Chapter 18: Carbonyl Compounds III

Learning Objectives:

1. Write the mechanism for keto-enol tautomerization and explain the consequence of such tautomerizarion in the optical chiral of compound.
2. Remember the approximate p*Ka* value for the α-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:

18.1 The Acidity of an α-Hydrogens*
18.2 Keto-Enol Tautomers*
18.3 Enolization
18.4 How Enols and Enolate Ions React*
18.5 Halogenation of the α-Carbon of Aldehydes and Ketones*
18.6 Halogenation of the α-Carbon of Carboxylic Acids: The Hell-Volhard-Zelinski (HVZ) Reaction
18.7 α-Halogenated Carbonyl Compounds Are Useful in Synthesis*
18.8 Using LDA to Form an Enolate*
18.9 Alkylation of the α-Carbon of Carbonyl Compounds*
18.10 Alkylation and Acylation of the α-Carbon Using an Enamine Intermediate
18.11 Alkylation of the β-Carbon: the Michael Reaction*
18.12 The Aldol Reaction Form β-Hydroxyaldehydes or β-Hydroxyketones*
18.13 Dehydration of Aldol Addition Products: Formation of α,β-Unsaturated Aldehydes and Ketones*
18.14 The Mixed Aldol Reaction
18.15 The Claisen Condensation Forms a β-Keto Ester*
18.16 The Mixed Claisen Condensation
18.17 Intramolecular Condensation and Addition Reactions*
18.18 3-Oxocarboxylic Acids Can Be Decarboxylated*
18.19 The Malonic Ester Synthesis: A Way to Synthesize a Carboxylic Acids
18.20 The Acetoacetic Ester Synthesis: A Way to Synthesize Methyl Ketones
18.21 Designing a Synthesis VII: Making New Carbon-Carbon Bonds
18.22 Reactions at the α-Carbon in Biological Systems[#]

* Sections that will be focused
[#] Sections that will be skipped

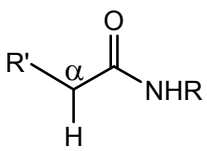
Recommended additional problems

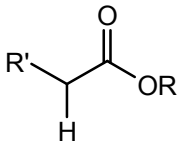
18.48 – 18.58, 18.60 – 18.70, 18.72 – 18.85

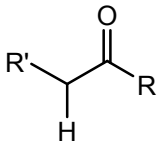
Class Note

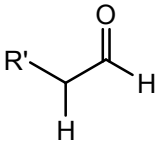
18.1 The Acidity of an α-Hydrogens*

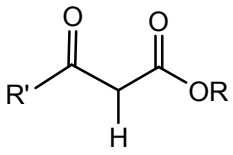
A. pKa of α-hydrogen of carbonyl derivatives

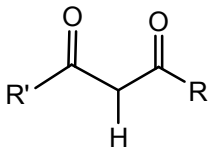


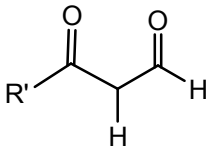






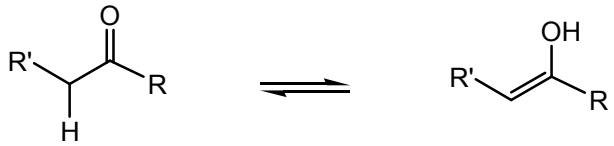






B. Resonance effect

18.2 Keto-Enol Tautomers*



A. Mechanism in acidic condition

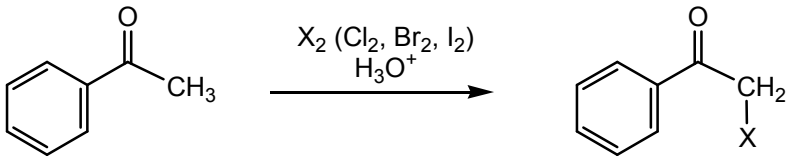
B. Mechanism in basic condition

18.3 Enolization and 18.4 How Enols and Enolate Ions React*

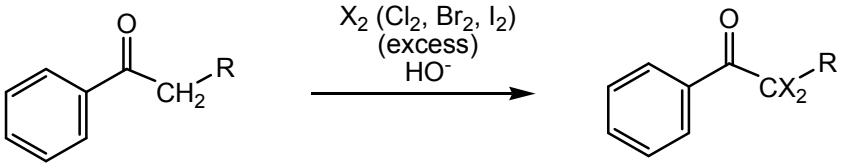
A. Analysis of enols and enolates

18.5 Halogenation of the α-Carbon of Aldehydes and Ketones*

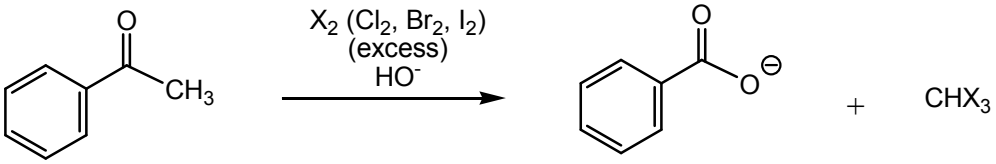
A. Acid-catalyzed halogenation



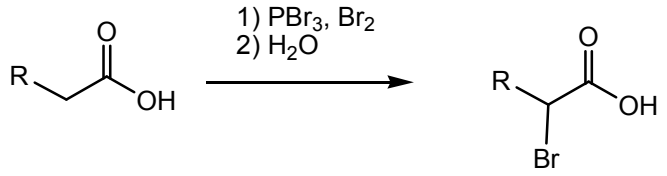
B. Base-promoted halogenation



C. Haloform reaction



18.6 Halogenation of the α-Carbon of Carboxylic Acids: The Hell-Volhard-Zelinski (HVZ) Reaction

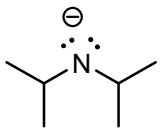


18.7 α-Halogenated Carbonyl Compounds Are Useful in Synthesis*

A. Analysis of α-halogenated carbonyl Compounds

B. Examples

18.8 Using LDA to Form an Enolate*



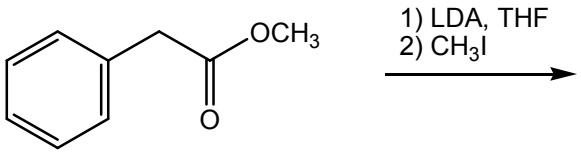
lithium diisopropylamide (LDA)

18.9 Alkylation of the α-Carbon of Carbonyl Compounds*

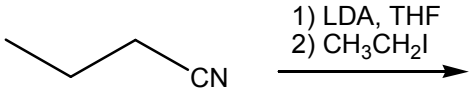
A. Analysis of the reaction

B. Examples

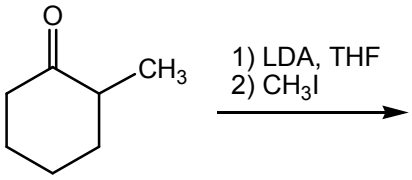
(i)



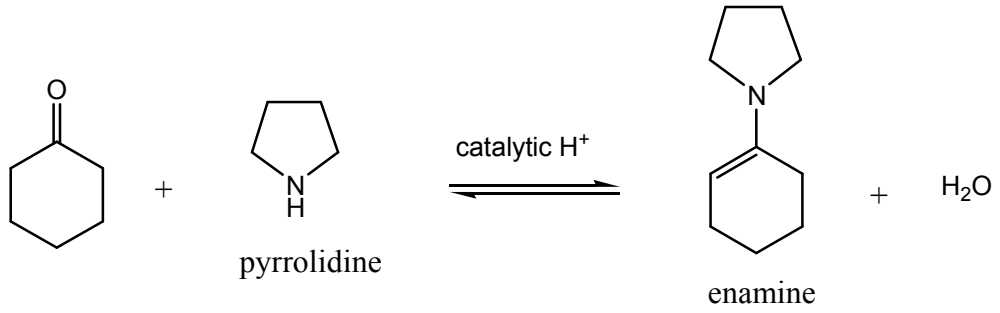
(ii)



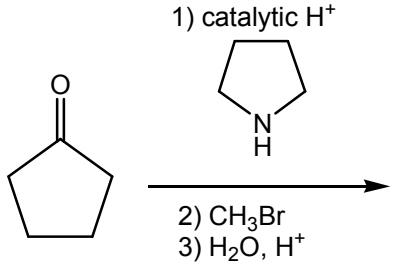
C. Potential problem in alkylation of the α-carbon of carbonyl compounds



18.10 Alkylation and Acylation of the α-Carbon Using an Enamine Intermediate

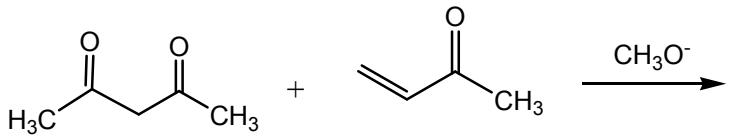


A. Examples



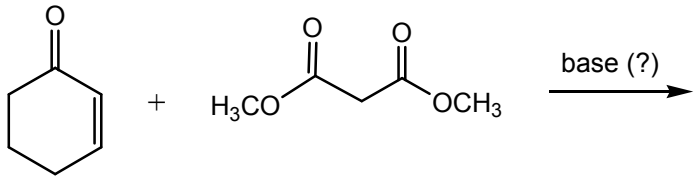
18.11 Alkylation of the β-Carbon: the Michael Reaction*

A. Michael reaction

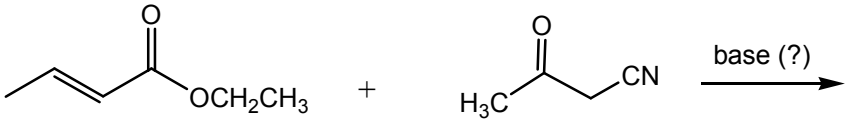


B. Examples

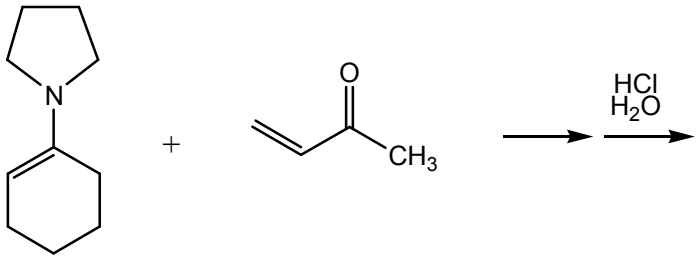
(i)



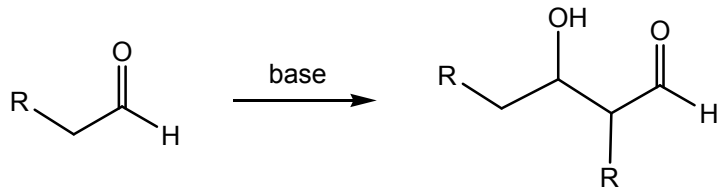
(ii)



C. Stork enamine reaction



18.12 The Aldol Reaction Form β-Hydroxyaldehydes or β-Hydroxyketones*



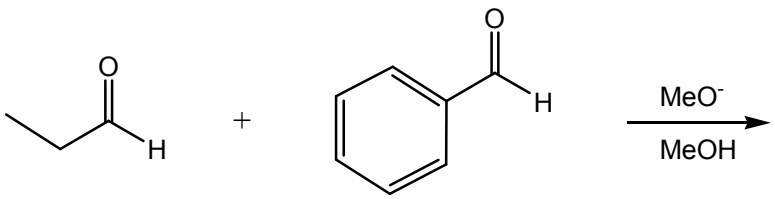
A. Mechanism

18.13 Dehydration of Aldol Addition Products: Formation of α,β-Unsaturated Aldehydes and Ketones*

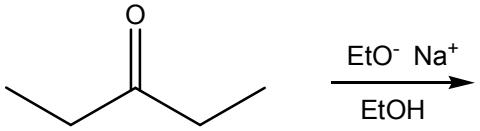
A. Aldol condensation

B. Examples

(i)



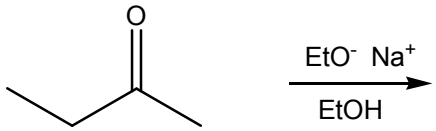
(ii)



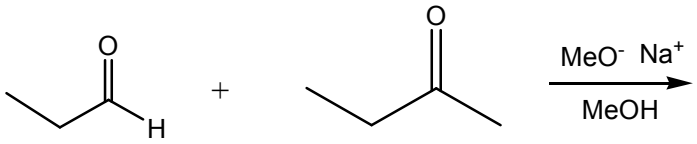
18.14 The Mixed Aldol Reaction

A. Potential problem in aldol reaction

(i)

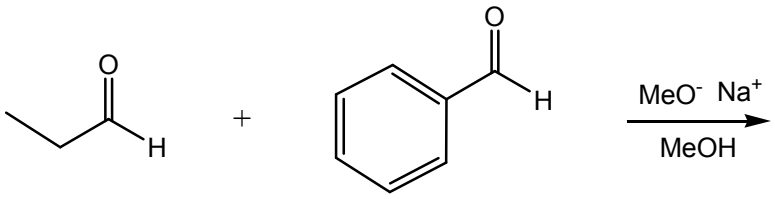


(ii)

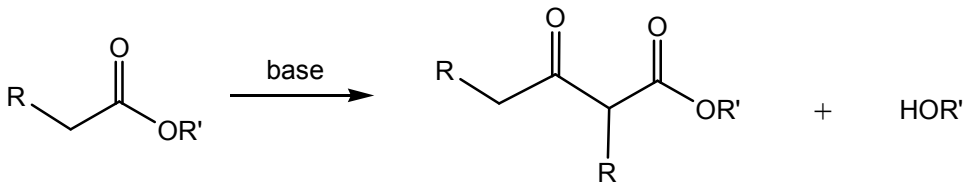


B. Solution

(i)



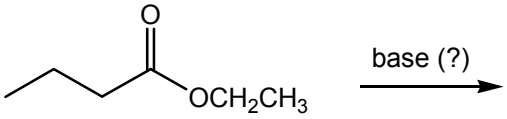
18.15 The Claisen Condensation Forms a β-Keto Ester* and 18.16 The Mixed Claisen Condensation



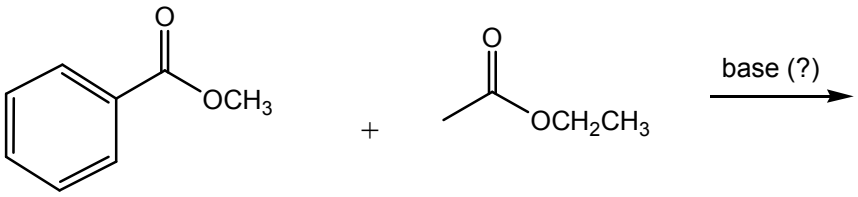
A. Mechanism

B. Examples

(i)



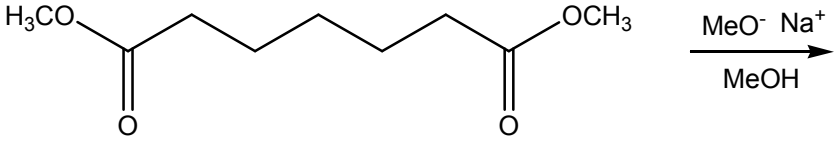
(ii)



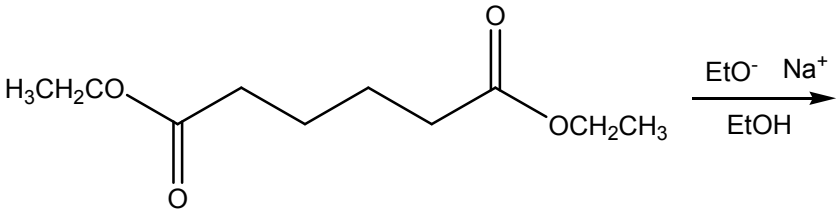
18.17 Intramolecular Condensation and Addition Reactions*

A. Intramolecular Claisen reaction (Dieckmann condensation)

(i)

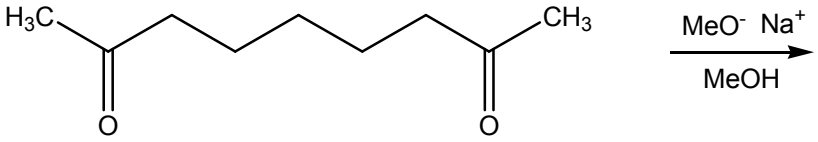


(ii)

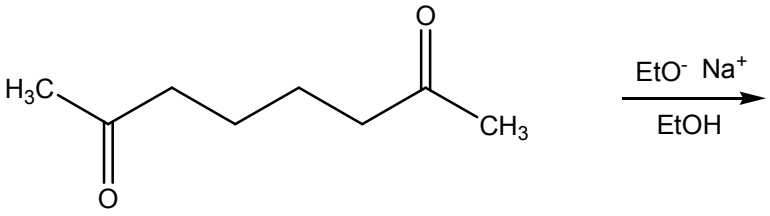


B. Intramolecular aldol reaction

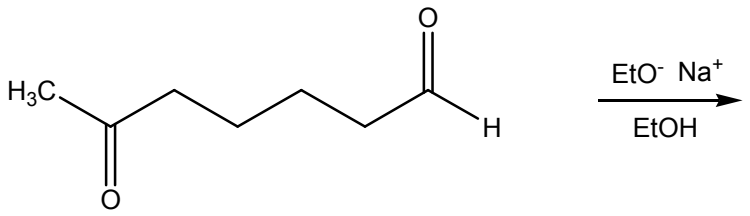
(i)



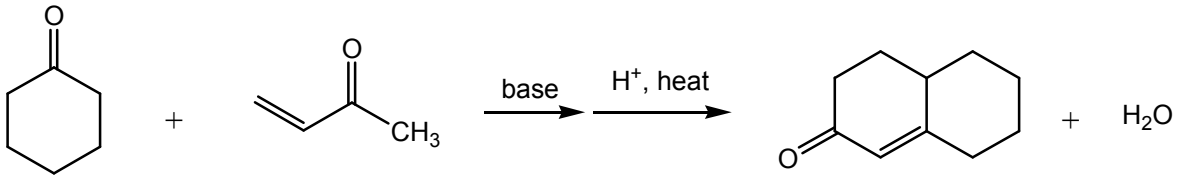
(ii)



(iii)

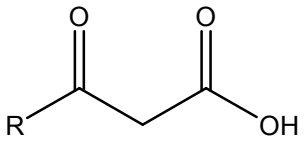


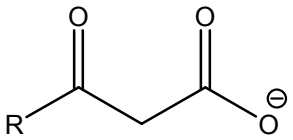
(iv) Robinson annulation



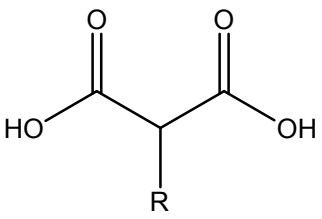
18.18 3-Oxocarboxylic Acids Can Be Decarboxylated*

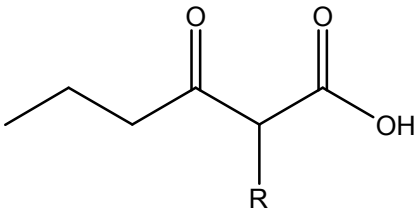
A. Easier in acidic condition: mechanism



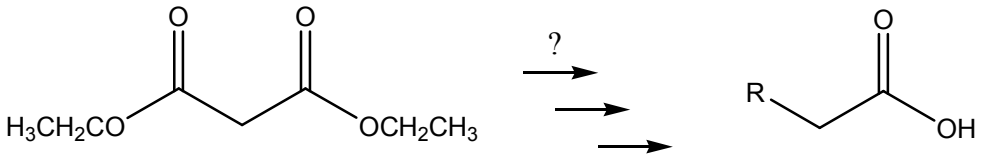


B. Examples of compounds containing 3-oxocarboxylic acid

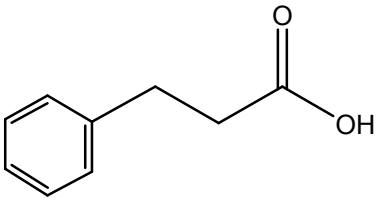


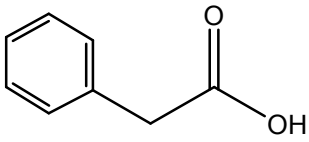


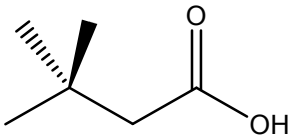
18.19 The Malonic Ester Synthesis: A Way to Synthesize a Carboxylic Acids and 18.20 The Acetoacetic Ester Synthesis: A Way to Synthesize Methyl Ketones



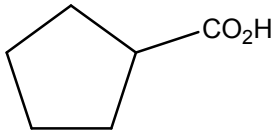
A. Examples:







18.21 Designing a Synthesis VII: Making New Carbon-Carbon Bonds

synthesis of 

from