

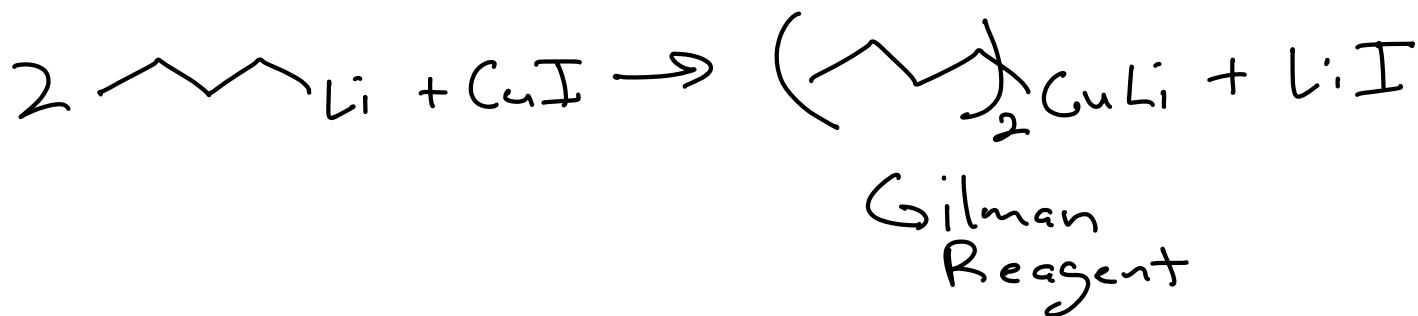
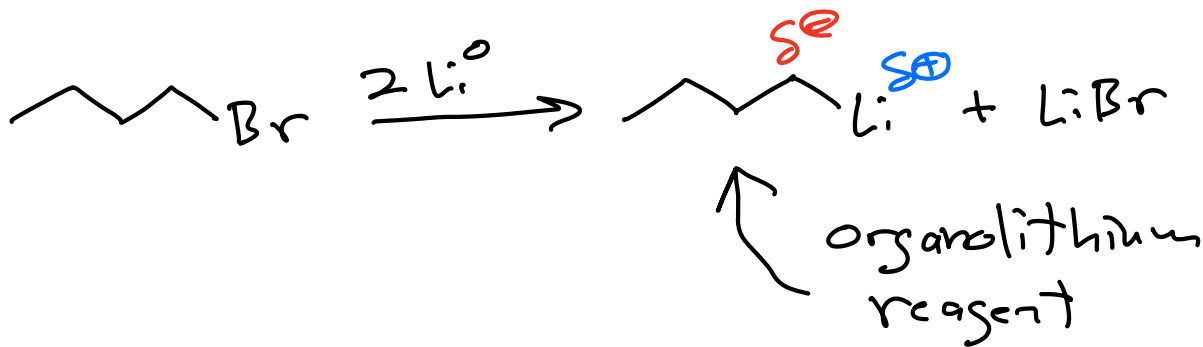
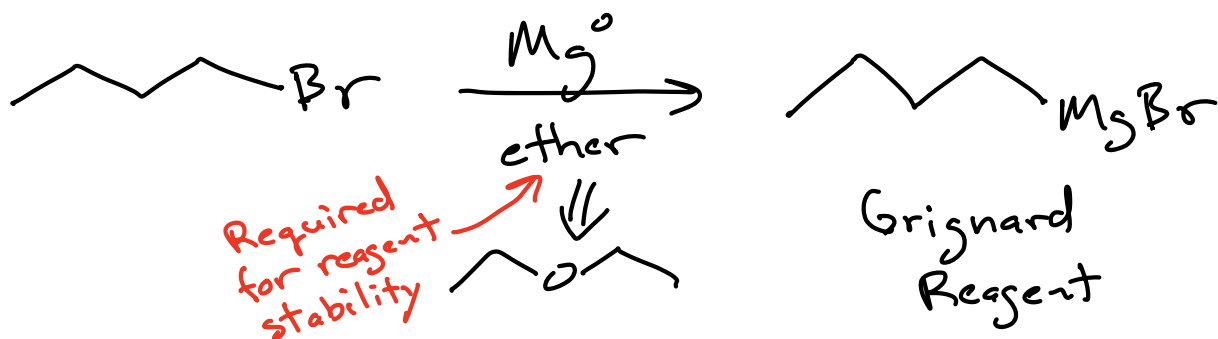


Preparation of Organometallic Reagents

C-metal bonds are more ionic than pure covalent bonds like C-C bonds

C-metal bond!

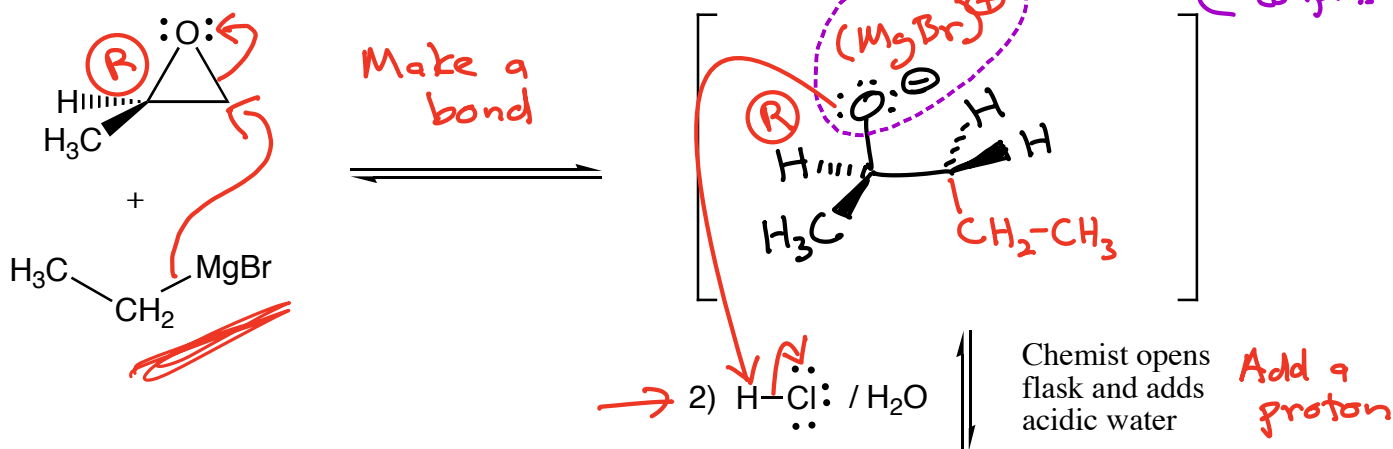
Prepared from haloalkanes



You are not responsible for these mechanisms!

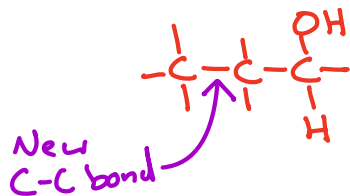
Organolithium and Gilman reagents react the same way as Grignard reagents in this reaction.

Grignard Reagent Reacting with an Epoxide

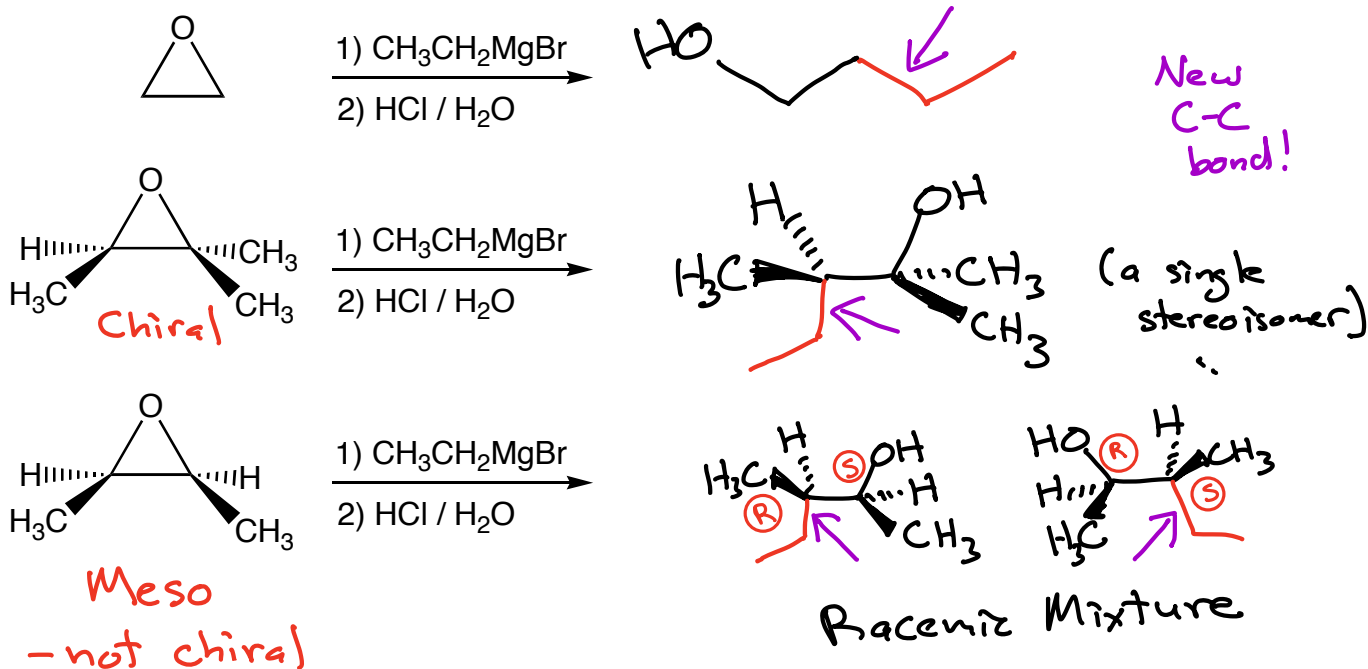
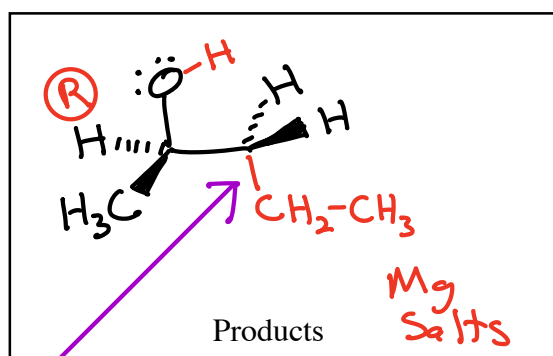


Key Recognition Element (KRE):

There is a new C-C bond that is two carbon atoms away from an OH group



New C-C bond!



Differences Between the Reagents

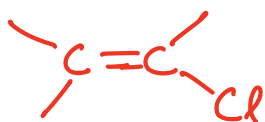
Alkyl lithium Reagents extremely basic
- limits their use

Grignard Reagents → will deprotonate anything more/ as acidic as an alcohol ($pK_a \sim 16$)

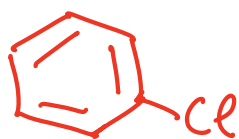
Gilman Reagents ([Watch the Gilman Reagent video](#)) → least basic → so they are the only reagents capable of reacting with:



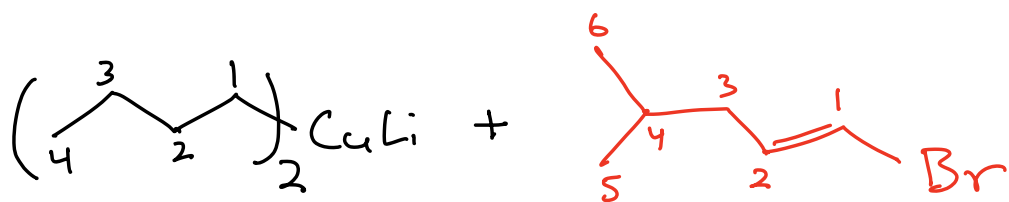
1) Primary haloalkanes



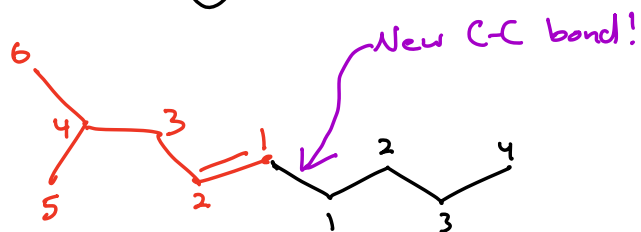
2) Vinyl halides



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)



Time Capsule

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

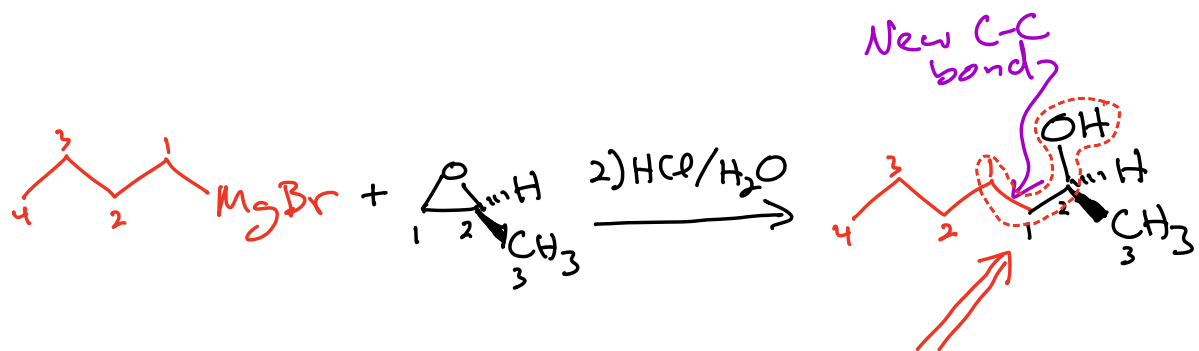
↳ So they can be used to react as nucleophiles with carbonyl compounds!

Synthesis \rightarrow New C-C bonds! \rightarrow
 \hookrightarrow Generate more complex molecules from simpler ones.

1) Retrosynthetic Analysis \rightarrow
Work backwards from the product.

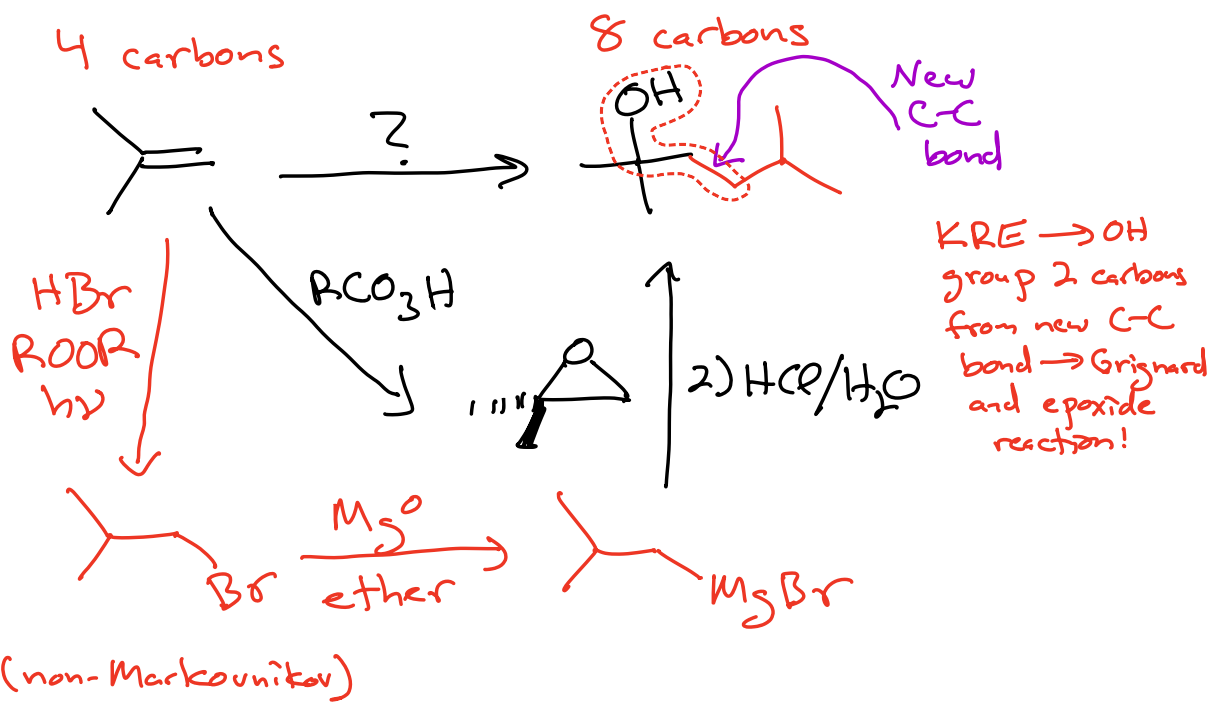
2) Count the number of carbon atoms in the starting material versus the product \rightarrow
Allows you to identify the location of any new C-C bonds.

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



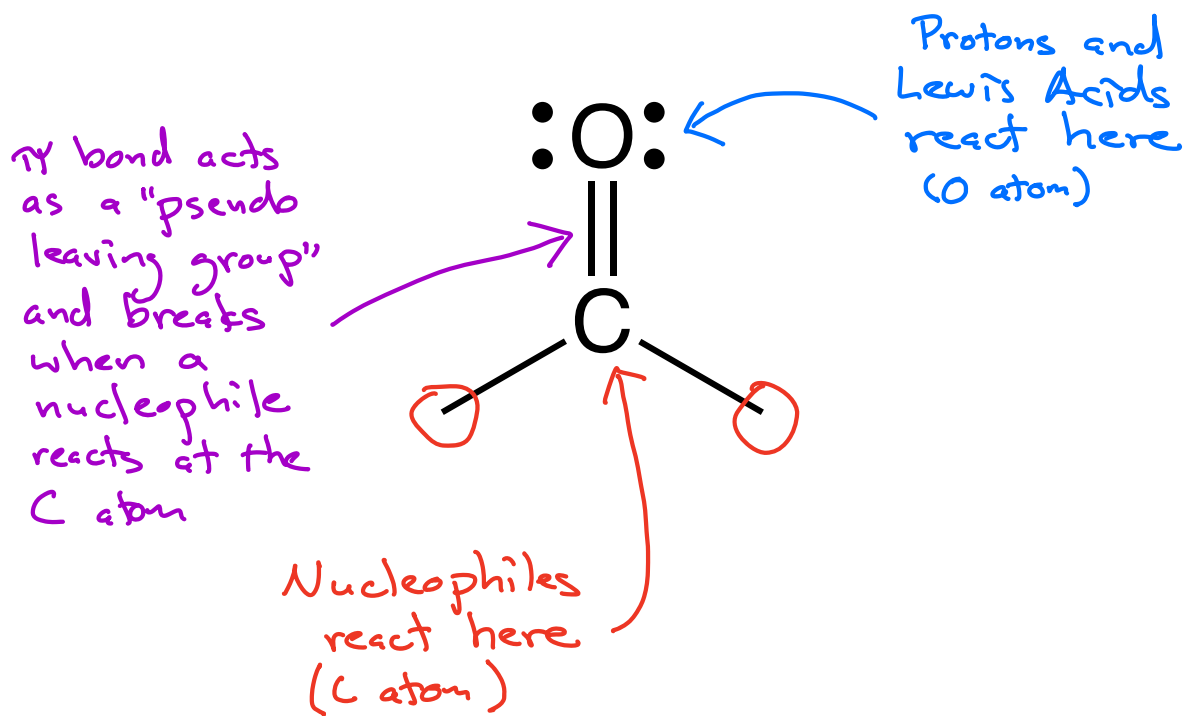
KRE → An alcohol group 2 carbons from a new C-C bond

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 Mechanisms A-D

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

1) There are basically four different mechanism 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

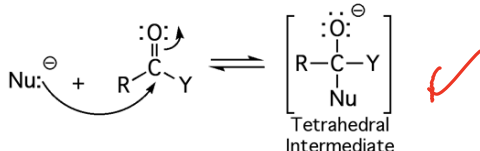
2) These same four mechanism elements describe most of the other mechanisms you have/will learn!!! (Yes, organic chemistry really is this simple if you look at it this way!!)

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.

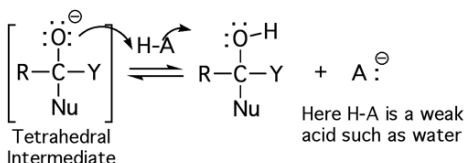
~~Four Mechanisms for the Reaction of Nucleophiles with Carbonyl Compounds~~

MECHANISM A: Reaction with a Strong Nucleophile

Step 1 Make a new bond between a nucleophile and electrophile

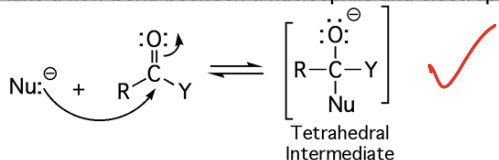


Step 2 Add a proton

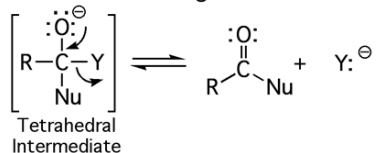


MECHANISM B: Reaction with a Strong Nucleophile When "Y" is a Good Leaving Group (-OR, -Cl, etc.).

Step 1 Make a new bond between a nucleophile and electrophile

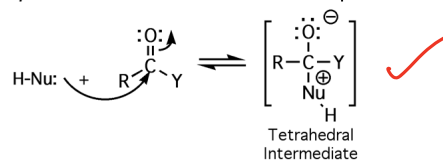


Step 2 Break a bond to give stable molecules or ions

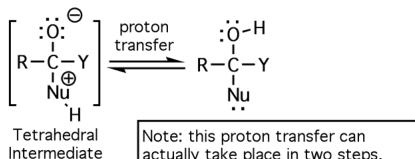


MECHANISM C: Reaction with a Weak Nucleophile

Step 1 Make a new bond between a nucleophile and electrophile



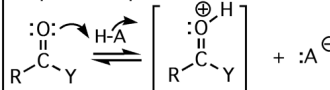
Step 2 Add a proton and Take a proton away



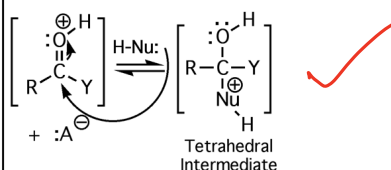
Note: this proton transfer can actually take place in two steps, i.e. Add a proton then Take a proton away or vice versa.

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

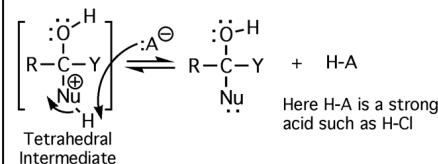
Step 1 Add a proton



Step 2 Make a new bond between a nucleophile and electrophile



Step 3 Take a proton away



Organic Chemistry is the study of carbon-containing molecules. This class has two points.

The first point of the class is to understand the organic chemistry of living systems. We will teach you how to think about and understand the most amazing molecules on the planet!!

You will learn how MRI scans work. 1/14/26

You will learn the basic principles of pharmaceutical science and how many drugs work. 1/21/26

You will learn about the special bond that holds carbohydrates such as glucose in six-membered rings, connects carbohydrate monomers together to make complex carbohydrate structures and is critical to DNA and RNA structure.

You will learn how soap is made from animal fat and how it works to keep us clean.

You will learn the important structural reason proteins, the most important molecular machines in our bodies, can support the chemistry of life.

You will learn how important antibiotics like penicillins work, including ones that make stable covalent bonds as part of their mode of action.

You will learn why carrots are orange and tomatoes are red.

You will learn the very cool reason that the DNA and RNA bases are entirely flat so they can stack in the double helix structure.

You will learn how energy drinks work.

You will learn even more about why fentanyl is such a devastating part of the opioid problem and how Naloxone is an antidote for a fentanyl overdose.

You will learn even more details about why Magic Johnson is still alive, decades after contracting HIV, and how the same strategy is being used to fight COVID.

You will learn about the surprising chemical reason the Pfizer and Moderna mRNA vaccines elicit strong immune responses.

The second point of organic chemistry is the synthesis of complex molecules from simpler ones by making and breaking specific bonds, especially carbon-carbon bonds.

You will learn how carbon-metal bonds lead to new carbon-carbon bonds. 1/21/26

You will learn how most reactions of carbonyl compounds involve only the four common mechanistic elements operating in only a few common patterns. 1/21/26

You will learn how, by simply adding a catalytic amount of base like HO^- to aldehydes or ketones, you can make new carbon-carbon bonds, giving complicated and useful products.

You will learn a reaction that can convert vinegar and vodka into a common solvent.

You will learn why molecules with six-membered rings and alternating double bonds are stable.

You will learn a reaction that can turn model airplane glue into a powerful explosive.

Most important, you will develop powerful critical thinking skills:

1. You will learn how to look at a molecule and accurately predict which atoms will react to make new bonds, and which bonds will break during reactions.
2. You will learn how to analyze a complex molecule's structure so that you can predict ways to make it via multiple reactions starting with less complex starting molecules.

All of these mechanisms have a tetrahedral intermediate ✓

Mechanism A \Rightarrow Use this with strong nucleophiles

(
 \Rightarrow 1) Make a bond
2) Add a proton

Grignard Reagent Reacting with an Aldehyde or Ketone

