

# Organic Chem

## Chapter 12:

### Alcohols

ACCORDING TO  
CHEMISTRY  ALCOHOL  
IS A SOLUTION

# Did you ever wonder...

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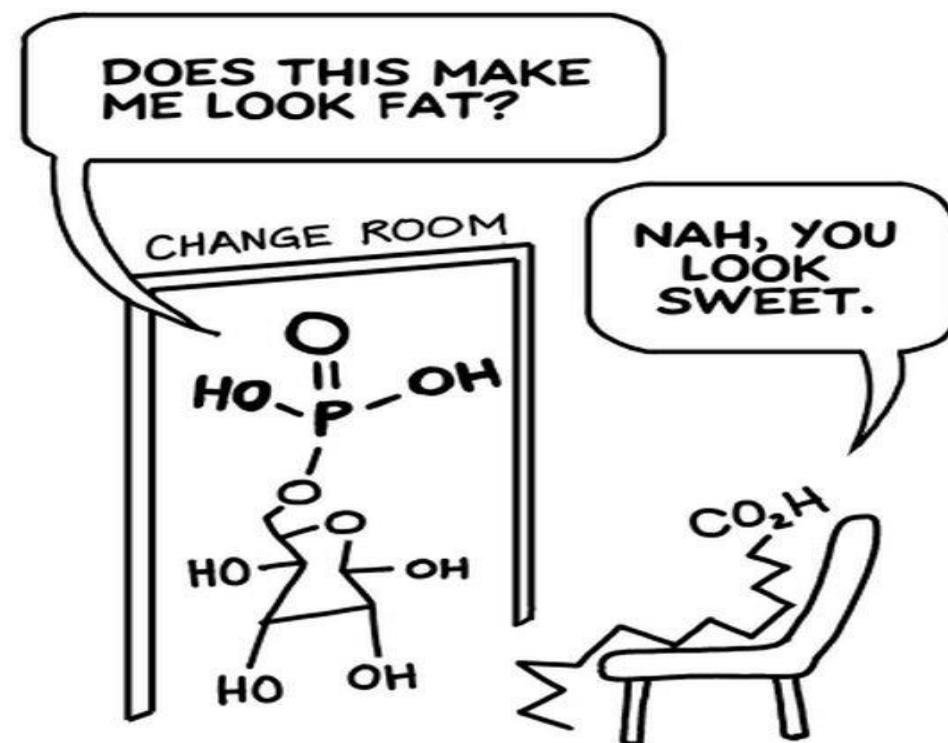
what causes the hangover associated with drinking alcohol and whether anything can be done to prevent a hangover? (p. 505)

## CH 12.1

Topic: Structure and Properties of Alcohol

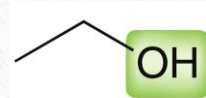
EQ: How are alcohols different in structure?

READ pg. 506 - 510  
then take notes

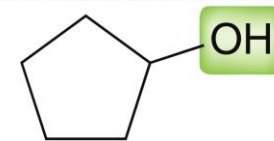


# Structure and properties of Alcohol

- Alcohols → compounds that have hydroxyl group (OH) connected to an  $sp^3$ -hybridized carbon atom
- Name ending in “ol”

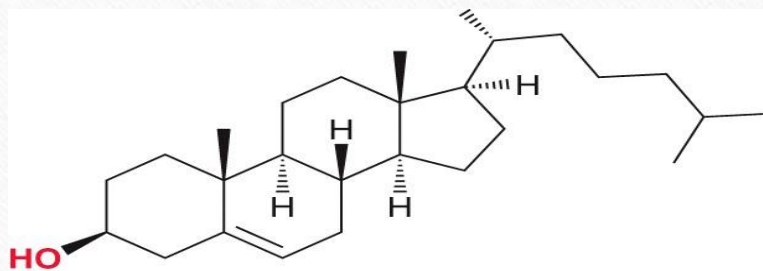


Ethanol



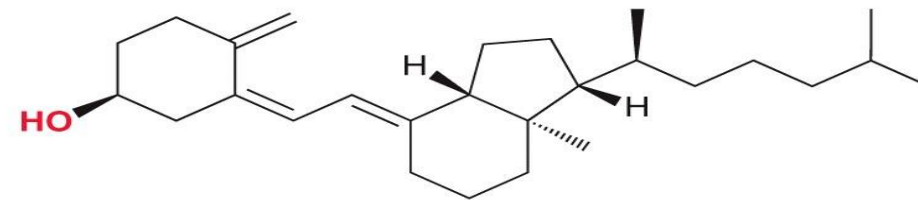
Cyclopentanol

- large number of compounds contain hydroxyl groups. (Examples)



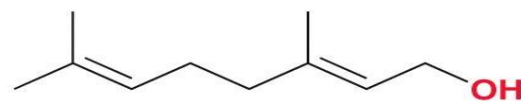
Cholesterol

Plays a vital role in the biosynthesis of many steroids



Cholecalciferol (vitamin D<sub>3</sub>)

Regulates calcium levels and helps to form and maintain strong bones



Geraniol

Isolated from roses and geraniums. Used in perfumes

# Nomenclature

- Remember: 4 steps to name alkanes, alkenes, & alkynes

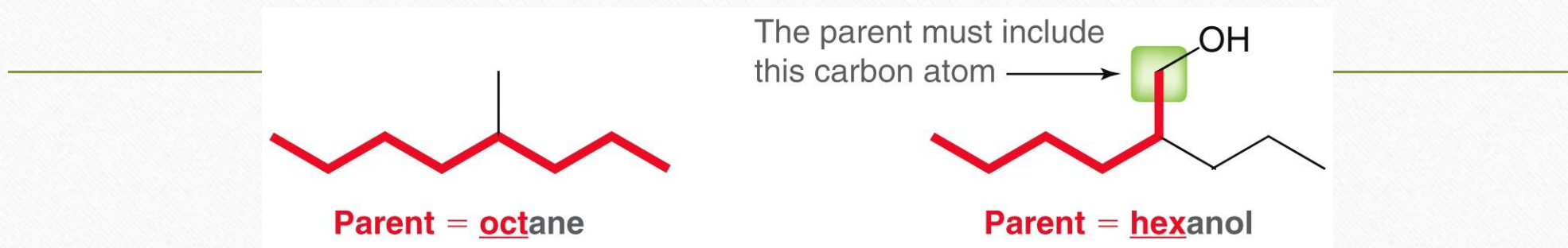
- 1) Identify & name parent
- 2) Identify & name substituent
- 3) Assign a locant to each substituent
- 4) Assemble the substituents alphabetically

Alcohols are named the same way (just add 1 more rule)

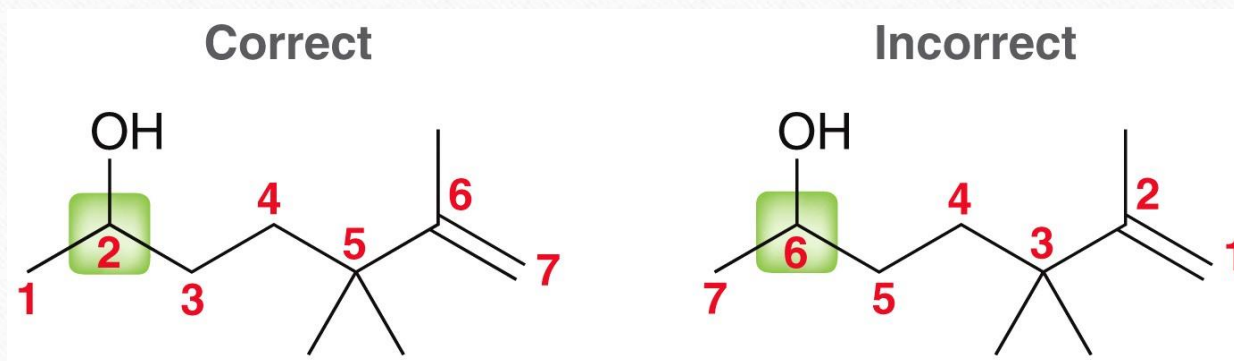
- *When naming parent, change ending of “e” to “ol” (letting know that OH is present)*



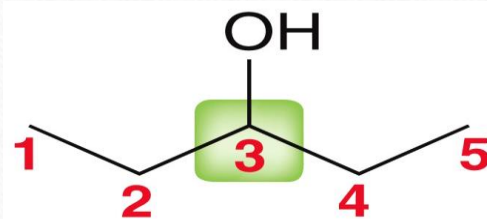
- When finding parent, get *longest chain attached to the "OH"* (must include the C attached to the OH as well)



- When numbering chain, *OH* must get the *lowest number possible*



- Position of OH is indicated by *locant*
- Locant can be placed before parent (or before suffix “ol”)

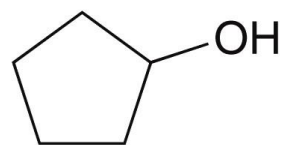


**3**-Pentanol  
or  
Pentan-**3**-ol

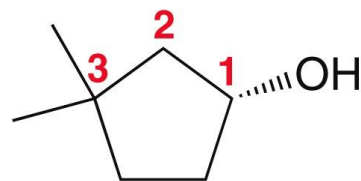
- A chiral center must be indicated at the beginning of the name

• **Cyclic alcohols** → numbering starts where OH is located

- no need to indicate where OH is since its always C-1)

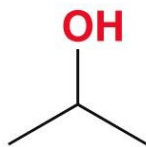


Cyclopentanol



(*R*)-3,3-Dimethylcyclopentanol

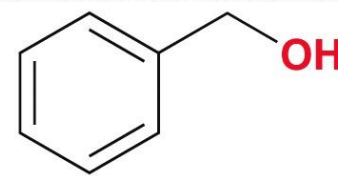
• Common names for alcohol (IUPAC nomenclature recognizes these)



Isopropyl alcohol  
(2-propanol)



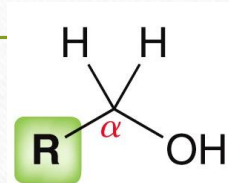
*tert*-Butyl alcohol  
(2-methyl-2-propanol)



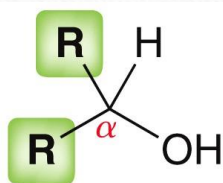
Benzyl alcohol  
(phenylmethanol)



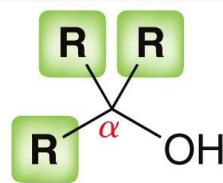
- Alcohols designated as **primary, secondary, or tertiary** depending on the number of alkyl groups are on the alpha position
- Alpha position** → C where the OH is attached to



Primary

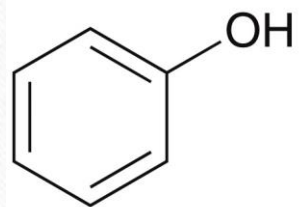


Secondary

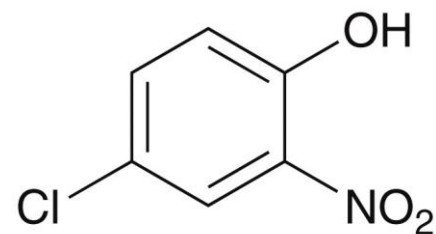


Tertiary

- “Phenol”** describes specific compound (**hydroxybenzene**) → used as parent when substituents are attached



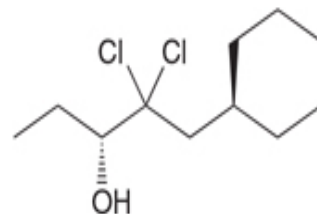
Phenol



4-Chloro-2-nitrophenol

# Skill Builder12.1

Assign an IUPAC name for the following alcohol:

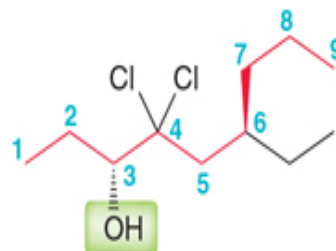


## SOLUTION

Begin by identifying and naming the parent. Choose the longest chain that includes the carbon atom connected to the hydroxyl group and then number the chain to give the hydroxyl group the lowest number possible.

### STEP 1

Identify and name the parent.



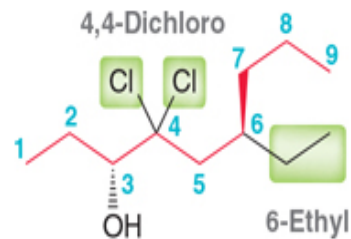
3-Nonanol

Then identify the substituents and assign locants.

# Skill Builder 12.1

## STEP 2 AND 3

Identify the substituents and assign locants.



Next, assemble the substituents alphabetically: 4,4-dichloro-6-ethyl-3-nanol.

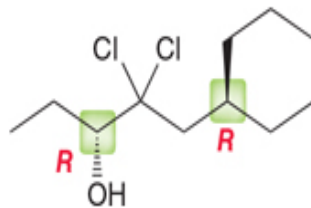
Before concluding, we must always check to see if there are any chiral centers. This compound has two chiral centers. Using the skills from [Section 5.3](#), we can assign the *R* configuration to each chiral center.

## STEP 4

Assemble the substituents alphabetically.

## STEP 5

Assign the configuration of any chiral centers.



Therefore, the complete name is (3*R*,6*R*)-4,4-dichloro-6-ethyl-3-nanol.

# Commercially important alcohols

- **Methanol** ( $\text{CH}_3\text{OH}$ ) is the simplest alcohol (yet toxic → causes blindness & death)
- AKA: “wood alcohol” b/c methanol can be made by heating up wood with the absence of air
- With a suitable catalyst, about 2 billion gallons of methanol is made industrially from  $\text{CO}_2$  and  $\text{H}_2$  every year
- Methanol is poisonous, but it has many uses
  1. Solvent
  2. Precursor for chemical syntheses
  3. Fuel

- **Ethanol** ( $\text{CH}_3\text{CH}_2\text{OH}$ ), produced by fermentation of grains or fruits
- Industrially, ethanol is made via acid-catalyzed hydration of ethylene (5 billion gallons/year in the U.S. alone)
- Ethanol has many uses
  1. Solvent fuel - precursor for chemical syntheses
  2. Human consumption – ethanol suitable for drinking

- **Isopropanol**  $\text{CH}_3\text{CH}(\text{OH})\text{CH}_3$ , a.k.a. rubbing alcohol.
- Isopropanol is made industrially from the acid-catalyzed hydration of propylene

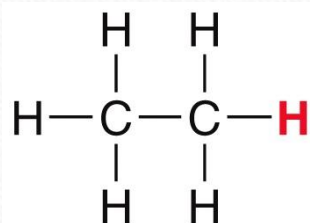
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- Isopropanol is poisonous, but it has many uses
  1. Industrial solvent
  2. Antiseptic
  3. Gasoline additive

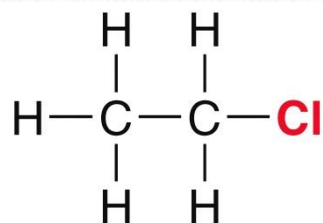
# Physical properties of alcohol

- Physical properties of alcohol different from physical properties of alkanes/ alkyl halides
- The  $\text{-OH}$  of an alcohol has a big effect on its physical properties

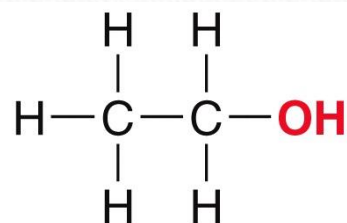
(Compare the boiling points(BP) below)



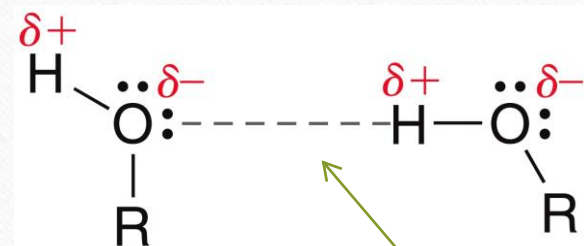
Ethane  
bp =  $-89^{\circ}\text{C}$



Chloroethane  
bp =  $12^{\circ}\text{C}$

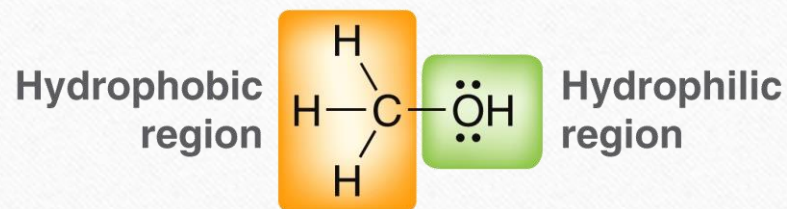


Ethanol  
bp =  $78^{\circ}\text{C}$



- Ethanol has a higher BP than other two compounds due to **H-bonding interaction that occurs between molecules**

- Alcohols with 3 carbons or less are **miscible** in water
- **miscible** – methanol can be mixed with water in any proportion (never separate in layers like water & oil)



- Alcohols with large carbon chains **DO NOT** readily mix with water





Let's try HMWK #1

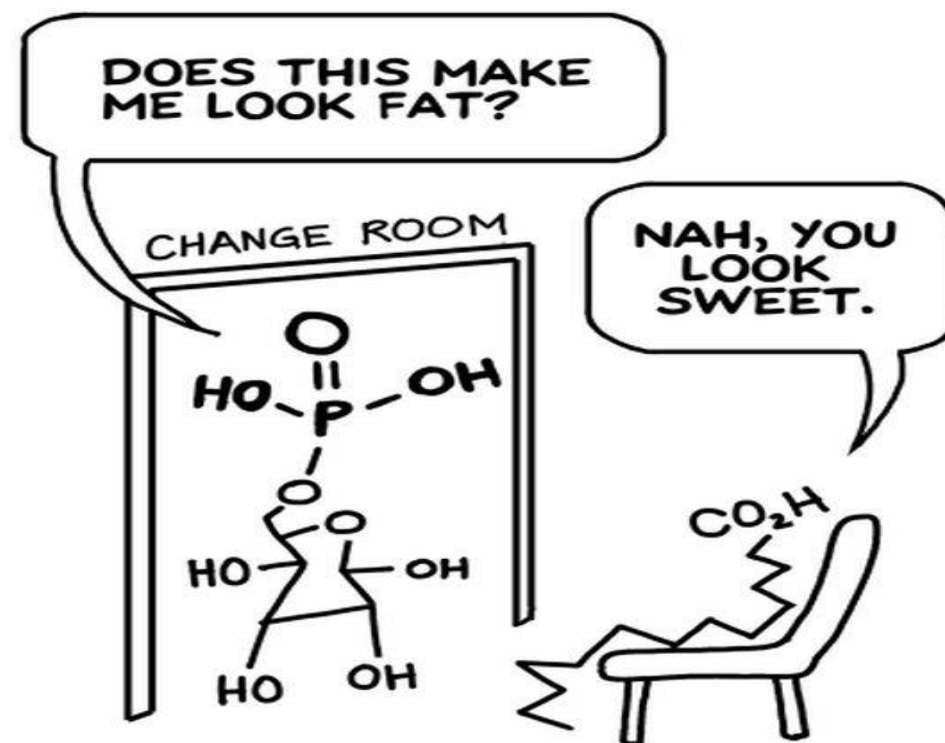
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## CH 12.2

Topic: Acidity of alcohols and phenols  
EQ: How acidic are alcohols compared to hydrogen halides ?

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READ pg. 510 - 512  
then take notes



Let's read p. 510

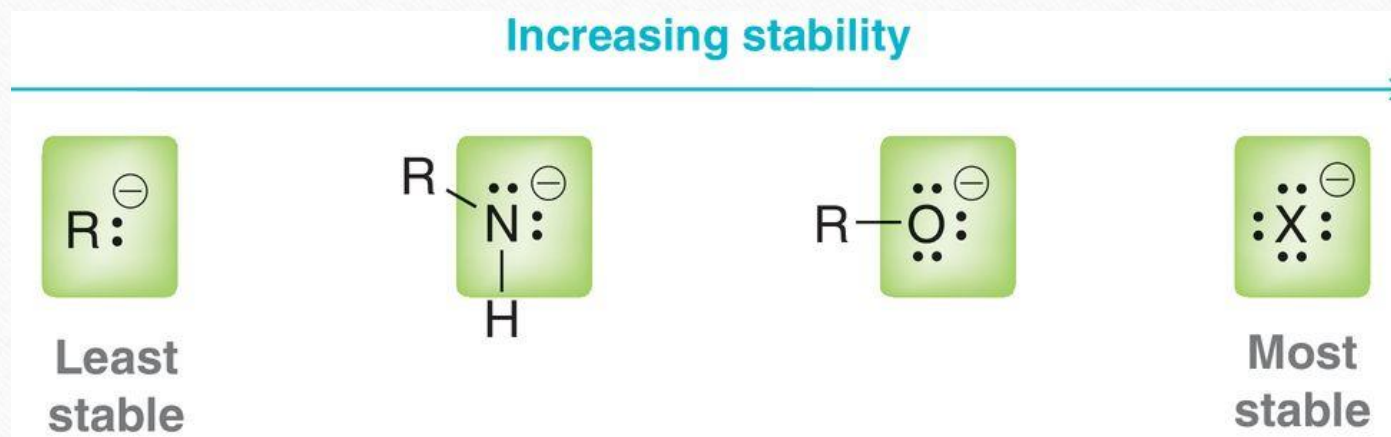
- 
- Chain length as a factor in drug design

# Acidity of the hydroxyl functional group

- Acidity of compound can be evaluated by the stability of conjugate base (CB)
- **Alkoxide ion** (AKA: conjugate base (CB) of alcohol) – exhibits a negative charge on an oxygen atom

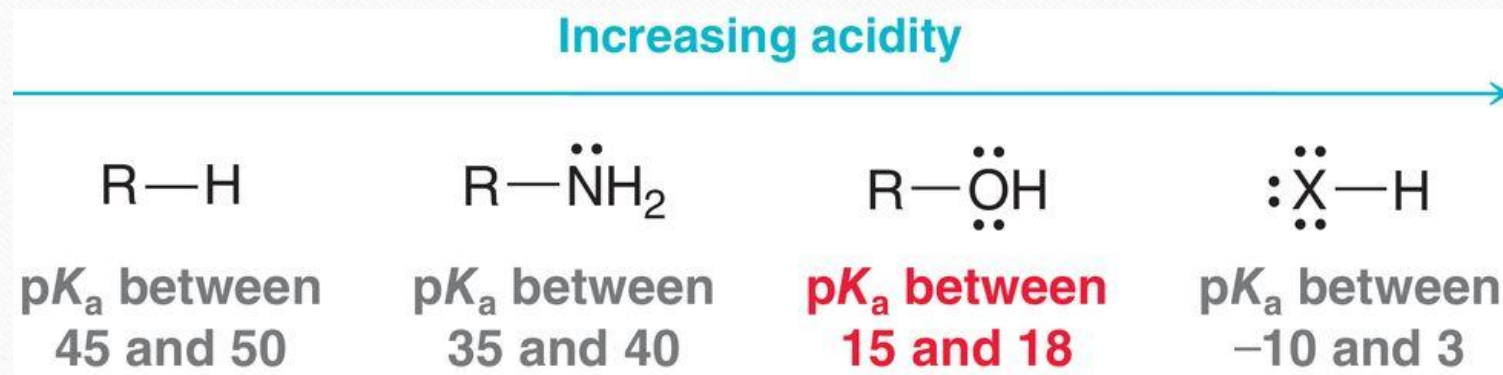
## Stability Ex:

- negative charge on Oxygen > negative charge on Carbon/ Nitrogen
- negative charge on Oxygen < negative charge on a Halogen



Continue →

- Therefore, alcohols are more acidic than amines & alkanes
  - BUT.... Less acidic than hydrogen halides
  - pK<sub>a</sub> for most alcohols fall in the range of 15 -18
- 
- (Remember **ARIO**... to rationalize the relative acidity of an alcohol)

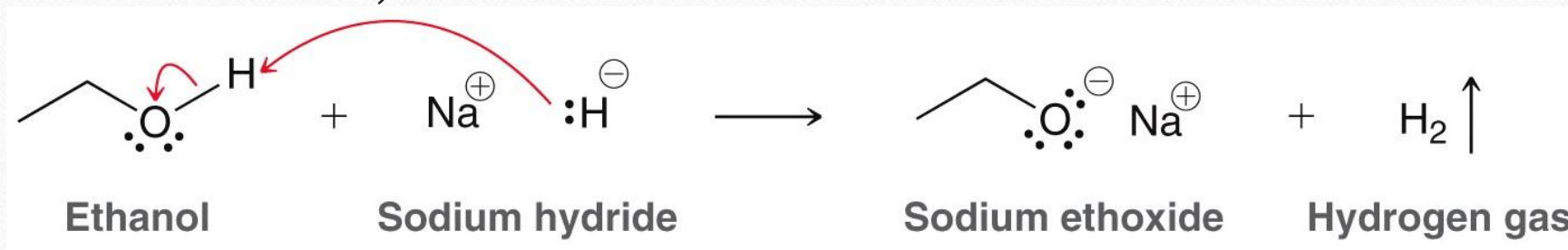


# Reagents for Deprotonating an alcohol

- Two ways to deprotonate an alcohol...

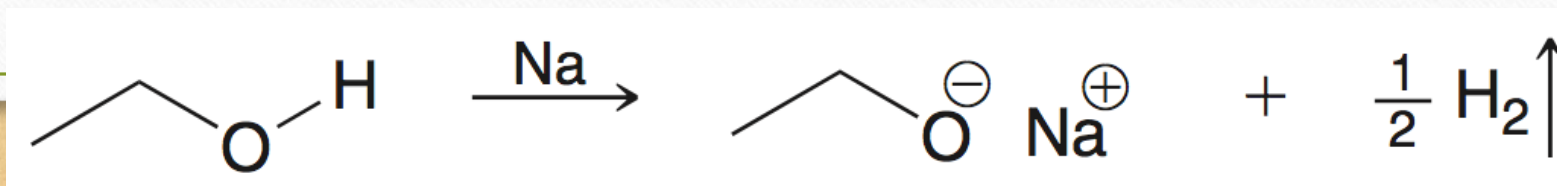
## 1) A strong base is necessary to deprotonate an alcohol.

- NaH is often used to generate the corresponding **alkoxide** because hydride deprotonates the alcohol to generate hydrogen gas (which bubbles out of the solution) :



## 2) Alternatively, metals (Na, K, or Li) are often used as well

- These metals react with the alcohol to liberate hydrogen gas (alkoxide ion produced) :



Lets do problem #4 p. 511

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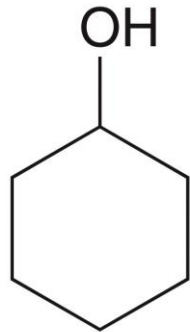
# Factors affecting the acidity of alcohols and phenols

*How can we predict which, of a number of alcohols, is more acidic?*

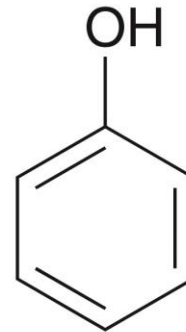
- 3 different ways

1) **Resonance**: a significant factor affecting acidity

Example → (phenol is millions of times more acidic because the conjugate base (CB), **phenoxide**, is resonance stabilized)



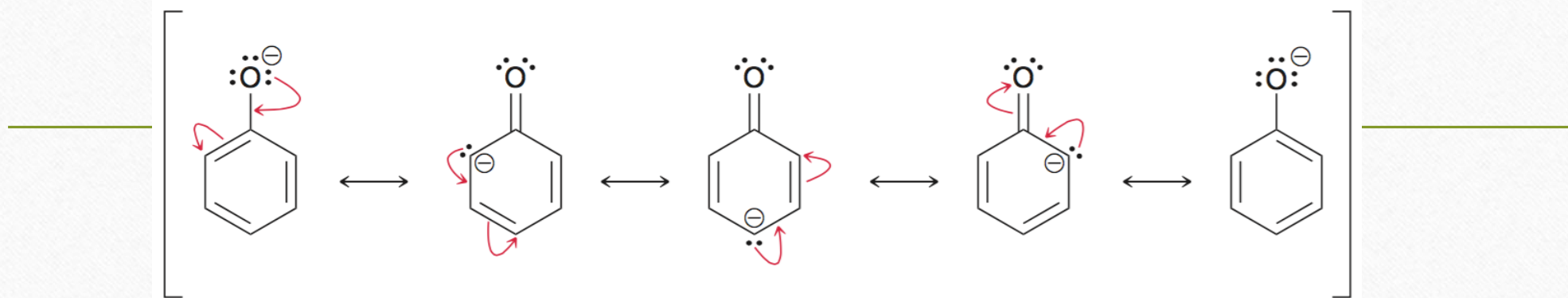
**Cyclohexanol**  
( $pK_a = 18$ )



**Phenol**  
( $pK_a = 10$ )



- Phenol deprotonated  $\rightarrow$  CB is stabilized by resonance



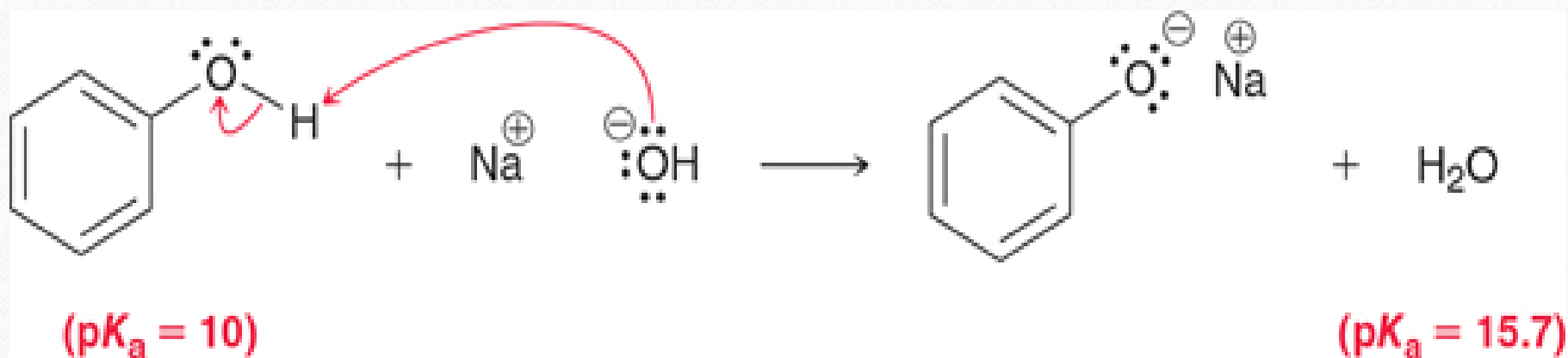
- Resonance-stabilized anion is called a **phenolate** or **phenoxide** ion
- Resonance stabilization of the phenoxide ion explains why phenol is eight orders of magnitude (100,000,000 times) more acidic than cyclohexanol.

- Phenol doesn't need to be deprotonated with a very strong base

- Doesn't need NaH to deprotonate

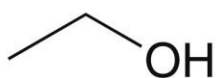
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- Could have  $\text{OH}^-$  to deprotonate

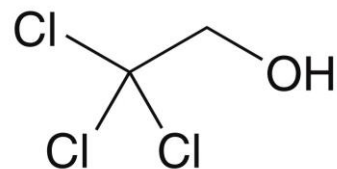


**2. Induction** – presence of electron withdrawing groups increases the acidity of an alcohol or phenol

- Trichloroethanol is four orders of magnitude more acidic than ethanol because the CB is stabilized by the electron-withdrawing effect of the near by chlorine atoms

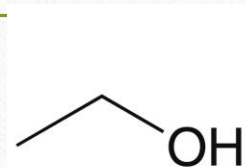


**Ethanol**  
( $pK_a = 16$ )

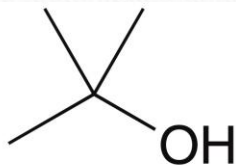


**Trichloroethanol**  
( $pK_a = 12.2$ )

3. **Solvation Effects** – The more poorly solvated a conjugate base, the less stable it is, and the less acidic it's conjugate acid



Ethanol  
( $pK_a = 16$ )

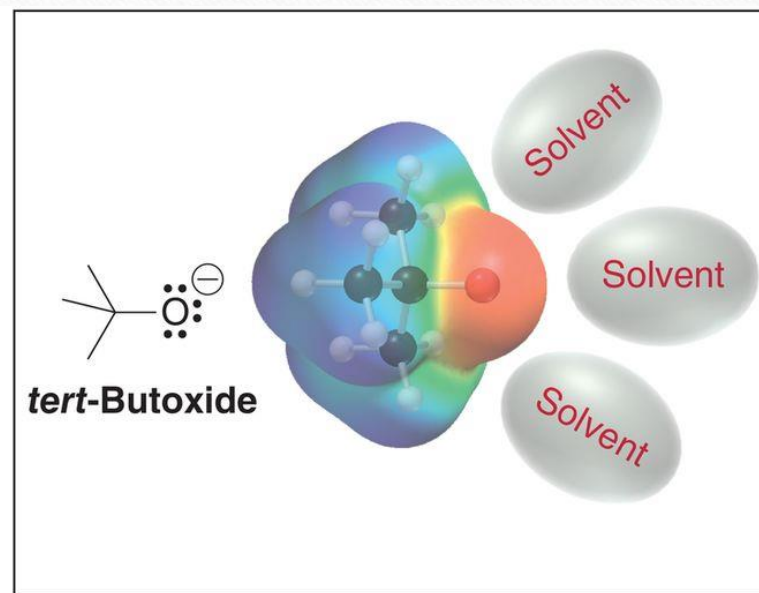
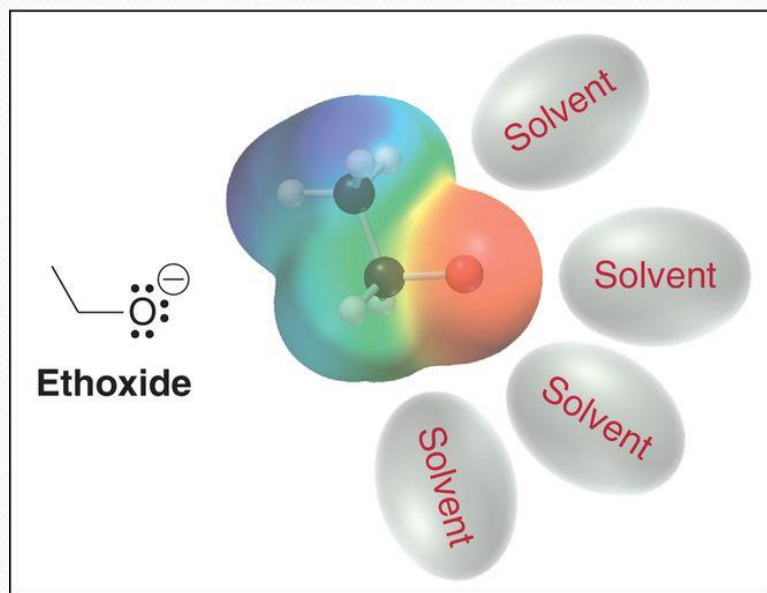


*tert*-Butanol  
( $pK_a = 18$ )

The conjugate base of *tert*-butanol is less stable due to solvation effects

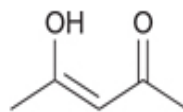
- The  $pK_a$  values indicate that *tert*-butanol is less acidic than ethanol

- Ethoxide ion not sterically hindered (easily solvated by solvent)
- Tert-butoxide is sterically hindered and is less easily solvated

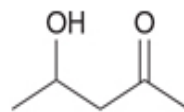


# Skill builder 12.2

Identify which of the following compounds is expected to be more acidic:



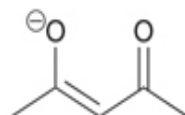
Compound A



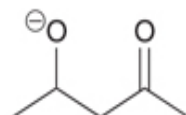
Compound B

## SOLUTION

Begin by drawing the conjugate base of each and then compare the stability of those conjugate bases.

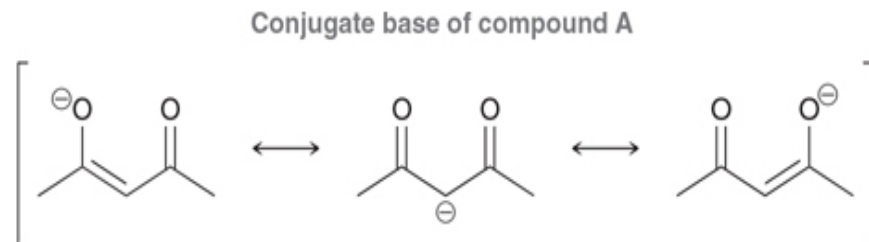


Conjugate base of compound A



Conjugate base of compound B

The conjugate base of compound **B** is not resonance stabilized, but the conjugate base of compound **A** is resonance stabilized.



The conjugate base of compound **A** will be more stable than the conjugate base of compound **B**. Therefore, compound **A** will be more acidic.

We expect compound **B** to have a  $pK_a$  somewhere in the range of 15–18 (the range expected for alcohols). The  $pK_a$  of compound **A** will be more difficult to predict. However, we expect that it will be lower (more acidic) than a regular alcohol. In other words, the  $pK_a$  value will be lower than 15.

Lets do problem #5 p. 513

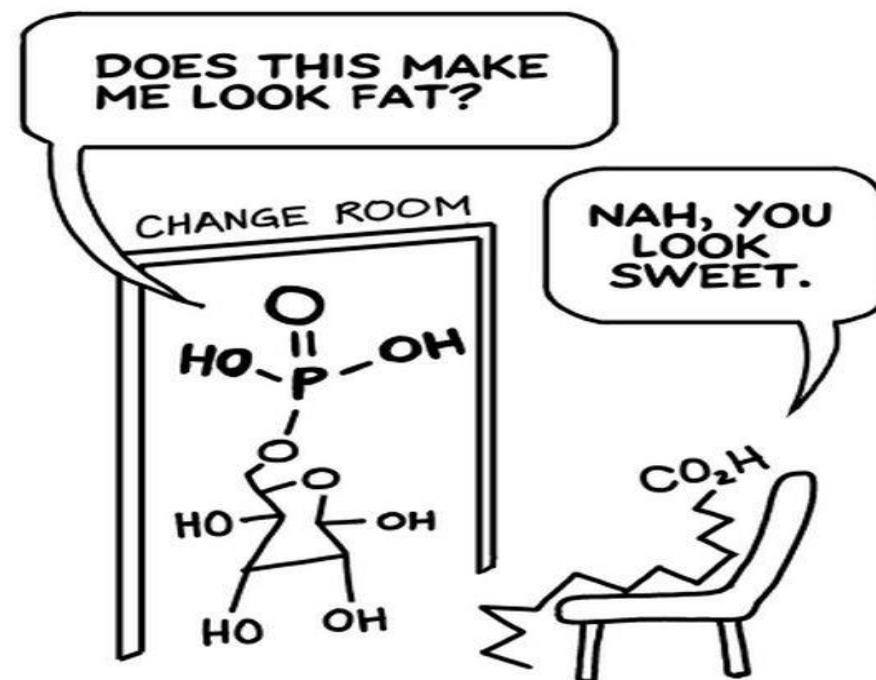
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# CH 12.3

Topic: Preparation of alcohol via substitution  
or addition

EQ: How are alcohols prepared by substitution  
reactions?

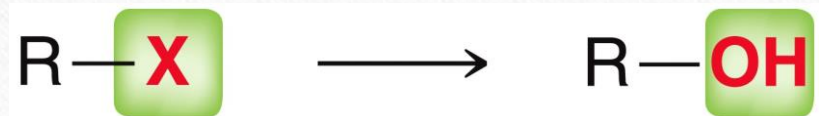
READ pg. 514 then  
take notes





# Substitution rxn

- Alcohols can be synthesized from alkyl halides via substitution:



- The substitution occurs by  $\text{S}_{\text{N}}1$  or  $\text{S}_{\text{N}}2$ , depending on the substrate

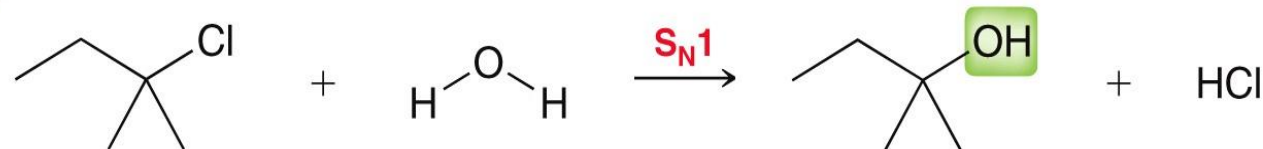
- $\text{S}_{\text{N}}2$  = strong nucleophile

- $\text{S}_{\text{N}}1$  = weak nucleophile

Primary:

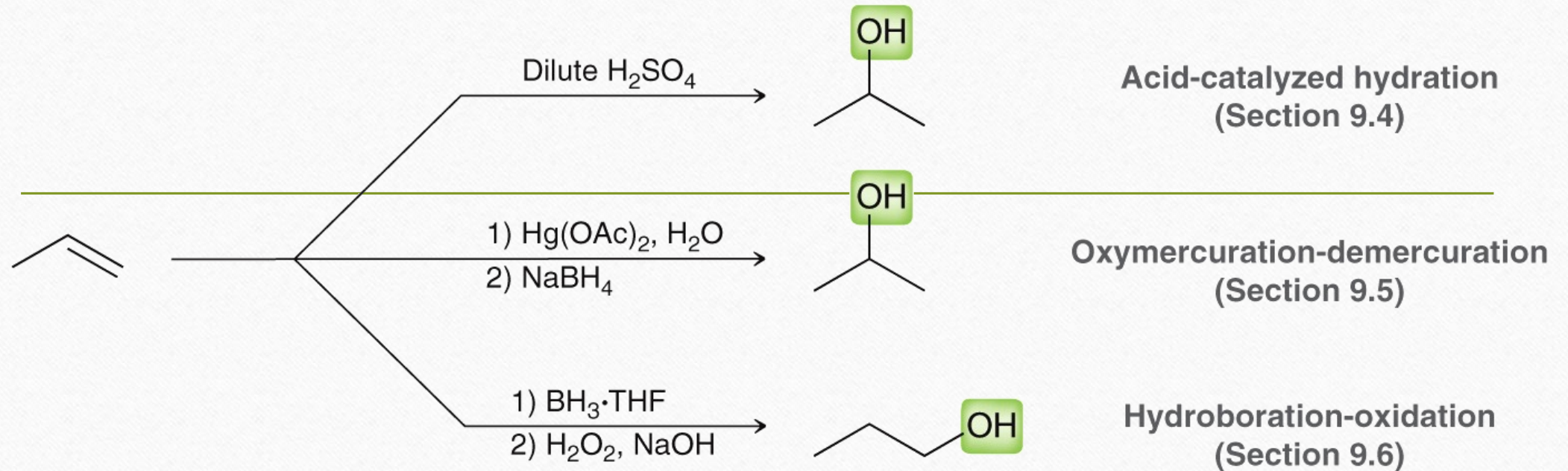


Tertiary:



# Addition rxn

- Several addition rxns can produce alcohols



- Recall that **acid-catalyzed hydration yield Markovnikov addition**
- Hydroboration-oxidation yields *anti* Markovnikov addition**

Lets do problem #7-8 p. 514

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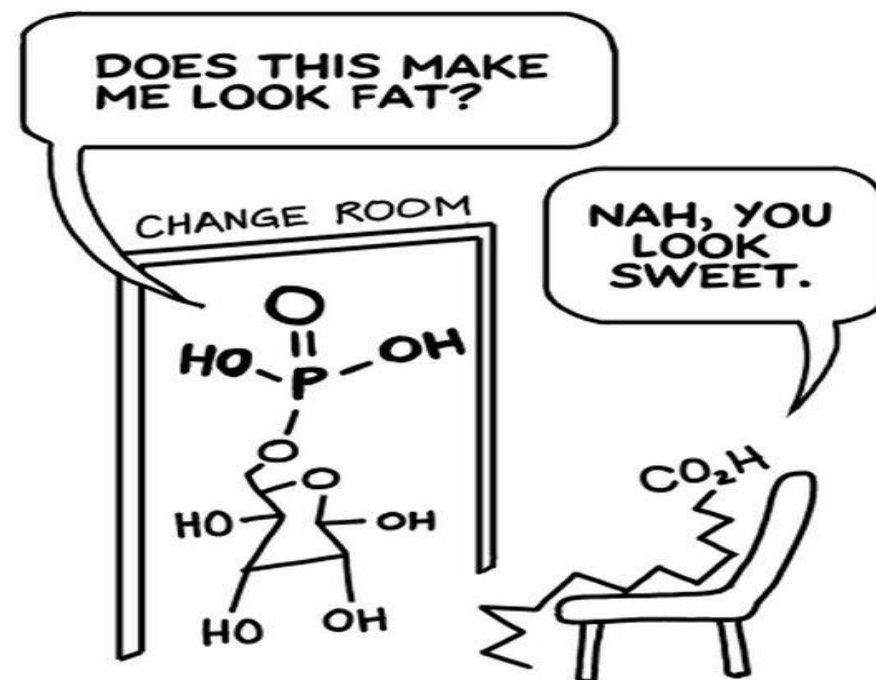
## CH 12.4

Topic: Preparation of Alcohols via Reduction

EQ: How are alcohols prepared by reduction reactions?

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READ pg. 515 - 521  
then take notes



# Preparation of Alcohols via Reduction

- Learn new methods to prepare, alcohols involving a change in *oxidation state*
- A third method to prepare alcohols is by the reduction of a carbonyl.  
What is a carbonyl?

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- Reductions involve a change in oxidation state
- Oxidation state refers to a method of electron bookkeeping
- Formal charge as a method of electron bookkeeping
  - Each atom is assigned half of the electrons it is sharing with another atom

# Oxidation States

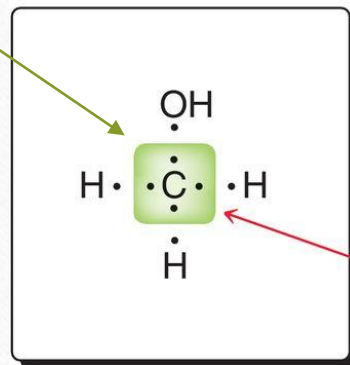
- To calculate formal charge, treat all bonds as *covalent* and break them *homolytically*
- To calculate oxidations states, treat all bond as *ionic*, and break them *heterolytically* (giving each pair of electrons to the most electronegative atom)

- To determine the oxidation state of an atom, imagine the electrons in a bond as a lone pair on the more electronegative atom.

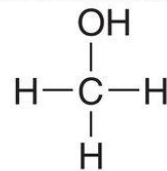
Formal charge of the carbon atom is zero – 4 electrons on the central atom, which is equivalent to the number of valence electrons a carbon atom is supposed to have

Treat all bonds as **covalent** and break them homolytically

Formal charge

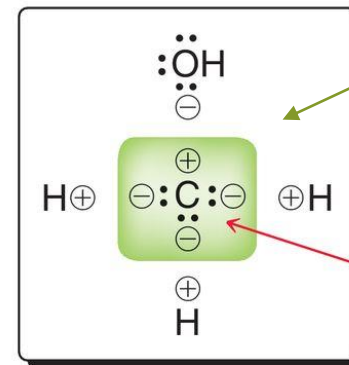


Four electrons



Treat all bonds as **ionic** and break them heterolytically

Oxidation state

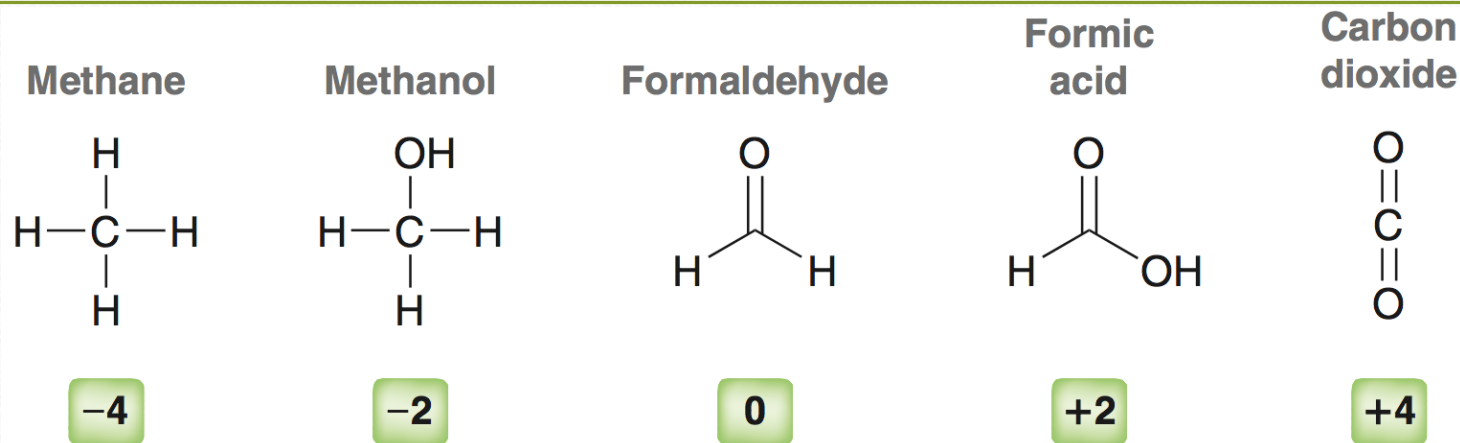


Six electrons

the same carbon atom has an oxidation state of  $-2$ , because we count six electrons on the carbon atom, which is two more electrons than it is supposed to have.

# Oxidation States

- Oxidation states for carbon ranges from -4 to +4 (**C with 4 bonds will always have NO formal charge**)

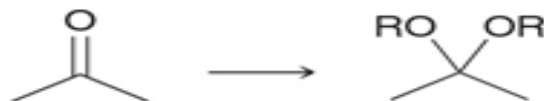


- **Oxidation Rxn** – carbon's oxidation state is **increased**
- **Reduction Rxn** – carbon's oxidation state is **decreased**



# Skill builder 12.3 p. 515

In the following transformation, identify whether the compound has been oxidized, reduced, or neither:

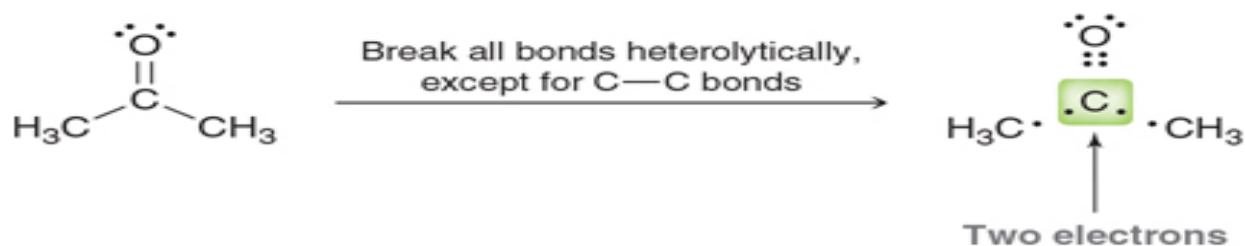


## SOLUTION

Focus on the carbon atom where a change has occurred and determine whether the oxidation state has changed as a result of the transformation. Let's begin with the starting material:

### STEP 1

Determine the oxidation state of the starting material.



Each C—O bond is broken heterolytically, giving all four electrons of the C=O bond to the oxygen atom. Each C—O bond cannot be broken heterolytically, because C and C have the same electronegativity. For each C—C bond, just divide the electrons between the two carbon atoms, breaking the bond homolytically. This leaves a total of two electrons on the central carbon atom. Compare this number with the number of valence electrons that a carbon atom is supposed to have (four). The carbon atom in this example is missing two electrons. Therefore, it has an oxidation state of +2.

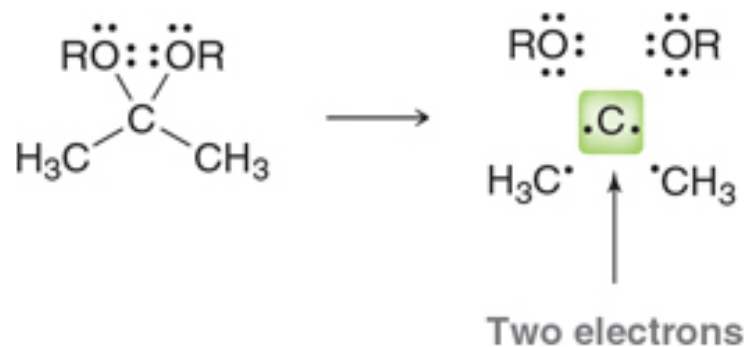
# Skill builder 12.3 p. 515

## STEP 2

Determine the oxidation state of the product.

## STEP 3

Determine if there has been a change in oxidation state.



Now analyze the carbon atom in the product. The same result is obtained: an oxidation state of +2. This should make sense, because the reaction has simply exchanged one  $\text{C}=\text{O}$  bond for two  $\text{C}-\text{O}$  single bonds. The oxidation state of the carbon atom has not changed during the reaction, and therefore the starting material has been neither oxidized nor reduced.

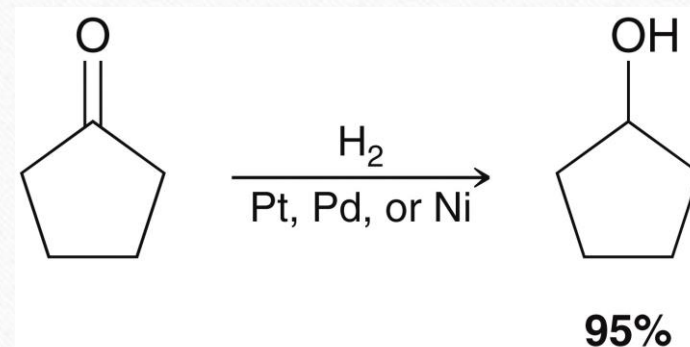
# Reducing Agents

- The conversion of a ketone to an alcohol is a reduction (requires a *reducing agent*)

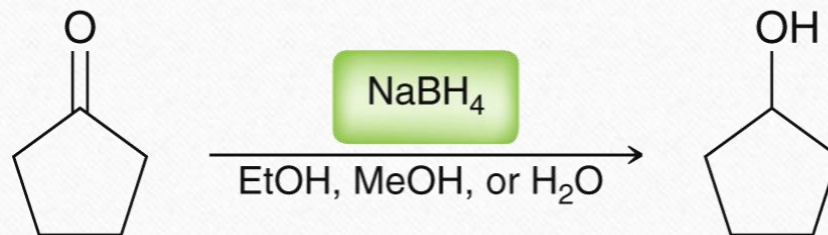


- ***Reducing agent*** – itself oxidized as a result of the rxn
- The reducing agent is then oxidized in the process, while the substrate (carbonyl is reduced)
- The reduction of the carbonyl group, overall, results in the **addition of H and H across the  $\pi$  bond**

- Alkene can undergo hydrogenation in the presence of a metal catalyst (Pt, Pd, or Ni)
  - Similar rxn occur for ketones or aldehydes (more forcing conditions required)
- There are three reducing agents that can be used:
  1. **Catalytic Hydrogenation:**
- This method is rarely used;  
high temp and pressure is required



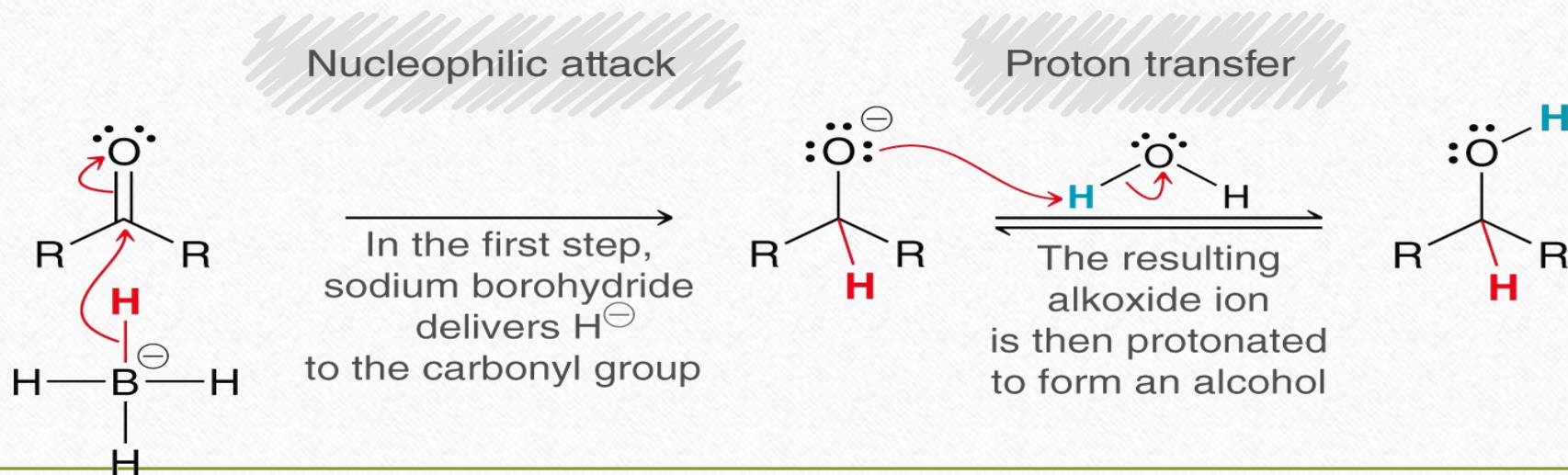
**2. Sodium Borohydride ( $\text{NaBH}_4$ )** – common reducing agent for aldehydes and ketones



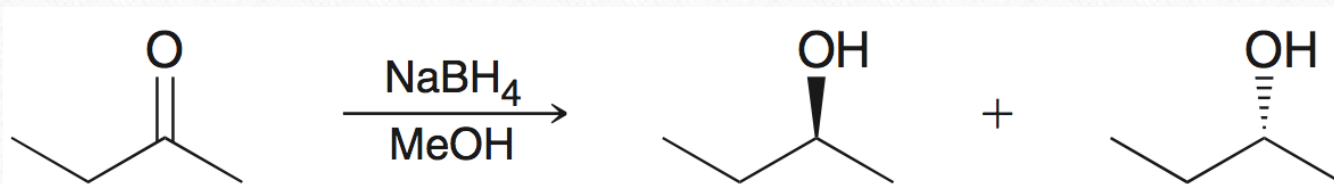
90%

- $\text{NaBH}_4$  acts as a source of hydride ( $\text{H}^-$ ) & the solvent function as the source of a proton ( $\text{H}^+$ ) which could be ethanol, methanol, or water

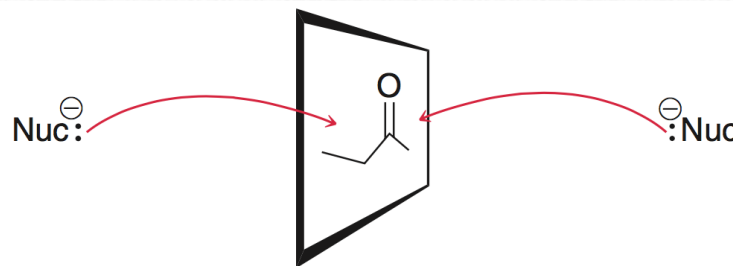
- First step involves the transfer of hydride to the *carbonyl group* (C=O bond)...Second step is a proton transfer
  - As a result, the reaction above cannot be achieved by using NaH (sodium hydride).
- 
- NaH only functions as a base, not as a nucleophile.
  - **But NaBH<sub>4</sub> does function as a nucleophile. Specifically, NaBH<sub>4</sub> functions as a *delivery agent* of nucleophilic H:<sup>-</sup>**



- When nucleophilic  $\text{H}^-$  attacks a carbonyl group, an important change in geometry occurs.
- Prior to the attack, the carbon atom of the carbonyl group is  $sp^2$ -hybridized and has trigonal planar geometry.
- But as a result of the attack, this carbon atom becomes  $sp^3$ -hybridized, with tetrahedral geometry.
- When an *unsymmetrical* ketone is reduced, a new chiral center is created and a pair of stereoisomers is obtained

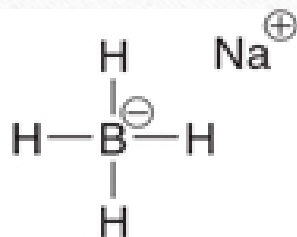


- **Unsymmetrical ketone** has two different R groups
- Reduction of the ketone gives a racemic mixture of enantiomers, because the hydride nucleophile can attack either face of the planar carbonyl group with equal likelihood

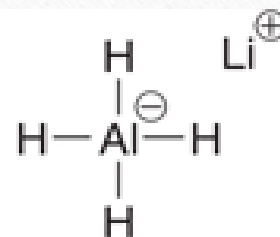




3. **Lithium Aluminum Hydride (LiAlH<sub>4</sub>)** – another common reducing agent for reducing carbonyl compounds



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



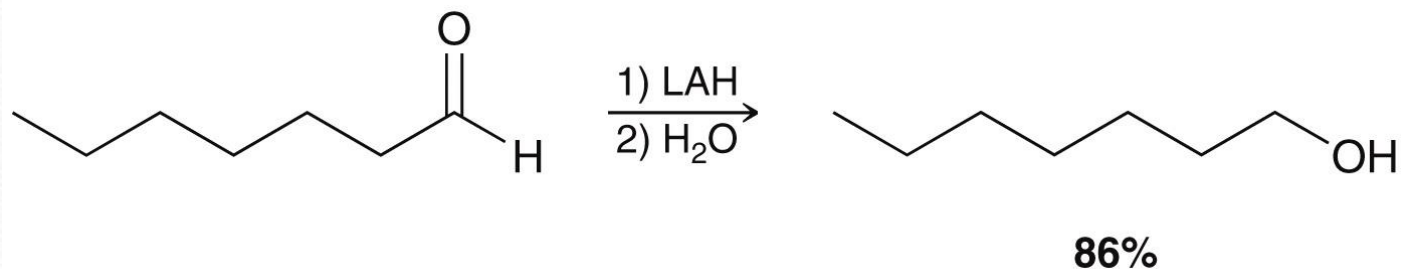
Lithium aluminum hydride  
(LiAlH<sub>4</sub>)

**L**ithium **A**luminum **H**ydride is often abbreviated as **LAH** (delivery agent of H:- , but it is much stronger reagent)

- Water can be used as proton source as well as H<sub>3</sub>O<sup>+</sup>

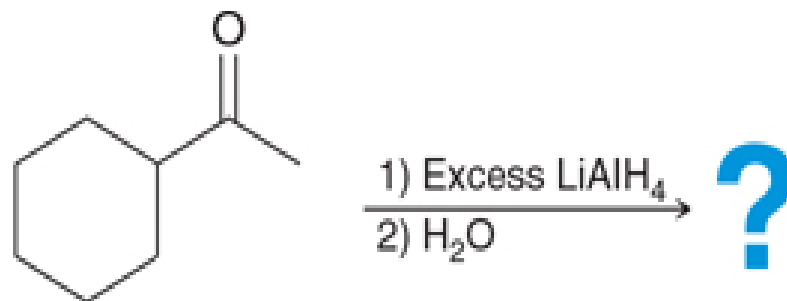
First the ketone or aldehyde is treated with  $\text{LiAlH}_4$ , and then, in a separate step, the proton source is added to the reaction flask. Water ( $\text{H}_2\text{O}$ ) can serve as a proton source, although  $\text{H}_3\text{O}^+$  can also be used as a proton source:

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## Skill Builder 12.4 p. 520

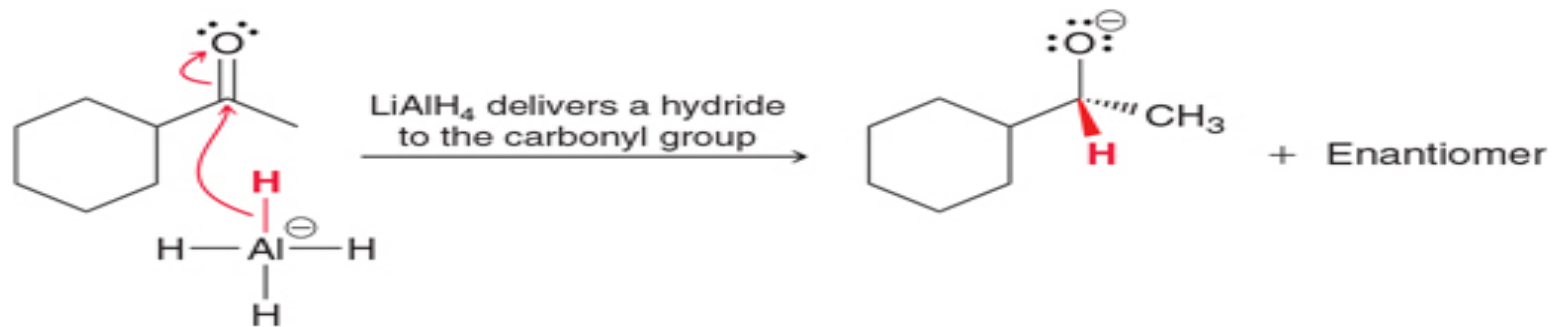
Draw a mechanism and predict the product for the following reaction:



### SOLUTION

LiAlH<sub>4</sub> is a hydride reducing agent, and the starting material is a ketone. When a hydride reducing agent reacts with a ketone or aldehyde, we can draw a mechanism that consists of two steps: nucleophilic attack, followed by proton transfer. In the first step, draw the structure of LiAlH<sub>4</sub> and show a hydride being delivered to the carbonyl group. Do not simply draw H:<sup>-</sup> as the reagent, because H:<sup>-</sup> is not nucleophilic by itself. It must be delivered by the delivery agent (LiAlH<sub>4</sub>). Draw the complete structure of LiAlH<sub>4</sub> (showing all bonds) and then draw a curved arrow that shows the electrons coming from one Al—H bond and attacking the carbonyl group.

# Skill Builder 12.4 p. 520



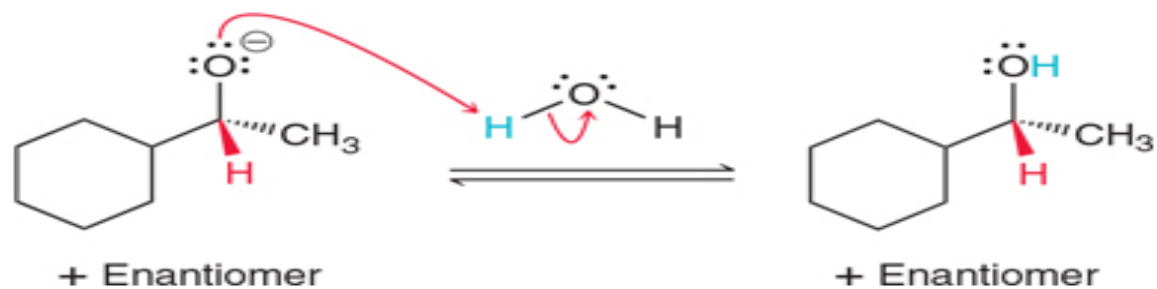
## STEPS 1 AND 2

Draw the two curved arrows that show the delivery of a hydride and then draw the resulting alkoxide ion.

Notice that a chiral center is created during this reduction process, so we expect the alkoxide ion to be produced as a racemic mixture of enantiomers. Then, in the final step of the mechanism, the alkoxide ion is protonated by a proton source, in this case, water.

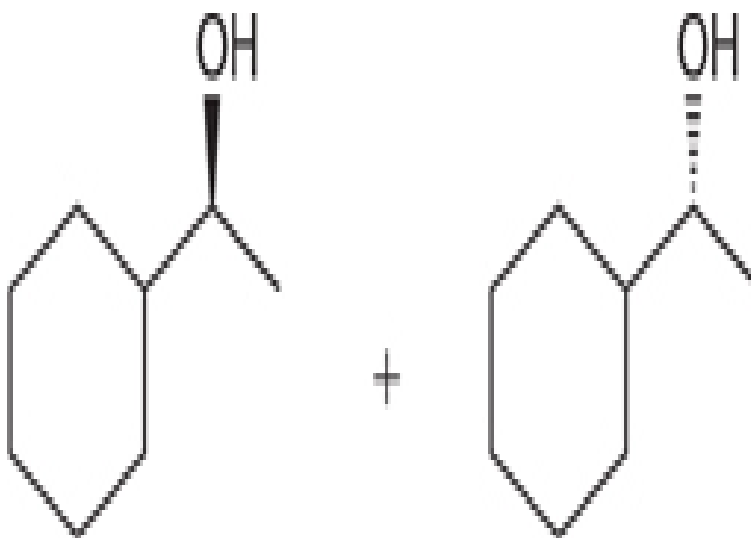
## STEP 3

Draw the two curved arrows showing the alkoxide ion being protonated by the proton source.



## Skill Builder 12.4 p. 520

The product is a racemic mixture of a secondary alcohol, which is what we expect from reduction of a ketone. The enantiomeric products can also be drawn like this:



# Ch 12.5

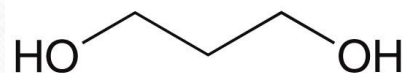
## Preparation of Diols

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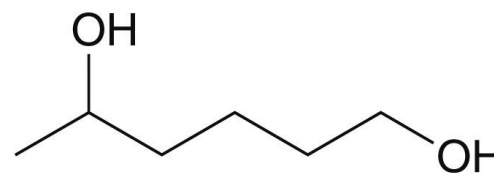
EQ:

# Preparation of Diols

- **Diols** – compounds with 2 hydroxyl groups (additional rules to be able to name them)
    1. Position of both hydroxyl groups are identified with #s placed before the parent
    2. Suffix “diol” is added to the end of the name
- Diols are named using the same method as alcohols, except the “e” is not dropped from the alkane name, and the suffix “**diol**” is used.



1,3-Propanediol

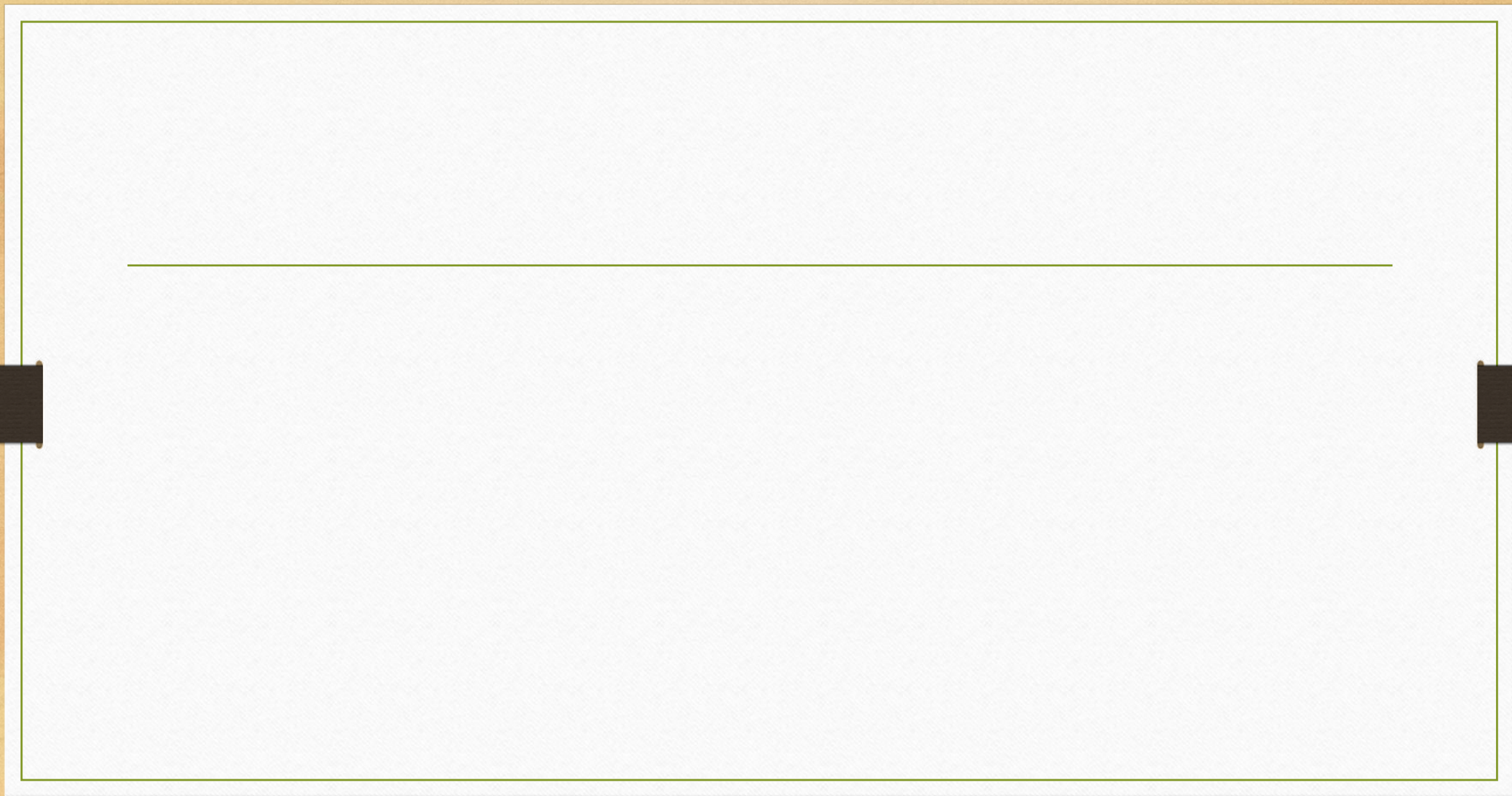


1,5-Hexanediol

**Don't go on !!!**

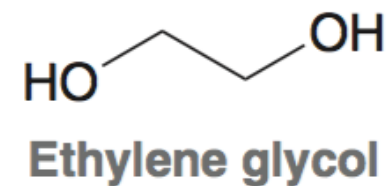
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# Preparation of Diols

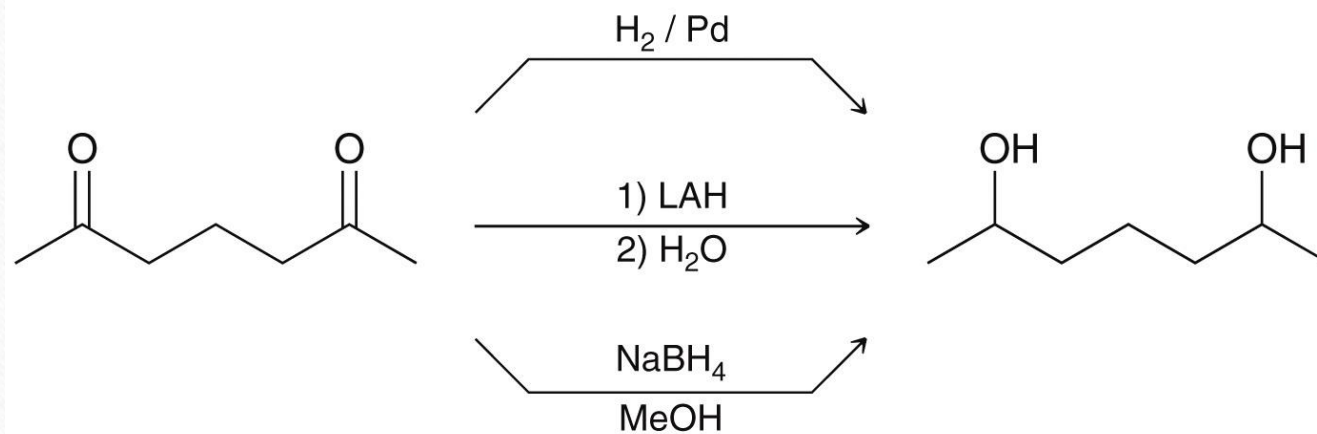
- The term **glycol** is also used to describe a compound with two hydroxyl groups



- Diols** can be prepared from the

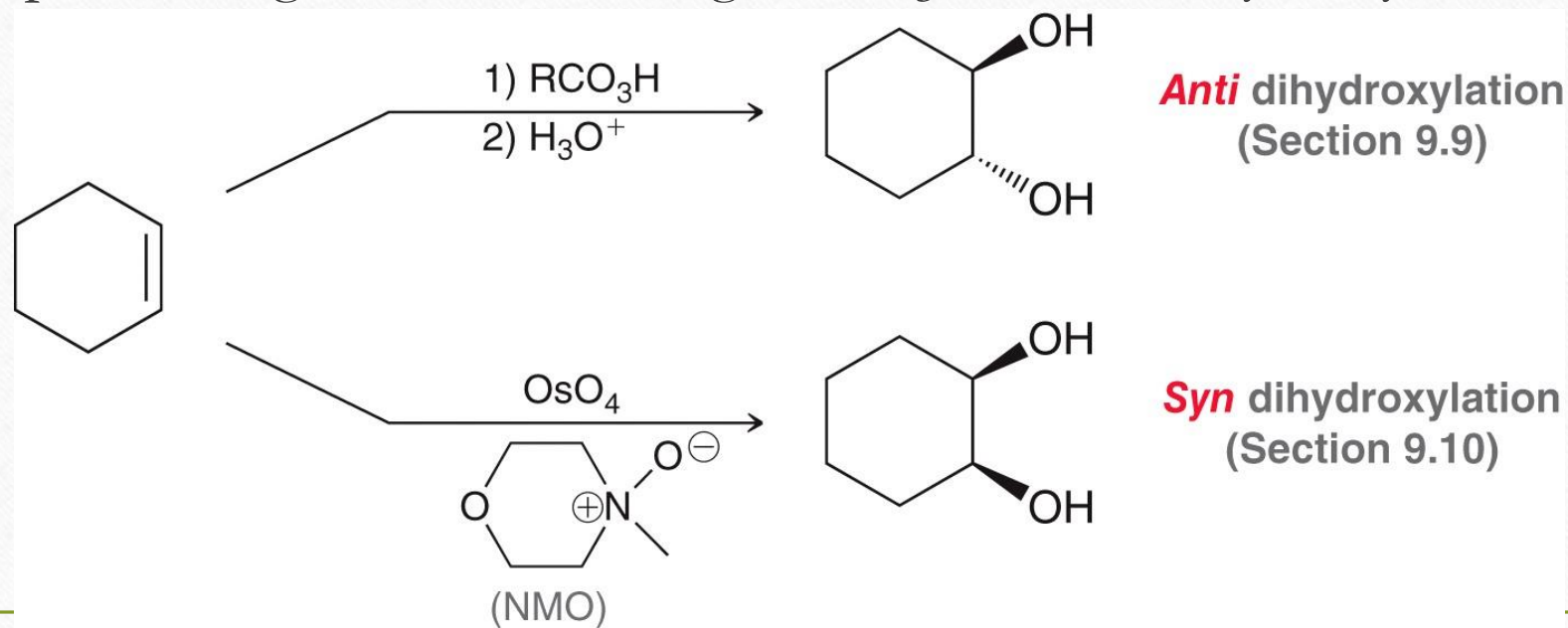
**reduction of diketones**

(using any of the reducing agents)



# Preparation of Diols

- Recall the methods we discussed in chapter 9 to convert an alkene into a diol (we explored reagents for achieving either *syn* or *anti* dihydroxylation...ch.8)



# Ch 12.6

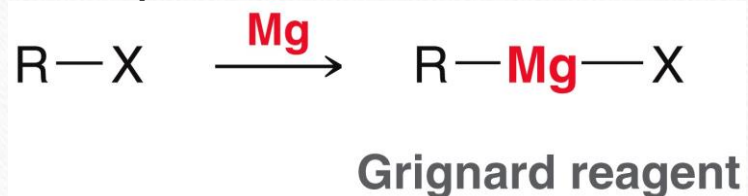
## Topic: Preparation of Alcohols via Grignard Reagents

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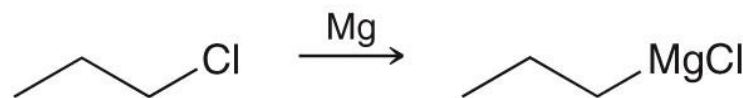
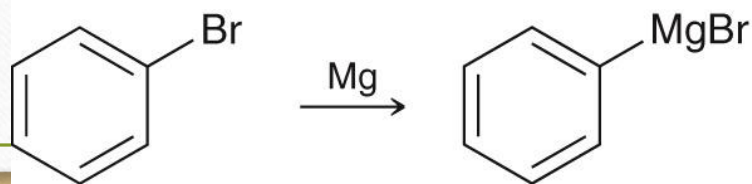
EQ:

# Preparation of Alcohols via Grignard Reagents

- **Grignard reagents** are often used in the synthesis of alcohols
- To form a Grignard, an alkyl halide is treated with Mg metal

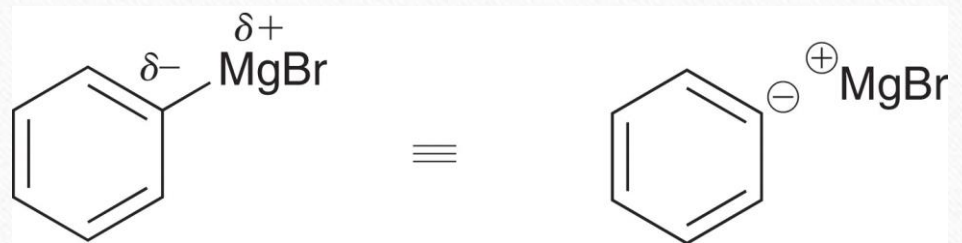


- Named after French chemist (Victor Grignard) who demonstrated their utility in preparing alcohol



# Preparation of Alcohols via Grignard Reagents

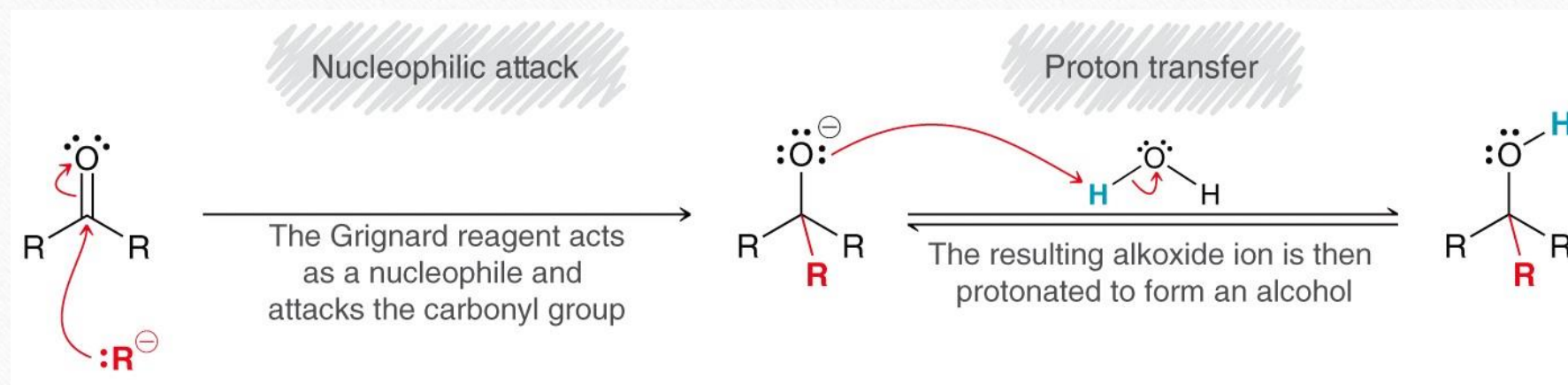
- The electronegativity difference between C (2.5) and Mg (1.3) is great enough that the bond has significant ionic character (a partial negative charge ( $\delta^-$ ) on the C atom)



- The carbon atom behaves like a **carbon anion**, and is a **strong nucleophile**, as well as a **strong base**

# Preparation of Alcohols via Grignard Reagents

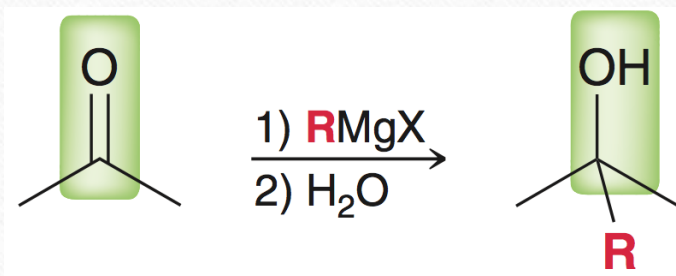
- Grignard reagents react like LAH, and will attack the carbonyl group of a ketone or an aldehyde



# Preparation of Alcohols via Grignard Reagents

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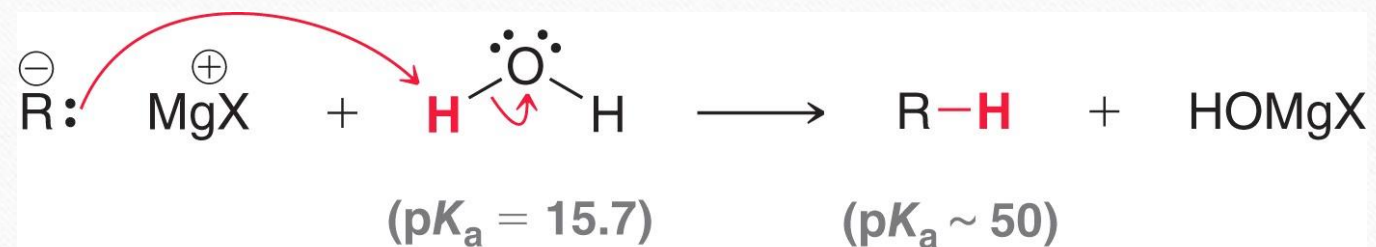
- The key difference – Grignard reaction give a **new C-C bond!**
- Product is an alcohol, and mechanism here is similar to the one in LiAlH<sub>4</sub> & NaBH<sub>4</sub>
- Rxn is reduction as well (*involves introduction of an **R** group*)





# Preparation of Alcohols via Grignard Reagents

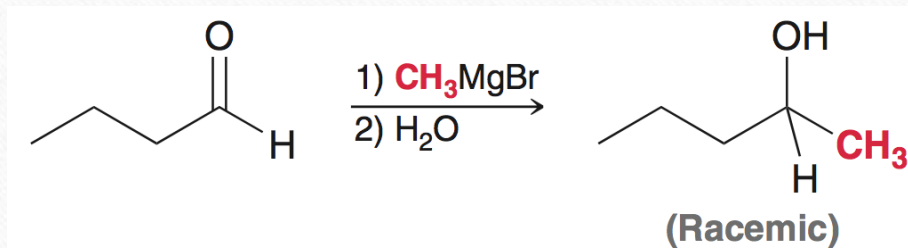
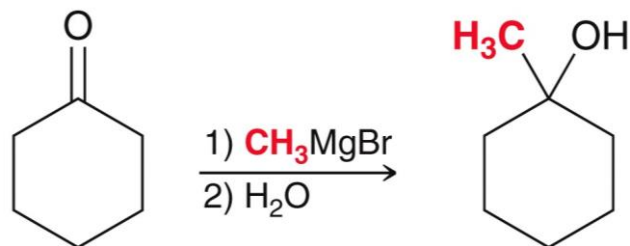
- Because the **Grignard is both a strong base and a strong nucleophile**, care must be taken to protect it from exposure to water or alcohols



- Anhydrous ethers are usually used as solvents for Grignard reactions

# Preparation of Alcohols via Grignard Reagents

• Ex



# Skill Builder 12.5

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