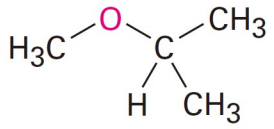
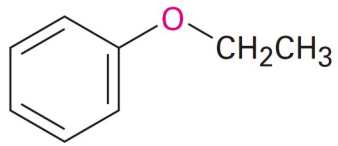
The appalling and unforgettable odor of skunks is due to a mixture of several simple thiols. Comstock Images/Jupiterimages

18 醚，环氧化物，硫化物

18.1 命名和性质

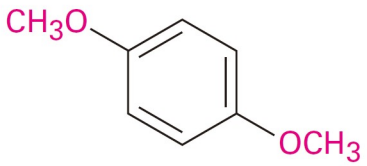


Isopropyl methyl ether

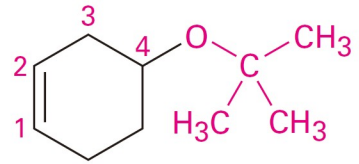


Ethyl phenyl ether

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

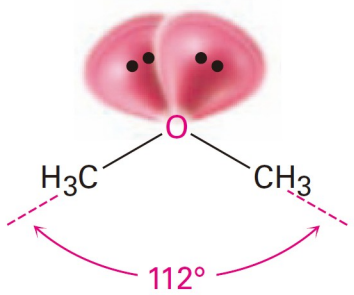


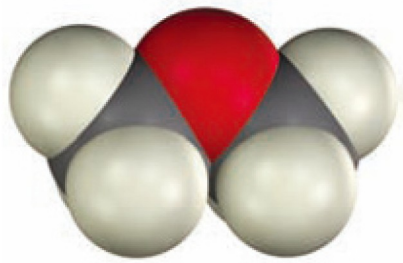
***p*-Dimethoxybenzene**

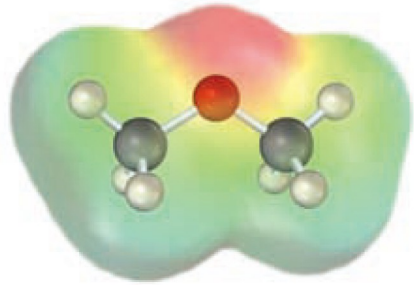


4-*tert*-Butoxy-1-cyclohexene

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 sp^3-hybridized.



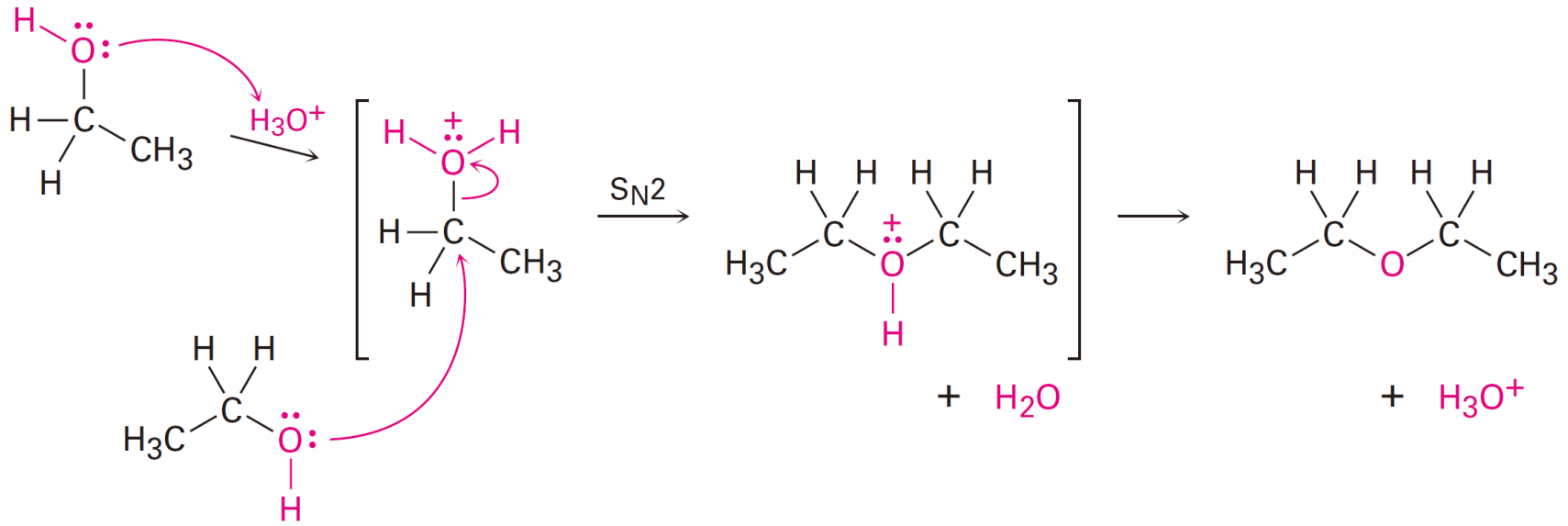




18.2 醚的合成

- 工业制法

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, the method is limited to use with primary alcohols because secondary and tertiary alcohols dehydrate by an E1 mechanism to yield alkenes **(Section 17.6)**.

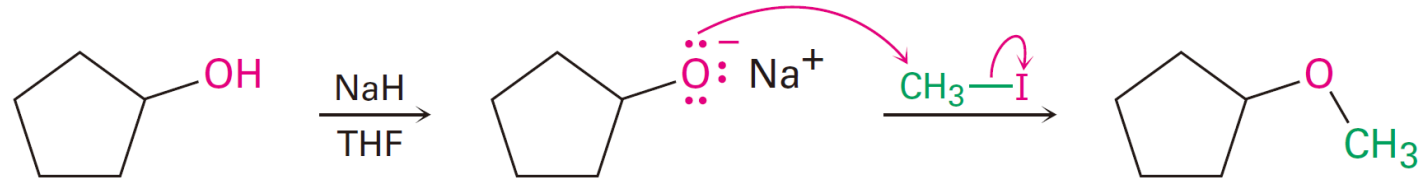


18.2 醚的合成

- 威廉森醚化反应

The Williamson Ether Synthesis

The most generally useful method of preparing ethers is by the *Williamson ether synthesis,* in which an alkoxide ion reacts with a primary alkyl halide or tosylate in an S_N2 reaction. As we saw earlier in **Section 17.2**, the alkoxide ion is normally prepared by reaction of an alcohol with a strong base such as sodium hydride, NaH.

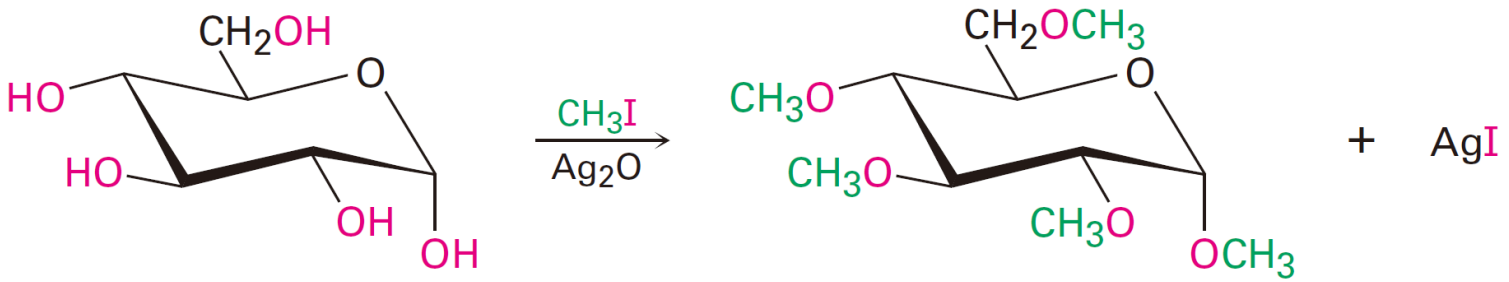


Cyclopentanol **Alkoxide ion** **Cyclopentyl methyl ether (74%)**

18.2 醚的合成

- Ag_2O 作为更温和的碱使用

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 preform the metal alkoxide intermediate. Sugars react particularly well; glucose, for example, reacts with excess iodomethane in the presence of Ag_2O to generate a pentaether in 85% yield.

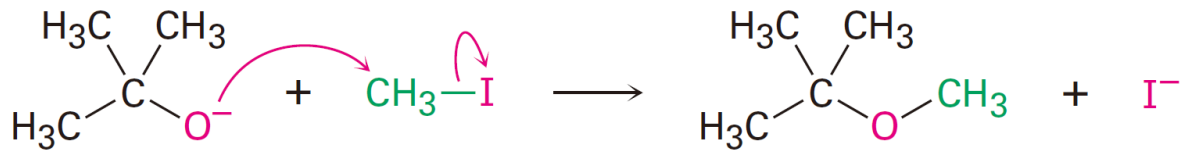


α-D-Glucose

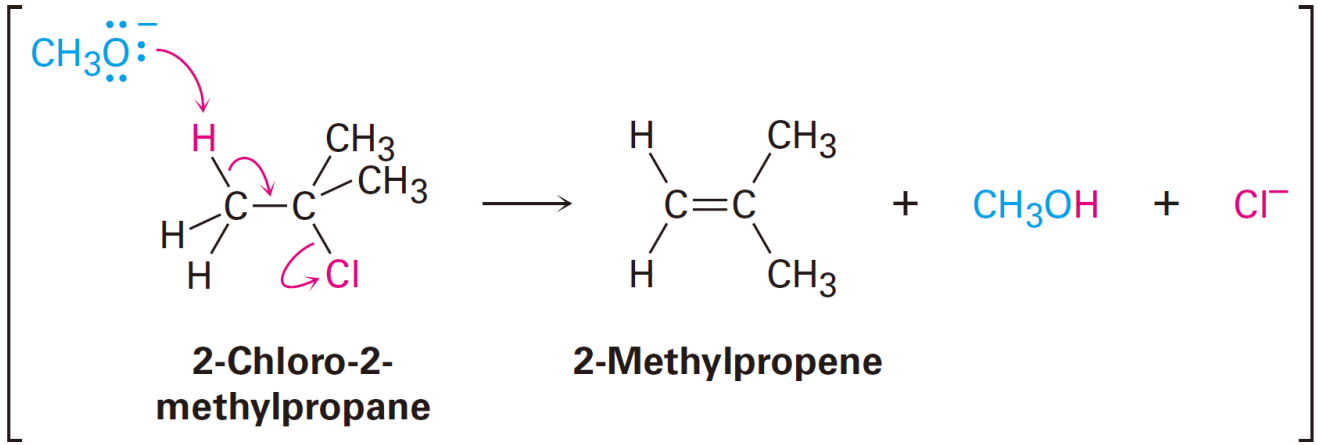
α-D-Glucose pentamethyl ether (85%)

18.2 醚的合成

- 注意选择合适的醇和卤化物



***tert*-Butoxide** **Iodomethane** ***tert*-Butyl methyl ether**



2-Chloro-2-methylpropane **2-Methylpropene**

Problem 18.3

How would you prepare the following ethers using a Williamson synthesis?

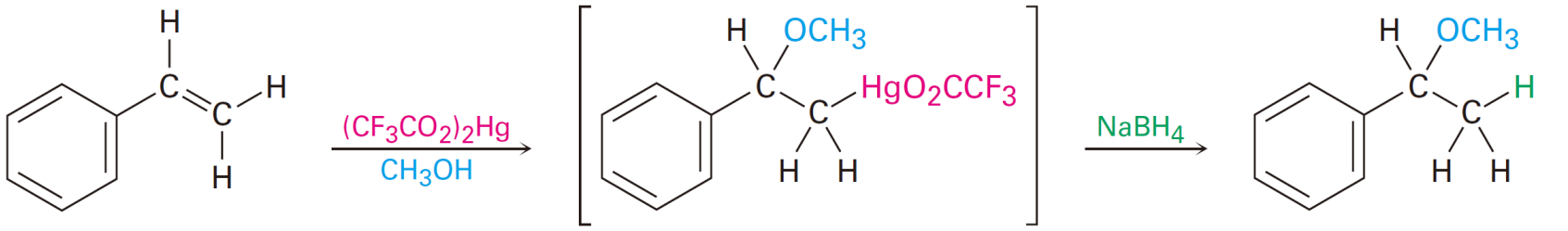
(a) Methyl propyl ether **(b)** Anisole (methyl phenyl ether)

(c) Benzyl isopropyl ether **(d)** Ethyl 2,2-dimethylpropyl ether

18.2 醚的合成

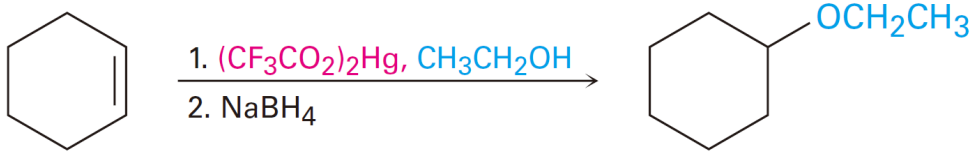
Alkoxymercuration of Alkenes

We saw in **Section 8.4** that 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 an ether. The net result is Markovnikov addition of the alcohol to the alkene.



Styrene

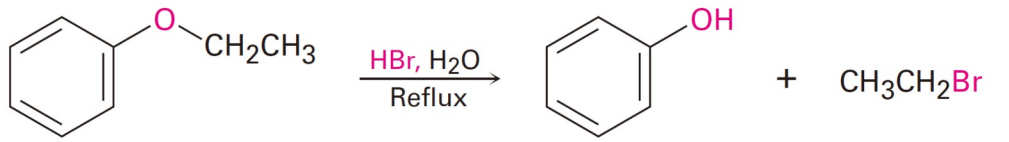
1-Methoxy-1-phenylethane (97%)



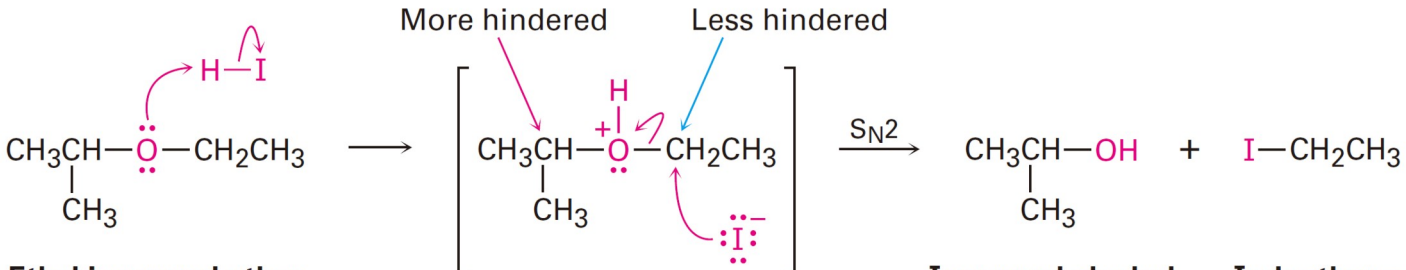
Cyclohexene

Cyclohexyl ethyl ether (100%)

18.3 醚的反应：酸催化切断

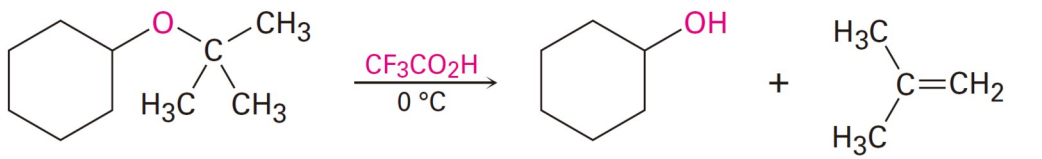


Ethyl phenyl ether **Phenol** **Bromoethane**



Ethyl isopropyl ether **Isopropyl alcohol** **Iodoethane**

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. We'll see in **Section 26.7** that the reaction is often used in the laboratory synthesis of peptides.

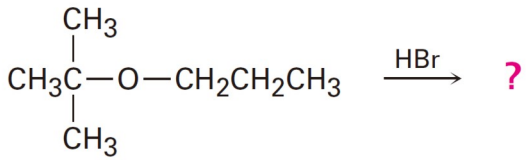


***tert*-Butyl cyclohexyl ether** **Cyclohexanol (90%)** **2-Methylpropene**

18.3 醚的反应：酸催化切断

Predicting the Product of an Ether Cleavage Reaction

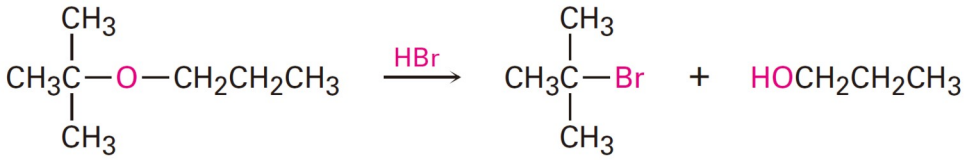
Predict the products of the following reaction:



Strategy

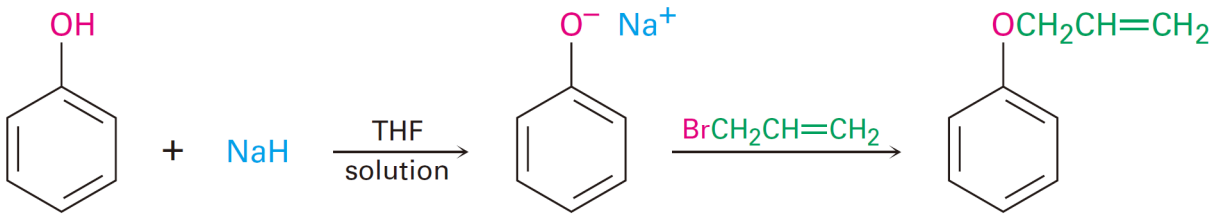
Identify the substitution pattern of the two groups attached to oxygen—in this case a tertiary alkyl group and a primary alkyl group. Then recall the guidelines for ether cleavages. An ether with only primary and secondary alkyl groups usually undergoes cleavage by S_N2 attack of a nucleophile on the less hindered alkyl group, but an ether with a tertiary alkyl group usually undergoes cleavage by an S_N1 mechanism. In this case, an S_N1 cleavage of the tertiary C—O bond will occur, giving 1-propanol and a tertiary alkyl bromide. In addition, a competitive E1 reaction leading to alkene might occur.

Solution

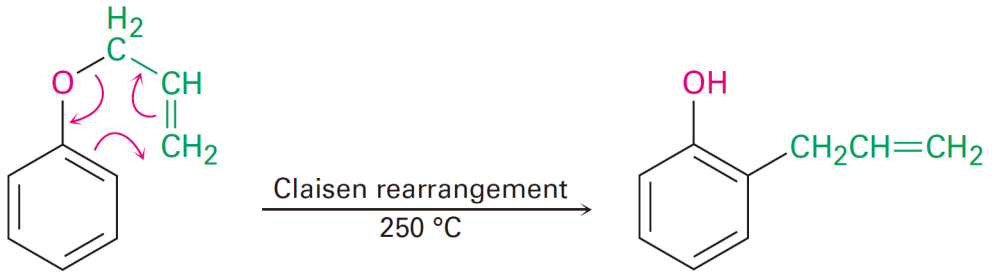


***tert*-Butyl propyl ether** | **2-Bromo-2-methylpropane** | **1-Propanol**

18.4 克莱森重排

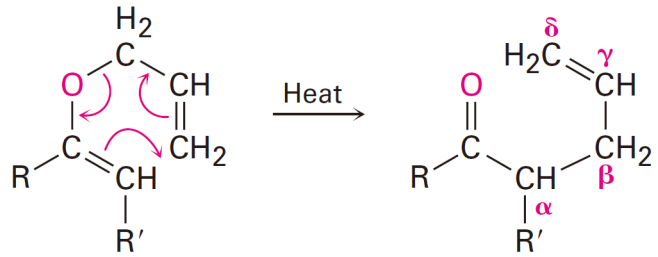


Phenol **Sodium phenoxide** **Allyl phenyl ether**



Allyl phenyl ether ***o*-Allylphenol**

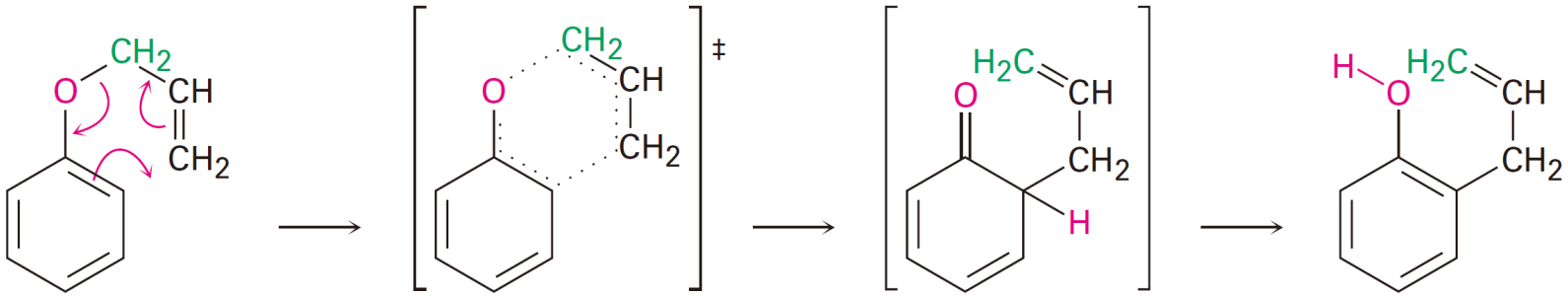
A similar rearrangement takes place with allyl vinyl ethers, leading to a so-called γ,δ-unsaturated ketone or aldehyde.



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

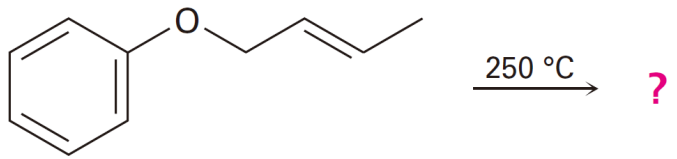
18.4 克莱森重排

Like the Diels–Alder reaction discussed in **Sections 14.4 and 14.5**, the Claisen rearrangement reaction takes place in a single step through a pericyclic mechanism in which a reorganization of bonding electrons occurs through a six-membered, cyclic transition state. The 6-allyl-2,4-cyclohexadienone intermediate then isomerizes to *o*-allylphenol **(Figure 18.1)**.



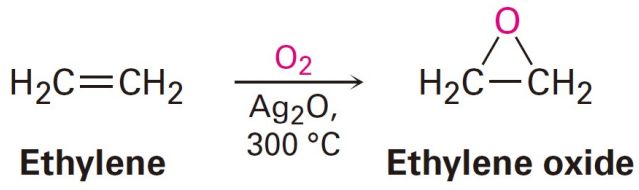
Problem 18.10

What product would you expect from Claisen rearrangement of 2-butenyl phenyl ether?

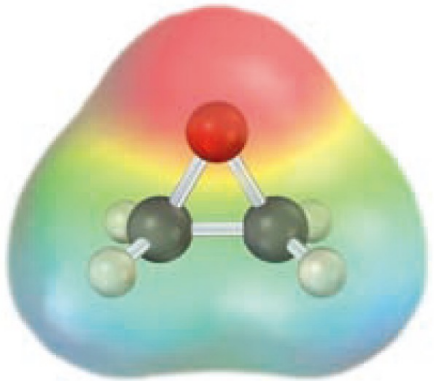


2-Butenyl phenyl ether

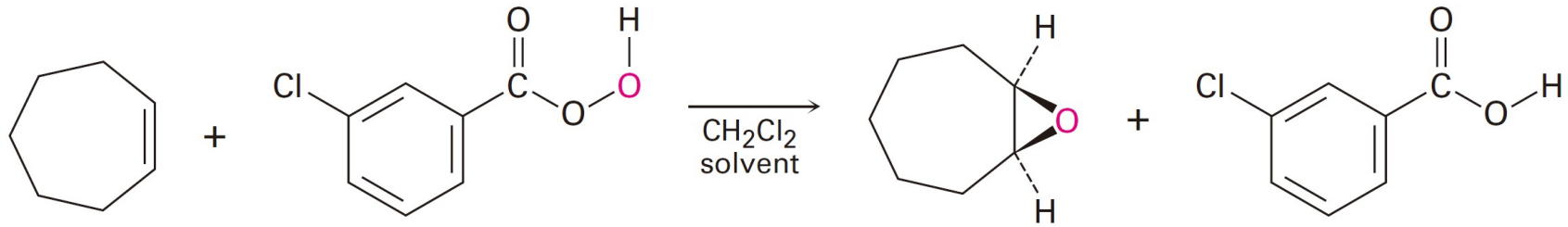
18.5 环醚



Ethylene **Ethylene oxide**

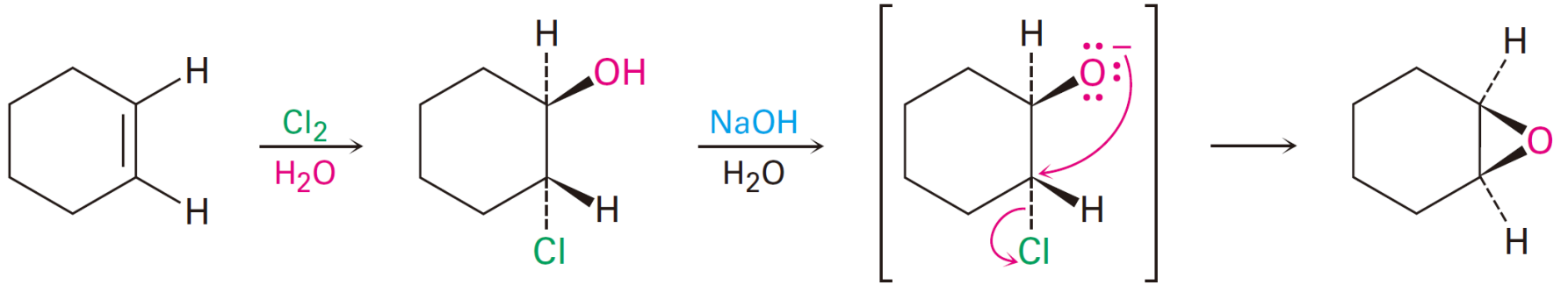


In the laboratory, as we saw in **Section 8.7**, epoxides are usually prepared by treatment of an alkene with a peroxyacid (RCO_3H), typically *m*-chloroperoxybenzoic acid.



Cycloheptene ***meta*-Chloroperoxybenzoic acid** **1,2-Epoxycycloheptane** ***meta*-Chlorobenzoic acid**

18.5 环醚



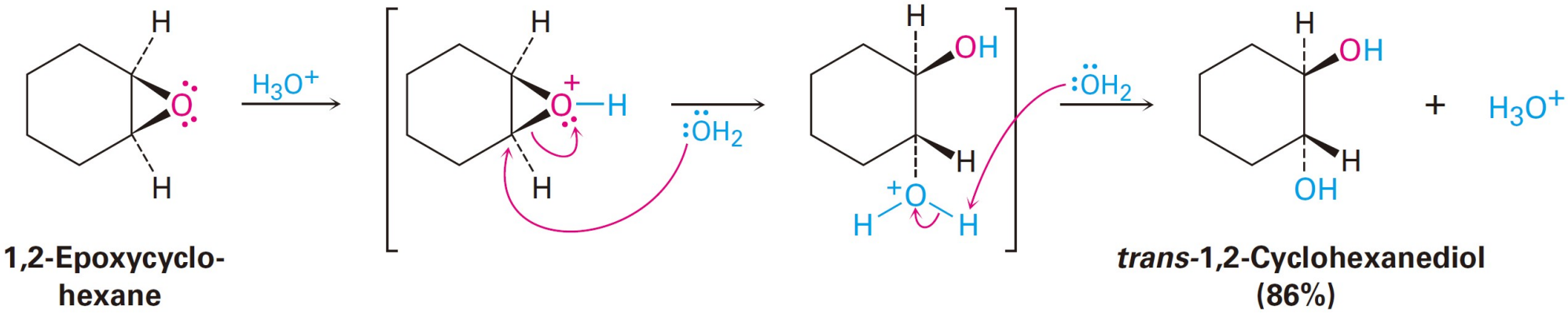
Cyclohexene | ***trans*-2-Chloro-cyclohexanol** | **1,2-Epoxy-cyclohexane**

Problem 18.11

Reaction of *cis*-2-butene with *m*-chloroperoxybenzoic acid yields an epoxide different from that obtained by reaction of the trans isomer. Explain.

18.6 环醚的开环反应

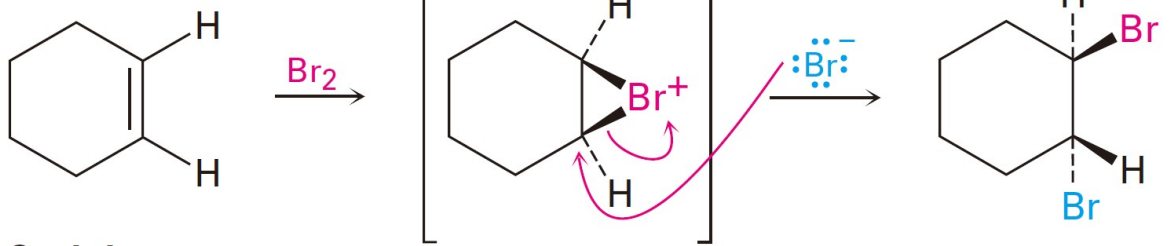
- 酸催化开环



1,2-Epoxycyclo-hexane

***trans*-1,2-Cyclohexanediol (86%)**

Recall the following:

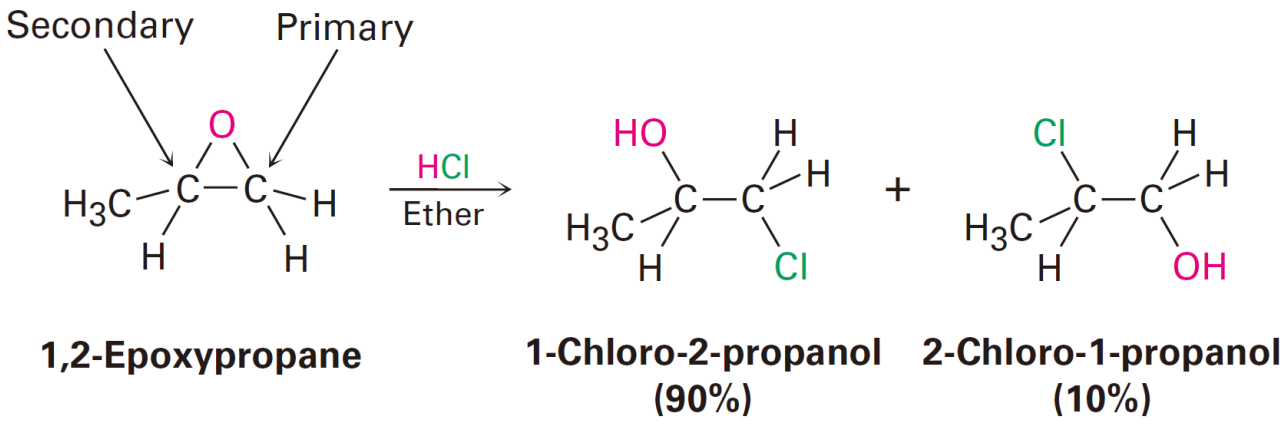


Cyclohexene

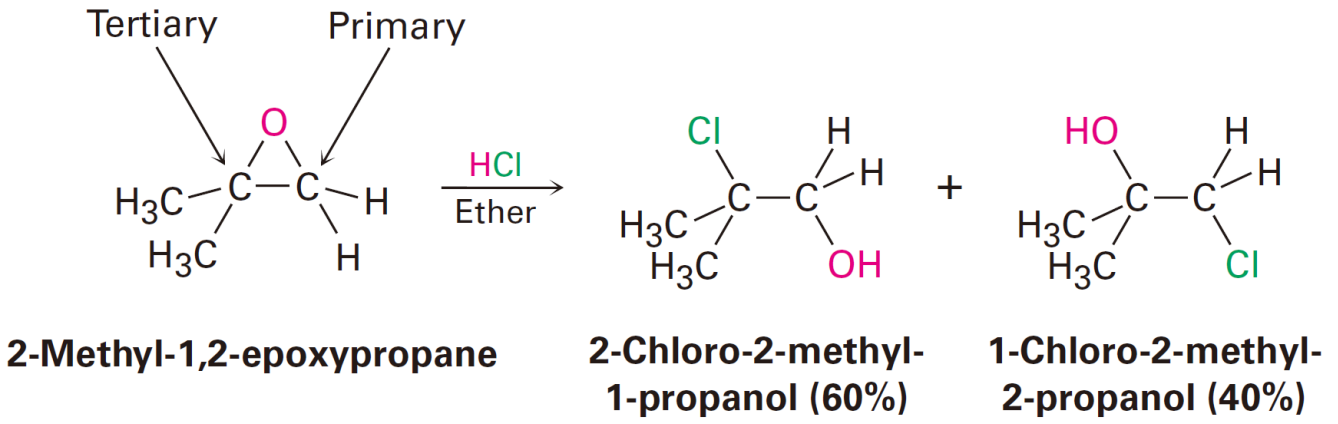
***trans*-1,2-Dibromo-cyclohexane**

18.6 环醚的开环反应

- 酸催化开环：不对称底物通常给出混合产物



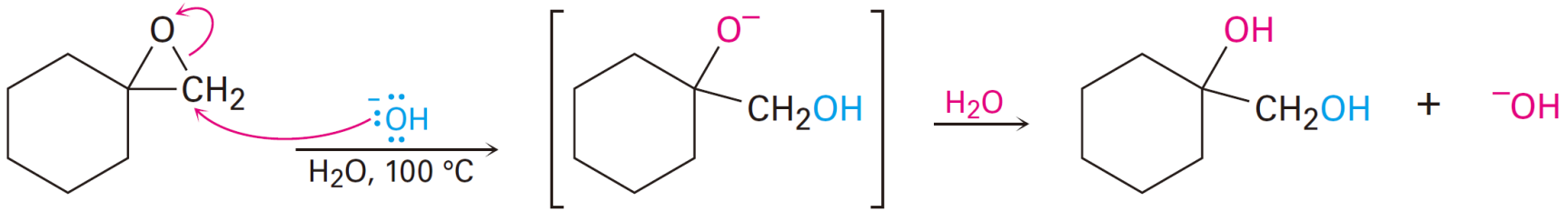
1,2-Epoxypropane **1-Chloro-2-propanol (90%)** **2-Chloro-1-propanol (10%)**



2-Methyl-1,2-epoxypropane **2-Chloro-2-methyl-1-propanol (60%)** **1-Chloro-2-methyl-2-propanol (40%)**

18.6 环醚的开环反应

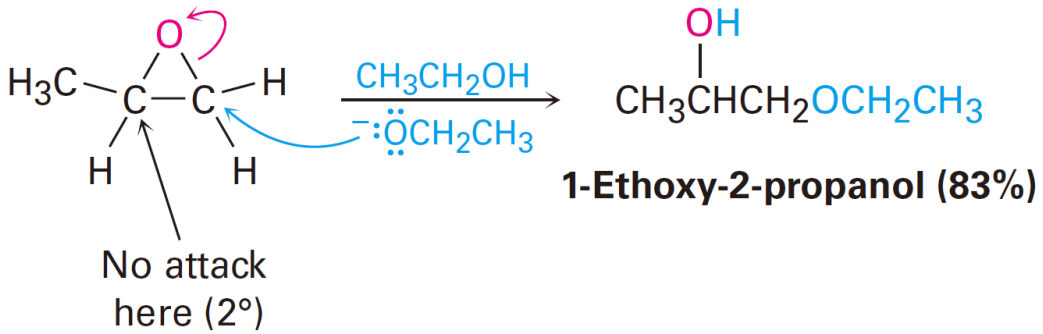
- 碱性条件开环



Methylenecyclohexane oxide

1-Hydroxymethyl-cyclohexanol (70%)

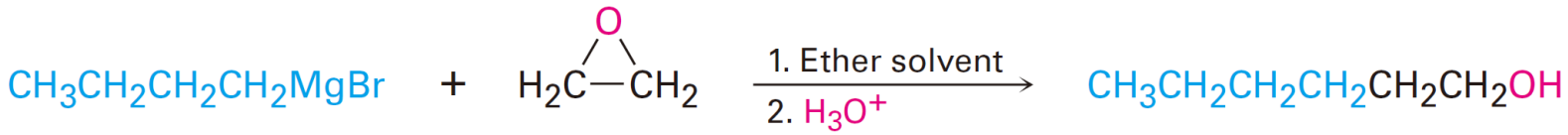
Base-catalyzed epoxide opening is a typical S_N2 reaction in which attack of the nucleophile takes place at the less hindered epoxide carbon. For example, 1,2-epoxypropane reacts with ethoxide ion exclusively at the less highly substituted, primary, carbon to give 1-ethoxy-2-propanol.



1-Ethoxy-2-propanol (83%)

18.6 环醚的开环反应

- 碱性条件开环

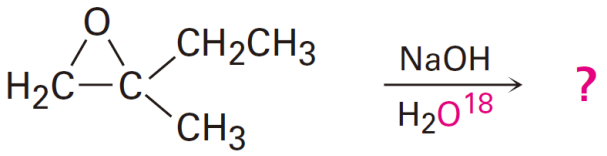


Butylmagnesium bromide **Ethylene oxide** **1-Hexanol (62%)**

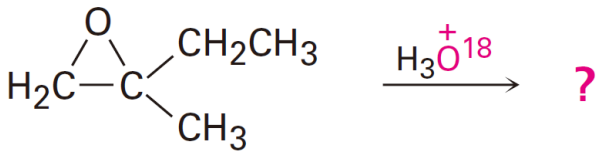
Problem 18.14

Predict the major product of the following reactions:

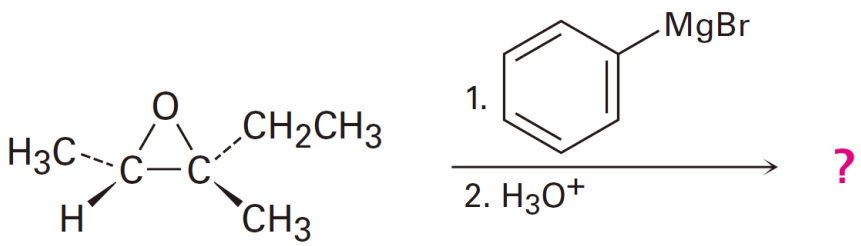
(a)



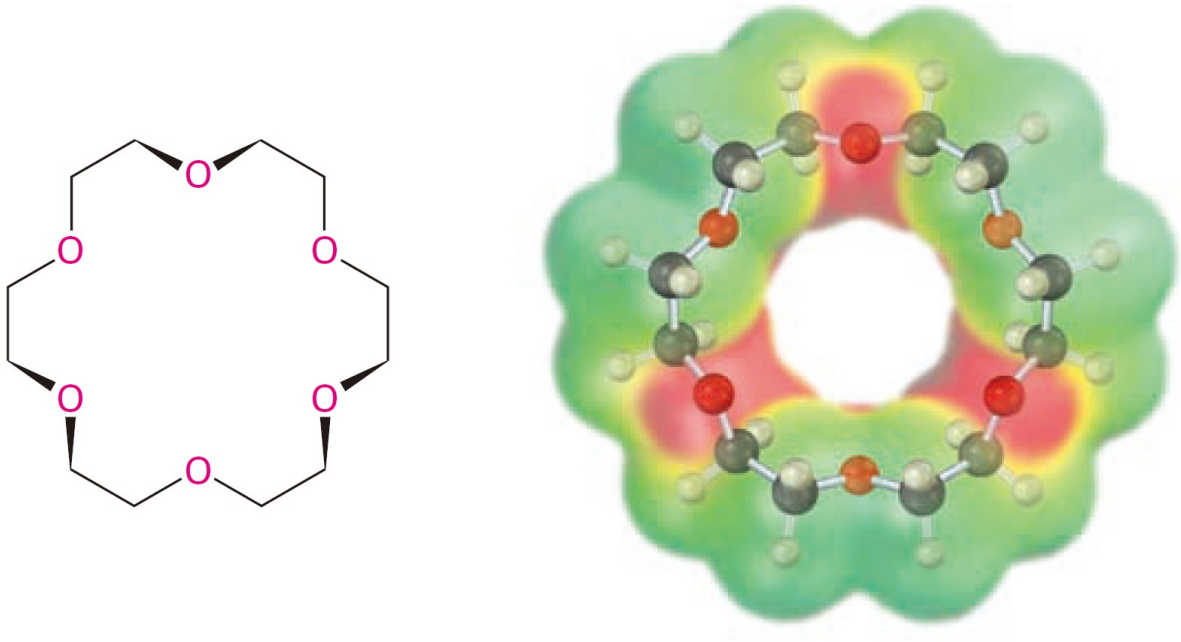
(b)



(c)



18.7 冠醚



18-Crown-6 ether

The importance of crown ethers derives from their ability to sequester specific metal cations in the center of the polyether cavity. 18-Crown-6, for example, binds strongly with potassium ion. As a result, a solution of 18-crown-6 in a nonpolar organic solvent will dissolve many potassium salts. Potassium permanganate, $KMnO_4$, dissolves in toluene in the presence of 18-crown-6, for instance, and the resulting solution is a valuable reagent for oxidizing alkenes.

18.7 冠醚

- 1987 年诺贝尔化学奖：主客体化学

The Nobel Prize in Chemistry 1987

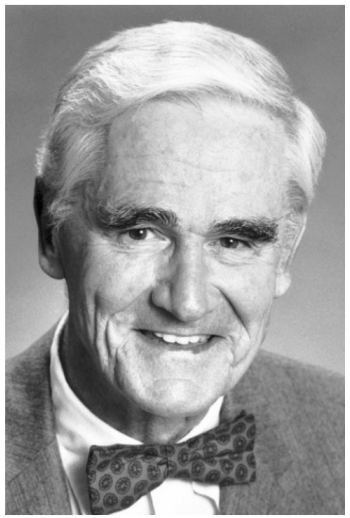


Photo from the Nobel Foundation archive.

Donald J. Cram

Prize share: 1/3

Photo from the Nobel Foundation archive.

Jean-Marie Lehn

Prize share: 1/3

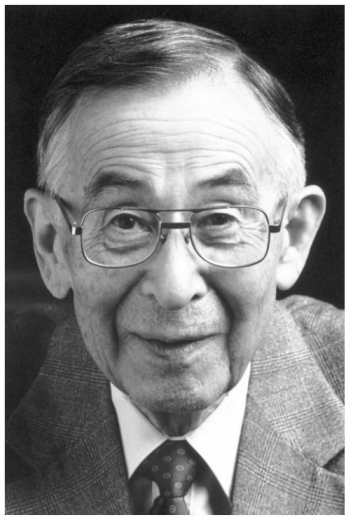


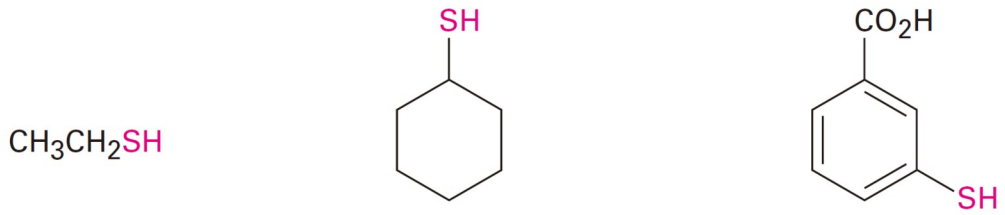
Photo from the Nobel Foundation archive.

Charles J. Pedersen

Prize share: 1/3

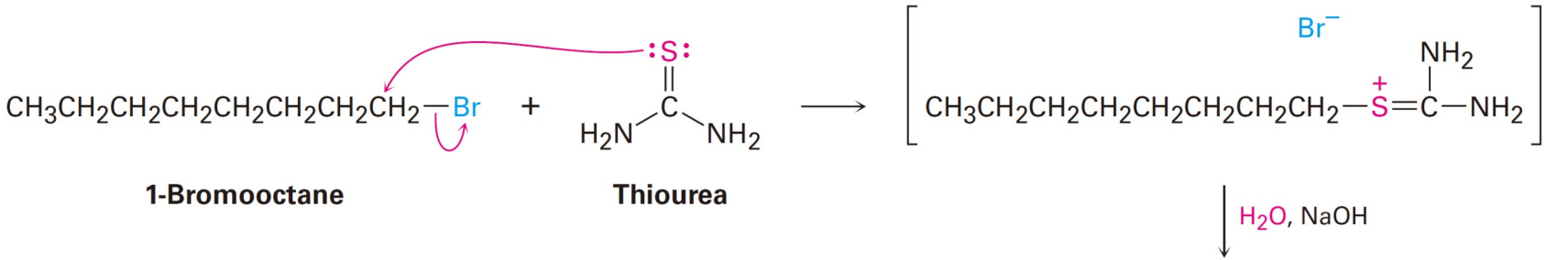
The Nobel Prize in Chemistry 1987 was awarded jointly to Donald J. Cram, Jean-Marie Lehn and Charles J. Pedersen "for their development and use of molecules with structure-specific interactions of high selectivity."

18.8 硫醇和硫醚



Ethanethiol **Cyclohexanethiol** ***m*-Mercaptobenzoic acid**

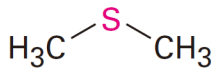
1-Bromooctane **1-Octanethiol (83%)**



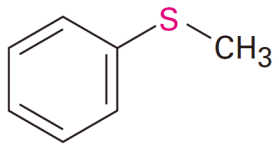
1-Bromooctane **Thiourea**

1-Octanethiol (83%) **Urea**

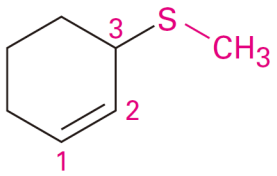
18.8 硫醇和硫醚



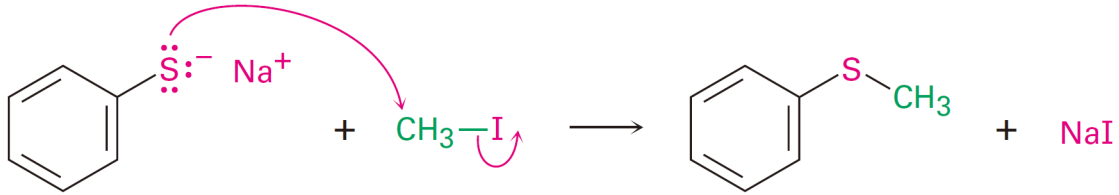
Dimethyl sulfide



Methyl phenyl sulfide

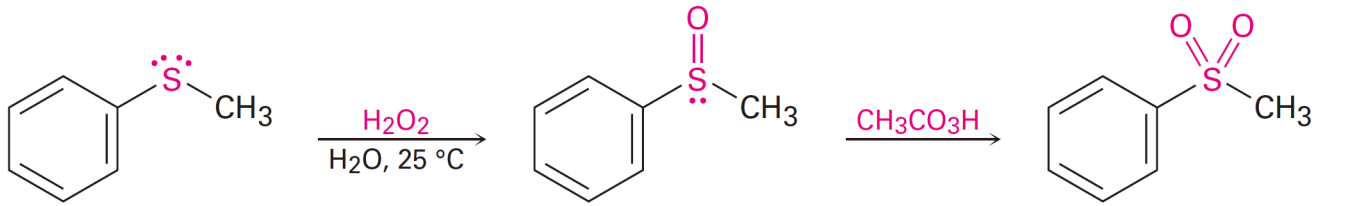


3-(Methylthio)cyclohexene



Sodium benzenethiolate

Methyl phenyl sulfide
(96%)



Methyl phenyl sulfide

Methyl phenyl sulfoxide

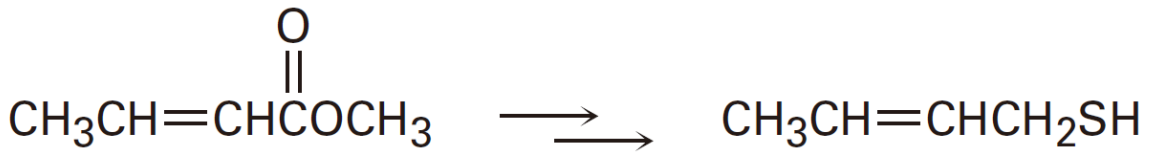
Methyl phenyl sulfone

18.8 硫醇和硫醚

- 课堂练习

Problem 18.17

2-Butene-1-thiol is one component of skunk spray. How would you synthesize this substance from methyl 2-butenoate? From 1,3-butadiene?



Methyl 2-butenoate **2-Butene-1-thiol**

18.9 波谱分析

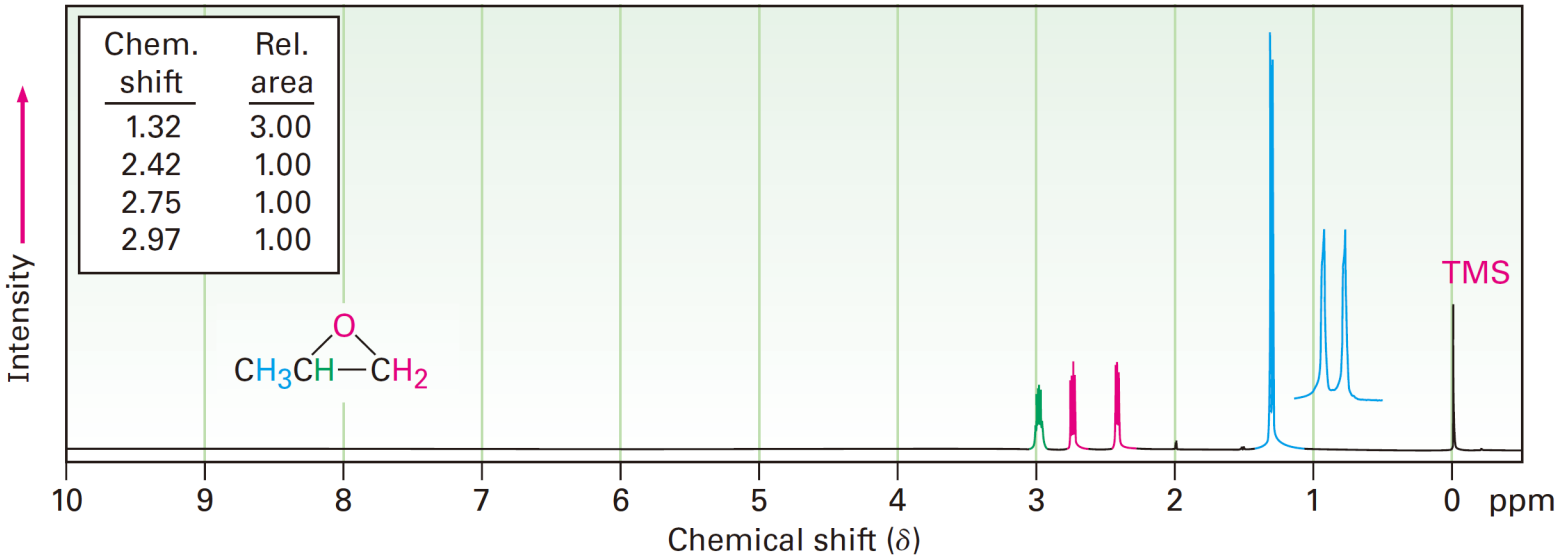
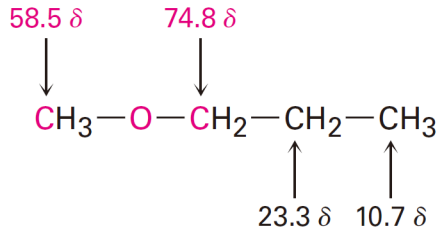
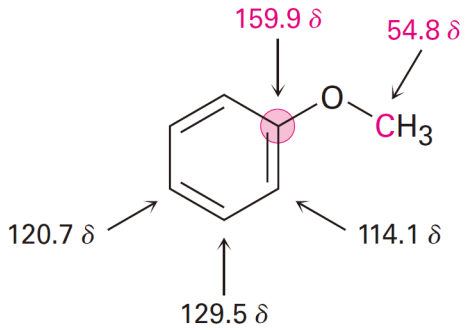


Figure 18.5 The ^{1}H NMR spectrum of 1,2-epoxypropane.

Ether carbon atoms also exhibit a downfield shift in the ^{13}C NMR spectrum, where they usually absorb in the 50 to 80 δ range. For example, the carbon atoms next to oxygen in methyl propyl ether absorb at 58.5 and 74.8 δ. Similarly, the methyl carbon in anisole absorbs at 54.8 δ.



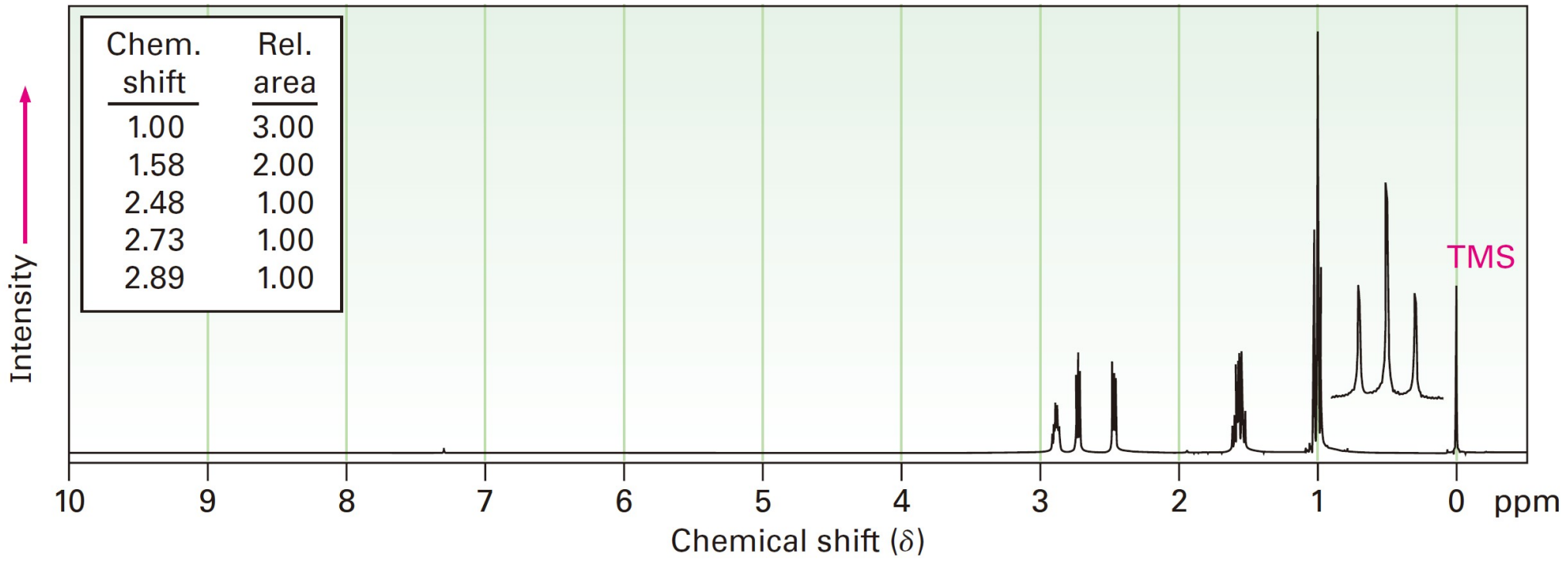


18.9 波谱分析

- 课堂练习

Problem 18.18

The ^{1}H NMR spectrum shown is that of a cyclic ether with the formula C_4H_8O. Propose a structure.



作业

- 18.47, 18.53, 18.55, 18.58, 18.61