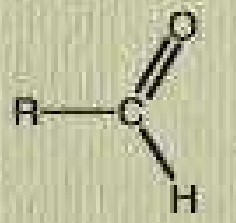
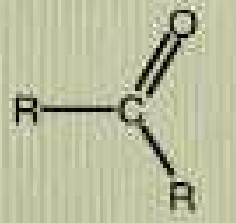
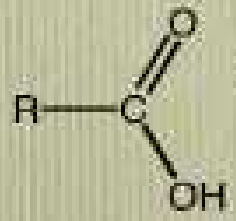
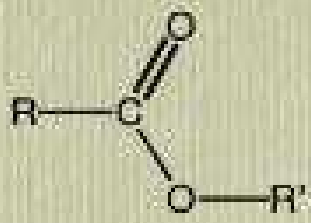
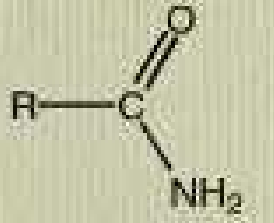
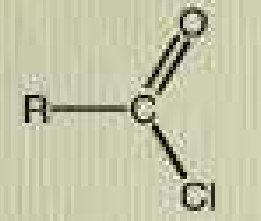
Carboxylic acids and Their Derivatives

Carbonyl containing compounds

Formula	Family
	Aldehyde
	Ketone
	Carboxylic acid

Formula	Family
	Ester
	Amide
	Acid Chloride

Examples

$CH_3CH_2CH_2CH(CH_3)CH_2COOH$

Parent compound = 6 carbons, hexane

Drop -e and add -oic acid

hexanoic acid

Carboxylic carbon is #1

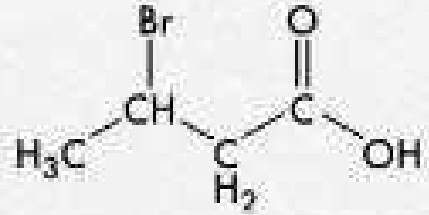
Name remaining substituents

3-methylhexanoic acid

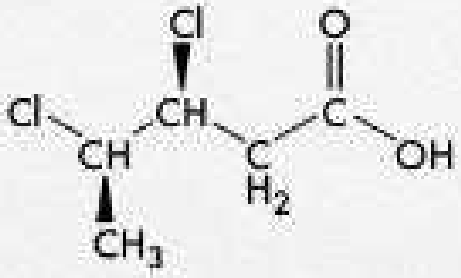
TABLE 10.1 ALIPHATIC CARBOXYLIC ACIDS

Carbon atoms	Formula	Source	Common name	IUPAC name
1	HCOOH	ants (Latin, *formica*)	formic acid	methanoic acid
2	CH_3COOH	vinegar (Latin, *acetum*)	acetic acid	ethanoic acid
3	CH_3CH_2COOH	milk (Greek, *protos pion*, first fat)	propionic acid	propanoic acid
4	$CH_3(CH_2)_2COOH$	butter (Latin, *butyrum*)	butyric acid	butanoic acid
5	$CH_3(CH_2)_3COOH$	valerian root (Latin, *valere*, to be strong)	valeric acid	pentanoic acid
6	$CH_3(CH_2)_4COOH$	goats (Latin, *caper*)	caproic acid	hexanoic acid
7	$CH_3(CH_2)_5COOH$	vine blossom (Greek, *oenanthe*)	enanthic acid	heptanoic acid
8	$CH_3(CH_2)_6COOH$	goats (Latin, *caper*)	caprylic acid	octanoic acid
9	$CH_3(CH_2)_7COOH$	pelargonium (an herb with stork-shaped seed capsules; Greek, *pelargos*, stork)	pelargonic acid	nonanoic acid
10	$CH_3(CH_2)_8COOH$	goats (Latin, *caper*)	capric acid	decanoic acid

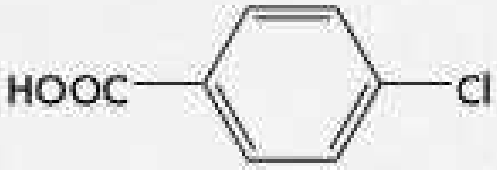
Examples



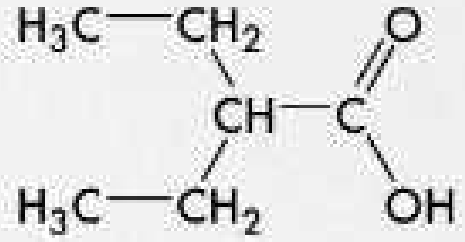
3-bromobutanoic acid



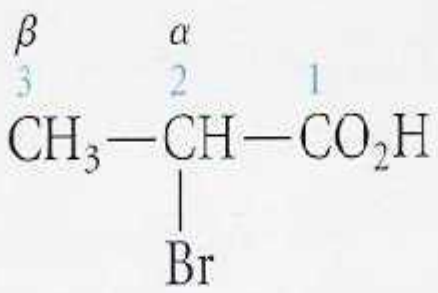
3,4-dichloropentanoic acid



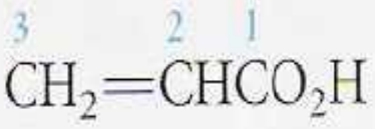
p-chlorobenzoic acid
or 4-chlorobenzoic acid



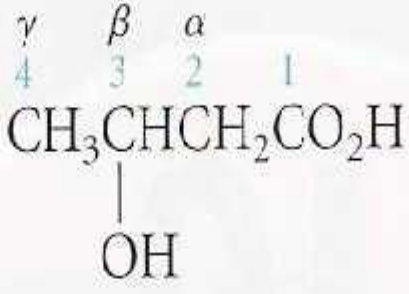
2-ethylbutanoic acid



2-bromopropanoic acid
(α-bromopropionic acid)

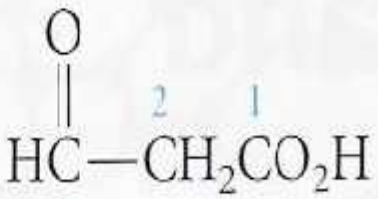


propenoic acid
(acrylic acid)

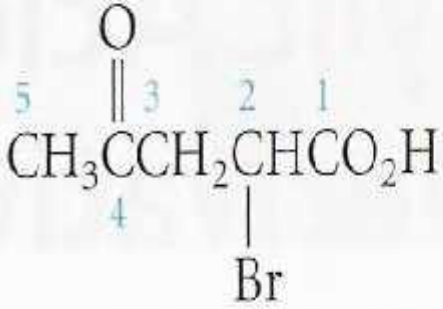


3-hydroxybutanoic acid
(β-hydroxybutyric acid)

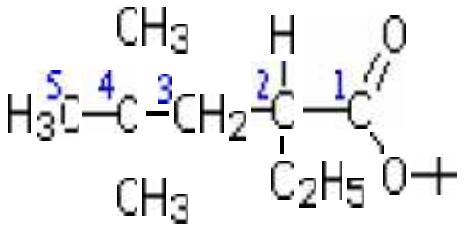
The carboxyl group has priority over alcohol, aldehyde, or ketone functionality in naming. In the latter cases, the prefix *oxo-* is used to locate the carbonyl group of the aldehyde or ketone, as in these examples:



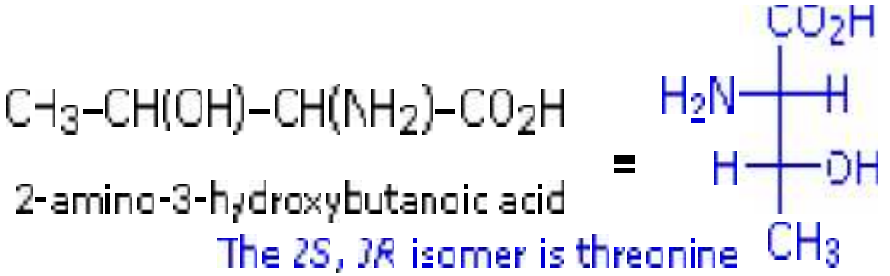
3-oxopropanoic acid



2-bromo-4-oxopentanoic acid

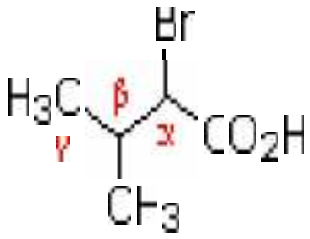


2-ethyl-4,4-dimethylpentaroic acid



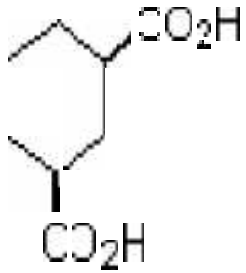
2-amino-3-hydroxybutanoic acid

The *2S, 3R* isomer is threonine



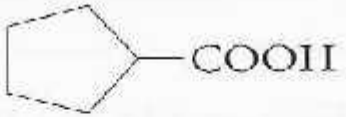
2-bromo-3-methylbutanoic acid

α-bromoisovaleric acid

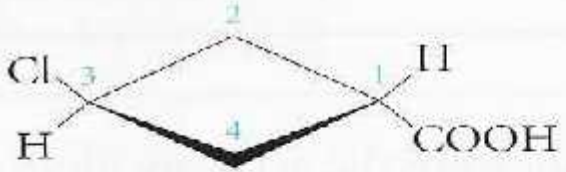


cis-1,3-cyclohexanedicarboxylic acid

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

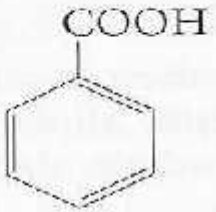


cyclopentanecarboxylic acid

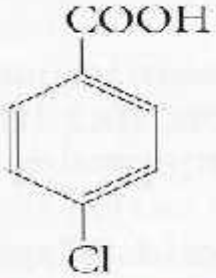


trans-3-chlorocyclobutanecarboxylic acid

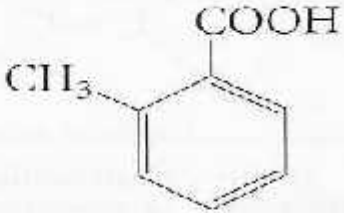
Aromatic acids are named by attaching the suffix *-oic acid* or *-ic acid* to an appropriate prefix derived from the aromatic hydrocarbon.



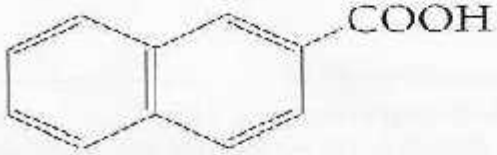
benzoic acid
(benzenecarboxylic acid)



p-chlorobenzoic acid
(4-chlorobenzenecarboxylic acid)



o-toluic acid
(2-methylbenzenecarboxylic acid)



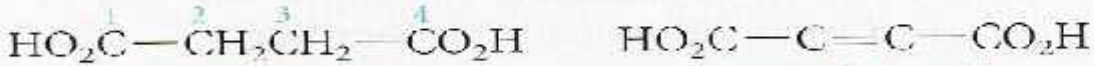
2-naphthoic acid
(2-naphthalenecarboxylic acid)

Diacids

TABLE 10.2 ALIPHATIC DICARBOXYLIC ACIDS

Formula	Common name	Source	IUPAC name
HOOC—COOH	oxalic acid	plants of the *oxalic* family (for example, sorrel)	ethanedioic acid
HOOC—CH_2—COOH	malonic acid	apple (Gk. *malon*)	propanedioic acid
HOOC—$(CH_2)_2$—COOH	succinic acid	amber (L. *succinum*)	butanedioic acid
HOOC—$(CH_2)_3$—COOH	glutaric acid	gluten	pentanedioic acid
HOOC—$(CH_2)_4$—COOH	adipic acid	fat (L. *adeps*)	hexanedioic acid
HOOC—$(CH_2)_5$—COOH	pimelic acid	fat (Gk. *pimele*)	heptanedioic acid

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



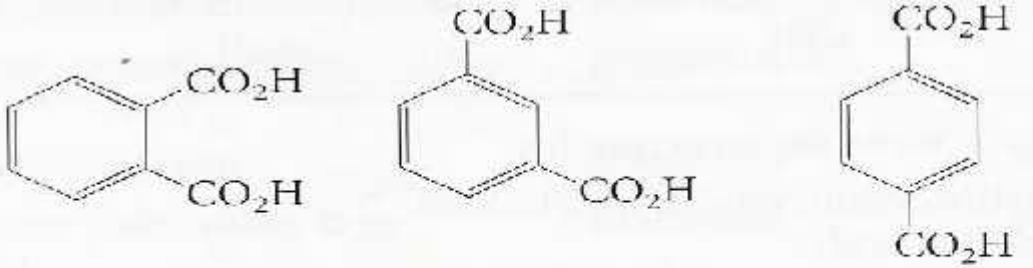
butanedioic acid — butynedioic acid

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

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

maleic acid (*cis*-2-butenedioic acid) — fumaric acid (*trans*-2-butenedioic acid)

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



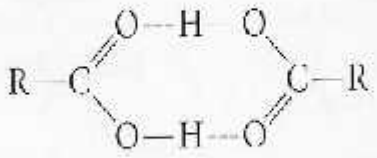
phthalic acid — isophthalic acid — terephthalic acid

Physical Properties of carboxylic acids

Hydrogen bonding

Solubility in water

(lower acids)



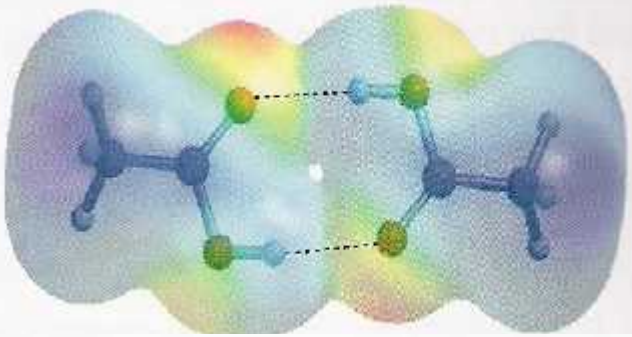


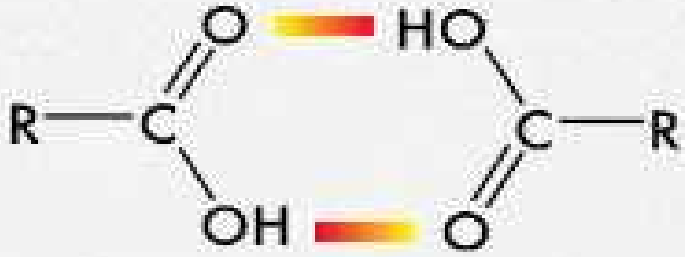
TABLE 10.3 PHYSICAL PROPERTIES OF SOME CARBOXYLIC ACIDS

Name	bp, °C	mp, °C	Solubility, g/100 g H_2O at 25°C
formic acid	101	8	miscible (∞)
acetic acid	118	17	
propanoic acid	141	−22	
butanoic acid	164	−8	
hexanoic acid	205	−1.5	1.0
octanoic acid	240	17	0.06
decanoic acid	270	31	0.01
benzoic acid	249	122	0.4 (but 6.8 at 95°C)

Properties

Acids

- Very polar with high boiling points
- Exhibit hydrogen bonding



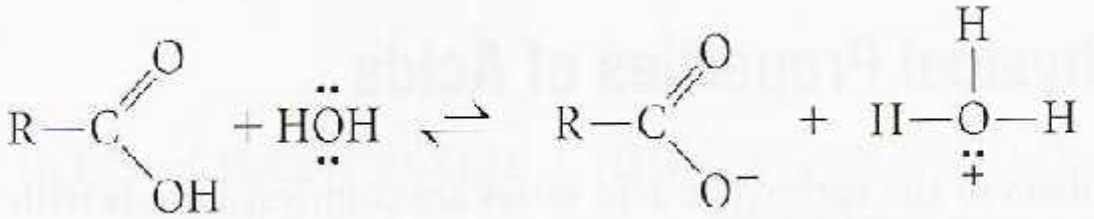
- Can dissociate - acid character

$$R\text{-}COOH \rightleftharpoons R\text{-}COO^- + H^+$$

Acidity of carboxylic acids

10.3 Acidity and Acidity Constants

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



(10.1)

Their acidity constant K_a in water is given by the expression

$$K_a = \frac{[RCO_2^-][H_3O^+]}{[RCO_2H]} \qquad (10.2)$$

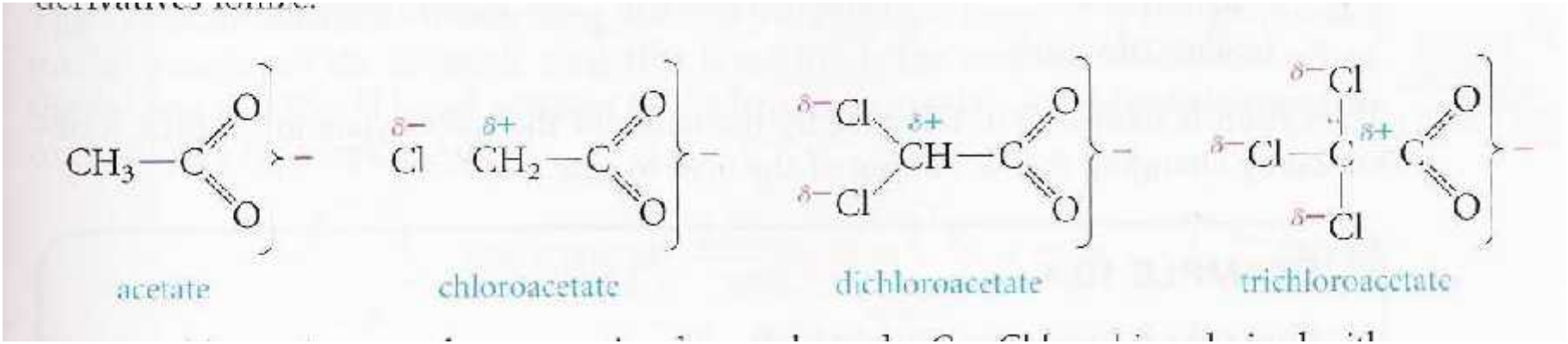
$pK_a = -\log K_a$

As K_a increase or pK_a decrease, the acidity increase

TABLE 10.4 THE IONIZATION CONSTANTS OF SOME ACIDS

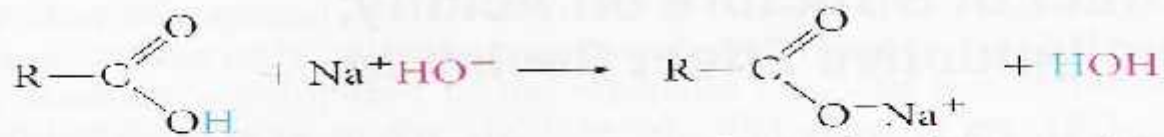
Name	Formula	K_a	pK_a
formic acid	HCOOH	2.1×10^{-4}	3.68
acetic acid	CH_3COOH	1.8×10^{-5}	4.74
propanoic acid	CH_3CH_2COOH	1.4×10^{-5}	4.85
butanoic acid	$CH_3CH_2CH_2COOH$	1.6×10^{-5}	4.80
chloroacetic acid	$ClCH_2COOH$	1.5×10^{-3}	2.82
dichloroacetic acid	$Cl_2CHCOOH$	5.0×10^{-2}	1.30
trichloroacetic acid	CCl_3COOH	2.0×10^{-1}	0.70
2-chlorobutanoic acid	$CH_3CH_2CHClCOOH$	1.4×10^{-3}	2.85
3-chlorobutanoic acid	$CH_3CHClCH_2COOH$	8.9×10^{-5}	4.05
benzoic acid	C_6H_5COOH	6.6×10^{-5}	4.18
o-chlorobenzoic acid	*o*-Cl—C_6H_4COOH	12.5×10^{-4}	2.90
m-chlorobenzoic acid	*m*-Cl—C_6H_4COOH	1.6×10^{-4}	3.80
p-chlorobenzoic acid	*p*-Cl—C_6H_4COOH	1.0×10^{-4}	4.00
p-nitrobenzoic acid	*p*-NO_2—C_6H_4COOH	4.0×10^{-4}	3.40
phenol	C_6H_5OH	1.0×10^{-10}	10.00
ethanol	CH_3CH_2OH	1.0×10^{-16}	16.00
water	HOH	1.8×10^{-16}	15.74

Resonance and Inductive effect



Conversion of acids to salts

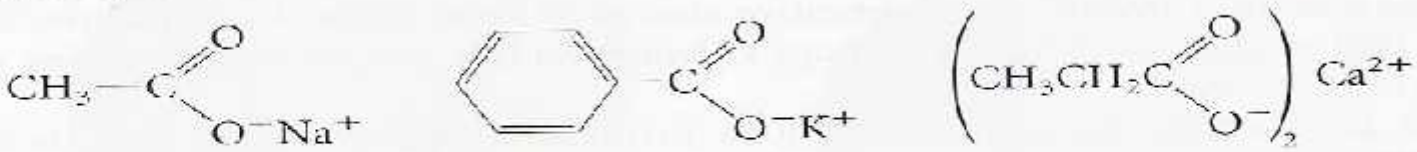
Carboxylic acids, when treated with a strong base, form carboxylate salts. For example,



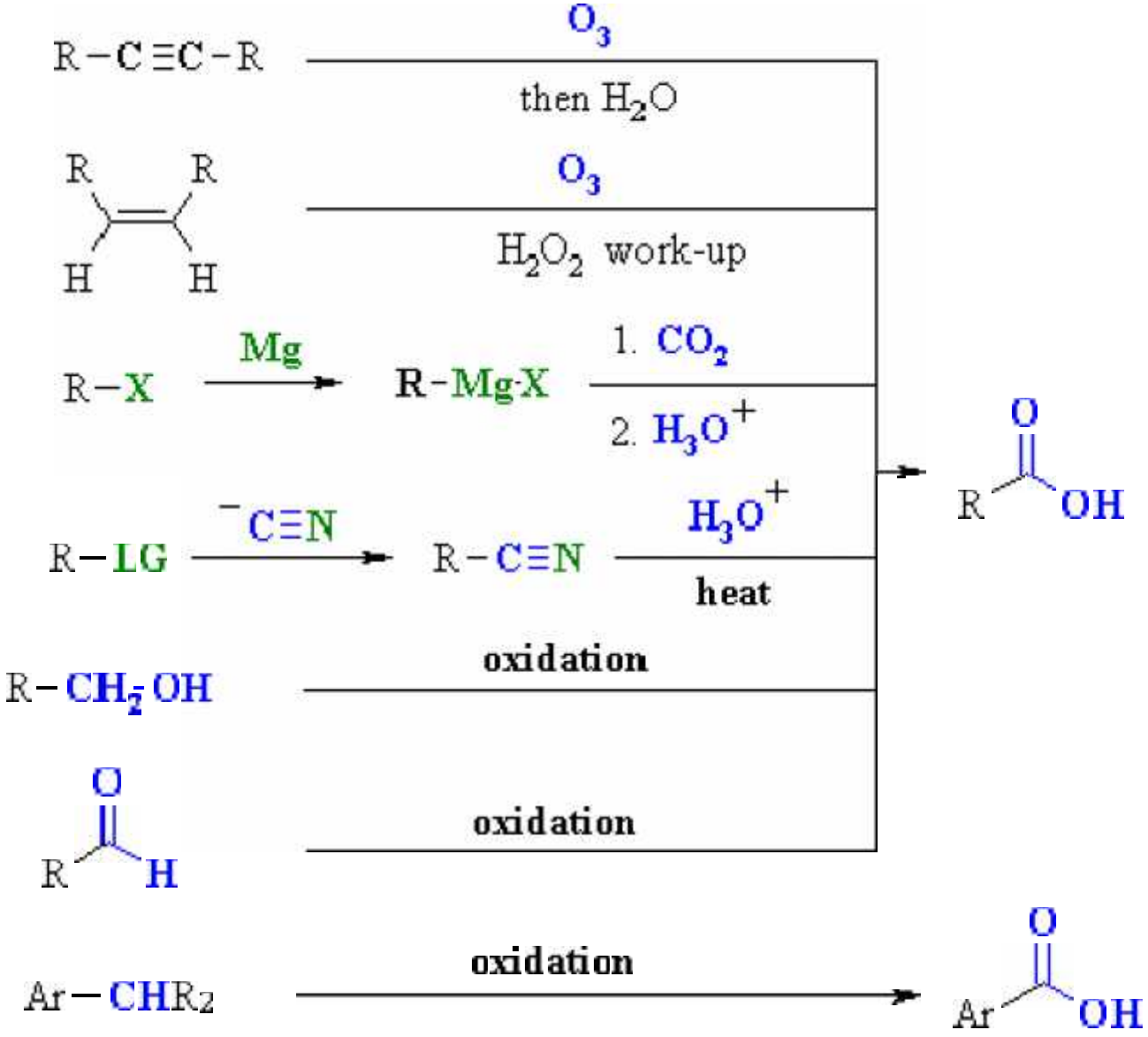
(10.5)

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

Carboxylate salts are named as shown in the following examples:

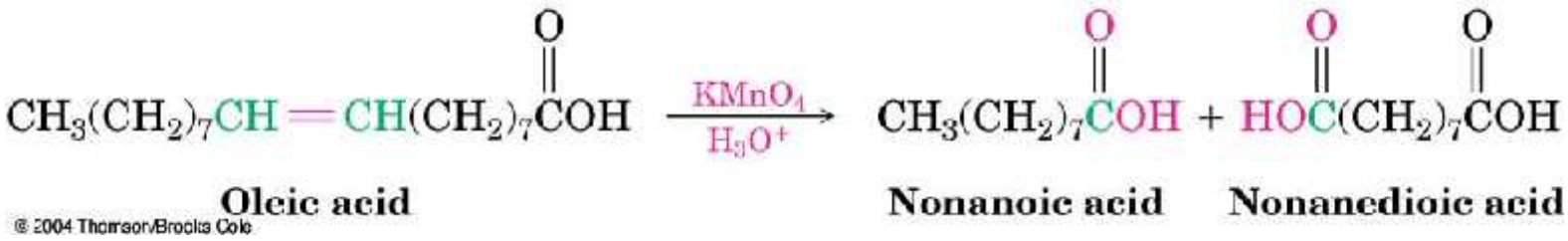


Preparation of carboxylic acids



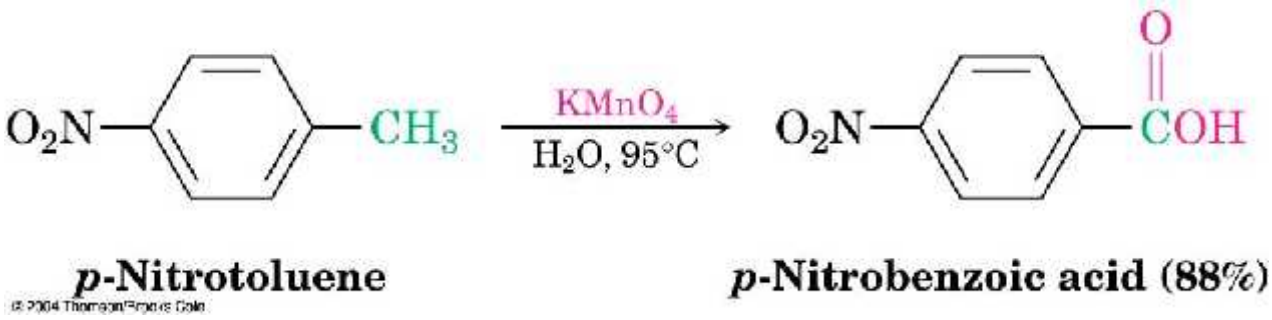
From Alkenes

- Oxidative cleavage of an alkene with $KMnO_4$ gives a carboxylic acid if the alkene has at least one vinylic hydrogen (see Section 7.8)



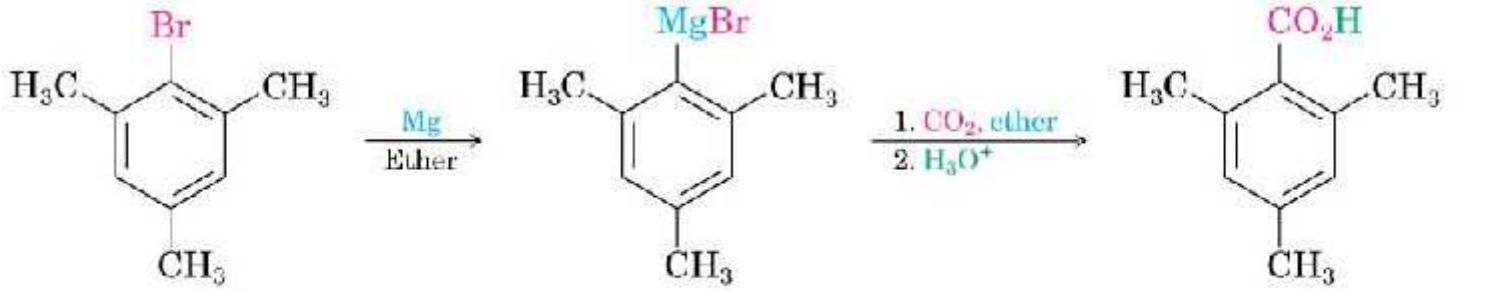
20.6 Preparation of Carboxylic Acids

- Oxidation of a substituted alkylbenzene with $KMnO_4$ or $Na_2Cr_2O_7$ gives a substituted benzoic acid (see Section 16.10)
- 1° and 2° alkyl groups can be oxidized, but tertiary groups are not



Carboxylation of Grignard Reagents

- Grignard reagents react with dry CO_2 to yield a metal carboxylate
- Limited to alkyl halides that can form Grignard reagents (see 17.6)

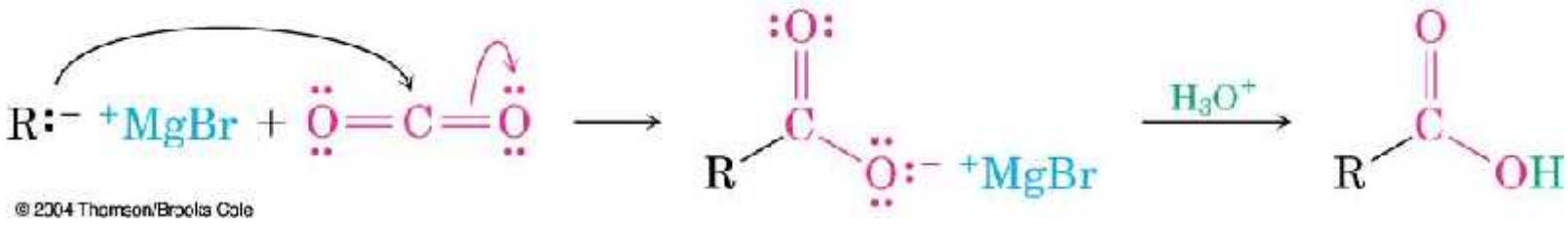


1-Bromo-2,4,6-trimethyl-benzene

2,4,6-Trimethylbenzoic acid (87%)

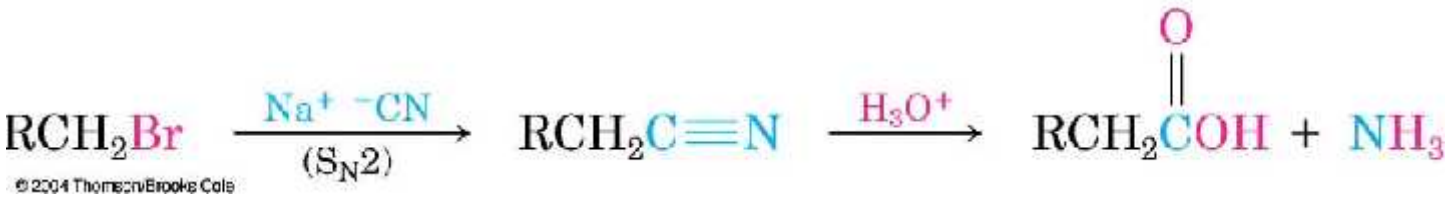
Mechanism of Grignard Carboxylation

- The organomagnesium halide adds to C=O of carbon dioxide
- Protonation by addition of aqueous HCl in a separate step gives the free carboxylic acid



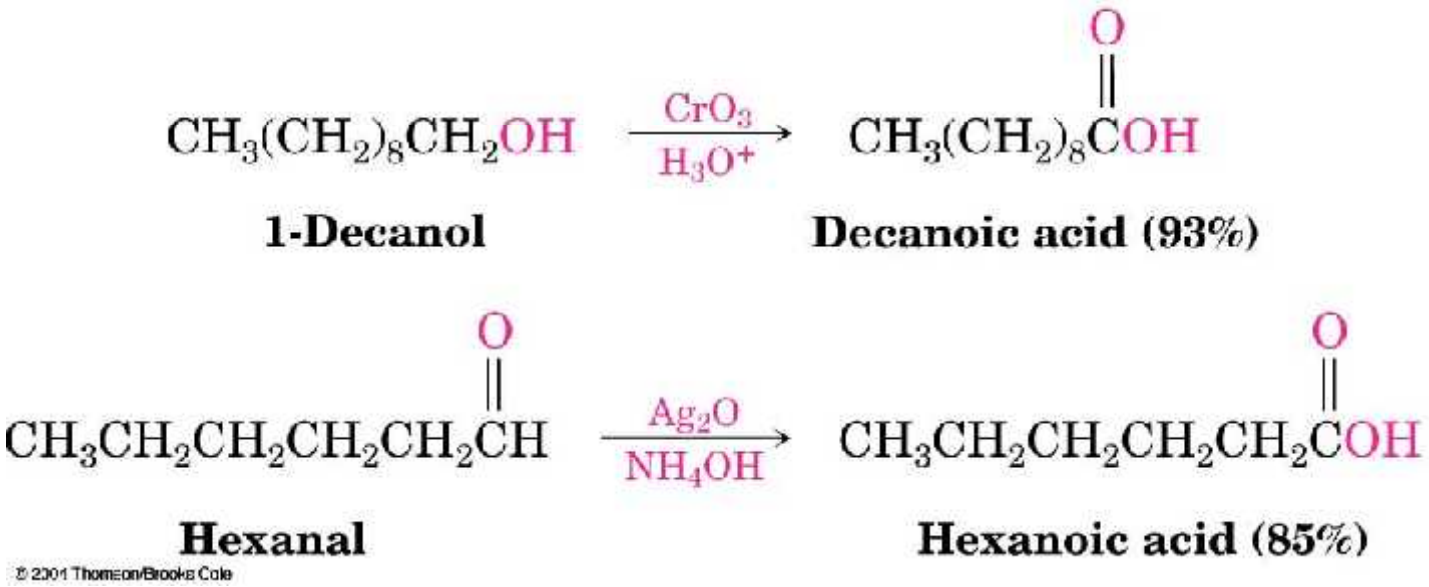
Hydrolysis of Nitriles

- Hot acid or base yields carboxylic acids
- Conversion of an alkyl halide to a nitrile (with cyanide ion) followed by hydrolysis produces a carboxylic acid with one more carbon ($RBr \rightarrow RC{\equiv}N \rightarrow RCO_2H$)
- Best with primary halides because elimination reactions occur with secondary or tertiary alkyl halides

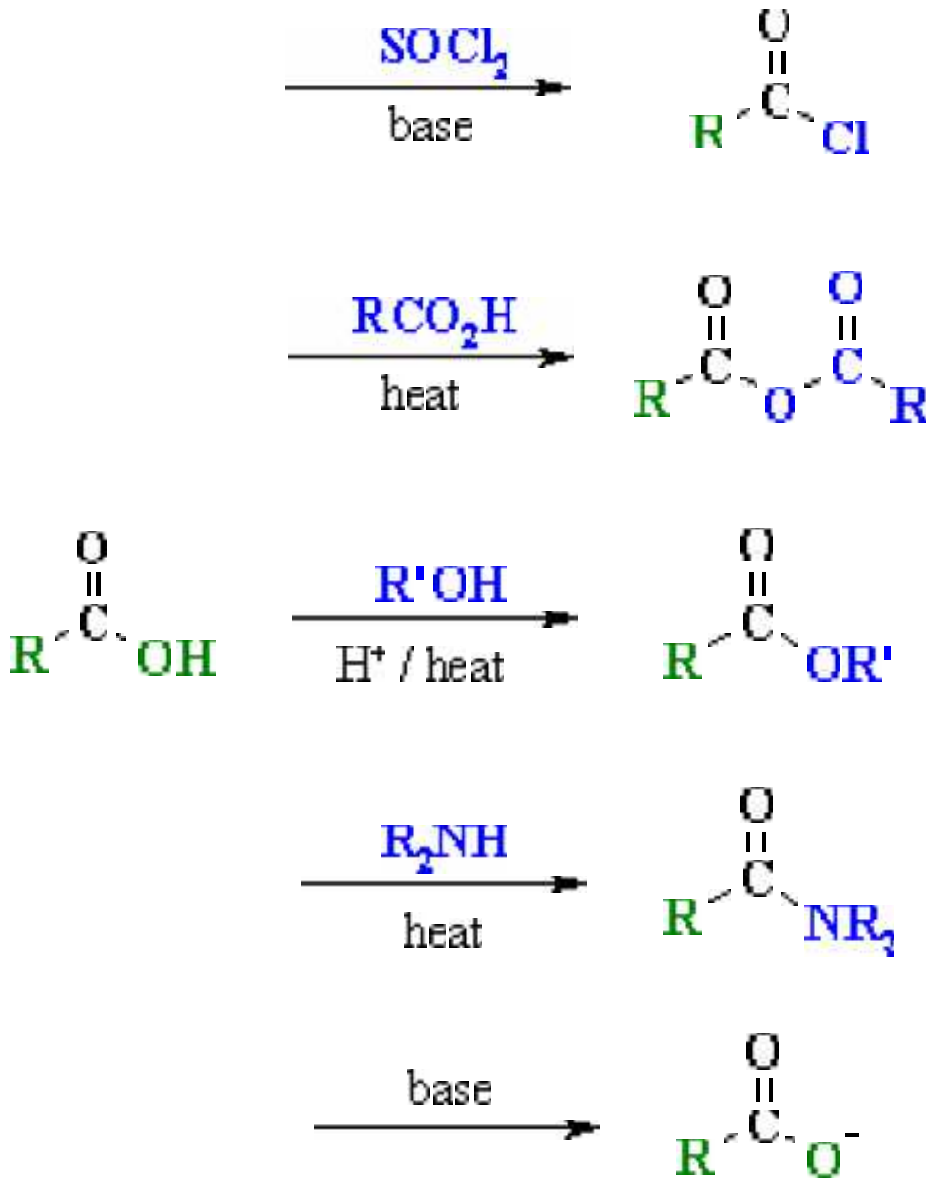


From Alcohols

- Oxidation of a primary alcohol or an aldehyde with CrO_3 in aqueous acid

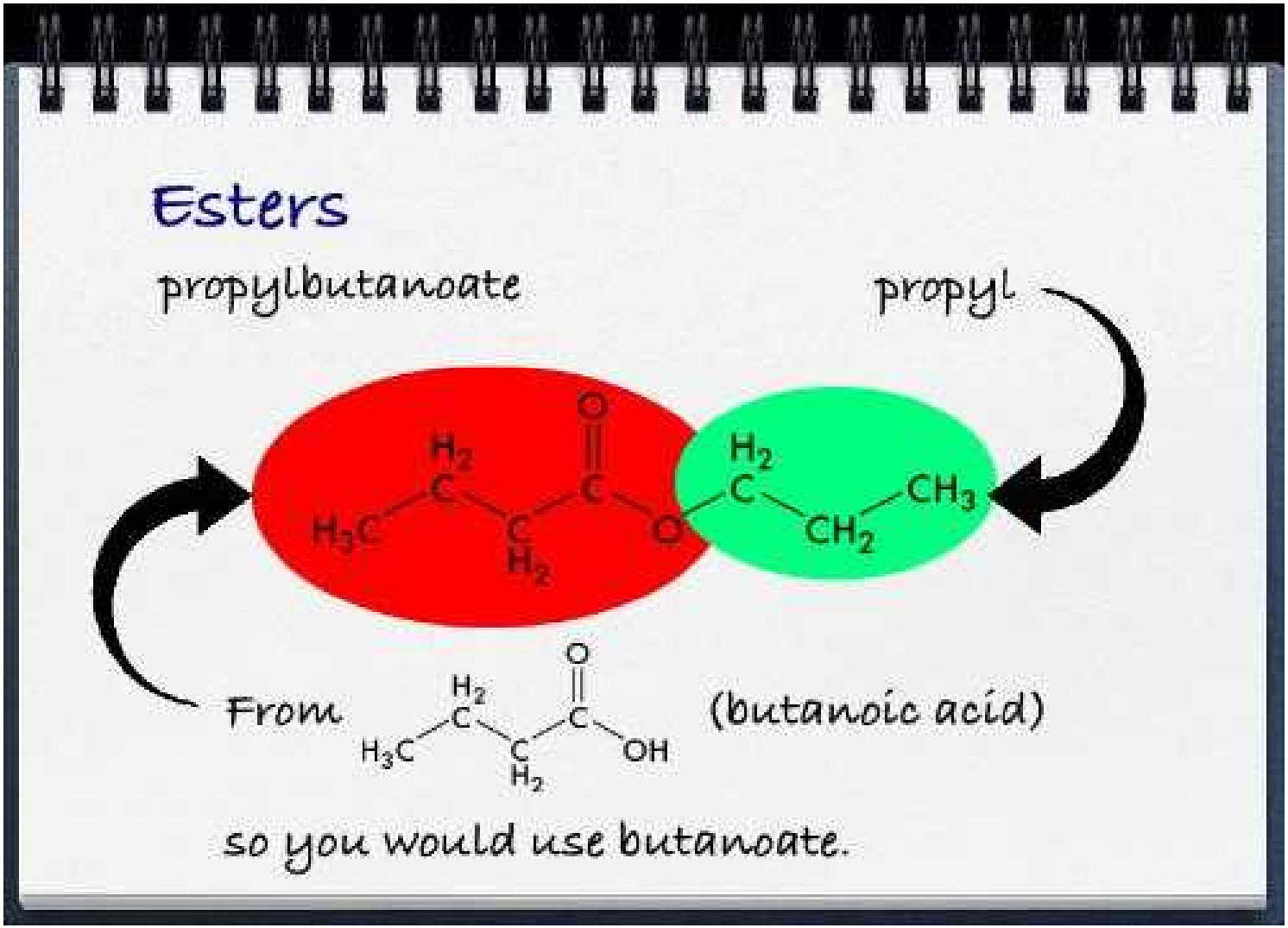


Reactions of carboxylic acids



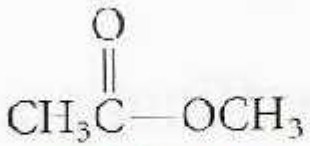
Esters

Nomenclature

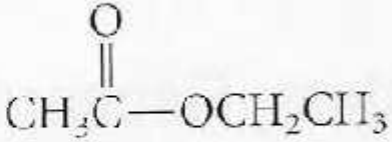


10.9 Esters

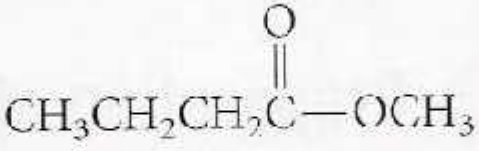
Esters are derived from acids by replacing the —OH group by an —OR group. They are named in a manner analogous to carboxylic acid salts. The R part of the —OR group is named first, followed by the name of the acid, with the *-ic* ending changed to *-ate*.



methyl acetate
(methyl ethanoate)
bp 57°C

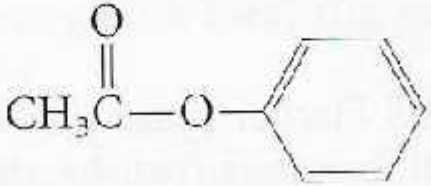


ethyl acetate
(ethyl ethanoate)
bp 77°C

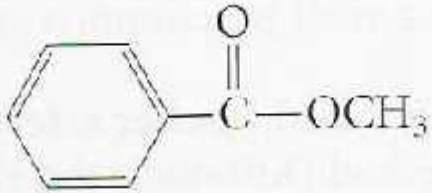


methyl butanoate
bp 102.3°C

Notice the different names of the following pair of isomeric esters, where the R and R′ groups are interchanged.

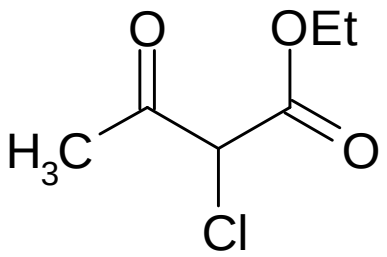


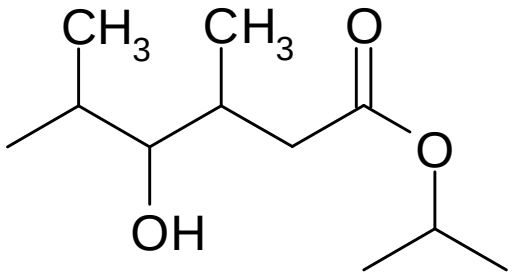
phenyl acetate
bp 195.7°C

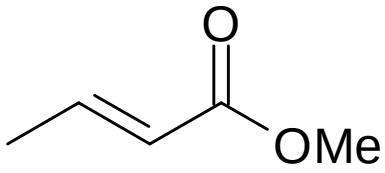


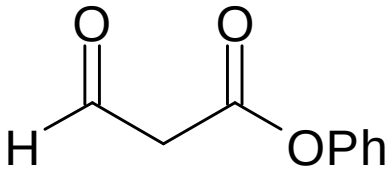
methyl benzoate
bp 196.6°C

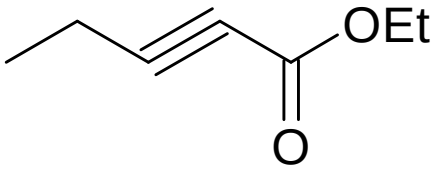
Examples





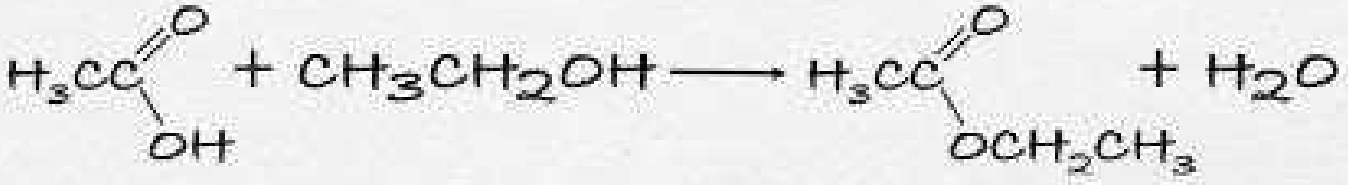




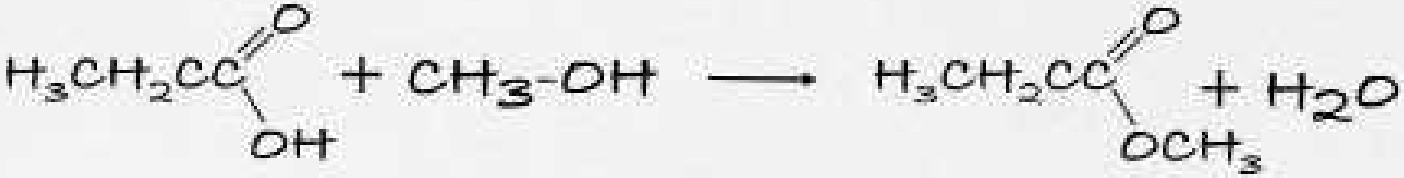


Reactions of carboxylic acids

Formation of Esters



ethyl ethanoate



methyl propanoate

Smelly stuff

methybutanoate

Apples

methythiobutanoate

Strawberries

ethybutanoate

Pineapples

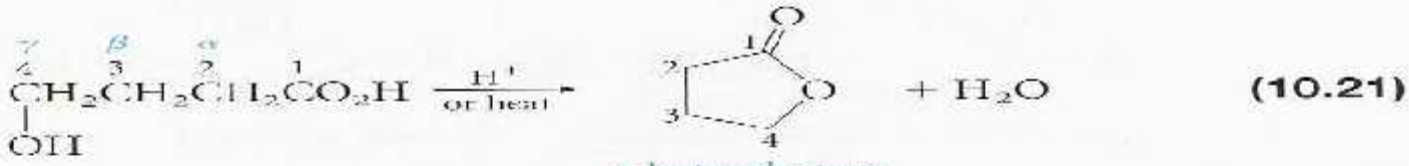
pentylbutanoate

Apricots

Lactones (Cyclic Esters)

10.12 Lactones

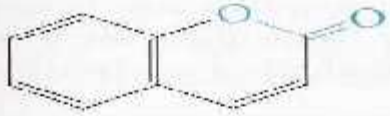
Hydroxy acids contain both functional groups required for ester formation. If these groups can come in contact through bending of the chain, they may react with one another to form **cyclic esters** called **lactones**. For example,



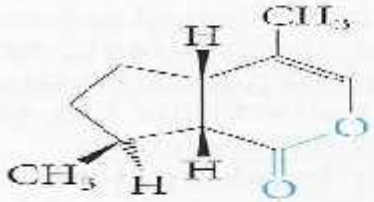
(10.21)

γ-butyrolactone

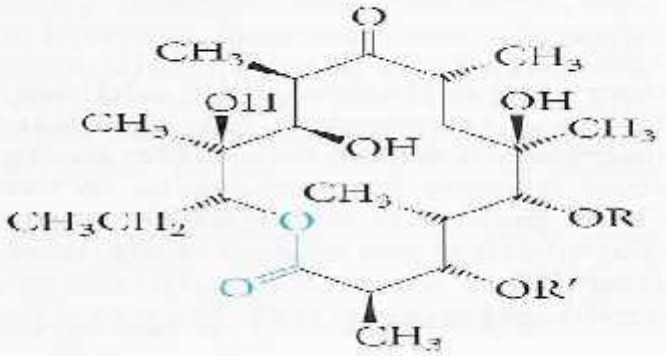
Most common lactones have five- or six-membered rings, although lactones with smaller or larger rings are known. Two examples of six-membered lactones from nature are **coumarin**, which is responsible for the pleasant odor of newly mown hay, and **nepetalactone**, the compound in catnip that excites cats. **Erythromycin**, widely used as an antibiotic, is an example of a macrocyclic lactone.[3]



coumarin



nepetalactone

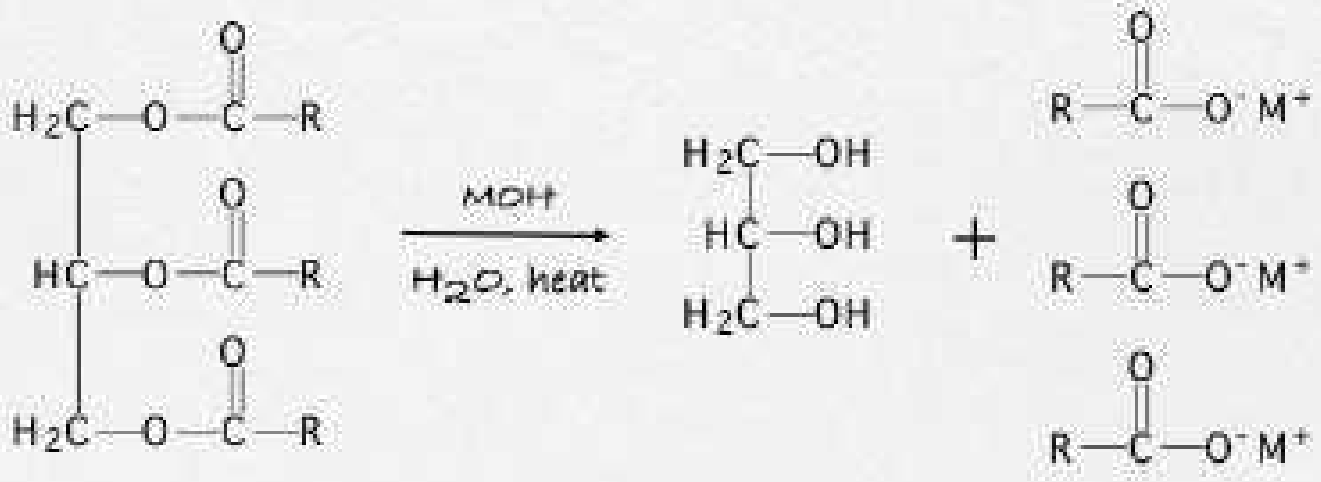


erythromycin

Reactions of carboxylic acids

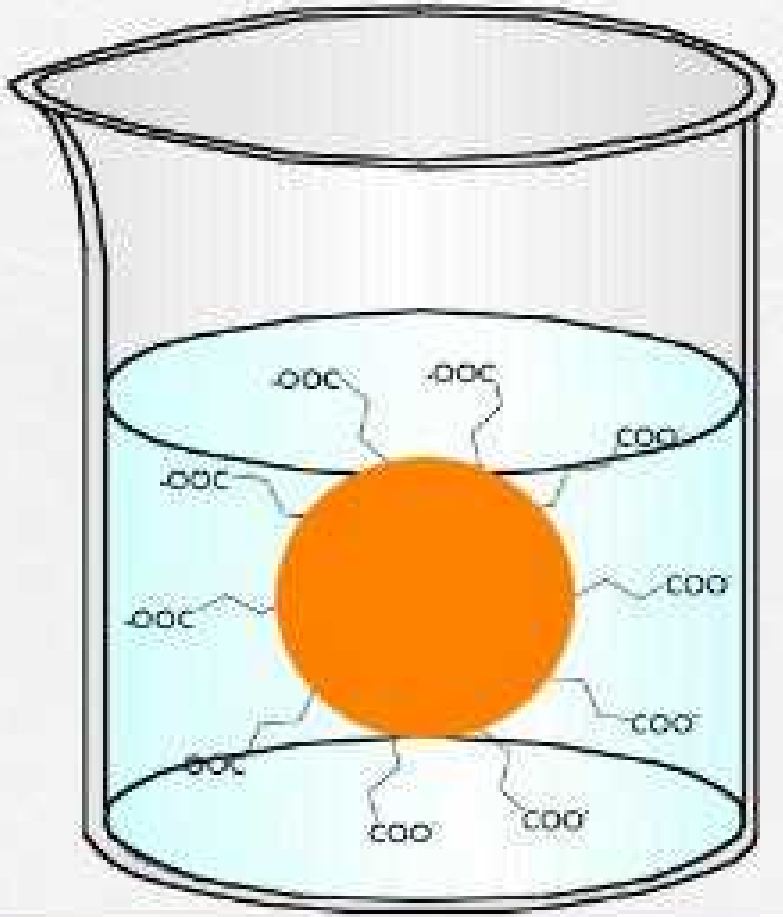
Soap formation

Produced from long-chain acids



$M = Na^+$ or K^+

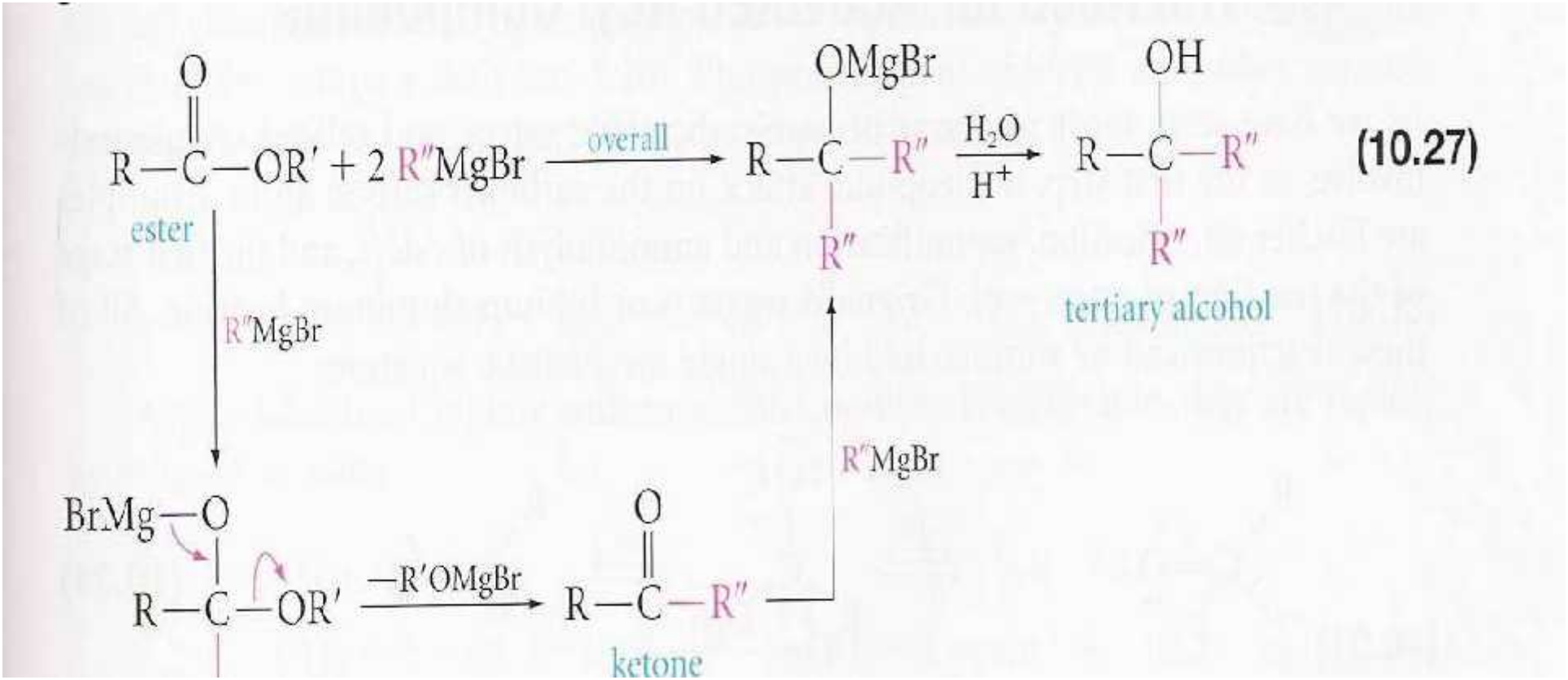
How soap works



Nonpolar tail dissolves in oil.

Polar 'heads' are attracted to the water.

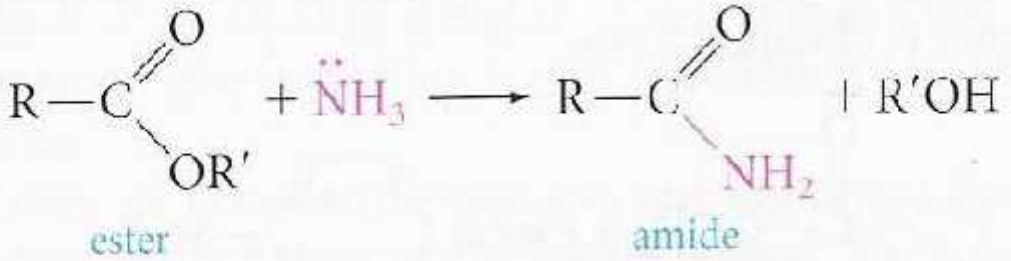
Reactions of Esters with Grignard Reagent



Formation of Amides (Ammonolysis of Esters)

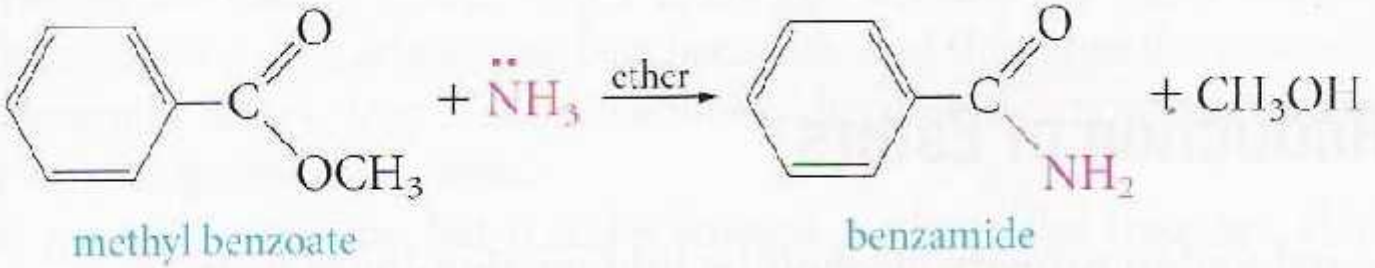
10.14 Ammonolysis of Esters

Ammonia converts esters to amides.



(10.24)

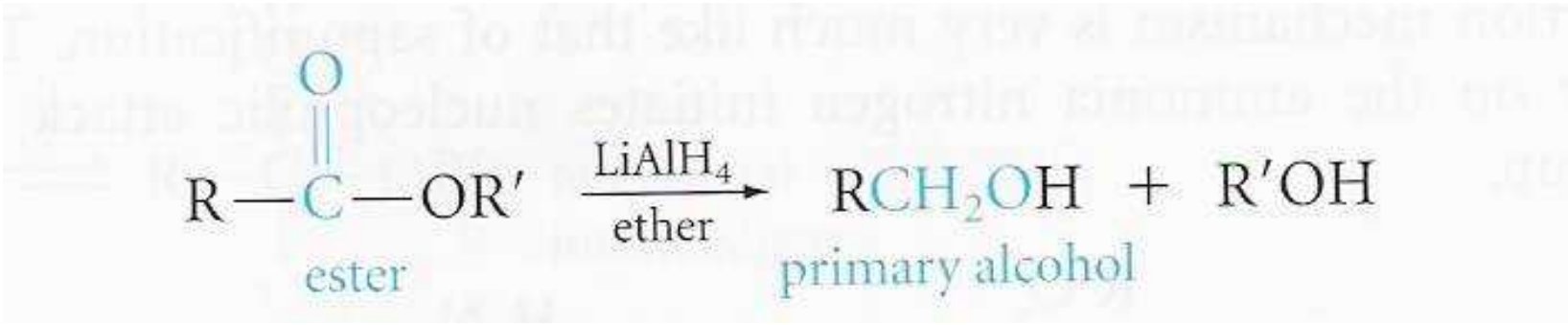
For example,



(10.25)

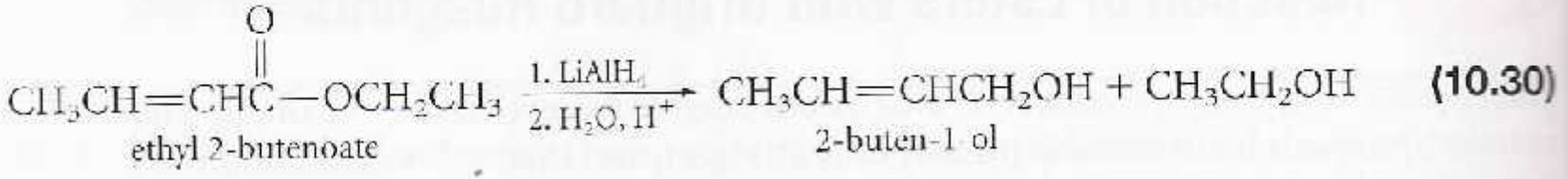
Reduction of Esters

Esters can be reduced to primary alcohols

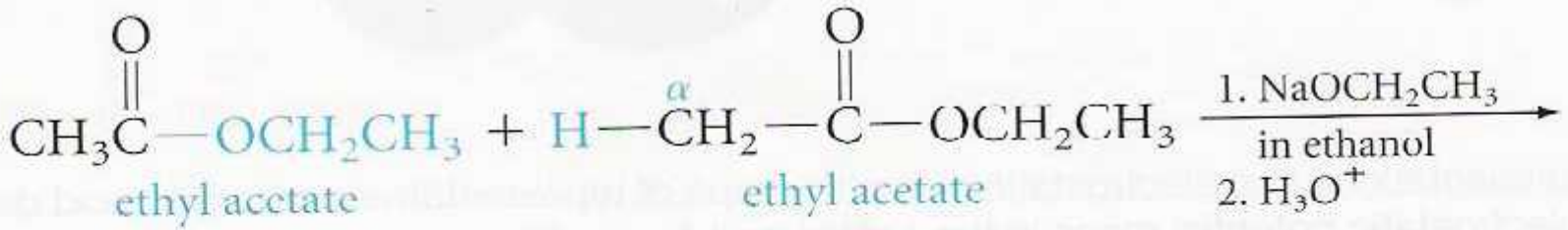


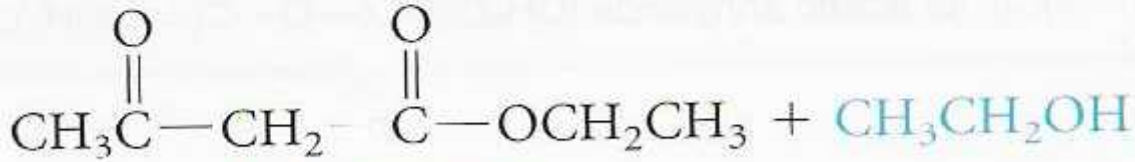
hydride to produce the alcohol.

It is possible to reduce an ester carbonyl group without reducing a C—C bond in the same molecule. For example,

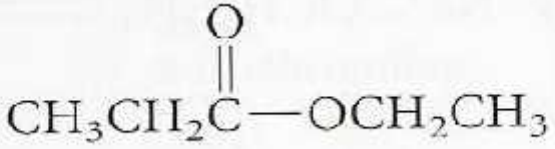


The Cliasen Condensation

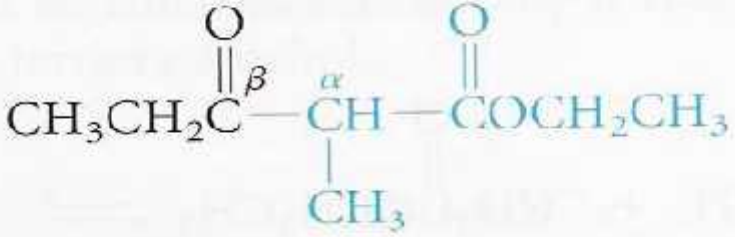




ethyl acetoacetate
(ethyl 3-oxobutanoate)

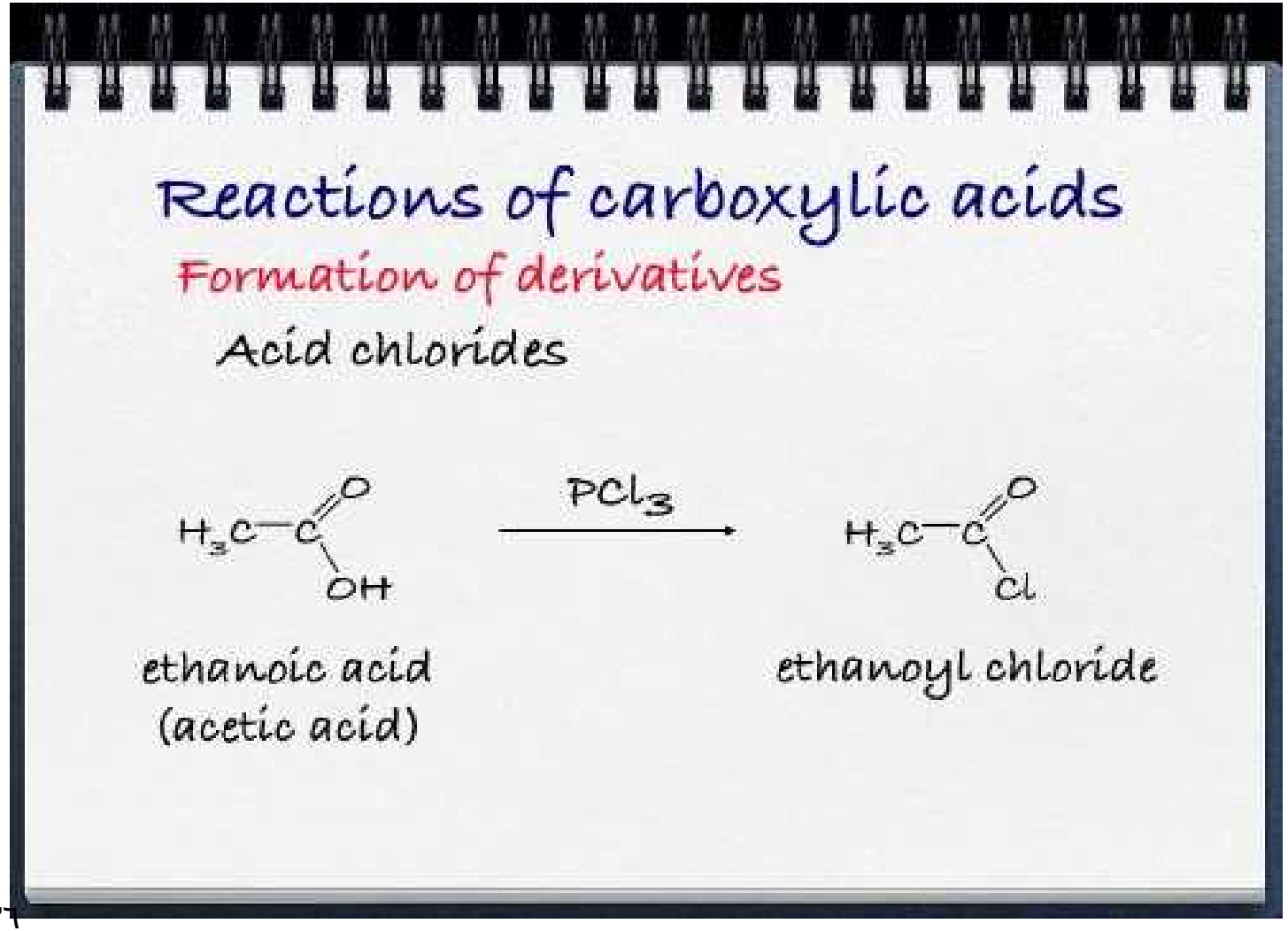


SOLUTION The product is



Acid Halides

They are prepared from the reaction of acids with thionyl chloride or phosphorus halides



Properties

Derivatives

Acid chlorides

Noxious, irritating, slightly polar

React violently with water

Esters

Slightly polar, pleasant odor

Low MW species are water soluble

Acid anhydrides

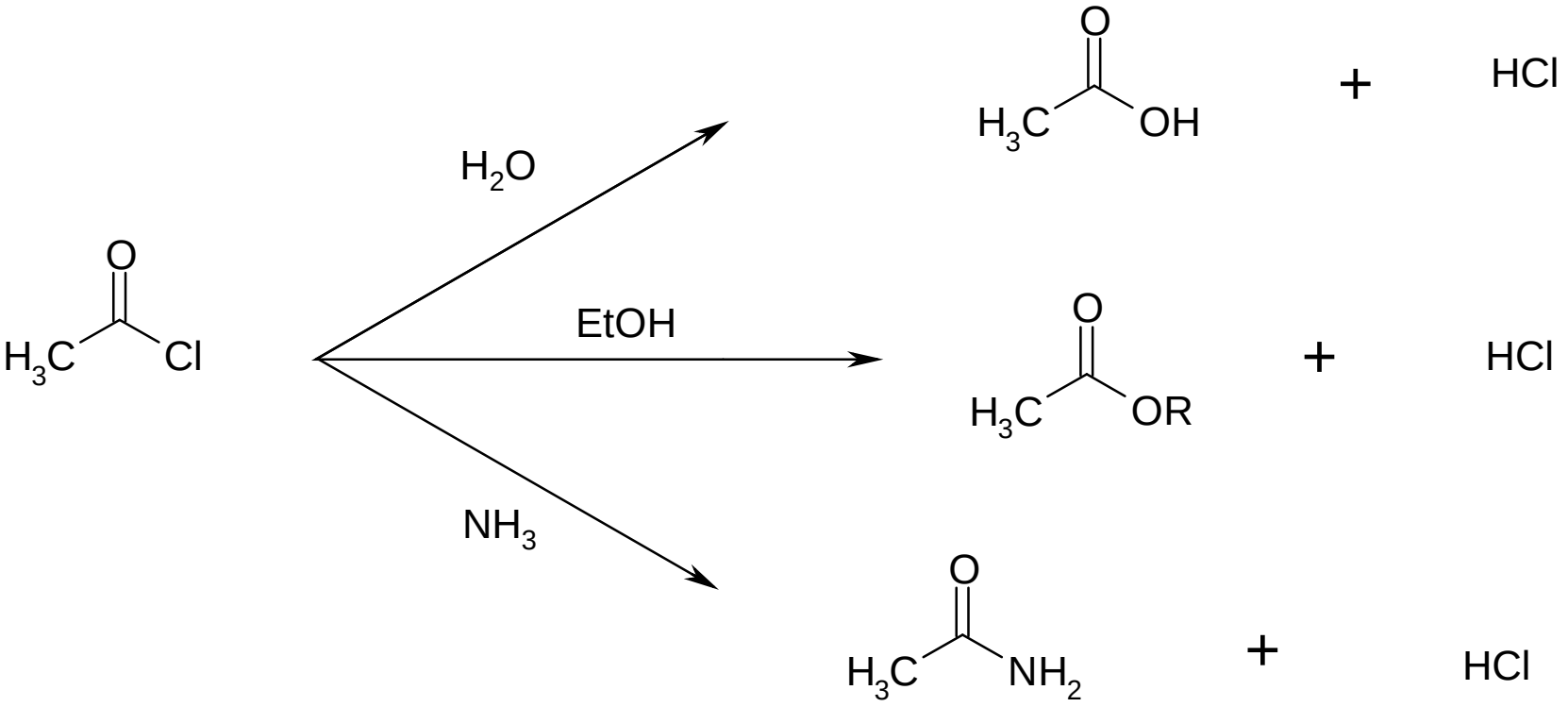
Not as polar as acids

May decompose in water

Reactions of acid chlorides

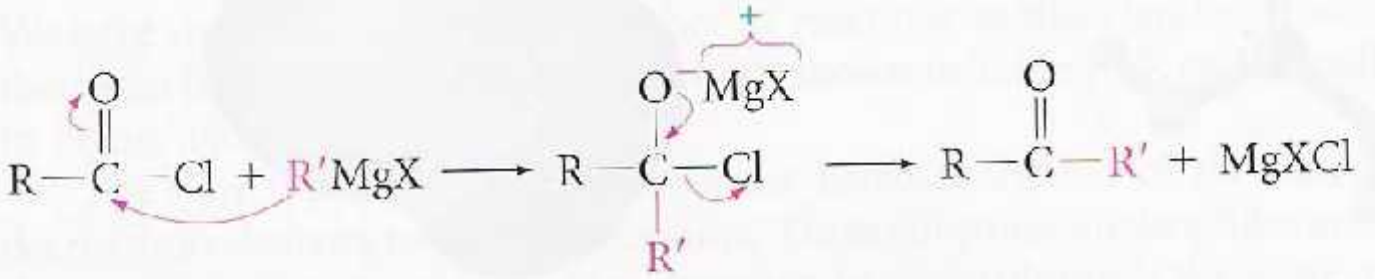
Acid chlorides react rapidly with most nucleophiles such as water, alcohols and ammonia

Acyl halides have irritating odors. Benzoyl chlorid is a lachrymator (tear gas)



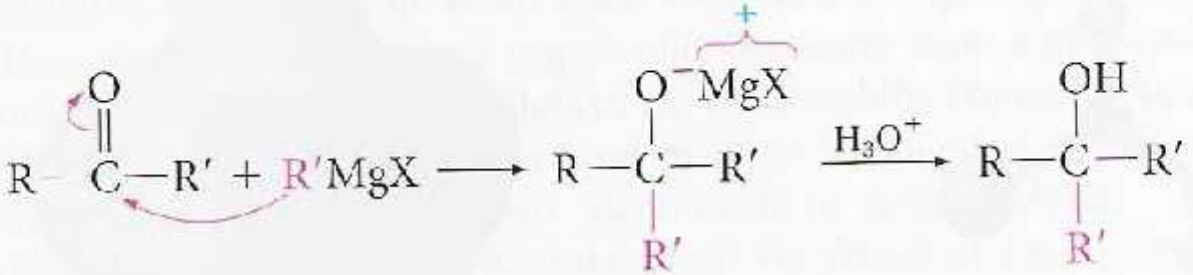
Reaction with Grignard Reagent

that acyl halides also react with Grignard reagents to give tertiary alcohols. The first steps involve ketone formation as follows:



(10.44)

The ketone can sometimes be isolated, but usually it reacts with a second mole of Grignard reagent to give a tertiary alcohol.

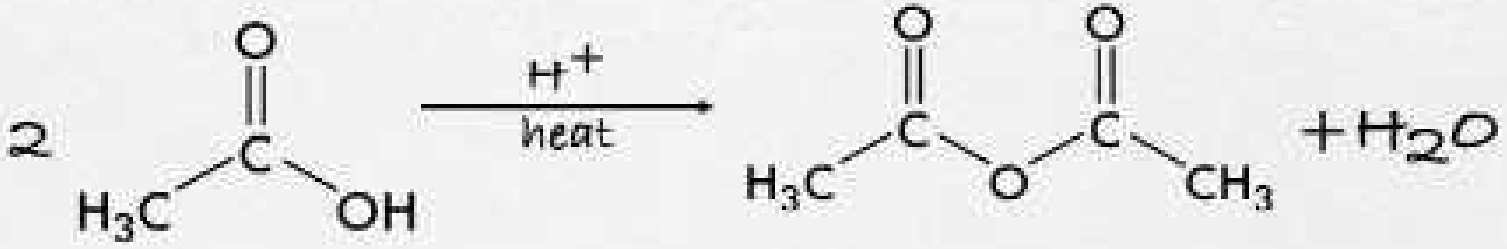


(10.45)

PROBLEM 10.35 Predict the product from the reaction of phenylmagnesium bromide (C_6H_5MgBr) with benzoyl chloride (C_6H_5COCl).

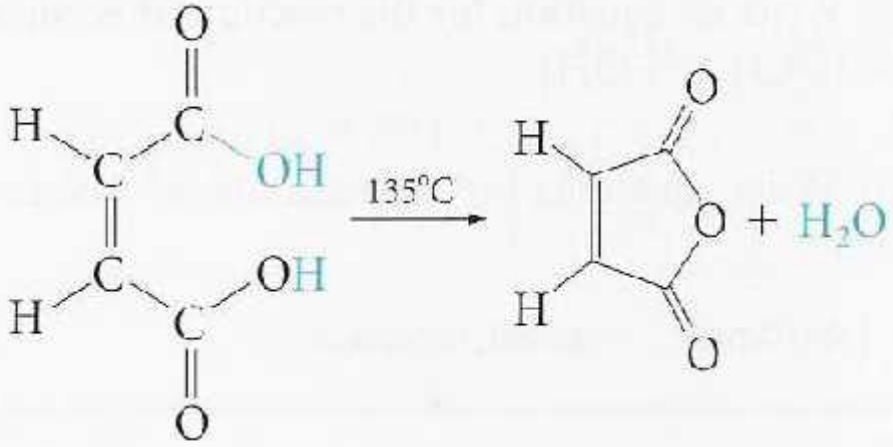
Acid anhydrides

Formed from the combination of two acids and the loss of water.



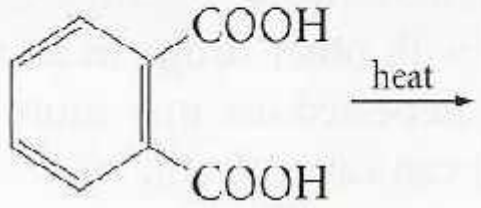
2 ethanoic acids

ethanoic anhydride



maleic acid maleic anhydride

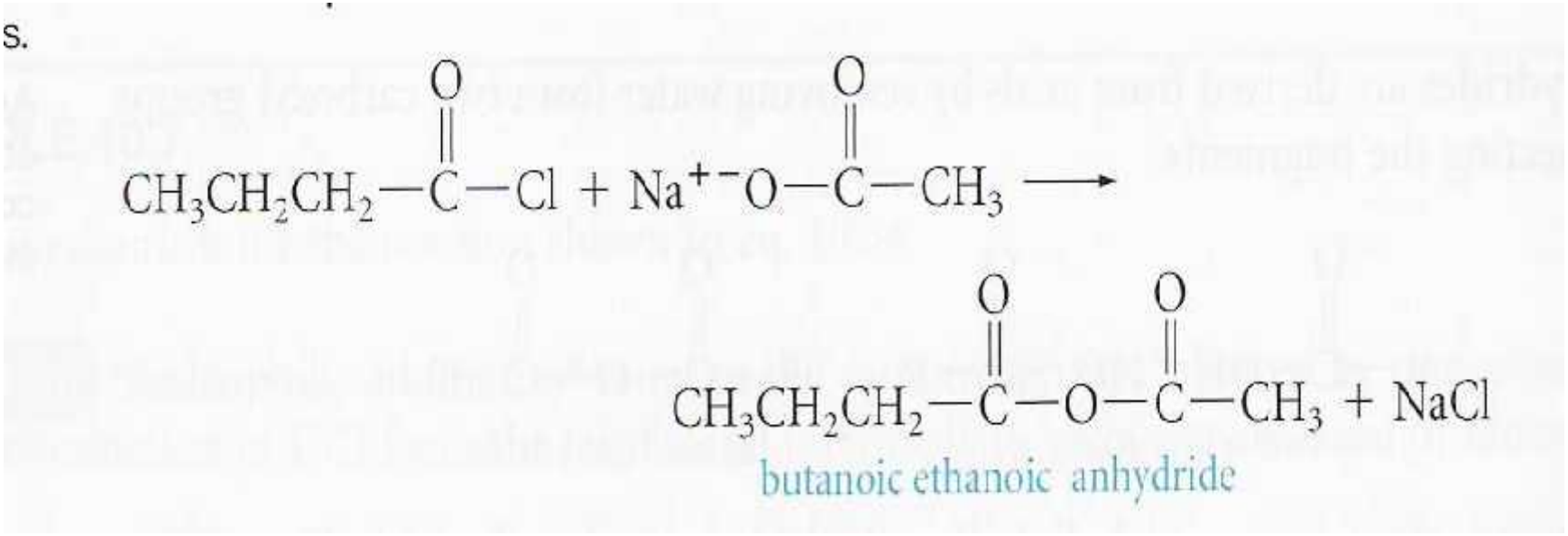
PROBLEM 10.27 Predict and name the product of the following reaction:



PROBLEM 10.28 Do you expect fumaric acid (page 288) to form a cyclic anhydride on heating? Explain.

Preparation of mixed anhydrides

s.

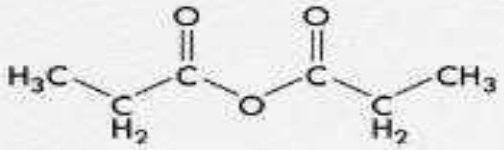


Acid anhydrides

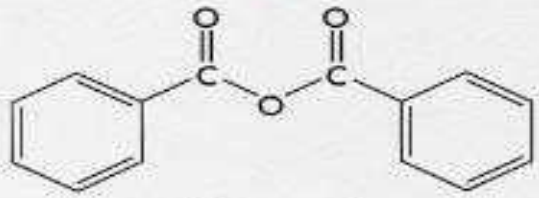
Nomenclature

Simple example: both halves are from the same acid.

Name by changing acid ending to anhydride.

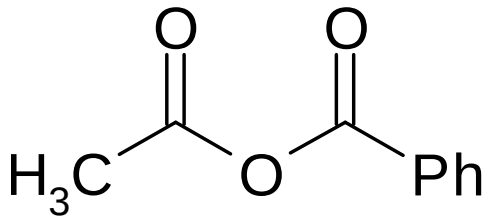


propanoic anhydride



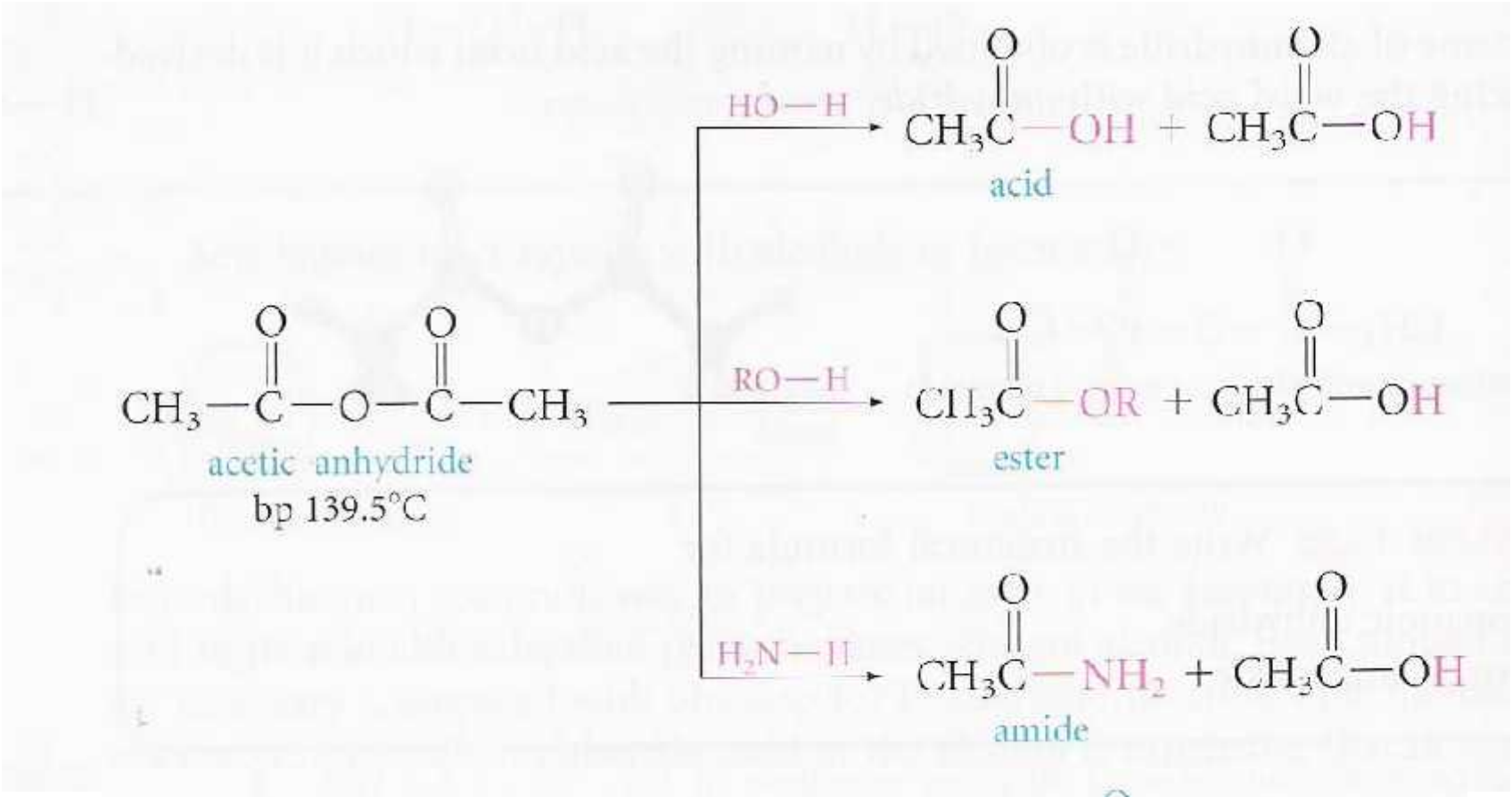
benzoic anhydride

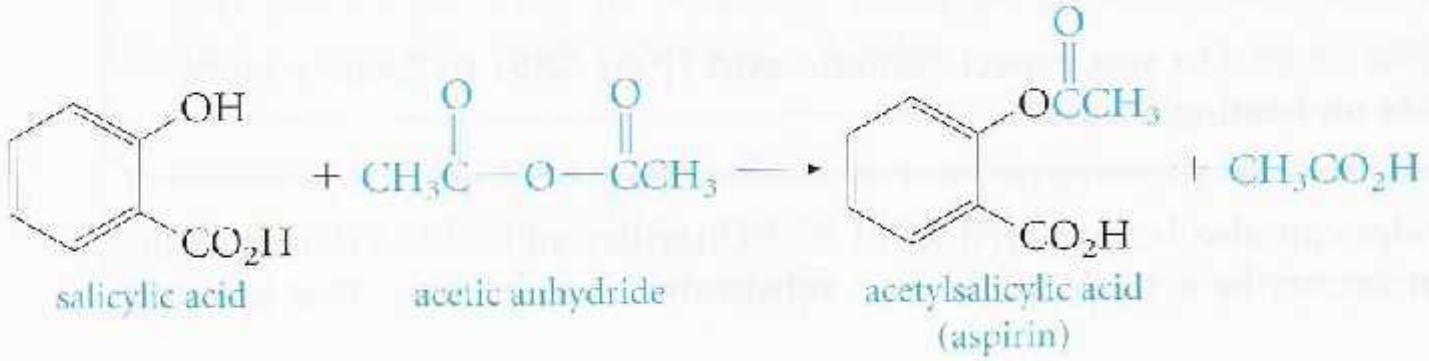
- Mixed anhydrides



Acetic benzoic anhydride

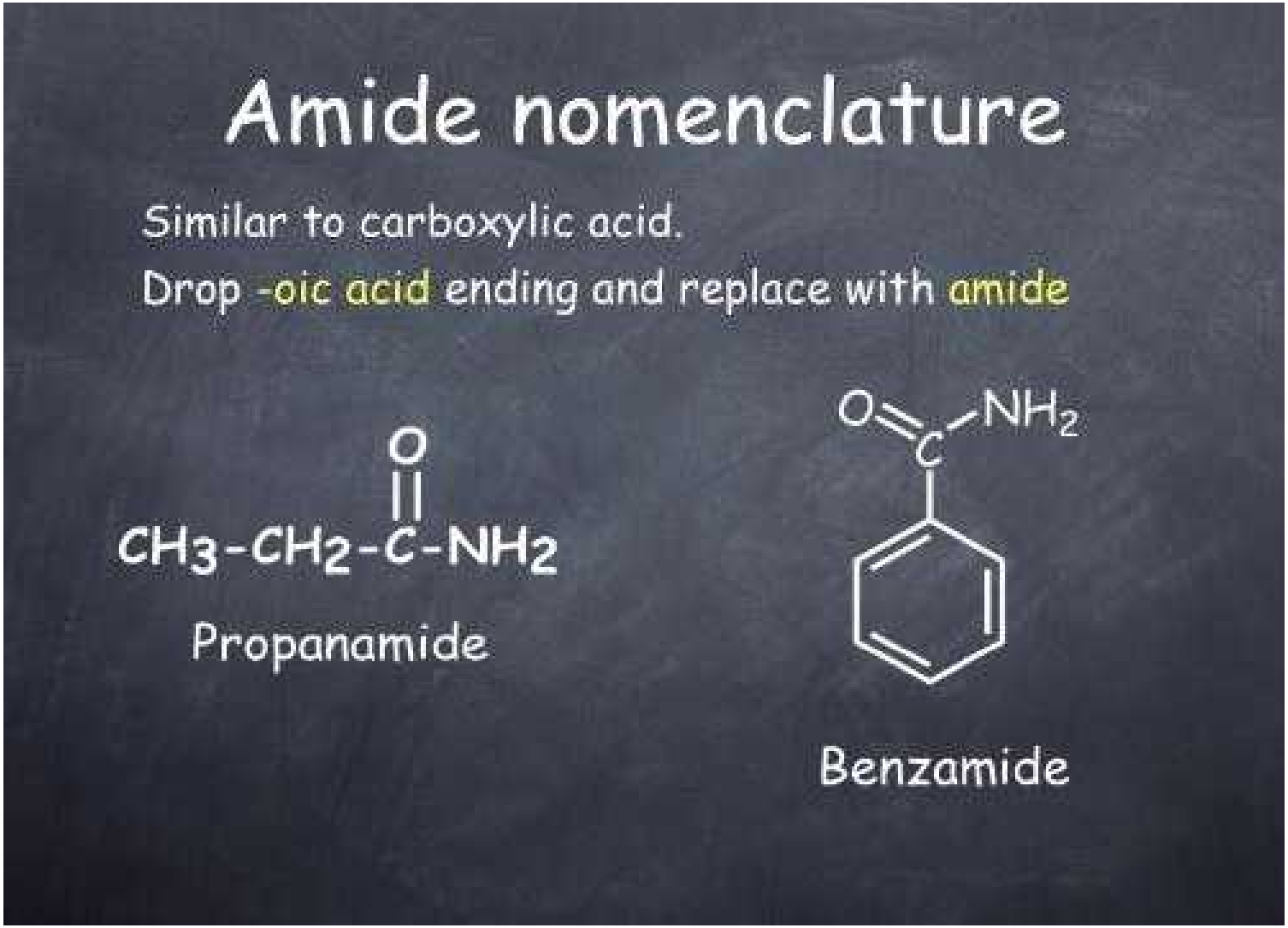
Nucleophilic substitution of anhydrides



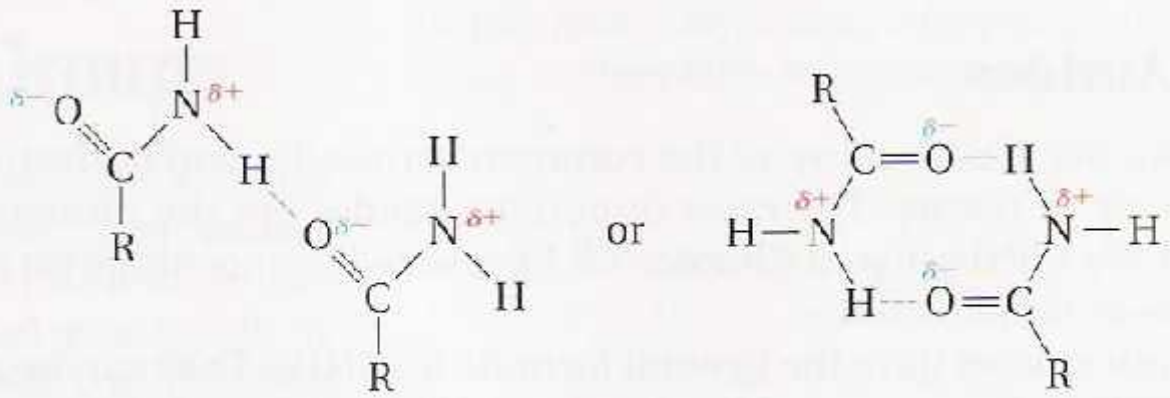


Amides

- **Nomenclature**



- **Properties of Amides**



They 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:

$HCONH_2$	$HCON(CH_3)_2$	CH_3CONH_2	$CH_3CON(CH_3)_2$
formamide	*N,N*-dimethylformamide	acetamide	*N,N*-dimethylacetamide
bp 210°C	153°C	222°C	165°C
mp 2.5°C	−60.5°C	81°C	20°C

Preparation of amides

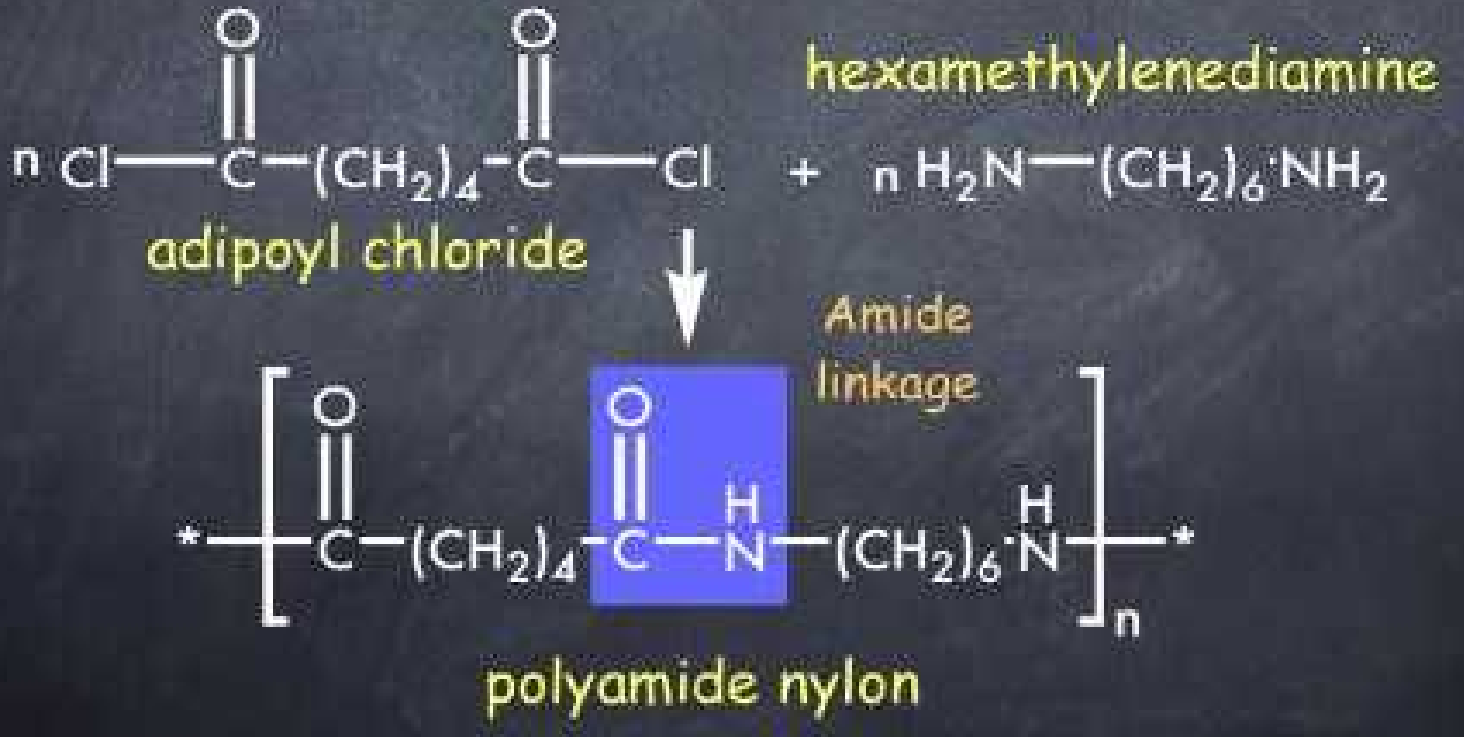
Production from a carboxylic acid

Production from an acid chloride

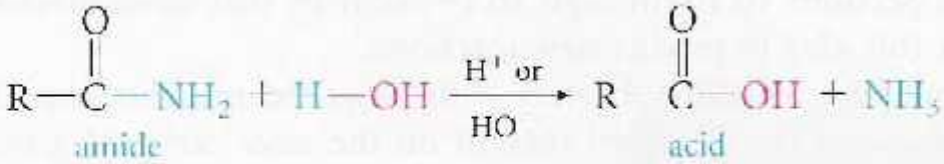
Amide Resonance

Nylon

If we have a diamine and a diacid chloride, we can produce a polymer using amide bonds. Nylon is an example.



Reactions of Amides (Hydrolysis and Reduction)

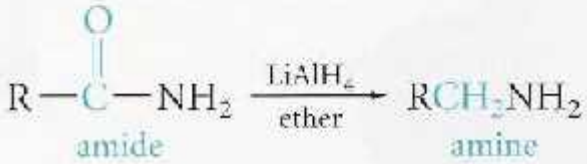


(10.42)

The reactions are slow, and prolonged heating or acid or base catalysis is usually necessary.

PROBLEM 10.33 Using eq. 10.42 as a model, write an equation for the hydrolysis of acetamide.

Amides can be reduced by lithium aluminum hydride to give amines.



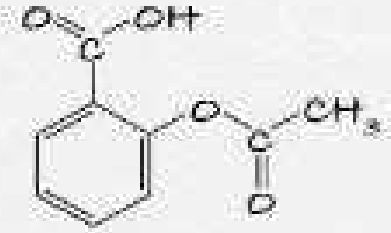
(10.43)

This is an excellent way to make primary amines, whose chemistry is discussed in the next chapter.

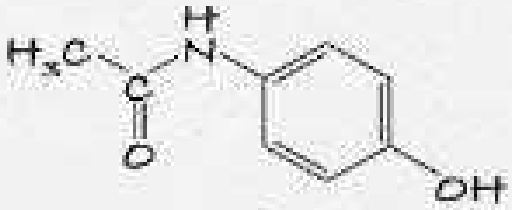
PROBLEM 10.34 Using eq. 10.43 as a model, write an equation for the reduction of acetamide with $LiAlH_4$.

Some significant examples

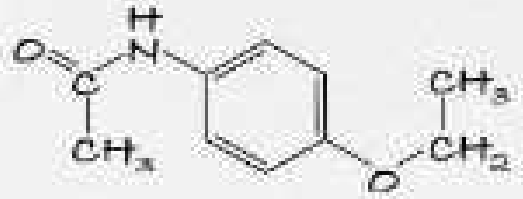
Analgesics - pain killers
Antipyetics - fever reducers



Acetylsalicyle acid
(Aspirin)



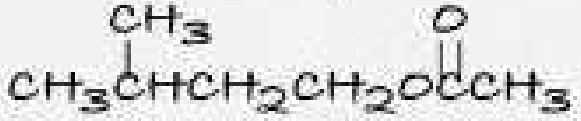
Acetaminophen
(Tylenol)



Phenacetin
(APC tablets)

More examples, pheromones

Pheromones – chemicals secreted by animals alter the behavior of other members of the same species.



isoamyl acetate
(honey bee alarm)

tetracecenyl acetate
(european corn borer sex pheromone)