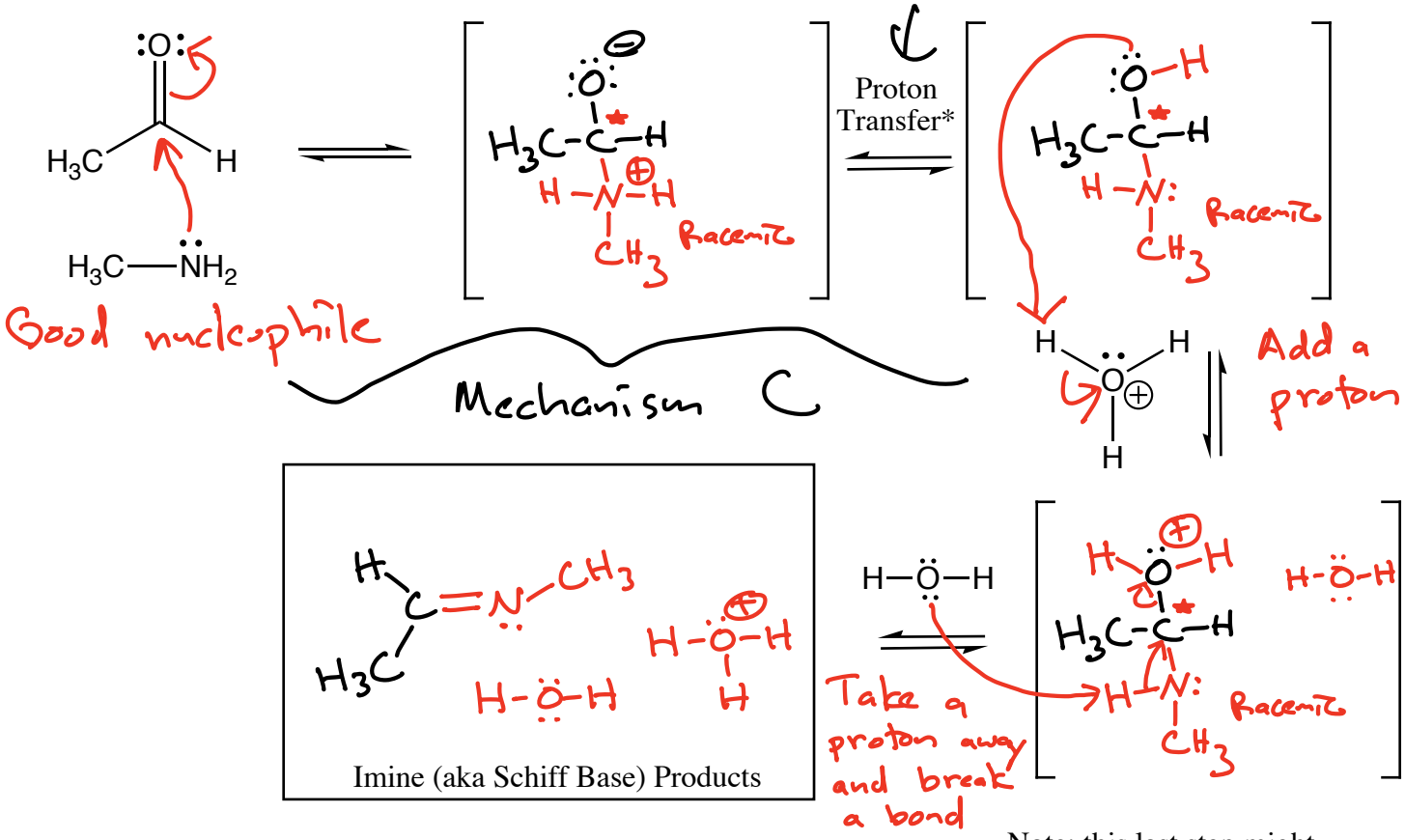
```
Placental Mammals
│
└── Glires
    │
    ├── Lagomorpha  (Rabbits & Relatives)
    │   │
    │   ├── Rabbits
    │   ├── Hares
    │   └── Pikas
    │       (Family: Ochotonidae)
    │
    └── Rodentia  (Rodents)
        │
        ├── Squirrels
        │   │
        │   ├── Prairie Dogs
        │   │   (Genus: Cynomys)
        │   │
        │   └── Marmots
        │       └── Groundhog / Woodchuck
        │           (Genus: Marmota)
        │
        ├── Mice & Rats
        ├── Beavers
        └── Porcupines
```

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



Key Recognition Element (KRE):

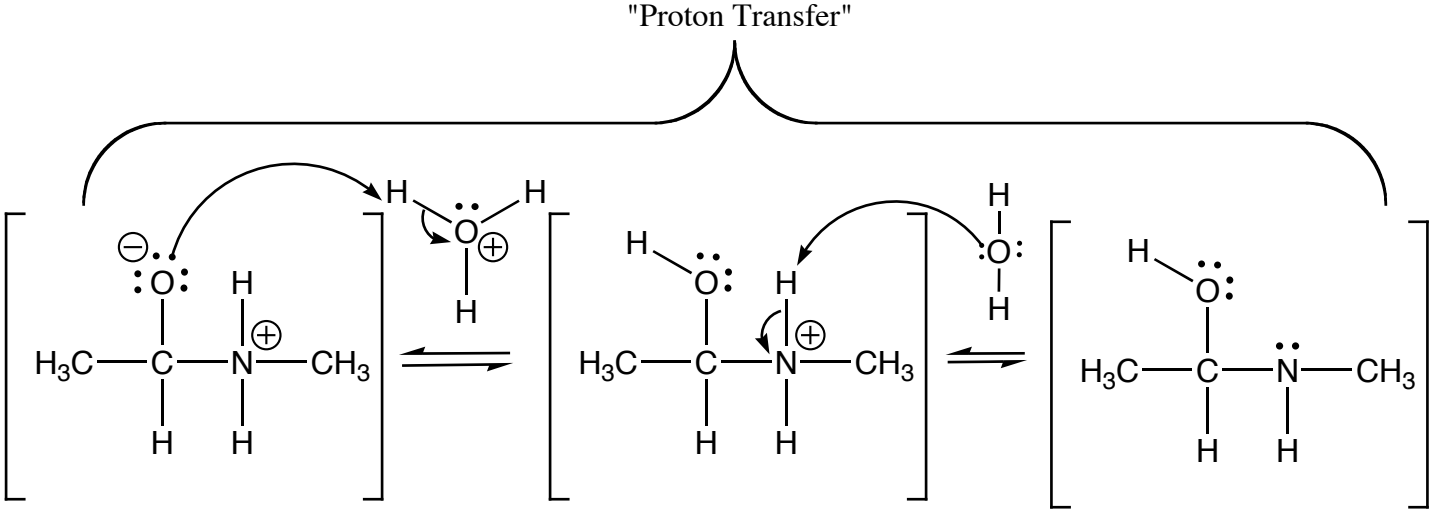
A C=N double bond

A C=O is converted to a C=N

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. Becuase of all the ambiguity, we just write "Proton Transfer" and do not bother with arrows.



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

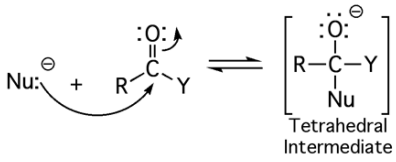
2) These same four mechanism elements describe most of the other mechanisms you have/will learn!!! (Yes, organic chemistry really is this simple if you look at it this way!!)

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.

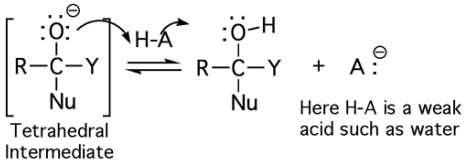
Four Mechanisms for the Reaction of Nucleophiles with Carbonyl Compounds

MECHANISM A: Reaction with a Strong Nucleophile

Step 1 Make a new bond between a nucleophile and electrophile

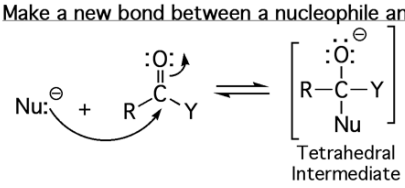


Step 2 Add a proton

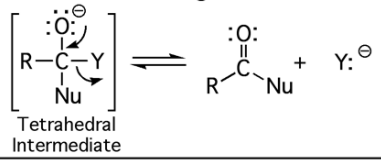


MECHANISM B: Reaction with a Strong Nucleophile When "Y" is a Good Leaving Group (-OR, -Cl, etc.).

Step 1 Make a new bond between a nucleophile and electrophile

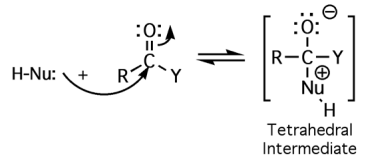


Step 2 Break a bond to give stable molecules or ions

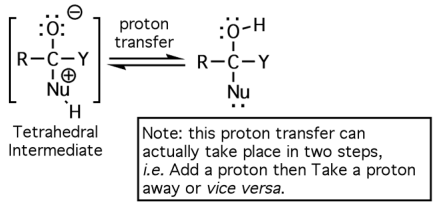


MECHANISM C: Reaction with a Weak Nucleophile

Step 1 Make a new bond between a nucleophile and electrophile

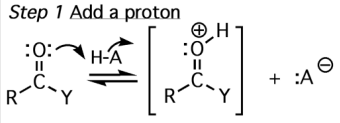


Step 2 Add a proton and Take a proton away

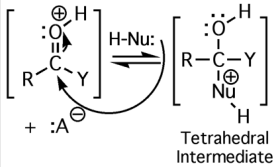


MECHANISM D: Reaction with a Weak Nucleophile in the Presence of Acid (H-A)

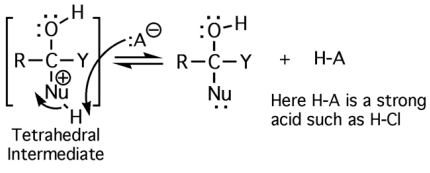
Step 1 Add a proton



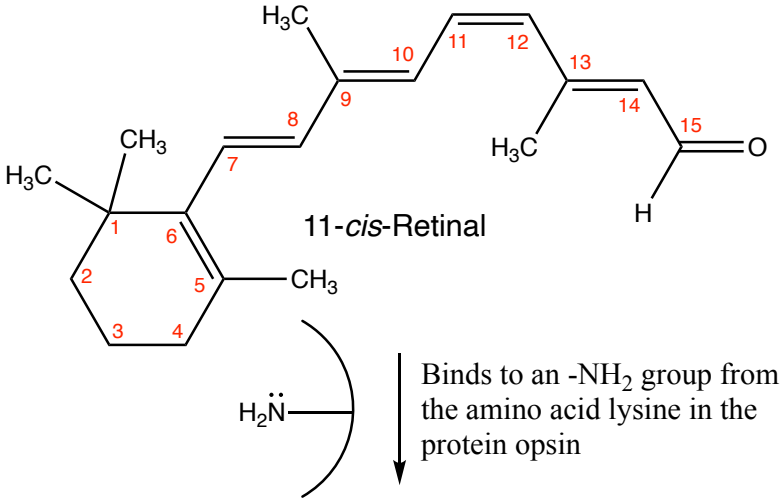
Step 2 Make a new bond between a nucleophile and electrophile



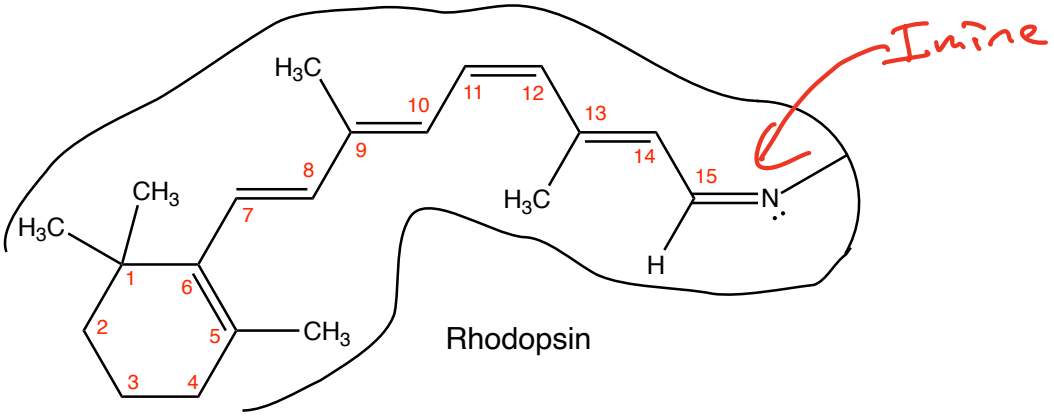
Step 3 Take a proton away



How vision works

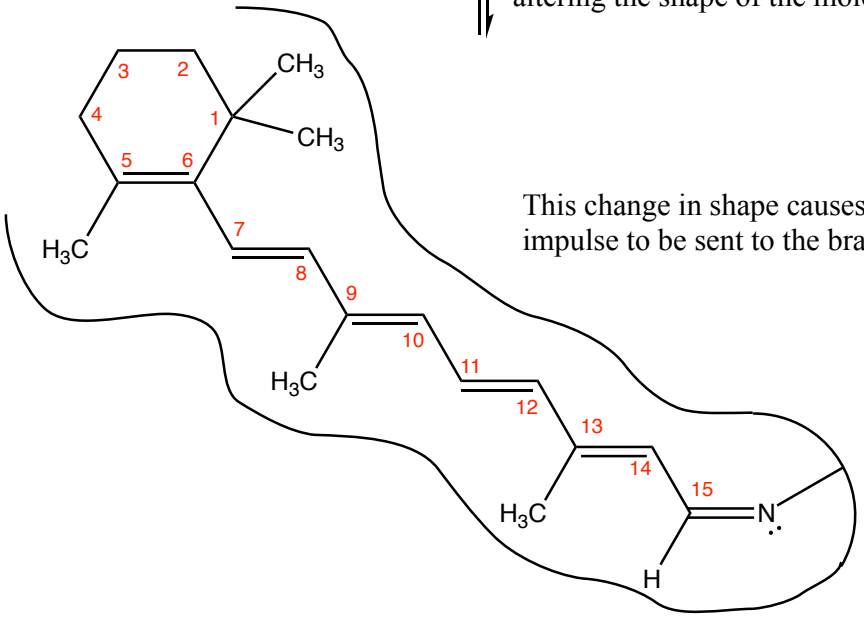


Binds to an -NH_2 group from the amino acid lysine in the protein opsin



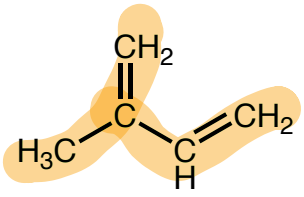
Molecule resets

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

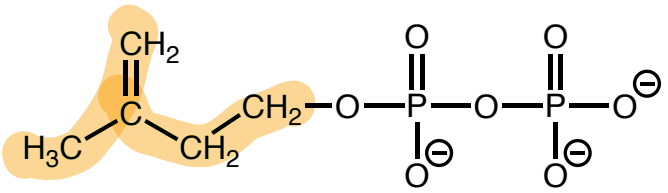


This change in shape causes a nerve impulse to be sent to the brain

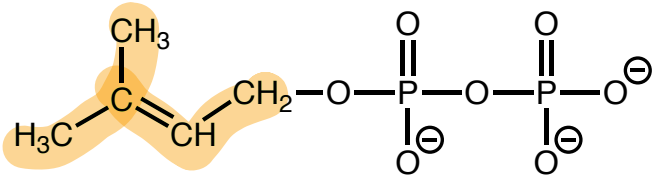
Terpenes



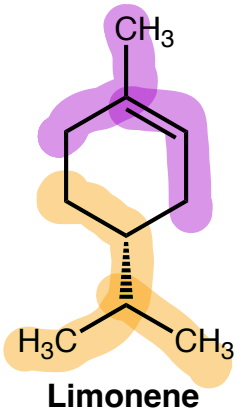
Isoprene



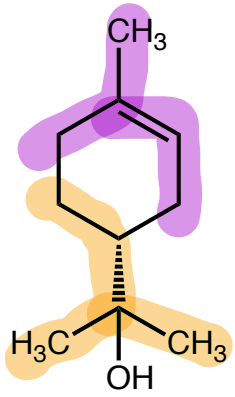
Isopentanyl diphosphate



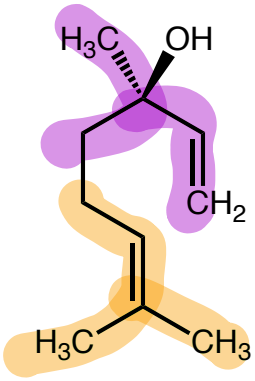
Dimethylallyl diphosphate



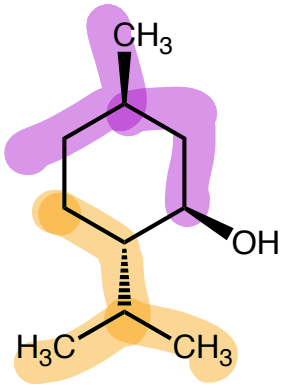
Limonene
(citrus flavor)



α-Terpineol
(from lilacs, used in perfume)

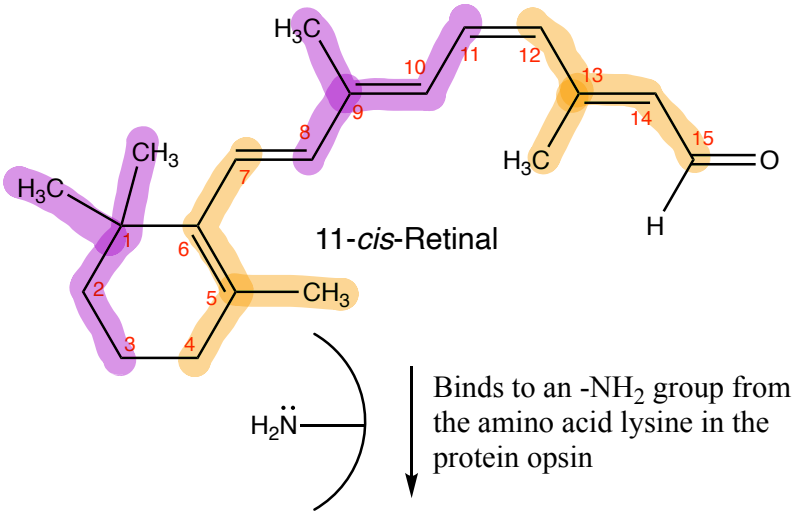


(*R*)-(-)-Linalool
(from lavender, used in perfume)

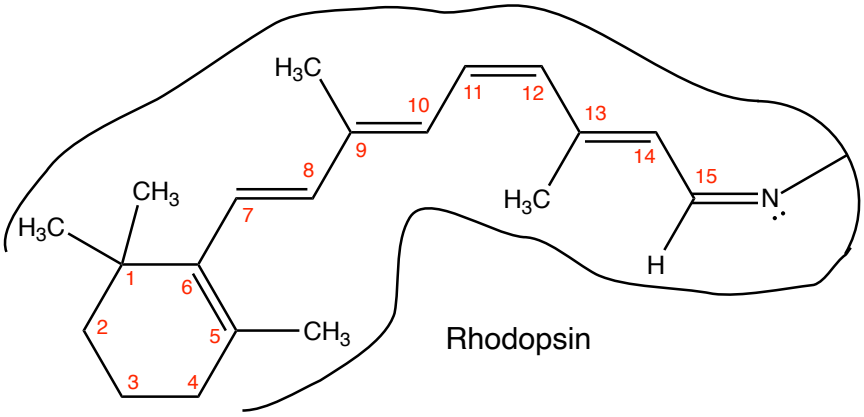


(-)-Menthol
(common flavoring from peppermint)

How vision works

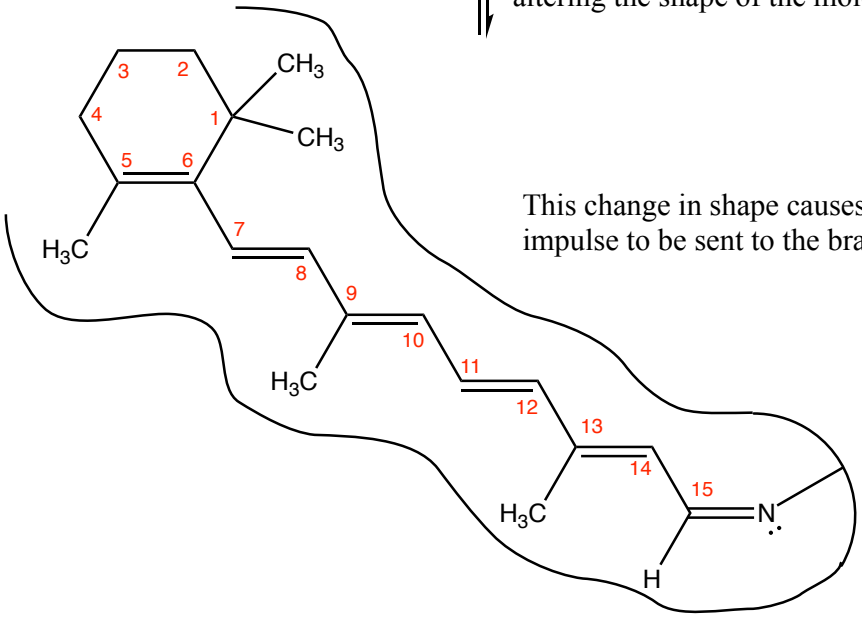


Binds to an -NH_2 group from the amino acid lysine in the protein opsin

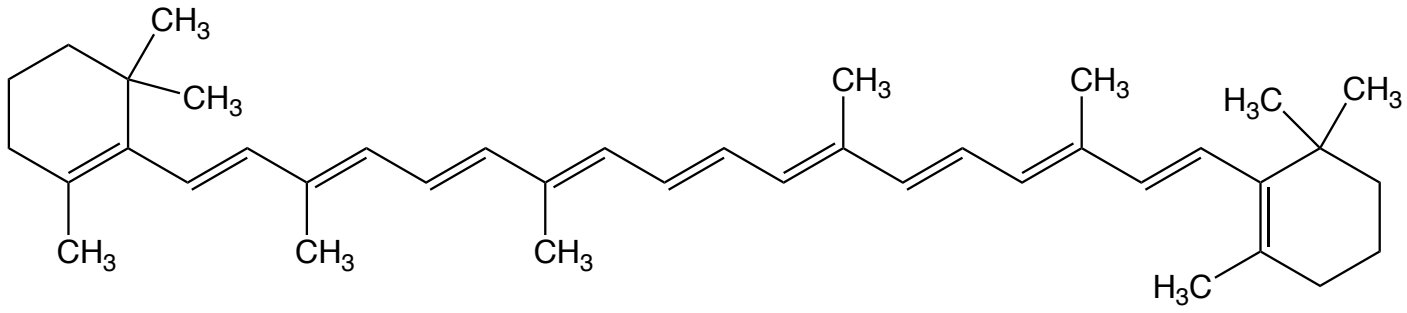


Molecule resets

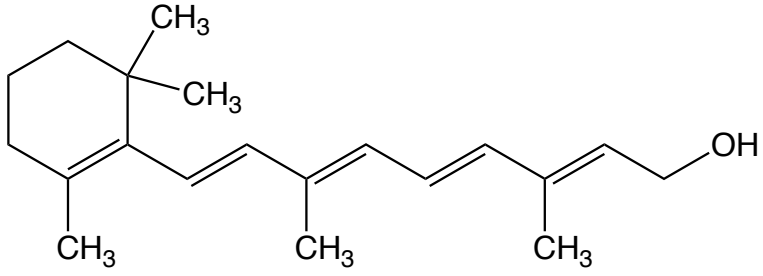
A photon of visible light is absorbed by the retinal, isomerizing the *cis* bond to *trans*, dramatically altering the shape of the molecule



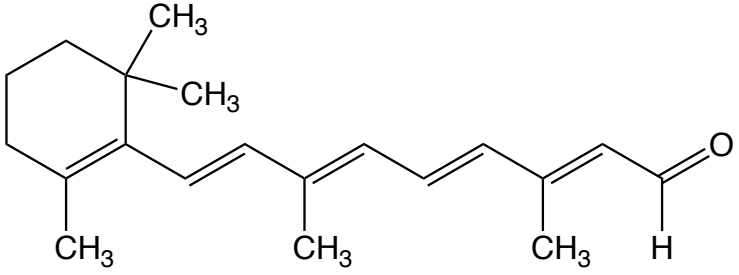
This change in shape causes a nerve impulse to be sent to the brain



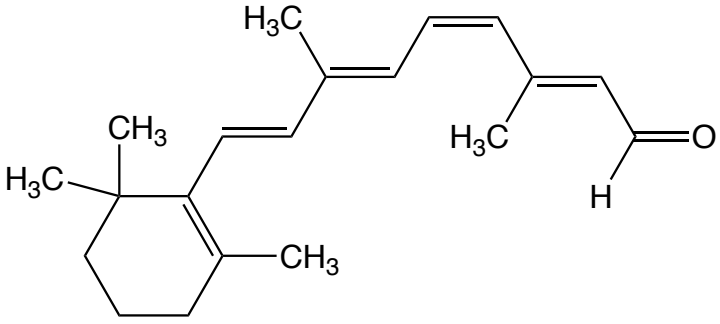
β-Carotene



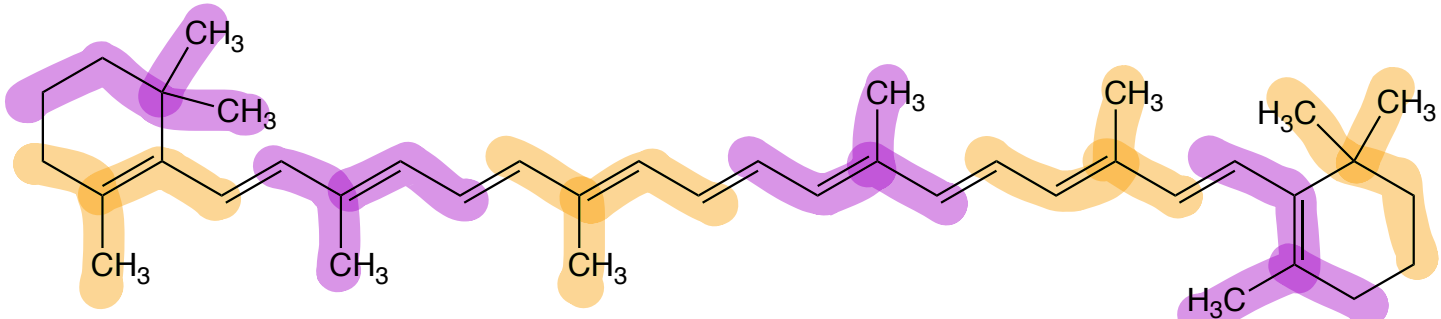
Vitamin A



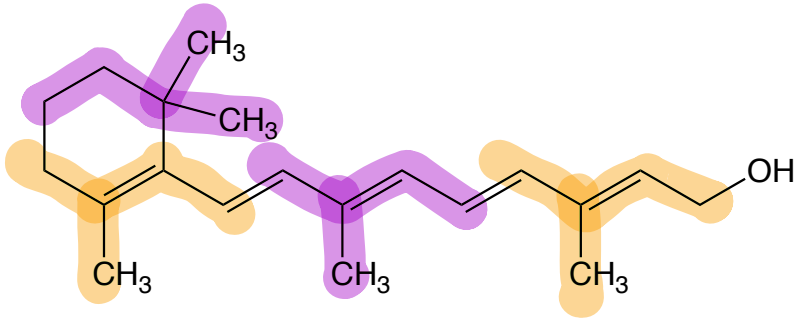
All *trans* Retinal



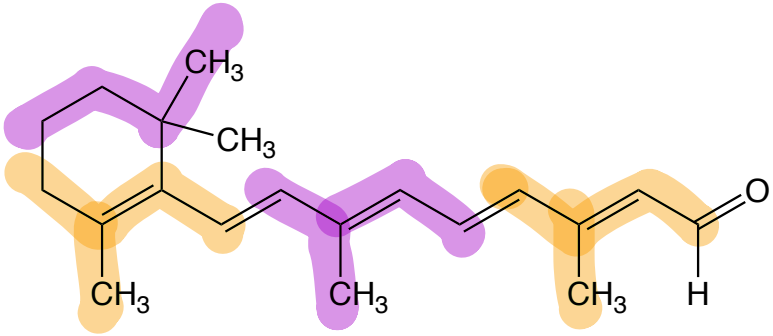
11-*cis*-Retinal



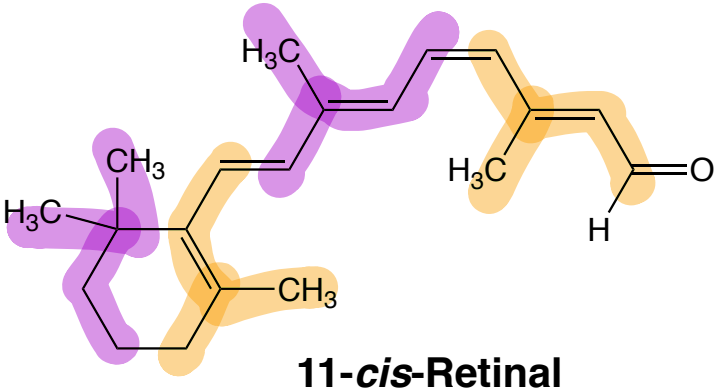
β-Carotene



Vitamin A

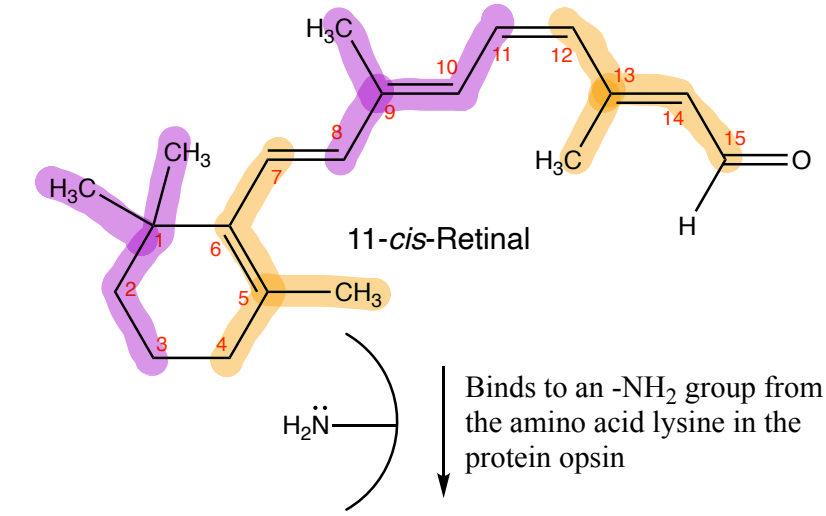


All *trans* Retinal

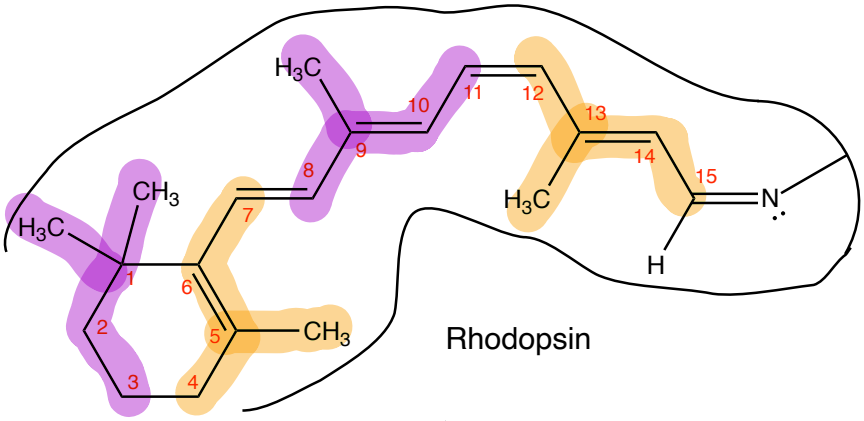


11-*cis*-Retinal

How vision works

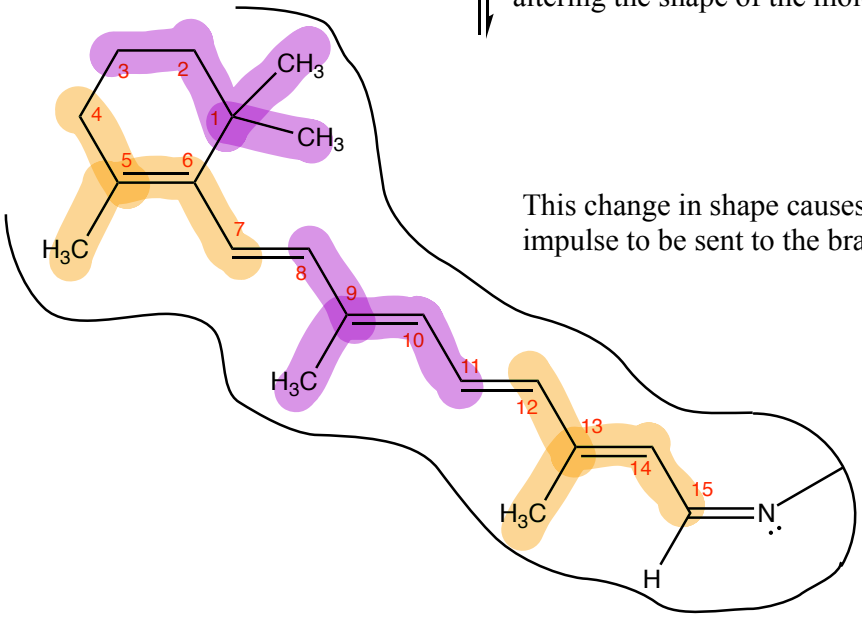


Binds to an -NH_2 group from the amino acid lysine in the protein opsin



Molecule resets

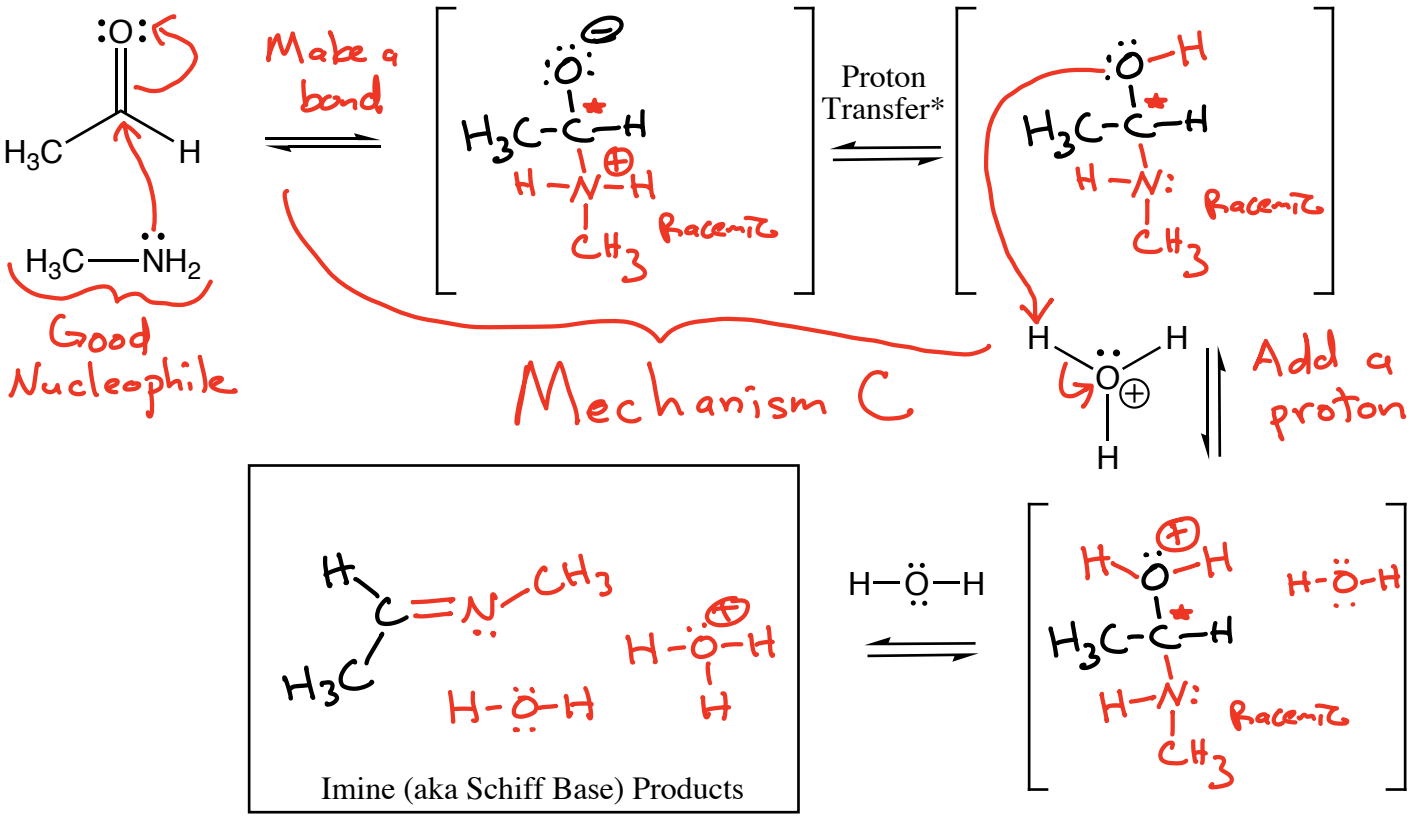
A photon of visible light is absorbed by the retinal, isomerizing the *cis* bond to *trans*, dramatically altering the shape of the molecule



This change in shape causes a nerve impulse to be sent to the brain

Recall:

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



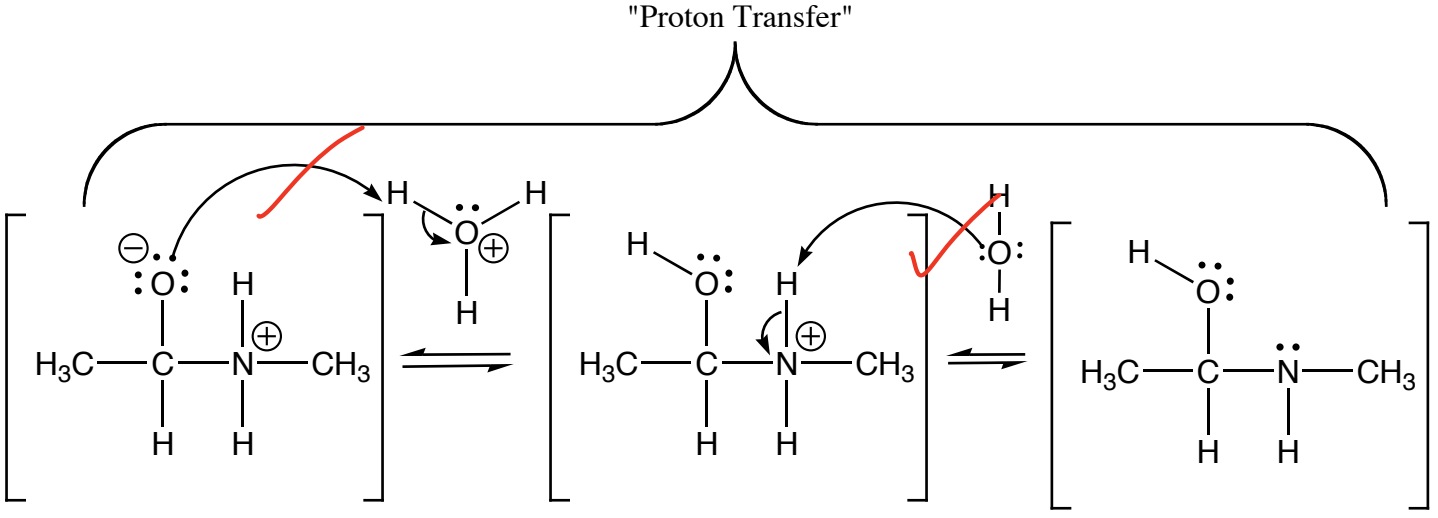
Key Recognition Element (KRE):

The C=O is converted to C=N

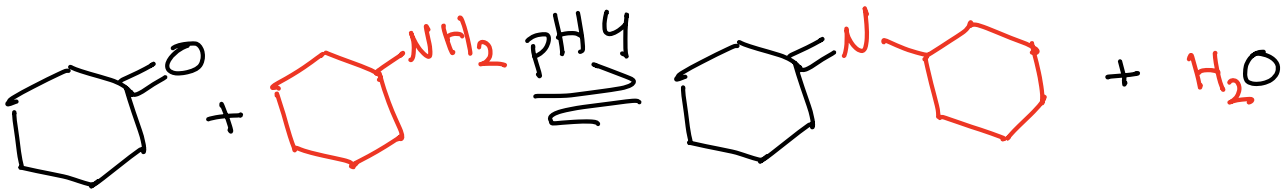
(Note: this last step might actually occur as two steps in some cases.)

---

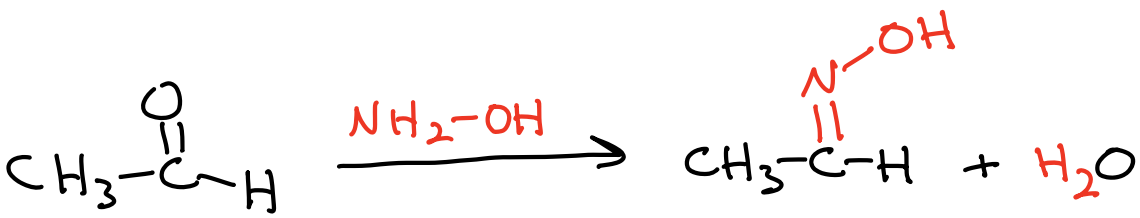
* "Proton Transfer" refers to a situation in which a proton moves from one part of a molecule to another on the SAME MOLECULE. We do not draw arrows for proton transfer steps because that would be deceptive. In some cases, the same proton may move from one part of the molecule to the other directly, 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. Becuase of all the ambiguity, we just write "Proton Transfer" and do not bother with arrows.



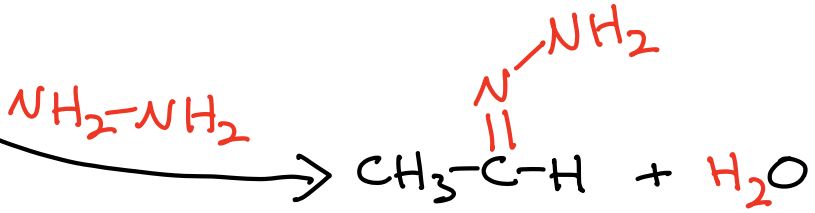
This is reversible:



Other similar reagents react the same way:

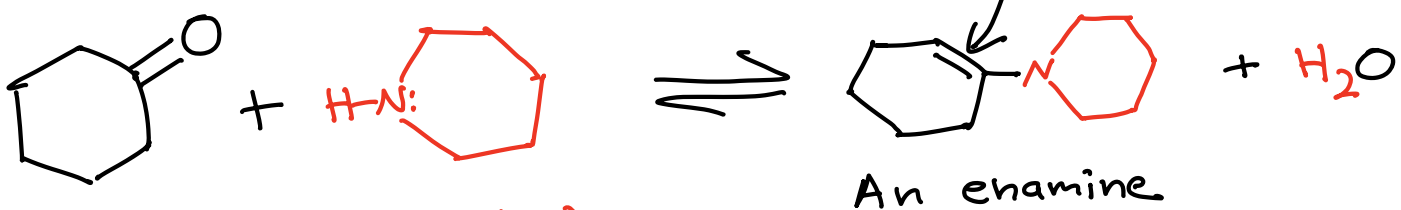


An oxime



A hydrazone

2° Amines



An enamine

2° (secondary) Amine – only one H atom

Time capsule – enamines are great nucleophiles

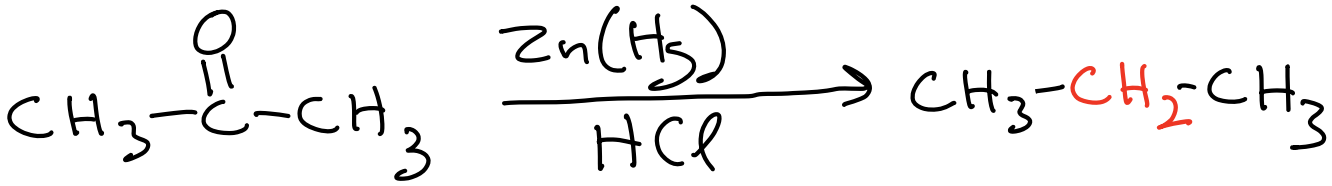
Conversion of ketone and aldehyde C=O groups to $-CH_2-$

In acid

Clemmenson Reduction → you are not responsible for the mechanism

↓

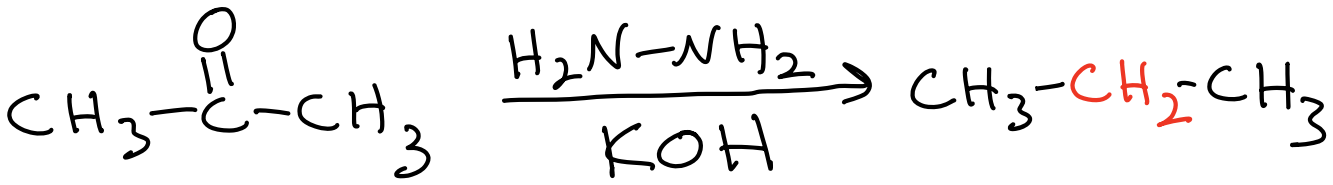
Relatively harsh conditions



↳ Strong acid - cannot be used with acid-sensitive groups like 3° alcohols (they dehydrate to give alkenes)

In base

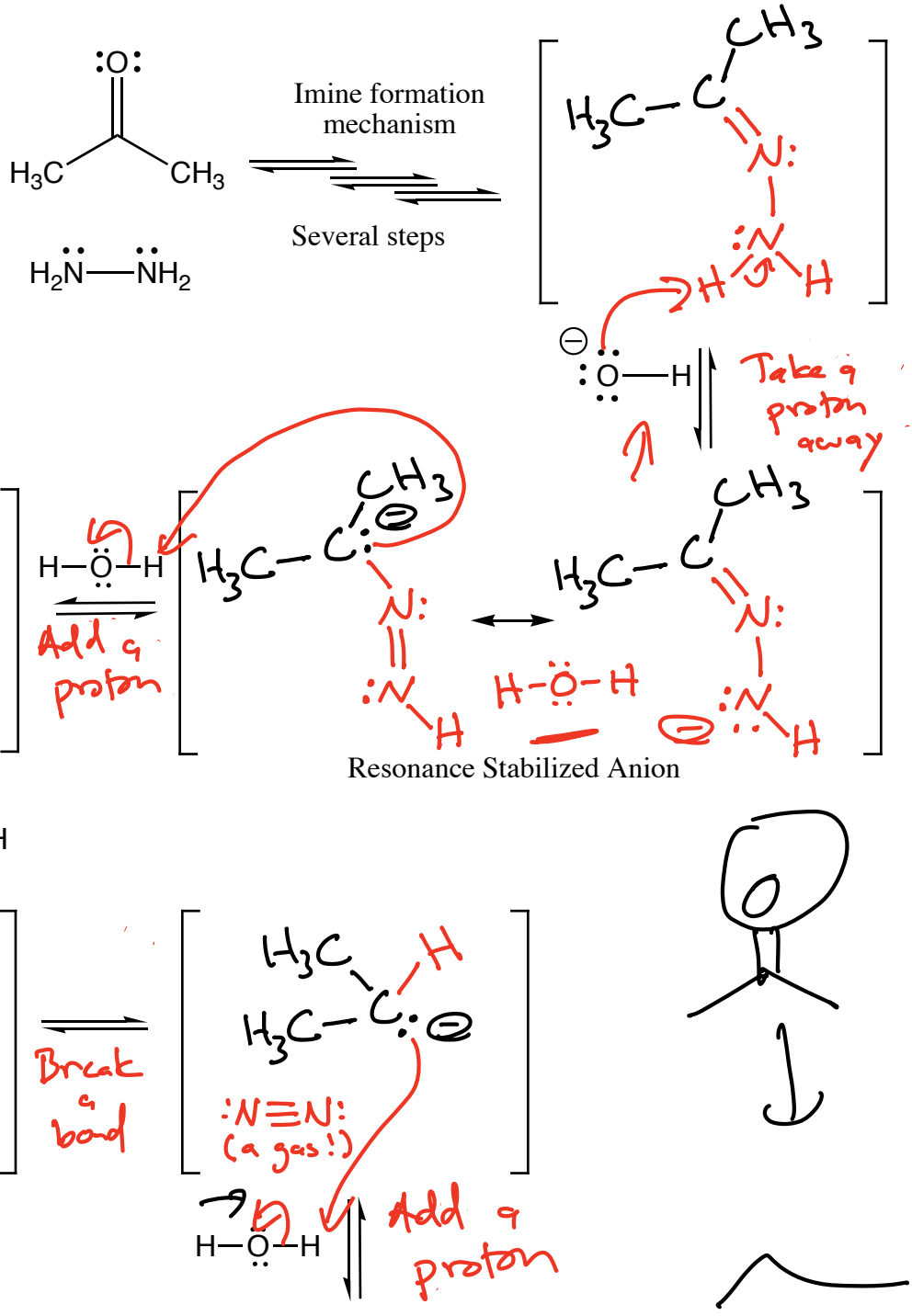
Wolff-Kishner Reduction



Used when there are acid-sensitive groups on a molecule

VERY COOL MECHANISM

Wolff-Kishner Reduction of an Aldehyde or Ketone



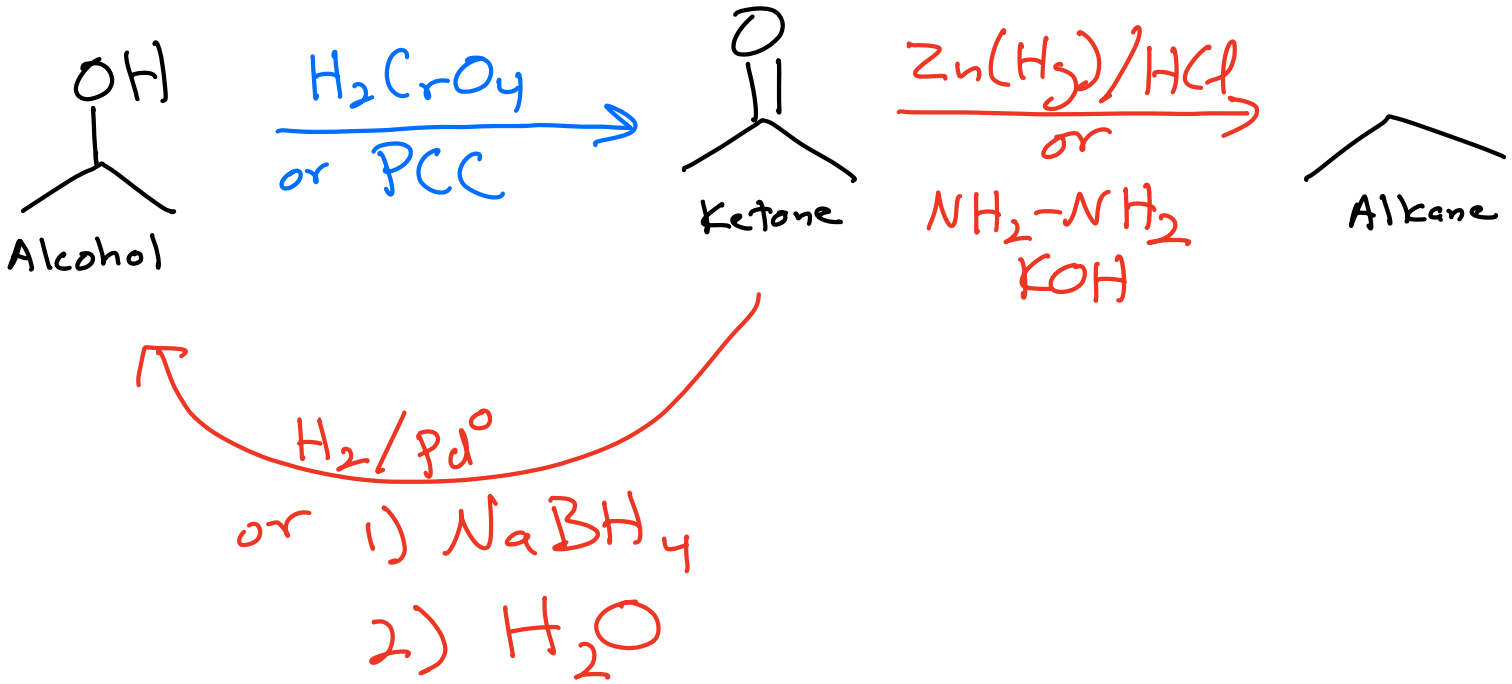
Key Recognition Element (KRE):

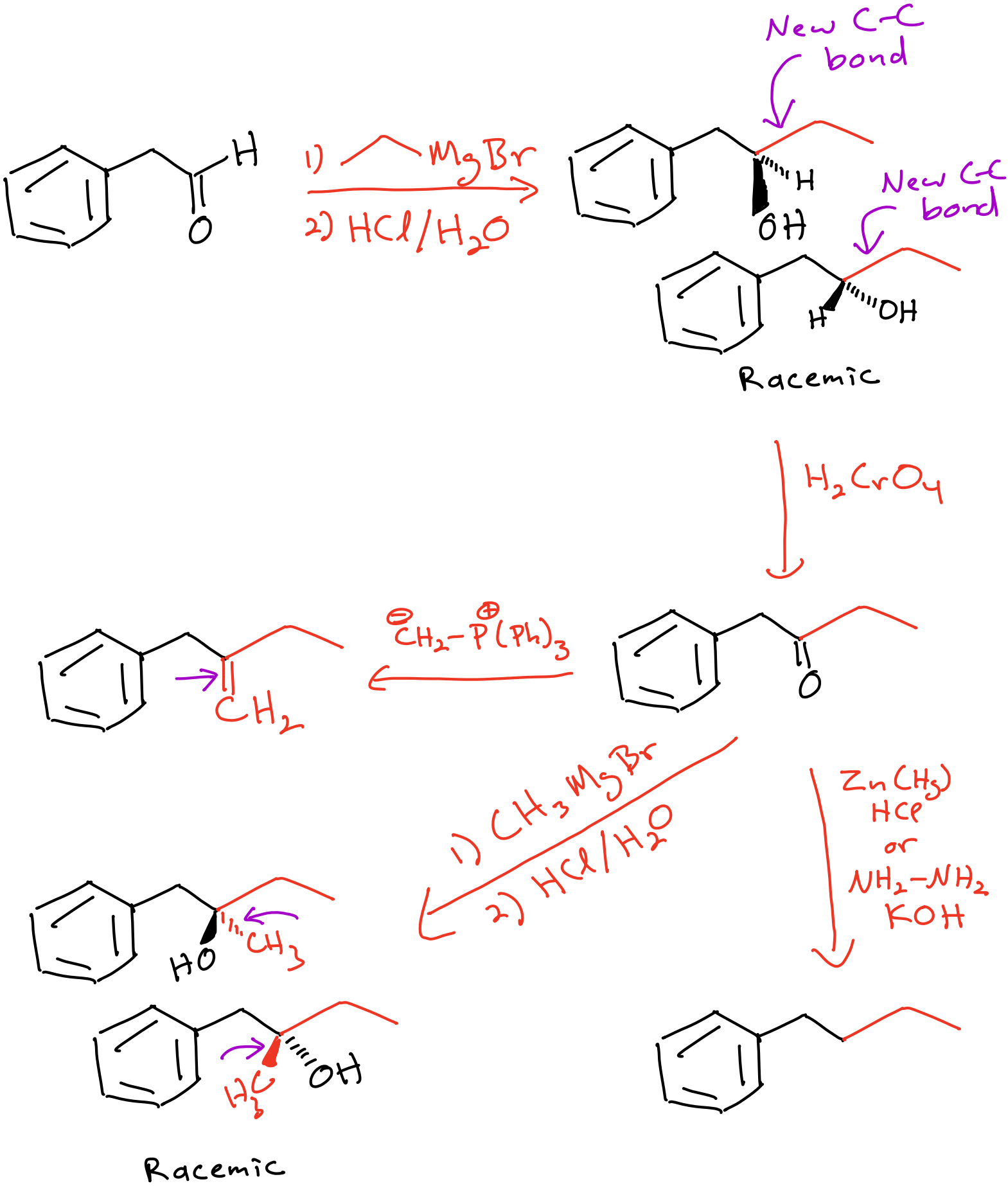
$-CH_2-$ where there was $C=O$

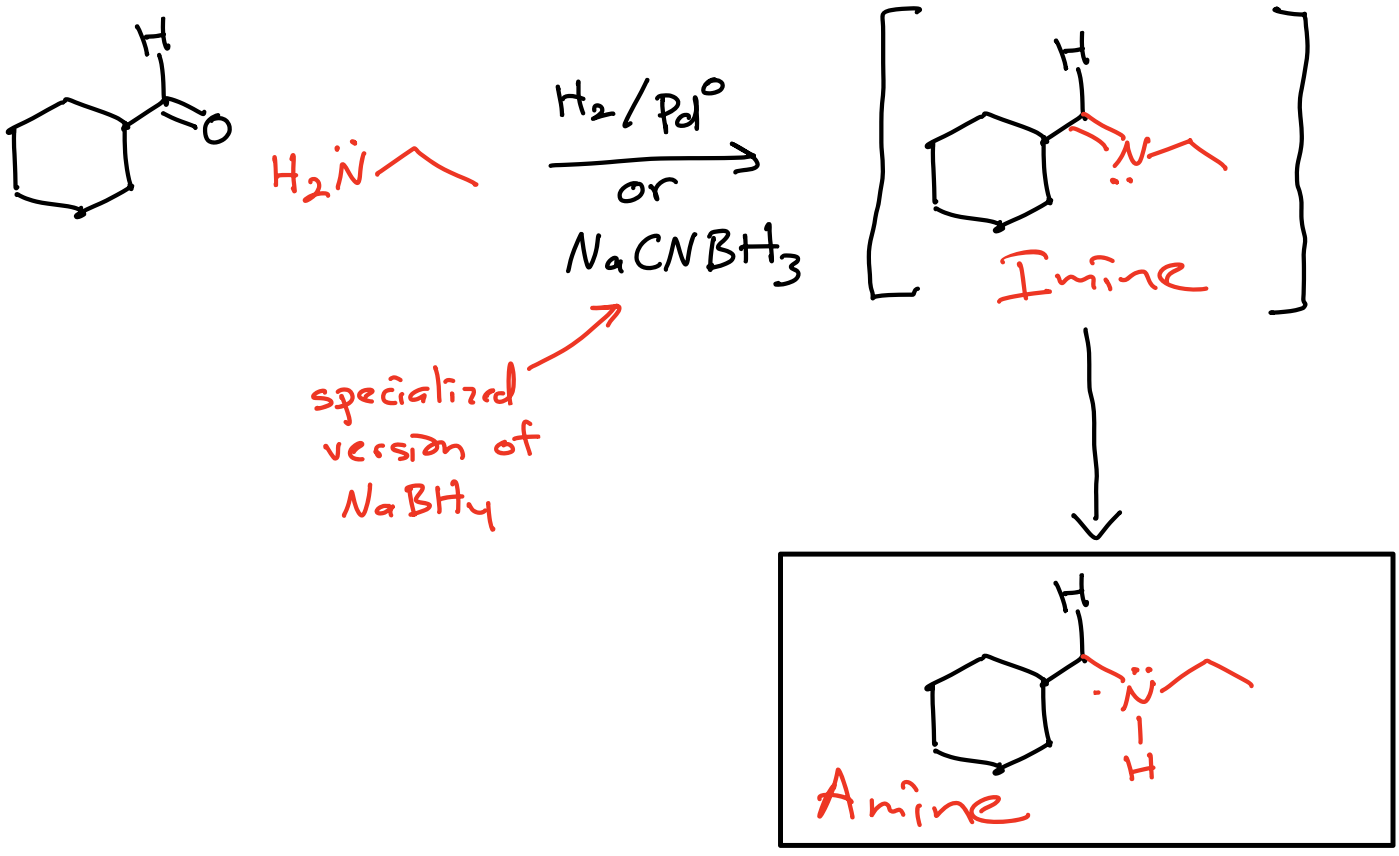
Products


Eek! Don't bite my head off!
O
NH_2-NH_2
KOH

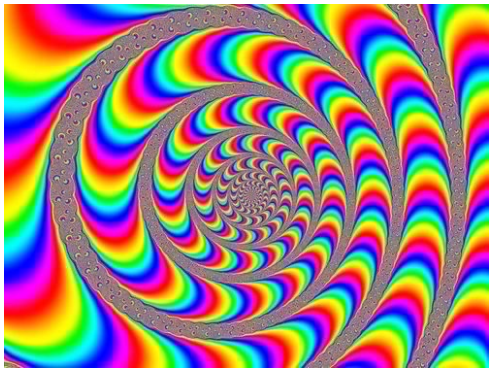
Putting these oxidation and reduction reactions to work in synthesis

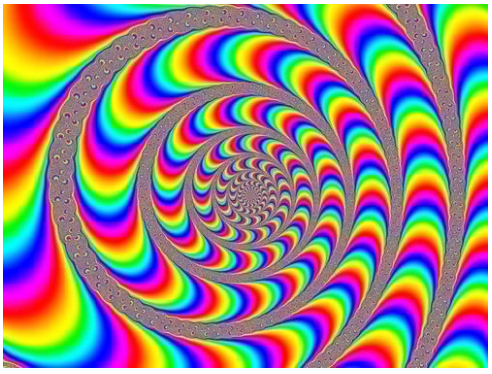



New C-C bond
1) MgBr
2) HCl/H2O
H
O
OH
New C-C bond
H
OH
Racemic
H2CrO4
CH2-P(Ph)3
CH2
O
1) CH3MgBr
2) HCl/H2O
Zn(Hg)
HCl
or
NH2-NH2
KOH
HO
CH3
OH
H
Racemic

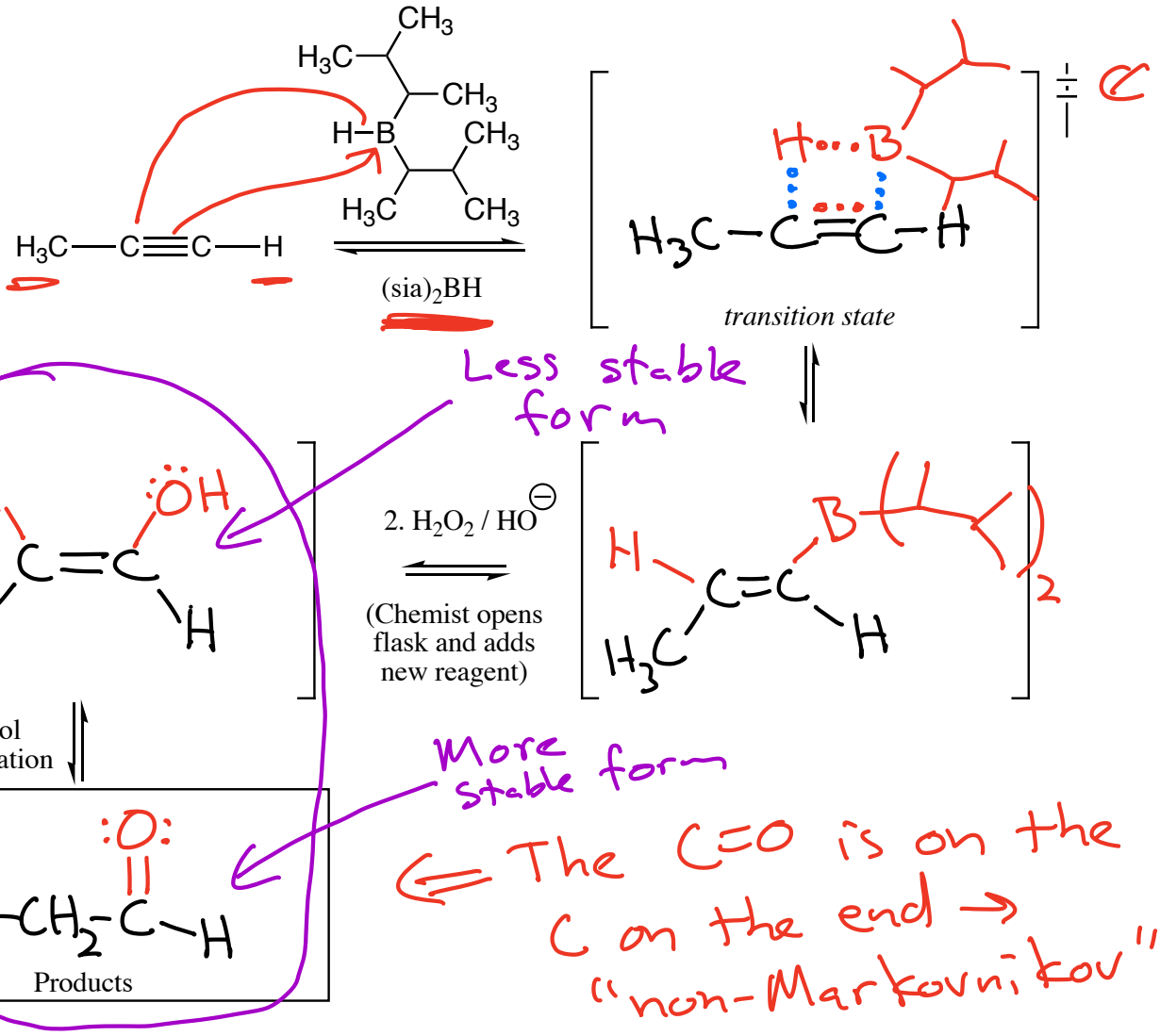


Reductive amination → reducing the C=N of an imine as it forms in the reaction.





Terminal Alkyne Hydroboration

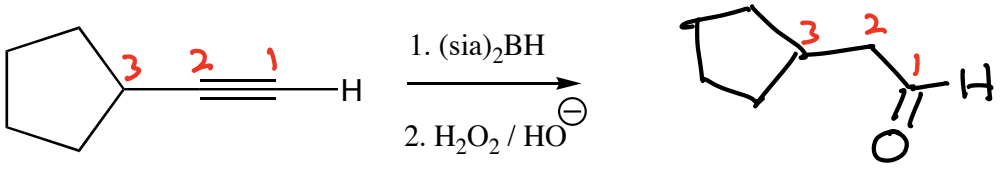


Summary: The $(sia)_2BH$ reacts so the B atom attaches to the C atom on the end. The four-membered ring transition state makes both bonds simultaneously. 2. $H_2O_2/HO^{\ominus}$ → enol → keto

Regiochemistry: non-Markovnikov

Stereochemistry: N/A

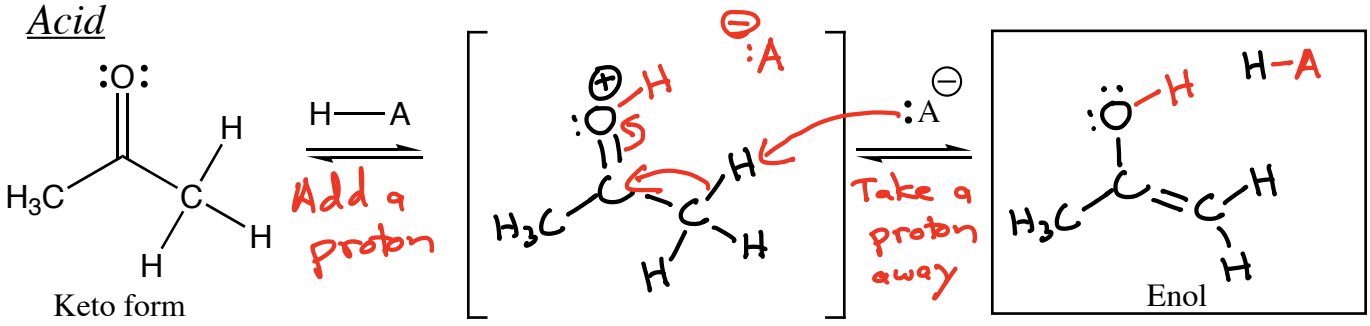
Example:



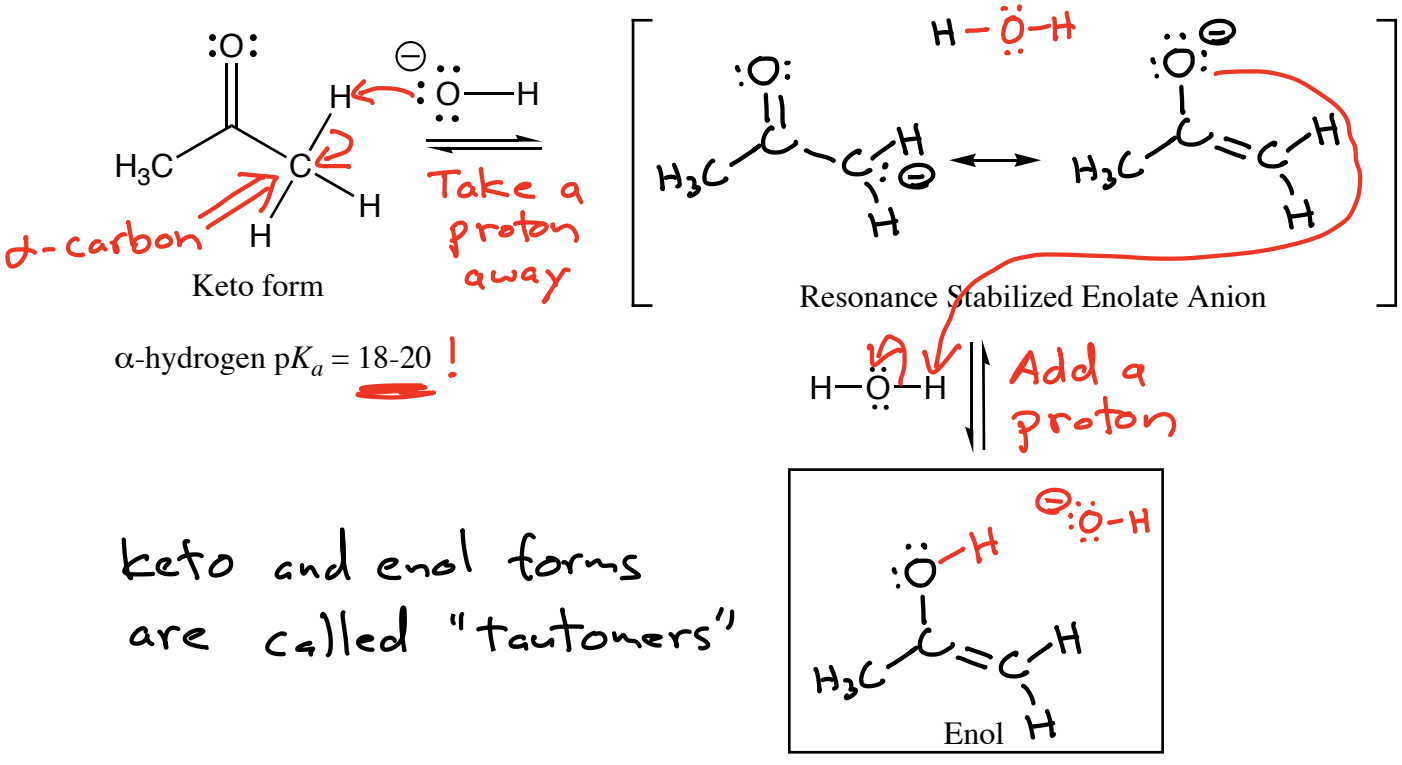
The process of interconverting the keto and enol forms is called "tautomerization"

Keto-Enol Equilibrium Catalyzed by Acid or Base

Acid



Base



α-hydrogen pK_a = 18-20 !

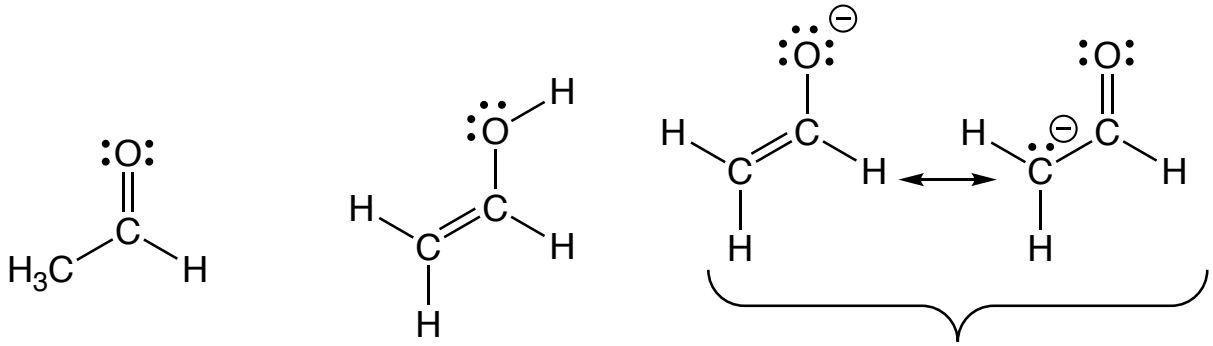
keto and enol forms are called "tautomers"

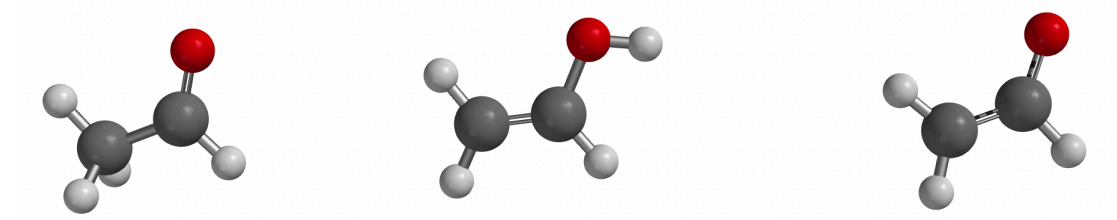
For both aldehydes and ketones, the keto form predominates at equilibrium, because C=O bonds are stronger than C=C bonds.

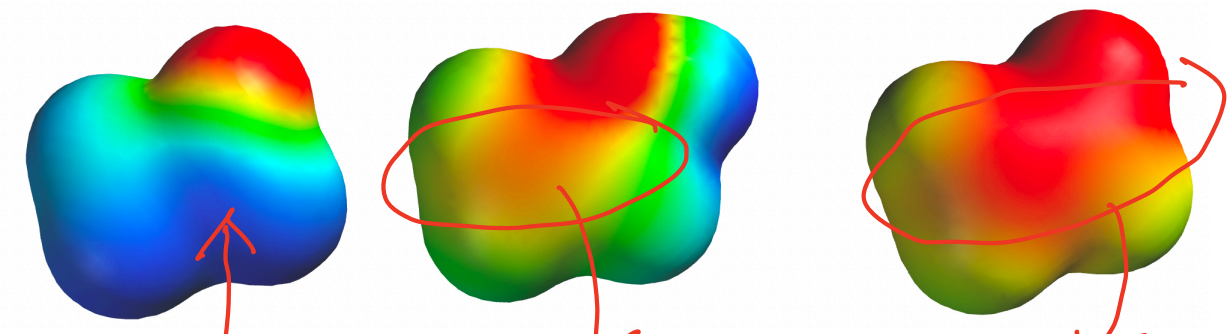
Enols are significant, however, because they react like nucleophile, not carbonyls, and this is important in certain situations.

Changing Personality:

An aldehyde or ketone is a weak electrophile.
An enol of that same aldehyde or ketone has a π bond that is a weak nucleophile!

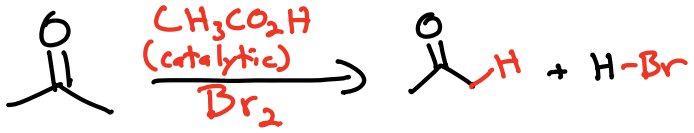




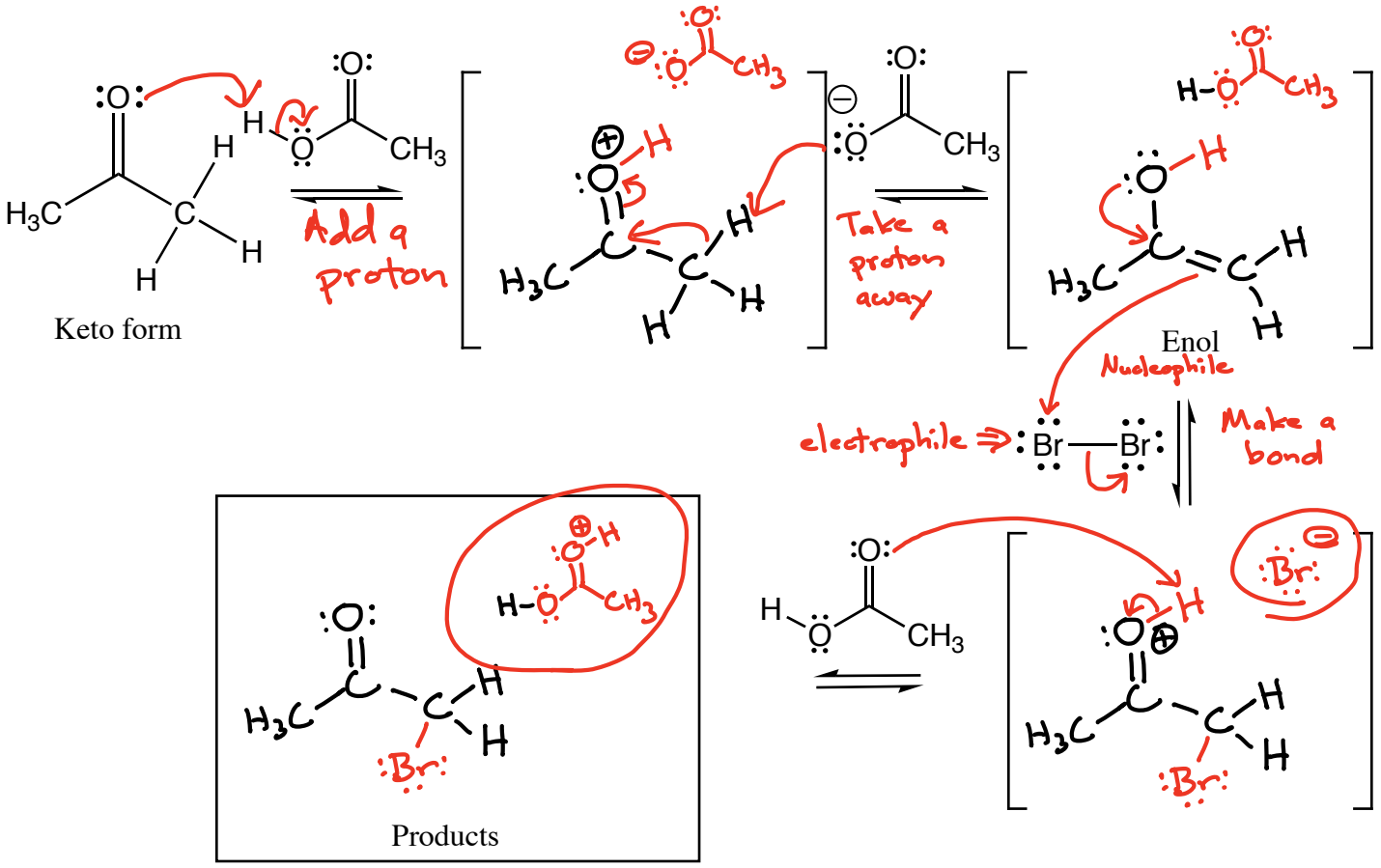


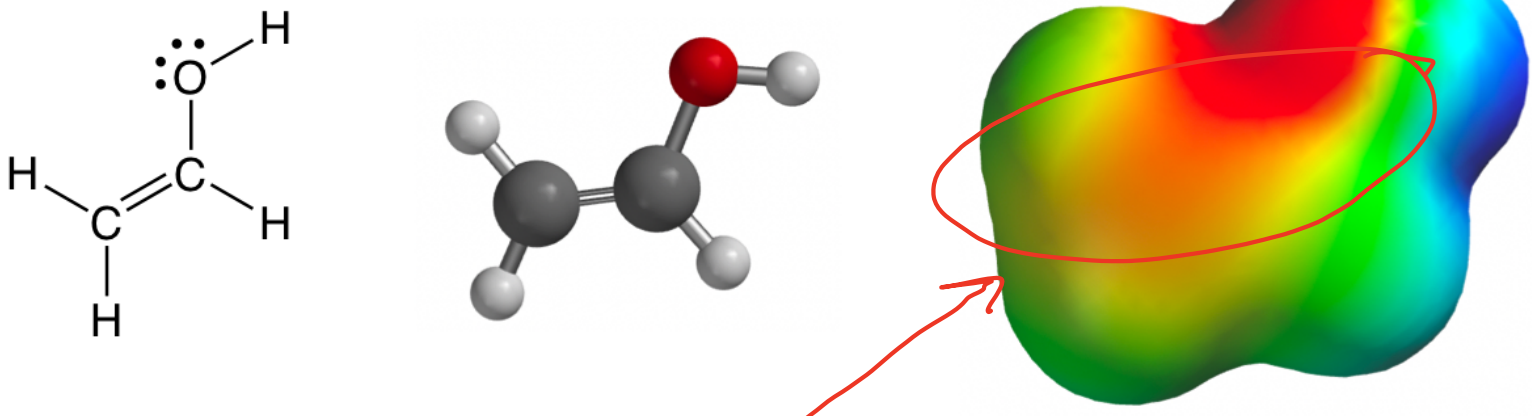
α-Halogenation of Aldehyde or Ketone in Acid

<u>Overall Reaction</u>



α-Halogenation of an Aldehyde or Ketone Catalyzed by Acid





Nucleophile