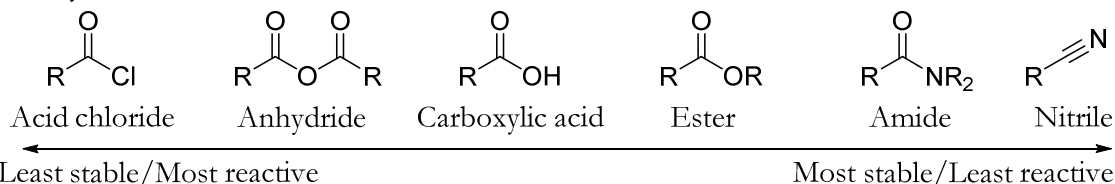


Loudon Chapter 20 Review: Carboxylic Acids

Jacque Richardson, CU Boulder – Last updated 10/21/2016

These two chapters cover compounds which are all at the “three bonds to more electronegative atoms” oxidation state. They’re called carboxylic acid derivatives, because they all have a carboxylic acid as the parent compound. If you want to make any of them, you often have to go through the acid form first, although there are cases where you can go directly from one derivative to another.



You can rank them by stability based on the size of the delta plus at the carbon. Acyl chlorides have the biggest delta positive and nitriles have the smallest.

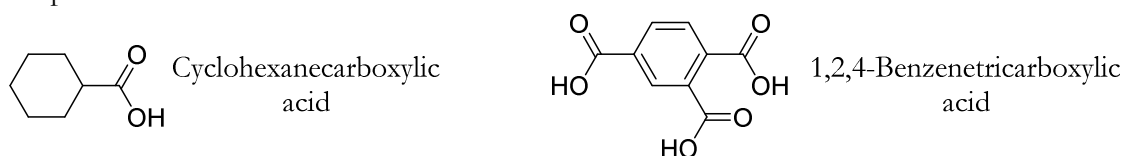
Chapter 20 mostly just covers how to make carboxylic acids in the first place, and how to make each of the derivatives from acids. Chapter 21 gets more into reactions you can do with the derivatives.

Nomenclature

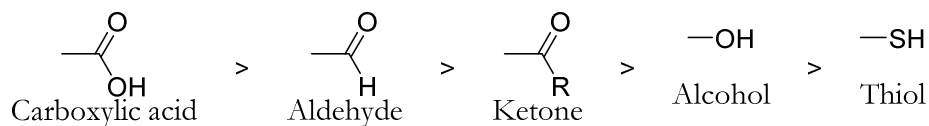
Under the IUPAC system, acids are named by taking the parent chain name (based on the total number of carbons, including the one in the acid group), dropping the “e” and adding “oic acid”. The acid carbon is at position one, and other substituents can be named as necessary. If there is an acid group at each end, the “e” is kept and “dioic acid” is added.



If there's no way to include the acid as part of the parent chain, it may still be possible to have a COOH group attached to the parent. In this case, add “carboxylic acid” to the end of the parent name.

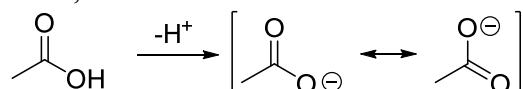


For choosing the parent chain in the first place, acids outrank all of the other principal FGs we've seen so far.



Acidity of Carboxylic Groups

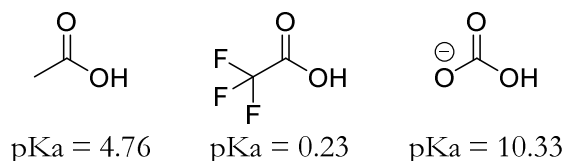
Carboxylic acids are acidic because they can easily use resonance to stabilize the negative charge after they lose a proton. Another factor that contributes is the large partial positive charge on the carbonyl carbon, which stabilizes the anion.



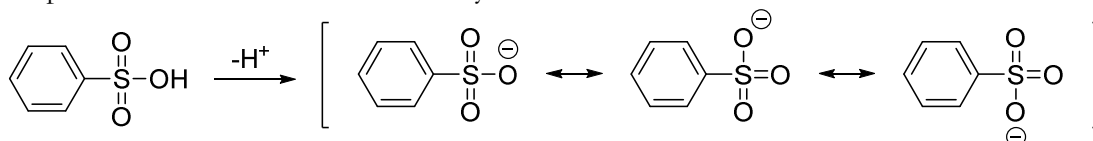
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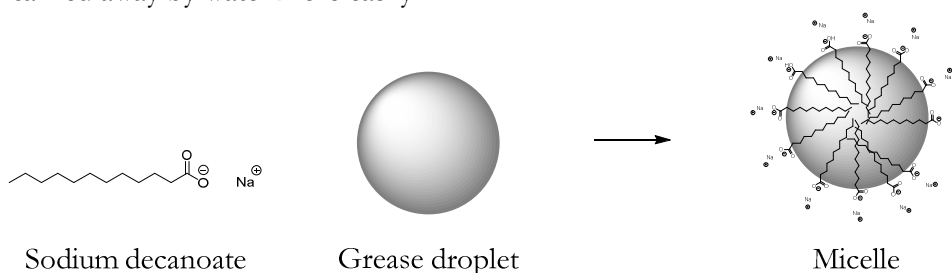
Most carboxylic acids have pK_as in the 4-5 range, though they can be higher or lower if there is a group elsewhere in the molecule that stabilizes or destabilizes the charge.



Sulfonic acids are even more acidic because they have three possible resonance forms, and also a bigger partial positive charge on sulfur. They usually have pK_as around -3. These are compounds that we saw how to make by sulfonation reactions in Ch. 16.



Deprotonated carboxylic acids are called carboxylates. These are commonly used as soaps, especially if they have long alkyl chains, because the polar “head” is soluble in water and the nonpolar “tail” is soluble in grease. This allows them to break the grease into micelles, which can be carried away by water more easily.

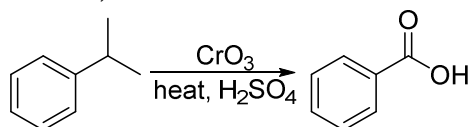


Making carboxylic acids

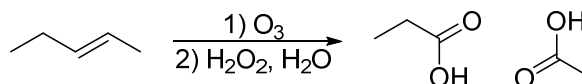
- 1) Oxidation of primary alcohols and aldehydes: This normally uses something like CrO₃ and pyridine, or stronger conditions. We've seen this in Ch. 10 and 19.



- 2) Oxidation at the benzylic position: This uses an oxidizer like CrO₃, but in vigorous conditions (usually acid and heat.) This was in Ch. 17.



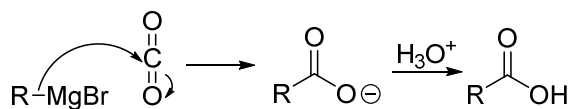
- 3) Ozonolysis: This is less useful because you have to break carbon-carbon bonds to do it. This is from Ch. 5.



- 4) Grignards attacking CO₂: This is a new one in Ch. 20, but it's similar to something we saw before. Ch. 19 shows how to use a Grignard to attack a carbonyl. We can do the same thing by attacking carbon dioxide, which is kind of like a “double carbonyl”. Then, we just finish it off the same way, with an acid workup.

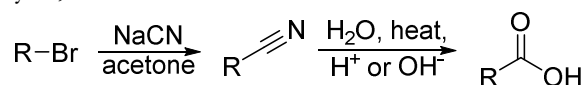
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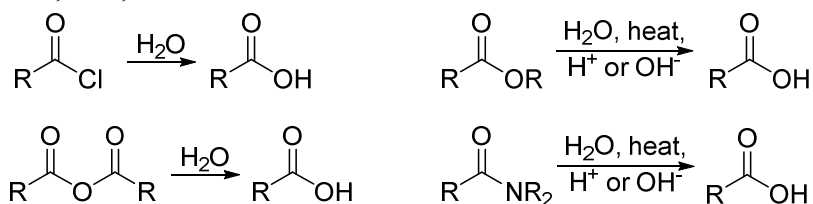
Note that whatever R was, we've just added one carbon to it overall. This is a useful way of extending chains one carbon at a time. The only limitation is that R has to be compatible with Grignards – no alcohols or unprotected carbonyls, etc.

- 5) S_N2 with a cyano group, followed by hydrolysis: This one doesn't show up until Ch. 22, but it's a useful complement to the Grignard/ CO_2 reactions shown above, and worth mentioning here. In this case, we can make a particular acid derivative by using S_N2 to replace a leaving group with a $^- \text{CN}$. Then, we can convert the nitrile to the parent acid compound by hydrolysis, which we'll look at the mechanism for shortly.



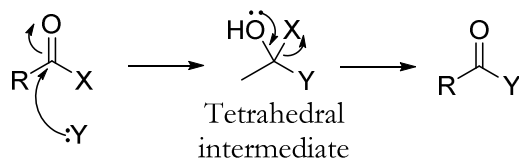
Like the Grignard reaction above, this ends up extending the chain length by one carbon. The only requirement is that R has to be S_N2 -capable, so primary is best.

- 6) Conversion from any other acid derivative: Again, this is Ch. 21 chemistry, but you can take any of the compounds shown at the beginning of this packet and convert them to the acid by hydrolysis. We'll see the mechanism later. If it's something more reactive than acid (like anhydrides and acid chlorides), you only need water. If it's less reactive, you need water, heat, and either acid or base.



General idea of mechanisms

Most of the reactions in Ch. 20 and 21 involve swapping out the group beside the carbonyl. Unlike S_N2 , you can't just attack and kick out the leaving group at the same time. You attack first and break up the carbon-oxygen double bond. This gets you to a point where the central carbon has four total groups attached – the tetrahedral intermediate. Then the oxygen's lone pair comes back down and kicks out the leaving group. The general idea looks like this.



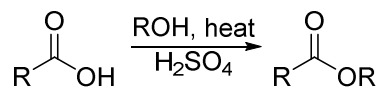
Depending on what you're doing and whether it's in acidic or basic conditions, there might be a few extra steps somewhere in there to account for protonation or deprotonation. But the general pattern is still the same for most of the reactions in these chapters.

Making esters from acids

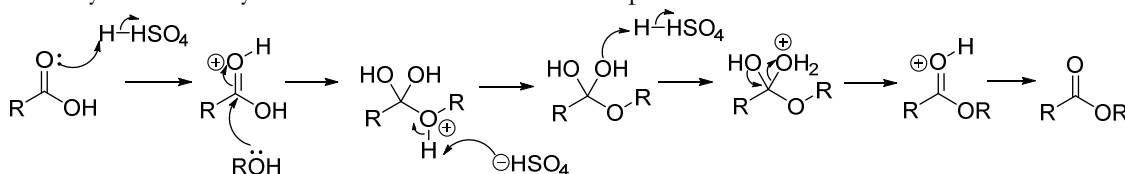
Fischer esterification is the simplest way of making esters. You can react the carboxylic acid with the alcohol and some catalytic H_2SO_4 .

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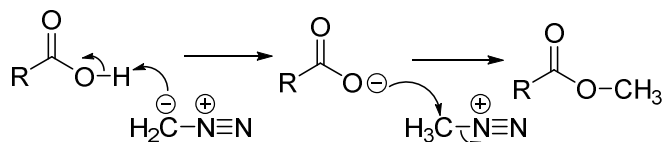
The mechanism is pretty much the same as the general pattern, but you protonate the carbonyl first since you're in acid. You also need to protonate the OH before it will leave.



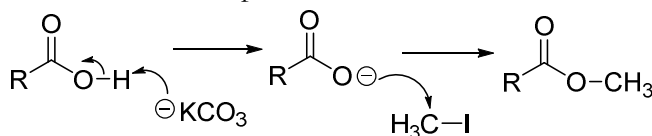
Note that in the middle you have the neutral tetrahedral intermediate.

Another option we have is different from that general reaction pattern shown above.

Instead, we keep both the oxygens that started out in the acid, and just stick an R group onto one of them. This is called alkylation, and you need a good leaving group on R to do it. One way is with diazomethane, CH_2N_2 . The leaving group here is spectacularly good, since it's nitrogen gas which leaves. Diazomethane also acts as its own base first, to deprotonate the acid.



Note that the oxygens stay on the molecule the entire time, just one of them gets alkylated. The other option uses a slightly less good leaving group, and you need a different mild base to deprotonate the acid in the first step.



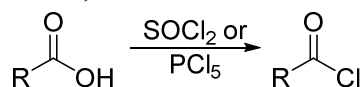
Overall, these are written as:



You can sometimes use different R groups instead of just CH_3 , but they have to be very good at doing $\text{S}_{\text{N}}2$. Benzylic positions are an okay choice. Usually, though, these reactions are considered the best way to make methyl esters (with an OCH_3 group) and not much else.

Making anhydrides and chlorides from acids

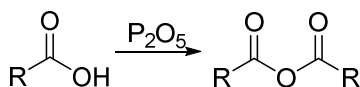
For chlorides, we can use the same special reagent we used to turn alcohols into alkyl chlorides: SOCl_2 or a similar molecule, PCl_5 . We still don't cover the mechanism.



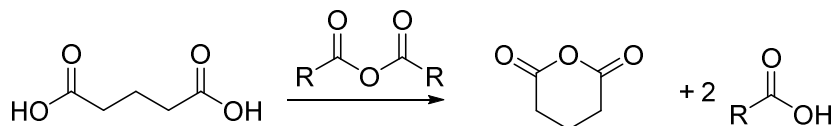
To make the anhydride, we have a couple of options. The name 'anhydride' means it's had a molecule of water removed. If you take two carboxylic acid molecules, stick them together, and remove a water, you get an anhydride. You can do this by using a very powerful dehydrating reagent, P_2O_5 . This takes two copies of the same acid and converts them to the anhydride.

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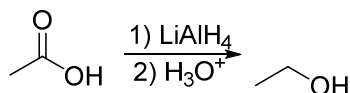


There's another option that only works to make five- or six-membered cyclic anhydrides. If you mix it with an acyclic anhydride, they'll swap which one is the acid and which is the anhydride.



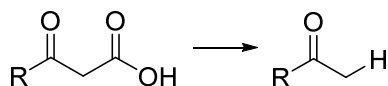
Reductions

Like we saw in Ch. 19, you can reduce carbonyl compounds with hydrides. You can do the same with acids, which are reduced from the “three bonds to more electronegative atoms” oxidation state to the “one bond to more electronegative atoms” oxidation state. An important thing to point out is that NaBH_4 *does not work for acids* – it only works for aldehydes and ketones. LiAlH_4 is what you want to use here. Since acids have an acidic hydrogen, that reacts first with the AlH_4^- . Then the remaining AlH_3 reduces the acid to the aldehyde. Finally, the aldehyde gets reduced by LiAlH_4 like in Ch. 19. Overall it looks like this:



Decarboxylation

The general idea here is that if you have a β -ketoacid - a carboxylic acid two carbons away from any type of carbonyl (often a ketone, but can be aldehyde, acid, ester, etc.), then the entire CO_2 unit can detach. The H that was part of the acid ends up attached where the CO_2 used to be.



The mechanism for this is actually not too different from that for Diels-Alder. It helps to keep in mind that the molecule is capable of hydrogen-bonding to itself, so it normally looks a little different than what's shown up there. There's already a partial bond between the other carbonyl and the H. To do this mechanism, you just show it going and picking up the H fully. Everything else clicks around the six-membered ring, like in Diels-Alder. Then to finish it up, you do a keto-enol tautomerization under acidic conditions.

