CHM-134 ORGANIC CHEMISTRY
CHAPTER-8: ETHERS

8.1 NAMES AND PHYSICAL PROPERTIES OF ETHERS

In the IUPAC system, ethers are alkoxyalkanes.

IUPAC:

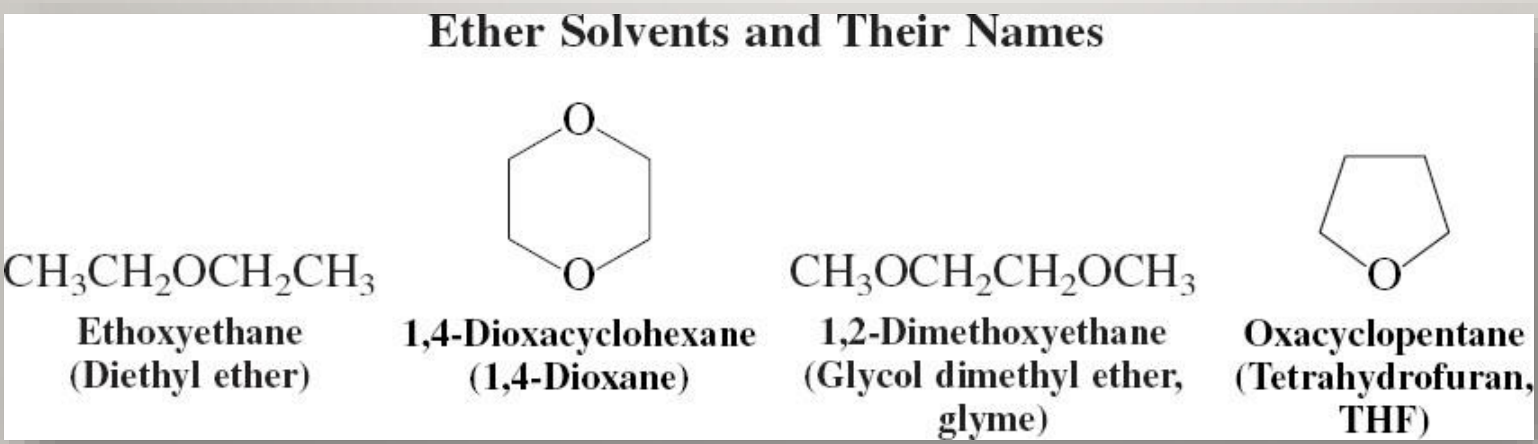
Ethers are alkanes bearing an alkoxy substituent.

The larger substituent is the stem and the smaller substituent is the alkoxy group (methoxyethane).

Common Names:

The names of the two alkyl groups are followed by the word "ether" (ethyl methyl ether).

- Except for strained cyclical derivatives, ethers are fairly unreactive and are often used as solvents in organic reactions.
- Cyclic ethers are members of the class of cycloalkanes called heterocycles, in which one or more carbon atoms have been replaced by a heteroatom.



Ether Solvents and Their Names

$CH_3CH_2OCH_2CH_3$		$CH_3OCH_2CH_2OCH_3$	
Ethoxyethane (Diethyl ether)	**1,4-Dioxacyclohexane (1,4-Dioxane)**	**1,2-Dimethoxyethane (Glycol dimethyl ether, glyme)**	**Oxacyclopentane (Tetrahydrofuran, THF)**

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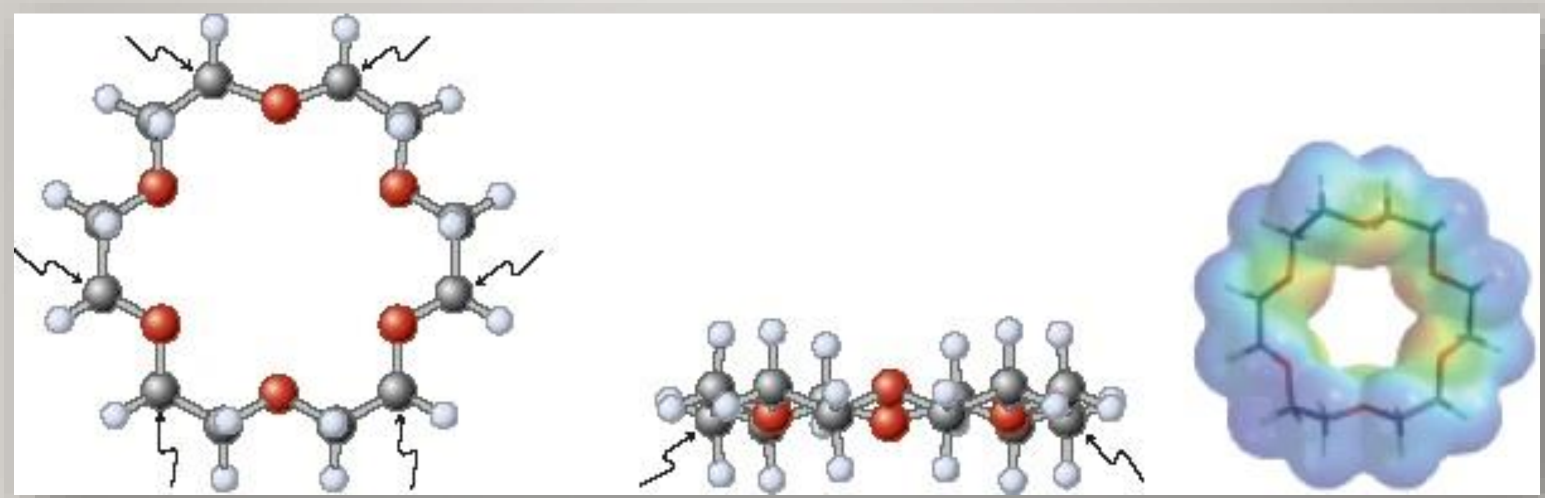
Cyclic polyethers based on the 1,2-ethanediol unit are called crown ethers. The crown ether 18-crown-6 contains 18 total atoms and 6 oxygen atoms.



Note that the inside of the ring is electron rich.

The absence of hydrogen bonding affects the physical properties of ethers.

The smaller alkoxyalkanes are water soluble, however solubility decreases with increasing hydrocarbon size.
Methoxymethane → completely water soluble
Ethoxyethane →10% aqueous solution

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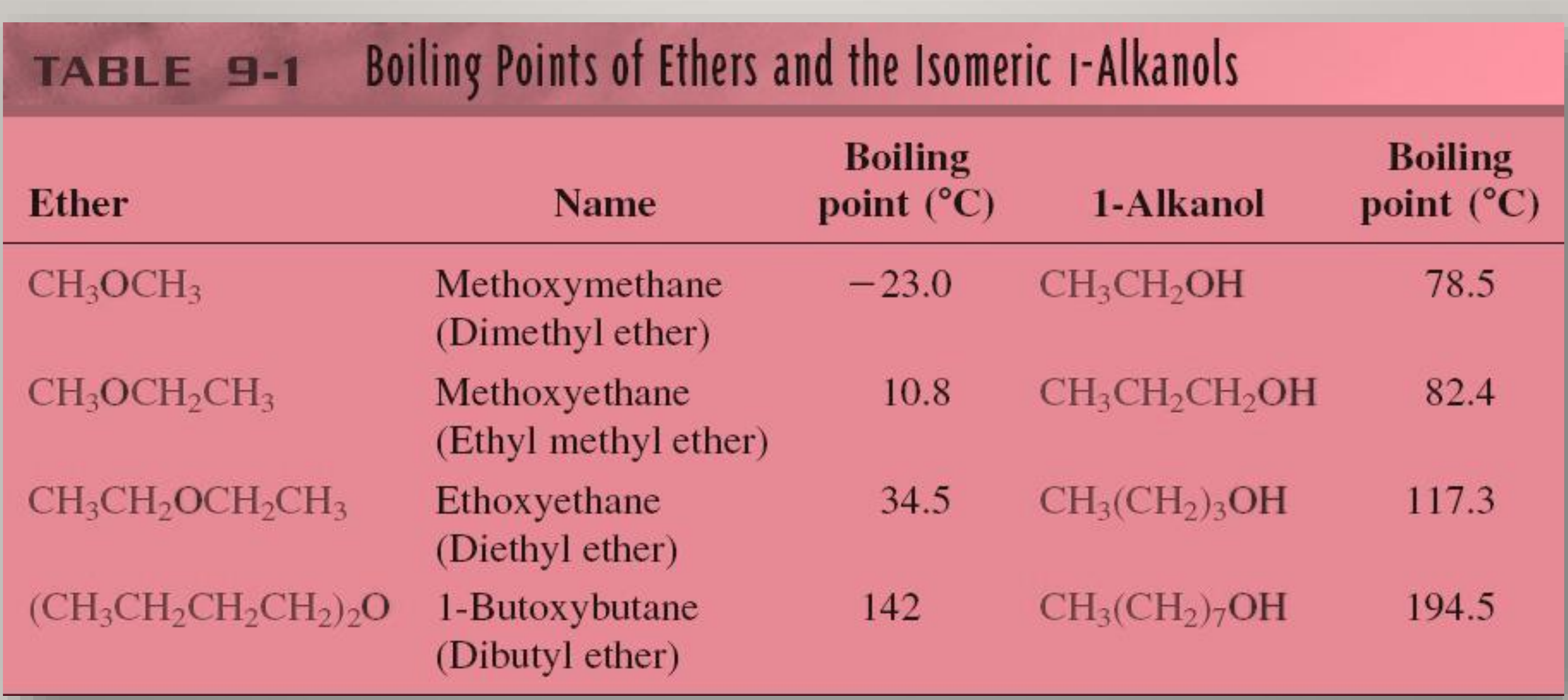

TABLE 9-1 Boiling Points of Ethers and the Isomeric 1-Alkanols

Ether	Name	Boiling point (°C)	1-Alkanol	Boiling point (°C)
CH_3OCH_3	Methoxymethane (Dimethyl ether)	−23.0	CH_3CH_2OH	78.5
$CH_3OCH_2CH_3$	Methoxyethane (Ethyl methyl ether)	10.8	$CH_3CH_2CH_2OH$	82.4
$CH_3CH_2OCH_2CH_3$	Ethoxyethane (Diethyl ether)	34.5	$CH_3(CH_2)_3OH$	117.3
$(CH_3CH_2CH_2CH_2)_2O$	1-Butoxybutane (Dibutyl ether)	142	$CH_3(CH_2)_7OH$	194.5

Simple alkoxyalkanes have the same molecular formula as the equivalent alkanols, $C_nH_{2n+2}O$, but have much lower boiling points due to the absence of hydrogen bonding.

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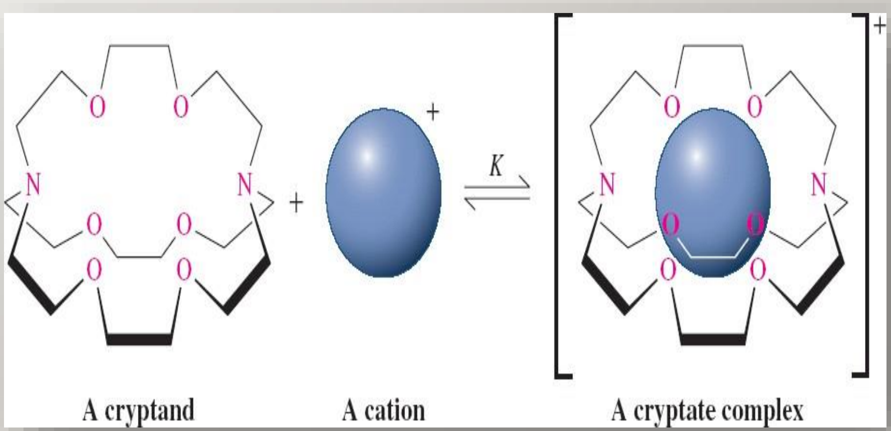
8.1 NAMES AND PHYSICAL PROPERTIES OF ETHERS

Polyethers solvate metal ions:crown ethers and ionophores.

Crown ethers can render salts soluble in organic solvents by chelating the metal cations. This allows reagents such as $KMnO_4$ to act as an oxidizing agent in the organic solvents.

The size of the central cavity can be tailored to selectively bind cations of differing ionic radii.

Three-dimensional analogs of crown ethers are polyethers called cryptands. These are highly selective in alkali and other metal cation binding.



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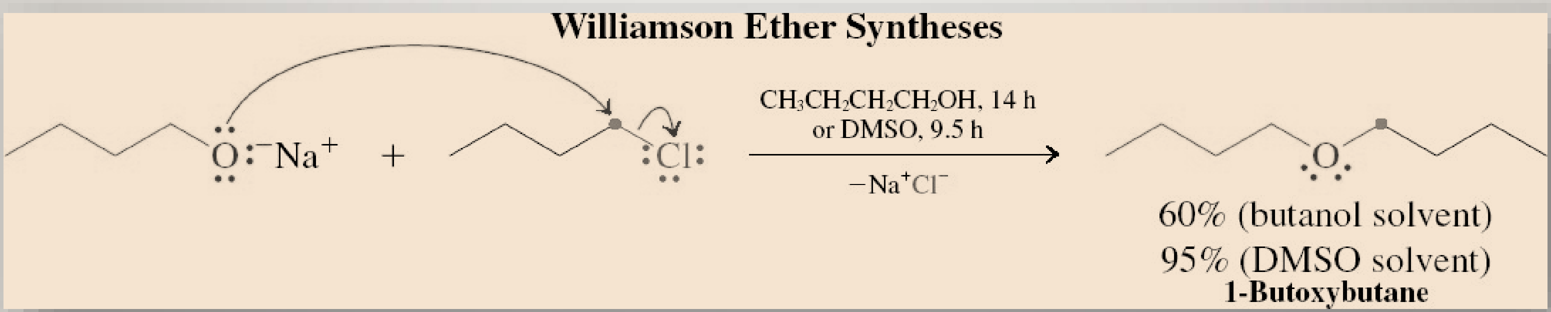
8.2 SYNTHESIS OF ETHERS

Williamson Ether Synthesis

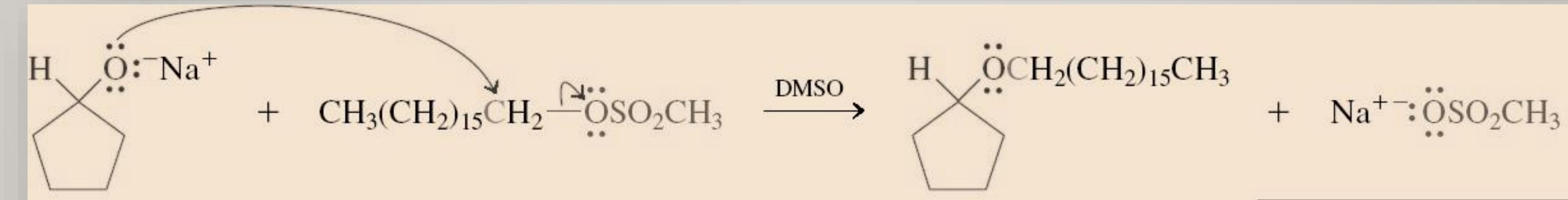
Ethers are prepared by SN_2 reactions.

Ethers can be prepared by the reaction of an alkoxide with a primary haloalkane or sulfonate ester under SN_2 conditions.

The parent alcohol of the alkoxide can be used as the solvent, however other polar solvents are often better, such as DMSO (dimethyl sulfoxide) or HMPA (hexamethylphosphoric triamide).



60% (butanol solvent)
95% (DMSO solvent)
1-Butoxybutane



91%
Cyclopentoxyheptadecane

Nucleophile: red
Electrophile: blue
Leaving group: green

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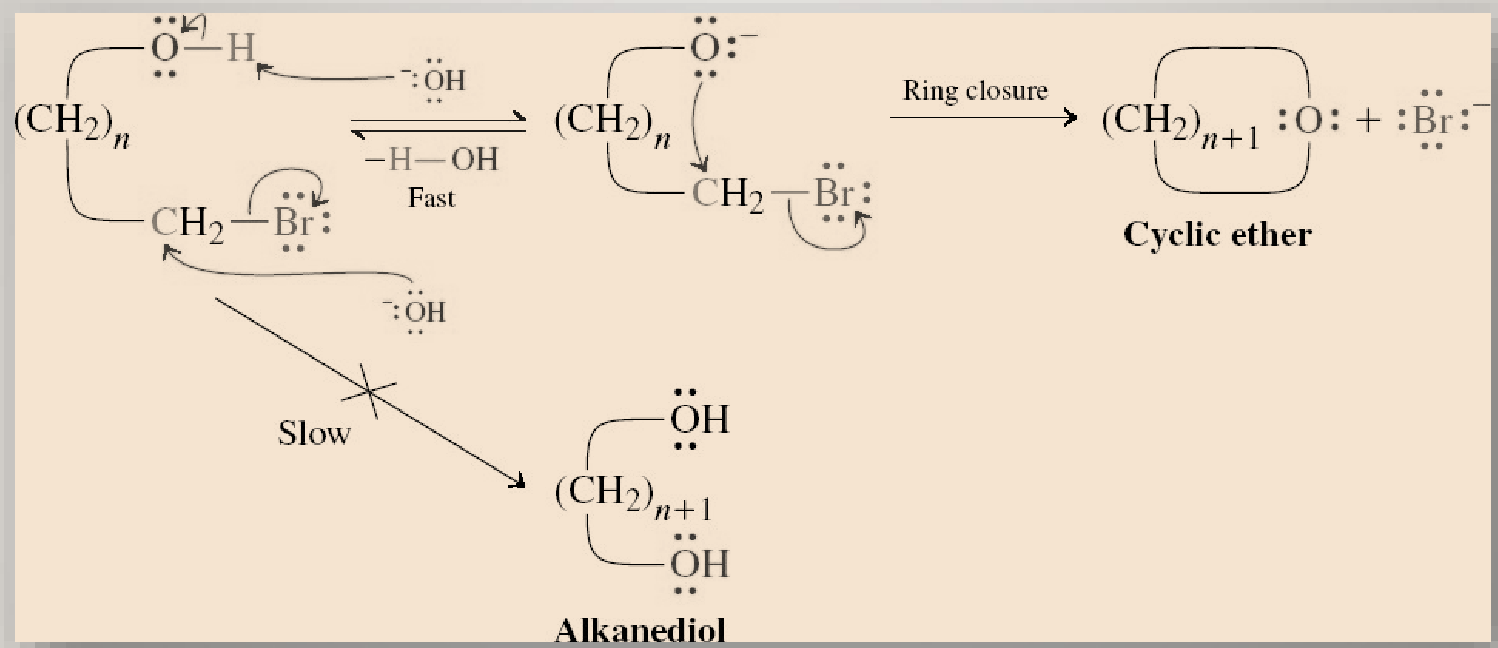
8.2 SYNTHESIS OF ETHERS

Cyclic ethers can be prepared by intramolecular Williamson synthesis.

Haloalcohols serve as the starting point for the Williamson synthesis of cyclic ethers.



The intramolecular reaction is usually much faster than the intermolecular reaction. If necessary, the intermolecular reaction can be suppressed by using a high dilution of the haloalcohol.

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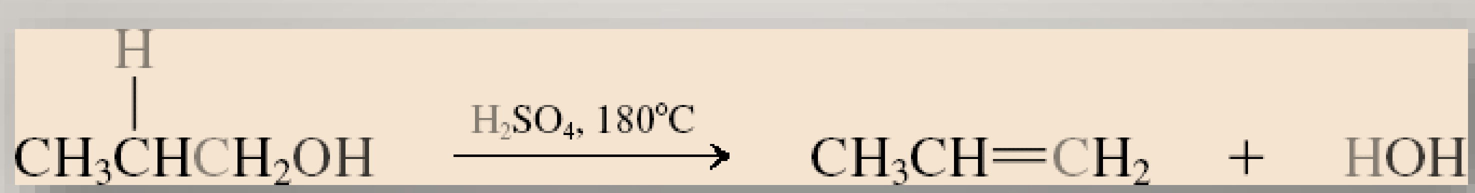
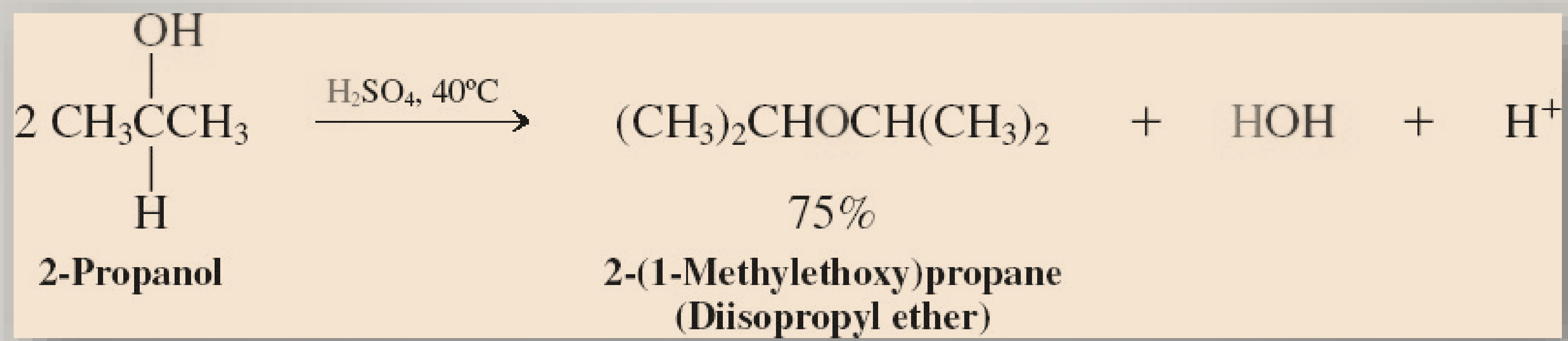


$$\mathrm{CH_3\overset{H}{C}HCH_2OH \xrightarrow{H_2SO_4,\ 180^\circ C} CH_3CH{=}CH_2 + HOH}$$



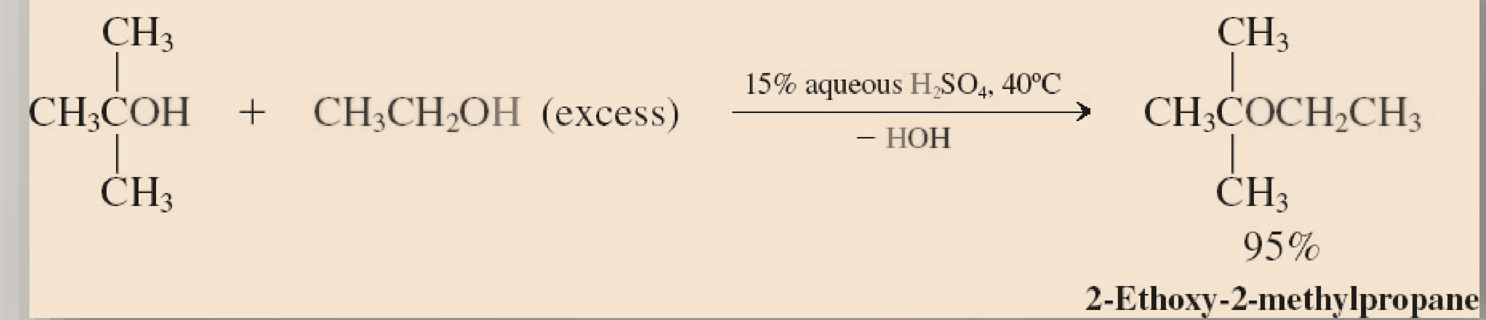
$$\mathrm{2\ CH_3\underset{H}{\overset{OH}{C}}CH_3 \xrightarrow{H_2SO_4,\ 40^\circ C} (CH_3)_2CHOCH(CH_3)_2 + HOH + H^+}$$

75%

2-Propanol

2-(1-Methylethoxy)propane
(Diisopropyl ether)

Synthesis of a Mixed Ether



$$\mathrm{CH_3\underset{CH_3}{\overset{CH_3}{C}}OH + CH_3CH_2OH\ (excess) \xrightarrow[-\ HOH]{15\%\ aqueous\ H_2SO_4,\ 40^\circ C} CH_3\underset{CH_3}{\overset{CH_3}{C}}OCH_2CH_3}$$

95%

2-Ethoxy-2-methylpropane

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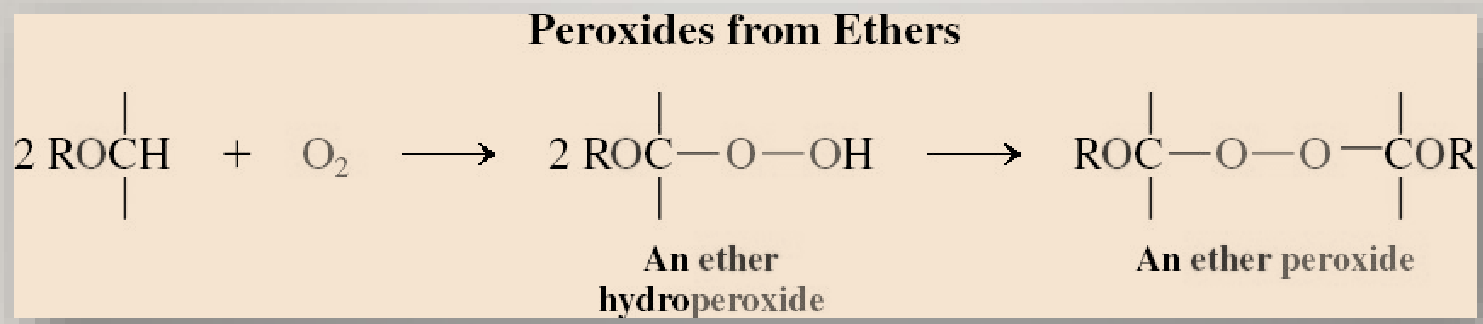
8.2 REACTIONS OF ETHERS

Ethers are usually inert; however, they do react slowly with oxygen to form hydroperoxides and peroxides which can decompose explosively.



Peroxides from Ethers

$$2\,\mathrm{ROCH} + \mathrm{O_2} \longrightarrow 2\,\mathrm{ROC{-}O{-}OH} \longrightarrow \mathrm{ROC{-}O{-}O{-}COR}$$

An ether hydroperoxide

An ether peroxide

The ether oxygen atom can be protonated to generate alkyloxonium ions.
With primary groups and strong nucleophilic acids (HBr), SN_2 displacement takes place.

Ether Cleavage with HBr

$$\underset{\textbf{Ethoxyethane}}{\mathrm{CH_3CH_2OCH_2CH_3}} \xrightarrow{\mathrm{HBr}} \underset{\textbf{Bromoethane}}{\mathrm{CH_3CH_2Br}} + \underset{\textbf{Ethanol}}{\mathrm{CH_3CH_2OH}}$$

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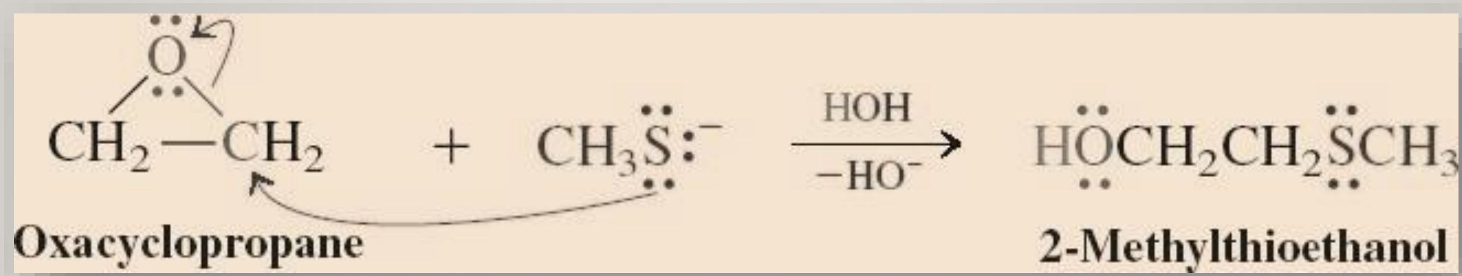
8.2 REACTIONS OF ETHERS

Nucleophilic ring opening of oxacyclopropanes by S_N2 is regioselective and stereospecific.

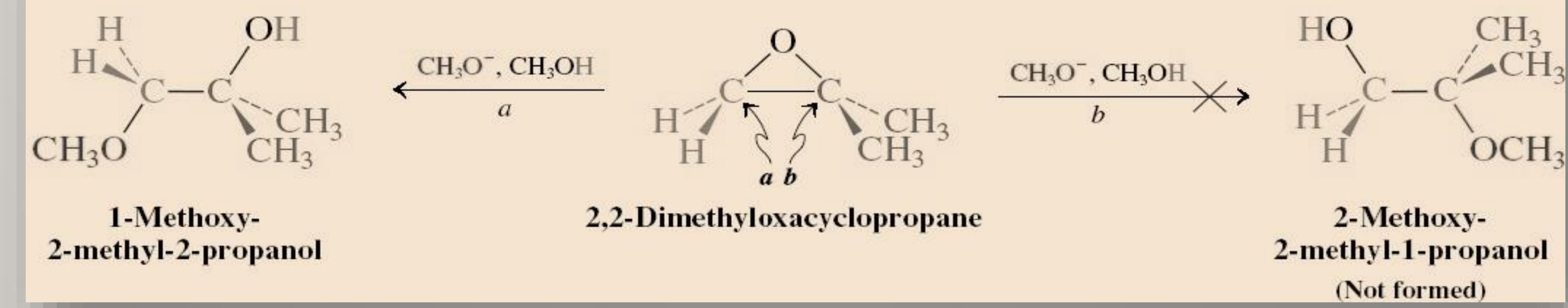
Oxacyclopropane can be ring-opened by anionic nucleophiles. Because the molecule is symmetric, nucleophilic attack can be at either carbon atom.



The driving force for this reaction is the release of ring strain.

With unsymmetrical systems, attack will be at the less substituted carbon center. This selectivity is referred to as "regioselectivity."

Nucleophilic Ring Opening of an Unsymmetrically Substituted Oxacyclopropane



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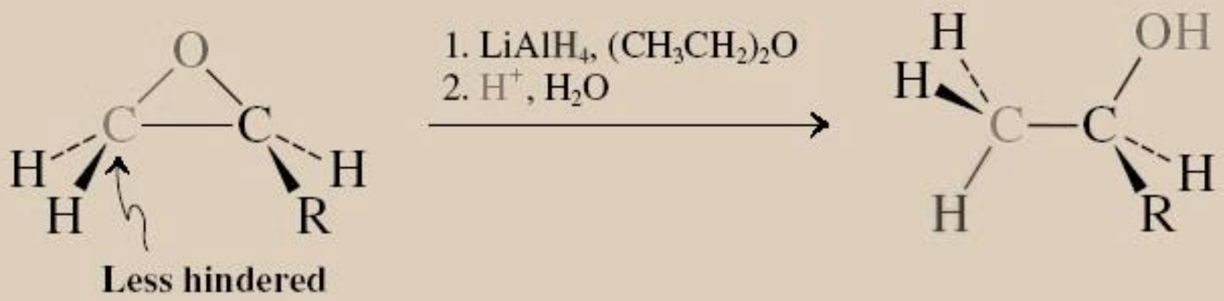
8.2 REACTIONS OF ETHERS

- Hydride and organometallic reagents convert strained ethers into alcohols.
- $LiAlH_4$ can open the rings of oxacyclopropanes to yield alcohols. (Ordinary ethers do not react.)
- In asymmetrical systems, the hydride attacks the less substituted side.

Ring Opening of an Oxacyclopropane by Lithium Aluminum Hydride



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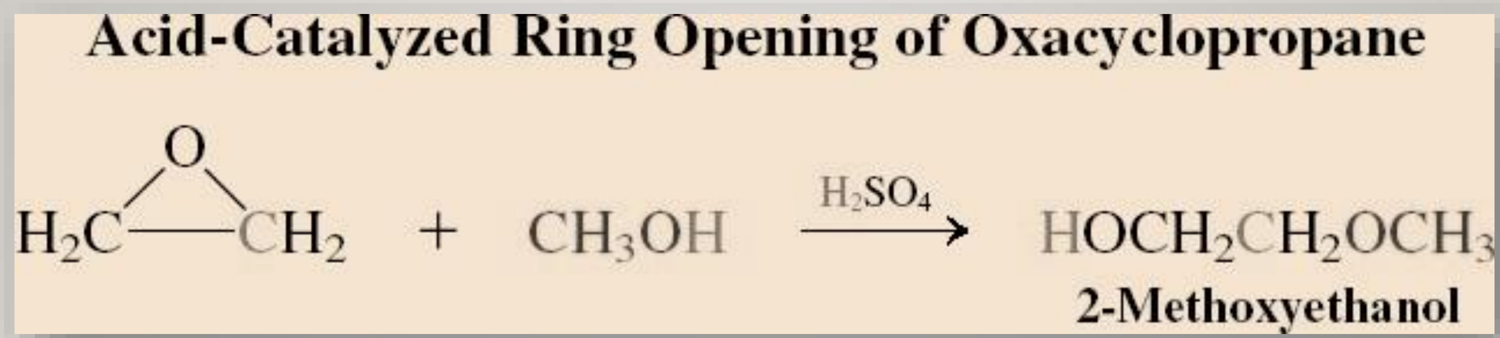
8.2 REACTIONS OF ETHERS

Ring opening of oxacyclopropane by acid catalysis proceeds through an initial cyclic alkyloxonium ion.

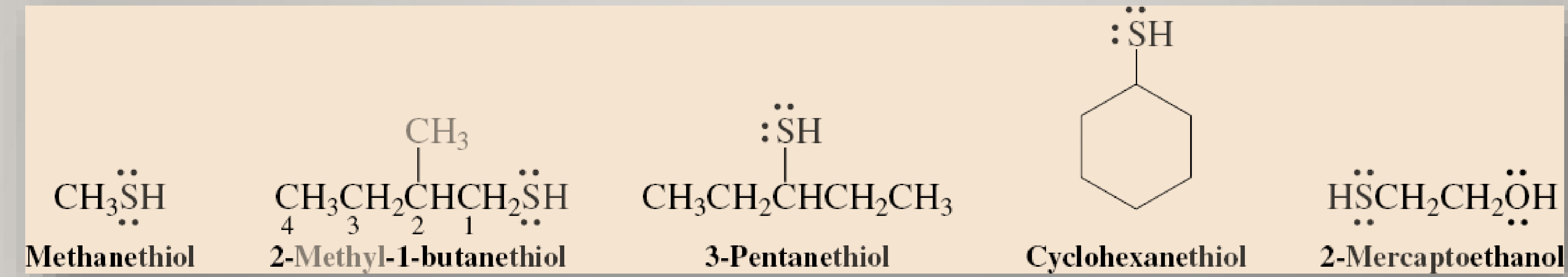


Acid-Catalyzed Ring Opening of Oxacyclopropane

This acid catalyzed ring opening is both regioselective and stereospecific.

8.3 SULFUR ANALOGS OF ALCOHOLS AND ETHERS

The sulfur analogs of alcohols and ethers are thiols and sulfides.
The IUPAC system calls the sulfur analogs of alcohols, R-SH, "thiols." The –SH group in more complicated compounds is referred to as "mercapto".



CH_3SH **Methanethiol**

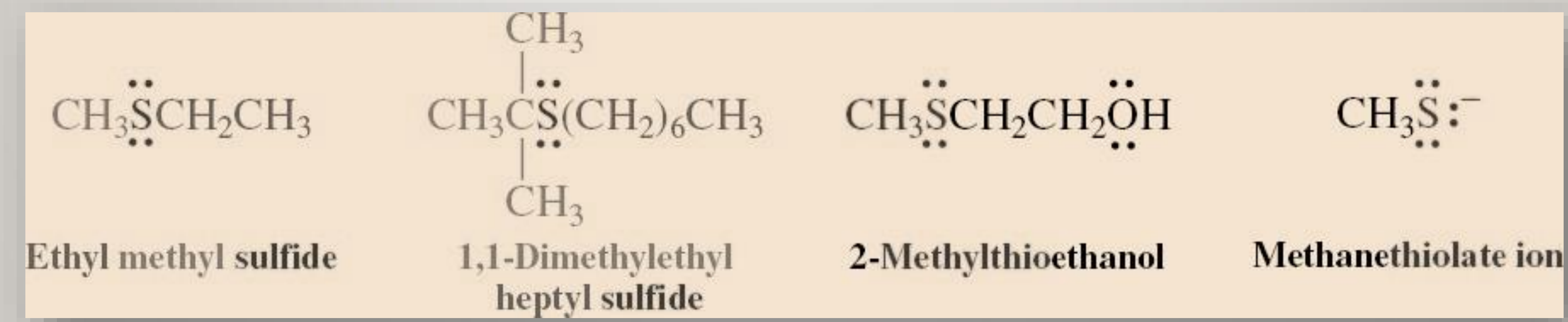
$\overset{CH_3}{CH_3CH_2CHCH_2SH}$ (4 3 2 1) **2-Methyl-1-butanethiol**

$CH_3CH_2\overset{SH}{C}HCH_2CH_3$ **3-Pentanethiol**

Cyclohexanethiol

$HSCH_2CH_2OH$ **2-Mercaptoethanol**

The sulfur analogs of ethers are called "sulfides" (common name, thioethers). The RS group is called "alkylthio," and the RS- group is called "alkanethiolate."



$CH_3SCH_2CH_3$ **Ethyl methyl sulfide**

$CH_3\underset{CH_3}{\overset{CH_3}{C}}S(CH_2)_6CH_3$ **1,1-Dimethylethyl heptyl sulfide**

$CH_3SCH_2CH_2OH$ **2-Methylthioethanol**

$CH_3S:^-$ **Methanethiolate ion**

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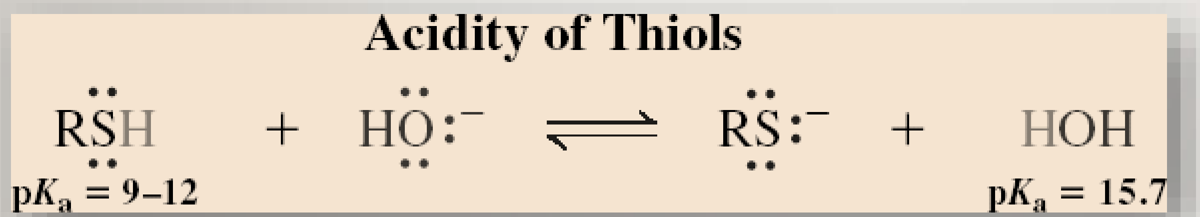
8.3 SULFUR ANALOGS OF ALCOHOLS AND ETHERS

Thiols are less hydrogen-bonded and more acidic than alcohols.

Compared to oxygen, sulfur has a large size, diffuse orbitals and a relatively nonpolarized S-H bond.

The boiling points of thiols are similar to those of the analogous haloalkanes.

Thiols are more acidic than water and can therefore be easily deprotonated by hydroxide and alkoxide ions:



Acidity of Thiols

$$\mathrm{RSH} + \mathrm{HO}^- \rightleftharpoons \mathrm{RS}^- + \mathrm{HOH}$$

$pK_a = 9\text{–}12$ (RSH); $pK_a = 15.7$ (HOH)

Thiols and sulfides react much like alcohols and ethers.

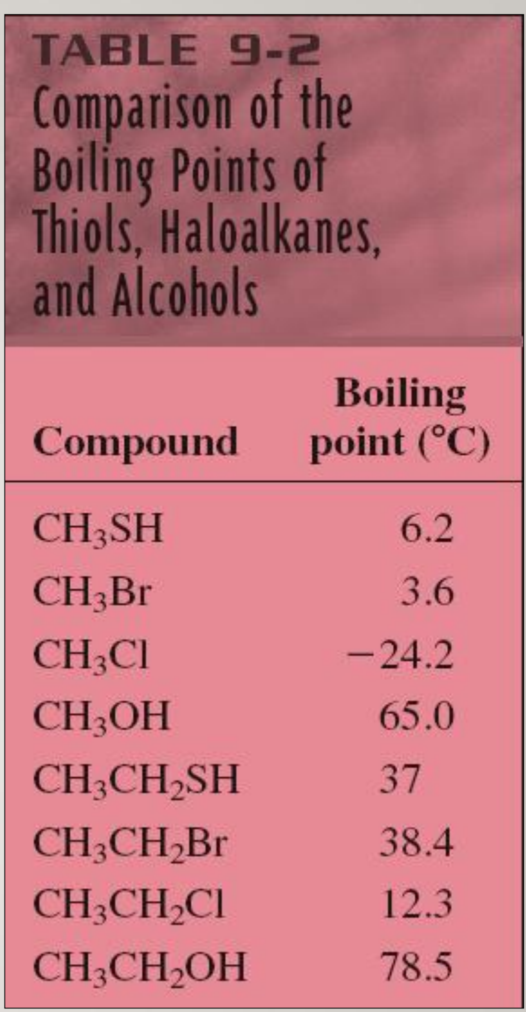


TABLE 9-2
Comparison of the Boiling Points of Thiols, Haloalkanes, and Alcohols

Compound	Boiling point (°C)
CH_3SH	6.2
CH_3Br	3.6
CH_3Cl	−24.2
CH_3OH	65.0
CH_3CH_2SH	37
CH_3CH_2Br	38.4
CH_3CH_2Cl	12.3
CH_3CH_2OH	78.5

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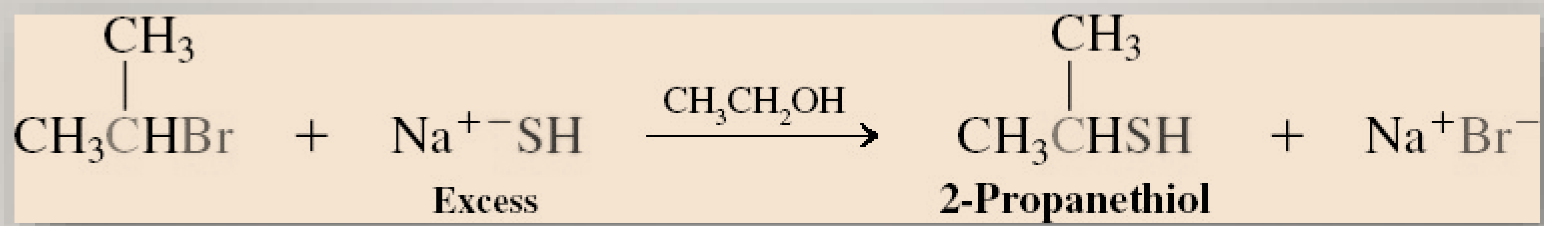
8.3 SULFUR ANALOGS OF ALCOHOLS AND ETHERS

The sulfur in thiols and sulfides is more nucleophilic than the oxygen in the analogous compounds.

Thiols and sulfides are readily made through nucleophilic attack by RS- or HS- on haloalkanes:



$$CH_3\overset{\displaystyle CH_3}{\overset{|}{C}}HBr + \underset{\text{Excess}}{Na^{+}\,{}^{-}SH} \xrightarrow{CH_3CH_2OH} \underset{\text{2-Propanethiol}}{CH_3\overset{\displaystyle CH_3}{\overset{|}{C}}HSH} + Na^{+}Br^{-}$$

A large excess of HS- is used to prevent the reaction of the product with the starting halide.

Sulfides are prepared by the alkylation of thiols in the presence of a base, such as hydroxide. The nucleophilicity of the generated thiolates is much greater than that of hydroxide which eliminates the competing SN_2 substitution by hydroxide ion.

Sulfides by Alkylation of Thiols

$$RSH + R'Br \xrightarrow{NaOH} RSR' + NaBr + H_2O$$

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