

Chemistry 0310 - Organic Chemistry 1

Chapter 8. The Hydroxy Functional Group & Alcohols

Alcohols can act both as acids as well as bases; the relevant pK_a 's for MeOH are 15.5 and -2.2 , respectively. The introduction of electron-withdrawing groups can increase or decrease these values.

The synthesis of alcohol proceeds by way of S_N1 AND S_N2 reactions from halides or sulfonates. In order to reduce the amount of elimination side products, carboxylic acid salts can be used for their higher nucleophilicity, and the resulting esters can be cleaved to the desired alcohols by treatment with aqueous NaOH, a process known as saponification.

Another major route toward alcohols uses the reduction of carbonyl compounds. $LiAlH_4$ (LAH) and $NaBH_4$ are the most common reducing agents and can donate 4 hydride ions each to a suitably electrophilic acceptor $C=O$. Organometallic agents such as organolithium and organomagnesium (Grignard) derivatives follow very similar mechanisms to hydride additions and provide a third major pathway to alcohols. The reverse reaction to reduction is oxidation. Important oxidizing agents are PCC (pyridine, HCl, and CrO_3), Jones reagent (CrO_3/H_2SO_4 in acetone), and $KMnO_4$.

The following table gives a brief summary of the reactions between major classes of functional groups and reducing, oxidizing, and organometallic agents (A/B = acid/base reaction = simple proton transfer; - = no reaction). Mechanisms of these processes are provided in lecture notes and in the textbook.

Substrate →	<u>RCH₂OH</u>	<u>RR'CHOH</u>	<u>RR'R''COH</u>	<u>RCHO</u>	<u>RCOR'</u>	<u>RCO₂R'</u>	<u>RCO₂H</u>
Reagent ↓							
LAH	A/B	A/B	A/B	RCH ₂ OH	RR'CHOH	RCH ₂ OH + HOR'	RCH ₂ OH
NaBH ₄	A/B	A/B	A/B	RCH ₂ OH	RR'CHOH	-	A/B
PCC	RCHO	RCOR'	-	-	-	-	-
CrO ₃ /H ₂ SO ₄	RCOOH	RCOR'	-	RCOOH	-	-	-
R*-Li	A/B	A/B	A/B	RR*CHOH	RR'R*COH	RR'R*COH + HOR'	RCOR*
R*-MgX	A/B	A/B	A/B	RR*CHOH	RR'R*COH	RR'R*COH + HOR'	A/B

Organometallic reagents can be prepared from the corresponding organohalides and Li or Mg metal. Another important pathway is proton transfer to generate an organometallic compound of decreased basicity from a derivative of higher basicity. The differential reactivity of different reducing, oxidizing, and organometallic agents allows the selective bond formation and structure manipulation, a strategy that is employed in the process of **retrosynthetic analysis**.

Retrosynthesis is the process of “deconstructing” a target molecule into readily available starting materials by means of

- imaginary breaking of bonds (*disconnections*) and by the
- conversion of one functional group into another (*functional group interconversions*).

