

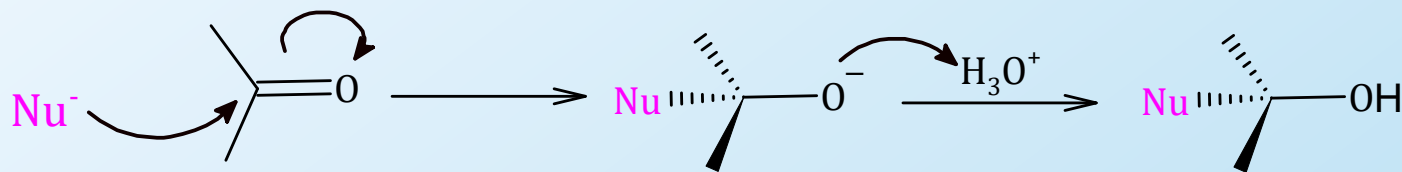
**Aldehydes and Ketones**  
**4 – Carbon, Nitrogen and  
Hydrogen Nucleophiles and  
Oxidation Reactions**

*Dr. Sapna Gupta*

# Reactions of Aldehydes and Ketones

Aldehyde and ketones will undergo nucleophilic addition reactions.

- A strong nucleophile attacks the carbonyl carbon, forming an alkoxide ion that is then protonated to form an alcohol.
- A weak nucleophile will attack a carbonyl if it has been protonated, thus increasing its reactivity.
- Aldehydes are more reactive than ketones. (WHY?)
- Also note that after the addition reaction, a  $sp^2$  carbon is converted to  $sp^3$ , a tetrahedral geometry. This can lead to formation of a chiral center depending on the groups around carbonyl.



# Reactions of Aldehydes and Ketones

Different nucleophiles can be used for addition reactions. We will cover them as different types of nucleophiles.

## 1) Nucleophilic addition

### a) Oxygen nucleophile

- i. Addition of water
- ii. Addition of alcohol

### b) Carbon nucleophile

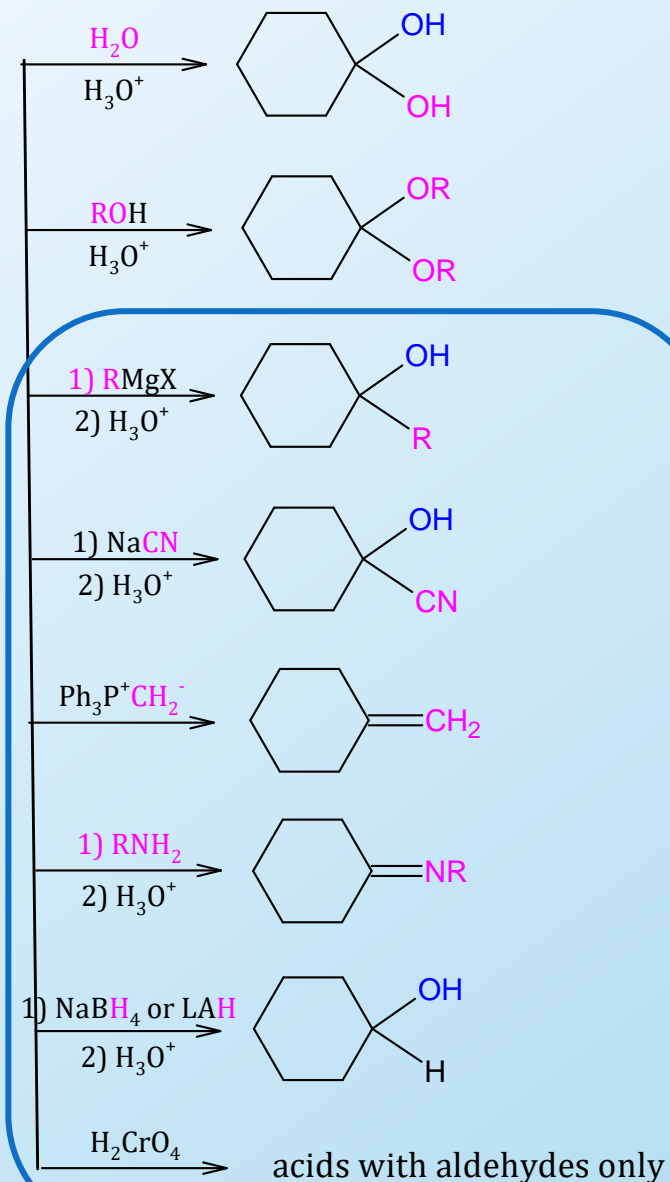
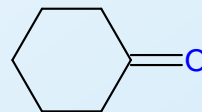
- i. Grignard reaction
- ii. Addition of HCN
- iii. Wittig reaction

### c) Nitrogen nucleophile

## 2) Hydrogen nucleophile - Reduction

## 3) Oxidation

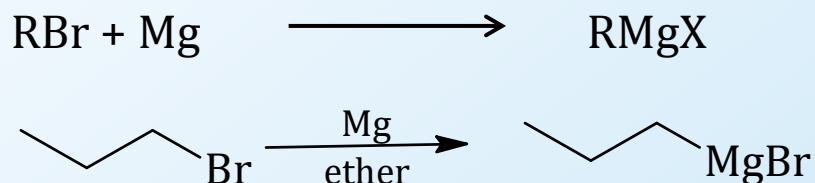
***Oxygen nucleophiles are NOT covered in this power point.***



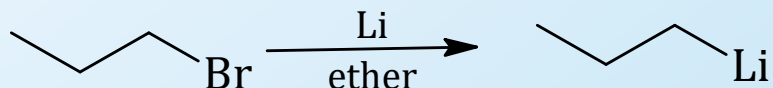
# (C-Nu) - Grignard Reagents

Grignard reagents (GR) are organometallics which make the carbons a strong carbonanion. These nucleophiles help to form C-C bond and an alcohol as product.

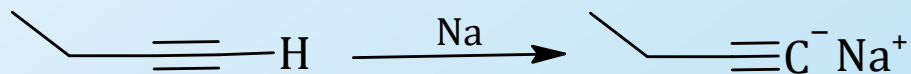
Grignard reagents can be synthesized by using the required alkyl halide with magnesium.



Other organometallics are organolithium reagents, made in similar manner to Grignards.

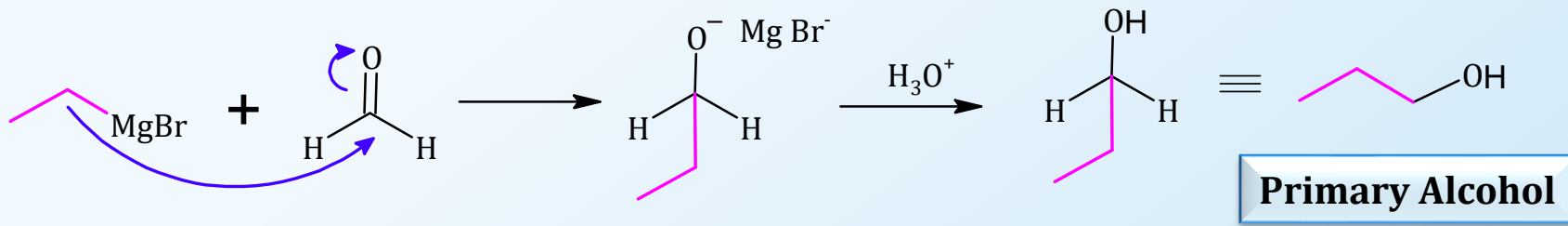


Alkynes can also be treated with  $\text{NaNH}_2$  to generate an alkynide ion which can also then be used as a nucleophile.

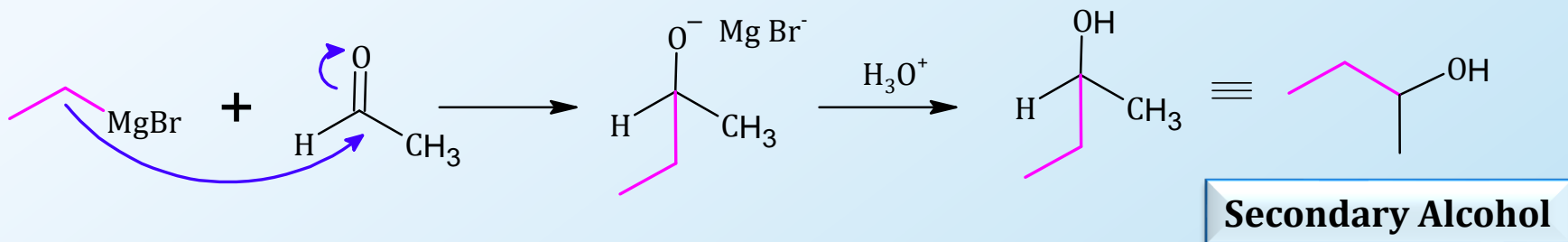


# (C-Nu) - Grignard Reactions

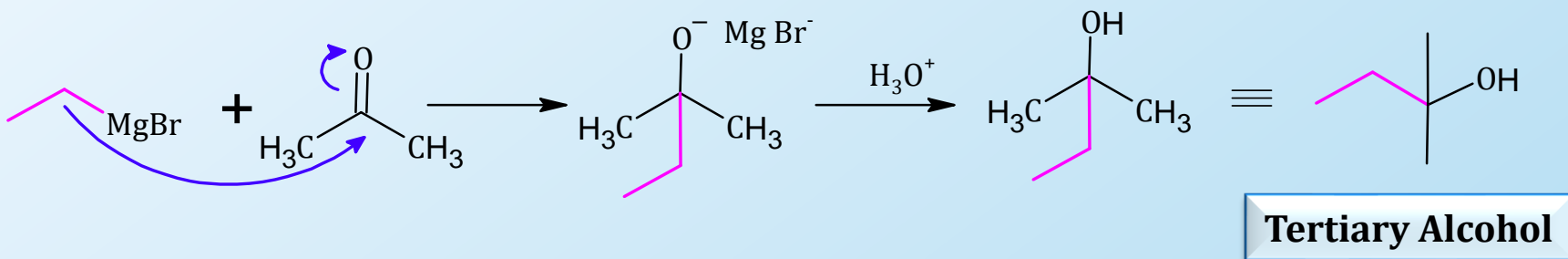
- GR + Formaldehyde gives a 1° alcohol.



- GR + any other RCHO gives a 2° alcohol.

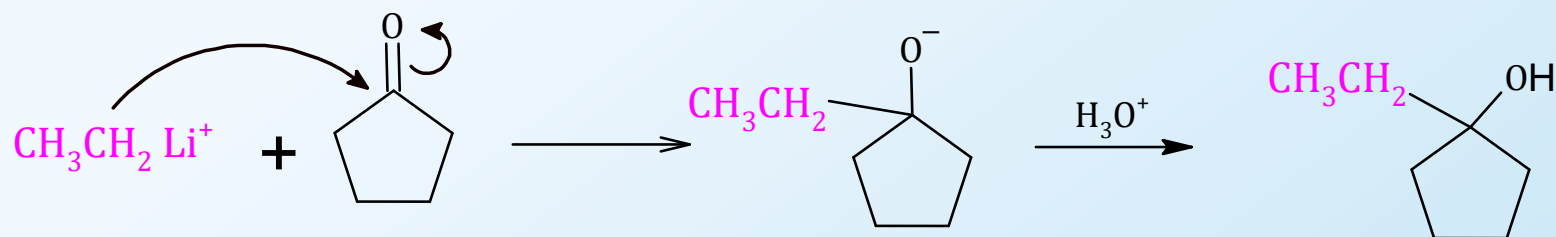


- GR + ketone gives a 3° alcohol.

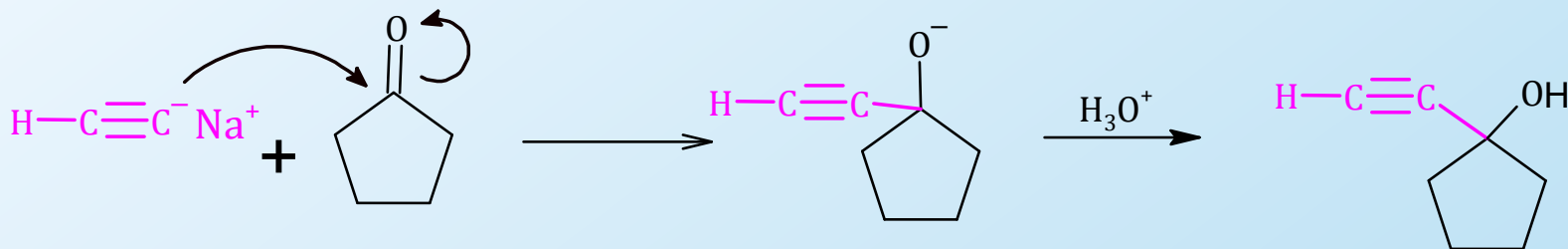


# (C-Nu) - Other Organometallics

**Organolithium Nucleophile:** These organometallics are more reactive in C=O addition reactions than RMgX, and typically give higher yields of product, and the product is still an alcohol. A C-C bond formation occurs just like in Grignard reagent.



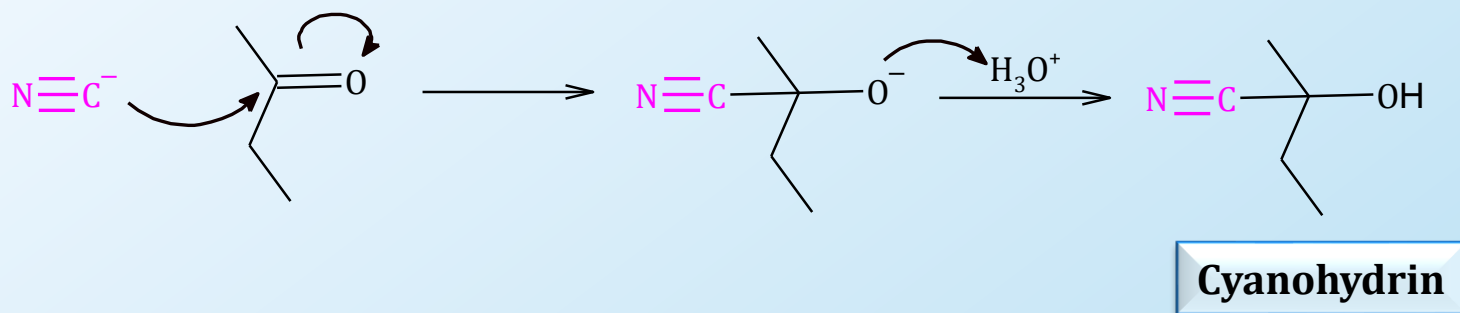
**Alkynide Nucleophile:** Addition of an alkyne anion followed by treatment with  $\text{H}_3\text{O}^+$  gives an  $\alpha$ -acetylenic alcohol.



# (C-Nu) - Addition of CN<sup>-</sup>

NaCN or KCN is used to add a cyanide group to the carbonyl, then protonated to add H to alcohol.

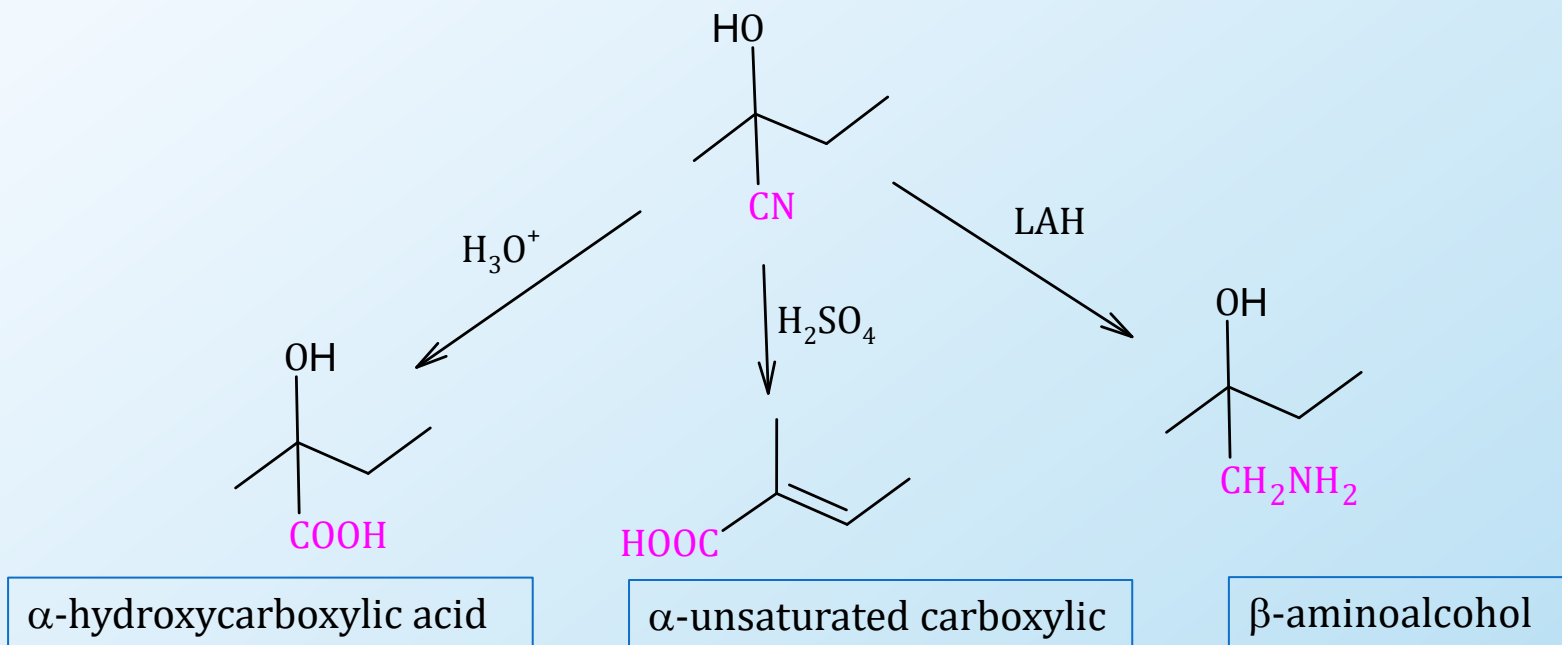
- HCN can also be used but it is more toxic.
- Reactivity formaldehyde > aldehydes > ketones >> bulky ketones.
- The cyanide group in an organic compound is called “nitrile”. The nitrile group is usually not the final product. They can be transformed into other functional groups, as shown on the next slide.



# (C-Nu) – Transformation of Cyanohydrin

The cyano/nitrile group can be hydrolyzed or reduced to give other functional groups.

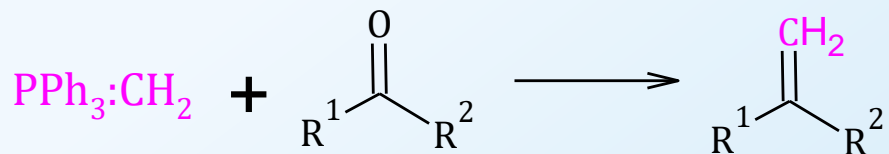
- Hydrolysis of a cyanohydrin produces an  $\alpha$ -hydroxycarboxylic acid.
- Concentrated acid can dehydrate the alcohol to give  $\alpha$ -unsaturated carboxylic acid.
- Reduction of a cyanohydrin produces a  $\beta$ -aminoalcohol.



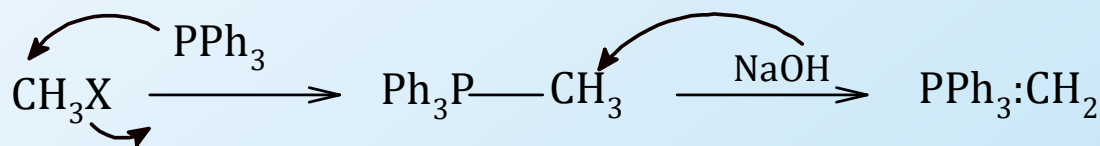


# (C-Nu) - Wittig Reaction

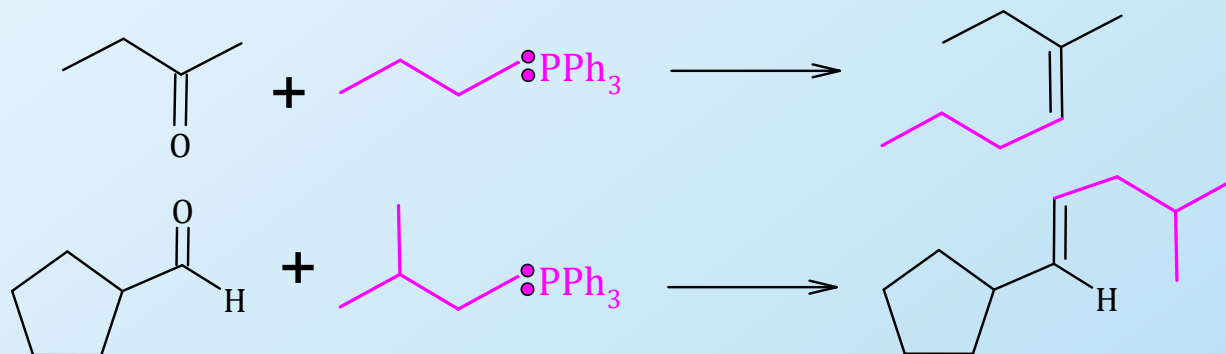
George Wittig created this reaction in which a phosphorous nucleophilic ylide is added to give alkenes. C=O becomes C=C.



Formation of the Ylide: An alkyl halide is treated with a phosphine reagent – triphenyl phosphine or a trialkyl phosphine. The phosphine-alkyl complex is treated with a strong base, NaOH which abstracts a proton and creates the ylide or Wittig reagent. The carbon attached to phosphorous is the nucleophile.

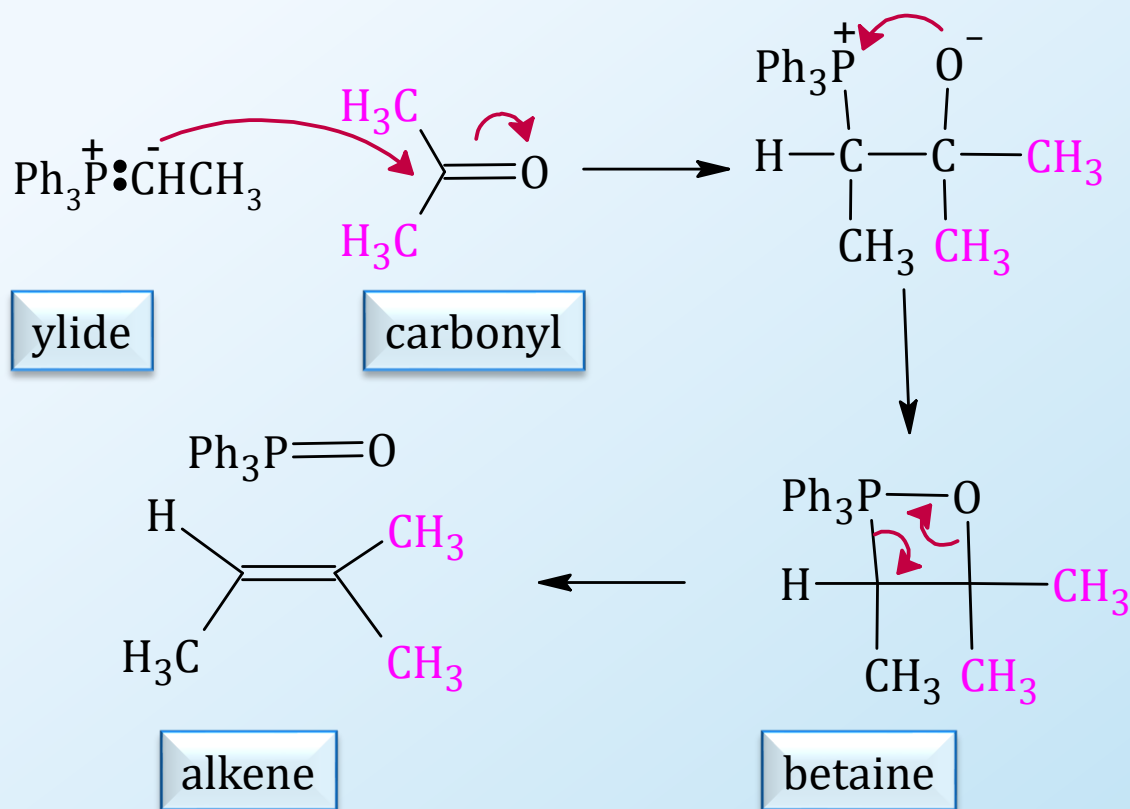


Examples:

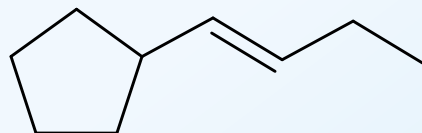


# (C-Nu) - Mechanism of Wittig Reaction

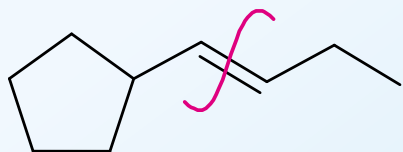
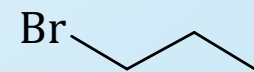
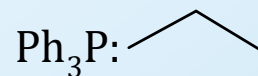
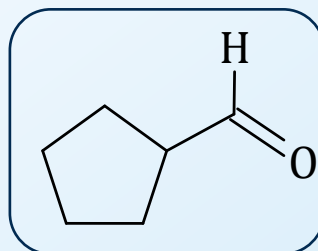
The negative C of ylide attacks the positive C of carbonyl to form a betaine. Note that the C attached to phosphorous has a lone pair of electrons and thus negatively charged. Oxygen combines with phosphine to form the phosphine oxide and alkene.



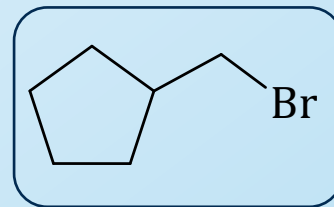
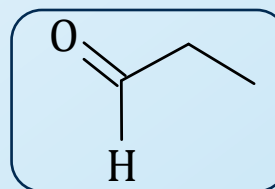
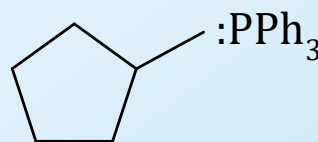
**Worked Example:** Give any carbonyls and alkyl halides needed to make the following alkene.



**Answer 1:**

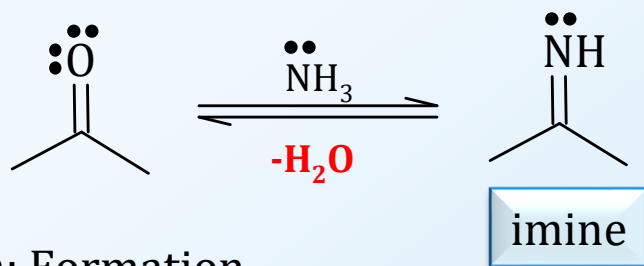


**Answer 2:**



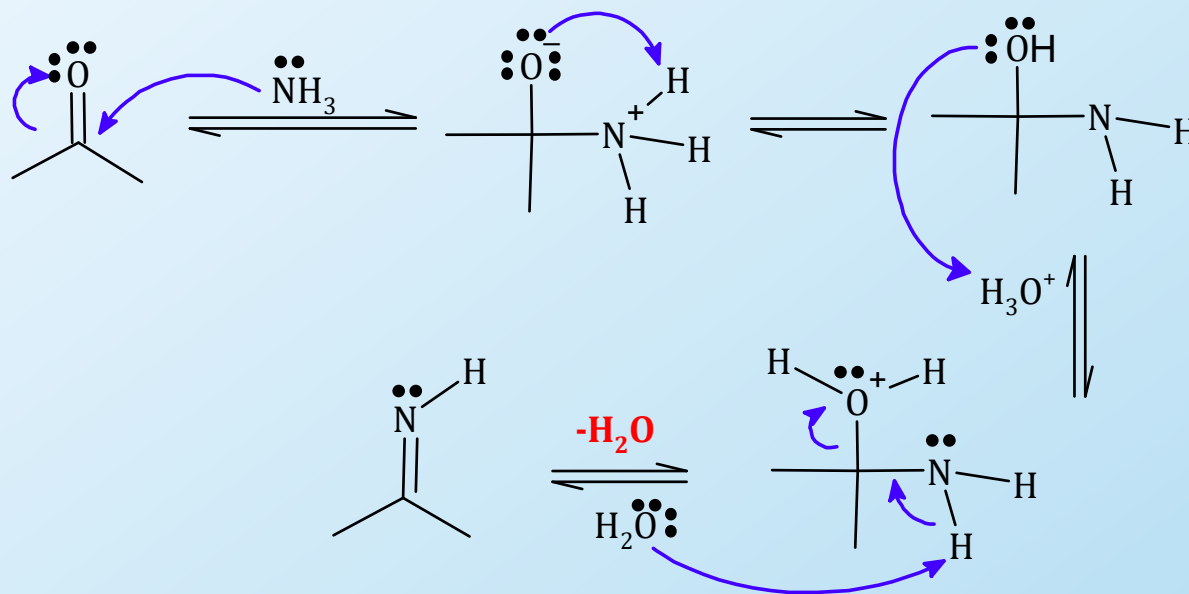
# (N-Nu) - Addition of Ammonia and Amines

Ammonia, 1° aliphatic amines, and 1° aromatic amines react with the C=O group of aldehydes and ketones to give **imines** (Schiff bases).

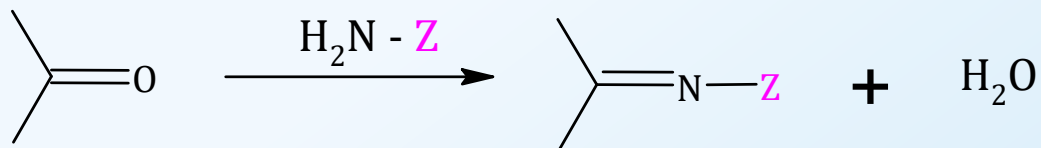


**Mechanism:** Formation of an imine occurs in two steps:

- Step 1: Addition of N group to carbonyl followed by proton transfer.
- Step 2: Loss of  $\text{H}_2\text{O}$  and proton transfer to solvent.



# (N-Nu) - Other Ammonia Derivatives

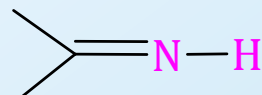
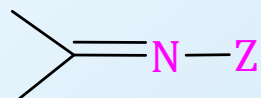


Z in H<sub>2</sub>N - Z

—H

H<sub>2</sub>N—H

Ammonia

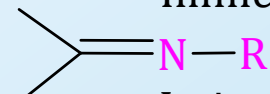


Imine

—R

H<sub>2</sub>N—R

Primary amine

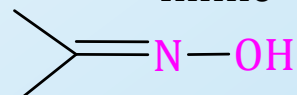


Imine

—OH

H<sub>2</sub>N—OH

Hydroxyl amine

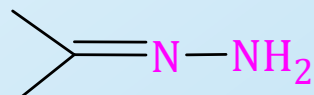


Oxime

—NH<sub>2</sub>

H<sub>2</sub>N—NH<sub>2</sub>

Hydrazine

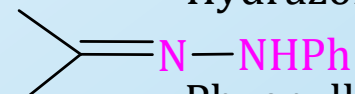


Hydrazone

—NHPh

H<sub>2</sub>N—NHPh

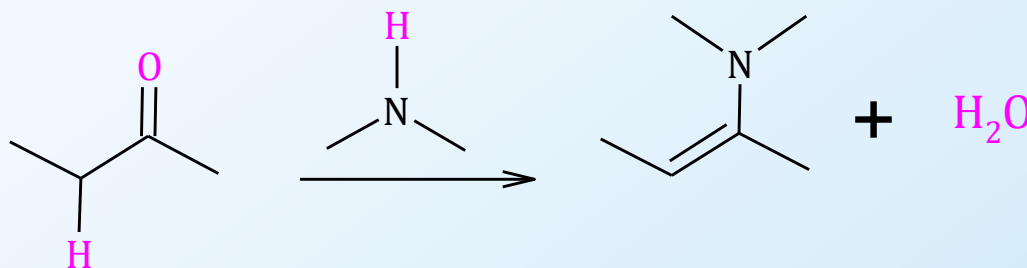
Phenylhydrazine



Phenylylhydrazone

# (N-Nu) - Reactions with Secondary Amines

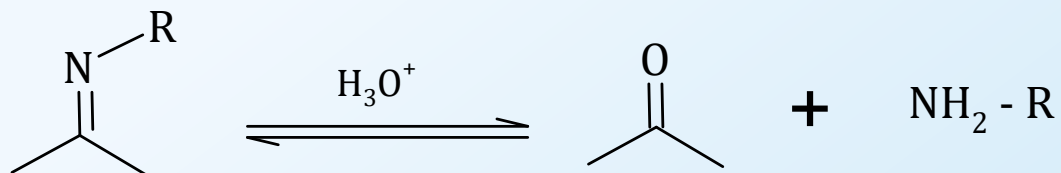
Secondary amines react with the C=O group of aldehydes and ketones to form enamines.



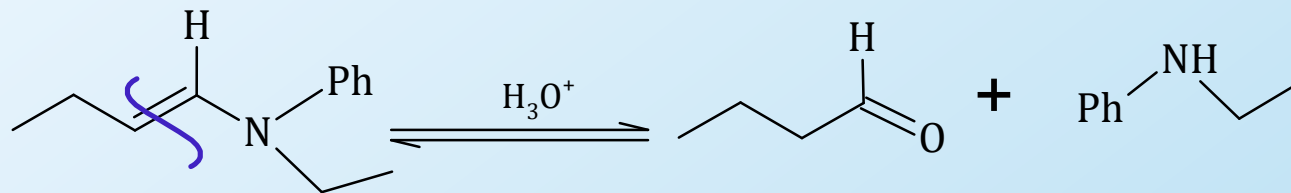
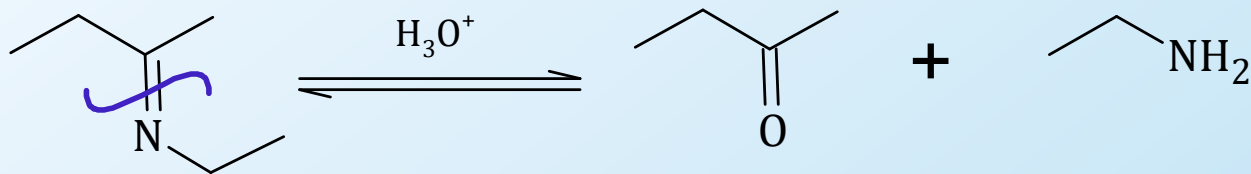
The mechanism of enamine formation involves formation of a tetrahedral carbonyl addition compound followed by its acid-catalyzed dehydration. The more stable alkene, Zaitsev's product, is formed.

# (N-Nu) – Hydrolysis of Imines

Formation of imines is a mechanism in equilibrium so hydrolysis of imine can give the amine and carbonyl.

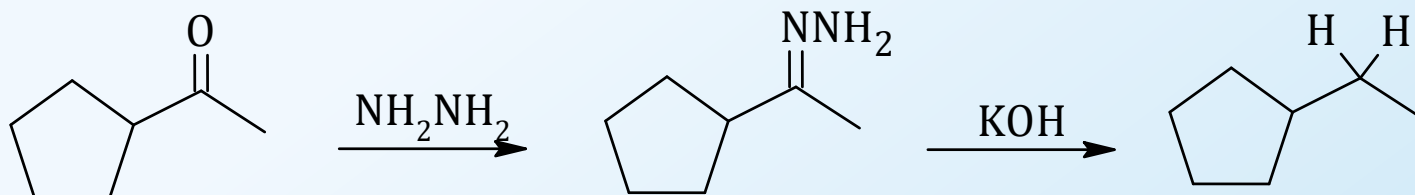


Examples:

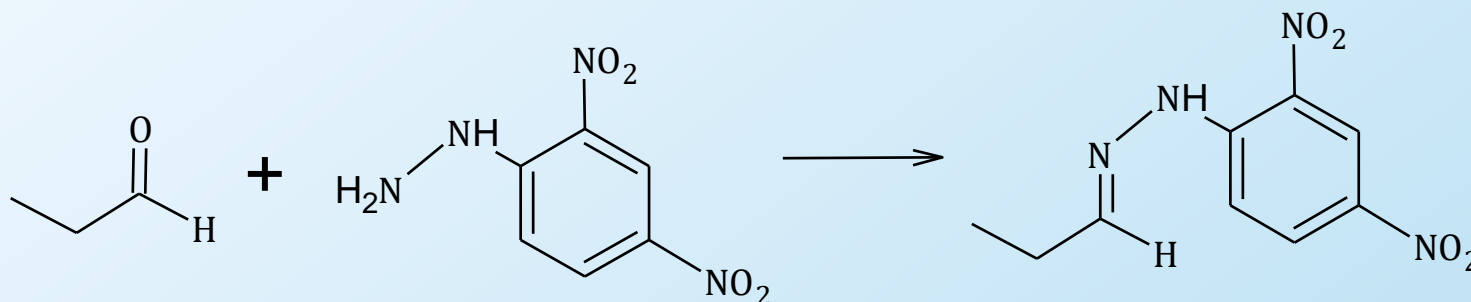


# (N-Nu) - Specific Reactions of Amines

**Wolf Kishner Reduction:** Reaction with hydrazine followed by reaction with KOH reduces the aldehydes and ketone to methylene.



**Qualitative Test:** The reaction of carbonyl with 2,4-dinitrophenyl hydrazine is used as a qualitative test. The product is usually a solid and a stable compound (and orange!) and is used to identify an aldehyde or ketone.

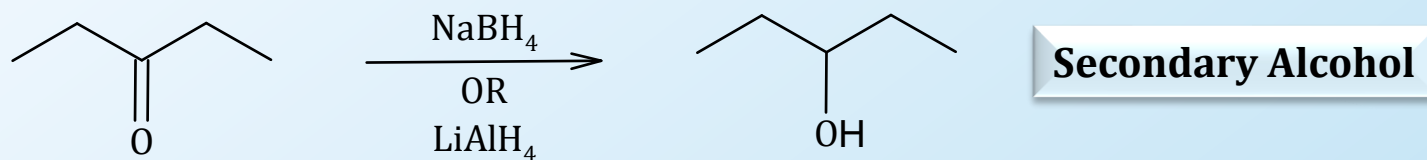
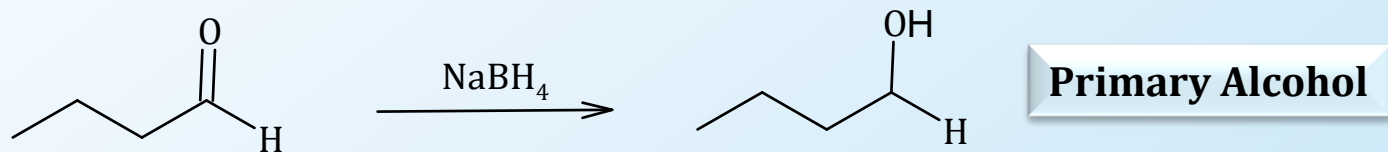




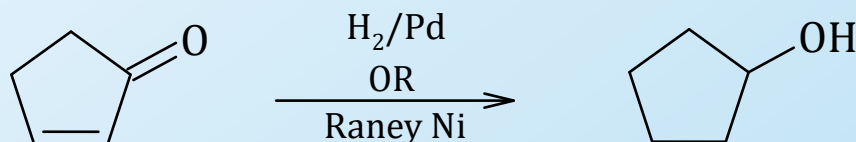
# (H-Nu) Reduction – Aldehydes and Ketones

Aldehydes and ketones can be reduced using a weak ( $\text{NaBH}_4$ ) or strong reducing agent ( $\text{LiAlH}_4$ ) to form alcohols. Aldehydes give primary alcohols while ketones give secondary alcohol.

Sodium borohydride and Lithium aluminum hydride can both reduce  $\text{C}=\text{O}$ , but not  $\text{C}=\text{C}$ . LAH is much stronger, difficult to handle.

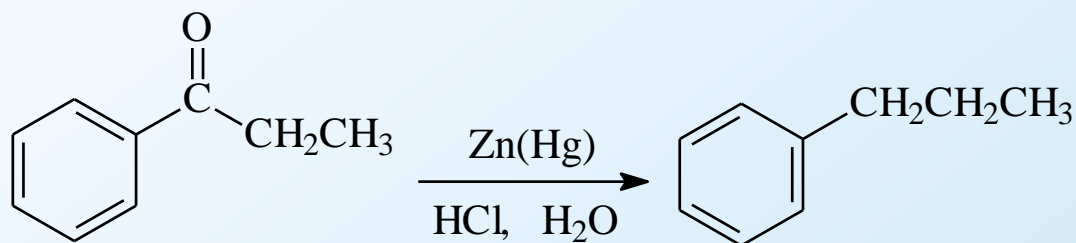


**Catalytic Hydrogenation**: Hydrogenation with catalyst ( $\text{H}_2/\text{Pt}$ ) and Raney Ni can reduce both the  $\text{C}=\text{O}$  and the  $\text{C}=\text{C}$  bond.

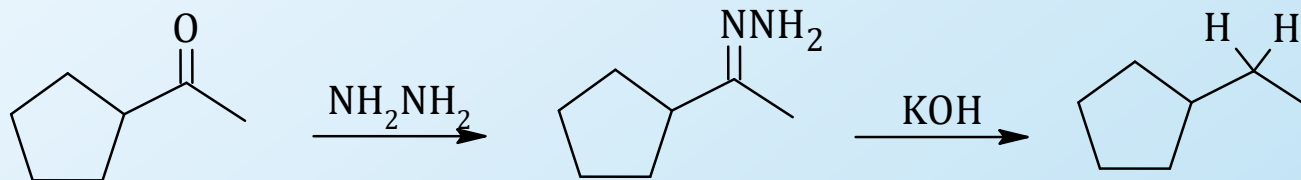


# Reduction - Carbonyl to Methylene

**Clemmensen reduction**: If molecule is stable in hot acid, then zinc and mercury in concentrated acid can be used to reduce carbonyl to a  $\text{CH}_2$  group.

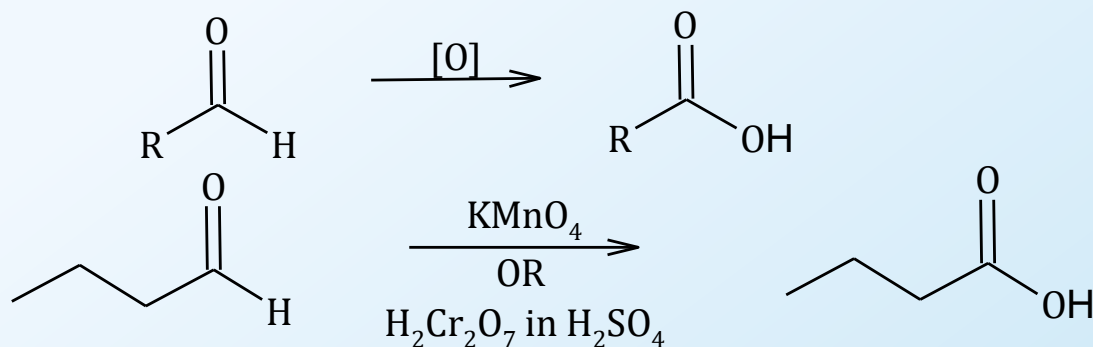


**Wolff-Kishner reduction**: Hydrazine can be used, as we learned in treating a carbonyl with an ammonia derivative to form an imine, followed by treating with KOH to reduce the carbonyl to  $\text{CH}_2$ .



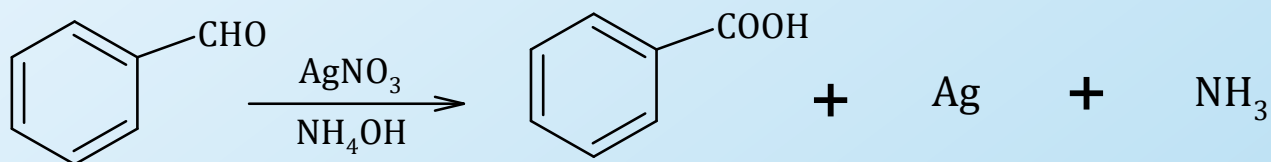
# Oxidation - Aldehydes

Aldehydes are easily oxidized to carboxylic acids. Chromate oxidation can also be used as a **qualitative test** for aldehydes as chromate ion reduces from  $\text{Cr}^{6+}$  (orange color) to  $\text{Cr}^{3+}$  (green color).



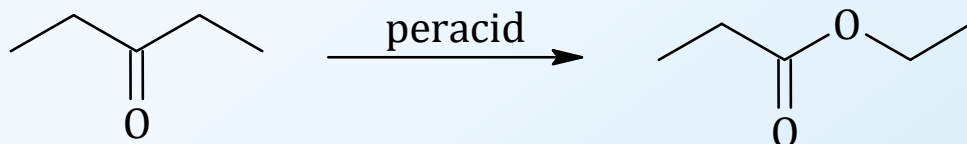
## Oxidation using Ammoniacal Silver - Tollens Test

Aldehydes can be oxidized using silver nitrate in ammonium hydroxide. The silver ion causes aldehyde to oxidize it reduces to silver precipitate. This is also known as the silver mirror test. This is not the ideal way to oxidize aldehydes, but it is a good qualitative test.

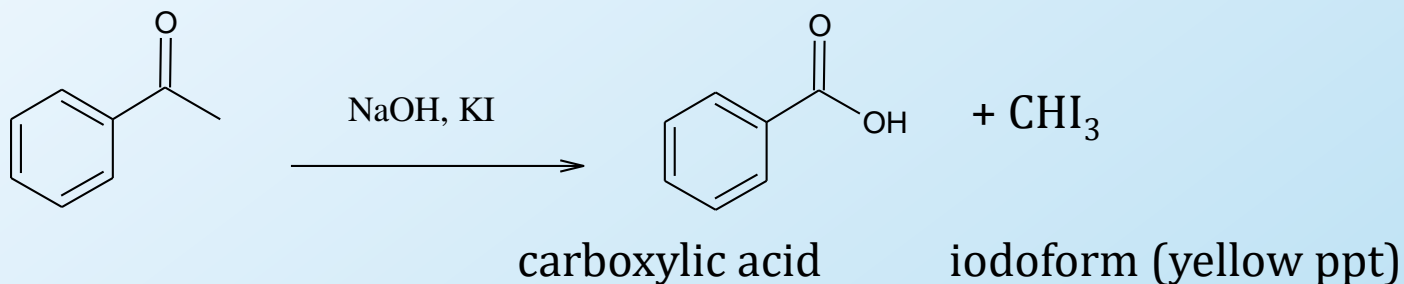


# Oxidation of Ketones

Ketones cannot be oxidized to acids as they are internal groups. A reaction devised by Baeyer and Villiger oxidation can produce esters.



Methyl ketones can be oxidized to form carboxylic acids using potassium iodide in presence of a strong base. One the products formed is iodoform, which is a yellow precipitate. (*We will learn about this reaction in detail in later chapters*). This is not an ideal way to form carboxylic acids, but it is a good qualitative test, called iodoform test, for methyl ketones, e.g., acetone, acetophenone etc.



# Qualitative Tests of Aldehydes and Ketones

## **Dinitrophenyl Hydrazine (DNP) Test for Aldehydes and Ketones:**

When an aldehyde or ketone is added to 2,4-dinitrophenyl hydrazine the product is usually an orange precipitate.

## **Tollens Test for Aldehydes**

This test is specific for aldehydes. Ammonia solution is added to  $\text{AgNO}_3$  until precipitate dissolves. When an aldehyde is added to it, the result is a silver mirror from the precipitating silver. This is also known as the silver mirror test.

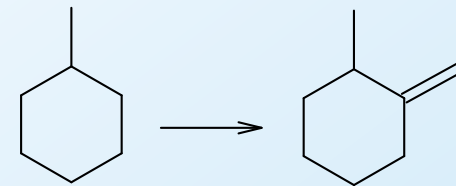
## **Chromic Acid Oxidation Test for Aldehydes**

Aldehydes will oxidize to give acids using chromic acid. As the aldehyde oxidizes, the chromate ion reduces from  $\text{Cr}^{6+}$  (orange color) to  $\text{Cr}^{3+}$  (green color).

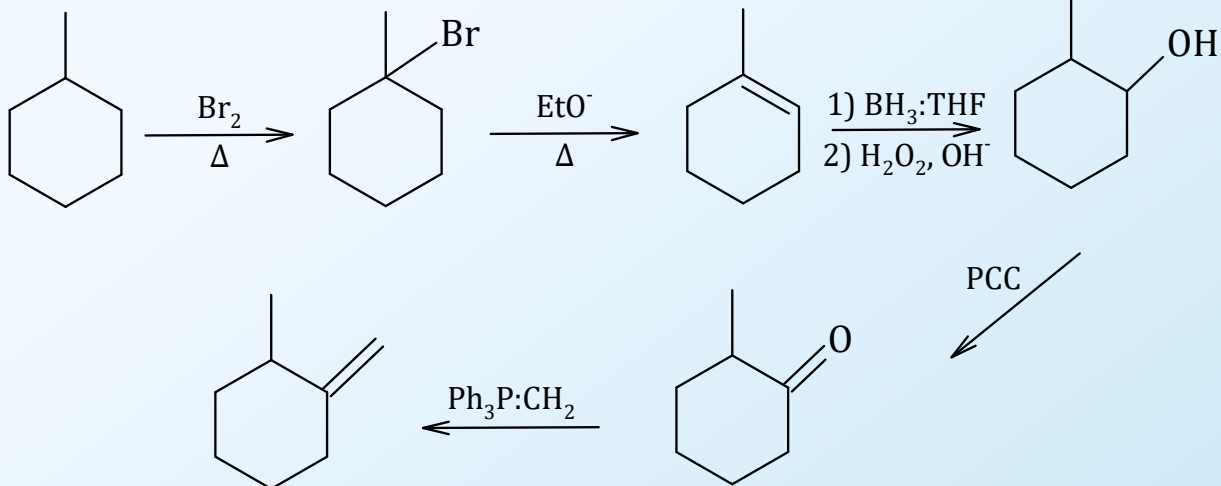
## **Iodoform Test for Methyl Ketones:** Iodoform Test

Methyl ketones oxidize to carboxylic acids with  $\text{NaOH}$  and  $\text{KI}$  and give the precipitate of  $\text{CHI}_3$ , iodoform as one of the products.

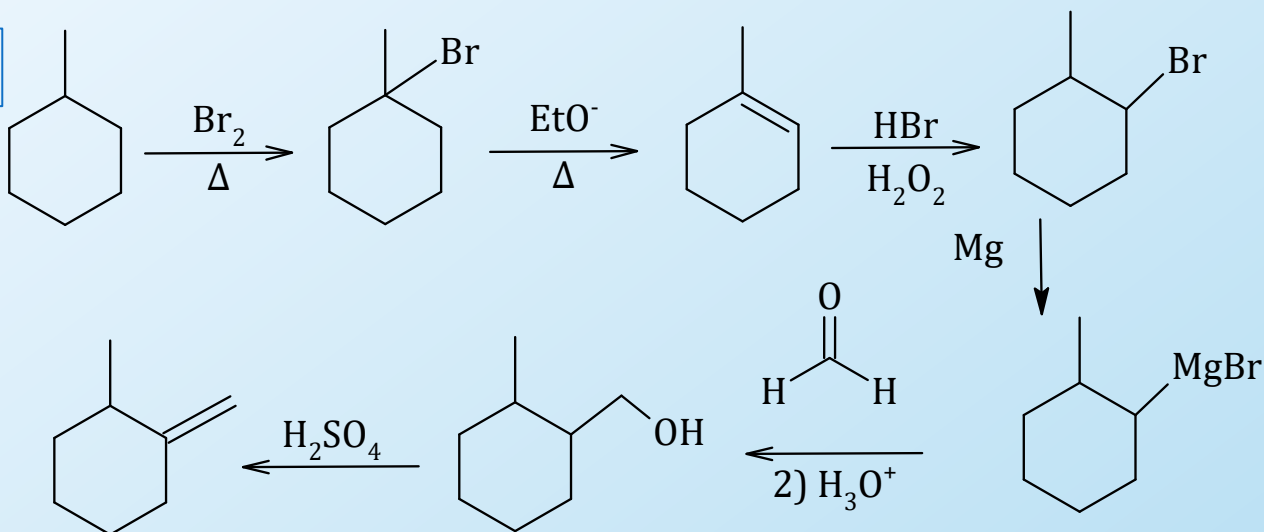
**Solved Example:** Carry out the following transformation using the reactions you have learned so far.



**One Way**



**Another Way**



# Key Concepts

- 1) Nucleophilic addition
  - a) Carbon nucleophile
    - i. Grignard reaction
    - ii. Addition of HCN
    - iii. Wittig reaction
  - b) Nitrogen nucleophile
- 2) Reduction
- 3) Oxidation
- 4) Qualitative tests