Reactions of Alkenes
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• Most characteristic reaction of alkenes is addition to the carbon-carbon double bond
  • The π bond is broken, and, in its place, σ bonds form to two new atoms or groups of atoms
  • **Addition reaction**: Two atoms or ions react with a double bond, forming a compound with the two new groups bonded to the carbon of the original double bond

• **Formation of chain-growth polymers**
  • In the presence of initiators, many alkenes form polymers made by the addition of monomers to a growing polymer chain
  • Example - Formation of polyethylene from ethylene

$$nCH_2=CH_2 \xrightarrow{\text{initiator}} (CH_2CH_2)_n$$
Which of the following monomers would give the polymer shown below?
# Characteristic Alkene Addition Reactions

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<th>Reaction</th>
<th>Descriptive Name(s)</th>
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<td>Hydrochlorination (hydrohalogenation)</td>
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<td>$\text{C} = \text{C} + \text{H}_2\text{O}$</td>
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<td>$\text{C} = \text{C} + \text{Br}_2 \quad \text{(X}_2\text{)}$</td>
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<td>$\text{C} = \text{C} + \text{Br}_2 \quad \text{(X}_2\text{)}$</td>
<td>Bromo(halo)hydrid formation</td>
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<td>( \text{C} = \text{C} + \text{Hg(OAc)}_2 + \text{H}_2\text{O} \rightarrow \text{C} - \text{C} - \text{HgOAc} )</td>
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<td>Hydrogenation (reduction)</td>
</tr>
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An Introduction to Reactions of Alkenes

• A review: What are the important orbitals in an alkene?

• Let’s see if we can predict what will happen in the following reaction:
Regioselectivity: “Markovnikov’s Rule”

• Now consider the following reaction. Can you predict what will happen?

\[
\text{烯烃} + \text{HBr} \rightarrow \text{产物}
\]

• What is the observed product of this reaction? What does this observation tell you about the mechanism of this reaction?

• Is there a general rule that we can formulate about alkene additions?

• The central lesson: First, predict what will happen. Then, compare that prediction with the experimental result. Finally, refine your understanding of the reaction. PCR!
The Stability of Carbocations

- The relative stability of carbocations exhibits the following trend:

\[
\text{Methyl cation (Methyl)} < \text{Ethyl cation (1°)} < \text{Isopropyl cation (2°)} < \text{tert-Butyl cation (3°)}
\]

- How can we explain this trend?

- Here are two other examples of “carbocations.” Can you make any statement about their stability, relative to the carbocations above (and relative to each other)?

\[
\begin{align*}
\text{CH}_3 & \text{C}^+ \text{O} \text{CH}_3 \\
\text{H}_3\text{C} & \text{C}^+ \text{CH}_3
\end{align*}
\]
Hyperconjugation

• Interaction of electrons in a sigma-bonding orbital with the vacant 2p orbital of an adjacent positively charged carbon

(a) Cartoon diagram of the ethyl cation. There is delocalization of C—H bonding electrons into the empty 2p orbital of the positively charged carbon. The orbital that results from this delocalization contains two electrons [see (b)].

(b) A calculated orbital populated with two electrons. This orbital is delocalized over the C—H bond and the 2p orbital of the positively charged carbon of the ethyl cation.

(c) Calculated empty orbital residing mostly on the positively charged carbon of ethyl cation. Some empty orbital character exists on the methyl group also.
Energy Diagram for a Two-Step Reaction Involving Formation of an Intermediate

**Reactive intermediate** corresponds to an energy minimum between two transition states.

**Rate-determining step**: Step that crosses the highest energy barrier:

Slowest step in a multistep reaction
• If \( \text{D} = {}^2\text{H} \) reacts in the same way as \( {}^1\text{H} \), what would be the most likely product of the following addition run under conditions that favor rearrangements?

\[
\text{propene} + \text{D-Cl} \rightarrow ?
\]

- a) \( \text{CH}_3\text{CH} \equiv \text{CHCH}_2\text{Cl} \)
- b) \( \text{CH}_3\text{CH} \equiv \text{CDCl} \)
- c) \( \text{CH}_3\text{CD} \equiv \text{CDCl} \)
- d) \( \text{CH}_3\text{CDCl} \)
- e) \( \text{CH}_3\text{CD} \equiv \text{CDCl} \)
• Which of the marked bonds in the carbocation shown below is the most likely to migrate to generate another carbocation?

1. A  
2. B  
3. C  
4. D  
5. E
Reactive Intermediates and Hammond’s Postulate

- For the following reaction, draw out the **reaction coordinate** for the reaction that leads to the observed (“Markovnikov”) product. Then, draw the reaction coordinate for the reaction that leads to the other (“anti-Markovnikov”) product.

- How can we analyze these reaction coordinate diagrams?

- Does this help to explain why the Markovnikov product is the one that is observed?
Carbocations Do Funky Things

• Predict the product of the following reaction:

\[ \text{substrate} + \text{H-Cl} \rightarrow \]

• What is the actual product of the reaction? What happened?

• Here’s another example. What’s going on here?

\[ \text{substrate} + \text{H-Br} \rightarrow \text{product}_1 + \text{product}_2 \]
• What is the best starting material for the following reaction?

\[ ? + \text{HBr} \rightarrow \text{Br} \]

1. \( \text{a) } \)
2. \( \text{b) } \)
3. \( \text{c) } \)
4. \( \text{d) } \)
5. \( \text{e) } \)
More Reactions of Alkenes

• Can you *predict* the product of the following reaction?

\[
\text{alkene} + \text{H}_3\text{O}^+ \rightarrow \text{product}
\]

• What’s really going on here? Why would this reaction be described as “the acid-catalyzed addition of water to an alkene”? How would we ordinarily write this reaction?

• What is meant by “acid-catalyzed”?
Still More Reactions of Alkenes

• You try this one: Can you predict the product of the following reaction?

\[ \text{Alkene} + \text{CH}_3\text{OH} \xrightarrow{\text{H}^+ \text{ cat.}} \]
Stereochemistry of Alkene Additions

- Consider adding HBr to a cyclic alkene, like the one shown below. The two new groups that are added (H and Br) could be added in two different ways: syn (both added to the same face of the alkene) or anti (added to opposite faces of the alkene):

- Work through the mechanism of HBr addition. Which is preferred: syn or anti?

- The addition of H₂ to the same cyclic alkene gives only one product. What type of addition is this, and why is only one product observed?
Addition of \( \text{Br}_2 \) or \( \text{Cl}_2 \) to Alkenes

- First, let’s *predict* what we expect to happen when an alkene reacts with Br2. How do we make such a prediction?

- What would your proposed mechanism predict about the *stereochemistry* of the outcome?

- The actual outcome of the reaction is shown below. What type of addition is this? Is this stereochemical outcome consistent with your proposed mechanism?
The Mechanism of Br$_2$ or Cl$_2$ Addition

• Is there a mechanism of Br$_2$ addition that is consistent with the observed stereochemistry?

\[
\text{C=C} + \text{Br} = \text{Br} \rightarrow \text{C=C-Br}
\]

• Consider the following alkene additions. Rearrangement is observed in one case but not in the other. Can you explain why?

\[
\begin{align*}
\text{C=C} + \text{H} = \text{Br} & \rightarrow \text{C=C-H} \quad \text{(Rearrangement observed)} \\
\text{C=C} + \text{Br} = \text{Br} & \rightarrow \text{C=C-Br} \quad \text{(No rearrangement)}
\end{align*}
\]
Electrophilic Additions - Addition of Bromine with Anti Stereoselectivity

• Step 1: Make a new bond between a nucleophile ($\sigma$ bond) and an electrophile
  • The product is a bridged bromonium ion
• Step 2: Make a new bond between a nucleophile and an electrophile from the side opposite to the bromonium ion, which opens the three-membered ring.

![Diagram showing the reaction involving a bromonium ion and nucleophile to form a new bond, with annotations for anti-coplanar orientation and Newman projection of the product.](image-url)
• Addition of chlorine or bromine to cyclohexene and its derivatives gives a \textit{trans} dixial product
  • Initial \textit{trans} dixial conformation is in equilibrium with the more stable \textit{trans} diequatorial conformation
  • Because the bromonium ion can form on either face of the double bond with equal probability, both \textit{trans} enantiomers are formed as a racemic mixture
  • \textbf{Anti stereoselectivity}: Addition of atoms or groups of atoms to opposite faces of a carbon-carbon double bond
Addition of $X_2$ with Water or Alcohols

• If Br$_2$ or Cl$_2$ is added to an alkene in the presence of water (HOH) or an alcohol (ROH), a different product is formed. Can you propose a mechanism for this reaction?

\[
\text{alkene} + \text{Br}_2 + \text{H}_2\text{O} \rightarrow \text{product}
\]

• Now that you’ve seen the mechanism, can you predict which of the following products will be produced in the reaction of cyclohexene with bromine in water?

\[
\text{cyclohexene} + \text{Br}_2 + \text{H}_2\text{O} \rightarrow \text{product}
\]
The Structure of the Bromonium Ion

• Explain why *only one product* is observed in the following reaction:

\[
\begin{align*}
\text{\ce{CH2=CH2}} & \text{ Br}_2 \\
& \text{ H}_2\text{O} \\
& \rightarrow \\
\text{Br} & \text{ HO}
\end{align*}
\]

• Is this observation consistent with Markovnikov’s Rule? Why or why not?

• Given all that you know about the addition of Br\(_2\) to alkenes, *predict* which of the four products shown below would be the main product observed in the addition of bromine to 1-methylcyclohexene in the presence of water:

\[
\begin{align*}
\text{\ce{CH2=CH2}} & \text{ Br}_2 \\
& \text{ H}_2\text{O} \\
& \rightarrow \\
\text{A} & \text{ B} & \text{ C} & \text{ D}
\end{align*}
\]
Conversions of Alkenes into Alcohols: Review of Alkene Hydration

• You already know one method for accomplishing the following transformation. What is that method? What is its mechanism?

\[
\text{\[\text{Alkene}\]} \rightarrow \text{\[\text{Alcohol}\]}
\]

• Now suppose you want to carry out the following transformation. Can you use the same method as you did above? Why or why not?

\[
\text{\[\text{Alkene}\]} \rightarrow \text{\[\text{Alcohol}\]}
\]

• What kinds of reactions might we want to avoid when carrying out organic synthesis in the laboratory?
Conversions of Alkenes into Alcohols: Oxymercuration-Reduction

- We can convert an alkene into an alcohol with the following *two-step* process:

  ![Chemical Reaction Diagram]

- What is the mechanism of this reaction? Why are carbocation rearrangements not observed?

- Why might we say that this two-step sequence results in the “Markovnikov addition of water to an alkene”?
Forming and Opening 3-Membered Rings

• Let’s take a close look at the mechanisms of the following reactions. Do you notice any similarities? Are there any generalizations you can make?
Conversions of Alkenes into Alcohols: Hydroboration-Oxidation

• We can accomplish the “anti-Markovnikov” addition of water to an alkene with the following two-step process:

![Chemical reaction diagram]

• Let’s take a closer look at the first step of this reaction:

• Would you say that the first step of this reaction obeys “Markovnikov’s Rule”?
Conversions of Alkenes into Alcohols: Hydroboration-Oxidation

Now, let’s look at the mechanism of the second step of the hydroboration-oxidation sequence:

- Intermediate (not usually isolated)
Which of the following compounds would yield trialkylborane shown below when treated with BH₃/THF?

1. 2-methylbut-1-ene
2. 2-methylbut-2-ene
3. 3-methylbut-1-ene
4. 2-methylpropene
5. (E)-2-pentene
Stereochemistry of Hydroboration-Oxidation

• Explain why hydroboration-oxidation of 1-methylcyclohexene gives only the product shown below:
Summary of Alkene Addition Reactions

- Show the product of each of the following alkene addition reactions, and include some brief notes about the mechanism of each reaction.
Oxidation and Reduction

- **Oxidation**: Loss of electrons
  - Alternatively, the loss of H, the gain of O, or both

- **Reduction**: Gain of electrons
  - Alternatively, the gain of H, the loss of O, or both

- Recognized using a balanced half-reaction

  - **Steps**
    - Write a half-reaction showing one reactant and its product(s)
    - Complete a material balance
      - Use H₂O and H⁺ in acid solution
      - Use H₂O and OH⁻ in basic solution
    - Complete a charge balance using electrons, e⁻
Oxidation and Reduction of Alkenes

• Balanced half-reactions for the hydration, oxidation, and reduction of propene

\[ \text{CH}_3\text{CH}═\text{CH}_2 + 2 \text{H}_2\text{O} \rightarrow \text{CH}_3\text{CH}─\text{CH}_2 + 2 \text{H}^+ + 2e^- \]

Propene 1,2-Propanediol

\[ \text{CH}_3\text{CH}═\text{CH}_2 + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{CHCH}_3 \]

Propene 2-Propanol

\[ \text{CH}_3\text{CH}═\text{CH}_2 + 2 \text{H}^+ + 2e^- \rightarrow \text{CH}_3\text{CH}_2\text{CH}_3 \]

Propene Propane
Oxidation with OsO$_4$

- OsO$_4$ is an effective oxidizing agent in the conversion of an alkene to a glycol or vicinal diol, a compound with $\text{—OH}$ groups on adjacent carbons.
  - Oxidation of an alkene by OsO$_4$ is syn stereoselective.

- Note that OsO$_4$ is both expensive and highly toxic.
  - Used in catalytic amounts with another oxidizing agent whose purpose is to reoxidize reduced forms of osmium and, thus, recycle the osmium reagent to reduce cost.
  - Commonly used oxidizing agents are hydrogen peroxide (HOOH) and tert-butyl hydroperoxide ($t$-BuOOH).
Ozonolysis of Alkenes

• Consider the following very interesting reaction sequence:

\[ \text{alkene} \xrightarrow{\text{O}_3} \text{aldehyde} + \text{aldehyde} \]

• What are the functional groups of the products of this reaction sequence?

• We won’t worry (for now) about the real mechanism for this reaction, but we can write a fake mechanism:

• Using that fake mechanism, predict the product(s) of the following reactions:
Ozonolysis of Alkenes, With Oxidation

- If the second step of ozonolysis is *oxidative*, then slightly different products are obtained:

\[
\text{O}_3 \quad \text{H}_2\text{O}_2 \quad \text{C}=\text{O} \quad + \quad \text{COH}
\]

- What are the functional groups of the products of this reaction sequence? How is this different from the reductive “workup” (with Me\textsubscript{2}S)?

- Predict the product(s) of the following reactions:

- Ozonolysis of a hydrocarbon (with oxidative workup) gave the following products. What are some possible structures for the original hydrocarbon?
• What is the major product of the following reaction?

\[ \text{1. OsO}_4 \] \[ \text{2. NaHSO}_3/H_2O \]

\[ \begin{align*}
\text{a)} & \quad \text{O} \quad \text{OH} \\
\text{b)} & \quad \text{O} \\
\text{c)} & \quad \text{HO} \quad \text{OH} \\
\text{d)} & \quad \text{HO} \quad \text{OH} \\
\text{e)} & \quad \text{OH} \\
\end{align*} \]
Wow, There Are Lots of Reactions of Alkenes

- Consider the following reaction:

```
\[ \text{CH}_2=\text{CH}_2 + \text{H}_2 \xrightarrow{\text{Pt/C}} \text{CH}_3\text{CH}_3 \]
```

- Is there any way you could have predicted the product of this reaction? Does this reaction even make sense?

- How does this reaction take place? What is the *mechanism* of this reaction?
Anti-Markovnikov Addition of HBr to Alkenes: Free-Radical Addition

• In the presence of certain compounds, notably peroxides (R–O–O–R), the addition of HBr (but not HCl or HI) takes place with anti-Markovnikov regiochemistry:

• Let’s see if we can understand why this is so. First, we need to see the mechanism for HBr addition under these conditions. Note that this is not a mechanism that I would expect you to be able to guess or predict!
Anti-Markovnikov Addition of HBr to Alkenes: Relative Stability of Free-Radical Intermediates

• Now let’s see if we can explain why the addition of HBr under free-radical conditions gives the “anti-Markovnikov” product. Consider the mechanisms for forming the Markovnikov and anti-Markovnikov products. What intermediates are formed in each case?

• Markovnikov Regiochemistry:

\[
\text{ROOR} \quad \text{HBr} \quad \text{ROOR} \quad \begin{array}{c}
\text{H} \\
\text{Br}
\end{array}
\]

• Anti-Markovnikov Regiochemistry:

\[
\text{ROOR} \quad \text{HBr} \quad \text{ROOR} \quad \begin{array}{c}
\text{Br} \\
\text{H}
\end{array}
\]

• How can we explain why the anti-Markovnikov product is preferred?
Reactions of Alkenes: Stereoisomerism
Addition of Bromine to \textit{cis}-2-Butene

- Step 1: Make a bond between a nucleophile (\(\pi\) bond) and an electrophile
  - A bridged bromonium ion intermediate is formed
Addition of Bromine to cis-2-Butene (continued)

- Step 2: Make a new bond between a nucleophile and an electrophile
Addition of Bromine to \textit{trans}-2-Butene

- Step 1: Make a new bond between a nucleophile (\(\pi\) bond) and an electrophile
Addition of Bromine to trans-2-Butene

• Step 2: Make a new bond between a nucleophile and an electrophile
Addition of Bromine to 2-Butene

- Addition of Br₂ or Cl₂ to an alkene is stereospecific
  - **Stereospecific reaction**: Stereochemistry of the product depends on the stereochemistry of the starting material
  - Addition of bromine to cis-2-butene gives the enantiomers of 2,3-dibromobutane as a racemic mixture
  - Addition of bromine to trans-2-butene gives meso-2,3-dibromobutane
Reaction of a Chiral Starting Material in an Achiral Environment

• Bromination of \((R)-4\text{-}\text{tert}\text{-}\text{butylcyclohexene}\)
  • Only a single diastereomer is formed

• Presence of the bulky \text{tert}-\text{butyl} group controls the orientation of the two bromine atoms added to the ring
Reactions of Achiral Starting Materials in a Chiral Environment

• BINAP [2,2-bis(diphenylphosphanylidene)-1,1′-binaphthyl] can be resolved into its $R$ and $S$ enantiomers.
Treating \((R)\)-BINAP with ruthenium chloride forms a complex in which ruthenium is bound in the chiral environment of the larger BINAP molecule:

\[
(R)\text{-BINAP} + \text{RuCl}_3 \rightarrow (R)\text{-BINAP-RuCl}_3
\]

Using \((R)\)-BINAP-RuCl\(_3\) as a hydrogenation catalyst, \((S)\)-naproxen is formed in greater than 98% enantiomeric excess (ee).
Reaction of Achiral Starting Materials in a Chiral Environment

- BINAP-RuCl$_3$ complexes are somewhat specific for the types of C=C reductions they catalyze
- To be reduced, the double bond must have some kind of neighboring group that serves as a directing group
- In the following example, the directing group is the hydroxyl —OH group

\[
\text{(E)-3,7-Dimethyl-2,6-octadien-1-ol (Geraniol)} + \text{H}_2 \xrightarrow{\text{(S)-BINAP-RuCl}_3} \text{(R)-3,7-Dimethyl-6-octen-1-ol} \\
\text{} \xrightarrow{\text{(R)-BINAP-RuCl}_3} \text{(S)-3,7-Dimethyl-6-octen-1-ol}
\]
Problem

• Treating 4-penten-1-ol with bromine in water forms a cyclic bromoether
  • Propose a mechanism for the formation of this product
Solution

• Step 1: Make a new bond between a nucleophile (π bond) and an electrophile
  • This reaction of the alkene with bromine gives a bridged bromonium ion intermediate
• Step 2: Make a new bond between a nucleophile and an electrophile
  • Reaction of this intermediate with the hydroxy group followed by proton transfer gives the cyclic oxonium ion
• Step 3: Take a proton away
  • A chiral center has been created, so a racemic mixture is produced
How Can I Possibly Learn All of These Reactions?
An Introduction to Organic Synthesis

• Propose a synthesis of the following product, starting with only hydrocarbons and inorganic reagents: