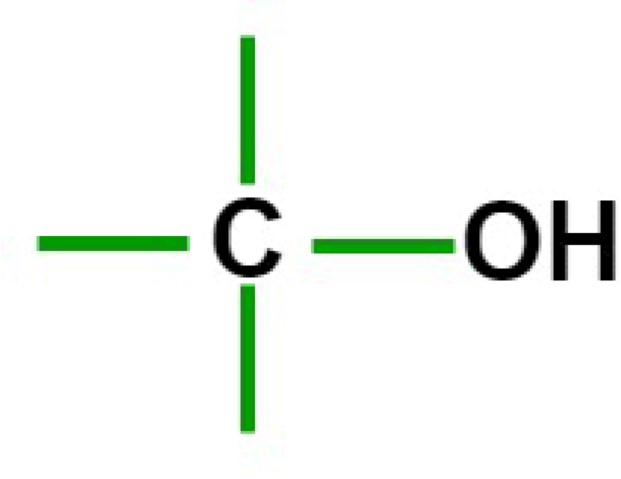
The Islamic University

Department of Pharmaceutical Chemistry

Title of the course: *Organic Chemistry* I

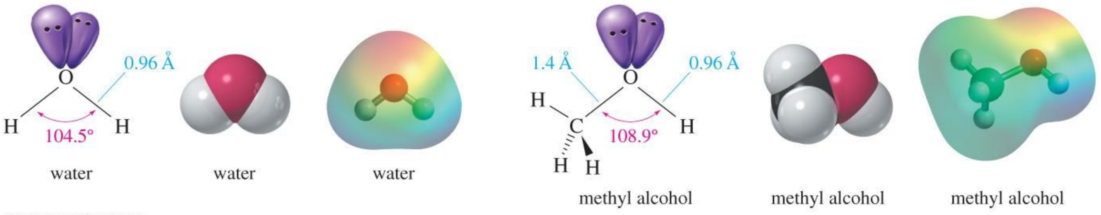
Level: 1st Class, 2nd Semester

Alcohols



Dr.Tabarek Alnaqib

- Alcohols contain a hydroxy group (OH) bonded to an *sp*3 hybridized carbon.

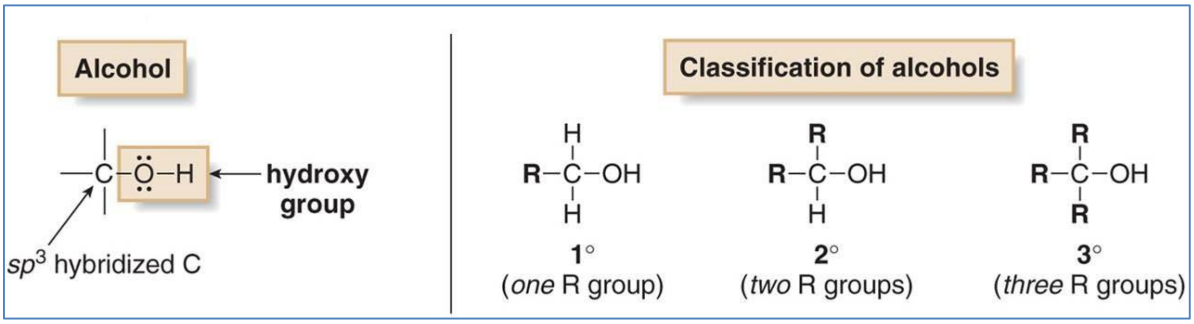


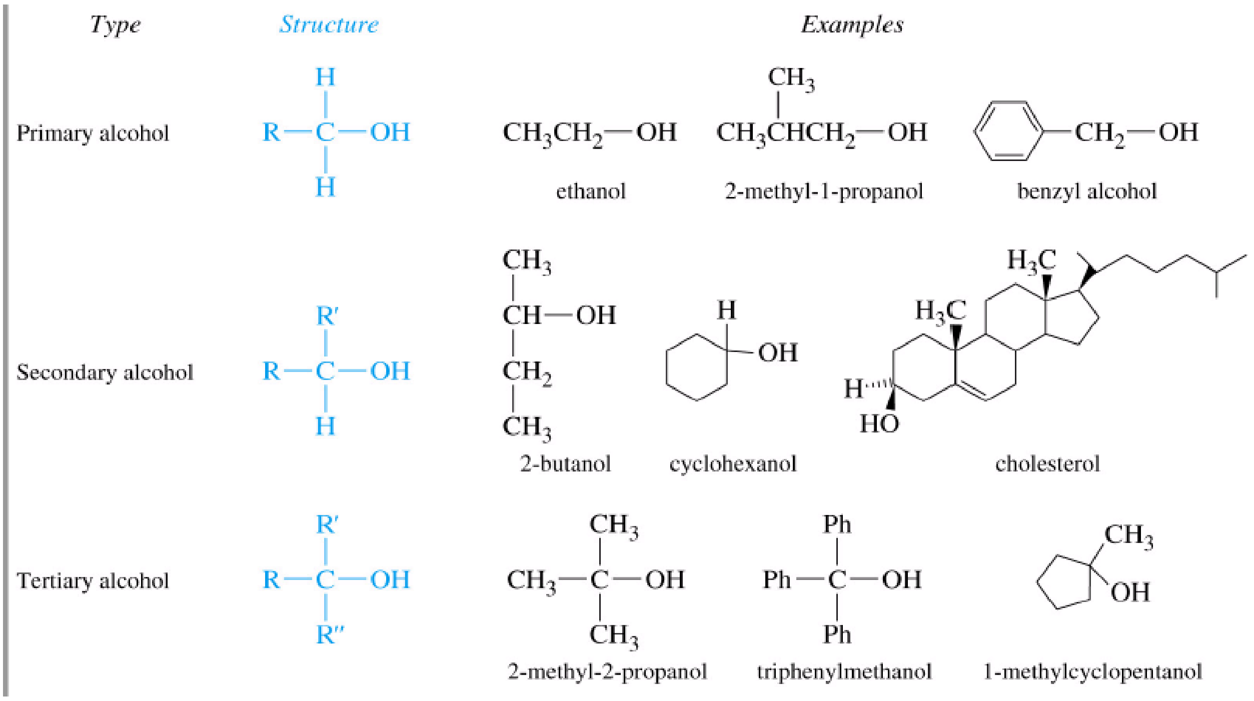
Oxygen is sp^3 hybridized and tetrahedral.

The **H—O—H** angle in water is 104.5°.

The **C—O—H** angle in methyl alcohol is 108.9°.

- They are classified according to the number of alkyl groups attached to carbon bearing the OH.





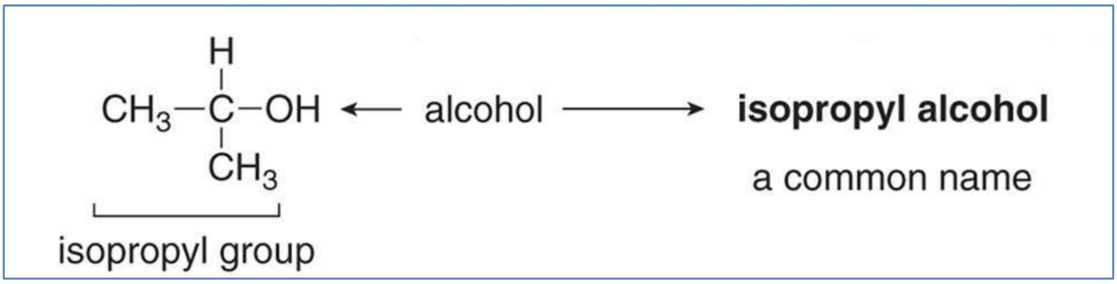
Nomenclature of Alcohols

The IUPAC System Rules

- Common names are often used for simple alcohols. To assign a common name:

- Name all the carbon atoms of the molecule as a single alkyl group.

- Add the word alcohol, separating the words with a space. Naming Alcohols Attached to Rings



- When an OH group is bonded to a ring, the ring is numbered beginning with the OH group.

- Because the functional group is at C1, the 1 is usually omitted from the name.

- The ring is then numbered in a clockwise or counterclockwise fashion to give the next substituent the lowest number.

In the IUPAC system, the hydroxyl group in alcohols is indicated by the ending **-ol.** In common names, the separate word *alcohol* is placed after the name of the alkyl group. The following examples illustrate the use of IUPAC rules, with common names given in parentheses.

CH_3OH

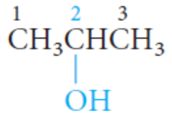
methanol
(methyl alcohol)

CH_3CH_2OH

ethanol
(ethyl alcohol)

$\overset{3}{C}H_3\overset{2}{C}H_2\overset{1}{C}H_2OH$

1-propanol
(*n*-propyl alcohol)

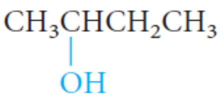


$\overset{1}{C}H_3\underset{\displaystyle OH}{\overset{2}{C}H}\overset{3}{C}H_3$

2-propanol
(isopropyl alcohol)

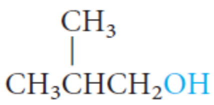
$CH_3CH_2CH_2CH_2OH$

1-butanol
(*n*-butyl alcohol)



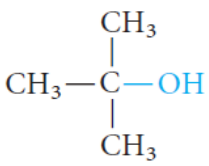
$CH_3\underset{\displaystyle OH}{CH}CH_2CH_3$

2-butanol
(*sec*-butyl alcohol)



$CH_3\overset{\displaystyle CH_3}{CH}CH_2OH$

2-methyl-1-propanol
(isobutyl alcohol)

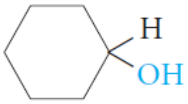


$CH_3-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{C}}-OH$

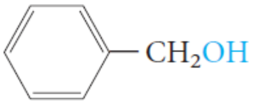
2-methyl-2-propanol
(*tert*-butyl alcohol)

$CH_2{=}CHCH_2OH$

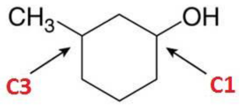
2-propen-1-ol
(allyl alcohol)



cyclohexanol
(cyclohexyl alcohol)

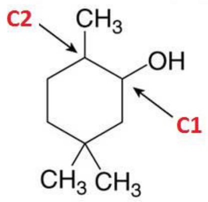


phenylmethanol
(benzyl alcohol)



3-methylcyclohexanol

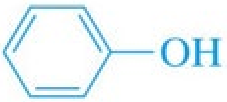
[The OH group is at C1; the second substituent (CH_3) gets the lower number.]

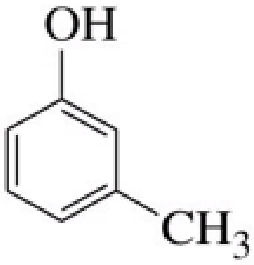


2,5,5-trimethylcyclohexanol

[The OH group is at C1; the second substituent (CH_3) gets the lower number.]

Phenols





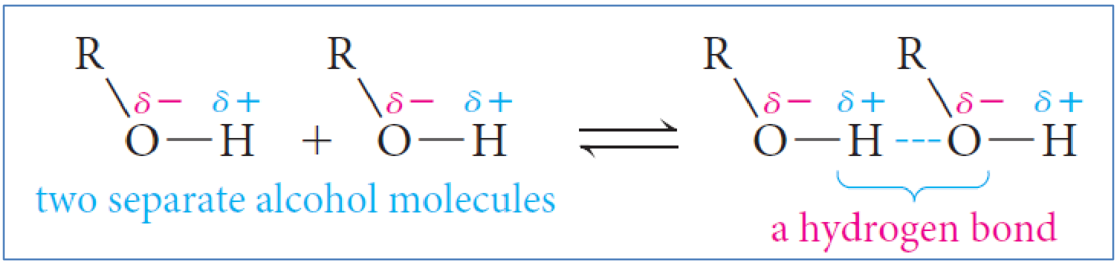
3-methylphenol

Hydrogen Bonding in Alcohols

The boiling points (bp,s) of alcohols are much higher than those of ethers or hydrocarbons with similar molecular weights.

	CH_3CH_2OH	CH_3OCH_3	$CH_3CH_2CH_3$
mol wt	46	46	44
bp	+78.5°C	−24°C	−42°C

The O-H bond is polarized by the high electronegativity of the oxygen atom. This polarization places a partial positive charge on the hydrogen atom and a partial negative charge on the oxygen atom. Because of its small size and partial positive charge, the hydrogen atom can link two electronegative atoms such as oxygen.



Water, of course, is also a hydrogen-bonded liquid. The lower molecular-weight alcohols can readily replace water molecules in the hydrogen bonded network.

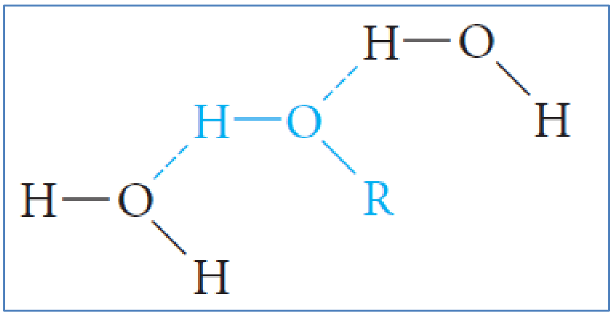
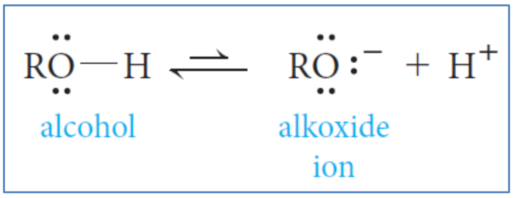


TABLE 10-2 Physical Properties of Selected Alcohols

IUPAC Name	Common Name	Formula	mp (°C)	bp (°C)	Density (g/mL
methanol	methyl alcohol	CH_3OH	−97	65	0.79
ethanol	ethyl alcohol	CH_3CH_2OH	−114	78	0.79
propan-1-ol	*n*-propyl alcohol	$CH_3CH_2CH_2OH$	−126	97	0.80
propan-2-ol	isopropyl alcohol	$(CH_3)_2CHOH$	−89	82	0.79
butan-1-ol	*n*-butyl alcohol	$CH_3(CH_2)_3OH$	−90	118	0.81
butan-2-ol	*sec*-butyl alcohol	$CH_3CH(OH)CH_2CH_3$	−114	100	0.81
2-methylpropan-1-ol	isobutyl alcohol	$(CH_3)_2CHCH_2OH$	−108	108	0.80
2-methylpropan-2-ol	*tert*-butyl alcohol	$(CH_3)_3COH$	25	83	0.79
pentan-1-ol	*n*-pentyl alcohol	$CH_3(CH_2)_4OH$	−79	138	0.82

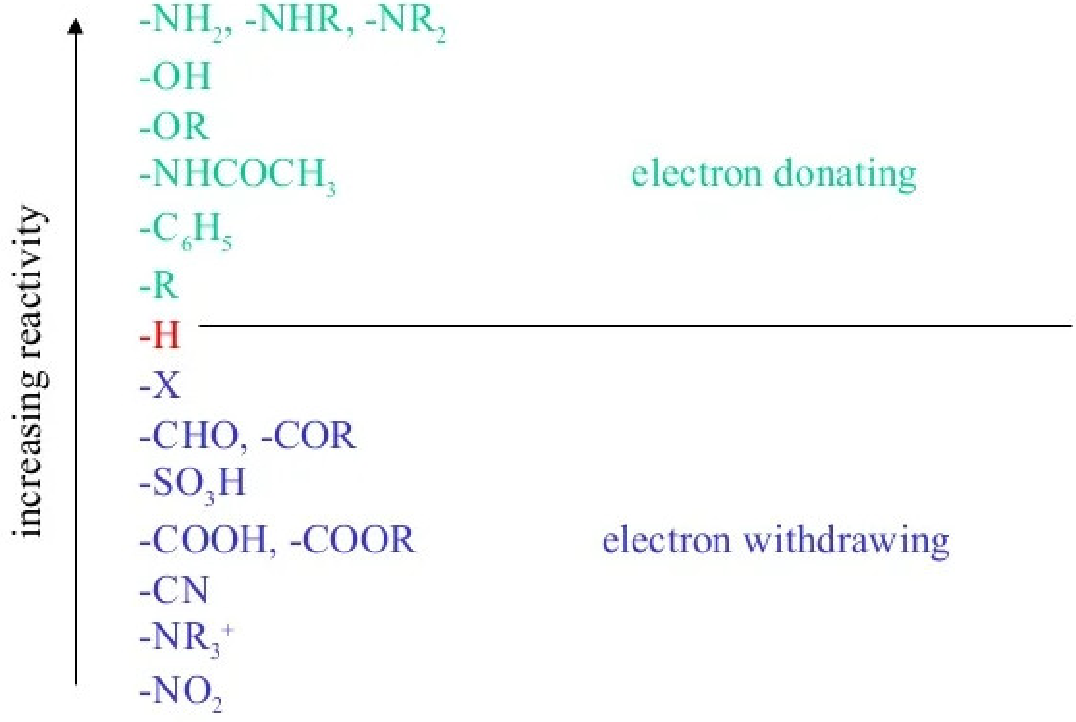
The Acidity of Alcohols and Phenols

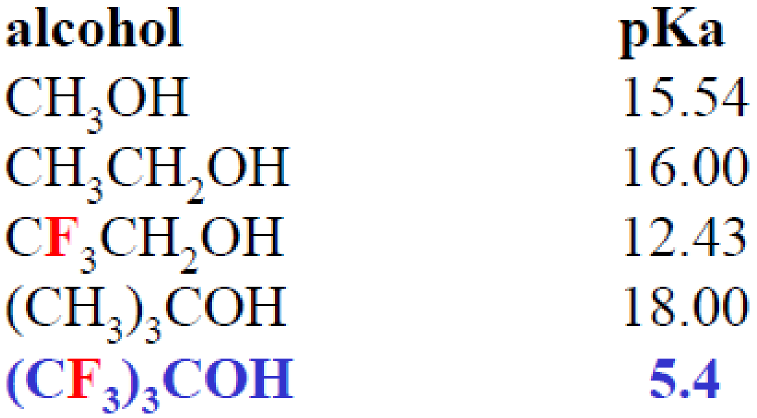
Like water, alcohols and phenols are weak acids. The hydroxyl group can act as a proton donor, and dissociation occurs in a manner similar to that for water:



The conjugate base of an alcohol is an **alkoxide ion** (for example, *meth*oxide ion from *meth*anol, *eth*oxide ion from *eth*anol, and so on).

Withdrawing Groups Enhance Acidity





alcohol	pKa
CH_3OH	15.54
CH_3CH_2OH	16.00
CF_3CH_2OH	12.43
$(CH_3)_3COH$	18.00
$(CF_3)_3COH$	**5.4**

Formation of Alkoxide Ions

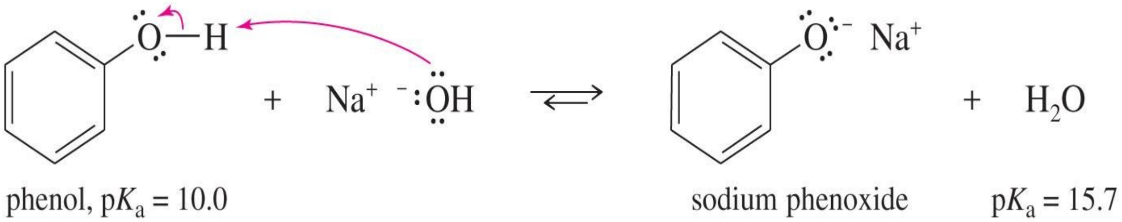
$$\mathrm{R{-}O{-}H} \; + \; \mathrm{Na} \; \longrightarrow \; \mathrm{R{-}O^{-}Na^{+}} \; + \; \tfrac{1}{2}\mathrm{H_2}\uparrow$$

Example

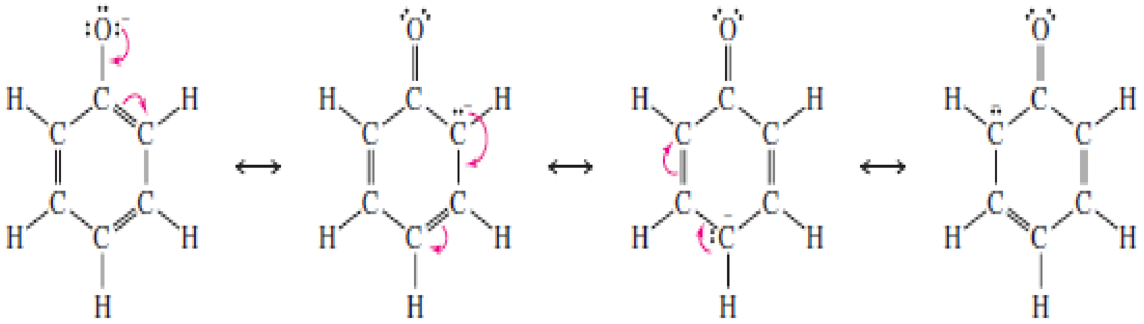
$$\underset{\text{ethanol}}{\mathrm{CH_3CH_2OH}} \; + \; \underset{\text{sodium metal}}{\mathrm{Na}} \; \longrightarrow \; \underset{\text{sodium ethoxide}}{\mathrm{CH_3CH_2O^{-}\,Na^{+}}} \; + \; \underset{\text{hydrogen gas}}{\tfrac{1}{2}\mathrm{H_2}\uparrow}$$

Ethanol reacts with sodium metal to form sodium ethoxide ($NaOCH_2CH_3$), a strong base commonly used for elimination reactions.

Formation of Phenoxide Ion



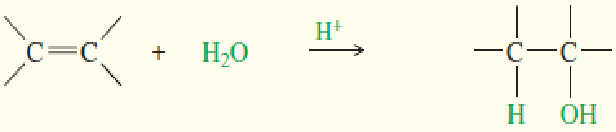
The aromatic alcohol phenol is more acidic than aliphatic alcohols due to the ability of aromatic rings to delocalize the negative charge of the oxygen within the carbons of the ring.



Preparation of Alcohols

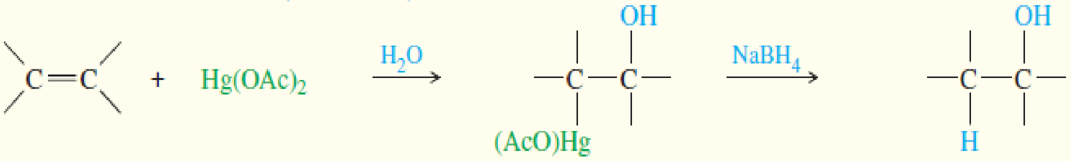
Synthesis of Alcohols from Alkenes **(Chapter 8)**

1. Acid-catalyzed hydration (Section 8-4)



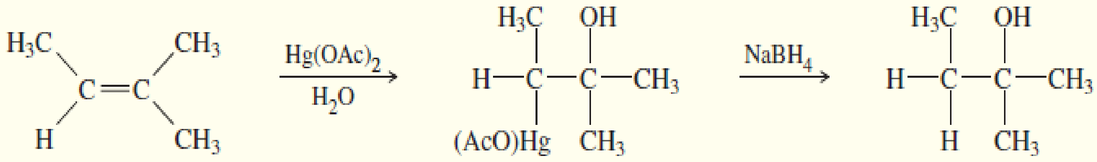
Markovnikov orientation

2. Oxymercuration–demercuration (Section 8-5)



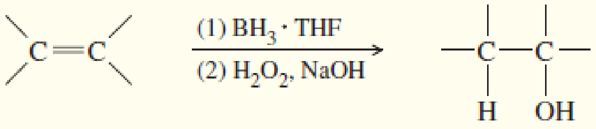
Markovnikov orientation

Example



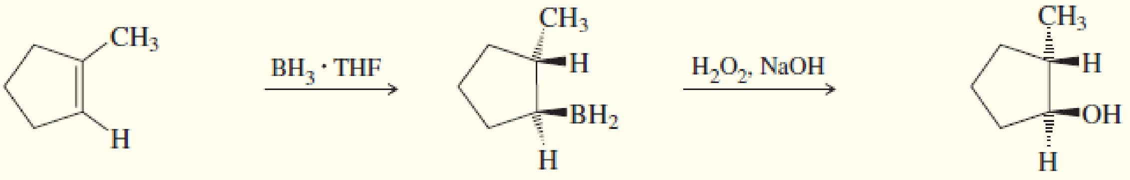
(90% overall)

3. Hydroboration–oxidation (Section 8-7)



syn addition, anti-Markovnikov orientation

Example

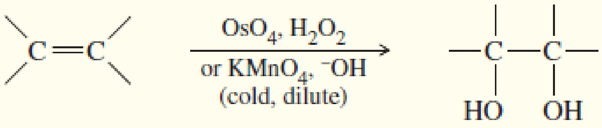


1-methylcyclopentene

trans-2-methylcyclopentanol (85%)

4. Dihydroxylation: synthesis of 1,2-diols from alkenes (Sections 8-13 and 8-14)

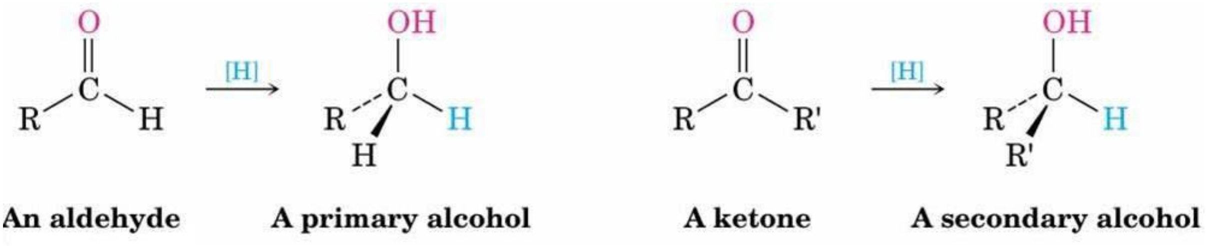
Syn Dihydroxylation



syn dihydroxylation

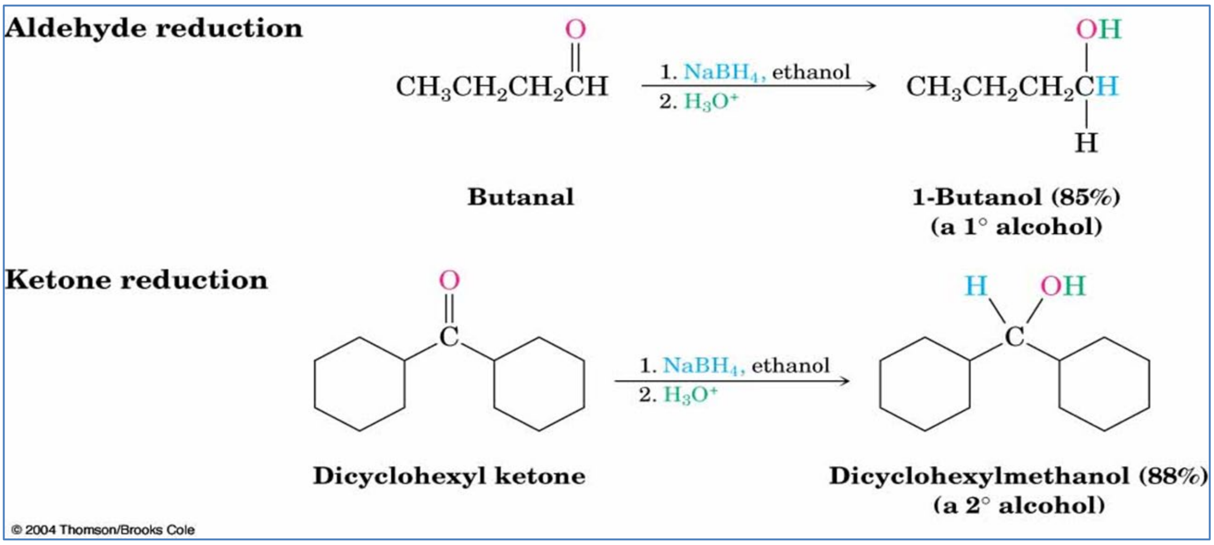
6.Reduction of Aldehydes and Ketones

- **Aldehydes give primary alcohols**
- **Ketones give secondary alcohols**



Reduction Reagent: Sodium Borohydride

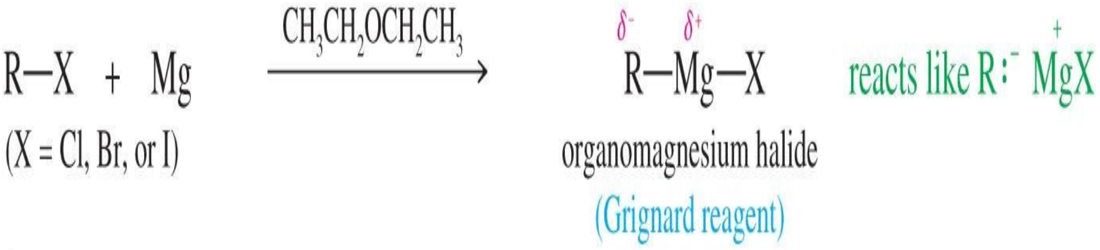
- **Sodium Borohydride (NaBH4) is not sensitive to moisture and it does not reduce other common functional groups.**



7. Grignard Reagents

Grignard and organolithium reagents provide some of the best methods for assembling a carbon skeleton. These strong nucleophiles add to ketones and aldehydes to give alkoxide ions, which are protonated to give alcohols.

A.Formation of the Grignard reagent: Magnesium reacts with an alkyl halide in an anhydrous ether solution.



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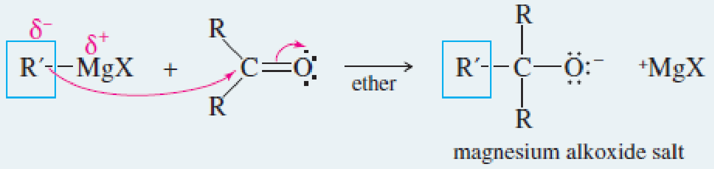
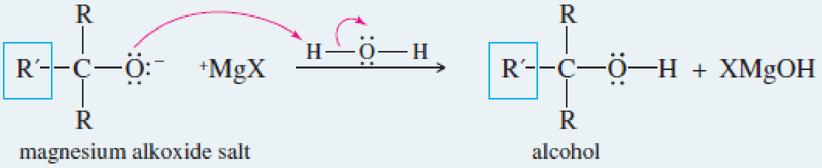
- Formula R—Mg—X (reacts like R:–+MgX).

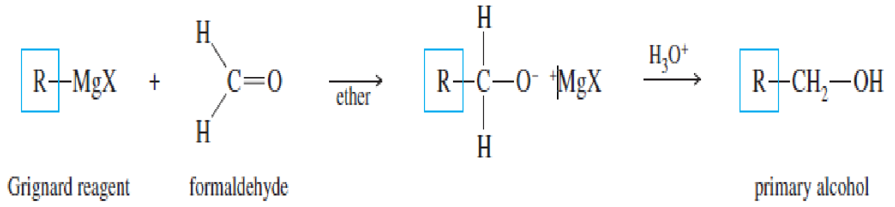
Reaction 1: The Grignard reagent attacks a carbonyl compound to form an alkoxide salt.



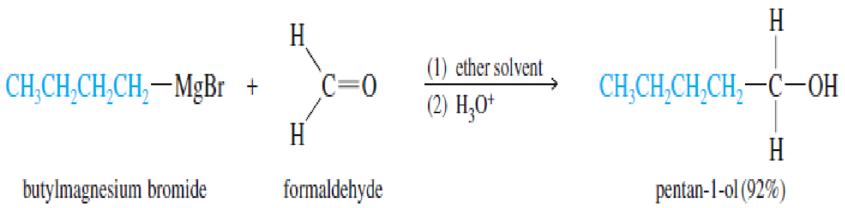
Reaction 2: After the first reaction is complete, water or dilute acid is added to protonate the alkoxide and give the alcohol.



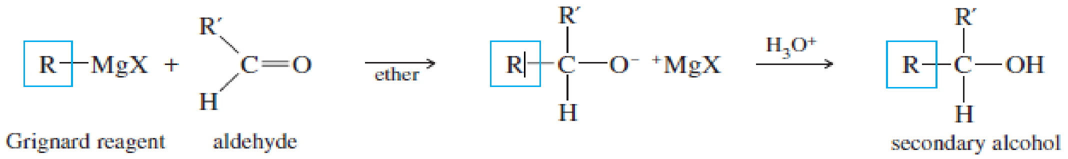
B. Addition of a Grignard reagent to formaldehyde, followed by protonation, gives a primary alcohol with one more carbon atom than in the Grignard reagent.



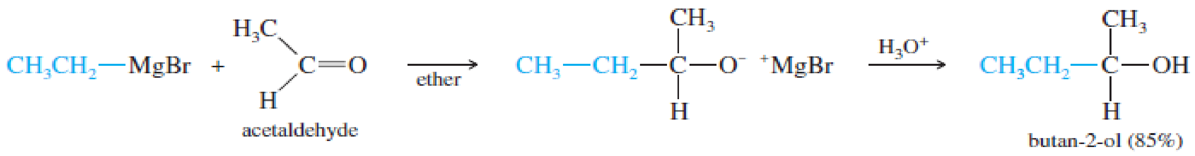
For example,



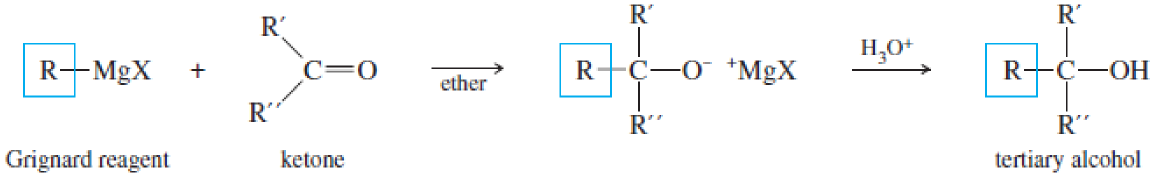
C. Grignard reagents add to aldehydes to give, after protonation, secondary alcohols.



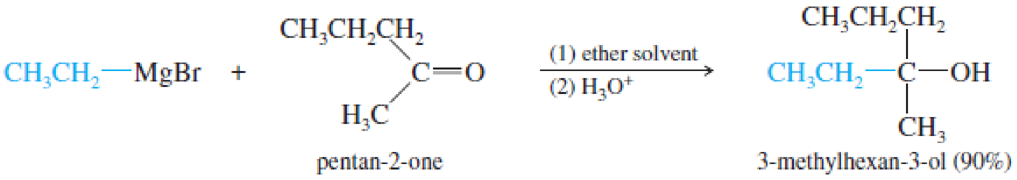
The two alkyl groups of the secondary alcohol are the alkyl group from the Grignard reagent and the alkyl group that was bonded to the carbonyl group of the aldehyde.



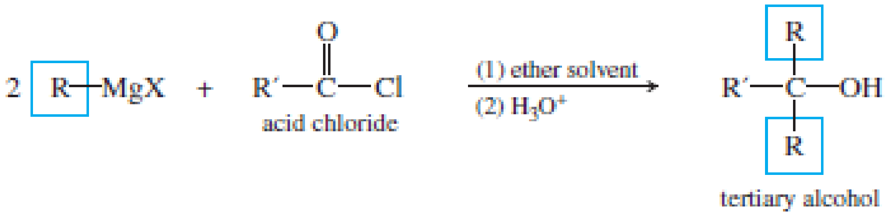
D. A ketone has two alkyl groups bonded to its carbonyl carbon atom. Addition of a Grignard reagent, followed by protonation, gives a tertiary alcohol, with three alkyl groups bonded to the carbinol carbon atom.

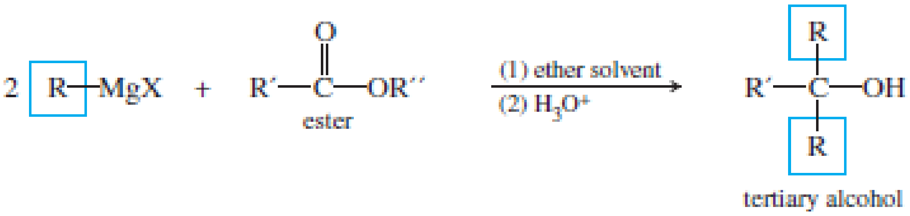


Two of the alkyl groups are the two originally bonded to the ketone carbonyl group. The third alkyl group comes from the Grignard reagent.



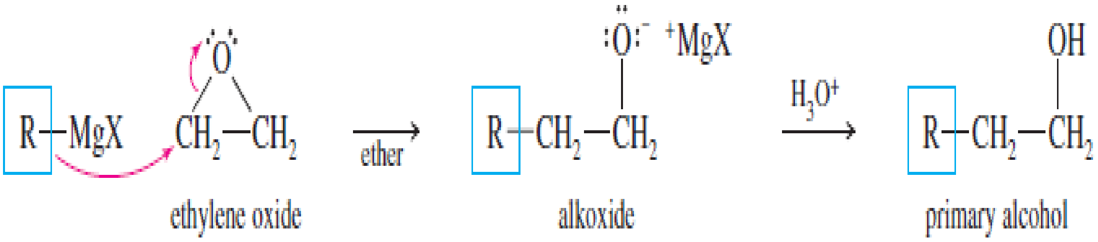
E. Acid chlorides and esters react with two equivalents of Grignard reagents to give (after protonation) tertiary alcohols.





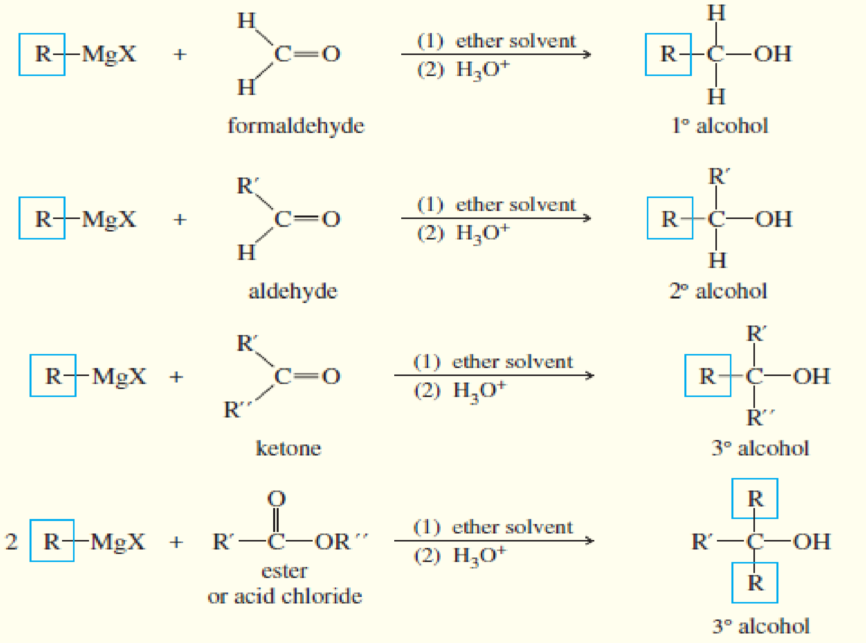
Addition of the first equivalent of the Grignard reagent produces an unstable intermediate that expels a chloride ion (in the acid chloride) or an alkoxide ion (in the ester), to give a ketone. The alkoxide ion is a suitable leaving group in this reaction because its leaving stabilizes a negatively charged intermediate in a fast, strongly exothermic step.

F. Addition to Ethylene Oxide

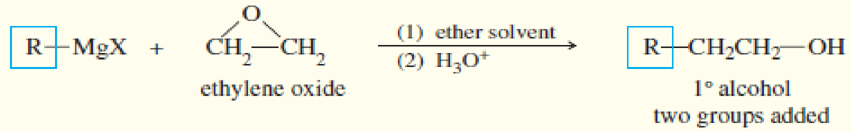


SUMMARY Grignard Reactions

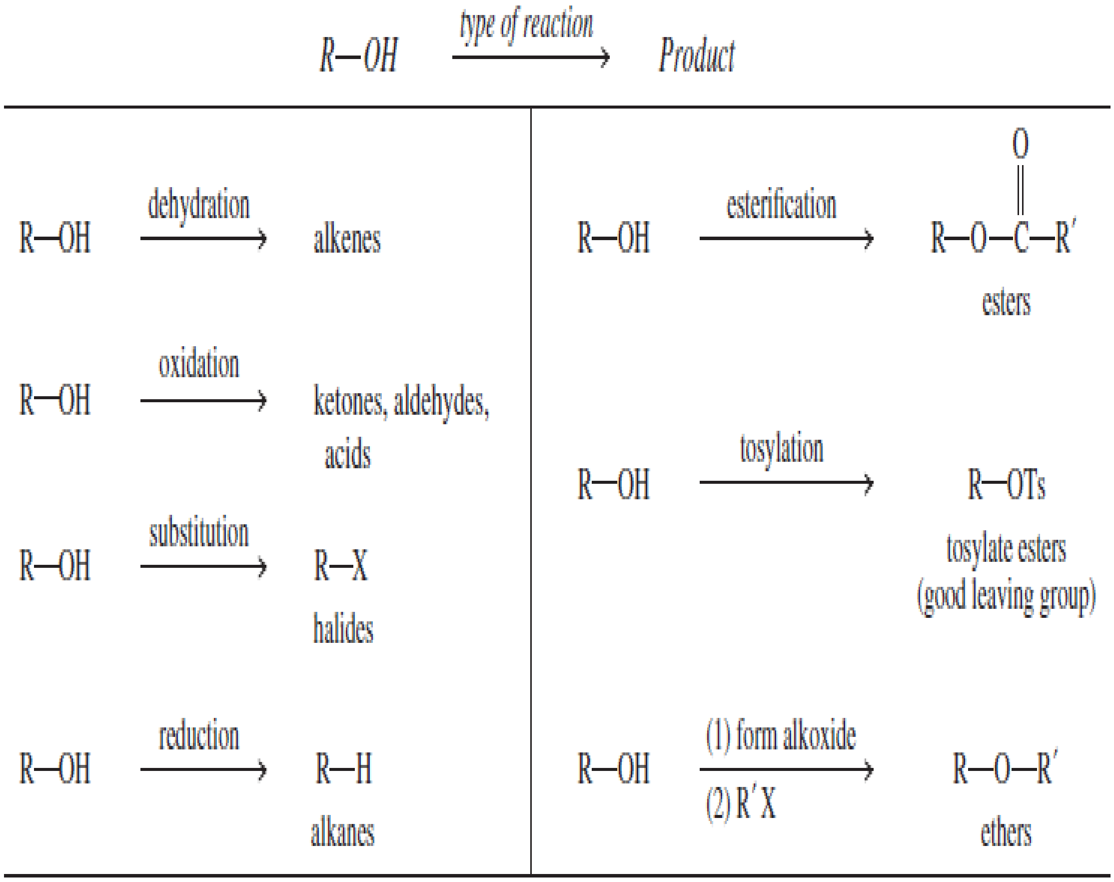
1. *Nucleophilic Additions to Carbonyl Compounds*



2. *Nucleophilic Displacement of Epoxides*



Types of Reactions of Alcohols



$$R\text{—}OH \xrightarrow{\textit{type of reaction}} \textit{Product}$$

$$\text{R—OH} \xrightarrow{\text{dehydration}} \text{alkenes}$$

$$\text{R—OH} \xrightarrow{\text{oxidation}} \text{ketones, aldehydes, acids}$$

$$\text{R—OH} \xrightarrow{\text{substitution}} \underset{\text{halides}}{\text{R—X}}$$

$$\text{R—OH} \xrightarrow{\text{reduction}} \underset{\text{alkanes}}{\text{R—H}}$$

$$\text{R—OH} \xrightarrow{\text{esterification}} \underset{\text{esters}}{\text{R—O—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—R}'}$$

$$\text{R—OH} \xrightarrow{\text{tosylation}} \underset{\substack{\text{tosylate esters}\\ \text{(good leaving group)}}}{\text{R—OTs}}$$

$$\text{R—OH} \xrightarrow[\text{(2) R}'\text{X}]{\text{(1) form alkoxide}} \underset{\text{ethers}}{\text{R—O—R}'}$$