Differences Between the Reagents

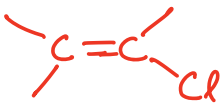
Alkyllithium Reagents → extremely basic — limits their use

Grignard Reagents → will deprotonate anything more/as acidic as an alcohol (pKa ~ 16)

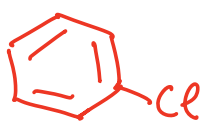
Time Capsule: These won't make enolates with carbonyl compounds

Gilman Reagents → least basic → so they are the only reagents capable of reacting with:

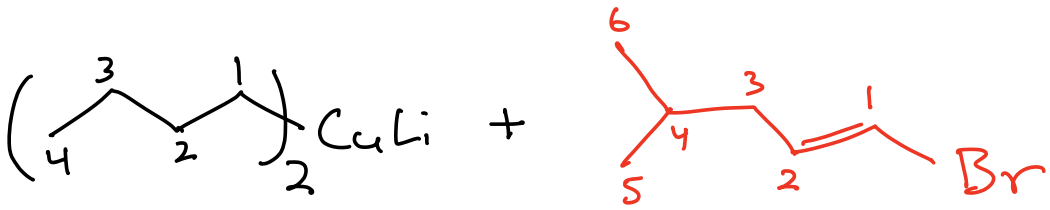
1) Primary haloalkanes



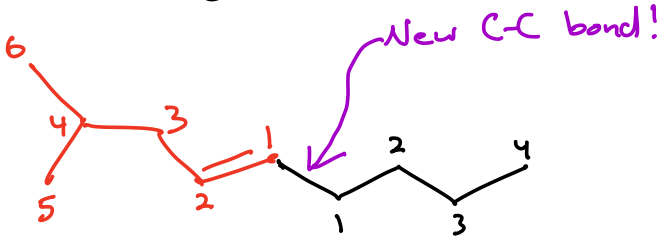
2) Vinyl halides



3) Aryl halides



(Not an S_N2 mechanism)



Cu salts

(you are not responsible for writing these)

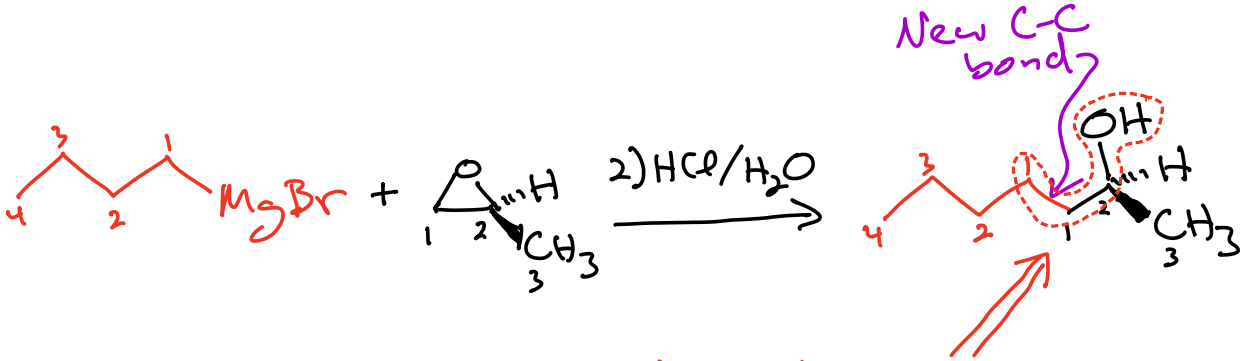
Watch the new video called "Gilman Reagents Explained" after hitting "Helpful Short Videos" on the main course web page (7th from the top on the left column)

Synthesis → New C-C bonds! →
↳ Generate more complex molecules from simpler ones.

1) Retrosynthetic Analysis →
Work backwards from the product.

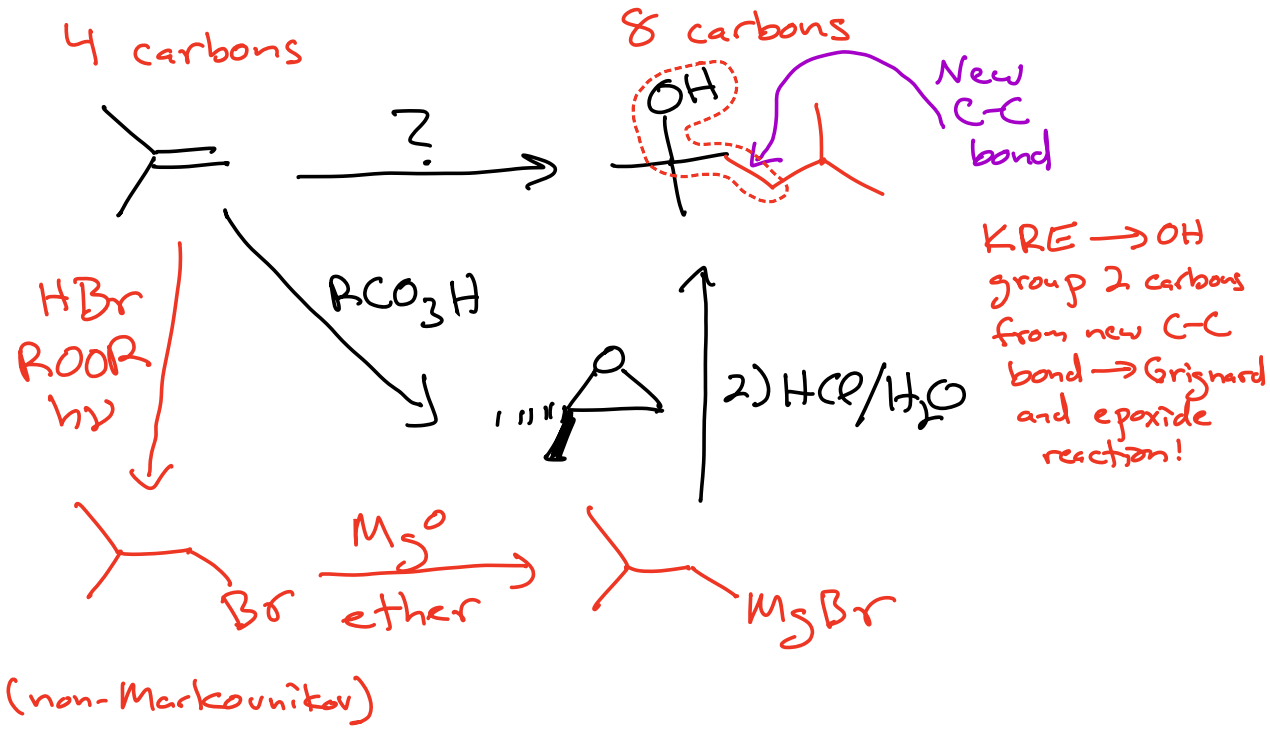
2) Count the number of carbon atoms in the starting material versus the product →
Allows you to identify the location of any new C-C bonds.

3) Learn to recognize the Key Recognition Elements (KRE) in the product → tells you what the final reaction had to be.



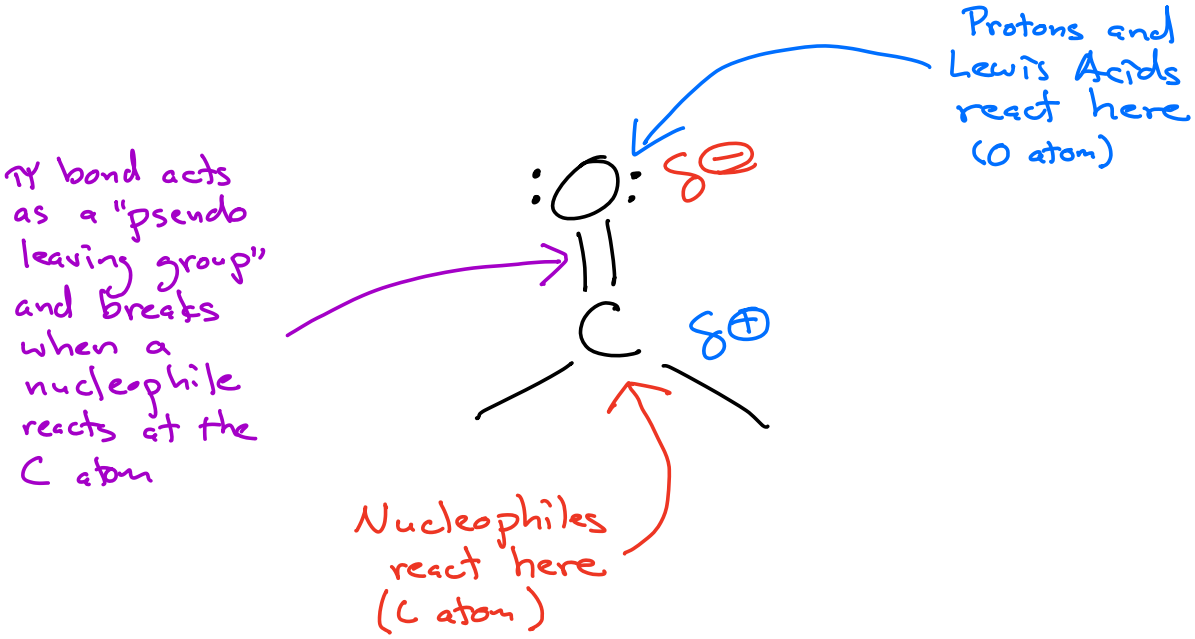
KRE → An alcohol group 2 carbons from a new C-C bond

Synthesis Example



Functional groups such as carbonyl groups undergo characteristic reactions.

There are common themes → the different reactions are variations on these themes



There are four common mechanisms seen when carbonyl compounds react with nucleophiles

→ We will call these Mechanism A-D

Here are the keys to understanding mechanisms in 320N!!

1) There are basically four different mechanisms elements that make up the steps of carbonyl reactions.

A) Make a bond between a nucleophile and an electrophile
B) Break a bond to give stable molecules or ions
C) Add a proton
D) Take a proton away

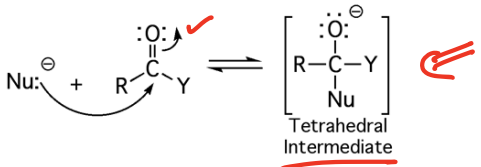
2) These same four mechanism elements describe most of the other mechanisms you have/will learn!!! (Yes, organic chemistry really is this simple if you look at it this way!!)

There are basically four different mechanisms that describe the vast majority of carbonyl reactions and these mechanisms are different combinations/ordering of the four mechanism elements listed above. In this class, I have termed them "Mechanism A", "Mechanism B", "Mechanism C", and "Mechanism D". They all involve a nucleophile attacking the partially positively charged carbon atom of the carbonyl to create a tetrahedral intermediate. Different reaction mechanisms are distinguished by the timing of protonation of the oxygen atom as well as the presence or absence of a leaving group attached to the carbonyl.

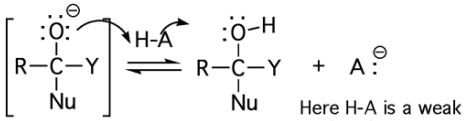
Four Mechanisms for the Reaction of Nucleophiles with Carbonyl Compounds

MECHANISM A: Reaction with a Strong Nucleophile

Step 1 Make a new bond between a nucleophile and electrophile

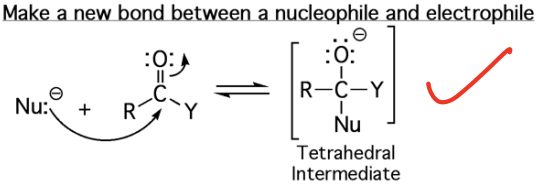


Step 2 Add a proton

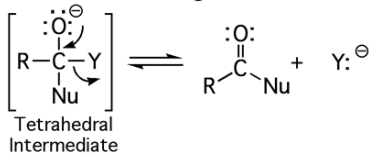


MECHANISM B: Reaction with a Strong Nucleophile When "Y" is a Good Leaving Group (-OR, -Cl, etc.).

Step 1 Make a new bond between a nucleophile and electrophile

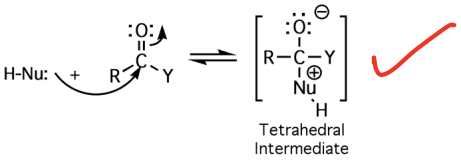


Step 2 Break a bond to give stable molecules or ions

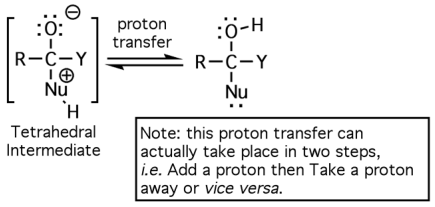


MECHANISM C: Reaction with a Weak Nucleophile

Step 1 Make a new bond between a nucleophile and electrophile

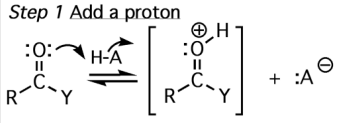


Step 2 Add a proton and Take a proton away

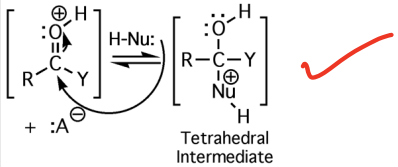


MECHANISM D: Reaction with a Weak Nucleophile in the Presence of Acid (H-A)

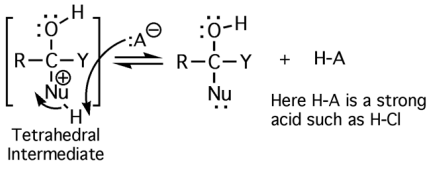
Step 1 Add a proton



Step 2 Make a new bond between a nucleophile and electrophile



Step 3 Take a proton away

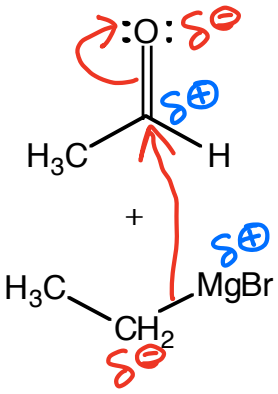


All of these mechanisms have a tetrahedral intermediate ✓

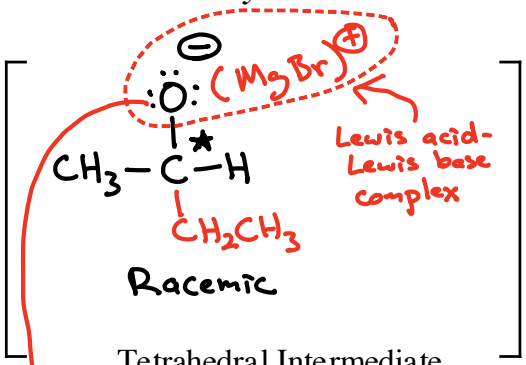
Mechanism A → Use this mechanism with strong nucleophiles

1) Make a bond
2) Add a proton

Grignard Reagent Reacting with an Aldehyde or Ketone



Make a bond



Chemist opens the flask

2) H–Cl: / H_2O

Add a proton

Mechanism A

Key Recognition Element (KRE):

-OH group attached the same C atom as a new C–C bond