Chapter 17: Carbonyl Compounds II

Learning Objectives:

1. Recognize and assign names to aldehydes and ketones.
2. Write the mechanism for nucleophilic addition and nucleophilic addition-elimination reactions of aldehydes and ketones, and be able to predict the products of such reactions.
3. Be able to explain the relative reactivity of carbonyl compounds toward nucleophilic addition.
4. Be able to describe the concept of employing protecting groups.
5. Predict the products of the reactions of carbonyl compounds with Grignard reagents, hydride ion donors, sulfur nucleophiles, and with phosphonium ylides (the Wittig reaction).
6. Be able to recognize *Re* and *Si* faces of carbonyl compounds, and the stereochemistry outcomes from a nucleophilic addition.
7. Predict the products of addition reactions to α,β-unsaturated carbonyl compounds.

Sections:

17.1 Nomenclature of Aldehydes and Ketones
17.2 Relative Reactivities of Carbonyl Compounds*
17.3 How Aldehydes and Ketones React*
17.4 Reaction of Carbonyl Compounds with Grignard Reagents*
17.5 Reaction of Carbonyl Compounds with Acetylide Inos
17.6 Reaction of Carbonyl Compounds with Hydride Ion*
17.7 Reaction of Aldehydes and Ketones with Hydrogen Cyanide
17.8 Reaction of Aldehydes and Ketones with Amines and Derivatives of Amines*
17.9 Reaction of Aldehydes and Ketones with Water
17.10 Reaction of Aldehydes and Ketones with Alcohol*
17.11 Protecting Groups*
17.12 Addition of Sulfur Nucleophiles
17.13 The Wittig Reaction Forms an Alkene*
17.14 Stereochemistry of Nucleophilic Addition Reactions: *Re* and *Si* Faces[#]
17.15 Designing a Synthesis VI: Disconnections, Synthones, and Synthetic Equivalents
17.16 Nucleophilic Addition to α,β-Unsaturated Aldehydes and Ketones*
17.17 Nucleophilic Addition to α,β-Unsaturated Carboxylic Acid Derivatives
17.18 Enzyme-catalyzed Additions to α,β-Unsaturated Carbonyl Compounds[#]

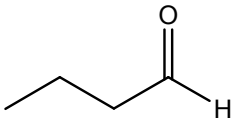
* Sections that will be focused
[#] Sections that will be skipped

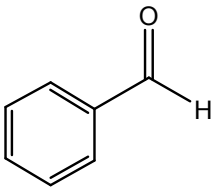
Recommended additional problems

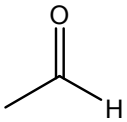
17.45 – 17.65, 17.67 – 17.70, 17.73 – 17.77, 17.79 – 17.82, 17.84

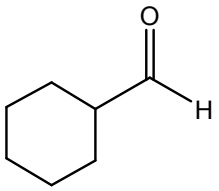
Class Note

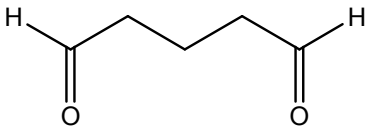
17.1 Nomenclature of Aldehydes and Ketones

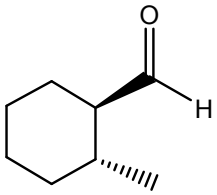


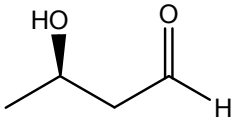


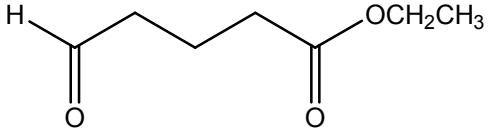


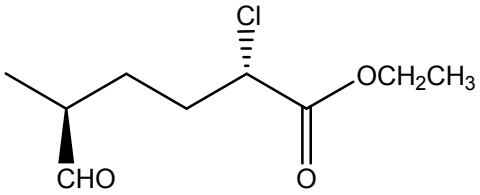


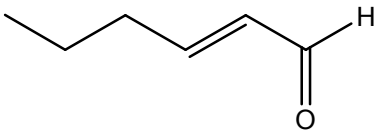











H
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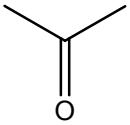
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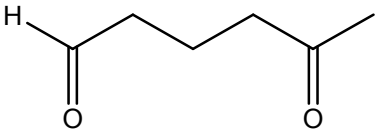
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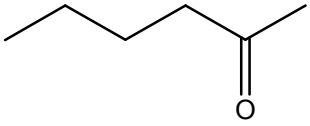
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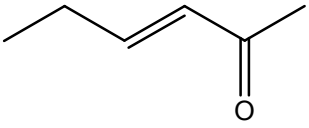
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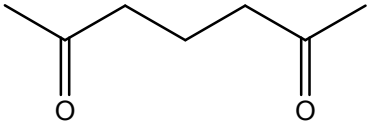
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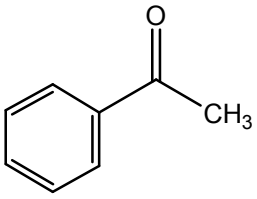
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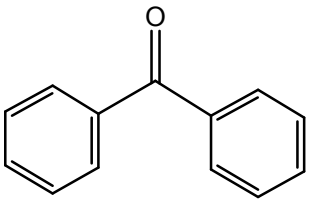
CH3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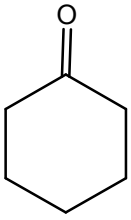
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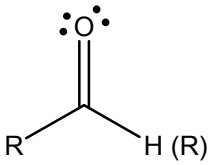
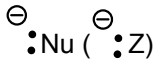
17.2 Relative Reactivities of Carbonyl Compounds*

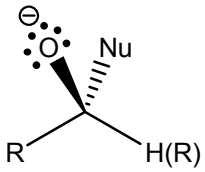
Nucleophilic addition

17.3 How Aldehydes and Ketones React*

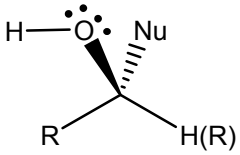
A. In basic condition



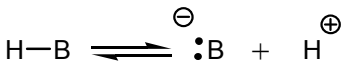


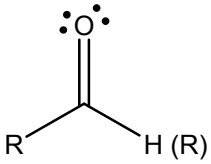


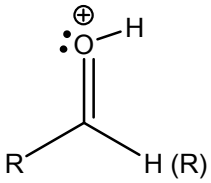
tetrahedral
intermediate

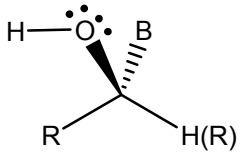


B. In acidic condition









17.4 Reaction of Carbonyl Compounds with Grignard Reagents*

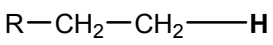
A. Carbon nucleophile (basic or acidic?)

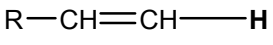
B. Reaction of aldehydes and ketones with Grignard reagent

C. Reactions of ester and carboxylic acid with Grignard reagent

17.5 Reaction of Carbonyl Compounds with Acetylide Inos

(i) *p*Ka of





(ii) Mechanism

17.7 Reaction of Aldehydes and Ketones with Hydrogen Cyanide

(i) *p*Ka of H-CN

(ii) Mechanism

(iii) Synthesis of α-hydroxy carboxylic acid

17.6 Reaction of Carbonyl Compounds with Hydride Ion*

A. Source of hydride

B. Reduction of aldehydes and ketones

C. Reduction of esters

D. Reduction of carboxylic acids

E. Reduction of amides

17.8 Reaction of Aldehydes and Ketones with Amines and Derivatives of Amines*

A. *p*Ka of amines

B. Addition of primary amines

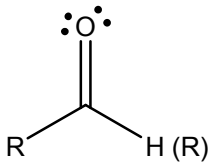
C. Addition of secondary amines

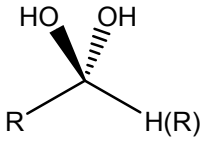
D. Addition of hydrazine, hydroxyamine

E. Mechanism of Wolff-Kishner reduction

17.9 Reaction of Aldehydes and Ketones with Water

A. Addition of water (formation of hydrate, *gem*-diol, geminal diol)





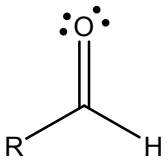
H_2O

(i) Consideration of *p*Ka

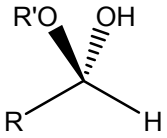
(ii) Stability consideration

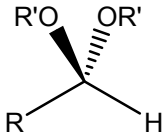
17.10 Reaction of Aldehydes and Ketones with Alcohol*

A. Addition of alcohol (formation of hemiacetal, acetal, hemiketal, and ketal)

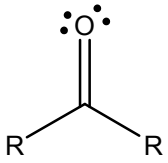


HOR'
(2 equivalents)

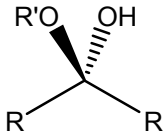


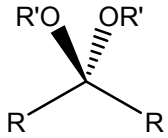


H_2O



HOR'
(2 equivalents)





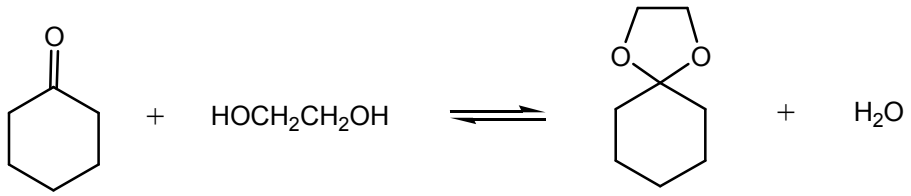
H_2O

C. Mechanism

17.11 Protecting Groups*

A. Stability of acetals and ketals

B. Example



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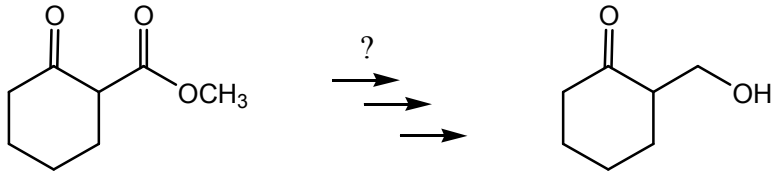
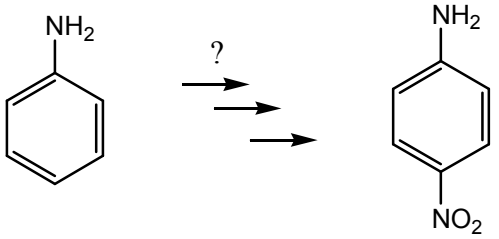
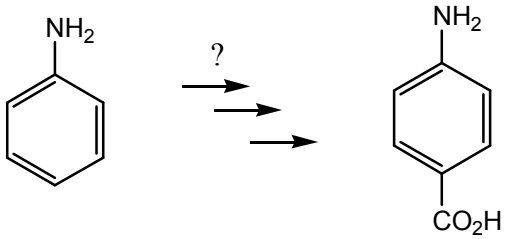


C. More examples

(i)



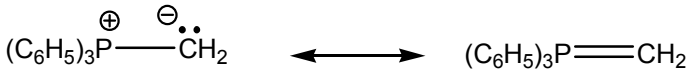
(ii)



17.12 Addition of Sulfur Nucleophiles

17.13 The Wittig Reaction Forms an Alkene*

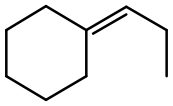
A. Wittig reagents

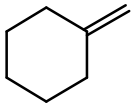


phosphonium ylide

B. Formation of Wittig reagents

C. Reactions

(i) Synthesis of 

(ii) Synthesis of 

D. Stereoselectivity (*E* vs. *Z*)

E. Arbuzov (Perkow) reaction and Horner-Emmons reaction

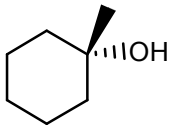
(i) Horner-Emmons reaction

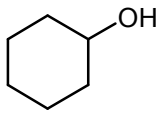
(ii) Arbuzov (Perkow) reaction

17.15 Designing a Synthesis VI: Disconnections, Synthones, and Synthetic Equivalents

A. Retrosynthetic analysis

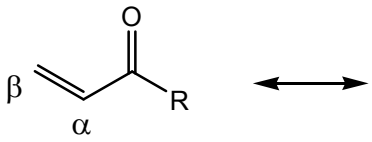
Example

synthesis of 

from 

17.16 Nucleophilic Addition to α,β-Unsaturated Aldehydes and Ketones*

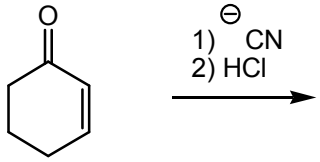
A. Analysis of α,β-unsaturated aldehydes and ketones



B. Direct addition (1,2-addition) and conjugate addition (1,4-addition)

C. Examples

(i)



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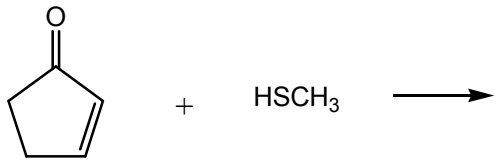

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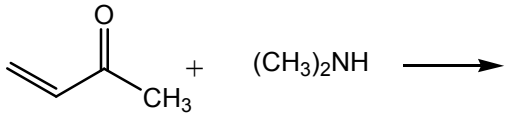
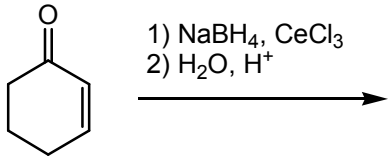
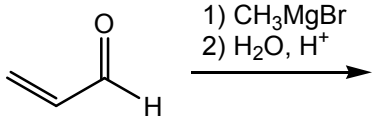


(iv)



(v)



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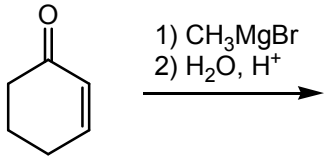
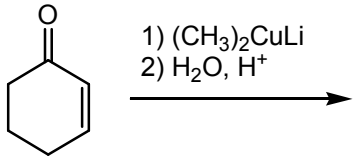


(vii)



17.17 Nucleophilic Addition to α,β-Unsaturated Carboxylic Acid Derivatives