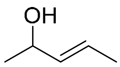
Chapter 8: Alcohols, Ethers, and Thiols

8.1 Structure, Nomenclature and Properties of Alcohols

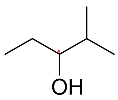
Naming Priority
Carbonyl (C=O) groups
OH
NH
SH
C≡C
C=C
Ethers, sulfides, alkyl, halogens

a) Nomenclature of Alcohols

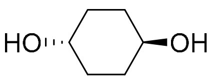
1. Find the longest chain containing the –OH substituent and if C=C or C≡C are present, include them in the longest chain
2. Replace –e on the parent name with –ol
3. Number the chain beginning at the end closest to the –OH
4. Number all substituents according to their position (don't forget to give the –OH a number!)
5. Write the complete name.



(E)-pent-3-en-2-ol
tran

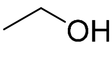


2-methyl pent-3-ol

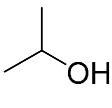


tran cyclo hexan-1,4-diol

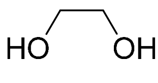
b) Common Alcohols



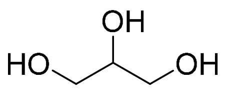
Ethanol
ethyl alcohol



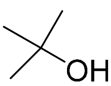
Isopropanol
isopropyl alcohol



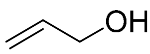
ethylene glycol
ethane-1,2-diol



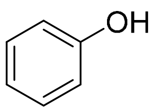
glycerol or glycerin
propane-1,2,3-triol



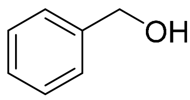
tert-Butanol



Allyl-alcohol



phenol



Benzyl-alcohol

c) Properties of Alcohols

Hydrogen bonding

- Alcohols and phenols have significantly higher boiling points than alkanes or haloalkanes due to hydrogen bonding
- Accounts for complete miscibility of lower alcohols with water

Reactivity of alcohols

- Alcohols and phenols are weakly basic and weakly acidic:

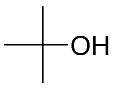
as base $R{-}O{-}H + H{-}X \rightleftharpoons R{-}\overset{\oplus}{O}H_2 + X^-$

as acid $R{-}O{-}H + H_2O \rightleftharpoons RO^{\ominus} + H_3O^+$

alkoxide ion

- Alcohols react with alkali metals such as sodium and potassium to form the sodium or potassium alkoxide and hydrogen gas:

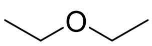
$2\ CH_3OH + 2\ Na \longrightarrow$ 2Na $+ 2CH_3O^- + H_2$

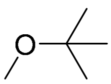
2  + 2 K ⟶

8.2 Structure, Nomenclature and Properties of Ethers

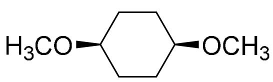
a) Nomenclature of Ethers

- Simple ethers with no other functional groups:
  Name the two oxygen substituents and add the word ether

 diethyl ether

 tert-butyl methyl ether

- More complex ethers which contain more than one ether or other functional groups: Longest carbon chain as parent name and -OR part becomes an alkoxy substituent

 cis 1,4 dimethoxy cyclohexane

1,2-Dimethoxyethane (DME)

b) Common Ethers

diethyl ether 'ether' | Tetrahydrofuran 'THF' | 1,4-dioxane 'dioxane' | ethyleneoxide

c) Properties of Ethers

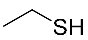
- Ethers have lower boiling points than alcohols (closer to hydrocarbons)
- Relatively inert –good solvents for reactive compounds
- Important in Grignard reactions: Ether solvents are required as they stabilize Grignard reagents (Chapter 12)
- Ethers oxidize upon exposure to air-to peroxides which can be explosive

$$R{-}O{-}CH_2R \xrightarrow{O_2} R{-}O{-}\underset{\displaystyle OOH}{\underset{|}{C}}HR$$

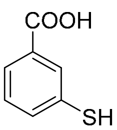
8.3 Structure, Nomenclature and Properties of Thiols

a) Nomenclature of Thiols

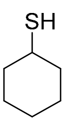
- Same as alcohols, with –thiol suffix
- -SH as a substituent = mercapto



ethanethiol



3-mercapto-benzoic acid



cyclohextane-thiol

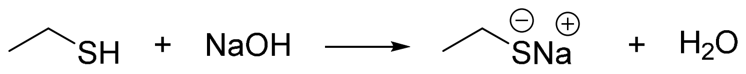
?

b) Properties of Thiols

- Low molecular weight thiols stink
- Responsible for unpleasant odor from skunk, rotten eggs, and sewage

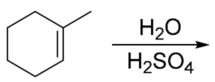
Acidity

- H_2S is a stronger acid than H_2O and RSH is a stronger acid than ROH

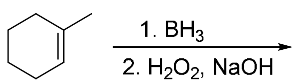


8.4 Synthesis of Alcohols from Alkenes (see Chapter 5)

a) Acid catalyzed hydration:

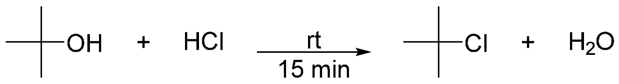


b) Hydroboration-Oxidation:



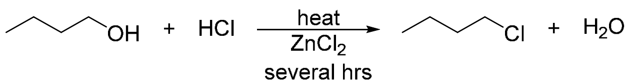
8.5 Conversion of Alcohols into Alkyl Halides

a) using HX



Reactivity of alcohols:

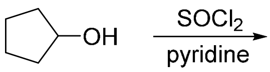
Reactivity of HX:

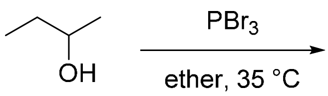


Because chloride is such a weak nucleophile, $ZnCl_2$ (or another Lewis acid) is required for converting primary or secondary alcohols to alkyl chlorides.

b) using PBr_3 or $SOCl_2$

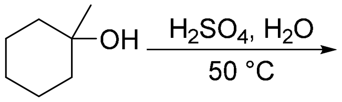
Only works with primary and secondary alcohols.

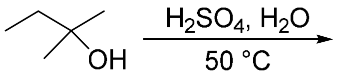




8.6 Acid Catalyzed Dehydration of Alcohols to Alkenes

E1 mechanism

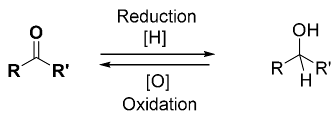




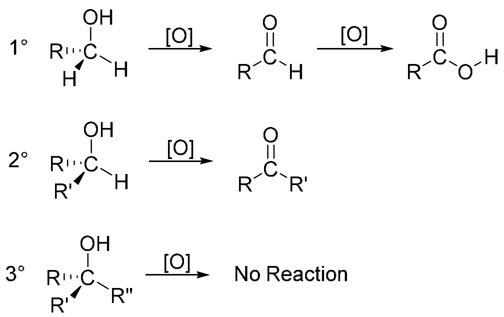
Reactivity of alcohols:

8.7 Oxidation of Alcohols to Carbonyl Compounds

Redox reactions in organic chemistry:



Oxidation of alcohols:



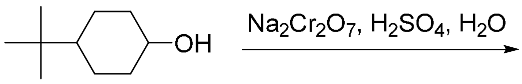
Oxidation methods for alcohols (there are more)

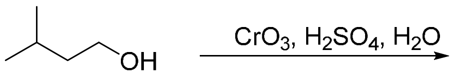
	Method of Oxidation/Product	
Substrates	aq H_2CrO_4 (Jones Reagent)	PCC
primary alcohol	carboxylic acid	aldehyde
secondary alcohol	ketone	ketone
tertiary alcohol	-	-

a) Chromic Acid (H_2CrO_4) Oxidation ("Jones Oxidation")

The ***Jones Reagent*** is a mixture of chromic trioxide or sodium dichromate in diluted sulfuric acid, which forms chromic acid in situ:

The Jones Oxidation allows a relatively inexpensive conversion of secondary alcohols to ketones and of most primary alcohols to carboxylic acids.

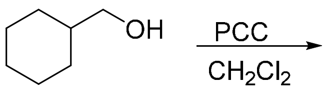


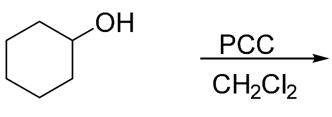


b) Pyridinium Chlorochromate (PCC) Oxidation of Alcohols

Chlorochromic acid can by prepared by the dissolution of chromium trioxide in 6 M aq. hydrochloric acid. Addition of pyridine gives pyridinium chlorochromate (**PCC**) as orange crystals.

Oxidation of primary alcohols with PCC yields aldehydes while secondary alcohols give ketones.

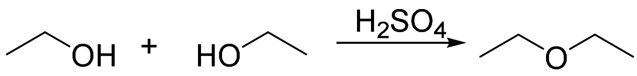




8.8 Synthesis of Ethers

a) Synthesis of Symmetrical Ethers

Under acid catalysis primary alcohols can form symmetrical ethers by intermolecular dehydration:



b) Synthesis of Unsymmetrical Ethers: Williamson Ether Synthesis

S_N2 process works that works best with primary alkyl halides which are attacked by an alkoxide.

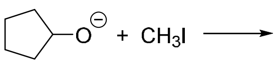
Formation of alkoxide:

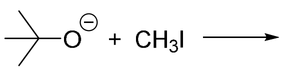
$$2\ R{-}OH \quad + \quad 2\ Na \longrightarrow 2\ \ R{-}O^{\ominus}\ Na^{\oplus} \quad + \quad H_2$$

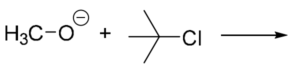
or

$$R{-}OH \quad + \quad NaH \longrightarrow R{-}O^{\ominus}\ Na^{\oplus} \quad + \quad H_2$$

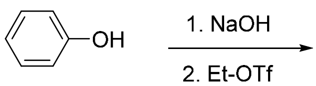
Williamson ether synthesis:







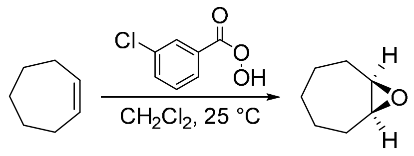
Phenols in the Williamson ether synthesis:



8.9 Synthesis of Epoxides (Oxiranes)

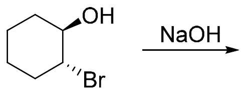
a) Synthesis of Epoxides by Epoxidation of Alkenes

Alkene + peroxyacid (RCO_3H) → epoxide



Stereochemical Outcome:

b) Synthesis of Epoxides in 2 Steps from Alkenes via Halohydrins



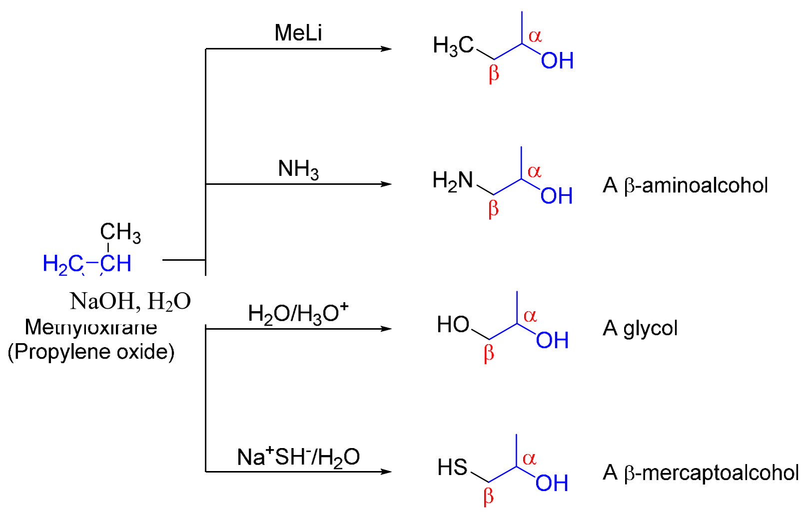
8.10 Reactions of Epoxides

Epoxides are very reactive ethers due to ring strain.

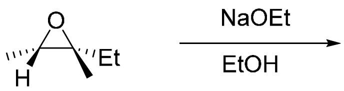
a) Base-Catalyzed Ring Opening

Base-catalyzed ring opening of an unsymmetrical epoxide occurs by attack of the nucleophile at the less substituted carbon atom.

Examples:



Stereochemistry: Epoxide opening is a stereospecific reaction:

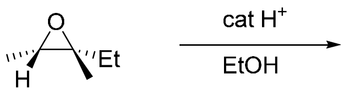


b) Acid-Catalyzed Ring Opening

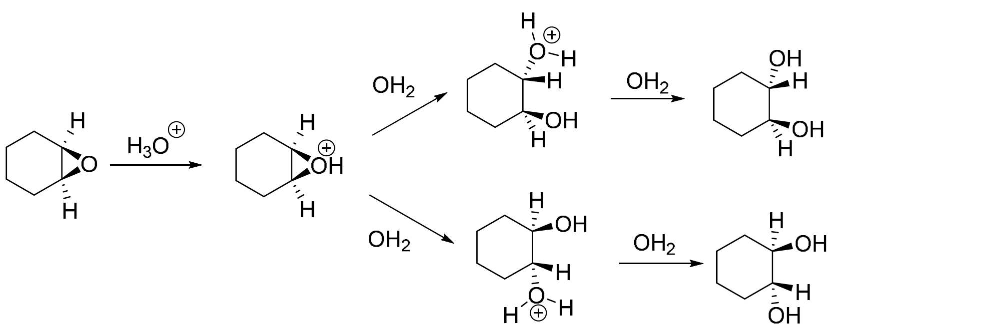
b) Acid-Catalyzed Ring Opening

- Acid-catalyzed ring opening of an unsymmetrical epoxide occurs by attack of the nucleophile at the more substituted carbon atom.

Stereochemistry: Epoxide opening is a stereospecific reaction:

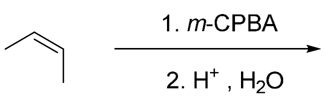


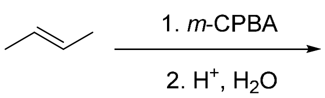
c) Anti 1,2-dihydroxylation of Alkenes via Epoxides



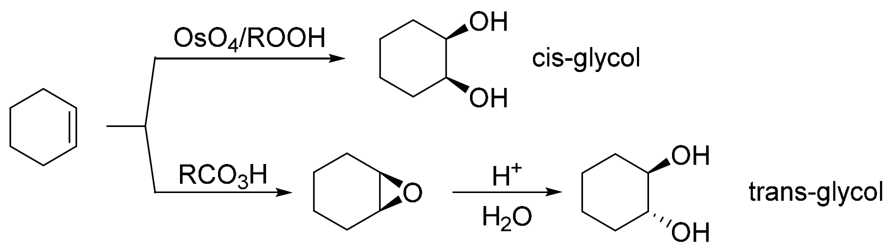
Trans-glycols obtained

Stereochemical outcome:

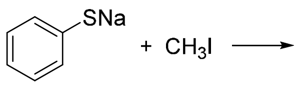




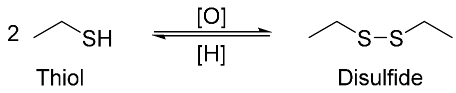
Cis vs Trans Glycols



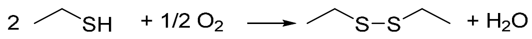
8.11 Thiol Synthesis and Reactions

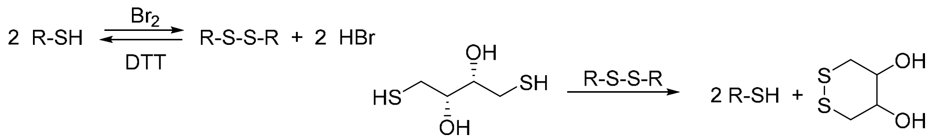


Oxidation:



Thiols are susceptible to oxidation in the presence of air:





DTT = Dithiothreitol

Protein−SH + HS−Protein ⟶

disulfide "bridges"
stabilize 3-D protein structure

8.12 Exercise