

Chemistry

B.Sc. Second Sem.

Nucleophilic substitution

in Alkyl and Aryl Halides

(Unit-2)

LECTURE-1

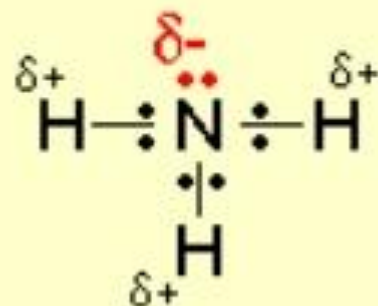
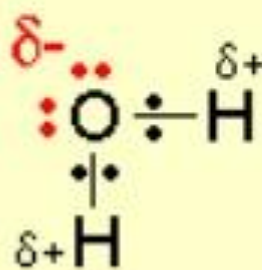
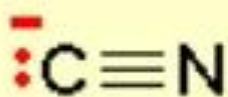
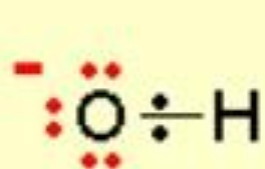
Nucleophilic Substitution



R = aliphatic as well as aromatic

Nucleophile + Substrate \longrightarrow Product + Leaving group

Examples of nucleophiles :



OH^-

CN^-

H_2O

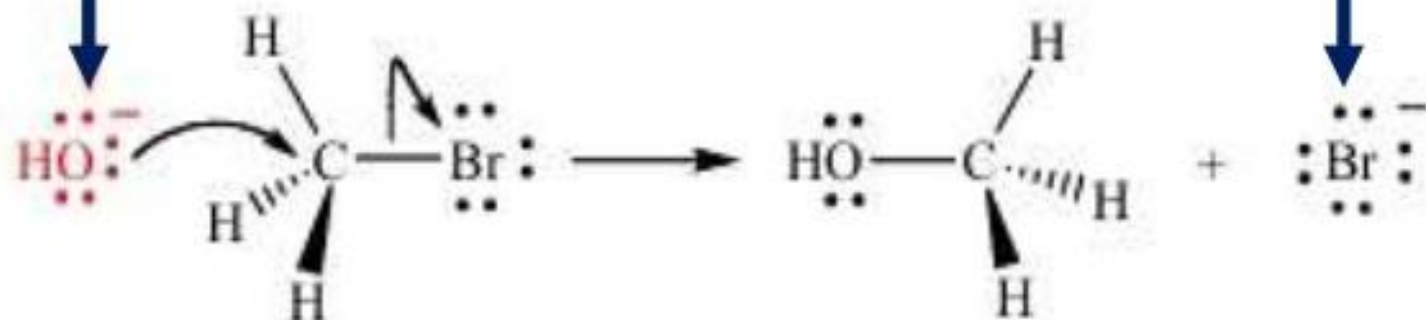
NH_3

Leaving group

- Substituent that leave substrate.
 - Good substituent
 - Leave in stable condition
 - Weak molecule
 - Example(s) :
 - F (strong base)
 - Br
 - Cl
 - I
- } (weak base)

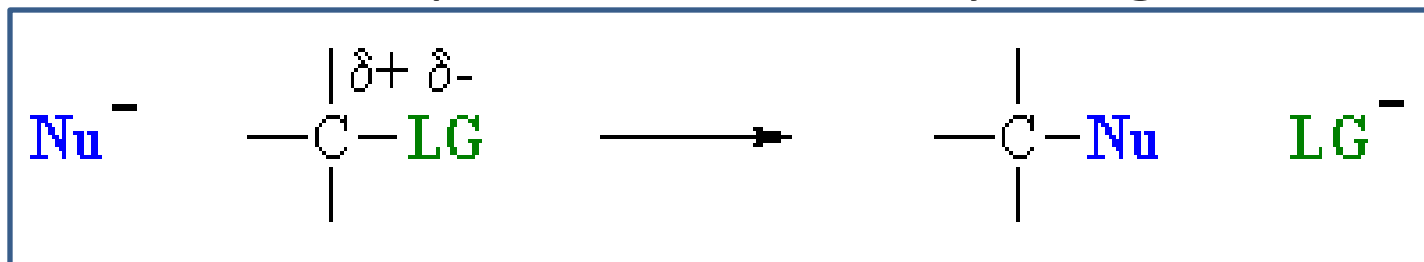
Nucleophile

Leaving group



- **Nucleophilic substitution is a fundamental class of reactions in which an electron rich Nucleophile selectively bonds with or attacks the positive or partially positive charge of an atom or a group of atoms to replace a leaving group; the positive or partially positive atom is referred to an Electrophile**

- Nucleophilic substitution reactions occur when an electron rich species, the **nucleophile**, reacts at an **electrophilic** saturated **C** atom attached to an electronegative group (important), the **leaving group**, that can be displaced as shown by the general scheme:



- The electrophilic C can be recognised by looking for the polar σ bond due to the presence of an electronegative substituent (esp. **C-Cl**, **C-Br**, **C-I** and **C-O**) Nucleophilic substitution reactions are an important class of reactions that allow the interconversion of functional groups.
- Of particular importance are the reactions of alkyl halides (**R-X**) and alcohols (**R-OH**)

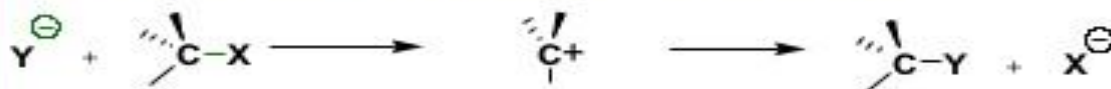
Types of

Nucleophilic Substitution

S_N1

S: Substitution
N: Nucleophilic
1: unimolecular

leaving group goes first and nucleophile comes later



S_N2

S: Substitution
N: Nucleophilic
2: Bimolecular

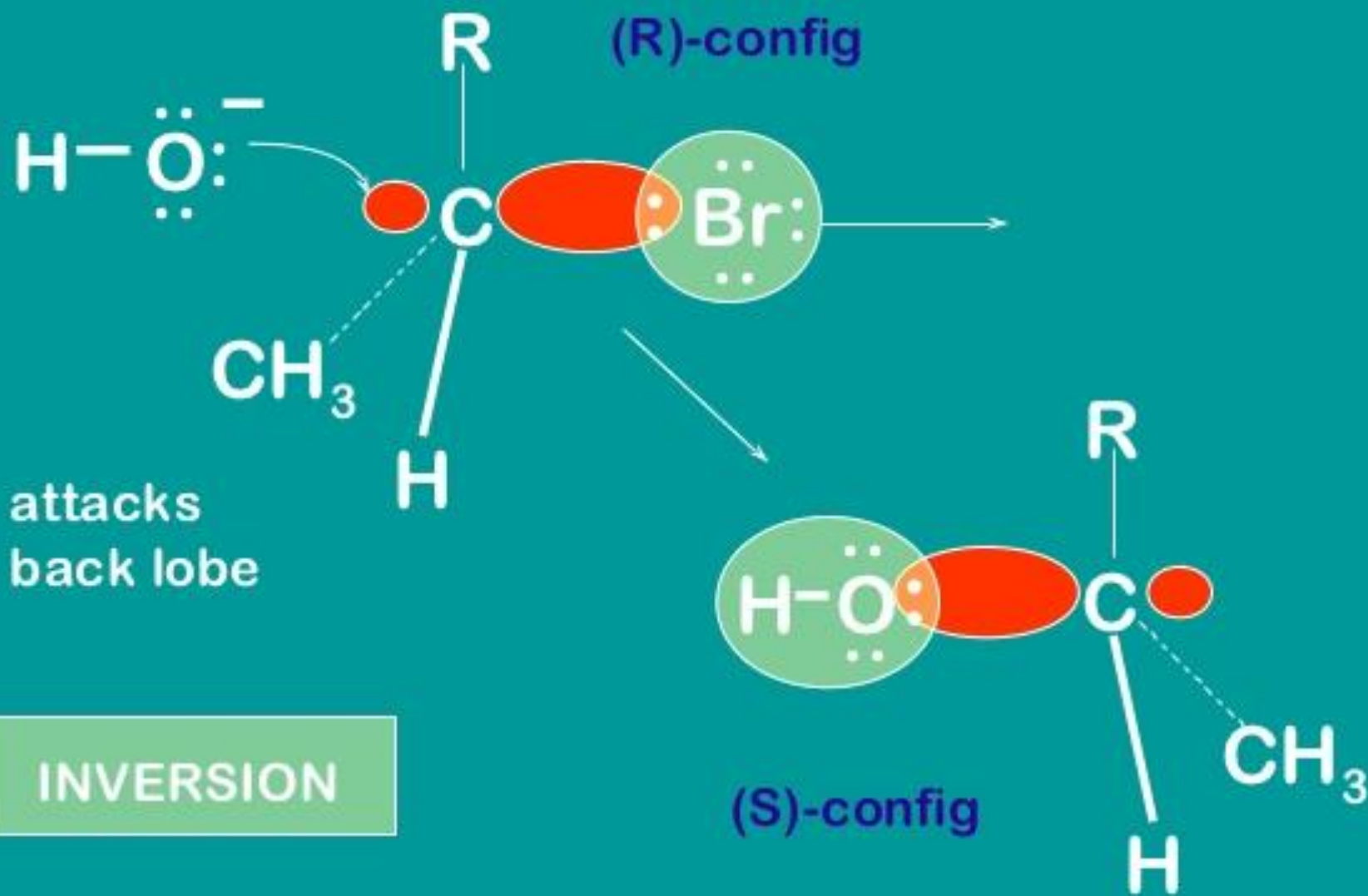
nucleophile attacks and leaving group goes simultaneously



- In the SN2 reaction, the addition of the nucleophile and the elimination of leaving group take place simultaneously. SN2 occurs where the central carbon atom is easily accessible to the nucleophile. By contrast the SN1 reaction involves two steps. SN1 reactions tend to be important when the central carbon atom of the substrate is surrounded by bulky groups, both because such groups interfere sterically with the SN2 reaction (discussed above) and because a highly substituted carbon forms a stable **carbocation**.

S_N2 MECHANISM

nucleophilic attack



Synthetic Utility of the S_N2 Reaction

A variety of functional groups can be prepared employing a good nucleophile and an electrophile with a good leaving group:



S_N2 reaction : Kinetics



Obtained experimentally:

$$\text{rate} = k [\text{alkyl halide}][\text{nucleophile}]$$

the rate constant

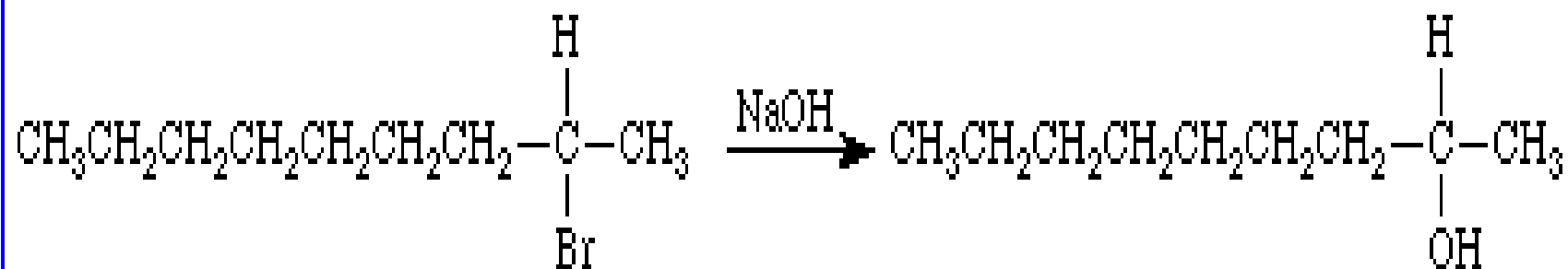
Rate law includes both the alkyl halide and the nucleophile, a second-order process

Walden Inversion

- The term Walden inversion is used to describe the stereochemical outcome of aliphatic bimolecular nucleophilic substitution reactions. For many years chemists suspected that a bimolecular nucleophilic substitution reaction at a chiral carbon atom produced a product that had the opposite stereochemistry from that of the reactant.

Example OF WALDEN INVERSION:

The specific rotations of the enantiomers of 2-bromooctane are -34.6° and $+34.6^\circ$. The specific rotations of the enantiomers of 2-octanol are -9.9° and $+9.9^\circ$. When a sample of 2-bromooctane with a specific rotation of -34.6° was treated with NaOH, the 2-octanol that was produced had an optical rotation of $+9.9^\circ$.



2-bromooctane

$$[\alpha]_{\text{D}}^{20} = -34.6^\circ$$

2-octanol

$$[\alpha]_{\text{D}}^{20} = +9.9^\circ$$

Factors influencing SN2 Reactions

- **Effect of Nucleophile**

- The nucleophilicity may be correlated with the availability of the electron pairs and the ease with which it is donated

Trends in Nuc. Strength

- Increases down Periodic Table, as size and polarizability increase:



- Of a conjugate acid-base pair, the base is stronger:



S_N2 : Nucleophilic Strength

- Stronger nucleophiles react faster.
- Strong bases are strong nucleophiles, but not all strong nucleophiles are basic.


TABLE 6-3 Some Common Nucleophiles, Listed in Decreasing Order of Nucleophilicity in Hydroxylic Solvents Such as Water and the Alcohols

strong nucleophiles	$(\text{CH}_3\text{CH}_2)_3\text{P:}$ $:\ddot{\text{S}}-\text{H}$ $:\ddot{\text{I}}^-$ $(\text{CH}_3\text{CH}_2)_2\ddot{\text{N}}\text{H}$ $:\text{C}\equiv\text{N}$ $(\text{CH}_3\text{CH}_2)_3\text{N:}$ $\text{H}-\ddot{\text{O}}^-$ $\text{CH}_3-\ddot{\text{O}}^-$	moderate nucleophiles	$:\ddot{\text{Br}}^-$ $:\text{NH}_3$ $\text{CH}_3-\ddot{\text{S}}-\text{CH}_3$ $:\ddot{\text{Cl}}^-$ $\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{C}-\ddot{\text{O}}^- \end{array}$ $:\ddot{\text{F}}^-$ $\text{H}-\ddot{\text{O}}-\text{H}$ $\text{CH}_3-\ddot{\text{O}}-\text{H}$
		weak nucleophiles	

Effect of Leaving group

- A good leaving group needs to be a Stable anions that are weak bases which can delocalize charge

Relative reactivity	OH^- , NH_2^- , OR^-	F^-	Cl^-	Br^-	I^-	TosO^-
	$\lll 1$	1	200	10,000	30,000	60,000

 Leaving group reactivity

Effect of Solvent

- SN2 Reaction prefers polar aprotic solvent.

For example : Acetone

Ether

Solvent Effects (2)

- Polar aprotic solvents (no O-H or N-H) do not form hydrogen bonds with nucleophile

End
of
Lecture 1