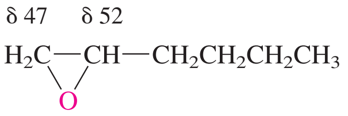
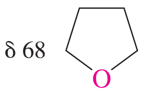
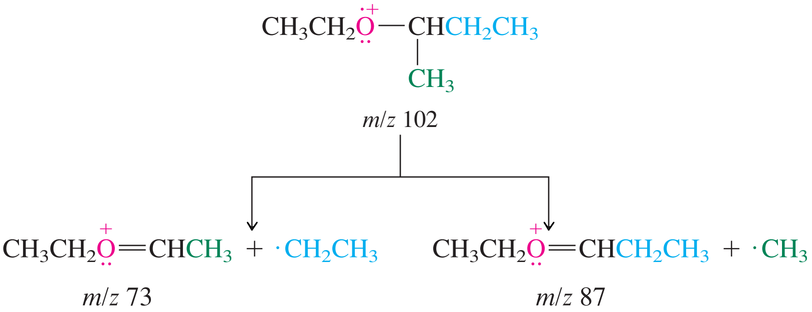




UV-VIS: Simple ethers have their absorption maximum at about 185 nm and are transparent to ultraviolet radiation above about 220 nm.

Mass Spectrometry: Ethers, like alcohols, lose an alkyl radical from their molecular ion to give an oxygen-stabilized cation. Thus, *m*/*z* 73 and *m*/*z* 87 are both more abundant than the molecular ion in the mass spectrum of *sec*-butyl ethyl ether.



PROBLEM 16.19 There is another oxygen-stabilized cation of *m/z* 87 capable of being formed by fragmentation of the molecular ion in the mass spectrum of *sec*-butyl ethyl ether. Suggest a reasonable structure for this ion.

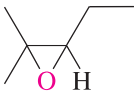
An analogous fragmentation process occurs in the mass spectra of sulfides. As with other sulfur-containing compounds, the presence of sulfur can be inferred by a peak at *m*/*z* of M+2.

16.19 SUMMARY

Section 16.1 **Ethers** are compounds that contain a C—O—C linkage. In substitutive IUPAC nomenclature, they are named as *alkoxy* derivatives of alkanes. In functional class IUPAC nomenclature, we name each alkyl group as a separate word (in alphabetical order) followed by the word *ether.*

$CH_3OCH_2CH_2CH_2CH_2CH_2CH_3$ **Substitutive IUPAC name:** 1-Methoxyhexane
Functional class name: Hexyl methyl ether

Epoxides are normally named as *epoxy* derivatives of alkanes or as substituted *oxiranes*.



2-Methyl-2,3-epoxypentane
3-Ethyl-2,2-dimethyloxirane

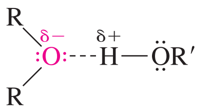
Sulfides are sulfur analogs of ethers: they contain the C—S—C functional group. They are named as *alkylthio* derivatives of alkanes in substitutive IUPAC nomenclature. The functional class IUPAC names of sulfides are derived in the same manner as those of ethers, but the concluding word is *sulfide*.

$CH_3SCH_2CH_2CH_2CH_2CH_2CH_3$ **Substitutive IUPAC name:** 1-(Methylthio)hexane
Functional class name: Hexyl methyl sulfide

Section 16.2 The oxygen atom in an ether or epoxide affects the shape of the molecule in much the same way as an sp^3-hybridized carbon of an alkane or cycloalkane.

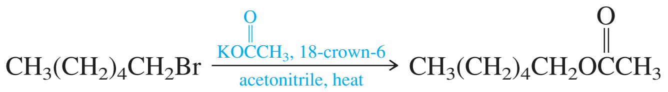
Pentane Diethyl ether

Section 16.3 The carbon–oxygen bond of ethers is polar, and ethers can act as proton *acceptors* in hydrogen bonds with water and alcohols.



But ethers lack OH groups and cannot act as proton *donors* in forming hydrogen bonds.

Section 16.4 Ethers form Lewis acid-Lewis base complexes with metal ions. Certain cyclic polyethers, called **crown ethers,** are particularly effective in coordinating with Na^+ and K^+, and salts of these cations can be dissolved in nonpolar solvents when crown ethers are present. Under these conditions the rates of many reactions that involve anions are accelerated.



$$CH_3(CH_2)_4CH_2Br \xrightarrow[\text{acetonitrile, heat}]{\overset{O}{\overset{\parallel}{\text{KOCCH}_3}}\text{, 18-crown-6}} CH_3(CH_2)_4CH_2O\overset{O}{\overset{\parallel}{C}}CH_3$$

1-Bromohexane Hexyl acetate (96%)

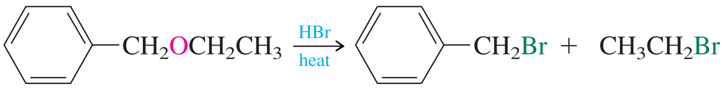
Sections 16.5 and 16.6 The two major methods for preparing ethers are summarized in Table 16.1.

Section 16.7 Dialkyl ethers are useful solvents for organic reactions, but must be used cautiously due to their tendency to form explosive hydroperoxides by air oxidation in opened bottles.

Section 16.8 The only important reaction of ethers is their cleavage by hydrogen halides.

$$\underset{\text{Ether}}{ROR'} + \underset{\substack{\text{Hydrogen}\\\text{halide}}}{2HX} \longrightarrow \underset{\substack{\text{Alkyl}\\\text{halide}}}{RX} + \underset{\substack{\text{Alkyl}\\\text{halide}}}{R'X} + \underset{\text{Water}}{H_2O}$$

The order of hydrogen halide reactivity is HI > HBr > HCl.



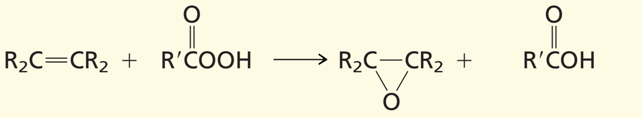
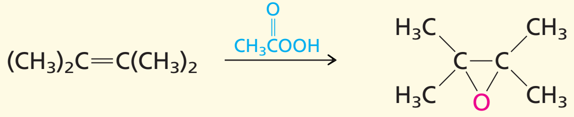
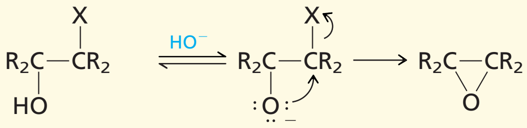
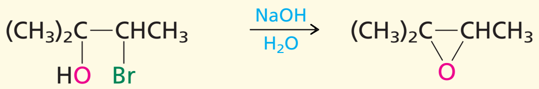
Benzyl ethyl ether Benzyl bromide Ethyl bromide

Sections 16.9 and 16.10 Epoxides are prepared by the methods listed in Table 16.2.

TABLE 16.1 Preparation of Ethers

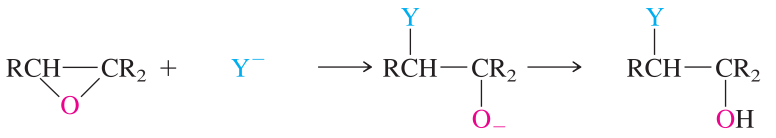
Reaction (section) and comments	General equation and specific example
Acid-catalyzed condensation of alcohols (Sections 15.7 and 16.5) Two molecules of an alcohol condense in the presence of an acid catalyst to yield a dialkyl ether and water. The reaction is limited to the synthesis of symmetrical ethers from primary alcohols.	$2RCH_2OH \xrightarrow{H^+} RCH_2OCH_2R + H_2O$ Alcohol Ether Water $CH_3CH_2CH_2OH \xrightarrow[\text{heat}]{H_2SO_4} CH_3CH_2CH_2OCH_2CH_2CH_3$ Propyl alcohol Dipropyl ether
The Williamson ether synthesis (Section 16.6) An alkoxide ion displaces a halide or similar leaving group in an S_N2 reaction. The alkyl halide cannot be one that is prone to elimination, and so this reaction is limited to methyl and primary alkyl halides. There is no limitation on the alkoxide ion that can be used.	$RO^- + R'CH_2X \longrightarrow ROCH_2R' + X^-$ Alkoxide ion Primary alkyl halide Ether Halide ion $(CH_3)_2CHCH_2ONa + CH_3CH_2Br \longrightarrow (CH_3)_2CHCH_2OCH_2CH_3 + NaBr$ Sodium isobutoxide Ethyl bromide Ethyl isobutyl ether (66%) Sodium bromide

TABLE 16.2 Preparation of Epoxides

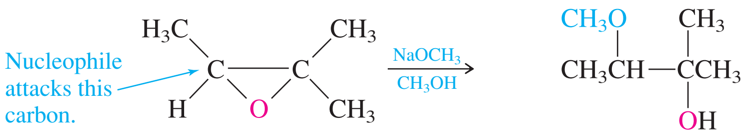
Reaction (section) and comments	General equation and specific example
Peroxy acid oxidation of alkenes (Sections 6.18 and 16.9) Peroxy acids transfer oxygen to alkenes to yield epoxides. Stereospecific syn addition is observed.	 Alkene Peroxy acid Epoxide Carboxylic acid  2,3-Dimethyl-2-butene 2,2,3,3-Tetramethyloxirane (70–80%)
Base-promoted cyclization of vicinal halohydrins (Section 16.10) This reaction is an intramolecular version of the Williamson ether synthesis. The alcohol function of a vicinal halohydrin is converted to its conjugate base, which then displaces halide from the adjacent carbon to give an epoxide.	 Vicinal halohydrin Epoxide  3-Bromo-2-methyl-2-butanol 2,2,3-Trimethyloxirane (78%)

Section 16.11 Epoxides are much more reactive than ethers, especially in reactions that lead to cleavage of their three-membered ring.

Section 16.12 Anionic nucleophiles usually attack the less substituted carbon of the epoxide in an S_N2-like fashion.



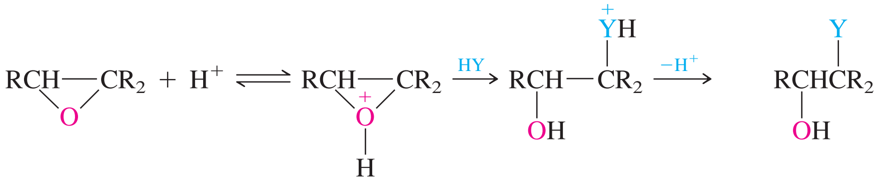
Epoxide Nucleophile β-substituted alcohol



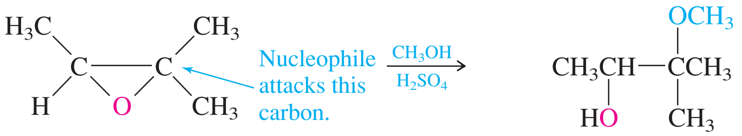
2,2,3-Trimethyloxirane

3-Methoxy-2-methyl-2-butanol (53%)

Section 16.13 Under conditions of acid catalysis, nucleophiles attack the carbon that can better support a positive charge. Carbocation character is developed in the transition state



Epoxide β-substituted alcohol



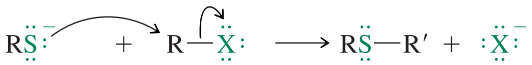
2,2,3-Trimethyloxirane

3-Methoxy-3-methyl-2-butanol (76%)

Inversion of configuration is observed at the carbon that is attacked by the nucleophile, irrespective of whether the reaction takes place in acidic or basic solution.

Section 16.14 Epoxide functions are present in a great many natural products, and epoxide ring opening is sometimes a key step in the biosynthesis of other substances.

Section 16.15 Sulfides are prepared by nucleophilic substitution (S_N2) in which an alkanethiolate ion attacks an alkyl halide.

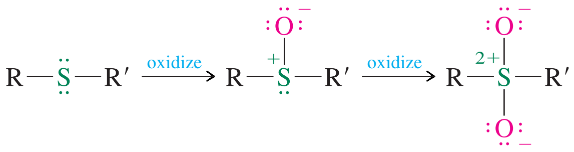


Alkanethiolate Alkyl halide Sulfide Halide

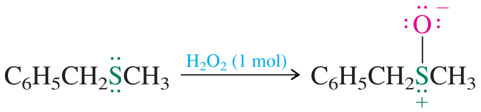
$$C_6H_5SH \xrightarrow{NaOCH_2CH_3} C_6H_5SNa \xrightarrow{C_6H_5CH_2Cl} C_6H_5SCH_2C_6H_5$$

Benzenethiol — Sodium benzenethiolate — Benzyl phenyl sulfide (60%)

Section 16.16 Oxidation of sulfides yields sulfoxides, then sulfones. Sodium metaperiodate is specific for the oxidation of sulfides to sulfoxides, and no further. Hydrogen peroxide or peroxy acids can yield sulfoxides (1 mole of oxidant per mole of sulfide) or sulfone (2 moles of oxidant per mole of sulfide).



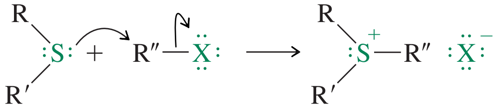
Sulfide — Sulfoxide — Sulfone



$$C_6H_5CH_2SCH_3 \xrightarrow{H_2O_2\ (1\ mol)} C_6H_5CH_2\overset{+}{S}(\overset{-}{O})CH_3$$

Benzyl methyl sulfide — Benzyl methyl sulfoxide (94%)

Section 16.17 Sulfides react with alkyl halides to give sulfonium salts.



Sulfide — Alkyl halide — Sulfonium salt

$$CH_3—\ddot{S}—CH_3 + CH_3I \longrightarrow (CH_3)_3\overset{+}{S}\ I^-$$

Dimethyl sulfide — Methyl iodide — Trimethylsulfonium iodide (100%)

Section 16.18 An H—C—O—C structural unit in an ether resembles an H—C—O—H unit of an alcohol with respect to the C—O stretching frequency in its infrared spectrum and the H—C chemical shift in its ^{1}H NMR spectrum. Because sulfur is less electronegative than oxygen, the ^{1}H and ^{13}C chemical shifts of H—C—S—C units appear at higher field than those of H—C—O—C.

PROBLEMS

16.20 Write the structures of all the constitutionally isomeric ethers of molecular formula $C_5H_{12}O$, and give an acceptable name for each.

16.21 Many ethers, including diethyl ether, are effective as general anesthetics. Because simple ethers are quite flammable, their place in medical practice has been taken by highly halogenated nonflammable ethers. Two such general anesthetic agents are *isoflurane* and *enflurane*. These compounds are isomeric; isoflurane is 1-chloro-2,2,2-trifluoroethyl difluoromethyl ether; enflurane is 2-chloro-1,1,2-trifluoroethyl difluoromethyl ether. Write the structural formulas of isoflurane and enflurane.