

Organic Chemistry Anchoring Concepts Content Map

Jeffrey R. Raker,[†] Thomas Holme^{†*} and Kristen Murphy[‡]

[†]Department of Chemistry, Iowa State University, Ames, Iowa 50011 United States;

*taholme@iastate.edu

[‡]Department of Chemistry and Biochemistry, University of Wisconsin–Milwaukee, Milwaukee, Wisconsin 53201 United States

The outline below delineates the anchoring concepts content map for organic chemistry.

I. Atoms: Matter consists of atoms that have internal structures that dictate their chemical and physical behavior.

A. *Atoms have unique chemical identities based on the number of protons in the nucleus.*

1. The atomic number and mass number are used to determine average atomic weight and identify isotopes, which play a part in understanding techniques such as MS, NMR, or IR and rates of reactions via kinetic isotope effects.

B. *Electrons play the key role for atoms to bond with other atoms.*

1. Electrons play a role in understanding the relative stability of resonance structures.
 - a. Stabilization of anions helps to explain pK_a values and relative acidities of protons.
2. Some reactions occur because molecules that are electrophilic are prone to react with regions where electron density is high.
 - a. Electron-deficient atoms that seek electron-rich atoms are called electrophiles (meaning “electron seeking”). Electrophiles are commonly neutral or positively charged.
 - b. Alkenes and alkynes are electron-rich and therefore are susceptible to electrophilic addition. Alcohols and alkyl halides are often formed from alkenes via electrophilic addition.
3. Some reactions occur because molecules that are nucleophilic are prone to react with regions where electron density is low.
 - a. Electron-rich atoms that seek electron-deficient atoms are called nucleophiles (meaning “nucleus seeking”). Nucleophiles are commonly neutral or negatively charged.

C. *Atoms display a periodicity in their structures and observable phenomena that depend on that structure.*

1. The valence of the various atoms commonly found in organic molecules shows the periodicity in structure and the phenomena that result from it (e.g., nucleophilicity trends, pK_a properties).
2. Organic molecules reflect the periodicity of atoms via bond strengths and bond lengths.

D. *Most information about atoms is inferred from studies on collections of atoms often involving an interaction with electromagnetic radiation.*

1. A discussion of the major historical developments in organic chemistry highlights how organic chemistry discoveries were made.
2. Key techniques for structural elucidation include UV, IR, NMR, and MS.

- E. *Macroscopic samples of matter contain so many atoms that they are counted in moles.*
1. Mole-based stoichiometry calculations (i.e., molar equivalents and limiting reagents) are used to determine percentage yield, particularly in the laboratory.
- F. *Atoms maintain their identity, except in nuclear reactions.*
- G. *Ions arise when the number of electrons and protons are not equal, and can be formed from atoms.*
1. Metal–nonmetal bonds have a large dipole and can function in organic reactions as a strong base or strong nucleophile.

II. Bonding: Atoms interact via electrostatic forces to form chemical bonds.

- A. *Because protons and electrons are charged, physical models of bonding are based on electrostatic forces.*
1. Organic molecules are held together with covalent bonds that arise from the sharing of electron pairs between nuclei.
 - a. In alkanes, carbons can be labeled as primary, secondary, tertiary, or quaternary, depending on the number of non-hydrogen substituents (i.e., 1, 2, 3, or 4 respectively) on the labeled carbon.
 2. An uneven sharing of the electrons in a chemical bond leads to a bond dipole moment.
 - a. Polar bonds (such as cyano groups) result from unequal sharing of electrons (due to electronegativity differences) between two covalently bonded atoms, resulting in a bond dipole moment.
 - b. Carbonyls are an extremely polar functional group; the carbon is partially positive and the oxygen is partially negative. Therefore, the carbon of a carbonyl is very electrophilic.
 - c. Conversion of an alkyl halide to an organomagnesium (or lithium–lithium and copper) results in a partially negative carbon that functions as a nucleophile. Organometallic reagents (e.g., Grignard or Gilman) are strong nucleophiles and participate in a variety of reactions that involve nucleophilic substitution or addition.
- B. *Because chemical bonds arise from sharing of negatively charged electrons between positively charged nuclei, the overall electrostatic interaction is attractive.*
1. Chemical bonds result from shared electrons; nuclei involved in the sharing and number of electrons shared results in differences in bond energy.
 - a. Single, double, and triple bonds between atoms give rise to patterns in bond energies and lengths.
- C. *When chemical bonds form, the overall energy of the bonding atoms is lowered relative to free atoms, and therefore energy is released.*
1. A chemical bond results in the lowest energy orbitals being filled such that the overall energy change of the system is negative.
 2. Chemical bonds can interact in ways to lower the overall energy of the molecule.
 - a. Conjugated alkenes are uniquely stable due to conjugation (p-orbital overlap).

- b. Benzene is uniquely stable (i.e., aromatic) due to cyclic conjugation of π -bonds.
 - c. Aromatic compounds are flat, continuous cyclic arrays of p-orbitals that contain $4n+2$ electrons (anti-aromatic compounds have $4n$ electrons).
- D. *To break a chemical bond requires an input of energy.*
- 1. The breaking of a bond homolytically requires the input of energy, measured as the bond dissociation energy.
- E. *A theoretical construct that describes chemical bonding utilizes the construction of molecular orbitals for the bond based on overlap of atomic orbitals on the constituent atoms.*
- 1. Hybridization, resonance, and molecular orbital theory provide information about bond formation.
 - a. Molecular orbital theory is based on the wavelike nature of electrons. Atomic orbitals (i.e., s, p, d, f; based on the atomic orbitals of hydrogen) are mathematical probability functions for finding an electron in the circumscribed space for a given atom. Orbitals can be “hybridized” through a process of linear combinations of atomic orbitals’ hybridized orbitals (such as sp or sp³), and are used to better represent actual bond lengths, angles, and energies for molecules. Atomic and hybridized orbitals can be overlapped to form bonding and antibonding molecular orbitals and thus theoretical models of electronic structure and molecular geometry.
 - b. Resonance structures are two or more Lewis structures that differ only in the absolute location of electrons. A weighted linear combination of resonance structures for a given molecule best represents the “actual” electron density of the molecule.
 - c. Allylic radicals, cations, and anions are uniquely stable due to resonance stabilization.
 - 2. The stereochemistry and regiochemistry of cycloaddition reactions is related to the symmetry of the orbitals.
 - a. The products formed in a Diels–Alder reaction retain the stereochemistry of the starting materials.
 - 3. Atomic orbitals mix to form bonding, nonbonding, and antibonding molecular orbitals such that the number of molecular orbitals produced equals the number of atomic orbitals used initially.
 - a. Hybrid orbitals are necessary to describe the geometry of substituents on individual atoms (e.g., the tetrahedral geometry of carbon in methane).
 - b. Orbital diagrams reduced to just p-orbitals are used to understand the differences between aromatic and anti-aromatic compounds.
- F. *Covalent bonds can be categorized based on the number of electrons (pairs) shared. The most common categories are single, double, and triple bonds.*
- 1. Single, double, and triple bonds are discussed in terms of sigma and pi bonds, and the differences in the relative bond lengths and strengths.
 - a. Bonds formed by the overlap of s-orbitals or s-containing hybrid orbitals result in the formation of sigma (σ) bonds; sigma bonds are also formed from the end-to-end overlap of p-orbitals; bonds formed by the side-to-side overlap of p-orbitals result in the formation of pi (π) bonds.

- b. The “degree(s) of unsaturation” (or index of hydrogen deficiency) is equal to the number of π -bonds or rings in a given molecule. In general, it is the difference between the number of hydrogens in a corresponding fully saturated molecule minus the actual number of hydrogens in the molecule divided by two. Incorporation of heteroatoms (e.g., N or halogens) impacts the way in which unsaturation is calculated.
 2. Sigma and pi bonds have effects on geometric structure; in particular, rotation about a single bond occurs readily, while rotation about a double bond is hindered.
 - a. Molecules can adopt conformations based on free rotation around σ -bonds. Relationships between atoms and substituent groups can be described as staggered or eclipsed, gauche or anti using Newman projections. Each conformation has a relative energy; molecules, in general, seek the lowest energy conformation. However, any conformation at an energy minimum can potentially be observed via spectroscopic methods.
 - b. Cyclohexane adopts three main conformations: chair (major conformer), boat, twist-boat. With sufficient energy, a cyclohexane molecule can interconvert between all possible conformations.
- G. *Metallic bonding arises in many solids and fundamentally involves the sharing of valence electrons among many positively charged “cores” over extended distances.*

III. Structure and Function: Chemical compounds have geometric structures that influence their chemical and physical behaviors.

- A. *Atoms combine to form compounds that have new properties based on structural and electronic features.*
1. Molecular properties (e.g., boiling point) can be the result of differing combinations of atoms (such as $-\text{OH}$, the hydroxyl group), referred to as functional groups.
 2. Molecular properties (e.g., chirality) can be the result of differing orientations of atoms (such as four different substituents bound to a tetrahedral configured carbon), referred to as stereocenters.
 3. The properties of polymers and the different allotropes of carbon are related to their structure, and in the case of crystals, to their crystal structure.
- B. *Models exist that allow the prediction of the shape of chemicals about any bonding atom in a molecule.*
1. Molecular shapes can be predicted using VSEPR theory, bond angles, and polarity.
 - a. Lewis structures are used to note the location of valence electrons in bonds and lone pairs. Lewis structures can be used to predict bond lengths, angles, and energies; in addition, overall three-dimensional geometry of molecules can be predicted.
 - b. Substituent groups on a cyclohexane molecule can be labeled as axial or equatorial when the molecule is in the chair conformation. Axial groups are parallel to an axis drawn through the center of the ring; equatorial groups stick out from the ring at an $\sim 109.5^\circ$ angle from the

- axial groups. Larger, more bulky substituents preferentially orient in the equatorial direction to reduce torsional and steric strain.
- c. Cyclic structures can be strained due to non-ideal bond angles and steric repulsion; these causes are respectively called bond-angle and torsional strain.
 - d. Two or more rings can be bridged or fused. Fused cycles share 2 atoms (1 bond) and bridged cycles share 3 or more atoms (2 or more bonds).
2. The molecular shape is especially important with regards to stereochemistry.
- a. Stereocenters are atoms with four different substituents, and are labeled R or S, depending on the three-dimensional arrangement of the four substituents based on substituent group priority as defined by the Cahn-Ingold-Prelog rules.
 - b. Nitrogens can be chiral; however, interconversion of the lone pair keeps the nitrogen in constant racemization. If interconversion can be stopped, the nitrogen can be chiral (the lone pair receives lowest Cahn-Ingold-Prelog priority when assigning R or S).
 - c. Alkenes can be labeled as terminal or internal. Likewise, through Cahn-Ingold-Prelog rules, E (trans) or Z (cis) isomers are used to identify the arrangement of the priority groups on alkenes.
 - d. Diels-Alder products can be labeled *endo* or *exo*, depending on the orientation of substituent groups in the product.
- C. *Theoretical models are capable of providing detail structure for whole molecules based on energy minimization methods.*
1. Molecular modeling computer programs can provide information about structures, and are predicated on these theoretical models.
- D. *Symmetry, based on geometry, plays an important role in how atoms interact within molecules and how molecules are observed in many experiments.*
1. Spectroscopy is related to the symmetry of the molecules being studied.
 - a. Symmetry impacts the visibility of some absorption peaks in an infrared spectrum.
 - b. The number of infrared spectrum peaks increase with the decrease of a molecule's symmetry.
 2. The symmetry of molecules may result in some ^1H or ^{13}C atoms having identical NMR characteristics (chemical shift and coupling patterns).
 - a. Equivalent protons do not couple with each other.
- E. *Three-dimensional structures may give rise to chirality, which can play an important role in observed chemical and physical properties.*
1. Enantiomers and diastereomers describe structural relationships between stereoisomers.
 - a. Isomers are two or more molecules of the same molecular formula, but differ in either connectivity (i.e., constitutional isomers) or three-dimensional arrangement (i.e., stereoisomers).
 - b. Chiral compounds are nonsuperimposable on their mirror image. Chiral compounds lack an internal mirror plane; achiral compounds do have an internal mirror plane. A special class of achiral compounds is called meso: these compounds contain chiral centers; however, the presence of an internal mirror plane makes the overall molecule achiral.

- c. Stereoisomers include cis (same) or trans (opposite) relationships of substituents; these terms are commonly used when describing substituents on cyclic alkene compounds.
 - d. Enantiomers are two stereoisomers that are nonsuperimposable mirror images of each other.
 - e. Diastereomers are two stereoisomers of the same connectivity, but are nonsuperimposable and nonmirror images.
 2. Reactions can be regiospecific, regioselective, stereospecific, stereoselective, or neither.
 - a. Markovnikov's rule—Addition across an alkene involves the addition of the electrophile to the least substituted carbon, resulting in a stable carbocation intermediate, followed by the attack of the nucleophile to the residual carbocation. Anti-Markovnikov reactions proceed via a different mechanism and add the nucleophile at the least substituted carbon.
 - b. Zaitsev's rule—Using a nonsterically hindered base, the major product of an alkene forming reaction is the most highly substituted (non-hydrogen) alkene.
 - c. Hofmann's Rule—Using a sterically hindered base, the major product of an alkene forming reaction is the least substituted (nonhydrogen) alkene.
 - d. Stereospecific reactions result in the formation of a single stereocenter configuration (R or S). S_N2 reactions are stereospecific, resulting in inversion of the stereocenter at the site of displacement.
 - e. Stereoselective reactions preferentially form one stereoisomer in a greater quantity than another possible stereoisomer.
 3. The stereochemistry of the starting material and reactive intermediates can affect the stereochemistry of the product(s).
 - a. Achiral starting materials give a racemic mixture of products or an achiral product (such as a meso compound).
 4. The three-dimensional structure of molecules can lead to different transition states, reaction intermediates, and different isomeric products of a reaction.
 5. Stereoisomers may be observed with polarized light; diastereomers may be separated based on differences in their physical properties.
 - a. Chiral compounds are optically active, meaning they rotate plane-polarized light. Specific rotation of a single enantiomer is an experimentally determined value (using a polarimeter) that can in turn be used as a constant to determine enantiomeric excess (i.e., optical purity).
 - b. A racemic mixture is a 1:1 mixture of enantiomers. Enantiomers can be separated from each other through a process called resolution.
 - c. Meso compounds contain two or more stereocenters, but have an internal mirror plane and therefore are achiral (optically inactive).
- F. *Reactions of molecules can often be understood in terms of subsets of atoms, called functional groups.*
 1. The reactivity of functional groups is related to their structures.
 - a. Functional groups can be stabilized or destabilized by resonance and inductive effects.
- G. *Many solid state, extended systems exist and geometric structures play an important role in understanding the properties of these systems.*

IV. Intermolecular Interactions: Intermolecular forces, electrostatic forces between molecules, dictate the physical behavior of matter.

- A. *Intermolecular forces are generally weaker, on an individual basis, than chemical bonds, but the presence of many such interactions may lead to overall strong interactions.*
1. Intermolecular forces play a role in spectroscopy and the physical properties displayed by molecules.
 - a. Hydrogen bonding causes peak broadening in both infrared and NMR spectroscopy.
 2. Intermolecular forces can lead to differences in solubility and melting and boiling points, and change the reactivity in polar versus nonpolar solvents.
 3. Hydrogen bonding is a particularly important intermolecular force in organic chemistry.
- B. *For large molecules, intermolecular forces may occur between different regions of the molecule. In these cases, they are sometimes termed noncovalent forces.*
1. Noncovalent forces can play a role for compounds that disperse hydrophobic molecules or ions into aqueous layers.
 2. For large molecules such as polymers, proteins, and DNA, intermolecular forces can affect their binding strength, and secondary and tertiary structure.
- C. *Intermolecular forces can be categorized based on the permanence and structural details of the dipoles involved.*
1. Intermolecular interactions can play a role in how molecules collide.
- D. *For condensed phases that are not structures of extended chemical bonds, the physical properties of the state are strongly influenced by the nature of the intermolecular forces.*
1. The type of intermolecular forces present in reactants can affect what solvent is used in a reaction.
 2. The nature of intermolecular forces can have an effect on green chemistry because choices of solvent can be environmentally important.
- E. *The energy consequences of chemical reactions that take place in condensed phases (solution) usually must include intermolecular forces to be correctly and completely explained.*
1. Choice of solvents is an important factor in organic reactions.
 2. Changing solvent polarity can cause a change in mechanisms and lead to different products.

V. Chemical Reactions: Matter changes, forming products that have new chemical and physical properties.

- A. *In chemical changes, matter is conserved and this is the basis behind the ability to represent chemical change via a balanced chemical equation.*
1. Equations for organic reactions are rarely explicitly balanced; reagents are often indicated over the arrow rather than to the left of it.
 2. Reaction yields are important.

3. Organic reactions can be carried out and techniques for maximizing yield and purity can be determined experimentally.
 4. Series of reactions are used to produce larger and more complex molecules.
 - a. Retrosynthetic analysis is a process of identifying a set of reagents that could be used to obtain the desired target. This backwards thought process continues until all reagents are commercially available or methods are known for the formation of the desired reagents.
- B. Chemical change involves the breaking or forming of chemical bonds, or typically both.*
1. The synthesis of organic compounds involves breaking and forming chemical bonds; energetics plays a part in which bonds are broken or formed.
 - a. When carbocations are formed as intermediates, the opportunity for rearrangement arises. Rearrangement is the process of a hydride or alkyl shift to produce a more stable carbocation intermediate. Only one shift is normally observed.
 - b. Radicals and cations are stable relative to each other such that tertiary are more stable than secondary, more stable than primary, more stable than methyl carbons. Allylic radical cations and anions are more stable than respective nonallylic radical cations and anions. Carbanions follow an inverse relative stability scale (i.e., methyl more stable than primary, etc.).
 - c. S_N2 reactions at α -allylic and benzylic sites are faster because of transition state stabilization by the allyl or benzyl group.
 - d. The rate of S_N1 and E1 reactions is dependent on the stability of the intermediate carbocation.
 - e. The rate of nucleophilic substitution is dependent on the leaving group ability, nucleophilicity, solvent polarity and proton donation ability, and steric hindrance at the site of leaving group displacement.
 - f. Carboxylic acid derivatives have differing degrees of susceptibility to nucleophilic attack such that amides are the least, then esters, anhydrides, with acid chlorides as the most reactive.
- C. Chemical change can be observed at both the nanoscopic and macroscopic levels, and models exist that allow the translation between these two levels of observation.*
1. Visualizing molecules and how they react is a key skill for organic chemistry.
 2. Different representations can be used to depict the structure of organic molecules.
 - a. Molecular geometry is depicted using several representational typologies, each with a specific purpose of communicating molecular geometry, properties, and reactivity. Representations include dashed-wedged line drawings, skeletal structures, and Newman and Fischer projections.
- D. There are a large number of possible chemical reactions, and categories have been devised to organize understanding of these reaction types.*
1. Addition, elimination, rearrangement, substitution, and redox reactions represent broad categories that are helpful in understanding organic reactions.

2. Key categories of organic reactions that students should be able to recognize include: S_N1 , S_N2 , E1, E2, and electrophilic and nucleophilic aromatic substitution.
 - a. Nucleophilic substitution occurs when a nucleophile displaces a leaving group. Bimolecular substitution (S_N2) occurs via a concerted mechanism in which the nucleophile directly displaces the leaving group. Unimolecular substitution (S_N1) occurs when the leaving group first leaves in a rate-determining step, followed by nucleophilic attack at the resultant carbocation intermediate.
 - b. Bimolecular (S_N2) and unimolecular (S_N1) nucleophilic substitution reactions compete with elimination reactions (E2 and E1, respectively). Preference for substitution or elimination is governed by steric hindrance and basicity of the reagent.
 - c. Elimination reactions (E2 and E1) occur via beta deprotonation to the site of the leaving group displacement. The resultant electron pair after deprotonation forms a π -bond with the carbon at the site of leaving group displacement. Elimination reactions occur in the presence of a strong base nucleophile.
 - d. S_N1 reactions result in racemization (or near racemization) at the site of displacement due to the attack of the planar carbocation from above or below.
 - e. Electrophilic aromatic substitution is a reaction between an electrophile and an aromatic compound (electron-rich component). The electrophile replaces hydrogen on the aromatic species. Electrophilic aromatic substitution reactions include bromination, nitration, sulfonation, Friedel-Crafts alkylation, and acylation.
 - f. Nucleophilic substitution occurs via an addition-elimination or elimination-addition mechanism. Electrophilic substitution occurs exclusively via an addition-elimination mechanism.
 3. Radical reactions, which show single electron movement, represent another broad category.
 - a. Radical reactions are regioselective, dependent on the stability of all possible reactive intermediates. More than one product is possible for a radical reaction; products (two or more) are labeled major or minor corresponding to predicted or observed relative yields.
 - b. Radical reactions follow a sequence of initiation, propagation, and termination steps.
 4. It is important to recognize reaction conditions in an environmentally responsible (green) manner whenever possible.
- E. *Chemical change can be controlled by choices of reactants, reaction conditions, or use of catalysts.*
1. Organic chemistry can be understood by studying the structure and reactivity of different functional groups. Reactions can be understood in collections by functional groups, collections including reactions leading to formation of functional groups, and reactions using the given functional group to form other functional groups. While key reactions of functional groups can be listed, such lists are not intended to be exhaustive within this map.

- a. Key reactions of alkanes include combustion and free radical halogenation.
 - b. Key reactions of alkyl halides include S_N1 and S_N2 substitution, E1 and E2 elimination, and the formation of organometallic reagents.
 - c. Key reactions that include alkenes are reduction to alkanes, Diels–Alder, formation of alkyl halides, electrophilic addition, free radical reactions, and oxidative cleavage reactions.
 - d. Alkynes undergo many of the same reactions as alkenes, and can also be selectively reduced to *cis*- or *trans*-alkenes.
 - e. Key reactions of alcohols include oxidation to aldehydes, ketones, and carboxylic acids, conversion to a chloride using sulfonyl chloride, and dehydration to form alkenes.
 - f. Key reactions of ethers include their formation by the Williamson ether synthesis and their reduction to alkyl halides.
 - g. Epoxides are highly reactive heterocyclic compounds; their key reactions include their formation via peroxy acid conditions and stereoselective opening in the presence of a strong acid or nucleophile.
 - h. Aromatic systems display a fairly broad array of important reactions, including: electrophilic or nucleophilic substitution; the oxidation of benzyl hydrogens to ketones, aldehydes, and carboxylic acids; reduction of aromatic nitro groups; and reactions of atoms that are alpha to aromatic rings, such as oxidation.
 - i. Aldehydes and ketones undergo many of the same key reactions, including: conversion to acetals; reduction to a $-CH_2-$ group via imine intermediates; combination into alkenes using Wittig reagents; nucleophilic attack at the carbonyl carbon; aldol and Claisen (reactions that depend on the acidity of hydrogens on the carbon alpha to the carbonyl group); conversion to complex alcohols by nucleophilic attack of organomagnesium and organocuprates; reduction to alcohols by hydride donors or Grignard reagents; and alpha-substitutions via basic and acidic conditions.
 - j. Key reactions of carboxylic acids and their derivatives include: interconversion via an addition–elimination mechanism; conversion to ketones or aldehydes by nucleophilic attack by organomagnesium; organocuprates; decarboxylation at high temperatures when the carboxylic acid group is beta to carbonyl groups; and conversion to enols or enolates when beta-carbonyl groups are present.
 - k. Key reactions of amines include their formation via substitution chemistry and Hoffman elimination reactions.
 - l. Substituents on an aromatic ring either activate or deactivate the ring (i.e., increase or decrease the electron density and susceptibility to electrophilic attack). Also, substituents serve to direct the adding group to an ortho, para, or meta relationship to it via resonance (electronic effect) stabilization of mechanistic intermediates, or via inductive effects.
2. The control of a reaction is important and is affected by time, temperature, catalysts, and solvent, etc.
- F. *Controlling chemical reactions is a key requirement in the synthesis of new materials.*

1. Different reagents or reaction conditions can control the regio- and stereochemistry of a reaction.
2. Different reagents or reaction conditions can control the regiochemistry of a reaction.

VI. Energy and Thermodynamics: Energy is the key currency of chemical reactions in molecular-scale systems as well as macroscopic systems.

- A. *Most chemical changes are accompanied by a net change of energy of the system.*
1. Thermodynamics is important in explaining energy changes.
 2. Energy diagrams provide an important tool for understanding and illustrating reaction energetics.
 - a. Energies for reactants, intermediates, and products can be combined to model energy diagrams for reaction mechanisms.
- B. *Many chemical reactions require an energy input to be initiated.*
1. Reactions generally require an input of energy to overcome the energy of activation.
- C. *The type of energy associated with chemical change may be heat, light, or electrical energy.*
1. Heat and light are common types of energy associated with reactions.
 2. The source of energy input can affect mechanisms and change the products of pericyclic reactions.
- D. *Breaking chemical bonds requires energy, and formation of chemical bonds releases energy.*
1. In a reaction, often there is both bond breaking and bond formation, so the energy consequences depend on both.
 - a. The transition state of an S_N2 reaction has concurrent bond making and bond breaking.
- E. *The forces that are associated with energy change in chemical processes are electrostatic forces.*
1. Interactions with solvent can be described in terms of dipole–dipole or induced-dipole interactions.
- F. *In accord with thermodynamics, energy is conserved in chemical changes, but the change of form in which the energy is present may be harnessed via natural or human-made devices.*
1. Hydrocarbon compounds are commonly combusted for energy.
- G. *Thermodynamics provides a detailed capacity to understand energy change at the macroscopic level.*
1. Bond energies of reactants and products can be used to estimate macroscopic enthalpy changes for reactions.
- H. *The tendency of nature to disperse, particularly in terms of energy distribution, is embodied in the state function called entropy.*
- I. *Energy changes associated with nuclear chemistry are many orders of magnitude larger than those of classical chemical change.*

VII. Kinetics: Chemical changes have a time scale over which they occur.

- A. *Chemical change can be measured as a function of time and occurs over a wide range of time scales.*
1. Differences between fast and slow reactions can play a vital role in determining what product forms in a reaction.
- B. *Empirically derived rate laws summarize the dependence of reaction rates on concentrations of reactants and temperature.*
1. Rate laws can provide clues to reaction mechanisms, particularly substitution and elimination reactions.
 - a. Rate laws can be developed from reaction equations or reaction mechanisms.
- C. *Most chemical reactions take place by a series of more elementary reactions, called the reaction mechanism.*
1. Reaction steps are fundamental to understanding each functional group's reactivity in organic chemistry.
 - a. The slowest step is the rate-determining step.
 2. Functional groups consist of polar or polarizable bonds that dictate reactivity.
 3. Curved arrow mechanisms show electron movement from nucleophiles to electrophiles in elementary reactions.
 - a. Reaction mechanisms can be depicted illustrating the movement of electrons for every bond broken or formed.
- D. *An elementary reaction requires that the reactants collide (interact) and have both enough energy and appropriate orientation of colliding particles for the reaction to occur.*
1. Transition state theory is used mainly to explain kinetics in S_N2 reactions.
- E. *Catalysis increases the rate of reaction and has important applications in a number of subdisciplines of chemistry.*
1. Catalysis changes the path of a reaction to a lower activation energy, which can be shown through changes in the reaction rates.
- F. *Reaction products can be influenced by controlling whether reaction rate or reaction energy plays the key role in the mechanism.*
1. Kinetic versus thermodynamic control of a reaction and reaction coordinate diagrams are used to discuss how to control the reaction products.
 2. The role of reaction intermediates and concepts such as resonance and hyperconjugation inform the manner in which this type of reaction control is understood.

VIII. Equilibrium: All chemical changes are, in principle, reversible and chemical processes often reach a state of dynamic equilibrium.

- A. *Both physical and chemical changes may occur in either direction (e.g., from reactants to products, or products to reactant).*
1. The position of equilibrium can affect the amount of product formed by a reaction.
 - a. Enols and enolate ions are in equilibrium with their respective ketones or aldehydes.

- B. *When opposing processes both occur at the same rate the net change is zero.*
1. Reversible reactions reach equilibrium.
- C. *For chemical reactions, the equilibrium state can be characterized via the equilibrium constant.*
1. An equilibrium state can be shown using a reaction-coordinate diagram, by performing a conformational analysis or using instrumentation.
 2. pK_a is a measure of the equilibrium between the protonated and deprotonated forms of a molecule.
 - a. Terminal alkyne hydrogens are more acidic ($pK_a \approx 25$) than most C–H bonds due to the s-character of the hybrid orbital (sp) containing the conjugate base lone pair. Deprotonated terminal alkynes are good nucleophiles.
 - b. The acidity of phenols is the result of resonance stabilization within the aromatic ring of the conjugate base's negative charge.
 - c. Alpha-hydrogens to carbonyl groups are acidic due to resonance stabilization of the conjugate base (i.e., an enolate). Enolates can be used as nucleophiles and therefore can be involved in any nucleophilic reaction (e.g., aldol or Claisen condensation).
 - d. Any H on an O is more acidic than carbon or nitrogen due to the ability of O to handle a negative charge.
- D. *When the equilibrium constant is very large or small, products or reactants, respectively, are primarily present at equilibrium. Systems with K near 1 have significant amounts of both reactants and products present.*
1. When the equilibrium constant K is very large, product formation is strongly favored.
- E. *If perturbed, a system at equilibrium will respond in the direction that tends to offset the perturbation.*
1. It is possible to use Le Châtelier's principle to force a reaction to form product.
- F. *Thermodynamics provides mathematical tools to understand equilibrium systems quantitatively.*
- G. *Equilibrium concepts have important applications in several subdisciplines of chemistry.*
1. Protonation of functional groups in organic molecules is an equilibrium process (and it is essential to acid-catalyzed processes, for example).
 - a. Brønsted acids are proton donors; bases are proton acceptors. Lewis acids are electron-pair acceptors; Lewis bases are electron-pair donors.
 - b. The reversibility of many reactions is important in understanding mechanisms and in predicting reaction outcomes.

IX. Experiments, Measurement and Data: Chemistry is generally advanced via empirical observation.

- A. *Quantitative observation of matter can be made at a wide range of distance and/or time scales.*
1. Data collected can be measured at the macroscopic level using chemical tests.

2. Data collected can be measured at the microscopic level using instruments such as X-ray, NMR, IR, MS, and EPR.
 3. Wet chemical methods may take time to provide results and results may be unclear due to multiple functional groups, particularly when compared with instrumental methods.
- B. Because there are a large number of compounds, a system of naming these compounds is used.*
1. In order to be able to organize observations on vast numbers of compounds, a systematic nomenclature system has been devised to name compounds.
 - a. IUPAC has outlined a set of systematic guidelines for naming all organic structures based on carbon chain length, rings, functional groups, and substituents.
 - b. Hydrocarbons contain carbon and hydrogen atoms. Hydrocarbons with only carbon-carbon single bonds are called alkanes; they can be straight-chained or branched.
 - c. Substituents on a di-substituted benzene ring can be labeled as ortho, meta, or para to each other.
- C. Experimental control of reactions plays a key role in the synthesis of new materials and analysis of composition.*
1. Experimental measures provide data to determine whether desired products are obtained.
 2. Measures of products can include stereochemical specificity.
- D. Chemical measurements are based on mass, charge, or interaction with electrons or photons.*
- E. Observations are verifiable, so experimental conditions, including considerations of the representativeness of samples, must be considered for experiments.*
- F. Fidelity of inferences from data requires appropriate experimental design.*
- X. Visualization: Chemistry constructs meaning interchangeably at the particulate and macroscopic levels.**
- A. Many theoretical models are constructed at the particulate level, while many empirical observations are made at the macroscopic level.*
1. Spectroscopic probes are especially important in organic labs where instruments such as NMR, MS, IR, chromatography, and GC as well as techniques such as melting points, boiling points, optical activities, and refractive indices are used to study the reactants and products of organic reactions.
 - a. Ultraviolet-visible light (UV-vis) spectroscopy can be used to observe the π -bond structure (especially conjugation) of molecules.
 - b. Infrared (IR) spectroscopy uses electromagnetic radiation to probe functional groups through energy absorption in bending and stretching molecular motions. Observed vibrations result from a change in dipole moment from the bending and stretching motion.
 - c. Nuclear magnetic resonance (NMR) spectroscopy is the result of observing the α and β spin-state transitions of atomic nuclei with odd mass numbers caused by radio-frequency radiation in an external

- magnetic field. NMR is most commonly used to observe ^1H and ^{13}C nuclei.
- d. Proton NMR signals are characterized by number (denoting the number of “kinds” of chemically equivalent protons), chemical shift (relative shielding or deshielding due to electron density relative to tetramethylsilane), integration (number of each “kind” of proton relative to every other “kind”), and splitting (number of “kinds” of protons alpha to the kind of proton causing the observed signal).
 - e. Carbon-13 NMR signals are characterized by number (denoting the number of “kinds” of chemically equivalent carbons), and chemical shift (relative shielding or deshielding due to electron density relative to tetramethylsilane). Specialized methods can be used to determine the number of non-hydrogen substituents on the number of carbons.
 - f. Mass spectrometry utilizes ionizing energy to fragment larger molecules that are then observed based on charged mass. Isotopes and fragmentation data can be used to predict the original molecule.
- B. The mole represents the key factor for translating between the macroscopic and particulate levels.*
1. Reaction yields obtained in the laboratory at the macroscopic scale are often explained in terms of molecular-scale models of the reaction.
- C. Macroscopic properties result from large numbers of particles, so statistical methods provide a useful model for understanding the connections between these levels.*
- D. Quantitative reasoning within chemistry is often visualized and interpreted graphically.*