

Fundamentals of Organic Chemistry

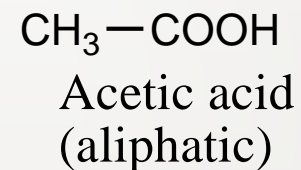
CHEM 245

4. Carboxylic Acids

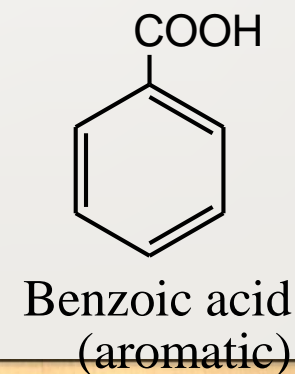
- ⇒ All carboxylic acids contain the **carboxyl group**, -COOH.
- ⇒ Depending on whether an **R or an Ar.** residue is attached to the carboxyl group;

Carboxylic acids are classified as aliphatic or aromatic.

→ **Aliphatic Carboxylic Acids.**



→ **Aromatic Carboxylic Acids.**



Nomenclature of Carboxylic Acids

⇒ The common names of carboxylic acids all end in *-ic acid*.

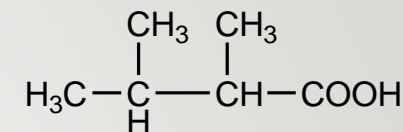
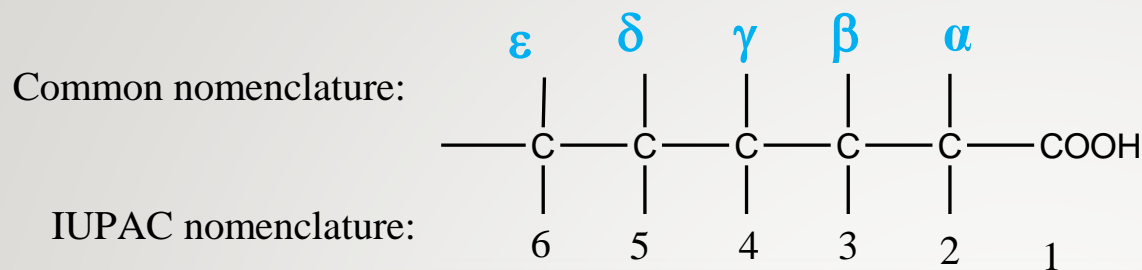
For example

- Formic acid is the acid that gives the characteristic sting to an ant bite (from the Latin *formica*, ant).
- Acetic acid is vinegar (from the Latin *acetum*, vinegar).
- Butyric acid is the compound that gives rancid butter its putrid smell (from the Latin *butyrum*, butter).
- Fatty acids.
Long straight-chain carboxylic acids with even numbers of carbons, which were first isolated from fats and waxes.

Nomenclature of Carboxylic Acids

- ⇒ In the **IUPAC system** the acids are named in the usual way.
 - ↪ The **ending -e** of the corresponding alkane is replaced by **-oic acid**.
 - ↪ For example
 - HCOOH** is called **methanoic acid**.
 - CH₃COOH** is called **ethanoic acid**.
 - ↪ If substituents are present on the acid chain.
 - ▶ **Common nomenclature**
Their positions are located by Greek letters.
α, β, γ, δ, ε,....etc
 - ▶ **IUPAC system**
Numbers are used and the **carboxylic carbon is numbered 1**.

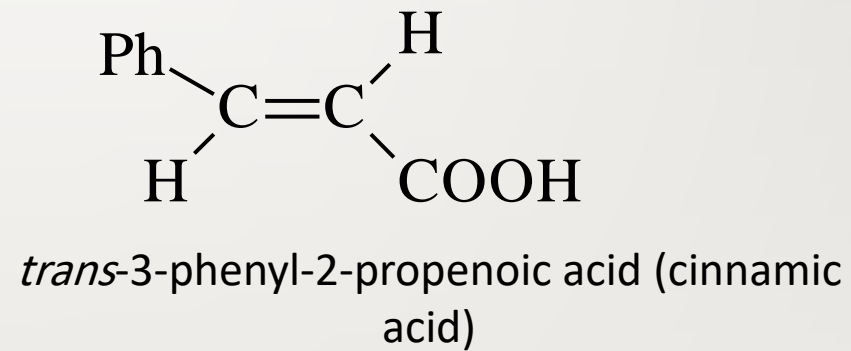
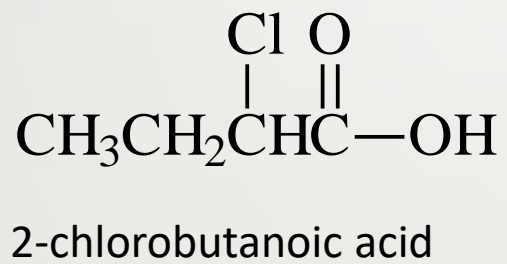
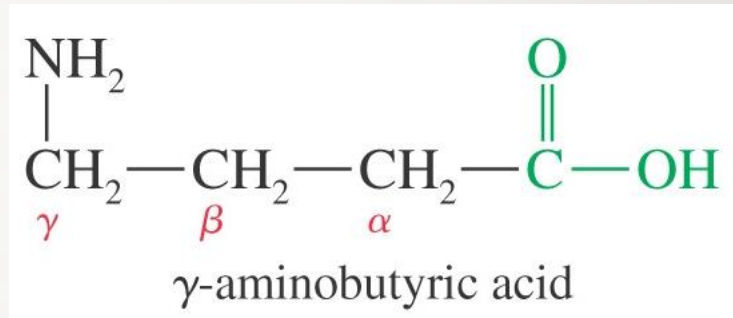
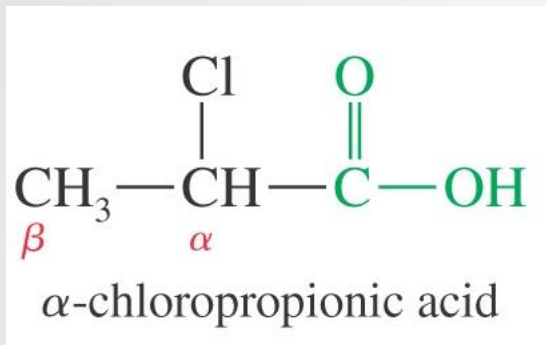
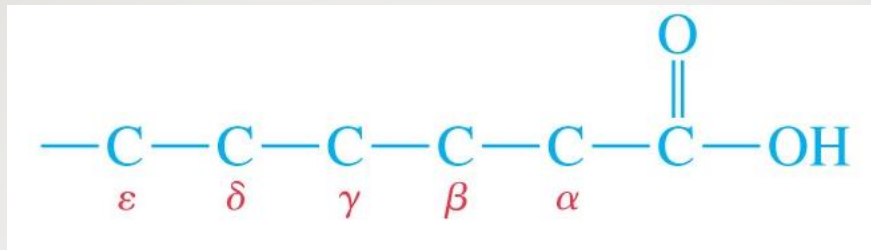
Nomenclature of Carboxylic Acids



Common name: α,β -Dimethylbutyric acid
 IUPAC nomenclature: 2,3-Dimethylbutanoic acid

IUPAC and Common Names of Some Normal carboxylic Acids.

No. of carbon atoms	Formula	IUPAC name	Common name
1	HCOOH	Methanoic acid	Formic acid
2	CH ₃ COOH	Ethanoic acid	Acetic acid
3	CH ₃ CH ₂ COOH	Propanoic acid	Propionic acid
4	CH ₃ (CH ₂) ₂ COOH	Butanoic acid	Butyric acid
5	CH ₃ (CH ₂) ₃ COOH	Pentanoic acid	Valeric acid



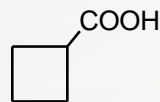
Nomenclature of Carboxylic Acids

⇒ Cycloalkane carboxylic acid

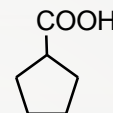
When the carboxyl group is attached to a saturated ring.



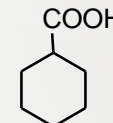
Cyclopropanecarboxylic acid



Cyclobutanecarboxylic acid

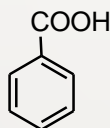


Cyclopentanecarboxylic acid

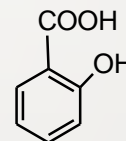


Cyclohexanecarboxylic acid

⇒ **Aromatic carboxylic acids** are generally called by their **common names**.



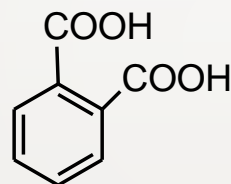
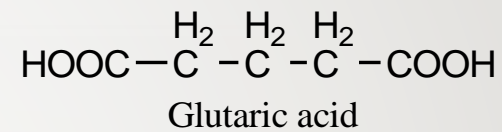
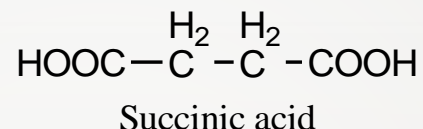
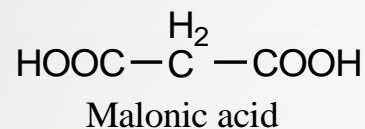
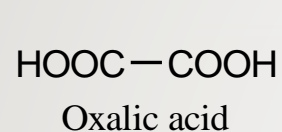
Common name: Benzoic acid
IUPAC name: Benzenecarboxylic acid
(used as germicide and as food preservative)



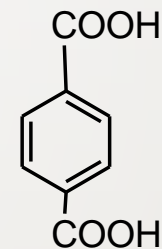
Common name: Salicylic acid
IUPAC name: 2-Hydroxybenzenecarboxylic acid
(raw material for aspirin)

Nomenclature of Carboxylic Acids

⇒ **Dicarboxylic acids** (acids that contain two carboxyl groups) are known almost exclusively by their common names.



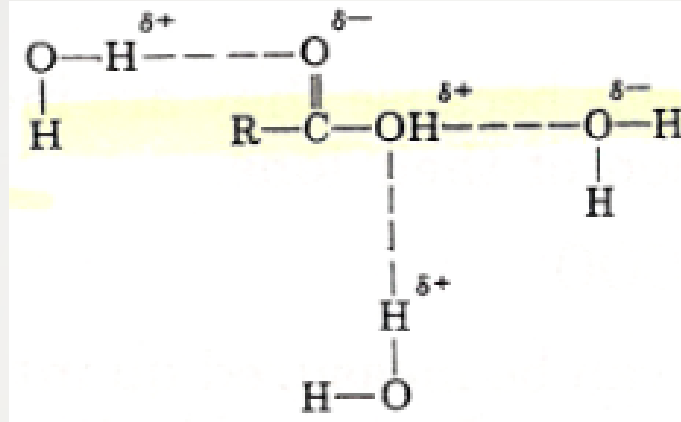
Common name: Phthalic acid
IUPAC name: Benzene-1,2-dicarboxylic acid
(medicinal uses; synthetic perfumes)



Common name: Terephthalic acid
IUPAC name: Benzene-1,4-dicarboxylic acid
(constituent of Dacron)

Physical Properties of Carboxylic Acids

⇒ Carboxylic acids are capable of hydrogen bonding .



⇒ Solubility in water.

- ➔ The **first four aliphatic acids** (formic through butyric) are **completely miscible in water**.
- ➔ **Higher members** of the series are **less soluble** because the long alkyl chain gives them alkane like characteristics.
- ➔ **Aromatic acids are insoluble in water**.

Physical Properties of Carboxylic Acids

⇒ Boiling points.

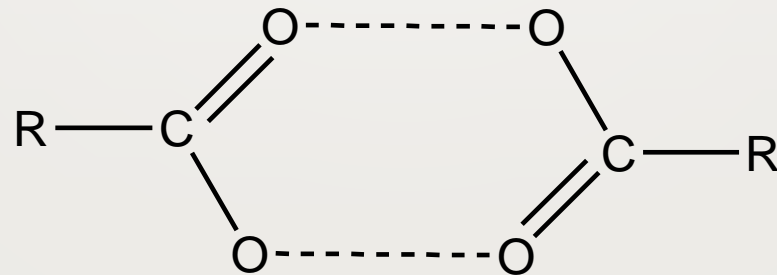
→ The boiling points of carboxylic acids indicate a greater degree of association than for alcohols of comparable molecular weights.

→ For example,

→ Acetic acid (mol wt = 60) boils at 118°C.

n-Propyl alcohol (mol wt = 60) boils at only 97° C.

→ In fact, simple carboxylic acids exist as *hydrogen-bonded dimers* .



Physical Properties of Carboxylic Acids

- ⇒ The first nine aliphatic acids are colorless liquids that have sharp, acrid odors.
- ⇒ Pure acetic acid is called *glacial acetic acid* because it solidifies into ice-like crystals at temperatures slightly below normal room temperature (about 17°C).
- ⇒ Butyric acid smells like rancid butter and strong cheese.
- ⇒ Acids of five to ten carbons have goat-like smells because they are present in the skin secretion of goats.
- ⇒ Higher acids are wax-like solids and are practically odorless.
- ⇒ Aromatic acids are also high-melting odorless solids.

Physical Properties of Carboxylic Acids

Some Physical Properties of Acids and Alcohols of Corresponding Molecular Weights:

Structure	Name	Mol. Wt.	b.p. °C	Solubility in H ₂ O at 25°C
HCOOH	Formic acid	46	100	Very soluble
CH ₃ CH ₂ OH	Ethyl alcohol	46	78	Very soluble
CH ₃ COOH	Acetic acid	60	118	Very soluble
CH ₃ CH ₂ CH ₂ OH	<i>n</i> -Propyl alcohol	60	97	Very soluble
CH ₃ (CH ₂) ₃ COOH	Valeric acid	102	187	4.0 g/100 g H ₂ O
CH ₃ (CH ₂) ₄ CH ₂ OH	<i>n</i> -Hexyl alcohol	102	156	0.6 g/100 g H ₂ O
Ph-COOH	Benzoic acid	122	250	Insoluble
Ph-CH ₂ CH ₂ OH	3-Phenylethanol	122	250	Insoluble

Acid Strength

- ⇒ The strength of an acid depends on the extent it ionizes.
- ⇒ Common mineral acids, such as HCl or HNO₃, ionize completely and are considered therefore to be strong acids.



⇒ Carboxylic acids are weak acids

Because they are incompletely ionized and exist in equilibrium with a solution of their ions.



Acid Strength

⇒ The strength of an acid can be measured quantitatively by determining the value of its ionization constant, K_a .

→ An acid with a higher K value is stronger than one with a lower K .

→ Strong acids have K_a values higher than 10^2 .

→ weak acids have K_a s of 10^{-2} or less.

⇒ The K_a s of most carboxylic acids fall in the range of 10^{-4} to 10^{-5} .

HCOOH
Formic acid

$$K_a = 1.8 \times 10^{-4}$$

CH₃COOH
Actic acid

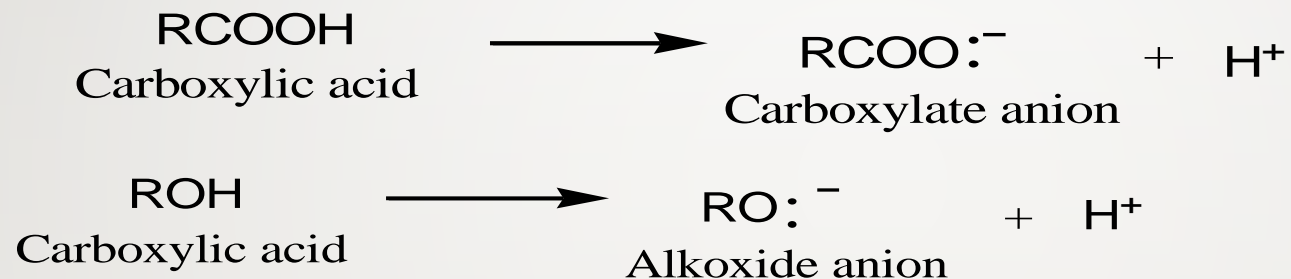
$$K_a = 1.8 \times 10^{-5}$$

Acid Strength and Acid Structure

⇒ **Carboxylic acids** are much **more acidic than are alcohols** even though both classes of compounds contain an OH group.

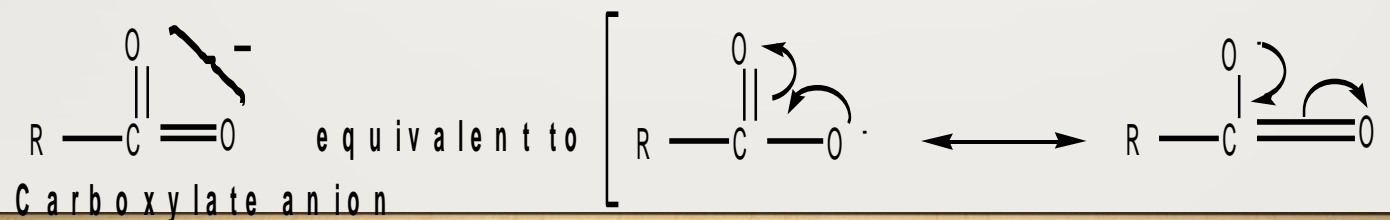
→ Why is this so?

The structures of their conjugate bases, the carboxylate anion and the alkoxide anion,



⇒ **Carboxylic acids** are stronger acid than alcohols because

*Carboxylate anions are stabilized by resonance; whereas **Alkoxide anions are not.***



Acid Strength and Acid Structure

⇒ Acid strength among carboxylic acids.

→ Generally, any factor that *stabilizes* the carboxylate anion of an acid will give it *greater* acid strength than an acid lacking that factor.

→ Conversely, any factor that *destabilizes* the carboxylate anion of an acid will make that acid *less* strong.

⇒ The **stronger acid** is the one with the **electron-withdrawing group** compared to unsubstituted acid.

By dispersing the negative charge.

⇒ Examples of common electron-withdrawing, and acid-strengthening, groups are



Acid Strength and Acid Structure

- ⇒ Addition of any **electron-donating substituent** on the R (or Ar) portion of an acid **decreases its acid strength** relative to the parent unsubstituted acid.
 - The electron-donating group destabilizes the carboxylate anion.
By intensifying the negative charge.
- ⇒ The most common electron-donating, acid-weakening substituent is *the alkyl group (methyl, ethyl, propyl, and so on).*
- ⇒ Formic acid (no alkyl group) is a stronger acid than acetic acid (one alkyl group).

Acid Strength and Acid Structure

Comparison of Acid Strengths of Acetic Acid and Chlorinated Acetic Acids

Name	Structure	pK_a	Relative acid strength
Acetic acid	CH_3COOH	4.7	1
Chloroacetic acid	ClCH_2COOH	2.8	80
Dichloroacetic acid	Cl_2CHCOOH	1.3	2800
Trichloroacetic acid	Cl_3CCOOH	0.7	11000

Comparison of Acid Strengths of Butyric Acid and the Monochlorinated Acids

Name	Structure	pK_a	Relative acid strength
Butyric acid	$\text{CH}_3\text{CH}_2\text{CH}_2\text{COOH}$	4.82	1
α -Chlorobutyric acid	$\text{CH}_3\text{CH}_2\text{CHClCOOH}$	2.85	92
β -Chlorobutyric acid	$\text{CH}_3\text{CHClCH}_2\text{COOH}$	4.05	6
γ -Chlorobutyric acid	$\text{ClCH}_2\text{CH}_2\text{CH}_2\text{COOH}$	4.52	2

Acid Strength and Acid Structure

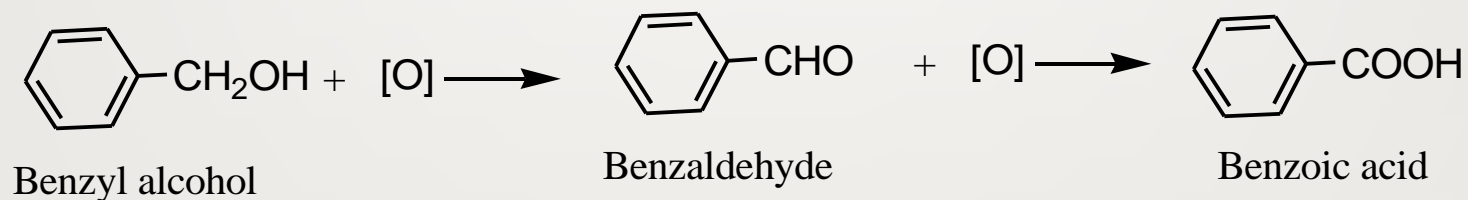
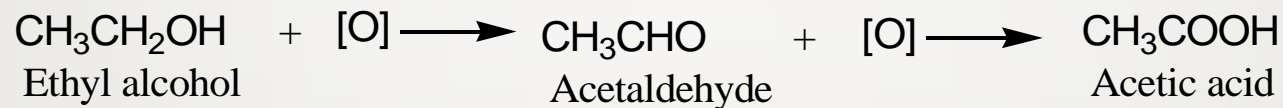
- ⇒ The electronic effect of a substituent transmitted through single bonds, be it electron-withdrawing or electron-donating, is called the **inductive effect**.
- ⇒ α -chlorobutyric acid is about 15 times more acidic than β -chlorobutyric acid.

Preparation of Carboxylic Acids

Preparation of Acids by Oxidation

A. Oxidation of Primary Alcohols or Aldehydes

⇒ **Primary alcohols** are oxidized quickly to carboxylic acids by potassium permanganate, KMnO_4 , or by a mixture of potassium dichromate, $\text{K}_2\text{Cr}_2\text{O}_7$, and sulfuric acid.

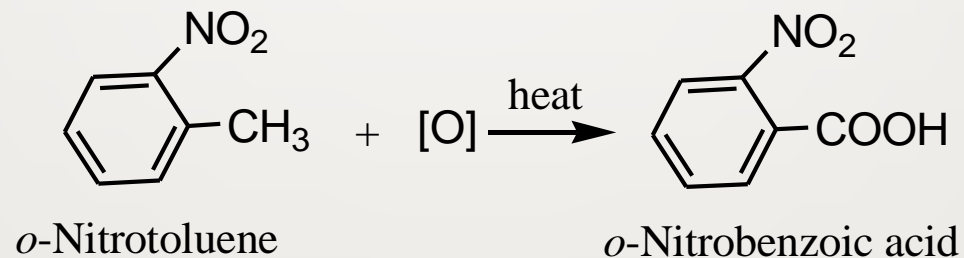
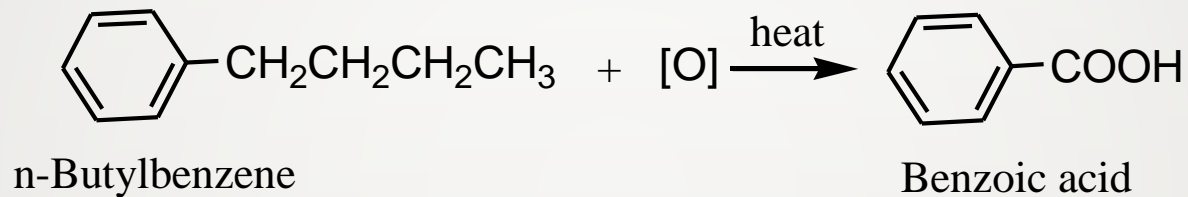


Preparation of Carboxylic Acids

Preparation of Acids by Oxidation

B. Oxidation of Alkylbenzenes

⇒ Vigorous oxidation of alkylbenzenes yields benzoic acid.

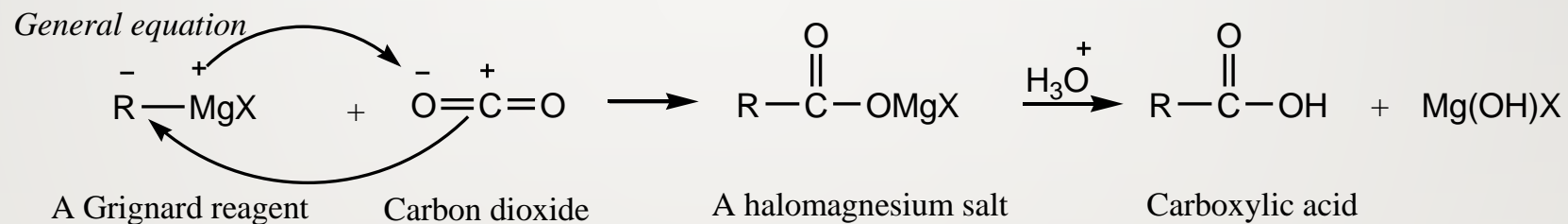


Preparation of Carboxylic Acids

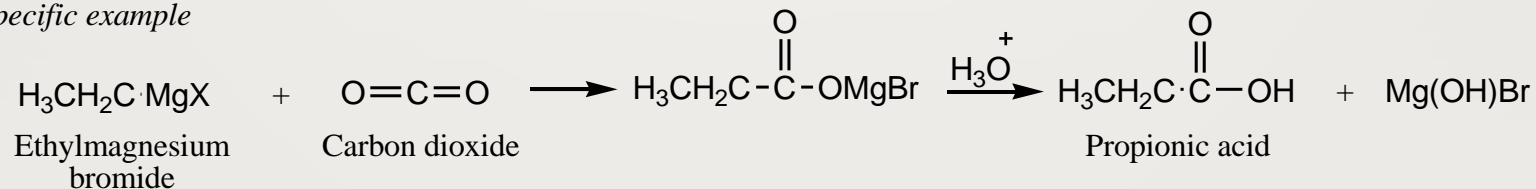
Carbonation of Grignard Reagents

⇒ The **addition of Grignard reagents to CO₂** in the form of dry ice proceeds in a similar fashion and yields the halomagnesium salt of a carboxylic acid.

⇒ Hydrolysis of the salt gives an acid with **one carbon more** than the original Grignard reagent



Specific example

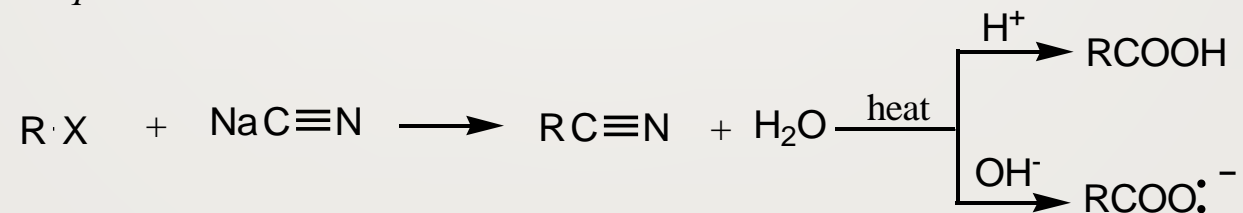


Preparation of Carboxylic Acids

Hydrolysis of Nitriles

- ⇒ **Nitriles** are compounds with the general formula RCN or ArCN .
- ⇒ They are prepared by reacting a 1° or 2° alkyl halide with a cyanide salt.
- ⇒ Acid hydrolysis of a nitrile yields a carboxylic acid. Alkaline hydrolysis yields a carboxylate salt.
- ⇒ The carboxylate acid or salt contain **one carbon more** than the starting alkyl halide.

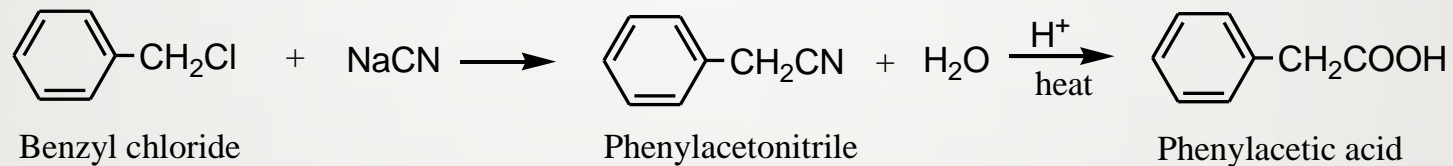
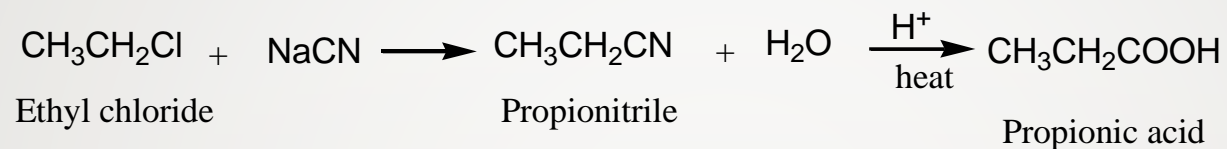
General equation



Preparation of Carboxylic Acids

Hydrolysis of Nitriles

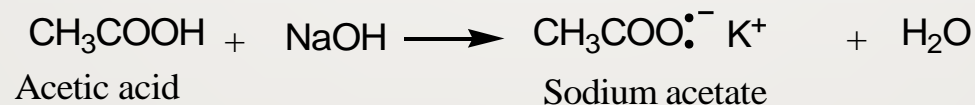
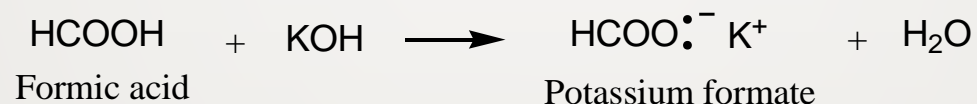
Specific example



Preparation of Carboxylic Acids

Reactions with Bases: Salt Formation

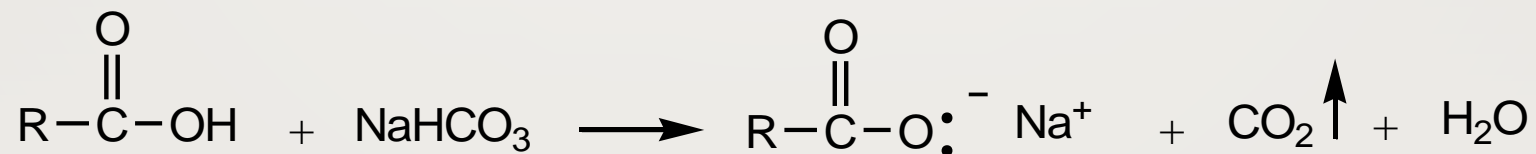
- ⇒ Carboxylic acids react quantitatively with bases to form **water-soluble salts**.
- ⇒ The **metal cation is named first**, followed by the name of the carboxylate anion.
- ⇒ The latter is named by dropping the ***-ic acid*** ending from the name of the parent acid and replacing it with ***-ate***.



Preparation of Carboxylic Acids

Reactions with Bases: Salt Formation

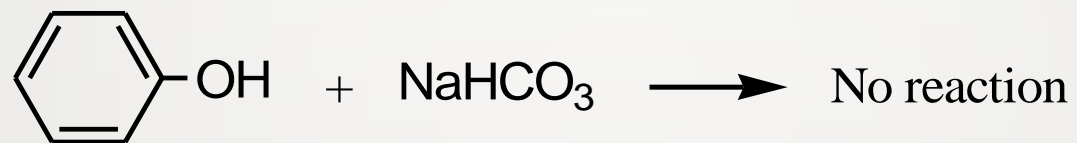
- ⇒ Sodium acetate is used in dyeing.
- ⇒ Sodium propionate, $\text{CH}_3\text{CH}_2\text{COO}^- \text{Na}^+$, and calcium propionate, $(\text{CH}_3\text{CH}_2\text{COO}^-)_2\text{Ca}^{2+}$, are used in bread to prevent molding.
- ⇒ Sodium benzoate is a food preservative.
- ⇒ Carboxylic acids will also react with a weak base like sodium bicarbonate, NaHCO_3 , to form
 - ↪ Water-soluble salts.
 - ↪ Carbon dioxide is liberated as a by-product.



Preparation of Carboxylic Acids

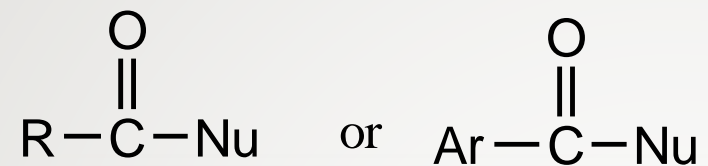
Reactions with Bases: Salt Formation

⇒ Weaker acids like phenols react only with strong bases (NaOH or KOH) and will not react with NaHCO_3 .



Carboxylic Acid Derivatives

⇒ When the OH of a carboxylic acid is replaced by a **nucleophile, : Nu**, a carboxylic acid derivative is produced.

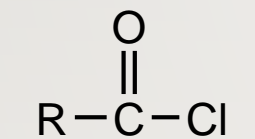


Carboxylic acid derivatives

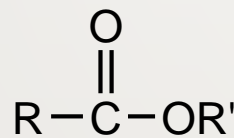
⇒ The **RCO-** portion of acid derivatives is called the **acyl group**.

Aromatic acid derivatives contain the **aryl group**.

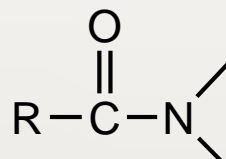
⇒ The **carboxylic acid derivatives** are



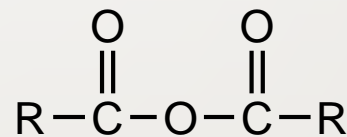
Acyl chloride
Acid chloride



Ester



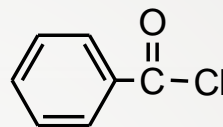
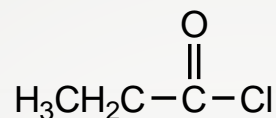
Amide



Acid anhydride

Nomenclature of Acid Derivatives

⇒ **Acyl chlorides, or acid chlorides**, are named by replacing the *-ic acid* ending of the parent acid by *-yl chloride*.

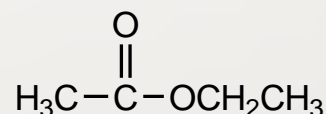
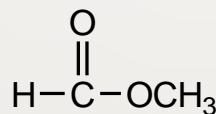


IUPAC name: Propanoyl chloride
Common name: Propionyl chloride

Benzoyl chloride

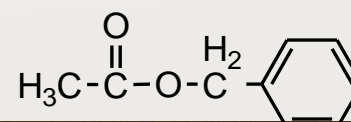
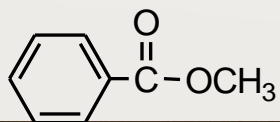
⇒ **Esters** are named as if they were formed from **replacement of the carboxyl hydrogen by an alkyl group**.

➡ The **alkyl group** is named first followed by the name of the parent acid with the ending *-ate* in place of *-ic acid*.



IUPAC name: Methyl methanoate
Common name: Methyl formate

Ethyl ethanoate
Ethyl acetate

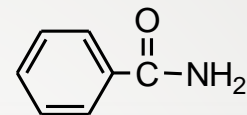
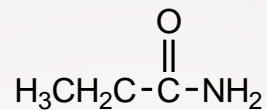


IUPAC name: Methyl benzoate
Common name:

Benzoyl ethanoate
Benzyl acetate

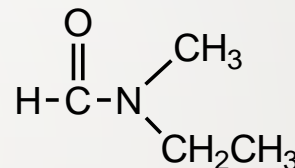
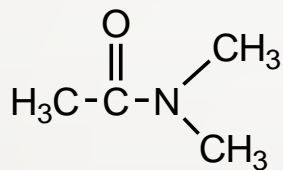
Nomenclature of Acid Derivatives

⇒ **Amides** are named by replacing the *-oic acid* or *-ic acid* of the parent acid's name by *-amide*.



IUPAC name: Propanamide
Common name: Propionamide

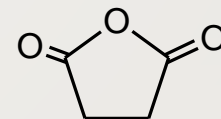
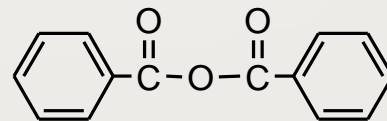
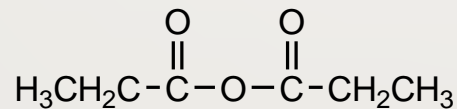
Benzamide



IUPAC name: *N,N*-Dimethylethanamide
Common name: *N,N*-Dimethylacetamide

N-Ethyl-*N*-methylmethanamide
N-Ethyl-*N*-methylformamide

⇒ An **anhydride** is named by replacing the word *acid* with *anhydride* in the name of the acid from which it was formed.



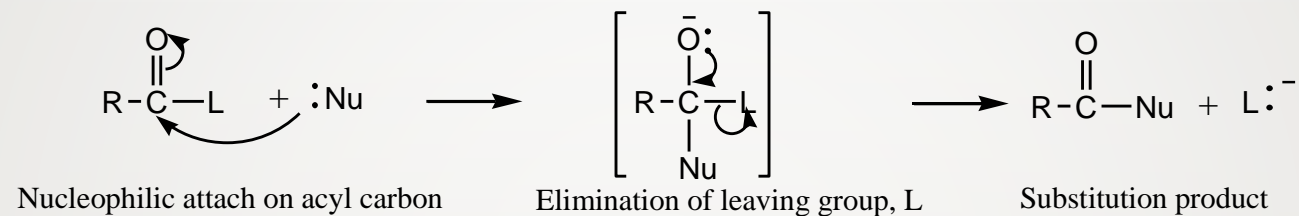
IUPAC name: Propanoic anhydride
Common name: Propionic anhydride

Benzoic anhydride

Succinic anhydride

Nucleophilic Substitution of Acid Derivatives

➡ Most reactions of acids and acid derivatives proceed by a common mechanism: **nucleophilic substitution**.



➡ The **leaving group, L**, may be **OH, OR, Cl, OCOR or NH₂**.

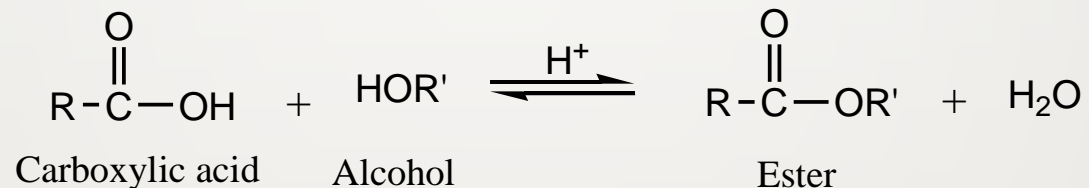
Nucleophilic Substitution of Acid Derivatives

Esters from Carboxylic Acids: Esterification

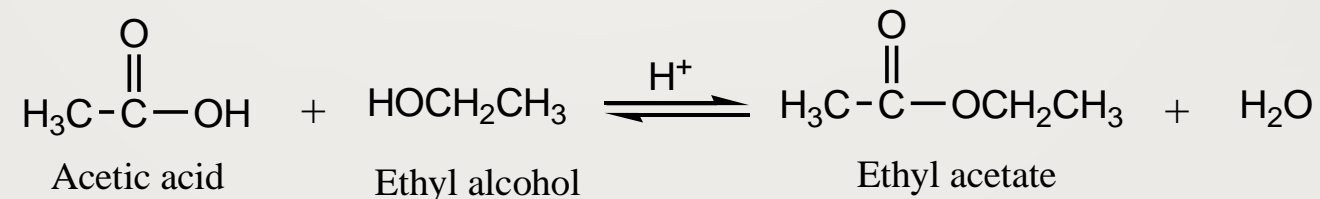
⇒ **Esters** are formed by treatment a carboxylic acid with a primary or secondary alcohol.

⇒ A small amount of mineral acid catalyst (H^+) is required to speed up esterification.

General equation



Specific example



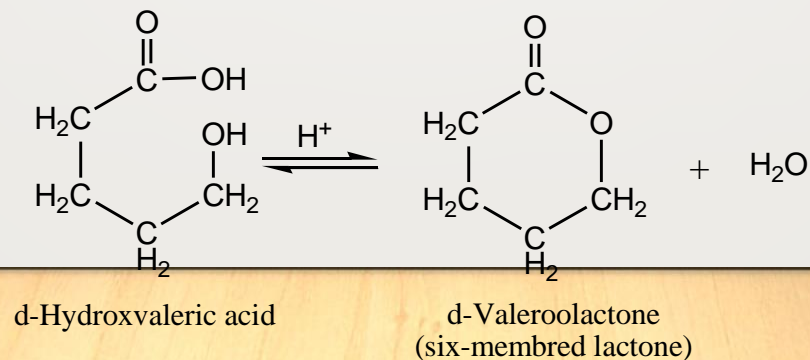
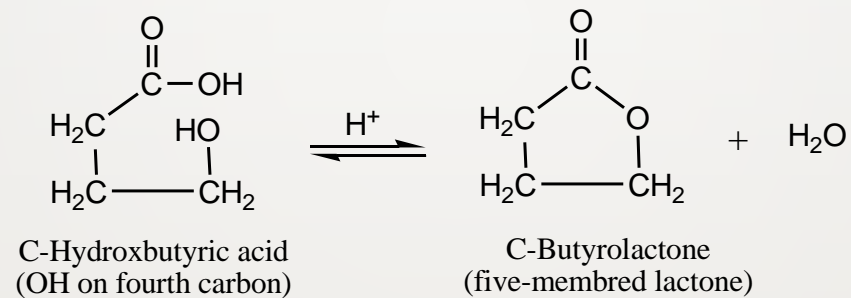
Nucleophilic Substitution of Acid Derivatives

Esters from Carboxylic Acids: Esterification

⇒ *Intramolecular esterification.*

➡ If the acid and alcohol functions are part of the same molecule.

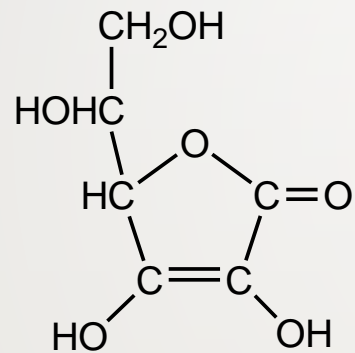
➡ The product, in such cases, is *a cyclic ester* or **lactone**.



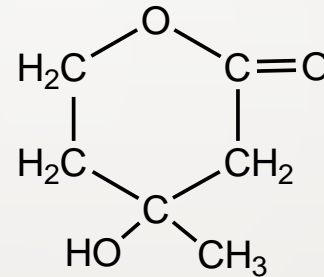
Nucleophilic Substitution of Acid Derivatives

Esters from Carboxylic Acids: Esterification

→ Ascorbic acid (vitamin C) and the lactone of mevalonic acid are two naturally occurring lactones.



L-Ascorbic acid
(Vitamin C)



Lactone of mevalonic acid
(precursor of cholesterol)

Nucleophilic Substitution of Acid Derivatives

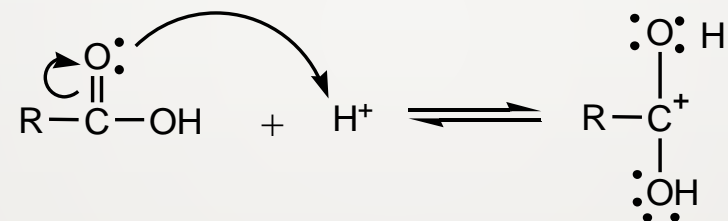
Esters from Carboxylic Acids: Esterification

Mechanism of Esterification.

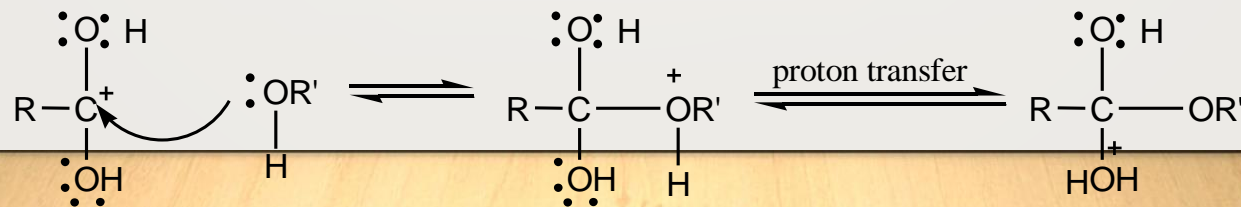
➔ Esterification is a **nucleophilic substitution** reaction.

➔ **The steps in the mechanism are**

Step 1. Protonation of the acyl group oxygen.



Step 2. Attack by alcohol nucleophile on positively charged carbon, followed by proton transfer.

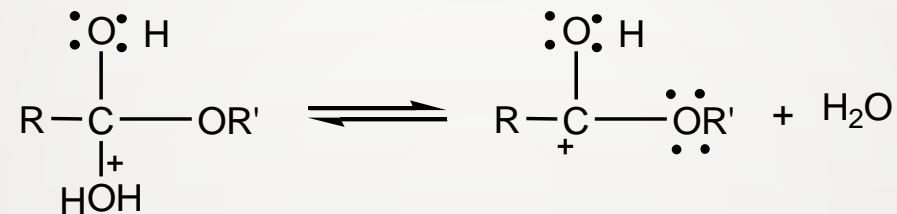


Nucleophilic Substitution of Acid Derivatives

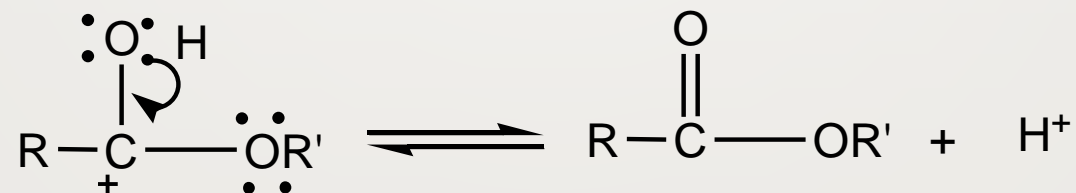
Esters from Carboxylic Acids: Esterification

Mechanism of Esterification.

Step 3. Elimination of H₂O.



Step 4. Regeneration of proton catalyst and formation of ester.

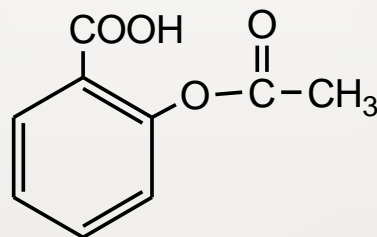


Nucleophilic Substitution of Acid Derivatives

Esters from Carboxylic Acids: Esterification

Sources and Uses of Esters

- ➔ **Fats, oils, and waxes** are naturally occurring esters of high molecular weight.
- ➔ A very common ester of medicinal importance is acetylsalicylic acid (aspirin).



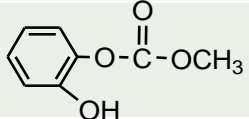
Acetylsalicylic acid
(Aspirin)

- ➔ Lower-molecular-weight esters are excellent solvents for many organic compounds.

Nucleophilic Substitution of Acid Derivatives

Esters from Carboxylic Acids: Esterification

Low-molecular-weight esters are **pleasant-smelling substances**.

Flavor	Name	Structure
Apricot	<i>n</i> -Pentyl butyrate	$\text{H}_3\text{CH}_2\text{CH}_2\text{C}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}(\text{CH}_2)_4\text{CH}_3$
Banana	<i>n</i> -Pentyl acetate	$\text{H}_3\text{C}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}(\text{CH}_2)_4\text{CH}_3$
Orange	<i>n</i> -Octyl acetate	$\text{H}_3\text{C}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}(\text{CH}_2)_7\text{CH}_3$
Pineapple	Ethyl butyrate	$\text{H}_3\text{CH}_2\text{CH}_2\text{C}-\overset{\text{O}}{\parallel}{\text{C}}-\text{OCH}_2\text{CH}_3$
Rum	Ethyl formate	$\text{H}-\overset{\text{O}}{\parallel}{\text{C}}-\text{OCH}_2\text{CH}_3$
Wintergreen	Methyl salicylate	

Nucleophilic Substitution of Acid Derivatives

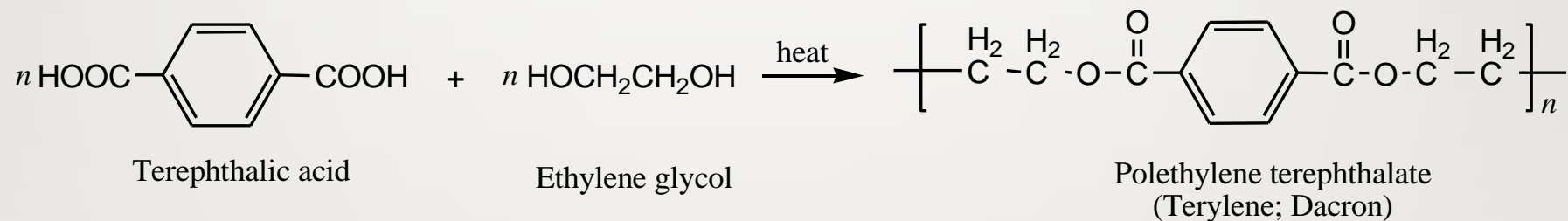
Esters from Carboxylic Acids: Esterification

Sources and Uses of Esters

➔ Other esters are suitable textile fibers.

The best-known polyester, Dacron, is polyethylene terephthalate,

formed from the polymerization of ethylene glycol and terephthalic acid

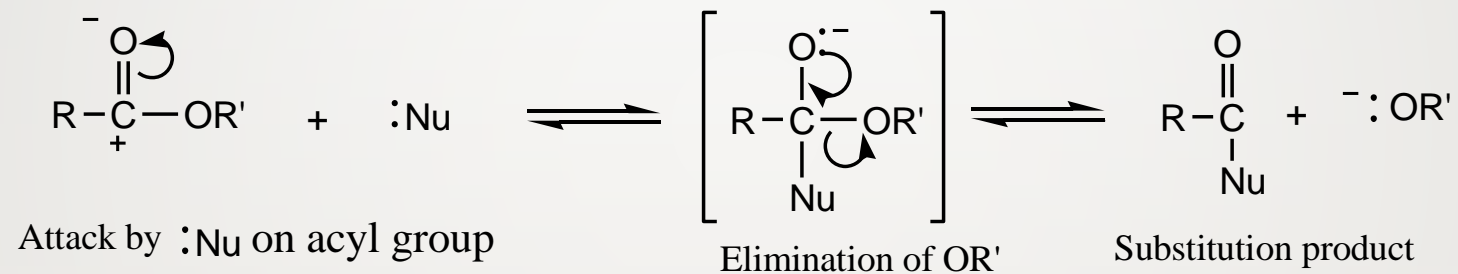


Nucleophilic Substitution of Acid Derivatives

Esters from Carboxylic Acids: Esterification

Reactions of Esters

➔ Nucleophilic attack on the acyl carbon followed by elimination of the OR group.



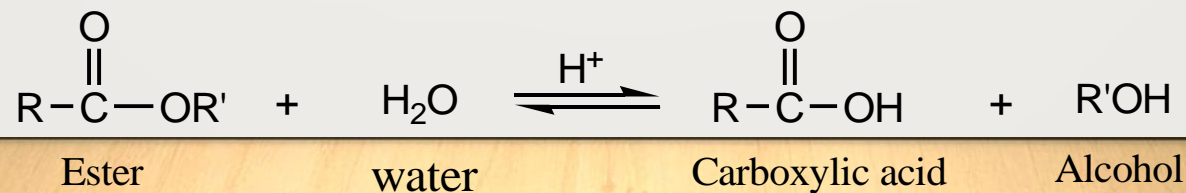
Nucleophilic Substitution of Acid Derivatives

Esters from Carboxylic Acids: Esterification

Reactions of Esters

A. Acid-Catalyzed Hydrolysis of Esters

- ➔ When a compound is broken down by the action of water, the reaction is called **hydrolysis**.
- ➔ The hydrolysis of an ester gives a carboxylic acid and an alcohol.
- ➔ The reaction is catalyzed by strong mineral acids H^+ .
- ➔ Acid-catalyzed hydrolysis, like acid-catalyzed esterification, is an equilibrium reaction that does not go to completion



Nucleophilic Substitution of Acid Derivatives

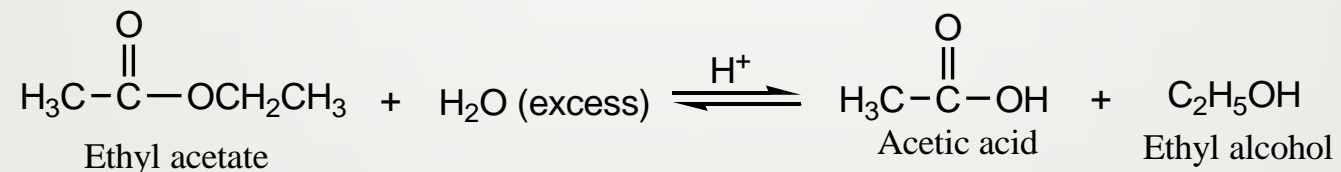
Esters from Carboxylic Acids: Esterification

Reactions of Esters

A. Acid-Catalyzed Hydrolysis of Esters



Excess water can be used to drive the equilibrium to the right.



Nucleophilic Substitution of Acid Derivatives

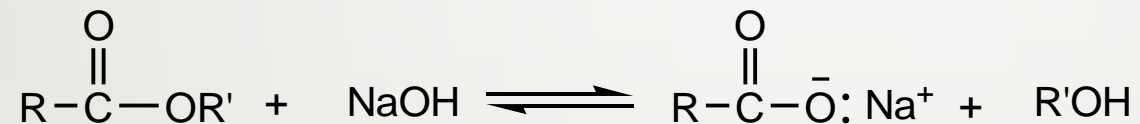
Esters from Carboxylic Acids: Esterification

Reactions of Esters

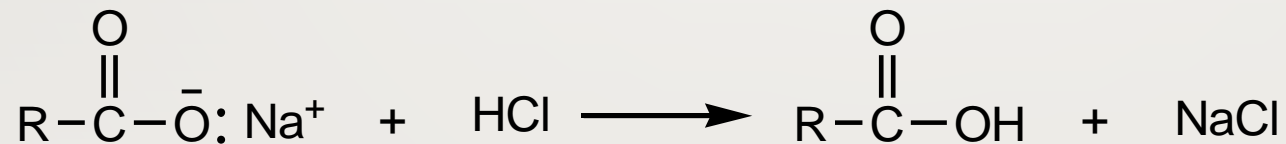
B. Alkaline Hydrolysis of Esters: Saponification

➔ *Alkaline hydrolysis* of an ester is called **saponification**.

because soap is the product of alkaline hydrolysis of esters of glycerol and long-chain fatty acids.



➔ Treatment of the salt with mineral acid regenerates the organic acid.



Nucleophilic Substitution of Acid Derivatives

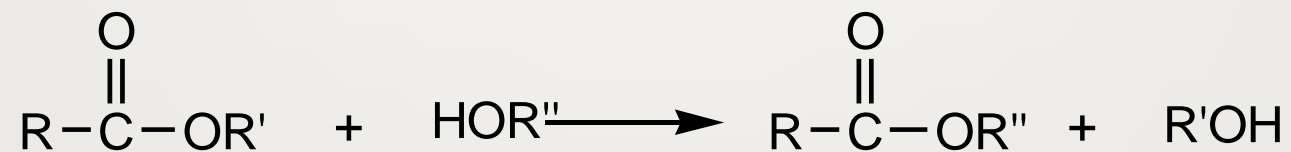
Esters from Carboxylic Acids: Esterification

Reactions of Esters

C. Alcoholysis: Transesterification

➔ **Alcoholysis** is the acid-catalyzed reaction between an ester and an alcohol to give an equilibrium mixture with another ester and another alcohol.

Ester interchange, or transesterification.



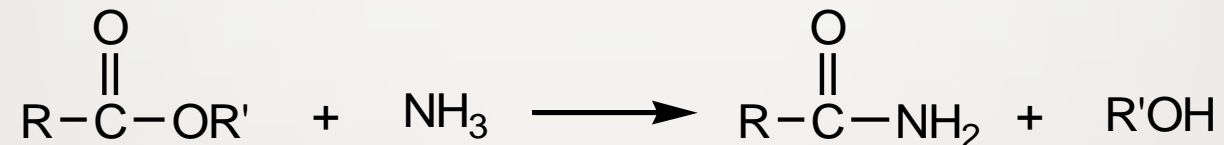
Nucleophilic Substitution of Acid Derivatives

Esters from Carboxylic Acids: Esterification

Reactions of Esters

D. Ammonolysis of Esters

➡ **Ammonolysis** is the reaction of esters with ammonia to form an amide and an alcohol.



➡ The amide group, -CON-, is widely distributed in nature, especially in protein molecules

Nucleophilic Substitution of Acid Derivatives

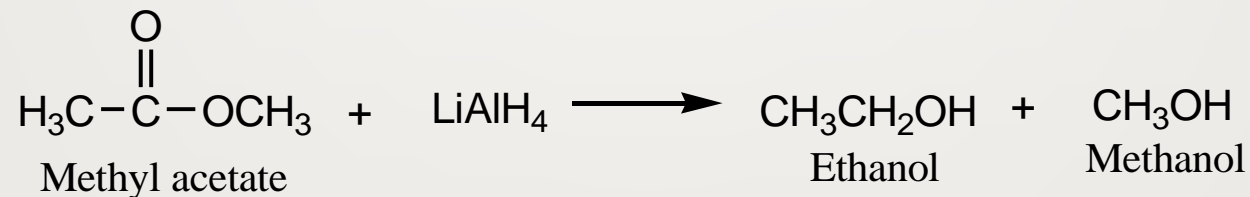
Esters from Carboxylic Acids: Esterification

Reactions of Esters

E. Reduction of Esters

➡ The reduction of esters with lithium aluminum hydride, LiAlH_4 produces two moles of alcohol:

- one from the acid part of the ester
- the other from the alcohol part.



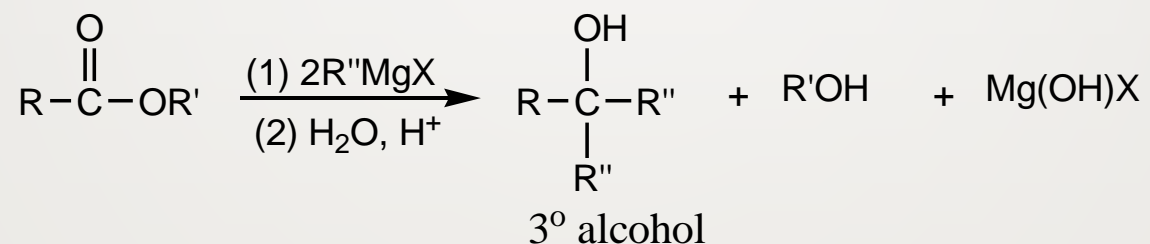
Nucleophilic Substitution of Acid Derivatives

Esters from Carboxylic Acids: Esterification

Reactions of Esters

F. Esters and Grignard Reagents

The carbonyl group of an ester can react with a Grignard reagent to form a *tertiary alcohol*.

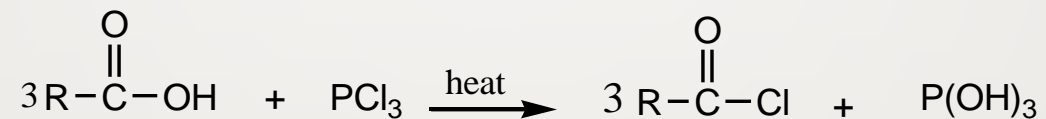


Nucleophilic Substitution of Acid Derivatives

Acid Chlorides: Preparation

⇒ **Acid chlorides** are reactive compounds and are important intermediates for the synthesis of other acid derivatives.

⇒ They are prepared by reaction of a carboxylic acid with phosphorus chlorides (PCl_5 or PCl_3) or with thionyl chloride (SOCl_2).



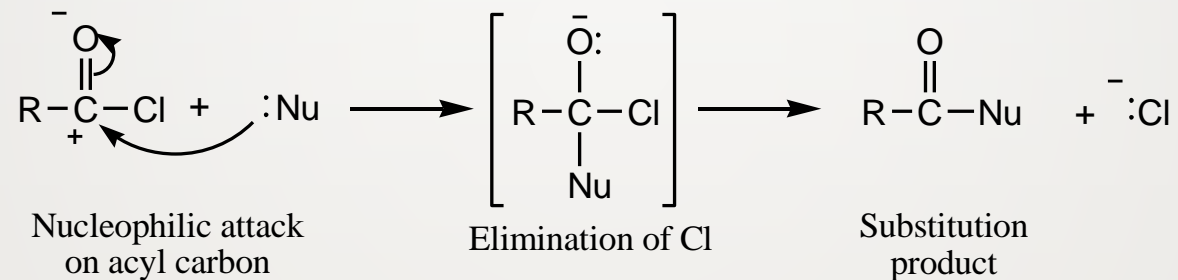
⇒ **Acid chlorides** are low-boiling liquids of irritating odors.

Nucleophilic Substitution of Acid Derivatives

Acid Chlorides: Preparation

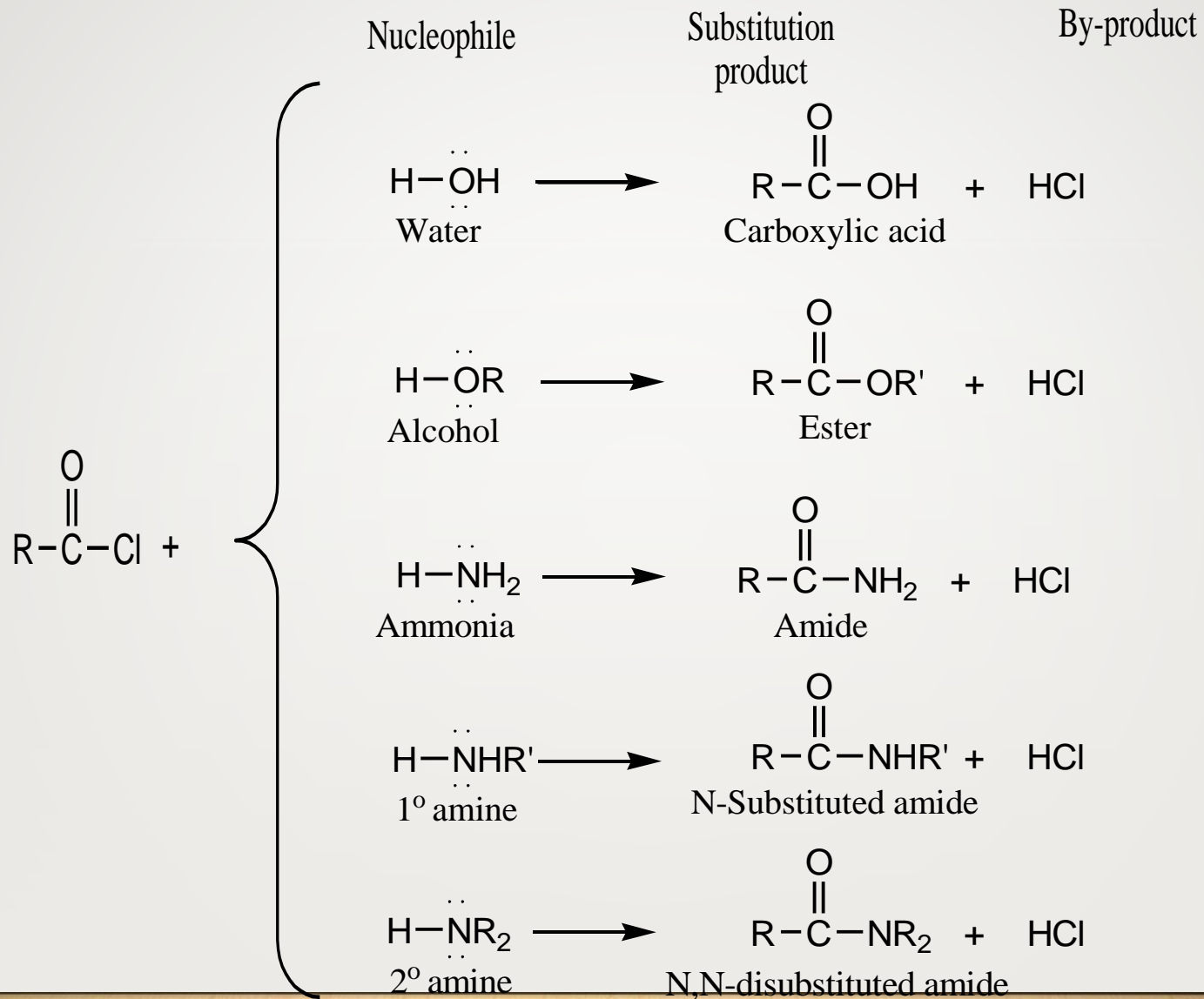
⇒ **Acid chlorides** are very reactive compounds because the inductive effect of the chlorine atom.

⇒ The mechanism of nucleophilic substitution of acid chlorides is similar to the one.



⇒ The attacking nucleophiles may be water, alcohol, ammonia, or amines.

⇒ Acid chlorides also form aromatic ketones *via* the Friedel-Crafts acylation.



Nucleophilic Substitution of Acid Derivatives

Acid Anhydrides: Preparation

⇒ **Anhydrides** are compounds that may be thought of as being formed by loss of water between two molecules of an acid.



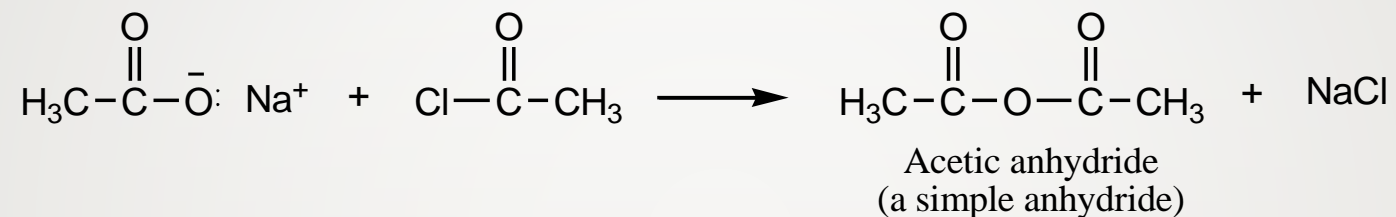
⇒ Most anhydrides are prepared by reaction between the sodium salt of the acid and an acid chloride.



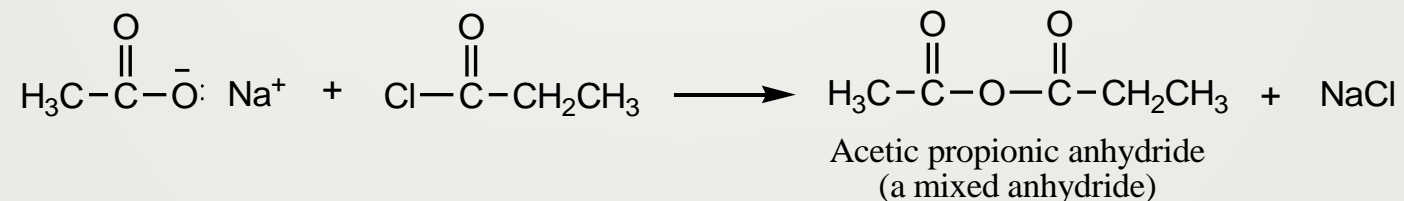
Nucleophilic Substitution of Acid Derivatives

Acid Anhydrides: Preparation

⇒ If the R groups of the acid salt and acid chloride are identical, we get a *anhydride*.



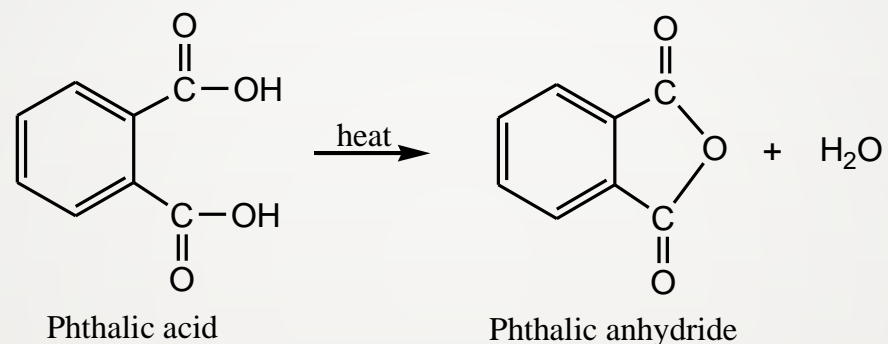
⇒ If the R groups are not the same, we get a *mixed anhydride*



Nucleophilic Substitution of Acid Derivatives

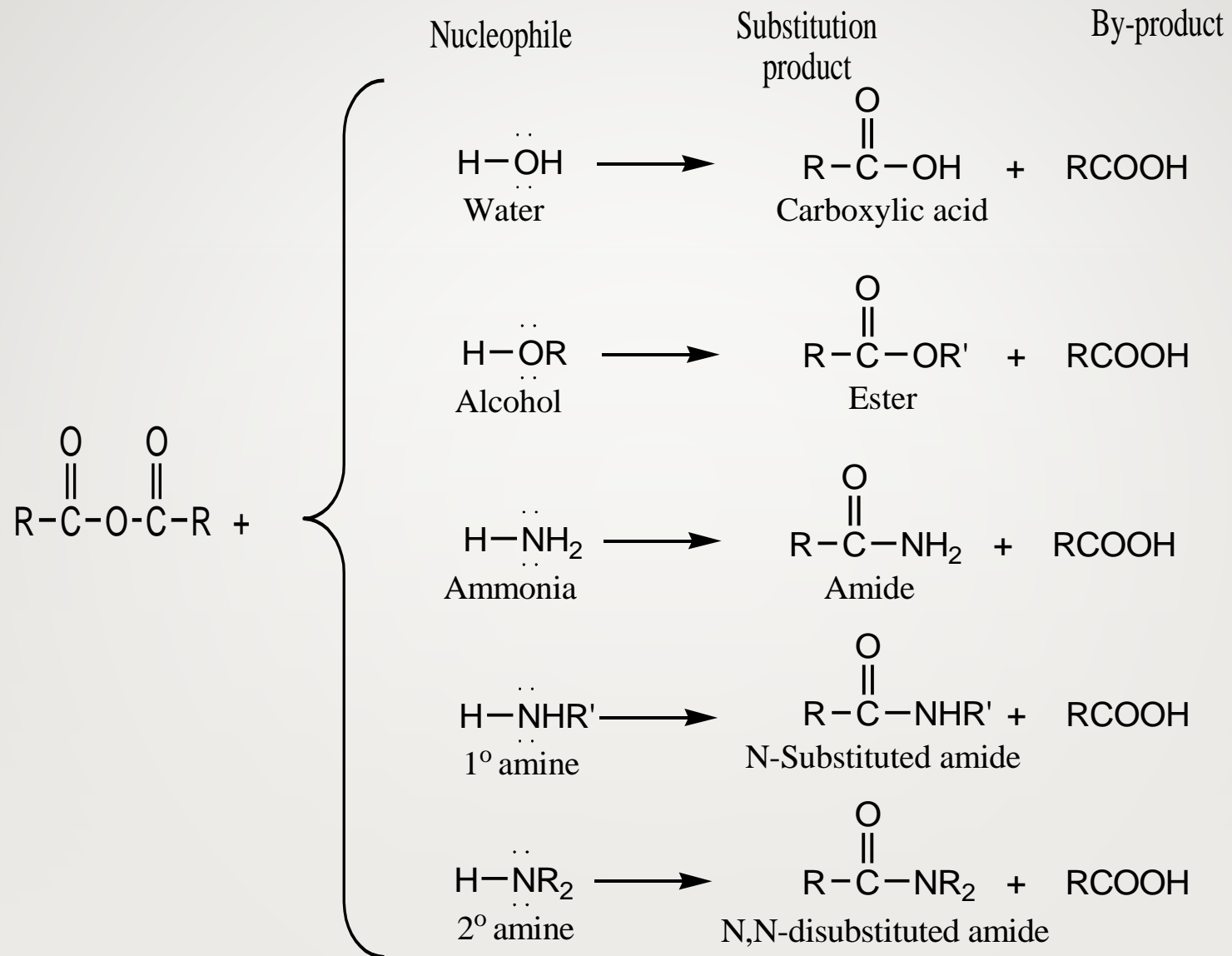
Acid Anhydrides: Preparation

⇒ **Cyclic anhydrides** are prepared by **intramolecular dehydration**.



⇒ The reactions of acid anhydrides with water, alcohols, ammonia, or amines parallel those already shown for the acid chlorides.

⇒ The by-product in all reactions of acid anhydrides is always a carboxylic acid



Nucleophilic Substitution of Acid Derivatives

Amides

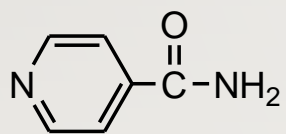
⇒ **Amides** are commonly prepared in the laboratory by the ammonolysis of acid chlorides or acid anhydrides.

⇒ For example,

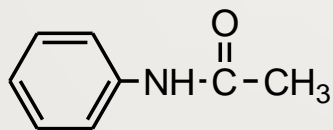
→ **Nicotinamide**, the amide of nicotinic acid (niacin), is essential in the diet to prevent pellagra.

→ **Acetanilide** and a derivative ***p*-hydroxyacetanilide**, are used as pain killers.

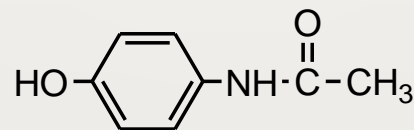
→ **Lidocaine** is a widely used local anesthetic.



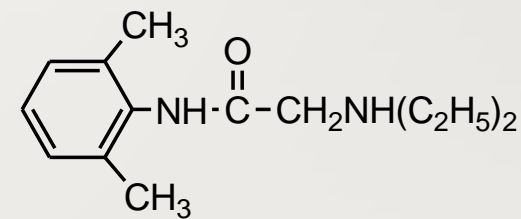
Nicotinamide
(prevents pellagra)



Acetanilide
(a pain killer)



p-Hydroxyacetanilide
(a pain killer)

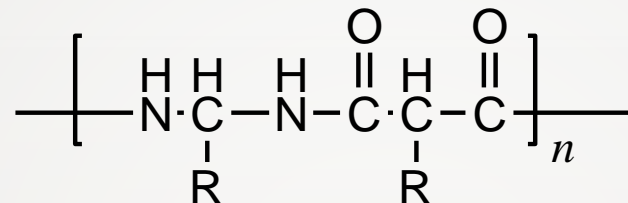


Lidocaine
(a local anesthetic)

Nucleophilic Substitution of Acid Derivatives

Amides

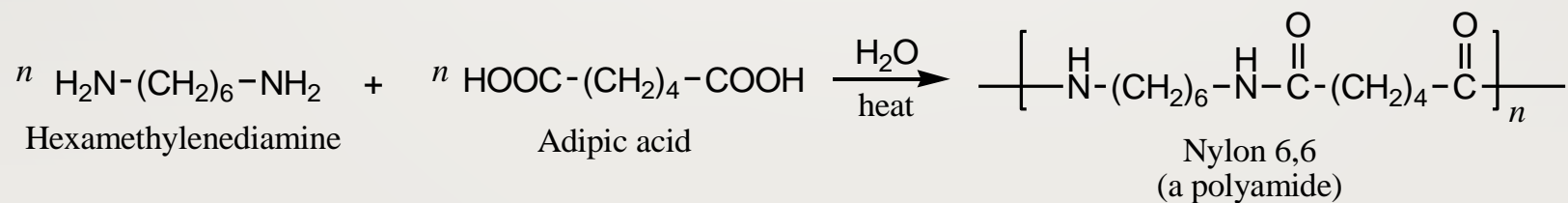
Proteins are polyamides containing amide linkage.



Polyamide polymer

Simpler polyamides make up the industrially important Nylon 6,6, used in the production of stockings and other textiles, and in the manufacture of brushes and plastic toys.

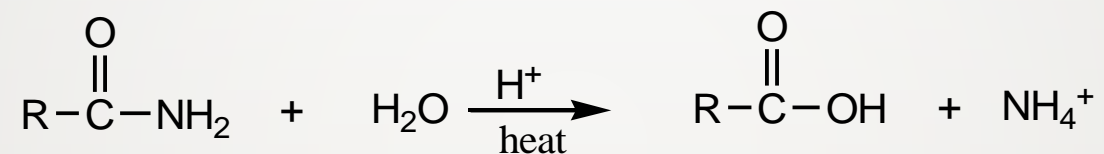
Nylon 6,6 is made from the reaction of hexamethylenediamine and adipic acid.



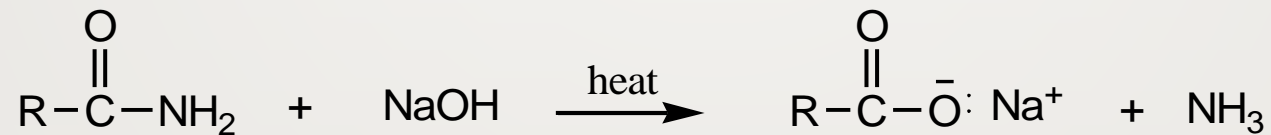
Nucleophilic Substitution of Acid Derivatives

Amides

- ⇒ **Amides** can be hydrolyzed in acid or in alkaline solution.
- ⇒ Acid-catalyzed hydrolysis produces the free organic acid and an ammonium salt.



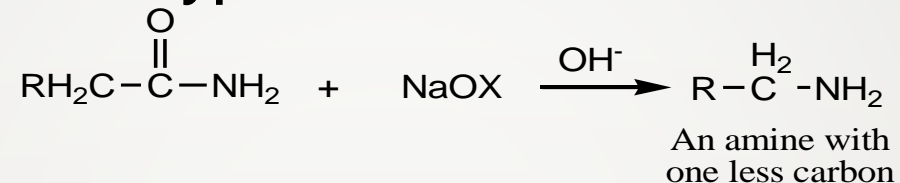
- ⇒ **Base-catalyzed hydrolysis** produces a carboxylate salt and free ammonia.



Nucleophilic Substitution of Acid Derivatives

Amides

Simple amides can be reduced to amines containing *one less carbon atom* by reaction with alkaline hypohalite solution.



Amides, when treated with lithium aluminum hydride, are reduced to amines.

The net reaction is the conversion of the C=O in amides to CH₂.

