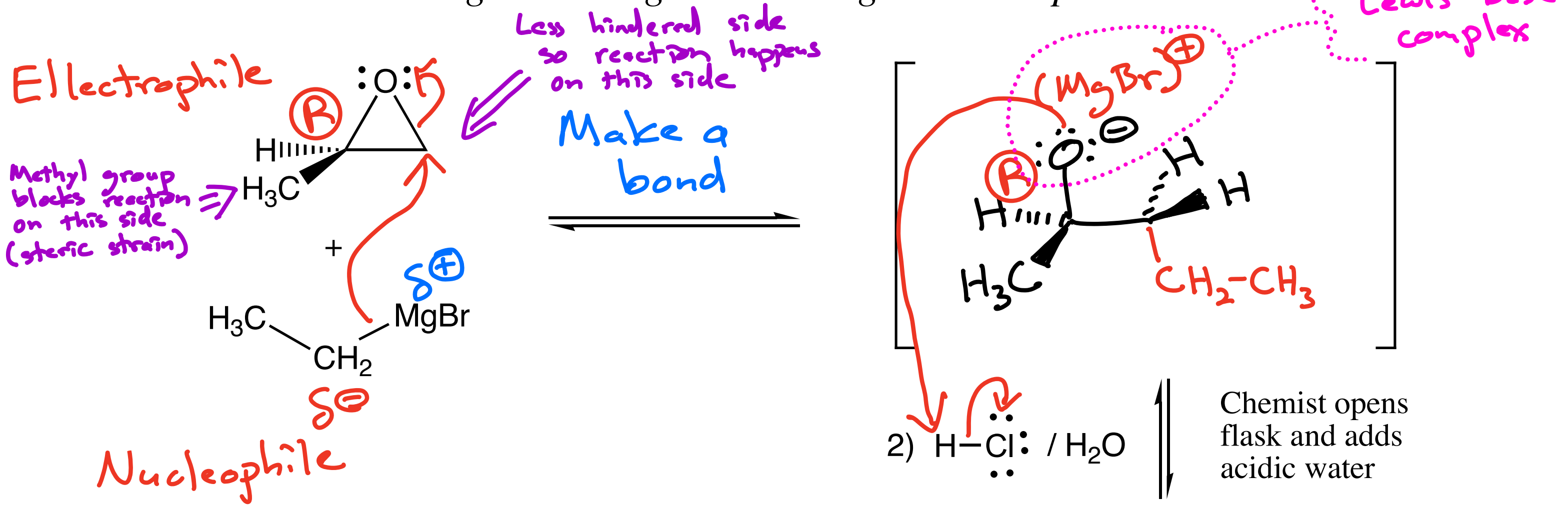
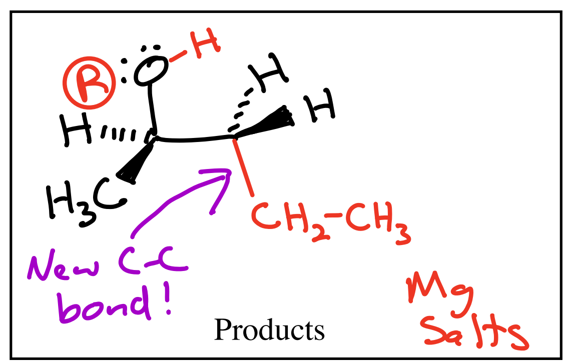
Organolithium and Gilman reagents react the same as Grignard reagents with epoxides

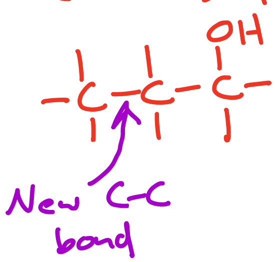
Grignard Reagent Reacting with an Epoxide

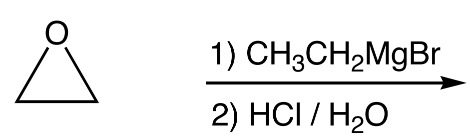


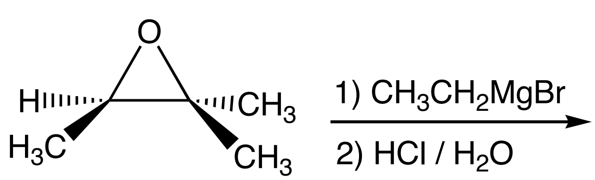


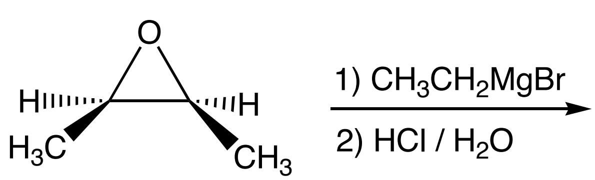
Key Recognition Element (KRE):

There is a new C–C bond that is two carbons from the –OH group







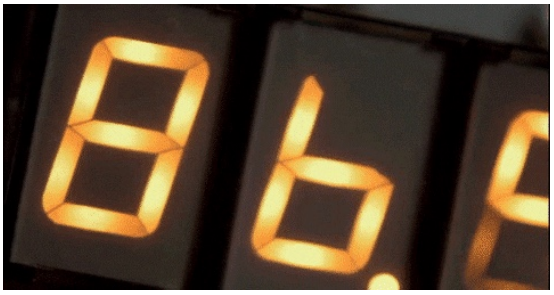


Differences Between the Reagents

Alkyllithium Reagents

Grignard Reagents

Gilman Reagents (Watch the Gilman Reagent video)



Time Capsule!

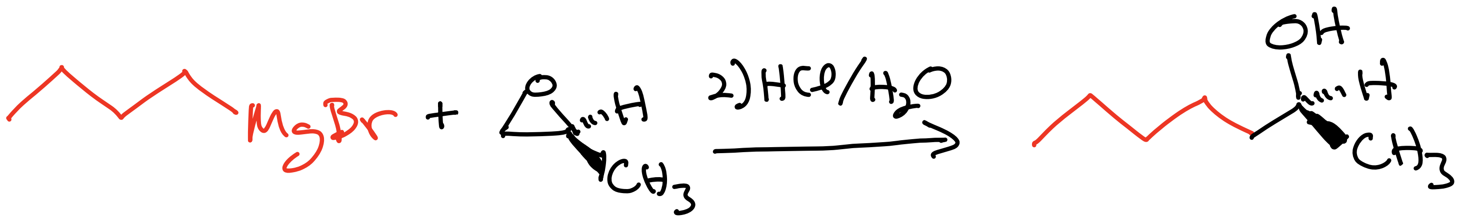
Grignard and Gilman Reagents are not basic enough to make enolates from carbonyl compounds

Synthesis

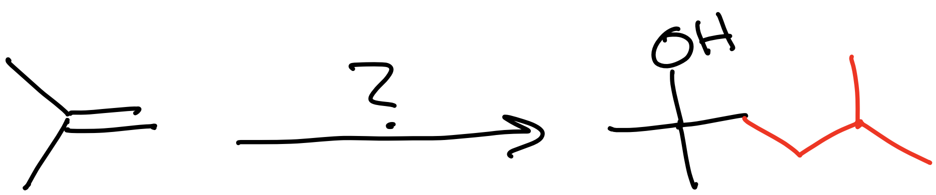
1) Retrosynthetic Analysis

2) Count the number of carbon atoms in the starting material versus the product

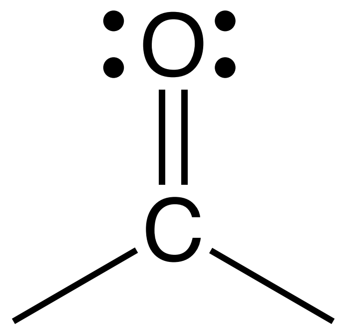
3) Learn to recognize the Key Recognition Elements (KRE) in the product



Synthesis Example



Functional Groups Such as Carbonyl Groups Undergo Characteristic Reactions



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

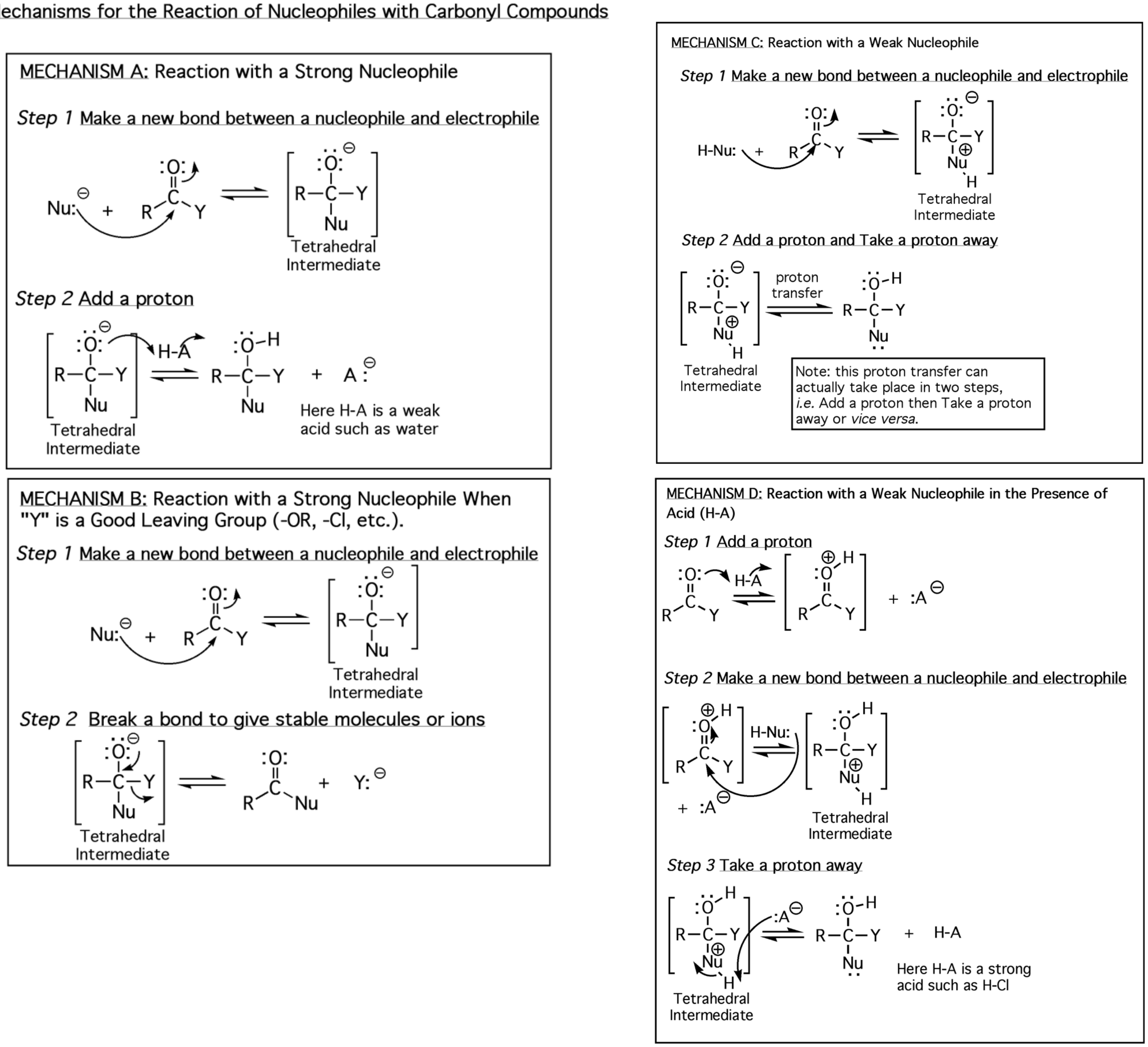
1) There are basically four different mechanisms elements that make up the steps of carbonyl reactions.

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

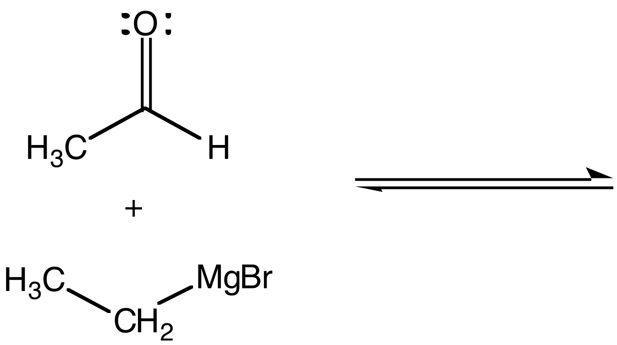
2) These same four mechanism elements describe most of the other mechanisms you have/will learn!!! (Yes, organic chemistry really is this simple if you look at it this way!!)

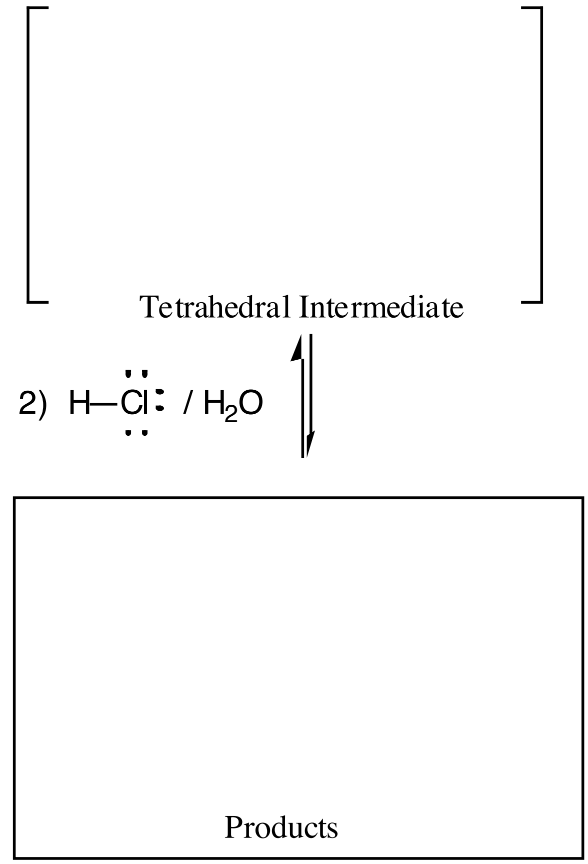
There are basically four different mechanisms that describe the vast majority of carbonyl reactions and these mechanisms are different combinations/ordering of the four mechanism elements listed above. In this class, I have termed them "Mechanism A", "Mechanism B", "Mechanism C", and "Mechanism D". They 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

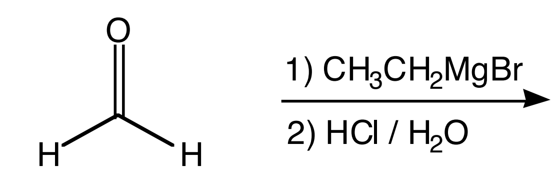


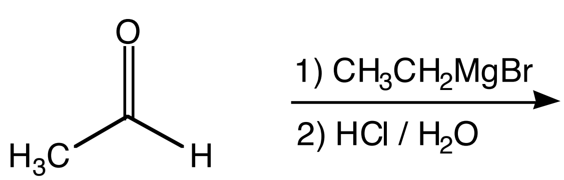
Grignard Reagent Reacting with an Aldehyde or Ketone

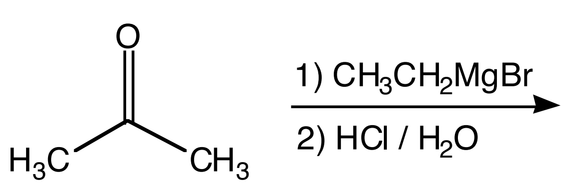


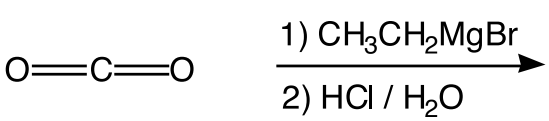


Key Recognition Element (KRE):










Make a Bond
Add a Proton
Break a Bond
Take a Proton Away
“The most important widsom in the universe, found, I have”

Lesson for Today:

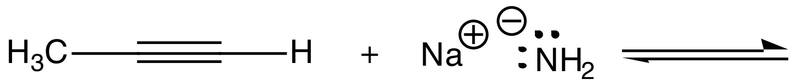
Strong nucleophiles react directly at the electrophilic C atom of carbonyls to

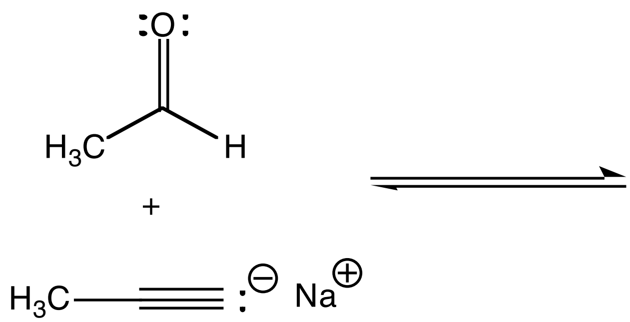
as the carbonyl π bond

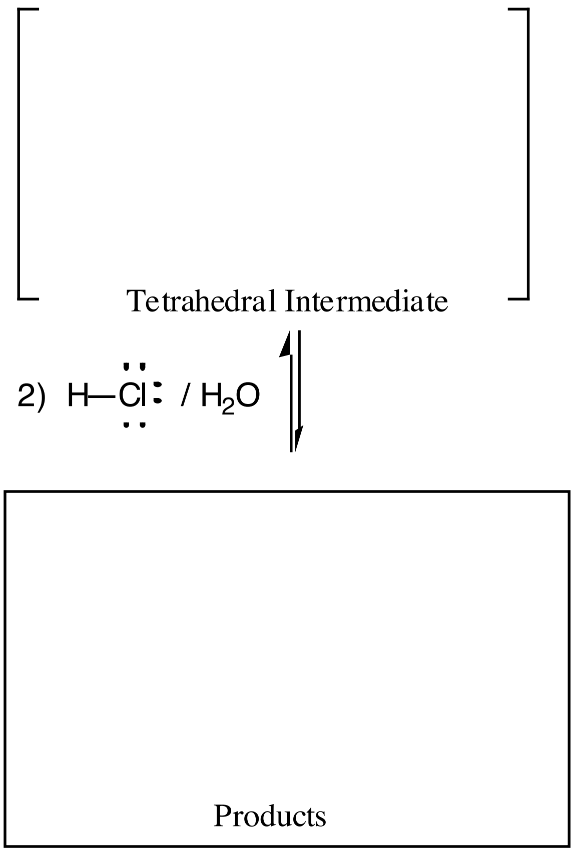
breaks. to

the O atom.

Alkyne Anion Reacting with an Aldehyde or Ketone

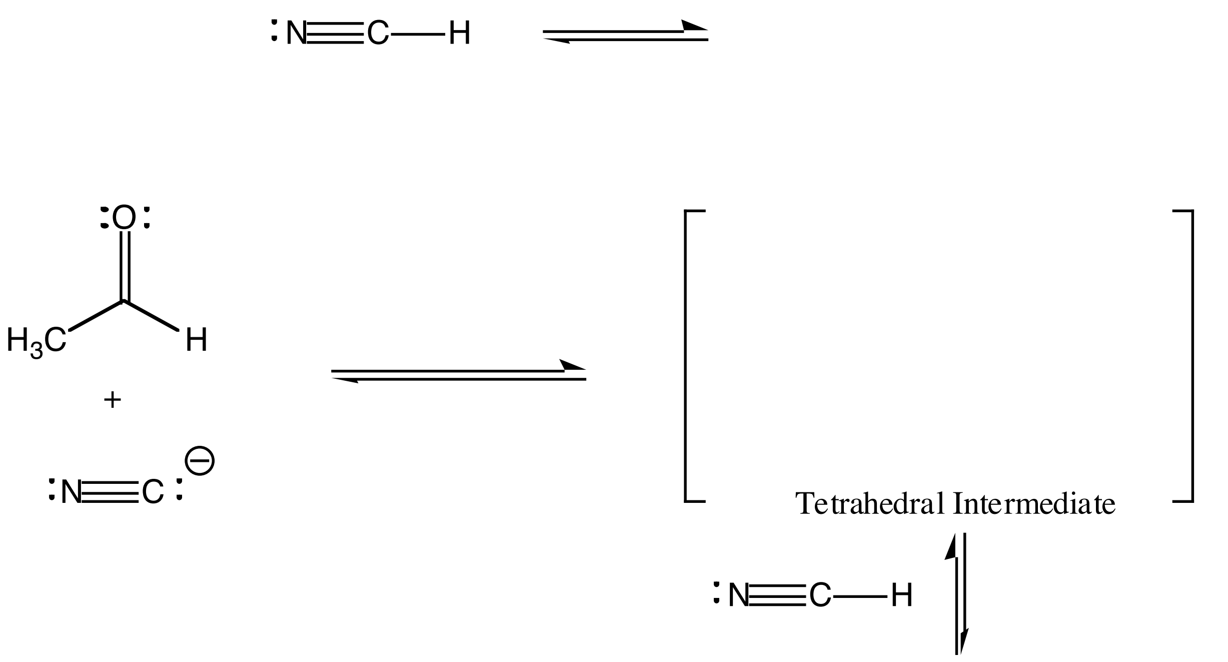




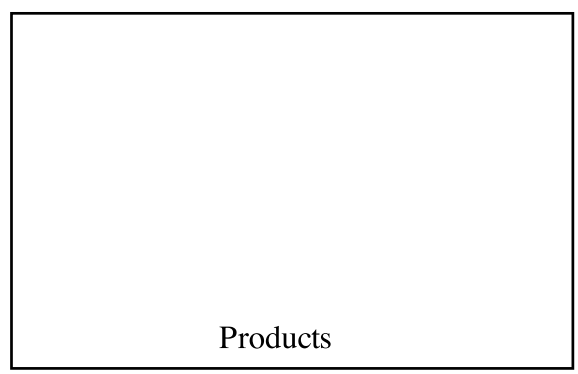


Key Recognition Element (KRE):

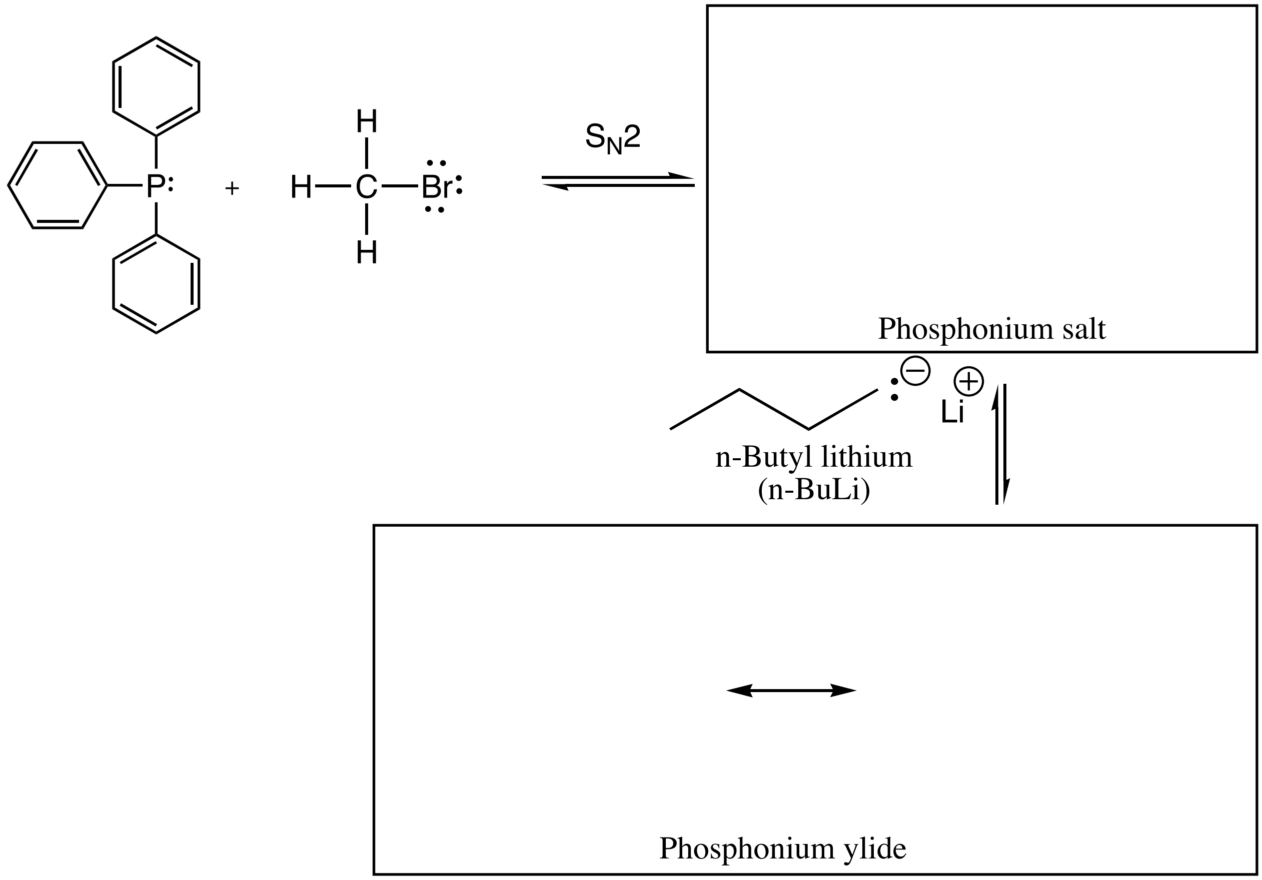
HCN Reacting with an Aldehyde or Ketone

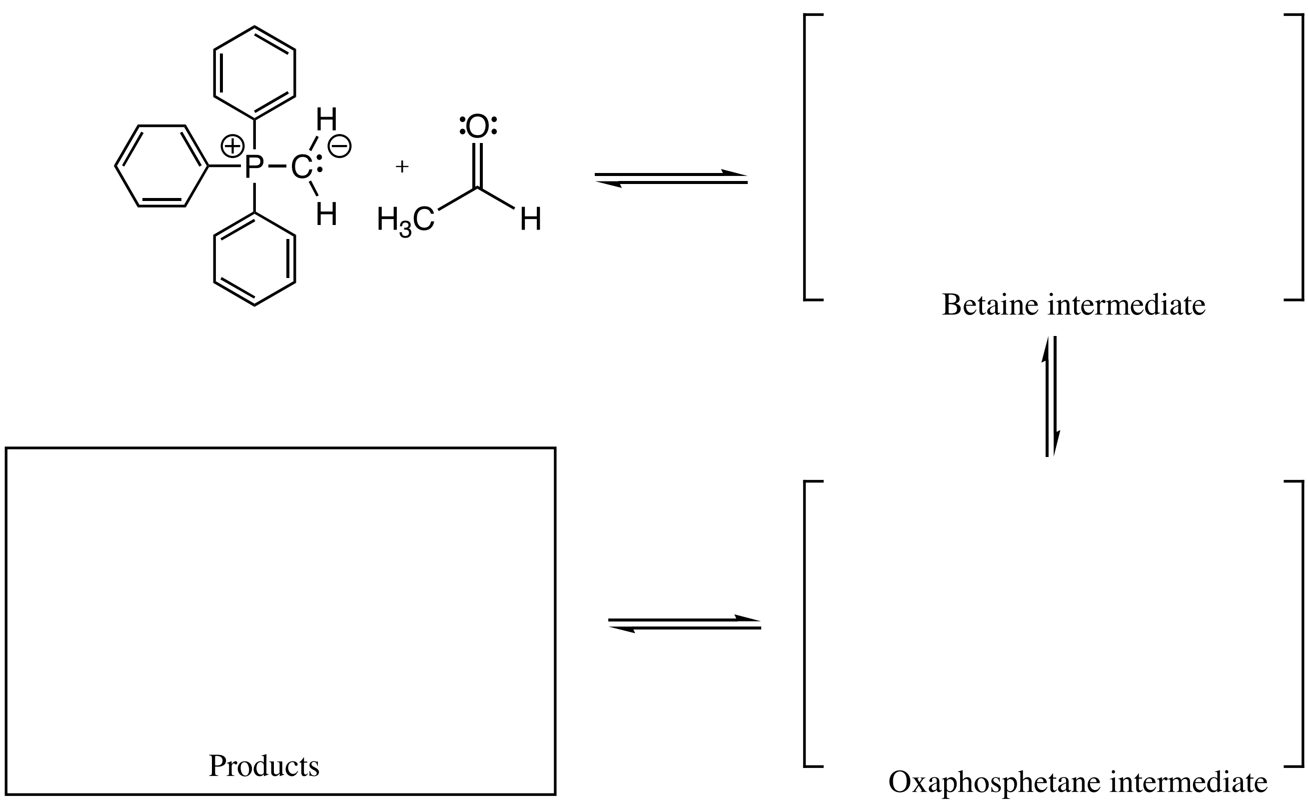


Key Recognition Element (KRE):



Wittig Reaction



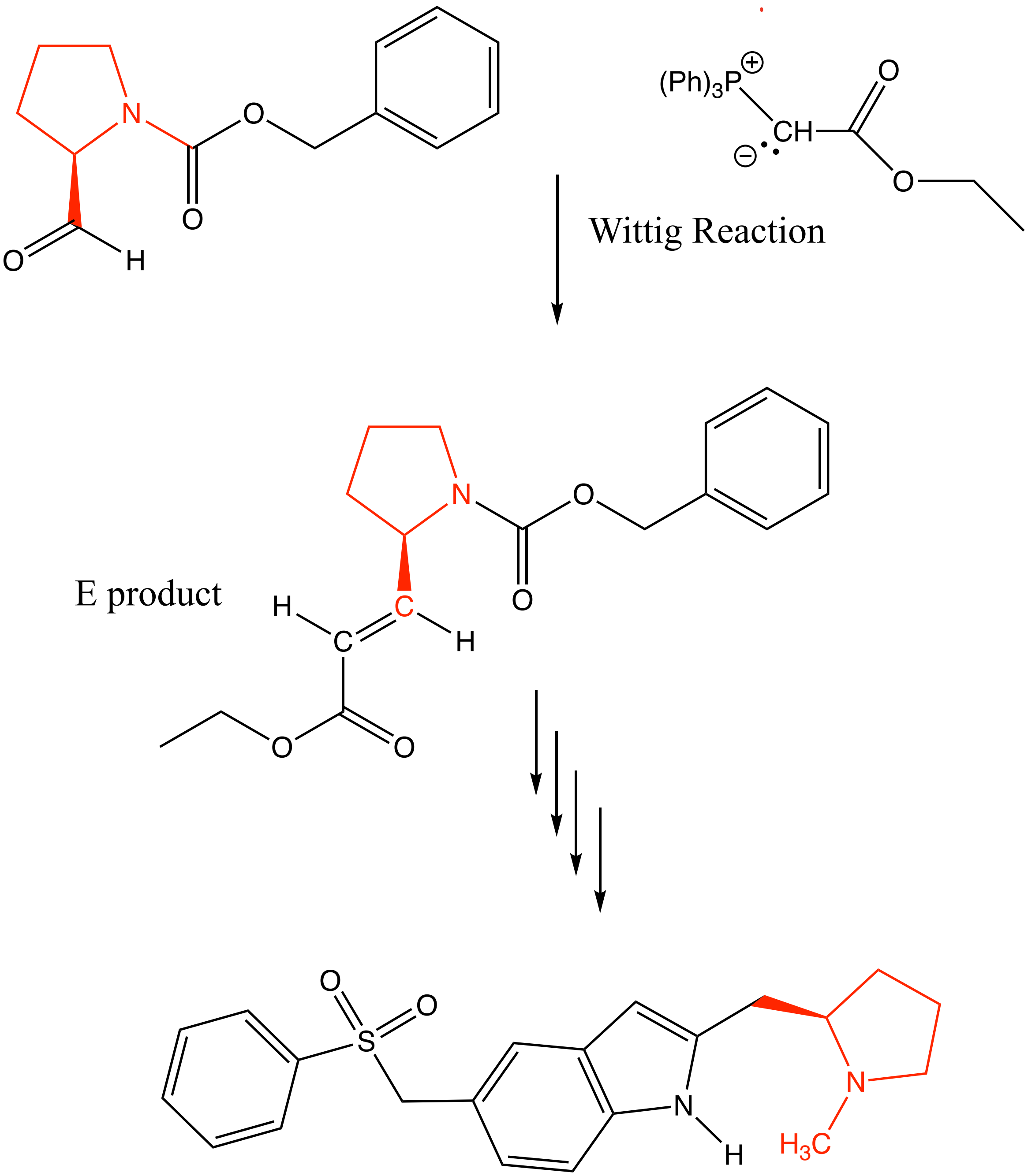


Key Recognition Element (KRE):

E vs. Z → Which product alkene?

1) With alkyl Wittig reagents, the Z alkene product predominates

2) When using Wittig reagents that have a carbonyl attached to the C atom that is bonded to the $P^{\oplus}$ atom — **E alkenes** predominate



Eletriptan - used to treat migraine headaches
A seratonin receptor agonist (5-$HT_{1B,1D,1F}$)