

**PHARMACEUTICAL ORGANIC CHEMISTRY-I  
(BP202T)**

**B. PHARM. FIRST YEAR (Second Sem.)**

Answer book

Of

First Sessional Examination-2019-20

**SHAMBHUNATH INSTITUTE OF PHARMACY, JHALWA,  
PRAYAGRAJ**

## SECTION-A

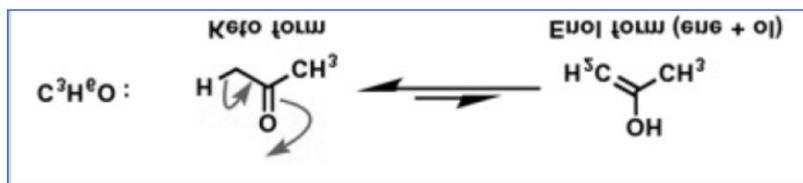
 Q.1a. Differentiate between E<sub>1</sub> and E<sub>2</sub> reaction.

Ans:

	E1	E2
1. Steps	Two step process $\begin{array}{c} \text{H} \\   \\ -\text{C}-\text{C}-\text{X} \\   \\ \text{H} \end{array} \xrightarrow{-\text{X}} \begin{array}{c} \text{H} \\   \\ -\text{C}-\text{C}^{\oplus} \\   \\ \text{H} \end{array}$ $\begin{array}{c} \text{H} \\   \\ -\text{C}-\text{C}^{\oplus} \\   \\ \text{H} \end{array} \xrightarrow{-\text{H}} >\text{C}=\text{C}<$	One step process $\begin{array}{c} \text{H} \\   \\ -\text{C}-\text{C}-\text{X} + \text{B}^{\ominus} \\   \\ \text{H} \end{array} \downarrow$ $>\text{C}=\text{C}< + \text{BH}^{\oplus}$
2. RI or TS	Carbocation as RI	TS
3. Kinetics	First order, unimolecular; Rate = K <sub>1</sub> [RX]; rate of ionisation	Second order, bimolecular Rate = K <sub>2</sub> [R-X][B]
4. Driving force	Ionisation of R-X	Attack by base on β-hydrogen
5. Stereochemistry	Nonstereospecific non-stereoselective	Stereoselective and stereospecific
6. Regioselectivity	Saytzeff	Saytzeff as well as Hofmann
7. Rearrangement	Common	No rearrangement except for , allylic (SN2')
8. Completing reaction	SN1	SN2
9. Reactivity order	3° > 2° > 1°	3° > 2° > 1°

Q1b. What is tautomerization? Give some suitable example.

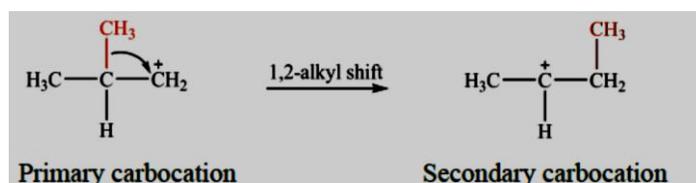
- This isomerism is due to spontaneous interconversion of two isomeric forms with different functional groups.
- Tautomerism:** Process by which two isomers are interconverted by the movement of an atom or a group. Enolization is a form of tautomerism.
- The prerequisites for this is the presence of the C=O, C=N or N=O in the usual cases and an alpha H atom. The most usual is the 'keto-enol' tautomerism, but there can be others like amine-imine forms.
- In general the Keto form is more stable. Enols can be formed by acid or base catalysis from the ketone and are extensively used in making C-C single bonds in organic synthesis.
- For example-



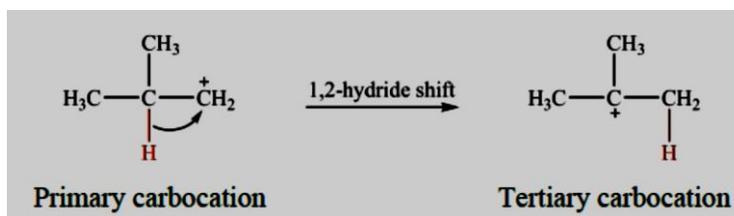
**Q1c. Write rearrangement of carbocation.**

**Solution:**

- The bonding electrons of a carbocation may shift between adjacent atoms to form a more stable carbocation.
- For example, rearrangement will occur if a secondary carbocation can be formed from a primary carbocation because a secondary carbocation is more stable than the primary carbocation.
- There can be two types of rearrangements-
  - Shift of an alkyl group is called a 1, 2-alkyl shift.
  - 1, 2-hydride shift
- In the following example the migrating methyl group-



- Shift of a hydrogen atom is called a 1, 2-hydride shift (or a 1,2-H shift).
- Hydride ion = H<sup>-</sup>. In the following example the migrating hydrogen atom and the associated electron pair-

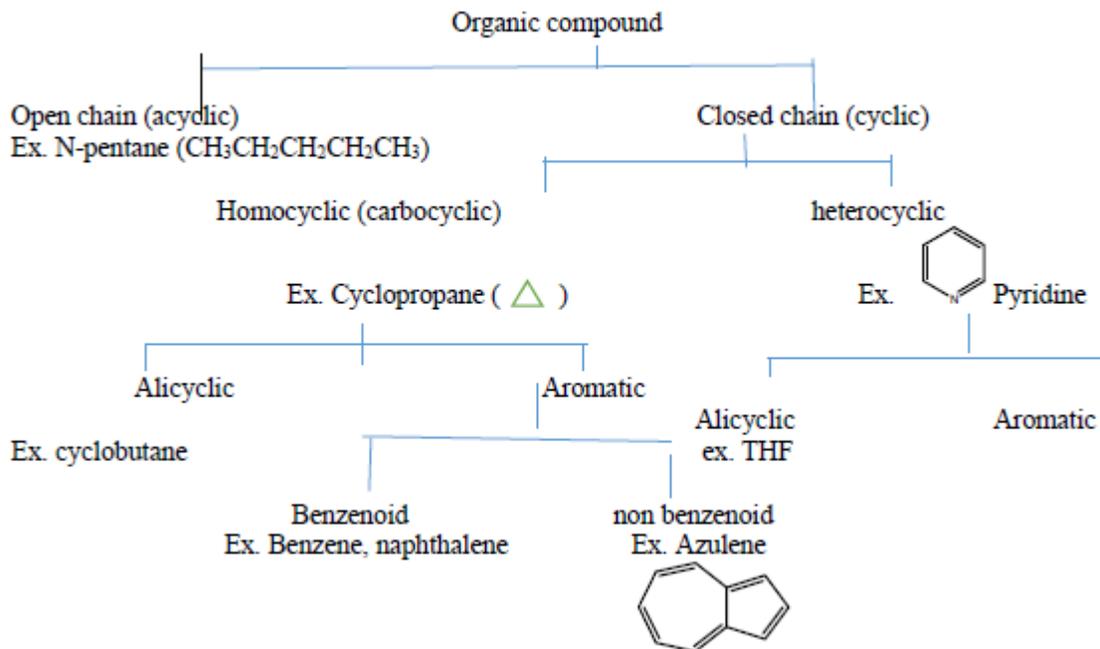


- Of these two rearrangement examples, hydride shift leads to a tertiary carbocation whereas alkyl shift leads to a secondary carbocation. Because a tertiary carbocation is more stable than a secondary carbocation, the hydride shift is favored in preference to the alkyl shift.
- Any C-H or C-C bond adjacent to a carbocation may shift (including C-C bonds that are part of a ring), but only C-C and C-H bonds can migrate during carbocation rearrangement.
- The most common carbocation rearrangements involve a carbocation rearranging into a more stable carbocation, such as 2° → 3° with resonance. (So use these rearrangements with impunity.)
- Rearrangements that transform a carbocation into another of apparently equal stability are less common, but they do occur.
- Rearrangement to a less stable carbocation is very unusual, but also does occur.

Q1d. Explain classification of organic compound.

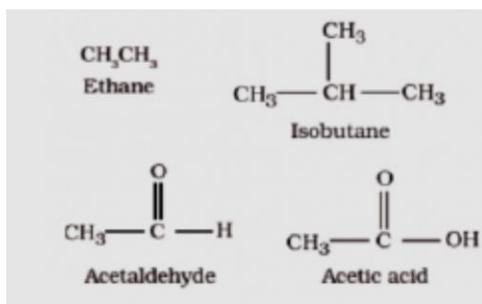
Solution:

**CLASSIFICATION AND NOMENCLATURE OF ORGANIC COMPOUND**



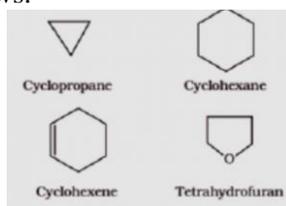
**1. Acyclic or Open Chain Compounds:**

- These compounds are also known as aliphatic compounds, they have branched or straight chains. Following are the examples in this category.



**2. Alicyclic or Closed Chain or Ring Compounds:**

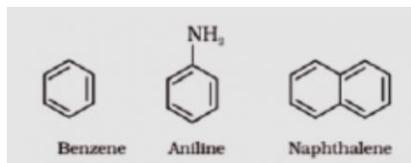
- These are cyclic compounds which contain carbon atoms connected to each other in a ring (homocyclic). When atoms other than carbon are also present then it is called as heterocyclic. Examples of this type are as follows:



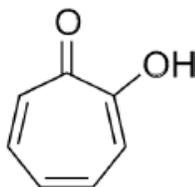
**3. Aromatic Compounds**

- They are a special type of compounds which contain benzene and other ring related compounds. Similar to alicyclic, they can also have heteroatoms in the ring. Such compounds are called heterocyclic aromatic compounds. Some of the examples are as follows:

(a) Benzenoid aromatic compounds



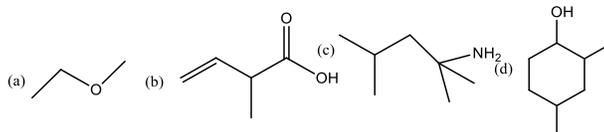
(b) Non-benzenoid aromatic compounds



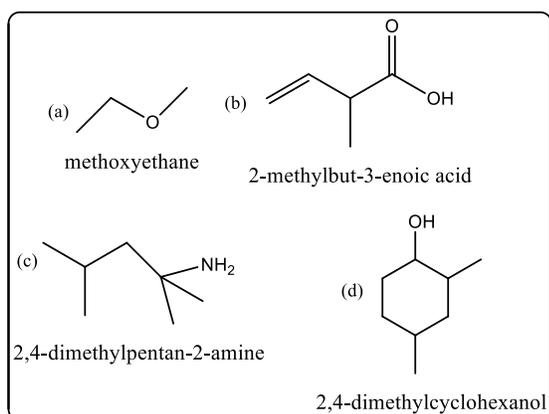
4. Heterocyclic Aromatic Compounds



Q1f. Give the IUPAC names of the following compounds:



Solution:

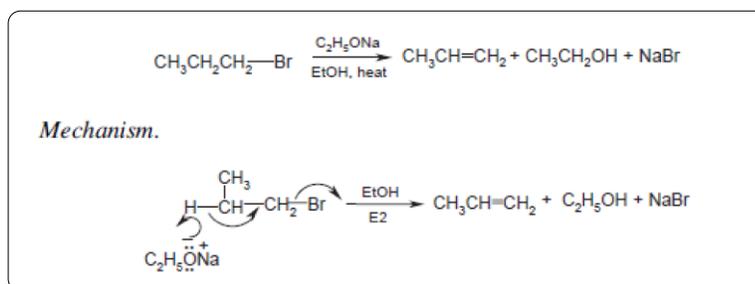




- Identity of R group – More substituted halides react faster
  - Rate:  $R_3CX > R_2CHX > RCH_2X$
  - Strength of the base – Favored by weaker bases such as H<sub>2</sub>O and ROH
  - Leaving group – Better leaving group leads to faster reaction rates. The rate determining step involves the C—X bond cleavage
  - Type of solvent – Favored by **polar Protic solvents**, which can stabilize the ionic intermediates
- E<sub>2</sub> REACTION or second order elimination of HX (formation of alkenes)**

#### Characteristics of an E<sub>2</sub> Reaction

- Kinetics – Second order
  - Mechanism – Single step
  - Identity of R group – More substituted halides react faster
  - Rate:  $R_3CX > R_2CHX > RCH_2X$
  - Strength of the base – Stronger bases favor the reaction
  - Leaving group – Better leaving group leads to faster reaction rates
  - Type of solvent – Favored by polar aprotic solvents
  - E<sub>2</sub> reactions are stereo selective, resulting in the formation of trans-double bonds preferably.
- Dehydrohalogenation of sec- and ter- alkyl halides undergo both E<sub>1</sub> and E<sub>2</sub> reactions. However, primary halides undergo only E<sub>2</sub> reactions.
  - They cannot undergo E<sub>1</sub> reaction because of the difficulty of forming primary carbocations.
  - E<sub>2</sub> elimination is stereospecific,
  - The E<sub>2</sub> reaction is the most effective for the synthesis of alkenes from primary alkyl halides.



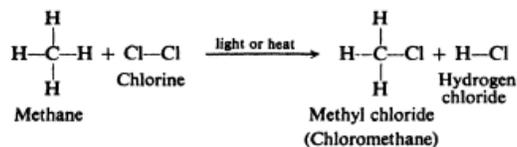
#### Q2b. Discuss halogenations of alkane with mechanism.

##### ALKANES

- General formula-  $C_nH_{2n+2}$  where n=1, 2, 3, 4.....etc.
- Alkanes are relatively inert because of strong C-C and C-H bond hence these are called as Paraffin's (Latin-*Parumaffinis* means little affinity)

##### Halogenation:

- When the substitution of alkane hydrogen by a halogen atom under the influence of UV light or 250-400°C.
- Chlorination is a typical example of a broad class of organic reactions known as substitution.
- A chlorine atom has been substituted for a hydrogen atom of methane, and the hydrogen atom thus replaced is found combined with a second atom of chlorine.

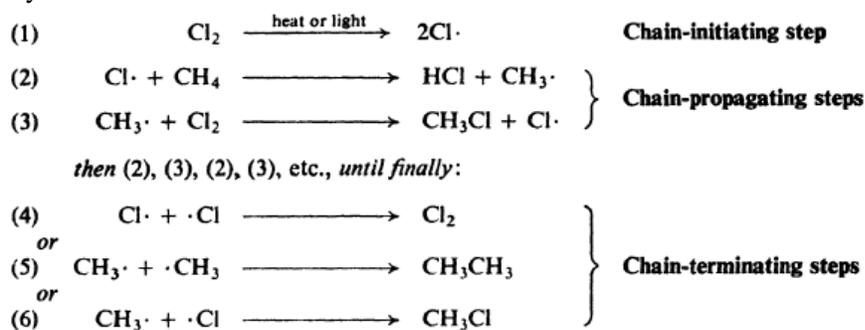


- Bromination takes place somewhat less readily than chlorination.
- Methane does not react with iodine at all.
- With fluorine it reacts so vigorously that, even in the dark and at room temperature, the reaction must be carefully, controlled: the reactants, diluted with an inert gas, are mixed at low pressure.
- We can, therefore, arrange the halogens in order of reactivity.

**Reactivity of halogens**  $\text{F}_2 > \text{Cl}_2 > \text{Br}_2 (> \text{I}_2)$

**Reaction mechanisms (Free radical):**

- The detailed, step-by-step description of a chemical reaction, is called a mechanism.
- An atom or group of atoms possessing an odd (unpaired) electron is called a free radical.
- The chlorination of methane is an example of a chain reaction, a reaction that involves a series of steps, each of which generates a reactive substance that brings about the next step.
- **Chain-initiating step:** In this energy is absorbed and a reactive particle generated; in the present reaction it is the cleavage of chlorine into atoms (step 1).
- **Chain-propagating steps:** In this step consumes a reactive particle and generates another; here they are the reaction of chlorine atoms with methane (step 2), and of methyl radicals with chlorine (step 3).
- **Chain-terminating steps:** in which reactive particles are consumed but not generated; in the chlorination of methane these would involve the union of two of the reactive particles, or the capture of one of them by the walls of the reaction vessel.



**Q2C. Write a short note on- (any two)**

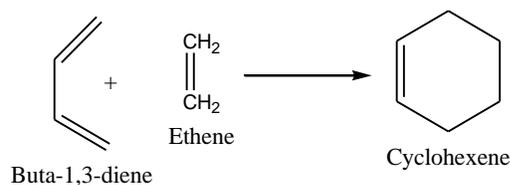
- Diel's Alder reaction**
- Saytzeff's Rule**
- Ozonolysis**

**Solution:**

**(i) DIELS ALDER REACTION**

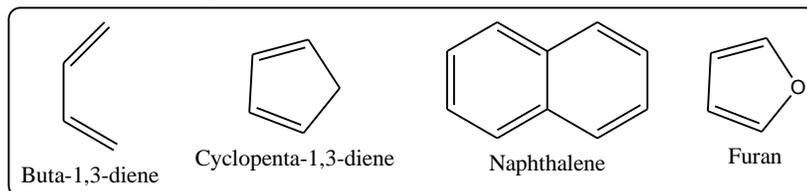
- Addition of a conjugated diene to an unsaturated molecule to give six membered ring compound is known as **Diels alder reaction**.

- Example-

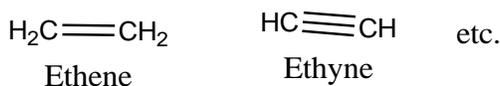


**Component of Diels alder reaction:**

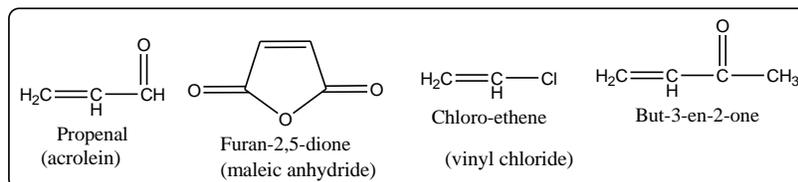
1. **Diene:** A conjugated diene, either open chain or cyclic is required for the reaction.
  - The presence of electron releasing groups (+I) increase the reactivity of diene.
  - Cis-diene undergoes the reaction, while Trans- Diene does not. Examples of Diene:



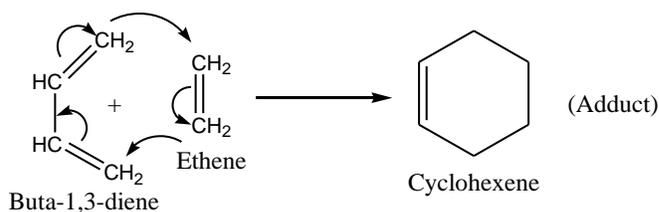
2. **Dienophile (diene loving):** any unsaturated species which tend to react with diene is called Dienophile. Examples:



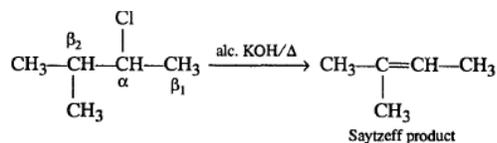
- The presence of electron withdrawing group (-I effect) increase the reactivity of Dienophile.
- Examples:



**Mechanism of reaction:**

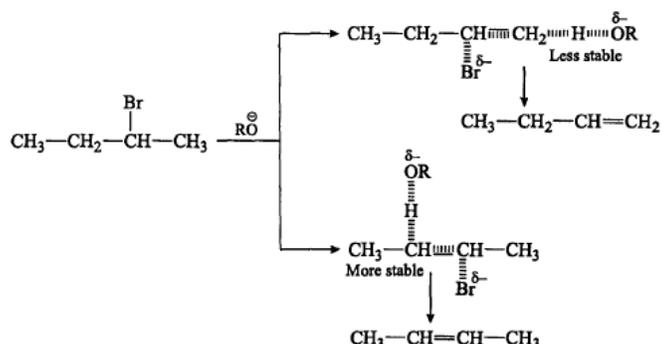


**(ii) Saytzeff Rule (Zaitsev Rule):** According to this rule, major product is the most substituted alkene, *i.e.*, the most stable alkene. Thus, the major product is obtained by elimination of  $\text{H}^+$  from that  $\beta$ -carbon which has the least number of hydrogen. Product of the reaction in this case is known as Saytzeff product.



### Theoretical Explanation for Saytzeff Rule

- Explanation for the more stable alkene (Saytzeff product) being formed in preference to the less stable alkene, is available from the transition states leading to these two alkenes.
- In either transition state, the removal of a proton and the formation of the double bond is taking place simultaneously.
- The transition state has some double-bond character which is represented by the dotted line.



## SECTION C

**Q3a. Explain the addition of HBr to propylene in accordance with Markonikov's and anti-Markonikov's rule with mechanism.**

**Solution:**

### Electrophilic addition to symmetrical and unsymmetrical $\pi$ bonds

- When the same substituents are at each end of the double or triple bond, it is called symmetrical.
- Unsymmetrical means different substituents are at each end of the double or triple bond.
- Electrophilic addition of unsymmetrical reagents (HX, H<sub>2</sub>O or ROH) to unsymmetrical double or triple bonds follows Markovnikov's rule.

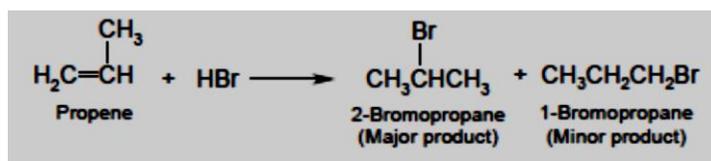
### MARKOVNIKOV'S RULE

- In the ionic addition of an acid to the carbon-carbon double bond of an alkene, the hydrogen of the acid attaches itself to the carbon atom that already holds the greater number of hydrogen. This statement is generally known as **Markovnikov's rule**.

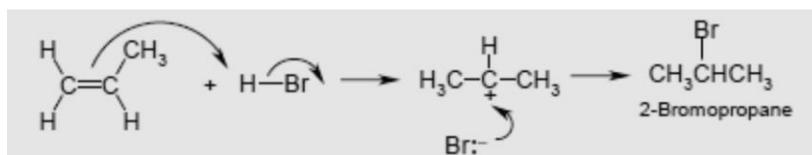


### Modern Markovnikov rule states

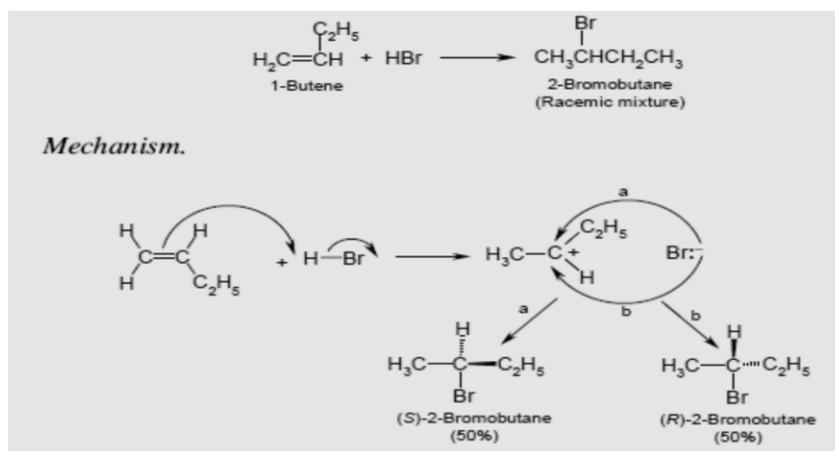
- The modern Markovnikov rule states that, in the ionic addition of an unsymmetrical reagent to a double bond, the positive portion of the adding reagent adds to a carbon atom of the double bond to yield the more stable carbocation as an intermediate.
- For example, Alkenes are converted to alkyl halides by the addition of HX (HCl, HBr or HI). Addition of HX to unsymmetrical alkenes follows Markovnikov's rule.
- addition of hydrogen bromide (HBr) to propene yields 2-bromopropane as the major product.



**Mechanism.** The double bond  $\pi$  electrons attack the electrophile. Protonation of the double bond yields a secondary carbocation intermediate. The bromine nucleophile attacks the carbocation to form 2-bromopropane.



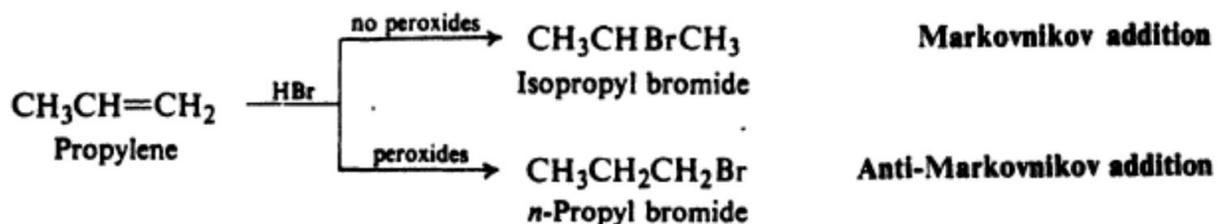
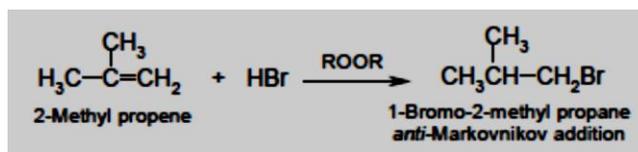
- Addition of HBr to 1-butene yields a chiral molecule. The reaction is regioselective and a racemic mixture is formed.



### Peroxide Effect or Kharasch Effect or Anti-Markovnikov Rule

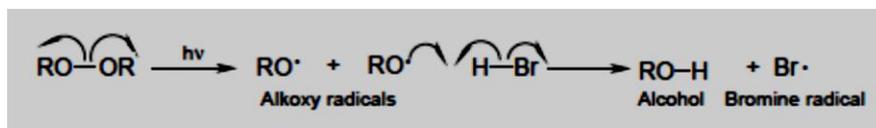
- In the absence of peroxides, hydrogen bromide 'adds to alkenes in agreement with Markovnikov's rule; in the presence of peroxides, the direction of addition is exactly reversed.

- When HBr is added to alkenes in the presence of free radical initiators, e.g. hydrogen peroxide (HOOH) or alkyl peroxide (ROOR).
- For example, 2-methyl propene reacts with HBr in the presence of peroxide (ROOR) to form 1-bromo-2-methyl propane, which is an anti-Markovnikov product.
- Radical additions do not proceed with HCl or HI.



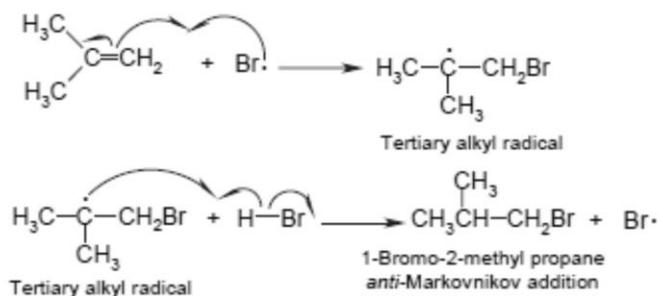
**Mechanism:** Free radicals reaction occurs in three steps

1. **Initiation** The oxygen–oxygen bond is weak, and is easily homolytically cleaved to generate two alkoxy radicals, which in turn abstract hydrogen to generate bromine radicals.

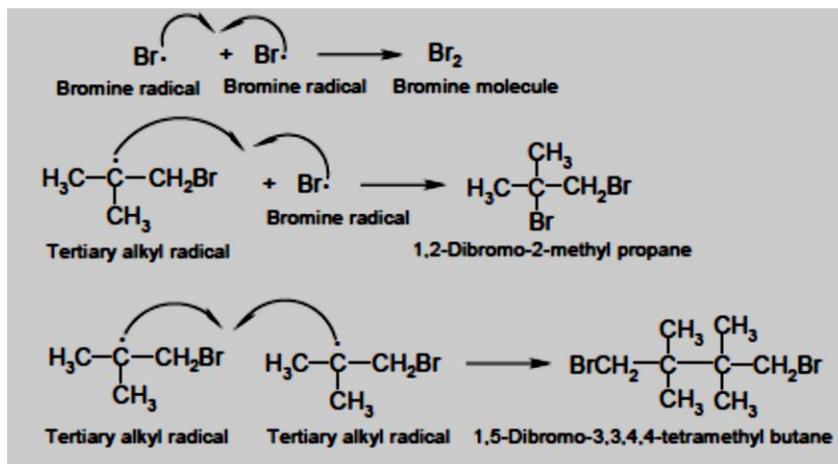


2. **Propagation** The bromine radical is electron deficient and electrophilic.

- The radical adds to the double bond, generating a carbon-centered radical. This radical abstracts hydrogen from HBr, giving the product and another bromine radical.
- The orientation of this reaction is **anti-Markovnikov**. The reversal of regiochemistry through the use of peroxides is called the **peroxide effect**.



3. **Termination** Any two radicals present in the reaction mixture can combine in a termination step, and end the radical chain reaction. Thus, radical reactions produce a mixture of products.



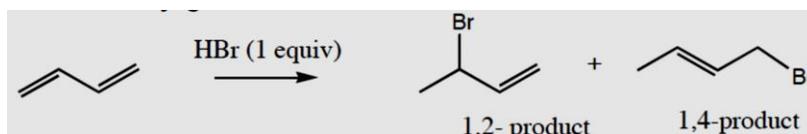
**Q3b. Discuss electrophilic addition reaction of conjugated diene with mechanism.**

**Solution:**

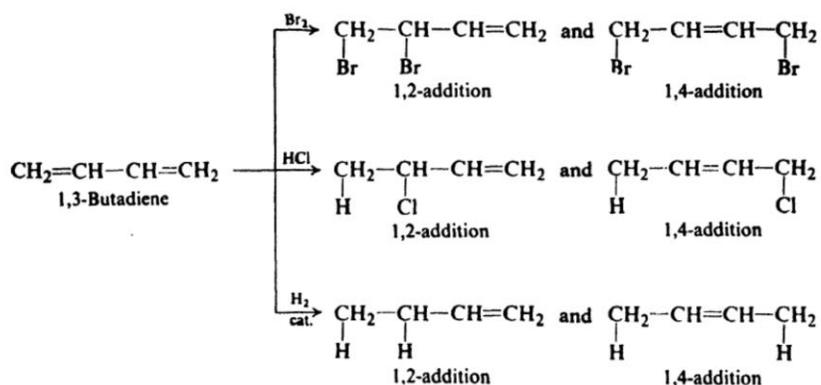
**Electrophilic addition reaction**

- With conjugated dienes, electrophilic addition of one equivalent of HBr gives two products;
  1. 1,2-product from Markovnikov addition
  2. 1,4-product from conjugate addition

For example-

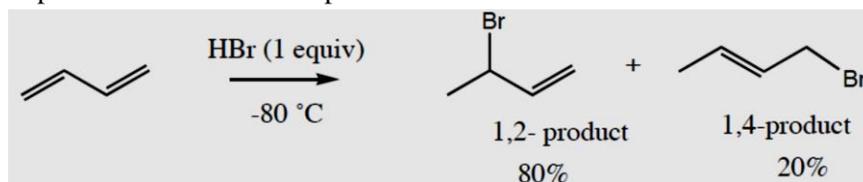


- Addition of HX to a conjugated diene forms 1,2- and 1,4-products because of the resonance stabilized allylic carbocation intermediate.
- When **1, 3-butadiene** is treated with bromine under similar conditions, there is obtained not only the expected 3,4-dibromo-1-butene, but also 1,4-dibromo-2-butene.
- Treatment with HCl yields not only 3-chloro-1-butene, but also 1-chloro-2-butene.
- Hydrogenation yields not only 1-butene but also 2-butene,

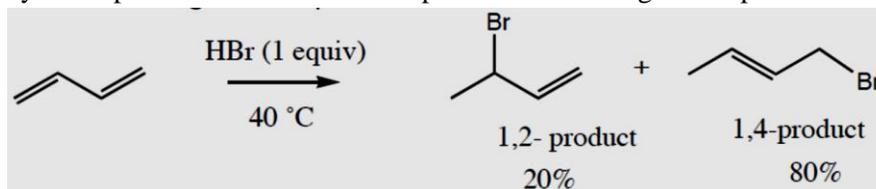


### Kinetic versus thermodynamic products

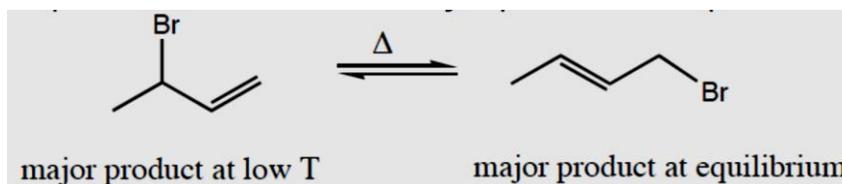
- The amount of 1,2- and 1,4-addition products formed in electrophilic addition reactions of conjugated dienes depends greatly on the reaction conditions:
- At low temperatures, the major product is formed by 1,2-addition. The kinetic product is formed faster and predominates at low temperature:



- At higher temperatures, the major product is formed by 1,4-addition. The more slowly formed thermodynamic product is more stable and predominates at higher temperatures.



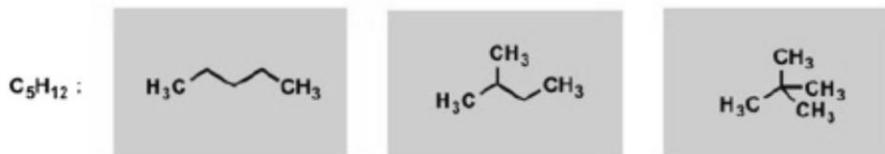
- In fact, when a mixture containing mainly the 1,2-product is heated, the 1,4-addition product becomes the major product at equilibrium:



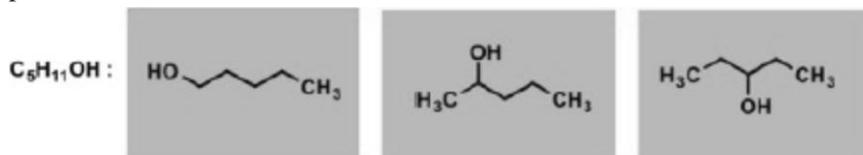
- Why is the 1,4-addition product the more stable (thermodynamic) product?
- Because more substituted alkenes are more stable (Remember, increasing alkyl substitution stabilizes an alkene by an electron-donating inductive effect)

**Q. 4a. Explain Chain OR Positional and Functional isomerism with suitable example.**

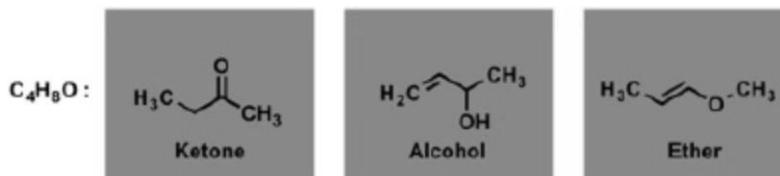
**Solution: Chain Isomerism:** It occurs when carbon atoms are linked to the main chain in different ways. For example:



**Positional Isomerism:** It occurs when functional groups are attached on different positions on a carbon chain. For example:



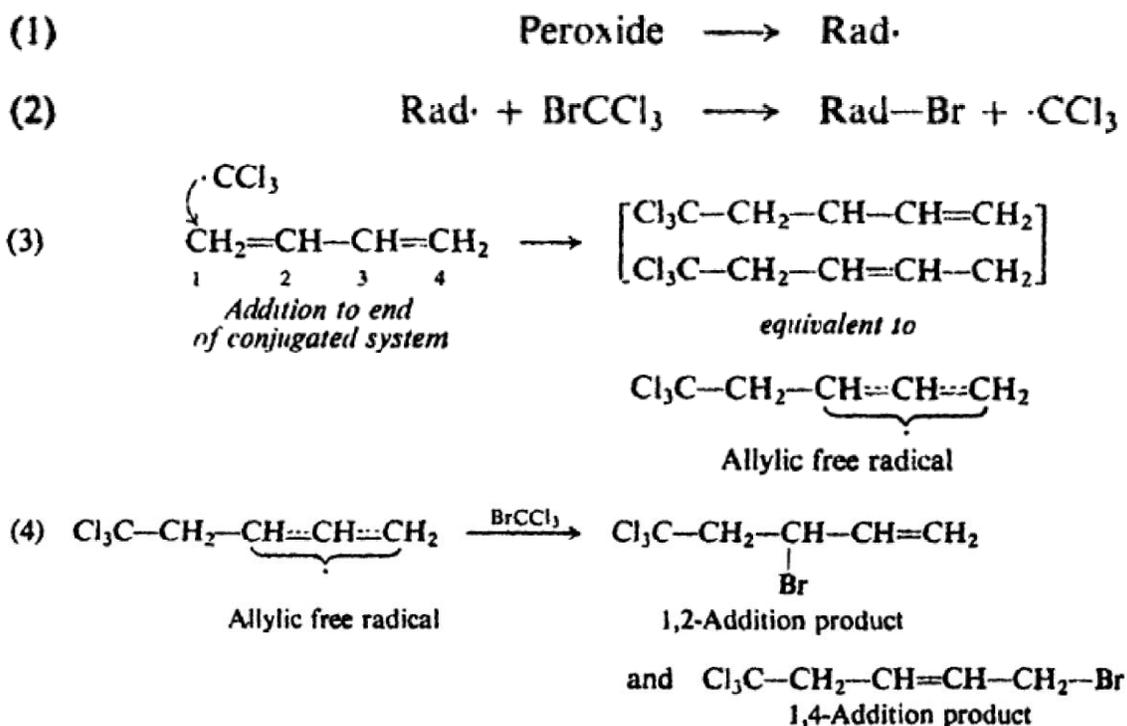
**Functional isomerism:** It is a very interesting form of isomerism where the compounds are different due to different arrangements of atoms leading to different functional groups. As functional groups are usually the reactive centre of a molecule this leads to entirely different properties. For example:



**Q. 4b. Discuss the free radical addition reaction of conjugated diene with suitable example.**

**Solution: Free-radical addition to conjugated dienes**

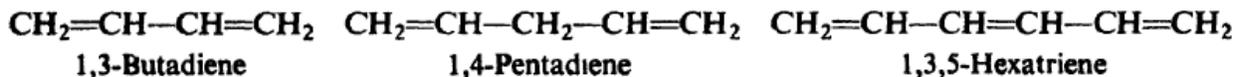
- In free-radical addition, conjugated dienes show two special features:
- They undergo 1, 4-addition as well as 1, 2-addition, and they are much more reactive than ordinary alkenes.
- Addition of BrCCl<sub>3</sub> to 1, 3-butadiene in the presence of a peroxide.
- The peroxide decomposes (**step 1**) to yield a free radical, which abstracts bromine from BrCCl<sub>3</sub>(**step 2**) to generate a ·CCl<sub>3</sub> radical.
- The ·CCl<sub>3</sub> free radical thus formed adds to the butadiene (**step 3**).
- Addition to one of the ends of the conjugated system is the preferred reaction, since this yields a resonance-stabilized allyl free radical.
- The allyl free radical then abstracts bromine from a molecule of BrCCl<sub>3</sub>(**step 4**) to complete the addition, and in doing so forms a new ·CCl<sub>3</sub> radical which can carry on the chain. In step (4) bromine can become attached to either C-2 or C-4 to yield either the 1, 2- or 1, 4-product.



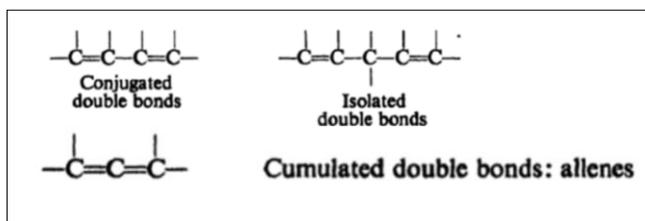
5(a). What are diene? Classified with suitable examples. Explain stability of conjugated diene over isolated diene.

- A diene is a hydrocarbon chain that has two double bonds that may or may not be adjacent to each other. The arrangements of these double bonds can have varying effects on the compounds reactivity and stability.
- Diene is used, with two numbers to indicate the positions of the two double bonds. This system is easily extended to compounds containing any number of double bonds.

Examples

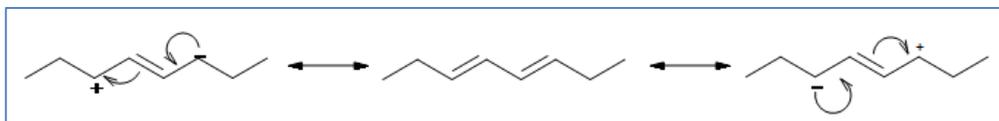


- Dienes are divided into two important classes according to the arrangement of the double bonds.
  1. Double bonds that alternate with single bonds are said to be **conjugated**;
  2. Double bonds that are separated by more than one single bond are said to be **isolated**.
  3. Contain **cumulated** double bonds; these compounds are known as **allenes**.



### Stability of conjugated diene

- Conjugated dienes are more stable than non-conjugated dienes (both isolated and cumulated) due to factors such as delocalization of charge through resonance and hybridization energy.
- This can also explain why allylic radicals are much more stable than secondary or even tertiary carbocations. This is all due to the positioning of the pi orbitals and ability for overlap to occur to strengthen the single bond between the two double bonds.
- The resonance structure shown below gives a good understanding of how the charge is delocalized across the four carbons in this conjugated diene. This delocalization of charges stabilizes the conjugated diene:



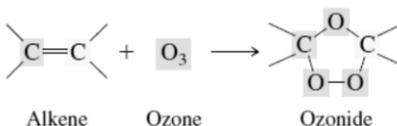
### 5 (b). Write Ozonolysis reaction for alkenes with suitable example.

#### OZONOLYSIS OF ALKENES

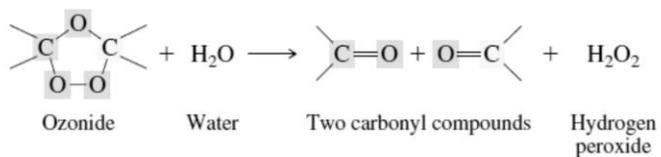
- Ozone (O<sub>3</sub>) is the triatomic form of oxygen.
- It is a neutral but polar molecule that can be represented as a hybrid of its two most stable Lewis structures.



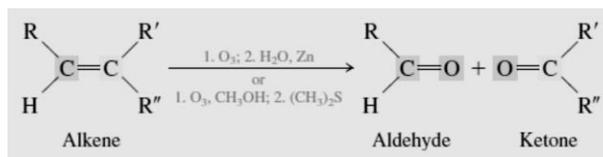
- Ozone is a powerful electrophile and undergoes a remarkable reaction with alkenes in which both the  $\sigma$  and  $\pi$  components of the carbon-carbon double bond are cleaved to give a product referred to as an **ozonide**.



- Ozonides undergo hydrolysis in water, giving carbonyl compounds.



- The two-stage reaction sequence is called **ozonolysis** and is represented by the general equation



- Each carbon of the double bond becomes the carbon of a carbonyl group.
- Ozonolysis has both synthetic and analytical applications in organic chemistry. In synthesis, Ozonolysis of alkenes provides a method for the preparation of aldehydes and ketones.