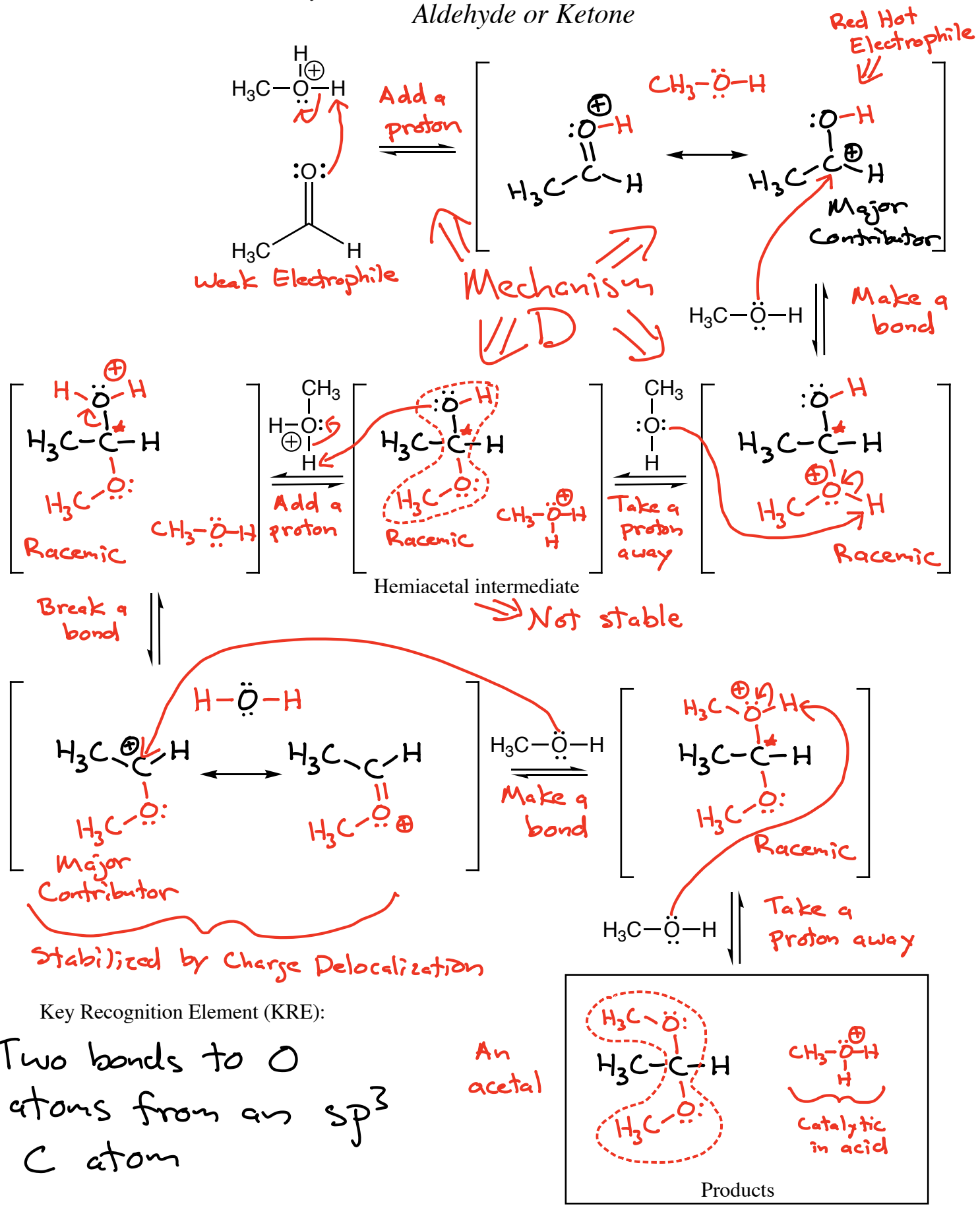




"Catching the O Chem Wave"

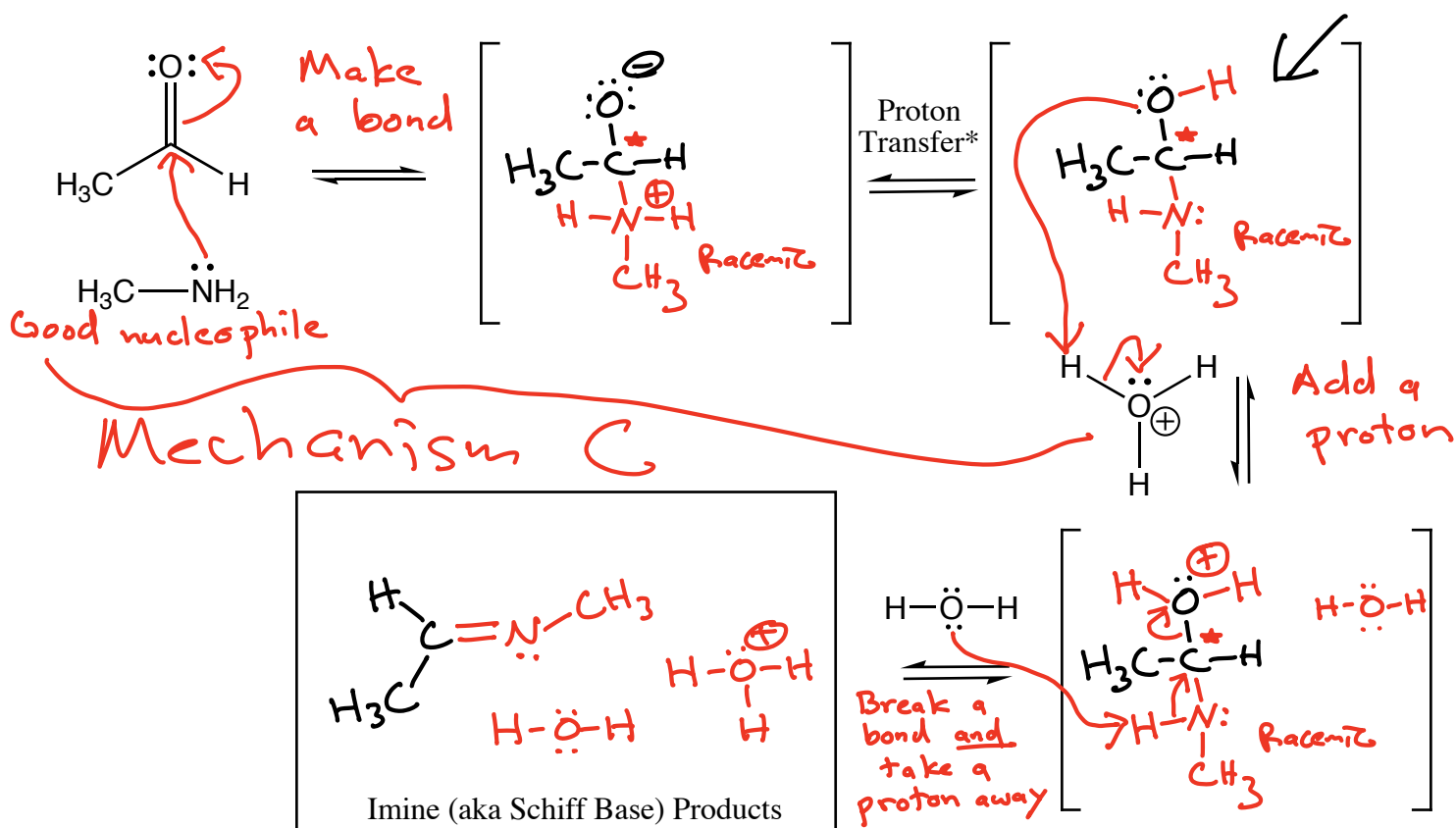
H₂SO₄
 "Hey, does that thing have a hemi in it?" "SWEET!"
 Acid Catalyzed Hemiacetal and Acetal Formation From an Aldehyde or Ketone



Key Recognition Element (KRE):

Two bonds to O atoms from an sp³ C atom

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



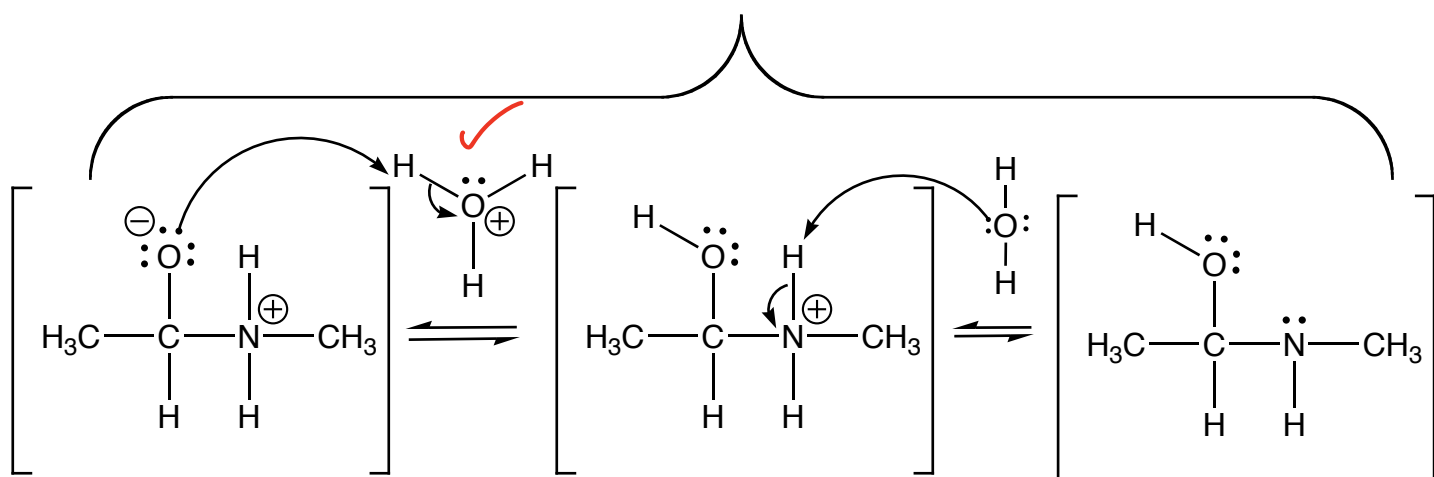
Key Recognition Element (KRE):



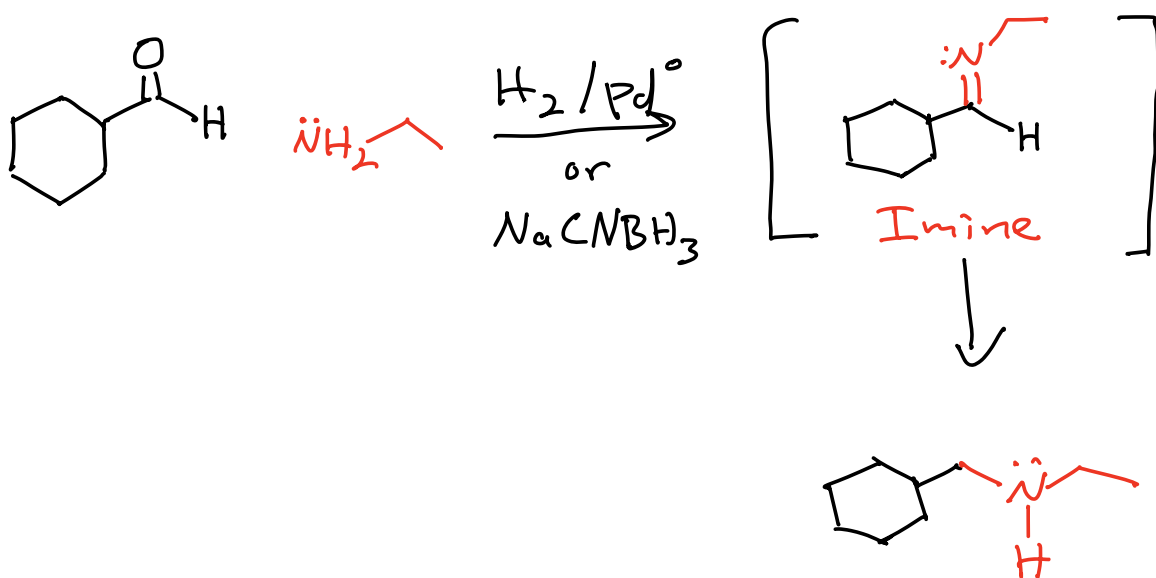
Note: this last step might actually occur as two steps in some cases.

* "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"



Reductive Amination \rightarrow reducing
the $C=N$ of an imine
as it forms in the
reaction $\rightarrow H_2/Pd^0$ or
 $NaCNBH_3$

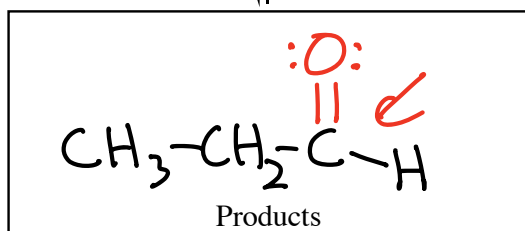
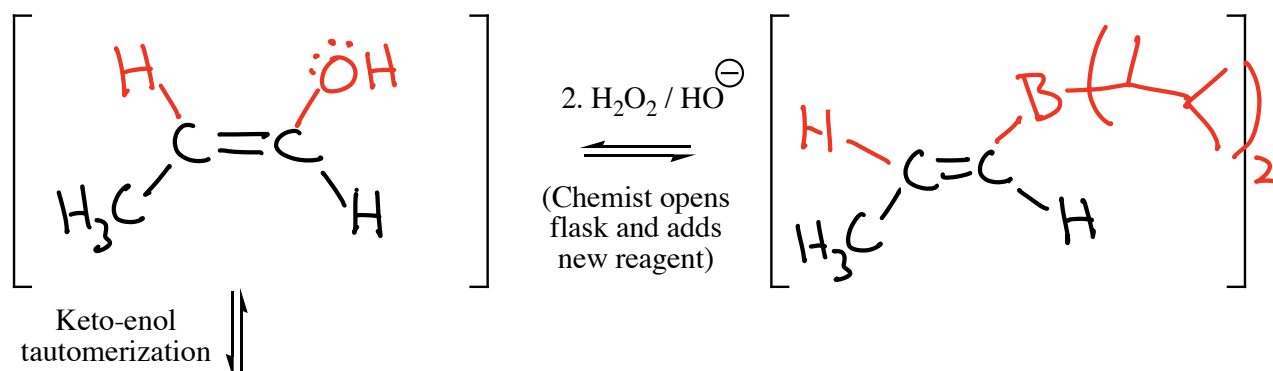
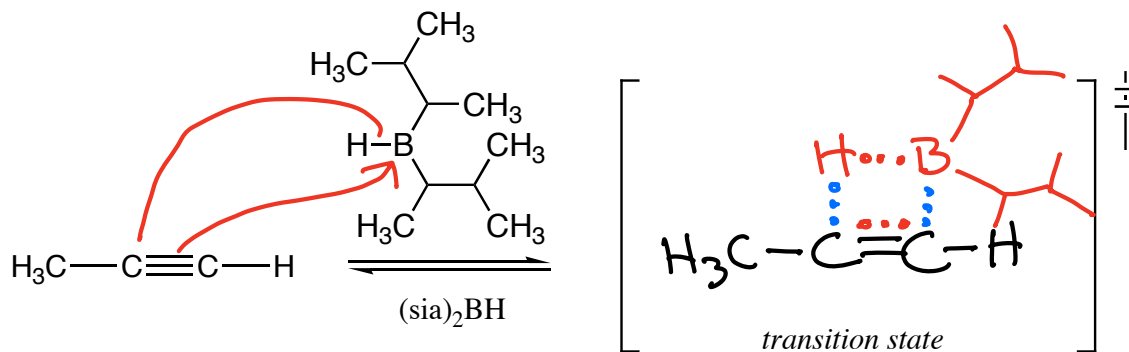




"Catching the O Chem Wave"



Terminal Alkyne Hydroboration



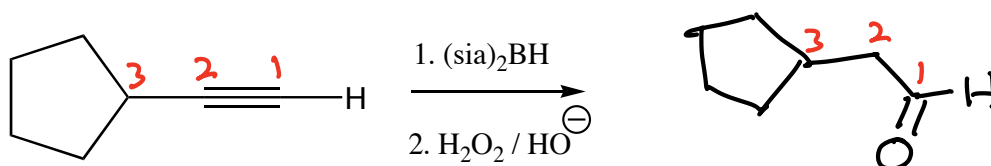
⇐ The C=O is on the C on the end → "non-Markovnikov"

Summary: The $(\text{sia})_2\text{BH}$ reacts so the B atom attaches to the C atom on the end. The four-membered ring transition states makes both bonds simultaneously. $2. \text{H}_2\text{O}_2 / \text{HO}^- \rightarrow \text{enol} \rightarrow \text{keto}$

Regiochemistry: non-Markovnikov

Stereochemistry: N/A

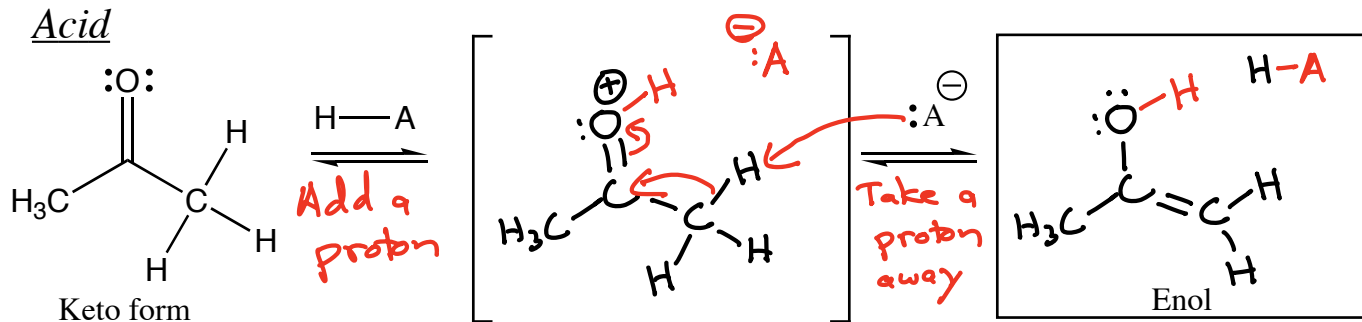
Example:



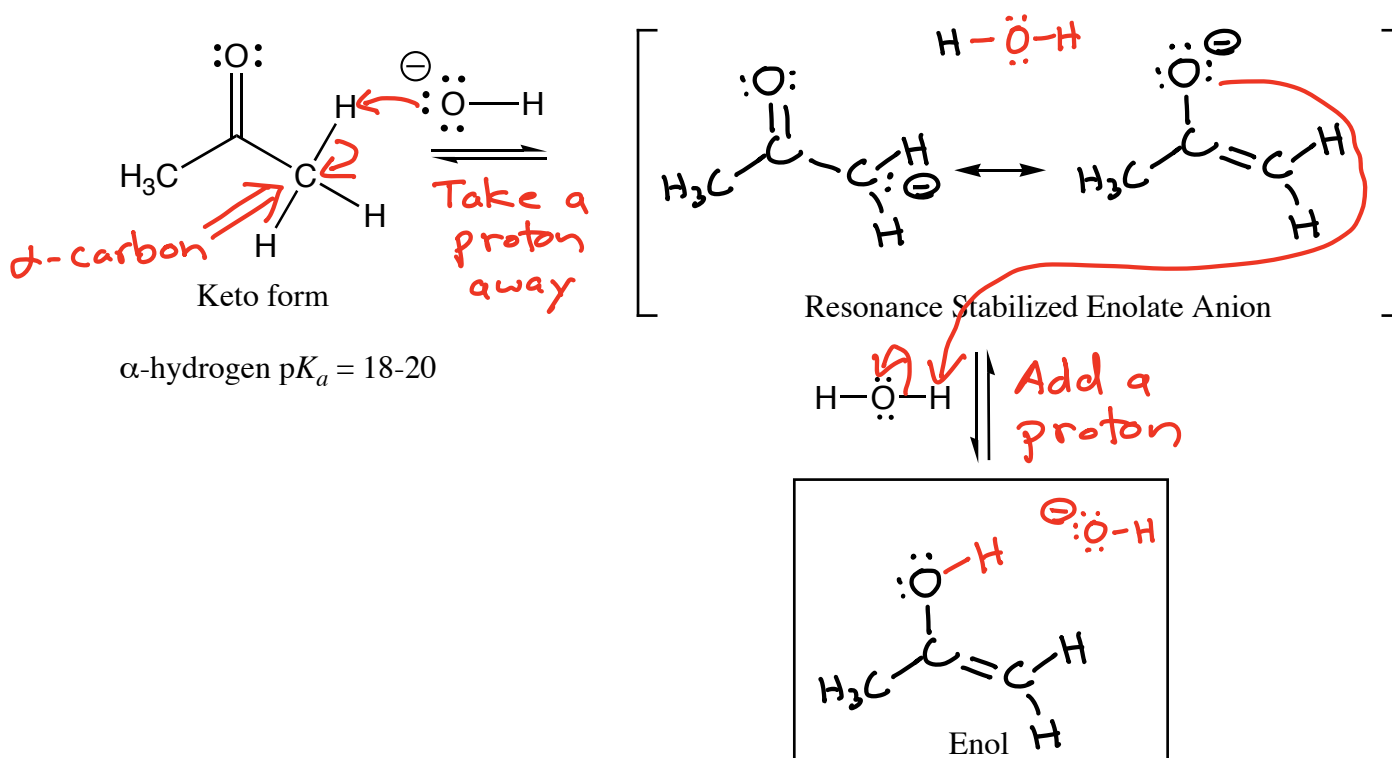
Tautomerization

Keto-Enol Equilibrium Catalyzed by Acid or Base

Acid

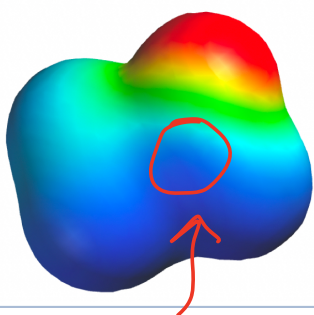
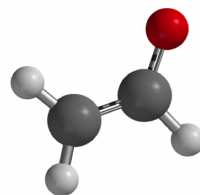
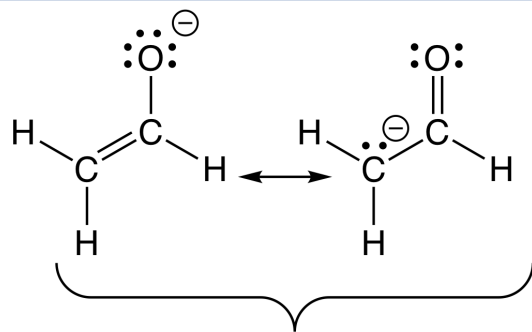
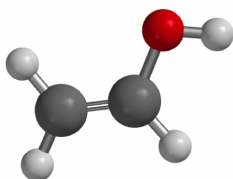
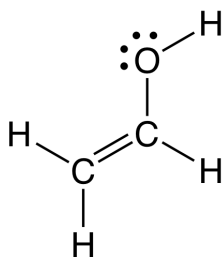
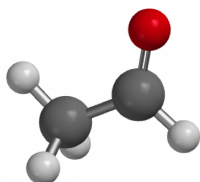
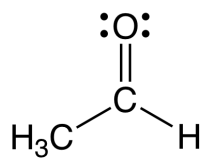


Base

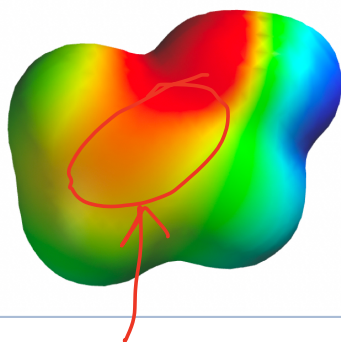


For both aldehydes and ketones, the keto form predominates at equilibrium, because $\text{C}=\text{O}$ bonds are stronger than $\text{C}=\text{C}$ bonds.

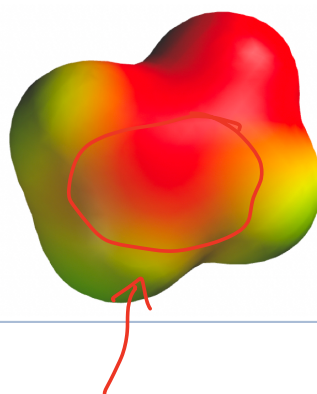
Enols are significant, however, because they react like nucleophile, not carbonyls, and this is important in certain situations.



electrophile



weak nucleophile

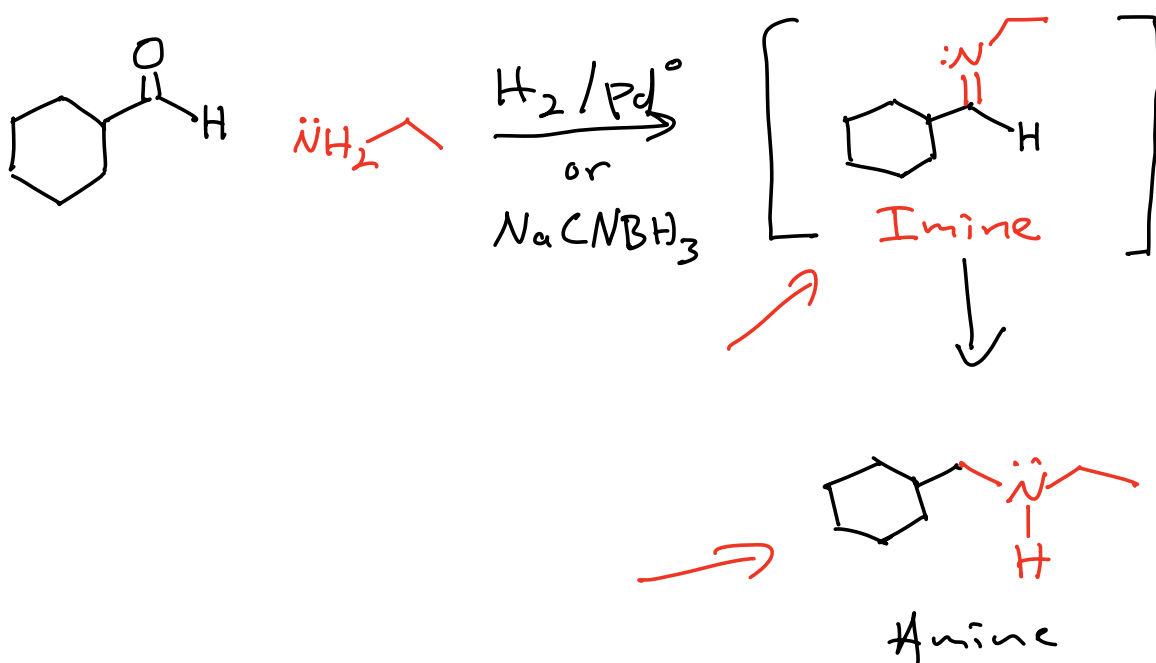


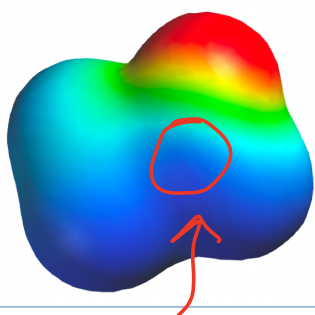
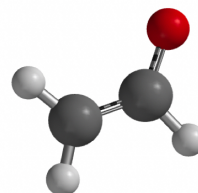
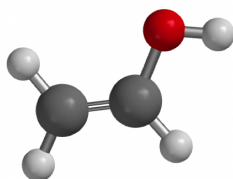
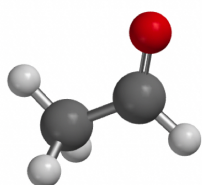
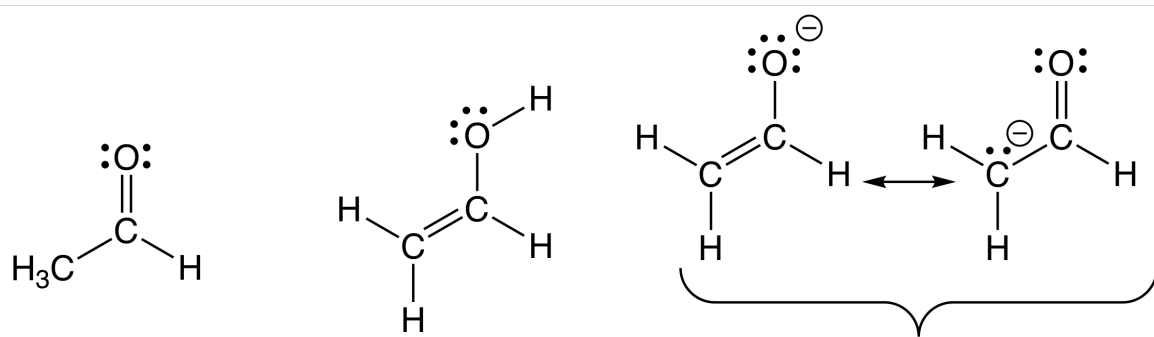
strong nucleophile



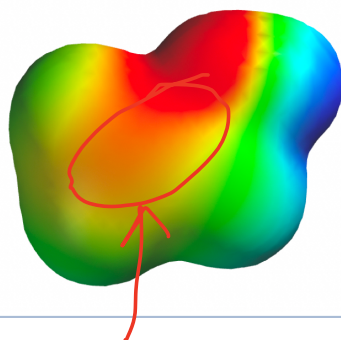
"Catching the O Chem Wave"

✓
Reductive Amination → reducing
the C=N of an imine
as it forms in the
reaction → H_2/Pd^0 or
 $NaCNBH_3$

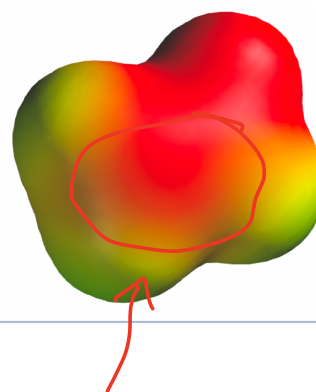




electrophile

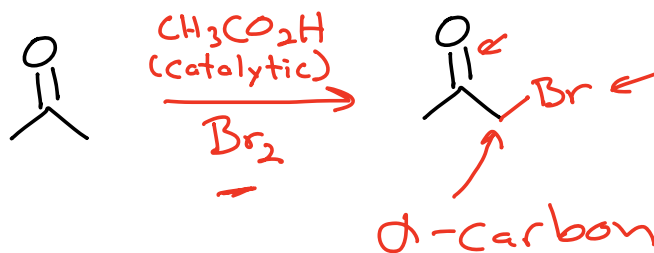


weak nucleophile

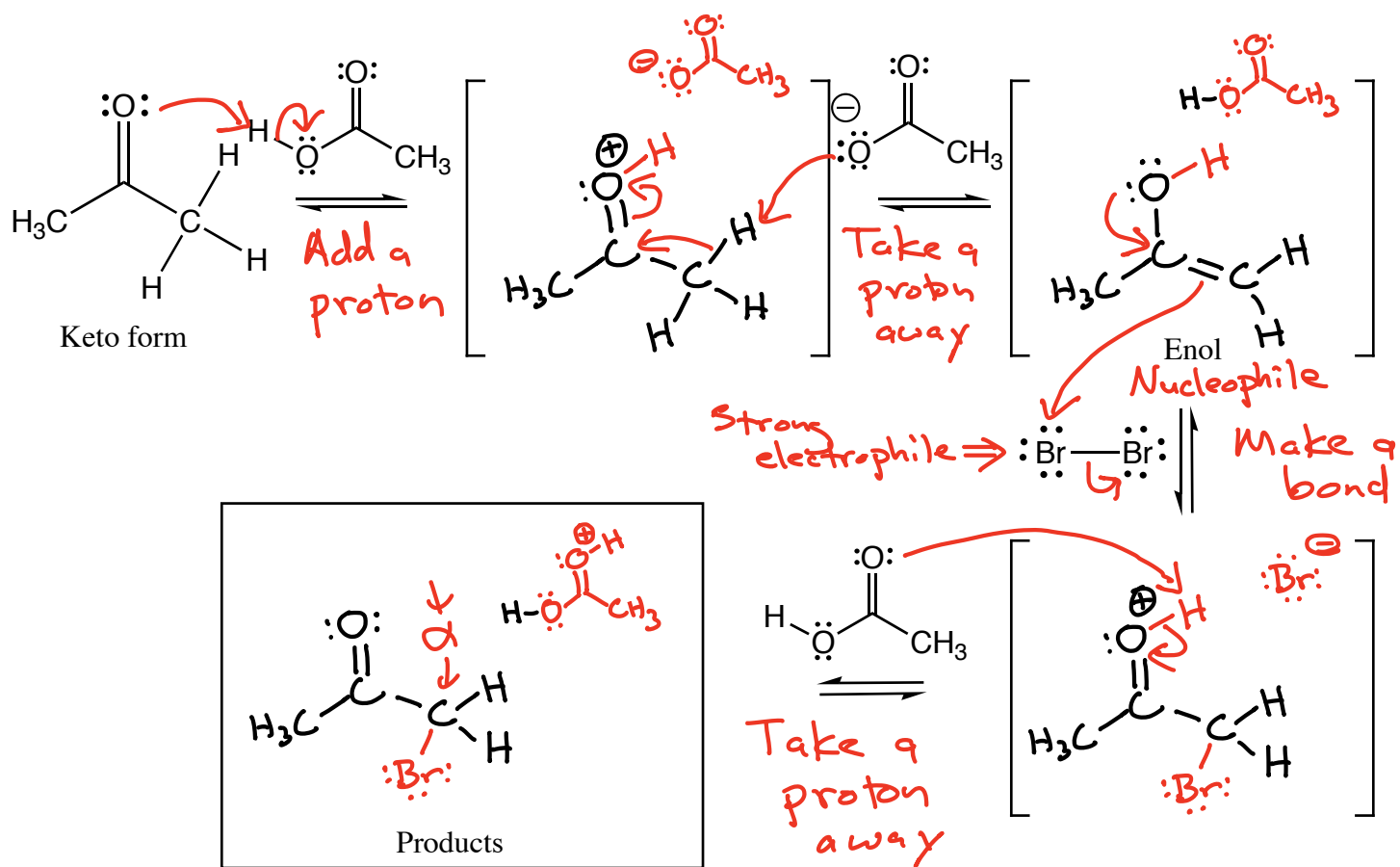


strong nucleophile

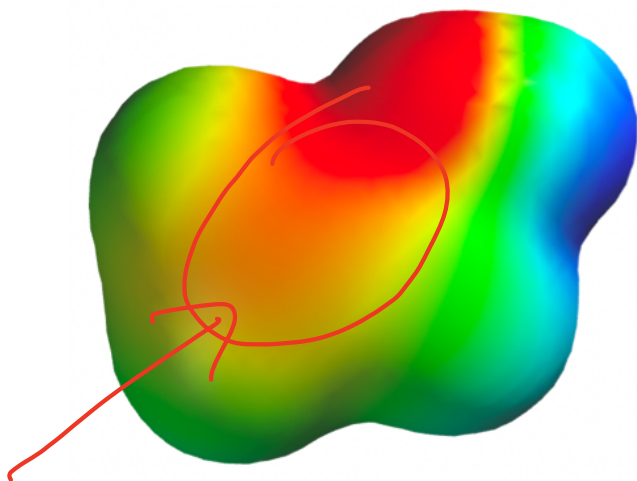
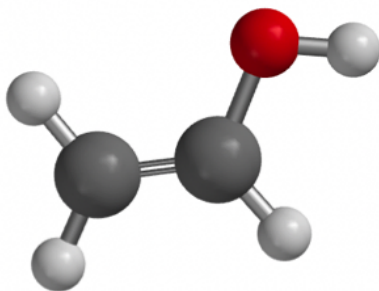
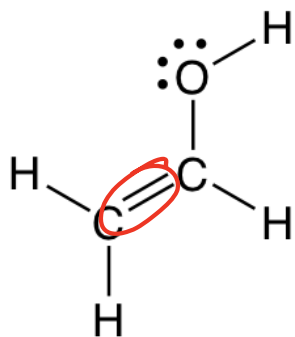
α-Halogenation of Aldehydes or Ketones

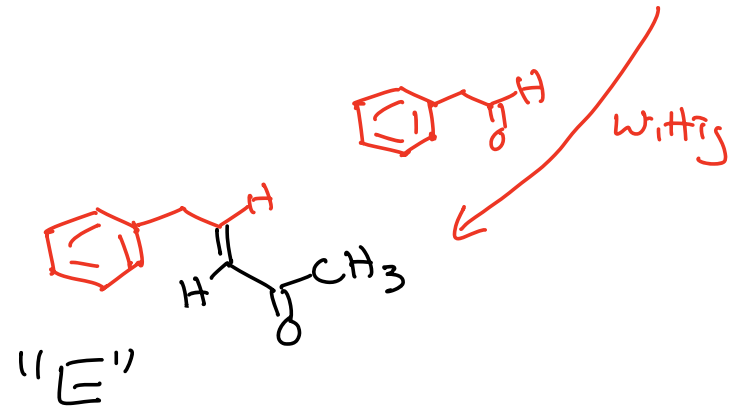
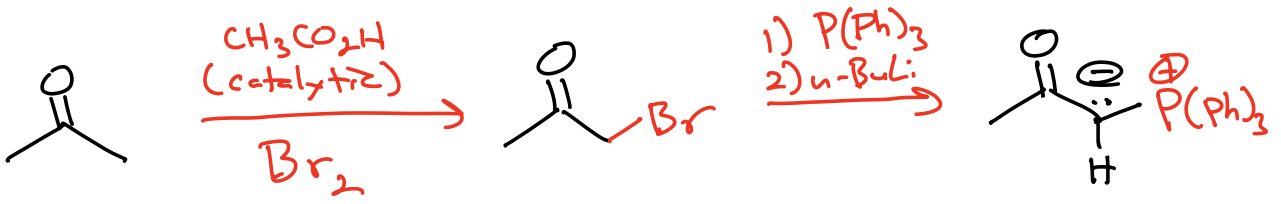


α -Halogenation of an Aldehyde or Ketone Catalyzed by Acid



KRE: A new bond to Br at the α -carbon position

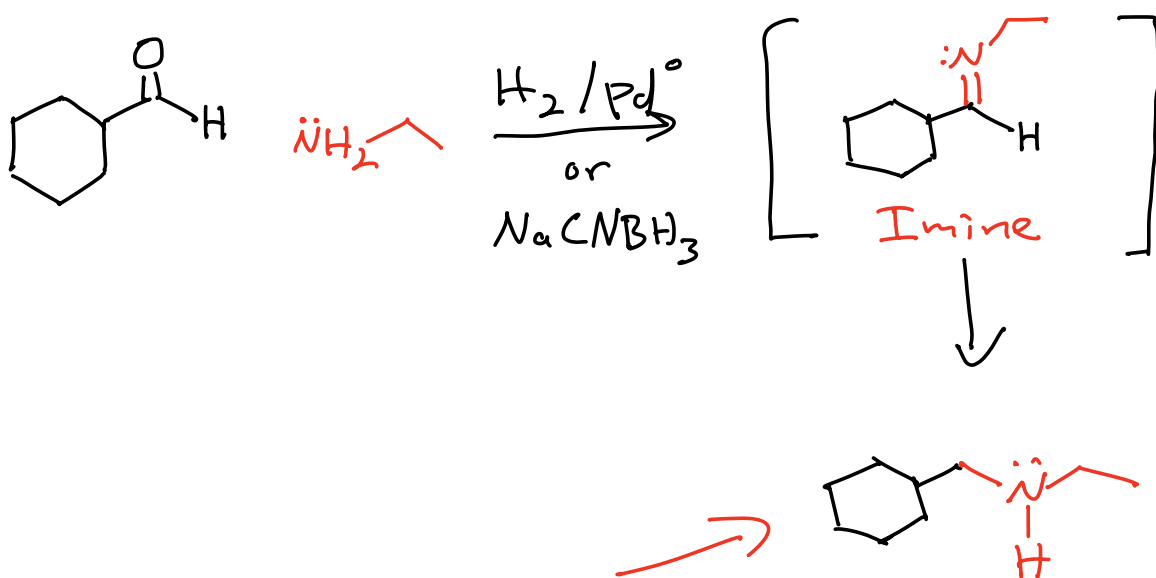


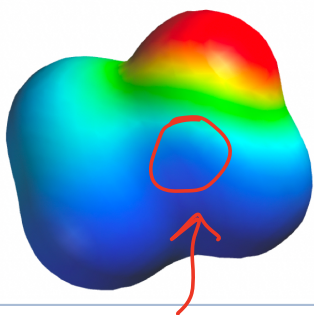
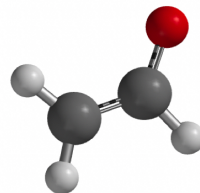
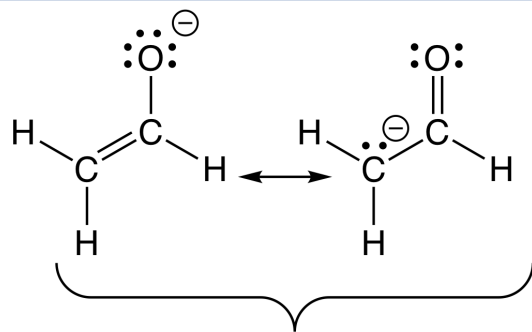
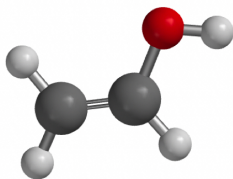
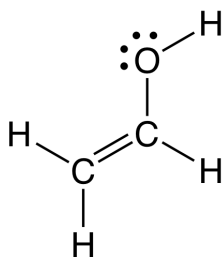
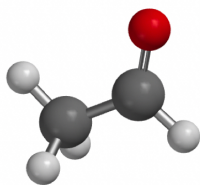
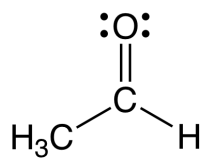




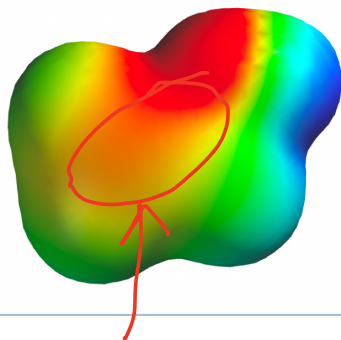
"Catching the O Chem Wave"

Reductive Amination \rightarrow reducing
the $C=N$ of an imine
as it forms in the
reaction $\rightarrow H_2/Pd^0$ or
 $NaCNBH_3$

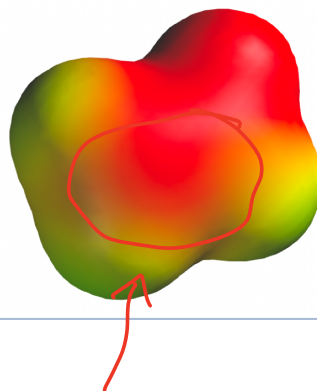




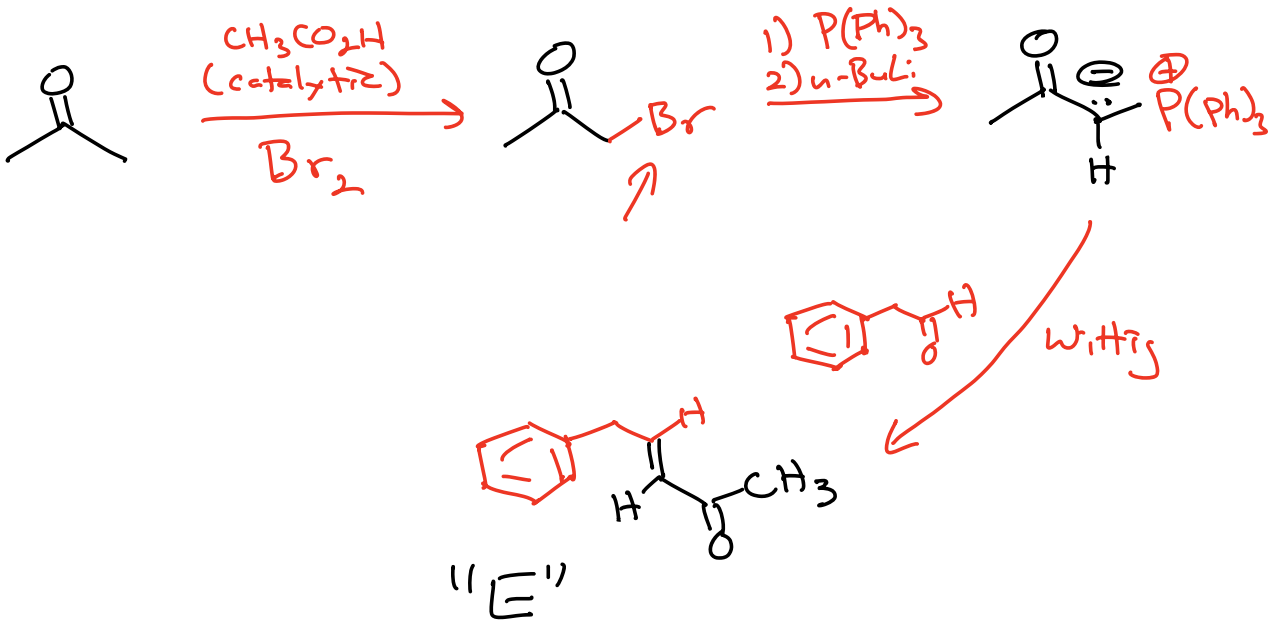
electrophile



weak nucleophile

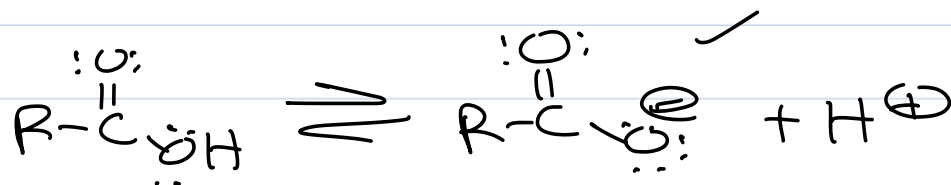
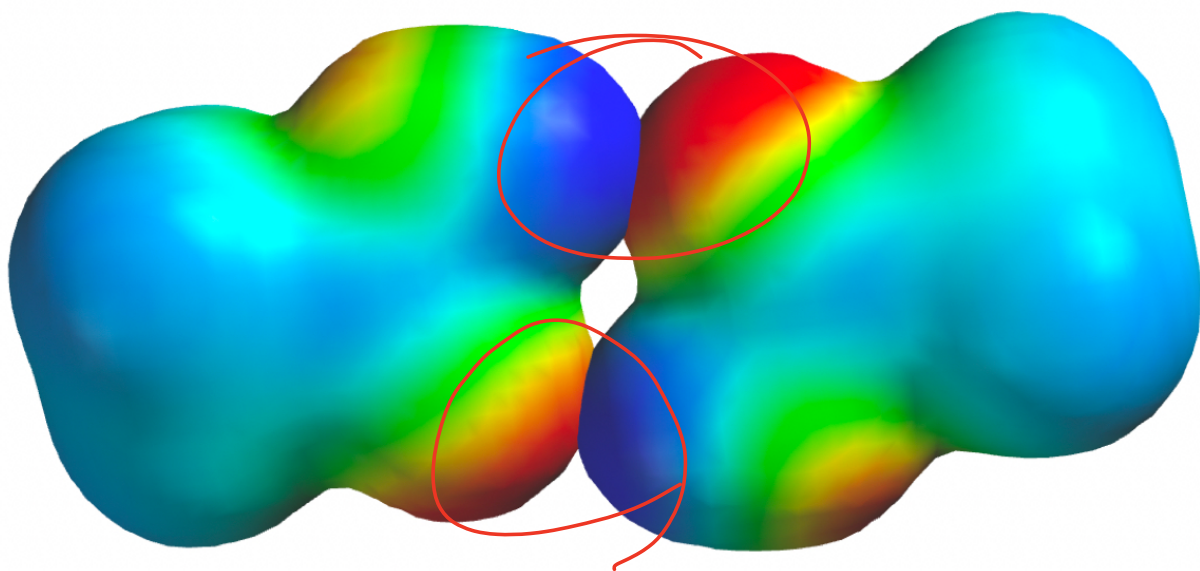
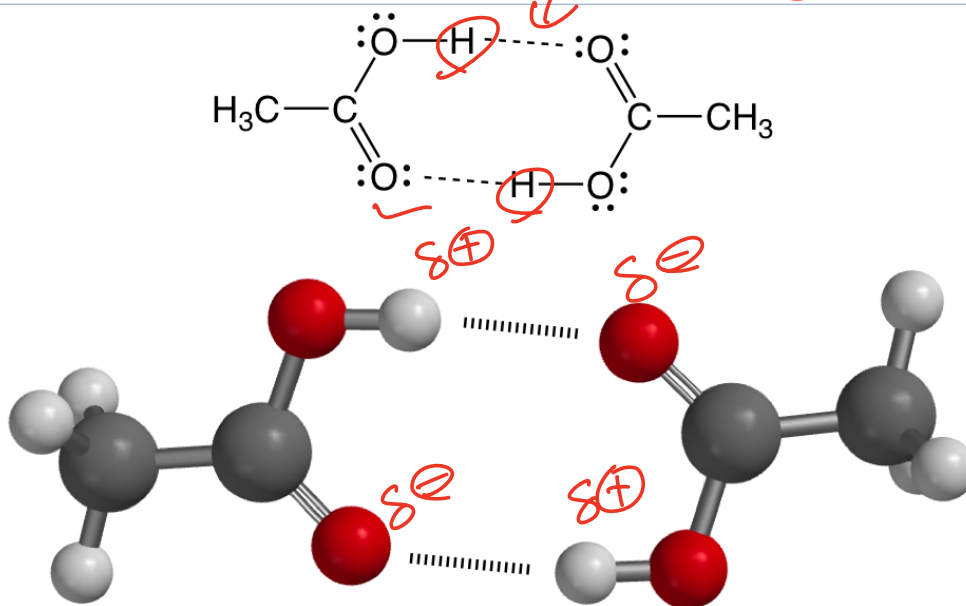


strong nucleophile

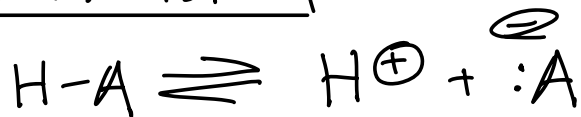


Carboxylic Acids

hydrogen bonds



Acidity Revisited



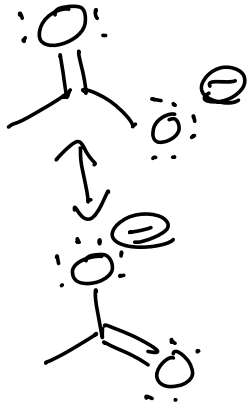
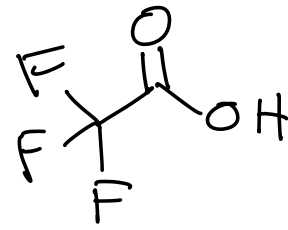
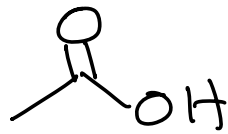
$$K_a = \frac{[\text{A}^{\ominus}][\text{H}^{\oplus}]}{[\text{HA}]}$$

$$\text{p}K_a = -\log_{10} K_a$$

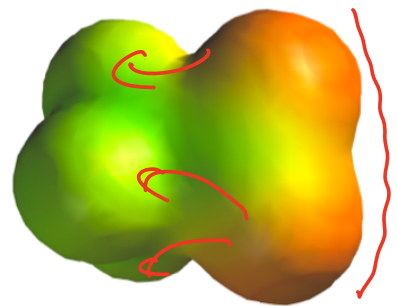
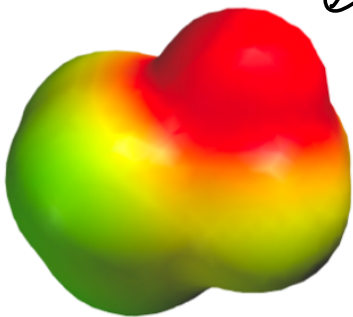
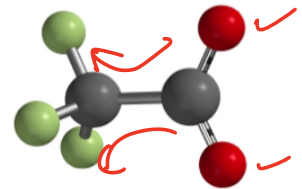
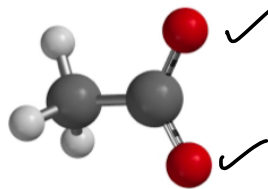
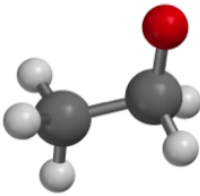
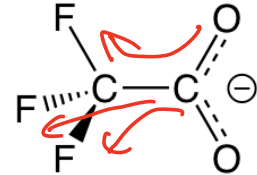
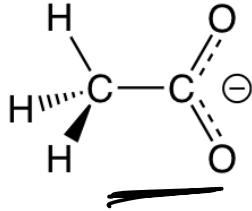
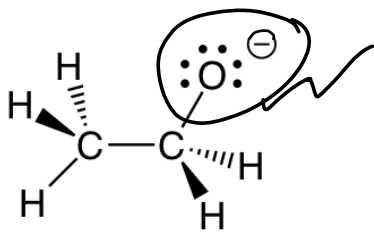
The lower the $\text{p}K_a$ value,
the stronger the acid

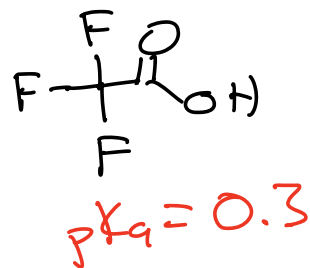
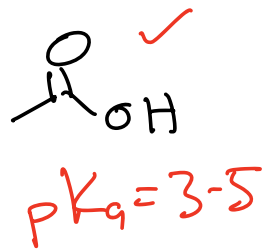
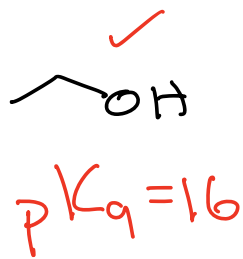
If an anion is created when
an acid dissociates \rightarrow the
more stable the anion, the
stronger the acid

Anions are stabilized when
the negative charge is
distributed over more atoms



Inductive effect
F is electronegative





For an acid H-A ✓

$$K_a = \frac{[A:^{\ominus}][H^{\oplus}]}{[HA]}$$

$$pK_a = -\log_{10} K_a$$

$$pH = -\log_{10} [H^{\oplus}]$$

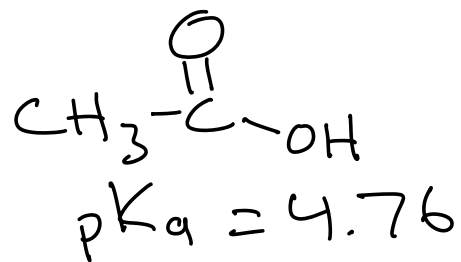
$$\left(\frac{K_a}{[H^{\oplus}]} = \frac{[A:^{\ominus}]}{[HA]} \right) = 10^{(pH - pK_a)} \quad \checkmark$$

If $pH = 7$ and $pK_a = 3$ ✓

$$\frac{[A:^{\ominus}]}{[HA]} = 10^{(pH - pK_a)} = 10^{(7-3)} = 10^4 \quad \checkmark$$

1) If the pH of a solution is above (larger) than the pK_a of an acid, the acid will be largely deprotonated

2) If the pH of a solution is below (smaller) than the pK_a of an acid, the acid will be largely protonated.

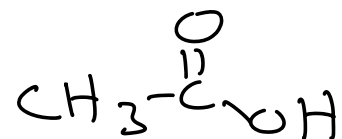


at pH 7.0



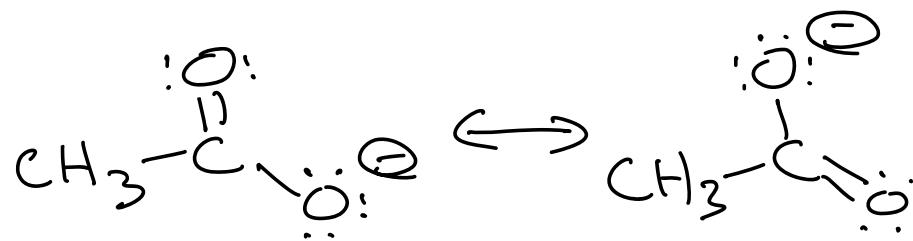
Deprotonated

at pH 2.0



Protonated

In biochemistry \rightarrow at neutral pH, carboxylic acids are deprotonated and negatively charged!!



Not only is the negative charge split between both O atoms, there is a "π-way", namely a π bonds that extend over 3 atoms \rightarrow also stabilizing