

Classification of Reagents in Chemistry IV: Nucleophiles and Electrophiles

- Electrophiles and nucleophiles are a very broad classification system of reactions and mechanisms that is commonly used in organic chemistry. Nearly all acid/base and redox reactions can be described in terms of electrophiles and nucleophiles.
- Typically reactions that involve the transfer of H^+ are described using the language of acid/base reactions, while reactions that involve the full transfer of an electron are described using the language of redox reactions. The descriptors electrophiles and nucleophiles are used to talk about reactions that fall between these two extremes.

Electrophiles – Literally ‘electron-loving’ electrophiles are atoms that are electron deficient and are going to react to increase their electron density. Electrophiles want to gain more electrons. Electrophiles can be neutral or charged, but tend to have a partial or full positive charge, or if neutral will not have a full electron shell. A general abbreviation for electrophiles is E^+ . All Lewis acids are electrophiles, but there are many more compounds that are also electrophiles that do not have a fully empty orbital. Electrophiles accept a pair of electrons, Lewis acids accept a pair of electrons into an empty orbital.

Common Electrophiles - H^+ , Zn^{2+} , Fe^{3+} , CH_3^+ , BH_3 , BF_3 , $AlCl_3$, $FeBr_3$, $H_2C=O$, $R_2C=O$, $R-X$, Br_2 , Cl_2 , I_2 , HX , H_2O , NH_3 , $RCOOH$, $RCOX$

Nucleophiles – Literally ‘nucleus-loving’, nucleophiles are atoms that are electron rich and are going to react to decrease their electron density. Nucleophiles have extra electrons and want to give them away. Nucleophiles can be neutral or charged, but tend to have partial or full negative charges, or if neutral will have a lone pair. The general abbreviation for nucleophiles is Nu^- when negative or $:Nu$ when neutral. All Bronsted-Lowry bases and Lewis bases are nucleophiles and all nucleophiles are Bronsted-Lowry and Lewis bases. Nucleophiles donate electrons, Lewis bases donate electrons into an empty orbital, and Bronsted-Lowry bases donate electrons to H^+ .

Common Nucleophiles - $R-Li$, $NaNH_2$, KH , $RONa$, $NaOH$, KCN , $NaSH$, $RCOONa$, $NaCl$, NH_3 , H_2O , ROH , HX , $H_2C=O$, $R_2C=O$, Br_2 , Cl_2 , I_2 , pi bonds.

- Note: Many neutral molecules are both electrophiles and nucleophiles. Any polar bond will tend to act nucleophilic at the more negative side and electrophilic at the more positive side of the dipole.

Nucleophilic Acids – Acids can be classified as nucleophilic when the counterion is a good nucleophile (e.g. HCl, HBr, HI) or non-nucleophilic when the counterion is not a good nucleophile (e.g. H₂SO₄, H₃PO₄, HClO₄). While all of these are fairly strong acids the presence or absence of the nucleophile significantly affects their reactivity and kinds of product formed (e.g. HBr tends to do substitution type reactions with an alcohol while H₂SO₄ tends to do elimination type reactions with the same alcohol).

Strength of Nucleophiles – Nucleophilicity (and electrophilicity) is used as a descriptor of reaction kinetics (how fast does the reaction occur), not as a descriptor of the reaction thermodynamics (most stable product of the reaction). Since all nucleophiles are also bases we will use pK_a to determine the ultimate stability of the product and nucleophilicity to determine which product forms faster. Typically stronger bases make better nucleophiles, as the base specifically wants H⁺ back, and the nucleophile just wants to give away electrons to form a bond, however many weaker bases are also good nucleophiles due to charge, electronegativity, polarizability, and solvation effects.

- Less electronegative atoms make better nucleophiles as they are more willing to share electrons (Left on table)

$$\text{NH}_3 > \text{H}_2\text{O} > \text{HF}$$
- More negative atoms make better nucleophiles as they have more electrons to share.

$$\text{NH}_2^- > \text{NH}_3 \quad \text{and} \quad \text{OH}^- > \text{H}_2\text{O}$$
- Larger atoms make better nucleophiles due to polarizability (Down on table)

$$\text{H}_2\text{Se} > \text{H}_2\text{S} > \text{H}_2\text{O} \quad \text{and} \quad \text{PH}_3 > \text{NH}_3$$
- Better bases make better nucleophiles with charged ions in aprotic solvents due to pK_a as they are more willing to share electrons.

$$\text{F}^- > \text{Cl}^- > \text{Br}^- > \text{I}^-$$
- Larger atoms make better nucleophiles with charged ions in protic solvents due to looser solvation shells, which allows the nucleophile to more easily approach the electrophile.

$$\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$$
- Less sterically hindered groups make better nucleophiles as they can more easily approach the electrophile.

$$\text{CH}_3\text{O}^- > \text{CH}_3\text{CH}_2\text{O}^- > (\text{CH}_3)_2\text{CHO}^- > (\text{CH}_3)_3\text{CO}^-$$

Mechanisms – There are many organic mechanisms that use the descriptions of electrophiles and nucleophiles. Typically these mechanisms are named by the pattern of what kind of group is reacting with the carbon in the organic molecule (nucleophile or electrophile), what kind of functional group is reacting (alkene, aromatic, acyl etc.) and what kind of process is occurring (addition, elimination, substitution etc.).

Common mechanisms in the 118 series that use this terminology:

- Bimolecular nucleophilic substitution (S_N2) (of haloalkanes)
- Unimolecular nucleophilic substitution (S_N1) (of haloalkanes)
- Electrophilic addition to alkenes (or alkynes)
- Electrophilic aromatic substitution (EAS)
- Nucleophilic acyl addition
- Nucleophilic acyl substitution (addition-elimination)
- Nucleophilic aromatic substitution