

**CHEM 322 Organic Chemistry II - Professor Kathleen V. Kilway**  
**"Organic Chemistry" by Maitland Jones, 3rd edition**

Chapter 15 - 5, 6, 8, 11, 13, 14, 15, 16, 18, 20, 23, 31, 32, 36, 37, 38, 40, 45, 46, 52, 53, 57, 62, 63.

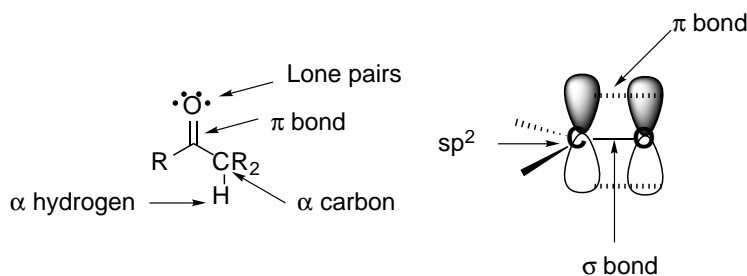
## CHAPTER 16 - CARBONYL CHEMISTRY 1: ADDITION REACTIONS

### Section 16.1

#### I. Preview

##### A- Carbonyl Groups

- 1- They are "not just another double bond".
- 2- They are similar to a C=C bond but have different reactivity.
- 3- It's the basic building block of synthetic organic chemistry.
- 4- There is a dipole moment between the C=O, where the oxygen has two lone pairs of electrons.
- 5- The H on the adjacent carbon, next to the C=O group, which is called the  $\alpha$ -carbon (which will be discussed in Chapter 17).



##### B- Essential Skills

- 1- This chapter involves the nucleophilic addition to the carbonyl carbon.
- 2- Many of these additions are reversible.
- 3- The ones that are irreversible usually involved a reduction reaction, carbon-carbon or carbon-hydrogen bond formation.
- 4- There will be some synthesis of alcohols using organometallic reagents or metal hydrides.

##### C- Important Details

- 1- The reactive compound may not be the favored one by equilibrium.
- 2- The redox cycle of converting alcohols to ketones/aldehydes and reducing the ketones/aldehydes to alcohols is important.
- 3- Protecting groups are used to "protect" attack of the carbonyl group.
- 4- This chapter involves the nucleophilic addition to the carbonyl carbon.

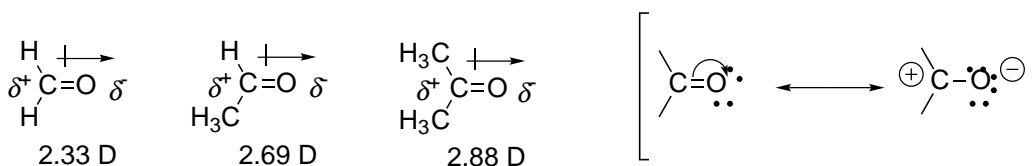
### Section 16.2

#### II. Structure of the Carbon-Oxygen Double Bond

##### A- There are similarities and differences between the carbonyl group and alkenes.

- 1- The carbon atom of the carbonyl group has similar  $sp^2$  hybridization to the carbon of an alkene.

- a- Bond angles are close to  $120^\circ$ .
- b- Bond lengths are similar to alkenes, but  $C=O$  bond is shorter and stronger.
- 2- The  $2p$  orbitals form a bonding  $\pi$  and antibonding  $\pi^*$  molecular orbitals, like alkenes.
  - a- In alkenes the  $2p$  orbitals have equal energy, contributing equally to  $\pi$  and  $\pi^*$  formation.
  - b- But in carbonyls, the oxygen is more electronegative so its  $2p$  orbital contributes more to  $\pi$ , whereas the carbon contributes more to  $\pi^*$ .
- 3- Carbonyls are very polar compared to alkenes.
  - a- The  $\pi$  and  $\pi^*$  orbitals of carbonyls are unsymmetrical in nature.
  - b- More electrons are found in the  $\pi$  orbital close to oxygen so there is a strong dipole moment.
- 4- The two major resonance forms show the Lewis acid character of  $C=O$ . (Fig. 16.6)

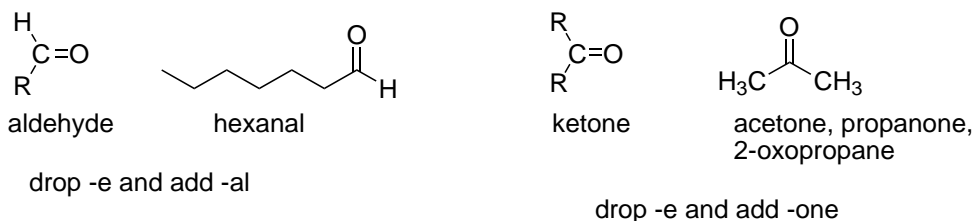


## Section 16.3

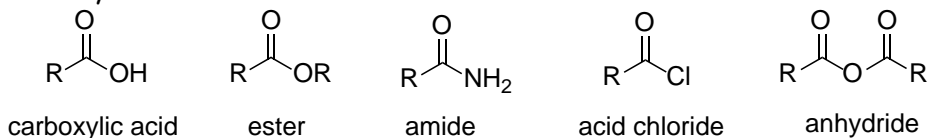
### III. Nomenclature of Carbonyl Compounds

A- Generic carbonyl compound takes the form  $R_2C=O$

- 1- Aldehydes carry a hydrogen in place of one R-group; formaldehyde has a hydrogen in place of both R groups.
  - a- Some common names are retained for aldehydes with four carbons or less.
  - b- Under IUPAC, drop "e" of the parent name and add "al".
  - c- Compounds with two aldehydes are called **dials**; the parent "e" is not dropped and "dial" is added. (e.g. propanedial.)
- 2- Ketones have two alkyl, alkenyl, or aryl substituents.
  - a- The only common name that has been retained is **acetone**, or dimethyl ketone.
  - b- The most common method of naming ketones is to drop the "e" of the parent name and add "one," (e.g., propanone)
  - c- Ketones have more than one way to be named; for example acetone can be 2-oxopropane, propanone, or dimethyl ketone.
  - d- Compounds with two ketones are called **diones**; the parent "e" is retained and "dione" is added, as in 2,4-Pentanedione.



- 3- Compounds with both an aldehyde and ketone are named as aldehydes because aldehydes have higher priority than ketones.
- 4- Many aromatic aldehydes and ketones have retained common names. (Fig. 16.12 & 16.13)
- 5- Other compounds with carbonyl groups include:
  - a- Carboxylic acid
  - b- Ester
  - c- Amide
  - d- Acid chloride
  - e- Anhydride

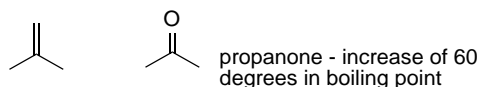


### Section 16.4

#### IV. Physical Properties of Carbonyl Compounds

A- Carbonyl compounds are polar and some are even water soluble.

- 1- Boiling points are considerably higher than hydrocarbons with the same number of heavy atoms.
  - a- Acetaldehyde boils at  $\sim 63^\circ$  higher than propane and propylene
  - b- Acetone boils at  $\sim 60^\circ$  higher than isobutene.



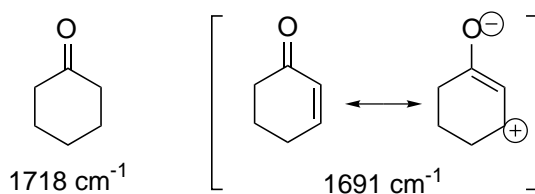
- 2- See Table 16.1 for physical properties of some common carbonyl compounds.

### Section 16.5

#### V. Spectroscopy of Carbonyl Compounds

A- Infrared Spectroscopy

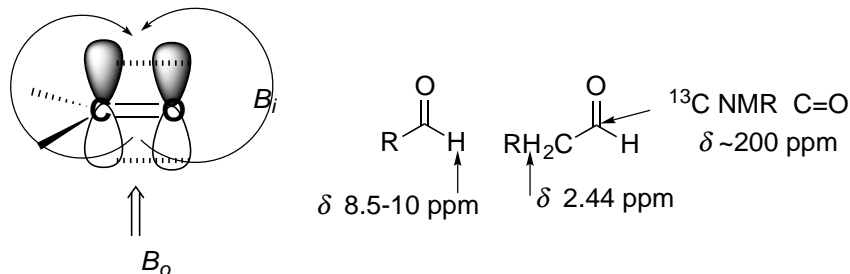
- 1- Carbonyl groups show a strong stretching frequency at  $\sim 1700\text{ cm}^{-1}$ .
- 2- Aldehydes show a pair of bands in the C-H stretching region at  $\sim 2850$  and  $2750\text{ cm}^{-1}$ .
- 3- Conjugated carbonyl compounds appear at lower frequency than unconjugated carbonyls due to resonance effects.
- 4- See Table 16.1 for spectral properties of selected carbonyl compounds.



B- Nuclear Magnetic Resonance Spectroscopy

- 1- The carbonyl group inductively withdraws electrons from nearby positions, causing a deshielding effect.

- The further away from the carbonyl group, the less deshielding is observed.
- Aldehydic hydrogens appear at very low field,  $\delta$  8.5-10 ppm.
- The carbon atom of the carbonyl group are at especially low field in the  $^{13}\text{C}$  NMR.

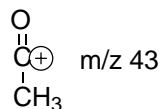


### C- Ultraviolet Spectroscopy

- It is possible to detect a weak absorption through the promotion of a nonbonding, or  $n$ , electron to the antibonding  $\pi^*$  orbital, the  $n \rightarrow \pi^*$  absorption. (See Table 16.2.)
- In unsaturated carbonyl compounds, the strong  $\pi \rightarrow \pi^*$  transition can be detected because of the conjugation-induced shift to longer wavelengths. (Table 16.2)

### D- Mass Spectrometry

- The diagnostic cleavage reaction for many simple carbonyl compounds causes a resonance-stabilized acylium ion to be generated.
- Mass/charge ratio:  $m/x = 43$ .

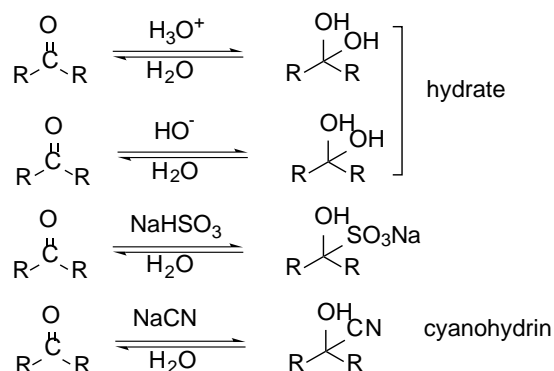


## Section 16.6

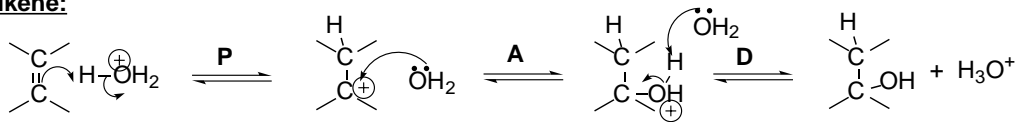
### VI. Reactions of Carbonyl Compounds: Simple Reversible Additions

#### A- The reaction between water and a carbonyl compound forms a hydrate.

- In addition reactions, carbonyl compounds can behave as both Lewis acids and Lewis bases, depending on the reagents.
- There are some similarities between addition to  $\text{C}=\text{C}$  and  $\text{C}=\text{O}$ , and some important differences.
- Thermodynamic influences determine whether water will add to the carbon or oxygen.
  - Addition to the carbon puts the negative charge on the electronegative oxygen.
  - Adding to oxygen forms a weaker bond, whereas addition to carbon gives a stronger bond.

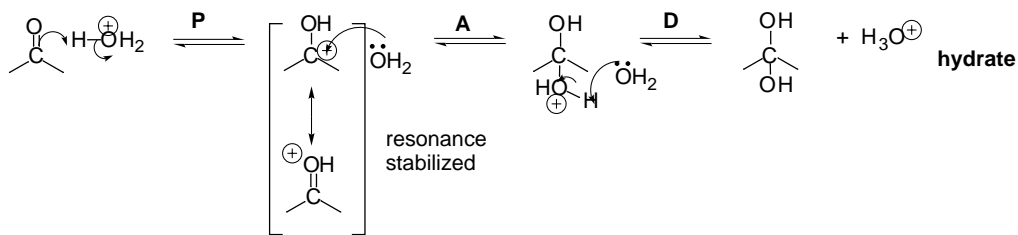


- 4- Molecular orbital interaction also helps determine whether water will add to carbon or oxygen.
- The filled  $n$  orbital of water (the nucleophile) overlaps with the empty  $\pi^*$  of the carbonyl group (Lewis acid).
  - This is a very stabilizing interaction.
- 5- In an acid-catalyzed reaction, hydration is very similar to acid-catalyzed additions of water to an alkene.

**Alkene:**

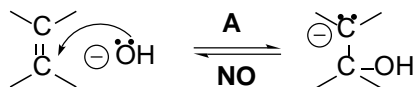
a- It is a three-step process:

- Protonation: the oxygen of the carbonyl group is a strong Lewis base and will be protonated first, which gives a resonance-stabilized carbocation.
- Addition: water acts as nucleophile and adds to carbocation (a Lewis Acid.)
- Deprotonation: by another water molecule and the acid catalyst ( $\text{H}_3\text{O}^+$ ) is regenerated.

**Carbonyl:**

b- The 1,1-diol, or hydrate, is formed. (Fig. 16.26)

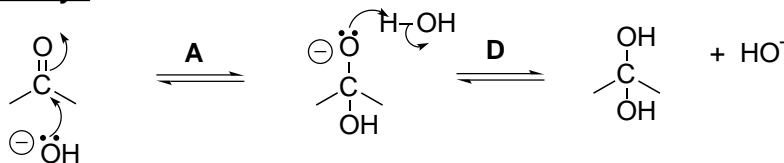
- 6- Under basic conditions, there is no counterpart to the chemistry of simple alkenes.

**Alkene:**

a- It is a two-step process:

- Addition: hydroxide (a strong nucleophile) attacks the carbon of the carbonyl group.
- Protonation: proton transfers from water to new alkoxide, and hydroxide ion is regenerated.

b- The 1,1-diol, or hydrate is formed. (Fig. 16.27)

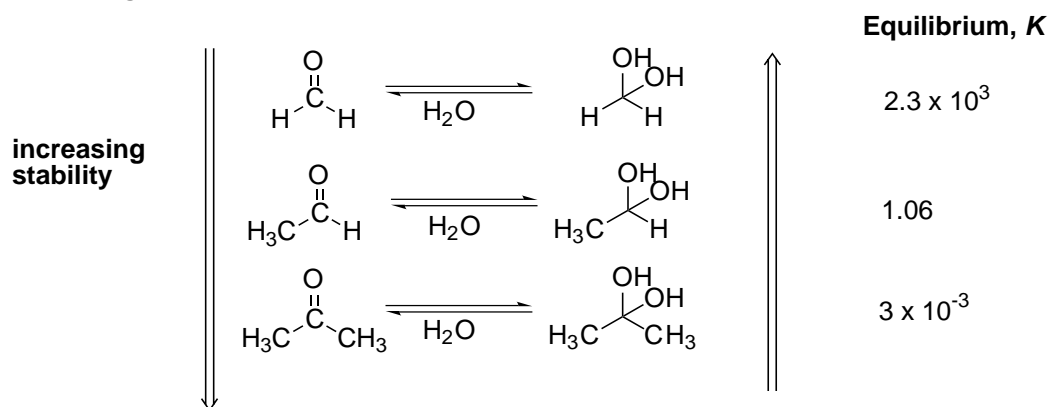
**Carbonyl:**

## Section 16.7

## VII. Equilibrium in Addition Reactions

A- The equilibrium constant ( $K_{eq}$ ) is different by a factor of  $10^6$  for each of the species, formaldehyde, acetaldehyde and acetone.

- 1- Energy factors: the more substituted the double bond for alkenes and carbonyls, the more stable it is.
- 2- Steric factors: the less substituted the double bond, the more stable the hydrate.  
[Fig. 16. 28 and 16.29]



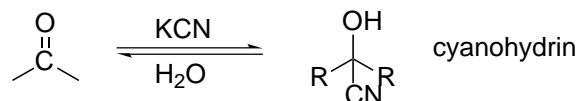
## 3- Other effects:

- a- Benzene rings decrease quantity of hydrate at equilibrium by interacting with C=O through resonance.
    - i- Electron-withdrawing groups  $\alpha$  to carbonyl favor hydrate.
    - ii- Large alkyl groups favor carbonyl over hydrate. (See Table 16.3)
  - b- Electron-withdrawing groups that are in  $\alpha$ -position, such as fluorine, cause hydrate to be favored at equilibrium.
  - c- Steric effects tend to favor the carbonyl at equilibrium.
- 4- If even a small amount of the higher energy partner is present at equilibrium, i.e. the disfavored species, it can be used to generate further reactions. (A consequence of Le Chatelier's principle.)

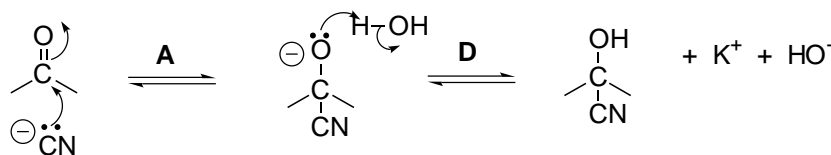
## Section 16.8

## IIX. Other Addition Reactions: Additions of Cyanide and Bisulfite

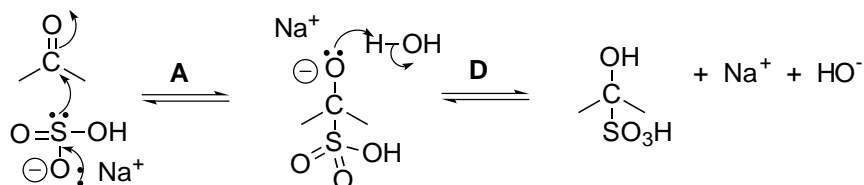
A- Other addition reactions can follow the pattern of hydration.



- 1- Cyanohydrin formation is usually base catalyzed.
  - a- Cyanide ion is a good nucleophile and attacks the carbonyl (a Lewis acid) to give the alkoxide.
  - b- Water is usually used as solvent to protonate the alkoxide and produce the cyanohydrin.



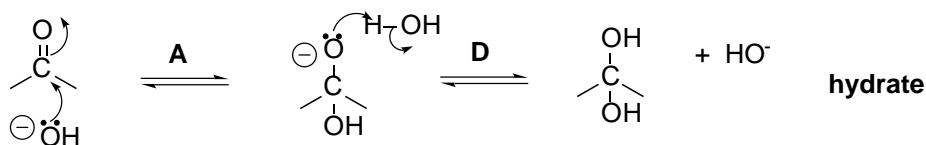
- 2- Bisulfite addition is also usually base catalyzed.
- Sulfur acts as the nucleophile in this case.
  - Sodium bisulfite will add to many aldehydes and ketones.



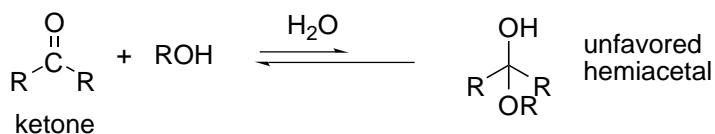
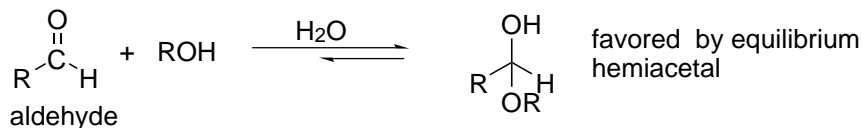
## Section 16.9

### IX. Addition Reactions Followed by Water Loss: Acetal and Ketal Formation

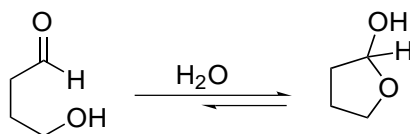
A- Aldehydes and ketones can form a similar hydration product in alcohol (ROH) as in water (HOH): **acetals or hemiacetals**.



- 1- Hemiacetal formation in basic conditions:
- Aldehydes tend toward the hemiacetal form at equilibrium.
  - Hemiacetal formation is not favored by ketones.



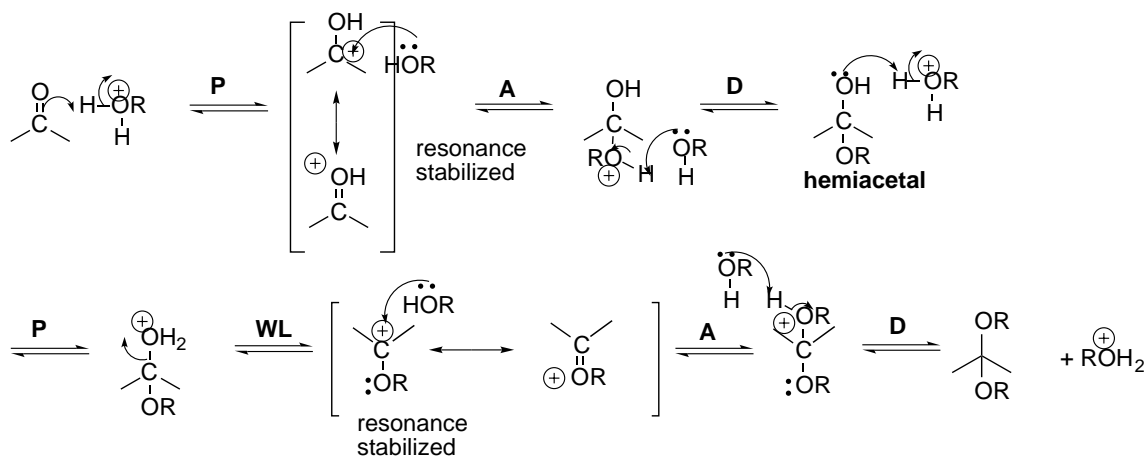
c- Most simple hemiacetals are not isolable, but cyclic ones are. (Fig. 16.40)



- 2- Hemiacetal formation progresses to acetal formation in acidic conditions:

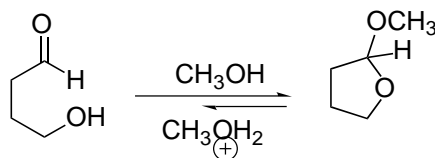
a- The mechanism parallels hydration through the hemiacetal then goes on to form the acetal in a seven-step process.

- i- Protonation of carbonyl oxygen.
- ii- Addition of ROH to resonance-stabilized carbocation.
- iii- Deprotonation of ROH to give hemiacetal.
- iv- Protonation of OH on hemiacetal.
- v- Water leaves.
- vi- Addition of second ROH to resonance-stabilized carbocation.
- vii- Deprotonation of ROH to give full acetal.



3- Since carbonyls are sensitive to base, acetal formation provides a **protecting group**.

- a- In excess acid, this equilibrium reaction will be driven to the right to form the acetal.
- b- In excess water, the reaction will be driven to the left to regenerate the carbonyl.



## Section 16.10

### X. Protecting Groups in Synthesis

#### A- Acetals as Protecting Groups for Aldehydes and Ketones

- 1 - Acetals are stable in basic conditions but not in acidic conditions
- 2 - It is the first example of a protecting group.

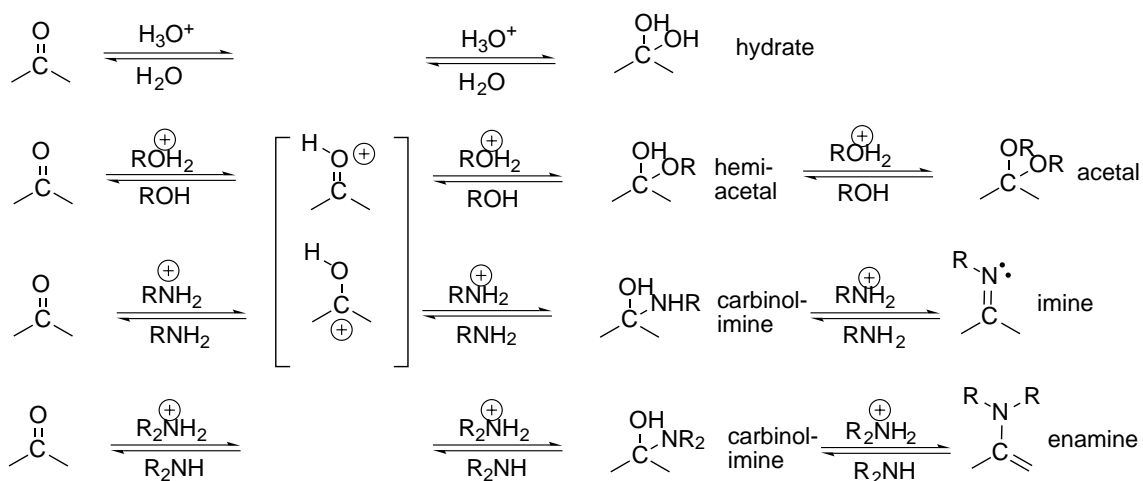
#### B- Protecting Groups for Alcohols

- 1 - Tetrahydropyranyl ether (THP) and Trialkylsilyl halides are examples of alcohols which are used in the protection of ketones and aldehydes.
- 2 - They are removed (cleaved) using NH<sub>4</sub>F.

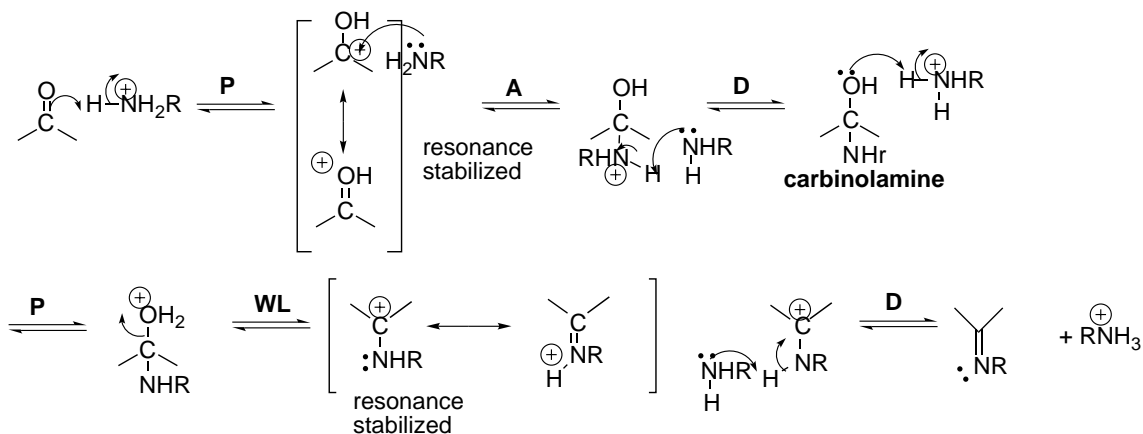
## Section 16.11

### XI. Addition Reaction of Nitrogen Bases: Imine and Enamine Formation

A- Since the nitrogen of an amine (RNH<sub>2</sub>) is a nucleophile, it can also add to carbonyls.

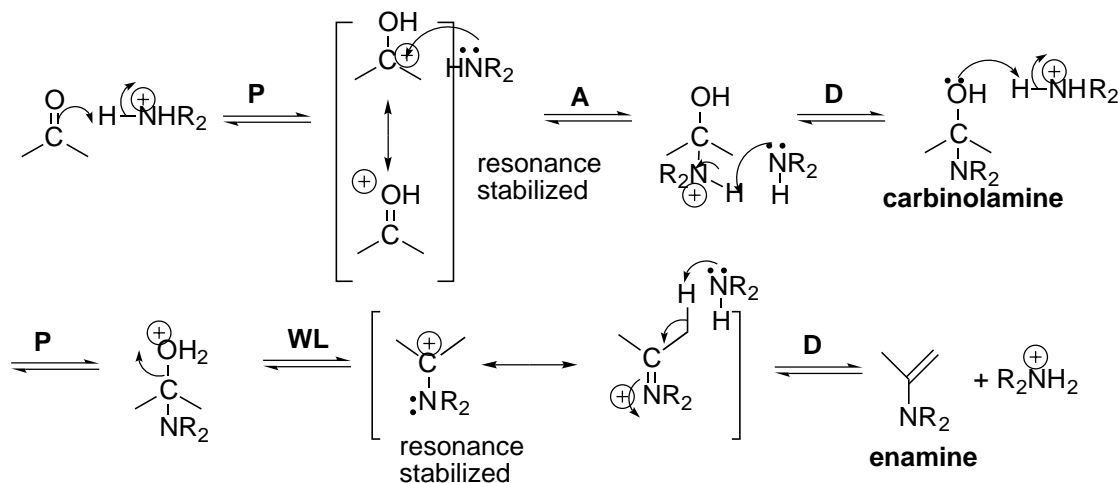


- 1- The reaction of a primary amine is similar to that of hydrate and hemiacetal formation.
- The intermediate is called a **carbinolamine**.
  - The product is a **Schiff base**, or **imine**.
  - At least 2 hydrogens are required on the starting amine for this reaction to go.



- 2- A secondary amine ( $\text{R}_2\text{NH}$ ) can also form a carbinolamine.
- Since only one H can be lost, the reaction proceeds through an **immonium ion**.
  - Deprotonation of the immonium ion is just like deprotonation of a carbocation to give an alkene.

c-The final product is an **enamine**.



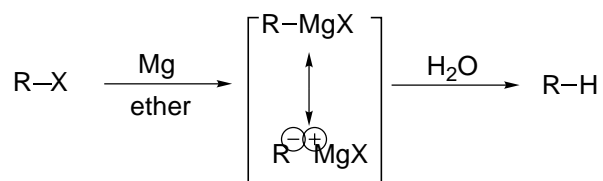
3- A tertiary amine ( $\text{R}_3\text{N}$ ) can add to the carbonyl, but since there is no available hydrogen for the deprotonation step, the reaction can only reverse to starting material.

## Section 16.12

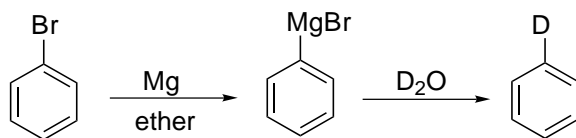
### XII. Organometallic Reagents

#### A- Grignard Reagent ( $\text{R-Mg-X}$ )

1- Generic example.

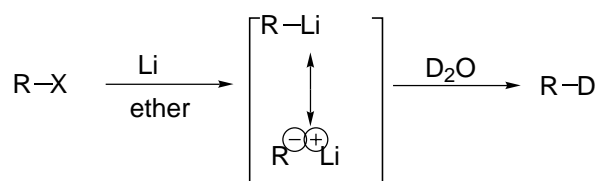


2- Specific example.

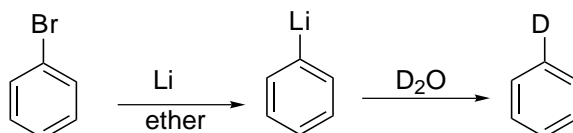


#### B- Organolithium Reagent ( $\text{R-Li}$ )

1- Generic example.

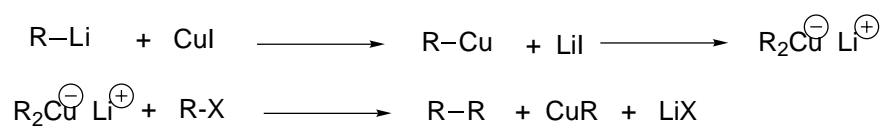


2- Specific example.

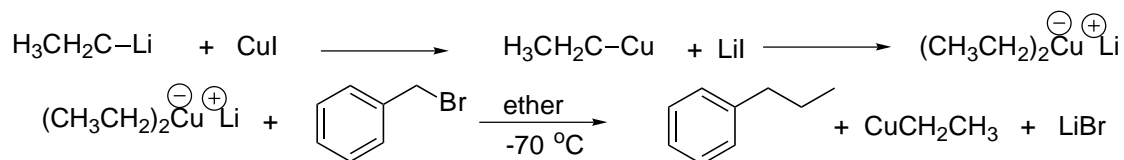


### C- Organocopper ( $R_2CuLi$ )

1- Generic example.



2- Specific example.

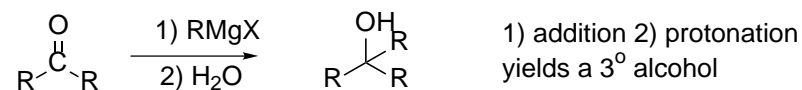
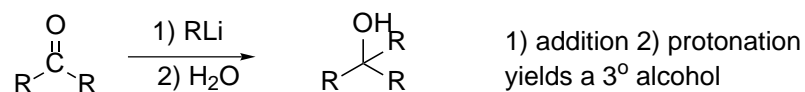


## Section 16.13

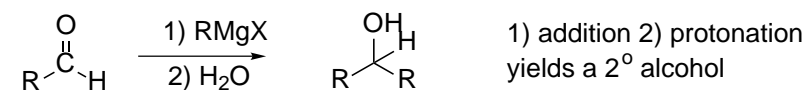
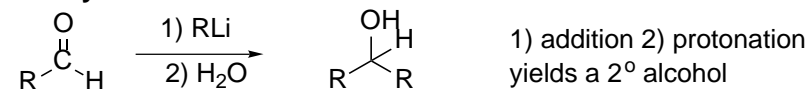
### XIII. Irreversible Addition Reactions: A General Synthesis of Alcohols

A- Addition of organolithium and grignard reagents is irreversible.

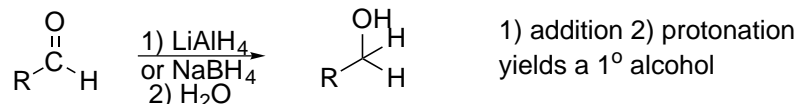
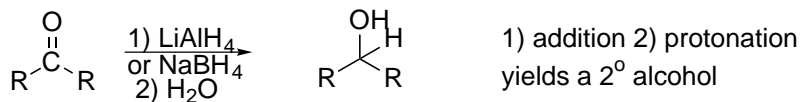
#### Ketones



#### Aldehydes



B- Addition of hydrides is also irreversible to yield alcohols.



### Section 16.14

#### XIV. Retrosynthetic Alcohols Synthesis

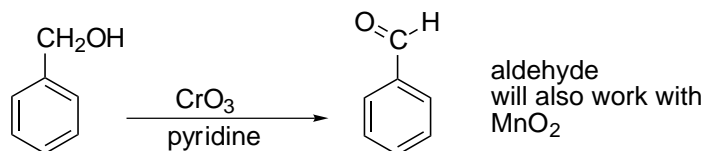
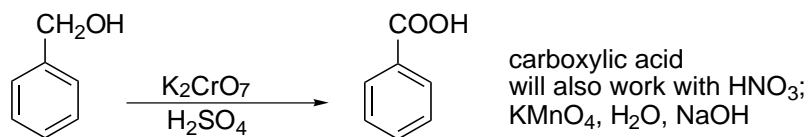
A- See problem 16.23.

### Section 16.15

#### XV. Oxidation of Alcohols to Carbonyl Compounds

A- Reduction of ketones and aldehydes is affected using metal hydrides (sodium or lithium aluminum hydride).

B- Oxidation of the alcohols to ketones, aldehydes and carboxylic acids is depicted in the figure below.



C- Oxidative cleavage of 1,2-diols is performed using HIO<sub>4</sub>/H<sub>2</sub>SO<sub>4</sub> which will form ketones and/or aldehydes.

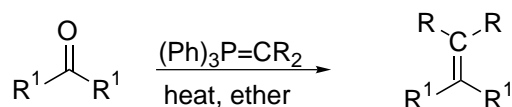
### Section 16.16

#### XVI. Oxidation of Thiols and Other Sulfur Compounds.

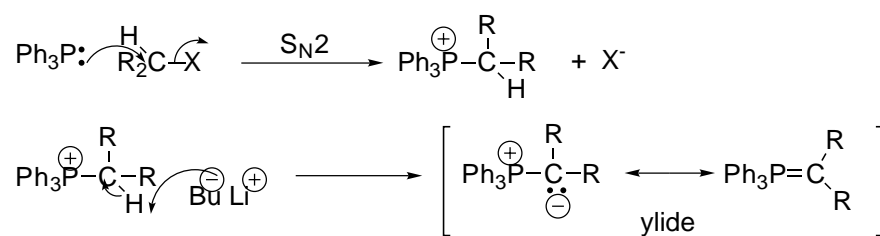
### Section 16.17

#### XVII. Wittig Reaction

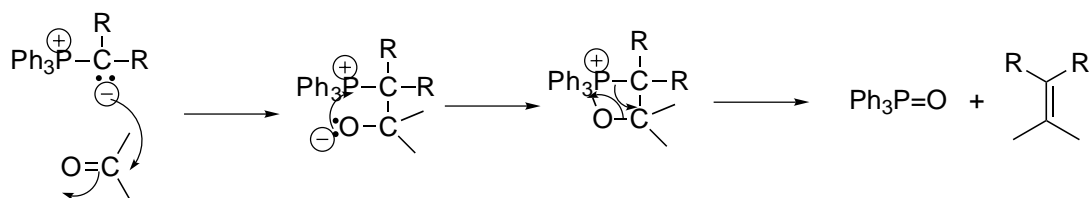
A- Overall reaction.



B- Formation of the ylide.



C- Addition of the ylide to the double bond.



D- Overall reaction.

