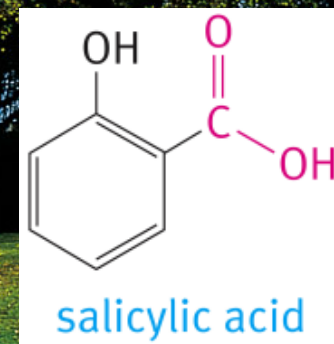


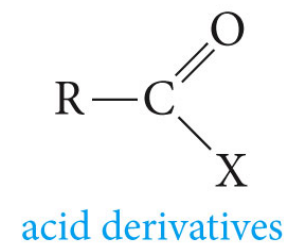
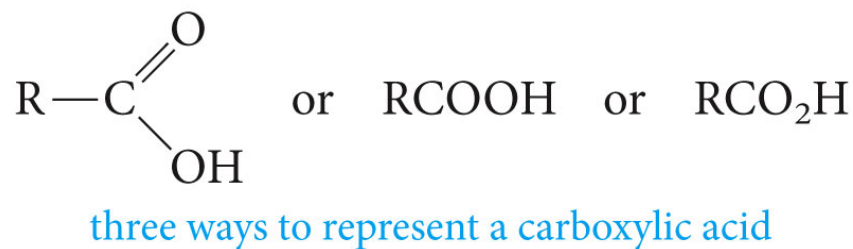
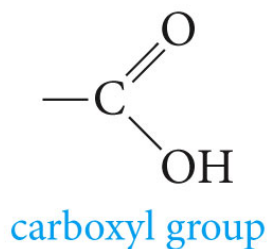
# Chapter 10: Carboxylic Acids and Their Derivatives



The bark of the white willow tree (*Salix alba*) is a source of salicylic acid which is used to make aspirin (acetylsalicylic acid)



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.





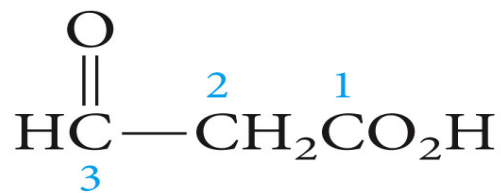


**Table 10.1** ▀ **Aliphatic Carboxylic Acids**

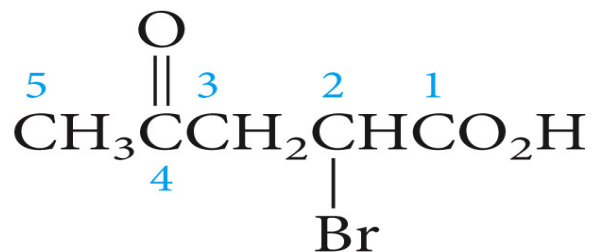
<b>Carbon atoms</b>	<b>Formula</b>	<b>Source</b>	<b>Common name</b>	<b>IUPAC name</b>
1	HCOOH	ants (Latin, <i>formica</i> )	formic acid	methanoic acid
2	CH <sub>3</sub> COOH	vinegar (Latin, <i>acetum</i> )	acetic acid	ethanoic acid
3	CH <sub>3</sub> CH <sub>2</sub> COOH	milk (Greek, <i>protos pion</i> , 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



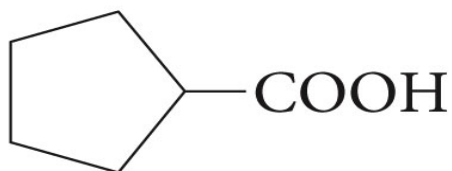




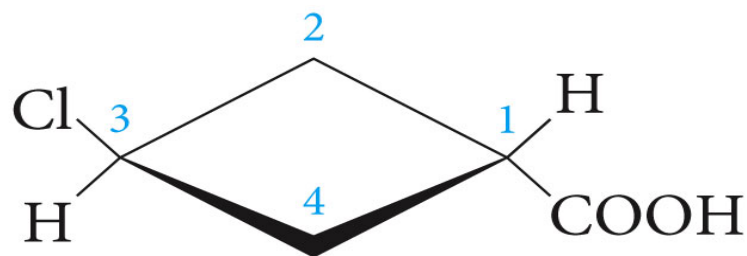
3-oxopropanoic acid



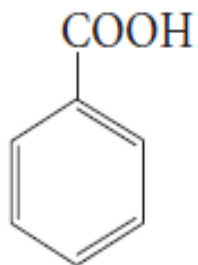
2-bromo-4-oxopentanoic acid



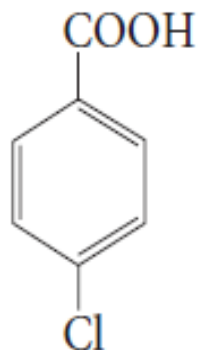
cyclopentanecarboxylic acid



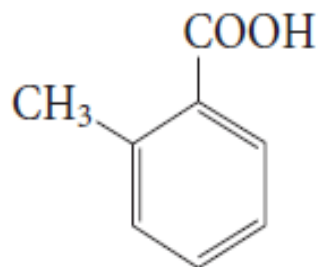
*trans*-3-chlorocyclobutanecarboxylic acid



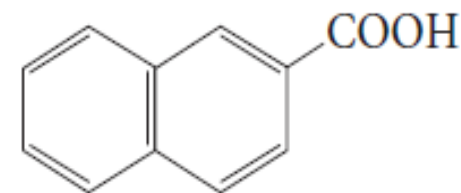
benzoic acid  
(benzenecarboxylic acid)



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



*o*-toluic acid  
(2-methylbenzenecarboxylic acid)



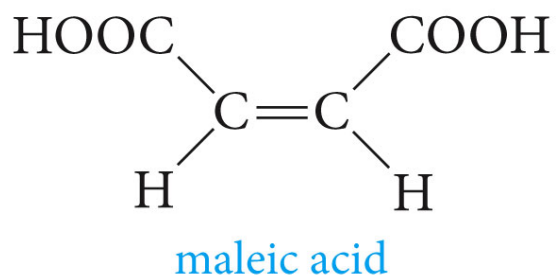
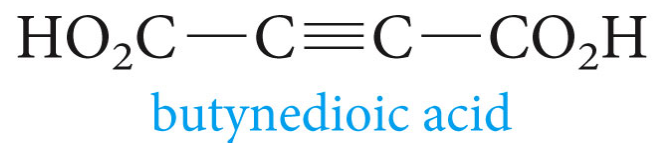
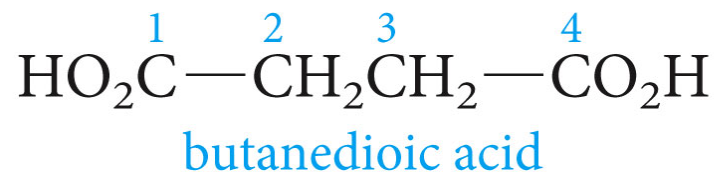
2-naphthoic acid  
(2-naphthalenecarboxylic acid)



**Table 10.2** ■ **Aliphatic Dicarboxylic Acids**

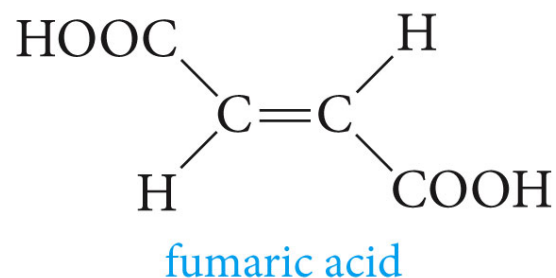
<b>Formula</b>	<b>Common name</b>	<b>Source</b>	<b>IUPAC name</b>
HOOC—COOH	oxalic acid	plants of the <i>oxalic</i> family (for example, sorrel)	ethanedioic acid
HOOC—CH <sub>2</sub> —COOH	malonic acid	apple (Gk. <i>malon</i> )	propanedioic acid
HOOC—(CH <sub>2</sub> ) <sub>2</sub> —COOH	succinic acid	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





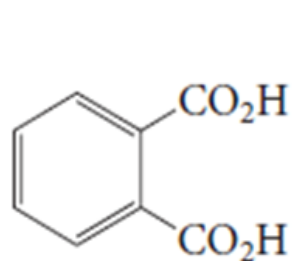
(*cis*-2-butenedioic acid)

and

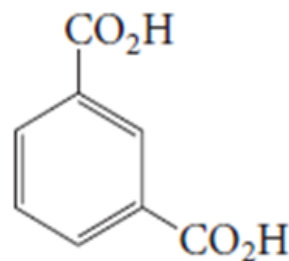


(*trans*-2-butenedioic acid)

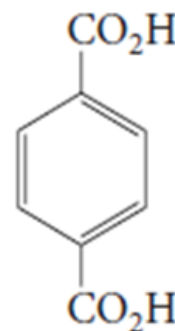
The three benzenedicarboxylic acids are generally known by their common names.



phthalic acid



isophthalic acid

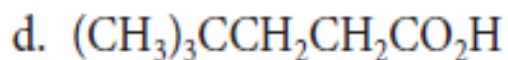
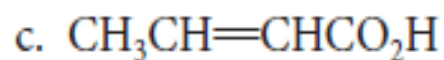
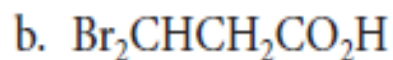
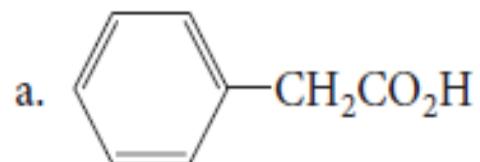


terephthalic acid





**PROBLEM 10.2** Give an IUPAC name for



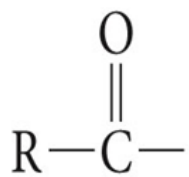
a. phenylethanoic acid

b. 3,3-dibromopropanoic acid

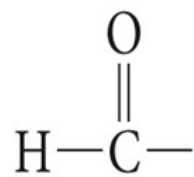
c. 2-butenoic acid

d. 5,5-dimethylpentanoic acid

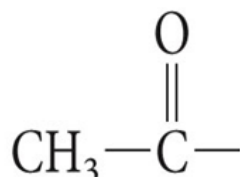




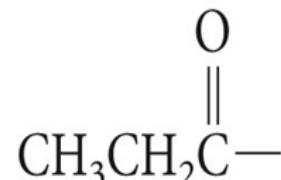
an acyl group



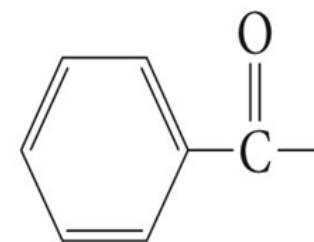
formyl  
(methanoyl)



acetyl  
(ethanoyl)



propanoyl



benzoyl

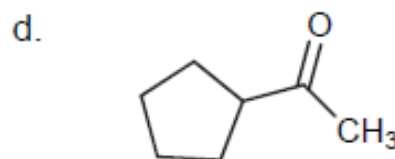
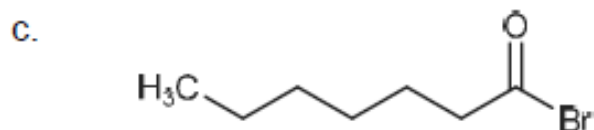
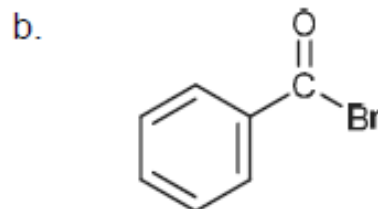
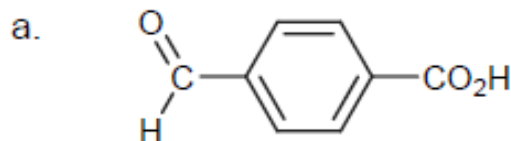
### PROBLEM 10.5 Write the formula for

a. 4-formylbenzoic acid

c. octanoyl bromide

b. benzoyl bromide

d. acetylcyclopentane



## 9.2 Physical Properties of 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 ( $\infty$ )
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)

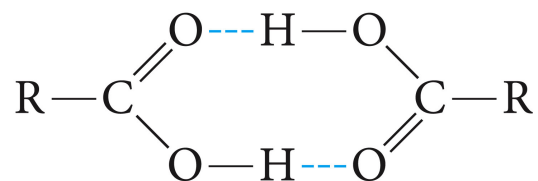




Carboxylic acids are polar. Like alcohols, they form hydrogen bonds with themselves or with other molecules. Therefore, they have high boiling points for their molecular weights—higher even than those of comparable alcohols.

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.

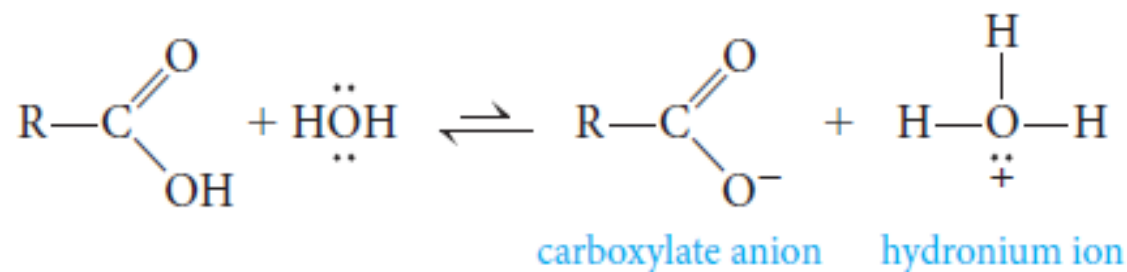


Hydrogen bonding also explains the water solubility of the lower molecular weight carboxylic acids.



## 10.3 Acidity and Acidity Constants

Carboxylic acids ( $\text{RCO}_2\text{H}$ ) dissociate in water, yielding a carboxylate anion ( $\text{RCO}_2^{2-}$ ) and a hydronium ion.



Their acidity constants  $K_a$  in water are given by the expression

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



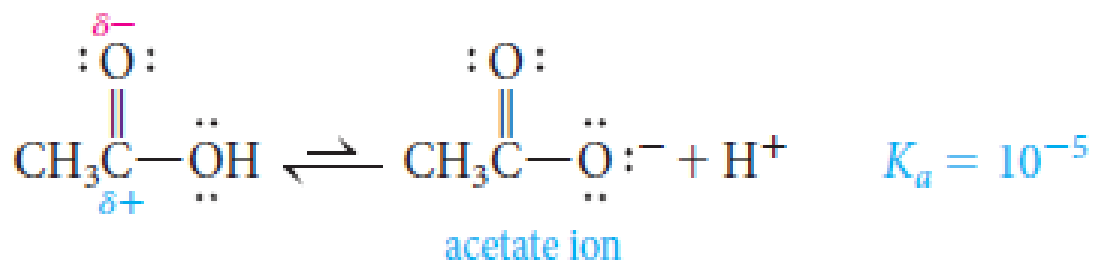
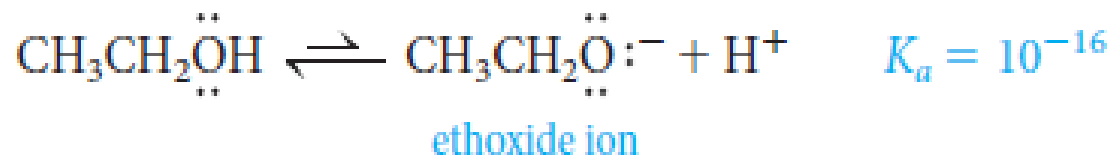
**Table 10.4** The Ionization Constants of Some Acids

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	Cl <sub>3</sub> CCOOH	$2.0 \times 10^{-1}$	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





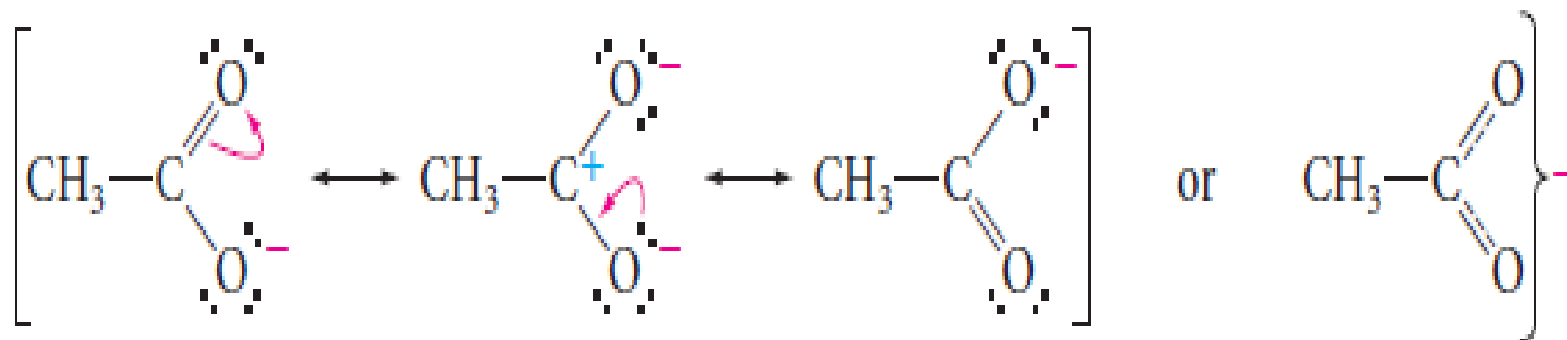
## 10.4 What makes carboxylic acids acidic?



1-The only difference between the structures of acetic acid and ethanol is the replacement of a CH<sub>2</sub> group (in ethanol) by a carbonyl group (in acetic acid). But carbonyl carbon atom carries a substantial *positive* charge (δ<sup>+</sup>). 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.



2- 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)

.1

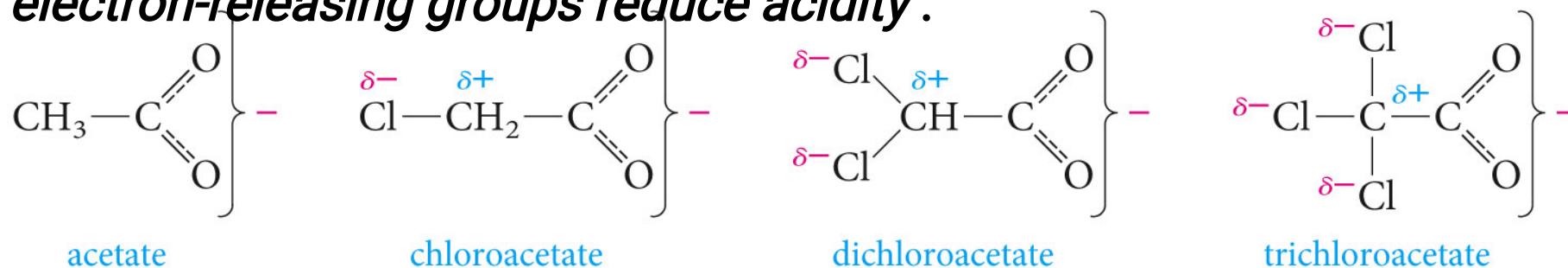


## 10.5 Effect of Structure on Acidity

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.

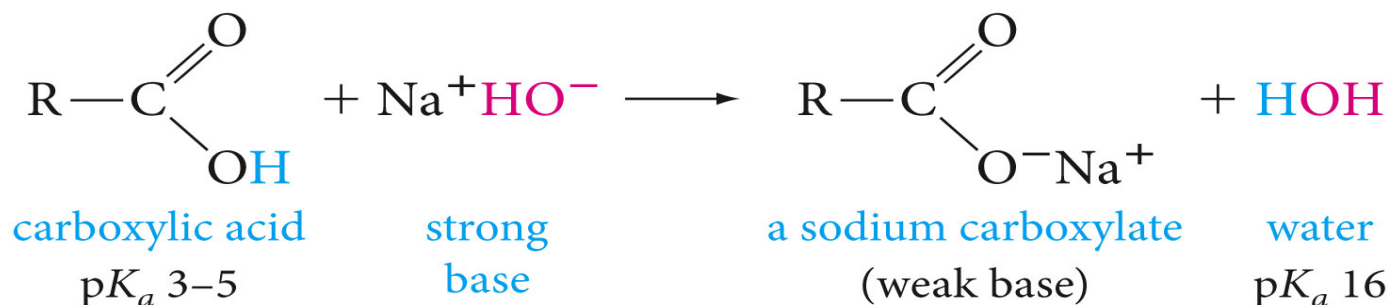
Remember that *electron-withdrawing groups enhance acidity, and electron-releasing groups reduce acidity*.



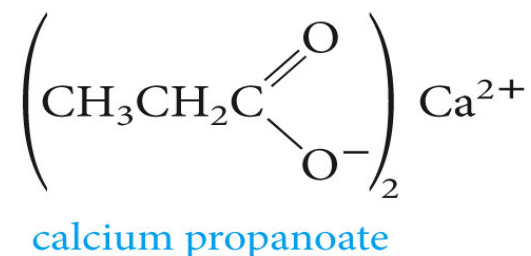
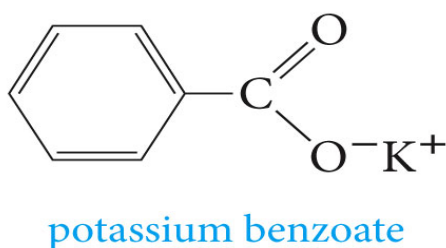
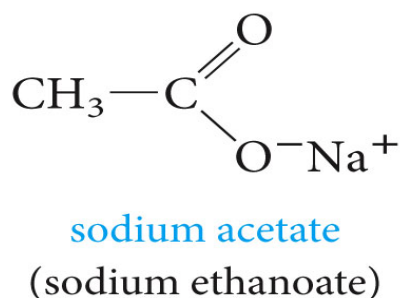


# 10.6 Conversion of Acids to Salts

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



Carboxylate salts are named as shown in the following examples:

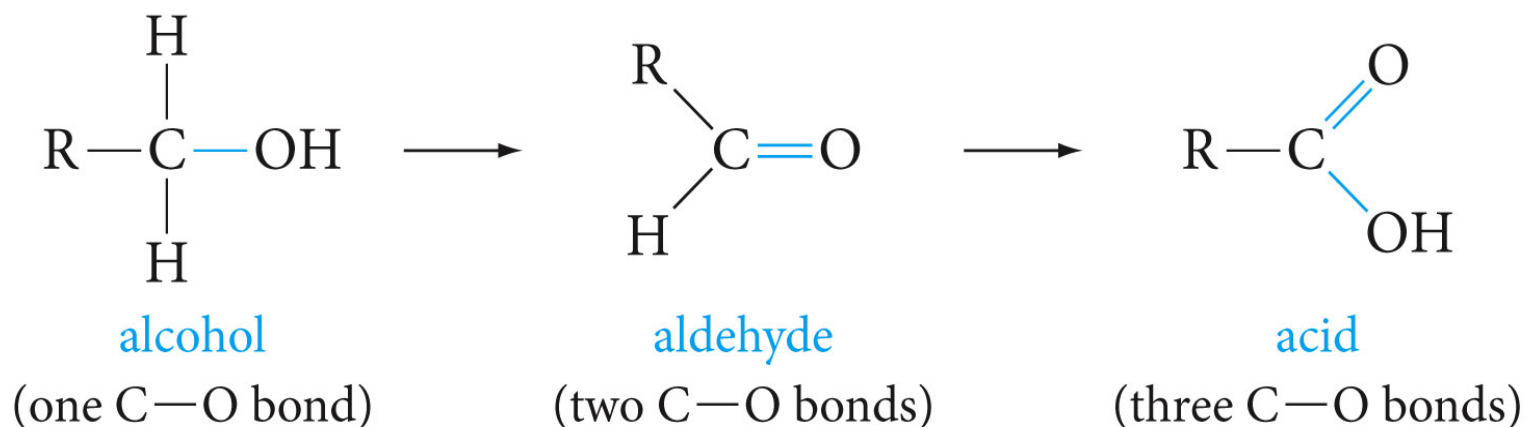


The cation is named first, followed by the name of the carboxylate ion, which is obtained by changing the *-ic* ending of the acid to *-ate*.



# 10.7 Preparation of Acids

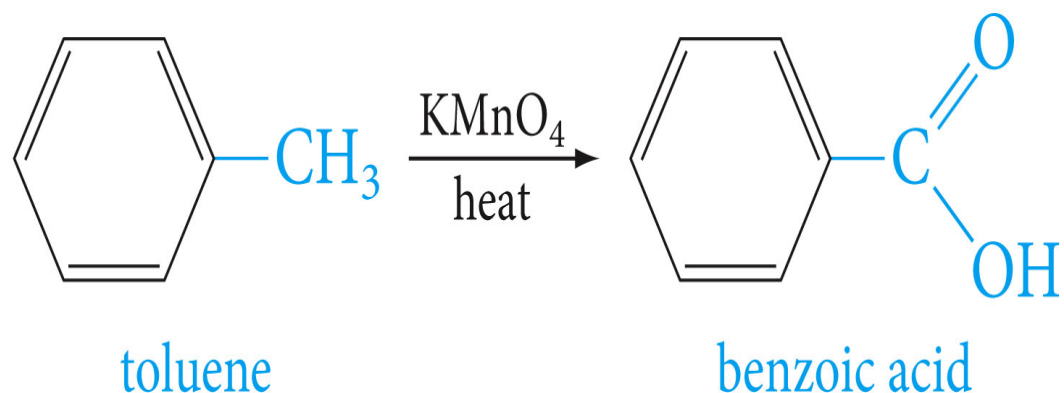
## a. Oxidation of primary alcohol and aldehyde



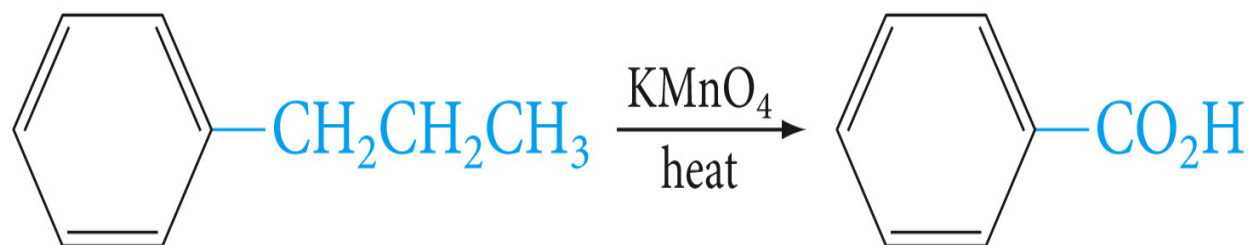
The most commonly used oxidizing agents for these purposes are potassium permanganate ( $\text{KMnO}_4$ ), chromic acid anhydride ( $\text{CrO}_3$ ), nitric acid ( $\text{HNO}_3$ ), and, with aldehydes only, silver oxide ( $\text{Ag}_2\text{O}$ ).



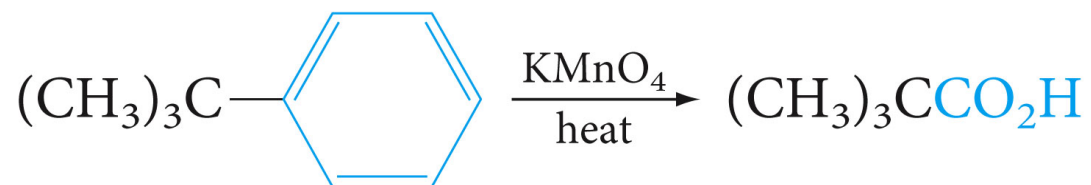
## b. Oxidation of Aromatic Side Chains



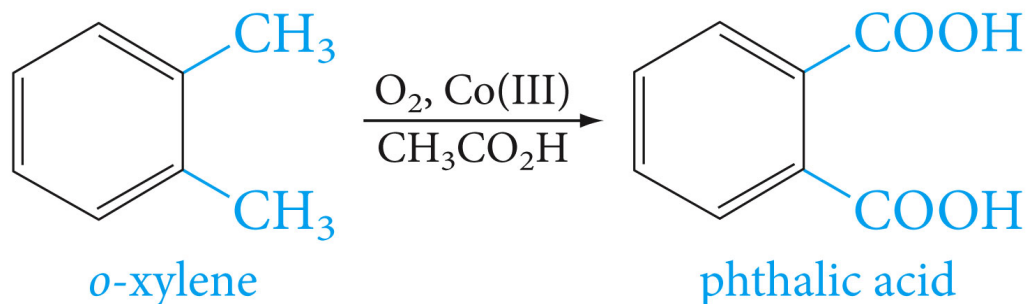
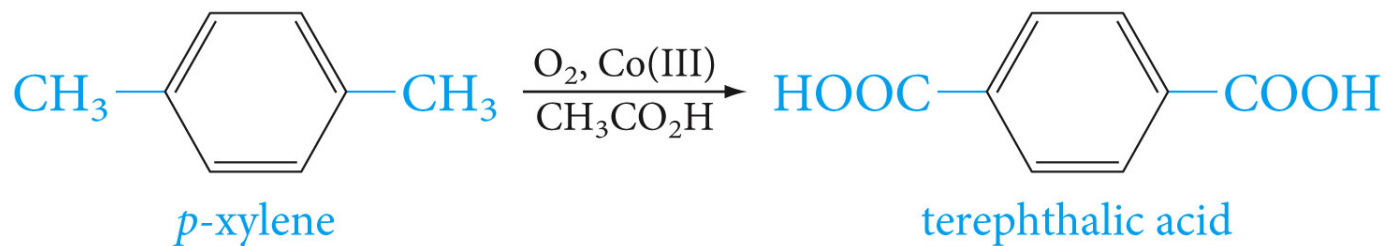
The reaction involves attack of the oxidant at a C-H bond adjacent to the benzene ring. Longer side chains are also oxidized to a carboxyl group.



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



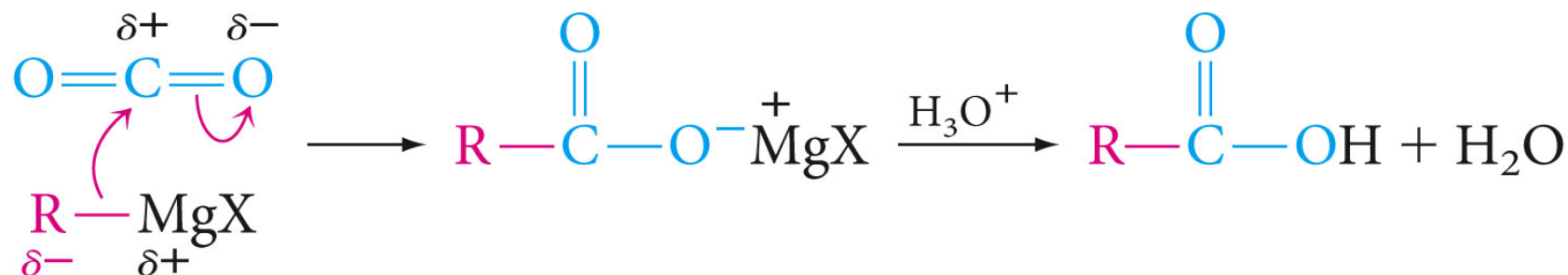
With oxidants other than potassium permanganate, this reaction is commercially important. For example, terephthalic acid





## c. Reaction of Grignard Reagents with Carbon Dioxide

Grignard reagents 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.

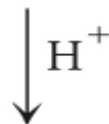
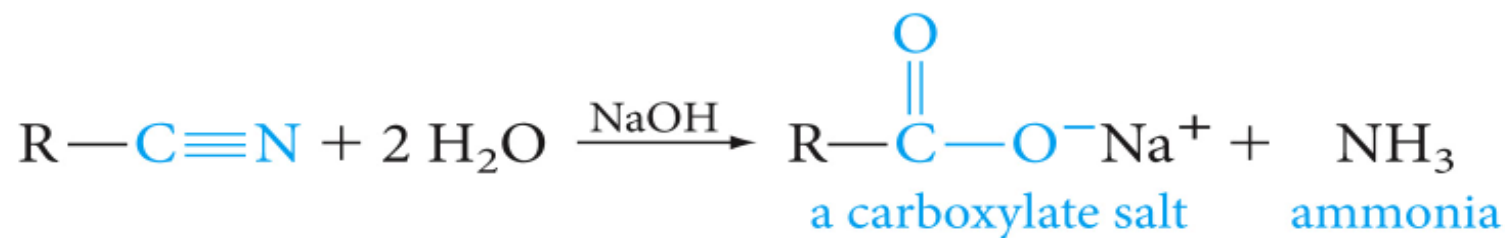
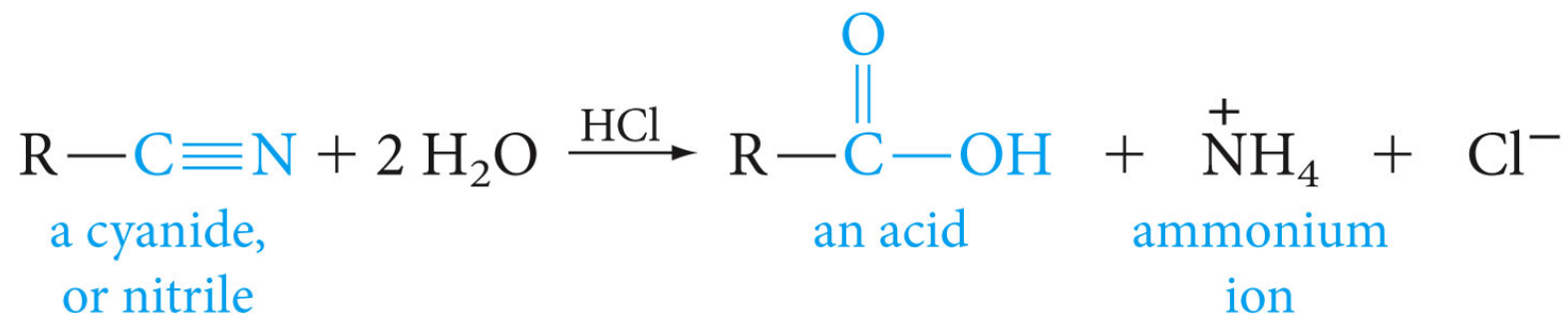


Note that the acid obtained has one more carbon atom than the alkyl or aryl halide from which the Grignard reagent is prepared, so the reaction provides a way to increase the length of a carbon chain.

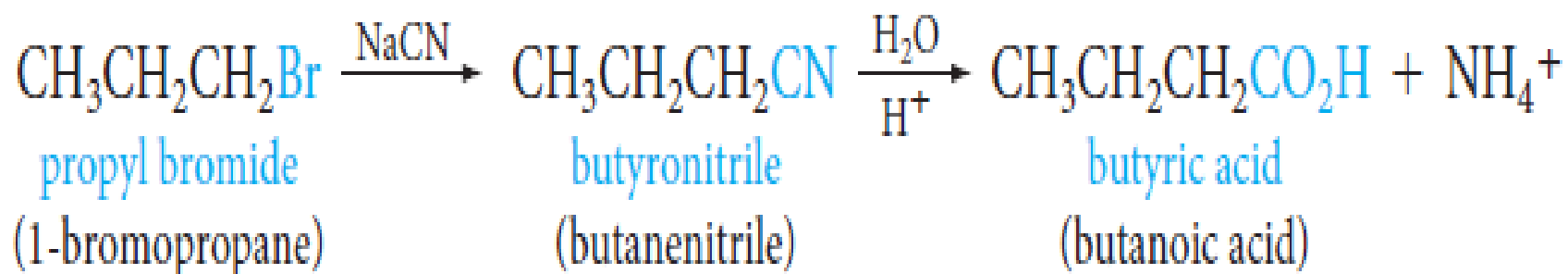


## d. Hydrolysis of Cyanides

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.

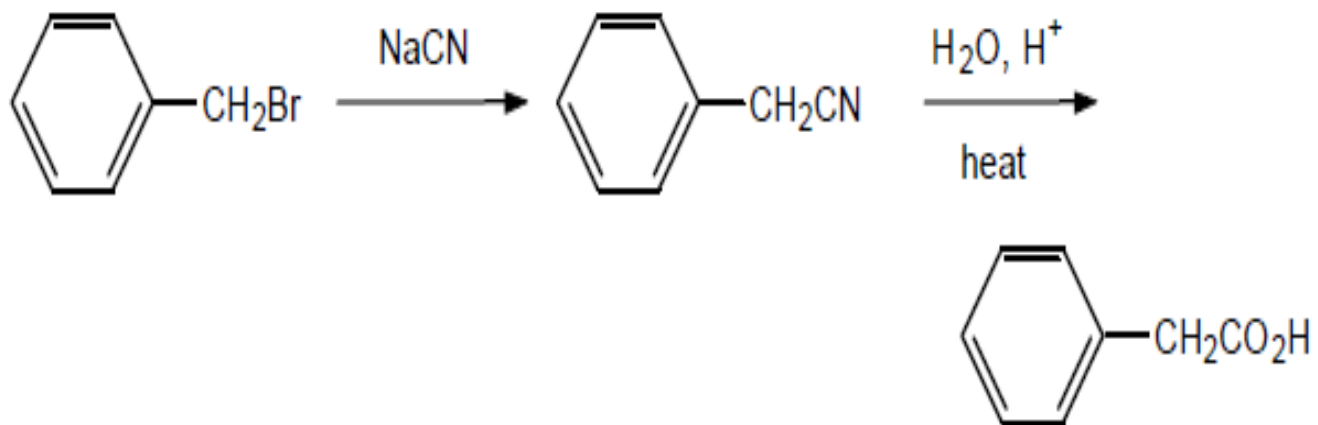
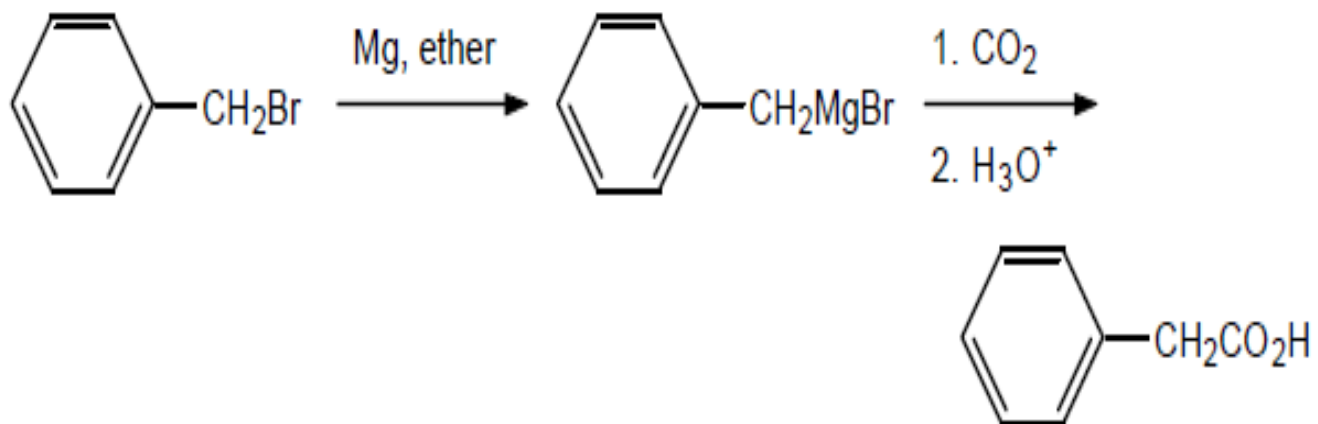


Alkyl cyanides are generally made from the corresponding alkyl halide (usually primary) and sodium cyanide by an  $S_N2$  displacement, as shown in this synthesis of an acid:



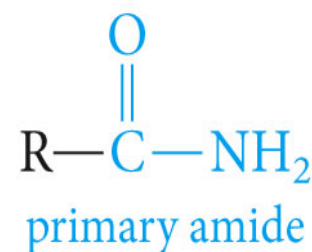
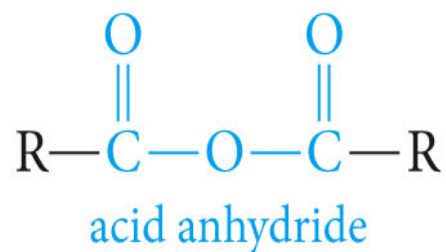
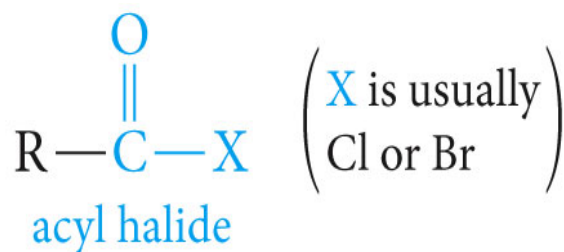
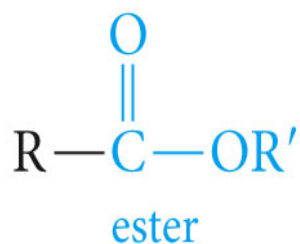
**PROBLEM 10.13** Write equations for synthesizing phenylacetic acid ( $\text{C}_6\text{H}_5\text{CH}_2\text{CO}_2\text{H}$ ) from benzyl bromide ( $\text{C}_6\text{H}_5\text{CH}_2\text{Br}$ ) by two routes.





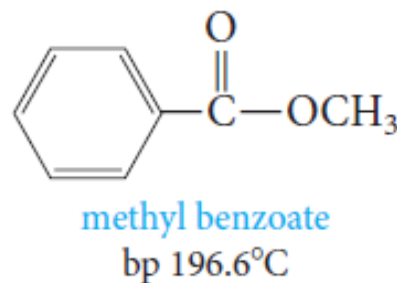
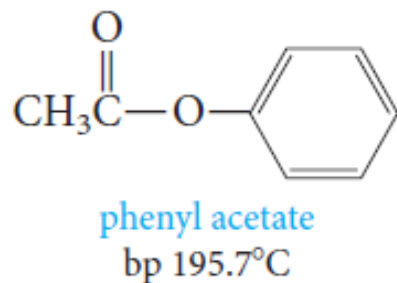
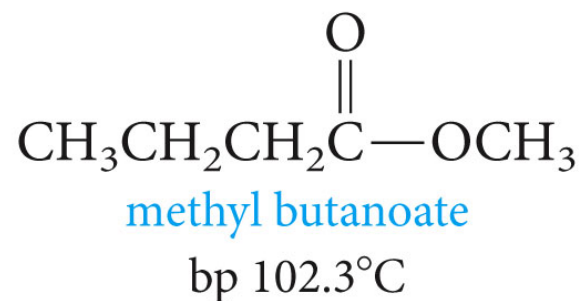
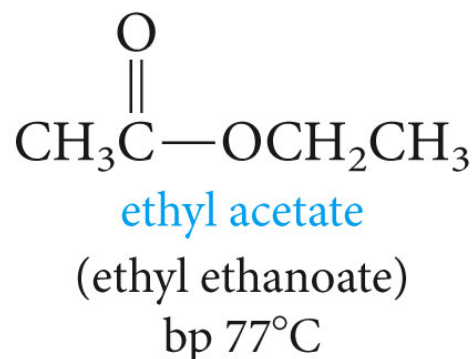
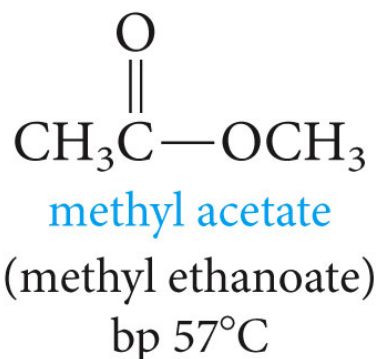
# 10.8 Carboxylic Acid Derivatives

Carboxylic acid derivatives are compounds in which the hydroxyl part of the carboxyl group is replaced by various other groups. All acid derivatives can be hydrolyzed to the corresponding carboxylic acid.



# 10.9 Esters

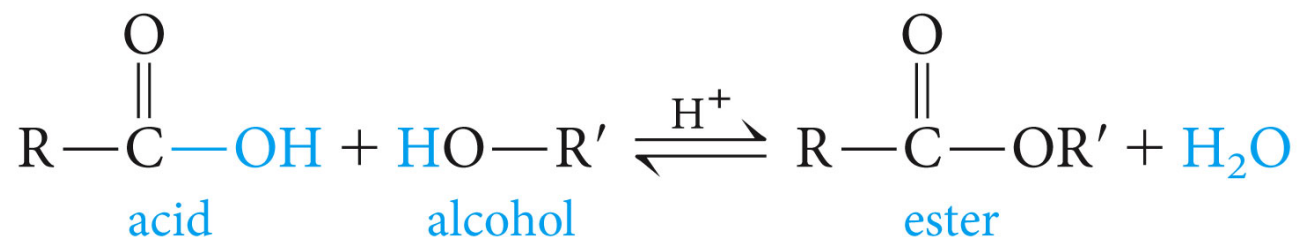
**Esters** are derived from acids by replacing the -OH group by an -OR group. They are named in a manner analogous to carboxylic acid salts. The R part of the -OR group is named first, followed by the name of the acid, with the *-ic* ending changed to *-ate*.





## 10.10 Preparation of ester, Fischer Esterification

When a carboxylic acid and an alcohol are heated in the presence of an acid catalyst (usually HCl or H<sub>2</sub>SO<sub>4</sub>), an equilibrium is established with the ester and water.

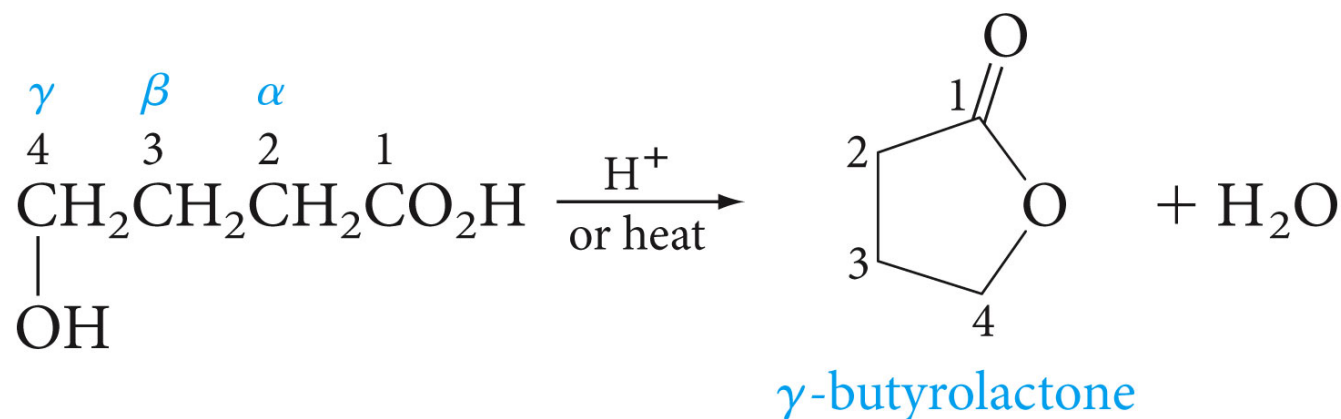


Although the reaction is an equilibrium, it can be shifted to the right in several ways. If either the alcohol or the acid is inexpensive, a large excess can be used. Alternatively, the ester and/or water may be removed as formed (by distillation, for example), thus driving the reaction forward.



## 10.12 Lactones

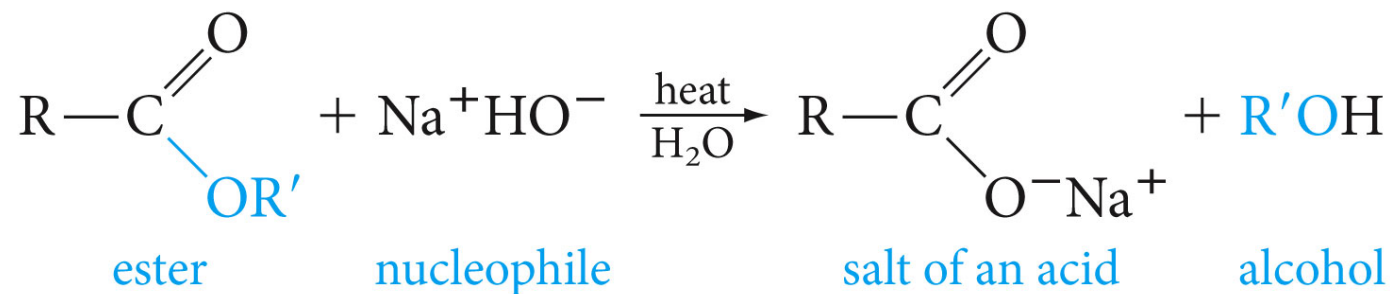
**Hydroxy acids** contain both functional groups required for ester formation. If these groups can come in contact through bending of the chain, they may react with one another to form **cyclic esters** called **lactones**. For example,



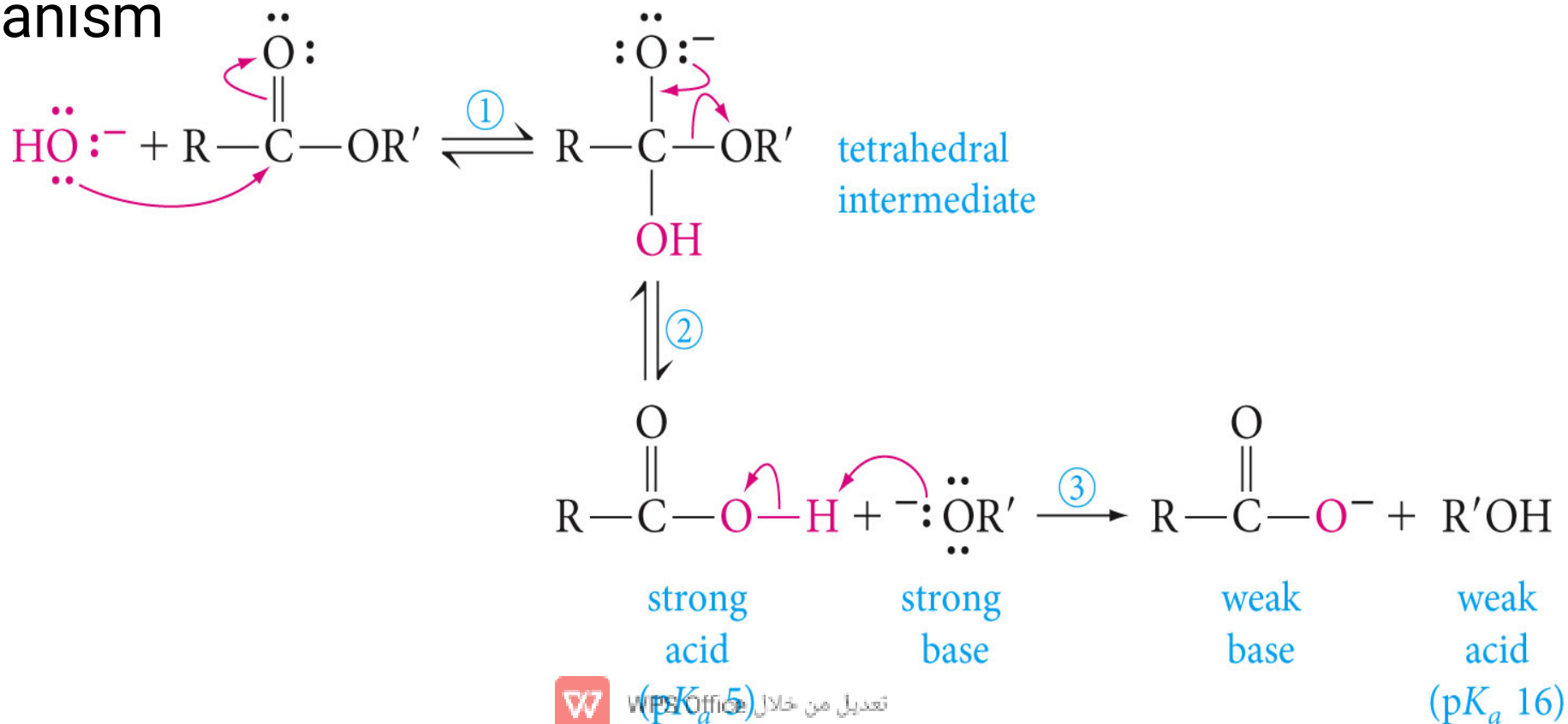


# 10.13 Saponification of Esters

Saponification is the hydrolysis of an ester with a base.

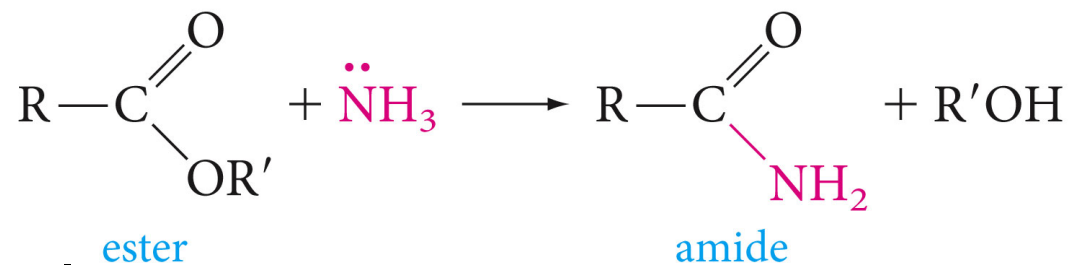


Mechanism

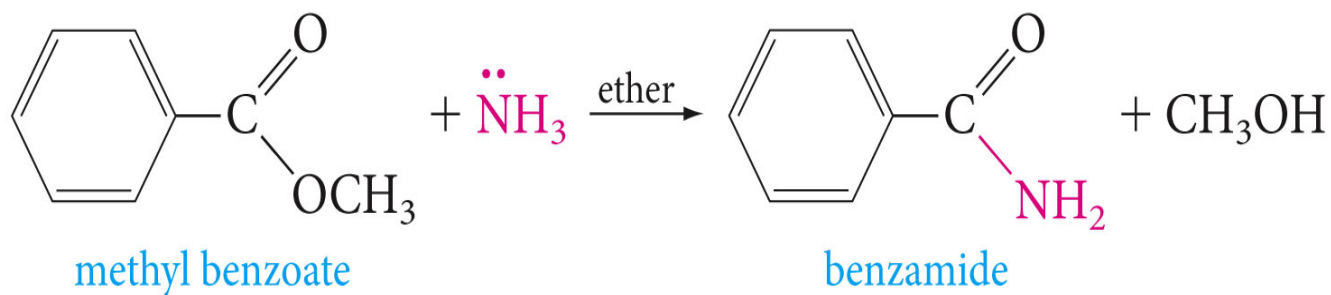


# 10.14 Ammonolysis of Esters

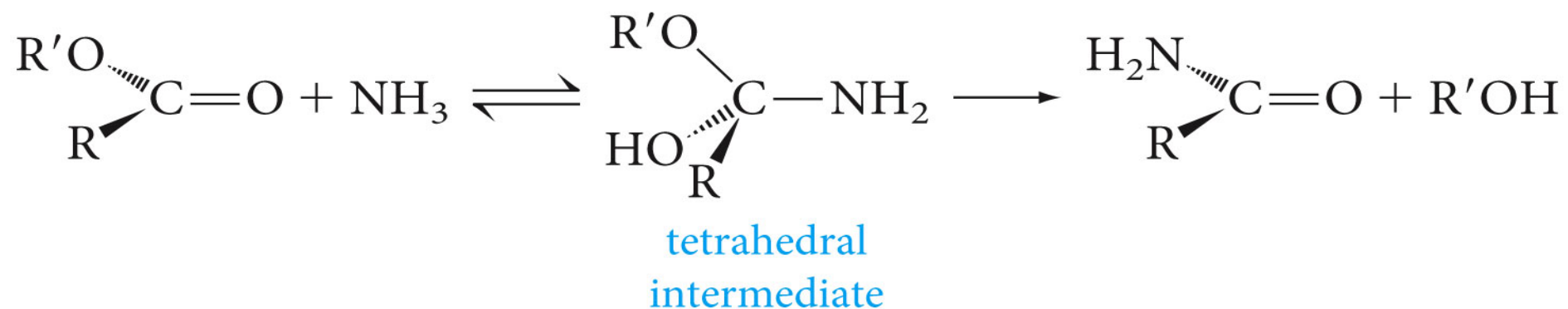
Ammonia converts esters to amides.



For example,



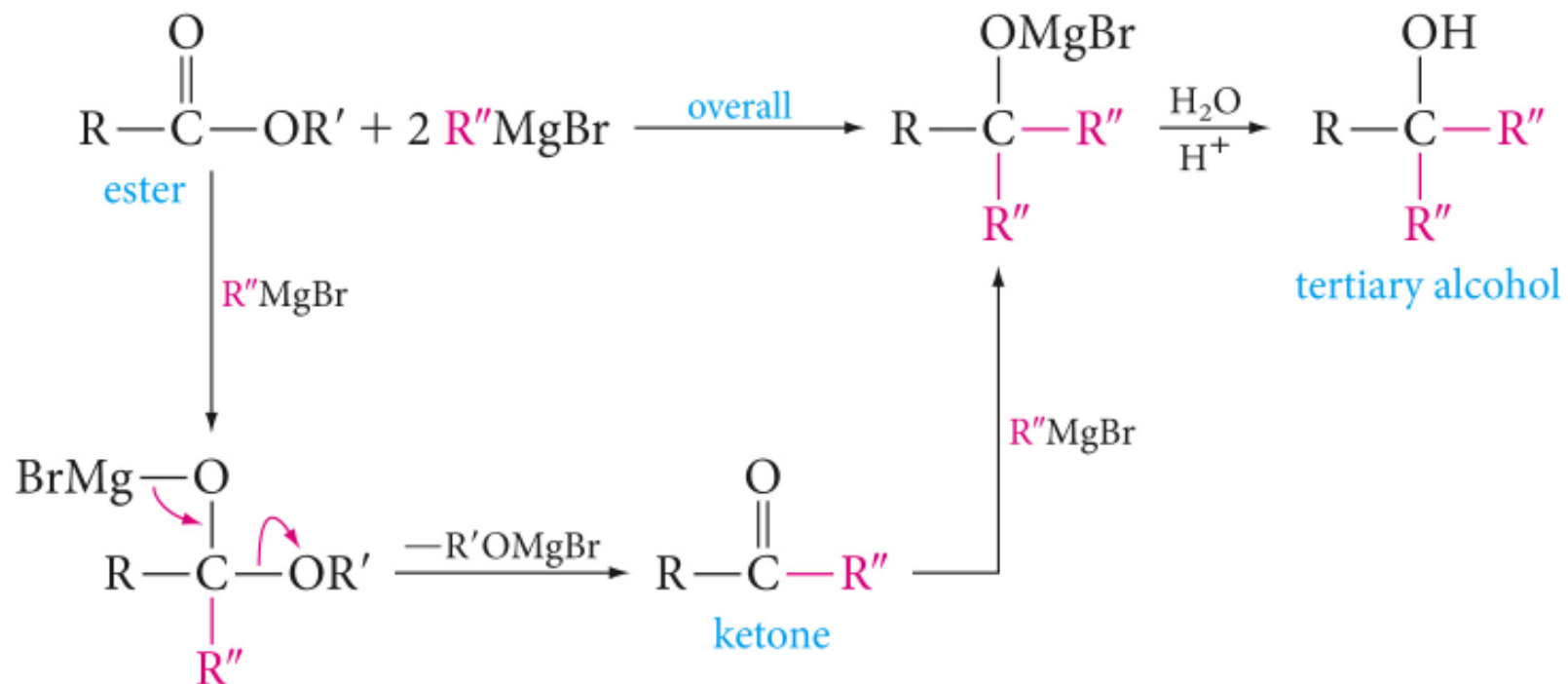
The reaction mechanism is very much like that of saponification. The unshared electron pair on the ammonia nitrogen initiates nucleophilic attack on the ester carbonyl group.



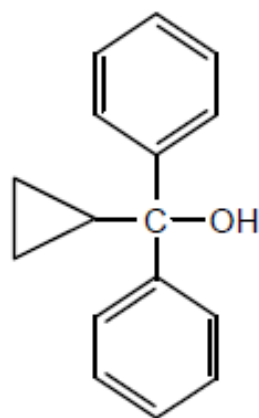
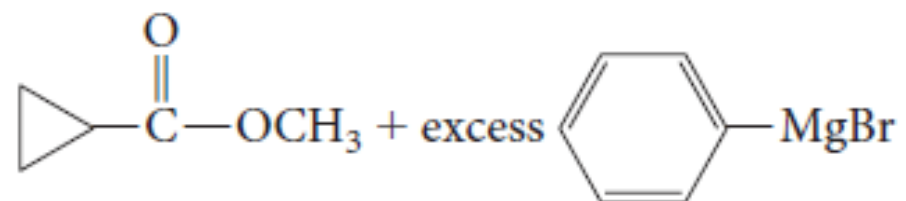


# 10.14 Reaction of Esters with Grignard Reagents

Esters react with two equivalents of a Grignard reagent to give tertiary alcohols. The reaction proceeds by *irreversible* nucleophilic attack of the Grignard reagent on the ester carbonyl group. The initial product, a ketone, reacts further in the usual way to give the tertiary alcohol.

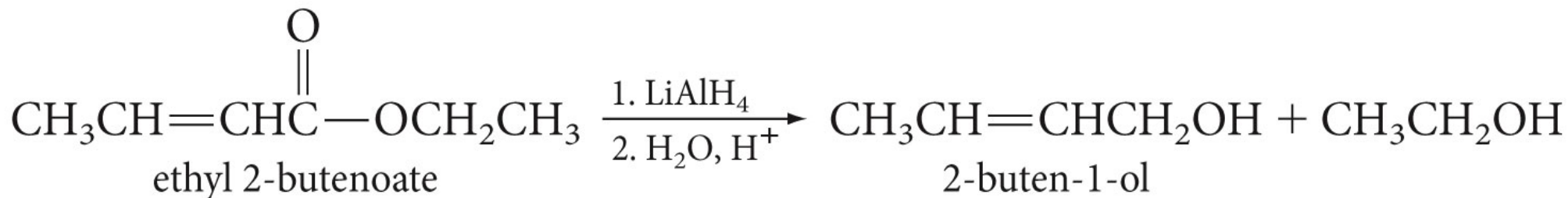
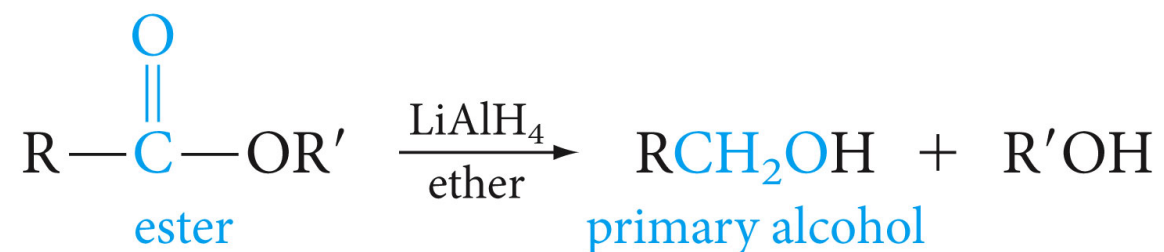


**PROBLEM 10.21** Using eq. 10.27 as a guide, write the structure of the tertiary alcohol that is obtained from



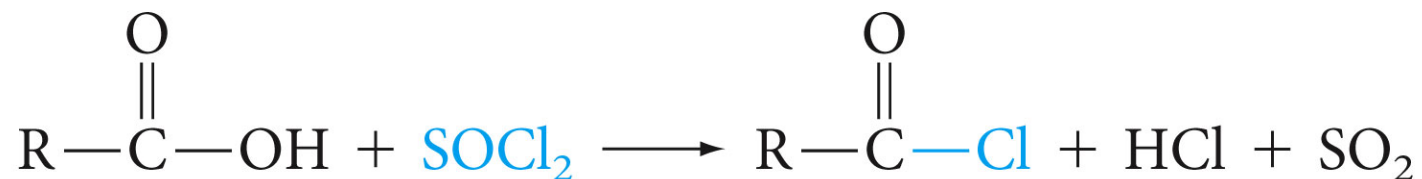
## 10.16 Reduction of Esters

Esters can be reduced to primary alcohols by lithium aluminum hydride ( $\text{LiAlH}_4$ ).

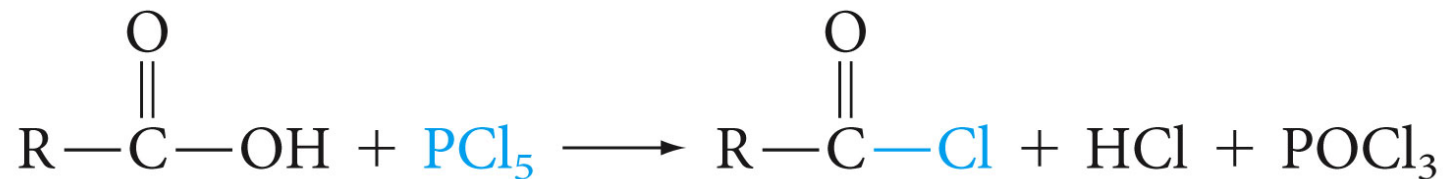


## 10.18 Acyl Halides

**Acyl halides** are among the most reactive of carboxylic acid derivatives. *Acyl chlorides* are more common and less expensive than bromides or iodides. They can be prepared from acids by reaction with thionyl chloride.



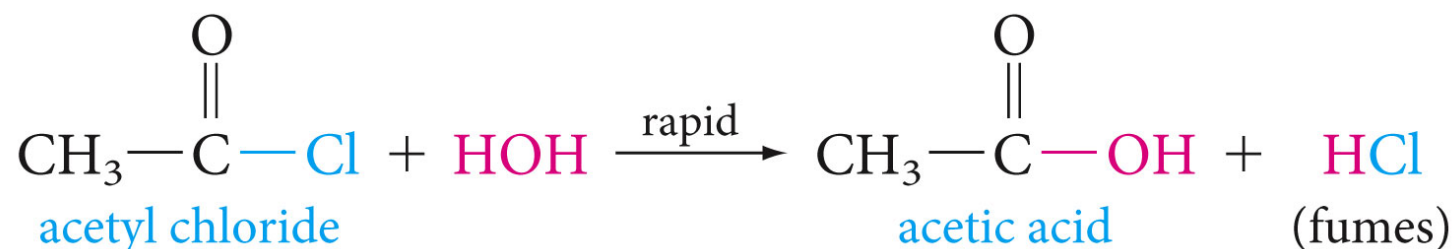
Phosphorus pentachloride and other reagents can also be used to prepare acyl chlorides from carboxylic acids.



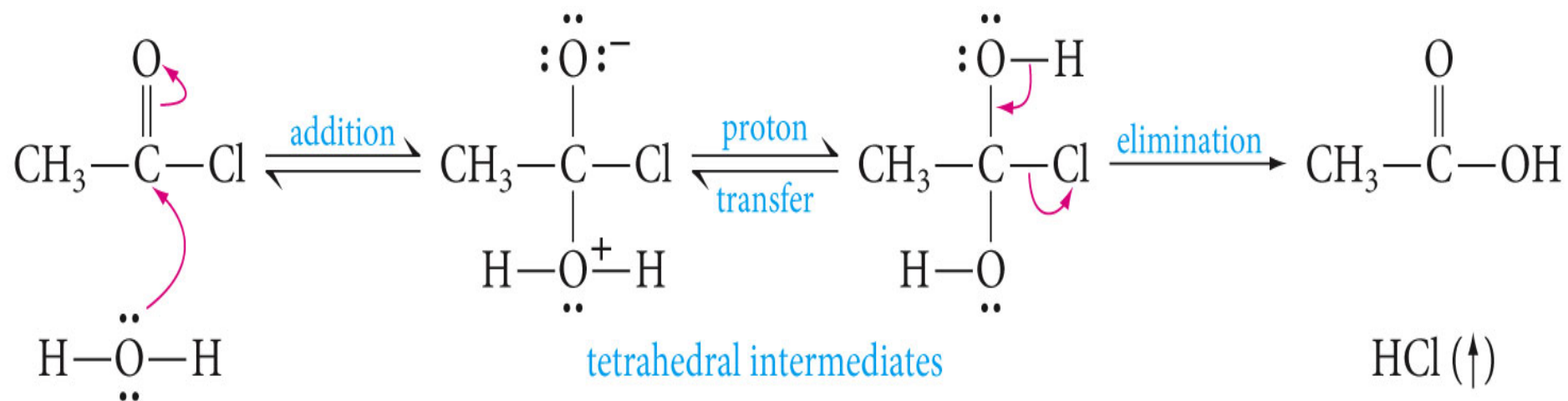
# Reactions

Acyl halides react rapidly with most nucleophiles.

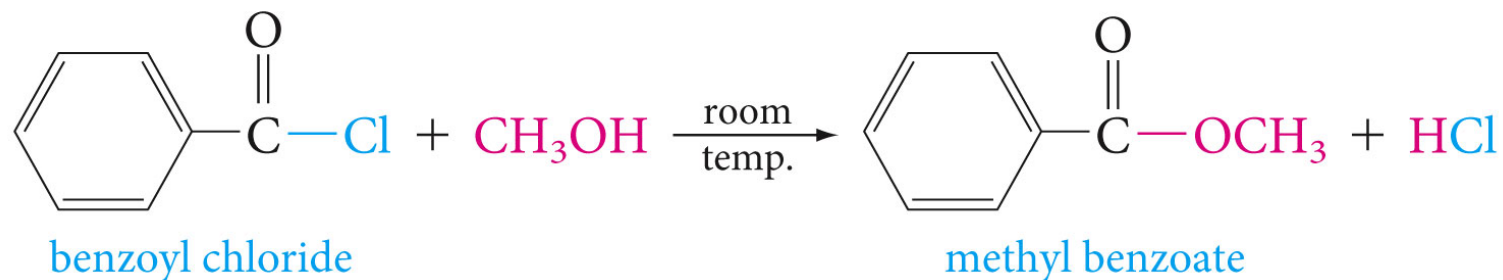
## 1. hydrolysis by water.



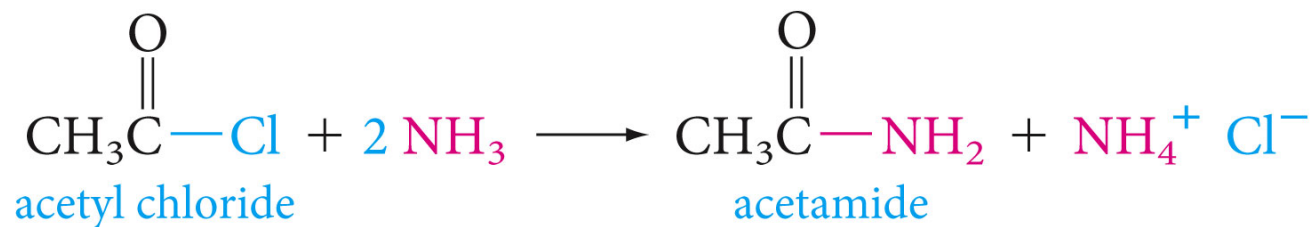
## Reaction mechanism



## 2. Acyl halides react rapidly with alcohols to form esters.

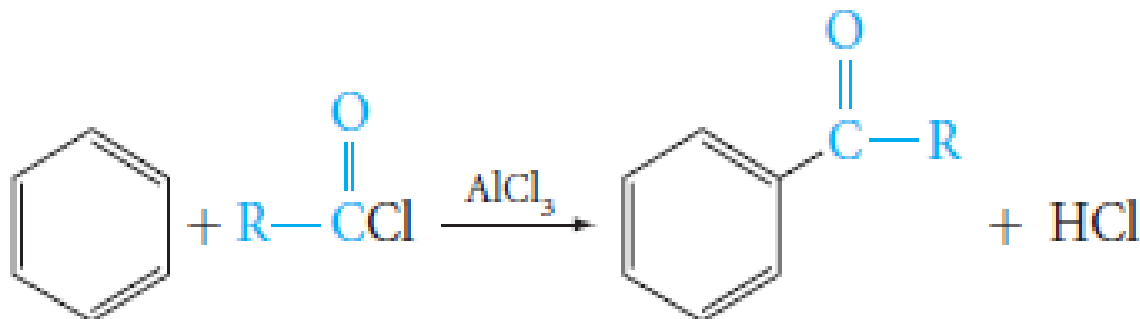


## 3. Acyl halides react with ammonia to form amides

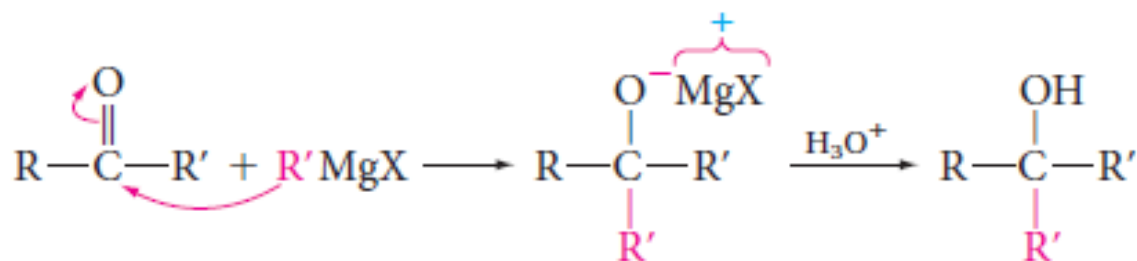
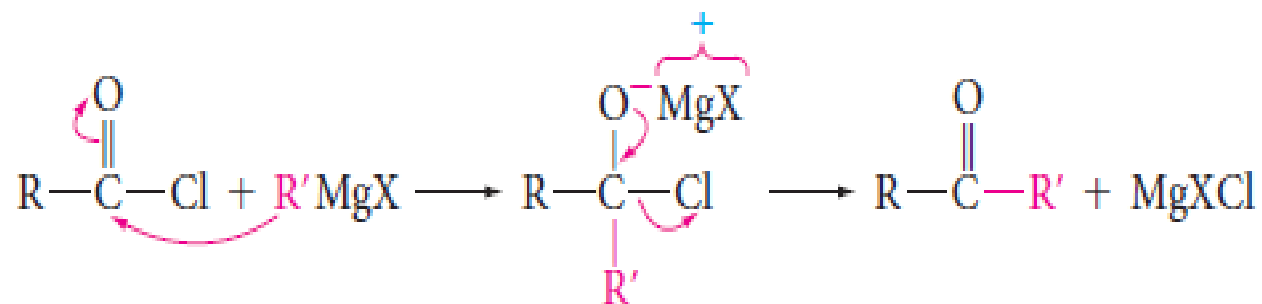




4. Acyl halides are used to synthesize aromatic ketones, through Friedel–Crafts acylation of aromatic rings.

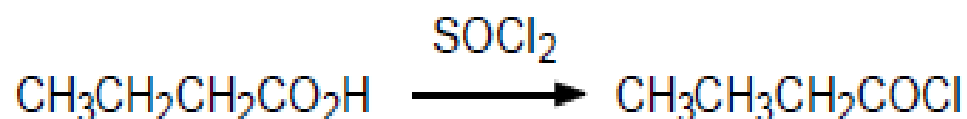


5. Acyl halides also react with Grignard reagents to give tertiary alcohols.

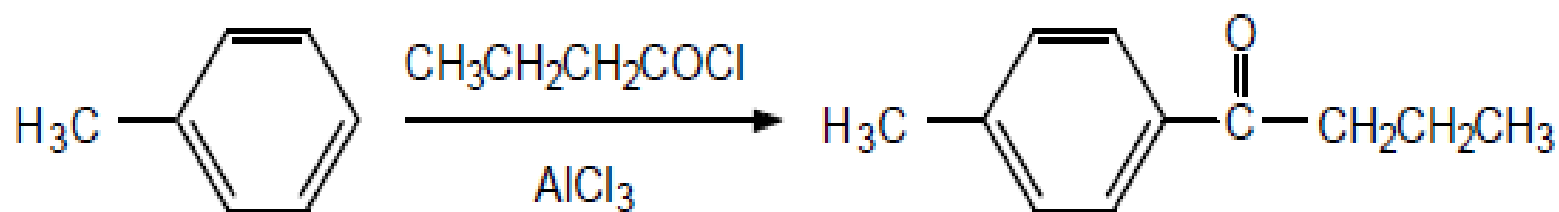


**PROBLEM 10.25** Devise a synthesis of 4-methylphenyl propyl ketone from toluene and butanoic acid as starting materials.

First prepare butanoyl chloride:

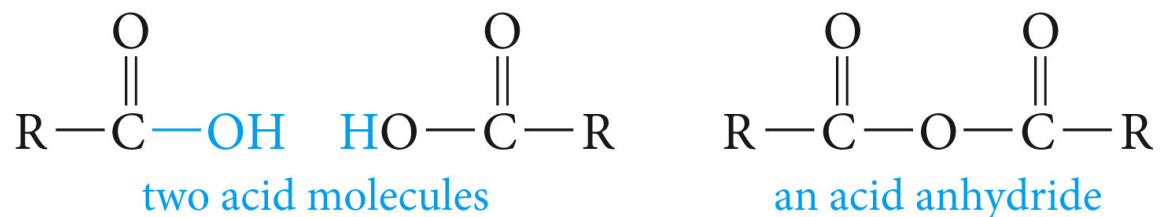


Then perform a Friedel–Crafts acylation:

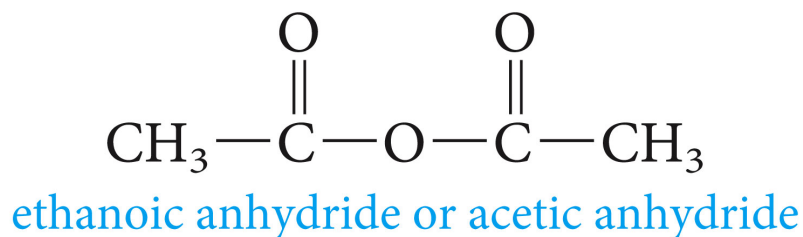


## 10.19 Acid Anhydrides

**Acid anhydrides** are carboxylic acid derivatives formed by condensing two carboxylic acid molecules.

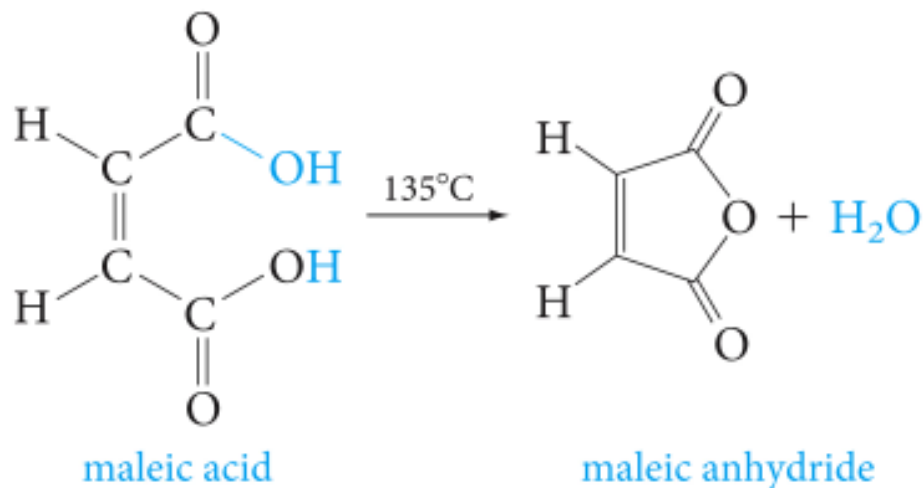


The name of an anhydride is obtained by naming the acid from which it is derived and replacing the word *acid* with *anhydride*.

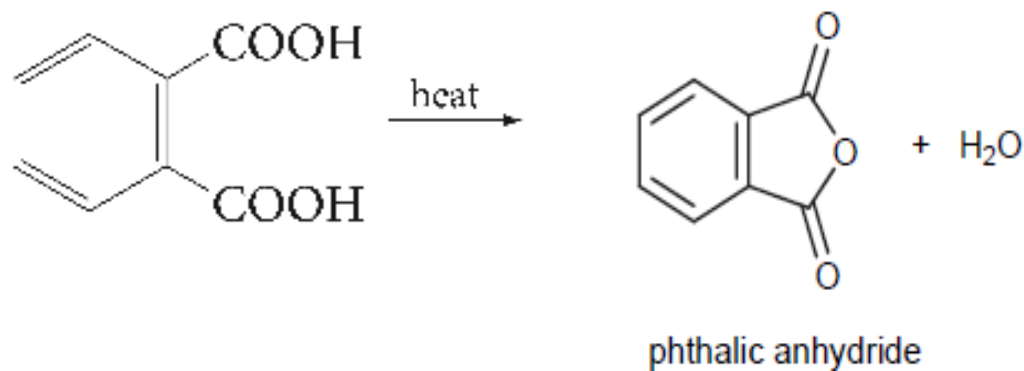


# Preparation

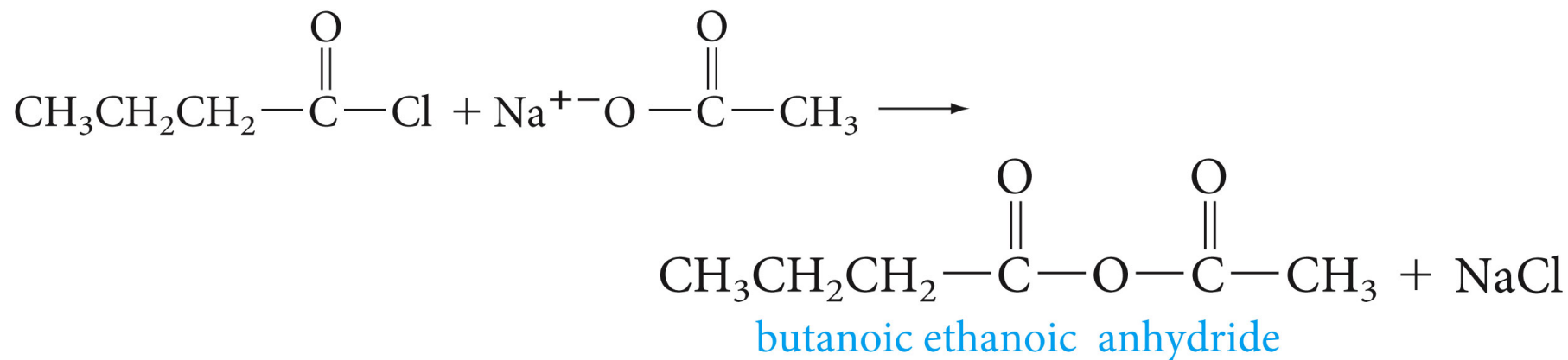
1. Anhydrides are prepared by dehydration of acids.



Predict the structure of the anhydride product of the reaction below.



2. Anhydrides can also be prepared from acid chlorides and carboxylate salts.

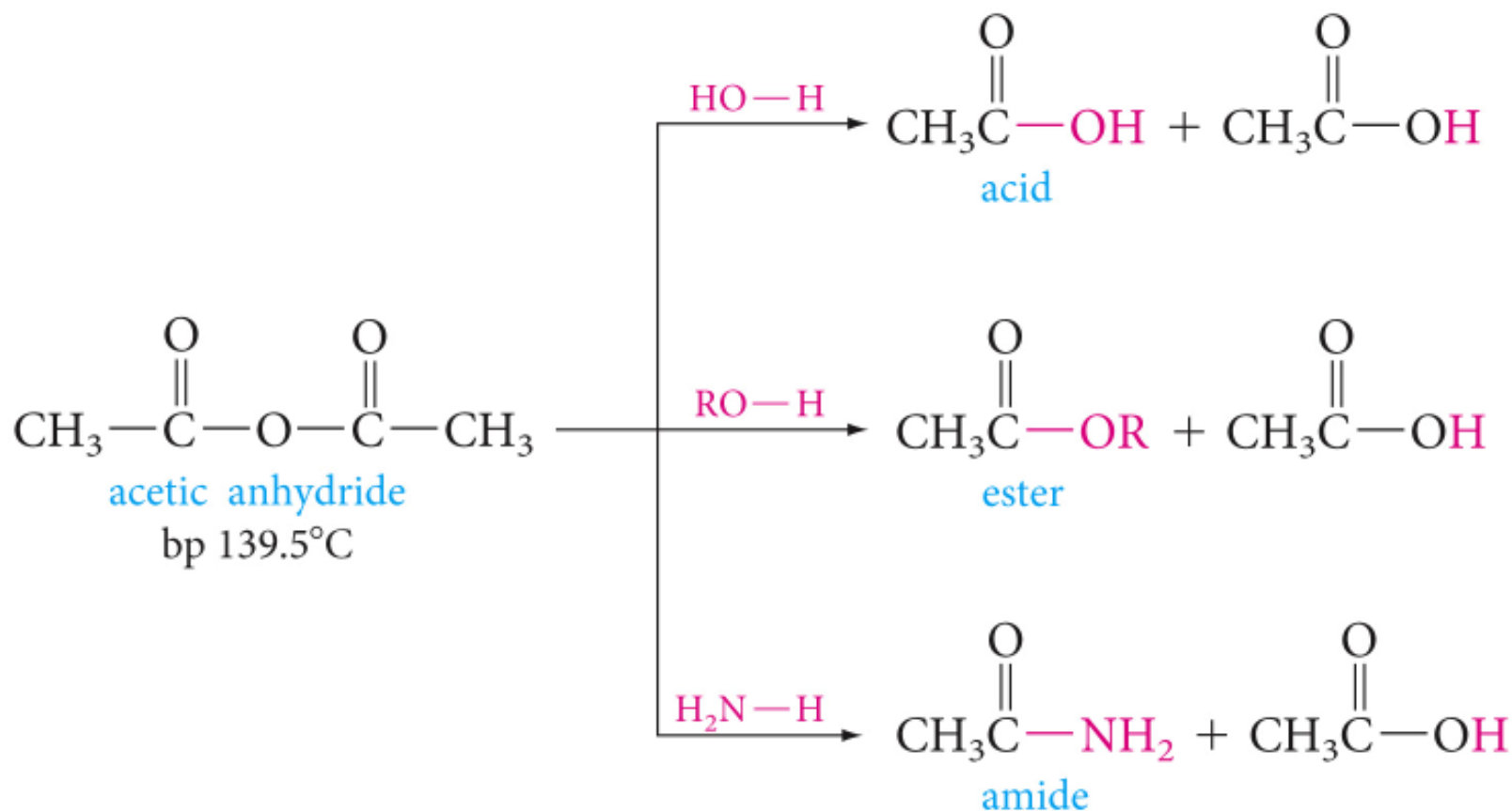


**Mixed anhydrides** are prepared from two different carboxylic acids.



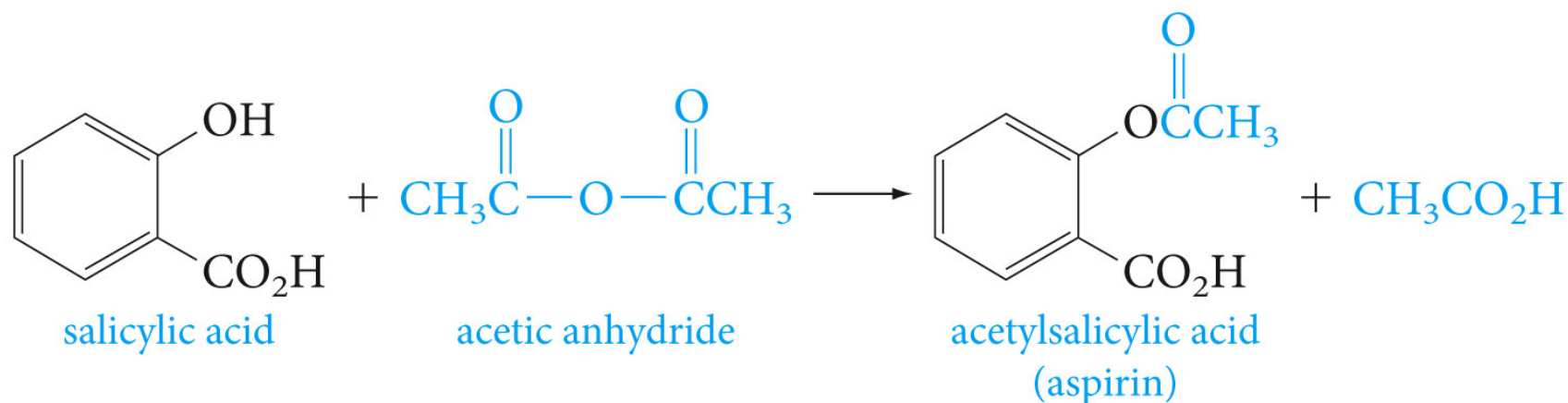
## Reactions

Anhydrides undergo nucleophilic acyl substitution reactions. They are more reactive than esters, but less reactive than acyl halides, toward nucleophiles. Below are some typical reactions with acetic anhydride



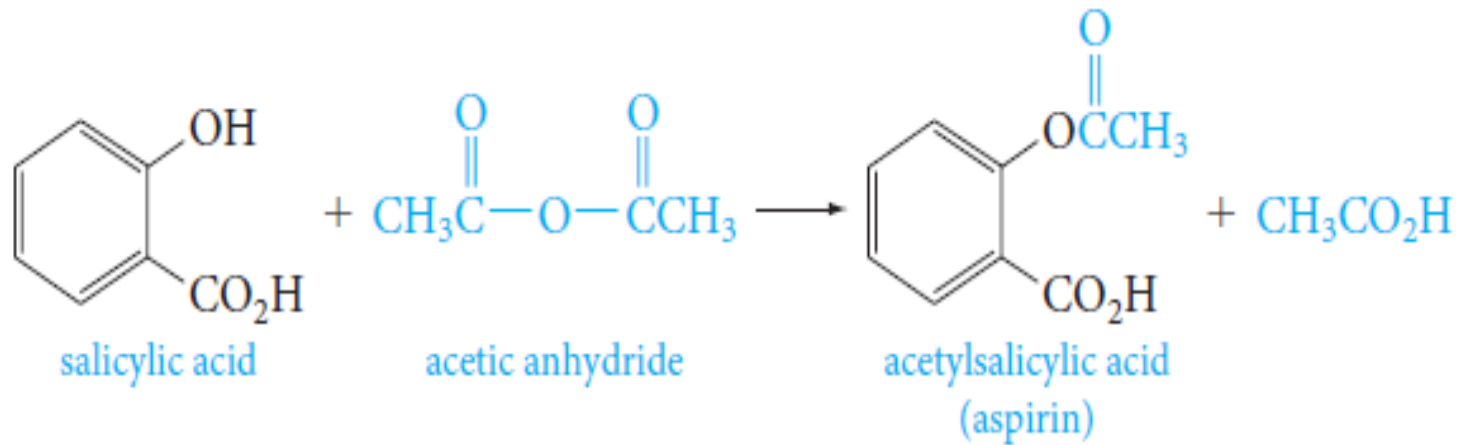
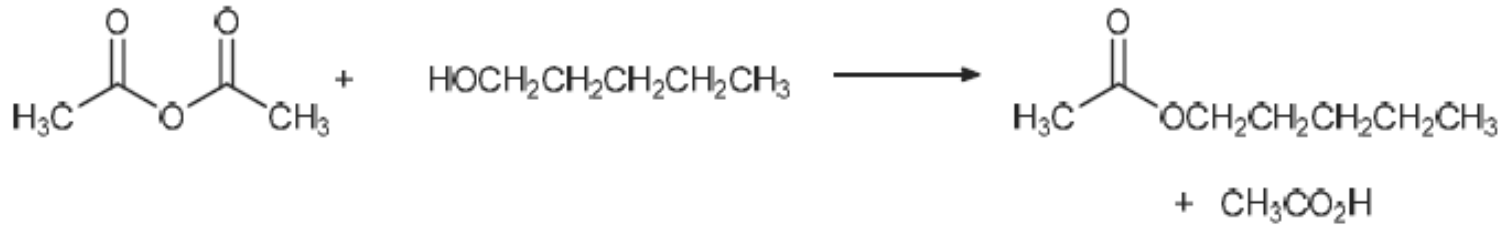


Aspirin can be prepared by the reaction of acetic anhydride with salicylic acid (o-hydroxybenzoic acid).



**PROBLEM 10.29** Write an equation for the reaction of acetic anhydride with 1-pentanol (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH).

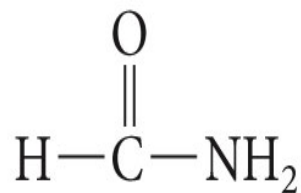




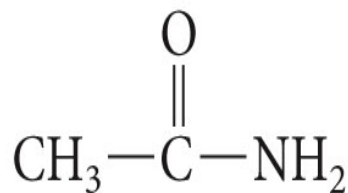
## 10.20 Amides

Amides are carboxylic acid derivatives in which the -OH group is replaced by -NH<sub>2</sub>, -NHR, or -NR<sub>2</sub>.

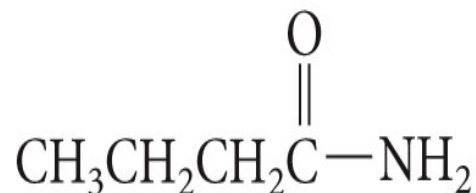
**Amides** are the least reactive of the common carboxylic acid derivatives.



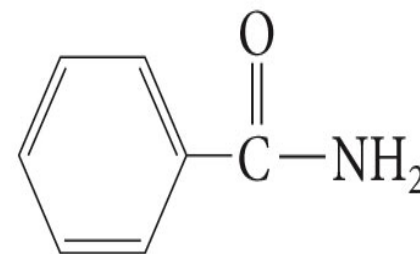
formamide  
(methanamide)



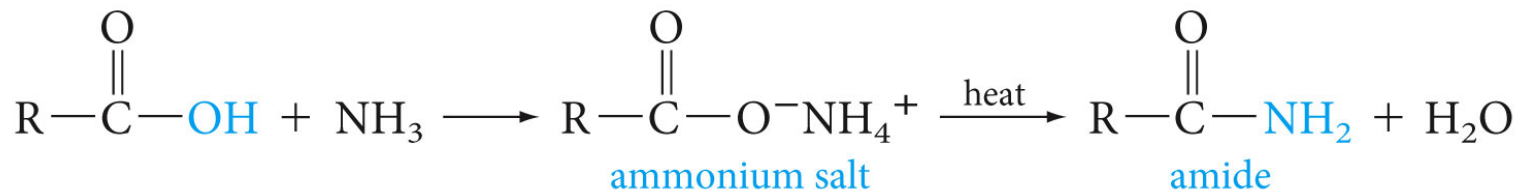
acetamide  
(ethanamide)



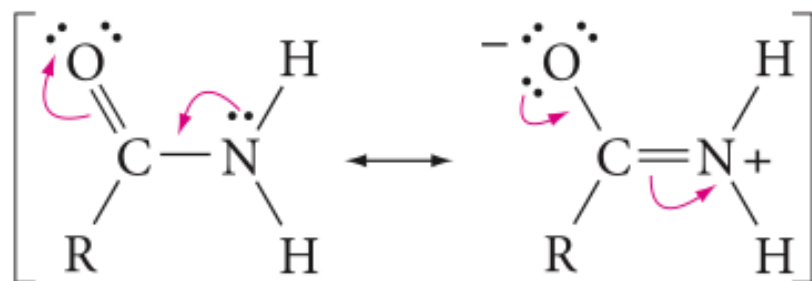
butanamide



benzamide  
(benzenecarboxamide)

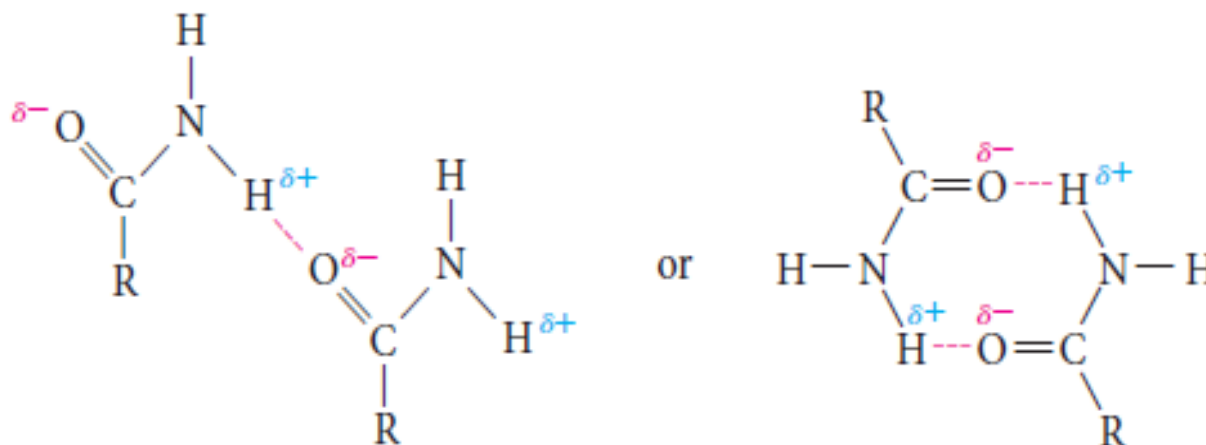


Amides have planar geometry, this is because of the C-N double bond character resulting from the resonance.

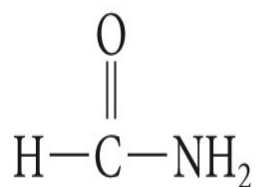


amide resonance

As the dipolar resonance contributor suggests, amides are highly polar and form strong hydrogen bonds.



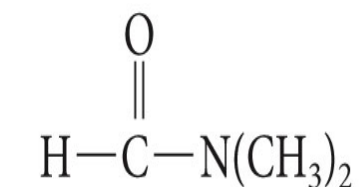
Amides have exceptionally high boiling points for their molecular weights, although alkyl substitution on the nitrogen lowers the boiling and melting points by decreasing the hydrogen-bonding possibilities, as shown in the following two pairs of compounds:



formamide

bp 210°C

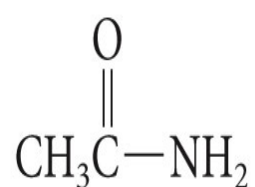
mp 2.5°C



*N,N*-dimethylformamide

153°C

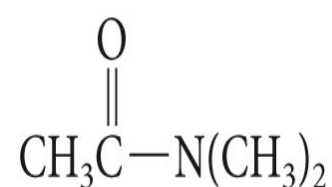
-60.5°C



acetamide

222°C

81°C



*N,N*-dimethylacetamide

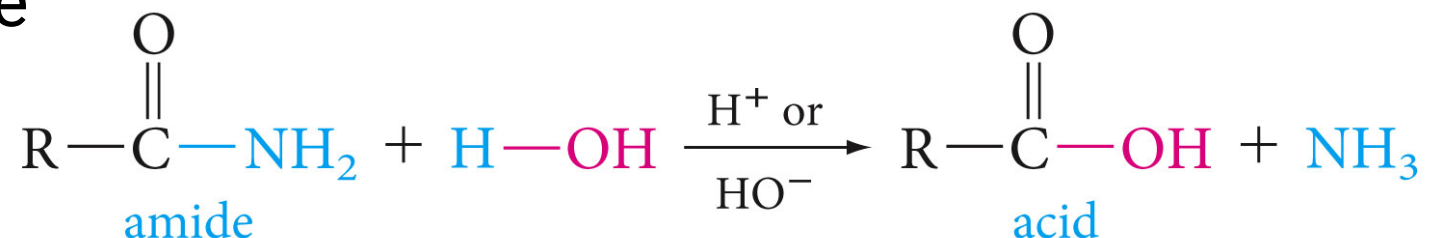
165°C

-20°C



## Reactions of amides:

-Like other acid derivatives, amides react with nucleophiles. Above is an example of hydrolysis of an amide



- Amides can be reduced to primary amines by Lithium aluminum hydride

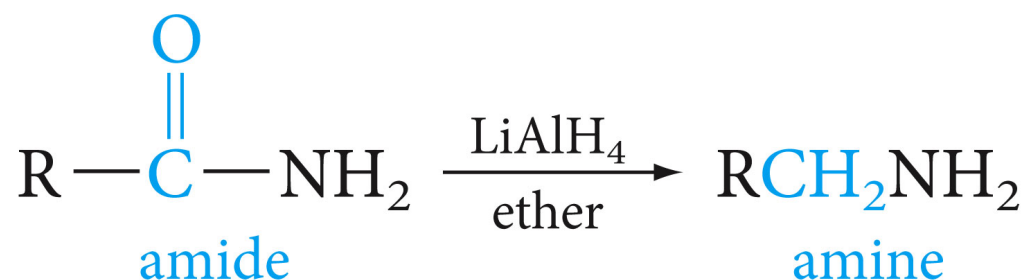


Table 10.5 ■ Reactions of Acid Derivatives with Certain Nucleophiles

Acid derivative	Nucleophile		
	HOH (hydrolysis)	R'OH (alcoholysis)	NH <sub>3</sub> (ammonolysis)
$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{Cl} \\ \text{acyl halide} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{OH} + \text{HCl} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{OR}' + \text{HCl} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{NH}_2 + \text{NH}_4^+\text{Cl}^- \end{array}$
$\begin{array}{c} \text{O} \qquad \text{O} \\ \parallel \qquad \parallel \\ \text{R}-\text{C}-\text{O}-\text{C}-\text{R} \\ \text{acid anhydride} \end{array}$	$2 \begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{OH} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{OR}' + \text{RCO}_2\text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{NH}_2 + \text{RCO}_2\text{H} \end{array}$
$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{O}-\text{R}'' \\ \text{ester} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{OH} + \text{R}''\text{OH} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{OR}' + \text{R}''\text{OH} \\ \text{(ester interchange)} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{NH}_2 + \text{R}''\text{OH} \end{array}$
$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{NH}_2 \\ \text{amide} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{R}-\text{C}-\text{OH} + \text{NH}_3 \end{array}$	$\text{---}$	$\text{---}$
<i>Main organic product</i>	acid	ester	amide

decreasing reactivity ↓

