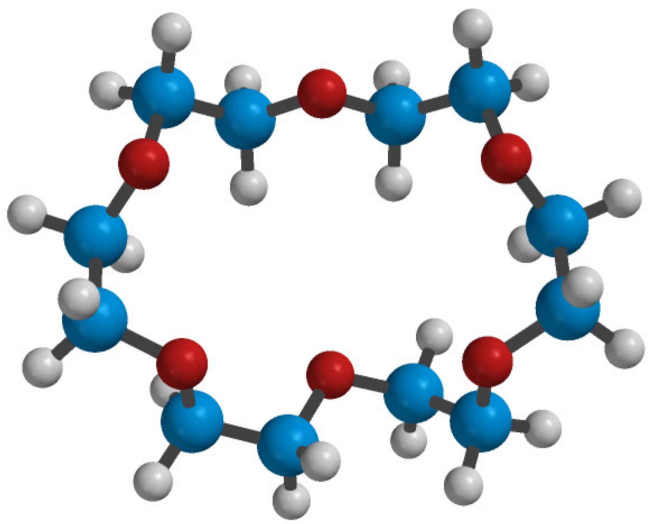
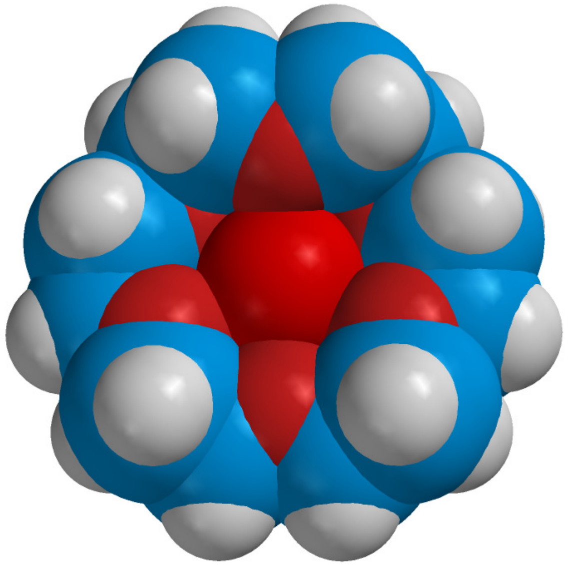
16

ETHERS AND EPOXIDES



The cyclic ether 18-crown-6

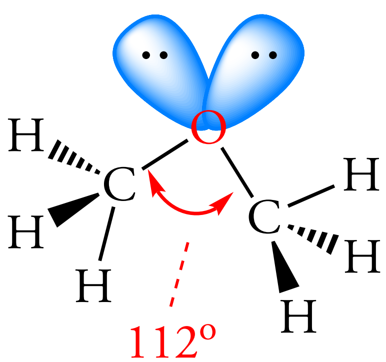


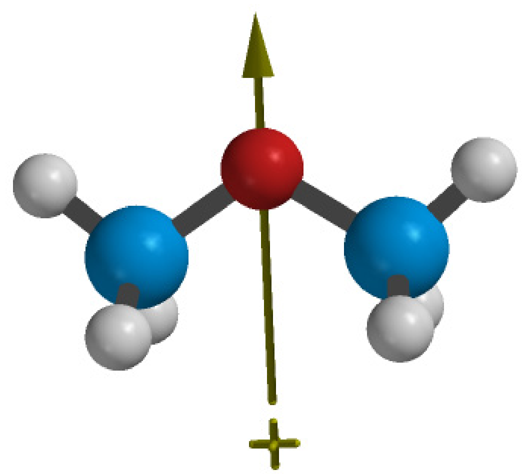
K^+ ion solvated by the cyclic ether 18-crown-6

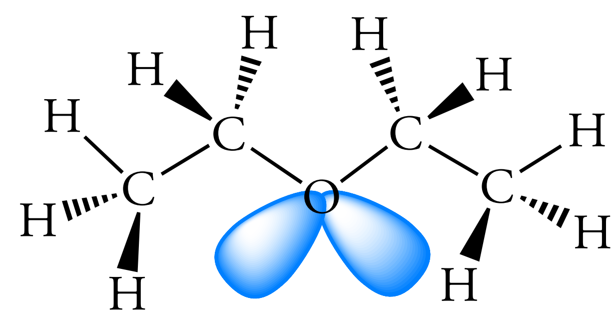
16.1 STRUCTURE OF ETHERS

Figure 16.1 Structure of Dimethyl Ether

The oxygen atom of methanol is sp^3-hybridized. The C—O—C bond angle, 112°, is close to the tetrahedral bond angle (109.5). The two sets of lone pair electrons are in sp^3 hybrid orbitals that are directed to two of the corners of a tetrahedron.

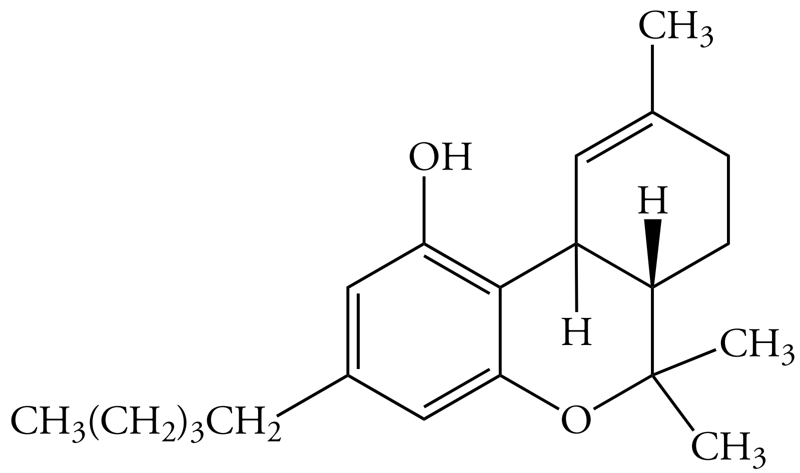




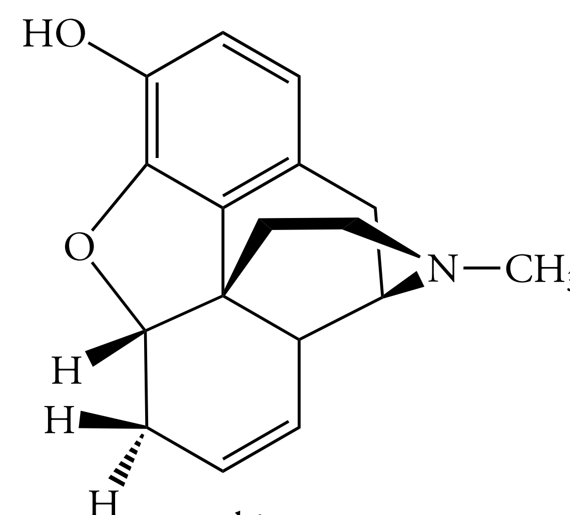


ethoxyethane
(diethyl ether)

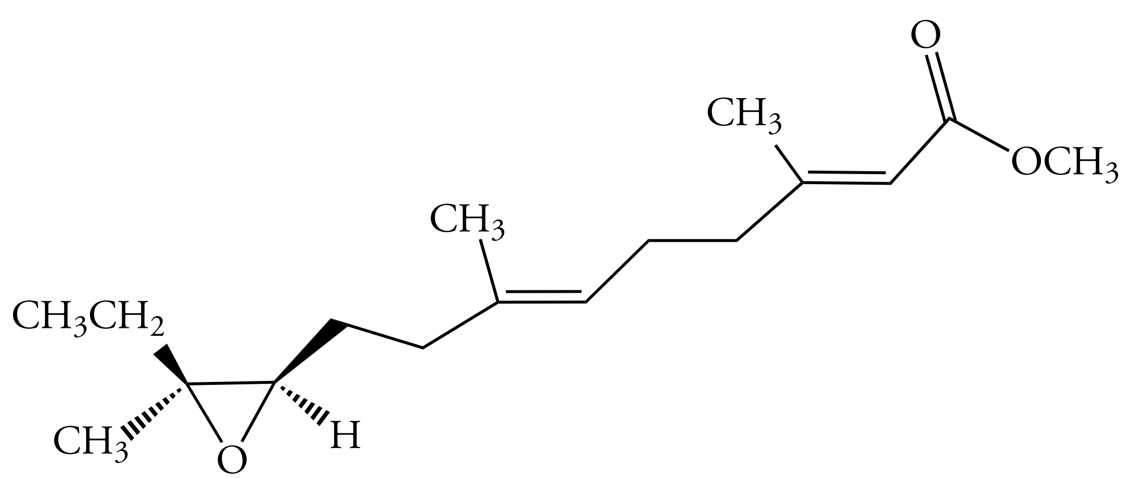
Figure 16.2 Structures of Naturally Occurring Ethers



tetrahydrocannabinol



morphine



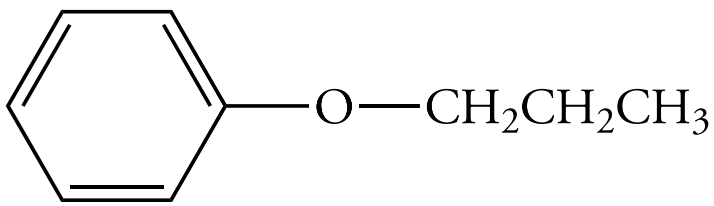
insect juvenile growth hormone

16.2 NOMENCLATURE OF ETHERS

Common Names

$$CH_3CH_2—O—CH_2CH_3$$

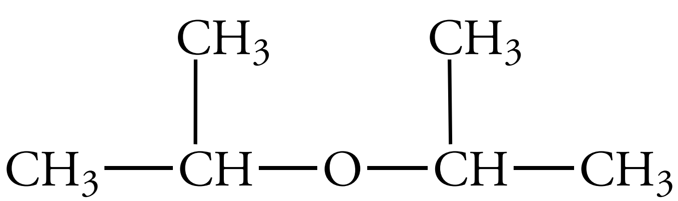
diethyl ether
(a symmetrical ether)



phenyl propyl ether
(an un symmetrical ether)

$$CH_3—O—CH_2CH_2CH_2CH_3$$

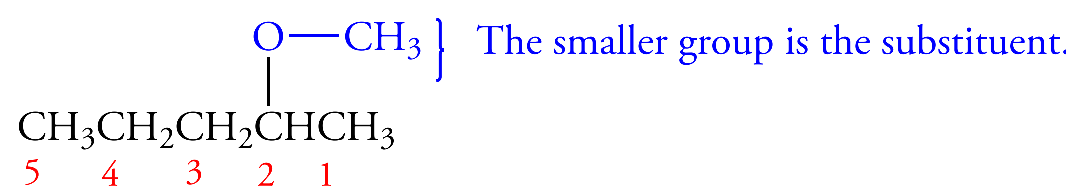
n-butylmethyl ether



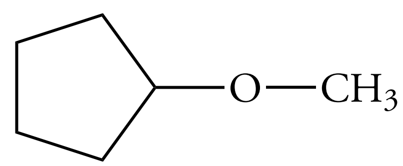
diisopropyl ether

16.2 NOMENCLATURE OF ETHERS
IUPAC Names

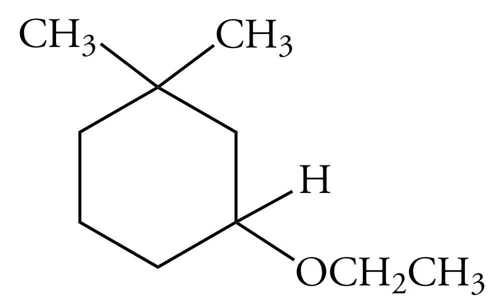
Figure 16.3 IUPAC Names of Ethers



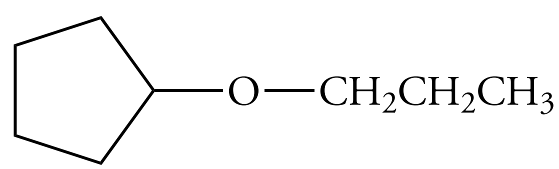
2-methoxypentane



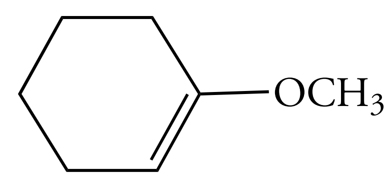
methoxycyclopentane



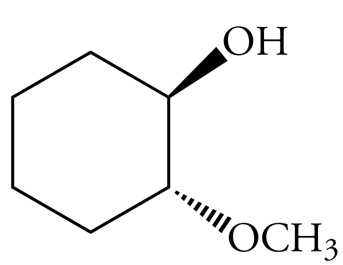
3-ethoxy-1,1-dimethylcyclohexane



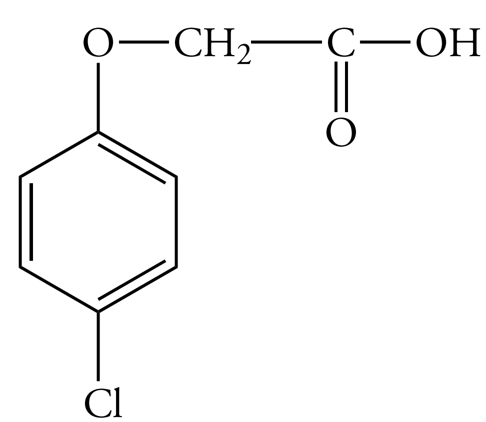
propoxycyclopentane



1-methoxycyclohexene

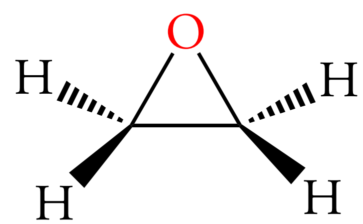


trans-2-methoxycyclohexanol

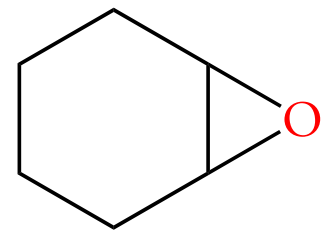


p-chlorophenoxyacetic acid

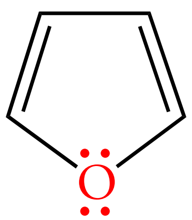
16.2 NOMENCLATURE OF ETHERS
Cyclic Ethers



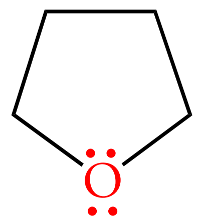
ethylene oxide
(oxirane)



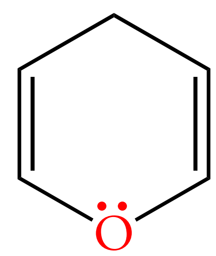
cyclohexene oxide



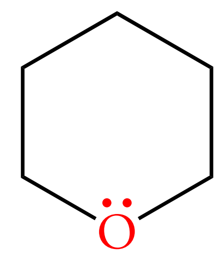
furan



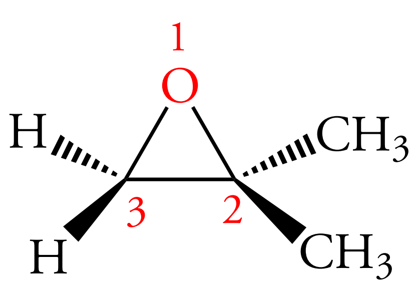
tetrahydrofuran



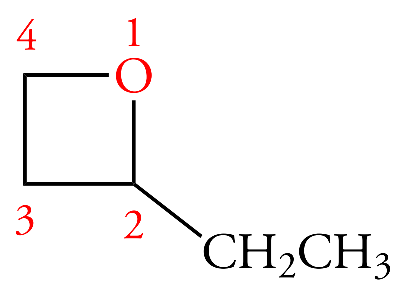
pyran



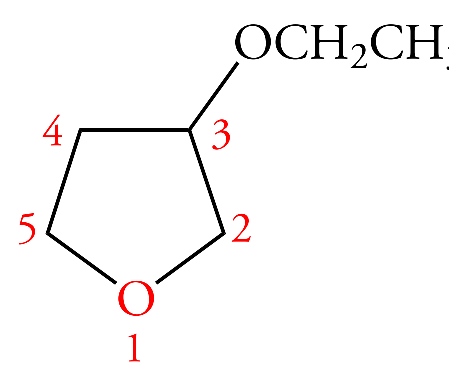
tetrahydropyran



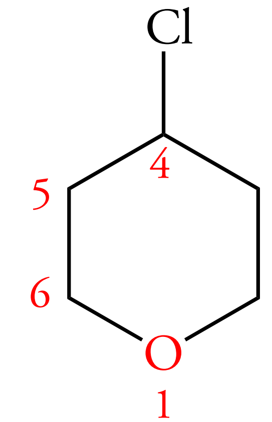
2,2-dimethyloxirane



2-ethyloxetane



3-ethoxyoxolane



4-chlorooxane

16.3 PHYSICAL PROPERTIES OF ETHERS

Dipole Moments and Boiling Points

$CH_3—CH_2—CH_2—CH_2—CH_3$

pentane (0.1 D)
bp 35 °C

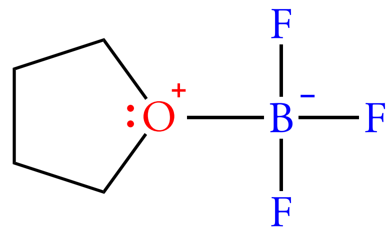
$CH_3—CH_2—O—CH_2—CH_3$

diethyl ether (1.2 D)
bp 35 °C

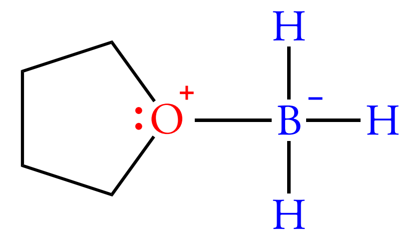
$CH_3—CH_2—CH_2—CH_2—OH$

1-butanol (1.7 D)
bp 117 °C

Ethers as Solvents

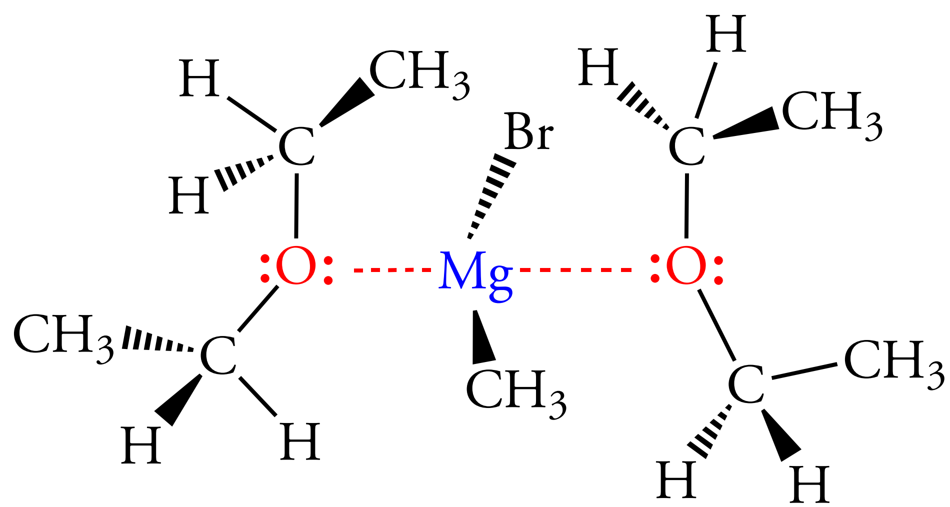


BF_3-THF complex



BH_3-THF complex

Figure 16.4 Solvation of a Grignard Reagent by Diethyl Ether



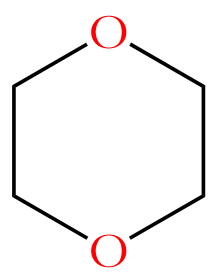
16.3 PHYSICAL PROPERTIES OF ETHERS
Polyethers

$$CH_3{-}O{-}CH_2CH_2{-}O{-}CH_3$$

glyme

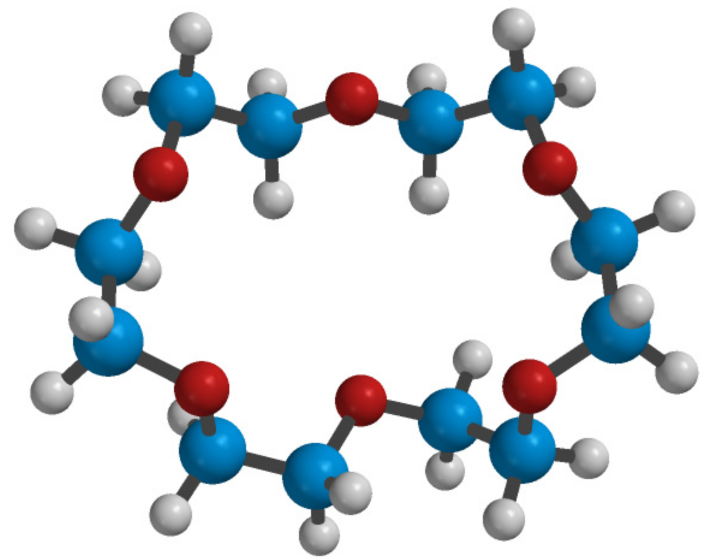
$$CH_3{-}O{-}CH_2CH_2{-}O{-}CH_2CH_2{-}O{-}CH_3$$

diglyme



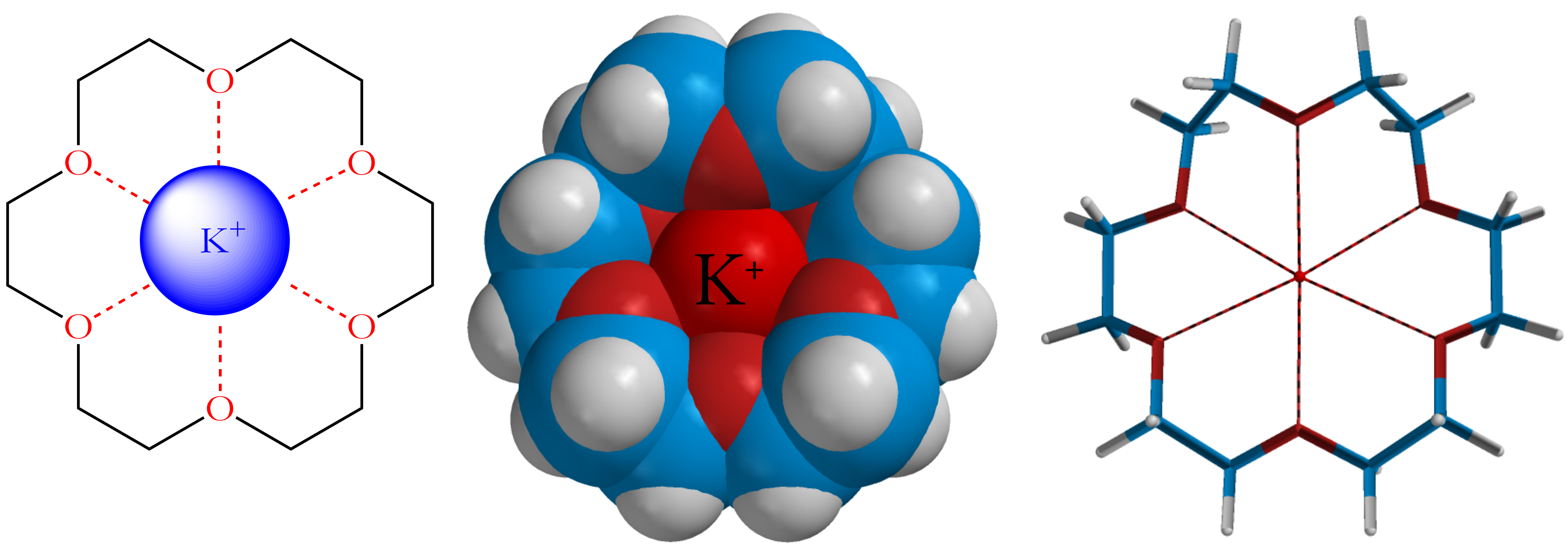
1,4-dioxane

Figure 16.5
(a) Crown ether 18-crown-6
(b) Solvation of Potassium by a 18-crown-6



18-crown-6

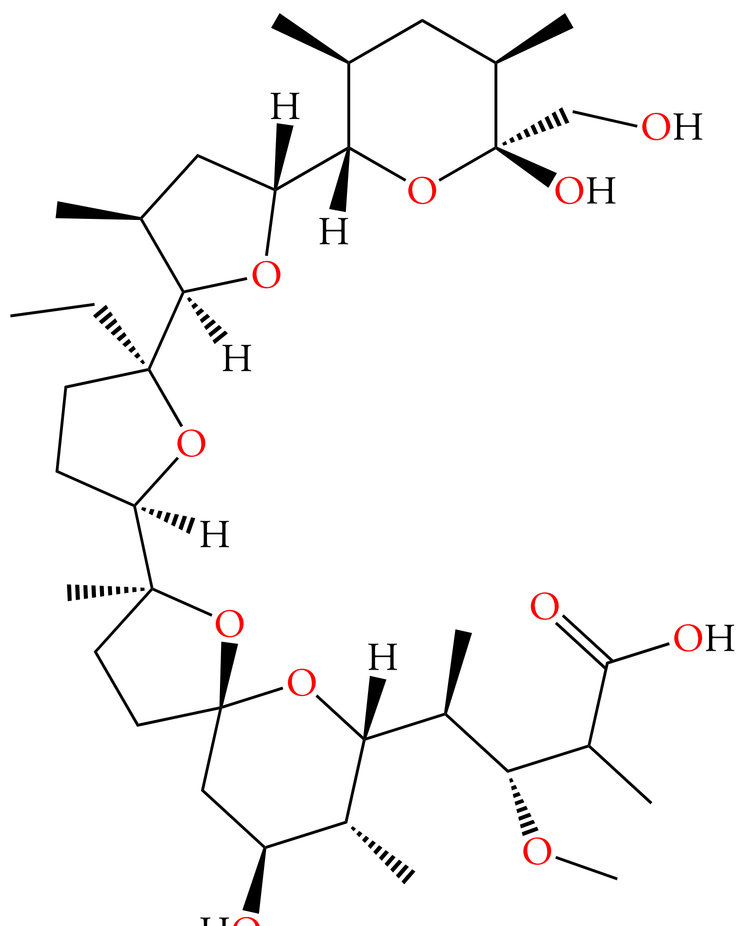
(b)



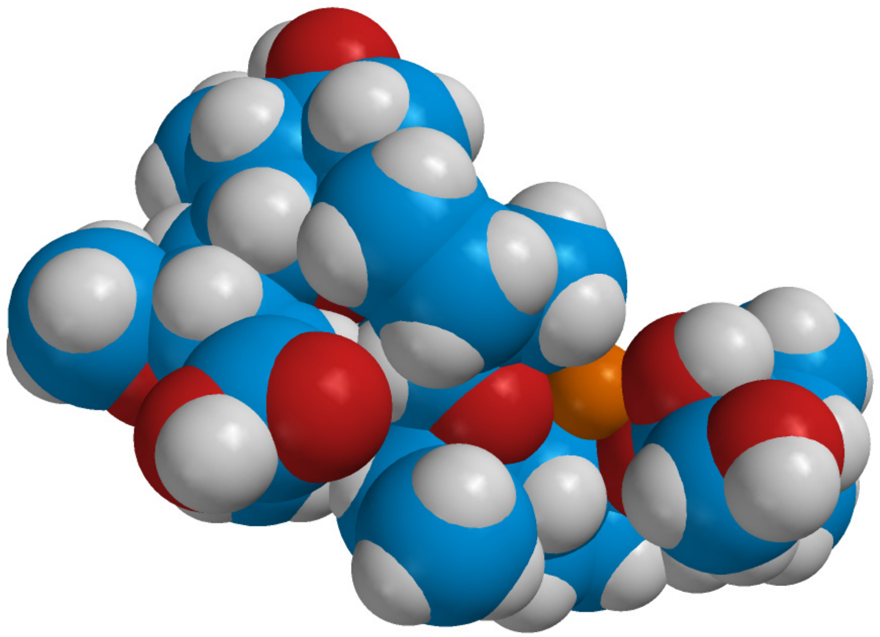
K^+ ion solvated by the cyclic ether 18-crown-6

Figure 16.6 Cation Solvation by Polyethers

Cyclic polyethers such as nonactin and monensin coordinate with alkali metal ions. The selectivity of the ether for one metal ion over another depends on, the geometry of the polyether and the location of the ether oxygen atoms.

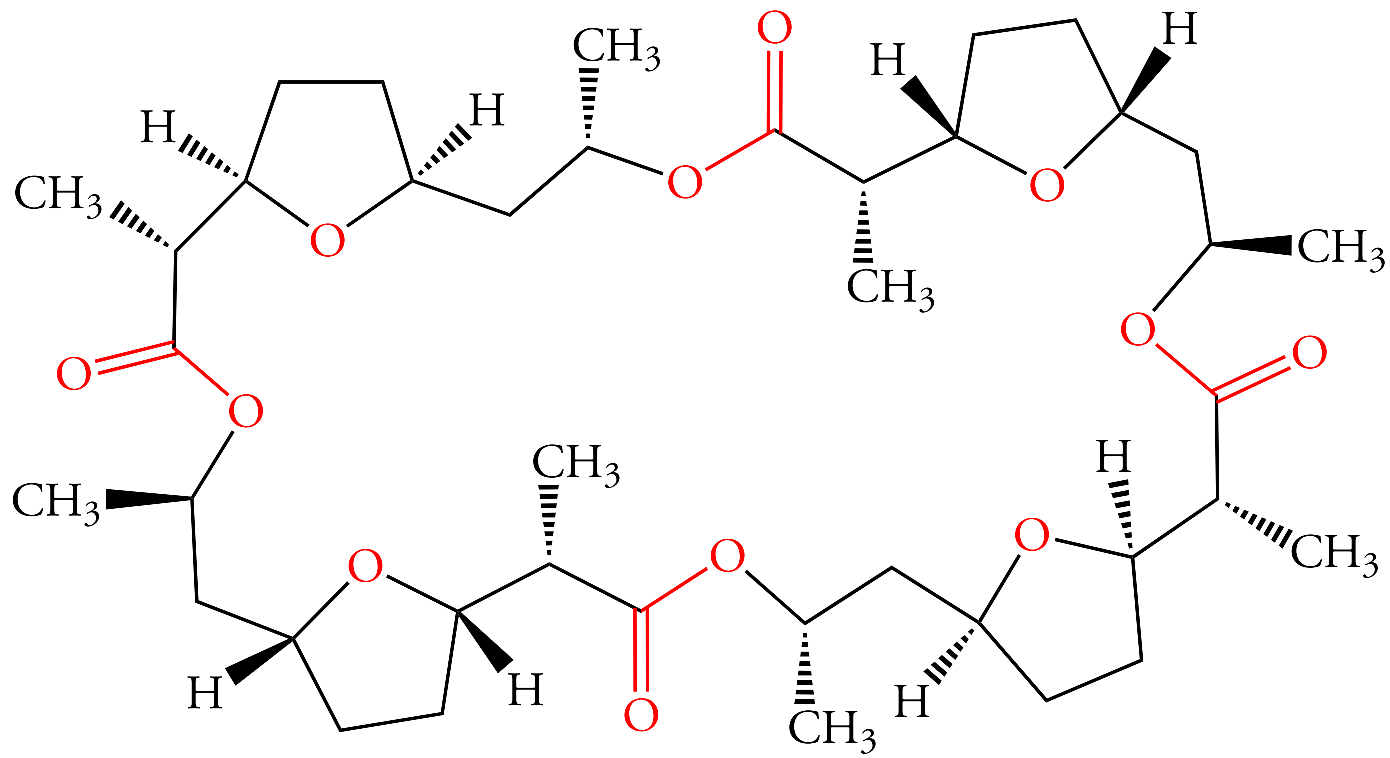


monensin



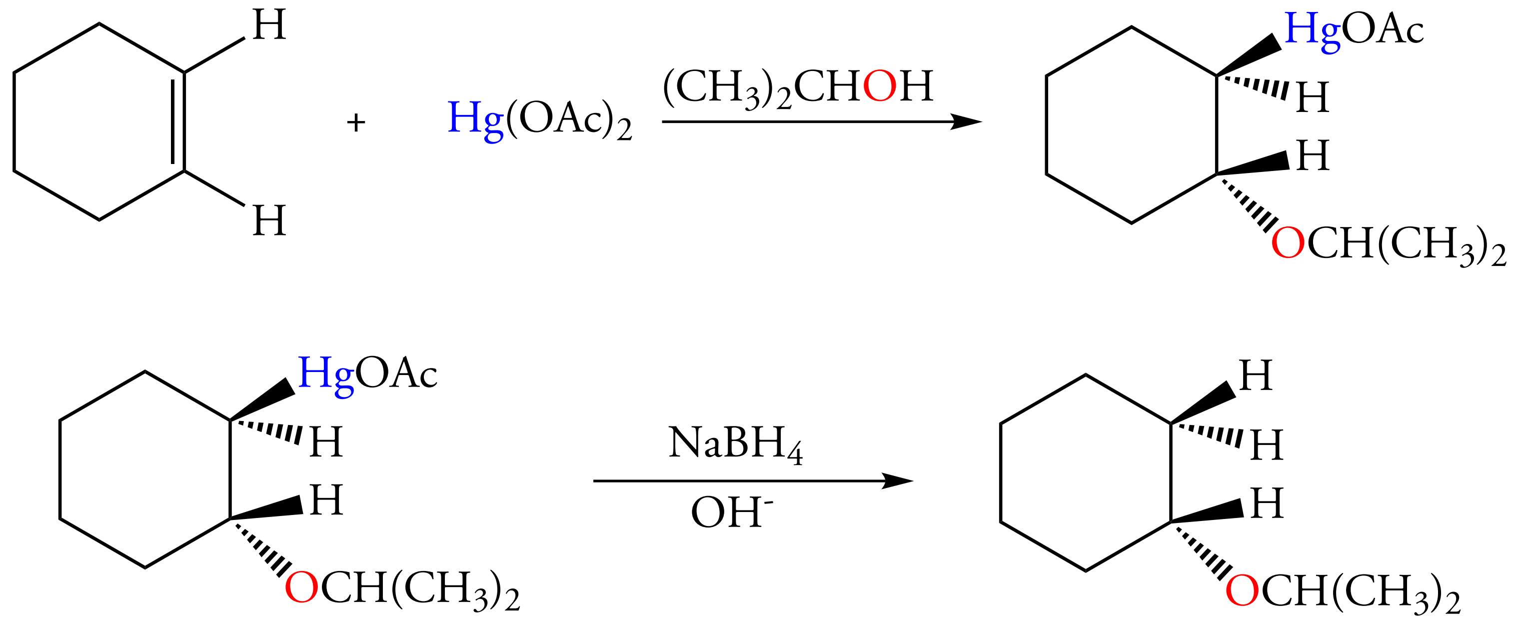
monensin-Na^+ complex

16.4 POLYETHER ANTIBIOTICS

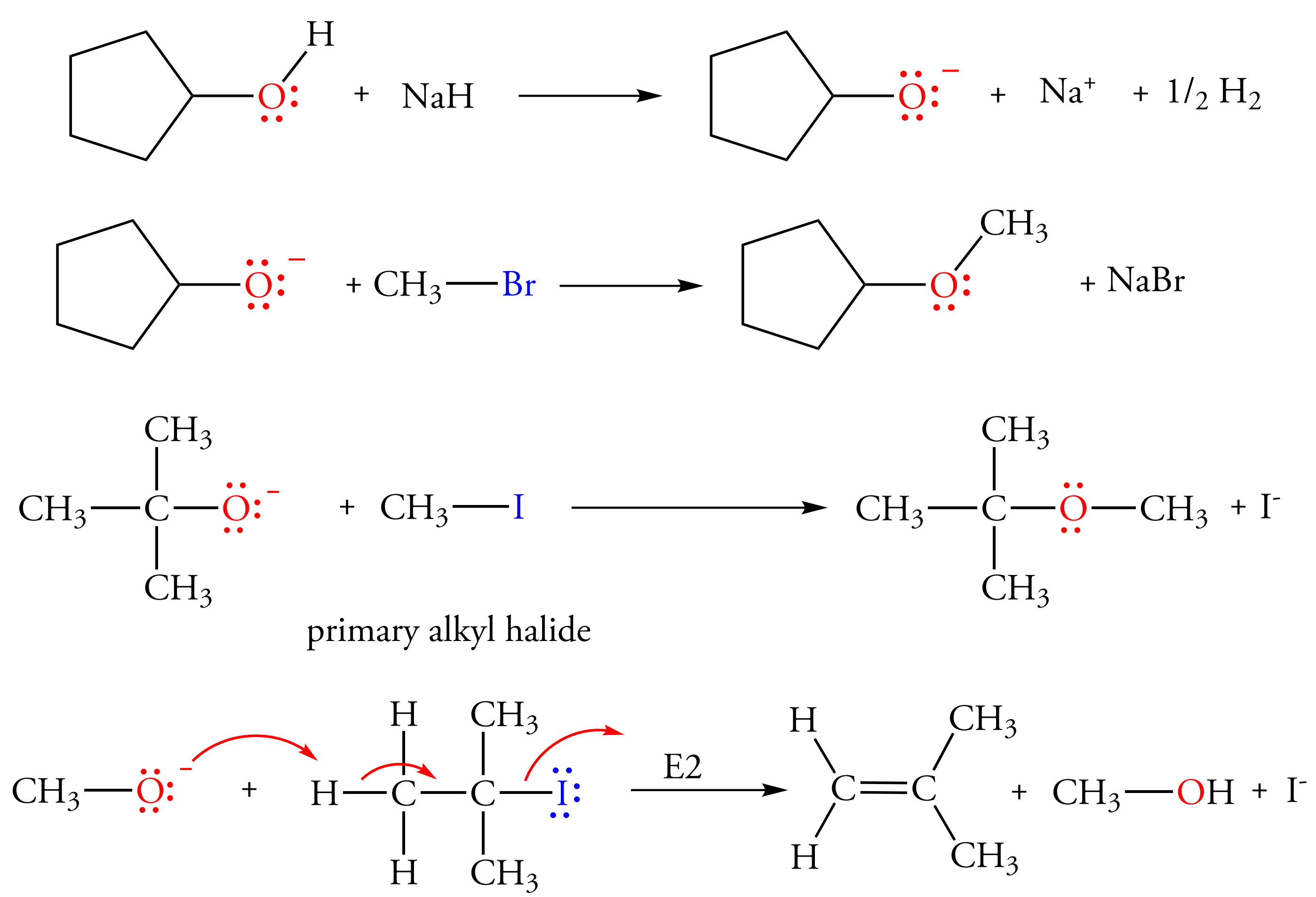


nonactin

16.5 SYNTHESIS OF ETHERS: ALKOXYMERCURATION- DEMERCURATION OF ALKENES

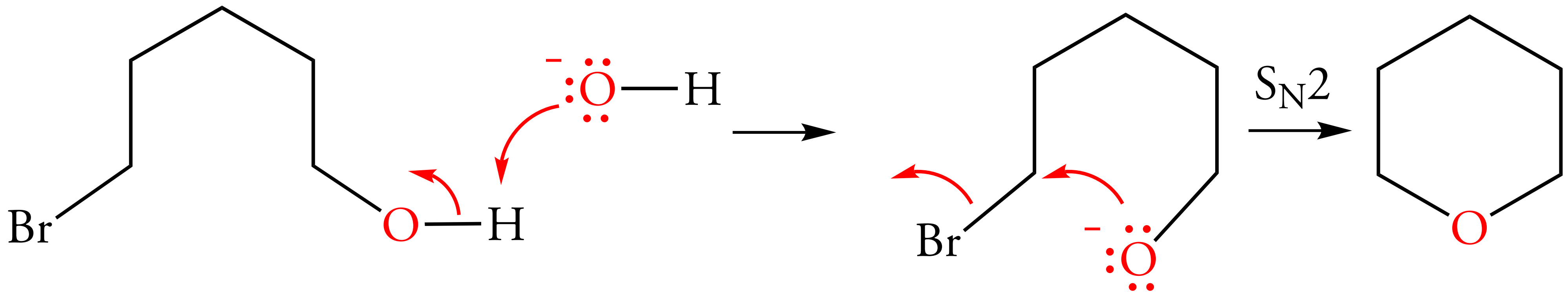


16.6 THE WILLIAMSON ETHER SYNTHESIS



16.6 THE WILLIAMSON ETHER SYNTHESIS

Formation of Cyclic Ethers



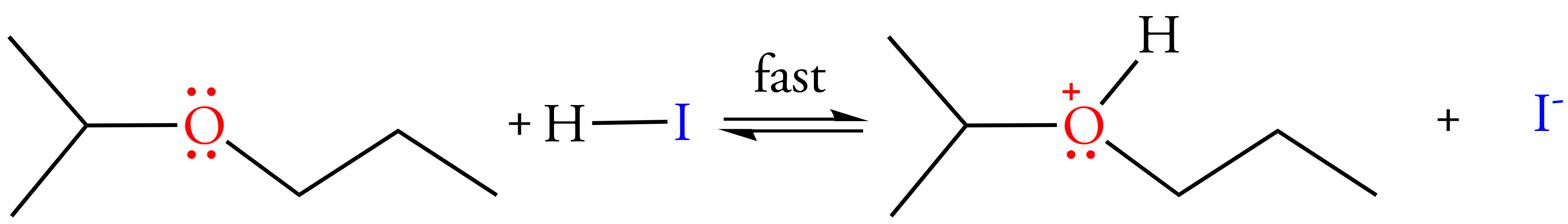
Rates of cyclization and ring size: 3 > 5 > 6 > 4 > 7 > 8

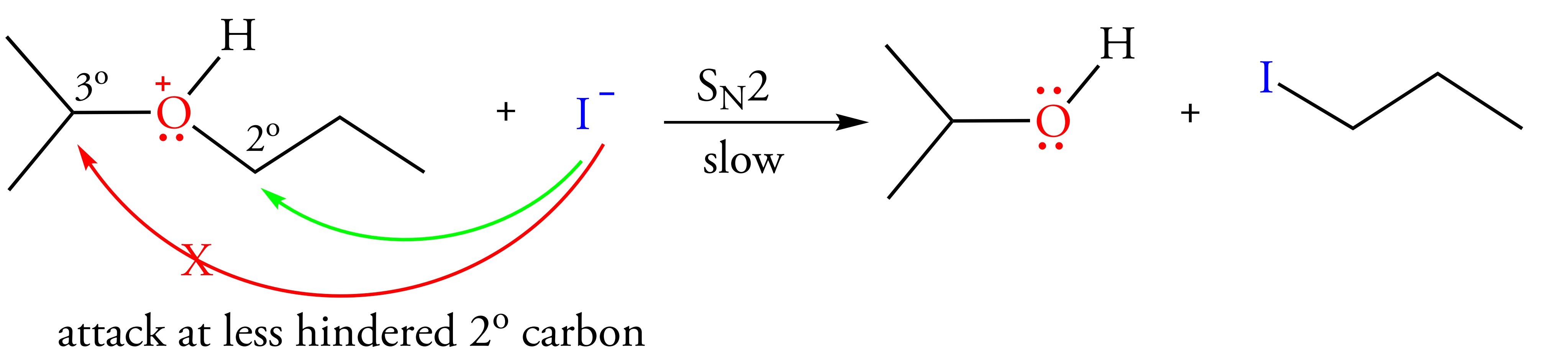
Predicted rates based on strain energy: 3 = 4 > 5 = 6 = 7 = 8

Predicted rates based on probability: 3 > 4 > 5 > 6 > 7 > 8

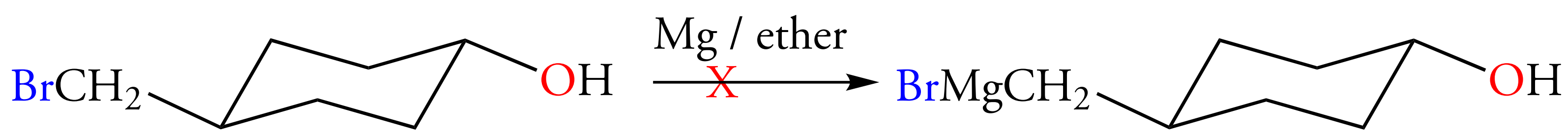
16.7 REACTIONS OF ETHERS

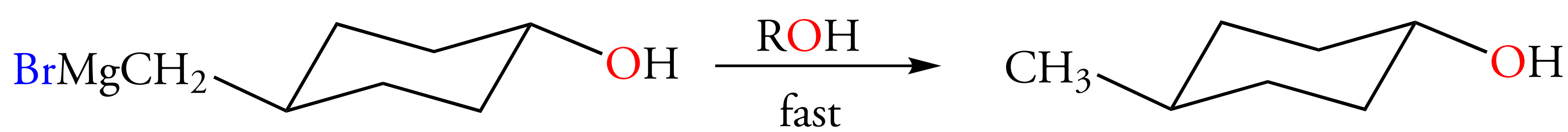
$$R-O-R' \xrightarrow{HX} R-O-H + R'-X \xrightarrow{HX} R-X + R'-X$$

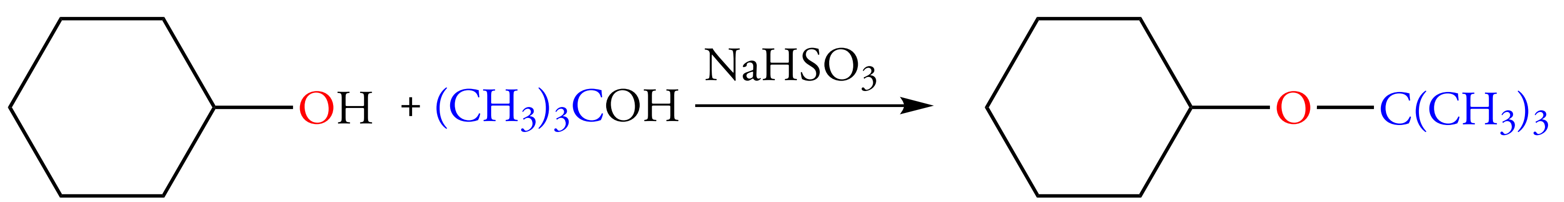


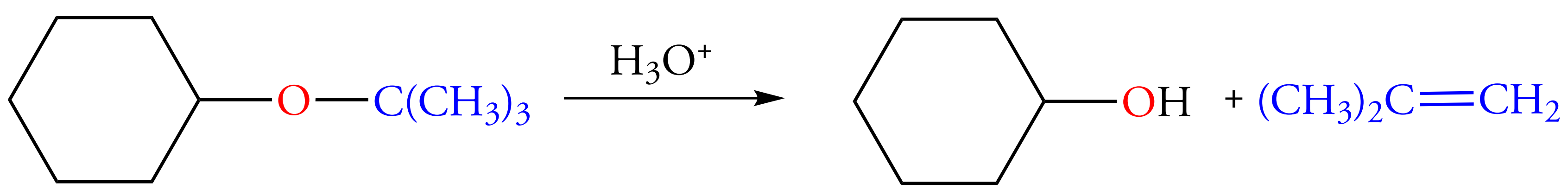


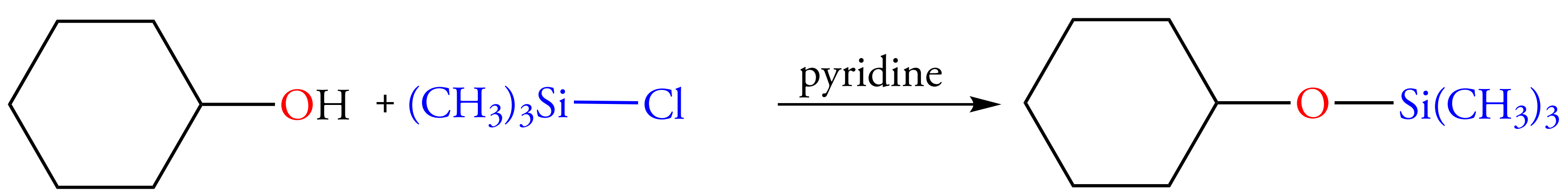
16.8 ETHERS AS PROTECTING GROUPS





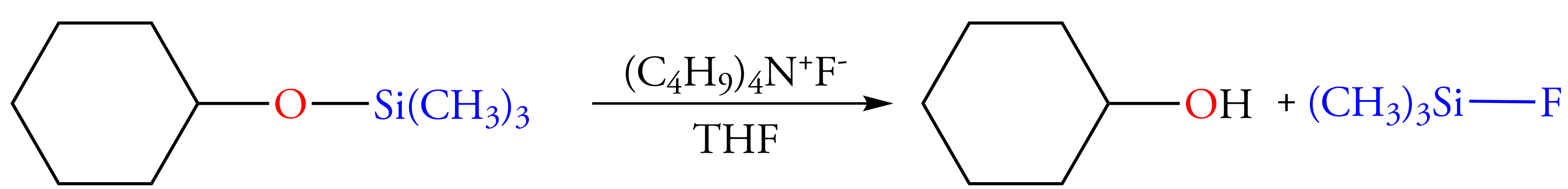






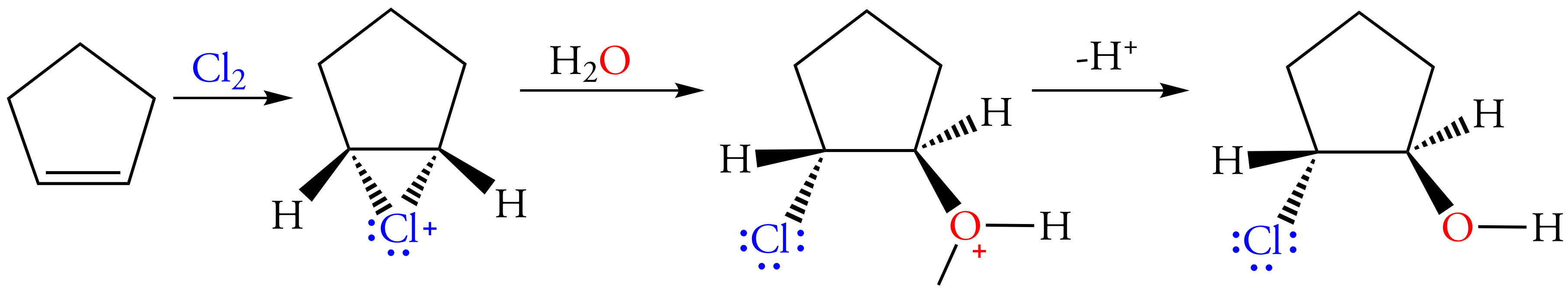
chlorotrimethylsilane

(a trimethylsilyl ether)

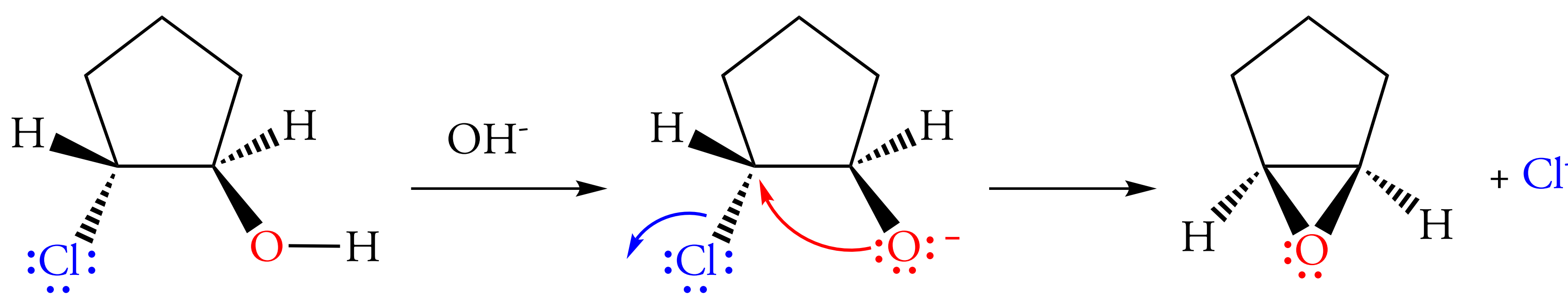


(a trimethylsilyl ether)

16.9 SYNTHESIS OF EPOXIDES

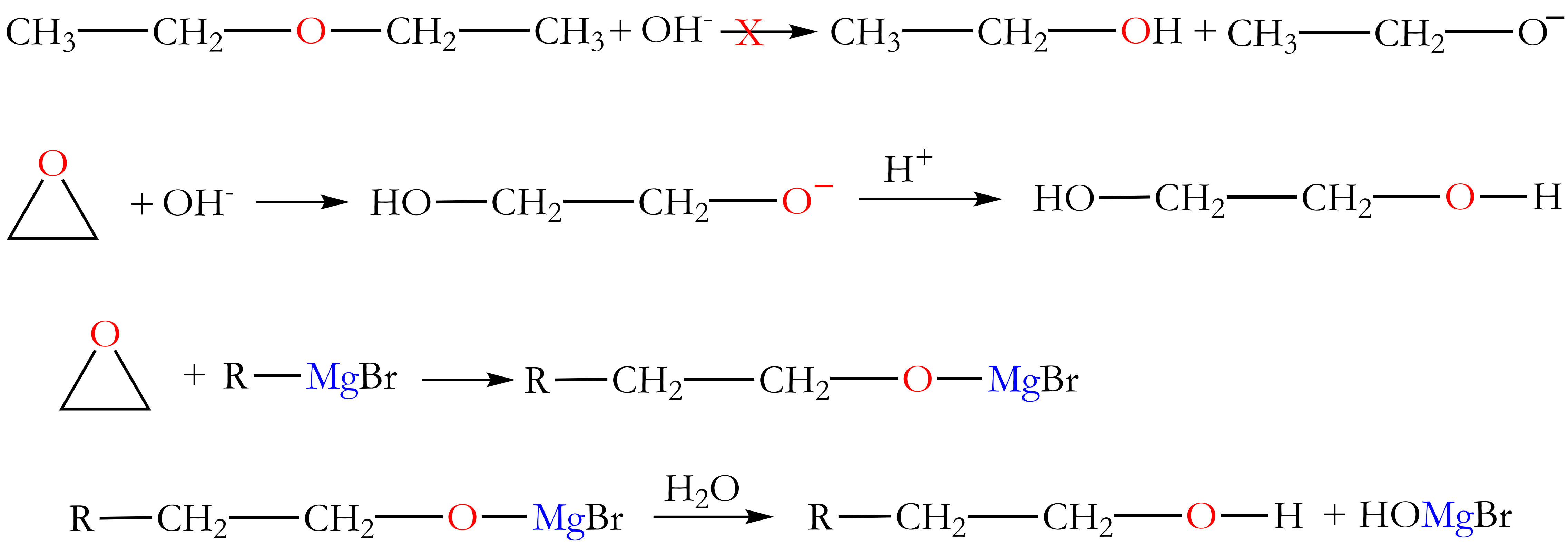


(a chlorohydrin)



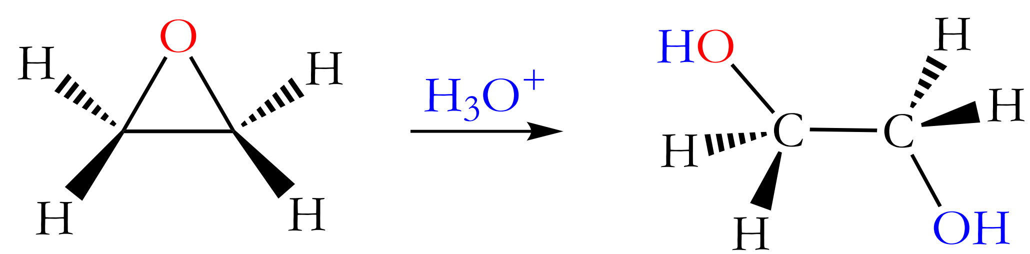
16.10 REACTIONS OF EPOXIDES

Ring Opening by Nucleophiles



16.10 REACTIONS OF EPOXIDES

Acid-Catalyzed Ring Opening



1,2-ethanediol
(ethylene glycol)

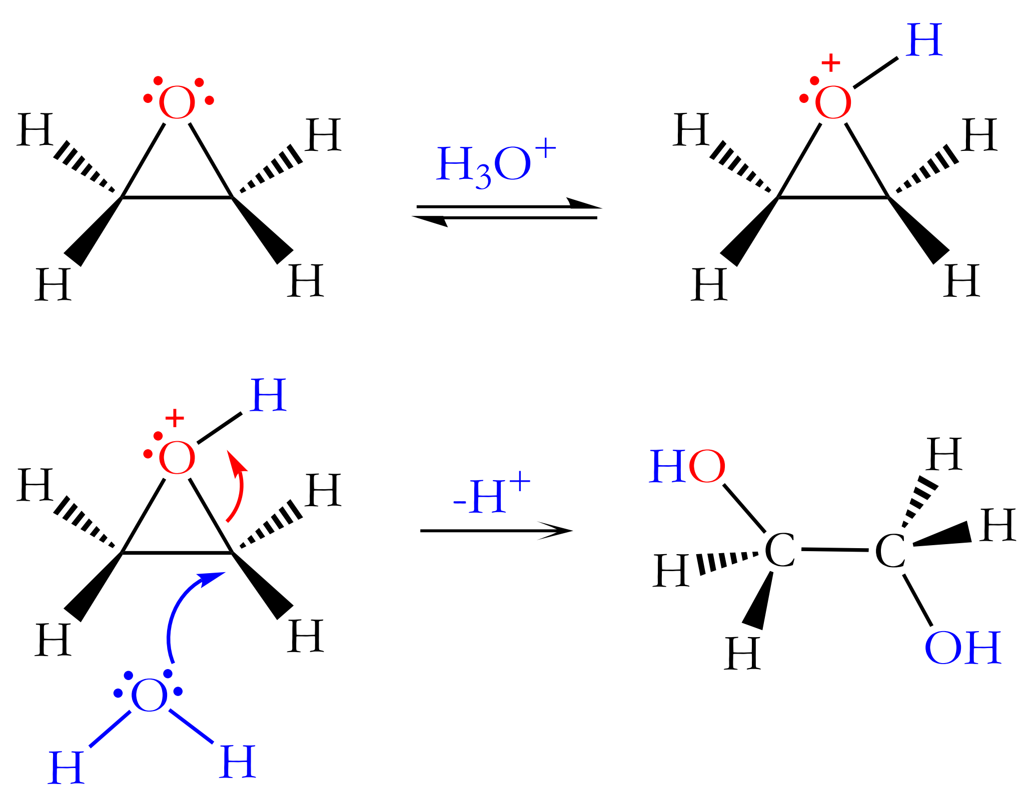
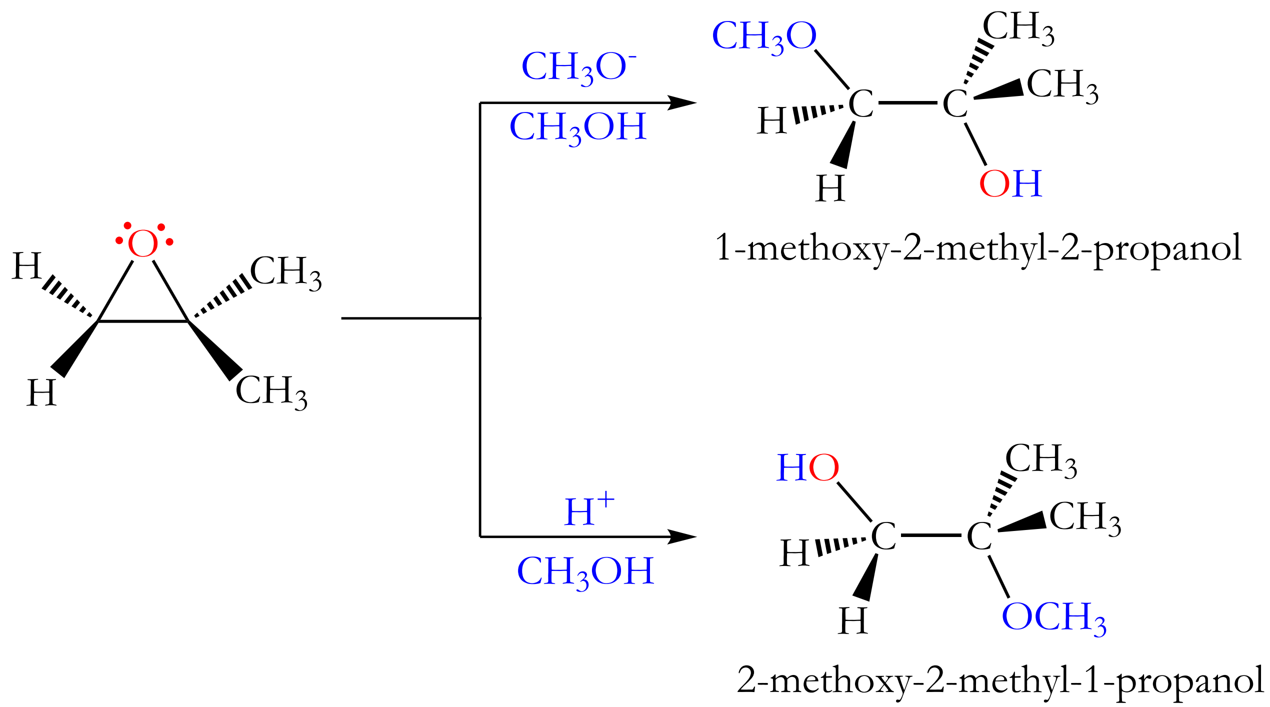
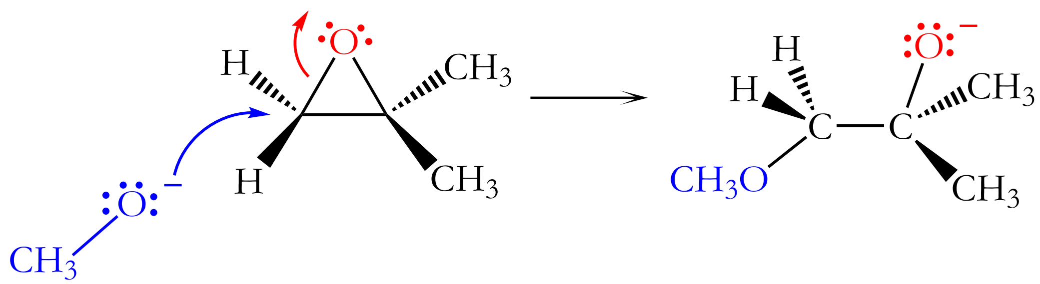


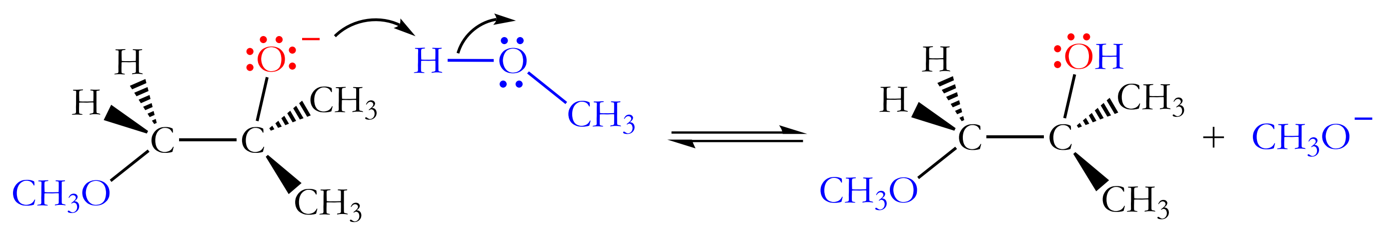
Figure 16.7 Regioselectivity of Epoxide Ring Opening

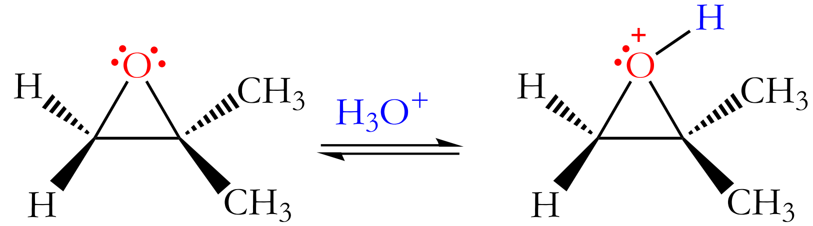


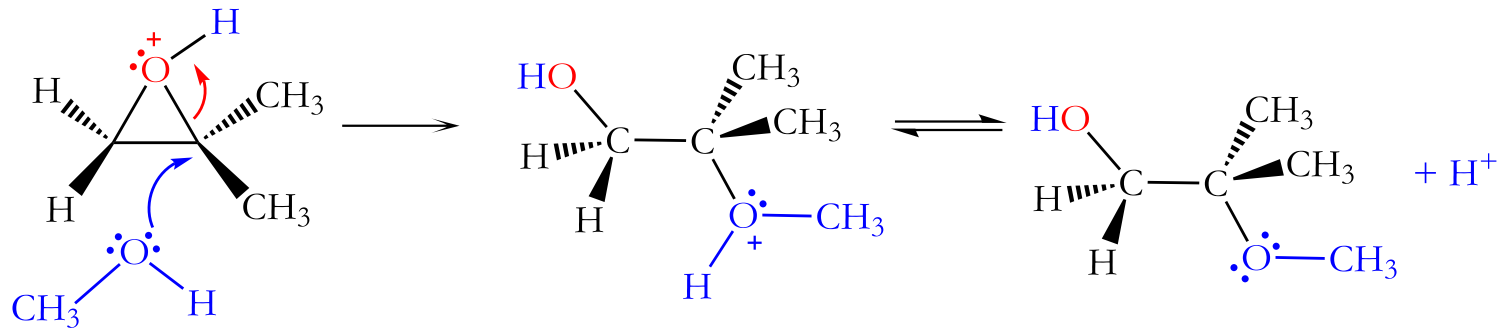
16.10 REACTIONS OF EPOXIDES

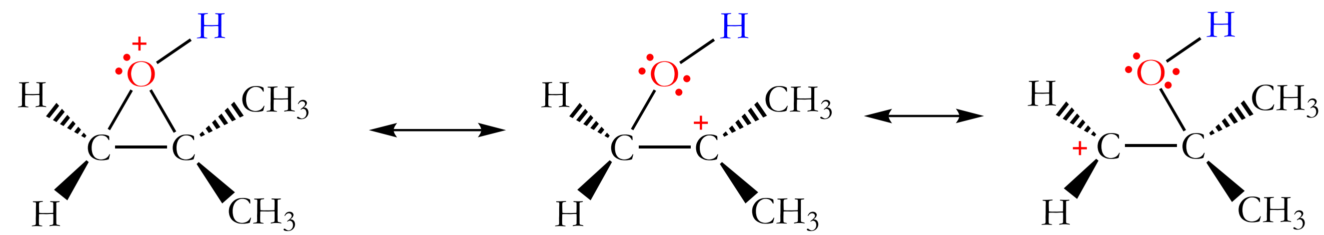
Regioselectivity of Ring Opening





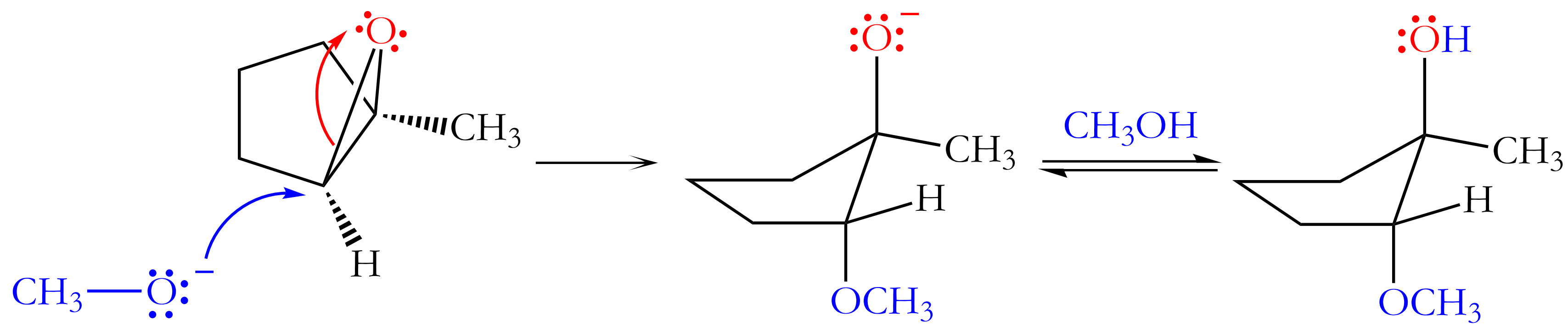


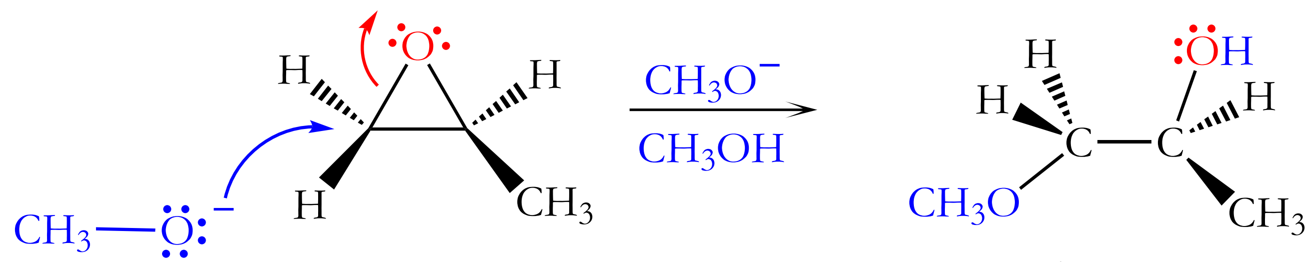




oxonium ion — tertiary carbocation — primary carbocation

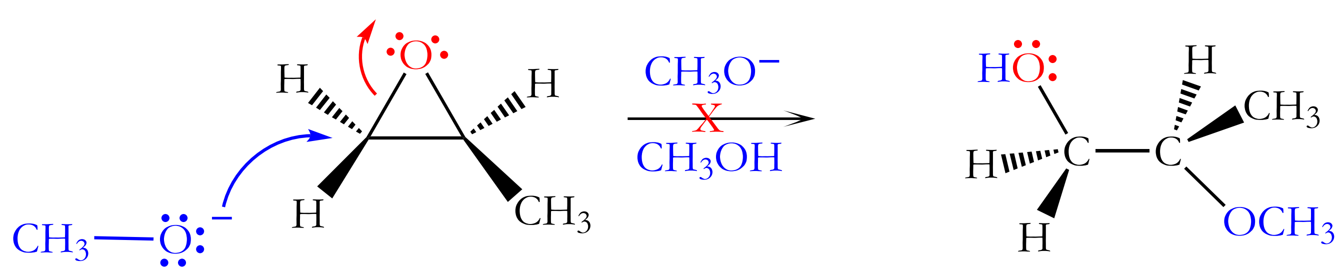
16.10 REACTIONS OF EPOXIDES
Stereochemistry of Ring Opening





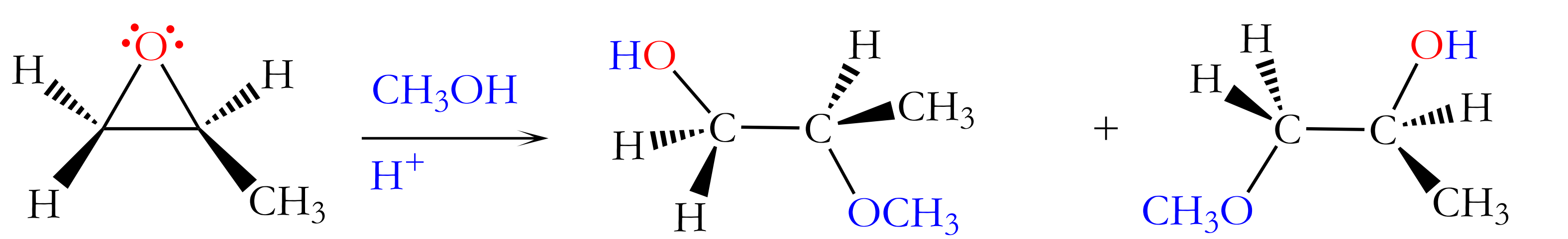
(S)-2-methyloxirane

(S)-1-methoxy-2-propanol



(S)-2-methyloxirane

not observed



(R)-2-methoxy-1-propanol
(major product)

(S)-1-methoxy-2-propanol
(minor product)

16.10 REACTIONS OF EPOXIDES

Biochemical Reactions of Epoxides

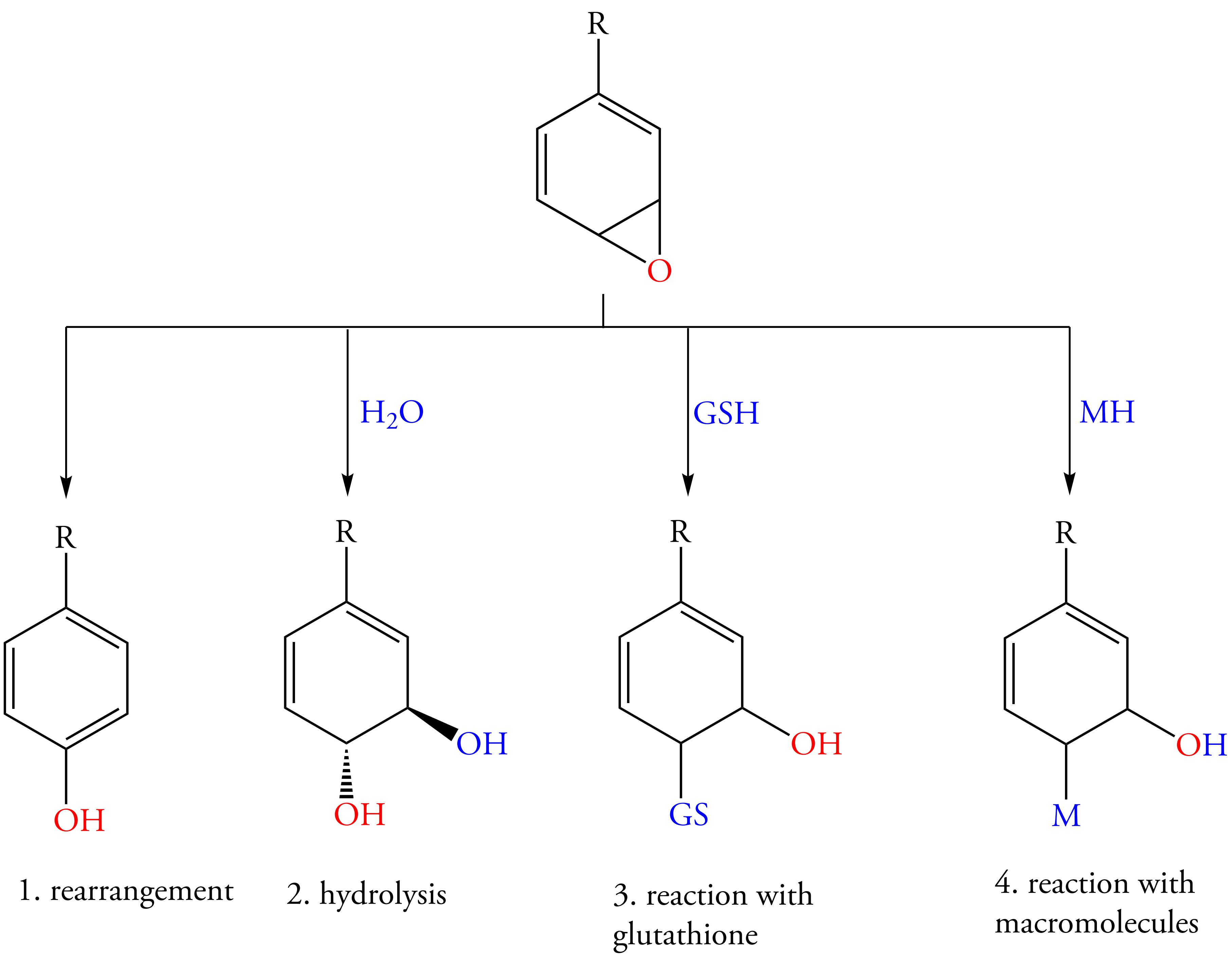
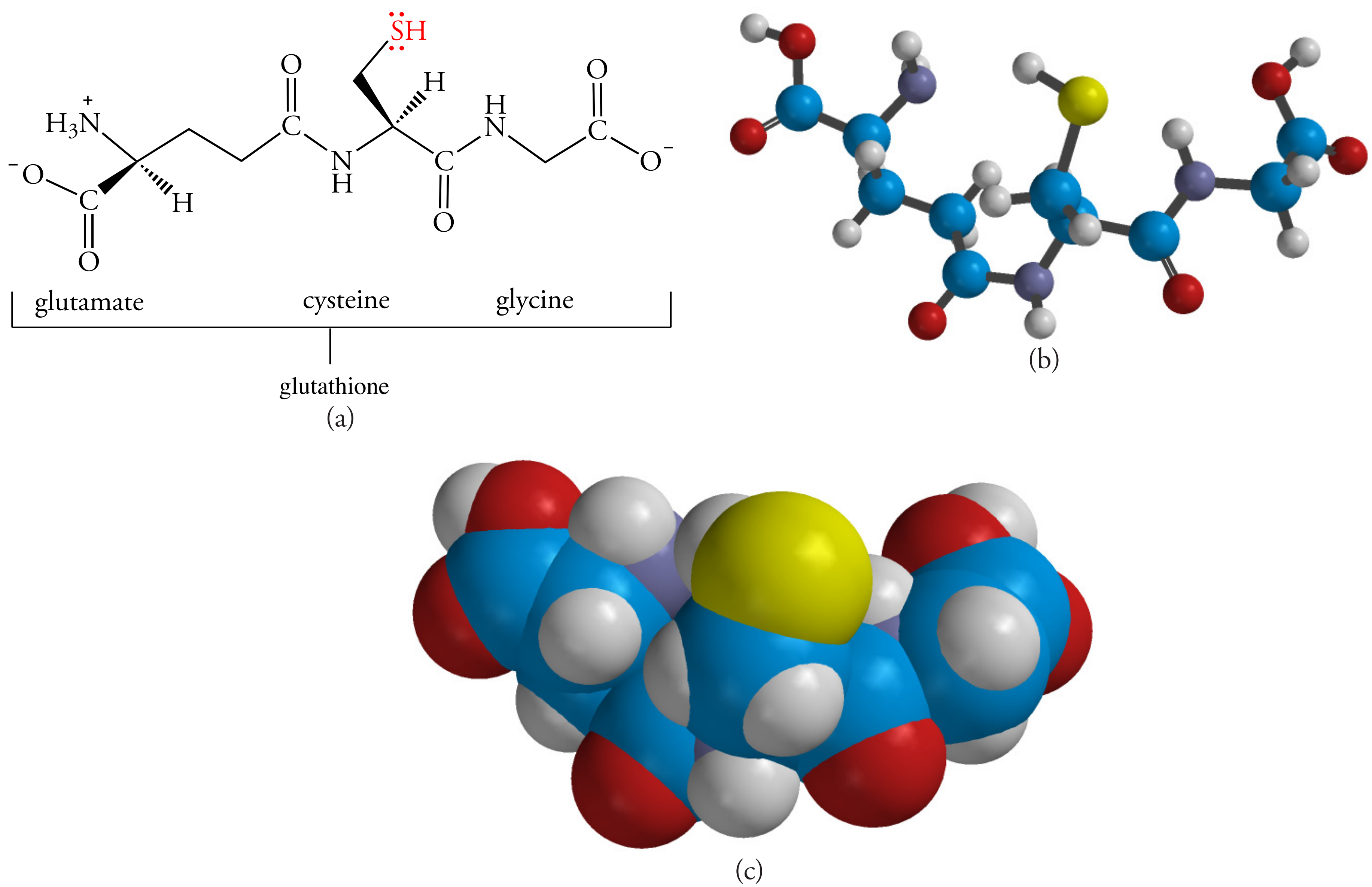
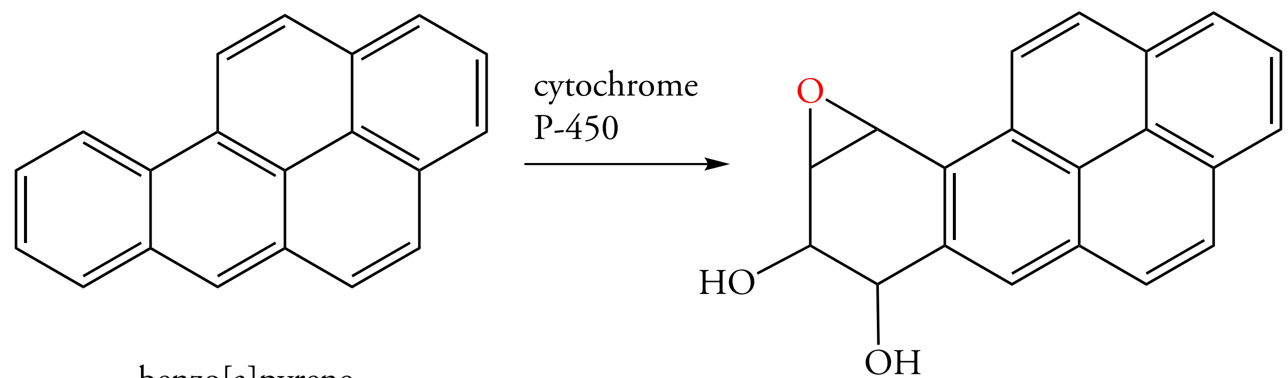


Figure 16.8 Structure of Glutathione

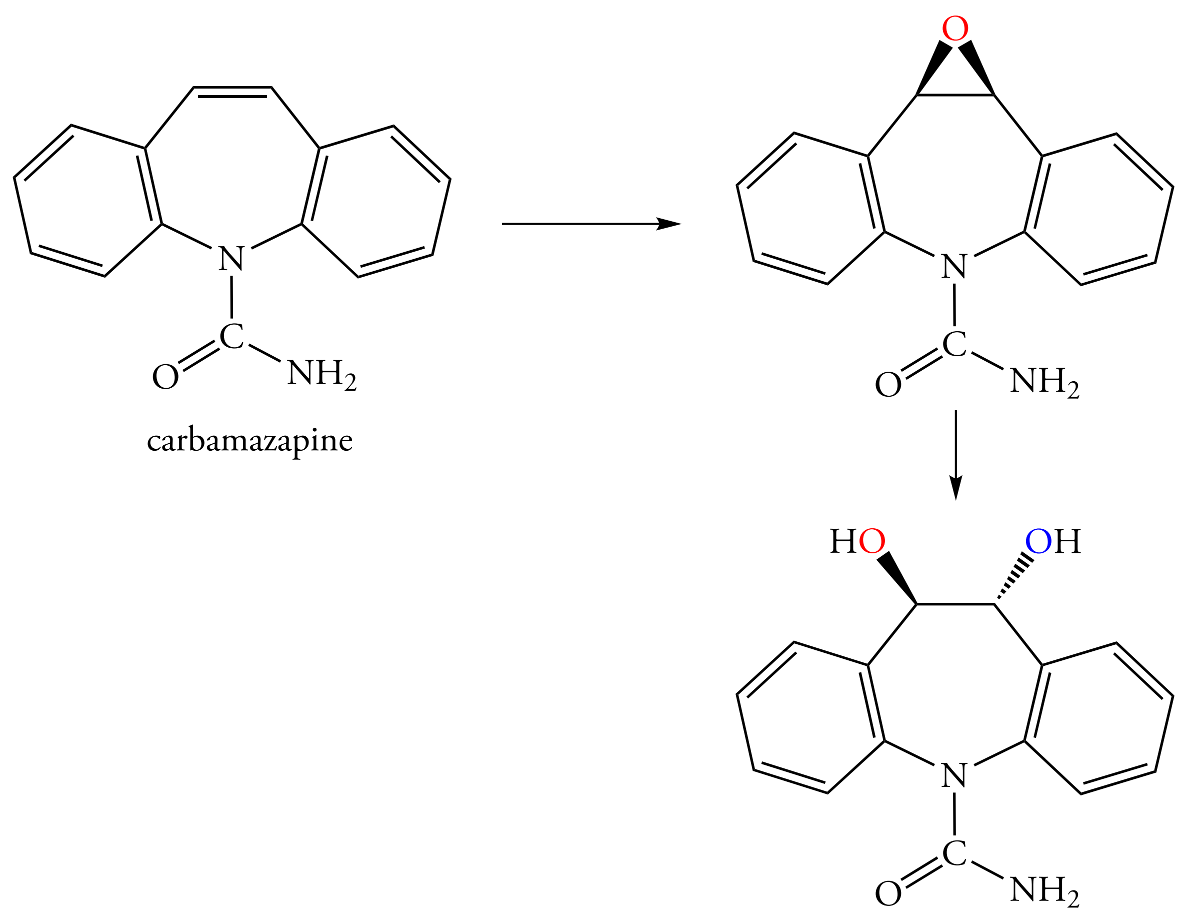
(a) Bond-line structure of glutathione at pH 7. (b) Ball-and-stick structure. (c) Space-filling structure.



16.10 REACTIONS OF EPOXIDES
Biochemical Reactions of Epoxides



benzo[a]pyrene

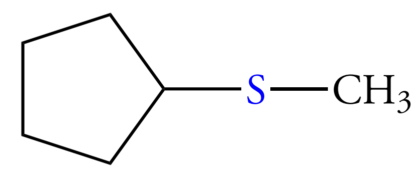


carbamazapine

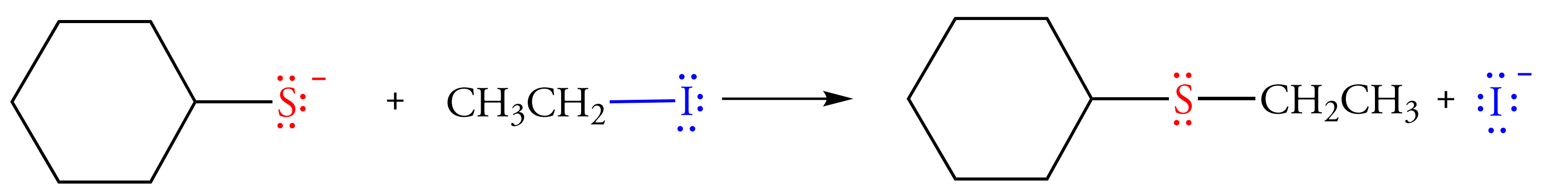
16.11 SULFIDES
Synthesis of Sulfides

$CH_3CH_2—S—CH_2CH_3$

1-(ethylthio)butane
(butyl ethyl sulfide)



methylthiocyclopentane
(cyclopentyl methyl sulfide)



16.11 SULFIDES

Oxidation of Sulfides

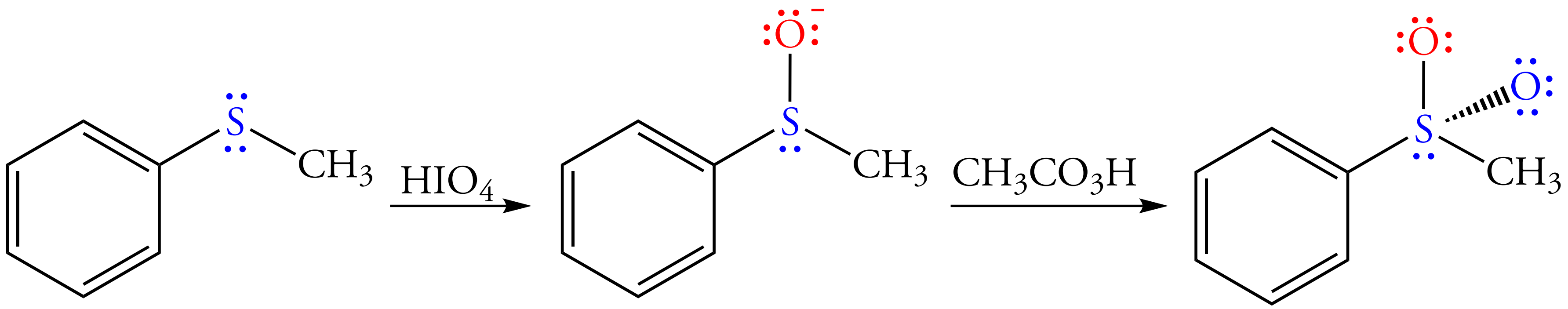
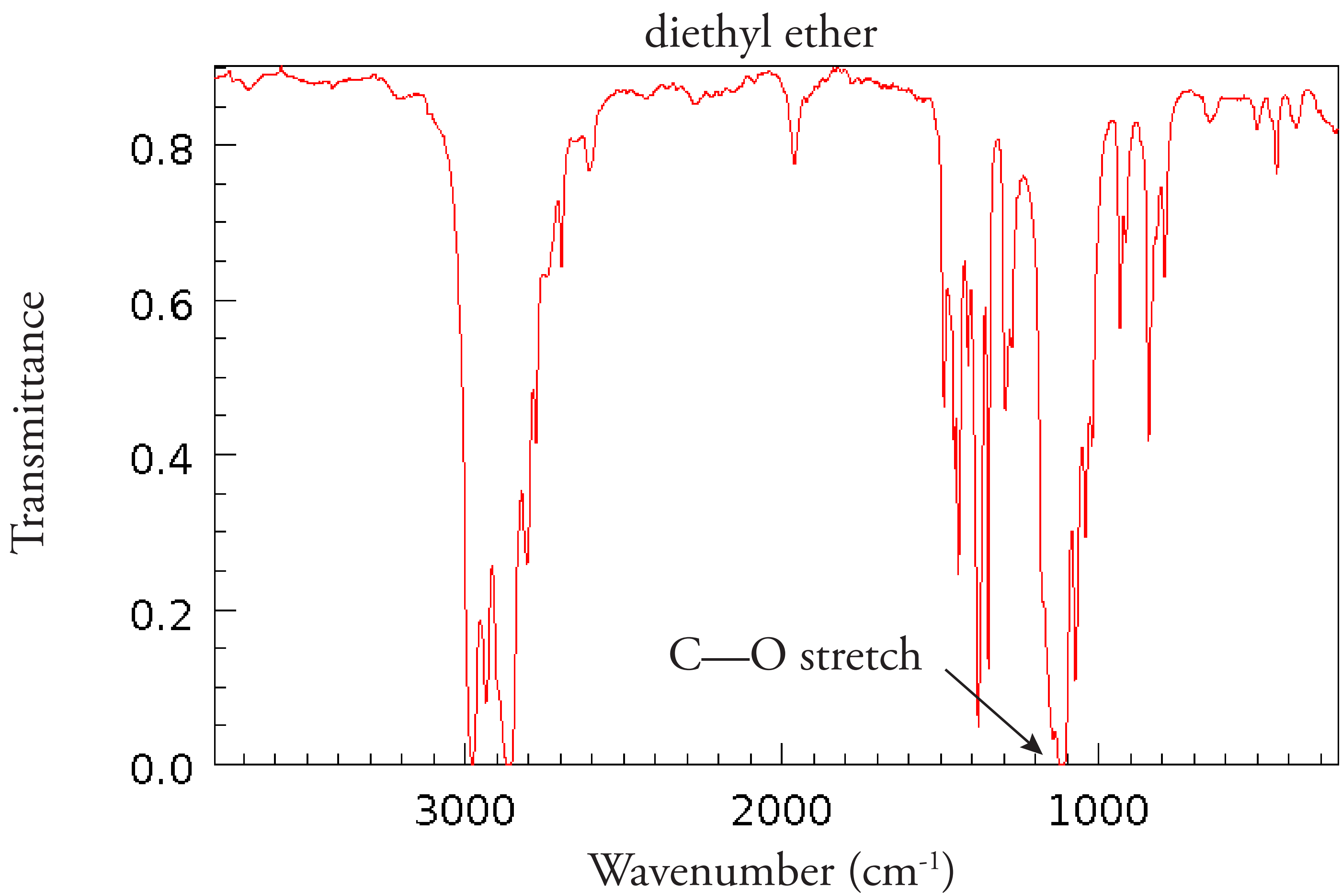


Figure 16.8 Infrared Spectrum of Diethyl Ether

The IR spectrum of diethyl ether has a characteristic C—O bond stretching frequency at about 1100 cm^{-1}.



16.12 SPECTROSCOPY OF ETHERS, THIOLS AND AND SULFIDES

Proton NMR Spectroscopy

Chemical Shifts

$CH_3—CH_2—OH$

1.15 δ   3.59 δ

$CH_3—CH_2—CH_2—OH$

0.93 δ   1.53 δ   3.49 δ

$CH_3—CH_2—SH$

1.25 δ   2.44 δ

$CH_3—CH_2—CH_2—SH$

1.02 δ   1.57 δ   2.49 δ

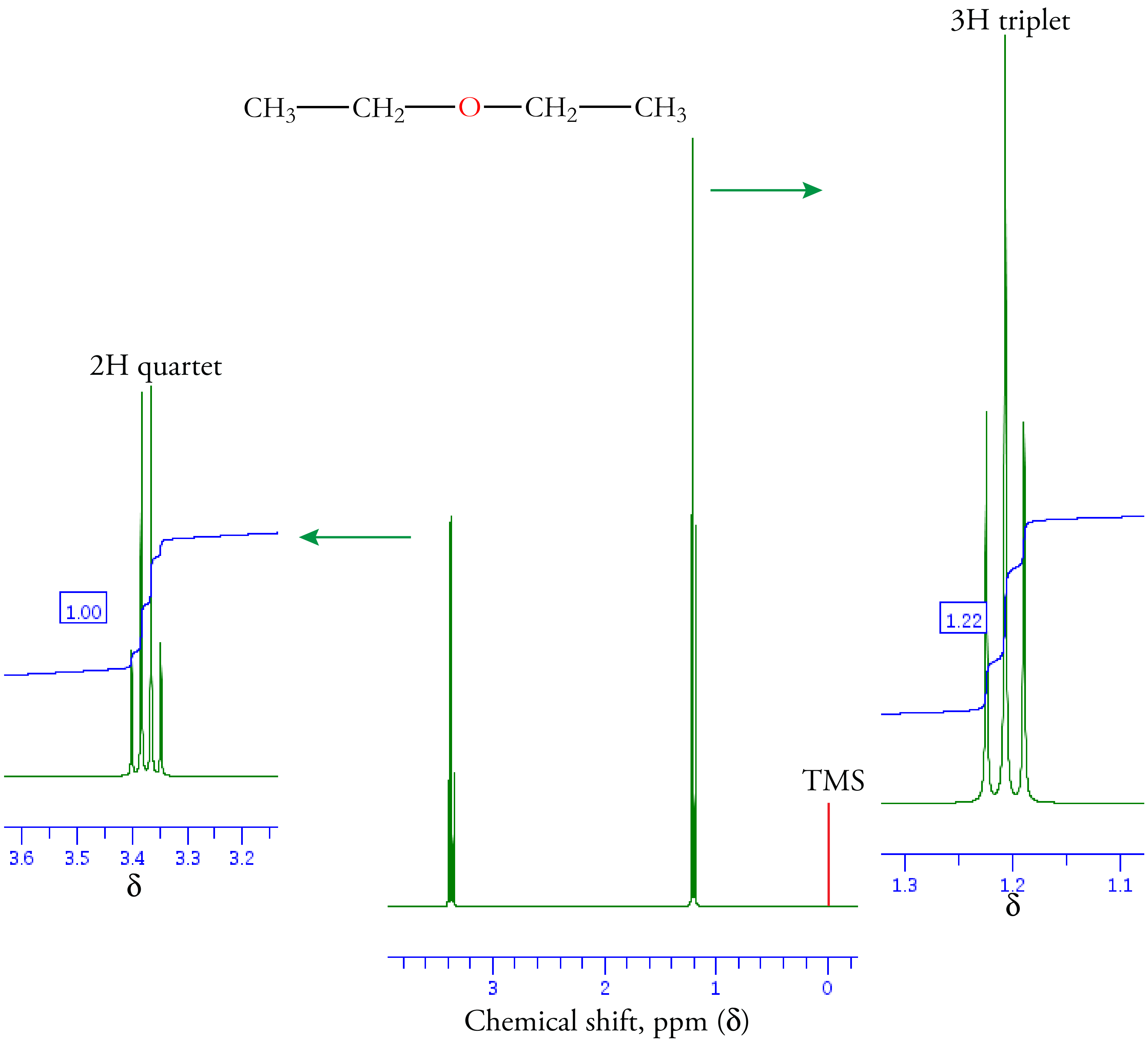
$CH_3—CH_2—O—CH_2—CH_3$

1.18 δ   3.37 δ

$CH_3—CH_2—S—CH_2—CH_3$

1.25 δ   2.49 δ

Figure 16.9 NMR Spectrum of Diethyl Ether



16.12 SPECTROSCOPY OF ETHERS, THIOLS AND AND SULFIDES

C-13 NMR Spectroscopy

Chemical Shifts

$CH_3—CH_2—CH_2—CH_2—OH$

14.8 δ   20.3 δ   36.2 δ   62.6 δ

$CH_3—CH_2—O—CH_2—CH_3$

17.1 δ   67.4 δ

$CH_3—CH_2—CH_2—CH_2—SH$

24.6

$CH_3—CH_2—S—CH_2—CH_3$

25.5 δ