Chapter 8
Alcohols, Ethers, and Thiols

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Alcohols - Structure

- Figure 8.1 The functional group of an alcohol is an -OH (hydroxyl) group bonded to an sp³ hybridized carbon.
  - Bond angles about the hydroxyl oxygen atom are approximately 109.5°.
- Oxygen is also sp³ hybridized.
  - Two sp³ hybrid orbitals form sigma bonds to carbon and hydrogen.
  - The remaining two sp³ hybrid orbitals each contain an unshared pair of electrons.

“...and the waters that were in the river were turned to blood. And the fish that were in the river died; and the river stank and the Egyptians could not drink of the water of the river...”
Exodus 7:20-21
Alcohols - Nomenclature

- **IUPAC names**
  - The parent chain is the longest chain that contains the -OH group.
  - Number the parent chain in the direction that gives the -OH group the lower number.
  - Change the suffix -e to -ol.

- **Common names**
  - Name the alkyl group bonded to oxygen followed by the word alcohol.

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**Examples:**

- Ethanol (Ethyl alcohol)
- 1-Propanol (Propyl alcohol)
- 2-Propanol (Isopropyl alcohol)
- 1-Butanol (Butyl alcohol)
- 2-Butanol (Isobutyl alcohol)
- 2-Methyl-1-propanol (Isobutyl alcohol)
- 2-Methyl-2-propanol (Isobutyl alcohol)
- Cyclohexanol (Cyclohexyl alcohol)

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**Problem:** Write the IUPAC name of each alcohol.

- (a) CH₃CH₂CH₂OH
- (b) CH₃CH₂OH
- (c) CH₃CH₂CH₂CH₂OH

---

**Compounds containing**

- two -OH groups are named as diols,
- three -OH groups are named as triols.
- Compounds containing two -OH groups on are called glycols.

- CH₂CH₂OH
- CH₃CH₂OH
- CH₃CH₂OH
  - 1,2-Ethandiol (Glycol)
  - 1,2-Propanediol (Propylene glycol)
  - 1,2,3-Propanetriol (Glycerol, Glycerin)
Alcohols - Nomenclature

- **Unsaturated alcohols**
  - The double bond is shown by the infix -en-.
  - The hydroxyl group is shown by the suffix -ol.
  - Number the chain to give OH the lower number.

  \[ \text{trans-3-hexene-1-ol} \]
  \[ (E)-3-hexene-ol \]

Physical Properties

- **Figure 8.2** Polarity of the C-O-H bond in methanol.
  (a) Partial positive charges on carbon and hydrogen and a partial negative charge on oxygen.
  (b) An electron density map showing the partial negative charge (red) and the partial positive charge (blue).

Hydrogen Bonding

- Alcohols associate in the liquid state by hydrogen bonding.

  - **Hydrogen bonding**: The attractive force between a partial positive charge on hydrogen and a partial negative charge on a nearby oxygen, nitrogen, or fluorine atom.
    - The strength of hydrogen bonding in alcohols is approximately 2 to 5 kcal/mol.
    - Hydrogen bonds are considerably weaker than covalent bonds (for example, 110 kcal/mol for an O–H bond).
    - Nonetheless, hydrogen bonding can have a significant effect on physical properties.
Hydrogen Bonding Erythromycin

**Problem:** Following is a structural formula for Erythromycin A, a widely used antibiotic. See next screen for questions.

![Structural formula of Erythromycin A](image)

**Solution:** Shown are the four intramolecular hydrogen bonds. They create one six-membered ring and three five-membered rings.

![Intramolecular hydrogen bonds](image)

---

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---

**Boiling Points**

<table>
<thead>
<tr>
<th>Structural Formula</th>
<th>Name</th>
<th>Molecular Weight</th>
<th>Boiling Point (°C)</th>
<th>Solubility in Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃OH</td>
<td>methanol</td>
<td>32</td>
<td>65</td>
<td>infinite</td>
</tr>
<tr>
<td>CH₃CH₂OH</td>
<td>ethanol</td>
<td>30</td>
<td>-89</td>
<td>insoluble</td>
</tr>
<tr>
<td>CH₃CH₂CH₂OH</td>
<td>propane</td>
<td>44</td>
<td>-42</td>
<td>insoluble</td>
</tr>
<tr>
<td>CH₃CH₂CH₃CH₂OH</td>
<td>1-propanol</td>
<td>60</td>
<td>97</td>
<td>infinite</td>
</tr>
<tr>
<td>CH₃CH₂CH₃CH₃OH</td>
<td>butane</td>
<td>58</td>
<td>0</td>
<td>insoluble</td>
</tr>
<tr>
<td>CH₃CH₂CH₃CH₄OH</td>
<td>1-butanol</td>
<td>74</td>
<td>117</td>
<td>8 g/100 g</td>
</tr>
<tr>
<td>CH₃CH₂CH₃CH₅OH</td>
<td>pentane</td>
<td>72</td>
<td>36</td>
<td>insoluble</td>
</tr>
<tr>
<td>CH₃CH₂CH₃CH₆OH</td>
<td>1,2-pentanediol</td>
<td>88</td>
<td>138</td>
<td>2.3 g/100 g</td>
</tr>
<tr>
<td>HOCH₂CH₃CH₂CH₃OH</td>
<td>1,4-butandiol</td>
<td>90</td>
<td>230</td>
<td>infinite</td>
</tr>
<tr>
<td>CH₃CH₂CH₃CH₅CH₆OH</td>
<td>hexane</td>
<td>86</td>
<td>69</td>
<td>insoluble</td>
</tr>
</tbody>
</table>
**Acidity of Alcohols**

- Most alcohols are about the same or slightly weaker acids than water.

$$\text{CH}_3\text{OH} \rightarrow +\text{H}^+ + \text{CH}_3\text{O}^- + \text{H}_2\text{O}^- + \text{H} \rightarrow \text{CH}_3\text{O}^- + \text{H}^+ + \text{H}_2\text{O}^- + \text{H}$$

$$pK_a = 15.5 \quad (pK_a = 15.7)$$

- Aqueous solutions of alcohols have the same pH as that of pure water.

**Acidity of Alcohols**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structural Formula</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogen chloride</td>
<td>HCl</td>
<td>-7</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>CH₃COOH</td>
<td>4.8</td>
</tr>
<tr>
<td>Methanol</td>
<td>CH₃OH</td>
<td>14.4</td>
</tr>
<tr>
<td>Water</td>
<td>H₂O</td>
<td>15.7</td>
</tr>
<tr>
<td>Ethanol</td>
<td>CH₃CH₂OH</td>
<td>15.9</td>
</tr>
<tr>
<td>2-Propanol</td>
<td>(CH₃)₂COH</td>
<td>17</td>
</tr>
<tr>
<td>2-Methyl-2-propanol</td>
<td>(CH₃)₂COH</td>
<td>18</td>
</tr>
</tbody>
</table>

*Also given for comparison are $pK_a$ values for water, acetic acid, and hydrogen chloride.

**Basicity of Alcohols**

- In the presence of strong acids, the oxygen atom of an alcohol behaves as a weak base.

- Proton transfer from the strong acid forms an oxonium ion.

$$\text{CH}_3\text{OH} \rightarrow +\text{H}^+ + \text{CH}_3\text{O}^- + \text{H}_2\text{O}^- + \text{H} \rightarrow \text{CH}_3\text{O}^- + \text{H}^+ + \text{H}_2\text{O}^- + \text{H}$$

- Alkoxides are somewhat stronger bases than OH⁻.
- Alkoxides can be used as nucleophiles in nucleophilic substitution reactions.
- They can also be used as bases in β-elimination reactions.

**Reaction with Active Metals**

- Alcohols react with Li, Na, K, and other active metals to liberate hydrogen gas and form metal alkoxides.

$$2 \text{CH}_3\text{OH} + 2 \text{Na} \rightarrow 2 \text{CH}_3\text{O}^- \text{Na}^+ + \text{H}_2$$

- Na is oxidized to Na⁺ and H⁺ is reduced to H₂.

- Alkoxides can be used as nucleophiles in nucleophilic substitution reactions.
- They can also be used as bases in β-elimination reactions.
Conversion of ROH to RX

- Water-soluble 3° alcohols react very rapidly with HCl, HBr, and HI.

\[
\text{CH}_3\text{OH} + \text{HCl} \xrightarrow{25 \degree C} \text{CH}_3\text{Cl} + \text{H}_2\text{O}
\]

2-Methyl-2-propanol 2-Chloro-2-methylpropane

- Low-molecular-weight 1° and 2° alcohols are unreactive under these conditions.

Conversion of ROH to RX

- Water-insoluble 3° alcohols react by bubbling gaseous HCl through a solution of the alcohol dissolved in diethyl ether or THF.

\[
\text{OH} + \text{HCl} \xrightarrow{1-2 \degree C} \text{Cl} + \text{H}_2\text{O}
\]

1-Methyl-cyclohexanol 1-Chloro-1-methyl-cyclohexane

1-Butanol 1-Butanobutane (Butyl bromide)

- 1° and 2° alcohols require concentrated HBr and HI to form alkyl bromides and iodides.

Reaction of a 3° ROH with HX

- 3° Alcohols react with HX by an S_n^1 mechanism.

**Step 1:** Add a proton. Rapid and reversible proton transfer from the acid to the —OH group.

- This proton-transfer converts the leaving group from OH^−, a poor leaving group, to H_2O, a better leaving group.

**Step 2:** Break a bond to form a stable molecule or ion. Loss of H_2O gives a 3° carbocation.

**Step 3:** Reaction of an electrophile and a nucleophile to form a new covalent bond completes the reaction.
Reaction of a 1° ROH with HX
• 1° alcohols react with HX by an $S_N$2 mechanism.

  – **Step 1:** Add a proton. Proton transfer to OH converts OH$^-$, a poor leaving group, to H$_2$O a better leaving group.

  

  Reaction of ROH with HX
  • Reactions are governed by a combination of electronic and steric effects

  ![Reaction mechanism](image.png)

Dehydration of Alcohols
• An alcohol can be converted to an alkene by elimination of $-\text{H}$ and $-\text{OH}$ from adjacent carbons (a $-\text{elimination}$).

  – 1° alcohols must be heated at high temperature in the presence of an acid catalyst, such as H$_2$SO$_4$ or H$_3$PO$_4$.

  – 2° alcohols undergo dehydration at somewhat lower temperatures.

  – 3° alcohols often require temperatures at or only slightly above room temperature.

Dehydration of Alcohols
– examples:

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Temperature</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_3$CH$_2$OH</td>
<td>$180^\circ$C</td>
<td>CH$_3$ == CH$_2$ + H$_2$O</td>
</tr>
<tr>
<td>Cyclohexanol</td>
<td>H$_2$SO$_4$</td>
<td>Cyclohexene + H$_2$O</td>
</tr>
<tr>
<td>CH$_3$COH</td>
<td>50$^\circ$C</td>
<td>CH$_3$C == CH$_2$ + H$_2$O</td>
</tr>
<tr>
<td>2-Methyl-2-propanol</td>
<td>(t-butyl alcohol)</td>
<td>2-Methylpropene (Isobutylene)</td>
</tr>
</tbody>
</table>
Dehydration of Alcohols

- When isomeric alkenes are obtained, the more stable alkene (the one with the greater number of substituents on the double bond) generally predominates (Zaitsev's rule).

**Dehydration of a 2° Alcohol**

- A three-step mechanism
  - **Step 1**: Add a proton. Proton transfer from $H_2O^+$ to the $-OH$ group converts $OH^-$, a poor leaving group, into $H_2O$, a better leaving group.

**Dehydration of a 2° Alcohol**

- **Step 2**: Break a bond to form a stable molecule or ion. Loss of $H_2O$ gives a carbocation intermediate.

- **Step 3**: Take a proton away. Proton transfer from an adjacent carbon to $H_2O$ gives the alkene and regenerates the acid catalyst.

**Dehydration of a 1° Alcohol**

- A two-step mechanism
  - **Step 1**: Add a proton. Proton transfer from the acid gives an oxonium ion.

  - **Step 2**: Take a proton away and loss of $H_2O$ gives the alkene and regenerates the acid catalyst.
**Hydration-Dehydration**

- Acid-catalyzed hydration of an alkene and dehydration of an alcohol are competing processes.

\[ \text{C=} \xrightarrow{\text{acid catalyst}} \xleftarrow{\text{dehydration}} \text{C} \quad \text{H} \quad \text{OH} \]

An alkene \quad \text{An alcohol}

- Large amounts of water favor alcohol formation.
- Scarcity of water or experimental conditions where water is removed favor alkene formation.

**Ethers - Structure**

- **Figure 8.4** The functional group of an ether is an oxygen atom bonded to two carbon atoms.
  
  - Oxygen is \( sp^3 \) hybridized with bond angles of approximately 109.5°.
  
  - In dimethyl ether, the C–O–C bond angle is 110.3°.

![](ether_structures.png)

**Ethers - Nomenclature**

- **IUPAC**
  
  - The parent alkane is longest carbon chain.
  
  - Name the -OR group as an alkoxy substituent.

- **Common names**:

  - Name the groups bonded to oxygen followed by the word ether.

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Structural Formulas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethoxethane (Diethyl ether)</td>
<td>CH₃CH₂OCH₂CH₃</td>
</tr>
<tr>
<td>2-methyl-2-methoxypropanol (sec-butylmethyl ether)</td>
<td>CH₃CH₂CH₂OCH₂CH₃</td>
</tr>
<tr>
<td>(1R,2R)-2-ethoxycyclohexanol</td>
<td><img src="cyclohexanol.png" alt="Structure" /></td>
</tr>
</tbody>
</table>

**Ethers - Nomenclature**

- Although cyclic ethers have IUPAC names, their common names are more widely used.

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Structural Formulas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylene oxide</td>
<td><img src="ethyleneoxide.png" alt="Structure" /></td>
</tr>
<tr>
<td>Tetrahydrofuran (THF)</td>
<td><img src="tetrahydrofuran.png" alt="Structure" /></td>
</tr>
<tr>
<td>1,4-Dioxane</td>
<td><img src="14dioxane.png" alt="Structure" /></td>
</tr>
</tbody>
</table>
Ethers - Physical Properties

- **Figure 8.5** Ethers are polar molecules.
  - Each C-O bond is polar covalent.
  - However, only weak attractive forces exist between ether molecules in the pure liquid.

Ethers - Physical Properties

- **Figure 8.6** Ethers are hydrogen bond acceptors only. They are not hydrogen bond donors.

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**Table 8.3** Boiling Points and Solubilities in Water of Some Alcohols and Ethers of Comparable Molecular Weight

<table>
<thead>
<tr>
<th>Structural Formula</th>
<th>Name</th>
<th>Molecular Weight</th>
<th>Boiling Point (°C)</th>
<th>Solubility in Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CH₂OH</td>
<td>ethanol</td>
<td>46</td>
<td>78</td>
<td>infinite</td>
</tr>
<tr>
<td>CH₃OCH₃</td>
<td>dimethyl ether</td>
<td>46</td>
<td>-24</td>
<td>7.4 g/100 g</td>
</tr>
<tr>
<td>CH₃CH₂CH₂CH₂OH</td>
<td>1-butanol</td>
<td>74</td>
<td>117</td>
<td>7.4 g/100 g</td>
</tr>
<tr>
<td>CH₃CH₂OCH₂CH₃</td>
<td>diethyl ether</td>
<td>74</td>
<td>35</td>
<td>8 g/100 g</td>
</tr>
<tr>
<td>CH₃CH₂CH₂OH</td>
<td>1-pentanol</td>
<td>88</td>
<td>138</td>
<td>2.3 g/100 g</td>
</tr>
<tr>
<td>CH₃CH₂OCH₂CH₂OH</td>
<td>1,4-butane diol</td>
<td>90</td>
<td>230</td>
<td>infinite</td>
</tr>
<tr>
<td>CH₃CH₂OCH₂CH₂CH₃</td>
<td>butyl methyl ether</td>
<td>88</td>
<td>71</td>
<td>slight</td>
</tr>
<tr>
<td>CH₃CH₂OCH₂CH₂CH₂CH₃</td>
<td>ethylene glycol dimethyl ether</td>
<td>90</td>
<td>84</td>
<td>infinite</td>
</tr>
</tbody>
</table>

Ethers - Physical Properties

- The effect of hydrogen bonding is illustrated by comparing the boiling points of ethanol and dimethyl ether.

- Ethanol: bp 78 °C
- Dimethyl ether: bp -24 °C
Epoxides

- Epoxide: A cyclic ether in which oxygen is one atom of a three-membered ring.

![Epoxide structures](image)

Ethylene oxide

- Ethylene oxide is synthesized from ethylene and O₂

\[2 \text{CH}_2=\text{CH}_2 + \text{O}_2 \rightarrow 2 \text{HOCH}_2\text{CH}_2\text{O} \]

Ethylene Ethylene oxide

Epoxide Ring Openings

- The mechanism of acid-catalyzed hydrolysis of an epoxide involves three steps.
  - Step 1: Add a proton
  - Step 2: Reaction of an electrophile and a nucleophile to form a new covalent bond.
  - Step 3: Take away a proton.

![Epoxide ring openings](image)

Epoxides as Building Blocks

- Following are structural formulas for two common drugs, each synthesized in part with ethylene oxide as a building block.

![Structural formulas](image)
Thiols - Structure

- Figure 8.7 The functional group of a thiol is an -SH (sulfhydryl) group bonded to an sp³ hybridized carbon.

(a) 
(b) 

Thiols - Nomenclature

IUPAC names
- The parent chain is the longest chain that contains the -SH group.
  - Add -thiol to the name of the parent chain.
Common names
- Name the alkyl group bonded to sulfur followed by the word mercaptan.
- Alternatively, indicate the -SH by the prefix mercapto.

Ethanethiol  2-Methyl-1-propanethiol  2-Mercaptobenzyl alcohol
(Ethyl mercaptan)  (Isobutyl mercaptan)  (2-Methylpropyl mercaptan)

Thiols - Physical Properties

- Low-molecular-weight thiols have a STENCH

<table>
<thead>
<tr>
<th>Thiol</th>
<th>Boiling Point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methanethiol</td>
<td>6</td>
</tr>
<tr>
<td>Ethanethiol</td>
<td>35</td>
</tr>
<tr>
<td>1-Butanethiol</td>
<td>98</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Boiling Point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methanol</td>
<td>65</td>
</tr>
<tr>
<td>Ethanol</td>
<td>78</td>
</tr>
<tr>
<td>1-Butanol</td>
<td>117</td>
</tr>
</tbody>
</table>

- The difference in electronegativity between S and H is 2.5 – 2.1 = 0.4
- Because of their low polarity, thiols
  - show little association by hydrogen bonding.
  - have lower boiling points and are less soluble in water than alcohols of comparable MW.
Acidity of Thiols

- Thiols are stronger acids than alcohols.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{OH} + \text{H}_2\text{O} & \rightleftharpoons \text{CH}_3\text{CH}_2\text{O}^- + \text{H}_3\text{O}^+ \quad pK_a = 15.9 \\
\text{CH}_3\text{CH}_2\text{SH} + \text{H}_2\text{O} & \rightleftharpoons \text{CH}_3\text{CH}_2\text{S}^- + \text{H}_3\text{O}^+ \quad pK_a = 8.5 
\end{align*}
\]

- Thiols react with strong bases to form salts.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{SH} + \text{Na}^+\text{OH}^- & \rightarrow \text{CH}_3\text{CH}_2\text{S}^-\text{Na}^+ + \text{H}_2\text{O} \\
pK_a 8.5 & \quad pK_a 15.7 \\
\text{Stronger} & \quad \text{Stronger} & \quad \text{Weaker} & \quad \text{Weaker}
\end{align*}
\]

- Thiols react with strong bases to form salts.