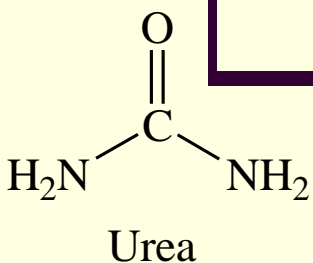




Timberlake, *General, Organic, and Biological Chemistry*. Copyright © Pearson Education Inc., publishing as Benjamin Cummings

# Aldehydes and Ketones

Based on McMurry's *Organic Chemistry*, 7<sup>th</sup> edition  
**Assistant Lecturer:- Jalal Hasan Mohammed**



# Aldehydes and Ketones



- Aldehydes ( $\text{RCHO}$ ) and ketones ( $\text{R}_2\text{CO}$ ) are characterized by the the carbonyl functional group ( $\text{C}=\text{O}$ )
- The compounds occur widely in nature as intermediates in metabolism and biosynthesis

Class	General Formula	Class	General Formula
ketones	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}'$	aldehydes	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{H}$
carboxylic acids	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{OH}$	acid chlorides	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{Cl}$
esters	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{R}'$	amides	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$

# Naming Aldehydes and Ketones

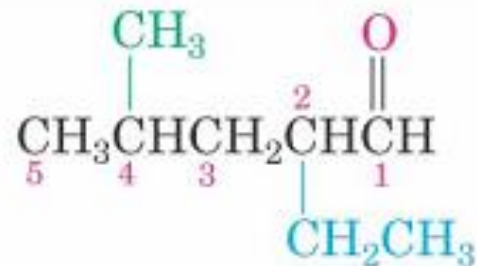
- Aldehydes are named by replacing the terminal *-e* of the corresponding alkane name with *-al*
- The parent chain must contain the  $\text{—CHO}$  group
  - The  $\text{—CHO}$  carbon is numbered as C1
- If the  $\text{—CHO}$  group is attached to a ring, use the suffix carbaldehyde.
- See Table 19.1 for common names



**Ethanal**  
(Acetaldehyde)



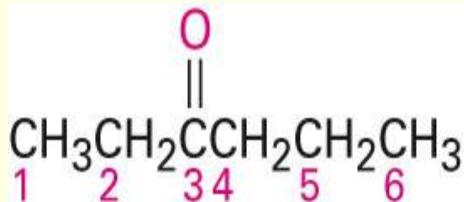
**Propanal**  
(Propionaldehyde)



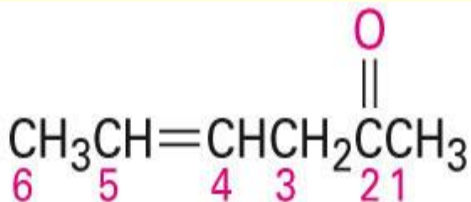
**2-Ethyl-4-methylpentanal**

# Naming Ketones

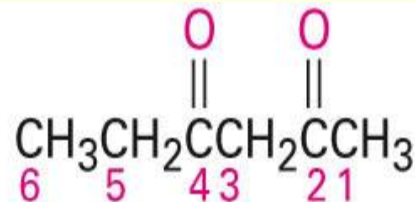
- Replace the terminal *-e* of the alkane name with *-one*
- Parent chain is the longest one that contains the ketone group
  - Numbering begins at the end nearer the carbonyl carbon



**3-Hexanone**  
(New: Hexan-3-one)



**4-Hexen-2-one**  
(New: Hex-4-en-2-one)



**2,4-Hexanedione**  
(New: Hexane-2,4-dione)

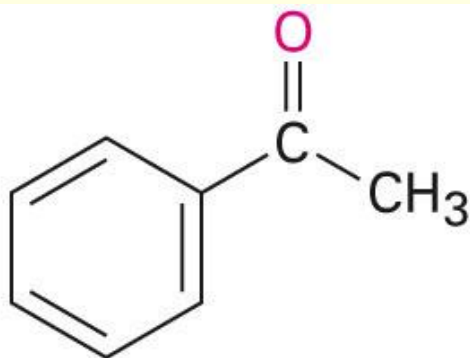
# Ketones with Common Names

- IUPAC retains well-used but unsystematic names for a few ketones

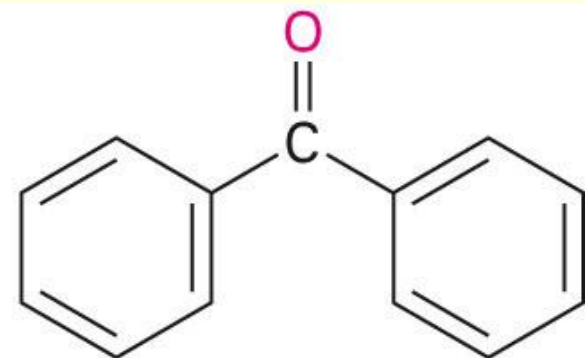


**Acetone**

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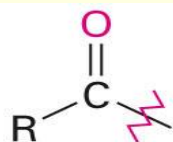
**Acetophenone**



**Benzophenone**

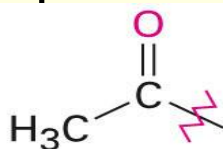
# Ketones and Aldehydes as Substituents

- The R–C=O as a substituent is an acyl group, used with the suffix -yl from the root of the carboxylic acid
  - CH<sub>3</sub>CO: acetyl; CHO: formyl; C<sub>6</sub>H<sub>5</sub>CO: benzoyl
- The prefix *oxo-* is used if other functional groups are present and the doubly bonded oxygen is labeled as a substituent on a parent chain

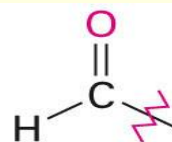


An acyl group

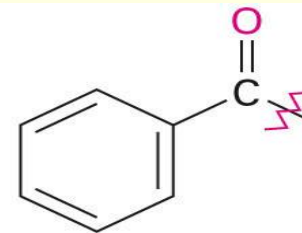
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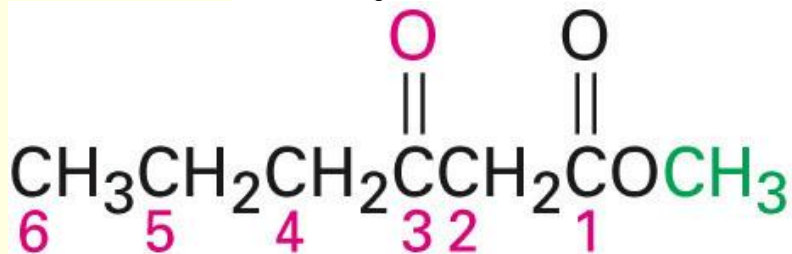
Acetyl



Formyl



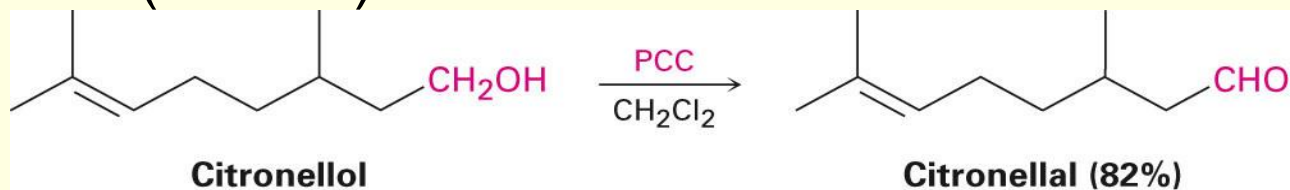
Benzoyl



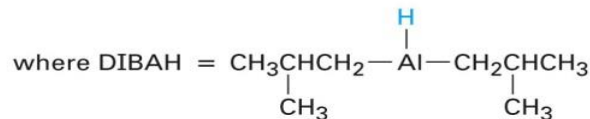
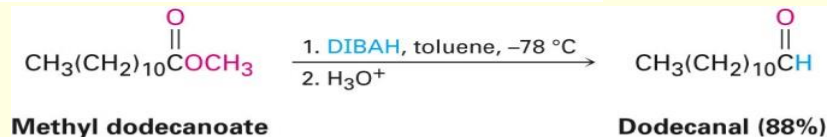
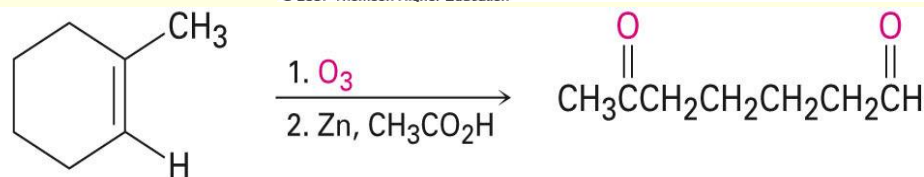
Methyl 3-oxohexanoate

# Preparation of Aldehydes and Ketones

- **Preparing Aldehydes**
- Oxidize primary alcohols using pyridinium chlorochromate
- Alkenes with a vinylic hydrogen can undergo oxidative cleavage when treated with ozone, yielding aldehydes
- Reduce an ester with diisobutylaluminum hydride (DIBAH)

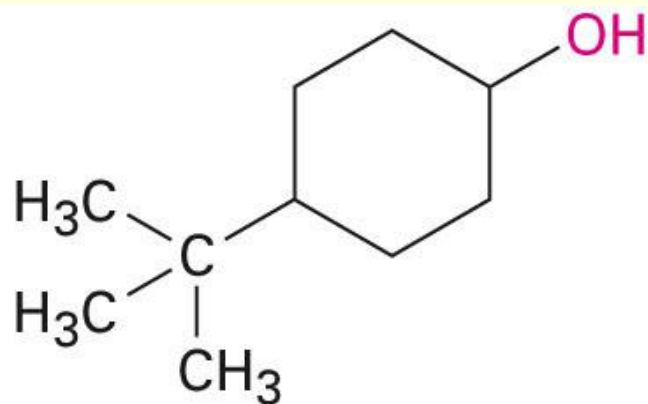


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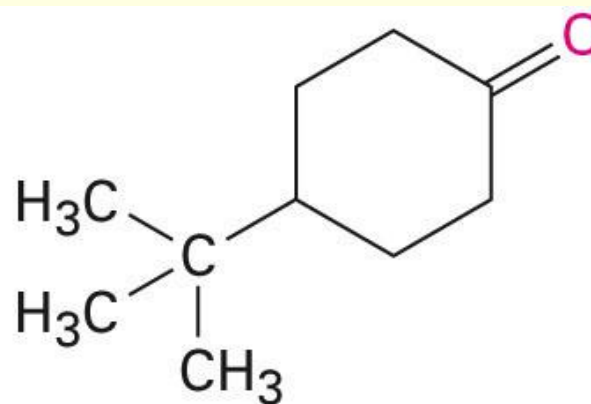
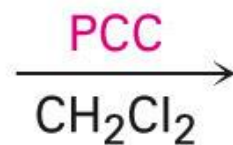


# Preparing Ketones

- Oxidize a 2° alcohol
- Many reagents possible: choose for the specific situation (scale, cost, and acid/base sensitivity)



**4-*tert*-Butylcyclohexanol**

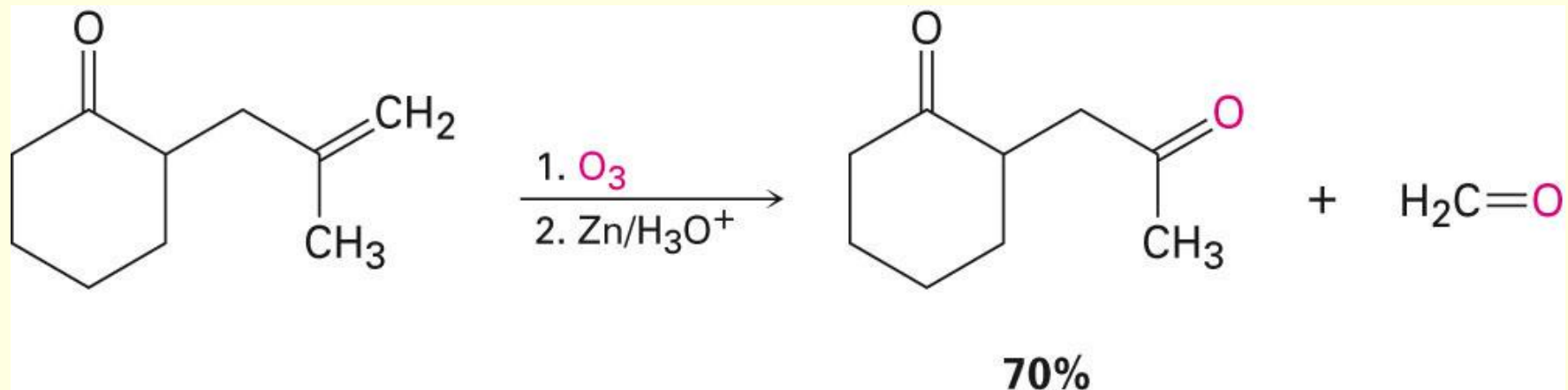


**4-*tert*-Butylcyclohexanone (90%)**



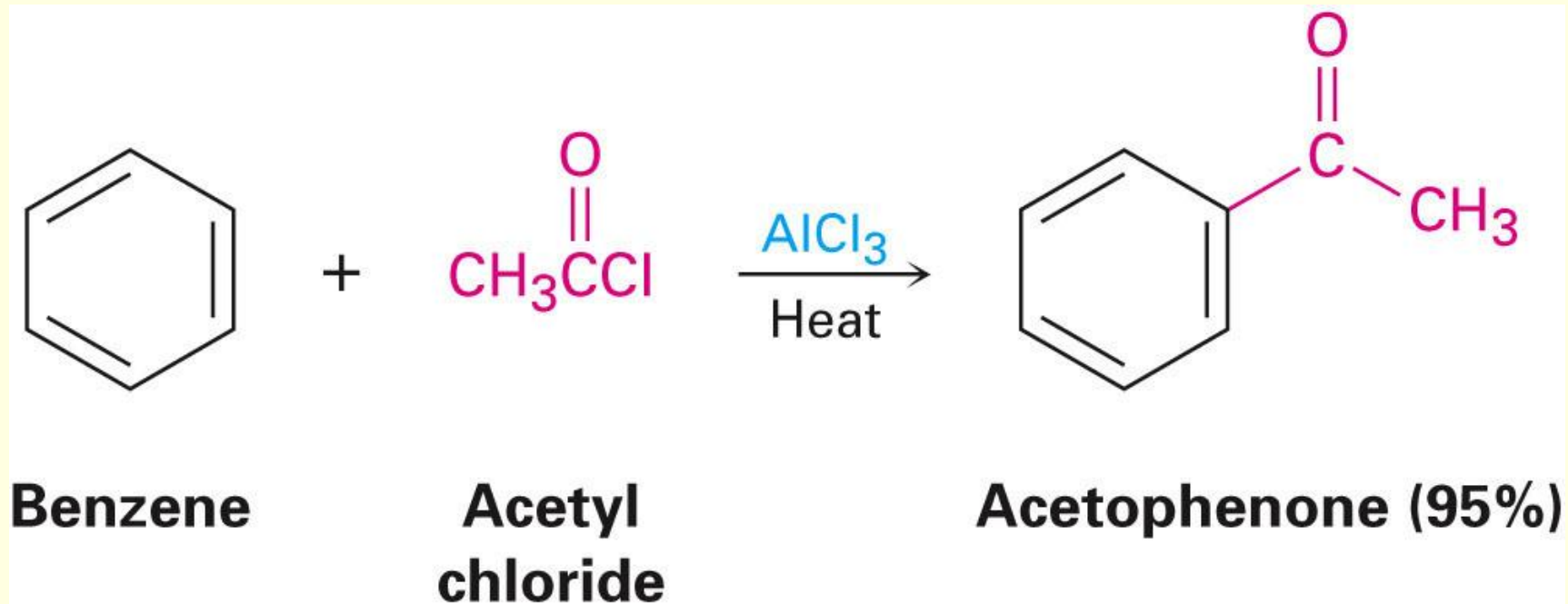
# Ketones from Ozonolysis

- Ozonolysis of alkenes yields ketones if one of the unsaturated carbon atoms is disubstituted



# Aryl Ketones by Acylation

- Friedel–Crafts acylation of an aromatic ring with an acid chloride in the presence of  $\text{AlCl}_3$  catalyst



# Methyl Ketones by Hydrating Alkynes

- Hydration of terminal alkynes in the presence of  $\text{Hg}^{2+}$  (catalyst: Section 8.4)



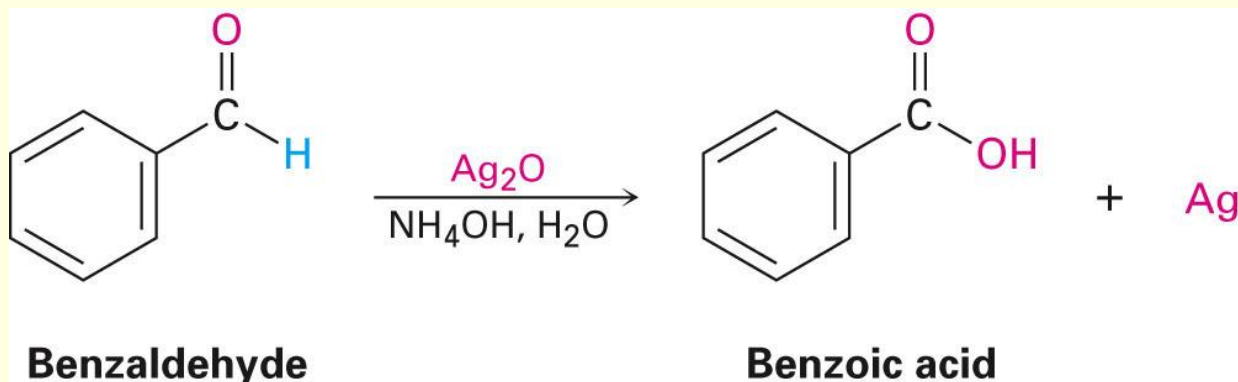
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# Oxidation of Aldehydes and Ketones

- $\text{CrO}_3$  in aqueous acid oxidizes aldehydes to carboxylic acids efficiently
- Silver oxide,  $\text{Ag}_2\text{O}$ , in aqueous ammonia (Tollens' reagent) oxidizes aldehydes (no acid)



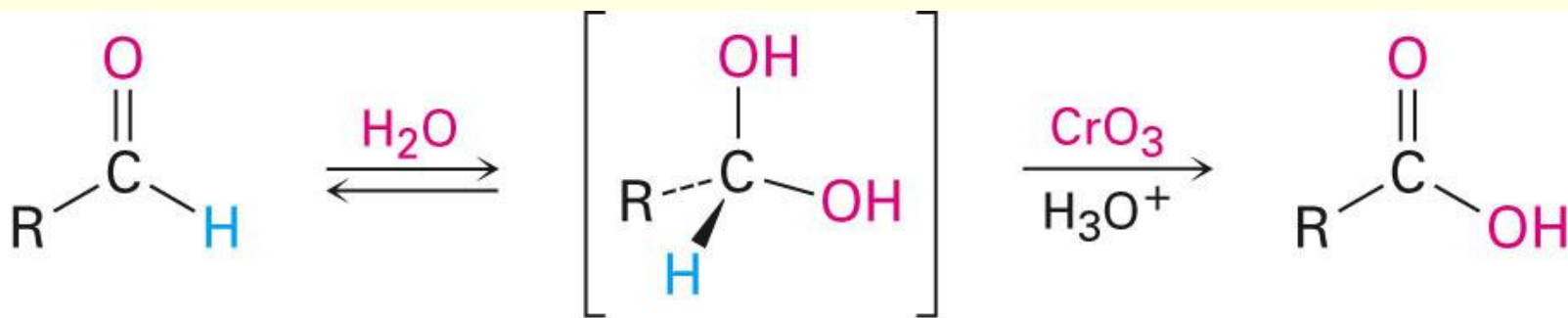
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# Hydration of Aldehydes

- Aldehyde oxidations occur through 1,1-diols (“hydrates”)
- Reversible addition of water to the carbonyl group
- Aldehyde hydrate is oxidized to a carboxylic acid by usual reagents for alcohols



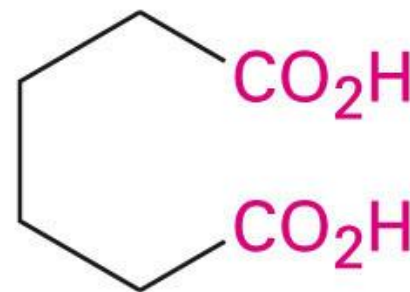
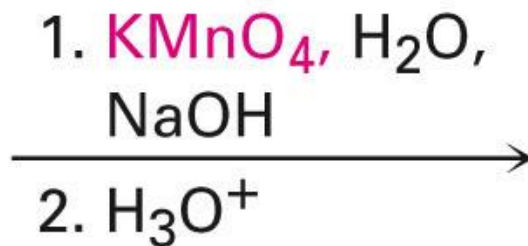
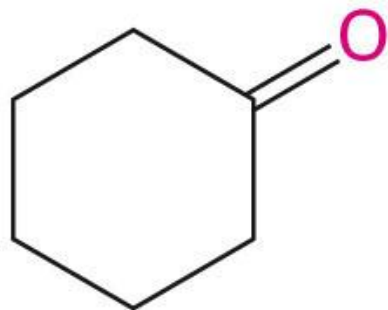
**An aldehyde**

**A hydrate**

**A carboxylic acid**

# Ketones Oxidize with Difficulty

- Undergo slow cleavage with hot, alkaline  $\text{KMnO}_4$
- C–C bond next to  $\text{C}=\text{O}$  is broken to give carboxylic acids
- Reaction is practical for cleaving symmetrical ketones



**Cyclohexanone**

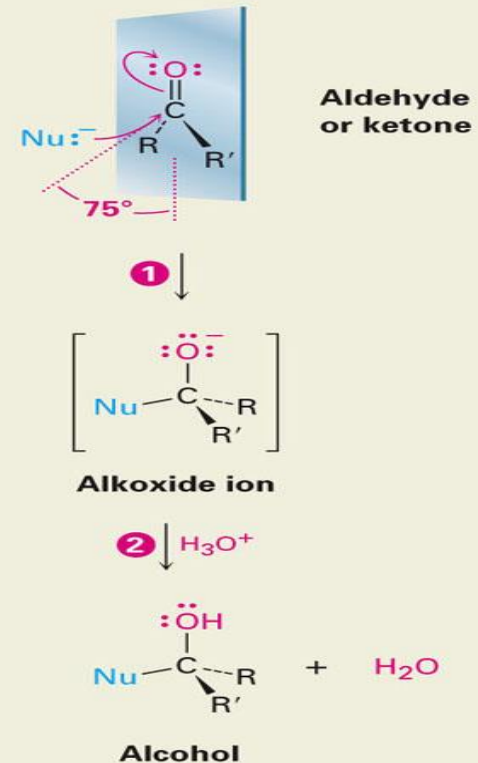
**Hexanedioic acid (79%)**

# Nucleophilic Addition Reactions of Aldehydes and Ketones

- Nu<sup>-</sup> approaches 75° to the plane of C=O and adds to C
- A tetrahedral alkoxide ion intermediate is produced

1 An electron pair from the nucleophile adds to the electrophilic carbon of the carbonyl group, pushing an electron pair from the C=O bond onto oxygen and giving an alkoxide ion intermediate. The carbonyl carbon rehybridizes from  $sp^2$  to  $sp^3$ .

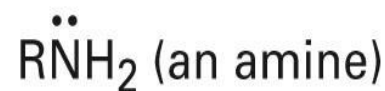
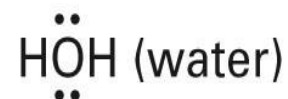
2 Protonation of the alkoxide anion intermediate gives the neutral alcohol addition product.



# Nucleophiles

- Nucleophiles can be negatively charged ( $: \text{Nu}^-$ ) or neutral ( $: \text{Nu}$ ) at the reaction site
- The *overall charge* on the nucleophilic species is not considered

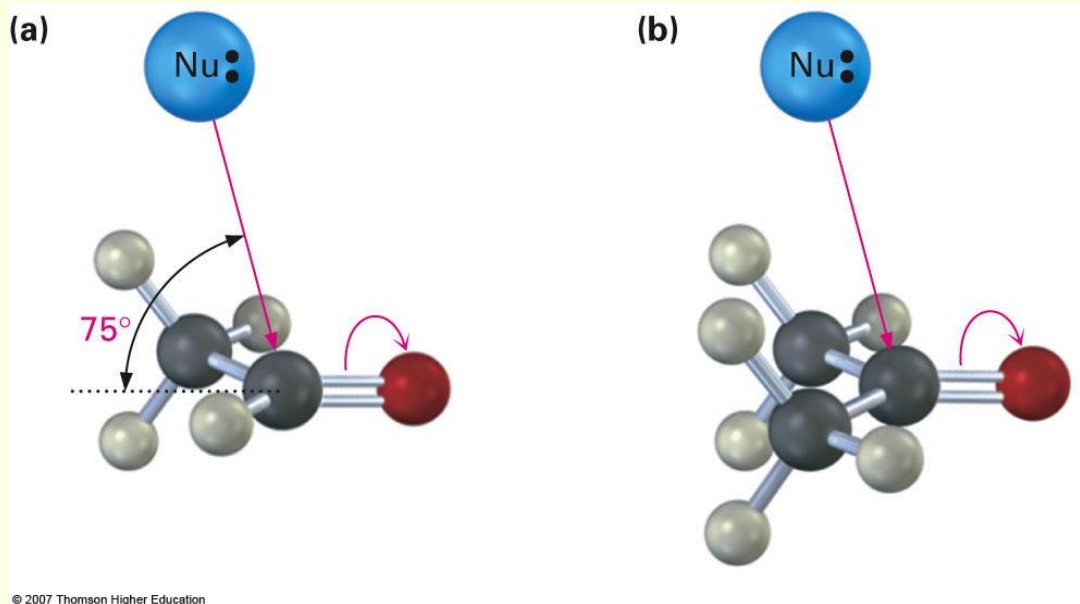
## Some neutral nucleophiles





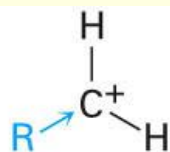
# Relative Reactivity of Aldehydes and Ketones

- Aldehydes are generally more reactive than ketones in nucleophilic addition reactions
- The transition state for addition is less crowded and lower in energy for an aldehyde (a) than for a ketone (b)
- Aldehydes have one large substituent bonded to the C=O: ketones have two

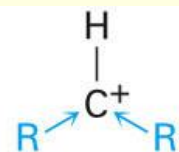


# Electrophilicity of Aldehydes and Ketones

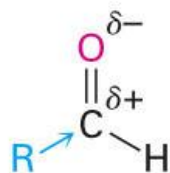
- Aldehyde C=O is more polarized than ketone C=O
- As in carbocations, more alkyl groups stabilize + character
- Ketone has more alkyl groups, stabilizing the C=O carbon inductively



**1° carbocation**  
(less stable, more reactive)



**2° carbocation**  
(more stable, less reactive)



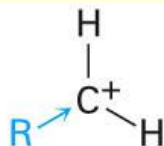
**Aldehyde**  
(less stabilization of  $\delta+$ , more reactive)



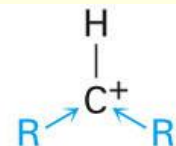
**Ketone**  
(more stabilization of  $\delta+$ , less reactive)

# Reactivity of Aromatic Aldehydes

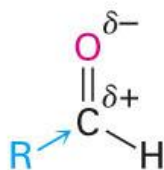
- Less reactive in nucleophilic addition reactions than aliphatic aldehydes
- Electron-donating resonance effect of aromatic ring makes C=O less reactive electrophile than the carbonyl group of an aliphatic aldehyde



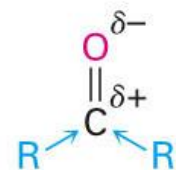
**1° carbocation**  
(less stable, more reactive)



**2° carbocation**  
(more stable, less reactive)



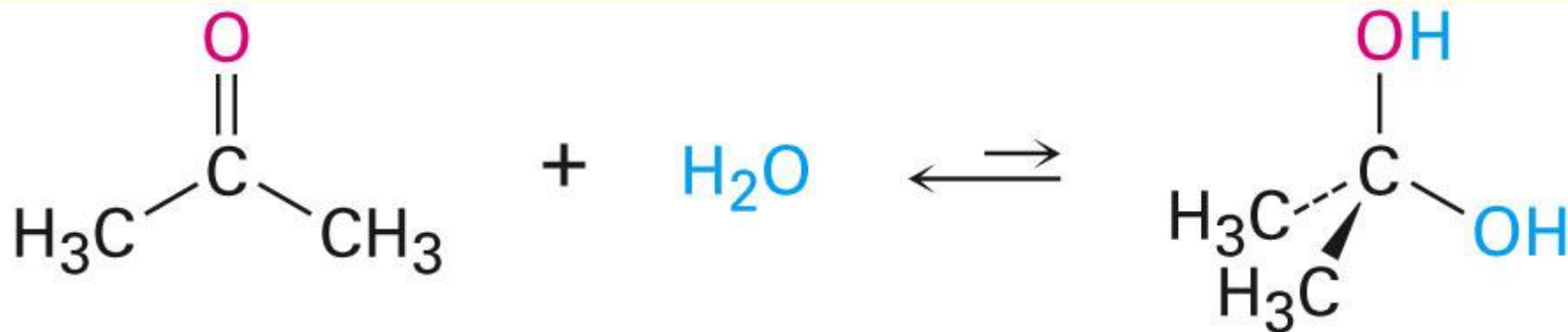
**Aldehyde**  
(less stabilization of  $\delta+$ , more reactive)



**Ketone**  
(more stabilization of  $\delta+$ , less reactive)

# Nucleophilic Addition of H<sub>2</sub>O: Hydration

- Aldehydes and ketones react with water to yield 1,1-diols (**geminal (gem) diols**)
- Hydration is reversible: a gem diol can eliminate water



**Acetone (99.9%)**

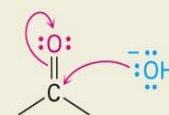
**Acetone hydrate (0.1%)**

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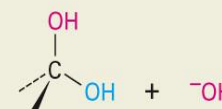
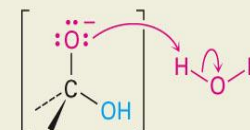
# Base-Catalyzed Addition of Water

- Addition of water is catalyzed by both acid and base
- The base-catalyzed hydration nucleophile is the hydroxide ion, which is a much stronger nucleophile than water

1 The nucleophilic hydroxide ion adds to the aldehyde or ketone and yields a tetrahedral alkoxide ion intermediate.



2 The alkoxide ion is protonated by water to give the gem diol product and regenerate the hydroxide ion catalyst.

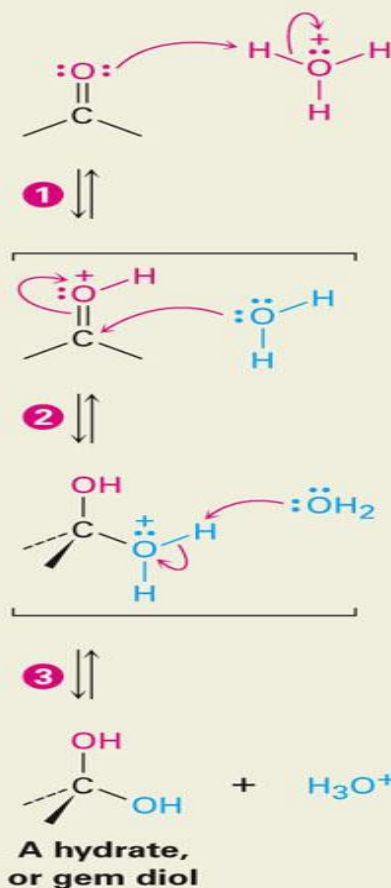


A hydrate,  
or gem diol

# Acid-Catalyzed Addition of Water

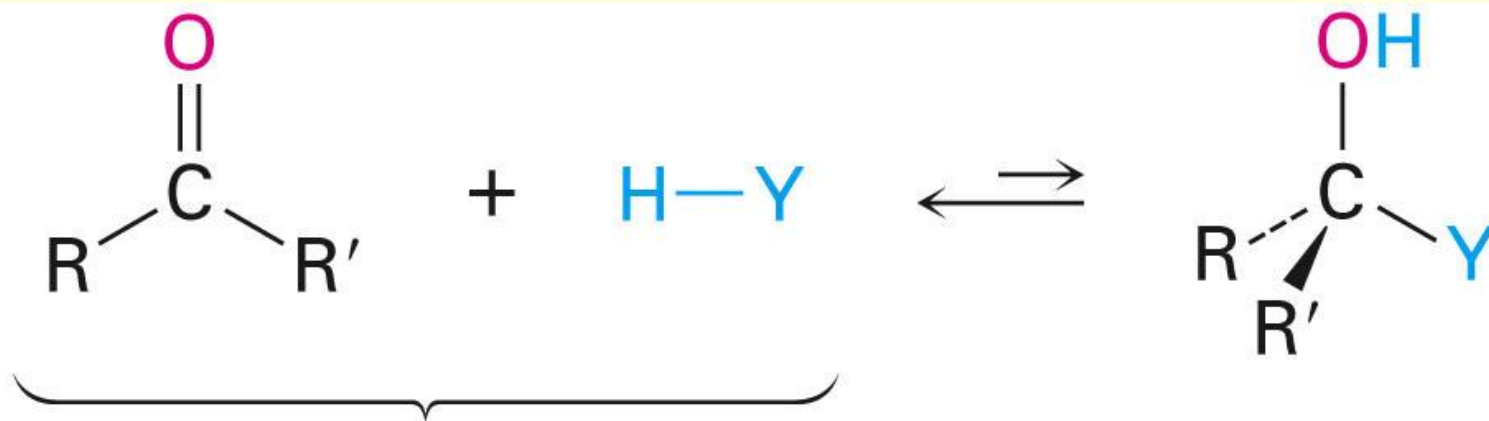
- Protonation of C=O makes it more electrophilic

- 1** Acid catalyst protonates the basic carbonyl oxygen atom, making the aldehyde or ketone a better acceptor for nucleophilic addition.
- 2** Addition of water to the protonated carbonyl compound gives a protonated gem diol intermediate.
- 3** Deprotonation of the intermediate by reaction with water yields the neutral gem diol and regenerates the acid catalyst.



# Addition of H-Y to C=O

- Reaction of C=O with H-Y, where Y is electronegative, gives an addition product (“adduct”)
- Formation is readily reversible

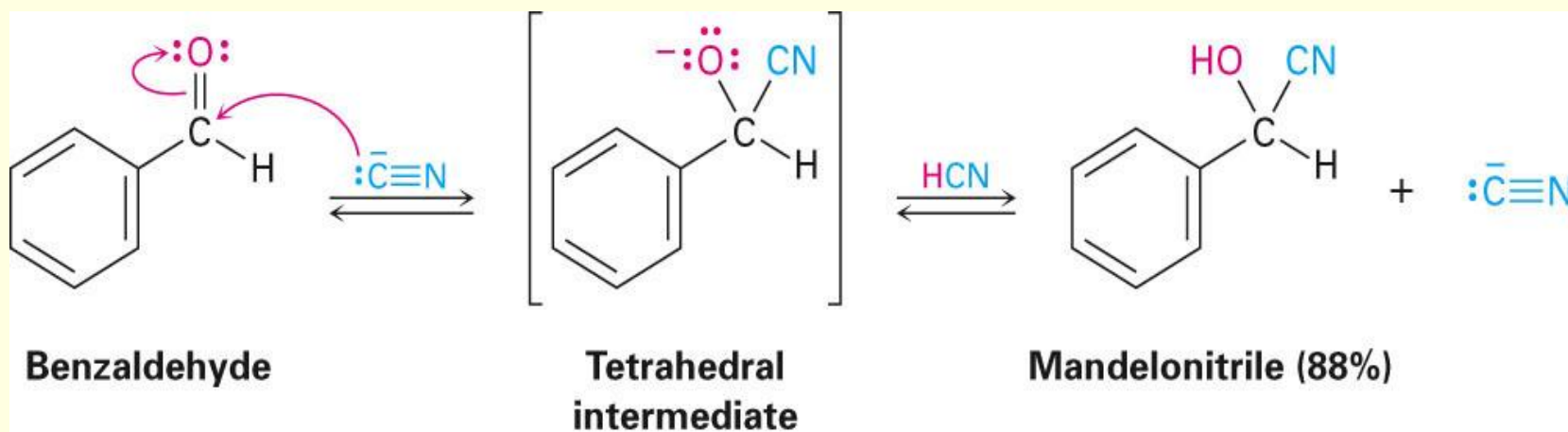


Favored when



# Nucleophilic Addition of HCN: Cyanohydrin Formation

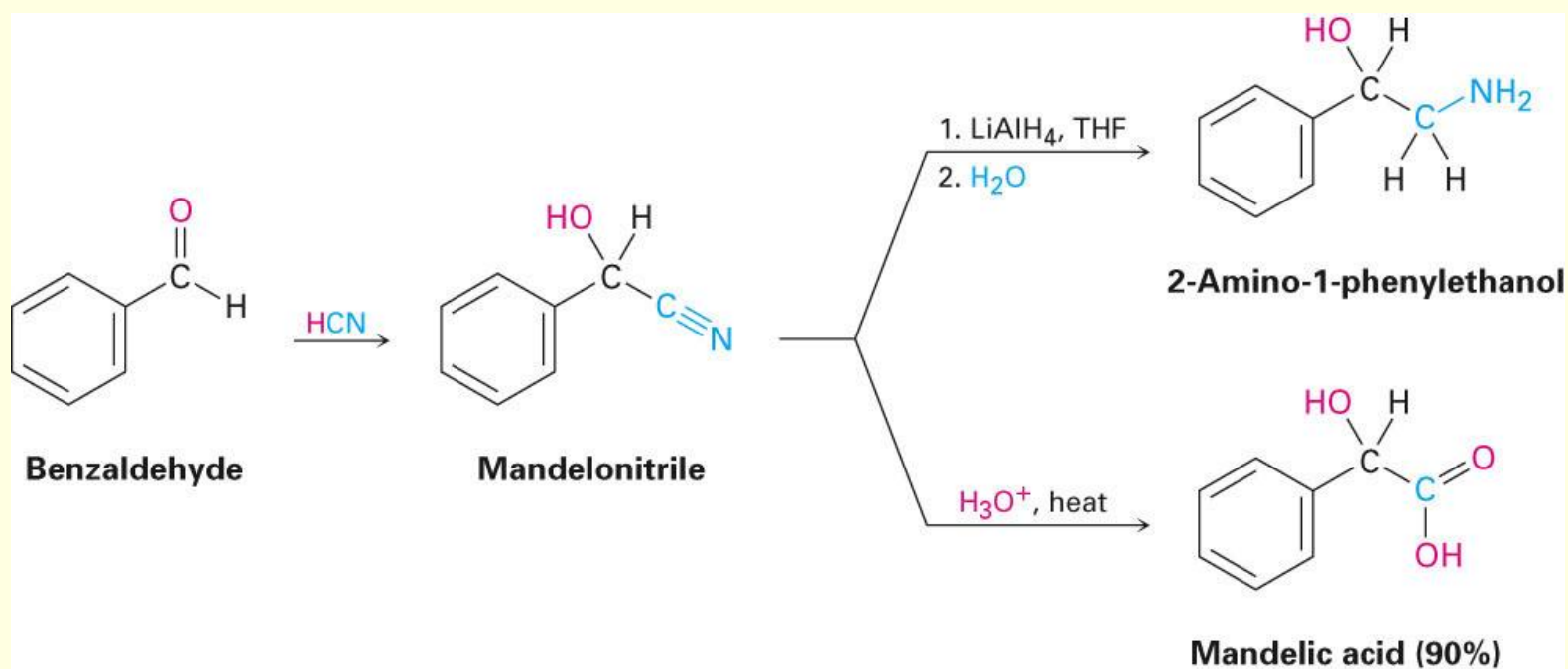
- Aldehydes and unhindered ketones react with HCN to yield cyanohydrins,  $\text{RCH(OH)C}\equiv\text{N}$
- Addition of HCN is reversible and base-catalyzed, generating nucleophilic cyanide ion,  $\text{CN}^-$
- Addition of  $\text{CN}^-$  to  $\text{C}=\text{O}$  yields a tetrahedral intermediate, which is then protonated
- Equilibrium favors adduct





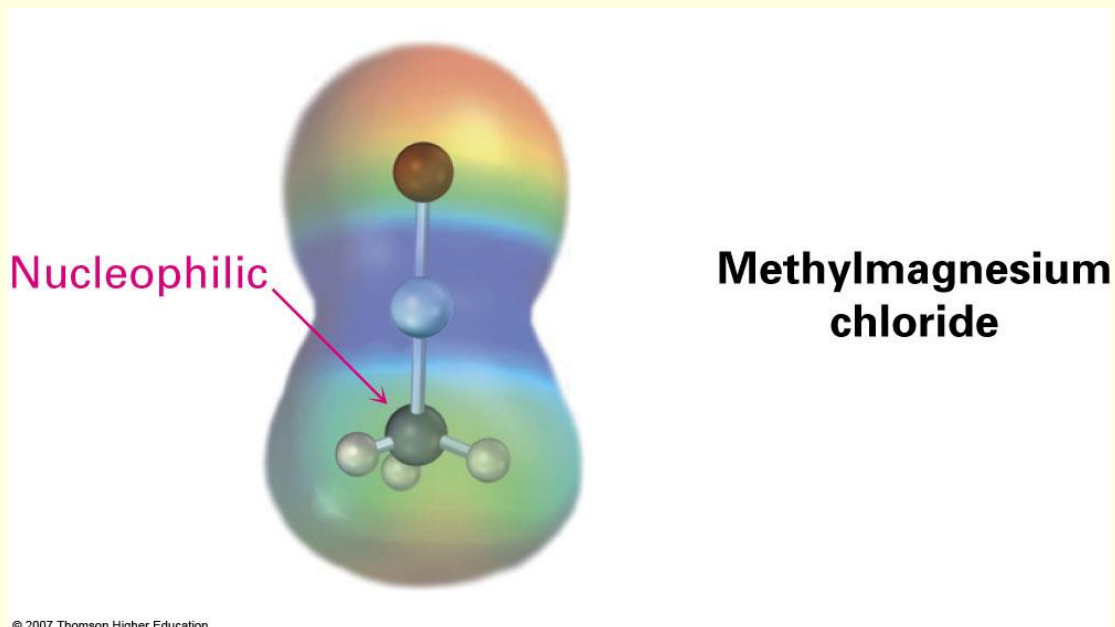
# Uses of Cyanohydrins

- The nitrile group ( $\text{—C}\equiv\text{N}$ ) can be reduced with  $\text{LiAlH}_4$  to yield a primary amine ( $\text{RCH}_2\text{NH}_2$ )
- Can be hydrolyzed by hot acid to yield a carboxylic acid



# Nucleophilic Addition of Grignard Reagents and Hydride Reagents: Alcohol Formation

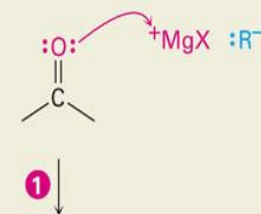
- Treatment of aldehydes or ketones with Grignard reagents yields an alcohol
  - Nucleophilic addition of the equivalent of a *carbon* anion, or **carbanion**. A carbon–magnesium bond is strongly polarized, so a Grignard reagent reacts for all practical purposes as  $R : ^- MgX ^+$ .



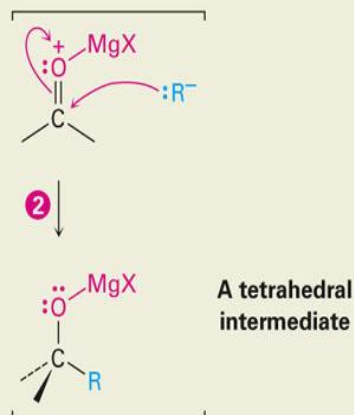
# Mechanism of Addition of Grignard Reagents

- Complexation of C=O by  $Mg^{2+}$ , Nucleophilic addition of  $R^-$ , protonation by dilute acid yields the neutral alcohol
- Grignard additions are irreversible because a carbanion is not a leaving group

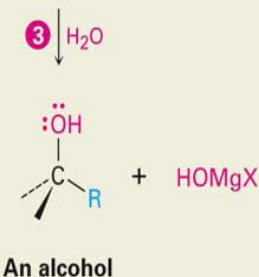
1 The Lewis acid  $Mg^{2+}$  first forms an acid-base complex with the basic oxygen atom of the aldehyde or ketone, thereby making the carbonyl group a better acceptor.



2 Nucleophilic addition of an alkyl group  $:R^-$  to the aldehyde or ketone produces a tetrahedral magnesium alkoxide intermediate . . .

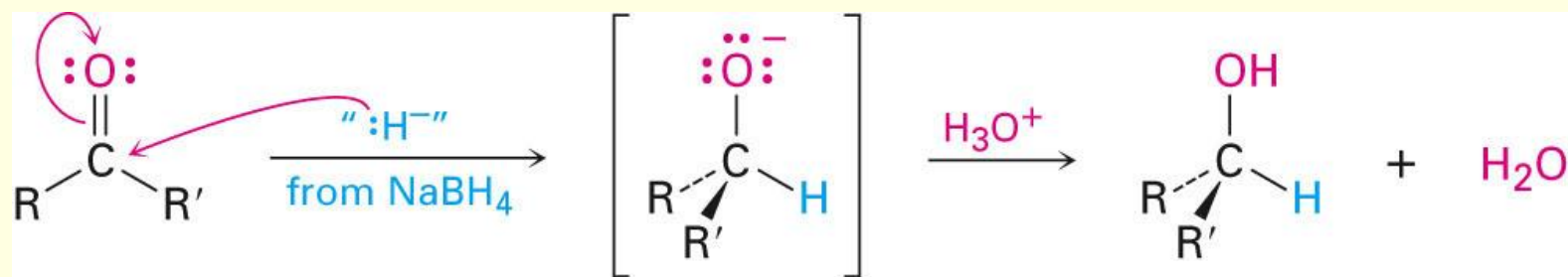


3 . . . which undergoes hydrolysis when water is added in a separate step. The final product is a neutral alcohol.



# Hydride Addition

- Convert C=O to CH-OH
- $\text{LiAlH}_4$  and  $\text{NaBH}_4$  react as donors of hydride ion
- Protonation after addition yields the alcohol

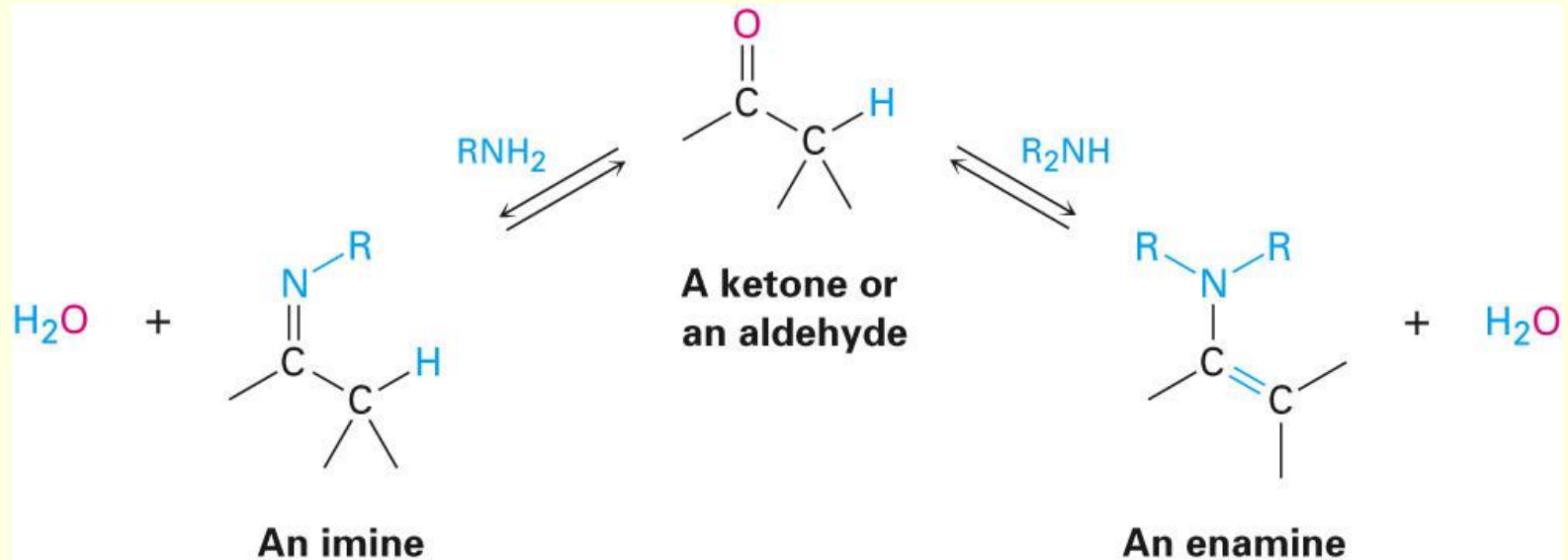


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# Nucleophilic Addition of Amines: Imine and Enamine Formation

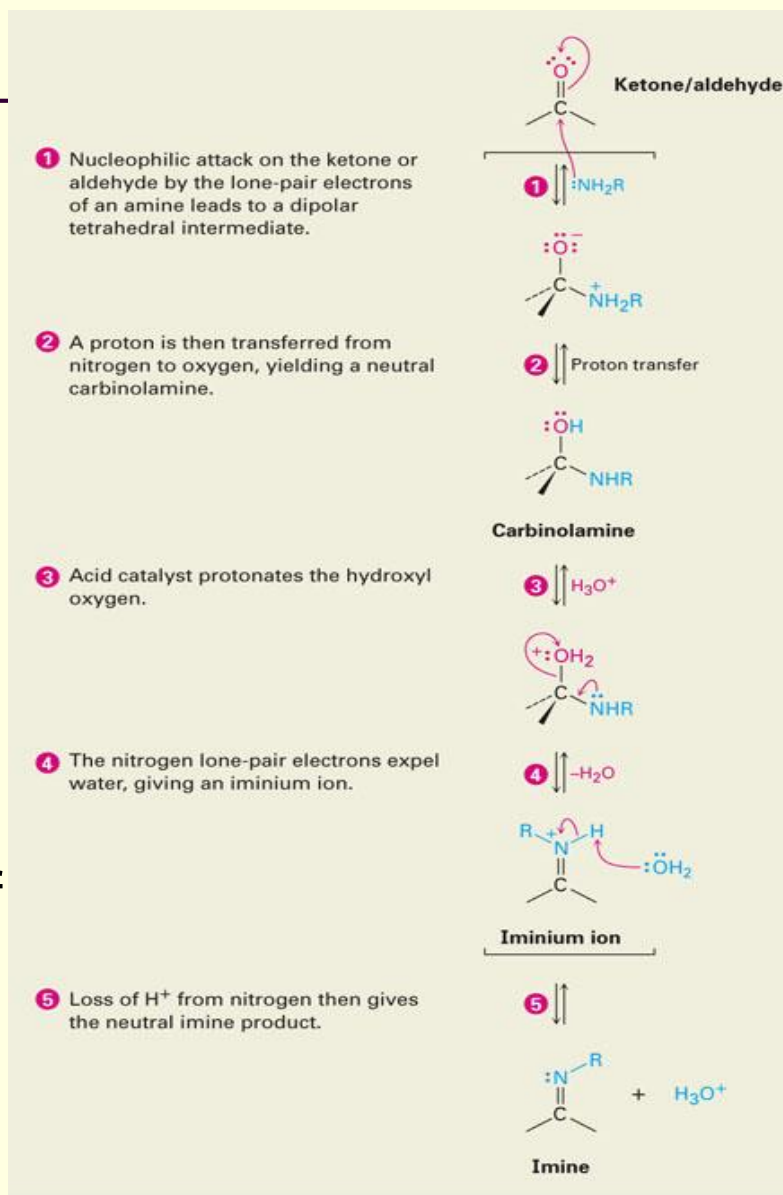
$\text{RNH}_2$  adds to  $\text{C}=\text{O}$  to form imines,  $\text{R}_2\text{C}=\text{NR}$  (after loss of  $\text{HOH}$ )  
 $\text{R}_2\text{NH}$  yields enamines,  $\text{R}_2\text{N}-\text{CR}=\text{CR}_2$  (after loss of  $\text{HOH}$ )  
(*ene* + *amine* = unsaturated amine)

“Thompson Now” (Section 19.8)



# Mechanism of Formation of Imines

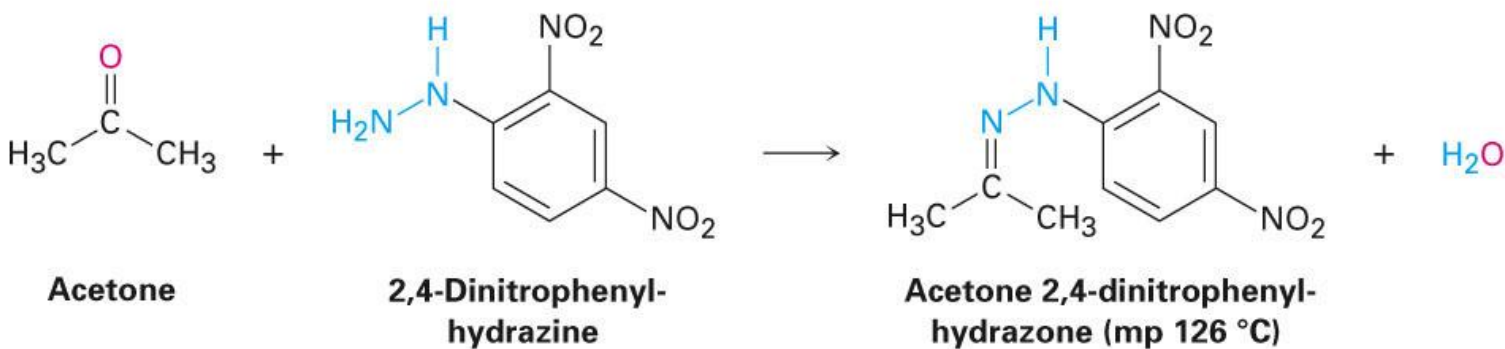
- Primary amine adds to C=O
- Proton is lost from N and adds to O to yield a neutral amino alcohol (carbinolamine)
- Protonation of OH converts into water as the leaving group
- Result is iminium ion, which loses proton
- Acid is required for loss of OH – too much acid blocks  $\text{RNH}_2$



# Imine Derivatives

- Addition of amines with an atom containing a lone pair of electrons on the adjacent atom occurs very readily, giving useful, stable imines
- For example, hydroxylamine forms oximes and 2,4-dinitrophenylhydrazine readily forms 2,4-dinitrophenylhydrazones
  - These are usually solids and help in characterizing liquid ketones or aldehydes by melting points

## 2,4-Dinitrophenylhydrazone



# Enamine Formation

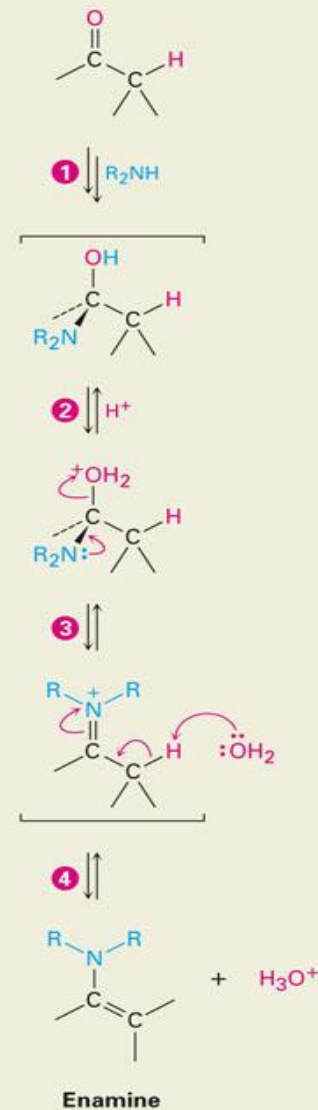
- After addition of  $R_2NH$ , proton is lost from adjacent carbon

1 Nucleophilic addition of a secondary amine to the ketone or aldehyde, followed by proton transfer from nitrogen to oxygen, yields an intermediate carbinolamine in the normal way.

2 Protonation of the hydroxyl by acid catalyst converts it into a better leaving group.

3 Elimination of water by the lone-pair electrons on nitrogen then yields an intermediate iminium ion.

4 Loss of a proton from the alpha carbon atom yields the enamine product and regenerates the acid catalyst.





# Nucleophilic Addition of Hydrazine: The Wolff–Kishner Reaction

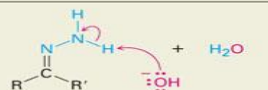
- Treatment of an aldehyde or ketone with hydrazine,  $\text{H}_2\text{NNH}_2$  and  $\text{KOH}$  converts the compound to an alkane
- Originally carried out at high temperatures but with dimethyl sulfoxide as solvent takes place near room temperature

1 Reaction of the aldehyde or ketone with hydrazine yields a hydrazone in the normal way.



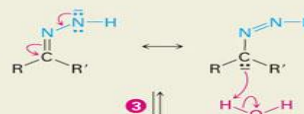
1 ↓

2 Base abstracts a weakly acidic N–H proton, yielding a hydrazone anion. This anion has a resonance form that places the negative charge on carbon and the double bond between nitrogens.



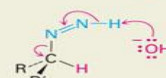
2 ↓

3 Protonation of the hydrazone anion takes place on carbon to yield a neutral intermediate.



3 ↓

4 Deprotonation of the remaining weakly acidic N–H occurs with simultaneous loss of nitrogen to give a carbanion . . .

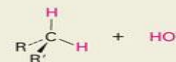


4 ↓

5 . . . which is protonated to give the alkane product.

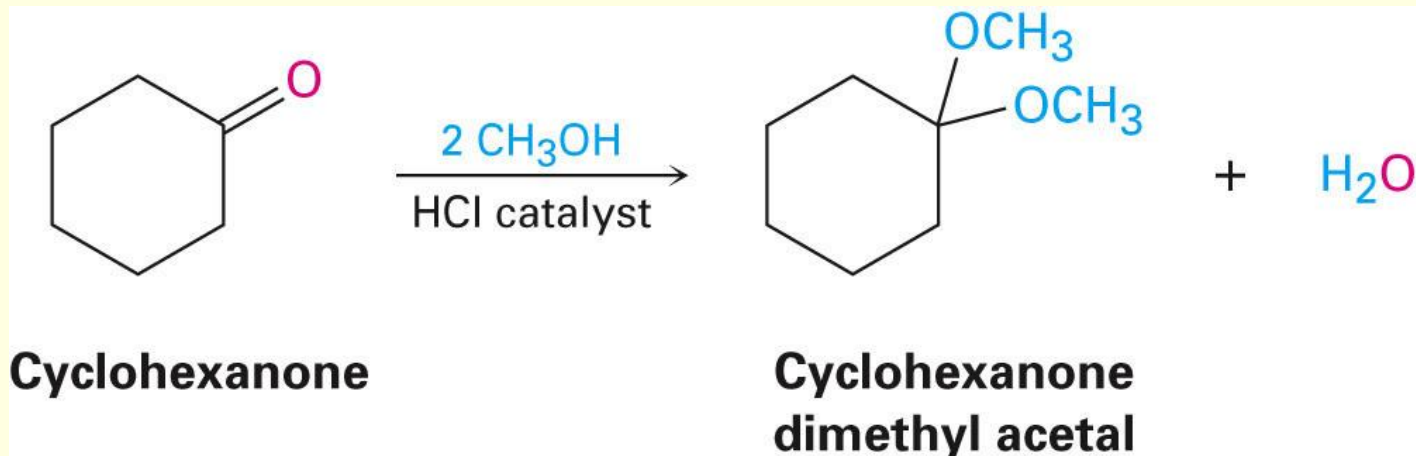


5 ↓



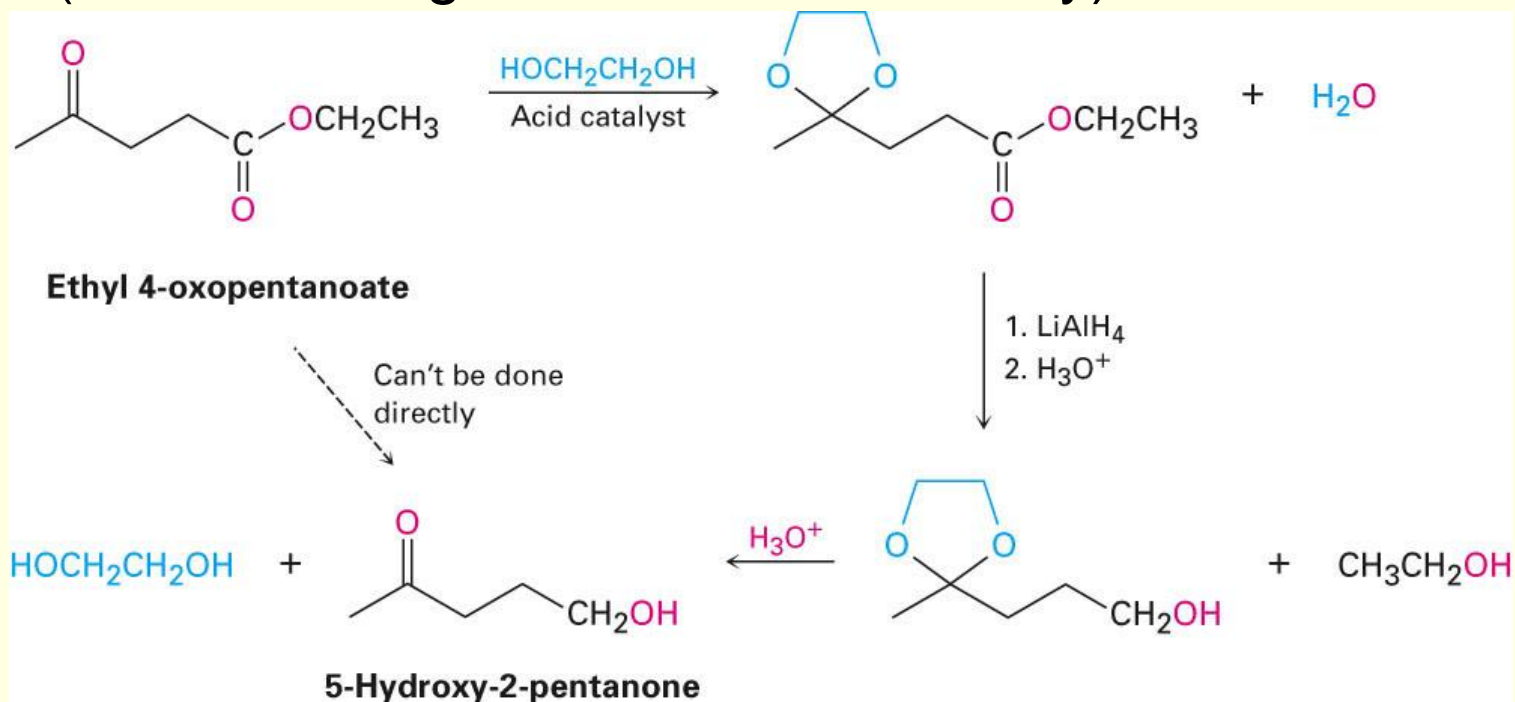
# Nucleophilic Addition of Alcohols: Acetal Formation

- Alcohols are weak nucleophiles but acid promotes addition forming the conjugate acid of C=O
- Addition yields a hydroxy ether, called a hemiacetal (reversible); further reaction can occur
- Protonation of the —OH and loss of water leads to an oxonium ion,  $R_2C=OR^+$  to which a second alcohol adds to form the acetal



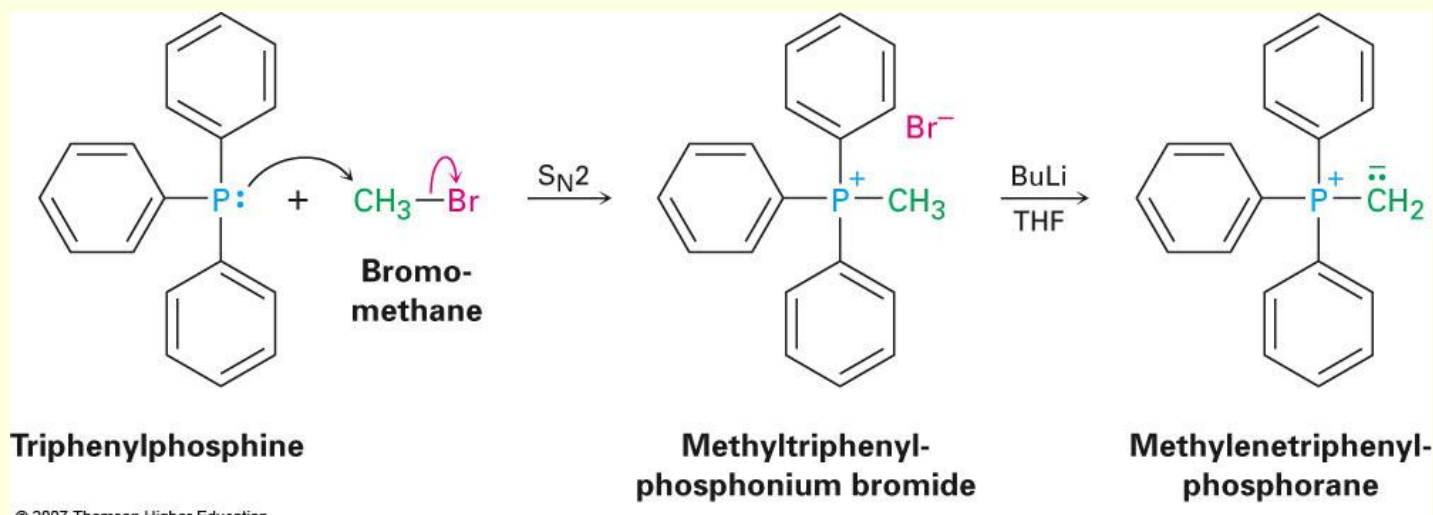
# Uses of Acetals

- Acetals can serve as protecting groups for aldehydes and ketones
- It is convenient to use a diol, to form a *cyclic* acetal (the reaction goes even more readily)



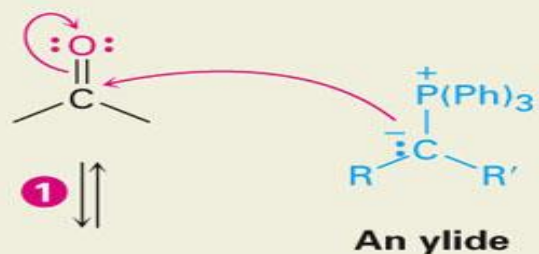
# Nucleophilic Addition of Phosphorus Ylides: The Wittig Reaction

- The sequence converts C=O to C=C
- A phosphorus *ylide* adds to an aldehyde or ketone to yield a dipolar intermediate called a *betaine*
- The intermediate spontaneously decomposes through a four-membered ring to yield alkene and triphenylphosphine oxide,  $(\text{Ph})_3\text{P}=\text{O}$
- Formation of the ylide is shown below

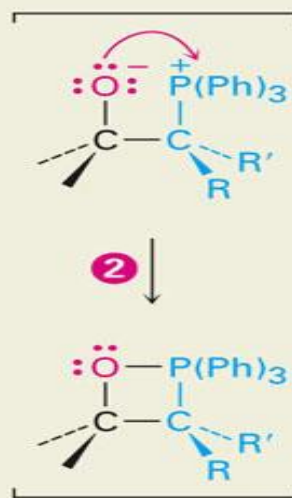


# Mechanism of the Wittig Reaction

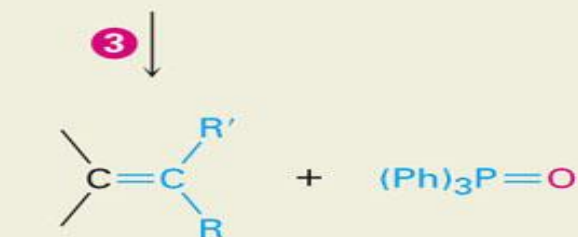
- 1 The nucleophilic carbon atom of the phosphorus ylide adds to the carbonyl group of a ketone or aldehyde to give an alkoxide ion intermediate.



- 2 The alkoxide ion then undergoes intramolecular O-P bond formation to produce a four-membered ring . . .

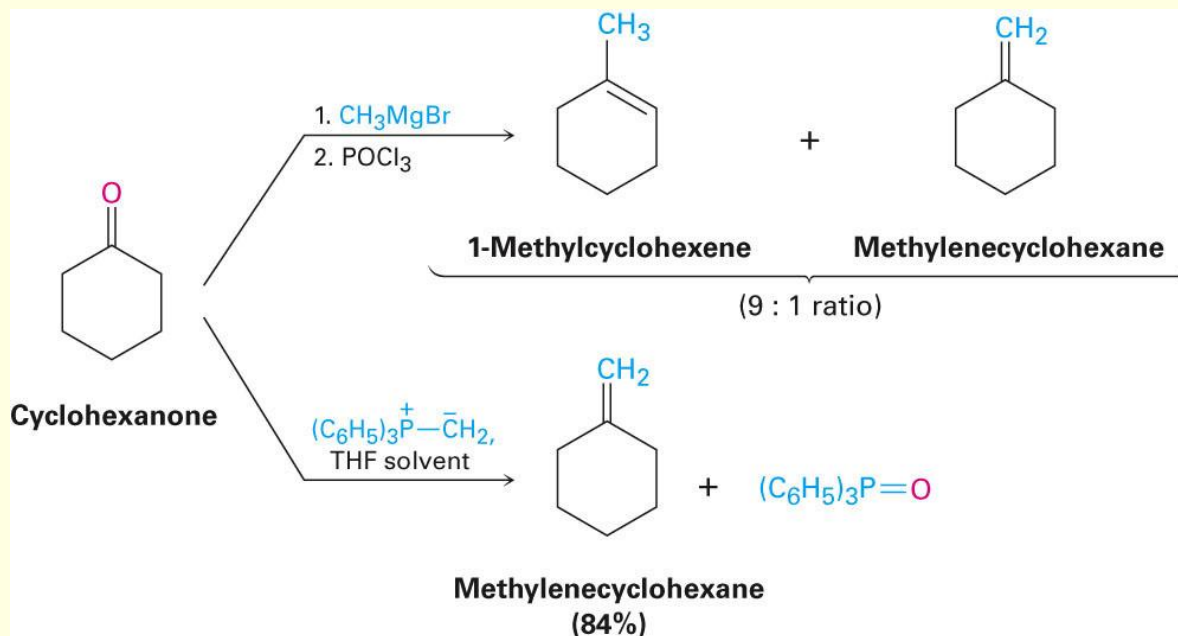


- 3 . . . which spontaneously decomposes to give an alkene and triphenylphosphine oxide.



# Uses of the Wittig Reaction

- Can be used for monosubstituted, disubstituted, and trisubstituted alkenes but not tetrasubstituted alkenes  
The reaction yields a pure alkene of known structure
- For comparison, addition of  $\text{CH}_3\text{MgBr}$  to cyclohexanone and dehydration with, yields a mixture of two alkenes



# The Cannizzaro Reaction

- The adduct of an aldehyde and  $\text{OH}^-$  can transfer hydride ion to another aldehyde  $\text{C}=\text{O}$  resulting in a simultaneous oxidation and reduction (*disproportionation*)

