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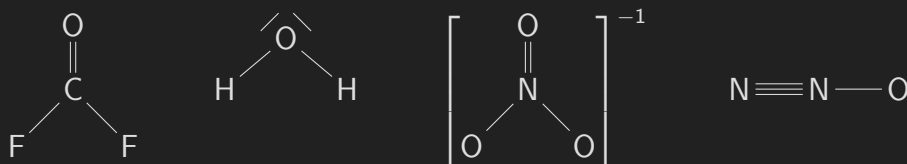
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1 General Chemistry Review

Electrons, Bonds, and Lewis Structures

- ▷ **Covalent bond:** two atoms sharing a pair of electrons.
- ▷ **Octet rule:** *main group elements* that tend to bond in a way that each atom has **eight** electrons in its valence shell.
 - Atoms that do not have eight will share electrons with other elements in order to maintain a stable state.
- ▷ **Main group elements:** sometimes called representative elements, are groups 1, 2 and 13–18 in periodic table.
 - Some elements in group 3 and 12 share properties between transition metals and the main group.
- ▷ The lowest energy (most stable) state of two atoms is determined both by bond length and bond strength.
- ▷ Valence electrons are determined by the group, 1A–8A, of the periodic table.
- ▷ **Lone pair:** unshared, or nonbonding, electrons.
- ▷ **Lewis structures:** 2D model that represents covalent bonds as straight lines and lone pairs as dots.
- ▷ Examples: COF_2 , H_2O , NO_3^- , N_2O :



- ▷ **Resonance structures:** a set of two or more Lewis structures that collectively describe the electronic bonding of a single polyatomic species, including fractional bonds.

Identifying Formal Charges

- **Formal charge:** any atom that does not exhibit the appropriate number of valence electrons.
- Determining formal charge:
 - Formula: $FC = V - N - \frac{B}{2}$
 - V = valence electrons of element
 - N = lone pair electrons
 - B = bonded electrons

- Less than expected number of valence electrons results in a positive charge.
- More than expected number of valence electrons results in a negative charge.
- The lower the magnitude of formal charge, the greater the stability of the whole molecule.
- Atoms that are more electronegative hold negative formal charges better, which results in greater stability vs when the negative charge is spread on less electronegative elements in a polyatomic species.
 - The dominant resonance structure will be that of the greatest stability.

Induction and Polar Covalent Bonds

- ▷ Bonds can be classified into three categories: covalent, polar covalent, and ionic.
- ▷ The categories emerge from the electronegativity values of the atoms sharing a bond.
- ▷ **Electronegativity**: a measure of the ability of an atom to attract electrons.
 - Electronegativity generally increases left to right, and from the bottom to top of the periodic table.
 - F, O, N, Cl (Br, I). Most electronegative elements, from left to right, that are often encountered.
- ▷ **Covalent bond**: when the difference in electronegativity is less than 0.5.
- ▷ **Polar covalent bond**: when the difference in electronegativity is between 0.5 and 1.9, then the electrons are not equally shared and become polar.
- ▷ **Induction**: the withdrawal of electrons towards a more electronegative atom. δ^+ represents partial positive charge gained when electrons are pulled away, while δ^- represents the partial negative charge pulled closer.
- ▷ **Ionic bond**: when the difference in electronegativity is greater than 1.9.
 - Electrons are not shared in this case, and attraction is instead just the result of oppositely charged ions.

Dipole Moments and Molecular Polarity

- **Dipole moment (μ):** defined as the amount of partial charge, δ , on either end of the dipole multiplied by the distance separation, d :
 - $\mu = \delta d$
 - μ generally has an order of magnitude of 10^{-18} esu·cm due to general partial charge (esu) and distance (cm) values.
 - 1 debye (D) = 10^{-18} esu·cm
- **Molecular dipole moment:** the vector sum of the individual dipole moments.
 - Lone pairs have significant effect on the molecular dipole moment.
 - Also called the net dipole moment.

Atomic Orbitals

- ▷ **Atomic orbital (AO):** standing quantum wave (excitation in electron field) around an atom.
 - More energy leads to higher orbitals levels.
 - Gives principle quantum number, n , as is associated with distance from nucleus.
 - Orbital levels: s(1 pair), p(3 pairs), d(5 pairs), f(7 pairs).
 - Angular momentum quantum number that describes three-dimensional region of space that the electron density occupies.
 - Magnetic quantum number describes orientation in space of electron density.
 - $m_l = 0$; s orbital
 - $m_l = -1, 0, 1$; p_x, p_y, p_z orbitals.
 - Locations where ψ (quantum wave function) is zero are called **nodes**.
 - The more nodes that an orbital has, the greater it's energy.
 - *Spin*: allows an orbital to contain only two electrons, $\pm\frac{1}{2}$
- ▷ **Degenerate orbitals:** orbitals with the same energy level.
- ▷ Order in which orbitals are filled is determined by three principles:
 - **Aufbau principle:** lowest energy orbital is filled first.
 - **Pauli exclusion principle:** each orbital can accommodate a maximum of two electrons that have opposite spin.

- **Hund's rule:** electrons are placed in each degenerate orbital before being paired up.
- ▷ Describing the nature of atomic orbital is done with two commonly used theories: *Valence Bond Theory* and *Molecular Orbital Theory*.
- ▷ The commonly used theories give a deeper understanding of covalent bonds, which is essentially just the **overlap of atomic orbitals**.
- ▷ **Constructive/destructive interference:** the result of two waves that approach each other, or overlap.
 - Constructive interference produces a wave with the vector sum of both waves.
 - Destructive interference cancel each other out and produces a node.

Valence Bond Theory

- **Valence bond theory:** the sharing of electron density between two atoms is a result of the constructive interference of their atomic orbitals.
- *Bond axis:* the line that can be drawn between two hydrogen atoms.
- **Sigma bond (σ):** a particular type of covalent bond that has circular symmetry with respect to the bond axis.
 - All single bonds are σ bonds.
 - The strongest type of covalent bond.
- **Pi bond (π):** covalent bonds where two lobes of an orbital overlap with two lobes of another atom.
 - Each atomic orbital has zero electron density at a shared nodal plane, passing through the two bonded nuclei.
 - π bonds form double ($\sigma + \pi$) and triple bonds ($\pi + \sigma + \pi$).
 - Individual π bonds are weaker than σ bonds.

Molecular Orbital Theory

- **Molecular orbital theory (MO):** uses linear combinations of atomic orbitals to model and explore the consequences of orbital overlap.
 - The newly described orbitals are called **molecular orbitals** according to MO theory.
- Atomic orbitals refer to an individual atom, while molecular orbitals is associated with an entire molecule.

- In other words, MO theory states that atomic orbitals cease to exist when they overlap. Instead they are replaced with multiple molecular orbitals which span the entire molecule.
- Molecular orbitals are more stable (lower energy) since electrons are attracted by both nuclei.
- When there are **nodes** between the nuclei, then the resulting σ^* orbitals become **antibonding**, as they **destabilize** (increase the energy) of a molecular orbital.
- Best used to produce a quantitative picture of bonding.
 - Describes strength, order, and polarity of bonds.
 - Allows for the presence of paired or unpaired electrons.
 - Has spectroscopic properties.

Hybridized Atomic Orbitals

- **sp^3 -hybridized orbitals:** produced by averaging one s orbital and **three** p orbitals.
 - Hybridized orbitals explains to geomtry of methane, which results form the **now four degenerate** orbitals pushing apart to achieve tetrahedral geometry.
 - Hybridized orbitals become **unsymmetrical**, producing a larger front lobe that is more efficient than standard p orbitals in the ability to form bonds.
 - All bonds in are **σ bonds**, and thus can be individually represented by the overlap of atomic orbitals.
- **sp^2 -hybridized orbitals:** produced by averaging the s orbital with only **two** of p orbitals.
 - The remaining p orbital is unaffected, and free multiple p orbitals results in a π bond.
 - This is done to expain geometry of compounds bearing a double bond.
 - A double bond if formed from one σ bond and one π bond.
 - Associated with *trigonal planar geometry*.
- **sp -hybridized orbitals:** produced by averaging of one s orbital and **one** p orbital.
 - Leaves two p orbitals and resulting in two π bonds.

- A triple bond is formed with the addition of one σ bond due to the overlap of the sp orbitals.
- Geometry of a triple bond has *linear geometry*.
- Finding the hybridization of any atom can be done simply:
 1. Look at the central item.
 2. Determin groups (number of bonds, π bonds count as 1, and lone pairs attached) of atom.
 - groups aka regions of electron density.
 3. For groups 1-4: sp^x ; $x = \text{groups} - 1$
 4. For groups 5-6: sp^3d^x ; $x = \text{groups} - 4$
- Bond Strength and Bond Length:
 - Bond length **decreases** with more bonds.
 - Bond strength **increases** with more bonds.
 - The more **s character**, the **shorter** and **stronger** the bond, and the **larger** the bond angle.
 - *s-character*: contribution of the σ bond in a hybridization.
 - e.g. $sp = 50\%$, $sp^2 = 33\%$, $sp^3 = 25\%$
 - sp - sp bond is the strongest, sp^3 - sp^3 is the weakest.

Molecular Geometry

- ▷ **Valence shell electron pair repulsion (VSEPR) theory**: enables the **prediction of molecular geometry** due to the presumption that all electron pairs repel each other; resulting in a three-dimensional space that **maximizes distance** from each other.
- ▷ **Steric number**: the total number of electron pairs in a molecule. Can be bonds or lone pairs.
- ▷ **Tetrahedral geometry**: result of four σ bonds and zero lone pairs.
 - produces a tetrahedron with bond angles of 109.5° .
- ▷ **Trigonal pyramidal geometry**: three σ bonds and one lone pair.
 - The lone pair occupy more space than bonded electron pairs, so the remaining angles are slightly less than a tetrahedral, at 107° .
 - The lone pair sits atop the base forming a pyramid like structure.
- ▷ **Bent geometry**: two σ bonds and two lone pairs.
 - VSEPR predicts the lone pairs to be in two corners of the tetrahedral, producing bond angles of 105° .

- VSEPR predicts geometry H₂O correctly, but for wrong reasons.
 - The lone pairs in H₂O have different energy levels, suggesting one pair occupies a *p* orbital with the other in a lower-energy hybridized orbital.
- ▷ VSEPR theory is best used for a first approximation and is mostly accurate for most small molecules.
- ▷ **Trigonal planar geometry:** three electron pairs forming three bond angles of 120° and lie on the same plan.
- ▷ **Linear geometry:** two electron pairs that oppose each other at 180°, forming a linear structure.
- ▷ General method of determining structure:
 1. Count steric number—the total number of electron pairs in a molecule. Can be bonds or lone pairs.
 2. Determine predicted geometrical structure predicted (EDG) by VSEPR using steric number.
 - Octahedral:6, Bipyrmaid:5, Tetrahedral:4, Trigonal:3, Linear:2
 3. Determin impact (the MG) of lone pairs; more lone pairs results in less space between bonded pairs. Shape depends on EDG.

Intermolecular Forces and Physical Properties

- ▷ **Intermolecular forces:** the attractive forces between individual molecules that determed the physical properties of a compound.
- ▷ *Electrostatic:* forces that occur as a result of the attraction between opposite charges.
- ▷ Electrostatic interactions for neutral molecules (no formal charge) are often classified as into the following categories:
 - **Dipole-dipole interaction:** Compounds with **net dipole** moments.
 - In **solid** space these intereactions either **repel or attract** each other.
 - In **liquid** space these interactions tend to **attract more often**, raising melting/boiling point.
 - **Ion-dipole:** electrostatic interaction between an ion and a molecule with a dipole.
 - **Hydrogen bonding:** molecules with a hydrogen attached to an F, O, or N.
 - Not actually a bond, just an interaction.
 - When hydrogen bonds to a electronegative atom, then the hydrogen will have a **δ⁺**.

- Hydrogen bonding is strong due to size of hydrogen atom, resulting in very close partial charge interactions.
- The **more** hydrogen bonds, the **higher** the boiling point tends to be.
- Stronger than dipole-dipole interactions.

○ **Fleeting dipole-dipole interactions:**

- Electrons are considered to be in constant motion, which result in the center of negative charge to vary.
- **London Dispersion Forces (LDFs):** On average, the dipole moment is zero, though it can experience transient dipole moments, initiating fleeting attraction/repulsion.
 - All atoms and molecules have LDFs.
 - Weakest, but the dominant force in non-polar molecules.
 - Dispersion forces directly related to molar mass.
- Heavier hydrocarbons generally experience a stronger force due to increased surface area, and thus greater chance for non-zero dipole moments, which results in higher boiling points.
- Branched hydrocarbons generally have decreased surface area, decreasing boiling point relative to others of similar weight.

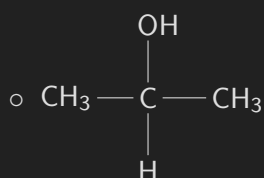
▷ When comparing boiling points of compounds, look for following factors:

- Any dipole-dipole interactions? (increases boiling point)
- Formation of hydrogen bonds? (increase boiling point)
- Number of electrons. (more electrons, higher boiling point)
- Number of carbon atoms. (more surface area, higher boiling point)
- Degree of branching of compound. (more branching, more surface area)

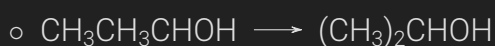
2 Molecular Representations

Types of Molecular Representations

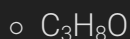
- ▷ **Partially condensed structures:** the C–H bonds are not always drawn, saving space.



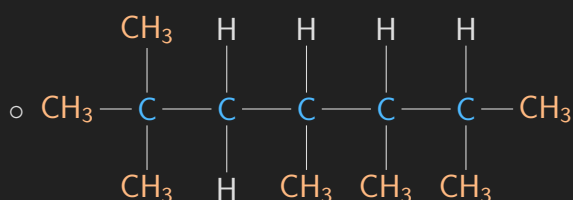
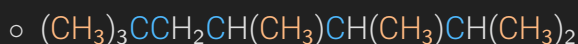
- ▷ **Condensed structures:** single bonds are not drawn and groups of atoms are clustered when possible.



- ▷ **Molecular formula:** simply shows number of each type of atom with no structural information.



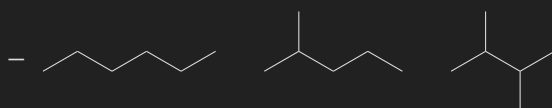
- ▷ Example of converting a condensed structure into a partially condensed structure:



- This shows just one isomer, more partially condensed structures are possible.

Bond-Line Structures

- **Bond-line structures;** aka skeletal structures; simplify drawing process of chemical structures and are easier to read.
- Each corner or endpoint represents a carbon atom.



- All examples have 6 carbon atoms

- Double bonds are shown with two lines, triple with three.

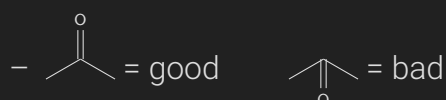


- Triple bonds are drawn linearly due to sp-hybridization

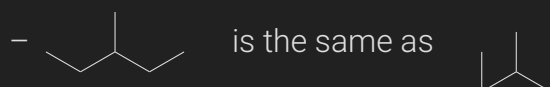
- Hydrogens are not shown; it is assumed that each carbon possesses enough to satisfy octet rule.

Notes on Drawing Bond-Line Structures

- Carbon atoms in a straight chain should be drawn in zigzag format in order to accurately show each carbon.
- Double bonds should be drawn as far apart as possible:



- Direction of a single bond is irrelevant:



- All **heteroatoms** (atoms other than carbon and hydrogen) must be drawn.
 - Hydrogens next to heteroatoms must be shown.
- Carbons cannot have more than four bonds.

Hydrogen Deficiency Index: Degrees of Unsaturation

Excerpt from Chapter 14: Infrared Spectroscopy and Mass Spectrometry

- **Saturated compounds:** the maximum number of hydrogen atoms possible, relative to number of carbon present.
 - Determining saturation using molecular formula: C_nH_{2n+2} n = carbon atoms
 - Halogens:** takes the place of a hydrogen atom; **add one H** for each halogen.
 - Oxygen:** no affect on saturation; **ignore**.
 - Nitrogen:** needs an extra hydrogen; **subtract one H** for each nitrogen.
- **Unsaturated compounds:** a compound that contains at least one π bond, resulting fewer than the maximum number of hydrogen atoms.
 - Compounds with rings also result in an unsaturated compound.
 - Degree of unsaturation:** a number that represents **half** the "missing" number of hydrogen atoms when compared to a saturated compound.
- **Hydrogen deficiency index (HDI):** the measure of degrees of unsaturation.
 - e.g. two degrees of unsaturation results in a HDI of 2.

- Degrees of freedom help represent possible structures, indicating possible double bonds, triple bonds, rings, or various combinations of each.
- Only helpful when molecular formula is known for certainty.
- Formula: $\text{HDI} = \frac{1}{2}(2C + 2 + N - H - X)$
 - X : halogen atoms.

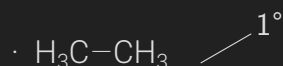
Identifying Functional Groups

- ▷ **Functional group (R)**: specific substituents or moieties within molecules that may be responsible for the characteristic chemical reactions.
 - **Substituents**: an atom or group of atoms which replaces one or more hydrogen atoms on the parent hydrocarbon chain.
 - **Moiety**: a part of a molecule which is typically found within other molecules and often given a specific name.

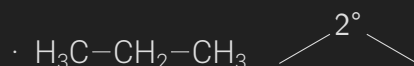
Characterizing Carbon Centers and Functional Groups

Characterizing Carbon Centers

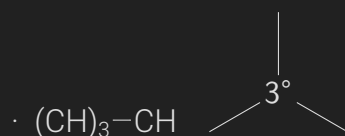
- Primary 1° : a carbon with only one carbon-carbon bond.



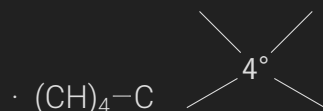
- Secondary 2° : a carbon with two carbon-carbon bonds.



- Tertiary 3° : a carbon with 3 carbon-carbon bonds.



- Quaternary 4° : a carbon with four carbon-carbon bonds.



Characterizing Functional Groups

- Certain functional groups can be characters as 1° , 2° , or 3° , based on how many carbon bonds are attached to the carbon with the functional group.

Identifying Lone Pairs

- ▷ Formal charges must always be drawn on bond line structures, otherwise the resulting bond line structures would be inferred incorrectly.
- ▷ Lone pairs do not have to be drawn and usually are omitted.
- ▷ The formal charge allows you to determine lone pairs.
 - Formula: $FC = V - N - \frac{B}{2}$
 - V = valence electrons of element
 - N = lone pair electrons
 - B = bonded electrons
 - Solve for lone pairs: $N = V - FC - \frac{B}{2}$
- ▷ Frequent usage will allow for intuition for lone pairs.

Common Patterns Between Formal Charge and Lone Pairs

o Associated Patterns for Oxygen

- A **negative** (\ominus) charge corresponds with **1 bond** and **3 lone pairs**.
- The absence of charge corresponds with **2 bonds** and **2 lone pairs**.
- A **positive** (\oplus) charge corresponds with **3 bonds** and **1 lone pair**.

o Associated Patterns for Nitrogen

- A **negative** charge corresponds with **2 bonds** and **2 lone pairs**.
- The absence of charge corresponds with **3 bonds** and **1 lone pair**.
- A **positive** charge corresponds with **4 bonds** and **0 lone pairs**.

Resonance

- ▷ **Resonance:** description of bonding in molecules or ions by the combination of multiple contributing structures.
- o **Resonance structures:** each contributing structure of the resonance hybrid.
 - Formal charges are important to include when drawing resonance structures as it clarifies where locations of lone pairs and movement of electrons.
 - Total charge must remain the same between structures.
- ▷ Resonance does not describe any real process, rather it's a method to overcome inadequacy of bond-line drawings.
- ▷ Different from isomerism, which differs in arrangements of atomic nuclei in space, rather than how the electrons are assigned to the depictions.

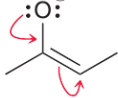

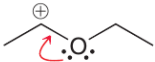


Resonance: Curved Arrows

- o **Curved arrows:** a tool used to help draw resonance structures by **representing electrons as if** they were moving.
 - Somewhat different from curved arrow notation in reactions, which actually represent the flow of electron density.
 - Can help show how to change the formal charge:
 - Formal charges at the **tail** become more **positive**, since it's losing an electron.
 - Formal charges at the **head** more **negative**, since it's gaining an electron.
- o **Avoid breaking a single bond.**

- Structures must have atoms connected in same order, though there are minor exceptions that *will be discussed later*.
- This rule affects the placement of the **tail** of the arrow, as it represents distribution of previous electrons.
- **Never exceed an octet for second-row elements.**
 - Not a violation to have less than an octet.
 - This rule affects the placement of the **head** of the arrow, as it represents sharing of new electrons.
- Can only be used on adjacent atoms, though the electrons can be pushed multiple times.
- "Legal" moves:
 - π bond \rightarrow lone pair.
 - Lone pair $\rightarrow \pi$ bond.
 - π bond $\rightarrow \pi$ bond.
 - Every resonance structure can be built through a combination of above three moves.

Common Patterns of Resonance Structures

- **Vinylic:** the two carbon atoms bearing the double bond of a carbon-carbon double bond.
- **Allylic:** atoms connected directly to vinylic positions.

Allylic lone pair 	Allylic carbocation 	Lone pair adjacent to C+ 	π bond between two atoms of differing electronegativity 	Conjugated π bonds enclosed in a ring 
Two curved arrows	One curved arrow	One curved arrow	One curved arrow	Three curved arrows

Resonance Hybrid

- **Resonance hybrid:** represents the *average* of the contributing structures, with bond lengths and partial charges taking on intermediate values.
- No matter how many resonance structures are drawn, they collectively represent one entity.
- Drawn partial bonds and charges to illustrate the delocalization of electrons.

Delocalization

- **Delocalization:** the spreading of electrons between multiple atoms or covalent bonds.
 - **Resonance stabilization:** molecules and ions that are stabilized by the delocalization of electrons.
 - Plays a major role in the outcome of many reactions.
- with
- When a lone pair participates in resonance, it will occupy a p orbital rather than hybridized; important for 3d shapes of proteins.
- **Localized lone pair:** when a lone pair is not allylic to a π bond.
 - Whenever an atom possesses both a π bond and a lone pair, they will not both participate in resonance.
 - Usually π bonds participate first.

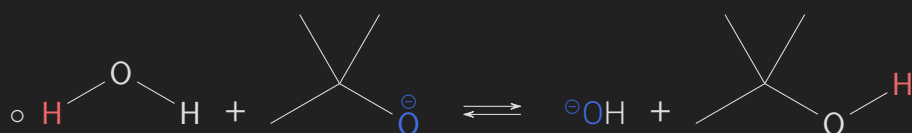
Contributor Significance

- Some resonance structures may resemble the actual molecule more than another, in regards to energy and stability.
- Structures with low potential energy are more stable compared to those of higher values and resemble the actual structure more.
- **Major contributors:** the most stable contributing structures.
- **Minor contributors:** less favorable contributing structures.
- Rules for contributing significance, descending:
 - The greatest number of filled octets.
 - The greatest number of covalent bonds.
 - Minimize formally charged atoms.
 - Separation of unlike and like charges, minimized and maximized respectively.
 - Negative charges placed on the most electronegative atoms, positive charges placed on the less electronegative atoms.
 - Do not deviate substantially from idealized bond lengths and angles.
 - Maintain aromatic substructures locally while avoiding anti-aromatic ones.

3 Acids and Bases

Brønsted-Lowry Acids and Bases

- ▷ **Acid:** a proton donor; i.e., a H^+ donor.
- ▷ **Base:** a proton acceptor; i.e., a OH^- (hydroxide ion), which wants a H^+ to form the more stable H_2O .
- ▷ General definition: acid + base \rightleftharpoons conjugate base + conjugate acid
 - Symbolically: $HA + B \rightleftharpoons A^- + HB^+$
 - The strength of the acid/base is inversely proportional to the strength of the conjugate acid/base.
- ▷ Most acid-base reactions are reversible.
 - Strong acids tend to be less reversible.
- ▷ Example using bond-line structures:



Quantitative Perspective

- **Equilibrium:** when there is no longer an observable change in concentrations of reactants and products.
 - $K_{eq} = \frac{[H_3O^+][A^-]}{[HA][H_2O]}$
 - Water concentration is fairly constant and can be removed, giving K_a .
 - $K_a = K_{eq} [H_2O] = \frac{[H_3O^+][A^-]}{[HA]}$
 - K_a tends to be large, so it's converted to pK_a .
 - $pK_a = -\log K_a$
 - Generally ranges from -10 (strong acid) to 50 (strong base).
 - $pK_a (H^+)$ can be easily converted to $pK_b (OH^-)$:
 - $pK_b = 14 - pK_a$
- Equilibrium favors formation of the weaker (higher pK_a) acid.
 - Reactions with vastly different pK_a values make the reverse process is negligible.
 - Can ignore the reverse reaction in such cases and treat it as a reaction in one direction.

Qualitative Perspective

- Relative acid strength can be determined by comparing conjugate bases.
 - The **more stable** (weaker) the conjugate base, the **stronger** the acid.
 - Does not predict pK_a , just a means of comparing relative acid strengths without known pK_a .
- **Stabilization factors:** (1) **atom bearing the charge**, (2) **resonance**, (3) **induction**, and (4) **orbitals**.
 - Generally follow descending order of significance; absence of difference in earlier factors allow for later factors to express more significance.
- **Atom bearing the charge:** Compare atoms bearing negative charge in each conjugate base after deprotonation.
 - First determine if atoms are in same row or column in the periodic table.
 - **Row comparison:** **electronegativity** is the dominant effect; stability is greater when the negative charge is on the **more electronegative** element.
 - **Column comparison:** **size** is the dominant effect; stability is greater when the negative charge is on the **larger** element.
- **Resonance:** charge that is delocalized across multiple atoms will lead to more stable structures compared to molecules with no resonance.
 - Helps determine relative stability when both molecules have the same elements that have a difference in charge.
 - Again, more stability means it's the weaker conjugate base, meaning the proton removed from the atom creating the resonance hybrid will be more acidic.
- **Induction:** induction of other atoms can act to withdraw the negative charge away from the new electronegatively charged atom due to deprotonation.
 - Inductive effect diminishes the further the electronegative atom is away from the deprotonated atom.
- **Orbitals:** negative charges on atoms with lower hybridization result in greater stability due to proximity to positive nucleus, i.e., $sp > sp^2 > sp^3$
 - sp = triple bond, sp^2 = double bond, sp^3 = three σ bonds.

Lewis Acids and Bases

- ▷ The lewis definition is more broad than the Brønsted-Lowry definition.
- ▷ Lewis describes acidity in terms of **electrons**, rather than protons.
- ▷ **Lewis acid**: electron-pair **acceptor**.
- ▷ **Lewis base**: electron-pair **donor**.
- ▷ All Brønsted-Lowry acids and bases are Lewis acid and bases, but the inverse is not always true.
- ▷ Most reactions are described in terms of lewis base and acids, since molecules without donatable protons are unable to be described by the Brønsted-Lowry definition.

Nucleophiles and Electrophiles

Excerpt from Chapter 6: Chemical Reactivity and Mechanisms ⇨

Mechanisms and Arrow Pushing may also be useful.

- ▷ **Ionic reactions**, aka polar reactions: reactions that involve the participation of ions as reactants, intermediates, or products.
 - Most cases ions act as intermediates.
 - Radical reactions and pericyclic reactions are also major categories, but are typically not discussed in undergraduate courses.
 - Ionic reactions occur when one reactant has a site of **high electron density** and the other reactant has a site of **low electron density**.
- ▷ **Nucleophiles**: an electron rich atom that is capable of donating a pair of electrons.
 - **Lewis bases are nucleophiles**, but not all nucleophiles are lewis bases.
 - Any atom that possesses a localized lone pair can be nucleophilic.
 - π bonds can also function as nucleophiles due to their region of space having high electron density.
- ▷ **Electrophiles**: an electron-deficient atom that is capable of accepting a pair of electrons.
 - **Lewis acids are electrophiles**, but not all electrophiles are lewis acids.

Flow of Electron Density: Curved-Arrow Notation

- ▷ All reactions are accomplished via a flow of electron density.
- ▷ Electron density flow is illustrated with curved arrows.
 - **Reaction mechanism:** how the reaction occurs in terms of the motion
 - All ionic mechanisms, regardless of complexity, are combinations of four characteristic patterns of electron flow (*discussed later*).

Notes on Drawing Curved Arrows

- **Tails** must be placed on either a bond or a lone pair.
 - Shows the **source**, i.e., the electron donor (base).
 - Electrons can only be found in lone pairs or bonds, so **never place the tail** of a curved arrow on a **positive charge**.
- **Heads** must be placed so that it shows either the formation of a bond or the formation of a lone pair.
 - Shows the **destination**, i.e., the electron acceptor (acid).
 - Avoid drawing an arrow that violates the octet rule, so never draw an arrow that gives more than four orbitals to a second-row element.

4 Alkanes and Cycloalkanes

Nomenclature of Alkanes

- ▷ **Alkane:** acyclic (linear structure) saturated hydrocarbons (no π bonds).
 - General chemical formula: C_nH_{2n+2}
- ▷ **Substituents:** branches connected to the parent chain.

Selecting the Parent Chain

- **Parent chain:** the longest carbon chain in an alkane.

Parent Names for Alkanes

Number of Carbons	Parent	Name
1	meth	methane
2	eth	ethane
3	pro	propane
4	but	butane
5	pent	pentane
6	hex	hexane
7	hept	heptane
8	oct	octane
9	non	nonane
10	dec	decane
11	undec	undecane
12	dodec	dodecane
13	tridec	tridecane
14	tetradec	tetradecane
15	pentadec	pentadecane
20	eicos	eicosane
30	triacont	triacontane
40	tetracont	tetracontane
50	pentacont	hectane
100	hect	hectane

- **Substituents:** branches connected to the parent chain, can be a single atom, groups of atoms, that replace one or more hydrogen atoms.
 - If there is competition between chains of **equal length**, then **choose the chain with greatest number of substituents**.
- **Cycloalkanes (cyclo):** presence of a ring in an alkane.

Naming Substituents

- **Alkyl groups:** Substituents that are named the same as the parents, but with the added letters **yl**.


Names of Alkyl Groups

Substituent Carbons	Terminology
1	methyl
2	ethyl
3	propyl
4	butyl
5	pentyl
6	hexyl
7	heptyl
8	octyl
9	nonyl
10	decyl


- When a group is connected to the ring, then the ring is generally treated as the parent.
 - If the ring has fewer atoms than the rest of the structure, then it becomes a substituent.



Naming Complex substituents

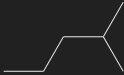

- **Complex substituents:** branched alkyl substituents.
- Begin by numbering carbons going **away** from the parent chain, then name it as if it's a parent chain itself.
 - Complex substituents are placed in parentheses, indicating it as a single substituent of the parent chain.
- Some complex substituents have common names that are so well established and allowed by IUPAC.
 - An alkyl group bearing **three** carbon atoms; only one way to branch it.

· **Isopropyl group:** (1-methylethyl): 

- Alkyl groups bearing **four** carbon atoms, which can be branched three different ways:

· **sec-butyl** (1-methylpropyl): 

- **isobutyl** (2-methylpropyl): 
- **tert-butyl** (1,1-dimethylethyl): 
- Alkyl groups bearing **five** carbons, which can be branched many more ways. Two common ways:

- **isopentyl (isoamyl)** (3-methylbutyl): 
- **neopentyl** (2,2-dimethylpropyl): 

Assembling the Systematic Name

- **Locant:** the location of a carbon numbered parent chain.
- Rules for assigning locant:
 - If one substituent is present, then assign the lowest number possible.
 - When multiple substituents are present, then the first substituent receives the lowest number.
 - If there is a tie, the second locant should be as low as possible.
 - If tie cannot be broken, then lowest number is assigned alphabetically.
 - Prefixes are used when the same substituent appears more than once.
 - di:2, tri:3, tetra:4, penta:5, 6:hexa
 - Hyphens are used to separate numbers from letters, while commas are used to separate numbers from each other.
 - Substituents are alphabeticalized after all locants are correctly assigned.
 - Prefixes are ignored during alphabeticalization.
- Summary of discrete steps:
 1. **Identify parent chain**
 2. **Identify and name substituents**
 3. **Number the parent chain and assign a locant to each substituent**
 4. **Arrange the substituents alphabetically**

Constitutional Isomers of Alkanes

- ▷ For an alkane, the number of possible constitutional isomers increases with increasing molecular size.
- ▷ Determining IUPAC name is the best way to tell if two alkanes are constitutional isomers, or just different representations of the same one.

Constitutional Isomers for Various Alkanes

Molecular Formula	Constitutional Isomers
C_3H_8	1
C_4H_{10}	2
C_5H_{12}	3
C_6H_{14}	5
C_7H_{16}	9
C_8H_{18}	18
C_9H_{20}	35
$C_{10}H_{22}$	75
$C_{15}H_{32}$	4,347
$C_{20}H_{42}$	366,319
$C_{40}H_{82}$	4,111,846,763

Newman Projections

- ▷ **Conformations:** the variety of possible three-dimensional shapes of a molecule that are interchangeable by low energy pathways.
 - Conformations vary in potential energy.
 - Changes due to rotation about σ bonds.
- ▷ **Configurations:** refer to different orientations in space that require breaking of bonds (high energy pathway) to change.
 - Cis and trans isomers in alkenes (*discussed later*)
- ▷ **Newman projections:** a type of representation of compounds specially designed for showing the conformation of a molecule.
 - Drawn from the angle of the observer, with the front carbon represented in front of the circle, and the back carbon behind the circle.
 - ***Chemmacros package is broken due to font usage, need to figure out how to fix that before inserting drawings***

Conformational Analysis of Ethane and Propane

- **dihedral (torsional) angle:** the angle between substituents of front and back carbons as the σ bonds rotates.
- There are an infinite number of possible conformations, but there are conformations of maximum and minimum energy.
 - **Staggered conformation:** **lowest energy** conformation, when two substituents are at maximum dihedral angle from each other.
 - **Eclipsed conformation:** the **highest energy** conformation, when two substituents are at the minimum dihedral angle from each other.
- **Degenerate:** when all staggered conformations have the same amount of energy.
 - All staggered and eclipsed conformations of ethanes are degenerate.
- **Torsional strain:** the difference in energy between staggered and eclipsed conformations.
 - Recent quantum methods suggest conformation possesses a favorable interaction between occupied, bonding molecular orbitals and unoccupied, antibonding molecular orbitals.
 - An increase in potential energy occurs when the favorable overlap is broken.
 - A sample of ethane gas at room temperature will have $\approx 99\%$ of its molecules staggered.
- Ethane has total cost of 12 kJ/mol (4 kJ/mol/H), while propane has total cost of 14 kJ/mol.
 - Reasonable estimates of energy cost of an H eclipsing a CH_3 group must be 6 kJ/mol.

Conformational Analysis of Butane

- Butane has three eclipsed conformations that are **not degenerate**.
 - Dihedral angle of 0° has the highest eclipsed energy, while both conformations at $\pm 120^\circ$ are second highest in energy and degenerate.
 - Likewise, a dihedral angle of 180° has the lowest staggered energy, while both conformations at $\pm 60^\circ$ are second lowest in energy and degenerate.
- **Anti conformation:** the conformation with a dihedral angle of 180° ; the lowest staggered energy.

- Occurs when the methyl groups are farthest apart.
- **Steric interaction:** nonbonding interactions that influence energy levels and conformations.
- **Gauche interaction:** unfavorable interaction between substituents, causing an increase in energy due to electron cloud repulsion.
 - Gauche interaction is a type of steric interaction present at $\pm 60^\circ$ of the next eclipsed conformation.
- Costs of butane: 19 kJ/mol, 16 kJ/mol, 3.8 kJ/mol
 - Energy cost of eclipsing CH_3/CH_3 : 11 kJ/mol
 - Energy cost for gauche interaction of CH_3/CH_3 : 3.8 kJ/mol for butane.
 - Energy cost of eclipsing CH_3/H : 6 kJ/mol
 - Energy cost of eclipsing H/H : 4 kJ/mol

Cycloalkanes

- ▷ **Angle strain:** the increase in energy associated with a bond angle that has deviated from the preferred angle of 109.5° .
 - Cyclic alkanes, except cyclopropane, are **not planar**.
 - Expected angles are different than originally proposed by Adolph von Baeyer, which assumed rings were planar.
 - Angle strain is only one factor that contributes to the energy of various ring sizes.
- ▷ **Cyclopropane:**
 - Under significant angle strain.
 - Locked into an eclipsed conformation due to triangular structure; exhibiting significant torsional strain.
 - Thus highly reactive and very susceptible to ring-opening reactions.
- ▷ **Cyclopentane:**
 - Less angle strain than cyclopropane.
 - More torsional strain than cyclopropane due to four sets of eclipsing hydrogens.
 - Adopts slightly "puckered" shape, which is the cause of reduced angle strain.
- ▷ **Cyclohexane:**
 - Less total strain than both cyclopropane and cyclopentane.
 - Can adopt a relatively low strained conformation.

Conformations of Cyclohexane

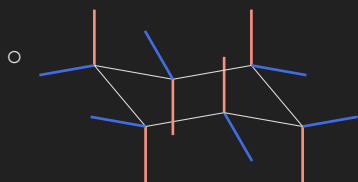
- **Chair conformation:**
 - Bond angles close to 109.5° ; little angle strain.
 - No torsional strain; all hydrogens are staggered.
 - Least potential energy of cyclohexane conformations.
 - **Half-chair:** highest potential energy, formed via interchange between alternate chair form; leads into twisted boat.
- **Boat conformation:**
 - Bond angles also close to 109.5° ; little angle strain.
 - Two sources of torsional strain; many of hydrogens are eclipsed.
 - One hydrogen on each side experiences a steric interaction called the **flagpole interaction**.
 - Second highest potential energy.
 - **Twisted boat:** second lowest potential energy, a slightly less strained version of boat that avoids some of the flagpole interaction.
- Majority of cyclohexanes are found in chair form. All other forms are intermediates between alternate chair forms.

Drawing Chair Conformations



- **Axial position:** parallel to a vertical axis passing through the center of the ring.
 - less stable than equatorial due to steric strain.

- **Equatorial:** positioned approximately along the equator of the ring.



- The chair is more stable when the methyl (substituent) group is in the **equatorial** position.
 - The larger the substituent, the more equatorial-substituted conformer is favored.

5 Stereoisomerism

Overview of Stereoisomerism

- ▷ **Constitutional isomers:** aka structural isomers; same **chemical formula**, but different in the way the **atoms are connect**, i.e. their constitution is different.
- ▷ **Stereoisomers:** isomers that differ in **spatial arrangement** of atoms, rather than connectivity.
 - **Geometric isomerism:** aka cis–trans; **locked into spatial positions** due to double bonds or a ring structure.
 - **Cis:** functional groups that are on the **same side** of the carbon chain.
 - **Trans:** functional groups on **opposite sides** of the carbon chain.
 - *Cis-trans* terminology is used to describe disubstituted alkenes (carbon chain with π bond), even when the the two substituents are different from each other.
 - Does not apply to disubstituted alkenes in which the substituents are connect in the same position.

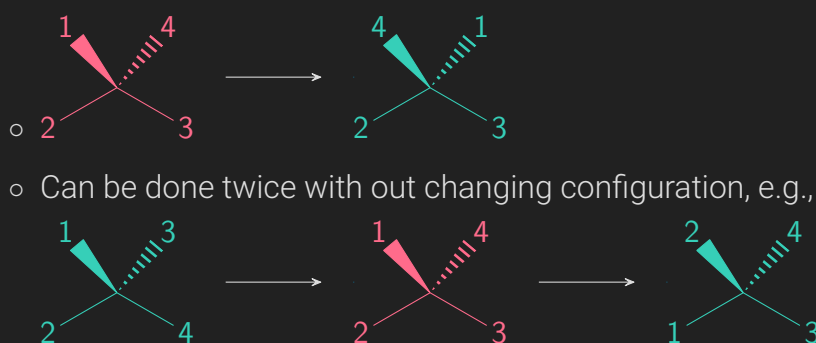
Chirality

- **Superimposable (achiral):** when an an object's mirrored version is identical to the actual object.
- **Chiral:** objects that are not superimposable.
- All three-dimensional objects can be classified as either chiral or achiral.
- **Enantiomer:** the nonsuperimposable mirror image of a chiral compound.
 - Can be used in speech the same way **twin** is used
 - Easiest way to draw enantiomers is to just change wedges and dashes, but there are multiples ways to mirror a molecule, so it can be more complex.
- The most common source of molecular chirality is the presence of a carbon bearing **four different groups**.
 - **Chirality (chiral) center:** a tetrahedral carbon that bears four different groups.
- **Diastereomers:** non-identical stereoisomers (nonsuperimposable) that are **not mirror images** of one another.
 - Enantiomers have the same physical properties, while diastereomers have **different physical properties**.

- Differences between enantiomers and diastereomers are especially relevant when comparing compounds with **more than one chiral center**.
- Maximum number of stereoisomers: 2^n
 - n : number of chiral centers
 - $\frac{2^n}{2}$: pairs of enantiomers.

Cahn-Ingold-Prelog System

- ▷ **Cahn-Ingold-Prelog system:** a system of nomenclature for identifying each enantiomer individually.
 1. Assign priorities to each of the four groups based on atomic number; the highest atomic number has the highest priority.
 2. Rotate the molecule so that the fourth priority group is on a dash (behind)
 3. Determine the configuration, i.e., sequence of 1-2-3 groups.
 - **clockwise (R)** or **counterclockwise (S)**.
- ▷ If there is a tie between the atoms connected, then continue outward until a difference is found.
 - Do not add the sum of all atomic numbers attached to each atom, just the first in which the atoms differ.
 - Any multiple bonded atom, (2 or 3) is treated as if connected to multiple atoms equal to number of bonds.
- ▷ Switching any two groups on a chiral center will invert the configuration, e.g.,



Configuration in IUPAC nomenclature:

- The configuration of the chiral center is indicated at the beginning of the name, italicized, and surrounded by parentheses.
- When multiple centers are present, then each must be preceded by a locant.

Optical Activity

- ▷ Enantiomers exhibit identical physical properties, but different behavior to plane-polarized light.
 - **Polarization**: the orientation of electric field of the electromagnetic wave.
 - **Plane-polarized light**: a filter that only allows light of a particular polarization through.
- ▷ **Optically active**: property of compounds that rotate the plane-polarized light.
 - Can be measured using a polarimeter.
 - Chiral compounds are optically active, while achiral compounds are not optically active.
- ▷ **Observed rotation (α)**: the rotation of light due to chiral compounds, which depends on the number of molecules light encounters.
 - Doubling the concentration or pathlength both double the observed rotation.
- ▷ **Specific rotation $[\alpha]$** : a standard concentration (1 g/mL) and a standard pathlength (1 dm) that allows for meaningful comparison between compounds.
 - $[\alpha] = \frac{\alpha}{cl}$
 - c: concentration, l: pathlength
 - Temperature (T) and wavelength (λ) both have a nonlinear relationship, so it is often noted as: $[\alpha]_{\lambda}^T$
- ▷ Specific rotation for enantiomers are equal in magnitude but opposite in direction.
 - **dextrorotatory**: a compound exhibiting positive rotation.
 - **levorotatory**: a compound exhibiting negative rotation.
 - No direct relationship between R/S system of nomenclature, as that is independent of conditions, but dependent on observation angle.
 - The direction of polarized light, however, is dependent on conditions, and can change based on temperature or wavelength even with the same given configuration.

Enantiomeric Excess

- **Optically (enantiomerically) pure:** a solution containing a single enantiomer.
- **Racemic mixture:** a solution containing equal amounts of both enantiomers, resulting in an optically inactive appearance.
- **Enantiomeric excess (ee):** when a solution containing both enantiomers in unequal amounts, appearing optically active.

$$- \% ee = \frac{|\text{observed } (\alpha)|}{|\text{specific } [\alpha]|} \times 100\%$$

Symmetry and Chirality

- ▷ Any compound with a single chiral center must be chiral, however, the same is not always true for two or more.
- ▷ **Reflectional symmetry:** when an object has a **plane of symmetry** that can be reflected across and still generate the same image.
 - Any compound that possesses a **plane of symmetry** in any conformation will be **achiral**.
- ▷ **Rotational symmetry:** when an object has an **axis of symmetry**, i.e., it can be rotated around a single point and appear 2 or more times.
 - Order: how many times the object appears.
 - Chirality is **not dependent** on rotational symmetry.
- ▷ **Point symmetry (inversion):** when every part of an object has a matching part, i.e., **equal distance** from the **central point**, but in **opposite direction**.
 - Absence of a plane of symmetry does not mean it is chiral.
 - If a compound exhibits **inversion**, then it is **achiral**.
- ▷ Summary of relationship between symmetry and chirality:
 - The presence or absence of rotational symmetry is irrelevant to chirality.
 - A compound that has a plane of symmetry will be achiral.
 - A compound that lacks a plane of symmetry will most likely be chiral, with some exceptions.
- ▷ **Meso compounds:** achiral compounds (possess plane of symmetry or can be inverted) that have multiple chiral centers.
 - A family of stereoisomers containing a meso compound will have less than 2^n stereoisomers.

Fischer Projections

- **Fischer projections:** two-dimensional representations of organic molecules by projection.
 - Limited to carbohydrates/sugars with multiple chiral centers.
- **Horizontal** lines are considered to be coming **out** of the page.
- **Vertical** lines are considered to be going **behind** the page.
- Helpful for quickly comparing relationship between stereoisomers with multiple chiral centers;
 - Enantiomers will have opposite configurations, while diastereomers will not.
 - Assuming the north is priority 2, and the south is priority 3:
 - If the atom with priority 1 is on the **right**, then it will have an **R** configuration.
 - If the atom with priority 1 is on the **left**, then it will have an **S** configuration.

6 Chemical Reactivity and Mechanisms

Enthalpy

- ▷ **Enthalpy**: the sum of the system's internal energy and the product of its pressure and volume.
 - A convenient state function preferred in measurements at constant pressure.
 - **State function (function of state, point function)**: a system relating several state variables (variables of dynamic system) or quantities that depends on the current equilibrium of the system.
 - As a state function, enthalpy depends only on the final configuration, not the path taken to achieve it.
- ▷ $\Delta H = q$ (at constant pressure)
 - ΔH the exchange of kinetic energy, or heat (q).
 - Primary determined by the amount of energy necessary to break the bond **homolytically**.
 - **Homolytic bond cleavage**: generates two radicals (uncharged species), each which bears an unpaired electron.
 - **Heterolytic bond cleavage**: generation of charged species, i.e., ions.
- ▷ **Bond dissociation energy (ΔH°)**: the energy required to break a covalent bond via Homolytic bond cleavage under **standard conditions** (pressure 1 atm and standard state—gas, liquid, or solid).
 - I.e., enthalpy.

Heat of Reaction

- **Heat of reaction**: the total change in enthalpy (ΔH°).
 - The sign indicates the direction in which the energy is exchanged from the **perspective of the system**.
 - A **positive ΔH°** indicates that the system **increased** in energy due to transfer **from the surroundings**.
 - I.e., indicates an **endothermic** process.
 - A **negative ΔH°** indicates that the system **decreased** in energy due to transfer **to the surroundings**.
 - i.e., indicates an **exothermic** process.
 - Physicists think of ΔH° as moving from system \longrightarrow surroundings

- Chemists think of ΔH° as moving from the surroundings \longrightarrow system.
- o Predicting sign and magnitude:
 1. Identify all bonds that are **broken** (gained energy from surroundings) or **formed** (lost energy to the surroundings).
 2. Then find the bond dissociation energies.
 3. Apply the sign to the bonds in respect to the system based on **breakage** (+) or **formation** (-).
 4. Sum to find ΔH° .

Entropy

- ▷ **Entropy**: informally defined as the measure of disorder associated with a system.
 - o Essentially it represents the gradual decline towards disorder since random occurrences resulting order is less ultimately probable than disordered results.
- ▷ **Spontaneous**: a process that involves an **increase in entropy**, which will always occur given enough time.
 - o $\Delta S^\circ = \Delta S_{\text{surr}} + \Delta S_{\text{sys}}$
 - o ΔS° is the total change in entropy associated with the reaction.
 - Sometimes referred to as just S , ΔS , or ΔS_{total}
- ▷ Entropy of the **system (reaction)** can decrease, as long as the entropy of the **surroundings** increases by a greater amount.
- ▷ Thus, ΔS° must be **positive** for a reaction to be spontaneous.
- ▷ A larger number of possible states corresponds with larger entropy.
 - o Acyclic compounds can adopt more conformations, so they have more entropy than cyclic compounds.

Gibbs Free Energy

- ▷ Under constant pressure and temperature, ΔS_{surr} can be measured:
 - $\Delta S_{\text{surr}} = -\frac{\Delta H^\circ}{T}$
 - Both ΔH° and temperature (in Kelvin) can be easily measured, which means ΔS_{surr} can be measured.
 - Applying this definition:

$$\Delta S^\circ = -\frac{\Delta H^\circ}{T} + \Delta S_{\text{sys}}$$

$$-T\Delta S^\circ = \Delta H^\circ - T\Delta S_{\text{sys}}$$

$$\Delta G^\circ = \Delta H^\circ - T\Delta S_{\text{sys}}$$
 - ΔH is then associated with the change in entropy of the surroundings, as a transfer in energy to/from the surroundings from the system increases/decreases entropy of the surroundings.
 - ΔS° is associated with the change of entropy of the system.
- ▷ **Gibbs free energy (ΔG°)**: the maximum amount of non-expansion work that can be extracted from a closed system.
 - Essentially a repackaged way of expressing entropy in a closed system.
 - ΔG° is just ΔS° multiplied by the negative temperature in order to measure the entropy of the surroundings.
 - Thus, ΔG° must be negative for a reaction to be spontaneous. (second law of thermodynamics)
- ▷ Often ΔH° has a much greater contribution than $T\Delta S^\circ$, so enthalpy is commonly an indicator of the spontaneity.
 - When more bond energy is broken ($+\Delta H^\circ$), then the ΔG° is decreased, which increases spontaneity.
 - When more bond energy is formed ($-\Delta H^\circ$), then the ΔG° is increased, which decreases spontaneity.
- ▷ However, temperature has a large influence on the entropy of the system:
 - An **increase in temperature** (endothermic) leads to more bond energy being broken ($+\Delta S_{\text{sys}}$) since energy is transferred from the surroundings ($-\Delta S^\circ$), which is unfavorable, as it increases ΔG° .
 - **Endergonic**: nonspontaneous ($+\Delta G^\circ$) processes.
 - A **decrease in temperature** (exothermic) leads to more bond energy being formed ($-\Delta S_{\text{sys}}$) since energy is transferred to the surroundings ($+\Delta S^\circ$), which is favorable, as it decreases ΔG° .
 - **Exergonic**: spontaneous ($-\Delta G^\circ$) processes.

Equilibria

- ▷ **Reaction quotient** (Q_r , Q_c , Q): a measurement of the relative quantities of products and reactants present in a reaction at a particular point in time.
 - Defined as the ratio of the effective (molar) concentrations of the product over the reactants.
 - General chemical reaction with α moles of reactant A and β moles of reactant B to give ρ moles of product R and σ moles of product S:

$$-\alpha A + \beta B \rightleftharpoons \rho R + \sigma S$$
 - Reaction quotient as a function of time:

$$-Q_r(t) = \frac{R_t^\rho S_t^\sigma}{A_t^\alpha B_t^\beta}$$
- ▷ **Equilibrium constant** (K_{eq} , K^\ominus): a chemical reaction's reaction quotient (Q_r) at chemical equilibrium given sufficient time.
 - $K_{eq} = \frac{R^\rho S^\sigma}{A^\alpha B^\beta} = \frac{\text{products}}{\text{reactants}}$
 - $Q_r = K_{eq}$: the system is at equilibrium.
 - $Q_r < K_{eq}$: more reactants than products—reaction will shift towards the products. (right)
 - $Q_r = 0$: $Q_r \ll K_{eq}$ —reaction will shift towards products.
 - $K_{eq} < Q_r$: more products than reactants—reaction will shift towards the reactants. (left)
 - $Q_r = \infty$: $Q_r \gg K_{eq}$ —reaction will shift towards reactants.
- ▷ The ultimate direction of a reaction is governed by ΔG^\ominus .
 - $\Delta G^\ominus = -RT \ln K_{eq}$
 - R : gas constant 8.314 J/mol·K
 - T : temperature in Kelvin ($C^\ominus + 273.15$).
 - $-\Delta G^\ominus$: the products are favored. ($1 < K_{eq}$)
 - $+\Delta G^\ominus$: the reactants are favored. ($K_{eq} < 1$)
 - A small difference in ΔG^\ominus can have significant impact on the K_{eq} and ultimately determines the yield of products that can be expected from any reaction.
- ▷ The relationship between ΔG^\ominus and equilibrium falls under the realm of thermodynamics, i.e., the study of how energy is distributed under influence of entropy, i.e., the spontaneity/direction of reactions.

Kinetics

- ▷ **Kinetics (reaction kinetics)**: the investigation of experimental conditions that influence the **speed (rate)** of chemical reactions.
 - Spontaneity has nothing to do with the rate of a reaction.
 - Reveals information about *reaction mechanisms* and *transition states*, as well as the construction of models that describe reactions.
- ▷ **Rate equation (general)**: $\text{rate} = k[\text{reactants}]$
 - k : a constant value that is specific to each reaction and dependent on a number of factors, such as, substrate type, physical state, surface area, concentration, temperature, catalysts, pressure, and light absorption.
 - Can be reduces to more general factors: **concentration**, **energy of activation**, **temperature**, and **steric considerations**.
 - Reaction speed is positively correlated with the rate of reaction.
 - The *steric considerations*, or the geometry and orientation, of collisions have an impact as well, and will be discussed later.

Concentration

- Reactions are result of collision between reactants, thus increases concentration should the rate of reactions.
- Precise effect must be determined experimentally:
 - $\text{Rate} = k[A]^x[B]^y$
 - **Rate order**: the sum of exponents of the reactants.
 - E.g., kA = first, kAB = second, kA^2B = third.

Energy of Activation

- **Energy of activation (E_a)**: the energy barrier between reactants and the products.
 - Represents the minimum amount of energy required for a reaction to occur between two reactants that collide.
 - Number of successful interactions depends on the number of molecules that have more than a certain threshold kinetic energy required to form the products.
 - **Catalysts**: a compound that can speed the reaction up without being consumed by lowering the activation energy of a reaction.

Temperature

- Raising the temperature causes the rate of the reaction to increase due to a larger portion of molecules passing the kinetic threshold for the reaction to occur.
- Generally raising the temperature by 10 °C doubles the rate.

Energy Diagrams

- ▷ Kinetics refers to the rate of a reaction, while thermodynamics refers to the equilibrium concentrations of the reactants and products.
- ▷ Different sets of products can be favored from the reactants depending on activation energy, regardless of the stability of the products.
- ▷ Products that require lower activation energy will be favored when environmental potential energy is low.
- ▷ More stable products will be favored when potential energy in the environment is high, or other means at overcoming the larger activation energy are present.
- ▷ Reactions often require multiple steps:
 - **Intermediates:** represent local minima of the reaction.
 - Have a certain, albeit short, lifetime.
 - Very common in reactions and widely observed.
 - **Transition states:** represent local maxima of the reaction.
 - Cannot be isolated.
 - Represents high-energy states where bonds are being simultaneously broken and formed.
- ▷ **Hammond postulate:** states that the transition state of a reaction resembles either the reactants or the products depending on proximity in terms of potential energy.
 - **Endothermic** reactions represent transition states that are closer to the products, since more energy **remains** in the system leaving **less stable** products.
 - **Exothermic** reactions represent transition states that are closer to the reactants, since more energy **leaves** the system leaving **more stable** products.

Mechanisms and Arrow Pushing

- ▷ Previously excerpted section, Nucleophiles and Electrophiles, contains relevant information.
- ▷ There are four distinct characteristic patterns that **make up all ionic mechanisms** through various combinations; nucleophilic attacks, loss of a leaving group, proton transfers, and rearrangements.

Nucleophilic Attack

- When a **nucleophile** (**electron dense atom/lewis base/donator**) attacks (donates electrons) a **electrophile** (**electron lacking/lewis acid/acceptor**).
- Involves just one curved arrow, with tail on the nucleophile and the head on the electrophile.
- Often a nucleophilic attack causes a second **resonance arrow** to be drawn, showing the actual flow of electron density caused by the initial attack.
- π Bonds often serve as nucleophiles, as they are relatively more electron dense compared to nearby σ bonds.

Loss of a Leaving Group

- When a substituent (group) is forced off (leaves) a molecule due to change in electron density.
- Often more than one arrow is drawn, again representing resonance arrows (or changes in electron density), that ultimately force the group to leave.

Proton Transfers

- Previously discussed in terms of Brønsted acid and bases in chapter 3.
- Characterized by two curved arrows due to the combination of a new molecule that causes a compound to be protonated, or deprotonated, transferring the proton to a different atom.
- Sometimes the arrow from the proton is omitted.
- Sometimes there is more than two arrows due to resonance structures that can be created from the change, or again just the flow in electron density.

Rearrangements

- There are several kind of rearrangements, but carbocation rearrangements are focused here.
- **Hyperconjugation:** carbocations that can be stabilized by neighboring groups due to molecular orbitals that slightly overlap with empty p orbitals, placing some of its electron density there.
 - **Primary, secondary, and tertiary:** refer to the number of groups directly attached to the carbocation.
 - Tertiary are the most stable (more slight overlap) and primary are the least (less overlap)
- **Hydride shift:** involves the migration of a H^- .
 - Involves the rearrangement of the carbocation to a more stable variant due to charge migration of the H^- .
- **Methyl shift:** similar to a hydride, except a whole methyl group is migrated instead.
 - The methyl group must be attached to the carbon atom that is adjacent to the carbocation for this to occur.
- Again, there are more, but hydride and methyl shifts are the most common.

Reversible and Irreversible Reaction Arrows

- Reversible arrows can be the result of nucleophilic attacks that leave the nucleophile being capable of a functioning leaving group (weak bases).
 - Non-reversible arrows show the opposite, i.e., poor leaving groups (strong bases).
- Likewise, reversible arrows can show when leaving groups, caused by any means, are capable of functioning as a good nucleophile.
 - Most leaving groups can also function as leaving groups, so most are reversible.
- All protons are technically reversible, however many have very minute reversible reactions.
 - A strong difference in pK_a represents this fact, while a small difference allows for protons to be transferred back and forth.
- Carbocation rearrangements tend to only occur when all possible carbocations are present, which means they are hardly ever reversible.

7 Alkyl Halides: Nucleophilic Substitution and Elimination Reactions

Introduction to Substitution And Elimination Reactions

- ▷ **Alkyl halides:** compounds in which a halogen (Cl, Br, I) is connected to an sp^3 hybridized carbon atom.
 - Alkyl halides are electrophiles since they contain such electron deficient halogens—making them easily accept new electrons.
- ▷ **Substitution reaction:** when a nucleophile replaces a halogen.
- ▷ **Elimination reaction:** when an alkyl halide is treated with a base, allowing for the formation of a π bond, eliminating the halogen.
- ▷ Many reagents (e.g., OH^-) can function either as a nucleophile or as a base, so substitution and elimination often compete with each other.
- ▷ Often the word substrate is used to refer to the alkyl halide since substitution and elimination can occur for a variety of substrates, not just alkyl halides.
- ▷ In an alkyl halide, the halogen serves two critical functions that render the alkyl halide reactive:
 - The halogen withdraws electron density via induction, rendering the adjacent carbon atom electrophilic, and therefore subject to nucleophilic attack.
 - The halogen can serve as the leaving group for the compound, vital for substitution or an elimination to occur.
 - Good leaving groups are conjugate bases of strong acids, i.e., good groups are weak bases.
 - Generally an acid with a $pK_a < 0$ generates a stable enough base to be a good leaving group, which is why F (pK_a of HF is 3.2) is not one, despite being a halogen.
- ▷ The most common leaving groups are halides (I^- , Br^- , and Cl^-) and sulfonate ions (RSO_3^-)

Nomenclature and Uses of Alkyl Halides

- **α position:** the position connected directly next to the halogen.
 - **β position:** positions connected to the α position.
 - As many as 3 β positions; following familiar naming structure of primary (1°), secondary (2°), or tertiary (3°) based on number of β connected to the α position.
- **Naming Alkyl Halides:**
 - Halogens are simply treated as substituents, receiving fluoro-, chloro-, bromo-, and iodo-.
 - **Haloalkane:** formal name for alkane containing a halogen substituent.
 - **Alkyl halide:** the common name that treats the compound as with an alkyl substituent connected to a halide.
 - **Organohalide:** any organic compound containing a halogen, including alkyl halides.
- Many organohalides are toxic and have been used as insecticides.
- Sucralose, which contains three chlorine atoms, is sold under the name of Splenda.
- Organohalides often serve as the synthesis of more complex molecules, especially aryl and vinyl halides (not discussed yet).
- ▷ Early investigation by Ingold and Hughes revealed **concerted**, i.e., simultaneous occurrences of reaction mechanisms (S_N2 , $E2$), and **stepwise**, i.e., one mechanism that allows for a different mechanism(s) to take place (S_N1 , $E1$).

S_N2 Reactions

- ▷ **Kinetics of S_N2 reactions:** a bimolecular (2) nucleophilic (N) substitution (S) reaction.
 - **Bimolecular:** a step that involves two chemical entities, such as when the alkyl halide and nucleophile collide during the substitution reaction mechanism.
 - Occur in a **concerted**, one-step, process.
 - Rate: $v_0 = k[\text{alkyl halide}][\text{nucleophile}]$
 - Second-order rate is means it shows a linear dependent relationship between rate and chemicals; any change in concentrations will have a proportional effect on the rate.

- Nucleophilic strength effects the rate of the reaction, which is effected by: charge, electronegativity, polarizability, resonance stability, and steric hinderance.

Stereospecificity

- **Inversion of configuration:** when an α position is a chiral center, then a change in configuration is generally observed after a reaction takes place.
 - **back-side attack:** a requirement for the inversion to take place; a nucleophile can only attack from the back side opposite to the leaving group.
 - Lone pairs of the leaving group act as regions of high electron density that block the front side of the substrate and thus the nucleophile attack.
 - The incoming electron pair must go through an empty orbital on the back, and cannot go through the occupied orbital in the front.
 - The result is like the chiral center with an umbrella top(filled orbital/halogen) flipping (leaving group) due to the wind (nucleophilic attack) hitting the back (empty orbital).
- **Stereospecific:** when the configuration of the product is dependent on the configuration of the starting material.

Effect of Substrate Structure on Rate

- The rate of an S_N2 reaction is extremely sensitive to the nature of the starting alkyl halide.
 - The presence of substituent the α or β positions can significantly reduce the rate.
- The rate of an S_N2 reaction is more sensitive to the number of substituents at the α position.
 - Methyl halides and primary alkyl halides are the most effective.
 - t-butyl (a tertiary alkyl halide) is unreactive.
- The effect of β substituents is not as great.
 - However it still has noticeable impact; even with just two substituents the rate is moderately reduced.
 - With three substituents the rate is too generally slow to be of any use.

- The more substituents, the more bonds that need to be broken/changed and the more steric interactions there are during the transition state—leading to higher activation energy and thus a slower reaction.

Nucleophilic Strength and Solvent Effects

- **Nucleophilicity:** the rate at which a nucleophile will attack a suitable electrophile.
 - A high rate leads to a relatively fast reaction, while a slow rate leads to a slow one.
 - Generally means a strong nucleophile is required for practical S_N2 reactions.
 - Nucleophilicity decreases as electronegativity increases.
- **Polarizability:** the ability of an atom to distribute its electron density unevenly in response to external influences.
 - Correlated with size of the atom, which increases the number of electrons that are distant from the nucleus.
 - Has a significant effect on nucleophilicity, often more so than degree of negative charge.
 - Another contributing factor that makes fluoride behave as a weak nucleophile.
- S_N2 reactions are generally ionic, as is the leaving group, so polar solvent is required in order to solvate the ionic species.
 - The transition state also often has ionic character, which helps the stability of the state.
- **Protic solvents:** polar solvent that contains a hydrogen atom connected directly to an electronegative atom.
 - E.g., water, methanol (O–H), ethanol (O–H), ammonia (N–H), acetic acid (O–H).
 - Allows for **stabilization of added nucleophiles** in the solution, reducing potential energy and thus a **higher activation energy** for a reaction to take place.
 - S_N2 reactions are generally **slower in protic solvents**.
- **Polar aprotic solvents:** protic solvents lacking a hydrogen atom connected to electronegative atoms.
 - Lack of hydrogen **fails to stabilize added nucleophiles**, leaving compounds with higher potential energy and thus a **lower activation energy** for a reaction to take place.

- S_N2 reactions are generally much faster in polar aprotic solvents.

E2 Reactions

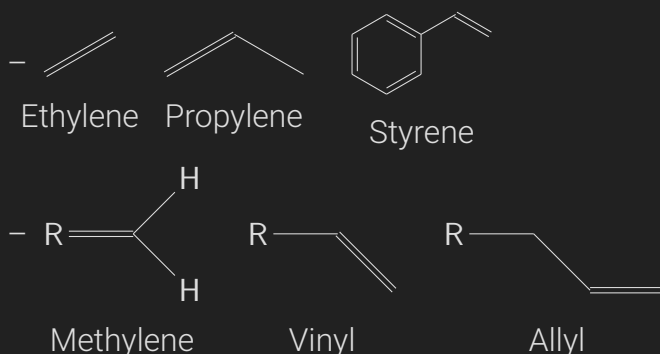
- ▷ Elimination reactions involve the use of bases, rather than nucleophiles (causes substitution).
- ▷ Base strength review:
 - Anionic bases are bases carrying a negative charge.
 - A weak base is stabilized (lower energy), while a strong base is unstable (higher energy).
 - There is inverse relations with pK_a between base stability and acid strength.
- ▷ **Beta elimination (1,2-elimination):** when an alkyl halide is treated with a strong base, causing deprotonation from the β position, ejecting the halide as a leaving group (X^-) from the α position—leaving a π bond to be formed between the α and β positions and forming an alkene.
 - **Dehydrohalogenation:** another name for beta elimination, since H and X are removed from the substrate.
 - I.e., the base accepts a hydrogen (Brønsted base) and the alkyl drops the alkyl in order to form the now needed π bond between carbons.
- ▷ **Kinetics of E2 reaction:** a bimolecular (2) elimination (E) reaction mechanism.
 - *Bimolecular:* a step that involves two chemical entities, such as when the alkyl halide and nucleophile collide during the elimination reaction mechanism.
 - Occur in a concerted, one-step, process.
 - Rate: $v_0 = k[\text{alkyl halide}][\text{base}]$

Substrate Structure Effect on Rate

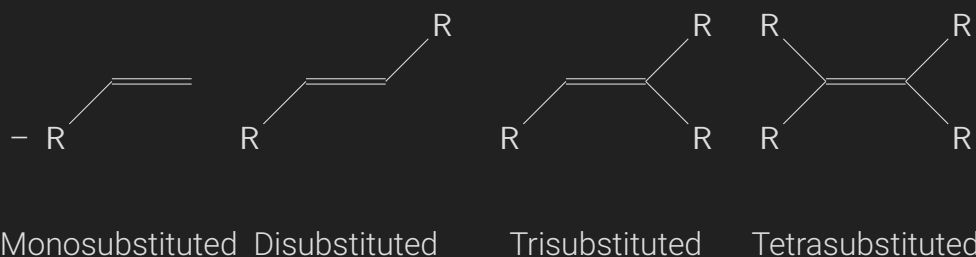
- Unlike S_N2 reactions, steric hindrance has less of an effect on elimination.
 - A substitution reaction occurs when reagent functions as a nucleophile that attacks the α position, while elimination functions as a base and removes a proton from the β position.
 - Thus, the steric hindrance impacts the ability to attack, but not the ability to deprotonate the molecule.

Nomenclature of Alkenes

- Beta elimination results in the formation of alkenes (series of unsaturated hydrocarbons contain a π bond).
- Alkenes are named using the same four steps in the previously used nomenclature, though the suffix of "ane" is replaced with "ene."
- When choosing the parent chain, choose the parent chain that **includes** the π bond.
- When numbering the parent chain, the π bond should receive the **lowest** number possible, **despite the presence of alkyl substituents**.
- The locant of the π bond should be placed right before the suffix of "ene," though, it was previously recommended before the parent (both are acceptable).
- Common recognized names:



- **Degree of substitution:** not substitution reaction, but the **number of alkyl groups** connected to the double bond.



Stability of Alkenes and Cycloalkenes

- In general, a *cis* alkene is **less stable** than its stereoisomeric *trans* alkene.
 - *trans* configurations help reduce steric strain that otherwise would be present in a *cis* alkene.
- Alkenes are **more stable** the greater the degree of substitution that is present.
 - This is due to the electronic through sharing of C–C bonds that allows for greater stability of the electrons compared to C–H bonds.

- Similar to hyperconjugation, which stabilizes through the delocalization of electron density; π bonds have a similar effect on delocalization.
- o Cycloalkenes can only accommodate a π bond in *cis* configuration, and thus cannot accommodate *trans* π bonds.
 - Generally no need to specify configuration when naming.
 - Though, cyclooctene (and other larger rings) can accommodate *trans* π bonds at room temperature.
 - **Bredt's rule**: it is not possible for a bridgehead carbon of a bicyclic system to possess a C=C bond if it involves a *trans* π bond being incorporated in a small ring.

Regioselectivity and Stereospecificity of E2 Reactions

- o **Regiochemistry**: when a chemical reaction is said to produce two different regiochemical outcomes.
 - **Regiochemical**: preference of chemical bonding or breaking **direction**.
- o **Regioselective**: when there is a preference in products of a regiochemical reaction.
- o **Zaitsev product**: name of the more substituted alkene that is generally observed to be the major product.
- o **Hofmann product**: name of the less substituted alkene.
- o The ratio between the Zaitsev and Hofmann product is dependent on a number of factors and often difficult to predict.
 - Steric hindrance of the base often plays a major role, often increasing the Hofmann product.
 - The outcome of E2 reactions can often be carefully **controlled by choosing the base**, despite difficulty in overall prediction.
- o **Stereospecific**: when the stereoisomeric product of the E2 process depends on the configuration of the starting alkyl halide (stereoisomeric substrate).
 - The stereospecificity is only relevant when the **β position has only one proton**.
- o **Stereoselective**: when the substrate itself is not necessarily stereoisomeric, but can yield two stereoisomeric products, one of which that often has a higher yield.
 - Occurs when there are **more than one proton in the β position**.

- **Coplanar**: when the proton in the β position, the leaving group, and the two carbons atoms that form a π bond lie on the same plane.
 - Often leads only one stereoisomer product being formed, thus more often stereospecific.
 - If it stereoselective, than usually *trans* conformation is favored.
 - **Periplanar**: when the proton and leaving group are **nearly** coplanar; often is used in place of coplanar to incorporate both situations.
- **syn-coplanar**: when the proton and the leaving group are **eclipsed** in a coplanar conformation.
 - Elimination in this state involves a higher energy transition state due to eclipsed geometry, and is **slower** than anti-coplanar arrangement.
- **anti-coplanar**: when the proton and the leaving group are **staggered** in a coplanar conformation.
 - Elimination in this state involves a lower energy transition state due to staggered geometry, leading to a **faster** reaction relative to syn-coplanar.

Unimolecular Reactions

- ▷ S_N1 and E2 reactions that are linearly dependent on the concentration of only one compound (the substrate).
 - A first order rate: $v_0 = k[\text{substrate}]$
 - The substrate varies, and can be more than just an alkyl halide, but alkyl halides are very common.
 - Occurs in a **stepwise** fashion with carbocation intermediate.
 - Occurs in **3° (tertiary) alkyl halides**.
 - Generally occurs at a slow rate, and a mixture of products are often produced.
 - Formation intermediate carbocation allows for both inversion and retention of configuration to remain the same.
- ▷ **Ionization**: when the tertiary alkyl halide dissociates into pair of ions.
 - Pair of ions: a **carbocation** and more often a **halide anion**.
 - The carbocation then determines the resulting product depending on solvents:
 - If the solvent is a nucleophile, then it's substitution.
 - If the solvent can function as a base, then it's elimination.

S_N1 Mechanism

- **Solvolysis:** when an alkyl halide undergoes ionization in a polar solvent (hydrogen connects to electronegative atom), and the solvent functions as a **nucleophile** which attacks the intermediate carbocation, resulting in a two-step substitution.
 - The concentration of the **alkyl halide** acts as the **rate-determining** step, since the loss of the leaving group, and the formation of the carbocation, represents the highest energy transition state of the multi-step process.
 - Loss of leaving group (formation of carbocation) → nucleophilic attack
- If the nucleophile is uncharged, which is often the case for S_N1 reactions, then there will be an additional step at the end of the mechanism in which the extra proton is removed by a solvent molecule.

E1 Mechanism

- When a 3° alkyl halide undergoes ionization in a polar solvent and can function as a **base** and deprotonate the intermediate carbocation, resulting in a two-step elimination.
 - The **loss of the leaving group** also is the **rate-determining** step for eliminations.
- Often the second rate-limiting step is either the substitution or elimination.
 - Usually substitution is favored due to the lower energy transition state requirement.
 - Elimination is favored when potential energy is high enough for the more stable product of elimination to have a greater determining effect.
 - E.g, when the resulting alkene is tri- or Tetrasubstituted; more stability in the end product is favored.
 - This is why a mixture of products is often observed.

Solvent and Substrate Effects on Ionization Rates

- Ionization process occurs most readily in **protic solvents**, since both ionization products are well solvated in protic solvents.
 - Carbocations are stabilized by interacting with lone pairs of the oxygen atoms.
 - Chloride ions are stabilized via hydrogen bonds.
 - Aprotic cannot stabilize both equally, as there is little free hydrogen, thus unfavorable for solvolysis reactions.
- To contrast, S_N2 reactions are enhanced by the **strength of the nucleophile**, which allows them to overcome activation energy of the reaction.
 - Lack of stabilization increases energy of nucleophiles.
- Protic solvents stabilize the ionic intermediates and transition states, allowing for smaller activation energy barrier due to loss of leaving group being the rate-limiting step.
- **Effect of Substrate**
 - Alkyl iodides are the most reactive, while fluorides are the least.
$$I^- > Br^- > Cl^- > F^-$$

Predicting Products: Substitution vs Elimination

- ▷ Often elimination and substitution are in competition with each other, with sometimes one product dominating, or reactions resulting in multiple products.
- ▷ Main steps in determining products:
 - Determine the function of the reagent.
 - Analyze the substrate and determine the expected mechanism(s).
 - Consider any relevant regiochemical and stereochemical requirements.

Determining the Function of the Reagent

- To recap: substitution occurs when the reagent functions as a nucleophile, while an elimination reaction occurs when the reagent functions as a base.
- Major factors (not all) that determine nucleophilicity: presence of high electron density and polarizability, while basicity is determined by base stability.
 - Strong acids have weaker conjugate bases. The weaker the base, then the more stability the molecule has, and the less likely to act as base rather than nucleophile.
 - Often bases bear negative charges, allowing them to also function as nucleophiles.
 - Small size often decreases polarizability, which makes some weak bases unable to be nucleophiles.
- Common reagents can be classified into four categories, with two-dimensions based on base and nucleophile strength.
 - **Strong base, weak nucleophile:** NaH, DBN, DBU
 - Strong tendency to give up hydrogens leads reagents functioning almost exclusively as bases, leading to the elimination reaction.
 - **Strong base, strong nucleophile:** HO^- , MeO^- , EtO^-
 - Can act as both, often producing mixture of products.
 - Such reagents are generally used for biomolecular processes.
 - **Weak base, strong nucleophile:** I^- , Br^- , Cl^- , RS^- , HS^- , RSH, H_2S
 - Reagents mainly function as nucleophiles due to high polarizability, despite being weak bases, leading to substitution reactions.
 - **Weak base, weak nucleophile:** H_2O , MeOH, EtOH
 - Can act as both a nucleophile and base.
 - Mainly used in unimolecular reactions.

	Expected Mechanism(s)			
	Strong Base Weak Nucleo	Strong Base Strong Nucleo	Weak Base Strong Nucleo	Weak Base Weak Nucleo
1°	E2	E2, S _N 2	S _N 2	—
2°	E2	E2, S _N 2	S _N 2	—
3°	E2	E2	S _N 1	E1, S _N 1

Determining the Expected Mechanism(s)

- After determining categories, then the next step is to identify likely mechanisms, which is done by analyzing the substrate (3°, 2°, 1°).
- The identify of the substrate plays a vital role in determining reactions when the reagent is a strong nucleophile and a strong base.
 - If both are weak, then substitution and elimination can only occur in 3° due the need of carbocation intermediate (some rare exceptions with 2° allylic and benzylic compounds).
- Elimination is not hindered by steric interactions, so generally it will prevail long as substitution isn't favored.
 - Except in unimolecular, where E1 is favored when the products is tri- or tetrasubstituted, and S_N1 with mono- and disubstituted.

Considering Regiochemical and Stereochemical Outcomes

- Much of follow information was already discussed, but will be recapped here.
- S_N2:
 - Regiochemical: the nucleophile attacks the α position where the leaving group is connected.
 - Stereochemical: the nucleophile replaces the leaving group with inversion of configuration.
- E2:
 - Regiochemistry: The Zaitsev product (more hydrogen-dense) is generally favored over Hofmann product (less hydrogen-dense), unless sterically hindered, then Hofmann will be favored.
 - Stereochemical: stereoselective, with preference for *trans* over *cis* in disubstituted alkene.
 - Also stereospecific: when the β position has only one proton, then the stereoisomeric alkene resulting from the anti-periplanar elimination will be obtained.

- S_N1 :
 - Regiochemical: nucleophile attacks the carbocation, which is where leaving group is originally connected, unless carbocation rearrangement took place.
 - Stereochemical: nucleophile replaces the leaving group, giving a nearly racemic mixture of inverted and retained configurations.
 - Often though there is slight preference on inversion as a result of the ion pairs effect.
- E1:
 - Regiochemical: Zaitsev product will always be favored over the Hofmann product.
 - Stereochemical: Stereoselective, with the *trans* disubstituted alkene often being favored.