Summary of Alkene Reactions, Ch. 8.
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 HBr (no peroxides)</td>
<td>Markovnikov</td>
<td>None</td>
<td>Be able to draw completely</td>
</tr>
<tr>
<td>2 HBr peroxides both cis and trans</td>
<td>Anti-Markovnikov</td>
<td>Nonselective. Both cis and trans</td>
<td>Be able to draw propagation steps.</td>
</tr>
<tr>
<td>3 H2O, H+</td>
<td>Markovnikov</td>
<td>None</td>
<td>Be able to draw completely</td>
</tr>
<tr>
<td>4 1. Hg(OAc)2, H2O 2. NaBH4</td>
<td>Markovnikov</td>
<td>None</td>
<td>Not responsible</td>
</tr>
<tr>
<td>5 1. BH3•THF 2. H2O2, NaOH</td>
<td>Anti-Markovnikov</td>
<td>Cis</td>
<td>Not responsible</td>
</tr>
<tr>
<td>6 1. Hg(OAc)2, ROH 2. NaBH4</td>
<td>Markovnikov</td>
<td>None</td>
<td>Not responsible</td>
</tr>
<tr>
<td>7 H2, Pt</td>
<td>None</td>
<td>Cis</td>
<td>Not responsible</td>
</tr>
<tr>
<td>Reaction</td>
<td>Orientation</td>
<td>Stereo</td>
<td>Mechanism</td>
</tr>
<tr>
<td>----------</td>
<td>-------------</td>
<td>--------</td>
<td>-----------</td>
</tr>
<tr>
<td>8</td>
<td>None</td>
<td>Trans</td>
<td>Be able to draw completely</td>
</tr>
<tr>
<td>9</td>
<td>Markovnikov</td>
<td>Trans</td>
<td>Be able to draw completely</td>
</tr>
<tr>
<td>10</td>
<td>None</td>
<td>Cis</td>
<td>Not responsible</td>
</tr>
<tr>
<td>11</td>
<td>None</td>
<td>Trans</td>
<td>Be able to draw acid-catalyzed epoxide hydrolysis</td>
</tr>
<tr>
<td>12</td>
<td>None</td>
<td>Cis</td>
<td>Not responsible</td>
</tr>
<tr>
<td>13</td>
<td>None</td>
<td>None</td>
<td>Not responsible</td>
</tr>
<tr>
<td>14</td>
<td>None</td>
<td>None</td>
<td>Not responsible</td>
</tr>
</tbody>
</table>

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

H-bearing alkene carbon ends as carboxylic acid.
Alkene Synthesis and Reactions.

1. \[
\text{HBr} \quad \text{HBr} \quad \text{HBr}
\]

(no peroxides)

2. \[
\text{HBr} \quad \text{HBr} \quad \text{HBr}
\]

peroxides

both cis and trans

3. \[
\text{H}_2\text{O}, \text{H}^+ \quad \text{H}_2\text{O}, \text{H}^+
\]

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

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

Note: For unsymmetrical alkenes, protonation again occurs at the less substituted end of the alkene, in order to produce the more stable radical intermediate \((3^\circ > 2^\circ > 1^\circ)\).
Chem 350  Jasperse  Ch. 8 Handouts

### Notes

1. **Concerted Addition of B-H across C=C**
   - Explains the cis stereochemistry
   - In step one, the B-H addition is Markovnikov; the H is δ−, and the B is δ+.
   - The H₂O₂, NaOH process is complex, but replaces the B with OH with complete retention of stereochemistry.
   - The cis stereochemistry established in step one is preserved in step two.

2. **Capture with Hg(OAc)₂**
   - Deprotonation with NaBH₄

3. **Additional Reactions**
   - 1. Hg(OAc)₂, ROH
   - 2. NaBH₄
**Chem 350  Jasperse  Ch. 8 Handouts**

**3 Notes**
1. Cation intermediate is cyclic bromonium (or chloronium) ion
2. The nucleophile captures the bromonium ion via backside attack - this leads to the trans stereochemistry
3. The nucleophile attacks the bromonium ion at the *more* substituted carbon

**4 Notes**
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
   a. There is more + charge at the more substituted carbon
   b. 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

Notes:
- The nucleophile (water) attacks from the more substituted end of the protonated epoxide
  - More $\delta^+$ charge there
  - The C-O bond to the more substituted end is much weaker
- The nucleophile adds via S$_N$2-like backside attack. Inversion at the top stereocenter, but not the bottom, explains the trans stereochemistry.

Notes:
1. The nucleophile (water) attacks from the more substituted end of the protonated epoxide
   - More $\delta^+$ charge there
   - The C-O bond to the more substituted end is much weaker
2. The nucleophile adds via S$_N$2-like backside attack. Inversion at the top stereocenter, but not the bottom, explains the trans stereochemistry.
Chapter 7 Reactions and Mechanisms, Review

E2
On R-X, Normal Base

Mech:

Notes
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.

E2, On R-X, Bulky Base

Mech:

Notes:
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.

Acid-Catalyzed E1-Elimination Of Alcohols

Mech

Notes:
1. Zaytsev elimination
2. Cationic intermediate means 3° > 2° > 1°
3. 3-Step mechanism
8-1,2 Introduction

1. Thermodynamics: Usually exothermic
   - $1 \pi + 1 \sigma \rightarrow 2 \sigma$ bonds
2. Kinetics: $\pi$ 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
1. Orientation
   - Matters only if both of two things are true:
     a. The alkene is unsymmetrical, and
     b. 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
8.3 H-X Hydrogen Halide Addition: Ionic/Cationic Addition in the Absence of Peroxides

(Reaction 1)

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

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

**Markovnikov’s Rule (For Predicting Products):** When H-X (or any unsymmetrical species \( \text{A}^\delta \text{B}^\delta \)) adds to an unsymmetrical alkene:
- the \( \text{H}^+ \) (or \( \text{A}^\delta \)) adds to the less substituted carbon (the one with more H’s)
- the \( \text{X}^- \) (or \( \text{B}^\delta \)) 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?

Yes

1. \[
\text{HBr} \quad \xrightarrow{\text{no peroxides}} \quad \text{Br}
\]

2. \[
\text{HCl} \quad \xrightarrow{} \quad \text{Cl}
\]

3. \[
\text{HI} \quad \xrightarrow{} \quad \text{I}
\]

4. \[
\text{HBr} \quad \xrightarrow{} \quad \text{Br}
\]

5. \[
\text{HBr} \quad \xrightarrow{} \quad \text{Br}
\]

6. \[
\delta^+ \quad \delta^- \quad \text{Cl} \quad \text{I}
\]
Mechanism

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

Rank the Reactivity of the following toward HBr addition.

3 (2º) 2 (3º) 1 (3º allylic)

Issue: Cation stability

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 (3º > 2º > 1º), 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:
8.3B Free Radical Addition of HBr with Peroxide Initiator: Anti-Markovnikov Addition (Rxn 2)

- Peroxides are radical initiators, and cause the mechanism to shift to a radical mechanism.
- 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.
  - No peroxides: Br goes to more substituted end
  - With peroxides: Br goes to less substituted end
- The anti-Markovnikov radical process works only with HBr, not HCl or HI.
- 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 AntiMarkovnikov Orientation

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

Examples, Predict the Products.

1. \[ \text{HBr, peroxides} \quad \text{HBr, no peroxides} \]
   - Yes

2. \[ \text{HBr, peroxides} \quad \text{HBr, no peroxides} \]
   - Yes

3. \[ \text{HBr, peroxides} \quad \text{HBr, no peroxides} \]
   - No
8.4 Addition of H-OH. Direct acid-catalyzed addition. (Reaction 3)

**General:**

\[
\text{C} = \text{C} + \text{H-OH} \xrightarrow{\text{H}^+} \text{C} - \text{C} - \text{OH}
\]

3. \[
\text{CH}_2\text{CH}_{\text{H}_2}\text{O, H}^+ \xrightarrow{\text{H}_2\text{O}, \text{H}^+} \text{CH}_3\text{H}_2\text{O, H}^+
\]

*Markovnikov:* \(\text{H}^+\text{OH}^+ \rightarrow \) 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

- The sequence in which key step (cation capture in this case) is sandwiched by proton on-proton off protonation-deprotonation is super common for acid-catalyzed reactions.
  - Whenever you see an acid-catalyzed process, expect to use \(\text{H}^+\) in first step and to deprotonate in the last step
- Cation stability dictates reactivity
- Cation stability explains why the Markovnikov orientation occurs. This involves the more substituted, more stable carbocation product in the rate-determining step.
- 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 \(\rightarrow\) 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. \[ \text{Markovnikov's Rule matter?} \]
   - Yes

2. \[ \text{Markovnikov's Rule matter?} \]
   - Yes

3. \[ \text{Markovnikov's Rule matter?} \]
   - No

4. \[ \text{Markovnikov's Rule matter?} \]
   - No

5. \[ \text{Markovnikov's Rule matter?} \]
   - Yes

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 rearrangements can be 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:

[Chemical diagrams]

General: \[ \text{C=C} \xrightarrow{1. \text{Hg(OAc)}_2, \text{H}_2\text{O}} \text{C-CH}_3 \xrightarrow{2. \text{NaBH}_4} \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} \]

4

1. Hg(OAc)$_2$, H$_2$O
2. NaBH$_4$

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?
Yes

**H$_2$O/H$^+$ vs Oxymercuration/Demercuration:** Which should I use?
- Both normally give same product
- For predict-the-product problems, be able to handle either recipe
- **For provide-the-right-recipe problems, I will accept either answer.**
  - H$_2$O/H$^+$ is easier to write!
- 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: \[\text{Hg(OAc)}_2 + \text{C} = \text{C} \rightarrow \text{NaBH}_4 \rightarrow \text{H}_2\text{O} \rightarrow \text{Hg(OAc)}_2\]

"Oxymercuration"  "Demercuration"

More Details for the Oxymercuration Phase

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

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\text{-Complex}" Perspective

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.
8.7 Indirect anti-Markovnikov Addition of H-OH via Hydroboration/Oxidation. Reaction 5.

Overall pathway:

1. BH₃·THF → H[1. BH₃·THF] → C[1. BH₃·THF] → C
   "Hydroboration"

   "Oxidation"

plus enantiomer

5

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>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Examples:

1. 1. BH₃·THF
   2. H₂O₂, NaOH
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 → H-C-H₂ → "Hydroboration"
2. H₂O₂, NaOH → H-OH → "Oxidation"

"π-Complex" Perspective

Electrophilic BH₃ Adds → H-BH₂ → H₂-BH₂ → "π-Complex"

Notes
1. Free BH₃ is actually the electrophile
2. Because BH₃ does not have octet rule, the boron is very electrophilic for an extra electron pair
3. BH₃-THF is a convenient complex in which the oxygen provides the extra electron pair. But the complex is weak, and always provides a small equilibrium amount of free, reactive BH₃
4. The electrophilic boron originally makes a π-complex, but then you get actual hydroboration via a 4-centered ring
5. 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
6. 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.
7. 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 one is preserved in the oxidation.
8.6 Alkoxymercuration-Demercuration: Markovnikov Addition of H-OR (Reaction 6)

General:
\[
\begin{align*}
\text{C} &=& \\
1. & \text{Hg(OAc)}_2, \text{ROH} \quad & \text{Markovnikov} \\
2. & \text{NaBH}_4 & \text{Stereo: None} \\
\end{align*}
\]

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.

1. \[
\begin{align*}
\text{1. } & \text{Hg(OAc)}_2, \text{CH}_3\text{CH}_2\text{OH} \\
2. & \text{NaBH}_4
\end{align*}
\]
   Yes
   No

2. \[
\begin{align*}
\text{1. } & \text{Hg(OAc)}_2, \text{OH} \\
2. & \text{NaBH}_4
\end{align*}
\]
   Yes
   No
Ether Synthesis: Two Routes
1. From Alkene and Alcohol: By Oxymercuration/Demercuration
2. From R-Br and Alkoxide Anion: By S_N2
3. Multistep Syntheses: Design Reactants for the Following Conversions
   - Note: It is often most strategic to think backward from product to precursor.
   - Then think back how you could access the precursor from the starting material.
   - There may sometimes be more than one suitable route.

a. \[
\begin{align*}
\text{1. HBr, peroxides} \\
\text{2. NaOCH}_3
\end{align*}
\]

b. \[
\begin{align*}
\text{1. Hg(OAc)_2, CH}_3\text{OH} \\
\text{2. NaBH}_4
\end{align*}
\]

c. \[
\begin{align*}
\text{1. H}_2\text{SO}_4, \text{heat} \\
\text{2. BH}_3\text{-THF} \\
\text{3. NaOH, H}_2\text{O}_2
\end{align*}
\]

d. \[
\begin{align*}
\text{1. Br}_2, \text{hv} \\
\text{2. NaOCH}_3 \text{ (or other small, normal base)}
\end{align*}
\]

e. \[
\begin{align*}
\text{1. Br}_2, \text{hv} \\
\text{2. NEt}_3 \text{ (or KOCMe}_3\text{)}
\end{align*}
\]

f. \[
\begin{align*}
\text{1. H}_2\text{SO}_4, \text{heat} \\
\text{2. HBr}
\end{align*}
\]

g. \[
\begin{align*}
\text{1. H}_2\text{SO}_4, \text{heat} \\
\text{2. HBr, peroxides}
\end{align*}
\]
8-10. H-H addition. Catalytic Hydrogenation (Reaction 7)

General: \[ \text{C} \equiv \text{C} \xrightarrow{\text{H}_2, \text{Pt}} \text{C} \equiv \text{C} \]
(or Pd, or Ni, etc.)

7 \[
\begin{align*}
\text{H}_2, \text{Pt} & \quad \text{H}_2, \text{Pt} \\
| & | \\
\text{H} & \text{H} \\
\end{align*}
\]

Orientation: None  Stereo: Cis  Mech: Not responsible

plus enantiomer

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>No</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
8.8 X-X Dihalogen Addition: Trans Addition (Reaction 8)

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

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Orientation</th>
<th>Stereo</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<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>Reaction</th>
<th>Does Mark. matter?</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>No</td>
<td>Yes</td>
<td>Yes</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: Br₂ in CCl₄ solvent is reddish/brown color. Add a few drops to an unknown organic:
- If the color stays reddish/brown → the unknown does not contain any alkenes
- If the reddish/brown color goes away → the unknown did have an alkene that is reacting with the bromine

Mechanism (Very important)

![Mechanism Diagram]

Notes
1. Cation Formation: Step 1
2. Cation capture: Step 2
3. Br₂ and Cl₂ 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 π-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_N2
   - Trans addition results
7. The nucleophile actually attacks at the more substituted carbon!
   - This is contrary to S_N2 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:

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

9. Orientation   Stereo   Mechanism

Markovnikov    Trans    Be able to draw completely

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 Br$_2$ or Cl$_2$ recipes, check whether there is a water (or alcohol) solvent

Mechanism

1. 3 Steps:
   a. bromonium formation (cation formation)
   b. cation capture/nucleophile addition
   c. deprotonation (since the nucleophile was neutral)
2. The mechanism is closely analogous to the Br$_2$ or Cl$_2$ additions
3. Water is a better bromonium (chloronium) capture nucleophile than bromide (or chloride) anion
   a. The large population of water molecules in the solvent give it a statistical advantage
   b. 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.
   c. 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

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

![Mechanism Diagram]

Examples, Predict the Products.

<table>
<thead>
<tr>
<th></th>
<th>Does Mark. matter?</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Does Mark. matter?</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Does Mark. matter?</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Does Mark. matter?</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Does Mark. matter?</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
8-12 Epoxidation. Addition of one Oxygen (Reaction)

General:
\[ \text{C=C} \overset{\text{PhCO}_3\text{H}}{\rightarrow} \text{C-C} \]
"peracid"
"epoxide"

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

10

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

plus enantiomer

None  \textbf{Cis}  Not responsible

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

Mechanism: No test Responsibility

\[ \text{Carbonyl-hydrogen}
\text{Hydrogen-bonded reactant} \]

- Any peracid with formula RCO$_3$H has an extra oxygen relative to a carboxylic acid.
- Any peracid can deposit the extra oxygen onto the p-bond to make the epoxide
- No ions are actually involved, because the leaving group is the neutral carboxylic acid

Examples, Predict the Products.

<table>
<thead>
<tr>
<th></th>
<th>Does Mark.</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
8-13 Trans OH-OH addition. Epoxidation in water. The initially formed epoxide undergoes Acid-Catalyzed Ring Opening. Reaction 11.

General: \[
\begin{align*}
\text{C} & \text{= C} \\
& \text{H}_2\text{O} \\
& \text{CH}_3\text{CO}_3\text{H}
\end{align*}
\] \[
\text{OH} \quad \text{OH}
\]

11

\[
\begin{align*}
\text{CH}_3\text{CO}_3\text{H} & \quad \text{H}_2\text{O} \\
\text{OH} \quad \text{OH} & \quad \text{None} \\
& \quad \text{Trans} \quad \text{Be able to draw acid-catalyzed epoxide hydrolysis}
\end{align*}
\]

Examples, Predict the Products.

<table>
<thead>
<tr>
<th>Does Mark.</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Mech

11

Notes:

a. The nucleophile (water) attacks from the more substituted end of the protonated epoxide
   - More \( \delta^+ \) charge there
   - The C-O bond to the more substituted end is much weaker
b. The nucleophile adds via \( S_N^2 \)-like backside attack. Inversion at the top stereocenter, but not the bottom, explains the trans stereochemistry.
8-14 Cis OH-OH addition. Catalytic Osmylation. Reaction 12.

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

12

$$\text{Cyclic } \xrightarrow{\text{OsO}_4, \text{H}_2\text{O}_2} \text{CH}_3 \xrightarrow{\text{OH}} \text{C}$$

plus enantiomer

Examples, Predict the Products.

<table>
<thead>
<tr>
<th>Number</th>
<th>Reaction</th>
<th>Product</th>
<th>Does Mark.</th>
<th>Does Stereo?</th>
<th>Chiral?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\text{OsO}_4, \text{H}_2\text{O}_2$</td>
<td>$\text{CH}_3\text{OH}$</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>$\text{OsO}_4, \text{H}_2\text{O}_2$</td>
<td>$\text{OH}$</td>
<td>No</td>
<td>Yes</td>
<td>No, Yes</td>
</tr>
<tr>
<td>3</td>
<td>$\text{OsO}_4, \text{H}_2\text{O}_2$</td>
<td>$\text{OH}$</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>$\text{OsO}_4, \text{H}_2\text{O}_2$</td>
<td>$\text{OH}$</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Mech: (Not required)

12

Concerted cis addition

Os (VIII) $\xrightarrow{\text{OsO}_4, \text{H}_2\text{O}_2} \text{Os (VI)}$ Osmate Ester Hydrolysis

Os (VIII) $\xrightarrow{\text{KMnO}_4, \text{H}_2\text{O}} \text{Os (VIII)}$ Alternative Recipe. Cheaper, Less Reliable

KMnO$_4$, NaOH, H$_2$O
Stereochemically complementary methods

Skills:

a. Given starting material and product, provide reagent
b. Given product and reagent, what was the starting material?

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

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

trans addition

\[
\text{cis addition} \\
\]

2. Stereochemistry Problems. Given product and reagent, what was the starting material?

\[
\text{OsO}_4 \rightarrow \text{trans addition} \\
\text{cis addition} \\
\]

but trans in product so carbons need to be different in start from at end.

trans addition

trans in product so carbons should be zig-zag trans at start

\[
\]

1. BH$_3$-THF
2. NaOH, H$_2$O$_2$
8.15-B Ozonolysis. Cleavage of Alkenes. Reaction 13

General:

\[
\begin{align*}
\text{C} & \equiv \text{C} \\
\xrightarrow{1. \text{ O}_3} & \text{C} = \text{O} \\
\xrightarrow{2. \text{ Me}_2\text{S}} & \text{O} = \text{C} \\
\end{align*}
\]

13

\[
\begin{align*}
\text{C}_\text{H} & \equiv \text{C} \\
\xrightarrow{1. \text{ O}_3} & \text{O} \\
\xrightarrow{2. \text{ Me}_2\text{S}} & \text{H} \\
\end{align*}
\]

None

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

Notes
1. Double bond gets sliced in half
2. Get two corresponding carbonyls
3. Alkene bonds and nothing else are oxidized.
4. Get ketones and/or aldehydes and/or formaldehyde

8.15-A Oxidative Cleavage of Alkenes by Permanganate. Reaction 14

General:

\[
\begin{align*}
\text{C} & \equiv \text{C} \\
\xrightarrow{\text{K Mn O}_4 \text{ heat}} & \text{C} = \text{O} \\
\xrightarrow{\text{K Mn O}_4 \text{ heat}} & \text{O} = \text{C} \text{H} \\
\end{align*}
\]

14

\[
\begin{align*}
\text{C}_\text{H} & \equiv \text{C} \\
\xrightarrow{\text{K Mn O}_4 \text{ heat}} & \text{H} \\
\end{align*}
\]

None

Notes
1. Double bond gets sliced in half
2. Get two corresponding carbonyls
3. Alkene C-H bonds are also oxidized to C-OH bonds.
4. Get ketones and/or carboxylic acids and/or carbonic acid.
4.  \[
\begin{align*}
\text{H} &\quad \text{O} \quad \text{H} \\
\text{O} &\quad \text{C} \quad \text{H} \\
\text{O} &\quad \text{C} \\
\text{H} &\quad \text{O} \\
\text{H} &\quad \text{O} \\
\end{align*}
\]
1. \(\text{O}_3\) \\
2. \(\text{Me}_2\text{S}\) \\
\[
\text{KMN}_4
\]

5. Identify reactants.

6. Identify A, B, and C.

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

a. \[ \text{OH} \xrightarrow{1. \ H_2SO_4, \ \text{heat}} \xrightarrow{2. \ OsO_4, \ H_2O_2} \]

b. \[ \text{OH} \xrightarrow{1. \ Br_2, \ H_2O} \xrightarrow{2. \ NEt_3} \]

c. \[ \text{Br} \xrightarrow{1. \ NEt_3} \xrightarrow{2. \ Cl_2} \]

d. \[ \text{Br} \xrightarrow{1. \ Br_2, \ hv} \xrightarrow{2. \ NaOH \ (or \ other \ normal \ base)} \xrightarrow{3. \ O_3} \xrightarrow{4. \ Me_2S} \]

e. \[ \text{OH} \xrightarrow{1. \ Br_2, \ hv} \xrightarrow{2. \ NaOH \ (or \ other \ normal \ base)} \xrightarrow{3. \ CH_3CO_3H, \ H_2O} \]

f. \[ \text{OH} \xrightarrow{1. \ H_2SO_4, \ \text{heat}} \xrightarrow{2. \ PhCO_3H} \]
Elements of Unsaturation Problems

9. What is a structure for C₃H₆, if it reacts with Br₂?

   Formula: 1 element of unsaturation
   Br₂ Test: proves element of unsaturation is an alkene

   Answer: CH₃CH=CH₂

10. What is a structure for C₅H₁₀O, if it does not react with H₂/Pt, but does react with H₂SO₄ to give 2 different isomeric alkenes C₅H₈?

   EU = 1
   H₂ Test: proves element of unsaturation is NOT an alkene and must be a ring
   Sulfuric acid reactions suggests that it is an alcohol, since it results in dehydration

   OH
   or
   OH

11. What is a possible structure for C₅H₈, if it reacts with H₂/Pt to give C₅H₁₀?

   1 ring, 1 alkene

   etc.

12. Identify products A-C.

   A
   HBr,
   Peroxides

   B
   Br
   NaOCH₂CH=CH₂

   C
   1. BH₃-THF
   2. NaOH, H₂O₂