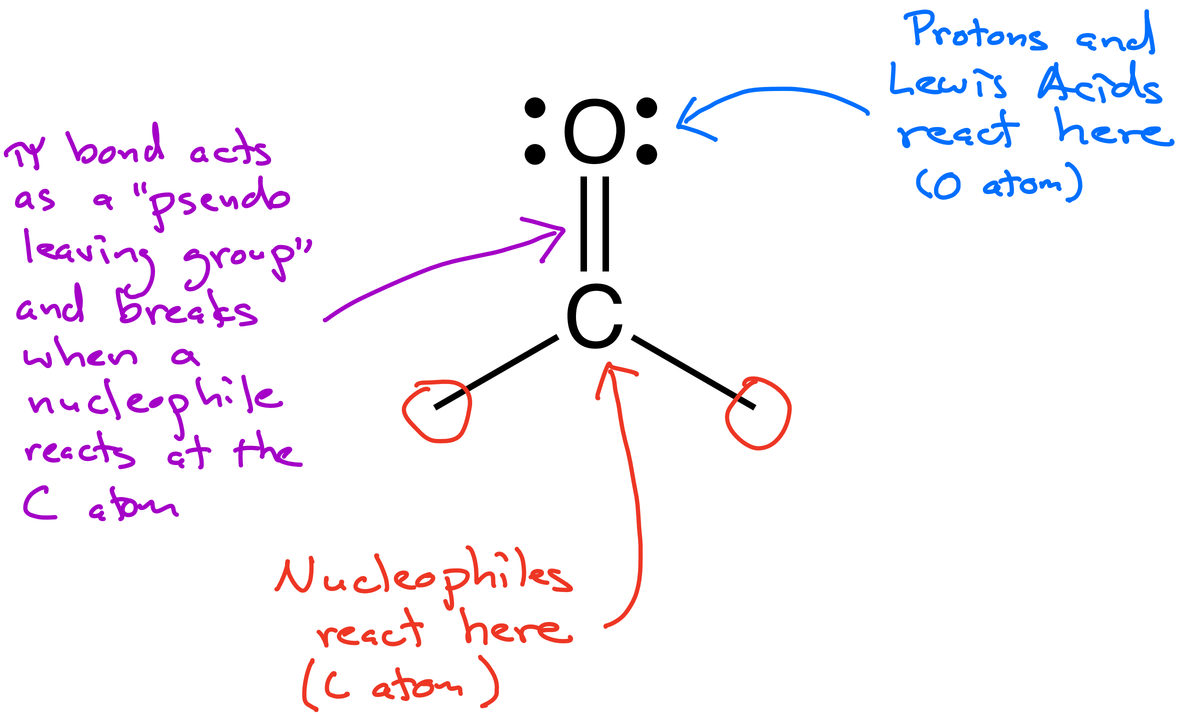
I am

I can

I will

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!!

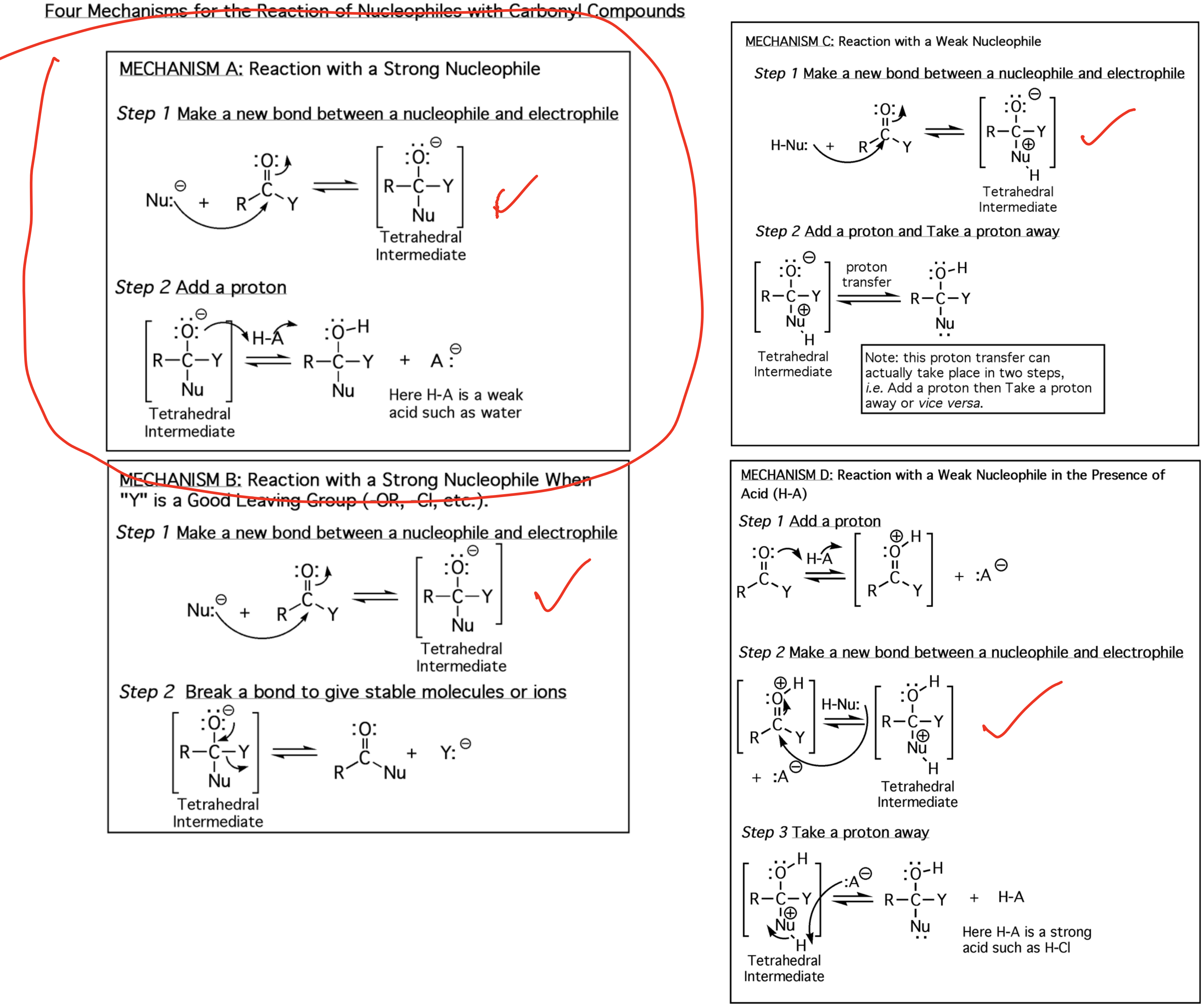
1) There are basically four different mechanisms elements that make up the steps of carbonyl reactions.

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



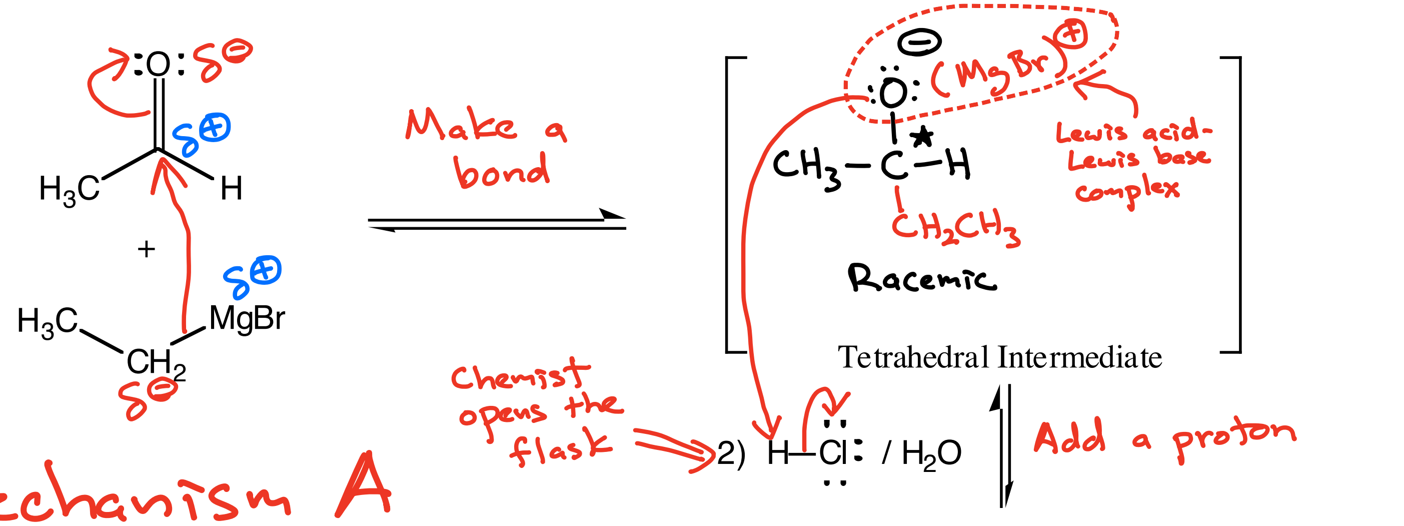
All of these mechanisms have a tetrahedral intermediate ✓

Mechanism A ⇒ Use this with strong nucleophiles

⇒ 1) Make a bond

2) Add a proton

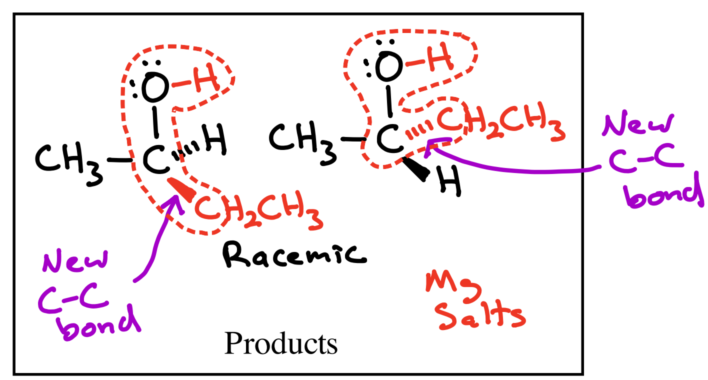
Grignard Reagent Reacting with an Aldehyde or Ketone

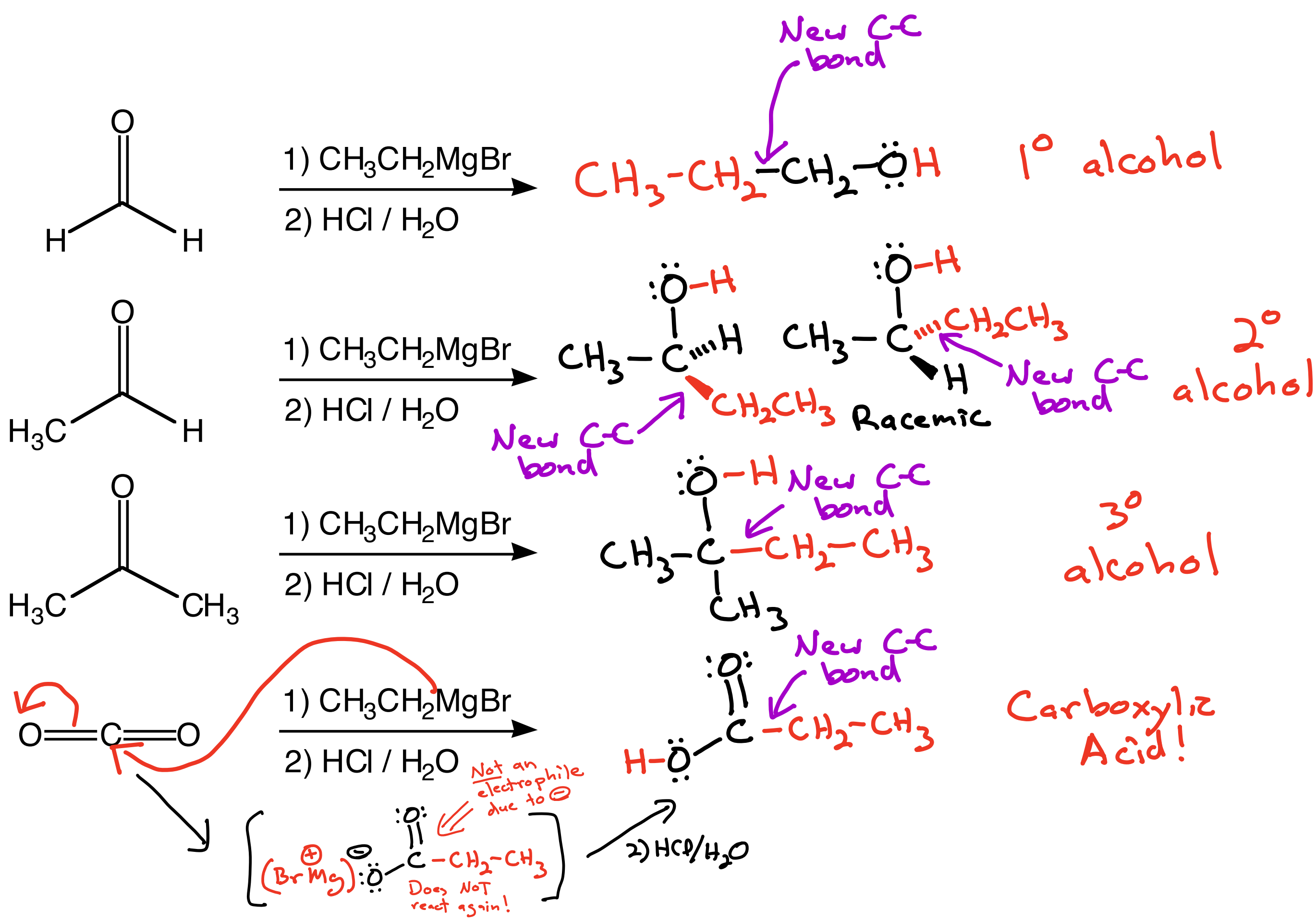


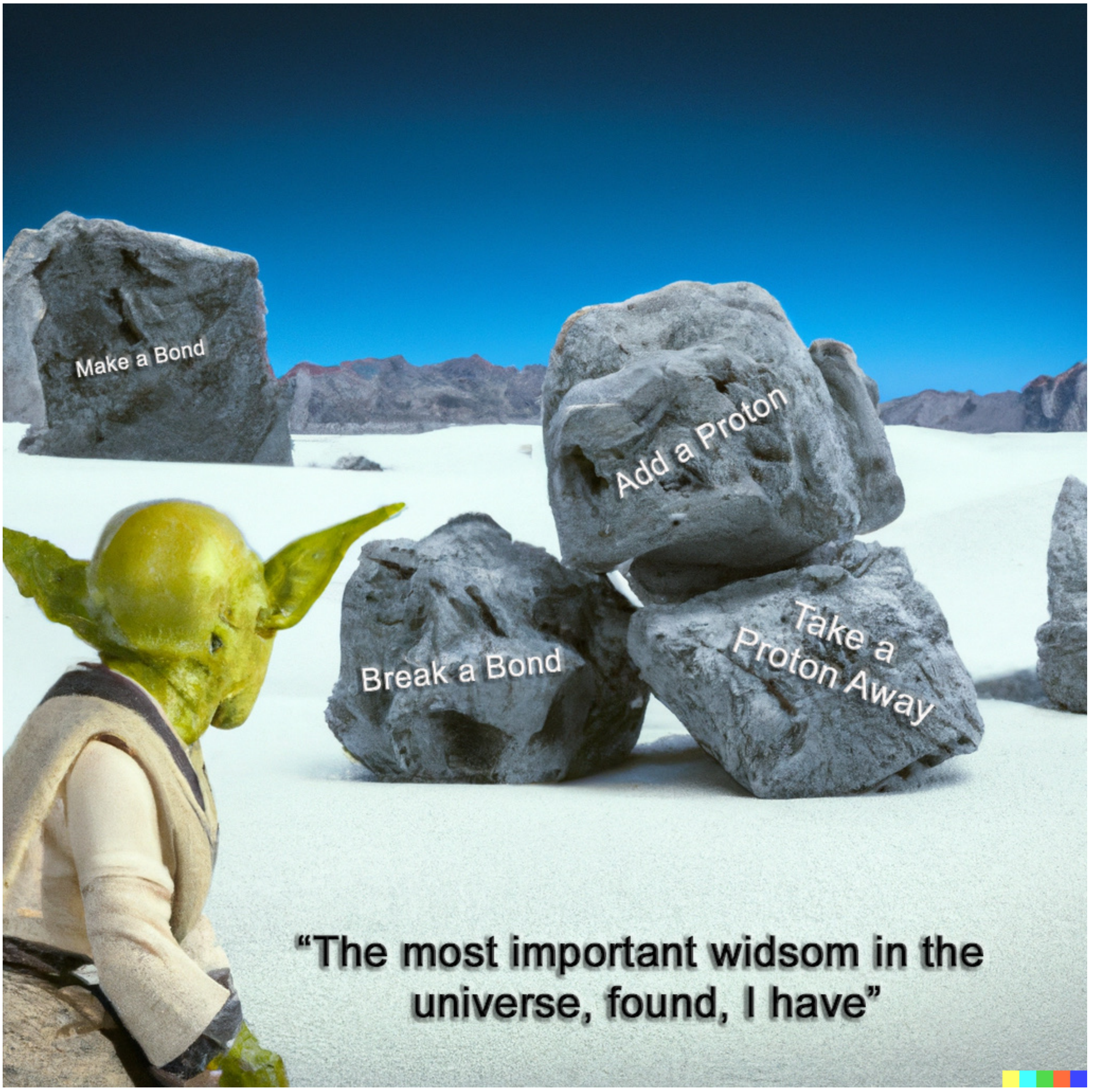
Mechanism A

Key Recognition Element (KRE):

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






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

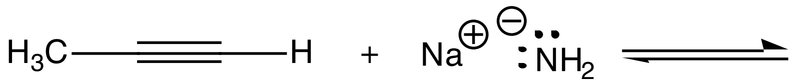
Lesson for Today:

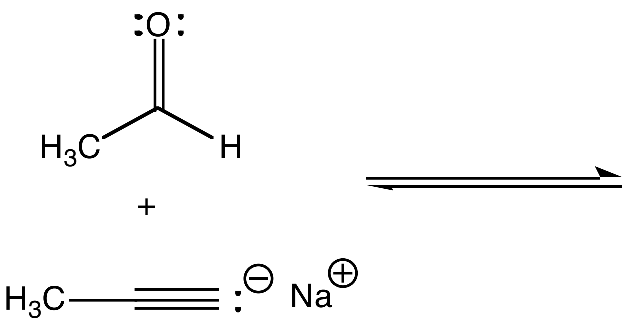
Strong nucleophiles react directly at the electrophilic C atom of carbonyls to

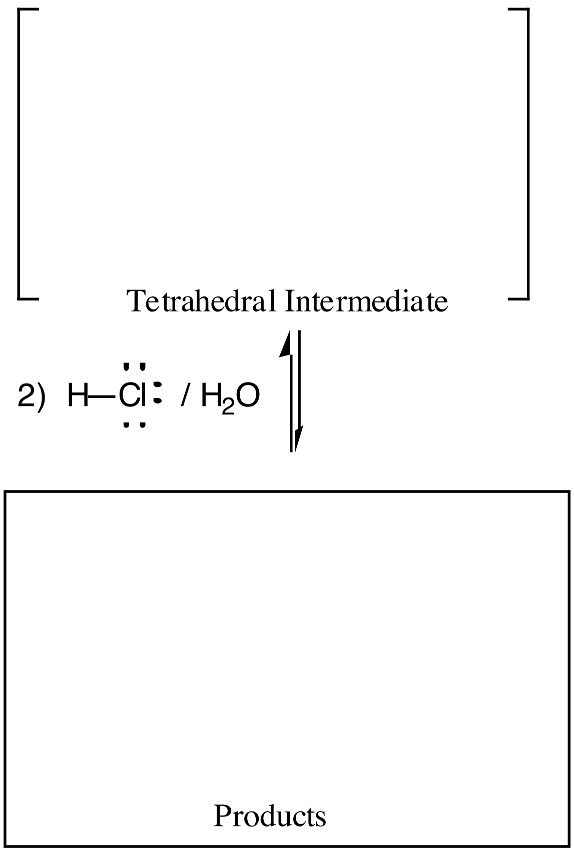
as the carbonyl π bond breaks. to

the O atom.

Alkyne Anion Reacting with an Aldehyde or Ketone

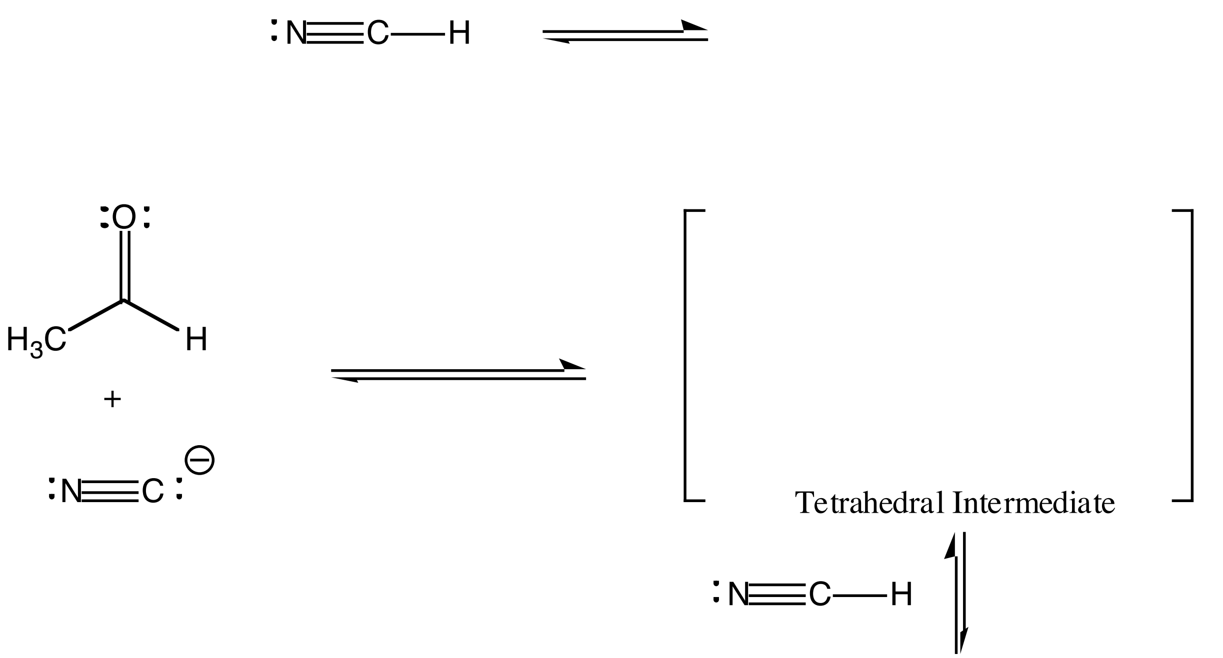




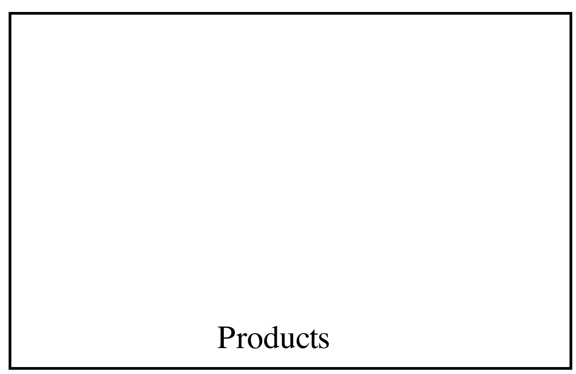


Key Recognition Element (KRE):

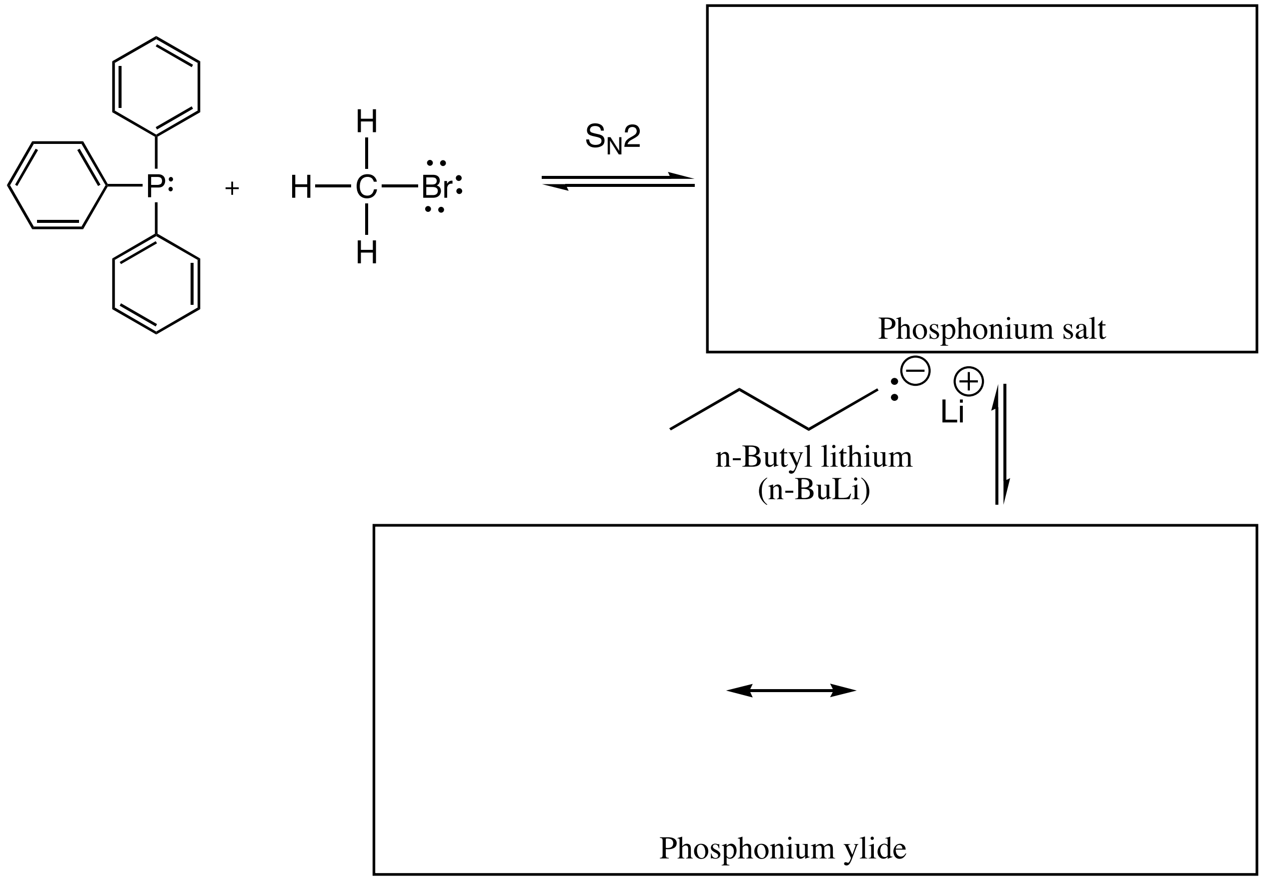
HCN Reacting with an Aldehyde or Ketone

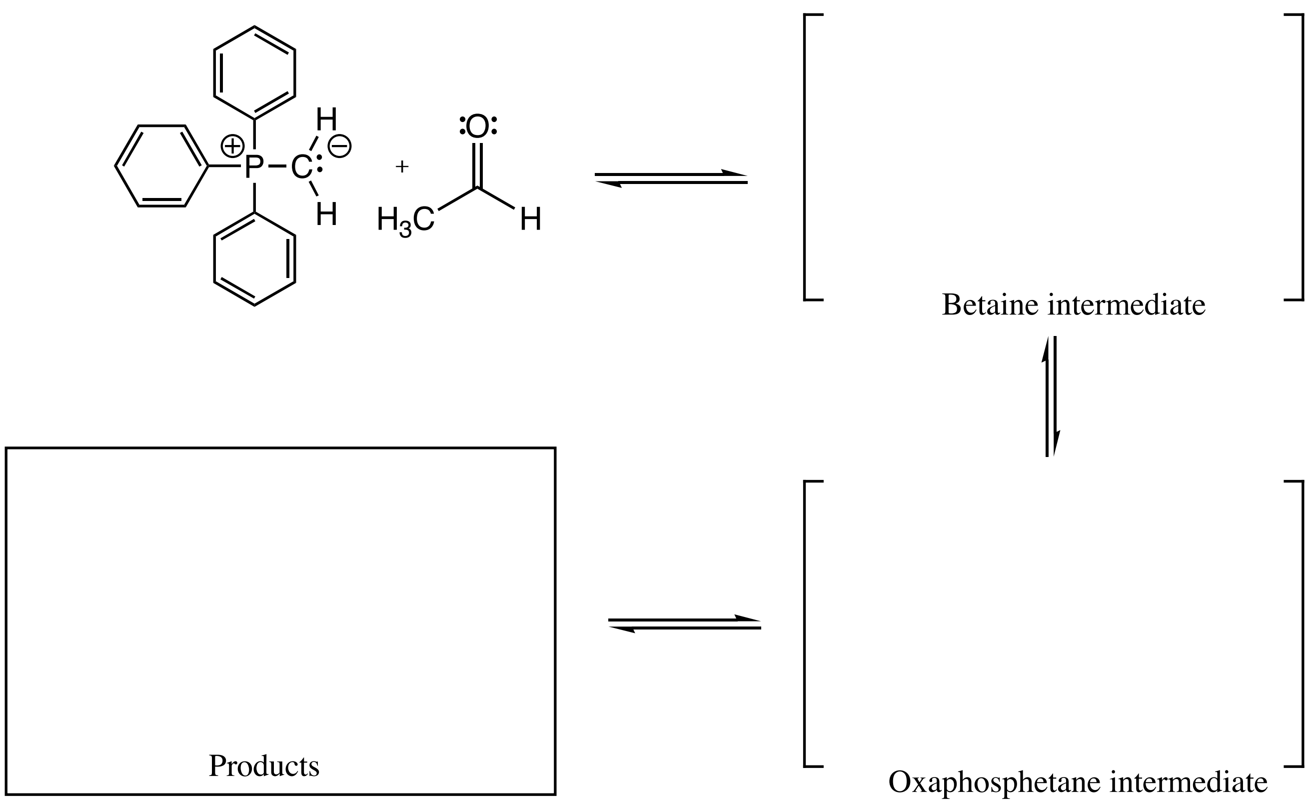


Key Recognition Element (KRE):



Wittig Reaction



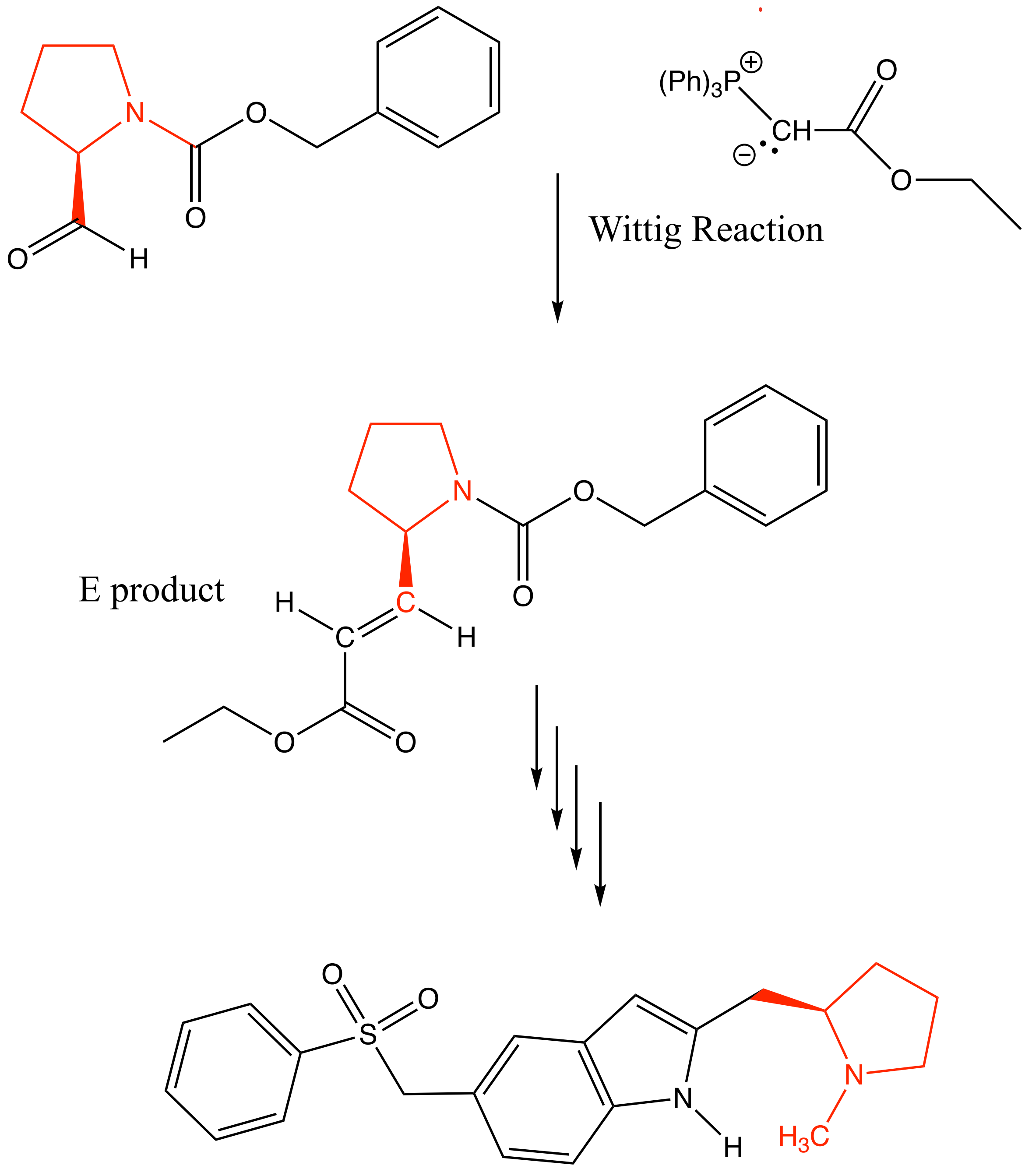


Key Recognition Element (KRE):

E vs. Z → Which product alkene?

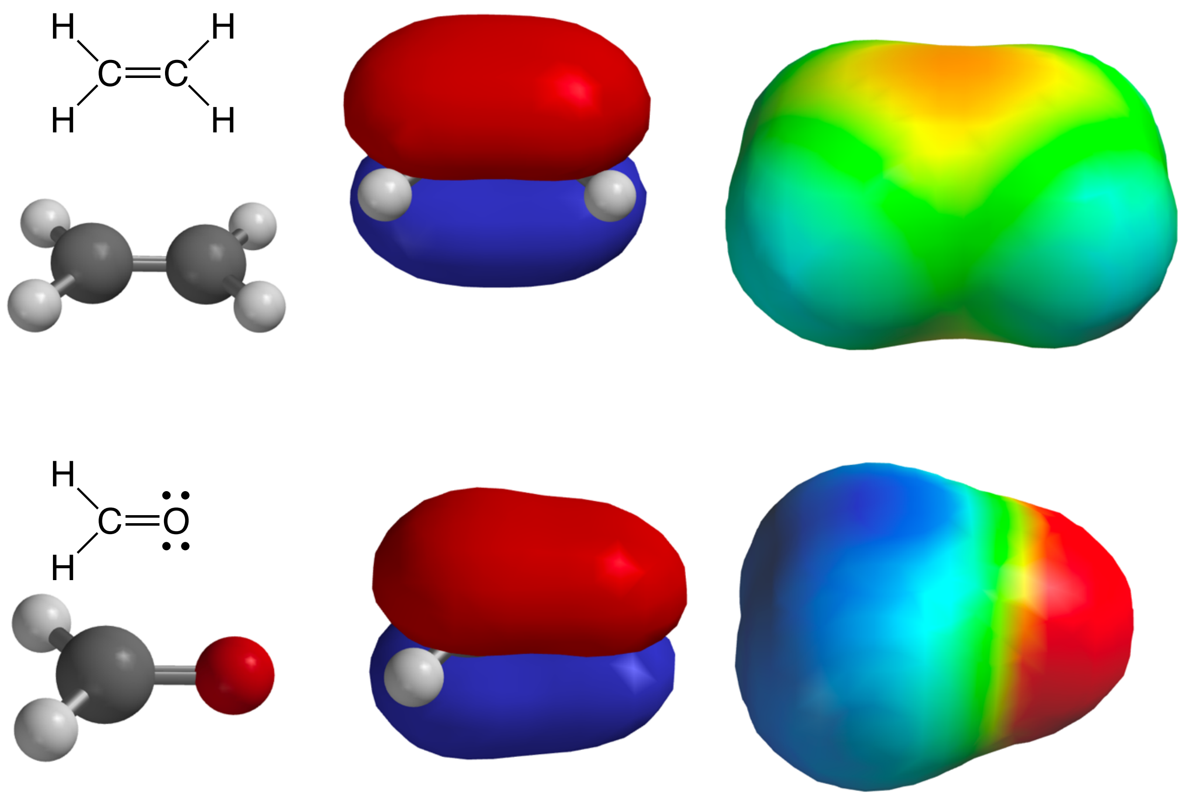
1) With alkyl Wittig reagents, the Z alkene product predominates

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

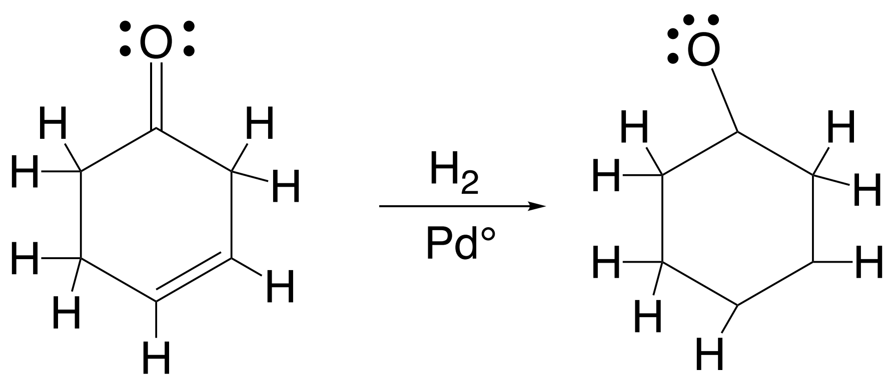


Eletriptan - used to treat migraine headaches
A seratonin receptor agonist (5-HT$_{1B,1D,1F}$)

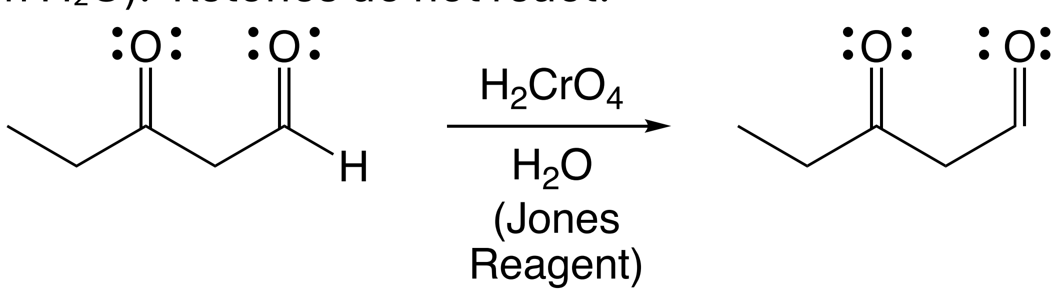
Detour: Hydrogenation and Oxidation of Aldehydes and Ketones



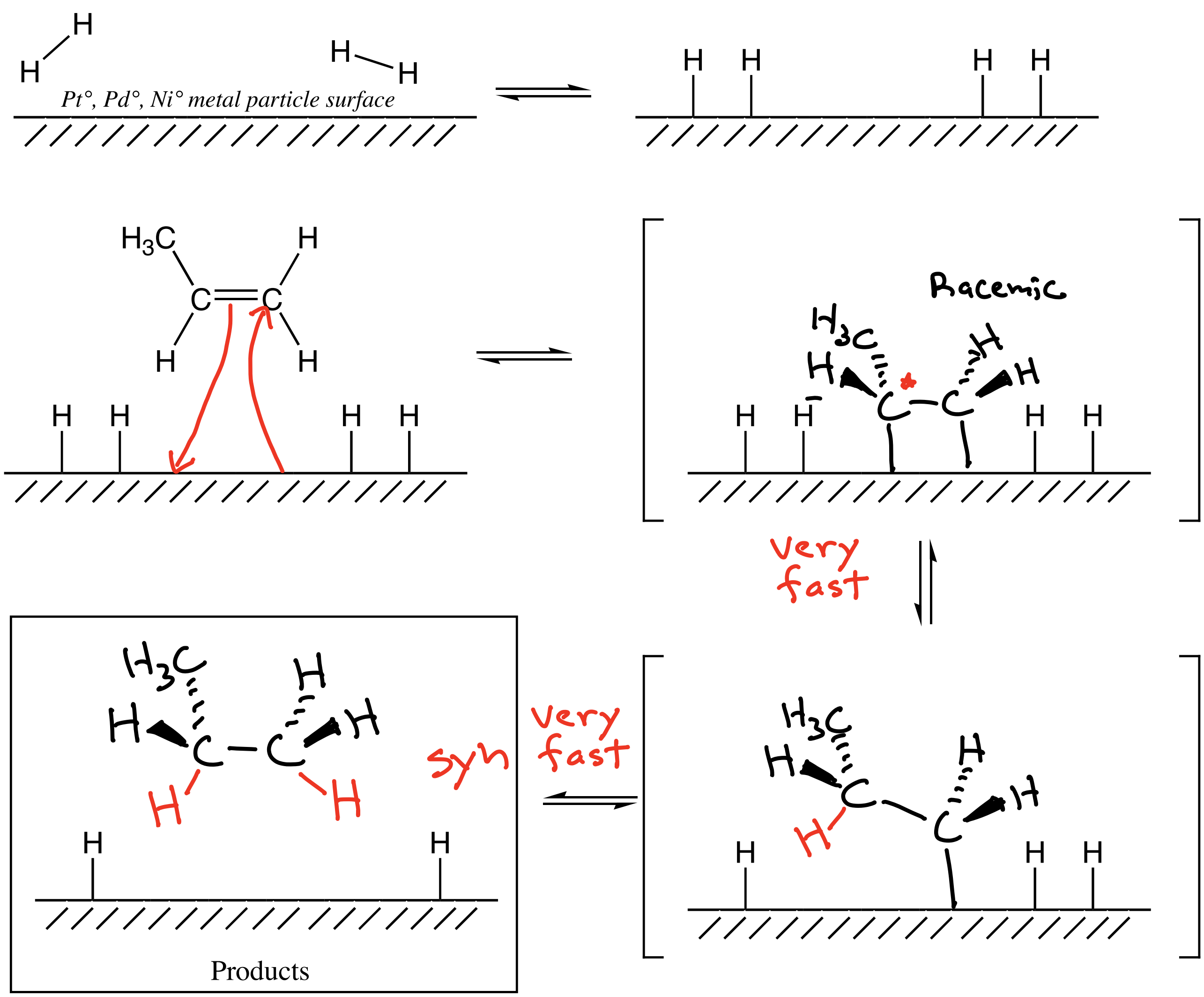
The pi bonds of carbonyls react the same as pi bonds of alkenes with H_2 in the presence of Pt°, Pd° or Ni°



Aldehydes are oxidized to carboxylic acids using the Jones Reagent (H_2CrO_4 in H_2O). Ketones do not react.



Hydrogenation: H_2 with Pt°, Pd°, Ni°

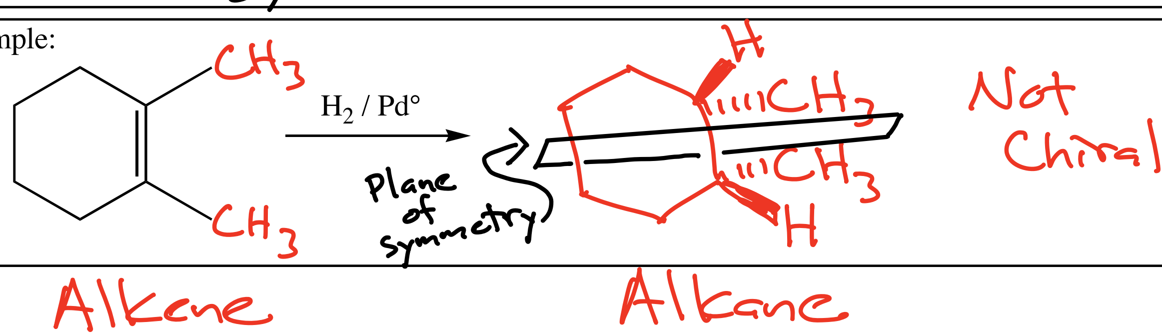


Summary: H_2 adsorbs onto the metal surface.
The alkene adsorbs onto the metal surface.
H atoms transfer to both C atoms →
on the same face → before the C-C bond rotates

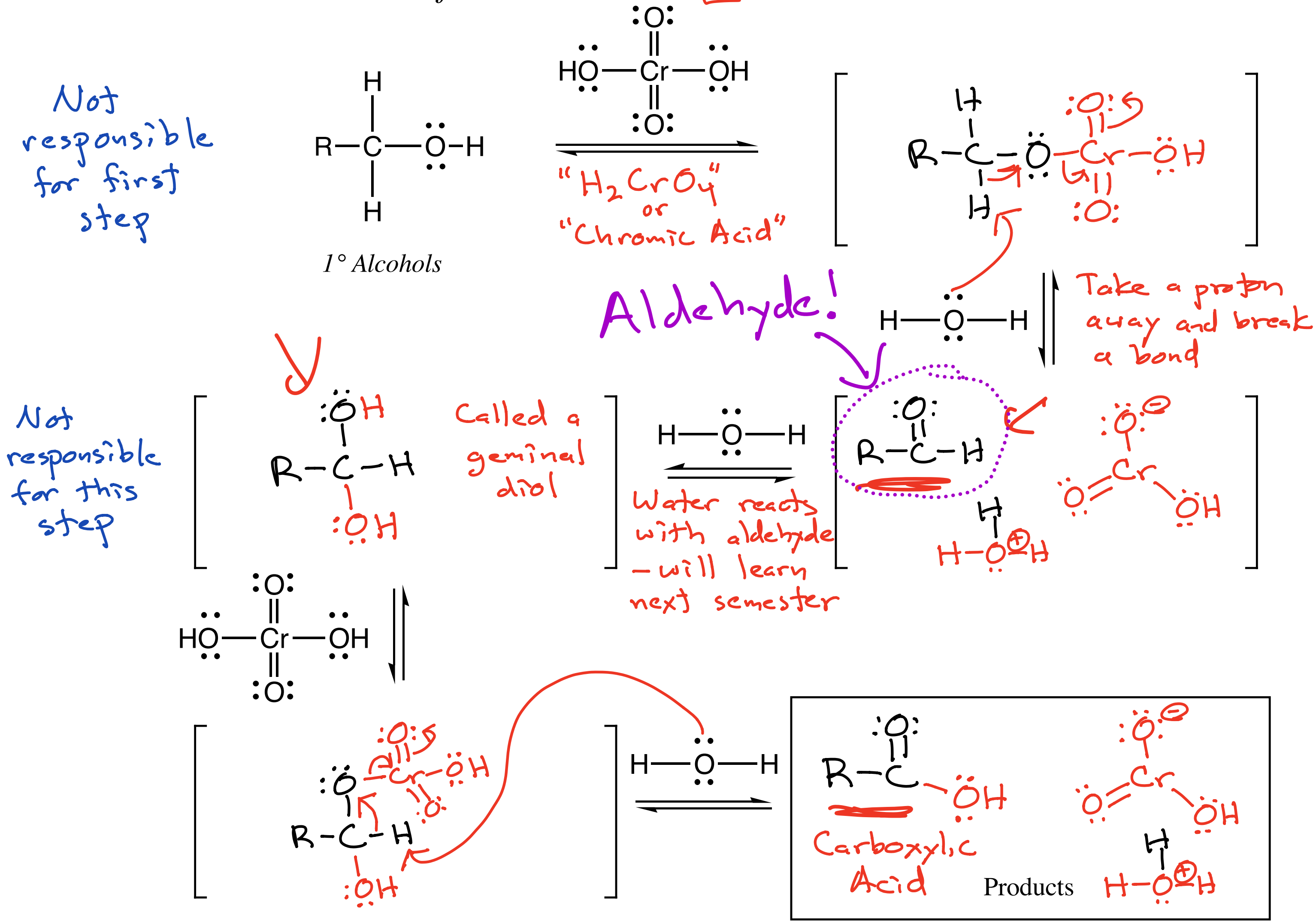
Regiochemistry: N/A

Stereochemistry: Syn

Example:



Chromic Acid Oxidation of Alcohols



Summary:

- $1°$ alcohols ⇒ Carboxylic Acid (R–C(=O)–OH)
- $2°$ alcohols ⇒ Ketone (R–C(=O)–R)
- $3°$ alcohols ⇒ NO REACTION

Regiochemistry: N/A

Stereochemistry: N/A

Example:

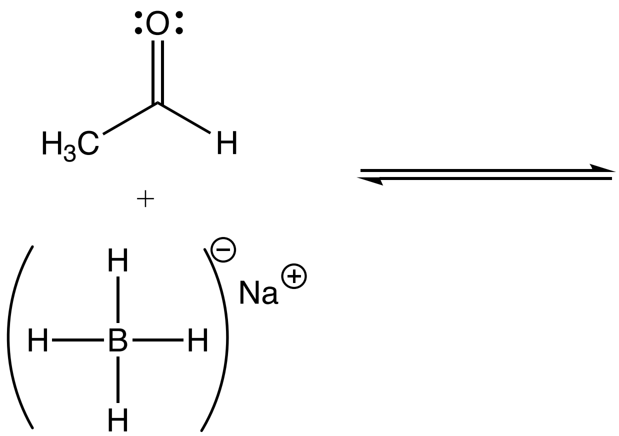
We now return to our regularly scheduled discussion of Mechanism A

Metal Hydride Reduction

How to think about the reagent:

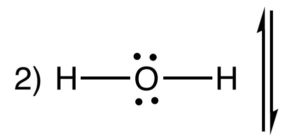
$\Rightarrow$

Sodium Borohydride Reacting with an Aldehyde or Ketone



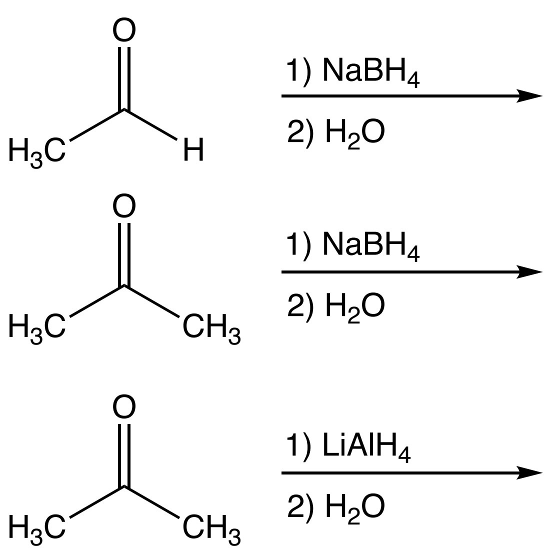
$NaBH_4$

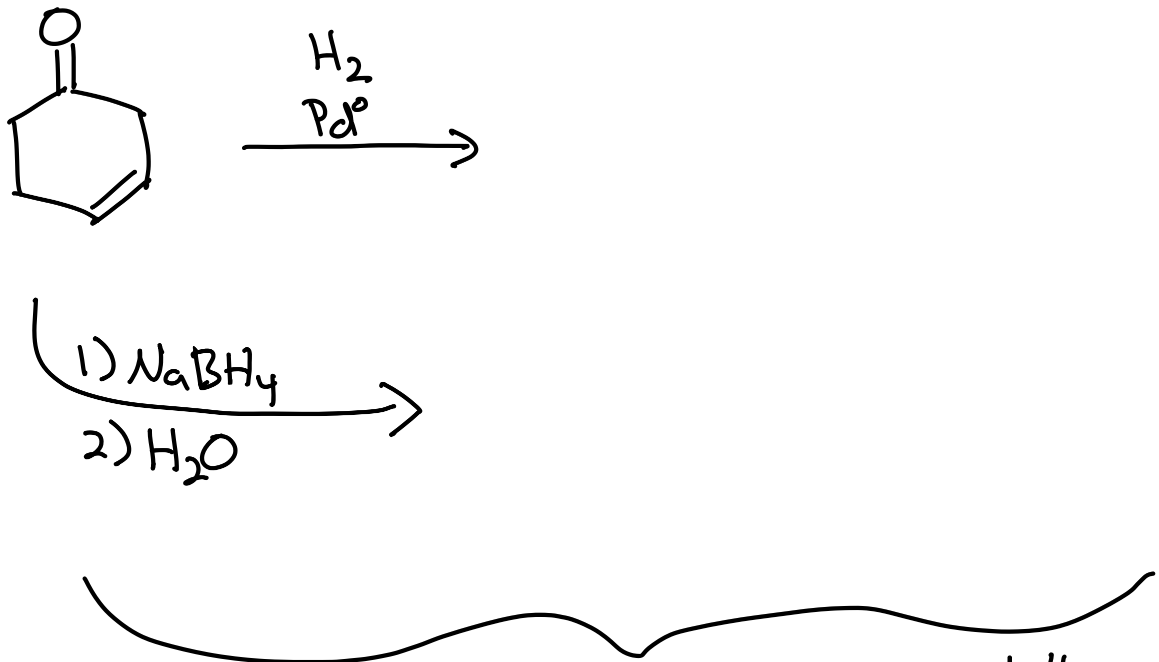
Tetrahedral Intermediate



Key Recognition Element (KRE):

Products





"hydride"

This makes sense because $H:^{\ominus}$ is a and C=O is an , while C=C is so it cannot react!

Weak nucleophiles such as $R-\ddot{\underset{..}{O}}-H$ are not strong enough to react with a C=O of a ketone or aldehyde

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

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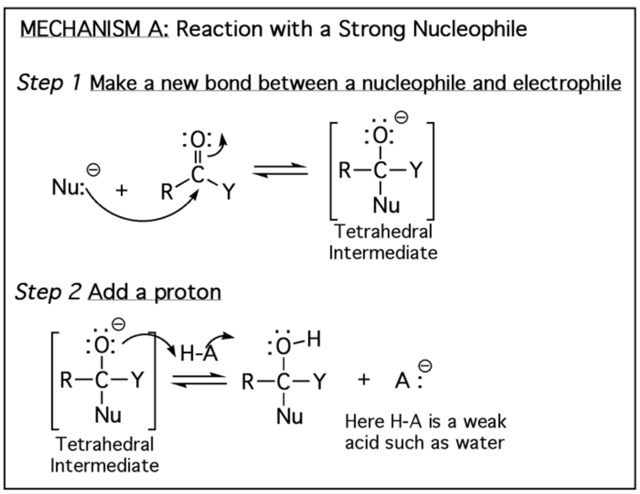
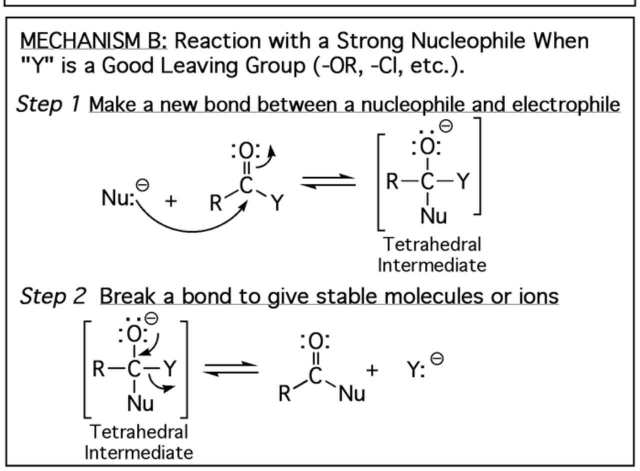
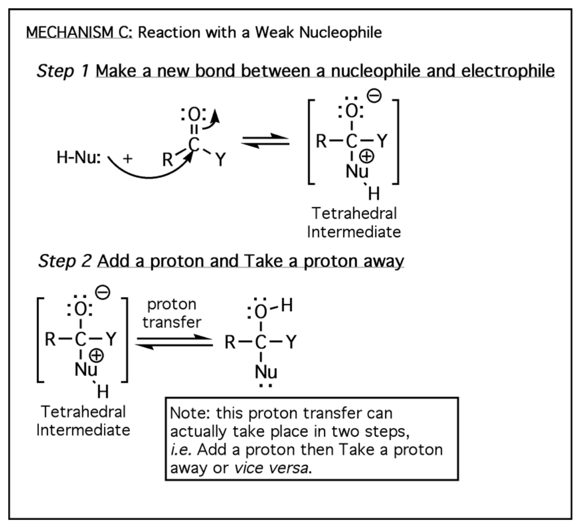
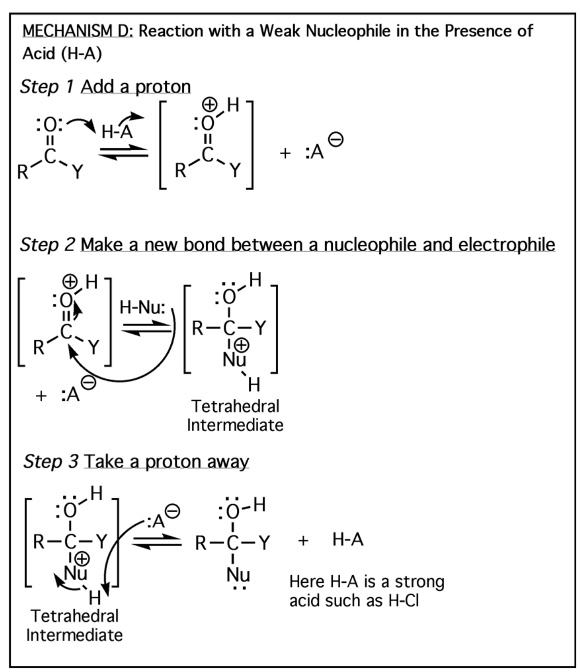
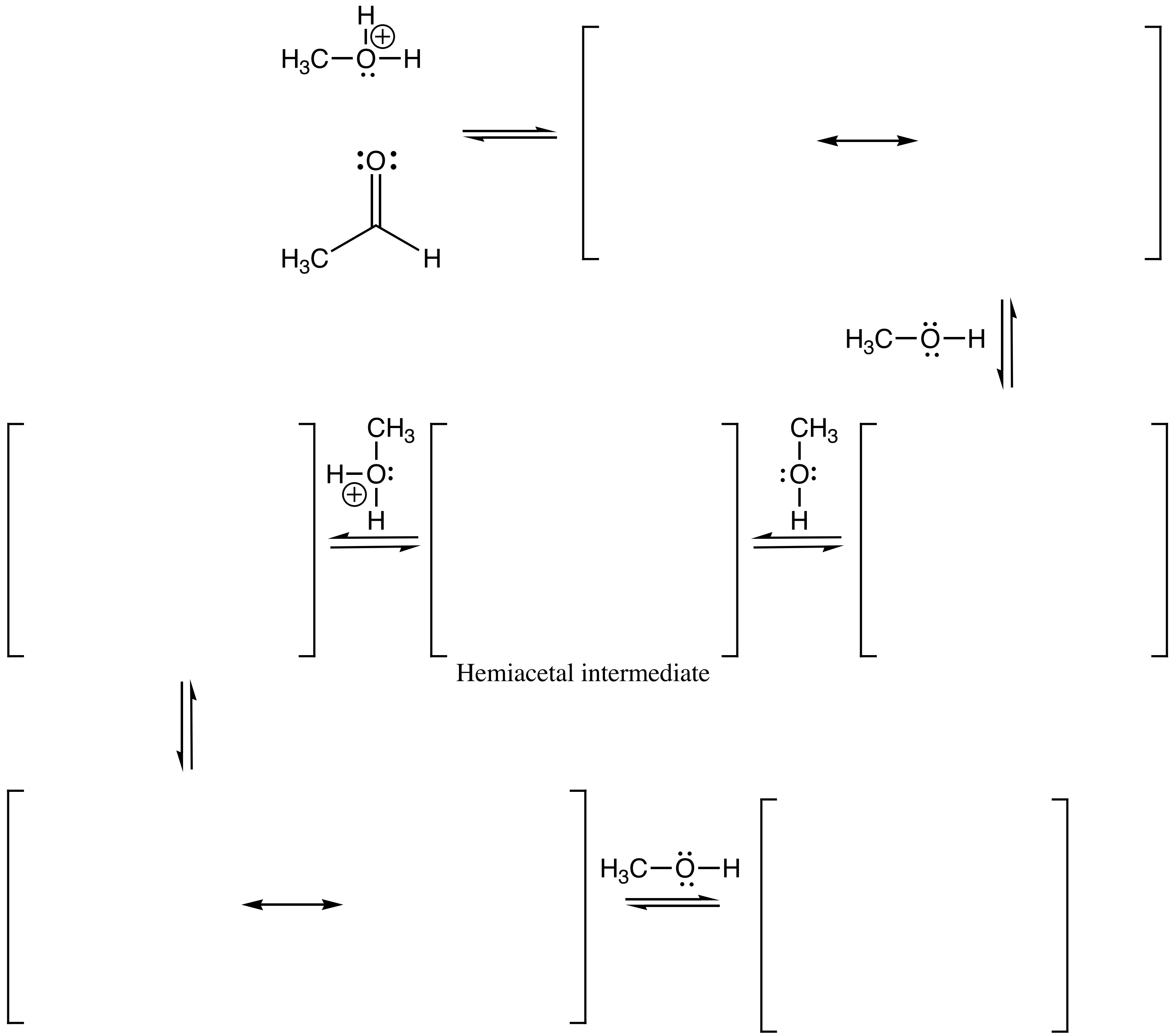


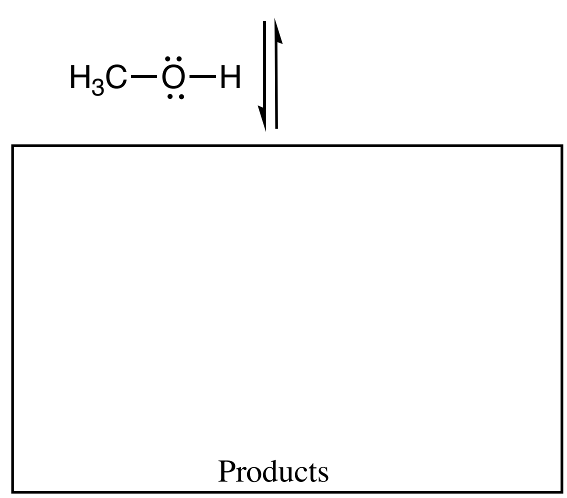






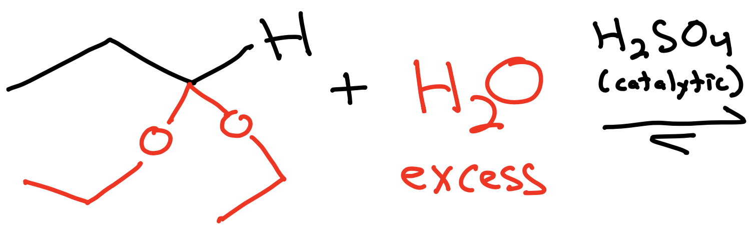
Acid Catalyzed Hemiacetal and Acetal Formation From an Aldehyde or Ketone



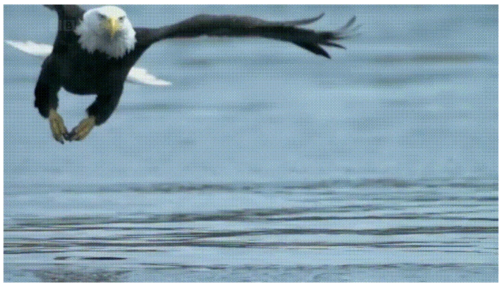


Key Recognition Element (KRE):

Just like alkene hydration last semester, this acetal formation reaction is REVERSIBLE



Le Chatlier's Principle

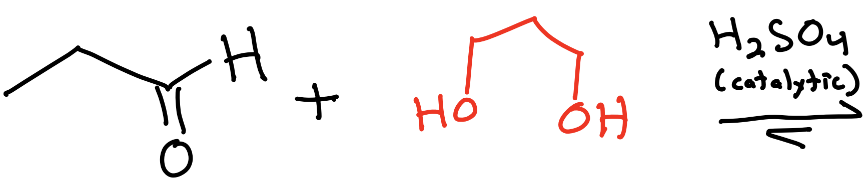


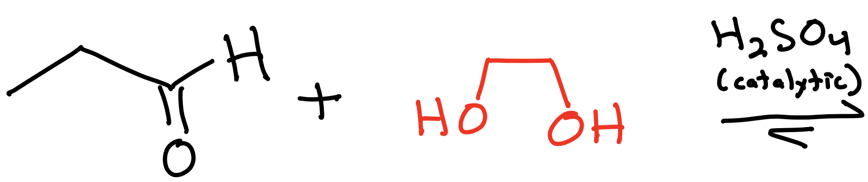
"The Claw"

Cyclic acetals are more stable than "normal" acetals because of the chelate effect.

"Normal" acetal

Cyclic acetals → 5 and 6-membered rings!



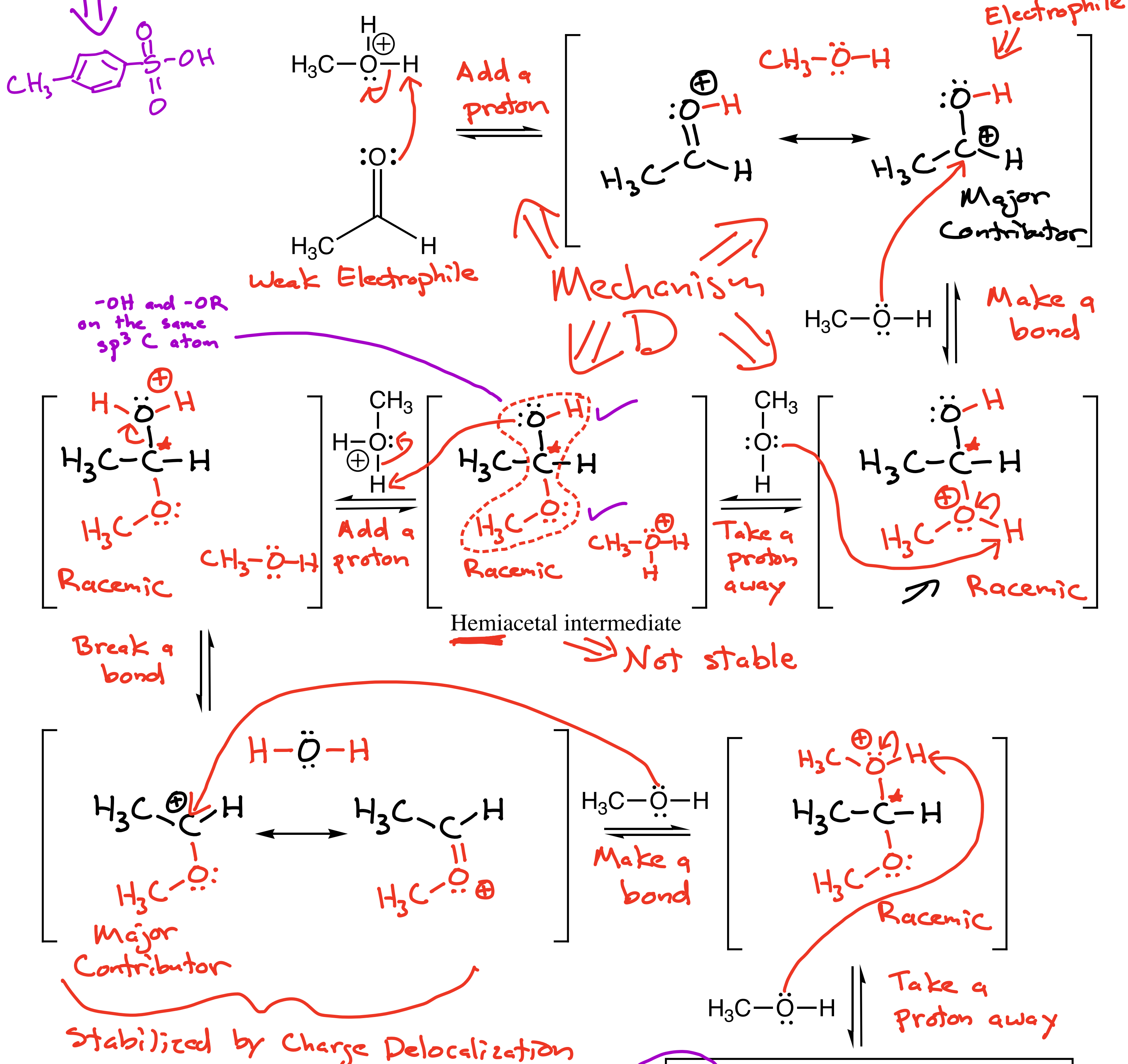


TsOH or H_2SO_4

Tosylic Acid

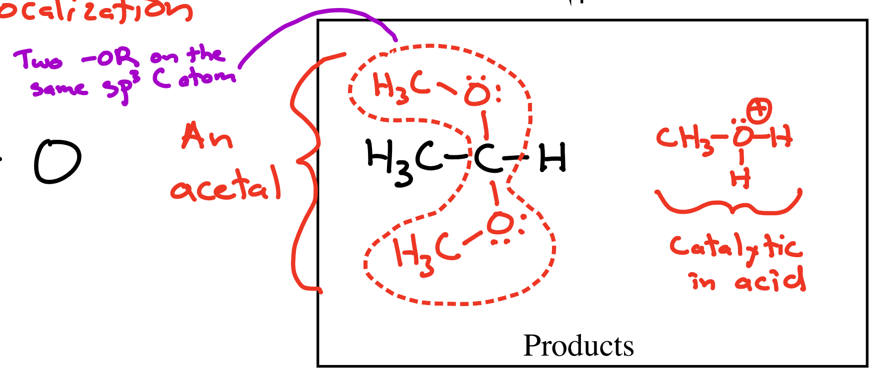
"Hey, does that thing have a hemi in it?" "SWEET!" !

Acid Catalyzed Hemiacetal and Acetal Formation From an Aldehyde or Ketone



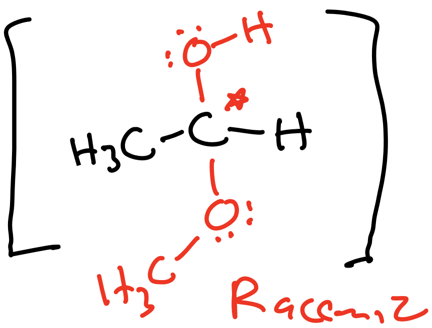
Key Recognition Element (KRE):

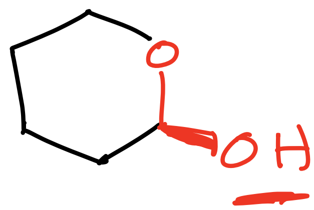
Two bonds to ether O atoms to an sp^3 C atom

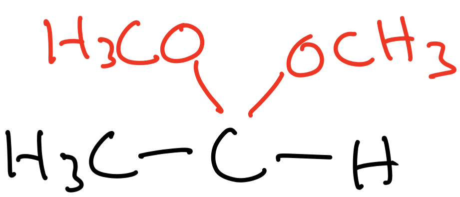


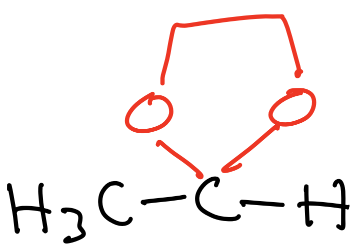
Recap

Hemiacetal →

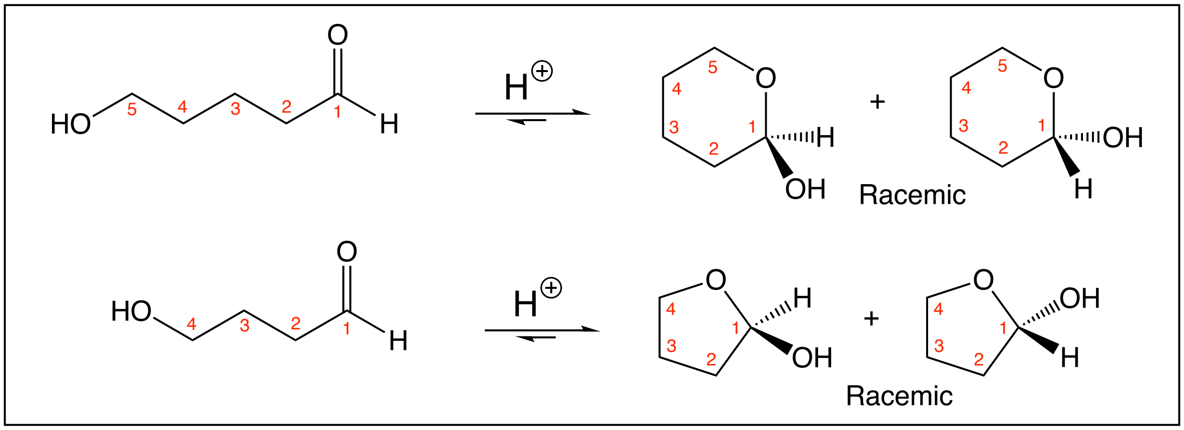


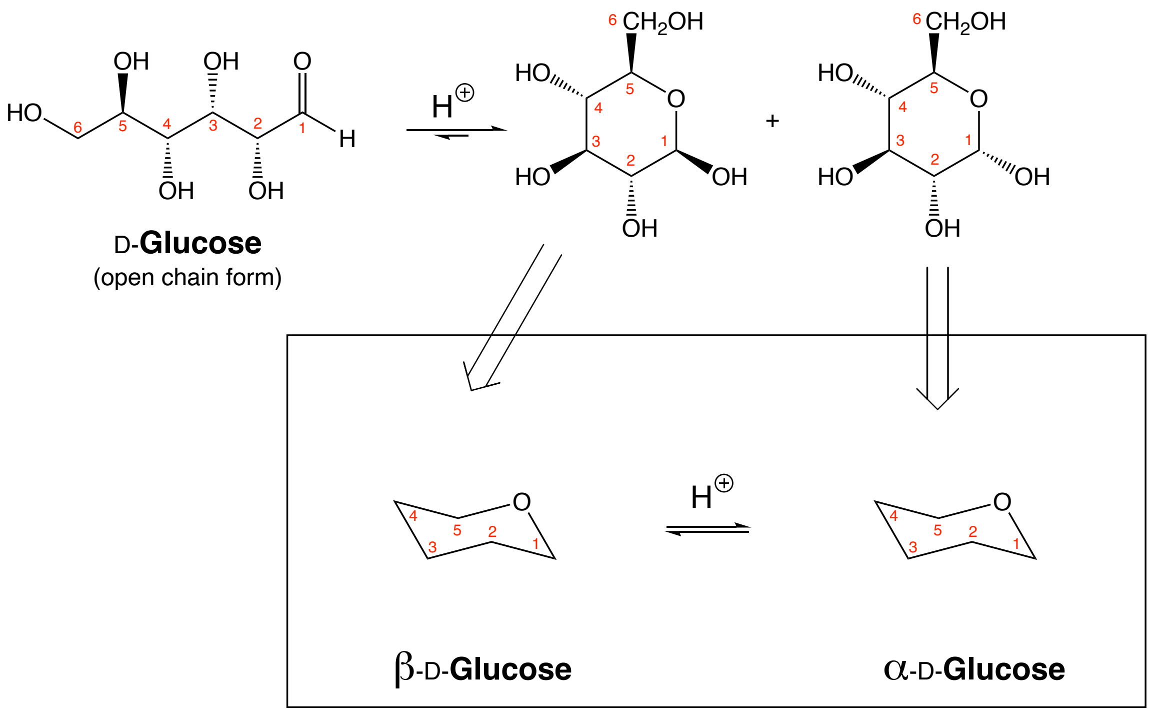


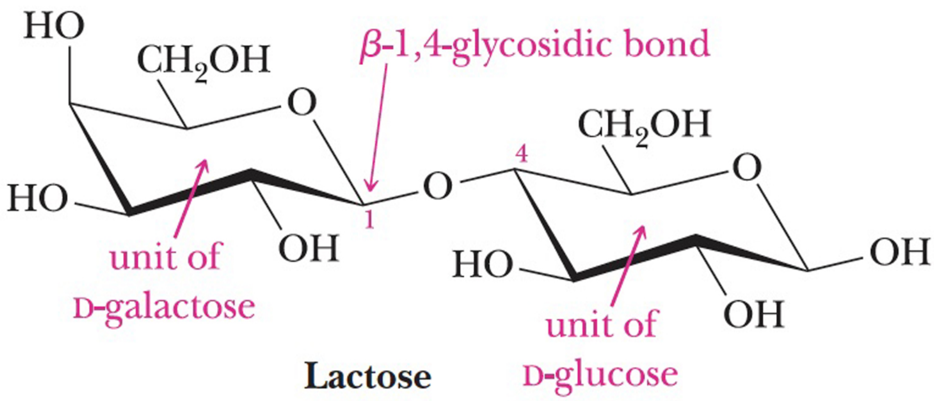




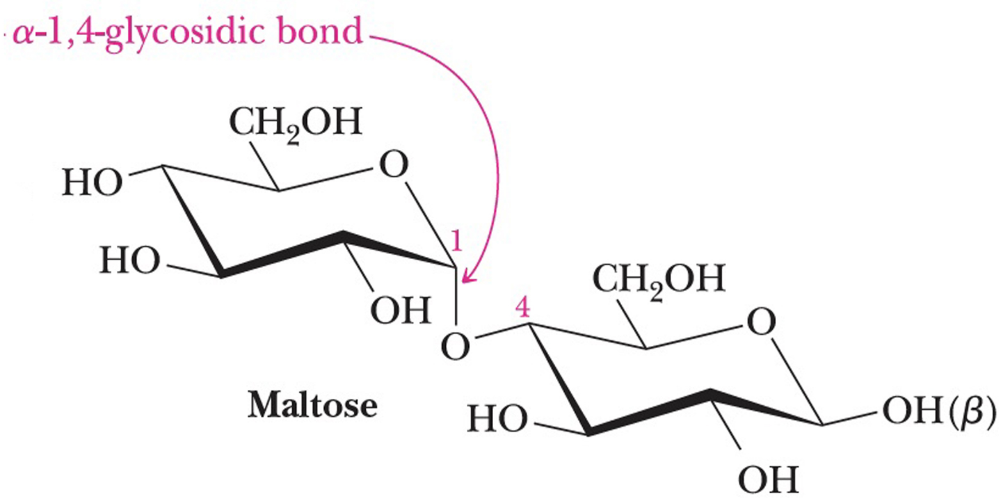
Cyclic Hemiacetals and Carbohydrates



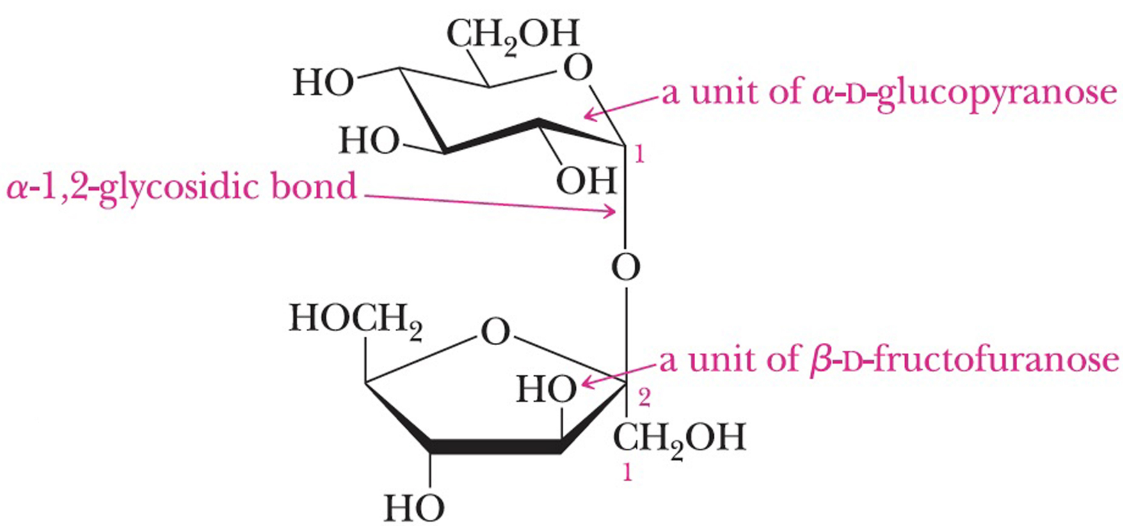




Lactose



Maltose



Sucrose