

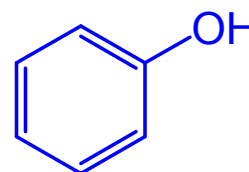
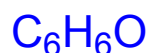
8. Alcohols, Ethers, and Thiols (text 8.1 – 8.7)

A. Structure and Nomenclature

- Alcohols have the general formula R–OH
- The O atom has a valence of 2, and one of these is taken by the H. Thus, the OH group substitutes an H atom in general formulas.
- So, the O atom is always ignored in unsaturation calcs.

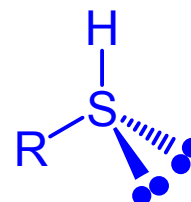
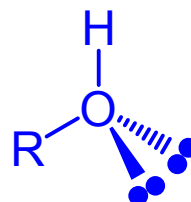


0 units unsat.

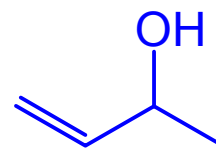


4 units unsat.

- The O has sp^3 hybridization, with two non-bonding pairs occupying the two sp^3 orbitals. The R–OH bond angle is about 104° (i.e. $< 109.5^\circ$).
- Thiols have the general formula R–SH and are structurally similar to alcohols, except the O is replaced by S.

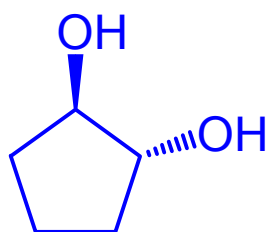


- In nomenclature, the OH or SH group is given the lowest possible number in the carbon chain. These groups take priority over π bonds.



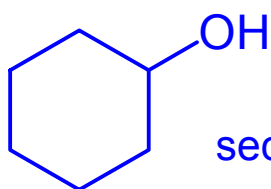
3-buten-2-ol

- However, in complex molecules, OH can be treated as a simple **hydroxy** substituent.

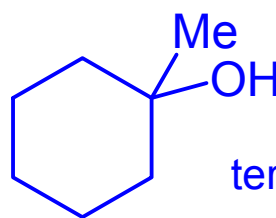


trans-cyclopentane-1,2-diol
or
trans-1,2-dihydroxycyclopentane

- Like alkyl halides, alcohols are classified as 1°, 2°, or 3° depending on the carbon atom to which OH is bonded.



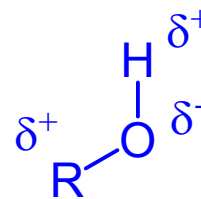
secondary



tertiary

B. Physical Properties

- The properties of alcohols stem from the high electronegativity of O, resulting in polar bonds. Effect is less in thiols (S less electronegative).



- Due to hydrogen bonding, alcohols have very high boiling points for their molar mass.

C_5H_{12} 36°

$\text{C}_5\text{H}_{11}\text{Cl}$ 108°

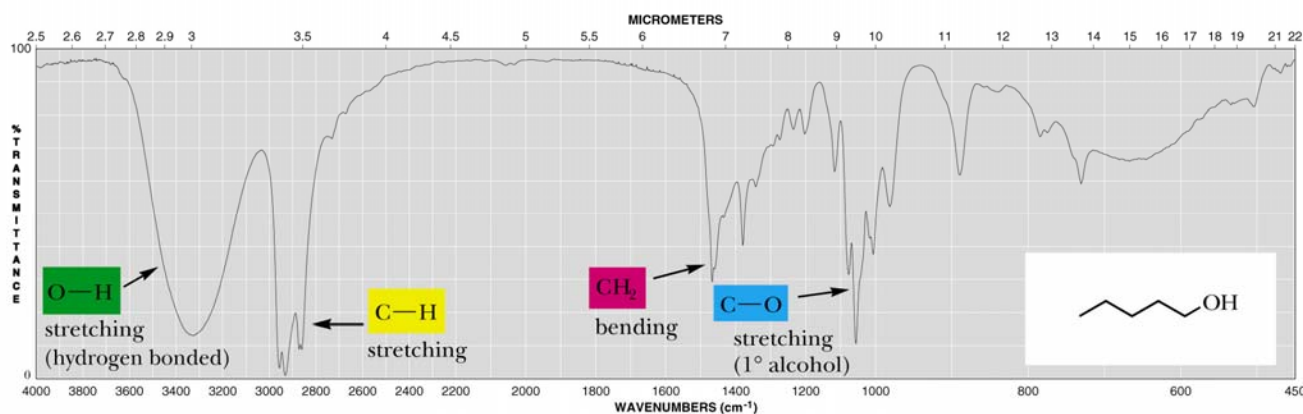
$\text{C}_5\text{H}_{11}\text{OH}$ 136°

CH_4 -136°

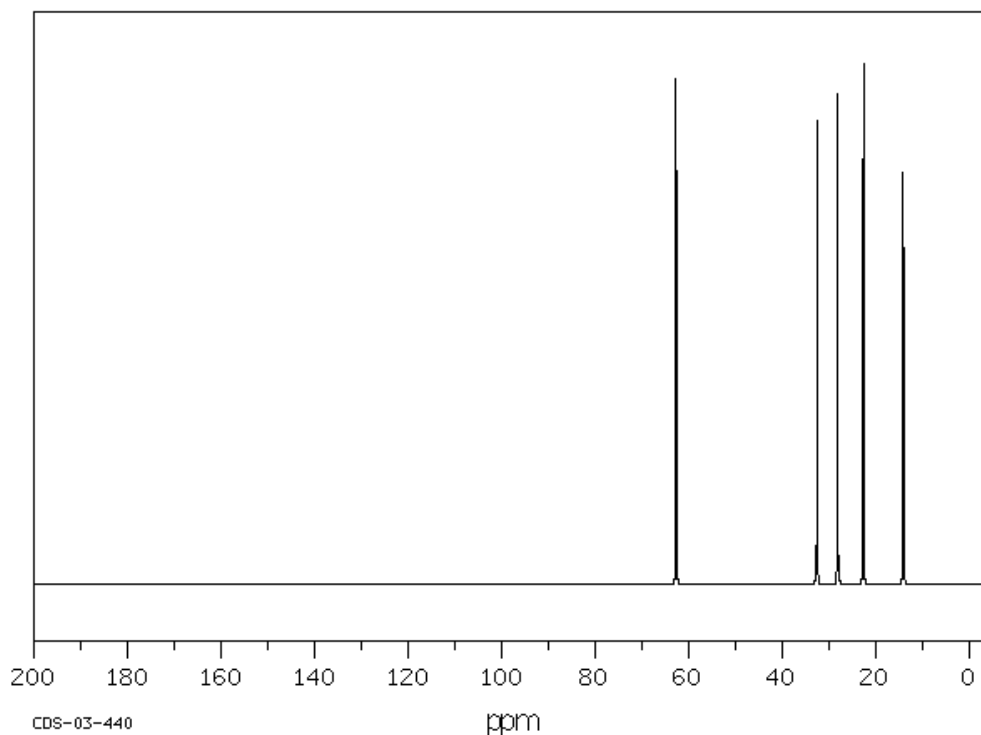
H_2O 100°

C. Spectroscopy

- In IR, alcohols have a strong, broad OH stretch at $3200 - 3500\text{ cm}^{-1}$, and a strong CO stretch at $1050 - 1250\text{ cm}^{-1}$.
- These absorptions are easily seen in 1-pentanol.

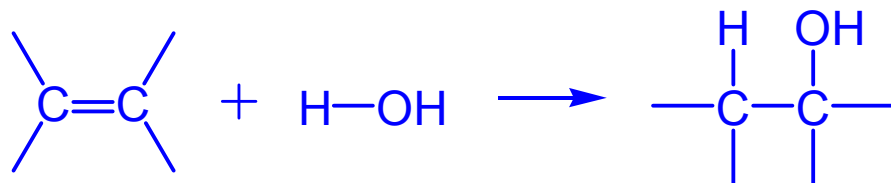


- The ^{13}C -NMR spectrum of 1-pentanol shows the five signals, with the ones furthest downfield closest to the OH.

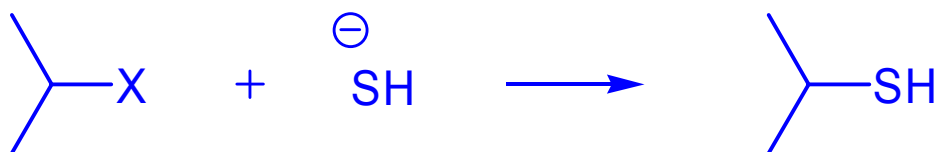
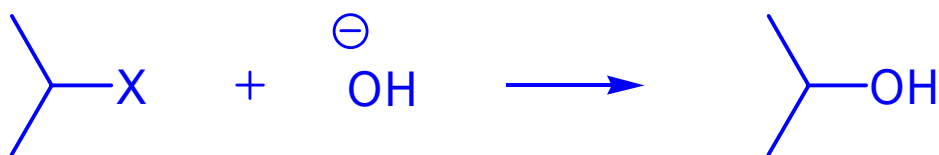


D. Preparation

- We have learned two ways for the preparation of alcohols, and one way for thiols.
- Hydration of alkenes to alcohols



- Substitution of alkyl halides \rightarrow alcohols and thiols

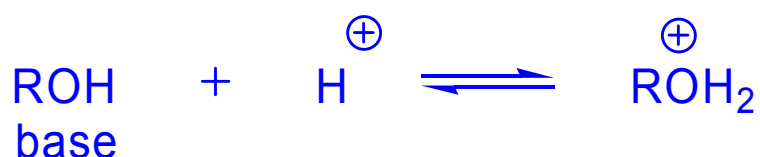
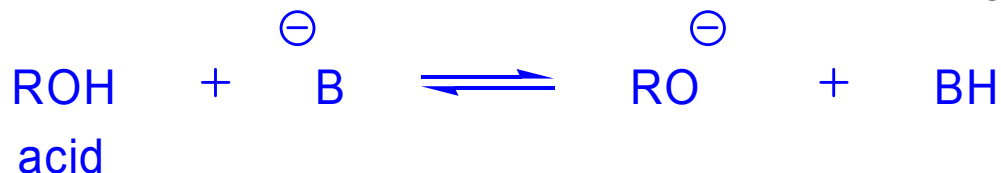


E. Reactions of Alcohols and Thiols

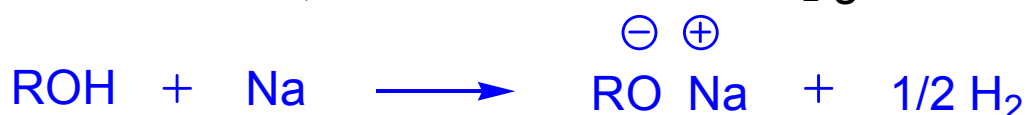
- Alcohols and thiols undergo a series of common reactions: acid-base reactions, conversion to alkyl halides, dehydrations to alkenes, and oxidations.

1. Acid-base reactions

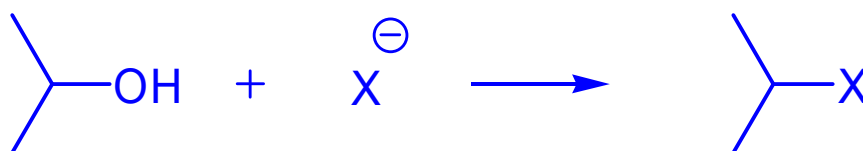
- Like water, alcohols/thiols are amphiprotic (amphoteric): they can function as acids (in the presence of strong bases), and also as bases (in the presence of strong acids).



- Alcohols, like water, also react with Group 1 and 2 metals to form alkoxide salts, with the liberation of H₂ gas.



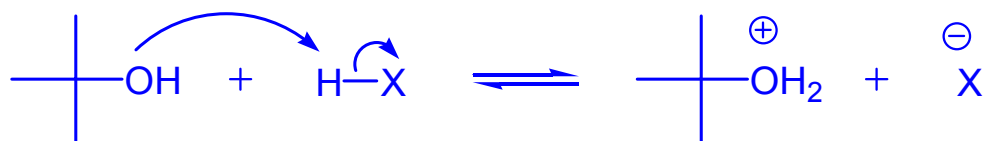
2. Conversion to alkyl halides



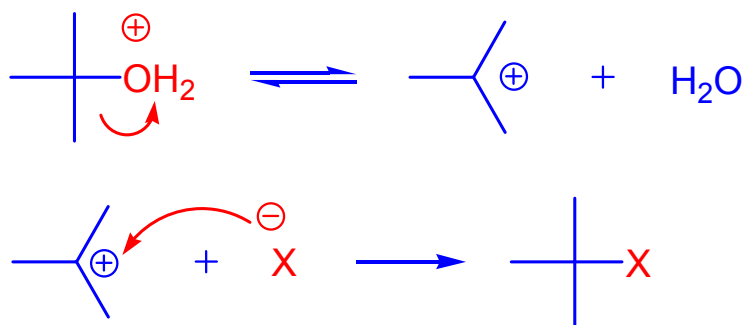
- Alcohols can be converted to RX by substitution mechanisms S_N1 or S_N2, depending on the structure.
- The nucleophilic halogen can be supplied by different reagents.

1. Reaction with HX ($X = \text{Cl}, \text{Br}, \text{I}$)

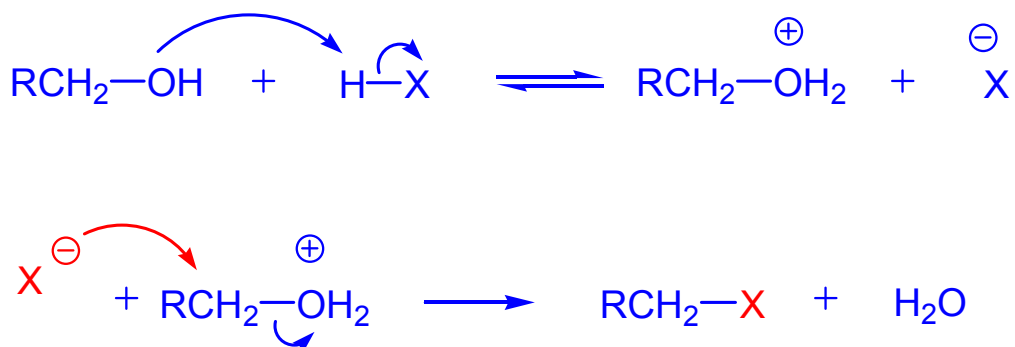
- In acidic solutions, alcohols act as bases and can be protonated.



- After the OH group is protonated to form an oxonium ion, an S_N1 reaction can occur if a stable carbocation is formed.



- Alcohols that do not form stable carbocations usually react via an S_N2 mechanism. After protonation, there is concerted attack of the nucleophile and the departure of the LG.



2. Reaction with thionyl chloride (SOCl_2)

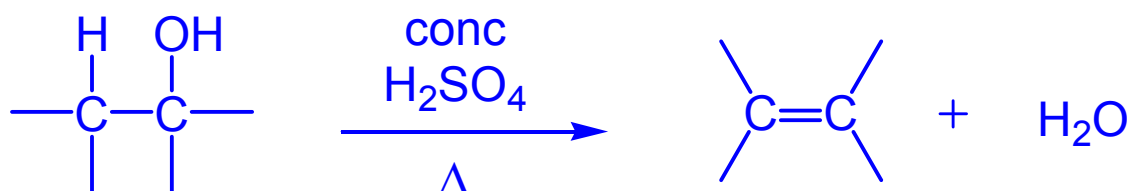
- Better yields of chloroalkanes are obtained from **1° and 2°** alcohols when SOCl_2 is a chlorine source. This is because the co-products made are gases and bubble out of solution, rendering the reaction irreversible.



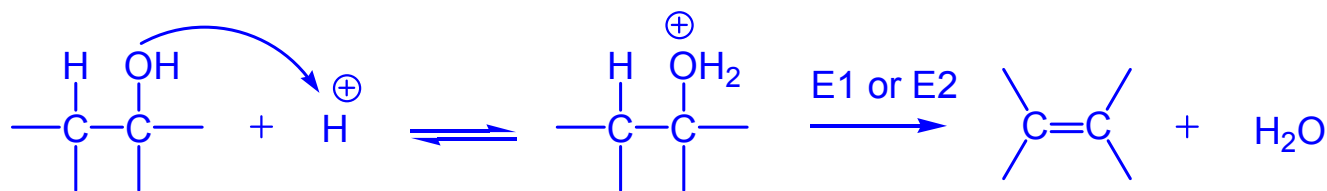
- This occurs by $\text{S}_{\text{N}}2$, but we will not examine it in detail. Because it occurs $\text{S}_{\text{N}}2$, **3° alcohols will not react with SOCl_2** .
- Remember, OH groups bonded to a benzene ring (and sp^2 carbons) do not substitute by the above mechanisms.

3. Dehydration to alkenes

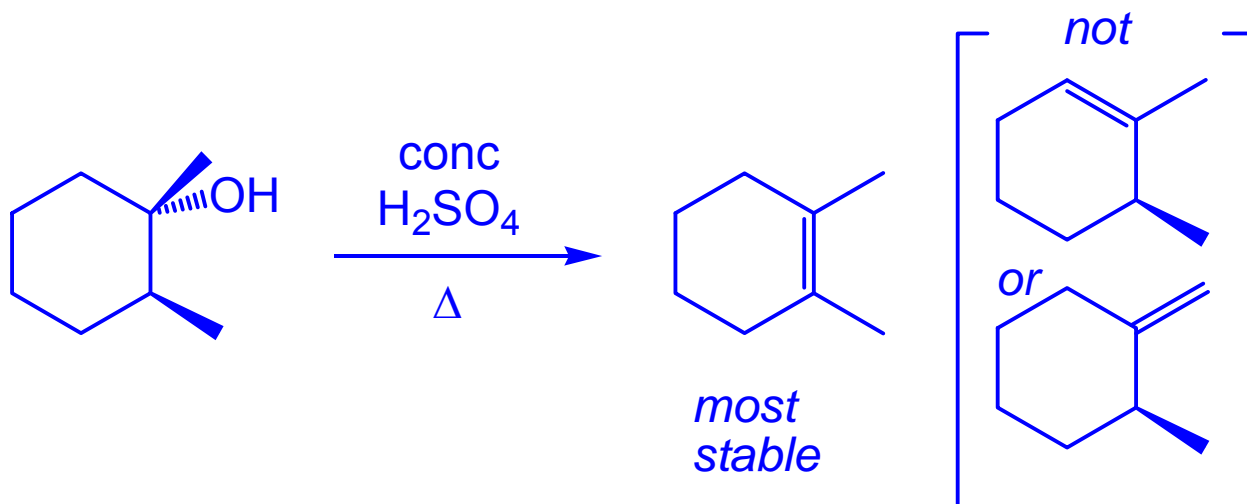
- Elimination of water in the presence of conc. H_2SO_4 or H_3PO_4 . Heating is required (denoted by Δ).



- The acid is necessary to protonate the OH, generating the good leaving group H_2O .

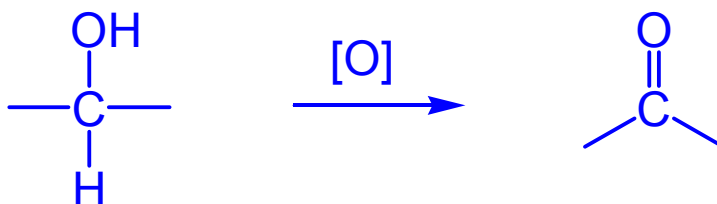


- Elimination to form double bonds is especially favoured when stable double bonds are formed.
- Recall Zaitsev's Rule... alkyl groups stabilize C=C bonds

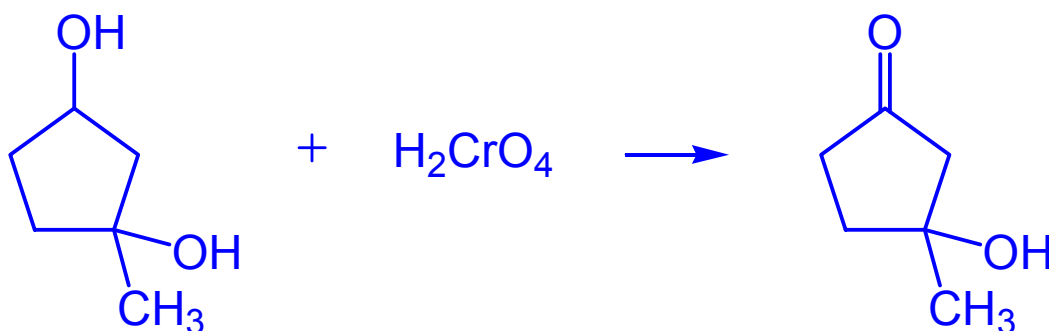


4. Oxidation of 1° and 2° alcohols

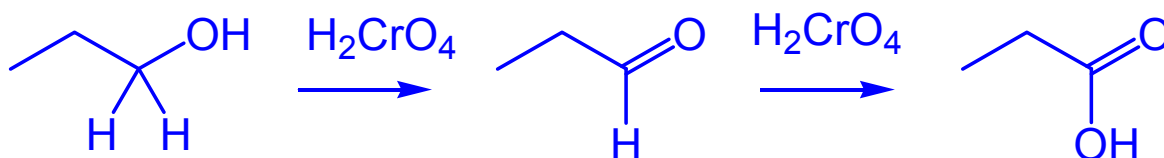
- Primary and secondary alcohols are easily oxidized to carbonyl compounds (aldehydes and ketones, respectively).



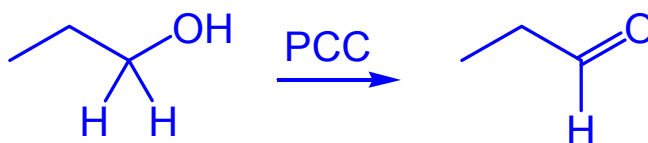
- Because oxidation removes H atoms from both the OH and the CH, only 1° and 2° alcohols can be oxidized (not 3°) to simple carbonyl compounds.



- Oxidation of alcohols is a great way to prepare carbonyl compounds. However, the aldehyde is also easily oxidized to carboxylic acid, so the reaction directly results in the acid.

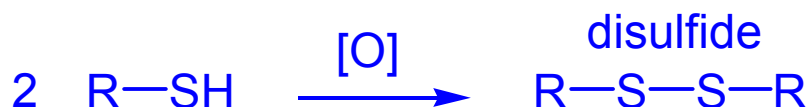


- Sometimes its possible to isolate the aldehyde before it reacts, but it's usually difficult to stop the reaction at the aldehyde stage for most oxidizing agents.
- Yet, the weak oxidant **pyridinium chlorochromate (PCC)** oxidizes alcohols to carbonyl compounds only. Primary alcohols stop at aldehydes do not continue to carboxylic acids. Secondary alcohols are oxidized to ketones.

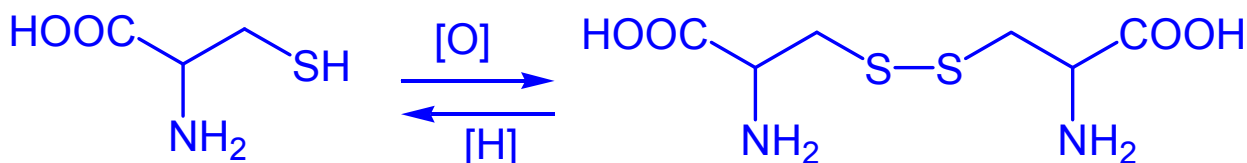


5. Oxidation of thiols

- Unlike alcohols, thiols are oxidized to disulfides. Thiols oxidize very easily and can be oxidized by most oxidizing agents (even oxygen in air).



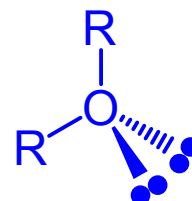
- Commonly, oxidation of thiols on neighbouring regions of proteins results in “disulfide bridging” (e.g. human hair).
- Disulfides can also be reduced back to thiols by reducing agents. This happens when you get a hair perm.



F. Ethers and Epoxides

1. Structure and Nomenclature

- General formula R-O-R. As in alcohols, the O is ignored in unsaturation calculations. O is sp^3 with 2 non-bonding pairs.
- In IUPAC nomenclature, both R groups are named as adjectives, followed by the word ether.



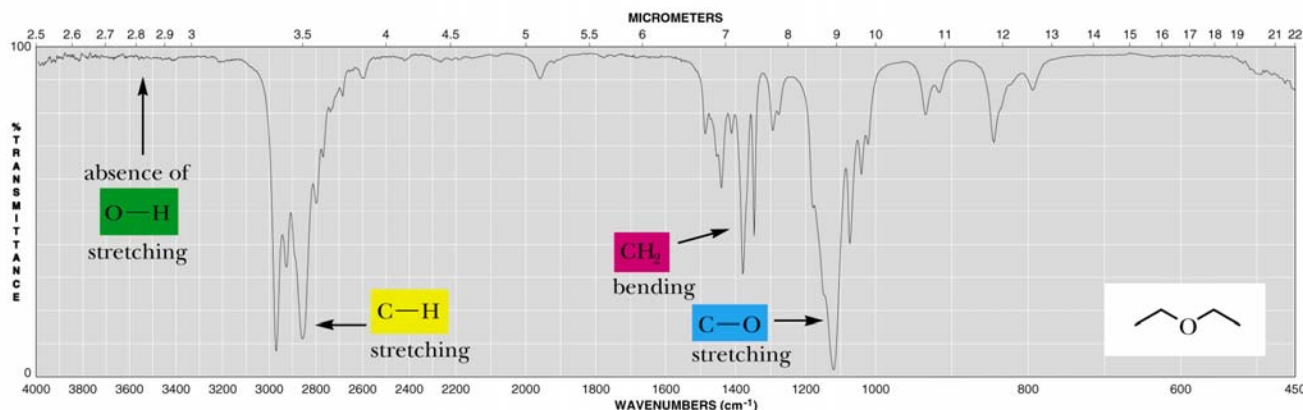
- Epoxides are cyclic ethers and are named as “oxides” according to the parent alkene.



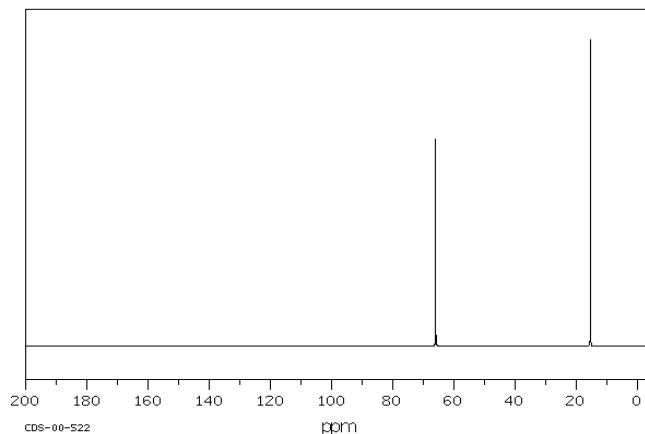
- Ethers contain 2 polar bonds and have a small dipole moment, but they cannot hydrogen-bond to themselves.
- Ethers are also low-boiling compounds like alkanes, but because of their polarity they are much better solvents than alkanes. They're also quite unreactive. This is why you used diethyl ether in Expt. 2.

2. Spectroscopy of Ethers

- Ethers have a strong C-O stretch between 1070 – 1150 wavenumbers, like alcohols. There is no OH stretch.

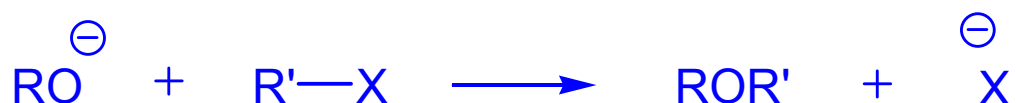


- The carbon NMR of diethyl ether shows two signals.

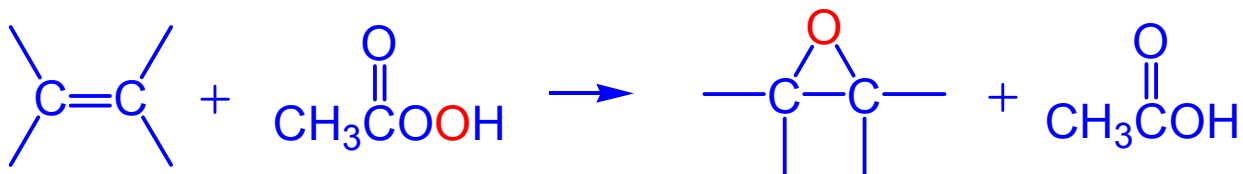


3. Preparation

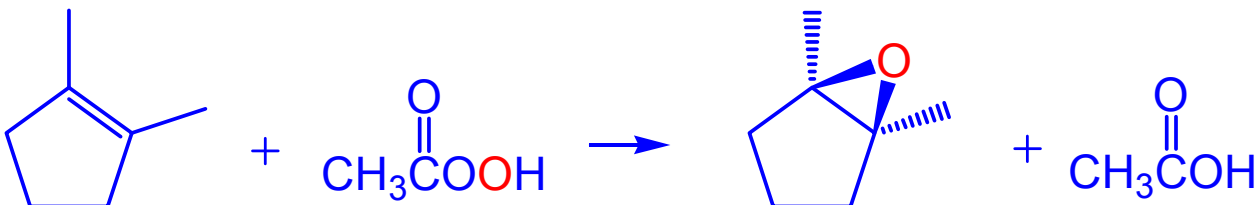
- Ethers are usually prepared by the S_N2 attack of alkoxide nucleophiles on 1° or 2° alkyl halides. This does not work for 3° because elimination products are formed instead.



- Epoxides are prepared from the oxidation of alkenes, e.g. using **peroxyacetic acid**. During the reaction it is reduced to acetic acid.

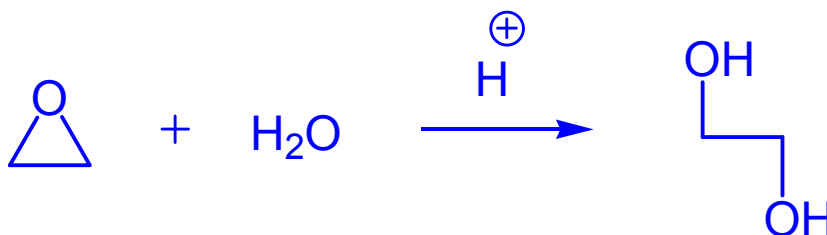


- The addition of the O atom to the alkene is stereoselective and gives only syn addition (*i.e.* adds to one side of C=C).

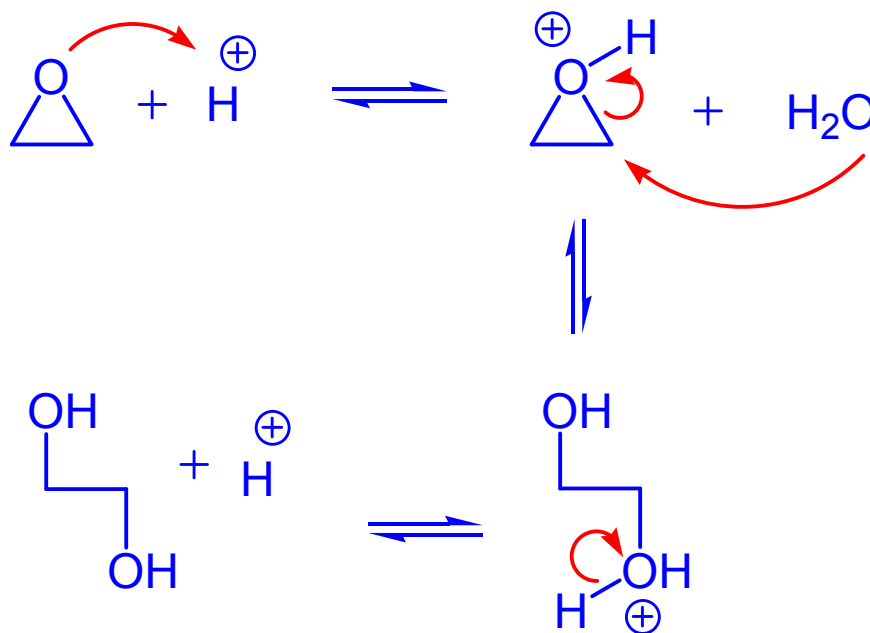


4. Reactions

- Ethers are quite unreactive.
- Epoxides, because of the strained three-membered ring, are very reactive towards electrophiles. We'll look at one reaction only, the acid-catalyzed hydration of epoxides.

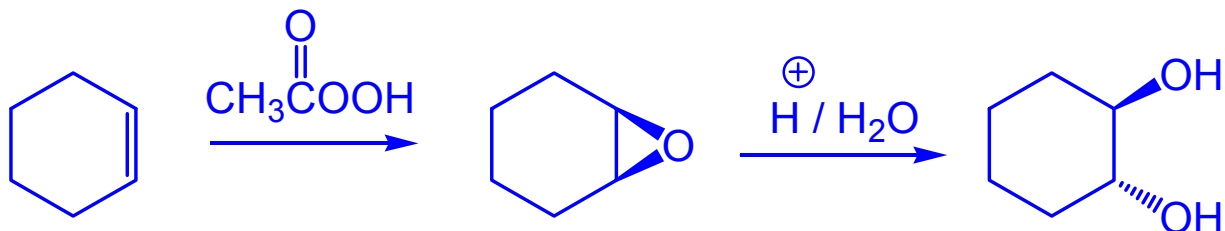


- This ring-opening proceeds by the *anti* addition of water, by a mechanism similar to the hydration of alkenes.

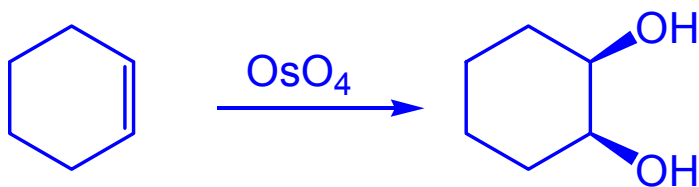


- Note the positively charged cyclic ion... recall the *anti* addition of halogens to alkenes. Water can attack either of the two carbons, but it would prefer the less-hindered one.

- Epoxidation of ring alkenes followed by acid-catalyzed ring opening results in *trans* glycols.

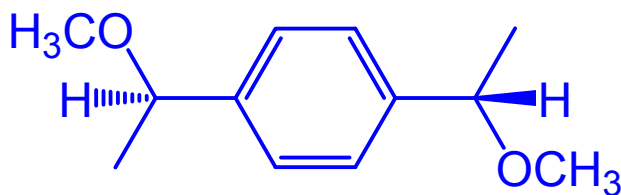


- Recall that oxidation by OsO_4 results in *cis* glycols.



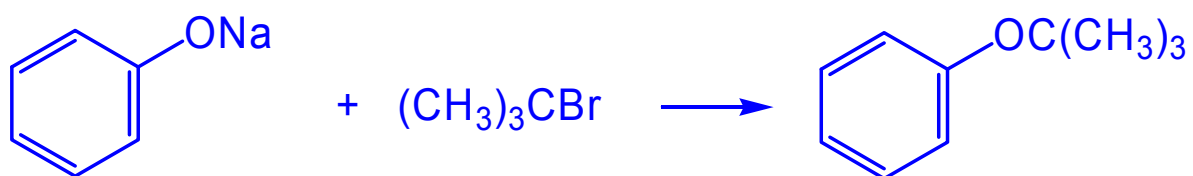
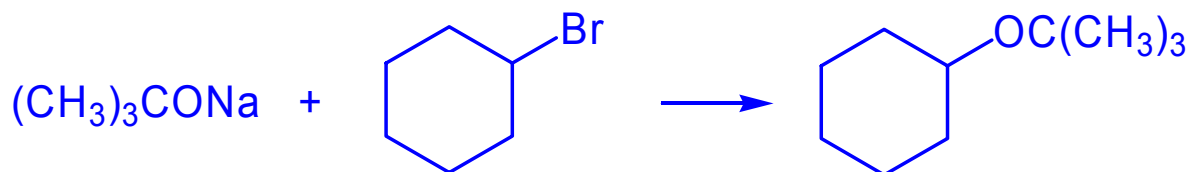
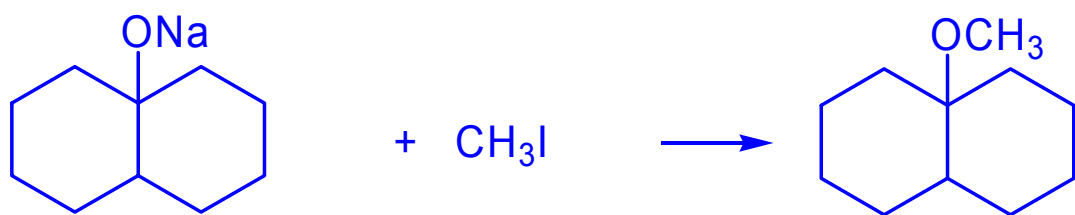
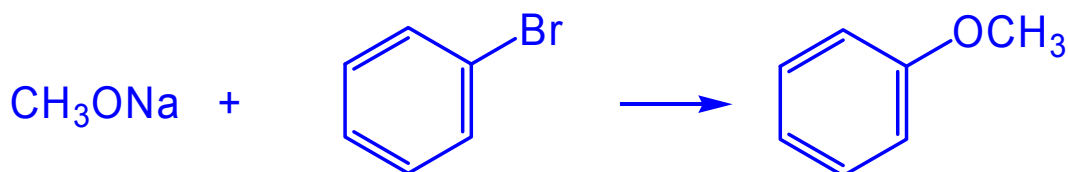
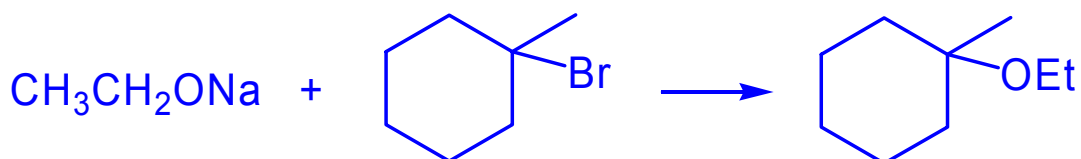
- This shows how different procedures can be used depending on whether *cis* or *trans* products are wanted.
- Pages covered: Chapter 8, p. 197-227
- Problems: 14, 16, 17, 25, 28, 31, 34, 36, 37, 43, 44, 46, 48, 50. Also try Chapter 11 #13.
- Dec 2005: 23 – 27
Dec 2006: 22 – 25
Dec 2007: 24, 25
Dec 2008: 22 – 25

- Past test question: How many lines there in the ^{13}C -NMR spectrum of this compound?

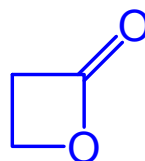
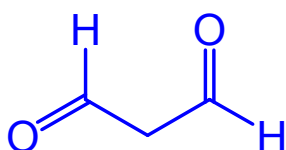
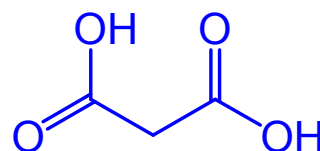
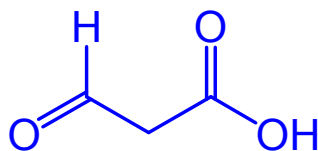
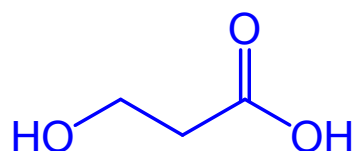
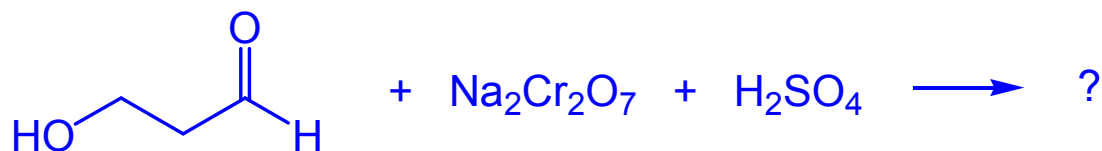


5 6 8 11 12

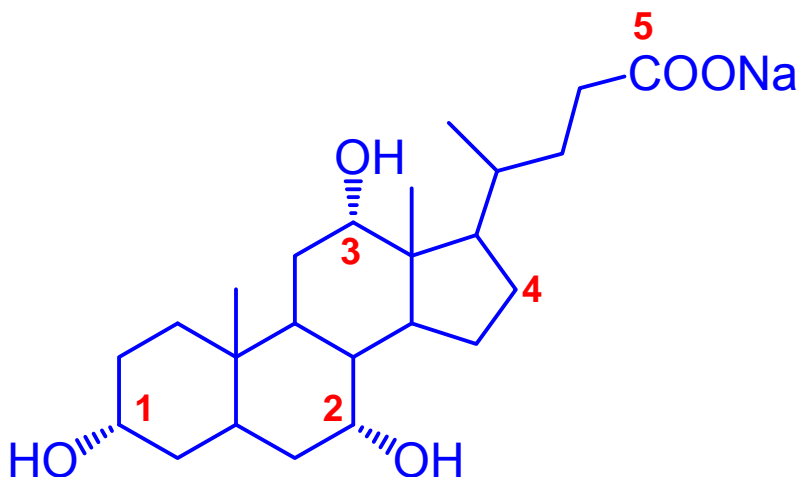
- Past test question: Which one of the following reactions gives the best yield of the ether shown?



- Past test question: What is the major product of...

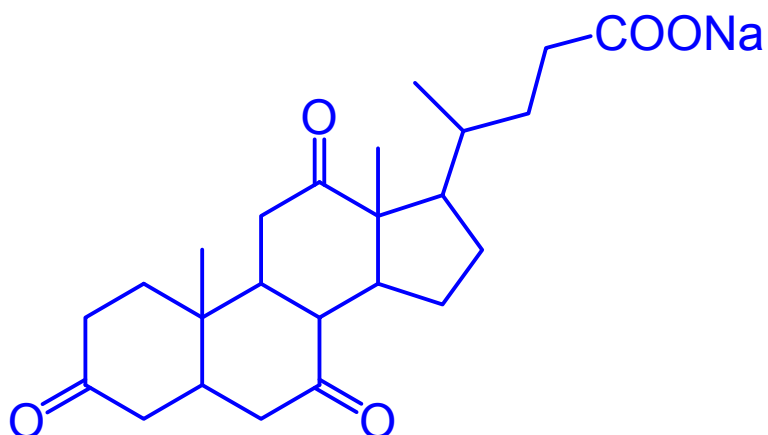


- MCAT question: Shown is the structure of sodium cholate, a detergent used to purify proteins.



- Which of the three hydroxyl carbon atoms is least sterically hindered?

- Which of the reagents shown would convert sodium cholate to the product shown below?



$\text{CH}_3\text{CO}_3\text{H}$

HBr

H_2CrO_4

conc H_2SO_4

- Which of the carbons in sodium cholate has the highest oxidation number?

Carbon 1

Carbon 3

Carbon 4

Carbon 5