

# **Chapter 11:**

# **Reactions of Alcohols**

- Alcohols are often referred to as the central functional group (FG) because all other FG can be obtained from alcohols. Here is a summary of some of the possible transformations of alcohols.

**TABLE 11-1**

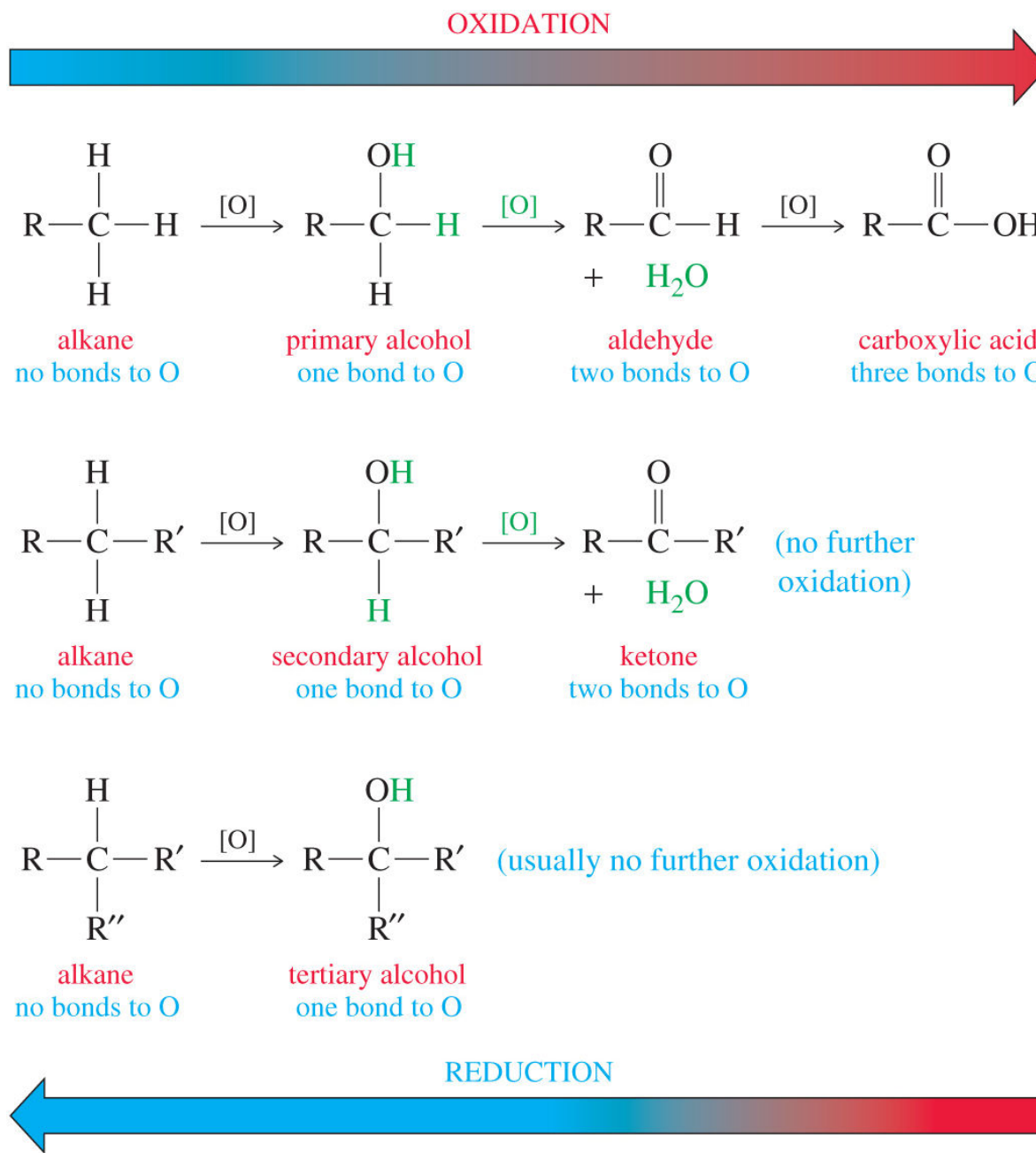
Types of Reactions of Alcohols

$R-OH$		$\xrightarrow{\text{type of reaction}}$	Product
$R-OH$	$\xrightarrow{\text{dehydration}}$	alkenes	
$R-OH$	$\xrightarrow{\text{oxidation}}$	ketones, aldehydes, acids	
$R-OH$	$\xrightarrow{\text{substitution}}$	$R-X$ halides	
$R-OH$	$\xrightarrow{\text{reduction}}$	$R-H$ alkanes	
$R-OH$	$\xrightarrow{\text{esterification}}$		$R-O-\overset{\text{O}}{\parallel}{C}-R'$ esters
$R-OH$	$\xrightarrow{\text{tosylation}}$		$R-OTs$ tosylate esters (good leaving group)
$R-OH$	$\xrightarrow{\begin{matrix} (1) \text{ form alkoxide} \\ (2) R'X \end{matrix}}$		$R-O-R'$ ethers

- **Oxidation States of Alcohols (11.1)**

**Alcohols are more oxidized than alkanes but less oxidized than the corresponding carbonyl compounds such as ketones and aldehydes. The oxidation state of organic molecules can be summarized in the figure on the next slide.**

**In the presence of an oxidizing agent [O], it is possible to change the alcohols into a ketone, aldehyde or carboxylic acid.**

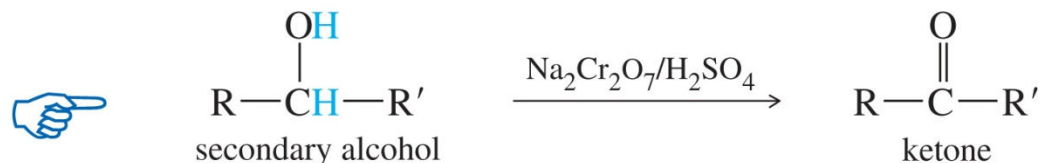


- **Oxidation of Alcohols (11.2)**

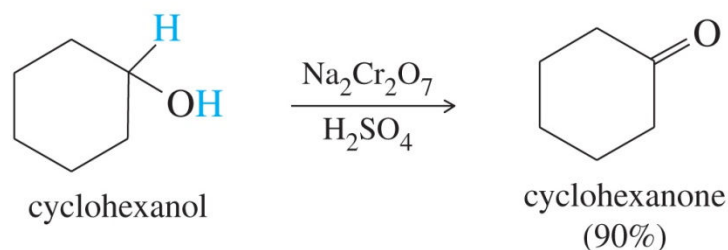
**Oxidizing agents such as those listed below are often used.**

- Cr (VI) reagents (Chromic acid) (most common)**
- KMnO<sub>4</sub>**
- HNO<sub>3</sub>**
- NaOCl (hypochlorite: bleach)**

- **Secondary alcohols will always produce ketones. Chromic acid is a common reagent used to carry out oxidation of alcohols.**



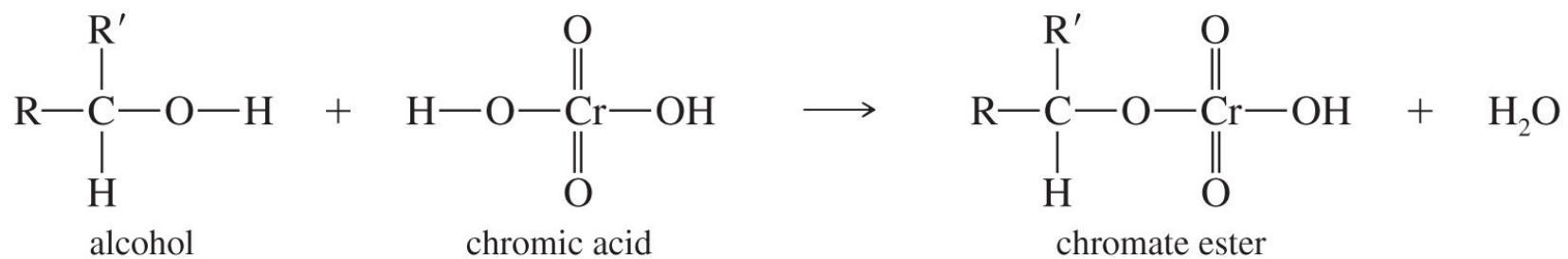
*Example*



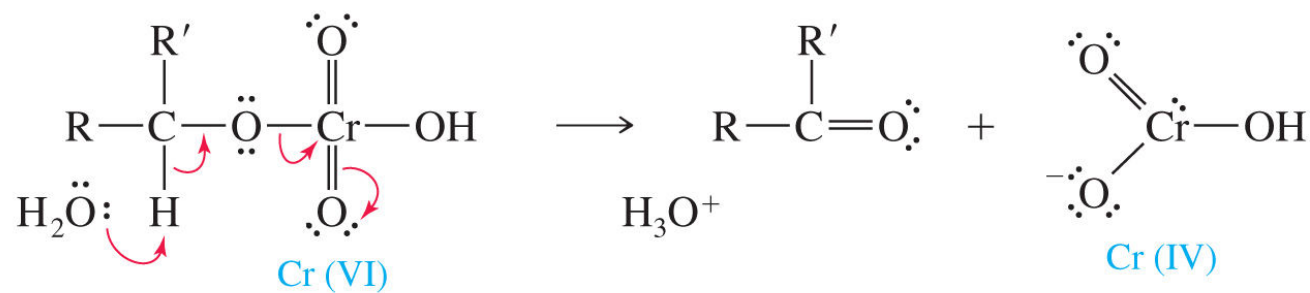
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**Note: When  $\text{CrO}_3$  or  $\text{Na}_2\text{Cr}_2\text{O}_7$  or  $\text{K}_2\text{Cr}_2\text{O}_7$  is dissolved in aqueous acid, chromic acid ( $\text{H}_2\text{CrO}_4$ ) is formed and is the oxidizing agent.**

*Formation of the chromate ester*

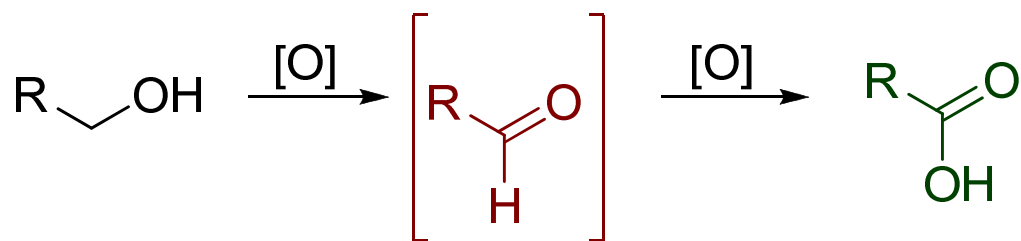


*Elimination of the chromate ester and oxidation of the carbinol carbon*

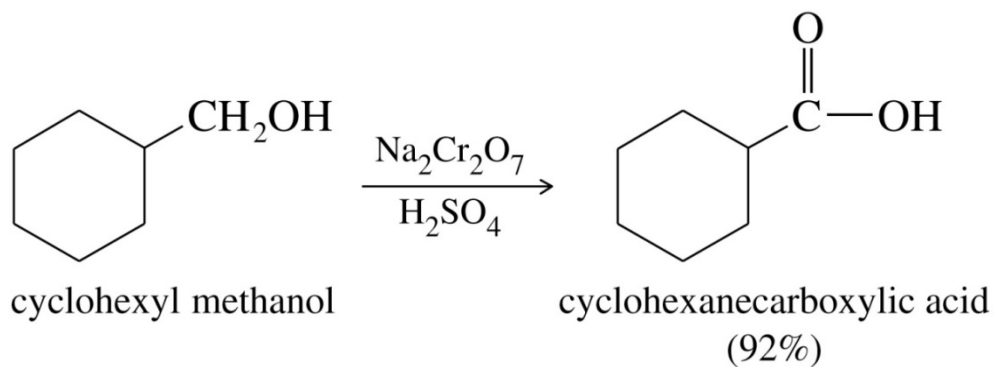


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- **Primary alcohols will also be oxidized by chromic acid. An aldehyde is first produced and react further to give the corresponding carboxylic acid. Other reagents listed on slide 137 will also give **carboxylic acids**.**

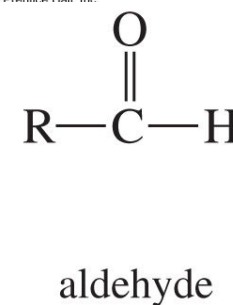
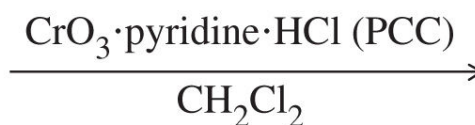
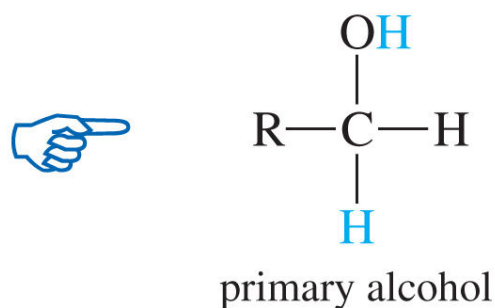


Chromic acid is too reactive and the aldehyde formed cannot be isolated. It is further oxidized to the product, a carboxylic acid

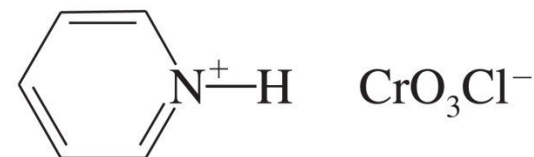




- **Primary alcohols can be oxidized to the aldehydes using a less reactive oxidant, PCC**



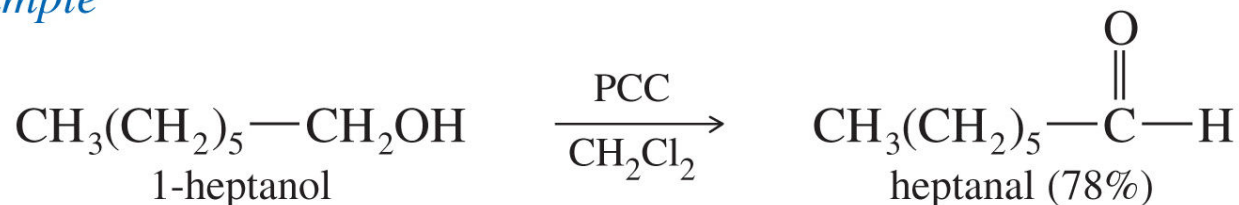
*Pyridinium chlorochromate (PCC):*



$\text{CrO}_3 \cdot \text{pyridine} \cdot \text{HCl}$   
or  $\text{pyH}^+ \text{CrO}_3\text{Cl}^-$

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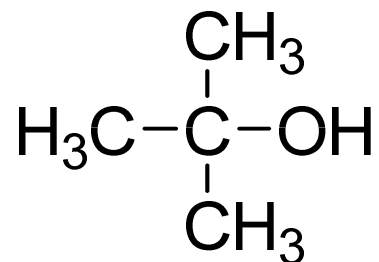
*Example*



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- **PCC will also transform a 2° alcohol into the corresponding ketone**

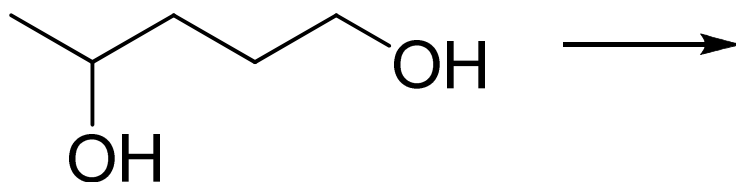
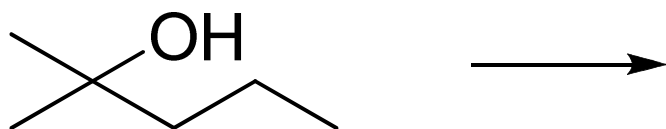
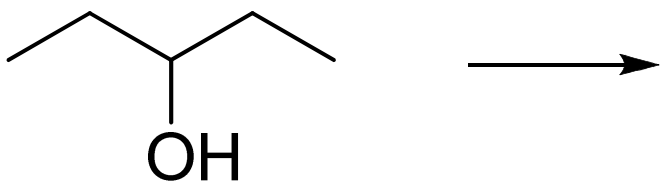
- **Tertiary alcohols cannot be oxidized to a carbonyl compound, as it would involve the breaking of one C-C bond in the process.**



tertiary alcohol..no  
oxidation possible

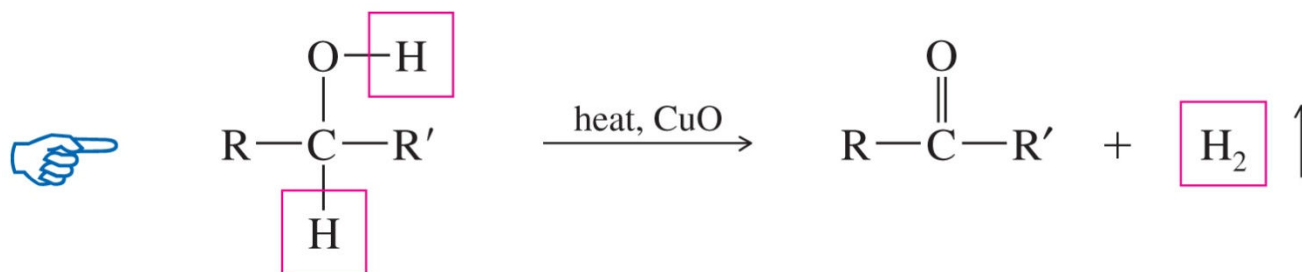
# Practice Questions

- What are the major products in each of the following oxidation with sodium dichromate in sulfuric acid?



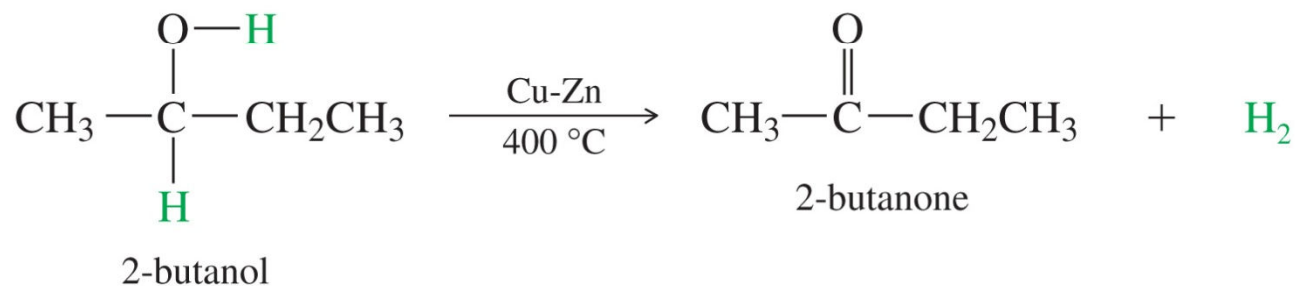
- Additional Methods of Oxidizing Alcohols (11.3)

There are many other methods available to oxidize alcohols. Here are examples:



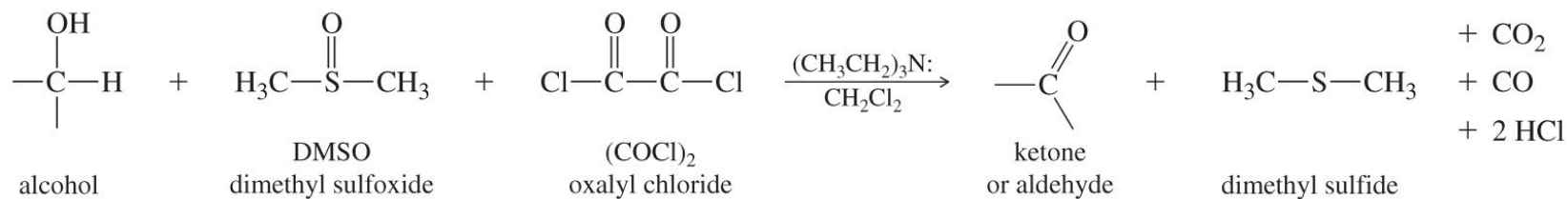
**A dehydrogenation reaction**

*Example*

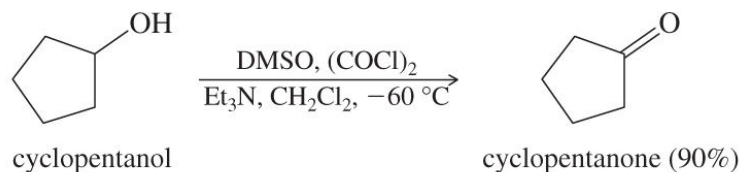


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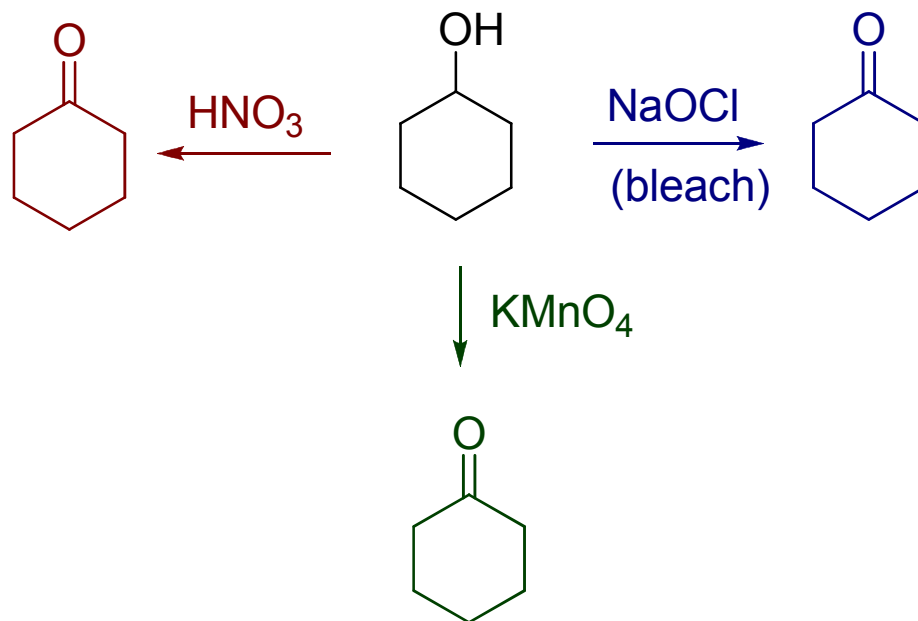
## • Swern Oxidation:



### Examples



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# Summary

## Summary of Alcohol Oxidations

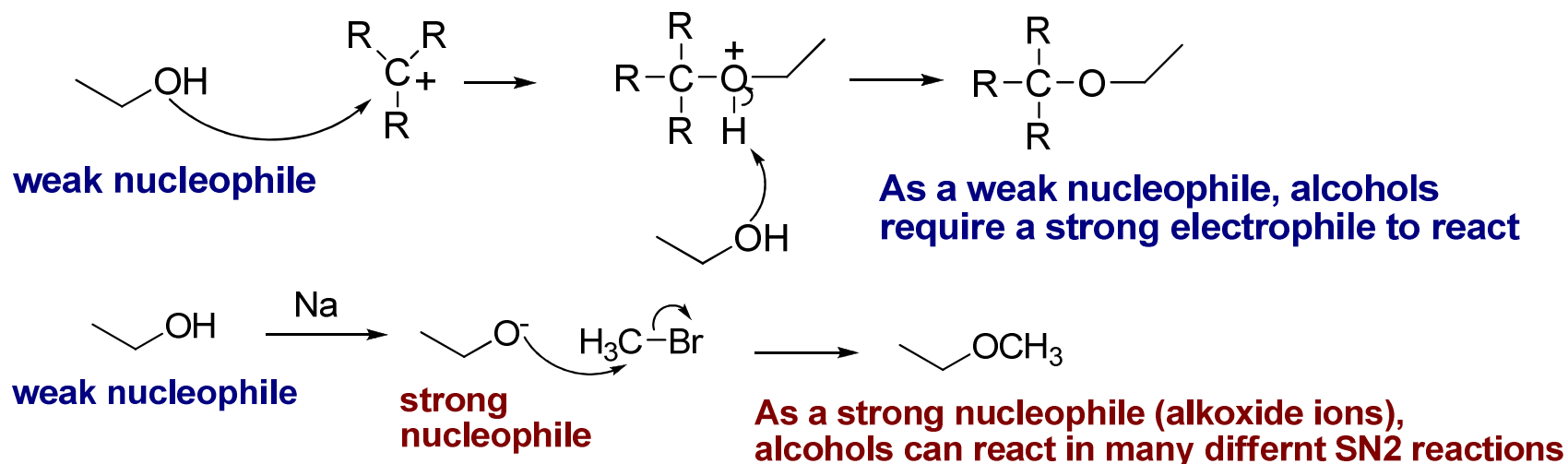
To Oxidize	Product	Reagent
2° alcohol	ketone	chromic acid (or PCC)
1° alcohol	aldehyde	PCC
1° alcohol	carboxylic acid	chromic acid

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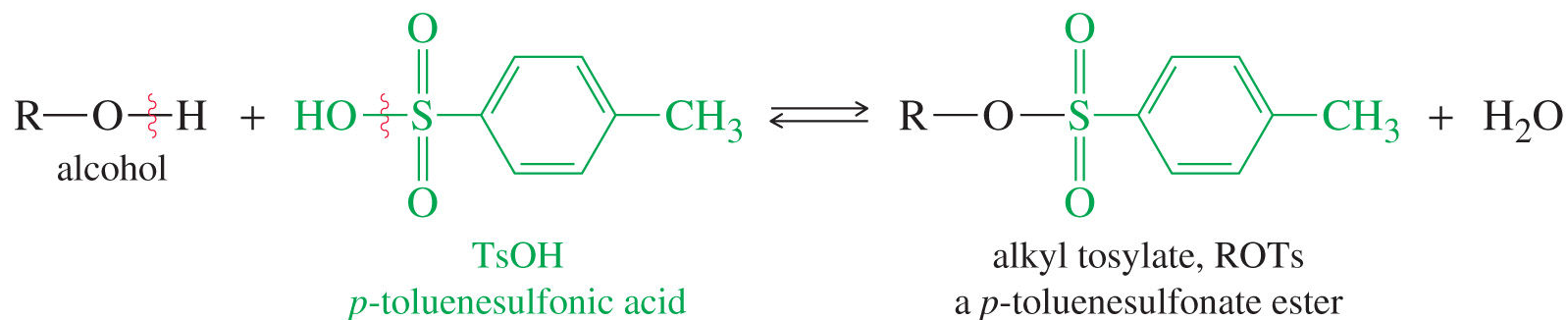
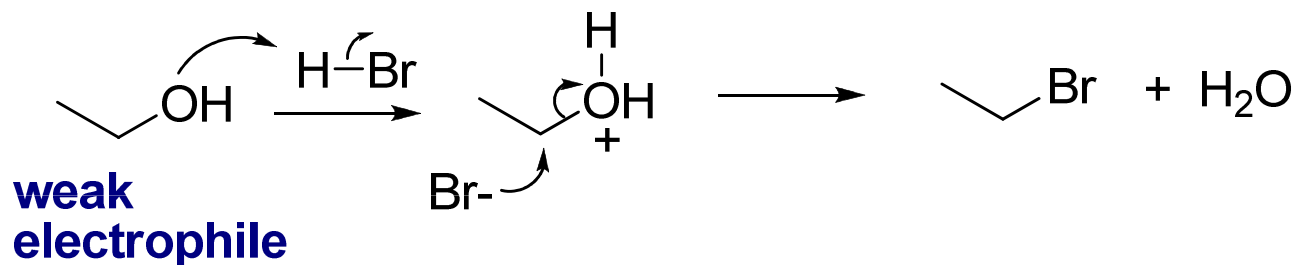
- Alcohols as Nucleophiles or Electrophiles (11.5)

Alcohols are highly versatile and can be used as both electrophile or nucleophile in organic reactions.

Alcohols can be used as a weak or strong nucleophile. This is the natural reactivity of alcohols.



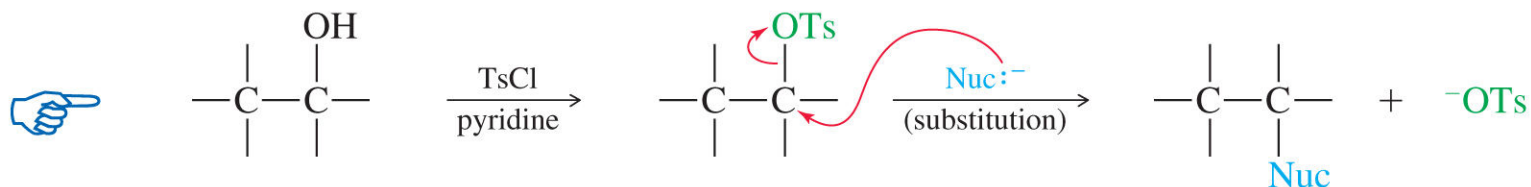
**As electrophiles, alcohols are considered weak because the hydroxyl group is a poor leaving group. As such, the hydroxyl group must be transformed into a good leaving group prior to reacting as an electrophile.**



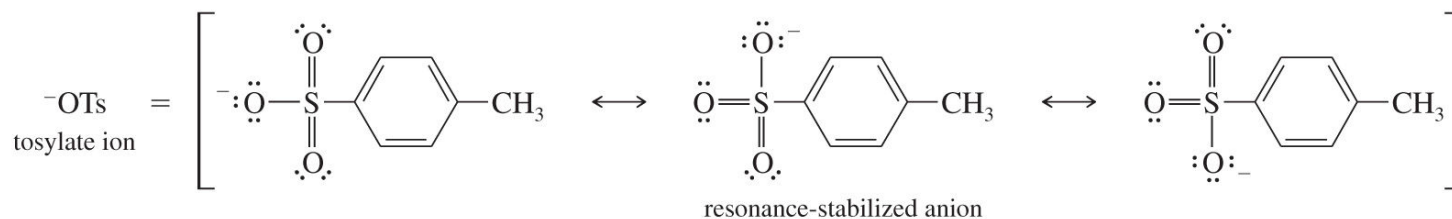
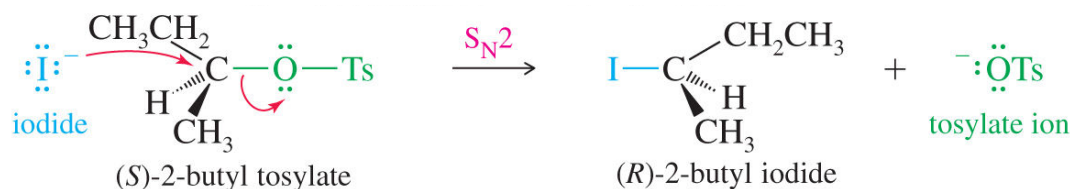
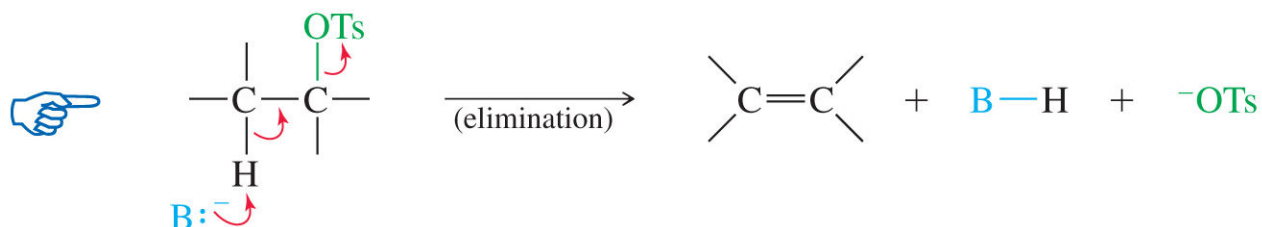
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**Sulfonate Esters are equivalent or better leaving groups than halides. They are easily prepared from alcohols and react just like halides in S<sub>N</sub>1 or S<sub>N</sub>2 reactions**

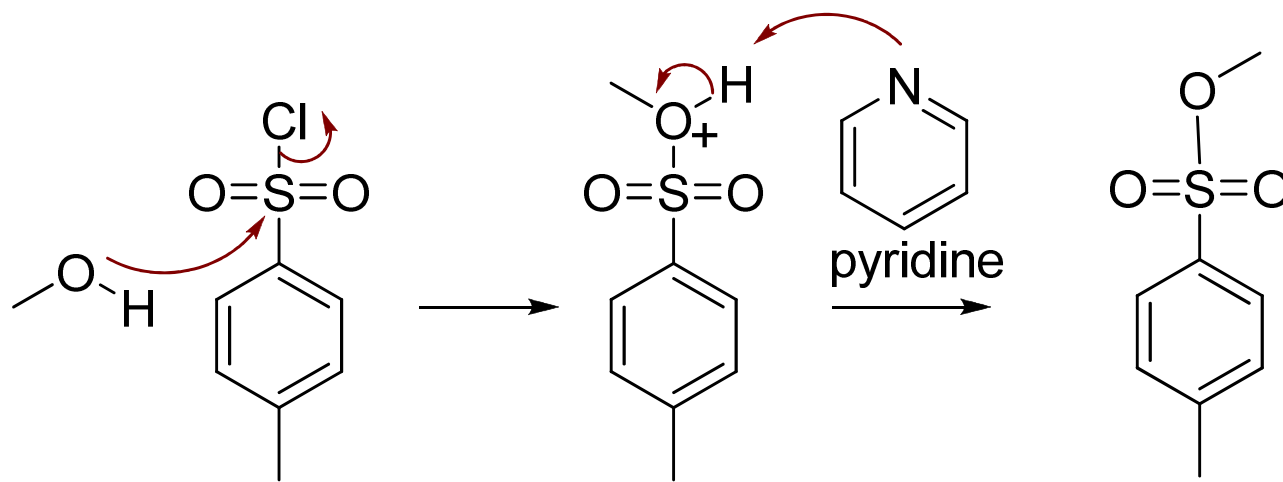


or elimination:



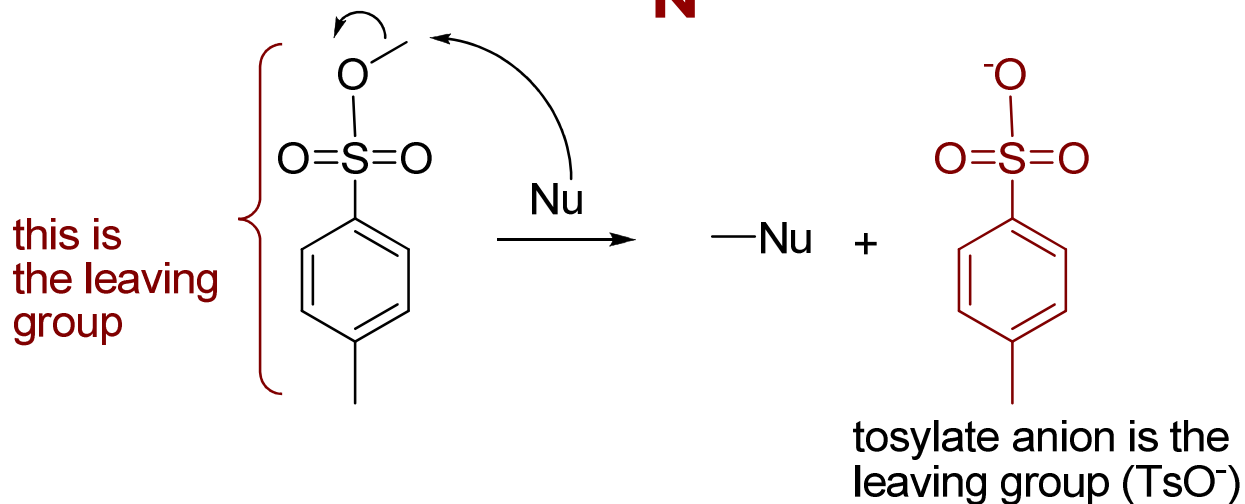
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# Mechanism of Formation of Tosylates



ROTs, a tosylate ester

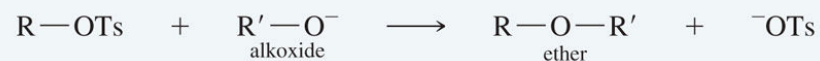
## Mechanism of $S_N2$ reactions



# Summary of Tosylate Reactions

## SUMMARY

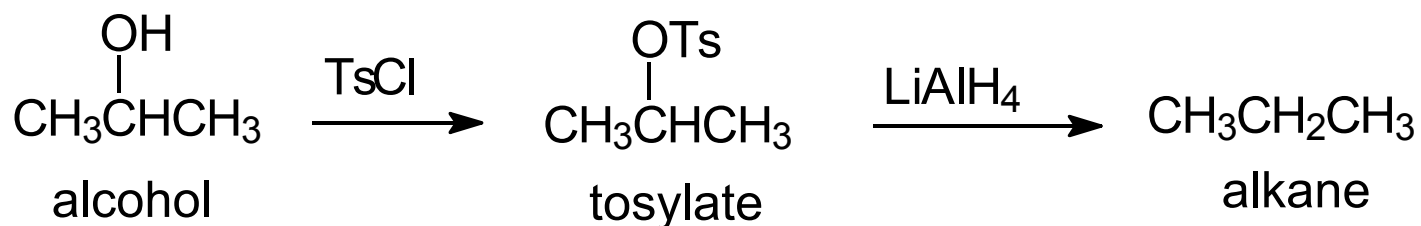
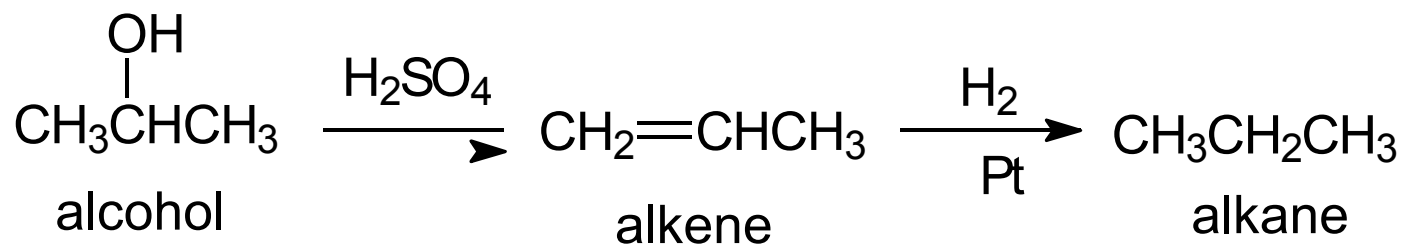
### S<sub>N</sub>2 Reactions of Tosylate Esters



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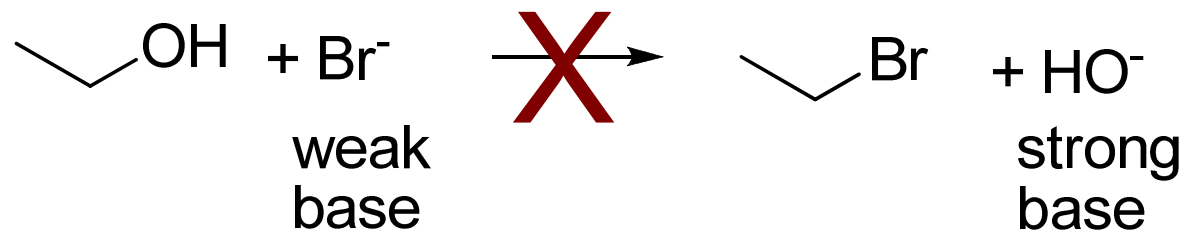
- Reduction of Alcohols (11-6)

**Reduction of alcohols is rare since it removes the functional group. However, it can be easily accomplished if necessary using two common methods.**



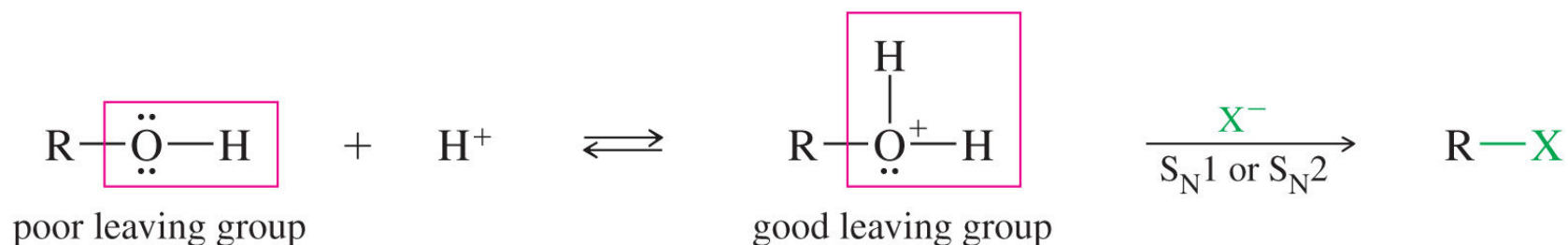
- Reactions of Alcohols with HX (11.7)

We have just seen that alcohol have a strongly basic leaving group ( $\text{HO}^-$ ) that cannot be displaced by a nucleophile. Therefore, an alcohol cannot undergo a nucleophilic substitution reaction.



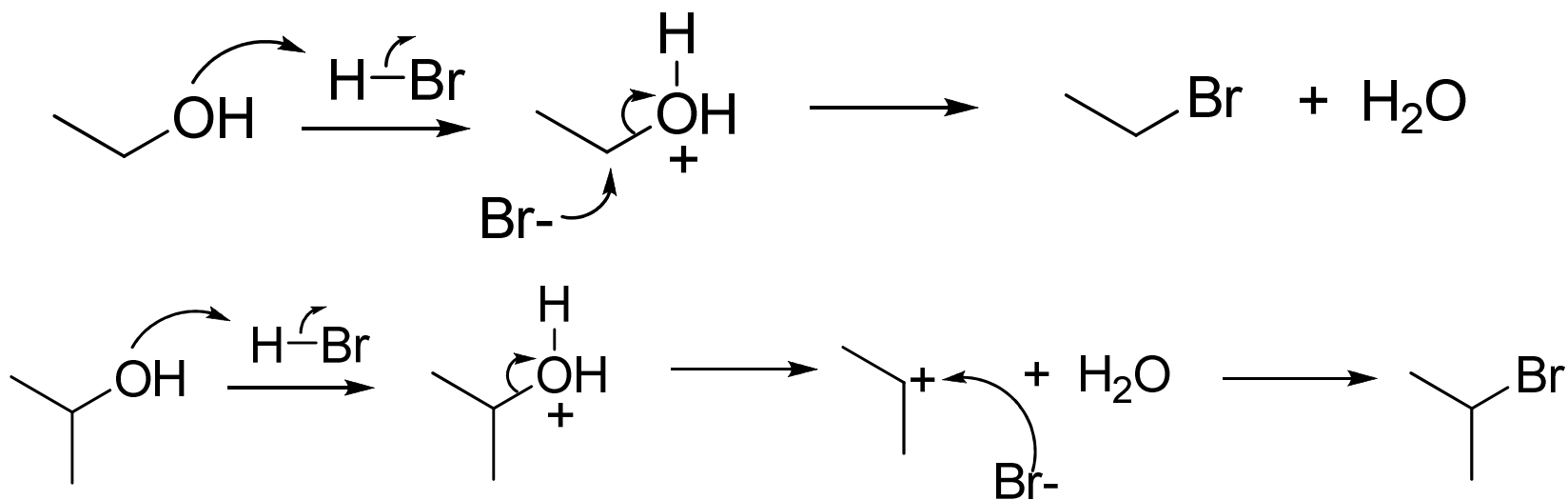
$\text{S}_{\text{N}}2$  reaction directly on alcohols is not possible since the leaving group ( $\text{HO}^-$ ) is usually more basic than the nucleophile

**However, if the alcohol's OH group is converted into a group that is a weaker base (and therefore a better leaving group), a nucleophilic substitution reaction can occur. One way to convert an OH group into a weaker base is to protonate it by adding acid to the solution.**

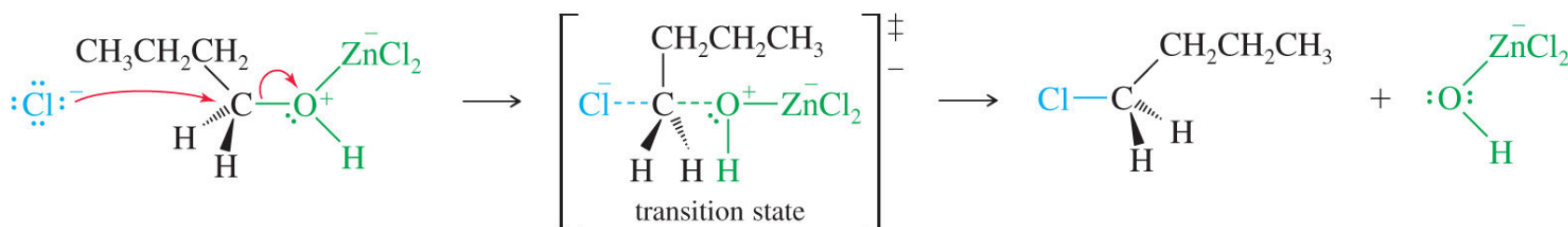
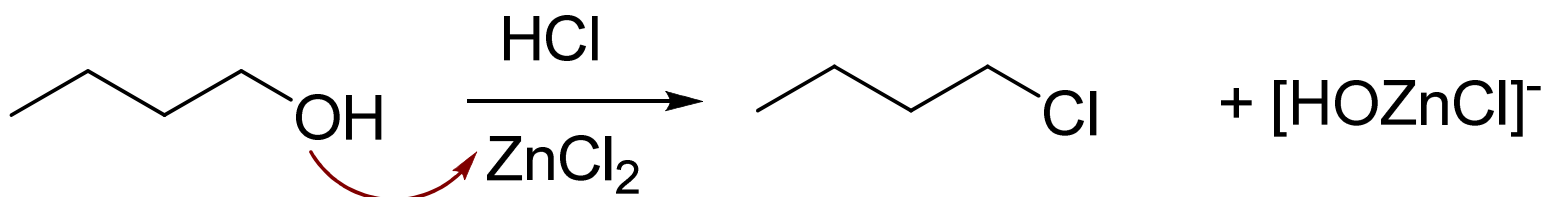


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- 1°, 2° and 3° alcohols will react with HBr to give R-Br. Reactions with HCl are not good with 1° and 2° alcohols, but work well with 3° alcohols. Reactions with HI are almost impossible.
- 1° alcohols follow a S<sub>N</sub>2 mechanism, while 2° and 3° will follow a S<sub>N</sub>1 mechanism



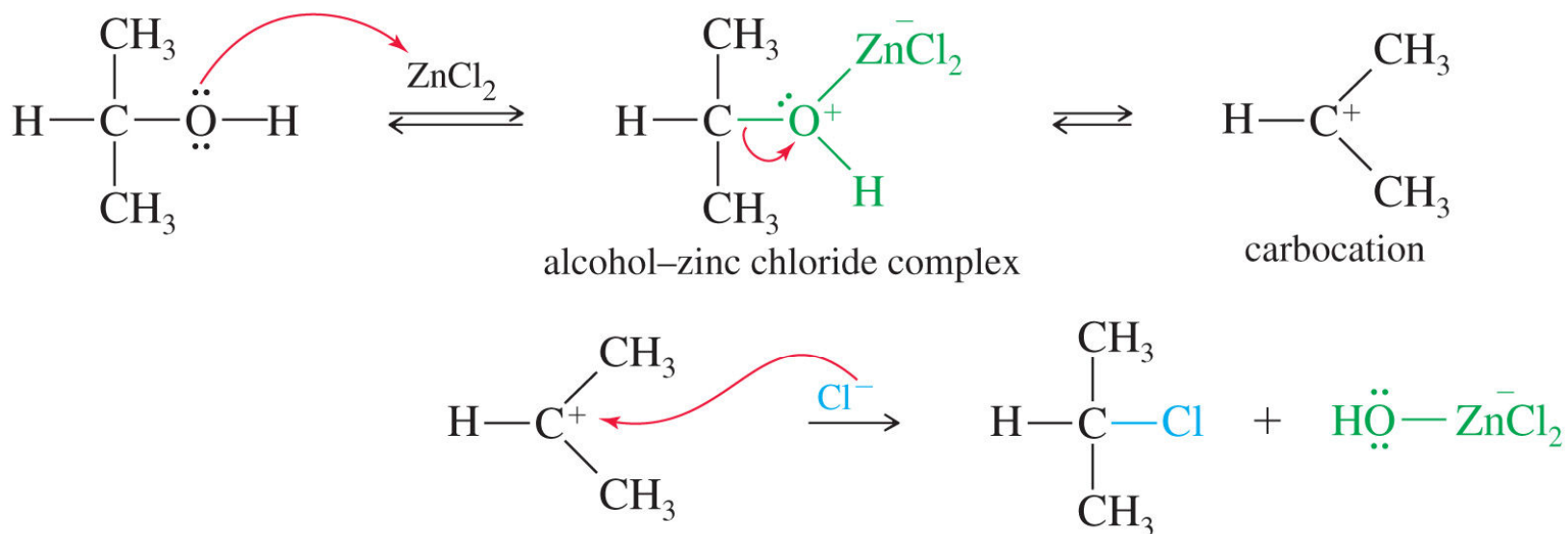
- When HCl is used with 1° and 2° alcohols, a Lewis acid (ZnCl<sub>2</sub>) is needed to carry out the reaction. 3° Alcohols react with HCl without the need for ZnCl<sub>2</sub>. The combination of HCl and ZnCl<sub>2</sub> is known as the Lucas reagent. 1° alcohols follow an S<sub>N</sub>2 mechanism,



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**while secondary alcohols follow a SN1 mechanism as shown below.**

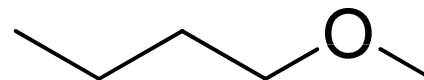


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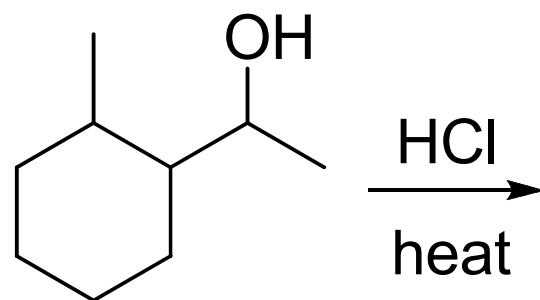
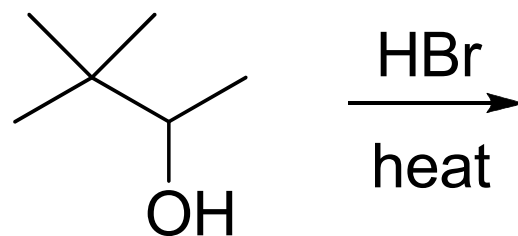
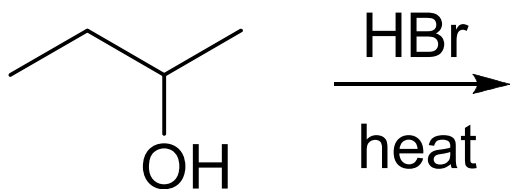
- **The transformation of R-OH into R-X now allows for any other transformation of R-X via  $S_N1$  or  $S_N2$  reactions. (see CHEM201, Chapter 6)**
- **The reactions of Alcohols with HX has limitations:**
  - **Poor yields with HCl for  $1^\circ$  and  $2^\circ$  alcohols**
  - **Eliminations are often a side reaction (sometimes provide the major product)**
  - **Rearrangement of carbocations are possible**
  - **Alkyl iodides are difficult to obtain using this method**

# Practice Questions

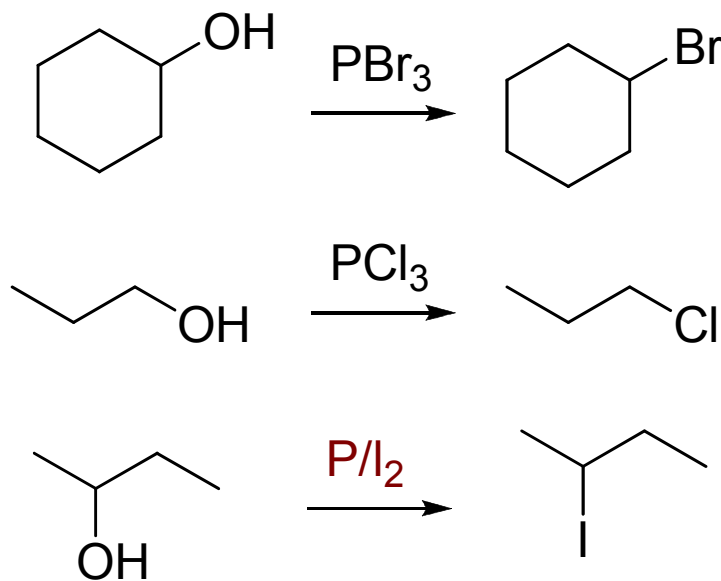
- Show how 1-butanol can be converted to the following compounds.



- What is the major organic product of the following reactions?

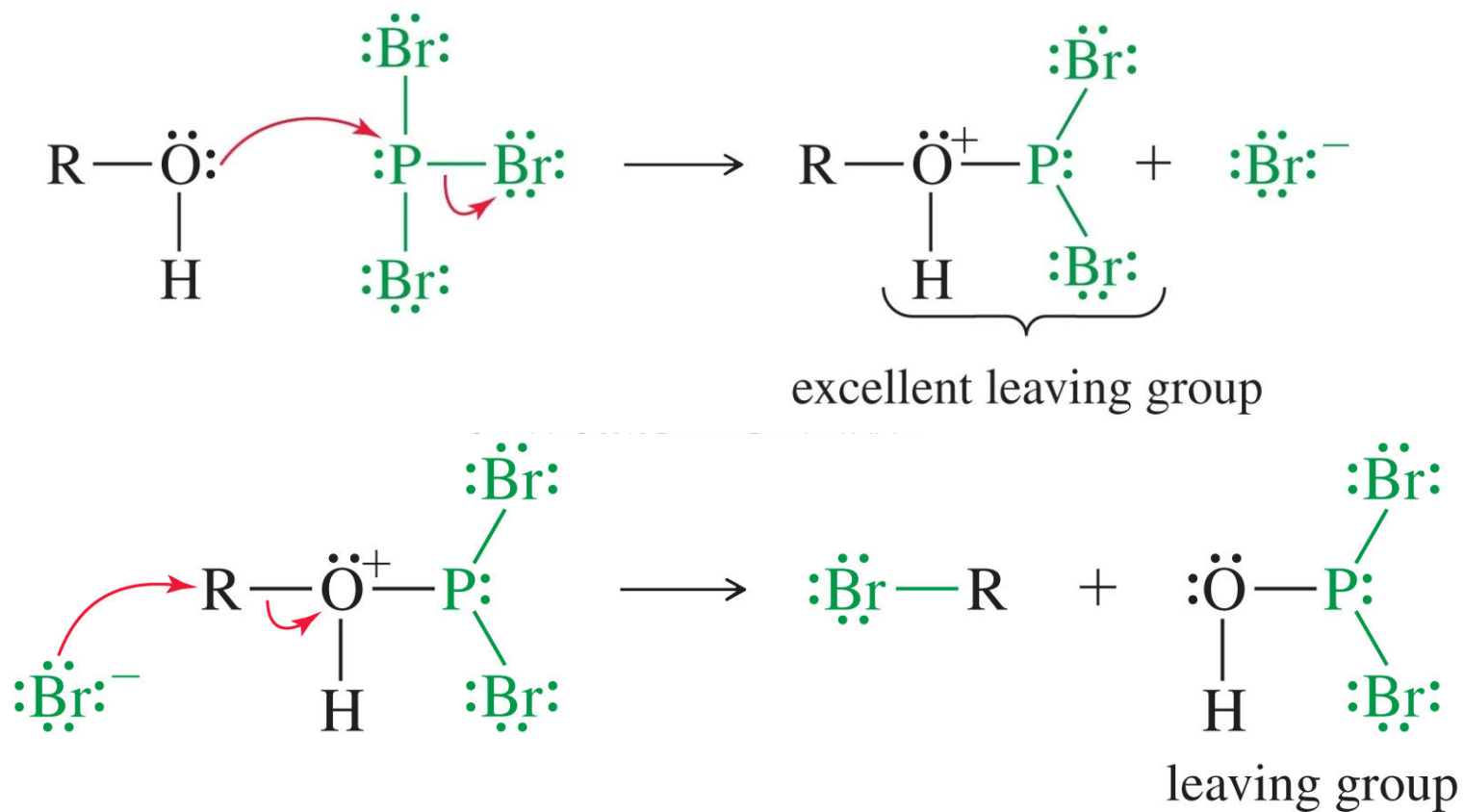


- Reaction of Alcohols and  $PX_3$  (11.8)
- Other ways are available to change the hydroxyl group into a halide. One common method is to treat the alcohols with  $PBr_3$ ,  $PCl_3$  or  $P/I_2$  (because  $PI_3$  is unstable), leading to alkyl bromides, chlorides and iodides. Reaction is good with  $1^\circ$  and  $2^\circ$  alcohols.



$P$  and  $I_2$  will produce  $PI_3$  in solution

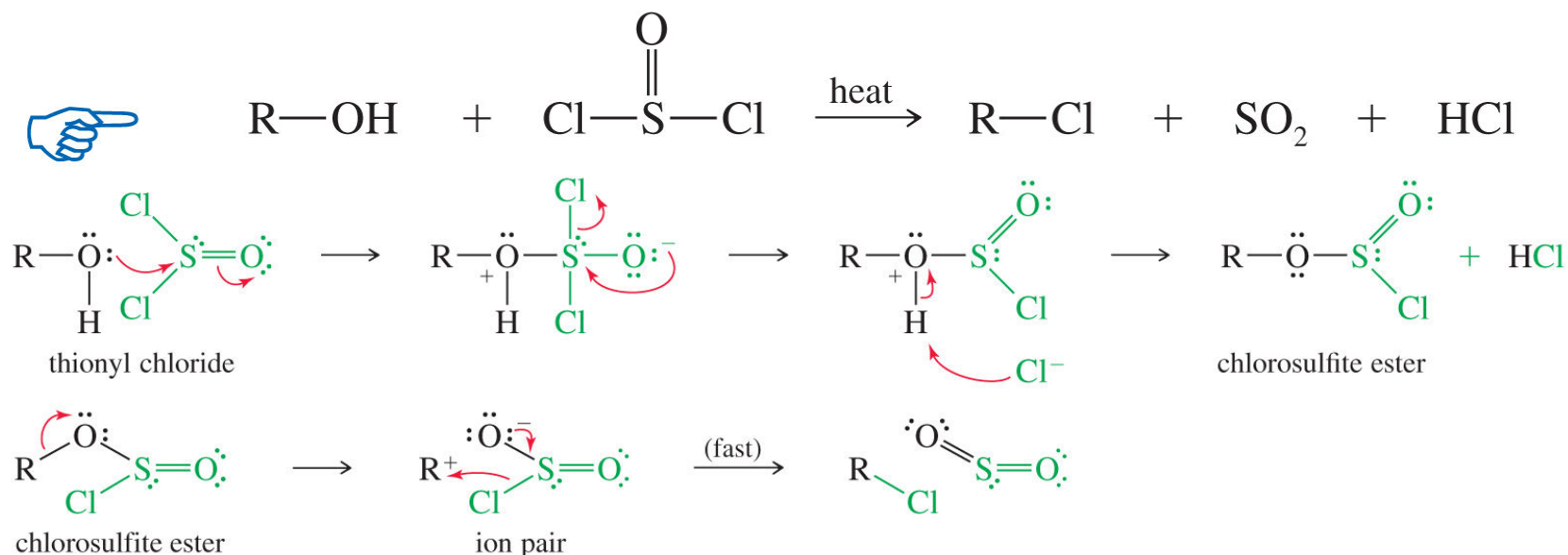
## Mechanism of Reaction between Alcohols and $PX_3$



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- Reaction of Alcohols with SOCl<sub>2</sub> (11.9)

This is the best way to make alkyl chlorides from 1°, 2° and 3° alcohols. The reaction proceeds via the chlorosulfite ester by S<sub>N</sub>2 mechanism for 1° alcohols and S<sub>N</sub>1 mechanism for 2° and 3° alcohols.



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- **Dehydration** (11.10)

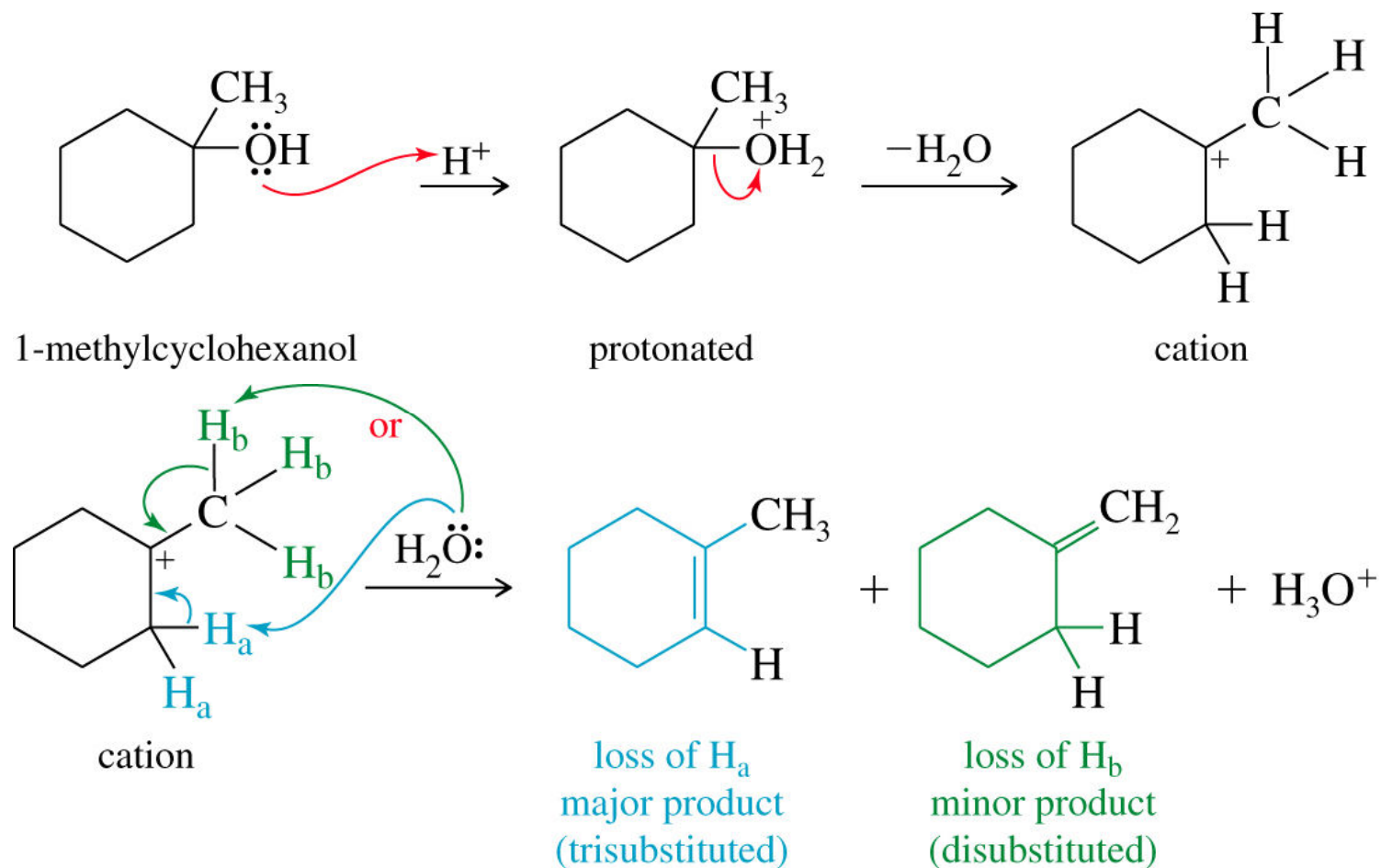
**Dehydration of alcohols is done under acidic conditions and will produce alkenes via E1 mechanisms. Carbocation rearrangement is possible and will be the key step especially for 1° alcohols since the rearrangement and formation of the carbocation is concerted. (see page 485)**

**The ease of dehydration depends on the structure of the alcohol.**





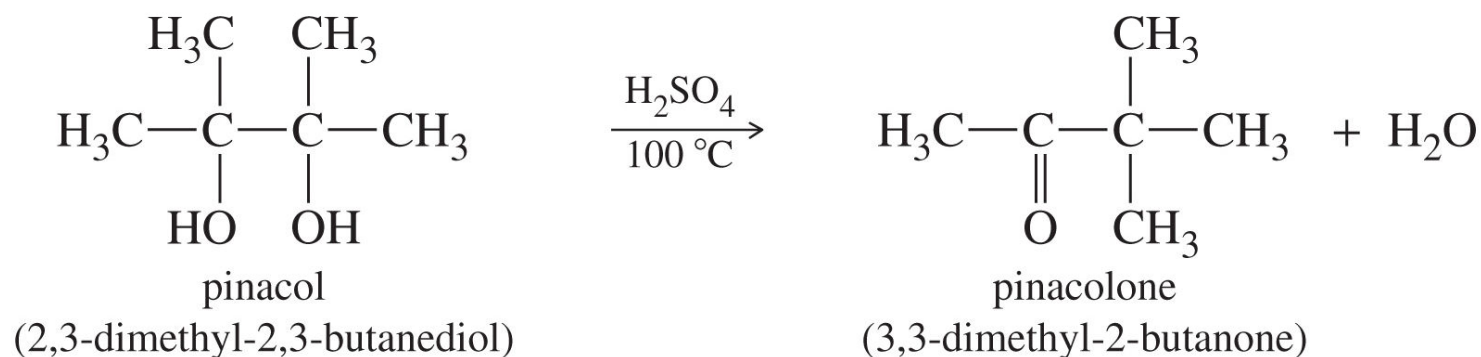
# E<sub>1</sub> mechanism of Dehydration



**Remember that the more stable alkene is always the major product**

- Unique Reactions of Diols (11.11)

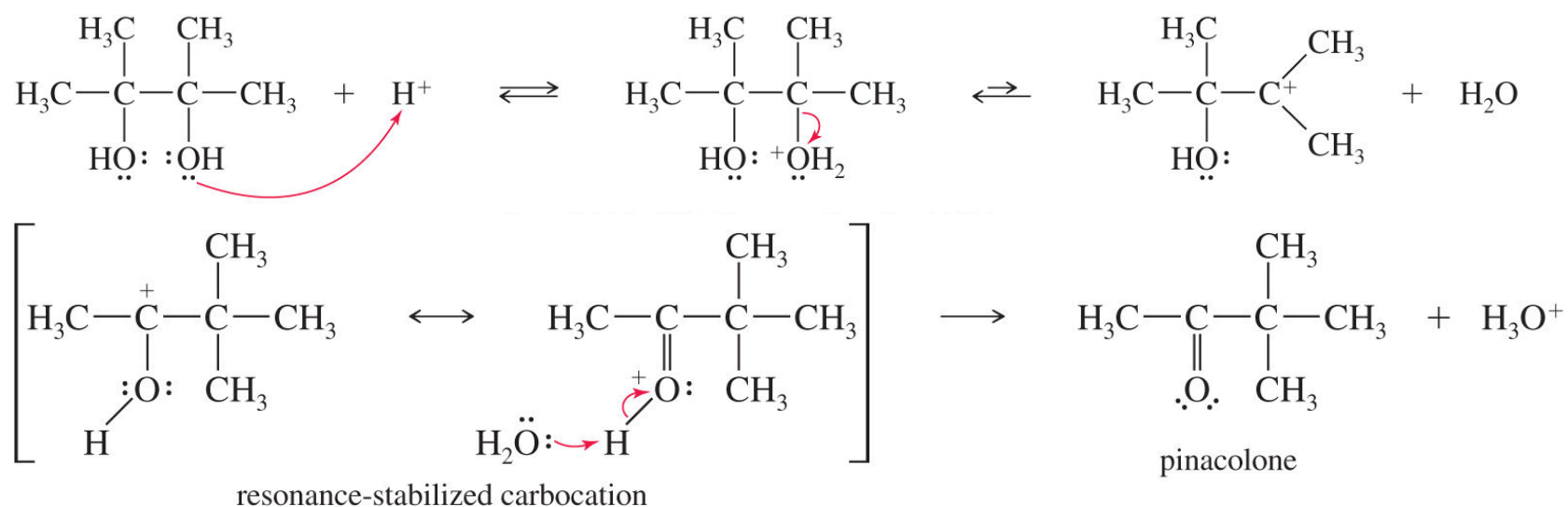
The dehydration of vicinal diols is unique simply because of the product that is generated. In this reaction known as the **Pinacol Rearrangement**, the product is no longer an alkene but rather a ketone.



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# Mechanism of Pinacol Rearrangement

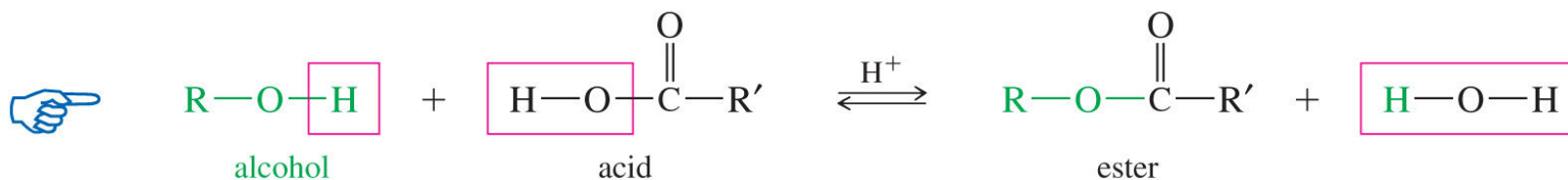
- The difference with other alcohol is that the carbocation rearranges to a more stable resonance-stabilized carbocation leading to the ketone.**



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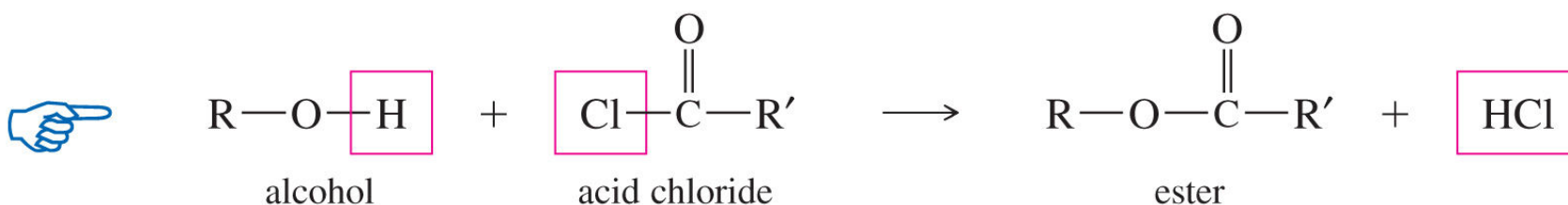
- Esterification of Alcohols (11.12)

**Organic esters are easily formed from the corresponding carboxylic acid and alcohols following an acyl substitution mechanism. The reaction is catalyzed by a strong acid and is known as the Fisher Esterification. Esters can easily be detected due to their common smell such as apple, strawberries, banana...and even goat!!!!**



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- Because esterification of alcohols is an equilibrium, it is often difficult to get good yield of the ester. Another method that not an equilibrium employs an acid derivative (acid chloride) to carry out the reaction and good yields of esters can be obtained. We will see the mechanism of both of these reaction later in the semester.



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# Practice Question

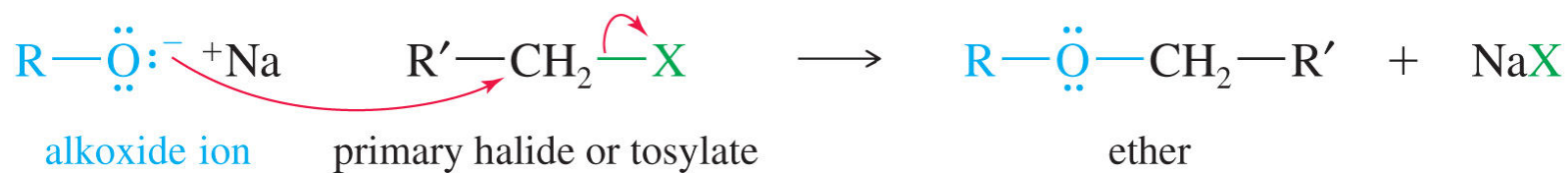
- **How would you prepare the following esters using an alcohol and a carboxylic acid? Methyl butanoate (odor of apples) and octyl ethanoate (odor of oranges).**

- Reactions of Alkoxides (11-14)

[Williamson Synthesis]

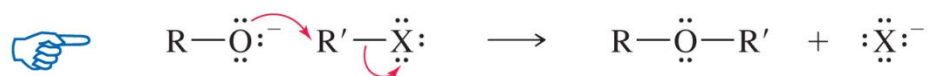
Ethers can be prepared from alcohols via  $S_N2$  reaction of the corresponding alkoxide ions.

The halides should be sterically unhindered (primary is best). The more steric factors, the least amount of ether will be obtained.



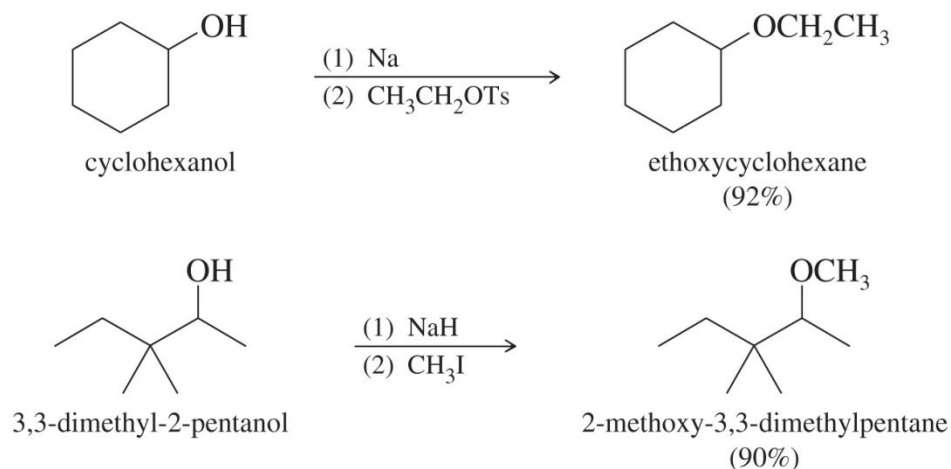
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- **The formation of the alkoxide ion is done by deprotonation of the alcohols. Since alcohols have a pKa ~ 15-16, hydroxide ion is not a suitable base. Normally Na<sub>(s)</sub> or NaH are used (K<sub>(s)</sub> or KH can also be used)**



The alkoxide is commonly made by adding Na, K, or NaH to the alcohol (Section 11-14).

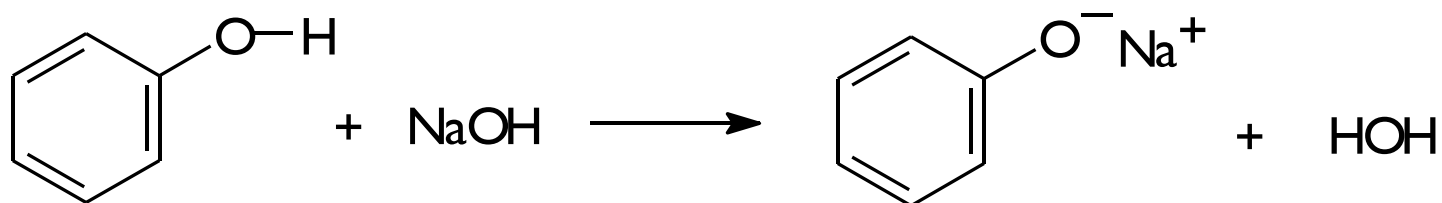
*Examples*



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- Phenoxide ions are easily produced for because the alcohol proton is acidic.
- Phenyl halides or tosylates cannot be used in this synthesis method.



# Practice Question

- **How could the following ethers be prepared using an alkyl halides and an alcohol?**

