

PROBLEM 16.20

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

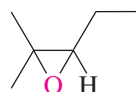
An analogous fragmentation process occurs in the mass spectra of sulfides. As with other sulfur-containing compounds, the presence of sulfur can be inferred by a peak at m/z of $M+2$.

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*.

$\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ **Substitutive IUPAC name:** 1-Methoxyhexane
Functional class name: Hexyl methyl ether

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



2,3-Epoxy-2-methylpentane
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*.

$\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ **Substitutive IUPAC name:** 1-(Methylthio)hexane
Functional class name: Hexyl methyl sulfide

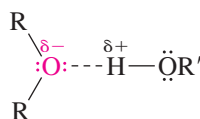
Section 16.2 The oxygen atom in an ether or epoxide affects the shape of the molecule in much the same way as an sp^3 -hybridized carbon of an alkane or cycloalkane.



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.

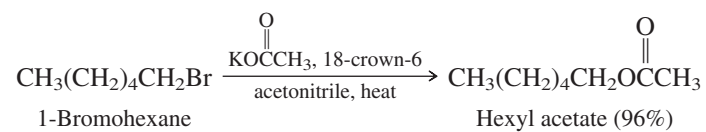


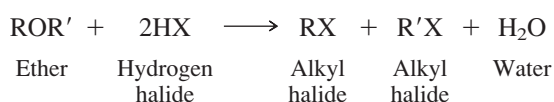
TABLE 16.2 Preparation of Ethers

| 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. | $2\text{RCH}_2\text{OH} \xrightarrow{\text{H}^+} \text{RCH}_2\text{OCH}_2\text{R} + \text{H}_2\text{O}$ <p style="text-align: center;">Alcohol Ether Water</p> |
| | $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH} \xrightarrow[\text{heat}]{\text{H}_2\text{SO}_4} \text{CH}_3\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{CH}_3$ <p style="text-align: center;">Propyl alcohol Dipropyl ether</p> |
| The Williamson ether synthesis (Section 16.6) An alkoxide ion displaces a halide or similar leaving group in an S _N 2 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. | $\text{RO}^- + \text{R}'\text{CH}_2\text{X} \longrightarrow \text{ROCH}_2\text{R}' + \text{X}^-$ <p style="text-align: center;">Alkoxide ion Primary alkyl halide Ether Halide ion</p> |
| | $(\text{CH}_3)_2\text{CHCH}_2\text{ONa} + \text{CH}_3\text{CH}_2\text{Br} \longrightarrow (\text{CH}_3)_2\text{CHCH}_2\text{OCH}_2\text{CH}_3 + \text{NaBr}$ <p style="text-align: center;">Sodium isobutoxide Ethyl bromide Ethyl isobutyl ether (66%) Sodium bromide</p> |

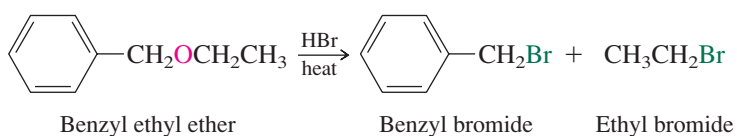
Sections 16.5 and 16.6 The two major methods for preparing ethers are summarized in Table 16.2.

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.



The order of hydrogen halide reactivity is $\text{HI} > \text{HBr} > \text{HCl}$.



Sections 16.9 and 16.10 Epoxides are prepared by the methods listed in Table 16.3.

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.

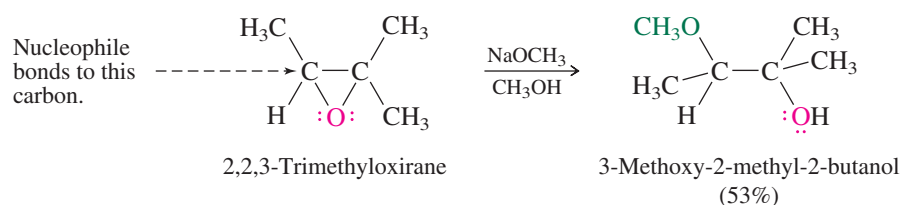
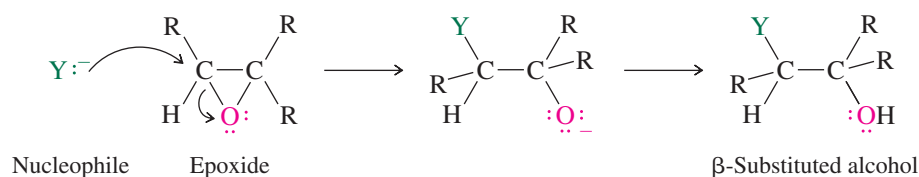
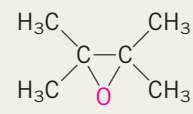
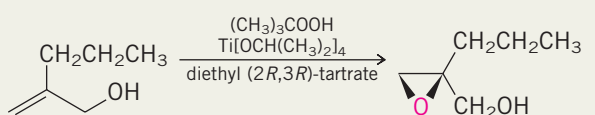
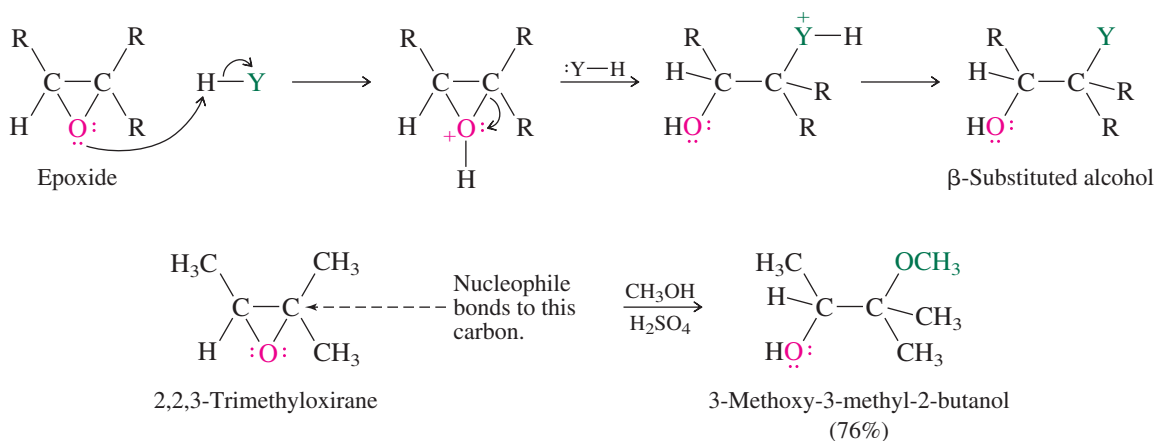


TABLE 16.3 Preparation of Epoxides

| Reaction (section) and comments | General equation and specific example |
|---|--|
| Peroxy acid oxidation of alkenes (Sections 6.19 and 16.9) Peroxy acids transfer oxygen to alkenes to yield epoxides. Stereospecific syn addition is observed. | $R_2C=CR_2 + R'COOH \longrightarrow R_2C \begin{array}{c} \diagup \\ O \\ \diagdown \end{array} CR_2 + R'COH$ <p>Alkene Peroxy acid Epoxide Carboxylic acid</p> <p>$(CH_3)_2C=C(CH_3)_2 \xrightarrow{CH_3COOH}$ </p> <p>2,3-Dimethyl-2-butene 2,2,3,3-Tetramethyloxirane (70–80%)</p> |
| Sharpless epoxidation (Section 16.9) Allylic alcohols are converted to epoxides by treatment with <i>tert</i> -butyl hydroperoxide and titanium(IV) alkoxides. The reaction is highly enantioselective in the presence of enantiomerically pure diethyl tartrate. | $R_2C=CR_2 + (CH_3)_3COOH \xrightarrow[\text{diethyl (2R,3R)- or (2S,3S)-tartrate}]{Ti[OCH(CH_3)_2]_4} R_2C \begin{array}{c} \diagup \\ O \\ \diagdown \end{array} CR_2 + (CH_3)_3COH$ <p>Alkene <i>tert</i>-Butyl hydroperoxide Epoxide <i>tert</i>-Butyl alcohol</p> <p></p> <p>2-Propyl-2-propen-1-ol (<i>S</i>)-2,3-Epoxy-2-propylpropan-1-ol (88% yield; 95% enantiomeric excess)</p> |
| 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. | $R_2C \begin{array}{c} X \\ \\ HO \end{array} - CR_2 \xrightleftharpoons{HO^-} R_2C \begin{array}{c} X \\ \\ :O^- \end{array} - CR_2 \longrightarrow R_2C \begin{array}{c} \diagup \\ O \\ \diagdown \end{array} CR_2$ <p>Vicinal halohydrin Epoxide</p> <p>$(CH_3)_2C \begin{array}{c} HO \\ \\ Br \end{array} - CHCH_3 \xrightarrow[H_2O]{NaOH} (CH_3)_2C \begin{array}{c} \diagup \\ O \\ \diagdown \end{array} - CHCH_3$</p> <p>3-Bromo-2-methyl-2-butanol 2,2,3-Trimethyloxirane (78%)</p> |

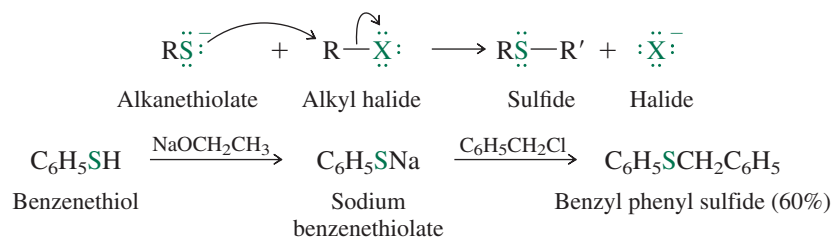
Section 16.13 Under conditions of acid catalysis, nucleophiles attack the carbon that can better support a positive charge. Carbocation character is developed in the transition state



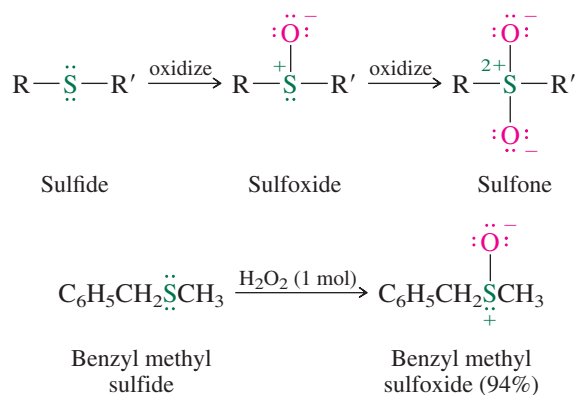
Inversion of configuration is observed at the carbon that is attacked by the nucleophile, irrespective of whether the reaction takes place in acidic or basic solution.

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.

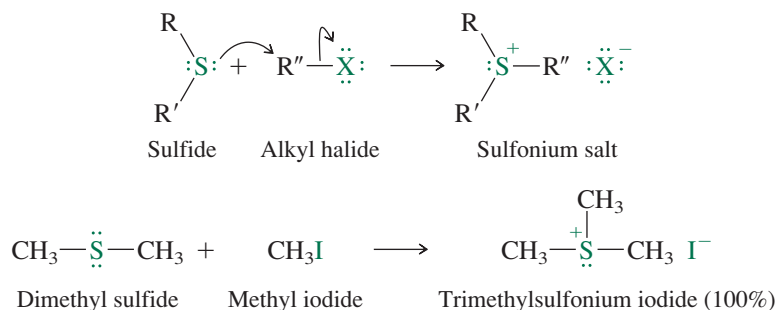
Section 16.15 Sulfides are prepared by nucleophilic substitution (S_N2) in which an alkanethiolate ion reacts with an alkyl halide.



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 mol of oxidant per mole of sulfide) or sulfones (2 mol of oxidant per mole of sulfide).



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



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 ^1H NMR spectrum. Because sulfur is less electronegative than oxygen, the ^1H and ^{13}C chemical shifts of H—C—S—C units appear at higher field than those of H—C—O—C.