Nuggets of Knowledge for Chapter 7 – Introduction to Reactions Chem 2310

I. Introduction to Chemical Reactions

What a chemical reaction is

- A chemical reaction involves the making and breaking of chemical bonds to form new compounds.
 - Since chemical bonds are made of shared or transferred electrons, when a chemical reaction occurs, it is the electrons that change. The nucleus is not changed, so the same atoms are present at the beginning and the end. Only the connections between the atoms change.

How to represent chemical reactions

- In order to talk about chemical reactions without using specific examples, we need a way to represent reactions in a general way.
 - For example, we can use this format: $A + B \rightarrow C + D$. A and B are reactants, while C and D are products.

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- In organic chemistry we often use this format: $A \rightarrow C + D$.
 - Sometimes in organic chemistry, we refer to organic reactants as starting materials, and inorganic reactants are reagents. We think of a reagent causing a change to a starting material. In the equation above, A is a starting material, and B is a reagent.

Reversibility of reactions (moved)

• Most reactions are reversible. The reaction can run in the "forward" direction (A + B --> C + D) or in the "backward" direction (C + D --> A + B). This is usually written by drawing equilibrium arrows between the reactants and products. Which direction is forward and which is backward depends on how we have chosen to write it.

Energy diagrams for chemical reactions

- The energy of a reaction can be represented by an energy diagram, in which energy is on the y-axis and time on the x-axis.
 - The energy pathway of a reaction always starts low, goes up to a high point, and goes down again. The high energy point in the middle is called the transition state.
 - Since the bonds that are breaking and being formed are half-way through the process, the transition state is higher in energy than either the products or the reactants.
 - The energy needed to get from the starting materials to the transition state is called the activation energy. Molecules must have this much energy in order to react.

- Enthalpy (H) is the difference between the energy of the reactants and products, and given by H of the products H of the reactants.
 - If the energy of the reactants is lower than the products, then the reaction is endothermic. If the energy of the reactants is higher than the products, then the reaction is exothermic.
 - Endothermic reactions absorb energy, while exothermic reactions give off energy. Endothermic reactions have a positive H, while exothermic reactions have a negative H.
 - The reason for the difference in energy is the energy of the chemical bonds.
 - In an exothermic reaction, stronger bonds which are lower in energy are being formed, so the excess energy is given off.
 - In an endothermic reaction, weaker bonds which are higher in energy are being formed, so additional energy is needed.

How free energy relates to enthalpy (moved)

- H isn't the whole story entropy is involved too
- G comes from a combination of the change in enthalpy and entropy: G = H T S.
 - H is the change in enthalpy, which comes from the energy of the bonds being broken and formed.
 - S is the change in entropy, and can be significant if the number of molecules changes. If the number of molecules increases, the entropy increases, and S is positive.
 - S usually much smaller than H. If the H is near zero (bonds formed and broken are about the same energy), then S can be important.

II. Kinetics of Reactions

- The kinetics of a reaction tells you how fast a reaction occurs; in other words, how many molecules of product are formed per second.
 - This matters because it tells us how long we will have to wait for a reaction to be done, or how fast an undesirable reaction will occur.
- To understand kinetics, we must look at what is happening on the molecular level. In order for a reaction to occur, two molecules must collide so that their orbitals will come close enough to react.

- They must also have the correct orientation; in other words, the right atoms must bump into each other at the right angles.
- They must also have sufficient energy to react; they must have equal to or greater than the activation energy.
- Therefore, anything which affects the frequency of collisions or the energy of the molecules will affect the rate of the reaction.
- The activation energy and orientation are always the same for a given reaction; however the concentration of the reactants and the temperature of the reaction may be changed.
 - The lower the activation energy for a reaction is, the faster the reaction will be.
 - The higher the probability that the molecules will collide with the correct orientation, the faster the reaction will be. The probability factor is represented by A, and has to do with how narrow the acceptable approach angle is.
 - A higher concentration of reactants will cause the reaction to speed up, since it causes more collisions between molecules. Concentration is represented by putting the molecule in brackets [].
 - A higher temperature will cause the reaction to speed up for two reasons: 1) the molecules are moving faster, so there are more collisions, and 2) more molecules have enough energy to overcome the activation energy. Temperature is represented by T.
- The rate law of a reaction is a mathematical expression: rate = $k_r[A]^x[B]^y$.
 - Rate is the number of molecules formed per second.
 - k_r is the rate constant; it is given by the equation $k_r = Ae^{Ea/RT}$. A gives the probability that the molecules will collide at an appropriate angle, while the rest of the equation gives the proportion of molecules with enough energy to react.
 - [A] and [B] are the concentrations of the reactants.
 - X and y give the order of the reaction; by adding the exponents for all reactants, you can get the overall order of the reaction.
- The rate of the reaction can be affected differently by the concentration of different reagents, depending on the role they play in the reaction. These must be determined experimentally, but once they are known, they can be used to help determine how the reaction proceeds.
 - If the mechanism is known it can also be used to determine the order of the reactants. The mechanism gives the individual collisions required for a reaction to be completed.

- In a simple, one-step reaction involving a collision of two molecules, both reactants are first order, and the reaction is second order overall.
 - The rate law would be rate = $k_r [A][B]$.
 - Increasing the concentration of either reactant would increase the rate of the reaction by that same amount.
 - Note that only the concentration of the reactants appears in the rate law; the concentration of products does not affect the rate of the reaction. If the reaction is reversible, then the reverse reaction will have its own rate law, which will include the concentration of its reactants, which were the products of the forward reaction.
- In a reaction with two or more steps, you must determine which step is the slowest, and is therefore rate-limiting. The reactants of this step will be included in the rate law; all others will be 0 order, and not appear in the rate law (anything to the power of 0 = 1).
 - With more than one step, there is often the formation of an unstable intermediate which quickly reacts again to form another product. The formation of the intermediate is often endothermic and rate-limiting.

III. Thermodynamics of Reactions

What thermodynamics tells you

- While kinetics tell you how fast a reaction will go, thermodynamics tell you how far a reaction will go.
 - This is important because we need to know if a desirable reaction is favorable or not, as well as whether undesirable reactions are favorable or not.

What equilibrium is

- If a reaction is reversible, then both the forward and backward reactions are occurring at the same time. If they are allowed enough time, they will reach a state in which they are both occurring at the same rate. This is called equilibrium.
 - When equilibrium is reached, the concentrations of all reactants and products does not change with time.

The Equilibrium Constant

- Since at equilibrium the concentration of products and reactants isn't changing over time, we can use these concentrations to define how far a reaction will go to reach equilibrium.
- The equilibrium constant, K_{eq} , is defined as the concentration of the products over the concentration of the reactants at equilibrium.

- An equilibrium constant greater than 1 (or having a positive exponent) indicates that the forward reaction is more favorable; in other words, there is more of the products at equilibrium than the reactants.
- An equilibrium constant less than 1 (or having a negative exponent) indicates that the backward reaction is more favorable; in other words, there is more of the reactants at equilibrium than the products.
- An equilibrium constant will be the same for a given reaction at a given temperature no matter what concentrations you start with.

Independence of rate and equilibrium constant

- The rate of the reaction and the equilibrium constant are independent.
 - A reaction could have a large equilibrium constant but a slow rate, or a small equilibrium constant but a fast rate.
 - It could also have a large equilibrium constant and a fast rate, or a small equilibrium constant and a slow rate.

Relationship between equilibrium constant and change in free energy

- The equilibrium constant comes from the difference between the free energies of the products and the reactants: G = G(products) G(reactants).
 - The change in free energy is related to the equilibrium constant by the equation $G = -RTlnK_{eq}$.
 - If the free energy of the reactants is lower than the free energy of the products, then G is positive, and the reaction is unfavorable. The natural log of K_{eq} will be negative, and K_{eq} will be less than one.
 - If the free energy of the reactants is higher than the free energy of the products, then G is negative, and the reaction is favorable. The natural log of K_{eq} will be positive, and K_{eq} will be greater than one.

How concentration and activation energy combine to give equal rates

- The equilibrium constant, change in free energy, activation energy of the forward and backward reactions, and the concentrations of the reactants and products are all related.
 - \circ When K_{eq} =1, the free energy of the reactants and products are equal. This means that the activation energy of both reactions is the same, so the forward and backward reactions will proceed at the same rate when the amount of reactants and products are equal.

- \circ When K_{eq} is greater than 1, the free energy of the reactants is higher than the products. This means that the activation energy of the backward reaction is higher than the forward reaction, so it takes a higher concentration of the products to make the reaction rates equal.
- \circ When K_{eq} is less than 1, the free energy of the reactants is lower than the products. This means that the activation energy of the backward reaction is lower than the forward reaction, so it takes a higher concentration of the reactants to make the reaction rates equal.

How systems reach and maintain equilibrium

- If a reaction is not at equilibrium, the concentrations of the reactants and products will cause the rates of the reactions to shift under the equilibrium is reached. This is often known as Le Chatelier's principle: if the equilibrium of a system is disturbed, the system will shift to minimize the change and restore equilibrium.
 - If a reactions starts with all reactants and no products, then at the beginning the forward reaction will be much faster. As the forward reaction causes reactants to be turned into products, the backward reaction will speed up, and the forward reaction will slow down, until they become equal.
 - If a reactant is added to the reaction, the forward reaction will initially increase to create more products, then gradually decrease as the backward reaction decreases until the equilibrium is restored. Overall, both reaction rates would increase. The amount of products would increase, but the amount of other reactants would decrease. A corresponding change would occur if a product were added to the reaction.
 - If a reactant is removed from the reaction, the forward reaction will initially decrease, allowing the backward reaction to create more products, then gradually the forward reaction would increase and the backward reaction decrease until the equilibrium is restored. Overall, both reaction rates would decrease. The amount of products would decrease, but the amount of the other reactants would increase. A corresponding change would occur if a product were removed from the reaction.
 - If one reactant is present in excess, the others will be nearly used up in order to achieve equilibrium.
 - If the K_{eq} is very large or very small, adding or removing a reagent won't have much effect; this is only useful in practice when the K_{eq} is near 1.
 - In a two step reaction, if the K_{eq} of the first reaction is small, but the K_{eq} of the second reaction is large, as soon as any of the intermediate is formed, it will react, effectively removing a product, and causing more to be produced. Eventually all of the reactants will end up as products.

III. Nucleophiles and Electrophiles

Definitions of Acids and Bases

- There are two definitions of acids and bases that are useful in organic chemistry: Lewis acids and bases, and Bronsted-Lowry acids and bases.
 - Lewis acids and bases are defined in terms of electron pairs. A Lewis base is an electron pair donor, while a Lewis acid is an electron pair acceptor.
 - Bronsted-Lowry acids and bases are defined in terms of hydrogen atoms. A Bronsted-Lowry acid is a hydrogen donor, while a Bronsted-Lowry base is a hydrogen acceptor.
 - All Bronsted-Lowry acid/base reactions are also Lewis acid/base reactions. Whenever a base takes a hydrogen from an acid, it does so by donating a pair of electrons to the hydrogen. However, not all Lewis acid/base reactions are Bronsted-Lowry acid/base reactions, since the electron pair can be donated to atoms other than a hydrogen.
 - To avoid confusion, Lewis acids and bases which are not also Bronsted-Lowry acids and bases are generally known by the terms electrophile and nucleophile. We can then reserve the terms acid and base only for Bronsted-Lowry acids and bases.
 - A Lewis acid is an electrophile, because it accepts a pair of electrons; we often say that it is attacked.
 - A Lewis base is a nucleophile, because in donating a pair of electrons, it becomes attached to a new nucleus; we often say that it is the attacker.

Reactions of Nucleophiles and Electrophiles

- There are three general types of Lewis acid/base reactions: association, dissociation, and displacement.
 - In an association, an electron-deficient atom (the electrophile) accepts an electron pair from an atom with a lone pair (the nucleophile), forming a bond between them. Only one arrow is needed to describe the movement of electrons.
 - In a dissociation, a weak bond breaks apart, and the electron pair goes to the more electronegative atom. There are no nucleophiles or electrophiles in this reaction, since there is only one reactant. Only one arrow is needed to describe the movement of electrons.
 - In a displacement, a nucleophile donates a pair of electrons to an electrophile, forming a new bond between them; a bond is also broken on the electrophile to make room for the new bond formed. Two or more arrows are needed to describe the movement of electrons.
- Charge must always be conserved in a reaction.

- Nucleophiles must always have a lone pair of electrons to attack with.
 - They may be negatively charged or neutral. If they are negative, they become neutral after attacking; if they are neutral, they become positive.
- An electrophile must always have either an empty orbital that can be filled, or a bond that can leave to make room for a new one.
 - They may be positive or neutral. If they are positive, they become neutral after being attacked; if they are neutral, the atom that is pushed off becomes negative.

Curved Arrow Notation

- In both Lewis acid/base reactions and Bronsted-Lowry acid/base reactions, the movement of electrons is demonstrated by using curved arrow notation.
 - An arrow begins at an electron pair located on an atom (a lone pair) or in a bond, and goes to the atom where a new bond is being formed or a lone pair is being formed, or to the space where a bond will be (when forming a double bond where a single bond already exists).
 - Arrows describe the motion of electrons, not of atoms. The electrons are what cause a reaction to occur; the atoms just go along for the ride.
 - Arrows are not used for positive or negative charges, either. Charges change based on where the electrons go.
 - \circ There are only three basic things that an electron pair can do:
 - A lone pair can become a bond (between the atom it was on and a new atom).
 - A bond can become a lone pair (it will always go to the more electronegative end of the bond it was in).
 - A bond can pivot to become a new bond (one end will still be attached to the original atom, while the other end is attached to a new atom).
 - Electrons cannot jump from one atom to another atom that they were not previously associated with, leaving the original atom behind.
 - There are two important skills to have when working with curved arrow notation: you must be able to supply the products of a reaction when given the arrows, or supply the arrows when given the products of a reaction.
 - If you are given the products, consider what bonds have been formed, and what lone pairs are new. Move the electrons in such a way as to form these bonds and electron pairs without changing anything else.

- Curved arrow notation can also be used to describe the relationship between resonance structures.
 - The arrows show how electrons "move" to create one resonance structure out of another. However, remember that the electrons are actually spread across both locations, rather than moving.

Strengths of nucleophiles and electrophiles

- There are several principles which can allow us to predict the relative strengths of two nucleophiles.
 - A negatively charged nucleophile is stronger than a neutral nucleophile when the attacking atom is the same element. This is because negatively charged atoms become neutral when then attack, while neutral atoms become positively charged when they attack.
 - If the attacking atom of two nucleophiles are different, but in the same period, the less electronegative atoms is a stronger nucleophile than the more electronegative atom. This is because electronegative atoms hold onto their electrons more strongly, and are not as willing to give them up to form a new bond to another atom.
 - If the attacking atom of two nucleophiles are different, but in the same family, the larger atom is a stronger nucleophile than the smaller atom. This is because the electrons are farther from the nucleus and are therefore easier to donate to form a new bond.
 - If the attacking atom of one nucleophile is more hindered than that of another (and they are the same element), then the unhindered nucleophile is a stronger than the hindered one. This is because the hindered nucleophile is blocked by other atoms in the molecule from reaching the electrophile.
- There are several principles which allow us to predict the relative strengths of two electrophiles.
 - An electrophile with an empty orbital is much stronger than an electrophile with a complete octet. Electron-deficient atoms are highly reactive, but with an electrophile with a complete octet, something must be pushed off in order for the reaction to occur.
 - An electrophile with a weak bond to its leaving group is stronger than an electrophile with a stronger bond to its leaving group. A weaker bond is more easily broken, allowing the bond to the nucleophile to form.
 - An electrophile with a leaving group that is low in energy (for example, stabilized by resonance) is stronger than an electrophile with a leaving group that is higher in energy (in other words, more reactive). The energy of the leaving group contributes to the overall energy of the products, and the higher the energy of the products, the less favorable the reaction.

• An electrophile with a positively charged atom next to the atom being attacked is stronger than an electrophile without this. This is because when the electrophile is attacked, the electrons are pushed onto the positively charged atom, making it neutral, while otherwise it would have to become negative.

V. Bronsted-Lowry Acids and Bases

- Bronsted-Lowry acid/base reactions are usually reversible. When the acid loses its H, it becomes a base, and when the base loses its H, it becomes an acid. An acid base reaction could therefore be represented as follows:
 - \circ H-base₁ + base₂ --> base₁ + H-base₂
 - H-base₁ and H-base₂ are the acids, while base₁ and base₂ are the bases. In effect, the reaction is like two bases passing a H back and forth.
 - Each molecule in its acid and base form is called a conjugate acid base pair. H-base₁ is the conjugate acid of base₁, and base₁ is the conjugate base of H-base₁.
- A compound that can act as an acid or a base is said to be amphoteric. It must have a pair of electrons with which to attack a H, as well as a H that can be removed.
 - Water, bicarbonate, ammonia, alcohols, amines, ketones, and carboxylic acids are examples of amphoteric compounds we will encounter.

<u>Mechanisms</u>

• The mechanism of a reaction is a series of individual Lewis or Bronsted-Lowry acid/base reaction steps which show how the electrons move to accomplish the changes that occur. Some reactions take place in only one step, while others may have up to 8 steps.

Using pKa's to determine acid and base strength

- The strength of an acid is measured by its pKa.
 - The pKa of an acid is equal to the negative logarithm of the Ka, the equilibrium constant for the reaction of the acid with water:
 - acid/base reaction: acid + H₂O --> conjugate base + H₃O⁺
 - equilibrium equation: $Ka = [base] [H_3O^+] / [acid]$
 - definition of pKa: pKa = -logKa

- The negative sign is used because most Ka's are very small, making the exponent negative in most cases. The log is used because Ka's occupy such a large scale that it is simpler to look at the exponent (Ka = 10^{pKa}).
- The larger the pKa, the weaker the acid.
 - A large pKa means that the Ka is a large, negative exponent, indicating that the reaction of the acid with water is very unfavorable. This means that the acid is very weak.
 - As the pKa decreases, the reaction of the acid with the water becomes less unfavorable, and the acid is somewhat stronger.
 - If the pKa is negative, this means that Ka is a positive exponent, indicating that the reaction of the acid with water is favorable. This means that the acid is very strong.
- The strength of a base is measured by looking at its conjugate acid.
 - The stronger an acid is, the weaker its conjugate base will be. Likewise, the weaker an acid is, the stronger its conjugate base will be.
 - On the pKa chart given out in class, the strongest acids are on the top, and the weakest acids are on the bottom. Therefore, the weakest conjugate bases are at the top, and the strongest conjugate acids are at the bottom.

Using pKa's to predict whether an acid/base reaction will be favorable

- The equilibrium constant for an acid/base equilibrium can be determined by looking at the pKa's for the two acids in the reaction.
 - Use the following procedure:
 - Locate the acid on each side of the equation.
 - Determine the pKa of each acid.
 - Compare them to determine which acid is stronger, and which is weaker.
 - The side of the reaction with the weaker acid will be more favorable.
 - The pKa of the acid in the products minus the pKa of the acid in the reactants gives the exponent on the equilibrium constant: $K_{eq} = 10^{pKa(product) pKa(reactant)}$.
 - You can also determine which of the conjugate bases will be weaker or stronger. The stronger base will be on the same side of the equation as the stronger acid.
 - The K_{eq} of the acid/base reaction can be used to determine if a given base is strong enough to deprotonate a given acid, or if an acid is strong enough to protonate a base.
 - The base should have a conjugate acid pKa larger than that of the acid in order to deprotonate it.

• An acid with a pKa smaller than the pKa of the conjugate acid of the base will protonate the base.

Predicting relative acid and base strength

- In addition to using pKa values, there are some underlying reasons why some acids are stronger or weaker than others. These can be used to predict the relative strength of two acids.
 - Electronegativity: The more electronegative an atom is, the more acidic a H will be when attached to it. This is because it is more stable when left with the electron pair when the H is removed.
 - Size: The larger an atom is, the more acidic a H will be when attached to it. This is because the larger the atom the weaker the bond will be.
 - Hybridization: The more "s" character an atom has, the more acidic a H will be when attached to it; sp³ atoms have only $\frac{1}{4}$ s, sp² atoms have $\frac{1}{3}$ s, and sp atoms have $\frac{1}{2}$ s, so acidity will go sp³ < sp² < sp.
 - Electronegative atoms nearby: The presence of an electronegative atom near, but not attached to the H will increase its acidity. The closer the group is, the more of them there are, and the more electronegative the group is, the more acidic the H will be. This is because electronegative atoms draw electrons towards them, stabilizing the negative charge created when the H is removed.
 - Resonance: If the conjugate base has more than one resonance structure, this will increase the acidity of the molecule. Resonance spreads negative charge around, stabilizing the conjugate base.
- These same principles can be used to predict the relative strength of two bases.
 - A more electronegative atom makes a weaker base.
 - A larger atom makes a weaker base.
 - Nearby electronegative atoms make a weaker base.
 - More "s" character makes a weaker base.
 - Resonance stabilization makes a weaker base.