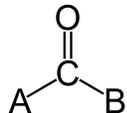


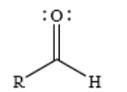
# Carbonyl Chemistry – Fundamentals

## Introduction

Carbonyl group:



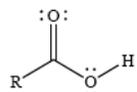
Carbonyl functional groups:



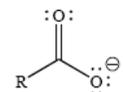
Aldehyde



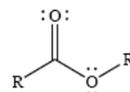
Ketone



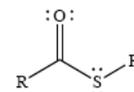
Carboxylic acid



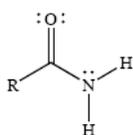
Carboxylate



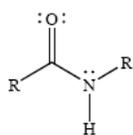
Ester



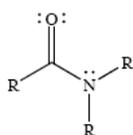
Thioester



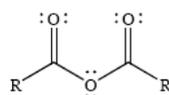
1° Amide



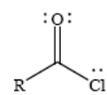
2° Amide



3° Amide



Anhydride



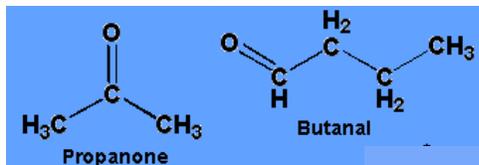
Acid chloride  
(Acyl chloride)

## Brief Nomenclature of Aldehydes & Ketones<sup>1</sup>

IUPAC system:

- add -al to aldehydes

- add -one to ketones



## Comparing Alkenes & Carbonyls<sup>2</sup>

<p>Alkenes (ethylene)</p>	<p>Carbonyls</p>
Double bond is nonpolar and longer	Double bond is polar and shorter
	Due to polarity, double bond can be an H-bond acceptor
Both sides of an alkene undergo nucleophilic or electrophilic attack	Carbonyls undergo regioselective attack by nucleophile or electrophile
The lack of a polar bond results in alkenes having a lower boiling point than carbonyls that are about the same size. (Fig.1)	Due to polar character (& for some carbonyls, the ability to form H-bonds) of the carbonyl group, carbonyls have higher boiling points. (Fig.1)

<sup>1</sup> <http://www.elmhurst.edu/~chm/vchembook/700carbonyls.html>

<sup>2</sup> <http://www.cem.msu.edu/~reusch/VirtualText/aldket1.htm>

	Relative boiling points <sup>3</sup> : (higher bp) amide > carboxylic acid > nitrile >> ester ~ acyl chloride ~ aldehyde ~ ketone (lower bp)
C=C bond has a bond energy of ~146 kcal/mole.	C=O bond has bond energy that varies: H <sub>2</sub> C=O 170 kcal/mole RCH=O 175 kcal/mole R <sub>2</sub> C=O 180 kcal/mole

Higher bond energy of the C=O bond of carbonyls suggests that they are thermodynamically unfavorable. How can carbonyls undergo a reaction?  
 → The polarity of the carbonyl group and its higher basicity than alkenes lower the transition state energy of activation and therefore result in a faster rate.

Fig. 1

Compound	Mol. Wt.	Boiling Point
(CH <sub>3</sub> ) <sub>2</sub> C=CH <sub>2</sub>	56	-7.0 °C
(CH <sub>3</sub> ) <sub>2</sub> C=O	58	56.5 °C
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH=CH <sub>2</sub>	70	30.0 °C
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH=O	72	76.0 °C
	96	103.0 °C
	98	155.6 °C

### Reactivity of Carbonyls

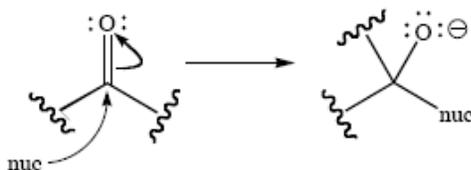
- Polar double bond creates a partial positive charge on the carbonyl carbon and a partial negative charge on the oxygen.  $\delta^+ \text{C}=\text{O} \delta^-$

### Three C=O Fates

Polar double bond → plays a role in determining mechanism of reaction

1. Nucleophilic attack at  $\delta^+$  carbon

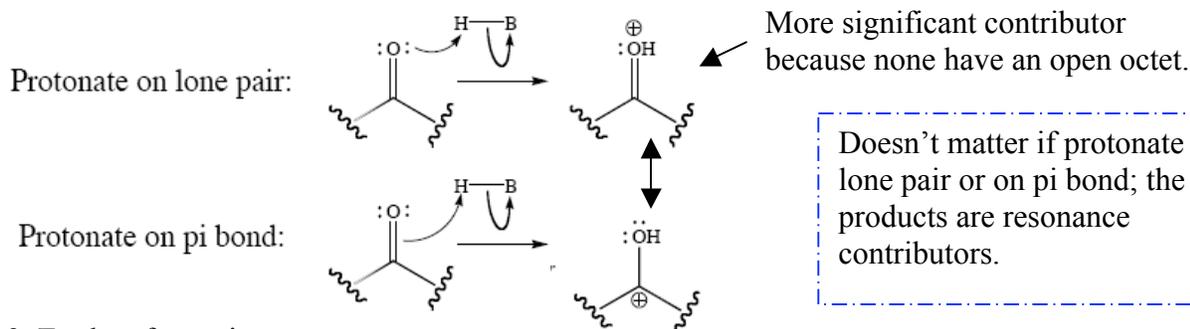
- oxygen (high electronegativity) accepts electron pair → helps nucleophilic attack



- The product of nucleophilic attack is called a “tetrahedral adduct”; it is formed when an  $sp^2$  carbon is changed to an  $sp^3$  carbon.

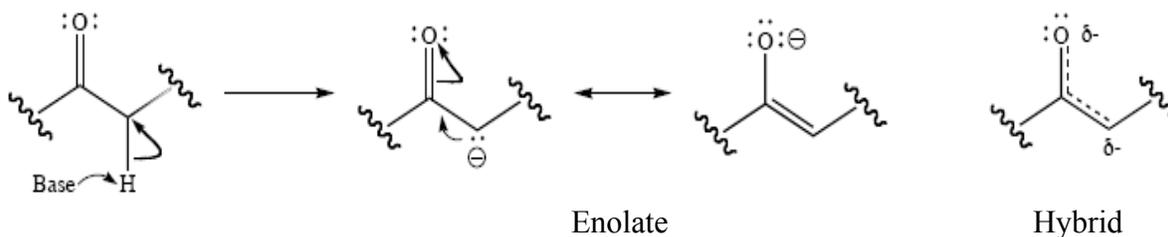
<sup>3</sup> Bruice, Paula Y. “Carbonyl Compounds I.” *Organic Chemistry*. 4<sup>th</sup> ed. Pg. 677.

- Attack on a carbonyl could create a new stereocenter<sup>4</sup>
2. Electrophilic attack at  $\delta^-$  oxygen
- lone pairs & pi bond  $\rightarrow$  help electrophilic attack
  - requires strong acid ( $\text{H}_2\text{SO}_4$ ,  $\text{H}_3\text{O}^+$ ,  $\text{ROH}_2^+$ ) for protonation



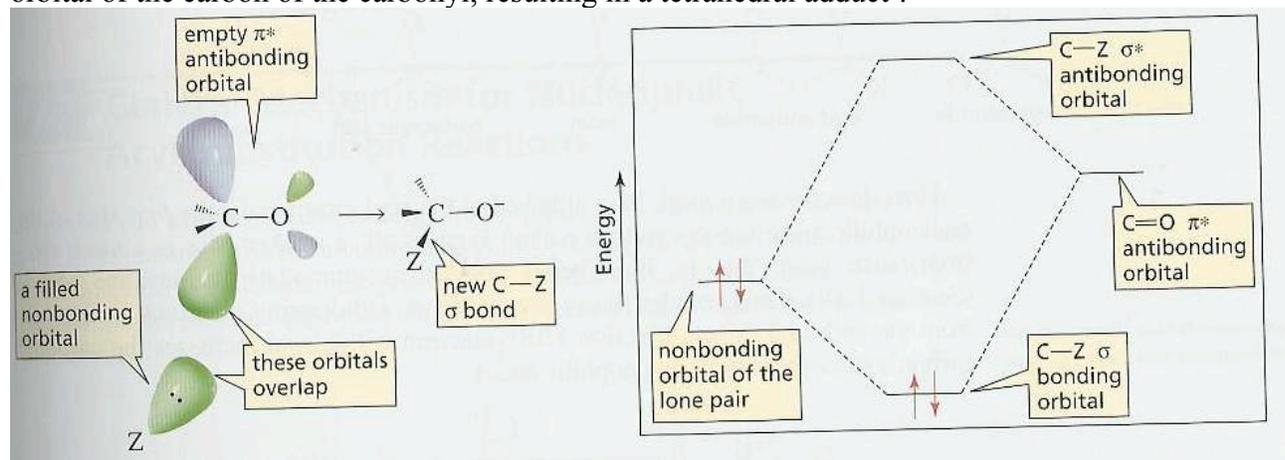
### 3. Enolate formation

- resonance stabilization of conjugate base  $\rightarrow$  helps enolate formation



### Molecular Orbital Diagram of Carbonyl Reactions

The orbital that contains the lone pairs of the nucleophile overlaps the empty  $\pi^*$  antibonding orbital of the carbon of the carbonyl, resulting in a tetrahedral adduct<sup>5</sup>.



### Two Generalized Carbonyl Reaction Mechanisms

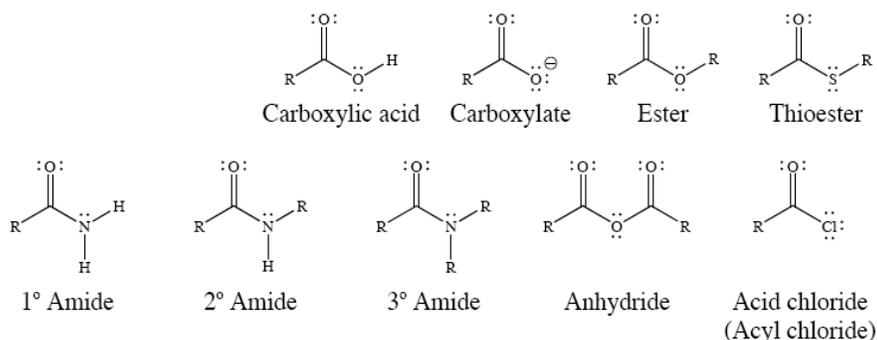
#### 1. Nucleophilic carbonyl/acyl substitution

- substitution occurs when  $\text{C}=\text{O}$  bears a LG (ie. ester, amide, anhydride, acid chloride, etc.)

<sup>4</sup> <http://www.colby.edu/chemistry/OChem/DEMOS/ketones.html>

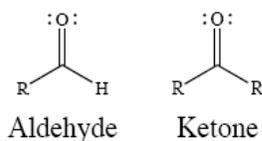
<sup>5</sup> Bruice, Paula Y. "Carbonyl Compounds I." *Organic Chemistry*. 4<sup>th</sup> ed. Pg. 683.

Carbonyls that undergo substitution:



## 2. Addition

- addition products result when C=O does not have a LG (ie. aldehydes & ketones)
- Carbonyls that undergo addition:



Note: Substitution is usually considered first because it is *intramolecular* (within the molecule) and is therefore faster.

### Four Factors that Affect Carbonyl Reaction Rate

*Carbonyl carbon*  $\delta^+$ :

- larger carbonyl carbon  $\delta^+$   $\rightarrow$  carbonyl more electronegative  $\rightarrow$  faster nucleophilic attack

*Resonance*:

- more (significance) resonance  $\rightarrow$  spreading of e- density  $\rightarrow$  carbonyl less electronegative  $\rightarrow$  slower nucleophilic attack
- When the tetrahedral adduct is formed, resonance may be disrupted. The loss of resonance results in a higher transition state energy, and would therefore slow the carbonyl reaction rate.

*Leaving group*:

- better LG  $\rightarrow$  quicker breaking up of tetrahedral adduct  $\rightarrow$  faster reaction

*Steric effects*:

- more steric hindrance on carbonyl carbon  $\rightarrow$  slower nucleophilic attack

Relative reactivities of carbonyl compounds toward nucleophilic attack<sup>6</sup>:

(most reactive) acyl halide > acid anhydride > aldehyde > ketone > ester ~ carboxylic acid > amide > carboxylate ion (least reactive)

<sup>6</sup> Bruice, Paula Y. "Carbonyl Compounds II." *Organic Chemistry*. 4<sup>th</sup> ed. Pg. 736.



