Chapter 14
Ethers, Epoxides, and Sulfides

Chem 233
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Introduction

- Formula R-O-R’ where R and R’ are alkyl or aryl.
- Symmetrical or unsymmetrical
- Examples:

$$\text{CH}_3-\text{O-CH}_3$$

$$\text{C}=$$

$$\text{O-CH}_3$$
Structure and Polarity

- Bent molecular geometry
- Oxygen is $sp^3$ hybridized
- Tetrahedral angle

Boiling Points

Similar to alkanes of comparable molecular weight.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>MW</th>
<th>bp (°C)</th>
<th>Dipole Moment (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>water</td>
<td>$H_2O$</td>
<td>18</td>
<td>100</td>
<td>1.9</td>
</tr>
<tr>
<td>ethanol</td>
<td>$CH_3CH_2OH$</td>
<td>46</td>
<td>78</td>
<td>1.7</td>
</tr>
<tr>
<td>dimethyl ether</td>
<td>$CH_3OCH_3$</td>
<td>46</td>
<td>-25</td>
<td>1.3</td>
</tr>
<tr>
<td>propane</td>
<td>$CH_3CH_2CH_3$</td>
<td>44</td>
<td>-42</td>
<td>0.1</td>
</tr>
<tr>
<td>n-butanol</td>
<td>$CH_3CH_2CH_2OH$</td>
<td>74</td>
<td>118</td>
<td>1.7</td>
</tr>
<tr>
<td>tetrahydrofuran</td>
<td></td>
<td>72</td>
<td>66</td>
<td>1.6</td>
</tr>
<tr>
<td>diethyl ether</td>
<td>$CH_3CH_2OCH_2CH_3$</td>
<td>74</td>
<td>35</td>
<td>1.2</td>
</tr>
<tr>
<td>pentane</td>
<td>$CH_3CH_2CH_2CH_2CH_3$</td>
<td>72</td>
<td>36</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Note: The alcohols are hydrogen bonded, giving them much higher boiling points. The ethers have boiling points that are closer to those of alkanes with similar molecular weights.
Hydrogen Bond Acceptor

- Ethers cannot H-bond to each other.
- In the presence of -OH or -NH (donor), the lone pair of electrons from ether forms a hydrogen bond with the -OH or -NH.

Solvent Properties

- Nonpolar solutes dissolve better in ether than in alcohol.
- Ether has large dipole moment, so polar solutes also dissolve.
- Ethers solvate cations.
- Ethers do not react with strong bases.
Ether Complexes

- Grignard reagents
- Electrophiles
- Crown ethers

Common Names of Ethers

- Alkyl alkyl ether
- Current rule: alphabetical order
- Old rule: order of increasing complexity
- Symmetrical: use dialkyl, or just alkyl.
- Examples:

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{O}\text{CH}_2\text{CH}_3 & \quad \text{diethyl ether or ethyl ether} \\
\text{CH}_3\text{O}\text{C}\text{CH}_3 & \quad \text{t-butyl methyl ether or methyl t-butyl ether}
\end{align*}
\]
IUPAC Names

- Alkoxy alkane
- Examples:

\[
\begin{align*}
\text{CH}_3\text{O-CH}_3 & \quad \text{CH}_3\text{O-C-CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\end{align*}
\]

2-methyl-2-methoxypropane \quad \text{Methoxycyclohexane}

Cyclic Ethers

- Heterocyclic: oxygen is in ring.

- Epoxides (oxiranes)

- Oxetanes

- Furans (Oxolanes)

- Pyrans (Oxanes)

- Dioxanes
Naming Epoxides

- Alkene oxide, from usual synthesis method

\[ \text{peroxybenzoic acid} \rightarrow \text{cyclohexene oxide} \]

- Epoxy attachment to parent compound, 1,2-epoxy-cyclohexane

- Oxirane as parent, oxygen number 1

\[ \text{trans-2-ethyl-3-methyloxirane} \rightarrow \]

Spectroscopy of Ethers

- IR: Compound contains oxygen, but O-H and C=O stretches are absent.
- MS: α-cleavage to form oxonium ion, or loss of either alkyl group.
- NMR: \(^{13}\)C-O signal between δ65-δ90, \(^1\)H-C-O signal between δ3.5-δ4.

=>
Williamson Synthesis

- Alkoxide ion + 1° alkyl bromide (or tosylate)
- Example:

\[
\begin{align*}
\text{CH}_3\text{O}^- + \text{K} & \rightarrow \text{CH}_3\text{O}^- \text{K}^+ \\
\text{CH}_3\text{O}^- + \text{CH}_3\text{CH}_2\text{C}=\text{Br} & \rightarrow \text{CH}_3\text{O}^-\text{CH}_2\text{CH}_2\text{CH}_3 + \text{Br}^-
\end{align*}
\]

Phenyl Ethers

- Phenoxide ions are easily produced for use in the Williamson synthesis.
- Phenyl halides or tosylates cannot be used in this synthesis method.

\[
\begin{align*}
\text{C}=\text{O}^- + \text{NaOH} & \rightarrow \text{C}=\text{O}^-\text{Na}^+ + \text{HOH} 
\end{align*}
\]
Alkoxymercuration-Demercuration

Use mercuric acetate with an alcohol to add RO-H to a double bond and form the Markovnikov product.

\[
\begin{align*}
\text{CH}_3\text{(CH}_2\text{)}_3\text{CH}==\text{CH}_2 & \xrightarrow{\text{(1) Hg(OAc)}_2, \text{CH}_3\text{OH}} \text{CH}_3\text{(CH}_2\text{)}_3\text{CH}--\text{CH}_3 \\
& \xrightarrow{\text{(2) NaBH}_4} \text{CH}_3\text{(CH}_2\text{)}_3\text{CH}--\text{CH}_3 \\
& \quad \quad \quad \text{(Markovnikov product)}
\end{align*}
\]

Bimolecular Dehydration of Alcohols

- Industrial method, not good lab synthesis.
- If temperature is too high, alkene forms.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{O}--\text{H} + \text{H--OCH}_2\text{CH}_3 & \xrightarrow{\text{H}_2\text{SO}_4, 140^\circ\text{C}} \text{CH}_3\text{CH}_2\text{O}--\text{CH}_2\text{CH}_3 \\
& \Rightarrow
\end{align*}
\]
Cleavage of Ethers

- Ethers are unreactive toward base, but protonated ethers can undergo substitution reactions with strong acids.
- Alcohol leaving group is replaced by a halide.
- Reactivity: HI > HBr >> HCl

=>

Mechanism for Cleavage

- Ether is protonated.
  \[
  \text{CH}_3\text{--O--CH}_3 + \text{HBr} \rightarrow \text{CH}_3\text{--O}^+\text{--CH}_3 + \text{Br}^- \]
- Alcohol leaves as halide attacks.
  \[
  \text{Br}^- \text{--O--CH}_3 + \text{H} \rightarrow \text{Br--CH}_3 + \text{H--O--CH}_3 \]
- Alcohol is protonated, halide attacks, and another molecule of alkyl bromide is formed.

=>
Phenyl Ether Cleavage

- Phenol cannot react further to become halide.
- Example:

\[
\begin{align*}
\text{PhCH}_2\text{OH} + \text{CH}_3\text{CH}_2\text{Br} & \rightarrow \text{PhCH} = \text{CH}_{\text{Br}} + \text{CH}_3\text{CH}_2\text{OH}
\end{align*}
\]

Autoxidation of Ethers

- In the presence of atmospheric oxygen, ethers slowly oxidize to hydroperoxides and dialkyl peroxides.
- Both are highly explosive.
- Precautions:
  - Do not distill to dryness.
  - Store in full bottles with tight caps.
Sulfides (Thioethers)

- R-S-R’, analog of ether.
- Name sulfides like ethers, replacing “sulfide” for “ether” in common name, or “alkylthio” for “alkoxy” in IUPAC system.
- Example:

\[
\begin{align*}
\text{S—CH}_3 & \quad \text{methyl phenyl sulfide} \\
\text{or} & \\
\text{methylthiobenzene} & \Rightarrow
\end{align*}
\]

Thiols and Thiolates

- R-SH about same acidity as phenols.

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{SH} + \text{NaOH} & \quad \text{CH}_3\text{CH}_2\text{S}^- \quad \text{Na}^+ + \text{HOH}
\end{align*}
\]

- Thiolates are better nucleophiles, weaker bases, than alkoxides.

\[
\begin{align*}
\text{CH}_3- & \quad \text{Br} \quad \text{CH}_3\text{S}^- \quad \text{CH}_3- \\
\text{CH}_3- & \quad \text{H} \quad \text{CH}_3\text{OH} \quad \text{CH}_3- \\
2^\circ \text{halide} & \quad \text{Substitution product} \quad \Rightarrow
\end{align*}
\]
Sulfide Reactions

- Sulfides are easily oxidized to sulfoxides and sulfones.

\[ \text{CH}_3\text{S}-\text{CH}_3 + \text{H}_2\text{O}_2 \xrightarrow{\text{CH}_3\text{COOH}} \text{CH}_3\text{O}=\text{S}-\text{CH}_3 \]

\[ \text{CH}_3\text{S}-\text{CH}_3 + \text{H}_2\text{O}_2 \xrightarrow{\text{CH}_3\text{COOH}} \text{CH}_3\text{O}=\text{S}=\text{O} \]

- Sulfides react with unhindered alkyl halides to give sulfonium salts.

\[ \text{CH}_3\text{S}-\text{CH}_3 + \text{CH}_3\text{I} \xrightarrow{} \text{CH}_3\text{S}^+\text{CH}_3 \text{I}^- \]

Synthesis of Epoxides

- Peroxyacid epoxidation

- Cyclization of Halohydrin
Ring Opening in Acid

- Trans diol formed in water solvent.
- Alkoxy alcohol formed in alcohol solvent.
- 1,2-Dihalide formed with HI or HBr.

Biosynthesis of Steroids

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Ring Opening in Base

Epoxide’s high ring strain makes it susceptible to nucleophilic attack.

Epoxide Opening in Base

• With aqueous hydroxide, a trans 1,2-diol is formed.
• With alkoxide in alcohol, a trans 1,2-alkoxy alcohol is formed.
• These are the same products that were formed in acid.
• Different products are formed in acid and base if epoxide is unsymmetrical.
Orientation of Epoxide Opening

- Base attacks the least hindered carbon.

![Reaction diagram showing base attack]

- In acid, the nucleophile attacks the protonated epoxide at the most substituted carbon.

![Reaction diagram showing acid attack]

Reaction with Grignard and R-Li

- Strong base opens the epoxide ring by attacking the less hindered carbon.
- Example:

![Reaction diagram showing Grignard reaction]
Epoxy Resins

Polymer of bisphenol A and epichlorohydrin

\[
\text{bisphenol A} \quad \text{O} \quad \text{H}_2\text{C} - \text{CHCH}_2\text{Cl} \\
\text{epichlorohydrin}
\]

=>

End of Chapter 14
Homework: 33, 35, 37, 39, 40, 42, 45-47