

The bark of the white willow tree (*Salix alba*) is a source of salicylic acid, from which aspirin (acetylsalicylic acid) is made.

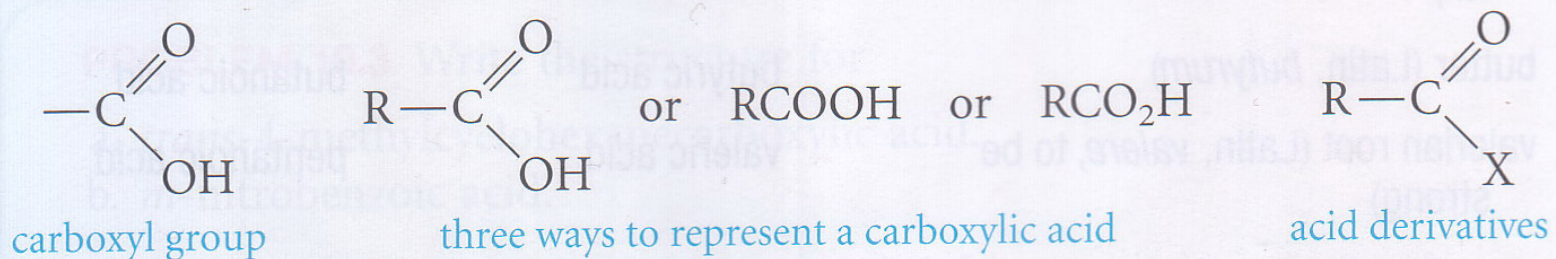


10

## Carboxylic Acids and Their Derivatives



**T**he taste of vinegar, the sting of an ant, the rancid smell of butter, the relief derived from aspirin or ibuprofen—all of these are due to compounds that belong to the most important family of organic acids, the **carboxylic acids**. The resilience of polyester and nylon fabrics, the remarkable properties of Velcro, the softness of silk, the strength of bacterial cell walls and our own cell membranes—all of these are due to properties of derivatives of carboxylic acids. The functional group common to all carboxylic acids is the **carboxyl group**. The name is a contraction of the parts: the *carbonyl* and *hydroxyl* groups. The general formula for a carboxylic acid can be written in expanded or abbreviated forms.



In this chapter, we will describe the structures, properties, preparation, and reactions of carboxylic acids and will also discuss some common **carboxylic acid derivatives**, in which the hydroxyl group of an acid is replaced by other functional groups.



## 10.1 Nomenclature of Acids

Because of their abundance in nature, carboxylic acids were among the earliest classes of compounds studied by organic chemists. It is not surprising, then, that many of them have common names. These names usually come from some Latin or Greek word that indicates the original source of the acid. Table 10.1 lists the first ten unbranched carboxylic acids, with their common and IUPAC names. To obtain the IUPAC name of a carboxylic acid, we replace the final *e* in the name of the corresponding alkane with the suffix *-oic* and add the word *acid*. Substituted acids are named in two ways. In the IUPAC system, the chain is numbered beginning with the carboxyl carbon atom, and substituents are located in the usual way. If the common name of the acid is used, substituents are located with Greek letters, beginning with the  $\alpha$ -carbon atom. IUPAC and common naming systems should not be mixed.

# Nomenclature of Carboxylic Acids

**Common names** are frequently used for the simpler carboxylic acids that have been known for hundreds of years.

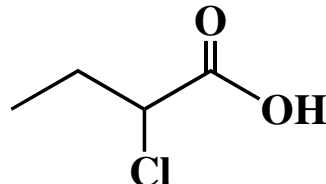
**HCOOH**  
**Formic acid**  
(from Latin  
*formica*, ant)

**CH<sub>3</sub>COOH**  
**Acetic acid**  
(from Latin  
*acetum*, vinegar)

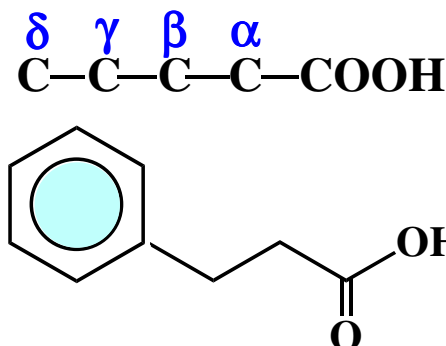
**CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>COOH**  
**Butyric acid**  
(from Latin  
*butyrum*, butter)

In common names, the positions of substituents are often given by  $\alpha$ ,  $\beta$ ,  $\gamma$ ...

Examples



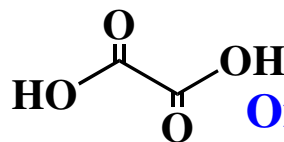
**$\alpha$ -Chlorobutyric acid**



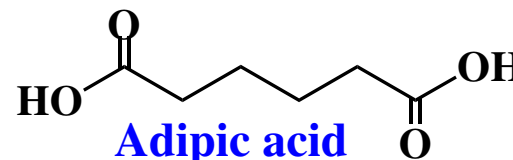
**$\beta$ -Phenylpropionic acid**

The simple dicarboxylic acids have common names, they are the ones usually used, and it is advisable to learn them at least through the six-carbon one. These are oxalic, malonic, succinic, glutaric, and adipic acid.

Examples



**Oxalic acid**



**Adipic acid**

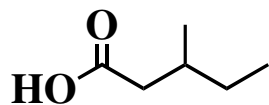


## Systematic Names of Carboxylic Acids

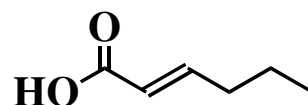
**IUPAC systematic names** are derived from the name of the longest-chain alkane present (the parent compound), dropping the final **-e**, and adding **-oic acid**.

**Note:** Count carboxyl carbon as part of the parent chain.

### Examples

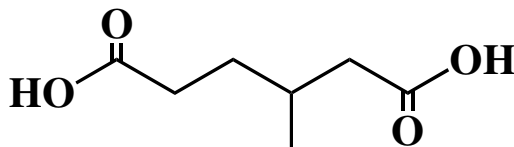


**3-Methylpentanoic acid**

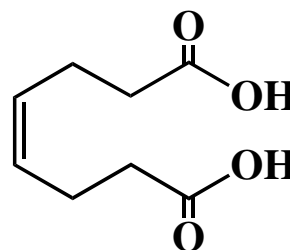


**(E)-2-Hexenoic acid**

Dicarboxylic acids can be named similarly although most have common names that are the ones usually used.



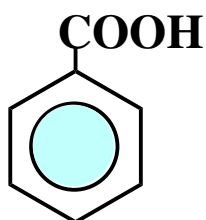
**3-Methylhexanedioic acid**



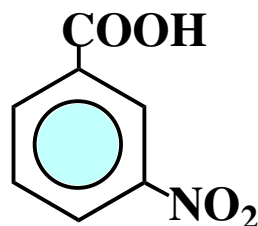
**(Z)-4-Octenedioic acid**

## Aromatic Acids: Benzoic Acids

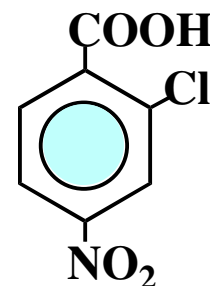
The carboxylic acids derived from benzene are named as derivatives of **benzoic acid**, using the standard notations to indicate positions of substituent groups.



**Benzoic acid**



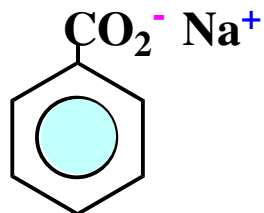
***m*-Nitrobenzoic acid**



**2-Chloro-4-nitrobenzoic acid**

## Salts of Carboxylic Acids

To name a salt, use the name of the **cation** (sodium, ammonium, etc.) followed by the name of the acid with "**ic acid**" changed to "**ate**."



**Sodium benzoate**

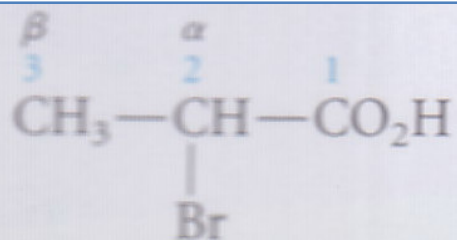


**Magnesium propanoate**

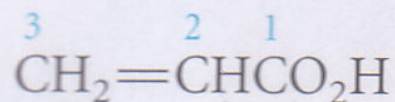
or

**Magnesium propionate**

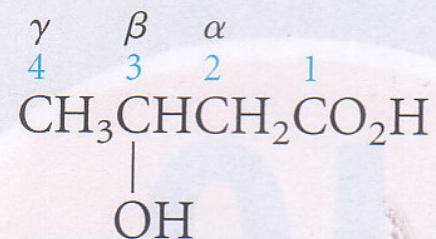




2-bromopropanoic acid  
( $\alpha$ -bromopropionic acid)

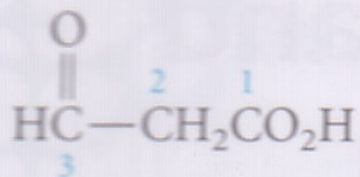


propenoic acid  
(acrylic acid)

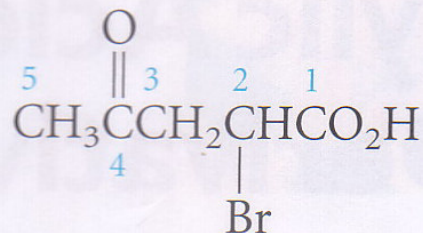


3-hydroxybutanoic acid  
( $\beta$ -hydroxybutyric acid)

The carboxyl group has priority over alcohol, aldehyde, or ketone functionality in naming. In the latter cases, the prefix *oxo-* is used to locate the carbonyl group of the aldehyde or ketone, as in these examples:



3-oxopropanoic acid



2-bromo-4-oxopentanoic acid

**Table 10.1** Aliphatic carboxylic acids

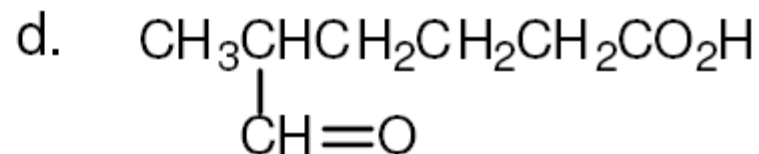
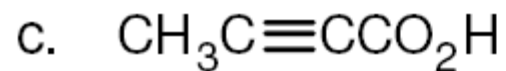
Carbon atoms	Formula	Source	Common name	IUPAC name
1	HCOOH	ants (Latin, <i>formica</i> )	formic acid	methanoic acid
2	CH <sub>3</sub> COOH	vinegar (Latin, <i>acetum</i> )	acetic acid	ethanoic acid
3	CH <sub>3</sub> CH <sub>2</sub> COOH	milk (Greek, <i>protos pion</i> , first fat)	propionic acid	propanoic acid
4	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> COOH	butter (Latin, <i>butyrum</i> )	butyric acid	butanoic acid
5	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> COOH	valerian root (Latin, <i>valere</i> , to be strong)	valeric acid	pentanoic acid
6	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> COOH	goats (Latin, <i>caper</i> )	caproic acid	hexanoic acid
7	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> COOH	vine blossom (Greek, <i>oenanthe</i> )	enanthic acid	heptanoic acid
8	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>6</sub> COOH	goats (Latin, <i>caper</i> )	caprylic acid	octanoic acid
9	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>7</sub> COOH	pelargonium (an herb with stork-shaped seed capsules; Greek, <i>pelargos</i> , stork)	pelargonic acid	nonanoic acid
10	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> COOH	goats (Latin, <i>caper</i> )	capric acid	decanoic acid



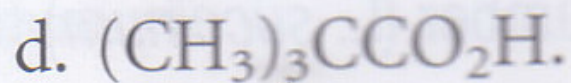
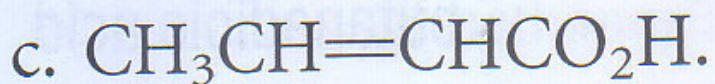
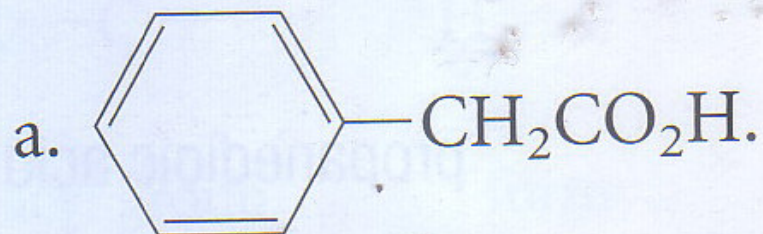
**PROBLEM 10.1** Write the structure for

c. 2-butynoic acid.

d. 5-methyl-6-oxohexanoic acid.



**PROBLEM 10.2** Give an IUPAC name for



a. phenylethanoic acid

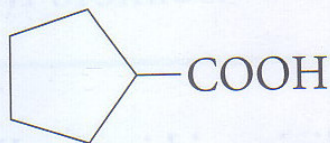
b. Dibromoethanoic acid

c. 2-butenic acid

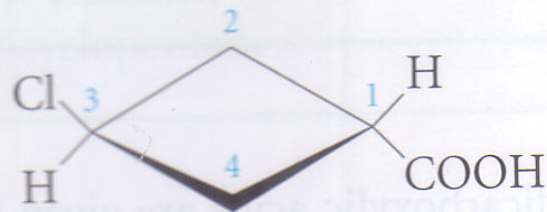
d. 2,2-dimethylpropanoic acid



When the carboxyl group is attached to a ring, the ending *-carboxylic acid* is added to the name of the parent cycloalkane.

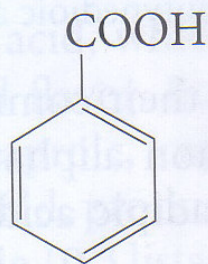


cyclopentanecarboxylic acid

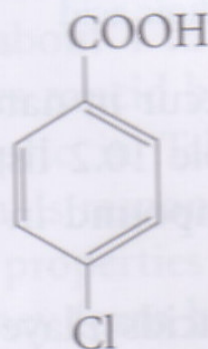


*trans*-3-chlorocyclobutanecarboxylic acid

Aromatic acids are named by attaching the suffix *-oic acid* or *-ic acid* to an appropriate prefix derived from the aromatic hydrocarbon.

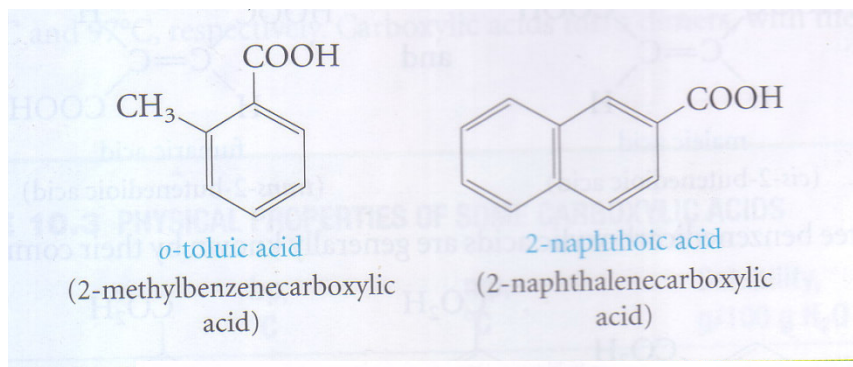


benzoic acid  
(benzenecarboxylic acid)



*p*-chlorobenzoic acid  
(4-chlorobenzenecarboxylic acid)





The root of Garden Heliotrope is a source of valeric acid,  $\text{CH}_3(\text{CH}_2)_3\text{COOH}$ .



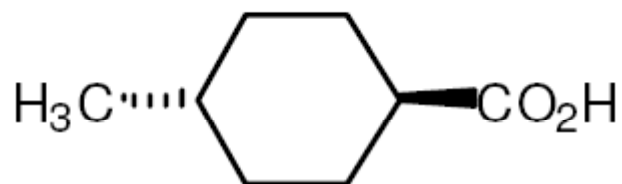
Goats, source of caproic, caprylic, and capric acids:  $\text{CH}_3(\text{CH}_2)_n\text{COOH}$ ,  $n = 4, 6, 8$ .

**PROBLEM 10.3** Write the structure for

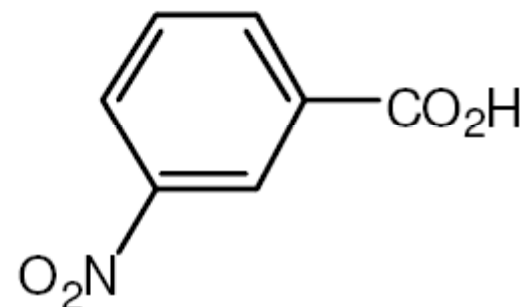
a. *trans*-4-methylcyclohexanecarboxylic acid.

b. *m*-nitrobenzoic acid.

a.

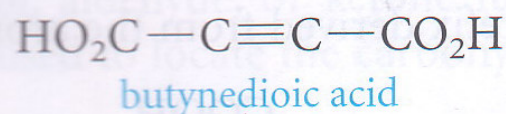
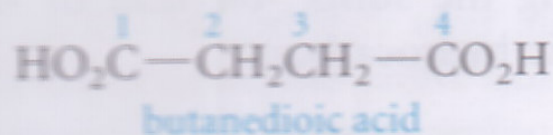


b.



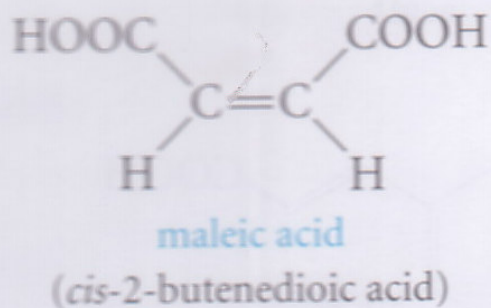


Aliphatic dicarboxylic acids are given the suffix *-dioic acid* in the IUPAC system. For example,

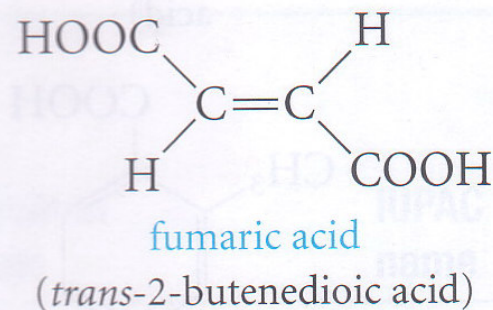


Many dicarboxylic acids occur in nature and go by their common names, which are based on their source. Table 10.2 lists some common aliphatic diacids.\* The most important commercial compound in this group is adipic acid, used to manufacture nylon.

The two butenedioic acids played a historic role in the discovery of *cis-trans* isomerism and are usually known by their common names **maleic**\*\* and **fumaric**\*\*\* acid.



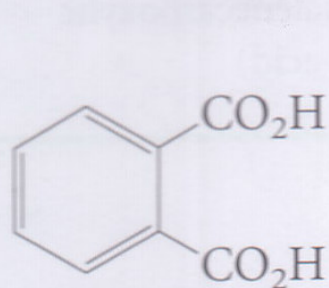
and



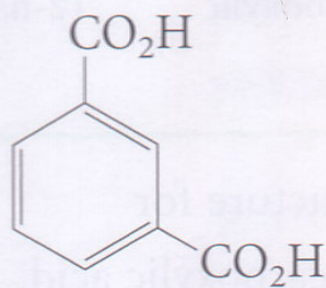
**Table 10.2** Aliphatic dicarboxylic acids

Formula	Common name	Source	IUPAC name
HOOC—COOH	oxalic acid	plants of the <i>oxalic</i> family (for example, sorrel)	ethanedioic acid
HOOC—CH <sub>2</sub> —COOH	malonic acid	apple (Gk. <i>malon</i> )	propanedioic acid
HOOC—(CH <sub>2</sub> ) <sub>2</sub> —COOH	succinic acid	amber (L. <i>succinum</i> )	butanedioic acid
HOOC—(CH <sub>2</sub> ) <sub>3</sub> —COOH	glutaric acid	gluten	pentanedioic acid
HOOC—(CH <sub>2</sub> ) <sub>4</sub> —COOH	adipic acid	fat (L. <i>adeps</i> )	hexanedioic acid
HOOC—(CH <sub>2</sub> ) <sub>5</sub> —COOH	pimelic acid	fat (Gk. <i>pimele</i> )	heptanedioic acid

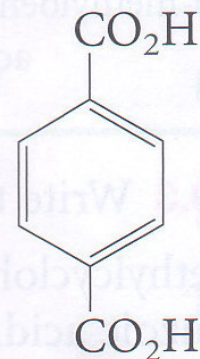
The three benzenedicarboxylic acids are generally known by their common names.



phthalic acid



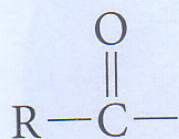
isophthalic acid



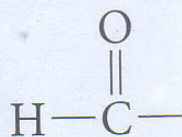
terephthalic acid

Materials.

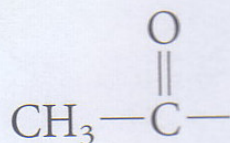
Finally, it is useful to have a name for an **acyl group**. Particular acyl groups are named from the corresponding acid by changing the *-ic* ending to *-yl*.



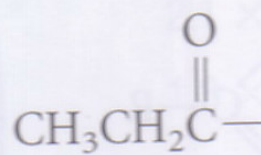
an acyl group



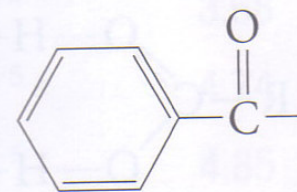
formyl  
(methanoyl)



acetyl  
(ethanoyl)



propanoyl



benzoyl



**PROBLEM 10.5** Write the formula for

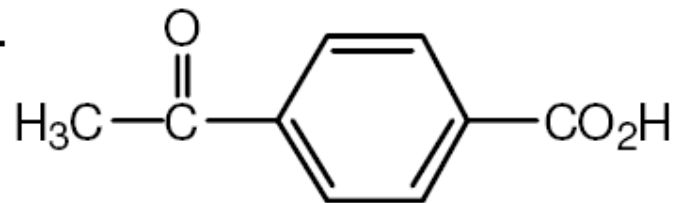
a. 4-acetylbenzoic acid.

b. benzoyl chloride.

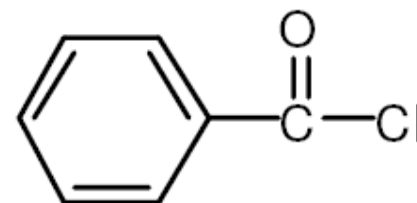
c. butanoyl bromide.

d. formylcyclopentane.

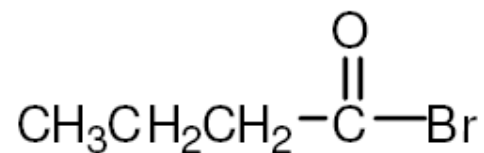
a.



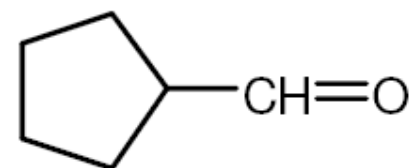
b.



c.



d.



## 10.2 Physical Properties of Acids

The first members of the carboxylic acid series are colorless liquids with sharp or unpleasant odors. Acetic acid, which constitutes about 4 to 5% of vinegar, gives it its characteristic odor and flavor. Butyric acid gives rancid butter its disagreeable odor, and the goat acids (caproic, caprylic, and capric in Table 10.1) smell like goats. 3-Methyl-2-hexenoic acid, produced by bacteria, is responsible for the offensive odor of human armpits. Table 10.3 lists some physical properties of selected carboxylic acids.

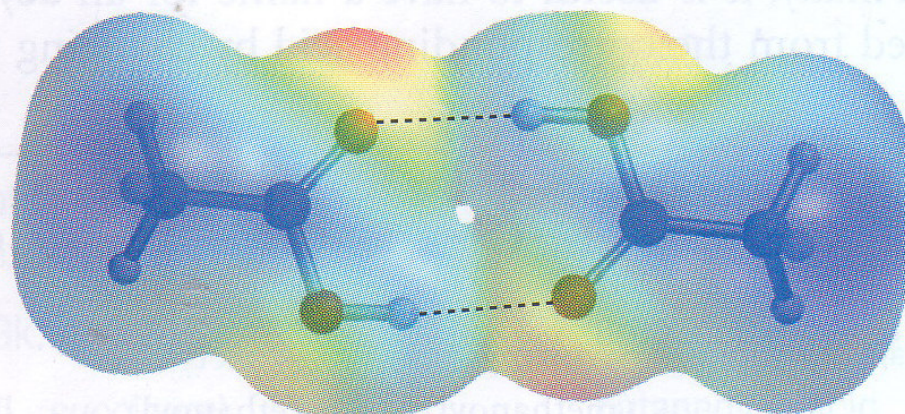
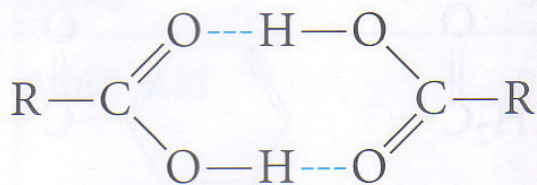
**Table 10.3** Physical properties of some carboxylic acids

Name	bp, °C	mp, °C	Solubility, g/100 g H <sub>2</sub> O at 25°C
formic acid	101	8	miscible (∞)
acetic acid	118	17	
propanoic acid	141	-22	
butanoic acid	164	-8	
hexanoic acid	205	-1.5	1.0
octanoic acid	240	17	0.06
decanoic acid	270	31	0.01
benzoic acid	249	122	0.4 (but 6.8 at 95°C)



Carboxylic acids are polar. Like alcohols, they form hydrogen bonds with themselves or with other molecules (Sec. 7.4). They therefore have high boiling points for their molecular weights—higher even than those of comparable alcohols. For example, acetic acid and propyl alcohol, which have the same formula weights (60 g/mol), boil at 118°C and 97°C, respectively. Carboxylic acids form dimers, with the individual

units neatly held together by *two* hydrogen bonds between the electron-rich oxygens and the electron-poor hydrogens (see Sec. 7.4).

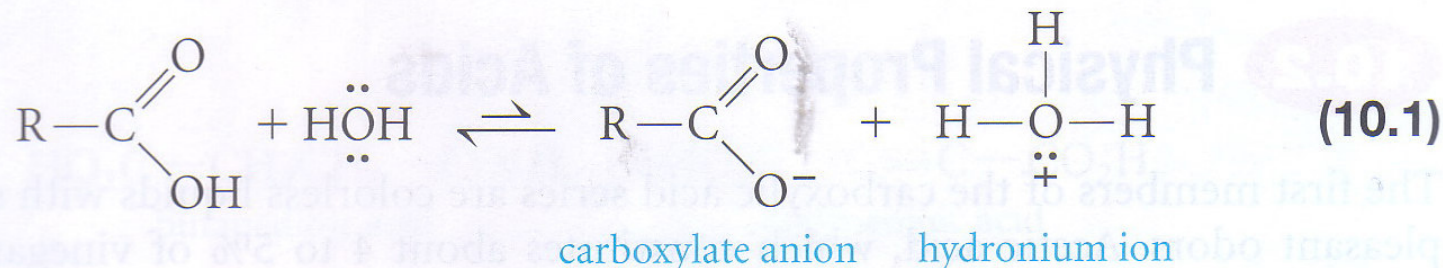


Hydrogen bonding also explains the water solubility of the lower molecular weight carboxylic acids.



### 10.3 Acidity and Acidity Constants

Carboxylic acids dissociate in water, yielding a **carboxylate anion** and a hydronium ion.



Their acidity constant  $K_a$  in water is given by the expression

$$K_a = \frac{[\text{RCO}_2^-][\text{H}_3\text{O}^+]}{[\text{RCO}_2\text{H}]} \quad (10.2)$$

(Before proceeding further, it would be a good idea for you to review Secs. 7.5 and 7.6.)

Table 10.4 lists the acidity constants for some carboxylic and other acids. In comparing data in this table, remember that the larger the value of  $K_a$  or the smaller the value of  $\text{p}K_a$ , the stronger the acid.

**Table 10.4** The ionization constants of some acids

Name	Formula	$K_a$	$pK_a$
formic acid	HCOOH	$2.1 \times 10^{-4}$	3.68
acetic acid	CH <sub>3</sub> COOH	$1.8 \times 10^{-5}$	4.74
propanoic acid	CH <sub>3</sub> CH <sub>2</sub> COOH	$1.4 \times 10^{-5}$	4.85
butanoic acid	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> COOH	$1.6 \times 10^{-5}$	4.80
chloroacetic acid	ClCH <sub>2</sub> COOH	$1.5 \times 10^{-3}$	2.82
dichloroacetic acid	Cl <sub>2</sub> CHCOOH	$5.0 \times 10^{-2}$	1.30
trichloroacetic acid	CCl <sub>3</sub> COOH	$2.0 \times 10^{-1}$	0.70
2-chlorobutanoic acid	CH <sub>3</sub> CH <sub>2</sub> CHClCOOH	$1.4 \times 10^{-3}$	2.85
3-chlorobutanoic acid	CH <sub>3</sub> CHClCH <sub>2</sub> COOH	$8.9 \times 10^{-5}$	4.05
benzoic acid	C <sub>6</sub> H <sub>5</sub> COOH	$6.6 \times 10^{-5}$	4.18
<i>o</i> -chlorobenzoic acid	<i>o</i> -Cl—C <sub>6</sub> H <sub>4</sub> COOH	$12.5 \times 10^{-4}$	2.90
<i>m</i> -chlorobenzoic acid	<i>m</i> -Cl—C <sub>6</sub> H <sub>4</sub> COOH	$1.6 \times 10^{-4}$	3.80
<i>p</i> -chlorobenzoic acid	<i>p</i> -Cl—C <sub>6</sub> H <sub>4</sub> COOH	$1.0 \times 10^{-4}$	4.00
<i>p</i> -nitrobenzoic acid	<i>p</i> -NO <sub>2</sub> —C <sub>6</sub> H <sub>4</sub> COOH	$4.0 \times 10^{-4}$	3.40
phenol	C <sub>6</sub> H <sub>5</sub> OH	$1.0 \times 10^{-10}$	10.00
ethanol	CH <sub>3</sub> CH <sub>2</sub> OH	$1.0 \times 10^{-16}$	16.00
water	HOH	$1.8 \times 10^{-16}$	15.74

Which is the stronger acid, formic or acetic, and by how much?

**SOLUTION** Formic acid is stronger; it has the larger  $K_a$ . The ratio of acidities is

$$\frac{2.1 \times 10^{-4}}{1.8 \times 10^{-5}} = 1.17 \times 10^1 = 11.7$$

This means that formic acid is 11.7 times stronger than acetic acid.

**PROBLEM 10.6** Using the data given in Table 10.4, determine which is the stronger acid, acetic or chloroacetic, and by how much.

$K_a$  is  $1.8 \times 10^{-5}$  for acetic acid and  $1.5 \times 10^{-3}$  for chloroacetic acid.  $K_a$  is larger for chloroacetic acid; it is the stronger acid. The ratio is:

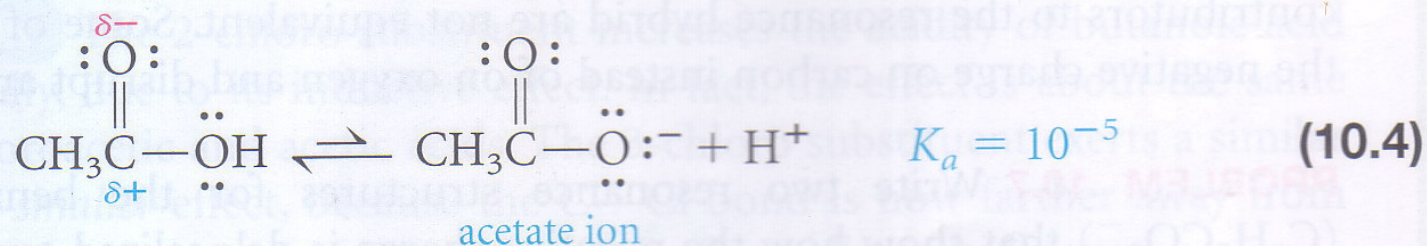
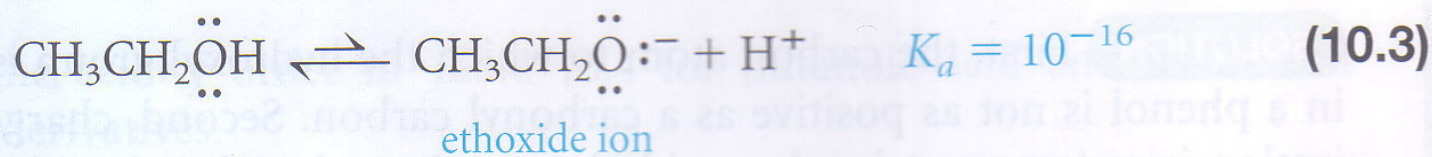
$$\frac{1.5 \times 10^{-3}}{1.8 \times 10^{-5}} = 0.83 \times 10^2$$



## 10.4 What Makes Carboxylic Acids Acidic?

You might wonder why carboxylic acids are so much more acidic than alcohols, since each class ionizes by losing  $\text{H}^+$  from a hydroxyl group. There are two reasons, which can best be illustrated with a specific example.

From Table 10.4, we see that acetic acid is approximately  $10^{11}$ , or one hundred thousand million, times stronger an acid than ethanol.

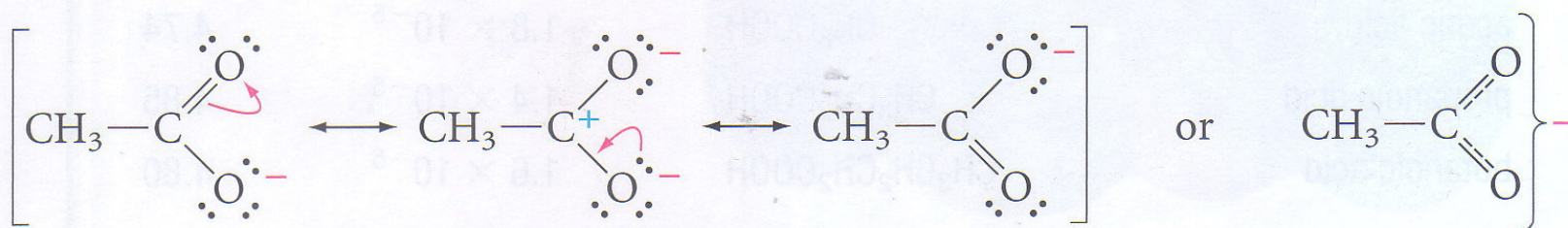


The only difference in their structures is the replacement of a  $\text{CH}_2$  group (in ethanol) by a carbonyl group. But we saw (Sec. 9.5) that a carbonyl carbon atom carries a

## The carbonyl carbon carries

substantial *positive* charge ( $\delta+$ ). This charge makes it much easier to place a *negative* charge on the adjacent oxygen atom, which is exactly what happens when we ionize a proton from the hydroxyl group.

In ethoxide ion, *the negative charge is localized on a single oxygen atom*. In acetate ion, on the other hand, *the negative charge can be delocalized through resonance*.



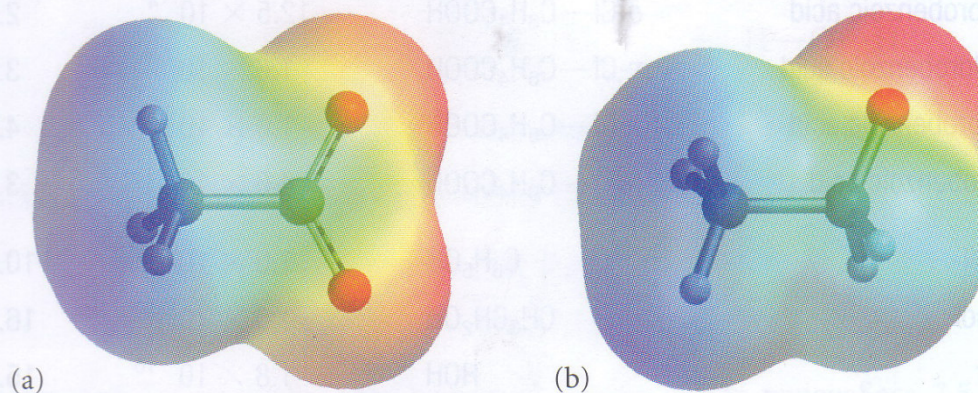
resonance in a carboxylate ion (acetate ion)

The negative charge is spread *equally* over the two oxygens, so that each oxygen in the carboxylate ion carries only half the negative charge (Figure 10.1). The acetate ion is stabilized by resonance compared to the ethoxide ion, and this stabilization helps to drive the equilibrium more to the right in eq. 10.4 than in eq. 10.3. Consequently, more  $\text{H}^+$  is formed from acetic acid than from ethanol.



■ **FIGURE 10.1**

Electrostatic potential map of (a) acetate ion and (b) ethoxide ion. Note the negative (red) character for *both* oxygens in (a).

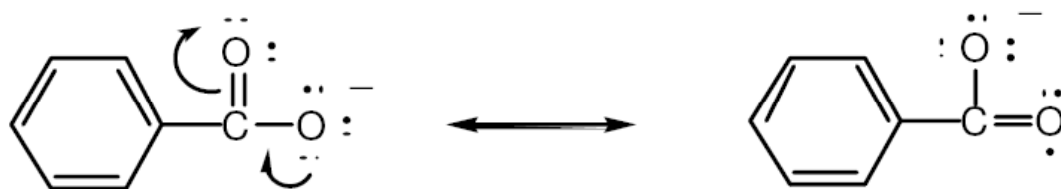


For both these reasons, the positive charge on the carbonyl carbon and delocalization of the carboxylate ion, carboxylic acids are much more acidic than alcohols.

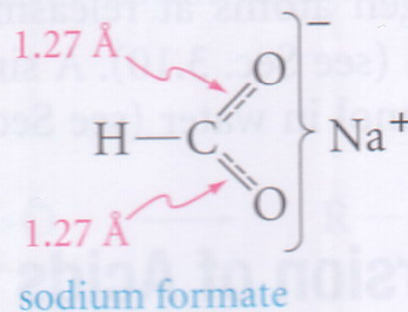
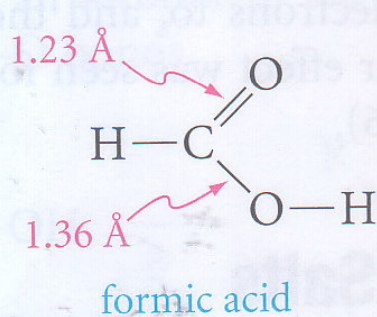


**PROBLEM 10.7** Write two resonance structures for the benzoate ion ( $\text{C}_6\text{H}_5\text{CO}_2^-$ ) that show how the negative charge is delocalized over the two oxygens. Can the negative charge in the benzoate ion be delocalized into the aromatic ring?

The negative charge in the benzoate anion cannot be delocalized into the aromatic, but can be distributed over the two oxygen atoms.



Physical data support the importance of resonance in carboxylate ions. In formic acid molecules, the two carbon–oxygen bonds have different lengths. But in sodium formate, both carbon–oxygen bonds of the formate ion are identical, and their length is between those of normal double and single carbon–oxygen bonds.



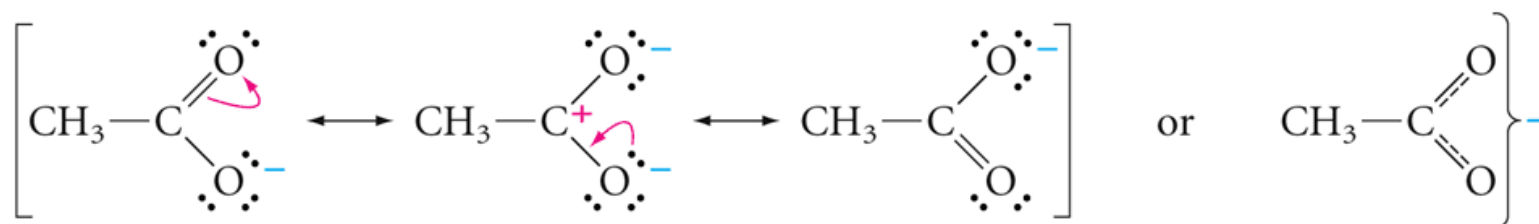
## 10.5 Effect of Structure on Acidity; the Inductive Effect Revisited

The data in Table 10.4 show that even among carboxylic acids (where the ionizing functional group is kept constant), acidities can vary depending on what other groups are attached to the molecule. Compare, for example, the  $K_a$  of acetic acid with those of mono-, di-, and trichloroacetic acids, and note that the acidity varies by a factor of 10,000.

The most important factor operating here is the inductive effect of the groups close to the carboxyl group. This effect relays charge through bonds, by displacing bonding electrons toward electronegative atoms, or away from electropositive atoms. Recall that *electron-withdrawing groups enhance acidity, and electron-releasing groups reduce acidity* (see Sec. 7.6).

Let us examine the carboxylate ions formed when acetic acid and its chloro derivatives ionize:



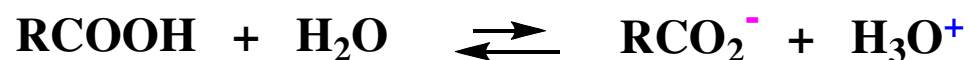


resonance in a carboxylate ion (acetate ion)

Because chlorine is more electronegative than carbon, the C—Cl bond is polarized with the chlorine partially negative and the carbon partially positive. Thus, electrons are pulled away from the carboxylate end of the ion toward the chlorine. The effect tends to spread the negative charge over more atoms than in acetate ion itself and thus stabilizes the ion. The more chlorines, the greater the effect and the greater the strength of the acid.

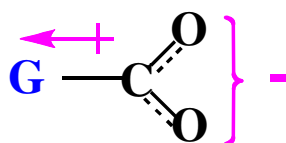
## Effect of Substituents on Acidity

Any factor that stabilizes the anion more than it stabilizes the acid should **increase acidity** (decrease the magnitude of  $pK_a$ ). Any factor that destabilizes the anion relative to the acid should **decrease acidity**.



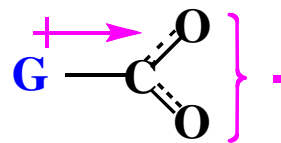
### Electronic Influences

The electronic effect of a substituent **G** operates more strongly on the anion (charged species) than on the carboxylic acid (neutral species).



*Electron withdrawal*

Stabilizes the anion and  
increases acidity

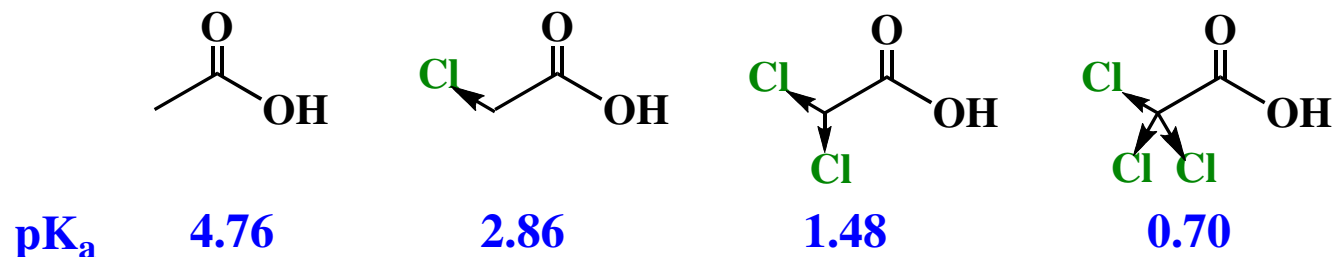


*Electron release*

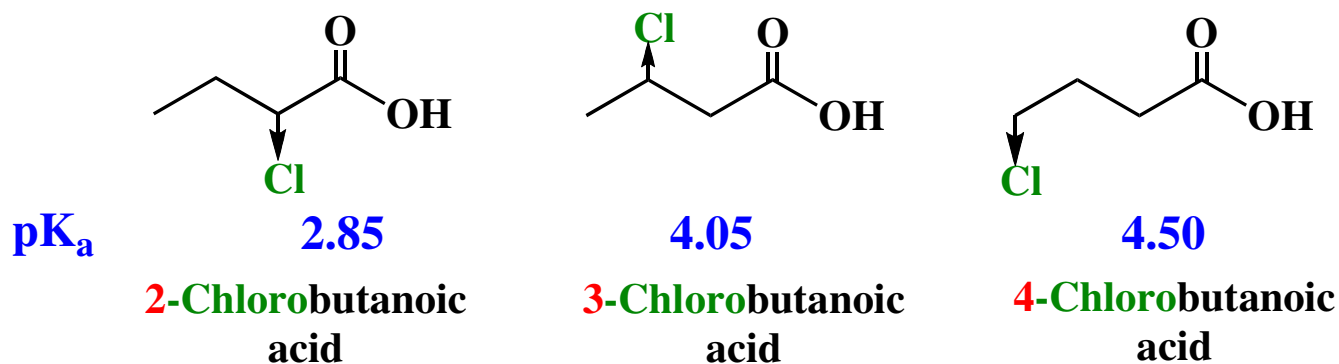
Destabilizes the anion  
and decreases acidity

## Some Examples of Substituent Effects

Electron-withdrawing  $\alpha$ -substituents increase acidity:



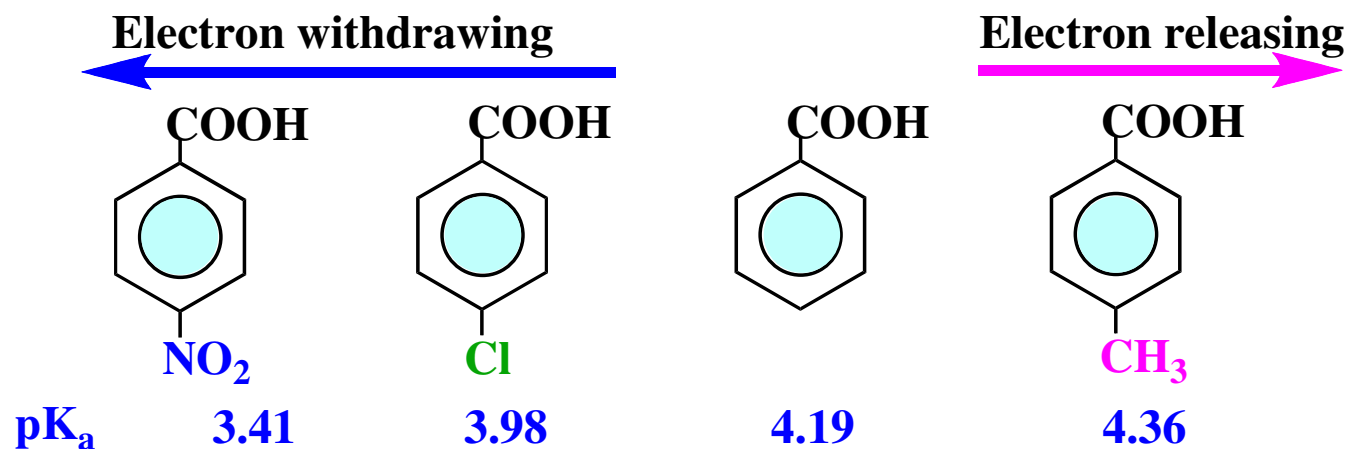
The more remote an electron-withdrawing substituent is from the carbonyl group, the less its effect:





## Substituent Effects in Benzoic Acids

Substituents introduced into the *para* position of a benzoic acid affect the acidity as expected for the electronic influence on the stability of the benzoate anion.



The substituent influence is from a combination of resonance and inductive effects because direct resonance interaction between the benzene ring and the carboxylate anion is not important.

**PROBLEM 10.8** Account for the relative acidities of benzoic acid and its *ortho*, *meta*, and *para* chloro derivatives (Table 10.4).

benzoic acid	$\text{C}_6\text{H}_5\text{COOH}$	$6.6 \times 10^{-5}$	4.18
<i>o</i> -chlorobenzoic acid	<i>o</i> -Cl— $\text{C}_6\text{H}_4\text{COOH}$	$12.5 \times 10^{-4}$	2.90
<i>m</i> -chlorobenzoic acid	<i>m</i> -Cl— $\text{C}_6\text{H}_4\text{COOH}$	$1.6 \times 10^{-4}$	3.80
<i>p</i> -chlorobenzoic acid	<i>p</i> -Cl— $\text{C}_6\text{H}_4\text{COOH}$	$1.0 \times 10^{-4}$	4.00

$K_a$  for benzoic acid is  $6.6 \times 10^{-5}$  or  $0.66 \times 10^{-4}$ . For *o*-, *m*-, and *p*-chlorobenzoic acids,  $K_a$  is 12.5, 1.6, and  $1.0 \times 10^{-4}$ , respectively. All three chloro acids are stronger than benzoic acid. However, the difference is greatest for the *ortho* isomer since, in this isomer, the chloro substituent is closest to the carboxyl group and exerts the maximum electron-withdrawing inductive effect. The effect decreases as the distance between the chloro substituent and the carboxyl group increases.

Which is the stronger acid, formic or acetic, and by how much?

**SOLUTION** Formic acid is stronger; it has the larger  $K_a$ . The ratio of acidities is

$$\frac{2.1 \times 10^{-4}}{1.8 \times 10^{-5}} = 1.17 \times 10^1 = 11.7$$

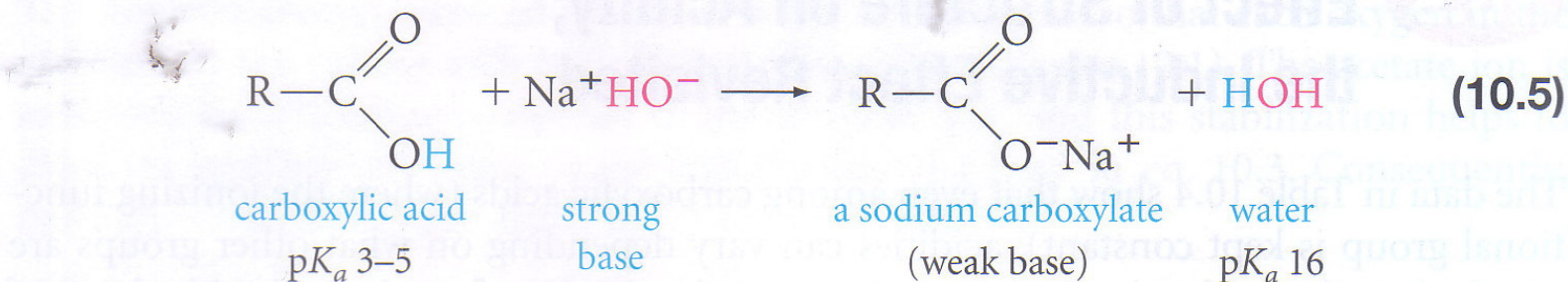
This means that formic acid is 11.7 times stronger than acetic acid.

We saw in Example 10.1 that formic acid is a substantially stronger acid than acetic acid. This suggests that the methyl group is more electron-releasing (hence anion destabilizing and acidity-reducing) than hydrogen. This observation is consistent with what we have already learned about carbocation stabilities—that alkyl groups are more effective than hydrogen atoms at releasing electrons to, and therefore stabilizing, a positive carbon atom (see Sec. 3.10). A similar effect was seen for the relative acidity of ethanol and *t*-butanol in water (see Sec. 7.6).



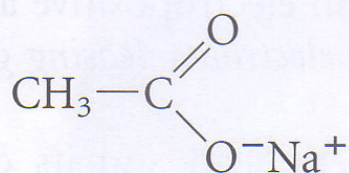
## 10.6 Conversion of Acids to Salts

Carboxylic acids, when treated with a strong base, form carboxylate salts. For example,

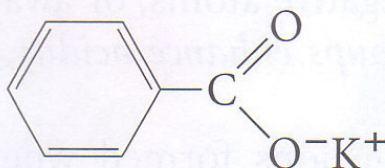


The salt can be isolated by evaporating the water. As we will see in Chapter 15, carboxylate salts of certain acids are useful as soaps and detergents.

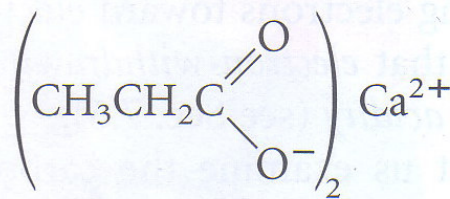
Carboxylate salts are named as shown in the following examples:



sodium acetate  
(sodium ethanoate)



potassium benzoate

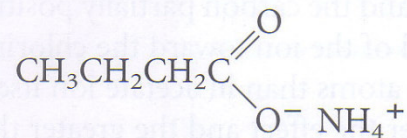


calcium propanoate

The cation is named first, followed by the name of the carboxylate ion, which is obtained by changing the *-ic* ending of the acid to *-ate*.

**EXAMPLE 10.4**

Name the following carboxylate salt:



**SOLUTION** The salt is ammonium butanoate (IUPAC) or ammonium butyrate (common).

**PROBLEM 10.9** Write an equation, analogous to eq. 10.5, for the preparation of potassium 3-bromopropanoate from the corresponding acid.



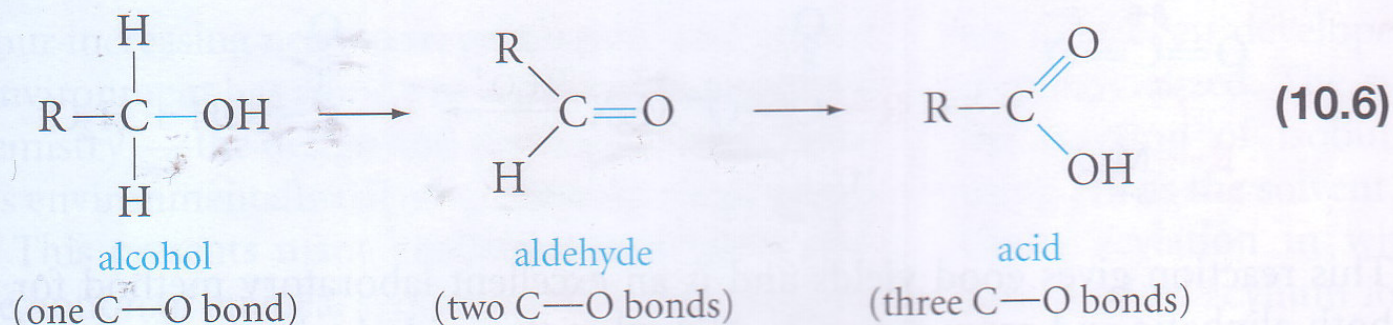


## 10.7 Preparation of Acids

Organic acids can be prepared in many ways, four of which will be described here: (1) oxidation of primary alcohols or aldehydes, (2) oxidation of alkyl side chains on aromatic rings, (3) reaction of Grignard reagents with carbon dioxide, and (4) hydrolysis of alkyl cyanides (nitriles).

### 10.7.a Oxidation of Primary Alcohols and Aldehydes

The oxidation of primary alcohols (Sec. 7.12) and aldehydes (Sec. 9.13) to carboxylic acids has already been mentioned. It is easy to see that these are oxidation reactions because going from an alcohol to an aldehyde to an acid requires replacement of C—H bonds by C—O bonds.



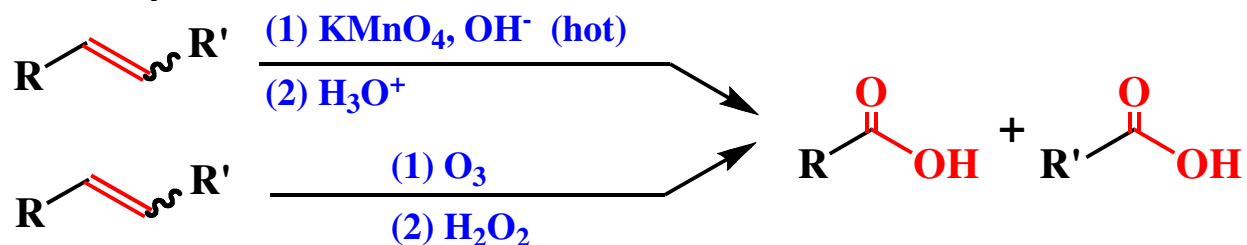
The most commonly used oxidizing agents for these purposes are potassium permanganate ( $\text{KMnO}_4$ ), chromic acid anhydride ( $\text{CrO}_3$ ), nitric acid ( $\text{HNO}_3$ ), and with aldehydes only, silver oxide ( $\text{Ag}_2\text{O}$ ). For specific examples, see eqs. 7.37, 9.37, 9.38, and 9.41.



# Preparation of Carboxylic Acids

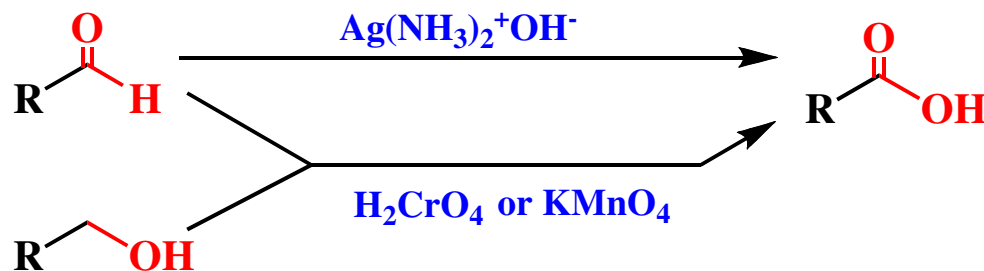
## Oxidation of Alkenes

Alkenes can be oxidatively cleaved to carboxylic acids by use of either  $\text{KMnO}_4$  or ozone.



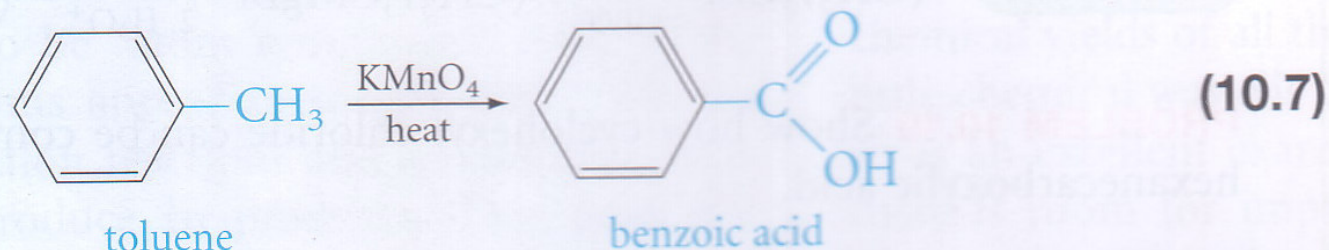
## Oxidation of Aldehydes and 1° Alcohols

Aldehydes are easily oxidized to carboxylic acids, even by mild oxidants such as  $\text{Ag}(\text{NH}_3)_2^+\text{OH}^-$ , which is used in the Tollens' test for distinguishing aldehydes from ketones. Stronger reagents such as chromic acid ( $\text{H}_2\text{CrO}_4$ ) or  $\text{KMnO}_4$  can oxidize either aldehydes or 1° alcohols to carboxylic acids.

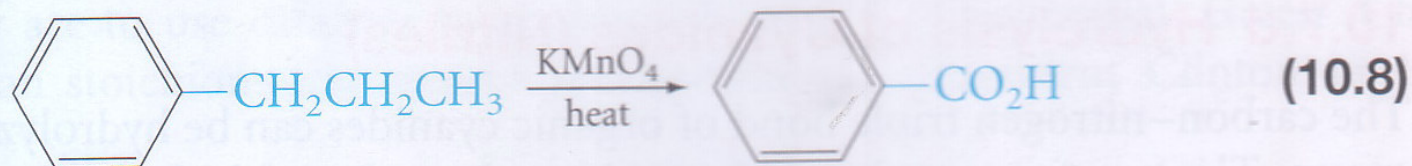


## 10.7.b Oxidation of Aromatic Side Chains

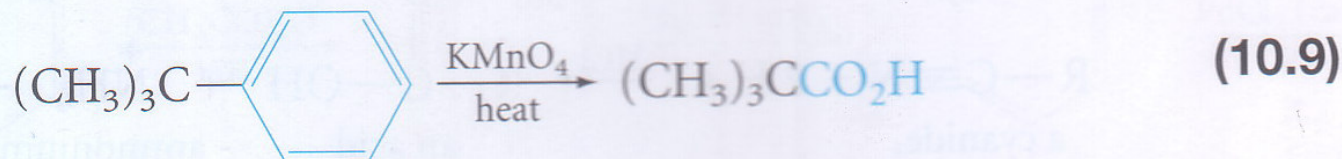
Aromatic acids can be prepared by oxidizing an alkyl side chain on an aromatic ring.



This reaction illustrates the striking stability of aromatic rings; it is the alkane-like methyl group, not the aromatic ring, that is oxidized. The reaction involves attack of the oxidant at a C—H bond adjacent to the benzene ring. Longer side chains are also oxidized to a carboxyl group.

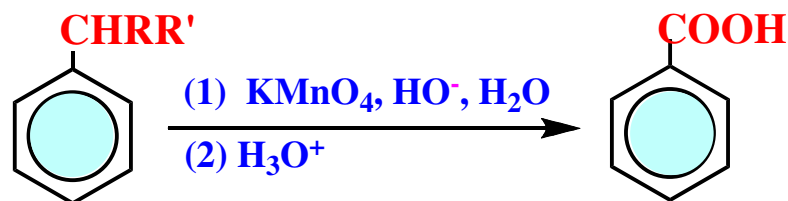


If no C—H bond is in the benzylic position, however, the aromatic ring is oxidized, although only under severe reaction conditions.



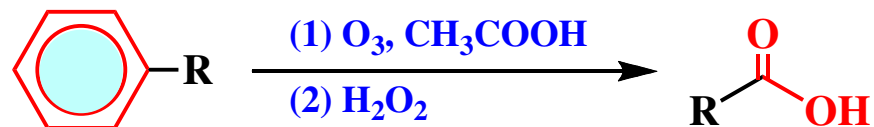
## Oxidation of Alkylbenzenes

Vigorous oxidation by  $\text{KMnO}_4$  of primary and secondary (but not tertiary) alkyl groups directly attached to a benzene ring produces aromatic acids.



## Oxidation of Alkylbenzenes

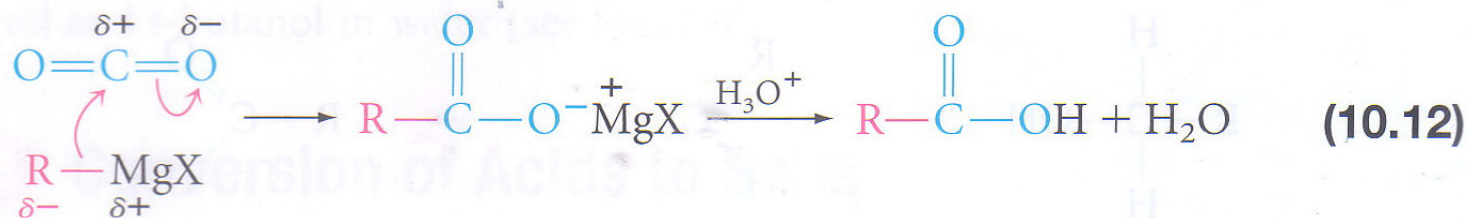
The benzene ring of an alkylbenzene can be converted to a carboxyl group by ozonolysis.





### 10.7.c Reaction of Grignard Reagents with Carbon Dioxide

As we saw previously, Grignard reagents add to the carbonyl groups of aldehydes or ketones to give alcohols. In a similar way, they add irreversibly to the carbonyl group of carbon dioxide to give acids, after protonation of the intermediate carboxylate salt with a mineral acid like aqueous HCl.

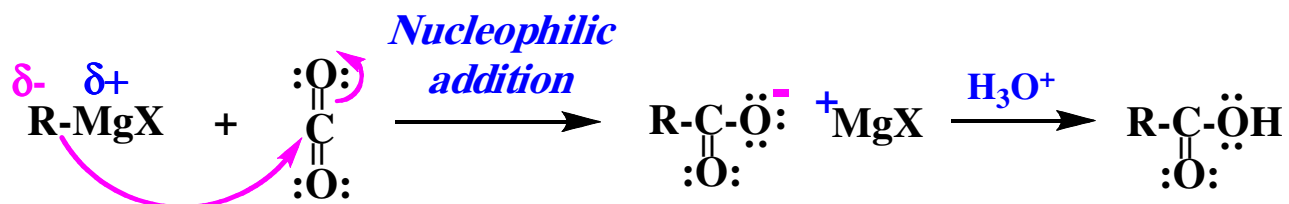


This reaction gives good yields and is an excellent laboratory method for preparing both aliphatic and aromatic acids. Note that the acid obtained has one more carbon atom than the alkyl or aryl halide from which the Grignard reagent is prepared, so the reaction provides a way to increase the length of a carbon chain.

## Carbonation of Grignard Reagents

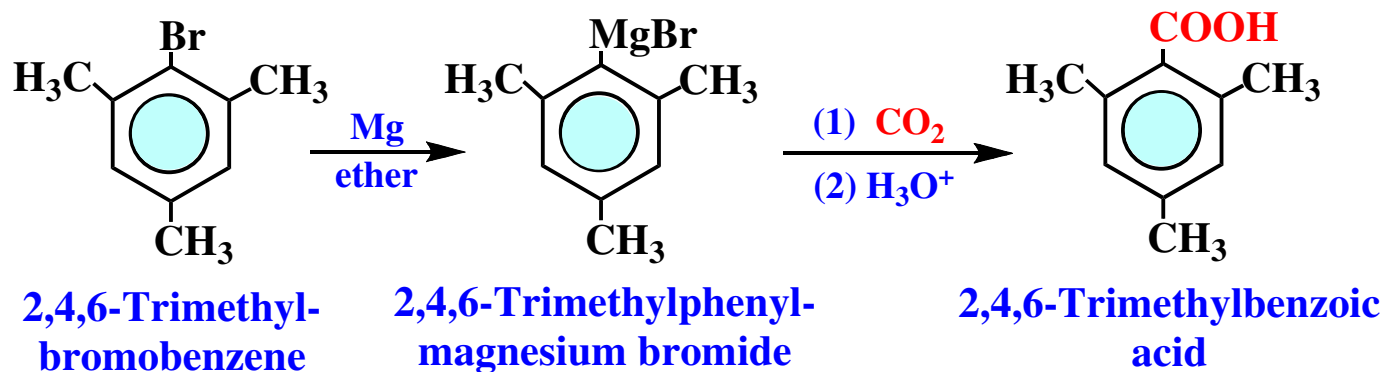
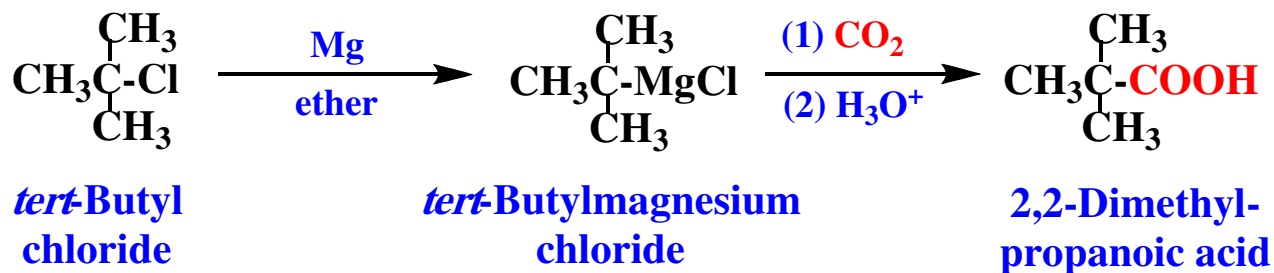
A more general way to prepare carboxylic acids from alkyl or aryl halides is by carbonation (reaction with  $\text{CO}_2$ ) of the corresponding Grignard reagents.

The **strongly nucleophilic** organomagnesium reagents add to  $\text{CO}_2$  to produce magnesium carboxylates. Acidification of these salts yields the carboxylic acids.



All alkyl ( $1^\circ$ ,  $2^\circ$ ,  $3^\circ$ ) and aryl Grignard reagents undergo the carboxylation reaction. This reaction is accomplished by either bubbling dry gaseous  $\text{CO}_2$  through an ether solution of the Grignard reagent or by pouring the Grignard reagent onto crushed dry ice (solid  $\text{CO}_2$ ).

## Syntheses Using the Grignard Carbonation Reaction

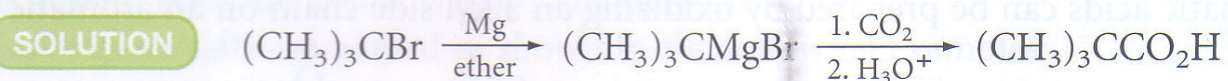




### EXAMPLE 10.5

Show how  $(\text{CH}_3)_3\text{CBr}$  can be converted to  $(\text{CH}_3)_3\text{CCO}_2\text{H}$ .

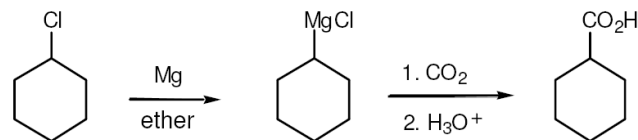
**SOLUTION**



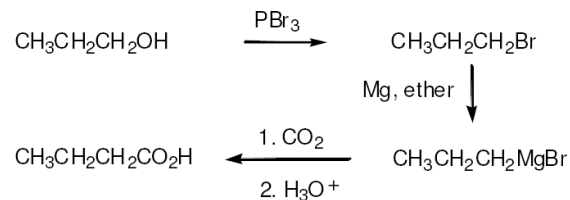
**PROBLEM 10.10** Show how cyclohexyl chloride can be converted to cyclohexanecarboxylic acid.

**PROBLEM 10.11** Devise a synthesis of butanoic acid ( $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$ ) from 1-propanol ( $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ ).

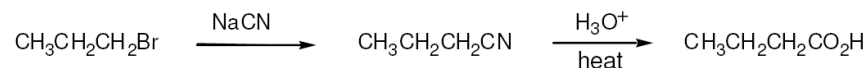
10.10 The halide can be converted to the corresponding Grignard reagent, which can react with carbon dioxide to give the carboxylic acid.



10.11 There are several possible approaches. First, the alcohol must be converted to a halide. The halide can then be converted to the corresponding Grignard reagent, which can react with carbon dioxide to provide the carboxylic acid.

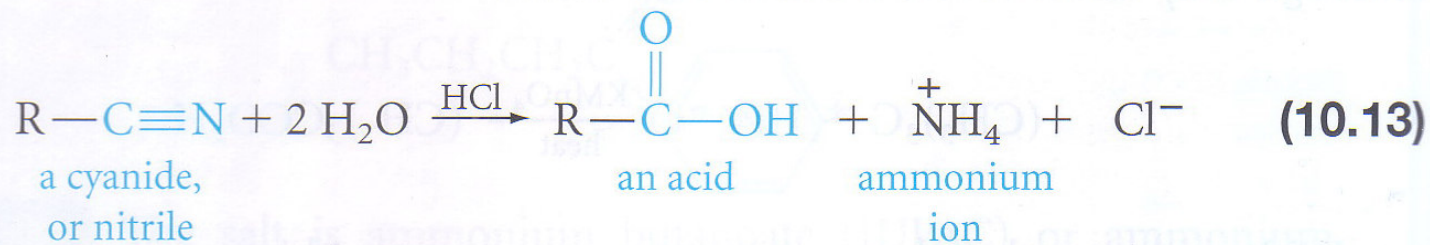


Conversion of the halide to a nitrile followed by hydrolysis would also provide the carboxylic acid. This reaction is introduced in the next section (10.7d), so do not be concerned if it did not occur to you when initially working this problem.

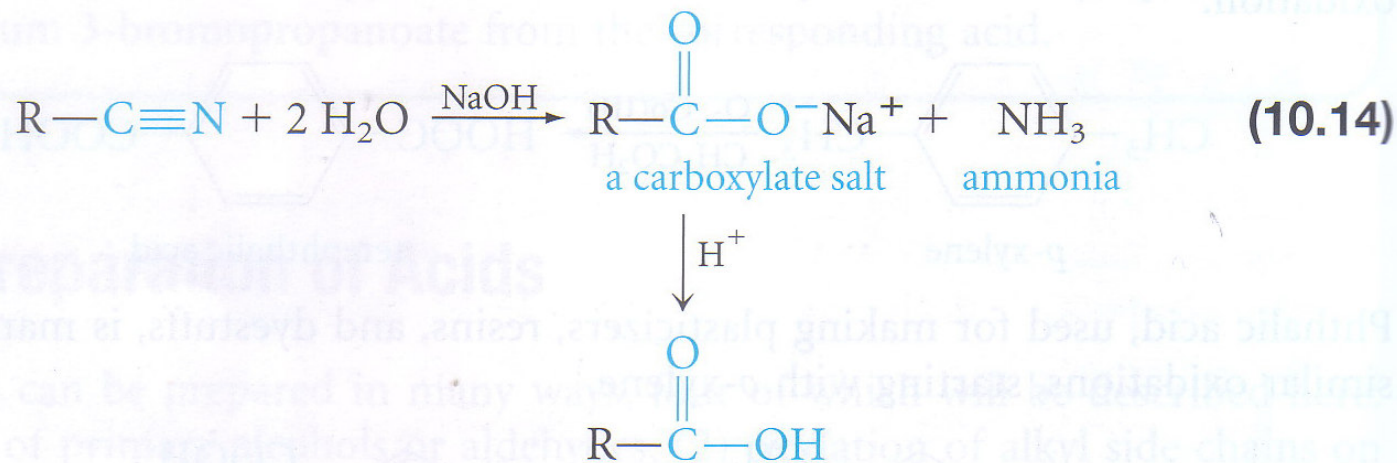


### 10.7.d Hydrolysis of Cyanides (Nitriles)

The carbon–nitrogen triple bond of organic cyanides can be hydrolyzed to a carboxyl group. The reaction requires either acid or base. In acid, the nitrogen atom of the cyanide is converted to an ammonium ion.

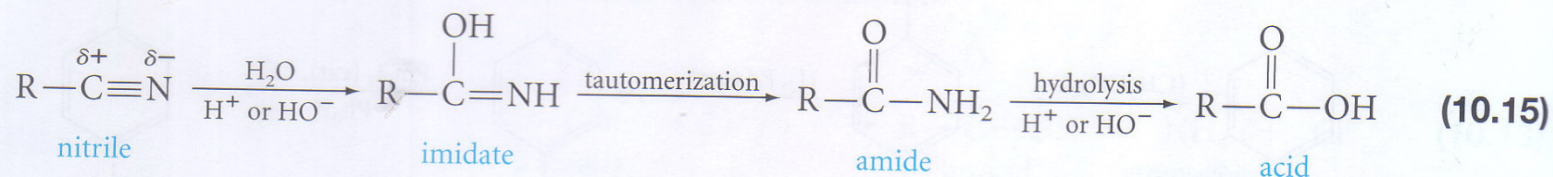


In base, the nitrogen is converted to ammonia and the organic product is the carboxylate salt, which must be neutralized in a separate step to give the acid.

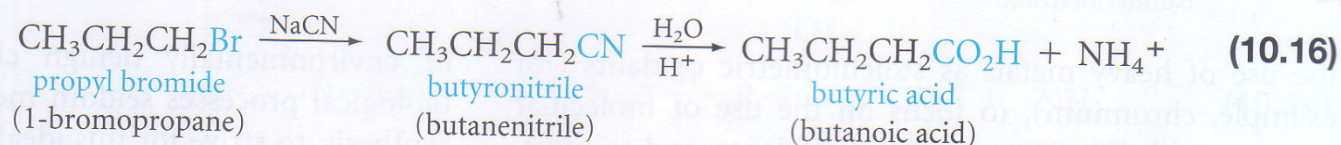




The mechanism of nitrile hydrolysis involves acid or base promoted addition of water across the triple bond. This gives an intermediate imidate that tautomerizes to an amide. The amide is then hydrolyzed to the carboxylic acid. The addition of water to the nitrile resembles the hydration of an alkyne (eq. 3.52). The oxygen of water behaves as a nucleophile and bonds to the electrophilic carbon of the nitrile. Amide hydrolysis will be discussed in Sec. 10.20.



Alkyl cyanides are generally made from the corresponding alkyl halide (usually primary) and sodium cyanide by an S<sub>N</sub>2 displacement, as shown in this synthesis of an acid:



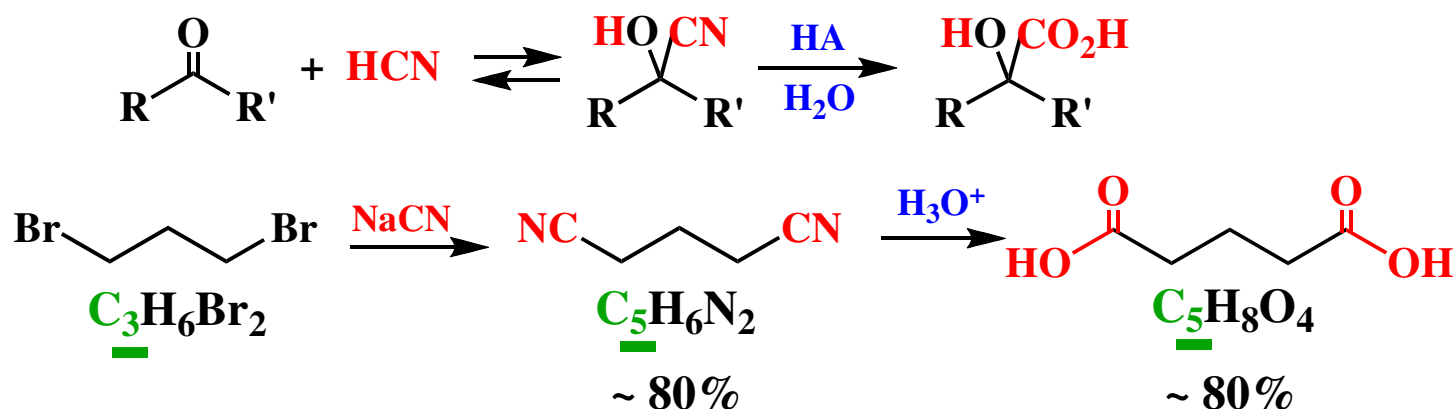
Organic cyanides are commonly named after the corresponding acid, by changing the *-ic* or *-oic* suffix to *-onitrile* (hence, butyronitrile in eq. 10.16). In the IUPAC system, the suffix *-nitrile* is added to the name of the hydrocarbon with the same number of carbon atoms (hence butanenitrile in eq. 10.16).



## Hydrolysis of Cyanohydrins and Other Nitriles

Cyanohydrins, prepared by addition of HCN to aldehydes or ketones, can be hydrolyzed to  $\alpha$ -hydroxy acids.

Nitriles can also be prepared by nucleophilic substitution reactions of 1° alkyl halides with sodium cyanide. Hydrolysis then provides a carboxylic acid of increased chain length .

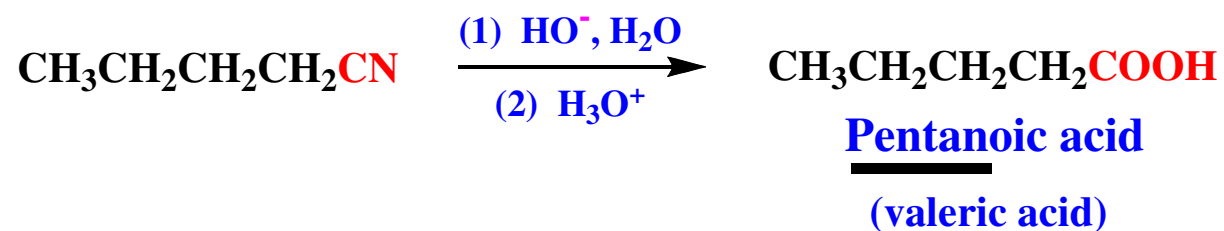
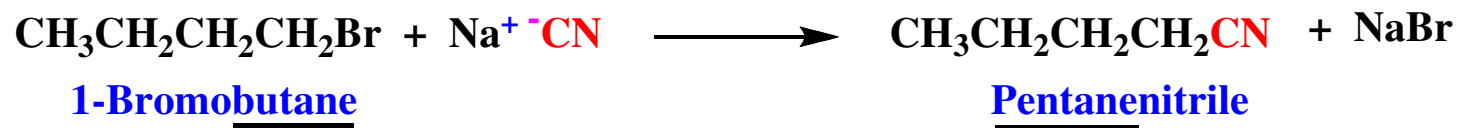


Because of the elimination-promoting basicity of cyanide ion, the  $\text{S}_{\text{N}}2$  reaction proceeds in good yield only with  $\text{CH}_3\text{X}$  and 1° halides. Aryl halides (except for those with *o*- or *p*-nitro groups) do not readily undergo nucleophilic substitution reactions.

Hydrolysis of nitriles may be carried out under either basic or acidic conditions.

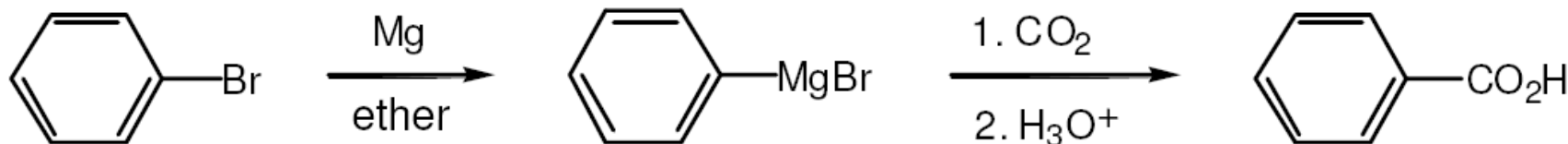
## An Example: The Synthesis of Pentanoic Acid from 1-Bromobutane

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**PROBLEM 10.12** Why is it *not* possible to convert bromobenzene to benzoic acid by the nitrile method? How could this conversion be accomplished?

It is not possible to conduct  $S_N2$  displacements at  $sp^2$ -hybridized (aryl, vinyl) carbon atoms. The conversion can be accomplished via the Grignard reagent:





Note that with the hydrolysis of nitriles, as with the Grignard method, the acid obtained has one more carbon atom than the alkyl halide from which the cyanide is prepared. Consequently, both methods provide ways of increasing the length of a carbon chain.

**PROBLEM 10.13** Write equations for synthesizing phenylacetic acid ( $\text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{H}$ ) from benzyl bromide ( $\text{C}_6\text{H}_5\text{CH}_2\text{Br}$ ) by two routes.

