Ch. 5 Structure and Synthesis of Alkenes

7.2 Review

<table>
<thead>
<tr>
<th>Bond Strength</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>C-C $\sigma$ Bond</td>
<td>83 kcal/mol</td>
</tr>
<tr>
<td>C=C $\pi$ Bond</td>
<td>63 kcal/mol</td>
</tr>
</tbody>
</table>

a. $\pi$ Bonds are much weaker
b. $\pi$ Bonds are thus more breakable and more reactive

Double Bonds can’t rotate

7.3 Elements of Unsaturation (“EU”)/Index of Hydrogen Deficiency ) (13.25)

• **Saturated Alkane**: $C_nH_{2n+2}$
• **Unsaturated** Formula: Has less than the maximum $2N+2$ number of hydrogens

1. **Element of Unsaturation**: Something that reduces the hydrogen count by two
   a. Double bond
   b. Ring

2. Each element of unsaturation reduces the hydrogen count by two
3. A molecule may well have several elements of unsaturation, each one progressively reducing it’s hydrogen count by two.

4. Knowing how many elements of unsaturation are present helps to classify, and helps in isomer problems.

5. Calculating EU

   **General Concept**
   \[ EU = \frac{\text{Theory # H's} - \text{Actual # H's}}{2} \]

   For Formulas With Nothing Other than C, H, or O
   \[ EU = \frac{(2C + 2) - H}{2} \]

   For Formulas That May Include Nitrogen or Halogens
   \[ EU = \frac{(2C + 2 + N) - (H + X)}{2} \]

   C = # C’s
   H = # H’s
   N = # N’s
   X - # halogens

6. **Heteroatom Effect:**
   - Oxygens: No effect
   - Nitrogen: each nitrogen increases the theory # H’s by 1
   - Halogen: each halogen takes the place of a hydrogen and reduces the theory # H’s by 1.

   ![Oxygen: no impact](image1)
   ![Nitrogen: adds one](image2)
   ![Halogen: replaces one](image3)
Calculate how many elements of unsaturation are in the following formulas:

1. \( \text{C}_5\text{H}_{12} \)

2. \( \text{C}_4\text{H}_8 \)

3. \( \text{C}_3\text{H}_4\text{O} \)

4. \( \text{C}_5\text{H}_9\text{Cl} \)

5. \( \text{C}_4\text{H}_{11}\text{N} \)

**Distinguishing Rings from Double Bonds by \( \text{H}_2/\text{Pt} \) Hydrogenation**

a. \( \text{H}_2/\text{Pt} \) will “saturate” all \( \text{C} = \text{C} \) double bonds by adding \( \text{H}_2 \) across each one.

b. However, rings will not add hydrogen upon treatment with \( \text{H}_2/\text{Pt} \)

c. Thus you can count how many of your EU’s are rings versus double bonds

d. Note: 2H’s add per 1 double bond

<table>
<thead>
<tr>
<th>Structure</th>
<th>After H2/Pt</th>
<th>EU</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{C}<em>6\text{H}</em>{10} )</td>
<td>( \text{C}<em>6\text{H}</em>{12} )</td>
<td>2</td>
</tr>
<tr>
<td>( \text{C}<em>6\text{H}</em>{10} )</td>
<td>( \text{C}<em>6\text{H}</em>{14} )</td>
<td>0</td>
</tr>
<tr>
<td>( \text{C}<em>6\text{H}</em>{10} )</td>
<td>No Reaction</td>
<td>2</td>
</tr>
</tbody>
</table>

6. For \( \text{C}_4\text{H}_8 \), draw all possible structures for isomer A and isomer B, given the following:

   a. \( \text{C}_4\text{H}_8 \) (A) \( \xrightarrow{\text{H}_2, \text{Pt}} \) \( \text{C}_4\text{H}_{10} \)

   b. \( \text{C}_4\text{H}_8 \) (B) \( \xrightarrow{\text{H}_2, \text{Pt}} \) No reaction

7. Which of the following is possible for structure C?

\( \text{C}_5\text{H}_8 \) (C) \( \xrightarrow{\text{H}_2, \text{Pt}} \) \( \text{C}_5\text{H}_{10} \)
5.1.4 Alkene Nomenclature
A. When the Alkene is in the Core Name (the priority functional group)
1. Number the longest continuous alkene-containing C-chain from the end nearest the alkene → core name = “alk-x-ene”
2. Designate the position of the alkene by using the lower-numbered of the two alkene carbons
3. Attach and number substituents
4. When alkene stereoisomer issues apply:
   • Designate stereochemistry as (E) or (Z)

Give formal names for the following alkenes
Simple Acyclics

1. 
2. 

Rings

3. 

B. Alkenes as Substituents
• Many functional groups have higher priority than alkenes, so that alkenes may need to be named as substituents rather than in the core name

Four to Memorize:

<table>
<thead>
<tr>
<th>Vinyl</th>
<th>Allyl</th>
<th>Methylene</th>
<th>Phenyl = &quot;Ph&quot;</th>
</tr>
</thead>
</table>

Name the following:
1. 
2. 
3. 
4. 
(E)-(Z) for Alkene Stereochemistry (5.4)

- Each carbon of an alkene has two attachments.

1. Check whether (E)/(Z) stereochemistry is relevant. If so:
2. Identify which of the two attachments on the left alkene carbon has higher priority.
   - Use the same priority rules as were used in R/S chirality context
3. Then identify which attachment on the right alkene carbon has higher priority.
4. Assign (E) or (Z) based on whether the two priority attachments are on same or opposite side
   - (Z) (“zusammen” = “together”): the priority attachments are cis
   - (E) (“entgegan = “opposite”): the priority attachments are trans

When does (E)/(Z) apply?
- If either alkene carbon has two common attachments, then stereo doesn’t apply

Assign as (Z) or (E)

1.  
2.  
3.  
4.  
5.  
6.  
7.  
8.  
9.  
10.  
5.6 Alkene Stability Pattern

1. Increasing Substitution (# of non-hydrogens directly attached to alkene carbons) → Increased Stability
     a. Alkene carbons are somewhat electron poor due to the inferior overlap of pi bonds. (One carbon doesn’t really “get” as much of the other carbon’s electron as is the case in a nice sigma bond).
     b. Since alkyl groups are electron donors, they stabilize electron-deficient alkene carbons.
     c. Analogous to why electron-donating alkyls give the 3° > 2° > 1° stability pattern for cations and radicals

2. Trans is more stable than cis for 1,2-disubstituted alkenes
   - Why? Steric Reasons

3. Measuring Relative Stability of Isomers by Heats of Hydrogenation or Heats of Combustion (6.2)

   \[
   \text{CH}_2=\text{CH}_2 + \text{H}_2 \xrightarrow{\text{Pt}} \text{CH}_3\text{CH}_3 \quad \Delta H = -30.3 \text{ kcal/mol}
   \]
   - More exo, more energy released

   \[
   \text{CH}_2=\text{CH}_2 + \text{H}_2 \xrightarrow{\text{Pt}} \text{CH}_3\text{CH}_3 \quad \Delta H = -26.9 \text{ kcal/mol}
   \]
   - Less exo, less energy released

   - When 2 isomers can be converted to a common product, the relative magnitude of \(\Delta H\) tells which isomer is more stable
   - The more heat released, the less stable the isomer. The less heat released, the more stable.
   - Heat of combustion works the same way (converts products to common CO\(_2\) and H\(_2\)O)
1. List the number of non-hydrogen substituents on each alkene; rank the relative stability; rank by heat of hydrogenation, from 1 (most) to 4 (least)

\[
\begin{array}{cccc}
\text{\includegraphics[width=1cm]{alkene1.png}} & \text{\includegraphics[width=1cm]{alkene2.png}} & \text{\includegraphics[width=1cm]{alkene3.png}} & \text{\includegraphics[width=1cm]{alkene4.png}} \\
\end{array}
\]

Stability:

Heat:

2. List the number of non-hydrogen substituents on each alkene; rank the relative stability; When the following are burned, rank from the largest heat of combustion (1) to the smallest.

\[
\begin{array}{ccc}
\text{\includegraphics[width=1cm]{alkene5.png}} & \text{\includegraphics[width=1cm]{alkene6.png}} & \text{\includegraphics[width=1cm]{alkene7.png}} \\
\end{array}
\]

Stability:

Heat:

3. Which isomer is more stable, given the indicated heats of hydrogenation?

\[
\begin{array}{cc}
\text{\includegraphics[width=1cm]{alkene8.png}} & \text{\includegraphics[width=1cm]{alkene9.png}} \\
80 \text{ kcal/mol} & 74 \text{ kcal/mol} \\
\end{array}
\]

5.5 Physical Properties of Alkenes
- Nonpolar
- No hydrogen bonding
  - low boiling
  - Hydrophilic
5.14 Synthesis of Alkenes by E2 Elimination of Alkyl Halides (7.9A)

Factors to Consider
1. $3^\circ$ R-X or $2^\circ$ R-X
   a. $3^\circ$ R-X gives E2 with any base
   b. $2^\circ$ R-X gives largely SN2 with normal anions.
   c. $2^\circ$ R-X gives largely E2 with a bulky base. E2 prevails over SN2.
      • Because SN2 backside attack is so sterically sensitive, bulky bases have problems doing SN2. Get E2 instead.
2. Base Size: Bulky Base versus Normal Base
   a. Normal anions:
      • $3^\circ$ R-X give E2 only, no SN2
      • $2^\circ$ R-X give predominantly SN2 rather than E2
      • E2 eliminations proceed with Zaytsev orientation: more-subbed alkene predominates
   b. Bulky base.
      • $3^\circ$ R-X gives E2 only, no SN2.
      • $2^\circ$ R-X gives E2 only, no SN2.
3. E2’s proceed via Hofmann orientation: less-subbed alkene predominates
   • For steric reasons: base goes after less sterically hindered neighbor hydrogen
4. 2 Bulky Bases to Memorize:
   • NEt3 (Triethylamine)
   • KOC(CH3)3 (potassium t-butoxide)
### Bulky Bases: 2 to remember

<table>
<thead>
<tr>
<th>Bulky Bases</th>
<th>Normal Bases</th>
</tr>
</thead>
<tbody>
<tr>
<td>NE₃ = &quot;triethylamine&quot;</td>
<td>NaOH, KOH, LiOH</td>
</tr>
<tr>
<td>Neutral but amines are basic anyway</td>
<td>NaOCH₃, NaOCH₂CH₃, NaOCH₂CH₂CH₃</td>
</tr>
<tr>
<td>KOC(CH₃)₃ = KOCMe₃ = OCH₃ CH₃</td>
<td>KOCH₃, KOCH₂CH₃, KOCH₂CH₂CH₃</td>
</tr>
<tr>
<td>&quot;potassium t-butoxide&quot;</td>
<td>etc.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bulky bases are:</th>
<th>Normal bases are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Good SN₂ nucleophiles only for 1° R-X</td>
<td>1. Anionic</td>
</tr>
<tr>
<td>2. Do clean E2 with both 3° R-X and 2° R-X</td>
<td>2. Not especially bulky</td>
</tr>
<tr>
<td>3. Give Hofmann elimination (less substituted alkene major)</td>
<td>3. Good SN₂ nucleophiles for 1° or 2° R-X</td>
</tr>
<tr>
<td></td>
<td>4. Only do clean E2 with 3° R-X</td>
</tr>
<tr>
<td></td>
<td>5. Give Zaitsev elimination (more substituted alkene preferred)</td>
</tr>
</tbody>
</table>

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5. **Alkene Orientation: Zaytsev versus Hofmann Elimination**

   a. **Zaytsev:** most subbed alkene
      - The major E2 product involves removal of a hydrogen from the most substituted neighbor carbon
      - This results in a maximally substituted, maximally stable alkene (product stability)
      - Normal-sized bases give predominantly Zaytsev elimination

   b. **Hofmann:** least subbed alkene
      - The major E2 product involves removal of a hydrogen from the least substituted neighbor carbon
      - This results in a less substituted, less stable alkene
      - Bulky bases give predominantly Hofmann elimination

   c. **Why:** Steric reasons. A bulky base ends up having an easier time reaching a hydrogen on a less substituted carbon than on a more substituted carbon (transition-state stability-reactivity principle)

6. **Stereochemistry:** A trans-hydrogen is required.

7. **Mechanism: Concerted.**

   ![Mechanism Diagram]

   Predicting E2 Eliminations:
   1. Is the base normal or bulky?
   2. Is the R-X 3°, 2°, or 1°?
   3. Will E2 or S_N2 occur predominantly?
   4. Will you get Zaitsev or Hoffman elimination?
   5. Is there a trans hydrogen available?
Draw the major Product for each of the following Reactions.

1. \[ \text{Br} \rightarrow \text{NaOH} \]
   \[ \rightarrow \text{NEt}_3, \text{heat} \]

2. \[ \text{Br} \rightarrow \text{NaOCH}_3 \]
   \[ \rightarrow \text{KOC(Me)}_3 \]

3. \[ \text{Br} \rightarrow \text{NaOH} \]
   \[ \rightarrow \text{NEt}_3, \text{heat} \]

4. \[ \text{Br} \rightarrow \text{NaOH} \]
   \[ \rightarrow \text{NEt}_3, \text{heat} \]

5. \[ \text{Br} \rightarrow \text{CH}_3 \rightarrow \text{CH}_2=\text{CH}_2 \]

6. \[ \text{Br} \rightarrow \text{C}_5 \rightarrow \text{C}_4 \]
**Indirect Route to Alkenes from Alkanes**

Via 2 Reactions:
1. **Bromination (reaction 1)** followed by
2. **Elimination (reaction 2)**

Provide Recipe:

1. \[ \text{alkane} \xrightarrow{\text{Br}_2, \text{hv}} \text{alkyl bromide} \xrightarrow{\text{Base}} \text{alkene} \]

2. \[ \text{alkane} \xrightarrow{\text{Br}_2, \text{hv}} \text{alkyl bromide} \xrightarrow{\text{NaOCH}_3} \text{alkene} \]
Synthesis of Alkenes from Alcohol (5.9-12)

General: \[ \text{H}_2\text{SO}_4, \Delta \text{ or H}_3\text{PO}_4 \rightarrow \text{C=C} + \text{H}_2\text{O} \]

1. Zaitsev, not Hoffman elimination.
2. No requirement for a trans hydrogen.
3. Acidic conditions, need an acidic mechanism.

Mechanism (Memorize)

3 steps: Protonation – Elimination – Deprotonation
1. Protonation converts OH, a bad leaving group, into a very good leaving group (neutral water)
2. Carboxation formation is slow step (like E1 mechanism)
   - Cation stability dictates reactivity
   - Reactivity: allylic > 3º R-OH > 2º R-OH >>> 1º R-OH > vinyl, aryl
   - Allylic, 3º, and 2º work; 1º, vinyl, and aryl do not.
3. C-H cleavage comes last.
   - Protonation and deprotonation sandwich the key step.
5. Strong acidic conditions \(\rightarrow\) intermediates should be positive, not negative
6. Because the cation is flat, and forgets original stereochemistry, there is no trans-H requirement.
7. The reaction is actually reversible, an equilibrium
8. Get complete E1, not S\(_N\)1, because the water that falls off in step 2 is converted to hydronium H\(_3\)O\(^+\).
9. Often the equilibrium is driven by distilling the alkene off as it forms (if it's low boiling due to loss of weight and being non-polar) or phase separating out from the acid layer.
**Draw Products**

a. 

b. 

c. 

d. 


e. Rank the reactivity of the following toward H$_2$SO$_4$-catalyzed elimination (1 most). Why?

Key Issue:

Reactivity:
Reaction Mechanisms (Summary and Practice)

A. Recognizing/Classifying as Radical, Cationic, or Anionic

1. Radical
   - initiation requires both energy (either hv or Δ) and a weak, breakable heteroatom-heteroatom bond
     - Cl-Cl, Br-Br, O-O (peroxide), N-Br, etc..
   
   2 Guides for That are Usually Reliable:
   - hv $\rightarrow$ radical mechanism
   - peroxides $\rightarrow$ radical mechanism

2. Anionic
   - **a strong anion/base appears in the recipe**
   - no strong acids should appear in the recipe
   - mechanisms should involve anionic intermediates and reactants, not strongly cationic ones
     - (except for do-nothing spectators like metal cations)
   - The first step in the mechanism will involve the strong anion/base that appears in the recipe

3. Cationic
   - **a strong acid/electrophile appears in the recipe**
   - no strong anion/base should appear in the recipe
   - mechanisms should involve cationic intermediates and reactants, not strongly anionic ones
     - (except for do-nothing spectators like halide or hydrogen sulfate anions)
   - The first step in the mechanism will involve the acid that appears in the recipe. The last step will often involve a deprotonation step. Often the main step occurs in between the proton-on and proton-off steps

B. Miscellaneous Mechanism Tips

1. Keep track of hydrogens on reacting carbons
2. **Each step in a mechanism must balance**
3. The types of intermediates involved (cation, anion, or radical) should be consistent with the reaction classification above
   - a. If the reaction is cationic, don’t show anionic intermediates
   - b. If the reaction is anionic, don’t show cationic intermediates
4. Usually conditions are ionic.
5. **Use a reactive species, whether strong anion or an acid, to start the first step**
   - a. If acidic, first step will involve protonation of the organic
   - b. If anionic, the first step will involve anion attacking the organic.
6. While it isn’t always easy to figure out what is a good mechanism, you should often be able to eliminate an unreasonable mechanism.
1. Classify each mechanism as radical, cationic, or anionic.

   a. \[
   \text{CH}_2\text{CH} = \text{CH}_2 \xrightarrow{\text{HBr}} \text{CH}_2\text{CH} = \text{CH}\text{Br}
   \]

   b. \[
   \text{CH}_2=\text{CH} \xrightarrow{\text{hv}, \text{H}_2\text{C}\text{O} - \text{O} - \text{O} \text{CH}_3} \text{CH}_2\text{CH} = \text{CH}_2 \text{Cl}
   \]

   c. \[
   \text{HO} = \text{O} \xrightarrow{\text{NaOH}} \text{O} = \text{O}
   \]

   d. \[
   \text{CH}_2\text{CH} = \text{CH} = \text{CO} \xrightarrow{\text{NaCH}_3} \text{CH} = \text{CH}_2 \text{OCH}_3
   \]

2. Which of the following mechanisms is reasonable or unreasonable for the transformation shown. Identify recognition keys for things wrong with those that aren’t right.

   \[
   \text{HO} = \text{O} \xrightarrow{\text{NaOH}} \text{O} = \text{O}
   \]

Problems

1. \[
   \text{CH}_3\text{CH} = \text{CH} = \text{CH} = \text{CO} \xrightarrow{\text{OH}} \text{CH}_3\text{CH} = \text{CH} = \text{CH}_2
   \]

2. \[
   \text{HO} = \text{O} \xrightarrow{\text{OH}} \text{O} = \text{O} \xrightarrow{\text{CH}_3\text{CO}} \text{CH}_3\text{CH} = \text{CH}_2
   \]

3. \[
   \text{HO} = \text{O} \xrightarrow{\text{OH}} \text{O} = \text{O} \xrightarrow{\text{CH}_3\text{CO}} \text{CH}_3\text{CH} = \text{CH}_2
Q: Which of the following mechanisms is reasonable or unreasonable for the transformation shown:

Identify recognition keys for things wrong with those that aren’t right.

Problems

1. 

2. 

3. 

4. 

5. 
## Summary of Alkene Reactions, Ch. 6.

Memorize Reaction, **Orientation where Appropriate, Stereochemistry where Appropriate, and Mechanism where Appropriate.**

-all are drawn using 1-methylcyclohexene as a prototype alkene, because both orientation and stereochemistry effects are readily apparent.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Orientation</th>
<th>Stereo</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Markovnikov</td>
<td>None</td>
<td>Be able to draw completely</td>
</tr>
<tr>
<td>2</td>
<td>Anti-Markovnikov</td>
<td>Cis and trans</td>
<td>Not responsible</td>
</tr>
<tr>
<td>3</td>
<td>Markovnikov</td>
<td>None</td>
<td>Be able to draw completely</td>
</tr>
<tr>
<td>4</td>
<td>Markovnikov</td>
<td>None</td>
<td>Not responsible</td>
</tr>
<tr>
<td>5</td>
<td>Anti-Markovnikov</td>
<td>Cis</td>
<td>Not responsible</td>
</tr>
<tr>
<td>6</td>
<td>Markovnikov</td>
<td>None</td>
<td>Not responsible</td>
</tr>
<tr>
<td>7</td>
<td>None</td>
<td>Cis</td>
<td>Not responsible</td>
</tr>
<tr>
<td></td>
<td>Reaction</td>
<td>Orientation</td>
<td>Stereo</td>
</tr>
<tr>
<td>----</td>
<td>----------</td>
<td>-------------</td>
<td>--------</td>
</tr>
<tr>
<td>8</td>
<td>$\text{Br}_2$ (or Cl$_2$)</td>
<td>None</td>
<td>Trans</td>
</tr>
<tr>
<td>9</td>
<td>$\text{Br}_2, \text{H}_2\text{O}$ (or Cl$_2$)</td>
<td>Markovnikov</td>
<td>Trans</td>
</tr>
<tr>
<td>10</td>
<td>PhCO$_2$H</td>
<td>None</td>
<td>Cis</td>
</tr>
<tr>
<td>11</td>
<td>CH$_3$CO$_2$H</td>
<td>None</td>
<td>Trans</td>
</tr>
<tr>
<td>12</td>
<td>OsO$_4$, H$_2$O</td>
<td>None</td>
<td>Cis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>1. O$_3$</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>2. Me$_2$S</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

- **Note:** H-bearing alkene carbon ends up as aldehyde.
- **Note:** Zn common option to (CH$_3$)$_2$S in step 2

- $\text{t}$-butyl hydroperoxide often used instead of hydrogen peroxide.

H-bearing alkene carbon ends as carboxylic acid.
Summary of Mechanisms, Ch. 7 + 8.
Alkene Synthesis and Reactions.

1. HBr
(no peroxides)

2. Test Responsible
HBr
peroxides
both cis and trans

3. Not test responsible
H₂O, H⁺

Note: For unsymmetrical alkenes, protonation occurs at the less substituted alkene carbon so that the more stable cation forms (3° > 2° > 1°), in keeping with the product stability-reactivity principle.

Note 1: For unsymmetrical alkenes, bromination occurs at the less substituted alkene carbon so that the more stable radical forms (3° > 2° > 1°), in keeping with the product stability-reactivity principle.

Note 2: Hydrogenation of the radical comes from either face, thus cis/trans mixture results.

Test Responsible
4. 

\[
\text{Hg(OAc)}_2, \text{H}_2\text{O} \\
\text{NaBH}_4
\]

Not test responsible

5. 

\[
\text{BH}_3\cdot\text{THF} \\
\text{H}_2\text{O}_2, \text{NaOH}
\]

Not test responsible

Notes:

a. concerted addition of \(\text{B-H}\) across \(\text{C=C}\)
   - explains the cis stereochemistry
b. the B-H addition is Markovnikov; the B is \(\delta^+\), the H is \(\delta^-\)
c. The \(\text{H}_2\text{O}_2, \text{NaOH}\) process is complex, but replaces the B with OH with complete retention of stereochemistry
   - the explains why the cis stereochemistry established in step one is preserved in step 2.

6. 

\[
\text{Hg(OAc)}_2, \text{ROH} \\
\text{NaBH}_4
\]

Not test responsible
1. Cation intermediate is cyclic bromonium (or chloronium) ion
2. The nucleophile captures the bromonium ion via backside attack (ala SN2)
   - this leads to the trans stereochemistry
3. The nucleophile attacks the bromonium ion at the *more* substituted carbon
   - There is more + charge at the more substituted carbon
   - The Br-C bond to the more substituted carbon is a lot weaker
4. Alcohols can function in the same way that water does, resulting in an ether OR rather than alcohol OH.
Notes
1. Complex arrow pushing
2. No ions required
3. The carbonyl oxygen picks up the hydrogen, leading directly to a neutral carboxylic acid
   - The peracid is already pre-organized for this via internal H-bonding between carbonyl and H

Not Test Responsible

Notes:
a. The nucleophile (water) attacks from the more substituted end of the protonated epoxide
   • More δ+ charge there
   • The C-O bond to the more substituted end is much weaker
b. The nucleophile adds via S_N2-like backside attack. Inversion at the top stereocenter, but not the bottom, explains the trans stereochemistry.

Test Responsible for Epoxide Opening

Not Test Responsible
Chapter 7 Reactions and Mechanisms, Review

**E2**

On R-X, Normal Base

1. Trans hydrogen required for E2
2. Zaytsev elimination with normal bases
3. For 3° R-X, E2 only. But with 2° R-X, S_N2 competes (and usually prevails)
4. Lots of “normal base” anions.

**Test Responsible**

**E2**, On R-X, Bulky Base

1. Hoffman elimination with Bulky Bases
2. E2 dominates over S_N2 for not only 3° R-X but also 2° R-X
3. Memorize NEt_3 and KOC(CH_3)_3 as bulky bases.

**Test Responsible**

**Acid-Catalyzed E1-Elimination Of Alcohols**

Mech

Notes:
1. Zaytsev elimination
2. Cationic intermediate means 3° > 2° > 1°
3. 3-Step mechanism
Ch. 6 Reactions of Alkenes

**Introduction**

\[ \text{CH}_3 = CH_2 + A-B \rightarrow \text{CH}_3CH(B=CH_2)A \]

1. Thermodynamics: Usually exothermic
   - \( 1\pi + 1\sigma \rightarrow 2\sigma \) bonds
2. Kinetics: p bond is exposed and accessible

**Generic Electrophilic Addition Mechanism**

2 Steps: Cation formation and cation capture
- Cation formation is the slow step
  - Cation stability will routinely determine the orientation in the first step
    - Which is preferred, \( A \rightarrow B \) or \( A \rightarrow C \)?
- Often the cation is a normal cation B. Sometimes 3-membered ring cations D will be involved.
- In some cases, the cation will be captured by a neutral species (like water), in which case an extra deprotonation step will be involved

**4 Aspects to Watch For in Addition Reactions**
1. Orientation
   - Matters only if both of two things are true:
     - The alkene is unsymmetrical, and
     - The electrophile is unsymmetrical

2. Relative Stereochemistry
   - Matters only if both the first and the second alkene carbons are transformed into chiral centers

3. Mechanism

4. Relative Reactivity of Different Alkenes
   - Stability of cation formed is key
6.4-6 H-X Hydrogen Halide Addition: Ionic/Cationic Addition in the Absence of Peroxides

(Reaction 1)

General: \[ \text{C} = \text{C} + \text{H-X} \rightarrow \text{C} - \text{C} \]

<table>
<thead>
<tr>
<th>Orientation</th>
<th>Stereo</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Markovnikov</td>
<td>None</td>
<td><strong>Be able to draw completely</strong></td>
</tr>
</tbody>
</table>

Markovnikov’s Rule (For Predicting Products): When H-X (or any unsymmetrical species A\(\delta^+\)B\(\delta^-\)) adds to an unsymmetrical alkene: (6.5)
- the H\(^+\) (or A\(^+\)) adds to the less substituted carbon (the one with more H’s)
- the X\(^-\) (or B\(^-\)) adds to the more substituted carbon (the one with more non-H’s).
- Note: Markovnikov’s rule does not apply if either the alkene or the atoms that are adding are symmetrical

Examples, Predict the Products.

Does Markovnikov’s Rule matter?

1

2

3

4

5

6
Mechanism (6.6)

- Protonate first
- Capture cation second
- Cation formation (step 1) is the slow step

Rank the Reactivity of the following toward HBr addition.

\[ \text{Issue:} \]

- Formation of the most stable carbocation results in Markovnikov orientation

For unsymmetrical alkenes, protonation occurs at the 
less substituted alkene carbon so that the more stable cation forms
\((3^\circ > 2^\circ > 1^\circ)\), in keeping with the product stability-reactivity principle
- This same logic applies anytime something adds to an alkene.
- You want to make the best possible intermediate in the rate-determining step.

Draw the mechanism for the following reaction:  \[ \text{HBr} \]
6.18 Free Radical Addition of HBr with Peroxide Initiator: Anti-Markovnikov Addition (Rxn 2)

1. Peroxides are radical initiators, and cause the mechanism to shift to a radical mechanism.
2. With peroxides, the orientation is reversed to anti-Markovnikov: now the Br adds to the less substituted end and the H adds to the more substituted end of an unsymmetrical alkene.
   a. No peroxides: Br goes to more substituted end
   b. With peroxides: Br goes to less substituted end
3. The anti-Markovnikov radical process works only with HBr, not HCl or HI.
4. The radical process is faster, and wins when peroxides make it possible. In the absence of peroxides, the slower cationic process happens.

Mechanism, and Reason for Anti-Markovnikov Orientation

For unsymmetrical alkenes, bromination occurs at the less substituted alkene carbon so that the more stable radical forms ($3^o > 2^o > 1^o$), in keeping with the product stability-reactivity principle.

Examples, Predict the Products.

1. HBr, peroxides  
   HBr, no peroxides

2. HBr, peroxides  
   HBr, no peroxides

3. HBr, peroxides  
   HBr, no peroxides

Does Markovnikov’s Rule matter?
6.9 Addition of H-OH. Direct acid-catalyzed addition. (Reaction 3)

General: 

\[
\begin{align*}
\text{C} &= 
\begin{array}{c}
\text{C} \\
\text{C} \\
\text{H}_{2}\text{OH} \\
\text{H} \\
\text{H}
\end{array}
\end{align*}
\]

Markovnikov: Hδ⁺OHδ⁻ → H adds to the less substituted end of the alkene, OH adds to the more substituted end
- OH ends up on more substituted end of the alkene

Mechanism: 3 Steps.
1. Protonation
2. Cation Capture
3. Deprotonation

Notes
1. Whenever you see an acid-catalyzed process, expect to use H⁺ in first step and to deprotonate in the last step
2. Cation stability dictates reactivity
3. Cation stability explains why the Markovnikov orientation occurs. This involves the more substituted, more stable carbocation product in the rate-determining step.
4. The actual reaction is an equilibrium.
   - The reverse of alcohol dehydration to make alkenes!
   - A key drive is to have excess water. That pushes the equilibrium to the alcohol side.
   - Under alcohol → alkene conditions, the equilibrium is often driven to the alkene side by having no water, or by distilling off the lower-boiling alkene as it forms.
Examples, Predict the Products.

1. \( \text{H}_2\text{O}, \text{H}^+ \)

2. \( \text{H}_2\text{O}, \text{H}^+ \)

3. \( \text{H}_2\text{O}, \text{H}^+ \)

4. \( \text{H}_2\text{O}, \text{H}^+ \)

5. \( \text{H}_2\text{O}, \text{H}^+ \)

Does Markovnikov’s Rule matter?

Problems with Acid-Catalyzed Addition of Water to Alkenes

1. Alkenes with poor water solubility often don’t add very well.
   - Can’t drive the equilibrium strongly to the alcohol side in that case
   - Solvent mixtures can often help, but not always good enough
2. Alcohol/Alkene equilibrium sometimes poor
3. Carbocation rearrangement is a problem
4. The degree of Markovnikov selectivity isn’t always satisfactory
   - 99:1 isomer selectivity is a lot nicer than 90:10…
   - Especially if you have to purify!
5. Obviously you can’t get the reverse, anti-Markovnikov alcohol products.

Each of these limitations, when they are a problem, can be solved by alternative recipes that indirectly add H-OH.

Draw the mechanism for the following reaction: \( \text{H}_2\text{O}, \text{H}^+ \)

General: \[ \text{C}\equiv\text{C} \quad \begin{array}{c} 1. \text{Hg(OAc)}_2, \text{H}_2\text{O} \\ 2. \text{NaBH}_4 \end{array} \rightarrow \text{C} - \text{C} - \text{OH} \]

4 \[ \text{CH}_2 = \text{CH}_2 \quad \begin{array}{c} 1. \text{Hg(OAc)}_2, \text{H}_2\text{O} \\ 2. \text{NaBH}_4 \end{array} \rightarrow \text{CH}_3 \text{CH}_2 \text{CH(OH)} \text{CH}_3 \]

Markovnikov Stereo: None Mech: Not responsible

Notes:
1. Often higher yields, cleaner, faster, and easier
2. No restrictions
3. No cation rearrangements
4. **Very strong**, often superior **Markovnikov selectivity**
   - OH adds to the more substituted end, H to the less substituted end

Does Markovnikov’s Rule matter?

\[ \text{H}_2\text{O}, \text{H}^+ \]

1 \[ \text{CH}_2 = \text{CH}_2 \quad \begin{array}{c} 1. \text{Hg(OAc)}_2, \text{H}_2\text{O} \\ 2. \text{NaBH}_4 \end{array} \]

2 \[ \text{CH}_2 = \text{CH}_2 \quad \begin{array}{c} 1. \text{Hg(OAc)}_2, \text{H}_2\text{O} \\ 2. \text{NaBH}_4 \end{array} \]

\[ \text{H}_2\text{O}/\text{H}^+ \text{ vs Oxymercuration/Demercuration: Which should I use?} \]
1. Both normally give same product
2. For predict-the-product problems, be able to handle either recipe
3. **For provide-the-right-recipe problems, I will accept either answer.**
   - H$_2$O/H$^+$ is easier to write!
4. In the real lab, the choice is decided on a case-by-case basis.
   - Default to H$_2$O/H$^+$
   - Go to oxymercuration/demercuration when direct acid-catalyzed hydration doesn’t work as well as you’d like
Mechanism (For interest sake. Not for memorization, not for test.)

Overall pathway:

```
\[
\text{C} = \text{C} \xrightarrow{\text{Hg(OAc)}_2} \text{OH} \xrightarrow{\text{HgOAc}} \xrightarrow{\text{NaBH}_4} \text{OH}
\]
```

"Oxymercuration"  "Demercuration"

More Details for the Oxymercuration Phase

```
\[
\text{Hg(OAc)}_2 \xrightarrow{\text{HgOAc}} \xrightarrow{\text{OH}_2} \xrightarrow{-\text{H}^+} \xrightarrow{\text{Deprotonate}} \xrightarrow{\text{NaBH}_4} \text{HgOAc}
\]
```

OAc = "acetate" = \( \text{OAc} = \text{O}_2\text{C}^- \)

Notes:
1. “demercuration” with NaBH4 replaces the mercury with a hydrogen
2. The initial “oxymercuration” essentially adds (HgOAc)\(^+\)(OH\(^-\)), and follows Markov.’s rule
3. The interesting new thing here is the “mercuronium” ion
4. This is normally drawn as a 3-ring, but can also be viewed as a resonance structure of a hybrid

Mercuronium Ion

```
\[
\text{HgOAc} \xrightarrow{\text{A}} \xrightarrow{\text{B}} \xrightarrow{\text{C}} \text{HgOAc}
\]
```

Mercuronium Ring

```
\text{A} \xrightarrow{\text{3° Cation}} \xrightarrow{\text{B}} \xrightarrow{\text{2° Cation}} \text{HgOAc}
```

Both participation from structures A and B are required to explain everything

- A explains why you don’t get cation rearrangements, ever: you don’t have a free carbocation
- A also explains structure studies, which show that the mercury is weakly bonded to the more substituted carbon
- B helps to explain why water adds to the more substituted carbon, which has extensive positive charge
- C doesn’t contribute, isn’t really involved

In the real thing, there is a long, very weak and super breakable bond between mercury and the more substituted carbon. The bond to the less substituted carbon is much shorter and stronger.

"\(\pi\)Complex" Perspective

```
\[
\text{C} = \text{C} \xrightarrow{\text{Electrophilic \text{HgOAc}}} \xrightarrow{\text{Add}} \text{HgOAc}
\]
```

"\(\pi\)-complex"

Overall pathway: \[ \text{Overall pathway: } \begin{array}{c}
\text{C} = \text{C} \\
1. \text{BH}_3\cdot\text{THF} & \overset{\text{"Hydroboration"}}{\rightarrow} & \text{H} & \text{H} \\
2. \text{H}_2\text{O}_2, \text{NaOH} & \overset{\text{"Oxidation"}}{\rightarrow} & \text{C} & \text{C} \\
\end{array} \]

\[ \text{5. } \begin{array}{c}
\text{1. BH}_3\cdot\text{THF} \\
\text{2. H}_2\text{O}_2, \text{NaOH} \\
\text{plus} \\
\text{Anti-Markovnikov} \\
\text{Cis} \\
\text{Not responsible} \\
enantiomer
\end{array} \]

Notes:

1. **Anti-Markovnikov orientation**: the OH ends up on the less substituted end of an unsymmetrical alkene; the H adds to the more substituted end.
2. **Cis addition. Both the H and the OH add from the same side.**
3. When does cis/trans addition stereochemistry matter?
   - Only when both alkene carbons turn into chiral centers in the product.
   - If one does but not both, then the relative stereochemistry doesn’t matter.
   - For Markovnikov additions involving H-Br or H-OH, the H usually adds to a carbon that already has an H, so that in the product it is not a stereocenter.
   - In anti-Markovnikov additions, much more common for both carbons to become chiral carbons.
4. **Chiral products are Racemic (two enantiomers form) but not optically active**
   - When only one chiral center forms (often in the Markovnikov additions), any chiral product will always be racemic.
   - When two chiral centers form, as in the example above, of the four possible stereoisomers, you get only two of them, in racemic mixture.

Examples, Predict the Products.

<table>
<thead>
<tr>
<th>Does Markov.</th>
<th>Does Stereo Matter?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. BH₃·THF</td>
<td>2. H₂O₂, NaOH</td>
</tr>
</tbody>
</table>
1. Which starting alkenes would produce the following products following hydroboration-oxidation? Factor in the stereochemistry of the products in considering what starting materials would work.

2. Fill in recipes for converting 1-butene into the three derivatives shown.
Mechanism (For interest sake. Not for memorization, not for test.)

Overall pathway:

1. BH₃·THF  "Hydroboration"  H C BH₂  2. H₂O₂, NaOH  "Oxidation"  H C OH

5

1. BH₃·THF
2. H₂O₂, NaOH

"π-Complex" Perspective

Electrophilic BH₃ Adds

BH₃-THF  "π-complex"

Notes
1. Other recipes (B₂H₆, etc. are common)
2. BH₃·THF is a convenient complex in which the oxygen provides the extra electron pair. But the weak complex provides a small equilibrium amount of free, reactive BH₃
3. Free BH₃ is actually the electrophile
4. Because BH₃ does not have octet rule, the boron is very electrophilic
5. The electrophilic boron originally makes a π-complex, but then you get actual hydroboration via a 4-centered ring
6. The key is that both the boron and the hydrogen enter from the same side of the alkene
   - **concerted addition of B-H across C=C**
   - **cis addition**
7. Why do you get the orientation?
   - the B-H addition actually does follow Markovnikov’s rule
     - H₂Bδ+Hδ−
     - The B is δ+, the H is δ−, because boron is a semi-metal and less electronegative than hydrogen! The only case this chapter where the hydrogen is δ- rather than δ+
   - Sterics: The Boron end is pretty big, so it prefers to go to the less substituted, less hindered end of the alkene for steric as well as electronic reasons.
8. The NaOH/H₂O₂ workup is complex and beyond our scope, but replaces the B with OH with complete retention of stereochem
   - the cis stereochemistry established in the hydroboration
   - the oxygen stereo is preserved in the oxidation.
Alkoxymercuration-Demercuration: Markovnikov Addition of H-OR (Reaction 6)

General: \[ \text{C} = \text{C} \rightarrow 1. \text{Hg(OAc)}_2, \text{ROH} \rightarrow \text{C} - \text{C} \]
2. NaBH₄

Mechanism

Notes:
1. Everything is the same as with oxymercuration-demercuration to form an alcohol, except you use an alcohol instead of water
2. This results in an oxygen with it’s spectator carbon chain adding rather than an OH
3. Strong Markovnikov orientation
   - The OR adds to the more substituted end of the alkene
   - The Hydrogen ends up on the less substituted end of the alkene
4. The mechanisms are analogous.

Examples, Predict the Products.

Does Does Mark’s Stereo? Rule matter?

1. \[ \text{CH}_3\text{CH}_2\text{OH} \]
2. NaBH₄

2. \[ \text{Hg(OAc)}_2, \text{OH} \]
2. NaBH₄
Ether Synthesis: Two Routes
1. From Alkene and Alcohol: By Oxymercuration/Demercuration
2. From R-Br and Alkoxide Anion: By $S_N2$

Multistep Synthetic Design: Design Reactants for the Following Conversions
1. Note: It is often most strategic to think backward from product to precursor.
2. Then think back how you could access the precursor from the starting material.
3. There may sometimes be more than one suitable route.
4. There will be problems of this style/format on the next test.

1. \[
\begin{align*}
&\text{CH}_3\text{C} = \text{CH}_2 \quad \rightarrow \quad \text{CH}_3\text{OCH}_3 \\
\end{align*}
\]

2. \[
\begin{align*}
&\text{CH}_3\text{C} = \text{CH}_2 \quad \rightarrow \quad \text{CH}_3\text{OCH}_3 \\
\end{align*}
\]

3. \[
\begin{align*}
&\text{CH}_3\text{OH} \quad \rightarrow \quad \text{CH}_3\text{OH} \\
\end{align*}
\]

4. \[
\begin{align*}
&\text{CH}_3\text{OH} \quad \rightarrow \quad \text{CH}_3\text{OH} \\
\end{align*}
\]

5. \[
\begin{align*}
&\text{CH}_3\text{OH} \quad \rightarrow \quad \text{CH}_3\text{OH} \\
\end{align*}
\]

6. \[
\begin{align*}
&\text{CH}_3\text{OH} \quad \rightarrow \quad \text{CH}_3\text{Br} \\
\end{align*}
\]

7. \[
\begin{align*}
&\text{CH}_3\text{OH} \quad \rightarrow \quad \text{CH}_3\text{Br} \\
\end{align*}
\]

**General:** \[ 
\text{C} = \text{C} \xrightarrow{\text{H}_2, \text{Pt} \text{ or Pd, or Ni, etc.}} \text{C} - \text{C} 
\]

\[ \text{CH}_3 \]

Orientation: None  
Stereo: Cis  
Mech: Not responsible

**Notes:**
1. Since both atoms adding are the same (H), Markovnikov orientation issues don’t apply  
   - You’re adding a hydrogen to both the more and less substituted alkene carbon!
2. Stereochemistry isn’t often relevant, but when it is it’s cis  
   - Rarely relevant because if either alkene carbon has even one hydrogen attached,  
     addition of an additional hydrogen will result in an achiral carbon.
3. The reaction is substantially exothermic
4. But some kind of transition-metal catalyst is required to active the otherwise strong H-H bonds.

**Examples. Predict the Products.**

<table>
<thead>
<tr>
<th>Example</th>
<th>Does Mark’s Rule matter?</th>
<th>Does Stereo?</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>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6.14-17 X-X Dihalogen Addition: Trans Addition (Reaction 8)

General: \[ \text{Br}_2 \text{ or } \text{Cl}_2 \rightarrow \text{C} \rightarrow \text{C} \]

<table>
<thead>
<tr>
<th>Orientation</th>
<th>Stereo</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>Trans</td>
<td>Be able to draw completely</td>
</tr>
</tbody>
</table>

Notes:
1. **Orientation**: Non-issue, since you’re adding the same atom to each alkene carbon
2. **Trans addition**
3. **Solvent** matters: to get X-X addition, you need a solvent other than water or alcohol.
   - With water or alcohol, you get different products, see reaction 9

Examples, Predict the Products.

<table>
<thead>
<tr>
<th>Does Mark.</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Br₂</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Br₂</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Cl₂</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Cl₂</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Br₂</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Br₂</td>
<td></td>
</tr>
</tbody>
</table>

Notes:
1. Cis and trans reactants give different products!
2. For any product (in this and other reactions), be able to identify whether it is chiral or not
Chemical Test for Alkenes: \( \text{Br}_2 \) in \( \text{CCl}_4 \) solvent is reddish/brown color. Add a few drops to an unknown organic:

a. If the color stays reddish/brown \( \rightarrow \) the unknown does not contain any alkenes

b. If the reddish/brown color goes away \( \rightarrow \) the unknown did have an alkene that is reacting with the bromine

**Mechanism (Very important) (6.16)**

Notes
1. **Cation Formation: Step 1**
2. **Cation capture: Step 2**
3. \( \text{Br}_2 \) and \( \text{Cl}_2 \) are exceptionally good electrophiles
4. **The cation that forms is a 3-membered ring**
   - “Bromonium ion”
   - “Chloronium ion”
5. Or, it can be viewed as a \( \pi \)-complex, with a halogen cation sitting on a p-bond
6. When the nucleophile captures the cation, it must come in from the opposite face
   - **Backside attack, ala S\text{N}2**
   - **Trans addition results**
7. **The nucleophile actually attacks at the more substituted carbon!**
   - This is contrary to \( \text{S}_\text{N}2 \) expectations!
8. Resonance pictures A and B help to explain things
   a. The cyclic form A explains stereochemistry
      - If acyclic form B was all there was, you wouldn’t need backside attack and you wouldn’t get trans stereochemistry
   b. Form B helps explains why the nucleophile attacks the more substituted carbon.
      - Of the two carbons, the more substituted one has the positive charge and is thus more electrophilic, in spite of steric issues.

**Solvent Limitation:** Solvents that are nucleophilic (water or alcohols...) successfully compete with bromide or chloride in the cation capture step.

**Draw the mechanism for:**
**Br-OH or Cl-OH Addition.** Markovnikov Addition, Trans Addition, to form “Halohydrins” (reaction 9) (6.17)

General: \[ \text{C} = \text{C} \xrightarrow{\text{Br}_2 \text{ or } \text{Cl}_2} \text{H}_2\text{O} \quad \text{Br-OH or Cl-OH Addition} \]

9 \[ \text{Br}_2, \text{H}_2\text{O} \quad \text{(or Cl}_2\text{)} \quad \text{Orientation} \quad \text{Stereo} \quad \text{Mechanism} \]

plus enantiomer

**Notes:**

1. **Markovnikov Orientation**
   - OH adds to more substituted alkene carbon
   - Br or Cl adds to less substituted alkene carbon
   - This literally follows Markovnikov’s Rule, since the relative electronegativity makes for BrOH (or ClOH) is Brδ+(OH)δ-

2. **Trans addition**
3. **Solvent** matters: whenever you see Br₂ or Cl₂ recipes, check whether there is a water (or alcohol) solvent

**Mechanism**

1. 3 Steps:
   - bromonium formation (cation formation)
   - cation capture/nucleophile addition
   - deprotonation (since the nucleophile was neutral)
2. The mechanism is closely analogous to the Br₂ or Cl₂ additions
3. Water is a better bromonium (chloronium) capture nucleophile than bromide (or chloride) anion
   - The large population of water molecules in the solvent give it a statistical advantage
   - When the bromide anion forms in step one, it is initially formed on the wrong side of the bromonium. It needs to swim around to the opposite side in order to attack. Usually water has already captured the cation before then.
   - Water really is inherently a better electron donor than bromide anion. This is why in water a proton goes onto water to make hydronium ion rather than going onto bromide to make covalent HBr
4. Notice that the water attacks the **more substituted** carbon of the bromonium (chloronium) ion

**Alcohol Reactions**

\[ \text{Br}_2, \text{HOCH}_3 \]
Draw the mechanism for the following reaction:

Examples, Predict the Products.

1.  

2.  

3.  

4.  

5.  

6.  

Does Does Chiral?  
Mark. Stereo?  
matter?
6.19 Epoxidation. Addition of one Oxygen (Reaction

General: \[ \text{C} = \text{C} \xrightarrow{\text{PhCO}_3\text{H}} \text{C} = \text{C} \]

"peracid"
"epoxide"

\[ \text{PhCO}_3\text{H} \]

plus enantiomer

Notes:
1. No orientation issues, since the same oxygen atom connects to both bonds
2. Cis addition: both oxygen bonds come from the same direction

Mechanism: No test Responsibility

\[ \text{PhCO}_3\text{H} \]

Carbonyl-hydrogen
Hydrogen-bonded reactant

a. Any peracid with formula RCO_2H has an extra oxygen relative to a carboxylic acid.
b. Any peracid can deposit the extra oxygen onto the p-bond to make the epoxide
c. No ions are actually involved, because the leaving group is the neutral carboxylic acid

Examples, Predict the Products.

1. \[ \text{PhCO}_3\text{H} \]

2. \[ \text{PhCO}_3\text{H} \]

3. \[ \text{PhCO}_3\text{H} \]

4. \[ \text{PhCO}_3\text{H} \]

Does Does Chiral?
Mark. Stereo? matter?
15.4,5 Trans OH-OH addition. Epoxidation in water. The initially formed epoxide undergoes Acid-Catalyzed Ring Opening. Reaction 11. (15.5)

General: \[
\begin{array}{c}
C\equiv C \\
\text{CH}_3\text{CO}_2\text{H} \\
\text{H}_2\text{O}
\end{array} \rightarrow \begin{array}{c}
\text{CH}_3\text{CO}_2\text{H} \\
\text{H}_2\text{O}
\end{array}
\]

<table>
<thead>
<tr>
<th>Example</th>
<th>Reaction</th>
<th>Products</th>
<th>Mark</th>
<th>Stereo</th>
</tr>
</thead>
</table>
| 1       | \[
\begin{array}{c}
\text{CH}_3\text{CO}_2\text{H} \\
\text{H}_2\text{O}
\end{array}
\] | None | Trans | Be able to draw acid-catalyzed epoxide hydrolysis |
| 2       | \[
\begin{array}{c}
\text{CH}_3\text{CO}_2\text{H} \\
\text{H}_2\text{O}
\end{array}
\] | | |
| 3       | \[
\begin{array}{c}
\text{CH}_3\text{CO}_2\text{H} \\
\text{H}_2\text{O}
\end{array}
\] | | |
| 4       | \[
\begin{array}{c}
\text{CH}_3\text{CO}_2\text{H} \\
\text{H}_2\text{O}
\end{array}
\] | | |

Examples, Predict the Products.

Notes:
1. The nucleophile (water) attacks from the more substituted end of the protonated epoxide
   - More δ+ charge there
   - The C-O bond to the more substituted end is much weaker
2. The nucleophile adds via S$_\text{N}$2-like backside attack. Inversion at the top stereocenter, but not the bottom, explains the trans stereochemistry.
15.4, 5 Cis OH-OH addition. Catalytic Osmylation. Reaction 12. (15.5)

General: \[ \text{C}=\text{C} \xrightarrow{\text{OsO}_4, \text{H}_2\text{O}_2} \text{C} \text{-C} \text{-OH} \text{-OH} \]

12 \[
\text{OsO}_4, \text{H}_2\text{O}_2 \rightarrow \begin{array}{c}
\text{CH}_3 \\
\text{OH} \\
\text{OH} \\
\text{H}
\end{array}
\]

None \hspace{1cm} \textbf{Cis} \hspace{1cm} \text{Not responsible}

plus enantiomer

Examples, Predict the Products.

1 \[
\text{OsO}_4, \text{H}_2\text{O}_2
\]

2 \[
\text{OsO}_4, \text{H}_2\text{O}_2 \\
\text{CH}_3\text{CO}_3\text{H} \\
\text{H}_2\text{O}
\]

3 \[
\text{OsO}_4, \text{H}_2\text{O}_2 \\
\text{CH}_3\text{CO}_3\text{H} \\
\text{H}_2\text{O}
\]

4 \[
\text{OsO}_4, \text{H}_2\text{O}_2
\]

Does Mark. \hspace{1cm} Does \hspace{1cm} Chiral?

 DOESStereo?

Mech: (Not required)

12

\[
\text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \\
\text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os}
\]

Concerted cis addition \hspace{1cm} \text{Osmate Ester Hydrolysis} \hspace{1cm} \text{Osmium Reoxidation}

Alternative Recipe. Cheaper, Less Reliable

\[
\text{KMnO}_4, \text{NaOH, } \text{H}_2\text{O}
\]

\[
\text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \\
\text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os} \hspace{1cm} \text{Os}
\]
Stereochemically complementary methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Products</th>
<th>Skills:</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{CH}_3\text{CO}_2\text{H}/\text{H}_2\text{O} )</td>
<td>trans</td>
<td>1. Given starting material and product, provide reagent</td>
</tr>
<tr>
<td>( \text{OsO}_4/\text{H}_2\text{O}_2 )</td>
<td>cis</td>
<td>2. Given product and reagent, what was the starting material?</td>
</tr>
</tbody>
</table>

1. **Given starting material and product, provide reagent.** Consider stereo.

   ![Chemical structures](image1)

2. **Stereochemistry Problems. Given product + reagent, what was the starting alkene?**

   ![Chemical structures](image2)

General: \[
\begin{align*}
\text{C} & \rightarrow \text{C} \quad \xrightarrow{1. \text{O}_3} \quad \text{C} = \text{O} \quad \text{O} = \text{C} \\
\text{H} & \quad \xrightarrow{2. \text{Me}_2\text{S}} \quad \text{None} \\
\end{align*}
\]

Note: H-bearing alkene carbon ends up as aldehyde.

Notes
1. Double bond gets sliced in half, gives two corresponding carbonyls per alkene
2. Alkene bonds and nothing else are oxidized.
3. Get ketones and/or aldehydes and/or formaldehyde
4. Zn often used in workup step two instead of dimethylsulfide

Oxidative Cleavage of Alkenes by Permanganate. Reaction 14

General: \[
\begin{align*}
\text{C} & \rightarrow \text{C} \quad \xrightarrow{\text{KMN}O_4, \text{heat}} \quad \text{C} = \text{O} \quad \text{O} = \text{C} \\
\text{H} & \quad \xrightarrow{\text{KMN}O_4} \quad \text{None} \\
\end{align*}
\]

Note: H-bearing alkene carbon ends as carboxylic acid.

Notes
1. Double bond gets sliced in half, gives two carbonyls per alkene
2. Alkene C-H bonds are also oxidized to C-OH bonds.
3. Get ketones and/or carboxylic acids and/or carbonic acid.

1

2

3
4. Identify reactants.

1. Identify A, B, and C.

Review Problems.
3. “Roadmap format”. Identify products A-D.
1. Design a synthetic plan for the following conversions. (Several on test)

   a. 

   b. 

   c. 

   d. 

   e. 

   f.
1. What is a structure for $\text{C}_3\text{H}_6$, if it reacts with $\text{Br}_2$?

Elements of Unsaturation Problems

2. What is a structure for $\text{C}_5\text{H}_{10}\text{O}$, if it does not react with $\text{H}_2/\text{Pt}$, but does react with $\text{H}_2\text{SO}_4$ to give 2 different isomeric alkenes $\text{C}_5\text{H}_8$?

3. What is a possible structure for $\text{C}_5\text{H}_8$, if it reacts with $\text{H}_2/\text{Pt}$ to give $\text{C}_5\text{H}_{10}$?

4. Identify products $\text{A-}\text{C}$.

\begin{center}
\begin{align*}
\text{A} & \xrightarrow{\text{HBr, Peroxides}} \text{B} \\
\text{C} & \xrightarrow{1. \text{BH}_3/\text{THF}} \xrightarrow{2. \text{NaOH, H}_2\text{O}_2} \text{A}
\end{align*}
\end{center}