

## Klein Chapter 12 Outline - Alcohols (ROH) &amp; Phenols (ArOH)

- I. Nomenclature of alcohols and ethers (12.1, 13.2)
- II. Physical properties of alcohols and ethers (12.1, 13.3)
- III. Acidity of alcohols and phenols (12.2)
- IV. Preparation of alcohols
  - a. from alkyl halides, RX (12.3)
  - b. from alkenes (12.3, 12.5)
  - c. from ketones/aldehydes (12.4, 12.6)
- V. Reactions of alcohols
  - a. oxidation reactions (12.10)
  - b. tosylation (7.12)
  - c. reduction reactions
    - Not in Educator:* elimination reactions, E1 and E2 (7.12, 12.9)
  - d. conversion to alkyl halides, RX (12.9)
- VI. *Not in Educator:* Synthesis strategies (12.13)

**skip the following sections:**

- 12.7 protection of alcohols
- 12.8 preparation of phenols
- 12.11 biological redox rxns
- 12.12 oxidation of phenol

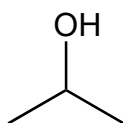
**I. Nomenclature of Alcohols and Ethers****Alcohol Nomenclature (12.1)**

Identify the longest parent carbon chain that contains the carbon bearing the OH group.

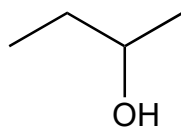
Number from the end of the chain closer to the OH.

Drop the alkane "e" and add "ol" to give "**#-alkanol**," where the # indicates the position of the OH group (or number can be inserted **alkan-#-ol**).

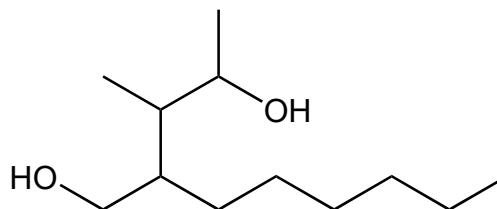
If there are two OH's, the parent is "**#, #-alkanediol**" (triol, tetraol, etc.).



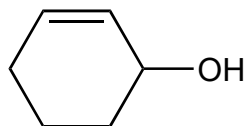
(isopropyl alcohol)



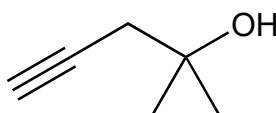
IUPAC:  
common:



Alcohol functional group (FG) has priority over alkene/alkyne.



**2-cyclohexen-1-ol** or  
cyclohex-2-en-1-ol

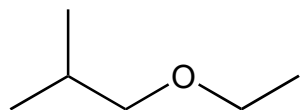
**Types of Alcohols**

RCH <sub>2</sub> OH	primary, 1°
R <sub>2</sub> CHOH	secondary, 2°
R <sub>3</sub> COH	tertiary, 3°

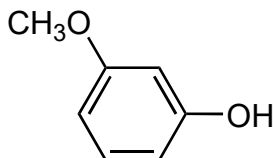
## Ether Nomenclature (13.2)

12-2

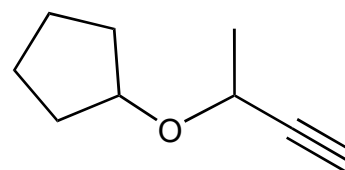
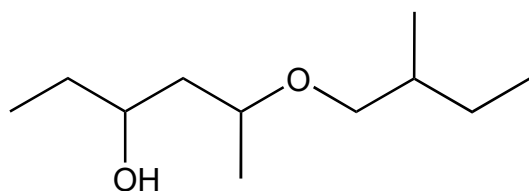
- \*\* Ethers have no effect on the name of the parent; they are simply named as a substituent (group) attached to the parent.
- \*\* Any -OR substituent is named by dropping the "yl" ending and adding "oxy" (e.g., ethyl becomes ethoxy).
- \*\* Simple ethers are often named as an "alkyl alkyl ether," but this is not IUPAC.



(isobutyl ethyl ether)



$\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$   
common: diethyl ether  
IUPAC:



*try SkillBuilder 12.1*

## II. Physical properties of alcohols and ethers (12.1, 13.3)



- very polar functional group
- alcohols can form hydrogen bonds with each other
- boiling point (bp)      water solubility
- OH group is acidic

### Boiling Point

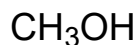
pentane	diethyl ether	ethanol	<i>n</i> -butanol	ethylene glycol
bp (°C)    36	35	79	117	197

### Water Solubility (g per 100 mL H<sub>2</sub>O)

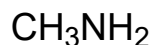
0 g	8.4 g	7.4 g	miscible

### III. Acidity of alcohols and phenols (12.2)

12-3



$$pK_a = 16$$



$$pK_a = 40$$

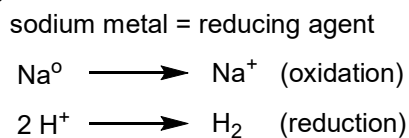
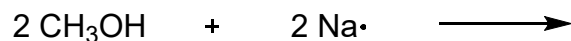
Why?  
Conj. base:

#### Preparations of Alkoxides ( $\text{RO}^-$ ) \*\*need to completely deprotonate ROH\*\*

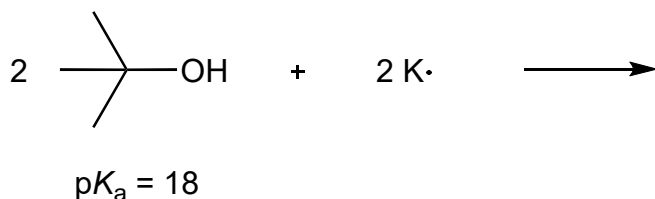
1. Can use strong base like sodium hydride



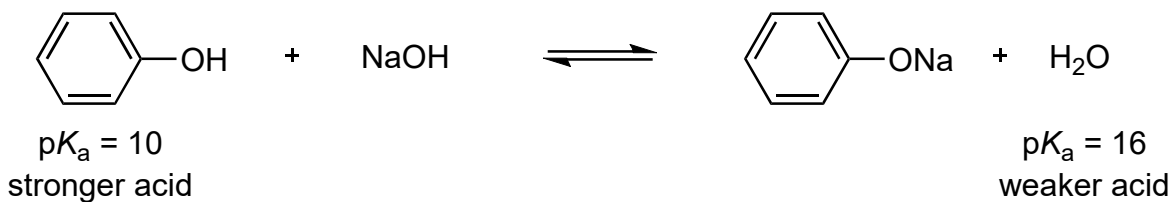
2. Can use a redox reaction



Can also use potassium metal (more reactive)



Note: phenols are more acidic than alcohols

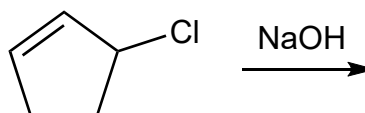
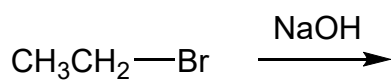


## IV. Preparation of alcohols, ROH

### a. from alkyl halides, RX (12.3)

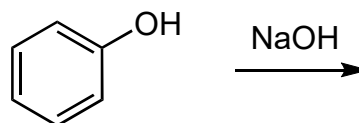
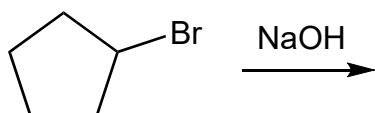
**S<sub>N</sub>2 with HO<sup>-</sup>** (remember, HO<sup>-</sup> is a strong nu: and a strong base)

- great for CH<sub>3</sub>X, 1° RX, allylic RX, benzylic RX



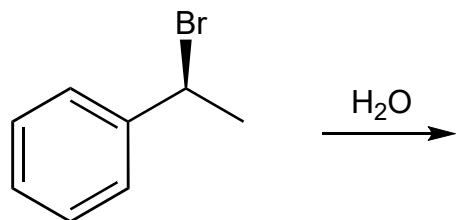
- unlikely on 2° RX (E2 favored)

- impossible on 3° RX (E2) and phenyl/vinyl (N/R)



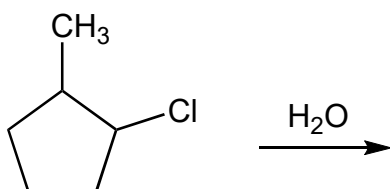
**S<sub>N</sub>1 with H<sub>2</sub>O** ("solvolysis" or "hydrolysis")

- good for allylic RX, benzylic RX, 3° RX (all good C<sup>+</sup>)



benzylic RX (X = Br)

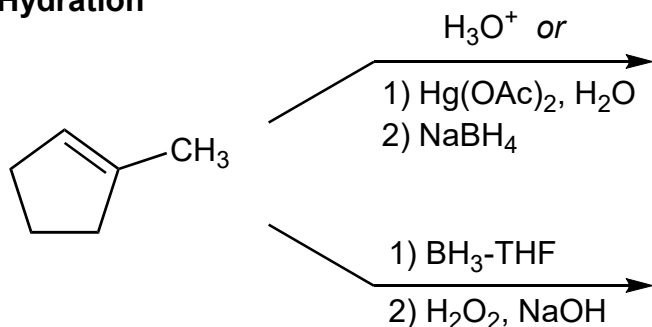
- carbocation can rearrange!



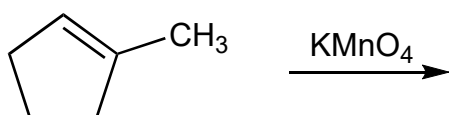
## b. Preparation of alcohols from alkenes (12.3, 12.5)

12-5

### Hydration



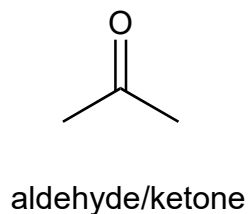
### Oxidation → Diol



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## c. Preparation of alcohols from ketones/aldehydes (12.4, 12.6)

General reaction:



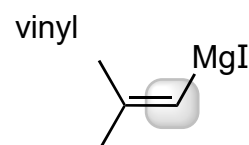
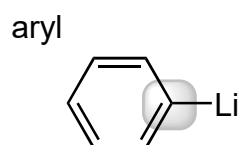
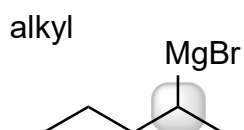
Nucleophile (Nu:) can be:  $\text{RC}\equiv\text{C}^-$  or  $\text{RMgX}$  or  $\text{LiAlH}_4$   
(acetylide) (Grignard) (Hydride)

### Organometallic Reagents (RM = $\text{RMgX}$ or $\text{RLi}$ )

#### a) Preparation of organometallic reagents

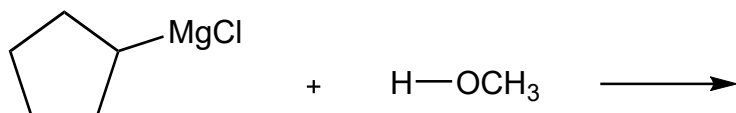


For RM, R can be...

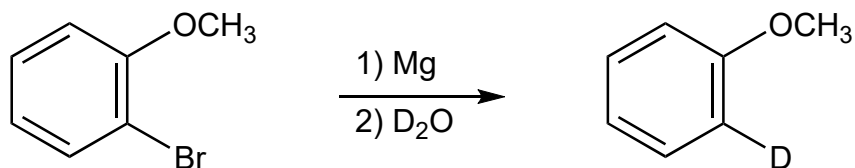

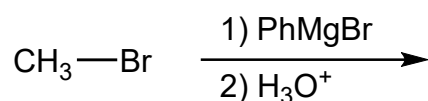
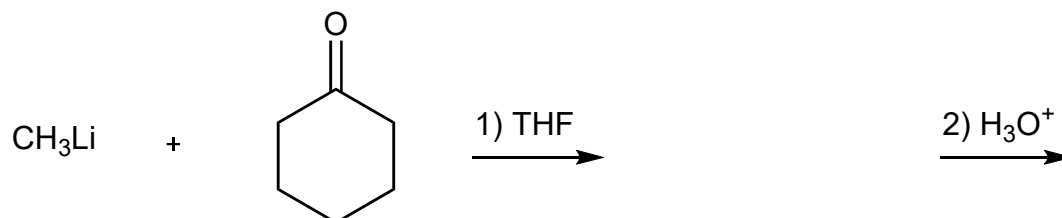


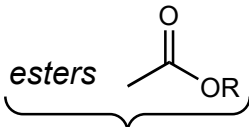
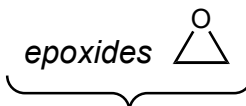
## b) Reactions of organometallic reagents

strong base (can be protonated)

\*\* Grignards will react with H<sub>2</sub>O and ROH!\*\* need to use aprotic solvents with organometallics (e.g., Et<sub>2</sub>O or THF)

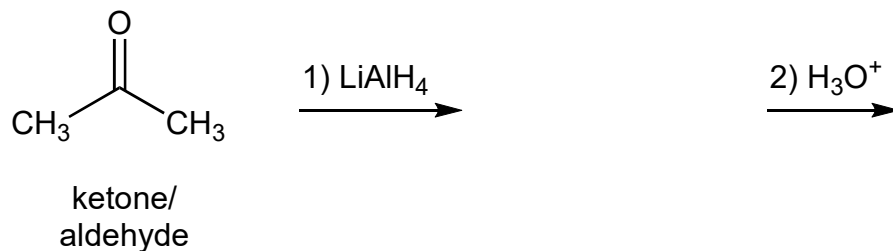
\*\* can be a useful reaction to introduce H or D

strong Nu: (reacts with E<sup>+</sup> like  but not RX)

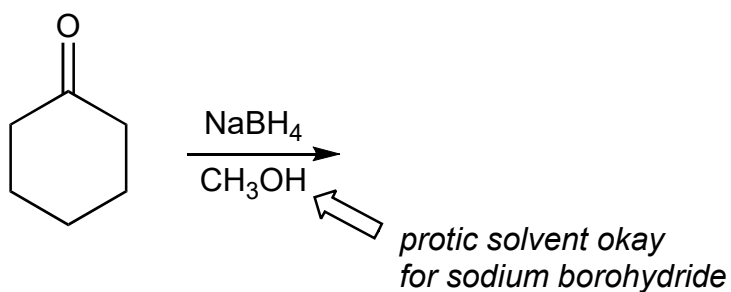
Note: for now, we will skip reactions with  and 

Chapter 20                      Chapter 13

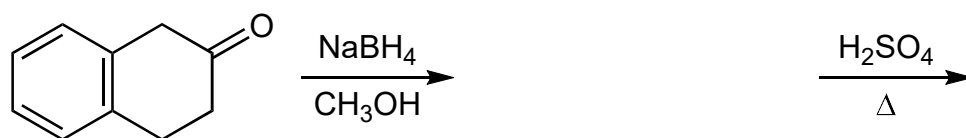
## Hydride Nucleophiles

LiAlH<sub>4</sub> – lithium aluminum hydrideNaBH<sub>4</sub> – sodium borohydride

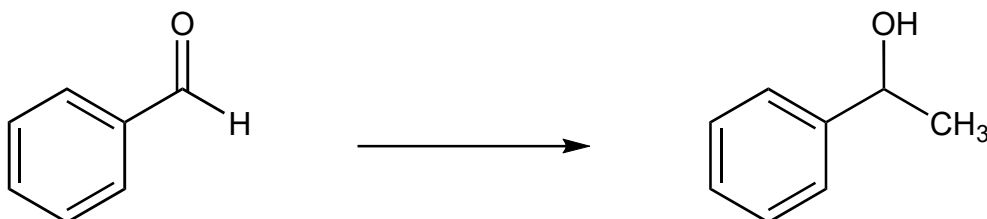
Predict the major product:



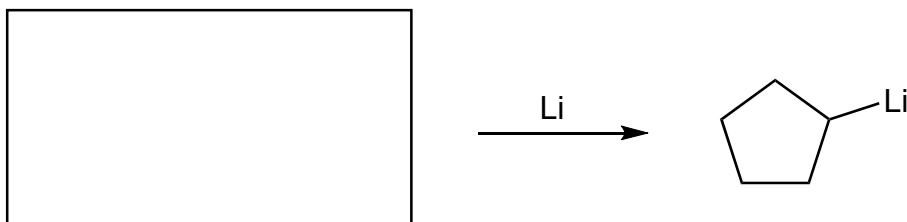
Predict the major product:



Transform:



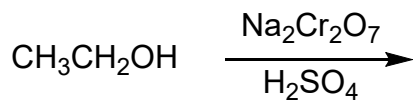
Provide a starting material:



## V. Reactions of alcohols

### a. oxidation reactions (12.10)    Oxidizing agents = Jones, PCC, Swern

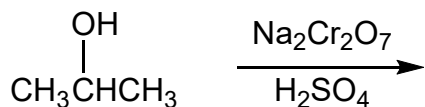
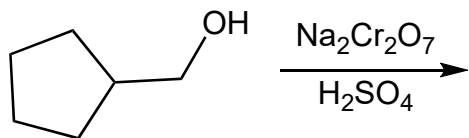
A) "Jones" oxidation: dichromate ( $\text{Cr}_2\text{O}_7^{2-}$ ) + acid, or  $\text{CrO}_3$  + acid



1° alcohol

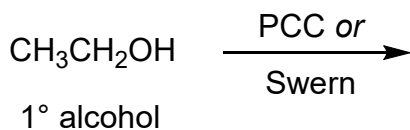
- complete [ox] with chromic acid "Jones" conditions
- harsh, strong reaction conditions (aq. acid)

Predict the major product:

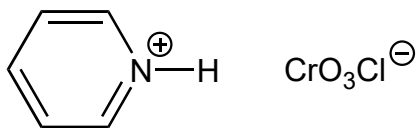


B) selective oxidizing agents (PCC and Swern)

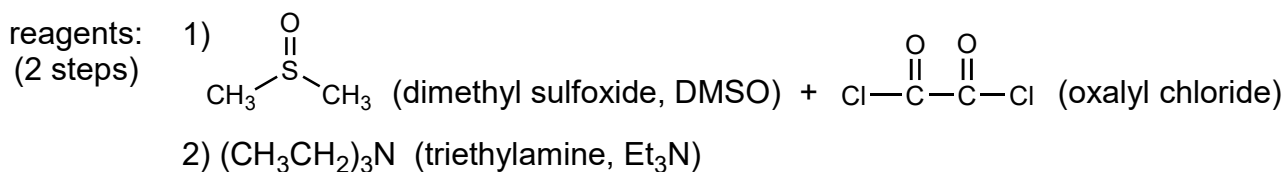
- milder reaction conditions are less reactive, so stop at aldehyde



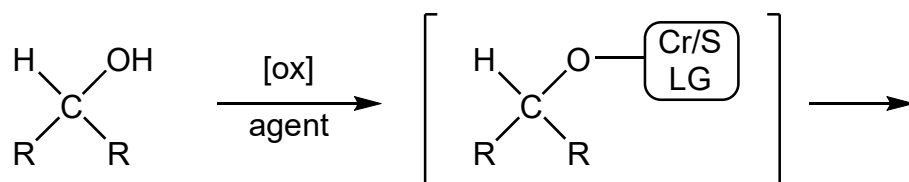
i) PCC = pyridinium chlorochromate



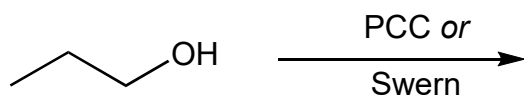
ii) Swern oxidation (great method since Cr waste is toxic)



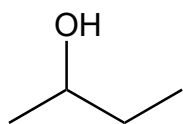
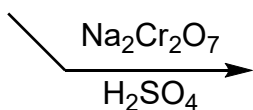




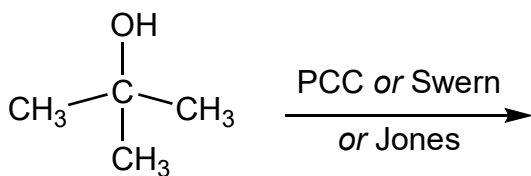
**Oxidation of Alcohols Summary** \*\* Primary ROH can overoxidize to choose [ox] agents wisely \*\*



1° alcohol

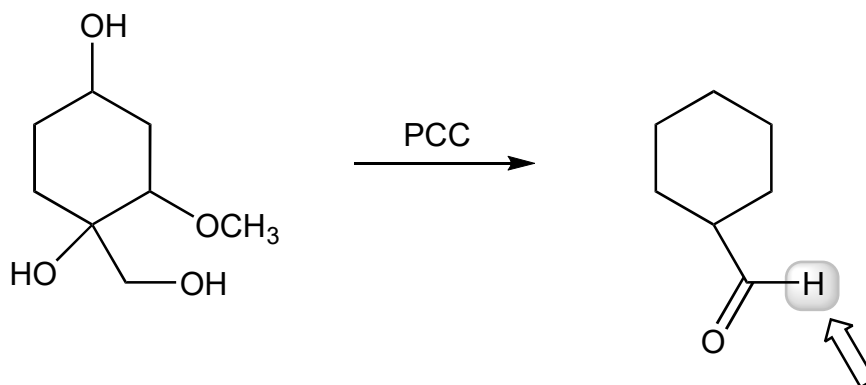


2° alcohol



3° alcohol

Predict the major product:



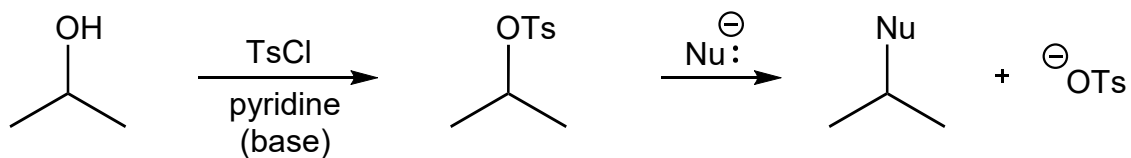
*Note: Educator lecture has an error in it! An aldehyde is formed at this position, because PCC is the reagent.*

## V. Reactions of alcohols

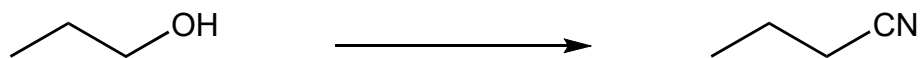
12-10

### b. tosylation (7.12)

Turns "OH" into a good leaving group "OTs"

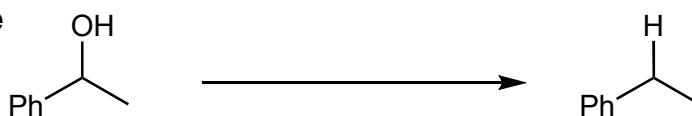


Transform

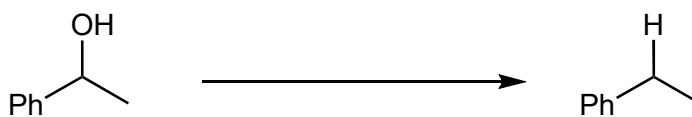


### c. Reductions of alcohols

A) via  $\text{S}_{\text{N}}2$  with hydride

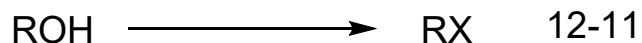


B) via dehydration



See also: elimination reactions, E1 and E2 (Klein sections 7.12, 12.9)

## V. Reactions of alcohols



### d. conversion to alkyl halides, RX (12.9)

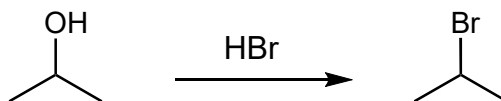
\*Key: need to make OH a good LG

#### A) via tosylate



#### B) use HX

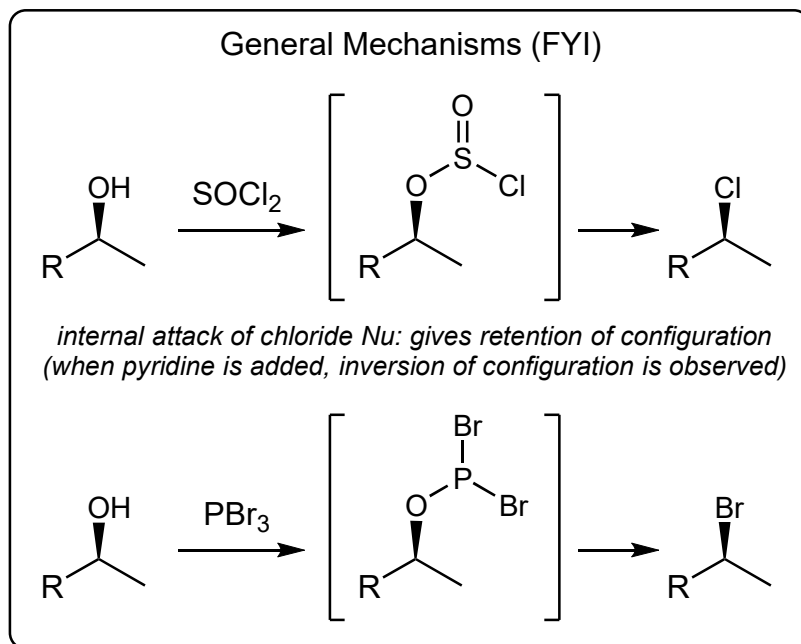
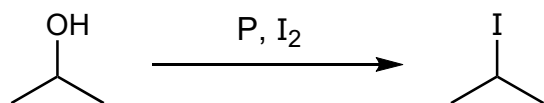
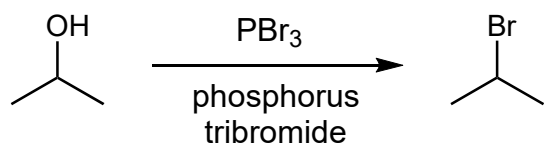
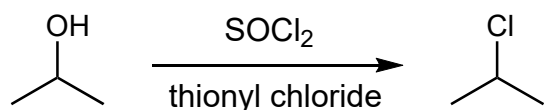
(HBr or HCl/ZnCl<sub>2</sub> cat.)



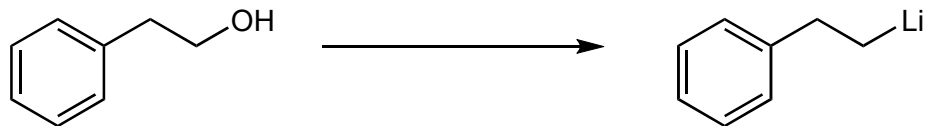
mechanism

Notes: - conditions favor carbocation (consider E1, rearrange, 3° is best)  
- HX can react with other functional groups (alkenes, ethers, etc.)

#### C) reagents that provide LG and Nu: in one "pot"



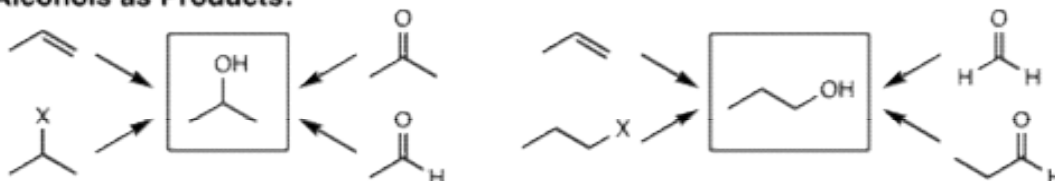
Transform:



- I. Nomenclature of alcohols and ethers (12.1, 13.2)
- II. Physical Properties of alcohols and ethers (b.p., H<sub>2</sub>O solubility, 12.1, 13.3)
- III. Acidity of alcohols & phenols, and preparation of alkoxides (RO<sup>-</sup>) (12.2)
- IV. Preparation of alcohols: review (12.3)
  - A) S<sub>N</sub>2 w/OH<sup>-</sup> on unhindered alkyl halides (E2 competes w/2°, 3° substrates)
  - B) S<sub>N</sub>1 w/H<sub>2</sub>O on 3° or allylic alkyl halides
  - C) hydration or dihydroxylation of alkenes (Ch. 8, 12.3, 12.5)
- V. Preparation of alcohols from ketones/aldehydes
  - A) organometallic reagents: Grignard (RMgX) and organolithium (RLi) (12.6)
    - i) prepared from alkyl halide (treat RX with Mg or Li metal)
    - ii) can be protonated by ROH or H<sub>2</sub>O
    - iii) Nu: that will react with carbonyl or epoxide E<sup>+</sup>, NOT RX
  - B) hydride Nu.: H<sup>-</sup> (LiAlH<sub>4</sub> or NaBH<sub>4</sub>, 12.4)
    - i) a reduction reaction that gives an alcohol product
- VI. Reactions of alcohols
  - A) Oxidation reactions (↑ # of C–O bonds, 12.10)
    - i) oxidizing agents [ox]
      - a) Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>/H<sub>2</sub>SO<sub>4</sub> (chromic acid)
      - b) pyridinium chlorochromate (PCC)
      - c) Dess-Martin periodinane (DMP)
      - d) DMSO, oxalyl chloride, Et<sub>3</sub>N (Swern)
    - ii) Summary for primary, secondary, tertiary alcohols (1°, 2°, 3° ROH)
  - B) Tosylation of alcohols (TsCl, pyridine) makes a good LG (7.12)
  - C) Elimination reactions (ROH → alkene, 12.9)
    - i) via E2 elimination
      - a) TsCl/py, followed by strong base
      - b) t-BuOK for Hofmann (less substituted alkene)
      - c) NaOH or any alkoxide other than t-BuOK (RONa) for Zaitsev
    - ii) via dehydration (E1 mechanism)
      - a) carbocation intermediate can rearrange
      - b) always give most stable alkene (Zaitsev)
  - D) Conversion to alkyl halides (ROH → RX, 12.9)
    - i) S<sub>N</sub>1/S<sub>N</sub>2 with HX
    - ii) SOCl<sub>2</sub>, PBr<sub>3</sub> or P/I<sub>2</sub>
- VII. Synthesis Strategies
  - A) ROH can be prepared from RX, alkene, or ketone/aldehyde
  - B) ROH can be used to prepare RO<sup>-</sup> (alkoxide), RX, ROTs (tosylate), alkene, or ketone/aldehyde

Skip Sections:  
 12.7, 12.8,  
 12.11, 12.12

**Alcohols as Products:**



**Alcohols as Starting Materials:**

