ORGANIC CHEMISTRY I

A Problem Set for
CHM 321

Martin Hulce
Academic Year 2011 – 2012

Creighton University
Department of Chemistry
2500 California Street
Omaha, NE 68178-0323
ORGANIC CHEMISTRY I

A Problem Set for CHM 321

Academic Year 2011-2012

Martin Hulce

Creighton UNIVERSITY

Department of Chemistry
2500 California Street
Omaha, NE 68178-0323
Note: Problems with italicized numbers are more challenging.
You may want to try them last.
Chapter One: Electrons, Bonds, and Molecular Properties

The simplest organic molecule: tetrahedral methane, CH$_4$
Concepts for Chapter 1: Electrons, Bonds, and Molecular Properties

I. Isomerism: The existence of molecules that have the same molecular formulas but differ in chemical or physical properties
   A. Constitutional isomers (also called structural isomers) differ in atomic connectivity
      1. Valence: The number of chemical bonds usually made by an uncharged atom

II. Bonding and Lewis Structures
   A. Covalent bonding: Lewis structural (valence bond) theory
      1. Valence electrons: The number of electrons in an atom’s outermost shell
      2. Valence bonds: Two valence electrons shared by two atoms
   B. Lewis structures and the octet rule
      1. Rules for writing Lewis structures
         a. Count the number of valence electrons for a compound
         b. Join atoms by single bonds, multiple bonds
         c. Check valence electrons for each atom, add lone pairs to fill octets
            d. Check for formal charge
               i. Formal charge =
                  (# valence electrons in electroneutral atomic species)
                  - (# valence electrons formally assigned to species in molecule)
               e. Eliminate as much formal charge as possible by making multiple bonds
      2. Relative stability of Lewis structures
         a. greatest number of covalent bonds
         b. have all octets filled
         c. have no formal charge separation
         d. have least amount of formal charge separation
         e. have formal charge assignments that are in agreement with relative electronegativities of atoms involved
   C. Lewis structures, electronegativity (EN), and dipole moment
      1. The extent of valence electron sharing by different atoms varies
         a. EN is the tendency of an atom to draw the electrons in a covalent bond towards itself
      2. Electronegativity values of atoms allow prediction of bond polarity to be
         a. ionic (ΔEN ≥ 1.7)
         b. polar covalent (ΔEN 0.5 - 1.7)
         c. a ΔEN ≤ 0.5 means the bond is essentially nonpolar: eg, C–H
         d. what’s the percent ionic character of a covalent bond? Here’s one approximation:
            \[ \text{% ionicity} = 16|\Delta \text{EN}| + 3.5(\Delta \text{EN})^2 \]

III. Atomic orbitals
   A. Electronic configuration diagrams: filling the 1s, 2s, 2p, etc orbitals
      1. Orbitals have phase
      3. Lewis structures and bonding geometry
         a. VSEPR theory
            i. Predicts three major bonding geometries
               I. linear
               II. trigonal planar
               III. tetrahedral
B. LCAO-MO: how bonds form from atomic orbitals
   1. Linear, head-on overlap of two atomic orbitals generates a $\sigma$ bond (having a circular cross-section) and a $\sigma^*$ bond (usually empty)
      a. Electronic configuration diagrams
C. Hybrid atomic orbitals and rehybridization–reconciling VSEPR and MO’s
   1. $sp^3$ orbitals
      a. Linear, head-on overlap of two atomic orbitals generates a $\sigma$ bond
      b. $sp^3$-hybridization of tetrahedral C atoms in molecules
      c. Orbital overlap diagrams of molecules
   2. $sp^2$ orbitals
      a. Linear, head-on overlap of two atomic orbitals generates a $\sigma$ bond and long-axis parallel overlap of two atomic orbitals generates a $\pi$ bond
      b. $sp^2$-hybridization of trigonal planar C atoms in molecules
      c. Orbital overlap diagrams of molecules
   3. $sp$ orbitals
      a. Linear, head-on overlap of two atomic orbitals generates a $\sigma$ bond and long-axis parallel overlap of two sets of atomic orbitals generates two $\pi$ bonds
      b. $sp$-hybridization of linear C atoms in molecules
      c. Orbital overlap diagrams of molecules

IV. Dipole moment and molecular polarity
   A. Along with $\Delta EN$ values, VSEPR allows prediction of molecular dipole moments
      1. Dipole moment, $\mu$, is readily approximated as the vector sum of all bond polarizations in a molecule

V. Intermolecular properties
   A. Dipole - dipole attractions
      1. Most important example: hydrogen bonding
   B. Induced dipole - induced dipole attractions
      1. Also called VanderWaals or London dispersion forces
1. Draw

   a. Four constitutional isomers that have the molecular formula $\text{C}_3\text{H}_9\text{N}$

   b. All of the constitutional isomers of molecular formula $\text{C}_2\text{H}_3\text{F}_3\text{O}$
2. Draw correct Lewis structures for each of the following chemical compounds.

a. $\text{H}_2\text{O}_2$

b. $\text{H}_2\text{CNH}$

c. $\text{CH}_3\text{CH}_2\text{NO}$
3. Using the atomic orbital energy level diagrams below, show how the electrons are distributed among the orbitals for the following chemical species:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>F</th>
<th>2p</th>
<th>2p</th>
<th>2p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2s</td>
<td>2s</td>
<td>2s</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1s</td>
<td>1s</td>
<td>1s</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3p</td>
<td>3p</td>
<td>3p</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3s</td>
<td>3s</td>
<td>3s</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>N</th>
<th>2p</th>
<th>2p</th>
<th>2p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1s</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Al³⁺</th>
<th>2p</th>
<th>2p</th>
<th>2p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2s</td>
<td>2s</td>
<td>2s</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1s</td>
<td>1s</td>
<td>1s</td>
</tr>
</tbody>
</table>

4. Using atomic orbital energy level diagrams and electron arrows, show how the electrons are distributed among the orbitals for the following chemical species:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Mg⁷⁺</th>
<th>Mg⁷⁺</th>
<th>Mg⁷⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>C⁻¹</td>
<td>C⁻¹</td>
<td>C⁻¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>sp³-hybridized O⁺¹</td>
<td>sp³-hybridized O⁺¹</td>
<td>sp³-hybridized O⁺¹</td>
</tr>
</tbody>
</table>
5. Using atomic orbital energy level diagrams and electron arrows, show how the electrons are distributed among the valence orbitals for the following chemical species:

   a. \( sp^3 \)-hybridized B\(^3\)

   b. \( sp^2 \)-hybridized O\(^+1\)

6. a. Consider the diatomic molecule, He\(_2\). Use the linear combination of atomic orbitals--molecular orbital (LCAO-MO) method to diagram the formation and relative energies of the molecular orbitals derived from the mixing of the 1s atomic orbitals. Label the type of orbitals formed and whether they are bonding or antibonding. Show how the electrons are distributed in these orbitals.

b. Would you expect a molecule of He\(_2\) to be more stable of less stable than two free He atoms? Explain your answer, being brief but clear.
7. Consider the molecule CH₃NHOH.

a. Draw an orbital overlap picture for the molecule, assuming \( sp^3 \)-hybridization for all row 2 elements. Label the hybridization state of each atom, the type of chemical bond formed from each overlap, and clearly indicate the distribution of electrons using half-arrows.

b. How many different types of covalent chemical bonds are there in the molecule?

c. What is the expected value for the bond angle \( \angle \text{HON} \)? Include the appropriate \( \approx \), \( > \), or \( < \) symbol in your answer.
8. Consider the molecule CH$_2$(OH)C≡N.

a. Draw an orbital overlap picture for the molecule, assuming $sp^3$-hybridization for oxygen and the carbon with hydrogens on it, and $sp$-hybridization for the other carbon and the nitrogen. Label the hybridization state of each atom, the type of chemical bond formed from each overlap, and clearly indicate the distribution of electrons using half-arrows.

b. How many different types of covalent chemical bonds are there in the molecule? List them.

c. What is the expected value for the bond angle $\angle$H-C-H? Include the appropriate $\approx$, $>$, or $<$ symbol in your answer.
9. The structural formula of 2-methyl-1-oxacyclopropane is

```
  O
 / \   
C---C
 |   |
H---C
  H   H
```

a. Draw an orbital overlap picture for the molecule, assuming $sp^3$-hybridization for all row 2 elements. Label the hybridization state of each atom, the type of chemical bond formed from each overlap, and clearly indicated the distribution of electrons using half-arrows.

b. How many different types of covalent chemical bonds are there in the molecule?
10. Silicon, which is isoelectronic with carbon, can be found immediately below carbon in the periodic table. Not surprisingly, silicon is very similar to carbon: it is tetravalent, and readily makes tetrahedral analogs of alkanes. Thus, tetramethyldisilane, Si(CH$_3$)$_4$ (bp 27°C), like 2,2-dimethylpropane C(CH$_3$)$_4$ (bp 10°C) is a tetrahedral molecule with CSiC bond angles of 109.5°. It is entirely reasonable to assume that the Si atom is $sp^3$-hybridized. The only difference appears to be that the Si–C bonds are 20% longer than the corresponding C–C bond lengths.

On the other hand, unlike carbon-carbon (C=C) double bonds, silicon-carbon double bonds (Si=C) are very rare and usually are never observed to form. Using what you have learned from our discussions of how the electronic properties of atoms and molecules determine their bonding characteristics, suggest (a) why the bp of Si(CH$_3$)$_4$ is 17°C higher than that of C(CH$_3$)$_4$, and (b) why Si=C bonds are very rare and usually are never observed to form.

11. Consider the molecule N-Nitrosofluoramine. It has the molecular formula N$_2$HFO and bonding pattern F-N-N-O. The hydrogen atom is attached to the nitrogen that is is bonded to the fluorine atom.

(a) Draw the best, correct, complete Lewis structure for this molecule. Be sure to include all bonded and lone pair electrons.

(b) How many non-bonding valence electrons does this Lewis structure have?

(c) Using VSEPR theory, predict the value of the bond angle $\angle$FNN in the Lewis structure you have drawn.
12. a. Circle the ions which possess electron configurations that are isoelectronic with that of neon:

\[
\begin{align*}
\text{Na}^+ & \quad \text{F}^+ & \quad \text{Ca}^{2+} & \quad \text{O}^2- \\
\text{Cl}^- & \quad \text{H} & \quad \text{S}^2- & \quad \text{Br}^+ \\
\end{align*}
\]

b. In the space below, draw an electron configuration diagram for the lowest energy configuration of \(sp\)-hybridized \(F^+\).

13. The Lewis structure of caffeine is shown below.

a. Clearly add lone pair electrons so as to fill the octets of all atoms of caffeine.

b. In the spaces provided, provide the hybridization state of the nitrogens indicated.

c. The bond that the squiggly arrow is pointed at is at a double bond. This bond has formed from overlap of a \(\text{________}\) orbital of carbon and a \(\text{________}\) orbital of nitrogen to form a \(\text{________}\) bond, and from overlap of a \(\text{________}\) orbital of nitrogen and a \(\text{________}\) orbital of carbon to form a \(\text{________}\) bond.
14. Briefly answer each of the following questions:

a. Rank the following molecules from highest (1) to lowest (3) dipole moment:

\[
\text{H}_2\text{SO}_3 \quad \text{H}_2\text{CO}_3 \quad \text{H}_2\text{CH}_3
\]

b. Circle the most covalent chemical bond in the following molecule:

\[
\text{H}_2\text{CO}_2\text{Br}
\]

c. Circle the least polar covalent chemical bond in the following molecule:

\[
\text{H}_2\text{BONCH}_3
\]
15. Circle the letters of the two molecules below that have identical dipole moments, $\mu$.

A          B
\[ \text{Br} \quad \text{C} \quad \text{O} \quad \text{H} \]
\[ \text{Br} \quad \text{C} \quad \text{F} \quad \text{F} \]
\[ \text{H} \quad \text{C} \quad \text{F} \]
\[ \text{H} \quad \text{C} \quad \text{H} \]
\[ \text{O} \quad \text{H} \]

Now, clearly circle the most polar, covalent bond in molecule A of this problem.

16. Molecule CH$_3$F has dipole moment $\mu = 1.81$ D. This is smaller than that of CH$_3$Cl, with $\mu = 1.87$ D. This is surprising at first glance: based upon the relative electronegativities of F and Cl, you would predict the opposite to be the case! Using concepts from your study of general and organic chemistry, clearly explain why CH$_3$Cl, the molecule with the less electronegative atom, has the greater dipole moment.
17. Answer the following:

a. Draw the ground state valence electron configuration diagram of $sp^2$-hybridized oxygen.

b. Is the S–H bond considered to be a polar or a nonpolar covalent bond

c. There are other atoms that make covalent bonds to hydrogen with exactly the same bond polarization as the S–H bond. Identify one of these atoms:
Chapter Two: Molecular Representations

A vector description (left) and electrostatic potential map (right) illustrating the polarization of chlorofluoromethane
Concepts for Chapter 2: Molecular Representations

I. Ways to write structures of molecules
   A. Lewis dot structures: a : between atoms represents a covalent bond. Otherwise, it represents a nonbonding pair (also called a lone pair) of electrons.
   B. Lewis bond-line formulas: a — represents a two-electron covalent bond between atoms.
      1. A wedged bond-line means the bond is pointing out of the plane of the surface upon which it is drawn:
         means A is in the plane of the writing surface and Z is above it, closer to the viewer than A is
         A→Z
      1. A hatched bond-line means the bond is pointing behind the plane of the surface upon which it is drawn:
         means A is in the plane of the writing surface and Z is below it, farther away from the viewer than A is
         A···Z
   C. Condensed formulas: can be written on one line; e.g. CH₃CH₂OH
      1. Structural formula hybrids of types A and B are called partially condensed formulas.
   D. Carbon skeleton formulas (also called bond-line formulas)
      1. Every line is a covalent bond
      2. Every intersection of two or more lines is a C
      3. Every terminus of a line is a C unless another atom explicitly replaces it
      4. H atoms are implicit; add them as necessary to fill octets of C atoms

II. Functional groups
   A. An atom or an ensemble of atoms within a molecule that has a characteristic and predictable chemical behavior
      1. see accompanying chart or table 2.1 of textbook for descriptions of the most common functional groups

III. Analyzing structural formulas
   A. Lewis structures and the octet rule revisited
      1. Recall the complete rules for writing Lewis structures
         a. Count the number of valence electrons for a compound
         b. Draw a skeleton structure, joining atoms by single bonds, multiple bonds
         c. Check valence electrons for each atom, add lone pairs to fill octets
            d. Check for formal charge
               i. Formal charge =
                  (# valence electrons in electroneutral atomic species)
                  - (# valence electrons formally assigned to species in molecule)
         e. Eliminate as much formal charge as possible by making multiple bonds
      2. Relative stability of Lewis structures
         a. greatest number of covalent bonds
b. have all octets filled

c. have no formal charge separation

d. have least amount of formal charge separation

e. have formal charge assignments that are in agreement with relative electronegativites of atoms involved

IV. Resonance isomers

A. Lewis structures that differ only by the location of their $\pi$ and nonbonding electrons; the constitution of the structures and hybridization states of their atoms remain the same

1. Curved electron arrows can be used to illustrate how electrons in adjacent $p$ orbitals are localized or delocalized on and between atoms

2. Resonance isomers provide alterative electronic configurations of electrons in adjacent $p$ orbitals

3. A double-headed arrow is used between resonance isomers to illustrate that the real electronic configuration of the molecule is a hybrid of all resonance isomers

i. Resonance isomers may or may not contribute equally to the description of the actual electronic configuration of the molecule: Ranking criteria of III.

A. 2. above apply
### IMPORTANT FAMILIES OF ORGANIC COMPOUNDS

<table>
<thead>
<tr>
<th>Family</th>
<th>Alkane</th>
<th>Alkene</th>
<th>Alkyne</th>
<th>Arene</th>
<th>Haloalkane</th>
<th>Alkanol</th>
<th>Alkyl Ether</th>
<th>Alkyl Amine</th>
<th>Alkanal</th>
<th>Alkane</th>
<th>Alkanoic Acid</th>
<th>Alkyl Alkanoate</th>
<th>Alkynamide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Common Name</strong></td>
<td>Alkane</td>
<td>Alkylene</td>
<td>Alkyne</td>
<td>Arene</td>
<td>Alkyl Halide</td>
<td>Alcohol</td>
<td>Ether</td>
<td>Amine</td>
<td>Aldehyde</td>
<td>Ketone</td>
<td>Carboxylic Acid</td>
<td>Ester</td>
<td>Amide</td>
</tr>
<tr>
<td><strong>Specific Example</strong></td>
<td>CH₃CH₃</td>
<td>CH₂=CH₂</td>
<td>HC≡CH</td>
<td></td>
<td>CH₃CH₂Cl</td>
<td>CH₃CH₂OH</td>
<td>CH₂OCH₃</td>
<td>CH₃NH₂</td>
<td>H₂C≡CH</td>
<td>H₂C=CH₃</td>
<td>H₂C=O</td>
<td>H₂C=O</td>
<td>H₂C=O</td>
</tr>
<tr>
<td><strong>IUPAC Name</strong></td>
<td>Ethane</td>
<td>Ethene</td>
<td>Ethyne</td>
<td>Benzene</td>
<td>Chloroethane</td>
<td>Ethanol</td>
<td>Dimethyl ether</td>
<td>Methanamine</td>
<td>Ethanal</td>
<td>Propanone</td>
<td>Ethanoic Acid</td>
<td>Methyl ethanoate</td>
<td>Ethanamide</td>
</tr>
<tr>
<td><strong>Common Name</strong></td>
<td>Ethane</td>
<td>Ethylene</td>
<td>Acetylene</td>
<td>Benzene</td>
<td>Ethyl chloride</td>
<td>Ethyl alcohol</td>
<td>Methyl ether</td>
<td>Methyl amine</td>
<td>Acetaldehyde</td>
<td>Acetone</td>
<td>Acetic acid</td>
<td>Methyl acetate</td>
<td>Acetamide</td>
</tr>
<tr>
<td><strong>Generic Formula</strong></td>
<td>RH</td>
<td>R₂C=CR₂</td>
<td>RC≡CR</td>
<td>ArH</td>
<td>RX</td>
<td>ROH</td>
<td>ROR</td>
<td>RNR₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Functional Group</strong></td>
<td>C−C</td>
<td>C≡C</td>
<td>C≡C</td>
<td>Aromatic ring</td>
<td>C−X</td>
<td>C−OH</td>
<td>C−O−C</td>
<td>C−N</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

|                | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] | [Image of molecules] |
1. Draw a clear, correct skeletal (bond-line) formula for the condensed formula \( \text{CH(CH}_3)_2\text{CH}_2\text{CH(CH}_3)\text{CHBrF} \).

2. Draw each of the following:
   
   (a) The Lewis bond-line structure of

   ![Lewis bond-line structure of a complex molecule]

   (b) The condensed structure of

   ![Condensed structure of a molecule]

   (c) The skeletal (bond-line) structure of \( \text{C(CH}_3)_2=\text{CHCH}_2\text{CH}_2\text{C(CH=CH}_2)=\text{CH}_2 \)
3. a. Provide the letter of the functional group class to which each of the following belongs:

- ester
- amide
- amine
- alkanol
- carboxylic acid
- nitroalkane
- ketone
- ether

b. For the third molecule down, provide both a molecular formula and a Lewis bond-line structural formula.
4. Draw correct Lewis bond-line structures for two resonance isomers of each of the following chemical compounds. Be sure to indicate lone pairs and formal charge when appropriate.

a. CH₃CNO  

b. (HCO₂)⁻  

c. HN₃

5. a. Explain the meaning of the double-headed arrow and the single-headed arrow in the following equation. Use only a single sentence for each explanation.

b. Circle the more stable isomer.

6. a. Draw correct Lewis structures for both of the following chemical compounds. Be sure to indicate lone pairs and formal charge when appropriate.

A (CH₂CHCHF)⁺ (three resonance isomers) B. (NNN)⁻ (the most important resonance isomer)

b. Draw two resonance isomeric Lewis structures for the molecule (CH₂CHO)⁻, and circle the resonance isomer which has greater importance in describing the resonance hybrid structure.
7. Consider a hypothetical compound, CH₂Br₂, which possesses a square planar geometry—that is, each of the four groups bonded to carbon is arranged so that all lie in the same plane. For such a compound, two distinct structures are possible.

   a. Draw these two structures.

   b. Are these two structures resonance structures? Why or why not?

   c. Suppose you had samples of each of the isomers, but did not know which was which. What physical property differences would you predict to help you identify the isomers?

   d. In fact, no more than one compound of formula CH₂Br₂ has ever been found in all of history. Explain why the failure to isolate more than one isomer of CH₂Br₂ is consistent with assigning the compound a tetrahedral geometry. Does this failure prove a tetrahedral structure? Why or why not?
8. a. Circle the resonance isomer which would be predicted to have the largest contribution to the molecule's resonance hybrid:

\[
\begin{array}{c}
\overset{-}{\overset{\Large{\text{O}}}{{\overset{\Large{\text{N}}}{\text{O}}}}} \\
\overset{\text{+}}{\overset{\text{O}}{\text{O}}} \\
\end{array}
\]

\[
\begin{array}{c}
\overset{-}{\overset{\Large{\text{O}}}{{\overset{\Large{\text{N}}}{\text{O}}}}} \\
\overset{\text{+}}{\overset{\text{O}}{\text{O}}} \\
\end{array}
\]

\[
\begin{array}{c}
\overset{-}{\overset{\Large{\text{O}}}{{\overset{\Large{\text{N}}}{\text{O}}}}} \\
\overset{\text{+}}{\overset{\text{O}}{\text{O}}} \\
\end{array}
\]

b. What is the molecular formula of the resonance isomer you have circled?

c. Are the molecular formulas of all three resonance isomers of this question the same?

d. Label the hybridization states of the carbon atoms of each of the three resonance isomers.

9. Consider the molecule with condensed formula \( \text{CH}_2=\text{NOH} \).

(a) Draw two nonidentical, correct and complete Lewis structure resonance isomers for this molecule. Be sure to include all bonded and lone pair electrons, any formal charges, and a double-headed resonance arrow.

(b) Of the two you have drawn, circle the better resonance isomer and briefly explain your choice.

(c) Using VSEPR theory, predict the value of the bond angle \( \angle \text{H-C-N} \).
10. Consider the following incorrect Lewis structure:

![Lewis structure](image)

(a) Provide two explanations why this Lewis structure is not correct as drawn.

11. Consider the molecule at right, which was prepared by Creighton graduate Derek Woodrum.

![Molecule](image)

a. How many $sp^3$-hybridized carbons does this molecule have? 

b. How many $\pi$ bonds does this molecule have?

c. How many lone pairs of electrons does this molecule have?
12. For A - D below, clearly add the nonbonding electrons.

Now, rank the relative importance of contribution of each resonance isomer to the resonance hybrid, from most important to least important:

(most important) __________ __________ __________

(least important) __________

13. Below is a multifunctional molecule:

a. Identify each of the circled functional groups by writing its name in the blank provided.

b. Briefly but clearly, explain what the wedged bonds in the skeletal structure indicate.
14. Let’s revisit a type of problem introduced in Chapter 1. This kind of problem may be easier for you now: Consider the molecule formoxime, which has the condensed formula CH$_2$=NOH.

   a. Draw the Lewis line-bond structure of this molecule. Be sure to include all nonbonding valence electrons in your structure.

   b. Draw an orbital overlap diagram of this molecule. Label the hybridization state of each atom, the type of each chemical bond formed by orbital overlap, and clearly indicate the distribution of electrons using half-arrows.

15. The structure of the antidepressant drug Pristiq, recently introduced by Wyeth, is shown at right.

   a. Count carefully: how many sp$^3$-hybridized carbon atoms does Pristiq have?

   b. What is the molecular formula of Pristiq?

   c. Indicate the value of the C–N–C bond angles of Pristiq in degrees. Use the term “a little greater than,” “a little less than,” or “about equal to” in your answer.
16. Consider the cation below, which can be drawn as number of resonance isomers. One of its resonance isomers is

\[ \begin{align*}
&\vdots Cl : \\
&\vdots \\
&\text{+} \\
&\text{C} \\
&\text{C} \\
&\text{C} \\
&\text{C} \\
&\text{C} \\
&\text{C} \\
\end{align*} \]

a. There five other resonance isomers of this molecule. Provide two of them, one of which must have all octets filled. Use correct and complete Lewis line-bond structures. Be sure to include all bonded and lone pair electrons, any formal charges, and a double-headed resonance arrow that connects your structures.

b. How many valence electrons does this molecule have? ____________

c. Do the carbon and chlorine atoms in this molecule have the same hybridization states? Circle the correct response.

\[ \begin{align*}
\text{YES} & \quad \text{NO} \\
\end{align*} \]

d. Use the resonance structure at the top of the page to clearly label the hybridization state of the chlorine atom.
17. Consider the skeletal structure of Minocin®, an tetracycline class antibiotic:

a. Explicitly add in all of the nonbonding electrons in the structure of Minocin.

b. How many hydrogen atoms does the molecular formula of Minocin have? 

 c. How many $sp^3$-hybridized carbon atoms does Minocin have? 

d. How many C–N $\sigma$ bonds does Minocin have? 

e. Minocin has two identical C–N–C bond angles. What is their approximate value in degrees?

f. What does the wedged C–N bond in the structural formula of Minocin mean?
17, 21-Dimethylheptatriacontane, a sex attractant pheromone of the tsetse fly
ChM 321: Summary of Important Concepts

Concepts for Chapter 3: Acids and Bases

I. Acid-base theories
   A. Brønsted-Lowry acid-base theory
      1. Brønsted-Lowry acids are proton donors
      2. Brønsted-Lowry bases are proton acceptors
      3. Relationships of conjugate acids and bases
   B. Curved electron arrows illustrate how acids and bases react
   C. pKₐ
      1. pKₐ = -logKₐ, where for the reaction HA + H₂O → H₃O⁺ + A⁻,
         \[ K_a = \frac{[H_3O^+][A^-]}{[HA]} \]
      2. Strong acids have pKₐ < 1
      3. Moderate acids have pKₐ = 1 - 10
      4. Weak acids have pKₐ > 16
      5. pKₐ's can be used to predict in which direction an acid-base equilibrium will lie
   D. Acidity as a function of structure
      1. Four general factors influencing the stability of an acid’s conjugate base determine how strong an acid is going to be:
         a. Intrinsic properties of the atom bonded to H
            i. Electronegativity
            ii. Size
         b. Resonance stabilization of the conjugate base
         c. Inductive stabilization of the conjugate base
         d. Hybridization effects
      2. Trends
         a. In any given row of the periodic table, acidity increases as ΔEN increases
         b. In any given column of the periodic table, the weaker the H-heteroatom bond, the stronger the acid
         c. For C-H bonds, pKₐ C₃p-H > C₃p²-H > C₃p³-H
   E. Acidity as a function of other factors
      1. Solvation
         a. Increased dipolar solvent-acid interactions decrease pKₐ
      2. Counterion of conjugate base
         a. Generally not significant
   F. Lewis acid-base theory
1. Lewis bases are electron donors
   a. Lewis bases which, by donating electrons, undergo formation of a covalent bond are called \textit{nucleophiles}.

2. Lewis acids are electron acceptors
   a. Lewis acids which, by accepting electrons, undergo formation of a covalent bond are called \textit{electrophiles}.
1. Provide short answers for each of the following:

a. If the pK_a of an organic compound is large, it must be a relatively ______________ acid.

b. If the pK_a of an organic compound is small, the conjugate base of that compound is a relatively ______________ base.

c. Borane, BH_3, should have a pK_a that is ______________ than that of ethanol, C_2H_5OH.

2. 2,2,2-Trifluoro-1-ethanol has a pK_a of 9.7 and ethanol a pK_a of 16.

a. Which is the stronger Brønsted-Lowry acid? ______________

b. Use your answer of part a to draw the equilibrium acid-base reaction between these two compounds. Include the curved electron arrows that illustrate how the proton of the acid is transferred to the base.

c. Label your equilibrium reaction with the terms stronger acid, weaker acid, stronger base, and weaker base.

d. Knowing that the pK_a of the conjugate acid of ethanol is 1.5 and that of 2,2,2-trifluoroethanol is -1.5, will the equilibrium lie to the left or right of the reaction you have written? ______________

e. Will the alkane ethane, CH_3CH_3, have a pK_a greater than or less than the pK_a of ethanol? ______________

3. Rank the following from 1 - 4 according to their relative pK_a values. Use 1 for the most acidic and 4 for
the least acidic:

\[ \text{Carboxyl} \quad \text{Aminohydroxide} \quad \text{Aldehyde} \quad \text{Thioester} \]

4. Consider the following Brønsted-Lowry acid-base reaction:

\[ \text{H}_2\text{O} + \text{H}_2\text{SO}_4 \rightleftharpoons \text{HSO}_4^- + \text{H}_2\text{O}^+ \]

a. Use curved electron arrows to show how the acid and base on the left of the equilibrium arrow undergo proton transfer to result in the products on the right.

b. Label the acid, base, conjugate acid, and conjugate base of the reaction.

c. Which is the stronger Brønsted-Lowry acid: one with \( K_{eq} = 3.5 \times 10^{-8} \) or one with \( K_{eq} = 1.4 \times 10^3 \)?
6. a. For the following chemical equilibrium, identify each chemical species on either side of the equilibrium arrow as being the strong acid (SA), weak acid (WA), strong base (SB), or weak base (WB) of the equilibrium. Refer to the table of pKₐ values to help you in your assignments.

\[
\text{OH} \quad + \quad \text{OCCF}_3 \quad \overset{k}{\Longleftrightarrow} \quad \text{HOCCF}_3
\]

<table>
<thead>
<tr>
<th>Species</th>
<th>pKₐ</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCl</td>
<td>-7</td>
</tr>
<tr>
<td>H₃O⁺</td>
<td>-1.7</td>
</tr>
<tr>
<td>HOCCF₃</td>
<td>0</td>
</tr>
<tr>
<td>H₂O</td>
<td>15.7</td>
</tr>
<tr>
<td>CH₃CH₂OH</td>
<td>16</td>
</tr>
</tbody>
</table>

b. Will the reaction equilibrium constant, \(k\), be greater or less than 1? ✅
7. This is a difficult problem that will really test your ability to use resonance and inductive effects to predict relative acidities! Rank these carboxylic acids according to their $pK_a$ values:

- **A**
- **B**
- **C**
- **D**

**highest $pK_a$**

**lowest $pK_a$**

8. Complete the phrase: Borane, BH$_3$, has a $pK_a$ that is _______________ than that of ethanol, C$_2$H$_5$OH.
9. a. Examine the following three acid-base equilibrium reactions, and fill in the table below them:

<table>
<thead>
<tr>
<th>Equilibrium reaction</th>
<th>What are the 2 letters of the reactants acting as acids?</th>
<th>What is the letter of the reactant that is the stronger base?</th>
<th>Is the equilibrium constant greater than 1, less than 1, or equal to 1?</th>
</tr>
</thead>
<tbody>
<tr>
<td>i.</td>
<td>H, S</td>
<td>H</td>
<td>&gt; 1</td>
</tr>
<tr>
<td>ii.</td>
<td>O, H</td>
<td>H</td>
<td>&gt; 1</td>
</tr>
</tbody>
</table>

b. Use curved electron arrow formalism to show how reactants A and B of equilibrium reaction i. are converted into reactants C and D.

<table>
<thead>
<tr>
<th>Some pKₐ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid</td>
</tr>
<tr>
<td>pKₐ</td>
</tr>
</tbody>
</table>
10. Consider the following chemical reaction:

a. Clearly label the compound acting as a Lewis acid and the compound acting as the Lewis base in this reaction.

b. Use curved electron arrow formalism to show how reactants on the left side of the equilibrium arrow form the product on the right side of the equilibrium arrow.
The most stable conformation of isopropylcyclohexane
Concepts for Chapter 4: Alkanes and Cycloalkanes

I. Alkanes: structure and bonding
   A. sp³-hybridization of carbons
   B. Constitutional isomerism
      1. Also known as structural isomerism
      2. Constitutional isomers have same molecular formula but different bonding patterns between atoms
      3. The only way to convert one into the other is to break and then remake chemical bonds between two or more atoms
   C. Relative stabilities
      1. branching effects
      2. measure relative stabilities by ΔH of combustion

II. Nomenclature of alkanes
   A. The IUPAC system
      1. alkanes
      2. branching substituents on parent alkane chain
      3. numbering parent chain
      4. alphabetizing substituents
   B. Common substituent names
      1. isopropyl
      2. isobutyl
      3. sec-butyl
      4. tert-butyl

III. Primary, secondary, tertiary and quaternary carbons and substituents in molecules
   A. Methyl, methylene, and methine hydrogens
   B. Chemically equivalent atoms in molecules

IV. Stereoisomerism
   A. Stereoisomers have the same molecular formula and the same constitution, but differ by the arrangement of their atoms in space.
   B. There are two classes of stereoisomers: conformational stereoisomers and configurational stereoisomers
V. Conformational stereoisomers (conformers or rotational isomers)
A. Have the same molecular formula and constitution but differ by the arrangement of their atoms in space. They can be converted into each other by rotations about sigma bonds
B. Structural representations (here, using a conformation of 3,4-dichloro-3,4-dimethylhexane as an example)
   1. Wedge and hatched line

   ![Wedge and hatched line](image)

   2. Sawhorse projection

   ![Sawhorse projection](image)

   3. Newman projection

   ![Newman projection](image)

C. Describing conformations
   1. Dihedral angles (torsion angles)
   2. Staggered conformations
      a. Anti relationship between adjacent substituents
      b. Gauche relationship between adjacent substituents
      c. Relative stabilities
   3. Eclipsed conformations
      a. Relative stabilities
   4. Staggered almost always more stable than eclipsed
   5. $\Delta E$ versus torsion angle plots

VI. Nomenclature of cycloalkanes
A. The IUPAC system
   1. Cycloalkane
   2. Otherwise, identical to alkanes
VII. Stereoisomerism

A. Configurational stereoisomerism of disubstituted cycloalkanes: cis-trans isomerism
   1. Stereoisomers have the same molecular formula and the same constitution, but differ by the arrangement of their atoms in space. Configurational stereoisomers can only be converted into each other by breaking bonds and reforming them.
   2. cis-trans isomers of disubstituted cyclohexanes belong to the diastereoisomer class of configurational stereoisomers.
      a. cis and trans nomenclature
         i. cis -- identical substituents on the same side of the ring
         ii. trans -- identical substituents on opposing sides of the ring

B. Conformational stereoisomerism of cycloalkanes
   1. Stereoisomers have the same molecular formula and constitution, but differ by the arrangement of their atoms in space. Conformational isomers can be converted into each other by rotations about sigma bonds.
   2. Cyclohexane and ring flipping
      a. chair
         i. axial and equatorial positions

\[ \text{Diagram: Chair conformation} \]

b. half-chair

\[ \text{Diagram: Half-chair conformation} \]

b. twist boat

\[ \text{Diagram: Twist boat conformation} \]
c. boat
   ii. "flagpole" interaction

\[ \text{Diagram of boat conformation} \]

d. chair almost always more stable than boat
e. an energy versus torsion diagram illustrates the relative energy of the
cyclohexane ring system as it changes conformation via the path chair–half-
chair–twist boat–boat–twist boat–half-chair–chair

2. Monosubstituted cyclohexane
   a. axial
      i. causes unfavorable (high energy) 1,3-diaxial interactions (really
gauche interactions)
   b. equatorial favored; removes 1,3-diaxial interactions

3. Disubstituted cyclohexanes
   a. cis and trans nomenclature (see above) – these diastereomers do not
      necessarily identical energy chair conformations
   b. table of findings:

<table>
<thead>
<tr>
<th>Substitution pattern</th>
<th>More stable conformer</th>
<th>More stable stereoisomer</th>
</tr>
</thead>
<tbody>
<tr>
<td>cis-1,2</td>
<td>ax–eq</td>
<td>trans</td>
</tr>
<tr>
<td>trans-1,2</td>
<td>dieq</td>
<td></td>
</tr>
<tr>
<td>cis-1,3</td>
<td>dieq</td>
<td>cis</td>
</tr>
<tr>
<td>trans-1,3</td>
<td>ax-eq</td>
<td></td>
</tr>
<tr>
<td>cis-1,4</td>
<td>ax-eq</td>
<td>trans</td>
</tr>
<tr>
<td>trans-1,4</td>
<td>dieq</td>
<td></td>
</tr>
</tbody>
</table>

4. Multisubstituted cyclohexanes are analyzed in the same manner: lower energy
   chair conformation is the one that minimizes the number and severity of 1,3-
diaxial interactions

VIII. Conformations of rings other than cyclohexane
   A. Cyclopropane
      1. flat, planar
      2. C–C \( \sigma \) bonds are bent and therefore weaker than normal \( \sigma \) bonds
      3. all C–H bonds are eclipsed
   B. Cyclobutane
      1. nonplanar bent (bird-like) form
2. bent form allows for some easing of C–H eclipsing interactions

C. Cyclopentane
   1. Envelope conformation preferred
   2. Pseudoaxial, pseudoequatorial positions

D. Medium and large rings

E. Structures containing more than one ring
   1. Spirocycloalkanes: two rings share one common atom
   2. Polycycloalkanes: two rings share two or more common atoms
   3. Catenanes and twistanes: two rings share no or all carbons

IX. Heterocycles and their conformations
   A. Heterocycles are cycloalkanes that have had one or more of their ring carbons replaced with other atoms. Most common are N, O, and S
1. Give a correct chemical structure or the best, correct IUPAC name for each of the following:

a. 

![Chemical structure](image)

b. 3-ethyl-2,2,5,5-tetramethylhexane

c. 3,4-Dimethyl-4-(1,1-dimethylethyl)heptane

d. 

![Chemical structure](image)
2. Provide structural formulas for three constitutional isomers of the alkane C₈H₁₈ and provide a correct, acceptable IUPAC name for each.

3. Provide brief answers to the following questions:
   a. Circle the compound with the lowest boiling point:

   ![Structural formulas]

   b. What type of intermolecular cohesive forces are operating when the compounds of part a above are the liquid state?
c. Rank the following molecules from lowest to highest boiling point:

A

B

C

D

d. Rank the following molecules from lowest (1) to highest (4) relative thermodynamic stability:

4. Consider the molecule at right, which was prepared by Creighton graduate Derek Woodrum.

a. How many of the \(sp^3\)-hybridized carbons are quaternary carbons?

b. How many methyl groups does this molecule have?

c. How many methylene groups does this molecule have?
5. Provide the best, most preferred IUPAC name for the following molecule:

![Molecule Diagram]

6. Draw C3–C4 Newman projections of the highest and lowest energy staggered conformations of 2,4,5-trimethyloctane. (A C3–C4 Newman projection is one where C3 is the steering wheel carbon and C4 is the dashboard carbon.)
7. Consider the molecule 2-methylpentane.

   a. Draw Newman projections of all staggered conformations of 2-methylpentane viewed along the C3–C4 bond.

   b. Draw Newman projections of all eclipsed conformations of 2-methylpentane viewed along the C3–C4 bond.
c. Place all of the structures drawn in parts a and b on the free energy diagram below. "Torsion angle" refers to the angle swept out between the C2–C3 and C4–C5 bonds as the molecule is rotated about the C3–C4 bond.

8. Consider the molecule 2,3-dimethylpentane.
   
a. Draw Newman projections of all staggered conformations of 2,3-dimethylpentane viewed along the C2–C3 bond.
b. Draw Newman projections of all eclipsed conformations of 2,3-dimethylpentane viewed along the C2–C3 bond.

c. Place all of the structures drawn in parts a and b on the free energy diagram below. "Torsion angle" refers to the angle swept out between the C1–C2 and C3–C4 bonds as the molecule is rotated about the C2–C3 bond.
9. Consider the amino acid derivative valinol, which has molecular formula (CH₃)₂CHCH(NH₂)CH₂OH

. a. Draw a Newman projection for this molecule, looking from the carbon bearing the oxygen to the carbon bearing the nitrogen.

b. The lowest relative energy conformation of valinol is observed to be one of its *eclipsed* conformations! Specifically, it is the one with the OH and NH₂ substituents eclipsed. Draw the Newman projection of this conformation and explain why it is of such low relative energy.

10. Consider the molecule 2-methylbutane.

a. Draw Newman projections of all eclipsed conformations of 2-methylbutane viewed along the C2–C3 bond. Label them with letters.
b. Draw Newman projections of all staggered conformations of 2-methylbutane viewed along the C2–C3 bond. Label them with letters as well.

c. Using the letter labels to identify the Newman projections drawn above, position each projection on the free energy diagram below and draw a curve showing how the energy of 2-methylbutane varies as its conformation changes. “Torsion angle” refers to the angle swept out between the C1–C2 and C3–C4 bonds as the molecule is rotated about the C2–C3 bond.
11. Give a correct chemical structure or a correct name for each of the following:

a.

![Chemical structure](image)

b. cis-1-ethyl-3-isopropylcyclopentane

c.

![Chemical structure](image)

12. Rank the following cycloalkanes according from least to most stable:

![Cycloalkanes](image)

A B C D
13. a. Provide the best, most preferred IUPAC name for the following molecule:

b. Draw a skeletal structure of any constitutional isomer of the molecule in part a.

c. Give a clear, correct structural formula for 2-cyclobutyl-3-isopropylbutane.

d. 2-Cyclobutyl-3-isopropylbutane is not the best IUPAC name for the molecule you just drew. Provide the best, correct IUPAC name for it.
14. Draw both the more stable and the less stable chair conformation of cis-1-isobutyl-2-methylcyclohexane. Then, supply answers to the question below.

<table>
<thead>
<tr>
<th>more stable conformation</th>
<th>less stable conformation</th>
</tr>
</thead>
</table>

**How many**

- axial substituents? ______________________ ________________ __
- equatorial substituents? ______________________ ________________ __
- non-H–H diaxial interactions? ______________________ ________________ __

15. Ignoring twist boat conformations, draw all the nonidentical boat conformations possible for the molecule cis-1-cyclopropyl-2-methylcyclohexane. Circle that boat conformation which you feel represents the lowest energy boat conformation of the molecule.
16. Consider the following pairs of conformations:

A. 

```
H
CH₃
H
```

1

```
CH₃
H
```

2

B. 

```
H
CH₃
H
```

3

```
H
CH₃
```

4

C. 

```
H
H
H
```

5

```
H
```

6

D. 

```
H
CH₃
H
```

7

```
H
CH₃
```

8

a. Circle the number of the more stable conformation in each pair. If both conformations of a pair are of equal stability, circle the numbers of both of those conformations.

b. How many CH₃–CH₃ gauche interactions and how many CH₃–H 1,3-diaxial interactions are present in the following conformations:

<table>
<thead>
<tr>
<th>Conformation</th>
<th>CH₃–CH₃ gauche</th>
<th>CH₃–H 1,3-diaxial</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>2</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>3</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>4</td>
<td>______</td>
<td>______</td>
</tr>
</tbody>
</table>

c. Name the type of conformation for 5 and 6.

5 ____________________

6 ____________________

d. For conformation 5, label the hydrogens shown as axial (a) or equatorial (e).
17. The stereoisomer of 1,2,3,4,5,6-hexaisopropylcyclohexane that has all of its isopropyl substituents in an alternating up and down arrangement is quite remarkable in that the thermodynamically preferred chair conformation has all of the isopropyl groups in axial positions! Carefully draw both possible chair conformations of this stereoisomer, then, using your knowledge of conformational analysis, explain the observed conformational preference of this molecule.

18. Draw the two possible chair conformations of 2-tert-butyl-1-ethyl-1-isopropylcyclohexane that have the ethyl and the tert-butyl groups in a trans orientation. Then, supply answers to the question below.

a. Circle the more stable conformation.
b. When the more stable conformation is viewed along the C1–C2 bond:
   • the tert-butyl group on C2 is ____________ to C6 of the cyclohexane ring.
   • the ethyl group on C1 is anti to the ___________ group of C2.

c. How many hydrogens are found in axial positions in the more stable conformation? __________

d. In the more stable conformation, is the equatorial hydrogen on C5 on the same or opposite side of the 
cyclohexane ring as the isopropyl group on C1? __________

19.  (a)  Draw both chair conformations for molecules A and B:

![A and B](image)

(b) Of the four chair conformations you have drawn, circle the lowest energy conformation.

(c) Using your knowledge of conformational analysis, briefly explain your choice of lowest energy conformation.
20. Do the following pair of structural formulas represent constitutional isomers, conformational isomers, stereoisomers, or are they identical structural formulas?

\[ \text{CH}_3 \quad \text{CuLi} \]

21. Consider the following reaction, which adds two CH\(_3\) groups to the starting material. Two isomeric products, A and B, are possible. In the laboratory, the only product that forms is A.

\[
\text{O} 
\begin{array}{c}
\text{1. (CH\(_3\))\(_2\)CuLi} \\
\text{2. CH\(_3\)I}
\end{array} 
\]

\[
\begin{array}{c}
\text{A} \\
\text{B}
\end{array} 
\]

This result might be surprising to some organic chemists. Using your knowledge of conformational analysis, draw the lowest energy chair conformations of A and B. Determine which will have the lower potential energy, and provide a brief chemical explanation that justifies your choice.
22. a. Provide the best, correct IUPAC name for the molecule below.

![Molecule with Cl](image)

b. In the conformation given, how many hydrogens are gauche to the chlorine-containing substituent in the molecule you have just named?

23. Clearly draw both chair conformations of the molecule below. Then, clearly circle the lower energy chair conformation.

![Molecule with O and NH2](image)

24. Consider cis-1,4-diethylcyclobutane and trans-1,4-dimethylcyclohexane.

a. Clearly and accurately draw trans-1,4-dimethylcyclohexane in both of its chair conformations, then circle the higher energy conformation.

b. Circle the term that best describes the relationship of cis-1,4-diethylcyclobutane and trans-1,4-dimethylcyclohexane:

- diastereomers
- configurational stereoisomers
- constitutional isomers
- conformational stereoisomers

iii. cis-1,4-Diethylcyclobutane is about 38 kcal/mol higher in energy than trans-1,4-dimethylcyclohexane. Briefly but clearly, explain why.
25.  

a. Provide the best, most correct IUPAC name for the following compound:

![Compound Image]

b. Now consider the molecule’s conformation. When viewed as indicated below, circle the word that best describes this conformation.

![Conformation Image]  
eclipsed  cis  chair
half-chair  staggered  trans

c. Draw a Newman projection of the highest energy eclipsed conformation and a Newman projection of the lowest energy staggered conformation of the molecule in part b viewed along the $\sigma$ bond indicated.

b. In the staggered conformation Newman projection you have drawn, what is the value of the dihedral angle of the ethyl substituent and the propyl substituent?

c. In the eclipsed conformation Newman projection you have drawn, how many methyl substituents are gauche to the propyl substituent?
(S)-(−)-Dopa, used to treat Parkinson's disease, and its medically ineffective (R)-(+) enantiomer.
Concepts for Chapter 5: Stereoisomerism

I. Types of stereoisomerism
   A. Stereoisomers have the same molecular formula and the same constitution. They differ by the arrangement of their atoms in space
      1. Conformational stereoisomers
         a. Conformational isomers are stereoisomers that are interconvertible by rotations about sigma bonds
      2. Configurational stereoisomers
         a. Configurational stereoisomers are stereoisomers that are interconvertible by breaking bonds and reforming them
         b. Configurational stereoisomer classes
            i. enantiomers
            ii. diastereomers

II. Enantiomers
   A. Compounds of the same molecular formula and constitution that differ only by the arrangement of their atoms in space, making them stereoisomers. The special way that the atoms are related are as object and its nonsuperimposable mirror image, defining them as enantiomers. They are convertible only by breaking and reforming chemical bonds.
      1. Physical properties
         a. identical in all respects except for rotation of plane polarized light in opposite directions
         b. compounds that rotate place polarized light are optically active
         c. are said to be dissymmetric (synonymous with "chiral")
         d. possess one or more stereogenic centers, usually tetrahedral carbons with four different groups attached
            i. stereogenic centers are also called chirality centers, chiral centers, or stereocenters
         e. have a specific rotation, $[\alpha]_D = 100\alpha/c_l$
      2. ($R$) and ($S$) nomenclature system to specify configuration
      3. Racemic mixture (racemate): A 50:50 mixture of enantiomers having optical rotation of 0.0°
         a. Other mixtures are characterized by enantiomeric excess (ee)

III. Diastereomers
   A. Stereoisomers that are not mirror image isomers (enantiomers) are diastereomers.
      1. cis, trans stereoisomers of disubstituted cycloalanes are diastereomers
      2. cis, trans stereoisomers of alkenes are diastereoisomers
      3. Maximum number of stereoisomers: the $2^n$ rule, where $n =$ number of stereogenic elements (stereocenters and double bonds)

IV. Meso isomers
   A. Compounds with stereocenters which have mirror images that are the same (that is, are superimposable upon each other) are symmetric molecules. They are achiral and are called meso isomers (mesomers).

V. Representations of enantiomers, diastereomers, and meso isomers
   A. Wedged-and-hatched line notation
B. Sawhorse projections  
C. Fisher (cruciform) projections (example below is (2S,3R)-2,3-dichlorohexane)

\[
\begin{align*}
   & \text{CH}_3 \\
   & \text{H} \quad \text{Cl} \\
   & \text{H} \quad \text{Cl} \\
\end{align*}
\]

IV. Reactions involving stereoisomers  
\[\text{CH}_2\text{CH}_2\text{CH}_3\]  
A. Optically inactive starting materials provide optically inactive products  
   1. Optically inactive starting materials that generate products with new  
      stereocenters produce racemic mixtures and/or meso isomers  
B. Optically active starting materials with stereocenters not involved in a reaction  
   provide optically active products  
   1. Optically active starting materials that generate products with new  
      stereocenters produce mixtures of diastereomers  
C. Optically active starting materials with stereocenters that are involved in a reaction  
   (that is, bonds are broken and made at stereocenters) can produce  
   1. products of the same configuration (called retention)  
   2. products of opposite configuration (called inversion)  
   3. products of mixed configurations (called racemization)  
   4. achiral products (e.g., eliminations) that may or may not still be formed  
      stereoselectively
1. Provide answers for each of the following questions:

a. Classify each pair of molecules shown as being enantiomers, diastereomers, constitutional isomers, or as being identical:

- Enantiomers
- Constitutional isomers
- Diastereomers
- Identical
b. Label the asymmetric center in each molecule as \( R \) or \( S \):
2. Consider the following reaction scheme which can be used to identify the structure of compound \( Y \), with molecular formula \( C_8H_{12} \): 

\[
\begin{align*}
\text{C}_8\text{H}_{12} & \xrightarrow{1. \text{O}_3} \text{O} & & \text{O} \\
\text{Y} & \xrightarrow{2. \text{Zn, H}_2\text{O}} \begin{array}{c}
\text{H}_3\text{C} \\
\text{H} \\
\text{O} \\
\text{H} \\
\text{O}
\end{array} & + & \begin{array}{c}
\text{H} \\
\text{O} \\
\text{H}
\end{array} \\
\text{xS} & \xrightarrow{\text{Pt}} \text{H}_2 \\
\text{H}_2 & \text{Pt} \\
\text{C}_8\text{H}_{16} & \text{Z}
\end{align*}
\]

a. Is the stereogenic center shown for one of the products \((R)\) or \((S)\)? 

3. Consider the following stereoisomer:

Is this compound capable of rotating plane-polarized light? Clearly explain your reasoning.
4. Classify each pair of molecules shown as being enantiomers, diastereomers, constitutional isomers, conformational isomers, meso, or as being identical:

a. 

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{Cl} & \quad \text{CH}_2\text{CH}_3 \\
\text{Cl} & \quad \text{H}
\end{align*}
\]

b. 

\[
\begin{align*}
\text{CH}_3 & \quad \text{H} \\
\text{H} & \quad \text{Br} \\
\text{Br} & \quad \text{H} \\
\text{Br} & \quad \text{H}
\end{align*}
\]

c. 

\[
\begin{align*}
\text{CH}_3 & \quad \text{Br} \\
\text{Br} & \quad \text{Br} \\
\text{Br} & \quad \text{CH}_3
\end{align*}
\]

d. 

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{SCH}_3 & \quad \text{SCH}_3\text{OCH}_3 \\
\text{OCH}_3 & \quad \text{H}_3\text{C} \quad \text{CH}_2\text{CH}_3
\end{align*}
\]

e. 

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*}
\]
5. Which compound, A or B, is capable of having an enantiomer? Explain your answer.

A

H
CH₂CH₃
F
H
CH₂CH₂F

B

H
CH₂CH₃
F
H
CH₂CH₂F

6. Circle the structure of the molecule that is not a meso-isomer:

7. a. Place an "X" before the correct identifying term for each pair of structures shown:

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CH₂H</td>
<td>H₃C</td>
</tr>
<tr>
<td>HO</td>
<td>OH</td>
</tr>
<tr>
<td>CH₃</td>
<td>CH₂CH₃</td>
</tr>
<tr>
<td>Cl</td>
<td></td>
</tr>
<tr>
<td>enantiomers</td>
<td>diastereomers</td>
</tr>
<tr>
<td>identical</td>
<td>conformational isomers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃</td>
<td>CH₂CH₂Br</td>
</tr>
<tr>
<td>HOCH₂</td>
<td>H</td>
</tr>
<tr>
<td>CH₃</td>
<td>CH₃</td>
</tr>
<tr>
<td>CH₂OH</td>
<td>CH₂CH₂Br</td>
</tr>
<tr>
<td>enantiomers</td>
<td>diastereomers</td>
</tr>
<tr>
<td>conformational isomers</td>
<td>constitutional isomers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Br</td>
<td>Br</td>
</tr>
<tr>
<td>enantiomers</td>
<td>diastereomers</td>
</tr>
<tr>
<td>identical</td>
<td>constitutional isomers</td>
</tr>
</tbody>
</table>
b. Label the stereogenic carbon in each case as \((R)\) or \((S)\):

Chlorpheniramine
(active ingredient in Coricidin)

Limonene
(smells like lemons)
8. When \((S)\)-4-\textit{tert}-butyl-1-methyl-1-cyclohexene is treated with bromine, a single cyclohexane product, \((1R,2R,4S)\)-1,2-dibromo-4-\textit{tert}-butyl-1-methylcyclohexane results.

   a. Draw structural formula of the product.

   b. In the product, is the methyl group is gauche or anti to the bromo substituent on carbon 2? \______________.
9. a. In the spaces provided, label stereogenic carbons of each molecule as \((R)\) or \((S)\):

![Molecule 1]

Efavirenz, an anti-HIV drug

![Molecule 2]

Meridia®, an antiobesity drug

b. Draw a clear, correct Fisher projection of the molecule \((3S,4R)\)-3,4-dimethylhexane.

c. Is \((3S,4R)\)-3,4-dimethylhexane a meso-isomer? Very briefly, explain your answer.
10. Draw a clear Newman projection of the highest energy conformation of (3R,4S)-4-ethyl-3-methylheptane viewed along the C3--C4 bond (carbon number 3 is the "steering wheel" and carbon number 4 is the "dashboard" of the Newman projection).

11. Place an "X" before the correct identifying term for each pair of structures shown:

- enantiomers
- diastereomers
- conformational isomers
- constitutional isomers
12.  Circle the correct stereochemical description for each of the following pairs of structures:

a.  
\[
\begin{align*}
\text{O} & \quad \text{C} & \quad 3\text{r} \\
\text{C} & \quad 3\text{l} & \quad 1\text{r} \\
\end{align*}
\]

identical  
enantiomers  
diastereoisomers  
constitutional isomers

b.  
\[
\begin{align*}
\text{CONH}_2 & \quad \text{C} & \quad \text{C} & \quad \text{N} & \quad \text{I} \\
\text{C} & \quad \text{C} & \quad \text{I} & \quad \text{C} & \quad \text{I} \\
\text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} \\
\end{align*}
\]

identical  
enantiomers  
diastereoisomers  
conformational isomers

c.  
\[
\begin{align*}
\text{Br} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} \\
\end{align*}
\]

identical  
enantiomers  
diastereoisomers  
constitutional isomers

13.  (10 points) a.  Provide a clear Fisher projection for the molecule named \((4S, 5R)-4\text{-isopropyl-5-ethyl-2-octyne}\)

b.  Which stereoisomer, \(cis\)-1,3-dimethylcyclohexane or \(trans\)-1,3-dimethylcyclohexane, is chiral?  
Briefly but clearly explain you answer using chemical concepts from class.
14. Aldopentols are reduced stereoisomeric versions of the sugar ribose, which is found in RNA. They have the general formula at right. Only four stereoisomeric aldopentols are known to exist. Using your knowledge of stereochemistry, deduce the structures of these four stereoisomeric aldopentols. (Hint: consider using Fisher projections to explore the relationships of the various isomers.)
A concerted rearrangement reaction
CHM 321: Summary of Important Concepts

Concepts for Chapter 6: Chemical Reactivity and Mechanisms

I. Reaction classes
   A. Additions
      \[ \text{A} + \text{B} \rightarrow \text{C} \]
   B. Eliminations
      \[ \text{A} \rightarrow \text{B} + \text{C} \]
   C. Substitutions
      1. \[ \text{A} - \text{B} + \text{C} - \text{D} \rightarrow \text{A} - \text{C} + \text{B} - \text{D} \]
   D. Rearrangements
      1. \[ \text{A} \rightarrow \text{B} \]

II. Descriptions of reactions: mechanisms
   A. A mechanism is a description of a sequence of bond breaking and bond making steps by which a set of starting materials are converted to the products of a chemical reaction.
      1. The sequence of bonding changes is described using the curved electron arrow formalism
   B. Bond breaking/making can be
      1. Homolytic / homogenic
         a. \[ \text{A} - \text{B} \rightarrow \text{A}^\cdot + \text{B}^\cdot \]
      2. Heterolytic / heterogenic
         a. \[ \text{A} - \text{B} \rightarrow \text{A}^+ + \text{B}^- \]
      3. Concerted: bond making and breaking occur at the same time

C. Sample reactions
   1. Radical substitution
      a. involves three steps: initiation, propagation, and termination
         \[ \text{Cl} - \text{Cl} \rightarrow \Delta \rightarrow \text{Cl}^\cdot + \text{Cl}^\cdot \]
         \[ \text{Cl}^\cdot + \text{H} - \text{H} \rightarrow \text{H} - \text{H} + \text{H} - \text{Cl} \]
         \[ \text{H} - \text{H} + \text{Cl} - \text{Cl} \rightarrow \text{Cl}^\cdot + \text{H} - \text{H} - \text{Cl} \]
         \[ \text{H} - \text{H} + \text{Cl}^\cdot \rightarrow \text{H} - \text{Cl} \]
2. Electrophilic addition
   a. Protonation of a Lewis base

   ![Chemical structure](image)

3. Nucleophilic substitution
   a. Displacement of a halide by a nucleophile

   ![Chemical structure](image)

4. Elimination
   a. Removal of HBr from a bromoalkane

   ![Chemical structure](image)

III. Descriptions of reactions: equilibrium, rate, $\Delta E$, and reaction coordinate diagrams

A. For example, for the electrophilic addition reaction

$$\text{CH}_3\text{CH}=\text{CH}_2 + \text{H–Br} \rightleftharpoons \text{CH}_3\text{CHBr–CH}_3$$

1. The equilibrium constant, $K_{eq}$, is

   $$K_{eq} = \frac{[\text{CH}_3\text{CHBr–CH}_3]}{[\text{CH}_3\text{CH}=\text{CH}_2][\text{HBr}]}$$

2. The Gibbs free energy of the reaction is

   $$\Delta G^\circ = -RT\ln K_{eq}$$

   and

   $$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

3. $\Delta H^\circ$ can be calculated using energies of bond formation:
\[ \Delta H^\circ = \sum [\Delta H^\circ(\text{the bonds that are broken in the reaction})] - \sum [\Delta H^\circ(\text{the bonds that are formed in the reaction})] \]

4. The mechanism is

\[
\begin{align*}
\text{H}_3\text{C} &- \text{CH}_3 + \text{H-Br} \rightleftharpoons \text{H}_3\text{C} - \text{CH} = \text{CH}_3 + \text{Br}^- \\
\end{align*}
\]

5. The reaction coordinate diagram is

\[
\begin{align*}
\text{SM} \quad \cdots \cdots \cdots \cdots \cdots \cdots \quad \text{P} \\
\end{align*}
\]

where

a. RLS = the rate limiting step of the reaction (here, the first step)
b. SM = the starting materials for the reaction
c. I = an intermediate formed during the reaction
d. P = the products of the reaction
e. \( E_a \) = the activation energy of the reaction
f. \( \Delta H_{\text{rxn}} \) = the heat of reaction (here, exothermic)
g. \( \ddagger \) = the transition state of the first step of the reaction mechanism

i. it looks like:
h. $\delta^+$ = the transition state of the second step of the reaction mechanism
   i. it looks like:

IV. A rearrangement class: Carbocation rearrangement
   A. Stabilities: $3^\circ > 2^\circ > 1^\circ$ > methyl carbocation
   B. Carbocations that can rearrange do rearrange
      – 1,2 hydride shifts
      – 1,2 alkyl shifts
   C. Most common rearrangements:
      – $2^\circ$ to $2^\circ$
      – $2^\circ$ to $3^\circ$
      – $3^\circ$ to $3^\circ$
1. Just like $\text{H}_3\text{O}^+$, $(\text{CH}_3\text{OH})^+$ will undergo electrophilic addition to C=C bonds. The product of the reaction is a methyl ether:

\[
\begin{array}{c}
\text{CH}_3\text{OH} : \text{H}_2\text{SO}_4 \\
\text{1:1} \\
\text{CH}_3\text{O} - \text{CH}_2
\end{array}
\]

a. Provide a clear, detailed, correct Brønsted-Lowry acid-base mechanism that describes how a 1:1 mixture of CH$_3$OH and sulfuric acid, HOSO$_2$OH, makes $(\text{CH}_3\text{OH})^+$ (OSO$_2$OH)$^-$.  

b. Draw a reaction coordinate diagram for the mechanism you have just drawn. Label it with the following: SM, P, $E_a$, $\Delta$, $\Delta_H$.  

c. Is an intermediate formed in the reaction whose mechanism you draw in part a? Explain your reasoning.
d. Draw the transition state, which you labeled with a $\ddagger$ in part b.

e. Finally, provide a clear, detailed, correct mechanism that describes how the alkene in the equation above is converted to the product ether, using $(\text{CH}_3\text{OH})^+$ as the electrophile. (Need a hint? The mechanism is analogous to the one shown on page 89).

f. Circle any nucleophile in the mechanism you just drew.
2. Hydrogen atoms that are on an $sp^3$-hybridized carbon that is adjacent to a double bond are called allylic hydrogens. Substitutions of these hydrogens by bromine (shown below using propene) occurs by the same reaction mechanism as the chlorination of methane:

$$\text{Br} + \text{Br}_2 \xrightarrow{\text{heat or } \nu} \text{Br}$$.  

Provide a mechanism for this reaction, clearly indicating the initiation step(s), propagation step(s), and any termination step(s). (Need a hint? The mechanism is analogous to the one shown on page 87).
3. Each of the following reactions can be best classified as an addition, elimination, substitution, or rearrangement. Identify each according to its reaction class:

a. 

b. 

4. When boron trifluoride is added to a mixture of 2-chloropropane and sodium iodide, a substitution reaction occurs. The mechanism of the reaction proceeds in two steps, with the formation of an intermediate carbocation:

(a) Clearly add curved electron arrows for both steps to indicate the sequence of bonds being broken and bonds being formed that communicates how the starting material is converted into the product.

(b) Clearly circle the substance acting as a Lewis acid in the first step.
5. a. Rank the following cations in order of relative thermodynamic stability, from least stable (1) to most stable (3):

\[ \text{Br} \quad \text{Br}^+ \quad \text{Br}^+ \]

b. The rightmost carbocation is known to rearrange. Draw two possible carbocations that could form from rearrangements, and explain if these rearrangements would be favored or disfavored.

6. a. Rank the following according to relative thermodynamic stability:

\[ 1 \quad 2 \quad 3 \quad 4 \quad 5 \]

b. Place the following in order from most stable to least stable:

\[ \text{A} \quad \text{B} \quad \text{C} \quad \text{D} \]
Draw the transition state of the following $S_n2$ reaction:

\[ \text{R} - \text{O} - \text{CF}_3 \quad \text{Na}^+ \text{N}_3^- \quad \text{DMF} \quad \text{R} - \text{H} - \text{N}_3 \]
Chapter Seven: Substitution Reactions

\[ \text{S}_{\text{N}2} \]
CHM 321: Summary of Important Concepts

Concepts for Chapter 7: Substitution Reactions

I. Nomenclature of alkyl halides, R–X
   A. Common name: alkyl halide
   B. IUPAC: Haloalkanes; the halo substituent
   C. Primary (1°), secondary (2°), tertiary (3°) classes

II. S\textsubscript{N}2 reactions of RX
   A. X of RX acts as a leaving group (LG); it is substituted by a nucleophile (Nu):

   \[ \text{Nu}^- + \text{R}–\text{X} \rightarrow \text{Nu–R} + \text{X}^- \]

   The reaction is a one-step, concerted reaction; in the transition state:
   bond making = bond breaking

   1. Examples: Transhalogenation and the Finkelstein reaction
   2. Relative RX reactivity (rate of S\textsubscript{N}2 as a function of RX identity)
      a. As a function of X: RF ≪ RCl < RBr < RI ≈ ROTs
         i. F\textsuperscript{-} is poorest LG; I\textsuperscript{-} is best LG
         ii. The sulfonate LG’s are good LG’s
      b. As a function of R: 3° < 2° < 1° < methyl
         i. Relates to amount of steric hindrance Nu encounters as it
            approaches the reactive C center
         ii. Branching on C adjacent to C–X bond causes additional steric
            hindrance
   3. Relative Nu reactivity (good and poor Nus; rate of S\textsubscript{N}2 as a function of Nu
      identity): Nucleophilicity
      a. Nus always are Lewis bases
      b. Usually they are anions or neutrals with lone pairs
      c. Comparing Nus in same row of periodic table: better bases are better
         Nus (that is, have greater nucleophilicity)
      d. Comparing Nus in the same column of periodic table: bigger Nus are
         better Nus
      e. Sterically hindered Nus usually are poor Nus
4. Role of the solvent
   a. Polar, aprotic solvents increase the $S_N2$ reaction rate
      i. They do this by raising the ground state energy of the Nu
   b. Polar, protic solvents slow down the $S_N2$ reaction rate
      ii. They do this by lowering the ground state energy of the Nu

5. Role of temperature
   a. The rate of $S_N2$ slows as temperature decreases

6. Stereochemical consequences
   a. Backside attack of Nu causes inversion of configuration at the electrophilic center

II. $S_N1$ reactions of RX
A. X of RX acts as a leaving group (LG); it is substituted by a nucleophile (Nu):

$$\text{Nu}^- + R^-X \rightarrow R^+ + X^- + \text{Nu}^-$$

$$X^- + R^+ + \text{Nu}^- \rightarrow R\text{Nu}^- + X^-$$

The reaction is a two-step reaction: bond-breaking and bond-making are separated by a carbocation intermediate

1. Examples: solvolysis of $3^\circ$ RX (the Nu is the solvent)

2. Relative RX reactivity (rate of $S_N1$)
   a. As a function of X: RF $<<$ RCl $< RBr < RI \approx$ ROTs
   b. As a function of R: allylic $> 3^\circ >> 2^\circ > 1^\circ >$ methyl
      Relates to the relative stability of carbocation intermediate

3. Role of the solvent
   a. Polar solvents increase the rate of a $S_N1$ reaction
      i. They do this by stabilizing the transition state of the RLS

4. Role of temperature
   a. The rate of $S_N1$ slows as temperature decreases

5. Stereochemical consequences
   a. Racemization
   b. Rearrangements of the intermediate carbocations
1. For each reaction shown below, predict the major organic product. If you decide that no reaction occurs for a given set of reaction conditions, write NR. Be sure to indicate the correct stereochemistry of the product when appropriate.

a. 
\[
\text{HO-Br} \xrightarrow{\text{NaI, acetone}}
\]

b. 
\[
\text{Br-H-Br} \xrightarrow{\text{Na\textsuperscript{+} N\textsubscript{3}\textsuperscript{-}, CH\textsubscript{3}OH}}
\]

c. 
\[
\text{H-C} \xrightarrow{\text{Na\textsuperscript{+} CN\textsuperscript{-}, DMSO}}
\]

d. 
\[
(S)-2\text{-Bromo-4-methylpentane} \xrightarrow{\text{K\textsuperscript{+} CN\textsuperscript{-}, DMSO, 25 ^\circ C}}
\]
2. Provide short answers for each of the following questions:

a. Define nucleophile.

b. Which will react faster in an $S_N2$ reaction with $Na^+ \cdot OH$ in aqueous ethanol: 1-iodo-2,2,3-trimethylbutane or 1-iodo-2,3,3-trimethylbutane? Why?

c. Circle which compound will react with $K^+N_3^-$ in $CH_3OH$ at 25°C more rapidly:

\[
(CH_3)_2CHCH_2CH_2Br \quad (CH_3)_2CHCH_2CH_2OSO_2CH_3
\]

3. Consider the following $S_N1$ reactions:

\[
\begin{align*}
\text{\textbullet SH} & \quad \xrightarrow{K^+ \ CN^-} \quad \text{\textbullet CN} \\
& \quad \text{H}_2\text{SO}_4, \text{DMSO} \\
\end{align*}
\]

\[
\begin{align*}
\text{\textbullet SH} & \quad \xrightarrow{K^+ \ CN^-} \quad \text{\textbullet CN} \\
& \quad \text{H}_2\text{SO}_4, \text{DMSO} \\
\end{align*}
\]

One of these reactions proceeds at a rate twice as fast as the other. Using what you have learned from your study of organic chemistry, decide which reaction is the slower reaction, and clearly explain your choice.
4. Provide reasonable, clear, detailed reaction mechanisms for the following reactions:

a. 

\[ \begin{align*}
\text{Na}^+ \cdot \text{SH} & \quad \text{O} \quad \text{O} \\
& \quad \text{OH} \quad \text{O} \\
& \quad \text{H}_2\text{O}
\end{align*} \]

b. 

\[ \begin{align*}
(\text{R}) \text{-enantiomer} & \quad \text{H}_2\text{O} \\
& \quad \text{OH}
\end{align*} \]
5. Rank each of the following isomeric bromoalkanes according to the rates they undergo $S_N2$ reaction with the nucleophile $\text{CH}_3\text{CH}_2\text{S}^-$:

\[
\begin{align*}
\text{1} & \quad \text{Br} & \quad \text{Br} & \quad \text{Br} & \quad \text{Br} \\
\text{2} & \quad \text{3} & \quad \text{4} & \quad & \\
\text{1} & \quad \text{2} & \quad \text{3} & \quad \text{4} & \\
\text{1} & \quad \text{2} & \quad \text{3} & \quad \text{4} & \\
\text{1} & \quad \text{2} & \quad \text{3} & \quad \text{4} & \\
\text{1} & \quad \text{2} & \quad \text{3} & \quad \text{4} & \\
\text{1} & \quad \text{2} & \quad \text{3} & \quad \text{4} & \\
\text{1} & \quad \text{2} & \quad \text{3} & \quad \text{4} & \\
\end{align*}
\]

_____ fastest
_____ slowest

6. Provide a structural formula for the principal organic product of each of the following reactions. Include stereochemistry where appropriate. If you determine that there will be no reaction given the starting materials and reaction conditions, indicate so by writing “NR” for “no reaction”.

a.

\[
\begin{align*}
\text{Cl} & \quad \text{H} \\
\text{O} & \quad \text{1. Na}^+\text{I}^- \text{, acetone} \\
\text{2. Na}^+\text{N}_3^- \text{, DMF} \\
\end{align*}
\]

b.

\[
\begin{align*}
\text{Br} & \\
\text{O} & \quad \text{K}^+\text{CN}^- \\
\text{acetone, 23 °C} \\
\end{align*}
\]
Chapter Eight:
Alkenes: Structure and Preparation via Elimination Reactions

5-Androstene, the parent alkene for most anabolic steroids
CHM 321: Summary of Important Concepts

Concepts for Chapter 8: Alkenes: Structure & Preparation via Elimination Reactions

I. Structure and Bonding of Alkenes
   A. \( \text{sp}^2 \)-hybridization of carbons in double bond
   B. \( \pi \), \( \sigma \) bonds
   C. relative stabilities

II. Nomenclature
   A. IUPAC system
   B. (\( E \)), (\( Z \)) and cis, trans systems for naming stereoisomeric alkenes
      1. Use of the Cahn-Ingold-Prelog priority rules

III. Preparations of Alkenes: Elimination Reactions

   \[
   \begin{array}{c}
   \text{LG} \\
   \text{H}
   \end{array}
   \quad \rightleftharpoons \quad \begin{array}{c}
   \text{H} \\
   \text{LG}
   \end{array}
   + \text{H}^+ + \text{LG}^-
   \]

   A. Industrial preparation: “thermal cracking” (dehydrogenation) of alkanes
      1. \( \text{LG}^- = \text{H}^- \)
      2. Almost never used to make alkenes in the laboratory
   B. Dehydrohalogen of haloalkanes: loss of HX
      1. \( \text{LG}^- = \text{X}^- \), a halide (or sulfonate)
   C. Dehydration of alcohols: loss of \( \text{H}_2\text{O} \)
      1. \( \text{LG}^- = \text{HO}^- \)

IV. E2 and E1 reactions of RX
   A. Elimination of HX from haloalkanes: dehydrohalogenation using bases
      1. Zaitsev’s rule
      2. E2 (usually) mechanism
         a. rearrangements are rare
         b. best way to make terminal alkenes
         c. anti-elimination stereochemistry
      3. E1 when 2° or 3° RX and weak base (Like ROH)
         a. weak base is usually the solvent
         b. expect rearrangement

IV. Substitution versus elimination
   A. Primary factors: RX class and basicity of Nu
      1. RX class
         a. \( \text{S}_\text{N}2 \): methyl > 1° > 2° > 3°
         b. \( \text{S}_\text{N}1 \): 3° > 2° > 1°
         c. \( \text{E}_2 \): 3° > 2° > 1°
         d. \( \text{E}_1 \): 3° > 2° > 1°
      2. Stronger and more hindered the Nu, the more it tends to act as a base
      3. General trends:
         a. For methyl-X and 1° RX, \( \text{S}_\text{N}2 \) is favored when
            i. Nu + methyl–X
            ii. 1° RX + Nu even if Nu is very strong base
iii. increased steric hindrance in RX or Nu increases amount of 
   $\text{E}_2$ products in the reaction

b. For $2\degree\text{RX}$
   i. When Nu is stronger base than HO$, expect elimination to 
      predominate
   ii. When Nu is weaker base than HO$, expect substitution to 
      predominate
   iii. Subject to same steric factors as above

c. For $3\degree\text{RX}$
   i. When Nu is an anion, usually elimination predominates
   ii. Expect substitution for neutral Nus and conjugate bases of 
      strong acids

d. All substitutions work better at lower temperatures whereas 
   eliminations work better at higher temperatures

V. E2 and E1 reactions of ROH

A. Elimination of H$_2$O from alcohols: dehydration using acids
   1. use H$_3$PO$_4$, H$_2$SO$_4$, heat
      a. relative reactivities
         i. $3\degree$ ROH $> 2\degree$ ROH $> 1\degree$ ROH
         ii. mechanism: E1
   2. use POCl$_3$
      a. mechanism: E2
1. Consider the following molecule:

![Molecule Image]

a. Provide a correct IUPAC name for this molecule.

b. Provide clear, unambiguous line-bond or skeletal structures for two stereoisomers of the molecule you have just named.

2. Consider the molecule \((1E,5Z)-1\text{-fluoro-1-iodo-2,3-dimethyl-1,5-heptadiene}\).

a. Provide a correct, unambiguous structural formula for this molecule.
b. Can any of the double bonds present in the molecule be unambiguously referred to as cis or trans double bonds? If so, circle those double bonds in the structure you have just drawn.

c. Provide clear, unambiguous structural formulas for two other nonidentical stereoisomers of the molecule you have just drawn.

3. Provide the principal organic reaction product for each of the following reactions. Include stereochemistry of the product when appropriate. If you believe there will be no reaction given the starting materials and the reaction condition, indicate so by writing "NR" for "no reaction".

a. 

\[ \begin{array}{c}
\text{Br} \\
\text{CH}_3\text{CH}_2\text{OH} \\
\end{array} \xrightarrow{\text{CH}_3\text{CH}_2\text{O}^+\text{Na}^+} \]

\[ \begin{array}{c}
\text{CH}_3\text{CH}_2\text{OH} \\
\end{array} \]
b.

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{OTs} \\
\text{H} & \quad \text{OTs}
\end{align*}
\]

\[
\text{CH}_3\text{CH}_2\text{OH}, \Delta
\]

c.

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{OTs} \\
\text{H} & \quad \text{OTs}
\end{align*}
\]

\[
\text{CH}_3\text{CH}_2\text{OH}, \Delta
\]

d.

\[
\begin{align*}
\text{Cl} & \quad \text{H} \\
\text{Cl} & \quad \text{Cl}
\end{align*}
\]

\[
\text{CH}_3\text{CH}_2\text{O}^- \text{Na}^+ \quad \text{CH}_3\text{CH}_2\text{OH}, \Delta
\]

e.

\[
\begin{align*}
\text{Cl} & \quad \text{H} \\
\text{Cl} & \quad \text{Cl}
\end{align*}
\]

\[
\text{CH}_3\text{CH}_2\text{OH}, \Delta
\]

f.

\[
\begin{align*}
\text{Br} & \quad \text{Br}
\end{align*}
\]

\[
\text{Na}^+ \text{ I}^- \quad \text{acetone}
\]
4. Provide short answers for each of the following questions.

a. *cis*-1-Chloro-2-isopropylcyclopentane provides a 80:20 mixture of two products when reacted with CH₃O⁻Na⁺ in CH₃OH at 25°C:

\[
\begin{align*}
\text{Cl} & \quad \text{CH₃O⁻Na⁺} \\
\text{CH₃OH, 23 °C} & \quad \text{OCH₃} \\
\end{align*}
\]

Circle the major product and suggest two things that could be done to increase the amount of the minor product that is formed.

b. Circle which of the following haloalkanes will provide 1-isopropyl-1-cyclohexene most rapidly when reacted with CH₃CH₂ONa in CH₃CH₂OH:

\[
\begin{align*}
\text{Br} & \\
\text{Cl} & \\
\text{Br} & \\
\text{Cl} & \\
\end{align*}
\]

c. Briefly, explain your choice of haloalkane for part e, above.

5. Provide brief answers for each of the following questions:

a. Rank the following alkenes of formula C₆H₁₂ from most to least relative thermodynamic stability:

\[
\begin{align*}
\text{A} & \\
\text{B} & \\
\text{C} & \\
\text{D} & \\
\end{align*}
\]
(3Z)-2,4-Dimethyl-1,3-hexadiene, shown below, forms as the only product from E2 elimination of (3S,4S)-3-bromo-2,4-dimethyl-1-hexene.

![Diagram of (3Z)-2,4-Dimethyl-1,3-hexadiene]

a. Clearly draw the starting material in a wedge-and-hatched line representation.

b. Use Newman projections to explain why only the (Z) isomer, rather than the thermodynamically stable (E) isomer, forms from this starting material.

c. Briefly but clearly, why doesn’t any 2,4-dimethyl-1,2-hexadiene form as a product of this reaction?

d. Will the enantiomeric (3R,4R)-3-bromo-2,4-dimethyl-1-hexene yield the same elimination product?
7. When trans-1-tert-butyl-2-chlorocyclohexane is treated with NaOCH$_2$CH$_3$ in CH$_3$CH$_2$OH, the major product alkene that forms is 3-tert-butyl-1-cyclohexene, apparently in violation of Zaitsev’s rule. Clearly draw the starting material in its lowest energy chair conformation and clearly explain why the unexpected alkene forms as the major product.
8. Consider the following reaction:

\[
\begin{array}{c}
\text{A} \\
\text{B}
\end{array}
\]

a. Using electron arrows to illustrate the sequence of bond-breaking and bond-making steps by which the reactant is transformed to products, provide a reasonable, clear, detailed reaction mechanism for the formation of both A and B.

b. Will A or B be the major product of this reaction? ________________

c. Using concepts of organic chemistry that you have learned in class, briefly explain your choice for part b.
9. Below is an energy vs. reaction coordinate diagram for a dehydration reaction (see page 364 of the textbook if you need a hint). Label it to clearly indicate its rate limiting step, the transition state for each step, the activation energy for the reaction, and the $\Delta G_{\text{rxn}}$. 
10. a. Provide the best, most correct IUPAC name for the following compound:

b. Clearly draw a skeletal formula for the molecule named (3E)-4-isopropyl-6,6-dimethyl-1,3-octadiene.

11. Label the stereochemistry of each carbon-carbon double bond indicated as $E$ or $Z$: 

![Diagram with stereochemistry labels]
12. Label each of the double bonds below as \((E)\) or \((Z)\).
Biosynthesis of a prostaglandin from arachidonic acid: intermediate intramolecular radical addition
I. Concepts for Chapter 9: Addition Reactions of Alkenes

A. Reactions of Alkenes

1. Electrophilic additions (all by very similar mechanisms)
   a. When carbocations are intermediates, remember to anticipate rearrangement
   b. Hammond postulate
   c. Hydrohalogenation: addition of HX to yield haloalkanes
      i. Markovnikov
         - In an addition of HX to C=C, HX adds so as to produce the thermodynamically more stable carbocation intermediate
      I. Bimolecular electrophilic addition
      II. Carbocations are intermediates
      III. Stabilities: 3° > 2° > 1° > methyl carbocation
      IV. Carbocations that can rearrange do rearrange
         - 1,2 hydride shifts
         - 1,2 alkyl shifts
      V. Most common rearrangements:
         - 2° to 2°
         - 2° to 3°
         - 3° to 3°
      ii. Anti-Markovnikov
         I. Radical addition of HBr to C=C

   d. Hydration: addition of \( H_2O \) to yield alcohols
      i. Markovnikov
         I. Addition of \( H_2SO_4 \), then \( H_2O \)
         II. 50:50 \( H_2SO_4:H_2O \)
         III. Oxymercuration-demercuration
      ii. Anti-Markovnikov
         I. Hydroboration-oxidation
            A. Syn-addition stereochemistry

   e. Dihalogenation: addition of \( X_2 \) to yield 1,2-dihaloalkanes
      i. Halonium ions
      ii. Anti-addition stereochemistry

   f. Halohydroxylation: addition of \( X-OH \) to yield halohydrins
      i. Halonium ions
      ii. Anti-addition stereochemistry
      iii. Mechanism similar to dihalogenation

   g. Methylenation: addition of \( :CH_2 \) to yield cyclopropanes
      i. Almost any carbene, \( :CR_2 \), will work
      ii. Most commonly used reaction: the Simmons-Smith reaction
         \[ 2 \text{CH}_2I_2 + \text{Zn}(\text{Cu}) \rightarrow \text{ICH}_2\text{ZnI} + \text{“CH}_2” \]
h. dihydroxylation: addition of OH and OH to C=C to yield 1,2-dihydroxyalkanes (common name: glycols)
   i. cold, dilute, aqueous alkaline KMnO₄ (yields only fair)
   ii. OsO₄ (yields are good)
   iii. syn-addition stereochemistry
i. epoxidation: addition of O to yield epoxides
   i. typical to use peracids like peracetic acid
   ii. basic hydrolysis causes net anti-dihydroxylation
2. hydrogenation: addition of H₂ with a noble metal catalyst to yield alkanes
   a. syn-addition stereochemistry
3. C=C cleavage reactions
   a. ozonolysis: addition of 2 O to yield formaldehyde, aldehydes, or ketones
   b. KMnO₄ in base or acid: addition of ≥ 2O to yield CO₂, carboxylic acids, or ketones
4. Cleavage of 1,2-diols
   a. HIO₄ yields two carbonyl compounds

II. Synthesis strategies
   A. One-step
      1. Substitutions
      2. Eliminations
      3. Additions
      4. Rearrangements
   B. Multistep
      1. Combine II.A.1. - II.A.4. in linear sequences
         a. Constitutional rearrangements
            i. Changing leaving group location
               > Elimination – Addition
            ii. Pi bond position
               > Addition – Elimination
1. Provide the principal organic reaction product for each of the following reactions. Include stereochemistry of the product when appropriate. If you believe there will be no reaction given the starting materials and the reaction condition, indicate so by writing "NR" for "no reaction".

a. \[
\text{CH}_2=\text{CH}_2 + \text{HCl} \xrightarrow{23 \ ^\circ \text{C}} \text{CH}_3\text{CH}_2\text{Cl}
\]

b. \[
\text{BrCH}_2\text{C}_5\text{H}_{11} \xrightarrow{1. \text{Hg}((\text{OCCH}_3)_2} \xrightarrow{2. \text{NaBH}_4, \text{HO}^-} \text{product}
\]

c. \[
\text{ClCH}_2\text{ClCH}_2\text{Cl} \xrightarrow{\text{CH}_3\text{COOH}} \text{product}
\]

d. \[
\text{CH}_3\text{CH}==\text{CHCH}==\text{C}==\text{CHCH}==\text{CHCH}_3 \xrightarrow{\text{xs H}_2, \text{Pt}} \text{product}
\]

e. \[
\text{CH}_2=\text{CHCH}==\text{CHCH}_2\text{OH} \xrightarrow{\text{Br}_2, \text{H}_2\text{O, dark}} \xrightarrow{0 \ ^\circ \text{C}} \text{product}
\]

f. \[
\text{product} \xrightarrow{\text{H}_2, \text{Pd/C}} \text{product}
\]
2. Provide brief answers for each of the following questions:

a. Circle which compound undergoes catalytic hydrogenation faster:

![Structures](image)

b. Draw the structure of the intermediate bromonium ion formed when Br₂ reacts with (Z)-2-butene to provide 2,3-dibromobutane:

![Intermediate structure]

c. Rank the following cations in order of relative thermodynamic stability, from least stable (1) to most stable (3):

![Cations](image)
d. Each of the following isomeric compounds of formula C₈H₁₄ release heat energy when hydrogenated with excess H₂ using Pt as catalyst. Rank the compounds in order of relative heat of hydrogenation, from largest (1) to smallest (4) heat of hydrogenation:

```
\[ \text{\includegraphics{diagram.png}} \]
```

e. Draw the structure of the only primary alcohol of molecular formula C₅H₁₂O which cannot be prepared from an alkene.

---

3. Muscalure is the common name given to a hydrocarbon pheromone of molecular formula C₂₃H₄₆ which the female housefly Musca domestica secretes to attract male houseflies. Ozonolysis of this compound, followed by workup using Zn and H₂O, yields two aldehydes with formulas CH₃(CH₂)₇CHO and CH₃(CH₂)₁₂CHO. What is the structure of muscalure?
4. When (6Z)-2,6-dimethyl-2,6-octadiene is heated with H₂SO₄ for two hours, a new compound, identified as 1,2,3,3-tetramethyl-1-cyclohexene, is isolated in good chemical yield.

Provide a clear, reasonable, detailed stepwise reaction mechanism for this chemical transformation.

5. 3-Methyl-3-(1-methylethyl)-1-cyclohexene is found to undergo acid-catalyzed hydration using 1 : 1 H₂SO₄ : H₂O to produce three isomeric alcohols, A, B, and C:

```
A  OH  +  B  OH  +  C  OH
  |     |     |     |
  |     |     |     |
  |     |     |     |
```

a. Provide a detailed, clear, accurate reaction mechanism that explains how the starting alkene provides product C. It is not necessary to show how the other two products form.
b. Would analogous oxymercuration–demercuration using aqueous \( \text{Hg(CO}_2\text{CH}_3\text{)}_2 \), followed by \( \text{NaBH}_4 \) in aqueous base, yield the same mixture of isomeric alcohol products as the above reaction?

c. Briefly, explain the reasoning that lead to your answer in part b.
6. When \( (E) \)-3-hexene is reacted with \( \text{Cl}_2 \) in the dark at 0 °C, a single isomer of molecular formula \( \text{C}_6\text{H}_{12}\text{Cl}_2 \) is produced.

a. Draw the structural formula of the product that forms, using wedge and hatched lines.

b. Draw the highest and the lowest energy Newman projections of the product, viewed along the C3–C4 sigma bond.
7. Like water, alkanols can add to double bonds in the presence of acid catalysts. For instance:

\[
\text{OH} + \text{C} = \text{C} \xrightarrow{\text{H}_2\text{SO}_4, \text{CH}_2\text{Cl}_2} \text{CH}_2\text{O}
\]

a. Account for the formation of the product of this reaction using an accurate, clear, detailed reaction mechanism.

b. Would this be considered to be a Markovnikov or an antiMarkovnikov addition? Briefly explain the reasoning that led you to your answer.
Unlike alkenes, dacarbazine, an antineoplastic drug, undergoes facile cis-trans isomerization of its N=N bond in the presence of an acid catalyst:

Provide a reasonable, clear, detailed mechanism that accounts for this isomerization.
9. The following mechanism describing the electrophilic addition of hydrogen chloride to an alkene has an awful error in each step:

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{H} & \quad \text{Cl} \\
\text{Cl} & \quad \text{H} \\
\end{align*}
\]

Error 1.

Error 2.

Correct mechanism:
10. Each of the following reactions provides a major product in good chemical yield. Provide a structural formula for each reaction’s major product, including stereochemistry where appropriate.

(a)

(b)

(c)

(d)

(e)
11. Δ³-Carene is a major component of turpentine. It has molecular formula C₁₀H₁₆. When it is hydrogenated at room temperature using excess hydrogen gas, compound Y with molecular formula C₁₀H₁₈ is isolated. Ozonolysis of Δ³-carene provides compound Z:

Draw the structural formulas of Δ³-carene and Y.
12. For the reactions shown below, predict the major organic product. If you decide that no reaction occurs for a given set of reaction conditions, write NR. Be sure to indicate the correct stereochemistry of the product when appropriate.

a. 

\[ \text{Na}^+ \text{CN}^- \longrightarrow \text{DMSO} \]

b. 

\[ \text{Br}_2 \text{CCl}_4 \longrightarrow \text{KI acetone} \]
13. The reaction below, which provides compound M as its major product, appears to defy the principles that we discussed in class. Draw the structures of the intermediate carbocations that form in this reaction, then clearly but briefly explain why M, and not L, is the major product of this reaction. Hint: draw a complete Lewis structure for the starting material.

\[
\begin{align*}
\text{CH}_2\text{CH}_2\text{NO}_2 & \xrightarrow{\text{HCl}} \text{Cl}\text{CH}_2\text{NO}_2 \quad + \quad \text{Cl}\text{CH}_3 \text{NO}_2 \\
\text{M} & \quad \text{L}
\end{align*}
\]

14. Consider the following series of carbocations:

\[
\begin{array}{cccccc}
\text{A} & & \text{B} & & \text{C} & & \text{D} & & \text{E} & & \text{F} \\
+ & & + & & + & & + & & + & & +
\end{array}
\]

a. Which carbocation is the thermodynamically least stable? ____________

b. Which carbocation is an intermediate in the Markovnikov addition of HCl to 4-ethyl-1,4-dimethyl-1-cyclopentene? ____________

c. Which carbocation rearranges to form ? ____________
15. (24 points) Treatment of 4-penten-1-ol with aqueous Br₂ yields a cyclic bromoether as the major product:

\[ \text{4-penten-1-ol} + \text{Br}_2 + \text{H}_2\text{O} \rightarrow \text{cyclic bromoether} + \text{HBr} \]

a. Propose a clear, detailed, correct reaction mechanism that explains how this product forms.

b. Draw the transition state of the first step of the mechanism you provided in part a of this question.

c. Yes or no: is this a regioselective reaction? ____________

d. Yes or no: is this a stereoselective reaction? ____________
Tazarotene, a synthetic acetylenic retinoid used to treat acne
CHM 321: Summary of Important Concepts

Concepts for Chapter 10: Alkynes

I. Structure and bonding
   A. sp-hybridization of carbons in triple bond
   B. 2 perpendicular $\pi$ and 1 $\sigma$ bonds
   C. relative stabilities
      1. disubstituted (interior or internal) > monosubstituted (terminal)

II. Nomenclature
   A. IUPAC system: alkyne (eg, t-C$_4$H$_9$C≡CH is 3,3-dimethyl-1-butyne)
   B. trivial: substituted acetylene (eg, t-C$_4$H$_9$C≡CH is t-butylacetylene)

III. Preparations of alkynes
   A. elimination reactions
      1. elimination of 2 HX from geminal, 1,1-dihaloalkanes: double dehydrohalogenation using very strong bases
         a. $E_2$ twice is usually mechanism
         b. must use strong base like NaNH$_2$
         c. anti-elimination stereochemistry of $E_2$ is followed
         d. an intermediate haloalkene is generated; this alkene is the major product if bases weaker than NaNH$_2$ (eg, alkoxides) are used
      2. elimination of 2 HX from vicinal, 1,2-dihaloalkanes: double dehydrohalogenation using very strong bases
         a. same comments as above
      3. alkylation of terminal alkynes
         a. C$_{sp}$–H bonds are quite short and relatively polarized so that the Hs are relatively acidic
            i. $pK_a$ of acetylene is 26
            ii. terminal acetylenes can be deprotonated by very strong bases (eg, NaNH$_2$) to form their conjugate bases which are called metal acetylides:
               \[
               \text{RC≡C–H} + \text{NaNH}_2 \rightarrow \text{RC≡CNa}^+ + \text{NH}_3
               \]
         b. metal acetylides are nucleophiles and participate in $S_N2$ reactions:
               \[
               \text{RC≡CNa}^+ + \text{R}^1–X \rightarrow \text{RC≡CR}^1 + \text{NaX}
               \]
            i. $\text{R}^1–X$ must be methyl or $1^o$ otherwise elimination predominates

IV. Reactions of alkynes
   A. addition reactions
      1. hydrogenation: addition of 1 mol H$_2$ to yield alkenes
         a. Lindlar's catalyst (Pd on BaSO$_4$ + quinoline) and H$_2$
            i. syn-addition stereochemistry yields 1-alkenes from terminal alkynes and (Z)-alkenes from internal alkynes
         b. dissolving metal reduction: Na in liquid NH$_3$
i. anti-addition stereochemistry yields 1-alkenes from terminal alkynes and (E)-alkenes from internal alkynes

2. double hydrogenation: addition of 2 mol of H₂ to yield alkanes
   a. noble metal catalyst + excess H₂

3. electrophilic additions (all by very similar mechanisms)
   a. hydrohalogenation: addition of HX to yield haloalkenes
      i. Markovnikov
      ii. anti-Markovnikov in presence of peroxides, light or heat
   b. double hydrohalogenation: addition of 2 HX to yield geminal dihaloalkanes
      i. Markovnikov
   c. hydration: addition of H₂O to yield aldehydes and ketones
      i. Markovnikov
      I. 50:50 H₂SO₄:H₂O; Hg²⁺ usually is added
      II. Mechanism is tricky, as it involves a rearrangement of the enol product to a thermodynamically more stable carbonyl-containing product
      III. Process is called tautomerization
      ii. anti-Markovnikov
      I. Borohydration-oxidation
   d. dihalogenation: addition of X₂ to yield dihaloalkenes
      i. halonium ion intermediate
      ii. anti-addition stereochemistry
   e. double dihalogenation: addition of 2 X₂ to yield tetrahaloalkanes
      i. halonium ion intermediate
      ii. anti-addition stereochemistry
      iii. mechanism is dihalogenation twice

4. electrophilic cleavage reactions
   a. ozonolysis: addition of ≥ O to yield formic acid and/or carboxylic acids

5. nucleophilic addition reactions
   a. conjugate bases of terminal alkynes are nucleophiles; see III. A. 3. above

V. Synthesis strategies: interconversions of single, double and triple bonds

A. Additions
   1. C≡C → C≡C → C=C

B. Eliminations
   1. C≡C → C=C
1. Write the structure(s) of the major product(s) expected in each of the following reactions:

a.  

b.  

c.  

d.  

e.  

f.  

1. Br₂, dark, 0 °C
2. 2 NaNH₂

NaNH₂
Δ, ether

Na
NH₃ (l)

Na
liquid NH₃
2. Describe chemical methods that would distinguish between the following pairs of compounds. Tell exactly what you would do and see:

a. 1-pentyne and 1-pentene

b. 2-hexyne and isopropanol

c. 2-pentyne and (Z)-2-pentene

3. Addition of HCl to 3,3-dimethyl-1-butyne gives the following products: 2,2-dichloro-3,3-dimethylbutane (44%), 2,3-dichloro-2,3-dimethylbutane (18%), and 1,3-dichloro-2,3-dimethylbutane (34%). Provide a clear, reasonable, detailed reaction mechanism that accounts for the formation of all three products.
4. Each of the following reactions provides products in good chemical yields. Provide structural formulas for each reaction’s major products, including stereochemistry where appropriate.

a. 
\[
\begin{align*}
\text{Na} & \quad \text{NH}_3 (l) \\
\end{align*}
\]

b. 
\[
\begin{align*}
1. O_3 & \\
2. \text{Zn, H}_2\text{O} &
\end{align*}
\]

5. (16 points) Consider the following addition reaction:

a. Propose a clear, detailed, correct reaction mechanism that explains how the product forms from the starting materials.
b. None of the material shown at right forms in this reaction. Explain why.

![Chemical Structure Image]

b. None of the material shown at right forms in this reaction. Explain why.

c. Would you expect rearrangement products to be formed in this reaction?

6. Using the table at right,

a. Which compound would be most likely to react with CH_3CH_2C=C: Na^+ to form a symmetrical internal alkyne?

b. Can CH_3CH_2C=C: Na^+ be prepared from CH_3CH_2C=CH using these bases?

<table>
<thead>
<tr>
<th>Compound</th>
<th>pK_a</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF_3CH_2OH</td>
<td>12</td>
</tr>
<tr>
<td>H_2O</td>
<td>16</td>
</tr>
<tr>
<td>(CH_3)_3COH</td>
<td>20</td>
</tr>
<tr>
<td>CHCl_3</td>
<td>21</td>
</tr>
<tr>
<td>CH_3CH_2C=CH</td>
<td>25</td>
</tr>
<tr>
<td>CH_2Cl_2</td>
<td>36</td>
</tr>
<tr>
<td>[(CH_3)_2CH]_2NH</td>
<td>36</td>
</tr>
<tr>
<td>CH_3CH_2Cl</td>
<td>45</td>
</tr>
<tr>
<td>(CH_3)_3CCl</td>
<td>50</td>
</tr>
</tbody>
</table>

Yes ☐ No ☐ (CH_3)_3CO^− Na^+ ☐ ☐

Yes ☐ No ☐ HO^− Na^+ ☐ ☐

Yes ☐ No ☐ [(CH_3)_2CH]_2N^− Na^+ ☐ ☐
7. Each of the following reactions provides a product in good chemical yield. Provide a structural formula for each reaction’s major product, including stereochemistry where appropriate.

(a) 

(b) 

8. Provide the best, most correct IUPAC name for the following molecule:
Chapter Eleven: Radical Reactions

$\alpha,\gamma$-Bisdiphenylene-$\beta$-phenylallyl, an unusual example of a persistent carbon radical
CHM 321: Summary of Important Concepts

- Concepts for Chapter 11: Radical Reactions

I. Nomenclature
   A. Alkyl

II. Properties
   A. $sp^2$-hybridized
   B. Stability
      a. $3^\circ > 2^\circ > 1^\circ >> CH_3$
      b. resonance stabilizes radicals
   C. Functions
      1. Homolytic / homogenic bond cleavage / coupling
         a. 

III. Reactions
   A. Radical substitution
      1. involves three steps: initiation, propagation, and termination
         a. initiation with heat, light, or peroxides: radicals are created
         b. propagation: one radical makes another
         c. termination: radicals are consumed

2. Selectivity
   a. Regioselectivity
      i. Chlorination is not regioselective; useful only with alkanes having Hs that are all the same
      ii. Bromination regioselectively brominates $3^\circ$ Hs; is useful
   b. Stereoselectivity
      i. Proceeds with racemization

B. Allylic halogenation
1. Allylic substituent groups
   a. \(-\text{CH}_2\text{CH}=\text{CH}_2\), the allyl substituent
   b. A C bonded to a C=C is an allylic C
      i. The Hs on that C are allylic Hs

2. Allylic free radicals
   a. Resonance stabilization

3. Allylic halogenation is highly selective and very useful
   a. Reaction conditions: NCS or NBS in CCl\(_4\) + heat

C. Anti-Markinikov addition of HBr to a pi bond

1. Mechanism
c. termination
   i. any two radicals combine to form a neutral
1. A. For each reaction, provide either an IUPAC name for the starting material shown OR draw the correct chemical structure of the starting material named.

B. Provide structural formulas for the principal product of each reaction, and describe its stereochemical outcome. If you believe there will be no reaction given the starting material and reaction conditions, indicate so by writing "NR" for "no reaction".

a.  

\[
\begin{array}{c}
\text{\textbf{Br}}_2 \\
300 \, ^\circ C
\end{array}
\]

b.  

\[
(6R)-6-(\text{chloromethyl})-2\text{-ethyl}1\text{-nonene} \xrightarrow{\text{HBr}} \text{hv}
\]

2. Provide the principal organic reaction product for each of the following reactions. If you believe there will be no reaction given the starting materials and the reaction condition, indicate so by writing "NR" for "no reaction".

a.  

\[
\begin{array}{c}
\text{Br}_2 \\
\text{light}
\end{array}
\]

b.  

\[
\begin{array}{c}
I_2 \\
0 \, ^\circ C, \text{dark}
\end{array}
\]
3. After initiation by homolysis of HBr to yield a hydrogen radical and a bromine radical, 1-pentene undergoes antiMarkovnikov addition according to these two propagation steps:

\[
\begin{align*}
\text{HBr} & \quad + \quad \cdot \text{Br} \\
\text{Br} & \quad + \quad \cdot \text{H} \\
\end{align*}
\]

Under the reaction conditions, it is *not* observed to undergo Markovnikov addition. This is because one of the two propagation steps required to form a Markovnikov addition product is endothermic, and therefore disfavored:

\[
\begin{align*}
\text{HBr} & \quad + \quad \cdot \text{H} \\
\text{Br} & \quad + \quad \cdot \text{H} \\
\end{align*}
\]

Use the table of bond disassociation energies at right to:

a. Identify which of the two propagation steps is endothermic by placing a star (☆) to its left.

b. Calculate the $\Delta H^\circ$ of that endothermic step. Show your work for full credit.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Energy of disassociation, $\Delta H$ (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C=C $\pi$</td>
<td>63</td>
</tr>
<tr>
<td>C=C $\sigma$</td>
<td>83</td>
</tr>
<tr>
<td>C–Br</td>
<td>70</td>
</tr>
<tr>
<td>C–H</td>
<td>98</td>
</tr>
<tr>
<td>H–Br</td>
<td>87.5</td>
</tr>
<tr>
<td>Br–Br</td>
<td>46</td>
</tr>
</tbody>
</table>
4. Provide a clear, detailed, complete, chemically correct mechanism for the following radical chlorination. Your mechanism must include labeled initiation, propagation, and one example termination steps. It must also include the two resonance isomers of the intermediate carbon radical that forms in the reaction.

\[
\text{\begin{align*}
\text{N} & \quad \text{O} \\
\text{O} & \quad \text{Cl}
\end{align*}} + \quad \Delta \quad \text{\begin{align*}
\text{N} & \quad \text{O} \\
\text{O} & \quad \text{H}
\end{align*}} \quad \text{\begin{align*}
\text{Cl} & \quad \text{O}
\end{align*}}
\]
5. Radical chlorination of alkanes is not generally useful because mixtures of products often result when more than one kind of C–H bond is present in the alkane.

a. Draw skeletal structures of all the monochloro substitution products \( C_6H_{13}Cl \) you might obtain by reaction of 2-methylpentane with \( Cl_2 \) and heat.

6. (16 points) The mechanisms of the reactions are the same, but radical monobomination, unlike radical monochlorination, is very selective: only one product forms. Consider this reaction:

\[
\text{Cyclic alkane} + \text{Br–Br} \xrightarrow{\Delta} \text{Product} \quad + \quad \text{H–Br}
\]

Use curved electron half-arrows to provide a clear, correct, detailed reaction mechanism that explains how the starting materials are converted into the observed products. Clearly label the initiation, propagation and termination steps of your mechanism. The mechanism that you provide needs only to have one example of a termination step: it is not necessary to provide every possible one that can occur.
7. Consider the radical *dibromination* of bicyclo[1.1.1]pentane:

\[
\begin{align*}
\text{C}_5\text{H}_6\text{Br}_2 \quad &\xrightarrow{\Delta} \quad 2 \text{Br}_2 \quad \rightarrow \\
\end{align*}
\]

a. Clearly draw structural formulas of all of the dibromobicyclo[1.1.1]pentane isomers that in theory can form from this reaction.

b. How many of the dibromobicyclo[1.1.1]pentane isomers that in theory can form from this reaction are chiral?

_______________

c. Two of the theoretical number of dibromobicyclo[1.1.1]pentane isomers are never found to form in this reaction. Draw which two and clearly explain why they are never found to form.
A two-step synthesis of simple carbohydrates
Concepts for Chapter 12: Synthesis

I. Functional group transformation
   A. Changes one functional group into another. This can be done in
      1. One step
      2. Multiple sequential steps (“multistep”)

II. Functional group transposition
   A. A rearrangement reaction
   B. Moves a functional group from one positional to another. This can be done in
      1. One step
      2. Multistep

III. Carbon chain elongation
   A. Increases the carbon count of the molecular formula of a starting material

IV. Creating a strategy to make a molecule using I-III in multiple, sequential steps
   A. Retrosynthetic analysis
      1. Recognize the functional groups of the starting material and product (“target”)
      2. Determine the molecular formulas of the starting material and target
         a. Are the starting material and target related by net addition, elimination, or substitution?
         b. Is there a one step reaction that will accomplish this?
            a. Increase in carbon count = strategy requires carbon chain elongation.
      3. Disconnect the product: what starting material(s) would be required to prepare the target by this strategic connection?
      4. Repeat until the connection is made to the given starting material.
      5. Assemble the multiple steps of the forward synthesis.
1. Write a synthetic route for a reasonable laboratory preparation of the following compounds, starting with the reactant(s) shown and any other needed organic or inorganic reagents:

a. 1-bromopentane from acetylene

b. \((Z)\)-2,5-Dimethyl-3-heptene from \((E)\)-2,5-dimethyl-3-heptene

c. \textit{meso}-3,4-Dibromohexane from acetylene and haloalkanes of four carbons or less as the only sources of carbon.

2. Provide a multistep route for reasonable laboratory syntheses of the following compound:
3. Using a sequence of chemical reactions that you have learned from your study of organic chemistry, provide a synthesis of cis-2-hexene using 1-propene as your only source of carbon. You may use any other reagents that you wish, but all of the carbons of the cis-2-hexene you make should be derived from 1-propene.
4. Provide multistep routes for reasonable laboratory syntheses of the following compounds using the starting materials and conditions given. You may use any other reagents you require, and as many moles of the starting materials as you need.

a. A racemic mixture of \( \text{OH} \) and \( \text{OH} \) from 1-propyne and any other reagents needed.

b. \( \text{O} \) using acetylene as the only source of carbon.