ORGANIC CHEM
CHAPTER 13:
ETHERS
DID YOU EVER WONDER……

- How cigarettes cause cancer? (p. 556)
CH 13.1
INTRODUCTION TO ETHERS
READ PG. 556-557 - THEN TAKE NOTES

STOP
no matter how hard you try, you will never be as cute as the Ether Bunny
- **Ethers** are compounds that *exhibit an oxygen atom bonded to two R groups*, where each R group can be an alkyl, aryl, or vinyl group:

  ![An ether](image)

- The ether group is a common structural feature of many natural and synthetic compounds; for example:

  ![Vitamin E](image)
  An antioxidant

  ![Fluoxetine](image)
  *(R)-Fluoxetine*
  A powerful antidepressant sold under the trade name Prozac

  ![Morphine](image)
  Morphine
  An opiate analgesic used to treat severe pain
CH 13.2
NOMENCLATURE OF ETHERS
READ PG. 557 - 559
THEN TAKE NOTES

STOP
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IUPAC rules allow two different methods for naming ethers:

1. A common name is constructed by identifying each R group, arranging them in alphabetical order, and then adding the word “ether”; for example:

In these examples, the oxygen atoms are connected to two different alkyl groups.
Ethers connected to two different alkyl groups are called **unsymmetrical ethers**

While ethers with identical alkyl groups are called **symmetrical ethers**, and are named as *dialkyl ethers*

For example, \((CH_3CH_2)_2\) is called diethyl ether

2. A systematic name is constructed by choosing the **larger group to be the parent alkane** and naming the smaller group as an **alkoxy substituent**.

Systematic names must be used for complex ethers that exhibit multiple substituents and/or chiral centers.
Skillbuilder 13.1

Name the following compounds:

(a)

(b)

SOLUTION

(a) To assign a common name, identify each group on either side of the oxygen atom, arrange them in alphabetical order, and then add the word “ether.”
Skillbuilder 13.1

To assign a systematic name, choose the more complex (larger) group as the parent and name the smaller group as an alkoxy substituent.

This compound therefore can be called methyl phenyl ether or methoxybenzene. Both names are accepted by IUPAC rules.

(b) The second compound is more complex. It has a chiral center and several substituents. Therefore, it will not have a common name. To assign a systematic name, begin by choosing the more complex group as the parent. The cyclopentane ring becomes the parent, highlighted below, and the ethoxy group is listed as one of the three substituents on the cyclopentane ring. Locants are then assigned so as to give the lowest possible numbers to all three substituents (1,1,3 rather than 1,3,3):

The configuration of the chiral center is identified at the beginning of the name:

(R)-1,1-Dichloro-3-ethoxycyclopentane
LET’S DO HMWK #1-2 (P. 559)
CH 13.3
STRUCTURE A
PROPERTIES OF
ETHERS
READ PG. 559 - 560
THEN TAKE NOTES
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The geometry of an oxygen atom is similar for water, alcohols, and ethers.

The bond angle depends on the groups attached to the oxygen atom, with ethers having the largest bond angles:

- Water (105°)
- Methanol (109°)
- Dimethyl ether (112°)

In the previous chapter, we saw that alcohols have relatively high boiling points due to the effects of hydrogen bonding.
An ether can only act as a hydrogen bond acceptor by interacting with the proton of an alcohol:

Ethers cannot form hydrogen bond with each other. As a result, the boiling points of ethers are significantly lower than their isomeric alcohols.

Ethanol: 78°C
Dimethyl ether: −25°C
Propane: −42°C
The boiling point of dimethyl ether is almost as low as the BP of propane.

Both dimethyl ether and propane lack the ability to form hydrogen bonds.

The slightly higher BP of dimethyl ether can be explained by considering the net dipole moment.

The oxygen atom has bent geometry, so the individual dipole moments do not fully cancel each other.

Together, they produce a molecular dipole moment.

As a result, dimethyl ether exhibits dipole-dipole interactions, which slightly elevate the boiling point relevant to propane.
Ethers with larger alkyl groups have even higher boiling points due to London dispersion forces between the alkyl groups on different molecules.

This trend is significant, as seen in the following examples:

- Dimethyl ether: $-25^\circ C$
- Diethyl ether: $35^\circ C$
- Dipropyl ether: $91^\circ C$
- Ethers are often used as solvents.
  - They are fairly unreactive
  - They dissolve a wide variety of organic compounds
  - Their low boiling points allow them to be readily evaporated after a reaction is complete.

![Chemical structures]

Diethyl ether  Tetrahydrofuran  1,4-Dioxane
CH 13.4 CROWN ETHERS

READ PG. 561 - 562
THEN TAKE NOTES
- Ethers can interact with metals that have either a full positive charge or a partial positive charge.
- Grignard reagents are formed in the presence of an ether, such as diethyl ether.
- The lone pairs on the oxygen atom serve to stabilize the charge on the magnesium atom.
- The interaction is weak, but it is necessary in order to form a Grignard reagent.
Charles J. Pederson, discovered that the interaction between ethers and metal ions is significantly stronger for compounds with multiple ether groups.

Such compounds are called polyethers.

Pederson prepared and investigated the properties of many cyclic polyethers, or also called crown ethers because of their molecular models.
These compounds contain multiple oxygen atoms and are therefore capable of binding more tightly to metal ions.

To name these compounds, Pederson used the formula **X-crown-Y**, where X represents the number of atoms in the ring and Y represents the number of oxygen atoms.

For example, 18-crown-6 contains 18 atoms and 6 of those are oxygen atoms.
The unique properties of these compounds derive from the size of their internal cavities.

In Figure 13.1a, it is clear that the oxygen atoms all face toward the inside of the cavity, where they can bind to the metal cation.

Figure 13.1b shows how a potassium cation fits perfectly into the internal cavity.
Once inside the cavity, the entire complex has an outer surface that resembles a hydrocarbon, rendering the complex soluble in the organic solvents.

In this way, 18-crown-6 is capable of solvating potassium ions in organic solvents.

The ability of crown ethers to solvate metal cations has enormous implications, in both synthetic organic chemistry and medicinal chemistry.

For example, consider what happens when KF and 18-crown-6 are mixed together in benzene.
Without the crown ether, KF would not dissolve in benzene. The presence of 18-crown-6 generates a complex that dissolves in benzene.

The result is a solution containing fluoride ions, which causes us to perform substitution reactions with $F^-$ as a nucleophile.

It is usually difficult to use $F^-$ as a nucleophile, because it usually interacts too strongly with the polar solvents in which it dissolves.

However, the use of 18-crown-6 allows the creation of free fluoride ions in a nonpolar solvent, making substitution reactions possible.
Other metal cations can be solvated by other crown ethers. For example:

- The discovery of these compounds led to a whole new field of chemistry, called host-guest chemistry
LET’S DO HMWK #4 (P. 562)
CH 13.5
PREPARATION OF ETHERS

READ PG. 563 - 566
THEN TAKE NOTES

STOP

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Diethyl ether is prepared industrially via the acid-catalyzed dehydration of ethanol.

The mechanism of this process is believed to involve an $S_N 2$ process.

A molecule of ethanol is protonated and then attacked by another molecule of ethanol in an $S_N 2$ process.

As a final step, deprotonation generates the product.
A proton is used in the first step of the mechanism, and then another proton is liberated in the last step of the mechanism.

The acid is therefore a catalyst that enables the $S_N2$ process to proceed.

This process has many limitations.
- For example, it only works well for primary alcohols, and it produces symmetrical ethers.
- As a result, this process for preparing ethers is too limited to be of any practical value for synthetic organic chemists.
Ethers can be readily prepared via a two-step process called a **Williamson ether synthesis**.

In the **first step**, the alcohol is deprotonated to form an alkoxide ion.

In the **second step**, the alkoxide ion functions as a nucleophile in an $S_N 2$ reaction.

\[
R\text{-}\overset{\ominus}{\text{OH}} \quad 1) \quad \text{NaH} \quad 2) \quad \text{RX} \quad \rightarrow \quad R\text{-}\overset{\ominus}{\text{O}}\text{-}R
\]

Proton transfer

Nucleophilic attack

The resulting alkoxide ion then functions as a nucleophile and attacks the alkyl halide in an $S_N 2$ process.
This process is named after Alexander Williamson, a British scientist who first demonstrated this method in 1850 as a way of preparing diethyl ether.

Since the second step is an $S_N\,2$ process, steric effects must be considered.

The process works best when methyl or primary alkyl halides are used.

Secondary alkyl halides are less efficient because elimination is favored over substitution, and tertiary alkyl halides cannot be used.

This limitation must be taken into account when choosing which C – O bond to form.
For example, consider the structure of **tert-butyl methyl ether**, also called MTBE.

There are two possible routes to consider in the preparation of MTBE, but only one is efficient.

- The **first route** is efficient because it employs a methyl halide, which is a suitable substrate for an $S_N 2$ process.

- The **second route** does not work because it employs a tertiary alkyl halide, which will undergo elimination rather than substitution.
Show reagents that you could use to prepare the following ether via a Williamson ether synthesis:

\[
\begin{align*}
\text{SOLUTION} \\
\text{In order to prepare this ether via a Williamson ether synthesis, we must identify a starting alcohol and a starting alkyl halide. To make the proper choice, we analyze the positions on either side of the oxygen atom.}
\end{align*}
\]

**STEP 1**

Classify the groups on either side of the oxygen atom.

The phenyl position is \(sp^3\) hybridized, and \(S_n2\) processes do not occur at \(sp^2\)-hybridized centers. The other position is a primary position, and \(S_n2\) processes can occur readily at primary substrates. Therefore, we must start with phenol and an ethyl halide.

**STEP 2**

Determine which side is more capable of serving as a substrate in an \(S_n2\) reaction.

The X can be any good leaving group, such as I, Br, Cl, or OTs. In general, iodide and tosylate are the best leaving groups. The alcohol in this case is phenol, which can be deprotonated with sodium hydroxide (as we saw in Section 12.2). We therefore propose the following synthesis:

\[
\begin{align*}
\text{OH} & \quad \text{X} \\
\text{Ph} & \quad \text{Ph} \\
\text{1) NaOH} & \quad \text{2) CH}_3\text{CH}_2\text{I} \\
\end{align*}
\]
LET’S DO HMWK #5 (P. 565)
Oxymercuration-demercuration is a process used to synthesize alcohols from alkenes.

The net result is a Markovnikov addition of water (H and OH) across an alkene.

That is, the hydroxyl group is ultimately placed at the more substituted position.

A mechanism for this process was discussed in Section 8.4.
If an alcohol (ROH) is used in place of water, then the result is a Markovnikov addition of the alcohol (RO and H) across the alkene.

This process is called **alkoxymercuration-demercuration**, and it can be used as a method for preparing ethers.
LET’S DO HMWK #7-9 (P. 566)
DON’T GO ON!!
CH 13.6 REACTIONS OF ETHERS
When heated with a concentrated solution of a strong acid (HX), an ether will undergo acidic cleavage, in which the ether is converted into two alkyl halides.

This process involves two substitution reactions:

**FORMATION OF FIRST ALKYL HALIDE**

- The ether is protonated, generating an oxonium ion.
- A halide ion functions as a nucleophile and attacks the oxonium ion, ejecting an alcohol as a leaving group.
The formation of the first alkyl halide begins with protonation of the ether to form a good leaving group, followed by an $S_N^2$ process in which a halide ion functions as a nucleophile and attacks the protonated ether.

FORMATION OF FIRST ALKYL HALIDE

Proton transfer

The ether is protonated, generating an oxonium ion

A halide ion functions as a nucleophile and attacks the oxonium ion, ejecting an alcohol as a leaving group.
- The second alkyl halide is then formed with the same two steps – protonation followed by an $S_N 2$ attack.

- If either R group is tertiary, then substitution is more likely to proceed via an $S_N 1$ process rather than $S_N 2$. 

**FORMATION OF SECOND ALKYL HALIDE**

- The alcohol is protonated, generating an oxonium ion.
- A halide ion functions as a nucleophile and attacks the oxonium ion, ejecting water as a leaving group.
- When a phenyl ether is cleaved under acidic conditions, the products are phenol and an alkyl halide

![Chemical reaction diagram]

- The phenol is not further converted into a halide, because neither $S_N 1$ nor $S_N 2$ processes are efficient at $sp^2$-hybridized centers

- Both HI and HBr can be used to cleave ethers. HCl is less efficient, and HF does not cause acidic cleavage of ethers

- This reactivity is a result of the relative nucleophilicity of the halide ions
Ethers undergo autooxidation in the presence of atmospheric oxygen to form hydroperoxides:

\[ \text{Ethers} + \text{O}_2 \rightarrow \text{Hydroperoxide} \]

This process occurs via a radical mechanism, which is initiated by a hydrogen abstraction.
**Initiation**

Hydrogen abstraction

![Chemical structure](image)

Forms a carbon radical

**Propagation**

Coupling

![Chemical structure](image)

A carbon radical couples with molecular oxygen

**Termination**

Coupling

![Chemical structure](image)

Destroys two carbon radicals

Gives the product and regenerates a carbon radical
As with all radical mechanisms, the net reaction is the sum of the propagation steps:

- **Coupling**
  \[ R' + {\cdot O\cdot O} \rightarrow R{\cdot O\cdot O} \]

- **Hydrogen abstraction**
  \[ R{\cdot O\cdot O} + H-R \rightarrow R{\cdot O\cdot OH} + R' \]

**Net reaction**
\[ R-H + O_2 \rightarrow R-O-O-H \]

- The reaction is slow, but old bottles of ether will invariably contain a small concentration of hydroperoxides, rendering the solvent very dangerous to use.
- Hydroperoxides are unstable and decompose violently when heated.
- Ethers used in laboratories must be frequently tested for the presence of hydroperoxides and purified prior to use.