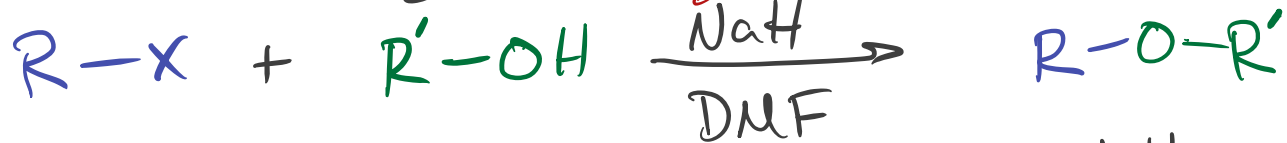


Using Alkyl Halides in Chemical Synthesis

① Williamson-Ether Synthesis

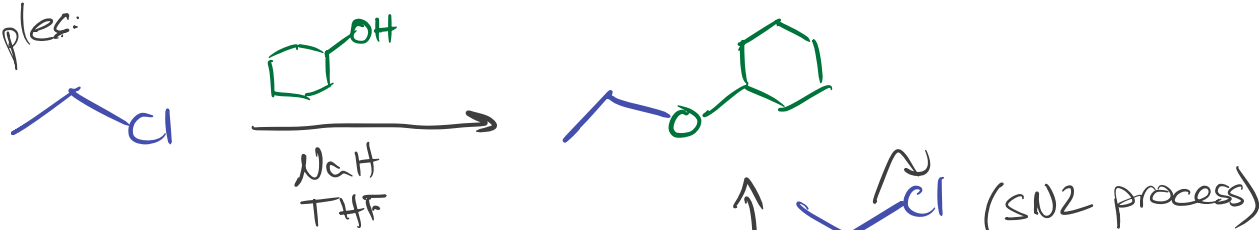


$R = \text{CH}_3, 1^\circ$, sometimes 2° Less hindered for backside attack

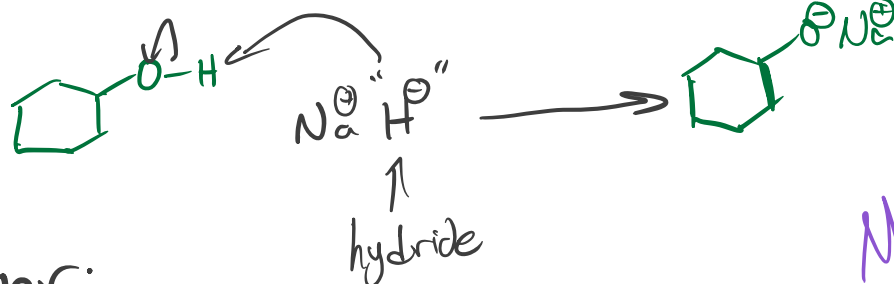
$RX = \text{CH}_3, 1^\circ, 2^\circ$, sometimes 3° , Ar-

(polar, aprotic solvents)

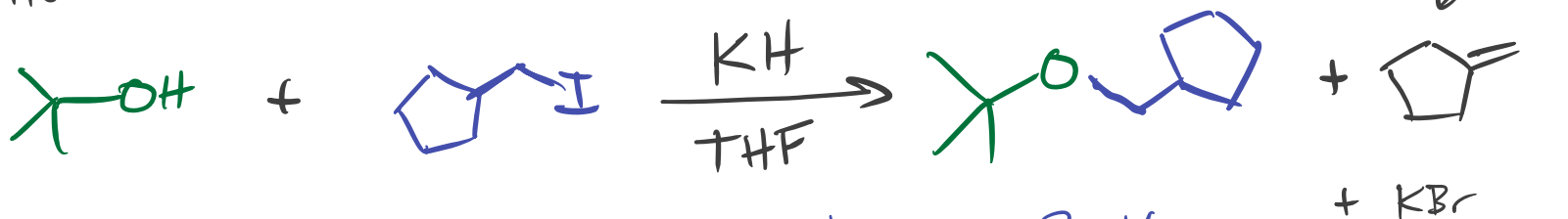
examples:



How?



However:



Notes:

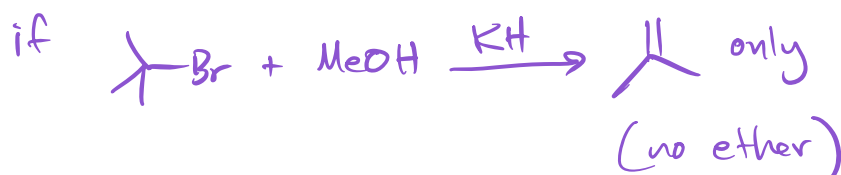
- S_N2 Rxn conditions
- Sometimes competes w/ $E1/S_N1$ due to Alkoxide.

(RO^-)

- KH also works

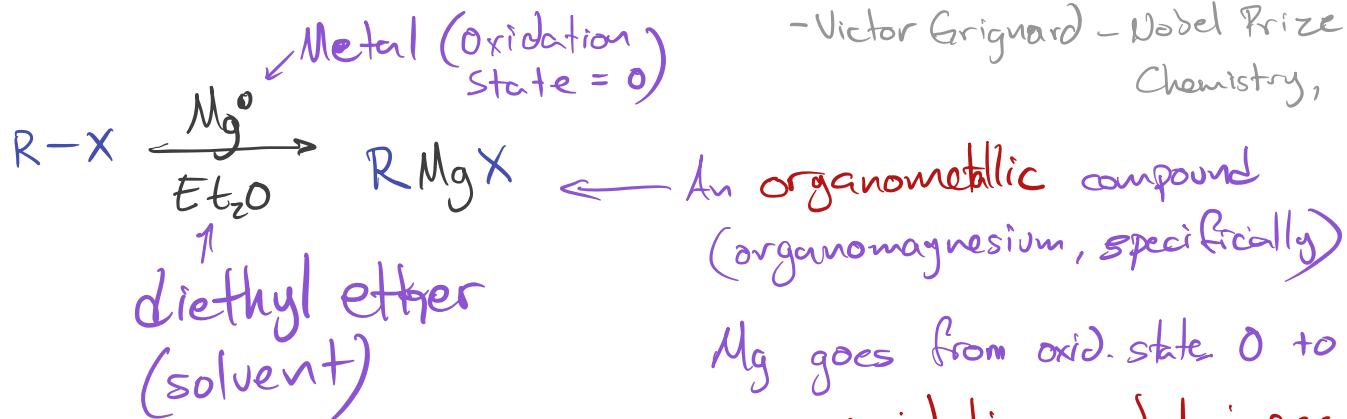
it works for $R-X$ without antiperiplanar orientation,

Plan on $R-X$ being less substituted than $R-OH$



ORGANOMAGNESIUM REAGENTS (Grignard Reagents)

- Victor Grignard - Nobel Prize in Chemistry, 1912



Mg goes from oxid. state 0 to 2^+
 "oxidative metal insertion"
 ⇒ Metal-halogen exchange

$R = 1^\circ \text{ alkyl}$ $X = \text{Cl, Br, I}$
 2° "
 3° "

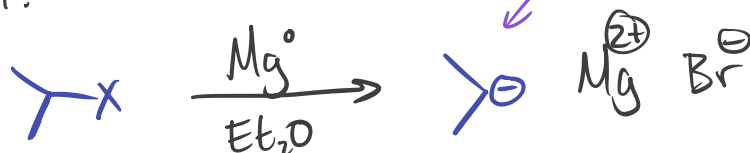
Alkenyl 

Aryl 

↑
 used most
 widely
 - reacts better
 than Cl &
 cheaper than I

carbon-based Nucleophile! (carbanion)

The Result:



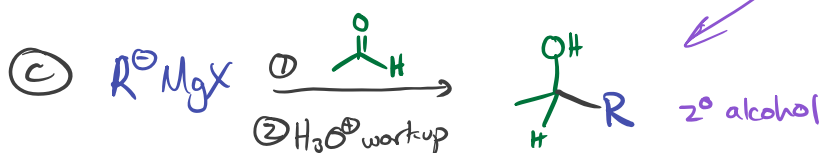
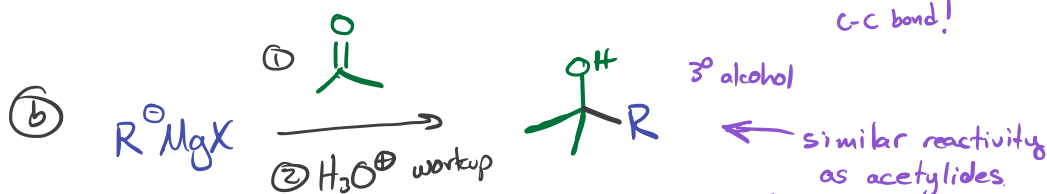
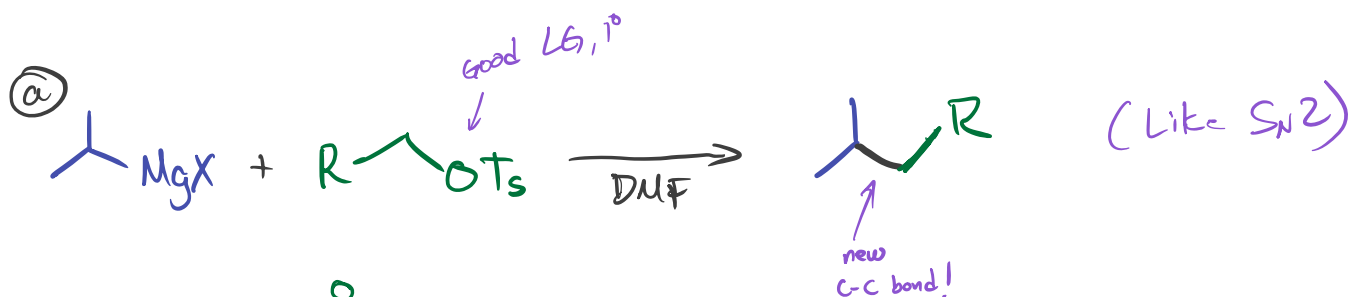
Essentially, an alkyl halide was turned into an alkane

Reactivity:

① as B^\ominus



② as Nu^\ominus

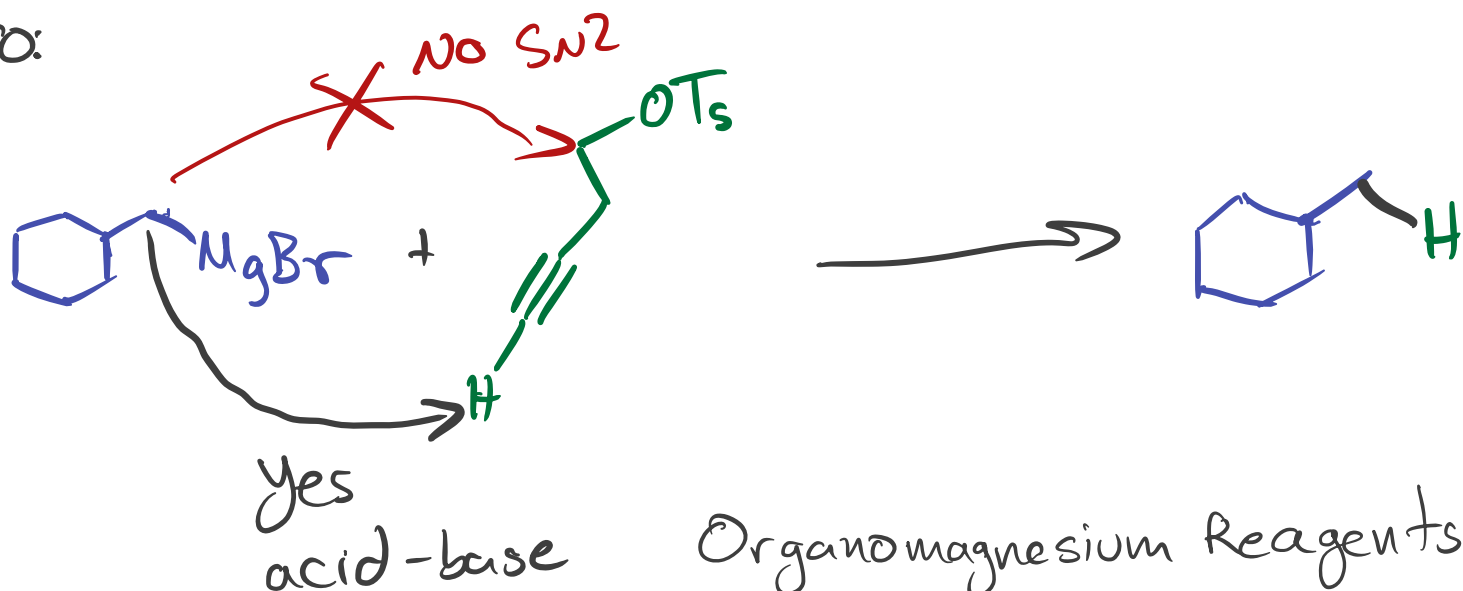


Reminder:

Acid Strength: $\text{HF} > \text{H}_2\text{O} > \text{ROH} > \text{R}-\text{C}\equiv\text{CH} > \text{NH}_3 > \text{CH}_4$

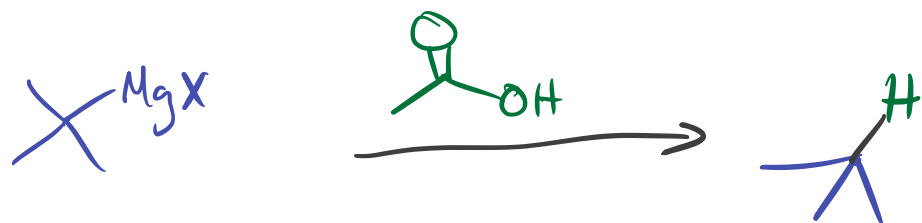
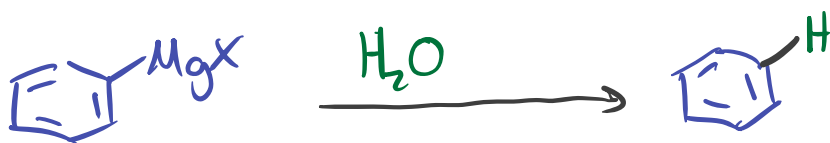
Base Strength: $\text{CH}_3^- > \text{NH}_2^- > \text{C}\equiv\text{C}^--\text{R} > \text{OR}^- > \text{OH}^- > \text{F}^-$

so:



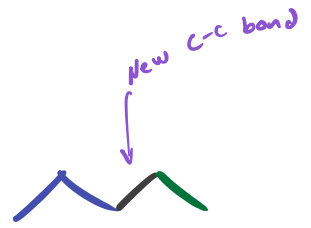
Organomagnesium Reagents will act as bases with protic solvents, reagents, or other functional groups

ex.

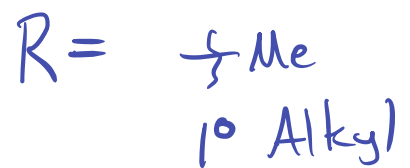
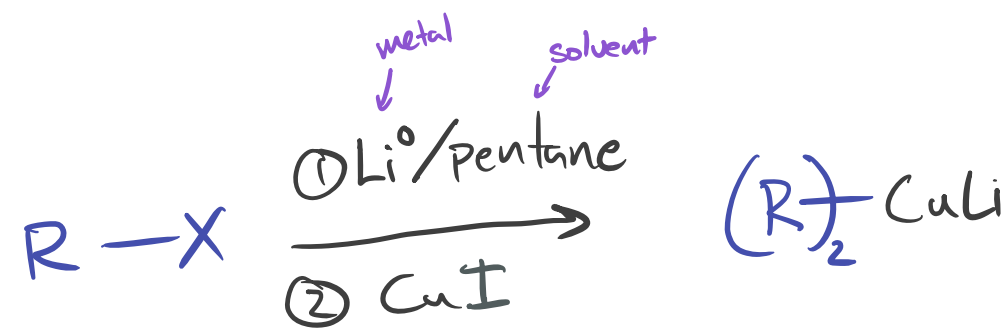


Organocuprate Reagents (Gillman Reagents)

A Gillman Reagent.



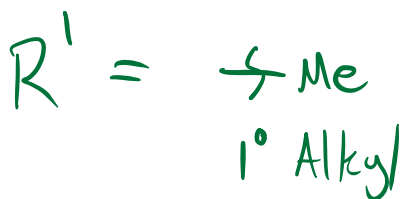
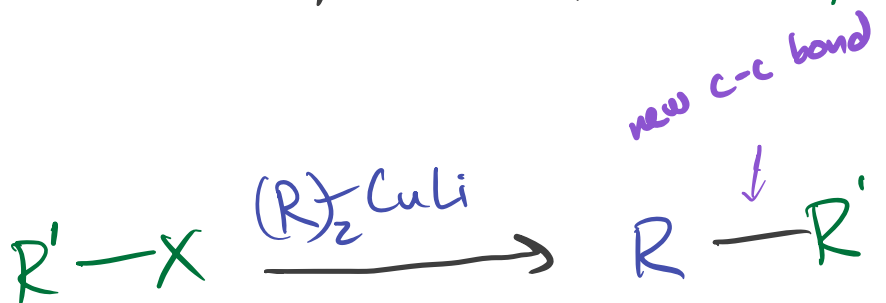
How to make the organocuprates?



No 2°
or 3°



The Organocuprate can be coupled to other R-X



No 2°
or 3°

Examples

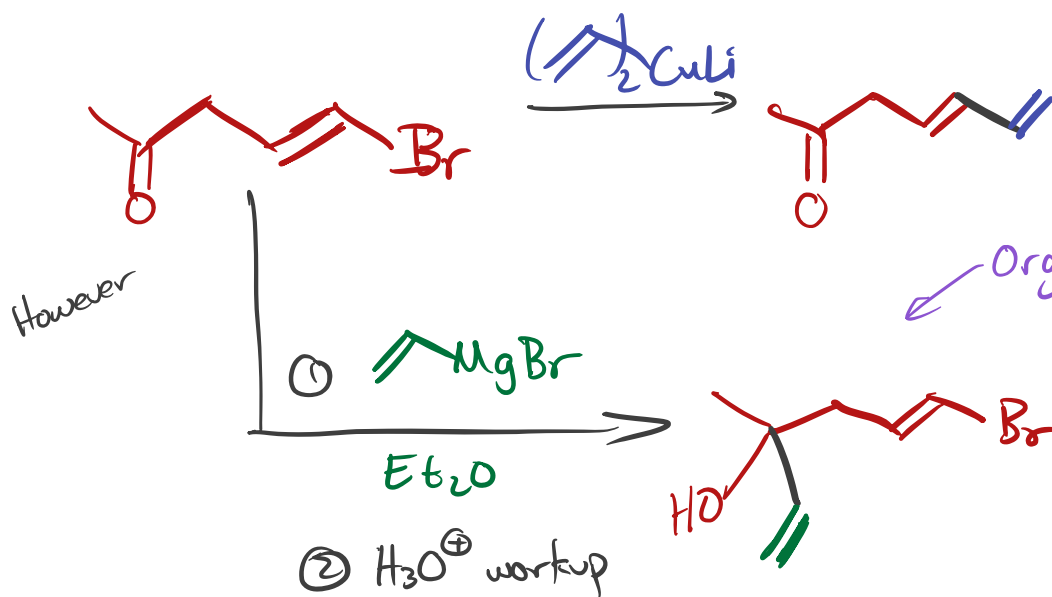


Retaining alkene stereochemistry



And check this out:

Organocuprate does NOT attack the carbonyl carbon!



Organomagnesium reagents attack the carbonyl

The Gilman reagents are not as nucleophilic as Grignard reagents!

Organocuprates are great for making trisubstituted alkenes

