Chapter 11

Reactions of Carboxylic Acids and Carboxylic Acid Derivatives

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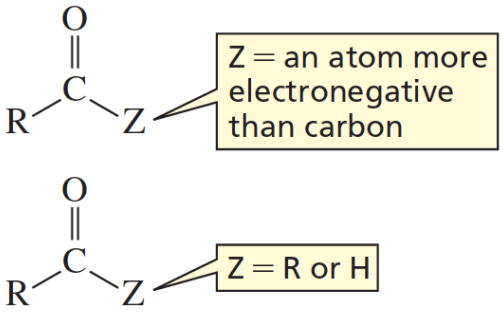
1

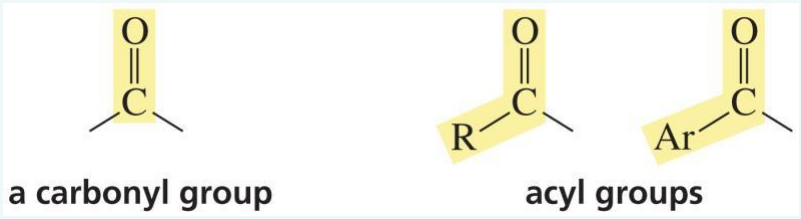
The Families in Group IV

Group IV



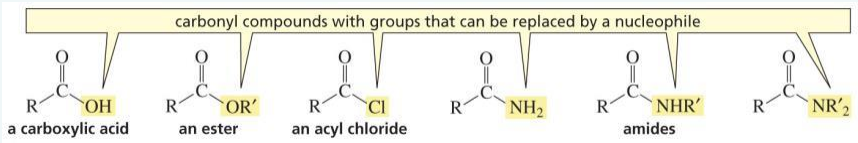
2

A Carbonyl Group an Acyl Group



3

Carbonyl Compounds that have a group that can be Substituted

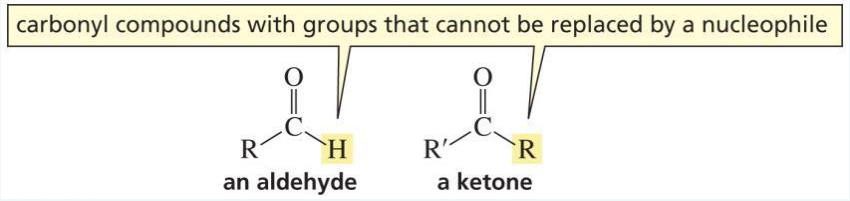


These carbonyl compounds have a group that can be substituted by another group.

4

Carbonyl Compounds that have a group that cannot be Substituted

carbonyl compounds with groups that cannot be replaced by a nucleophile



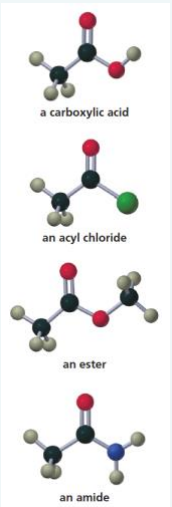
These carbonyl compounds do not have a group that can be substituted by another group.

5

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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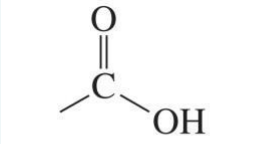
A Carboxyl Group



a carboxyl group

—COOH —CO_2H

carboxyl groups are frequently shown in abbreviated forms

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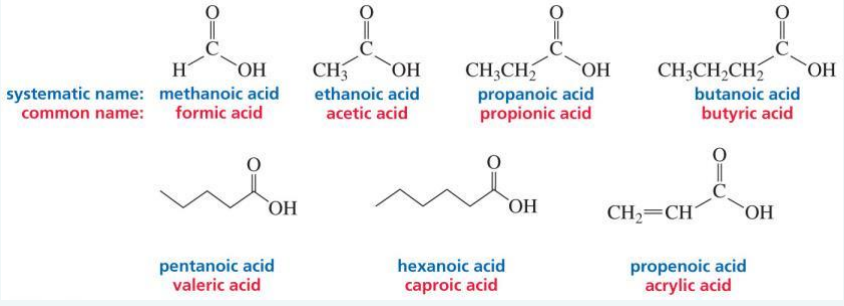
Naming Carboxylic Acids



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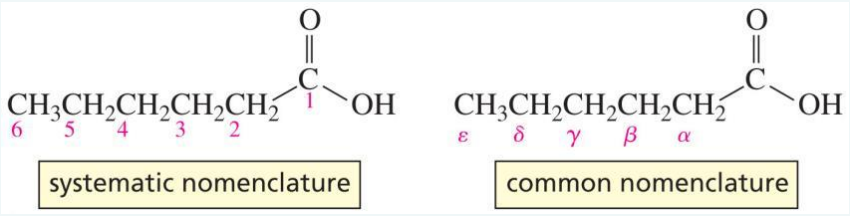
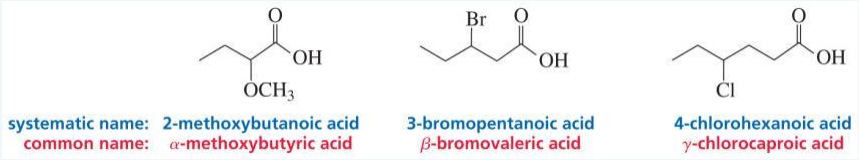
Naming Carboxylic Acids



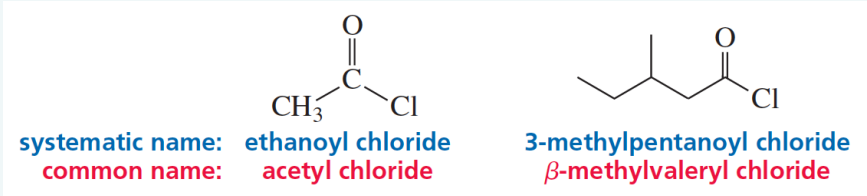
In systematic nomenclature, the carbonyl carbon is C-1.

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

Naming Carboxylic Acids



Naming Acyl Chlorides



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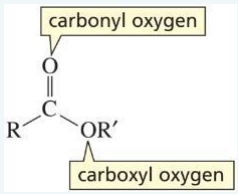
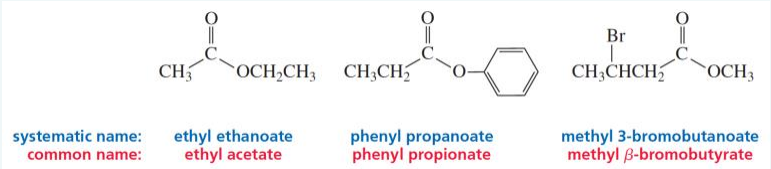
Naming Esters





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

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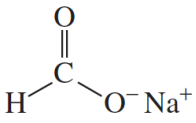
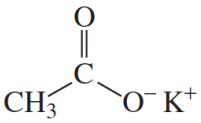
Naming Carboxylate Ions





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

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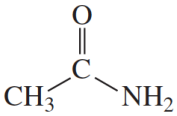
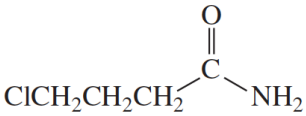
Naming Amides





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

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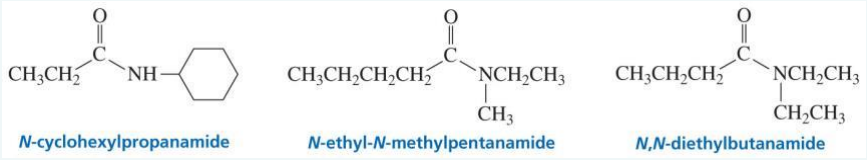
Naming Amides



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

The substituent attached to the nitrogen is stated first.

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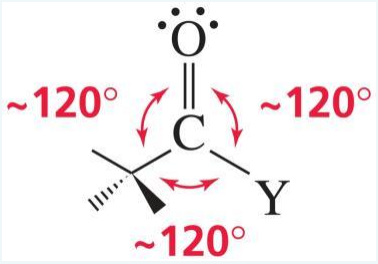
The Structure of a Carbonyl Compound



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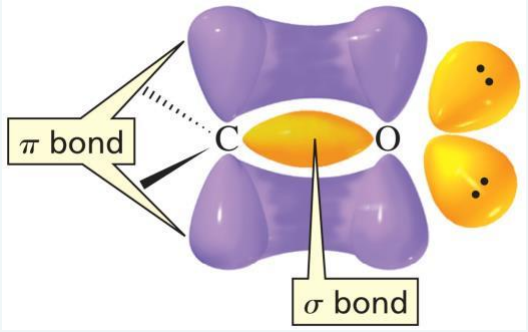
The Orbitals used in Carbonyl Group Formation



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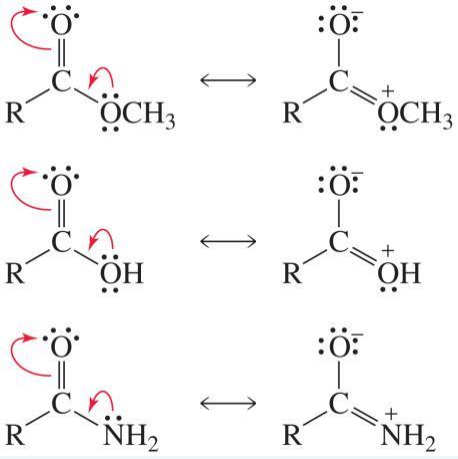
Resonance Contributors



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

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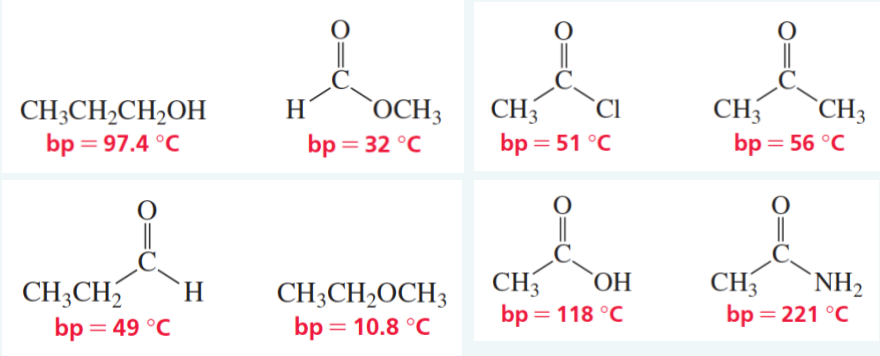
Physical Properties



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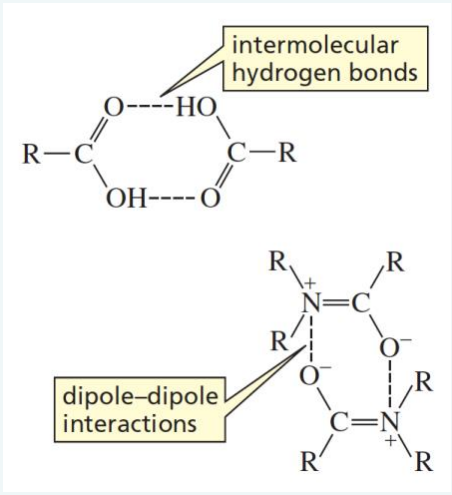
Amides and Nitriles have relatively high Boiling Points



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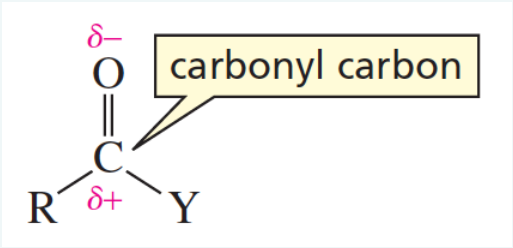
The Carbonyl Carbon is an Electrophile



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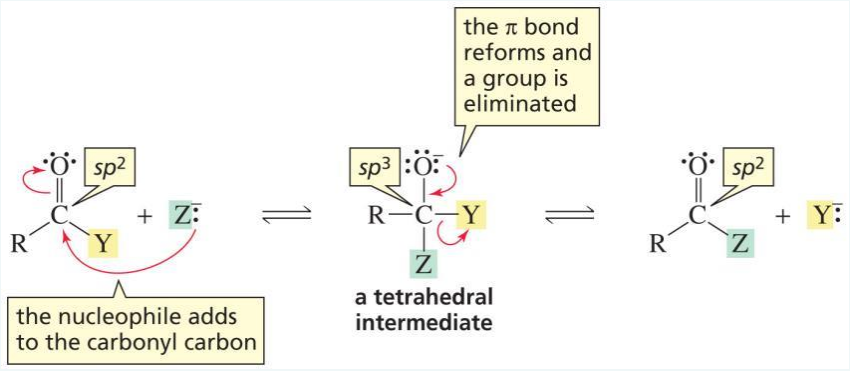
Nucleophilic Acyl Substitution Reaction



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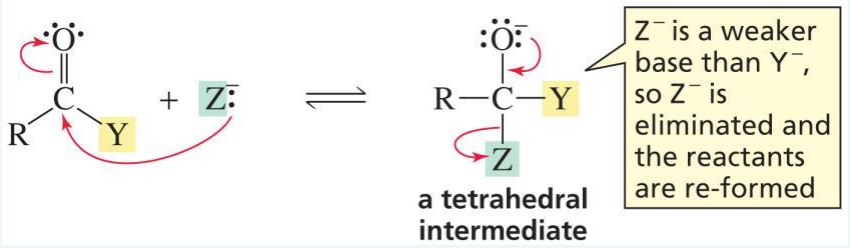
When the incoming Nucleophile (Z) is a weaker Base than the Base in the Reactant (Y)



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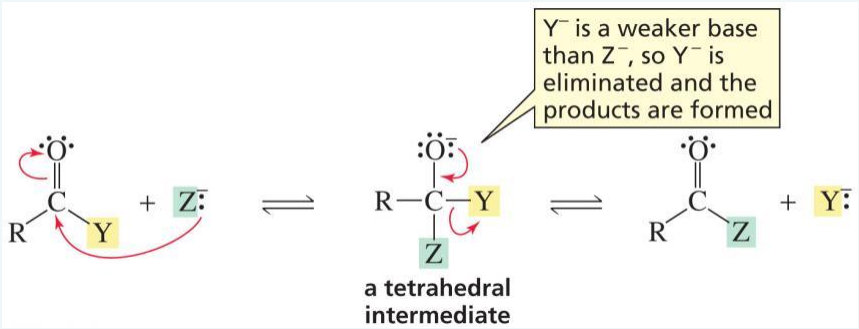
When the incoming Nucleophile (Z) is a stronger Base than the Base in the Reactant (Y)



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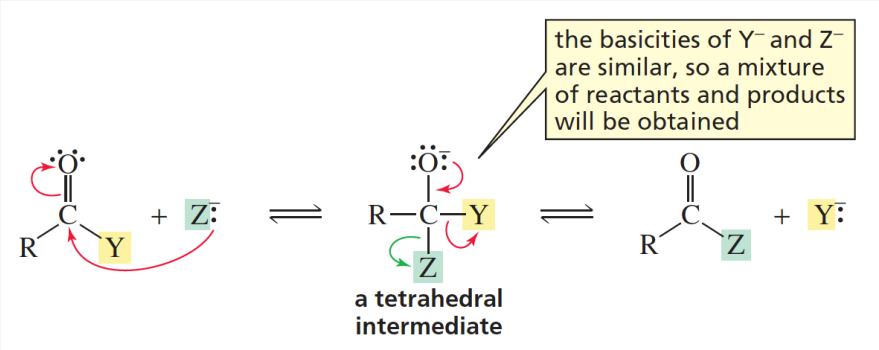
When the Reactant (Y) and the incoming Nucleophile (Z) have similar Base Strengths



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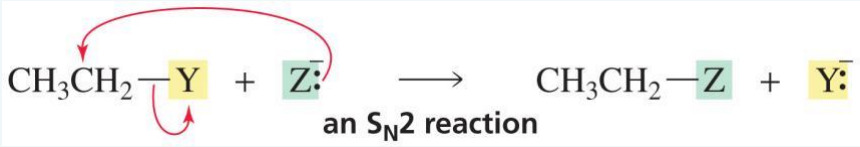
When a Nucleophile attacks a Carbon, the weakest Bond Breaks



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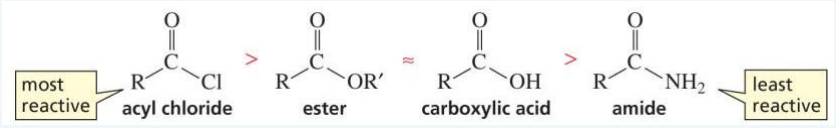
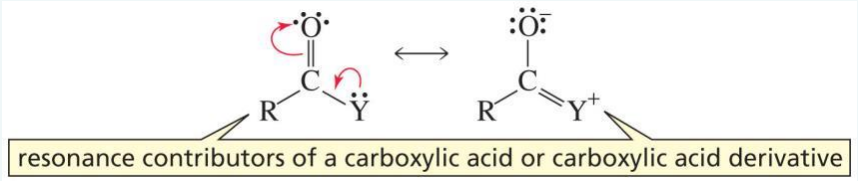
The Relative Reactivities depend on the Basicity of the substituent attached to the leaving Group



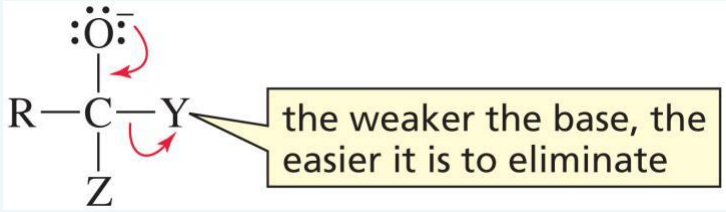
27

A weak base makes formation of the Tetrahedral Intermediate faster



28

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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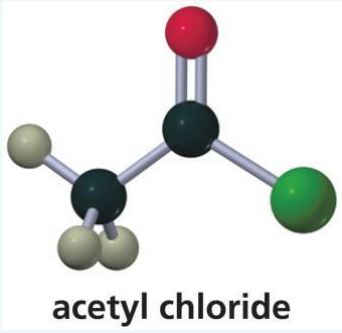
An Acyl Chloride



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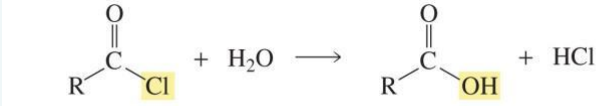
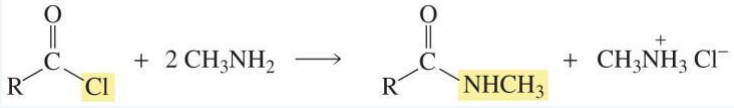
Reactions of Acyl Chlorides





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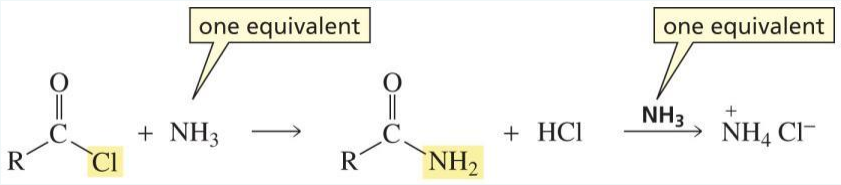
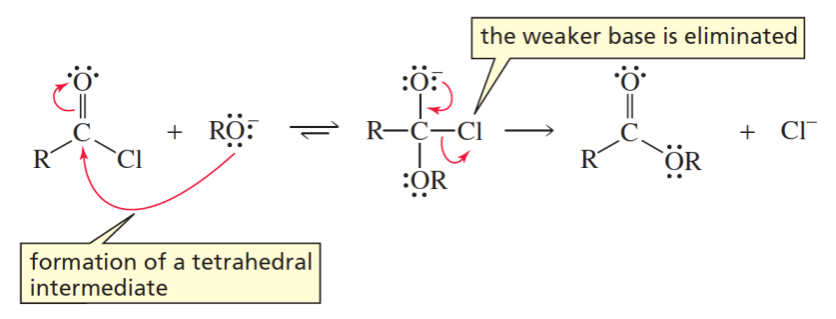
Two equivalents of Amine are Required



33

Mechanism for Reaction With a Negatively Charged Nucleophile



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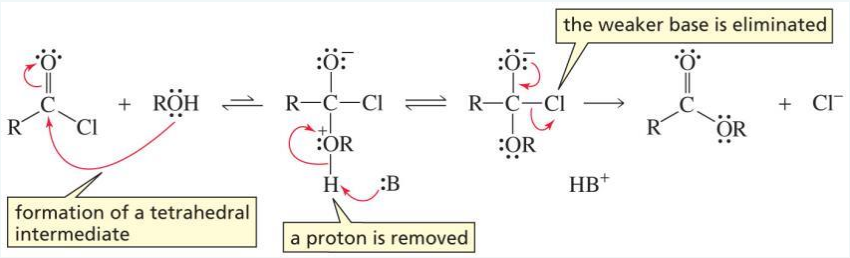
Mechanism for Reaction With a Neutral Nucleophile



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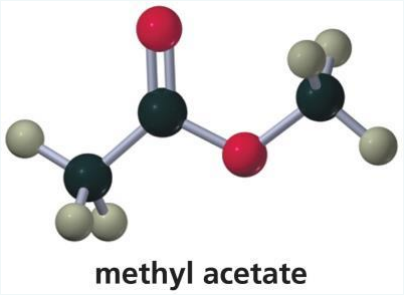
An Ester



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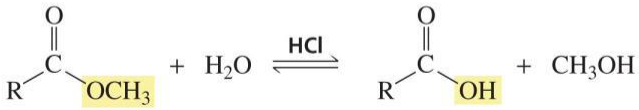
Reaction of an Ester with Water

a hydrolysis reaction



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

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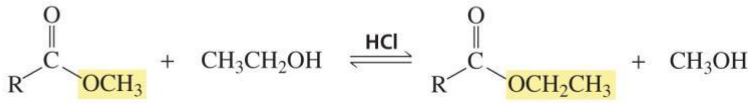
Reaction of an Ester with an Alcohol

a transesterification reaction



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

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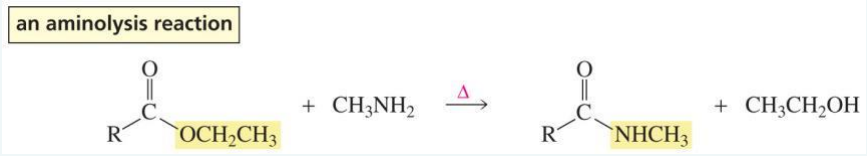
Reaction of an Ester with an Amine



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

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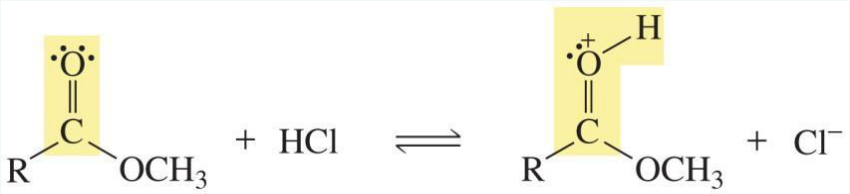
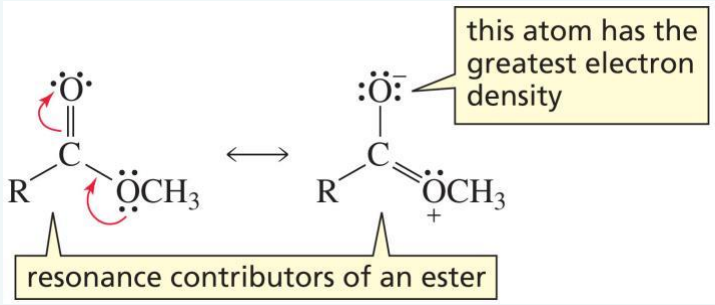
The Carbonyl Oxygen is the Oxygen that is Protonated



The acid protonates the atom with the greatest electron density.

40

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



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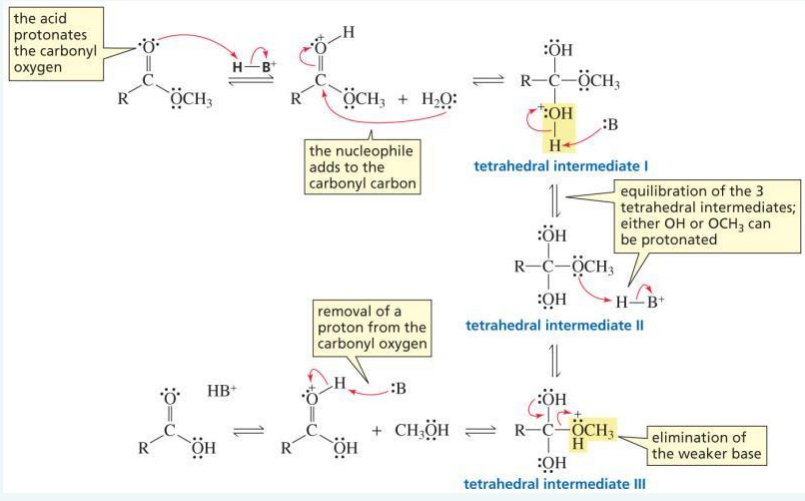
The Mechanism for the Acid-Catalyzed Hydrolysis of an Ester



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Use excess water to drive the Reaction to the right

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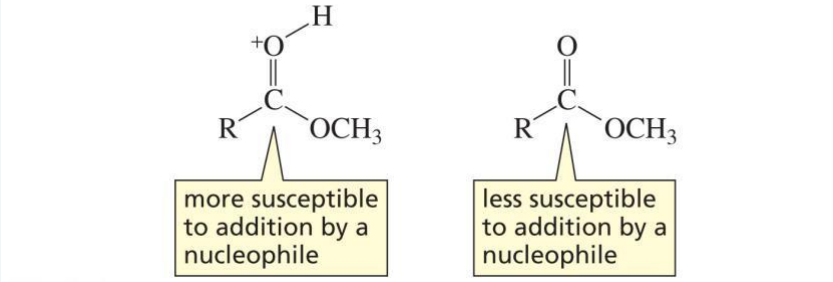
Protonation makes the Carbonyl Group more susceptible to Nucleophilic Addition

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



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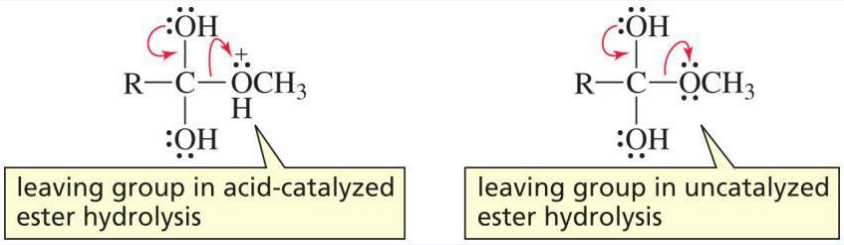
Protonation makes the Leaving Group a better Leaving Group



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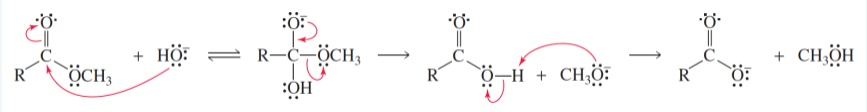
The Mechanism for Hydroxide-Ion Promoted Hydrolysis of an Ester



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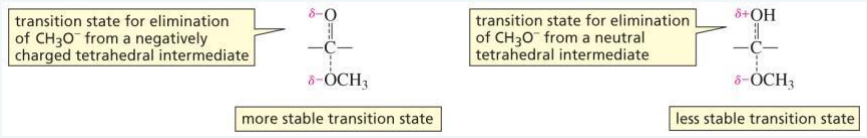
Why is collapse of the Tetrahedral Intermediate faster in a basic solution?



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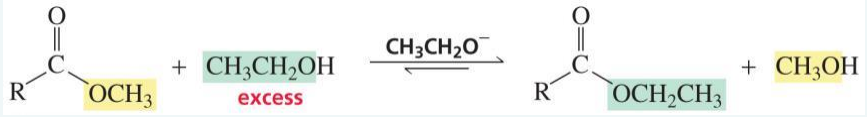
Reaction with an alcohol can be catalyzed by an Alkoxide Ion



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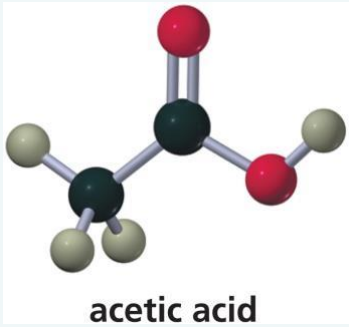
A Carboxylic Acid



acetic acid

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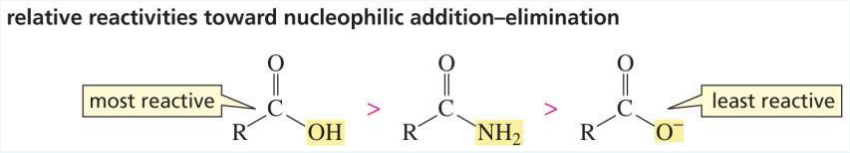
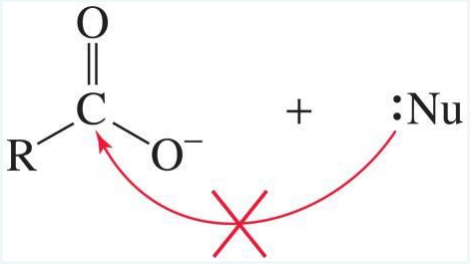
A Carboxylic Acid must be in its acidic form in order to undergo a Nucleophilic Acyl Substitution Reaction



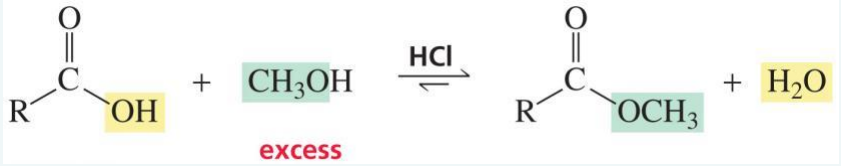
50

Carboxylate Ions do not react with Nucleophiles



51

Reaction of a Carboxylic Acid with an alcohol

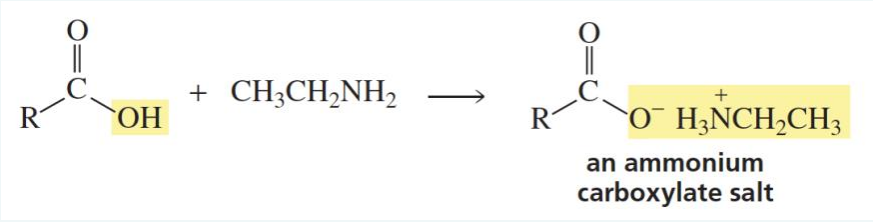


The reaction is catalyzed by acids.

Excess alcohol drives the reaction to the right.

52

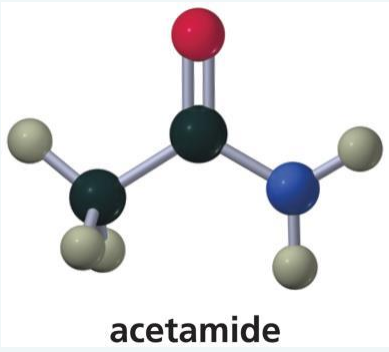
Reaction of a Carboxylic Acid with an Amine



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

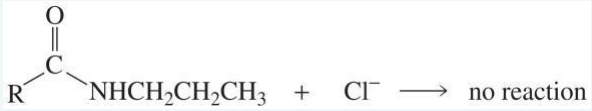
53

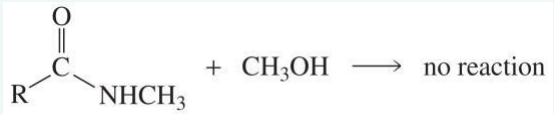
An Amide

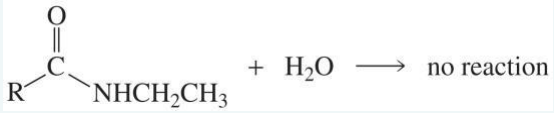


54

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

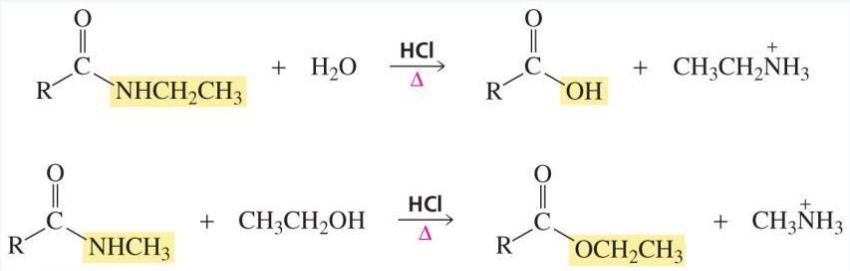






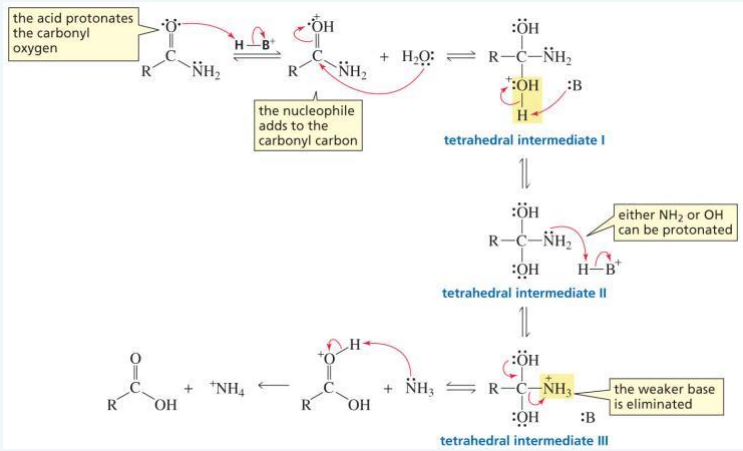
55

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



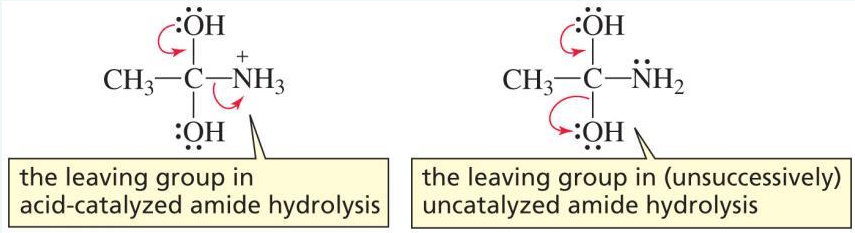
56

The Mechanism for the Acid-Catalyzed Hydrolysis of an Amide



57

The weakest base is the best Leaving Group

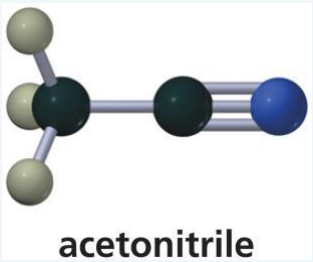


A protonated amino group is a weaker base than hydroxide ion.

An amino group is a stronger base than hydroxide ion.

58

A Nitrile



acetonitrile

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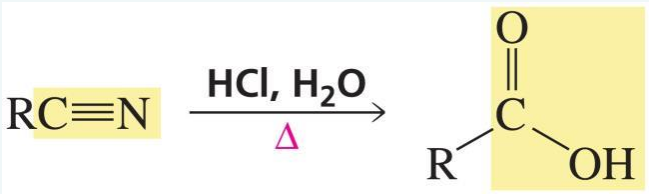
Nomenclature of Nitriles

	$CH_3C{\equiv}N$	$CH_3CHCH_2CH_2CH_2C{\equiv}N$ (with CH_3 branch)	$CH_2{=}CHC{\equiv}N$
systematic name:	ethanenitrile	5-methylhexanenitrile	propenenitrile
common name:	acetonitrile	δ-methylcapronitrile	acrylonitrile
	methyl cyanide	isohexyl cyanide	

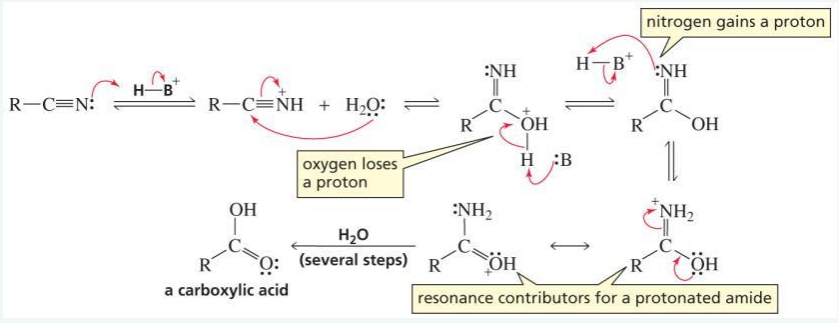
60

Acid-Catalyzed Hydrolysis of a Nitrile



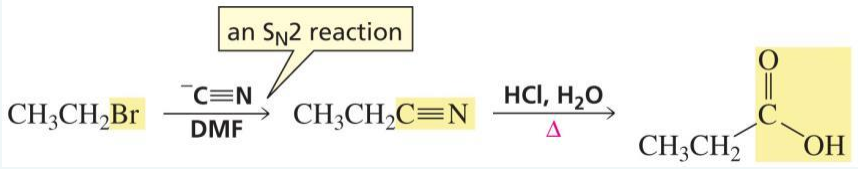
61

The Mechanism



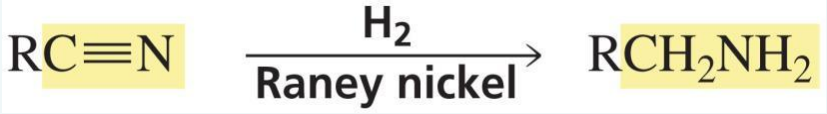
62

Synthesis of a Carboxylic Acid



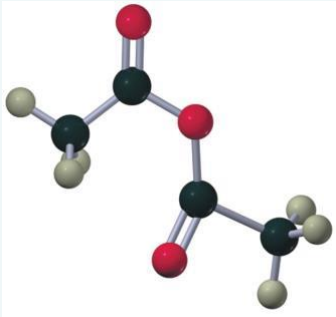
63

Synthesis of a Primary Amine



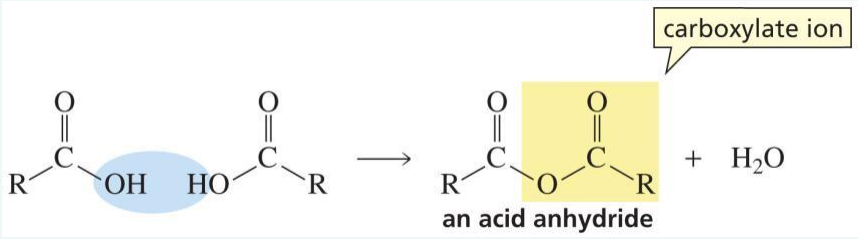
64

An Acid Anhydride



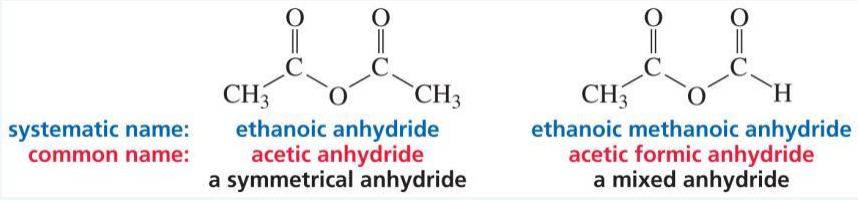
65

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



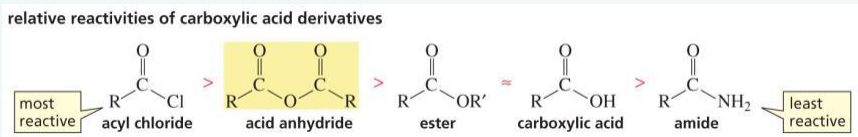
66

Nomenclature of Acid Anhydrides



67

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



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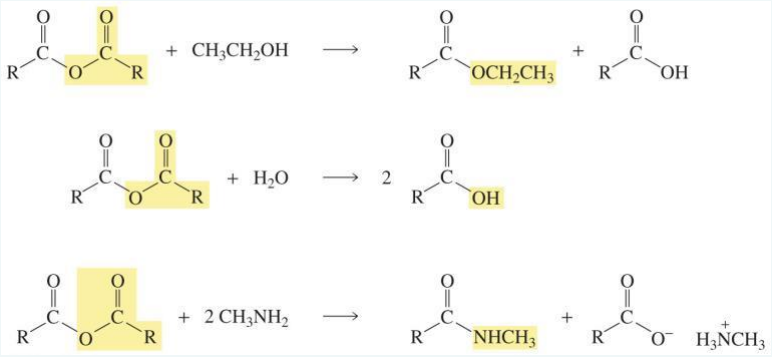
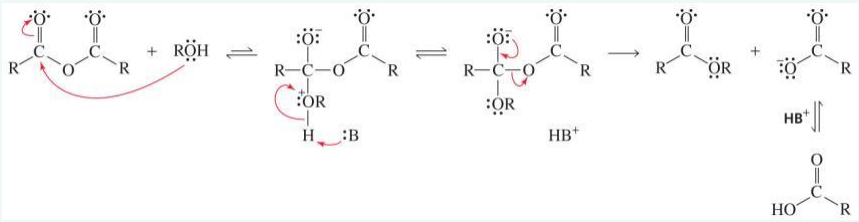
Reactions of Acid Anhydrides



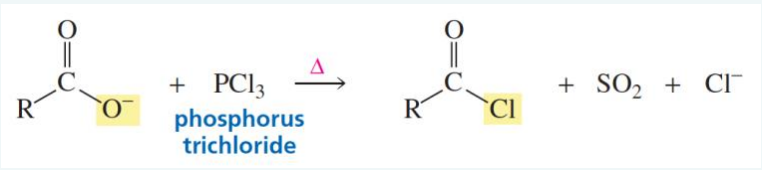
69

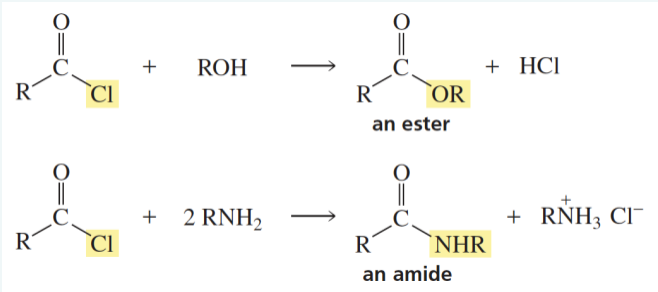
The Mechanism



70

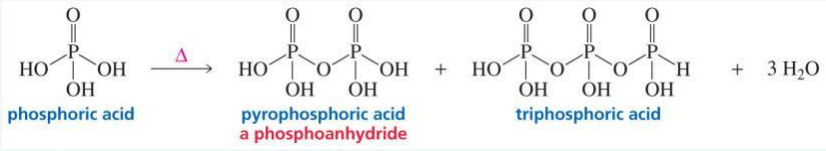
Activating Carboxylic Acids by converting them to Acyl Chlorides





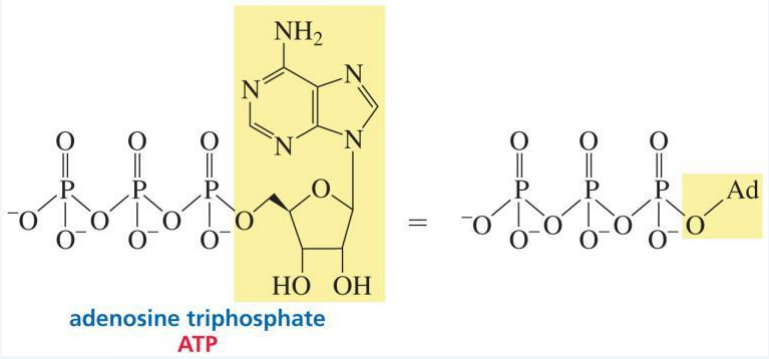
71

Heating Phosphoric Acid forms Pyrophosphoric Acid and Triphosphoric Acid



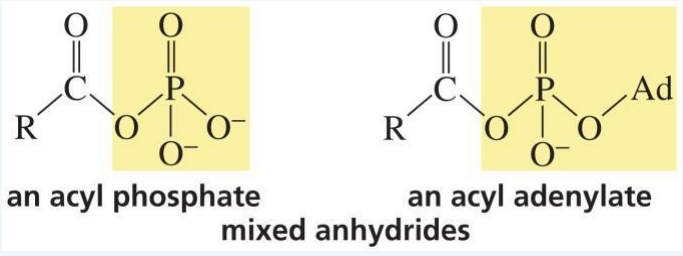
72

ATP



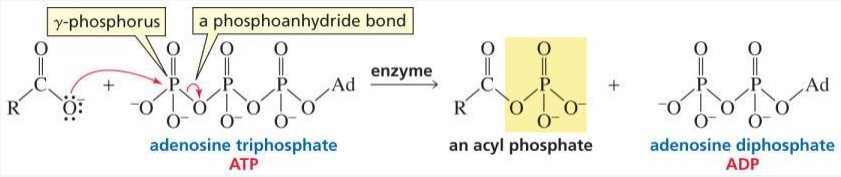
73

Mixed Anhydrides of a Carboxylic Acid and a Phosphoric Acid



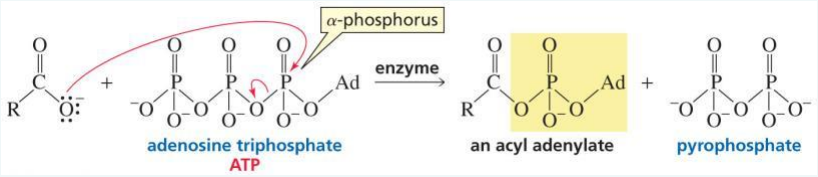
74

Forming an Acyl Phosphate



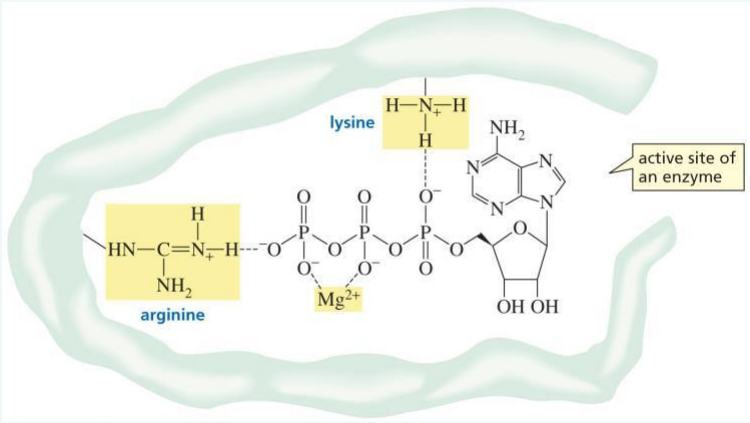
75

Forming an Acyl Adenylate



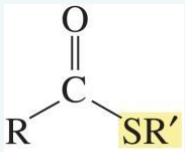
76

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

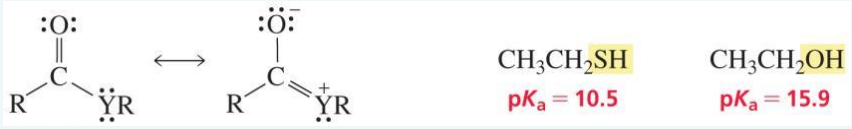


77

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



a thioester



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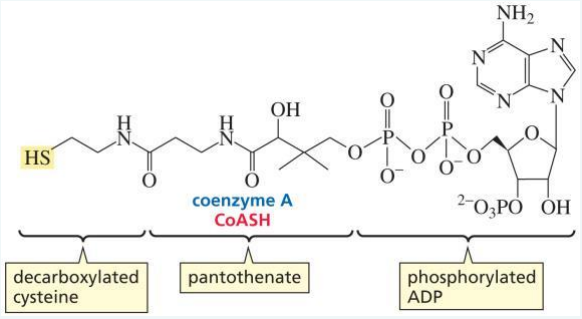
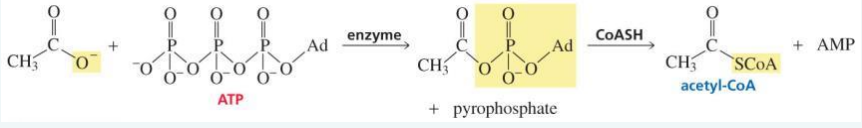
Coenzyme A



Coenzyme A is the thiol used in cells.

79

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



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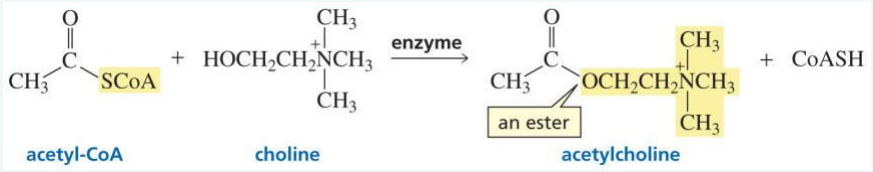
Using Acetyl-CoA to form Acetylcholine



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