Chapter 15: Alcohols, Diols, and Ethers

- Alcohols by reduction of aldehydes and ketones
- Metal hydride reagents for reducing carbonyls
- Reduction of carboxylic acid derivatives with LiAlH₄
- Alcohols by acid/base opening of epoxides
- Preparation of diols from alkenes
- Reactions of alcohols; oxidation, ether synthesis

Chapter 14
Alcohol synthesis using organometallic reagents
Chapter 15: Alcohols, Diols, and Ethers

Use of alcohols to make other functional groups

15.1 – Sources of Alcohols

Geraniol (component of the fragrant oil of many flowers)

Menthol (from oil of peppermint; used to flavor tobacco and food)
15.1 – Sources of Alcohols

Testosterone (male sex hormone)

Progesterone

Testosterone

(YSU)
Organic Synthesis: Molecular Engineering

Two main components

Carbon-Carbon bond formation – organometallics

Functional group manipulation – e.g. $\text{R}_2\text{CHOH}$ to $\text{R}_2\text{C}=\text{O}$

15.2 – Preparation of Alcohols by Reduction of $\text{RR'}\text{C}=\text{O}$

[Chemical reaction and mechanism diagrams]
15.3 – Preparation of Alcohols by Reduction of RCO₂R' 

\[ \text{RCO}_2\text{H} \rightarrow \text{H}_2\text{O}^+ \text{LiAlH}_4, \text{THF} \rightarrow \text{H}_2\text{O}^+ \text{LiAlH}_4, \text{THF} \]

Mechanism analogous to Grignard-Ester Reaction

15.4 – Preparation of Alcohols from Epoxides

\[ \text{m-CPBA} \rightarrow \text{CH}_3\text{MgBr} \rightarrow \text{H}_2\text{O}^+ \text{CH}_3\text{MgBr} \rightarrow \text{H}_2\text{O}^+ \]

Nucleophilic ring-opening is an $S_{n2}$ process governed by steric hindrance around the electrophilic carbon being attacked
15.5 – Preparation of Diols from Alkenes

Cis-dihydroxylation via an osmate ester intermediate

15.5 – Polyols in Nature and Medicine

D-glucose           D-galactose           D-glucosamine           D-GlcNAc

L-Fucose           D-ManAcA          D-Ribose           2-Deoxy-D-ribose
15.5 – Polyols in Nature and Medicine

Blood antigens

Oligo- & polysaccharides serve as molecular recognition motifs

15.6 – Reactions of Alcohols – Review

Hi, HBr, PBr₃, SOCl₂, TsCl, pyridine

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15.7 – Conversion of Alcohols to Ethers

- Acid-base reaction followed by $S_n2$ reaction on alkyl halide substrate
- Limited to primary alkyl halides (secondary give E2 in competition)

15.7 – Conversion of Primary Alcohols to Ethers

- Acid-base reaction followed by $S_n2$ reaction on alcohol
- Limited to primary alcohols ($2^o/3^o$ give elimination products)
15.7 – Conversion of Primary Alcohols to Ethers

Examples

15.8 – Esterification of Alcohols

Examples
**15.8 – Other Methods of Esterification**

**Acyl chlorides**

\[ R\text{Cl} \xrightarrow{\text{pyridine}} R\text{O} \]

**Acetic anhydride**

\[ \text{H}_2\text{C}==\text{O} \xrightarrow{\text{pyridine}} \text{H}_2\text{C}==\text{O} \]

Skip Section 15.9

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**15.10 – Oxidation of Alcohols**

**Primary**

\[ \text{H}_2\text{H} \xrightarrow{} \text{H} \xrightarrow{} \text{H} \]

**Secondary**

\[ \text{R}_2\text{H} \xrightarrow{} \text{R} \xrightarrow{} \text{R} \]

Useful chemical tests for classifying alcohols

**Tertiary**

\[ \text{R}_2\text{H} \xrightarrow{} \text{R} \xrightarrow{} \text{R} \]

no reaction under normal conditions

YSU
15.10 – Oxidation of Alcohols – Mechanism 15.3

**Mechanism 15.3**

Chromic Acid Oxidation of 2-Propanol

**Step 1:** Reaction of the alcohol with chromic acid gives an alkyl chromate.

```
CH₃CH₂OH + H₂CrO₄ → CH₃CH₂O⁻Cr₂O₇²⁻ + H₂O
```

**Step 2:** The oxidation step can be viewed as a β-elimination. Water acts as a base to remove a proton from carbon while the O–C₁ bond breaks.

```
CH₃CH₂O⁻Cr₂O₇²⁻ → CH₃CH⁺⁺⁻OH + Cr₂O₇²⁻ + H₂O
```

**Step 3:** A series of redox reactions converts chromium from the 4⁺ oxidation state in HCrO₄⁻ to the 3⁺ oxidation state.

15.10 – Oxidation of Alcohols – Stopping at the Aldehyde

**Pyridinium chlorochromate (PCC)**

```
+CH₃CH₂OH → +CH₃CH₂CHO
```

**Pyridinium dichromate (PDC)**

```
+CH₃CH₂OH → +CH₃CH₂CHO
```

*Also works for secondary alcohols to ketones*
15.11 – Oxidation of Alcohols – Biological Oxidation

Structure of NAD⁺

Figure 15.2

![Structure of NAD⁺]

15.11 – Oxidation of Alcohols – Biological Oxidation

**MECHANISM 15.4**

Oxidation of Ethanol by NAD⁺

![Oxidation of Ethanol by NAD⁺]

- Ethanol + NAD⁺ → Acetaldehyde + NADH

YSU
15.12 – Oxidative Cleavage of Vicinal Diols

Use:

\[
\text{Use:} \quad \text{O}_3 \xrightarrow{\text{BuOOH}} \xrightarrow{\text{NaOH}} \xrightarrow{\text{NaIO}_4} \xrightarrow{\text{H}_2\text{O}} \text{CHO} \]

Compare to ozonolysis:

\[
\text{Compare to ozonolysis:} \quad \text{O}_3 \xrightarrow{2. \text{Zn, Mo}_2\beta} \xrightarrow{1. \text{O}_3} \text{CHO} \]

15.13 – Thiols – Sulfur Equivalent of Alcohols

\[
\begin{align*}
\text{ethanethiol} & \quad \text{butanethiol} \\
\text{thiophenol} & \quad 3\text{-methyl-1-butethiol}
\end{align*}
\]

Important – more acidic than alcohols: pKa ~ 10