STEREOCHEMISTRY

Stereochemistry defines have the **same molecular formula** and sequence of bonded atoms, but **differs in the three-dimensional orientations of their atoms in space.**

Stereoisomer's: Compounds that have the same molecular formula and the same connectivity, but different arrangement of the atoms in 3-dimensional space. Stereoisomers cannot be converted into each other without breaking bonds.

DEFINITIONS IN STEREOCHEMISTRY

1. Stereoisomer's: Compounds that have the same molecular formula and the same connectivity, but different arrangement of the atoms in 3-dimensional space. Stereoisomers cannot be converted into each other without breaking bonds.

2. Enantiomers: Nonsuperposable mirror images (or) chiral molecules which are mirror images.

3. Chiral (or) asymmetric carbon: A tetrahedral carbon atom bearing four different substituents.

4. Chirality centers (or) stereocenters: Asymmetrically substituted atoms in a molecular structure.

5. Diastereomers: Stereoisomers which are not enantiomers (or mirror images).

6. Meso compounds (or) meso forms: Symmetric (or) achiral molecules that contain stereocenters. Meso compounds and their mirror images are not stereoisomers, since they are identical.

7. Optical activity: The ability of chiral substances to rotate the plane of polarized light by a specific angle.

8. Dextrorotatory: Ability of chiral substances to rotate the plane of polarized light to the right.

9. Levorotatory: Ability of chiral substances to rotate the plane of polarized light to the left.

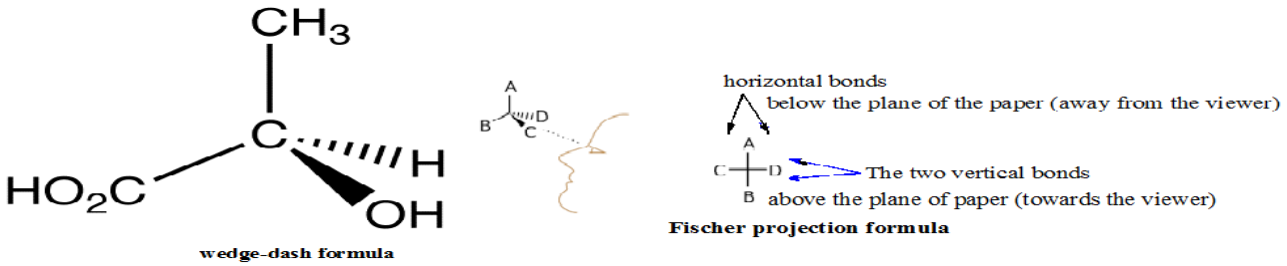
10. Racemic mixture (or) racemate - A mixture consisting of equal amounts of enantiomers. A racemic mixture exhibits no optical activity because the activities of the individual enantiomers are equal and opposite in value, therby canceling each other out.

11. Absolute configuration - A description of the precise 3-dimensional topography of the molecule.

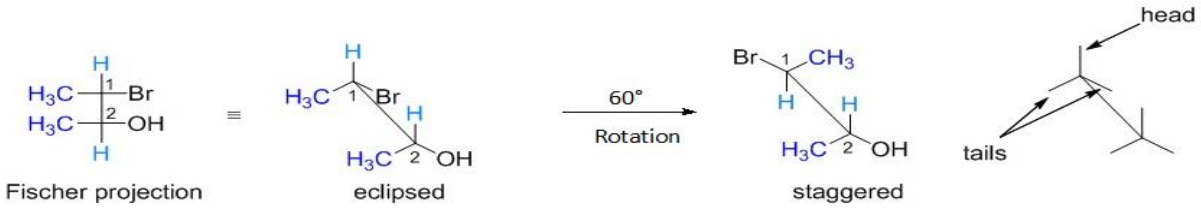
INTRODUCTION TO REPRESENTATION OF 3-DIMENSIONAL STRUCTURES

Fischer projection formula: It is a representation of a 3D molecule as a flat structure where a tetrahedral carbon is represented as two crossed lines. The two vertical bonds about the stereo centre

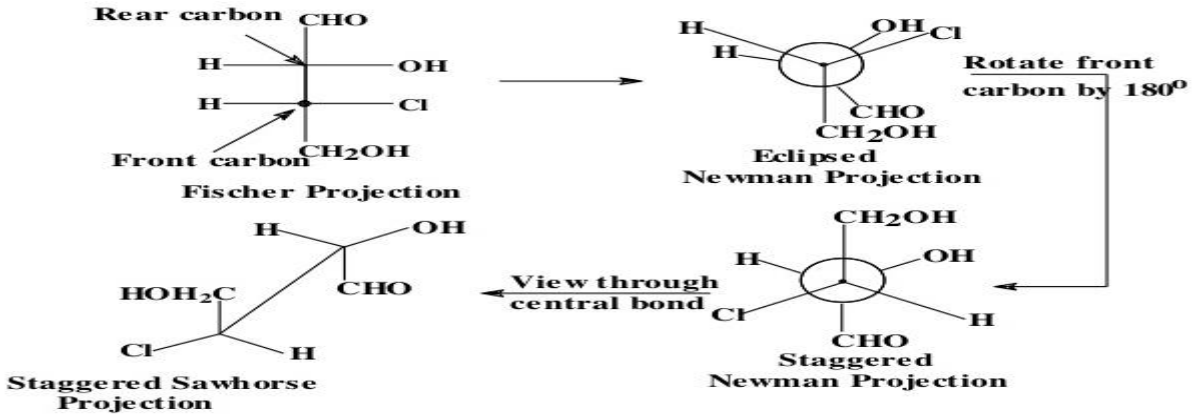
are above the plane of paper (towards the viewer) while the horizontal bonds are below the plane of the paper (away from the viewer)



Sawhorse projection formula: Sawhorse projection formulas are used to denote two principal stereo centers. It is a view of a molecule down a particular carbon- carbon bond, with the groups connected to both the front and back carbons are drawn using sticks at 120° angles. Sawhorse Projections can also be drawn so that the groups on the front carbon are staggered (60° apart) or eclipsed (directly overlapping) with the groups on the back carbon. The overall representation is given below.



Newmann projection formula: In this notion, the molecule is again viewed by looking down a particular carbon-carbon bond. The front carbon of this bond is represented by a dot, and the back



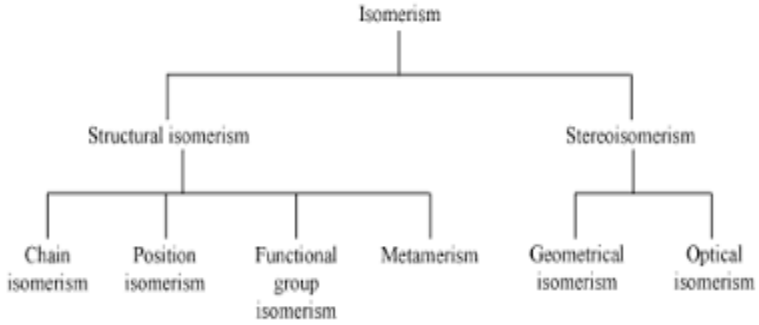
carbon is represented by a large circle. The three remaining bonds are drawn as sticks coming off the dot (or circle), separated by one another by 120°. Just like Sawhorse projection formula, Newman

Projection can be drawn such that the groups on the front carbon are staggered (60° apart) or eclipsed (directly overlapping) with the groups on the back carbon.

CLASSIFICATION OF STRUCTURAL AND STEREOISOMER'S

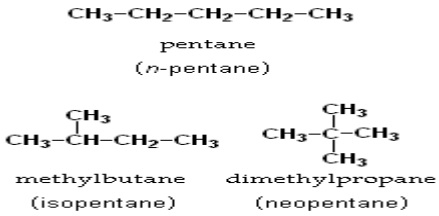
Compounds which have same molecular formula but differ in arrangement of atoms within the molecule are known as **isomers** and this phenomenon is known as isomerism. Isomers can have different physical or chemical properties.

Classification of isomerism: There are two main types of isomerism- structural isomerism and stereoisomerism. These can be further classified as:



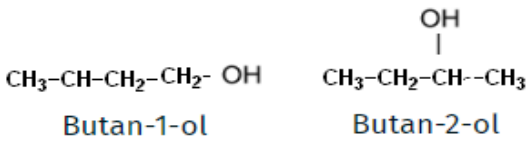
I. Structural Isomerism: Structural isomerism, or constitutional isomerism, is a type of isomerism where isomers have same molecular formula but have different arrangements of atoms within the molecule. Structural isomerism can be further classified as:

1. Chain isomerism:
Formula but they differ in the order in which the carbon atoms are bonded to each other.



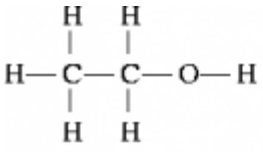
2. Position isomerism:

Position isomerism is a type of structural isomerism where the main carbon skeletons are same but they differ in the position of functional group attached to it.

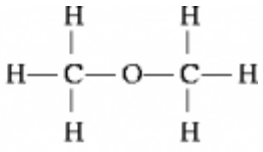


3. Functional group isomerism:

Functional group isomerism is a type of structural isomerism where isomers have same molecular formula but differ in functional group.



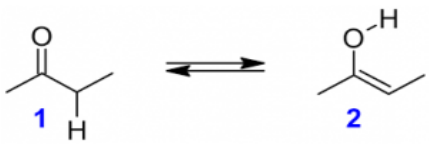
Ethanol (Alcohol)



Dimethylether

4. Tautomerism:

Tautomerism is a special type of structural isomerism where the isomer stays in dynamic equilibrium with each other by simple proton transfer in an intramolecular fashion.



II. Stereoisomerism:

Stereoisomer's are isomers that have same molecular formula, same sequence of bonding of atoms but differ in their three dimensional orientation of atoms in space. Stereoisomerisms are of two types: 1. Geometrical isomerism

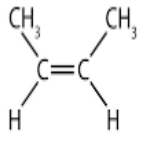
2. Optical isomerism

1. Geometrical isomerism: Geometrical isomers are molecules that are locked into their spatial positions with respect to one another due to a double bond.

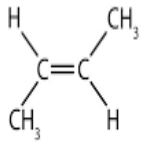
Geometric isomers differ from one another inphysical properties like melting and boiling points.

Geometrical isomers are two types that are *Cis–trans* isomerism

- Cis indicates that the functional groups are on the same side of the carbon chain.
- Trans conveys that functional groups are on opposing sides of the carbon chain.

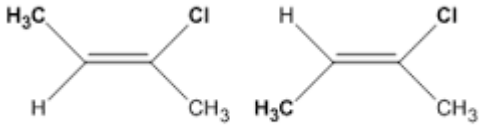


cis-2-butene



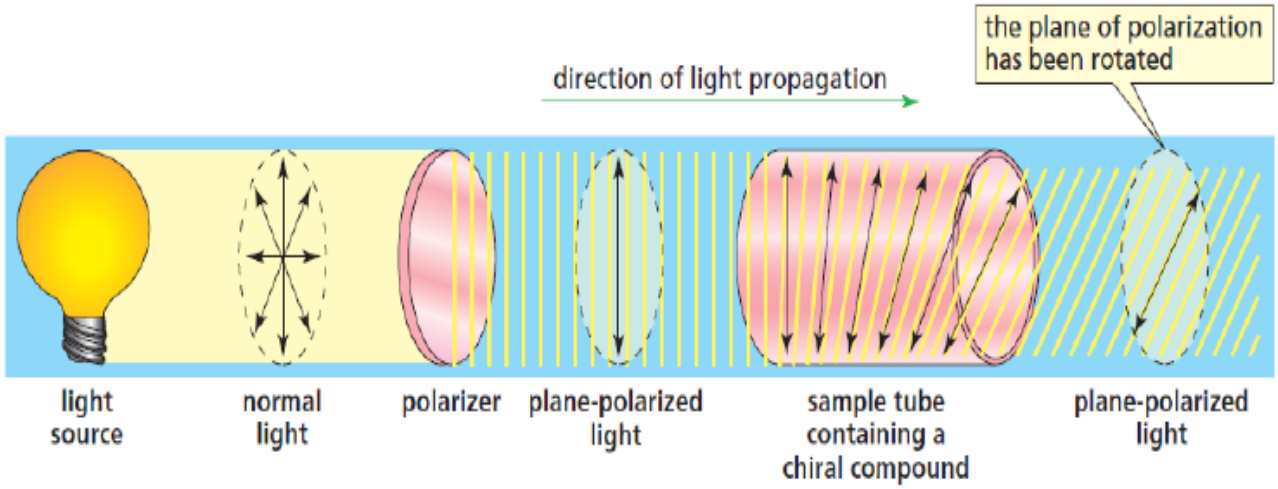
trans-2-butene

- It is not to be confused with E–Z isomerism, which is an absolute stereochemical description, and only to be used with alkenes. In general, stereoisomers contain double bonds that do not rotate, or they may contain ring structures, where the rotation of bonds is restricted or prevented.

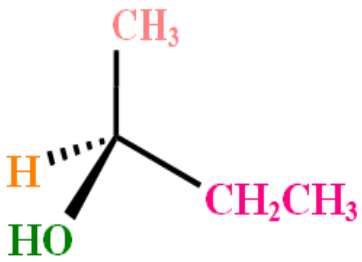


(Z) (E)

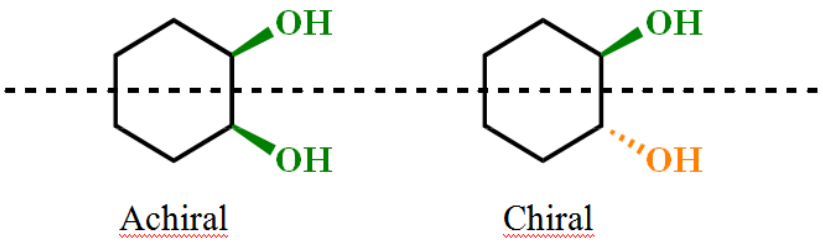
2. Optical isomerism: Compounds which have similar chemical and physical properties and differ only in their optical activity are known as optical isomers and phenomenon as optical isomerism.



- Certain substances have a remarkable power of rotating the plane polarized light (PPL) either towards left (or) towards right.
- The isomer which rotates the plane polarized light to left is known as laevo (l).
- The isomer which rotates the plane polarized light to right is known as dextro (d).
- The phenomenon of rotating the plane polarized light is known as optical activity and compounds exhibiting this property are known as **optically active** compounds.
- A carbon atom bonded to four different groups could lead to optical activity and is called a stereogenic center.
- **Ex:** 2-Butanol:



- In general organic compounds, which lack a plane of symmetry are optical active and are called **chiral** compounds.



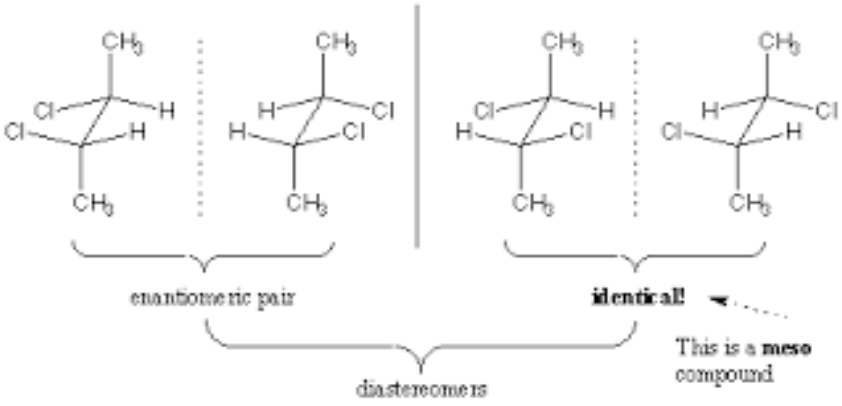
ENANTIOMERS

- Optical isomers that are mirror images are called Enantiomers.
- These always exist as discrete pairs.
- Enatiomers are stable, isolable compounds that differ from one another in three-dimensional spatial arrangements.
- Enantiomers have identical properties in all respects except in their interaction with plane of polarized light.
- Enantiomers have the same melting point, density, solubility, color and reactivity toward acids and bases.

- They differ, however, in the direction in which they rotate the plane polarized light.
- Both rotate the plane of polarized light to exactly the same extent (same angle) but one rotates the plane to the right (clockwise: called dextrorotatory). While the other rotates the plane to the left (anticlockwise: called levorotatory).

DIASTEREOMERS

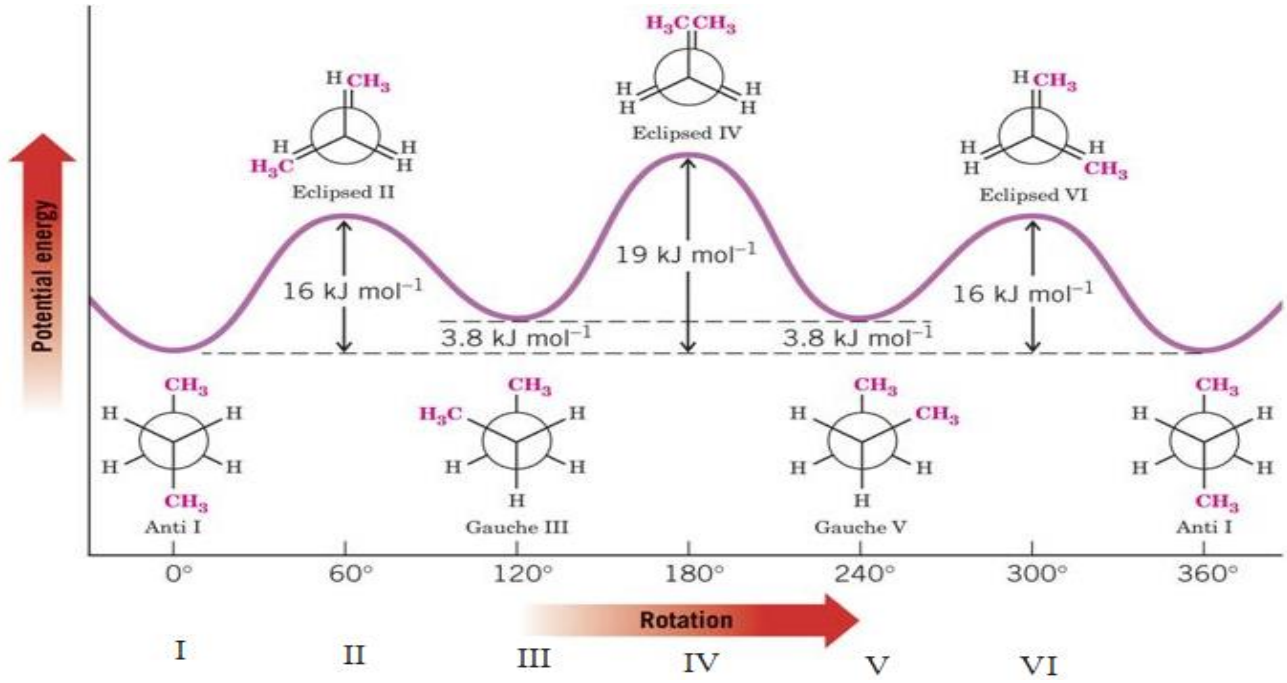
- Optical isomers that are are **not mirror images** of each other and **non-superimposable**.
- Diastereomers can have different physical properties and reactivity.
- They have different melting points and boiling points and different densities.
- They have **two or more** stereocenters.



CONFORMATION ANALYSIS OF n-BUTANE

The molecular formula of n-Butane is CH_3-CH_2-CH_2-CH_3, in this there are now three rotating carbon-carbon bonds to consider, but we will focus on the middle bond between C_2 and C_3. Below are two representations of butane in a conformation which puts the two CH_3 groups (C_1 and C_4) in the eclipsed position.

DIHEDRAL ANGLE	CONFORMATION OF BUTANE	ENERGY(kJ/mol)
Butane - 0°	Staggered	0
Butane - 60°	Partial Eclipsed	16
Butane - 120°	Gauche	3.8
Butane - 180°	Fully Eclipsed	19
Butane - 240°	Gauche	3.8
Butane - 300°	Partial Eclipsed	16
Butane - 360°	Staggered	0



Stability Order: I > III & V > II & VI > IV

- III and V conformations of Butane are enantiomers.
- I and III conformations of Butane are diastereomers.
- I and V conformations of Butane are diastereomers.

ABSOLUTE CONFIGURATION

There are three steps to assign ***R* or *S***, which is called the absolute configuration of the chiral carbon atom. Groups are first assigned a priority based on the atomic weight of the first atom bonded to the chiral carbon, which can be found on a periodic table. The higher the atomic weight, the higher priority.

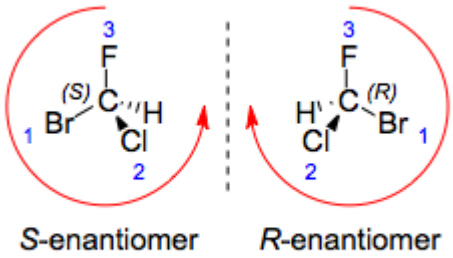
Rules for the absolute configuration:

1. Point the lowest priority group away from you. This means that the low priority group needs be on the dashed wedge in the example below.
2. Number the remaining three groups according to priority: 1 = highest priority and 3 = lowest priority.
3. Draw a circle beginning at the group numbered 1 that ends with an arrow at group 3.

If the arrow points **clockwise, the compound is *R***. If the arrow points in a **counterclockwise direction, the chiral carbon is *S***.

Assigning Chirality When the Group Contains Multiple Atoms:

When the groups contain more than one atom, we may need to look beyond the first atom to assign the absolute configuration. The example on the left is fairly straightforward. The first group is CH_2 in two chains, so we need to look beyond that position. As we move outward one atom, we can see that the nitrogen has higher priority than another carbon atom, which makes this compound *R*. In the example on the right, the groups contain only carbon and hydrogen, but they are different groups:



REACTION MECHANISMS

The chemical reactions happening between electron donors and acceptors are described by concepts like **electrophile and nucleophile**. These are the most important concepts in organic chemistry.

Electrophile:

The term electrophile can be split into "electro-electron" and "phile-loving".

- They are electron deficient and hence electrons loving.
- They are positively charged or neutrally charged, they attract electrons.
- Movement of electrons depends on the density. They move from high density area to low density area.
- They undergo electrophilic addition and electrophilic substitution reactions.
- Electrophile is also called as Lewis acid.

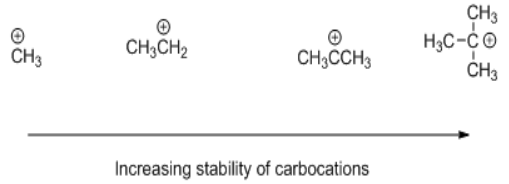
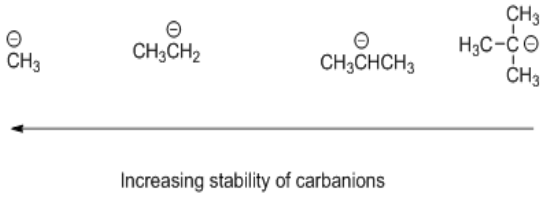
Nucleophile:

The term nucleophile can be split into "nucleo-nucleus" and "phile-loving".

- They are electron rich and hence nucleus loving.
- They are negatively charged or neutrally charged, they donate electrons.
- Movement of electrons depends on the density. They move from low density area to high density area.
- They undergo nucleophilic addition and nucleophilic substitution reactions.
- Nucleophile is also called as Lewis base.

DIFFERENCES BETWEEN ELECTROPHILES AND NUCLEOPHILES

ELECTROPHILE	NUCLEOPHILE
Electron deficient	Electron rich
They are positively charged / neutral	They are negatively charged / neutral
Also called as Lewis acid	Also called as Lewis base
They undergo electrophilic addition and electrophilic substitution reactions.	They undergo nucleophilic addition and nucleophilic substitution reactions.
It accepts pair of electron to form covalent bond	It donates pair of electron to form covalent bond
All carbocations	All carboanions
Example: Hydronium ion, Cl^+, NO_2^+, BF_3, CH_3^+	**Example:** Chloride ion, $C_2H_5O^-$, HS^-, H_2N^-, $(CH_3)_3N:^-$

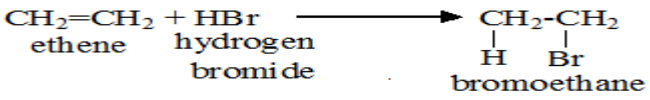
DIFFERENCES BETWEEN CARBOCATION AND CARBANION	
Carbocation	**Carbanion**
It is an electron deficient species.	It is an electron rich species.
The carbon involved is Sp_2 hybridized.	The carbon involved is Sp_3 hybridized.
It has a planar geometry.	It has a tetrahydral geometry.
It is lewis acid.	It is lewis base.
It is electrophile.	It is nucleophile.
It accepts pair of electron to form covalent bond.	It donates pair of electron to form covalent bond.
Stability order of Cabocations: 	Stability order of Cabanions: 
Example: Hydronium ion, Cl^+, NO_2^+, BF_3, CH_3^+	**Example:** Chloride ion, $C_2H_5O^-$, HS^-, H_2N^-, $(CH_3)_3N:^-$

ADDITION REACTIONS

These reactions are given by those compounds which have at least one π bond (>C=C<, −C≡C−).

In addition reaction there is loss of one π bond and gain of two σ bonds. Thus product of the reaction is generally more stable than the reactant. The reaction is a spontaneous reaction.

Ex: when hydrogen bromide reacts with ethene we, get bromoethane



Types of addition reactions:

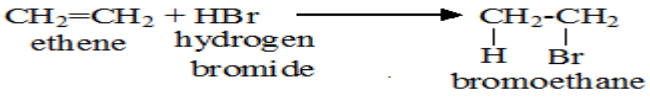
Addition reactions can be classified into three categories on the basis of the nature of initiating species. **i.** Electrophilic additions **ii.** Nucleophilic additions **iii.** Free radical additions

i. ELECTROPHILIC ADDITION REACTIONS:

- Electrophilic addition reactions are mainly given by alkenes and alkynes.
- Electrophilic addition reactions of alkenes and alkynes are generally two step reactions.
- Alkenes and alkynes give electrophilic addition with those reagents which on dissociation gives electrophile as well as nucleophile.

- If the reagent is a weak acid then electrophilic addition is catalysed by strong acids (Generally H_2SO_4).

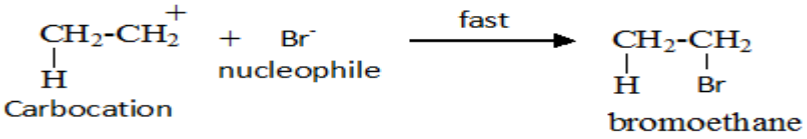
Ex: when hydrogen bromide reacts with ethene we, get bromoethane



Mechanism of Electrophile addition: *Ethene to hydrogen bromide:*

Step-1: Attack by the electrophile opening the double bond and producing an intermediate **Carbocation** and leaving a negative bromide ion.

Step-2: The intermediate, carbocation reacts with nucleophile and produce product, bromoethane.



MARKOWNIKOFFS RULE:

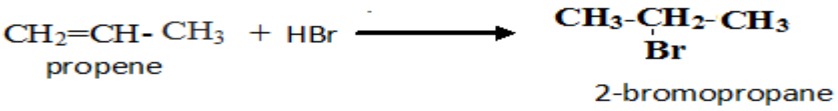
The negative part of the addendum adds on that doubly bonded carbon of the alkene which has least number of hydrogen atoms.

This rule can be used only in those alkenes which fulfill the following conditions:

- Alkene should be unsymmetrical.
- Substituent/substituents present on doubly bonded carbon/(s) should only be +I group.

Example: Addition of HBr to propene:

According to this rule, the product formed is 2-bromopropane as the major product.



Mechanism of Markownikoff's rule:

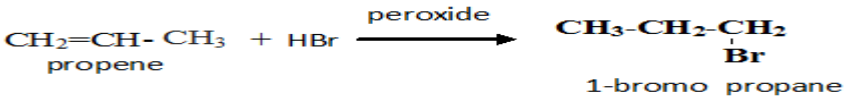
The secondary carbocation obtained in the below mechanism is more stable than the primary carbocation, therefore the product of secondary carbocation predominates because it is formed at a faster rate.

The secondary carbocation is attacked by Br^- ion to form 2-bromopropane as the major product.

Anti Markownikoff's rule:

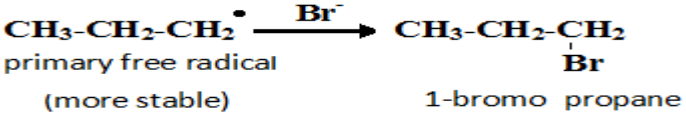
If negative part of the addendum gets attached to that carbon atom which possesses higher number of hydrogen atoms.

Example: Addition of HBr to propene: In the presence of peroxide, addition of HBr to propene takes place opposite to the Markovnikoff rule.



Mechanism of Anti Markownikoff's rule: The primary free radical obtained in the below mechanism is more stable than the secondary free radical.

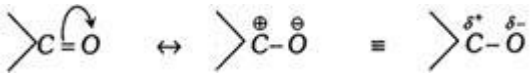
This explains the formation of 1-bromopropane as the major product.



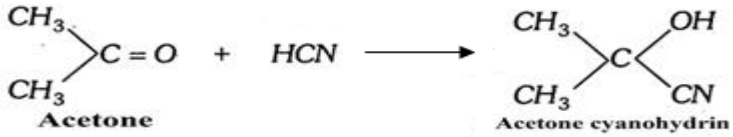
ii. NUCLEOPHILIC ADDITION REACTIONS:

- When the addition reaction occurs on account of the initial attack of nucleophile, the reaction is said to be a nucleophilic addition reaction.
- Due to presence of strongly electronegative oxygen atom, the π−electrons of the carbon-oxygen double bond in carbonyl group (C=O) get shifted towards the oxygen atom and thereby such bond is highly polarised.

- This makes carbon atom of the carbonyl group electron deficient.



Example: The addition of HCN to acetone is an example of nucleophilic addition.

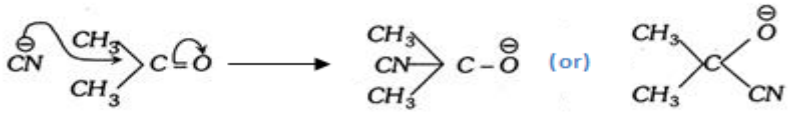


The mechanism of the reaction involves the following steps:

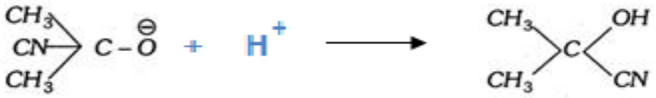
Step1: HCN gives a proton ($H^{\oplus}$) and a nucleophile, cyanide ion ($CN^{\ominus}$)

$$\mathbf{HCN \rightarrow H^{\oplus} + CN^{\ominus}}$$

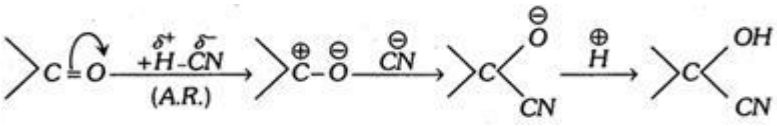
Step2: The nucleophile ($CN^{\ominus}$) attacks the positively charged carbon so as to form an anion ($H^{\oplus}$ does not initiate the negatively charged oxygen as anion is more stable than cation).



Step3: The proton ($H^{\oplus}$) combines with anion to form the addition product.



In C=O compounds, the addition of liquid HCN gives cyanohydrin and the addendum is CN^{-} ion and not HCN directly (addition is catalysed by bases or salts of weak acids and retarded by acids or unaffected by neutral compounds).



GRIGNARD ADDITION OF CARBONYL COMPOUNDS

When an alkyl halide reacts with Magnesium metal in presence of dry ether, the compound formed is Alkyl Magnesium halide, which is also known as Grignard reagent.

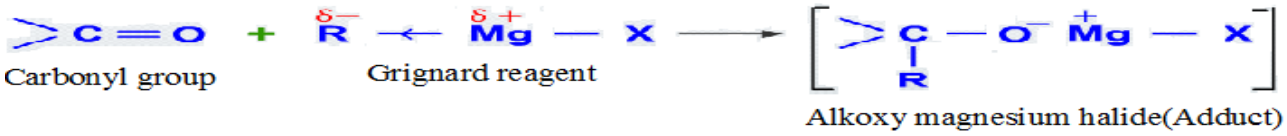
$$\text{R-X} + \text{Mg} \xrightarrow{\text{dry ether}} \text{R-MgX (\textbf{Grignard reagent})}$$

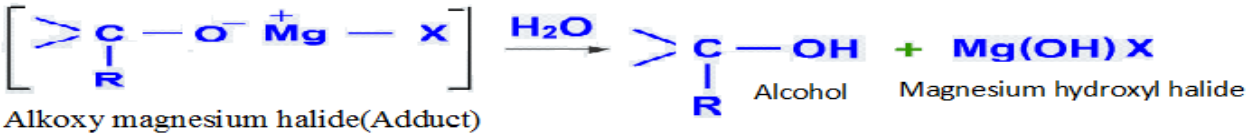
The Grignard reagent is represented as **R-Mg-X**, where **R** = alkyl / aryl / alkenyl / allyl group

X = Cl / Br / I

Note: Grignard reagent is highly polar compound. It is also known as Organometallic compound. When Grignard reagent reacts with such type of compounds, having active hydrogen atom, hydrocarbons are formed.

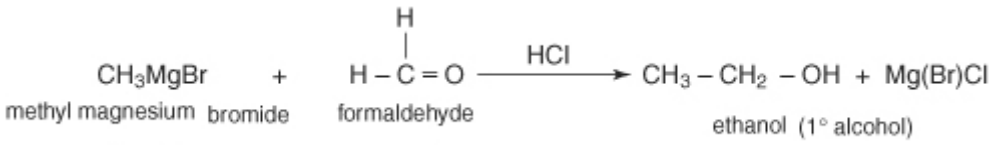
THE MECHANISM OF GRIGNARD ADDITION OF CARBONYL COMPOUNDS:





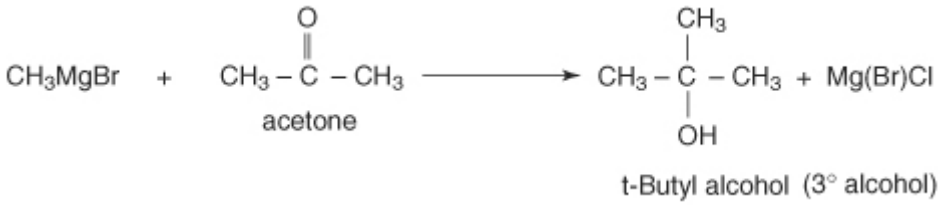
Grignard addition of carbonyl compounds: The Grignard reaction is the only simple method available that is capable of producing primary, secondary, and tertiary alcohols.

i. To produce a primary alcohol, the Grignard reagent is reacted with **formaldehyde**.



ii. Reacting a Grignard reagent with **any other aldehyde (acetaldehyde)** will lead to a secondary alcohol.

iii. Reacting a Grignard reagent with a **ketone (acetone)** will generate a tertiary alcohol.



SUBSTITUTION REACTIONS

A reaction in which the functional group of one chemical compound is substituted by another group
(or)

It is a reaction which involves the replacement of one atom or a molecule of a compound with another atom or molecule.

Ex: The reaction of Ethanol with the hydrogen iodide which forms iodoethane along with water.

$$CH_3CH_2OH + HI \longrightarrow CH_3CH_2I + H_2O$$

Conditions for Substitution Reaction:

- The strong base such as NaOH has to be in dilute form. Suppose if the base is of higher concentration, there are chances of dehydrohalogenation taking place.
- Maintaining low temperatures such as room temperature.
- The solution needs to be in an aqueous state such as water

Types of Substitution Reactions: Substitution Reactions are of two types

i. Electrophilic reactions **ii.** Nucleophilic reaction

These two types of reactions mainly differ in the kind of atom which is attached to its original molecule. In the nucleophilic reactions the atom is said to be electron-rich species, whereas, in the electrophilic reaction, the atom is an electron-deficient species.

i. **Electrophilic substitution reactions:** The electrophilic substitution reaction involves the electrophiles. Electrophiles are those which donate a pair of electrons in the formation of a covalent bond. The Electrophilic reactions occur mostly with the aromatic compounds. These compounds have about an excess of electrons that can be shared throughout the system of reaction.

The Electrophilic substitution reactions are basically defined as those chemical reactions where the electrophile replaces the functional group in a compound but not the hydrogen atom.

Example: The species of electrophiles include hydronium ion (H_3O^+), halides of hydrogen such as HCl, HBr, HI, sulfur trioxide (SO_3), the nitronium ion (NO_2^+), etc.

NUCLEOPHILIC SUBSTITUTION REACTIONS

The nucleophilic substitution reaction involves the nucleophiles. These are said to be fully charged (or) have negative ions present on a molecule. The common **examples** of nucleophiles are cyanide ions, water, hydroxide ions, and ammonia. In Nucleophilic substitution reaction, where a nucleophile gets attached to the positive charged atoms or molecules of the other substance.

Example: The hydrolysis of alkyl bromide (R-Br), under the basic conditions, where in the nucleophile is nothing but the base OH^-, whereas the leaving group is the Br^-. The reaction for the following is as given below

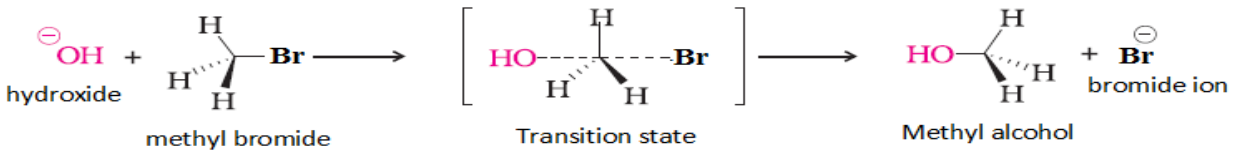
$$\mathbf{R\text{-}Br + OH^- \longrightarrow R\text{-}OH + Br^-}$$

The S_N2 (Bi molecular nucliophilic substitution reaction) Reaction Mechanism:

The reaction between methyl bromide and hydroxide ion to yield methanol follows second order kinetics; that is, the rate depends upon the concentrations of both reactants:

$$CH_3Br + OH^- \rightarrow CH_3OH + Br^- \quad \textbf{Rate} = K\,[CH_3Br]\,[OH^-]$$

The simplest way to account for the kinetics is to assume that reaction requires a collision between a hydroxide ion and a methyl bromide molecule. In its attack, the hydroxide ion stays far away as possible from the bromine; i.e. it attacks the molecule from the rear and begins to overlap with the tail of the sp^3 hybrid orbital holding 'Br'. The reaction is believed to take place as shown:



In the **Transition state** the carbon is partially bonded to both -OH and - Br; the C-OH bond is not completely formed, the C- Br bond is not yet completely broken. Hydroxide has a diminished -ve charge, since it has begun to share its electrons with carbon. Bromine has developed a partial negative charge, since it has partial removed a pair of electrons from carbon. At the same time, of course, ion dipole bonds between hydroxide ion and solvent are being broken and ion-dipole bonds between bromide ion and solvent are being formed.

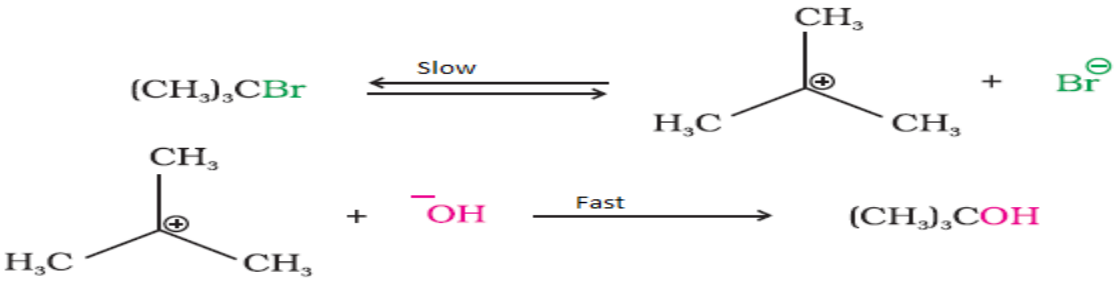
As the -OH becomes attached to C, 3 bonds are forced apart (120^o) until they reach the spoke arrangement of the **Transition state**; then as bromide is expelled, they move on to the tetrahedral arrangement opposite to the original one. The process has often been likened to the turning inside out of an umbrella in a gale.

Reactivity: In S_N2 reactions the order of reactivity of RX is ***$CH_3X > 1^o > 2^o > 3^o$*.**

Differences in rate between two S_N2 reactions seem to be chiefly due to **steric factors** (bulk of the substituents) and not due to electronic factors i.e. ability to withdraw or release electrons.

The S_N1 (Uni molecular nucliophilic substitution reaction) Reaction Mechanism:

The reaction between tert-butyl bromide and hydroxide ion to yield tert-butyl alcohol follows first order kinetics; i.e., the rate depends upon the concentration of only one reactant, tert-butyl bromide.

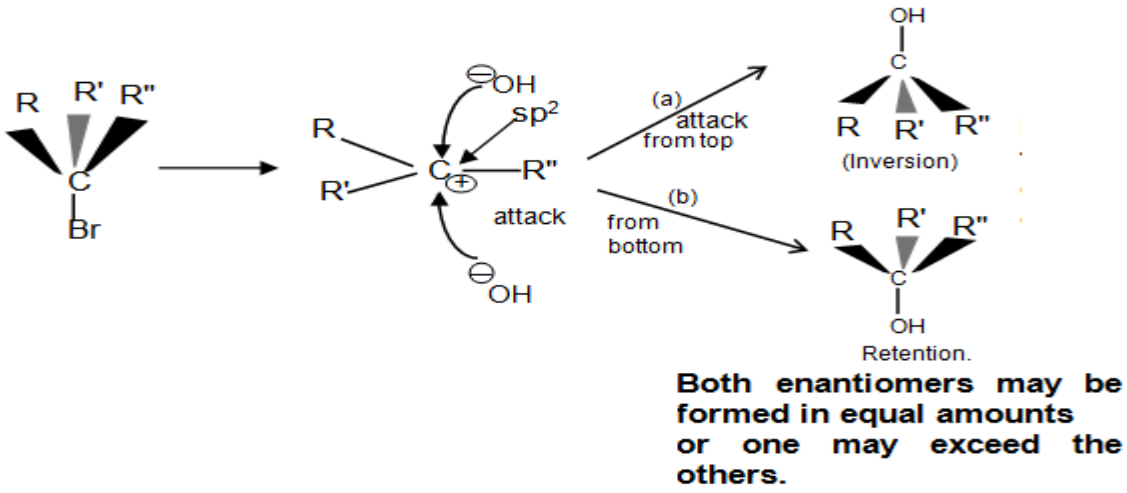


Rate = K[Br] S_N1 reaction K follows first order kinetics.

The optically active bromide ionizes to form bromide ion and the **flat carbocation**. The nucleophilic reagent then attaches itself to carbonium ion from either face of the flat ion.

It the attacks were purely random, we would expect equal amounts of two isomers; i.e. we would expect only the racemic modification. But the product is not completely racemized, for the inverted product exceeds its enantiomer.

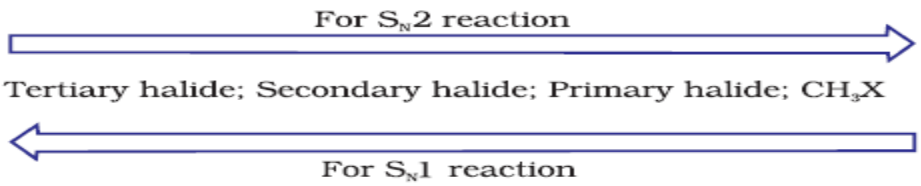
We can say in contrast to S_N2 reaction, which proceeds with complete inversion; **an S_N1 reaction proceeds with racemization though may not be complete.**



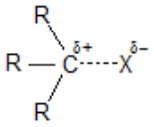
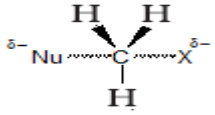
Reactivity of an alkyl halide depends chiefly upon how stable a carbonium ion it can form.

In S_N1 reactions the order of reactivity of alkyl halides is **Allyl, benzyl >3º>2º>1º>CH_3 X.** 3^0 alkyl halides undergo S_N1 reaction very fast because of the high stability of 3^0 carbocations.

Order of reactivity of alkyl halides towards S_N1 and S_N2 reactions as follows:



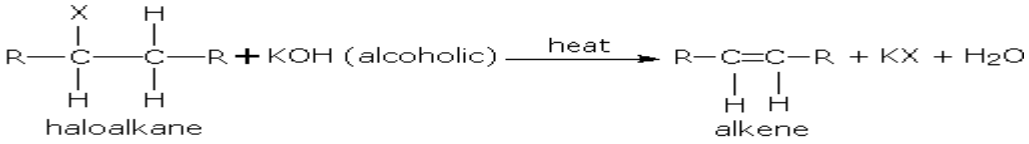
Differences between S_N1 and S_N2:

	S_N1 **(Uni molecular nucliophilic substitution reaction)**	**S_N2** **(Bi molecular nucliophilic substitution reaction)**
Steps	Two : **1:** $R:X \rightarrow R^+ + X^-$ **2:** $R^+ + Nu^- \rightarrow RNu$	One : $R:X + Nu^- \rightarrow RNu + X^-$
Rate	=K [RX] (1st order)	=K[RX] [$:Nu^-$] (2nd order)
Transition State of slow step		
Stereochemistry	Inversion and racemization (Top and bottom attack)	Inversion (backside attack)
Molecularity	Unimolecular	Bimolecular
Reactivity of 'R' Determining Factor	$3^o > 2^o > 1^o > CH_3$ (Stability of R^+)	$CH_3 > 1^o > 2^o > 3^o$ (Steric hindrance in R group)
Nature of 'X' **Solvent effect on rate**	RI> RBr> RCl> RF Rate increases in polar solvent	RI> RBr> RCl> RF with Nu^- Rate increase in polar aprotic solvents.
Effect of nucleophile	No effect as it does not appear in the rate expression.	Rate depends on nucleophilicity $I^- > Br^- > Cl^-$; $RS^- > RO^-$
Catalysis	Lewis acid, eg. Ag^+, $AlCl_3$, $ZnCl_2$	None
Competitive reaction	Elimination, rearrangement	Elimination

ELIMINATION REACTIONS

Elimination reactions are commonly known by the kind of atoms or groups of atoms leaving the molecule.

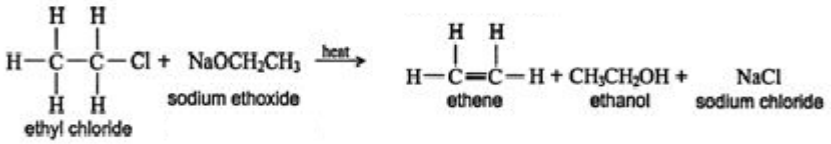
- The removal of a hydrogen atom and a halogen atom is known as **dehydrohalogenation.**
- When both leaving atoms are halogens, the reaction is known as **dehalogenation.**
- The elimination of a water molecule, usually from an alcohol, is known as **dehydration.**
- When both leaving atoms are hydrogen atoms, the reaction is known as **dehydrogenation.**



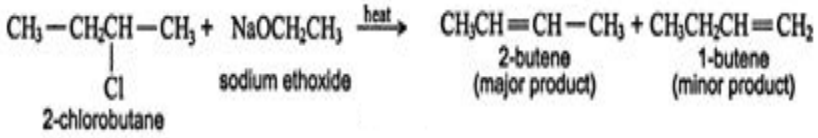
It is the principal process by which organic compounds containing only single carbon-carbon bonds (saturated compounds) are transformed to compounds containing double or triple carbon-carbon bonds (unsaturated compounds).

DEHYDROHALOGENATION OF ALKYL HALIDES:

The dehydrohalogenation of alkyl halides**,** another β elimination reaction, involves the loss of a hydrogen and a halide from an alkyl halide (RX). Dehydrohalogenation is normally accomplished by reacting the alkyl halide with a strong base, such as sodium ethoxide.

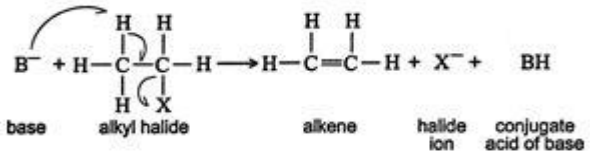


This reaction also follows the Saytzeff rule, so in the reaction of 2-chlorobutane with sodium ethoxide, the major product is 2-butene.



MECHANISM:

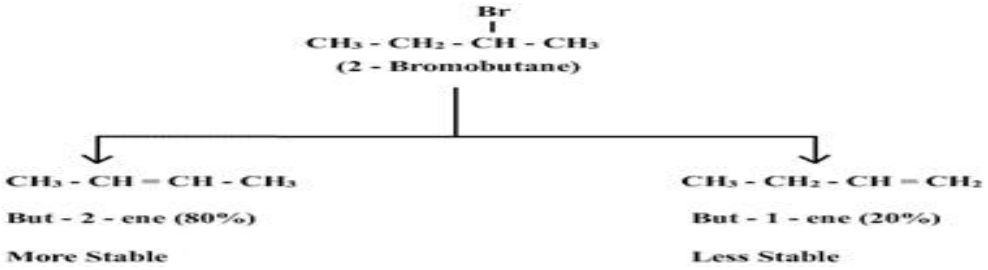
- A strong base removes a slightly acidic hydrogen proton from the alkyl halide via an acid-base reaction.
- The electrons from the broken hydrogen-carbon bond are attracted toward the slightly positive carbon atom attached to the chlorine atom. As these electrons approach the second carbon, the halogen atom breaks free, leading to the formation of the double bond.



The order of reactivity of haloalkanes in dehydrohalogenation is, Tertiary > Secondary > Primary.

SAYTZEFF'S RULE / ZAITSEV'S RULE

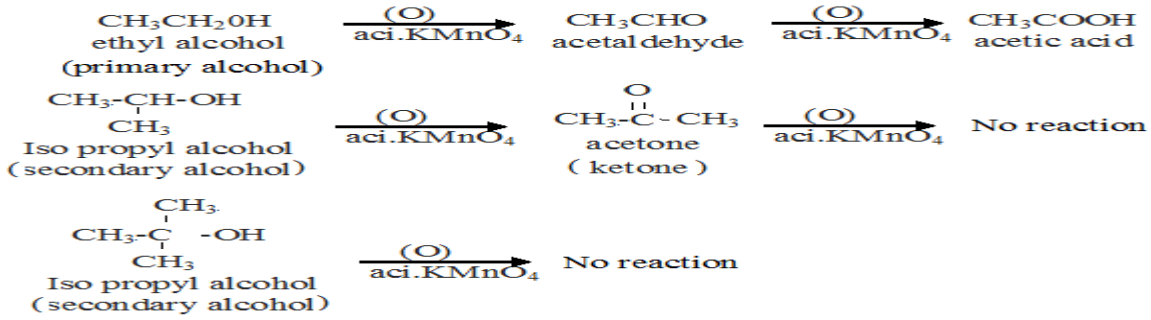
According to Saytzeff rule "In dehydrohalogenation reactions, the preferred product is that alkene which has the greater number of alkyl groups attached to the doubly bonded carbon atoms." For example: The dehydrohalogenation of 2-bromobutane yields two products 1-butene and 2-butene. Out of these 2-butene is the major product (80%) as it is more highly substituted and it is morestable.



OXIDATION REACTIONS

Oxidation of alcohols by using of Potassium permanganate ($KMnO_4$):
Potassium permanganate is a very strong oxidizing agent and able to react with many functional groups especially secondary alcohols. Under controlled conditions $KMnO_4$ oxidizes primary alcohols to Carboxylic acids very efficiently.

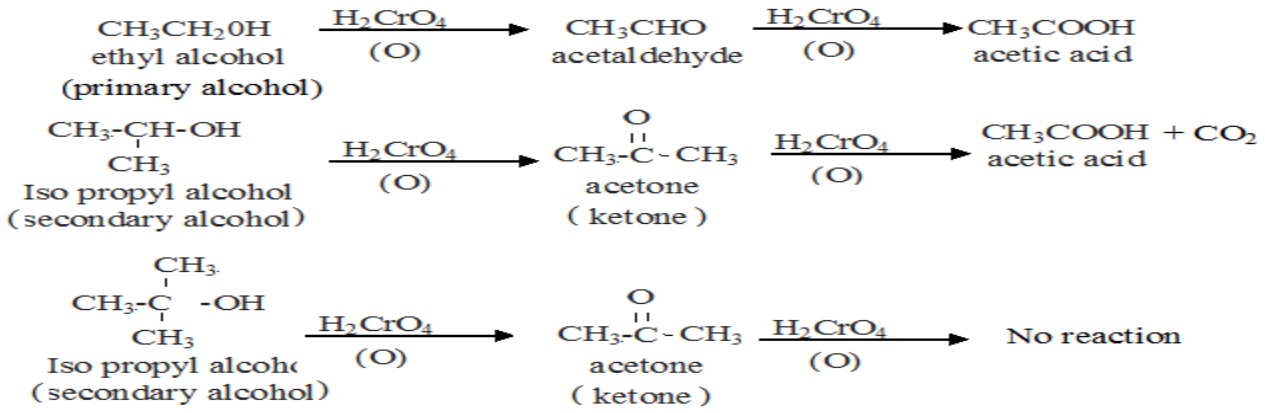
Example: Acidified $KMnO_4$ oxidizes the ethyl alcohol (primary alcohol) directly to the carboxylic acid. Acidified $KMnO_4$ oxidizes the Iso propyl alcohol (secondary alcohol) to ketone and no further



reaction. There is no reaction with Acidified $KMnO_4$ to tertiary alcohols.

Oxidation of alcohols by using of Chromic acid (H_2CrO_4):
Chromic acid strong acid and it is a reagent for oxidizing alcohols to ketones and carboxylic acids.

Example: Generally Chromic acid oxidizes primary alcohols (ethyl alcohol) to carboxylic acids (acetic acid), secondary alcohols (iso propyl alcohol) to ketones (acetone), Carbon dioxide and finally carboxylic acids (acetic acid). Chromic acid oxidizes the tertiary alcohol (secondary alcohol) to ketone and no further reaction.

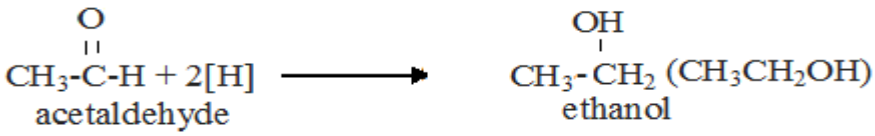


REDUCTION REACTIONS OF CARBONYL COMPOUNDS BY USING $LiAlH_4$ & $NaBH_4$

Metal hydrides like lithium aluminium hydride ($LiAlH_4$), sodium borohydride ($NaBH_4$) reduce carbonyl compounds to alcohols. These are hydride ion (H^-) donors. Hydride ion is a nucleophile, hence it is a nucleophilic addition reaction.

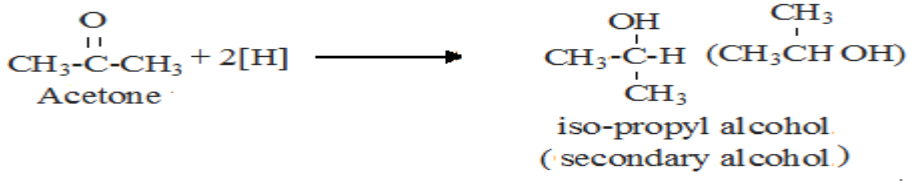
Reduction of an aldehyde using $LiAlH_4$ or $NaBH_4$:
Reduction of an aldehyde using lithium aluminium hydride ($LiAlH_4$) or sodium borohydride ($NaBH_4$) gives the same organic compound like alcohols.

Example: acetaldehyde to ethanol. Reduction of an aldehyde leads to primary alcohol.



Reduction of a ketone using $LiAlH_4$ or $NaBH_4$:
Reduction of a Ketone using lithium aluminium hydride ($LiAlH_4$) or sodium borohydride ($NaBH_4$) gives the same organic compound like alcohols.

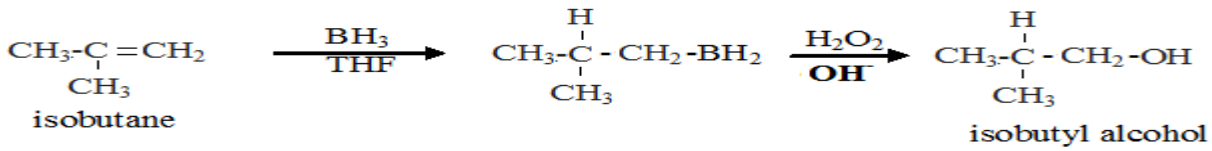
Example: Acetone to iso-propyl alcohol. Reduction of a ketone leads to secondary alcohol.



HYDROBORATION OF OLEFINS

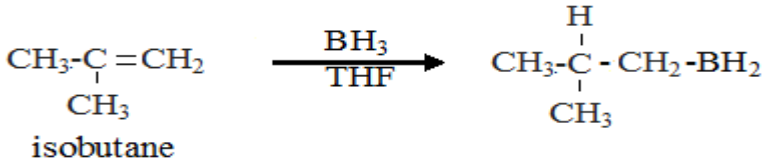
Hydroboration-Oxidation reaction is a two step organic reaction that converts an alkene into neutral alcohol by the net addition of water across the double bond. The hydrogen and hydroxyl group are added in a syn addition. Hydroboration-Oxidation reaction is an Anti Markovnikoff reaction with the hydroxyl group attaching to the less substituted carbon.

Example: Conversion of isobutane into isobutyl alcohol.

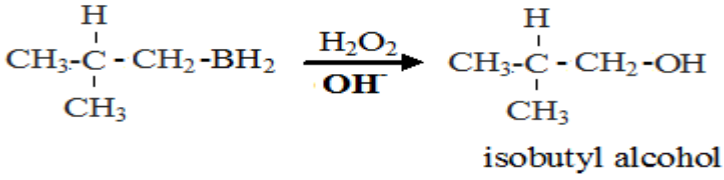


Mechanism of Hydroboration of olefins:

Step-1(Hydroboration): In the step-1, borane (BH_3) adds to the double bond transferring one of the hydrogen atoms to the carbon adjacent to the one that becomes bonded to the boron.



Step-2 (Oxidation): In the step-2, the nucleophilic hydroperoxide anion attacks the boron atom to give alcohol.



SYNTHESIS OF ASPIRIN

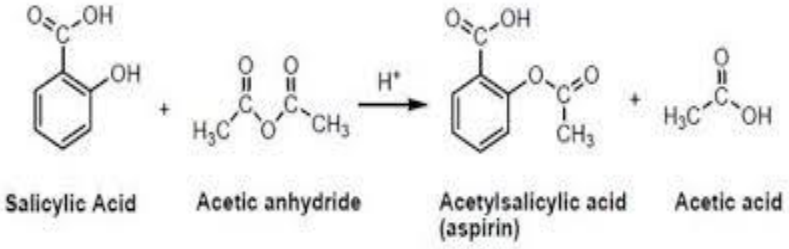
Aim: To prepare Aspirin from salicylic acid.

Chemicals: salicylic acid 2.5grams, acetic anhydride-5 ml and 3-4 drops Con.Sulphuric acid.

Apparatus: Conical flask, Measuring cylinder and filter paper.

Principle: Aspirin is prepared from salicylic acid by acetylating it with acetic anhydrade in the presence of 3-4 drops of Con.Sulphuric acid as catalyst.

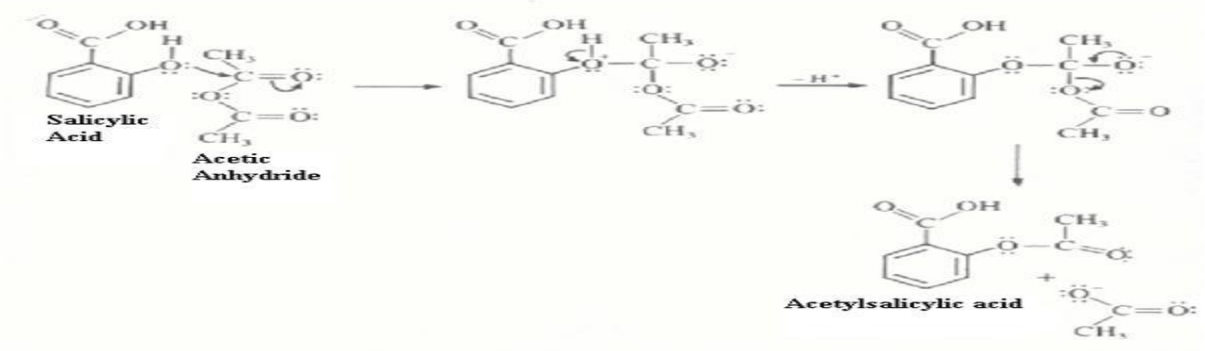
Reaction:



Procedure:

- Weigh 2.5 grams of salicylic acid and transfer to a 100ml cleaned and dried conical flask.
- Add 5ml of acetic anhydride and 3-4 drops Con.Sulphuric acid in to the flask.
- The contents of the flask should be thoroughly mixed.
- Warm the mixture on a water-bath maintaining 60 °C for about 20-25 min with constant stirring.
- Allow the contents of the flask to attain room temperature and pour it directly into a beaker having 100 ml cold water.
- Filter the crude product by using filter paper and dry it in hot air oven at 100 °C.
- Finally calculate yield of the Aspirin.

Mechanism:



Calculation:

138 gm/mole salicylic acid ($M.F = C_7H_6O_3$) ⟶ 180 gm/mole Aspirin ($M.F = C_9H_8O_4$)

Therefore, 2.5 grams of salicylic acid will form .....? (X) g Aspirin

$$X = (180 \times 2.5)/\ 138 = \mathbf{3.26}\ g$$

Theoretical yield = **3.26** g

% Yield = (Practical Yield)/(Theoretical Yield) × 100

Result:

1. Practical weight of the Aspirin _____ gm.
2. % yield of the Aspirin _____ %

SYNTHESIS OF PARACETAMOL

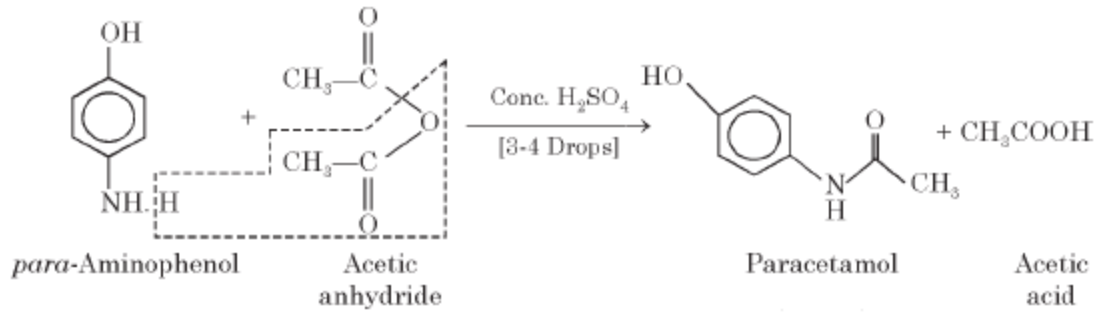
Aim: To prepare Paracetamol from p-aminophenol.

Chemicals: p-aminophenol-6grams, Acetic anhydride-6.5 ml and 3-4 drops Con.Sulphuric acid.

Apparatus: Conical flask, Measuring cylinder and filter paper.

Principle: Paracetamol is prepared from p-aminophenol by acetylating it with acetic anhydrade in the presence of 3-4 drops of Con.Sulphuric acid as catalyst.

Reaction:

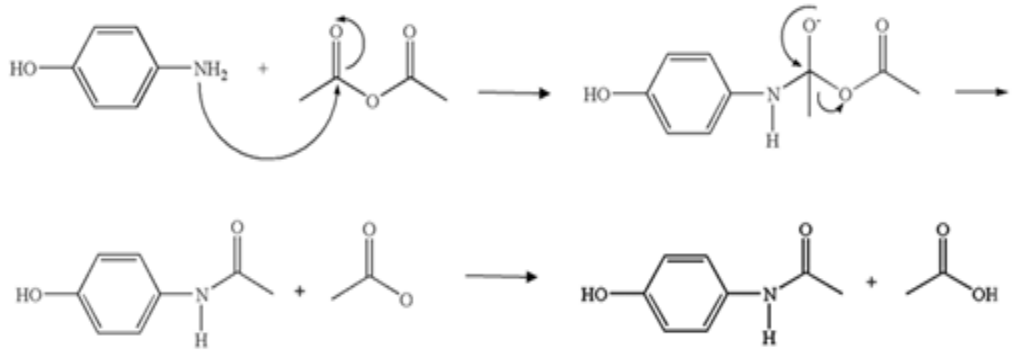


Procedure:

- Weigh 6 grams of p-aminophenol and transfer to a 100ml cleaned and dried conical flask.
- Add 6.5ml of acetic anhydride and 3-4 drops Con.Sulphuric acid in to the flask.
- The contents of the flask should be thoroughly mixed.

- Warm the mixture on a water-bath maintaining 60 °C for about 20-25 min with constant stirring.
- Allow the contents of the flask to attain room temperature and pour it directly into a beaker having 100 ml cold water.
- Filter the crude product by using filter paper and dry it in hot air oven at 100 °C.
- Finally calculate yield of the paracetamol.

Mechanism:



Calculation:

109 gm/mole p-aminophenol ($M.F=C_6H_7NO$) ⟶ 151 gm/mole paracetamol ($M.F=C_8H_8NO_2$)

Therefore, 6 g p-aminophenol will form .....? (X) g paracetamol

$$X = (151 \times 6)/109 = 8.31 \text{ g}$$

Theoretical yield = 8.31 g

% Yield = (Practical Yield)/(Theoretical Yield) × 100

Result:

3. Practical weight of the Paracetamol _____ gm.

4. % yield of the Paracetamol _____ %

Learning objectives:

After completion of this unit the student should be able to:

- Introduction to representation of 3-dimensional structures.
- Structural and stereoisomers.
- Configurations, symmetry and chirality.
- Enantiomers, diastereomers, optical activity.
- Absolute configuration. Conformation alanalysis of n- butane.

Nucleophilic Substitution reactions:

- Mechanism of S_N1, S_N2 reactions.
- Electrophilic and nucleophilic addition reactions:
- Addition of HBr to propene. Markownikoff and anti Markownikoff's additions.
- Grignard additions on carbonyl compounds.

Elimination reactions:

- Dehydro halogenation of alkylhalides. Saytzeff rule.

Oxidation reactions:

- Oxidation of alcohols using $KMnO_4$ and chromic acid.

Reduction reactions:

- Reduction of carbonyl compounds using $LiAlH_4$ & $NaBH_4$.
- Hydroboration of olefins.

Synthesis of drug molecules:

- Structure, synthesis and pharmaceutical applications of Paracetamol.
- Structure, synthesis and pharmaceutical applications of Aspirin.

Short Answer Questions:

1.Distinguish between Electrophilic addition reactions and nucleophilic addition reactions.

2.Explain Addition of HBr to propene by Markownikoff additions.

3.Write the Reduction of carbonyl compounds using $NaBH_4$.

4.Explain Dehydro halogenation of alkylhalides with Saytzeff rule.

5.Give one example for Hydroboration of Olefins.

6.Discuss the Oxidation of alcohols using chromic acid.

7.Explain Reduction of carbonyl compounds using $LiAlH_4$.

8.Explain Addition of HBr to propene by Markownikoff additions.

9.Write about optical activity with one example.

10. Define Diastereomers explain with one example.

11. Write about classification of isomers.

12. Define Enantiomers explain with one example.

Descriptive Questions:

1. Detail explanation of the Nucleophilic substitution reaction mechanism of S_N1, S_N2 reactions.

2. Describe the Oxidation of alcohols using $KMnO_4$ and Chromic acid.

3. Explain Structure, synthesis and pharmaceutical applications of Aspirin.

4. Explain the following:

i. Electrophilic addition reaction (Addition of HBr to propene by Markownikoff-rule).

ii. Nucleophilic addition reaction (Grignard additions on carbonyl compound)

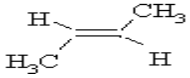
5. Explain Structure, synthesis and pharmaceutical applications of Paracetamol.

6. Explain Conformational analysis of n-butane.

Objective Questions:

1. Stereo chemistry explains the orientation of molecules in which of the following dimensional. **[c]**

(a) 1D (b) 2D (c) 3D (d) All

2. Write the name of this structure  **[b]**

(a) Cis-isomer (b Trans-isomer (c) Enantiomer (d)Diastereomer

3. Pair of molecules that are non-superimposable mirror images of each other is called **[a]**

(a) Enantiomer (b) Diastereomer (c) Anomer (d)Epimer

4. Which of the following compounds involved in nucleophilic addition reactions? **[c]**

(a)Acetaldehyde (b) Acetone (c)Both (d) Ethylene

5. When Methyl Magnesium Bromide reacts with acetone which of the following alcohol will be formed. **[c]**
(a)1°-Alcohol (b) 2°-Alcohol (c) 3°-Alcohol (d) 4°-Alcohol

6. The number of steps involved in Bimolecular nucleophilic substitution reaction is… **[a]**
(a)1 (b) 2 (c) Both (d) 3

7. Which of the following product is obtained when acetaldehyde is undergone reduction with $LiAlH_4$. **[d]**
(a) Formic acid (b) Acetic acid (c) CO_2 (d) Ethanol

8. Which of the following chemicals are used for preparation of Aspirin. **[c]**
(a) Salicylic acid (b) Acetic anhydride (c) Both (d) Acetic acid

9. According to the Anti-markownikoff rule, when 2-Butene is reacted with KBr which of the following is the major product. **[a]**
(a) 1-bromo butane (b) 2-bromo butane (c) Both (d) 2-bromo butane

10. According to the Saytzeff's rule, which of the following is the major product is formed, when 2-chloro butane is reacted with alcoholic KOH is.. **[b]**
(a) 1- butene (b) 2- butene (c) Both (d) 2- butanol

Fill in the blanks:

1. 2-chloropropane and 1-chloropropane are **position** isomers.

2. **Plane Polarized Light** is the full form of PPL in optical isomerism.

3. **Unsaturated** Hydrocarbon involved in electrophilic addition reactions.

4. **Tertiary (3°)** alkyl halide involved in uni molecular nucleophilic substitution reaction.

5. **Hydrogen** and **Halide** are eliminated in dehydrohalogenation reaction.

6. **Acetic Acid** obtained when acetaldehyde is undergone oxidation with $KMnO_4$.

7. **Alcohols** obtained by hydroboration of olefins.

8. **P-Amino Phenol** and **Acetic anhydride** chemicals are used in preparation of Paracetamol.

9. According to the Markownikoff rule, when 2-Butene is reacted with KBr **2-Bromo butane** is the major product.

10. Alkyl magnesium halide is called **Grignard** reagent.