Carboxylic Acids and Nitriles

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Reference Text Book:

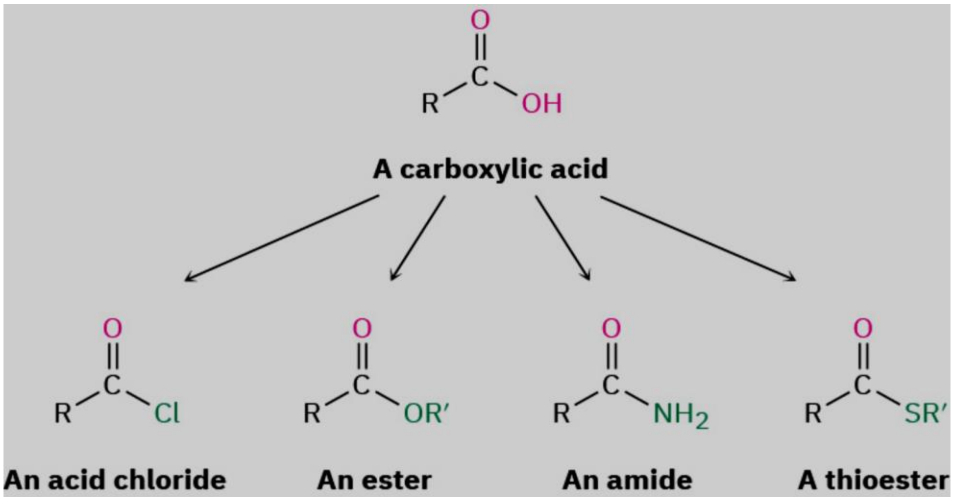
- **John McMurry "Organic Chemistry" 10th Edition, OpenStax, Rice University, USA (2023).**

WHY THIS CHAPTER?

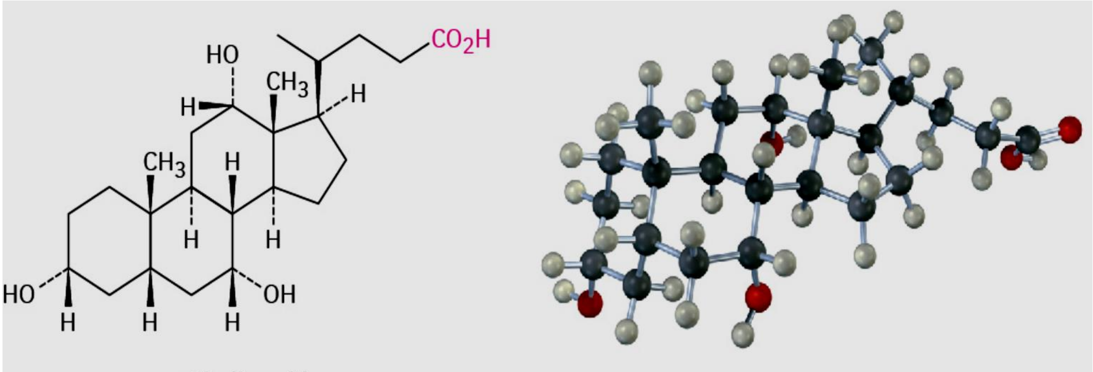
- Carboxylic acids are present in many industrial processes
- Most biological pathways and are the starting materials from which other acyl derivatives are made.
- Understanding of their properties and reactions is fundamental to understanding organic chemistry.
- We'll look both at acids and at their close relatives, nitriles ($RC\equiv N$), in this chapter and at carboxylic acid derivatives in the next chapter.

Carboxylic acids, RCO_2H,

- occupy a central place among carbonyl compounds.
- Not only are they valuable in themselves, they also serve as starting materials for preparing numerous carboxylic acid derivatives such as acid chlorides, esters, amides, and thioesters.
- In addition, carboxylic acids are present in the majority of biological pathways.

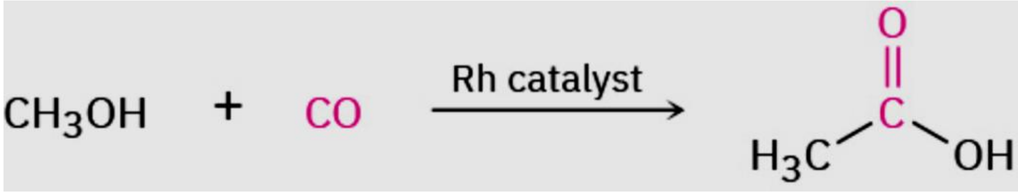


- A great many carboxylic acids are found in nature: acetic acid, **CH_3CO_2H**, is the chief organic component of vinegar;
- butanoic acid, **$CH_3CH_2CH_2CO_2H$**, is responsible for the rancid odor of sour butter; and
- hexanoic acid (caproic acid), **$CH_3(CH_2)_4CO_2H$**, is responsible for the unmistakable aroma of goats and dirty gym socks (the name comes from the Latin *caper*, meaning "goat").
- Other examples are cholic acid, a major component of human bile, and long-chain aliphatic acids such as palmitic acid, **$CH_3(CH_2)_{14}CO_2H$**, a biological precursor of fats and vegetable oils.



Cholic acid

Approximately 20 million tons of acetic acid is produced worldwide each year for a variety of purposes, including preparation of the vinyl acetate polymer used in paints and adhesives. About 20% of the acetic acid synthesized industrially is obtained by oxidation of acetaldehyde. Much of the remaining 80% is prepared by the rhodium-catalyzed reaction of methanol with carbon monoxide.

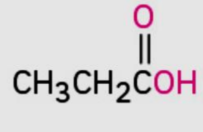


$$CH_3OH + CO \xrightarrow{\text{Rh catalyst}} H_3C\overset{\overset{\displaystyle O}{\|}}{C}OH$$

Naming Carboxylic Acids and Nitriles

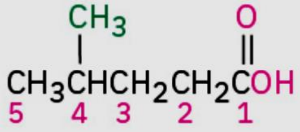
Naming Carboxylic Acids, RCO_2H

- Simple carboxylic acids derived from open-chain alkanes are systematically named by replacing the terminal ***-e*** of the corresponding alkane name with ***-oic*** *acid*.
- The $\mathbf{CO_2H}$ carbon atom is numbered $\mathbf{C_1}$.



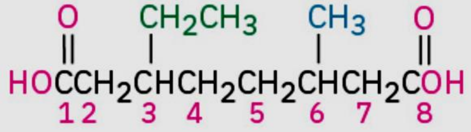
$CH_3CH_2\overset{O}{\overset{\|}{C}}OH$

Propanoic acid



$\underset{5}{CH_3}\underset{4}{\overset{CH_3}{\overset{|}{C}}}H\underset{3}{CH_2}\underset{2}{CH_2}\underset{1}{\overset{O}{\overset{\|}{C}}}OH$

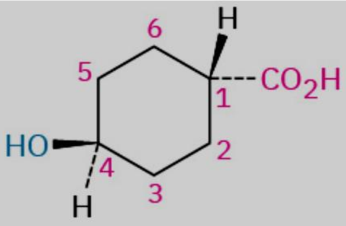
4-Methylpentanoic acid



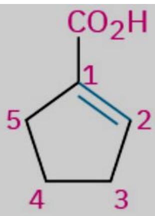
$HO\underset{1}{\overset{O}{\overset{\|}{C}}}\underset{2}{CH_2}\underset{3}{\overset{CH_2CH_3}{\overset{|}{C}}}H\underset{4}{CH_2}\underset{5}{CH_2}\underset{6}{\overset{CH_3}{\overset{|}{C}}}H\underset{7}{CH_2}\underset{8}{\overset{O}{\overset{\|}{C}}}OH$

3-Ethyl-6-methyloctanedioic acid

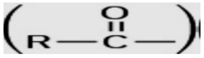
- Compounds that have a $\mathbf{-CO_2H}$ group bonded to a ring are named using the suffix ***-carboxylic acid***.
- The CO_2H carbon is attached to C1 in this system and is not itself numbered. As a substituent, the CO_2H group is called a **carboxyl group**.



***trans*-4-Hydroxycyclohexanecarboxylic acid**



1-Cyclopentenecarboxylic acid

Also listed in Table 20-1 are the names of acyl groups  $(R-\overset{O}{\overset{\|}{C}}-)$ derived from the parent acids. Except for the eight entries at the top of Table 20-1, whose names have a ***-yl*** ending, all other acyl groups are named using an ***–oyl*** ending.

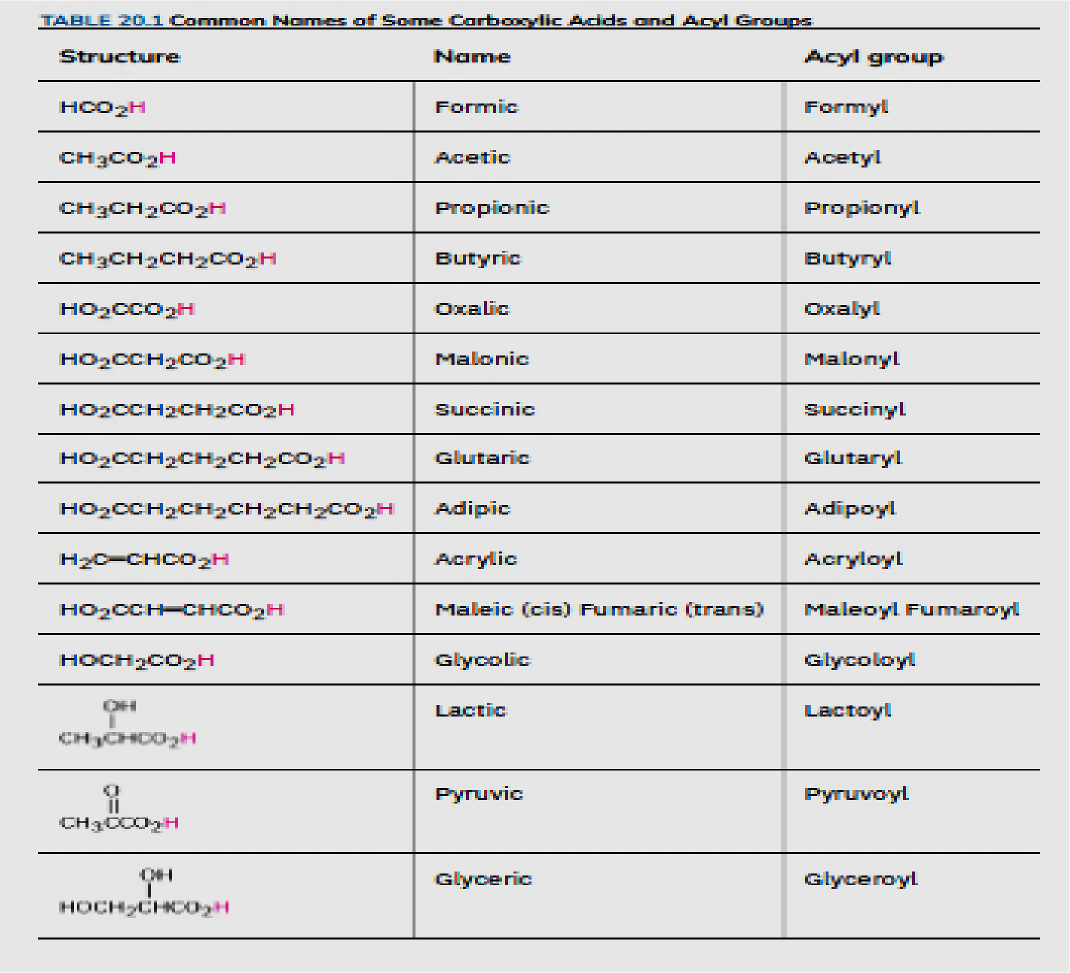


TABLE 20.1 Common Names of Some Carboxylic Acids and Acyl Groups

Structure	Name	Acyl group
HCO_2H	Formic	Formyl
CH_3CO_2H	Acetic	Acetyl
$CH_3CH_2CO_2H$	Propionic	Propionyl
$CH_3CH_2CH_2CO_2H$	Butyric	Butyryl
HO_2CCO_2H	Oxalic	Oxalyl
$HO_2CCH_2CO_2H$	Malonic	Malonyl
$HO_2CCH_2CH_2CO_2H$	Succinic	Succinyl
$HO_2CCH_2CH_2CH_2CO_2H$	Glutaric	Glutaryl
$HO_2CCH_2CH_2CH_2CH_2CO_2H$	Adipic	Adipoyl
$H_2C{=}CHCO_2H$	Acrylic	Acryloyl
$HO_2CCH{=}CHCO_2H$	Maleic (cis) Fumaric (trans)	Maleoyl Fumaroyl
$HOCH_2CO_2H$	Glycolic	Glycoloyl
$CH_3\overset{\text{OH}}{\overset{\vert}{C}}HCO_2H$	Lactic	Lactoyl
$CH_3\overset{\text{O}}{\overset{\Vert}{C}}CO_2H$	Pyruvic	Pyruvoyl
$HOCH_2\overset{\text{OH}}{\overset{\vert}{C}}HCO_2H$	Glyceric	Glyceroyl

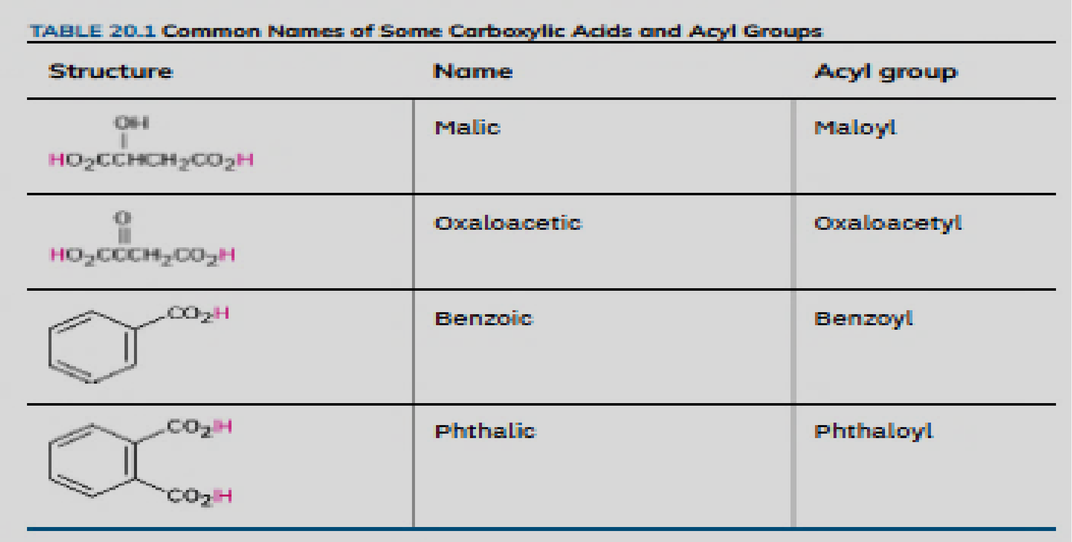
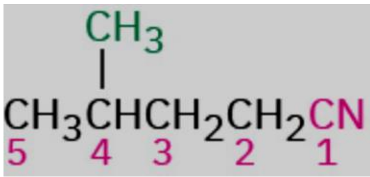


TABLE 20.1 Common Names of Some Carboxylic Acids and Acyl Groups

Structure	Name	Acyl group
$HO_2C\overset{\text{OH}}{\overset{\vert}{C}}HCH_2CO_2H$	Malic	Maloyl
$HO_2C\overset{\text{O}}{\overset{\Vert}{C}}CH_2CO_2H$	Oxaloacetic	Oxaloacetyl
CO_2H	Benzoic	Benzoyl
CO_2H CO_2H	Phthalic	Phthaloyl

Naming Nitriles, $RC\equiv N$

- Compounds containing the $—C\equiv N$ functional group are called **nitriles** and can undergo some chemistry similar to that of carboxylic acids.
- Simple open-chain nitriles are named by adding -nitrile as a suffix to the alkane name, with the nitrile carbon numbered **C_1.**

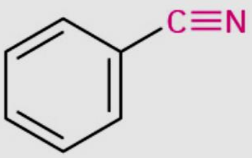

$CH_3\overset{\overset{CH_3}{|}}{C}HCH_2CH_2CN$

4-Methylpentanenitrile

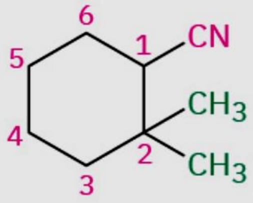
- Nitriles can also be named as derivatives of carboxylic acids by replacing the ***-ic acid*** or ***-oic acid*** ending with ***-onitrile,*** or by replacing the ***-carboxylic acid*** ending with ***-carbonitrile.***
- The nitrile carbon atom is attached to **C_1** but is not itself numbered.

$CH_3C\equiv N$

Acetonitrile
(from acetic acid)

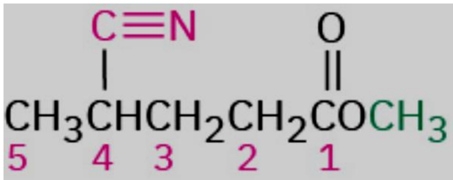


Benzonitrile
(from benzoic acid)



2,2-Dimethylcyclohexanecarbonitrile
(from 2,2-dimethylcyclohexane-carboxylic acid)

- If another carboxylic acid derivative is present in the same molecule, the prefix cyano- is used for the $C\equiv N$ group.


$CH_3\overset{\overset{C\equiv N}{|}}{C}HCH_2CH_2\overset{\overset{O}{\|}}{C}OCH_3$

Methyl 4-cyanopentanoate

Structure and Properties of Carboxylic Acids

Carboxylic acids are similar in some respects to both ketones and alcohols. Like ketones, the carboxyl carbon is *sp*^{2}-hybridized, and carboxylic acid groups are therefore planar with $C{-}C{=}O$ and $O{=}C{-}O$ $C{-}C{=}O$ and $O{=}C{-}O$ bond angles of approximately 120° **(Table 20-2)**.

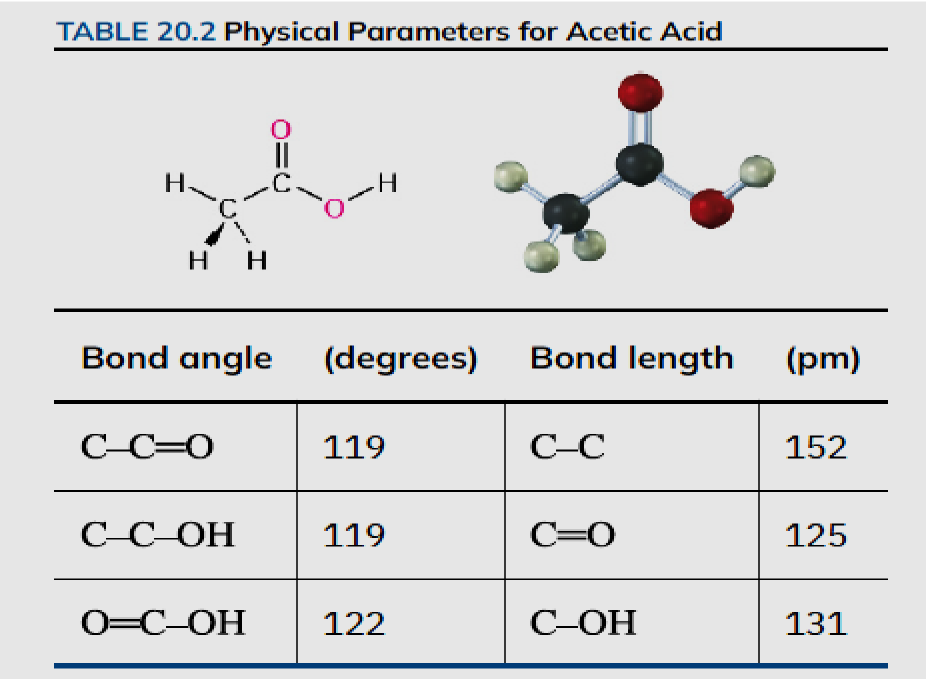
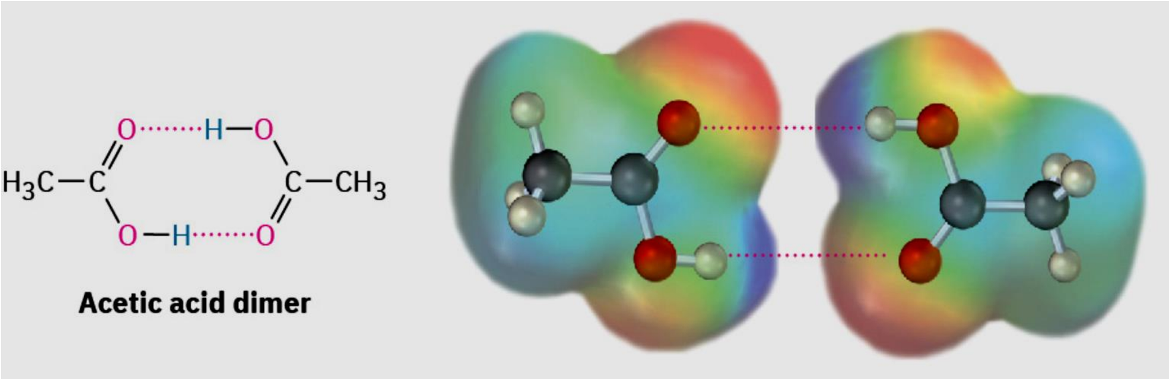


TABLE 20.2 **Physical Parameters for Acetic Acid**

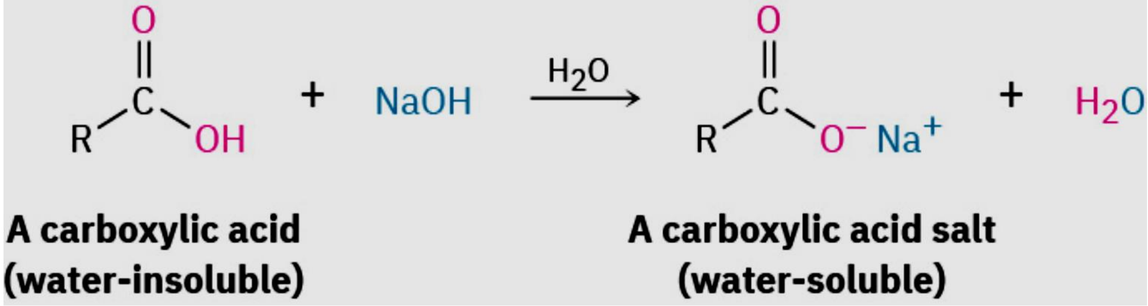
Bond angle	(degrees)	Bond length	(pm)
C–C═O	119	C–C	152
C–C–OH	119	C═O	125
O═C–OH	122	C–OH	131

Like alcohols, carboxylic acids are strongly associated because of hydrogen-bonding. Most carboxylic acids exist as cyclic dimers held together by two hydrogen bonds. This strong hydrogen-bonding has a noticeable effect on boiling points, making carboxylic acids boil far less easily than their corresponding alcohols. Acetic acid, for instance, has a boiling point of 117.9 °C, versus 78.3 °C for ethanol, even though both compounds have two carbons.

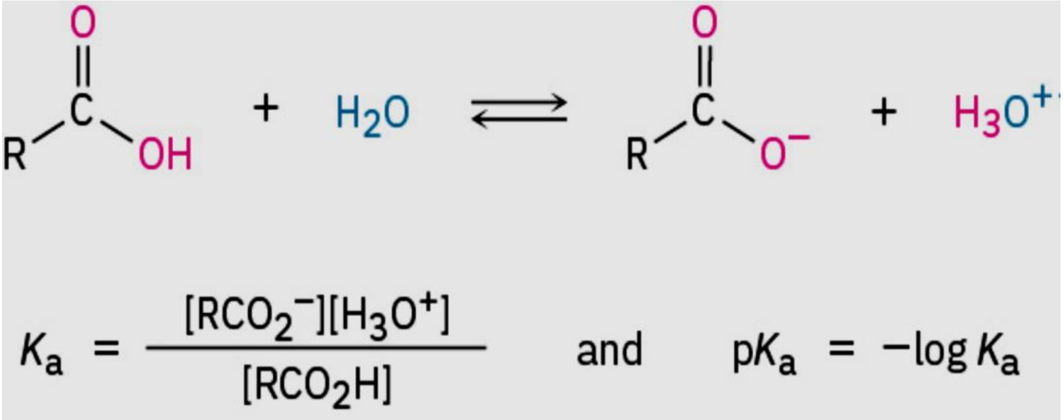


Acetic acid dimer

The most obvious property of carboxylic acids is implied by their name: carboxylic acids are *acidic*. They therefore react with bases such as NaOH and $NaHCO_3$ to give metal carboxylate salts, **RCO^-M^+**. Carboxylic acids with more than six carbons are only slightly soluble in water, but the alkali metal salts of carboxylic acids are often highly water-soluble. In fact, it’s often possible to purify an acid by extracting its salt into aqueous base, then reacidifying and extracting the pure acid back into an organic solvent.



Carboxylic acids dissociate slightly in dilute aqueous solution to give H_3O^+ and the corresponding carboxylate anions, **RCO_2^-**. The extent of dissociation is given by an acidity constant, ***Ka***.



$$K_a = \frac{[RCO_2^-][H_3O^+]}{[RCO_2H]} \quad \text{and} \quad pK_a = -\log K_a$$

A list of *K*a values for various carboxylic acids is given in **Table 20-3**. For most, *K*a is approximately 10^{-4} to 10^{-5}. Acetic acid, for instance, has $Ka=1.75\text{x}10^{-5}$ at 25 °C, which corresponds to a p*K*a of 4.76. In practical terms, a *K*a value near 10^{-5} means that only about 0.1% of the molecules in a 0.1 M solution are dissociated, as opposed to the 100% dissociation found with strong mineral acids like HCl.

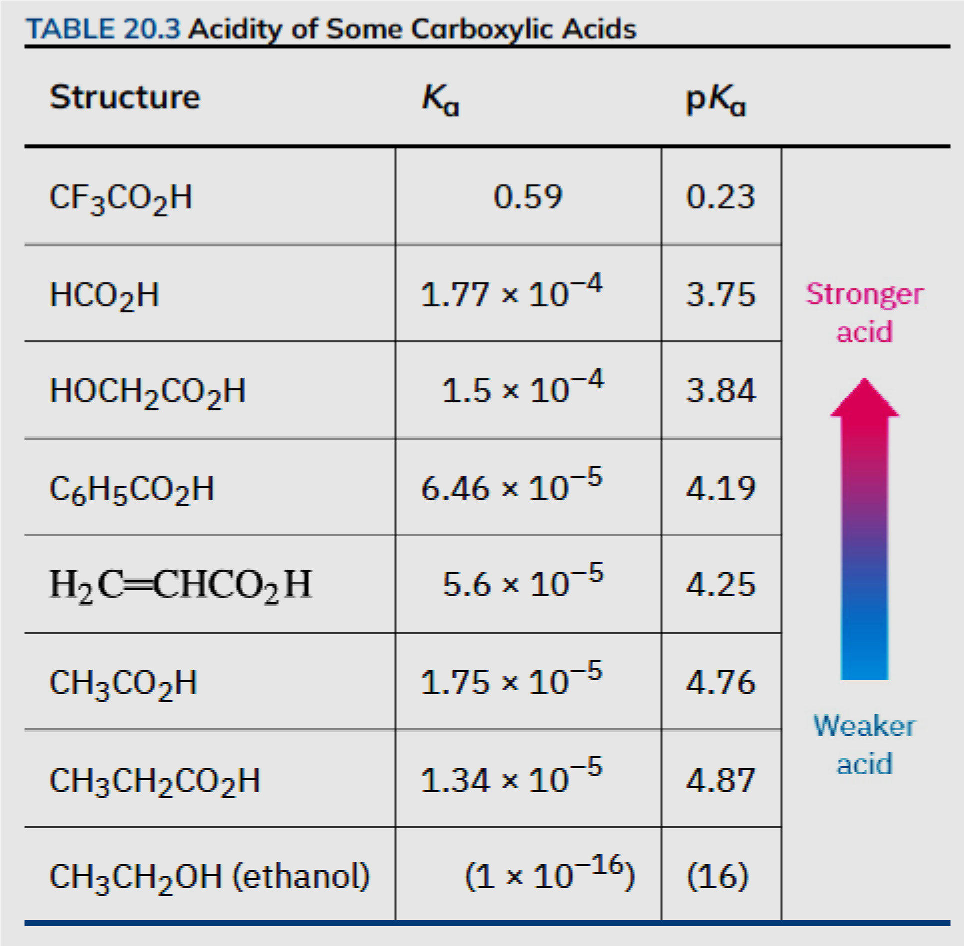
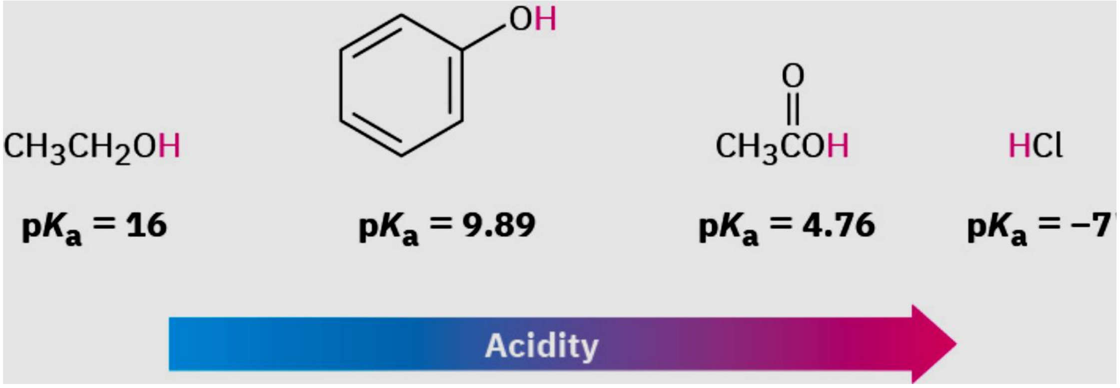


TABLE 20.3 Acidity of Some Carboxylic Acids

Structure	K_a	pK_a
CF_3CO_2H	0.59	0.23
HCO_2H	1.77×10^{-4}	3.75
$HOCH_2CO_2H$	1.5×10^{-4}	3.84
$C_6H_5CO_2H$	6.46×10^{-5}	4.19
$H_2C{=}CHCO_2H$	5.6×10^{-5}	4.25
CH_3CO_2H	1.75×10^{-5}	4.76
$CH_3CH_2CO_2H$	1.34×10^{-5}	4.87
CH_3CH_2OH (ethanol)	(1×10^{-16})	(16)

Although much weaker than mineral acids, carboxylic acids are nevertheless much stronger acids than alcohols and phenols. The *K*a of ethanol, for example, is approximately 10^{-16}, making it a weaker acid than acetic acid by a factor of 10^{11}.



- Why are carboxylic acids so much more acidic than alcohols, even though both contain **-OH** groups?
- An alcohol dissociates to give an alkoxide ion, in which the negative charge is localized on a single electronegative atom.
- A carboxylic acid, however, gives a carboxylate ion, in which the negative charge is delocalized over two equivalent oxygen atoms **(Figure 20-1)**.
- In resonance terms, a carboxylate ion is a stabilized resonance hybrid of two equivalent structures.
- Since a carboxylate ion is more stable than an alkoxide ion, it is lower in energy and more favored in the dissociation equilibrium.

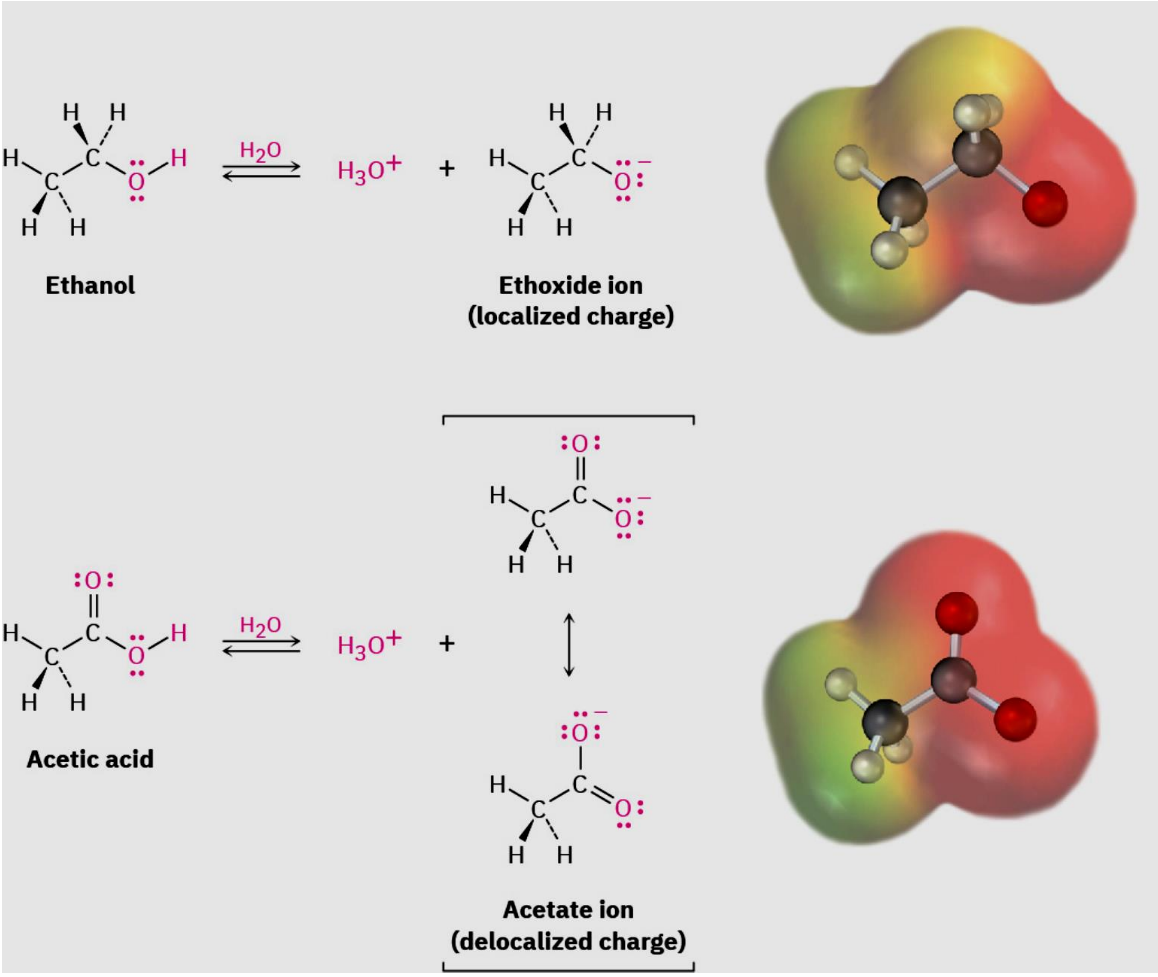
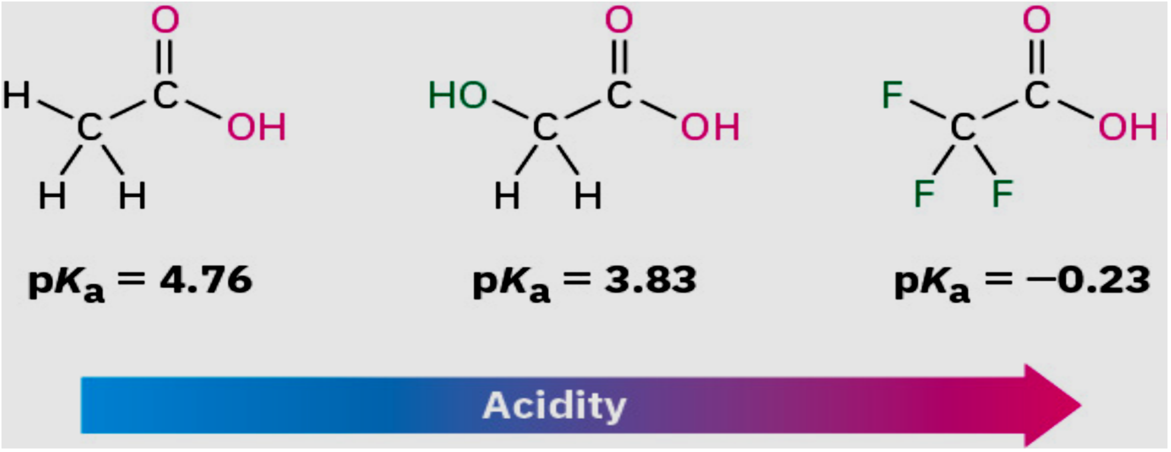


Figure 20-1 an alkoxide ion has its charge localized on one oxygen atom and is less stable, while a carboxylate ion has the charge spread equally over both oxygens and is therefore more stable.

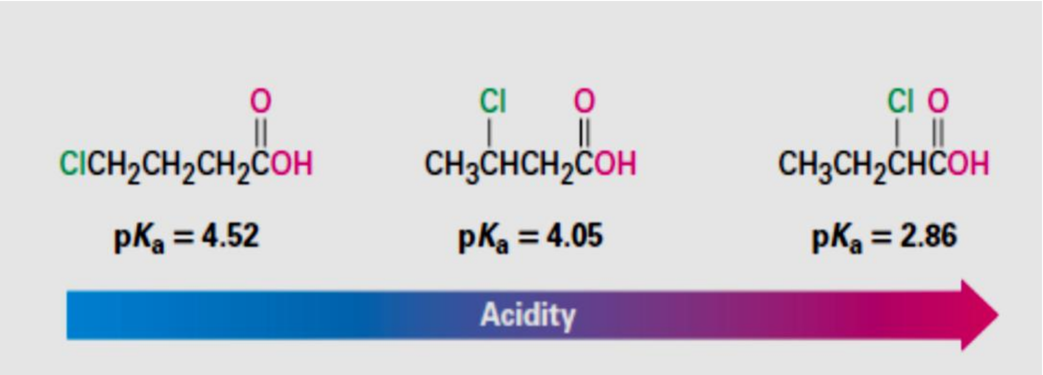
Substituent Effects on Acidity

The listing of p*K*a values shown previously in Table 20-3 indicates that there are substantial differences in acidity from one carboxylic acid to another. For example, trifluoroacetic acid (*K*a 5 0.59) is 33,000 times as strong as acetic acid (*K*a=1.75x10^{-5}). How can we account for such differences?

Because the dissociation of a carboxylic acid is an equilibrium process, any factor that stabilizes the carboxylate anion relative to undissociated carboxylic acid will drive the equilibrium toward increased dissociation and result in increased acidity. For instance, three electron-withdrawing fluorine atoms delocalize the negative charge in the trifluoroacetate anion, thereby stabilizing the ion and increasing the acidity of CF_3CO_2H. In the same way, glycolic acid ($HOCH_2CO_2H$; p*K*a= 3.83) is stronger than acetic acid because of the electron-withdrawing effect of the electronegative oxygen atom.



Because inductive effects operate through *s* bonds and are dependent on distance, the effect of halogen substitution decreases as the substituent moves farther from the carboxyl. Thus, 2-chlorobutanoic acid has p*K*a =2.86, 3-chlorobutanoic acid has p*K*a=4.05, and 4-chlorobutanoic acid has p*K*a =4.52, similar to that of butanoic acid itself



Substituent effects on acidity are also found in substituted benzoic acids. Aromatic rings with electron-donating groups are activated toward further electrophilic substitution, and aromatic rings with electron-withdrawing groups are deactivated. Exactly the same effects can be observed on the acidity of substituted benzoic acids **(Table 20-4)**.

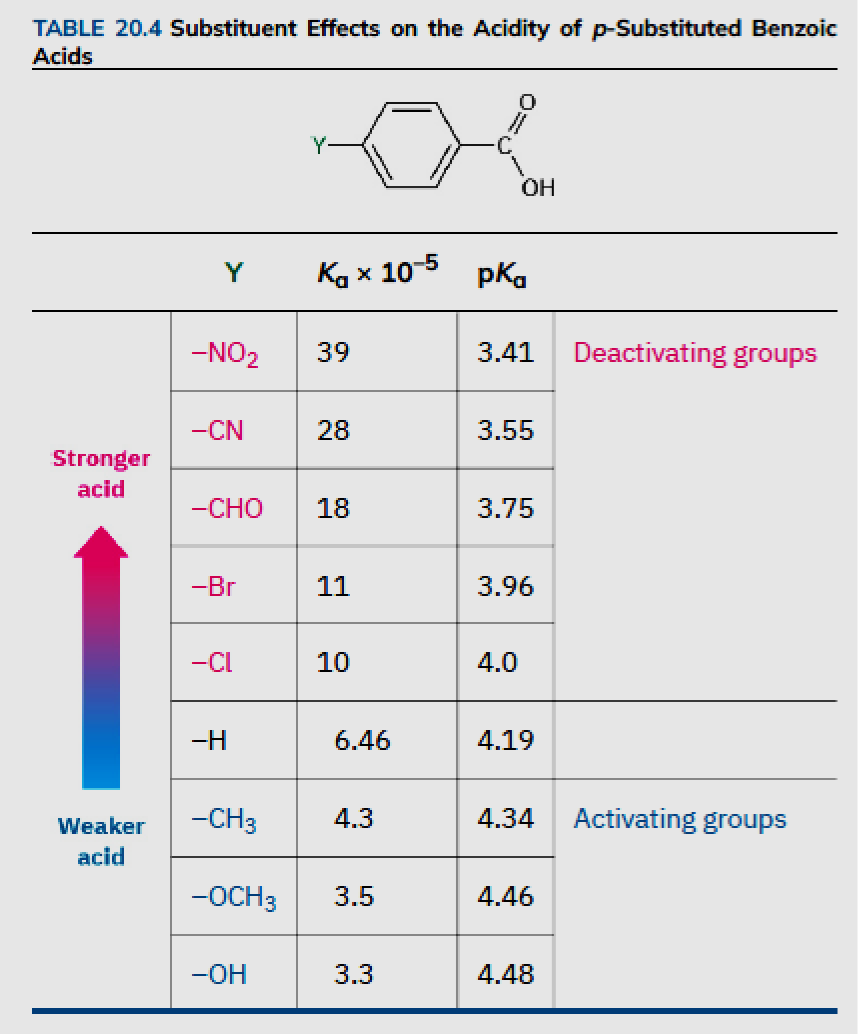
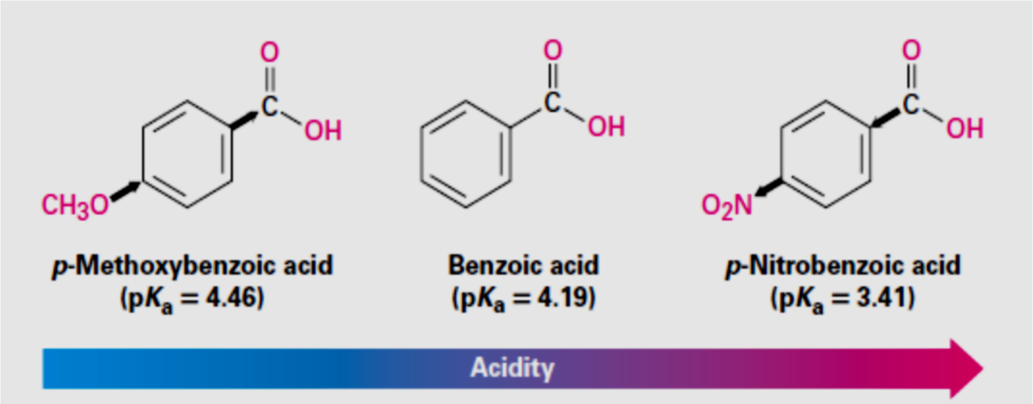


TABLE 20.4 Substituent Effects on the Acidity of *p*-Substituted Benzoic Acids

	Y	$K_a \times 10^{-5}$	pK_a	
Stronger acid	$-NO_2$	39	3.41	Deactivating groups
	$-CN$	28	3.55	
	$-CHO$	18	3.75	
	$-Br$	11	3.96	
	$-Cl$	10	4.0	
	$-H$	6.46	4.19	
Weaker acid	$-CH_3$	4.3	4.34	Activating groups
	$-OCH_3$	3.5	4.46	
	$-OH$	3.3	4.48	

As Table 20-4 shows, an electron-donating (activating) group such as methoxy decreases acidity by destabilizing the carboxylate anion, and an electron-withdrawing (deactivating) group such as nitro increases acidity by stabilizing the carboxylate anion.



Because it's much easier to measure the acidity of a substituted benzoic acid than it is to determine the relative reactivity of an aromatic ring toward electrophilic substitution, the correlation between the two effects is useful for predicting reactivity. If we want to know the effect of a certain substituent on electrophilic reactivity, we can simply find the acidity of the corresponding benzoic acid.