

16: Addition and Substitution Reactions of Carbonyl Compounds

16.1 Carbonyl Groups React with Nucleophiles

Overview (16.1A)

Addition and Substitution (16.1B)

Addition Reactions

Substitution Reactions

Addition and Substitution Mechanisms

Types of Nucleophiles (16.1C)

Enolate Ions

16.2 The Nucleophile HO^-

HO^- in HOH (16.2A)

Relative Nucleophilicities of HO^- and HOH

Competitive Enolate Ion Formation

HO^- Addition to Ketones and Aldehydes (16.2B)

1,1-Diols are Called Hydrates

Ketones, Aldehydes, and Their Hydrates

HO^- Substitution on $\text{R}-\text{C}(=\text{O})-\text{Z}$ Compounds (16.2C)

The Mechanism

When Z is OH

16.3 The Nucleophile HOH

Activation of $\text{C}=\text{O}$ by Protonation (16.3A)

Protonated $\text{C}=\text{O}$ Group

Reaction with HOH

Acid Catalyzed Addition of HOH to Aldehydes and Ketones (16.3B)

Acid Catalyzed Addition of Water to $\text{R}-\text{C}(=\text{O})-\text{Z}$ (16.3C)

The Overall Mechanism

The Tetrahedral Intermediate

Loss of the Z Group

Proton Shifts

Amide Hydrolysis as an Example

"Uncatalyzed" Addition of HOH to Carbonyl Compounds (16.3D)

Uncatalyzed Aldehyde Hydration

Uncatalyzed Hydrolysis of $\text{R}-\text{C}(=\text{O})-\text{Z}$

16.4 Alcohols (ROH) as Nucleophiles

ROH Addition to Aldehydes and Ketones gives Hemiacetals (16.4A)

Hemiacetal Formation Mechanism

Acid Catalyzed Formation of Acetals (16.4B)

Acetal Formation Mechanism

Acetals Serve as Protecting Groups

ROH Addition to $\text{R}-\text{C}(=\text{O})-\text{Z}$ (16.4C)

General Mechanism

ROH Reaction with Acid Halides

ROH Reactions with Carboxylic Acids and Esters

16.5 Amines (R_2NH) as Nucleophiles

Reaction of Amines with Ketones or Aldehydes (16.5A)

Imines

Enamines

Reaction of Amines with $R-C(=O)-Z$ (16.5B)

Amines and Anhydrides or Esters

Amines and Carboxylic Acids

Other Nitrogen Nucleophiles (16.5C)

Hydrazines as Nucleophiles

Wolff-Kishner Reaction

Hydroxylamine as a Nucleophile

16.6 Carbon Centered Nucleophiles

Different Types of C Nucleophiles (16.6A)

Organometallic Reagents (16.6B)

Overview

Magnesium, Lithium and Zinc Reagents

Addition of "R-M" to Aldehydes and Ketones (16.6C)

Stepwise Reactions

Solvents

Mechanisms

Side Reactions

Addition of "R-M" to Carbonyl Compounds $R-C(=O)-Z$ (16.6D)

A General Mechanism

3° Alcohol Formation

Ketone Formation

Reactions of "R-M" with Carboxylic Acids (16.6E)

Reactions with CO_2 (16.6F)

Reaction of Cyanide Ion with $C=O$ Groups (16.6G)

Cyanohydrins

Mechanism of Cyanohydrin Formation

Reaction of $Ph_3P=CR_2$ with $C=O$ Groups (16.6H)

Wittig Reaction

Formation of the Wittig Reagent

Mechanism of the Wittig Reaction

16.7 Other Nucleophiles

The Hydride Nucleophile (16.7A)

Chloride Ion as a Nucleophile (16.7B)

16.8 Nucleophilic Addition to $C=N$ and $C\equiv N$ Bonds

Additions to $C=N$ (16.8A)

Addition of Water

Addition of Organometallic Reagents

Addition of Cyanide Ion

Strecker Synthesis

Additions to $C\equiv N$ (16.8B)

Addition of Water

Hydrolysis Reaction Mechanism

Addition of Organometallic Reagents