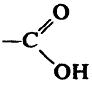
Chapter 18 Carboxylic Acids

18.1 Structure

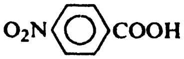
Of the organic compounds that show appreciable acidity, by far the most important are the carboxylic acids. These compounds contain the **carboxyl group**



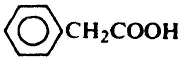
attached to either an alkyl group (RCOOH) or an aryl group (ArCOOH). For example:

$HCOOH$	CH_3COOH	$CH_3(CH_2)_{10}COOH$	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
Formic acid	Acetic acid	Lauric acid	Oleic acid
Methanoic acid	Ethanoic acid	Dodecanoic acid	*cis*-9-Octadecenoic acid

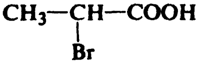
Benzoic acid



p-Nitrobenzoic acid

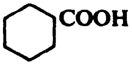


Phenylacetic acid



$$CH_3{-}\underset{\displaystyle Br}{\underset{|}{C}H}{-}COOH$$

α-Bromopropionic acid
2-Bromopropanoic acid



Cyclohexanecarboxylic acid

$CH_2{=}CHCOOH$

Acrylic acid
Propenoic acid

Whether the group is aliphatic or aromatic, saturated or unsaturated, substituted or unsubstituted, the properties of the carboxyl group are essentially the same.

18.2 Nomenclature

The aliphatic carboxylic acids have been known for a long time, and as a result have common names that refer to their sources rather than to their chemical structures. The **common names** of the more important acids are shown in Table 18.1. *Formic acid*, for example, adds the sting to the bite of an ant (Latin: *formica*, ant); *butyric acid* gives rancid butter its typical smell (Latin: *butyrum*, butter);

Table 18.1 CARBOXYLIC ACIDS

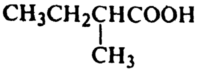
Name	Formula	M.p., °C	B.p., °C	Solub., g/100 g H_2O
Formic	$HCOOH$	8	100.5	∞
Acetic	CH_3COOH	16.6	118	∞
Propionic	CH_3CH_2COOH	−22	141	∞
Butyric	$CH_3(CH_2)_2COOH$	− 6	164	∞
Valeric	$CH_3(CH_2)_3COOH$	−34	187	3.7
Caproic	$CH_3(CH_2)_4COOH$	− 3	205	1.0
Caprylic	$CH_3(CH_2)_6COOH$	16	239	0.7
Capric	$CH_3(CH_2)_8COOH$	31	269	0.2
Lauric	$CH_3(CH_2)_{10}COOH$	44	225^{100}	i.
Myristic	$CH_3(CH_2)_{12}COOH$	54	251^{100}	i.
Palmitic	$CH_3(CH_2)_{14}COOH$	63	269^{100}	i.
Stearic	$CH_3(CH_2)_{16}COOH$	70	287^{100}	i.
Oleic	*cis*-9-Octadecenoic	16	223^{10}	i.
Linoleic	*cis,cis*-9,12-Octadecadienoic	− 5	230^{16}	i.
Linolenic	*cis,cis,cis*-9,12,15-Octadecatrienoic	−11	232^{17}	i.
Cyclohexanecarboxylic	*cyclo*-$C_6H_{11}COOH$	31	233	0.20
Phenylacetic	$C_6H_5CH_2COOH$	77	266	1.66
Benzoic	C_6H_5COOH	122	250	0.34
o-Toluic	*o*-$CH_3C_6H_4COOH$	106	259	0.12
m-Toluic	*m*-$CH_3C_6H_4COOH$	112	263	0.10
p-Toluic	*p*-$CH_3C_6H_4COOH$	180	275	0.03
o-Chlorobenzoic	*o*-ClC_6H_4COOH	141		0.22
m-Chlorobenzoic	*m*-ClC_6H_4COOH	154		0.04
p-Chlorobenzoic	*p*-ClC_6H_4COOH	242		0.009
o-Bromobenzoic	*o*-BrC_6H_4COOH	148		0.18
m-Bromobenzoic	*m*-BrC_6H_4COOH	156		0.04
p-Bromobenzoic	*p*-BrC_6H_4COOH	254		0.006
o-Nitrobenzoic	*o*-$O_2NC_6H_4COOH$	147		0.75
m-Nitrobenzoic	*m*-$O_2NC_6H_4COOH$	141		0.34
p-Nitrobenzoic	*p*-$O_2NC_6H_4COOH$	242		0.03
Phthalic	*o*-$C_6H_4(COOH)_2$	231		0.70
Isophthalic	*m*-$C_6H_4(COOH)_2$	348		0.01
Terephthalic	*p*-$C_6H_4(COOH)_2$	300 *subl.*		0.002
Salicylic	*o*-HOC_6H_4COOH	159		0.22
p-Hydroxybenzoic	*p*-HOC_6H_4COOH	213		0.65
Anthranilic	*o*-$H_2NC_6H_4COOH$	146		0.52
m-Aminobenzoic	*m*-$H_2NC_6H_4COOH$	179		0.77
p-Aminobenzoic	*p*-$H_2NC_6H_4COOH$	187		0.3
o-Methoxybenzoic	*o*-$CH_3OC_6H_4COOH$	101		0.5
m-Methoxybenzoic	*m*-$CH_3OC_6H_4COOH$	110		
p-Methoxybenzoic (Anisic)	*p*-$CH_3OC_6H_4COOH$	184		0.04

and *caproic*, *caprylic*, and *capric acids* are all found in goat fat (Latin: *caper*, goat).

Branched-chain acids and substituted acids are named as derivatives of the straight-chain acids. To indicate the position of attachment, the Greek letters, α-, β-, γ-, δ-, etc., are used; the α-carbon is the one bearing the carboxyl group.

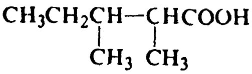
$$\overset{\delta}{C}—\overset{\gamma}{C}—\overset{\beta}{C}—\overset{\alpha}{C}—COOH \qquad \textit{Used in common names}$$

For example:



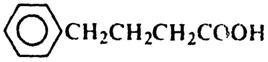
$\underset{CH_3}{CH_3CH_2CHCOOH}$

α-Methylbutyric acid

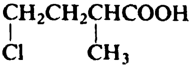


$CH_3CH_2\underset{CH_3}{CH}—\underset{CH_3}{C}HCOOH$

α,β-Dimethylvaleric acid

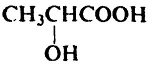


γ-Phenylbutyric acid



$\underset{Cl}{CH_2}CH_2\underset{CH_3}{C}HCOOH$

γ-Chloro-α-methylbutyric acid

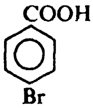


$CH_3\underset{OH}{C}HCOOH$

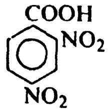
α-Hydroxypropionic acid
Lactic acid

Generally the parent acid is taken as the one of longest carbon chain, although some compounds are named as derivatives of acetic acid.

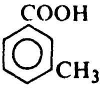
Aromatic acids, ArCOOH, are usually named as derivatives of the parent acid, **benzoic acid**, C_6H_5COOH. The methylbenzoic acids are given the special name of *toluic acids*.



p-Bromobenzoic acid



2,4-Dinitrobenzoic acid

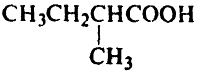


m-Toluic acid

The **IUPAC names** follow the usual pattern. The longest chain carrying the carboxyl group is considered the parent structure, and is named by replacing the -*e* of the corresponding alkane with **-oic acid**. For example:

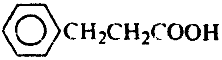
$CH_3CH_2CH_2CH_2COOH$

Pentanoic acid

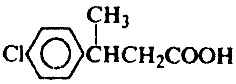


$CH_3CH_2\underset{CH_3}{C}HCOOH$

2-Methylbutanoic acid



3-Phenylpropanoic acid



3-(*p*-Chlorophenyl)butanoic acid

$CH_3CH=CHCOOH$

2-Butenoic acid

The position of a substituent is indicated as usual by a number. We should notice

$$\overset{5}{C}-\overset{4}{C}-\overset{3}{C}-\overset{2}{C}-\overset{1}{C}OOH \qquad \textit{Used in IUPAC names}$$

that the carboxyl carbon is always considered as C-1, and hence C-2 corresponds to α of the common names, C-3 to β, and so on. (*Caution:* Do not mix Greek letters with IUPAC names, or Arabic numerals with common names.)

The name of a **salt** of a carboxylic acid consists of the name of the cation (*sodium*, *potassium*, *ammonium*, etc.) followed by the name of the acid with the ending *-ic acid* changed to **-ate**. For example:

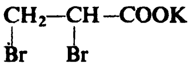
Sodium benzoate

$(CH_3COO)_2Ca$

Calcium acetate

$HCOONH_4$

Ammonium formate



$$\underset{Br}{CH_2}-\underset{Br}{CH}-COOK$$

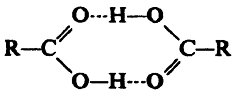
Potassium α,β-dibromopropionate
(Potassium 2,3-dibromopropanoate)

18.3 Physical properties

As we would expect from their structure, carboxylic acid molecules are polar, and like alcohol molecules can form hydrogen bonds with each other and with other kinds of molecules. The aliphatic acids therefore show very much the same solubility behavior as the alcohols: the first four are miscible with water, the five-carbon acid is partly soluble, and the higher acids are virtually insoluble. Water solubility undoubtedly arises from hydrogen bonding between the carboxylic acid and water. The simplest aromatic acid, benzoic acid, contains too many carbon atoms to show appreciable solubility in water.

Carboxylic acids are soluble in less polar solvents like ether, alcohol, benzene, etc.

We can see from Table 18.1 that as a class the carboxylic acids are even higher boiling than alcohols. For example, propionic acid (b.p. 141°) boils more than twenty degrees higher than the alcohol of comparable molecular weight, *n*-butyl alcohol (b.p. 118°). These very high boiling points are due to the fact that a pair of carboxylic acid molecules are held together not by one but by two hydrogen bonds:



Problem 18.1 At 110° and 454 mm pressure, 0.11 g acetic acid vapor occupies 63.7 cc; at 156° and 458 mm, 0.081 g occupies 66.4 cc. Calculate the molecular weight of acetic acid in the vapor phase at each temperature. How do you interpret these results?

The odors of the lower aliphatic acids progress from the sharp, irritating odors of formic and acetic acids to the distinctly unpleasant odors of butyric, valeric, and caproic acids; the higher acids have little odor because of their low volatility.

18.4 Salts of carboxylic acids

Although much weaker than the strong mineral acids (sulfuric, hydrochloric, nitric), the carboxylic acids are tremendously more acidic than the very weak organic acids (alcohols, acetylene) we have so far studied; they are much stronger acids than water. Aqueous hydroxides therefore readily convert carboxylic acids into their salts; aqueous mineral acids readily convert the salts back into the carboxylic acids. Since we can do little with carboxylic acids without encountering this conversion to and from their salts, it is worthwhile for us to examine the properties of these salts.

$$\underset{\text{Acid}}{\text{RCOOH}} \underset{\text{H}^+}{\overset{\text{OH}^-}{\rightleftarrows}} \underset{\text{Salt}}{\text{RCOO}^-}$$

Salts of carboxylic acid—like all salts—are crystalline non-volatile solids made up of positive and negative ions; their properties are what we would expect of such structures. The strong electrostatic forces holding the ions in the crystal lattice can be overcome only by heating to a high temperature, or by a very polar solvent. The temperature required for melting is so high that before it can be reached carbon–carbon bonds break and the molecule decomposes, generally in the neighborhood of 300–400°. A decomposition point is seldom useful for the identification of a compound, since it usually reflects the rate of heating rather than the identity of the compound.

The alkali metal salts of carboxylic acids (sodium, potassium, ammonium) are soluble in water but insoluble in non-polar solvents; most of the heavy metal salts (iron, silver, copper, etc.) are insoluble in water.

Thus we see that, except for the acids of four carbons or less, which are soluble both in water and in organic solvents, *carboxylic acids and their alkali metal salts show exactly opposite solubility behavior.* Because of the ready interconversion of acids and their salts, this difference in solubility behavior may be used in two important ways: for *identification* and for *separation.*

A water-insoluble organic compound that dissolves in cold dilute aqueous sodium hydroxide must be either a carboxylic acid or one of the few other kinds of organic compounds more acidic than water; that it is indeed a carboxylic acid can then be shown in other ways.

$$\underset{\substack{\text{Stronger acid}\\ \textit{Insoluble in } \text{H}_2\text{O}}}{\text{RCOOH} + \text{NaOH}} \longrightarrow \underset{\substack{\textit{Soluble in}\\ \text{H}_2\text{O}}}{\text{RCOONa}} + \underset{\substack{\text{Weaker}\\ \text{acid}}}{\text{H}_2\text{O}}$$

Instead of sodium hydroxide, we can use aqueous sodium bicarbonate; even if the unknown is water-soluble, its acidity is shown by the evolution of bubbles of CO_2.

$$\underset{\textit{Insoluble in } \text{H}_2\text{O}}{\text{RCOOH}} + \text{NaHCO}_3 \longrightarrow \underset{\textit{Soluble in } \text{H}_2\text{O}}{\text{RCOONa}} + \text{H}_2\text{O} + \text{CO}_2\uparrow$$

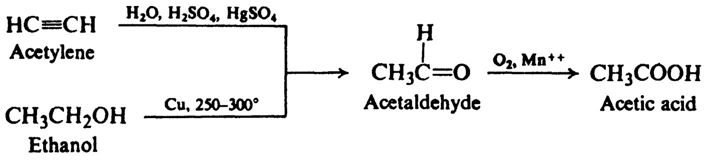
We can separate a carboxylic acid from non-acidic compounds by taking advantage of its solubility and their insolubility in aqueous base; once the separation has been accomplished, we can regenerate the acid by acidification of the aqueous solution. If we are dealing with solids, we simply stir the mixture with aqueous base and then filter the solution from insoluble, non-acidic materials; addition of mineral acid to the filtrate precipitates the carboxylic acid, which can be collected on a filter. If we are dealing with liquids, we shake the mixture with aqueous base in a separatory funnel and separate the aqueous layer from the insoluble organic layer; addition of acid to the aqueous layer again liberates the carboxylic acid, which can then be separated from the water. For completeness of separation and ease of handling, we often add a water-insoluble solvent like ether to the acidified mixture. The carboxylic acid is extracted from the water by the ether, in which it is more soluble; the volatile ether is readily removed by distillation from the comparatively high-boiling acid.

For example, an aldehyde prepared by the oxidation of a primary alcohol (Sec. 16.8) may very well be contaminated with the carboxylic acid; this acid can be simply washed out with dilute aqueous base. The carboxylic acid prepared by oxidation of an alkylbenzene (Sec. 12.10) may very well be contaminated with unreacted starting material; the carboxylic acid can be taken into solution by aqueous base, separated from the insoluble hydrocarbon, and regenerated by addition of mineral acid.

Since separations of this kind are more clear-cut and less wasteful of material, they are preferred wherever possible over recrystallization or distillation.

18.5 Industrial source

Acetic acid, by far the most important of all carboxylic acids, is prepared by air oxidation of acetaldehyde, which is readily available from the hydration of acetylene (Sec. 8.13), or the dehydrogenation of ethanol.

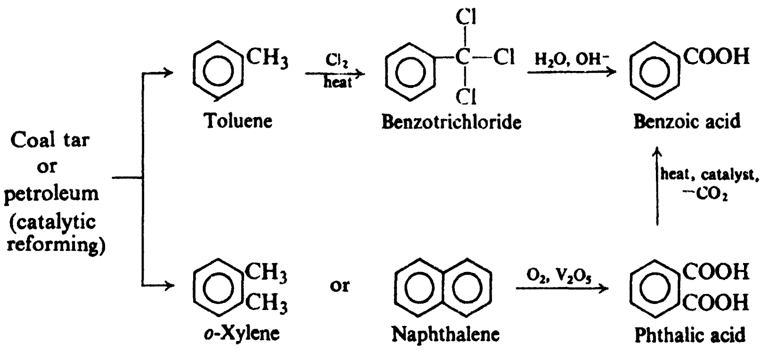


Large amounts of acetic acid are also produced as the dilute aqueous solution known as *vinegar*. Here, too, the acetic acid is prepared by air oxidation; the compound that is oxidized is ethyl alcohol, and the catalysts are bacterial (*Acetobacter*) enzymes.

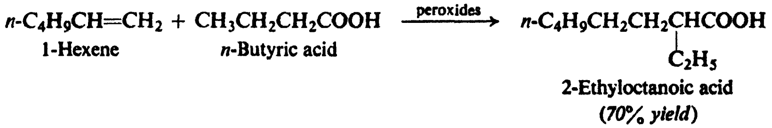
The most important sources of aliphatic carboxylic acids are the animal and vegetable **fats** (Secs. 33.2–33.4). From fats there can be obtained, in purity of over 90%, straight-chain carboxylic acids of even carbon number ranging from six to eighteen carbon atoms. These acids can be converted into the corresponding alcohols (Sec. 18.18), which can then be used, in the ways we have already studied (Sec. 16.10), to make a great number of other compounds containing long, straight-chain units.

The most important of the aromatic carboxylic acids, **benzoic acid** and the

phthalic acids, are prepared on an industrial scale by a reaction we have already encountered: oxidation of alkylbenzenes (Sec. 12.10). The toluene and xylenes required are readily available from coal tar and, by catalytic reforming of aliphatic hydrocarbons (Sec. 12.4), from petroleum; another precursor of phthalic acid (the *ortho* isomer) is the aromatic hydrocarbon *naphthalene*, also found in coal tar. Cheap oxidizing agents like chlorine or even air (in the presence of catalysts) are used.



Problem 18.2 In the presence of peroxides, carboxylic acids (or esters) react with 1-alkenes to yield more complicated acids. For example:



$$\underset{\text{1-Hexene}}{n\text{-}C_4H_9CH{=}CH_2} + \underset{n\text{-Butyric acid}}{CH_3CH_2CH_2COOH} \xrightarrow{\text{peroxides}} n\text{-}C_4H_9CH_2CH_2\underset{C_2H_5}{\underset{|}{C}}HCOOH$$

2-Ethyloctanoic acid
(70% yield)

(a) Outline all steps in a likely mechanism for this reaction. (*Hint:* See Sec. 6.18.) Predict the products of similar reactions between: (b) 1-octene and propionic acid; (c) 1-decene and isobutyric acid; and (d) 1-octene and ethyl malonate, $CH_2(COOC_2H_5)_2$.

Problem 18.3 (a) Carbon monoxide converts a sulfuric acid solution of each of the following into 2,2-dimethylbutanoic acid: 2-methyl-2-butene, *tert*-pentyl alcohol, neopentyl alcohol. Suggest a likely mechanism for this method of synthesizing carboxylic acids. (b) *n*-Butyl alcohol and *sec*-butyl alcohol give the same product. What would you expect it to be?

18.6 Preparation

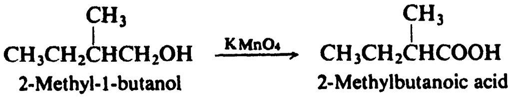
The straight-chain aliphatic acids up to C_6, and those of even carbon number up to C_{18}, are commercially available, as are the simple aromatic acids. Other carboxylic acids can be prepared by the methods outlined below.

PREPARATION OF CARBOXYLIC ACIDS

1. **Oxidation of primary alcohols.** Discussed in Sec. 16.8.

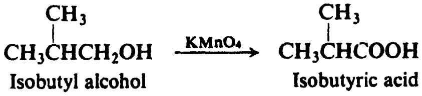
$$RCH_2OH \xrightarrow{KMnO_4} RCOOH$$

Examples:



$$CH_3CH_2\overset{CH_3}{\overset{|}{C}}HCH_2OH \xrightarrow{KMnO_4} CH_3CH_2\overset{CH_3}{\overset{|}{C}}HCOOH$$

2-Methyl-1-butanol → 2-Methylbutanoic acid



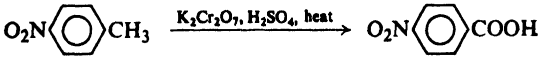
$$CH_3\overset{CH_3}{\overset{|}{C}}HCH_2OH \xrightarrow{KMnO_4} CH_3\overset{CH_3}{\overset{|}{C}}HCOOH$$

Isobutyl alcohol → Isobutyric acid

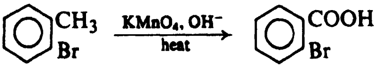
2. **Oxidation of alkylbenzenes.** Discussed in Sec. 12.10.

$$Ar—R \xrightarrow[K_2C_2O_7]{KMnO_4 \text{ or } K_2Cr_2O_7} Ar—COOH$$

Examples:



p-Nitrotoluene → *p*-Nitrobenzoic acid

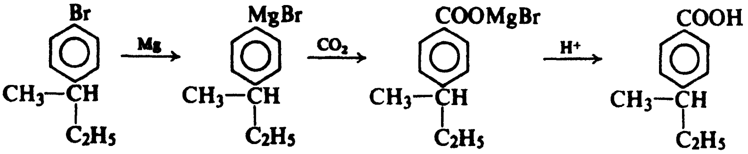


o-Bromotoluene → *o*-Bromobenzoic acid

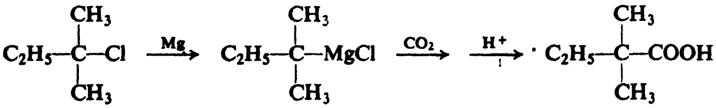
3. **Carbonation of Grignard reagents.** Discussed in Sec. 18.7.

$$\underset{\text{(or ArX)}}{RX} \xrightarrow{Mg} RMgX \xrightarrow{CO_2} RCOOMgX \xrightarrow{H^+} \underset{\text{(or ArCOOH)}}{RCOOH}$$

Examples:



p-Bromo-*sec*-butylbenzene → *p*-*sec*-Butylbenzoic acid



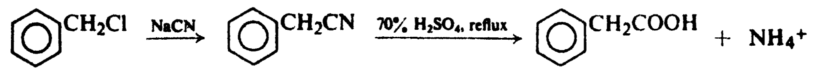
$$C_2H_5—\underset{CH_3}{\overset{CH_3}{C}}—Cl \xrightarrow{Mg} C_2H_5—\underset{CH_3}{\overset{CH_3}{C}}—MgCl \xrightarrow{CO_2} \xrightarrow{H^+} C_2H_5—\underset{CH_3}{\overset{CH_3}{C}}—COOH$$

tert-Pentyl chloride → Ethyldimethylacetic acid (2,2-Dimethylbutanoic acid)

4. **Hydrolysis of nitriles.** Discussed in Sec. 18.8.

$$\begin{matrix} R—C\equiv N \\ \text{or} \\ Ar—C\equiv N \end{matrix} + H_2O \xrightarrow{\text{acid or base}} \begin{matrix} R—COOH \\ \text{or} \\ Ar—COOH \end{matrix} + NH_3$$

Examples:



Benzyl chloride Phenylacetonitrile Phenylacetic acid

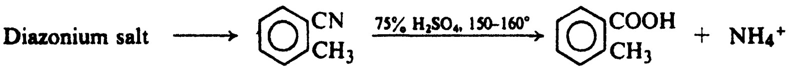
$$n\text{-}C_4H_9Br \xrightarrow{NaCN} n\text{-}C_4H_9CN \xrightarrow{\text{aq. alc. NaOH, reflux}} n\text{-}C_4H_9COO^- + NH_3$$

n-Butyl bromide *n*-Valeronitrile (Pentanenitrile)

$$\downarrow H^+$$

$$n\text{-}C_4H_9COOH + NH_4^+$$

n-Valeric acid (Pentanoic acid)



o-Tolunitrile *o*-Toluic acid

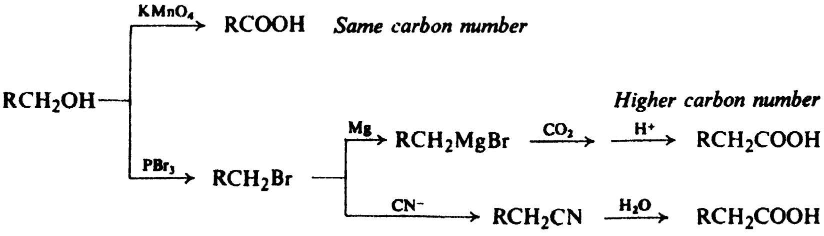
5. **Malonic ester synthesis.** Discussed in Sec. 26.2.

6. **Special methods for phenolic acids.** Discussed in Sec. 24.11.

All the methods listed are important; our choice is governed by the availability of starting materials.

Oxidation is the most direct and is generally used when possible, some lower aliphatic acids being made from the available alcohols, and substituted aromatic acids from substituted toluenes.

The **Grignard synthesis** and the **nitrile synthesis** have the special advantage of increasing the length of a carbon chain, and thus extending the range of available materials. In the aliphatic series both Grignard reagents and nitriles are prepared from halides, which in turn are usually prepared from alcohols. The syntheses thus amount to the preparation of acids from alcohols containing one less carbon atom.



Problem 18.4 What carboxylic acid can be prepared from *p*-bromotoluene: (a) by direct oxidation? (b) by free-radical chlorination followed by the nitrile synthesis?

Aromatic nitriles generally cannot be prepared from the unreactive aryl halides (Sec. 25.5). Instead they are made from diazonium salts by a reaction we shall discuss later (Sec. 23.13). Diazonium salts are prepared from aromatic amines, which in turn are prepared from nitro compounds. Thus the carboxyl group eventually occupies the position on the ring where a nitro group was originally introduced by direct nitration (Sec. 11.8).

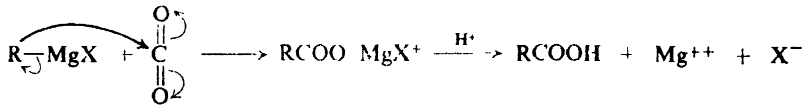
$$\text{ArH} \longrightarrow \underset{\text{Nitro compound}}{\text{ArNO}_2} \longrightarrow \underset{\text{Amine}}{\text{ArNH}_2} \longrightarrow \underset{\text{Diazonium ion}}{\text{ArN}_2^+} \longrightarrow \underset{\text{Nitrile}}{\text{ArC}\equiv\text{N}} \longrightarrow \underset{\text{Acid}}{\text{ArCOOH}}$$

For the preparation of quite complicated acids, the most versatile method of all is used, the *malonic ester synthesis* (Sec. 26.2).

18.7 Grignard synthesis

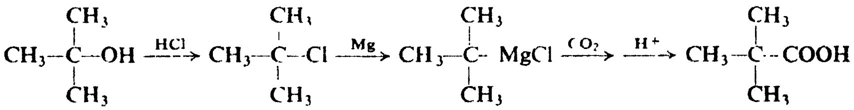
The Grignard synthesis of a carboxylic acid is carried out by bubbling gaseous CO_2 into the ether solution of the Grignard reagent, or by pouring the Grignard reagent on crushed Dry Ice (solid CO_2); in the latter method Dry Ice serves not only as reagent but also as cooling agent.

The Grignard reagent adds to the carbon–oxygen double bond just as in the reaction with aldehydes and ketones (Sec. 15.12). The product is the magnesium salt of the carboxylic acid, from which the free acid is liberated by treatment with mineral acid.

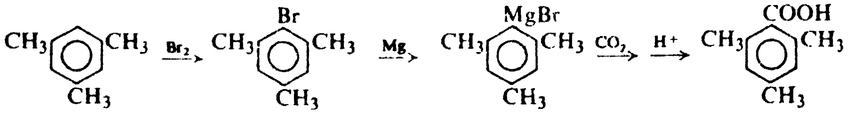


$$\text{R—MgX} + \text{O=C=O} \longrightarrow \text{RCOO}^- \text{MgX}^+ \xrightarrow{\text{H}^+} \text{RCOOH} + \text{Mg}^{++} + \text{X}^-$$

The Grignard reagent can be prepared from primary, secondary, tertiary, or aromatic halides; the method is limited only by the presence of other reactive groups in the molecule (Sec. 15.15). The following syntheses illustrate the application of this method:



tert-Butyl alcohol — *tert*-Butyl chloride — Trimethylacetic acid

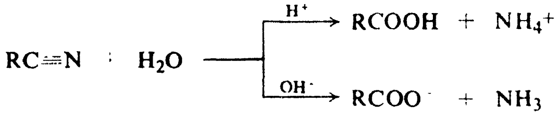


Mesitylene — Bromomesitylene — Mesitoic acid (2,4,6-Trimethylbenzoic acid)

18.8 Nitrile synthesis

Aliphatic nitriles are prepared by treatment of alkyl halides with sodium cyanide in a solvent that will dissolve both reactants; in dimethyl sulfoxide, reaction occurs rapidly and exothermically at room temperature. The resulting nitrile is then hydrolyzed to the acid by boiling aqueous alkali or acid.

$$RX + CN^- \longrightarrow RC{\equiv}N + X^-$$

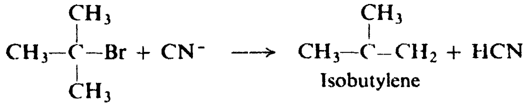


The reaction of an alkyl halide with cyanide ion involves nucleophilic substitution (Sec. 14.5). The fact that HCN is a very weak acid tells us that cyanide ion is a strong base; as we might expect, this strongly basic ion can abstract hydrogen ion and thus cause elimination as well as substitution. Indeed, with tertiary halides elimination is the principal reaction; even with secondary halides the yield of substitution product is poor. Here again we find a nucleophilic substitution reaction that is of synthetic importance *only when primary halides are used.*

$$CH_3CH_2CH_2CH_2Br + CN^- \longrightarrow CH_3CH_2CH_2CH_2CN$$

n-Butyl bromide Valeronitrile

1° halide: *substitution*



$$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-Br + CN^- \longrightarrow CH_3-\overset{CH_3}{C}{=}CH_2 + HCN$$

tert-Butyl bromide Isobutylene

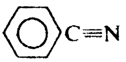
3° halide: *elimination*

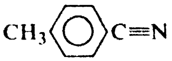
As already mentioned, aromatic nitriles are made, not from the unreactive aryl halides, but from diazonium salts (Sec. 23.13).

Although nitriles are sometimes named as *cyanides* or as *cyano* compounds, they generally take their names from the acids they yield upon hydrolysis. They are named by dropping *-ic acid* from the common name of the acid and adding **-nitrile**; usually for euphony an "o" is inserted between the root and the ending (e.g., *acetonitrile*). In the IUPAC system they are named by adding *-nitrile* to the name of the parent hydrocarbon (e.g., *ethanenitrile*). For example:

$CH_3C{\equiv}N$
Acetonitrile
(Ethanenitrile)

$CH_3(CH_2)_3C{\equiv}N$
n-Valeronitrile
(Pentanenitrile)


Benzonitrile


p-Tolunitrile

18.9 Reactions

The characteristic chemical behavior of carboxylic acids is, of course, determined by their functional group, **carboxyl**, —COOH. This group is made up of a carbonyl group ($C{=}O$) and a hydroxyl group (—OH). As we shall see, it is the —OH that actually undergoes nearly every reaction—loss of H^+, or replacement by another group—but *it does so in a way that is possible only because of the effect of the* C=O.

The rest of the molecule undergoes reactions characteristic of its structure; it may be aliphatic or aromatic, saturated or unsaturated, and may contain a variety of other functional groups.

REACTIONS OF CARBOXYLIC ACIDS

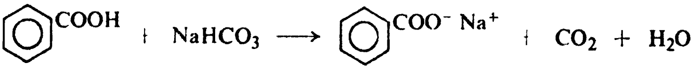
1. Acidity. Salt formation. Discussed in Secs. 18.4, 18.10–18.14.

$$\mathrm{RCOOH} \rightleftharpoons \mathrm{RCOO^-} + \mathrm{H^+}$$

Examples:

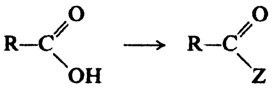
$$\underset{\text{Acetic acid}}{2\mathrm{CH_3COOH}} + \mathrm{Zn} \longrightarrow \underset{\text{Zinc acetate}}{(\mathrm{CH_3COO^-})_2\mathrm{Zn^{++}}} + \mathrm{H_2}$$

$$\underset{\text{Lauric acid}}{\mathrm{CH_3(CH_2)_{10}COOH}} + \mathrm{NaOH} \longrightarrow \underset{\text{Sodium laurate}}{\mathrm{CH_3(CH_2)_{10}COO^-Na^+}} + \mathrm{H_2O}$$



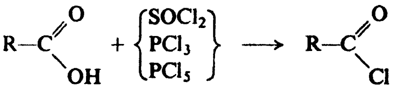
Benzoic acid Sodium benzoate

✓ **2. Conversion into functional derivatives**



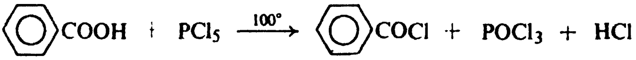
(Z = —Cl, —OR′, —NH$_2$)

(a) Conversion into acid chlorides. Discussed in Sec. 18.15.



Acid chloride

Examples:

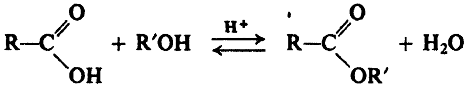


Benzoic acid Benzoyl chloride

$$\underset{\text{Stearic acid}}{n\text{-}\mathrm{C_{17}H_{35}COOH}} + \underset{\substack{\text{Thionyl}\\ \text{chloride}}}{\mathrm{SOCl_2}} \xrightarrow{\text{reflux}} \underset{\text{Stearoyl chloride}}{n\text{-}\mathrm{C_{17}H_{35}COCl}} + \mathrm{SO_2} + \mathrm{HCl}$$

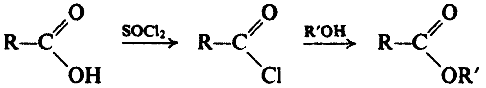
$$\underset{\text{Acetic acid}}{3\mathrm{CH_3COOH}} + \mathrm{PCl_3} \xrightarrow{50^\circ} \underset{\text{Acetyl chloride}}{3\mathrm{CH_3COCl}} + \mathrm{H_3PO_3}$$

(b) **Conversion into esters.** Discussed in Secs. 18.16 and 20.15.



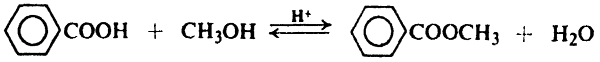
An ester

Reactivity of R'OH: 1°> 2° (> 3°)

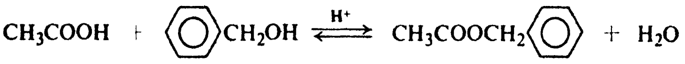


An acid chloride An ester

Examples:



Benzoic acid Methanol Methyl benzoate

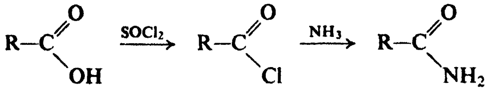


Acetic acid Benzyl alcohol Benzyl acetate

$$(CH_3)_3CCOOH \xrightarrow{SOCl_2} (CH_3)_3CCOCl \xrightarrow{C_2H_5OH} (CH_3)_3CCOOC_2H_5$$

Trimethylacetic acid Ethyl trimethylacetate

(c) **Conversion into amides.** Discussed in Sec. 18.17.



An acid chloride An amide

Example:

$$C_6H_5CH_2COOH \xrightarrow{SOCl_2} C_6H_5CH_2COCl \xrightarrow{NH_3} C_6H_5CH_2CONH_2$$

Phenylacetic acid Phenylacetyl chloride Phenylacetamide

3. **Reduction.** Discussed in Sec. 18.18.

$$RCOOH \xrightarrow{LiAlH_4} RCH_2OH$$

1° alcohol

Also reduced via esters (Sec. 20.22)

Examples:

$$4(CH_3)_3CCOOH + 3LiAlH_4 \xrightarrow{ether} [(CH_3)_3CCH_2O]_4AlLi \xrightarrow{H^+} (CH_3)_3CCH_2OH$$

$$+ 2LiAlO_2 + 4H_2$$

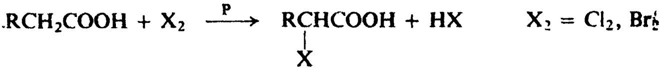
Trimethylacetic acid

Neopentyl alcohol (2,2-Dimethyl-1-propanol)

m-Toluic acid *m*-Methylbenzyl alcohol

4. Substitution in alkyl or aryl group

(a) Alpha-halogenation of aliphatic acids. Hell-Volhard-Zelinsky reaction. Discussed in Sec. 18.19.



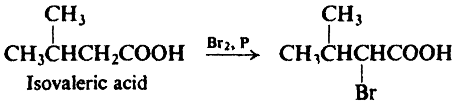
$$RCH_2COOH + X_2 \xrightarrow{P} \underset{\underset{X}{|}}{RCHCOOH} + HX \qquad X_2 = Cl_2, Br_2$$

An α-haloacid

Examples:

$$CH_3COOH \xrightarrow{Cl_2,\,P} ClCH_2COOH \xrightarrow{Cl_2,\,P} Cl_2CHCOOH \xrightarrow{Cl_2,\,P} Cl_3CCOOH$$

Acetic acid — Chloroacetic acid — Dichloroacetic acid — Trichloroacetic acid



$$CH_3\overset{\overset{CH_3}{|}}{C}HCH_2COOH \xrightarrow{Br_2,\,P} CH_3\overset{\overset{CH_3}{|}}{C}H\underset{\underset{Br}{|}}{C}HCOOH$$

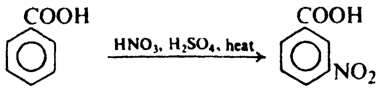
Isovaleric acid

α-Bromoisovaleric acid

(b) Ring substitution in aromatic acids. Discussed in Secs. 11.5 and 11.17.

—COOH: deactivates, and directs *meta* in electrophilic substitution.

Example:



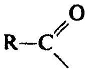
Benzoic acid

m-Nitrobenzoic acid

The most characteristic property of the carboxylic acids is the one that gives them their name: **acidity**. Their tendency to give up a hydrogen ion is such that in aqueous solution a measurable equilibrium exists between acid and ions; they are thus much more acidic than any other class of organic compounds we have studied so far.

$$RCOOH + H_2O \rightleftarrows RCOO^- + H_3O^+$$

The OH of an acid can be replaced by a number of groups—Cl, OR′, NH_2—to yield compounds known as *acid chlorides*, *esters*, and *amides*. These compounds are called **functional derivatives** of acids; they all contain the **acyl group**:

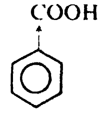


The functional derivatives are all readily reconverted into the acid by simple hydrolysis, and are often converted one into another.

One of the few reducing agents capable of reducing an acid directly to an alcohol is *lithium aluminum hydride*, $LiAlH_4$.

The hydrocarbon portion of an aliphatic acid can undergo the free-radical halogenation characteristic of alkanes, but because of the random nature of the substitution it is seldom used. The presence of a small amount of phosphorus, however, causes halogenation (by an ionic mechanism) to take place *exclusively at the alpha position*. This reaction is known as the **Hell-Volhard-Zelinsky reaction**, and it is of great value in synthesis.

An aromatic ring bearing a carboxyl group undergoes the aromatic electrophilic substitution reactions expected of a ring carrying a deactivating, *meta*-directing group. Deactivation is so strong that the Friedel-Crafts reaction does not take place. We have already accounted for this effect of the —COOH group on the basis of its strong electron-withdrawing tendencies (Sec. 11.18).



—COOH withdraws electrons
deactivates, directs meta in
electrophilic substitution

Decarboxylation—elimination of the —COOH group as CO_2—is of limited importance for aromatic acids, and highly important for certain substituted aliphatic acids: malonic acids (Sec. 26.2) and β-keto acids (Sec. 26.3). It is worthless for most simple aliphatic acids, yielding a complicated mixture of hydrocarbons.

18.10 Ionization of carboxylic acids. Acidity constant

In aqueous solution a carboxylic acid exists in equilibrium with the carboxylate anion and the hydrogen ion (actually, of course, the hydronium ion, H_3O^+).

$$RCOOH + H_2O \rightleftharpoons RCOO^- + H_3O^+$$

As for any equilibrium, the concentrations of the components are related by the expression

$$K_a = \frac{[RCOO^-][H_3O^+]}{[RCOOH]}$$

(Since the concentration of water, the solvent, remains essentially constant, this term is usually omitted.) The equilibrium constant is called here the **acidity constant**, K_a (*a for acidity*).

Every carboxylic acid has its characteristic K_a, which indicates how strong an acid it is. Since the acidity constant is the ratio of ionized to unionized material, the larger the K_a the greater the extent of the ionization (under a given set of conditions) and the stronger the acid. We use the K_a's, then, to compare in an exact way the strengths of different acids.

We see in Table 18.2 (p. 600) that unsubstituted aliphatic and aromatic acids have K_a's of about 10^{-4} to 10^{-5} (0.0001 to 0.00001). This means that they are weakly acidic, with only a slight tendency to release protons.

By the same token, carboxylate anions are moderately basic, with an appreciable tendency to combine with protons. They react with water to increase the concentration of hydroxide ions, a reaction often referred to as *hydrolysis*. As

$$\mathrm{RCOO^- + H_2O \rightleftharpoons RCOOH + OH^-}$$

a result aqueous solutions of carboxylate salts are slightly alkaline. (The basicity of an aqueous solution of a carboxylate salt is due chiefly, of course, to the carboxylate anions, not to the comparatively few hydroxide ions they happen to generate.)

We may now expand the series of relative acidities and basicities:

Relative acidities: $\mathrm{RCOOH > HOH > ROH > HC{\equiv}CH > NH_3 > RH}$

Relative basicities: $\mathrm{RCOO^- < HO^- < RO^- < HC{\equiv}C^- < NH_2^- < R^-}$

Certain substituted acids are much stronger or weaker than a typical acid like $\mathrm{CH_3COOH}$. We shall see that the acid-strengthening or acid-weakening effect of a substituent can be accounted for in a reasonable way; however, we must first learn a little more about equilibrium in general.

18.11 Equilibrium

So far we have dealt very little with the problem of equilibrium. Under the conditions employed, most of our reactions have been essentially irreversible; that is, they have been one-way reactions. With a few exceptions—1,4-addition, for example (Sec. 8.22)—the products obtained, and their relative yields, have been determined by how fast reactions go and not by how nearly to completion they proceed before equilibrium is reached. Consequently, we have been concerned with the relationship between structure and rate; now we shall turn to the relationship between structure and equilibrium.

Let us consider the reversible reaction between A and B to form C and D. The

$$\mathrm{A + B \rightleftharpoons C + D}$$

yield of C and D does not depend upon how fast A and B react, but rather upon how completely they have reacted when equilibrium is reached.

The concentrations of the various components are related by the familiar expression,

$$K_{eq} = \frac{[\mathrm{C}][\mathrm{D}]}{[\mathrm{A}][\mathrm{B}]}$$

in which K_{eq} is the equilibrium constant. The more nearly a reaction has proceeded to completion when it reaches equilibrium, the larger is [C][D] compared with [A][B], and hence the larger the K_{eq}. The value of K_{eq} is therefore a measure of the tendency of the reaction to go to completion.

The value of K_{eq} is determined by the change in *free energy*, G, on proceeding from reactants to products (Fig. 18.1). The exact relationship is given by the expression,

$$\Delta G^\circ = -2.303RT \log K_{eq}$$

where ΔG° is the *standard free energy change*.

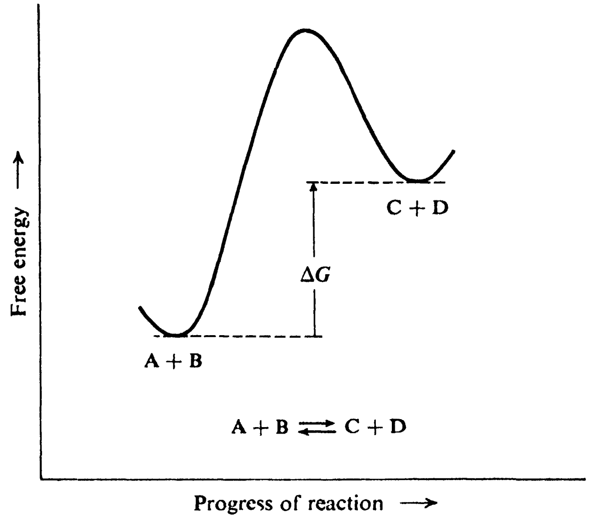


Figure 18.1. Free energy curve for a reversible reaction.

Free energy change is related to our familiar quantity ΔH (precisely $\Delta H°$, which is only slightly different) by the expression,

$$\Delta G° = \Delta H - T\Delta S°$$

where $\Delta S°$ is the *standard entropy change*. Entropy corresponds roughly, to the *randomness* of the system. To the extent that $T\Delta S°$ contributes to $\Delta G°$, equilibrium tends to shift toward the side in which fewer restrictions are placed on the positions of atoms and molecules. ("Die Energie der Welt ist constant. Die Entropie der Welt strebt einem Maximum zu." *Clausius, 1865.*)

Under the same experimental conditions two reversible reactions have K_{eq}'s of different sizes because of a difference in $\Delta G°$. In attempting to understand the effect of structure on position of equilibrium, we shall estimate differences in relative stabilities of reactants and products. Now, what we estimate in this way are not differences in free energy change but differences in potential energy change. It turns out that very often these differences are *proportional to* differences in $\Delta G°$. So long as we compare closely related compounds, the predictions we make by this approach are generally good ones.

These predictions are good ones despite the fact that the free energy changes on which they depend are made up to varying degrees of ΔH and $\Delta S°$. For example, *p*-nitrobenzoic acid is a stronger acid than benzoic acid. We attribute this (Sec. 18.14) to stabilization of the *p*-nitrobenzoate anion (relative to the benzoate anion) through dispersal of charge by the electron-withdrawing nitro group. Yet, in this case, the greater acidity is due about as much to a more favorable $\Delta S°$ as to a more favorable ΔH. How can our simple "stabilization by dispersal of charge" account for an effect that involves the randomness of a system?

Stabilization *is* involved, but it appears partly in the $\Delta S°$ for this reason.

Ionization of an acid is possible only because of solvation of the ions produced: the many ion–dipole bonds provide the energy needed for dissociation. But solvation requires that molecules of solvent leave their relatively unordered arrangement to cluster in some ordered fashion about the ions. This is good for the ΔH but bad for the $\Delta S°$. Now, because of its greater intrinsic stability, the *p*-nitrobenzoate anion does not *need* as many solvent molecules to help stabilize it as the benzoate anion does. The $\Delta S°$ is thus more favorable. We can visualize the *p*-nitrobenzoate ion accepting only as many solvent molecules as it has to, and stopping when the gain in stability (decrease in enthalpy) is no longer worth the cost in entropy.

(In the same way, it has been found that very often a more polar solvent speeds up a reaction—as, for example, an S_N1 reaction of alkyl halides (Sec. 14.16) —not so much by lowering E_{act} as by bringing about a more favorable entropy of activation. A more polar solvent is already rather ordered, and its clustering about the ionizing molecule amounts to very little loss of randomness—indeed, it may even amount to an *increase* in randomness.)

By the organic chemist's approach we can make *very* good predictions indeed. We can not only account for, say, the relative acidities of a set of acids, but we can correlate these acidities *quantitatively* with the relative acidities of another set of acids, or even with the relative rates of a set of reactions. These relationships are summarized in the Hammett equation (named for Louis P. Hammett of Columbia University),

$$\log\frac{K}{K_0} = \rho\sigma \qquad \text{or} \qquad \log\frac{k}{k_0} = \rho\sigma$$

where K or k refers to the reaction of a *m*- or *p*-substituted phenyl compound (say, ionization of a substituted benzoic acid) and K_0 or k_0 refers to the same reaction of the unsubstituted compound (say, ionization of benzoic acid).

The *substituent constant* (*σ, sigma*) is a number (+ or −) indicating the relative electron-withdrawing or electron-releasing effect of a particular substituent. The *reaction constant* (*ρ, rho*) is a number (+ or −) indicating the relative *need* of a particular reaction for electron withdrawal or electron release.

A vast amount of research has shown that the Hammett relationship holds for *hundreds of sets of reactions.* (Ionization of 40-odd *p*-substituted benzoic acids, for example, is *one* set.) By use of just two tables—one of σ constants and one of ρ constants—we can calculate the relative K_{eq}'s or relative rates for thousands of individual reactions. For example, from the σ value for *m*-NO_2 (+0.710) and the ρ value for ionization of benzoic acids in water at 25° (+1.000), we can calculate that K_a for *m*-nitrobenzoic acid is 5.13 times as big as the K_a for benzoic acid. Using the same σ value, and the ρ value for acid-catalyzed hydrolysis of benzamides in 60% ethanol at 80° (−0.298), we can calculate that *m*-nitrobenzamide will be hydrolyzed only 0.615 as fast as benzamide.

The Hammett relationship is called a *linear free energy relationship* since it is based on—and reveals—the fact that a linear relationship exists between free energy change and the effect exerted by a substituent. Other linear free energy relationships are known, which take into account steric as well as electronic effects, and which apply to *ortho* substituted phenyl compounds as well as *meta* and *para*, and to aliphatic as well as aromatic compounds. Together they make up what is perhaps the greatest accomplishment of physical-organic chemistry.

In dealing with rates, we compare the stability of the reactants with the stability of the transition state. In dealing with equilibria, we shall compare the stability of the reactants with the stability of the products. For closely related reactions, we are justified in assuming that the more stable the products relative to the reactants, the further reaction proceeds toward completion.

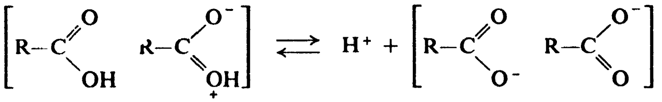
18.12 Acidity of carboxylic acids

Let us see how the acidity of carboxylic acids is related to structure. In doing this we shall assume that acidity is determined chiefly by the difference in stability between the acid and its anion.

First, and most important, there is the fact that carboxylic acids are acids at all. How can we account for the fact that the —OH of a carboxylic acid tends to release a hydrogen ion so much more readily than the —OH of, say, an alcohol? Let us examine the structures of the reactants and products in these two cases.

We see that the alcohol and alkoxide ion are each represented satisfactorily by a single structure. However, we can draw two reasonable structures (I and II) for the carboxylic acid and two reasonable structures (III and IV) for the carboxylate anion. Both acid and anion are resonance hybrids. But is resonance equally important in the two cases? By the principles of Sec. 6.27 we know that resonance is much more important between the exactly equivalent structures III and IV than between the non-equivalent structures I and II. As a result, although both acid and anion are stabilized by resonance, stabilization is far greater for the anion than for the acid (see Fig. 18.2). Equilibrium is shifted in the direction of increased ionization, and K_a is increased.

$$\mathrm{R{-}O{-}H} \rightleftarrows \mathrm{H^+ + R{-}O^-}$$



I II III IV

Non-equivalent: *resonance less important*

Equivalent: *resonance more important*

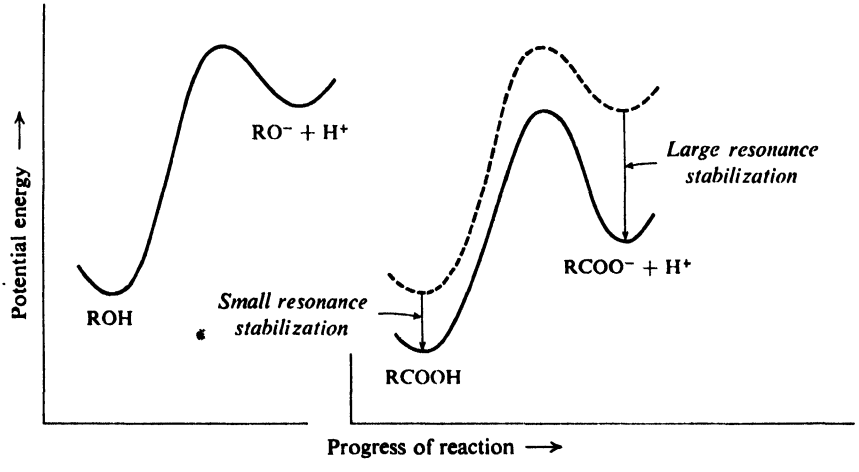


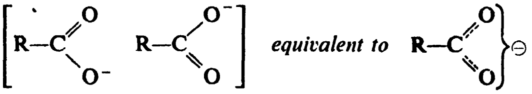
Figure 18.2. Molecular structure and position of equilibrium. Carboxylic acid yields resonance-stabilized anion; is stronger acid than alcohol. (Plots aligned with each other for easy comparison.)

Strictly speaking, resonance is less important for the acid because the contributing structures are of *different stability*, whereas the equivalent structures for the ion must necessarily be of *equal stability*. In structure II two atoms of similar electronegativity carry opposite charges; since energy must be supplied to separate opposite charges, II should contain more energy and hence be less stable than I. Consideration of *separation of charge* is one of the rules of thumb (Sec. 6.27) that can be used to estimate relative stability and hence relative importance of a contributing structure.

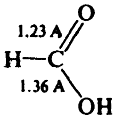
The acidity of a carboxylic acid is thus due to the powerful resonance stabilization of its anion. *This stabilization and the resulting acidity are possible only because of the presence of the carbonyl group.*

18.13 Structure of carboxylate ions

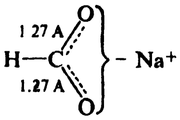
According to the resonance theory, then, a carboxylate ion is a hybrid of two structures which, being of equal stability, contribute equally. Carbon is joined to each oxygen by a "one-and-one-half" bond. The negative charge is evenly distributed over both oxygen atoms.



That the anion is indeed a resonance hybrid is supported by the evidence of bond length. Formic acid, for example, contains a carbon–oxygen double bond and a carbon–oxygen single bond; we would expect these bonds to have different lengths. Sodium formate, on the other hand, if it is a resonance hybrid, ought to contain two equivalent carbon–oxygen bonds; we would expect these to have the same length, intermediate between double and single bonds. X-ray and electron diffraction show that these expectations are correct. Formic acid contains one carbon–oxygen bond of 1.36 A (single bond) and another of 1.23 A (double bond); sodium formate contains two equal carbon–oxygen bonds, each 1.27 A long.



Formic acid



Sodium formate

Problem 18.5. How do you account for the fact that the three carbon–oxygen bonds in $CaCO_3$ have the same length, and that this length (1.31 A) is greater than that found in sodium formate?

What does this resonance mean in terms of orbitals? Carboxyl carbon is joined to the three other atoms by σ bonds (Fig. 18.3); since these bonds utilize sp^2 orbitals (Sec. 5.2), they lie in a plane and are 120° apart. The remaining *p* orbital of the carbon overlaps equally well *p* orbitals from *both* of the oxygens, to form hybrid bonds (compare benzene, Sec. 10.8). In this way the electrons are bound not just to one or two nuclei but to *three* nuclei (one carbon and two oxygens); they are therefore held more tightly, the bonds are stronger, and the

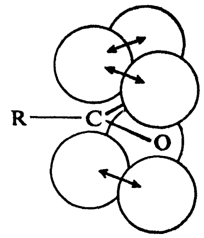
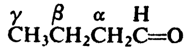


Figure 18.3. Carboxylate ion. Overlap of *p* orbitals in both directions: delocalization of π electrons, and dispersal of charge.

anion is more stable. This participation of electrons in more than one bond, this smearing-out or delocalization of the electron cloud, is what is meant by representing the anion as a resonance hybrid of two structures.

Problem 18.6 How do you account for the fact that the α-hydrogens of an aldehyde (say, *n*-butyraldehyde) are much more acidic than any other hydrogens in the molecule? (Check your answer in Sec. 21.1.)



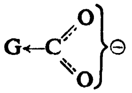
$$\overset{\gamma}{C}H_3\overset{\beta}{C}H_2\overset{\alpha}{C}H_2\overset{H}{C}{=}O$$

n-Butyraldehyde

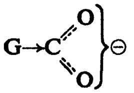
18.14 Effect of substituents on acidity

Next, let us see how changes in the structure of the group bearing the —COOH affect the acidity. Any factor that stabilizes the anion more than it stabilizes the acid should increase the acidity; any factor that makes the anion less stable should decrease acidity. From what we have learned about carbonium ions, we know what we might reasonably expect. Electron-withdrawing substituents should disperse the negative charge, stabilize the anion, and thus increase acidity. Electron-releasing substituents should intensify the negative charge, destabilize the anion, and thus decrease acidity.

Acid Strength



G withdraws electrons: *stabilizes anion, strengthens acid*



G releases electrons: *destabilizes anion, weakens acid*

The K_a's listed in Table 18.2 are in agreement with this prediction.

Looking first at the aliphatic acids, we see that the electron-withdrawing halogens strengthen acids: chloroacetic acid is 100 times as strong as acetic acid, dichloroacetic acid is still stronger, and trichloroacetic acid is more than 10,000 times as strong as the unsubstituted acid. The other halogens exert similar effects.

Table 18.2 ACIDITY CONSTANTS OF CARBOXYLIC ACIDS

	K_a		K_a
$HCOOH$	17.7×10^{-5}	$CH_3CHClCH_2COOH$	8.9×10^{-5}
CH_3COOH	1.75 ,,	$ClCH_2CH_2CH_2COOH$	2.96 ,,
$ClCH_2COOH$	136 ,,	FCH_2COOH	260 ,,
$Cl_2CHCOOH$	5530 ,,	$BrCH_2COOH$	125 ,,
Cl_3CCOOH	23200 ,,	ICH_2COOH	67 ,,
$CH_3CH_2CH_2COOH$	1.52 ,,	$C_6H_5CH_2COOH$	4.9 ,,
$CH_3CH_2CHClCOOH$	139 ,,	p-$O_2NC_6H_4CH_2COOH$	14.1 ,,

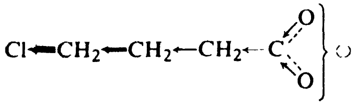
ACIDITY CONSTANTS OF SUBSTITUTED BENZOIC ACIDS

K_a of benzoic acid = 6.3×10^{-5}

	K_a		K_a		K_a
p-NO_2	36×10^{-5}	m-NO_2	32×10^{-5}	o-NO_2	670×10^{-5}
p-Cl	10.3 ,,	m-Cl	15.1 ,,	o-Cl	120 ,,
p-CH_3	4.2 ,,	m-CH_3	5.4 ,,	o-CH_3	12.4 ,,
p-OCH_3	3.3 ,,	m-OCH_3	8.2 ,,	o-OCH_3	8.2 ,,
p-OH	2.6 ,,	m-OH	8.3 ,,	o-OH	105 ,,
p-NH_2	1.4 ,,	m-NH_2	1.9 ,,	o-NH_2	1.6 ,,

Problem 18.7 (a) What do the K_a's of the monohaloacetic acids tell us about the relative strengths of the inductive effects of the different halogens? (b) On the basis of Table 18.2, what kind of inductive effect does the phenyl group, $—C_6H_5$, appear to have?

α-Chlorobutyric acid is about as strong as chloroacetic acid. As the chlorine is moved away from the —COOH, however, its effect rapidly dwindles: β-chlorobutyric acid is only six times as strong as butyric acid, and γ-chlorobutyric acid is only twice as strong. It is typical of inductive effects that they decrease rapidly with distance, and are seldom important when acting through more than four atoms.



Inductive effect: *decreases with distance*

The aromatic acids are similarly affected by substituents: $—CH_3$, —OH, and $—NH_2$ make benzoic acid weaker, and —Cl and $—NO_2$ make benzoic acid stronger. We recognize the acid-weakening groups as the ones that activate the ring toward electrophilic substitution (and deactivate toward nucleophilic substitution). The acid-strengthening groups are the ones that deactivate toward electrophilic substitution (and activate toward nucleophilic substitution). Furthermore, the groups that have the largest effects on reactivity—whether activating or deactivating—have the largest effects on acidity.

The —OH and $—OCH_3$ groups display both kinds of effect we have attributed to them (Sec. 11.20): from the *meta* position, an electron-withdrawing acid-strengthening inductive effect; and from the *para* position, an electron-releasing acid-weakening resonance effect (which at this position outweighs the inductive effect). Compare the two effects exerted by halogen (Sec. 11.21).

ortho-Substituted aromatic acids do not fit into the pattern set by their *meta* and *para* isomers, and by aliphatic acids. Nearly all *ortho* substituents exert an effect of the same kind—acid-strengthening—whether they are electron-withdrawing or electron-releasing, and the effect is unusually large. (Compare, for example, the effects of *o*-NO_2 and *o*-CH_3, of *o*-NO_2 and *m*- or *p*-NO_2.) This *ortho* effect undoubtedly has to do with the *nearness* of the groups involved, but is more than just steric hindrance arising from their bulk.

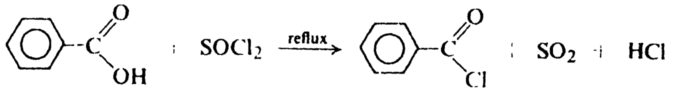
Thus we see that the same concepts—inductive effect and resonance—that we found so useful in dealing with rates of reaction are also useful in dealing with equilibria. By using these concepts to estimate the stabilities of anions, we are able to predict the relative strengths of acids; in this way we can account not only for the effect of substituents on the acid strength of carboxylic acids but also for the very fact that the compounds are acids.

Problem 18.8 There is evidence that certain groups like *p*-methoxy weaken the acidity of benzoic acids not so much by destabilizing the anion as by stabilizing the acid. Draw structures to show the kind of resonance that might be involved. Why would you expect such resonance to be more important for the acid than for the anion?

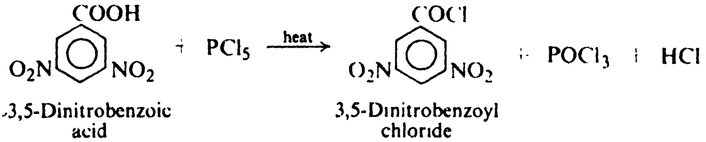
18.15 Conversion into acid chlorides

A carboxylic acid is perhaps more often converted into the acid chloride than into any other of its functional derivatives. From the highly reactive acid chloride there can then be obtained many other kinds of compounds, including esters and amides (Sec. 20.8).

An acid chloride is prepared by substitution of —Cl for the —OH of a carboxylic acid. Three reagents are commonly used for this purpose: *thionyl chloride*, $SOCl_2$; *phosphorus trichloride*, PCl_3; and *phosphorus pentachloride*, PCl_5. (Of what inorganic acids might we consider these reagents to be the acid chlorides?) For example:



Benzoic acid Benzoyl chloride



3,5-Dinitrobenzoic acid 3,5-Dinitrobenzoyl chloride

Thionyl chloride is particularly convenient, since the products formed besides the acid chloride are gases and thus easily separated from the acid chloride; any excess of the low-boiling thionyl chloride (79) is easily removed by distillation.

18.16 Conversion into esters

Acids are frequently converted into their esters via the acid chlorides:

$$\underset{\text{Acid}}{\text{RCOOH}} \xrightarrow{\text{SOCl}_2\text{, etc.}} \underset{\text{Acid chloride}}{\text{RCOCl}} \xrightarrow{\text{R'OH}} \underset{\text{Ester}}{\text{RCOOR}'}$$

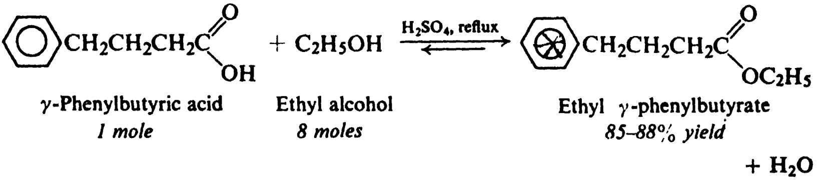
A carboxylic acid is converted directly into an ester when heated with an alcohol in the presence of a little mineral acid, usually concentrated sulfuric acid or dry hydrogen chloride. This reaction is reversible, and generally reaches equilibrium when there are appreciable quantities of both reactants and products present.

$$\underset{\text{Acid}}{\text{RCOOH}} + \underset{\text{Alcohol}}{\text{R'OH}} \overset{\text{H}^+}{\rightleftharpoons} \underset{\text{Ester}}{\text{RCOOR}'} + \text{H}_2\text{O}$$

For example, when we allow one mole of acetic acid and one mole of ethyl alcohol to react in the presence of a little sulfuric acid until equilibrium is reached (after several hours), we obtain a mixture of about two-thirds mole each of ester and water. and one-third mole each of acid and alcohol. We obtain this same equilibrium mixture, of course, if we start with one mole of ester and one mole of water, again in the presence of sulfuric acid. *The same catalyst, hydrogen ion, that catalyzes the forward reaction, esterification, necessarily catalyzes the reverse reaction, hydrolysis.*

This reversibility is a disadvantage in the preparation of an ester directly from an acid; the preference for the acid chloride route is due to the fact that both steps—preparation of acid chloride from acid, and preparation of ester from acid chloride—are essentially irreversible and go to completion.

Direct esterification, however, has the advantage of being a single-step synthesis; it can often be made useful by application of our knowledge of equilibria. If either the acid or the alcohol is cheap and readily available, it can be used in large excess to shift the equilibrium toward the products and thus to increase the yield of ester. For example, it is worthwhile to use eight moles of cheap ethyl alcohol to convert one mole of valuable γ-phenylbutyric acid more completely into the ester:



Sometimes the equilibrium is shifted by removing one of the products. An elegant way of doing this is illustrated by the preparation of ethyl adipate. The dicarboxylic acid adipic acid, an excess of ethyl alcohol, and toluene are heated with a little sulfuric acid under a distillation column. The lowest boiling component (b.p. 75°) of the reaction mixture is an azeotrope of water, ethyl alcohol, and toluene (compare Sec. 15.6); consequently, as fast as water is formed it is removed as the azeotrope by distillation. In this way a 95–97% yield of ester is obtained:

$$\underset{\substack{\text{Adipic acid}\\ \textit{Non-volatile}}}{HOOC(CH_2)_4COOH} + \underset{\substack{\text{Ethyl alcohol}\\ \textit{B.p. 78°}}}{2C_2H_5OH} \overset{\text{toluene (b.p. 111°),}}{\underset{}{\overset{H_2SO_4}{\rightleftharpoons}}} \underset{\substack{\text{Ethyl adipate}\\ \textit{B.p. 245°}}}{C_2H_5OOC(CH_2)_4COOC_2H_5} + \underset{\substack{\textit{Removed as}\\ \textit{azeotrope, b.p. 75°}}}{2H_2O}$$

The equilibrium is particularly unfavorable when phenols (ArOH) are used instead of alcohols; yet, if water is removed during the reaction, phenolic esters (RCOOAr) are obtained in high yield.

The presence of bulky groups near the site of reaction, whether in the alcohol or in the acid, slows down esterification (as well as its reverse, hydrolysis). This

Reactivity in esterification

$CH_3OH > 1° > 2° (> 3°)$

$HCOOH > CH_3COOH > RCH_2COOH > R_2CHCOOH > R_3CCOOH$

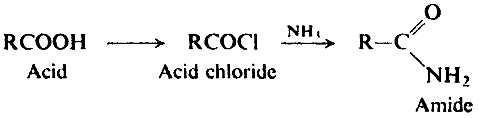
steric hindrance can be so marked that special methods are required to prepare esters of tertiary alcohols or esters of acids like 2,4,6-trimethylbenzoic acid (mesitoic acid).

The mechanism of esterification is necessarily the exact reverse of the mechanism of hydrolysis of esters. We shall discuss both mechanisms when we take up the chemistry of esters (Sec. 20.18) after we have learned a little more about the carbonyl group.

Problem 18.9 (a) In the formation of an acid chloride, which bond of a carboxylic acid is broken, C—OH or CO—H? (b) When labeled methanol, $CH_3{}^{18}OH$, was allowed to react with ordinary benzoic acid, the methyl benzoate produced was found to be enriched in ^{18}O, whereas the water formed contained only ordinary oxygen. In this esterification, which bond of the carboxylic acid is broken, C—OH or CO—H? Which bond of the alcohol?

18.17 Conversion into amides

Amides are compounds in which the —OH of the carboxylic acid has been



replaced by $—NH_2$. These are generally prepared by reaction of ammonia with acid chlorides.

18.18 Reduction of acids to alcohols

Conversion of alcohols into acids (Sec. 18.6) is important because, in general, alcohols are more available than acids. This is not always true, however; long straight-chain acids from fats are more available than are the corresponding alcohols, and here the reverse process becomes important: reduction of acids to alcohols.

Lithium aluminum hydride, $LiAlH_4$, is one of the few reagents that can reduce an acid to an alcohol; the initial product is an alkoxide from which the alcohol is liberated by hydrolysis:

$$4RCOOH + 3LiAlH_4 \longrightarrow 4H_2 + 2LiAlO_2 + (RCH_2O)_4AlLi \xrightarrow{H_2O} \underset{1^\circ \text{ alcohol}}{4RCH_2OH}$$

Because of the excellent yields it gives, $LiAlH_4$ is widely used in the laboratory for the reduction of not only acids but many other classes of compounds. Since it is somewhat expensive, it can be used in industry only for the reduction of small amounts of valuable raw materials, as in the synthesis of certain drugs and hormones.

As an alternative to direct reduction, acids are often converted into alcohols by a two-step process: esterification, and reduction of the ester. Esters can be reduced in a number of ways (Sec. 20.22) that are adaptable to both laboratory and industry.

We have seen (Sec. 18.5) that in the carboxylic acids obtained from fats we have available long straight-chain units for use in organic synthesis. Reduction of these acids to alcohols (either directly or as esters) is a fundamental step in the utilization of these raw materials, since from the alcohols, as we know, a host of other compounds can be prepared (Sec. 16.10). Although only acids of even carbon number are available, it is possible, of course, to increase the chain length and thus prepare compounds of odd carbon number. (For an alternative source of alcohols both of even and odd carbon number, see Sec. 32.6.)

Problem 18.10 Outline the synthesis from lauric acid (n-$C_{11}H_{23}COOH$, dodecanoic acid) of the following compounds: (a) 1-bromododecane; (b) tridecanoic acid (C_{13} acid); (c) 1-tetradecanol; (d) 1-dodecene; (e) dodecane; (f) 1-dodecyne; (g) methyl n-decyl ketone; (h) 2-dodecanol; (i) undecanoic acid; (j) 2-tetradecanol; (k) 2-methyl-2-tetradecanol.

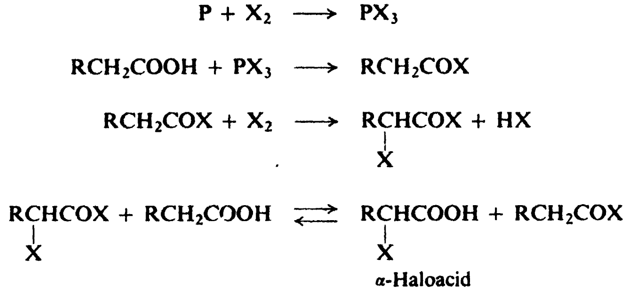
18.19 Halogenation of aliphatic acids. Substituted acids

In the presence of a small amount of phosphorus, aliphatic carboxylic acids react smoothly with chlorine or bromine to yield a compound in which α-hydrogen has been replaced by halogen. This is the **Hell-Volhard-Zelinsky reaction.** Because of its specificity—*only alpha halogenation*—and the readiness with which it takes place, it is of considerable importance in synthesis.

$$CH_3COOH \xrightarrow{Cl_2, P} ClCH_2COOH \xrightarrow{Cl_2, P} Cl_2CHCOOH \xrightarrow{Cl_2, P} Cl_3CCOOH$$

$$\begin{tikzcd} CH_3CH_2COOH \arrow[r, "Br_2, P"] & CH_3CHBrCOOH \arrow[r, "Br_2, P"] & CH_3CBr_2COOH \arrow[d, "Br_2, P"] \\ & & \text{no further substitution} \end{tikzcd}$$

The function of the phosphorus is ultimately to convert a little of the acid into acid halide. In this form (for reasons we cannot go into here) each molecule of acid sooner or later undergoes α-halogenation.



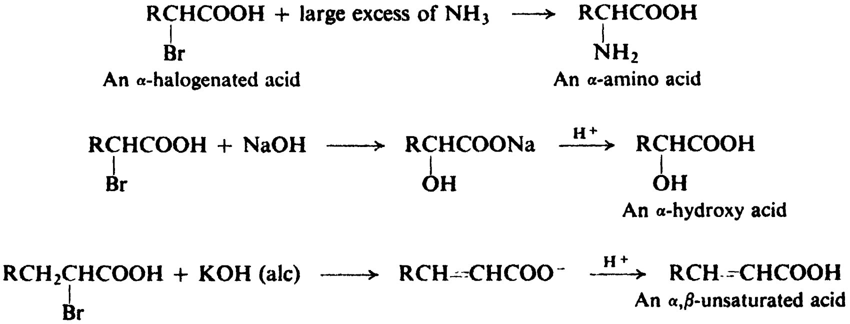
$$P + X_2 \longrightarrow PX_3$$

$$RCH_2COOH + PX_3 \longrightarrow RCH_2COX$$

$$RCH_2COX + X_2 \longrightarrow R\underset{\substack{|\\X}}{C}HCOX + HX$$

$$R\underset{\substack{|\\X}}{C}HCOX + RCH_2COOH \rightleftharpoons \underset{\alpha\text{-Haloacid}}{R\underset{\substack{|\\X}}{C}HCOOH} + RCH_2COX$$

The halogen of these halogenated acids undergoes *nucleophilic displacement* and *elimination* much as it does in the simpler alkyl halides (Secs. 14.5 and 5.12). Halogenation is therefore the first step in the conversion of a carboxylic acid into many important substituted carboxylic acids:



$$\underset{\text{An }\alpha\text{-halogenated acid}}{R\underset{\substack{|\\Br}}{C}HCOOH} + \text{large excess of } NH_3 \longrightarrow \underset{\text{An }\alpha\text{-amino acid}}{R\underset{\substack{|\\NH_2}}{C}HCOOH}$$

$$R\underset{\substack{|\\Br}}{C}HCOOH + NaOH \longrightarrow R\underset{\substack{|\\OH}}{C}HCOONa \xrightarrow{H^+} \underset{\text{An }\alpha\text{-hydroxy acid}}{R\underset{\substack{|\\OH}}{C}HCOOH}$$

$$RCH_2\underset{\substack{|\\Br}}{C}HCOOH + KOH\text{ (alc)} \longrightarrow RCH{=}CHCOO^- \xrightarrow{H^+} \underset{\text{An }\alpha,\beta\text{-unsaturated acid}}{RCH{=}CHCOOH}$$

These new substituents can, in turn, undergo *their* characteristic reactions.

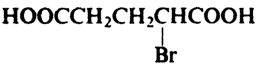
Problem 18.11 Predict the product of each of the following reactions:

(a) $CH_2{=}CHCOOH + H_2/Ni$
(b) *trans*-$CH_3CH{=}CHCOOH + Br_2/CCl_4$
(c) $C_6H_5CH(OH)CH_2COOH + H^+$, heat $\longrightarrow C_9H_8O_2$
(d) *o*-$HOOCC_6H_4CH_2OH + H^+$, heat $\longrightarrow C_8H_6O_2$

18.20 Dicarboxylic acids

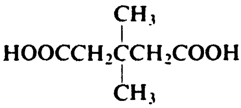
If the substituent is a second carboxyl group, we have a *dicarboxylic acid.* For example:

$HOOCCH_2COOH$	$HOOCCH_2CH_2COOH$	$HOOCCH_2CH_2CH_2CH_2COOH$
Malonic acid	Succinic acid	Adipic acid
Propanedioic acid	Butanedioic acid	Hexanedioic acid



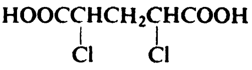
$HOOCCH_2CH_2CH(Br)COOH$

α-Bromoglutaric acid
2-Bromopentanedioic acid



$HOOCCH_2C(CH_3)_2CH_2COOH$

β,β-Dimethylglutaric acid
3,3-Dimethylpentanedioic acid



$HOOCCH(Cl)CH_2CH(Cl)COOH$

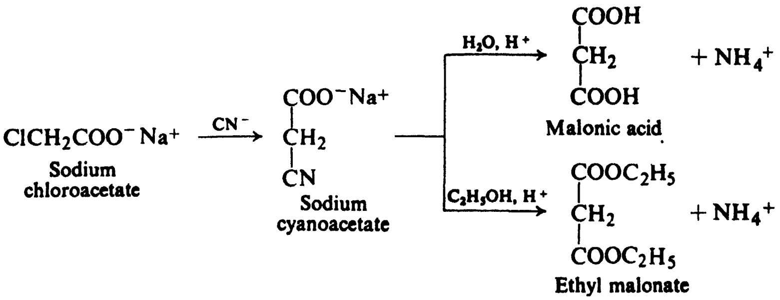
α,α'-Dichloroglutaric acid
2,4-Dichloro-pentanedioic acid

We have already encountered the benzenedicarboxylic acids, the *phthalic acids* (Sec. 12.10).

Table 18.3 DICARBOXYLIC ACIDS

Name	Formula	M.p., °C	Solub., g/100 g H_2O at 20°	K_1	K_2
Oxalic	HOOC—COOH	189	9	5400×10^{-5}	5.2×10^{-5}
Malonic	$HOOCCH_2COOH$	136	74	140	0.20
Succinic	$HOOC(CH_2)_2COOH$	185	6	6.4	0.23
Glutaric	$HOOC(CH_2)_3COOH$	98	64	4.5	0.38
Adipic	$HOOC(CH_2)_4COOH$	151	2	3.7	0.39
Maleic	*cis*-HOOCCH=CHCOOH	130.5	79	1000	0.055
Fumaric	*trans*-HOOCCH=CHCOOH	302	0.7	96	4.1
Phthalic	$1,2-C_6H_4(COOH)_2$	231	0.7	110	0.4
Isophthalic	$1,3-C_6H_4(COOH)_2$	348.5	0.01	24	2.5
Terephthalic	$1,4-C_6H_4(COOH)_2$	300 *subl*	0.002	29	3.5

Most dicarboxylic acids are prepared by adaptation of methods used to prepare monocarboxylic acids. Where hydrolysis of a nitrile yields a monocarboxylic acid, hydrolysis of a dinitrile or a cyanocarboxylic acid yields a dicarboxylic acid; where oxidation of a methylbenzene yields a benzoic acid, oxidation of a dimethylbenzene yields a phthalic acid. For example:



Problem 18.12 Why is chloroacetic acid converted into its salt before treatment with cyanide in the above preparation?

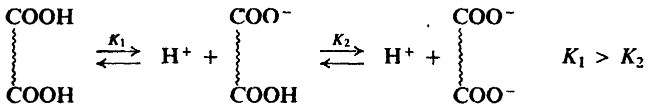
Problem 18.13 Outline a synthesis of: (a) pentanedioic acid from 1,3-propanediol (available from a fermentation of glycerol); (b) nonanedioic acid from *cis*-9-octadecenoic acid (oleic acid, obtained from fats); (c) succinic acid from 1,4-butynediol (available from acetylene and formaldehyde).

In general, dicarboxylic acids show the same chemical behavior as monocarboxylic acids. It is possible to prepare compounds in which only one of the carboxyl groups has been converted into a derivative; it is possible to prepare compounds in which the two carboxyl groups have been converted into different derivatives.

Problem 18.14 Predict the products of the following reactions:

(a) adipic acid (146 g) + 95% ethanol (146 g) + benzene + conc. H_2SO_4, 100°
(b) adipic acid (146 g) + 95% ethanol (50 g) + benzene + conc. H_2SO_4, 100°
(c) succinic acid + $LiAlH_4$
(d) pentanedioic acid + 1 mole Br_2, P
(e) terephthalic acid + excess $SOCl_2$
(f) maleic acid (*cis*-butenedioic acid) + Br_2/CCl_4

As with other acids containing more than one ionizable hydrogen (H_2SO_4, H_2CO_3, H_3PO_4, etc.), ionization of the second carboxyl group occurs less readily than ionization of the first (compare K_1's with K_2's in Table 18.3). More energy



$$\begin{matrix}\text{COOH}\\ \wr\\ \text{COOH}\end{matrix} \overset{K_1}{\rightleftharpoons} \text{H}^+ + \begin{matrix}\text{COO}^-\\ \wr\\ \text{COOH}\end{matrix} \overset{K_2}{\rightleftharpoons} \text{H}^+ + \begin{matrix}\text{COO}^-\\ \wr\\ \text{COO}^-\end{matrix} \qquad K_1 > K_2$$

is required to separate a positive hydrogen ion from the doubly charged anion than from the singly charged anion.

Problem 18.15 Compare the acidity (first ionization) of oxalic acid with that of formic acid; of malonic acid with that of acetic acid. How do you account for these differences?

Problem 18.16 Arrange oxalic, malonic, succinic, and glutaric acids in order of acidity (first ionization). How do you account for this order?

In addition to the reactions typical of any carboxylic acid, we shall find, some of these dicarboxylic acids undergo reactions that are possible only because there are two carboxyl groups in each molecule, and because these carboxyl groups are located in a particular way with respect to each other.

Problem 18.17 Give a likely structure for the product of each of the following reactions:

(a) oxalic acid + ethylene glycol $\longrightarrow$ $C_4H_4O_4$
(b) succinic acid + heat $\longrightarrow$ $C_4H_4O_3$
(c) terephthalic acid + ethylene glycol $\longrightarrow$ $(C_{10}H_8O_4)_n$, the polymer Dacron

18.21 Analysis of carboxylic acids. Neutralization equivalent

Carboxylic acids are recognized through their acidity. They dissolve in aqueous sodium hydroxide and in aqueous sodium bicarbonate. The reaction with bicarbonate releases bubbles of carbon dioxide (see Sec. 18.4).

(Phenols, Sec. 24.7, are more acidic than water, but—with certain exceptions—are considerably weaker than carboxylic acids; they dissolve in aqueous sodium hydroxide, but *not* in aqueous sodium bicarbonate. Sulfonic acids are even more acidic than carboxylic acids, but they contain sulfur, which can be detected by elemental analysis.)

Once characterized as a carboxylic acid, an unknown is identified as a particular acid on the usual basis of its physical properties and the physical properties of derivatives. The derivatives commonly used are *amides* (Secs. 20.11 and 23.6) and *esters* (Sec. 20.15).

Problem 18.18 Expand the table you made in Problem 17.24, p. 570, to include the kinds of compounds and tests we have taken up since then.

Particularly useful both in identification of previously studied acids and in proof of structure of new ones is the **neutralization equivalent**: *the equivalent weight of the acid as determined by titration with standard base.* A weighed sample of the acid is dissolved in water or aqueous alcohol, and the volume of standard base needed to neutralize the solution is measured. For example, a 0.224-g sample of an unknown acid (m.p. 139–140°) required 13.6 ml of 0.104 N sodium hydroxide solution for neutralization (to a phenolphthalein end point). Since each 1000 ml of the base contains 0.104 equivalents, and since the number of equivalents of base required equals the number of equivalents of acid present,

$$\frac{13.6}{1000} \times 0.104 \text{ equivalents of acid} = 0.224 \text{ g}$$

and

$$1 \text{ equivalent of acid} = 0.224 \times \frac{1000}{13.6} \times \frac{1}{0.104} = 158 \text{ g}$$

Problem 18.19 Which of the following compounds might the above acid be: (a) *o*-chlorobenzoic acid (m.p. 141°) or (b) 2,6-dichlorobenzoic acid (m.p. 139°)?

Problem 18.20 A 0.187-g sample of an acid (b.p. 203–205°) required 18.7 ml of 0.0972 N NaOH for neutralization. (a) What is the neutralization equivalent? (b) Which of the following acids might it be: *n*-caproic acid (b.p. 205°), methoxyacetic acid (b.p. 203°), or ethoxyacetic acid (b.p. 206°)?

Problem 18.21 (a) How many equivalents of base would be neutralized by one mole of phthalic acid? What is the neutralization equivalent of phthalic acid? (b) What is the relation between neutralization equivalent and the number of acidic hydrogens per molecule of acid? (c) What is the neutralization equivalent of 1,3,5-benzenetricarboxylic acid? Of mellitic acid, $C_6(COOH)_6$?

A metal salt of a carboxylic acid is recognized through these facts: (a) it leaves a residue when strongly heated (*ignition test*); (b) it decomposes at a fairly high temperature, instead of melting; and (c) it is converted into a carboxylic acid upon treatment with dilute mineral acid.

Problem 18.22 The residue left upon ignition of a sodium salt of a carboxylic acid was white, soluble in water, turned moist litmus blue, and reacted with dilute hydrochloric acid with the formation of bubbles. What was its probable chemical composition?

18.22 Spectroscopic analysis of carboxylic acids

Infrared. The carboxyl group is made up of a carbonyl group (C=O) and a hydroxyl group (OH), and the infrared spectrum of carboxylic acids reflects both these structural units. For hydrogen-bonded (dimeric) acids, O—H stretching gives a strong, broad band in the 2500–3000 cm^{-1} range (see Fig. 18.4, below).

O—H stretching, ***strong, broad***

—COOH and enols	2500–3000 cm^{-1}
ROH and ArOH	3200–3600 cm^{-1}

With acids we encounter, for the first time, absorption due to stretching of the carbonyl group. This strong band appears in a region that is usually free of other

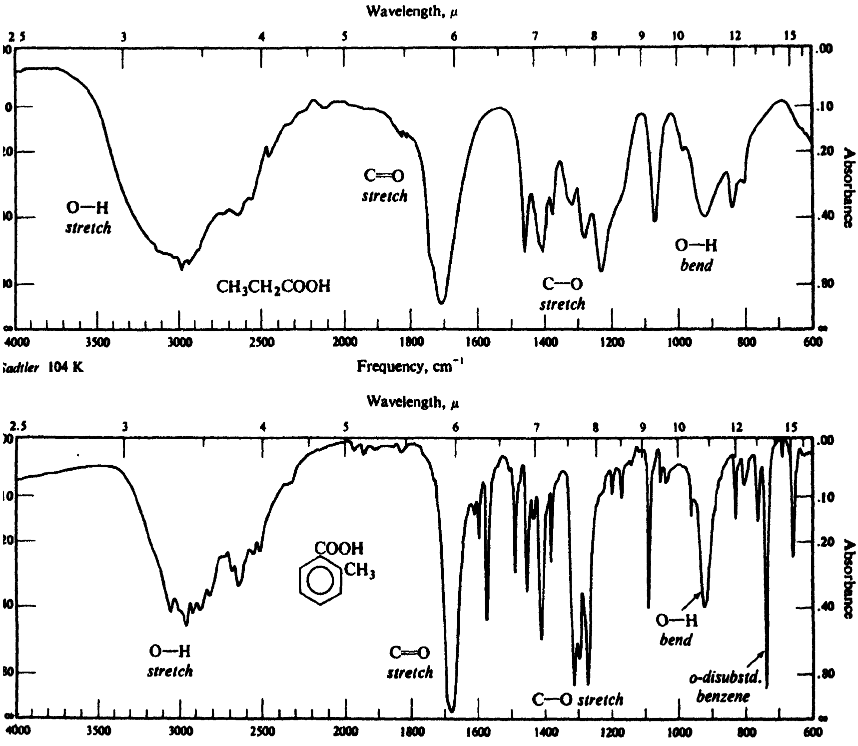


Figure 18.4. Infrared spectra of (*a*) propionic acid and (*b*) *o*-toluic acid.