Chapter 11

Reactions of Carboxylic Acids and Carboxylic Acid Derivatives

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University of California, Santa Barbara

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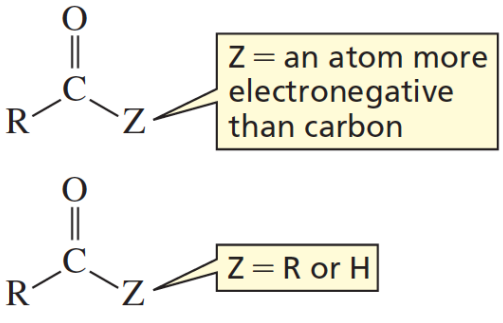
The Families in Group IV

Group IV



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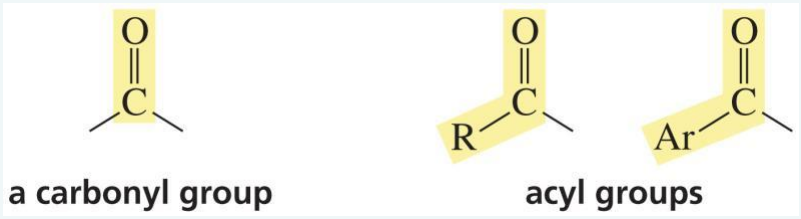
A Carbonyl Group an Acyl Group



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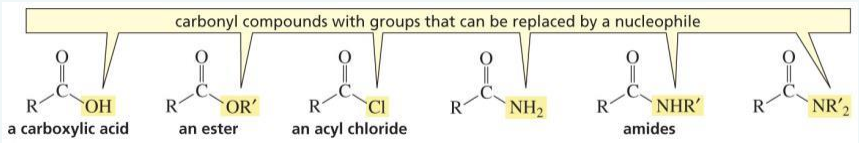
Carbonyl Compounds that have a group that can be Substituted



These carbonyl compounds have a group that can be substituted by another group.

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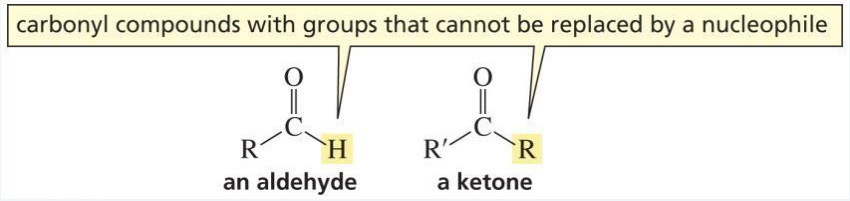
Carbonyl Compounds that have a group that cannot be Substituted

carbonyl compounds with groups that cannot be replaced by a nucleophile



These carbonyl compounds do not have a group that can be substituted by another group.

5

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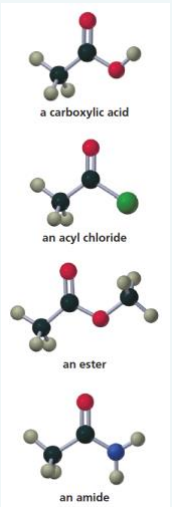
The Basicity of the group attached to the Acyl Group determines whether it can be Substituted

Table 11.1 The pK_a Values of the Conjugate Acids of the Leaving Groups of Carbonyl Compounds

Carbonyl compound	Leaving group	Conjugate acid of the leaving group	pK_a
Carboxylic Acids and Carboxylic Acid Derivatives			
	Cl^-	HCl	−7
	$^-OR'$	R′OH	~15–16
	^-OH	H_2O	15.7
	$^-NH_2$	NH_3	36*
Aldehydes and Ketones			
	H^-	H_2	35
	R^-	RH	> 60



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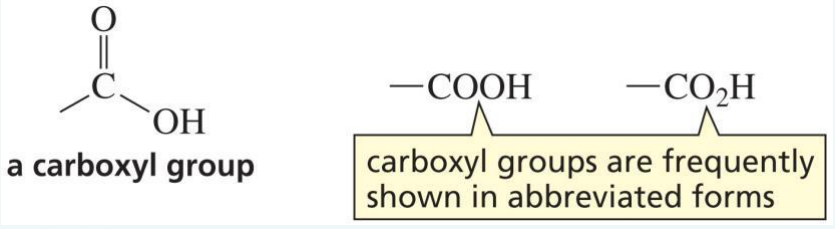
A Carboxyl Group



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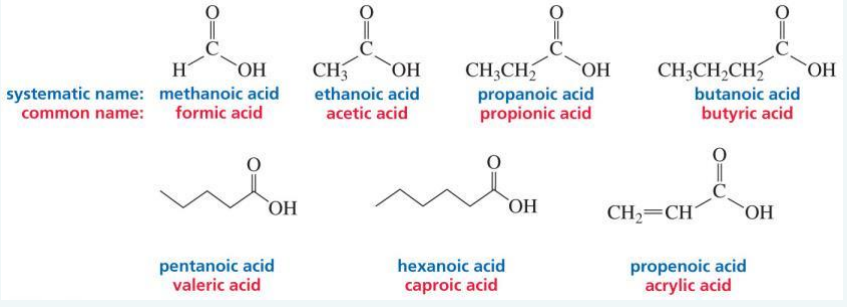
Naming Carboxylic Acids



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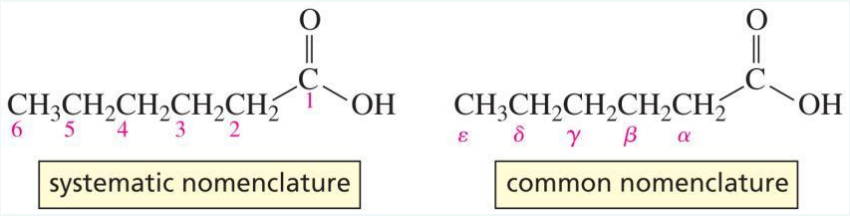
Naming Carboxylic Acids



In systematic nomenclature, the carbonyl carbon is C-1.

In common nomenclature, the carbon next to the carbonyl is the alpha–carbon.

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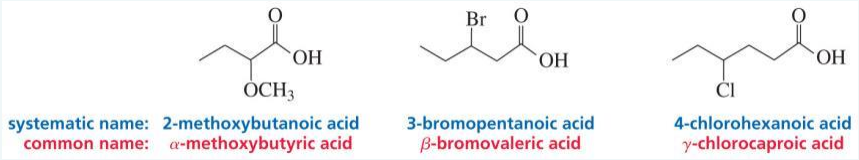
Naming Carboxylic Acids



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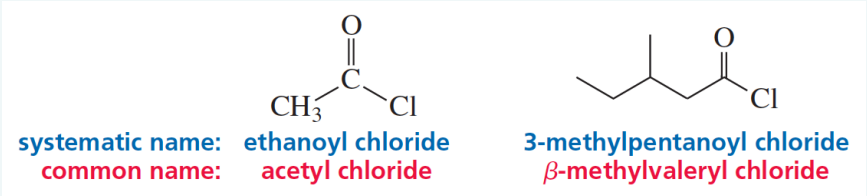
Naming Acyl Chlorides



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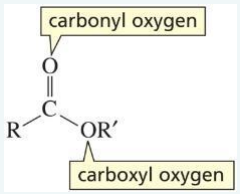
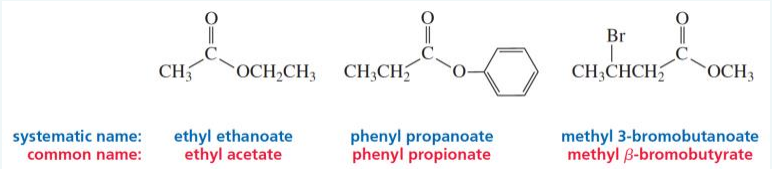
Naming Esters





state the substituent attached to the O
delete "ic acid"
add "ate"

12

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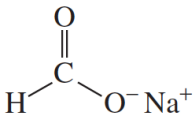
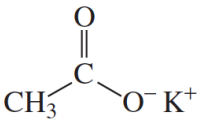
Naming Carboxylate Ions





systematic name:	sodium methanoate	potassium ethanoate
common name:	sodium formate	potassium acetate

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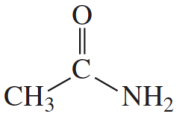
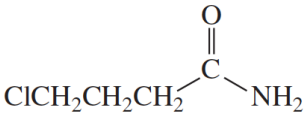
Naming Amides





systematic name:	ethanamide	4-chlorobutanamide
common name:	acetamide	γ-chlorobutyramide

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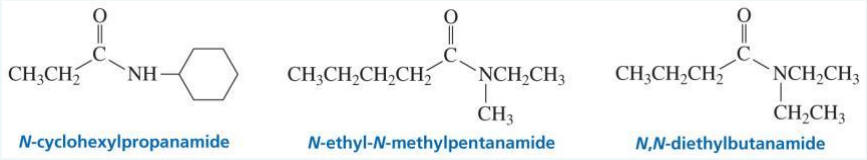
Naming Amides



N-cyclohexylpropanamide | *N*-ethyl-*N*-methylpentanamide | *N*,*N*-diethylbutanamide

The substituent attached to the nitrogen is stated first.

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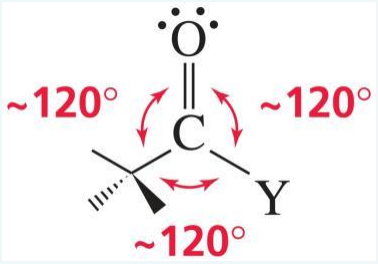
The Structure of a Carbonyl Compound



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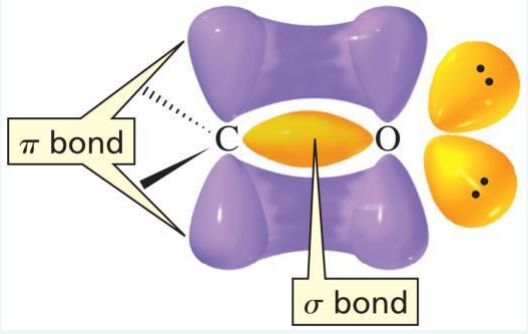
The Orbitals used in Carbonyl Group Formation



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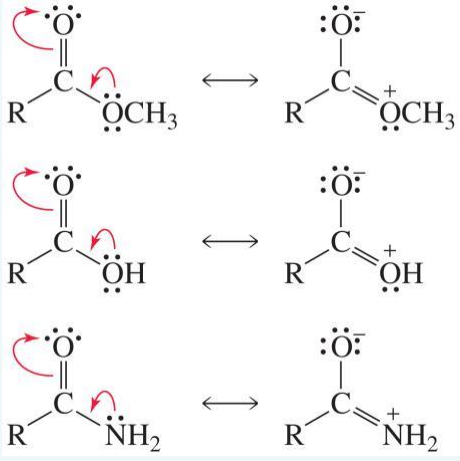
Resonance Contributors



Esters, carboxylic acids, and amines have two resonance contributors.

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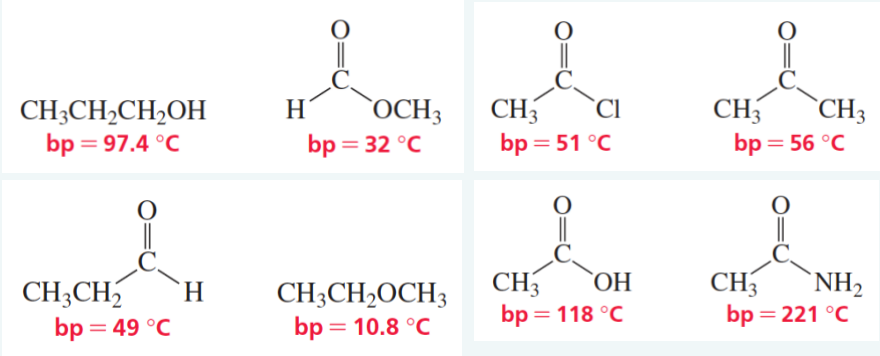
Physical Properties



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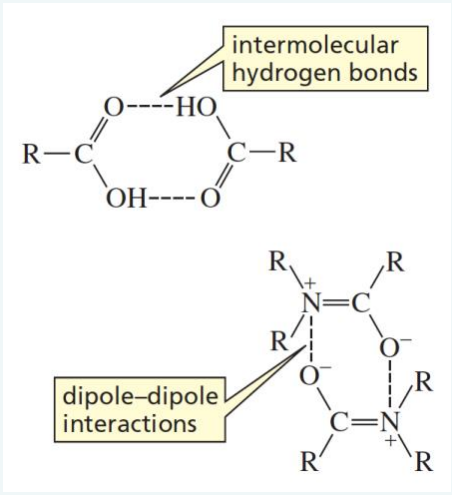
Amides and Nitriles have relatively high Boiling Points



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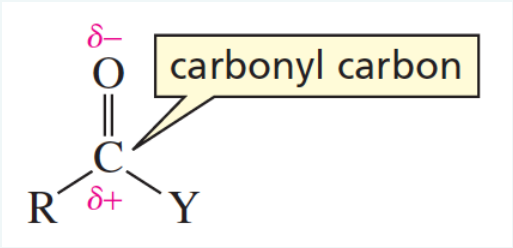
The Carbonyl Carbon is an Electrophile



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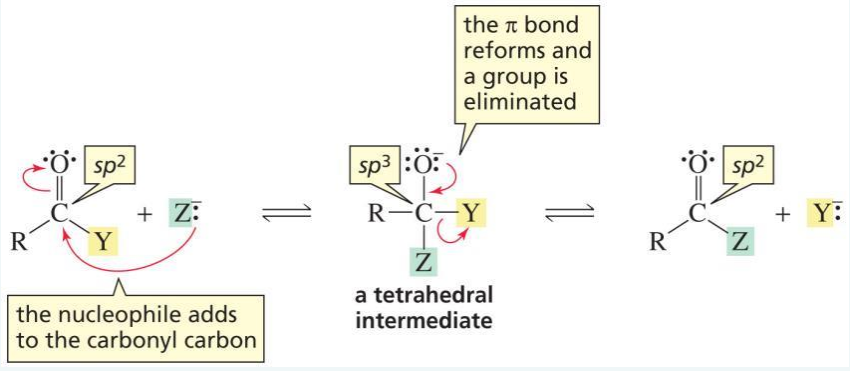
Nucleophilic Acyl Substitution Reaction



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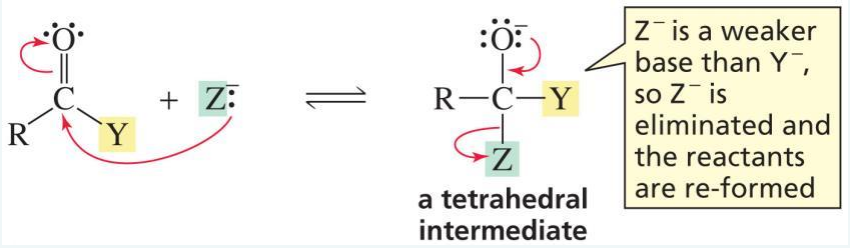
When the incoming Nucleophile (Z) is a weaker Base than the Base in the Reactant (Y)



The weakest base is eliminated from the tetrahedral intermediate.

If the incoming nucleophile (Z) is a weaker base than the base in the reactant (Y), the reactants will be reformed.

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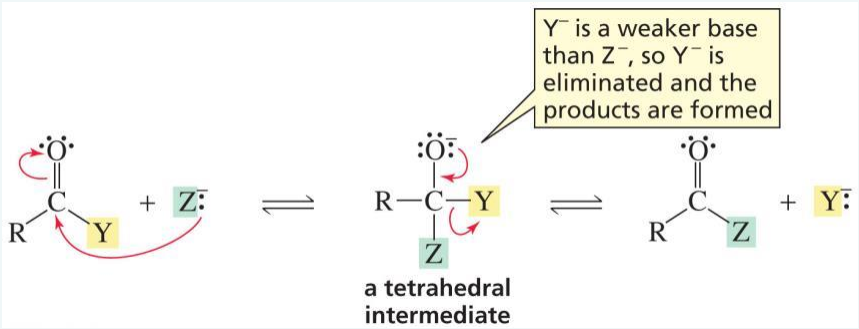
When the incoming Nucleophile (Z) is a stronger Base than the Base in the Reactant (Y)



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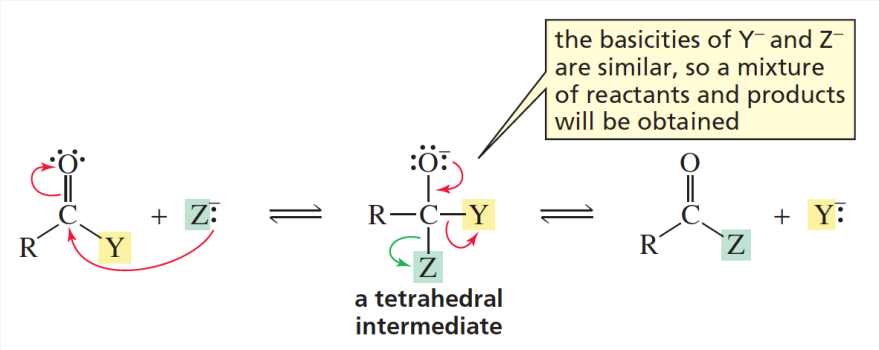
When the Reactant (Y) and the incoming Nucleophile (Z) have similar Base Strengths



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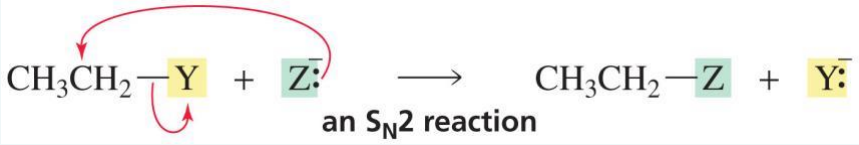
When a Nucleophile attacks a Carbon, the weakest Bond Breaks



When a nucleophile attacks an alkyl halide, the sigma bond breaks.

When a nucleophile attacks a carbonyl compound, the pi bond breaks.

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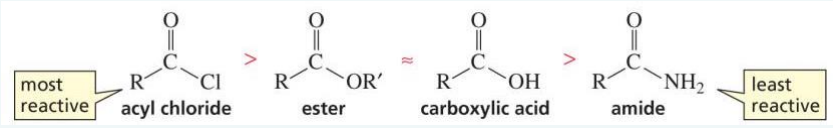
The Relative Reactivities depend on the Basicity of the substituent attached to the leaving Group



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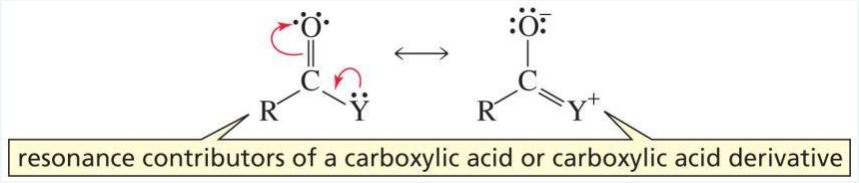
A weak base makes formation of the Tetrahedral Intermediate faster



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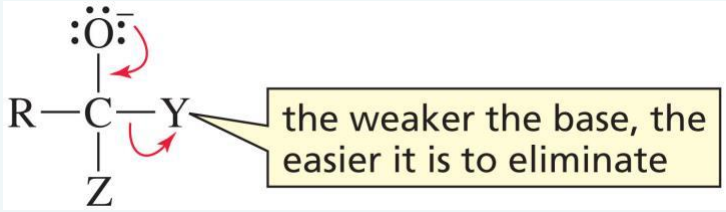
A weak base makes elimination from the Tetrahedral Intermediate faster



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A Carboxylic Acid Derivative can be converted into a less reactive Carboxylic Acid Derivative but not into a more reactive One

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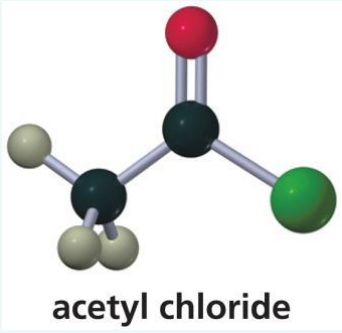
An Acyl Chloride



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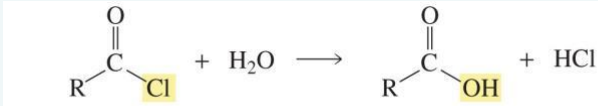
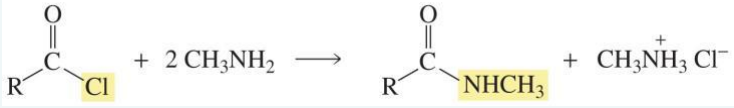
Reactions of Acyl Chlorides





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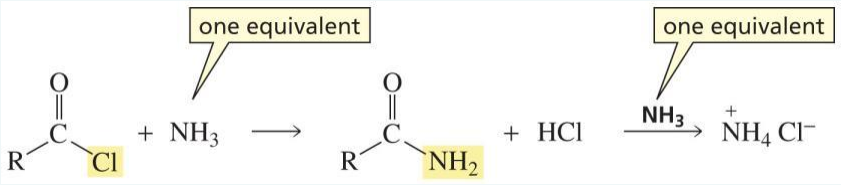
Two equivalents of Amine are Required



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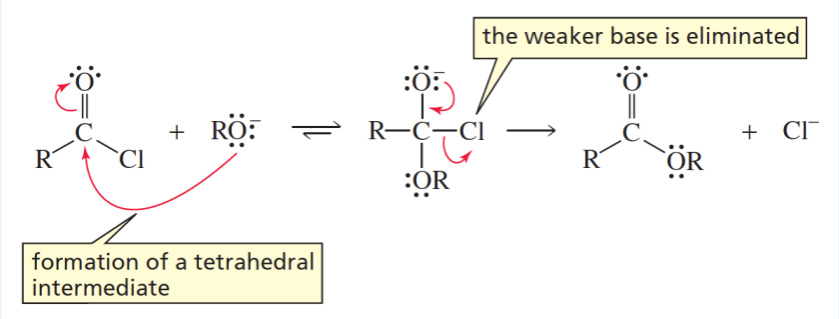
Mechanism for Reaction With a Negatively Charged Nucleophile



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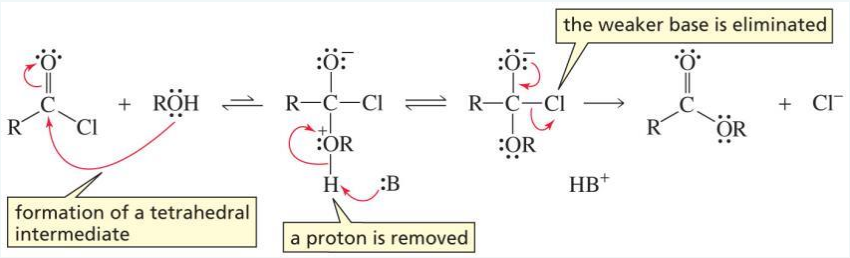
Mechanism for Reaction With a Neutral Nucleophile



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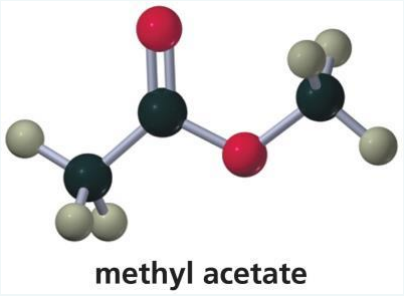
An Ester



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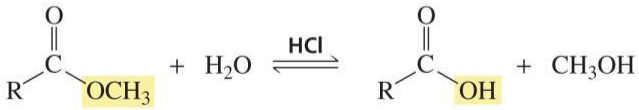
Reaction of an Ester with Water

a hydrolysis reaction



A hydrolysis reaction is a reaction with water that converts one compound into two compounds.

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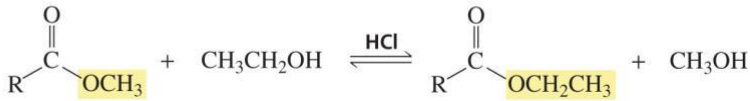
Reaction of an Ester with an Alcohol

a transesterification reaction



An alcoholysis reaction is a reaction with an alcohol that converts one compound into two compounds.

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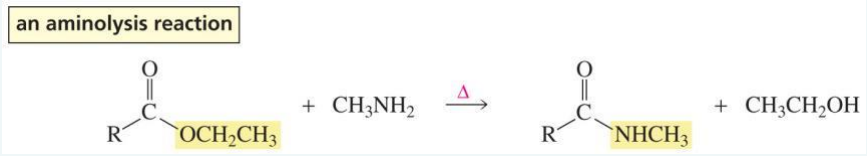
Reaction of an Ester with an Amine



An aminolysis reaction is a reaction with an amine that converts one compound into two compounds

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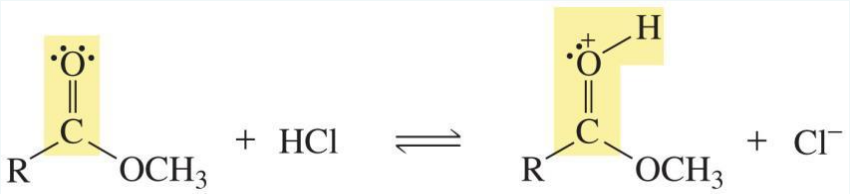
The Carbonyl Oxygen is the Oxygen that is Protonated



The acid protonates the atom with the greatest electron density.

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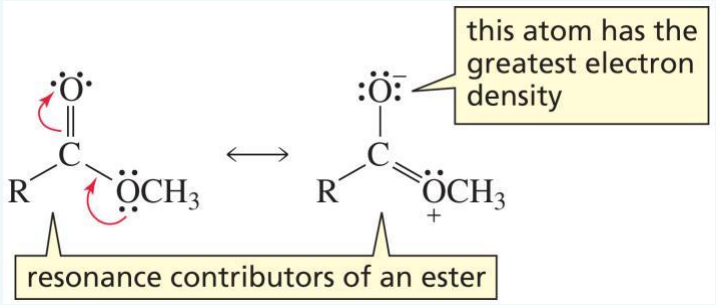
The Resonance Contributors show that the Carbonyl Oxygen has the Greatest Electron Density



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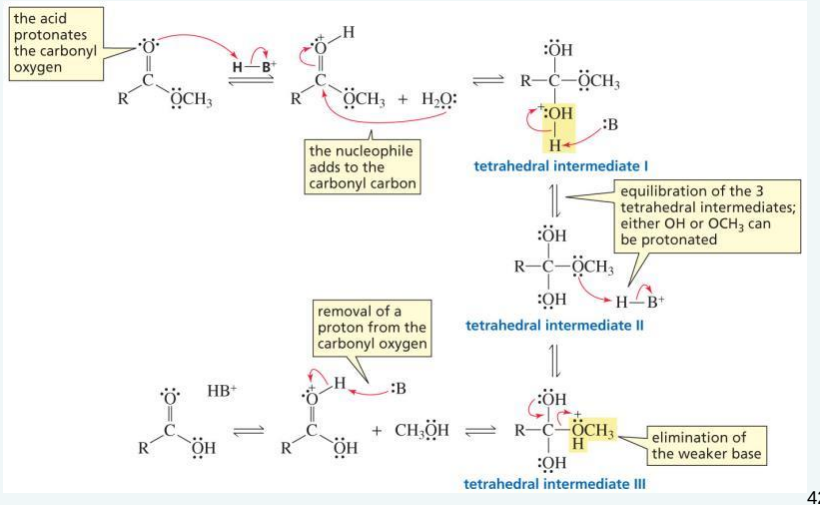
The Mechanism for the Acid-Catalyzed Hydrolysis of an Ester



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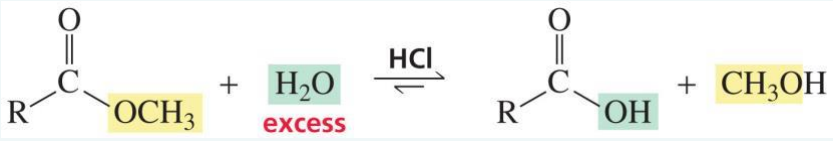
Use excess water to drive the Reaction to the right



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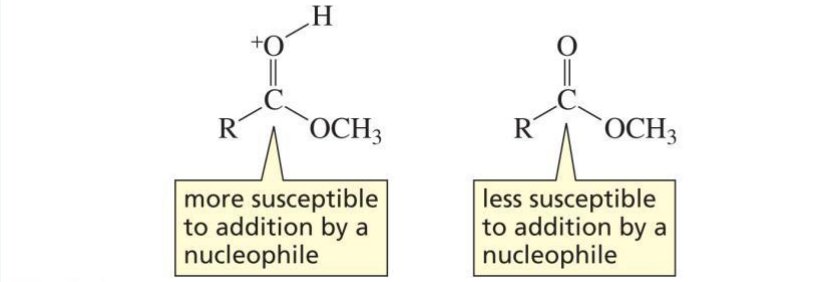
Protonation makes the Carbonyl Group more susceptible to Nucleophilic Addition

protonation of the carbonyl oxygen increases the susceptibility of the carbonyl carbon to nucleophilic addition



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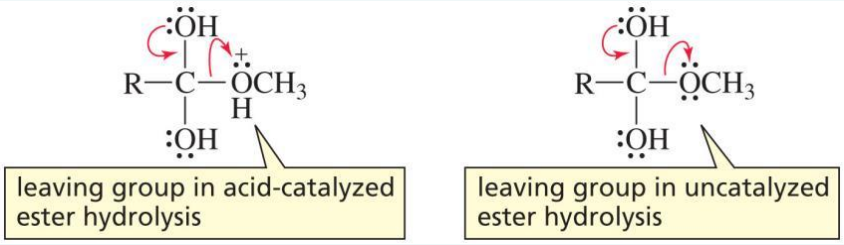
Protonation makes the Leaving Group a better Leaving Group



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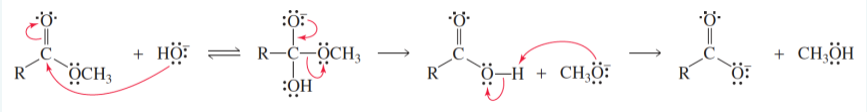
The Mechanism for Hydroxide-Ion Promoted Hydrolysis of an Ester



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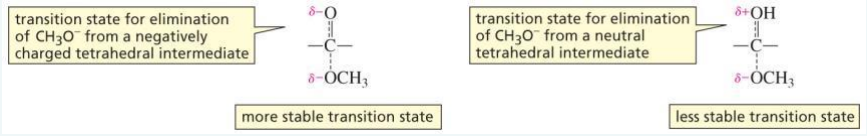
Why is collapse of the Tetrahedral Intermediate faster in a basic solution?



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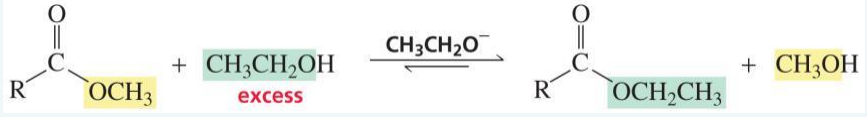
Reaction with an alcohol can be catalyzed by an Alkoxide Ion



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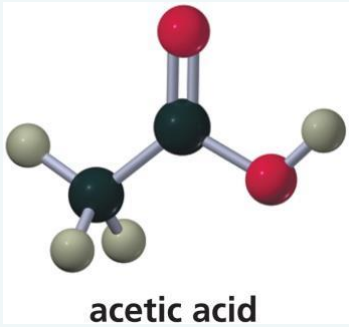
A Carboxylic Acid



acetic acid

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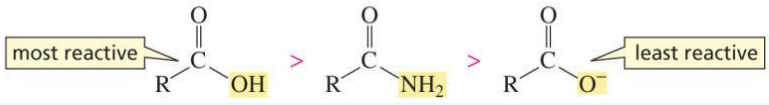
A Carboxylic Acid must be in its acidic form in order to undergo a Nucleophilic Acyl Substitution Reaction

relative reactivities toward nucleophilic addition–elimination



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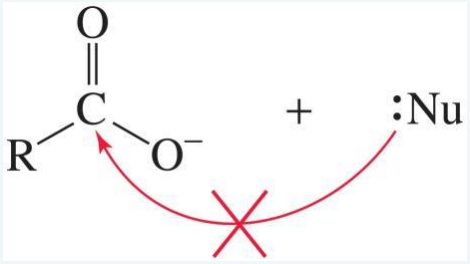
Carboxylate Ions do not react with Nucleophiles



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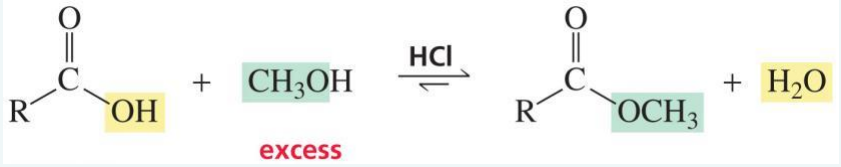
Reaction of a Carboxylic Acid with an alcohol



The reaction is catalyzed by acids.

Excess alcohol drives the reaction to the right.

52

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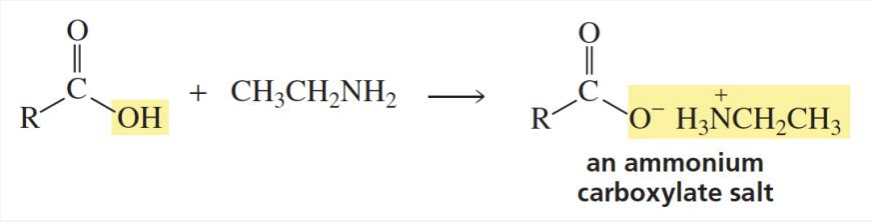
Reaction of a Carboxylic Acid with an Amine



A carboxylic acid is an acid and an amine is a base, so an acid-base reaction occurs.

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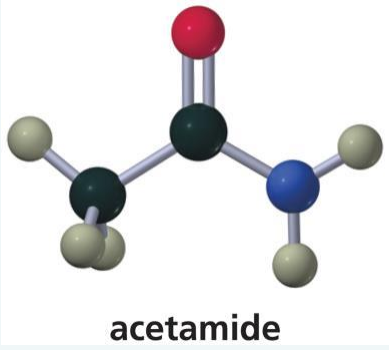
An Amide



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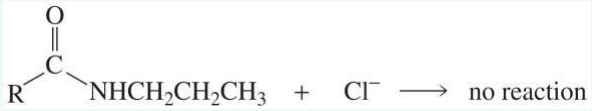
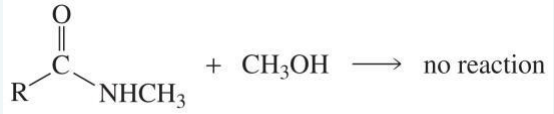
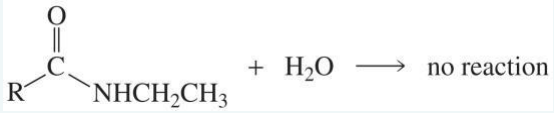
Amides do not undergo Nucleophilic Acyl Substitution Reactions (unless the reaction is acid catalyzed)







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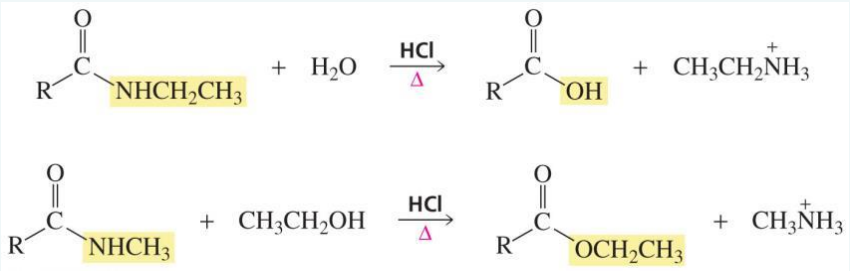
Amides react with water and alcohols if an Acid Catalyst is added



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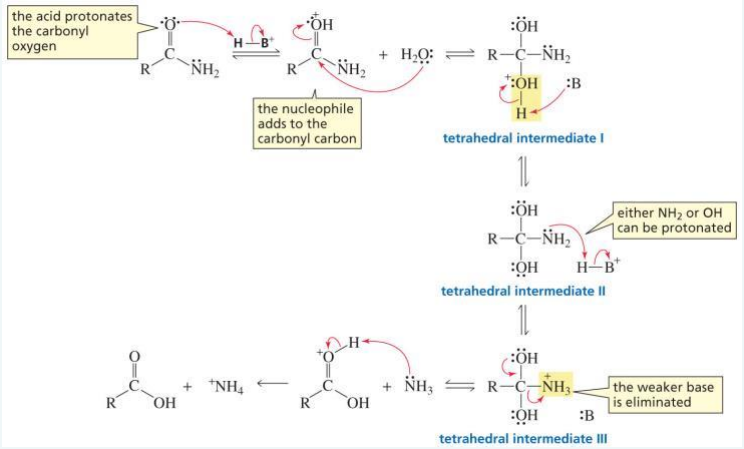
The Mechanism for the Acid-Catalyzed Hydrolysis of an Amide



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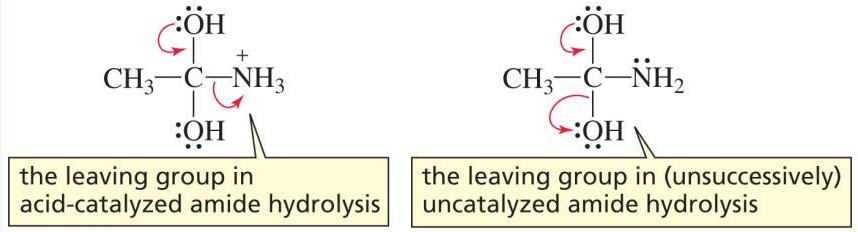
The weakest base is the best Leaving Group



A protonated amino group is a weaker base than hydroxide ion.

An amino group is a stronger base than hydroxide ion.

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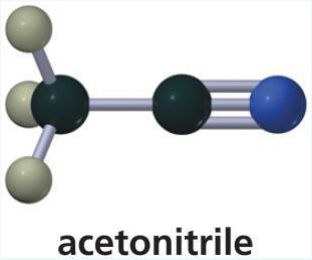
A Nitrile



acetonitrile

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Nomenclature of Nitriles

	$CH_3C{\equiv}N$	$CH_3CHCH_2CH_2CH_2C{\equiv}N$ (CH₃ on the CHCH₂ carbon)	$CH_2{=}CHC{\equiv}N$
systematic name:	ethanenitrile	5-methylhexanenitrile	propenenitrile
common name:	acetonitrile methyl cyanide	δ-methylcapronitrile isohexyl cyanide	acrylonitrile

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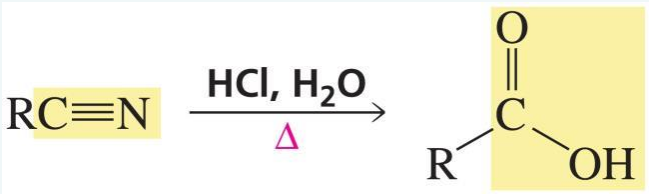
Acid-Catalyzed Hydrolysis of a Nitrile



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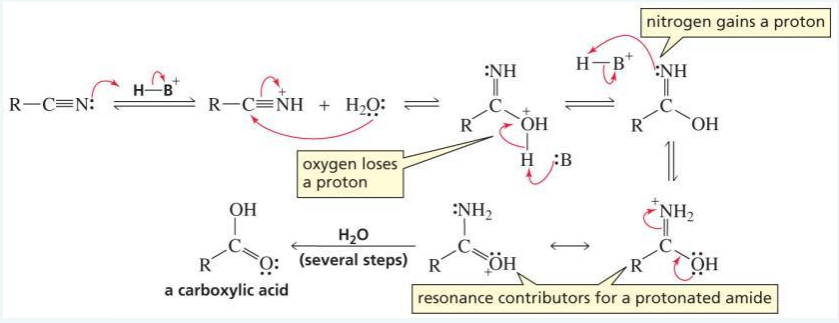
The Mechanism



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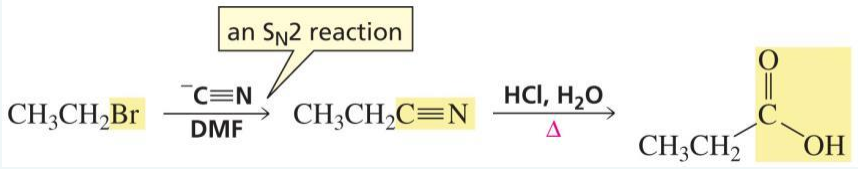
Synthesis of a Carboxylic Acid



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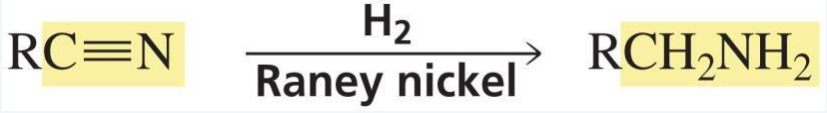
Synthesis of a Primary Amine



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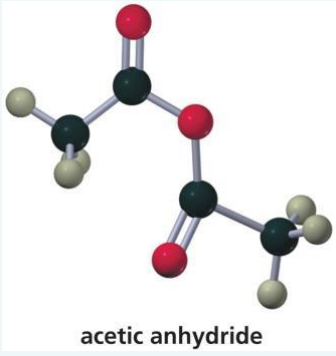
An Acid Anhydride



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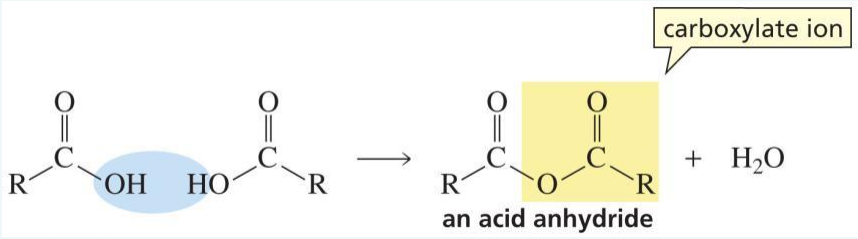
An Acid Anhydride is formed when water is lost from two molecules of a Carboxylic Acid



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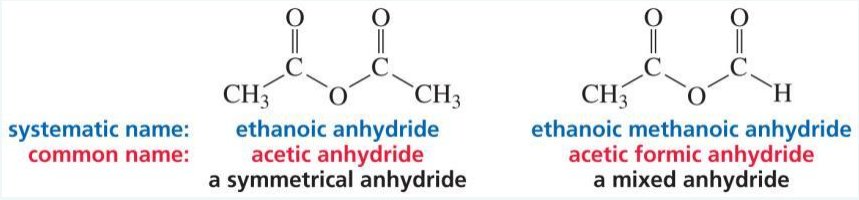
Nomenclature of Acid Anhydrides



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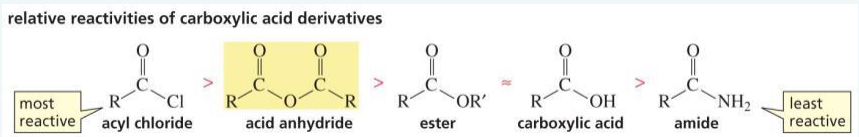
Acid Anhydrides are less reactive than Acyl Chlorides but more reactive than Esters



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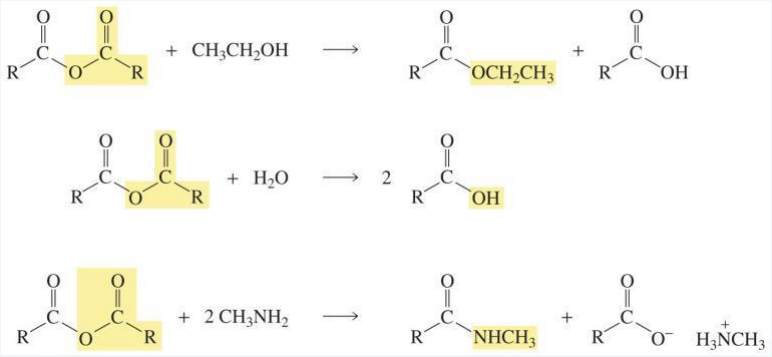
Reactions of Acid Anhydrides



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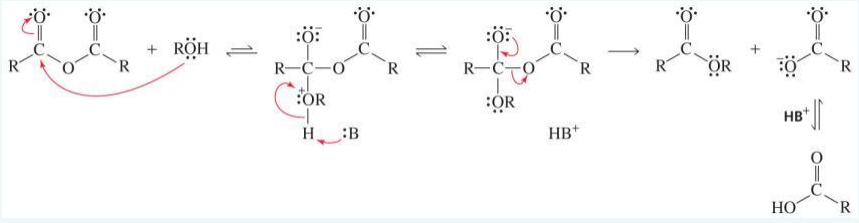
The Mechanism



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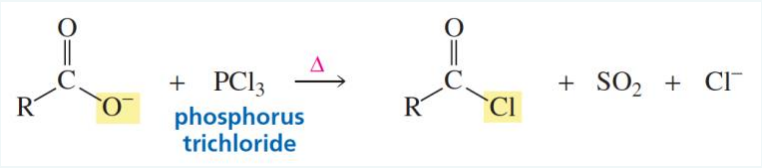
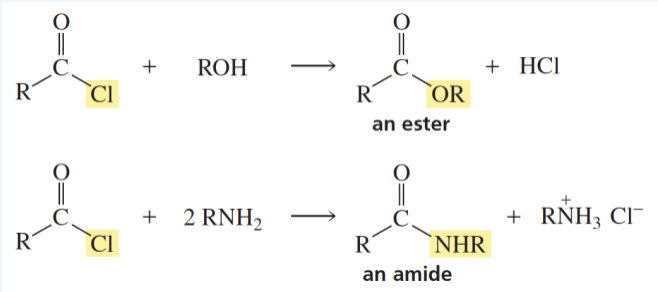
Activating Carboxylic Acids by converting them to Acyl Chlorides





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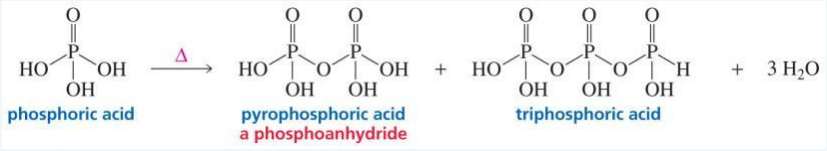
Heating Phosphoric Acid forms Pyrophosphoric Acid and Triphosphoric Acid



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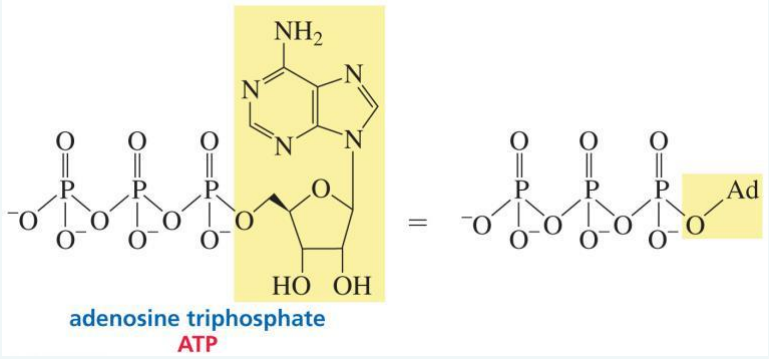
ATP



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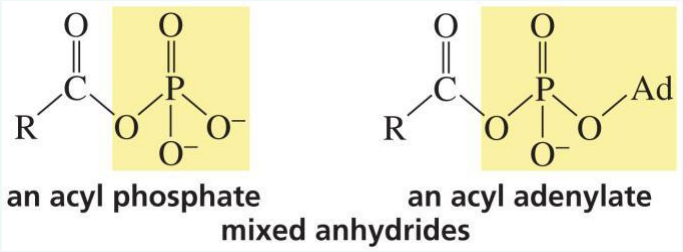
Mixed Anhydrides of a Carboxylic Acid and a Phosphoric Acid



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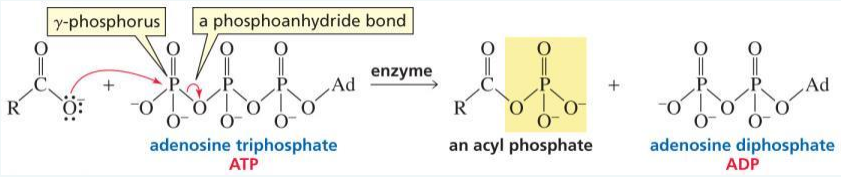
Forming an Acyl Phosphate



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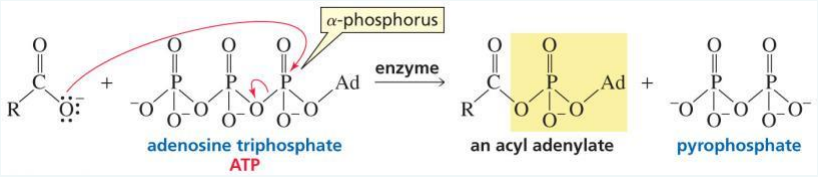
Forming an Acyl Adenylate



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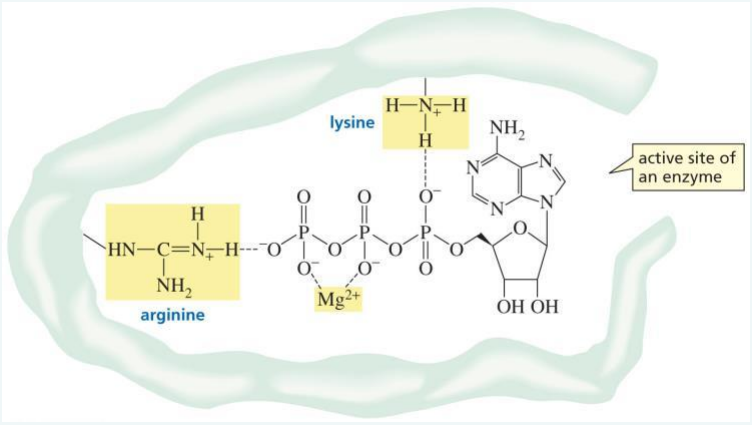
The negative charges on ATP are neutralized at the Active Site of an Enzyme



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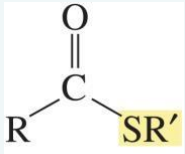
A Thioester is more susceptible to Nucleophilic Addition than an Oxygen Ester



a thioester

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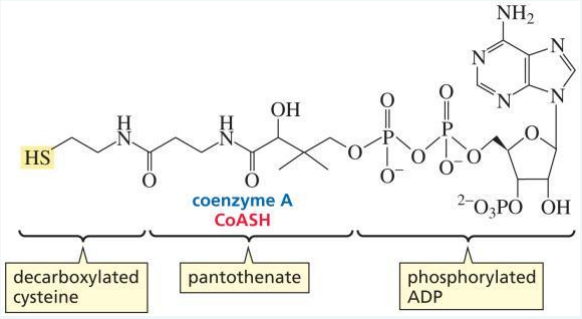
Coenzyme A



Coenzyme A is the thiol used in cells.

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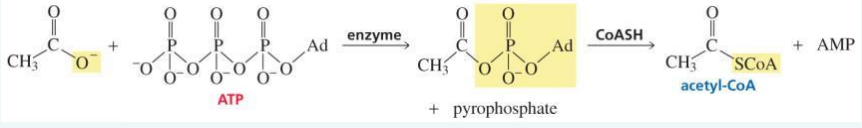
A Carboxylate Ion is first converted to an Acyl Adenylate and then to a Thioester



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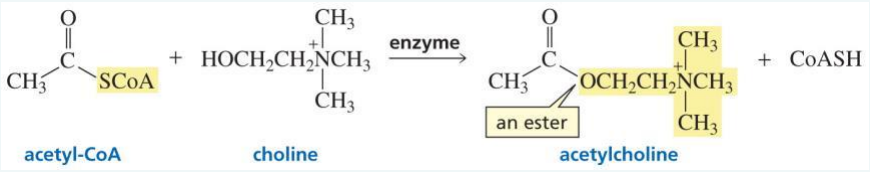
Using Acetyl-CoA to form Acetylcholine



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