

Notice, however, that there is a significant difference in the chemical shifts of the corresponding signals in the two spectra. The methyl singlet is more shielded (δ 2.0) when it is bonded to the carbonyl group of ethyl acetate than when it is bonded to the oxygen of methyl propanoate (δ 3.6). The methylene quartet is more shielded (δ 2.3) when it is bonded to the carbonyl group of methyl propanoate than when it is bonded to the oxygen of ethyl acetate (δ 4.1). Analysis of only the number of peaks and their splitting patterns does not provide an unambiguous answer to structure assignment in esters; chemical-shift data such as that just described must also be considered.

The chemical shift of the N—H proton of amides appears in the range δ 5–8. It is often a very broad peak; sometimes it is so broad that it does not rise much over the baseline and is easily overlooked.

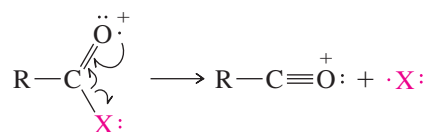
^{13}C NMR: The ^{13}C NMR spectra of carboxylic acid derivatives, like the spectra of carboxylic acids themselves, are characterized by a low-field resonance for the carbonyl carbon in the range δ 160–180. The carbonyl carbons of carboxylic acid derivatives are more shielded than those of aldehydes and ketones, but less shielded than the sp^2 -hybridized carbons of alkenes and arenes.

The carbon of a $\text{C}\equiv\text{N}$ group appears near δ 120.

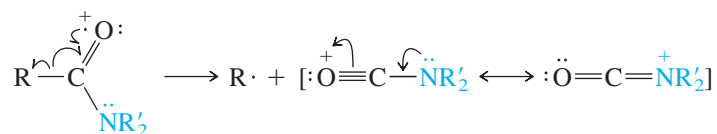
UV-VIS: The following values are typical for the $n\rightarrow\pi^*$ absorption associated with the $\text{C}=\text{O}$ group of carboxylic acid derivatives.

	$\text{CH}_3\overset{\text{O}}{\parallel}\text{CCl}$	$\text{CH}_3\overset{\text{O}}{\parallel}\text{C}\overset{\text{O}}{\parallel}\text{CCH}_3$	$\text{CH}_3\overset{\text{O}}{\parallel}\text{COCH}_3$	$\text{CH}_3\overset{\text{O}}{\parallel}\text{CNH}_2$
	Acetyl chloride	Acetic anhydride	Methyl acetate	Acetamide
λ_{max}	235 nm	225 nm	207 nm	214 nm

Mass Spectrometry: A prominent peak in the mass spectra of most carboxylic acid derivatives corresponds to an acylium ion derived by cleavage of the bond to the carbonyl group:

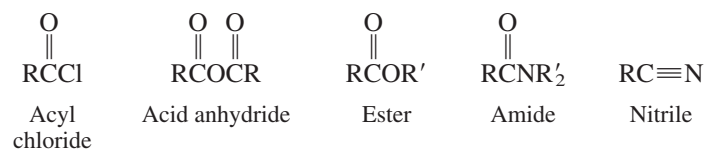


Amides, however, tend to cleave in the opposite direction to produce a nitrogen-stabilized acylium ion:

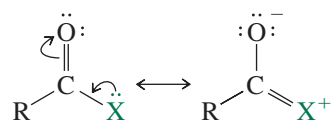


20.19 SUMMARY

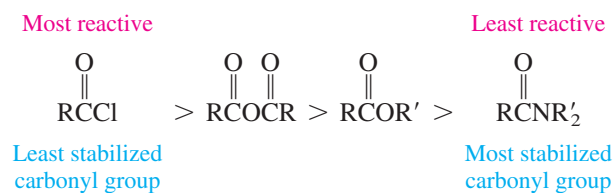
Section 20.1 This chapter concerns the preparation and reactions of *acyl chlorides*, *acid anhydrides*, *esters*, *amides*, and *nitriles*. These compounds are generally classified as carboxylic acid derivatives, and their nomenclature is based on that of carboxylic acids.



Section 20.2 The structure and reactivity of carboxylic acid derivatives depend on how well the atom bonded to the carbonyl group donates electrons to it.

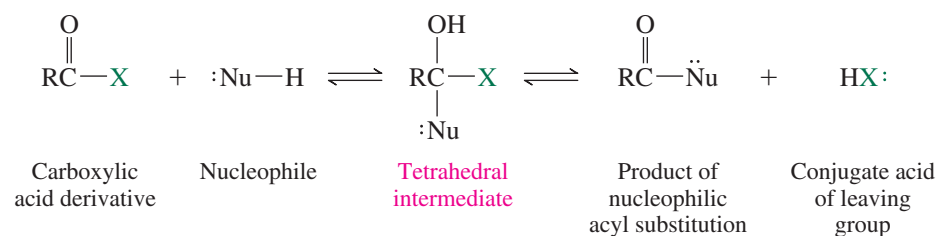


Electron-pair donation stabilizes the carbonyl group and makes it less reactive toward nucleophilic acyl substitution.

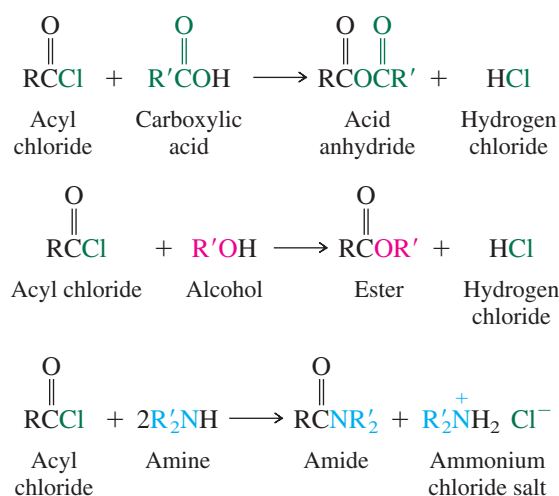


Nitrogen is a better electron-pair donor than oxygen, and amides have a more stabilized carbonyl group than esters and anhydrides. Chlorine is the poorest electron-pair donor, and acyl chlorides have the least stabilized carbonyl group and are the most reactive.

Section 20.3 The characteristic reaction of acyl chlorides, acid anhydrides, esters, and amides is **nucleophilic acyl substitution**. Addition of a nucleophilic reagent :Nu-H to the carbonyl group leads to a tetrahedral intermediate that dissociates to give the product of substitution:



Section 20.4 Acyl chlorides are converted to acid anhydrides, esters, and amides by nucleophilic acyl substitution.



Examples of each of these reactions may be found in Table 20.1.

Section 20.5 Acid anhydrides are less reactive toward nucleophilic acyl substitution than acyl chlorides, but are useful reagents for preparing esters and amides.

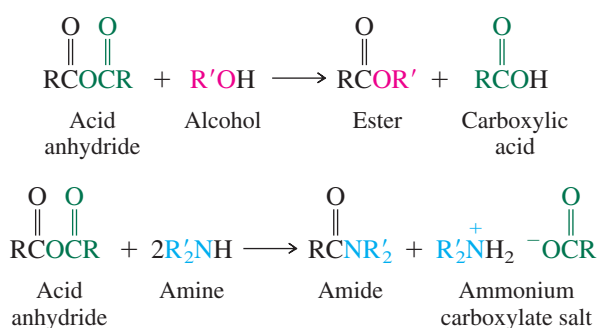


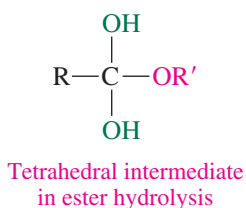
Table 20.2 presents examples of these reactions.

Section 20.6 Esters occur naturally or are prepared from alcohols by Fischer esterification or by acylation with acyl chlorides or acid anhydrides (Table 20.3).

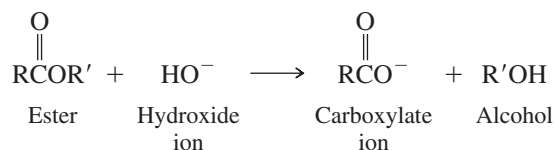
Section 20.7 Esters are polar and have higher boiling points than alkanes of comparable size and shape. Esters don't form hydrogen bonds to other ester molecules so have lower boiling points than analogous alcohols. They can form hydrogen bonds to water and so are comparable to alcohols in their solubility in water.

Section 20.8 Esters react with Grignard reagents and are reduced by lithium aluminum hydride (Table 20.4).

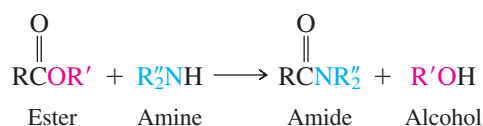
Section 20.9 Ester hydrolysis can be catalyzed by acids and its mechanism (Mechanism 20.3) is the reverse of the mechanism for Fischer esterification. The reaction proceeds via a tetrahedral intermediate.



Section 20.10 Ester hydrolysis in basic solution is called *saponification* and proceeds through the same tetrahedral intermediate (Mechanism 20.4) as in acid-catalyzed hydrolysis. Unlike acid-catalyzed hydrolysis, saponification is irreversible because the carboxylic acid is deprotonated under the reaction conditions.



Section 20.11 Esters react with amines to give amides.

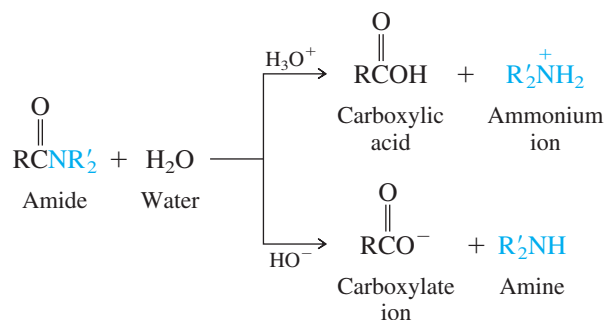


Section 20.12 Amides having at least one N—H unit can form intermolecular hydrogen bonds with other amide molecules. Compounds of this type have higher melting and boiling points than comparable compounds in which N—H bonds are absent.

870 CHAPTER TWENTY Carboxylic Acid Derivatives: Nucleophilic Acyl Substitution

Amides are normally prepared by the reaction of amines with acyl chlorides, anhydrides, or esters.

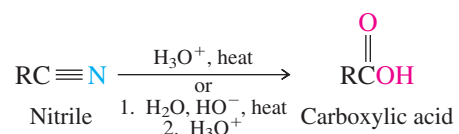
Section 20.13 Like ester hydrolysis, amide hydrolysis can be achieved in either aqueous acid or aqueous base. The process is irreversible in both media. In base, the carboxylic acid is converted to the carboxylate anion; in acid, the amine is protonated to an ammonium ion:



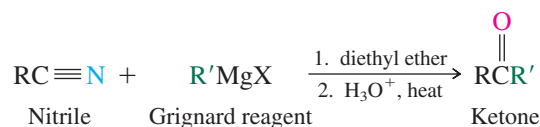
Section 20.14 Lactams are cyclic amides.

Section 20.15 Nitriles are prepared by nucleophilic substitution (S_N2) of alkyl halides with cyanide ion, by converting aldehydes or ketones to cyanohydrins (Table 20.6), or by dehydration of amides.

Section 20.16 The hydrolysis of nitriles to carboxylic acids is irreversible in both acidic and basic solution.



Section 20.17 Nitriles are useful starting materials for the preparation of ketones by reaction with Grignard reagents.



Section 20.18 Acyl chlorides, anhydrides, esters, and amides all show a strong band for C=O stretching in the infrared. The range extends from about 1820 cm^{-1} (acyl chlorides) to 1690 cm^{-1} (amides). Their ^{13}C NMR spectra are characterized by a peak near δ 180 for the carbonyl carbon. ^1H NMR spectroscopy is useful for distinguishing between the groups R and R' in esters ($\text{RCO}_2\text{R}'$). The protons on the carbon bonded to O in R' appear at lower field (less shielded) than those on the carbon bonded to C=O.

PROBLEMS

20.23 Write a structural formula for each of the following compounds:

- m*-Chlorobenzoyl chloride
- Trifluoroacetic anhydride
- cis*-1,2-Cyclopropanedicarboxylic anhydride
- Ethyl cycloheptanecarboxylate
- 1-Phenylethyl acetate
- 2-Phenylethyl acetate
- p*-Ethylbenzamide
- N*-Ethylbenzamide
- 2-Methylhexanenitrile