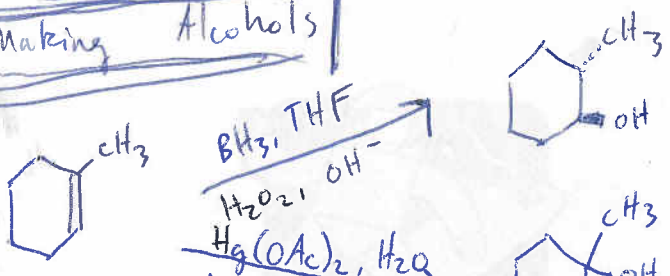
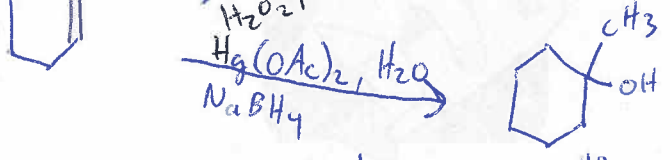


# Ch. 17 Alcohols (p. 1)

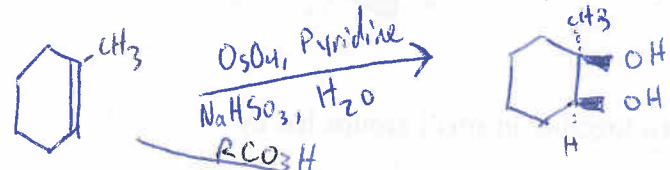
## Making Alcohols



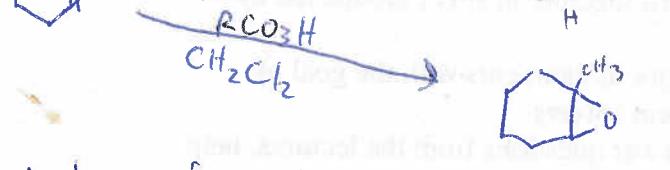
Trans-non-Markovnikov



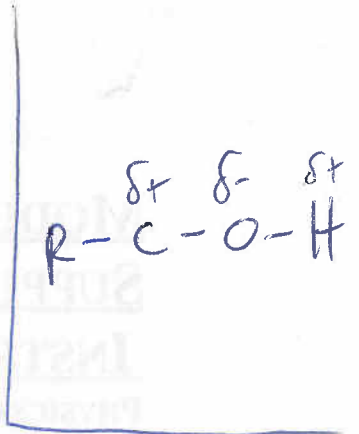
markovnikov



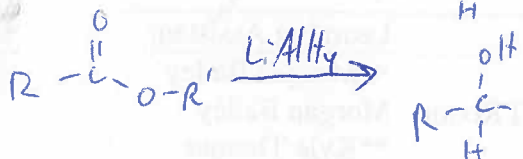
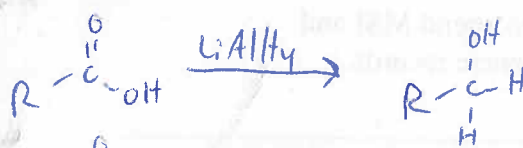
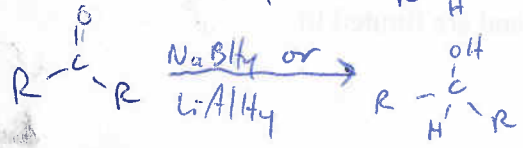
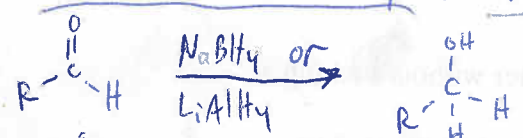
cis-diol



trans-diol

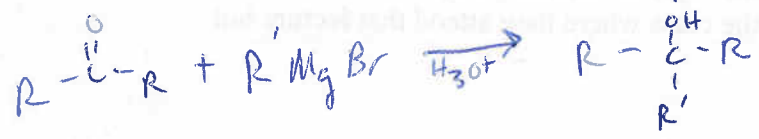


reduction of carbonyls:  $\text{LiAlH}_4$  must be used for Carboxylic Acids & Esters (always done in acidic conditions)

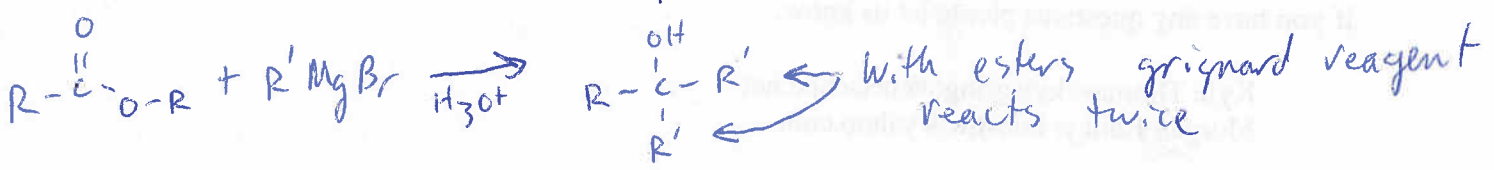


$\text{LiAlH}_4$  &  $\text{NaBH}_4$  are both equivalent to a hydride  $\text{H}^-$  ion & react by  $\text{S}_{\text{N}}2$ -like mechanism.  $\text{H}_3\text{O}^+$  Added at end to get extra protons.

Grignard & Carbonyls: Grignards are protonated by acids so  $-\text{OH}$   $-\text{NH}$   $-\text{SH}$  &  $\overset{\text{O}}{\parallel}{\text{C}}-\text{OH}$  can't be used in grignard reactions



$\text{S}_{\text{N}}2$




With esters grignard reagent reacts twice

$\text{RMgBr}$  is equivalent to  $\text{R}^- + \text{Mg}^+\text{Br}$  so  $\text{R}^- = \text{Nu}^-$

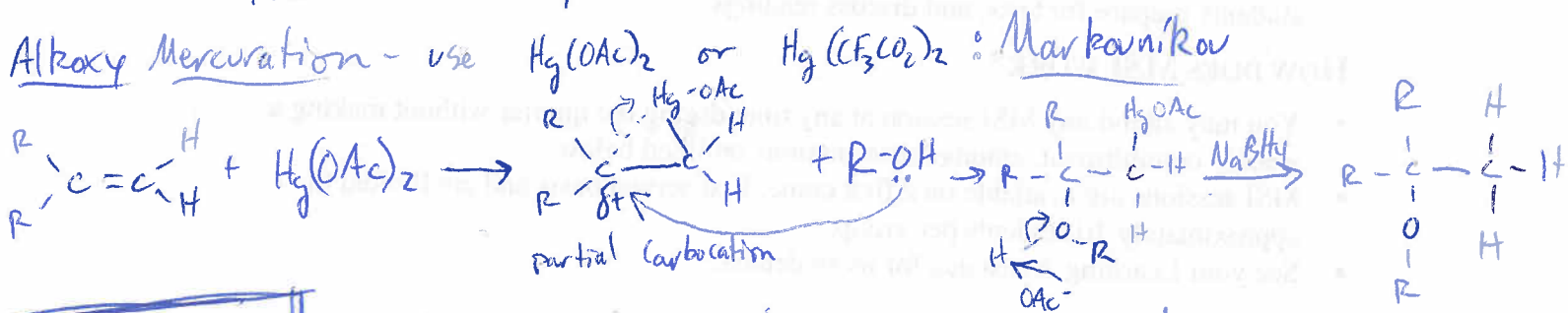
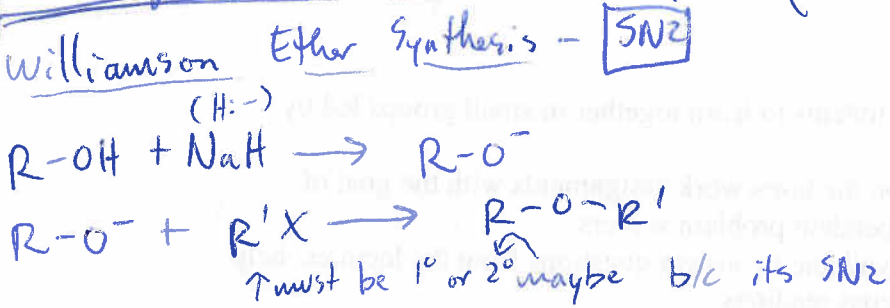


# Ch. 18 Ethers & Epoxides

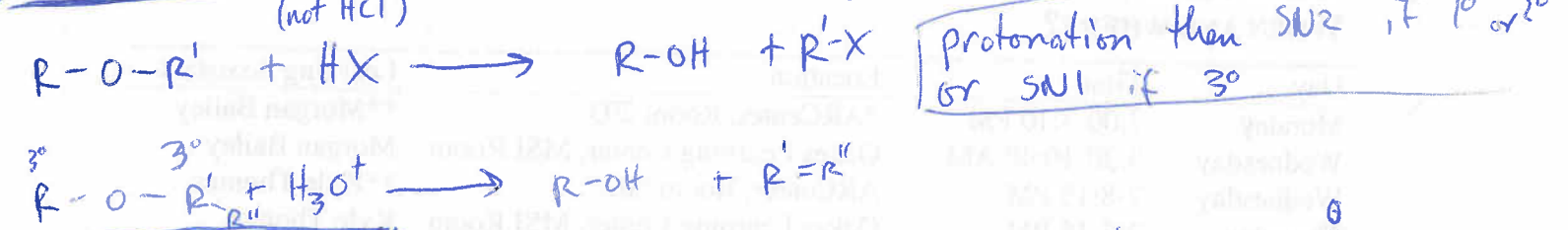
Epoxides are 3-membered-ring ethers  & are more reactive because of angle strain.  
Ethers are unreactive for the most part.

$\delta^+$   $\delta^-$   $\delta^+$   
 $R-O-R$   
 smaller dipole than any other R-O bonds like -OH or  $\overset{\delta^-}{O}H^{\delta^+}$  & that's why they are unreactive

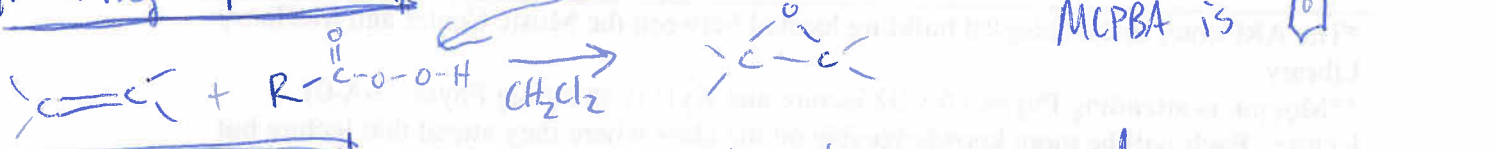
## Making Ethers - 2 ways (or from epoxides: see below)



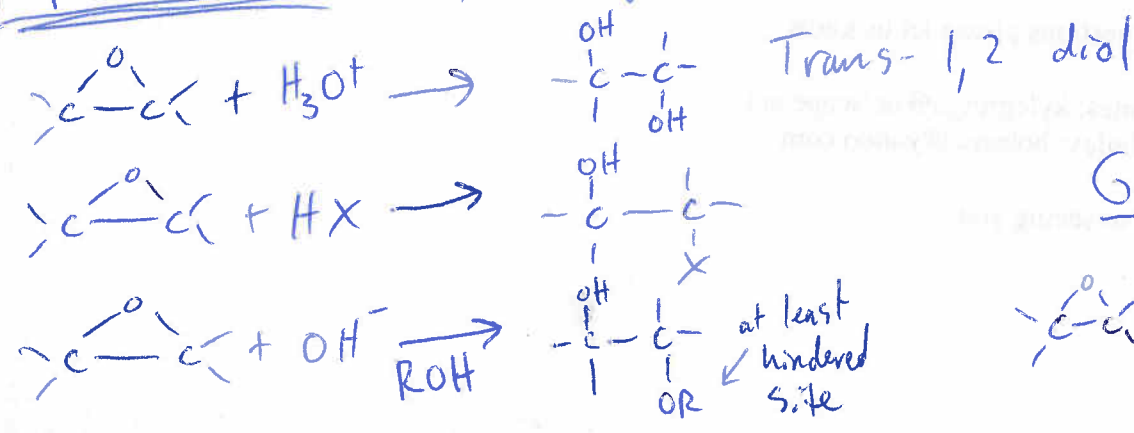
## Ether Rxns - only 1: ether cleavage by acids (not HCl)



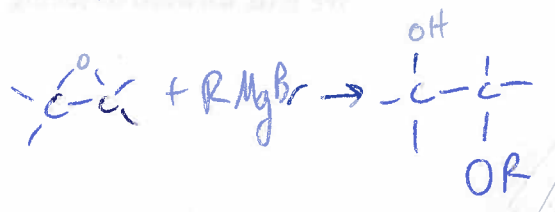
## Making Epoxides



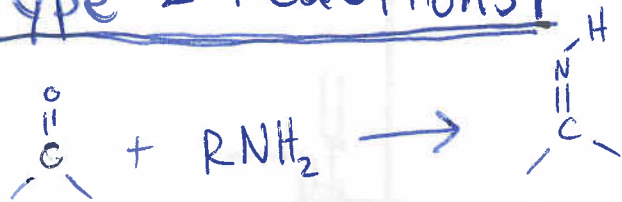
## Epoxide Rxns - only cleavage: by base or acid



## Grignard Cleavage



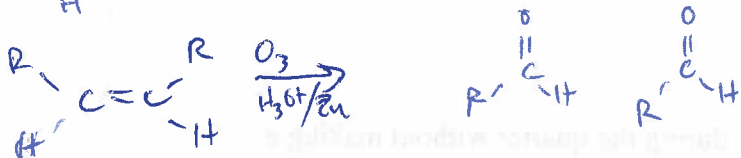
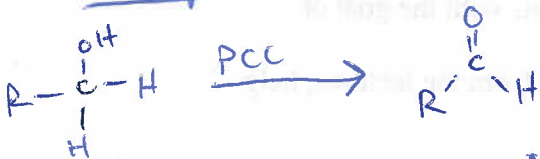
# Type 2 Reactions



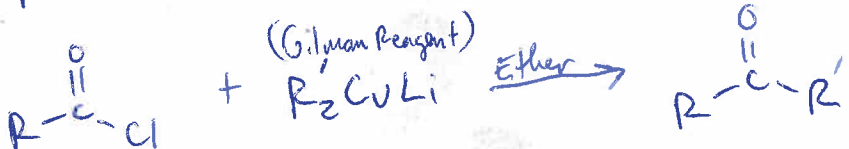
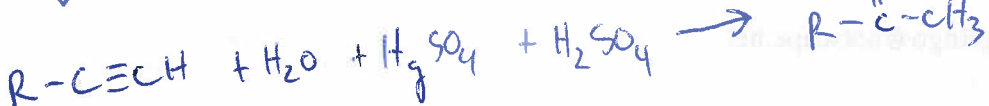
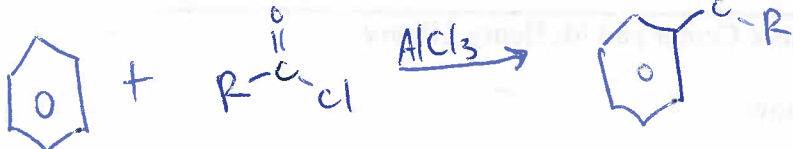
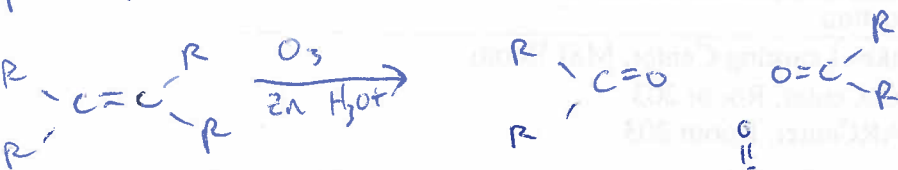
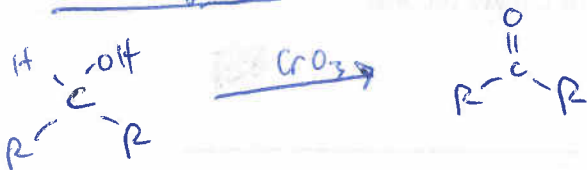
Mechanism is very similar to  $\text{RNH}_2$ , but because N is bonded to 2 R groups it can't form a double bond so  $\text{C}=\text{C}$  bond forms



## Making Aldehydes



## Making Ketones

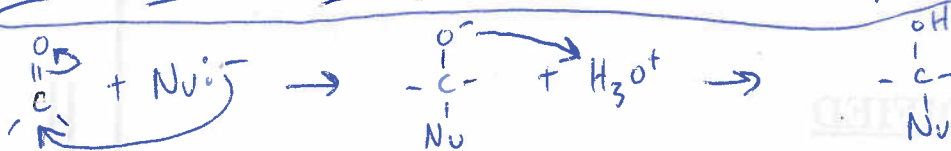


# CH. 19: Aldehydes & Ketones p.1

There are two basic reactions these both undergo.

## Reaction 1:

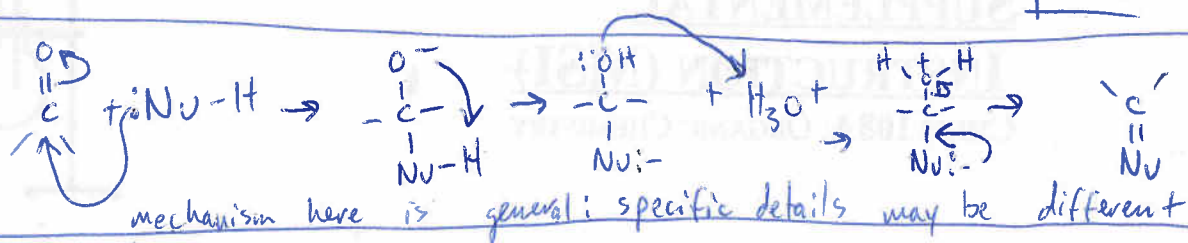
Nucleophilic Addition to yield alcohol



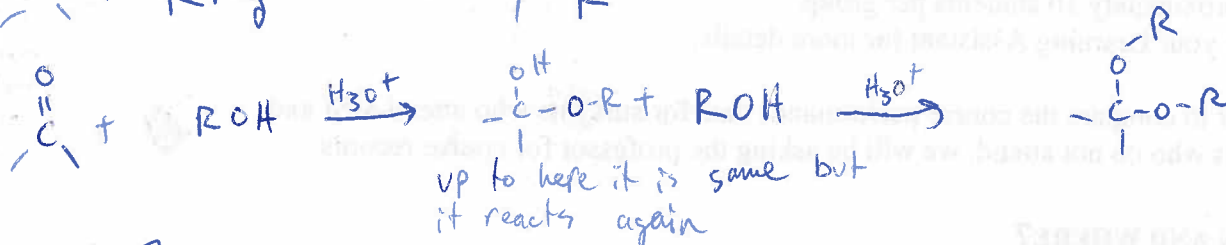
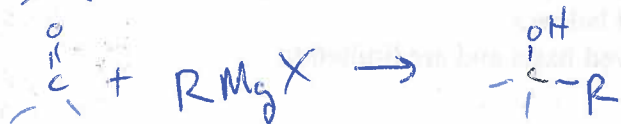
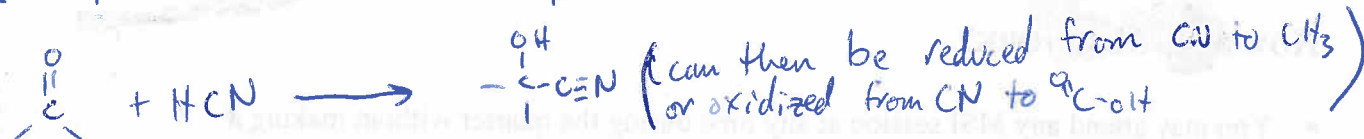
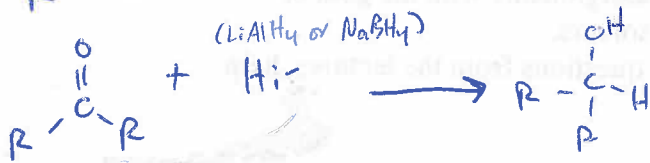
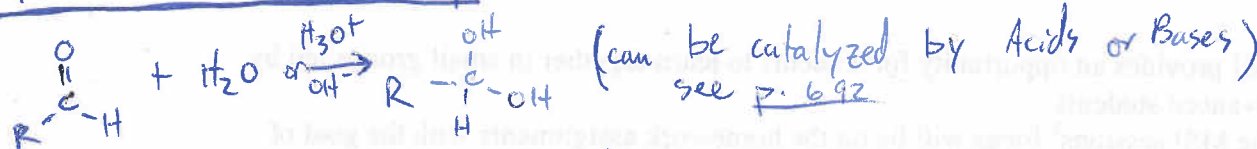
p.675

## Reaction 2:

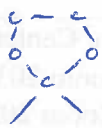
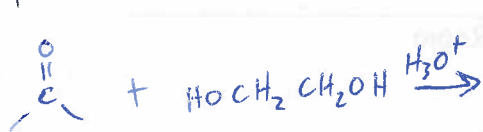
Nucleophilic addition to yield double-bonded C to Nucleophile



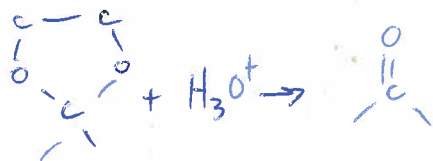
## Type 1 Reactions



This reaction can be used to protect Ketones



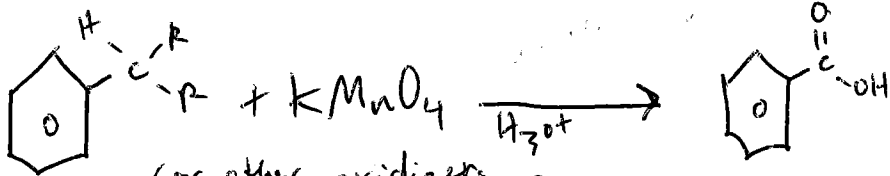
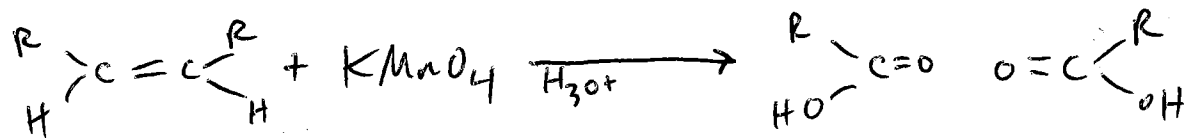
which protects ketone by making unreactive ethers & can then be converted back by adding  $\text{H}_3\text{O}^+$



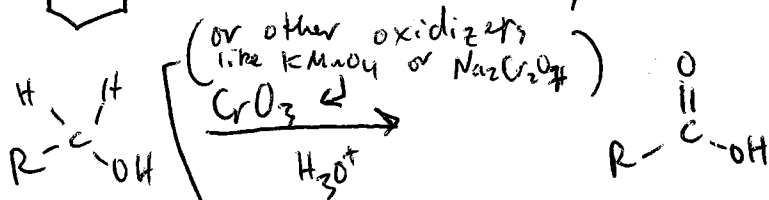
# Ch. 20 Carboxylic Acids & Nitriles (p.1)

## Making Carboxylic Acids

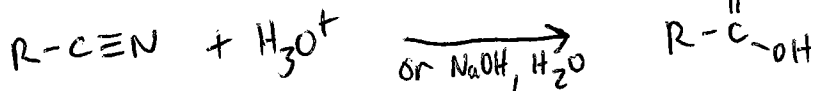
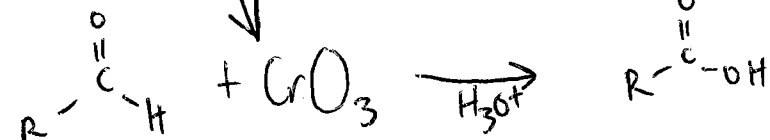
Carboxylic acids are most oxidized functional group so you can get there by using strong oxidizers on alcohols or other carbonyls



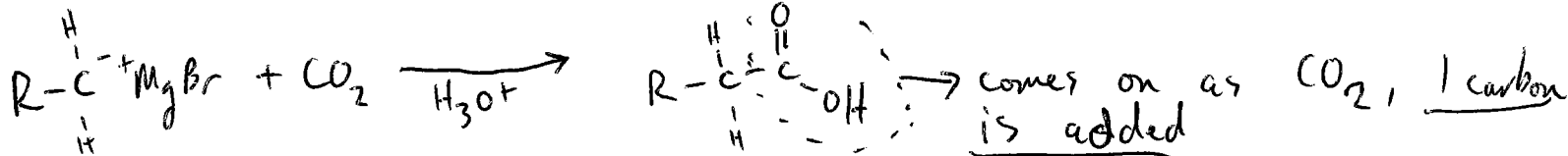
Alkanes oxidize to  $\overset{O}{\parallel}C-OH$  when attached to benzene only



Alcohol must be 1° because oxidizers can't break C-C bonds

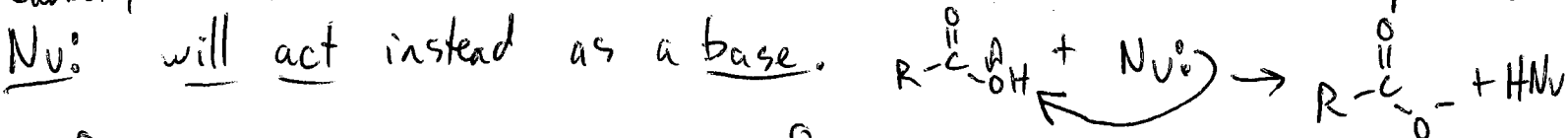


Both acids & bases cleave cyano-group but with different mechanism

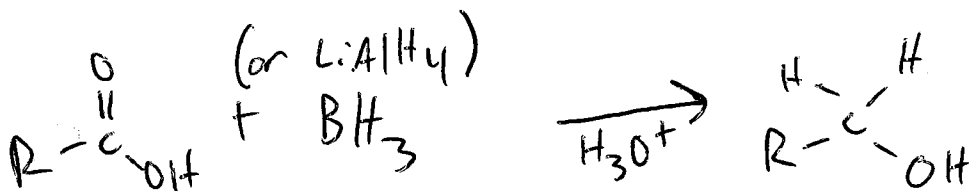


## Carboxylic Reactions

Carboxylic Acids tend to act as acids rather than electrophiles.



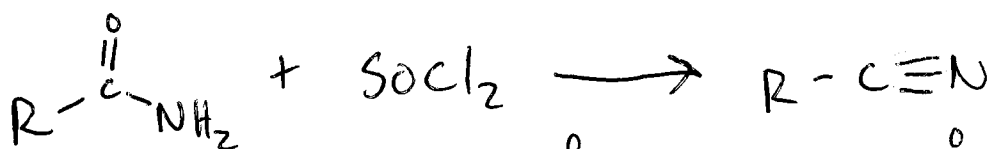
Acidic because product is so stable from resonance



# Ch. 20 Carboxylic Acids & Nitriles (p. 2)

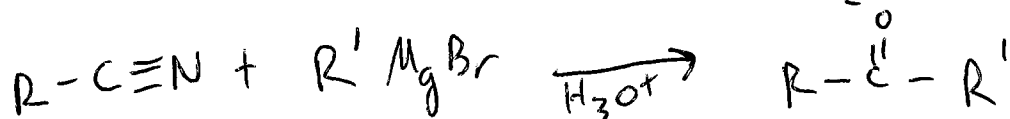
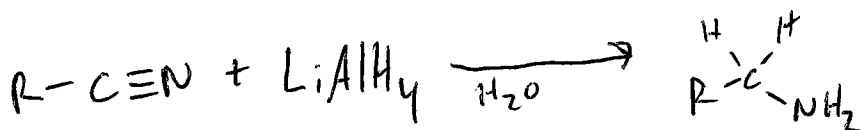
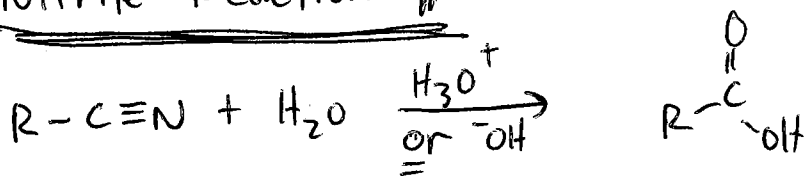
## Making Nitriles

There are 2 ways to make a nitrile. Adding a cyano group is  $\boxed{SN2}$  so other carbon must be  $1^\circ$  or possibly  $2^\circ$ . So a highly substituted carbon should be given cyano group through dehydration of Amines ( $SOCl_2$ ).



To make  $R-\overset{\overset{O}{\parallel}}{C}-NH_2$  1. take  $R-\overset{\overset{O}{\parallel}}{C}-OH$  & Add  $SOCl_2 + CHCl_3 \rightarrow R-\overset{\overset{O}{\parallel}}{C}-Cl$   
2. then take  $R-\overset{\overset{O}{\parallel}}{C}-Cl$  & Add  $NH_3 \rightarrow R-\overset{\overset{O}{\parallel}}{C}-NH_2$

## Nitrile Reactions

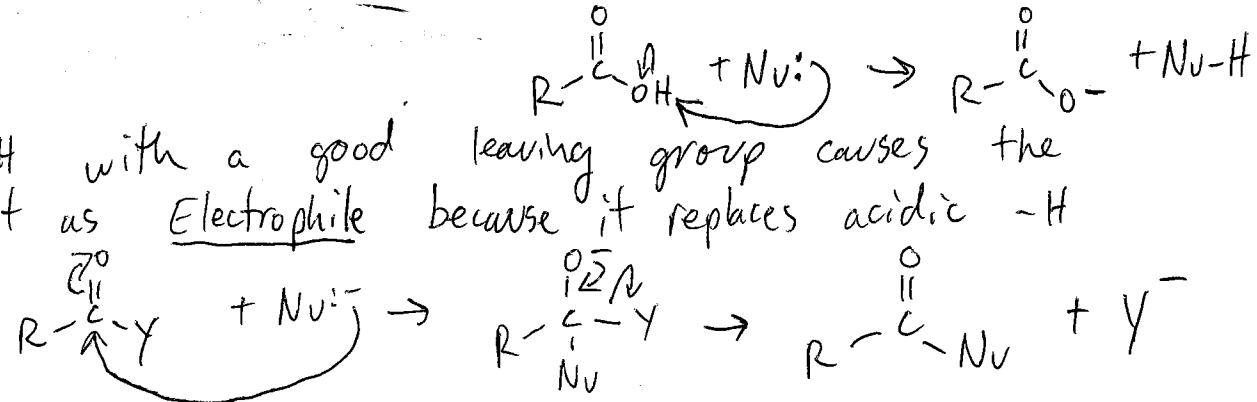


# CH. 21 Carboxylic Acid Derivatives (V.I)

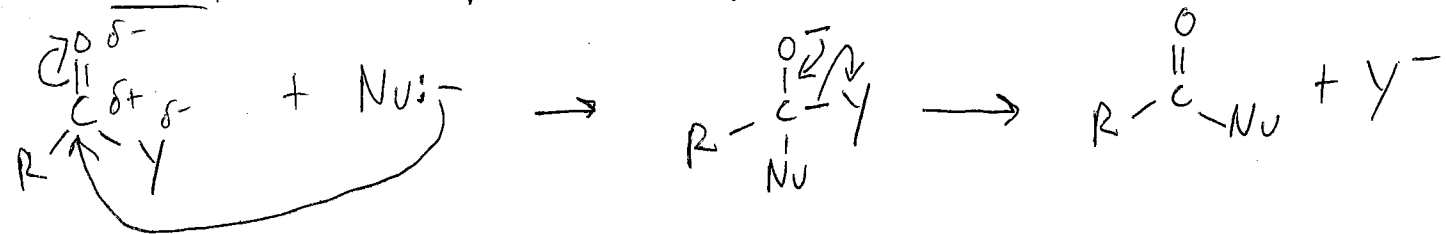
Carboxylic Acid Derivatives are Carboxylic Acids ( $R-C(=O)OH$ ) where  $-OH$  group is replaced by a good leaving group.

Carboxylic Acids act as acids instead of as Electrophiles ( $E^+$ )

Replacing  $-OH$  with a good leaving group causes the carbonyl to act as Electrophile because it replaces acidic  $-H$



The general mechanism for all Acid Derivative reactions is due to carbonyl with good leaving group. Nucleophile replaces leaving group

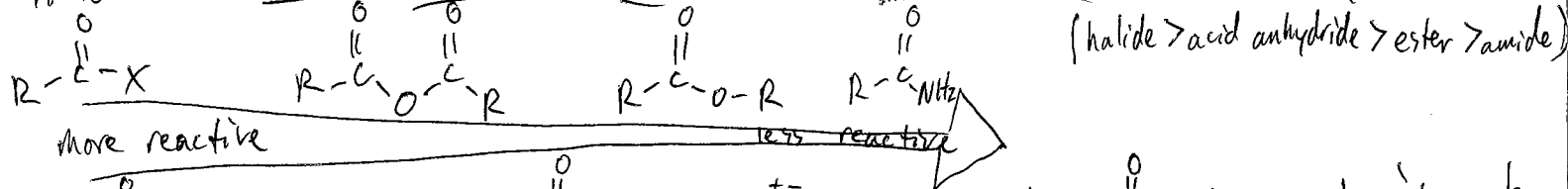


"Y" is good Leaving group because it is stable on its own supporting a negative charge (i.e.  $Cl^-$ ,  $-O-C(=O)R$ ).

Y is a halide ( $-X$ ), Acid Anhydride ( $-O-C(=O)R$ ), Ester ( $-O-R$ ), or an Amide ( $-NH_2$ ). It could also be  $-S-R$  or  $-O-P(=O)(O^-)-O^-$  (like ester).

All behave basically the same.

Reactivity Order A more reactive acid derivative can be converted into a less reactive one but not the other way around.



So  $R-C(=O)Br + 2NH_3 \rightarrow R-C(=O)NH_2 + NH_4^+ Br^-$  but  $R-C(=O)NH_2 + Br_2$  doesn't make  $R-C(=O)Br$



# CH. 21 Carboxylic Acid Derivatives (p. 2)

## Reactions

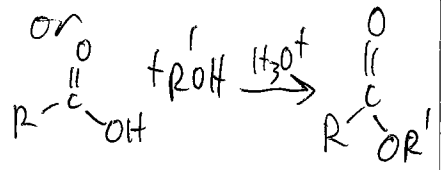
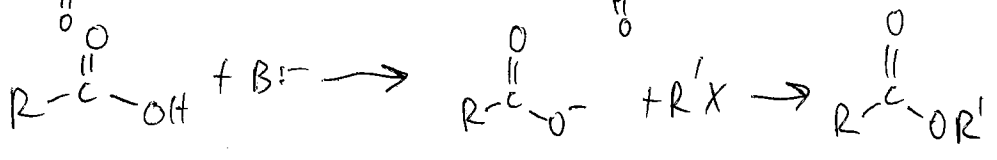
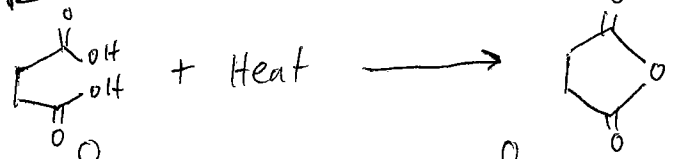
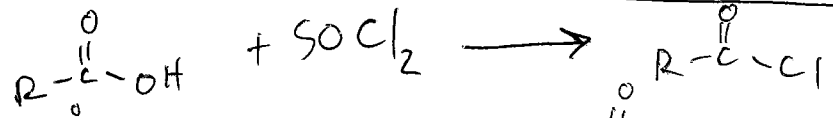
general reactions	what "y" is →	Halides -X	Acid Anhydrides $\begin{matrix} O \\    \\ -O-C-R \end{matrix}$	Ester -O-R	Amides -NH <sub>2</sub>
<u>Hydrolysis:</u> $R-\overset{O}{\parallel}C-y + \begin{matrix} H_3O^+ \\ \text{or } OH^- \end{matrix} \xrightarrow{H_2O} R-\overset{O}{\parallel}C-OH$		X	X	X	X
<u>Reduction:</u> $R-\overset{O}{\parallel}C-y + LiAlH_4 \xrightarrow{H_3O^+} R-\overset{H}{\underset{H}{\text{C}}}-OH$		X	X	2 Reductions possible X can also be reduced by DIBALH to Aldehyde → $R-\overset{H}{\underset{H}{\text{C}}}-NH_2$	X
<u>Amino lysis:</u> $R-\overset{O}{\parallel}C-y + 2NH_3 \longrightarrow R-\overset{O}{\parallel}C-NH_2$		X	X	X	
<u>Alcoholysis:</u> $R-\overset{O}{\parallel}C-y + R'-OH \longrightarrow R-\overset{O}{\parallel}C-O-R'$		X	X		* Also can Do $R-\overset{O}{\parallel}C-NH_2 + SOCl_2 \rightarrow R-\overset{O}{\parallel}C-N$
<u>Grignard:</u> $R-\overset{O}{\parallel}C-y + 2R'MgBr \xrightarrow{H_3O^+} R-\overset{R'}{\underset{R'}{\text{C}}}-OH$		X		X	
<u>Gilman:</u> $R-\overset{O}{\parallel}C-y + R'_2CuLi \longrightarrow R-\overset{O}{\parallel}C-R'$		X			

Notice reactivity order → most reactions least reactions

most reactive (Halides) undergo most reactions

least reactive (Amides) undergo least reactions

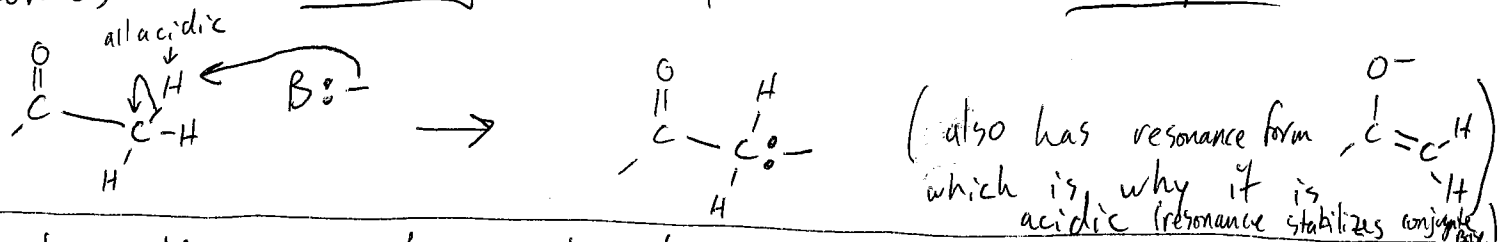
← most reactive reactivity → least reactive



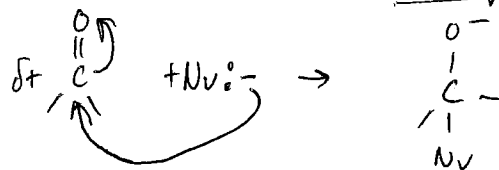
## Making Acid Derivatives

# CH. 22 Alpha-substitution (p.1)

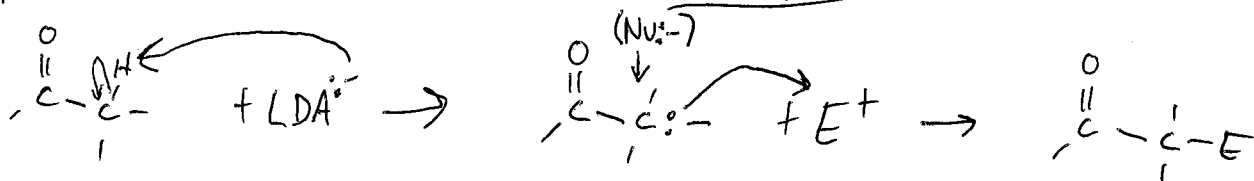
The  $\alpha$ -carbon is carbon next to carbonyl. Its hydrogens are acidic so when treated with base (LDA) the  $\alpha$ -carbon becomes a carbanion ( $C^-$ ) & acts as a nucleophile.



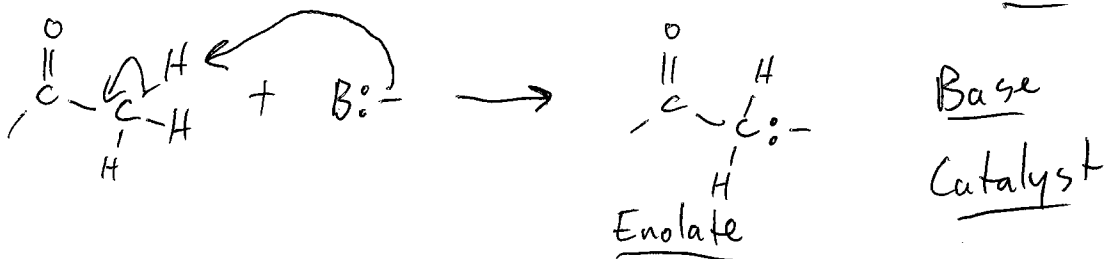
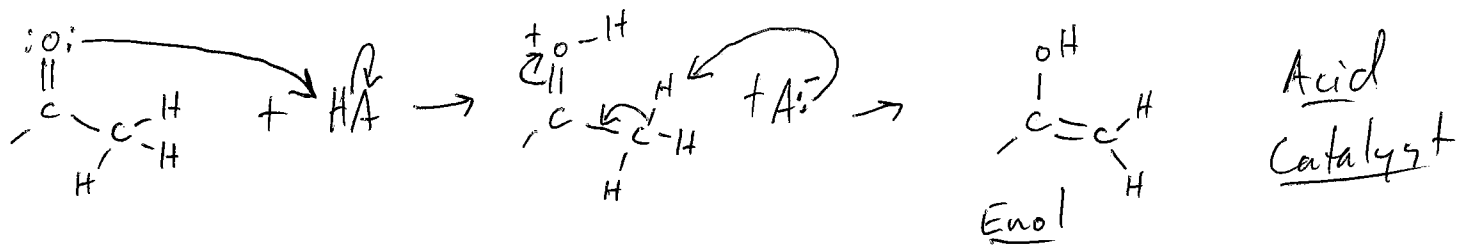
Up to this point carbonyls have been the Electrophile ( $E^+$ ) & undergo reactions with Nucleophiles:



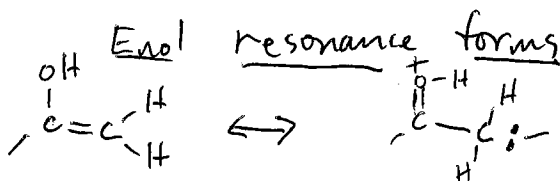
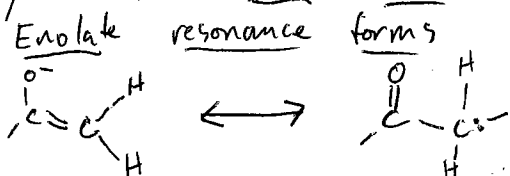
The  $\alpha$ -carbanion however is a nucleophile itself & reacts with electrophiles.



Alpha-substitution reactions can be catalyzed by acid or base. They yield different structural complements of enols. Acid yields enol. Base yields enolate.



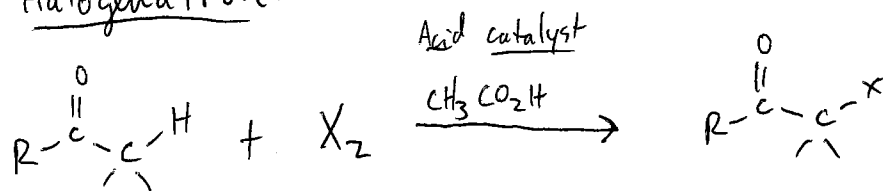
These are slightly different structures, but they have the same reactivity.



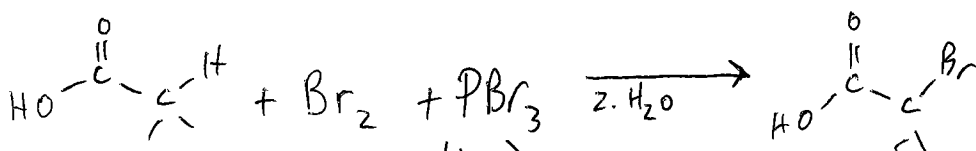
# Ch. 22 Alpha-substitution (p. 2)

## Reactions

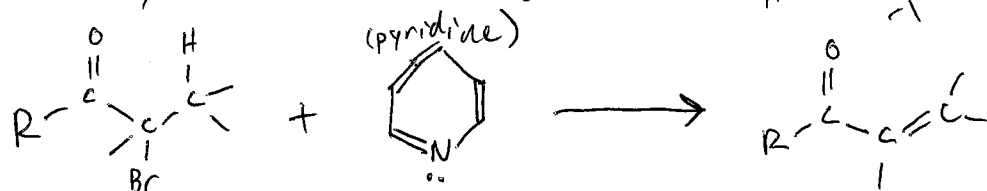
### Halogenations



If you use base catalyst you get haloform reaction (see below)

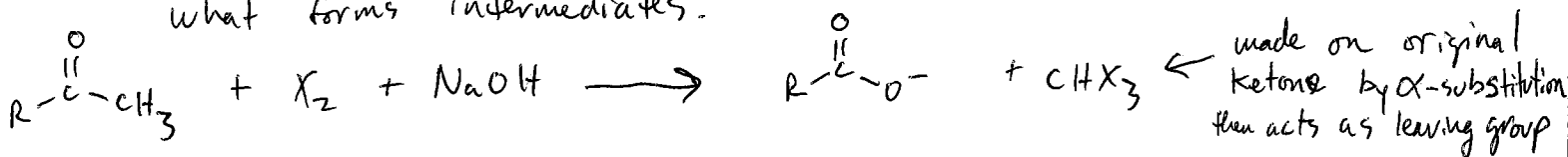


Hell-Volhard-Zelinski Reaction for Brominating Carboxylic Acids

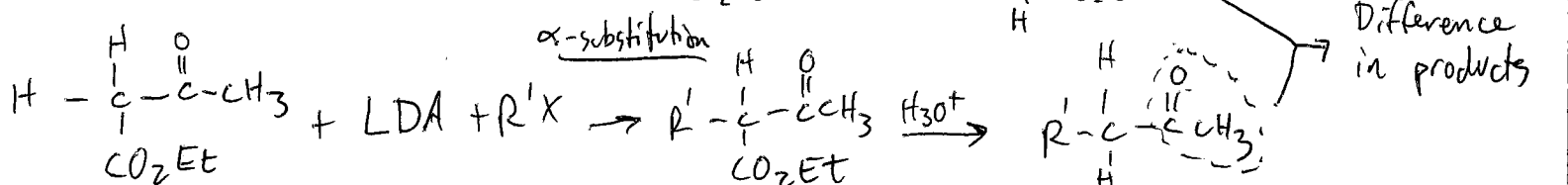
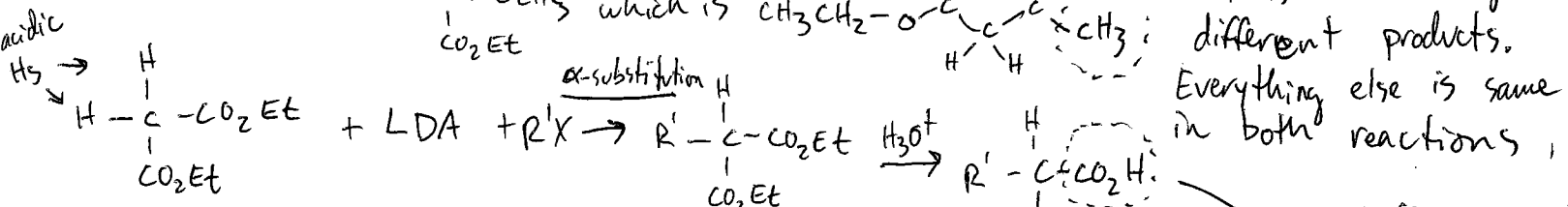
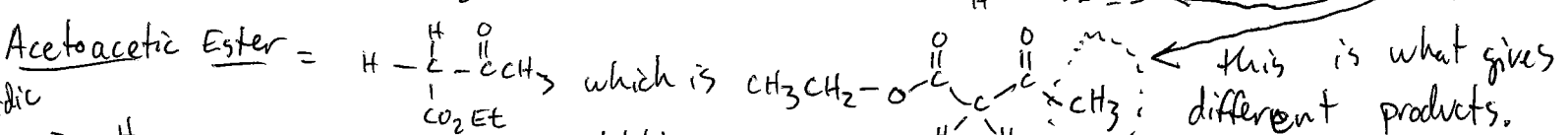
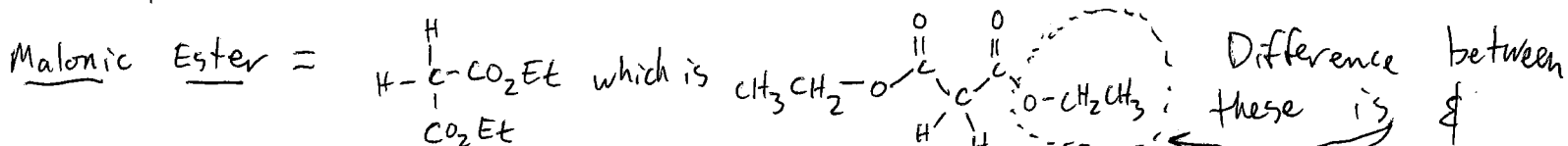
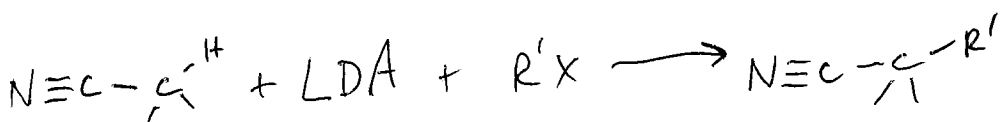
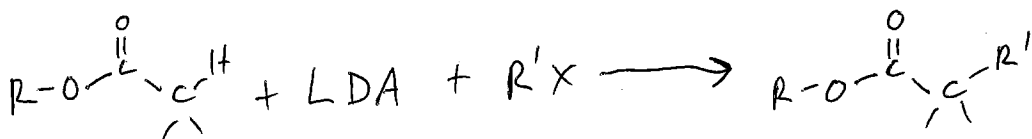
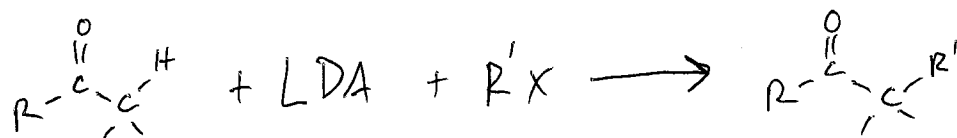


E2 Reaction with pyridine Base (De-Halogenation)

Haloform: Doesn't look like  $\alpha$ -substitution, but what forms intermediates.



### Alkylations



Difference between these is  $\alpha$  substitution. This is what gives different products. Everything else is same in both reactions. Difference in products.



# CH 23 Carbonyl Condensation (p.2)

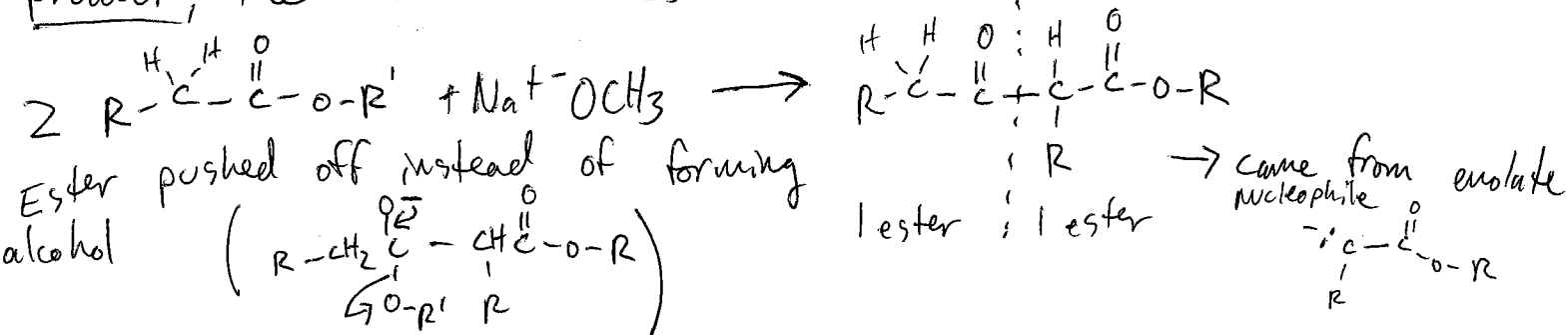
If you want to do α-substitution, you have to be careful your enolate  $R-\overset{\ominus}{C}-\overset{O}{\parallel}C$  doesn't react with itself  $R-\overset{\ominus}{C}-\overset{O}{\parallel}C + R-\overset{\ominus}{C}-\overset{O}{\parallel}C$  to get α-substitution & not condensation use ① strong base (LDA)

② 1 mol of base ③ nonprotic solvent.

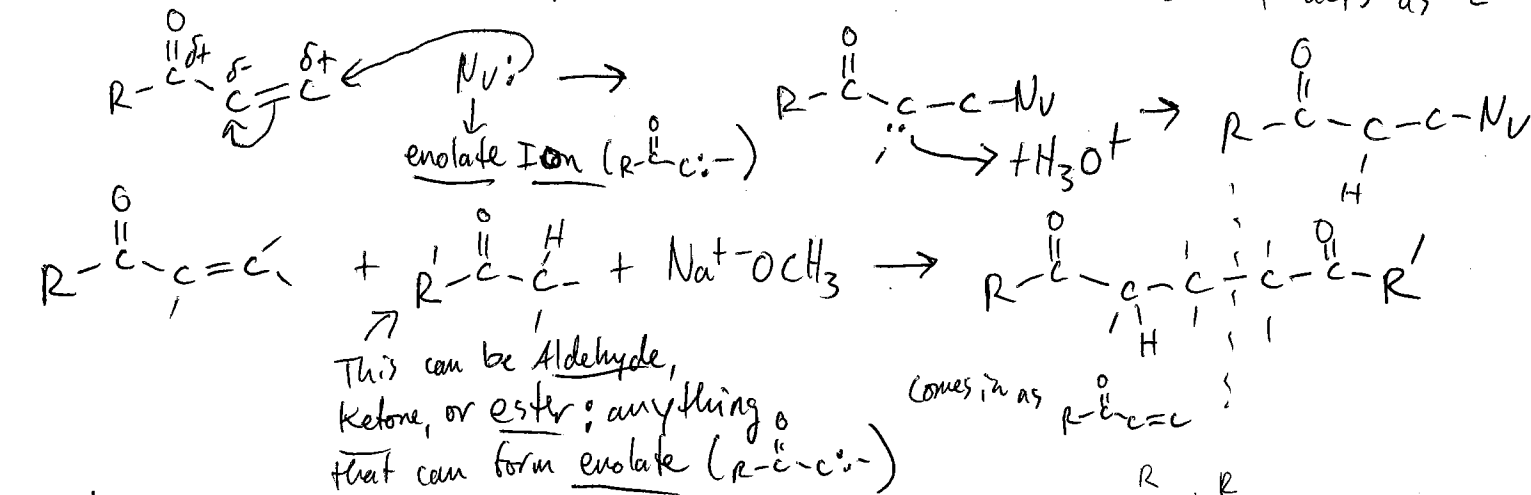
To get condensation use ① weak base ( $Na^+OCH_3$ ) ② catalytic amount of base (0.05 mol) ③ protic solvent.

## More Reactions

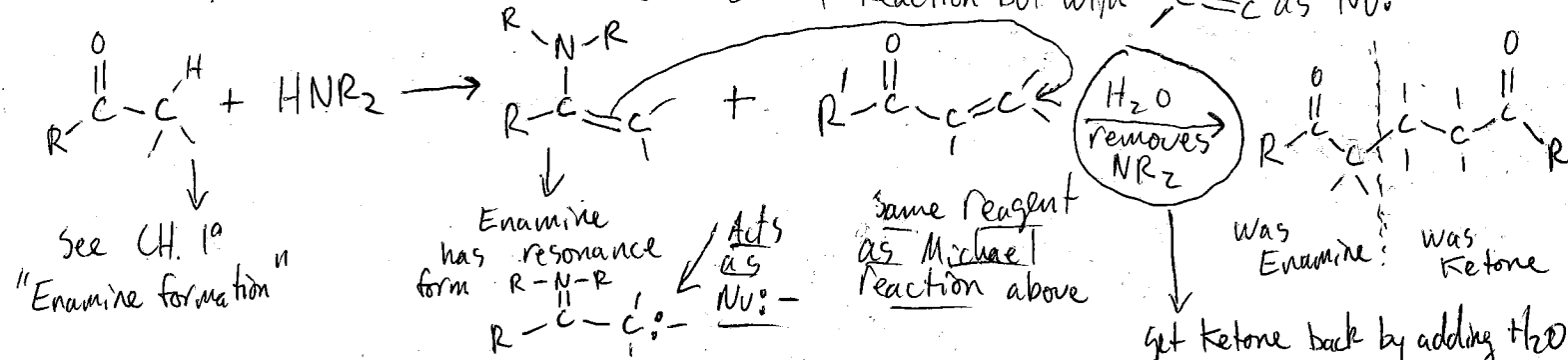
Claisen Condensation is with Esters ( $R-\overset{O}{\parallel}C-O-R$ ). 1 Ester remains in product, the other leaves



Michael Reaction takes place on β-carbon which is δ<sup>+</sup> & acts as E<sup>+</sup>



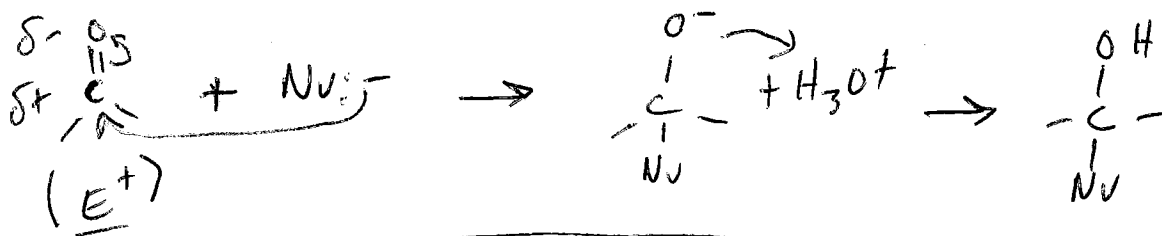
Stork Enamine Reaction - Like Michael Reaction but with  $\overset{R}{N}-R$  as Nu<sup>-</sup>



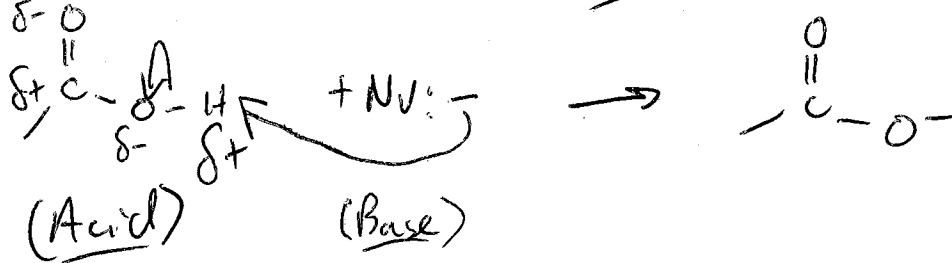
# Carbonyl Chemistry

Carbonyls act as both Electrophiles (E<sup>+</sup>) and Nucleophiles (Nu<sup>-</sup>)

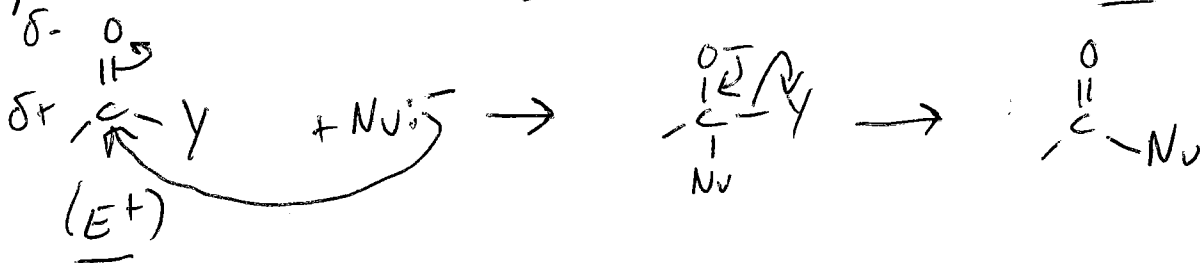
CH 19 Aldehydes & Ketones - carbonyl is electrophile



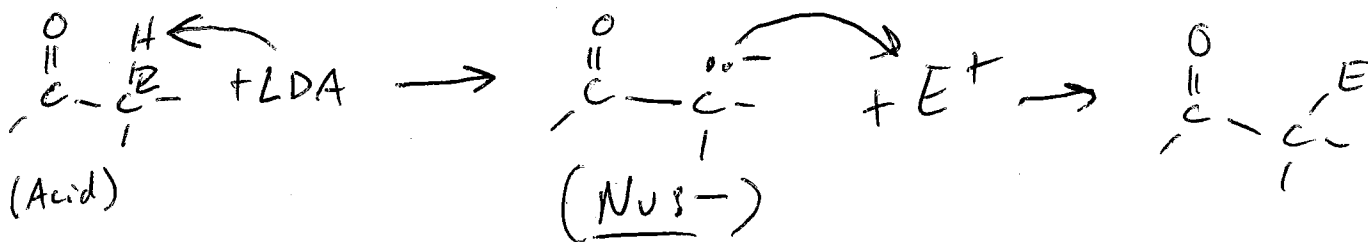
CH 20 Carboxylic Acids - these don't really act like electrophiles because they act as acids (H<sup>+</sup> is electrophile). Nucleophile acts as base



CH 21 Acid Derivatives - -OH in acid is replaced by good leaving group so carbonyl is electrophile. Nu<sup>-</sup> replaces leaving group



CH 22 α-substitution - α-carbon acts as nucleophile



CH 23 Condensations - basically combines nucleophilic carbonyls (CH 22)

& Electrophilic carbonyls (CH 19, 21)

