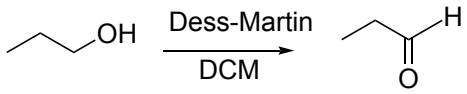
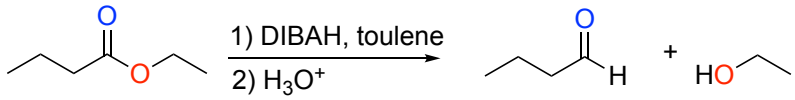
Chapter 19: Aldehydes and Ketones: Nucleophilic Addition Reactions

Preparation of Aldehydes

- **Method One:** Oxidation of primary alcohols

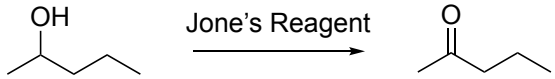


- **Method Two:** Partial reduction of esters

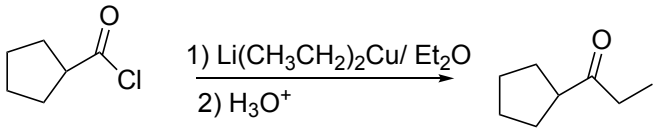


Preparation of Ketones

- **Method One:** Oxidation of secondary alcohols



- **Method Two:** Acyl chloride and Gilman
  - Reaction:

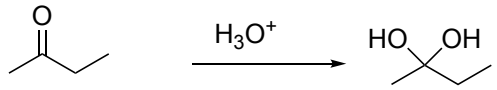


  - Notes:
    - Gilman is characterized by the general formula: R_2CuLi
    - Remove the chloride and replace with the alkyl group

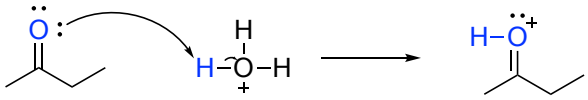
Nucleophilic Addition of Carbonyl Compounds: Alcohol Formation

Nucleophilic Addition of H_2O: Acidic Conditions Mechanism

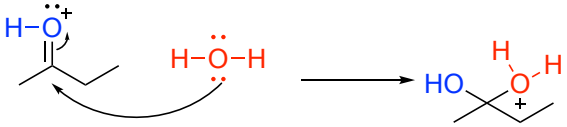
- Overall Reaction:



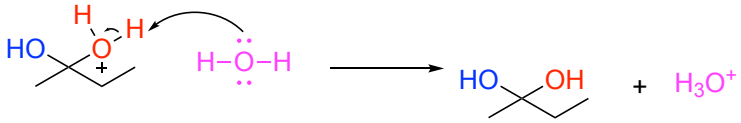
- Step One: Protonation



- Step Two: Nucleophilic attack by water

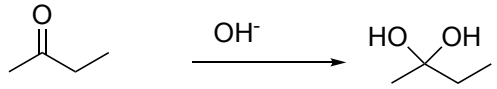


- Step Three: Proton transfer and acid regeneration

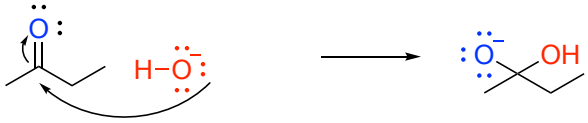


Nucleophilic Addition of H_2O: Basic Conditions Mechanism

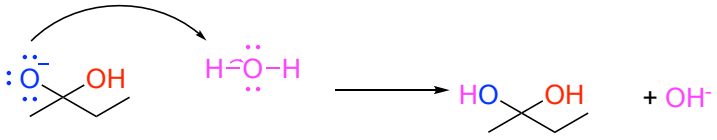
- Overall Reaction:



- Step One: Nucleophilic attack by hydroxide

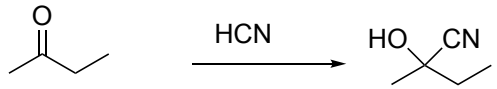


- Step Two: Alkoxide ion protonation by water and hydroxide regeneration

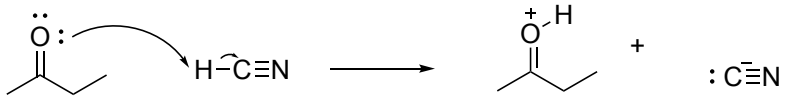


Nucleophilic Addition of HCN: Cyanohydrin Formation

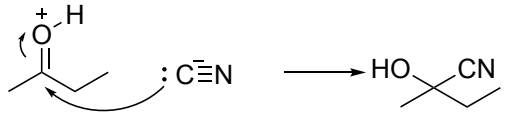
- Overall Reaction:



- Step One: Protonation of oxygen

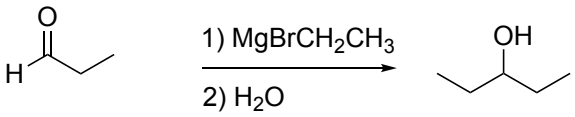


- Step Two: Nucleophilic attack on carbonyl carbon by cyanide

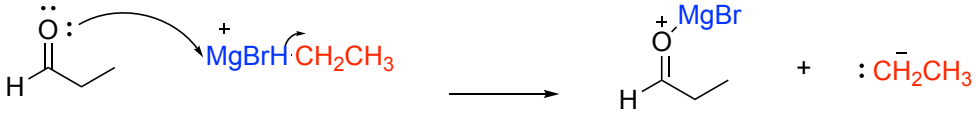


Nucleophilic Addition of Grignard Reagents with an Aldehyde

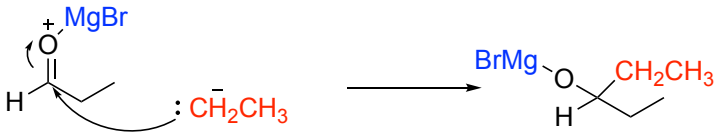
- Note: it will always produce a 2º alcohol
- Overall Reaction:



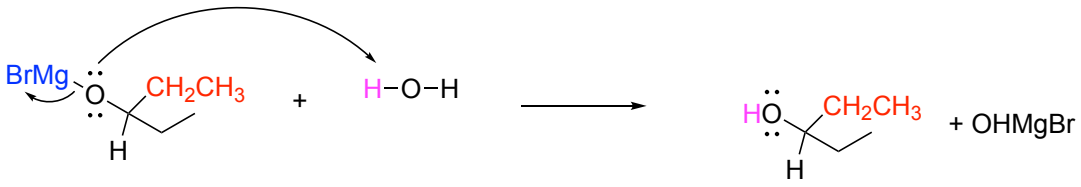
- Step One: Oxygen acts as a Lewis base, forming an acid-base complex with magnesium



- Step Two: Nucleophilic attack by the carbanion

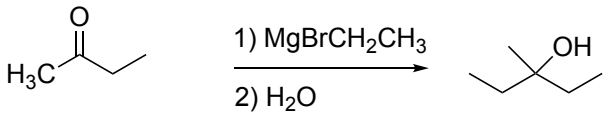


- Step Three: Water removes magnesium alkoxide

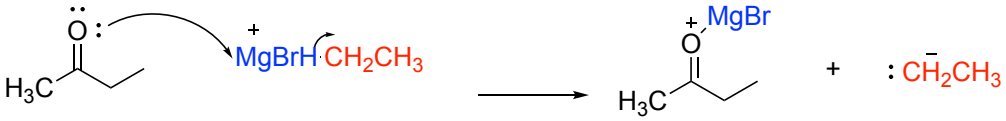


Nucleophilic Addition of Grignard Reagents with a Ketone

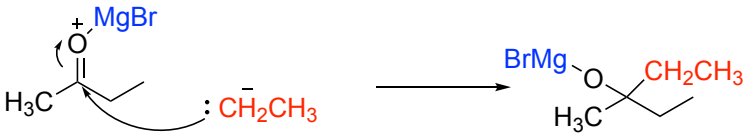
- Note: it will always produce a 3º alcohol
- Overall Reaction:



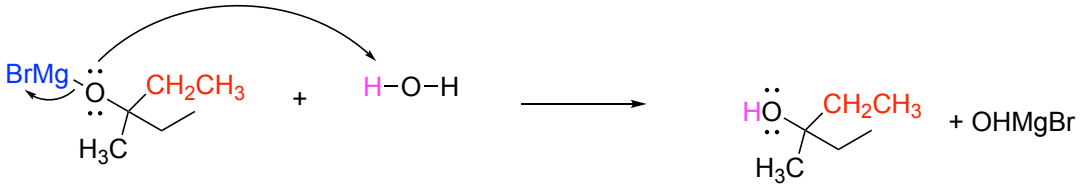
- Step One: Oxygen acts as a Lewis base, forming a acid-base complex with magnesium



- Step Two: Nucleophilic attack by the carbanion



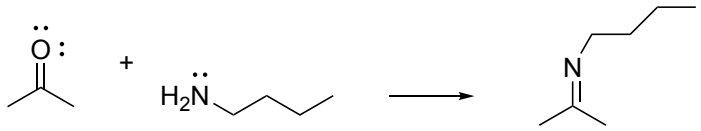
- Step Three: Water removes magnesium alkoxide



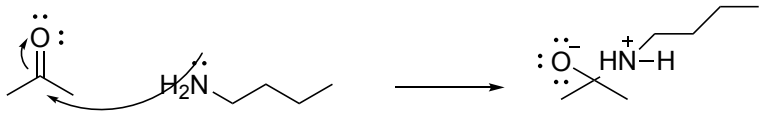
Nucleophilic Addition of Amines

Imine Formation: When you react a carbonyl compound with a primary amine.

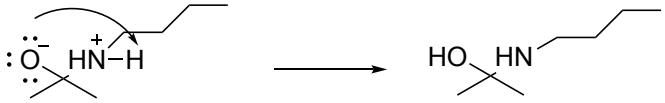
- Overall Reaction:



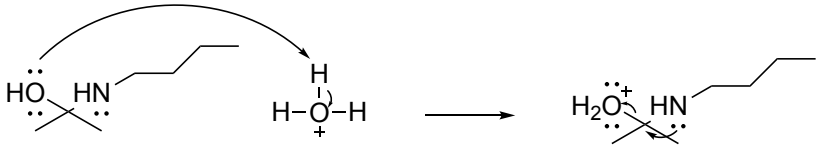
- Step One: Nucleophilic attack on the ketone by the amine



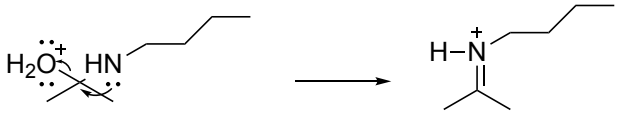
- Step Two: Proton transfer from the amine to the oxygen oxide ion



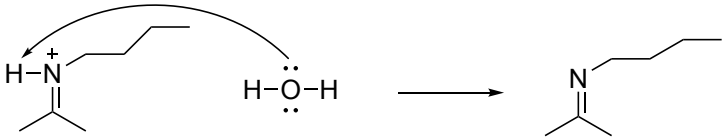
- Step Three: Hydroxyl gets protonated



- Step Four: Water group leaves and the lone pair of nitrogen creates a pi bond

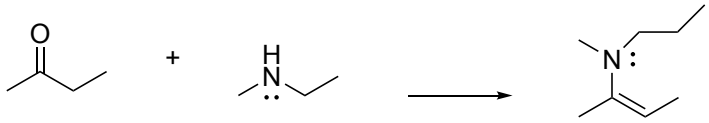


- Step Five: Loss of hydrogen atom by nearby water

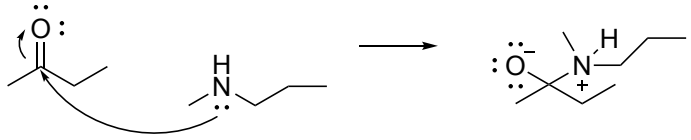


Enamine Formation: When you react a carbonyl compound with a secondary amine.

- Overall Reaction:



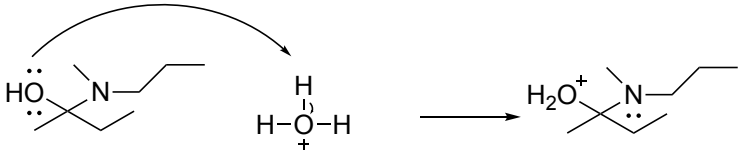
- Step One: Nucleophilic attack on the carbonyl carbon by the amine



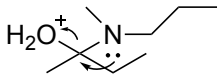
- Step Two: Proton transfer from the amine to the oxyanion



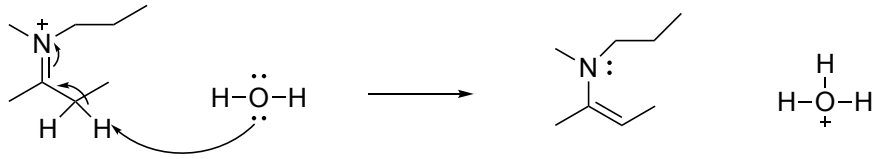
- Step Three: Protonation of the hydroxyl group



- Step Four: Water leaves, the lone pair of the nitrogen forms a pi bond

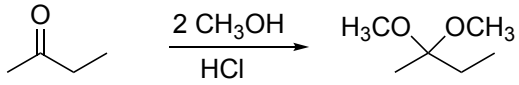


- Step Five: Alpha carbon gets deprotonated; those electrons form a pi bond between the alpha carbon and the carbon bonded to the nitrogen. The pi bond from the nitrogen, becomes lone pairs on the nitrogen.

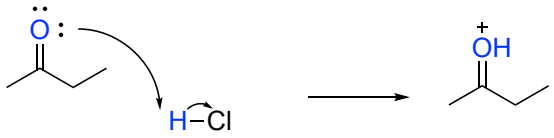


Acetal Formation

- When either an alcohol gets added ketone or aldehyde in acidic conditions
  - Note: If the conditions are basic a hemiacetal will form
- Overall Reaction:



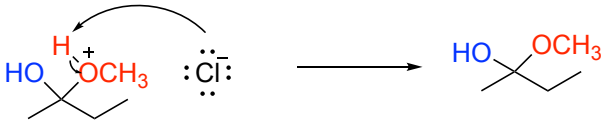
- Step One: Protonation of the oxygen



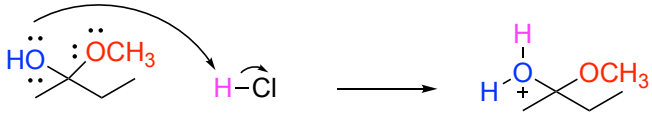
- Step Two: Nucleophilic attack of the carbonyl carbon by the alcohol



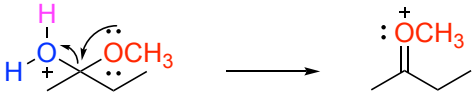
- Step Three: Deprotonation of the alcohol group



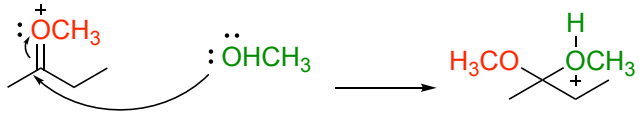
- Step Four: Protonation of the hydroxyl group



- Step Five: Water group leaves, lone pairs from the oxygen forms a pi bond



- Step Six: Alcohol group attacks the carbonyl carbon

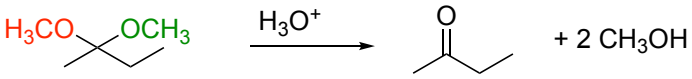


- Deprotonation of the alcohol group

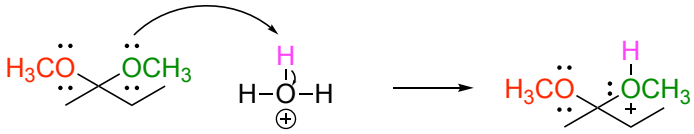


Acetal Hydrolysis

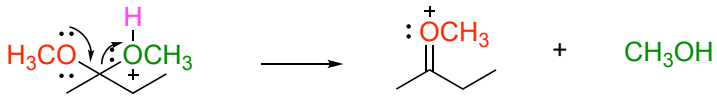
- When an acetal gets broken up into a ketone/ aldehyde and alcohol in acidic conditions
- Overall Reaction:



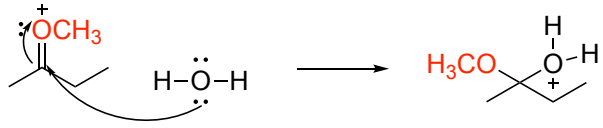
- Step One: Protonation of the oxygen:



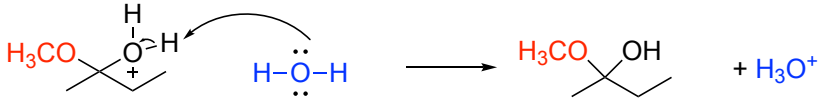
- Step Two: Elimination of the alcohol group, the lone pairs of the oxygen form a pi bond



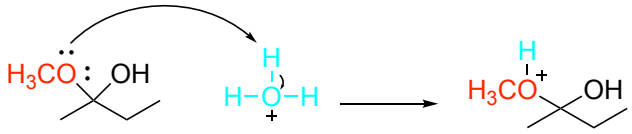
- Step Three: Nucleophilic attack of the carbonyl carbon by water



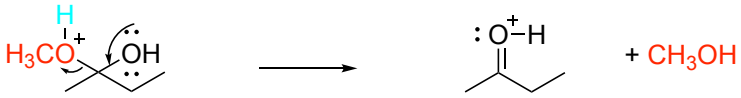
- Step Four: Deprotonation of water



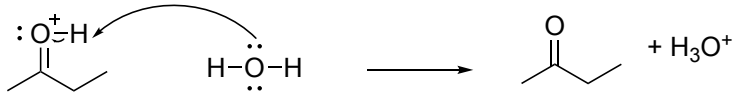
- Step Five: Protonation



- Step Six: Loss of alcohol group, lone pairs from oxygen forms a pi bond

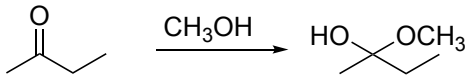


- Step Seven: Deprotonation of alcohol

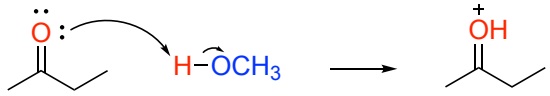


Hemiacetal Formation

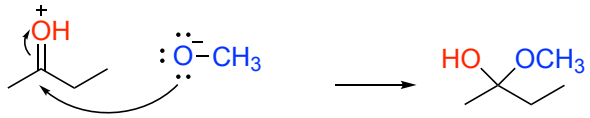
- Notes:
  - Occurs in basic conditions
  - Group: when a carbon is bonded to an alcohol (-OH) and alkoxy group (-OR)
- Overall Reaction:



- Step One: Protonation of oxygen



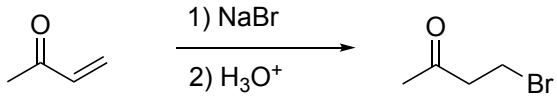
- Step Two: Nucleophilic attack on the carbonyl carbon



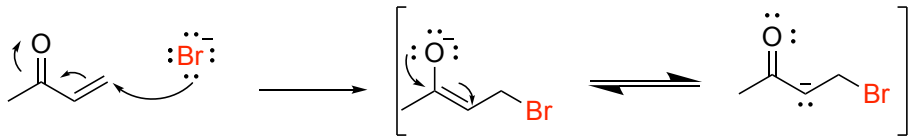
Conjugate Nucleophilic Addition to a,B-Unsaturated Aldehyde/ Ketone: 1,4-addition

Nucleophile Addition

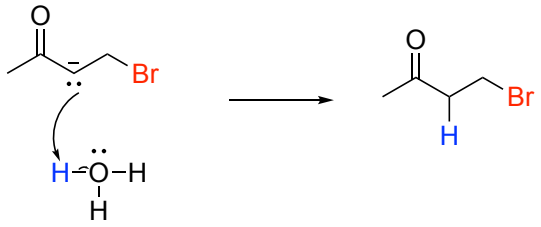
- Overall Reaction:



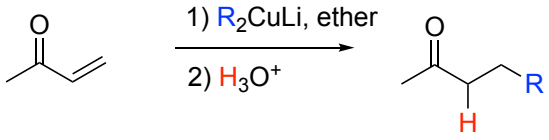
- Step One: Nucleophile Attacks beta carbon leading to a resonance structure



- Step Two: Carbanion gets protonated



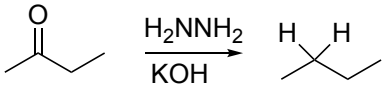
Alkyl group addition by diorganocopper reaction



Other Nucleophilic Addition Reactions of Aldehydes and Ketones

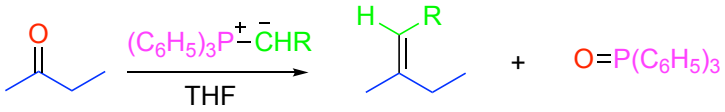
Wolff-Kishner reaction

- Ketone to alkane



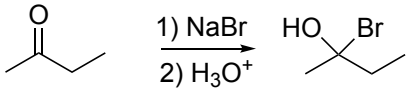
Wittig Reaction

- Addition of phosphorus ylides to give alkenes

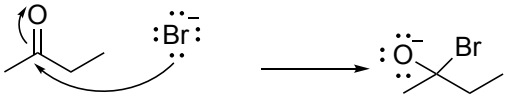


Direct 1,2-addition to Aldehyde/ Ketone

- Overall Reaction:



- Step One: Nucleophile (in this case bromide ion) attacks the carbonyl carbon



- Step Two: Protonation of the alkoxide via acidic workup

