Diethyl ether in starting fluid
Examples of compounds with ether groups

tetrahydrocannabinol (THC)

monensin
Nomenclature of Ethers

- Ethyl methyl ether
- Diethyl ether (the prefix "di-" is sometimes omitted)
- Diphenyl ether
- 2-Methoxypentane
- Trans-2-methoxycyclohexanol
- 1,3,5-Trimethoxybenzene
What are the correct names for the following ethers?

CH₃CHCH(CH₃)₂.

OCH₂CH₃

[Diagram of another ether structure]

O—CH₂CH₂CH₃
Physical Properties of Ethers

<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>bp</th>
<th>mol wt</th>
<th>Water solubility (g/100 mL, 20°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-butanol</td>
<td>CH₃CH₂CH₂CH₂OH</td>
<td>118°C</td>
<td>74</td>
<td>7.9</td>
</tr>
<tr>
<td>diethyl ether</td>
<td>CH₃CH₂–O–CH₂CH₃</td>
<td>35°C</td>
<td>74</td>
<td>7.5</td>
</tr>
<tr>
<td>pentane</td>
<td>CH₃CH₂–CH₂–CH₂CH₃</td>
<td>36°C</td>
<td>72</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Although ethers cannot form hydrogen bonds with one another, they do form hydrogen bonds with alcohols. This explains why ethers and alcohols are mutually soluble.
Ethers as Solvents

Ethers are relatively inert compounds. They do not usually react with dilute acids or bases or common oxidizing and reducing agents. They do not react with metallic sodium unlike alcohols. Their inert nature and the fact that most organic compounds are ether-soluble makes them excellent solvents for organic reactions.

\[
\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3 + \text{O}_2 \rightarrow \text{CH}_3\text{CH}_2\text{OCHCHCH}_3
\]

an ether hydroperoxide

When ethers are exposed to air for a long time, they form peroxides and may result to explosives. \(\text{FeSO}_4\) is usually added to destroy the peroxides.
The Grignard Reagent: an Organometallic Compound

Pronounced greenyär(d)

\[ R - X + Mg \xrightarrow{\text{dry ether}} R - MgX \]

R’—Mg—X

Acting as a Lewis base, ether stabilizes a Grignard reagent.
\[ \text{CH}_3\text{I} + \text{Mg} \xrightarrow{\text{ether}} \text{CH}_3\text{MgI} \]

\[ \text{Bromobenzene} + \text{Mg} \xrightarrow{\text{ether}} \text{Phenylmagnesium bromide} \]
A carbanion is an alkyl or aryl group with a negatively charged carbon atom. Carbanions are strong bases.

\[
\text{R} \rightarrow \text{MgX}
\]

\[
\text{R} \rightarrow \text{MgX} + \text{H} \rightarrow \text{OH} \rightarrow \text{R} \rightarrow \text{H} + \text{Mg}^{2+} \text{(OH)}^{-} \text{X}^{-}
\]

stronger base + stronger acid \rightarrow weaker acid + weaker base
Grignard reagent reaction with water

\[
\begin{align*}
\text{CH}_3\text{-}\text{Br} & \xrightarrow{\text{Mg} / \text{ether}} \text{CH}_3\text{-}\text{MgBr} & \xrightarrow{\text{D}_2\text{O}} \text{CH}_3\text{-}\text{D} \\
\text{p-bromotoluene} & \quad \text{p-tolylmagnesium bromide} & \quad \text{p-deuteriotoluene}
\end{align*}
\]

Reaction of Grignard reagent with water can be used to place deuterium isotopes by reacting them with heavy water (D\(_2\)O), where the deuterium substitutes the halogen.
Question: Show how to prepare CH₃CHDCH₃ from CH₂=CHCH₃
Organolithium compounds

\[
\begin{align*}
\delta^+ & \quad \delta^- \\
R-X + 2 \text{ Li} & \quad \text{ether} & \quad \delta^- & \quad \delta^+ \\
\text{an alkyl lithium} & \quad \text{Li}^+ X^- \\
\end{align*}
\]

These compounds contain carbon- metal (lithium) bond. They react in a similar manner to Grignard reagents, and are very useful in synthesis.
Preparation of Ethers

\[ \text{CH}_3\text{CH}_2\text{OH} + \text{HOCH}_2\text{CH}_3 \xrightarrow{\text{H}_2\text{SO}_4, 140^\circ\text{C}} \text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3 + \text{H}_2\text{O} \]

ethanol  
diethyl ether
Methyl *tert* Butyl Ether (MTBE) has a high octane value of about 110, it is used as an octane number enhancer in unleaded gasoline. It is prepared by the acid-catalyzed addition of methanol to 2-methylpropene.

\[
\text{CH}_3\text{OH} + \text{CH}_2\equiv\text{C}((\text{CH}_3)_2 \xrightarrow{\text{H}^+} \text{CH}_3\text{O} \equiv \text{C} \equiv \text{CH}_3
\]

methanol  2-methylpropene  \(t\)-butyl methyl ether
Williamson Synthesis

$$2 \text{ROH} + 2 \text{Na} \rightarrow 2 \text{RO}^-\text{Na}^+ + \text{H}_2$$

$$\text{RO}^-\text{Na}^+ + \text{R}'-\text{X} \rightarrow \text{ROR}' + \text{Na}^+\text{X}^-$$
\[
\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \quad \text{or} \quad \text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\]

from

\[
\text{CH}_3\text{O}^-\text{Na}^+ + \text{XCH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \quad \text{CH}_3\text{X} + \text{Na}^+\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3
\]

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

\[
\text{CH}_3\text{O}^-\text{Na}^+ + \text{CH}_3\text{CH}_2\text{CH}_2\text{X} \rightarrow \text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3 + \text{Na}^+\text{X}^-
\]
\[2 \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} + 2 \text{Na} \rightarrow 2\text{CH}_3\text{CH}_2\text{CH}_2\text{O}^-\text{Na}^+ + \text{H}_2\]
\[\text{CH}_3\text{CH}_2\text{CH}_2\text{O}^-\text{Na}^+ + \text{CH}_3\text{X} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{OCH}_3 + \text{Na}^+\text{X}^-\]
Show how this compound could be made

![Chemical structure of the compound](image)
Cleavage of Ethers

(a)

(b)
\[
\text{CH}_3\text{CH}_2\text{OCH(CH}_3\text{)}_2 + \text{HI} \xrightarrow{\text{heat}} \text{CH}_3\text{CH}_2\text{I} + \text{HOCH(CH}_3\text{)}_2 \\
\text{ethyl isopropyl ether} \quad \text{ethyl iodide} \quad \text{isopropyl alcohol}
\]

\[
\text{\begin{chemical}[depth=12pt]
\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {\begin{tikzpicture}
\begin{scope}[scale=0.5]
\node (o) at (0,0) {OCH}_3;\node (m) at (0,-1) {CH}_3;\node (a) at (0,-2) {CH}_3;
\end{scope}
\end{tikzpicture}
\end{center}
\end{chemical}
\text{OCH}_3 + \text{BBr}_3 \xrightarrow{1. \text{heat}} \xrightarrow{2. \text{H}_2\text{O}} \text{phenol} + \text{CH}_3\text{Br} \\
\text{anisole} \quad \text{phenol} \quad \text{methyl bromide}
\]
t-butyl phenyl ether $\xrightarrow{\text{H}^+ / \text{H}_2\text{O}}$ phenol + $t$-butyl alcohol (and $\text{(CH}_3\text{)}_2\text{C} \equiv \text{CH}_2$)
Ethers and Anesthesia
\[
\text{CH}_3\text{CH}_2\text{OCH}(\text{CH}_3)_2 \rightleftharpoons \text{CH}_3\text{CH}_2\text{OCH}(\text{CH}_3)_2 \quad \text{oxonium ion}
\]

\[
\text{I}^- + \text{CH}_3\text{CH}_2\text{OCH}(\text{CH}_3)_2 \rightarrow \text{CH}_3\text{CH}_2\text{I} + \text{HOCH}(\text{CH}_3)_2
\]
Epoxides (Oxiranes)

- Ethylene oxide (oxirane) bp 13.5°C
- cis-2-butene oxide (cis-2,3-dimethyloxirane) bp 60°C
- trans-2-butene oxide (trans-2,3-dimethyloxirane) bp 54°C
\[ \text{CH}_2=\text{CH}_2 + \text{O}_2 \xrightarrow{\text{silver catalyst, } 250^\circ\text{C, pressure}} \text{CH}_2-\text{CH}_2-\text{O} \]

ethylene oxide
cyclohexene + R-C-OOH → cyclohexene oxide + R-C-OH

organic peroxo acid

organic acid
*m*-chloroperbenzoic acid (MCPBA) is an oxidizing agent frequently used in epoxidation reactions.
\[
\text{muscalure} \\
\begin{align*}
\text{bombykol}
\end{align*}
\]
(CH₃)₂CH(CH₂)₄ \cdot \cdot \cdot 7 \quad 8 \cdot \cdot \cdot (CH₂)₉CH₃

H \quad O \quad H

(7R,8S)-(+)-7,8-epoxy-2-methyloctadecane

(disparlure)
Reactions of Epoxides

\[ \text{CH}_2\text{CH}_2 + \text{H}^+ \xrightarrow{\text{H}^+} \text{O} \xrightarrow{\text{OH}} \text{CH}_2\text{CH}_2 \]

ethylene oxide

ethylene glycol

\[ \text{CH}_2\text{CH}_2 + \text{H}^+ \xleftrightarrow{\text{H}^+} \text{CH}_2\text{CH}_2 \]

\[ \text{O} \xrightarrow{\text{H}^+} \text{O}^+ \xrightarrow{\text{H}^-} \text{H} \]
Grignard reagents and organolithium compounds are strong nucleophiles capable of opening the ethylene oxide (epoxide) ring. The initial product is a magnesium alkoxide of lithium alkoxide, but after hydrolysis, we obtain a primary alcohol with two carbon atoms than the organometallic reagent.
Cyclic Ethers

- Tetrahydrofuran (oxolane) bp 67°C
- Tetrahydropyran (oxane) bp 88°C
- 1,4-Dioxane bp 101°C
These compounds are called **Crown ethers** because their molecule have a crown-like shape. The bracket number represents the ring size and the terminal numbers gives the number of oxygens. The oxygens are usually separated by two carbons.

![Crown ethers](image)

- **[18]crown-6**
  - mp 39–40°C

- **[15]crown-5**
  - (liquid)

- **[12]crown-4**
Crown ethers have the unique property of forming complexes with positive ions (Na\(^+\), K\(^+\)) the positive ions fit within the macrocyclic rings selectively depending on the sizes. For example [18]crown-6 binds K\(^+\) more tightly than it does the smaller Na\(^+\) (too loose a fit) or the larger Cs\(^+\) (too large to fit in the hole). Similarly [15]crown-5 binds Na\(^+\), and [12]crown-4 binds Li\(^+\). The crown ethers act as hosts for their anionic guests.
Model of [18]crown-6 complex with $\text{K}^+$
The selective binding of metallic ions by macrocyclic compounds is important in nature. Several antibiotics, such as nonactin, have large rings that contain regularly spaced oxygen atoms. Nonactin (which contains four tetrahydrofuran rings joined by four ester links) selectively binds $K^+$ (in the presence of $Na^+$) in aqueous media. Thus allowing selective transport of $K^+$ (but not $Na^+$) through the cell membranes.