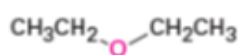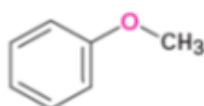# Ethers

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Ethers (R-O-R ̄), like the alcohols we saw in the preceding chapter, are also organic derivatives of water, but they have two organic groups bonded to the same oxygen atom rather than one. The organic groups might be alkyl, aryl, or vinylic, and the oxygen atom might be in an open chain or a ring. Perhaps the most well-known ether is diethyl ether, which has a long history of medicinal use as an anesthetic and industrial use as a solvent. Other useful ethers include anisole, pleasant-smelling aromatic ether used in perfumery, and tetrahydrofuran (THF), cyclic ether often used as a solvent
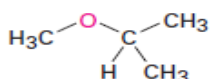

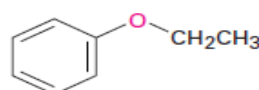| Diethyl ether	Anisole (methyl phenyl ether)	Tetrahydrofuran

Names and Properties of Ethers
Simple ethers with no other functional groups are named by identifying the two organic substituents and adding the word **ether.**
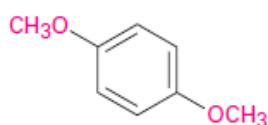

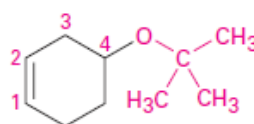Isopropyl methyl ether   Ethyl phenyl ether

If other functional groups are present, the ether part is considered an **alkoxy** substituent. For example:
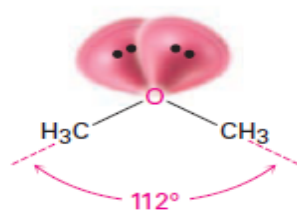

p-Dimethoxybenzene   4-*tert*-Butoxy-1-cyclohexene

Like alcohols, ethers have nearly the same geometry as water. The R-O-R bonds have an approximately tetrahedral bond angle (112° in dimethyl ether), and the oxygen atom is $sp3$-hybridized.

The electronegative oxygen atom gives ethers a slight dipole moment, and the boiling points of ethers are often slightly higher than the boiling points of comparable alkanes. **Table 18-1** compares the boiling points of some common ethers and their corresponding hydrocarbons.

TABLE 18-1 Comparison of Boiling Points of Ethers and Hydrocarbons

Ether	Boiling point °C	Hydrocarbon	Boiling point °C
CH_3OCH_3	−25	$CH_3CH_2CH_3$	−45
$CH_3CH_2OCH_2CH_3$	34.6	$CH_3CH_2CH_2CH_2CH_3$	36
(tetrahydrofuran)	65	(cyclopentane)	49
(anisole) OCH_3	158	(ethylbenzene) CH_2CH_3	136

Ethers are relatively stable and unreactive in many respects, but some ethers react slowly with the oxygen in air to give *peroxides,* compounds that contain an O-O bond. The peroxides from low molecular weight ethers such as diisopropyl ether and tetrahydrofuran are explosive and extremely dangerous, even in tiny amounts. Ethers are very useful as solvents in the laboratory, but they must always be used cautiously and should not be stored for long periods of time.

Preparing Ethers

Diethyl ether and other simple symmetrical ethers are prepared industrially by the sulfuric acid catalyzed reaction of alcohols. The reaction occurs by S_N2 displacement of water from a protonated ethanol molecule by the oxygen atom of a second ethanol. Unfortunately, this method is limited to use with primary alcohols because secondary and tertiary alcohols dehydrate by an E1 mechanism to yield alkenes.
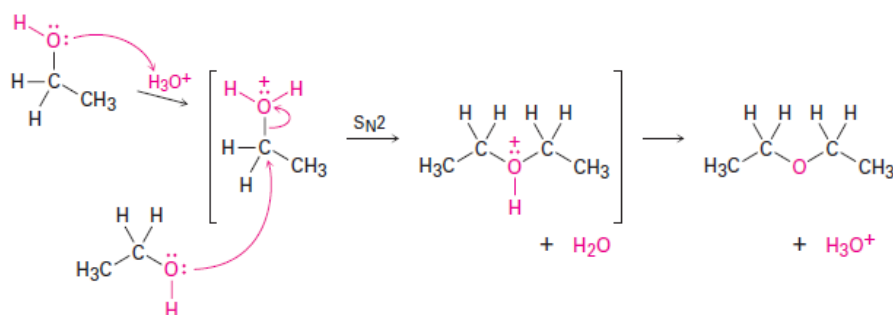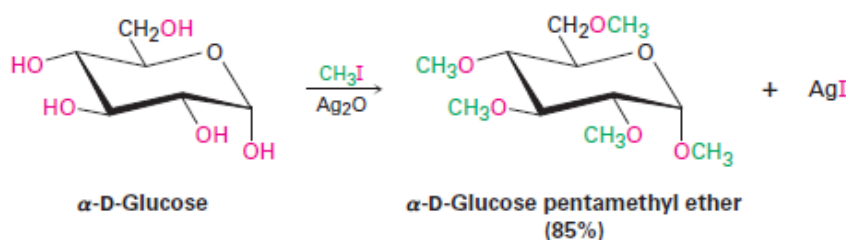
The Williamson Ether Synthesis

The most generally useful method of preparing ethers involves *Williamson ether synthesis,* in which an alkoxide ion reacts with a primary alkyl halide or tosylate in an S_N2 reaction. The alkoxide ion is normally prepared by reaction of an alcohol with a strong base such as sodium hydride, NaH.

Cyclopentanol   Alkoxide ion   Cyclopentyl methyl ether (74%)
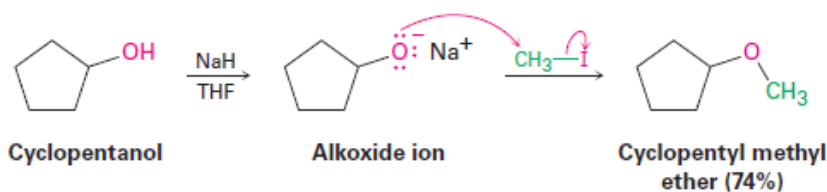
A useful variation of the Williamson synthesis involves silver oxide, Ag_2O, as a mild base rather than NaH. Under these conditions, the free alcohol reacts directly with alkyl halide, so there is no need to perform the metal alkoxide intermediate. Sugars react particularly well; glucose, for example, reacts with excess iodomethane in the presence of Ag_2O to generate penta ether in 85% yield.


α-D-Glucose   *α*-D-Glucose pentamethyl ether (85%)

Because the Williamson synthesis is an S_N2 reaction, it is subject to all the usual constraints. Primary halides and tosylates work best because competitive E2 elimination can occur with more hindered substrates. Unsymmetrical ethers should therefore be synthesized by reaction between the more hindered alkoxide partner and less hindered halide partner rather than vice versa. For example, *tert*-butyl methyl ether is best prepared by reaction of *tert*-butoxide ion with iodomethane rather than by reaction of methoxide ion with 2-chloro-2-methylpropane.

tert-Butoxide   Iodomethane   tert-Butyl methyl ether


2-Chloro-2-methylpropane   2-Methylpropene
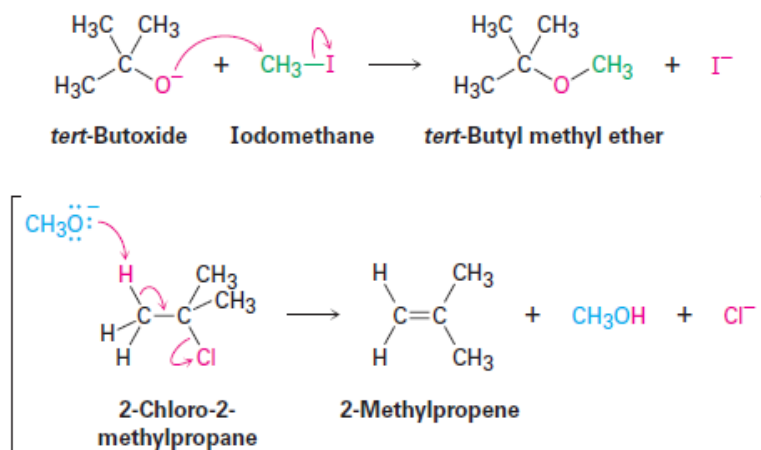
Alkoxymercuration of Alkenes

Alkenes react with water in the presence of mercuric acetate to yield a hydroxymercuration product. Subsequent treatment with $NaBH_4$ breaks the C-Hg bond and yields the alcohol. A similar **alkoxymercuration** reaction occurs when an alkene is treated with an *alcohol* in the presence of mercuric acetate or, even better, mercuric trifluoroacetate; $(CF_3CO_2)_2Hg$. Demercuration by reaction with $NaBH_4$ then yields ether. The net result is Markovnikov addition of the alcohol to the alkene

Styrene   1-Methoxy-1-phenylethane (97%)

Cyclohexene   Cyclohexyl ethyl ether (100%)
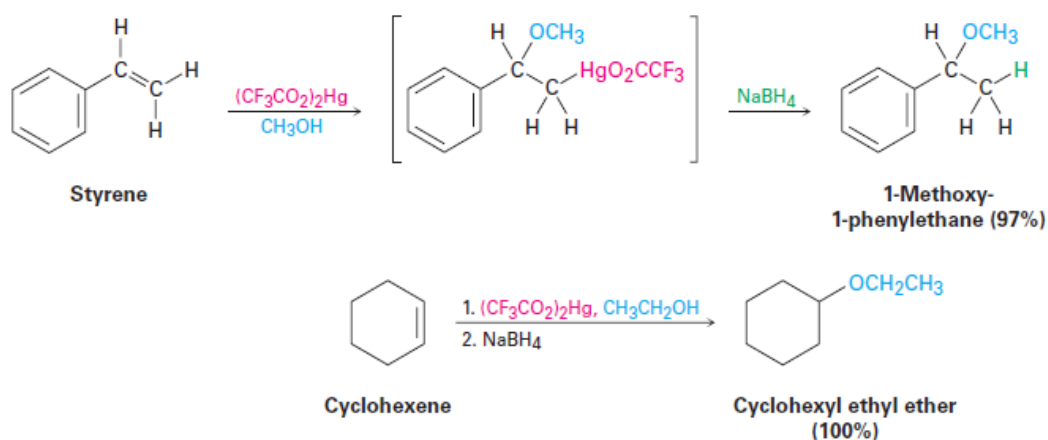
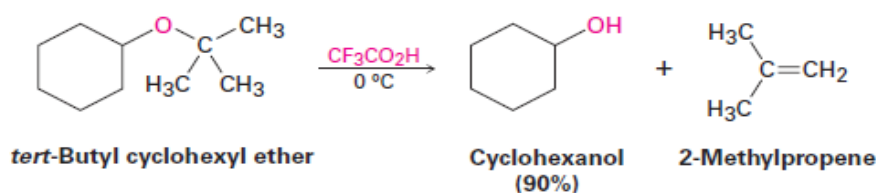## Reactions of Ethers: Acidic Cleavage

Ethers are unreactive to many reagents used in organic chemistry, a property that accounts for their wide use as reaction solvents. Halogens, dilute acids, bases, and nucleophiles have no effect on most ethers. In fact, ethers undergo only one truly general reaction they are cleaved by strong acids. Aqueous HBr and HI both work well, but HCl does not cleave ethers.

Ethyl phenyl ether   Phenol   Bromoethane
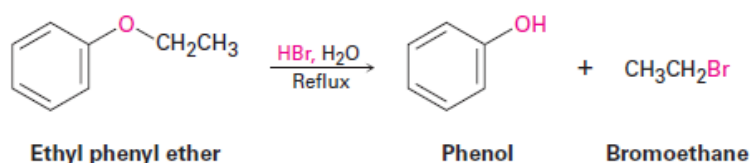
Acidic ether cleavages are typical nucleophilic substitution reactions and take place by either S_N1 or S_N2 mechanisms, depending on the structure of the substrate. Ethers with only primary and secondary alkyl groups react by an S_N2 mechanism, in which I_2 or Br_2 attacks the protonated ether at the less hindered site. This usually results in a selective cleavage into a single alcohol and a single alkyl halide. For example, ethyl isopropyl ether exclusively yields isopropyl alcohol and iodo ethane on cleavage by HI because nucleophilic attack by iodide ion occurs at the less hindered primary site rather than at the more hindered secondary site.
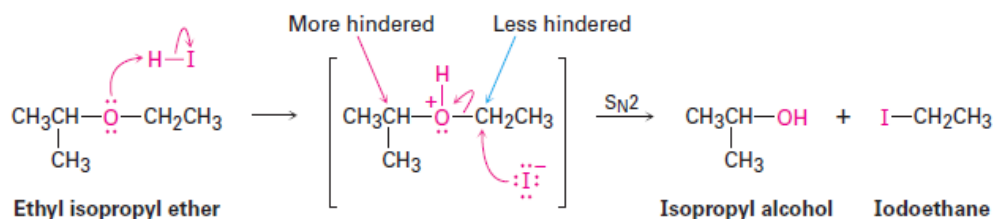

Ethers with a tertiary, benzylic, or allylic group cleave by either an S_N1 or E1 mechanism because these substrates can produce stable intermediate carbocations. These reactions are often fast and take place at moderate temperatures. *tert*-Butyl ethers, for example, react by an E1 mechanism on treatment with trifluoroacetic acid at 0 °C. This reaction is often used in the laboratory synthesis of peptides.
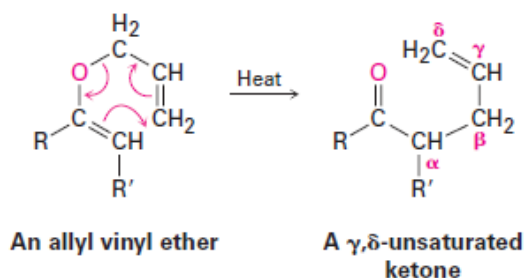

Reactions of Ethers: Claisen Rearrangement

Unlike the acid-induced ether cleavage reaction discussed in the previous section, which is general to all ethers, the **Claisen rearrangement** is specific to allyl aryl ethers
($H_2C=CHCH_2$-O-Ar) and allyl vinyl ethers ($H_2C=CHCH_2$-O-CH=CH_2). Treatment of a phenoxide ion with 3-bromopropene (allyl bromide) results in a Williamson ether synthesis and formation of an allyl aryl ether. Heating the allyl aryl ether to 200-250 °C then causes Claisen rearrangement, leading to an *o*-allylphenol. The net result is alkylation of the phenol in an ortho position.
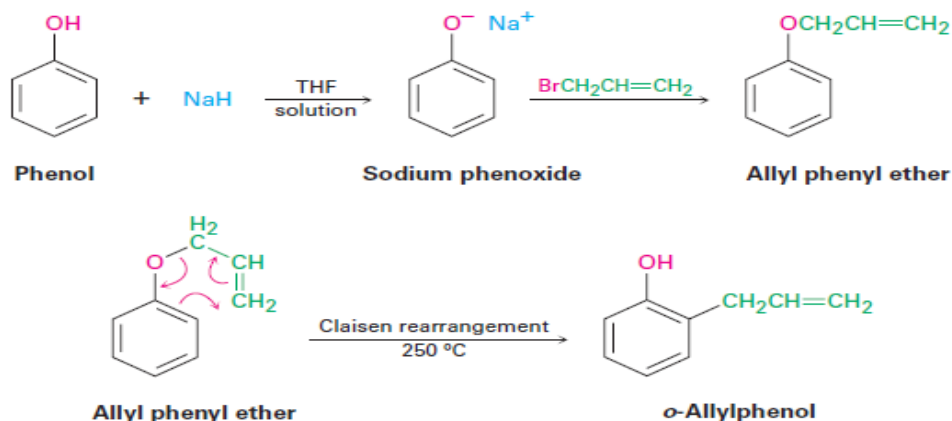
A similar rearrangement takes place with allyl vinyl ethers, leading to a so-called γ, δ-unsaturated ketone or aldehyde.

An allyl vinyl ether   **A γ,δ-unsaturated ketone**

Like the Diels–Alder reaction, the Claisen rearrangement reaction takes place in a single step through a pericyclic mechanism in which a reorganization of bonding electrons occurs in a six-membered, cyclic transition state. The 6-allyl-2,4-cyclohexadienone intermediate then isomerizes to *o*-allylphenol **(Figure 18-1)**.
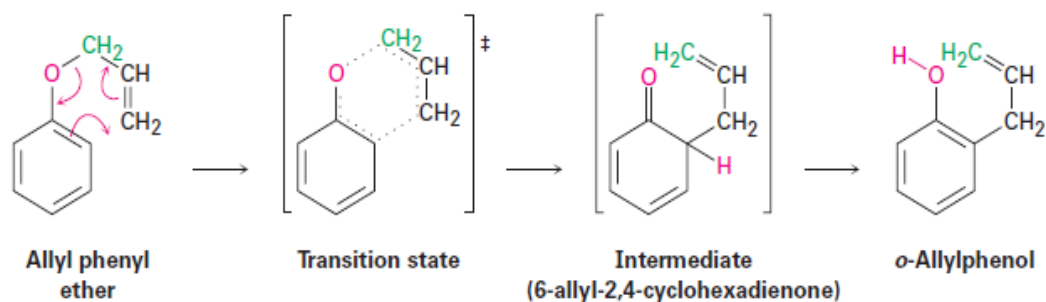

Allyl phenyl ether   **Transition state**   **Intermediate (6-allyl-2,4-cyclohexadienone)**   ***o*-Allylphenol**

Figure 18-1 The mechanism of Claisen rearrangement. The C-O bond-breaking and C-C bond making occur simultaneously.