

SN reactions (continued III)

Effect of Nucleophile:

Nucleophiles and bases are structurally similar: both have a lone pair or a π bond. They differ in what they attack

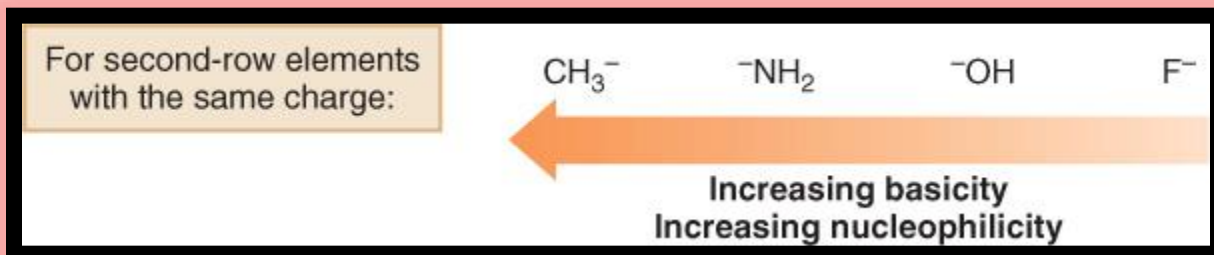
Although nucleophilicity and basicity are interrelated, they are fundamentally different.

Basicity is a measure of how readily an atom donates its electron pair to a proton. It is characterized by an equilibrium constant, K_a in an acid-base reaction, making it a thermodynamic property.

Nucleophilicity is a measure of how readily an atom donates its electron pair to other atoms. It is characterized by a rate constant, k , making it a kinetic property.

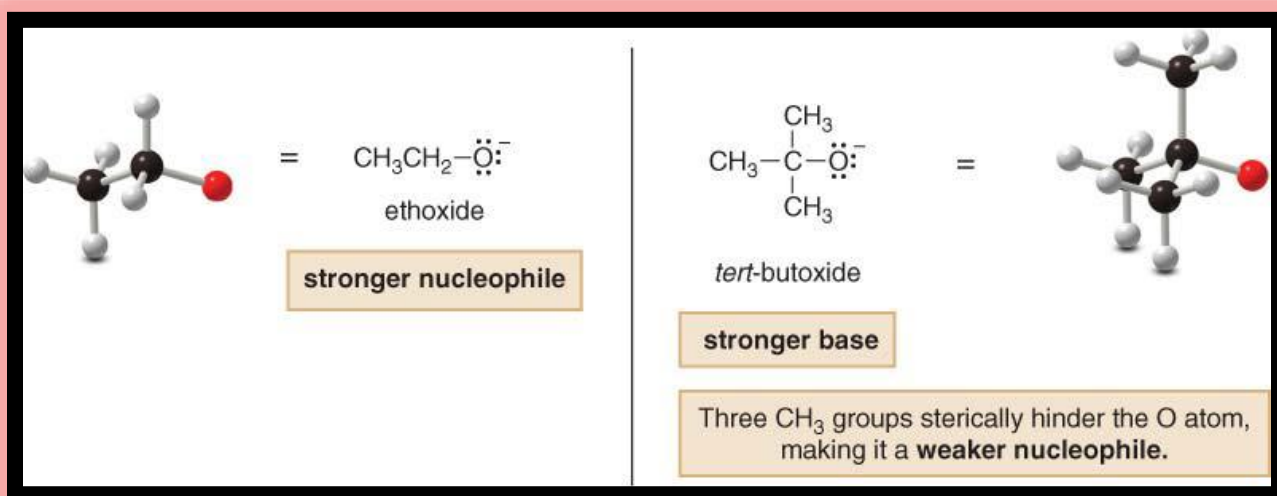
Nucleophilicity parallels basicity in three instances:

1. For two nucleophiles with the same nucleophilic atom, the stronger base is the stronger nucleophile. The relative nucleophilicity of HO^- and CH_3COO^- , two oxygen nucleophiles, is determined by comparing the $\text{p}K_a$ values of their conjugate acids ($\text{H}_2\text{O} = 15.7$, and $\text{CH}_3\text{COOH} = 4.8$). HO^- is a stronger base and stronger nucleophile than CH_3COO^- .
2. A negatively charged nucleophile is always a stronger nucleophile than its conjugate acid. HO^- is a stronger base and stronger nucleophile than H_2O .
3. Right-to-left-across a row of the periodic table, nucleophilicity increases as basicity increases:



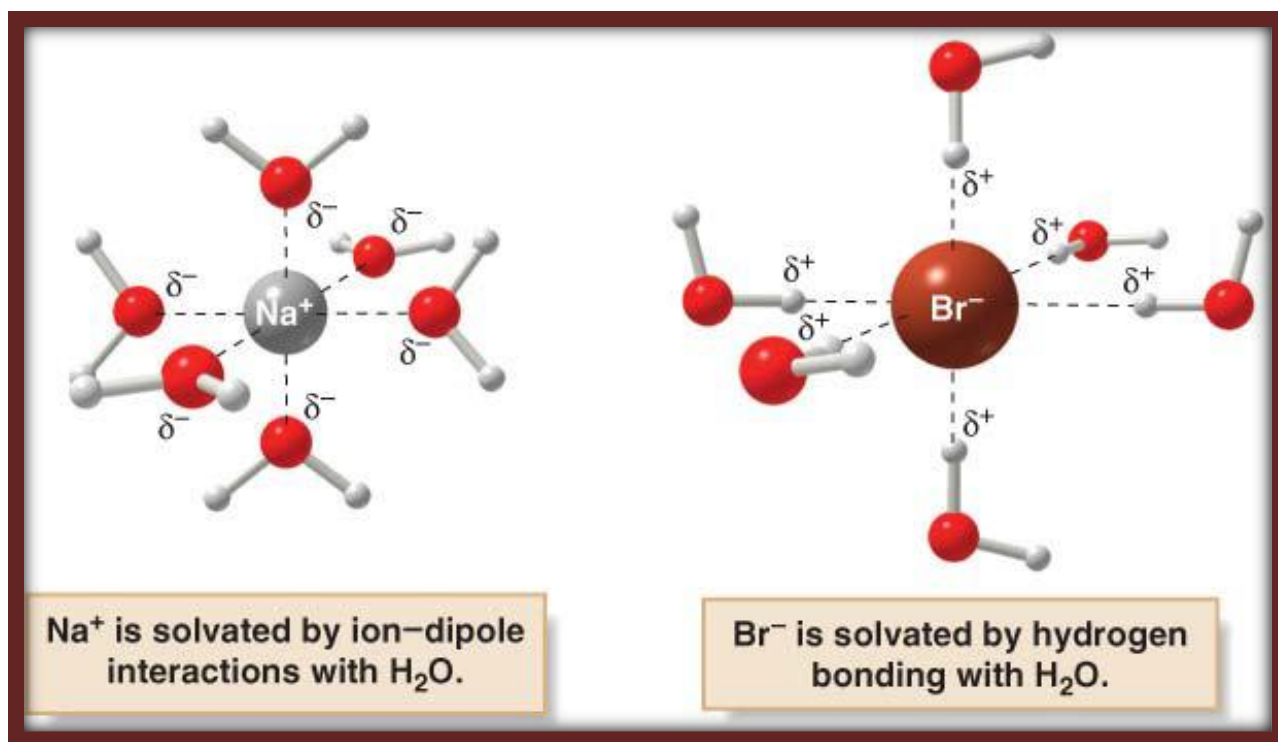
Nucleophilicity does not parallel basicity when steric hindrance becomes important.

- Steric hindrance is a decrease in reactivity resulting from the presence of bulky groups at the site of a reaction.
- Steric hindrance decreases nucleophilicity but not basicity.
- Sterically hindered bases that are poor nucleophiles are called non nucleophilic bases.



The ethoxide anion, for example, is both a strong base and nucleophile because it is very much unhindered. *tert*-Butoxide, on the other hand, is a strong base, but a poor nucleophile, because of its three methyl groups hindering its approach to the nucleophile than ethoxide. A strong/anionic nucleophile always favours $\text{S}_{\text{N}}2$ manner of nucleophilic substitution. Increasing the concentration of the nucleophile will enhance the rate of an $\text{S}_{\text{N}}2$ reaction since kinetically the reaction is first order in respect to the nucleophile concentration. This is in contrast to $\text{S}_{\text{N}}1$ where the concentration and nucleophilicity have no effect on the rate of an $\text{S}_{\text{N}}1$ reaction.

If the salt NaBr is used as a source of the nucleophile Br^- in H_2O , the Na^+ cations are solvated by ion-dipole interactions with H_2O molecules, and the Br^- anions are solvated by strong hydrogen bonding interactions.



In polar protic solvents, nucleophilicity increases down a column of the periodic table as the size of the anion increases. This is the opposite of basicity. In polar protic solvents, nucleophilicity increases down a column of the periodic table as the size of the anion increases. This is the opposite of basicity.

The Leaving Group

In most of nucleophilic substitution reactions alkyl halides are used as substrates in which halide ion acts as a leaving group. However, other groups can also act as good leaving groups if these are the conjugate bases of strong acids. For example, bisulphate ion, HSO₄⁻, which is the conjugate base of sulphuric acid, is a good leaving group.

In a nucleophilic substitution reaction of R—X, the C—X bond is heterolytically cleaved, and the leaving group departs with the electron pair in that bond, forming X:⁻. The more stable the leaving group X:⁻, the better able it is to accept an electron pair. For example, H₂O is a better leaving group than HO⁻ because H₂O is a weaker base.

As in both reactions, i.e., S_N1 and S_N2 the leaving group comes off along with its bonding electron pair. So, the group that can better accommodate the electron pair (or negative charge) is a better leaving group. For example, PhO⁻ is a

better leaving group than RO⁻ because the negative charge of phenoxide ion can be delocalized over to the ring. This type of delocalization is not possible in alkoxide ion. However, a poor leaving group like RO⁻ may be converted to a good leaving group by protonation, e.g., H₂O is a better leaving group than HO⁻ because H₂O is a weaker base than HO⁻.

The leaving group affects the rate of reaction because the more stable it is, the more likely that it will take the two electrons of its carbon-leaving group bond with it when the nucleophile attacks the carbon. Therefore, the weaker the leaving group is as a conjugate base, and thus the stronger its corresponding acid, the better the leaving group. Examples of good leaving groups are therefore the halides (except fluoride) and tosylate, whereas HO⁻ and H₂N⁻ are not.

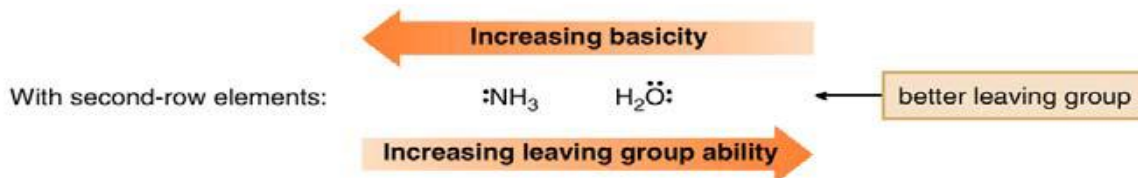
- In comparing two leaving groups, the better leaving group is the weaker base.



Nucleophilic substitution occurs with leaving groups that are weak bases.

There are periodic trends in leaving group ability:

- Left-to-right across a row of the periodic table, basicity *decreases* so leaving group ability *increases*.



- Down a column of the periodic table, basicity *decreases* so leaving group ability *increases*.

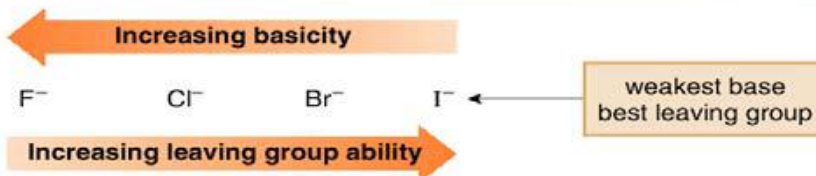


Table 7.2**Good Leaving Groups for Nucleophilic Substitution**

Starting material	Leaving group	Conjugate acid	pK _a
R-Cl	Cl ⁻	HCl	-7
R-Br	Br ⁻	HBr	-9
R-I	I ⁻	HI	-10
R-OH ₂ ⁺	H ₂ O	H ₃ O ⁺	-1.7

↑
These molecules undergo nucleophilic substitution.

↑
good leaving groups