Chapter 18: 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:

18.1 Nomenclature
18.2 Relative Reactivities of Carbonyl Compounds*
18.3 How Aldehydes and Ketones React*
18.4 Reaction of Carbonyl Compounds with Carbon Nucleophiles*
18.5 Reaction of Carbonyl Compounds with Hydride Ion*
18.6 Reaction of Aldehydes and Ketones with Nitrogen Nucleophiles*
18.7 Reaction of Aldehydes and Ketones with Oxygen Nucleophiles*
18.8 Protecting Groups*
18.9 Addition of Sulfur Nucleophiles
18.10 The Wittig Reaction*
18.11 Stereochemistry of Nucleophilic Addition Reactions: *Re* and *Si* Faces#
18.12 Designing a Synthesis V: Disconnections, Synthones, and Synthetic Equivalents
18.13 Nucleophilic Addition to α,β-Unsaturated Aldehydes and Ketones*
18.14 Nucleophilic Addition to α,β-Unsaturated Carboxylic Acid Derivatives
18.15 Enzyme-catalyzed Additions to α,β-Unsaturated Carbonyl Compounds#

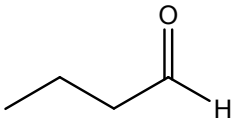
* Sections that will be focused
# Sections that will be skipped

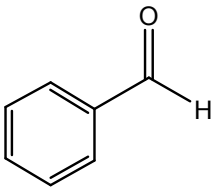
Recommended additional problems

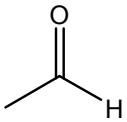
8.40 – 8.55, 8.58 – 8.61, 8.63 – 8.67, 8.69 – 8.72, 8.74

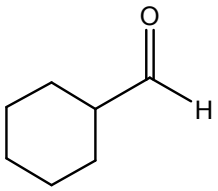
Class Note

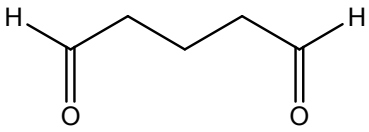
18.1 Nomenclature

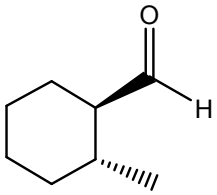


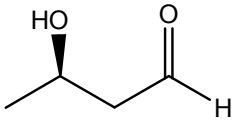


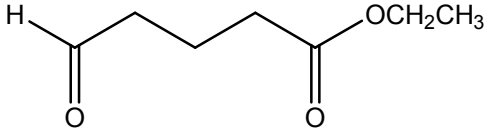


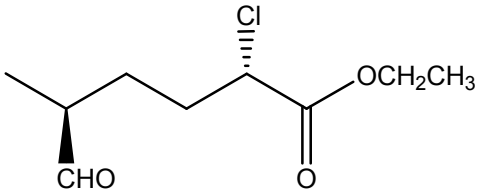


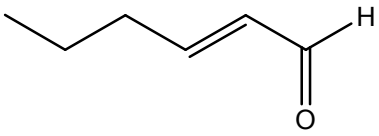








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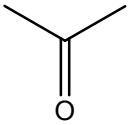
O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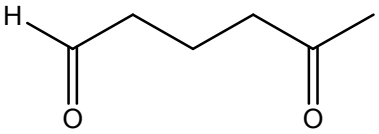
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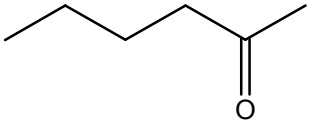
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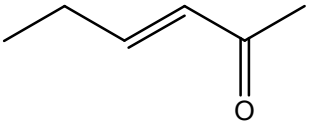
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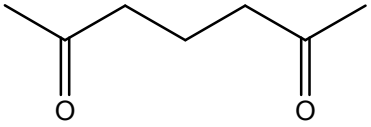
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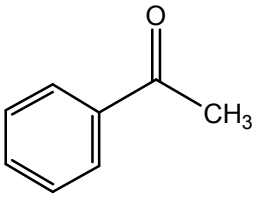
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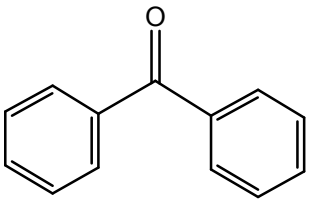
CH3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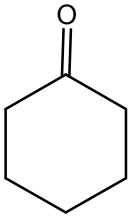
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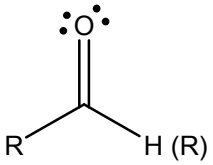
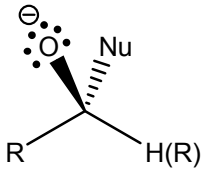
18.2 Relative Reactivities of Carbonyl Compounds

Nucleophilic addition

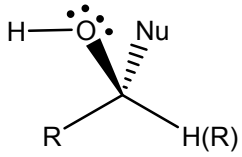
18.3 How Aldehydes and Ketones React

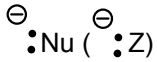
A. In basic condition



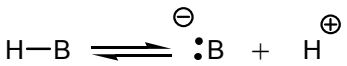


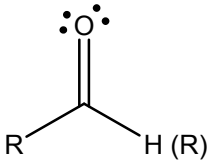
tetrahedral
intermediate

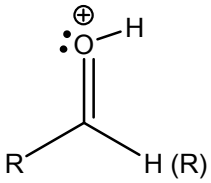


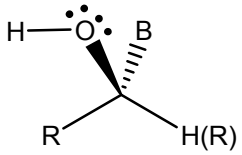


B. In acidic condition









18.4 Reaction of Carbonyl Compounds with Carbon Nucleophiles

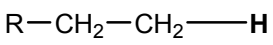
A. Carbon nucleophile (basic or acidic?)

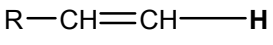
B. Reaction of aldehydes and ketones with Grignard reagent

C. Reactions of ester and carboxylic acid with Grignard reagent

D. Reactions of aldehydes and ketones with acetylide ions

(i) *p*Ka of





(ii) Mechanism

E. Reactions of aldehydes and ketones with hydrogen cyanide

(i) *p*Ka of H-CN

(ii) Mechanism

(iii) Synthesis of α-hydroxy carboxylic acid

18.5 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

18.6 Reaction of Aldehydes and Ketones with Nitrogen Nucleophiles

A. *p*Ka of amines

B. Addition of primary amines

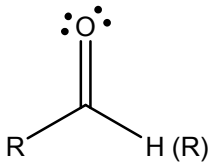
C. Addition of secondary amines

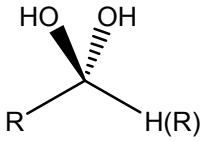
D. Addition of hydrazine, hydroxyamine

E. Mechanism of Wolff-Kishner reduction

18.7 Reaction of Aldehydes and Ketones with Oxygen Nucleophiles

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



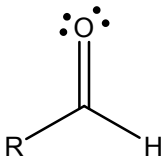


H_2O

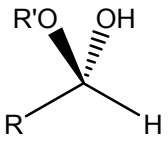
(i) Consideration of *p*Ka

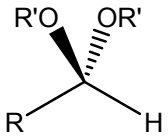
(ii) Stability consideration

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

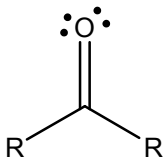


HOR'
(2 equivalents)

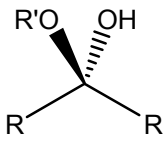


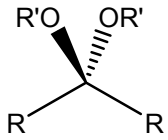


H_2O



HOR'
(2 equivalents)





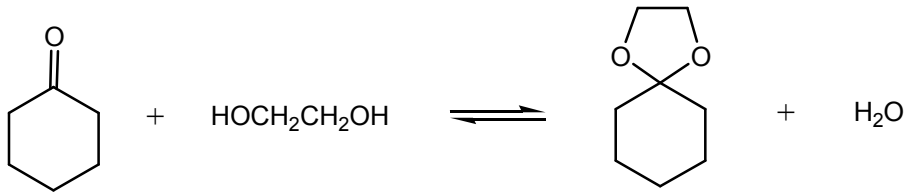
H_2O

C. Mechanism

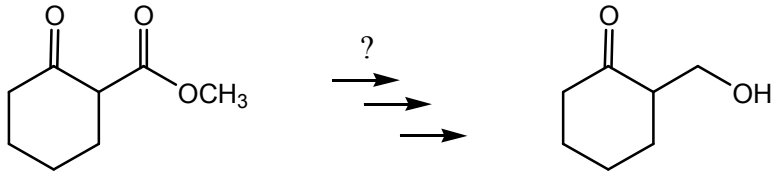
18.8 Protecting Groups

A. Stability of acetals and ketals

B. Example

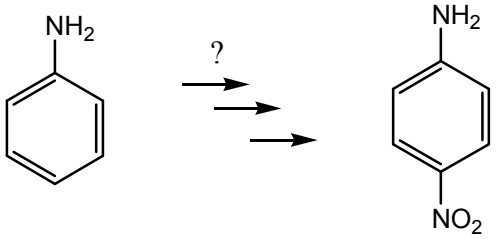


(i)



C. More examples

(i)



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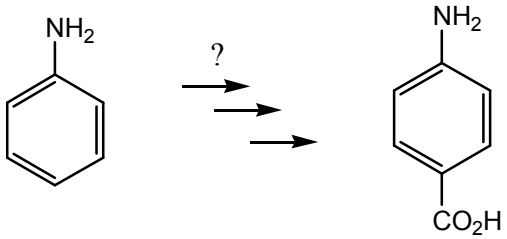
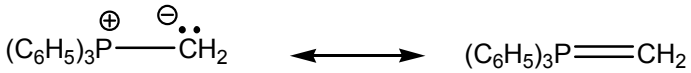


18.9 Addition of Sulfur Nucleophiles

18.10 The Wittig Reaction

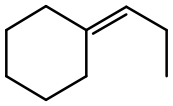
A. Wittig reagents

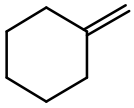


phosphonium ylide

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

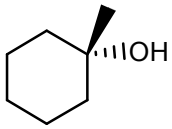
(i) Horner-Emmons reaction

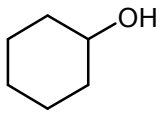
(ii) Arbuzov (Perkow) reaction

18.12 Designing a Synthesis V: Disconnections, Synthones, and Synthetic Equivalents

A. Retrosynthetic analysis

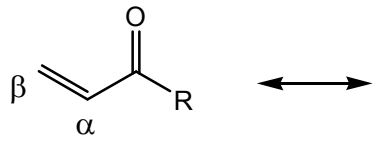
Example

synthesis of 

from 

18.13 Nucleophilic Addition to α,β-Unsaturated Aldehydes and Ketones

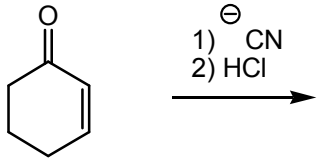
A. Analysis of α,β-unsaturated aldehydes and ketones



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

C. Examples

(i)



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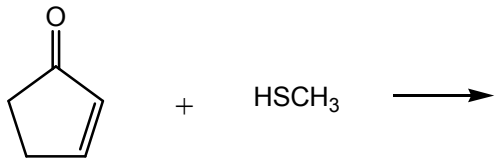

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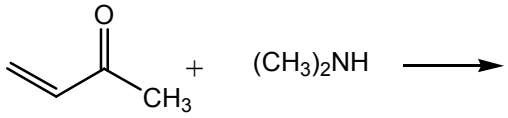

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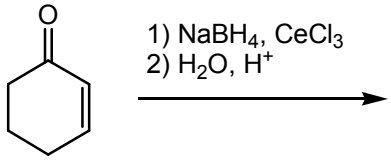
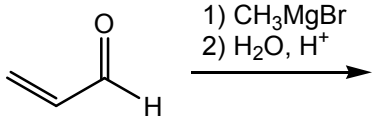


(v)



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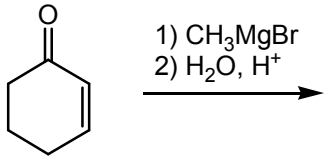
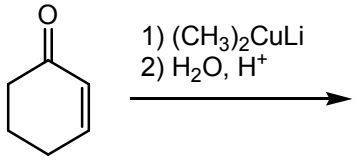


(vii)



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