INTRODUCTION TO LEWIS ACID-BASE CHEMISTRY

DEFINITIONS

Lewis acids and bases are defined in terms of electron pair transfers. A Lewis base is an electron pair donor, and a Lewis acid is an electron pair acceptor. An organic transformation (the creation of products from reactants) essentially results from a process of breaking bonds and forming new ones. This process basically amounts to electron pair transfers. Ionic mechanisms involve electron pair transfers and are therefore described by the Lewis acid-base theory.

The Lewis definition implies the presence of high electron density centers in Lewis bases, and low electron density centers in Lewis acids. In a reaction between a Lewis acid and a Lewis base the electron pair donated by the base is used to form a new sigma bond to the electron deficient center in the acid. The identification of Lewis bases follows basically the same guidelines as the identification of Bronsted bases. They frequently contain atoms that have nonbonding electrons, or lone pairs. On the other hand, Lewis acids frequently contain atoms with an incomplete octet, a full positive charge, or a partial positive charge.

Water is an example of a Lewis base. Carbocations are examples of Lewis acids. When water reacts with a carbocation as shown below, one of the electron pairs from oxygen is used to form a new sigma bond to the central carbon in the carbocation. As with Bronsted acid-base reactions, curved arrow are used to indicate the movement of electron pairs during the reaction process. The arrow always originates with the Lewis base and moves towards the area of electron deficiency in the Lewis acid.

![Lewis Reaction with Water and Carbocation]

To avoid confusion between the Lewis and the Bronsted definitions of acids and bases, Lewis bases are sometimes called nucleophiles, and Lewis acids are called electrophiles. In the example above, water acts as a nucleophile (donates electrons), and the carbocation acts as an electrophile (receives electrons).

Since Bronsted acids and bases are a subcategory of the more encompassing Lewis definition, it can be said that most Bronsted bases are also nucleophiles, and that the proton is a Lewis acid, or an electrophile. There are however some subtle differences to keep in mind.
**RECOGNIZING NUCLEOPHILES** - For the most part, the same criteria used for identifying Bronsted bases can also be used to identify nucleophiles. Here is a summary.

1. The most common type of nucleophiles are those containing atoms with unshared electron pairs, such as the following.

   \[
   \begin{align*}
   \text{H}_2\text{O} & \quad \Theta \text{OH} \\
   \text{NH}_3 & \quad \Theta \text{H} \\
   \text{RNH}_2 & \quad \Theta \text{CN}
   \end{align*}
   \]

   Notice that nonbonding electrons are frequently omitted from formulas. Always remember their presence on oxygen, nitrogen, and negatively charged carbon atoms.

2. A negatively charged species is usually a stronger nucleophile or base than its neutral analog. Thus, hydroxide ion is stronger, both as a base and as a nucleophile, than water.

3. Carbon bonded to a metal has strong negative character, revealed when writing resonance structures. The carbon atom in such molecules is considered a strong nucleophile. Recall the structures of \(n\)-butyllithium and Grignard (organomagnesium) reagents from previous notes.

4. The pi bond is a region of high electron density. Pi bonds are not as strong as sigma bonds, which means that pi electrons are more available for reactions because pi bonds are more easily broken. Molecules containing pi bonds are considered weak nucleophiles or bases, because they can react with strong acids or electrophiles. See examples under Bronsted acid-base chemistry.

5. Periodic trends in nucleophilicity are such that, other factors being similar, nucleophilicity increases from right to left across the same row, and from top to bottom across the same period or group. Make a note that this trend is different from the basicity trend, which increases in the same way across a row, but from bottom to top within a period.

6. **Basic vs. nucleophilic behavior.** There are some differences between Bronsted bases and nucleophiles. First, the term base is reserved for substances seeking acidic protons, whereas the term nucleophile is used for substances seeking electron-deficient centers, be they protons or other atoms (most commonly carbon).
Second, in acid-base reactions the size (or bulk) of the base seldom matters. In nucleophilic reactions, the size of the nucleophile can be an important (steric) factor. Smaller is more effective. Thus, although the nucleophilic atom in the two species below is the same (oxygen) and they have similar structures, methoxide ion is a more effective nucleophile than t-butoxide ion, even though they are about equally effective as bases. The larger t-butoxide ion has more difficulty reaching an electrophilic center, which is typically a carbon buried at the core of the molecular structure. That is not a problem when it acts as a base because acidic protons usually lie in the periphery of the molecule and are easily accessible.

![Nucleophile diagram]

**RECOGNIZING ELECTROPHILES** - There are two requirements for a molecule to be considered a good electrophile. First, it must contain an electrophilic center or atom. Second, the electrophilic atom must be able to accommodate a new sigma bond. Please keep in mind the difference between electrophile and electrophilic center. The term electrophile refers to the molecule. The term electrophilic center refers to the particular part of the molecule susceptible to nucleophilic attack.

To avoid confusion, the term *substrate* is frequently used in reference to electrophiles. This term denotes a molecule being acted upon by another agent. For example, an enzyme substrate is a molecule being modified by an enzyme. Likewise, an electrophile can be thought of as the substrate of a nucleophile when the latter “attacks” its electrophilic center.

Electrophilic centers are areas of low electron density. Most often they are atoms which (a) contain an incomplete octet, and/or (b) carry a full or a partial positive charge. A partial positive charge can be revealed by writing resonance structures, or by identifying a polar bond.

1. The following are examples of electrophiles containing atoms with incomplete octets:

![Electrophile examples]

proton

Molecules containing group III elements or transition metals

 carbocations
2. These are examples of electrophiles containing atoms with partial positive charges:

![Diagrams of electrophilic atoms](image)

3. Atoms of the second row like oxygen and nitrogen, which are more electronegative than carbon, seldom act as electrophilic centers, even if they carry a positive charge. In that situation they seek to lessen their positive character by sharing the charge with adjacent atoms, causing them to become acidic (protons) or electrophilic (carbon for instance). Resonance structures can reveal this shift of positive charge.

![Resonance structures](image)

The ammonium and hydronium ions are of moderate to high acidity because the highly electronegative oxygen and nitrogen seek to transfer their positive charge to the adjacent proton, making it acidic. In addition, those atoms cannot accommodate another bond without violating the octet rule.

![Additional examples](image)

In addition to making the protons acidic, a positive charge on oxygen can also make the adjacent carbon electrophilic by a similar transfer of positive character. Moreover, the oxygen atom becomes part of a good leaving group, in this case water. The stage is set for either a nucleophilic attack on carbon, or a reaction with a Bronsted base.

![Nucleophilic attack](image)

The reaction with a base (B') is an equilibrium process that normally has a low activation energy and is therefore relatively fast.
The reaction with a nucleophile (Nu⁻) is a kinetic process that normally has a higher activation energy than a proton transfer and is therefore slower. If the nucleophile being used is also a good base, it will prefer to take the proton.

An example of the above is the reaction of protonated \( n \)-butanol with either bromide ion or ammonia. Bromide ion is one of the best nucleophiles, but a weak base. It prefers to act as a nucleophile. Ammonia is a moderately good nucleophile but also a good base. Given the choice, it prefers to act as a base.

\[
\text{protonated } n\text{-butanol} \quad \text{OH}_2^+ \quad \text{Br}^- \quad \text{HBr} \quad \text{n-butanol}
\]

acid-base equilibrium favors the left side because bromide ion is a weak base

Bromide ion is an effective nucleophile, preferring to attack the electrophilic carbon displacing the water

Ammonia is a weak nucleophile and a moderate base. As long as it can act as a base, it will prefer to do so rather than engaging in a higher energy nucleophilic displacement.
4. Unlike their second row counterparts, some electronegative elements of the third row such as sulfur and phosphorus can sometimes act as electrophilic centers due to their larger size and the ability to accommodate a new sigma bond using their $d$-orbitals:

Unlike oxygen, sulfur can be electrophilic because it can accommodate a new sigma bond using its $d$-orbitals without violating the octet rule.

**REATIONS BETWEEN NUCLEOPHILES AND ELECTROPHILES** - As mentioned earlier, a good electrophile must be able to accommodate a new sigma bond between its electrophilic center and the nucleophile. When the electrophilic center is an atom with an incomplete octet, this is no problem.

For electrophiles containing polarized pi bonds such as carbonyl groups, at least one resonance form shows an atom with an incomplete octet.

You can use either resonance structure to write the reaction between the nucleophile and the electrophile. The following are acceptable representations of a nucleophilic attack of hydroxide ion on acetone, but the second one makes it more apparent that the central carbon can take the extra bond.
Sometimes the substrate has an electrophilic atom which is sp$^3$-hybridized and already has a complete octet. In this case there are no pi electrons to displace as the new $\sigma$-bond forms. The nucleophile must displace another group as it bonds to the electrophile. The displaced group is called a leaving group. The leaving group can be displaced only if it leaves as a weak base, because weak bases are stable molecules that can take the electrons with them. In the following example, hydroxide ion is the attacking nucleophile. As it bonds to the sp$^3$ electrophilic carbon, it must displace another group. The leaving group in this case is the bromine atom. It is a good leaving group because it leaves as bromide ion, which is a weak base and can take the electrons with it.

As OH$^-$ attacks, something must leave. Bromine acts as the leaving group here. 

The reverse reaction, however, could not happen. Although bromide is a good nucleophile and methyl alcohol contains an electron deficient center (the carbon bonded to oxygen), the molecule does not contain a good leaving group. Hydroxide ion is a strong base, therefore it cannot be displaced by bromide.
Although the hydroxide ion is not a good leaving group, it is possible to do nucleophilic displacements on alcohols by protonating them with acid first. The protonated hydroxyl group is a potential water molecule, which is a weak base and therefore a good leaving group.

This approach has limitations. The most important is that the nucleophile must be a weak base, or it will prefer to react with the acidic protons. For all practical purposes, the only nucleophiles that can be used in this way are chloride and bromide ions. But this provides a good way to convert alcohols into primary, secondary, or tertiary chlorides and bromides.

Notice that in these case the reverse reaction can happen. Water is a good nucleophile and chloride and bromide are good leaving groups. One must isolate the product as it forms to keep it from reacting with water and go back to alcohol.