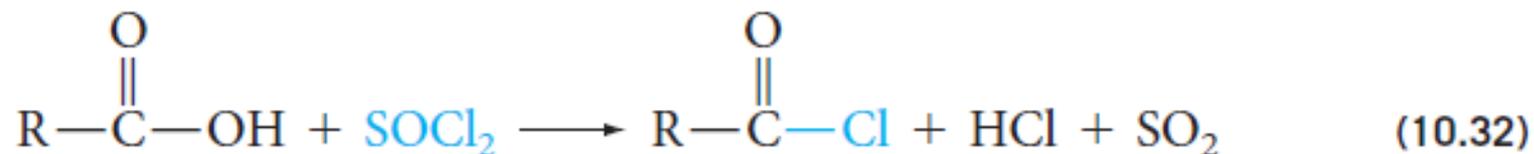


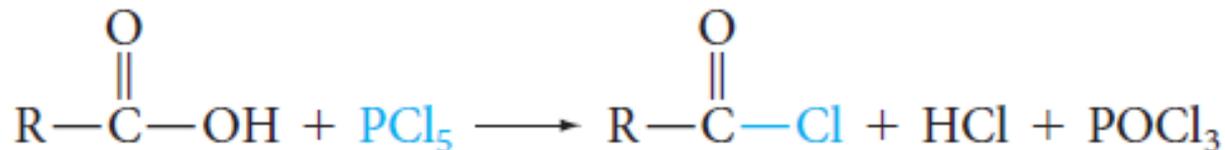
# Acyl Halides

An **acyl halide** is a carboxylic acid derivative in which the —OH group is replaced by a halogen atom.

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

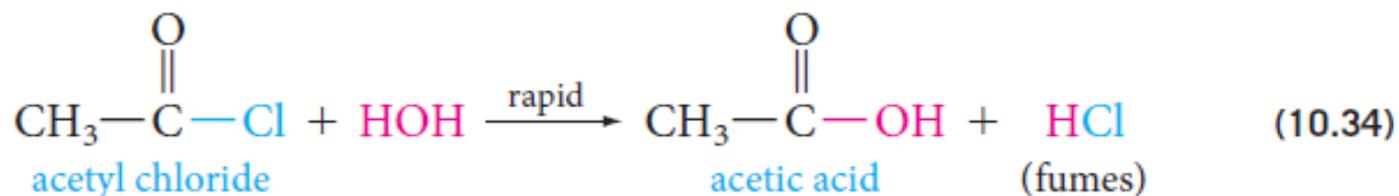


Phosphorus pentachloride and other reagents can also be used to prepare acyl chlorides from carboxylic acids.

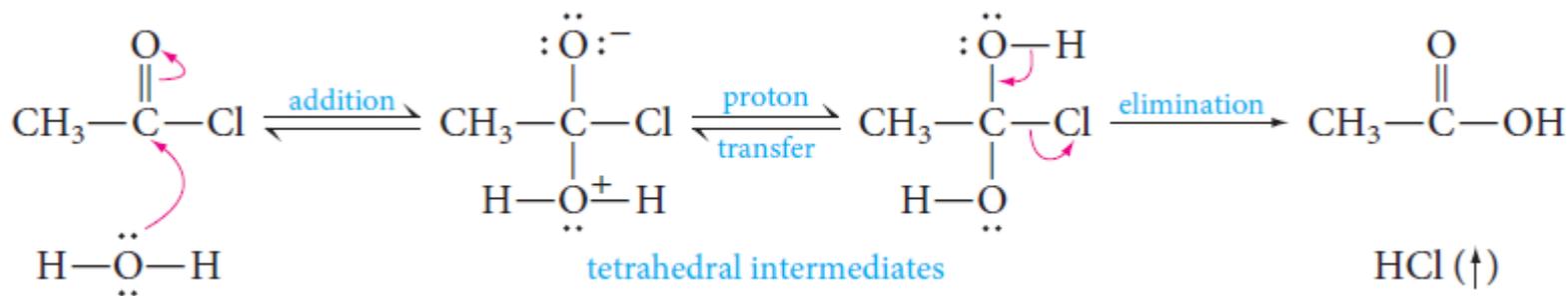


# Acyl Halides

Acyl halides react rapidly with most nucleophiles. For example, they are rapidly hydrolyzed by water.

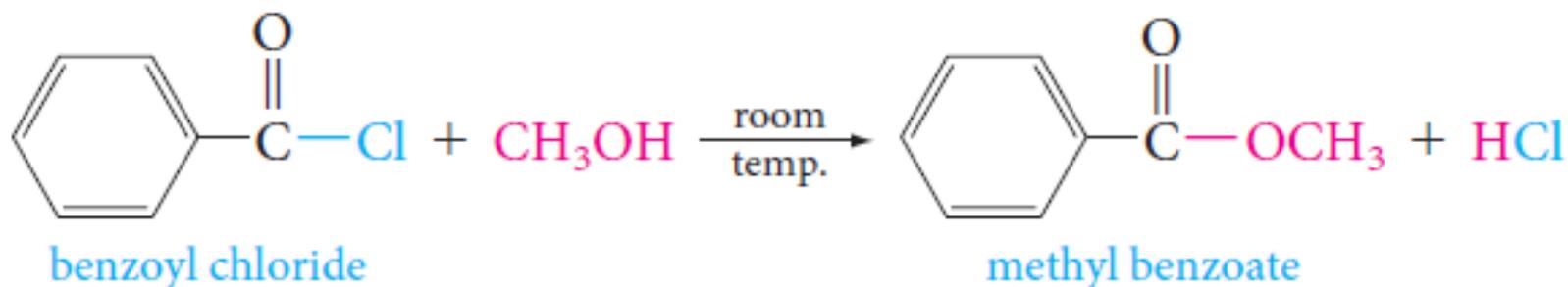


## Mechanism



# Acyl Halides

Acyl halides react rapidly with alcohols to form esters.

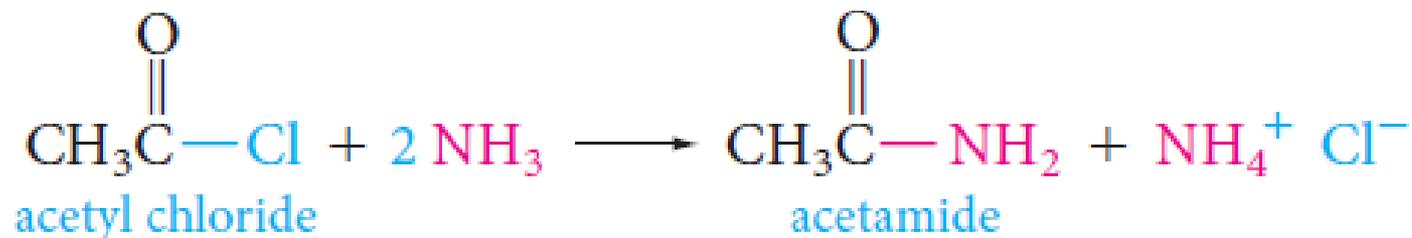


## Mechanism

????????????

# Acyl Halides

Acyl halides react rapidly with ammonia to form amides.

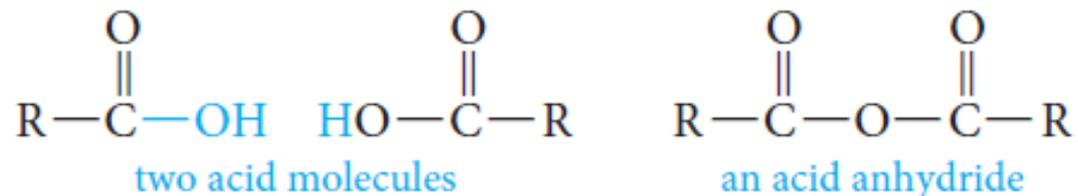


## Mechanism

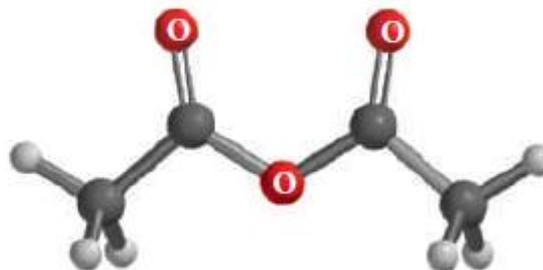
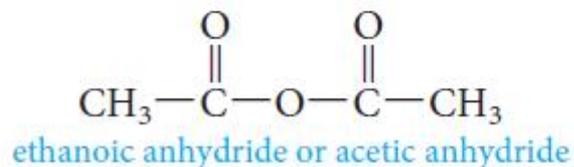
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# Acid Anhydrides

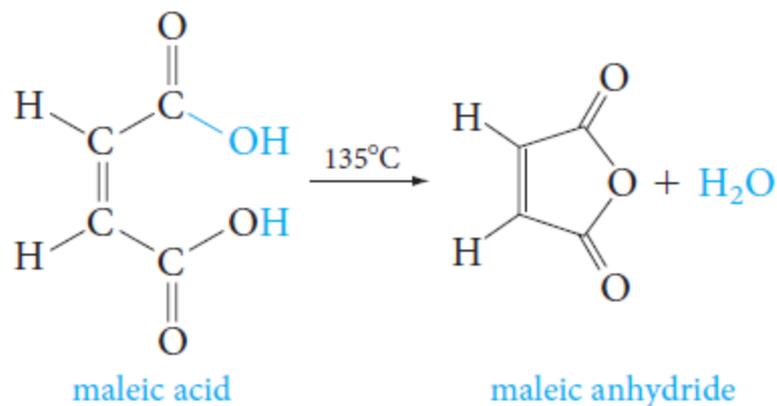
Acid anhydrides are derived from acids by removing water from two carboxyl groups and connecting the fragments.



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

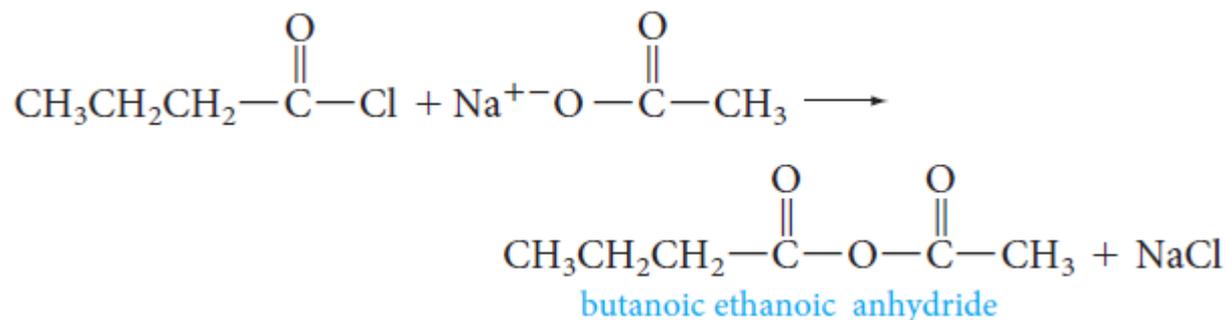


Anhydrides are prepared by dehydration of acids. Dicarboxylic acids with appropriately spaced carboxyl groups lose water on heating to form cyclic anhydrides with five- and six-membered rings. For example,



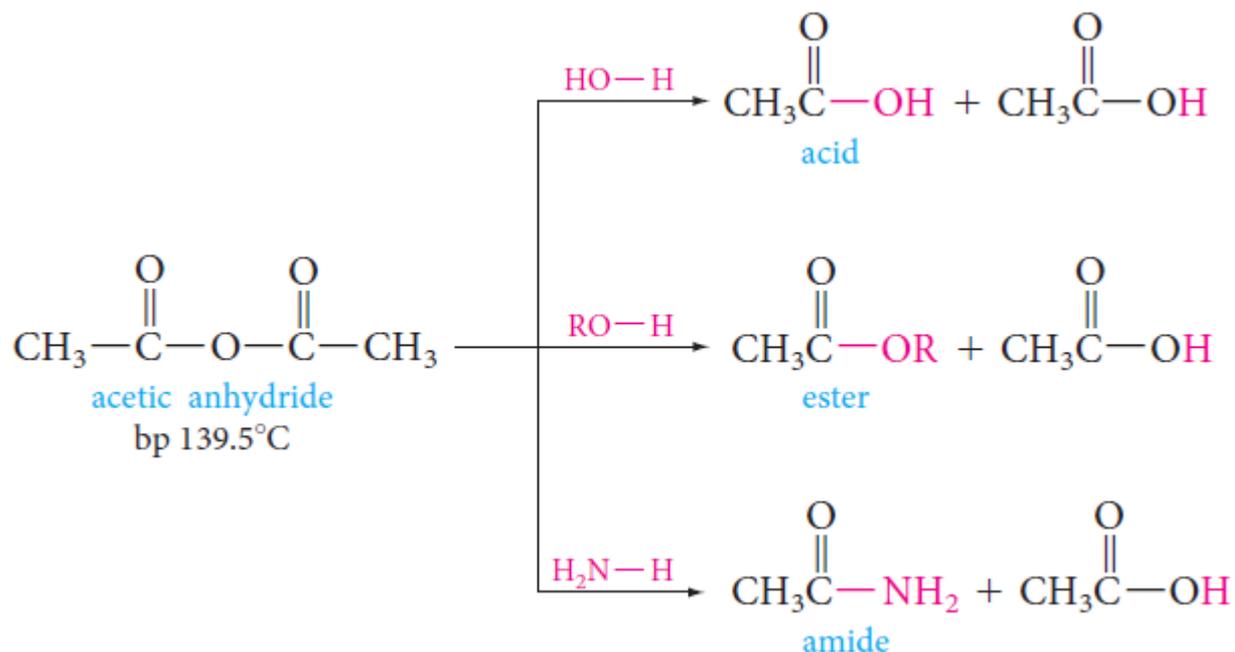
**Mixed anhydrides** are prepared from two different carboxylic acids.

Anhydrides can also be prepared from acid chlorides and carboxylate salts in a reaction that occurs by a nucleophilic acyl substitution mechanism. This is a good method for preparing anhydrides derived from two different carboxylic acids, called **mixed anhydrides**.



# Reactions of Anhydrides

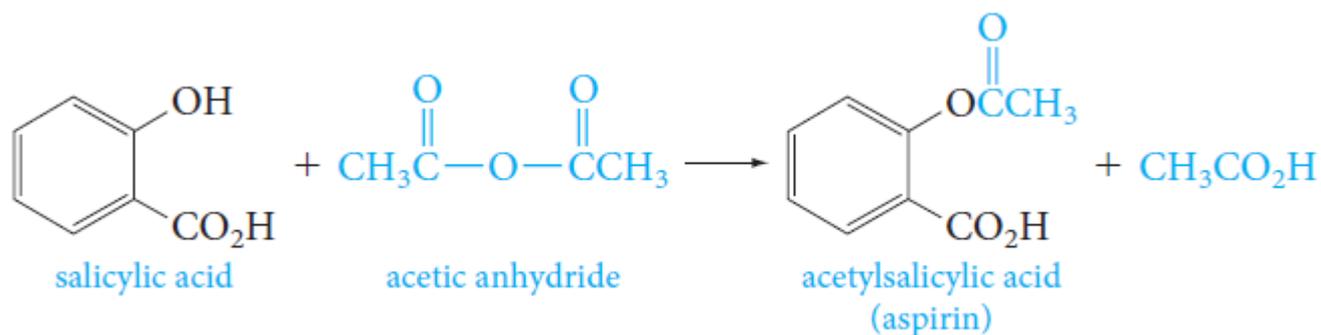
Anhydrides undergo nucleophilic acyl substitution reactions. They are more reactive than esters, but less reactive than acyl halides, toward nucleophiles. Some typical reactions of acetic anhydride follow:



# Aspirin

An alcohol is said to be **acetylated** when converted to its acetate ester.

The reaction of acetic anhydride with salicylic acid (*o*-hydroxybenzoic acid) is used to synthesize aspirin. In this reaction, the phenolic hydroxyl group is **acetylated** (converted to its acetate ester).

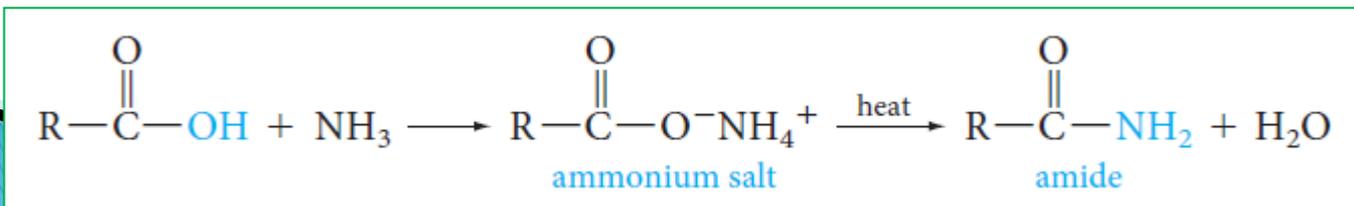
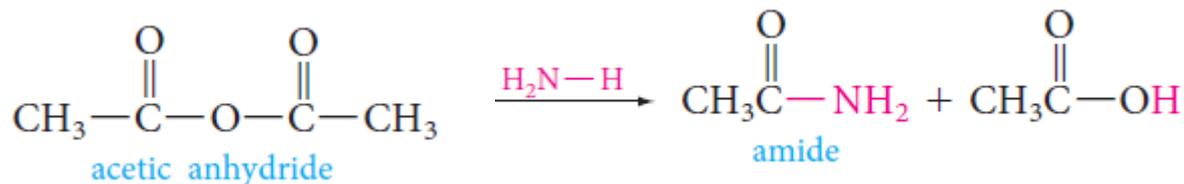
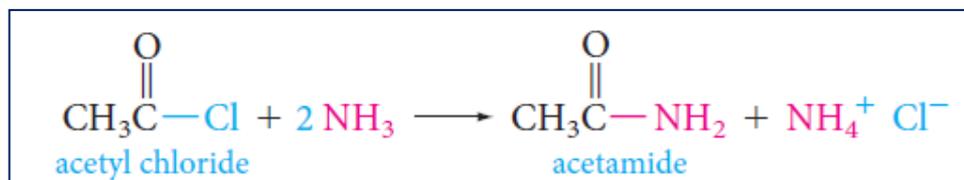
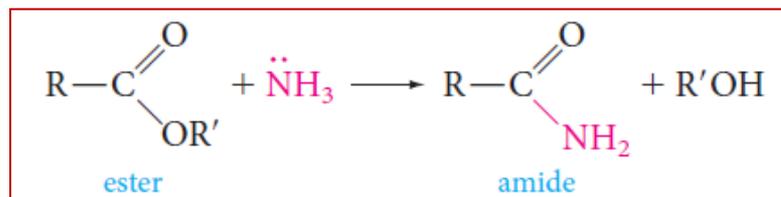


# Amides

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

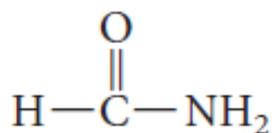
**Amides** are the least reactive of the common carboxylic acid derivatives. They occur widely in nature. The most important amides are the proteins

Primary amides have the general formula RCONH<sub>2</sub>. They can be prepared by the reaction of ammonia with esters, with acyl halides, or with acid anhydrides. Amides can also be prepared by heating the ammonium salts of acids.

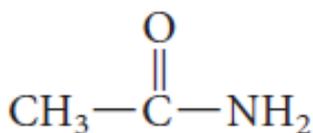


# Amides

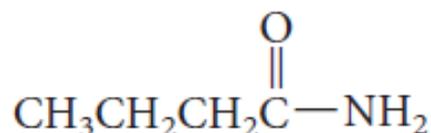
Amides are named by replacing the *-ic* or *-oic* ending of the acid name, either the common or the IUPAC name, with the *-amide* ending.



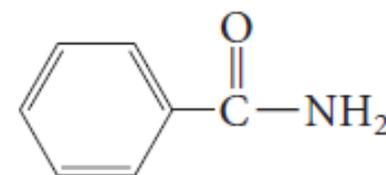
formamide  
(methanamide)



acetamide  
(ethanamide)



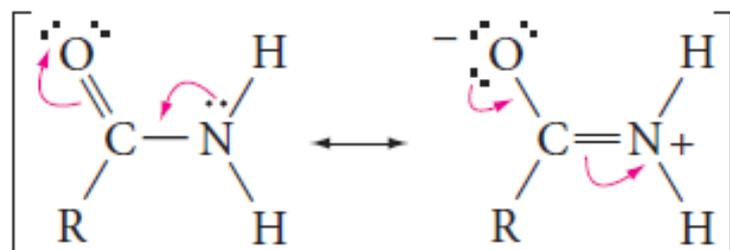
butanamide



benzamide  
(benzenecarboxamide)

# Amides

Amides have a planar geometry. Even though the carbon–nitrogen bond is normally written as a single bond, rotation around that bond is restricted because of resonance.

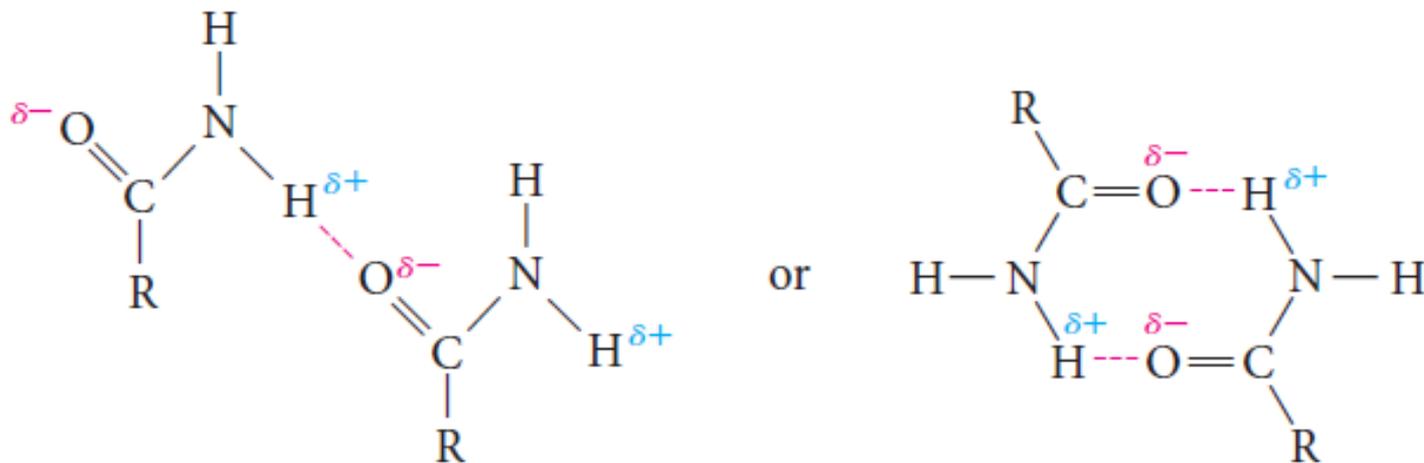


amide resonance

The dipolar contributor is so important that the carbon–nitrogen bond behaves much like a double bond. Consequently, the nitrogen and the carbonyl carbon, and the two atoms attached to each of them, lie in the same plane, and rotation at the C–N bond is restricted. Indeed, the C–N bond in amides is only 1.32 Å long—much shorter than the usual carbon–nitrogen single bond length (which is about 1.47 Å).

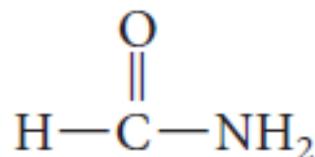
# Amides

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



# Amides

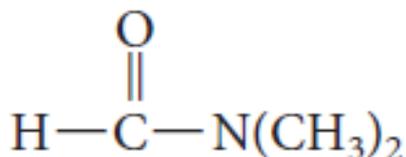
Amides have exceptionally high boiling points for their molecular weights, although alkyl substitution on the nitrogen lowers the boiling and melting points by decreasing the hydrogen-bonding possibilities, as shown in the following two pairs of compounds:



formamide

bp 210°C

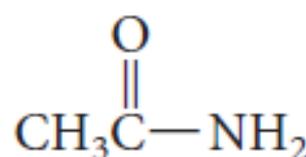
mp 2.5°C



*N,N*-dimethylformamide

153°C

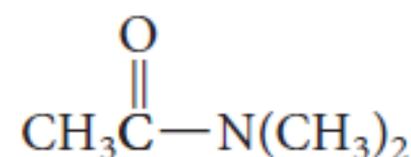
-60.5°C



acetamide

222°C

81°C



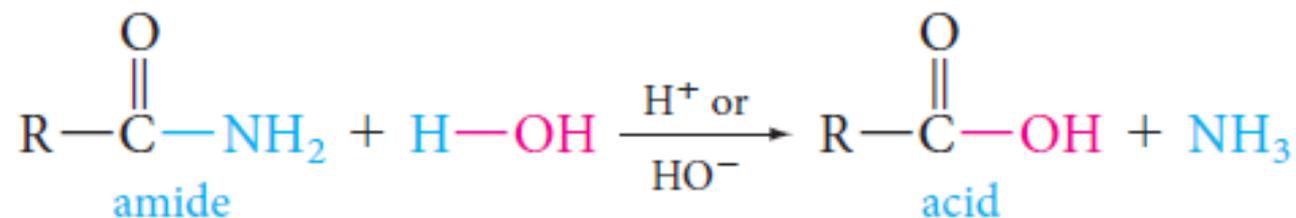
*N,N*-dimethylacetamide

165°C

-20°C

## Reactions of Amides

Amides react with nucleophiles. For example, they can be hydrolyzed by water.



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

