Chapter 12

Reactions of Aldehydes and Ketones

More Reactions of Carboxylic Acid Derivatives

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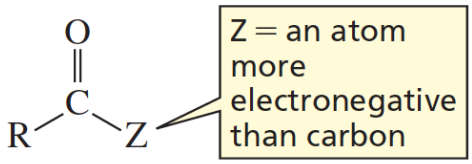
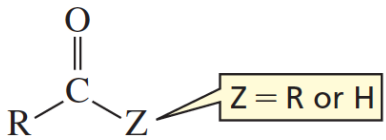
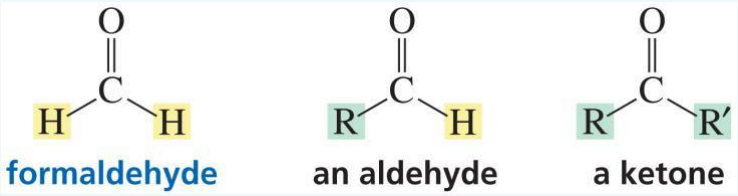
This chapter continues the discussion of the families of compounds in Group IV

Group IV





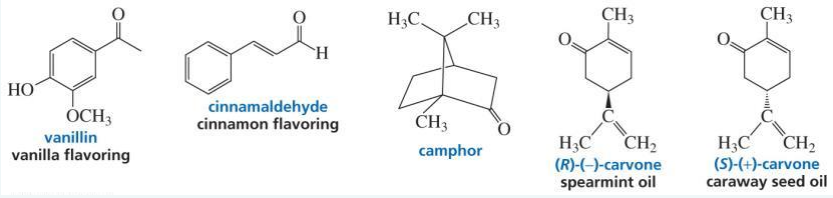
Aldehydes and Ketones



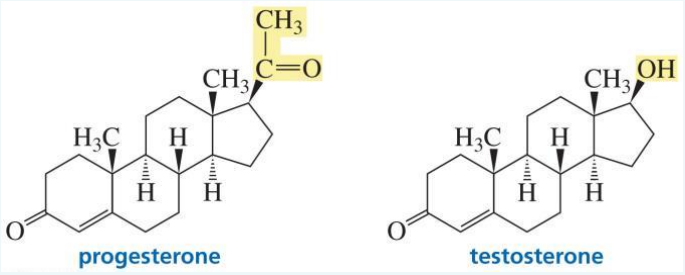
Carbonyl compounds with hydrogen and alkyl groups

- Formaldehyde: two hydrogens
- Aldehyde: a hydrogen and an alkyl group
- Ketone: two alkyl groups

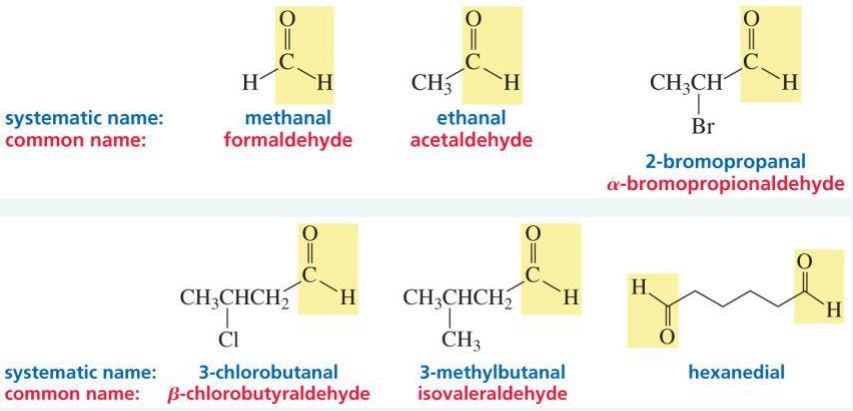
Some Aldehydes and Ketones found in Nature



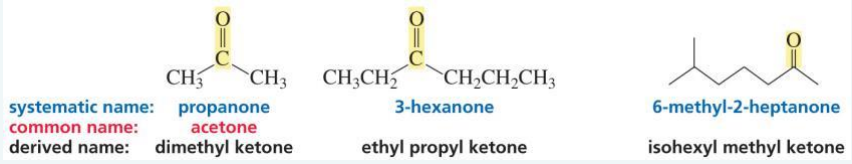
Biologically Important Ketones



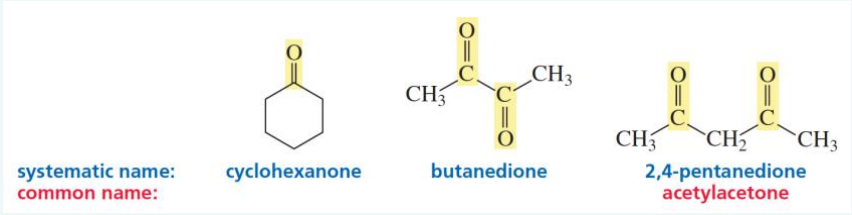
Naming Aldehydes



Naming Ketones

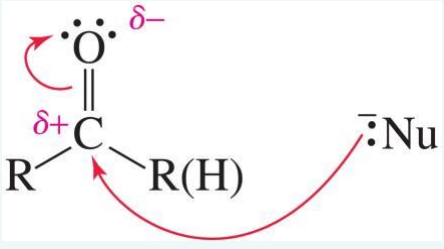


the carbonyl is assumed to be at the 1-position in cyclic ketones



Aldehydes and Ketones are attacked by Nucleophiles

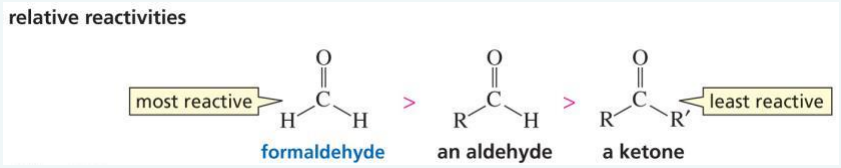
The partial positive charge on the carbonyl carbon causes it to be attacked by nucleophiles:



Aldehydes are more reactive than Ketones

Electronic Reason:

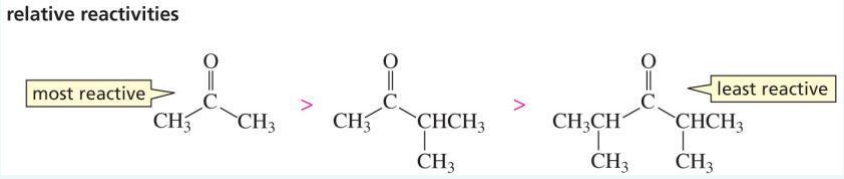
An aldehyde has a greater partial positive charge on its carbonyl carbon than does a ketone because a hydrogen is more electron withdrawing than an an alkyl group.



Aldehydes are more reactive than Ketones

Steric Reason:

The carbonyl carbon of an aldehyde is more accessible to the nucleophile.



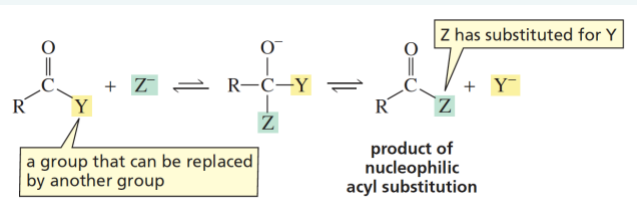
ketones with larger R groups are even less reactive

Aldehydes and Ketones are moderately reactive Carbonyl Compounds

Aldehydes and ketones are less reactive than acyl halides and acid anhydrides.

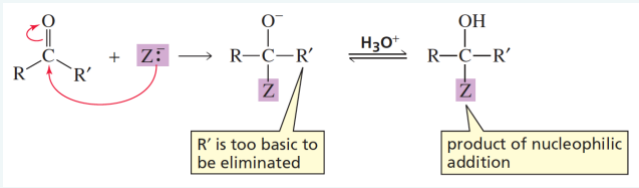
Aldehydes and ketones are more reactive than esters, carboxylic acids, amides, and carboxylate ions.

Aldehydes and Ketones react differently than do Carboxylic Acid Derivatives



In a carboxylic acid derivative, Y^- can leave.

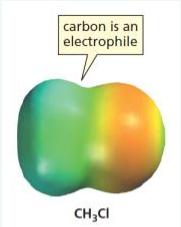
Nucleophilic acyl substitution is observed.

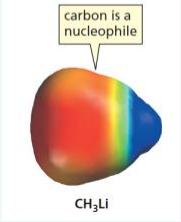


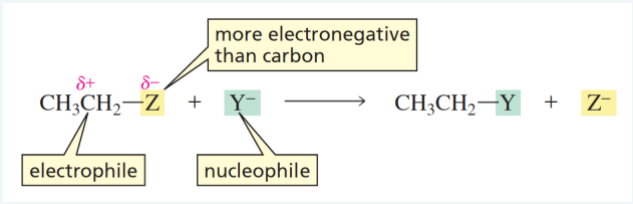
In aldehydes and ketones, neither alkyl nor hydride groups can leave.

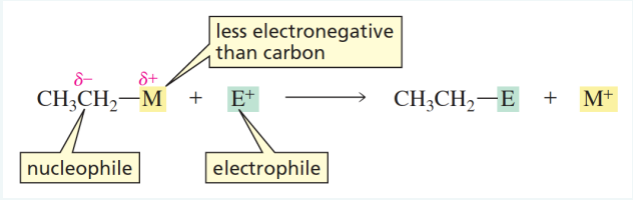
Nucleophilic addition is observed.

Organometallic Compounds









Organometallic Compounds: Grignard Reagents

$$CH_3CH_2Br \xrightarrow[Et_2O]{Mg} CH_3CH_2MgBr$$

CH_3CH_2MgBr **reacts as if it were** $CH_3\ddot{C}H_2\ \ \overset{+}{M}gBr$

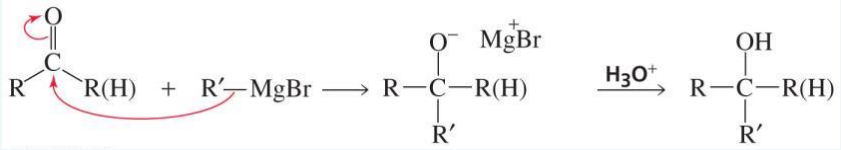
Grignard reagents react as carbanions.

$$CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 \xrightarrow[Et_2O]{Mg} CH_3CH_2\underset{\displaystyle MgBr}{\underset{|}{C}}HCH_3 \xrightarrow{H_2O} CH_3CH_2CH_2CH_3$$

They are strong bases and react vigorously with water.

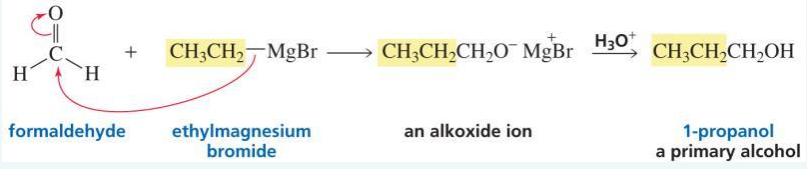
Mechanism for the reaction of an Aldehyde or a Ketone with a Grignard Reagent

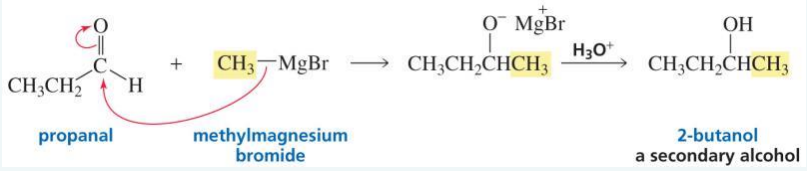
Grignard reagents react with aldehydes, ketones, and carboxylic acid derivatives.

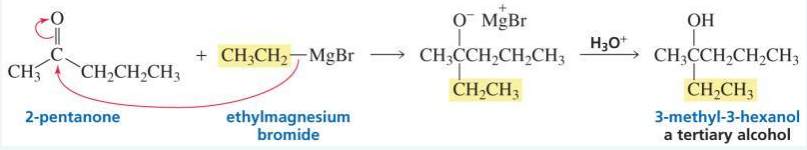


Addition of dilute acid breaks up the complex.

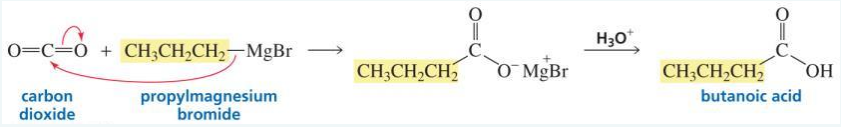
Grignard Reagents are used to prepare alcohols





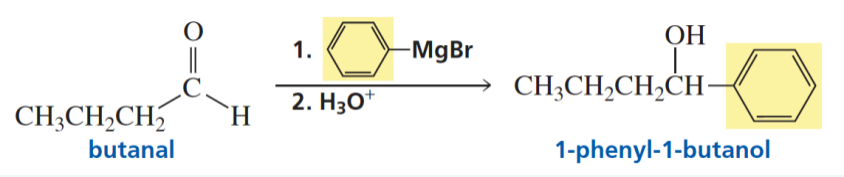


Grignard Reagents form Carboxylic Acids by reaction with Carbon Dioxide



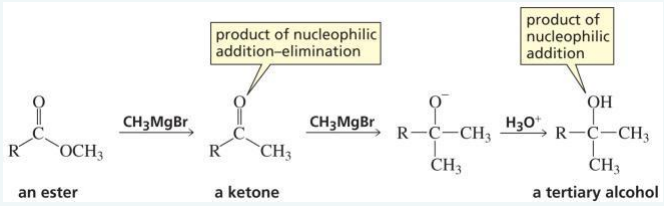
The carboxylic acid has one more carbon than the Grignard reagent.

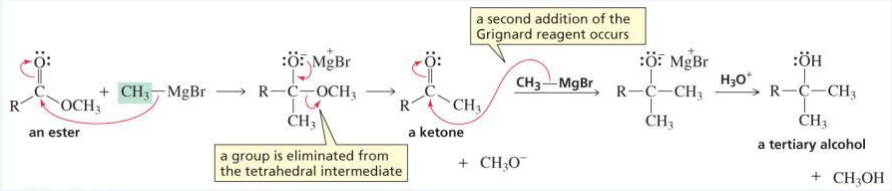
Examples of reactions with Grignard Reagents



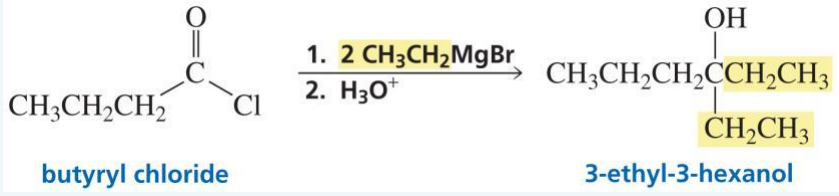
- The numbers above and below the arrows mean the acid is not added until the Grignard reagent has reacted with the carbonyl compound.
- The product of this reaction is a racemic mixture because a compound with an asymmetric center was created from a reactant without an asymmetric center.

Esters react with Grignard Reagents to form alcohols

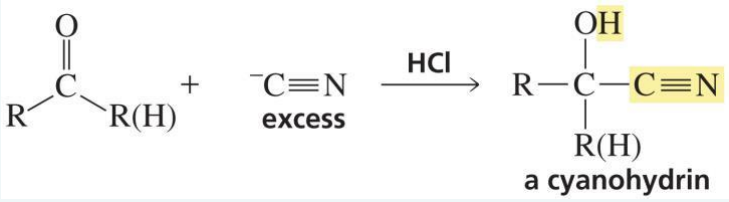


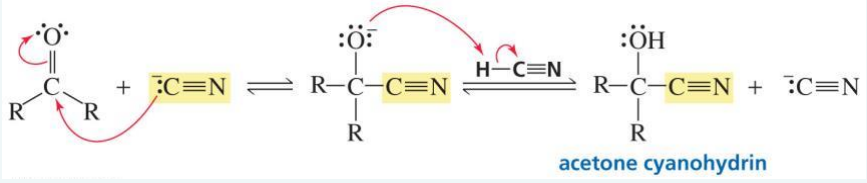


Acyl Chlorides react with Grignard Reagents to form alcohols

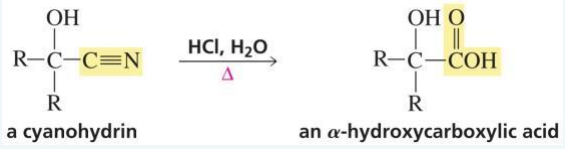


Reaction of Aldehydes and Ketones with Cyanide Ion

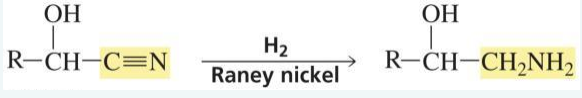




Reactions of Cyanohydrins

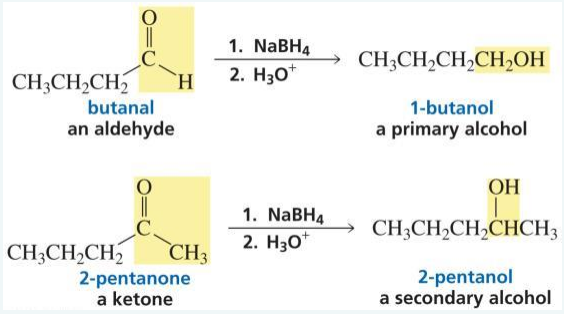


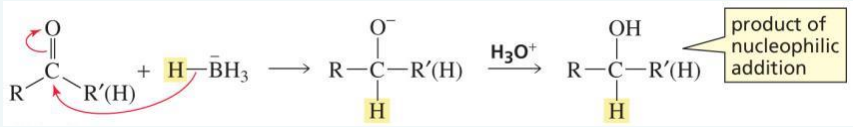
Hydrolysis to form an *α*-hydroxycarboxylic acid.



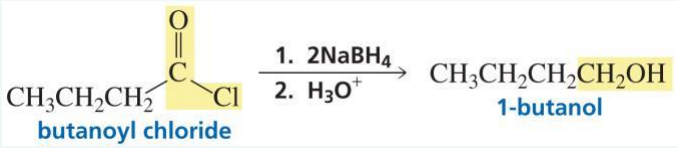
Reduction to a primary amine with an OH group on the *β*-carbon.

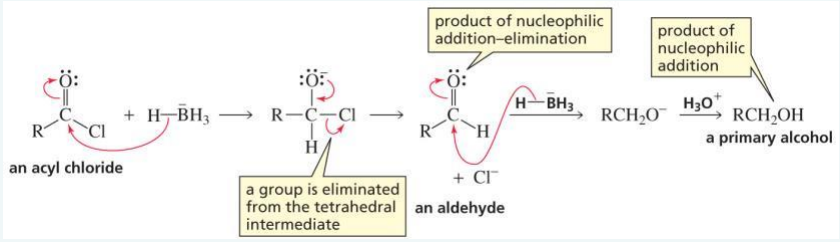
Reactions of Aldehydes and Ketones with Hydride Ion



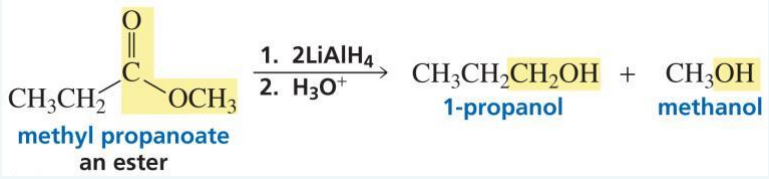


Reactions of Acyl Chlorides with Hydride Ion

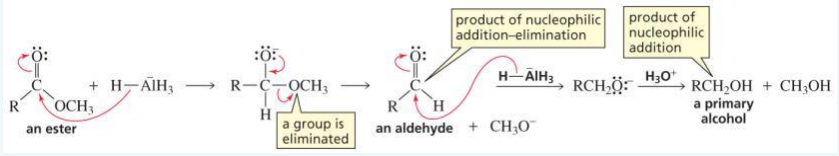




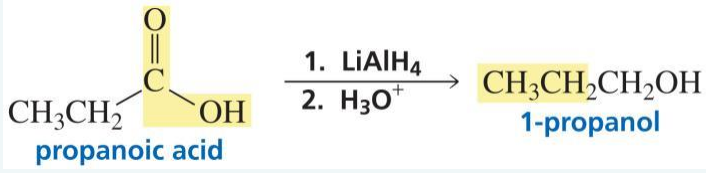
Reaction of an Ester with Hydride Ion



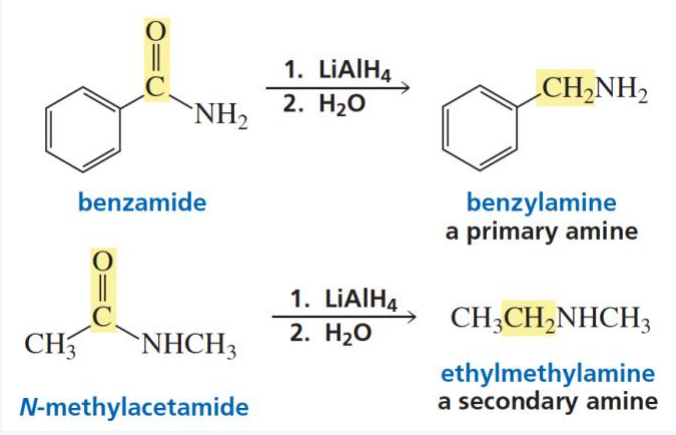
Mechanism for the reaction of an Ester with Hydride Ion



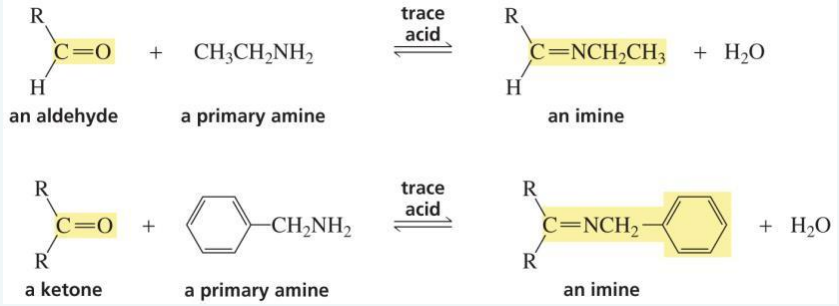
Reactions of Carboxylic Acids with Hydride Ion



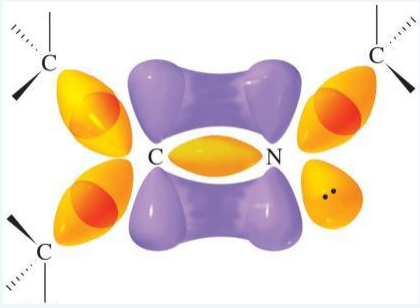
The Reactions of Amides with Hydride Ion



Aldehydes and Ketones form Imines with Primary Amines

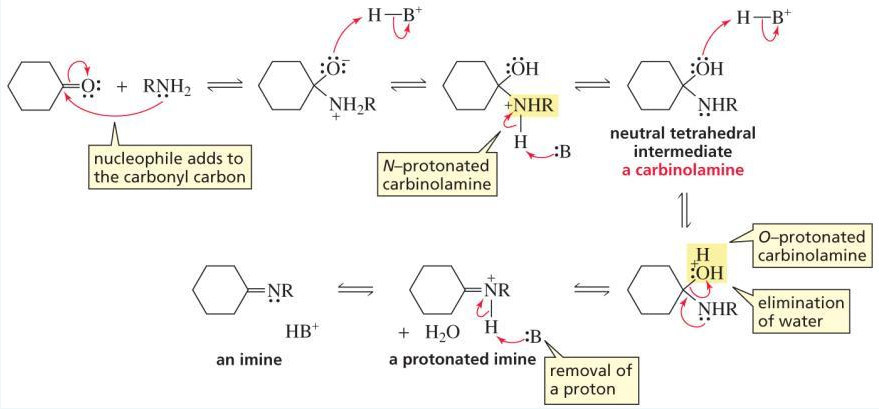


Bonding in an Imine

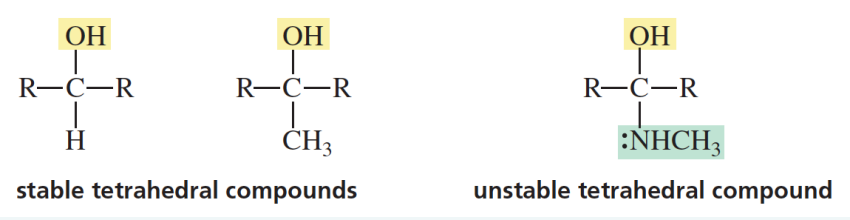


- The π bond is formed by side-to-side overlap of a *p* orbital of carbon with a *p* orbital of nitrogen.
- The π bond is perpendicular to the orange orbitals.

Mechanism for Imine Formation



Intermediates in Imine Formation are unstable



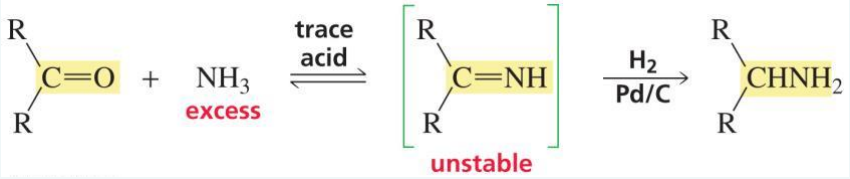
- Imine formation is reversible because there are two protonated intermediates in the mechanism that can eliminate a group.
- Imine formation can be pushed to completion by removing water as it is formed.

Imine Hydrolysis is Irreversible

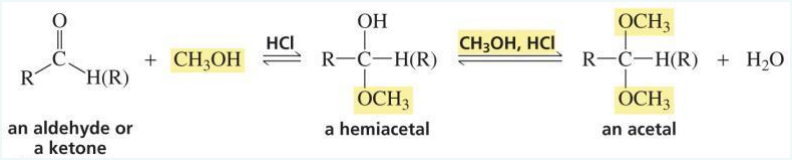
The amine is protonated in the acidic solution, so it is unable to react with the carbonyl compound.

Reductive Amination

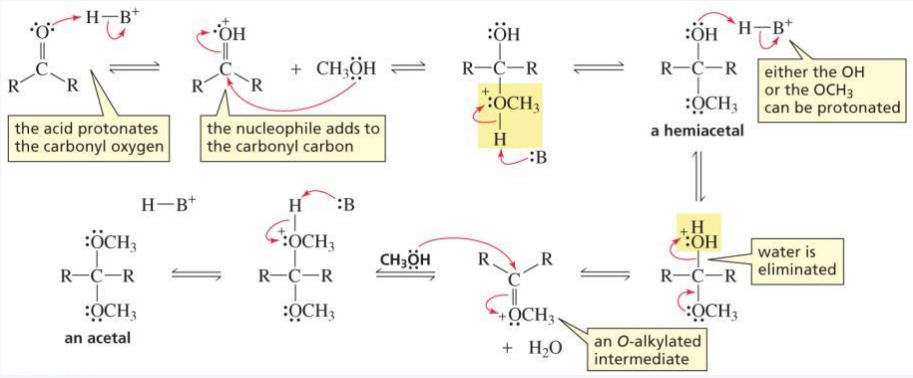
The unstable imine formed from ammonia is hydrogenated to an amine.



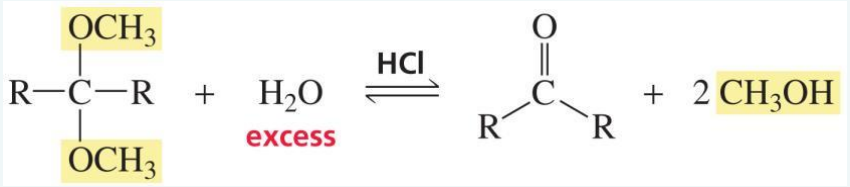
The reaction of an Aldehyde or Ketone with an alcohol



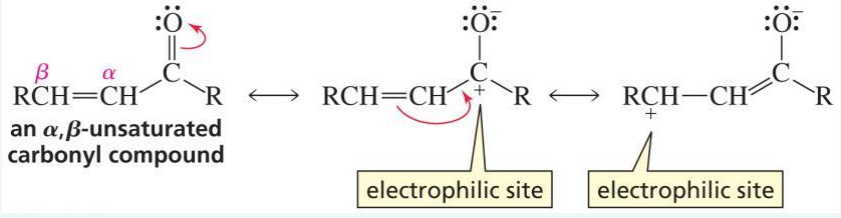
Mechanism for the reaction of an Aldehyde or Ketone with an alcohol



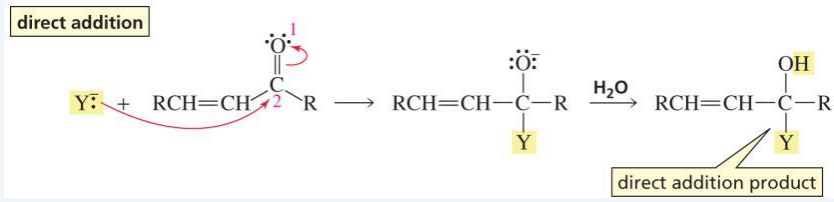
Acid-Catalyzed Hydrolysis of an Acetal



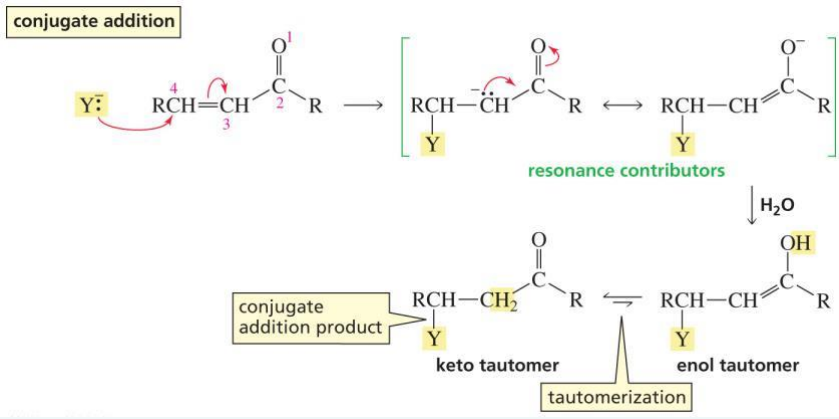
α,β-Unsaturated Aldehydes and Ketones have two Electrophilic Sites



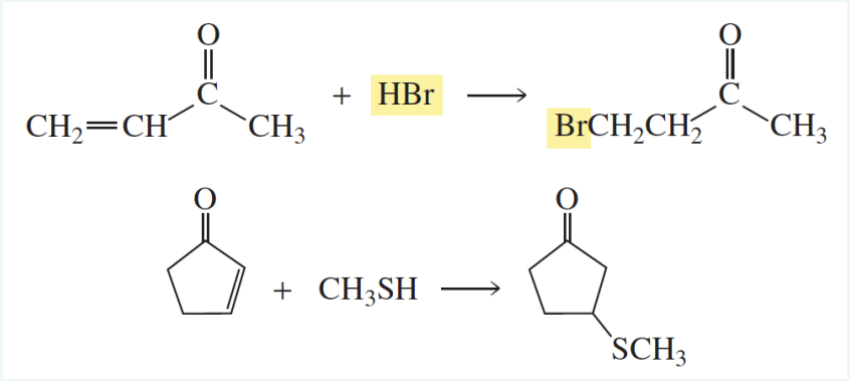
Direct addition to α,β-Unsaturated Aldehydes and Ketones



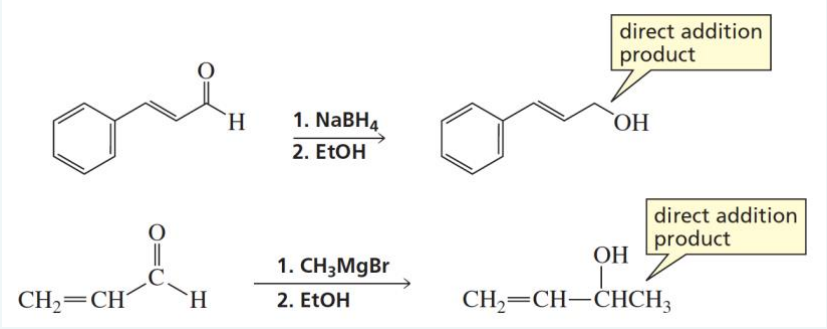
Conjugate addition to α,β-Unsaturated Aldehydes and Ketones



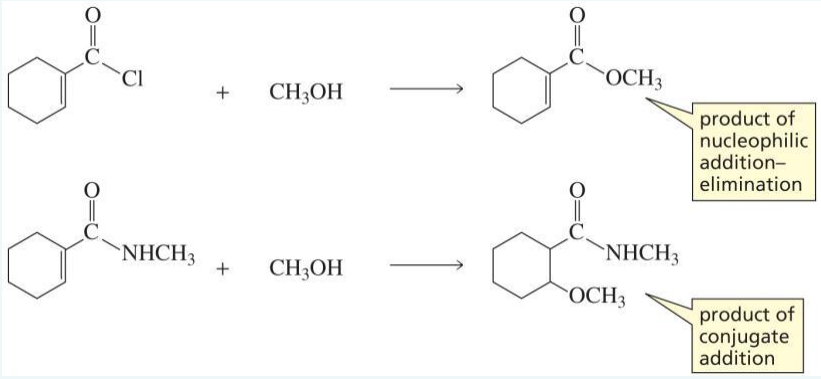
Weak Bases form Conjugate Addition products



Strong Bases form Direct Addition products



Nucleophilic Addition to α,β-Unsaturated Carboxylic Acid Derivatives



Conjugate Addition Reactions in Biological Systems