TOPIC 3. ALDEHYDES AND KETONES
(Chapters 12 and 16)

OBJECTIVES

1. Describe the synthesis aldehydes and ketones.

2. Describe the carbonyl group and oxidation-reductions reactions associated with alcohols and carbonyl groups.

3. Describe some the addition reactions of aldehydes and ketones in which nucleophiles add to the electrophilic carbonyl.

4. Describe the mechanisms by which carbonyl groups are transformed to alcohols in C-C bond forming reactions.

5. Describe how C-C bonds can be formed by other reactions of organometallic compounds (not involving the formation of alcohols).

6. Use this knowledge to predict the products of reactions and synthesize complex compounds using these procedures.
ALDEHYDES AND KETONES

\[ R_1 \text{C} \text{R}_2 \]
ketone
R₁ or R₂ = alkyl, aryl or alkenyl

\[ R \text{C} \text{H} \]
aldehyde
R = H, alkyl, aryl or alkenyl

Carbonyls are electrophilic

\[ \text{CO}^+ \]

Carbonyls are weakly basic; protonation makes the carbonyl more electrophilic

\[ \text{H}^+ \text{C} \text{O} \]

Nomenclature

alkane \( \rightarrow \) #-alkanone or alkyl alkyketone

alkane \( \rightarrow \) alkanal
Physical Properties

The carbonyl group has a permanent dipole moment and is therefore much more polar than a hydrocarbon, but less polar than an alcohol.

\[
\begin{align*}
\text{Boiling point} & \quad 0^\circ & 49^\circ & 56^\circ & 97^\circ \\
\text{MW} & \quad 58 & 58 & 58 & 60 \\
\text{Sol. in water in g/100 mL} & \quad \text{nil} & 20 & \text{miscible} & \text{miscible}
\end{align*}
\]

OXIDATIONS AND REDUCTIONS IN ORGANIC CHEMISTRY

Oxidation-Reduction Reactions in Organic Chemistry

Reduction - adding electrons, more hydrogens, less oxygen
Oxidation - removing electrons, less hydrogens, more oxygen

Calculating Oxidation State of Carbon Atoms in Organic Molecules

The oxidation state of a carbon balances the contributions from each of the bonds to its substituents:

- H = +1
- O and other electronegative atoms = -1
- C = 0
**Oxidation of Alcohols (-1 → +1 → +3)**

\[
\begin{align*}
RCH\text{OH} & \xrightarrow{[O]} RCH\text{O}^+ \\
& \xrightarrow{[O]} \text{RCHO} \\
& \xrightarrow{[O]} \text{RCO}_2\text{H}
\end{align*}
\]

**Strong Oxidants**

1. KMnO₄, KOH, H₂O
2. H₃O⁺ or Na₂Cr₂O₇, or CrO₃⁻

\[
\begin{align*}
RCH_2\text{OH} & \xrightarrow{[VII]} \text{RCH}_3\text{O}^+ \\
& \xrightarrow{[VI]} \text{RCHO} \\
& \xrightarrow{[VI]} \text{RCO}_2\text{H}
\end{align*}
\]
Chemical Tests for Functional Groups

The molecular formula indicates one site of unsaturation. Is it a ring, or an alkene?

Alkenes decolorize bromine

\[ \text{Br}_2 \text{ in CHCl}_3 \]

\[ \text{alkene} \rightarrow \text{alkane} \]

Infrared spectroscopy indicates the presence of an alcohol (strong, broad absorption at 3500 cm\(^{-1}\)). But what type of alcohol is it?

1° and 2° alcohols give a positive test with Jones reagent

\[ \text{Na}_2\text{Cr}_2\text{O}_7, \text{H}_2\text{SO}_4 \text{ in H}_2\text{O} \]
\[ (\text{orange} = \text{Cr}^{VI}) \]

1° of 2° alcohol

\[ \text{alkane} \rightleftharpoons \text{alkene} \]

\[ \text{Green solution} \]

\[ 2\text{Cr}_2\text{O}_7^{2-} + 3\text{C}_2\text{H}_5\text{OH} + 16\text{H}^+ \]

\[ 4\text{Cr}^{3+} + 3\text{CH}_3\text{CO}_2\text{H} + 11\text{H}_2\text{O} \]
**Oxidation of 1° Alcohols with Mild Oxidants**

\[ R-\text{CH}_2-\text{OH} \xrightarrow{\text{PCC}} \text{CH}_2\text{Cl}_2 \]

PCC = pyridinium chlorochromate

\[ \text{OH} \xrightarrow{\text{PCC}} \text{CH}_2\text{Cl}_2 \]

**Reduction (+3 → +1 → -1)**

**Reduction with LiAlH\(_4\) or NaBH\(_4\)**

\[ R-\text{CH}_2-\text{OH} \xrightarrow{1. \text{LiAlH}_4, 2. \text{H}_2\text{O}} \text{aldehyde or ketone} \]

\[ R-\text{CH}_2\text{OH} \xrightarrow{1. \text{NaBH}_4, 2. \text{H}_2\text{O}} \text{alcohol} \]

\[ R-\text{CO}_2\text{H} \xrightarrow{1. \text{LiAlH}_4, 2. \text{H}_2\text{O}} \text{acid or ester} \]

\[ R-\text{CO}_2\text{R} \xrightarrow{1. \text{NaBH}_4, 2. \text{H}_2\text{O}} \text{ester} \]

via

\[ R-\text{CO}_2\text{R} \]
Reduction of Carboxylic Acid Derivatives with Mild Reducing Agents

\[
\begin{align*}
\text{R}^-\text{C}^-\text{Cl} & \quad 1. \text{LiAlH}(t\text{-BuO})_3 \\
& \quad \text{-78}^\circ\text{C} \\
& \quad 2. \text{H}_2\text{O} \\
\text{R}^-\text{C}^-\text{OMe} & \quad 1. \text{DIBAL-H} \\
& \quad \text{-78}^\circ\text{C} \\
& \quad 2. \text{H}_2\text{O}
\end{align*}
\]

- LiAlH\((t\text{-BuO})_3\)
- DIBAL-H

SYNTHESIS OF ALDEHYDES

Oxidation of 1° Alcohols

\[
\text{C}_6\text{H}_5\text{CH}_2\text{-OH} \quad \xrightarrow{\text{PCC}}
\]

Reduction of Acid Derivatives

\[
\begin{align*}
\text{R}^-\text{C}^-\text{Cl} & \quad 1. \text{LiAlH}(t\text{-BuO})_3 \\
& \quad \text{-78}^\circ\text{C} \\
& \quad 2. \text{H}_2\text{O} \\
\text{R}^-\text{C}^-\text{OMe} & \quad 1. \text{DIBAL-H} \\
& \quad \text{-78}^\circ\text{C} \\
& \quad 2. \text{H}_2\text{O}
\end{align*}
\]
SYNTHESIS OF KETONES

Oxidation of $2^\circ$ Alcohols

$$\begin{align*}
1. \text{KMnO}_4, & \quad \text{KOH, H}_2\text{O} \\
2. \text{H}_3\text{O}^+ &
\end{align*}$$

Review: Ozonolysis of Alkenes

$$\begin{align*}
1. \text{O}_3 & \\
2. \text{Zn, HOAc} &
\end{align*}$$

Hydration of Alkynes

$$\begin{align*}
\text{Hyg}\text{ration of Alkynes} & \\
& \frac{\text{HgSO}_4}{\text{H}_2\text{SO}_4}
\end{align*}$$

Friedel-Crafts acylation

$$\begin{align*}
\text{H}_3\text{CO} & \\
\text{CH}_3\text{COCl} & \frac{\text{AlCl}_3}
\end{align*}$$

Problem - Provide a synthesis of 3-hexanone from starting materials with three of fewer carbon atoms.
Problem - Provide a synthesis of cyclohexanone from cyclohexane

Oxidation of Aldehydes

1. KMnO₄, KOH, H₂O
2. H₃O⁺ or
   Na₂Cr₂O₇, H₂SO₄, H₂O or CrO₃, H₂SO₄, H₂O

Ag₂O is a selective oxidant for aldehydes, avoids use of strong acid or base
Chemical Tests for Functional Groups

Infrared spectroscopy indicates the presence of an aldehyde or ketone (strong, sharp absorption at ca. 1720 cm\(^{-1}\)). Is the compound an aldehyde, or a ketone? Aldehydes give positive Tollen’s test (silver mirror).
**Oxidation of Ketones**  
*Oxidation with peracids: The Baeyer-Villiger reaction*

\[ R_1 R_2 CO_3H \rightarrow R_1 R_2 CO_2H \]

Oxidation with peracids results in the conversion of ketones to carboxylic acids. The reaction involves the addition of a peracid (\( RCO_3H \)) to a ketone (\( R_1 R_2 CO \)), leading to the formation of a carboxylic acid derivative (\( R_1 R_2 CO_2H \)).

**Migratory aptitude:** Ph > 3° > 2° > 1° > Me

**Reduction of Aldehydes and Ketones**

**Aldehydes**

\[ R'CH = O \]

1. LiAlH₄ or NaBH₄  
2. H₂O

**Ketones**

\[ R' R' CO \]

1. LiAlH₄ or NaBH₄  
2. H₂O
NUCLEOPHILIC ADDITION REACTIONS OF ALDEHYDES AND KETONES

General reaction

\[
\begin{align*}
O_{\delta^-} & : \text{Nu-H} \\
O_{\delta^+} & \quad \text{H} \quad \text{H}_3C
\end{align*}
\]

Examples

\[
\begin{align*}
H_3C - CH_3 & \quad HO-H \\
H_3C - H & \quad H_3CO-H
\end{align*}
\]

? Prob:16.27,29a,30a,b ?
OXYGEN NUCLEOPHILES:
ADDITION OF WATER AND ALCOHOLS

Structure

\[
\begin{align*}
\text{hydrate} & : \quad \text{OH} \quad R_1 - C - R_2 \\
\text{hemiacetal} & : \quad \text{OH} \quad R_1 - C - R_2 \\
\text{acetal} & : \quad \text{OR} \quad R_1 - C - R_2 \\
\end{align*}
\]

\( R_1 \text{ or } R_2 = \text{H or alkyl} \)
Hydrates

Example

Mechanism of base catalyzed reaction
Base catalysis increases the nucleophilicity of the nucleophile

Mechanism of acid catalyzed reaction
Acid catalysis increases the electrophilicity of the electrophile
Relative Reactivity (Electrophilicity) of Aldehydes and Ketones

*Equilibrium constants for Hydrate Formation*

<table>
<thead>
<tr>
<th>X</th>
<th>Y</th>
<th>$K_{eq}$</th>
<th>% hydrate at equilibrium</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>H</td>
<td>41</td>
<td>99.96</td>
</tr>
<tr>
<td>CH$_3$</td>
<td>H</td>
<td>$1.8 \times 10^{-2}$</td>
<td>50</td>
</tr>
<tr>
<td>C(CH$_3$)$_3$</td>
<td>H</td>
<td>$4.1 \times 10^{-3}$</td>
<td>19</td>
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<tr>
<td>CH$_3$</td>
<td>CH$_3$</td>
<td>$2.5 \times 10^{-5}$</td>
<td>0.14</td>
</tr>
<tr>
<td>CF$_3$</td>
<td>CF$_3$</td>
<td>22,000</td>
<td>99.9996</td>
</tr>
</tbody>
</table>

Data: 1 M carbonyl compound dissolved in H$_2$O

**Electronic factors**
Inductive electron donating groups decrease electrophilicity of carbonyl (and visa versa)

![Electronic Factors Diagram]

**Steric factors**
Bulky groups hinder attack of nucleophile and cause steric crowding in product

![Steric Factors Diagram]

$sp^2, \approx 120^\circ$

$sp^3, \approx 109.5^\circ$
Hemiacetals

*Example: Glucose*

Formation: **Base-catalyzed reaction**

$$
\text{ROH} + \text{B}^- \rightleftharpoons \text{OR}^- + \text{H}^- \\
\text{CHO} \rightleftharpoons \text{OR}^-
$$

Formation: **Acid-catalyzed reaction**

$$
\text{CHO} + \text{R}^+\text{OH} \rightleftharpoons \text{OR}^- + \text{H}^+ \\
\text{CHO} \rightleftharpoons \text{OR}^-
$$

**Problem:** Draw the mechanism for the acid-catalyzed formation of an hemiacetal (this is analogous to the acid-catalyzed hydration)
Acetals

Examples

\[
\text{C}=\text{O} + 2\text{OH} \rightarrow \text{H}^+ \\
\text{C}=\text{O} + \text{HO} \rightarrow \text{H}^+ 
\]

Only formed under acidic conditions

Mechanism for formation of acetals

All steps are reversible – must remove \(H_2O\) to drive reaction to completion.
Hydrolysis of Acetals: Mechanism for the REVERSE reaction

\[ 2 \text{CH}_3\text{OH} + \text{CHO} \rightleftharpoons \text{CH}_3\text{O} \text{CH}_3 + \text{H}_2\text{O} \]

Principle of microscopic reversibility: Forward and back reactions take place via the same intermediates and transition states.
Problem [Solomons 16.46] - Multistriatin is an aggregating pheromone of the European elm bark beetle, the vector of Dutch elm disease. Multistriatin is an acetal. What is the product of hydrolysis of multistriatin formed upon treatment with aqueous acid?

\[ \text{H}_3\text{O}^+ \]

NITROGEN NUCLEOPHILES: ADDITION-ELIMINATION

Addition-elimination of 1º Amines

\[ \text{ketone or aldehyde} + R\text{NH}_2 \xrightarrow{\text{H}_2\text{O}} \text{imine - } E \text{ and } Z \text{ isomers possible} \]
**Mechanism**

Acid or base catalyzed, but requires careful control of pH

\[ \text{R-NH}_2 + \text{H}_3\text{O}^+ \rightarrow \text{R-NH}_3 + \text{H}_2\text{O} \]

nucleophilic \[ \rightarrow \text{not nucleophilic} \]

\[ \text{carbonyl} + \text{H}_3\text{O}^+ \rightarrow \text{not nucleophilic} \]

less electrophilic \[ \rightarrow \text{not nucleophilic} \]

more electrophilic

\[ \text{H}_2\text{N}^\cdots\text{R} \]
Examples

\[
\begin{align*}
R' & \quad R''(H) \quad + \quad \text{CH}_3\text{--NH}_2 \quad \rightarrow \\
\text{aldehyde or ketone} & \quad 1^\circ \text{amine} \\
R' & \quad R''(H) \quad + \quad \text{HO--NH}_2 \quad \rightarrow \\
\text{aldehyde or ketone} & \quad \text{hydroxylamine} \\
R' & \quad R''(H)^+ \quad + \quad \text{H}_2\text{N--NH}_2 \quad \rightarrow \\
\text{aldehyde or ketone} & \quad \text{hydrazine} \\
R' & \quad R''(H) \quad + \quad \text{2,4-dinitrophenyl hydrazine} \quad \rightarrow \\
\text{aldehyde or ketone} & \quad \text{2,4-dinitrophenyl hydrazine}
\end{align*}
\]

Chemical Tests for Functional Groups
Aldehydes and ketones give positive 2,4-DNP test

2,4-DNP in EtOH

aldehyde or ketone

orange ppt (hydrazine)
CARBON NUCLEOPHILES: TWO CARBON NUCLEOPHILES WE HAVE SEEN BEFORE

Sodium Acetylides

\[
\text{Example}
\]

Addition of HCN

\[
\text{Example}
\]
ORGANOMETALLIC COMPOUNDS AS NUCLEOPHILES

Organometallic Compounds
Examples:

<table>
<thead>
<tr>
<th></th>
<th>RMgHal</th>
<th>RLi</th>
<th>RC≡CNa</th>
<th>RZnHal</th>
<th>R₂CuLi</th>
</tr>
</thead>
<tbody>
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<td></td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>C-Mg</td>
<td>1.2</td>
<td>1.0</td>
<td>1.0</td>
<td>1.7</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Contrast reactivity:

C-O  C-M

C-Br

ORGANOLITHIUM AND ORGANOMAGNESIUM COMPOUNDS

Preparation: Halogen-Metal Exchange

R-X + 2 Li →

R-X + Mg →

I > Br > Cl >> F

solvent is usually Et₂O or (THF)

Ph-Mg-X
Grignard and Lithium Reagents as Bases

Grignard And Lithium Reagents React with Epoxides

_Nucleophilic Ring opening of Epoxides (example from Organic-I)_

Organometallics as Nucleophiles
RMgX and RLi do not undergo S\textsubscript{N} reactions with alkyl halides

\[
\text{CH}_3\text{Br} + \text{H}_3\text{C}\text{Li} \rightarrow \text{CH}_3\text{CH}_3 + \text{LiBr}
\]

Lithium, Magnesium and Sodium Reagents Add to Carbonyl Groups

\[
\begin{align*}
\text{H}_3\text{C}\text{MgBr} & \quad \text{H}_2\text{O} \\
\text{Ph}\text{MgCl} & \quad \text{H}_2\text{O} \\
\text{H}_3\text{C}\text{Li} & \quad \text{PhH} \\
\text{PhNa} & \quad \text{H}_2\text{O}
\end{align*}
\]
**Problem** - Identify the structures of compounds A-E in the following scheme.

\[ \text{OH} \xrightarrow{\text{H}_2\text{CrO}_4, \text{acetone}} \text{A, C}_6\text{H}_{10}\text{O} \xrightarrow{1. \text{CH}_3\text{MgBr}, 2. \text{H}_2\text{O}} \text{B, C}_7\text{H}_{14}\text{O} \xrightarrow{\text{H}_2\text{SO}_4} \text{C, C}_7\text{H}_{12} \]

\[ \text{E, C}_7\text{H}_{12}\text{O}_3 \xrightarrow{1. \text{Ag}_2\text{O}, \text{OH}^-} \text{D, C}_7\text{H}_{12}\text{O}_2 \]

1. \text{CH}_3\text{MgBr}
2. \text{H}_2\text{O}

**Designing Organic Synthesis: Retroanalysis**

How would you make \( \text{H}_3\text{C} - \text{Ph} - \text{H} \)?

1. Locate the hydroxyl-bearing carbon. This carbon must have been part of the C=O group in the starting material.

2. "Disconnect" one of the substituents attached to the carbon bearing the hydroxyl group.

3. These steps reveal the carbonyl-containing substrate and the Grignard (nucleophilic) component.

4. Check that you can indeed perform the forward reaction!
Other ways to disconnect bonds in a Grignard alcohol synthesis

\[
\begin{align*}
\text{Ph} & \quad \text{H}_3\text{C}-\text{C}=\text{H} \\
\text{OH} & \quad \rightarrow \\
\text{Ph} & \quad \text{H}_3\text{C}-\text{C}=\text{H} \\
\text{OH} & \quad \rightarrow
\end{align*}
\]

**Preparation of Alcohols**

1º, 2º and 3º alcohols can all be made by addition of an appropriate carbon nucleophile to an appropriate carbonyl compound (aldehyde or ketone). Accordingly, alcohols are useful synthetic intermediates. When performing a retroanalysis, consider the possibility of making the product from an alcohol, and how this alcohol can be made from smaller molecules using this approach.

\[
\begin{align*}
\text{Target molecule} & \quad \rightarrow \quad \text{alcohol} & \quad \rightarrow & \quad + \\
& & & \quad \text{Grignard or lithium reagent} & \rightarrow \quad \text{alkyl or aryl halide} \\
& & & \quad \text{aldehyde or ketone} & \rightarrow \quad \text{alcohol}
\end{align*}
\]
Preparation of 1° Alcohols

\[
\text{formaldehyde} \\ 1. \text{R-MgBr} \\
\quad \quad \rightarrow \\
2. \text{H}_2\text{O}
\]

\[
\text{ethylene oxide} \\ 1. \text{R-MgBr} \\
\quad \quad \rightarrow \\
2. \text{H}_2\text{O}
\]

Preparation of 2° Alcohols

\[
\text{aldehyde} \\ 1. \text{R-MgBr} \\
\quad \quad \rightarrow \\
2. \text{H}_2\text{O}
\]

Preparation of 3° Alcohols

\[
\text{ketone} \\ 1. \text{R-MgBr} \\
\quad \quad \rightarrow \\
2. \text{H}_2\text{O}
\]
Problem - Propose a synthesis of 2-methyl-2-hexanol from starting materials with four or fewer carbon atoms

Prob: 12, 19, 20, 21, 24
Restrictions on the use of Grignard, Lithium and Sodium Reagents

Lithium, magnesium and sodium reagents are very reactive as nucleophiles and bases, limiting other functional groups in these reagents.

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{MgBr} & \quad \text{Ph} & \quad \text{MgCl} & \quad \text{H}_3\text{C} & \quad \text{Li} & \quad \text{Ph} & \quad \text{Na} \\
\text{Magnesium} & \quad \text{Lithium} & \quad \text{Sodium}
\end{align*}
\]

Will react with the following functional groups. This means that we can not prepare them from any starting material containing these functional groups.

- OH
- NH₂
- NHR
- CO₂H
- SO₃H
- SH
- C=CH
- NO₂
- C≡N
- CH
- CR
- COR
- CNR₂

Protecting Groups in Synthesis

How would you achieve the following transformation?

\[
\begin{align*}
\text{Br} & \quad \text{H} & \quad \text{OH} & \quad \text{H}
\end{align*}
\]
LITHIUM DIAKLYCUPRATES IN COUPLING REACTIONS

Problem: Grignard and lithium reagents are strongly basic and promote elimination reactions with alkyl halides, e.g.

\[
\begin{align*}
\text{Br} & \quad \text{R} \quad \text{Li} \\
\end{align*}
\]

Solution: Use dialkylcuprates – they are much less basic, but still nucleophilic

\[
\begin{align*}
\text{Cu}^{-} & \quad \text{Li}^{+} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\end{align*}
\]

Preparation of cuprates

\[
\begin{align*}
\text{R-X} + 2\text{Li} & \rightarrow \text{RLi} + \text{LiX} \\
2\text{RLi} + \text{CuI} & \rightarrow \text{LiI} + \text{R}_2\text{CuLi} - \text{"Lithium dialkyl cuprate"} \\
\text{H}_3\text{G-Li} & \quad \text{Cu-I} \\
\text{R'-X} + \text{R}_2\text{CuLi} & \rightarrow \\
\end{align*}
\]

\[\text{R'}-\text{X}: \text{R'}=\text{Me}, 1^\circ, 2^\circ, \text{vinyllic, phenyl} \]

\[\text{R}_2\text{CuCl}: \text{R}=\text{Me}, 1^\circ, 2^\circ, 3^\circ,\]
Comparison of reactions of alkyl halides with dialkycuprates and alkyllithium reagents

\[
\text{Br} + \text{CH}_3\text{Li} \rightarrow
\]

\[
\text{Br} + (\text{CH}_3)_2\text{CuLi} \rightarrow
\]

Reactions of cuprates with \(sp^2\) C-halides

Vinyl halides

\[
\text{Br} \rightarrow \text{Et}_2\text{CuLi}
\]

Aryl halides

\[
\text{I} \rightarrow \text{Bu}_2\text{CuLi}
\]
ADDITION OF YLIDES TO ALDEHYDES AND KETONES: THE WITTIG REACTION

What is an ylide?

\[
\begin{align*}
\text{carbanion next to a positively charged heteroatom, most often phosphorous}
\end{align*}
\]

Preparation of phosphonium ylides

\[
\begin{align*}
(H)R\text{C}^\text{Br}^\text{H} & \quad \text{\textbullet PPh}_3 \\
R\text{H} & \quad \text{\rightarrow}
\end{align*}
\]
Wittig Reaction: General Reaction

\[ R_1 \text{O} + \text{Ph}_3\text{P} \to R_3 \text{H} \]

Example

Mechanism of Wittig Reaction
Alternate method - use of a phosphonate ester

Planning a Wittig Synthesis of an Alkene
There are always two possible routes to make an alkene by Wittig chemistry. How could you make 2-methyl-2-heptene?

Either C₅ or C₃ can be the carbonyl or ylide
Problem [Solomons 16.39] - The sex attractant of the female tsetse fly can be prepared by the following route. Identify compounds A-C.

\[
\text{BrCH}_2-(\text{CH}_2)_7-\text{CH}_2\text{Br} \quad 1. \text{2 eq. Ph}_3\text{P} \quad \text{A, C}_{45}\text{H}_{46}\text{P}_2 \quad \text{CH}_3(\text{CH}_2)_{11}\text{CH}_3 \quad \text{H}_2/\text{Pt} \quad \text{B, C}_{37}\text{H}_{72} \quad \text{C, C}_{37}\text{H}_{76}
\]

Other Reactions of Organometallic Reagents (covered later):

- RMgX + CO₂
- RMgX + ester
- RMgX + RCN
- RCu, R₂CuLi + RCOCl
SPECTROSCOPIC PROPERTIES OF ALDEHYDES AND KETONES

Compound A: contains C, H, Br and O

M⁺=184 and 186

positive Tollen’s test

IR 1690 cm⁻¹

¹H NMR singlet at δ 10.1, doublets at 8.1 and 7.5 ppm.
REVIEW OF CARBONYL CHEMISTRY: REACTIONS AND MULTISTEP SYNTHESIS

Reactions

Oxidation and Reduction

\[
\begin{align*}
\text{H} & \quad \text{[O]} \quad \text{[H]} & \quad \text{OH} & \quad \text{[O]} \quad \text{[H]} & \quad \text{O} \quad \text{[O]} \quad \text{[H]} & \quad \text{O} \\
R\text{CH}_2\text{H} & \quad \text{[H]} & \quad R\text{CH}_2\text{H} & \quad \text{[H]} & \quad R\text{C}H & \quad \text{[H]} & \quad R\text{C}OH
\end{align*}
\]

Nucleophilic addition

\[
\text{RCO} \quad \text{R}_1 \quad \text{R}_2 \quad + \quad \text{NuH} \quad \longrightarrow \quad \text{R}_2 \quad \text{Nu} \quad \text{OH}
\]
Mestanaol, a component of modern birth control pills, using organometallic addition to carbonyl groups?
Problem: How could you make 2-phenyl-2-butanol from benzene and any other starting materials with two or fewer carbon atoms.

OH

Problem: How could you make 1,4-diphenylbutane from PhCH₂CO₂CH₃?
Problem: How could you make 1,3-diphenylpropanone from benzene?

Problem: How could you make 1-phenyl1-butene from benzene?
Problem: How could you prepare the following two alcohols from 2-propanol?

\[ \text{OH} \quad \text{OH} \]

TOPIC 3 ON EXAM 3

Types of Questions
- Predict the products obtained from given starting materials,
- Rationalize the outcome of a reaction (i.e., propose a mechanism, draw key intermediates)
- Develop multistep synthetic strategies.

Do the problems in the book; they are great examples of the types of problems on the exam!

Preparing for Exam 3
- Get up-to-date NOW!
- Work as many problems as possible. Do the problems first, then consult the solutions manual.
- Work in groups, discuss chemistry, teach and test each other.
- Do the “Learning Group Problem” at the end of the chapter.
**Problem:** How would you make the following 2° alcohol?

\[
\text{Ph} - \text{OH} - \text{H} \rightleftharpoons \text{Ph} - \text{H} - \text{CO}_2\text{Et}
\]

Grignard and lithium reagents react with esters!

**Solution:** Organozinc reagents do not react with esters

\[
\text{Ph} - \text{CO}_2\text{Et} \quad + \quad \text{Ph} - \text{Br} - \text{CO}_2\text{Et} \\
\text{1. Zn, benzene} \quad \quad \text{2. water}
\]

via:

Why are esters less electrophilic than ketones?