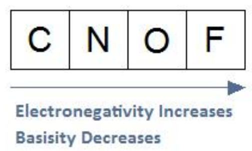
7.7: The Leaving Group

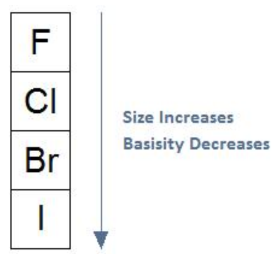
Our general discussion of nucleophilic substitution reactions, we have until now been designating the leaving group simply as “X". As you may imagine, however, the nature of the leaving group is an important consideration: if the C-X bond does not break, the new bond between the nucleophile and electrophilic carbon cannot form, regardless of whether the substitution is S_N1 or S_N2. In this module, we are focusing on substitution reactions in which the leaving group is a halogen ion, although many reactions are known, both in the laboratory and in biochemical processes, in which the leaving group is something other than a halogen.

In order to understand the nature of the leaving group, it is important to first discuss factors that help determine whether a species will be a strong base or weak base. If you remember from general chemistry, a Lewis base is defined as a species that donates a pair of electrons to form a covalent bond. The factors that will determine whether a species wants to share its electrons or not include electronegativity, size, and resonance.

As Electronegativity Increases, Basicity Decreases: In general, if we move from the left of the periodic table to the right of the periodic table as shown in the diagram below, electronegativity increases. As electronegativity increases, basicity will decrease, meaning a species will be less likely to act as base; that is, the species will be less likely to share its electrons.



As Size Increases, Basicity Decreases: In general, if we move from the top of the periodic table to the bottom of the periodic table as shown in the diagram below, the size of an atom will increase. As size increases, basicity will decrease, meaning a species will be less likely to act as a base; that is, the species will be less likely to share its electrons.

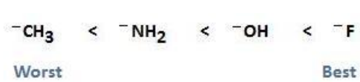


Resonance Decreases Basicity: The third factor to consider in determining whether or not a species will be a strong or weak base is resonance. As you may remember from general chemistry, the formation of a resonance stabilized structure results in a species that is less willing to share its electrons. Since strong bases, by definition, want to share their electrons, resonance stabilized structures are weak bases.Edit section

Now that we understand how electronegativity, size, and resonance affect basicity, we can combine these concepts with the fact that weak bases make the best leaving groups. Think about why this might be true. In order for a leaving group to leave, it must be able to accept electrons. A strong bases wants to donate electrons; therefore, the leaving group must be a weak base. We will now revisit electronegativity, size, and resonance, moving our focus to the leaving group, as well providing actual examples.

> **Note**
>
> As the Electronegativity of the group *Increases*, The propensity of the Leaving Group to Leave *Increases*

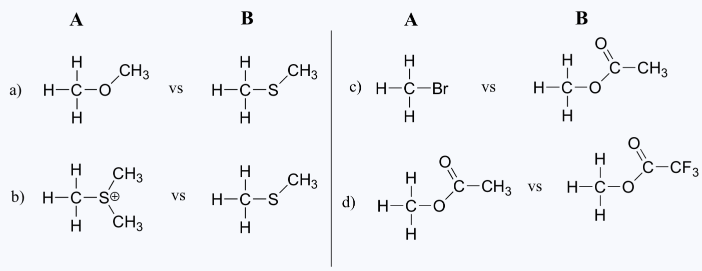
As mentioned previously, if we move from left to right on the periodic table, electronegativity increases. With an increase in electronegativity, basisity decreases, and the ability of the leaving group to leave increases. This is because an increase in electronegativity results in a species that wants to hold onto its electrons rather than donate them. The following diagram illustrates this concept, showing $^-CH_3$ to be the worst leaving group and F^- to be the best leaving group. This particular example should only be used to facilitate your understanding of this concept. In real reaction mechanisms, these groups are not good leaving groups at all. For example, fluoride is such a poor leaving group that S_N2 reactions of fluoroalkanes are rarely observed.



As Size Increases, The Ability of the Leaving Group to Leave Increases: Here we revisit the effect size has on basicity. If we move down the periodic table, size increases. With an increase in size, basicity decreases, and the ability of the leaving group to leave increases. The relationship among the following halogens, unlike the previous example, is true to what we will see in upcoming reaction mechanisms.

Example 7.7.1

In each pair (A and B) below, which electrophile would be expected to react more rapidly in an S_N2 reaction with the thiol group of cysteine as the common nucleophile?



Solution (8.13)

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