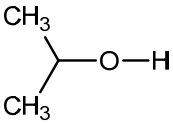
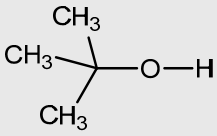
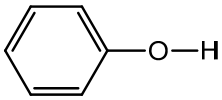
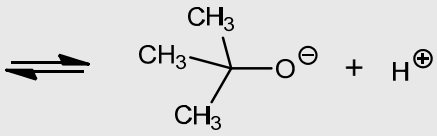
Acidity of Alcohols

	alcohol	pK_a
water	HO—H	15.7
methanol	CH_3O—H	15.5
ethanol	CH_3CH_2O—H	15.9
iso-propanol		16.5
tert-butanol		18.0
phenol		10.0

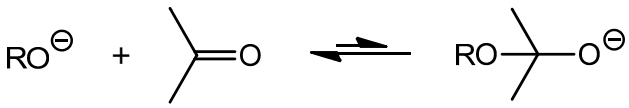
Increasing substitution pushes electron density onto oxygen, decreases acidity.



$^{\ominus}$O*t*Bu is 200 times more basic than $^{\ominus}$OH.

Nucleophilic Addition to Carbonyls

Heteroatom electron donors add reversibly to C=O groups.

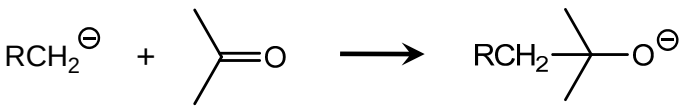


true for $Cl^{\ominus}$, $HS^{\ominus}$, NH_3…

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:

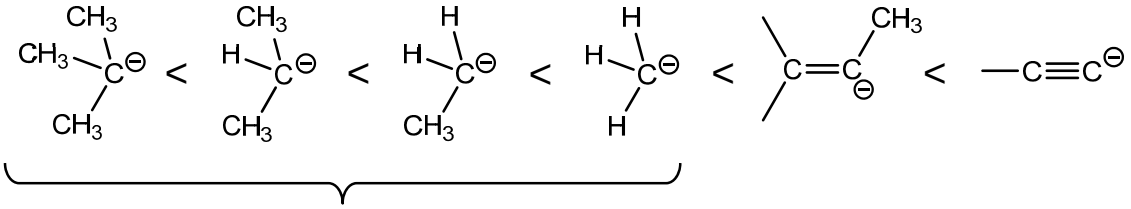
- instability of charge on RCH_2^-

Relative Stabilities of Carbanions

least stable, most reactive

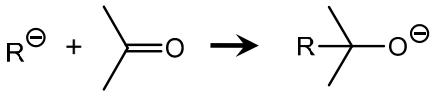
most stable, least reactive

sp^3 < sp^2 < sp

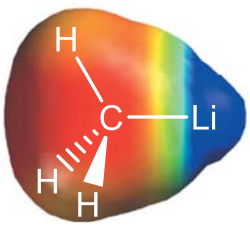


Increasing substitution pushes electron density onto carbon, destabilizes anion (and makes it more basic, and more reactive).

All of these anions add irreversibly to carbonyls,



Organometallic Reagents are Synthetically Equivalent to Carbanions



Computed electronic structure of CH_3Li

R—Li	alkyllithium (organolithium)
R—Mg—Br	Grignard reagent (organomagnesium halide)
R—C≡C—Na	alkynylsodium

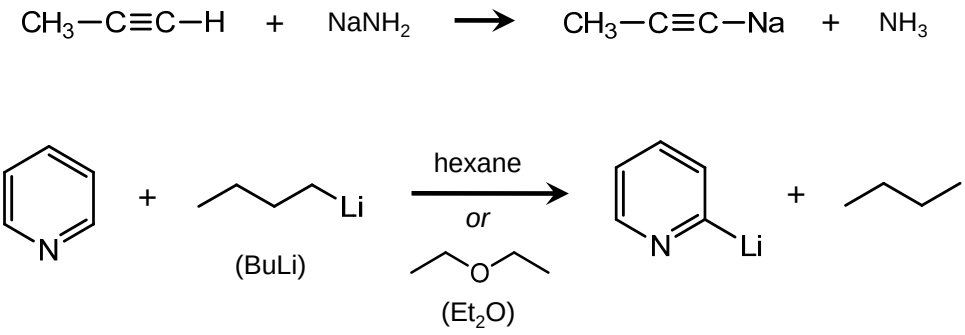
All of these react as "$R^{\ominus}$"

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:

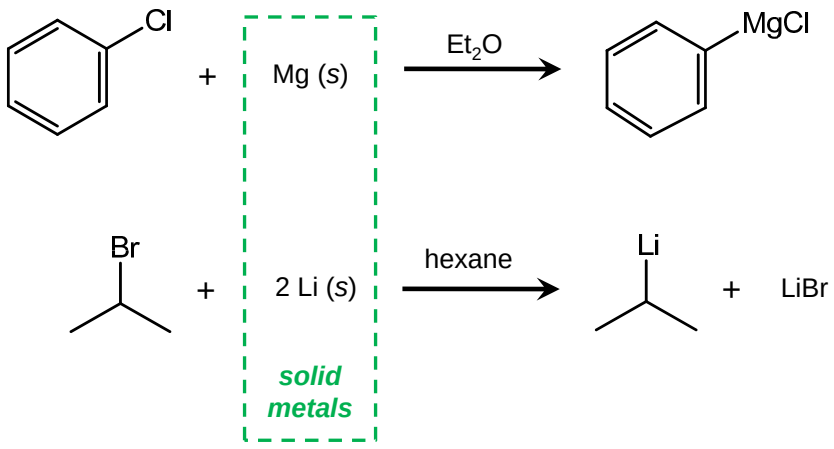


Generating Organometallic Reagents

2. Metalation of an alkyl halide.

Common for Grignard reagents, sp^3 alkyllithiums.

Examples:

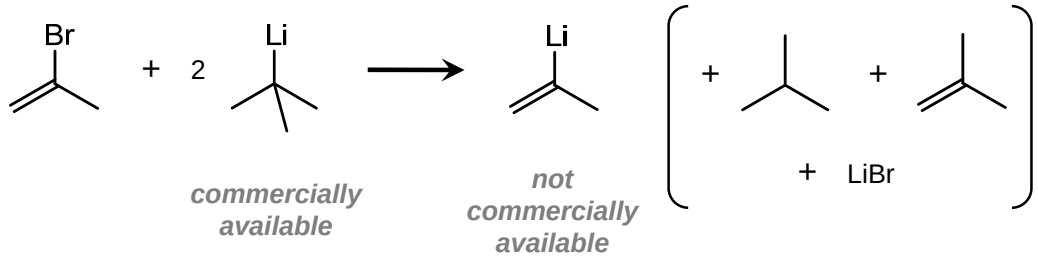


Generating Organometallic Reagents

3. Lithium-halogen exchange.

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

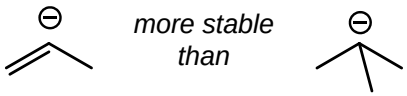
Example:



commercially available

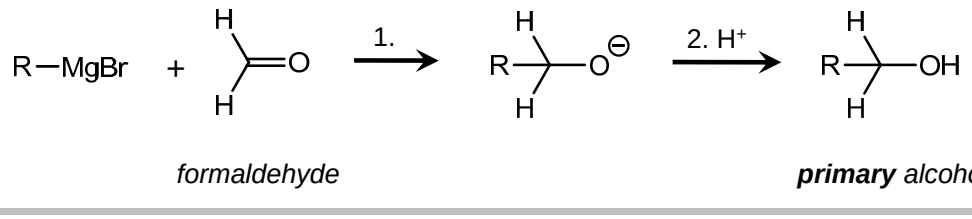
not commercially available

Reaction is driven by formation of more stable carbanion:

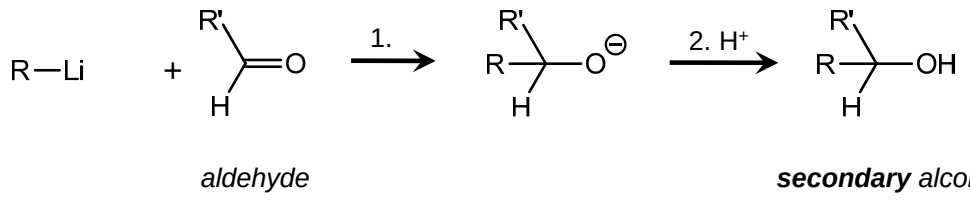


Reaction of Alkylmetals With C=O Bonds

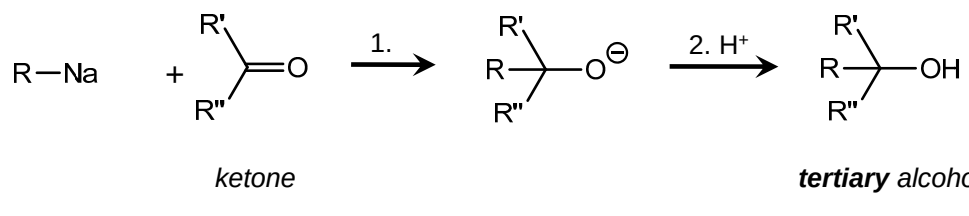
For any alkylmetal reagent,



formaldehyde — ***primary*** *alcohol*



aldehyde — ***secondary*** *alcohol*



ketone — ***tertiary*** *alcohol*