
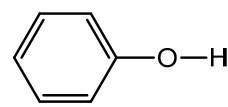


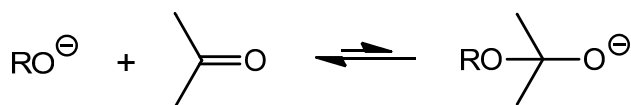
Acidity of Alcohols

	<u>alcohol</u>	<u>pK_a</u>	
water	HO—H	15.7	
methanol	CH ₃ O—H	15.5	
ethanol	CH ₃ CH ₂ O—H	15.9	
<i>iso</i> -propanol	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}-\text{O}-\text{H} \\ \\ \text{CH}_3 \end{array}$	16.5	
<i>tert</i> -butanol	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{C}-\text{O}-\text{H} \\ \\ \text{CH}_3 \end{array}$	18.0	$\rightleftharpoons \begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3-\text{C}-\text{O}^\ominus \\ \\ \text{CH}_3 \end{array} + \text{H}^\oplus$
phenol		10.0	<p>$\ominus\text{O}t\text{Bu}$ is 200 times more basic than $\ominus\text{OH}$.</p>

Increasing substitution pushes electron density onto oxygen, decreases acidity.

Nucleophilic Addition to Carbonyls

Heteroatom electron donors add reversibly to C=O groups.

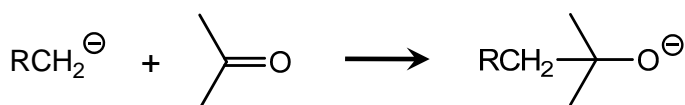


true for Cl[⊖], HS[⊖], NH₃...

Equilibrium driven to the left by:

- strength of C=O double bond
- entropy

Carbon anions add irreversibly to C=O groups.



true for all carbon anions.

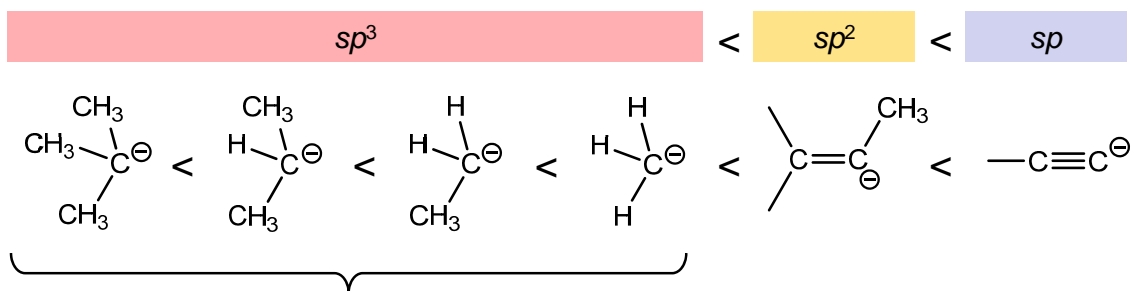
Reaction driven to the right by:

- instability of charge on RCH₂[⊖]

Relative Stabilities of Carbanions

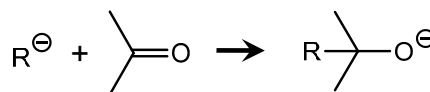
least stable,
most reactive

most stable,
least reactive

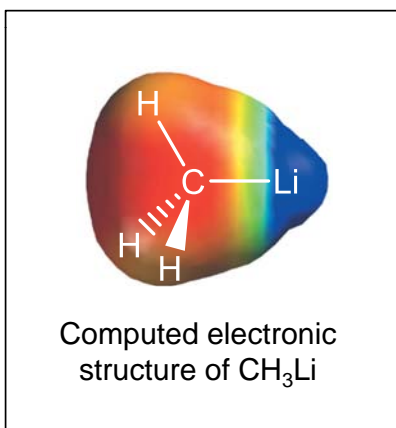


Increasing substitution pushes electron density onto carbon, destabilizes anion (and makes it more basic, and more reactive).

All of these anions add irreversibly to carbonyls,



Organometallic Reagents are Synthetically Equivalent to Carbanions



$\text{R}-\text{Li}$ alkyllithium (organolithium)

$\text{R}-\text{Mg}-\text{Br}$ Grignard reagent (organomagnesium halide)

$\text{R}-\text{C}\equiv\text{C}-\text{Na}$ alkynylsodium

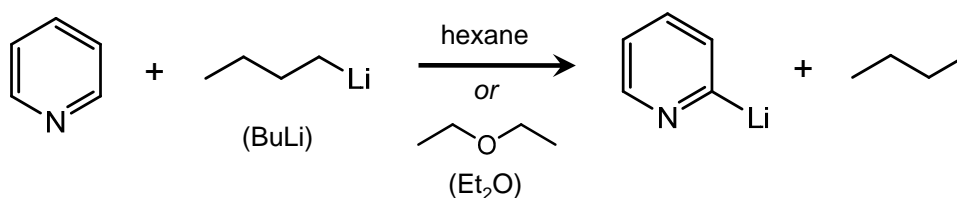
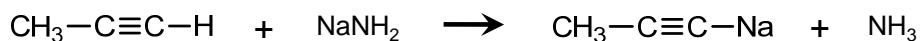
All of these react as " R^{\ominus} "

Generating Organometallic Reagents

1. Deprotonation.

Not common. Works for alkynyl, some sp^2 anions, but not for sp^3 (because alkanes are not acidic enough).

Examples:

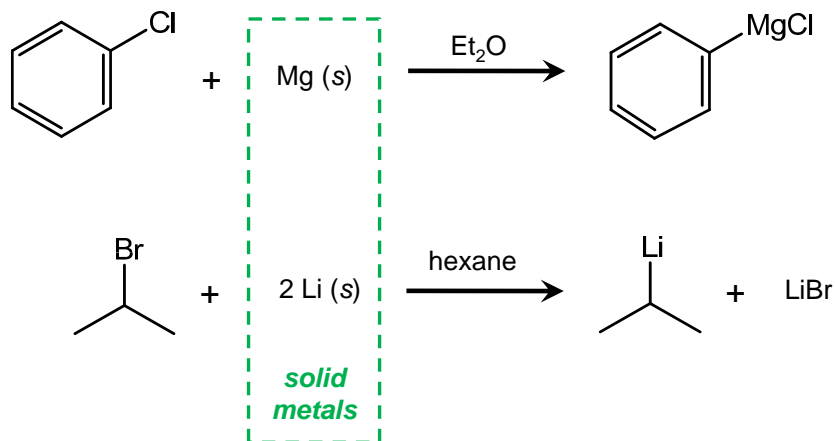


Generating Organometallic Reagents

2. Metalation of an alkyl halide.

Common for Grignard reagents, sp^3 alkylolithiums.

Examples:

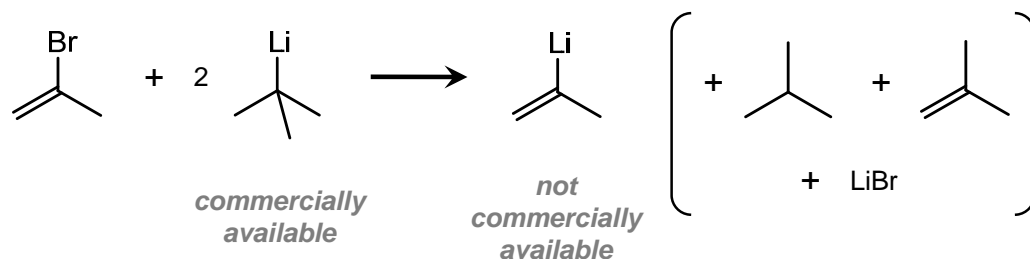


Generating Organometallic Reagents

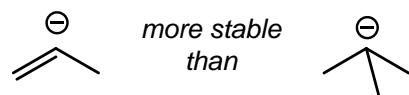
3. Lithium-halogen exchange.

Common for sp^2 alkyllithiums. Not useful for sp^3 alkyllithiums.

Example:

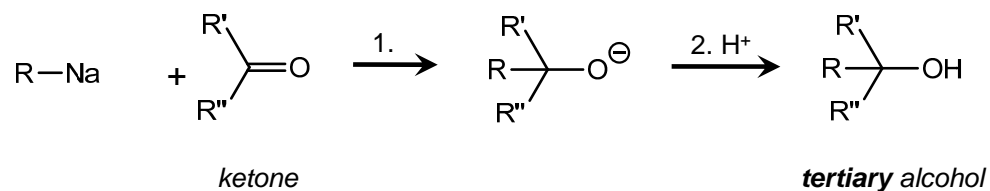
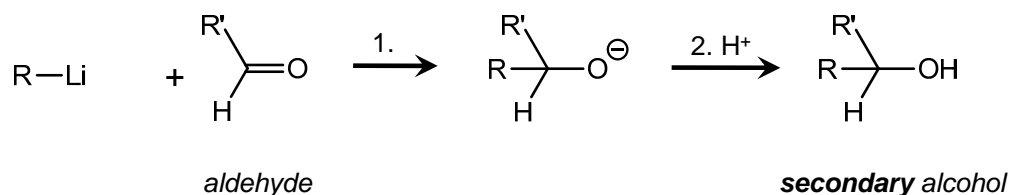
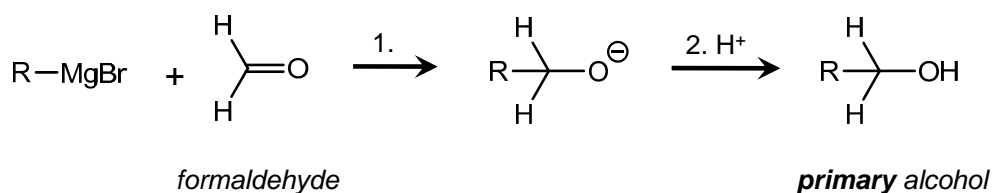


Reaction is driven by formation of more stable carbanion:

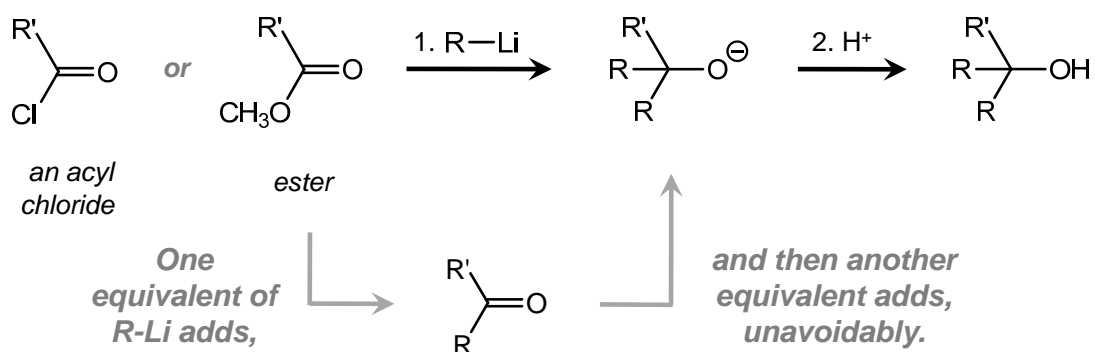


Reaction of Alkylmetals With C=O Bonds

For any alkylmetal reagent,

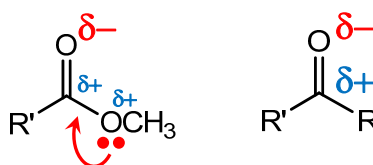


Double Addition of Alkylmetals to Esters and Acyl Halides



Why?

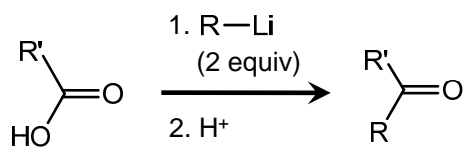
Ketones and aldehydes are more electrophilic than esters and acyl halides.



Lone pair donation by oxygen reduces partial positive charge on C=O carbon.

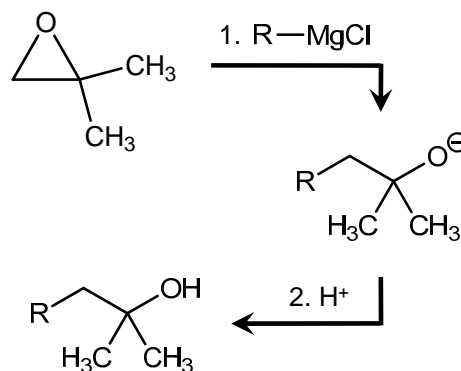
Single Addition of Alkylmetals to Carboxylates

Wade says:



- Only works for alkyllithiums.
- Other methods for making ketones are more common.

Alkylmetals Open Epoxides



- Another way of making new C-C bonds with alkylmetals.