Synthesis

- Why are organic chemists interested in synthesizing molecules?
  - to make biologically active compounds that may have been originally isolated from natural sources
  - to make medicinal products
  - to make many modern materials, such as polymers, dyes, and perfumes
- A synthetic organic chemist chooses his or her reactions much like an artist chooses pigments for a painting

Preparation of Alkenes

- Two most common ways to synthesize alkenes are:
  - Dehydrohalogenation of alkyl halides
  - Dehydration of alcohols
- Both of these reactions will be covered more thoroughly in Chapters 11 and 17
- Other methods also exist to make alkenes from alkynes, carbonyl compounds, and vicinal dihalides
- These will also be covered in other chapters
Dehydrohalogenation
- Occurs when an alkyl halide is treated with a strong base like OH⁻ or RO⁻
- Rate = k[RX] [Base]

Dehydration
- Elimination of H₂O from an alcohol in the presence of acid goes through a cation intermediate
- Usually the reaction is carried out with either 85% H₃PO₄ or concentrated H₂SO₄

Addition of Halogens to Alkenes
- Br₂, Cl₂, and I₂ can all add in an electrophilic fashion to C=C
  - F₂ is too reactive and I₂ is too unreactive to be very useful
  - As the halogen approaches the electron rich C=C, it momentarily becomes polarized forming an electrophilic Br.

What is the geometry around the carbocation?
What stereochemistry could the product show?
Problem: Only one Stereoisomer Formed

Thus we know the planar carbocation is not the intermediate because it does not explain the result. The trans cyclic isomer is formed by anti stereochemistry.

Proposed Anti - Mechanism

Each Br approaches the double bond from opposite sides – anti to each other. The resulting stereochemistry is easily observable in cyclic compounds because there is no free rotation around single bonds.

Another View of Cyclopentene Addition

- Addition to the double bond occurs through an anti mechanism
- The X attacks from the opposite face that the bromonium ion is formed on
- This addition is stereospecific

trans-1,2-Dibromocyclopentane
Anti-Stereochemistry in Bromination of General Alkenes

The reaction is stereoselective for anti-addition. Chlorine addition is less selective.

Bromonium Intermediate

- The intermediate forms due to overlap between an empty p orbital on a carbon and the lone pair electrons on Br.
- The drawback to this is the bond angle strain and the electronegativity of Br. Count the formal charges.
- The angles are much less than 109° and the positive charge is centered on an electronegative atom.
- The polarizability of Bromine helps in the formation of the bridge.

Halohydrin Formation

- Halohydrin addition is the formation of a compound with both a halogen and hydroxy group.
- Just as before, the X₂ is polarized and a three membered ring with the X⁺ is formed.
- But, now there is an additional Nu⁺ in solution.
- Addition is anti, with the H₂O attacking from the opposite face from the ring intermediate.
Stereochemistry of Halohydrin Addition

- Because the addition occurs in an anti fashion, the halogen atom and hydroxy group are trans to each other in the product.

Orientation of Halohydrin Addition

- The halogen is added to the less substituted carbon and the OH group adds to the more substituted carbon.
- This occurs because as the ring intermediate starts to open, a partial positive charge forms on one of the carbon atoms.
- The positive charge is stabilized by increased substitution on this carbon.

Note that Markovnikov’s rule means that the initial electrophile will attach to the least substituted carbon.

Source of Bromine

- Bromine is dangerous to use in its diatomic form.
- N-bromosuccinimide (NBS) is a stable and more easily handled source for Br.

Why is this compound a good source of Bromine for an electrophilic reaction?
Electrophilic Addition of $H_2O$ to C=C

- Acid-catalyzed
  - high temperature and acid conditions limit it to industry
- Carbocation intermediate
- Markovnikov Product

- Oxymercuration
  - 1. Mercury acetate/ 2. sodium borohydride
  - Markovnikov product

- Hydroboration
  - Borane in THF/peroxide in base
  - non-Markovnikov
  - Syn stereochemistry

Acid – Catalyzed Hydration

\[
\begin{align*}
CH_3CH_2CH=CH_2 + H_2O &\rightleftharpoons CH_3CH(=CH_2) + CH_3CH_2CHCH_3 + H_2O \\
CH_3CH(=CH_2) + H_2O &\rightleftharpoons CH_3CH=CHCH_3 + H_2O
\end{align*}
\]

Another Example

Two products formed
Oxymercuration-Demercuration

- Oxymercuration involves the use of Hg(OAc)₂

\[
\text{HgOAc} + \text{H}_2\text{C} = \text{CH}_2 \rightarrow \text{HgOAc} + \text{H}_3\text{COAc}
\]

- HgOAc⁺ can act as an electrophile toward C=C just as H⁺
- HgOAc⁺ adds to give the Markovnikov product
- There is no rearrangement

![Mechanism of Hg(OAc)₂ Addition](image)

- Attack by H₂O occurs on opposite face
- Anti-addition of H and OH groups

Hydroboration

- Hydroboration gives the anti-Markovnikov product, OH group ends up on the less substituted carbon.
- Developed by H.C. Brown who won a Nobel Prize in 1979
- Makes use of the fact that Boron is electron poor, good electrophile
- Reagent which is used is Diborane, B₂H₆
- In the mechanism, BH₃, Borane, is considered the active species

![Hydroboration](image)
**Mechanism of Hydroboration**

- The Boron is electron deficient and is attracted to the $\pi$ bond.
- The Boron becomes attached to the least substituted carbon in the C=C.
- A positive charge develops on the other carbon in the C=C.

![Mechanism of Hydroboration](image)

- Final step involves oxidation of BH$_2$ group to OH group - mechanism not understood.

**Stereochemistry of Hydroboration**

- Unlike Oxymercuration-Demercuration where addition is anti, Hydroboration occurs in a syn fashion.
- The Boron and Hydrogen add to the same face of C=C.

![Stereochemistry of Hydroboration](image)

**Problems**

React each of the following alkenes with Hg(OAc)$_2$, NaBH$_4$

React the same alkenes with BH$_3$ in THF, H$_2$O$_2$, HO$^-$

Compare the products.
Carbene Addition to \( \text{C} = \text{C} \)
Cycloaddition

- Carbenes are very reactive species where the carbon has two bonds and two unpaired electrons
- Carbenes can be treated as electrophiles and add to \( \text{C} = \text{C} \) in a concerted fashion
- The stereochemistry at the \( \text{C} = \text{C} \) is maintained after addition
- Carbene addition may occur through the Simmons-Smith Reaction or by Alpha Elimination
- The result of carbene addition is a cyclopropane ring

\[
\begin{align*}
\text{C} & \text{C} \\
\text{H} & \text{H}
\end{align*}
\rightarrow
\begin{array}{c}
\text{C} \\
\text{C} \\
\text{H} \\
\text{H}
\end{array}
\]

Formation of Free Carbenes

Usually done in solution with the alkene.

Carbene Structure
Compared to carbocation
Free Carbene Addition
with dichlorocarbene

- Forms dichlorocyclopropane
- Stereochemistry of double bond maintained in ring
- Very reactive – many side reactions

Simmons-Smith Reaction

- Forms nonhalogenated cyclopropanes
- Uses carbenoid – metal complexed carbene reagent
- Use dihalomethane in presence of Zn – Cu alloy
  - Forms the Simmons-Smith reagent

Examples of Carbene Addition

Note the stereochemistry of each species
Addition of H₂ to Alkenes

- Addition of H₂ to C=C is called hydrogenation
  - Also reduction
  - The reaction is exothermic but requires a catalyst such as Pt or Pd
  - H₂ adds in a syn fashion
  - Because of the mechanism of addition, the reaction is stereospecific and sensitive to steric interactions.

\[ \text{C} = \text{C} + \text{H}_2 \xrightarrow{\text{catalyst}} \text{C} - \text{C} \]

Mechanism of H₂ Addition

- Due to the mechanism of addition, only cis isomers are formed

\[ \text{CH}_2\text{CH}_3 + \text{H}_2 \xrightarrow{\text{Pt}} \text{CH}_2\text{CH}_3 \]

Stereochemistry of H₂ Addition

- Due to the mechanism of addition, only cis isomers are formed

\[ \text{CH}_2\text{CH}_3 \xrightarrow{\text{Pt}} \text{CH}_2\text{CH}_3 \]
Steric Consequences
Because the double bond has to approach the solid surface, it may react from one orientation.

Selectivity of H₂ Addition

\[
\text{Only product, C=O remains intact}
\]

Applications of Hydrogenation

Ester of hemic acid (a constituent of vegetable oil)

Ester of stearic acid
**Syn Hydroxylation of Alkenes**

- Syn hydroxylation of an alkene yields a 1,2-dialcohol
  - (diol or glycol)
- Oxidation – forms C-O bonds
- Two reagents are used for this purpose
  - Osmium Tetroxide, OsO₄
  - Potassium Permanganate, KMnO₄
- Both reagents give the same product with the same stereochemistry
  - OsO₄ gives better yields, but is expensive and very toxic
  - KMnO₄ yields are lower, but it is cheaper and less toxic

---

**Mechanism of OsO₄ Addition**

![Mechanism of OsO₄ Addition](image)

What stereochemistry is this addition?

---

**Oxidative Cleavage of Alkenes**

- Warm, concentrated KMnO₄ cleaves the C=C to make two C=O groups

![Oxidative Cleavage of Alkenes](image)
Oxidative Cleavage of Alkenes
- Ozone, O₃, reacts with C=C to give an ozonide
- Ozonides are unstable and can be reduced to form C=O groups
- Unlike with KMnO₄, aldehydes are not oxidized further to carboxylic acids

\[
\begin{align*}
\text{Ozone} & \quad \rightarrow \quad \text{Ozonide} \\
\text{Ozonide} & \quad \rightarrow \quad \text{molozonide} \\
\end{align*}
\]

Reduction of Ozonide
- Addition of the ozonide with zinc and acetic acid results in the formation of two C=O groups
- Unlike with KMnO₄, only ketones or aldehydes are formed

\[
\begin{align*}
\text{Zn, acetic acid} & \quad \rightarrow \quad 2 \text{C}=\text{O} \\
\end{align*}
\]

Example of Ozonolysis
- Addition of ozone to alkenes
- Subsequent reduction with zinc and acetic acid

\[
\begin{align*}
\text{Ozone} & \quad \rightarrow \quad \text{Ozonide} \\
\text{Ozonide} & \quad \rightarrow \quad \text{molozonide} \\
\end{align*}
\]
Using Ozonolysis to Determine Structure

The sex attractant of the female arctiid moth contains a compound of molecular formula C₂₁H₄₀. Upon ozonolysis, the following carbonyl compounds are formed. What is the structure of C₂₁H₄₀?

\[
\begin{aligned}
\text{CH}_3\text{(CH}_2\text{)}_{10}\text{CH}_2\text{CH}=&\text{CH}\text{CH}_2\text{CH}=&\text{CH}\text{(CH}_2\text{)}_{10}\text{CH}_3
\end{aligned}
\]

1,2-Diol Cleavage

- Vicinal or 1,2-diols can be cleaved under oxidative conditions to yield aldehydes or ketones
- Periodic acid, HIO₄, is used as the oxidizing agent

\[
\begin{aligned}
\text{R}^1\text{R}^2\text{OH} + \text{HIO}_4 &\rightarrow \text{R}^1\text{R}^2\text{O} + \text{HIO}_3 + \text{H}_2\text{O}
\end{aligned}
\]
Polymers from Alkenes

- A polymer is a large molecule composed of smaller repeating units called monomers
- Alkenes serve as the monomers for some of the more common polymers; polyethylene, polypropylene, polystyrene, and PVC (poly(vinylchloride))
- Many alkenes form polymers by a cationic process known as cationic polymerization
- Polyethylene cannot be prepared by cationic polymerization
- Polyethylene is prepared by free-radical polymerization

Free-Radical Polymerization

Step 1. Initiation

\[ \text{RO} - \text{OR} \rightarrow \text{RO}^* + \text{OR} \]

Step 2. Propagation

\[ \text{RO}^* \rightarrow \text{RO}^* + \text{CH}_2=\text{CH}_2 \rightarrow \text{RO} - \text{CH}_2\text{CH}_2 \]

\[ \text{RO} - \text{CH}_2\text{CH}_2 \rightarrow \text{RO} - \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2 \]

Step 3. Termination

\[ \text{RO} - \text{CH}_2\text{CH}_2 \rightarrow \text{RO} - \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2 \]

Cationic Polymerization

\[ \text{CH} = \text{CH}_2 + \text{BF}_3 \rightarrow \text{CH}^* - \text{CH}_2 - \text{BF}_3 \]

\[ \text{BF}_2\text{CH} - \text{CH} = \text{CH}_2 \rightarrow \text{BF}_2\text{CH} - \text{CH}_2 - \text{CH}_2\text{CH} \]
<table>
<thead>
<tr>
<th>Monomer name</th>
<th>Formula</th>
<th>Trade or common name of polymer</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylene</td>
<td>( \text{H}_2\text{C}=\text{CH}_2 )</td>
<td>Polyethylene</td>
<td>Packaging, bottles, cable insulation, filter and foams</td>
</tr>
<tr>
<td>Propene (propylene)</td>
<td>( \text{H}_2\text{C}==\text{CH}_3 )</td>
<td>Polypropylene</td>
<td>Antennas, molding, pipe, cable jackets</td>
</tr>
<tr>
<td>Chloromethylstyrene</td>
<td>( \text{H}_2\text{C}==\text{CHCl} )</td>
<td>Polychloroethylene</td>
<td>Healthcare, filters</td>
</tr>
<tr>
<td>Styrene</td>
<td>( \text{H}_2\text{C}==\text{CH}_2\text{H} )</td>
<td>Polystyrene</td>
<td>Foam and unrelated articles</td>
</tr>
<tr>
<td>Tetrafluoroethylene</td>
<td>( \text{FC}==\text{CF}_2 )</td>
<td>Teflon</td>
<td>Valves and通往significant valves</td>
</tr>
<tr>
<td>Acrylonitrile</td>
<td>( \text{H}_2\text{C}==\text{CHCN} )</td>
<td>Acrylonitrile</td>
<td>Fibers</td>
</tr>
<tr>
<td>Methacrylonitrile</td>
<td>( \text{H}_2\text{C}==\text{C}==\text{C}==\text{CH}_3 )</td>
<td>Polymethacrylonitrile</td>
<td>Molded articles, paints</td>
</tr>
<tr>
<td>Vinyl acetate</td>
<td>( \text{H}_2\text{C}==\text{C}==\text{O}\text{CH}_3 )</td>
<td>Polyvinyl acetate</td>
<td>Paints, adhesives</td>
</tr>
</tbody>
</table>

*Table 7.1: Some Alkene Polymers and Their Uses*