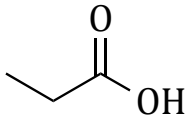
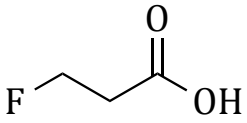
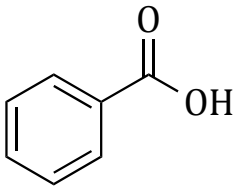
Acidity of Carboxylic Acids

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

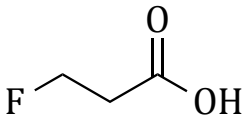
For each of the following carboxylic acids, change the structure slightly so that the acid becomes *more acidic*. Explain why that change is effective.

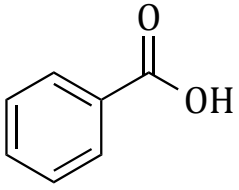






For each of the following carboxylic acids, change the structure slightly so that the acid becomes *less acidic*. Explain why that change is effective.





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

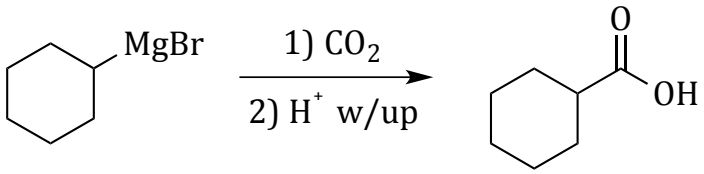
Nitrile

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?

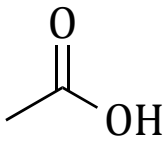


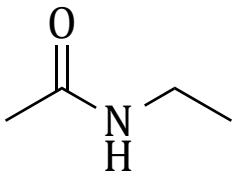
You also know some ways to make nitriles. What are they? Why are they special?

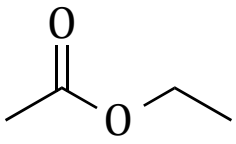
Reading: Section 20.6

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.





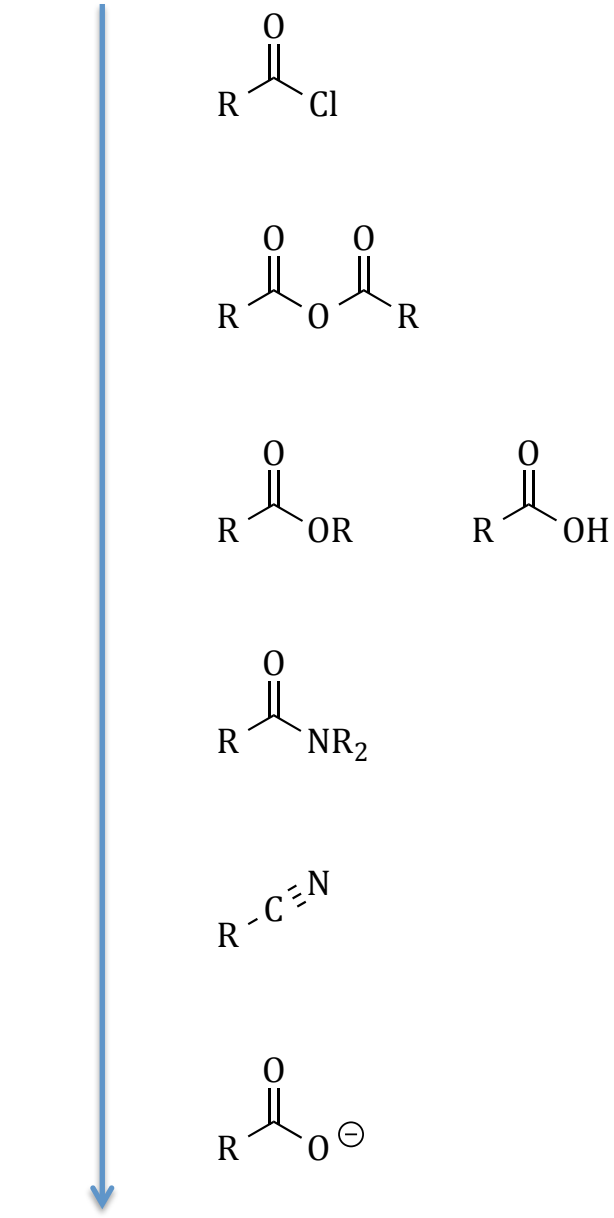


Reading: Section 20.7

Reactivity of Carboxylic Acids & Derivatives

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

more reactive



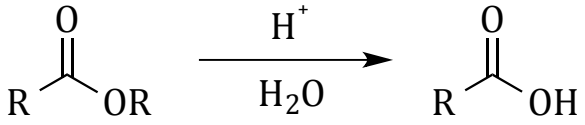
less reactive

Reading: Section 21.7

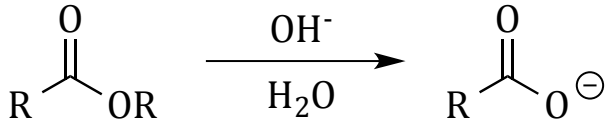
Converting Between Carboxylic Acid Derivatives

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.

Nucleophilic acyl substitution under **acidic conditions**:

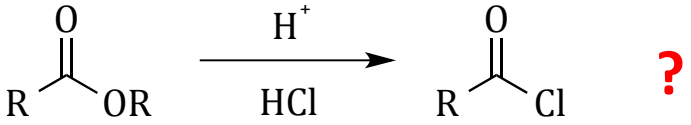


Nucleophilic acyl substitution under **basic conditions**:

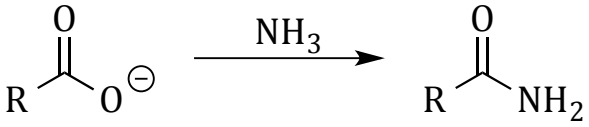


Reading: Section 21.7

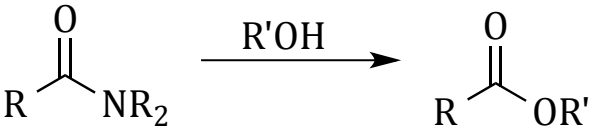
Converting Between Carboxylic Acid Derivatives: Some Problems



?



?



?

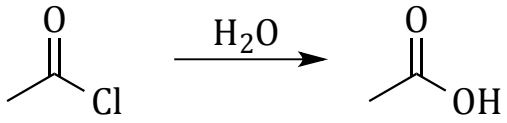
The nucleophile must be *nucleophilic enough*
The electrophile must be *electrophilic enough*
The incoming nucleophile must be a *worse leaving group* than the outgoing one.

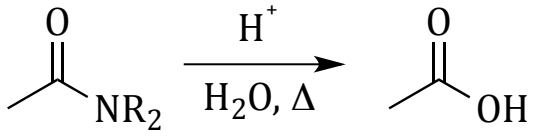
Reading: Section 19.13

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:



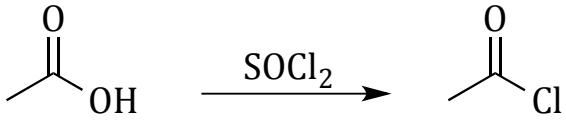


Acid halides & anhydrides react directly with water.
Esters require (mild) acid or base catalysis.
Amides and nitriles require strong acid/base and heat.

Reading: Section 21.7

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

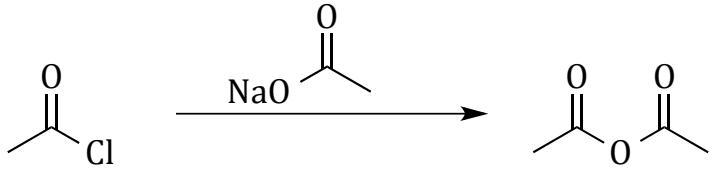
Draw complete curved-arrow mechanisms for the following reactions:

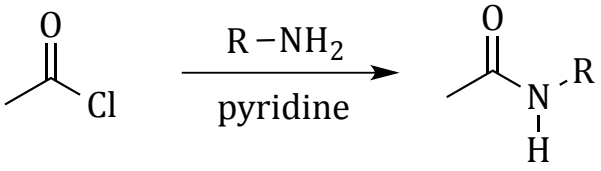


Reading: Section 20.9

Rule 3: Acid Chlorides be turned into any other CAD

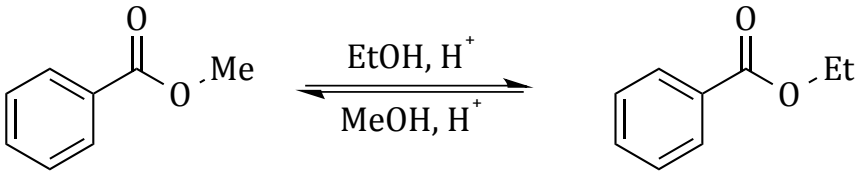
Draw complete curved-arrow mechanisms for the following reactions:





Reading: Section 20.9

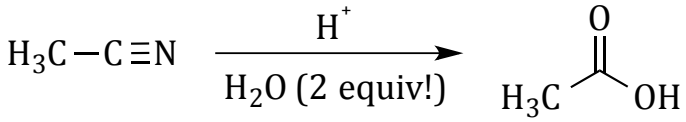
Transesterification:
Le Chatelier's Principle at work



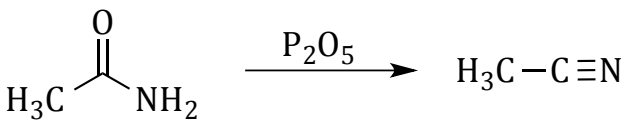
Reading: Section 21.8

Nitriles:
"Masked" 1° Amides

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

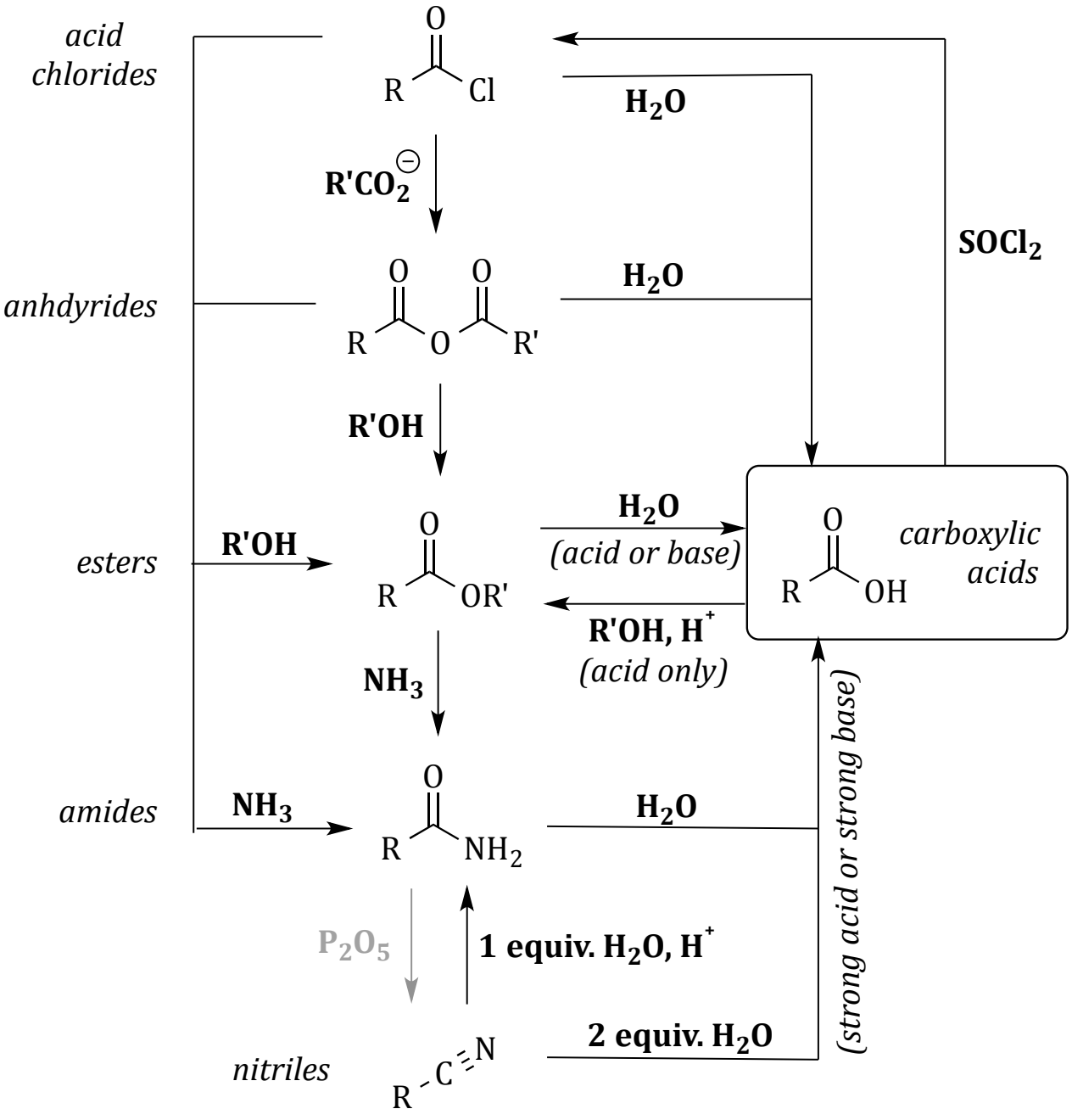


Nitriles can be synthesized by dehydration of primary amides:



Reading: Section 21.7

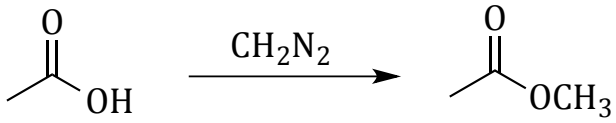
Putting it Together: Interconverting Between CADs



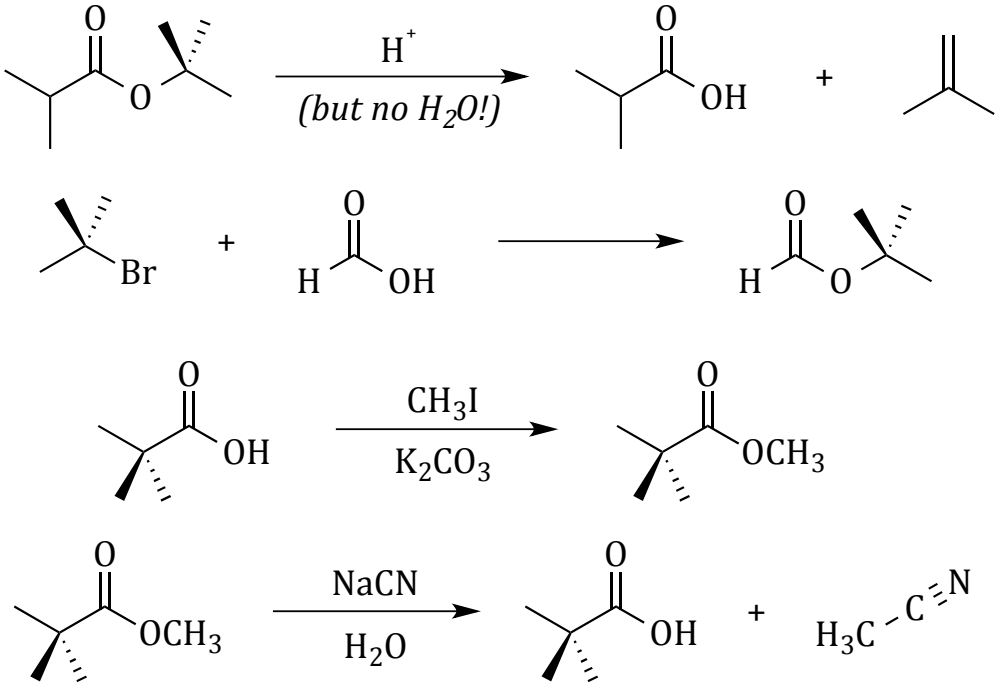
Reading: Section 20.9

Esters are Special:
Other Mechanisms of Formation/Hydrolysis

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



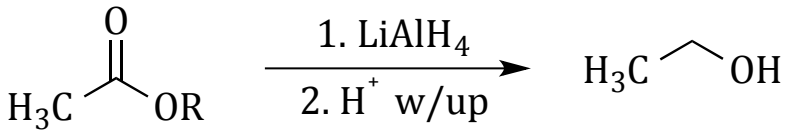
Here are several other reactions involving ester formation or "hydrolysis;" identify the types of mechanisms, and – on your own! – do the curved-arrow mechanisms.

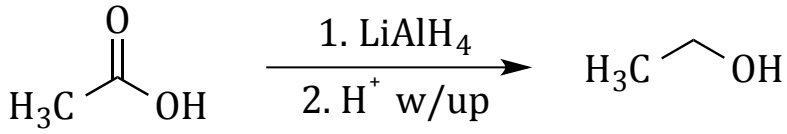


Reading: Section 20.8

Irreversible Addition to CADs: Reduction of Esters & Acids with $LiAlH_4$

Provide complete curved-arrow mechanisms for the following reactions:

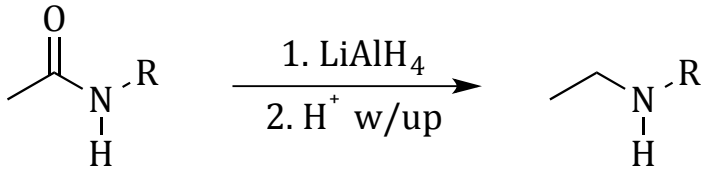


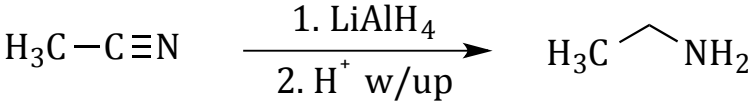


Reading: Sections 20.10, 21.8

Irreversible Addition to CADs: Reduction Amides and Nitriles with $LiAlH_4$

Provide complete curved-arrow mechanisms for the following reactions:

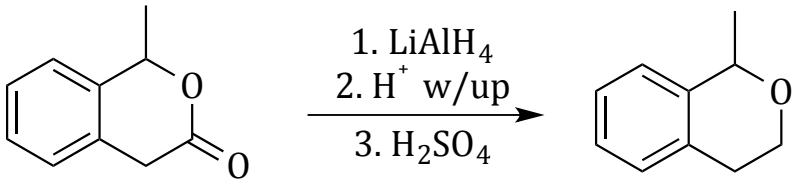




Reading: Section 21.8

Test Yourself Now!

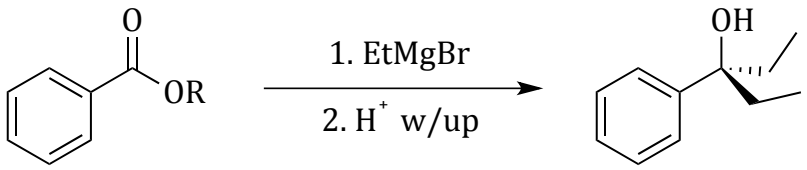
Provide a complete curved-arrow mechanism for the following reaction:

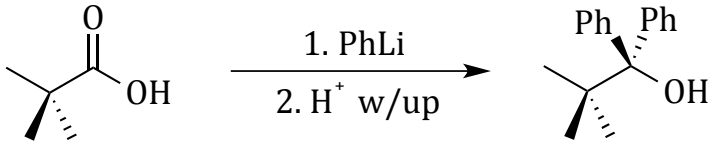


Reading: Section 21.8

Irreversible Addition to CADs:
Organometallic Reagents

Provide complete curved-arrow mechanisms for the following reactions:





Reading: Section 20.9