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Chapter 1

Fundamental Concepts In Organic Reaction Mechanism

1.1. Introduction

In an organic reaction, the organic molecule (substrate) reacts with an appropriate attacking reagent and leads to the formation of one or more intermediate(s) and finally give product(s).

The general reaction can be described in the following figure:



Substrate is that reactant which supplies carbon to the new bond and the other reactant is called reagent. In such a reaction a covalent bond between two carbon atoms or a carbon and some other atom is broken and a new bond is formed.

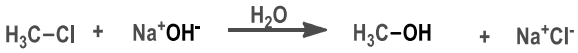
A sequential account of each step, describing details of electron movement, energetics during bond breaking (cleavage) and bond formation, and the rates of transformation of reactants into products is referred to as **reaction mechanism**.

1.2. Types of Organic Reactions

Mostly, all organic reactions fall into four categories: *substitutions (or displacement), additions, elimination, or rearrangements.*

1.2.1. Substitution:

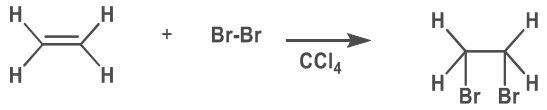
The substitution reactions are the characteristics of saturated compounds such as alkanes and alkyl halides and of aromatic compounds (even though they are unsaturated). In a substitution, *one group replaces other.* For e.g. chloromethane reacts with sodium hydroxide to produce methyl alcohol and sodium chloride as shown in figure:



In this reaction, a hydroxide ion from sodium hydroxide replaces the chlorine of methyl chloride.

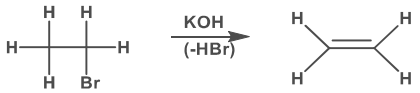
1.2.2. Addition:

Addition are characteristic of compounds of **multiple** (double or triple) bonds. Ethene, for example, reacts with bromine by an addition reaction. In an addition reaction, all parts of the adding reagent appear in the product: two molecules become one as shown in figure:



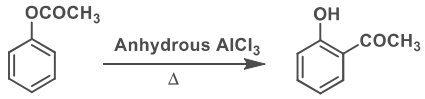
1.2.3. Elimination:

Eliminations are the opposite toadditions.*In an elimination one molecule loses the elements of another small molecule*. Elimination reactions give us a method for preparing compounds with double and triple bonds. In dehydrohalogenation, the elements of a hydrogen halide are eliminated and give product alkene as shown in figure:



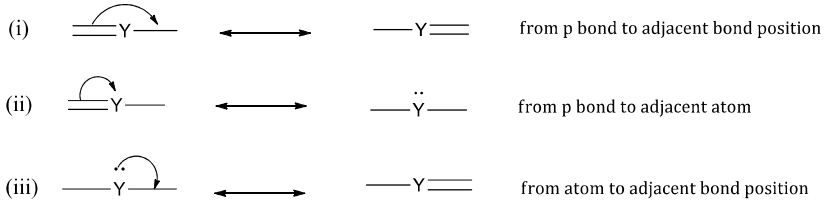
1.2.4. Rearrangement:

In a rearrangement a molecule undergoes a reorganization of its constitutent parts. For example, in the figure, the rearrangement reaction of a phenolic ester to a hydroxyl aryl ketone by catalysis of Lewis acids.

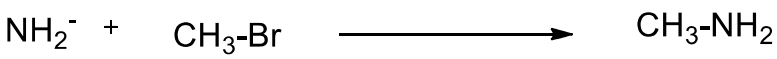


1.3 Electronic Movement in Organic Reactions

- The movement of electrons in organic reactions can be shown by curved-arrow notation (↷ or ↶).
- It shows how changes in bonding occure due to electronic redistribution during the reaction.
- To show the change in position of a pair of electrons, curved arrow starts from the point where an electron pair is shifted and it ends at a location to which the pair of electron may move.
- Presentation of shifting of electron pair is given below in figure:



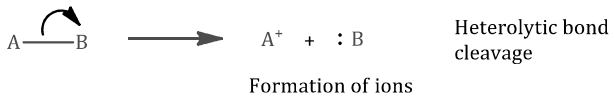
- Movement of single electron is indicated by a single barbed 'fish hooks' (i.e. half-headed curved arrow: ⇀ or ↼).
- For e.g. in transfer of amide ion giving methylamine and in the dissociation of bromomethane, the movement of electron using curved arrows can be depicted as follows:



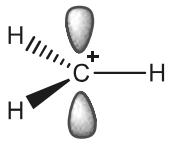
1.4 Fission of a Covalent Bond

- A covalent bond can get cleaved either by (i) Heterolytic cleavage or by (ii) Homolytic cleavage
- When a bond breaks such that one fragment takes away both electrons of the bond, leaving the other fragment with an empty orbital, this kind of cleavage is called ***heterolysis*** (Greek: *hetero*, different, + *lysis*, loosening or cleavage).
- Heterolysis produes charged fragment or ions and is termed an ***ionic reaction.***

- The broken bond is said to have cleaved *heterolytically*as shown in figure:

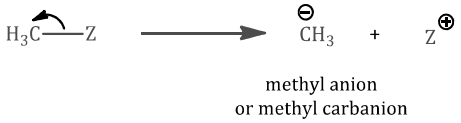


- For e.g. heterolytic cleavage of chloromethane will give methyl cation and chloride ion as shown below in figure:
- A species having a carbon atom possessing sextet of electrons and a positive charge is called a ***carbocation*** (earlier called ***carbonium ion***).

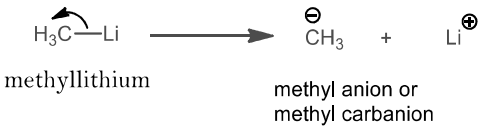


SP^2, Trigonal Planer

- The chlorine ion has octet of electrons has achieved a noble gas configuration.
- The reason for shift of electron pair from Carbon to chlorine is due to difference in electronegativity.
- Carbon has low electronegativity (χ = 2.5) as compared to chlorine (χ = 3.0) so the shared pair of electrons are polarized more towards chlorine than carbon, so after heterolytic cleavage the chlorine takes away both electrons of the bond, leaving the carbon atom possessing six pair of electrons and an empty p orbital.
- The heterolytic cleavage can also give a species in which carbon gets the shared pair of electrons as shown in figure below.
- For example, when group Z attached to the carbon leaves without electron pair, the methyl anion is formed. Such a carbon species carrying a negative charge on carbon atom is called ***carbanion***.



- For e.g. heterolytic cleavage of Methyllithium will give methyl anion and lithium ion as shown below in figure:



- The reason for shift of electron pair towards Carbon from lithium is due to difference in electronegativity.

- Carbon has high electronegativity (χ = 2.5) as compared to lithium (χ = 0.9) so the shared pair of electrons are polarized more towards carbon than lithium, so after heterolytic cleavage the carbon takes away both electrons of the bond, leaving the Lithium ion achieving noble gas configuration by losing electron.

When a bond breaks so that each fragment takes away one of the electrons of the bond, this process is called ***homolysis***(Greek: *homo,* the same, + *lysis,* loosening or cleavage).

Homolysis produces fragments with unpaired electrons called ***radicals*** as shown in figure:



1.5 Concept of Electrophiles and Nucleophiles

Polar reactions proceed by the movement of *pairs* of electrons from areas of high electron density (*nucleophiles*) to areas of low electron density (*electrophiles*), or from filled orbitals to empty orbitals.

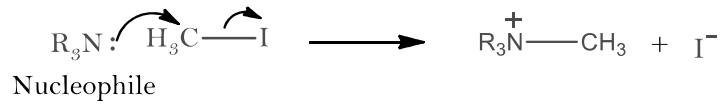
1.5.1 Nucleophiles (Nu^-)

- A *nucleophile* is a compound that has a relatively high energy pair of electrons available to make a new bond.
- A nucleophilic atom may be neutral or negatively charged molecule with an unshared electron pair.
- Examples of nucleophiles: $^-$OH, Halogens, N_3^-, NR_3, alkenes, alkynes,etc.
- There are three classes of nucleophiles: **Lone-Pair Nucleophiles**, **σ-Bond Nucleophiles**, and **π-Bond Nucleophiles**.

I. Types of Nucleophiles:

a. Lone-Pair Nucleophiles:

Lone-pair nucleophiles contain atoms with lone pairs. The lone pair is used to make a new bond to an electrophilic atom. Alcohols (ROH), alkoxides(RO^-), amines (R_3N), metal amides (R_2N^-), halides (X^-), thiols (RSH), sulfides (R_2S), and phosphines (R_3P) are all examples of lone-pair nucleophiles. When these compounds act as nucleophiles, the formal charge of the nucleophilic atom is *increased* by 1 in the product.

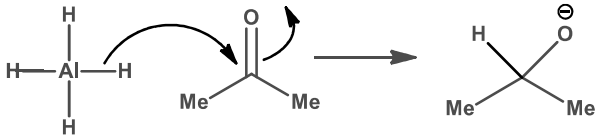


b. Sigma-Bond Nucleophiles:

Sigma-bond nucleophiles contain a bond between a nonmetal and a metal. The electrons of the element–metal bonds are used to form a bond between the nonmetal and the electrophile. The formal charge on the nucleophilic atom does not change; the metal increases its formal charge by 1.

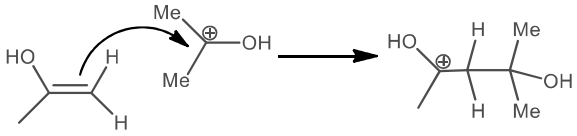
The nucleophilic atom may be a heteroatom (as in $NaNH_2$or KOH), carbon (as in Grignard reagents (RMgBr), organolithium reagents (RLi), and Gilman reagents (R_2CuLi), which have C–Mg, C–Li, and C–Cu bonds, respectively), or hydrogen (as in the complex metal hydrides $NaBH_4$and $LiAlH_4$).

For e.g. the Nucleophilic addition of Lithium Aluminum hydride with acetone.



c. π-Bond Nucleophiles:

- π *-bond nucleophiles* use the pair of electrons in a πbond, usually a C=Cbond, to form a σbond between one of the atoms in the *bond* and the electrophilic atom.
- The formal charge and total electron count of the nucleophilic atom of the πbond do not change, but the other atom of the πbond is made *electron-deficient*, and its formal charge increases by +1.
- The πbonds of simple alkenes and arenes are weakly nucleophilic; πbonds that are directly attached to heteroatoms, such as in enolates (C=C–O^-), enols (C=C–OH), enol ethers (C=C–OR), and enamines (C=C–NR_2), are much better nucleophiles.



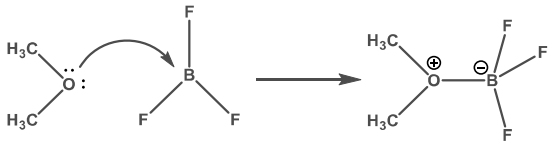
1.5.2 Electrophiles (E)

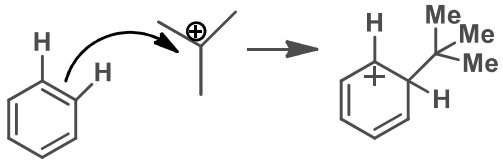
- An *electrophile* is a compound that has a relatively low energy empty orbital available for bond-making.
- An electrophile may be neutral or positively charged species.
- There are three types of electrophiles: **Lewis Acid Electrophiles**, **π-Bond Electrophiles**, and **σ-Bond Electrophiles**.

I. Types of Electrophiles:

a. Lewis Acid Electrophiles

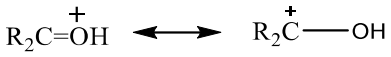
- *Lewis acid electrophiles* have an atom E that lacks an octet and has a low energy nonbonding orbital, usually a p orbital.
- A pair of electrons from the nucleophile is used to form a new bond to E, giving it its octet.
- The formal charge of E *decreases* by 1. Positive charged species(H^+, Cl^+, NO^+) Carbocations (R^+) , boron compounds, and aluminum compounds and other such as $AlCl_3$, $ZnCl_2$, $FeCl_3$, $TiCl_4$, $SnCl_4$ are common Lewis acid electrophiles.





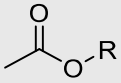
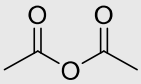
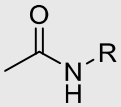
b. π - Bond Eelectrophiles

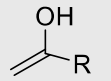
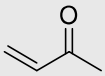
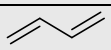
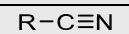
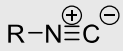
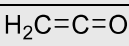
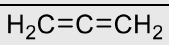
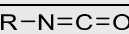
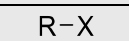
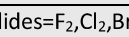
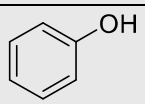
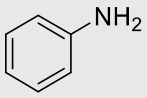
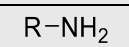
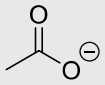
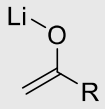
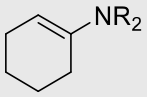
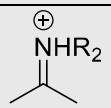
- In π-*bond electrophiles*, the electrophilic atom E has an octet, but it is attached by a πbond to an atom or group of atoms that can accept a pair of electrons.
- Electrophiles of the π -bond type commonly have C=O, C=N, or $C \equiv N$ bonds, in which the less electronegative atom is the electrophilic one. C=C and $C \equiv C$ bonds are electrophilic if they are attached to electrophilic atoms (see below).
- Miscellaneous π-bond electrophiles include SO_3 and RN=O.
- Certain cationic electrophiles can be classified as either the Lewis acid type or the π-bond type depending on whether the best or second-best resonance description is used e.g.,



- When a nucleophile attacks a π-bond electrophile, the πbond breaks, and the electrons move to the *other* atom of the πbond, whose formal charge is decreased by 1.

Table for nature of functional group:

Structure	Name of functional group	Nature
	Ketone	Electrophile
	Aldehyde	Electrophile
	Acyl chloride	Electrophile
	Ester	Electrophile
	Anhydride	Electrophile
	Substituted amide	Electrophile
	Amide	Electrophile

	Enol	Electrophile at C and O
	Methyl vinyl ketone (MVK)	Electrophile at Carbonyl carbon and beta carbon
	Alkene	Nucleophile
	Benzene	Nucleophile
	Diene	Nucleophile or elctrophile
	Cynide/ nitrile	Nucleophile or electrophile
	Isocynide	Nucleophile
	Ketene	Electrophile
	Allene	Electrophile
	Isocyanate	Electrophile
	Alkyl halide	Electrophile
	Halides	Electrophile
	Cyclopropane	Nucleophile
	Phenol	Nucleophile
	Aniline	Nucleophile
	Amine	Nucleophile
	Acetate anian	Nucleophile
	Enolate	Nucleophile at carbon and oxygen
	Enamine	Nucleophile
	Iminium ion	Electrophile at C
BX3	Boron halide	Electrophile