

## Chapter 19: Carbonyl Compounds III

### Learning Objectives:

1. Write the mechanism for keto-enol tautomerization and explain the consequence of such tautomerization in the optical chirality of compound.
2. Remember the approximate  $pK_a$  value for the  $\alpha$ -hydrogen of a carbonyl group.
3. Provide appropriate bases for the formation of enolate and use such enolate for halogenation and alkylation.
4. Be able to write the general electron-pushing (arrow-pushing) mechanisms of Aldol reaction, Michael reaction, Claisen condensation, and Dieckmann condensation.
5. Be able to write the general electron-pushing (arrow-pushing) mechanisms for decarboxylation of 3-oxocarboxylic acids
6. Be able to employ the above-mentioned reaction for the formation of new carbon-carbon bond

### Sections:

- 19.1 Acidity of  $\alpha$ -hydrogens\*
- 19.2 Keto-Enol Tautomerism\*
- 19.3 How Enols and Enolate Ions React\*
- 19.4 Halogenation of the  $\alpha$ -Carbon of Aldehydes and Ketones\*
- 19.5 Halogenation of the  $\alpha$ -Carbon of Carboxylic Acids: The Hell-Volhard-Zelinski (HVZ) Reaction
- 19.6  $\alpha$ -Halogenated Carbonyl Compounds in Synthesis\*
- 19.7 Using LDA to form an Enolate\*
- 19.8 Alkylation of the  $\alpha$ -Carbon of Carbonyl Compounds\*
- 19.9 Alkylation and Acylation of the  $\alpha$ -Carbon via an Enamine Intermediate
- 19.10 Alkylation of the  $\beta$ -Carbon: the Michael Reaction\*
- 19.11 The Aldol Reaction\*
- 19.12 Dehydration of Aldol Addition Products: Formation of  $\alpha,\beta$ -Unsaturated Aldehydes and Ketones\*
- 19.13 The Mixed Aldol Reaction
- 19.14 The Claisen Condensation\*
- 19.15 The Mixed Claisen Condensation
- 19.16 Intramolecular Condensation and Addition Reactions\*
- 19.17 Decarboxylation of 3-Oxocarboxylic Acids\*
- 19.18 The Malonic Ester Synthesis: Synthesis of Carboxylic Acids
- 19.19 The Acetoacetic Ester Synthesis: Synthesis of Methyl Ketones
- 19.20 Designing a Synthesis VI: Making New Carbon-Carbon Bonds
- 19.21 Reactions at the  $\alpha$ -carbon in Biological Systems<sup>#</sup>

\* Sections that will be focused

<sup>#</sup> Sections that will be skipped

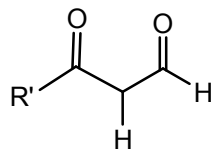
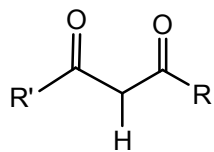
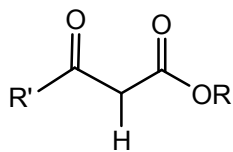
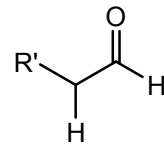
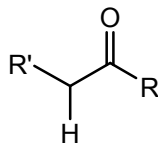
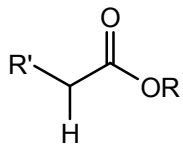
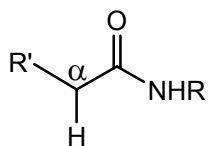
### Recommended additional problems

19.44 – 19.52, 19.54 – 19.64, 19.66 – 19.80

## Class Note

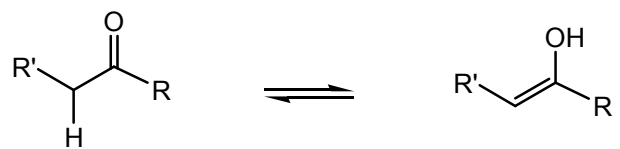
### 19.1 Acidity of $\alpha$ -hydrogens

#### A. pKa of $\alpha$ -hydrogen of carbonyl derivatives



#### B. Resonance effect

## 19.2 Keto-Enol Tautomerism



A. Mechanism in acidic condition

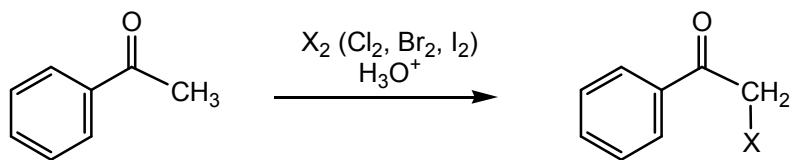
B. Mechanism in basic condition

## 19.3 How Enols and Enolate Ions React

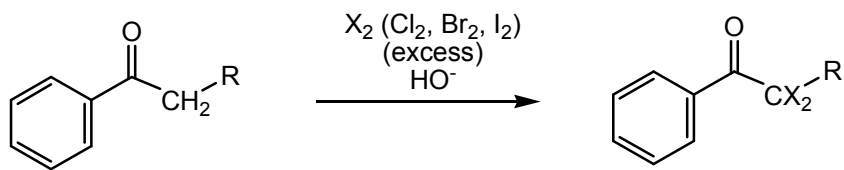
### A. Analysis of enols and enolates

## 19.4 Halogenation of the $\alpha$ -Carbon of Aldehydes and Ketones

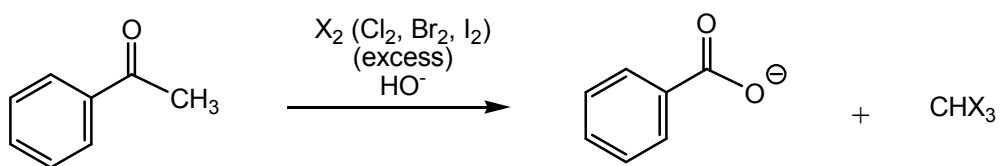
### A. Acid-catalyzed halogenation



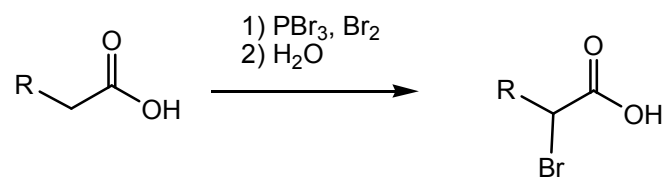
## B. Base-promoted halogenation



## C. Haloform reaction



19.5 Halogenation of the  $\alpha$ -Carbon of Carboxylic Acids: The Hell-Volhard-Zelinski (HVZ) Reaction

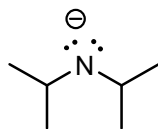


## 19.6 $\alpha$ -Halogenated Carbonyl Compounds in Synthesis

### A. Analysis of $\alpha$ -halogenated carbonyl Compounds

### B. Examples

19.7 Using LDA to form an Enolate



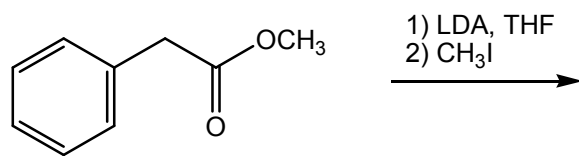
lithium diisopropylamide (LDA)

19.8 Alkylation of the  $\alpha$ -Carbon of Carbonyl Compounds

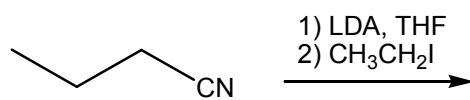
A. Analysis of the reaction

B. Examples

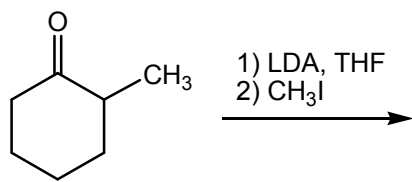
(i)



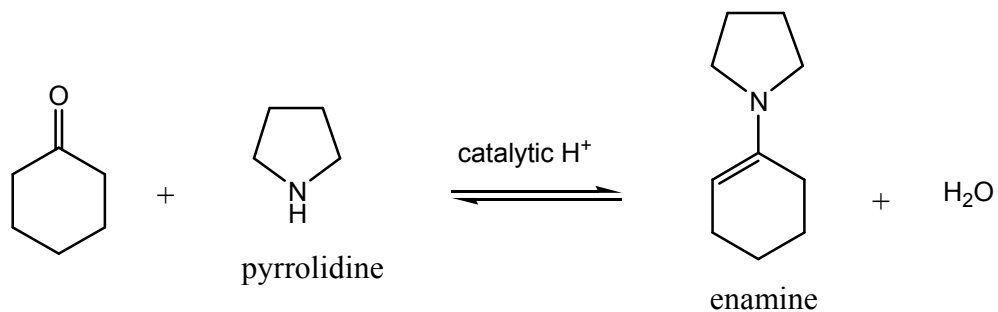
(ii)



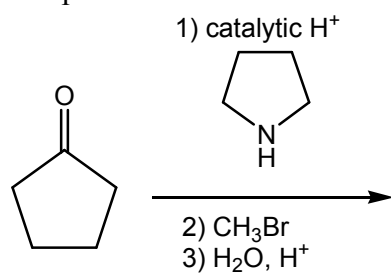
C. Potential problem in alkylation of the  $\alpha$ -carbon of carbonyl compounds



19.9 Alkylation and Acylation of the  $\alpha$ -Carbon via an Enamine Intermediate

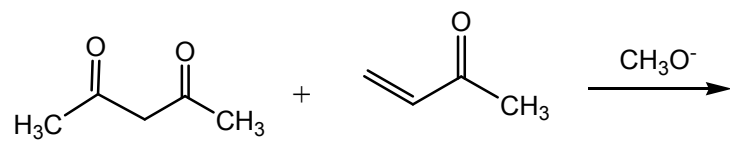


A. Examples



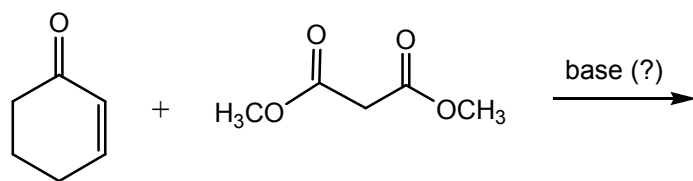
19.10 Alkylation of the  $\beta$ -Carbon: the Michael Reaction

A. Michael reaction

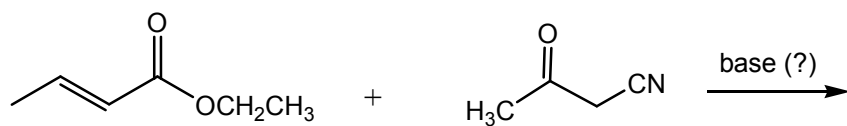


## B. Examples

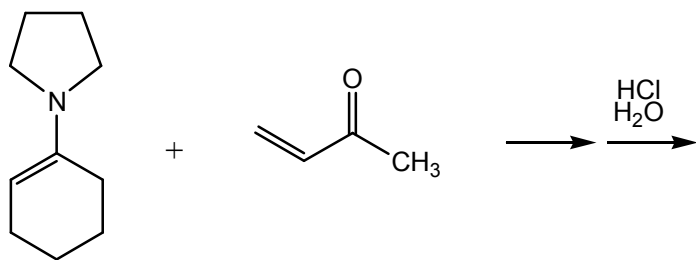
(i)



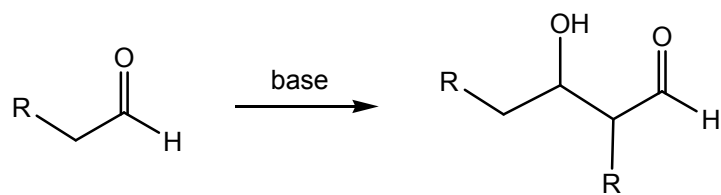
(ii)



C. Stork enamine reaction



## 19.11 The Aldol Reaction



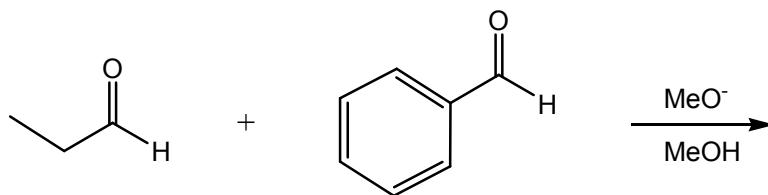
A. Mechanism

19.12 Dehydration of Aldol Addition Products: Formation of  $\alpha,\beta$ -Unsaturated Aldehydes and Ketones

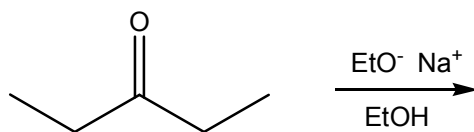
A. Aldol condensation

B. Examples

(i)

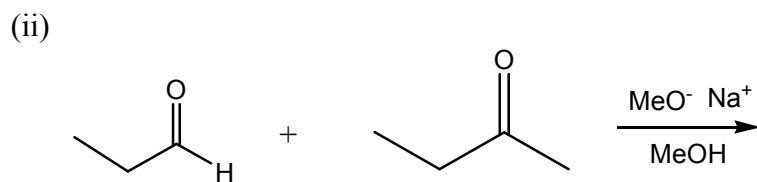
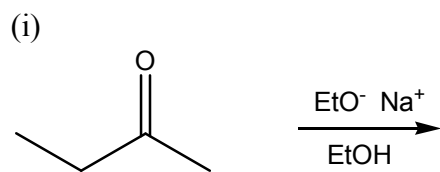


(ii)



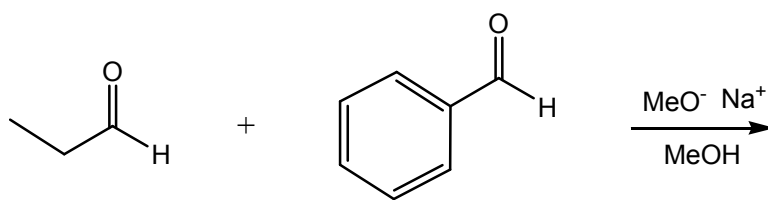
### 19.13 The Mixed Aldol Reaction

#### A. Potential problem in aldol reaction

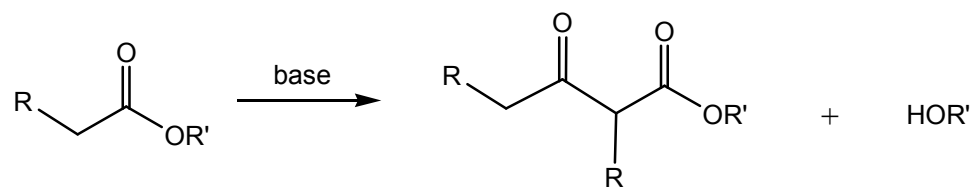


B. Solution

(i)



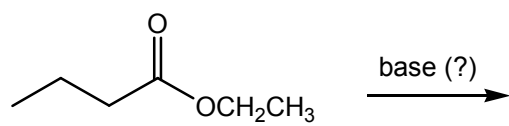
19.14 The Claisen Condensation and 19.15 The Mixed Claisen Condensation



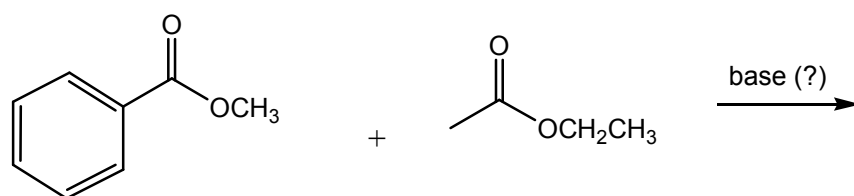
A. Mechanism

## B. Examples

(i)

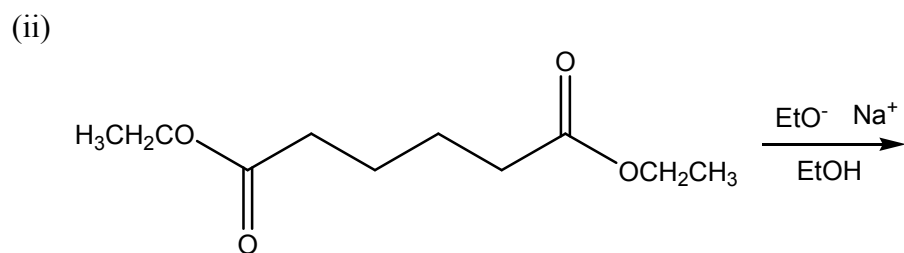
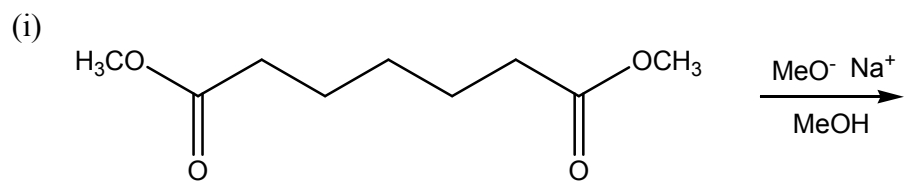


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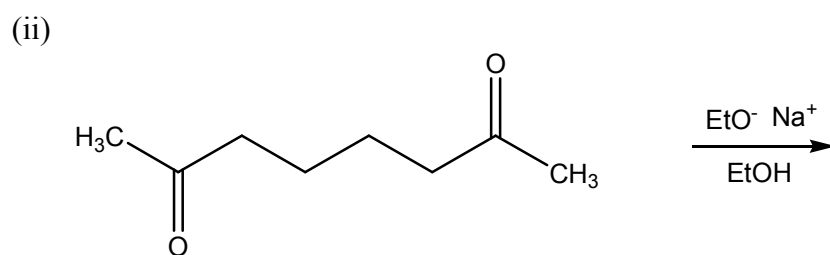
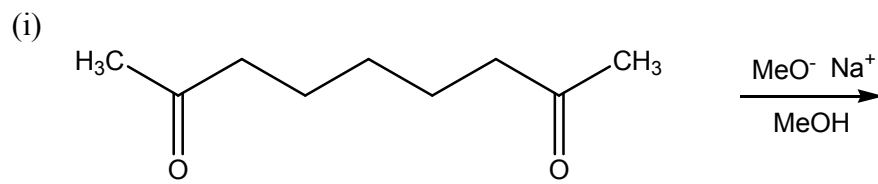


19.16 Intramolecular Condensation and Addition Reactions

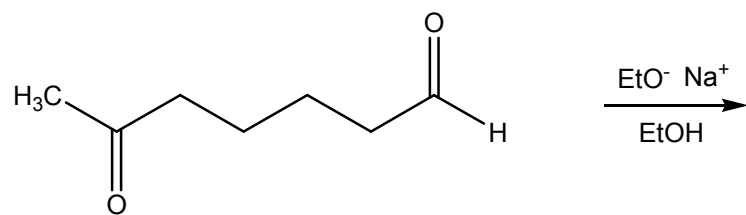
A. Intramolecular Claisen reaction (Dieckmann condensation)



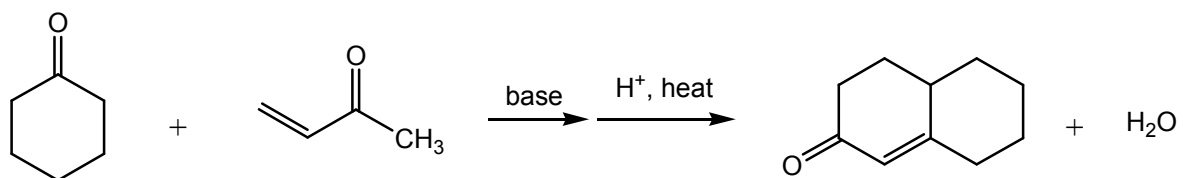
B. Intramolecular aldol reaction



(iii)

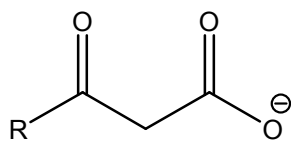
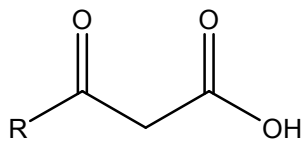


(iv) Robinson annulation

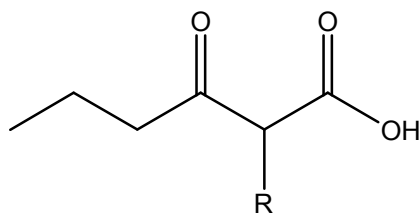
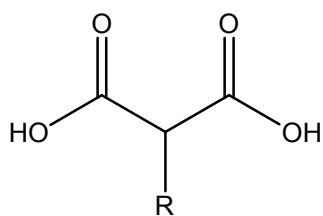


## 19.17 Decarboxylation of 3-Oxocarboxylic Acids

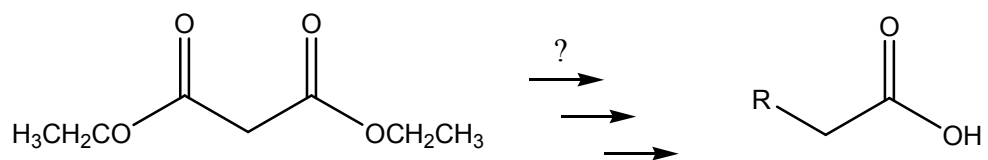
### A. Easier in acidic condition: mechanism



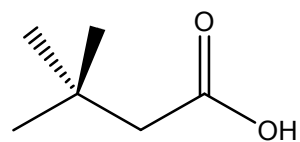
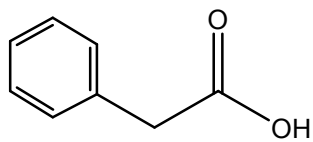
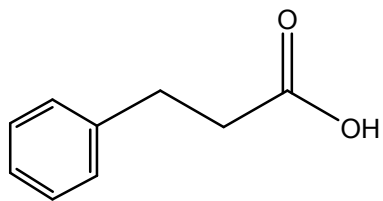
### B. Examples of compounds containing 3-oxocarboxylic acid



19.18 The Malonic Ester Synthesis: Synthesis of Carboxylic Acids and 19.19 The Acetoacetic Ester Synthesis: Synthesis of Methyl Ketones



A. Examples:



19.20 Designing a Synthesis VI: Making New Carbon-Carbon Bonds

