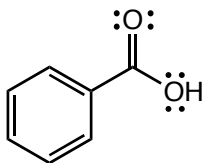


Notes on Chapter 21 - Carboxylic Acids

- I. Introduction to carboxylic acids
- II. Nomenclature of carboxylic acids
- III. Spectroscopy of carboxylic acids
- IV. Synthesis of carboxylic acids
- V. Reactions of carboxylic acids
 - Reduction of carboxylic acids
 - Reactions with organolithium reagents
 - Conversion to acid chlorides
 - Conversion to esters
 - Conversion to amides
 - Decarboxylation

I. Introduction to carboxylic acids

All compounds containing a carboxylic acid group have an OH attached directly to a C=O. This may be abbreviated as COOH or CO₂H.



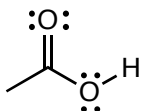
How are carboxylic acids different from alcohols?

What effects do you think this will have?

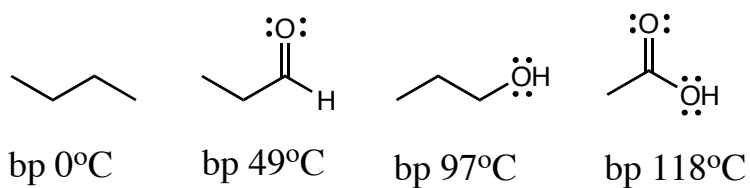
Carboxylic acids are important functional groups in biochemistry. What are some common biological molecules that contain carboxylic acids?

Physical properties

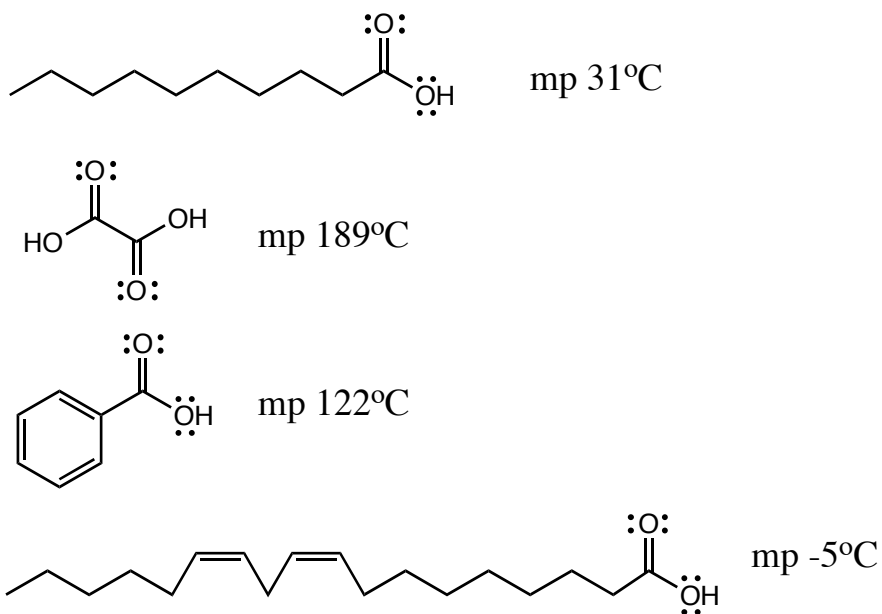
Carboxylic acids frequently form hydrogen bonded dimers, both in crystal structures and in solution. Where does this show up on the IR?



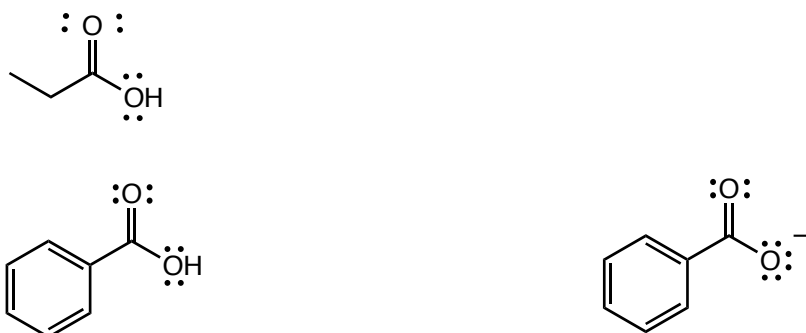
Boiling and melting points: Consider the following boiling points. What does this series tell you? How can you explain it?

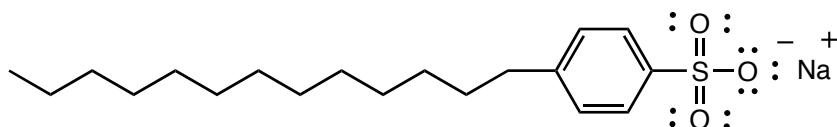
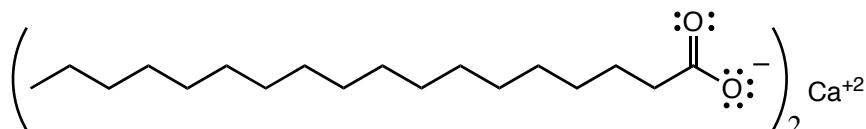
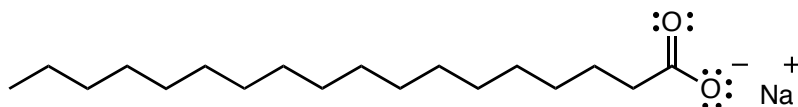
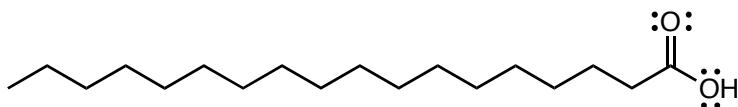


Consider the following melting points. What do they suggest about the physical state of carboxylic acids?



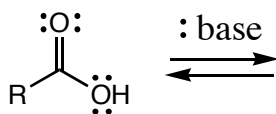
Water solubility: Predict the water solubility of the following compounds.





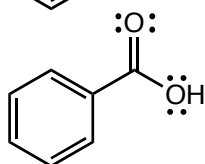
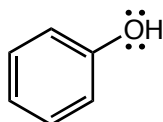
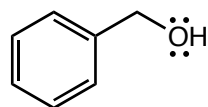
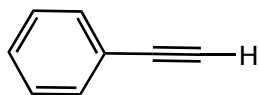
Acid/base properties

Carboxylic acids are the most acidic functional group. Write out the conjugate base and deduce the reason for this.

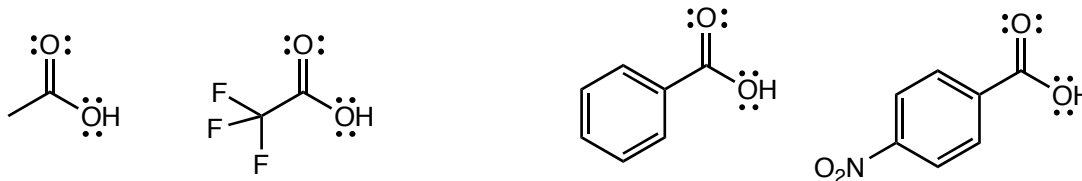


The deprotonated form of a carboxylic acid is called a carboxylate anion.

Compare carboxylic acids with the other acidic functional groups we have learned so far. What bases can be used to deprotonate them?

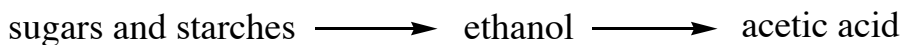


What effect will electronegative or electron-withdrawing groups have on the pKa of an acid?

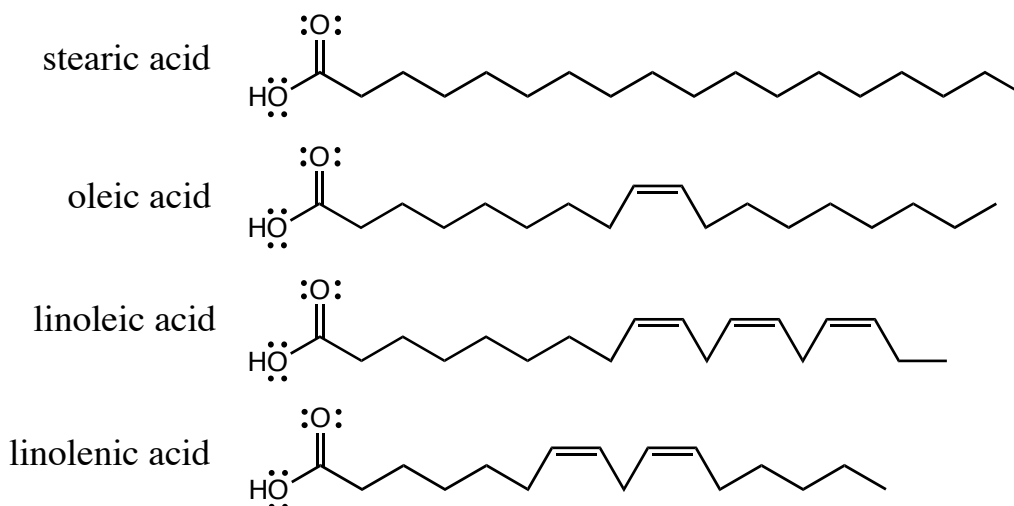


Examples of carboxylic acids

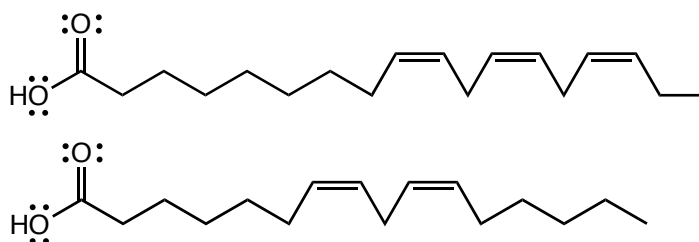
Acetic acid is the simplest and most common carboxylic acid. It is found as a 5% solution in vinegar, and is formed in when ethanol is oxidized by exposure to oxygen in the air. Acetic acid is used in industry as a solvent, starting material, or catalyst for a variety of reactions.



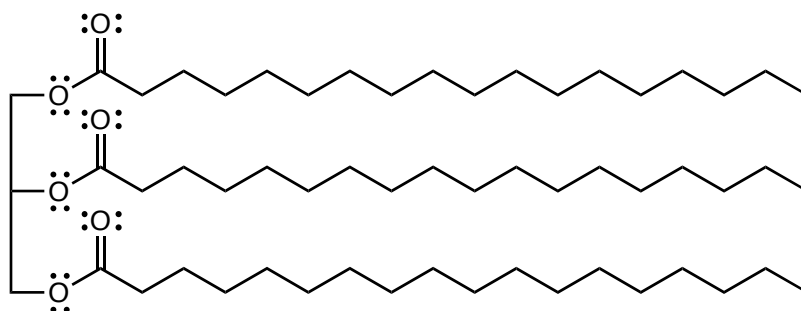
Fatty acids are long chain aliphatic carboxylic acids. Those with no C=C are called saturated fatty acids, while those with C=C are called unsaturated fatty acids. Unsaturated fatty acids are further divided into monounsaturated and polyunsaturated fatty acids.



Two of the polyunsaturated fatty acids - linoleic and linolenic acids - are essential nutrients. It has also been discovered that it is important to balance omega-6 fatty acids, which have a C=C six carbons from the end and are found in corn oil, safflower, cottonseed, and sesame, which omega-3 fatty acids, which are found in flaxseed, canola oil, salmon, and soybeans.



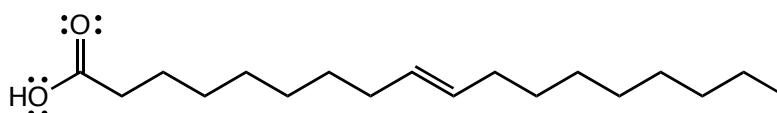
Fats are formed when three fatty acids join with glycerol to form a triester compound. Animal fats tend to contain a higher proportion of saturated fatty acids, and are usually solid. Fats obtained from plant sources are often called oils because they are liquids, and usually contain a higher proportion of unsaturated fatty acids.



Plant oils may be solidified by hydrogenation, which replaces the C=C's with C-C's - this process is used to make margarine. However, partial hydrogenation also isomerizes some of the C=C's that remain to the unnatural but more stable trans form. Trans fatty acids are being researched as culprits in a number of health problems including breast cancer.

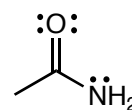
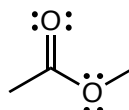
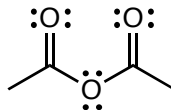
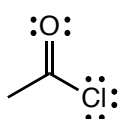
unsaturated fat \longrightarrow

unsaturated fat \longrightarrow



Since a law was passed requiring the amount of trans fats to be reported in the nutritional table, a number of zero trans fats have appeared on supermarket shelves.

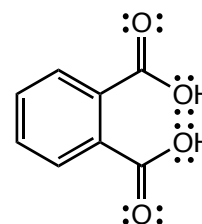
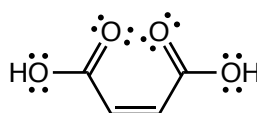
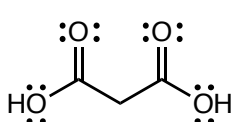
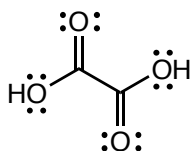
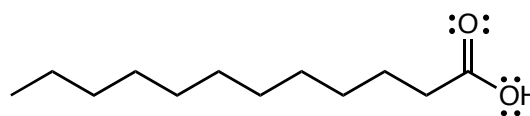
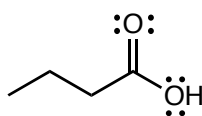
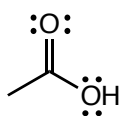
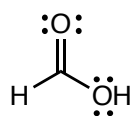
Carboxylic acids are considered the parent compounds of all other functional groups containing a halogen, oxygen, or nitrogen connected to a C=O. These are called carboxylic acid derivatives. The reactivity of these compounds will be considered together in chapter 22.



II. Nomenclature of Carboxylic Acids

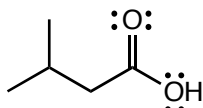
Common names

Because of their importance in biology, many simple carboxylic acids have been known since the 1800's, and have common names which are still in common use. When you see the name of an acid that you don't recognize, look at Tables 20-1 and 20-2. Here are some examples.

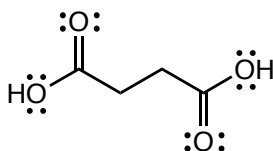


Substitutive names

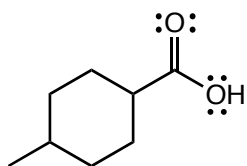
Carboxylic acids are a principle group, giving them priority in choosing and numbering the principle chain. How does the principle group name change?



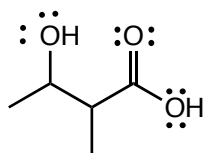
What happens when there are more than one carboxylic acid group?



Carboxylic acids attached directly to a ring are named in a way we haven't encountered before. The full name of the cyclic alkane is used, with "carboxylic acid" added to the end.



Carboxylic acids rank higher than alcohols, so when an alcohol is present, it will be named as a substituent.

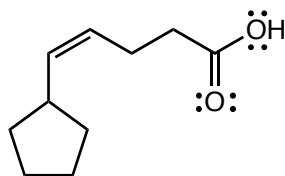


Draw structures for the following compounds.

o-hydroxybenzoic acid

1,2-cyclobutanedicarboxylic acid

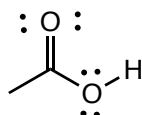
Name the following compound.

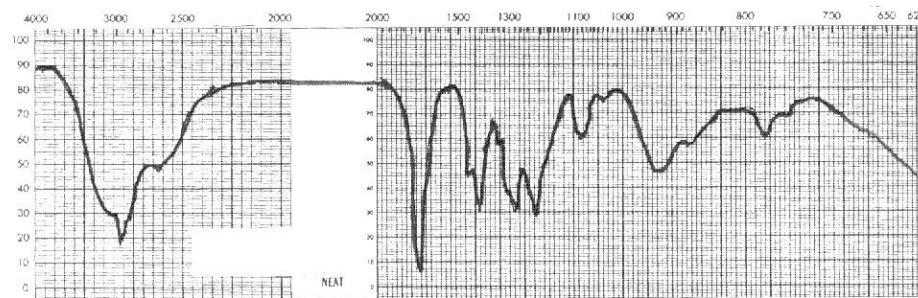


III. Spectroscopy of Carboxylic Acids

IR spectroscopy

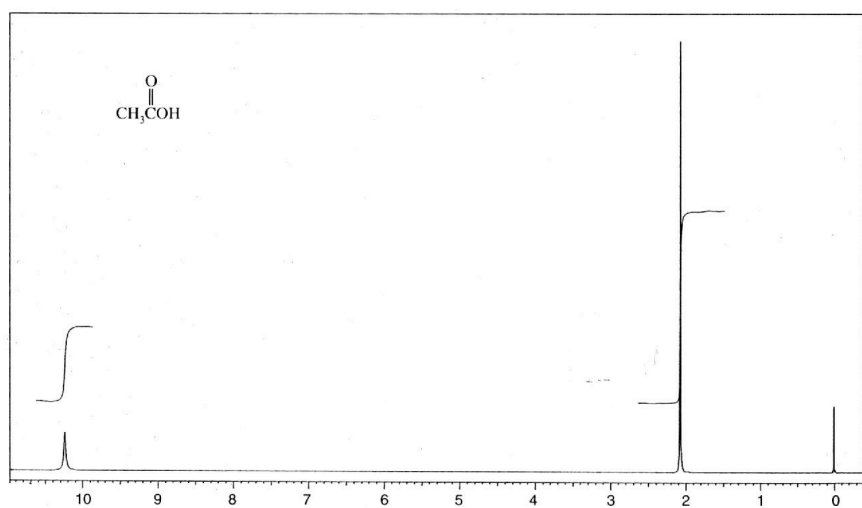
What are the distinctive features of an IR spectrum of a carboxylic acid?



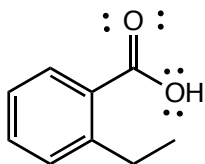


NMR spectroscopy

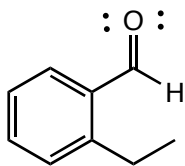
What chemical shifts are characteristic of an NMR spectrum of a carboxylic acid?



What peaks would appear on this compound?



How could this compound be distinguished from the one shown below?

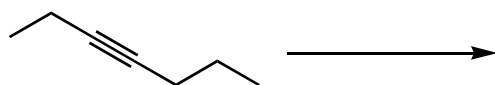
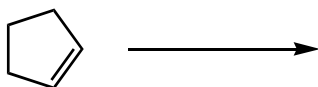
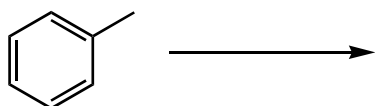
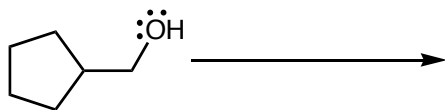


IV. Synthesis of carboxylic acids

LG Ch 21 p 9

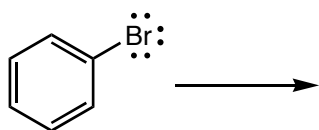
Reactions from previous chapters

So far we have seen three reactions that form carboxylic acids. They are oxidation of a primary alcohol, oxidation of a benzyl side chain, and ozonolysis of alkenes or alkynes.



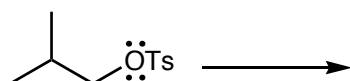
Addition of a Grignard to CO_2

Another useful method is the reaction of a Grignard reagent with carbon dioxide. When dry ice is added to a Grignard followed by mild acid, a carboxylic acid is formed.

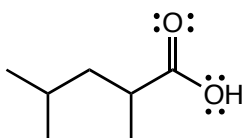
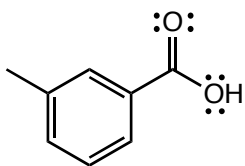


Hydrolysis of a nitrile

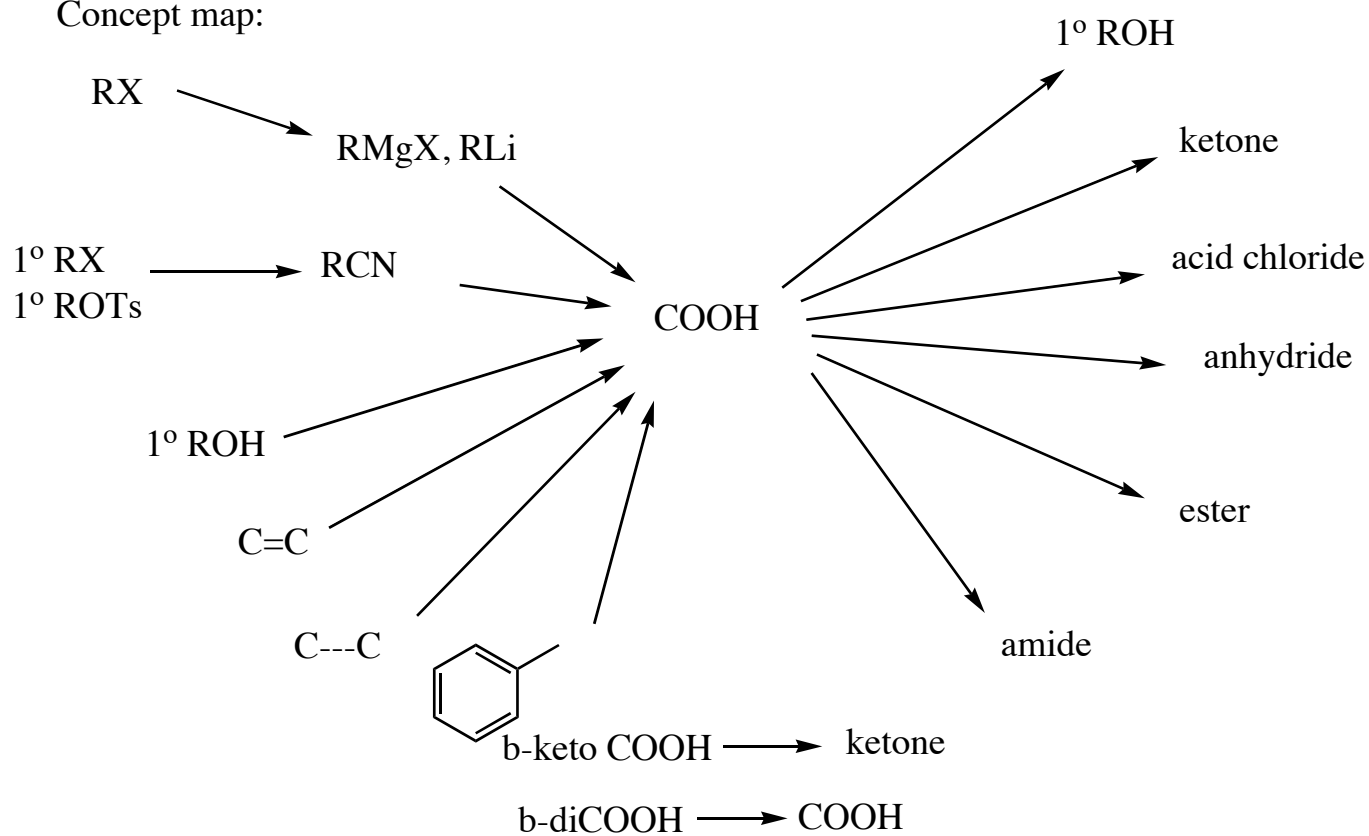
Nitriles can be hydrolyzed to form carboxylic acids by either acid or base in water with heat. Since nitriles are easily formed by $\text{S}_{\text{N}}2$ reactions with alkyl halides or tosylates, this is a useful synthetic pathway.



List as many ways as possible to form the following compounds.



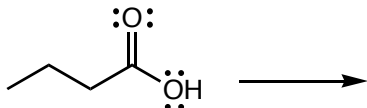
Concept map:



V. Reactions of carboxylic acids

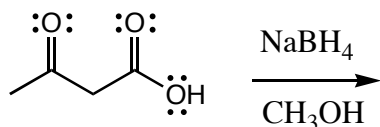
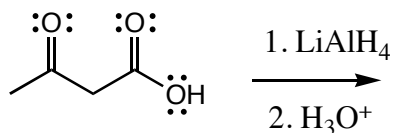
Reduction of carboxylic acids to alcohols (20-14)

What reagent is required in order to reduce carboxylic acids to primary alcohols?



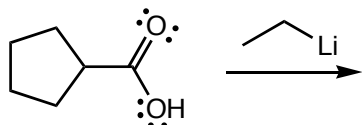
It is impossible to stop at the intermediate aldehyde stage. What does this tell you about the reaction sequence?

Recall that sodium borohydride and lithium aluminum hydride have somewhat different reactivity, which allows some control over which functional groups are reduced.



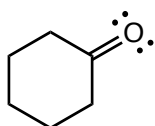
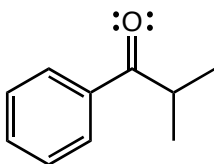
Reactions of carboxylate ions with organolithium reagents (20-15)

What will happen if a carboxylic acid reacts with an organolithium reagent?



This would be a pretty boring reaction, but if a second equivalent of the organolithium reagent is present, something else can happen.

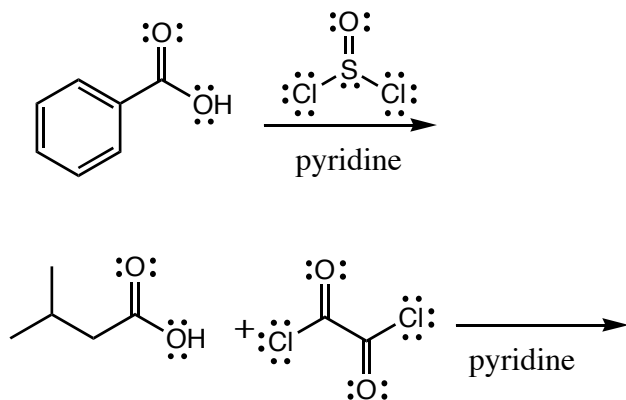
How could the following ketone be formed from a carboxylic acid?



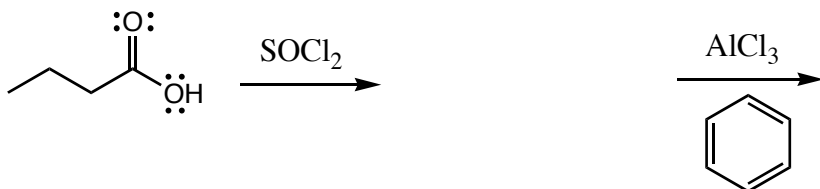
Conversion of carboxylic acids to acid chlorides (20-11)

Carboxylic acid derivatives are functional groups that can be converted to carboxylic acids by hydrolysis. We will study their reactions in chapter 22. All of them but one (nitriles) can also be made from carboxylic acids, as we shall now see.

Acid chlorides are the most reactive of the carboxylic acid derivatives. They are made from carboxylic acids by reacting them with thionyl chloride, SOCl_2 , or oxalyl chloride.

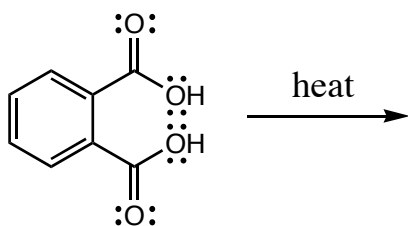
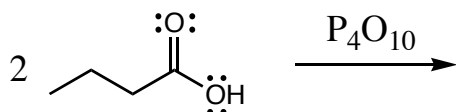


This is how you make acid chlorides to use in the Friedel-Craft reactions.



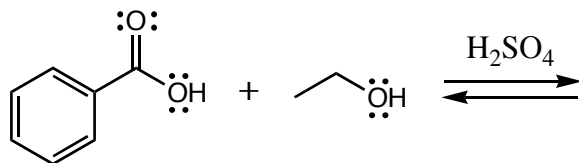
Converting carboxylic acids to anhydrides (21-5)

Carboxylic acids are converted to anhydrides by treatment with a good dehydrating agent such as P_4O_{10} . Cyclic anhydrides with 5 or 6 membered rings can be made simply by heating the dicarboxylic acid to drive off water.

Conversion of carboxylic acids to esters (20-10, 20-12)

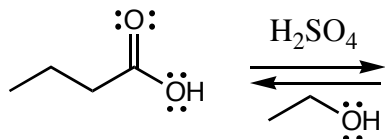
Carboxylic acids may be converted directly to esters through three different processes.

1 - Fischer Esterification



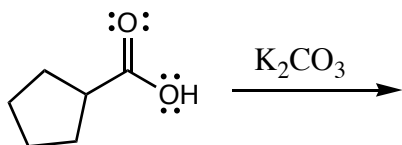
The free energies of the reactants and products are nearly the same, resulting in an equilibrium constant near 1. How can the concentration of ester be increased?

Mechanism:



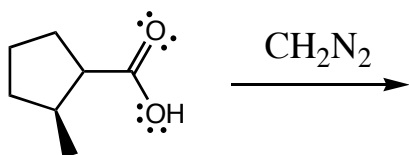
2 - S_N2 reaction between carboxylate and alkyl halide or tosylate

Carboxylate anions are not very good nucleophiles, but will react with methyl, allyl, or benzyl halides or tosylates to form esters.



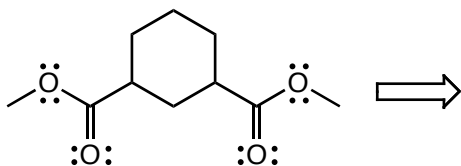
3 - Reaction with diazomethane

Reaction of carboxylic acids with diazomethane is a mild way to form methyl esters in very good yields with very little workup. However, diazomethane is explosive when dry, so special techniques must be employed.



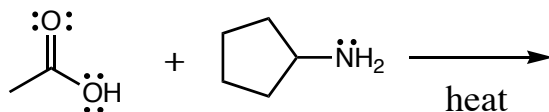
The mechanism involves protonation of diazomethane by the carboxylic acid, followed by attack of the resulting carboxylate anion on the methyldiazonium salt.

Show three ways in which the following ester could be formed.

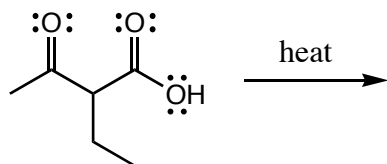


Conversion of carboxylic acids to amides (20-13)

Amides may be formed from carboxylic acids by reacting them with amines, then heating the resulting salt to over 100°C. This reaction is commonly used in industry.

Decarboxylation of β-ketocarboxylic acids and dicarboxylic acids

When a ketone is located two carbons away from a carboxylic acid, the compound can undergo a cyclic reaction in which the carboxylic acid is lost.



This mechanism is also effective with 1,3-dicarboxylic acids.

