

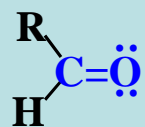
Chapter 12

ALCOHOLS FROM CARBONYL COMPOUNDS

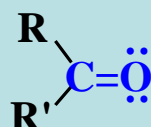
Oxidation-Reduction and Organometallic Compounds

INTRODUCTION

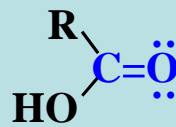
The **carbonyl group** is found in several classes of compounds. The principal types are:



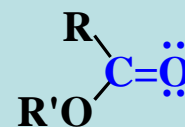
aldehyde



ketone

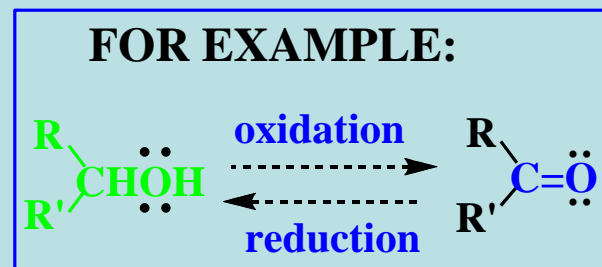


carboxylic acid

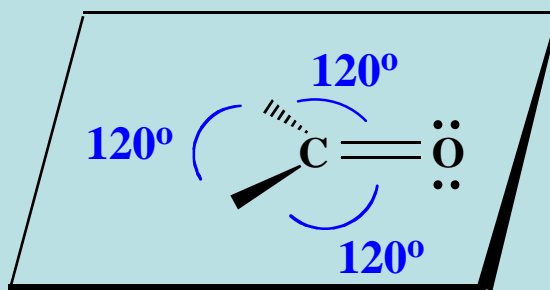
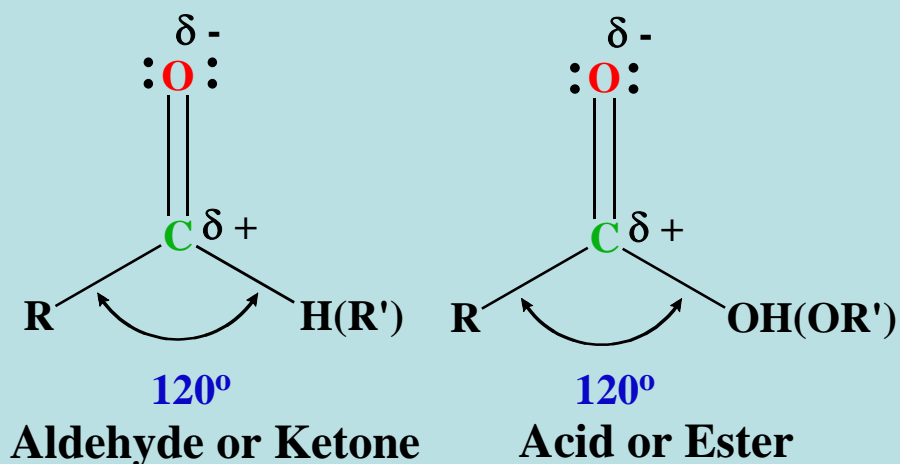


ester

Via one or more steps, these classes of compounds are interconvertible with **alcohols**.

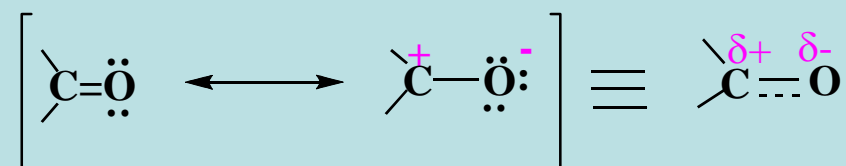


Important Types of Carbonyl Compounds; the Polarity of the Carbonyl Group



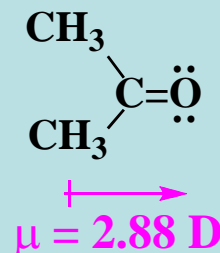
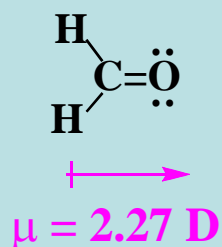
The carbonyl group
is locally planar.

Polarity and Reactivity of the Carbonyl Group



Resonance theory explanation of the polarity.

This polarity is indicated by the generally large **dipole moments** of carbonyl compounds.

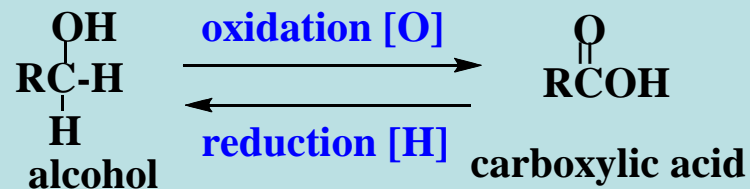


Oxidation-Reduction Reactions in Organic Chemistry

An **oxidation reaction** often can be recognized by an increase in oxygen content and/or a decrease in hydrogen content.

Similarly, a **reduction reaction** usually involves the opposite changes.

Example:



The symbol [H] means reduction and the symbol [O] means oxidation.

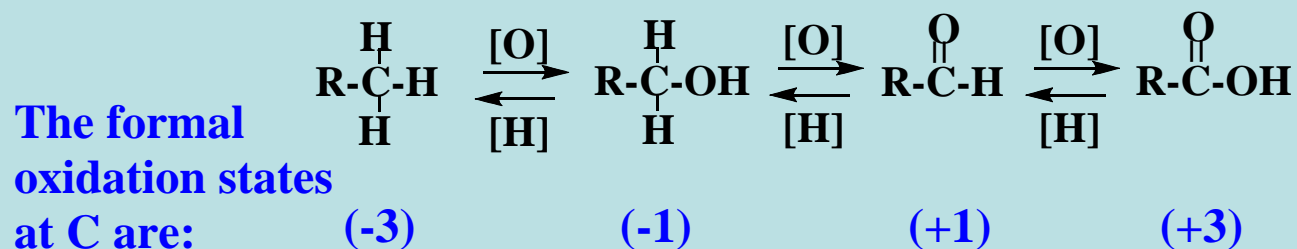
Alternatively, a formal oxidation state may be assigned to a carbon by **summing** the following:

For a bond to another carbon **0 (zero)**.

For a bond to H (or anything less electronegative than carbon) **-1**.

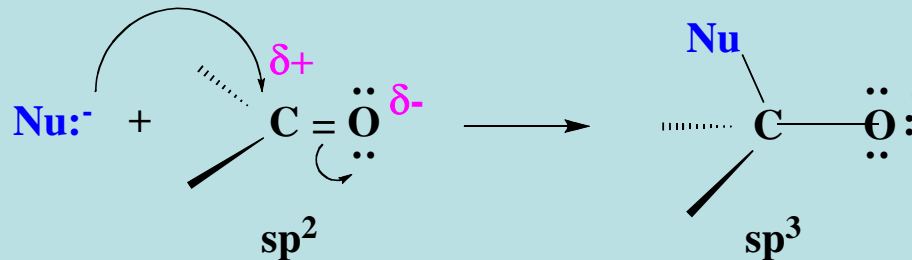
For a bond to a more electronegative atom than carbon (e.g., O, N, or halogen) **+1**.

Examples: For the sequences



Reactions of Carbonyl Compounds with Nucleophiles

Nucleophilic additions to the carbonyl function are common. The nucleophile (Nu^-) is attracted to the electropositive carbon and can attack from above or below the nodal plane.

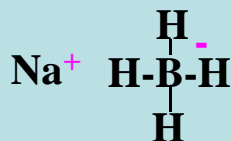


This nucleophilic attack shifts more π -electron density towards the electronegative oxygen.

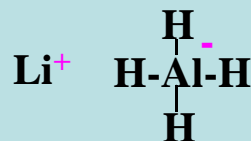
Hydride Ion and Carbanions as Nucleophiles



Hydride ions are readily available from **metal hydride reagents** like:

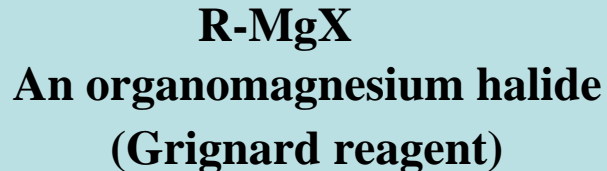


Sodium borohydride



Lithium aluminum hydride
(LAH)

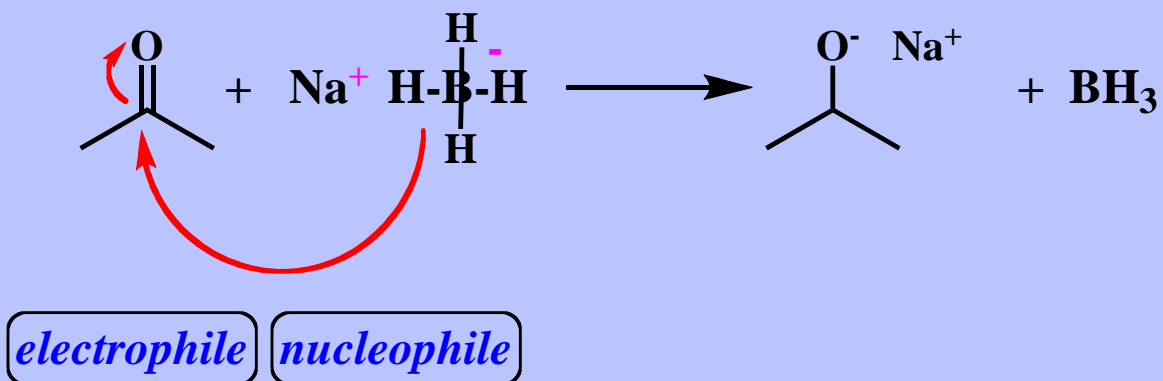
Carbanions are available from **organometallic reagents** such as:



The addition of a hydride ion or carbanion to a carbonyl group is formally a **reduction** of that function.

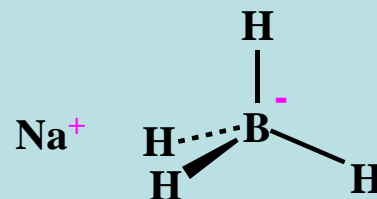
Quiz 12.01

In the following reaction, identify the nucleophile and electrophile and use curved arrows to show the movement of electron pairs.



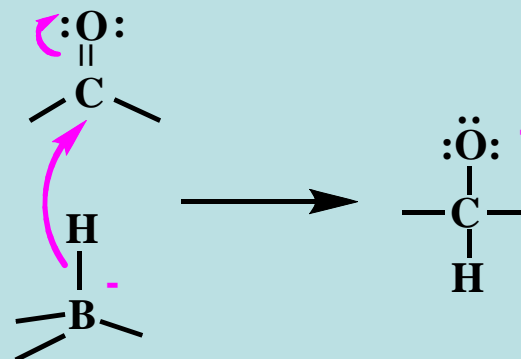
Reductions with Sodium Borohydride

Sodium borohydride (NaBH_4) is an ionic compound in which the anion has tetrahedral geometry.



It is a white crystalline solid, stable in dry air, insoluble in diethyl ether but soluble in water and methanol.

The borohydride anion is a source of **hydride ion** (H^-) in reduction reactions:

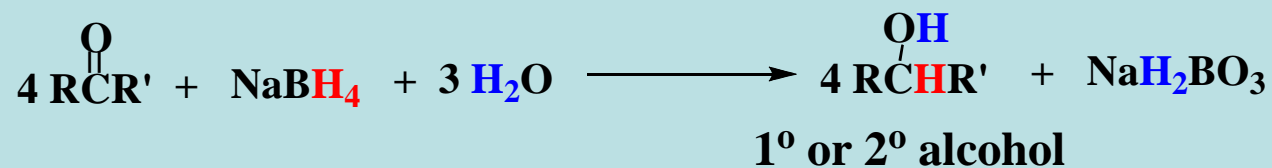


Because of the greater electronegativity of boron (compared with Al), the borohydride ion (BH_4^-) is more stable and **less reactive** than AlH_4^- .

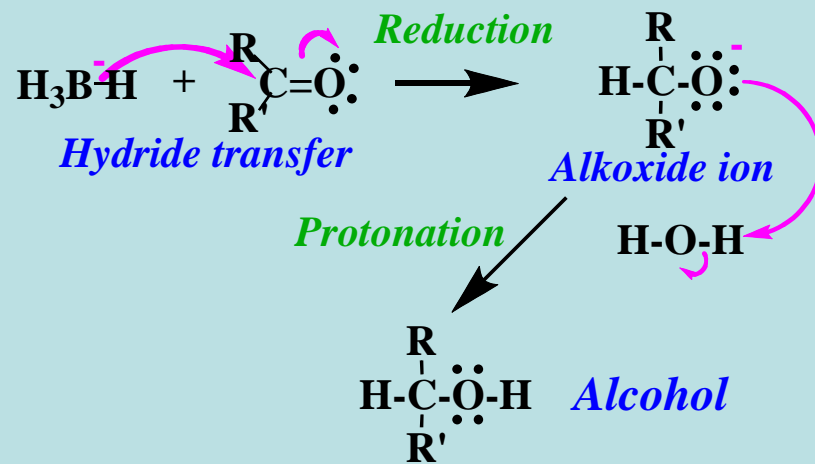
Key Observations about Sodium Borohydride Reductions:

- 1) NaBH_4 can be used in protic solvents because it abstracts protons from them (to form hydrogen) more slowly than it transfers hydride ions to aldehydes and ketones.
- 2) NaBH_4 is a **selective reducing agent**. It reduces aldehydes and ketones but not esters or carboxylic acids.
- 3) As with LiAlH_4 , all four H's may be transferred as hydride ions.

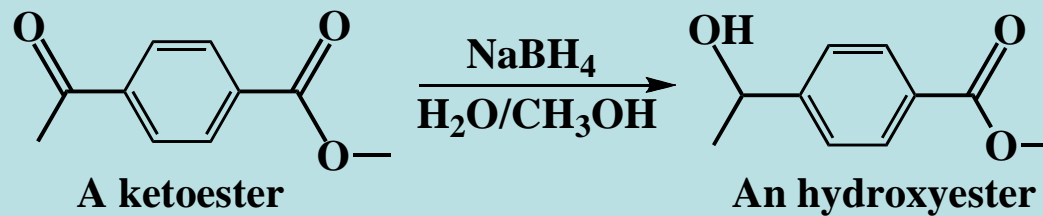
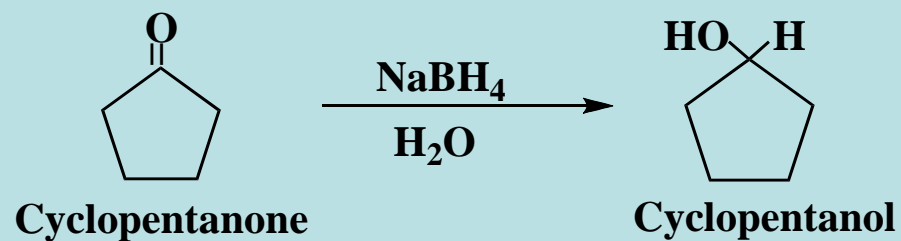
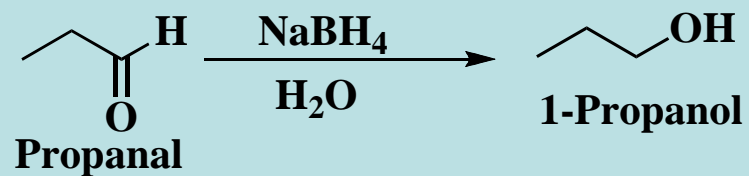
Overall Stoichiometry in Water



A Mechanism for Borohydride Reduction



Examples of Reduction by Sodium Borohydride

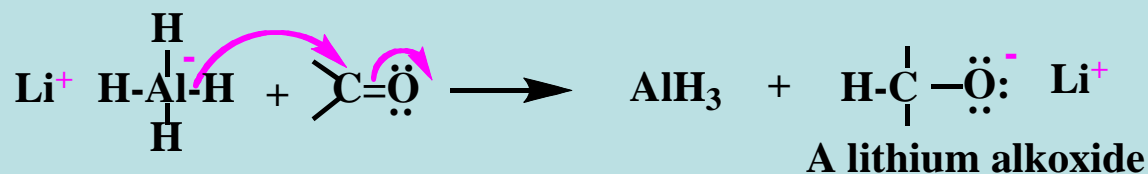
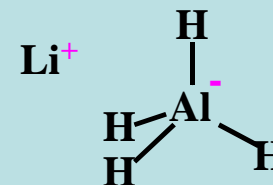


Selective reduction

Lithium Aluminum Hydride

Another important reducing agent is lithium aluminum hydride (LiAlH_4). Often referred to as "**LAH**", it is a nearly universal reducing agent for carbonyl compounds and also reduces many other functional groups by hydride transfer.

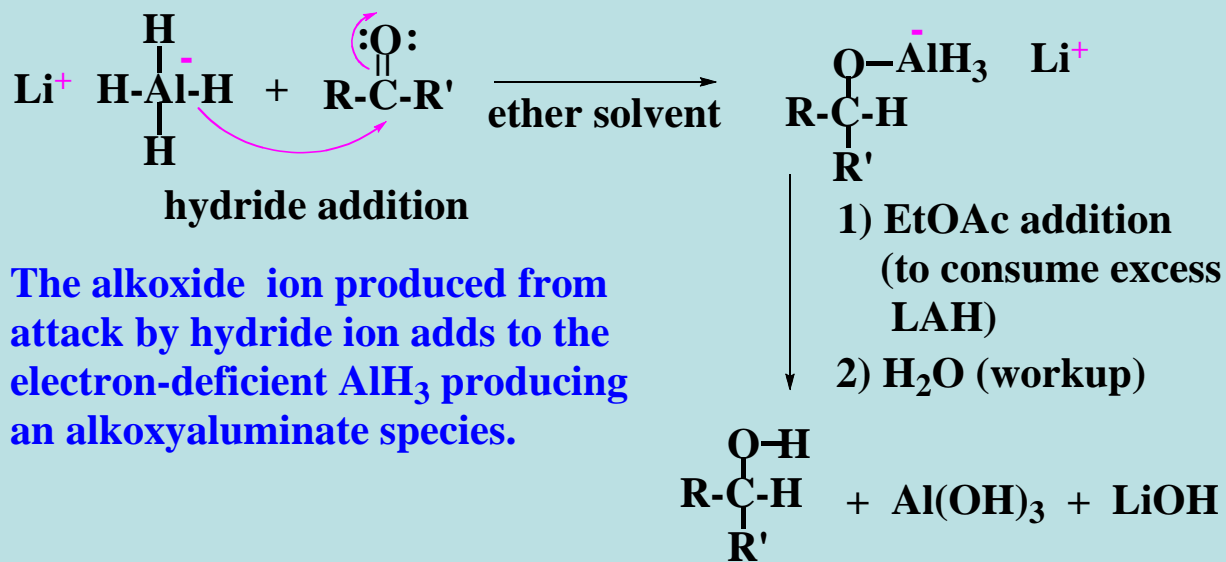
It is a nearly white, non-volatile crystalline solid soluble in various ethers, which are the usual reaction solvents.



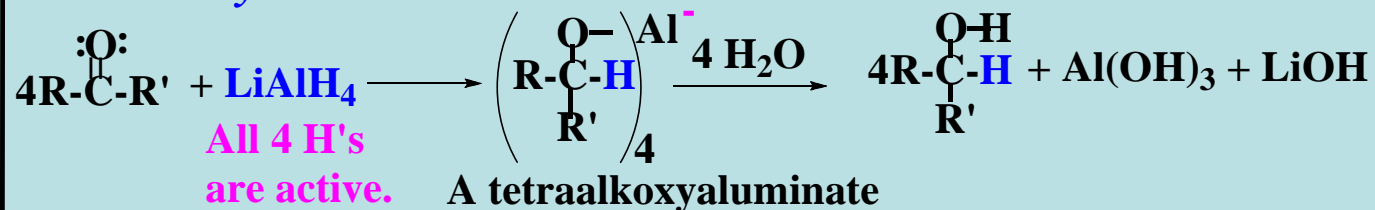
CAUTION: LAH reacts explosively with water and low molecular weight alcohols.

Reactions of Lithium Aluminum Hydride

With ALDEHYDES and KETONES

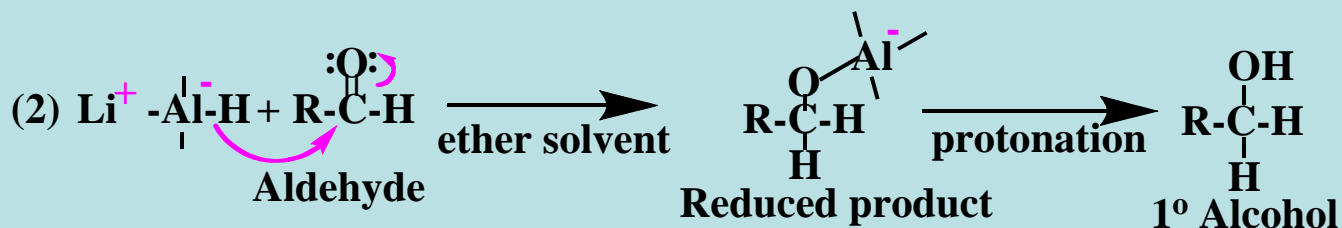
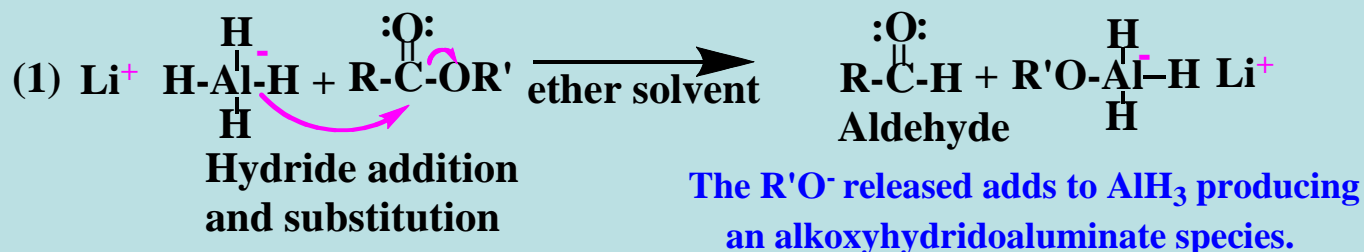


Stoichiometry

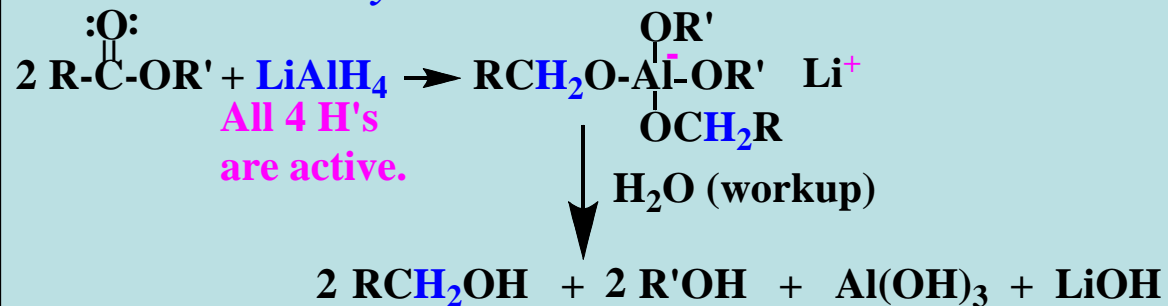


Reactions of Lithium Aluminum Hydride

With ESTERS: A Two-stage Reduction



Overall Stoichiometry



Reactions of Lithium Aluminum Hydride

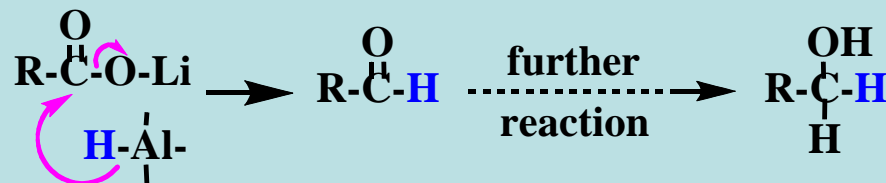
With CARBOXYLIC ACIDS

As with esters, carboxylic acids are reduced to primary alcohols. A fast, initial acid-base reaction gives the carboxylate salt.

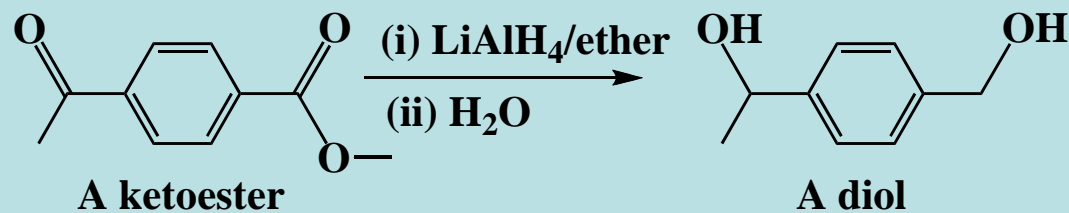
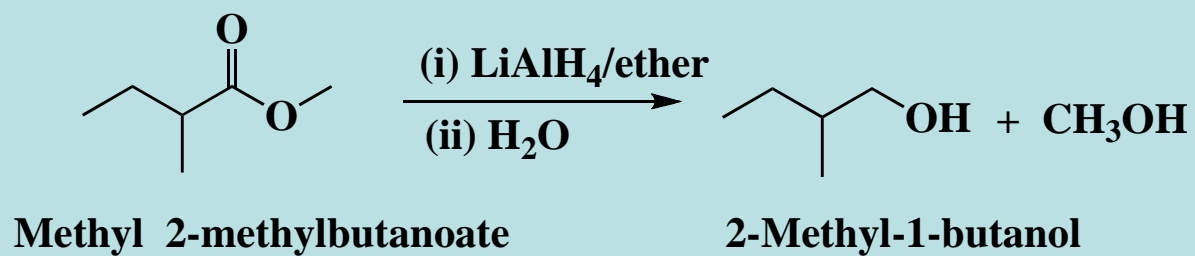
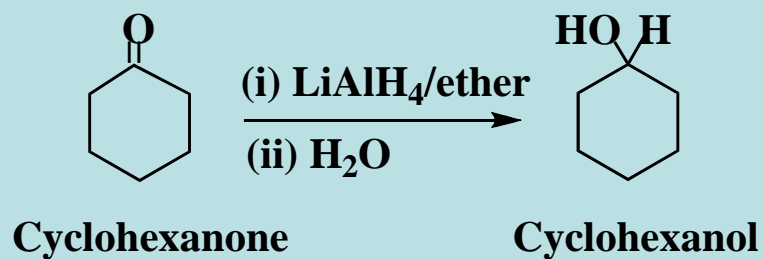


The salt can be reduced by the remaining LAH, but the reaction generally proceeds in low yield because of low solubility in the ether solvent. It is usually worthwhile doing a preliminary esterification of the carboxylic acid.

The key reduction step may occur via:

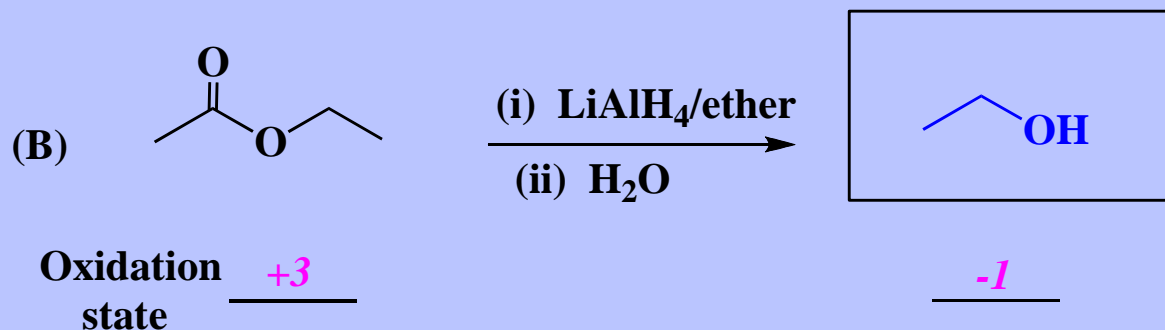
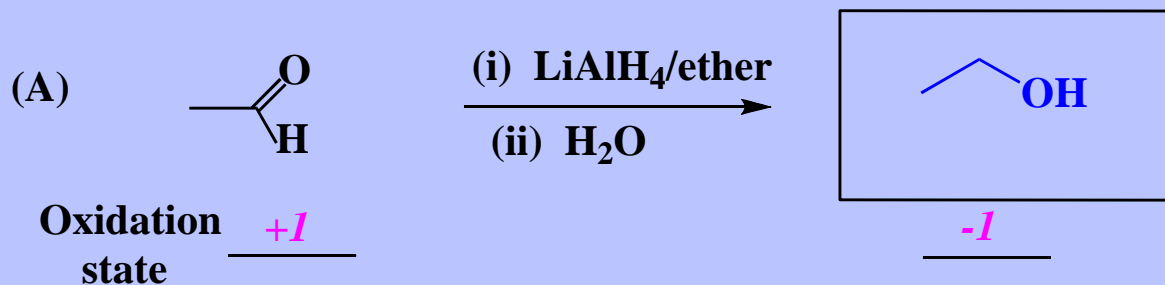


Examples of LAH Reductions



Quiz 12.02

Provide the organic products of the two reactions below. Assign formal oxidation states to the reacting carbon centers in the starting materials and the products.

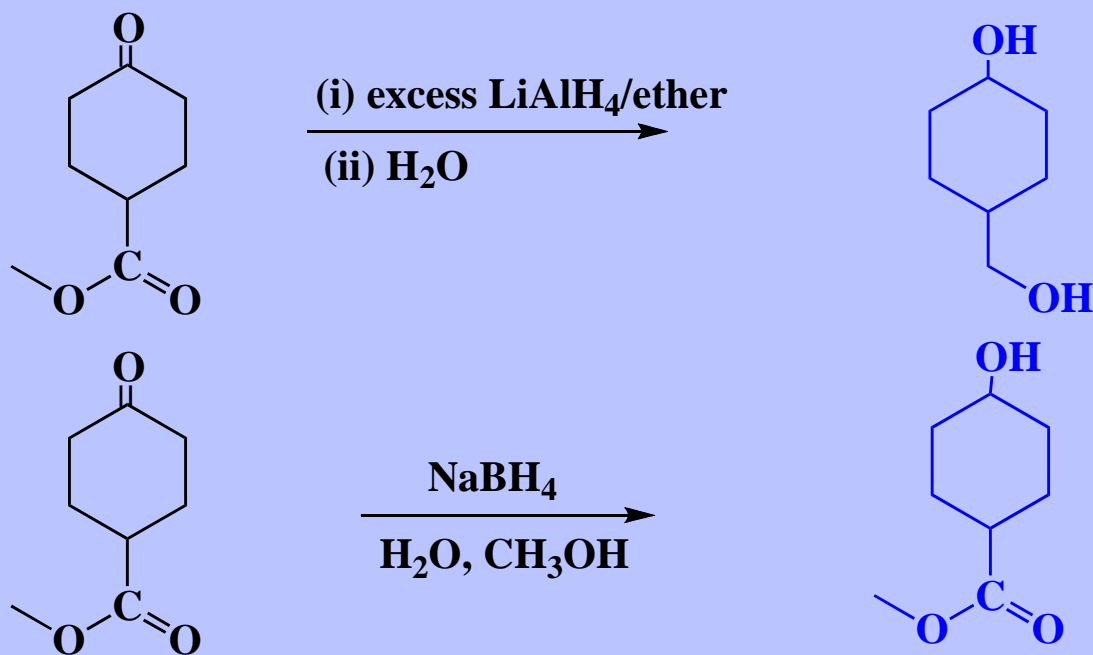


How many equivalents of hydride (H^-) are consumed in each reaction?

- (A) one
(B) two

Quiz 12.03

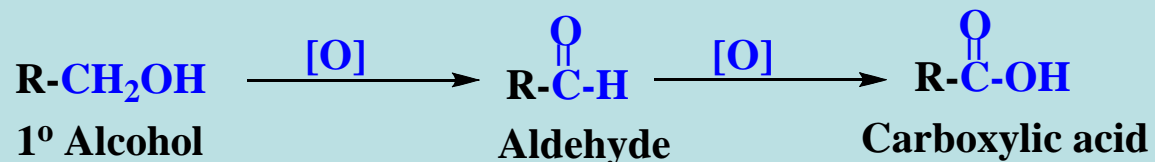
Provide the organic products of the following metal hydride reductions.



Oxidation of Alcohols

Primary Alcohols

Primary alcohols undergo stepwise oxidation to aldehydes and then carboxylic acids:

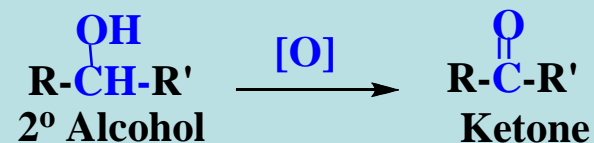


Selective Oxidation

Selective oxidation of a 1° alcohol to an aldehyde is difficult because aldehydes tend to undergo oxidation faster than primary alcohols. However, there are methods for carrying out this transformation.

Oxidation of Secondary Alcohols to Ketones

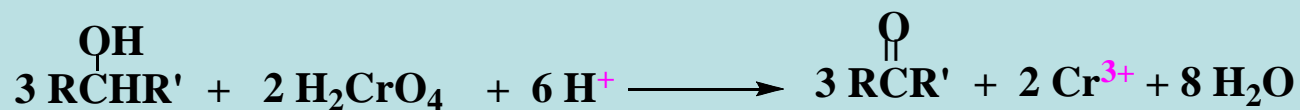
2° Alcohols are easily oxidized to ketones by a variety of reagents in good yields.



Chromium VI Reagents

Common oxidants are chromium VI reagents such as **potassium dichromate** ($\text{K}_2\text{Cr}_2\text{O}_7$), **sodium dichromate** ($\text{Na}_2\text{Cr}_2\text{O}_7$), and **chromium trioxide** (CrO_3). In sulfuric acid solution, all of these reagents yield chromic acid (H_2CrO_4), which is the actual oxidant.

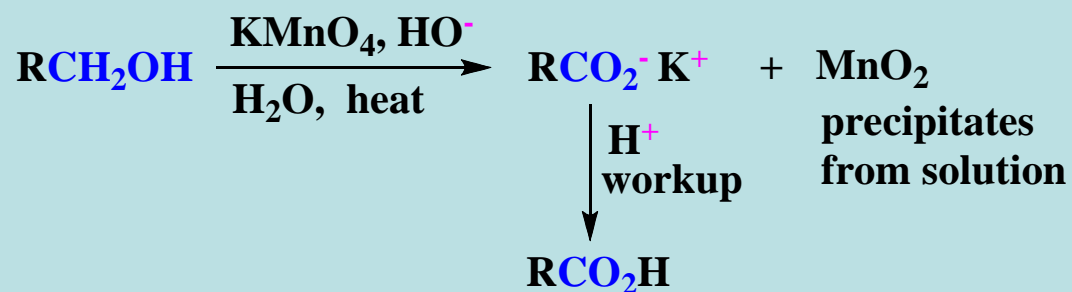
Stoichiometry



These oxidations typically are fast, even at about room temperature. Because of this and the very distinctive color change during the redox reaction as Cr^{VI} (**orange**) changes to Cr^{III} (**green**), the oxidant solution can be slowly titrated into the reaction mixture until one equivalent has been added.

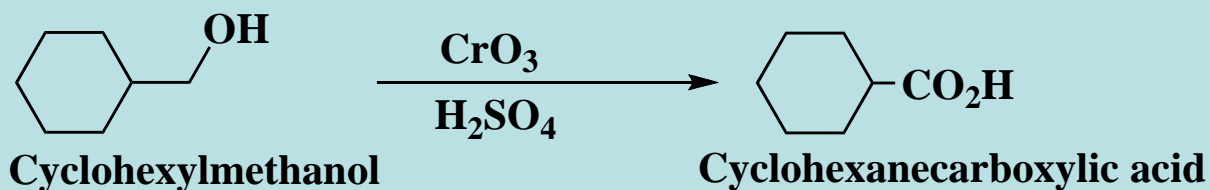
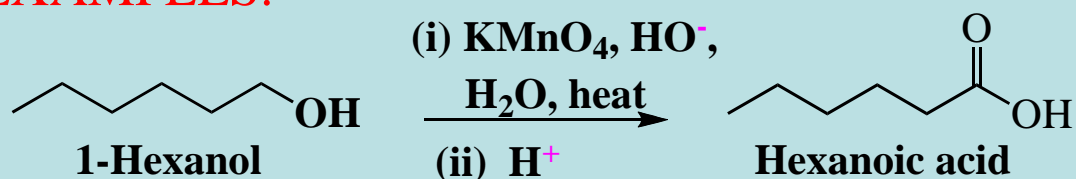
Oxidation of Primary Alcohols to Carboxylic Acids

A good reagent for oxidizing 1° alcohols to carboxylic acids is **potassium permanganate, KMnO_4** . In aqueous basic solutions, MnO_2 precipitates as the oxidation proceeds. The oxidation product is in solution as the carboxylate salt. The carboxylic acid is recovered by acidification.



Good yields are also obtained with Cr VI reagents in aqueous H_2SO_4 .

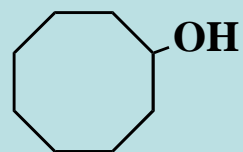
EXAMPLES:



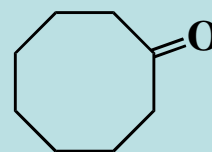
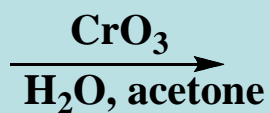
The Jones Oxidation

The **Jones oxidation** is a milder version of chromate oxidation in which chromium trioxide (CrO_3), a red solid, is used in aqueous acetone at room temperature.

Example



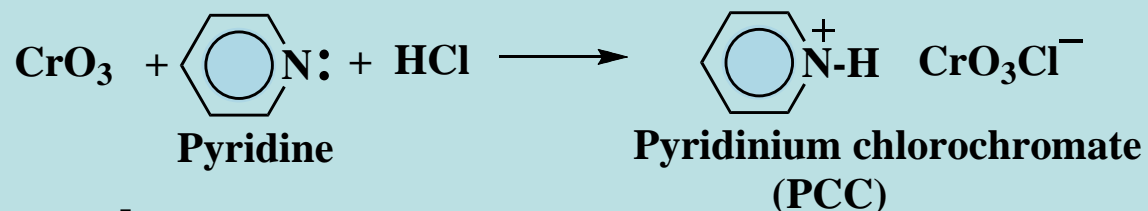
Cyclooctanol



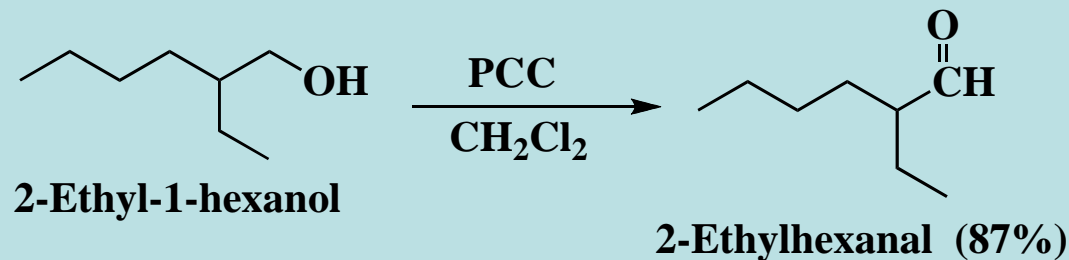
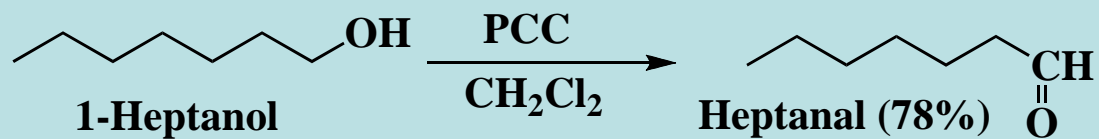
Cyclooctanone
(yield ~95%)

Selective Oxidation with Pyridinium Chlorochromate (PCC)

The oxidation of 1° alcohols to aldehydes may be accomplished with a reagent in which **chromium trioxide** (CrO_3) is complexed with **pyridine** and **HCl** in dichloromethane, CH_2Cl_2 . The resulting reagent is called **pyridinium chlorochromate**.



Examples



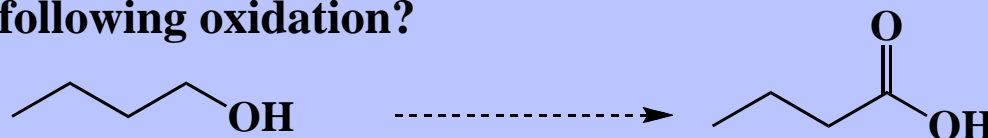
Why is PCC a selective reagent?

Summary of Oxidation Reactions

ALCOHOL	REAGENT	PRODUCT
RCH_2OH	PCC	$\text{R}\overset{\text{O}}{\parallel}\text{CH}$
RCH_2OH	$\text{H}_2\text{CrO}_4/\text{H}_2\text{SO}_4$ $\text{KMnO}_4/\text{HO}^-/\text{H}_2\text{O}$	RCO_2H
$\text{R}\overset{\text{OH}}{\parallel}\text{CHR}'$	$\text{H}_2\text{CrO}_4/\text{H}_2\text{SO}_4$ $\text{CrO}_3/\text{H}_2\text{O}$, acetone	$\text{R}\overset{\text{O}}{\parallel}\text{CR}'$
$\text{R}\overset{\text{OH}}{\parallel}\text{CR}''$ R'	No oxidation	

Quiz 12.04

Which of the following reagents will accomplish the following oxidation?



**CrO₃ in aqueous
H₂SO₄, heat**

PCC in CH₂Cl₂

**(i) KMnO₄, KOH in H₂O, heat
(ii) H₃O⁺**

Only the first and the third reagent systems.