

## Chapter 15: Alcohols, Diols, and Thiols

### 15.1: Sources of Alcohols (please read)

Hydration of alkenes (Chapter 6)

1. Acid catalyzed hydration
2. Oxymercuration
3. Hydroboration

Hydrolysis of alkyl halides (Chapter 8)  
nucleophilic substitution

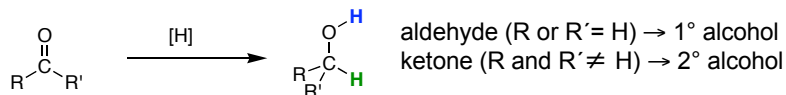
Reaction of Grignard or organolithium reagents with  
ketones, aldehydes, and esters. (Chapter 14)

Reduction of aldehydes, ketones, esters, and  
carboxylic acids (Chapter 15.2 - 15.3)

Reaction of epoxides with Grignard Reagents (Chapter 15.4)

Diols from the dihydroxylation of alkenes (Chapter 15.5)

### 15.2: Preparation of Alcohols by Reduction of Aldehydes and Ketones - add the equivalent of H<sub>2</sub> across the π-bond of the carbonyl to yield an alcohol

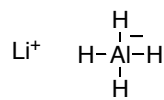
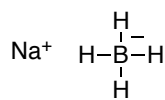


Catalytic hydrogenation is not typically used for the reduction of ketones or aldehydes to alcohols.

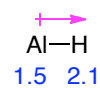
Metal hydride reagents: equivalent to H<sup>-</sup> (hydride)

sodium borohydride  
(NaBH<sub>4</sub>)

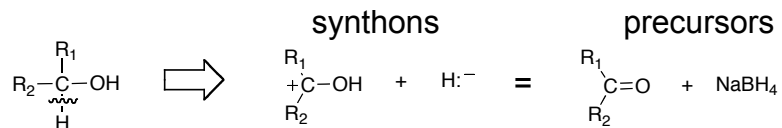
lithium aluminium hydride  
(LiAlH<sub>4</sub>)



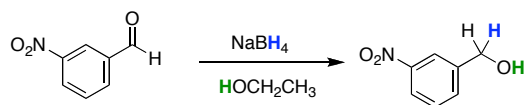
electronegativity



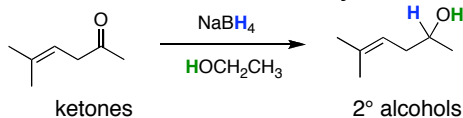
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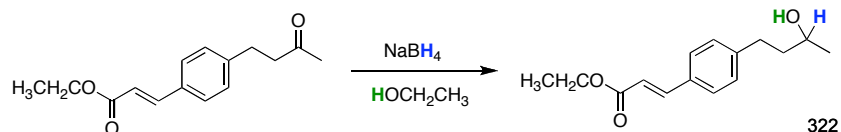
$NaBH_4$  reduces aldehydes to primary alcohols



$NaBH_4$  reduces ketones to secondary alcohols

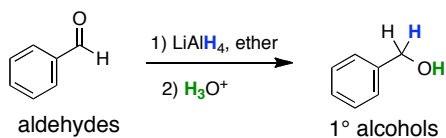
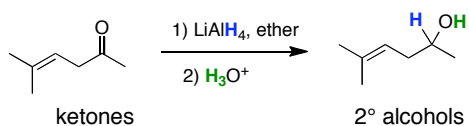


$NaBH_4$  does not react with esters or carboxylic acids



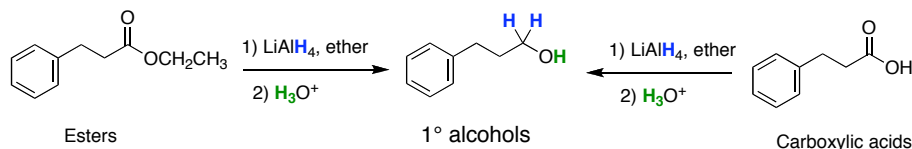
Lithium Aluminium Hydride ( $LiAlH_4$ , LAH) - much more reactive than  $NaBH_4$ . Incompatible with protic solvents (alcohols,  $H_2O$ ).

$LiAlH_4$  (in ether) reduces aldehydes, carboxylic acids, and esters to 1° alcohols and ketones to 2° alcohols.

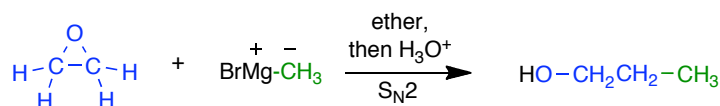


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**15.3: Preparation of Alcohols By Reduction of Carboxylic Acids and Esters - LiAlH<sub>4</sub> (but not NaBH<sub>4</sub> or catalytic hydrogenation).**

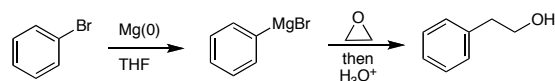
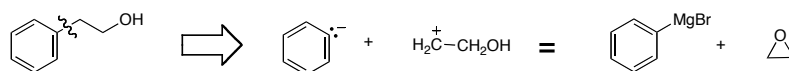


**15.4: Preparation of Alcohols From Epoxides - the three-membered ring of an epoxide is strained. Epoxides undergo ring-opening reaction with nucleophiles (Grignard reagents, organolithium reagents, and cuprates).**



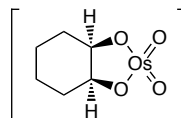
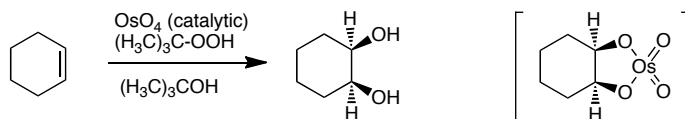
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disconnection                      synthons                      precursors



**15.5: Preparation of Diols - Vicinal diols have hydroxyl groups on adjacent carbons (1,2-diols, vic-diols, glycols)**

Dihydroxylation: formal addition of HO-OH across the  $\pi$ -bond of an alkene to give a 1,2-diol. This is an overall oxidation.



osmate ester intermediate

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### 15.6: Reactions of Alcohols: A Review and a Preview

Conversion to alkyl halides (Chapter 4)

1. Reaction with hydrogen halides
2. Reaction with thionyl chloride
3. Reaction with phosphorous trihalides

Acid-catalyzed dehydration to alkenes (Chapter 5)

Conversion to *p*-toluenesulfonate esters (Chapter 8)

Conversion to ethers (Chapter 15.7)

Conversion to esters (Chapter 15.8)

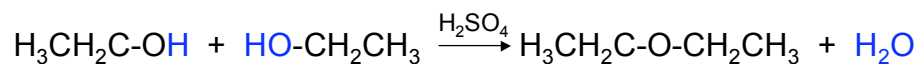
Esters of inorganic acids (Chapter 15.9)

Oxidation to carbonyl compounds (Chapter 15.10)

Cleavage of vicinal diols to ketones and aldehydes  
(Chapter 15.12)

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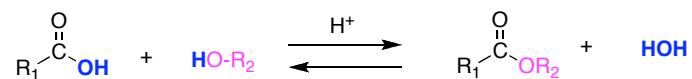
**15.7: Conversion of Alcohols to Ethers** - Symmetrical ethers can be prepared by treating the corresponding alcohol with a strong acid.



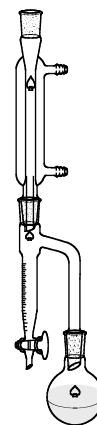
Limitations: ether must be symmetrical  
works best for 1° alcohols

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**15.8: Esterification** - Fischer esterification: acid-catalyzed reaction between a carboxylic acid and alcohol to afford an ester. The reverse reaction is the *hydrolysis* of an ester



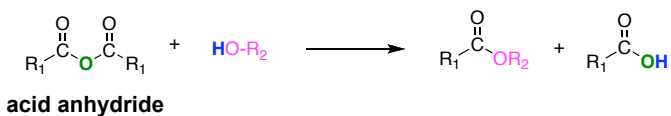
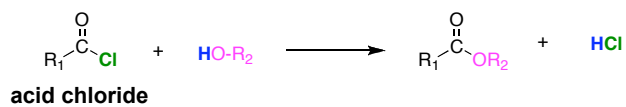
Mechanism (Chapters 19 and 20)



Dean-Stark Trap

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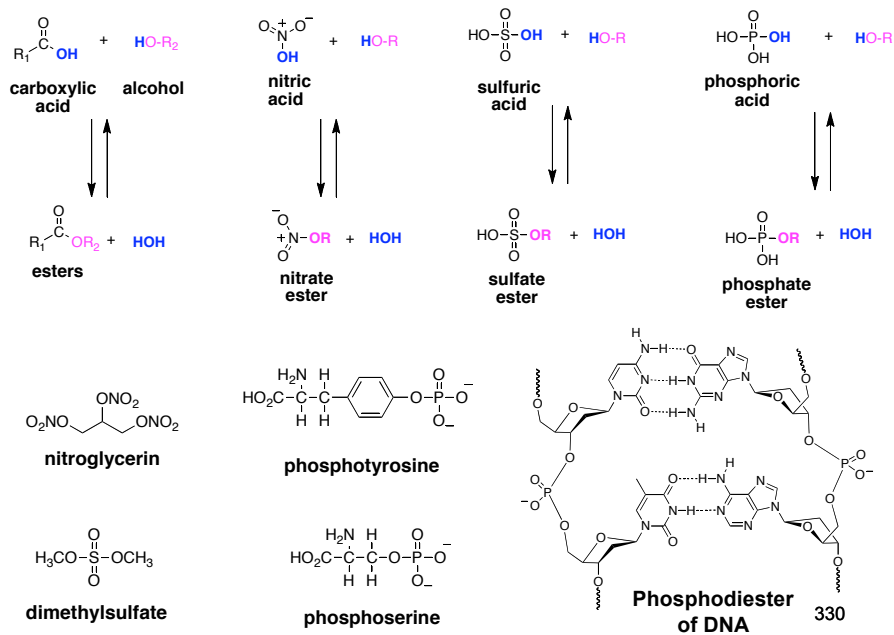
Ester formation via the reaction of an acid chloride or acid anhydride with an alcohol (nucleophilic acyl substitution)



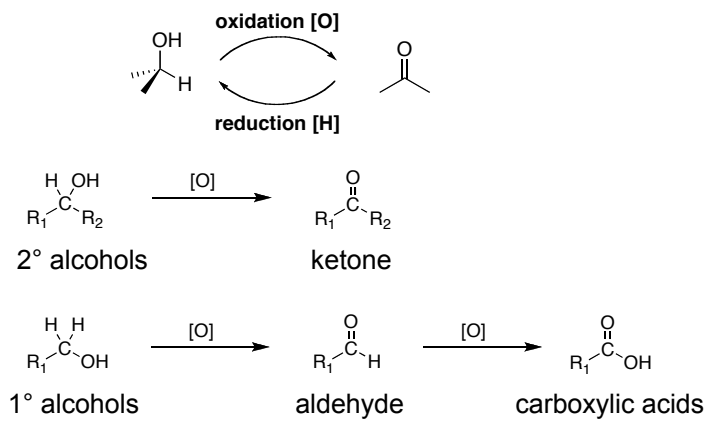
Mechanism (Chapters 20)

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### 15.9: Esters of Inorganic Acids (please read)



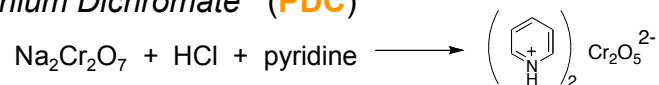
### 15.10: Oxidation of Alcohols



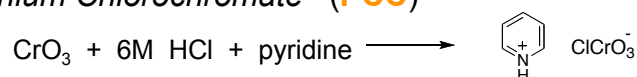
$\text{KMnO}_4$  and chromic acid ( $\text{Na}_2\text{Cr}_2\text{O}_7$ ,  $\text{H}_3\text{O}^+$ ) oxidize secondary alcohols to ketones, and primary alcohols to carboxylic acids.

Oxidation of primary alcohols to aldehydes

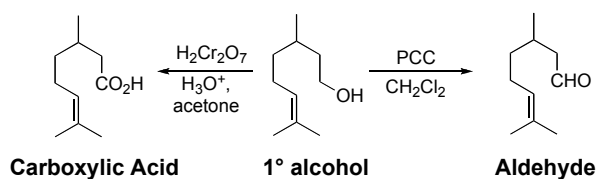
**Pyridinium Dichromate (PDC)**



**Pyridinium Chlorochromate (PCC)**



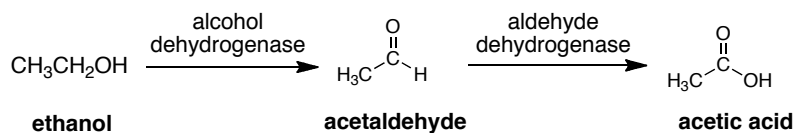
PCC and PDC are soluble in *anhydrous* organic solvent such as  $\text{CH}_2\text{Cl}_2$ . The oxidation of primary alcohols with PCC or PDC in anhydrous  $\text{CH}_2\text{Cl}_2$  stops at the aldehyde.



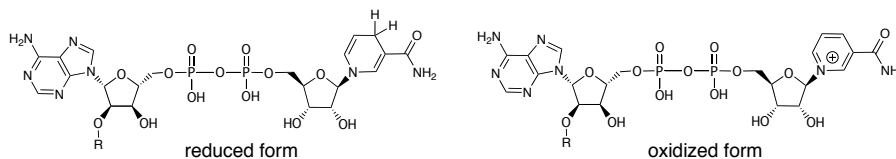
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### 15.11: Biological Oxidation of Alcohols (please read)

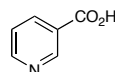
Ethanol metabolism:



Nicotinamide Adenine Dinucleotide (NAD)



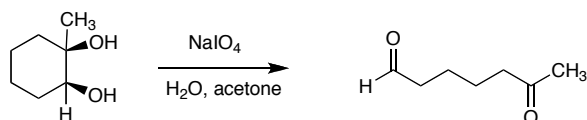
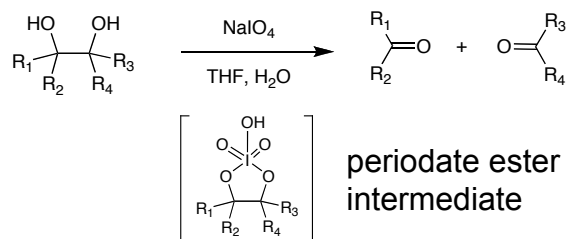
Vitamin B<sub>3</sub>, nicotinic acid, niacin



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### 15.12: Oxidative Cleavage of Vicinal Diols

Oxidative Cleavage of 1,2-diols to aldehydes and ketones with sodium periodate ( $\text{NaIO}_4$ ) or periodic acid ( $\text{HIO}_4$ )

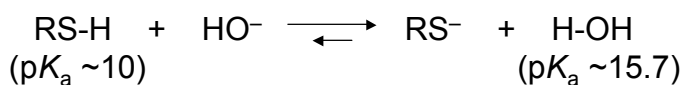


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### 15.13: Thiols

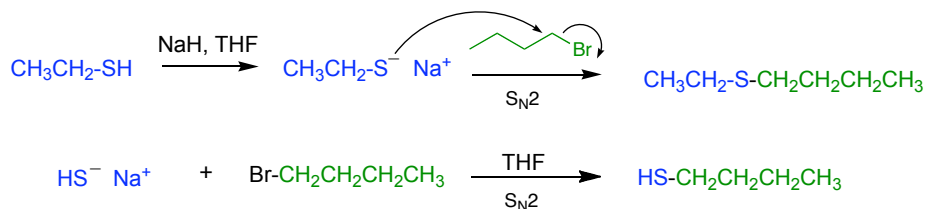
Thiols (mercaptans) are sulfur analogues of alcohols.

Thiols have a  $\text{p}K_a \sim 10$  and are stronger acids than alcohols.



$\text{RS}^-$  and  $\text{HS}^-$  are weakly basic and strong nucleophiles.

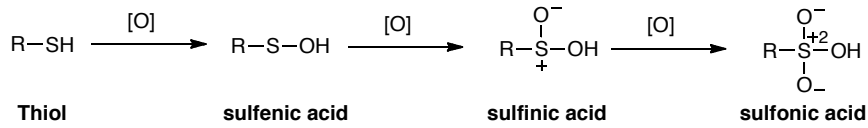
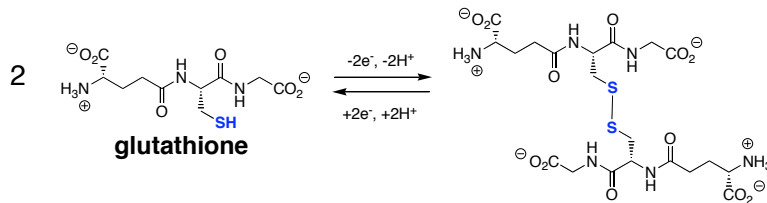
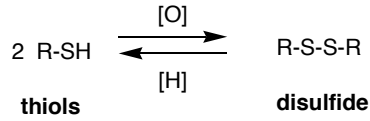
Thiolates react with  $1^\circ$  and  $2^\circ$  alkyl halides to yield sulfides ( $\text{S}_{\text{N}}2$ ).



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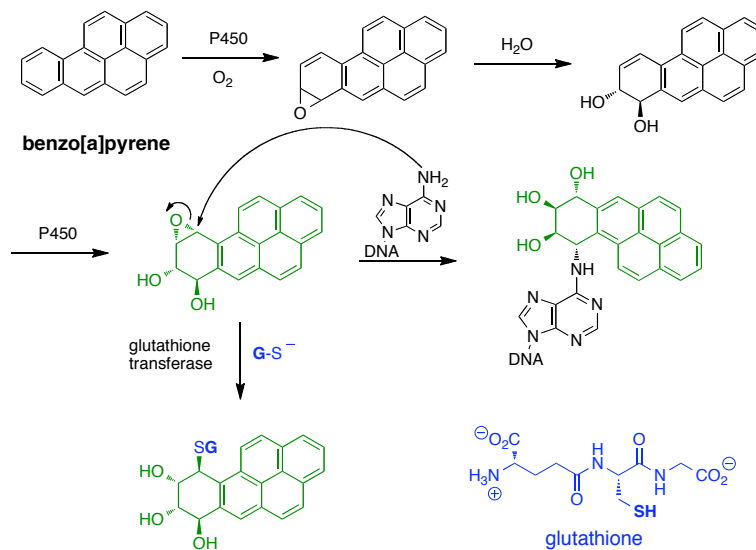


Thiols can be oxidized to disulfides



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**Bioactivation and detoxication of benzo[a]pyrene diol epoxide:**



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