# Chapter 19
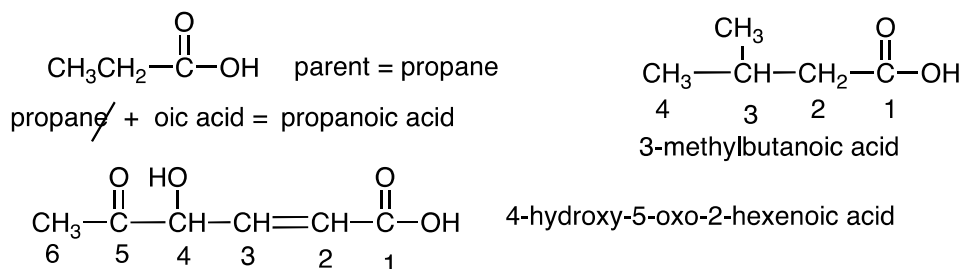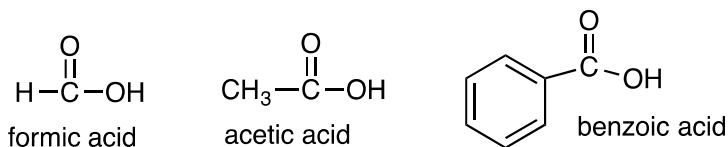# Carboxylic Acids

Carboxylic acids have the formula $RCO_2H$.

## Nomenclature

For the parent alkane, drop the terminal "e" and add the suffix "-oic acid".

The parent alkane is the longest continuous chain that contains the carboxylic acid functionality. The carbonyl carbon of the carboxylic acid receives the lowest number, C1, but this does not need to be specified. Recall that for carbons bearing oxygen, the higher oxidation state takes precedence. Therefore carboxylic acids > aldehydes > ketones > alcohols.

$$CH_3CH_2-\overset{O}{\underset{\|}{C}}-OH \quad \text{parent = propane}$$

propane + oic acid = propanoic acid

$$CH_3-\overset{CH_3}{\underset{|}{CH}}-CH_2-\overset{O}{\underset{\|}{C}}-OH$$
$$\quad\quad 4 \quad\;\; 3 \quad\; 2 \quad\; 1$$
3-methylbutanoic acid

$$CH_3-\overset{O}{\underset{\|}{C}}-\overset{HO}{\underset{|}{CH}}-CH=CH-\overset{O}{\underset{\|}{C}}-OH$$
$$\quad\;\; 6 \quad\;\; 5 \quad\;\; 4 \quad\; 3 \quad\;\; 2 \quad\;\; 1$$
4-hydroxy-5-oxo-2-hexenoic acid

Some common names:

$$H-\overset{O}{\underset{\|}{C}}-OH \qquad CH_3-\overset{O}{\underset{\|}{C}}-OH$$
formic acid          acetic acid

benzoic acid

Structure:
In formic acid one C-O bond is shorter than the other. The carbonyl carbon is $sp^2$ hybridized, making the carboxylic acid trigonal planar.

bond angles

| | |
|---|---|
| $H-C=O$ | 124 A° |
| $H-C-O$ | 111 A° |
| $O-C=O$ | 125 A° |

124°     1.2 A°
1.34 A°
1.11 A°
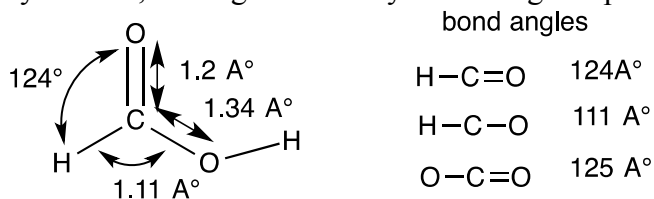
Lone pair donation from the alcohol OH decreases the electrophilicity of the carbonyl carbon. The negative charge is distributed equally over the two oxygens (each has a charge of -1/2) and the bond lengths are the same, 1.25 A°, about mid-way between a single and double bond.

bond length 1.25 A°
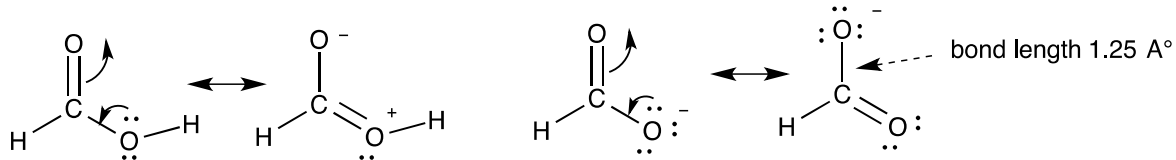
In the conjugate base, both oxygens are the same length and the negative charge is equally distributed over both oxygens.
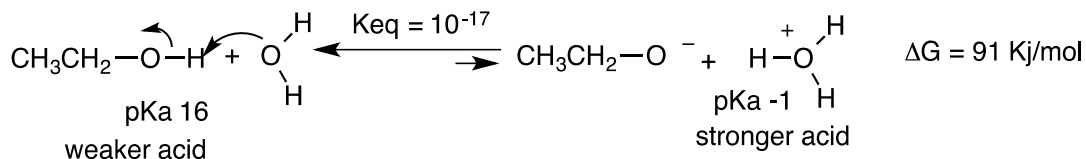
Carboxylic acids have higher boiling points that alcohols or ketones due to intermolecular hydrogen bonding. Two sets of hydrogen bonds are possible.



b. p.    31°        80°         99°          141°

Two sets of intermolecular H-bonds are possible.
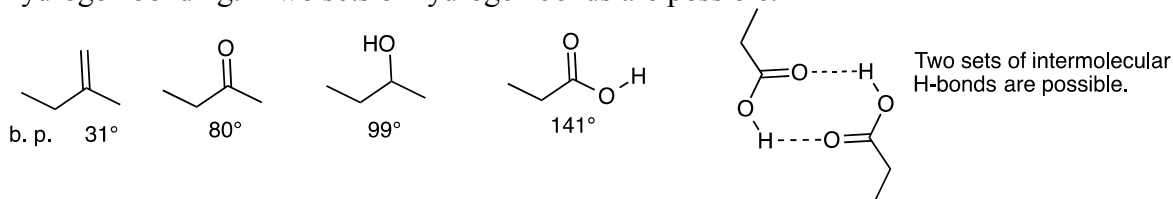
Carboxylic acids containing four carbons or less are miscible with water.


**Acidity of Carboxylic Acids**

Carboxylic acids are the most acidic compounds that contain only carbon, hydrogen and oxygen. They are much more acidic that $H_2O$ (pKa 15.7) or alcohols, ROH (pKa ~ 16), but they are still fairly weak acids when compared to the mineral acids such as HBr (pKa -7) or HCl (pKa -5). Carboxylic acids have pKa's of about 5 but this can be lowered considerably by electron withdrawing substituents.



$CH_3CH_2-O-H$ + $O$  $\xrightarrow{K_{eq} = 10^{-17}}$  $CH_3CH_2-O^-$ + $H-O$   $\Delta G = 91$ Kj/mol

pKa 16        pKa -1
weaker acid      stronger acid

Here the equilibrium is very unfavorable. As we know, the reaction proceeds in the direction of converting the stronger acid into the weaker acid. Here we see that the hydronium ion ($H_3O^+$) on the right is a much stronger acid (pKa -1) than the alcohol so the equilibrium lies way to the left. We can calculate the equilibrium constant by simply subtracting the exponents of the pKa's and adjusting the sign according to where the equilibrium lies: (-)-sign for the equilibrium to the left and (+)-sign for the equilibrium to the right.

With acetic acid in water, we see that the equilibrium is still unfavorable but less so.

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acetic acid
pKa 4.7
weaker acid

$K_{eq} = 10^{-5.7}$

pKa -1
stronger acid
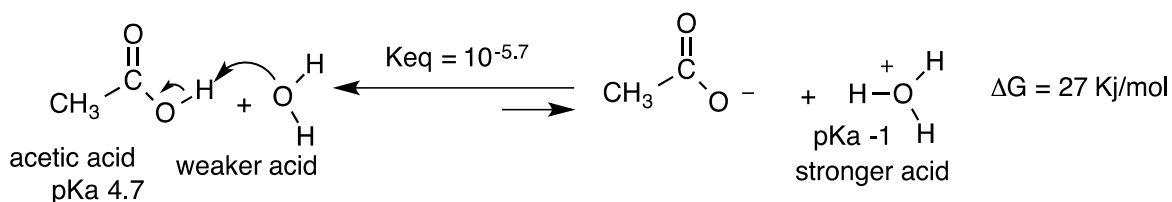
$\Delta G$ = 27 Kj/mol

The free energy of ionization for acetic acid (+27 KJ/mol) is still unfavorable but much less unfavorable than it is form ethanol (+ 91 KJ/mol). This is due to (1) the resonance stabilization of the resulting carboxylic acid anion, as shown above, and (2) to the inductive electron withdrawing effect of the carbonyl carbon.

We can use the Henderson-Hasselbalch equation to find the ratio of concentrations of an acid and its conjugate base. It is derived as follows.

For:



Acid
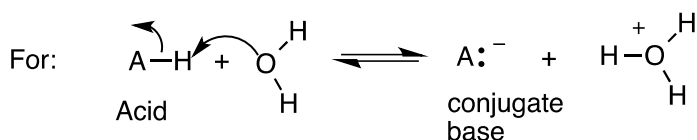
conjugate
base

$$K_a = \frac{[H_3O^+]\,[\text{Conjugate base}]}{[\text{acid}]}$$

Taking the log of both sides:

$$\log K_a = \log [H_3O^+] + \log \frac{[\text{Conjugate base}]}{[\text{acid}]}$$

Rearrange this to:
Rearrange this to:

$$-\log [H_3O^+] = -\log K_a + \log \frac{[\text{Conjugate base}]}{[\text{acid}]}$$

Since pH is by definition $-\log [H_3O^+]$ and pKa is $-\log K_a$, this expression is:
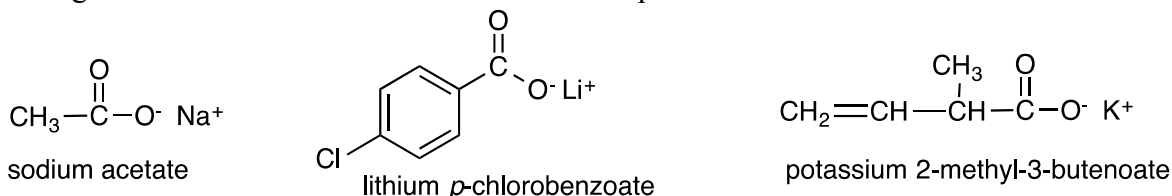
$$pH = pKa + \log \frac{[\text{Conjugate base}]}{[\text{acid}]}$$

This is the Henderson-Hasselbalch equation. This can be rearranged to:

$$pH - pKa = \log \frac{[\text{Conjugate base}]}{[\text{acid}]} \qquad \text{or:} \qquad \frac{[\text{Conjugate base}]}{[\text{acid}]} = 10^{(pH-pKa)}$$

$$pH - pKa = \log \frac{[\text{Conjugate base}]}{[\text{acid}]} \qquad \text{or:} \qquad \frac{[\text{Conjugate base}]}{[\text{acid}]} = 10^{(pH-pKa)}$$

3

**Salts of Carboxylic Acids, RCO$_2^-$ M$^+$**

These are named by taking the parent carboxylic acid, dropping the suffix "-oic acid" and adding the suffix "-ate".  The metal counterion is specified first.

CH$_3$—C(=O)—O$^-$ Na$^+$

sodium acetate

lithium p-chlorobenzoate

CH$_2$=CH—CH(CH$_3$)—C(=O)—O$^-$ K$^+$

potassium 2-methyl-3-butenoate

Carboxylic acid salts are soluble in water if the molecular weight is not too high.  If there are 12 – 18 carbons in the carboxylic acid salt then the behavior is unusual.  For example sodium stearate (sodium octadecanoate) is semi-soluble and forms micelles.  These are membrane-like structures that self-assemble in water into spherical shapes in which the polar head groups (-CO$_2^-$) are on the outside and the long, non-polar hydrocarbon chair are on the interior.

sodium octadecanoate

Non-polar hydrocarbon chain

polar headgroup
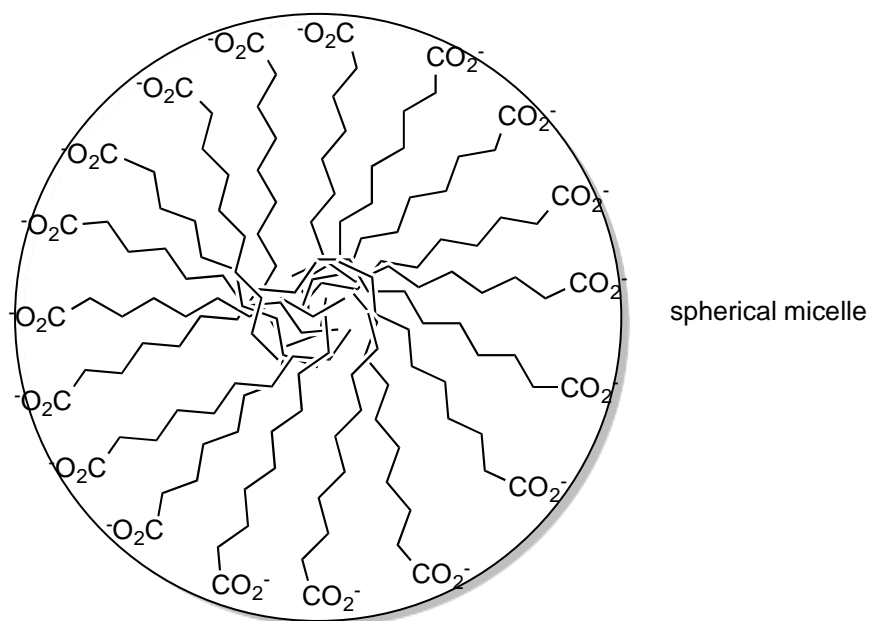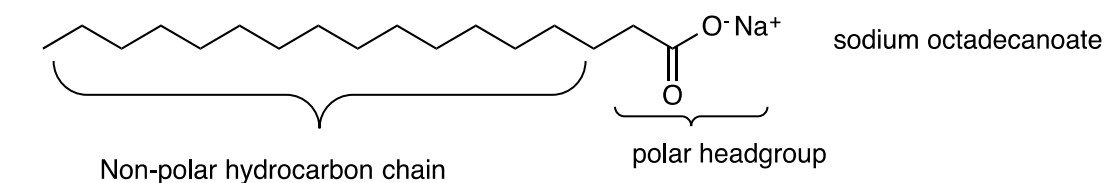
spherical micelle

The spherical shape exposes the minimum surface for a given volume.

This is how soaps work. They form micelles. Grease is non-polar and gets enclosed in the hydrophobic interior of the micelle and so is washed away.

Commercial detergents are similar to soaps except that they use synthetic head groups, like sulfates.



lauryl sulfate (sodium dodecyl sulfate)
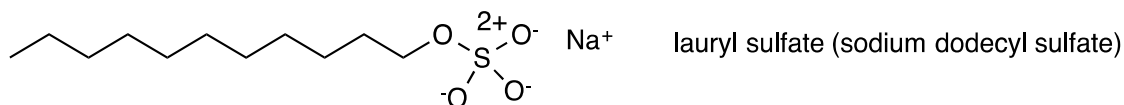
**Substituents and Acid Strength**

Electronegative substituents near an ionizable hydrogen increase its acidity. Alkyl groups have little effect.



pKa 4.7          pKa 4.9          pKa 4.8
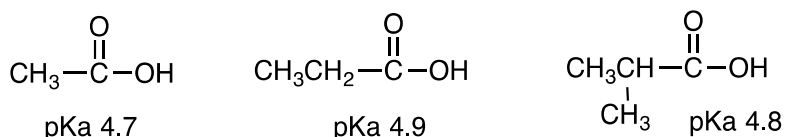
Halogens at the alpha position increase the acidity due to the inductive effect of the halogen. The electronegative chlorines withdraw electron density from the alpha-carbon, giving it a partial positive charge and also they help to stabilize the resulting anion by dispersing the negative charge.



pKa 2.9          pKa 1.3          pKa 0.9
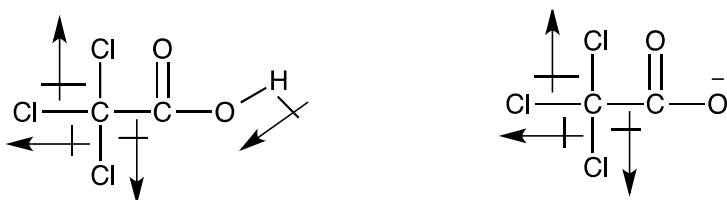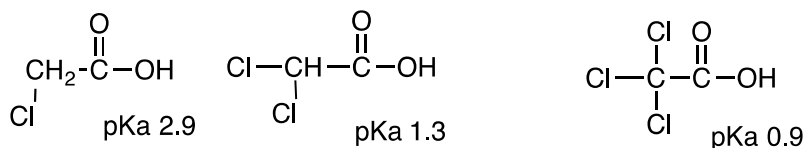


The effect of the chlorine weakens as it is moved away from the alpha position.



pKa 2.8          pKa 4.1          pKa 4.5
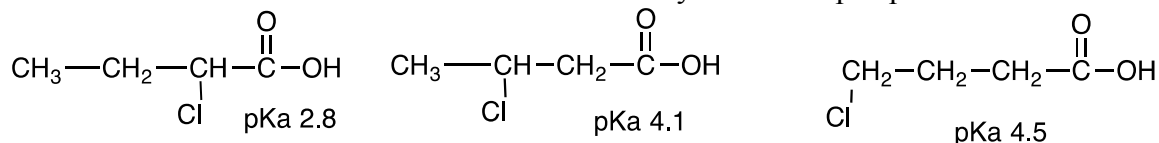
Note that there is also the field effect. This operates in the same direction as the inductive effect but the electronegative effect is communicated through the medium, usually the solvent. An electronegative substituent in a molecule polarizes the surrounding solvent

molecules. This polarization is transmitted through other solvent molecules to the remote site.

Substituents affect the entropy of ionization more than they do the enthalpy term. As we know, the free energy is the sum of the change in enthalpy or heat, $\Delta H°$, and the change in entropy or disorder, $-T\Delta S$:

$$\Delta G° = \Delta H° - T\Delta S°.$$

For most carboxylic acids, the enthalpy term is close to zero for ionization and so $\Delta G°$ is dominated by the $-T\Delta S°$ terms. Ionization is accompanied by an increase in solvation forces. This leads to a decrease in the entropy of the system. $\Delta S$ is negative so $-(-\Delta S)$ is positive.

Carboxylate ions with substituents capable of dispersing negative charge impose less order on the solvent (water) and less entropy is lost when they are ionized.


**Ionization of Substituted Benzoic Acids:**
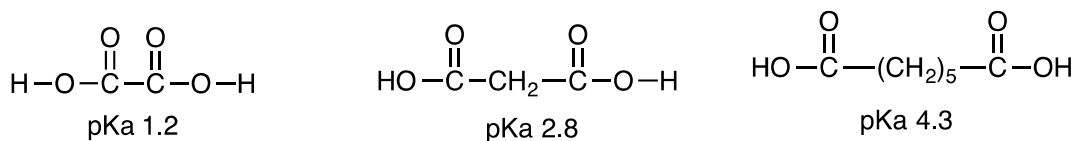Electron withdrawing groups (EWG's) increase acidity, especially at the *ortho* position.
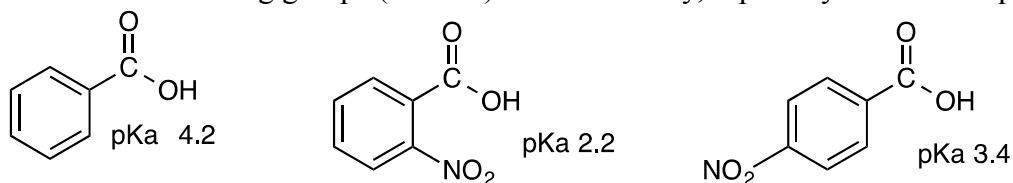


**Dicarboxylic Acids:**

Oxalic acid has two pKa's. The first one is lower than the second. The carboxylic acid functional group is a strong electron withdrawing group and we see that the first pKa is much lower than that of acetic acid. The carboxylate anion is not nearly as strong an electron withdrawing group and so the second pKa is much higher, not much lower than that of acetic acid. Note also that part of the increased acidity of oxalic acid as compared to the oxylate anion is due to the statistical effect. There are two potential sites for ionization in oxalic acid, making the effective concentration of carboxyl groups twice as large.
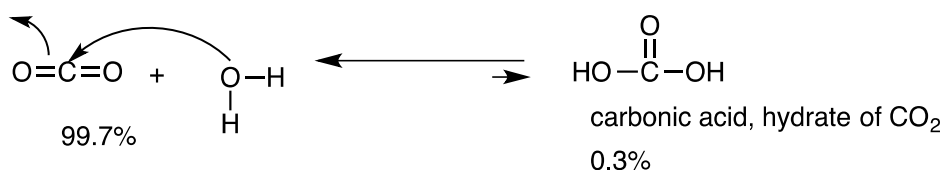


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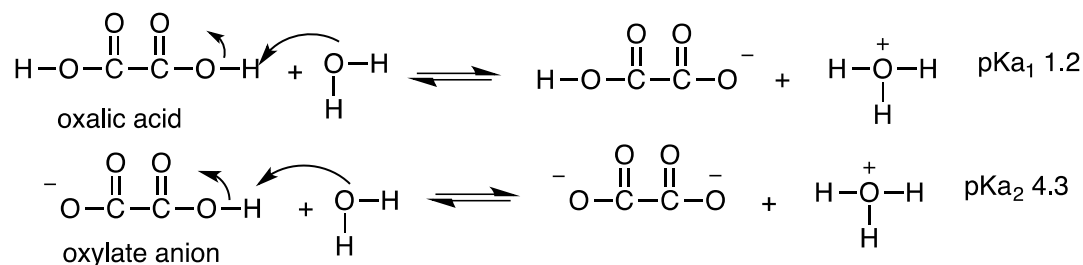
Note that the electron withdrawing effect of the carboxylic acid decreases as the distance between them increases.
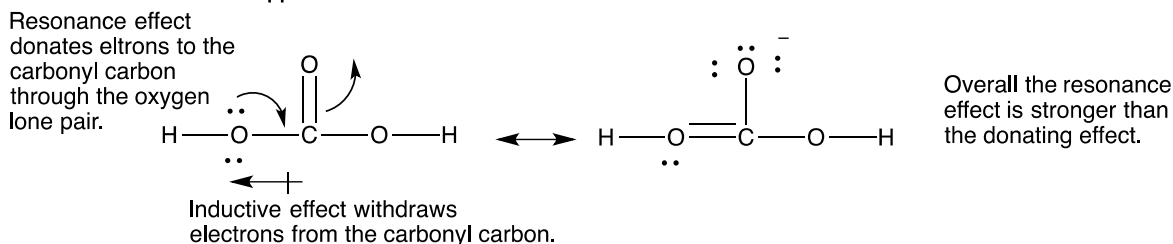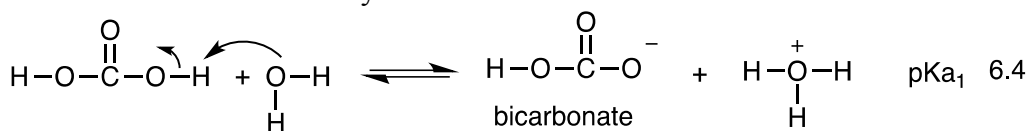
$$H-O-\overset{\overset{\displaystyle O}{\|}}{C}-\overset{\overset{\displaystyle O}{\|}}{C}-O-H \qquad HO-\overset{\overset{\displaystyle O}{\|}}{C}-CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-O-H \qquad HO-\overset{\overset{\displaystyle O}{\|}}{C}-(CH_2)_5-\overset{\overset{\displaystyle O}{\|}}{C}-OH$$

pKa 1.2 pKa 2.8 pKa 4.3

**Carbonic Acid**
Carbonic acid is unstable but exists in equilibrium with $CO_2$ and $H_2O$. Due to the two strong C=O bonds, carbon dioxide is more stable and the equilibrium greatly favors $CO_2$ and $H_2O$, with only a tiny amount of carbonic acid present.

$$O=C=O \quad + \quad \overset{\overset{\displaystyle |}{O}-H}{\underset{H}{}} \quad \rightleftarrows \quad HO-\overset{\overset{\displaystyle O}{\|}}{C}-OH$$

99.7% carbonic acid, hydrate of $CO_2$

0.3%

Carbonic acid is very important in blood chemistry. It carries $CO_2$ away from the cells to the lungs where it can be expunged. There is an enzyme, carbonic anhydrase, that catalyzes the hydration of $CO_2$, thereby effectively reversing the equilibrium so that it lies in favor of hydration. Carbonic anhydrase is said to be the perfectly evolved enzyme in that it is the fastest enzyme known. It can catalyze the hydration of $3.6 \times 10^7$ molecules of $CO_2$ per minute!

Carbonic acid is a weaker acid than acetic acid. This indicates that the hydroxyl group is actually an electron donating group (EDG). Remember that there are two effects operating here in opposition to each other. Oxygen, of course is more electronegative than carbon and so the oxygen withdraws electrons through the inductive effect but the oxygen lone pair can donate back to the C=O $\pi$–system. This resonance donation is stronger than the electron withdrawing inductive effect and so the overall effect of the oxygen is to release electrons to the electron deficient carbonyl.

$$H-O-\overset{\overset{\displaystyle O}{\|}}{C}-O-H \; + \; \overset{\overset{\displaystyle |}{O}-H}{\underset{H}{}} \; \rightleftharpoons \; H-O-\overset{\overset{\displaystyle O}{\|}}{C}-O^{-} \; + \; H-\overset{\overset{\displaystyle +}{O}-H}{\underset{H}{}} \qquad pKa_1 \; 6.4$$

bicarbonate

Resonance effect donates eltrons to the carbonyl carbon through the oxygen lone pair.

Inductive effect withdraws electrons from the carbonyl carbon.

Overall the resonance effect is stronger than the donating effect.

The second pKa, as we would expect, is higher than the first one, since the oxygen anion is an even better donating group.
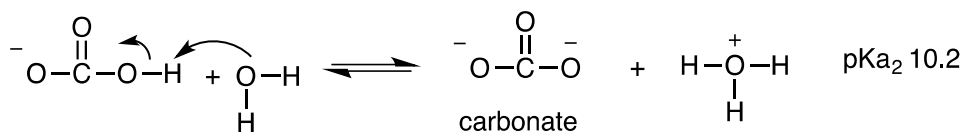
And the carbonate dianion (i.e. sodium carbonate) is a stronger base than bicarbonate.

But note, if there is an $sp^3$ carbon attached to the carbonyl and then an oxygen atom, the oxygen becomes a purely electron-withdrawing group through the inductive effect.



$CH_3O-CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-O-H$  pKa 3.7    $CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-O-H$  pKa 4.8
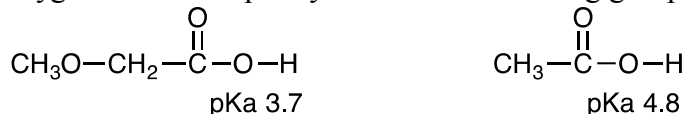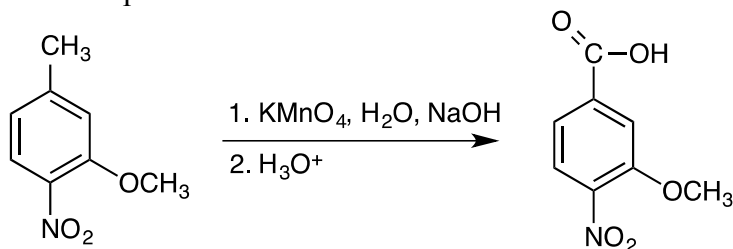
## Sources of Carboxylic Acids

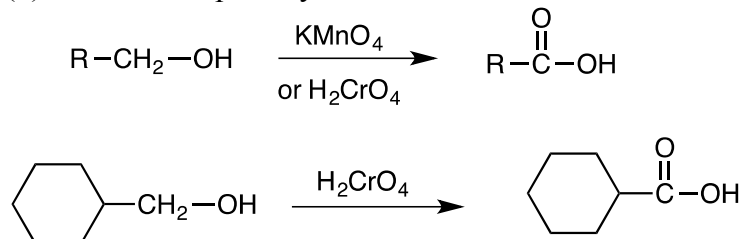### Previous Methods for Preparations of Carboxylic Acids

(1) Side chain oxidation of alkyl benzene derivatives. Potassium permanganate or chromic acid will oxidize any aryl side chain down to the carboxylic acid as long as there is at least one benzylic hydrogen.



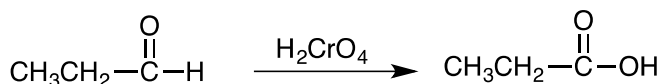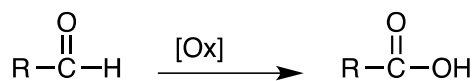$R_1, R_2$ = alkyl, alkenyl, etc
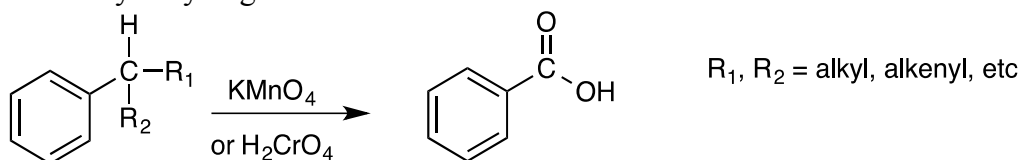
For example:



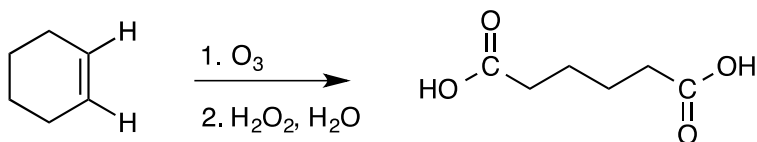(2) Oxidation of primary alcohols.



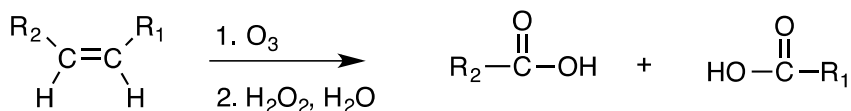

(3) Oxidation of Aldehydes.
A variety of reagents will oxidize aldehydes to carboxylic acids, including chromic acid.

$$R-\overset{\overset{\displaystyle O}{\|}}{C}-H \xrightarrow{\text{[Ox]}} R-\overset{\overset{\displaystyle O}{\|}}{C}-OH$$

$$CH_3CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-H \xrightarrow{H_2CrO_4} CH_3CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-OH$$
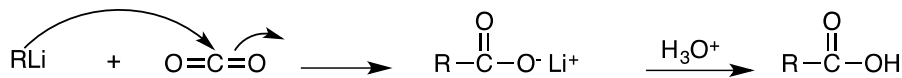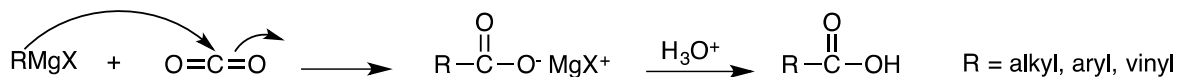
(4) Oxidative cleavage of alkenes using ozonolysis with oxidative work-up.
Recall that alkenes can be cleaved using ozonolysis and by using an oxidative work-up with a peroxide reagent we can form carboxylic acids.
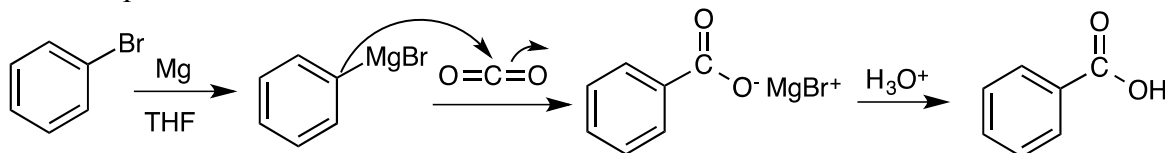
$$\underset{H}{\overset{R_2}{\diagdown}}C=C\underset{H}{\overset{R_1}{\diagup}} \quad \xrightarrow[\text{2. } H_2O_2,\ H_2O]{\text{1. } O_3} \quad R_2-\overset{\overset{\displaystyle O}{\|}}{C}-OH \quad + \quad HO-\overset{\overset{\displaystyle O}{\|}}{C}-R_1$$

**New Methods for Synthesis of Carboxylic Acids**

(5) Carbonylation of Grignard Reagents of Organolithium Reagents

Grignard reagents, RMgX, or organolithium reagents, RLi, both react with carbon dioxide to give, after acidic work-up, a carboxylic acid with the addition of one extra carbon. As we saw earlier, Grignards and organolithium reagents react with carbonyls and carbon dioxide, as a dicarbonyl is an excellent electrophile.

$$RMgX \quad + \quad O=C=O \quad \longrightarrow \quad R-\overset{\overset{\displaystyle O}{\|}}{C}-O^-\ MgX^+ \quad \xrightarrow{H_3O^+} \quad R-\overset{\overset{\displaystyle O}{\|}}{C}-OH \qquad R = \text{alkyl, aryl, vinyl}$$

$$RLi \quad + \quad O=C=O \quad \longrightarrow \quad R-\overset{\overset{\displaystyle O}{\|}}{C}-O^-\ Li^+ \quad \xrightarrow{H_3O^+} \quad R-\overset{\overset{\displaystyle O}{\|}}{C}-OH$$
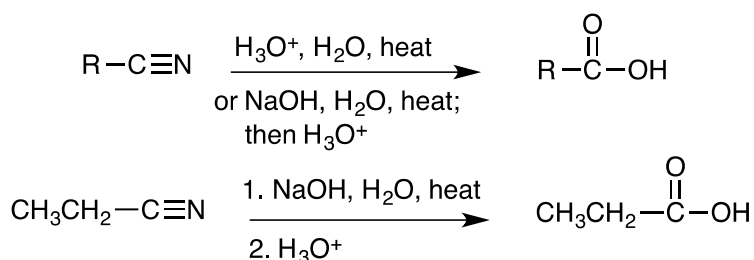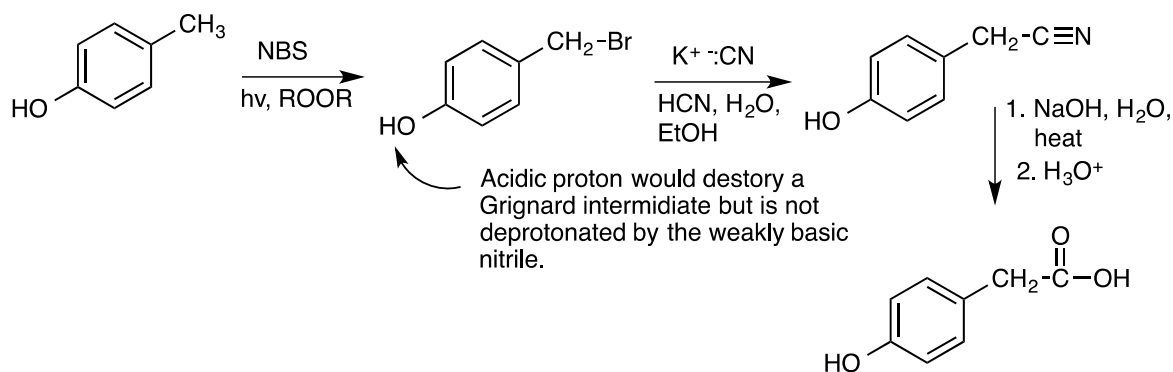
For example:

(6) Hydrolysis of Nitriles
Nitriles or cyano groups can be hydrolyzed to carboxylic acids in either aqueous acidic or aqueous basic conditions.

R$-$C$\equiv$N $\xrightarrow[\substack{\text{or NaOH, H}_2\text{O, heat;} \\ \text{then H}_3\text{O}^+}]{\text{H}_3\text{O}^+,\ \text{H}_2\text{O, heat}}$ R$-\overset{\overset{\displaystyle O}{\|}}{C}-$OH

CH$_3$CH$_2-$C$\equiv$N $\xrightarrow[\text{2. H}_3\text{O}^+]{\text{1. NaOH, H}_2\text{O, heat}}$ CH$_3$CH$_2-\overset{\overset{\displaystyle O}{\|}}{C}-$OH

As we know, we can make alkyl nitriles by reaction of alkyl halides with a nitrile salt. This is a simple S$_N$2 reaction that forms a new C-C bond in the process. Then we can hydrolyze the nitrile to the carboxylic acid derivative. This method is complementary to the carbonylation of Grignard or organolithium reagents and can be useful with molecules that have an acidic proton and so that would not be compatible with the strongly basic conditions of the Grignard or organolithium intermediate.



Acidic proton would destory a Grignard intermidiate but is not deprotonated by the weakly basic nitrile.

We can also hydrolyze cyanohydrins, which can be made from ketones or aldehydes by nucleophilic attack of the nitrile on the carbonyl carbon.
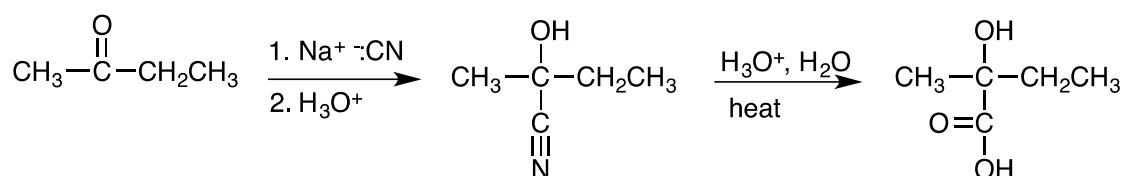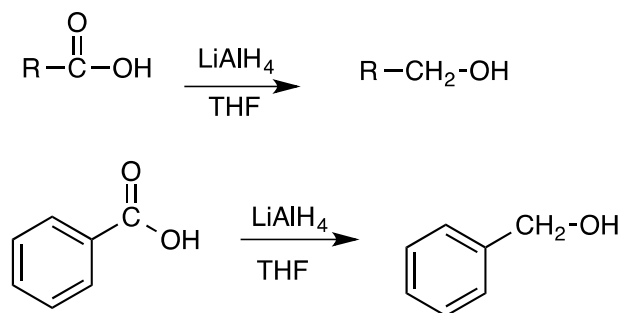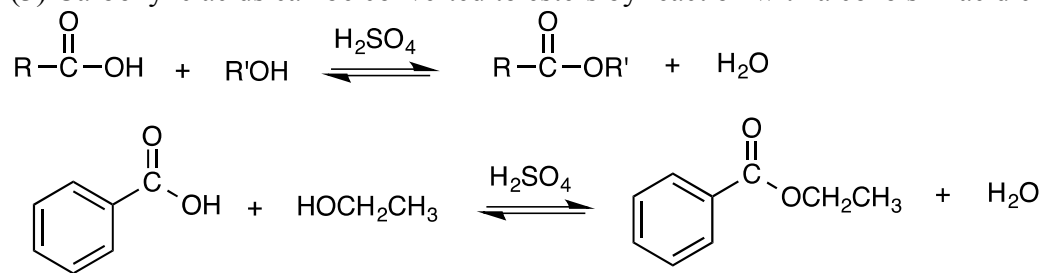


**Reactions of Carboxylic Acids**

(1) Carboxylic acids can be converted to acid chlorides by heating with thionyl chloride, SOCl$_2$.
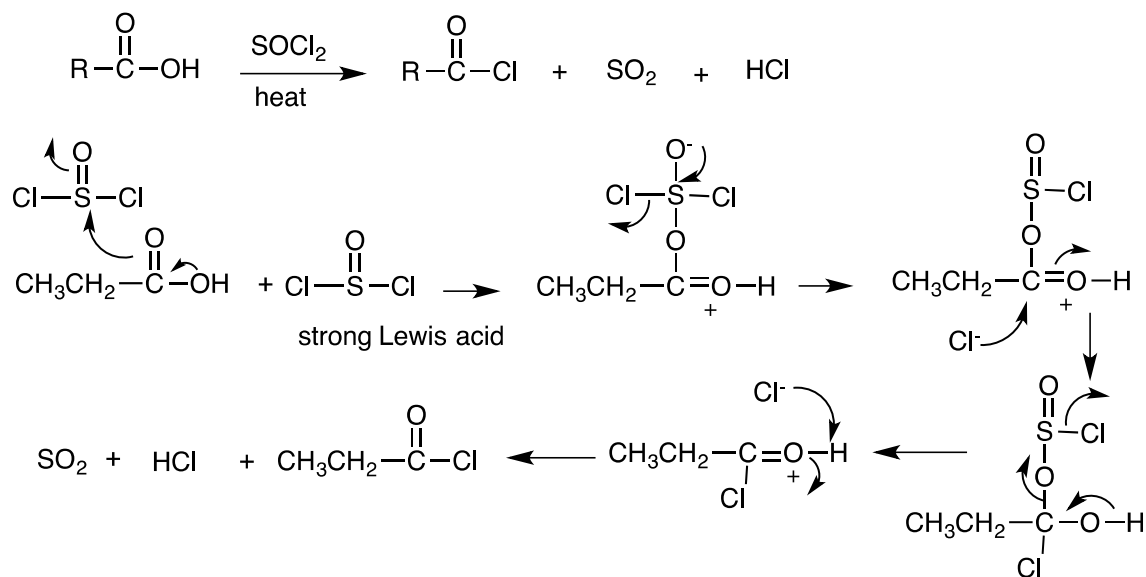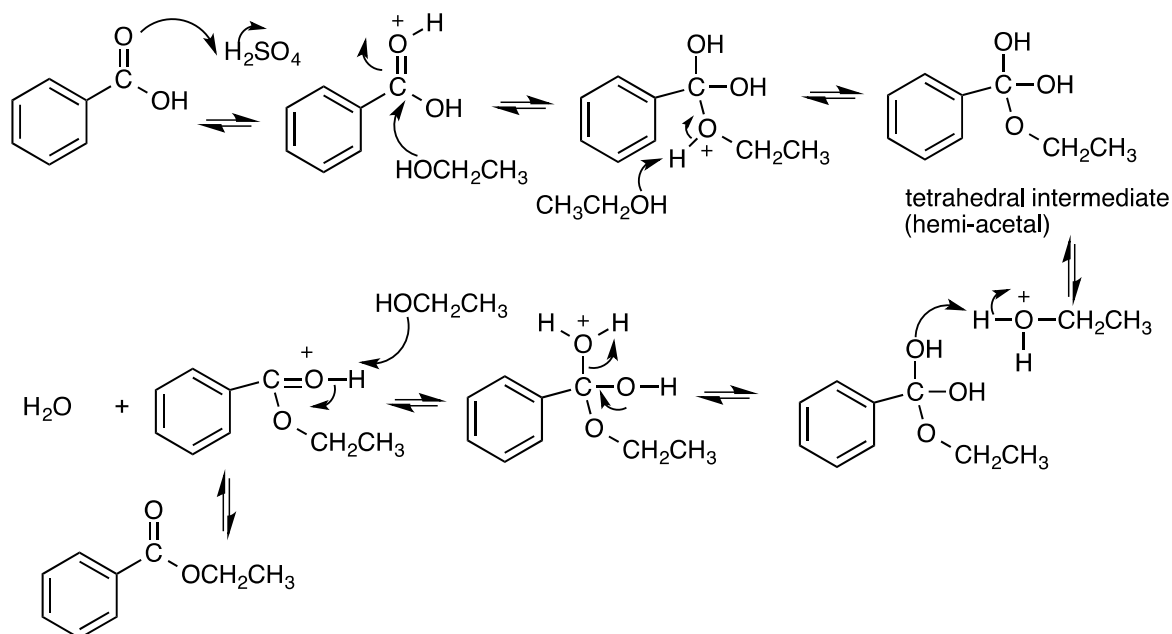
**(2) Carboxylic acids can be reduced to primary alcohols with lithium aluminum hydride.**



**(3) Carboxylic acids can be converted to esters by reaction with alcohols in acidic conditions.**



The mechanism is as follows:

The first steps are the same as the acetal formation. First we protonate the carbonyl carbon to make it more electrophilic and then the alcohol attacks to make, after proton transfer back to the ethanol solvent, the hemi-acetal. This is also called the tetrahedral intermediate. As we know, hemi-acetals are not stable. In this case, we now lose a molecule of water by first protonating one of the OH's so as to re-form the strong C=O bond.

Now, we can shorten the writing of this mechanism by combining some of the proton transfer steps. A shortened form of this is shown below.
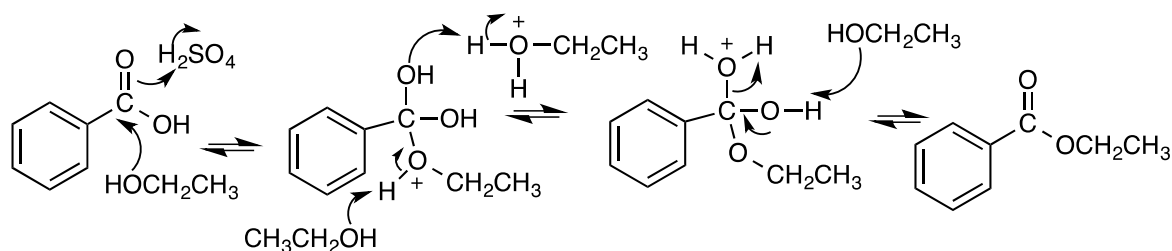
Notice that in the first step the carboxylic acid is protonated on the carbonyl oxygen rather than the hydroxyl group. This oxygen is more electron rich due to resonance.

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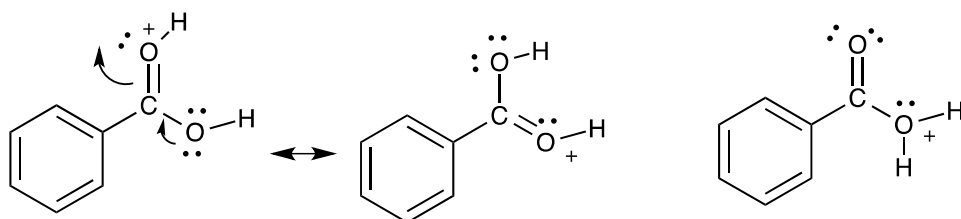
No resonance donation possible from the carbonyl oxygen since this would make a pentavalent carbon.

Note also that these reactions are completely reversible and as we shall see in the next chapter, we can also cleave esters in dilute aqueous acid. This is called hydrolysis. We drive the equilibrium in favor of ester formation by using an excess of the alcohol under anhydrous conditions and we drive the reaction in favor of ester hydrolysis by using an excess of water.

**Lactone Formation**

We can form esters intramolecularly to form cyclic esters. These are called lactones. These are favorable when we have a 4- or 5-hydroxy carboxylic acid that can cyclic to form a five- or six-membered ring.
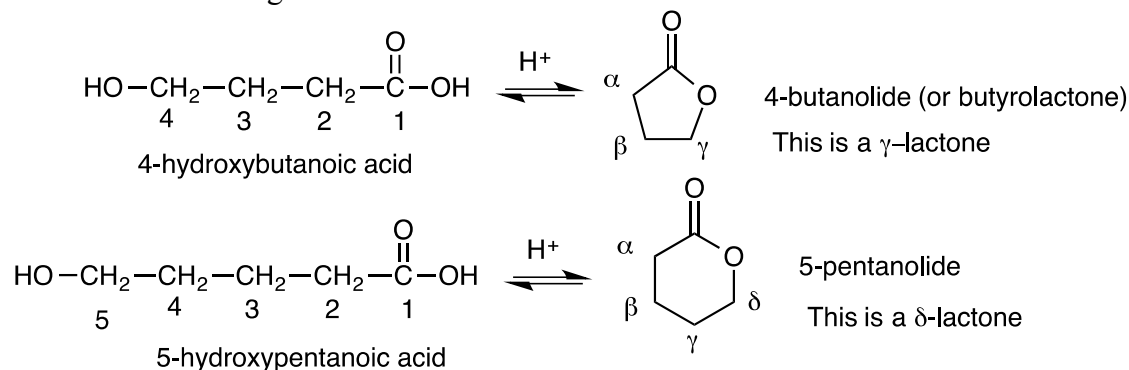


The mechanism is as shown below.
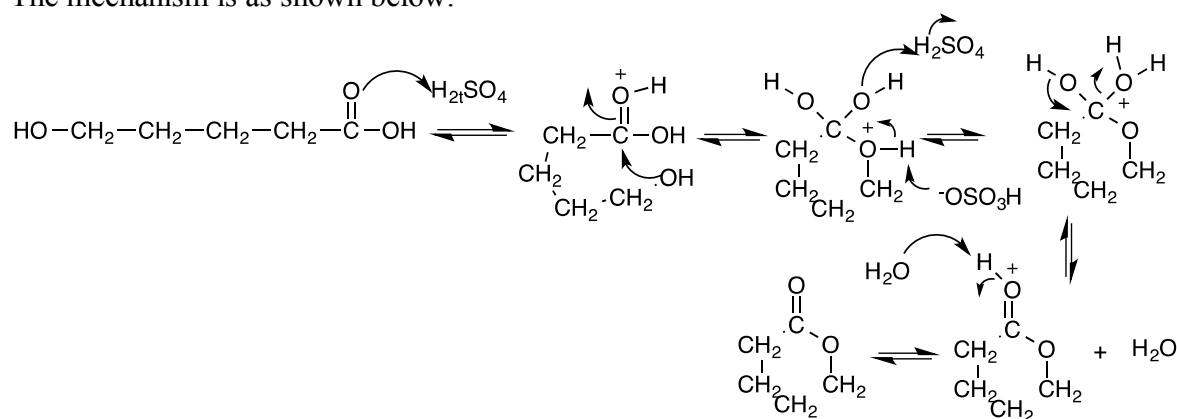


**Decarboxylation of Carboxylic Acids with a β-Carbonyl**

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Carboxylic acids that have a 1,3-relationship with a strong electron withdrawing group such as a carbonyl will lose carbon dioxide on heating. This is called a decarboxylation reaction and as we will see in a future chapter it is very useful in synthesis. The mechanism involves a six-membered ring transition state in which a C-C bond is broken. There is a relatively high energy barrier for this cleavage but the overall reaction is favorable thermodynamically since we are breaking a C-C bond and forming a much stronger C=O bond.

$$CH_3-\overset{O}{\underset{\|}{C}}-CH_2\text{-}\overset{O}{\underset{\|}{C}}-OH \quad \xrightarrow[\text{150-200°C}]{\text{heat}} \quad CH_3-\overset{O}{\underset{\|}{C}}-CH_3 \quad + \quad CO_2$$

$$HO-\overset{O}{\underset{\|}{C}}-CH_2\text{-}\overset{O}{\underset{\|}{C}}-OH \quad \xrightarrow[\text{150-200°C}]{\text{heat}} \quad HO-\overset{O}{\underset{\|}{C}}-CH_3 \quad + \quad CO_2$$

malonic acid



6-membered ring transition state

enol

$H_3O^+$

$$CH_3-\overset{O}{\underset{\|}{C}}-CH_3$$

keto form

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