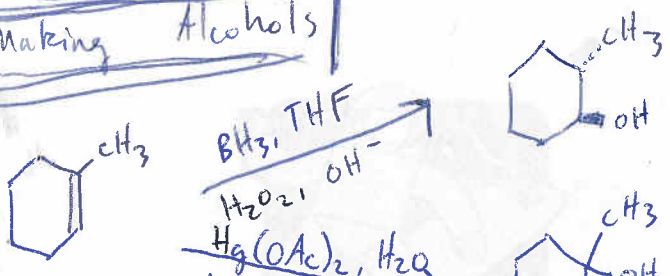
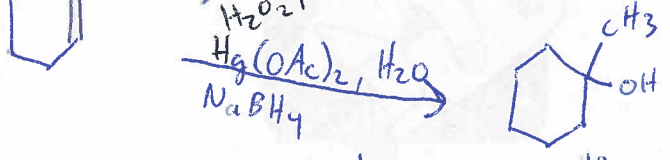


Ch. 17 Alcohols (p. 1)

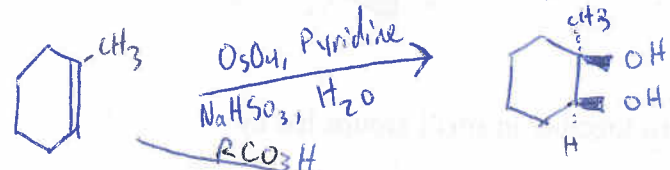
Making Alcohols



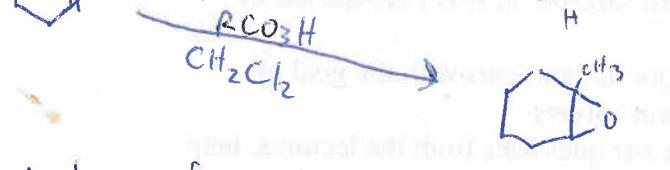
Trans-non-Markovnikov



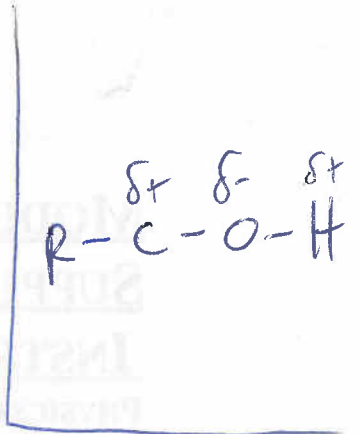
markovnikov



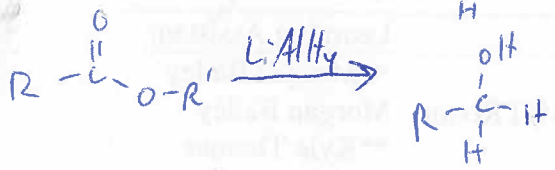
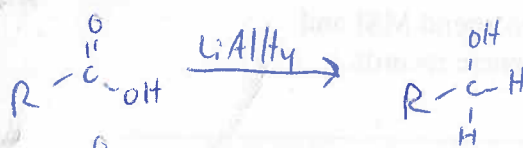
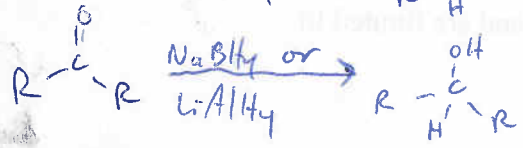
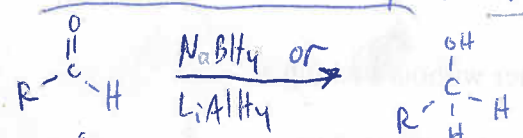
cis-diol



trans-diol

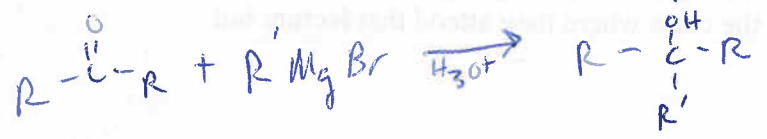
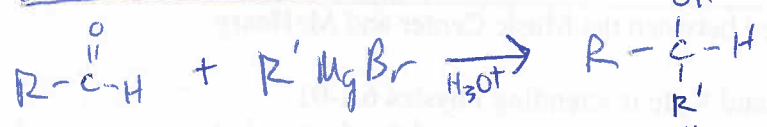


reduction of carbonyls: LiAlH_4 must be used for Carboxylic Acids & Esters (always done in acidic conditions)

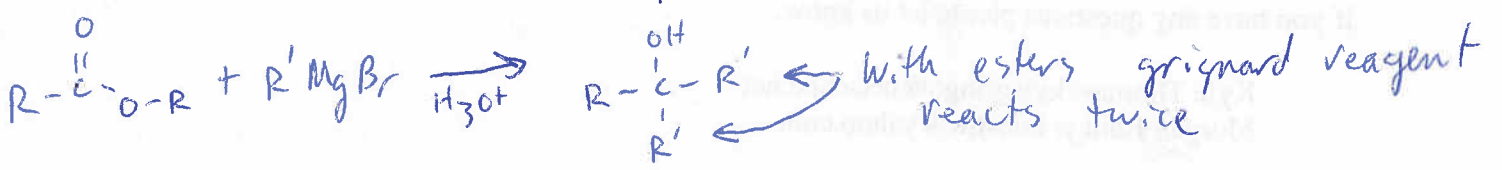


LiAlH_4 & NaBH_4 are both equivalent to a hydride H^- ion & react by $\text{S}_{\text{N}}2$ -like mechanism. H_3O^+ Added at end to get extra protons.

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

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

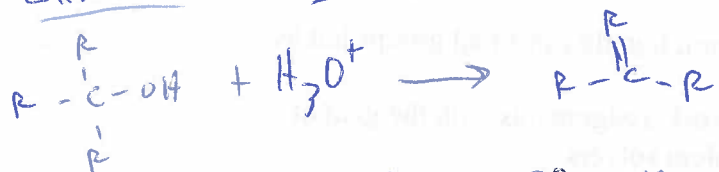
Ch. 17 Alcohols (p. 2)

Alcohol Reactions

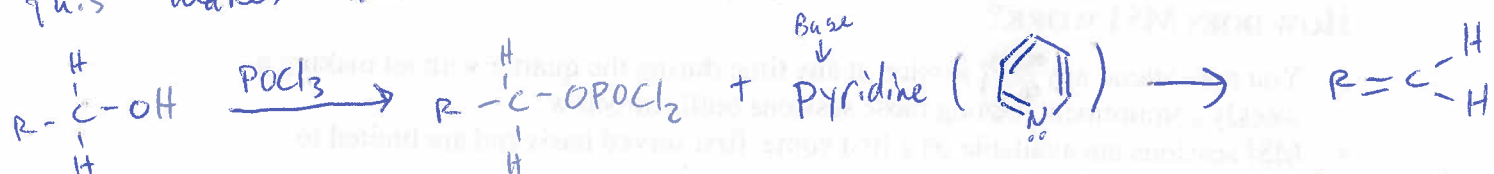
Alcohols can be acids when put with strong bases



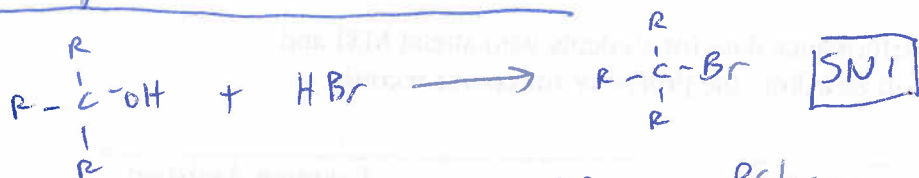
Elimination reactions; can be done with just H_3O^+ if alcohol is 3° $[E1]$



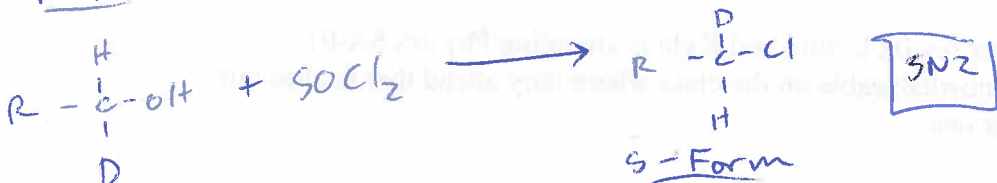
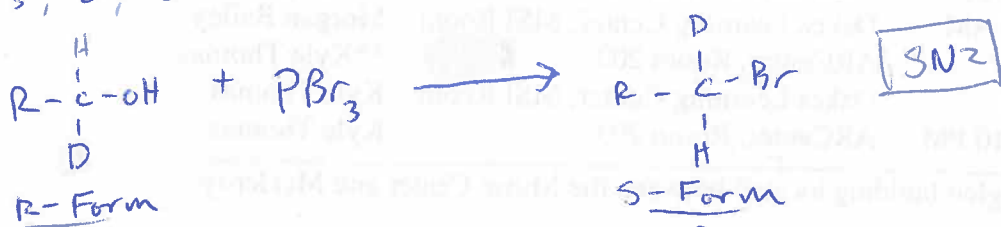
if Alcohol is 1° or 2° use $POCl_3$ which also works for 3° . This makes alcohol into a good leaving group for $[E2]$ reaction.



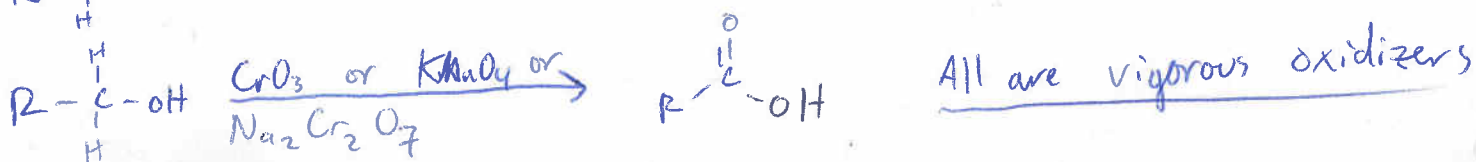
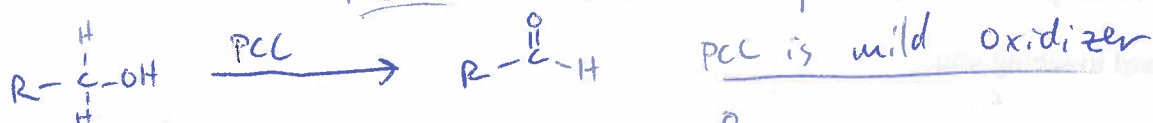
Halogenation of Alcohols: HX can react with 3° Alcohols (S_N1) but not 2° or 1°




$3^\circ, 2^\circ$, or 1° use $SOCl_2, PBr_3$, or PCl_5



Oxidation: see oxidation/reduction handout. 2° Alcohols always become ketones. 1° Alcohols depend on reagent. 3° Alcohols don't react

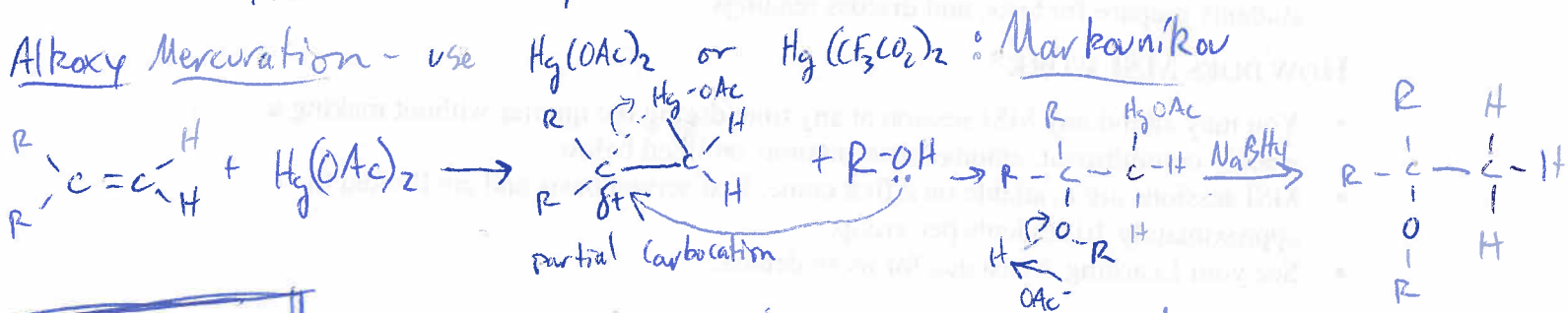
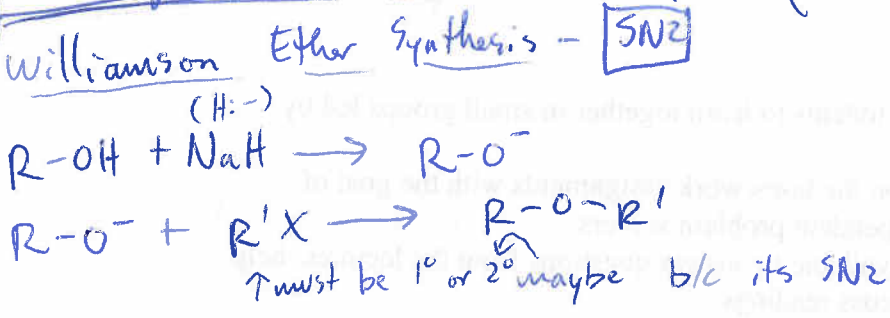


Ch. 18 Ethers & Epoxides

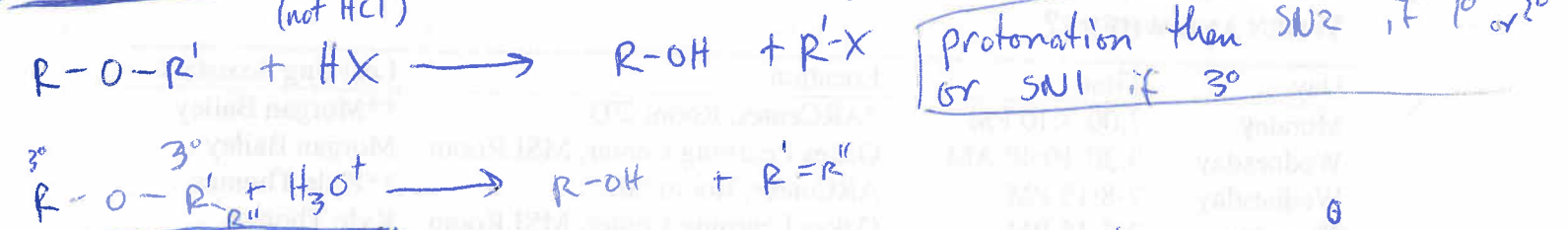
Epoxides are 3-membered-ring ethers  & are more reactive because of angle strain.
Ethers are unreactive for the most part.

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

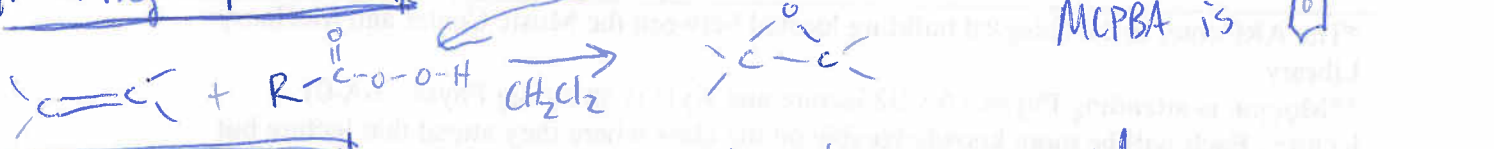
Making Ethers - 2 ways (or from epoxides: see below)



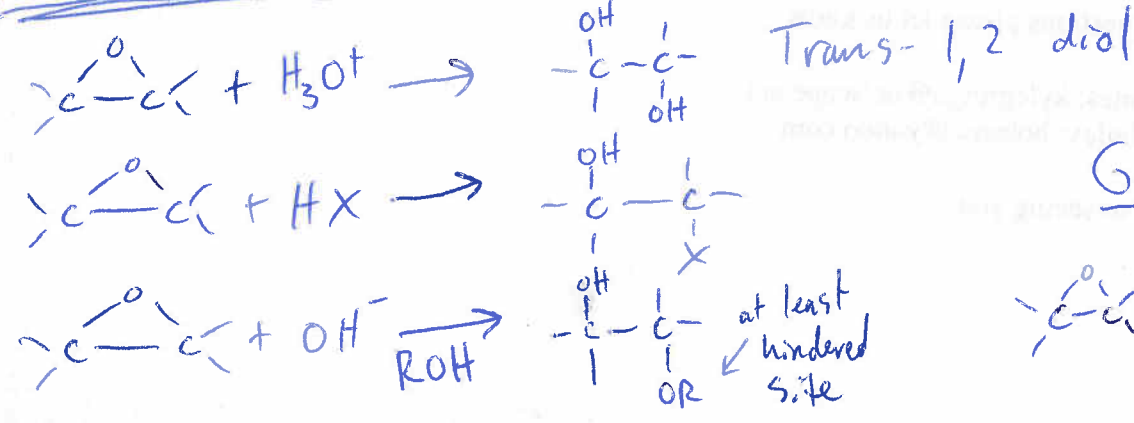
Ether Rxns - only 1: ether cleavage by acids (not HCl)



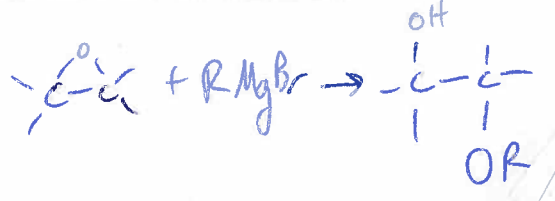
Making Epoxides



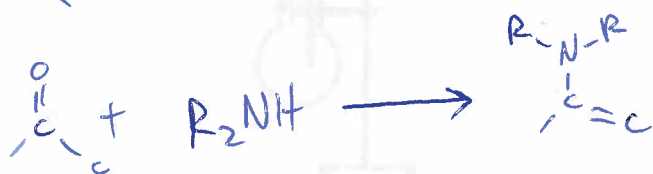
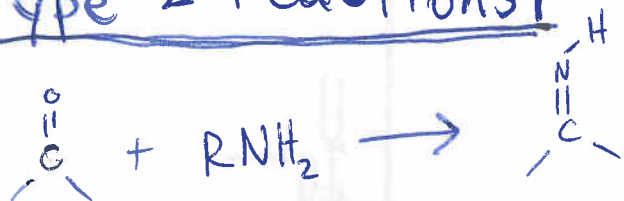
Epoxide Rxns only cleavage: by base or acid



Grignard Cleavage



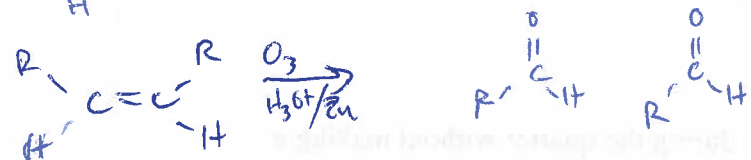
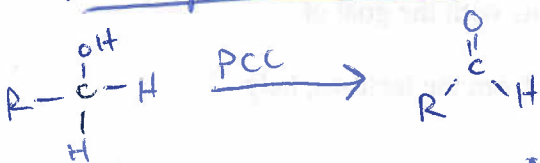
Type 2 Reactions



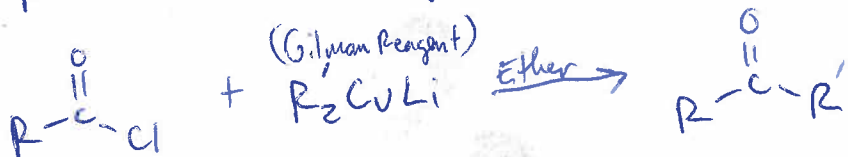
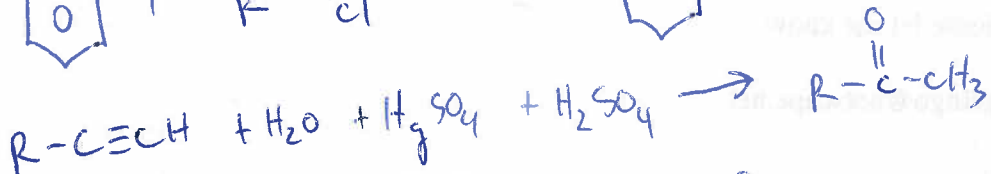
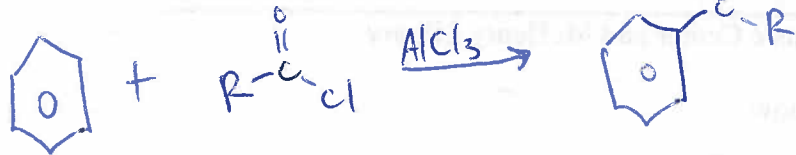
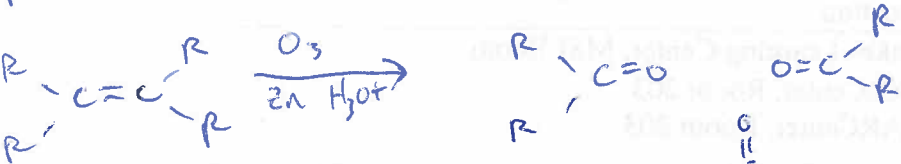
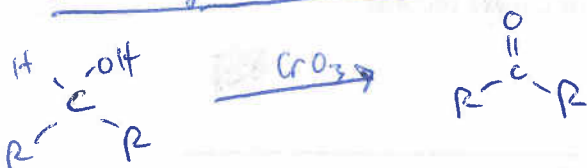
Mechanism is very similar to RNH_2 , but because N is bonded to 2 R groups it can't form a double bond so $\text{C}=\text{C}$ bond forms



Making Aldehydes



Making Ketones

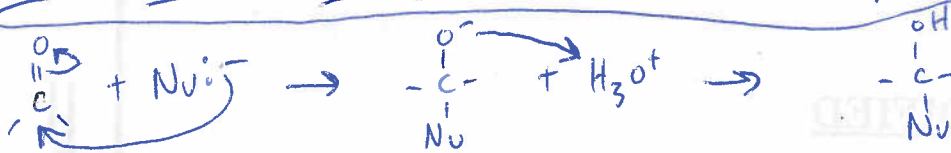


CH. 19: Aldehydes & Ketones p.1

There are two basic reactions these both undergo.

Reaction 1:

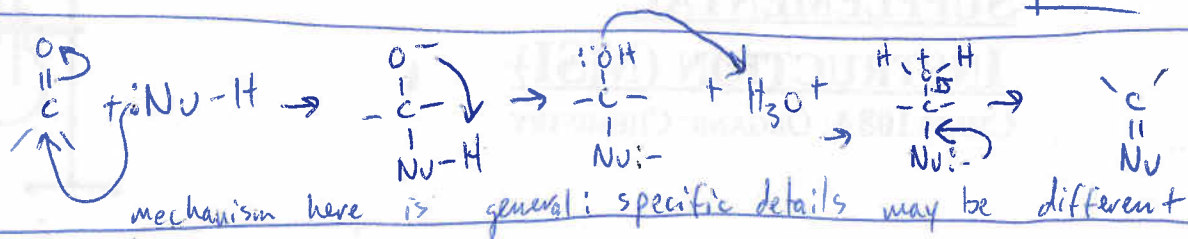
Nucleophilic Addition to yield alcohol



p.675

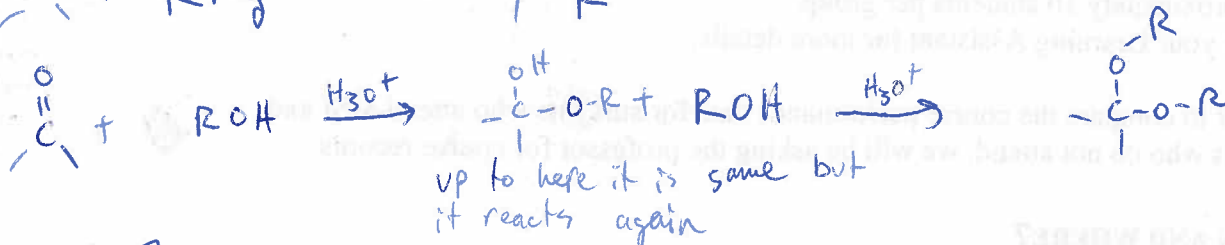
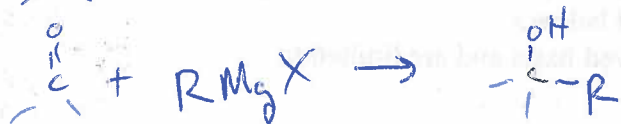
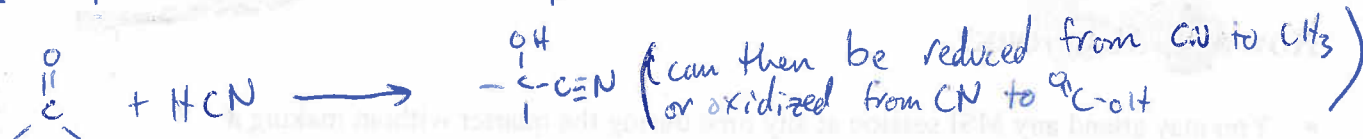
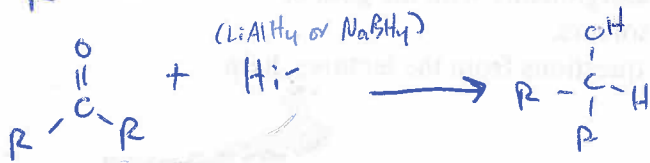
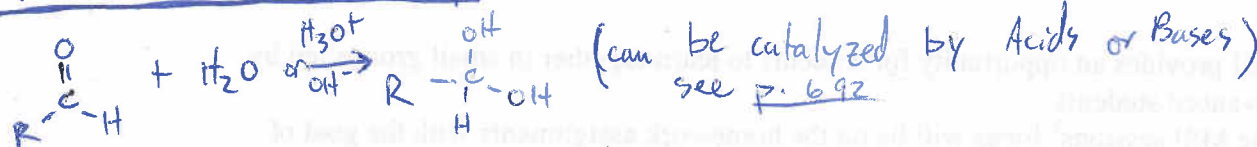
Reaction 2:

Nucleophilic addition to yield double-bonded C to Nucleophile

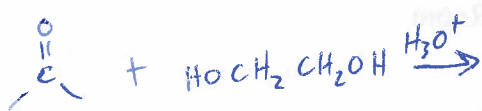


mechanism here is general: specific details may be different

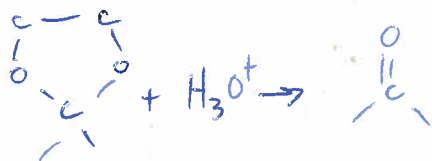
Type 1 Reactions



This reaction can be used to protect Ketones



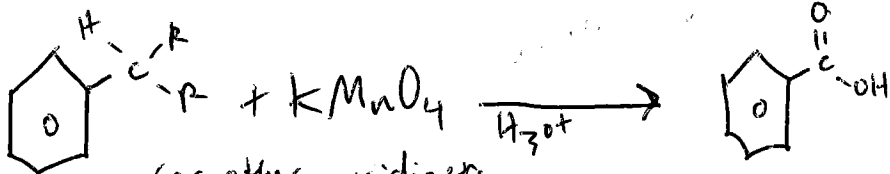
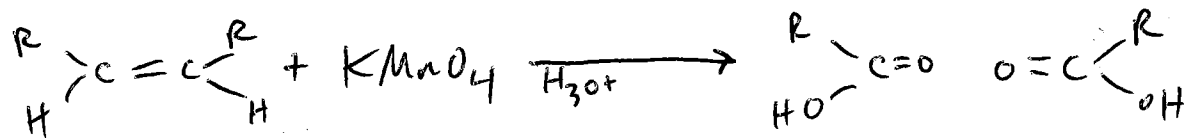
which protects ketone by making unreactive ethers & can then be converted back by adding H_3O^+



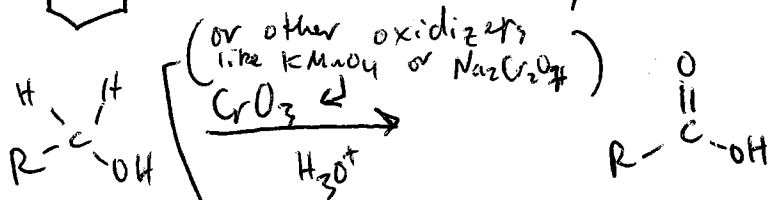
Ch. 20 Carboxylic Acids & Nitriles (p.1)

Making Carboxylic Acids

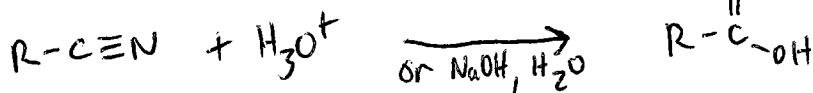
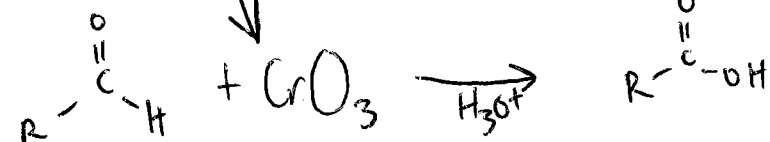
Carboxylic acids are most oxidized functional group so you can get there by using strong oxidizers on alcohols or other carbonyls



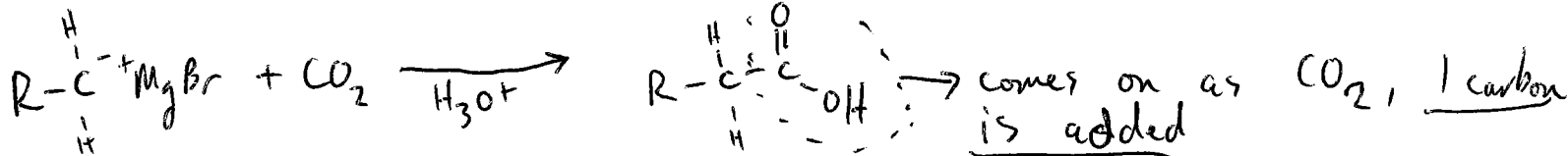
Alkanes oxidize to $\overset{O}{\parallel}C-OH$ when attached to benzene only



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

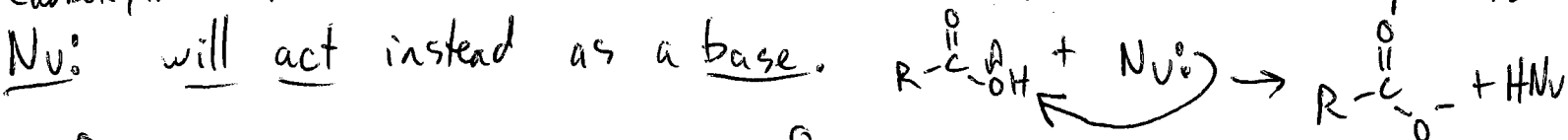


Both acids & bases cleave cyano-group but with different mechanism

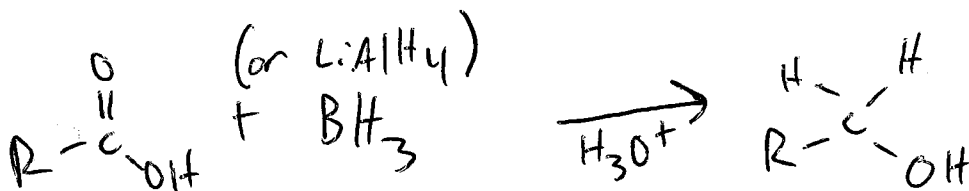


Carboxylic Reactions

Carboxylic Acids tend to act as acids rather than electrophiles.



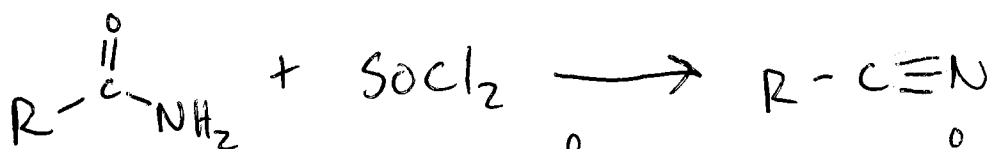
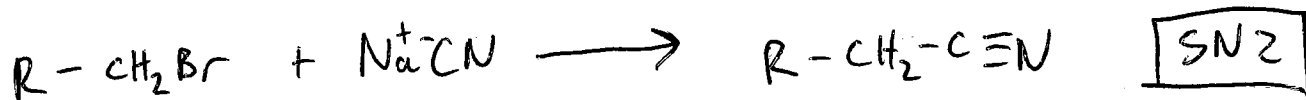
Acidic because product is so stable from resonance



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

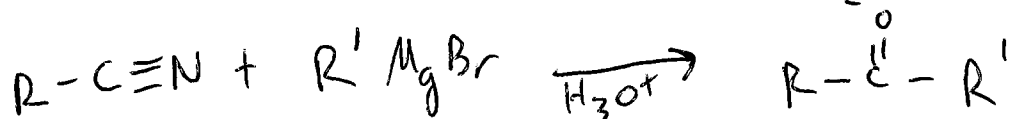
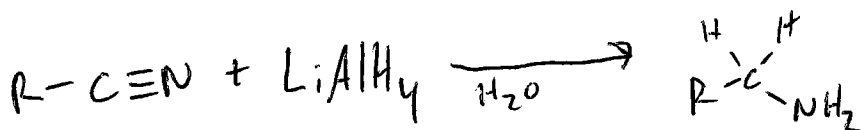
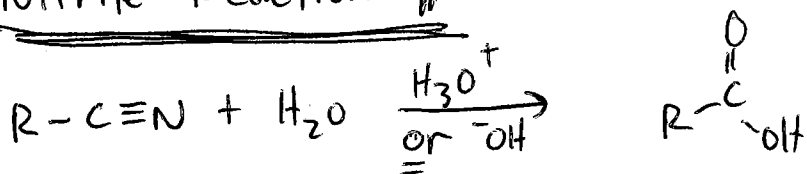
Making Nitriles

There are 2 ways to make a nitrile. Adding a cyano group is SN_2 so other carbon must be 1° or possibly 2° . So a highly substituted carbon should be given cyano group through dehydration of Amines (SOCl_2).



To make $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$ 1. take $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{OH}$ & Add $\text{SOCl}_2 + \text{CHCl}_3 \rightarrow \text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{Cl}$
2. then take $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{Cl}$ & Add $\text{NH}_3 \rightarrow \text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$

Nitrile Reactions

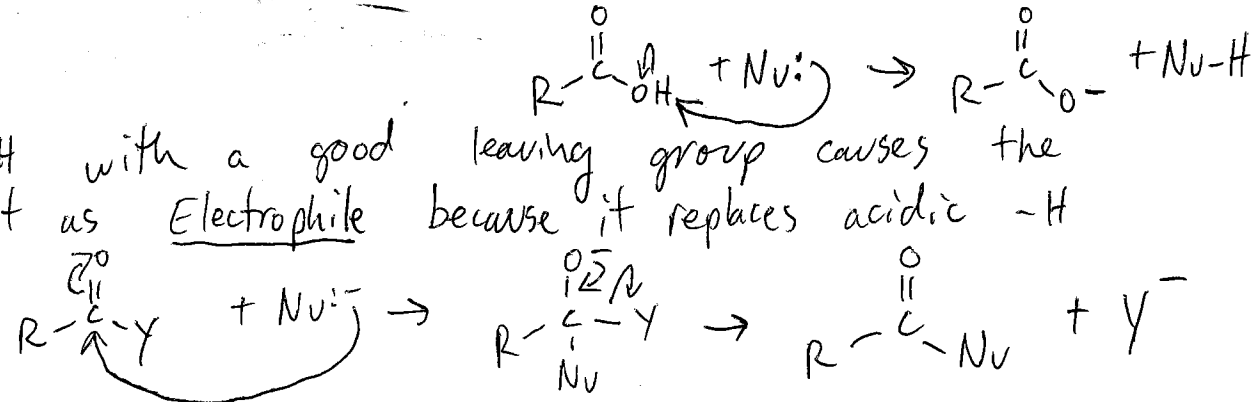


CH. 21 Carboxylic Acid Derivatives (V.I)

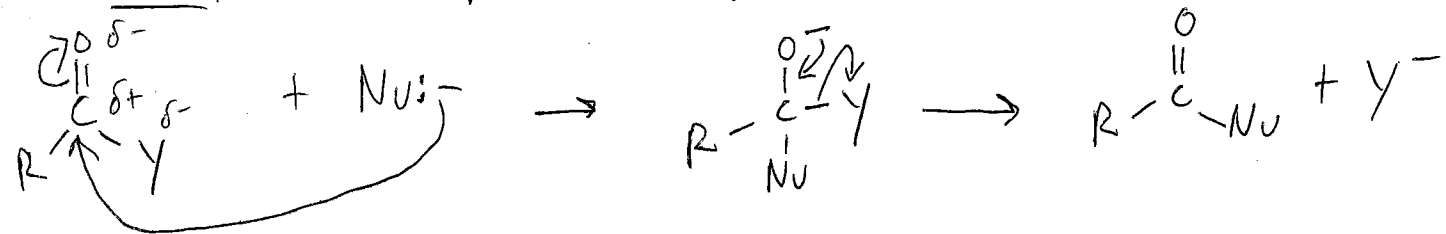
Carboxylic Acid Derivatives are Carboxylic Acids ($R-C(=O)OH$) where $-OH$ group is replaced by a good leaving group.

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

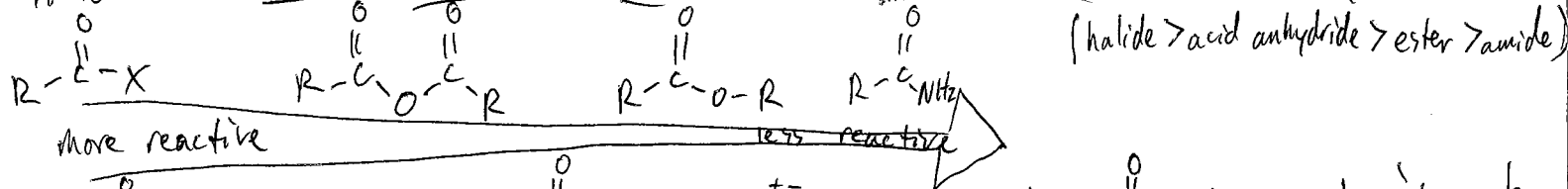


"Y" is good Leaving group because it is stable on its own supporting a negative charge (i.e. Cl^- , $-O-C(=O)R$).

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)

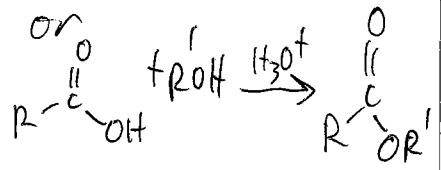
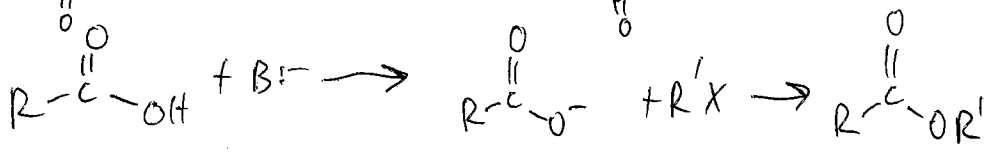
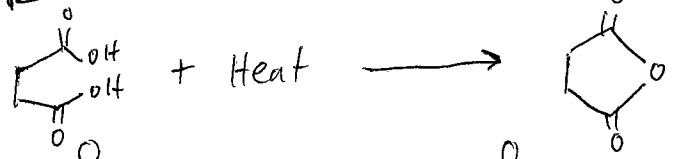
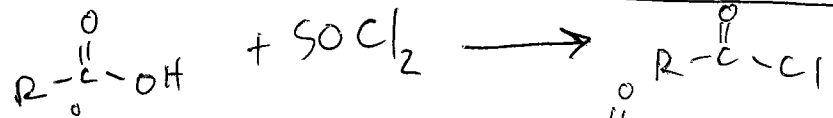
Reactions

general reactions	what "y" is →	Halides -X	Acid Anhydrides $\begin{matrix} O \\ \\ -O-C-R \end{matrix}$	Ester -O-R	Amides -NH ₂
<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 This $R-\overset{O}{\parallel}{C}-NH_2 + SOCl_2 \rightarrow R-\overset{O}{\parallel}{C}-N$
<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

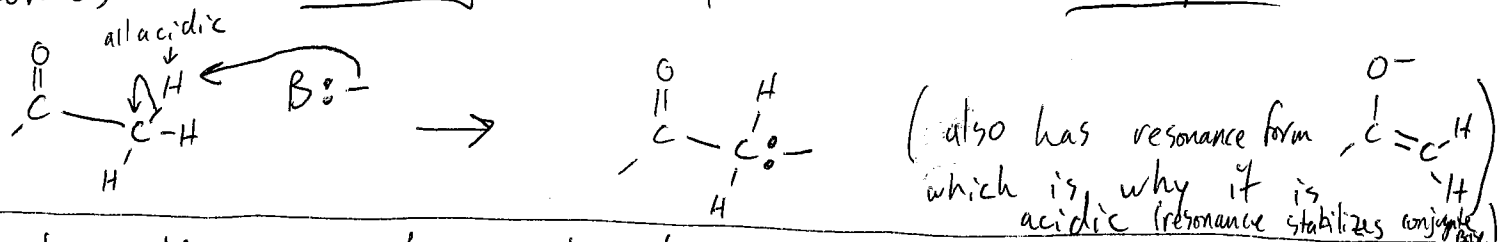
← most reactive reactivity → least reactive



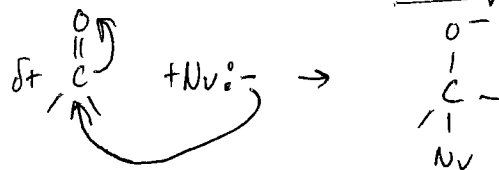
Making Acid Derivatives

CH. 22 Alpha-substitution (p.1)

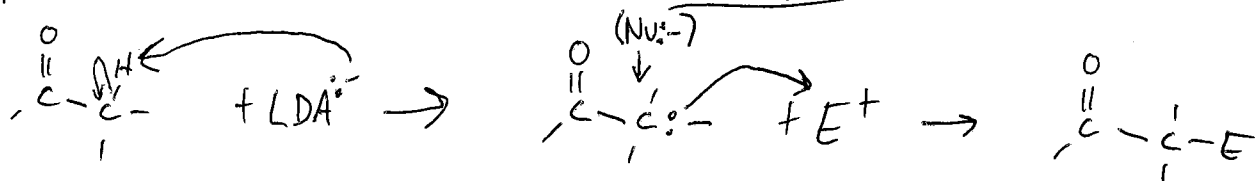
The α -carbon is carbon next to carbonyl. Its hydrogens are acidic so when treated with base (LDA) the α -carbon becomes a carbanion (C^-) & acts as a nucleophile.



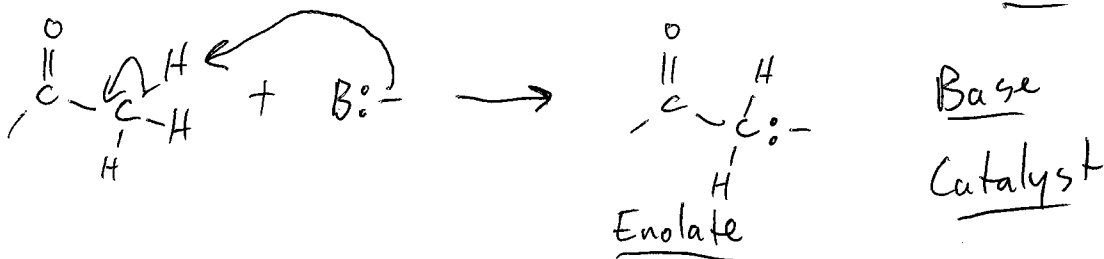
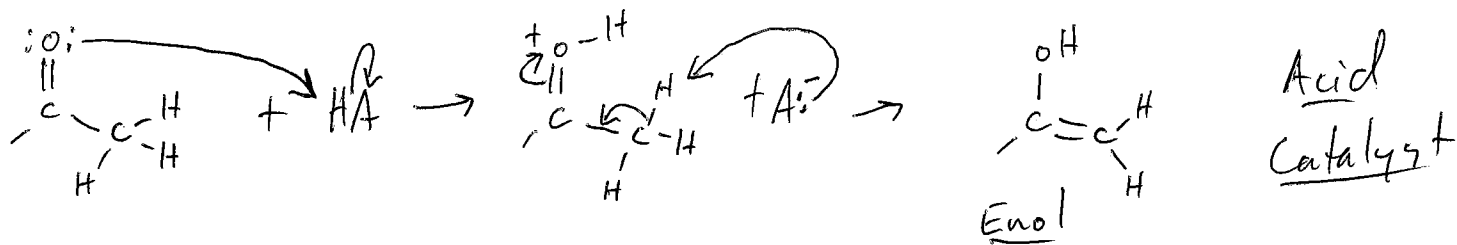
Up to this point carbonyls have been the Electrophile (E^+) & undergo reactions with Nucleophiles:



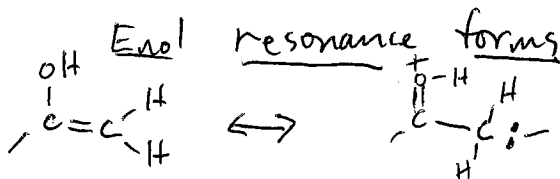
The α -carbanion however is a nucleophile itself & reacts with electrophiles.



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



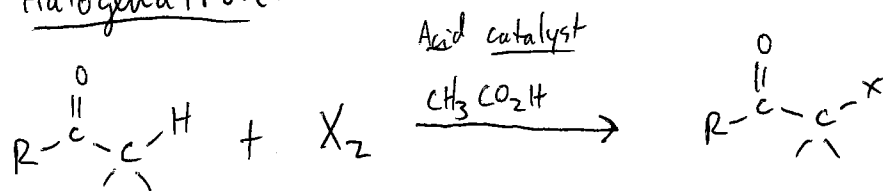
These are slightly different structures, but they have the same reactivity.



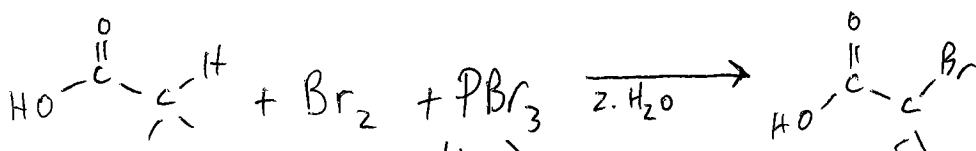
Ch. 22 Alpha-substitution (p. 2)

Reactions

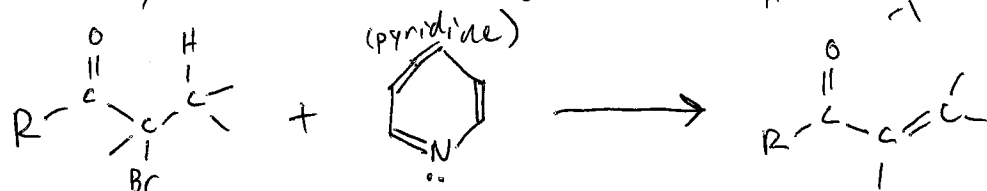
Halogenations



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

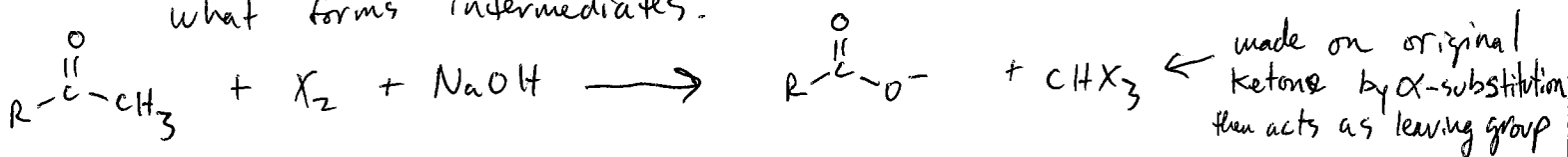


Hell-Volhard-Zelinski Reaction for Brominating Carboxylic Acids

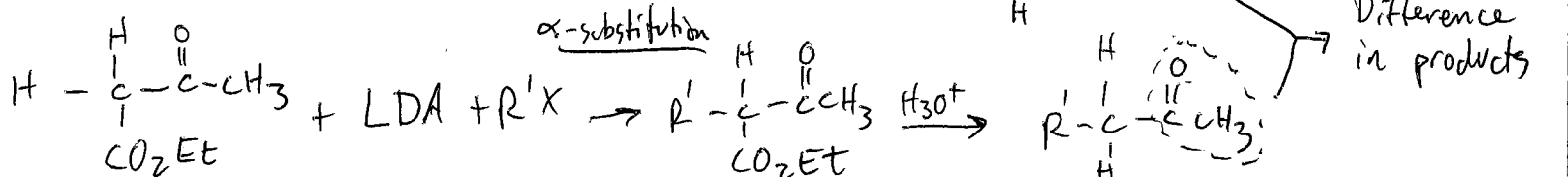
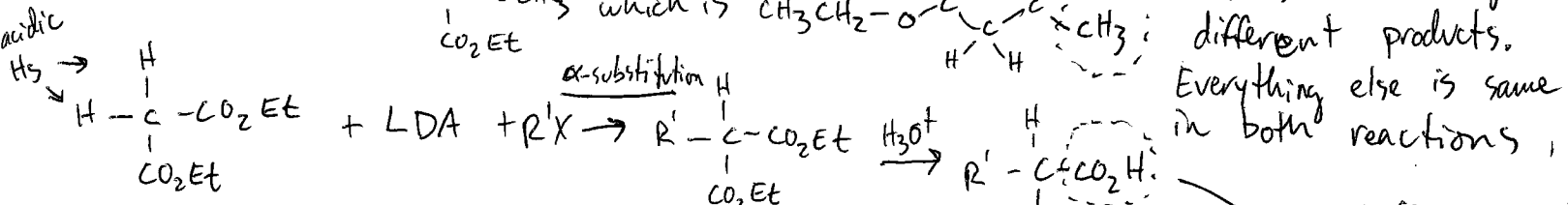
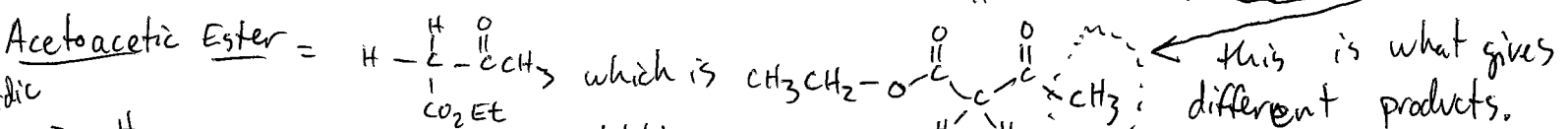
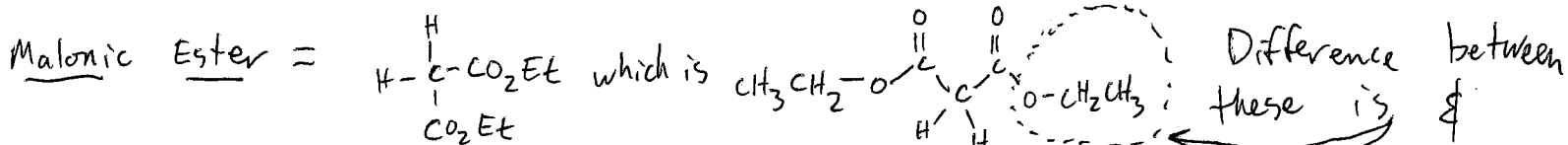
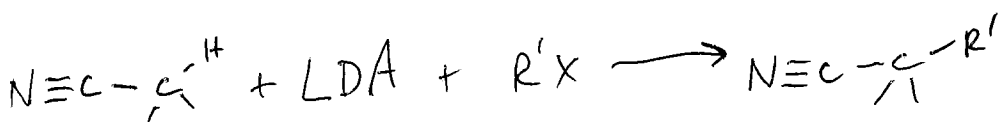
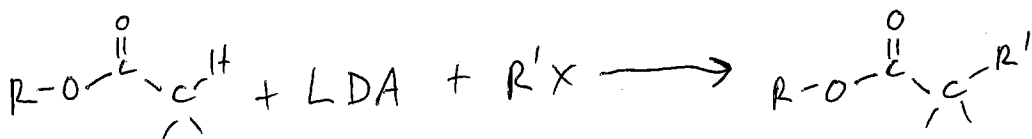
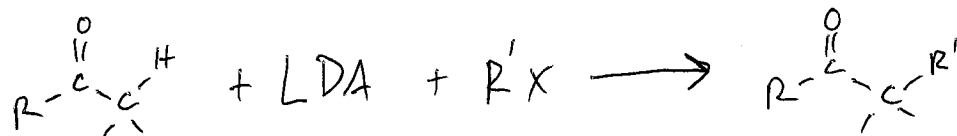


E2 Reaction with pyridine Base (De-Halogenation)

Haloform: Doesn't look like α -substitution, but what forms intermediates.



Alkylations

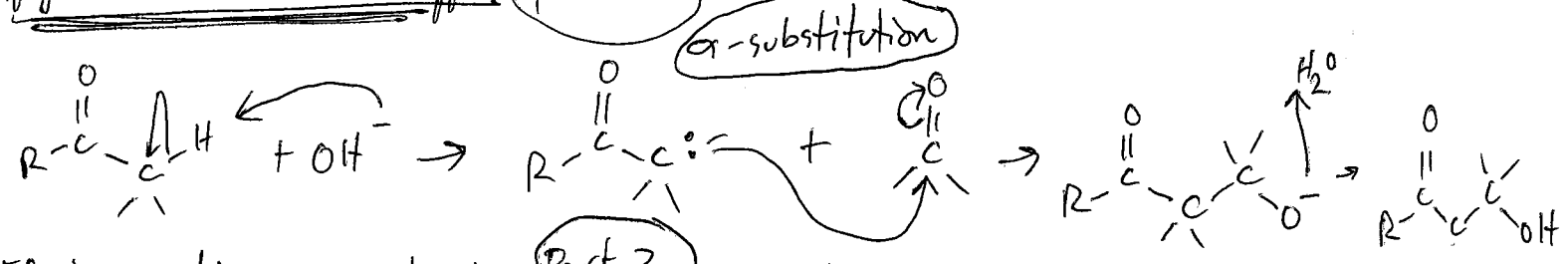


Difference between these is α (this is what gives different products). Everything else is same in both reactions. Difference in products

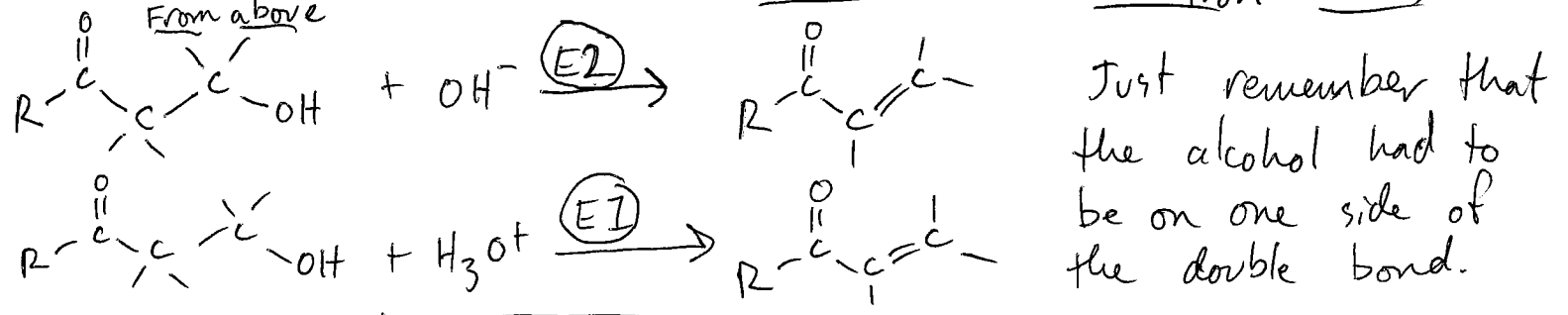
CH 23 Carbonyl Condensation (p.1)

Up to this point you have seen carbonyls act as Electrophiles ($\overset{\text{O}}{\parallel}{\text{C}}\delta^+$) & as Nucleophiles ($\overset{\text{O}}{\parallel}{\text{C}}-\overset{\text{H}}{\text{C}}\delta^-$). In Carbonyl Condensation reactions carbonyls act as both, that is both main reagents in reaction are carbonyls.

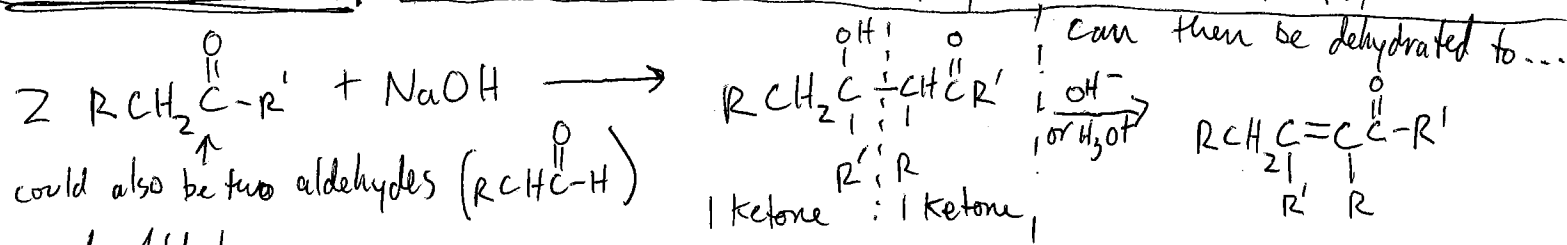
General Mechanism (part 1)



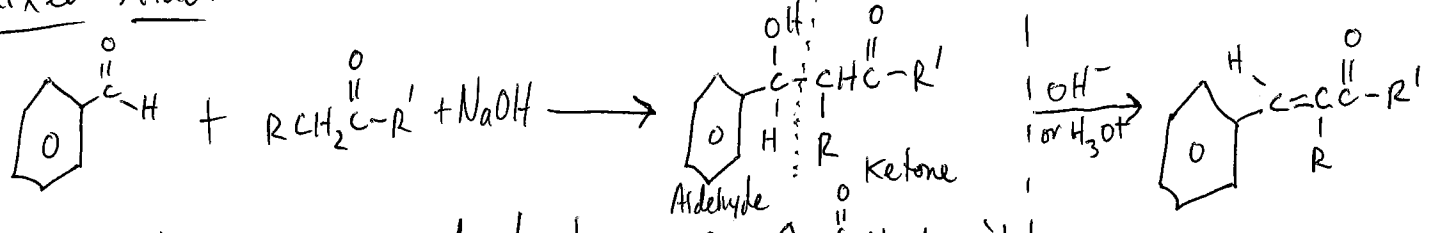
If in acidic or basic (part 2) conditions an elimination occurs



Aldol Reactions Can be two aldehydes ($\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{H}$), two ketones ($\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$), or both



Mixed Aldol



Above gives one product because $\text{C}_6\text{H}_5\overset{\text{O}}{\parallel}{\text{C}}-\text{H}$ doesn't have acidic Hs so can't form Nucleophile Enolate ion

mixed aldol will give a number of products which makes reaction useless. To get a single product one of 2 conditions must be met:

- One molecule has no α -Hs, but is good SN2 acceptor as above
- One molecule has extremely acidic α -Hs to make it most likely nucleophile ($\overset{\text{O}}{\parallel}{\text{C}}-\overset{\text{H}}{\text{C}}-\overset{\text{H}}{\text{C}}-\overset{\text{H}}{\text{C}}-\overset{\text{O}}{\parallel}{\text{C}}$)

CH 23 Carbonyl Condensation (p.2)

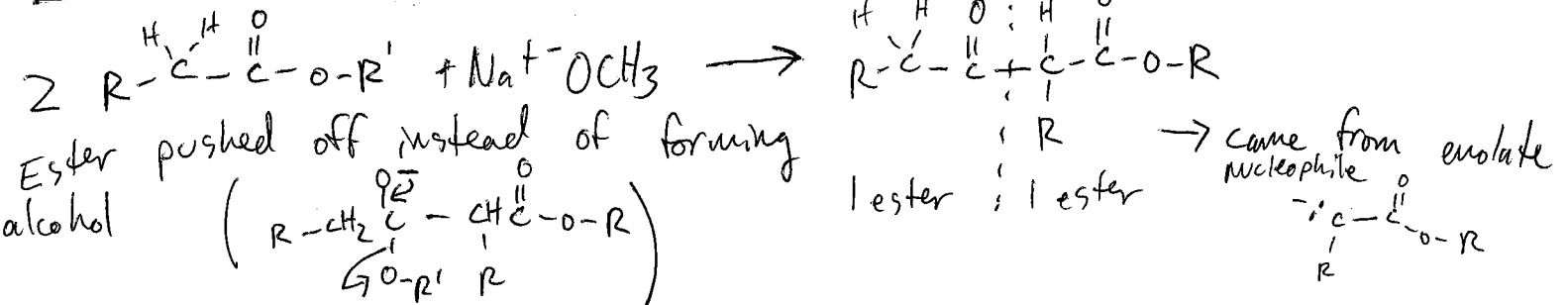
If you want to do α -substitution, you have to be careful your enolate $R-\overset{\ominus}{C}-\overset{O}{\parallel}-C:$ doesn't react with itself $R-\overset{\ominus}{C}-\overset{O}{\parallel}-C + R-\overset{\ominus}{C}-\overset{O}{\parallel}-C$ to get α -substitution & not condensation use ① strong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

② 1 mol of base ③ nonprotic solvent.

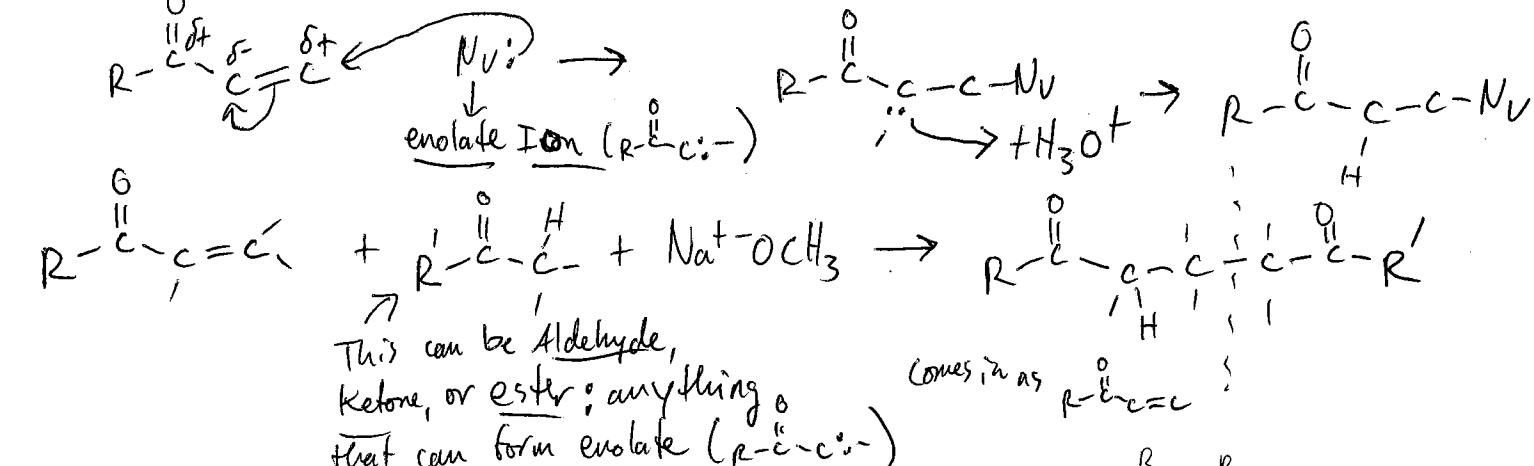
To get condensation use ① weak base (Na⁺OCH₃) ② catalytic amount of base (0.05 mol)
③ protic solvent.

More Reactions

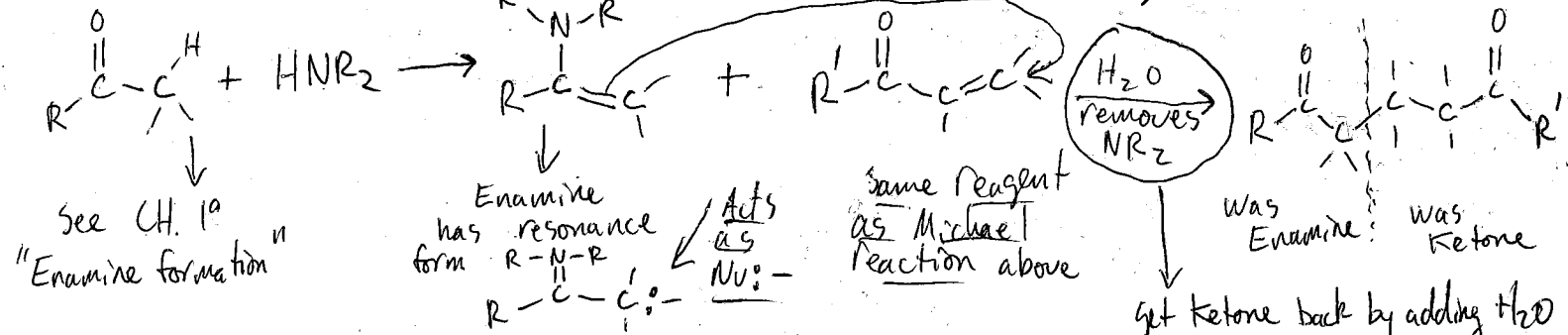
Claisen Condensation is with Esters ($R-\overset{O}{\parallel}-O-R$). 1 Ester remains in product, the other leaves



Michael Reaction takes place on β -carbon which is δ^+ & acts as E^+



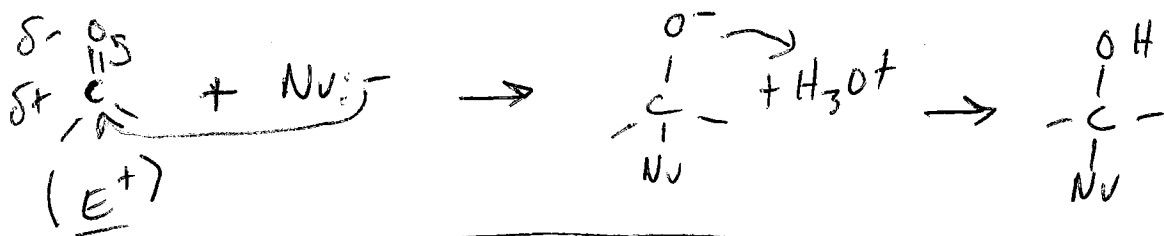
Stork Enamine Reaction - Like Michael Reaction but with $C=C$ as Nu^-



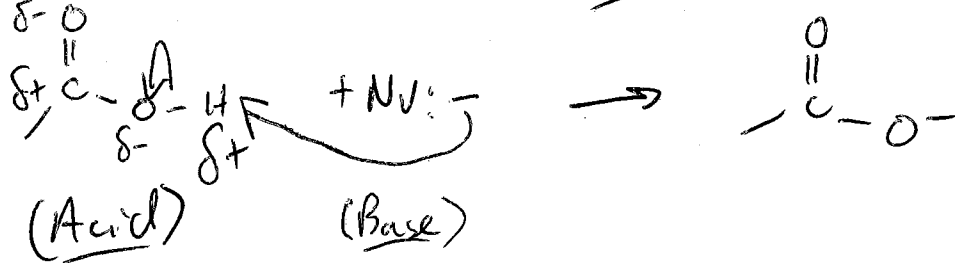
Carbonyl Chemistry

Carbonyls act as both Electrophiles (E⁺) and Nucleophiles (Nu⁻)

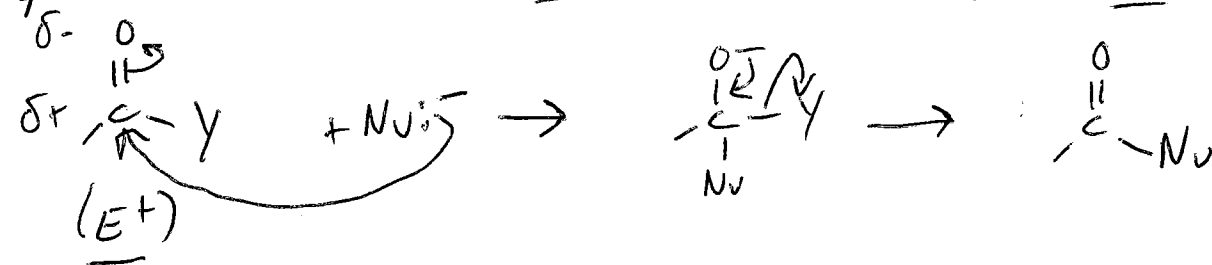
CH 19 Aldehydes & Ketones - carbonyl is electrophile



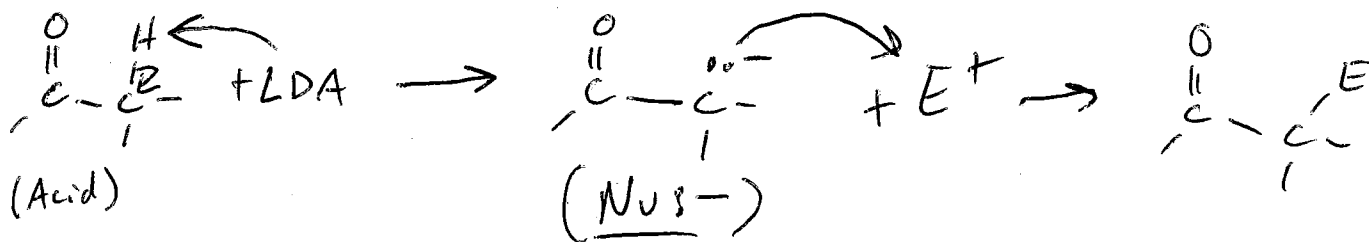
CH 20 Carboxylic Acids - these don't really act like electrophiles because they act as acids (H⁺ is electrophile). Nucleophile acts as base



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

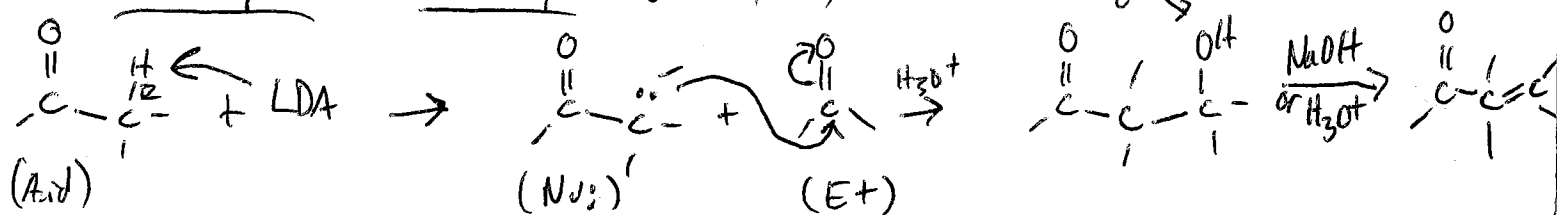


CH 22 α-substitution - α-carbon acts as nucleophile



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

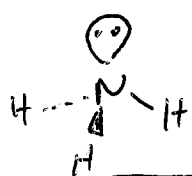
& Electrophilic carbonyls (CH 19, 21)



CH. 24 Amines (p.1)

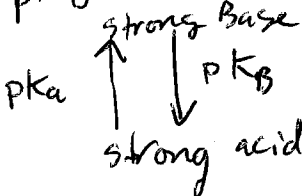
o Amines $-NR_3$ are different than Amides, reactions are different

o Amines are very similar to water, but have 1 less lone pair



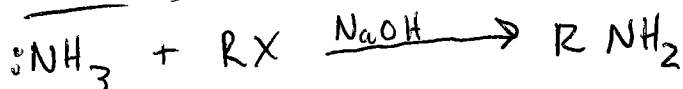
and just like water can be both basic and acidic

pK_b is inverse ($\frac{1}{pK_a}$) of pK_a . High pK_a = low pK_b = weak acid = strong base

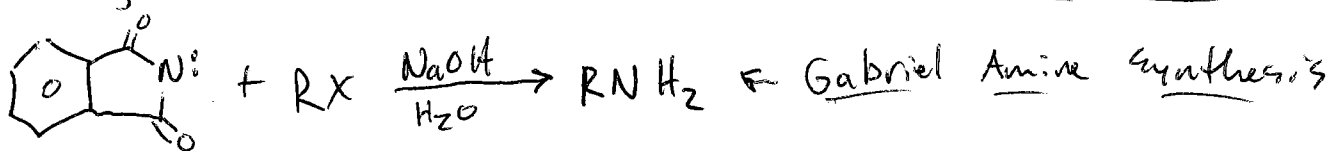


Reactions There are 3 types of syntheses: ① SN2, ② Reduction, ③ Rearrangement

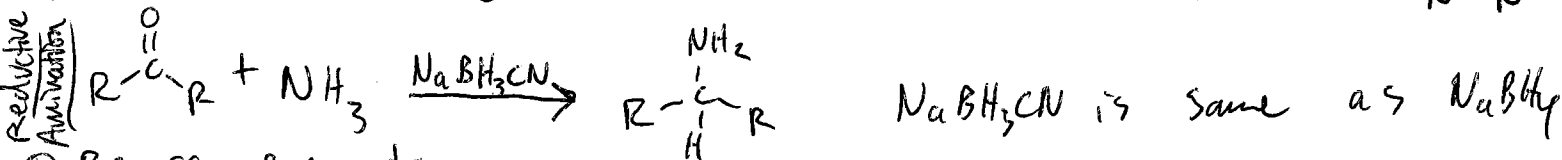
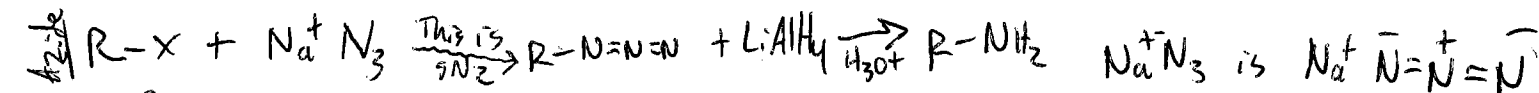
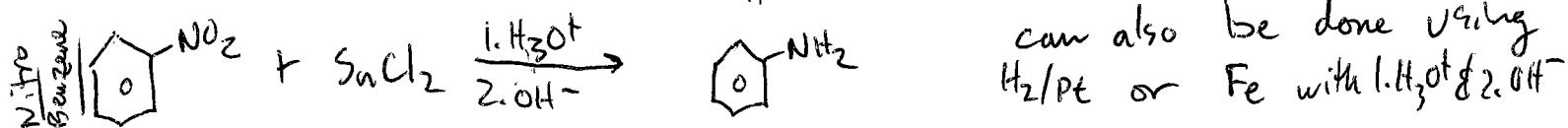
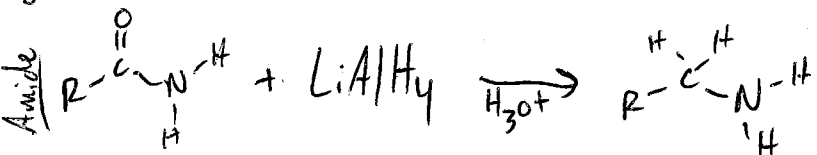
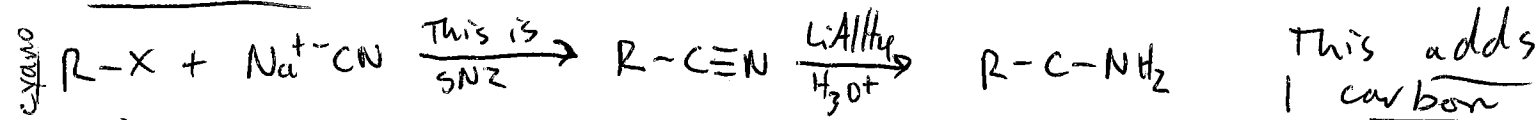
① SN2 Amine Reactions



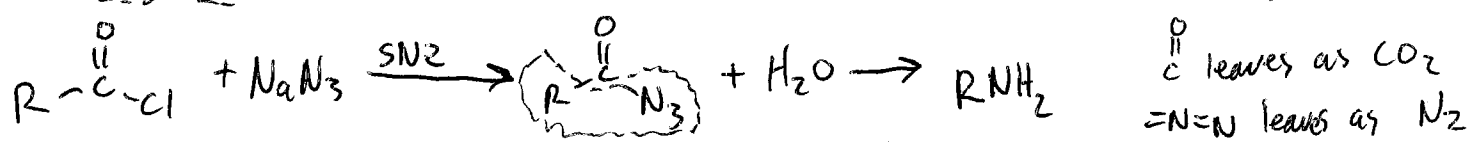
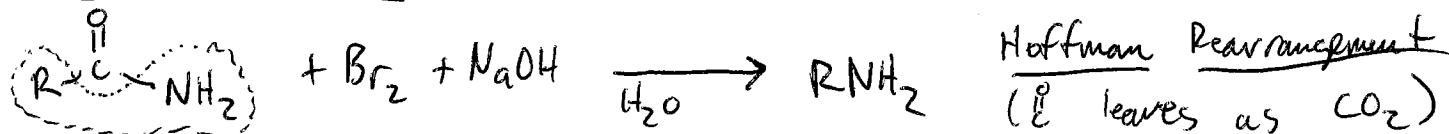
"NH₃" can be NH₃, NR₂H, NR₂H, or NR₃
all react the same



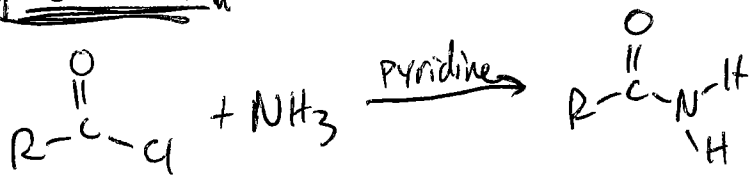
② Reductions



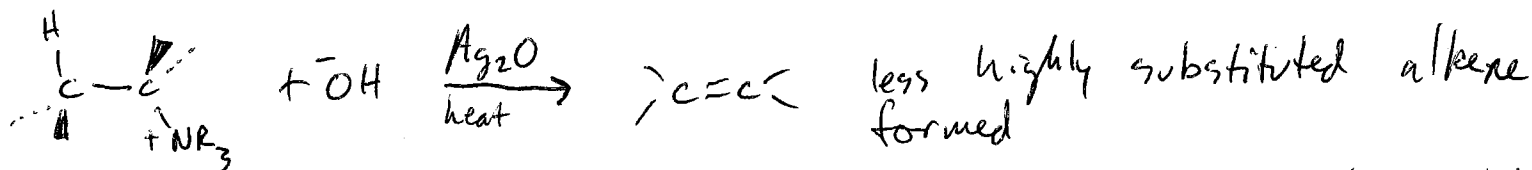
③ Rearrangements



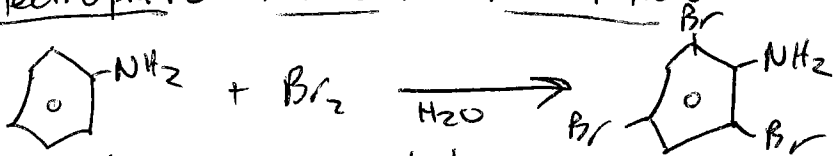
Reactions



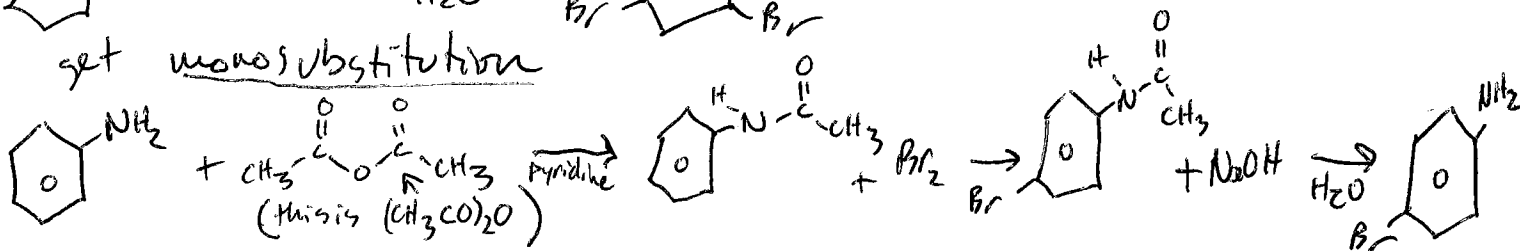
This is aminolysis as we saw in CH 21, -Cl could also be anhydride $-O-C(=O)-$, or ester $-O-R$



Electrophilic Aromatic substitution with just Amine gives polysubstitution



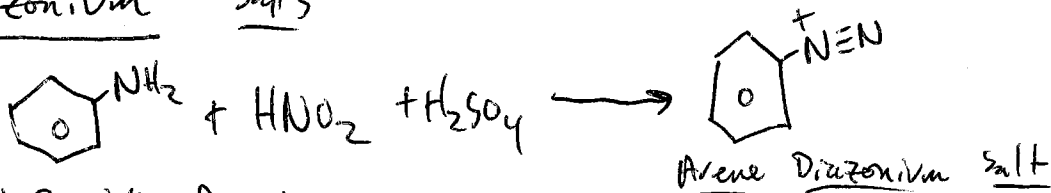
To get monosubstitution



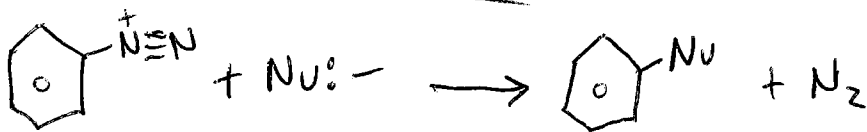
ortho-, para- director

Arene Diazonium Salts

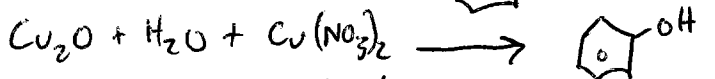
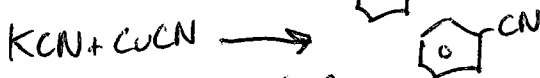
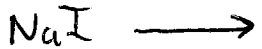
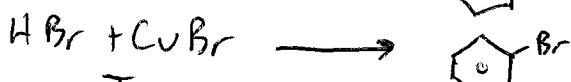
To make:



general Diazonium Reaction

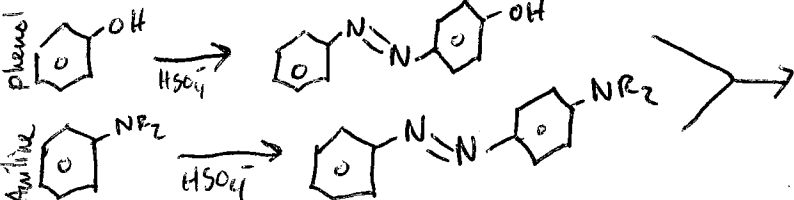


Nu⁻ can be



gives benzene

one of only ways to make phenol

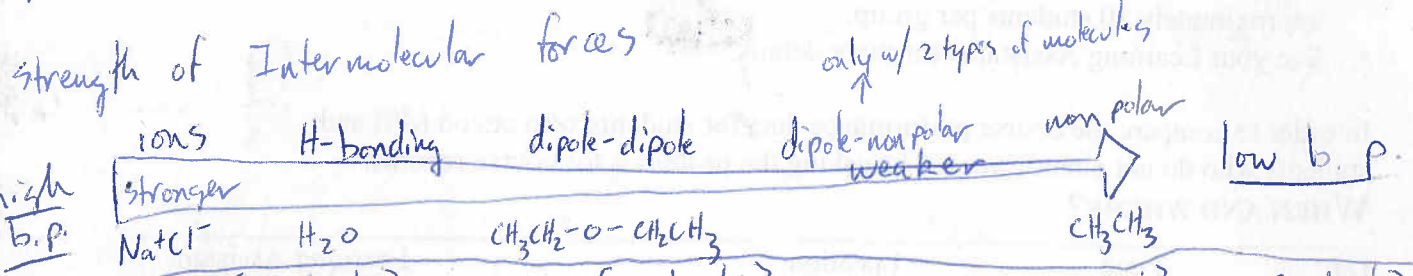


These are Diazonium coupling reactions same as other Arene Diazonium reactions where Nu⁻ is phenol or Aniline

Physical Properties

Boiling Point

What makes a substance a solid rather than liquid or a liquid rather than a gas is how strongly the molecules attract each other. So the stronger the intermolecular forces the higher the boiling point & melting point. Intermolecular forces come from charge differentials, so the more polarized a molecule is in general the higher the boiling point. So ions (Na^+Cl^-) tend to be solid at room temperature, molecules with dipoles & H-bonding tend to be liquid (H_2O , $\text{CH}_3\text{CH}_2\text{OH}$) and nonpolar molecules tend to be gases (H_2 , N_2 , O_2 , Cl_2 , etc.). So to compare relative boiling points you need to compare strengths of Intermolecular forces.



pKa



$$K_a = \frac{\{\text{A}^-\}\{\text{H}_3\text{O}^+\}}{\{\text{HA}\}\{\text{H}_2\text{O}\}} \quad \text{or} \quad \frac{\{\text{products}\}}{\{\text{reactants}\}}$$

so big $K_a = \frac{\{\text{P}\}}{\{\text{R}\}}$ or highly acidic

$\text{p}K_a = -\log K_a$ or $\text{p}K_a = 10^{-K_a} = \frac{1}{10^{K_a}}$ so bigger $K_a =$ smaller $\text{p}K_a$

Strong Acids have small $\text{p}K_a$'s & big K_a 's

What makes an acid an acid is that the products (conjugate base) are more stable than reactants. Anything that helps stabilize A^- makes HA more acidic. For example carboxylic Acids

