

Chapter 15

Carbonyl Compounds: Esters, Amides, and Related Molecules

from Organic Chemistry

by
Robert C. Neuman, Jr.
Professor of Chemistry, emeritus
University of California, Riverside

orgchembyneuman@yahoo.com
<<http://web.chem.ucsb.edu/~neuman/orgchembyneuman/>>

Chapter Outline of the Book

I. Foundations

1. Organic Molecules and Chemical Bonding
2. Alkanes and Cycloalkanes
3. Haloalkanes, Alcohols, Ethers, and Amines
4. Stereochemistry
5. Organic Spectrometry

II. Reactions, Mechanisms, Multiple Bonds

6. Organic Reactions **(Not yet Posted)*
7. Reactions of Haloalkanes, Alcohols, and Amines. Nucleophilic Substitution
8. Alkenes and Alkynes
9. Formation of Alkenes and Alkynes. Elimination Reactions
10. Alkenes and Alkynes. Addition Reactions
11. Free Radical Addition and Substitution Reactions

III. Conjugation, Electronic Effects, Carbonyl Groups

12. Conjugated and Aromatic Molecules
13. Carbonyl Compounds. Ketones, Aldehydes, and Carboxylic Acids
14. Substituent Effects
15. Carbonyl Compounds. Esters, Amides, and Related Molecules

IV. Carbonyl and Pericyclic Reactions and Mechanisms

16. Carbonyl Compounds. Addition and Substitution Reactions
17. Oxidation and Reduction Reactions
18. Reactions of Enolate Ions and Enols
19. Cyclization and Pericyclic Reactions **(Not yet Posted)*

V. Bioorganic Compounds

20. Carbohydrates
21. Lipids
22. Peptides, Proteins, and α -Amino Acids
23. Nucleic Acids

**Note: Chapters marked with an (*) are not yet posted.*

15: Carbonyl Compounds: Esters, Amides, and Related Molecules

15.1 Carbonyl Compounds with the Structure R-C(=O)-Z	15-3
<i>The C(=O)-Z Functional Group (15.1A)</i>	15-3
<i>The Z Group</i>	
<i>α-H Acidity and Enol Content</i>	
<i>R-C(=O)-Z Compounds are Interconvertible (15.1B)</i>	15-5
<i>Acid Chloride Interconversions</i>	
<i>Nucleophilic Acyl Substitution</i>	
<i>Oxidation States of R-C(=O)-Z Compounds (15.1C)</i>	15-6
<i>R-C\equivN versus R-C(=O)-Z (15.1D)</i>	15-6
<i>Comments about Nomenclature (15.1E)</i>	15-7
15.2 Acid Halides (R-C(=O)-X)	15-8
<i>Preparation, Reactivity, and Properties (15.2A)</i>	15-8
<i>Preparation</i>	
<i>Reactivity and Properties</i>	
<i>Nomenclature (15.2B)</i>	15-10
15.3 Esters (R-C(=O)-OR')	15-11
<i>Preparation, Reactivity, and Properties (15.3A)</i>	15-11
<i>Preparation</i>	
<i>Reactivity</i>	
<i>Properties</i>	
<i>Electron Delocalization</i>	
<i>Nomenclature (15.3B)</i>	15-12
<i>The R' Part</i>	
<i>The RC(=O)O Part</i>	
<i>Systematic or Common</i>	
15.4 Amides (R-C(=O)-NR'2)	15-13
<i>Preparation and Reactivity (15.4A)</i>	15-13
<i>Structure of Amides (15.4B)</i>	15-14
<i>Amides are Planar</i>	
<i>C-N Rotation is Restricted</i>	
<i>cis and trans Isomers of Amides</i>	
<i>Properties of Amides (15.4C)</i>	15-15
<i>Amide Basicity</i>	
<i>Amide Hydrogen Bonding</i>	
<i>Amides as Solvents</i>	
<i>Nomenclature (15.4D)</i>	15-17

(continued)

15.5 Anhydrides (R-C(=O)-O-C(=O)-R)	15-18
<i>Preparation, Reactivity, and Properties (15.5A)</i>	15-18
<i>Preparation of Symmetrical Anhydrides.</i>	
<i>Preparation of Mixed Anhydrides</i>	
<i>Reactivity of Anhydrides</i>	
<i>Nomenclature (15.5B)</i>	15-20
15.6 Nitriles (R-C≡N)	15-20
<i>Preparation and Properties (15.6A)</i>	15-20
<i>Alkyl Nitriles</i>	
<i>Aryl Nitriles</i>	
<i>Properties of Nitriles</i>	
<i>Nomenclature (15.6B)</i>	15-21
15.7 Lactones, Lactams, and Cyclic Anhydrides	15-22
<i>Structure (15.7A)</i>	15-22
<i>Cyclic Anhydrides</i>	
<i>Lactones and Lactams</i>	
<i>Nomenclature (15.7B)</i>	15-23
<i>Lactones</i>	
<i>Lactams</i>	
15.8 Biologically Important Molecules with R-C(=O)-Z Groups	15-24
<i>Esters (15.8A)</i>	15-25
<i>Waxes</i>	
<i>Fats and Oils</i>	
<i>Amides (15.8B)</i>	15-27
<i>Proteins</i>	
<i>Peptides</i>	
<i>Lactams (15.8C)</i>	15-28
15.9 Spectrometric Properties of R-C(=O)-Z and R-C≡N	15-28
<i>Ultraviolet-Visible Spectrometry (15.9A)</i>	15-28
<i>Infrared Spectrometry (15.9B)</i>	15-29
<i>C=O Stretch</i>	
<i>C-O Stretch</i>	
<i>N-H Stretch and N-H Bend</i>	
<i>C≡N Stretch</i>	
<i>NMR Spectrometry (15.9C)</i>	15-30
<i>¹³C NMR</i>	
<i>¹H NMR</i>	
<i>Determination of C-N Rotational Barriers in Amides</i>	

15: Carbonyl Compounds: Esters, Amides, and Related Molecules

- Carbonyl Compounds with the Structure $R-C(=O)-Z$
- Acid Halides ($R-C(=O)-X$)
- Esters ($R-C(=O)-OR'$)
- Amides ($R-C(=O)-NR'_2$)
- Anhydrides ($R-C(=O)-O-C(=O)-R$)
- Nitriles ($R-C\equiv N$)
- Lactones, Lactams, and Cyclic Anhydrides
- Biologically Important Molecules with $R-C(=O)-Z$ Groups
- Spectrometric Properties of $R-C(=O)-Z$ and $R-C\equiv N$

15.1 Carbonyl Compounds with the Structure $R-C(=O)-Z$

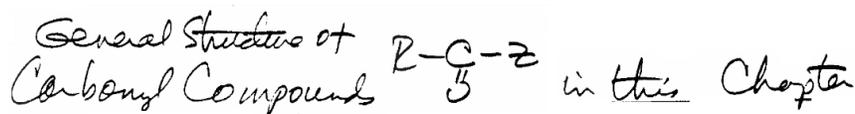
The carbonyl group ($C=O$) is one of the most important functional groups in organic chemistry. We have already described (Chapter 13) *ketones*, *aldehydes* and *carboxylic acids* (Figure 15.01) that contain the carbonyl group.

Figure 15.01



Now we introduce the remaining major classes of carbonyl compounds that all have the general formula $R-C(=O)-Z$ (Figure 15.02).

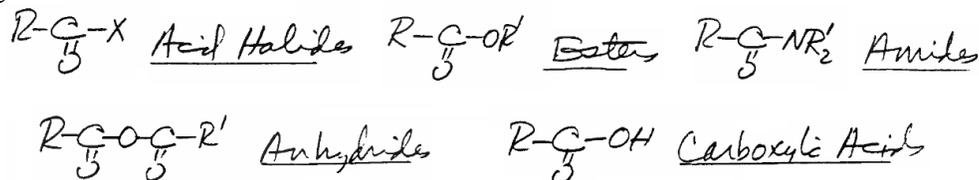
Figure 15.02



The $C(=O)-Z$ Functional Group (15.1A)

We give structures and names for these $R-C(=O)-Z$ compounds in Figure 15.03.

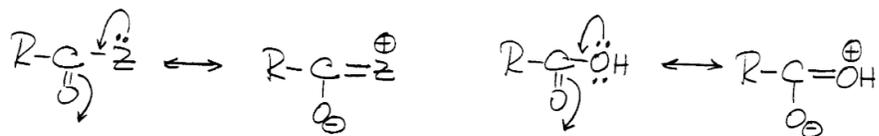
Figure 15.03



The Z Group. In each case, Z has an electronegative heteroatom (O, N, or halogen X), with one or more unshared pairs of electrons, directly bonded to $C=O$. We include carboxylic acids because their Z group (OH) fits these criteria. Although we discussed carboxylic acids

in Chapter 13, they are chemically more closely related to the other R-C(=O)-Z compounds that we describe here. In each of these compounds, an unshared electron pair on Z delocalizes into the C=O group as we show generally, and for a carboxylic acid, in Figure 15.04.

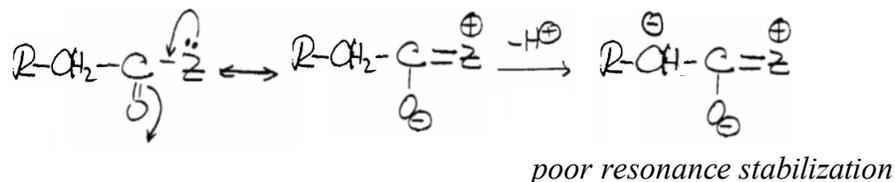
Figure 15.04



This does not occur with either ketones or aldehydes since they have H or R groups directly attached to C=O that do not have unshared electron pairs.

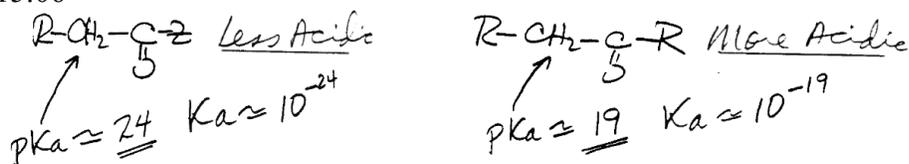
α-H Acidity and Enol Content. A consequence of this electron donation from Z to C=O is that α-H's of R-C(=O)-Z compounds are less acidic than α-H's of ketones and aldehydes. Electron donation from Z makes the C=O less able to stabilize a negative charge on the α-C arising from loss of a proton from the α-C (Figure 15.05)

Figure 15.05



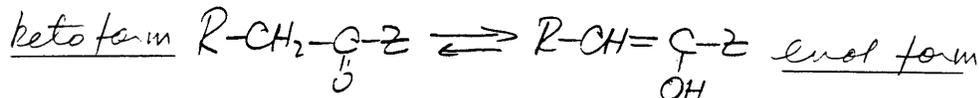
This is reflected in the data in Figure 15.06 where we compare typical acidity constants of the α-H's of R-CH₂-C(=O)-Z compounds with those of ketones.

Figure 15.06



Similarly, the relative amount of *enol form* in equilibrium with the *carbonyl form* of R-C(=O)-Z compounds (Figure 15.07) is less than that for ketones and aldehydes.

Figure 15.07

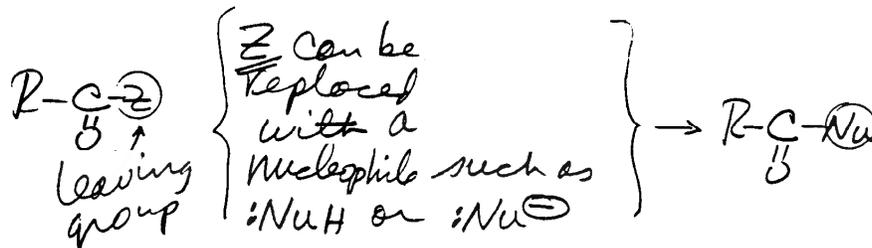


We gave quantitative estimates of the enol content of some aldehydes and ketones in Chapter 13, but the enol content of R-C(=O)-Z compounds is generally too small to measure. The extent of electron delocalization (Figure 15.04) depends on the specific heteroatom attached to C=O as we describe below in the detailed sections for each type of R-C(=O)-Z compound.

R-C(=O)-Z Compounds are Interconvertible (15.1B)

The Z groups in R-C(=O)-Z are leaving groups that we can replace with other nucleophiles (Figure 15.08).

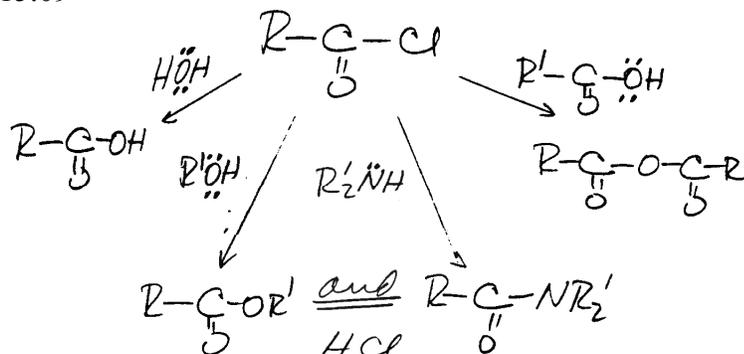
Figure 15.08



This enables us to interconvert different R-C(=O)-Z compounds. This is not possible with aldehydes or ketones since the H or R groups attached to C=O are not leaving groups.

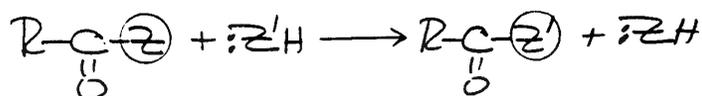
Acid Chloride Interconversions. Examples of these interconversions are transformations of acid chlorides into *carboxylic acids*, *esters*, *amides*, or *anhydrides* (Figure 15.09).

Figure 15.09



Each of these reactions is an example of the general reaction in Figure 15.08 where a nucleophilic species (:Nu-H) replaces Cl. Nu can be another Z group, so these nucleophilic substitution reactions interconvert different classes of R-C(=O)-Z compounds (Figure 15.10).

Figure 15.10



We list specific interconversions that use this type of reaction in Table 15.01.

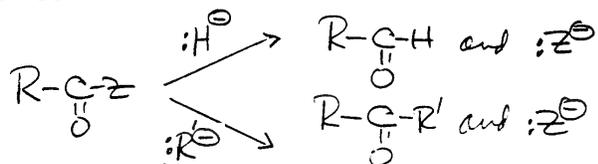
Table 15.01. Some Common Interconversions of R-C(=O)-Z

<u>acid halides to:</u>	<u>acids to:</u>	<u>anhydrides to:</u>	<u>esters to:</u>	<u>amides to:</u>
acids	acid halides	acids	acids	acids
esters	esters	esters	esters	
amides	amides	amides		
anhydrides	anhydrides			

Nucleophilic Acyl Substitution. The mechanisms of these interconversion reactions are called **nucleophilic acyl substitution**. In this mechanism, a *nucleophile* such as $:Z'-H$ reacts with $R-C(=O)-Z$ causing Z' to be *substituted* for Z on the *acyl* group $R-C(=O)$ (Figure 15.10). In the example in Figure 15.09, the nucleophile $R'O-H$ replaces Cl with $R'O$. We discuss this mechanism in detail in Chapter 16, but preview its mechanistic features later in the chapter.

In addition to the interconversions of various $R-C(=O)-Z$ compounds in Table 15.01, we can form aldehydes or ketones from some $R-C(=O)-Z$ compounds (Figure 15.11).

Figure 15.11

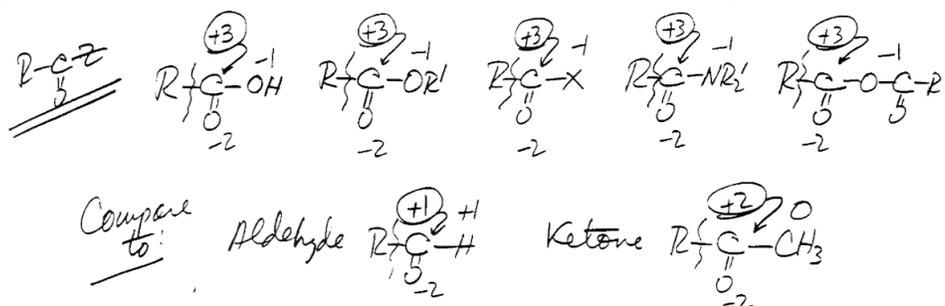


These reactions also occur by *nucleophilic acyl substitution* and we describe their mechanisms in detail in Chapter 16.

Oxidation States of $R-C(=O)-Z$ Compounds (15.1C)

A common feature of $R-C(=O)-Z$ compounds is that their $C=O$ C's all have the same oxidation number (Figure 15.12).

Figure 15.12

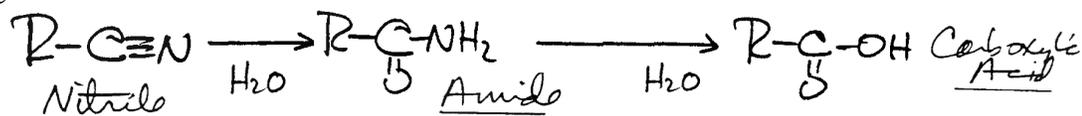


This contrasts with oxidation numbers for the $C=O$ C's of aldehydes or ketones that differ from those of the $C=O$ C's of $R-C(=O)-Z$ (Figure 15.12).

$R-C\equiv N$ versus $R-C(=O)-Z$ (15.1D)

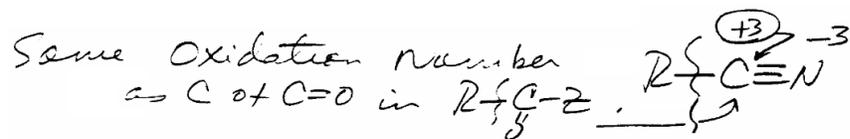
Organic nitriles ($R-C\equiv N$) are usually considered together with $R-C(=O)-Z$ compounds in organic chemistry textbooks. This is because *nitriles* ($R-C\equiv N$) are readily hydrolyzed to *carboxylic acids* ($R-C(=O)-OH$) via intermediate *amides* ($R-C(=O)-NH_2$) (Figure 15.13).

Figure 15.13



We will see in Chapter 16 that these hydrolysis reactions of R-C≡N compounds have mechanisms that are analogous to the *nucleophilic acyl substitution* mechanisms mentioned earlier. In addition, the C≡N carbon also has the same oxidation number as the C=O carbon in R-C(=O)-Z compounds (Figure 15.14).

Figure 15.14

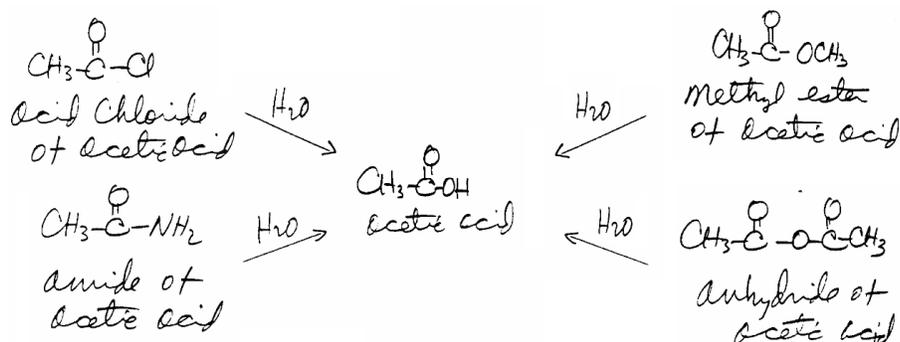


Comments about Nomenclature (15.1E)

We describe nomenclature, along with the physical and chemical properties of the various R-C(=O)-Z and R-C≡N compounds in the following sections. While we group all these classes together because they interconvert by *nucleophilic acyl substitution* reactions, you will see that nomenclature rules are significantly different for each class.

Before we present systematic names for these compounds, you need to know that organic chemists informally use a form of common nomenclature based on the specific carboxylic acid that forms during their hydrolysis (Figure 15.15).

Figure 15.15



The examples in this figure indicate why these R-C(=O)-Z compounds are frequently referred to as "derivatives" of carboxylic acids.

More on Nomenclature. The contrasting nomenclature rules for various R-C(=O)-Z compounds probably arose because common features and similar chemical reactions that now lead us to consider them together were not evident when they were first identified and named. The current systematic nomenclature balances the historical importance of the early nomenclature of these compounds with the need for a more modern systematic nomenclature. The results of these compromises can be confusing to the beginning student. But names must be learned as part of the process of learning organic chemistry. Recognizing systematic aspects of nomenclature, and learning names, helps you to feel more comfortable with all aspects of organic chemistry.

15.2 Acid Halides (R-C(=O)-X)

When Z of R-C(=O)-Z is a halogen atom (X), these compounds are equivalently referred to as **acid halides**, **acyl halides**, or **alkanoyl halides**.

Preparation, Reactivity, and Properties (15.2A)

The halogen atom of *acid halides* may be F, Cl, Br, or I, however acid chlorides (X = Cl) are most frequently encountered because of their ease of preparation and their use in organic synthesis.

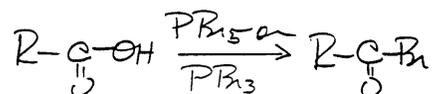
Preparation. We prepare acid chlorides from carboxylic acids using the reactions in Figure 15.16.

Figure 15.16



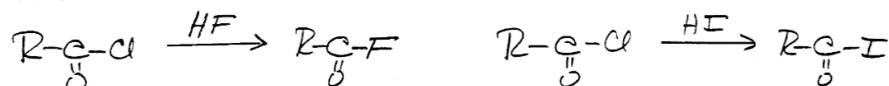
We prepare acid bromides by analogous reactions using PBr₃ or PBr₅ (Figure 15.17).

Figure 15.17



In contrast, we prepare acid fluorides and iodides using reactions of the corresponding acid chloride with HF or HI as we show in Figure 15.18.

Figure 15.18



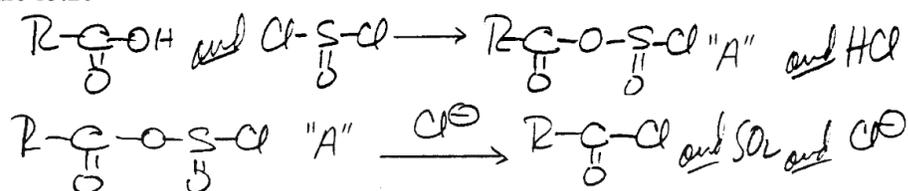
Mechanism for Acid Chloride Formation. We fully discuss the mechanisms for these reactions in Chapter 16, but give a preview here. The reactions in Figures 14.11 and 14.11a are analogous to those presented in Chapter 7 for the preparation of haloalkanes from alcohols (Figure 15.19).

Figure 15.19



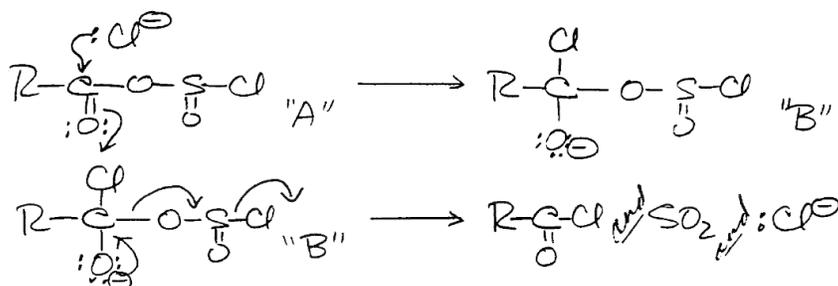
Carboxylic acids first react with SOCl₂ to form an intermediate "A" that then reacts with Cl⁻ to form the acid chloride (Figure 15.20).

Figure 15.20



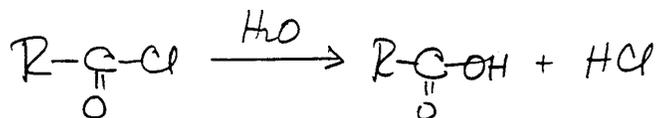
"A" reacts with chloride ion by a *nucleophilic acyl substitution* where the OS(=O)Cl group is substituted by Cl⁻ (Figure 15.21).

Figure 15.21



Reactivity and Properties. Acid halides are reactive compounds that serve as precursors to all of the other compounds with the structure R-C(=O)-Z (Figure 15.09 and Table 15.01). Since we prepare them from *carboxylic acids* (Figure 15.16 and Figure 15.17), they are usually not used as synthetic precursors to carboxylic acids. However they readily form carboxylic acids by *hydrolysis* (Figure 15.22).

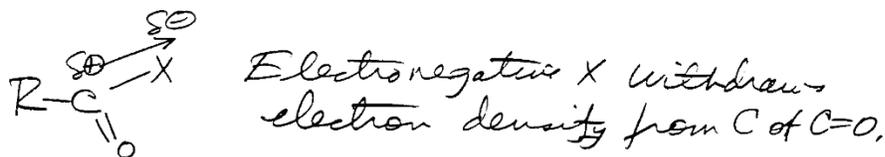
Figure 15.22



Caution. Hydrolysis of acid halides commonly occurs when they are not protected from atmospheric moisture (H₂O). HX formation during their hydrolysis, and in other reactions of acid halides, is one reason why they are toxic and corrosive compounds that you must handle with great care.

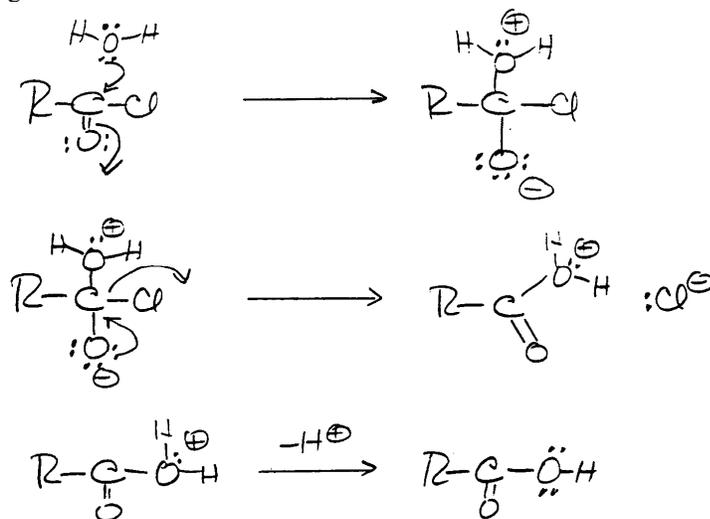
Acid halides are highly reactive because the electronegative halogens make the C=O group particularly susceptible to attack by nucleophiles. Inductive electron withdrawal (-I effect) by halogens is strong, while their resonance electron donation (+R effect) is relatively weak as we described in the previous chapter on substituent effects (Chapter 14). As a result, halogens generally decrease the electron density on the C=O group to which they are attached (Figure 15.23).

Figure 15.23



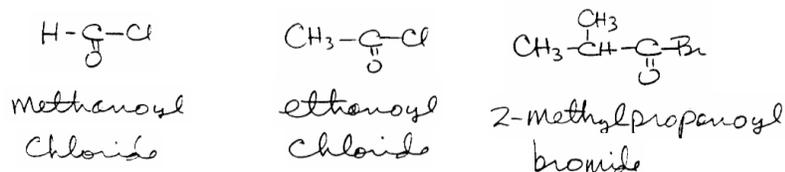
Mechanism for Acid Halide Hydrolysis. The reactions in Figure 15.09 and Table 15.01 all occur by *nucleophilic acyl substitution* mechanisms. We will describe these reaction mechanisms in detail in Chapter 16, but also show the mechanism for acid chloride hydrolysis in Figure 15.24 [next page].

Figure 15.24

**Nomenclature (15.2B)**

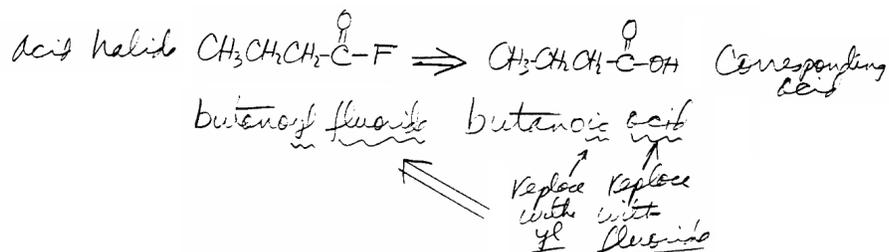
We show some acid halides and their systematic names in Figure 15.25.

Figure 15.25



We form these names from systematic names of the corresponding carboxylic acids by (1) dropping the word *acid* from the name and replacing it with the name of the specific *halide*, and (2) changing the ending *-ic* on the first word of the acid name to *-yl* (Figure 15.26).

Figure 15.26



We use the same procedure to name acid chlorides by common nomenclature except that we begin with the common names of the corresponding carboxylic acids (Figure 15.27).

Figure 15.27

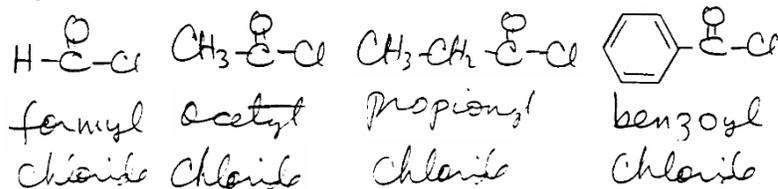
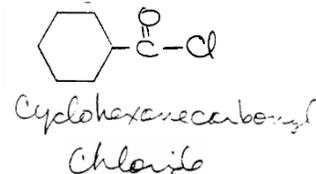


Figure 15.28



In cases where the acid name has the ending "carboxylic acid," the word *acid* is replaced with the name of the *halide*, and the ending *-carboxylic* is replaced with the ending *-carbonyl* as we illustrate above in Figure 15.28.

15.3 Esters (R-C(=O)-OR')

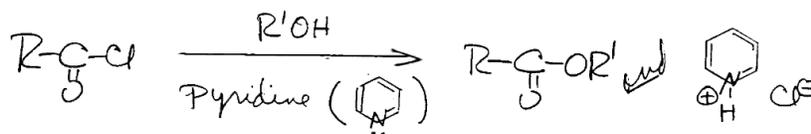
Esters are RC(=O)-Z compounds where Z is OR' , and R' groups are alkyl or aryl.

Preparation, Properties, and Reactivity (15.3A)

The differences between *esters* and *acid halides* are much greater than their similarities.

Preparation. We previously described the preparation of *esters* from acid halides and alcohols (Figure 15.09) and show this again in Figure 15.29.

Figure 15.29



The reagent *pyridine* shown in this reaction is basic, and reacts with HCl that forms in the reaction. We can also synthesize esters from other R-C(=O)-Z compounds as we showed in Table 15.01. We will describe these reactions in detail Chapter 16.

Properties. In contrast with *acid halides* that are unpleasant and toxic compounds, esters have very pleasant aromas. They provide many of the fragrances and flavors that characterize various fruits and artificial flavorings as we outline in Figure 15.30 [next page]. We show both the systematic and common names of the esters in Figure 15.30 and describe their origin in the nomenclature section below.

Figure 15.30

$\text{HC(O)OCH}_2\text{CH}_3$ ethyl methanoate ethyl formate <i>flavorful</i>	$\text{CH}_3\text{C(O)OCH}_2\text{CH}_3$ ethyl ethanoate ethyl acetate <i>flavorful</i>	$\text{CH}_3\text{CH}_2\text{CH}_2\text{C(O)OCH}_2\text{CH}_3$ ethyl butanoate ethyl butyrate <i>pineapple</i>
$(\text{CH}_3)_2\text{CHC(O)OCH}_2\text{CH}_3$ ethyl 2-methylpropanoate ethyl isobutyrate <i>fruity</i>	$(\text{CH}_3)_2\text{CHCH}_2\text{C(O)OCH}_2\text{CH}_3$ ethyl 3-methylbutanoate ethyl isovalerate <i>apple</i>	$\text{HC(O)OCH}_2\text{CH}(\text{CH}_3)_2$ 2-methylpropyl methanoate isoamyl formate <i>fruity</i>
$\text{CH}_3\text{C(O)OCH}_2\text{CH}(\text{CH}_3)_2$ 2-methylpropyl ethanoate isoamyl acetate <i>bannas, pears</i>	$\text{CH}_3\text{CH}_2\text{C(O)OCH}_2\text{CH}(\text{CH}_3)_2$ 2-methylpropyl propanoate isoamyl propionate <i>rum</i>	$\text{CH}_3\text{CH}_2\text{CH}_2\text{C(O)OCH}_2\text{CH}(\text{CH}_3)_2$ 2-methylpropyl butanoate isoamyl butyrate <i>pears</i>
$\text{CH}_3(\text{CH}_2)_3\text{C(O)OCH}_2\text{CH}(\text{CH}_3)_2$ 2-methylpropyl pentanoate isoamyl valerate <i>apple</i>	$(\text{CH}_3)_2\text{CHCH}_2\text{C(O)OCH}_2\text{CH}(\text{CH}_3)_2$ 2-methylpropyl 3-methylbutanoate isoamyl isovalerate <i>apple</i>	

Reactivity. As is the case with *acid halides*, we can also transform *esters* into other R-C(=O)-Z compounds as we showed in Table 15.01 and describe in Chapter 16. Esters are significantly less reactive than acid halides, but replacement of OR' with other Z groups by *nucleophilic acyl substitution* reactions has important synthetic utility.

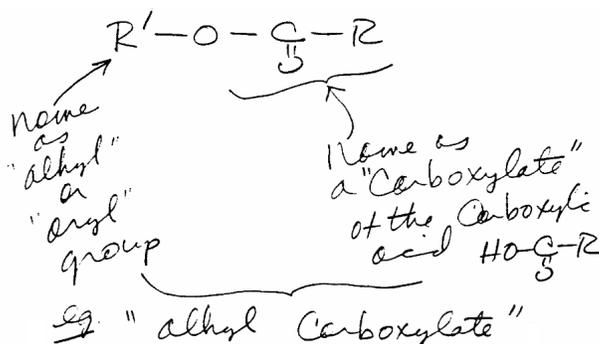
Electron Delocalization. An unshared electron pair on O of the OR' group of *esters* is more extensively delocalized into the C=O group than is the case for an unshared pair on the halogens of *acid halides*. As we mentioned earlier (Figure 15.06), this electron delocalization in esters increases electron density (decreases electron deficiency) on the C of C=O. A major result is that H's α to a C(=O)-OR' group are less acidic than α -H's of *ketones* and *aldehydes*.

Nomenclature (15.3B)

Whether esters are named using *systematic* or *common* nomenclature, their names are composed of two separate words (Figure 15.30) that each describe a specific part of the ester molecule RC(=O)O-R'.

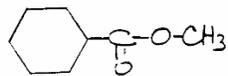
The R' Part. The first word in names of *esters* describes the R' group (Figure 15.31).

Figures 15.31

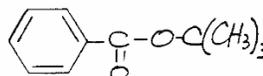


The R' group is often a relatively simple alkyl or aryl group as we showed in Figure 15.30 and show in Figure 15.32.

Figures 15.32



Methyl cyclohexanecarboxylate



t-butyl benzoate



We name that R' group using either its systematic or common alkyl or aryl group name depending on whether we are using systematic or common nomenclature.

The RC(=O)O Part. The second word in the *ester* name describes the RC(=O)O portion of the molecule. We name this part as if it is a *carboxylate anion* RC(=O)O⁻ formed from the carboxylic acid RC(=O)OH (see Figures 15.30-15.32). You can see that we drop the ending "-ic acid" of the acid name and replace it with the ending *-ate*.

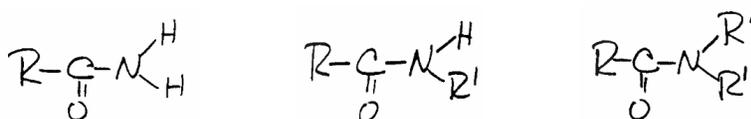
Systematic or Common. It is important to remember not to mix systematic and common nomenclature together in the name of an organic compound. For example, neither the name *isoamyl butanoate* or the name *2-methylpropyl butyrate* are correct for the ester CH₃CH₂CH₂C(=O)O-CH₂CH(CH₃)₂. It's systematic name is *2-methylpropyl butanoate* and its common name is *isoamyl butyrate*.

You can imagine complicated R' groups that may be much more difficult to name as *alkyl* or *aryl* groups than those we have shown in Figures 15.30 and 15.32. When faced with naming such complicated molecules, organic chemists often consult specialized books on organic nomenclature. However, many ester functional groups that we usually encounter have relatively simple alkyl or aryl R' groups such as those we have already seen.

15.4 Amides (R-C(=O)-NR'₂)

Amides are compounds RC(=O)-Z where Z is NR'₂. The two R' groups on N do not need to be the same as each other and can be any mixture of H, alkyl, or aryl groups (Figure 15.33).

Figure 15.33

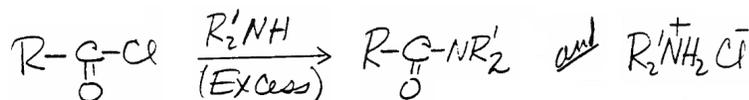


We find the *amide* functional group in many naturally occurring compounds. For example, we will see below, and in Chapter 22, that it is the repeating unit in the backbone of all *proteins*.

Preparation and Reactivity (15.4A)

We can make *amides* RC(=O)NR'₂ by reacting *acid halides* (RC(=O)X) with *amines* (R'₂NH) (Figures 15.09 and 15.34).

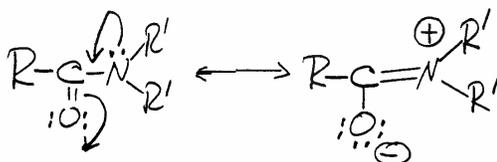
Figure 15.34



Amides are relatively unreactive compared to other R-C(=O)-Z compounds and their interconversion reactions are more limited. This is because the unshared electron pair on N of

NR'_2 is delocalized into the $\text{C}=\text{O}$ group more than in other compounds $\text{R}-\text{C}(=\text{O})-\text{Z}$. We illustrate this with the resonance structures in Figure 15.35.

Figure 15.35



Structure of Amides (15.4B)

The structural features of amides have been extensively studied because the amide functional group is the foundation of protein structure.

Amides are Planar. Electron delocalization in amides (Figure 15.35) causes amide functional groups to be planar (Figure 15.36).

Figure 15.36

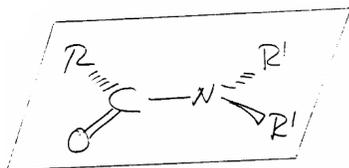
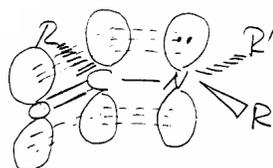


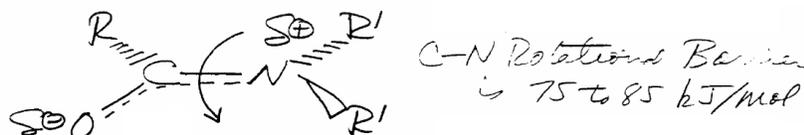
Figure 15.37



This planarity facilitates maximum delocalization of the unshared electron pair on N into the π system of the $\text{C}=\text{O}$ group. A planar N is hybridized sp^2 so its unshared electron pair is in a $2p$ orbital. As a result, it effectively overlaps the $\text{C}=\text{O}$ π molecular orbital (Figure 15.37).

C-N Rotation is Restricted. This electron delocalization in amides (Figure 15.35) causes the $\text{OC}-\text{N}$ bond to have double bond character. This in turn makes the energy required to rotate about that $\text{C}-\text{N}$ partial double bond of amides significantly higher than that for rotation about $\text{C}-\text{N}$ single bonds (Figure 15.38).

Figure 15.38



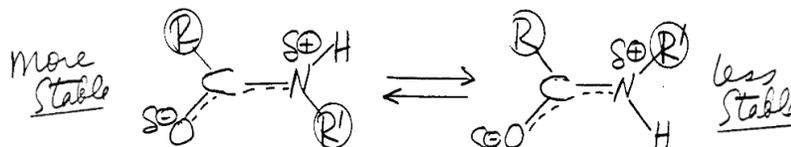
Experimentally determined activation energies required for $\text{C}-\text{N}$ rotation in amides (**$\text{C}-\text{N}$ rotational barrier**) are 75 to 85 kJ/mol. In contrast, rotational barriers for "normal" $\text{C}-\text{N}$ single bonds are about 8 kJ/mol while those for "normal" $\text{C}=\text{N}$ double bonds are on the order of 300 kJ/mol.

These relatively high $\text{C}-\text{N}$ rotational barriers in amides have several interesting consequences. They play a major role in determining the structures of protein molecules and stabilizing

these structures. We briefly discuss this later in this chapter, and in more detail in Chapter 22 where we describe aspects of protein structure. In addition, they affect the geometric structure of amides as we describe below.

cis and trans Isomers of Amides. Because of relatively high C-N rotational barriers, amides with two different R' groups on N are mixtures of geometric isomers (Figure 15.39) and these two isomers can have different stabilities. .

Figure 15.39



In general, the isomer where the larger N-R' group is *cis* to oxygen (closest to oxygen) is more stable than the isomer where that group is *trans* to the C=O oxygen. When the R' group is *trans* to O, the N-R' group is *cis* to the R group on the C=O and this is generally less sterically desirable than when R' is *cis* to O and *trans* to R.

In spite of the 75 to 85 kJ/mol rotational barriers for interconversion of these geometric isomers, we cannot isolate the individual isomers because their lifetimes at room temperature are on the order of 0.5 to 20 seconds. In contrast, you learned in Chapter 8 that we can isolate *cis* and *trans* geometric isomers of *alkenes*. Alkenes have C=C rotational barriers of about 270 kJ/mol, and as a result their lifetimes are essentially infinite ($>10^{26}$ years) at room temperature.

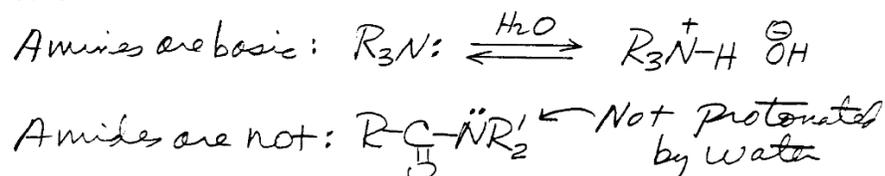
Chemists have determined the magnitude of amide C-N rotational barriers using NMR spectrometry. We describe this at the end of this chapter in the section on the spectrometric features of RC(=O)Z compounds.

Properties of Amides (15.4C)

The NR'₂ group of amides is much less basic than that of amines (R-NR'₂).

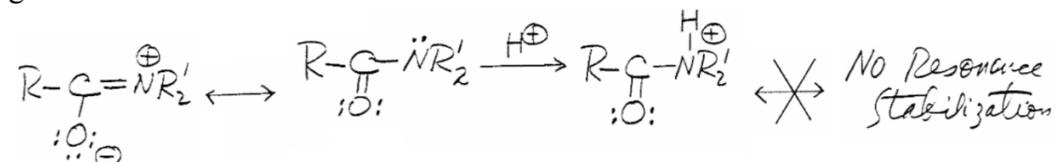
Amide Basicity. While *amines* are strong enough bases to be protonated by water as we described in Chapter 3 and illustrate again in Figure 15.40, this is not the case for *amides*.

Figure 15.40



Amides show no measurable basicity in water because the unshared electron pair on N is delocalized into the C=O group (Figure 15.35). If N is protonated by an acid, as we show in Figure 15.41, the electron pair becomes part of an N-H bond and is no longer available for delocalization.

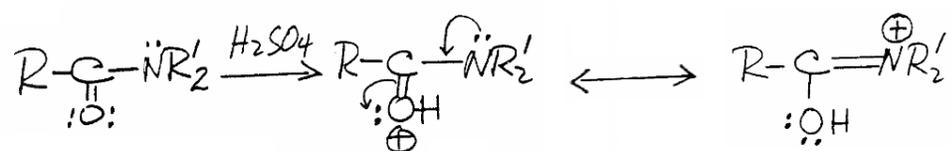
Figure 15.41



As a result, protonation of the NR'₂ group of an amide would cause all of the stabilization energy derived from electron delocalization in the amide to be lost.

In fact, we can protonate amides with strong acids such as sulfuric acid, but protonation does not occur on N. In sulfuric acid and other strong acids, protonation of amides occurs on the O atom of the C=O group as we show in Figure 15.42.

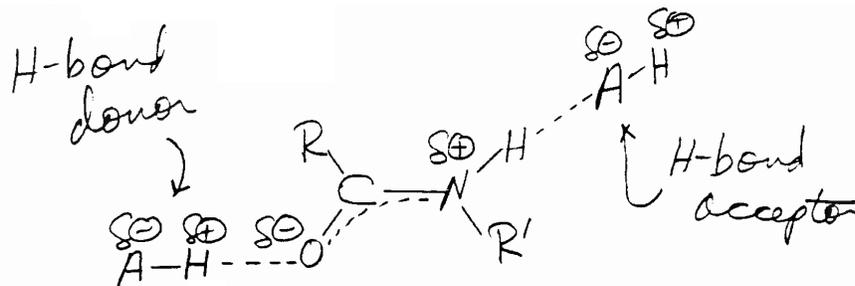
Figure 15.42



In spite of this O-protonation, we can see that the unshared electron pair on N remains conjugated with the C=O group (Figure 15.42).

Amide Hydrogen Bonding. The polar character of amides, resulting from electron delocalization, enables them to form relatively strong hydrogen bonds involving both their C=O group and any N-H protons. These hydrogen bonds may be between individual amide molecules in the same solution, or between an amide molecule and other molecules (H-A) that act as H-bond donors or acceptors (Figure 15.43).

Figure 15.43



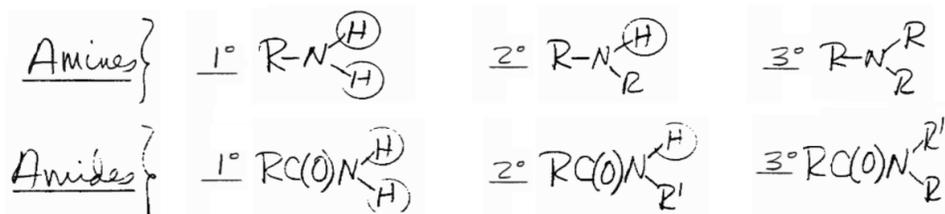
We will see in Chapter 22 that this hydrogen bonding is an important characteristic of protein structure.

Amides as Solvents. The simple amide $\text{H}-\text{C}(=\text{O})-\text{N}(\text{CH}_3)_2$ named *N,N*-dimethylformamide (DMF) (see next section), is frequently used as a reaction solvent. We classify it as a *polar aprotic* solvent because it is *polar* as described above, and *aprotic* (contains no H's attached to heteroatoms). It dissolves both polar and nonpolar substances, and we described its use in nucleophilic substitution reactions in Chapter 7. We explain its name in the next section on nomenclature.

Nomenclature (15.4D)

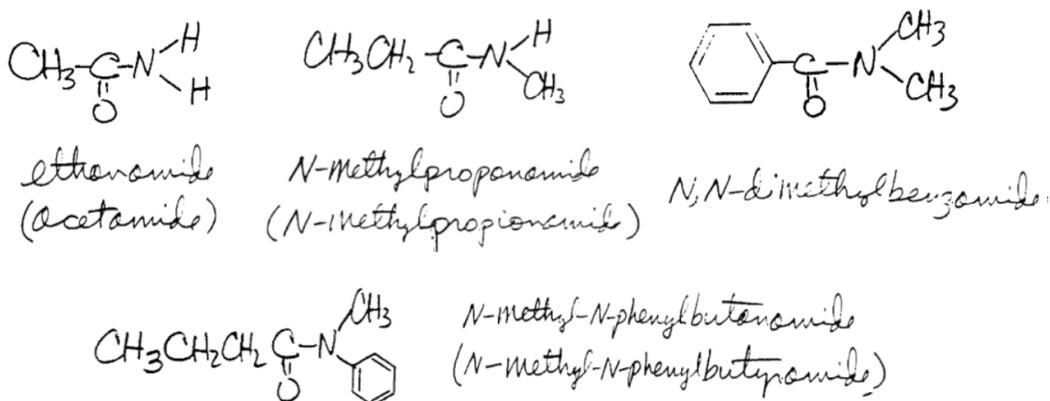
Amide nomenclature has similarities to nomenclature of amines (Chapter 2). As is the case for amines, designate amides as 1° , 2° or 3° , depending on the number of H's on their N atoms (Figure 15.44).

Figure 15.44



We also place the name or names of R' groups on the N atom first in the name of the amide (Figure 15.45) preceded by the prefix "N".

Figure 15.45



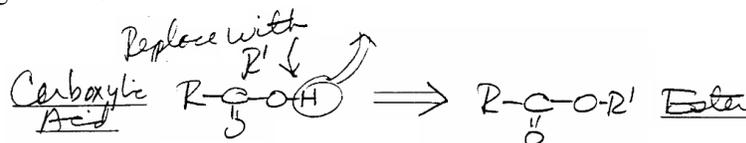
We similarly place the name of the R' group of esters ($\text{R}-\text{C}(=\text{O})\text{O}-\text{R}'$) first in ester names, but it is separated from the rest of the ester name by a space unlike amide names where there are no spaces.

The *parent name* of any amide is that of its corresponding 1° amide where NR'_2 is NH_2 ($\text{R}-\text{C}(=\text{O})\text{NH}_2$). We derive the name of this 1° amide from the name of the corresponding *carboxylic acid* $\text{R}-\text{C}(=\text{O})\text{OH}$. In *systematic names*, we drop the ending *-oic acid* from the carboxylic acid name, and add the ending *-amide*. When we use the *common* name of the acid

as the basis for amide nomenclature, we replace the ending *-ic acid* with *-amide*.

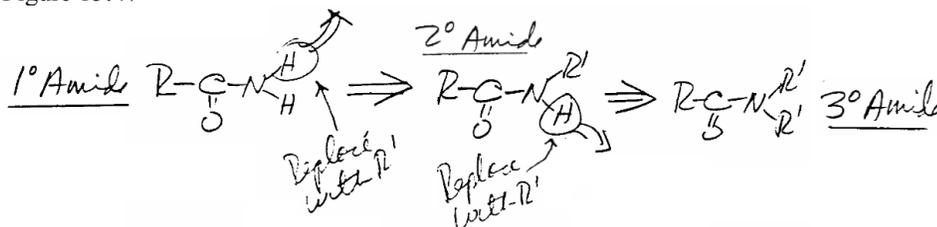
Nomenclature of Acids, Esters, and Amides. It is informative to compare the relationship between 1°, 2°, and 3° amides, with that between *carboxylic acids* and *esters*. Carboxylic acids ($\text{RC}(=\text{O})\text{OH}$) and esters ($\text{RC}(=\text{O})\text{OR}'$) are in different classes when an H or R' is bonded to the O of " $\text{RC}(=\text{O})\text{O}$ " (Figure 15.46).

Figure 15.46



Although a similar difference exists between 1° ($\text{RC}(=\text{O})\text{-NH}_2$), 2° ($\text{RC}(=\text{O})\text{-NHR}'$) and 3° ($\text{RC}(=\text{O})\text{-NR}'_2$) amides (Figure 14.2b), they are in the same class.

Figure 15.47

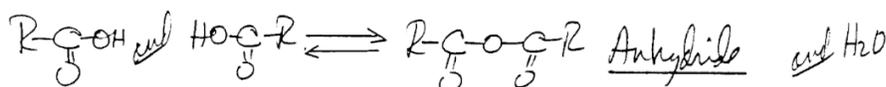


This historic inconsistency is probably the result of the comparative properties of these various compounds. *Carboxylic acids* are "acidic", while *esters* are not. In contrast, 1°, 2°, or 3° *amides* are all neutral compounds. We described a similar situation, in Chapter 3, for alcohols (R-OH) and ethers ($\text{R-OR}'$) compared to 1° (R-NH_2), 2° ($\text{R-NHR}'$), and 3° ($\text{R-NR}'_2$) amines.

15.5 Anhydrides ($\text{R-C}(=\text{O})\text{-O-C}(=\text{O})\text{-R}$)

Organic anhydrides are products of the reversible dehydration reaction of two carboxylic acids that we show in Figure 15.48.

Figure 15.48



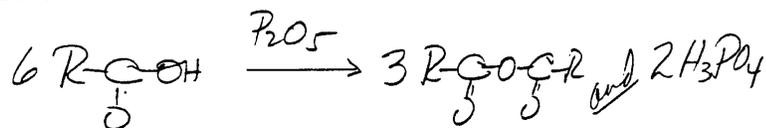
Preparation, Reactivity, and Properties (15.5A)

Anhydrides formed in the reaction above are **symmetrical anhydrides**, but **mixed anhydrides** also exist where the two R groups are not the same.

Preparation of Symmetrical Anhydrides. All carboxylic acids are in equilibrium with their anhydrides (Figure 15.48), but the equilibrium lies far on the side of the carboxylic acids. We can prepare anhydrides using the reaction in Figure 15.48, but we must drive the equilibrium

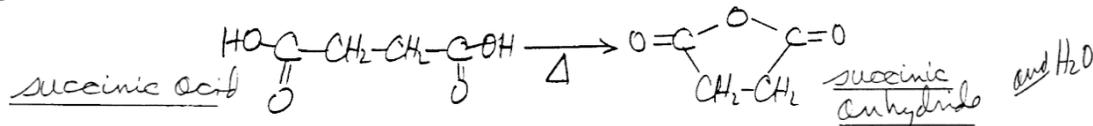
to the right side (product side) by removing water from the reaction mixture. We accomplish this by heating the carboxylic acid with a dehydrating agent such as P_2O_5 that reacts with the water to produce phosphoric acid (H_3PO_4) (Figure 15.49).

Figure 15.49



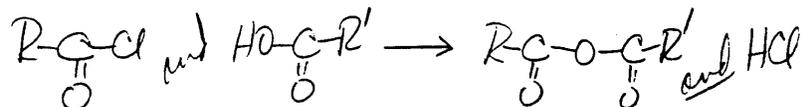
This reaction converts one anhydride into another anhydride since P_2O_5 is the anhydride of H_3PO_4 . With dicarboxylic acids that cyclize to give 5 or 6 membered ring anhydrides, we can form those anhydrides by just heating the dicarboxylic acid without a dehydrating reagent (Figure 15.50).

Figure 15.50



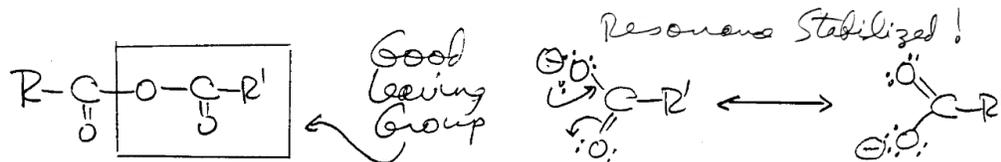
Preparation of Mixed Anhydrides. We can also form anhydrides from reaction of acid halides and carboxylic acids as we showed earlier in Figure 15.09. This type of reaction serves as a way to make *mixed anhydrides* where the two R groups are different (Figure 15.51).

Figure 15.51



Reactivity of Anhydrides. Anhydrides are less reactive in nucleophilic acyl substitution than *acid halides*, but are more reactive than *carboxylic acids*, *esters*, and *amides*. This is because *nucleophilic acyl substitution* reactions on anhydrides give carboxylate ions as leaving groups (Figure 15.52).

Figure 15.52

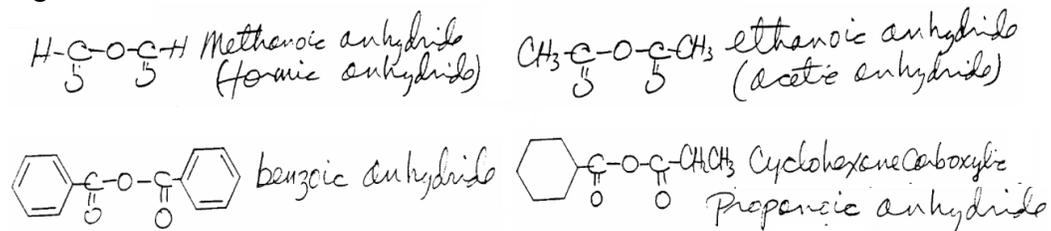


Carboxylate ions are relatively good leaving groups because they are resonance stabilized and we discuss this in more detail in Chapter 16. Since anhydrides are relatively reactive, they serve as precursors to several different compounds $\text{R}-\text{C}(=\text{O})-\text{Z}$ as we previously showed in Table 15.01.

Nomenclature (15.5B)

Names of *symmetrical anhydrides* are derived from the name of the acid from which they form. We replace the word *acid* with *anhydride* as we show in Figure 15.53.

Figure 15.53

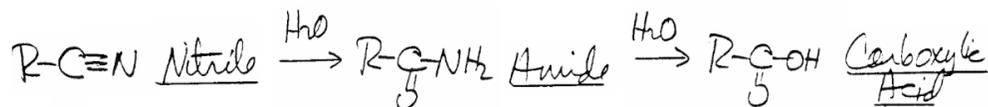


We name *mixed anhydrides* (Figure 15.53) by placing both acid names in alphabetical order before the word *anhydride*. This is analogous to the common nomenclature system for ethers (Chapter 2).

15.6 Nitriles (R-C≡N)

Nitriles (R-C≡N) are structurally very different from the R-C(=O)-Z compounds that we have discussed so far in this chapter. We include them here because they react similarly to R-C(=O)-Z compounds and also give R-C(=O)-Z compounds as reaction products. An example is the hydrolysis of nitriles to give amides, followed by amide hydrolysis to give carboxylic acids (Figure 15.54).

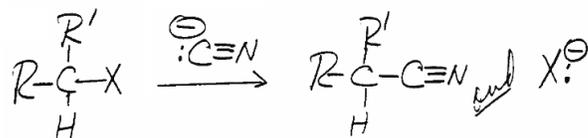
Figure 15.54

**Preparation and Properties (15.6A)**

The choice of reactions to prepare organic nitriles (R-C≡N) depends on whether the R group is *alkyl* or *aryl*.

Alkyl Nitriles. We can prepare a variety of *alkyl nitriles* with *nucleophilic substitution* reactions between haloalkanes and cyanide ion (Figure 15.55).

Figure 15.55



This reaction is especially useful because it (1) adds an additional C to the molecule, (2) forms a C-C bond, (3) provides a product that can be sequentially converted into all of the R-C(=O)-Z compounds, and (4) uses inorganic cyanide ion that is inexpensive and readily available as the source of the additional C.

Aryl Nitriles. In contrast, we cannot prepare *aryl nitriles* ($\text{Ar-C}\equiv\text{N}$) by nucleophilic substitution. Instead we use the **Sandmeyer reaction** in which an aromatic diazonium ion reacts with CuCN (Figure 15.56). We prepare *aromatic diazonium ions* from *aromatic amines* by reaction with nitrous acid (Figure 15.57).

Figure 15.56

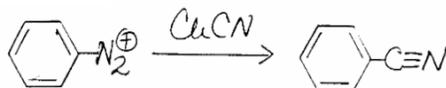
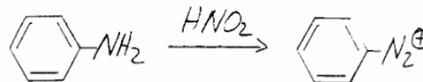


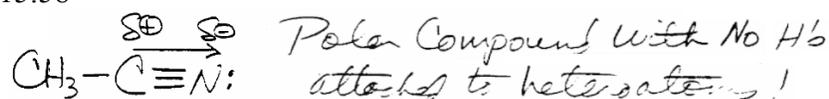
Figure 15.57



While the Sandmeyer reaction (Figure 15.56) looks like it could be a nucleophilic substitution reaction, it actually has a free radical mechanism that we do not describe here.

Properties of Nitriles. The lowest molecular weight nitrile, $\text{CH}_3\text{C}\equiv\text{N}$ (*acetonitrile*), is an important solvent for both polar and nonpolar compounds in a variety of reaction systems. It is polar (Figure 15.58), but has no H's attached to heteroatoms such as O or N.

Figure 15.58

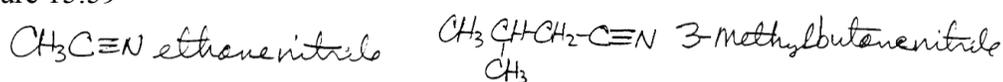


Like *N,N*-dimethylformamide (DMF) described earlier in this chapter, *acetonitrile* is one of a group of structurally diverse solvents called *polar aprotic solvents* described in Chapter 7.

Nomenclature (15.6B)

We use the longest hydrocarbon chain containing the nitrile ($\text{C}\equiv\text{N}$) group to systematically name nitriles as **alkanenitriles** (Figure 15.59).

Figure 15.59



The *alkane* portion of the name is that of an alkane chain with the same number of carbons. We include the C of the $\text{C}\equiv\text{N}$ group in the carbon chain length just as we did in systematic nomenclature of aldehydes, ketones, and carboxylic acids.

We name cyclic nitriles as **cycloalkanecarbonitriles** (Figure 15.60).

Figure 15.60

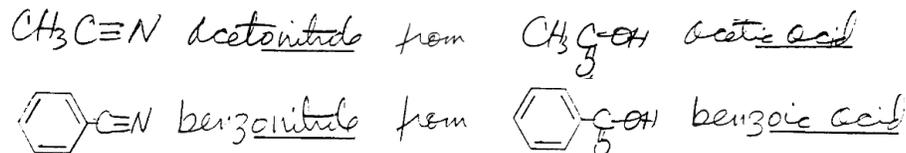


This nomenclature is analogous to that used for cycloalkanecarboxylic acids shown earlier.

Some simple nitriles have common names that are derived from the common names of the acids to which they are related. We form these names by dropping the ending *-ic acid* or *-oic*

acid from the name of the related acid and adding the ending *-onitrile* (Figure 15.61).

Figure 15.61



15.7 Lactones, Lactams, and Cyclic Anhydrides

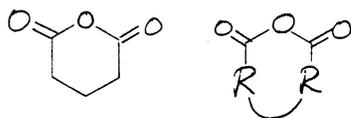
We have shown a number of examples of $\text{R}-\text{C}(=\text{O})-\text{Z}$ compounds in which the R group is a ring. In contrast to these "cyclic" compounds, we show examples here where the $\text{C}(=\text{O})-\text{Z}$ group is actually part of a ring structure.

Structure (15.7A)

Cyclic anhydrides, **lactones**, and **lactams** have the $\text{C}(=\text{O})\text{Z}$ group in a ring.

Cyclic Anhydrides. We showed examples of *cyclic anhydrides* in the anhydride section and redraw one of those here (Figure 15.62).

Figure 15.62



The two R groups in the general anhydride structure $\text{RC}(=\text{O})-\text{O}-(\text{O}=\text{C})\text{R}$ are both parts of the same organic unit. We can think of the R groups bonded to each other as we represent with the connecting line in the general structure above.

Lactones and Lactams. When the R group on the carbonyl of an ester or amide is "bonded" to the R' group on the OR' of esters, or on the NR'_2 of amides, the resulting cyclic compounds have the general structures in Figure 15.63.

Figure 15.63



These cyclic compounds are named *lactones* and *lactams*, respectively.

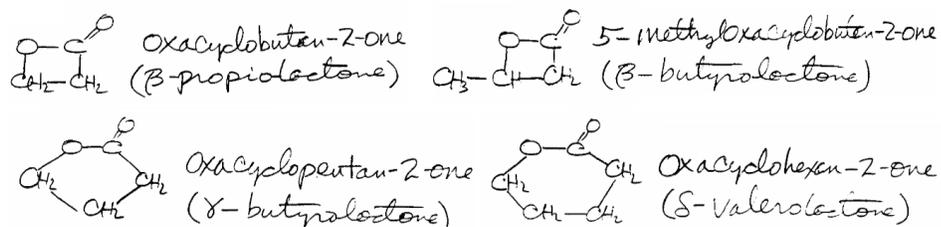
Their ring sizes can range from highly strained three-membered rings, through unstrained five and six membered rings, to ring sizes that are even greater. *Lactone* and *lactam* rings are frequently found in molecules that are biologically important and we give some examples at the end of this chapter.

Nomenclature (15.7B)

We named cyclic anhydrides earlier in the anhydride section. We describe the nomenclature for *lactones* and *lactams* here.

Lactones. We show some simple lactones in Figure 15.64 along with their *systematic* and *common* names.

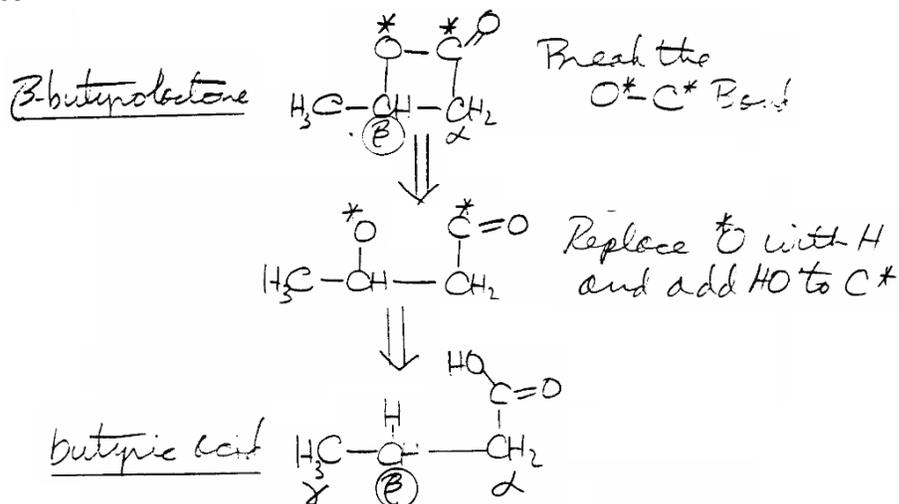
Figure 15.64



Their *systematic* names indicate that we can view lactones as having the dual functionality of *cyclic ethers* and *cyclic ketones*. We derive the root name of *lactones* from the total number of atoms in the lactone ring. We identify O atom in the ring using the prefix *oxa-* while we specify the adjacent C=O group using the number 2 in the name.

Common names in Figure 15.64 for the simple lactones are based on those of carboxylic acids with the same number of C's present in the lactone ring. We identify the carboxylic acid by breaking the O*-C*(=O) bond in the lactone (Figure 15.65), replacing O* with H, and adding HO to the C*.

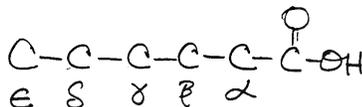
Figure 15.65



Use of Greek Letters. In common names we specify the lactone ring size using a Greek letter. For example, α , β , γ , δ , or ϵ , indicate a ring size of 3, 4, 5, 6, or 7 atoms, respectively. These Greek letters identify the C to which the *lactone* ring O is attached. We used these Greek letters in the

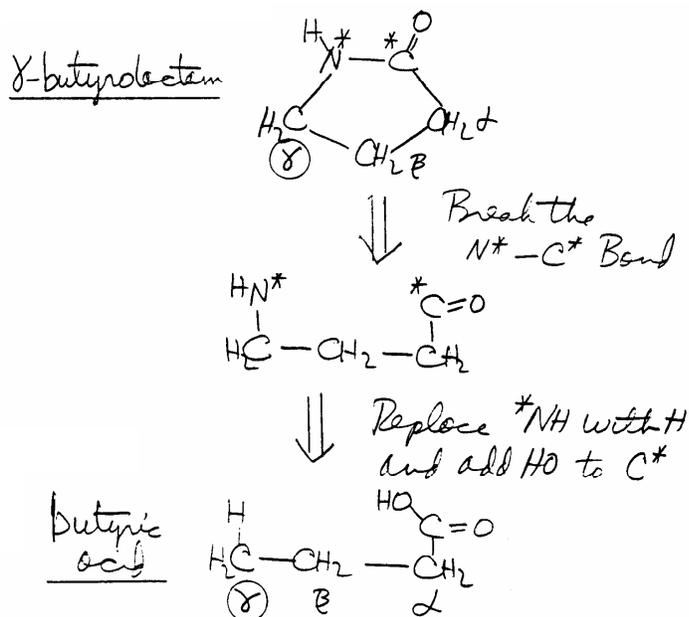
common nomenclature of both carboxylic acids and aldehydes (Chapter 13) to identify the location of C atoms with respect to the C=O group. We show that convention again in Figure 15.66 for carboxylic acids.

Figure 15.66



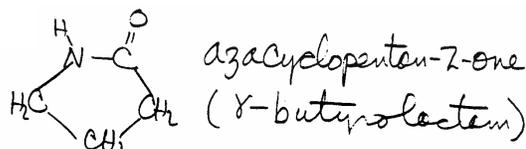
Lactams. *Lactam* systematic nomenclature is analogous to that of *lactones* but uses the prefix *aza-* to indicate the nitrogen atom in the ring. As with lactones, the common method of nomenclature for *lactams* uses the common name of the "parent" carboxylic acid that forms by breaking the N*-C*(=O) bond, replacing N* with H, and adding HO to the C* (Figure 15.67).

Figure 15.67



We compare the systematic and common names of a *lactam* in Figure 15.68.

Figure 15.68



15.8 Biologically Important Molecules with R-C(=O)-Z Groups

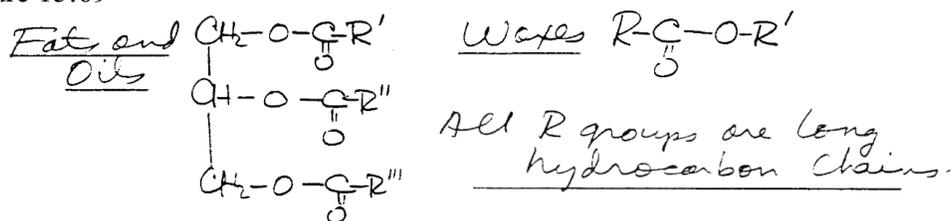
Most of the functional groups we have presented are found in molecules in living systems (bioorganic molecules), or in molecules that have biological effects such as pharmaceuticals or drugs (biologically active molecules). Three from this chapter that we describe here are the

ester functional group (R-C(=O)-OR'), the *amide* functional group (R-C(=O)-NR'₂), and the *lactam* (cyclic amide) functional group. Parts of this section preview material that we present in more detail in Chapters 20 to 23.

Esters (15.8A)

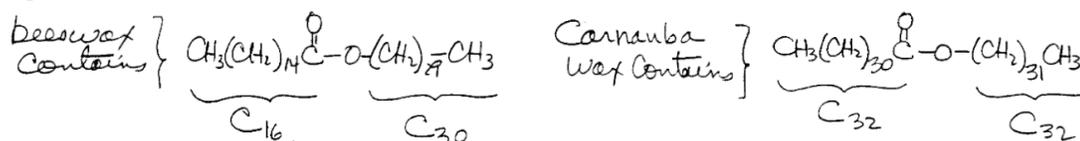
We find the ester functional group in **fats**, **oils**, and **waxes** that occur naturally in both plants and animals. In fact the ester functional group is the primary functional group in these biologically important compounds as we see in their general structures in Figure 15.69.

Figure 15.69



Waxes. Naturally occurring *waxes* are often mixtures of various compounds including esters where the R and R' groups have long straight alkyl chains as we show with two examples in Figure 15.70.

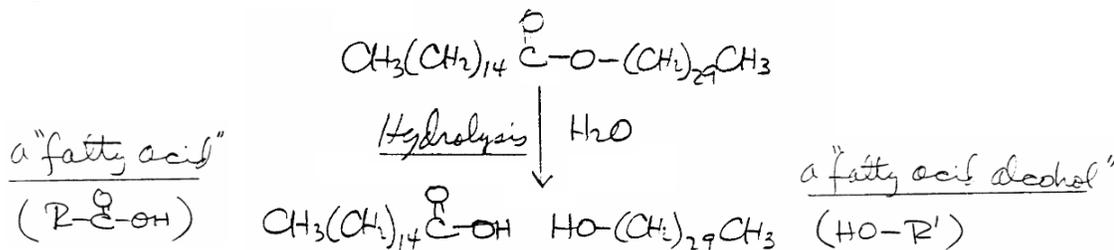
Figure 15.70



While the number of C's in the R-C(=O) and O-R' portions of these esters are sometimes the same, this is not always the case. However, in all cases the R-C(=O) and O-R' groups of esters in waxes contain an even number of C's. This occurs because these long chains are synthesized in the organism from two-carbon fragments called **acetate units** as we will describe in Chapter 21.

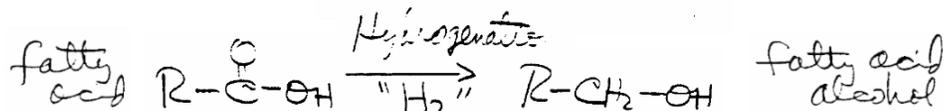
When we hydrolyze these naturally occurring esters found in waxes, we obtain a carboxylic acid and an alcohol just as we do for hydrolysis of any ester (Figure 15.71).

Figure 15.71



We refer to the long straight-chain carboxylic acid formed in this reaction as a **fatty acid**, while we can call the long straight-chain alcohol a **fatty acid alcohol**. These long chain carboxylic acids are called *fatty acids* because they also arise in hydrolysis of fats and oils as we describe below. The alcohols are called *fatty acid alcohols* because we can form them by hydrogenation (reduction) of *fatty acids* (Figure 15.72).

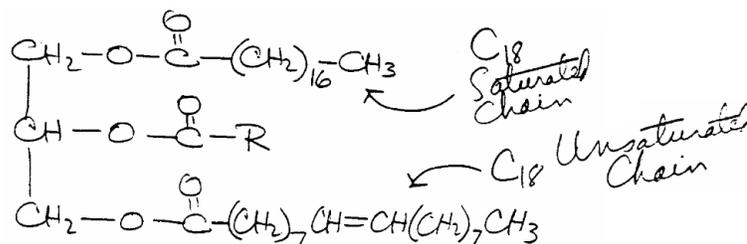
Figure 15.72



Fats and Oils. Naturally occurring *fats* and *oils* contain mixtures of **triesters** that have the general structure we showed in Figure 15.69. We call these triester mixtures *fats* if they are solids at "room temperature", and *oils* if they are liquids.

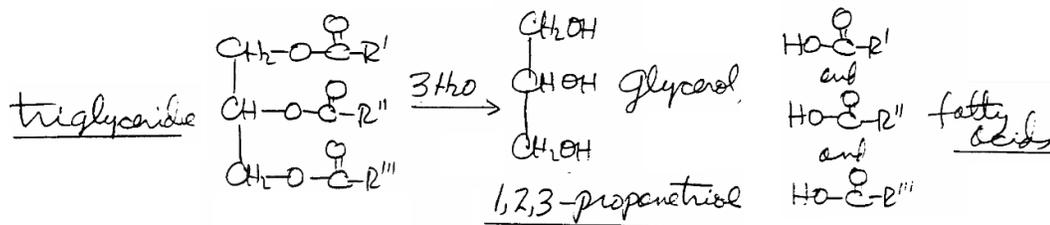
While the three triester R groups can be identical or different from each other, they are all long hydrocarbon chains. These chains can be *saturated* (contain linear alkyl groups) as in *waxes*, or *unsaturated* (contain one or more C=C groups) (Figure 15.73).

Figure 15.73



Hydrolysis of a typical *fat* or *oil*, gives glycerol (1,2,3-propanetriol) and three carboxylic acid (*fatty acid*) molecules (Figure 15.74).

Figure 15.74



Because they are triesters of glycerol, *fats* and *oils* are called **triglycerides**.

We show some of the more common *fatty acids* that arise by hydrolysis of fats and oils in Table 15.02 [next page]. These names are the *common* names of these fatty acids. We call those containing C=C groups **unsaturated fatty acids** while we call those without C=C groups **saturated fatty acids**. In the *unsaturated fatty acids* from fats and oils, the C=C

groups are *cis*. Whether saturated or unsaturated, they all contain an even number of C atoms.

Table 15.02. Some Common Fatty Acids

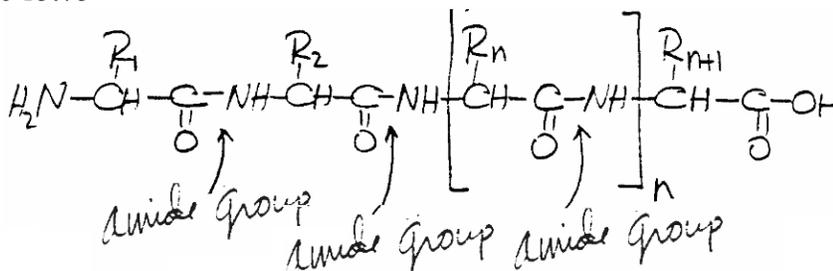
Fatty Acid (R-CO ₂ H)	Name	Number of C's
CH ₃ (CH ₂) ₁₀ CO ₂ H	lauric acid	C ₁₂
CH ₃ (CH ₂) ₁₂ CO ₂ H	myristic acid	C ₁₄
CH ₃ (CH ₂) ₁₄ CO ₂ H	palmitic acid	C ₁₆
CH ₃ (CH ₂) ₁₆ CO ₂ H	stearic acid	C ₁₈
CH ₃ (CH ₂) ₇ CH=CH(CH ₂) ₇ CO ₂ H	oleic acid	C ₁₈
CH ₃ (CH ₂) ₄ CH=CHCH ₂ CH=CH(CH ₂) ₇ CO ₂ H	linoleic acid	C ₁₈

Amides (15.8B)

The amide functional group is present in a variety of bioorganic compounds.

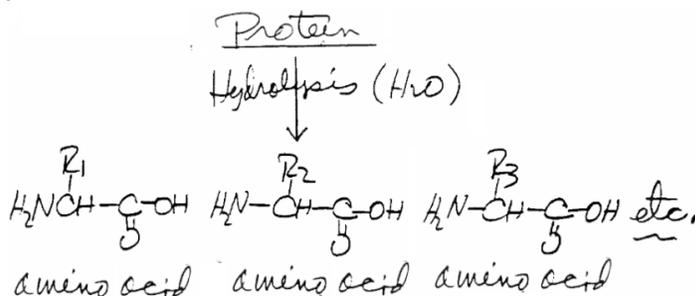
Proteins. Proteins are large molecules that contain a variety of functional groups. The major distinguishing feature common to all of them is a backbone composed of repeating amide units (Figure 15.75).

Figure 15.75



When we hydrolyze proteins, we hydrolyze the amide groups in the protein backbone leading to a mixture of **amino acids** that each contain at least one amino group (NH₂) and carboxylic acid group (CO₂H) (Figure 15.76).

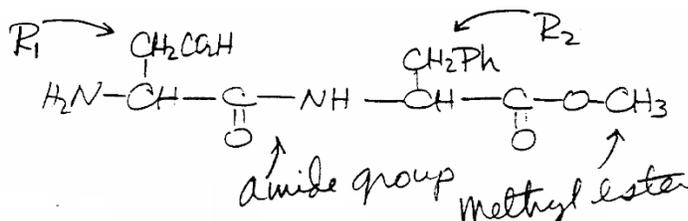
Figure 15.76



Amino acids differ from each other because of their different R' groups. There are more than 20 different R' groups typically found on *amino acids* that we describe in detail in Chapter 22.

Peptides. Peptides are structurally similar to proteins since they are made up of individual amino acids joined together by amide functional groups. But often they are small molecules that can include as few as two amino acids and they may or may not be biologically active. The artificial sweetener **aspartame** is the methyl ester of a dipeptide (Figure 15.77).

Figure 15.77

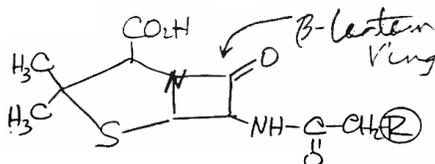


It has not only the "backbone" amide functional group, but also a carboxylic acid group, an ester group and an amino group.

Lactams (15.8C)

Some of the most well known *lactams* with biological activity are **penicillins**. There are several different penicillins, and all of them have the **general structure** that we show in Figure 15.78.

Figure 15.78



This general structure is composed of two fused rings with several substituent groups. The four-membered ring is a lactam ring, while the five-membered ring includes both N and S atoms. In addition to the lactam functional group, there is a side-chain amide group and a side-chain carboxylic acid group. The circled R group has a variety of different structures that distinguish the various types of penicillins.

15.9 Spectrometric Properties of R-C(=O)-Z and R-C≡N

The NMR, IR, and UV-Visible spectral properties of compounds of the structure R-C(=O)-Z are similar to the spectral properties of aldehydes, ketones, and carboxylic acids discussed in Chapter 13. We note important differences in the following sections and also describe the spectrometric properties of nitriles (R-C≡N).

Ultraviolet-Visible Spectrometry (15.9A)

The UV-Visible spectral features of the R-C(=O)-Z compounds are essentially the same as those of other carbonyl compounds already discussed. As is the case for ketones and

aldehydes, UV-Vis absorption of R-C(=O)-Z groups requires conjugation of the C=O with one or more multiple bonds in the molecule. The C≡N group is analogous to C=O groups and also requires conjugation with an extended π system for UV-Vis absorption.

Infrared Spectrometry (15.9B)

C=O Stretch. All R-C(=O)-Z compounds show strong absorption bands for C=O stretching. The position of this band is in the same general region of an IR spectrum as those for aldehydes and ketones, but the Z group does influence the frequency of its absorption maximum (Table 15.03).

Table 15.03. Frequency Ranges for C=O Stretching Bands in R-C(=O)-Z

Compound	Frequency (cm⁻¹)
Aldehyde	1740-1720
Ketone	1715
Acid Halide	1815-1785
Amide	1690-1650
Anhydrides (two bands)	
acyclic	1820 <u>and</u> 1750
cyclic (5-ring)	1865 <u>and</u> 1780
Carboxylic acid	
monomer	1760
dimer	1720-1706
Ester	1750-1735
δ -Lactone (six ring)	1750-1735
γ -Lactone (five ring)	1795-1760

The frequency of the C=O band for *amides* depends on whether the amide is 1°, 2°, or 3°, and also on its concentration in solution. This is the result of H-bonding involving N-H hydrogens as we described earlier. The C=O band frequency in amides is also lower than those for other carbonyl compounds due to the resonance interaction between the unshared electron pair on N and the C=O group.

Anhydrides show two C=O stretching bands that can overlap. The wavenumber (frequency) values given in Table 15.03 are for common saturated acyclic anhydrides such as *acetic anhydride* (CH₃C(=O)-O-C(=O)CH₃). Cyclic anhydrides such as succinic anhydride (Figure 15.50) with a five-membered ring show a band shift to higher frequencies. The effect of ring strain on the absorption frequency of a C=O is also evident in the data in Table 15.03 for the five-membered lactone. They show a shift of the C=O band to higher frequencies than those for acyclic esters or six-membered ring lactones.

C-O Stretch. Strong C-O stretching bands are visible in the IR spectra of *esters, lactones,* and *anhydrides.* Typical esters show this band at 1300-1000 cm^{-1} . There are two C-O stretching bands for anhydrides that are broad and occur over the regions of about 1300-1175 cm^{-1} and 950-910 cm^{-1} . This absorption often appears as a single broad band overlapping both of these spectral regions.

N-H Stretch and N-H Bend. 1° and 2° amides with N-H bonds show both N-H stretching and bending bands. 1° amides with two N-H bonds show two N-H stretching bands at about 3520 and 3400 cm^{-1} , while 2° amides with one N-H bond show a single band in the region of 3500-3400 cm^{-1} . N-H bending bands occur in the region 1620-1590 cm^{-1} .

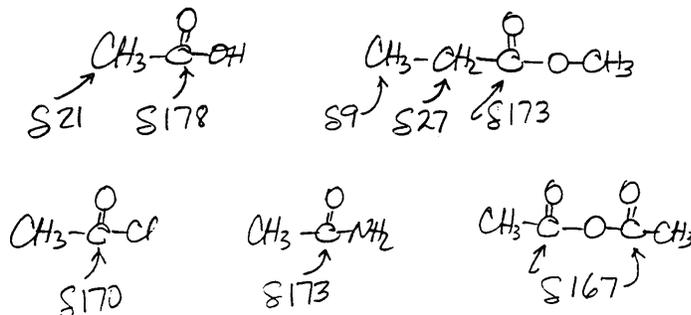
C≡N Stretch. Nitriles show a moderate band for C≡N stretch in the region of 2260-2240 cm^{-1} . Such an absorption is very useful in determining that a C≡N group is present because this IR spectral region is generally free of absorption bands except for compounds with triple bonds such as nitriles (C≡N) and alkynes (C≡C).

NMR Spectrometry (15.9C)

As is the case for all compounds containing the C=O group, the polar character and the sp^2 hybridization of the C=O carbon have strong influences on both the ^{13}C and ^1H NMR of carbonyl compounds. Although there are some specific differences, the general effects of the C=O group on NMR spectra for ketones, aldehydes, and carboxylic acids described in Chapter 12 also apply to the R-C(=O)-Z compounds in this chapter.

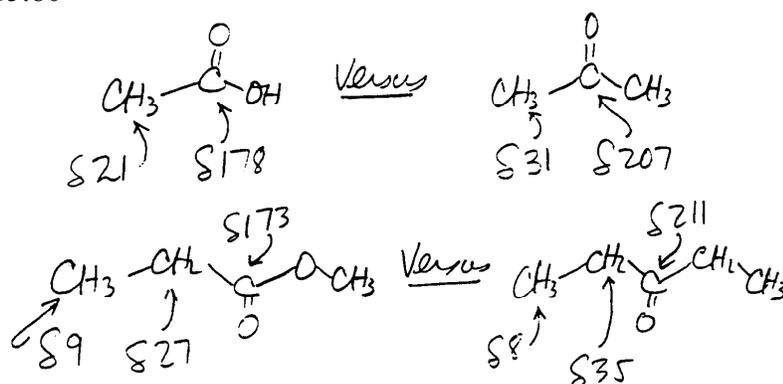
^{13}C NMR. As with ketones and aldehydes, $^{13}\text{C}=\text{O}$ resonance signals of R-C(=O)-Z have large chemical shift values. While these δ values range from $\delta 150$ to $\delta 185$ (Figure 15.79), they are smaller than those for ketones and aldehydes that are close to $\delta 200$.

Figure 15.79



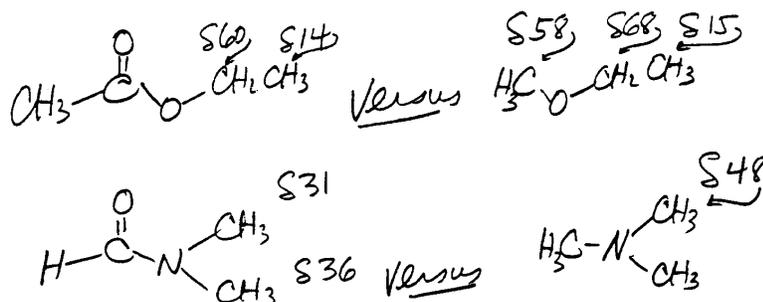
We see that the C=O group also influences the chemical shifts of neighboring ^{13}C atoms. However, the effect of the C(=O)-Z groups on these neighboring atoms is slightly less than that of C(=O)-R groups of ketones and aldehydes (Figure 15.80) [next page].

Figure 15.80



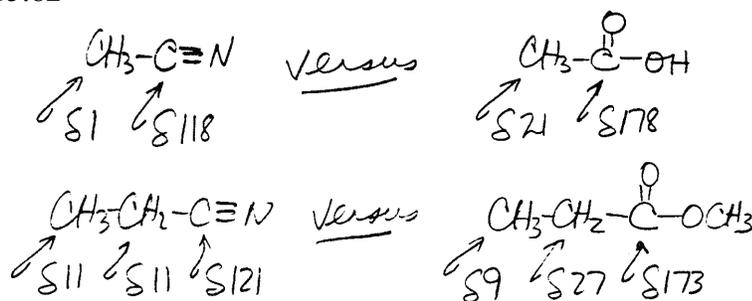
The chemical shifts of ^{13}C atoms directly attached to oxygen in the OR' groups of *esters* ($\text{R}-\text{C}(=\text{O})-\text{OR}'$) and to nitrogen in the NR'_2 groups of *amides* are large and comparable to those for ^{13}C atoms in alkyl groups of alcohols and amines (Figure 15.81)

Figure 15.81



In contrast, the δ value for the $^{13}\text{C}\equiv\text{N}$ carbon is somewhat smaller than those for $\text{C}=\text{O}$ groups (Figure 15.82).

Figure 15.82

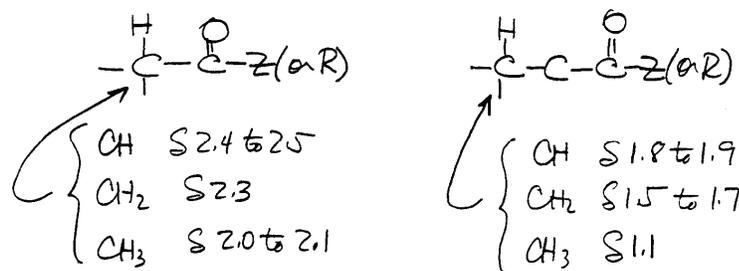


The effect of $\text{C}\equiv\text{N}$ on δ values of adjacent C atoms is much less than that of $\text{C}=\text{O}$. The origin of the anomalously small δ values for ^{13}C atoms directly attached to $\text{C}\equiv\text{N}$ is identical to that described for alkynes in Chapter 8.

^1H NMR. The effects of $\text{C}(=\text{O})-\text{Z}$ groups on the ^1H chemical shifts are very similar to those of the $\text{C}(=\text{O})-\text{R}$ groups of ketones and aldehydes. In the absence of other substituent groups, the chemical shift values of ^1H 's on C's that are α to $\text{C}=\text{O}$ groups range from $\delta 2$ to

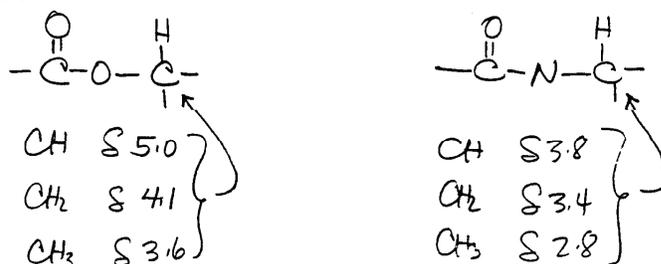
δ 2.5 depending on whether the other R groups on that carbon are H or alkyl, while those for ^1H 's on C's that are β to $\text{C}=\text{O}$ range from about δ 1.1 to δ 1.9 (Figure 15.83).

Figure 15.83



The electronegativities of O and N also affect the chemical shift of ^1H 's attached the C of a C-O or C-N in *esters* and *amides* (Figure 15.84).

Figure 15.84

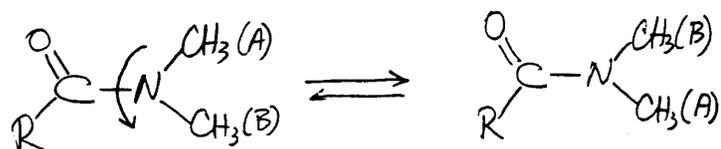


The O of an ester has a significantly greater effect than the N of an amide.

A $\text{C}\equiv\text{N}$ bond affects the δ values for ^1H 's in the same way as $\text{C}=\text{O}$ groups. Special effects associated with the $\text{C}\equiv\text{N}$ bond, like those for $\text{C}\equiv\text{C}$, do not extend beyond atoms directly attached to the $\text{C}\equiv\text{N}$ bond.

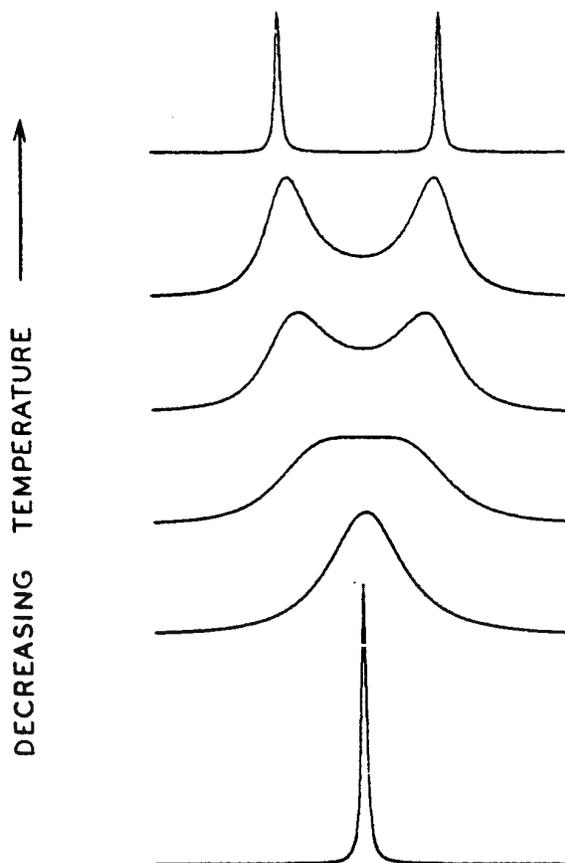
Determination of C-N Rotational Barriers in Amides. NMR is a valuable tool for determining the rate constants for certain very fast reactions. An example is rotation about the C-N bonds in amides mentioned earlier in this chapter and illustrated again in Figure 15.85 for an N,N-dimethylamide.

Figure 15.85



It turns out that the appearance of the ^1H NMR spectrum of amides depends on the temperature of the sample when the NMR spectrum is determined. We show this effect of temperature on the ^1H NMR lines for the N- CH_3 groups of an N,N-dimethylamide in Figure 15.86 [next page].

Figure 15.86



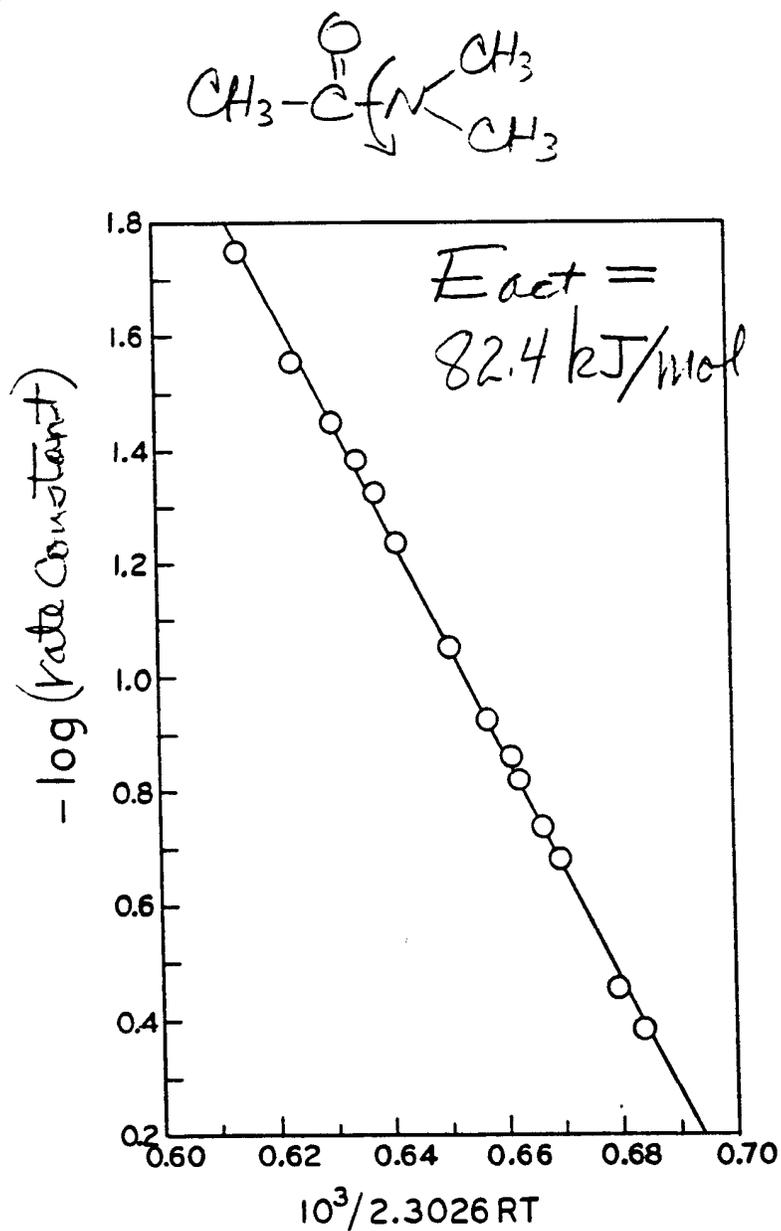
Note that there are separate NMR signals for each of the two N-CH₃ methyl groups of N,N-dimethylacetamide at temperatures below about 40°C, but just a single signal for these two N-CH₃ methyl groups at temperatures above 70°C.

We expect two separate peaks if each N-CH₃ group is restricted to its own location *cis* or *trans* to the O of the C=O group since the two locations are chemically nonequivalent. However, as we increase the temperature of the sample, the rate of rotation about the C-N bond increases. As a result the two N-CH₃ groups (labelled (A) and (B) in Figure 15.85) exchange positions with each other at an increasingly rapid rate. Ultimately, a rotational rate is reached that is faster than the ability of the NMR spectrometer to detect the N-CH₃ resonance signals in the separate locations *cis* and *trans* to C=O. At that point we observe only one peak that has a δ value halfway between that of the two individual N-CH₃ signal positions.

There is a range of temperature values where the N-CH₃ signals undergo a gradual transition from two peaks to one peak. We can use the exact line shape of the NMR spectrum, as the

two peaks coalesce into a single peak, to calculate a rate constant for C-N rotation corresponding to each temperature. We can then use these rate constants and their corresponding temperatures to calculate an activation energy for the C-N rotational process as shown in Figure 15.87.

Figure 15.87



This activation energy is the C-N rotational barrier described earlier in this chapter.