

Chapter 15

Alcohols, Diols, and Thiols

Chapter 15 suggested problems: 17, 19, 24, 28, 37, 39

I. Introduction

- A. The relevance of alcohols (from M&B: 497): "If an organic chemist were allowed to choose ten aliphatic compounds with which to be stranded on a desert island, he would almost certainly pick alcohols. From them he could make nearly every other kind of aliphatic compound: alkenes, alkyl halides, ethers, aldehydes, ketones, acids, esters, and a host of others. From the alkyl halides he could make Grignard reagents, and from the reaction between these and the aldehydes and ketones obtain more complicated alcohols and so on. Our stranded chemist would use his alcohols not only as raw materials but frequently as the solvents in which reactions are carried out and from which products are recrystallized.

"For alcohols to be such important starting materials in aliphatic chemistry, they must be not only versatile in their reactions but also available in large amounts and at low prices."

- B. Sources: there are two principal sources of simple aliphatic alcohols

1. Hydration of alkenes obtained by the cracking of petroleum

- a. 4-5 carbon alkenes are readily obtained during the cracking of raw petroleum
- b. These are easily converted to alcohols either by the direct addition of water or by the addition of sulfuric acid followed by hydrolysis
- c. Limitation: only alcohols formed in compliance with Markovnikov's rule are formed
 - i. Ethyl alcohol is the only primary alcohol formed through cracking
 - ii. isopropyl not n-propyl
 - iii. sec-butyl (1-methylpropyl) not n-butyl

iv. t-butyl not isobutyl (2-methylpropyl)

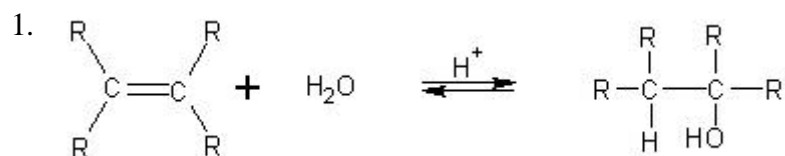
2. Fermentation of carbohydrate sources

a. Sugars from sugar cane and sugar beets; sorghum and molasses

b. Starches from grains (ethyl alcohol = grain alcohol)

II. Preparation of alcohols

A. Acid-catalyzed hydration of alkenes (Carey 6:10)



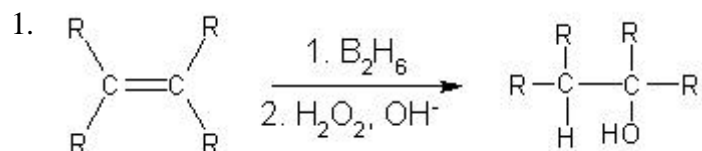
2. Dilute acid (50% sulfuric acid in water)

3. Carbocation mechanism affects reaction rates and potential rearrangements

4. Addition follows Markovnikov's rule

5. Example: the hydration of 2-butene

B. Hydroboration-oxidation (Carey 6:11)

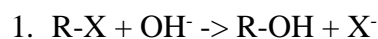


2. B_2H_6 is diborane, commonly used

3. Addition is anti-Markovnikov: boron is partially positive and hydrogen partially negative (although partial positive and negative charges have nothing to do with Markovnikov addition)

4. No rearrangements take place (not a carbocation mechanism, see Carey 6:13)

C. Hydrolysis of alkyl halides (Carey 8:1)



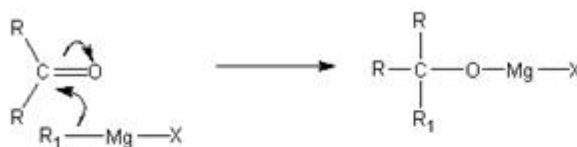
2. Rarely used in the synthesis of alcohols since alcohols are usually the starting materials of alkyl halides

- The products of E2 eliminations can compete with the formation of the desired alcohol

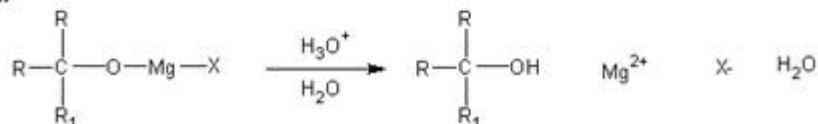
D. The reduction of aldehydes, ketones, and esters with organometallic compounds

- Result in the formation of new carbon-carbon bonds
- Can form primary, secondary, or tertiary alcohols when reducing aldehydes and ketones
- Can only form tertiary alcohols when acting on esters
- The reaction of Grignard reagents with aldehydes and ketones (Carey: 14.6 - 10)

Step 1.

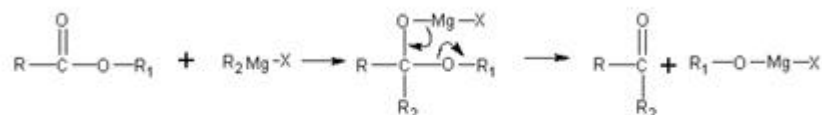


Step 2.

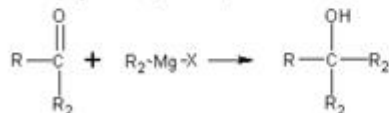


- The reaction of Grignard reagents with esters

Step 1. in diethyl ether



Step 2. in diethyl ether, then aqueous acid is added

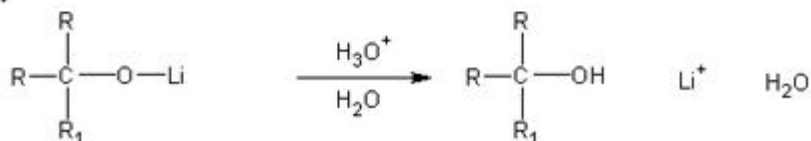


- The reaction of organolithium compounds with aldehydes and ketones

Step 1.



Step 2.

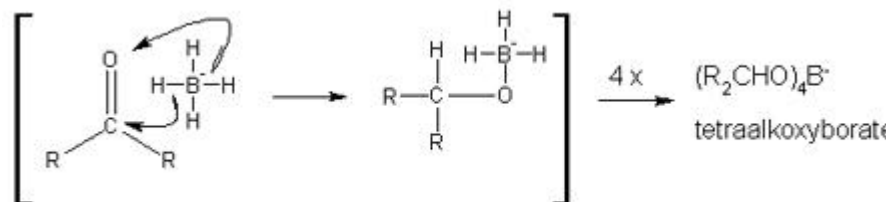


E. The reduction of aldehydes and ketones via catalytic hydrogenation

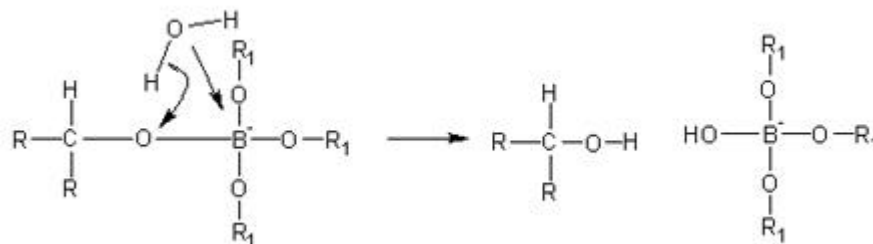
1. Catalysts: powdered Pt, Pd, Ni, Ru
2. Aldehydes: $\text{RCHO} + \text{H}_2 \rightarrow$ primary alcohol
3. Ketones: $\text{RCOR} + \text{H}_2 \rightarrow$ secondary alcohol

F. The reduction of aldehydes and ketones via metal hydrides

1. Sodium borohydride (NaBH_4) and lithium aluminum hydride (LiAlH_4) are powerful reducing agents i.e. hydride donors
2. The hydrogen is negatively charged (hydride)
3. Neither will reduce isolated carbon-carbon double bonds
4. Sodium borohydride
 - a. Easy to use but not as powerful a reducing agent as LiAlH_4
 - b. Simply add to an aqueous or alcohol solution of the aldehyde/ketone
 - c. Step 1: borohydride transfers a hydrogen with its electron pair to the carbonyl carbon, while the carbonyl oxygen attacks the central boron atom; this hydride transfer takes place four times until the tetraalkoxyborate is formed



- d. Step 2: hydrolysis or alcoholysis results in the breaking of the alkoxy-boron bond with the transfer of a hydrogen ion to the alkoxy group - resulting in alcohol formation - and the transfer of a hydroxide ion to the boron eventually resulting in the formation of tetrahydroxy boron compound



5. Lithium aluminum hydride

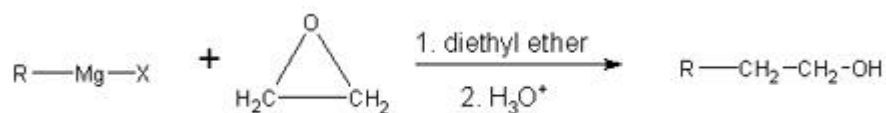
- a. Exact same transfers and mechanism as borohydride

G. The reduction of carboxylic acids and esters

1. Acids are very difficult to reduce
2. Can only be accomplished with lithium aluminum hydride
3. Primary alcohol is the product
4. Esters are more easily reduced than acids, but LiAlH_4 is still the reducing agent of choice
 - a. NaBH_4 will reduce esters but the reaction is extremely slow
 - b. Catalytic hydrogenation requires special catalysts and extremely high temperatures and pressures
5. Two alcohols are formed from each ester
6. The acyl portion of the ester gives a primary alcohol
7. The nature of the other alcohol depends on nature of the alcohol that was esterified

H. Preparation of alcohols from epoxides

1. Grignard reagents react with ethylene oxide to form primary alcohols two carbons longer than the original alkyl chain



III. Diols

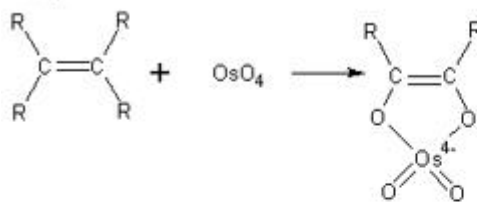
A. Nomenclature

1. Substitute "diol" for "ol" for alcohol name
2. Use locants as necessary
3. Note that the terminal "e" of the alkane name is dropped if the suffix begins with a vowel but is retained if it begins with a consonant
4. Common accepted IUPAC names: ethylene glycol, propylene glycol (glycol not otherwise accepted by IUPAC)
 - a. 1,2-ethanediol
 - b. 1,2-propanediol
 - c. 1,4-butanediol
5. Vicinal and geminal diols

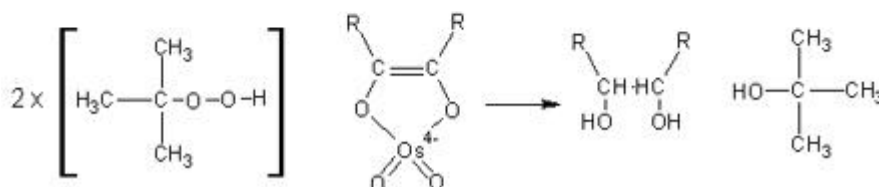
B. Preparation

1. Reduction of dialds and diones
2. Preparation of vicinal diols using osmium tetroxide
 - a. Hydroxylation: the process of adding a hydroxyl group to each of the two sp^2 -hybridized carbons in a double bond
 - b. Reaction of alkene with osmium tetroxide to form a cyclic osmate ester
 - c. Osmium tetroxide is a catalyst in this reaction
 - d. Oxidation of the ester t-butyl hydroperoxide to form the vicinal diol
 - e. Step 1: formation of the cyclic osmate ester
 - f. Step 2: oxidation of the ester and formation of the vicinal diol

Step 1.



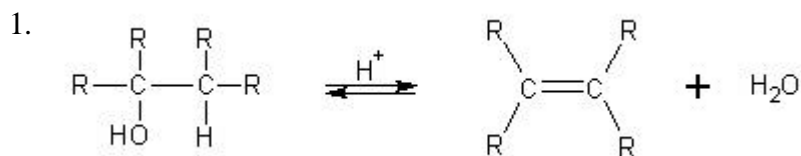
Step 2.



C. Reactions - chemistry similar to that of mono-ols

IV. Reactions of alcohols

A. Acid-catalyzed dehydration (Carey 5:9-13; March: 901ff)



2. Elimination reactions with carbocation mechanism

3. Order of reactivity: $3^\circ > 2^\circ > 1^\circ > \text{methyl}$

a. 3° alcohols dehydrate easily in the presence of even a trace of acid

4. Benzylic alcohols are very reactive

5. Dehydrations follow Zaitsev's rule: "the alkene formed in greatest amount is the one that corresponds to the removal of hydrogen from the beta carbon having the fewest hydrogens." (Carey: 184) - i.e., "the poor get poorer"

6. Rearrangements can complicate syntheses and are common with sulfuric and phosphoric acids

7. Vapor-phase eliminations over Al_2O_3 and other metal oxides greatly reduce side reactions

8. Numerous other ways of dehydrating alcohols

B. Reactions with hydrogen halides (Carey 4:8-13, March: 382ff)

1. $\text{ROH} + \text{HX} \rightarrow \text{RX} + \text{H}_2\text{O}$
2. Order of reactivity: $\text{HI} > \text{HBr} > \text{HCl} > \text{HF}$
3. Order of reactivity: $3^\circ > 2^\circ > 1^\circ > \text{methyl}$
4. Benzylic alcohols are very reactive
5. Alkyl iodides are generally made with HI, although more expensive reagents such as PI_5 , PI_3 , and SOI_2 can be used with equal success
6. Alkyl bromides are generally made with HBr, although more expensive reagents such as PBr_5 , PBr_3 , and SOBr_2 can be used with equal success
7. 3° alkyl chlorides are formed generally made with HCl, but 2° and 1° alcohols react so slowly with HCl that a catalyst is required
8. PCl_5 , PCl_3 , and SOCl_2 can be used with better success than HCl and with fewer problems with rearrangement
9. HF generally does not convert alcohols to alkyl fluorides
10. 3° and 2° react via an $\text{S}_{\text{N}}1$ mechanism (carbocation intermediate)
11. Because of the high energy associated with primary and methyl carbocations, 1° and methyl alcohols react via an $\text{S}_{\text{N}}2$ mechanism

C. Reactions with thionyl chloride (Carey 4:14)

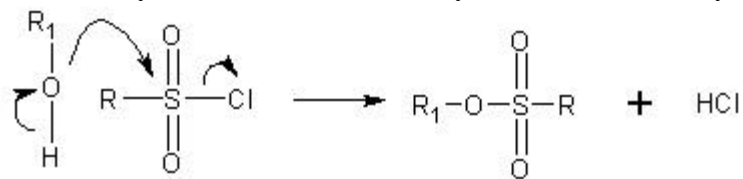
1. $\text{ROH} + \text{SOCl}_2 \rightarrow \text{RCl} + \text{SO}_2 + \text{HCl}$
2. That SO_2 and HCl are both gases at STP makes them easy to remove, which facilitates isolation of the alkyl chloride
3. Used to mostly to prepare 1° and 2° chlorides
4. Prepared in the presence of carbonate and pyridine

D. Reactions with phosphorus trihalides (Carey 4:14)

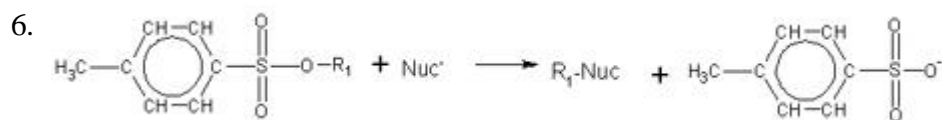
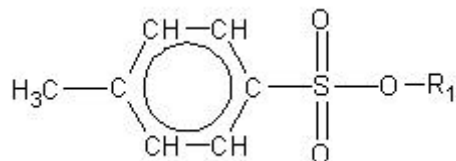
1. $3 \text{ROH} + \text{PX}_3 \rightarrow 3 \text{RX} + \text{H}_3\text{PO}_3$; $\text{X} = \text{Cl}, \text{Br}$
2. OH group is not broken during transfer to and formation of phosphorous acid

E. Conversion to p-toluenesulfonate esters (Carey 8:14)

1. Sulfonic acids: substituted sulfuric acid - RSO_3H
2. Sulfonic acid esters (sulfonates) are formed by substituting an alkyl group for the acidic proton
3. Alternatively, alcohol reacts with alkyl-substituted sulfonyl chloride



4. Alkyl sulfonate esters behave as alkyl halides w.r.t. participating in nucleophilic substitution and elimination reactions
5. p-toluenesulfonate (tosylate) is a better leaving group than iodide by a factor of nearly 1,000 (Table 8.8, Carey:327)



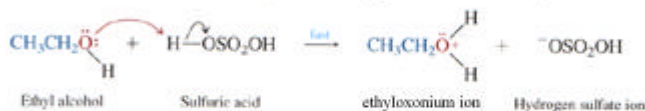
F. Acid-catalyzed conversion of primary alcohols to ethers

1. Condensation reactions: two molecules combine to form a larger molecule with incidental formation of a smaller molecule
2.
$$\text{R-CH}_2\text{-OH} \xrightarrow{\text{H}^+, \text{heat}} \text{R-CH}_2\text{-O-CH}_2\text{-R} + \text{H}_2\text{O}$$
3. Conditions are similar to those used to dehydrate alcohols, only at slightly lower temperatures
4. Mechanism of diethyl ether synthesis (Carey Figure 15.2, p. 592)

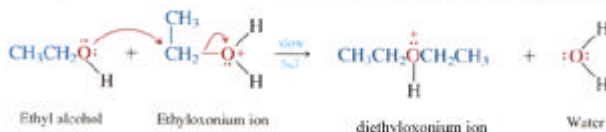
Overall Reaction:



Step 1: Proton transfer from the acid catalyst to the oxygen of the alcohol to produce an alkyloxonium ion



Step 2: Nucleophilic attack by a molecule of alcohol on the alkyloxonium ion formed in step 1



Step 3: The product of step 2 is the conjugate acid of the dialkyl ether. It is deprotonated in the final step of the process to give the ether.



5. Formation of cyclic ethers from diols

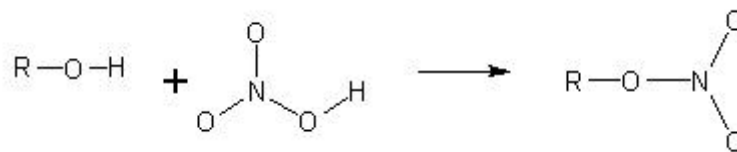
G. Fisher esterification: the reaction of an alcohol and a carboxylic acid to form an ester and water



2. The equilibrium conforms with LeChatlier's principle and product can be driven accordingly
3. Order of reactivity for alcohols determined by steric factors: methanol > 1° > 2° > 3°
4. Example: the reaction of acetic acid and ethanol
5. Esters can also be formed by the reactions of acid (acyl) chlorides or acid anhydrides with alcohols

H. Inorganic esters: alcohols can also react with inorganic acids to form inorganic esters

1. Alkyl nitrate synthesis: the reaction of alcohols and nitric acid

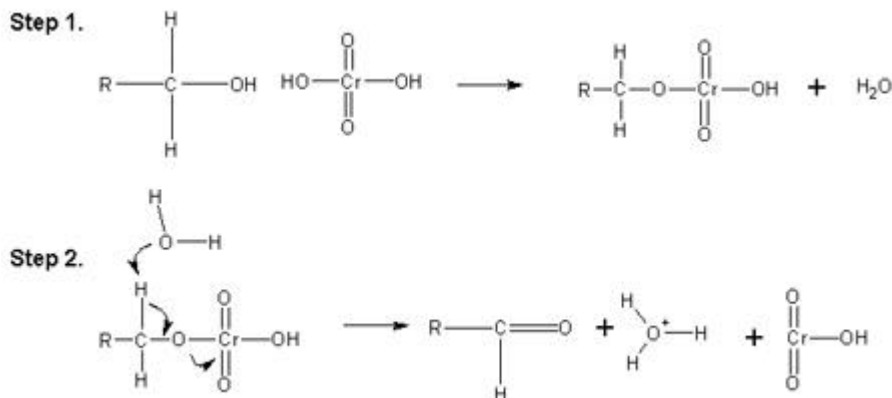


2. Alcohols react similarly with sulfuric acid to form dialkyl sulfates, and with

phosphorous and phosphoric acid to form trialkyl phosphites and phosphates respectively

I. Oxidation of alcohols

1. Primary alcohols can be oxidized to form aldehydes or carboxylic acids
2. Secondary alcohols can be oxidized to form ketones
3. Tertiary alcohols are generally unreactive toward oxidizing agents; at elevated temperatures strong oxidizing agents result in carbon-carbon bond cleavage
4. Oxidizing agents act on hydrogen atoms attached to the carbon bonded to the hydroxyl group
5. Common oxidizing agents
 - a. Potassium permanganate (usually results in oxidation from alcohol to acid)
 - b. Sodium dichromate in sulfuric acid (usually results in oxidation from alcohol to acid)
 - c. Pyridinium chlorochromate (PCC) and pyridinium dichromate (PDC) in methylene chloride permit oxidation of alcohols to aldehydes
6. Mechanism of action for chromic acid: formation of alkyl chromate ester and subsequent elimination of alpha hydrogen to form carbonyl group



J. Oxidative cleavage of vicinal diols

1. The carbon-carbon bond of vicinal diols is cleaved by periodic acid (HIO_4) and result in the formation of two carbonyl groups
2. Example: the reaction of 2-methyl-2,3-pentanediol

V. Thiols: sulfur analogues of alcohols (as compared to sulfides which are ether analogues)

A. Nomenclature

1. "Thiol" and "dithiol" used similarly to "ol" and "diol" for alcohols
 - a. 2,4-dimethyl-1-pentanethiol
 - b. 2,4-dimethyl-2-pentanethiol
 - c. 2,3-butanedithiol
2. As substituents referred to as "mercapto" (sulfhydryl) groups
 - a. 2-mercapto-1-propanol

B. Properties

1. Odor
2. Weak acids but more acidic than water or alcohols- pKa values around 10 and up
3. Oxidation of C-S bond to C=S does not occur
4. Oxidation of R-SH to R-S-S-R does occur

C. Preparation

1. Two step process
 - a. Reaction of alkyl halide with thiourea
 - b. Base-catalyzed hydrolysis of resulting ion to form thiol

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