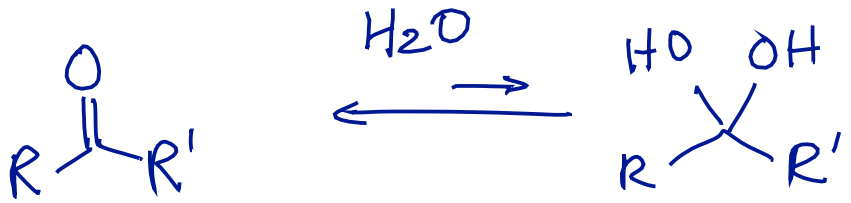
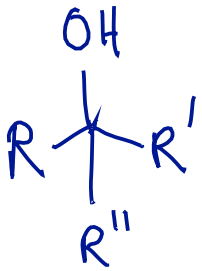
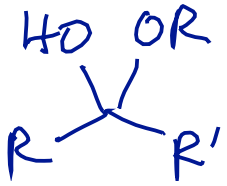
Recap: Aldehydes and Ketones

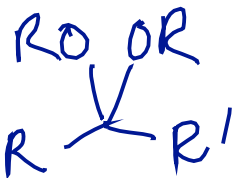


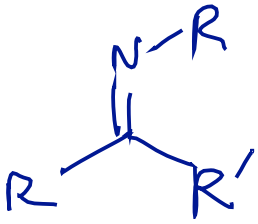
organometallic or hydride



or







Know reagents and mechanisms!

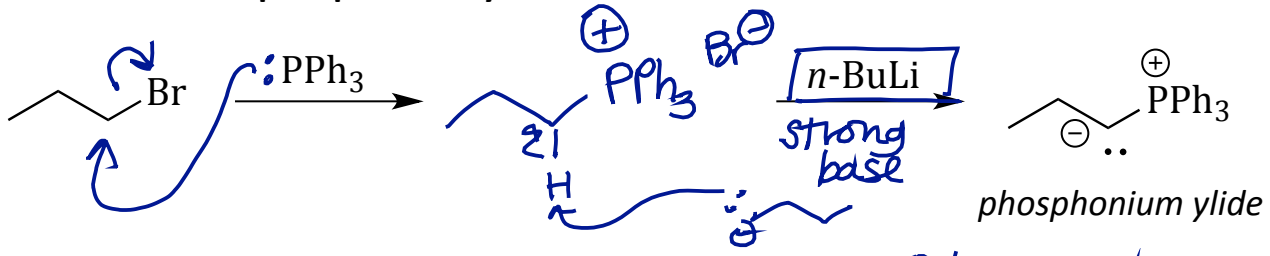
PINK THURSDAYS! (U)

pronounced "Vittig" 1979

Week 4 July 16, 2014

The Wittig Reaction:
Synthesizing Alkenes from Carbonyls

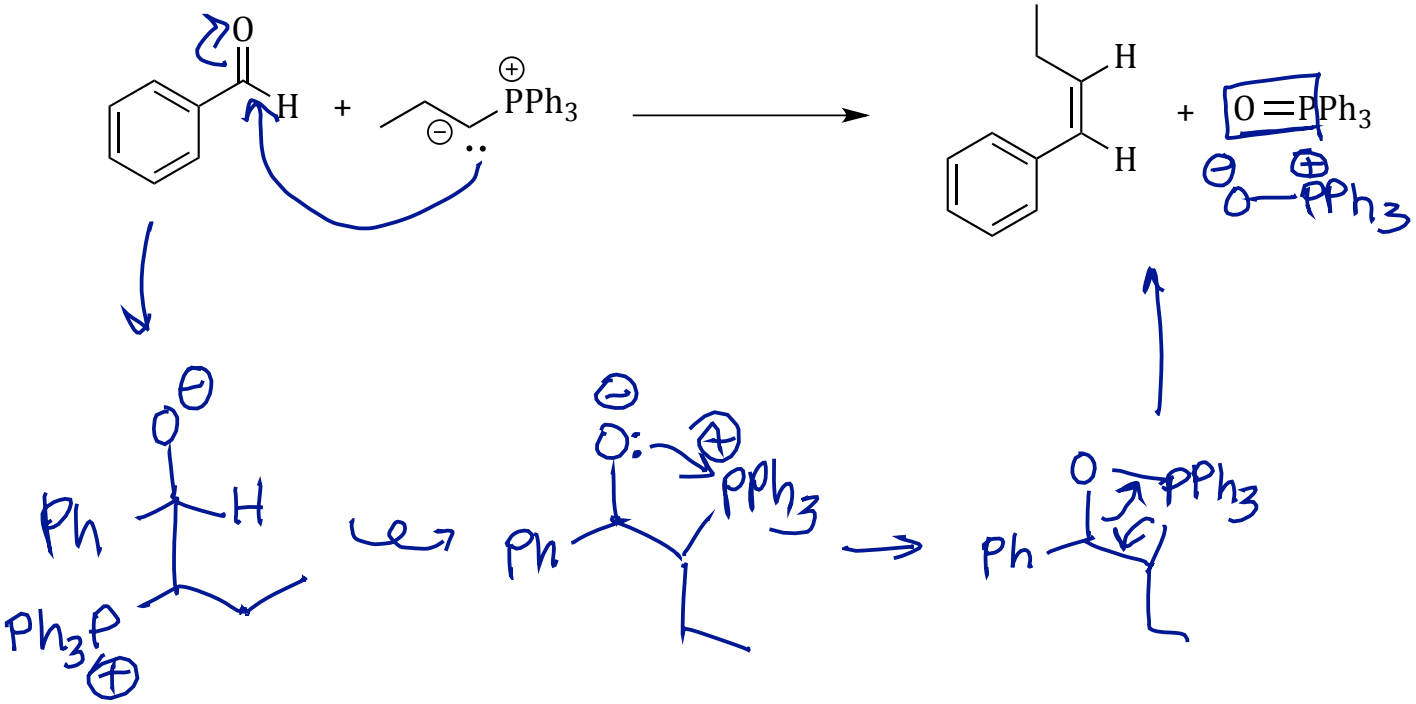
The Wittig reaction is a remarkably useful synthesis of alkenes. First, an alkyl halide is used to form a **phosphonium ylide.** Provide a curved-arrow mechanism.



phosphonium salt

⊕/⊖ on adjacent atoms

Then the phosphonium ylide is added to an aldehyde or ketone to yield a new carbon-carbon **double** bond! Provide a mechanism.



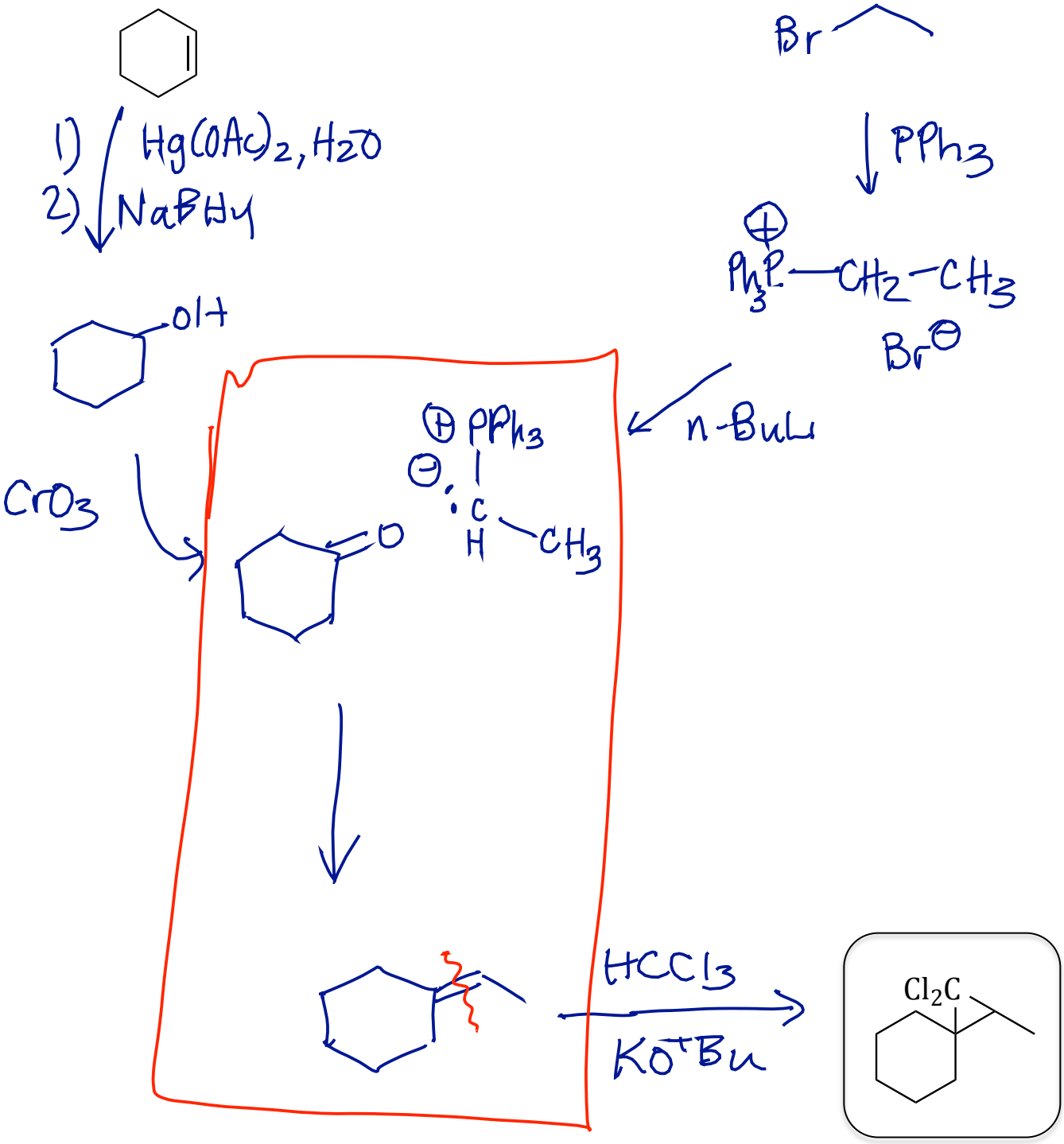
phosphorus is oxophilic

** The Wittig reaction tends to give *cis* alkenes when there is a choice. **

Reading: Section 19.13

The Wittig Reaction in Synthesis

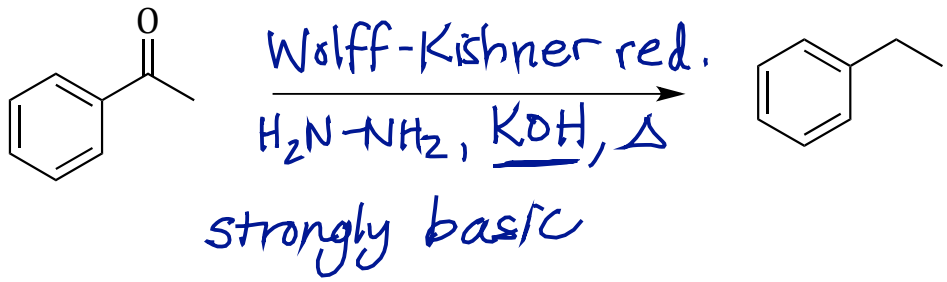
How would you carry out the following transformation?

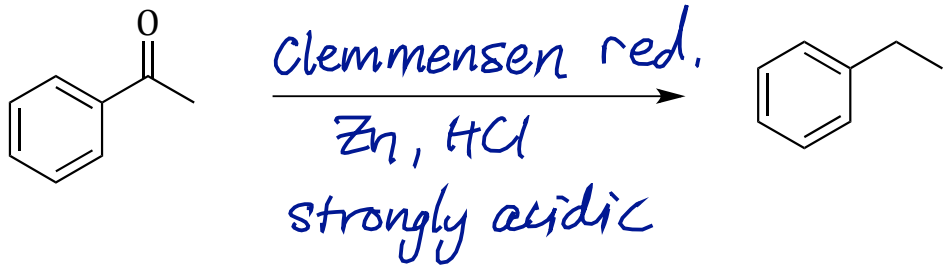


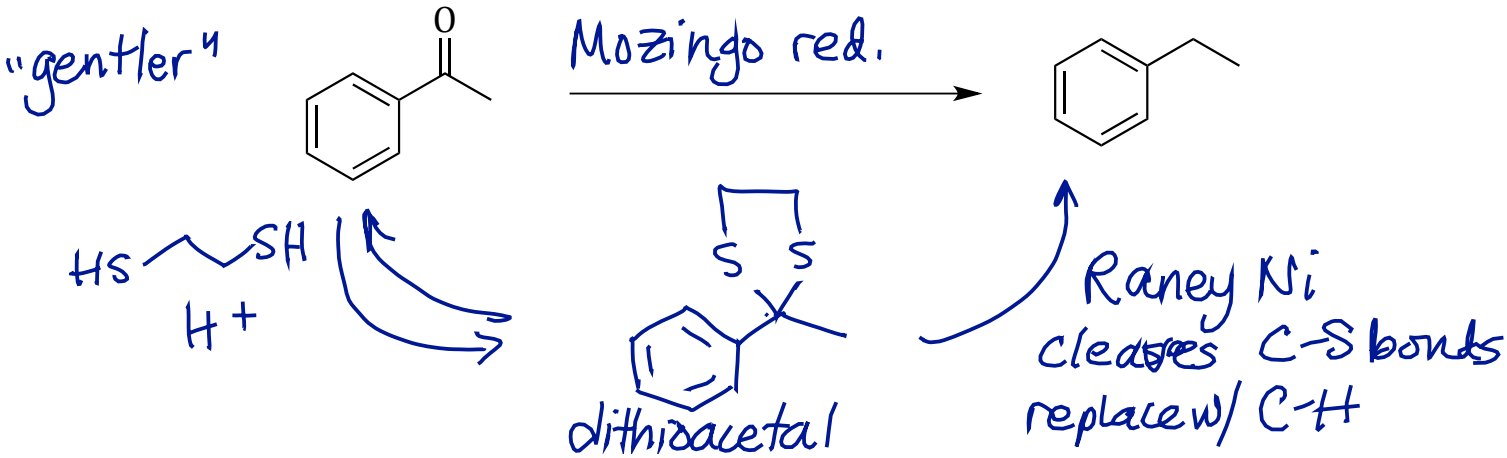
Reading: Section 19.13

"Removing" a Carbonyl Group from Aldehydes & Ketones

What reagents could you use to carry out the following transformations?







*** The Wolff-Kishner & Clemmensen reactions only work on carbonyl groups at the ketone oxidation level! ***

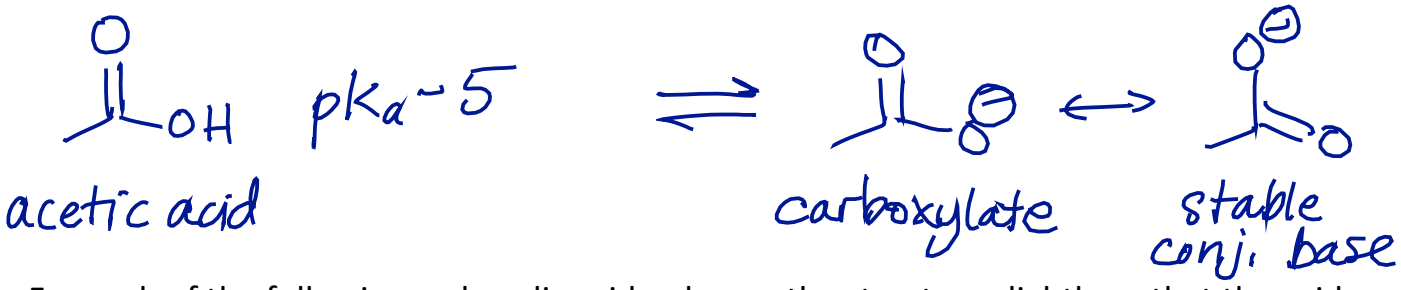
Reading: Section 19.12

carboxylic acid oxidation level!

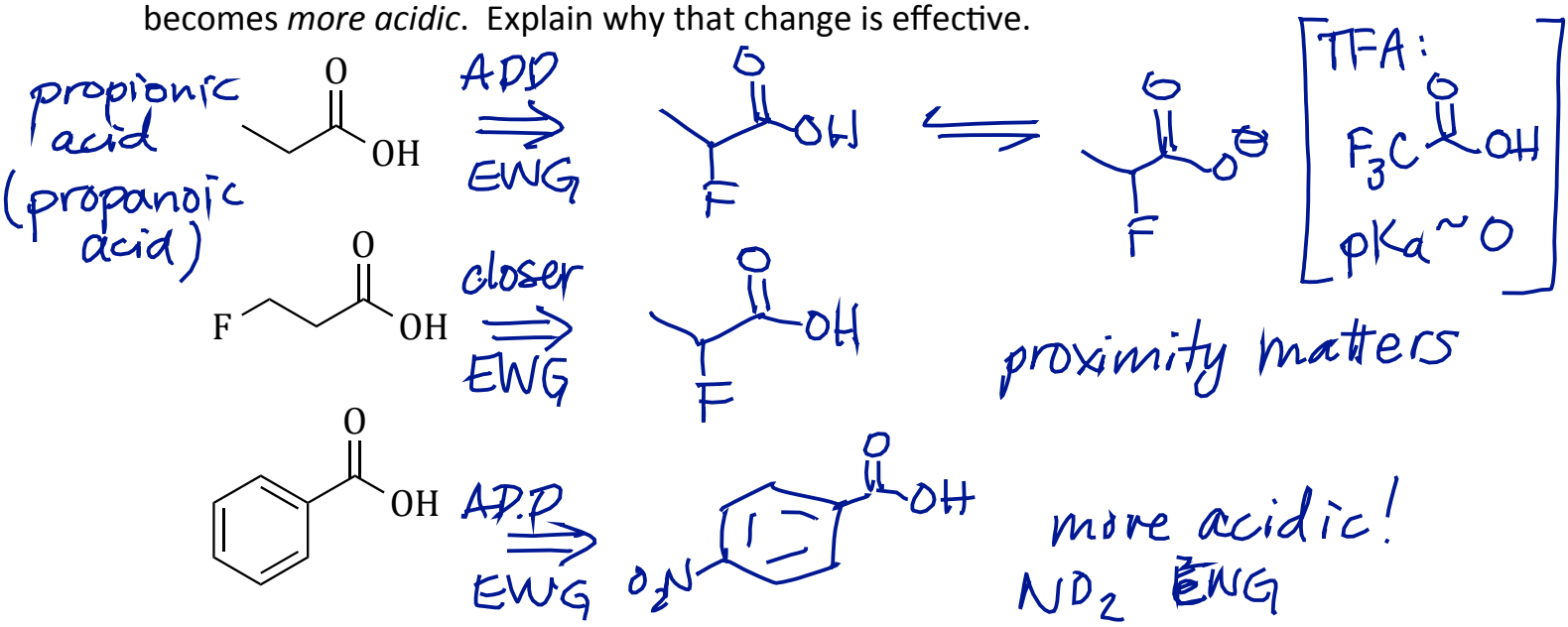
Week 4 July 17, 2014

Acidity of Carboxylic Acids

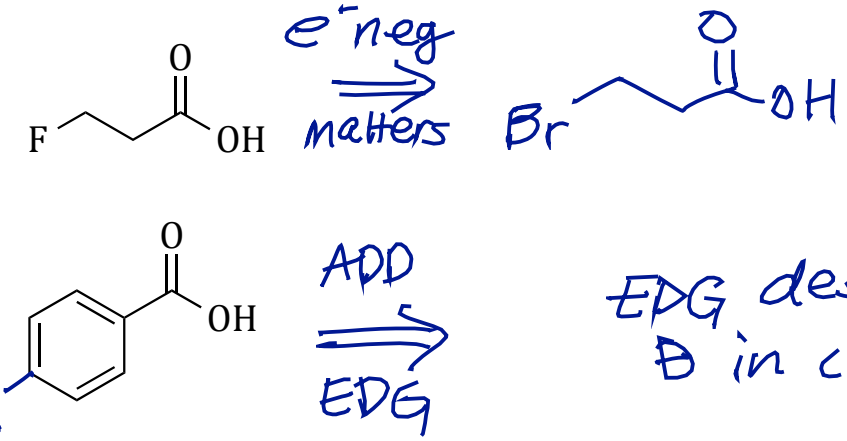
Draw some examples of carboxylic acids. Why are they acidic? What is a typical pK_a?



For each of the following carboxylic acids, change the structure slightly so that the acid becomes *more acidic*. Explain why that change is effective.



For each of the following carboxylic acids, change the structure slightly so that the acid becomes *less acidic*. Explain why that change is effective.

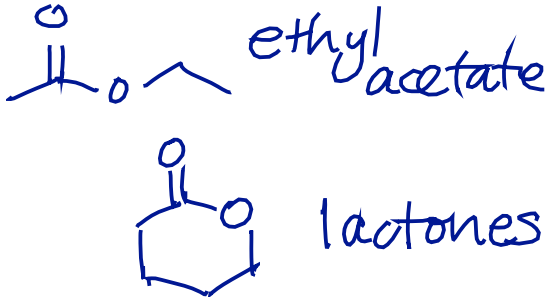


Reading: Section 20.1 and 20.4

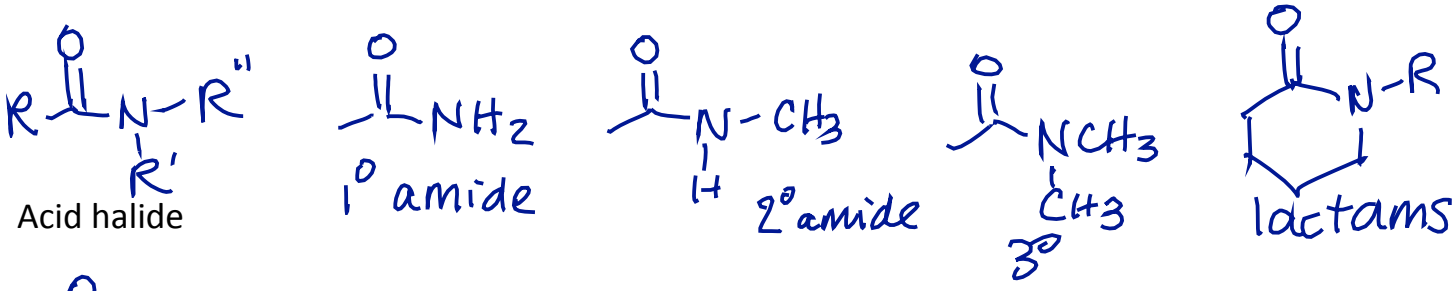
Carboxylic Acid Derivatives

Draw some examples of each of the following carboxylic acid derivatives (CADs):

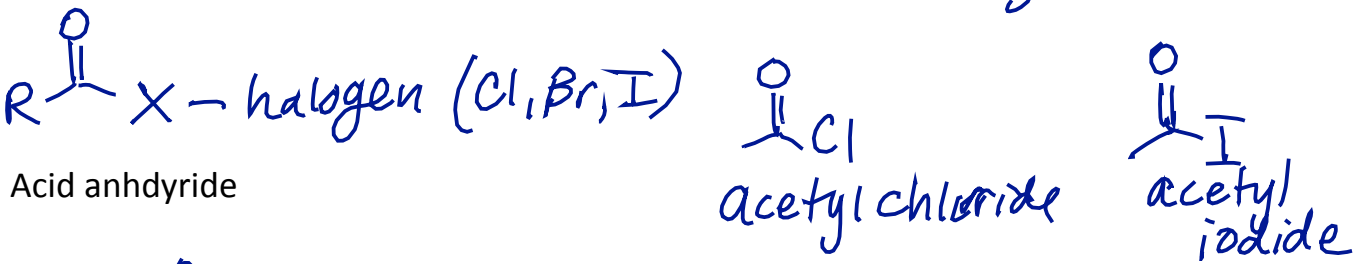
Ester (and lactone)



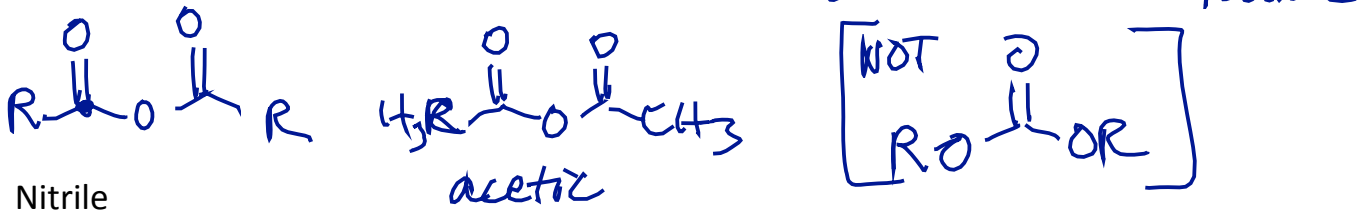
Amide (and lactam)



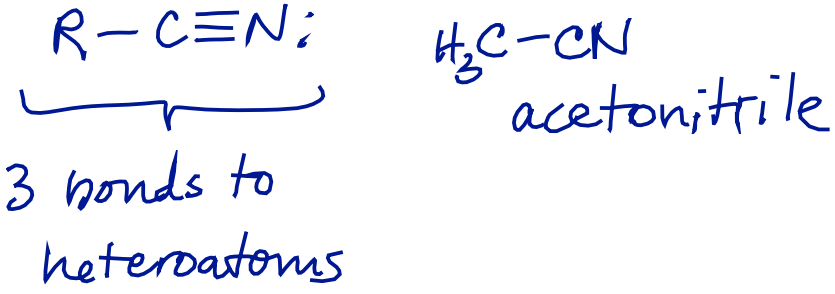
Acid halide



Acid anhdyride



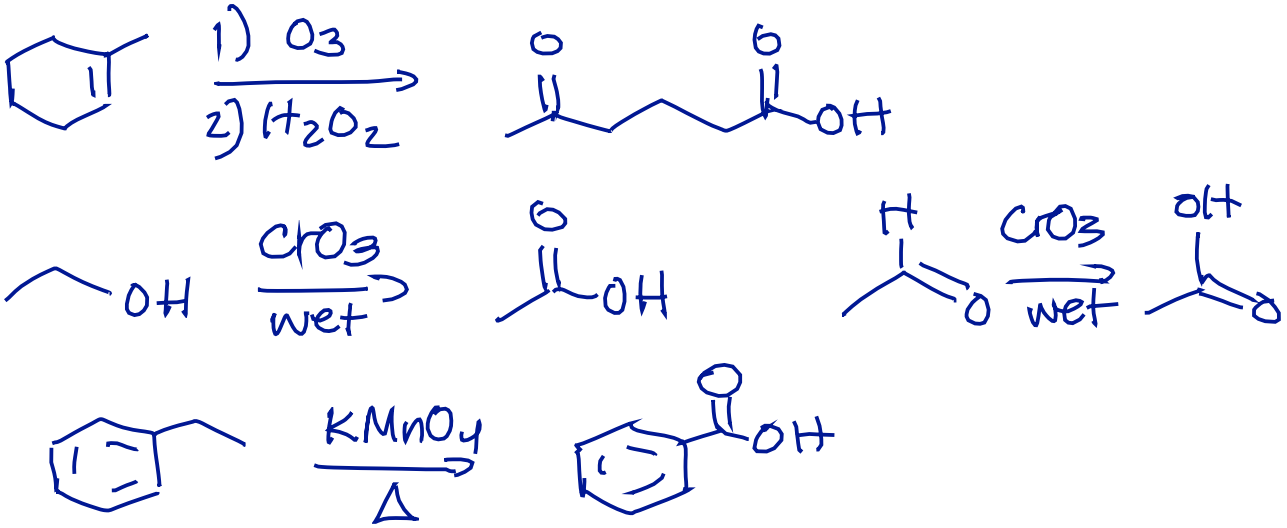
Nitrile



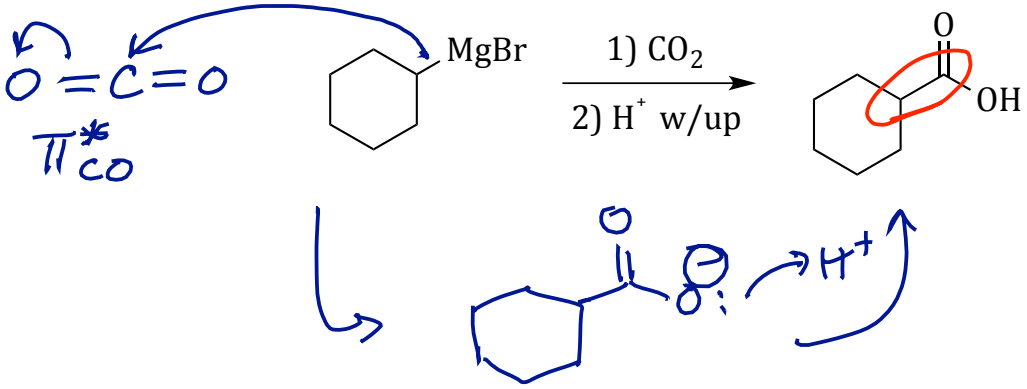
Reading: Section 21.1

Some Syntheses of Carboxylic Acids & Nitriles

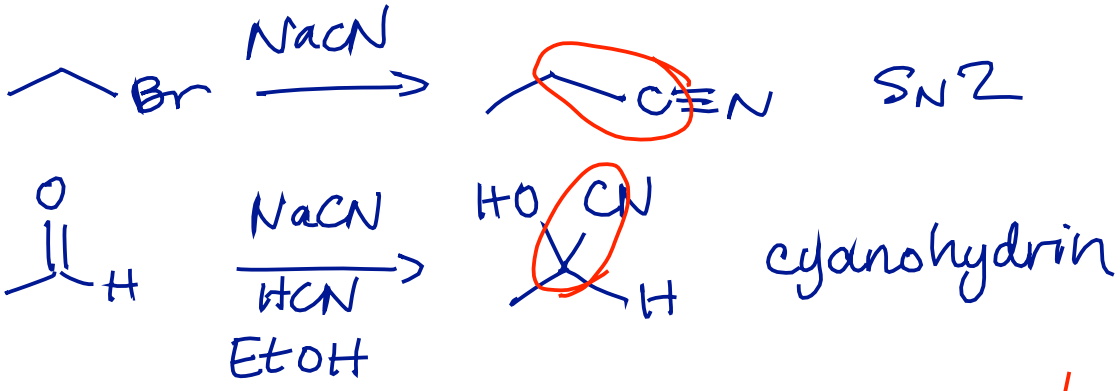
You already know some ways of making carboxylic acids. What are they?



Here's another way to make a carboxylic acid. Can you draw the mechanism?



You also know some ways to make nitriles. What are they? Why are they special?

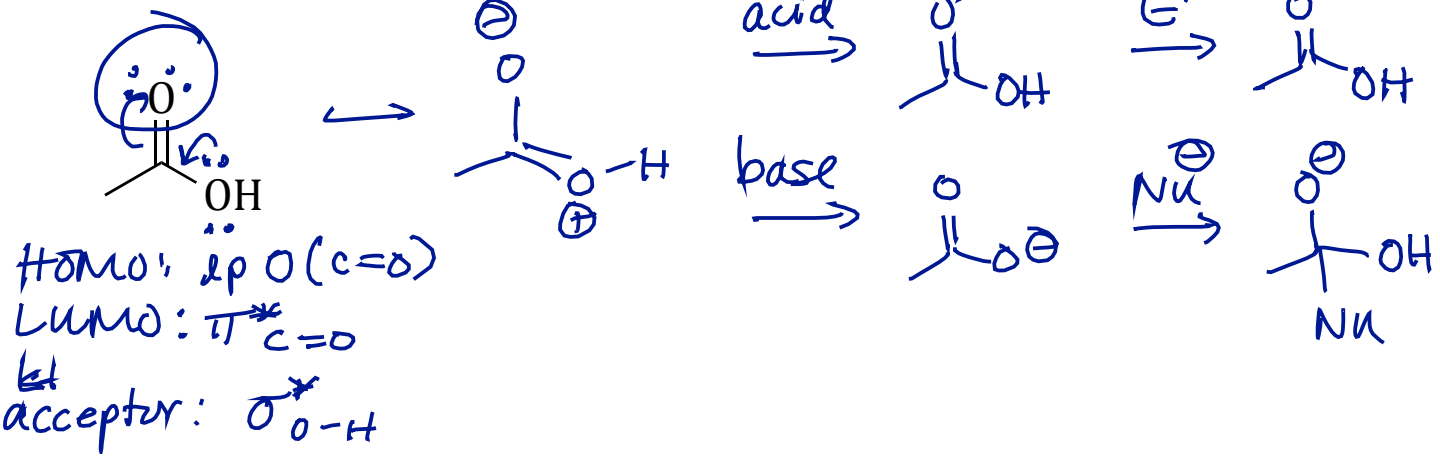


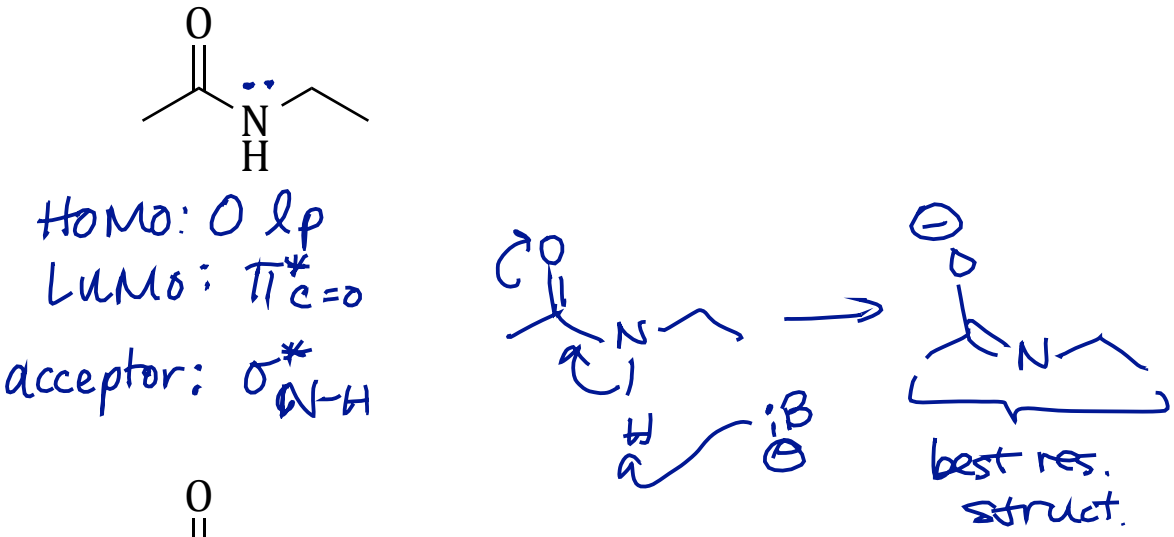
Reading: Section 20.6

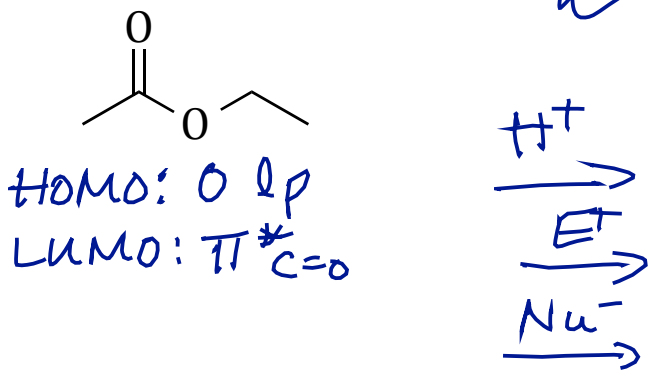
new C-C bonds!

Frontier Orbitals of Carboxylic Acids & Derivatives

For each of the following species, identify the HOMO and LUMO and predict how the molecule will react with an acid, with a base, with a nucleophile, and with an electrophile. Explain your reasoning in each case.

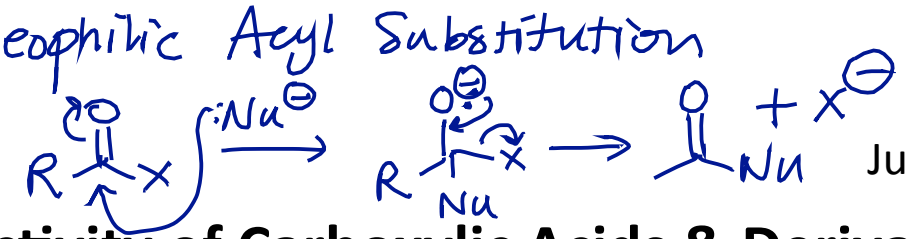






Reading: Section 20.7

Week 4

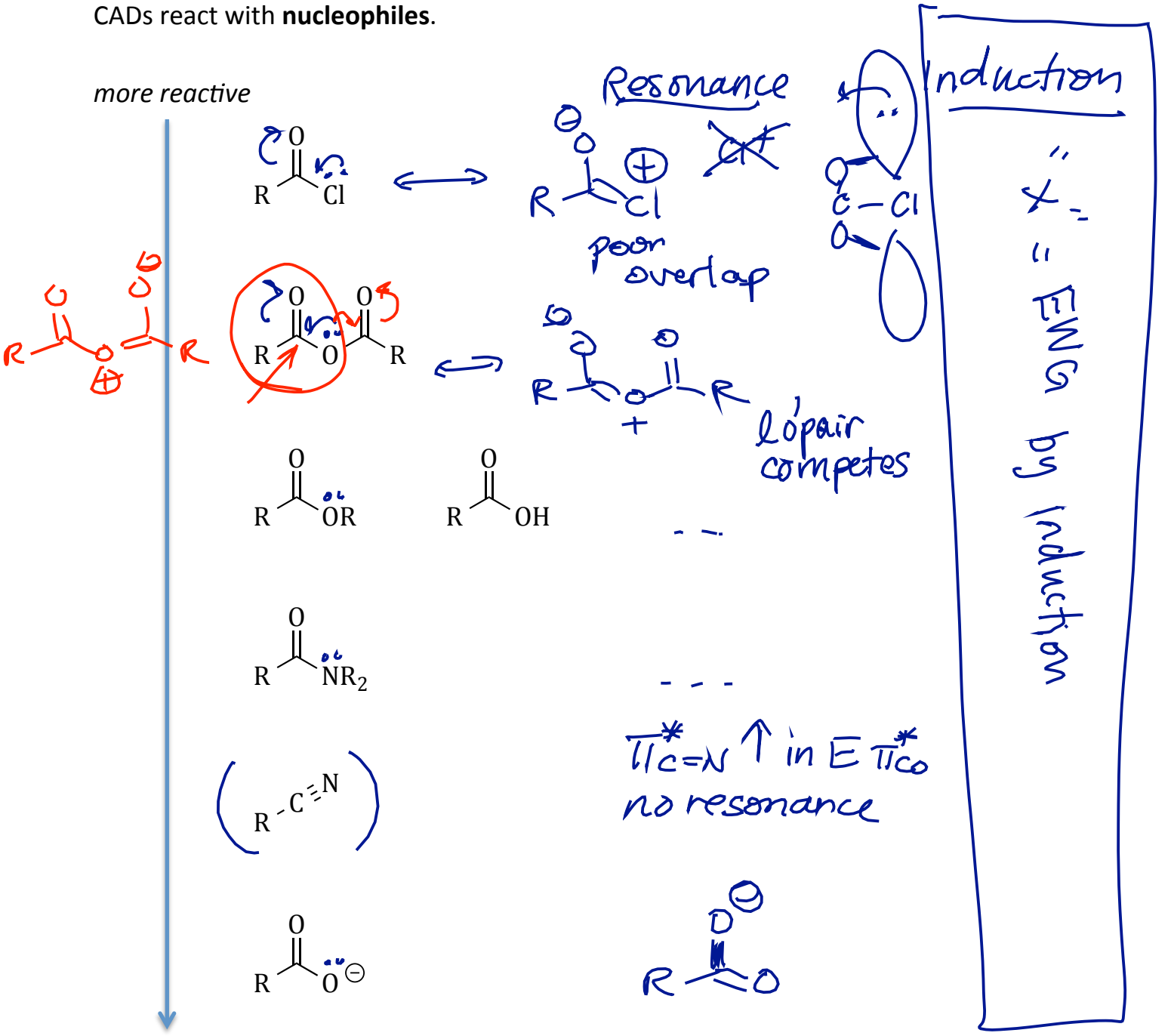


July 17, 2014

Reactivity of Carboxylic Acids & Derivatives

Explain the following relative order of reactivity, which is observed whenever these CADs react with **nucleophiles**.

more reactive



less reactive

Reading: Section 21.7

1) Nucl. Attack
2) LPP

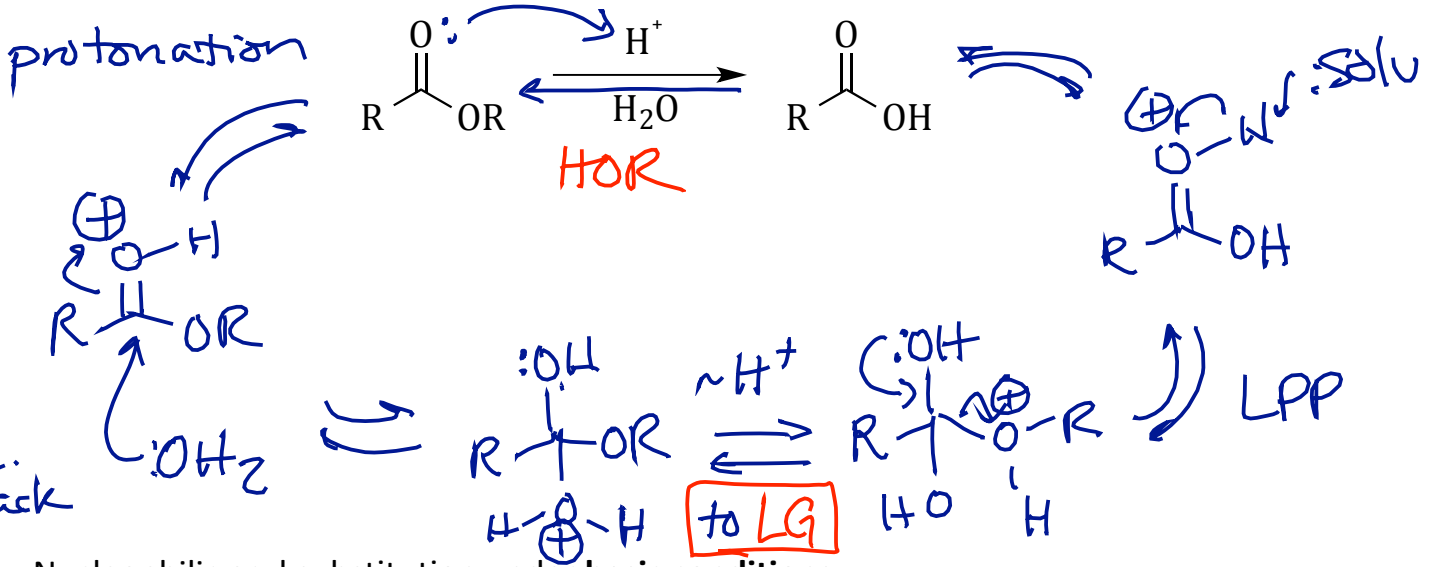
Week 4 July 17, 2014

Converting Between Carboxylic Acid Derivatives

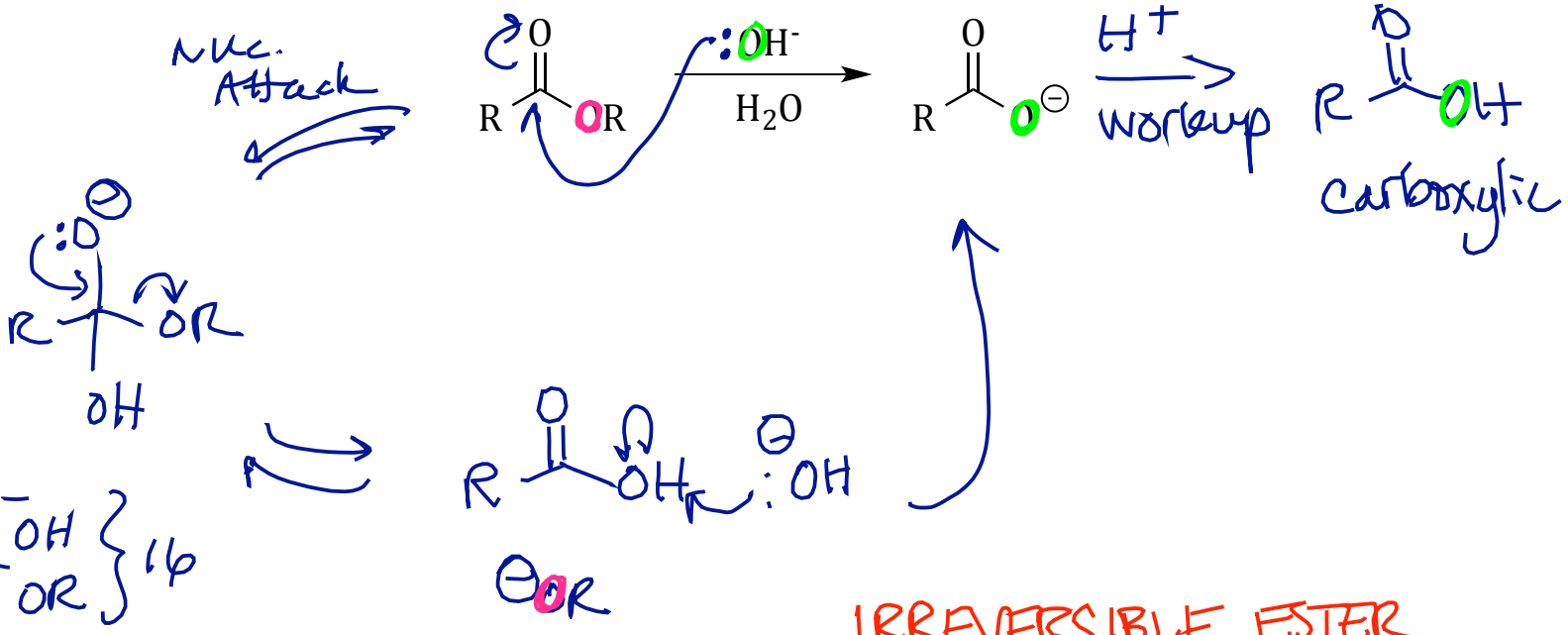
One carboxylic acid derivative can be converted into another by **nucleophilic acyl substitution**. There are two types of mechanisms; draw curved-arrow mechanisms for each.

REVERSIBLE ESTER HYDROLYSIS, H+

Nucleophilic acyl substitution under **acidic conditions**:



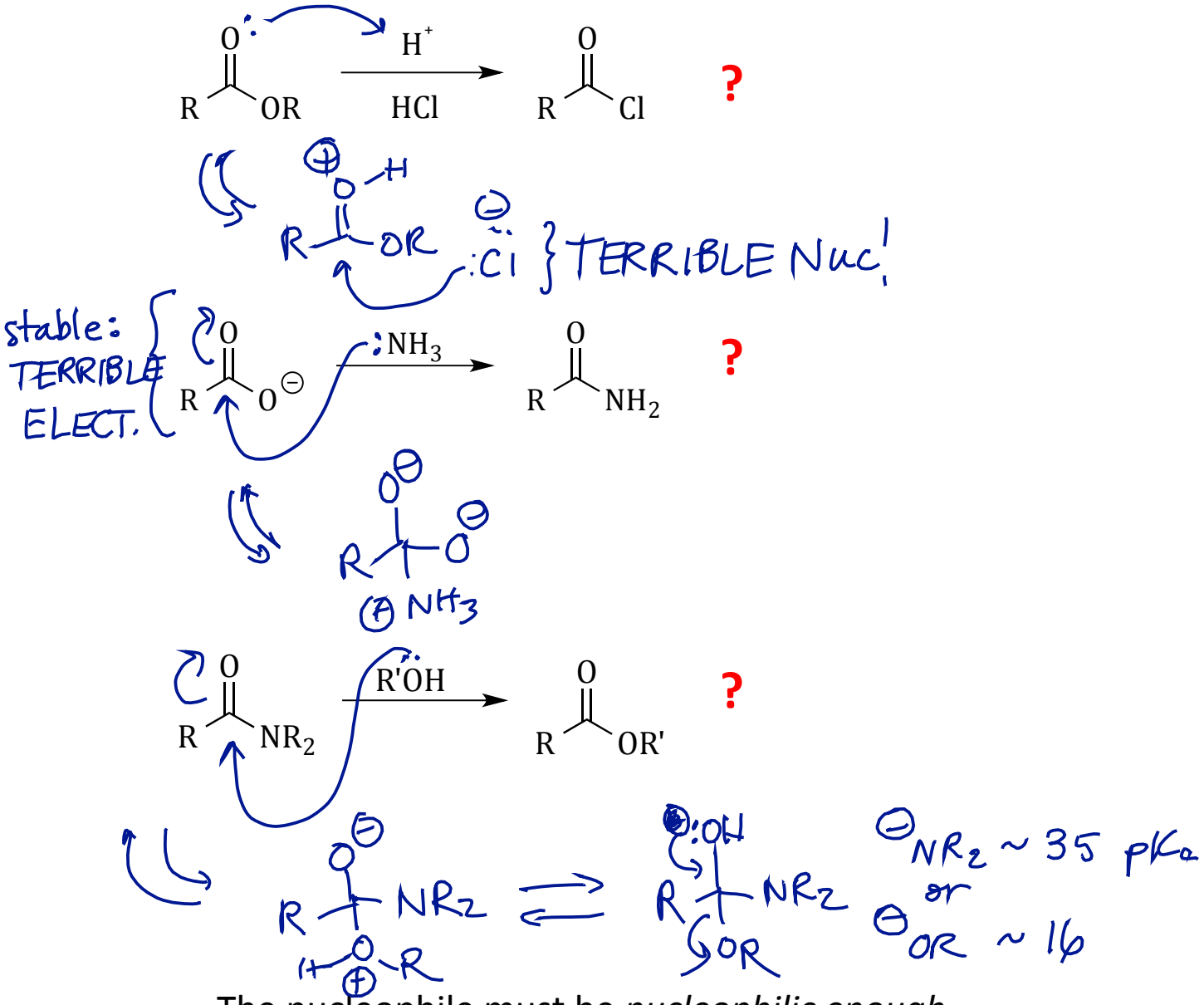
Nucleophilic acyl substitution under **basic conditions**:



IRREVERSIBLE ESTER HYDROLYSIS. BASIC

Reading: Section 21.7

Converting Between Carboxylic Acid Derivatives: Some Problems



The nucleophile must be *nucleophilic enough*

The electrophile must be *electrophilic enough*

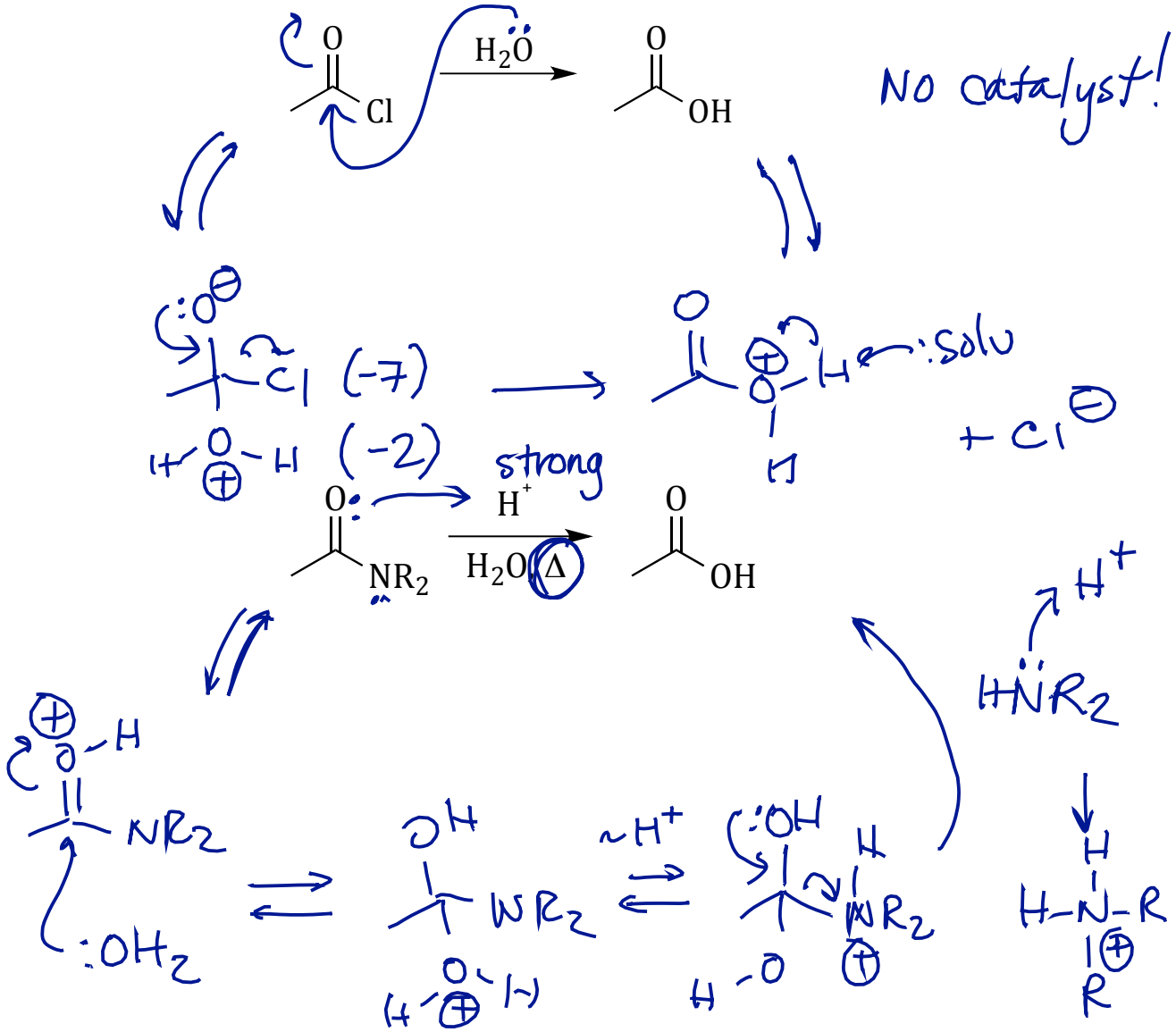
The incoming nucleophile must be a *worse leaving group* than the outgoing one.

Reading: Section 19.13

Making Carboxylic Acids from Other CADs

Rule 1: Any carboxylic acid derivative can be *hydrolyzed* to a carboxylic acid

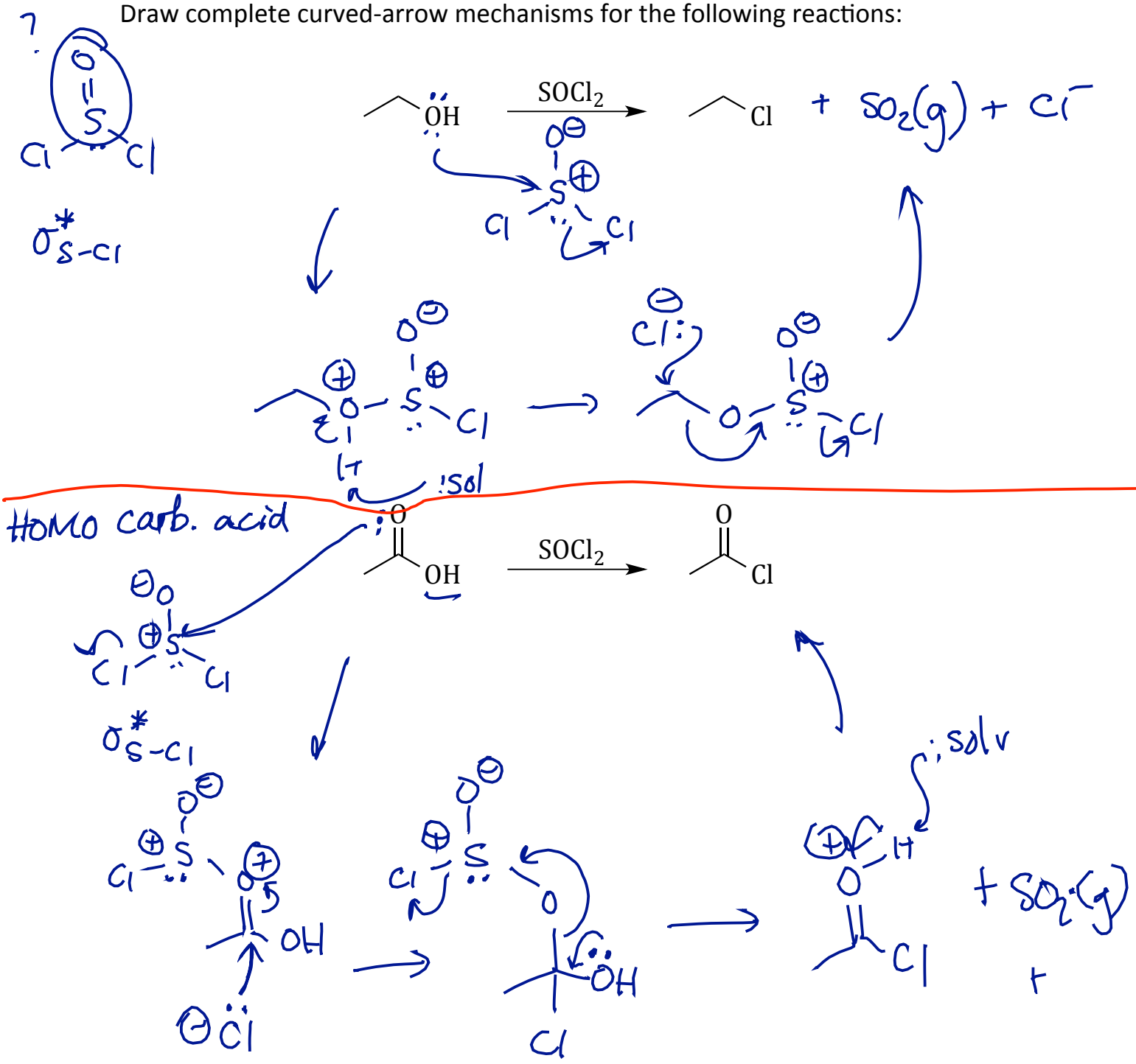
Draw complete curved-arrow mechanisms for the following reactions:



Reading: Section 21.7

Rule 2: Acid Chlorides can only be made from Carboxylic Acids

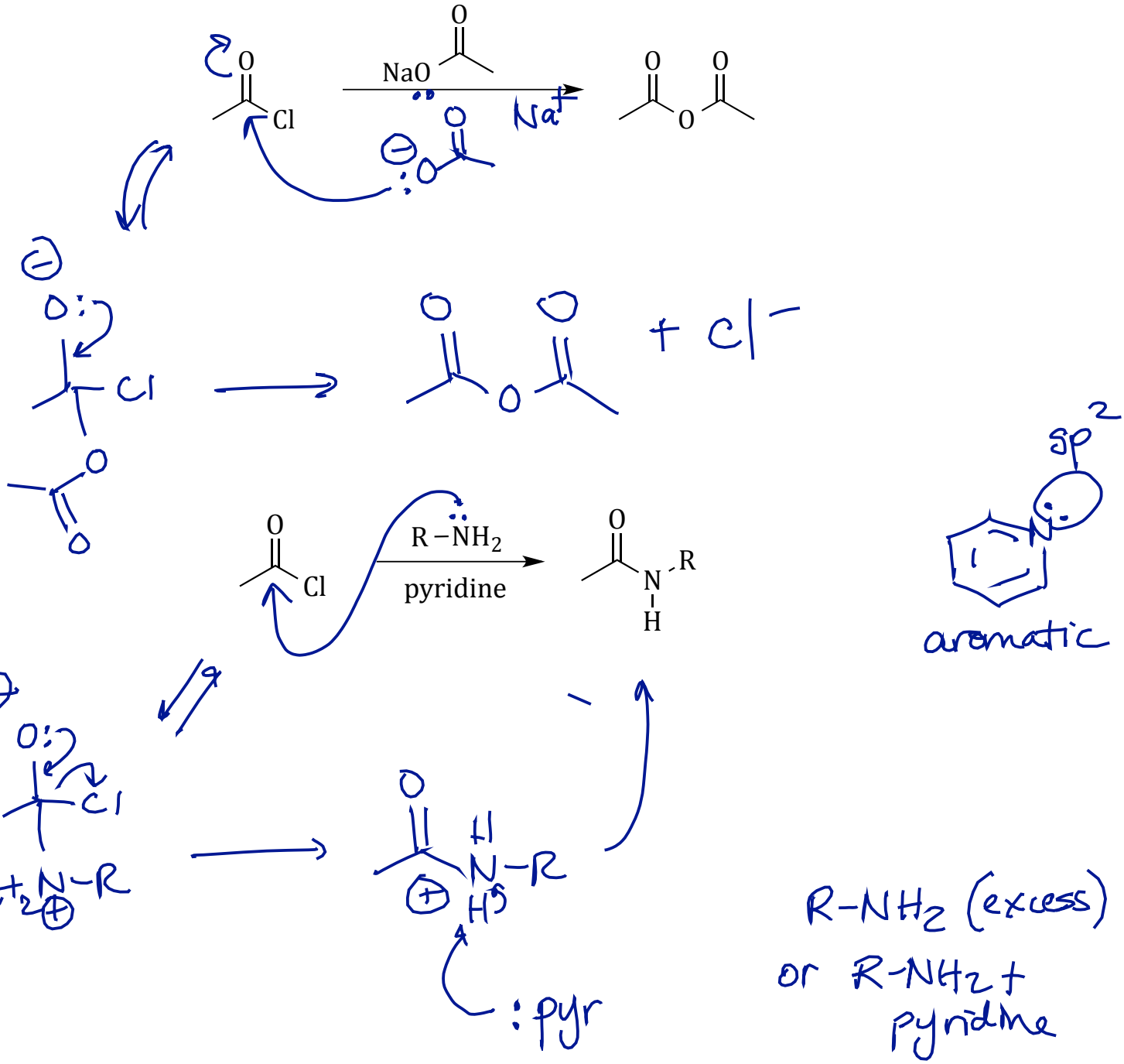
Draw complete curved-arrow mechanisms for the following reactions:



Reading: Section 20.9

Rule 3: Acid Chlorides be turned into any other CAD

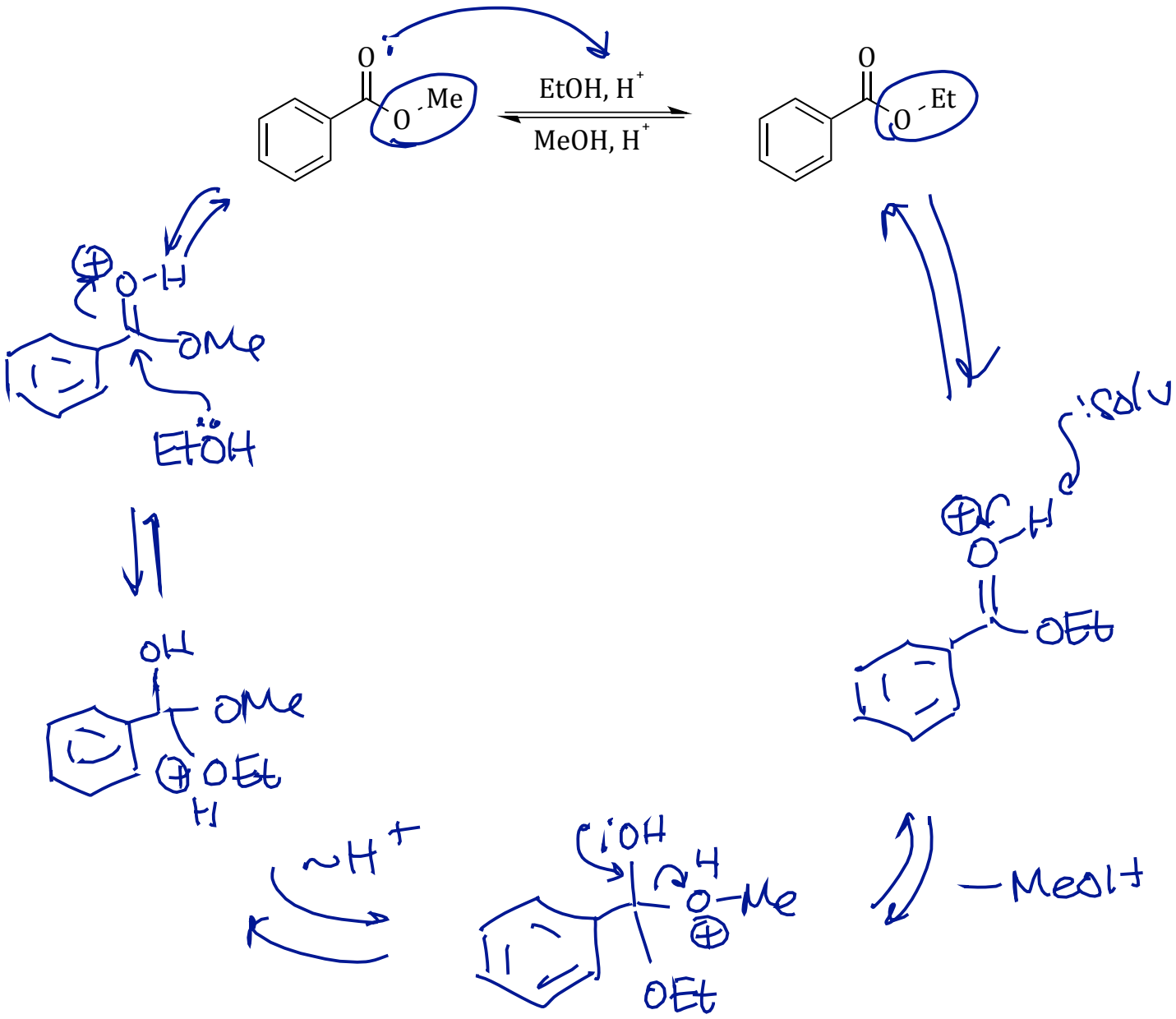
Draw complete curved-arrow mechanisms for the following reactions:



Reading: Section 20.9

Ester → A different Ester

Transesterification:
Le Chatelier's Principle at work



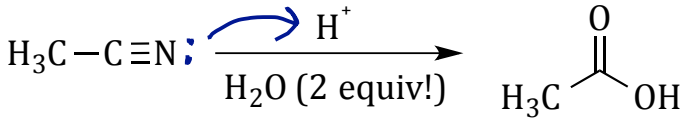
Reading: Section 21.8

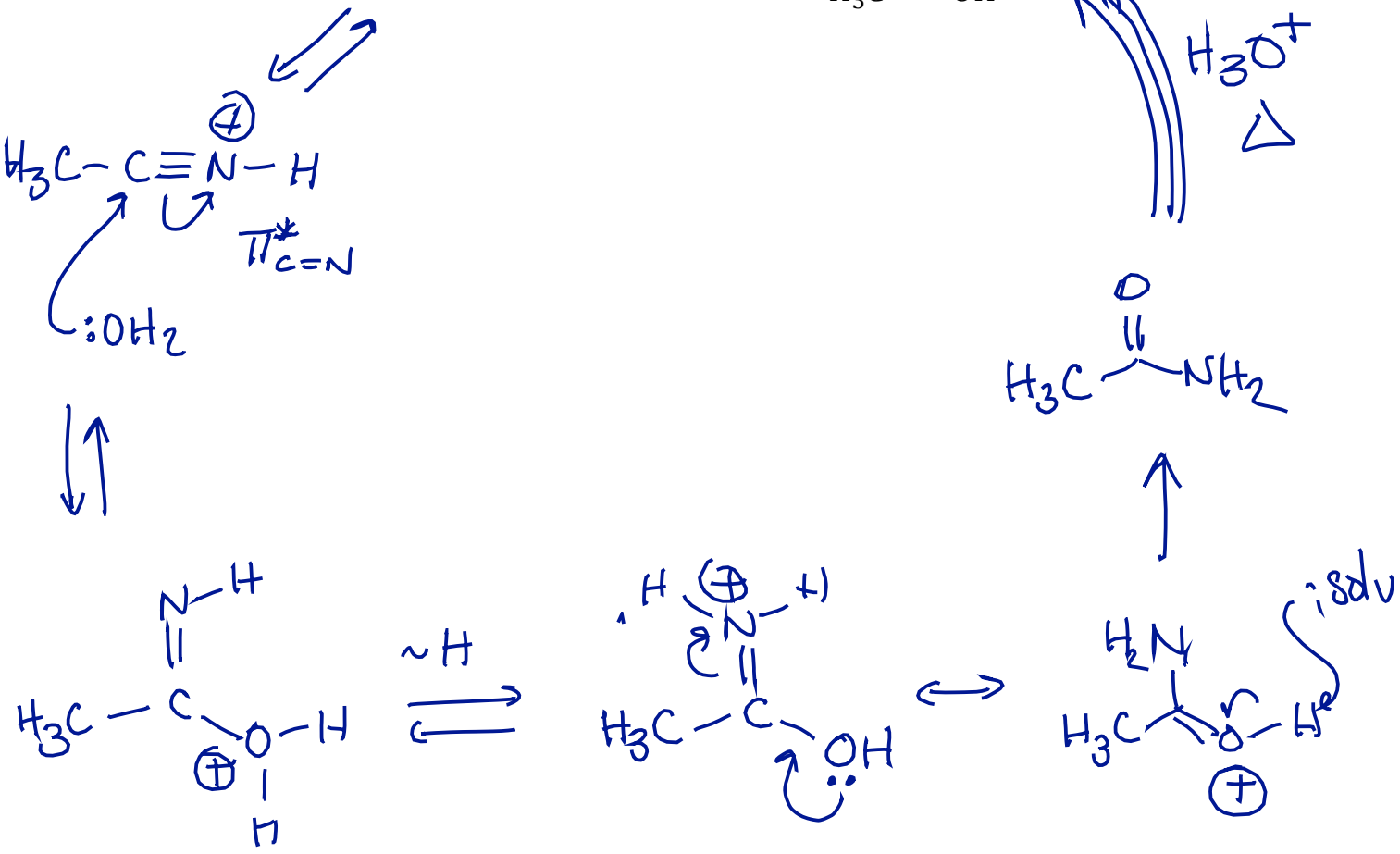
$R-C\equiv N:$

Week 4 July 17, 2014

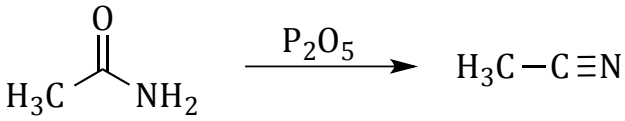
Nitriles:
"Masked" 1° Amides

Provide a complete curved-arrow mechanism for the following reaction:

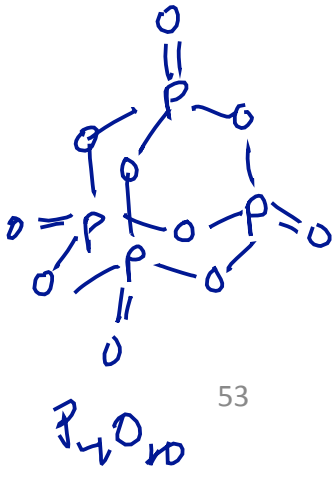




Nitriles can be synthesized by dehydration of primary amides:

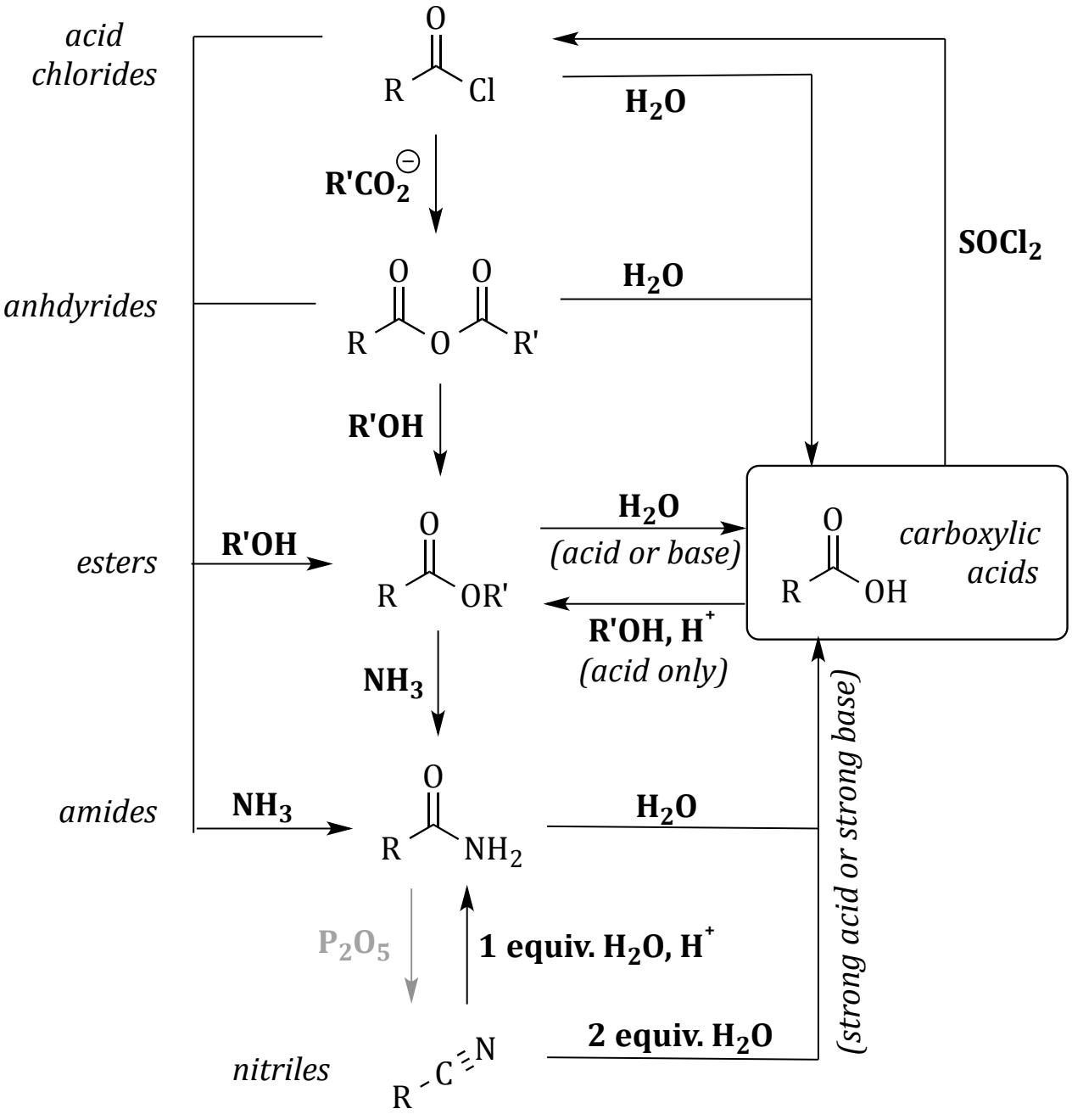


1° amide → nitrile

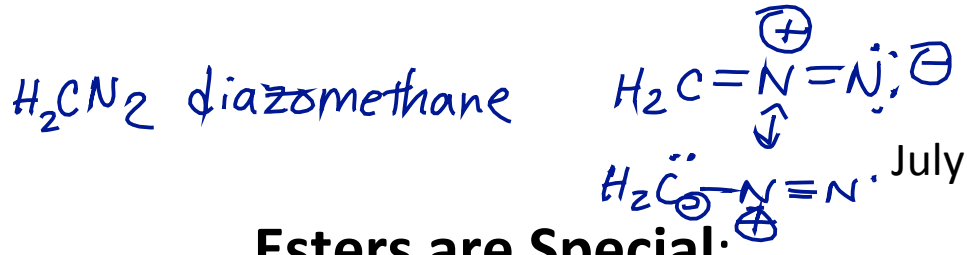


Reading: Section 21.7

Putting it Together: Interconverting Between CADs



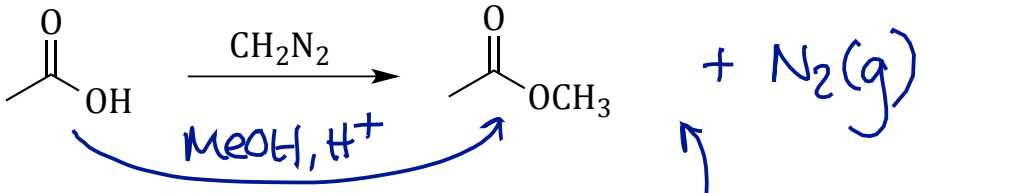
Reading: Section 20.9

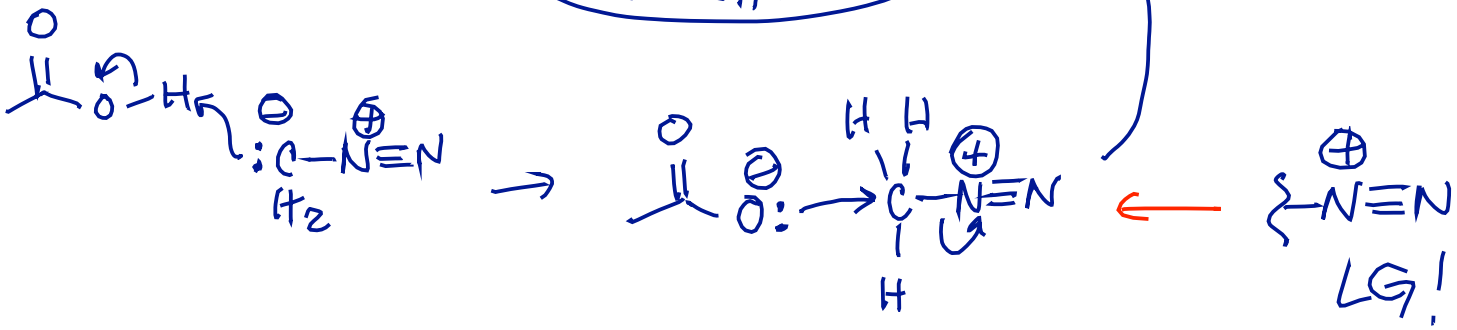


July 17, 2014

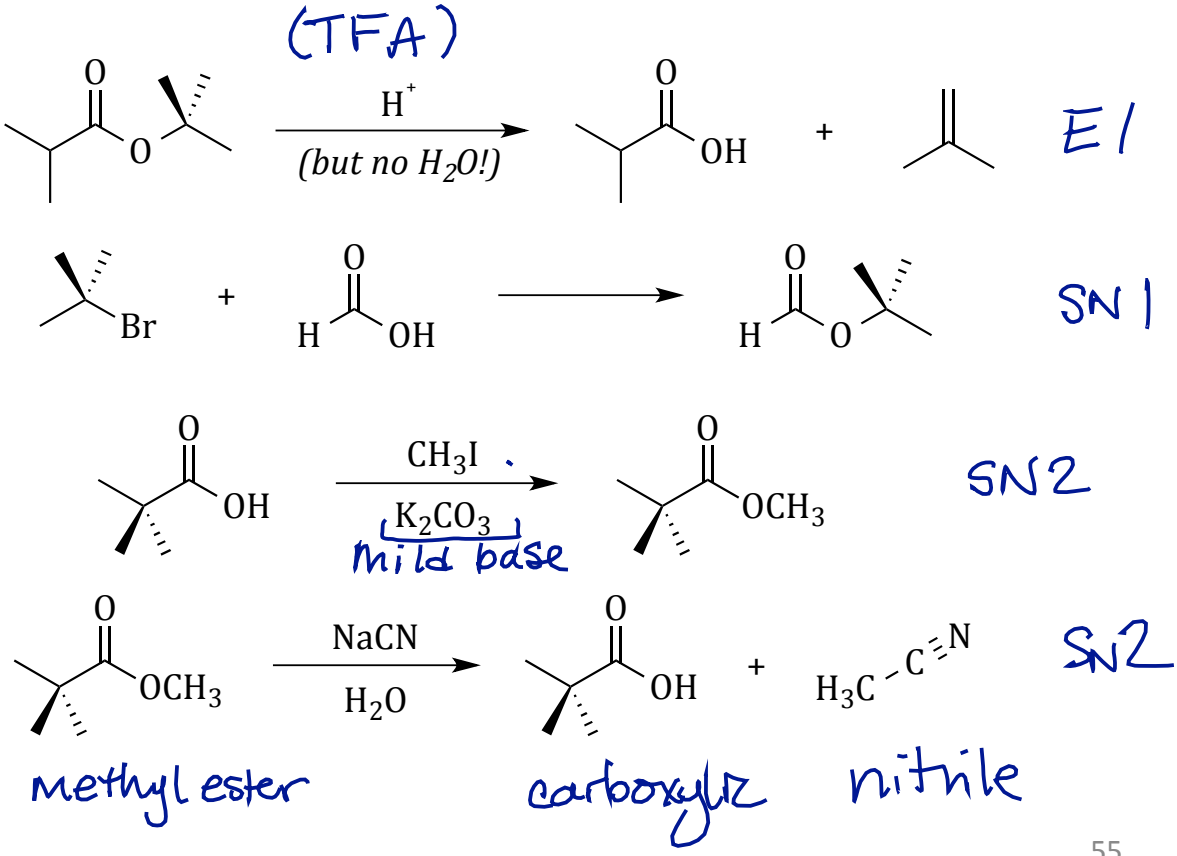
Esters are Special:
Other Mechanisms of Formation/Hydrolysis

Draw a complete curved-arrow mechanism for the following reaction:

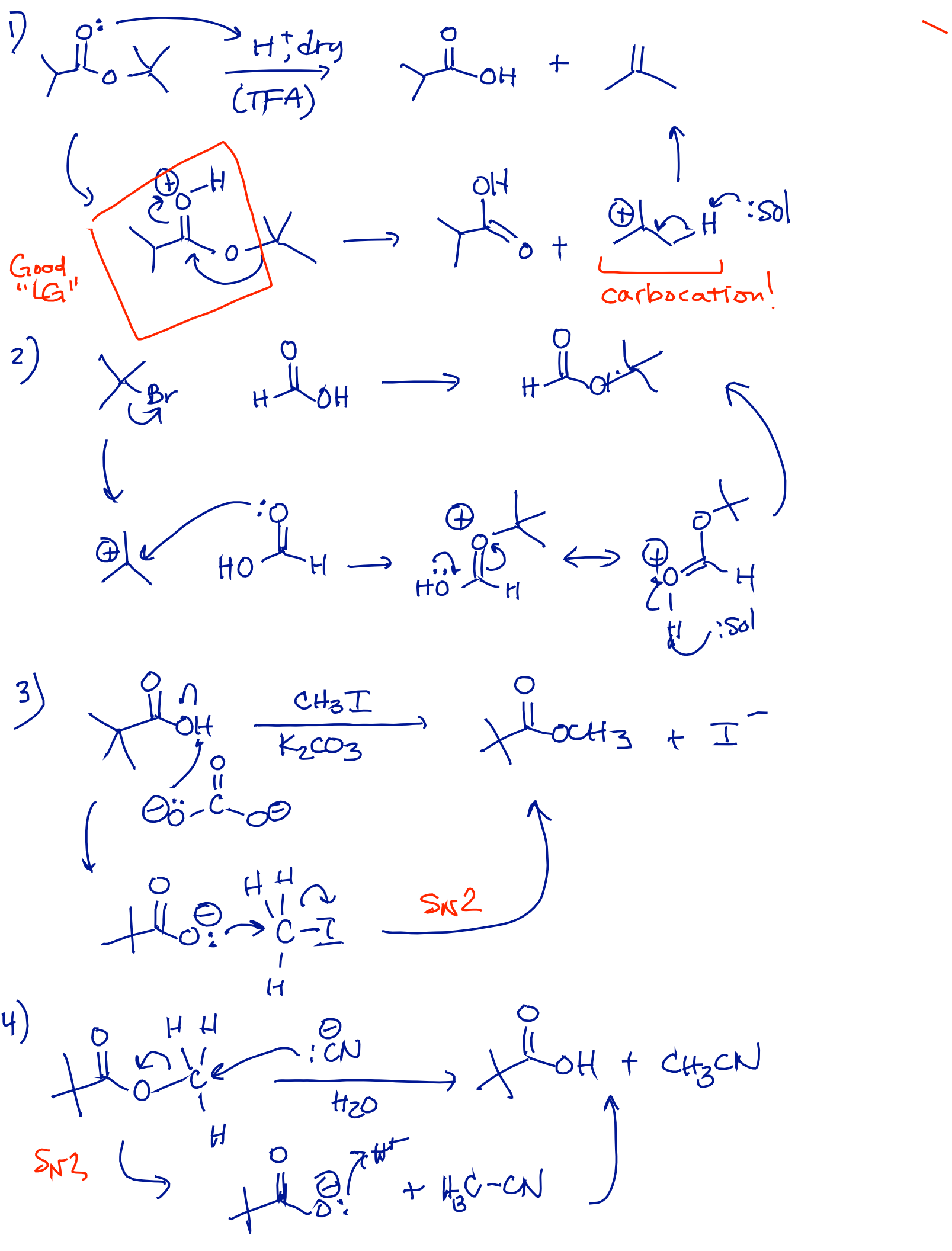




Here are several other reactions involving ester formation or "hydrolysis;" identify the types of mechanisms, and – on your own! – do the curved-arrow mechanisms.



Reading: Section 20.8


1)
H+; dry
(TFA)
OH
+
Good "LG"
carbocation!
:Sol
2)
Br
H
OH
HO
H
:Sol
3)
OH
CH3I
K2CO3
OCH3
+ I−
SN2
4)
:CN
H2O
OH
+ CH3CN
SN2
+ H3C-CN