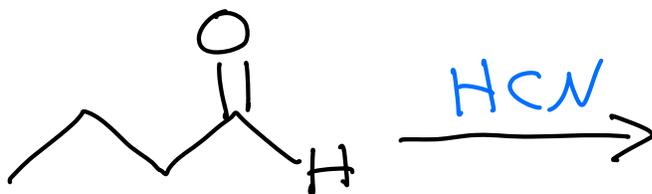
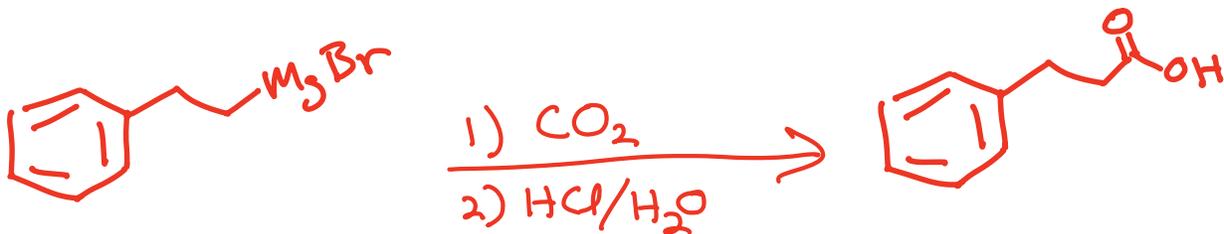
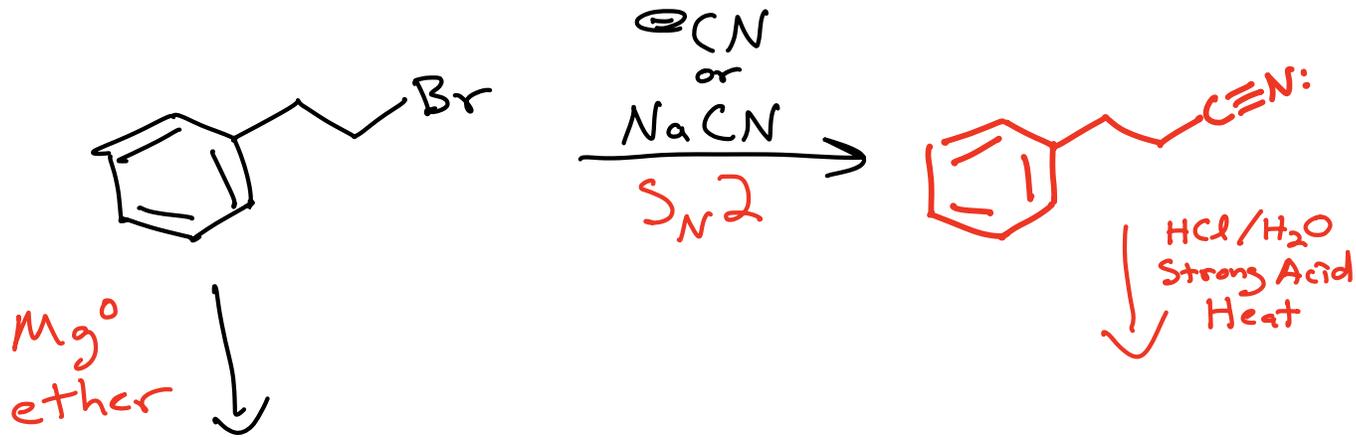


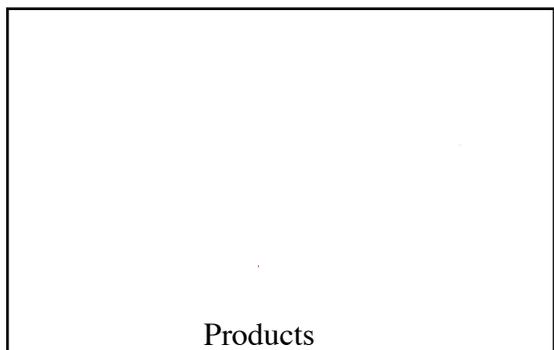
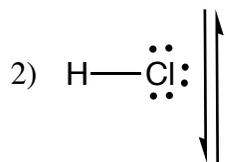
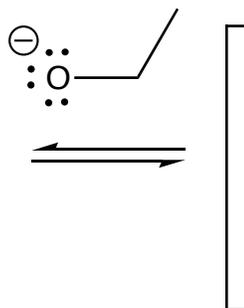
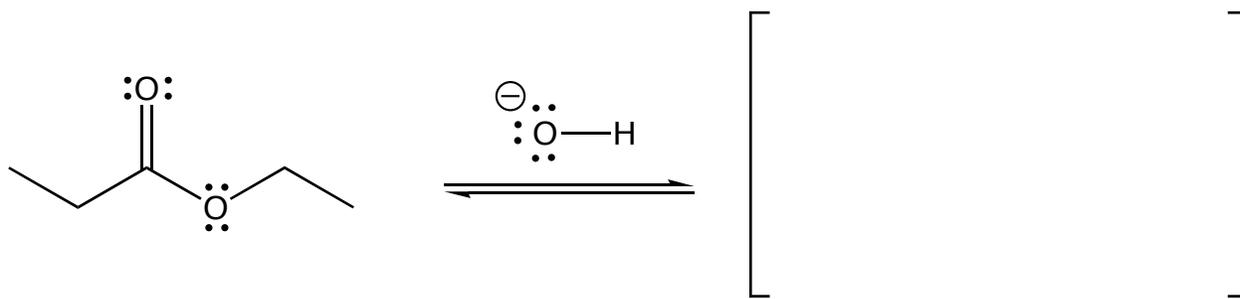
“I've missed more than 9000 shots in my career. I've lost almost 300 games. 26 times, I've been trusted to take the game winning shot and missed. I've failed over and over and over again in my life. And that is why I succeed.” Michael Jordan



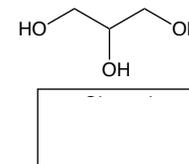
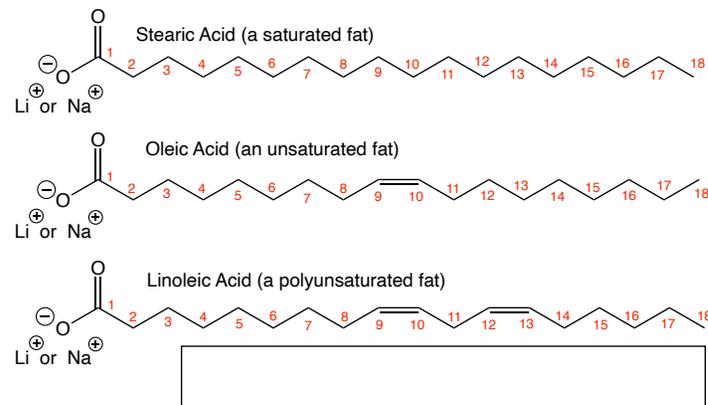
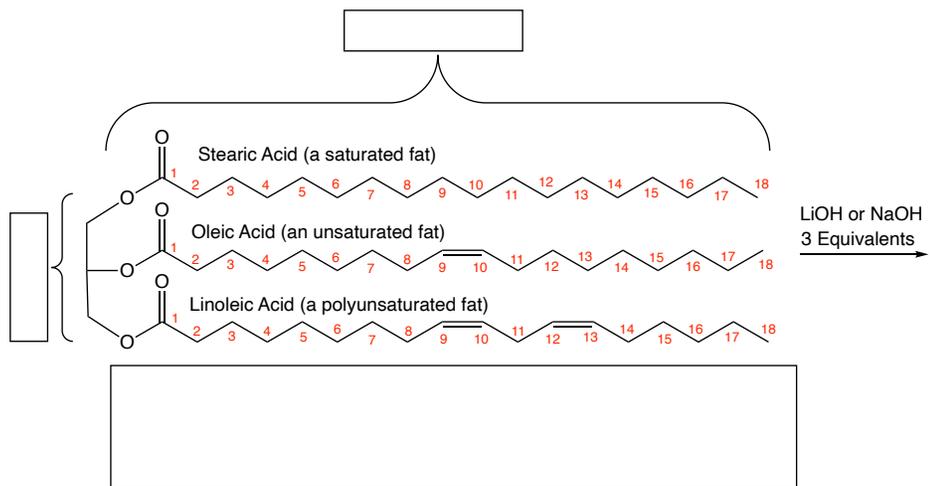
KRE →



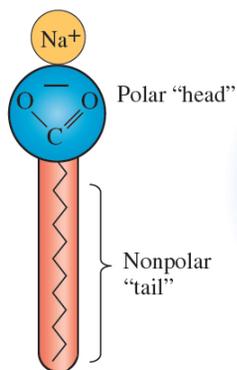
*Base-Promoted Ester Hydrolysis - Saponification*



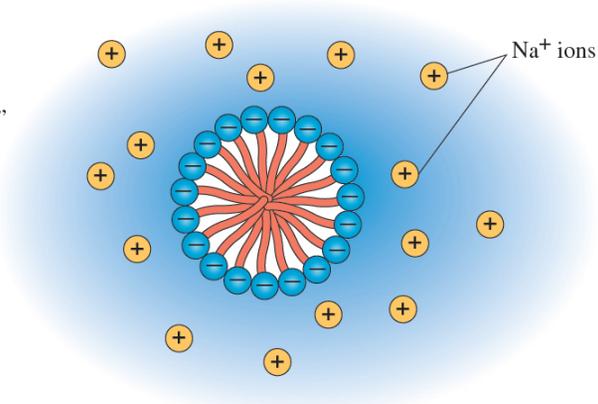
Driving force  $\rightarrow$



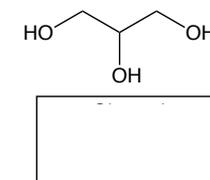
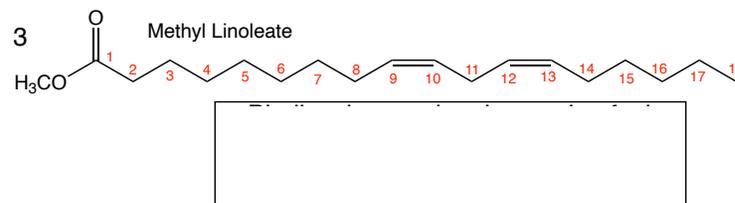
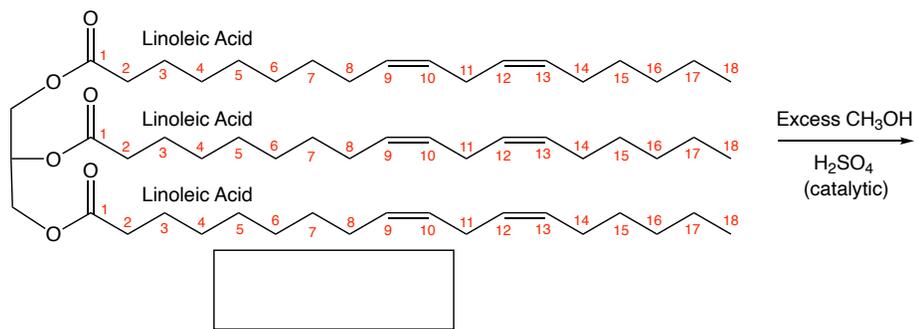
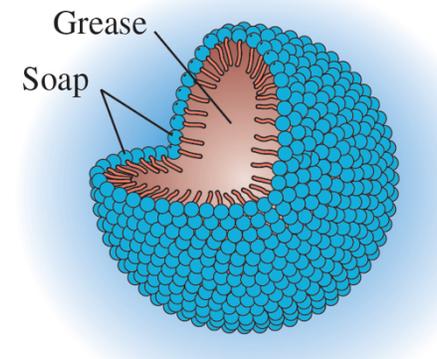
(a) A soap

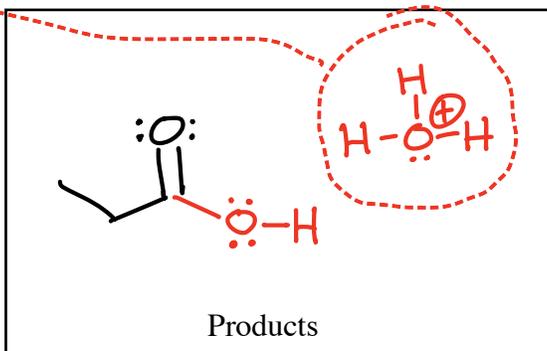
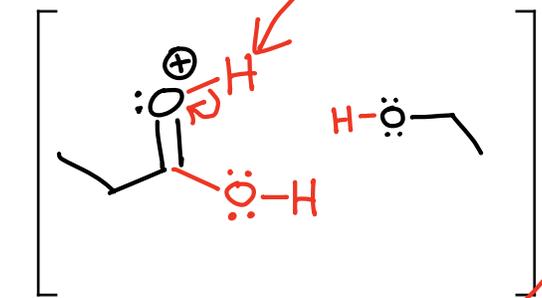
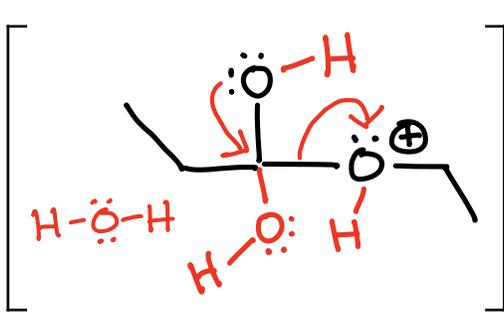
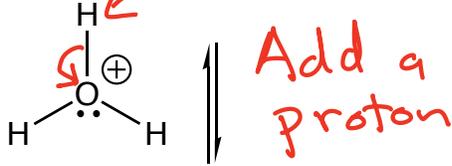
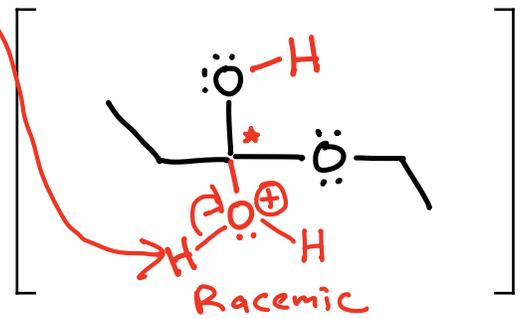
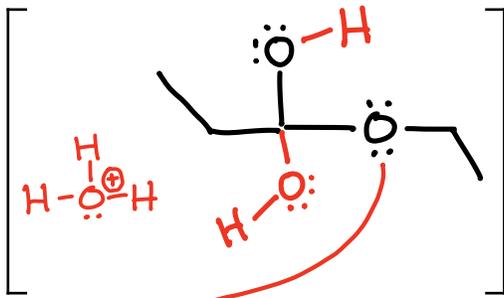
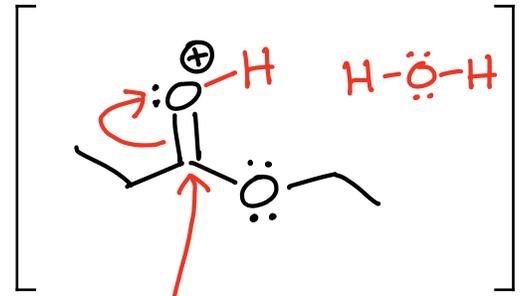
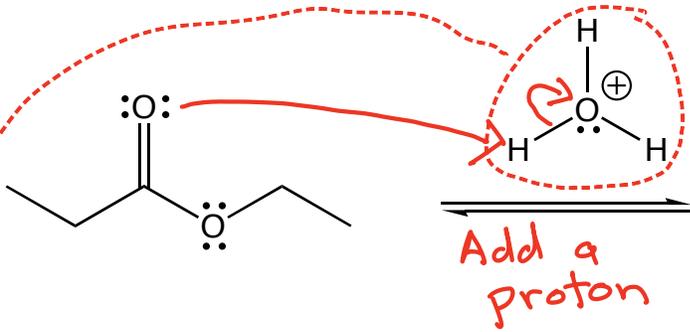
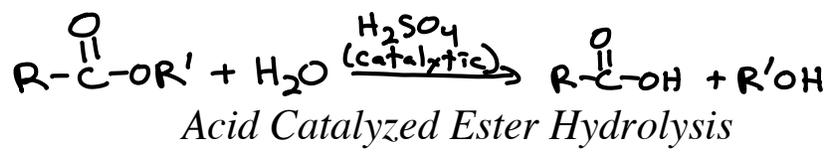


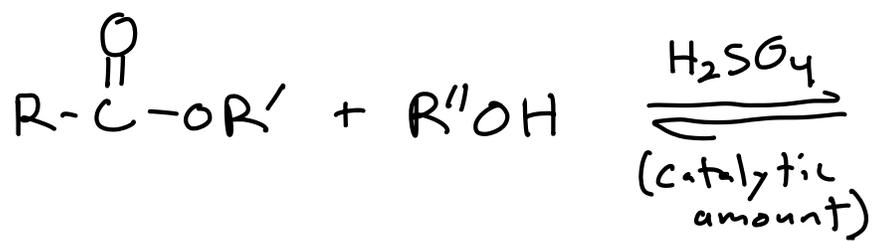
(b) Cross section of a soap micelle in water



Soap micelle with "dissolved" grease







Transesterification  $\rightarrow$

**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. 2/2/26

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  $\text{HO}^-$  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:

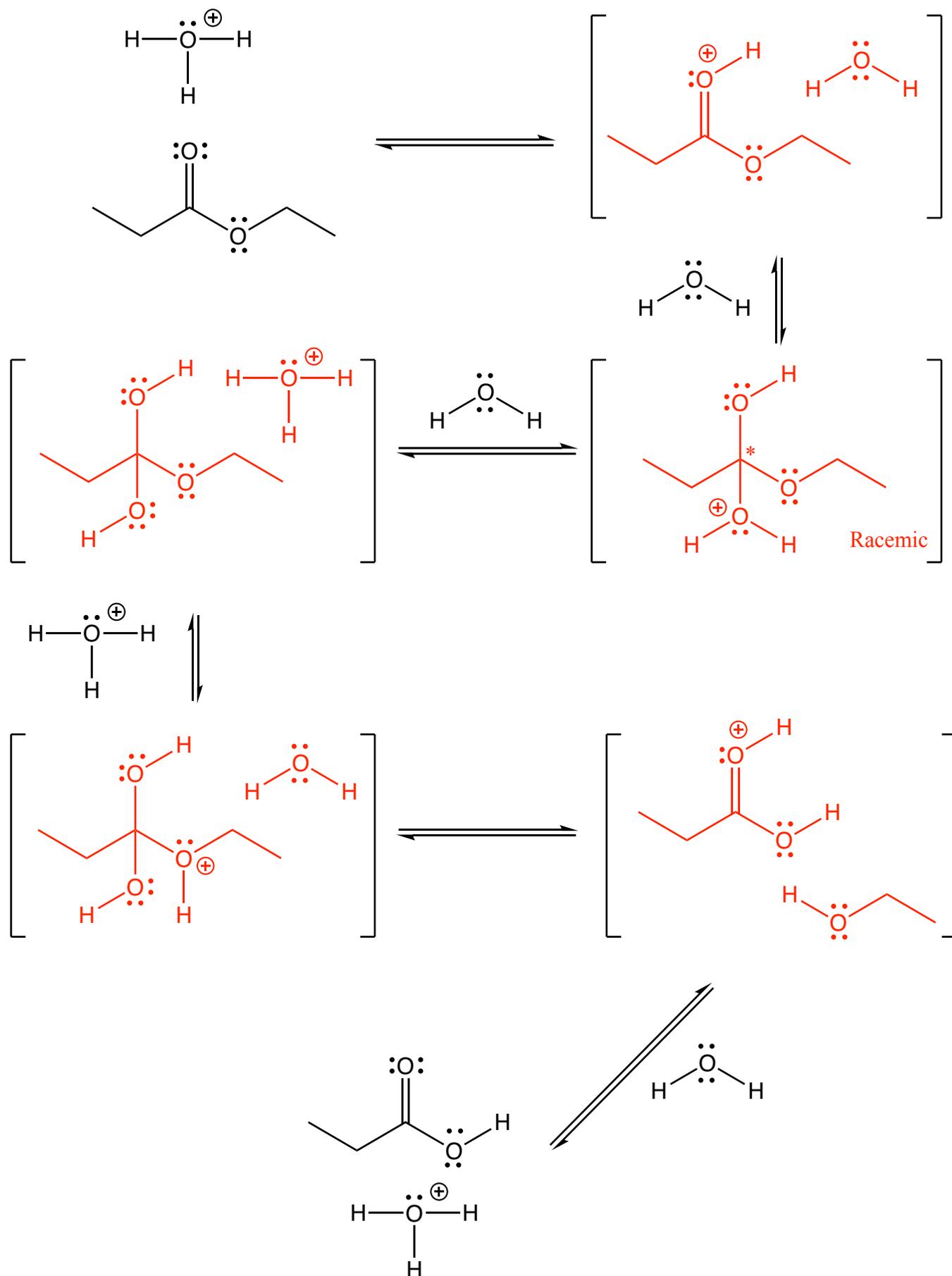
1. You will learn how to look at a molecule and accurately predict which atoms will react to make new bonds, and which bonds will break during reactions.
2. You will learn how to analyze a complex molecule's structure so that you can predict ways to make it via multiple reactions starting with less complex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

## Hydrolysis of Esters and Amides

Although either acid or base will work for both esters and amides, it is easiest (less harsh conditions required) to

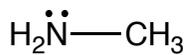
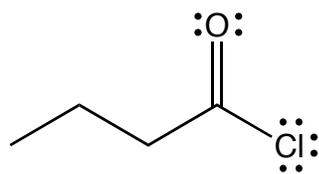
Warmup!

*Microscopic Reversibility: Acid Catalyzed Ester Hydrolysis-Fischer Esterification*

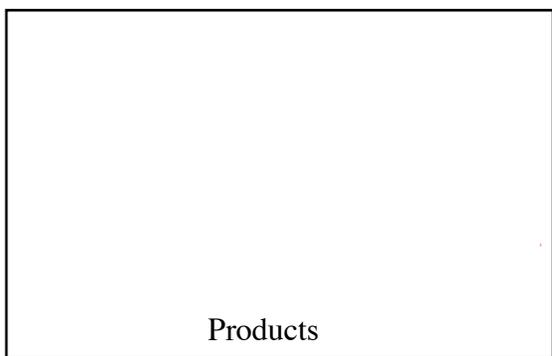
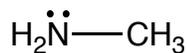


4 New Reactions

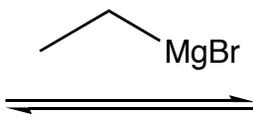
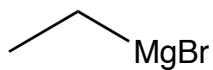
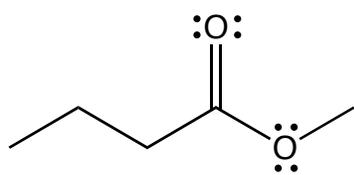
*Acid Chlorides Reacting with Amines*



Proton transfer

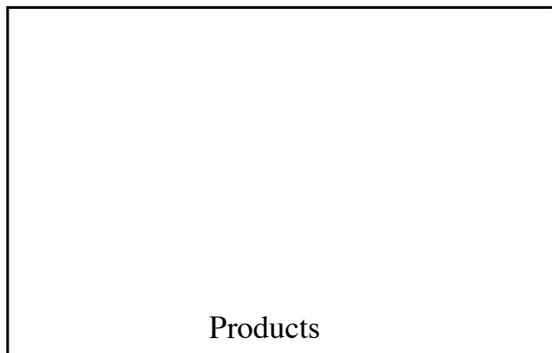
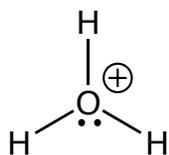


## Grignard Reacting with Esters

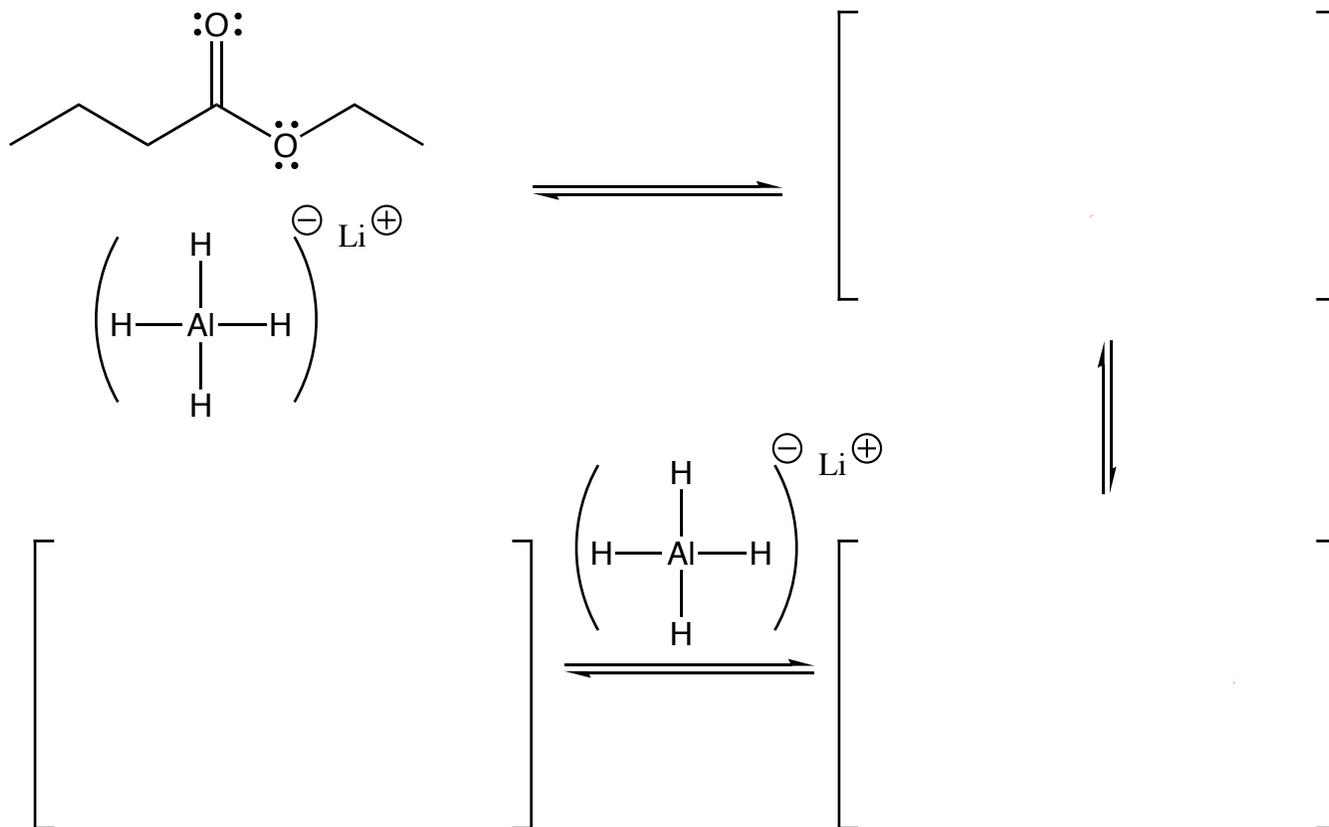


Chemist Opens Flask

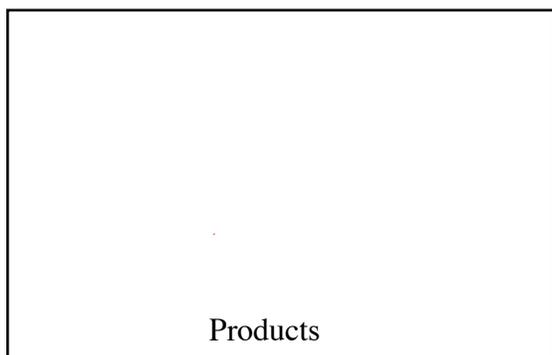
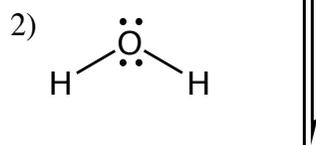
2)



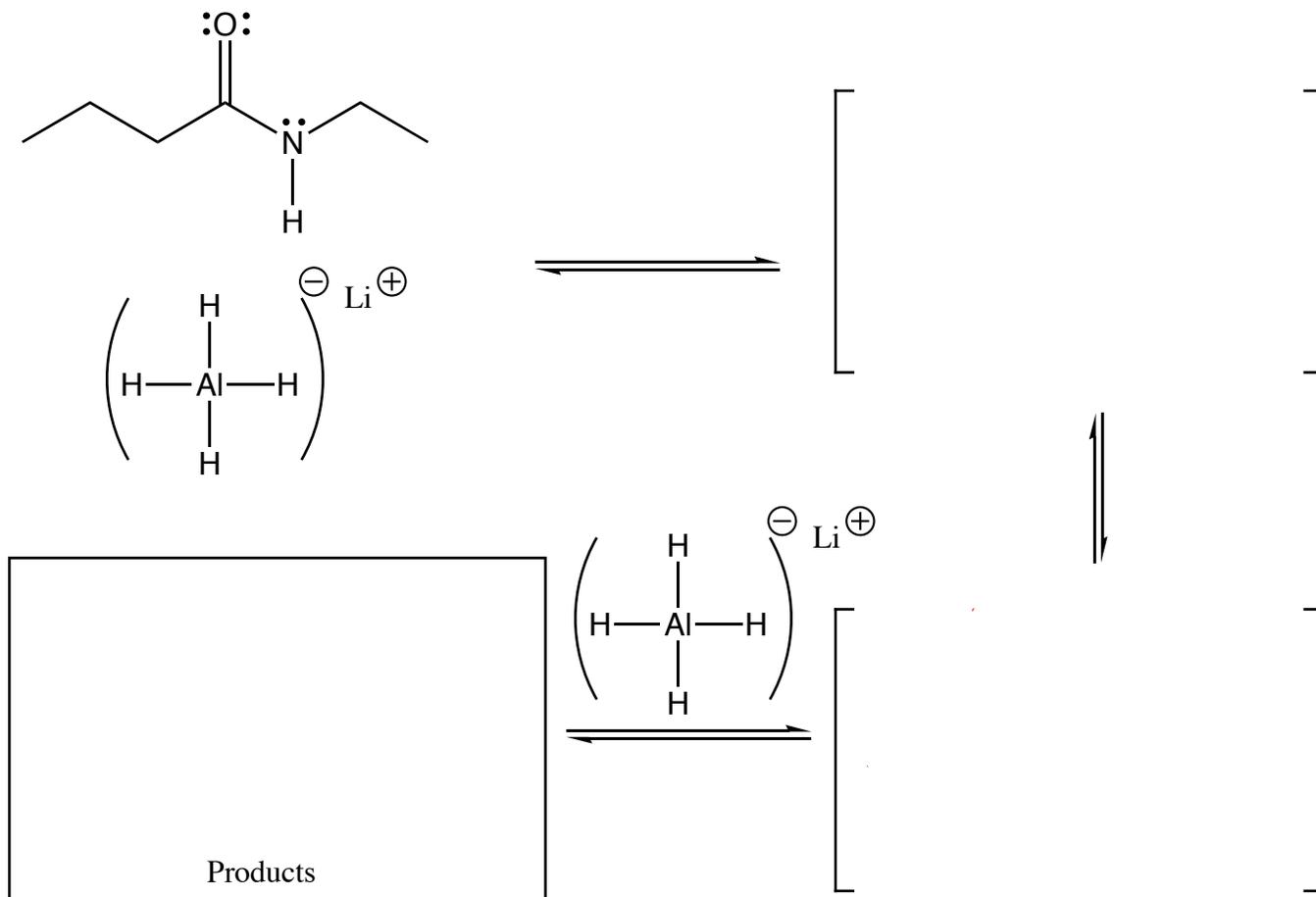
*Reduction of Esters with LiAlH<sub>4</sub>*



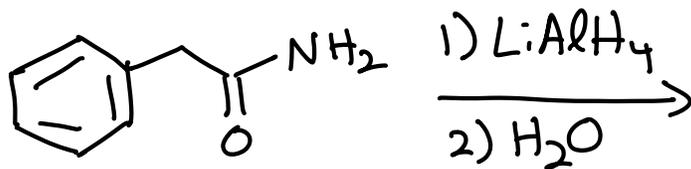
Chemist Opens Flask



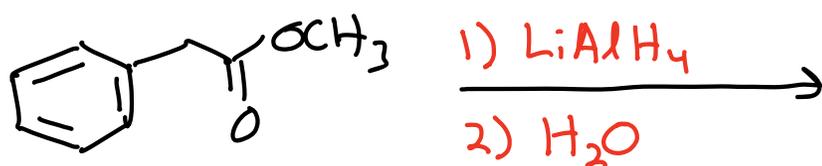
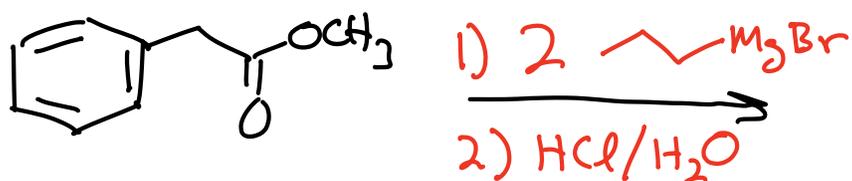
### Reduction of Amides with $\text{LiAlH}_4$



Note: In this reaction the chemist opens the flask and adds water in a second step that quenches any excess  $\text{LiAlH}_4$ . Therefore, you need a second step to add water when using this reaction in synthesis even though it is not shown in the mechanism above.

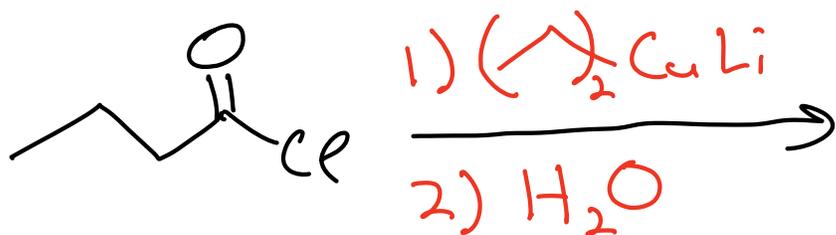


# Examples



Great new reaction  $\rightarrow$  Not responsible for the mechanism

$\rightarrow$  Reacting an acid chloride with a Gilman reagent to give a ketone



KRE  $\rightarrow$

Warning  $\rightarrow$  These  
two reactions are  
specific  $\rightarrow$

Grignard + Ester  $\rightarrow$  Alcohol

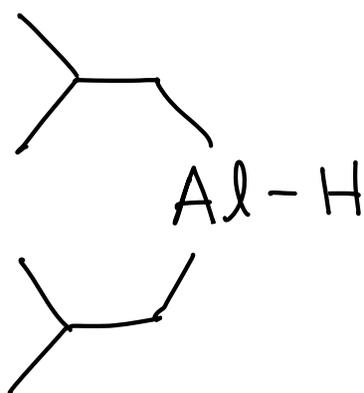
Gilman + Acid Chloride  $\rightarrow$  Ketone

Grignard + Acid Chloride

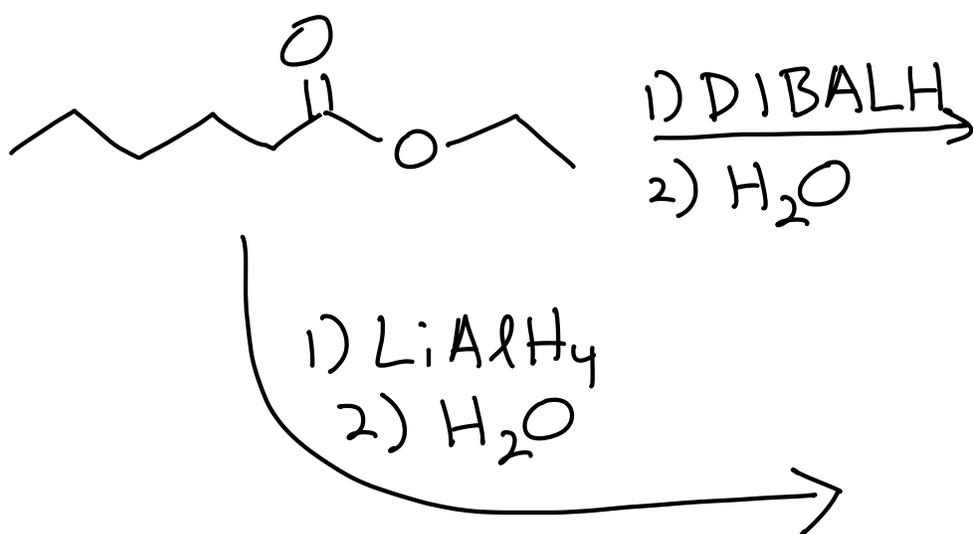
or

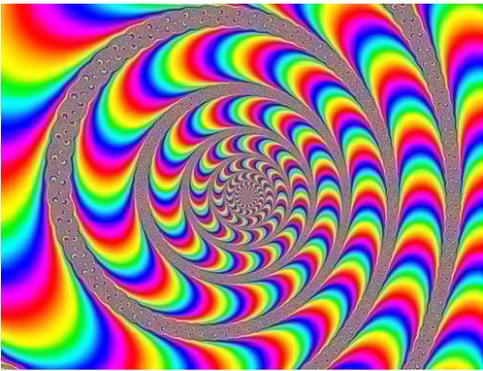
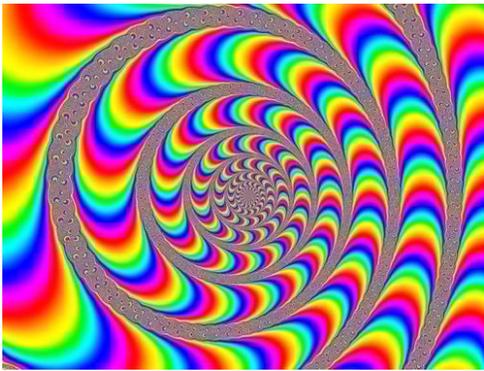
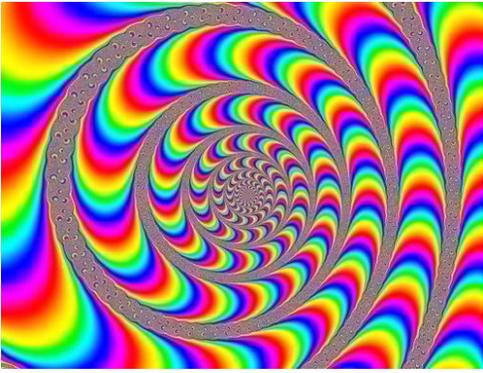
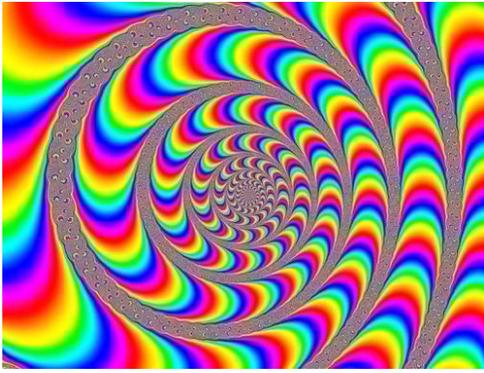
Gilman + Ester

Note: An aldehyde is produced as an intermediate when esters react with  $\text{LiAlH}_4$

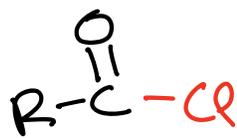


Diisobutylaluminum hydride  
DIBALH



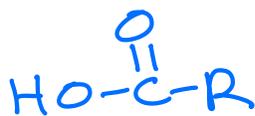
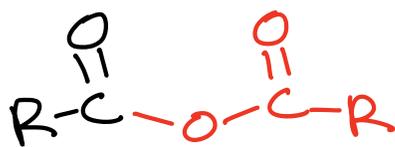


Acid Chloride



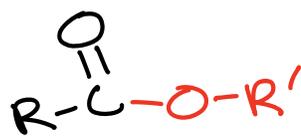
pK<sub>a</sub> -7

Anhydride



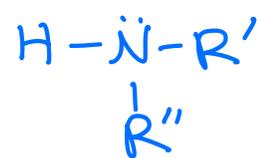
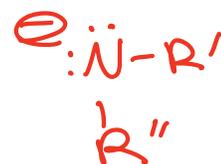
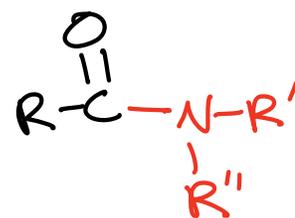
3-5

Ester



16

Amide



38

← Anion Stability

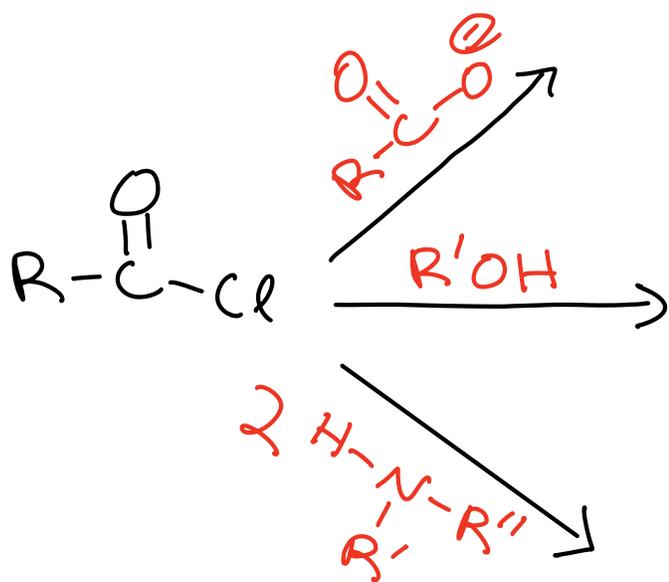
← Better Leaving Group Ability

← Reactivity of Carboxylic Acid Derivative

Think of carboxylic acid derivatives  
⇒ C=O with a leaving group attached

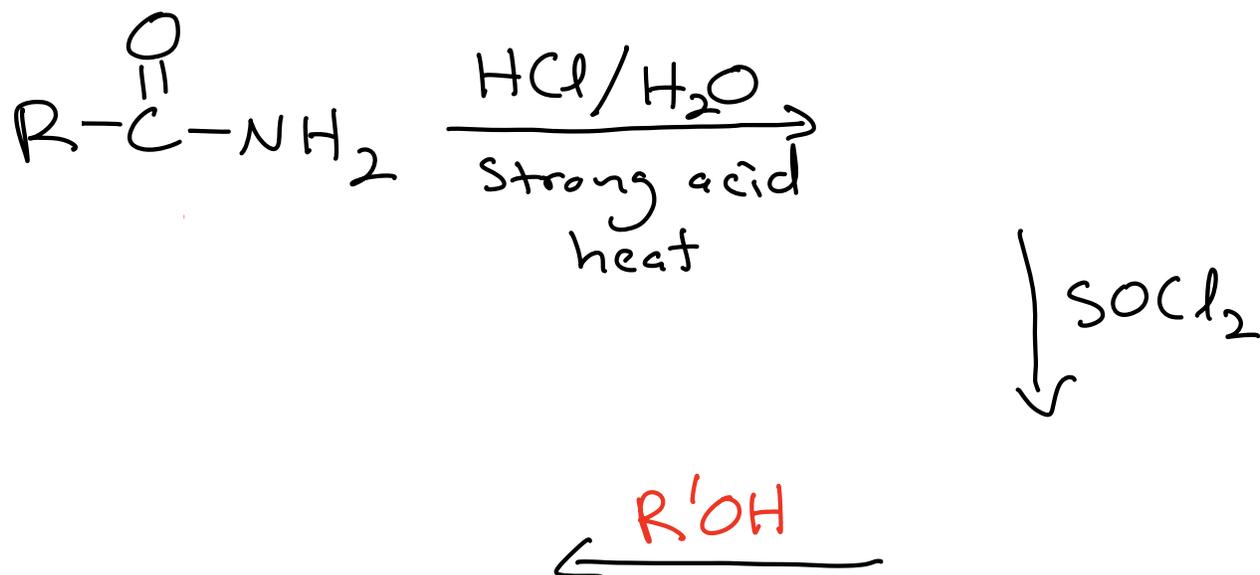
Here is the big rule →

Note: Acid chlorides and anhydrides spontaneously react with nucleophiles at room temperature, esters usually need some heat.

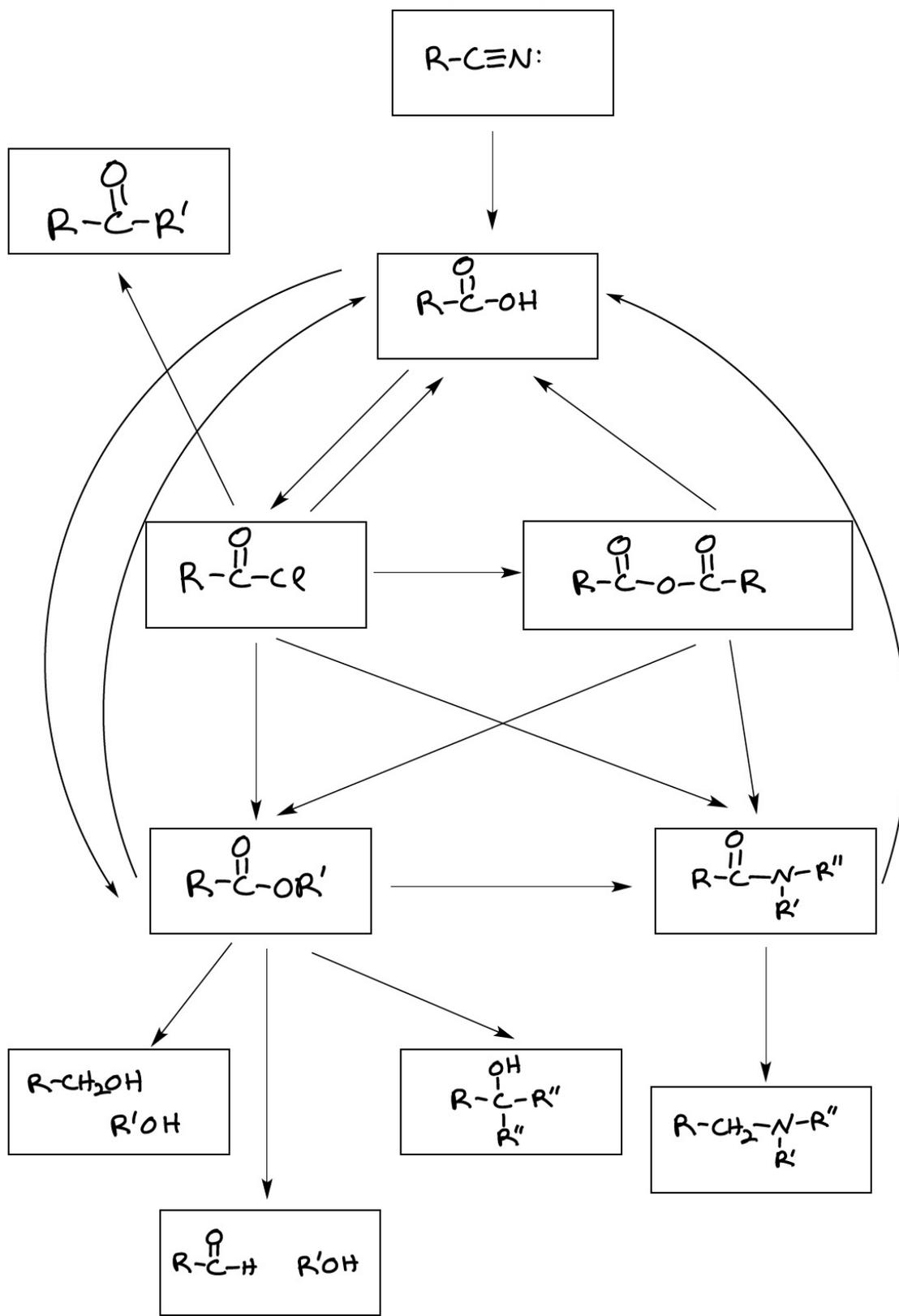


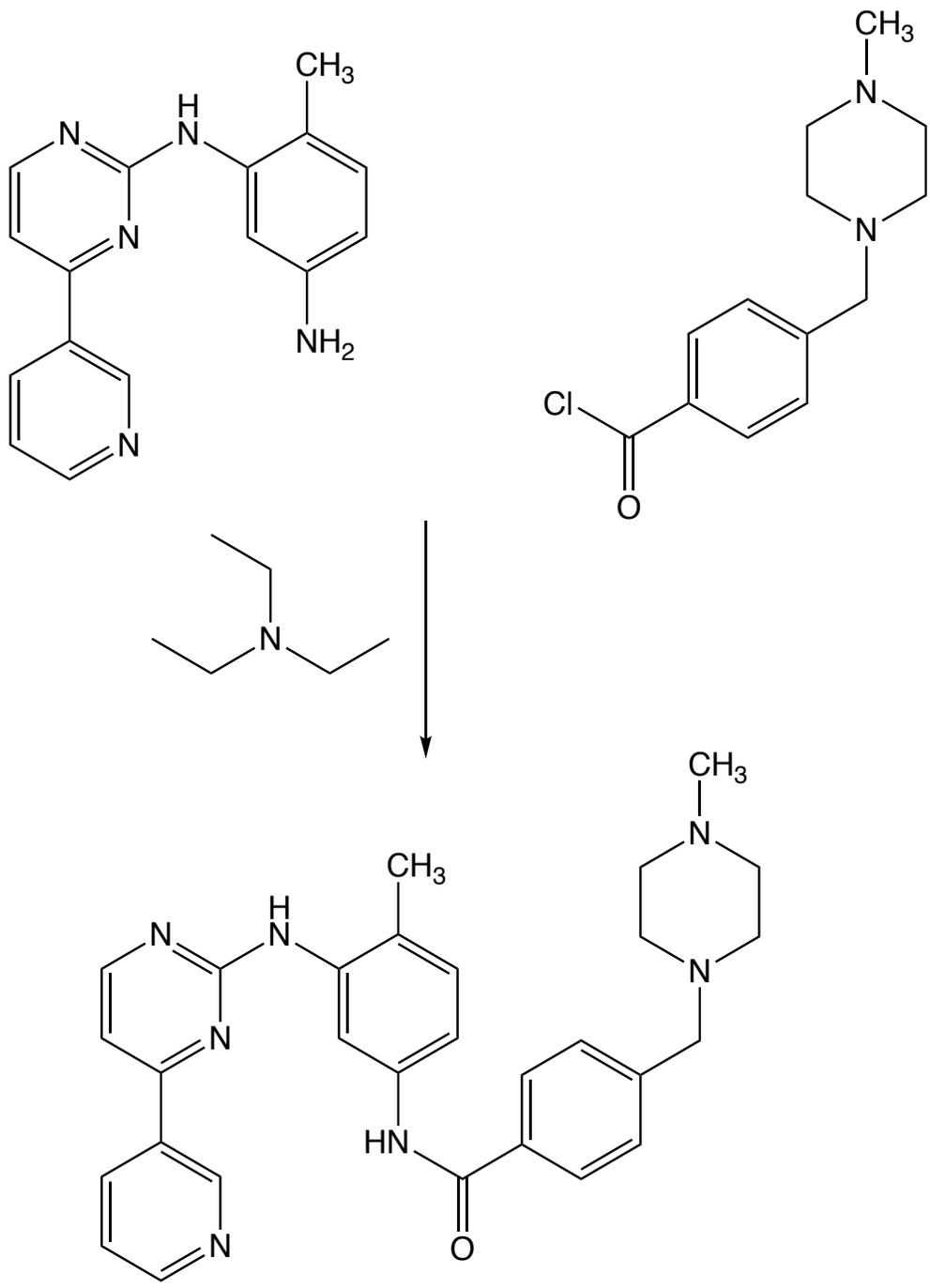


However: You can make a less stable carboxylic acid derivative from a more stable carboxylic acid derivative, but only if you:

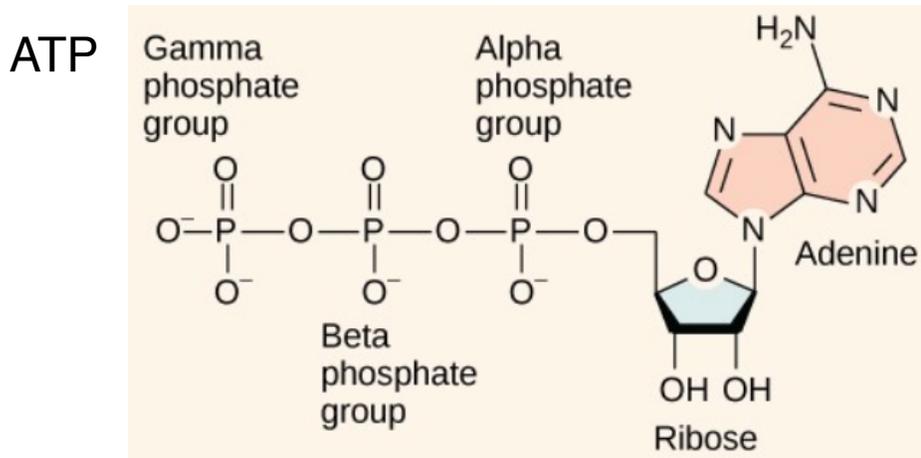
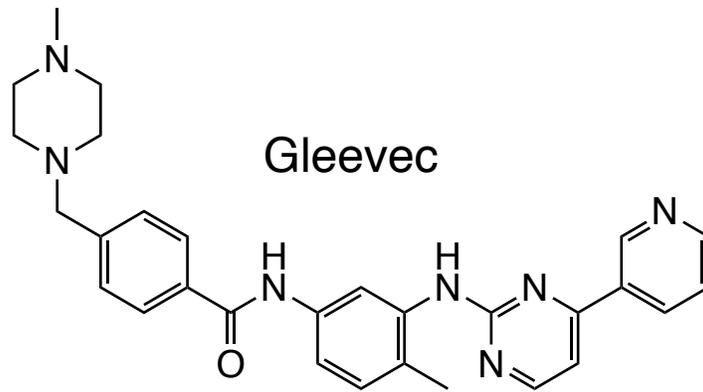


Interconversion of Carboxylic Acid Derivatives

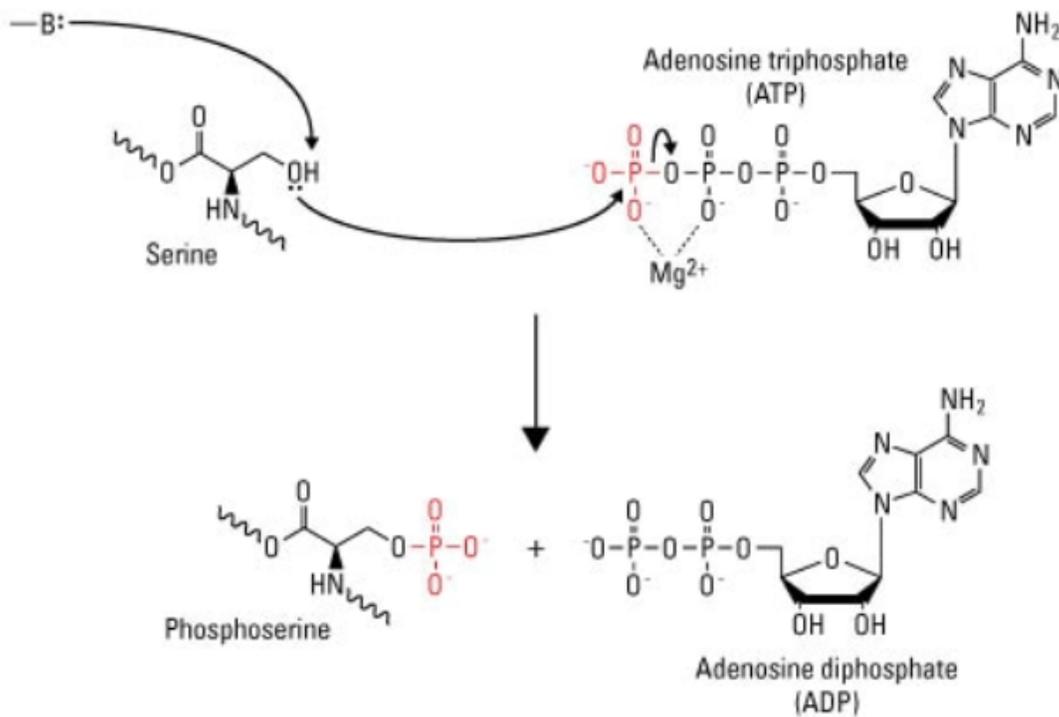




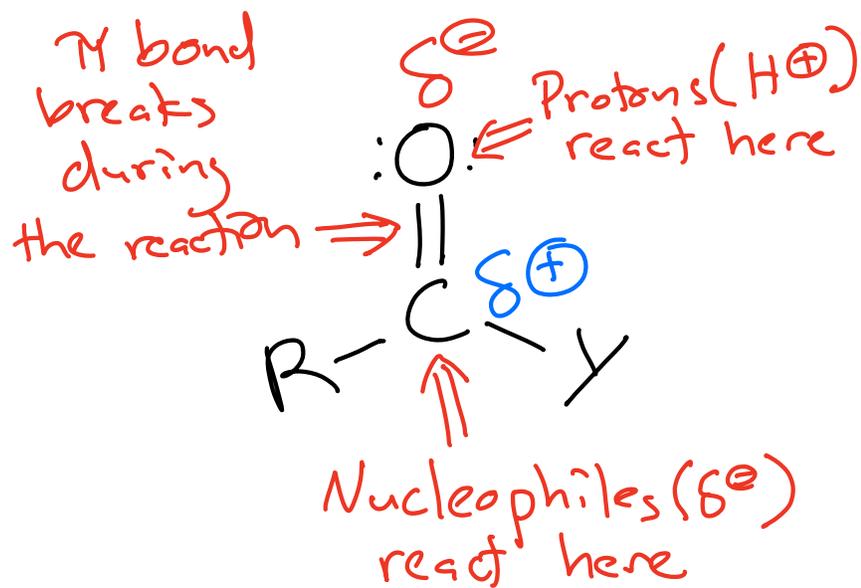
**Gleevec** – Novartis (\$4.65 Billion in sales in 2015). A kinase inhibitor, that is a first of its kind pill capable of treating certain blood cancers with only limited side effects. It was designed to combat leukemias with the relatively common “Philadelphia chromosome” (BCR-ABL kinase gene fusion)



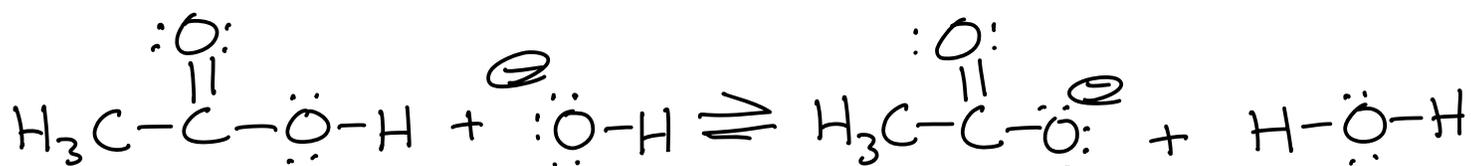
How Kinases Work:



# Carbonyl

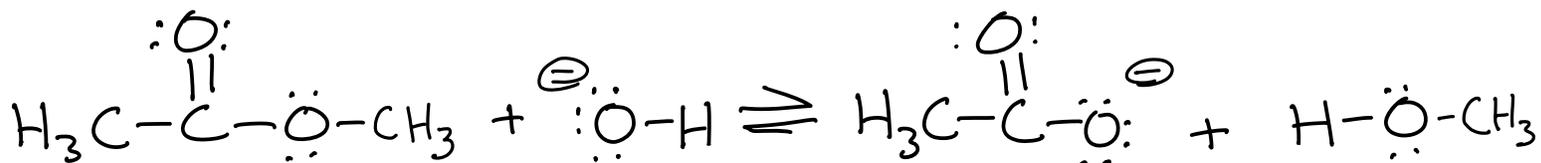


Equilibrium favors formation of the weaker base and weaker acid



Bottom line  $\rightarrow$  position of equilibrium favors the side with the more stable anion

The same logic holds for all reactions with anions on both sides of the equation:



# Weaker bases are favored at equilibrium

Compound	Chemical Structure	pK <sub>a</sub>
	H-Cl	-7
Carboxylic acids*	$\text{R}-\text{C}(=\text{O})-\text{OH}$	3-5
β-Dicarbonyls*	$\text{RC}(=\text{O})-\text{CH}_2-\text{CR}'(=\text{O})$	10
β-Ketoesters*	$\text{RC}(=\text{O})-\text{CH}_2-\text{COR}'$	11
β-Diesters*	$\text{ROC}(=\text{O})-\text{CH}_2-\text{COR}'$	13
Water	HOH	15.7
Alcohols	$\text{RCH}_2\text{OH}$	15-19
Acid chlorides*	$\text{RCH}_2-\text{COCl}$	16
Aldehydes*	$\text{RCH}_2-\text{CHO}$	18-20
Ketones*	$\text{RCH}_2-\text{CR}'(=\text{O})$	18-20
Esters*	$\text{RCH}_2-\text{COR}'$	23-25
Terminal alkynes	$\text{RC}\equiv\text{C}-\text{H}$	25
LDA	$\text{H}-\text{N}(\text{i-C}_3\text{H}_7)_2$	40
Terminal alkenes	$\text{R}_2\text{C}=\text{C}-\text{H}$	44
Alkanes	$\text{CH}_3\text{CH}_2-\text{H}$	51

Strongest Acid  
(Weakest conjugate base)



Weakest Acid  
(Strongest conjugate base)

A) Reactions are favored (i.e. have a motive) if they lead to formation of a weaker acid and/or weaker base.

B) Checking pK<sub>a</sub> values can predict if a reaction has a motive even if there are other steps besides a proton transfer.

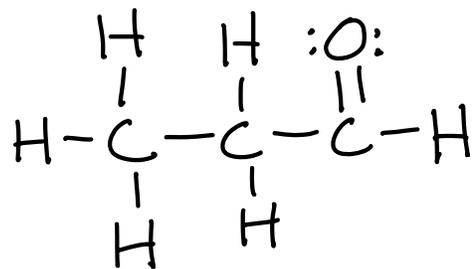
C) Recall that the conjugate base of a stronger acid (lower pK<sub>a</sub>) is a weaker base.

D) Check the pK's of the conjugate acid of the bases on either side of the equation. Lower pK<sub>a</sub> value corresponds to stronger acid of the conjugate acid, and thus weaker conjugate base. The base with a stronger conjugate acid (lower pK<sub>a</sub> value) will be the weaker base and will be favored at equilibrium.

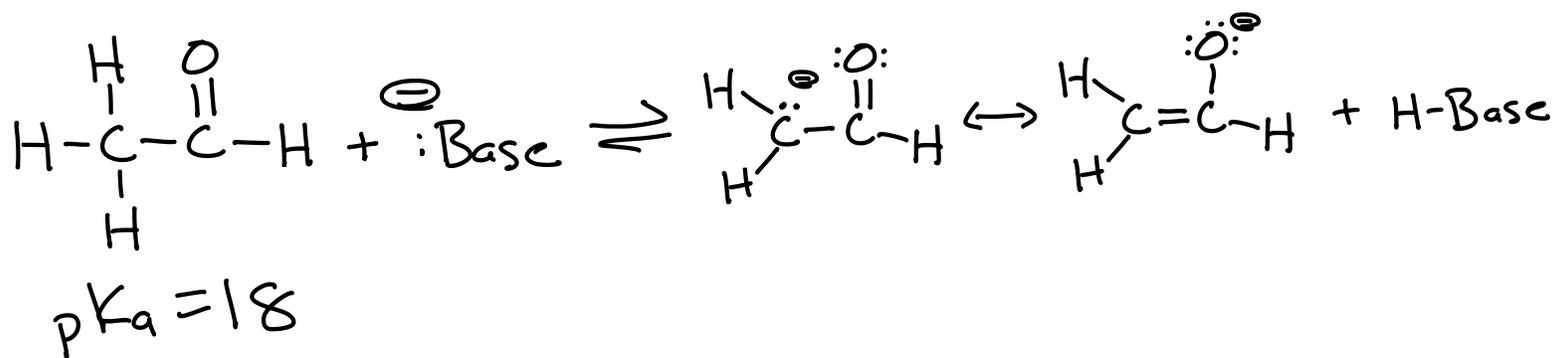
E) Another way to look at it is that the base that is favored at equilibrium is the one that has the more stabilized anion, i.e. the one with the charge spread around more (electronegative) atoms.

F) Above is a pK<sub>a</sub> table that we will refer to often.

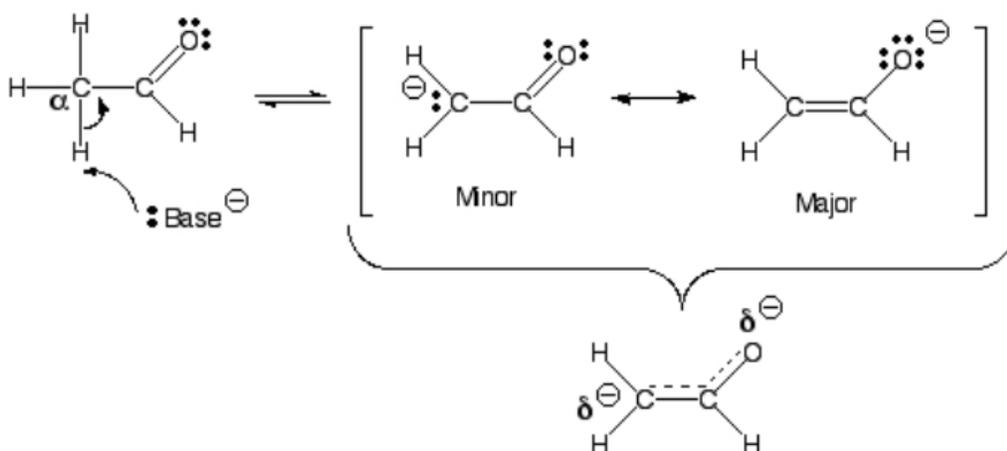
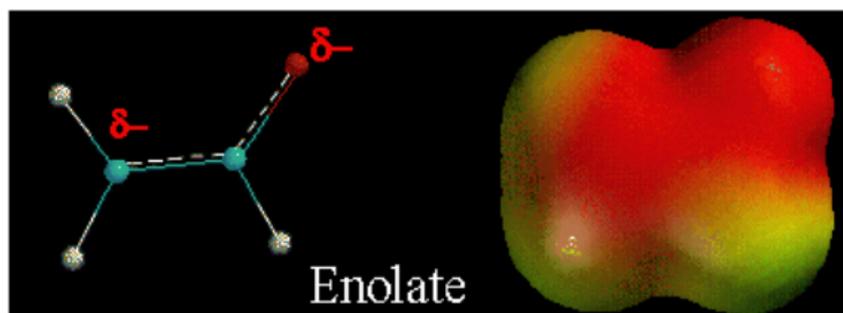
\*These have resonance stabilized anions



The H atoms on the  $\alpha$  carbon are called  $\alpha$  hydrogens

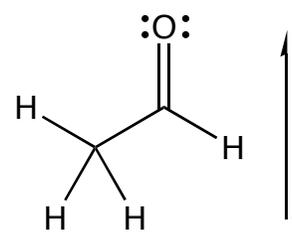
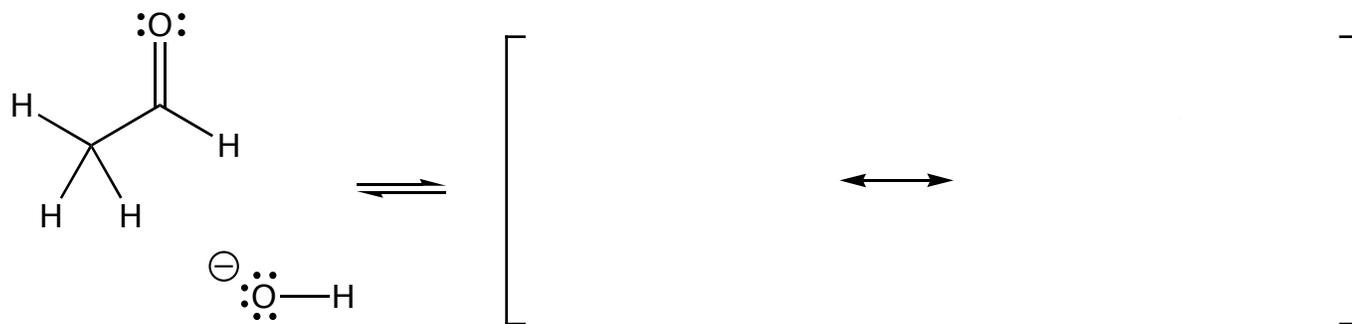


# Enolates as nucleophiles

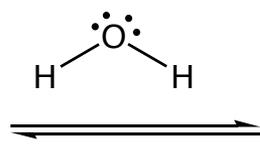


- A) Enolates are resonance stabilized, with a partial negative charge on carbon and oxygen.
- B) Enolates are nucleophiles, so they could react at either the carbon atom or oxygen atom. The partial negative charges give them the **opportunity** to react at either the carbon or oxygen.
- C) Reaction at the carbon atom gives the final product a C=O bond, while reaction at the oxygen atom gives the final product a C=C bond. However, C=O bonds are stronger than C=C bonds, **so the motive is to react at the carbon atom with most electrophiles.**

*Aldol Reaction*



Products



Draw both enantiomers

# Another Movie Rips Off Organic Chemistry

