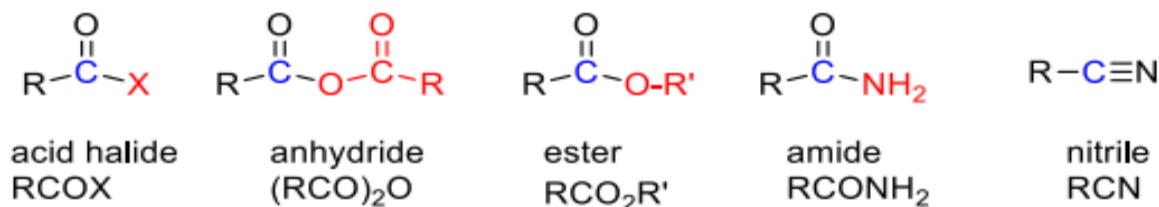


Chapter 7

Carboxylic Acid Derivatives

Compounds in which the –OH of the carboxyl group is replaced by certain other groups are called **carboxylic acid derivatives**, the most important of which are acyl halides, acid anhydrides, esters, Nitriles and amides.



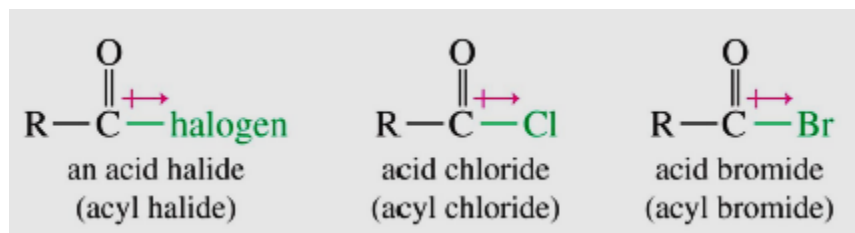
Reactivity of Acid Derivatives

<i>Reactivity</i>	<i>Derivative</i>	<i>Leaving group</i>	<i>Basicity</i>
<div style="display: flex; align-items: center;"> <div style="writing-mode: vertical-rl; transform: rotate(180deg); font-weight: bold; color: #800040;">more reactive</div> </div>	acid chloride $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{Cl}$	Cl^-	<div style="display: flex; align-items: center;"> <div style="writing-mode: vertical-rl; transform: rotate(180deg); font-weight: bold; color: #4682B4;">less basic</div> </div>
	anhydride $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$	$-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$	
	ester $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{R}'$	$-\text{O}-\text{R}'$	
	amide $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$	$-\text{NH}_2$	
<div style="display: flex; align-items: center;"> <div style="writing-mode: vertical-rl; transform: rotate(180deg); font-weight: bold; color: #800040;">less reactive</div> </div>	carboxylate $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}^-$	$-$	more basic

1. Acid Halides

Acid (or acyl) halides are *activated* derivatives of carboxylic acids, and are often used to prepare the other carboxylic acid derivatives.

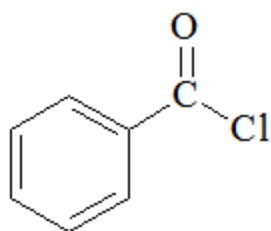
The most common examples of this class are acid *chlorides*, but acid *fluorides*, *bromides* and *iodides* do exist (but are rarely used).



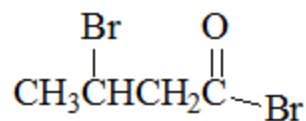
The halogen atom inductively withdraws electron density away from the already electrophilic carbon of the carbonyl group.

➤ Nomenclature

Acid halides are named by taking the *-ic acid* suffix of the related carboxylic acid, replacing it with *-yl*, and adding the *halide* name.



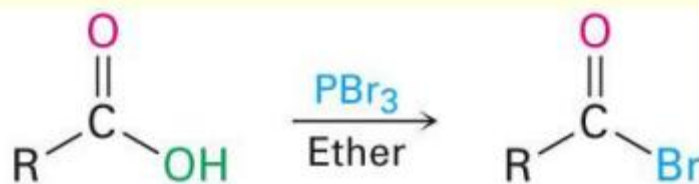
benzoyl chloride



3-bromobutanoyl bromide
 β -bromobutyryl bromide

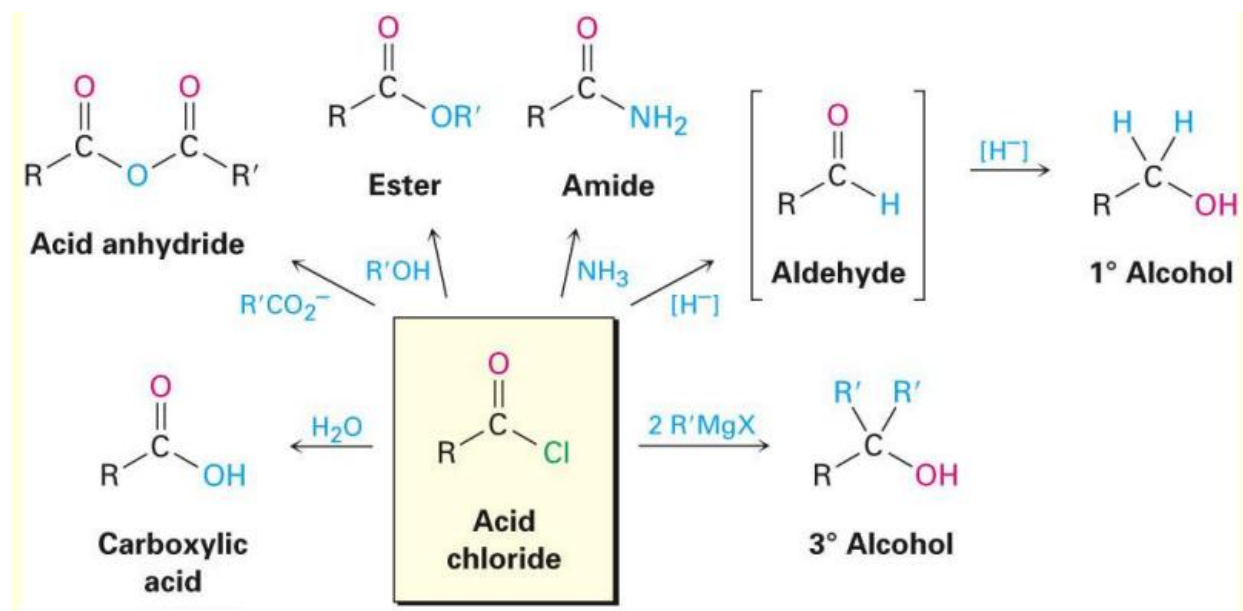
➤ Preparations:

- Acid chlorides are prepared from carboxylic acids by reaction with SOCl_2
- Reaction of a carboxylic acid with PBr_3 yields the acid bromide



➤ Reactions of Acid Halides

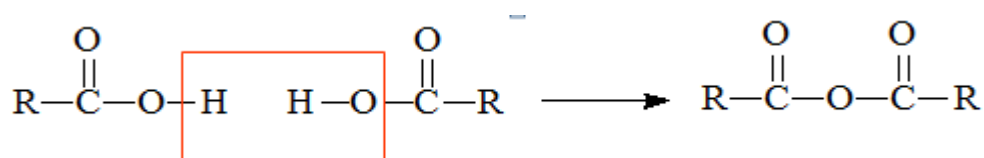
- Nucleophilic acyl substitution
- Halogen replaced by —OH, by —OR, or by —NH₂
- Reduction yields a primary alcohol



2. Acid Anhydrides

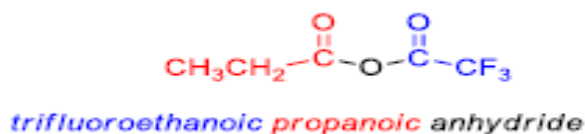
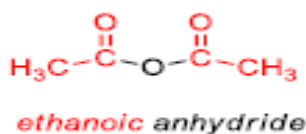
The word *anhydride* literally means *without water*, and an acid anhydride is the combination of two molecules of carboxylic acid with the elimination of one molecule of water.

- Anhydrides are more reactive than acids, but less reactive than acid chlorides.
- A carboxylate ion is the leaving group in nucleophilic acyl substitution reactions.



➤ Nomenclature:

(Simple) anhydrides are simply named by replacing the *-acid* suffix of the parent carboxylic acids with the word *anhydride*.



acetic anhydride

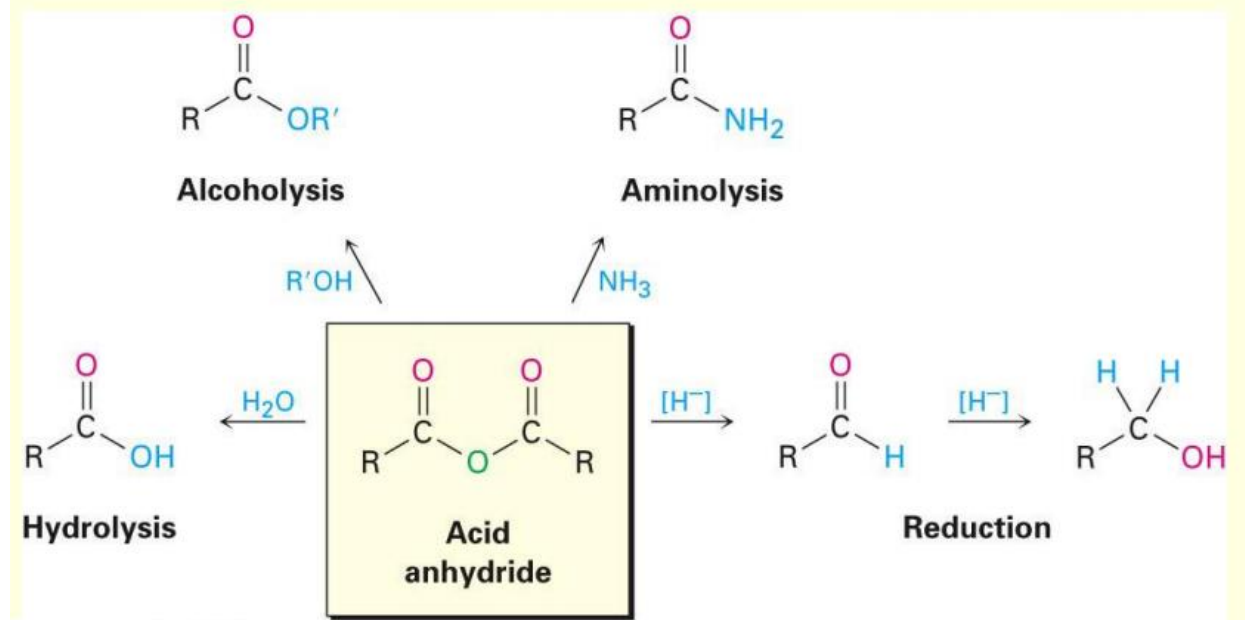
➤ Preparations of Acid Anhydride

Acid anhydrides are considered to be derived from carboxylic acids by the removal of a molecule of water from two molecules of acid. So acid anhydrides can be prepared by heating carboxylic acid in the presence of P₂O₅ in dehydrating agent.



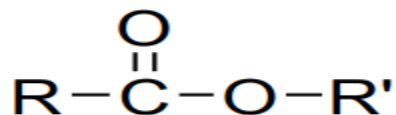
➤ Reactions of Acid Anhydrides

■ Similar to acid chlorides in reactivity



3. Esters of Carboxylic Acids

Structurally, an ester is a compound that has an alkoxy (**OR**) group attached to the carbonyl group.

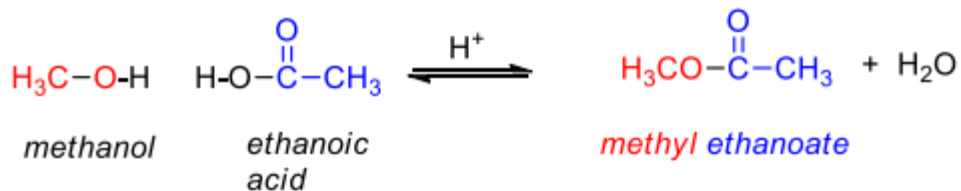


R may be **H**, alkyl or aryl, while **R'** may be alkyl or aryl only. Esters are widespread in nature. Many of the fragrances of flowers and fruits are due to the esters present.

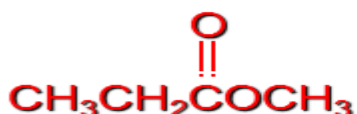
➤ Nomenclature:

The names of esters are derived from the names of the compounds that are used to create them. The first word of the name comes from the alkyl group of the alcohol, and the second part comes from the carboxylate group of the acid used (name as **alkyl alkanoates**, cite the alkyl group attached to oxygen first (**R'**) name the acyl group second; substitute the suffix **-ate** for the **-ic** ending of the corresponding acid)

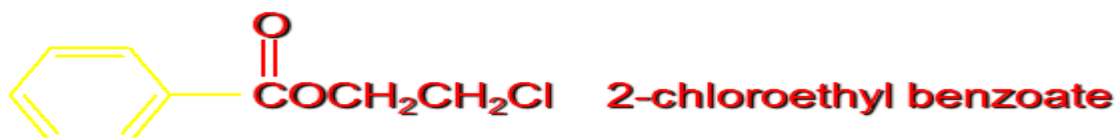
. E.g.



ethyl acetate

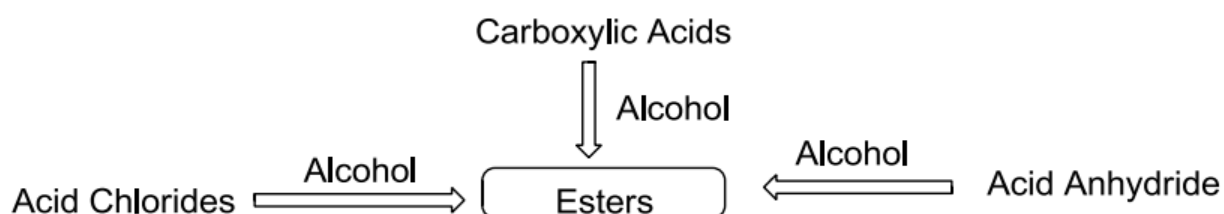


methyl propanoate

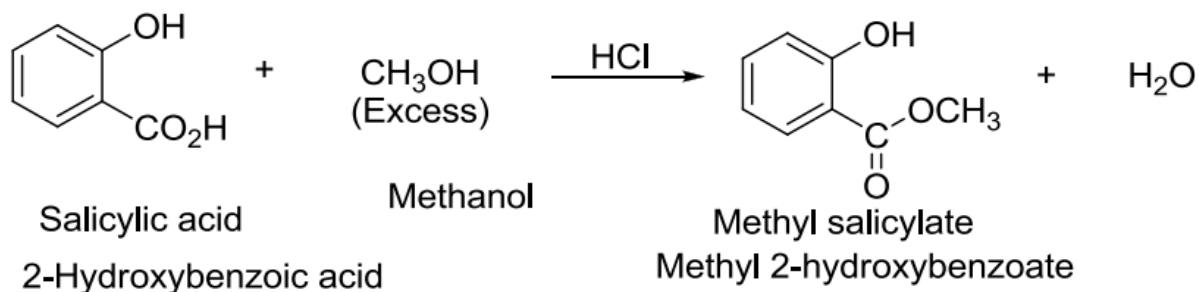


➤ Synthesis of Esters

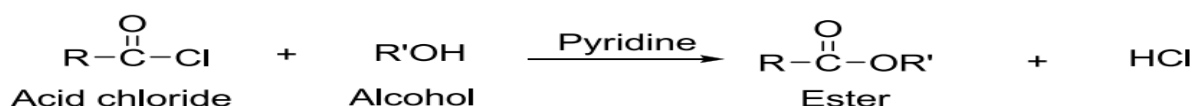
Highlighted below are some of the most common strategies by which esters are prepared. The esters are commonly prepared from the reaction of carboxylic acids, acid chlorides and acid anhydrides with alcohols.



1. Acid-Catalysed Esterification of a Carboxylic Acid and an Alcohol

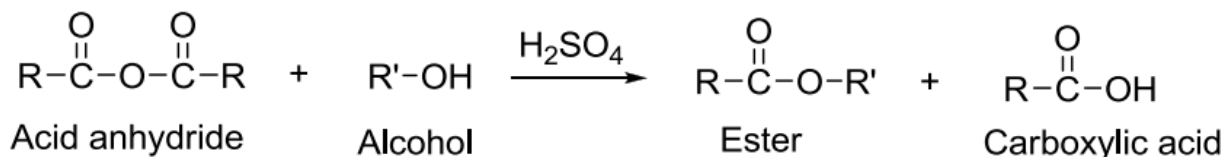


2. Esters Derived from an Acid Chloride and an Alcohol

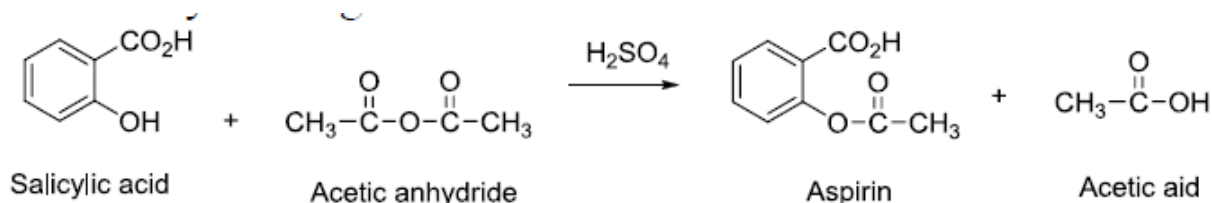


3. Esters

Derived from an Acid Anhydride and an Alcohol or a Phenol



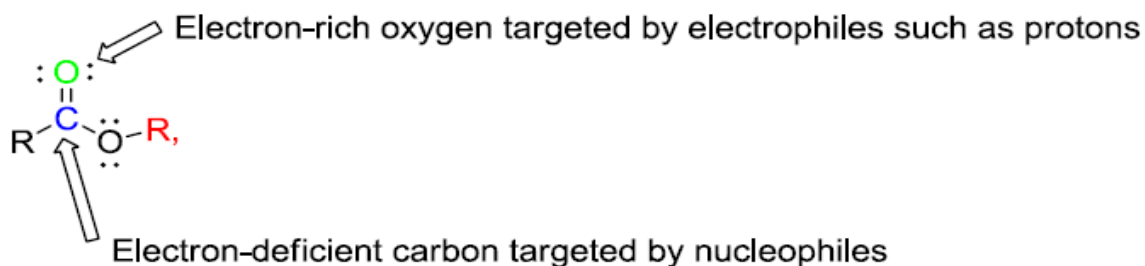
Acid anhydrides react with alcohols via nucleophilic acyl substitution to provide esters. The reaction may be catalysed by either a strong acid (H₂SO₄) or a weak base (pyridine) or effected by heating.



Reactions of Esters

Esters are less reactive compared to acid chlorides.

Reaction sites on the carboxyl group of Esters



The most common reactions of esters are with nucleophiles leading to nucleophilic acyl substitution.

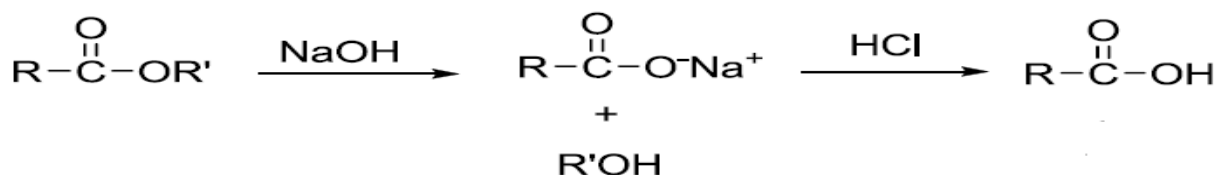


1. Hydrolysis of Esters in Basic Media

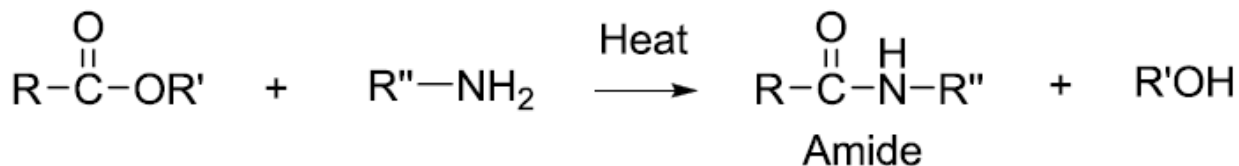
Unlike the acid chlorides that hydrolyse readily in water, esters do not hydrolyse readily in water. The hydrolysis of esters requires an acid or base catalyst.

The products of the hydrolysis depend on whether the reaction is conducted in a basic media or an acidic media.

Hydrolysis of esters in basic media provides a carboxylate salt and an alcohol, which when acidified provides a carboxylic acid and an alcohol.



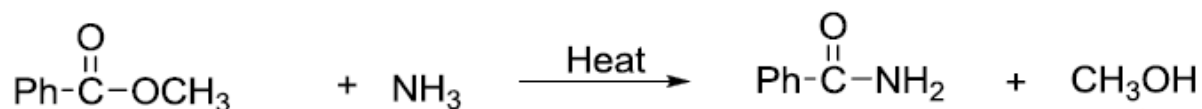
2. Reaction of Esters with Ammonia and Amines



Esters react with ammonia and amines in what amounts to a nucleophilic substitution at the carbonyl carbon to provide amides.

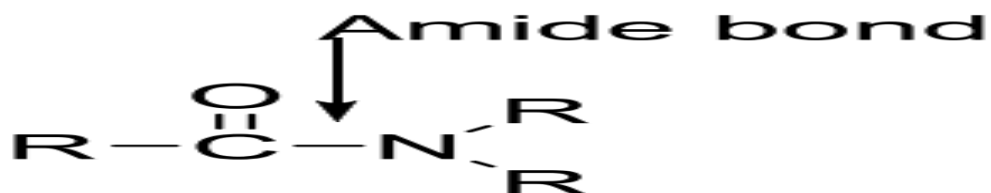
Note that ammonia and amines are more nucleophilic than water and alcohols. Consequently, these reactions can proceed even in presence of water or alcohol.

Example



4. Amides

Amides are functional groups in which a carbonyl carbon atom is linked by a single bond to a nitrogen atom and either a hydrogen or a carbon atom (an amide is a composite of a carboxylic acid and either ammonia or an amine).



R may be H, alkyl or aryl.

Classes of Amides:

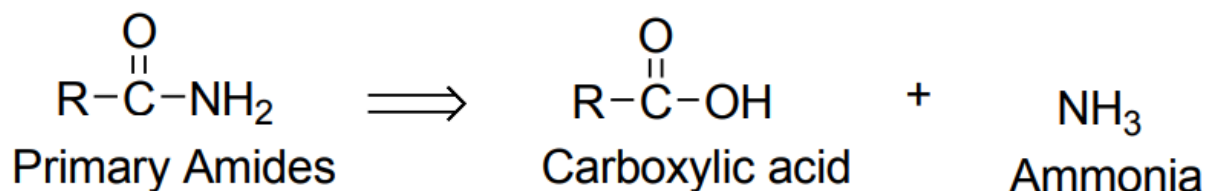
Amides are classified according to the number of substituents (non-hydrogen-like groups) connected to the nitrogen of the amide group. Note that the carboxyl group is also treated as a substituent to the nitrogen.

Structure	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\overset{\text{H}}{\text{N}}-\text{R}$	$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\overset{\text{R}}{\text{N}}-\text{R}$
# of groups on nitrogen	One	Two	Three
Classification	Primary amide	Secondary amide	Tertiary amide

➤ IUPAC Nomenclature of Amides

1. Primary

An amide is named based on the recognition that it is a composite of a carboxylic acid and ammonia or an amine.



Primary amides are, thus, named by replacing the suffix **-oic acid** in the IUPAC name of the parent carboxylic acid of the amide by the suffix **-amide**.

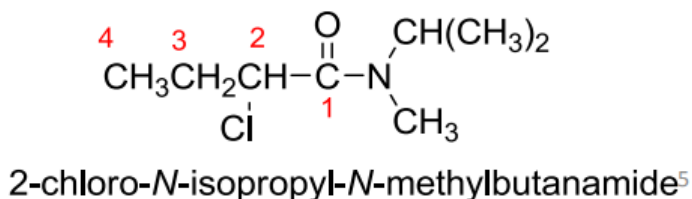
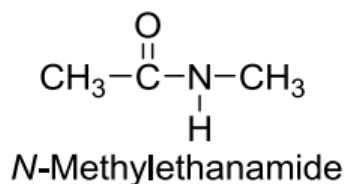
Examples



2. Names of Secondary and Tertiary Amides

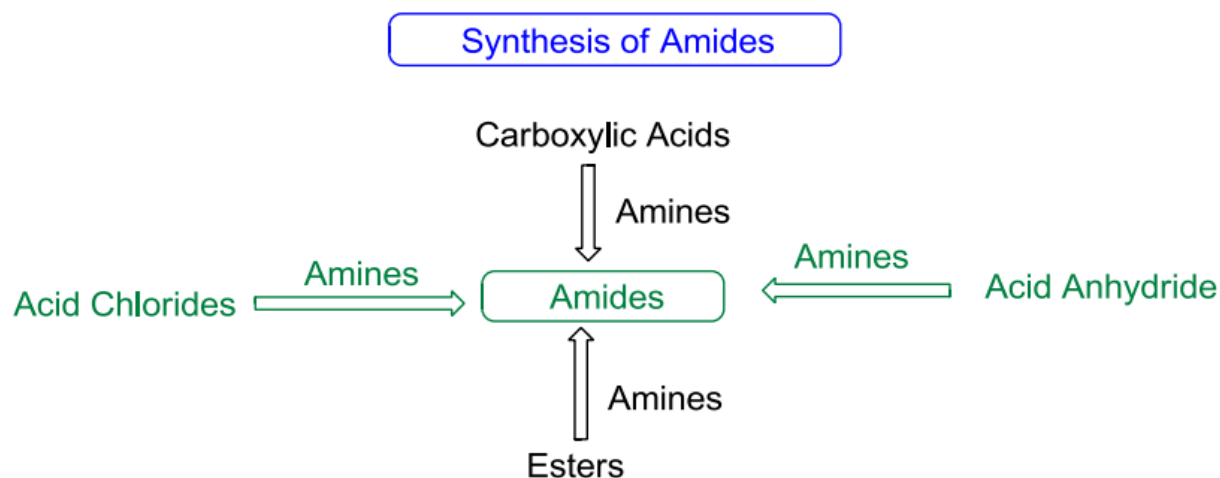
In the naming of secondary and tertiary amides, the **alkyl groups** on nitrogen are treated as substituents, and their position is specified by the **prefix N-** to differentiate them from any substituents located on the parent chain of the parent carboxylic acid. If more than one substituent is bonded to nitrogen, they are stated alphabetically followed by the name of the amide. Substituents on the acyl component are designated with the usual locators (2,3.. etc) as appropriate.

Example



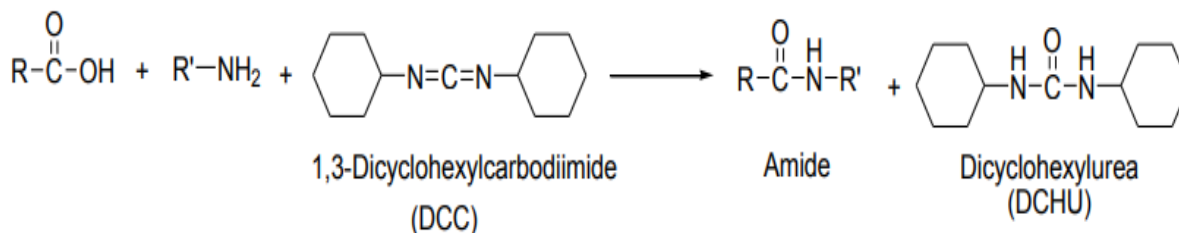
➤ Synthesis of Amides

Highlighted below are the most common strategies by which amides are prepared. The amides are commonly prepared from the reaction of carboxylic acids, acid chlorides and acid anhydrides with amines.

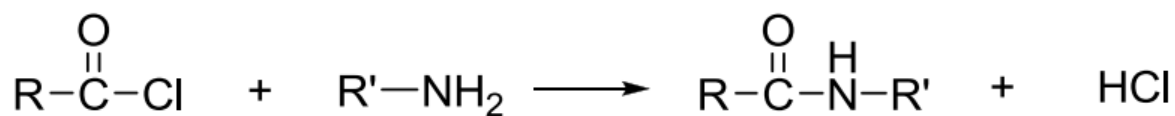


1. Reaction of Carboxylic Acids with Amines in Presence of DCC

Primary and secondary amines react with carboxylic acids in the presence of DCC to form amides.

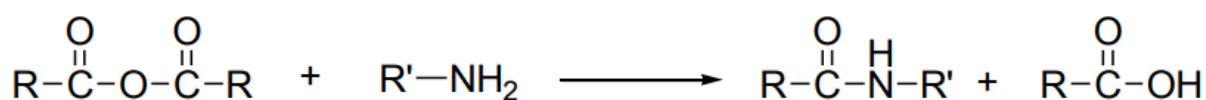


2. Reaction of Acid Chlorides with an Amine



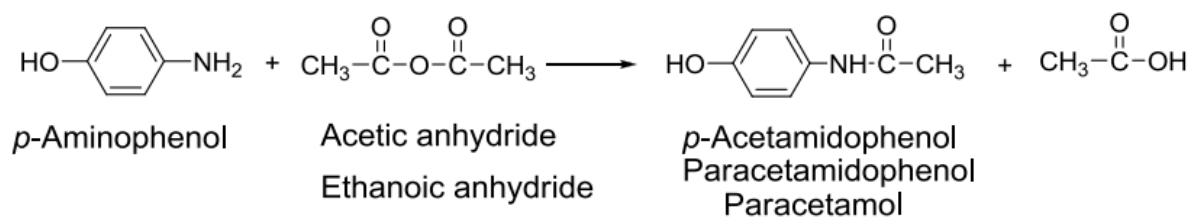
Acid chlorides, with a good leaving group attached to the carbonyl group, react with ammonia and amines through a nucleophilic acyl substitution to provide amides.

3. Reaction of Acid Anhydrides with an Amine

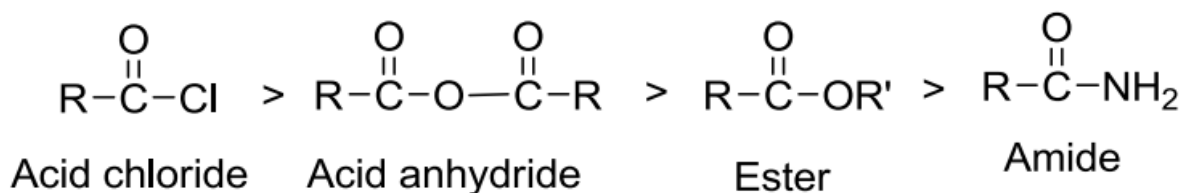


Just like acid chlorides, acid anhydrides also react with ammonia and amines through a nucleophilic acyl substitution to provide amides.

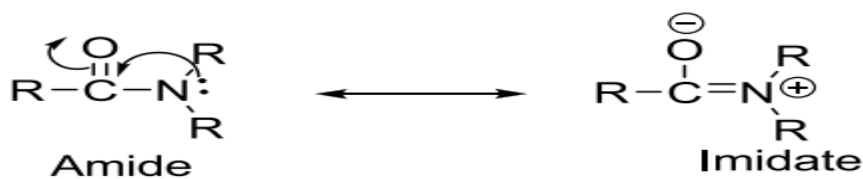
Example



➤ Reactions of Amides



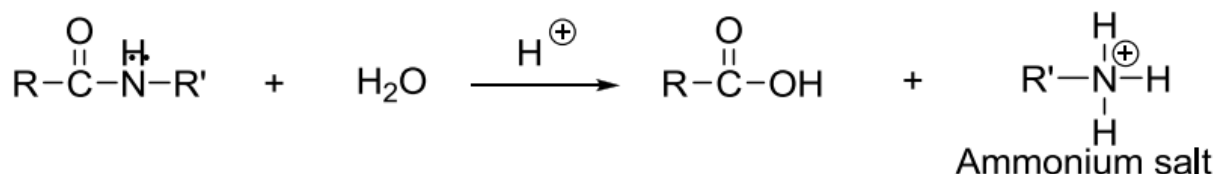
Amides are the most stable carboxylic acid derivatives and consequently the least reactive of the carboxylic acid derivatives.



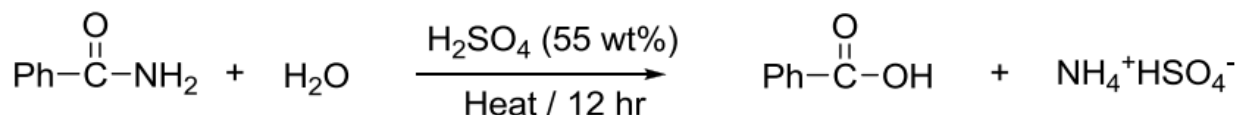
The diminished reactivity of amides is more because they exist in the imidate form rather than as a true amide. The imidate formation significantly reduces the electrophilicity of the carbon of the carbonyl. Consequently, amides undergo relatively fewer reactions.

1. Hydrolysis of Amides

The hydrolysis of amides is much more difficult compared to that of esters. Consequently, they require much harsher conditions usually by heating under either acidic or basic conditions for a prolonged period.

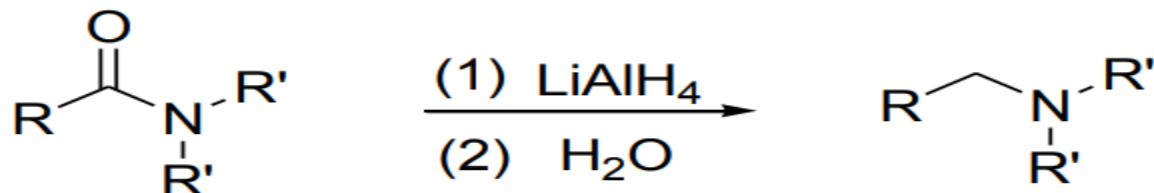


The hydrolysis of amides in acidic media provides a carboxylic acid and an ammonium salt.

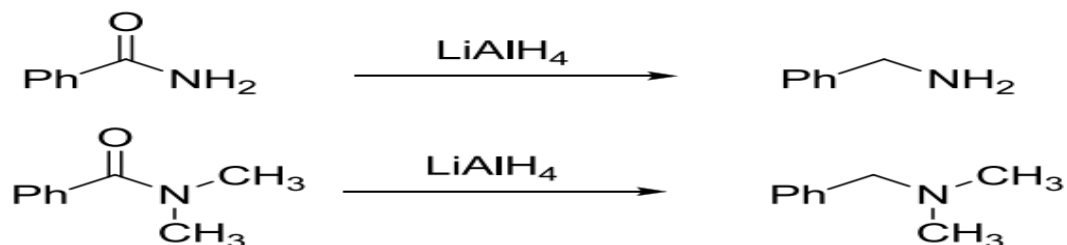


Due to the high stability of amides, their hydrolysis requires heating at 110 °C in concentrated acid for about 12 hours.

2. Reduction of Amides to Amines



The reduction of amides with a strong reducing agent (LiAlH_4) provides an amine of the same classification as the parent amide.

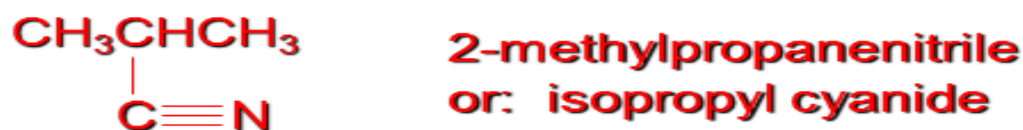
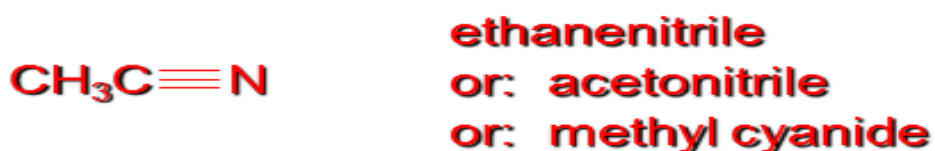


5. Nitriles

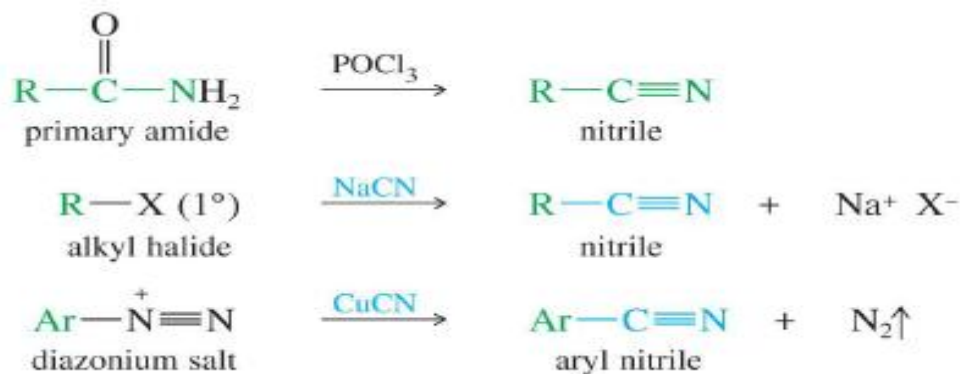
A nitrile is any organic compound that has a $-\text{C}\equiv\text{N}$ functional group



- **Nomenclature :**
- Add the suffix **-nitrile** to the name of the parent hydrocarbon chain (including the triply bonded carbon of CN)
- or: replace the **-ic acid** or **-oic acid** name of the corresponding carboxylic acid by **-onitrile**
- or: name as an **alkyl cyanide** (functional class name)



➤ Preparation of Nitriles



➤ Reactions of Nitriles:

Nitriles undergo *acidic* or *basic* hydrolysis to primary amides

