

Chapter 16

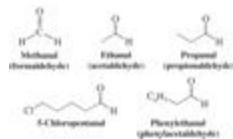
Aldehydes and Ketones I.

Nucleophilic Addition to the Carbonyl Group

Nomenclature of Aldehydes and Ketones

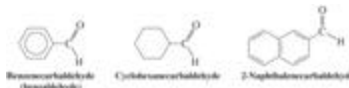
Aldehydes replace the -e of the parent alkane with -al

- The functional group needs no number

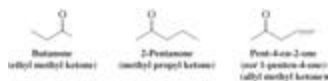


Aldehyde bonded to a ring are named using suffix carbaldehyde

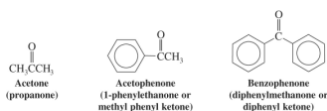
- Benzaldehyde is common short name for benzenecarbaldehyde



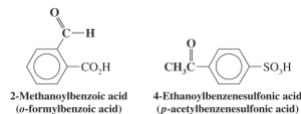
- Ketones: replacing the -e of the parent alkane with -one
 - Parent chain is numbered to give the ketone the lower number
 - Common names preceded the word ketone with names of two groups attached to the ketone carbonyl.



- Common names of ketones that are also IUPAC names

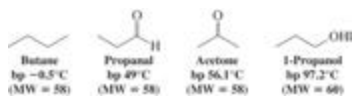


In complex structures, aldehyde or ketone must be named as an acyl group

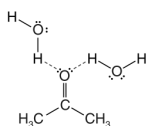


Physical Properties of Aldehydes and Ketones

- No hydrogen bonding to each other
- Rely only on intermolecular dipole-dipole interactions (C=O)
- Higher bp than non-polar alkanes, but lower bp than alcohols



Low molecular weight aldehydes and ketones have appreciable water solubility



Synthesis of Aldehydes

1. Oxidation of 1° Alcohols

- Pyridinium chlorochromate = PCC

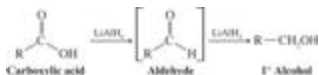


Stops at aldehyde because no water is present

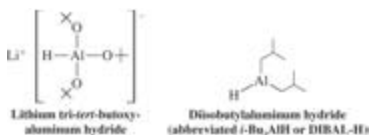
Synthesis of Aldehydes

2. Reduction of Carboxylic Acid Derivatives

Carboxylic acids themselves cannot be reduced directly to aldehydes



Aldehydes can be prepared by:
using more reactive carboxylic acid derivatives (RCO-X)
and a sterically hindered aluminum hydride reagent

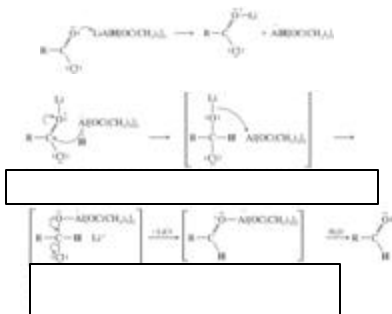


2a. Acid chlorides react with lithium tri-*tert*-butoxyaluminum hydride at low temperature to give aldehydes



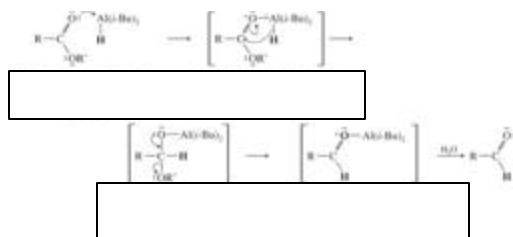
♦ Mechanism:

- Step 1: hydride transfer to carbonyl forms sp³ intermediate
- Step 2: good leaving group allows reformation of carbonyl



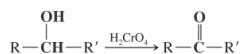
2b. Reduction of an ester to an aldehyde can be accomplished at low temperature using DIBAL-H

- Similar mechanism

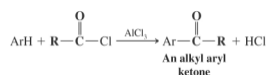


Synthesis of Ketones

1. From secondary alcohols by oxidation



2. From arenes by Friedel-Crafts Acylation

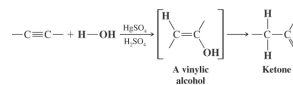


3. From alkenes by ozonolysis



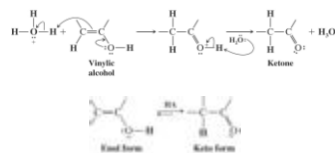
4. Ketones by addition of water to an alkyne

- ♦ Markovnikov hydration of an alkyne initially yields a vinyl alcohol (enol) which then rearranges rapidly to a ketone (keto)



♦ The rearrangement is called a keto-enol tautomerization

- An equilibrium which usually favors the keto form



Aldehydes are generally more reactive than ketones

- The tetrahedral addition product is less sterically hindered in an aldehyde



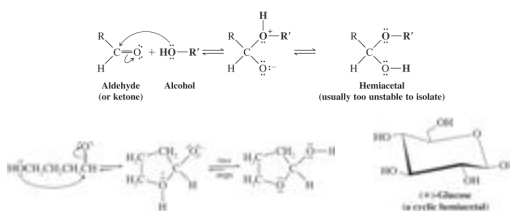
- Aldehyde carbonyl is more electron deficient because it has only one electron-donating group attached to the carbonyl carbon



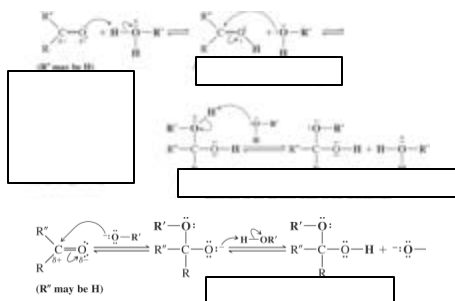
The Addition of Alcohols: Hemiacetals and Acetals

Hemiacetals

- An aldehyde or ketone dissolved in an alcohol will form an equilibrium mixture containing the corresponding hemiacetal
 - A hemiacetal has a hydroxyl and alkoxy group on the same carbon
 - Acyclic hemiacetals are generally not stable, however, cyclic five- and six-membered ring hemiacetals are

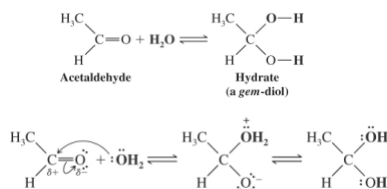


Hemiacetal formation is catalyzed by either acid or base



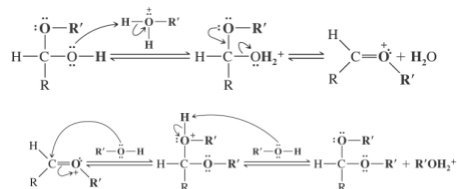
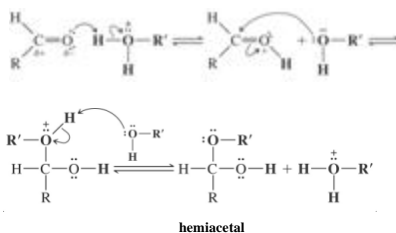
Dissolving aldehydes or ketones in water causes formation of an equilibrium between the carbonyl compound and its hydrate

- The hydrate is also called a *gem*-diol
- The equilibrium favors a ketone over its hydrate because the tetrahedral ketone hydrate is sterically crowded
- Aqueous solution of formaldehyde is largely in hydrated form



Acetals

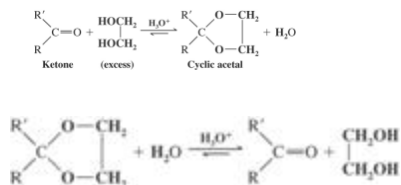
- An aldehyde (or ketone) in excess alcohol and an acid catalyst will form an acetal (two alkoxy groups bonded to same carbon)
 - Formation of the acetal proceeds via the corresponding hemiacetal



- Acetals are stable when isolated and purified
- Acetal formation is reversible
 - An excess of water in the presence of an acid catalyst will hydrolyze an acetal to the corresponding aldehyde (or ketone)

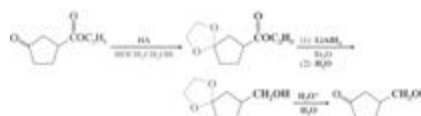


- ◆ Acetal formation from ketones and simple alcohols is less favorable than formation from aldehydes
- ◆ Formation of 5- or 6- membered ring acetals from ketones is favorable
- ◆ Cyclic acetals are used as protecting groups for aldehydes and ketones
- ◆ These protecting groups can be removed using dilute aqueous acid



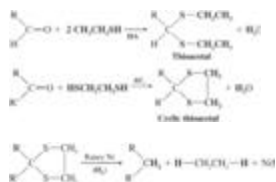
◆ Acetals as Protecting Groups

- Acetal protecting groups are stable to most reagents except aqueous acid
- Example: An ester can be reduced in the presence of a ketone protected as an acetal



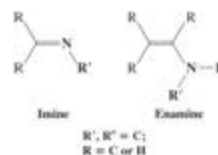
Thioacetals

- ◆ Thioacetals can be formed by reaction of an aldehyde or ketone with a thiol
 - Thioacetals can be converted to CH₂ groups by hydrogenation using a catalyst such as Raney nickel
 - This sequence provides a way to remove an aldehyde or ketone carbonyl oxygen



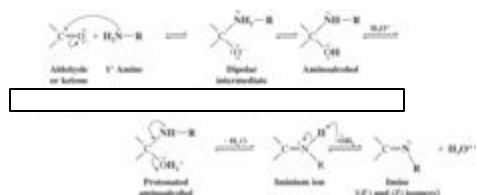
The Addition of Primary and Secondary Amines

- ◆ Aldehydes and ketones react with primary amines (and ammonia) to yield imines (C=N)
- They react with secondary amines to yield enamines



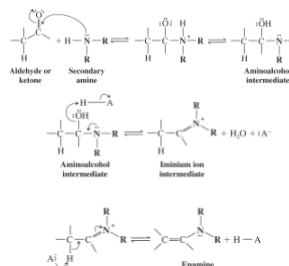
Formation of Imines

- ◆ These reactions occur fastest at pH 4-5
 - Mild acid facilitates departure of the hydroxyl group from the aminoalcohol intermediate without also protonating the nitrogen of the amine starting compound



Enamines

- ◆ Secondary amines cannot form a neutral imine by loss of a second proton on nitrogen
 - An enamine is formed instead

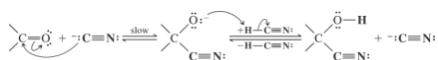


First two steps are the same as imine formation

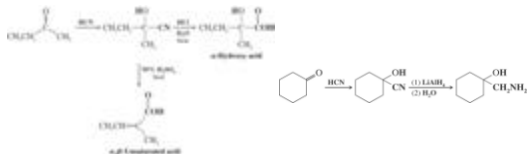
Why the different outcome?

The Addition of Hydrogen Cyanide

- Aldehydes and ketone react with HCN to form a cyanohydrin
 - A catalytic amount of cyanide speeds the reaction



- The cyano group can be hydrolyzed or reduced
 - Hydrolysis of a cyanohydrin produces an α -hydroxycarboxylic acid
 - Reduction of a cyanohydrin produces a β -aminoalcohol

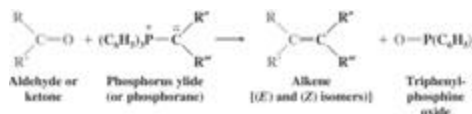


The Wittig Reaction: Addition of Ylides

Georg Wittig
The Nobel Prize in Chemistry 1979

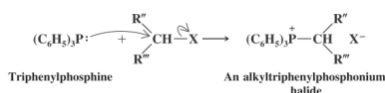


- Aldehydes and ketones react with phosphorous ylides to produce alkenes
- Ylide is a neutral molecule with adjacent positive and negative charges

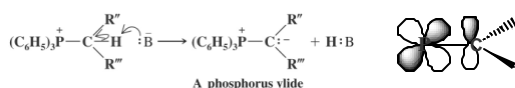


Ylide is formed in a two step process

- Reaction of triphenylphosphine with a primary or secondary alkyl halide produces a phosphonium salt



- The phosphonium salt is deprotonated by a strong base to form the ylide

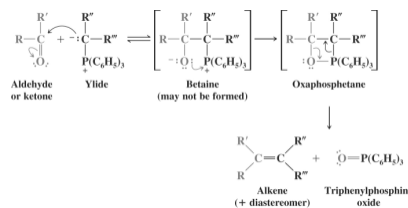


Empty d orbitals on P help stabilize carbanion

Ylide is then reacted with an aldehyde or ketone

- Attack of carbanion-like ylide on the carbonyl leads to formation of a four-membered ring oxaphosphetane

- The oxaphosphetane rearranges to the alkene and triphenylphosphine oxide
- The driving force for the last reaction is formation of the strong phosphorus-oxygen double bond in triphenylphosphine oxide

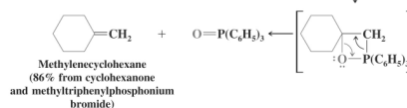
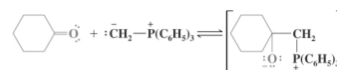
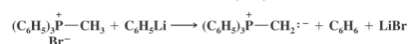
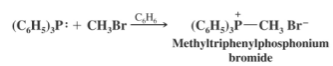


The overall result of a Wittig reaction is formation of a C=C bond from a C=O bond

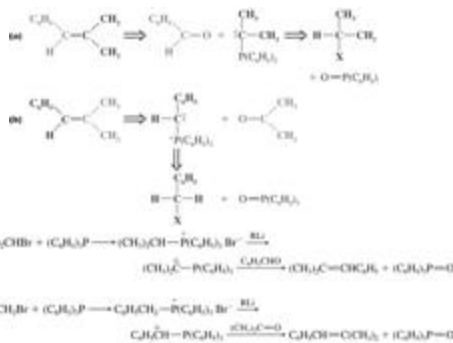


- Excellent way to extend carbon chains
- Puts alkene in a specific location

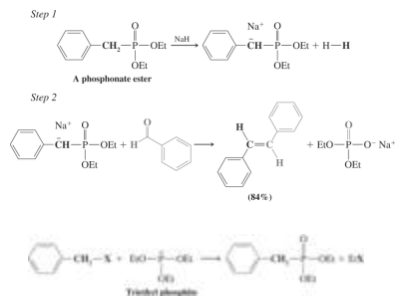
Example:



Problem: How to make 2-Methyl-1-phenylprop-1-ene by a Wittig reaction



◆ The Horner-Wadsworth-Emmons reaction employs a phosphonate ester and generally leads to formation of an (E)-alkene



The Addition of Organometallic Reagents

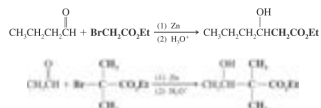
1. Grignards and organolithium: yields alcohols, review

2. The Reformatsky Reaction

- ◆ The Reformatsky reaction involves addition of an organozinc reagent to an aldehyde or ketone
- ◆ The organozinc reagent is made from an α-bromo ester; the reaction gives a β-hydroxy ester

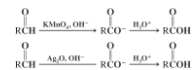


The β-hydroxyester is easily dehydrated to an α,β-unsaturated ester



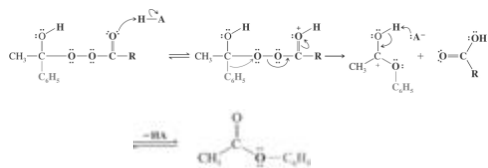
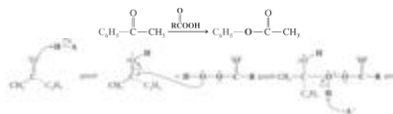
◆Oxidation of Aldehydes and Ketones

◆ Aldehydes are generally much more easily oxidized than ketones



◆ The Baeyer-Villiger Oxidation of Aldehydes and Ketones

- The Baeyer-Villiger reaction results in insertion of an oxygen atom adjacent to a ketone or aldehyde carbonyl
- ★ Oxidation of a ketone yields an ester
- ★ A peroxyacid such as *m*-chloroperbenzoic (MCPBA) acid is used



The migratory aptitude of a group attached to a carbonyl is
H > phenyl > 3° alkyl > 2° alkyl > 1° alkyl > methyl

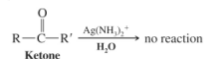
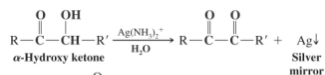
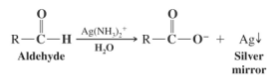


Chemical Analysis of Aldehydes and Ketones

◆ Tollens' Test (Silver Mirror Test)

- Aldehydes and ketones can be distinguished from each other on the basis of the Tollens test

- ◆ The presence of an aldehyde results in formation of a silver mirror (by oxidation of the aldehyde and reduction of the silver cation)
- ◆ α-Hydroxyketones also give a positive Tollens' test

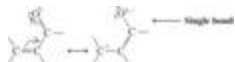


Spectroscopic Properties of Aldehydes and Ketones

- IR Spectra features strong carbonyl stretching frequencies in the 1665-1780 cm^{-1} region (1700)

C=O Stretching Frequencies			
Compound	Range (cm^{-1})	Compound	Range (cm^{-1})
$\text{R}-\text{CHO}$	1720-1740	$\text{R}_2\text{C}=\text{O}$	1710-1735
$\text{Ar}-\text{CHO}$	1680-1710	$\text{ArC}=\text{O}$	1680-1710
$\text{C}_6\text{H}_5\text{CHO}$	1680-1690	$\text{C}_6\text{H}_5\text{C}=\text{O}$	1680-1690
		Conjugated aldehydes	1680
		Conjugated ketones	1660

- ◆ Conjugation shifts the IR frequency about 40 cm^{-1} lower because the carbonyl has less double bond character



- ◆ Vibrations of the C-H bond in an aldehyde gives two weak but characteristic bands at 2700-2775 and 2820-2900 cm^{-1}

NMR Spectra of Aldehydes and Ketones

- ^{13}C NMR Spectra

- ➔ Aldehyde and ketone carbonyl carbons give characteristic signals at δ 180-220

- ^1H NMR Spectra

- ➔ Aldehyde protons give sharp signals at δ 9-12
- ➔ The aldehyde proton often shows coupling to the protons on the α -carbon
- ➔ Protons on the α carbon generally appear at δ 2.0-2.3

