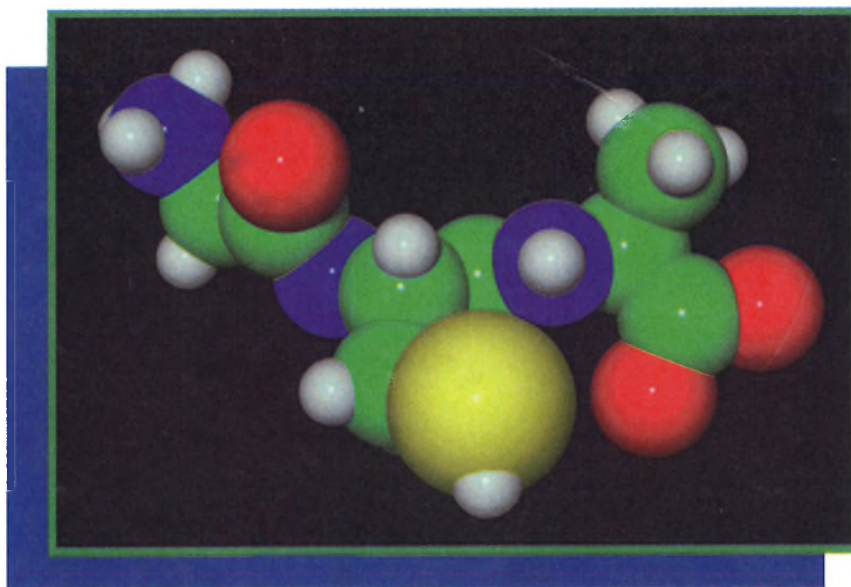


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A computer-generated representation of a tripeptide, glycylocysteylalanine. In this representation, carbon is green, hydrogen is white, nitrogen is blue, oxygen is red, and sulfur is yellow.

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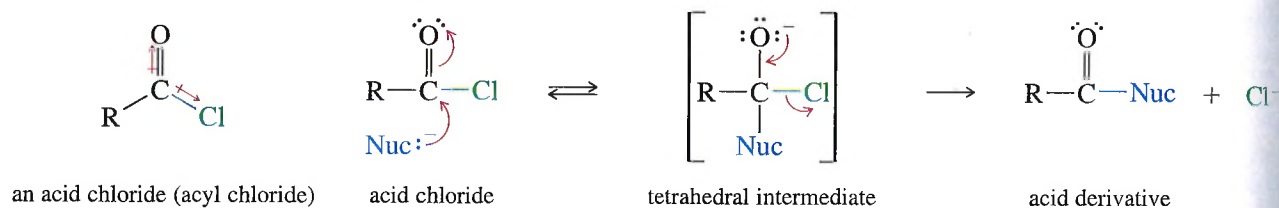
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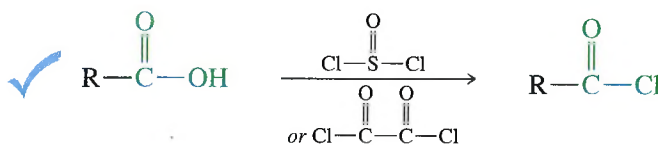
Reactions that convert carboxylic acids directly to these derivatives are covered in this chapter. Reactions that interconvert these and other acid derivatives are discussed in Chapter 21, Carboxylic Acid Derivatives.³

20-10 Synthesis and Use of Acid Chlorides

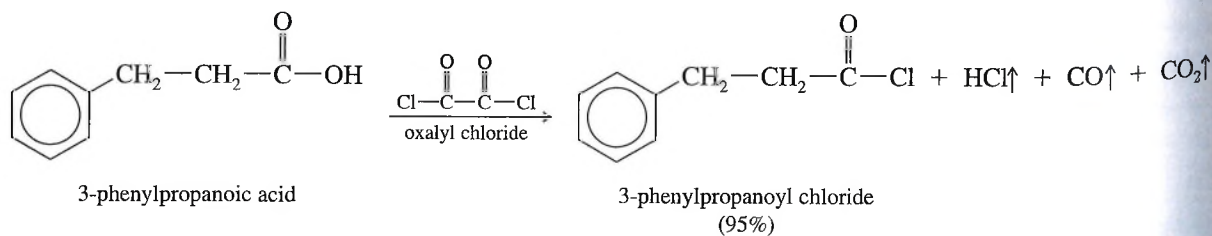
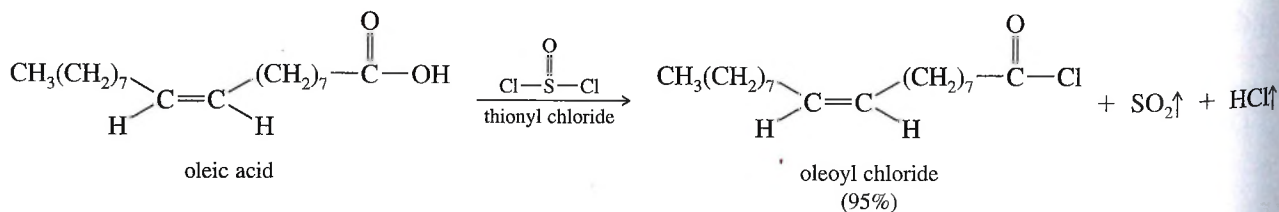
Halide ions are excellent leaving groups for nucleophilic acyl substitution; therefore, acyl halides are particularly useful intermediates for making acid derivatives. In particular, acid chlorides (acyl chlorides) are easily made and are commonly used as an activated form of a carboxylic acid. Both the carbonyl oxygen and the chlorine atom withdraw electron density from the acyl carbon atom, making it strongly electrophilic. Acid chlorides react with a wide range of nucleophiles, generally through the addition–elimination mechanism of nucleophilic acyl substitution.



The best reagents for converting carboxylic acids to acid chlorides are thionyl chloride (SOCl_2) and oxalyl chloride (COCl_2), because they form gaseous byproducts that do not contaminate the product. Oxalyl chloride is particularly easy to use because it boils at 62°C and is easily evaporated from the reaction mixture.

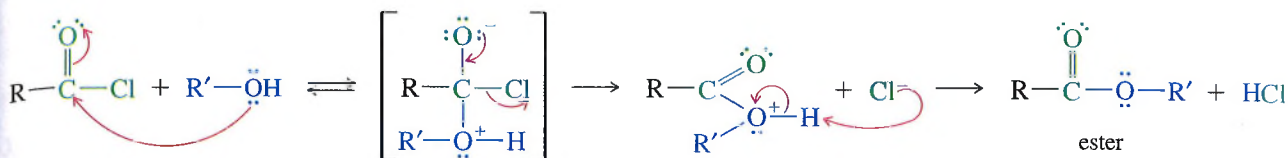


Examples

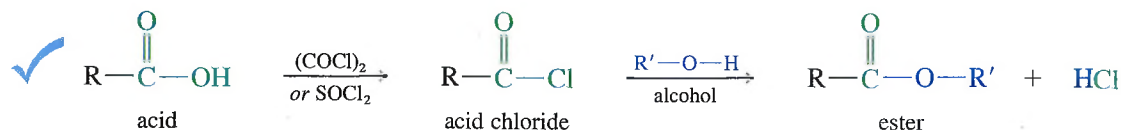


Acid chlorides react with alcohols to give esters through a nucleophilic acyl substitution by the addition–elimination mechanism discussed above. Attack by

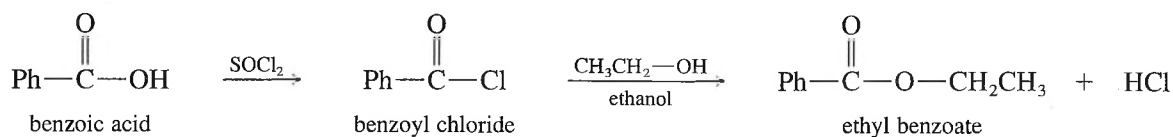
the alcohol at the electrophilic carbonyl group gives a tetrahedral intermediate. Loss of chloride and deprotonation give the ester.



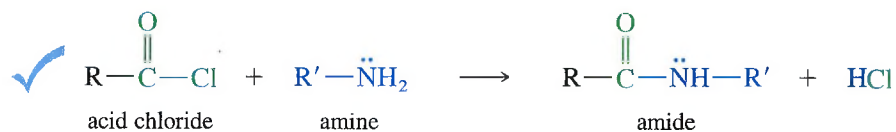
This reaction provides an efficient two-step method for converting a carboxylic acid to an ester. The acid is converted to the acid chloride, which reacts with an alcohol to give the ester.



Example



Ammonia and amines react with acid chlorides to give amides, also through the addition-elimination mechanism of nucleophilic acyl substitution. A carboxylic acid is efficiently converted to an amide by forming the acid chloride, which reacts with an amine to give the amide.



Example



PROBLEM 20-12

Give mechanisms for the nucleophilic acyl substitutions to form ethyl benzoate and *N*-methylacetamide as shown above.

PROBLEM 20-13

Show how you would use an acid chloride as an intermediate to synthesize

- N*-phenylbenzamide (PhCONHPh) from benzoic acid and aniline.
- Phenyl propionate (CH₃CH₂COOPh) from propionic acid and phenol.

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