Structure-Reactivity Relationships

A change in structure corresponds to a chemical reaction. **Reactivity** is the term we use to describe the potential of a structure to undergo chemical change. Some structures are more prone to react than others. Structures that are likely to undergo chemical change are said to be **reactive**. Structures that are resistant to chemical change are said to be unreactive. We sometimes choose to speak about the complementary property known as stability. Structures that are highly reactive are generally **unstable**. Structures that are unreactive are generally **stable**.

We want to view molecular structure from the perspective of potential to undergo chemical change. A goal is to establish trends that will allow you to examine a structure and make predictions about its chemical characteristics. Just like a physician diagnoses patients, chemists learn to associate certain features of structure with the tendency to react. From these trends emerge the **structure-reactivity relationships**.

Potential energy (specifically, **chemical potential**) is the link between structure and reactivity. The greater a structure's chemical potential, the greater is its reactivity. Understanding the link between structure and reactivity will help us decide which, among several possible changes, are most reasonable (e.g., pathways having intermediates with exceedingly high energies are not likely to be reasonable and should therefore be avoided, especially if a pathway with lower energy intermediates is available).

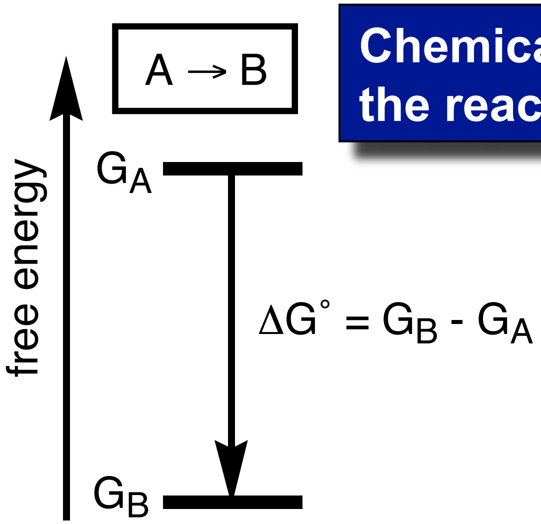
structure ⟺ **chemical potential** ⟺ **reactivity**

Analysis of Chemical Potential

Analysis of Chemical Potential: Chemical potential makes sense in the context of a chemical reaction because we can **compare** what's on the two sides of a reaction arrow (→) and determine the **difference** in chemical potential. By comparing what's on one side with what's on the other, it becomes possible to know if the chemical change is favored or not. Does the left-hand-side or the right-hand-side have greater chemical potential? The favored direction will be from high to low chemical potential.

An analysis of chemical potential can be done for individual elementary steps, or an overall chemical reaction, as the problem demands. The things that contribute to chemical potential - the things that need to be compared - are:

- Bond energy changes
- Strength (reactivity) of electrophiles and /or acids
- Strength (reactivity) of nucleophiles and/or bases



Chemical potential for the reaction A → B

What Factors Contribute to High Chemical Potential?

- Weak bonds
- Low energy LUMO = strong acid (reactive electrophile)
- High energy HOMO = strong base (reactive nucleophile)
- Permanent charges

Factors Contributing to Charge Stability

Charged species are commonly encountered in chemical reactions, either as starting components, end products, or as intermediates and TS$^{\neq}$ along a reaction pathway. **There is considerable energy associated with charged species**; consequently, the relative stability of charged atoms often provides important information about chemical reactivity. The four factors listed below are some of the most important aspects of structure that contribute to charge stability.

(1) Atom type and periodic table trends - The electronegativity and size of charged atoms contribute to its ability to stabilize charge.

(2) Delocalization - All other things being equal, greater charge delocalization leads to greater stability.

(3) Hybridization - All other things being equal, if negative charge is localized on an atom, the greater the s-character of that atom's hybrid orbitals, the greater the stability (for negative charge: sp is more stable than sp^2, which in turn is more stable than sp^3). Conversely, if positive charge is localized on an atom, the lesser the s-character of that atom's hybrid orbitals, the greater the stability (for positive charge: sp^3 is more stable than sp^2, which in turn is more stable than sp).

(4) Coulombic Like charges repel; opposite charges attract.