Chapter 3 - An Introduction to Organic Reactions and Their Mechanisms

3.1 - Reactions and Their Mechanisms
- **Substitutions** are the characteristic reactions of saturated compounds such as alkanes and alkyl halides and of aromatic compounds where one group replaces another.
- **Additions** are characteristic of compounds with multiple bonds where all parts of the adding reagent appear in the product.
- **Eliminations** are the opposite of additions where one molecule loses the elements of another small molecule.
- Eliminations are useful in creating compounds with multiple bonds.
- **Rearrangements** are when a molecule undergoes a reorganization of its constituent parts.
  - In cases where we want to indicate one electron moving (not a pair), we use a one-barbed arrow like the following: →
- **Heterolysis** is when a bond breaks such that one fragment takes away both electrons of the bond.
  - Heterolysis produces ions and is termed an ionic reaction with a broken bond that has been cleaved heterolytically.
- **Homolysis** is when a bond breaks so that each fragment takes away one electron from the bond.
  - Homolysis produces fragments with unpaired electrons known as radicals.
  - Heterolysis requires separation of oppositely charged ions, so it needs some input of energy typically from the addition of a molecule with an unshared pair that can form a bond to one of the atoms.

3.2 - Acid-Base Reactions
- **Brønsted-Lowry acid-base reactions** involve the transfer of protons.
  - A **Brønsted-Lowry acid** is a substance that can donate a proton.
  - A **Brønsted-Lowry base** is a substance that can accept a proton.
  - The molecule or ion that forms when an acid loses its proton is the conjugate base.
  - The molecule or ion that forms when a base accepts a proton is the conjugate acid.
  - The hydronium ion, \( \text{H}_3\text{O}^+ \), is the strongest acid that can exist in water with all stronger acids forming hydronium ions due to the leveling effect.
  - The hydroxide ion, \( \text{OH}^- \), is the strongest base that can exist in water with all stronger bases forming hydroxide ions due to the leveling effect.
  - **Spectator ions** do not play a part in an acid-base reaction.

3.3 - Lewis Acids and Bases
- According to **Lewis acid-base theory**, acids are electron pair acceptors while bases are electron pair donors.
  - By definition, Lewis theory includes Brønsted-Lowry reactions as well as more like electron-deficient atoms and metals such as elements of group IIIA, atoms with vacant orbitals, zinc, and iron(III) halides.

3.4 - Heterolysis of Bonds to Carbon: Carbocations and Carbanions
- A **carbocation** is an ion with a positive charge on the carbon atom while a **carbanion** is an ion with a negatively charge carbon atom.
- Carbocations act as Lewis acids while carbanions act as Lewis bases.
- Carbocations, and all Lewis acids, are **electrophiles**, which means that they are electron-seeking reagents to achieve a full octet.
- Even without a formal charge, a carbon atom can be an electrophile if it is electron poor ($\delta^+$) due to bond polarity.
- Carbanions, and all Lewis bases, are **nucleophiles**, which means they seek a positive center other than a proton, especially that of a positively charged carbon atom.

3.5 - How to Use Curved Arrows in Illustrating Reactions
- A curved arrow points from electrons to the atom receiving the electrons
- As an example, if a curved arrow has its tail at a lone pair of electrons on an oxygen atom of one molecule and the head of the arrow at the hydrogen atom of another second molecule, this means that the hydrogen from the second molecule is going to move to the first molecule and form a bond where the lone pair once was.

3.6 - The Strength of Brønsted-Lowry Acids and Bases: $K_a$ and $pK_a$
- **Acid strength** is characterized in terms of **acidity constant**, $K_a$, or $pK_a$ values
- The generic expression for weak acid in water is $HA + H_2O \rightleftharpoons H_3O^+ + A^-$ with an expression for the acidity constant as $K_a = \frac{[H_3O^+][A^-]}{[HA]}$
- A large $K_a$ value means the acid is a weak acid while a small value means the acid is strong
- The larger the value of $pK_a$, $-\log(K_a)$, the weaker the acid
- The stronger the acid, the weaker its conjugate base
- The larger the $pK_a$ value of the conjugate acid, the stronger the base

3.7 - How to Predict the Outcome of Acid-Base Reactions
- Acid-base reactions, which are under equilibrium control, always favor the formation of the weaker acid and the weaker base
- Some water-insoluble compounds, like amines and carboxylic acids of many carbon atoms, can be dissolved readily in hydrochloric acid or sodium hydroxide, respectively, due to an acid-base reaction.

3.8 - Relationships between Structures and Acidity
- Bond strength to the proton decreases as we move down a group. Therefore, acidity increases as we move down a group.
- Acidity increases from as we go across a period because electronegativity increases in the same fashion
- Having more $s$ character means that the electrons of the anion will, on average, be lower in energy, and the anion will be more stable. Consequently, more $s$ character causes a molecule to be more acidic.
- The **inductive effect**, which weakens with distance from the group, is an electronic effect transmitted through bonds that can be electron donating or electron withdrawing
- Eg: If we have $\text{CH}_3\text{CH}_2\text{F}$, the fluorine will have $\delta^-$. The $\text{CH}_3$ and $\text{CH}_2$ will have $\delta^+$

3.9 - Energy Changes
- Chemical energy is a form of potential energy, and the more potential energy an object has, the less stable it is.
- **Enthalpies**, $H$, represent the relative potential energies of molecules
- The sign for the **enthalpy change**, $\Delta H^\circ$, for **exothermic** reactions is negative while it is positive for **endothermic** reactions
3.10 - The Relationship between the Equilibrium Constant and the Standard Free-Energy Change, $\Delta G^\circ$
- Equation for standard free-energy change: $\Delta G^\circ = -RT \ln (K_{eq})$
- A negative value of $\Delta G^\circ$ is spontaneous while a positive value is nonspontaneous
- The relationship between enthalpy, entropy ($\Delta S^\circ$), and free-energy changes is: $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$
- Exothermic reactions and increases in molecular disorder, entropy, lead to spontaneous reactions

3.11 - The Acidity of Carboxylic Acids
- Carboxylic acids are weak acids while alcohols have negligible acidity
- Carboxylic acids are weakly basic because the carboxylate anion produced is relatively stable due to delocalization of charge from resonance structures as well as an inductive electron-withdrawing effect
- Charge delocalization due to resonance structures always increases stability
- The inductive electron-withdrawing effect for carboxylate anions is due to its two oxygen atoms versus the one oxygen atom of an alkoxide$^1$ anion. The negative charge is distributed through both the electronegative oxygen atoms in the carboxylate anion, but it is only distributed through one oxygen atom in an alcohol thus making the carboxylate anion more stable
- Also, there is an inductive effect in the neural molecule of the carboxylate because the two oxygen atoms create a larger polarized $\text{O}^-$-$\text{H}$ bond, which makes it easier for the $\text{H}$ to dissociate in solution
- The substituent effect is the acid-strengthening effect of other electron-attracting groups
- Any factor that stabilizes the conjugate base of an acid increases the strength of the acid

3.12 - The Effect of the Solvent on Acidity
- A protic solvent is one that has hydrogen bonding
- Solvation of any species decreases the entropy of the solvent because the solvent molecules become much more ordered as they surround the solute ($\Delta S = -$)

3.13 - Organic Compounds as Bases
- The conjugate acid of an alcohol is called a protonated alcohol, alkylxonium ion, or oxonium ion
- Since an atom with an unshared electron pair makes for a basic molecule, many organic molecules go through proton transfer reactions as a first step in a mechanism because of unshared electron pairs on an oxygen or nitrogen atom
- A $\pi$ bond, such as on an alkene, can also create basicity in a molecule in the presence of a strong acid by breaking the $\pi$ bond and taking the proton away from the strong acid
- As seen in the reaction below, the $\pi$ bond is broken, the bond between the proton and the atom, A, is broken, and a bond between a carbon of the alkene and the proton is formed, leaving that carbon with a formal positive charge (unstable carbocation)

\[
\begin{align*}
\text{H} & \quad \text{C} \quad \text{H} \\
\text{H} & \quad \text{C} \quad \text{H} \\
\text{H} & \quad \text{C}+ \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{H} \quad \text{A}^{-}
\end{align*}
\]

3.15 - Acids and Bases in Nonaqueous Solutions
- The leveling effect only applies to aqueous (water as solvent) solutions, so bases and acids stronger than the hydroxide anion and hydronium cation, respectively, can be created if a different solvent is used
- Terminal alkynes are alkynes with a proton attached to a triple bonded carbon

$^1$The anion of an alcohol
3.14 - A Mechanism for an Organic Reaction

3.16 - Acid-Base Reactions and the Synthesis of Deuterium- and Tritium-Labeled Compounds

- Using deuterium (²H) or tritium (³H) in an organic molecule is useful to label particular hydrogen atoms.
- If a very strong base is reacted with D₂O or T₂O, a good example being NH₂⁻, an acid-base reaction can occur to add the hydrogen isotope to the organic molecule (as well as OD⁻ or OT⁻).

Example: Note that C⁻ is a carbon atom with a lone pair. Both reactions occur in liquid NH₃.

Step 1: CH₃C≡CH + NH₂⁻ → CH₃C≡C⁻ + NH₃
Step 2: CH₃C≡C⁻ + D₂O → CH₃C≡CD + OD⁻

Systematic Approach to Acids and Bases

Factors Affecting Acidity (in decreasing significance): Acronym - ARIO (Atom-Resonance-Induction- Orbital)

- Factor 1 - What atom the charge is on for the conjugate base. Use periodic trends mentioned earlier.
- Factor 2 - Resonance structures. The more delocalized the better since charges will be spread over more atoms. However, one oxygen is better than many carbon atoms.
- Factor 3 - Inductive effect. Many electronegative atoms that pull electron density create more stable anions and thus more acidic molecules. However, if there are many alkyl groups, this is a process called hyperconjugation, and the molecule is less stable.
- Factor 4 - Orbital where the negative charge for the conjugate base is. More s character of a bond to hydrogen makes it more acidic.

Exception: When comparing H–C≡C–H and NH₃, it is true that NH₂⁻ is a more stable conjugate base due to Factor 1, but H–C≡C⁻ is a more stable conjugate base due to Factor 4. In this case, Factor 4 actually prevails, making NH₃ the stronger base.