



# 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**

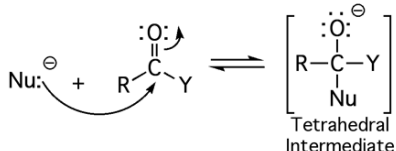
2) These same four mechanism elements describe most of the other mechanisms you have/will learn!!! (Yes, organic chemistry really is this simple if you look at it this way!!)

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.

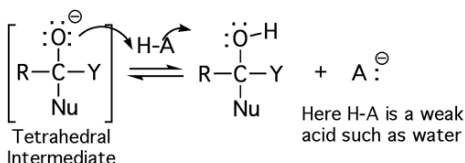
## Four Mechanisms for the Reaction of Nucleophiles with Carbonyl Compounds

### MECHANISM A: Reaction with a Strong Nucleophile

Step 1 Make a new bond between a nucleophile and electrophile

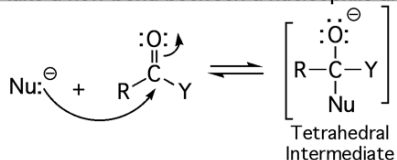


Step 2 Add a proton

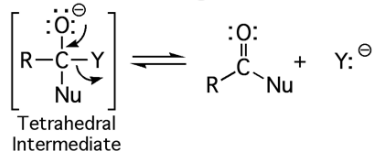


### MECHANISM B: Reaction with a Strong Nucleophile When "Y" is a Good Leaving Group (-OR, -Cl, etc.).

Step 1 Make a new bond between a nucleophile and electrophile

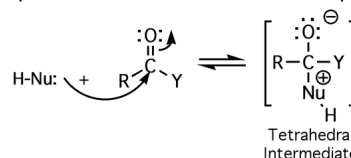


Step 2 Break a bond to give stable molecules or ions

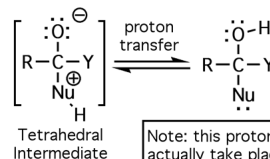


### MECHANISM C: Reaction with a Weak Nucleophile

Step 1 Make a new bond between a nucleophile and electrophile



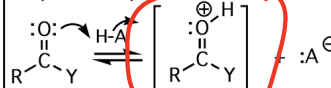
Step 2 Add a proton and Take a proton away



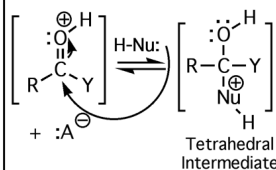
Note: this proton transfer can actually take place in two steps, i.e. Add a proton then Take a proton away or vice versa.

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

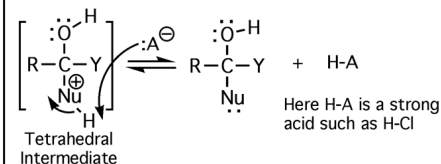
Step 1 Add a proton



Step 2 Make a new bond between a nucleophile and electrophile



Step 3 Take a proton away

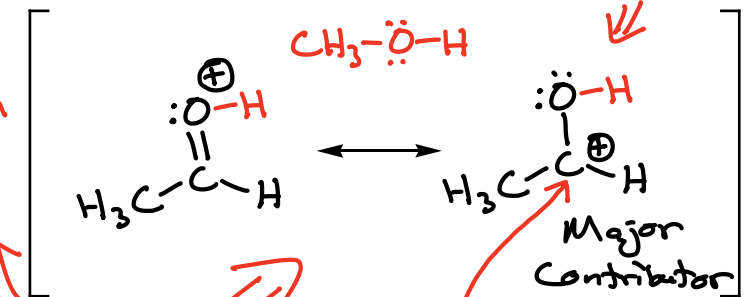
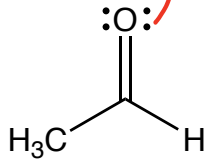
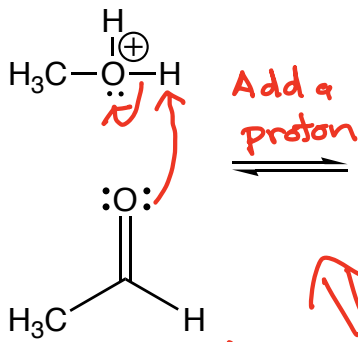
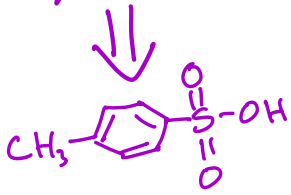


TsOH or H<sub>2</sub>SO<sub>4</sub>

Tosylic Acid

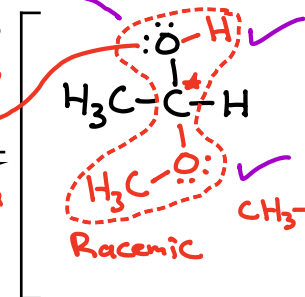
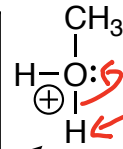
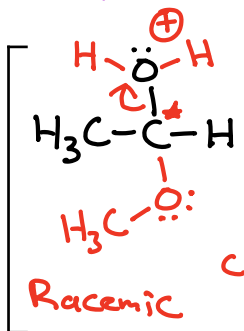
# Acid Catalyzed Hemiacetal and Acetal Formation From an Aldehyde or Ketone

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

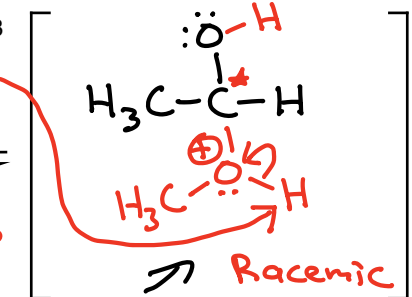
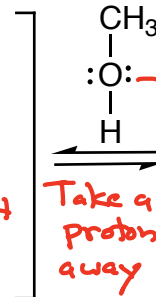


Mechanism

-OH and -OR on the same sp<sup>3</sup> C atom

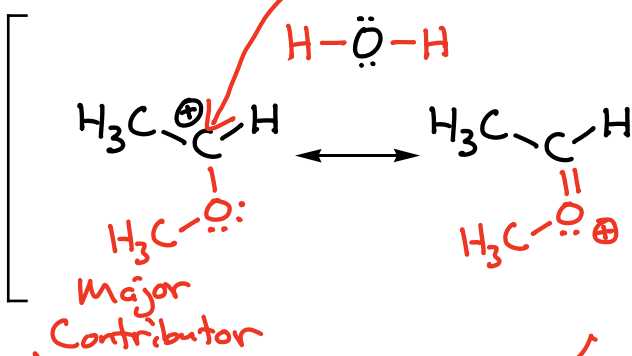


Hemiacetal intermediate

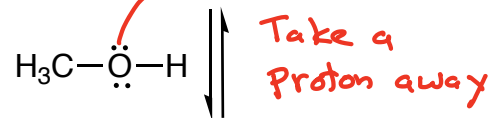
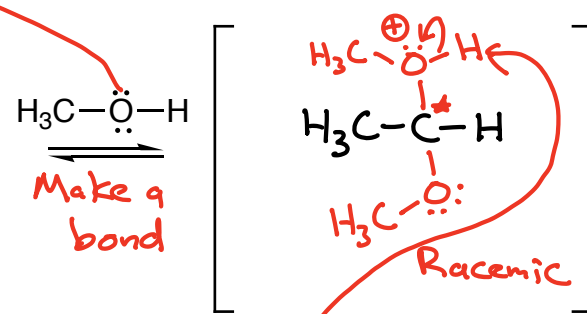


Break a bond

Not stable



Stabilized by Charge Delocalization

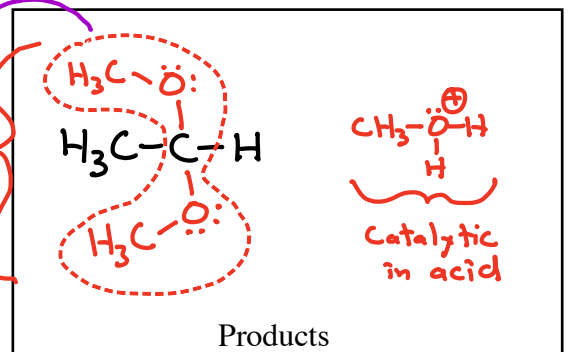


Key Recognition Element (KRE):

Two -OR on the same sp<sup>3</sup> C atom

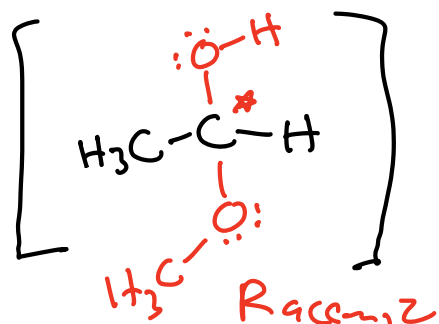
Two bonds to ether O atoms to an sp<sup>3</sup> C atom

An acetal

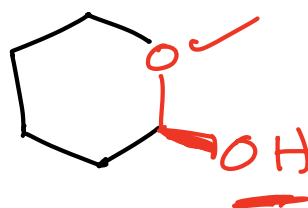


# Recap

**Hemiacetal** → One alcohol and one ether on same C atom

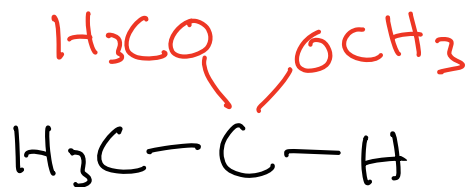


Not Stable

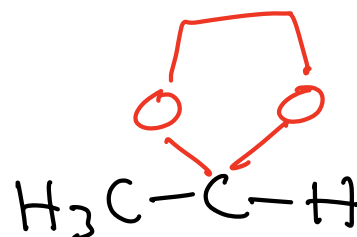


Stable  
(Chelate effect)

**Acetal** → two ethers on same C atom

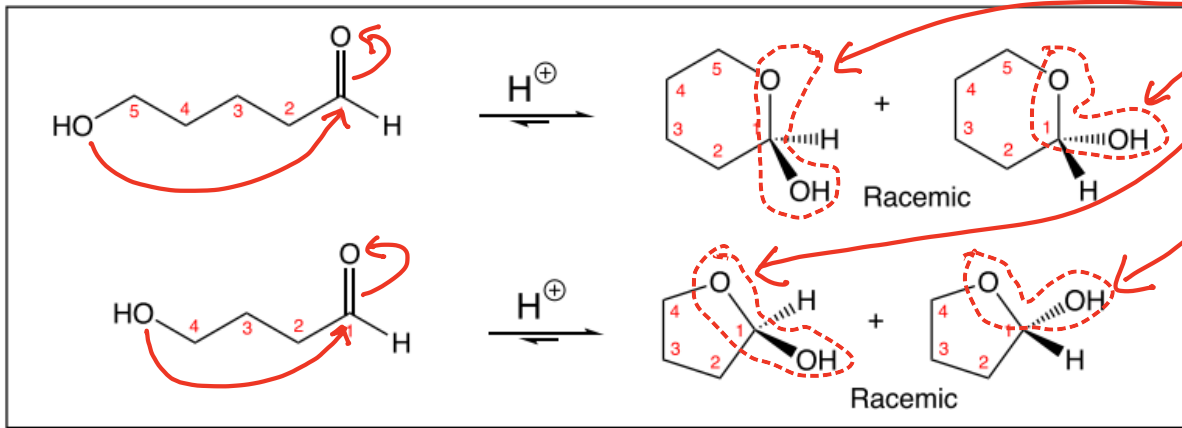


Stable



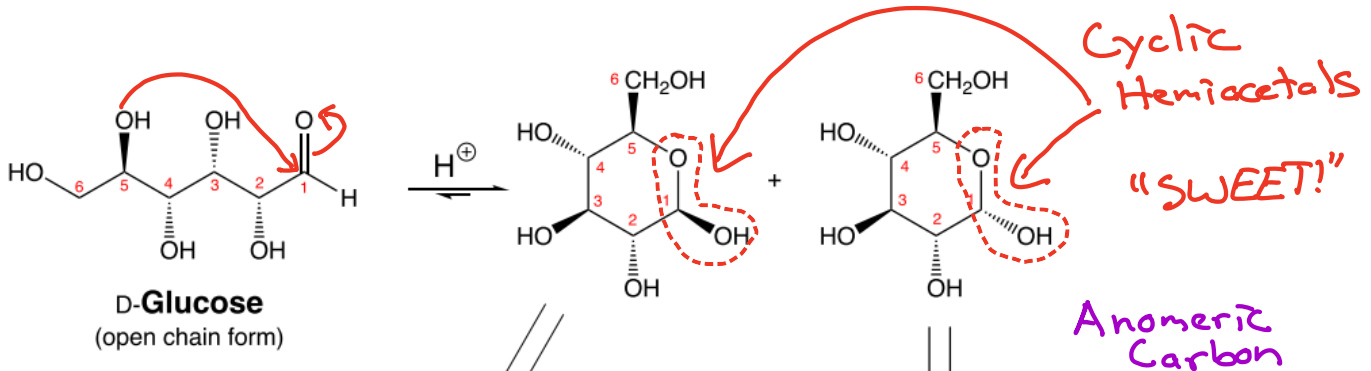
More Stable  
(Chelate effect)

# Cyclic Hemiacetals and Carbohydrates



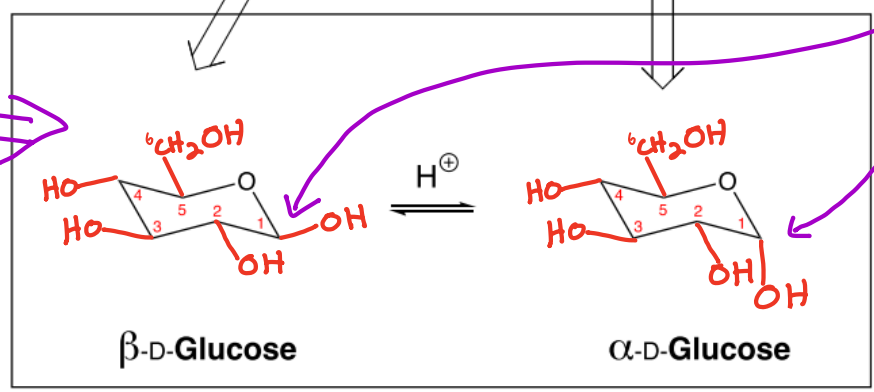
Cyclic hemiacetals

The cyclic form of hemiacetals are stable - "SWEET!"  
 → The chelate effect



Cyclic Hemiacetals  
 "SWEET!"

This interconversion is called "mutarotation"



Anomeric Carbon

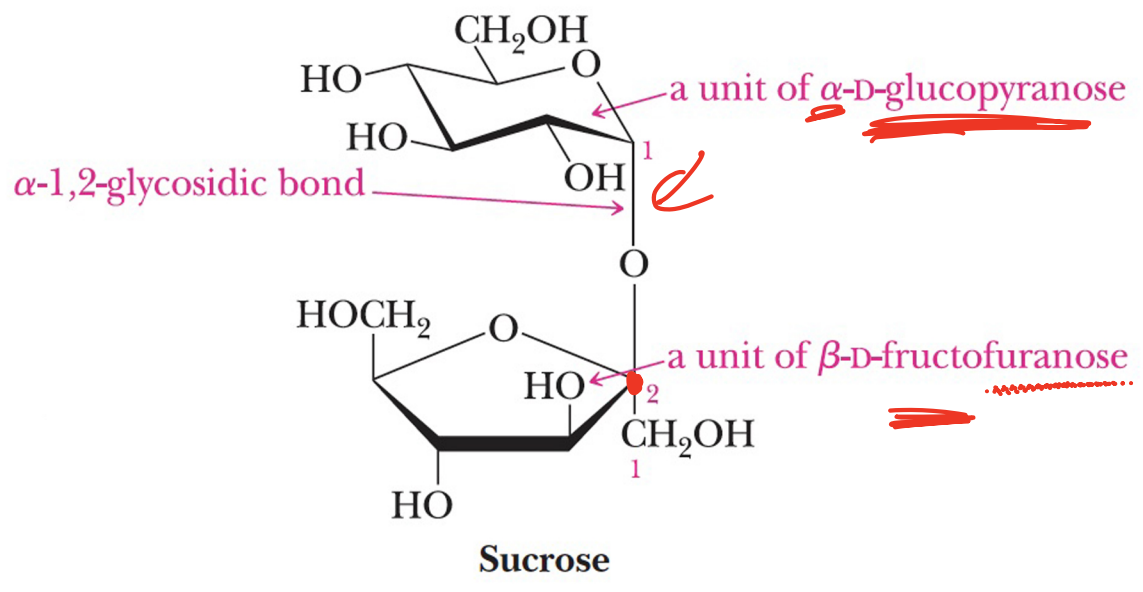
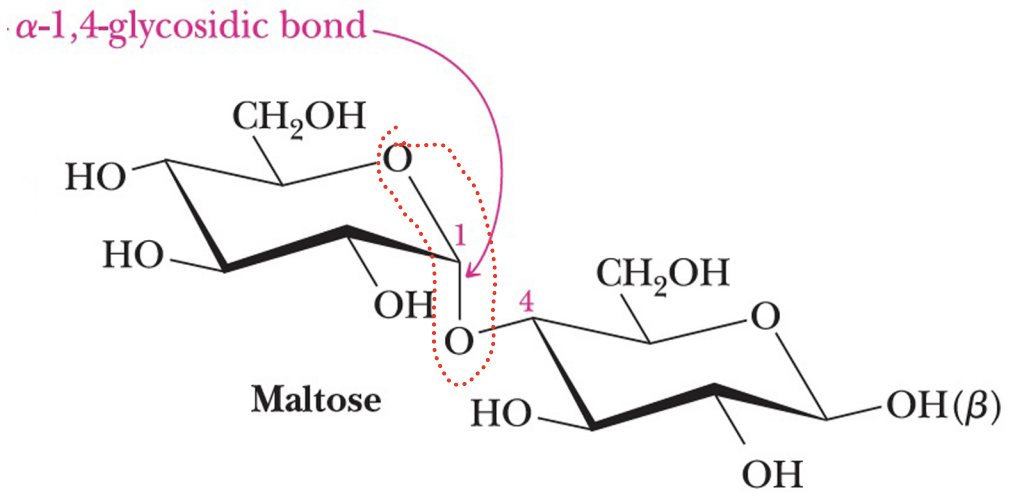
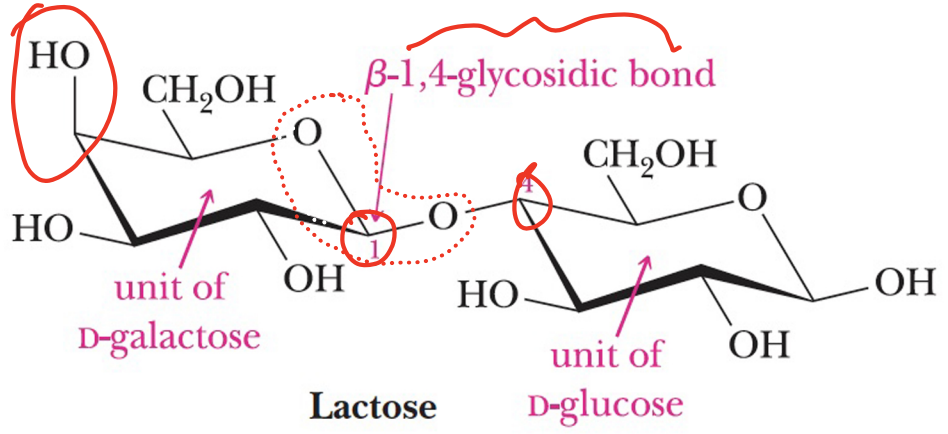
Biochemists call these two forms "anomers"

$\beta$ -D-Glucopyranose  
 means "6-membered ring"

$\alpha$ -D-Glucopyranose  
 Less stable → one -OH is axial

More stable → every group is equatorial!

biochemistry term for acetal



**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. 1/16/25

You will learn the basic principles of pharmaceutical science and how many drugs work. 1/21/25

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. 1/30/25

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 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. 1/16/25

You will learn how most reactions of carbonyl compounds involve only the four common mechanistic elements operating in only a few common patterns. 1/21/25

You will learn how, by simply adding a catalytic amount of base like  $\text{HO}^-$  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.

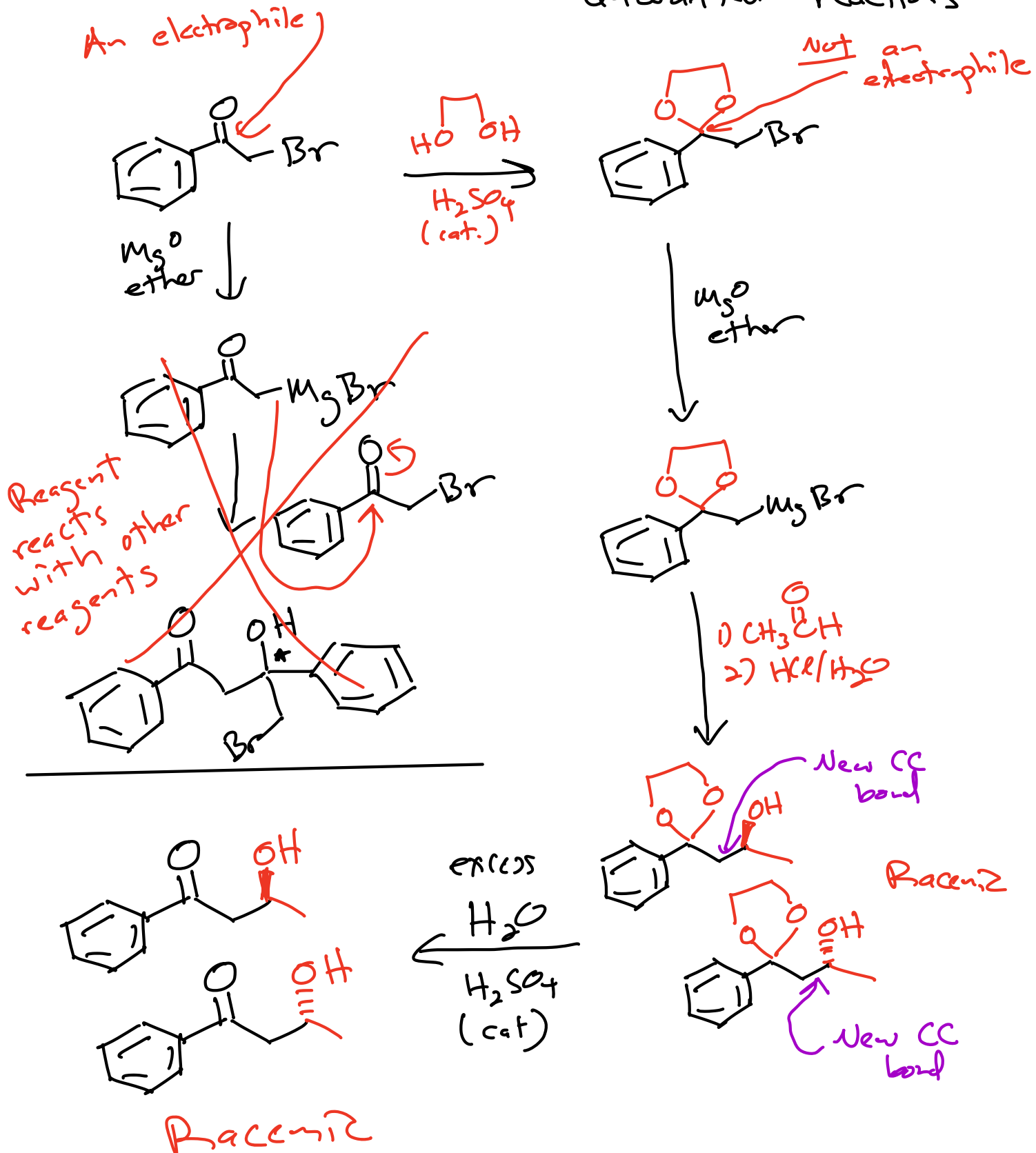
You will learn why molecules with six-membered rings and alternating double bonds are stable.

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

Most important, you will develop powerful critical thinking skills:

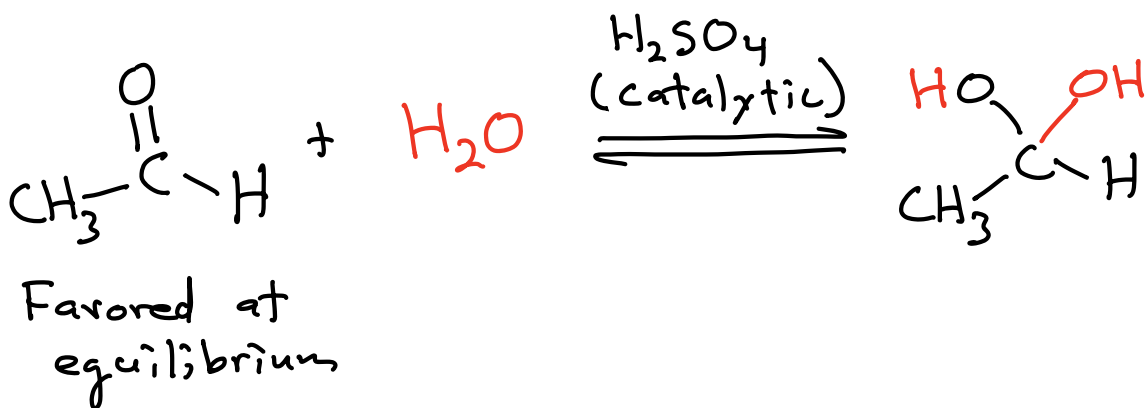
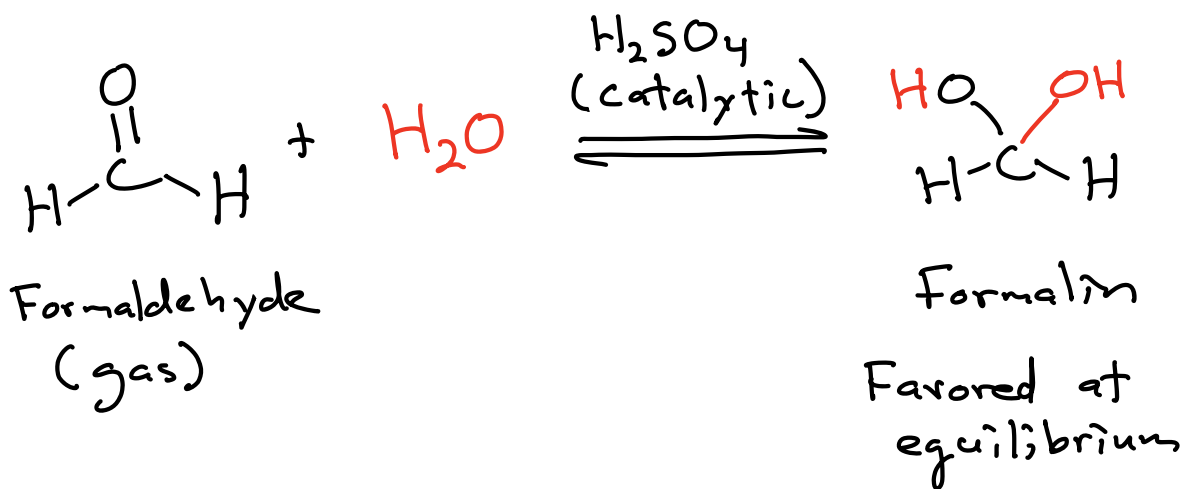
1. You will learn how to look at a molecule and accurately predict which atoms will react to make new bonds, and which bonds will break during reactions.
2. You will learn how to analyze a complex molecule's structure so that you can predict ways to make it via multiple reactions starting with less complex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

Protecting Group  $\rightarrow$  Reversibly mask the reactivity of a function to prevent unwanted reactions





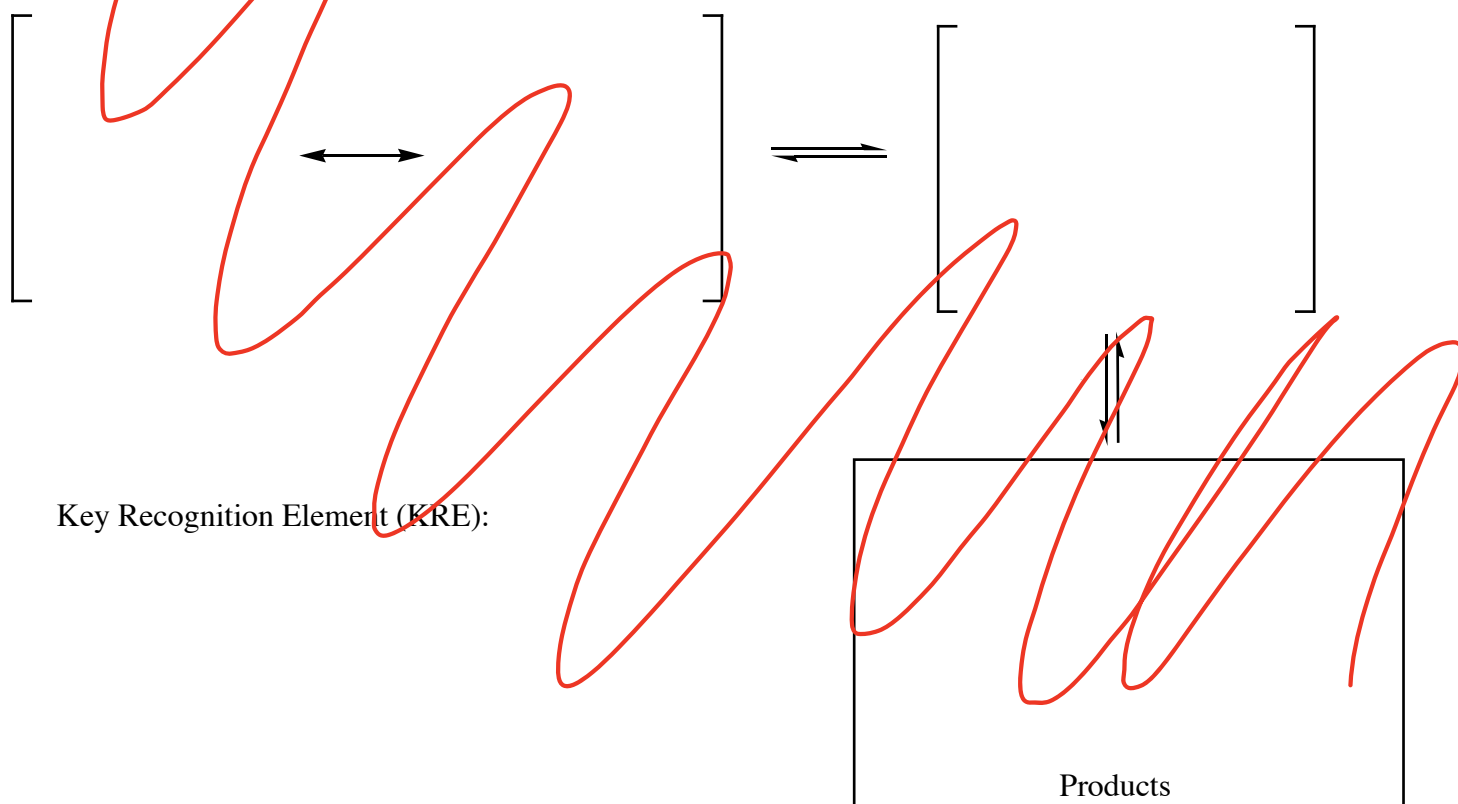
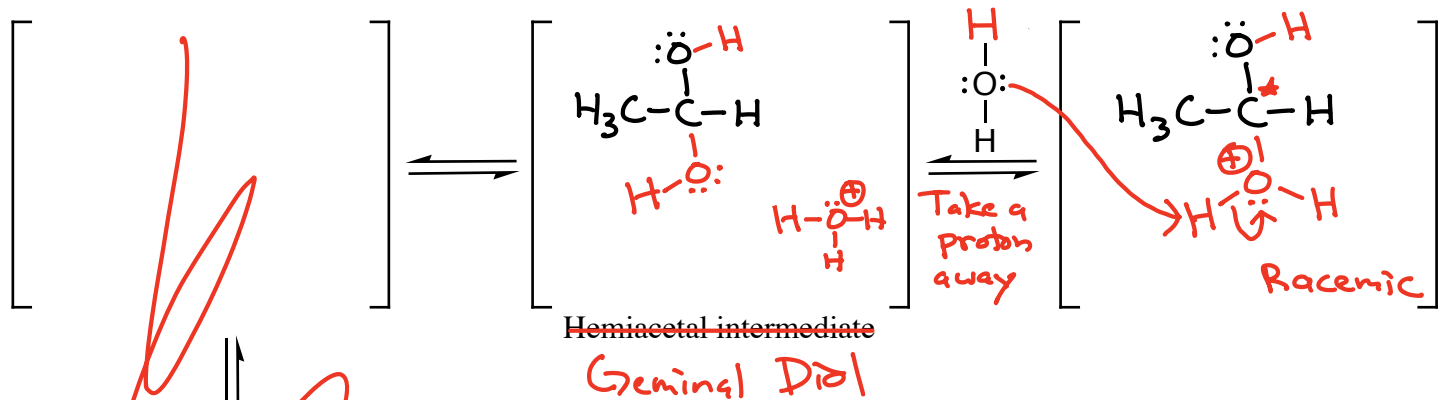
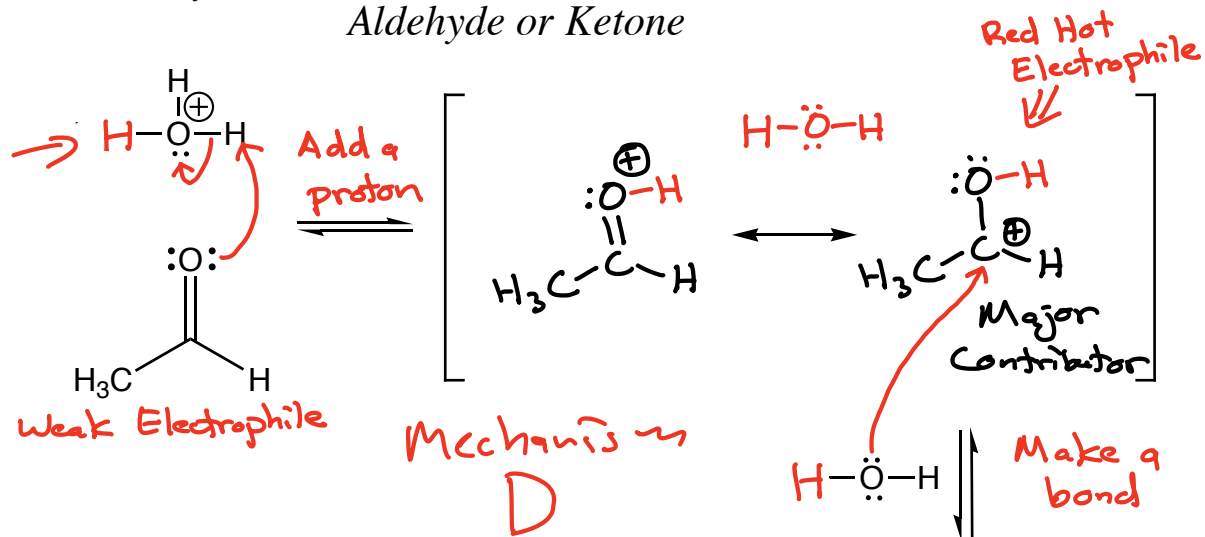
# Geminal Diols: $H_2O$ instead of $ROH$

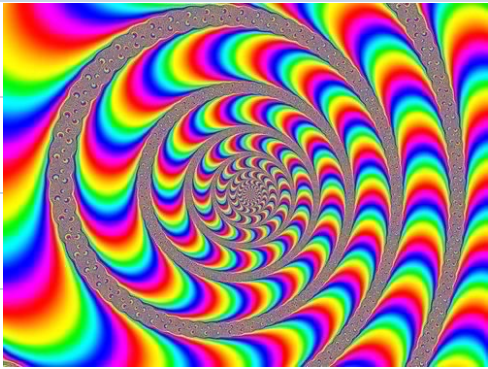
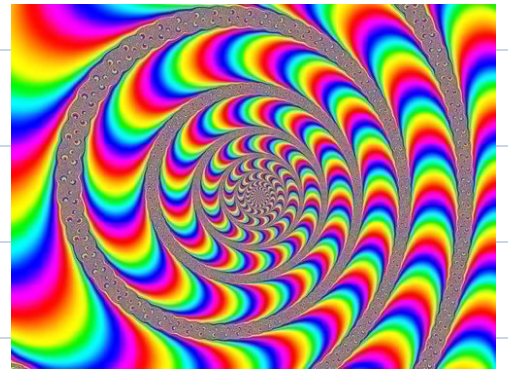


The geminal diol is in equilibrium with aldehydes and ketones, but it is only favored for the case of formaldehyde/formalin

# Geminal diol

Acid Catalyzed ~~Hemiacetal and Acetal~~ Formation From an Aldehyde or Ketone

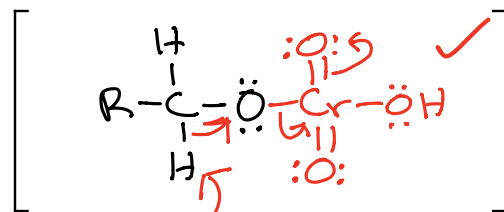
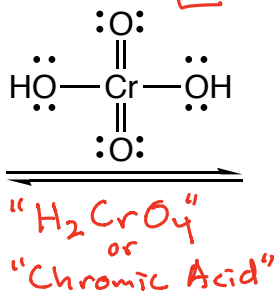
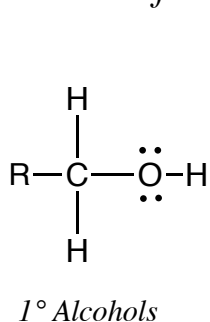




# Chromic Acid Oxidation of Alcohols

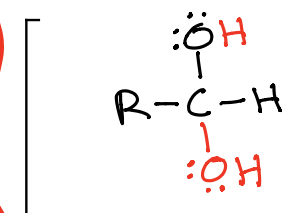
Called "Jones Reagent"  $(CrO_3 + H_2O)$  or  $K_2CrO_7 + H_2SO_4$

Not responsible for first step

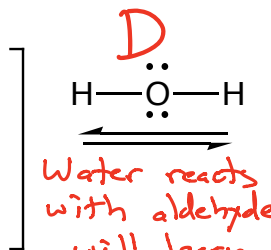


Mechanism

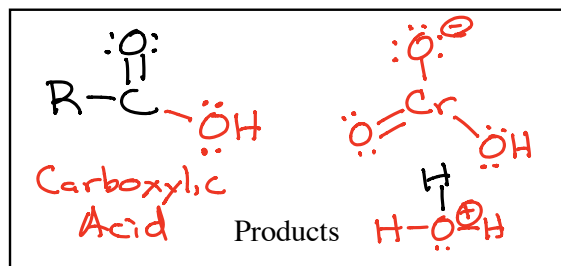
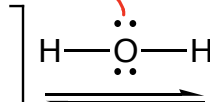
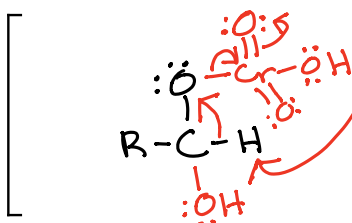
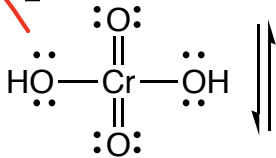
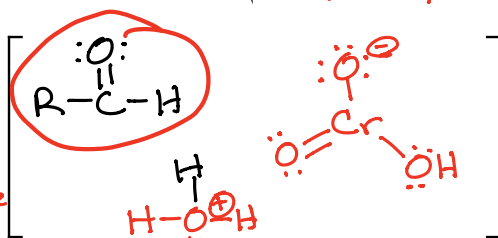
~~Not responsible for this step~~



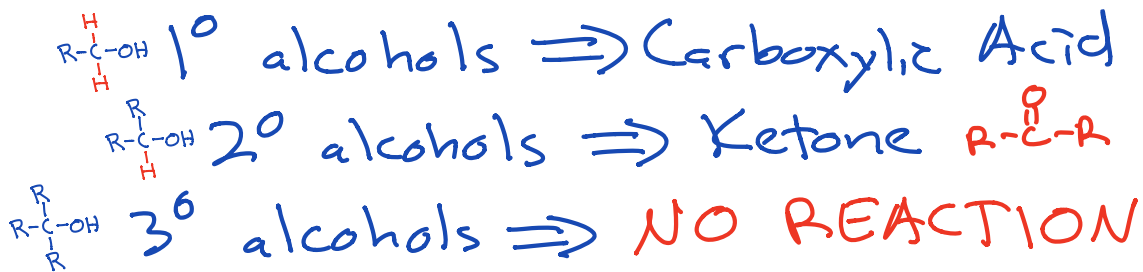
Called a geminal diol



Water reacts with aldehyde - will learn next semester



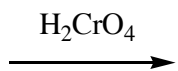
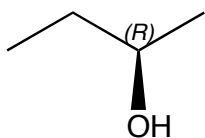
Summary:



Regiochemistry: N/A

Stereochemistry: N/A

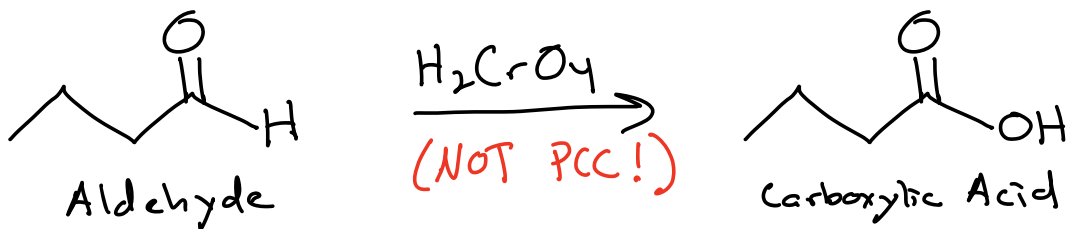
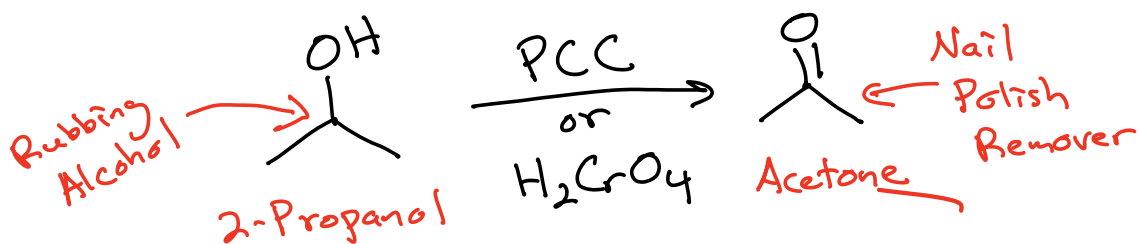
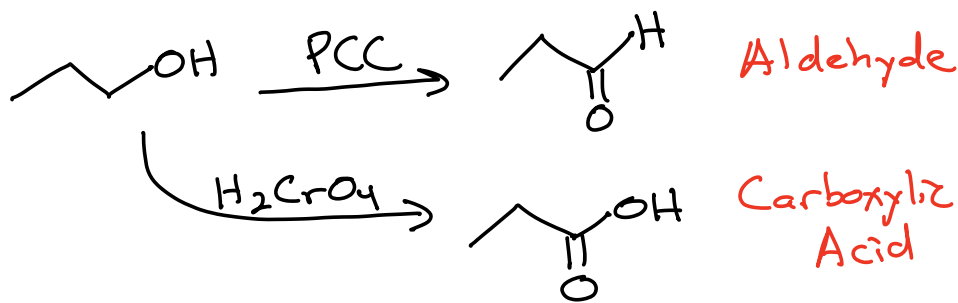
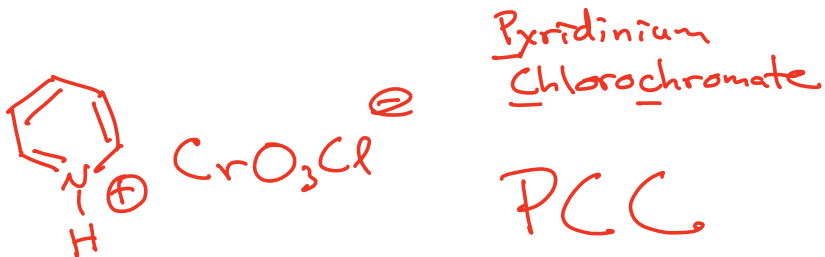
Example:

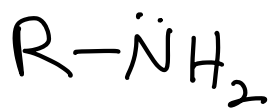


Ketone

From last semester

A chromic acid-like reagent WITHOUT WATER will stop at the aldehyde when using a primary alcohol as starting material





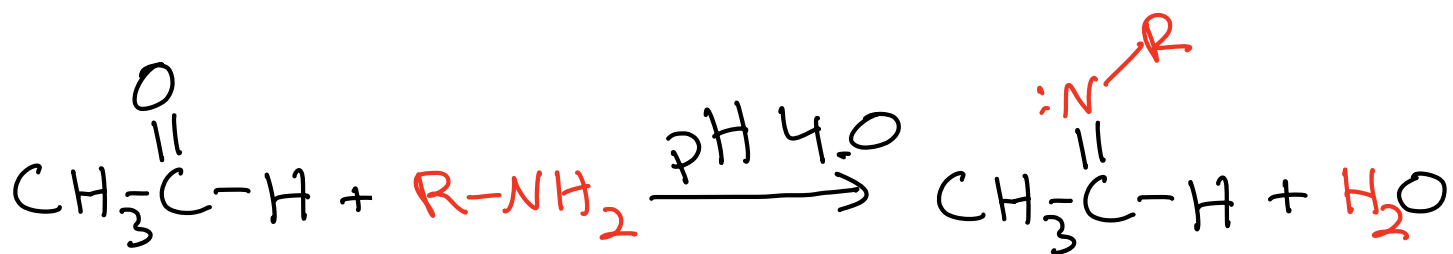
Amine

→ An amine is a fairly good nucleophile compared to  $R-\ddot{O}H$

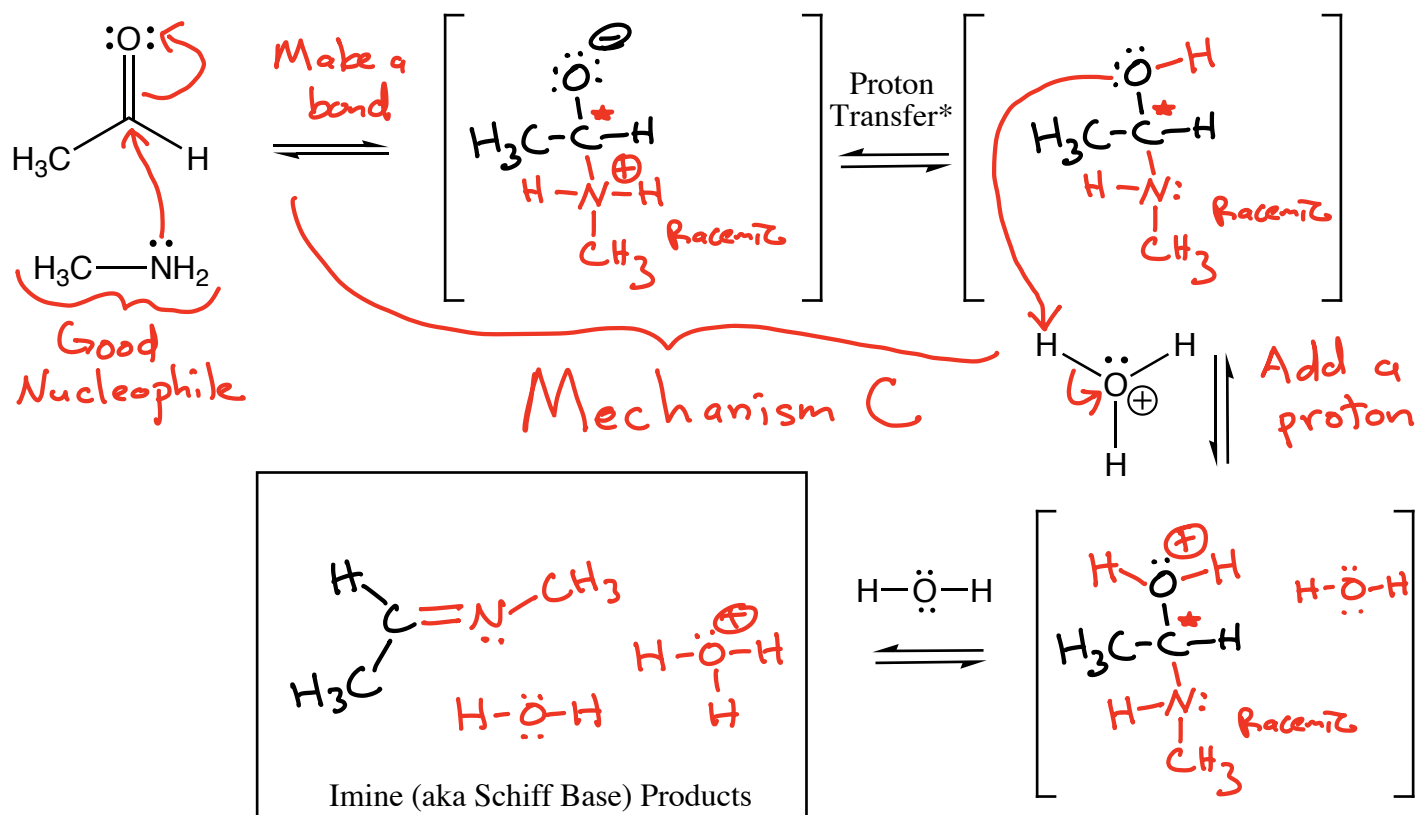
→ Can react with a carbonyl group directly →

However, there are "issues" with the protons in the mechanism!

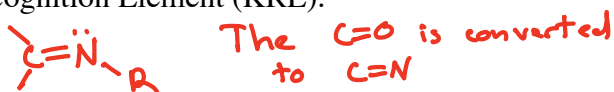
### Overall Process



## Formation of an Imine (Schiff Base) From an Aldehyde or Ketone Reacting with an Amine



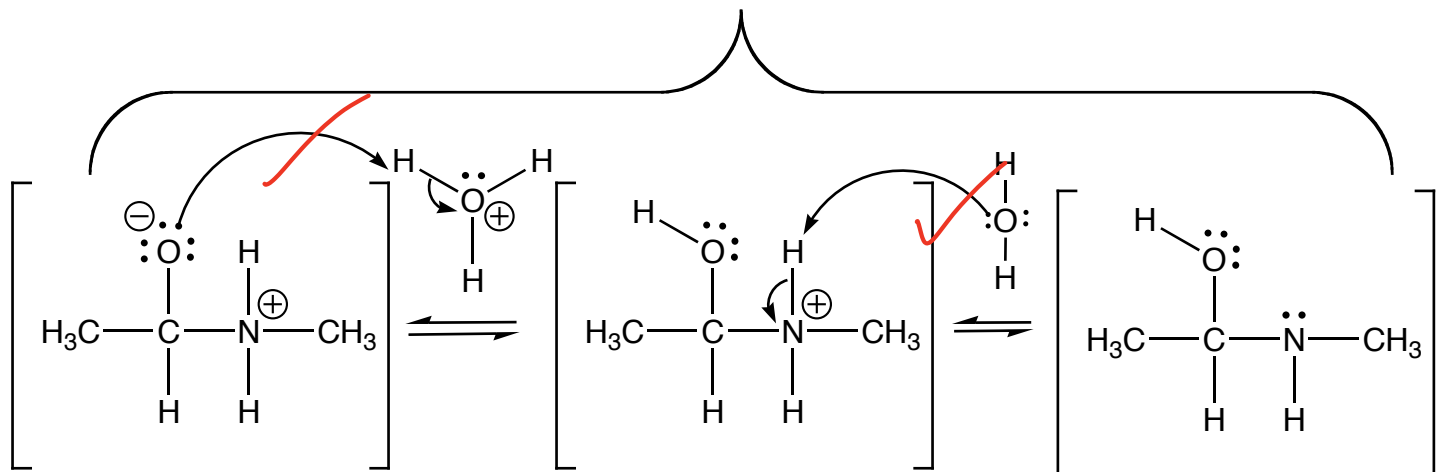
Key Recognition Element (KRE):



(Note: this last step might actually occur as two steps in some cases.)

\* "Proton Transfer" refers to a situation in which a proton moves from one part of a molecule to another on the SAME MOLECULE. We do not draw arrows for proton transfer steps because that would be deceptive. In some cases, the same proton may move from one part of the molecule to the other directly, but in other cases, solvent molecules may be involved as indicated in the following scheme. To make things even more interesting, the following two steps might even be reversed in some cases. Because of all the ambiguity, we just write "Proton Transfer" and do not bother with arrows.

"Proton Transfer"



# 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**

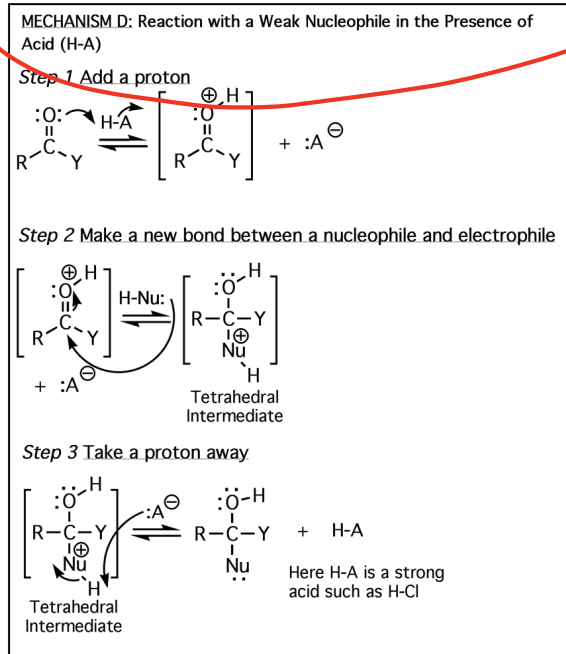
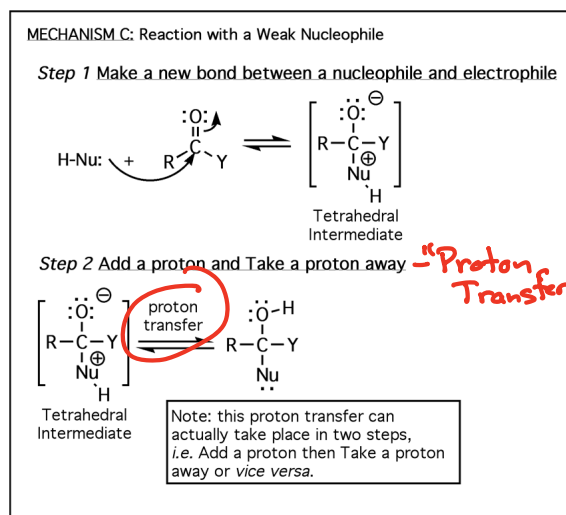
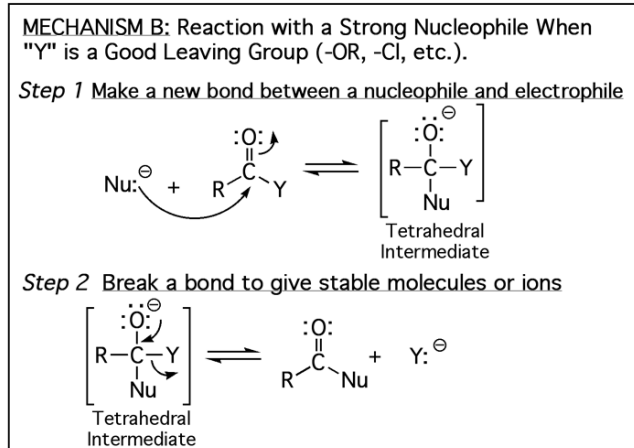
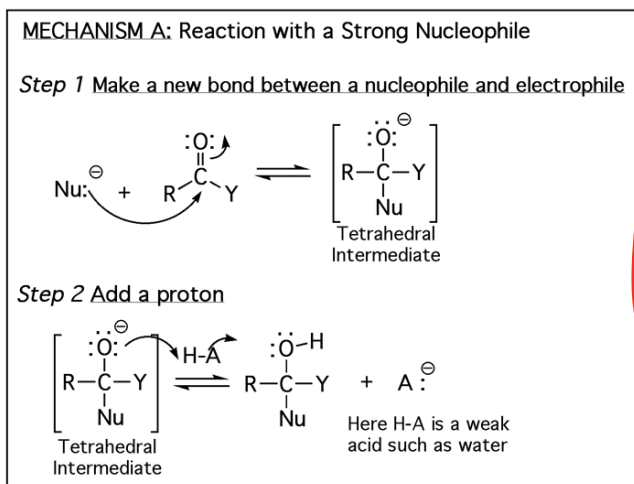
**C) Add a proton**

**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!!)

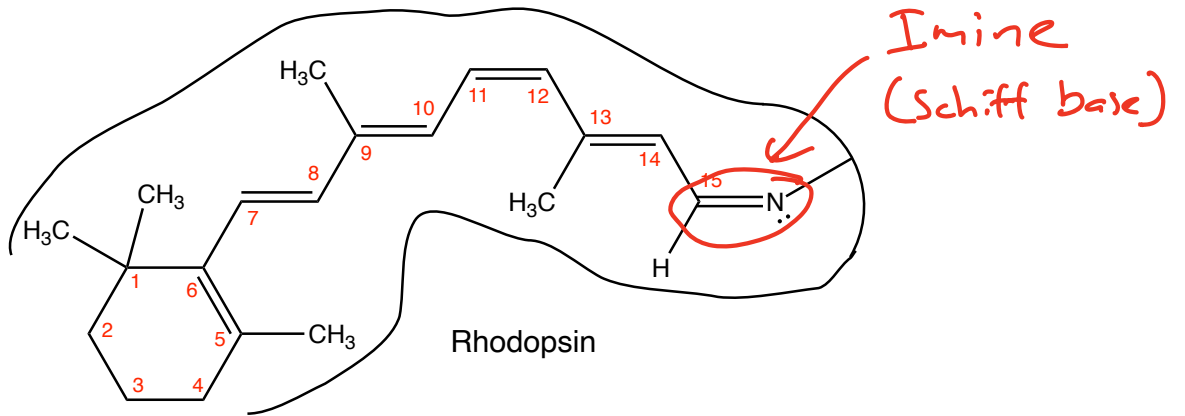
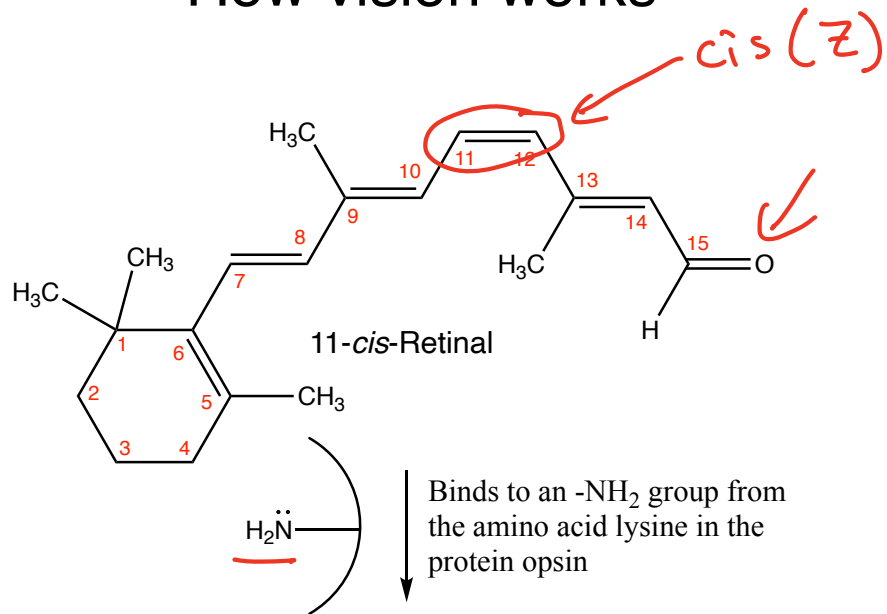
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## Four Mechanisms for the Reaction of Nucleophiles with Carbonyl Compounds



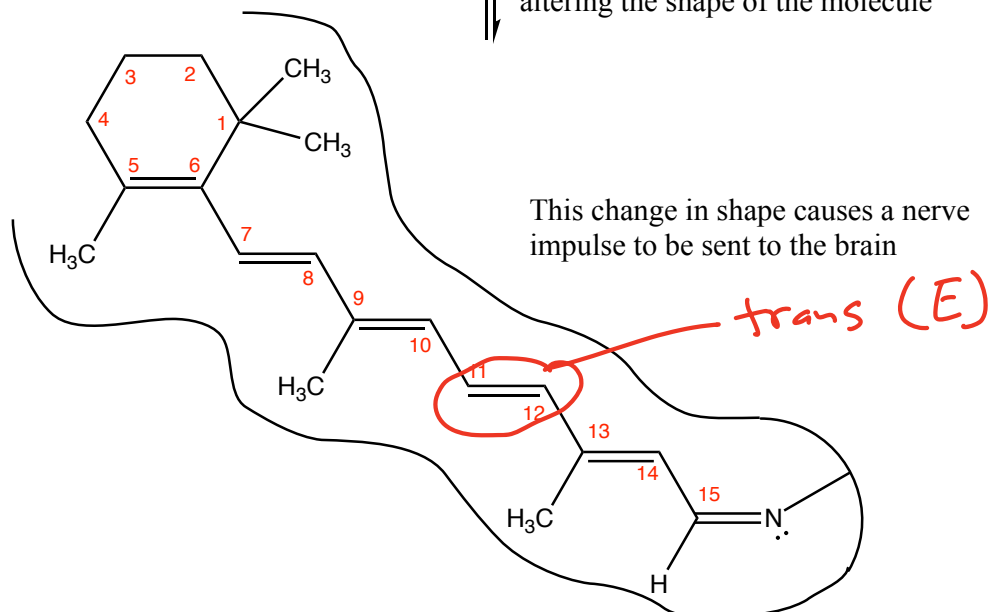


# How vision works



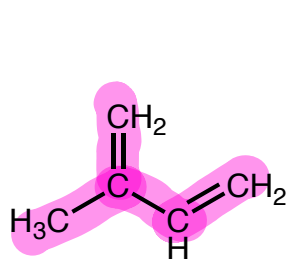
Molecule resets

A photon of visible light is absorbed by the retinal, isomerizing the *cis* bond to *trans*, dramatically altering the shape of the molecule

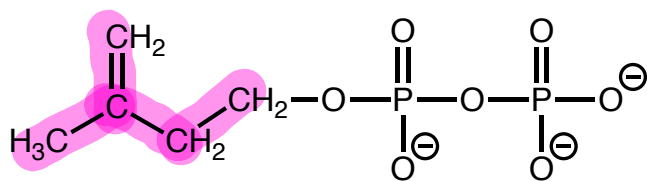




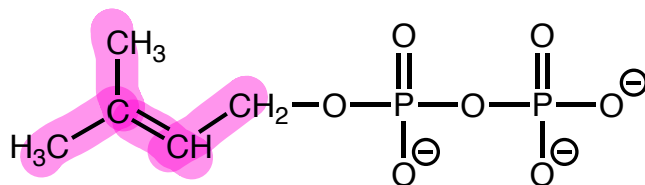
# Terpenes



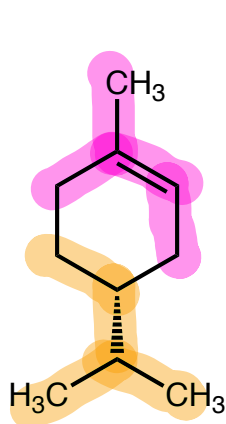
**Isoprene**



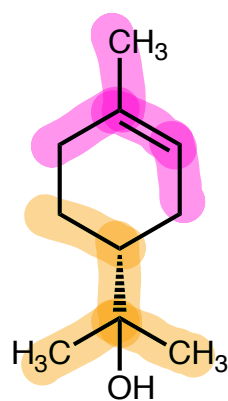
**Isopentanyl diphosphate**



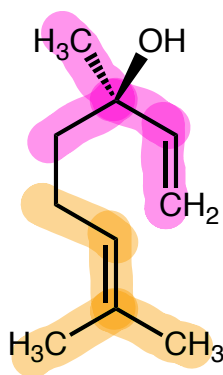
**Dimethylallyl diphosphate**



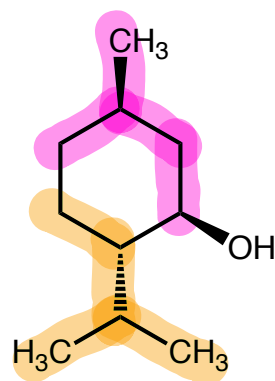
**Limonene**  
(citrus flavor)



**$\alpha$ -Terpineol**  
(from lilacs, used in perfume)

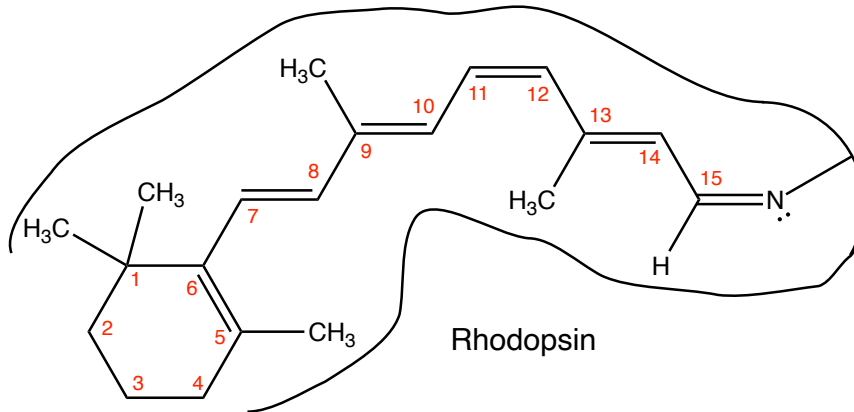
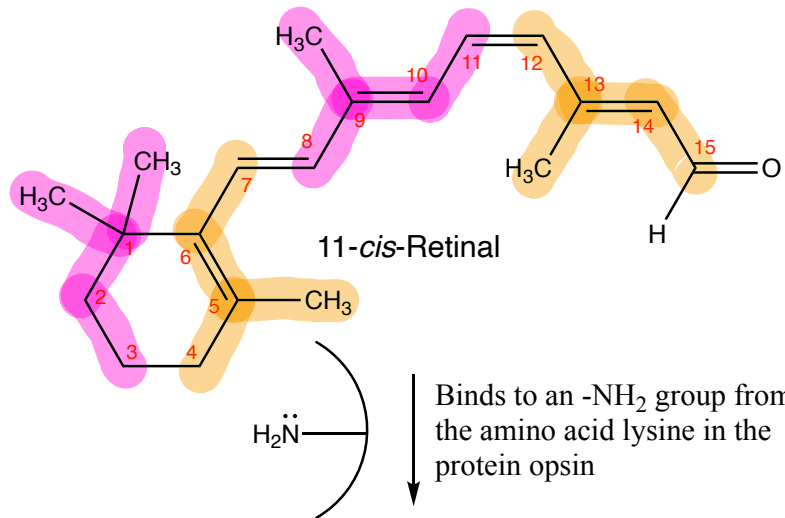


**(*R*)-(-)-Linalool**  
(from lavender, used in perfume)



**(-)-Menthol**  
(common flavoring from peppermint)

# How vision works



Molecule resets

A photon of visible light is absorbed by the retinal, isomerizing the *cis* bond to *trans*, dramatically altering the shape of the molecule

