8.14 Substitution vs. Elimination: Predicting the Products

\( \text{S}_\text{N}2 \) – nucleophile replaces the LG with inversion (backside attack) of stereochemistry (stereospecific).

\( \text{S}_\text{N}1 \) – nucleophile replaces the LG, unless the intermediate carbocation undergoes rearrangement. The \( \text{S}_\text{N}1 \) reaction is not stereospecific.

\( \text{E}2 \) – The more substituted alkene is usually favored (Zaitsev rule), unless bulky bases (e.g., t-butoxide) are used. The alkene geometry (\( E \) vs \( Z \)) is determined by the anti-periplanar conformation. In the case of a disubstituted alkene product, the trans geometry is favored.

\( \text{E}1 \) – The more thermodynamically favored alkene is favored. This will be the more substituted alkene product (Zaitsev rule), with the most sterically demanding groups trans.

---

Chapter 9. Addition Reactions of Alkenes
9.1 Introduction to Addition Reactions

Substitution Reactions: two reactants exchange parts to give new products (Chapter 7)

\[
\begin{align*}
\text{H}_3\text{C}-\text{H}_2\text{C-OH} + \text{H-Br} & \rightarrow \text{H}_3\text{C}-\text{H}_2\text{C-Br} + \text{H-OH}
\end{align*}
\]

Elimination Reaction: a single reactant is split into two (or more) products. Opposite of an addition reaction (Chapter 8)

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

\[
\text{NaOH} \rightarrow \begin{align*}
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*} + \text{H-OH} + \text{Na-Br}
\]

Addition Reaction: two reactants add to form a product with no (or few) atoms left over (Chapter 9).

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*} + \text{H-Br} \rightarrow \begin{align*}
\text{Br} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*}
\]
### 9.2: Addition vs. Elimination: A Thermodynamic Perspective

\[ \Delta G = \Delta H - T \Delta S \]

Addition reactions are usually enthalpically favorable, but entropically disfavored.

#### 9.3. Hydrohalogenation

Reactivity of \( HX \) correlates with acidity:

- slowest: HF \(<\) HCl \(<\) HBr \(<\) HI
- fastest
Regiochemistry

\[
\begin{align*}
& \text{H} \quad \underline{\text{C} = \text{C}} \quad \text{R'} \quad \underline{\text{H}} \quad \xrightarrow{\text{H-Br}} \quad \text{Br} \quad \underline{\text{R} - \text{C} - \text{C}} \quad \underline{\text{H}} \quad + \quad \text{H} \quad \underline{\text{Br}} \\
& \text{R} \quad \underline{\text{C} = \text{C}} \quad \text{R'} \quad \underline{\text{H}} \quad \xrightarrow{\text{H-Br}} \quad \text{Br} \quad \underline{\text{R} - \text{C} - \text{C}} \quad \underline{\text{H}} \quad + \quad \text{H} \quad \underline{\text{Br}}
\end{align*}
\]

Mechanism for hydrohalogenation
Stereochemistry of hydrohalogenation – hydrohalogenation proceeds through a carbocation intermediate. No stereochemical preference.

\[
\text{H} - \text{X} \rightarrow \text{H}^+ + \text{X}^-
\]

Carbocation rearrangements

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

Cationic polymerization

\[
\text{styrene} \rightarrow \text{polystyrene}
\]

9.4 Acid-Catalyzed Hydration – Alkenes - addition of water (H-OH) across the π-bond of an alkene to give an alcohol; opposite of dehydration

\[
\text{H}_3\text{C} - \text{C} = \text{CH}_2 \xrightarrow{\text{H}_2\text{SO}_4, \text{H}_2\text{O}} \text{H}_3\text{C} - \text{C} - \text{OH}
\]
This addition reaction follows Markovnikov’s rule. The more highly substituted alcohol is the product and is derived from the most stable carbocation intermediate. Reactions work best for the preparation of 3° alcohols, but poorly for 1° alcohols.

9.5 Oxymercuration-Demercuration – The acid-catalyzed hydration is not a general method for the hydration of an alkene.

Oxymercuration – Demercuration: a general (2-step) method for the Markovnikov hydration of alkenes.

NaBH₄ reduces the C-Hg bond to a C-H bond.
9.6 Hydroboration-Oxidation - *Anti*-Markovnikov addition of H-OH; *syn* addition of H-OH

CH₃

1) B₂H₆, THF
2) H₂O₂, NaOH, H₂O

Diborane

2 BH₃ → H₂B₄H₁₀

Mechanism of hydroboration

Hydration of alkenes summary: addition of water (H–OH) across the π-bond of an alkene to give an alcohol.

1. Acid catalyzed hydration- Markovnikov addition of H–OH
   Not a good method for hydration of an alkene

2. Oxymercuration- Markovnikov addition H–OH

3. Hydroboration- Anti-Markovnikov addition of H–OH,
   Syn addition of H–OH
9.7 Catalytic Hydrogenation – Addition of $\text{H}_2$ across the $\pi$-bond of an alkene to give an alkane. This is a reduction.

\[ \text{R} = \text{H}_2, \text{Pd} \rightarrow \text{R} \]

The catalysts (Pd, Pt, Rh, Ni) is not soluble in the reaction media; thus, this process is referred to as a *heterogenous* catalysis.

The reaction takes places on the surface of the catalyst. Thus, the rate of the reaction is proportional to the surface area of the catalyst.

Stereospecificity – The addition of $\text{H}_2$ across the $\pi$-bond is *syn*, i.e., from the same face of the double bond.

Mechanism: The catalyst assists in breaking the $\pi$-bond of the alkene and the H-H $\sigma$-bond.

Carbon-carbon $\pi$-bond of alkenes and alkynes can be reduced to the corresponding saturated C-C bond. Other $\pi$-bond bond such as C=O (carbonyls) and C≡N (nitriles) are not easily reduced by catalytic hydrogenation. The C=C bonds of aromatic rings are not easily reduced.
9.8 Halogenation and Hydrohydrin Formation
Addition of $X_2$ (Cl$_2$ and Br$_2$) to Alkenes

$$\text{alkene} + X_2 \rightarrow \text{1,2-dihalide}$$

Stereochemistry – *anti* addition of $X_2$ across the $\pi$-bond

Mechanism for halogenation

Bromonium ion intermediate explains the stereochemistry of Br$_2$ addition.
Regiochemistry of halohydrin formation – For unsymmetrical alkenes, halohydrin formation is Markovnikov-like in that the orientation of the addition of X–OH can be predicted by considering carbocation stability.
Organic molecules are sparingly soluble in water as solvent. The reaction is often done in a mix of organic solvent and water using N-bromosuccinimide (NBS) as the electrophilic bromine source.

Note that the aryl ring does not react!!!

9.9 Anti Dihydroxylation formal addition of HO-OH across the π-bond of an alkene to give a vicinal-diol. This is an overall oxidation. Vicinal diols have hydroxyl groups on adjacent carbons (vic-diols, 1,2-diols, glycols)

Epoxide (oxirane): three-membered ring, cyclic ethers.

Peroxyacids

Epoxidation mechanism

Stereochemistry of the epoxidation of alkenes: syn addition of oxygen. The geometry of the alkene is preserved in the product.

Groups that are trans on the alkene will end up trans on the epoxide product. Groups that are cis on the alkene will end up cis on the epoxide product.
Epoxide hydrolysis to anti vicinal diols

9.10 Syn Dihydroxylation

\[
\begin{align*}
\text{I} & \xrightarrow{\text{OsO}_4} \text{osmate ester intermediate} \xrightarrow{\text{NaHSO}_3, \text{H}_2\text{O}} \text{OH} \\
\end{align*}
\]

9.11 Oxidative Cleavage (ozonolysis) - oxidative cleavage of an alkene to carbonyl compounds (aldehydes and ketones). The \( \pi \)- and \( \sigma \)-bonds of the alkene are broken and replaced with C=O double bonds.

Ozone (\( \text{O}_3 \)): \( 3 \text{O}_2 \xrightarrow{\text{electrical discharge}} 2\text{O}_3 \) + \( \text{O}^=\text{O}^-\text{O}^=\text{O}^- \)

Mechanism

- Molozonide
- Ozonide
- Oxonide
- ZnO or (H\(_3\)C)\(_2\)SO

- \( \text{O}_3 \):
  - \( \text{H}_2\text{C}_2\text{S} \)
  - Zn, H\(_2\)O

- \( \text{O}_3 \):
  - \( \text{H}_2\text{C}_2\text{S} \)
  - Zn, H\(_2\)O

- \( \text{O}_3 \):
  - \( \text{H}_2\text{C}_2\text{S} \)
  - Zn, H\(_2\)O
9.12 Predicting the Products of an Addition Reaction

1. What atoms or groups are being added to the double bond. Account for these groups in the reagents.

2. What is the regiochemistry: Markovnikov vs anti-Markovnikov

3. What is the stereochemistry: Syn vs Anti addition, or no stereochemical preference.

9.13 Synthesis Strategies – Construct larger, more complex molecules out of smaller ones using known and reliable reactions

One-step synthesis:

- Substitution
- Elimination
- Addition

Change the position of the leaving group (halide or alcohol)

Change the position of a $\pi$-bond

*Retrosynthetic analysis* – working a synthesis problem backward from the desired product to the starting substrate.