

Nuggets of Knowledge for Chapter 8 – Chemical Reactions II
Chem 2310

I. Substitution, Addition, and Elimination Reactions

- The terms dissociation, association, and displacement are useful for describing what happens to the electrons in an individual step in a mechanism. There are other terms which are most useful for describing the overall result of a reaction.
- In an addition reaction, new atoms are added to a molecule, with loss of a double bond.
 - The new atoms are always next to each other, one on each of the atoms where the double bond was lost.
- In a substitution reaction, a bond to one atom is substituted for a bond to another atom.
 - Substitution reactions always involve a single carbon atom on the starting material – a bond is both lost and gained from that atom.
- In an elimination reaction, atoms are lost from a molecule, and a double bond is left in their place.
 - The atoms are always next to each other, so that the double bond can be formed between them.

II. Oxidation and Reduction Reactions

- In general chemistry, oxidation and reduction are most often defined in terms of loss or gain of electrons (and corresponding increase or decrease in charge). However, this won't work with organic molecules because they can be oxidized or reduced without changing charge. This makes oxidation states very difficult to calculate.
- In organic chemistry, oxidation and reduction are defined by looking at the bonds gained or lost to oxygen and hydrogen.
 - If a compound is oxidized, it gains bond to oxygen and/or loses bonds to hydrogen.
 - Examples include an alkene becoming an epoxide, an alcohol becoming a carboxylic acid, or a diol breaking apart to become two aldehydes (this is also called an oxidative cleavage).
 - If a compound is reduced, it loses bonds to oxygen and/or gains bonds to hydrogen.
 - Examples include an aldehyde becoming an alcohol, or an alkyne becoming an alkene.
- The highest oxidation state of carbon is carbon dioxide, in which it has 4 bonds to oxygen; the lowest oxidation state of carbon is methane, in which it has 4 bonds to hydrogen.

- Atoms other than carbon can sometimes be oxidized or reduced in organic molecules.
 - For example, if a nitro group becomes an amine, it has been reduced.
- Although oxygen is most often used, any other atom which is more electronegative than carbon can also count when deciding if a compound was oxidized or reduced.
 - For example, a alkyl halide becoming an alkane is a reduction.
- Not all reactions are oxidations or reductions. The following are examples where no oxidation or reduction has occurred:
 - the number of bonds to oxygen and hydrogen remain the same
 - one carbon is oxidized but another is reduced at the same time
 - exchange of oxygen for another electronegative atom
 - any acid base reaction (although this fits the definition for reduction with a loss of a bond to hydrogen, there is also a change of charge, which counteracts it)
- It is important for you to learn to recognize oxidizing and reducing agents. These are compounds which cause other molecules to be oxidized or reduced (oxidizing agents are easily reduced, while reducing agents are easily oxidized).
 - Oxidizing agents usually fit one of these two descriptions:
 - a transition metal in a high oxidation state and lots of oxygen atoms; for example, Na_2CrO_4 (sodium dichromate) and KMnO_4 (potassium permanganate)
 - oxygen in a high oxidation state (that is, bonded to itself); for example, H_2O_2 (hydrogen peroxide) or O_3 (ozone)
 - Reducing agents usually fit one of these three descriptions:
 - hydrogen gas (H_2) with some kind of catalyst
 - hydride reagents in which hydrogen is bonded to a group III atom; for example, NaBH_4 (sodium borohydride) or LiAlH_4 (lithium aluminum hydride)
 - metals in an elemental state; for example Na (sodium metal), or Sn (tin)

III. Radical Reactions

- A radical (often called a free radical) is an atom that has an unpaired electron, or a molecule with an atom that has an unpaired electron.

- Radicals are very reactive, since they do not have a complete octet.
- Radicals are also very dangerous when they are formed in the body, because they react with proteins and DNA, and can cause damage to cells. Radicals are thought to be involved in the aging process.
- Radicals are formed by an initiation step. This occurs when a molecule with a weak bond absorbs energy from light or heat and the bond breaks homolytically (one electron goes with each atom).
 - Molecules which typically undergo homolytic cleavage have highly electronegative atoms bonded to each other – for example, oxygen-oxygen bonds, and halogen-halogen bonds.
 - Molecules which can undergo homolytic cleavage must be stored in dark bottles to keep them away from light and in cold places to keep them from heat.
- Carbon radicals do not have high energy bonds that can break homolytically, so they are formed by reacting with radicals made by initiation reactions.
 - Whenever a radical reacts with a stable molecule to form a new radical, this is called a propagation step.
- Carbon radicals can become stable again by a propagation step or a termination step.
 - In a propagation step, the carbon radical reacts with an other stable molecule, taking an atom from it (usually a H).
 - In a termination step, the carbon radical combines with another radical, and a bond is formed between them.
- Termination steps can occur when any of the radicals in the reaction collide and form a bond.
 - Since radicals are so reactive, they are very short lived, and there are not ever many of them in the reaction at the same time. Therefore, a radical is more likely to collide with a stable molecule and undergo propagation than with another radical to undergo termination.
 - Termination steps usually happen at the end of the reaction, when most of the starting materials that the radicals could react with are used up.
- Radical mechanisms consist of three types of steps.
 - An initiation step is needed to get the reaction started.
 - The propagation steps are where the organic starting material reacts and forms products.

- Termination steps are side reactions that slow the reaction down. They produce small amounts of side products that are usually ignored in writing the overall reaction.
- The halogenation of alkanes is an example of a radical reaction.
 - The initiation step is homolytic cleavage of a halogen molecule to form two halogen radicals.
 - There are two propagation steps. In the first, the halogen radical takes a H from the alkane, leaving it as a radical. In the second, the carbon radical takes a halogen atom from a halogen molecule, leaving a halogen radical behind.
 - Possible termination steps involve combining of two halogen radicals, two carbon radicals, or a carbon and a halogen radical.
 - This reaction often does not stop at one substitution reaction. The alkyl halide product can still react with a halogen radical, so usually a mixture of products results.
 - This makes alkane halogenation useful only on an industrial scale, where all of the products can be distilled from each other.
- Many radical reactions (including alkane halogenation) are chain reactions. This is because the radical that is formed by initiation is often reformed by the propagation steps, so that initiation doesn't have to keep happening to keep the reaction running, so the reaction goes on without any more heat or light.
 - Another way to say this is that radical reactions have a high quantum yield – that is, they give a lot of product with only a small amount of light or heat added.
- Radical reactions are much different from reactions of nucleophiles and electrophiles (or acids and bases) because they involve movement of single, unpaired electrons rather than pairs of electrons together.
 - The mechanisms of radical reactions are shown using single-headed arrows to indicate that only a single electron is moving.
- Useful radical reactions are not as common as reactions of nucleophile and electrophiles in organic chemistry – we will study only a few during the semester. They can also be often unwanted reactions that create undesired products in other reactions.

IV. Reactive Intermediates

- In multistep reactions, there are often high energy intermediates. These are molecules which are not stable, but are formed, then quickly react. They are only present for a brief period of time.
 - They can strongly influence the outcome of the reaction because things which stabilize

or destabilize them have a big affect on the pathway the reaction will take.

- There are four types of carbon intermediates that we will encounter: carbocations, carbanions, carbon radicals, and carbenes.
 - Carbocations
 - Carbocations have three bonds and one empty orbital. They have an sp^2 hybridization, and a positive charge. Because of the lack of a complete octet of electrons, carbocations are very unstable and reactive.
 - Carbocations are formed by dissociation and by the reaction of alkenes with acid.
 - Carbocations are stabilized by resonance, and by the presence of other carbons bonded to them because of the overlap of the C-H bonds with the empty p orbital (this is called hyperconjugation).
 - Carbocations with three carbons attached are called tertiary or 3° carbons, and are the most stable.
 - Carbocations with two carbons attached are called secondary or 2° carbocations, and are not as stable, but can form.
 - Carbocations with one carbon attached are called primary or 1° carbocations, and do not usually form.
 - Carbocations with no carbons attached are called methyl carbocations, and do not usually form.
 - Carbocations react as electrophiles in association reactions, or as acids by donating a H from a carbon next to the carbocation. In either case, a new bond is formed which fills the octet of electrons.
 - Carbanions
 - Carbanions have three bonds and a pair of electrons. They may have sp^3 or sp^2 hybridization, and are negatively charged. Because carbon is not a very electronegative atom, carbanions are very reactive.
 - Carbanions are formed when a hydrogen is removed from a carbon atom. Since alkanes are the strongest bases, this cannot be accomplished unless the conjugate base is stabilized in some way. A carbanion may also be formed by a dissociation reaction if there is something to stabilize it.
 - Carbanions are most commonly stabilized by resonance, but may also be stabilized by nearby electronegative atoms.

- Carbanions react as nucleophiles or as bases, forming a new bond with the electron pair to restore the neutral charge.
- Carbon radicals
 - Carbon radicals have three bonds and an unpaired electron. This electron occupies a p orbital, so the radical has an sp^2 hybridization. They do not have a charge. They are highly reactive and unstable because they do not have an octet of electrons.
 - Carbon radicals are formed by reactions with other radicals, typically during propagation steps.
 - Carbon radicals are stabilized by having other carbons attached, and by resonance (the same as carbocations). Unlike carbocations, all carbon radicals of all substitutions can form.
 - Radical stability: $3^\circ > 2^\circ > 1^\circ > \text{methyl}$
 - Carbon radicals react to form other radicals in propagation steps, or by combining with other radicals in termination steps.
- Carbenes
 - Carbenes have two bonds, an empty orbital, and a lone pair of electrons. They have sp^2 hybridization, and they do not have a charge. They are highly reactive because the carbon does not have an octet of electrons.
 - Carbenes are formed by removal of a H by a base, followed by dissociation of a leaving group. Only a few types of molecules are capable of forming carbenes.
 - Carbenes typically have no other carbon groups attached, and are not stabilized by substituents.
 - Carbenes react in electrocyclic reactions in which they are both a nucleophile and an electrophile, most often with carbon-carbon double bonds.

Rearrangements of Carbocations

- Under certain conditions, a carbocation can rearrange to become more stable.
 - Rearrangements will not occur if the new carbocation is equally as stable or less stable than the original. They will only occur if the new carbocation is more stable than the original.
- Only 2° carbocations commonly undergo rearrangements.
 - Primary carbocations rarely undergo rearrangements because they are too unstable to

form in the first place, while tertiary carbocations are already as stable as they can be, so they do not usually undergo rearrangements.

- Secondary carbocations are stable enough to form, but if there is a way for them to rearrange and become tertiary, this can occur.
- There are two ways for a 2° carbocation to become tertiary by undergoing a rearrangement. Both of them involve electrons on a neighboring bond shifting to occupy the empty p orbital, leaving another, more stable one behind. They are called hydride shifts and alkyl shifts.
 - In a hydride shift, a hydrogen moves with its pair of electrons from a tertiary carbon to the carbocation, leaving the positive charge on the tertiary carbon.
 - In an alkyl shift, a carbon group moves with its pair of electrons from a quaternary carbon to the carbocation, leaving the positive charge on the now tertiary carbon.
 - When two possible alkyl groups could shift from a neighboring carbon, the smallest one is the most likely. The most common alkyl shifts are methyl shifts.
 - In both cases, it is the electrons that move, attracted by the positive charge and the empty orbital, carrying the atoms with them.
 - Alkyl and hydride shifts can only occur from a neighboring carbon atom. Electrons cannot leap over intervening carbons to the carbocation.

V. Stereochemistry of Reactions

- The stereochemistry of compounds is important when an existing stereocenter is involved in a reaction, or when one or two new stereocenters are formed by a reaction.
 - When a C=C undergoes a reaction creating two new asymmetric carbons, the carbons were actually already stereocenters, so we will use the term “new asymmetric carbons” for these situations.
- When an existing stereocenter is involved in a reaction (it gains and/or loses bonds), there are three possible outcomes: it may be conserved, inverted, or racemized. Which one will happen depends on the mechanism of the mechanism of the individual reaction.
 - If the stereocenter is conserved, this means that it has the same orientation in the product as it did in the starting material. (This is not very common – usually it happens when two inversions result in a net conservation.)
 - If the stereocenter is inverted, this means that it has the opposite orientation in the product as it did in the starting material. (This is quite common, as displacements usually result in inversion.)
 - If the stereocenter is racemized, this means that a racemic mixture has formed; an equal

number of molecules have the same orientation and opposite orientation in the starting material as in the product. (This is also quite common, and usually happens because of an achiral reactive intermediate such as a carbocation. It results in the loss of optical purity, which is generally bad.)

- If the starting material is racemic, it will be impossible to tell which of these has happened. The starting material must be enantiomerically pure, or at least optically active, for the results to show what happened.
- If the starting material is optically active, but the stereocenter is not involved in the reaction, the stereochemistry is unchanged.
- When one new asymmetric carbon is formed, most often a racemic mixture will result. This is because the two products are enantiomers, and have the same free energy, so the reactions that form them have the same activation energy and the same change in enthalpy. Both enantiomers are formed at the same rate.
- When one new asymmetric carbon is formed, but one enantiomer is favored over another, this is called a stereoselective reaction. There are two ways that this can be accomplished.
 - A chiral, enantiomerically pure reagent may be used. This will cause the activation energy of one reaction to be higher than the other, so that one enantiomer will be formed faster than the other and there will be more of it. This is a major area of research in organic chemistry.
 - You can't usually tell by looking at the structures which enantiomer will be favored; this is usually discovered by experiment.
 - A chiral starting material may be used in which the stereocenter is close to the new asymmetric carbon that will be formed, and affects the reaction. Both the activation energy and change in enthalpy will be different, again resulting in one of the products being formed faster than the other (in this case, they are diastereomers).
 - You can often tell by looking which diastereomer will be favored – it will be the one that is less sterically hindered.
- When two new asymmetric carbons are formed, each stereocenter may be R or S, creating four possible stereoisomers. Depending on the mechanism of the reaction, all four may form, or only two may form:
 - Syn addition – the stereoisomers in which the new substituents are added to the same side are formed, giving a maximum of 2 products.
 - Anti addition – the stereoisomers in which the new substituents are added to the opposite side are formed, giving a maximum of 2 products.
 - Nonselective addition – all possible stereoisomers are formed, giving a maximum of 4 products.