Study Guide for Exam 2- Aldehydes and Ketones

Nucleophilic Addition

Most of the reactions of aldehydes and ketones in these chapters are nucleophilic addition reactions. The oxygen in C=O polarizes the bond. Therefore, while electrophilic addition (electrophile first, followed by nucleophile) was favored for the comparatively non-polar, electron-rich alkene, carbonyls undergo nucleophilic addition (nucleophile first, followed by electrophile). Note how all the mechanisms begin exactly the same way:

Strong Nu: Mechanism (Ch 17)

Hydride

LiAlH₄ is similar

Carbanion

Grignard/Alkyllithium/Acetylide

Ylide

Wittig Reaction

The Wittig is unique in that the alkoxide oxygen in the tetrahedral intermediate attacks the phosphonium center forming an oxaphosphetane intermediate. Thus, the electrophile is not H⁺ as in the previous examples but the phosphonium center. The intermediate undergoes a reverse 2+2 process to form triphenylphosphine oxide and an alkene product to complete the process.
Weak Nu: Mechanism (Ch 18)

If the nucleophile is a weaker base than the alkoxide in the tetrahedral intermediate, an alternative mechanism is proposed. Here, the electrophile (usually $H^+$) is added first to enhance the polarity of the C=O bond, and reduce the energy of the tetrahedral intermediate (transition state resembles this intermediate; stabilizing it will increase the rate). The reverse reaction rates are also enhanced, so the mechanisms feature equilibria.

Alcohol as Nucleophile – Acetal/Ketal Formation

1° Amine as Nucleophile – Imine Formation

2° Amine as Nucleophile – Enamine Formation

Cyanide as Nucleophile – Cyanohydrin Formation

Peracid as Nucleophile – Baeyer-Villager Oxidation
Developmental Problems

1. Complete the following ‘reactivity tree’ for a ketone:

   \[ \text{H}_3\text{O}^+, \text{H}_2\text{O} \]

   \[ \text{ROH, H}_3\text{O}^+ \]

   \[ \text{HO} \rightarrow \text{OH}_2 \rightarrow \text{H}_3\text{O}^+ \]

   \[ \text{RNH}_2, \text{pH} \, 5.5 \]

   \[ \text{R}_2\text{NH}, \text{pH} \, 5.5 \]

   \[ \text{NH}_2\text{OH}, \text{pH} \, 5.5 \]

   \[ 1) \text{LiAlH}_4 \]

   \[ 2) \text{dil. H}_3\text{O}^+ \]

   \[ \text{PhMgBr} \]

   \[ \text{PPh}_3 \]

   \[ \text{HCN, KCN} \]

   \[ \text{H}_2\text{O}^+ \]

   \[ \text{RNH}_2, \text{pH} \, 5.5 \]

   \[ \text{R}_2\text{NH}, \text{pH} \, 5.5 \]

   \[ \text{NH}_2\text{OH}, \text{pH} \, 5.5 \]

   \[ 1) \text{LiAlH}_4 \]

   \[ 2) \text{dil. H}_3\text{O}^+ \]

2. Predict the products:
   a. \[
   \text{O} \quad 1) \text{LiAlH}_4 \\
   \quad 2) \text{dil. H}_3\text{O}^+ \\
   \]
   b. \[
   \text{O} \quad 1) \text{PhMgBr} \\
   \quad 2) \text{dil. H}_3\text{O}^+ \\
   \]
   c. \[
   \text{O} \quad \text{H}_2\text{C} \cdot \text{PPh}_3 \\
   \]
   d. \[
   \text{O} \quad \text{PPh}_3 \\
   \]
   e. \[
   \text{O} \quad \text{KCN} \\
   \quad \text{HCl / H}_2\text{O} \\
   \]
   f. \[
   \text{O} \quad \text{NH} \\
   \quad \text{pH} \, 5.5 \\
   \]
   g. \[
   \text{O} \quad \text{Ph}_3\text{PCHCH}_3 \\
   \]
3. Treatment of cathecol with formaldehyde in the presence of dilute acid leads to a product with formula \( C_7H_6O_2 \). Identify it!

4. How would you synthesize the following from cyclopentanone?
   a. 
   b. 
   c. 

5. Glutaraldehyde is a germicidal agent used to sanitize surgical equipment that cannot be autoclaved. Propose a mechanism for the following transformation:

6. Hydrolyze the following derivatives back to the original aldehydes and ketones:
   a. 
   b. 
   c. 
   d. 
   e. 

h. 

i. 

j. 

1) \( \text{KCN, HCl} \)
2) \( \text{HCl, H}_2\text{O} \)
1. Complete the following ‘reactivity tree’ for a ketone:

2. Predict the products:
   a. 
   b. 
   c. 
   d. 
   e. 
   f.
3. Treatment of cathecol with formaldehyde in the presence of dilute acid leads to a product with formula $C_7H_6O_2$. Identify it!

4. How would you synthesize the following from cyclopentanone?

a) 1) MeMgBr 2) $H_2O^+$

b) $Ph_3P$ -- $CH_2$

c) $KCN/HCl$
5. Glutaraldehyde is a germicidal agent used to sanitize surgical equipment that cannot be autoclaved. Propose a mechanism for the following transformation:

6. Hydrolyze the following derivatives back to the original aldehydes and ketones:

   a) \( \text{Cyclohexanone} \) + \(-\text{NH}_2\)   

   b) \( \text{2-Cyclopentanone} \) + \(-\text{NH}_2\)   

   c) \( \text{2-Cyclopentanone} \) + \(\text{OH}\)   

   d) \( \text{HO-} + \text{HO-} \)   

   e) \( \text{HO-} + \text{HO-} \)