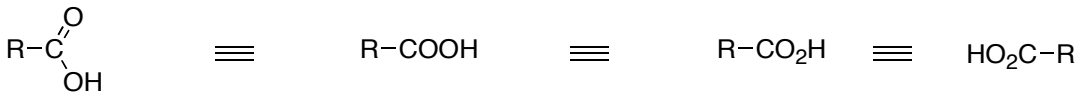
Carboxylic Acids and Derivatives

Carboxylic acids are very important compounds in nature and serve as building blocks for preparing related derivatives such as esters and amides.

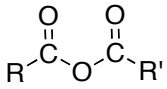
The general formula for a carboxylic acid includes a carbonyl and a hydroxyl group. The carboxylic acid can also be written in different ways and you should take note of these ways.



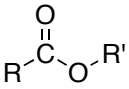
Many derivatives can be derived from carboxylic acids and below they are depicted in order of decreasing reactivity:

Acyl halides where X = F, Cl, Br, I

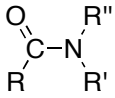
Anhydrides where R doesn't have to equal R'



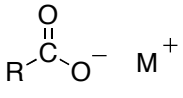
Esters where R doesn't have to equal R'



Amides where R doesn't have to equal R' or R''



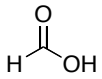
Carboxylate salts where M is usually a metal counter ion



Nomenclature of Carboxylic acids

Carboxylic acids are derived from open chain alkanes and are systematically named by replacing the terminal "-e" of the corresponding alkane name with "-oic acid". The carboxyl group is always numbered C1 in this system. Alternatively, compounds that have a –COOH group bonded to a ring are named with the suffix "-carboxylic acid". In this system, the carboxylic acid carbon is attached to C1 and is not itself numbered in this system.

For historical reasons having to do with the fact that many carboxylic acids were among the first compounds isolated and purified, there are several common names given to these acids. These common names, along with the systematic names are given below where the common names are given first. Know the names of the acids below.

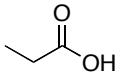


formic acid

methanoic acid

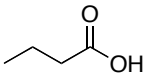
acetic acid

ethanoic acid



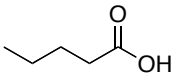
propionic acid

propanoic acid



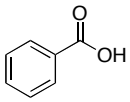
butyric acid

butanoic acid



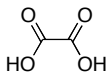
valeric acid

pentanoic acid



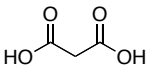
Benzoic Acid

Dicarboxylic acids are also common in nature. Know the first 5 common names:



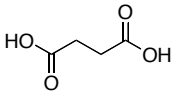
oxalic acid

ethanedioic acid



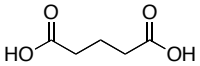
malonic acid

propanedioic acid



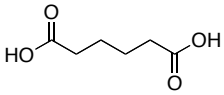
succinic acid

butanedioic acid



glutaric acid

pentanedioic acid



adipic acid

hexanedioic acid

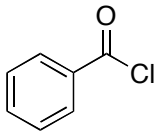
Acid halides, acyl halides

The acid/acyl halides are systematically named by dropping "ic acid" and adding "yl halide"

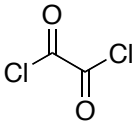
Examples:

acetyl chloride

ethanoyl chloride



benzoyl chloride

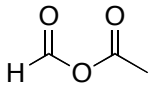


oxalyl dichloride

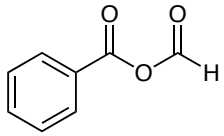
Anhydrides

The anhydrides are named by changing "acid" to "anhydride".

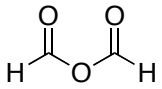
Examples:



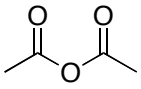
formic acetic anhydride



Benzoic formic anhydride

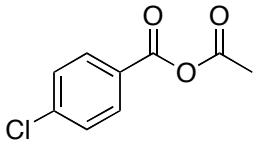


formic anhydride



acetic anhydride

ethanoic anhydride

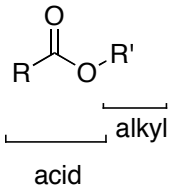


acetic 4-chlorobenzoic anhydride

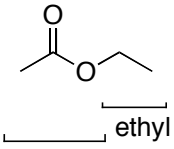
<u>Carboxylic Acids and Derivatives Nomenclature</u>

Esters

Systematic names for esters are derived by first giving the name of the alkyl group attached to the oxygen, and then identifying the carboxylic acid portion of the molecule. In doing so, the "-ic acid" is replaced with "-ate". When naming, the C1 carbon is always the carbon attached to the oxygen in the alkyl chain and the carbonyl in the acid portion.



In the below example, the alkyl chain is identified as an ethyl group and the carboxylic acid is identified as acetic acid. Identification of the alkyl chain and dropping the "-ic acid", replacing it with "-ate", gives the name ethyl acetate. The systematic name for this compound would be ethyl ethanoate.



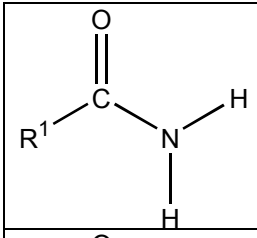
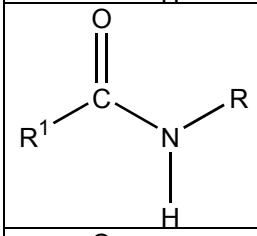
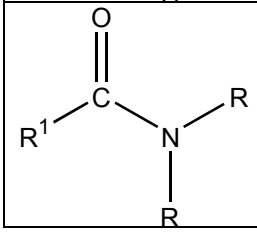
ethyl acetate

ethyl ethanoate

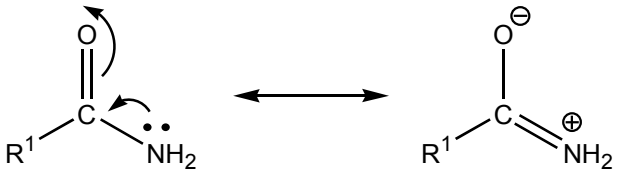
Amides

Name the corresponding acid, drop "-ic acid" or "oic acid", add "amide". If there is alkyl group on the amide nitrogen, then precede the chemical name with N-alkyl, such as N-methyl.

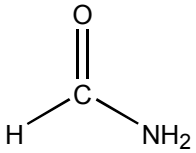
Classification:

	Primary amide where there are two hydrogens attached to amide nitrogen **If R^1 = H formamide** **methanamide**
	Secondary amide where there is one hydrogen attached to amide nitrogen **If R^1 = H N-methylformamide** **R = CH_3**
	Tertiary amide where there is no hydrogen attached to amide nitrogen **If R^1 = H dimethylformamide** **R = CH_3**

Usually amides are planar, because the lone pair on nitrogen can conjugate into the carbonyl.

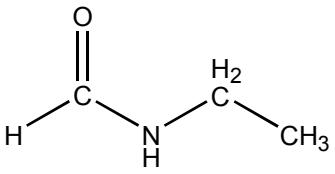


Example:



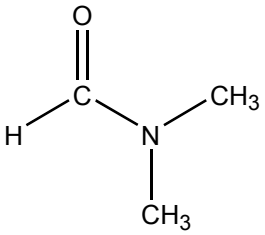
Nomenclature: **Formamide**. The corresponding parent acid is formic acid. Follow the rule above, drop "ic acid" and replace with "amide", the above molecule is named as formamide. Systematically, it is known as methanamide.

Example:



Nomenclature: **N-ethylformamide**. The letter "N" at the beginning of the name indicates that the ethyl group is attached on the nitrogen.

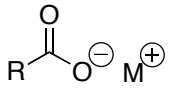
Example:



Nomenclature: **N, N-dimethylformamide** (DMF). This is a very common polar aprotic solvent. Make sure you know its name and structure. It may also be named N,N-dimethylmethanamide.

Carboxylate Salts

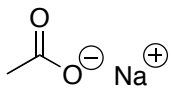
The general form of a carboxylate salt is:



where M is usually a metal ion.

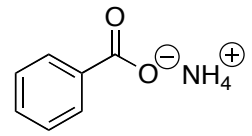
Carboxylate salts are named by first specifying the cation (such as sodium or ammonium), and then naming the carboxylic acid, where the "ic acid" is replaced with "ate."

Example:

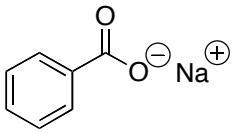


The counterion in this molecule is sodium, so we include it first. The carboxylic acid is acetic acid, so we replace the "ic acid" with "ate" and get acetate. Therefore, this molecule is known as sodium acetate.

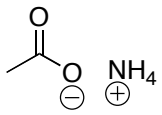
Examples:



Ammonium benzoate



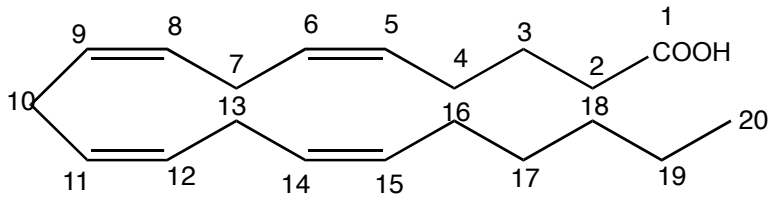
Sodium benzoate



Ammonium acetate

Nomenclature examples:

Example:

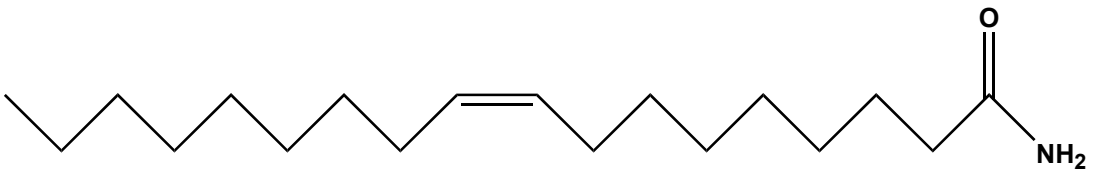


Arachidonic Acid

Arachidonic acid is a polyunsaturated fatty acid, and is one of the essential fatty acids required by most of mammals. It is a precursor in the production of eicosanoids: the prostaglandins, thromboxanes, prostacyclin and the leukotrienes (through enzymes including cyclooxygenase, lipoxygenase and peroxidase). Chemically, arachidonic acid is a carboxylic acid with a 20-carbon chain and four *cis* double bonds. Recall from previous lecture, a 20-carbon alkane is named eicosane.

To name the acid, you would drop '-e", add "oic acid". Since arachidonic acid has 4 double bonds, it would an eicosatetraene. All double bonds are cis, therefore are in Z configuration. Putting everything together, the systematic name is **5Z,8Z,11Z,14Z-eicosatetraenoic acid**.

Example:

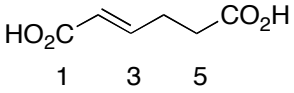


The molecule shown is oleamide, a sleep hormone.

It has 18 carbons. An 18-carbon alkane is called octadecane. The corresponding alkene would be octadecene. The corresponding acid would be 9-octadecenoic acid, and for the amide the systematic name is **9Z-octadecenamide**.

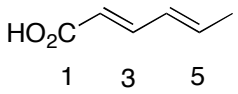
Example:

Below is an example of a molecule with two carboxylic acid groups. The first step to naming this compound is to find the parent alkane chain. Since it is a 6 carbon chain, it is a hexane. We then drop the "-e" and add "-oic acid" for the name to become hexanoic acid. Since there are two carboxylic acids present, the name becomes hexandioic acid. We notice that there is a double bond present in the molecule and therefore the name becomes hexendioic acid. The numbering of the chain should give the lowest number for the alkene, therefore the alkene is at C2 if you start numbering from the left, giving the name 2-hexendioic acid. Since the alkene is a trans double bond, the final name of this compound is 2E-hexendioic acid.



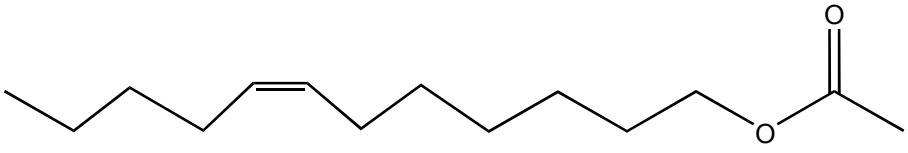
2E-hexendioic acid

Another naming example is given below. The first step is to find the parent alkane chain. This example once again has a 6 carbon chain and is a hexane. We then drop the "-e" and add "-oic acid" for the name to become hexanoic acid. There are two double bonds present in the molecule and therefore the name becomes hexadienoic acid. The numbering of the chain gives the carboxylic acid carbon C1 and therefore the alkenes are at C2 and C4 if you start numbering from the left giving the name 2,4-hexadienoic acid. Both alkenes are trans double bonds, therefore the final name for this molecule is 2E,4E-hexadienoic acid.

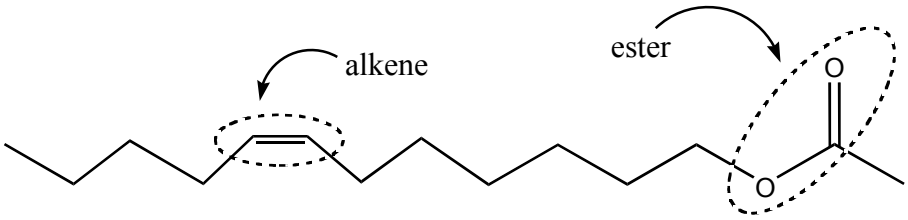


2E,4E-hexadienoic acid

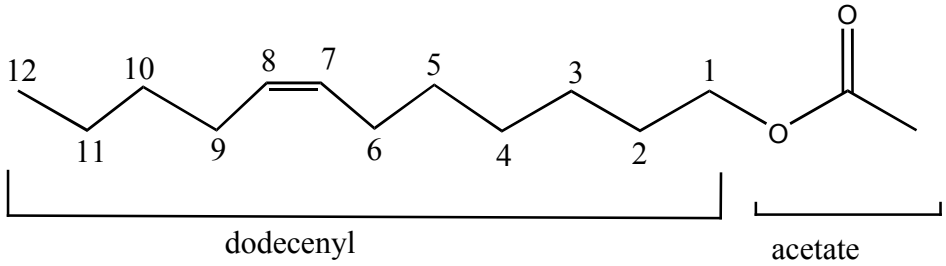
Example:



The molecule shown is a sex pheromone for elephants.
What kind of functional groups are present in this molecule?



Recall for esters, you name the alkyl part first (drop "e" and add "yl") and then the "ic acid" of the parent acid is replaced with "ate".
The alkyl group attached to oxygen has 12 carbons. A 12 carbon alkane is named a dodecane, and the corresponding alkene would be dodecene. The parent acid is acetic acid. When replaced with "-ate", it is acetate.

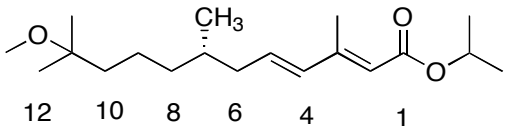


The systematic name for this pheromone is **7Z-dodecenyl acetate**.

If any part of this molecule is changed (remove a carbon, or extend by a carbon on the acetate part, or change the configuration of the double bond), it would not work as sex pheromone.

Examples

A more difficult example is the following growth inhibitor of fleas used in anti-flea powders on dogs and cats. When naming this compound, first the alkyl chain should be identified. The longest chain is 2 carbons and therefore is a substituted ethyl group. When numbering from the carbon attached to the oxygen, the methyl substituent is at C1 giving a 1-methylethyl (or isopropyl) chain. The acid portion of this molecule is a little more difficult. Firstly, we should identify the longest chain in the acid portion to get the parent alkane name. Since the longest chain is 12 carbons, it is a dodecane. Secondly, there are two trans alkenes in this molecule at the C2 and C4 positions when numbering starts at the carbonyl carbon to give dodeca-2E,4E-diene. The parent name for the acid would then be dodeca-2E,4E-dienoic acid. Since the molecule is an ester, dropping the "-ic acid" and replacing it with "-ate" gives the name dodeca-2E,4E-dienoate. Lastly is the naming of the substituents on the parent acid chain. At positions C3, C7, and C11 are methyl groups and at C11 is a methoxy group. The C7 methyl group is a stereogenic center and is in the S configuration. By combining the acid portion of the name and the alkyl portion, the final name for this molecule is isopropyl 11-methoxy-3,7S,11-trimethyldodeca-2E,4E-dienoate. Instead of isopropyl, one can call the alkyl part 1-methylethyl.

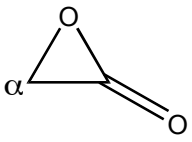


growth inhibitor of fleas
used in anti-flea powder

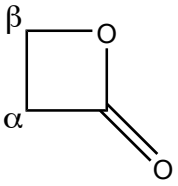
isopropyl 11-methoxy-3,7S,11-trimethyldodeca-2E,4E-dienoate

Lactones: Cyclic esters

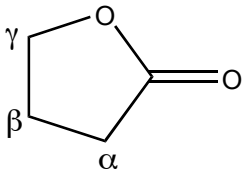
The ring size of the lactone can be described by starting at the carbonyl carbon and designating the other carbons in the ring with Greek letters (shown in figure) until the oxygen atom is reached.



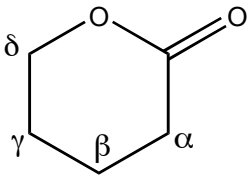
α-lactone



β-lactone



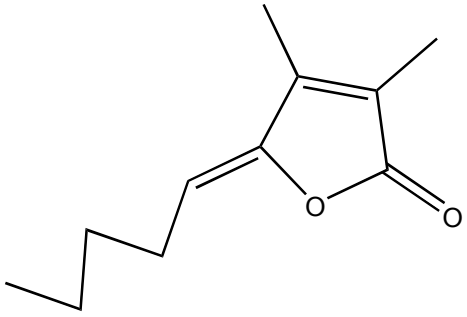
γ-lactone



δ-lactone

You should be able to recognize all four lactones shown above and know that lactones are cyclic esters.

Example:

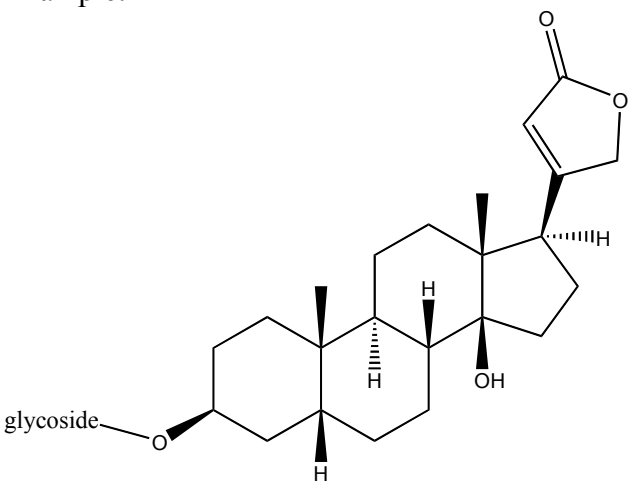


bovolide

Bovolide is produced by cows and is responsible for the butter flavor.

What kind of lactone is the above molecule?
Answer: It is a γ-lactone. Specifically, an α,β-unsaturated γ-lactone.

Example:



This molecule is digitoxin from the plant foxglove. It is a very toxic substance. In small amounts, it is a cardioactive drug. If taken in excess, it is a heart stimulant that can give instant heart attack.

Is the O at position 3 on the A ring α or β substituted?
Answer: it is β.

What kind of lactone does it have?
Answer: it is γ-lactone, since the lactone is 5-member ring.