

Week 10
CHE 3332 - Organic Chemistry 2

Hello and Welcome to the weekly resources for CHE 3332 – Organic Chemistry 2!

This week is Week 10 of class, and typically in this week of the semester your professors are covering these topics below. If you do not see the topics your particular section of class is learning this week, please take a look at other weekly resources listed on our website for additional topics throughout the semester.

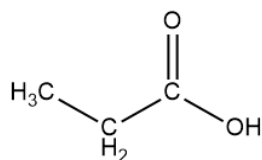
We also invite you to **look at the group tutoring chart on our website to see if this course has a group tutoring session offered this semester.** If you have any questions about these study guides, group tutoring sessions, private 30 minute tutoring appointments, the Baylor Tutoring YouTube channel or any tutoring services we offer, please visit our website www.baylor.edu/tutoring or call our drop in center during open business hours. M-Th 9am-8pm on class days 254-710-4135.

Keywords: Carboxylic Acids, Esters, Derivatives, Amides, Anhydrides

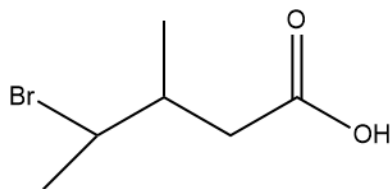
TOPIC OF THE WEEK: Carboxylic Acids & Derivatives (Chapter 20)

What are carboxylic acids?

Carboxylic acids in structure are simply aldehydes (meaning they have a terminal carbonyl group), with an -OH substituent, instead of an -H substituent. Because of this, nomenclature is very similar to both ketones and aldehydes, where we deal with the main chain and all its substituents, and add **-oic acid** to the end of their name.



Propanoic Acid

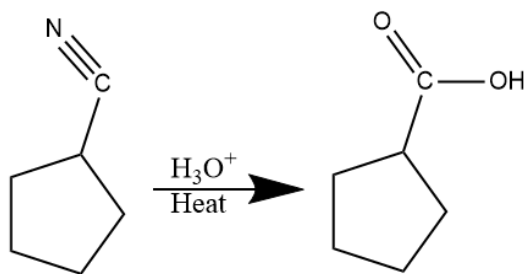
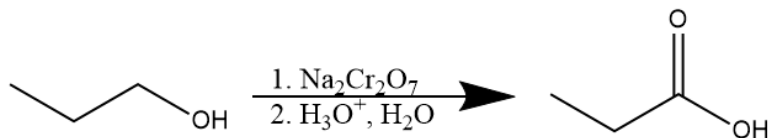


4-bromo-3-methylpentanoic acid

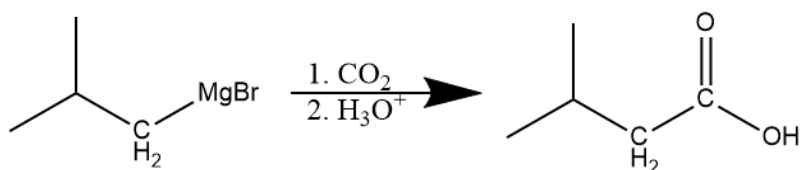
How can we make them?

Preparing carboxylic acids is quite simple. Some methods to do so have been covered in earlier chapters, such as the oxidation of primary alcohols, or through the oxidation of a benzylic

carbon. There are, however, two new ways to yield a carboxylic acid introduced in this chapter. The first method involves the hydrolysis of nitriles ($C\equiv N$). This reaction, using acid and heat, simply replaces the nitrogen bound to the carbon with the carboxylic acid's two oxygen atoms. Additionally, we can also get a carboxylic acid using a grignard reagent and CO_2 . The carbon on the grignard reagent will attack the carbon of CO_2 , forcing one of the double bonds to oxygen to be pushed up as a lone pair.



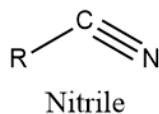
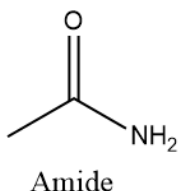
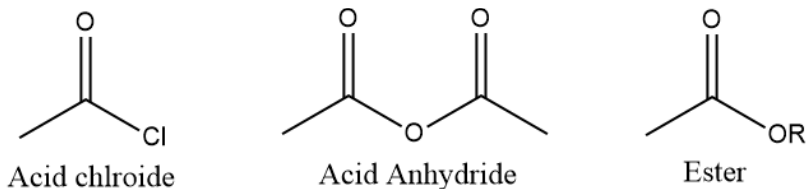
Preparation with a nitrile



Preparation using CO_2 .

Carboxylic Acid Derivatives:

A carboxylic acid derivative is a molecule which swaps the $-OH$ group for a different kind of substituent. For example, we can change the $-OH$ group to a $-Cl$ group, which would then give us an **acid chloride**. Through these types of reactions, there are five types of derivatives we can get to.

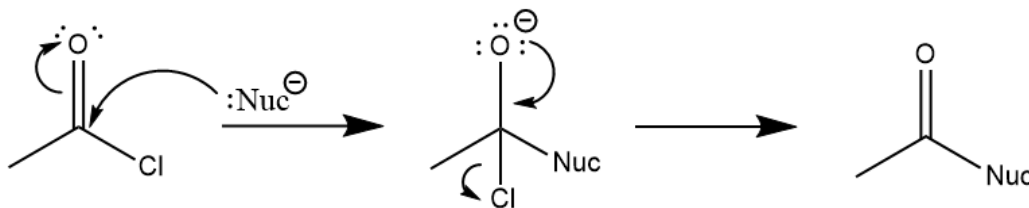


Acid Chlorides & Reactions

Acid Chlorides can be formed from carboxylic acids using SOCl_2 . This process can then be reversed using water. Because they are the **highest** in reactivity, they can **turn into any other derivative**, as well as taking part in a few other reactions.

Reaction	Reactants	Product
Alcoholysis	1. Primary Alcohol 2. Pyridine	Esters
Aminolysis	1. 2x NH_2 (or NHR/NR_2)	Amides
Reduction	1. LiAlH_4 2. H_2O	Primary alcohols
Reduction	1. $\text{LiAl}(\text{OR})_3\text{H}$ 2. H_2O	Aldehydes
Grignard Reaction	1. xs RMgBr 2. H_2O	Tertiary Alcohol
Gilman Reaction	1. R_2CuLi	Ketone

For the most part, these reactions all proceed with a similar mechanism. In this case, our reagent will usually be a nucleophile, which will want to attack at the slightly positive carbon on the carbonyl. Because chlorine (Cl^-) is such a great leaving group, it will easily let the nucleophile take over. Additionally, **Grignards will always add twice to acid chlorides**, and DO NOT give a ketone. Thus a **Gilman reagent** can be used to add a carbon group **once**.



General mechanism for reactions involving derivatives (not just acid chlorides)

IMPORTANT: Because of their high level of reactivity, acid anhydrides can undergo all of the same reactions listed above. The only different reaction to note is the one used to form anhydrides. It involves an acid chloride reacting with a deprotonated carboxylic acid, with both molecules melding together to yield an anhydride.

Esters & Reactions:

Like the two derivatives before it, esters can yield any other derivative that is lower on the reactivity scale. It cannot directly become an acid chloride or anhydride (as they are higher in reactivity). That being said, esters are involved in many reactions, both which can form it, as well as those which lead to different products.

Reaction Type	Reagents	Product
Preparation (S _N 2)	1. NaOH 2. RX	Ester
Preparation (Fischer Esterification)	1. ROH 2. H ⁺	Ester
Preparation (Using Acid Chlorides)	1. ROH 2. Pyridine	Ester
Saponification	1. NaOH 2. H ₃ O ⁺	Carboxylic Acid & Primary Alcohol
Acid Catalyzed Hydrolysis	H ₃ O ⁺	Carboxylic Acid & Primary Alcohol
Aminolysis	NH ₃	Amide
Reduction	1. xs LiAlH ₄ 2. H ₂ O	Primary Alcohol
Reduction	1. DIBAL 2. H ₂ O	Aldehyde
Grignard Reaction	1. xs RMgBr 2. H ₂ O	Tertiary Alcohol

Amides:

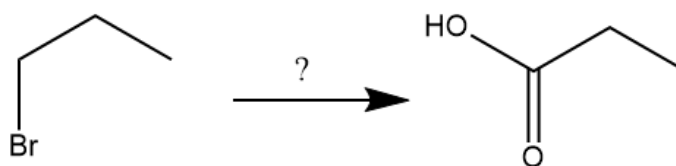
At this point, because of their low reactivity, we have already covered all the reactions used to form amides. This leaves only a handful of reactions; those which involve hydrolysis, and one which will yield the derivative with the lowest reactivity, nitriles.

Reaction	Reagent	Product
Acid Catalyzed Hydrolysis	1. H ₃ O ⁺ 2. Heat	Carboxylic Acid (& amine byproduct)
Base Catalyzed Hydrolysis	1. H ₂ O 2. Base 3. Heat	Carboxylic Acid (& amine byproduct)

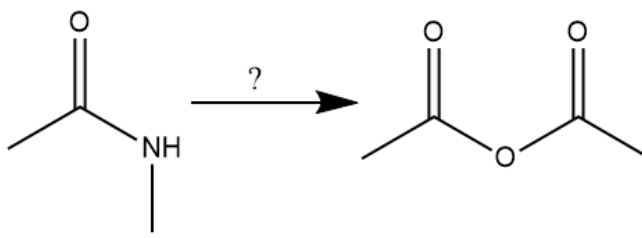
Conversion to a Nitrile (Primary Amides Only)	1. SOCl_2 2. $^- \text{OH}$	Nitrile
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CHECK YOUR LEARNING:

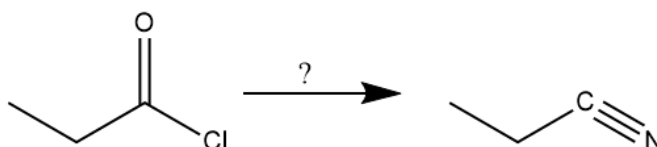
1. Provide a synthesis for this reaction:



2. Provide a synthesis for this reaction:



3. For the reaction below, give both the process and the mechanism for each step:



THINGS YOU MAY STRUGGLE WITH:

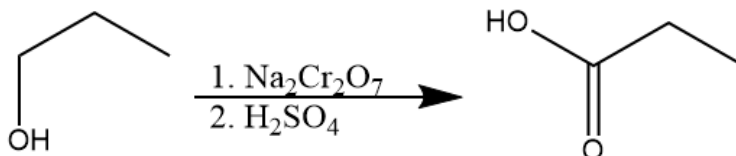
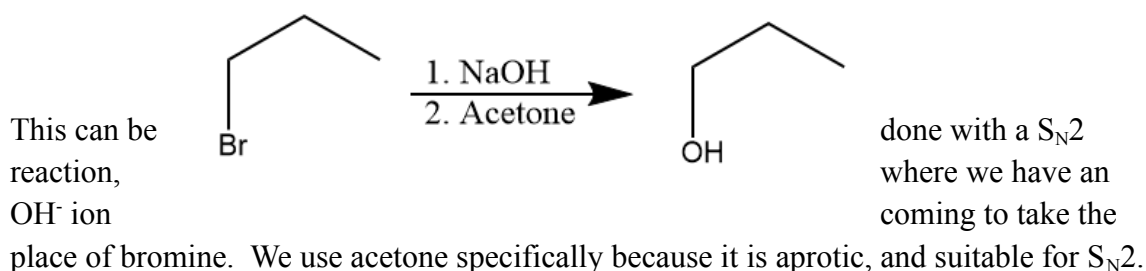
- It may seem quite daunting to be able to tackle all the different conversions that carboxylic acid and its derivatives can undergo, especially considering how interconnected everything is. At the end of chapter 20, there is a nice diagram that shows all the reactions, it is super helpful!
- A lot of questions in this chapter may draw upon knowledge of reactions from other chapters. Since we are getting farther into the semester, the number of reactions you may need to use is getting larger, so it is always a good idea to keep them fresh.

Thanks for checking out these weekly resources!

Don't forget to check out our website for group tutoring times, video tutorials and lots of other resources: www.baylor.edu/tutoring! Answers to check your learning questions are below!

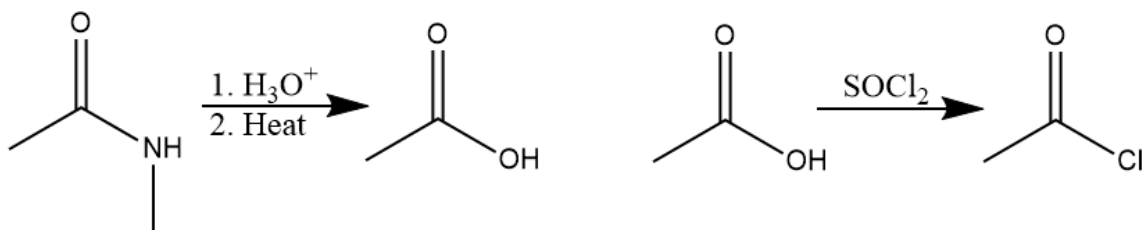
ANSWERS FOR THE PRACTICE PROBLEMS:

1. For the first question, we start with a halogen, and end up with a carboxylic acid. Because of this, we know that we want to put an alcohol where the halogen is.

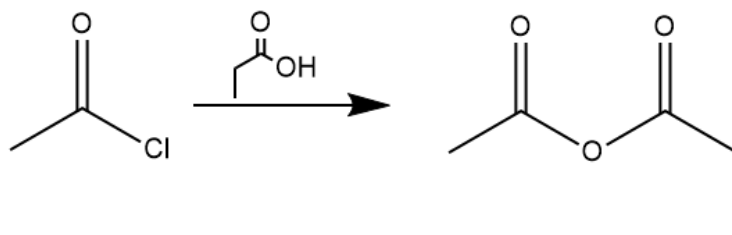


Finally, with a primary alcohol, we can oxidize it, to get the carboxylic acid.

2.

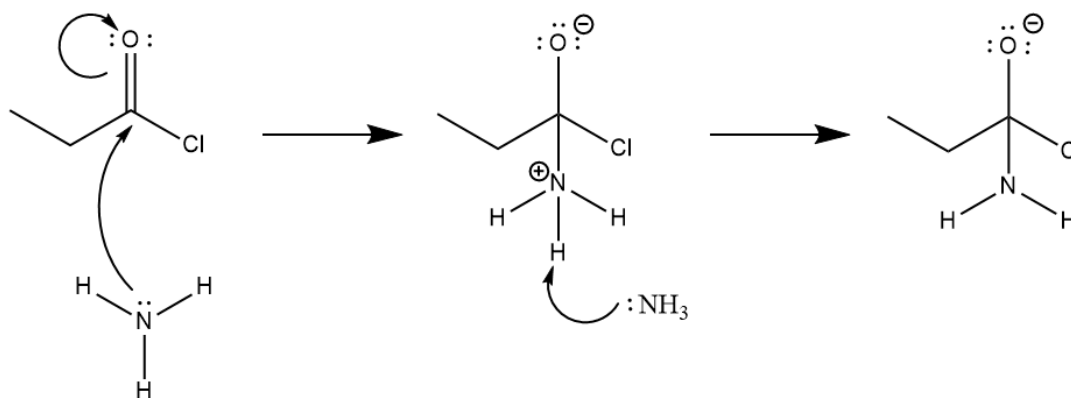


For this question, we are simply tasked with giving a synthesis that will get us from an amide to an anhydride. In doing so, we are moving up the reactivity ladder, so we cannot do this in one direct reaction. What we can do though, is get to a carboxylic acid, which can then go on to be anything. So, to start out, we can convert our amide to a carboxylic acid through a bit of acid and heat. Then we can get that to an acid chloride using SOCl_2 pretty easily.

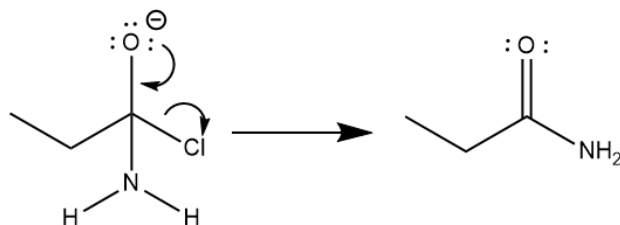


Now that we have an acid chloride, we can get to any derivative we want. To yield an anhydride, we can add the carboxylic acid precursor, which will then attack the carbonyl of the acid chloride.

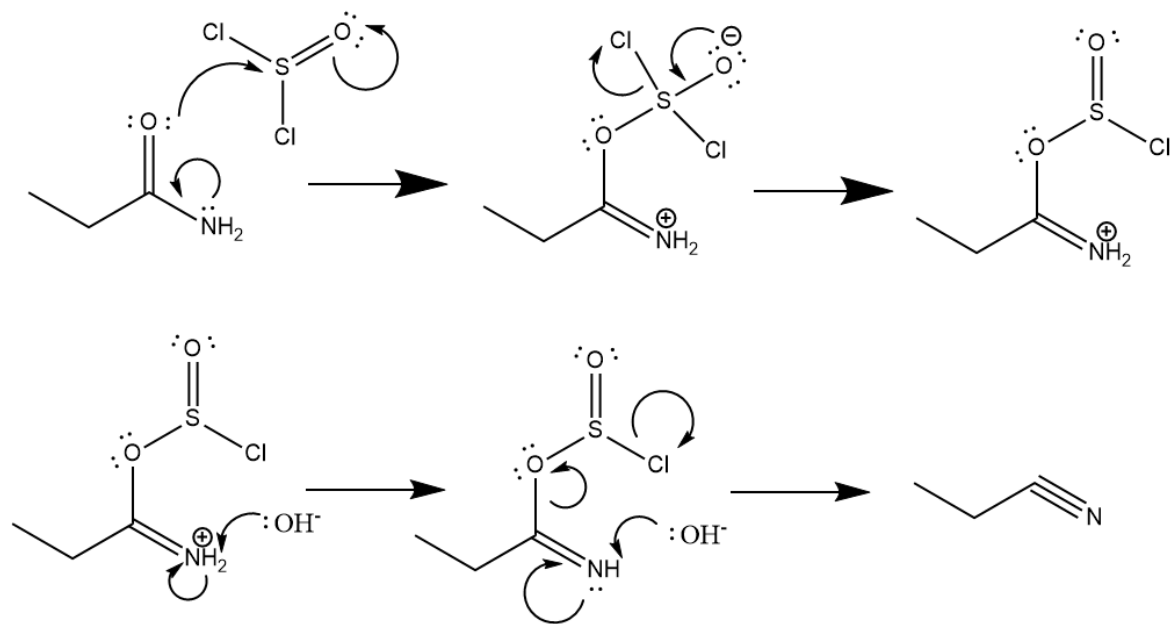
3.



For this reaction, the first step will be to switch the acid chloride to an amide. While this may seem arbitrary, amides are the only derivative we know of that can turn into a nitrile, so we have to get an amide at some point. So, our first step involves the **amine** (not amide yet), which will attack the carbonyl group. As is expected for nucleophilic attack on carbonyls, the electrons will be pushed upwards towards the oxygen. As a little aside, the NH₃ in solution will come in to pull a hydrogen off to neutralize the charge on our amine.



Next, to finally create our amide, the lone pair on the oxygen will go to create a carbonyl (oxygen does not want to have a charge), and the chlorine being a good leaving group will be plucked off.



Finally, we have the conversion from the amide to the nitrile. This is done with SOCl_2 and a base, which comprises the six steps above, giving us our nitrile.

All tables are courtesy of Organic Chemistry by David Klein. All drawings of molecules and mechanisms are made by me.