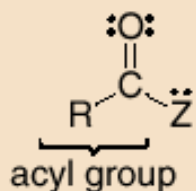


Carboxylic Acids and Nitriles

Chapters 20, 21
Organic Chemistry, *8th Edition*
John McMurry

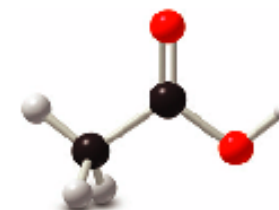
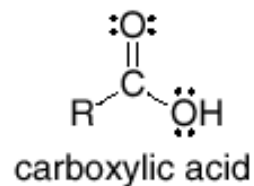
Carboxylic Acid Derivatives

General structure



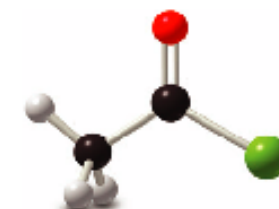
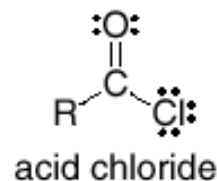
Z = electronegative atom

Z = OH



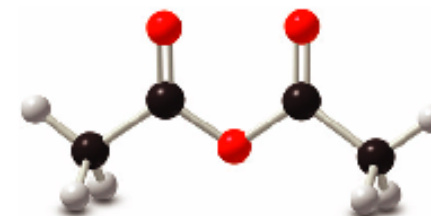
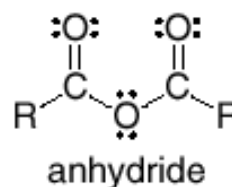
R = CH₃
acetic acid

Z = Cl



R = CH₃
acetyl chloride

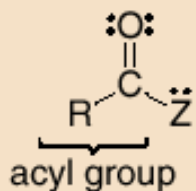
Z = OCOR



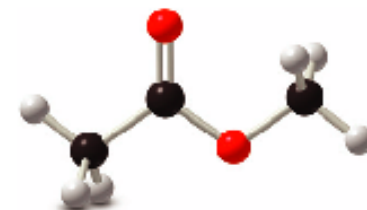
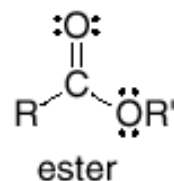
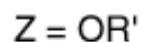
R = CH₃
acetic anhydride

Carboxylic Acid Derivatives

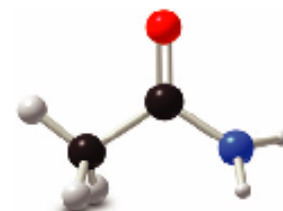
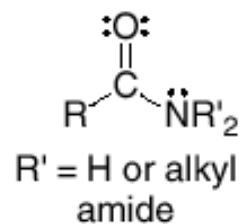
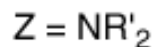
General structure



Z = electronegative atom



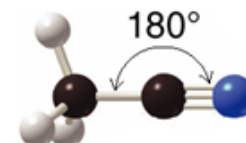
R = R' = CH₃
methyl acetate



R = CH₃, R' = H
acetamide

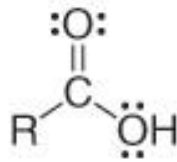


nitrile

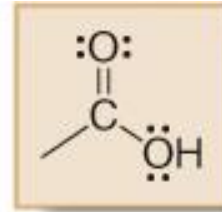


R = CH₃
acetonitrile

Structure and Bonding

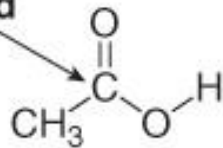


carboxylic acid



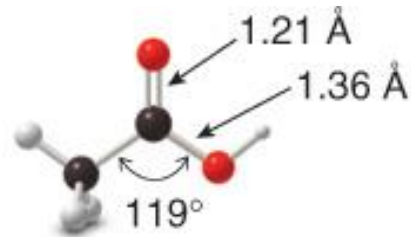
carboxy group

sp^2 hybridized



acetic acid

=

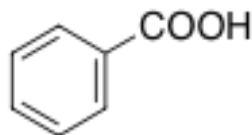


The C=O is shorter than the C-O.

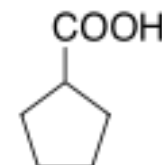
Nomenclature—The IUPAC System



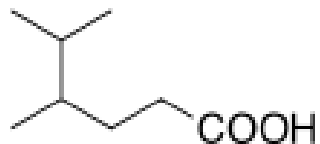
heptanoic acid



benzoic acid



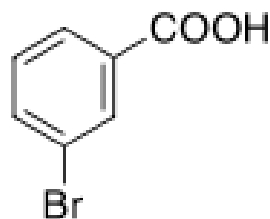
cyclopentane
carboxylic acid



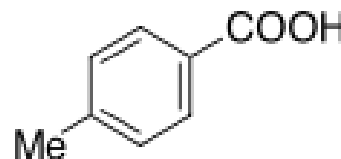
4,5-dimethyl
hexanoic acid



3-pentenoic
acid



3-bromobenzoic
acid



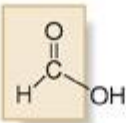
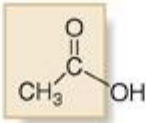
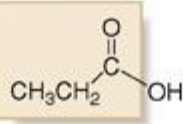
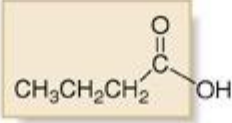
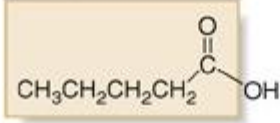
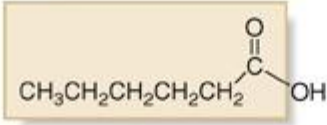
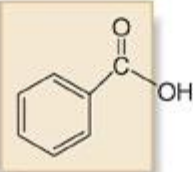
p-toluic
acid



1-methyl-
cyclopropanecarboxylic
acid

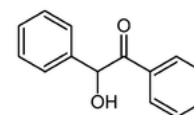
Nomenclature-Common Names

Table 19.1 Common Names for Some Simple Carboxylic Acids

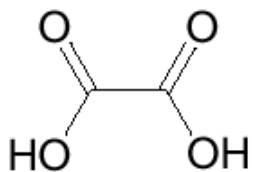
Number of C atoms	Structure	Parent name	Common name
1		form-	formic acid
2		acet-	acetic acid
3		propion-	propionic acid
4		butyr-	butyric acid
5		valer-	valeric acid
6		capro-	caproic acid
		benzo-	benzoic acid



(protos=primo + pion=grasso)
Il primo degli acidi grassi



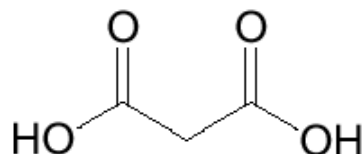
Nomenclature-Polyiacids



oxalic acid
(ethanedioic acid)



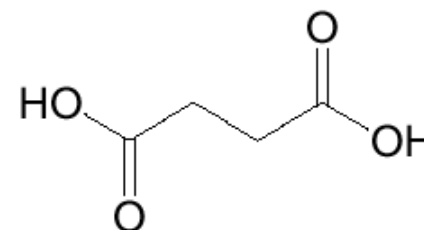
Oxalis acetosella



malonic acid
(propanedioic acid)



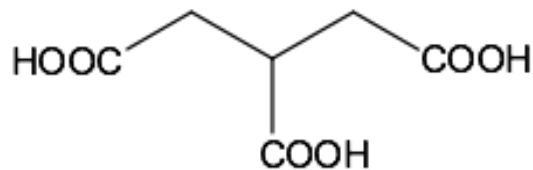
Malon



succinic acid
(butanedioic acid)



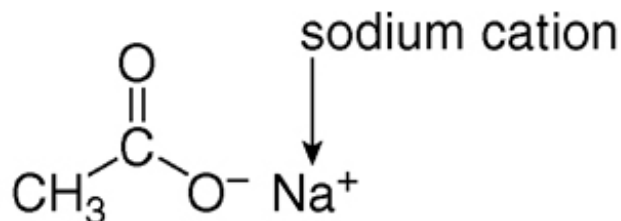
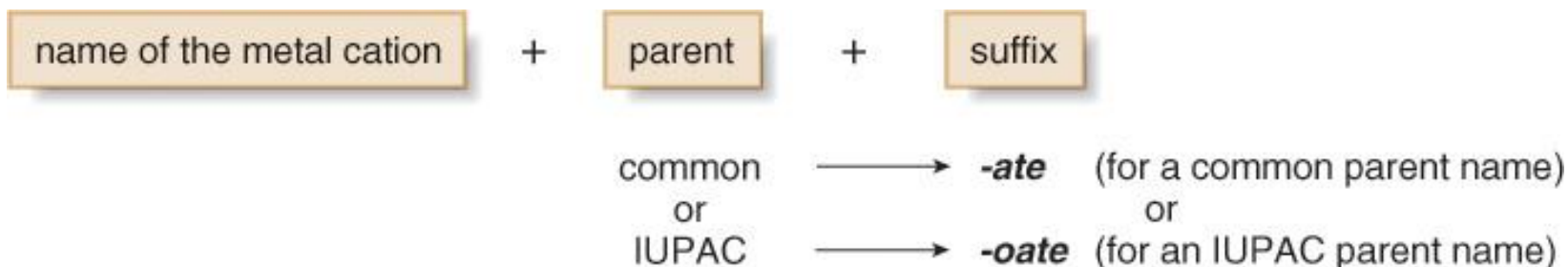
Succinum (ambra)



propane-1,2,3-tricarboxylic acid

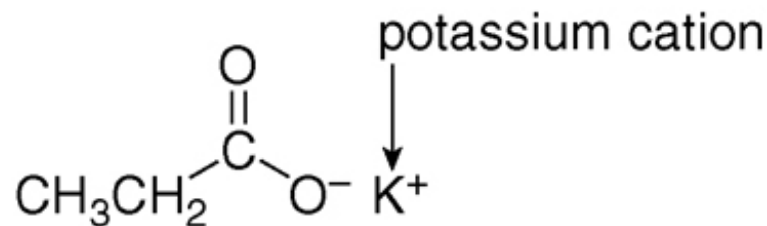
Nomenclature-Salts

- To name the metal salt of a carboxylate anion, put three parts together:



parent + suffix
acet- -ate

sodium acetate

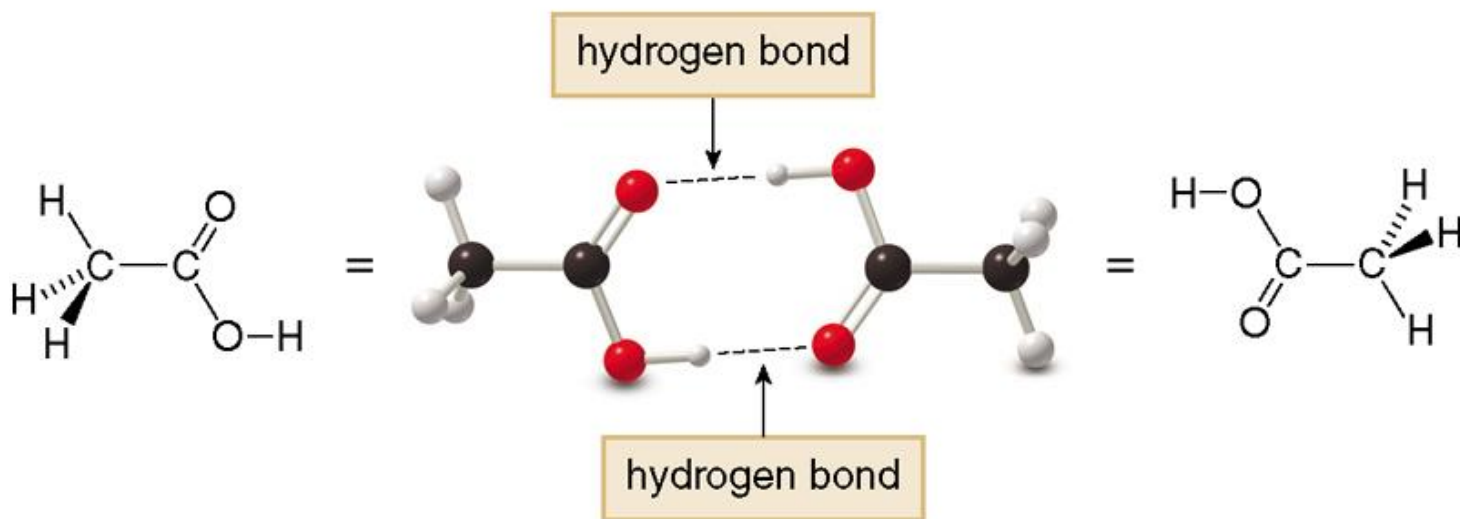


parent + suffix
propan- -oate

potassium propanoate


Physical Properties

- Carboxylic acids exhibit dipole-dipole interactions because they have polar C—O and O—H bonds.
- They also exhibit intermolecular hydrogen bonding.
- In the gas phase and in apolar solvents, carboxylic acids often exist as dimers held together by two intermolecular hydrogen bonds.



Physical Properties

Table 19.2 Physical Properties of Carboxylic Acids

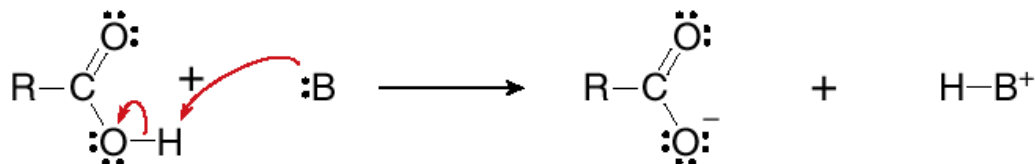
Property	Observation												
Boiling point and melting point	<ul style="list-style-type: none"> Carboxylic acids have higher boiling points and melting points than other compounds of comparable molecular weight. <table style="margin-left: auto; margin-right: auto; text-align: center;"> <tr> <td>$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$ VDW</td> <td>$\text{CH}_3\text{CH}_2\text{CHO}$ VDW, DD</td> <td>$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ VDW, DD, HB</td> <td style="border: 1px solid black;">CH_3COOH VDW, DD, two HB</td> </tr> <tr> <td>MW = 58</td> <td>MW = 58</td> <td>MW = 60</td> <td>MW = 60</td> </tr> <tr> <td>bp 0 °C</td> <td>bp 48 °C</td> <td>bp 97 °C</td> <td>bp 118 °C</td> </tr> </table> <p style="text-align: center; margin-top: 10px;">  Increasing strength of intermolecular forces Increasing boiling point </p>	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$ VDW	$\text{CH}_3\text{CH}_2\text{CHO}$ VDW, DD	$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ VDW, DD, HB	CH_3COOH VDW, DD, two HB	MW = 58	MW = 58	MW = 60	MW = 60	bp 0 °C	bp 48 °C	bp 97 °C	bp 118 °C
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$ VDW	$\text{CH}_3\text{CH}_2\text{CHO}$ VDW, DD	$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ VDW, DD, HB	CH_3COOH VDW, DD, two HB										
MW = 58	MW = 58	MW = 60	MW = 60										
bp 0 °C	bp 48 °C	bp 97 °C	bp 118 °C										
Solubility	<ul style="list-style-type: none"> Carboxylic acids are soluble in organic solvents regardless of size. Carboxylic acids having ≤ 5 C's are water soluble because they can hydrogen bond with H_2O (Section 3.4C). Carboxylic acids having > 5 C's are water insoluble because the nonpolar alkyl portion is too large to dissolve in the polar H_2O solvent. These "fatty" acids dissolve in a nonpolar fat-like environment but do not dissolve in water. 												

Key: VDW = van der Waals, DD = dipole–dipole, HB = hydrogen bonding, MW = molecular weight

Acidity of Carboxylic Acids

- Carboxylic acids react as Brønsted–Lowry acids—that is, as proton donors.

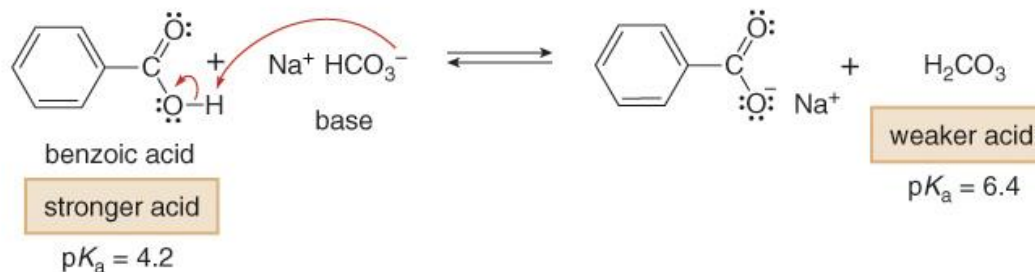
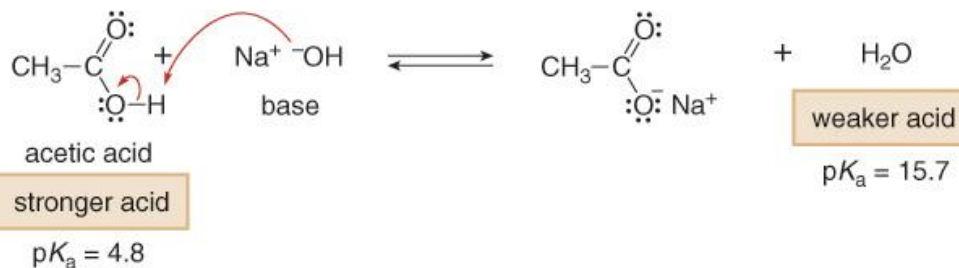
A Brønsted–Lowry acid–base reaction



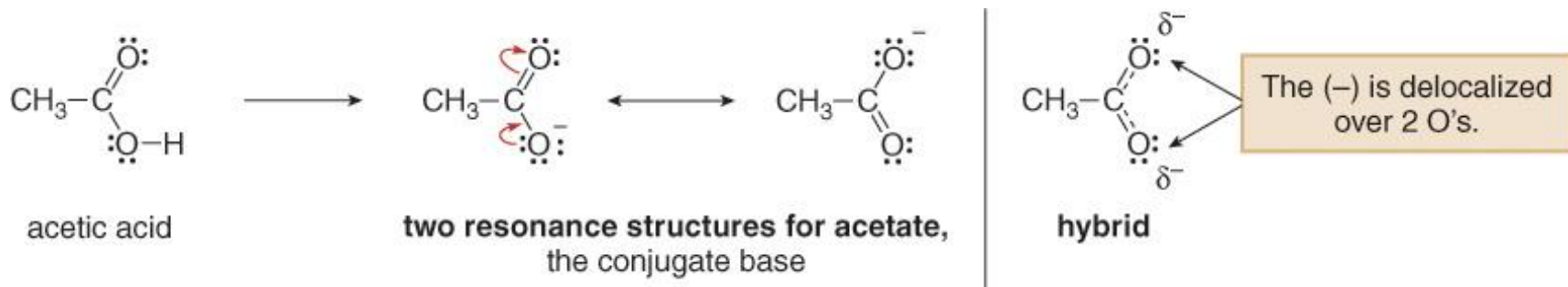
polar O–H bond

- Because the pK_a values of many carboxylic acids are ~ 5 , bases that have conjugate acids with pK_a values higher than 5 are strong enough to deprotonate them.

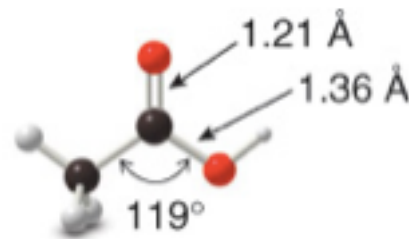
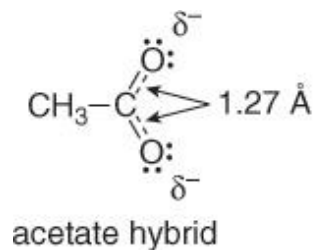
Examples



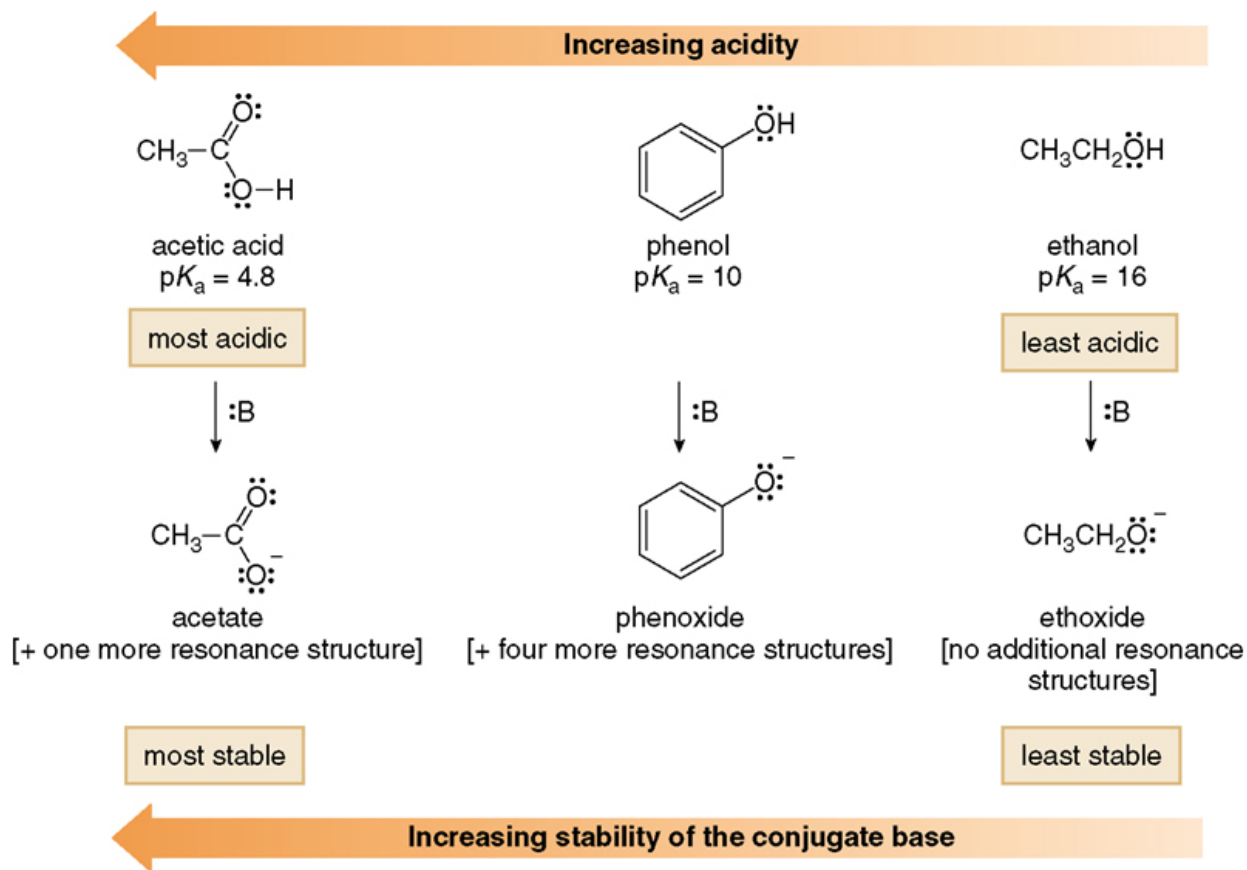
Acidity of Carboxylic Acids



- The acetate anion has two C—O bonds of equal length (1.27 Å) and intermediate between the length of a C—O single bond (1.36 Å) and C=O (1.21 Å).

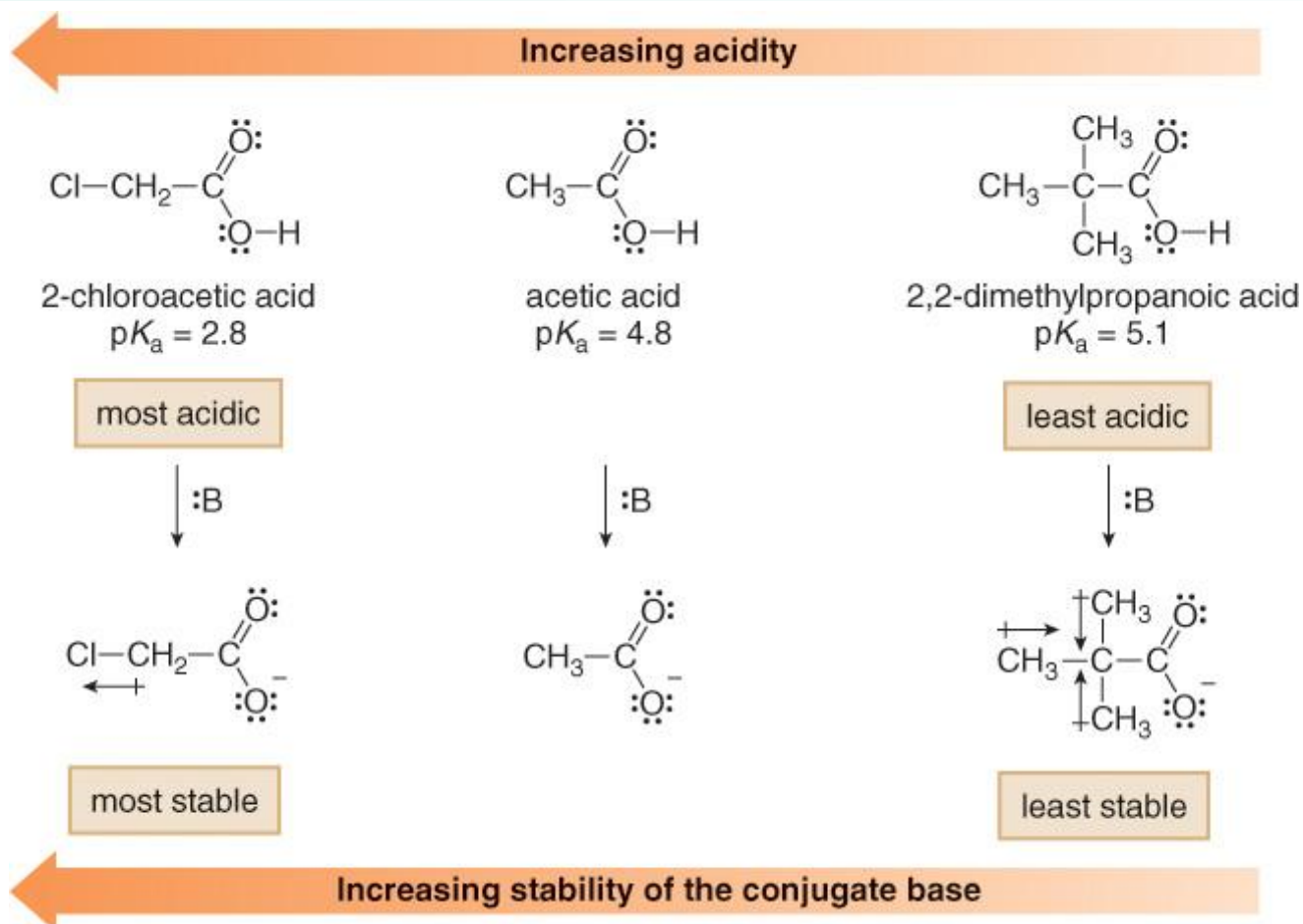


Carboxylic Acids—Strong Organic Brønsted-Lowry Acids



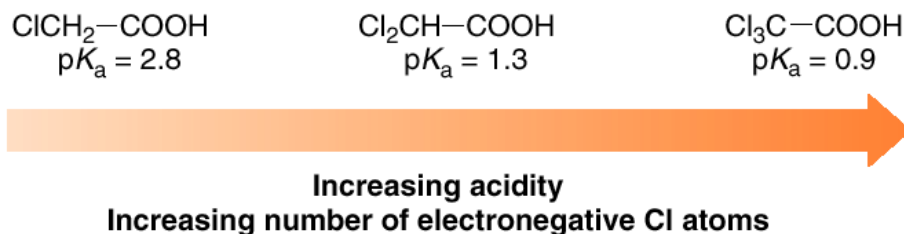
The Inductive Effect in Aliphatic Carboxylic Acids

- Electron-withdrawing groups stabilize a conjugate base, making a carboxylic acid more acidic.
- Electron-donating groups destabilize the conjugate base, making a carboxylic acid less acidic.

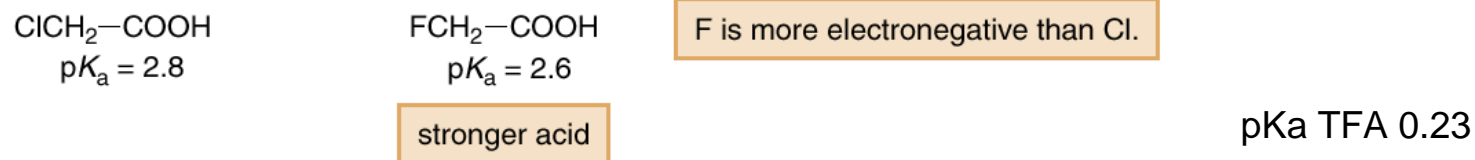


The Inductive Effect in Aliphatic Carboxylic Acids

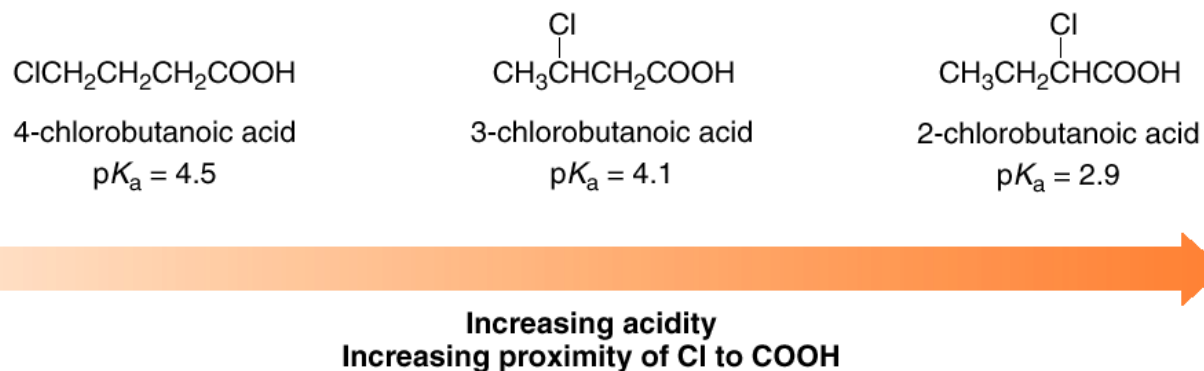
- The larger the number of electronegative substituents, the stronger the acid.



- The more electronegative the substituent, the stronger the acid.

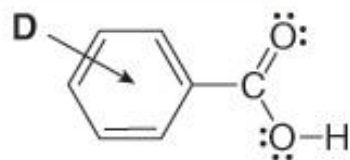


- The closer the electron-withdrawing group to the COOH, the stronger the acid.



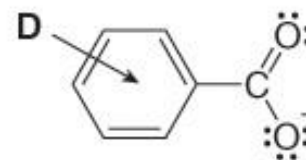
Substituted Benzoic Acids

D = Electron-donor group



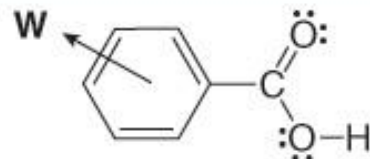
This acid is less acidic than benzoic acid.

$$pK_a > 4.2$$



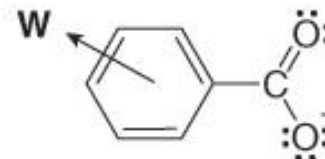
D destabilizes the carboxylate anion.

W = Electron-withdrawing group



This acid is more acidic than benzoic acid.

$$pK_a < 4.2$$



W stabilizes the carboxylate anion.

Substituted Benzoic Acids

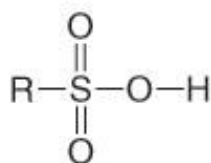
	Substituent	Effect in electrophilic substitution	Effect on acidity of substituted benzoic acids	
electron-donating groups	$-\ddot{\text{N}}\text{H}_2$ [$\ddot{\text{N}}\text{HR}$, $\ddot{\text{N}}\text{R}_2$]			
	$-\ddot{\text{O}}\text{H}$	activating groups	These groups make a benzoic acid less acidic .	
	$-\ddot{\text{O}}\text{R}$			
	$-\ddot{\text{N}}\text{HCOR}$			
	$-\text{R}$			
	$-\ddot{\text{X}}:$ [$\text{X} = \text{F}, \text{Cl}, \text{Br}, \text{I}$]			
electron-withdrawing groups	$-\text{CHO}$			deactivating groups
	$-\text{COR}$			
	$-\text{COOR}$			
	$-\text{COOH}$			
	$-\text{CN}$			
	$-\text{SO}_3\text{H}$			
	$-\text{NO}_2$			
	$-\overset{+}{\text{N}}\text{R}_3$			

Increasing acidity

Sulfonic Acids

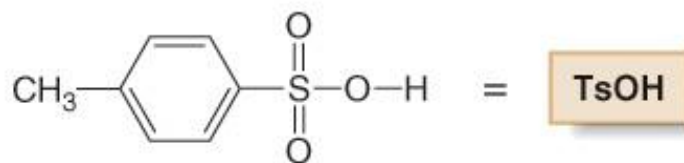
- Sulfonic acids have the general structure RSO_3H .
- The most widely used sulfonic acid is *p*-toluenesulfonic acid.

General structure

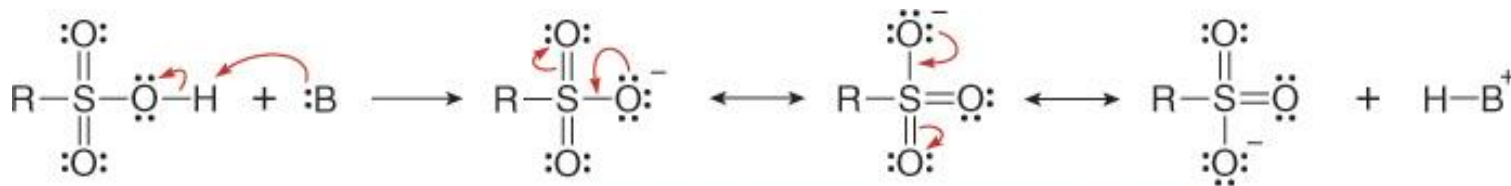


sulfonic acid

Example



p-toluenesulfonic acid

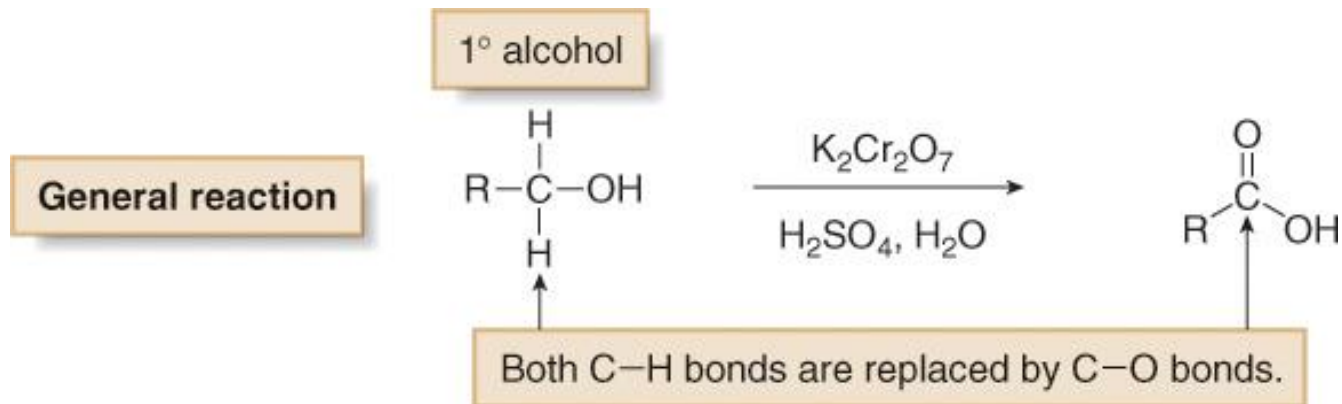


strong acid
 $\text{p}K_{\text{a}} \approx -7$

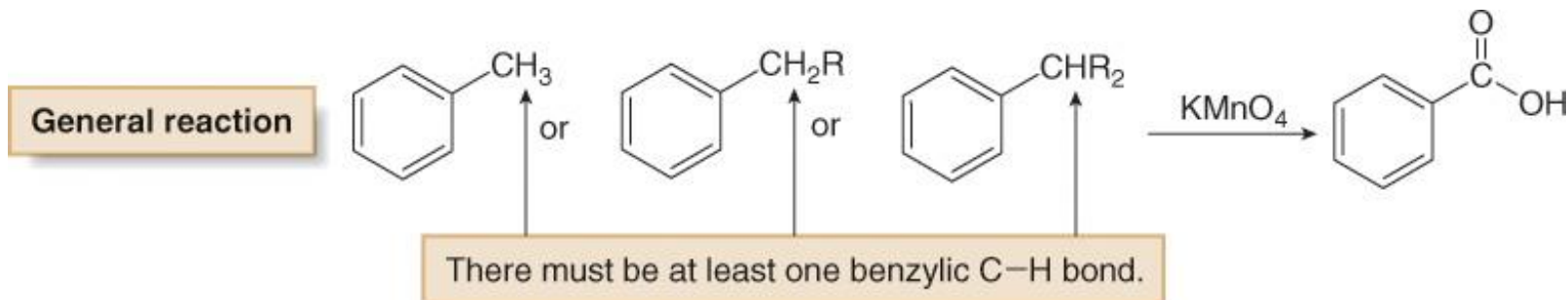
Three resonance structures—
All have a negative charge on oxygen.

Preparation of Carboxylic Acids

[1] Oxidation of 1° alcohols

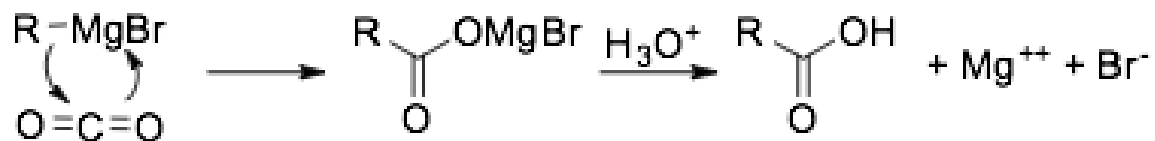
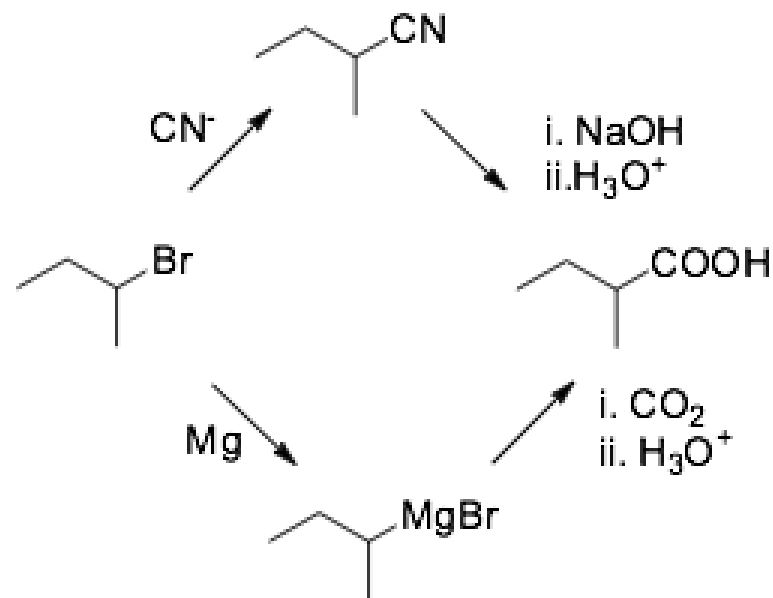


[2] Oxidation of alkyl benzenes



Preparation of Carboxylic Acids

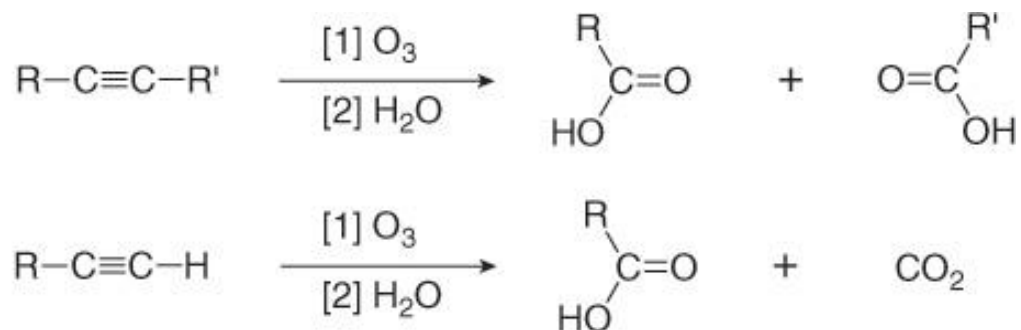
[3] From alkyl halides



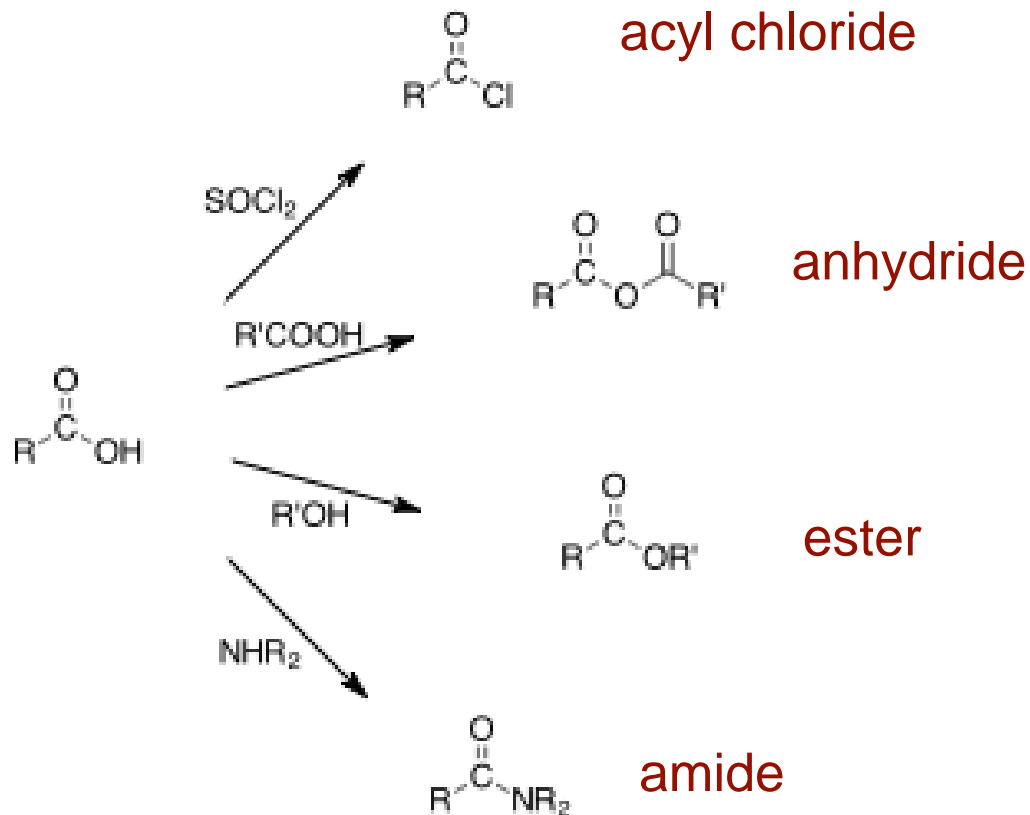
Preparation of Carboxylic Acids

[3] Oxidative cleavage of alkynes

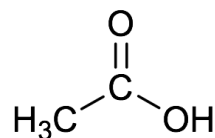
General reactions



Reactions of Carboxylic Acids



Derivatives: Physical Properties



MW = 60 bp 118 °C

Table 22.3

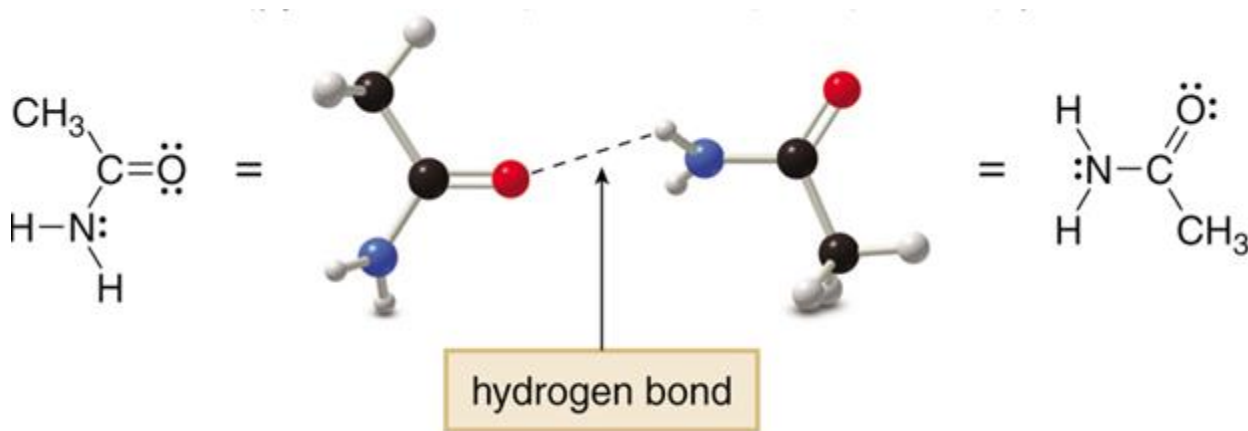
Physical Properties of Carboxylic Acid Derivatives

Property	Observation
Boiling point and melting point	<ul style="list-style-type: none"> Primary (1°) and 2° amides have <i>higher</i> boiling points and melting points than compounds of comparable molecular weight. The boiling points and melting points of other carboxylic acid derivatives are similar to those of other polar compounds of comparable size and shape. <div style="text-align: center; margin-top: 20px;"> <p style="text-align: center;"> $\text{CH}_3\text{C}(=\text{O})\text{Cl}$ $\text{CH}_3\text{C}(=\text{O})\text{OCH}_3$ $\text{CH}_3\text{C}(=\text{O})\text{CH}_2\text{CH}_3$ $\text{CH}_3\text{CH}_2\text{C}(=\text{O})\text{NH}_2$ MW = 78.5 MW = 74 MW = 72 MW = 73 bp 52 °C bp 58 °C bp 80 °C bp 213 °C </p> <p style="text-align: center;"> similar boiling points < higher boiling point 1° amide </p> </div>
Solubility	<ul style="list-style-type: none"> Carboxylic acid derivatives are soluble in organic solvents regardless of size. Most carboxylic acid derivatives having ≤ 5 C's are H₂O soluble because they can hydrogen bond with H₂O (Section 3.4C). Carboxylic acid derivatives having > 5 C's are H₂O insoluble because the nonpolar alkyl portion is too large to dissolve in the polar H₂O solvent.

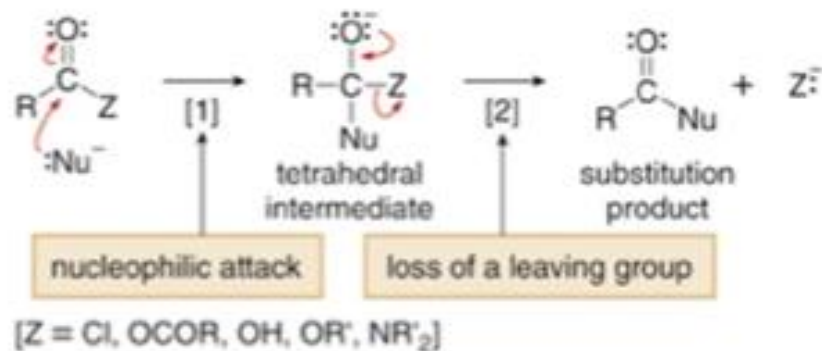
Key: MW = molecular weight

Derivatives: Physical Properties

- Because all carbonyl compounds have a polar carbonyl group, they exhibit dipole-dipole interactions.
- Because they contain one or two N—H bonds, 1° and 2° amides are capable of intermolecular hydrogen bonding.

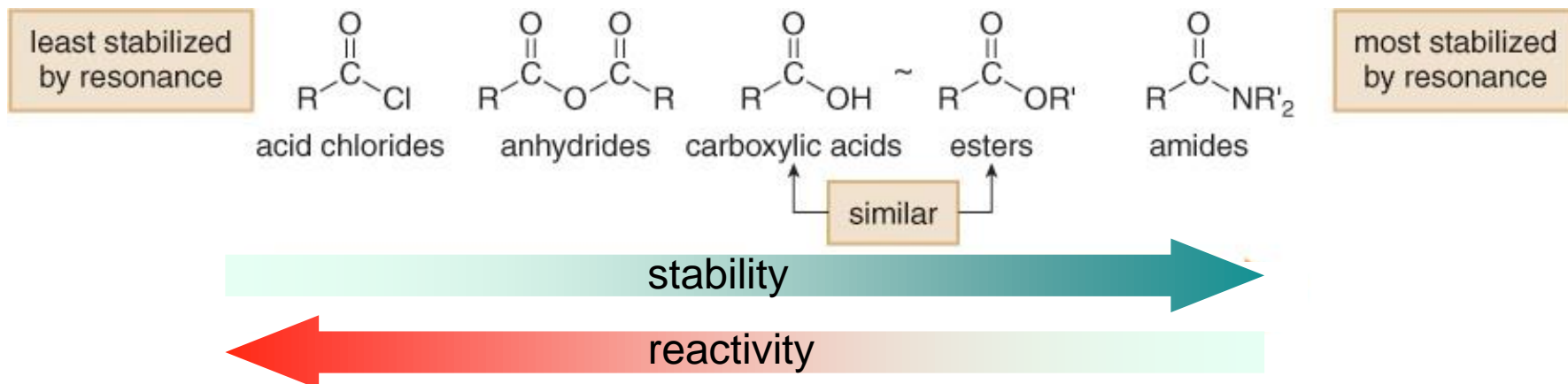
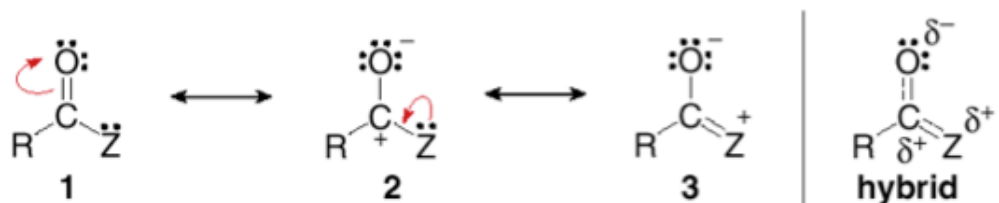


Reaction of Carboxylic Acid Derivatives: Nucleophilic Acyl Substitution

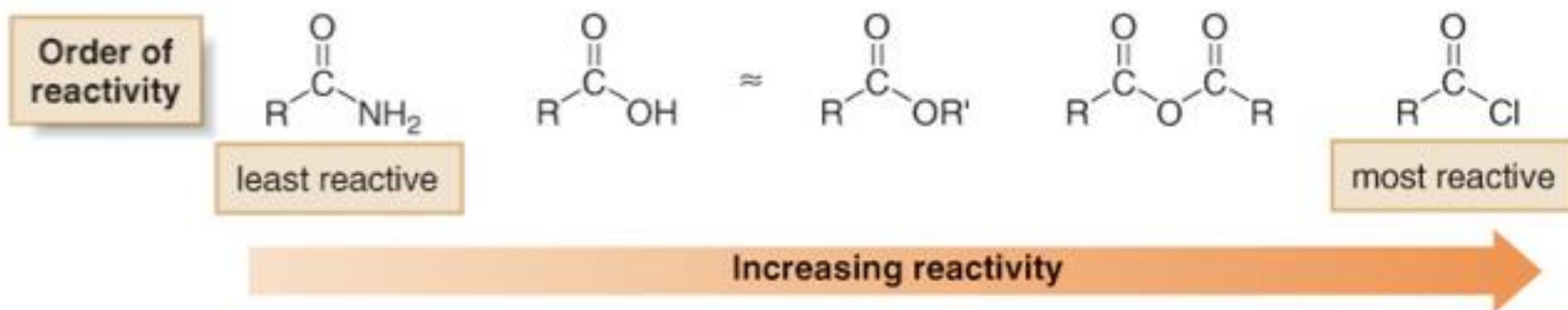


Derivatives: Structure and Bonding

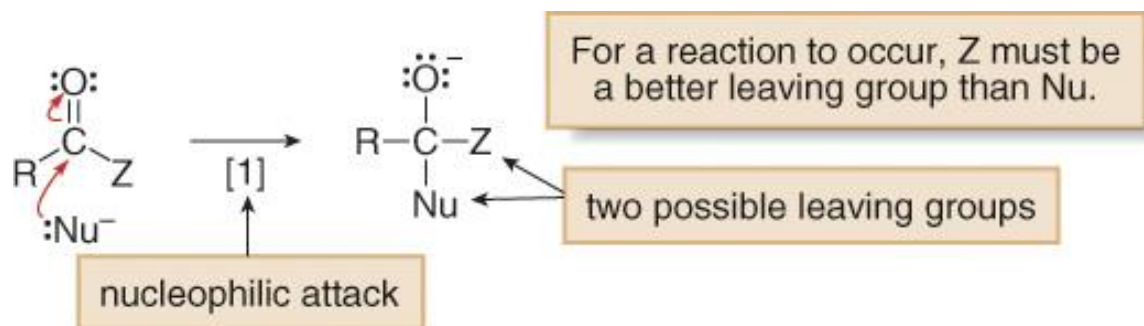
- Three resonance structures stabilize carboxylic acid derivatives (RCOZ) by delocalizing electron density.



Introduction to Nucleophilic Acyl Substitution



Based on this order of reactivity, more reactive compounds can be converted into less reactive ones. The reverse is not usually true.



Introduction to Nucleophilic Acyl Substitution

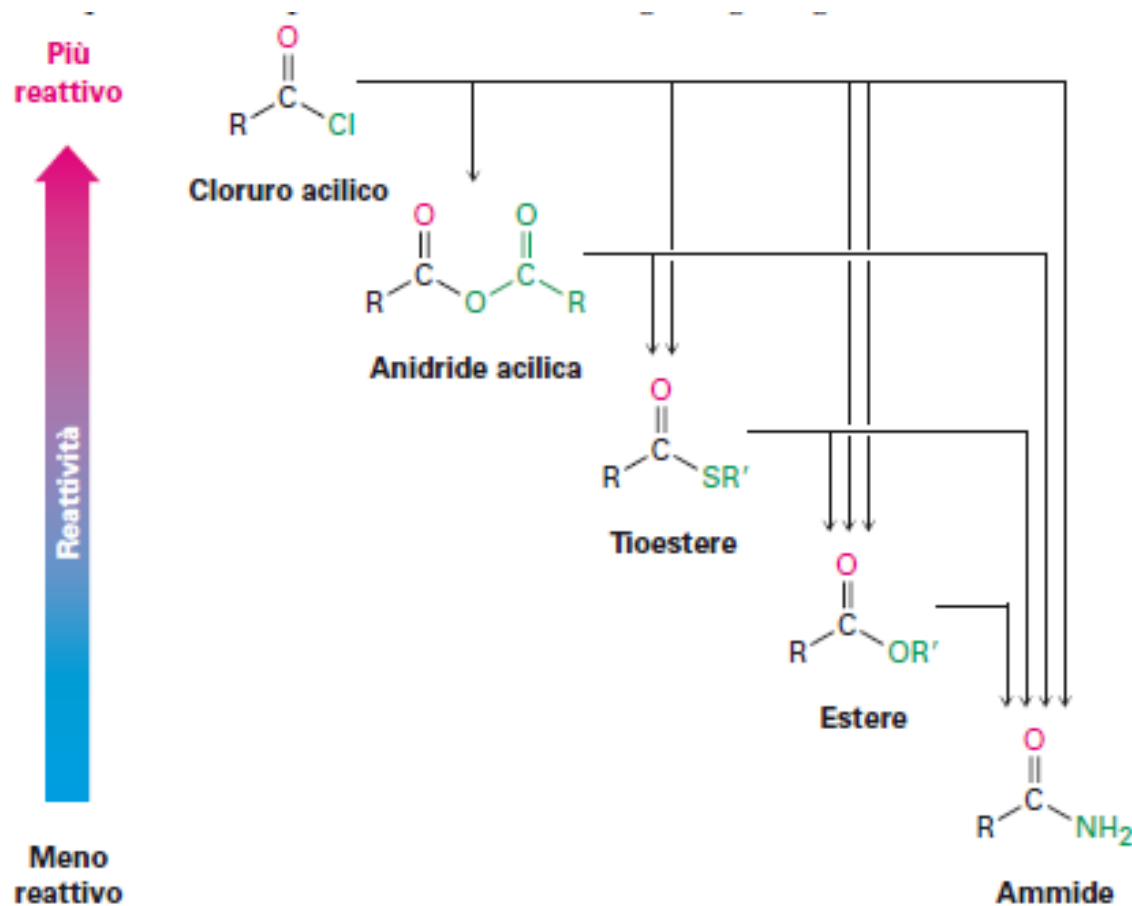
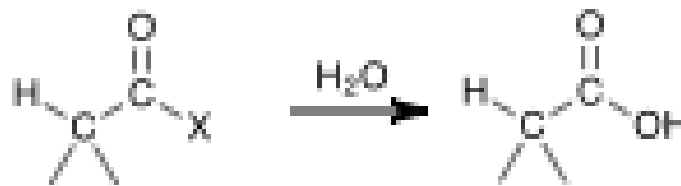


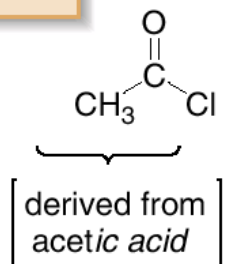
Figura 21.2 Interconversione di derivati degli acidi carbossilici. Un derivato acilico più reattivo può essere trasformato in uno meno reattivo, ma non vale il contrario.

All derivatives are hydrolysed to carboxylic acids

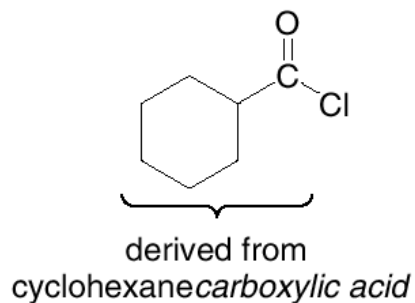


Acid Chlorides: Nomenclature

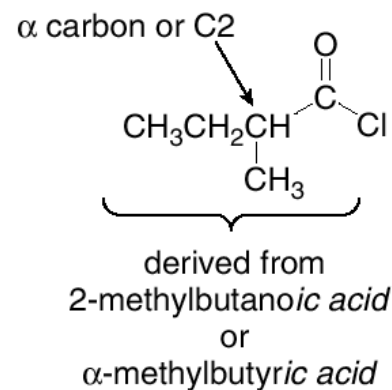
Naming acid chlorides



acetyl chloride



cyclohexanecarbonyl chloride



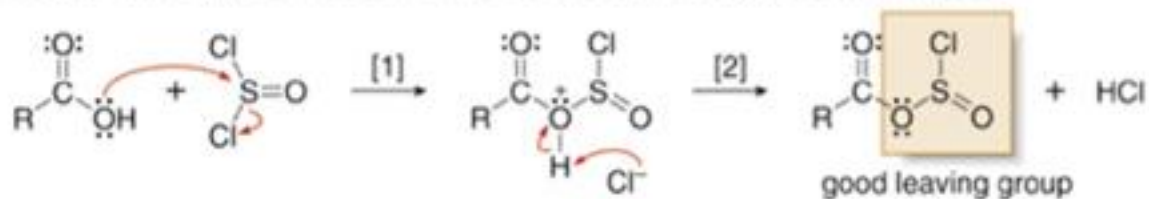
2-methylbutanoyl chloride
or
 α -methylbutyryl chloride

Acid Chlorides: Synthesis

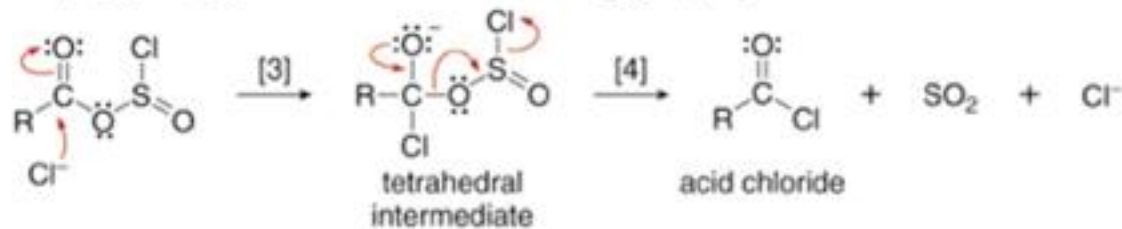
By the reaction of a carboxylic acid with thionyl chloride (SOCl_2).



Steps [1] and [2] Conversion of the OH group into a good leaving group

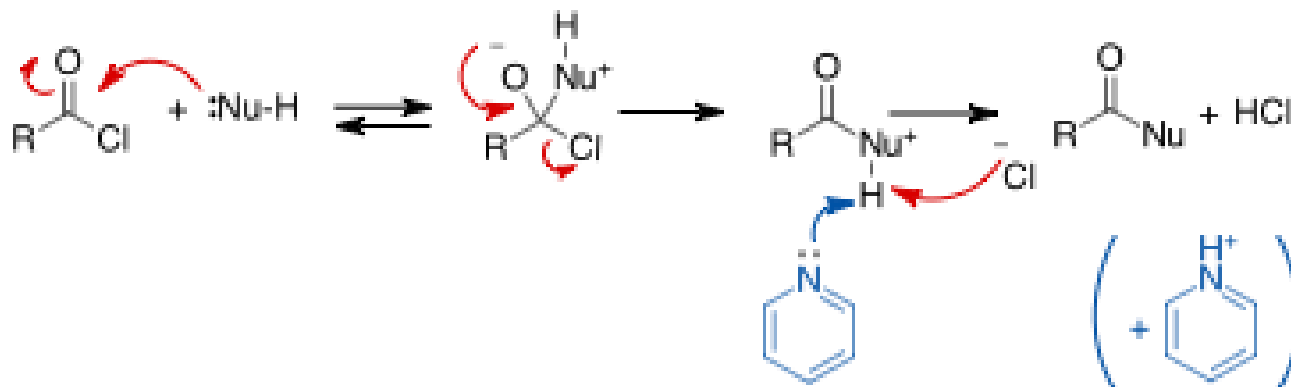


Steps [3] and [4] Substitution of the leaving group by Cl



Acid Chlorides: Reactions

- Acyl chlorides are the most reactive among carboxylic acid derivatives
- A weak, non nucleophilic, base like pyridine is often added to the reaction mixture to remove the byproduct HCl.



anhydride



ester



acid

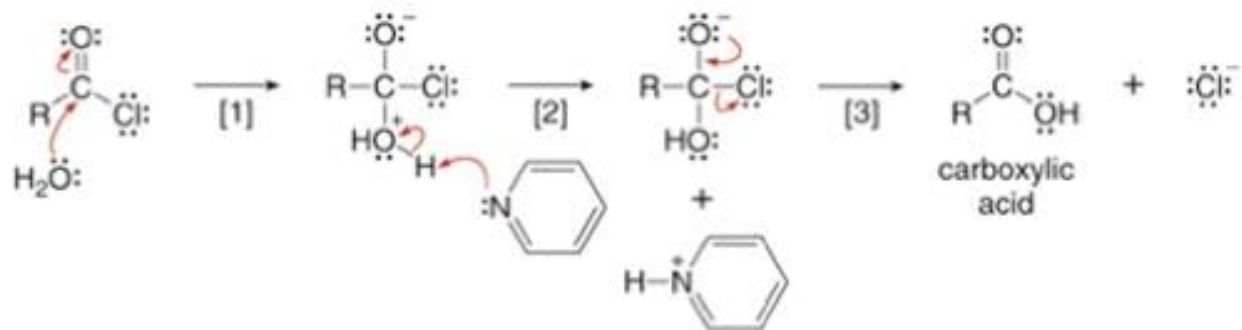
(acid chlorides are readily decomposed by water)



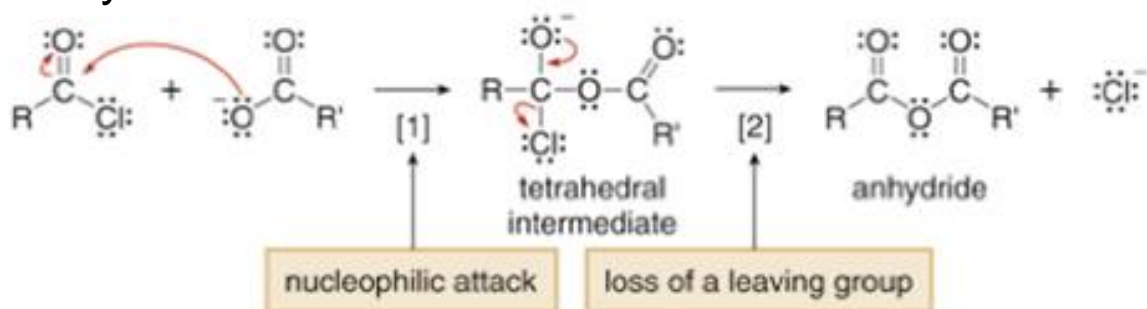
amide

Reactions of Acid Chlorides

Hydrolysis:

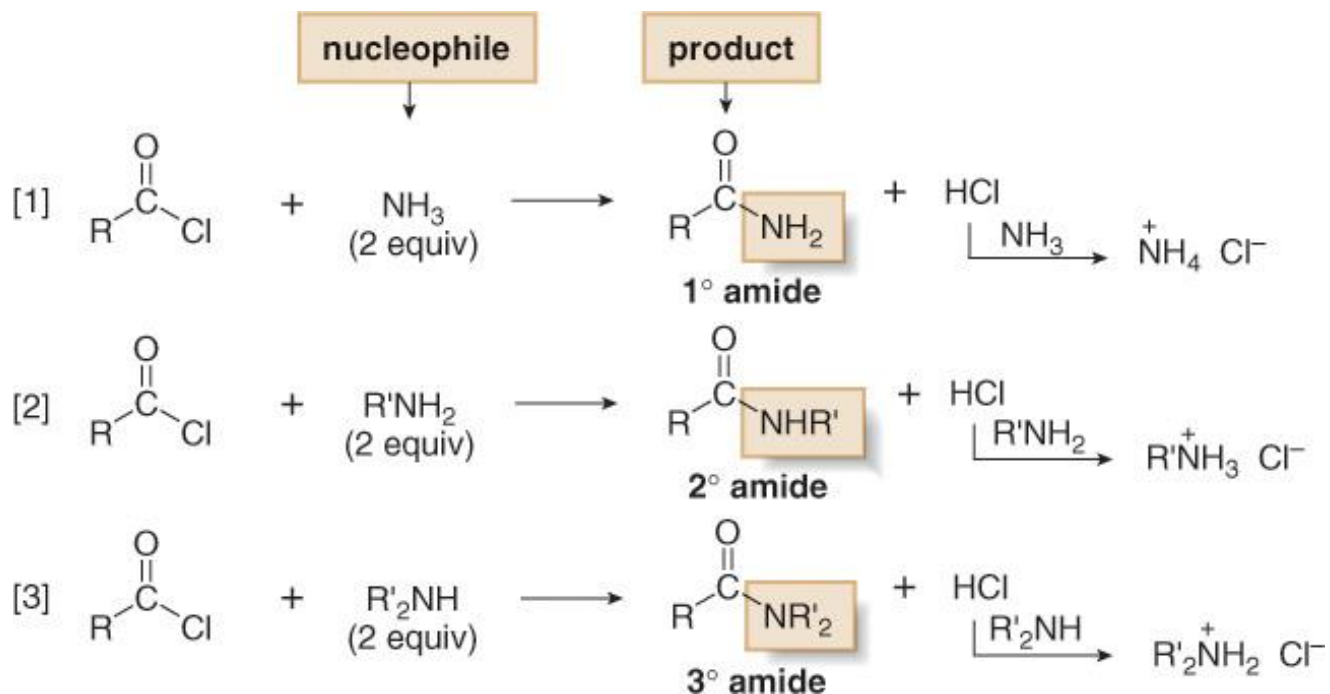


Formation of anhydrides:



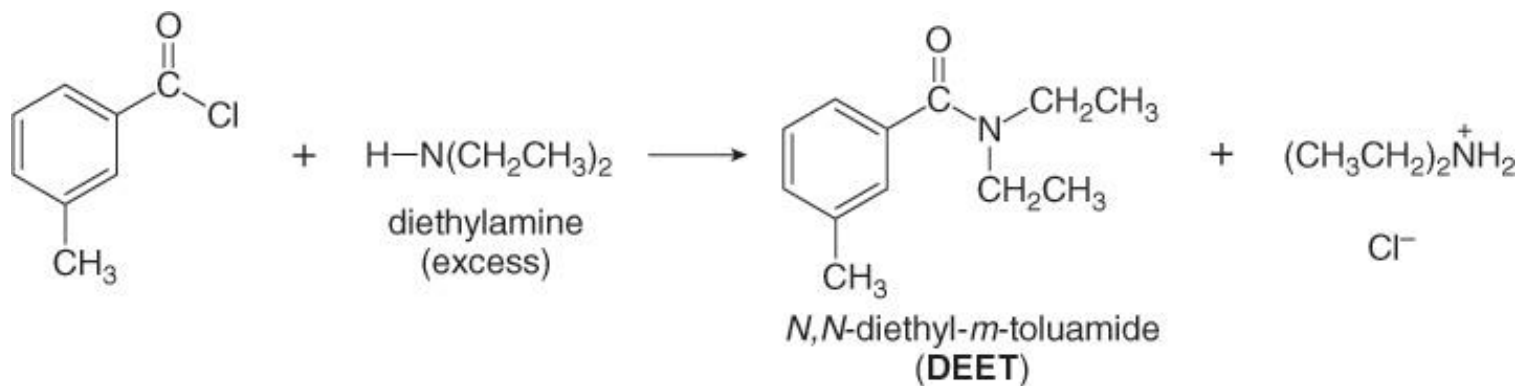
Reactions of Acid Chlorides

- Acid chlorides also react with ammonia and 1° and 2° amines to form 1°, 2° and 3° amides respectively.
- Two equivalents of NH₃ or amine are used.
- One equivalent acts as the nucleophile to replace Cl, while the other reacts as a base with the HCl by-product to form an ammonium salt.



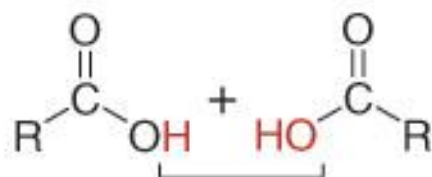
Reactions of Acid Chlorides

- **DEET** is the active ingredient in the most widely used insect repellents, and is effective against mosquitoes, fleas and ticks.

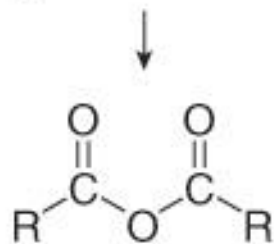


Anhydrides

The word anhydride means *without water*. Removing one molecule of water from two molecules of carboxylic acid forms an anhydride.

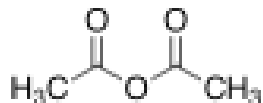


A molecule of
 H_2O is removed.

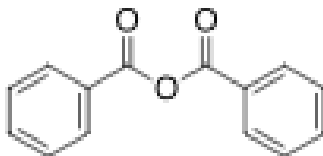


anhydride
+ H_2O

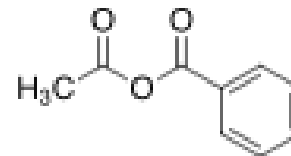
Anydrides: Nomenclature



acetic
anhydride



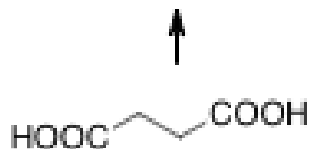
benzoic
anhydride



acetic benzoic
anhydride



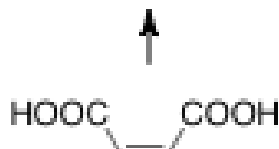
succinic
anhydride



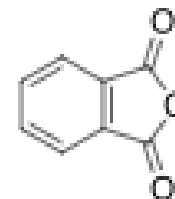
succinic
acid



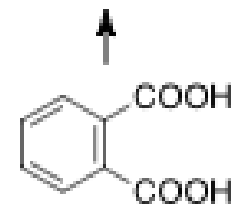
maleic
anhydride



maleic
acid



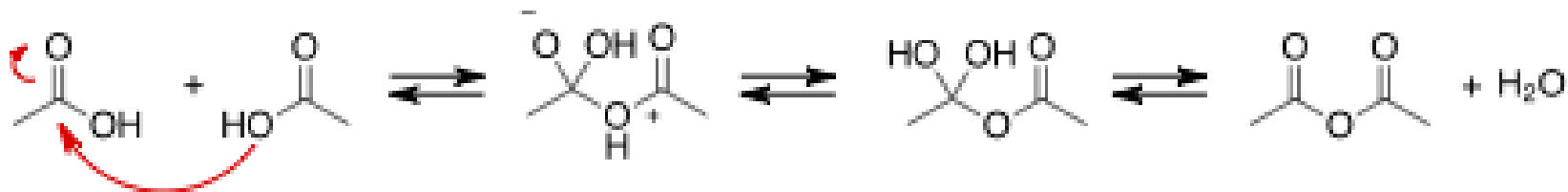
phthalic
anhydride



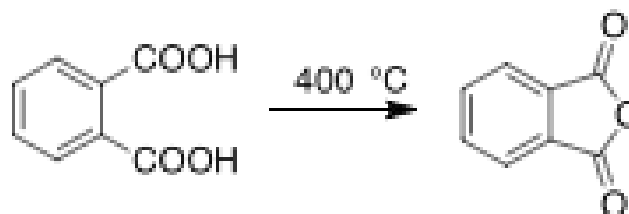
phthalic
acid

Anhydrides: Synthesis

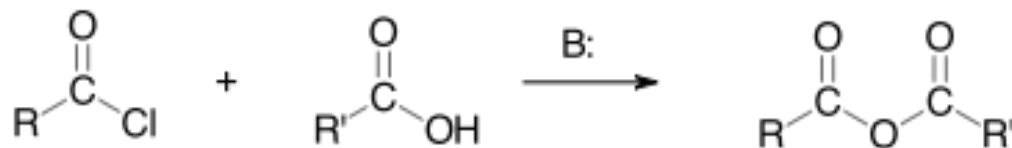
1. By dehydration of carboxylic acids at high temperatures (700-800 °C) and/or in the presence of condensing agents



Formation of cyclic anhydrides is easier

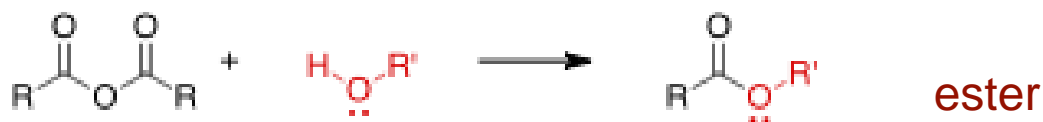
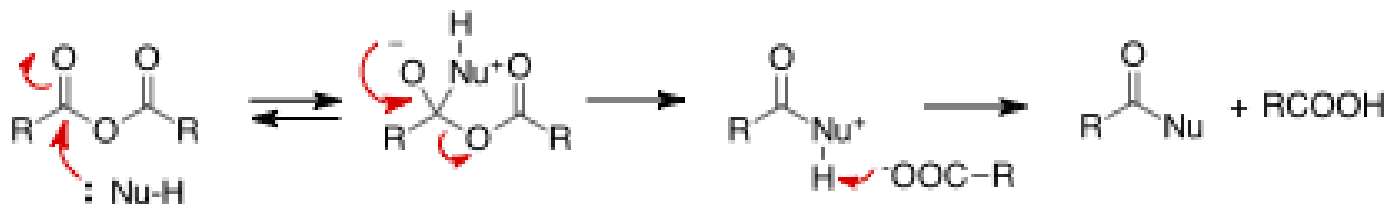


2. From an acid and an acyl chloride

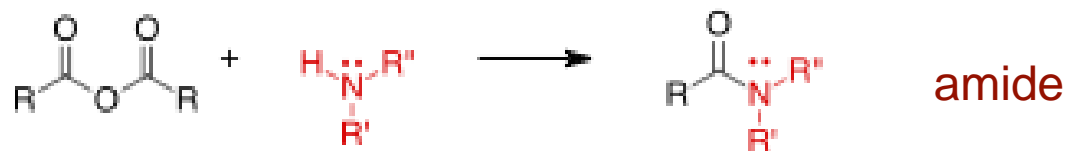


Anhydrides: Reactions

- Anhydrides are strong acylating agents a
- A weak acid is formed as by-product.

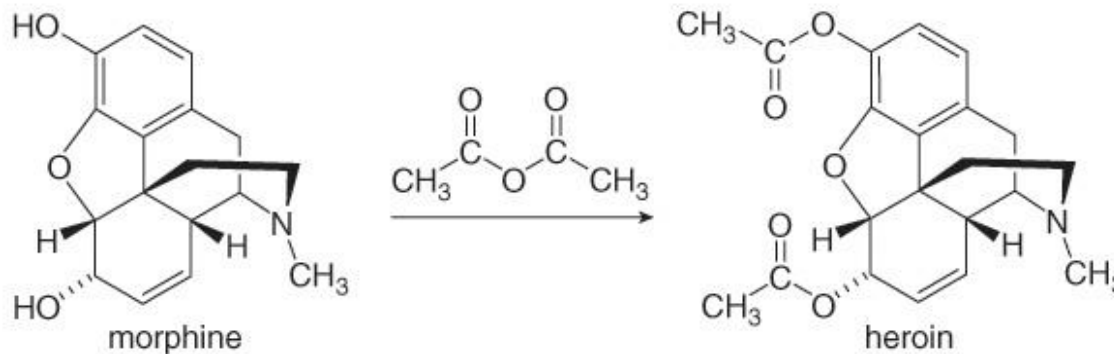
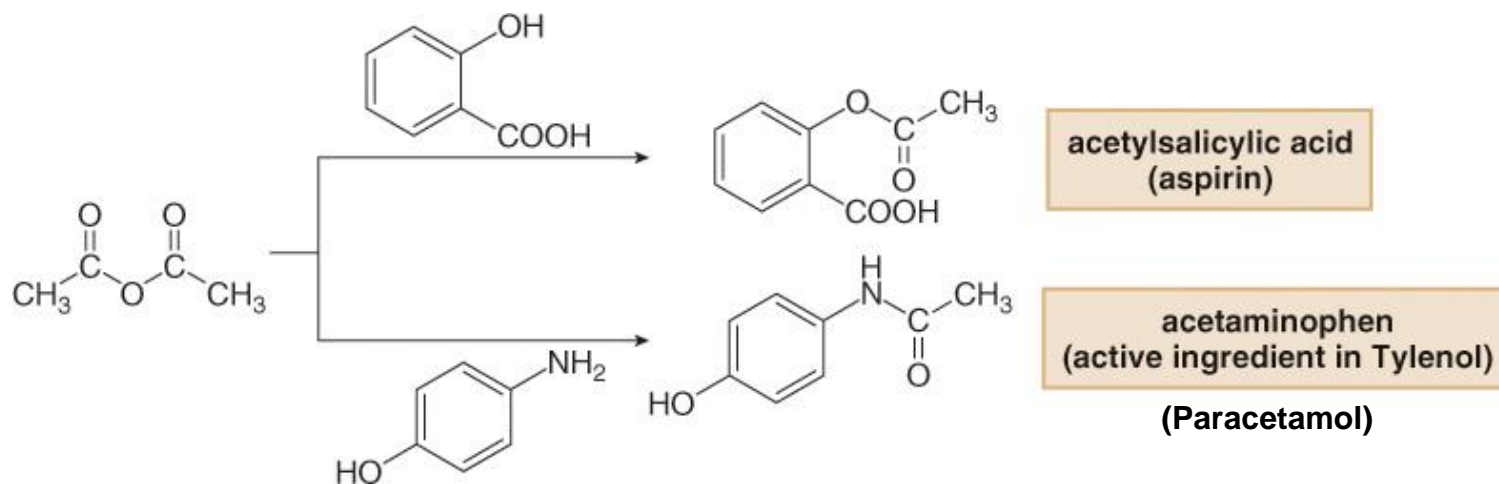


(anhydrides are readily decomposed by water)

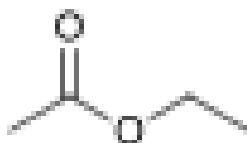


Reactions of Anhydrides

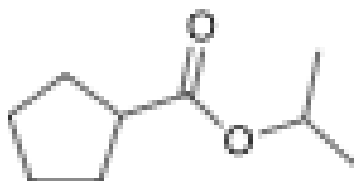
Anhydrides are very common acetylating agents for the synthesis of esters and amides:



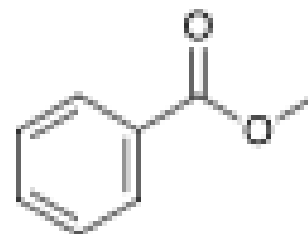
Esters: Nomenclature



Ethyl acetate

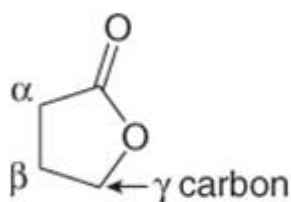


Isopropyl
cyclopentanecarboxylate



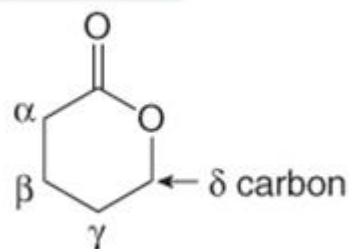
Methyl benzoate

Lactones—Cyclic esters



γ -lactone

Butyrolactone

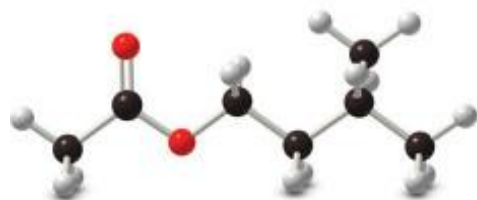
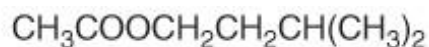


δ -lactone

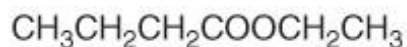
Valerolactone

Interesting Esters

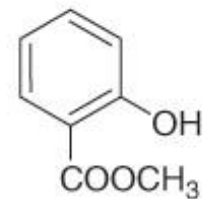
Many low molecular weight esters have pleasant and very characteristic odors.



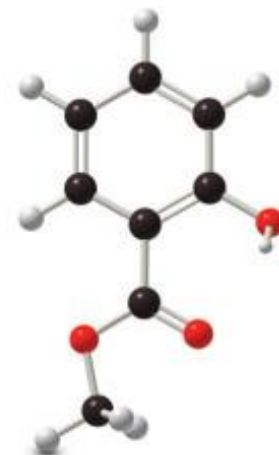
isoamyl acetate
odor of banana



ethyl butyrate
odor of pineapple

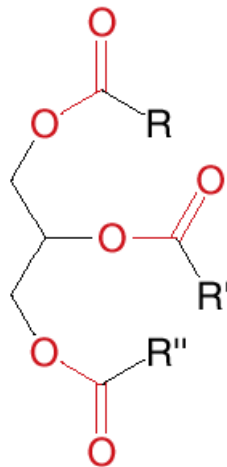


methyl salicylate
oil of wintergreen



Lipids

- Each triacylglycerol is a triester, containing three long hydrocarbon side chains.
- Unsaturated triacylglycerols have one or more double bonds in their long hydrocarbon chains, whereas saturated triacylglycerols have none.



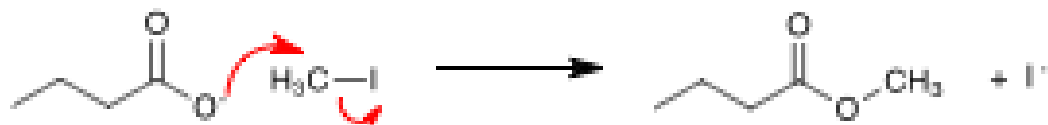
R groups have 11–19 C's.

[Three ester groups are labeled in red.]

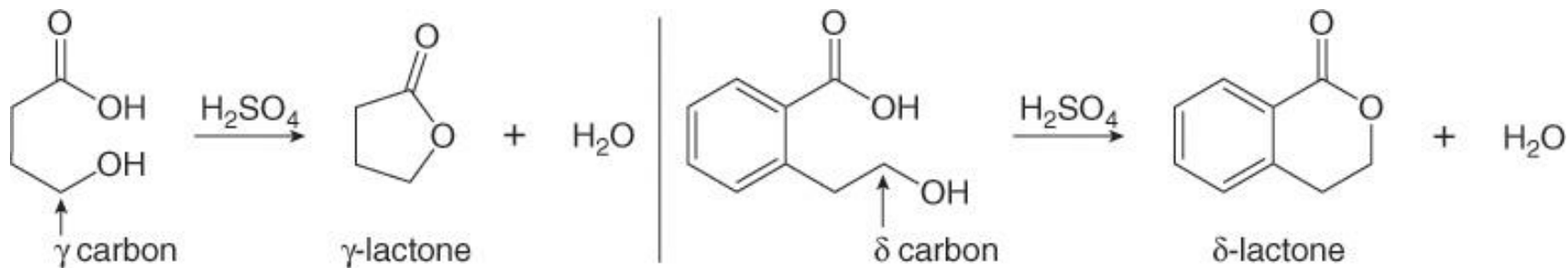
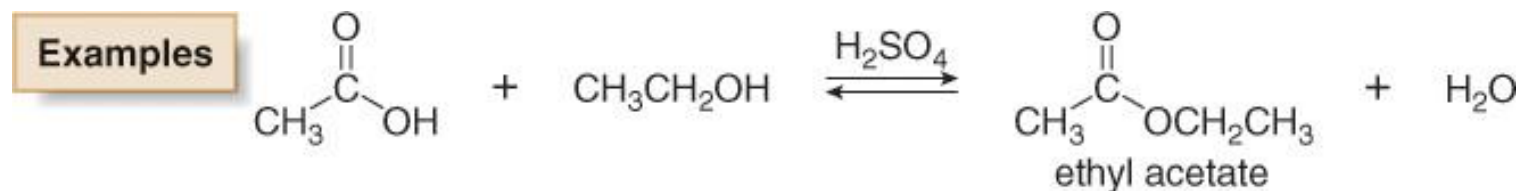
triacylglycerol
the most common type of lipid

Esters from Carboxylic Acids

- SN2 (mainly for methyl esters).

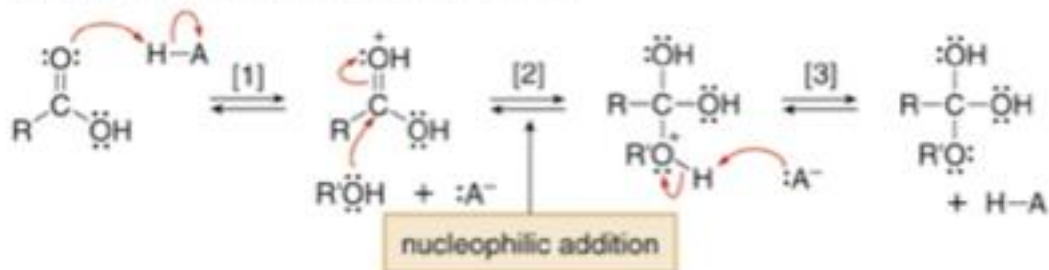


- Fischer esterification.

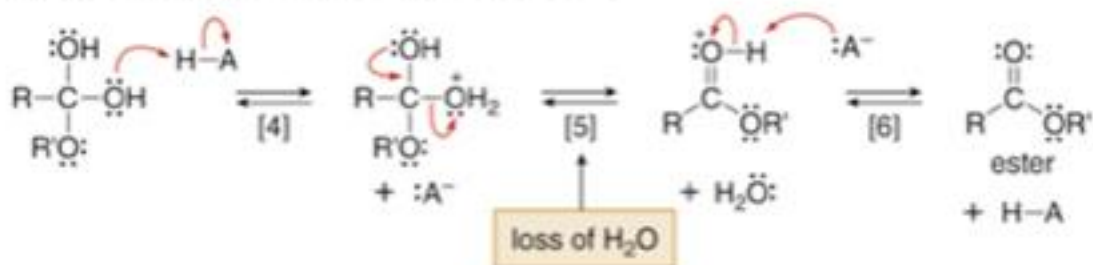


Fischer Esterification

Part [1] Addition of the nucleophile R'OH

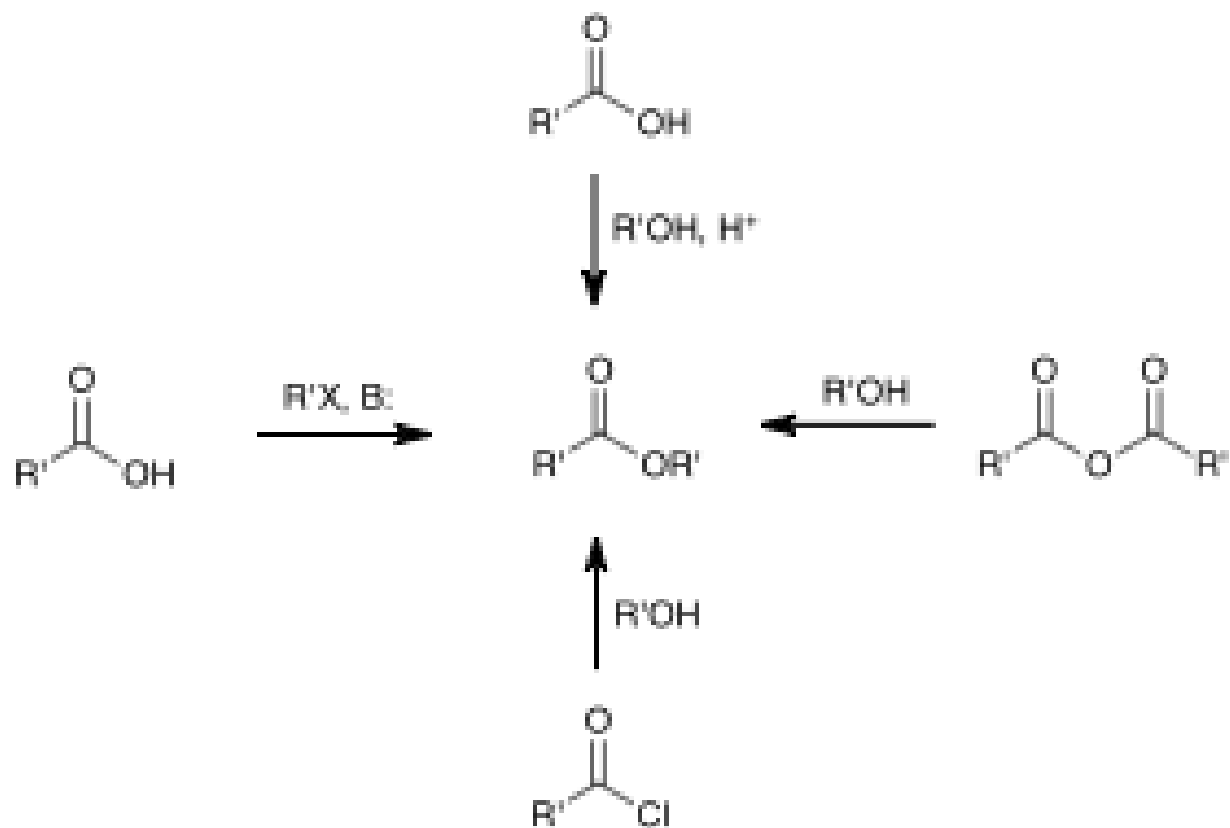


Part [2] Elimination of the leaving group H₂O



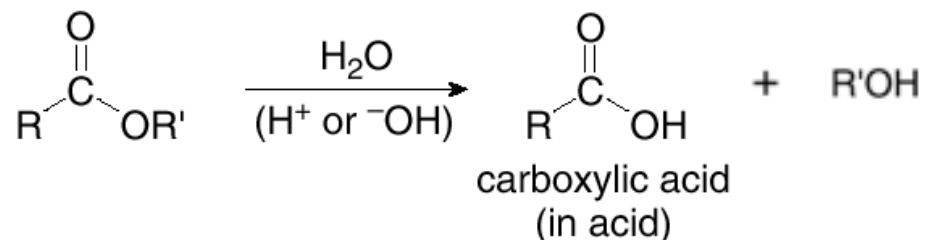
- The reaction is an equilibrium, so it is driven to the right by using excess alcohol or by removing water as it is formed.

Esters: Synthesis



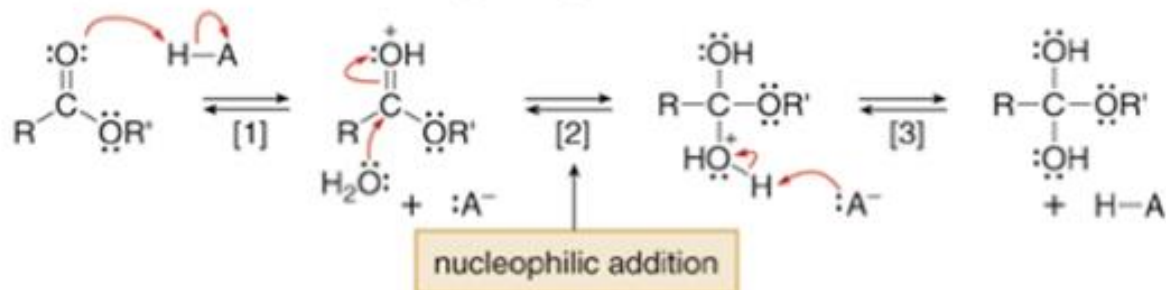
Esters: Reactions

Ester hydrolysis

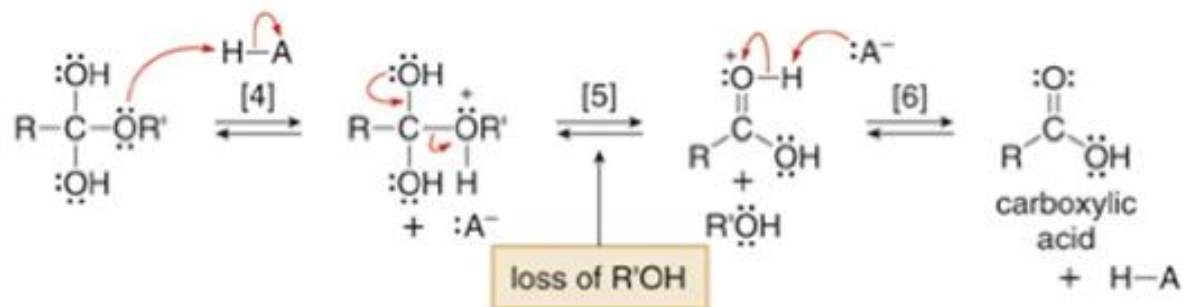


Acid hydrolysis

Part [1] Addition of the nucleophile H₂O

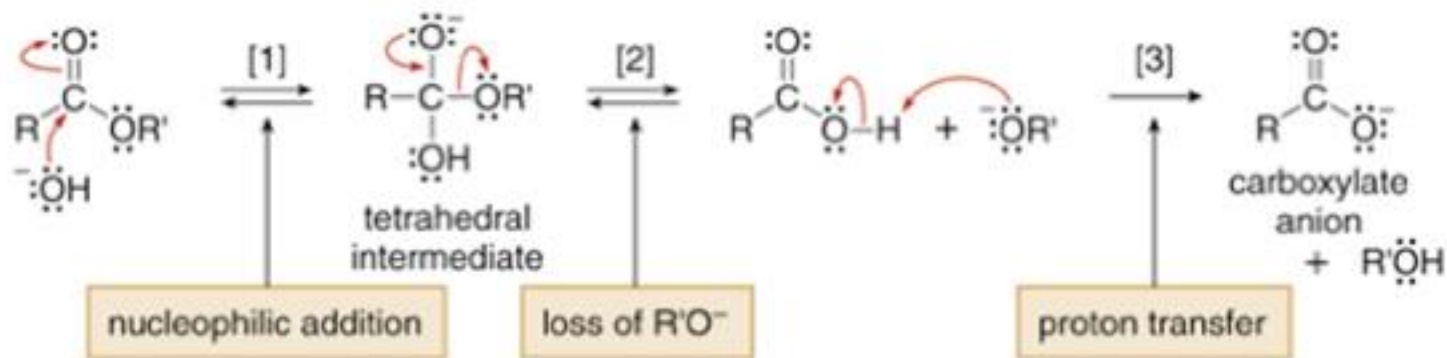


Part [2] Elimination of the leaving group R'OH



Esters: Reactions

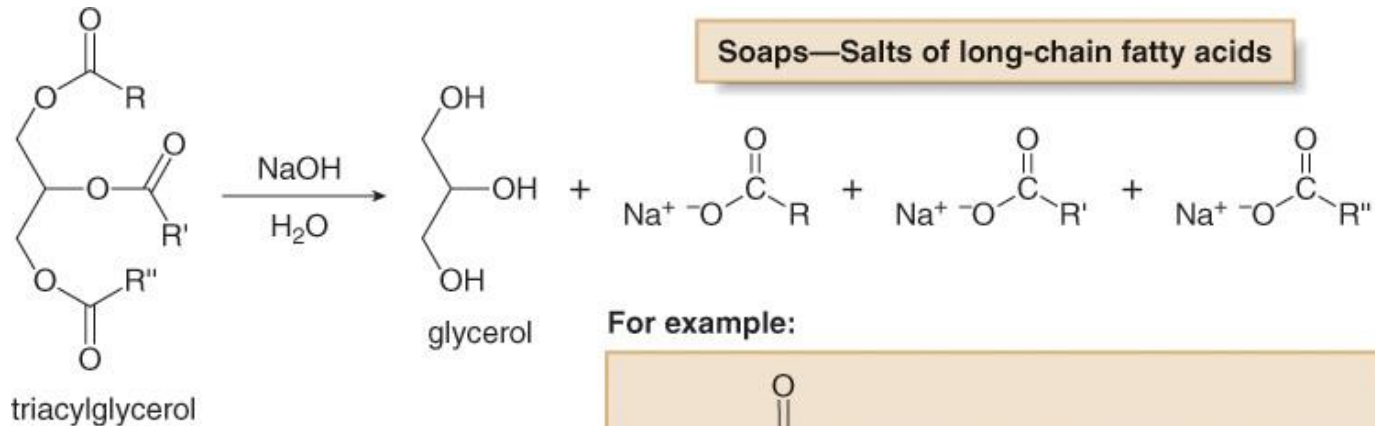
- Basic hydrolysis of an ester is also called saponification.



- Hydrolysis is base promoted, not base catalyzed, because the base (OH^-) is the nucleophile that adds to the ester and forms part of the product. It participates in the reaction and is not regenerated later.

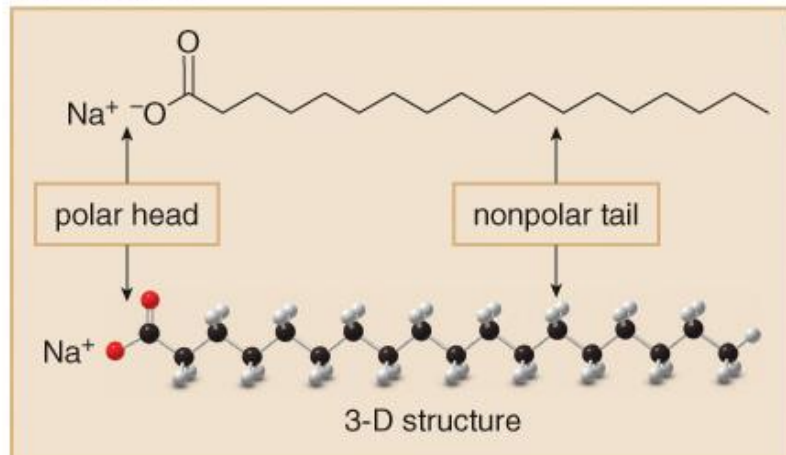
Lipid Hydrolysis

- Soap is prepared by the basic hydrolysis or saponification of a triacylglycerol. Heating an animal fat or vegetable oil with aqueous base hydrolyzes the three esters to form glycerol and sodium salts of three fatty acids. These carboxylate salts are soaps.



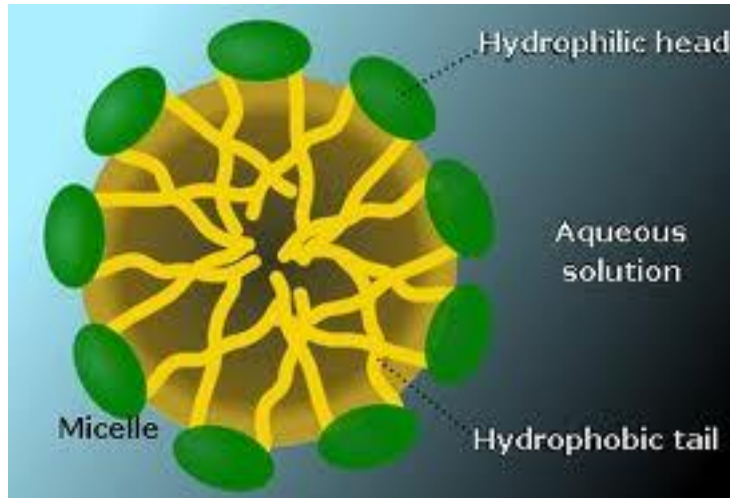
Soaps—Salts of long-chain fatty acids

For example:



Soap

- Soap molecules self-aggregate in water to form micelles



- Synthetic detergents

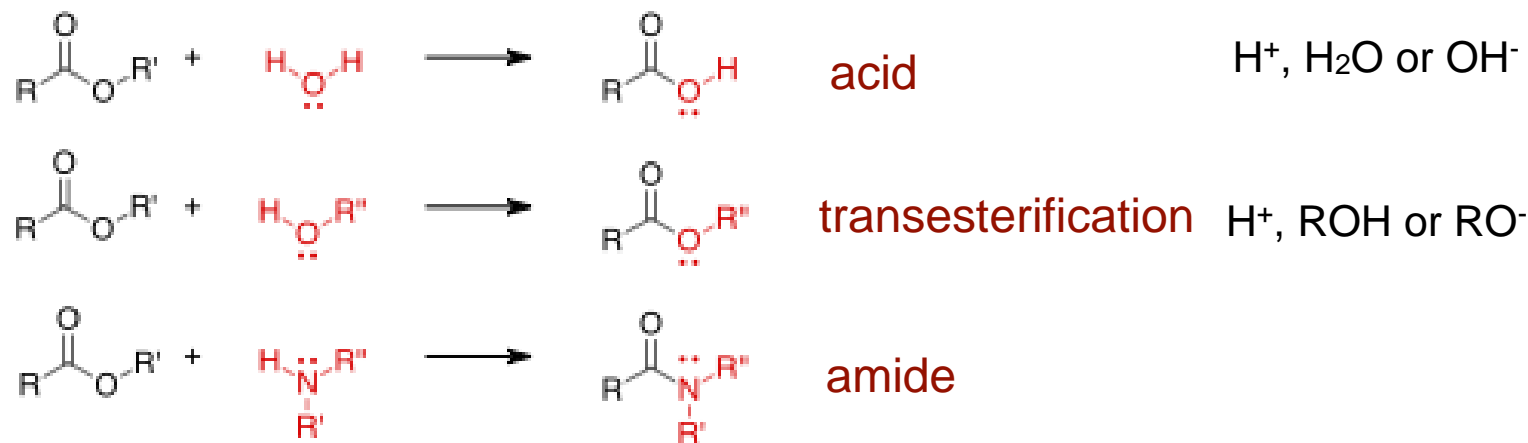


sodium laurylsulfate
SDS

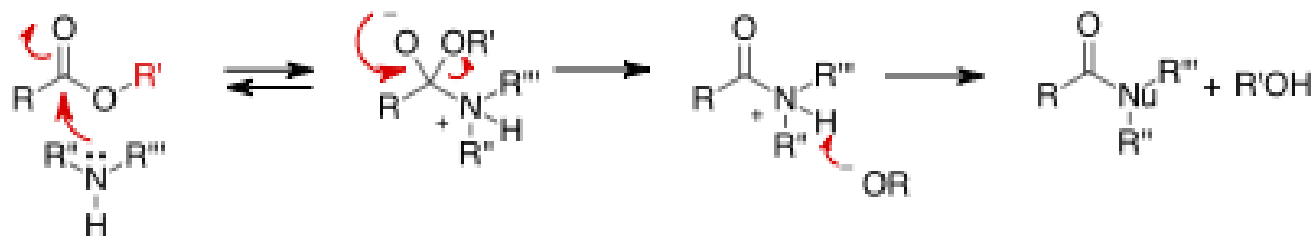


cetyltrimethylammonium
bromide
CTAB

Esters: Other Reactions

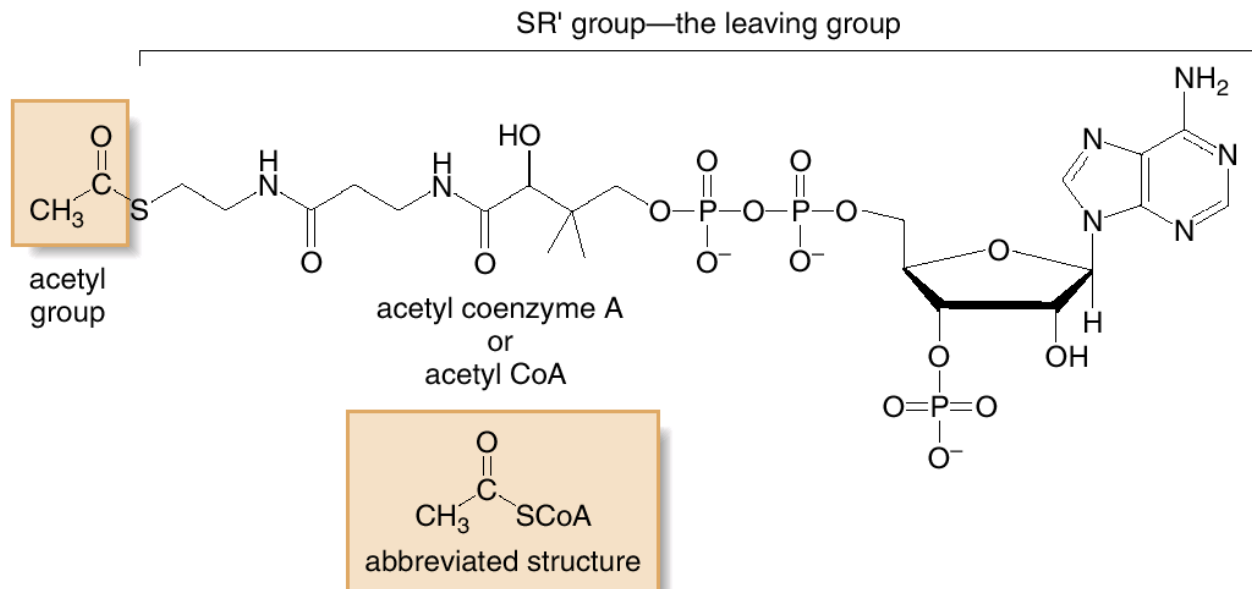


Mechanism of amide formation



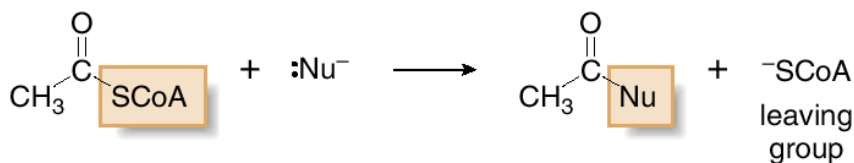
Biological Acylation Reactions

- In cells, acylations occur with the sulfur analogue of an ester (a thioester). The most common ester is **acetyl coenzyme A (acetyl CoA)**.



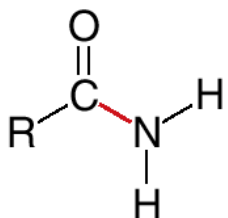
- A thioester (RCOSR') has a good leaving group ($^-SR'$), so, like other acyl compounds, it undergoes substitution reactions with other nucleophiles.

An acyl transfer reaction of a thioester

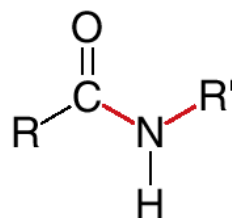


The acetyl group is transferred from SCoA to Nu.

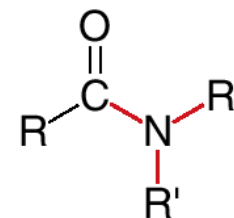
Amides: Structure



1° amide
1 C—N bond

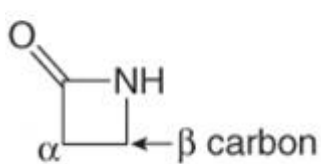


2° amide
2 C—N bonds

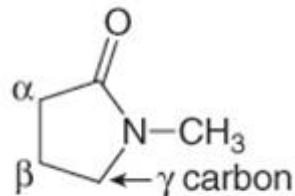


3° amide
3 C—N bonds

Lactams—Cyclic amides



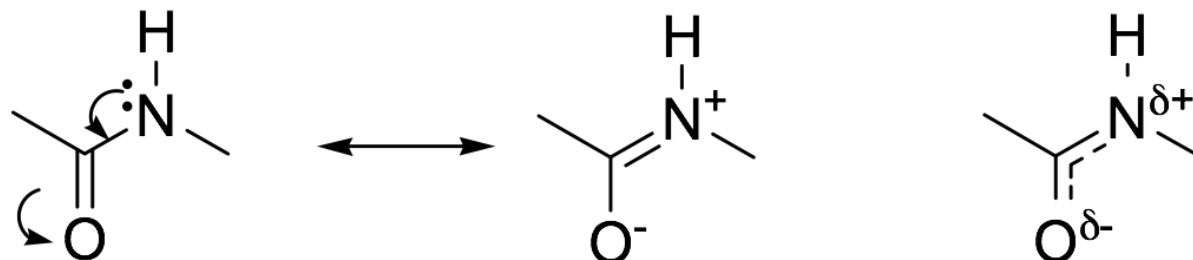
β-lactam



γ-lactam

Amides: Structure

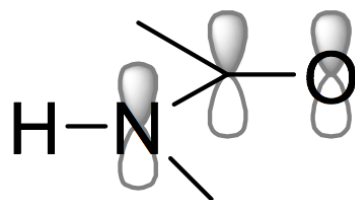
Amide resonance



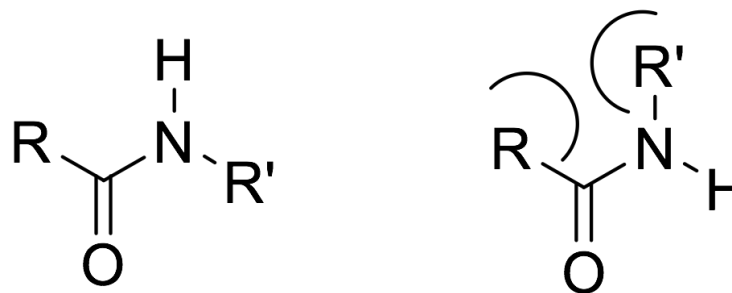
C, N, O: sp²

planar

Restricted rotation



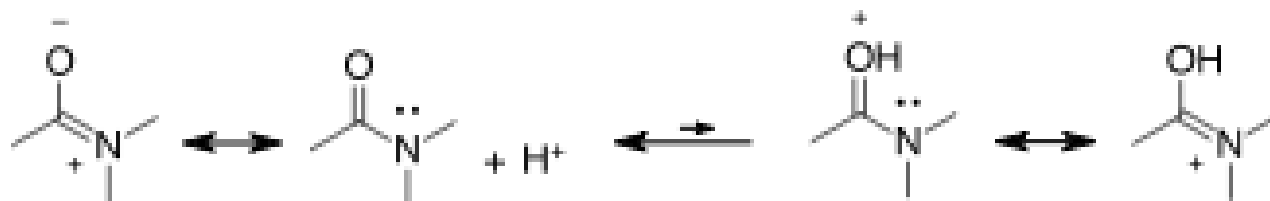
Trans amides are more stable than cis amides



Amides: Basicity



$pK_a = 9$

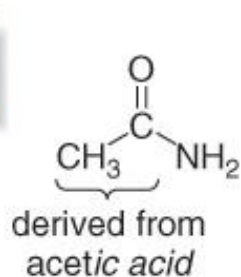


$pK_a = -1$

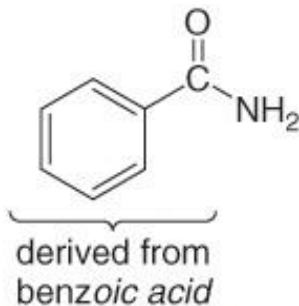
Amides: Nomenclature

- All 1° amides are named by replacing the *-ic acid*, *-oic acid*, or *-ylic acid* ending with the suffix amide.

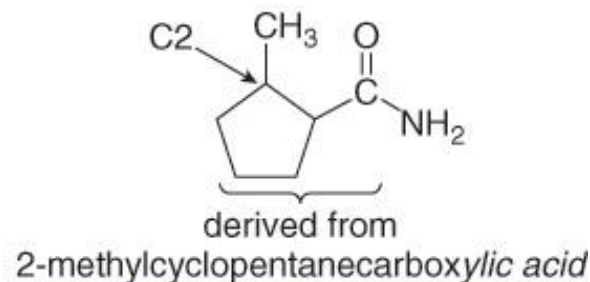
Naming 1° amides



acetamide

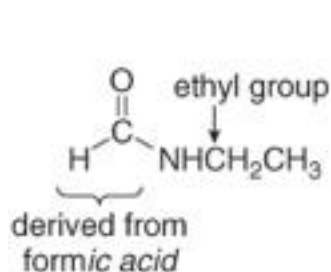


benzamide

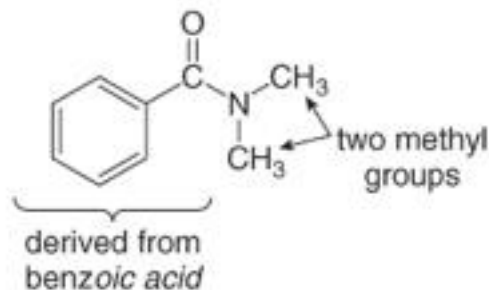


2-methylcyclopentanecarboxamide

- 2° and 3° amides are named as N-substituted (2°) or N,N-disubstituted (3°) derivatives of 1° amides



N-ethylformamide

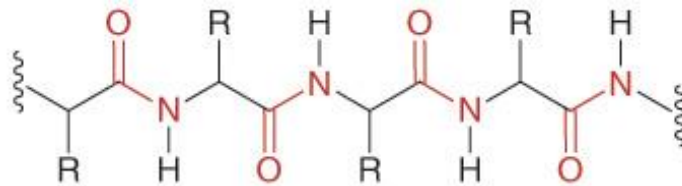


N,N-dimethylbenzamide

Interesting Amides

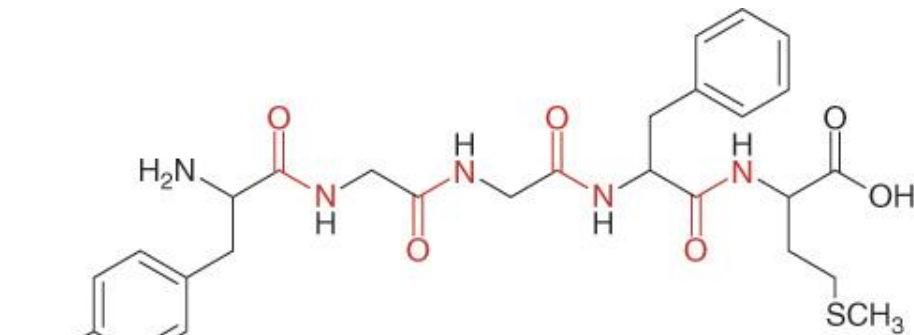
An important group of naturally occurring amides consists of proteins, polymers of amino acids joined together by amide linkages.

Portion of a protein molecule



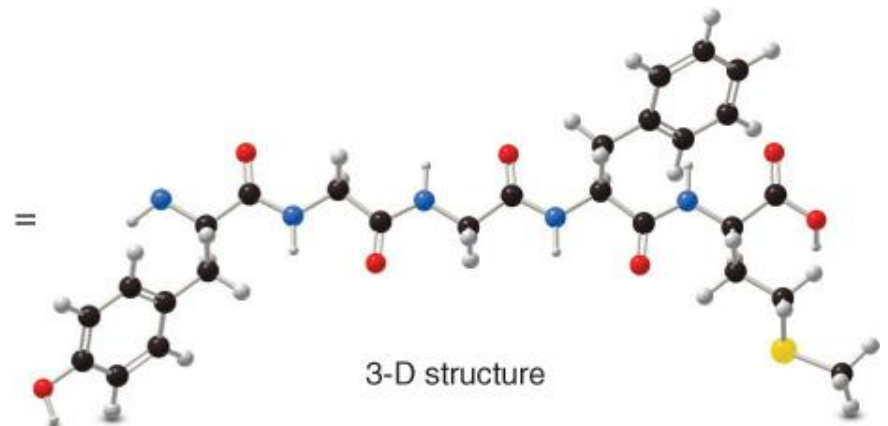
[Amide bonds are shown in red.]

The R groups come from amino acids joined together to form the protein.



met-enkephalin

[The four amide bonds are shown in red.]



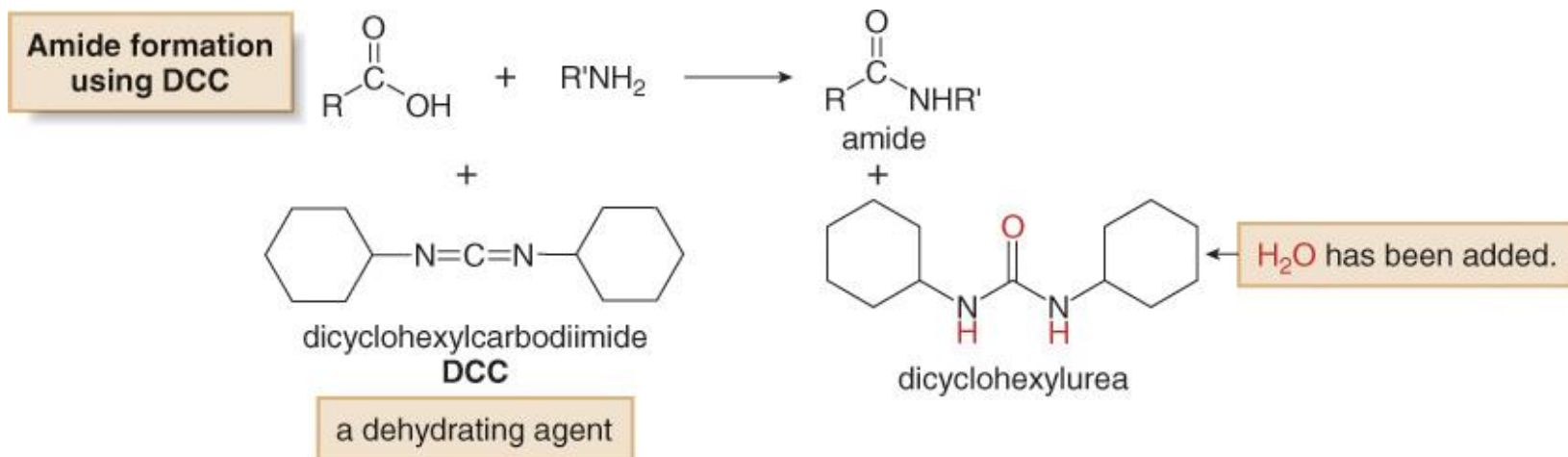
3-D structure

Amides from Carboxylic Acids

- Carboxylic acids cannot be converted into amides by reaction with NH_3 or an amine.

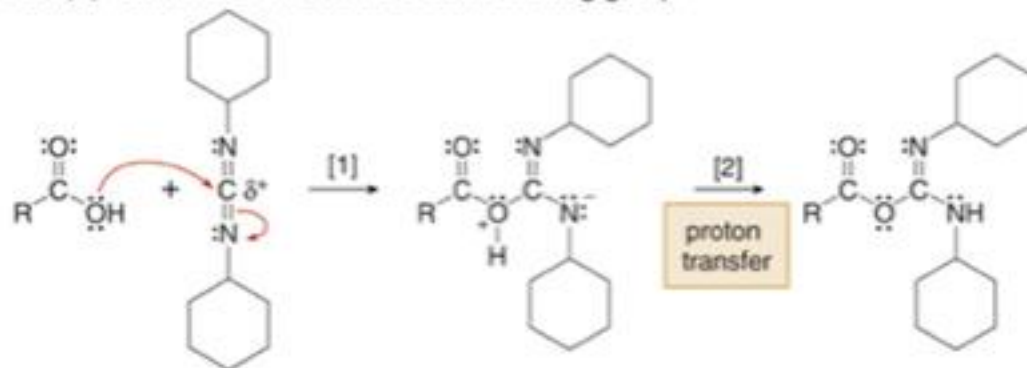


- Carboxylic acids are converted into amides by reaction with NH_3 or an amine in the presence of a condensing agent (DCC).

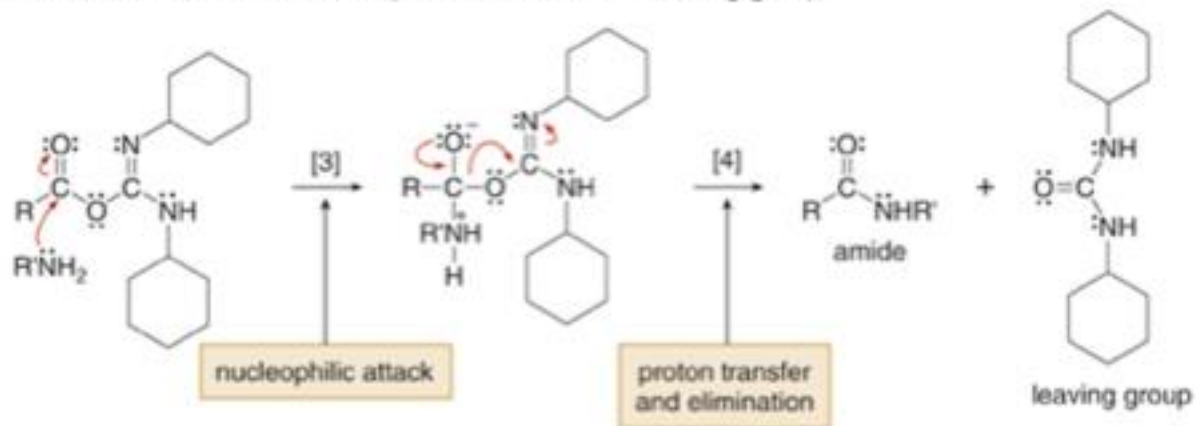


Reactions of Carboxylic Acids: Amides

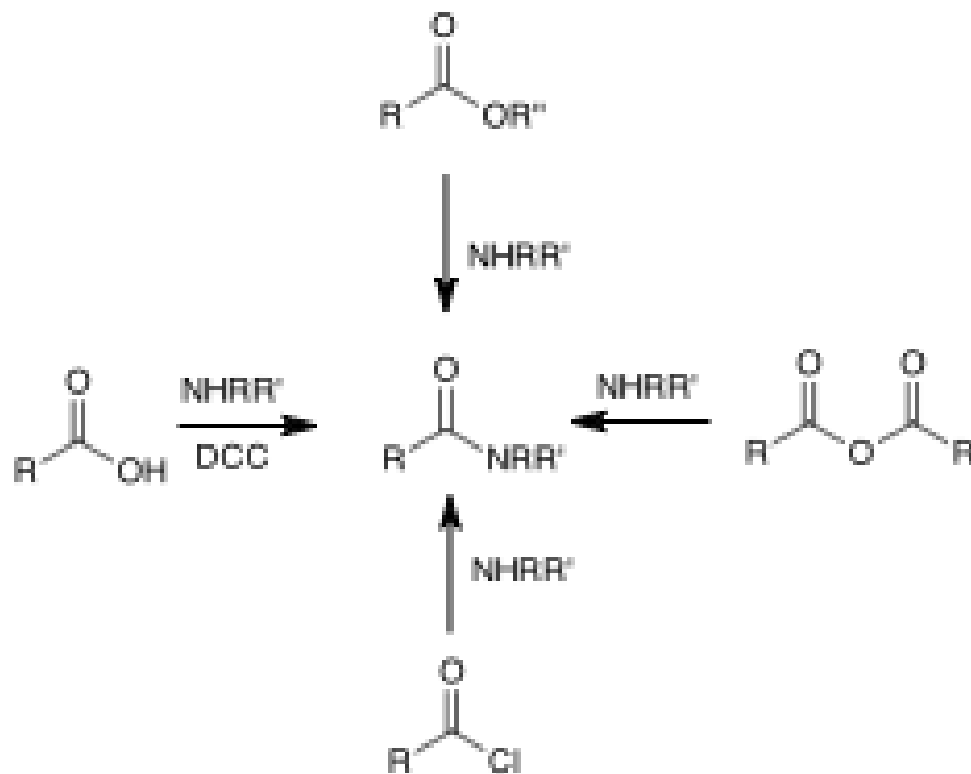
Part [1] Conversion of OH into a better leaving group



Part [2] Addition of the nucleophile and loss of the leaving group



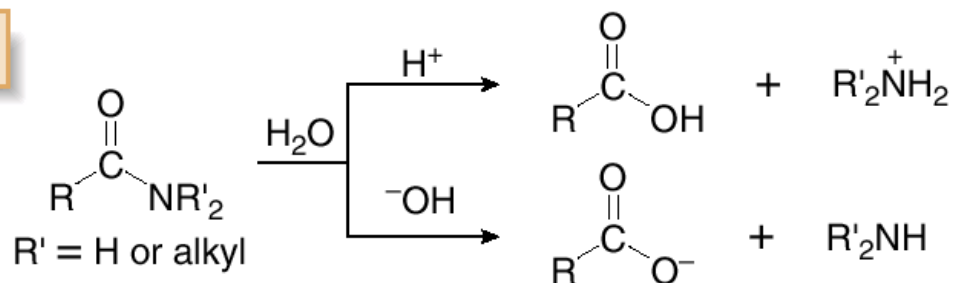
Synthesis of Amides



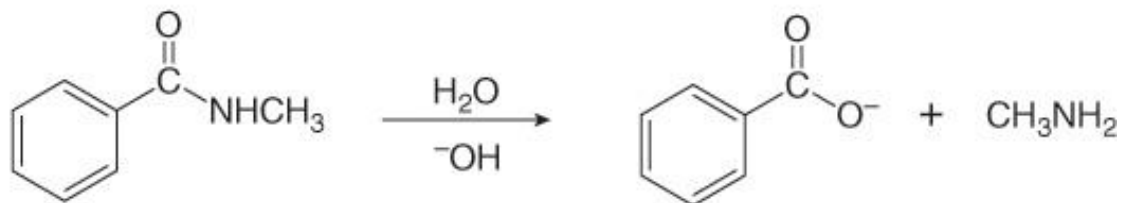
Amides: Reactions

- Amides are the least reactive of the carboxylic acid derivatives.

Amide hydrolysis

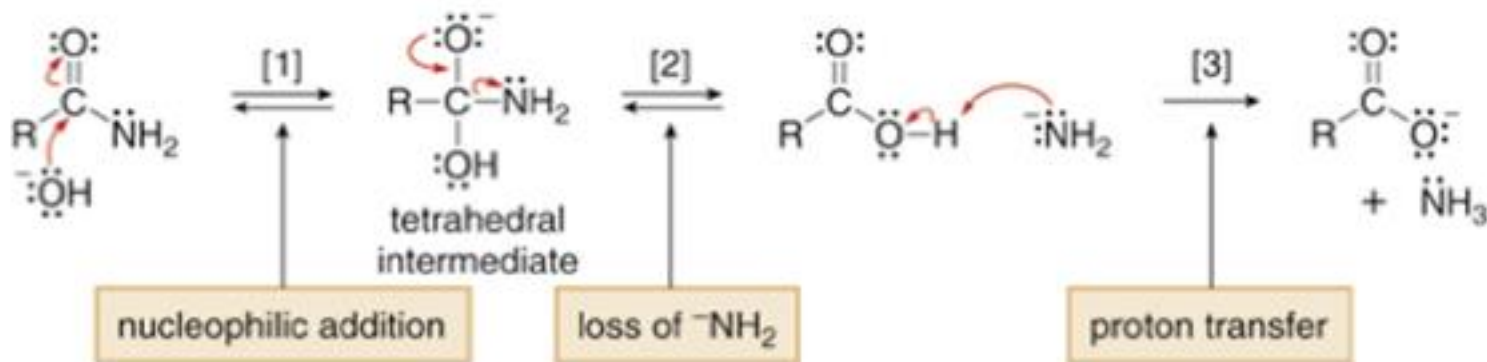
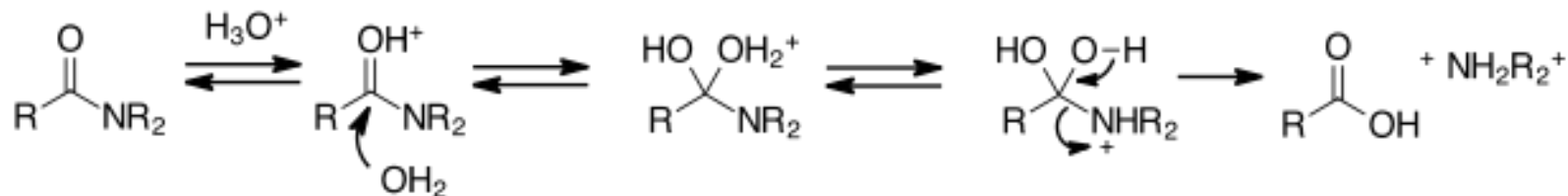


Examples



Amides: Reactions

- The mechanism of amide hydrolysis is exactly the same as the mechanism of ester hydrolysis.



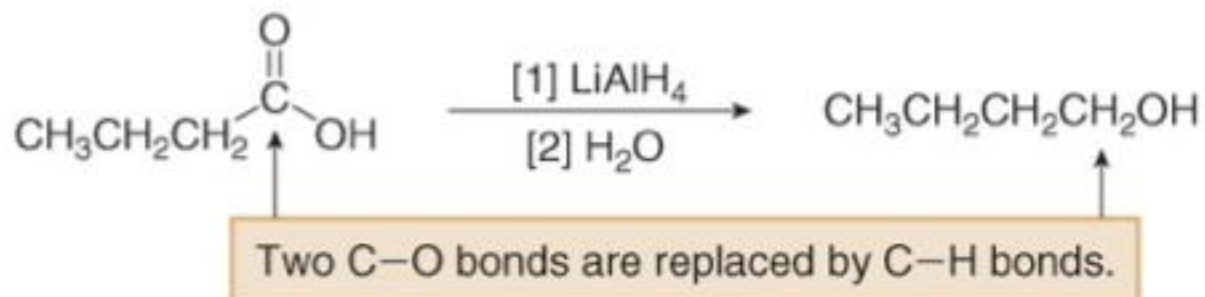
Amide hydrolysis is hard in acid because the nucleophile (H_2O) and the electrophile (amide) are poor.

Amide hydrolysis is hard in base because the electrophile and the leaving group (NR_2^-) are poor.

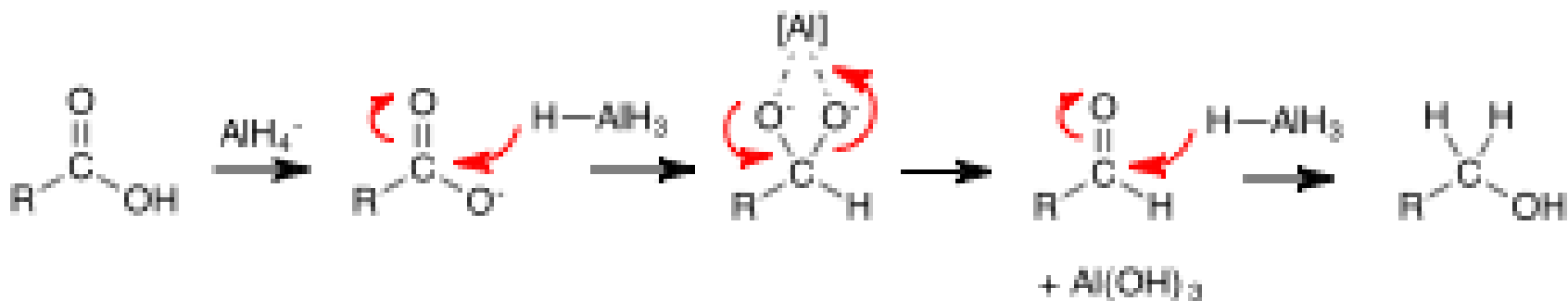
Reduction of Carboxylic Acids

Carboxylic acids are reduced to 1° alcohols with LiAlH_4 .

Example



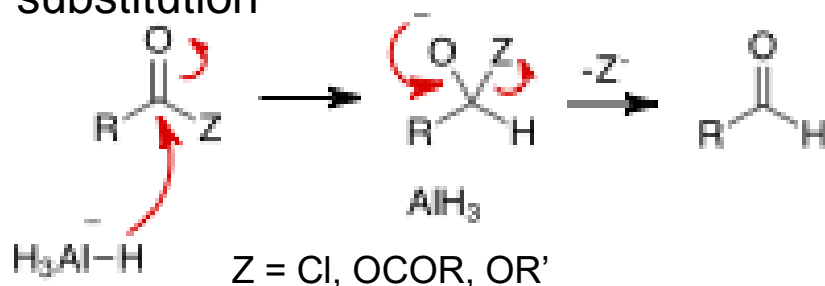
Mechanism:



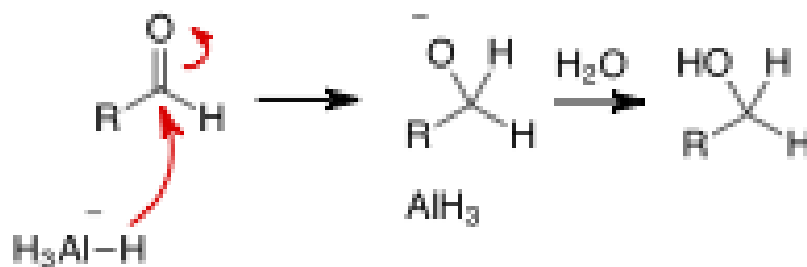
Reduction: acid chlorides, anhydrides and esters

- Acid chlorides, anhydrides and esters are reduced to 1^{ry} alcohols by Al hydrides, e.g. LiAlH₄
- A two-step reaction:

1. Nucleophilic acyl substitution

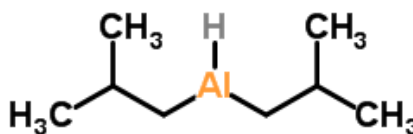


2. Nucleophilic addition



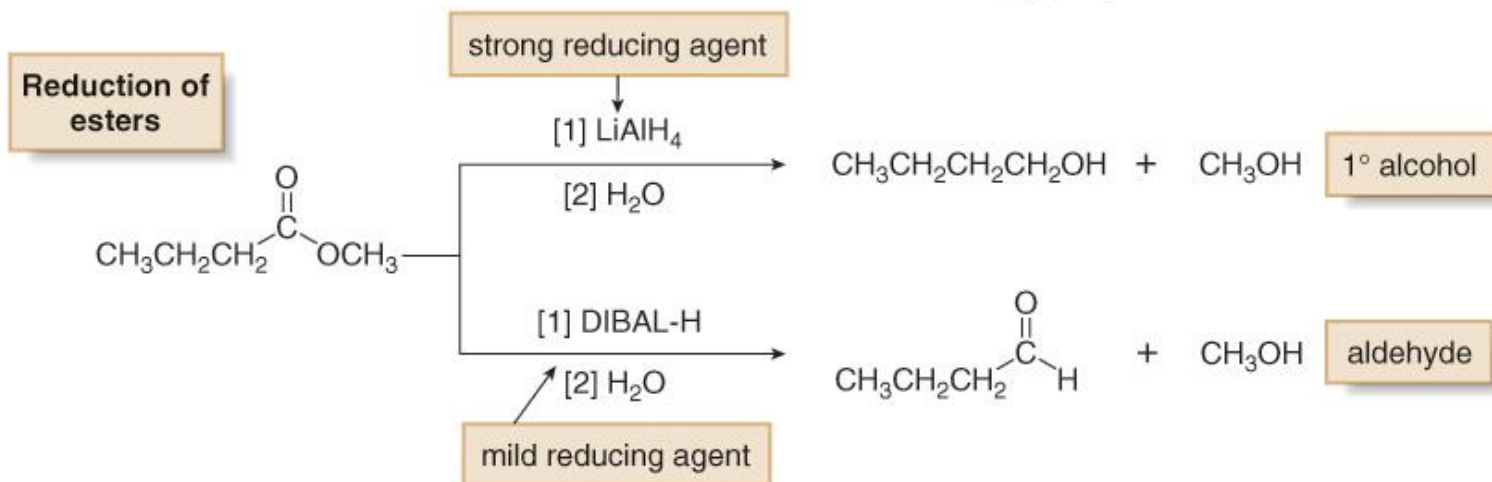
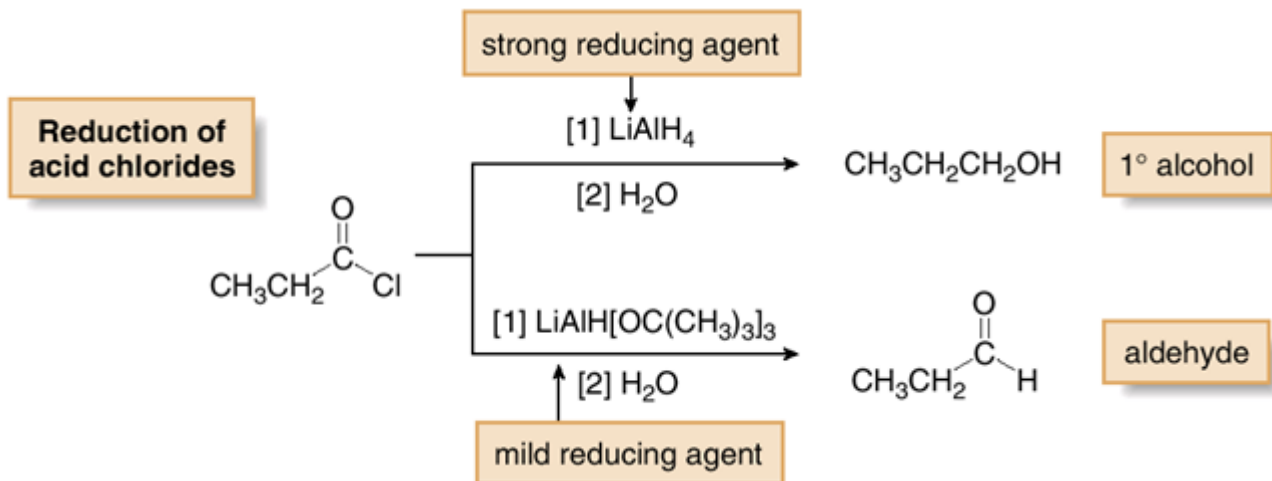
Reduction of acid chlorides, anhydrides and esters

- LiAlH_4 is a strong reducing agent that reduces acids, acid chlorides, anhydrides and esters to primary alcohols.
- Diisobutylaluminum hydride ($[(\text{CH}_3)_2\text{CHCH}_2]_2\text{AlH}$, abbreviated DIBAL-H, has two bulky isobutyl groups which makes this reagent less reactive than LiAlH_4 .
- DIBAL-H reduces acid chlorides, anhydrides and esters **to aldehydes**.

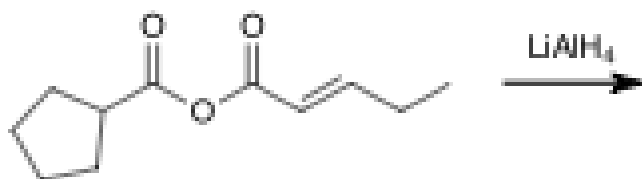
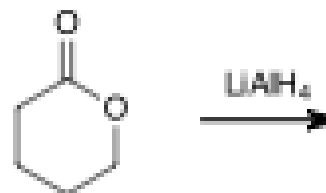
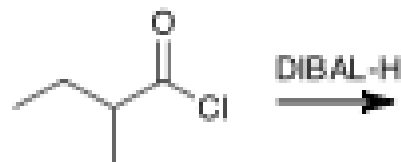


DIBAL-H

Reduction of acid chlorides, anhydrides and esters



Reduction of acid chlorides, anhydrides and esters

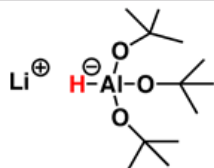


Reduction of Carboxylic Acids and Their Derivatives

Table 20.1

A Summary of Metal Hydride Reducing Agents

	Reagent	Starting material	→	Product
strong reagent	LiAlH ₄	RCHO	→	RCH ₂ OH
		R ₂ CO	→	R ₂ CHOH
		RCOOH	→	RCH ₂ OH
		RCOOR'	→	RCH ₂ OH
		RCOCl	→	RCH ₂ OH
milder reagents	NaBH ₄	RCHO	→	RCH ₂ OH
		R ₂ CO	→	R ₂ CHOH
	LiAlH[OC(CH ₃) ₃] ₃	RCOCl	→	RCHO
	DIBAL-H	RCOOR'	→	RCHO

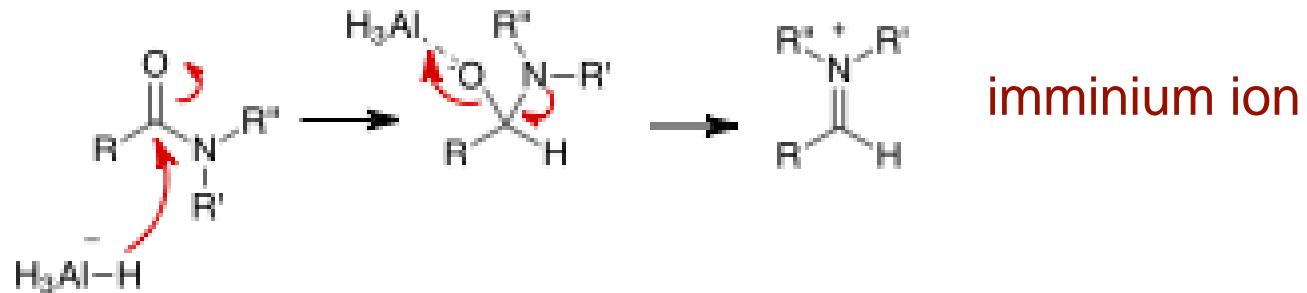


Lithium tri-*t*-butoxy aluminum hydride

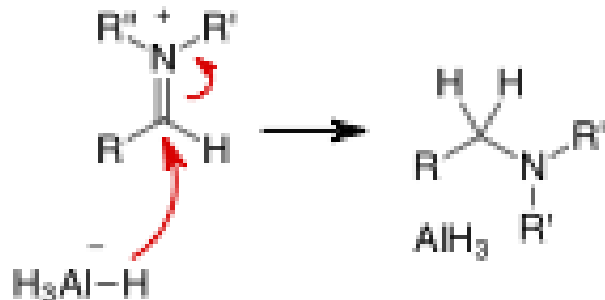
Reduction of Amides

- Amides are reduced to amines by Al hydrides, e.g. LiAlH_4
- A two-step reaction:

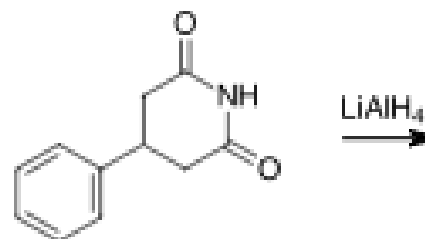
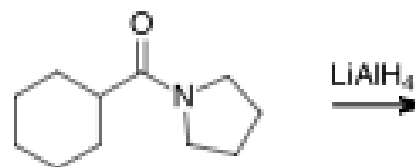
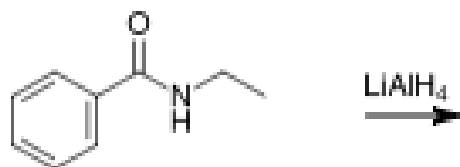
1. Nucleophilic addition-elimination



2. Nucleophilic addition



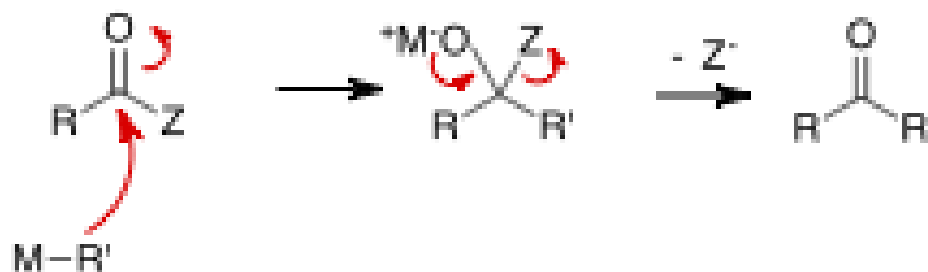
Reduction of Amides



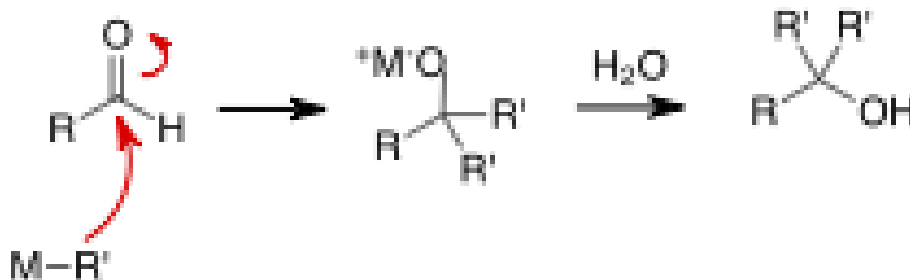
Reaction of Organometallic Reagents with Carboxylic Acid Derivatives.

- Both esters and acid chlorides form 3° alcohols when treated with two equivalents of either Grignard or organolithium reagents.
- A two-step reaction:

1. Nucleophilic acyl substitution



2. Nucleophilic addition

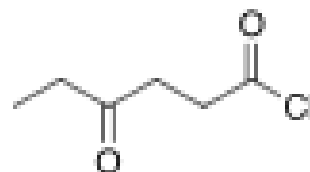
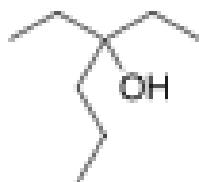
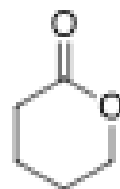
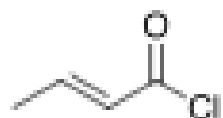
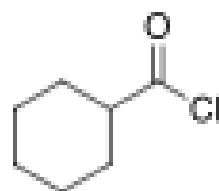
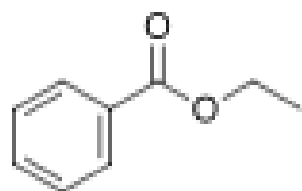


Reaction of Organometallic Reagents with Carboxylic Acid Derivatives.

- Organocuprates (R'_2CuLi) are less reactive than organolithium and organomagnesium compounds.
- R'_2CuLi react only with acid chlorides, which are the more reactive among carboxylic acid derivatives, to give a ketone as the product.
- Esters do not react with R'_2CuLi .

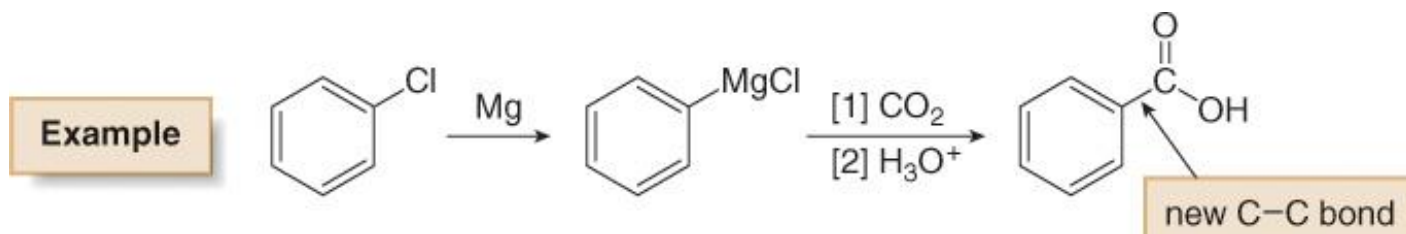
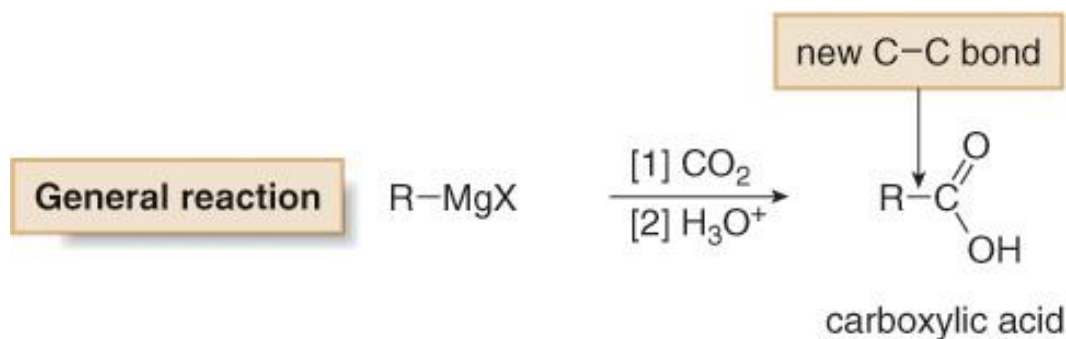


Reaction of Organometallic Reagents with Carboxylic Acid Derivatives.

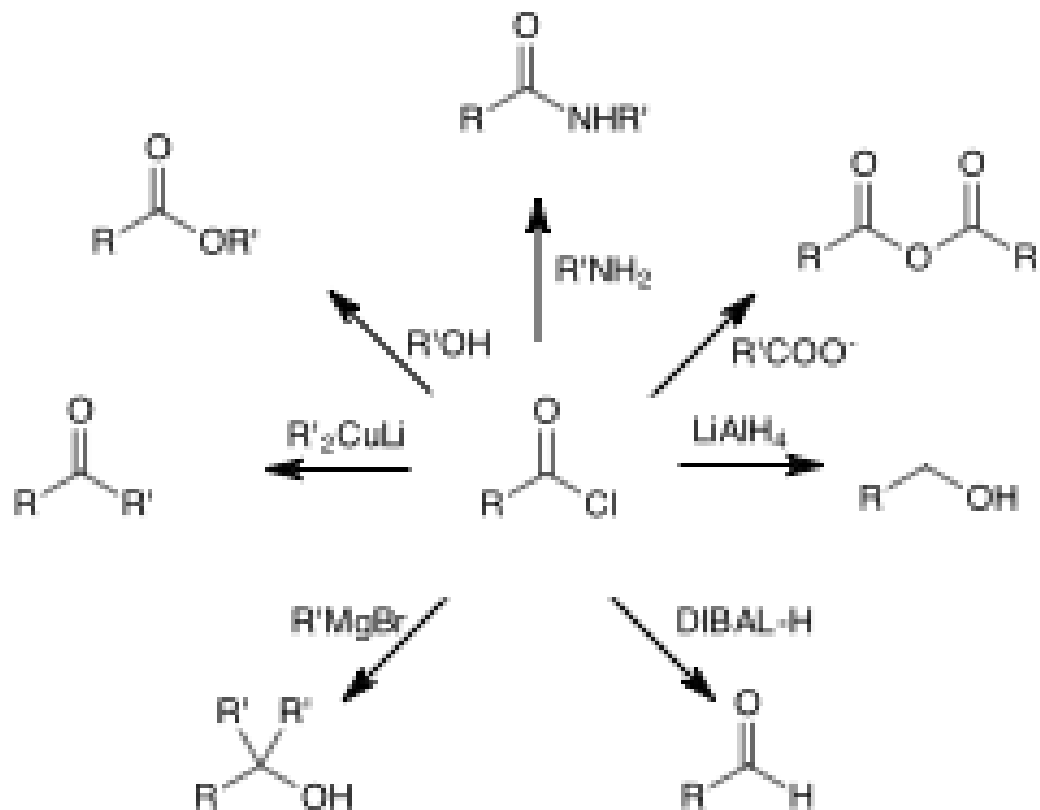


Reaction of Organometallic Reagents with CO₂

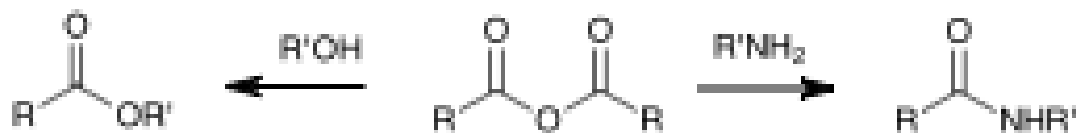
- Grignards react with CO₂ to give carboxylic acids after protonation with aqueous acid.
- This reaction is called carboxylation.
- The carboxylic acid formed has one more carbon atom than the Grignard reagent from which it was prepared.



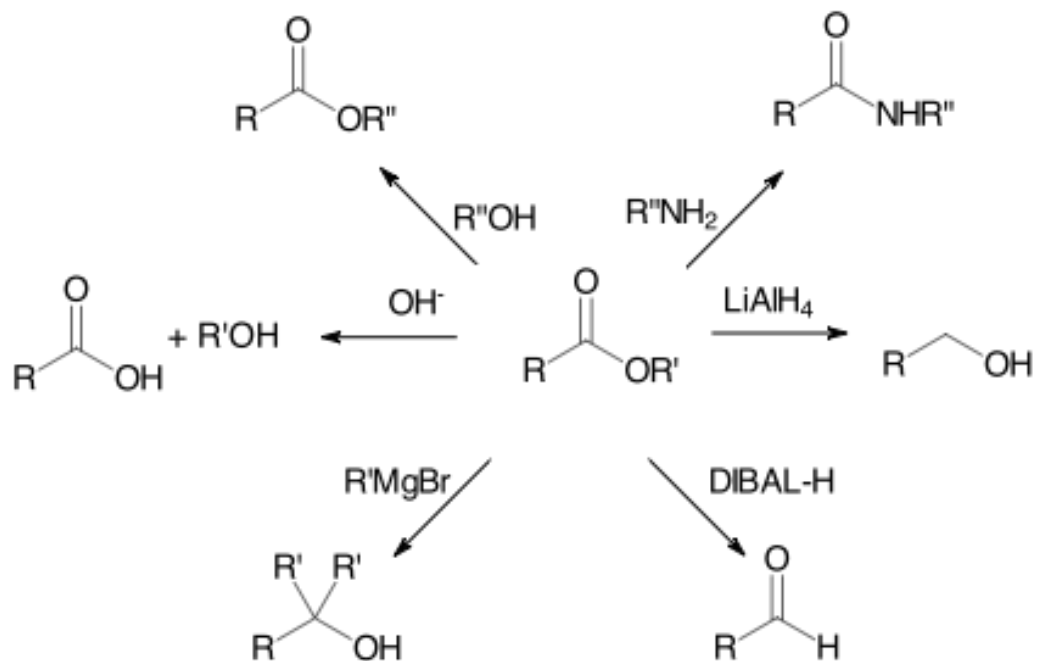
Summary: important reactions of acid chlorides.



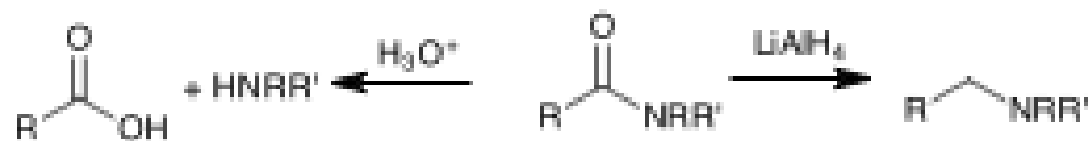
Summary: important reactions of anhydrides.



Summary: important reactions of esters.



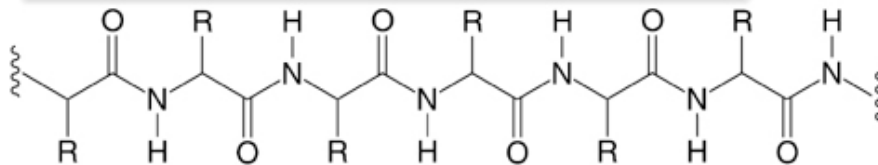
Summary: important reactions of amides.



Natural and Synthetic Fibers

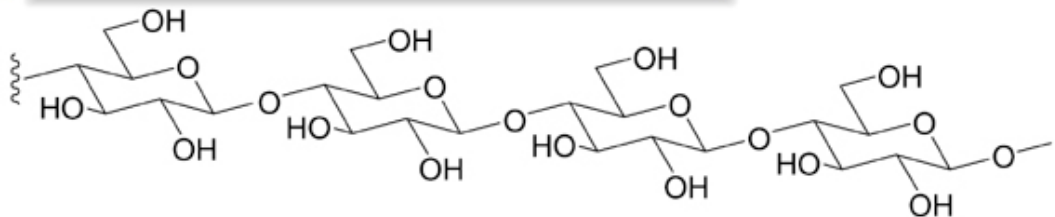
- Fibers like wool and silk are proteins obtained from animals.
- Cotton and linen are derived from carbohydrates having the general structure of cellulose.

Wool and silk—Proteins with many amide bonds



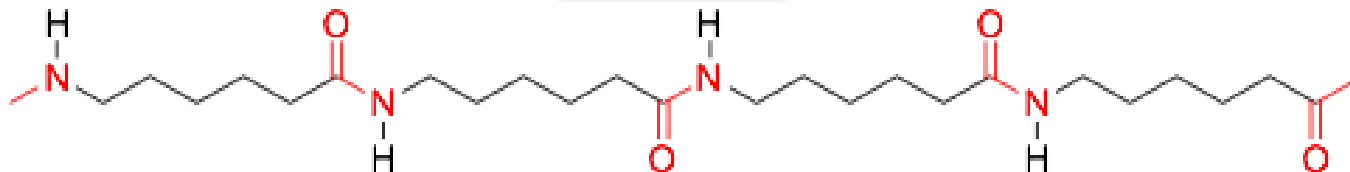
R groups contain C, H, and functional groups like NH_2 , COOH , OH , and SH .

Cotton and linen—Carbohydrates like cellulose



Natural and Synthetic Fibers: Nylon—A Polyamide

Nylon 6

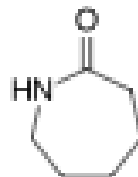


monomers:



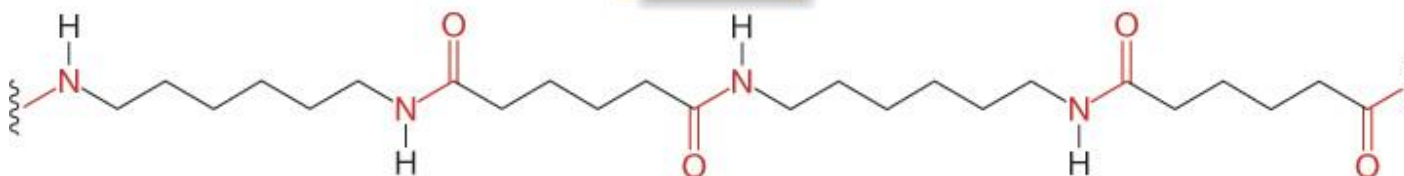
6-aminohexanoic acid

or



γ-caprolactam

Nylon 6,6



[The amide bonds are labeled in red.]

monomers:



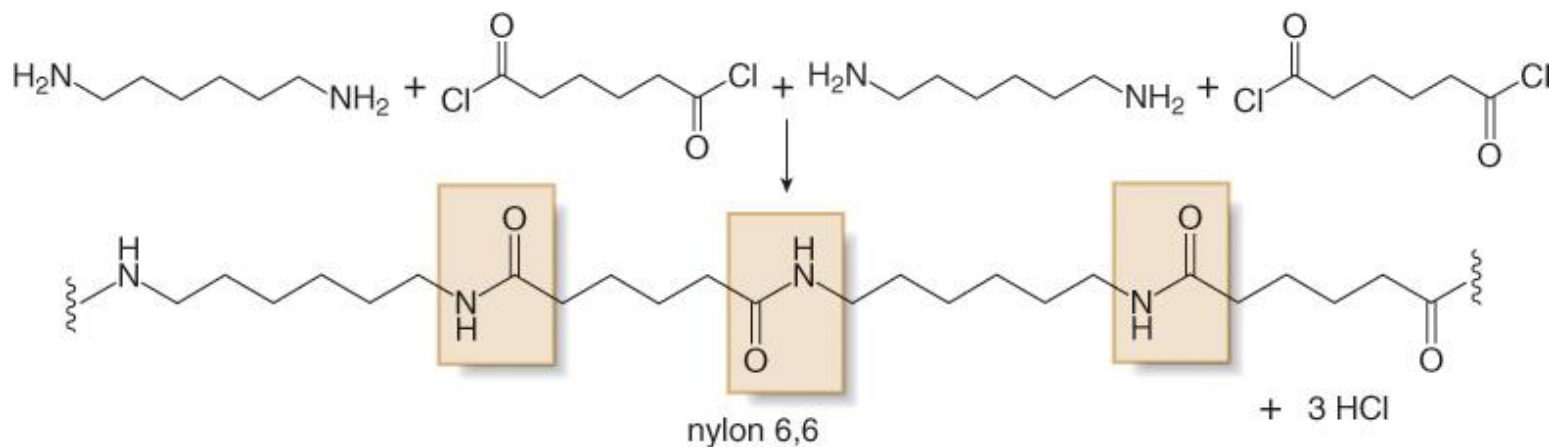
hexamethylenediamine



adipic acid

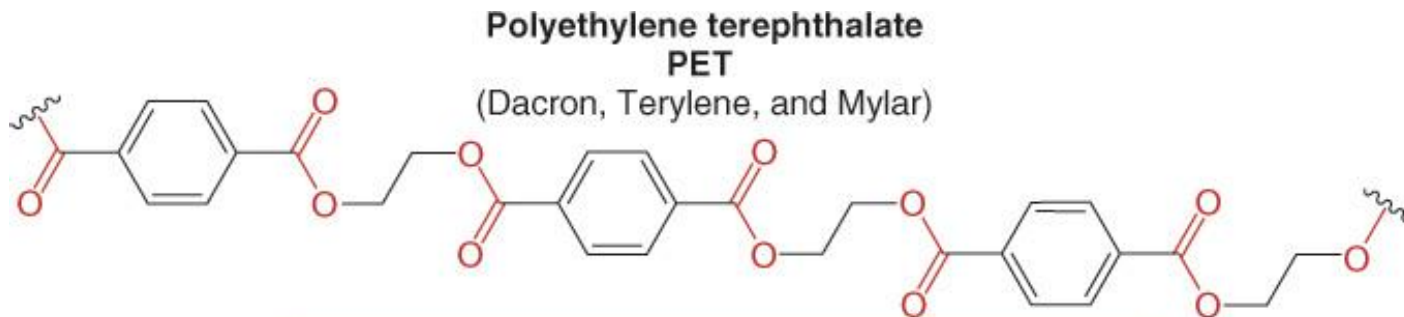
Natural and Synthetic Fibers: Nylon—A Polyamide

- Nylon is a **condensation polymer**



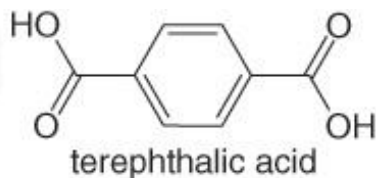
Three new amide bonds are shown.

Natural and Synthetic Fibers: Polyesters

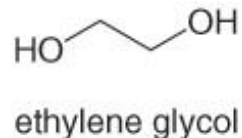


Ester bonds (in red) join the carbon skeleton together.

Synthesis of PET

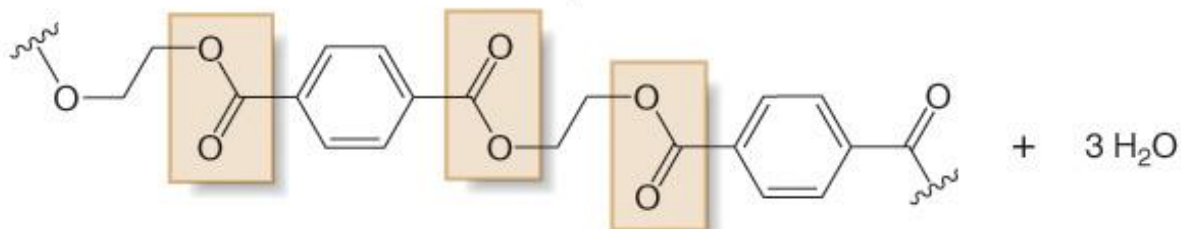


+



two monomers needed
for PET synthesis

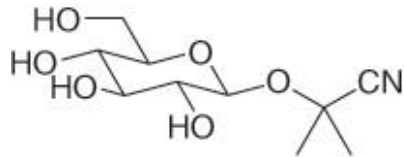
acid catalyst



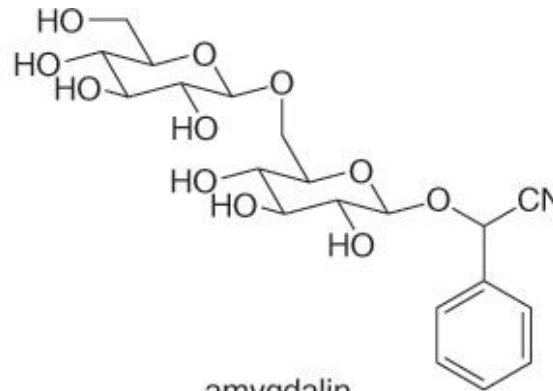
Three new ester bonds are shown.

Nitriles

- Nitriles are not common in nature.
- Cyanohydrins are the most common nitriles.



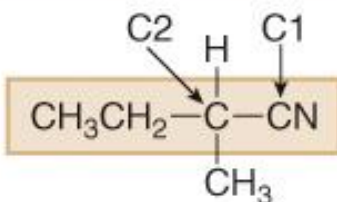
linamarin
(found in cassava root)



amygdalin
(commonly called laetrile)

Nomenclature—Nitriles

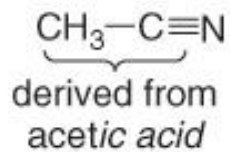
IUPAC name for a nitrile



(4 C's) → **butane** + **nitrile**

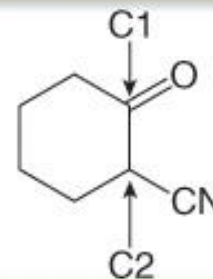
2-methylbutanenitrile

Common name for a nitrile



acetonitrile

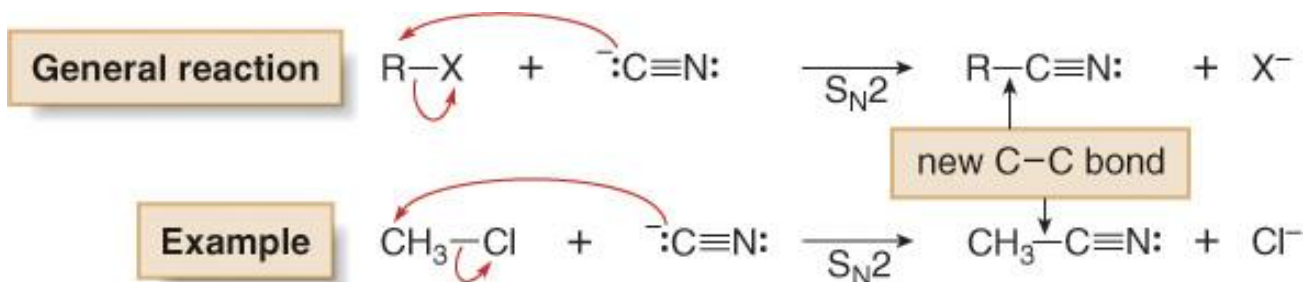
CN as a substituent



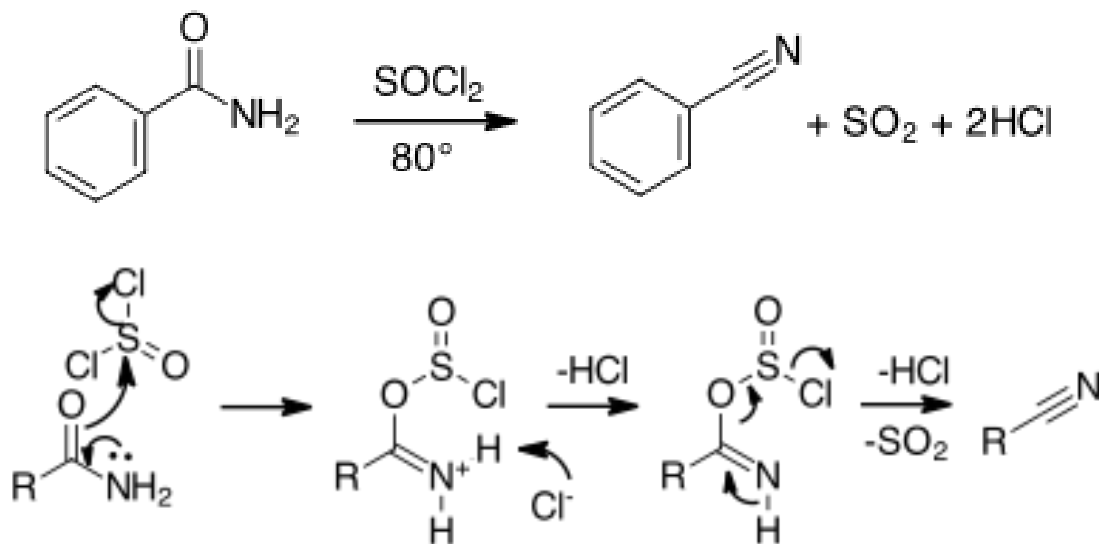
2-cyanocyclohexanone

Nitriles

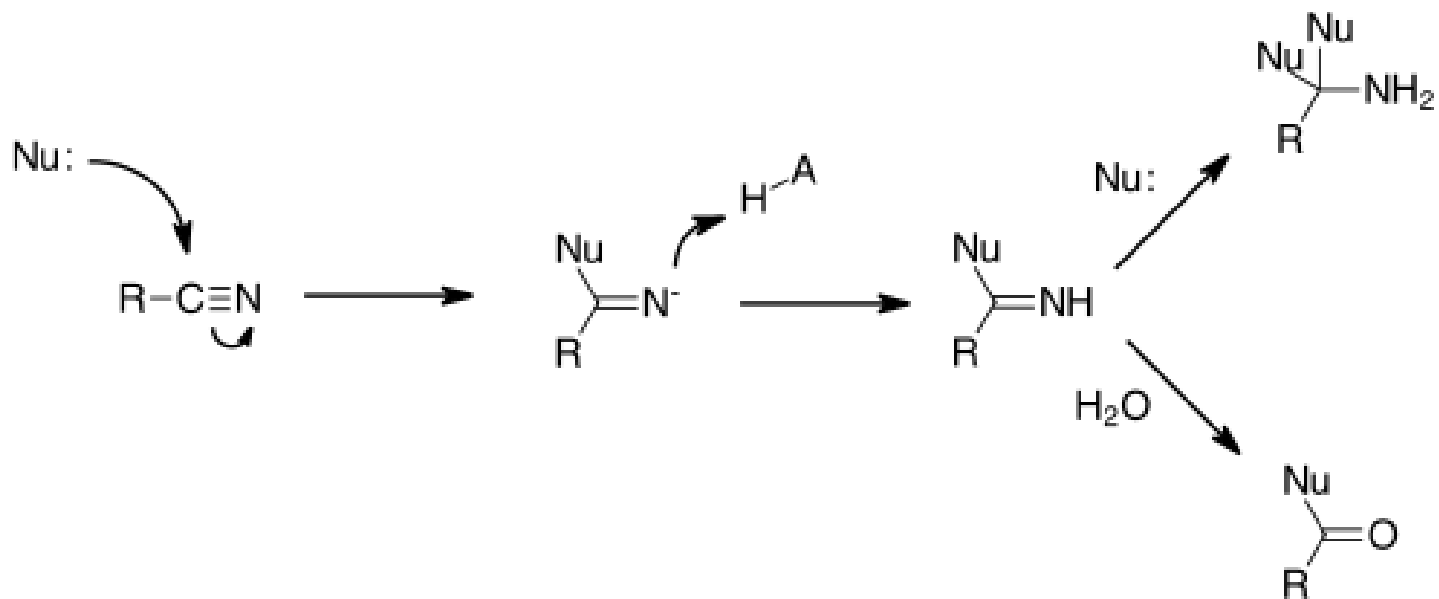
- Nitriles are prepared by S_N2 reactions of unhindered methyl and 1° alkyl halides with ^-CN .



- Nitriles are prepared by dehydration of amides (more general).



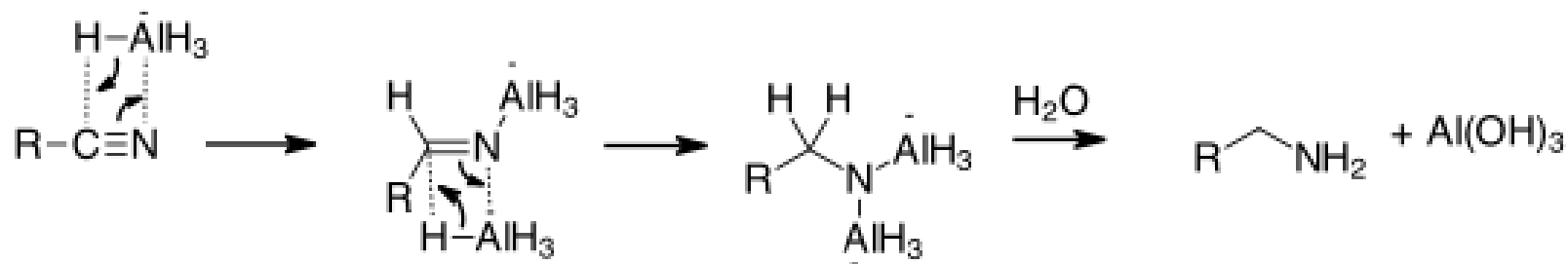
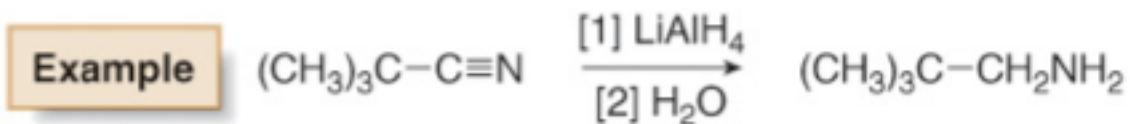
Reactions of Nitriles – Nucleophilic Addition to the CN Group



$Nu: = H^- ([Al]-H); R^- (R-[M]); H_2O$

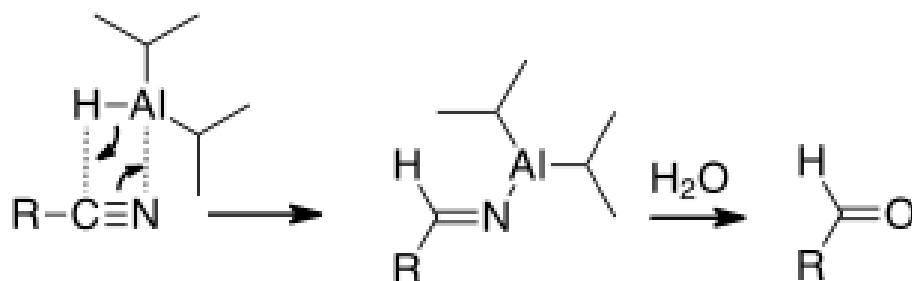
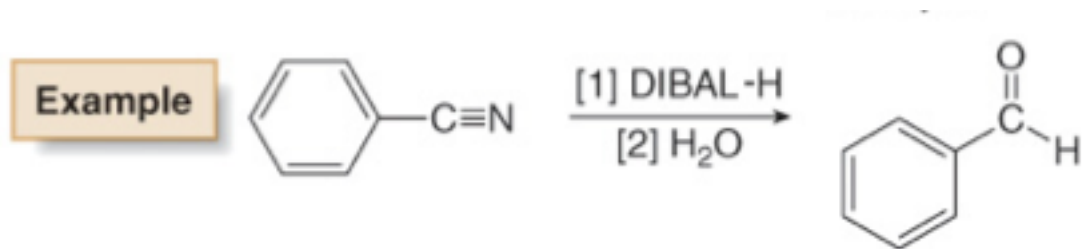
Reactions of Nitriles—Reduction

LiAlH_4 (more reactive)



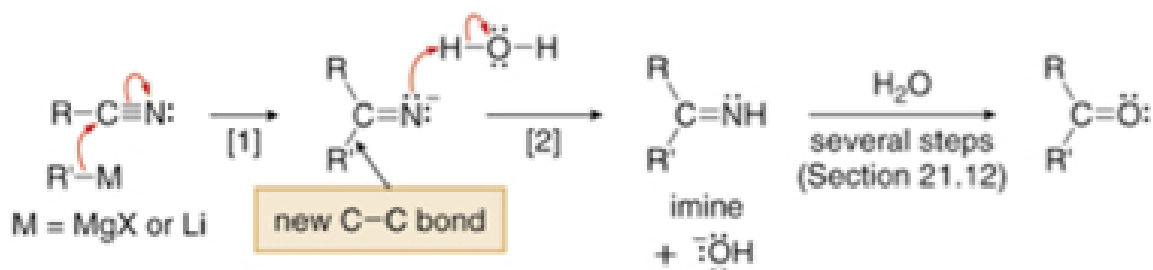
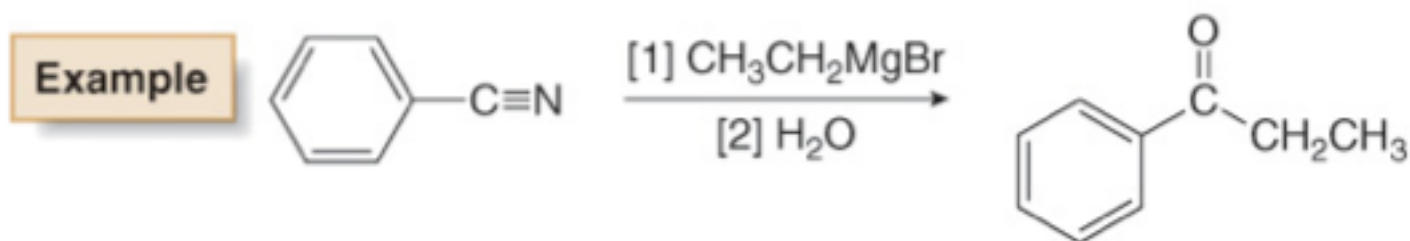
Reactions of Nitriles—Reduction

DIBAL-H (less reactive)



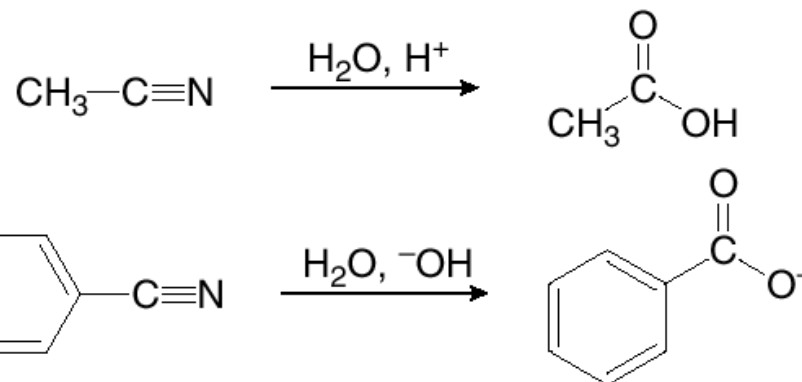
Addition of Organometallic reagents

- Both Grignard and organolithium reagents react with nitriles to form ketones with a new C—C bond.



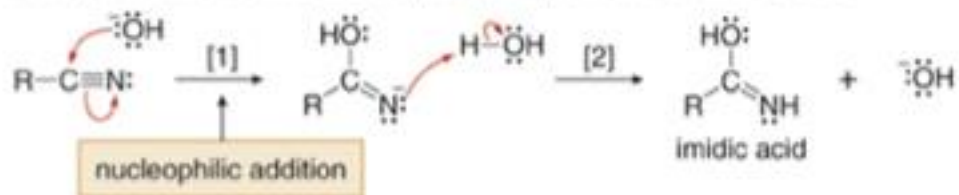
Reactions of Nitriles—Hydrolysis

Examples



Reactions of Nitriles—Hydrolysis

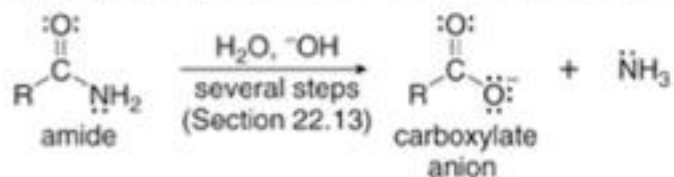
Part [1] Addition of the nucleophile (OH^-) to form an imidic acid



Part [2] Tautomerization of the imidic acid to an amide



Part [3] Hydrolysis of the 1° amide to a carboxylate anion



Summary: important reactions of nitriles.

