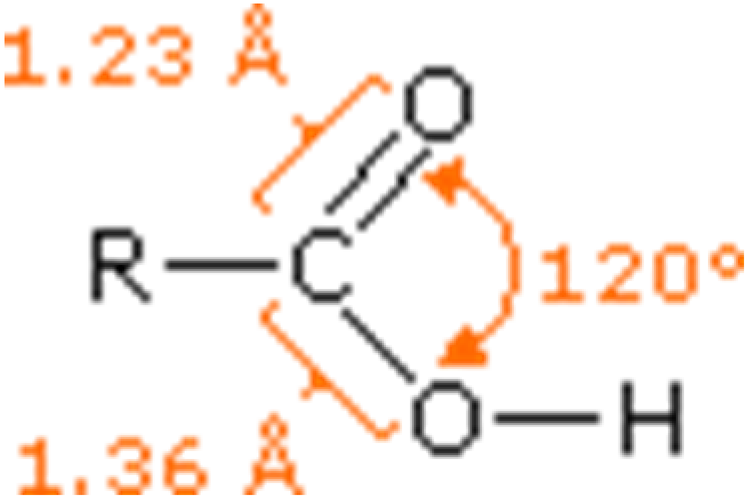
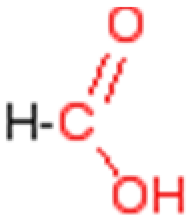
Carboxylic Acids

STRUCTURE

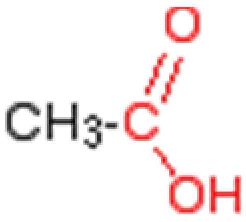


Nomenclature of Carboxylic Acids



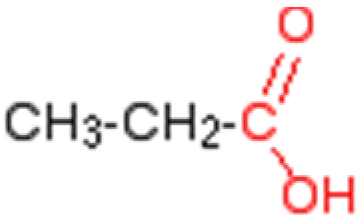
$\mathrm{H{-}C(=O){-}OH}$

methanoic acid



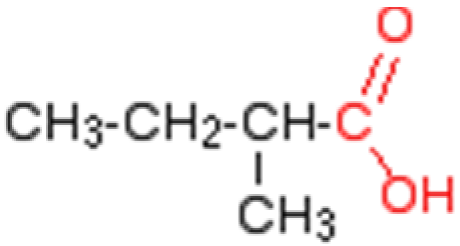
$\mathrm{CH_3{-}C(=O){-}OH}$

ethanoic acid



$\mathrm{CH_3{-}CH_2{-}C(=O){-}OH}$

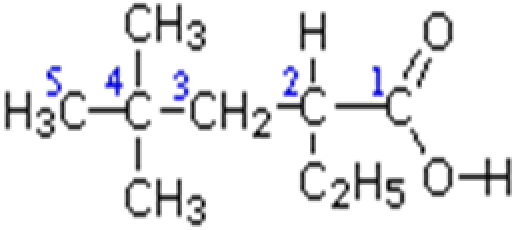
propanoic acid



$\mathrm{CH_3{-}CH_2{-}CH(CH_3){-}C(=O){-}OH}$

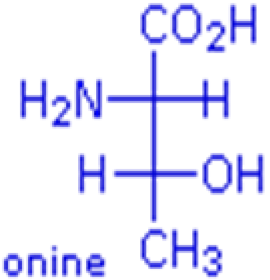
2-methylbutanoic acid

Formula	Common Name	Source	IUPAC Name	Melting Point	Boiling Point
HCO_2H	formic acid	ants (L. formica)	methanoic acid	8.4 ºC	101 ºC
CH_3CO_2H	acetic acid	vinegar (L. acetum)	ethanoic acid	16.6 ºC	118 ºC
$CH_3CH_2CO_2H$	propionic acid	milk (Gk. protus prion)	propanoic acid	-20.8 ºC	141 ºC
$CH_3(CH_2)_2CO_2H$	butyric acid	butter (L. butyrum)	butanoic acid	-5.5 ºC	164 ºC
$CH_3(CH_2)_3CO_2H$	valeric acid	valerian root	pentanoic acid	-34.5 ºC	186 ºC
$CH_3(CH_2)_4CO_2H$	caproic acid	goats (L. caper)	hexanoic acid	-4.0 ºC	205 ºC
$CH_3(CH_2)_5CO_2H$	enanthic acid	vines (Gk. oenanthe)	heptanoic acid	-7.5 ºC	223 ºC
$CH_3(CH_2)_6CO_2H$	caprylic acid	goats (L. caper)	octanoic acid	16.3 ºC	239 ºC
$CH_3(CH_2)_7CO_2H$	pelargonic acid	pelargonium (an herb)	nonanoic acid	12.0 ºC	253 ºC
$CH_3(CH_2)_8CO_2H$	capric acid	goats (L. caper)	decanoic acid	31.0 ºC	219 ºC



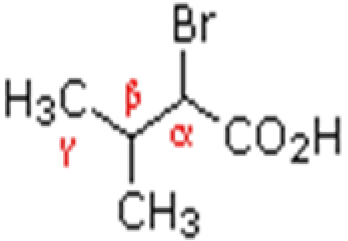
2-ethyl-4,4-dimethylpentanoic acid

$CH_3-CH(OH)-CH(NH_2)-CO_2H$ ≡



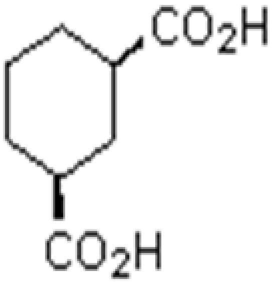
2-amino-3-hydroxybutanoic acid

The *2S*, *3R* isomer is threonine



2-bromo-3-methylbutanoic acid

α-bromoisovaleric acid

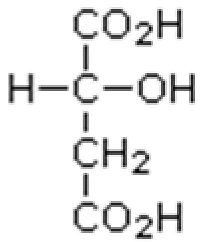


cis-1,3-cyclohexanedicarboxylic acid

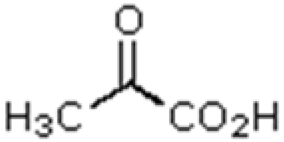
Carboxylic Acid Natural Products

Saturated		
Formula	**Common Name**	**Melting Point**
$CH_3(CH_2)_{10}CO_2H$	lauric acid	45 ºC
$CH_3(CH_2)_{12}CO_2H$	myristic acid	55 ºC
$CH_3(CH_2)_{14}CO_2H$	palmitic acid	63 ºC
$CH_3(CH_2)_{16}CO_2H$	stearic acid	69 ºC
$CH_3(CH_2)_{18}CO_2H$	arachidic acid	76 ºC

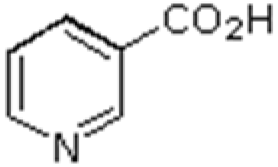
Formula	**Common Name**	**Melting Point**
$CH_3(CH_2)_5CH{=}CH(CH_2)_7CO_2H$	palmitoleic acid	0 ºC
$CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$	oleic acid	13 ºC
$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$	linoleic acid	-5 ºC
$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$	linolenic acid	-11 ºC
$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2CO_2H$	arachidonic acid	-49 ºC



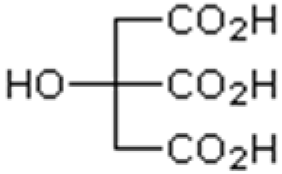
malic acid
(various fruits)



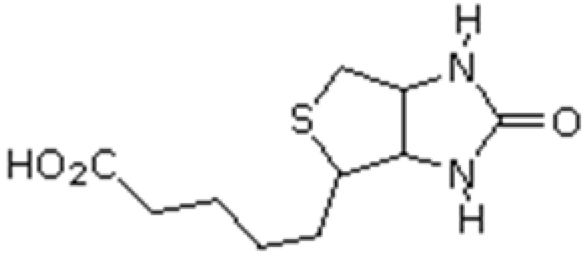
pyruvic acid
(a metabolic intermediate)



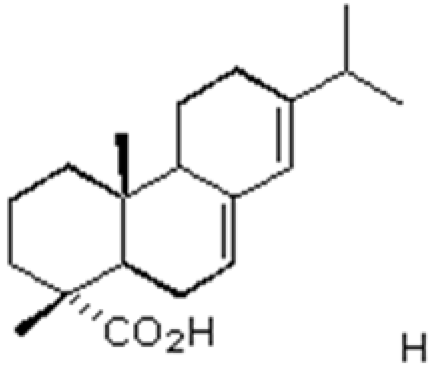
niacin
a vitamin



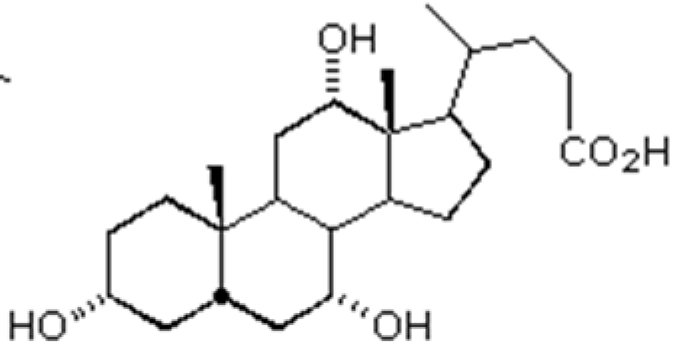
citric acid
(from citrus fruits)



biotin
(a cell growth factor)



abietic acid
(pine resin)



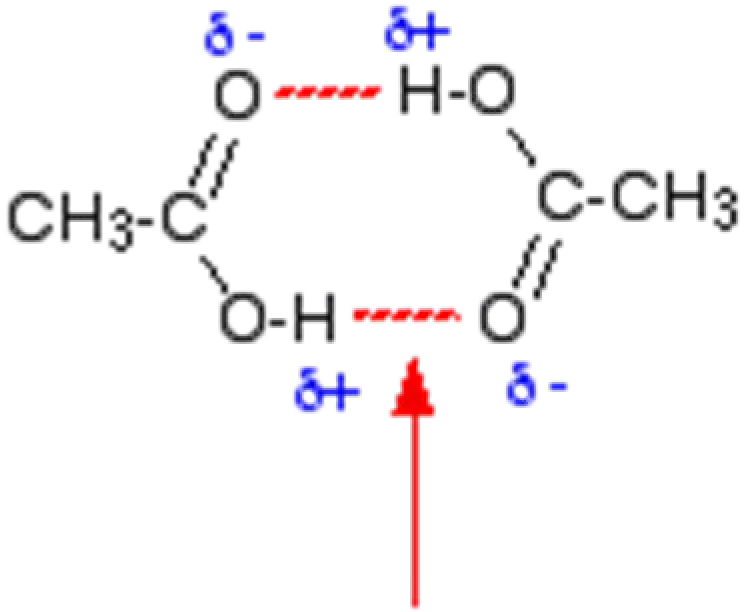
cholic acid
(from bile)

Physical Properties of Carboxylic Acids

Physical Properties of Some Organic Compounds

Formula	IUPAC Name	Molecular Weight	Boiling Point	Water Solubility
$CH_3(CH_2)_2CO_2H$	butanoic acid	88	164 ºC	very soluble
$CH_3(CH_2)_4OH$	1-pentanol	88	138 ºC	slightly soluble
$CH_3(CH_2)_3CHO$	pentanal	86	103 ºC	slightly soluble
$CH_3CO_2C_2H_5$	ethyl ethanoate	88	77 ºC	moderately soluble

$CH_3CH_2CO_2CH_3$	methyl propanoate	88	80 ºC	slightly soluble
$CH_3(CH_2)_2CONH_2$	butanamide	87	216 ºC	soluble
$CH_3CON(CH_3)_2$	N,N-dimethylethanamide	87	165 ºC	very soluble
$CH_3(CH_2)_4NH_2$	1-aminobutane	87	103 ºC	very soluble
$CH_3(CH_2)_3CN$	pentanenitrile	83	140 ºC	slightly soluble
$CH_3(CH_2)_4CH_3$	hexane	86	69 ºC	insoluble

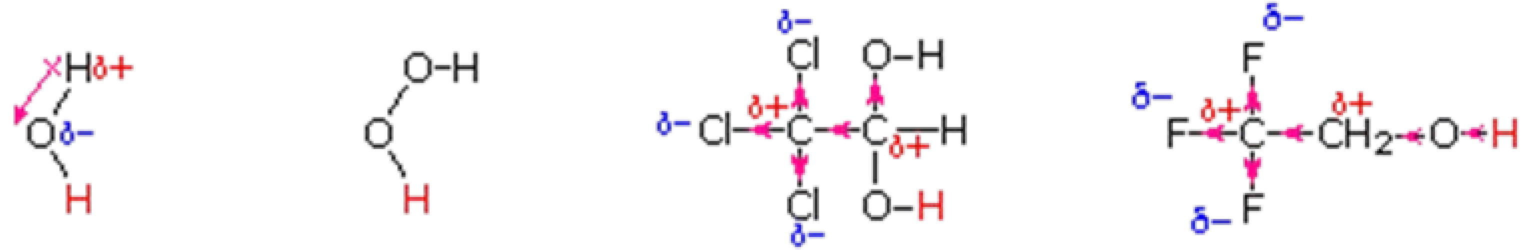


Hydrogen bond between the fairly positive hydrogen atom and a lone pair on the fairly negative oxygen atom.

Acidity of Carboxylic Acids

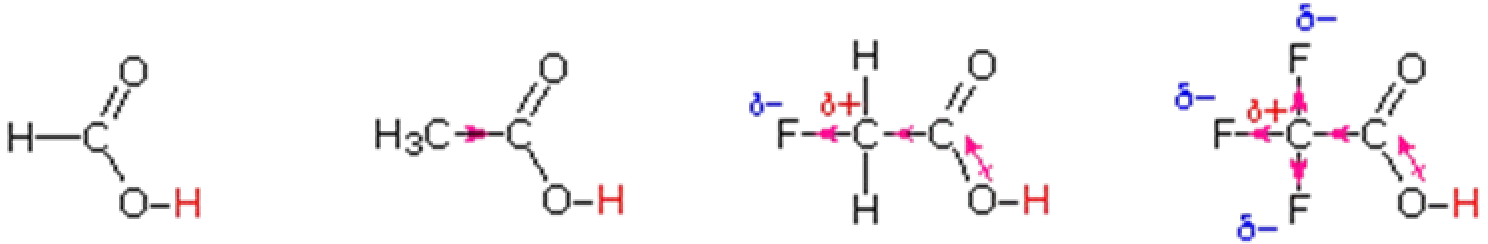
Compound	**pK_a**		**Compound**	**pK_a**
HCO_2H	3.75		$CH_3CH_2CH_2CO_2H$	4.82
CH_3CO_2H	4.74		$ClCH_2CH_2CH_2CO_2H$	4.53
FCH_2CO_2H	2.65		$CH_3CHClCH_2CO_2H$	4.05
$ClCH_2CO_2H$	2.85		$CH_3CH_2CHClCO_2H$	2.89
$BrCH_2CO_2H$	2.90		$C_6H_5CO_2H$	4.20
ICH_2CO_2H	3.10		p-$O_2NC_6H_4CO_2H$	3.45
Cl_3CCO_2H	0.77		p-$CH_3OC_6H_4CO_2H$	4.45

1.



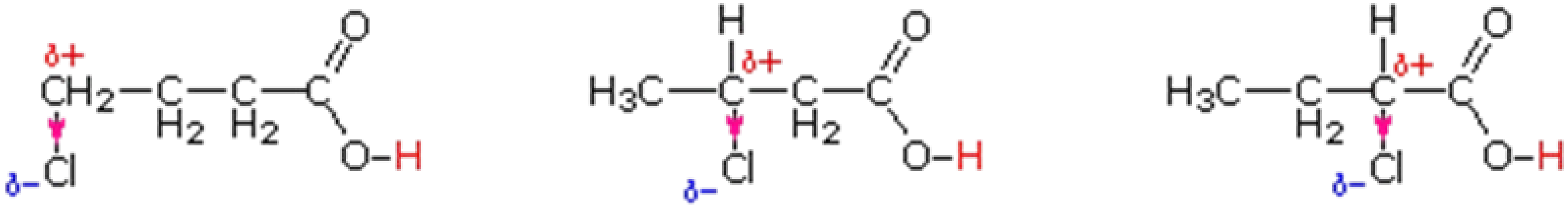
pK_a	15.7	11.6	10.0	12.2

2.



pK_a	3.75	4.74	2.65	0.0

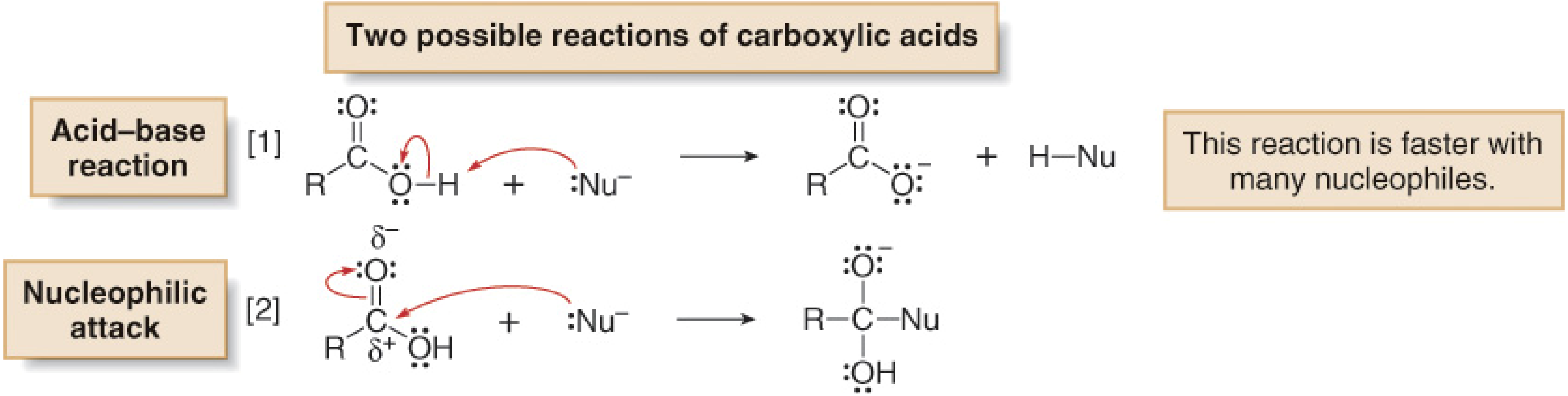
3.

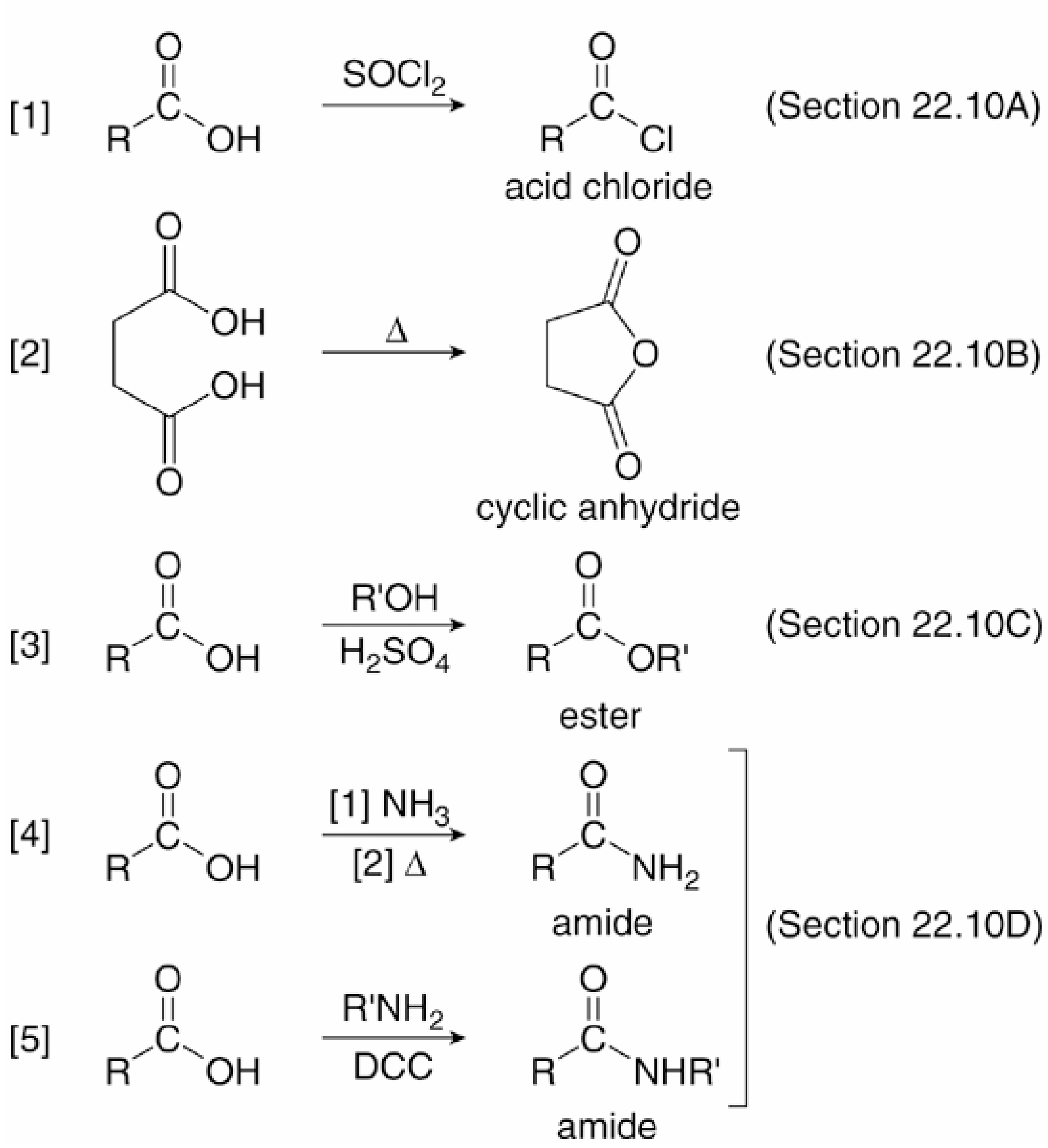


pK_a	4.53	4.05	2.89

Reactions of Carboxylic Acids

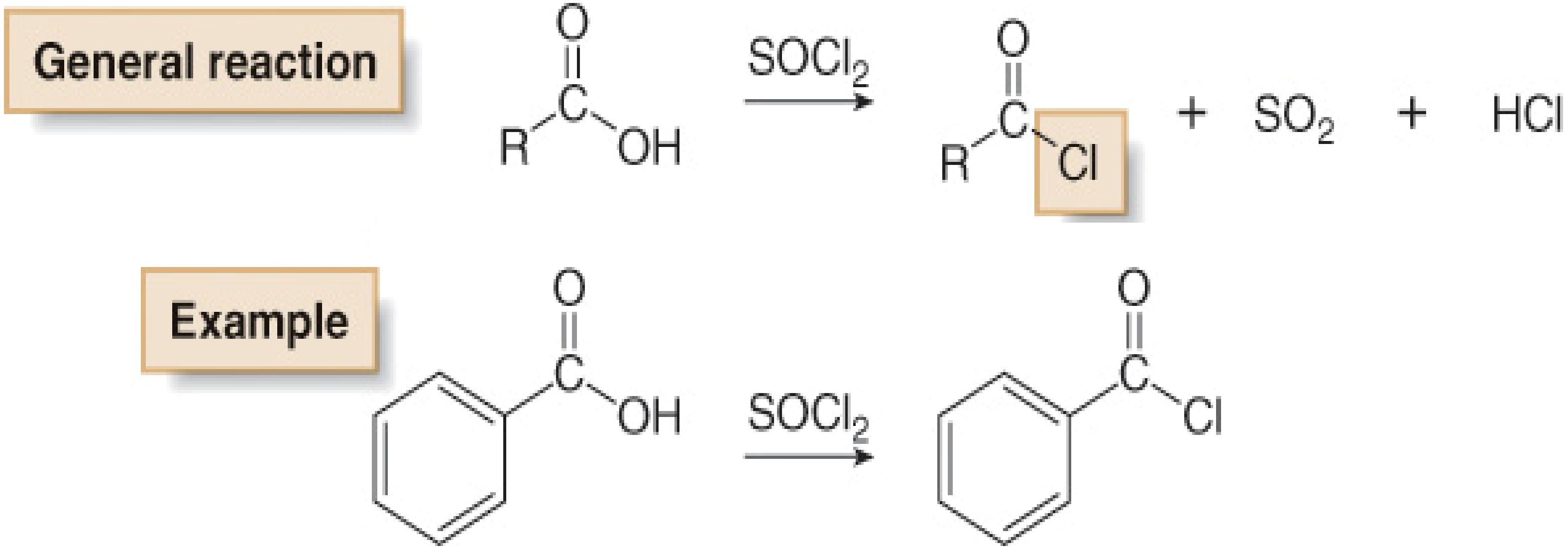
- **Nucleophiles that are also strong bases react with carboxylic acids by removing a proton first, before any nucleophilic substitution reaction can take place.**





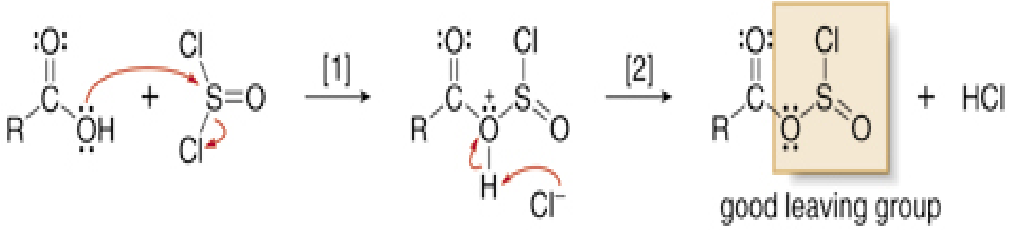
Nucleophilic acyl substitution reactions of carboxylic acids

- **Treatment of a carboxylic acid with thionyl chloride ($SOCl_2$) affords an acid chloride.**
- **This is possible because thionyl chloride converts the OH group of the acid into a better leaving group, and because it provides the nucleophile (Cl^-) to displace the leaving group.**



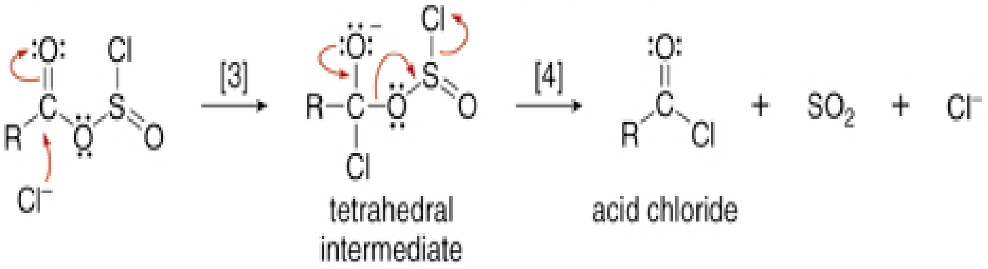
Mechanism 22.5 Conversion of Carboxylic Acids to Acid Chlorides

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



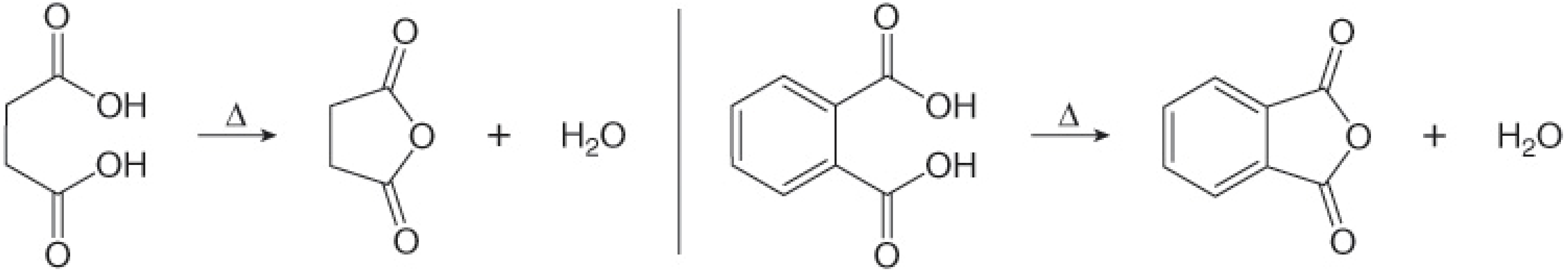
- Reaction of the OH group with $SOCl_2$ forms an intermediate that loses a proton in Step [2]. This two-step process converts the OH group into OSOCl, a **good leaving group.**

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



- **Nucleophilic attack by Cl^- and loss of the leaving group** ($SO_2 + Cl^-$) forms the acid chloride.

- **Although carboxylic acids cannot readily be converted into anhydrides, dicarboxylic acids can be converted to cyclic anhydrides by heating to high temperatures.**
- **This is a dehydration reaction because a water molecule is lost from the diacid.**



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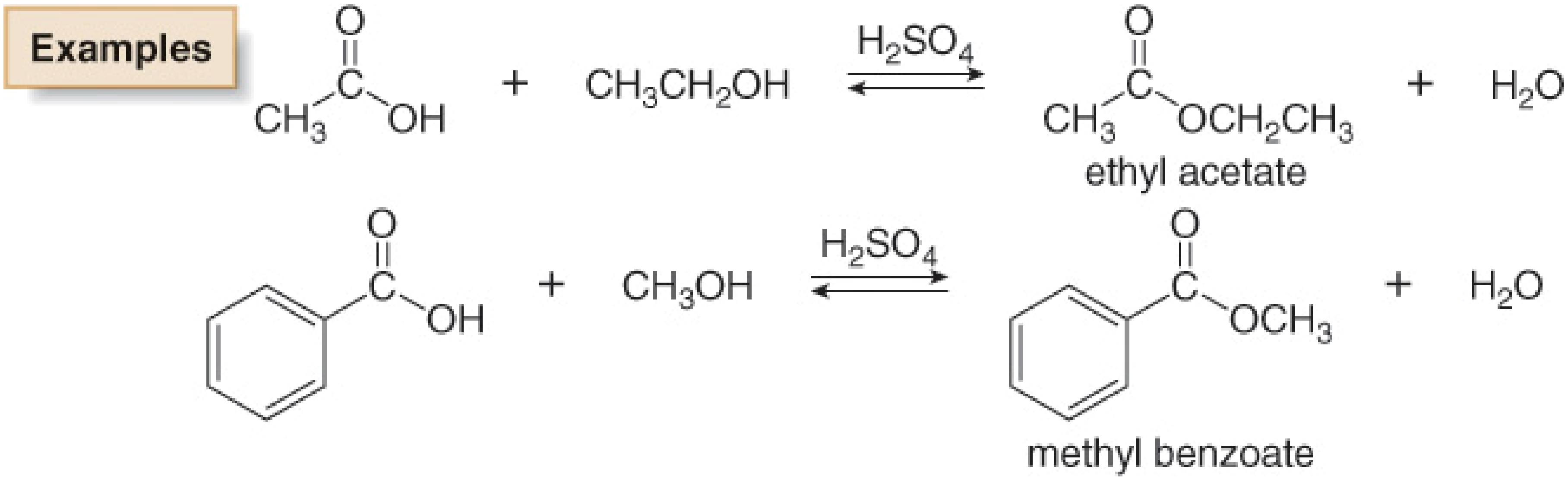
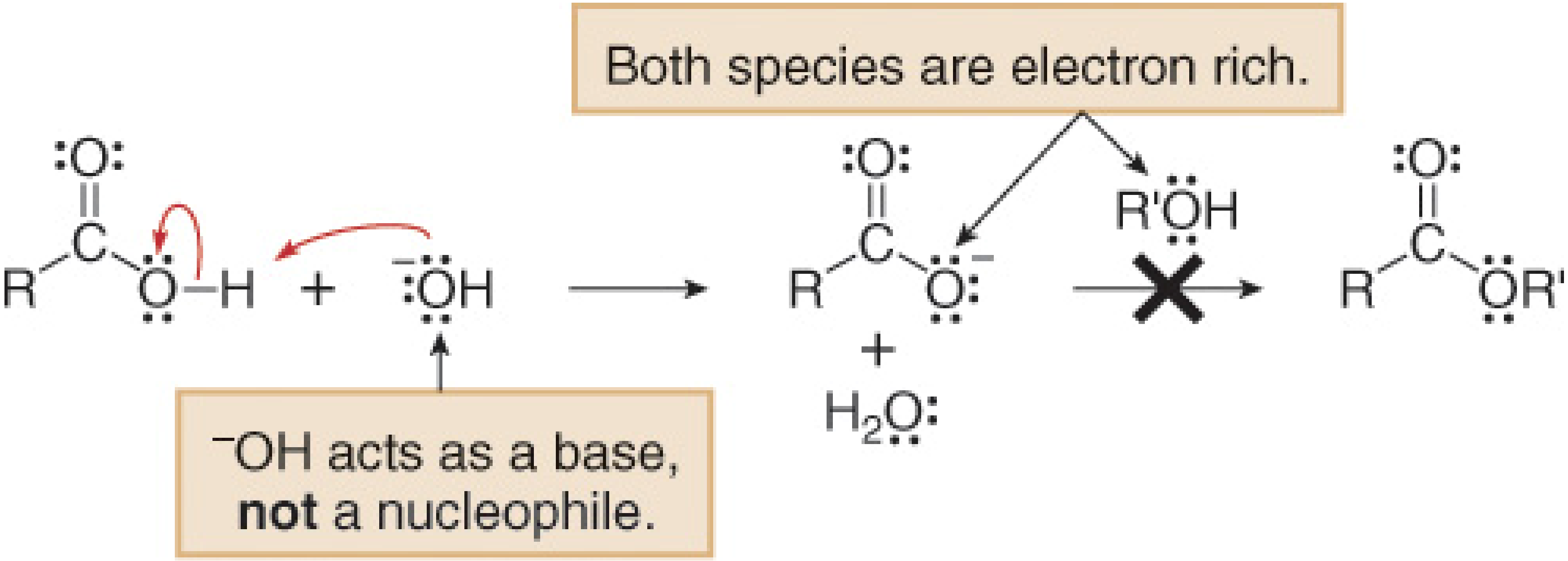


- **Esterification of a carboxylic acid occurs in the presence of acid but not in the presence of base.**
- **Base removes a proton from the carboxylic acid, forming the carboxylate anion, which does not react with an electron-rich nucleophile.**

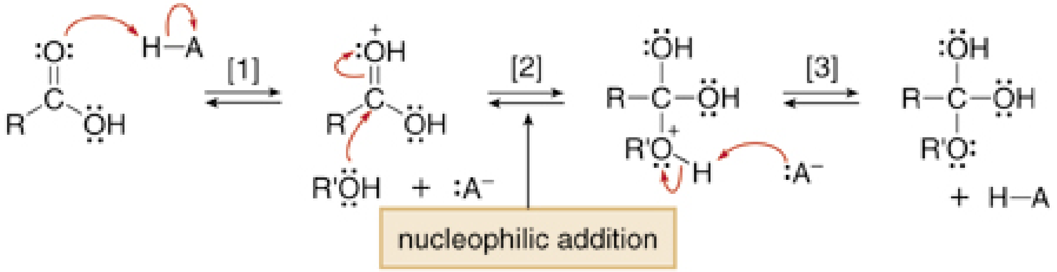


Both species are electron rich.

⁻OH acts as a base, **not** a nucleophile.

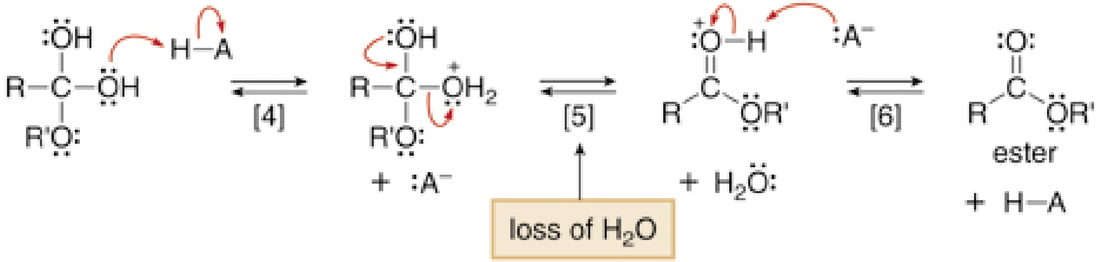
Mechanism 22.6 Fischer Esterification—Acid-Catalyzed Conversion of Carboxylic Acids to Esters

Part [1] Addition of the nucleophile R'OH



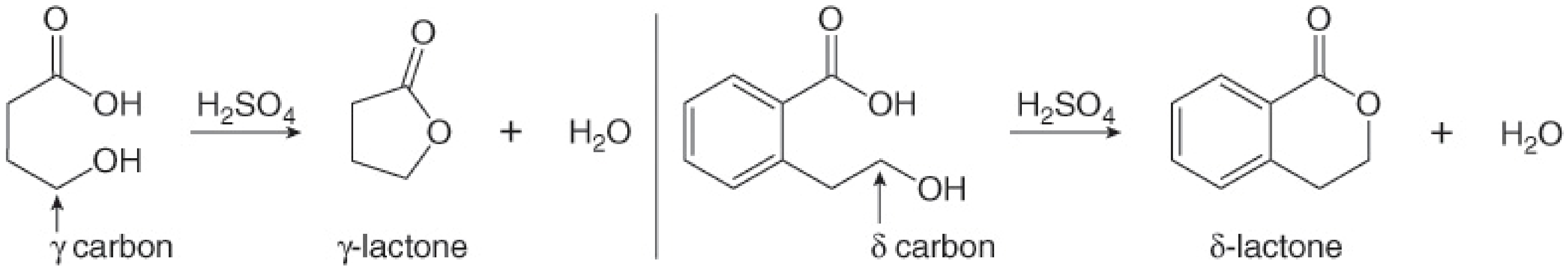
- **Protonation** in Step [1] makes the carbonyl group more electrophilic.
- **Nucleophilic addition of R'OH** forms a tetrahedral intermediate, and loss of a proton forms the neutral addition product (Steps [2]–[3]).

Part [2] Elimination of the leaving group H_2O

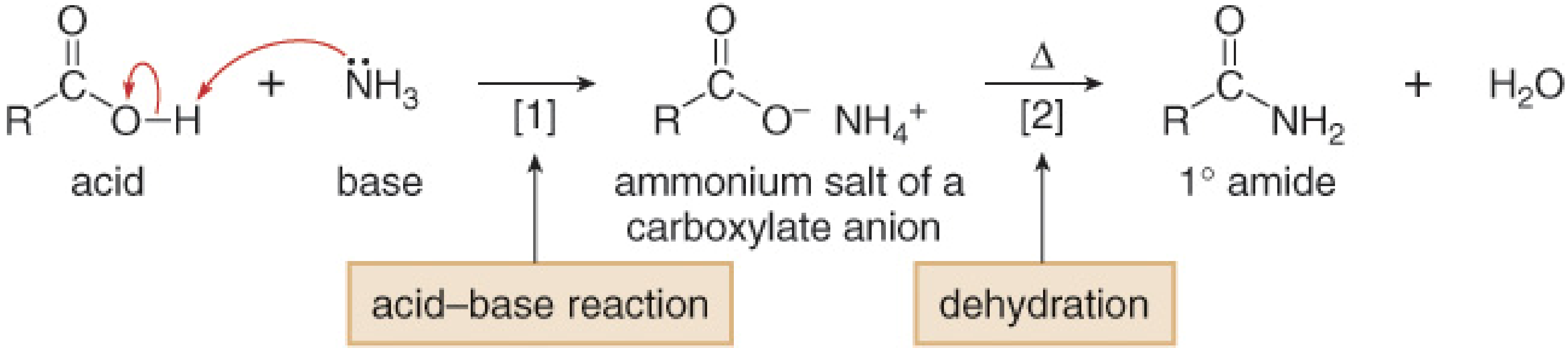


- Protonation of an OH group in Step [4] forms a good leaving group that is **eliminated in Step [5].**
- Loss of a proton in Step [6] forms the ester.

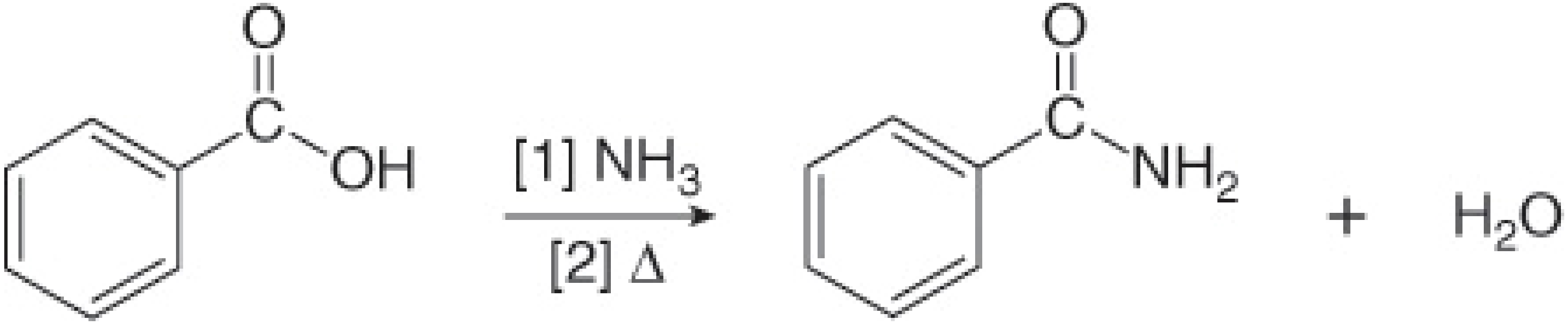
- **Intramolecular esterification of γ- and δ-hydroxyl carboxylic acids forms five- and six-membered lactones.**



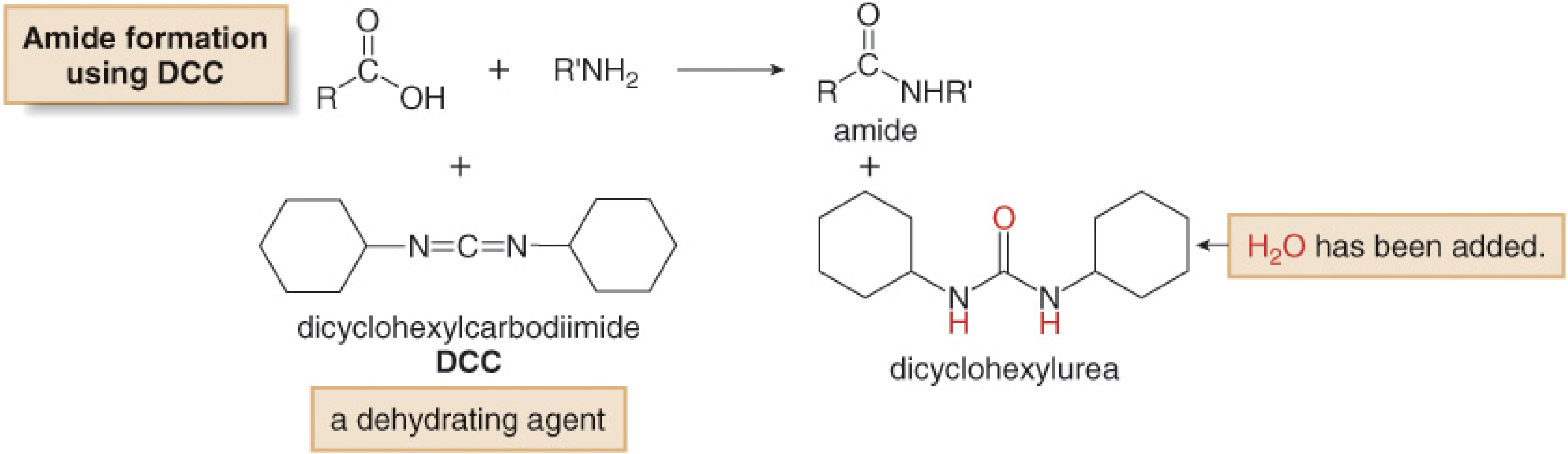
- **Carboxylic acids cannot be converted into amides by reaction with NH_3 or an amine because amines are bases, and undergo an acid-base reaction to form an ammonium salt before nucleophilic substitution occurs.**
- **However, heating the ammonium salt at high temperature (>100°C) dehydrates the resulting ammonium salt of the carboxylate anion to form an amide, although the yield can be low.**



- **The overall conversion of RCOOH to $RCONH_2$ requires two steps:**
  - **[1] Acid-base reaction of RCOOH with NH_3 to form an ammonium salt.**
  - **[2] Dehydration at high temperature (>100°C).**

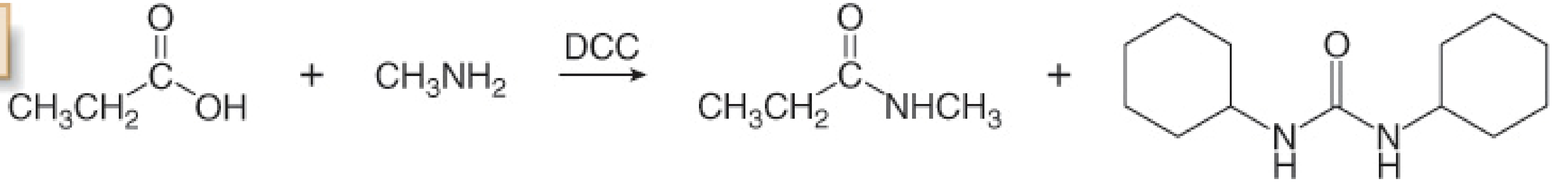


- **A carboxylic acid and an amine readily react to form an amide in the presence of an additional reagent, dicyclohexylcarbodimide (DCC), which is converted to the by-product dicyclohexylurea in the course of the reaction.**

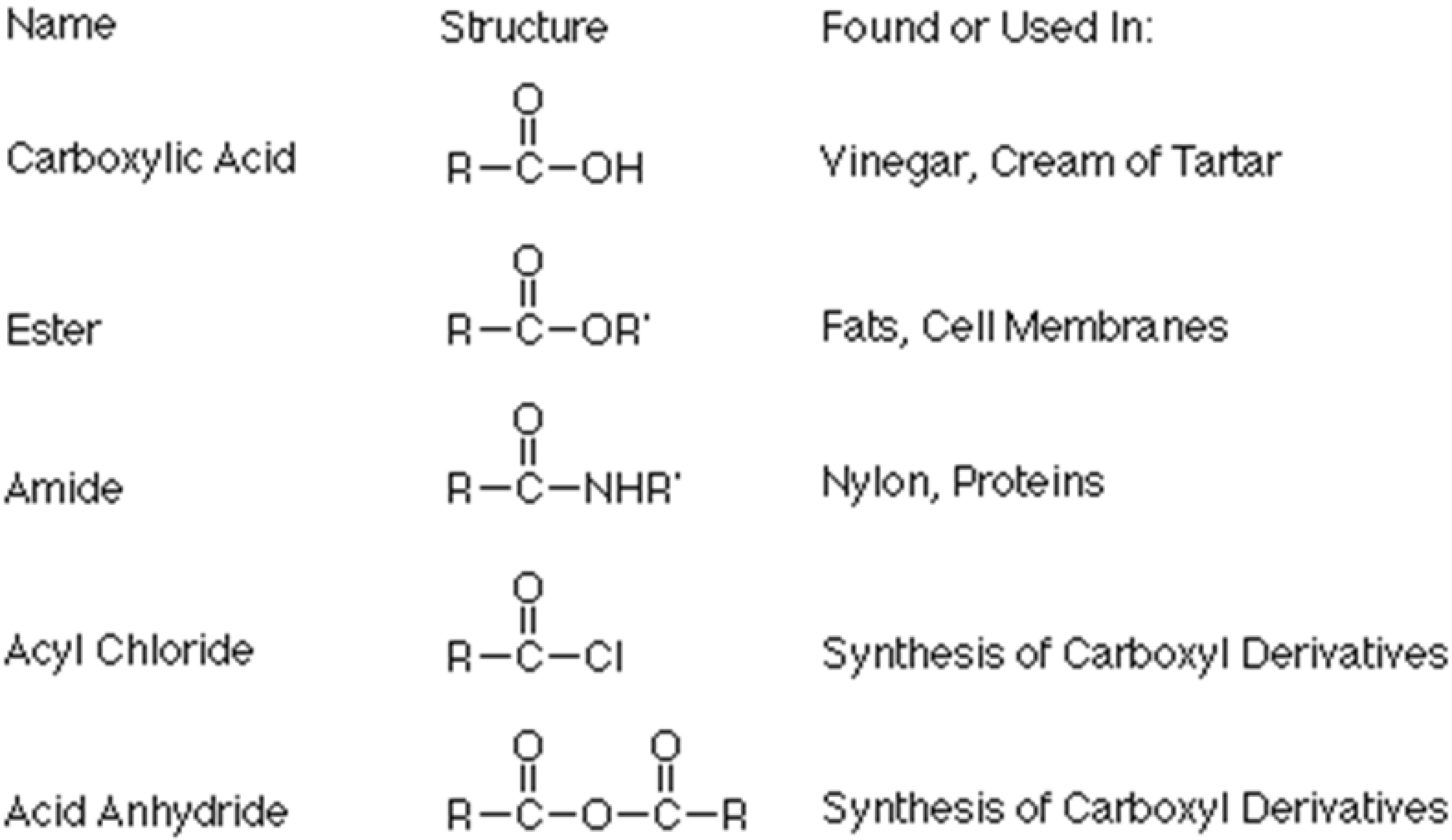


- **DCC is a dehydrating agent.**
- **The dicyclohexylurea by-product is formed by adding the elements of H_2O to DCC.**
- **DCC promotes amide formation by converting the carboxy group OH group into a better leaving group.**

Example



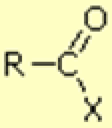
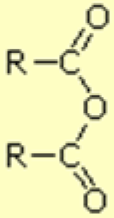
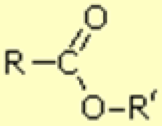
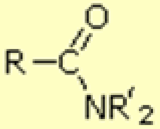
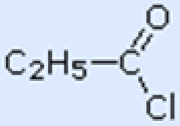
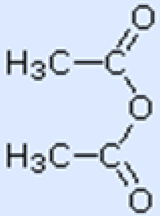
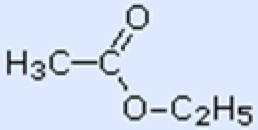
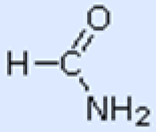
Carboxylic Acid Derivatives



Name	Structure	Found or Used In:
Carboxylic Acid	$R-\overset{O}{\overset{\Vert}{C}}-OH$	Vinegar, Cream of Tartar
Ester	$R-\overset{O}{\overset{\Vert}{C}}-OR'$	Fats, Cell Membranes
Amide	$R-\overset{O}{\overset{\Vert}{C}}-NHR'$	Nylon, Proteins
Acyl Chloride	$R-\overset{O}{\overset{\Vert}{C}}-Cl$	Synthesis of Carboxyl Derivatives
Acid Anhydride	$R-\overset{O}{\overset{\Vert}{C}}-O-\overset{O}{\overset{\Vert}{C}}-R$	Synthesis of Carboxyl Derivatives

Related Carbonyl Derivatives

Related Carbonyl Derivatives

acyl halide	**anhydride**	**ester**	**amide**	**nitrile**
 X = F, Cl, Br or I			 R′ = H or alkyl	$R-C\equiv N$
 propanoyl chloride	 acetic anhydride	 ethyl acetate	 formamide	$H_3C-C\equiv N$ acetonitrile