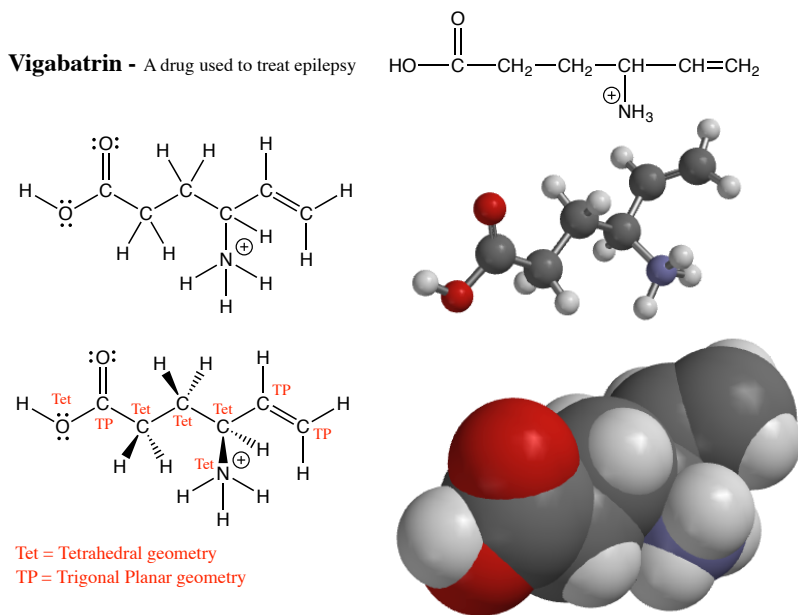


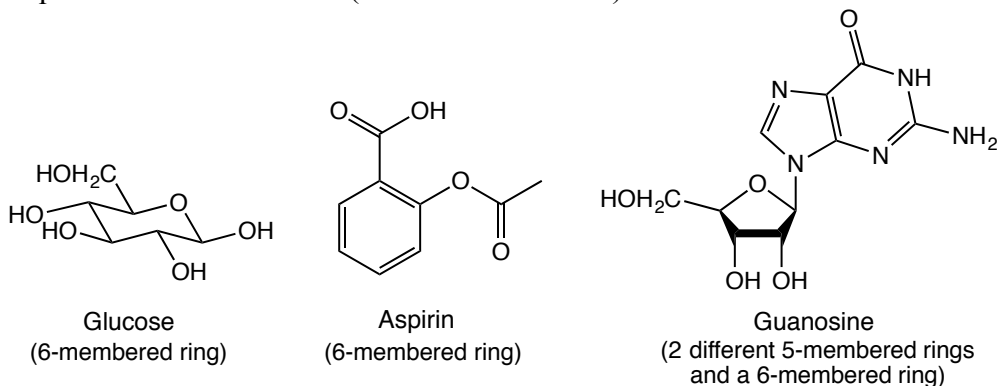
Your goal should be to understand, not memorize, the material presented in your organic chemistry course. The following principles should be learned as you begin your study of organic chemistry, then used as a solid foundation for building your understanding throughout the course. These simple ideas explain a great deal about the structures and properties of organic molecules, as well as the characteristic ways in which they react. Thoroughly understanding the following three key principles and related ideas will allow you to develop an intuitive feel for organic chemistry that avoids the necessity of resorting to the far less effective use of extensive memorization.

### *Predicting Structure and Bonding*

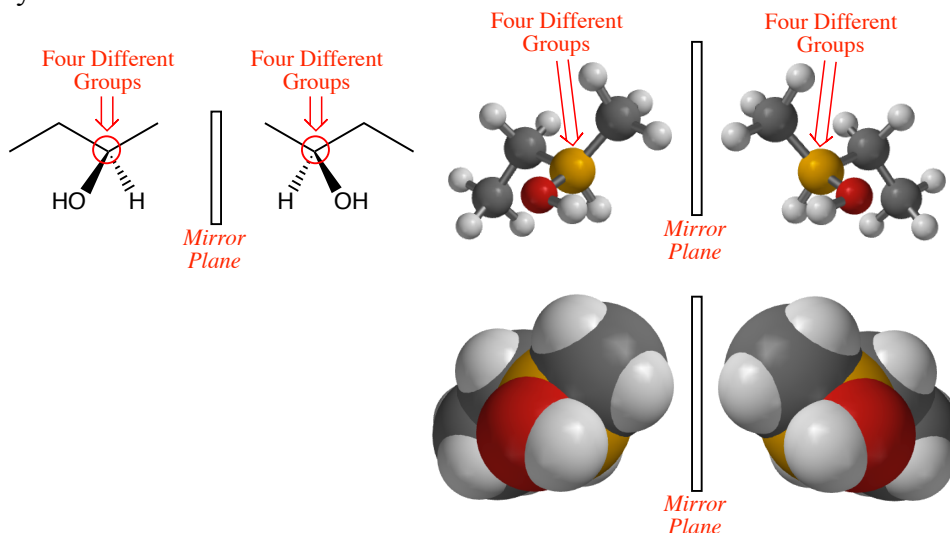
- 1. In most stable molecules, all the atoms will have filled valence shells.** This means that C, N, O and the halogens will have 8 electrons in their valence shells, and H atoms will have 2 electrons in their valence shells. This simple yet powerful principle predicts the type of bonds created (single, double or triple) and how many lone pairs are found around the different atoms of a molecule. In general, an atom surrounded by 4 atoms/lone pairs will have a tetrahedral geometry, an atom surrounded by 3 atoms/lone pairs will have a trigonal planar geometry and an atom surrounded by two atoms/lone pairs will have a linear geometry. You will encounter a small number of molecules containing an atom such as a C atom with only 6 or 7 electrons in its valence shell. Atoms such as this with only a partially filled valence shell are noteworthy and highly reactive. Note, however, that you can *never* overfill the valence shell of any atom in a molecule such as placing *more* than 8 electrons in the valence shells of C, N, or O. Study the structure of the anti-epilepsy drug Vigabatrin below. Each atom is surrounded by a filled valence shell (8 electrons for C,N,O and 2 electrons for H) when all the bonds and lone pairs of electrons are considered. All atoms surrounded by four bonds or lone pairs are tetrahedral in geometry, and atoms surrounded by three bonds (double bonds count once for this) are trigonal planar.



2. **Five- and six-membered rings are the most stable.** Molecules often contain rings of connected atoms, and by far the most common are five- and six-membered rings because the required bond angles for these rings require the least distortion (have the least strain).



3. **There are two possible arrangements of four different groups around a tetrahedral atom.** The two different arrangements are mirror images of each other, a property referred to as chirality and often compared to handedness. Chirality is especially important for the molecules in living systems.



### *Predicting Stability and Properties*

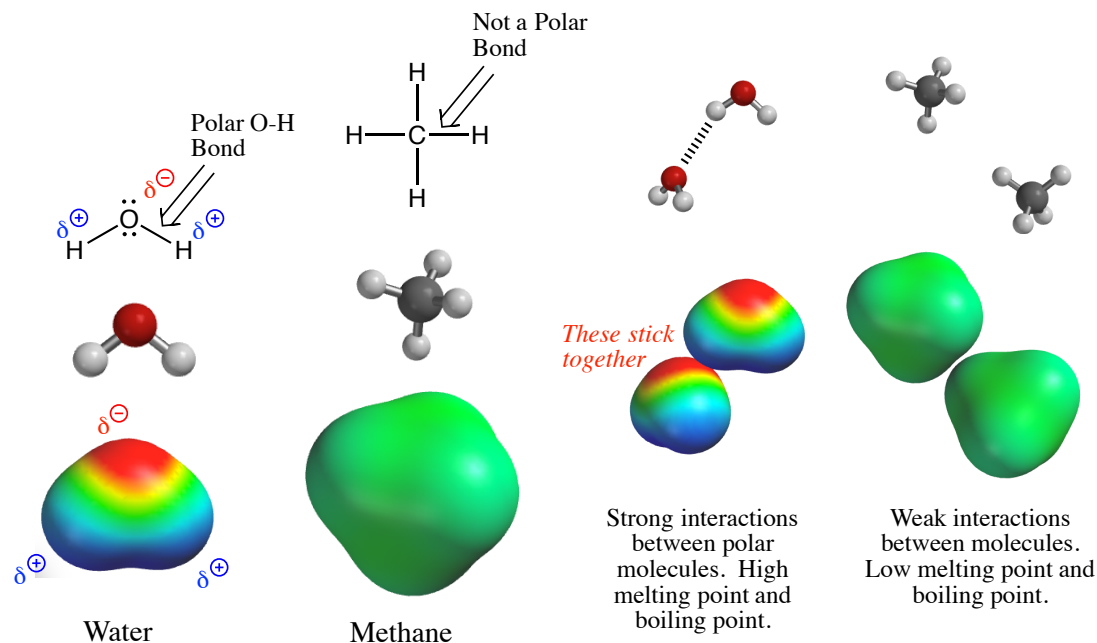
4. **The most important question in organic chemistry is "Where are the electrons?"** The answer is that electrons are generally in higher amounts around the more electronegative atoms (e.g. F, Cl, O, N) of a molecule. The electronegative atoms pull electron density away from the less electronegative atoms (e.g. C, H) to which they are bonded. Thus, understanding electronegativities provides a simple method of deciding which portions of a molecule have a relatively high electron density, and which portions have a relatively low electron density. Molecules with areas of high and low electron

density are referred to as 'polar' molecules. Molecules that have relatively uniform electron densities are referred to as 'nonpolar' molecules.

Electronegativities of the atoms we will normally encounter in organic chemistry:

H = 2.1, C = 2.5, S = 2.5, Br = 2.8, N = 3.0, Cl = 3.0, O = 3.5, F = 4.0

Physical properties such as melting points, boiling points and solubilities can be understood by analyzing distributions of electron density. All things being equal, molecules that are more polar will 'stick' to each other better, increasing both the melting points and boiling points (it takes more energy and thus heat to break apart the interactions between 'sticky' molecules). This is because unequal distributions of electrons in a polar molecule produce corresponding partial charges (remember that electrons are negatively charged), and opposite partial charges attract each other, making the molecules stick together. Nonpolar molecules do not have these partial charges, so they do not stick to each other as well. Also, polar molecules dissolve in polar solvents, again because of the attractions between partial charges on the solvent and the polar molecules. Nonpolar molecules dissolve in nonpolar solvents.



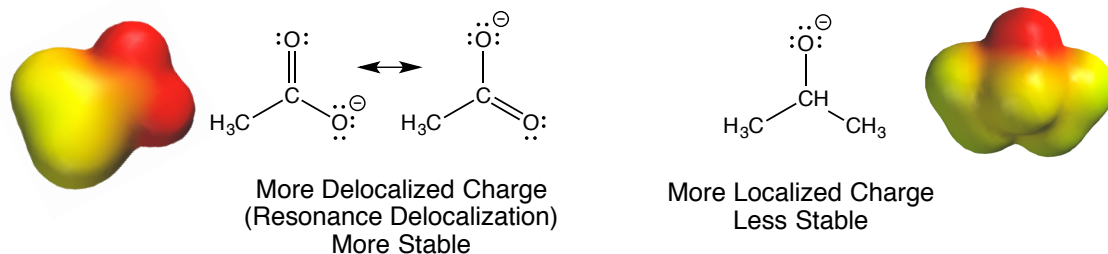
Relative acidities are also understood on the basis of electron distribution. When a molecule loses a proton, it is acting as a Bronsted acid. Because a proton has a positive charge, losing a proton generally leaves a negative charge behind. A molecule will be more willing to give up a proton (i.e. it will be a stronger acid) the better the negative charge can be absorbed after the proton leaves. A molecule can better absorb a negative charge if it has more electronegative atoms that can accommodate the negative charge. Later you will see how important it is to be

able to predict relative acidities of molecules in order to predict important attributes such as relative 'leaving group' abilities.

Finally, and most importantly, understanding where the electrons are located in a molecule allows for the understanding/prediction of reactions. As you will learn, the vast majority of reactions involve the electron rich portions of one molecule or species (the so-called 'nucleophile') reacting with the extremely electron deficient portion of another molecule (the so-called 'electrophile'). Being able to understand and predict reactions, then, comes down to being able to predict the locations of these reactive sites (i.e. where are the electrons?).

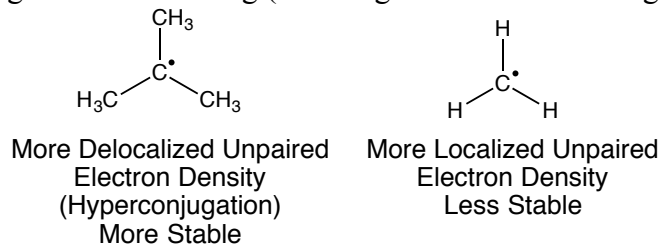
The bottom line. Understanding where electrons are in molecules (i.e. around the more electronegative atoms) allows you to understand/predict physical properties, acidities and reactions of molecules. It is just that simple. In short, you will understand organic chemistry, it will make sense to you, it will be far easier than trying to memorize a bunch of facts and your organic chemistry classes will be enjoyable. O.K., maybe the word 'enjoyable' was a stretch here, but it will be less painful than you are expecting. I guarantee it!

**5. Delocalization of charge over a larger area is stabilizing.** The majority of molecules you will encounter will be neutral, but some carry negative or positive charges because they contain an imbalance in their total number of electrons and protons. In general, charges are destabilizing (higher Gibbs free energy), increasing the reactivity of the molecules that possess them. Localized charges are the most destabilizing (highest Gibbs free energy). Delocalizing the charge over a larger area through interactions such as resonance, inductive effects, and hyperconjugation is stabilizing (lowering the Gibbs free energy). In addition, it is more stabilizing to have more negative charge on a more electronegative atom (e.g. O), and more positive charge on a less electronegative atom (e.g. C).



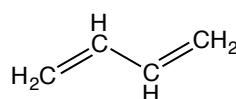
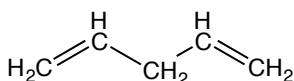
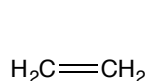
**6. Delocalization of unpaired electron density over a larger area is stabilizing.** The majority of molecules you will encounter will only have atoms with filled valence shells and therefore an even number of electrons. These electrons will have paired spins. However, especially in Chapter 8, you will encounter some molecules with an odd number of valence electrons and therefore an unpaired electron. In general, unpaired electron density is destabilizing (higher Gibbs free energy), dramatically increasing the reactivity of the molecules that possess it. Highly localized unpaired electron density is

the most destabilizing (highest Gibbs free energy). Delocalizing the unpaired electron density over a larger area through interactions such as resonance and hyperconjugation is stabilizing (lowering the Gibbs free energy).



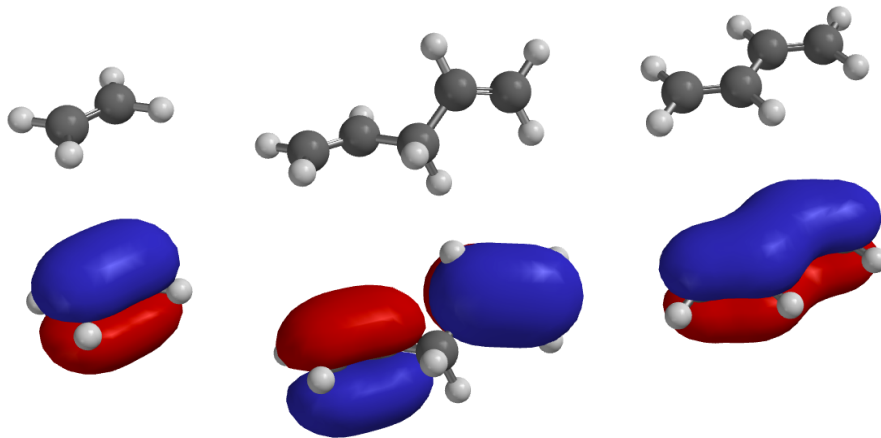
### 7. Delocalization of pi electron density over a larger area is stabilizing. Pi

electron density delocalization occurs through overlapping  $2p$  orbitals, so to take part in pi electron density delocalization atoms must be  $sp^2$  or  $sp$  hybridized and reside in the same plane. Pi electron delocalization can involve even large numbers of such atoms. Pi electron density cannot delocalize onto or through  $sp^3$  hybridized atoms because an  $sp^3$  atom has no  $2p$  orbital. Aromaticity is a special type of pi electron density delocalization involving rings and a specific number of pi electrons, and is the most stabilizing form of pi electron density delocalization.



No Pi Electron Delocalization  
Because  $-\text{CH}_2-$  Group  
Between Pi Bonds. Less  
Stable Pi Bonds.

Pi Electron Delocalization.  
More Stable Pi Bonds.



### *Predicting Reactions*

**8. Reactions will occur if the products are more stable than the reactants and the energy barrier is low enough.** Reactions will be thermodynamically *favorable* if the products are of lower Gibbs free energy than the starting materials, for example, if stronger bonds are made than are broken (enthalpy change is favorable), if a weaker acid or base is formed in the product (enthalpy change is

favorable) or if more molecules are created than consumed (entropy change is favorable). Even if thermodynamically *favorable*, a reaction will only occur if the energy barrier (Gibbs free energy of activation) has no step in the mechanism containing a species of such high energy that it cannot be formed at the temperature being used. Note that steric interactions (unreactive atoms bumping into each other) can prevent otherwise favorable reactions by keeping the reacting atoms away from each other.

**9. Functional groups react the same in different molecules.** Chemists classify groups of atoms that take part in characteristic reactions as functional groups such as –OH groups, carbonyls, haloalkanes or enolates. Although functional groups can influence each other in some complex molecules, functional groups serve as the most generally useful organizing principle in organic chemistry because they mostly react the same in different molecules. Recognizing functional groups and understanding their characteristic reactions are key to being able to predict reactions in molecules you have never seen before.

**10. A reaction mechanism describes the sequence of steps occurring during a reaction.** Gaining an intuitive understanding of reaction mechanisms allows the accurate prediction of products for new reactions, a key goal of any organic chemistry course. Most mechanisms involve combinations of the four elementary steps described as: 1) Make a bond, 2) Break a bond, 3) Add a proton or 4) Take a proton away. Learning how to predict which of these four, or perhaps some other less common elementary step, is appropriate at a given stage in a mechanism requires recognition of the properties of the participating molecules. When writing mechanisms, arrows are used to indicate the redistribution of electrons during each step.

**11. Most bond-making steps in reaction mechanisms involve nucleophiles reacting with electrophiles.** Nucleophiles are molecules that have a lone pair or bond that can donate electrons to make a new covalent bond, usually corresponding to an area of relatively high electron density. Electrophiles contain atoms that can accept the new covalent bond, usually corresponding to areas of relatively low electron density or even an unfilled valence shell. Note that often a covalent bond is broken in the electrophile to make room for the new covalent bond being made (although not in the example below).

