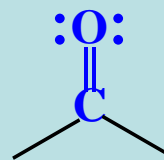


Chapter 16

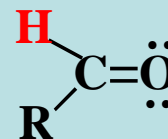
Aldehydes and Ketones I

Nucleophilic Addition to the Carbonyl Group

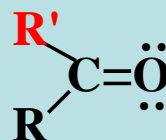
The general structure of the **carbonyl group** is



The general formula for an aldehyde is

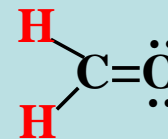


And that for a ketone is



The R groups can be either alkyl or aryl.

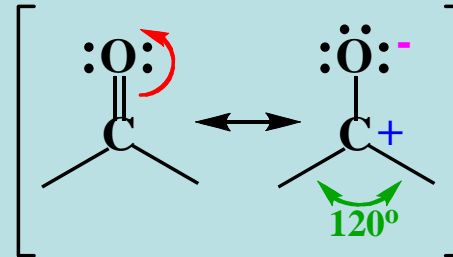
There is also the unique aldehyde, **formaldehyde**, in which there are two hydrogen atoms attached to the carbonyl group.



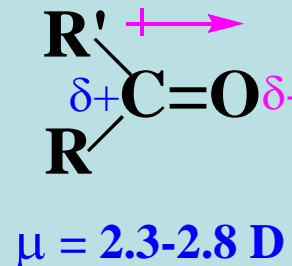
General Features of the Carbonyl Group

The contributing resonance structures are:

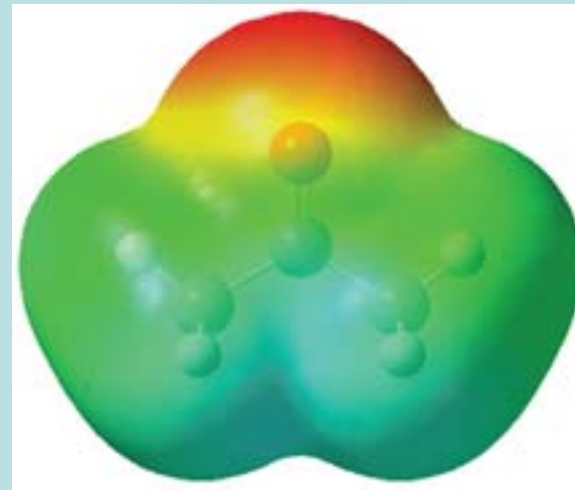
The carbon and oxygen atoms are both sp^2 hybridized.



The polarization of the double bond of the carbonyl group arises from the difference in electronegativities between C (2.5) and O (3.5).

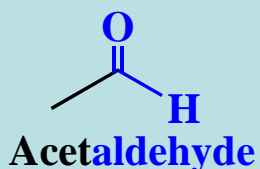
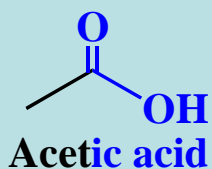


The $\text{C}=\text{O}$ bond polarization is clearly evident in this map of electrostatic potential for the simplest ketone, acetone (CH_3COCH_3).



Nomenclature of Aldehydes

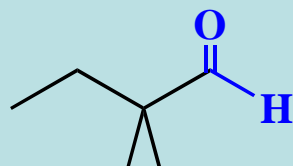
Common names are derived from those of the corresponding carboxylic acids by dropping the "(o)ic acid" and adding "aldehyde."



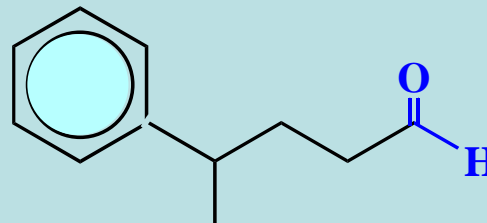
IUPAC (systematic) names are based on the following rules when the aldehyde function has priority and is named by use of a suffix.

- (1) Select the longest continuous chain containing the **-CHO** and use as the **parent** the name of the alkane of that chain length.
- (2) Replace "e" in the alkane name with "al."
- (3) Number from the end where the carbonyl group is located and follow all the other rules for locating substituent groups.

EXAMPLES:



2,2-Dimethylbutanal



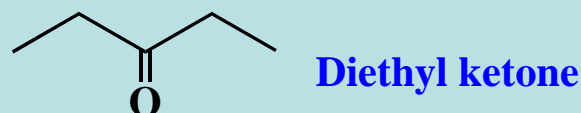
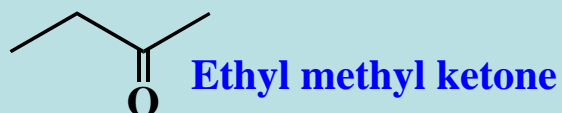
4-Phenylpentanal

Nomenclature of Ketones

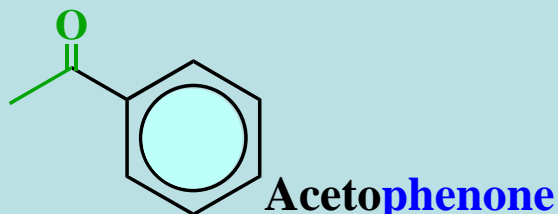
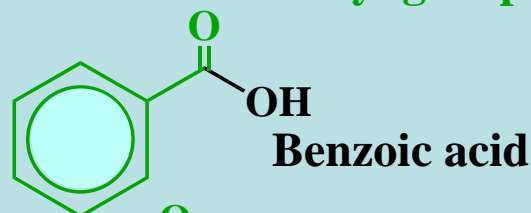
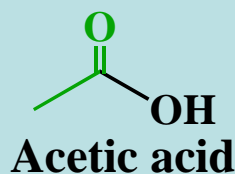
Common names are widely used for many of the simpler ketones.

Acetone, e.g., is the three carbon ketone: $\text{CH}_3\overset{\text{O}}{\parallel}\text{CCH}_3$

The common names of other aliphatic ketones are based on the **alkyl group names** for R and R' followed by "**ketone.**"

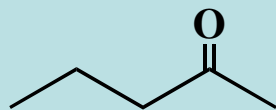


Common names of aryl ketones, where a benzene ring (phenyl group) is attached to the carbonyl, have a "**phenone**" ending. The prefix is derived from the carboxylic acid source of the **acyl group**.

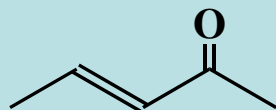


IUPAC systematic names for ketones are based on these rules:

- (1) The name of the longest alkane chain present that contains the carbonyl group is used as the **parent**.
- (2) Replace the "e" in the alkane name with the suffix "one" and indicate the carbonyl position by a number. Number from the end that gives the lower number to the ketone position.
- (3) Designate the substituents and their **positions** in the usual way.



2-Pentanone



(E)-3-Penten-2-one

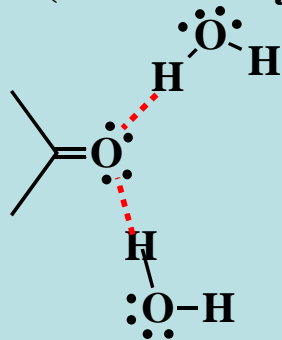
Note provision
for C=C bond.

Physical Properties of Aldehydes and Ketones

Because of the polar carbonyl group ($\mu \sim 2.3\text{-}2.8\text{ D}$), aldehydes and ketones have **higher boiling points than hydrocarbons** of comparable size. However, they have **lower boiling points than alcohols** of comparable size because only the latter have intermolecular hydrogen bonds.

$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$	$\text{CH}_3\text{CH}_2\overset{\text{O}}{\parallel}\text{CH}$	$\text{CH}_3\overset{\text{O}}{\parallel}\text{CCH}_3$	$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$
Butane	Propanal	Acetone	1-Propanol
MW 58	58	58	60
BP $-0.5\text{ }^\circ\text{C}$	$49.0\text{ }^\circ\text{C}$	$56.1\text{ }^\circ\text{C}$	$97.2\text{ }^\circ\text{C}$

Aldehydes and ketones form hydrogen bonds to water molecules and consequently the lower MW ones are **soluble in water** up to about C_6 . The smallest ones (formaldehyde and acetone) are miscible with water.

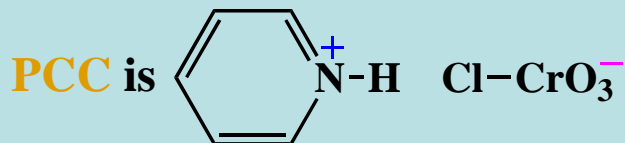
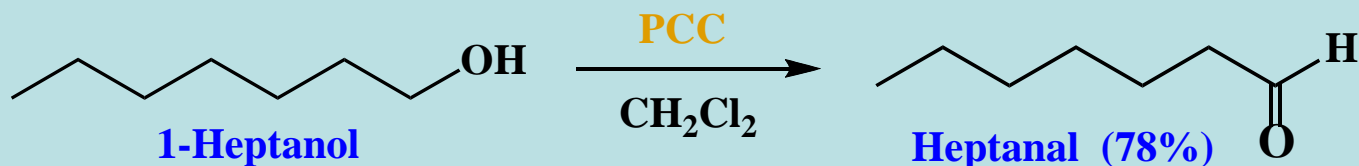


Synthetic Methods for Aldehydes

Because aldehydes are between 1° alcohols and carboxylic acids in the oxidation-reduction sequence, they can be synthesized by either **selective oxidation** of 1° alcohols or by **selective reduction** of carboxylic acid derivatives.



Selective Oxidation with Pyridinium Chlorochromate (PCC)



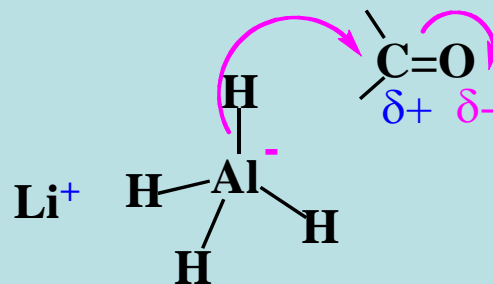
It is a unique **Cr +6** oxidant. Other oxidants carry oxidation on to the carboxylic acid stage because aldehydes are more easily oxidized than alcohols.

Reduction of Carboxylic Acids

Aldehydes can be prepared by **controlled** reduction of carboxylic acids. Acids can be reduced with **lithium aluminum hydride (LAH)**, a powerful reducing agent, but the process goes all the way to 1° alcohols.



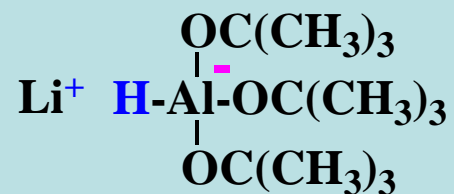
Lithium aluminum hydride (lithium tetrahydridoaluminate) and other metal hydride reducing agents, **transfer hydride ion (H⁻)** to the electropositive carbon of the carbonyl group.



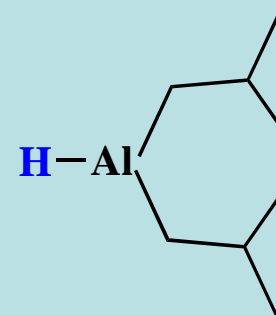
Selective Reductions by Metal Hydrides

Selective reduction of a carboxylic acid to an aldehyde can be achieved by first converting the acid to an acyl chloride (RCOCl) and then using a less powerful reducing agent.

Two selective reducing agents are:

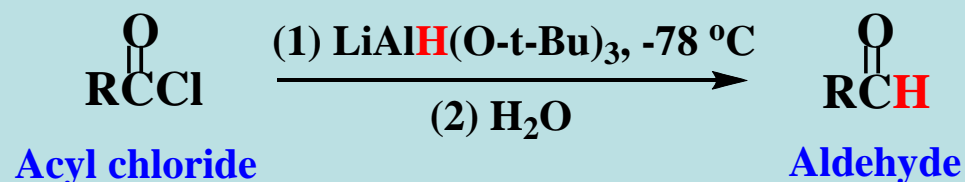


Lithium tri-*tert*-butoxyaluminum hydride

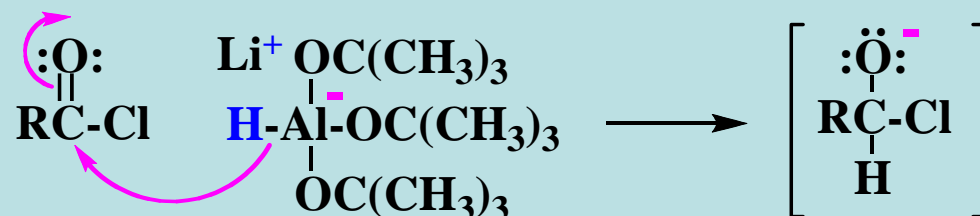


Diisobutylaluminum hydride
(*i*-Bu₂AlH or DIBAL-H)

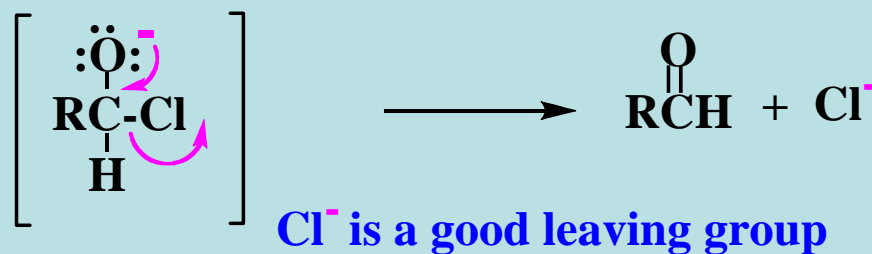
These reducing agents succeed in the controlled reduction:



Hydride Transfer Mechanism

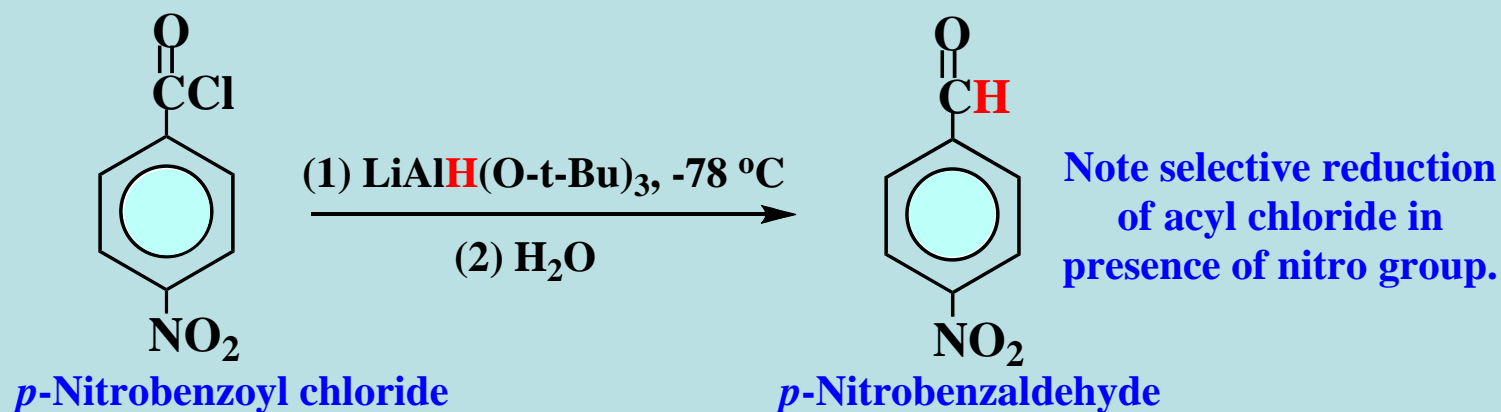


H^- is a nucleophile



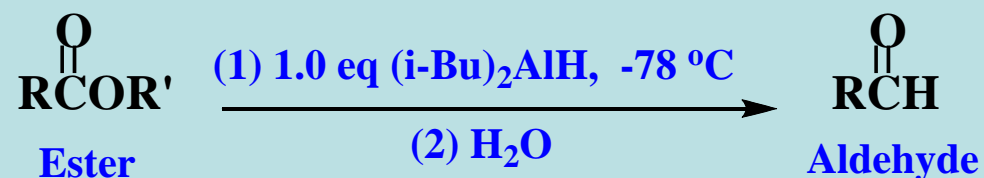
Cl^- is a good leaving group

A specific example:



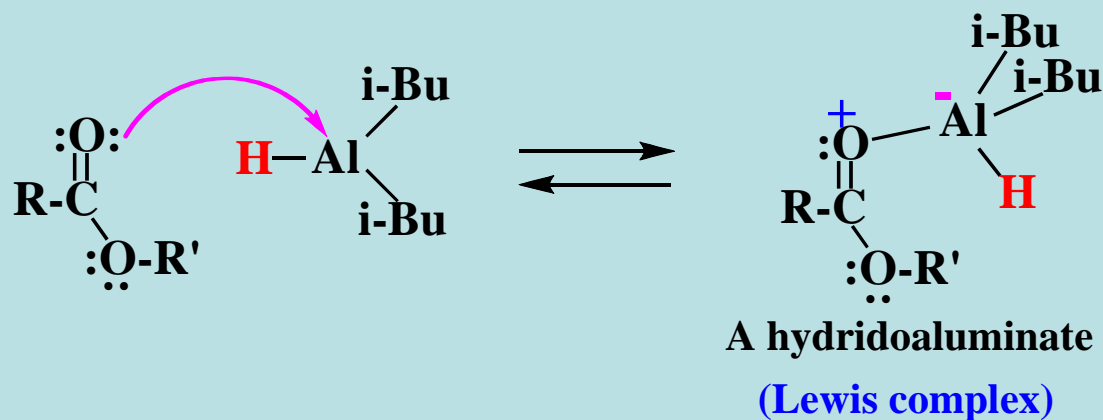
Reduction of Esters with DIBAL-H

Esters are selectively reduced to aldehydes with DIBAL-H when **one equivalent of the reducing agent** is used at low temperature.

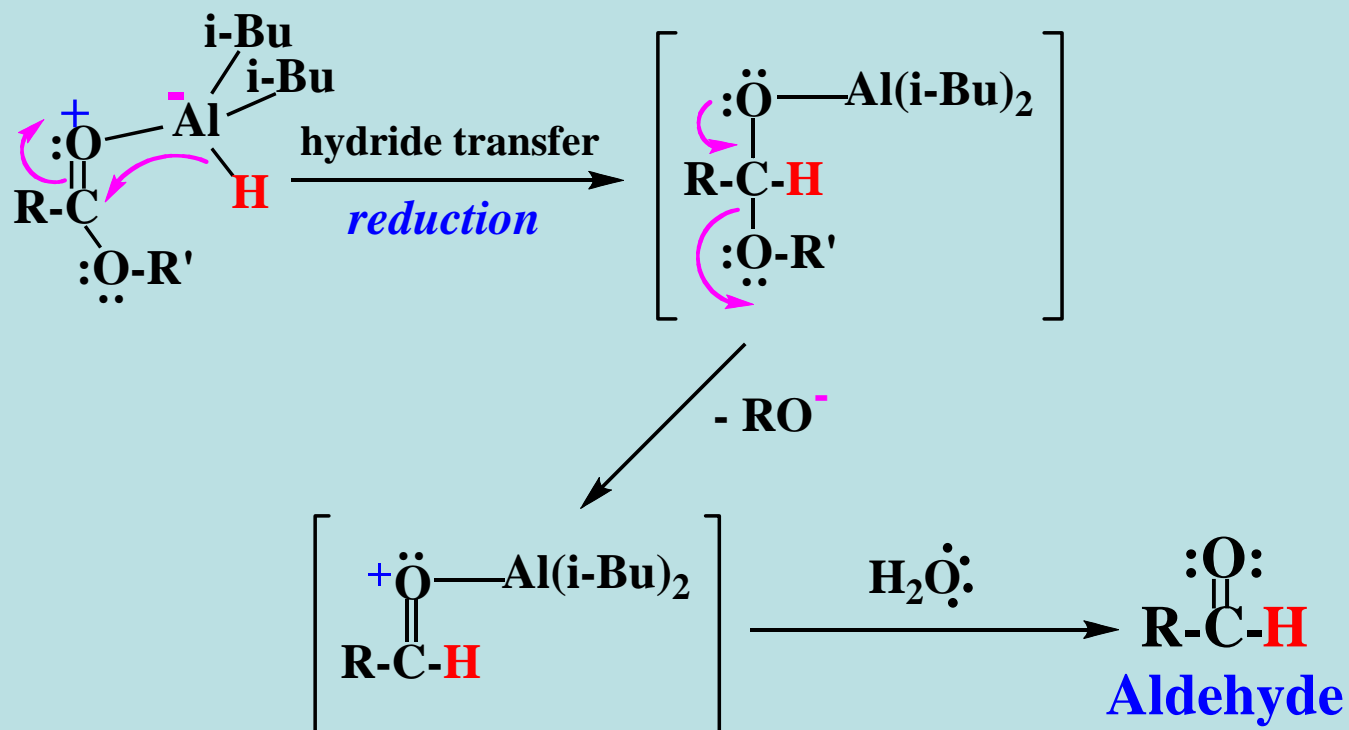


A Proposed Mechanism

DIBAL-H is a trivalent aluminum species and is **coordinatively unsaturated (i.e., a Lewis acid)**. The aluminum complexes with a nonbonding electron pair of the carbonyl oxygen:

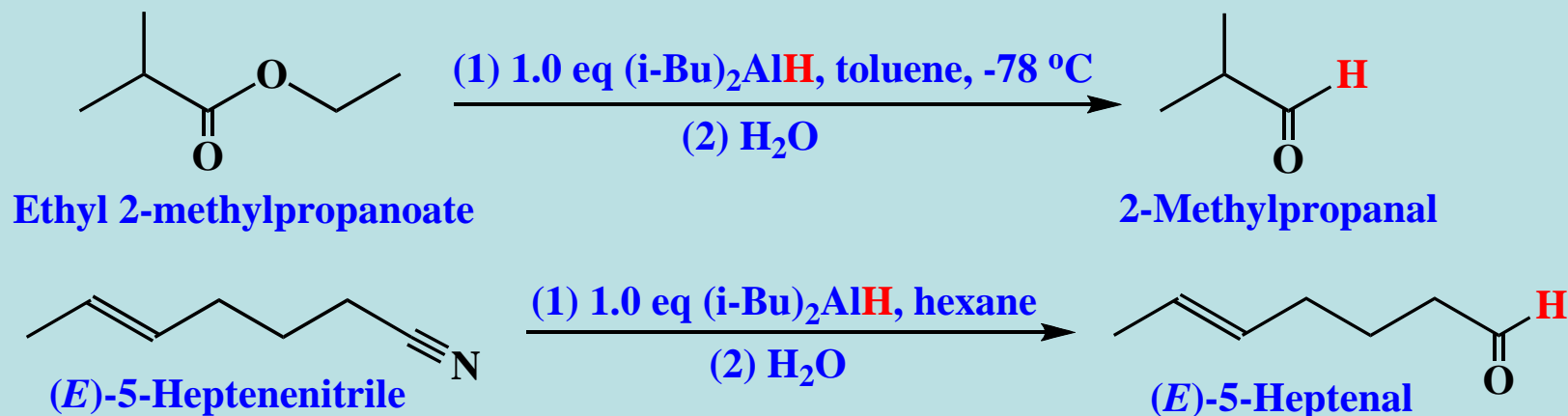


Hydride Transfer: Nucleophilic Addition to the Carbonyl

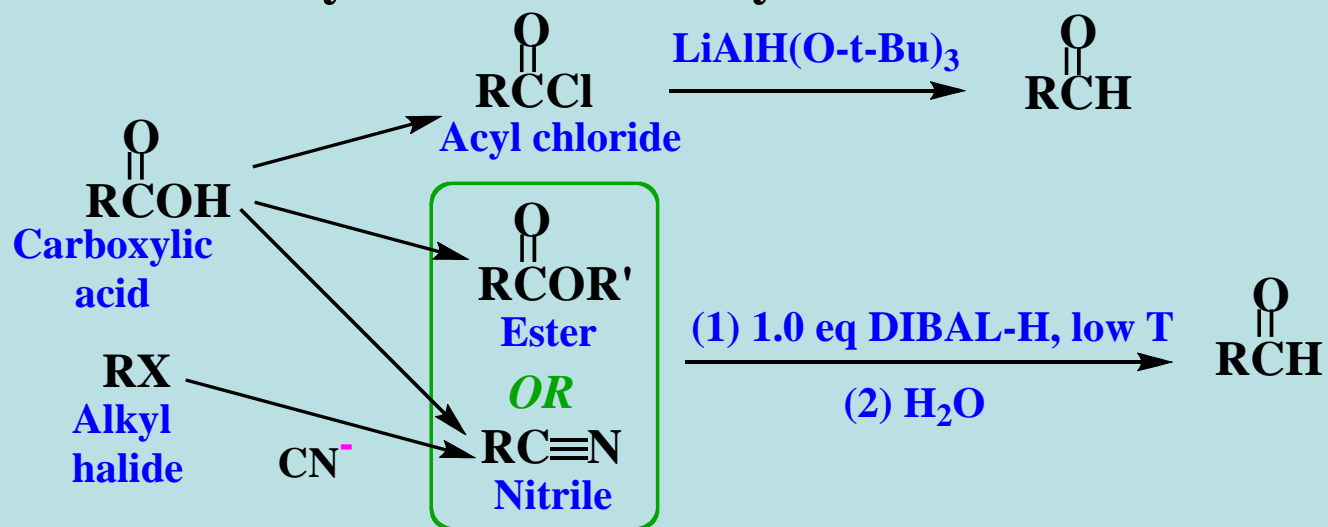


At higher temperature and with excess reagent, the aldehyde products are reduced to primary alcohols.

Ester and Nitrile Reductions by DIBAL-H

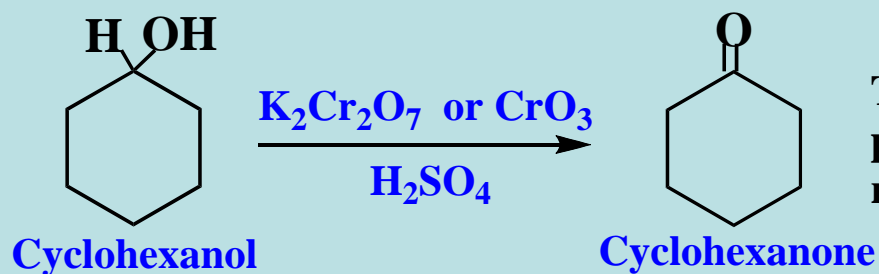


SUMMARY: General Synthetic Schemes for Reductive Synthesis of Aldehydes



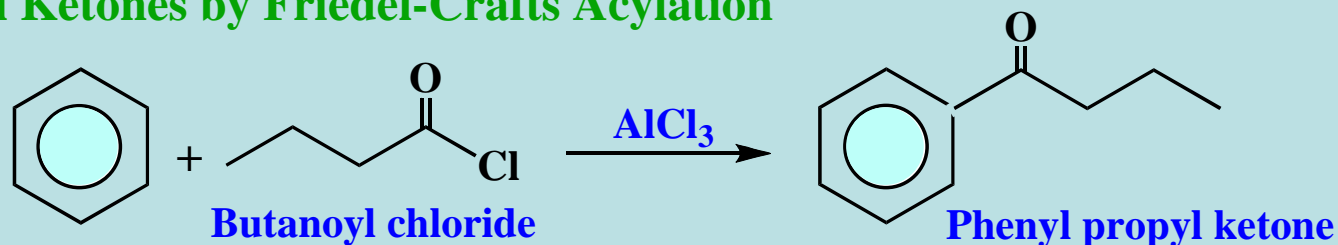
Ketone Syntheses

Oxidation of Secondary Alcohols

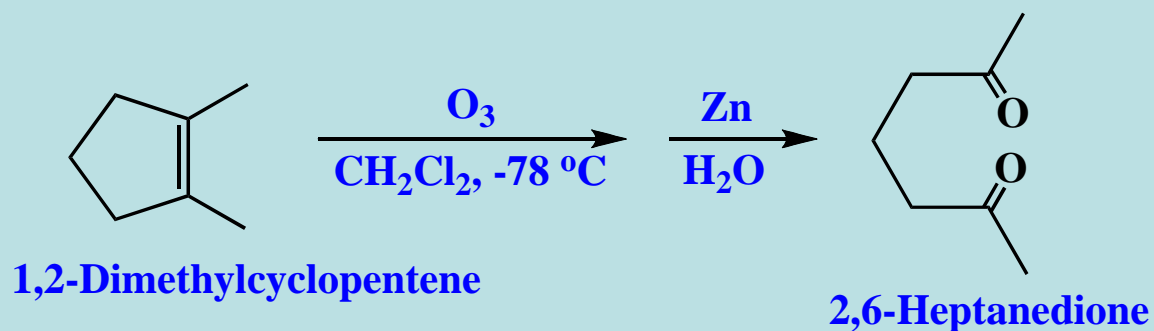


These oxidations generally proceed well with few side reactions.

Aryl Ketones by Friedel-Crafts Acylation

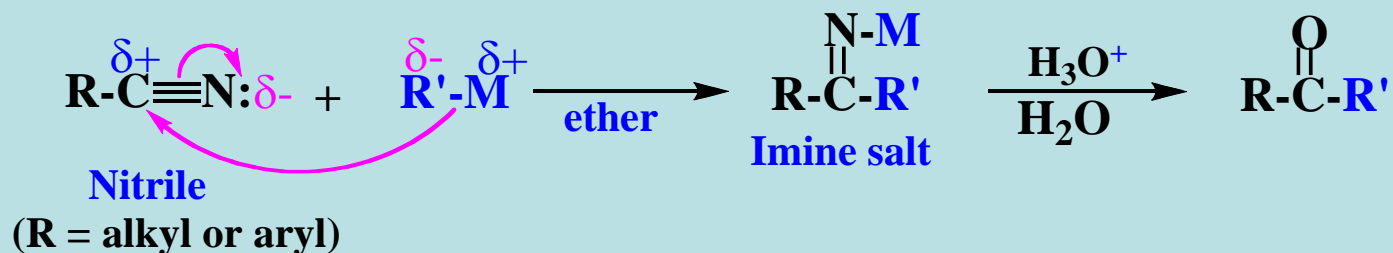


Ozonolysis of Alkenes



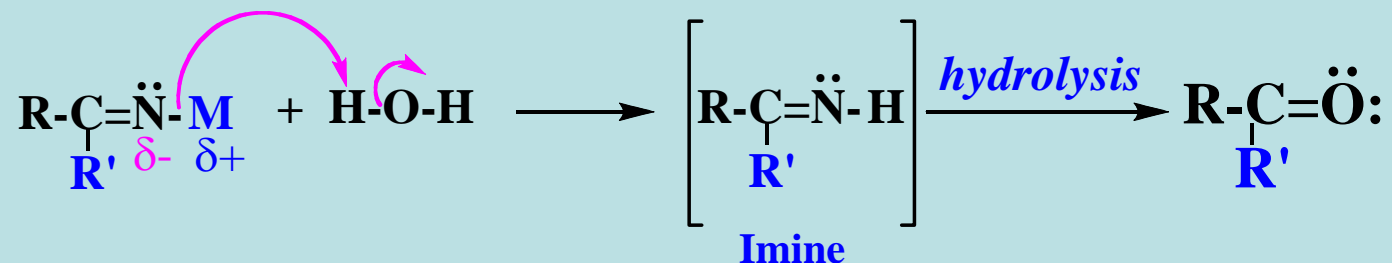
Ketones from Nitriles

Reaction of a **nitrile** with either a Grignard or organolithium reagent, followed by hydrolysis, yields a ketone.

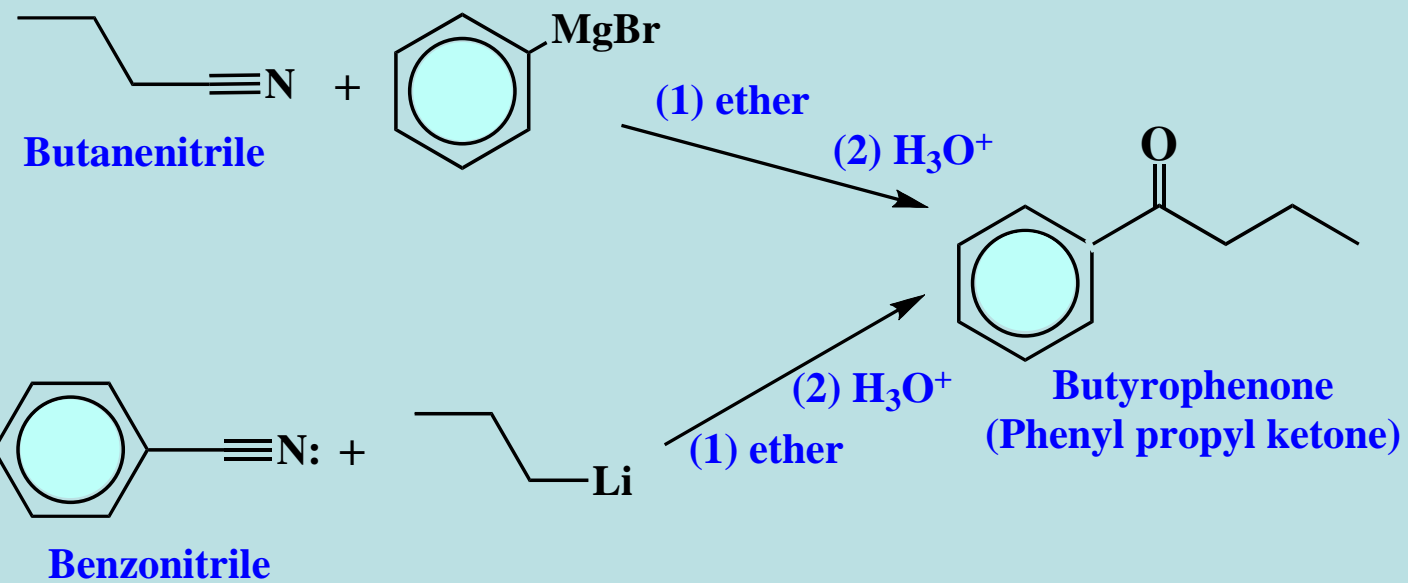


The nitrile is a **polar function** similar to a carbonyl. The carbanionic center of an organometallic reagent adds to the **electropositive carbon** of the nitrile producing the salt of an imine.

During aqueous workup, the imine is hydrolyzed to a ketone.

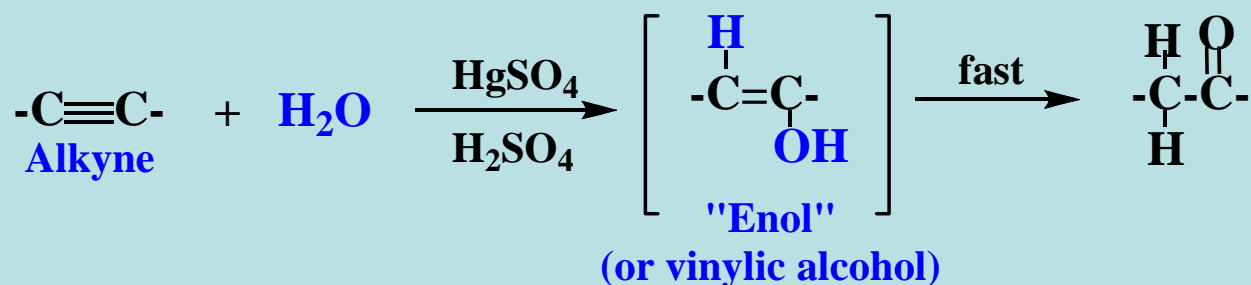


Examples

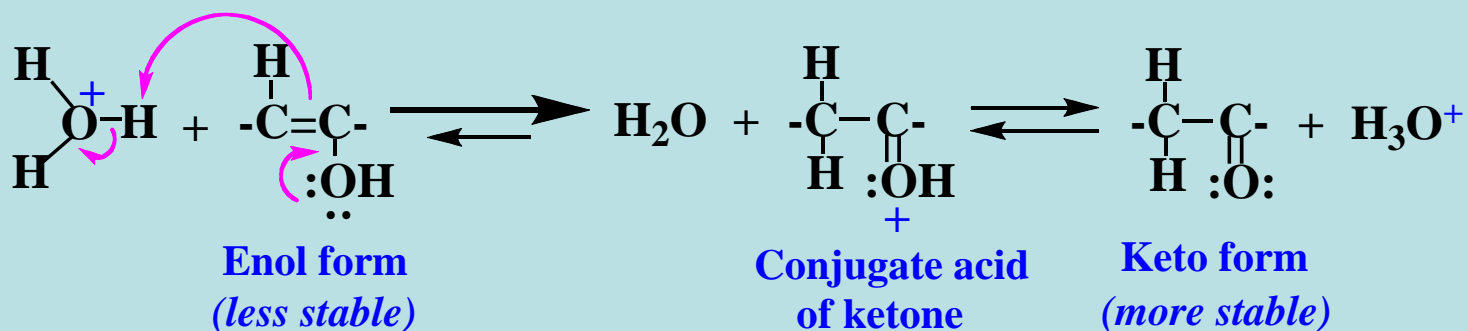


Ketones by Hydration of Alkynes

Alkynes, like alkenes, add water in the presence of electrophilic catalysts such as H^+ or Hg^{2+} . Hydration of alkynes is conducted in aqueous solutions of sulfuric acid with mercuric sulfate as catalyst. It follows Markovnikov's rule, with the hydrogen attaching to the carbon with the greater number of hydrogens.



The "enol" rapidly rearranges to the ketone. The enol and ketone constitutional isomers actually are connected by an equilibrium which usually lies heavily on the side of the ketone. This process called **tautomerization** is catalyzed by acid.



Designing a Multistep Synthesis by Retrosynthetic Analysis

Design a synthesis of **1-phenyl-2-butanone**.

