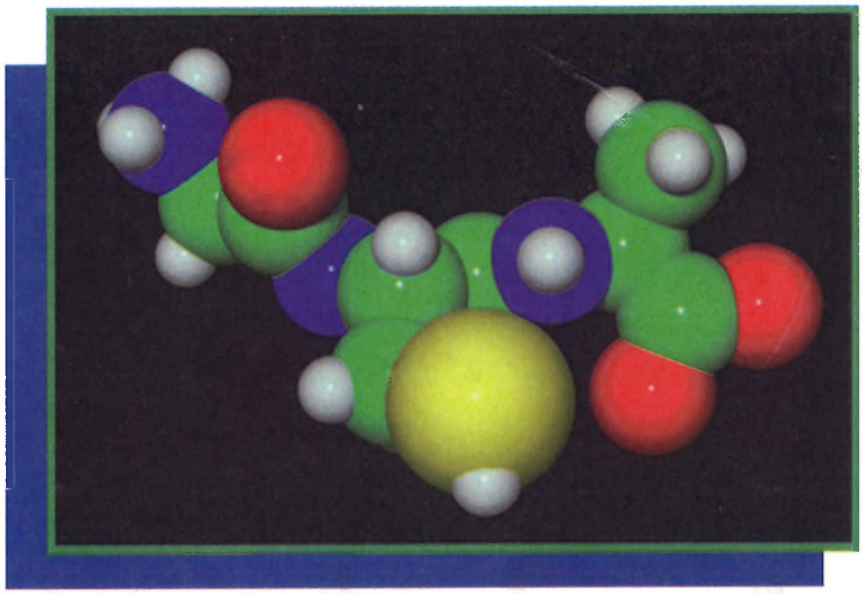
Organic Chemistry



Third Edition

L.G. WADE, JR.

Third Edition

Organic Chemistry

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Prentice Hall
Upper Saddle River, New Jersey 07458

Library of Congress Cataloging-in-Publication Data

WADE, L. G.
Organic chemistry/L. G. Wade, Jr.—3rd ed.

p. cm.
Includes index.
ISBN 0-13-301631-5
1. Chemistry, Organic. I. Title.
QD251.2.W33 1995
547—dc20

94-24693
CIP

Editorial/production supervision: *Barbara Marttine Cappuccio*
Acquisitions editor: *Deirdre Cavanaugh*
Interior design and page layout: *Lorraine Mullaney*
Cover design: *Tessie Lou*
Manufacturing buyer: *Lori Bulwin/Alan Fischer*
Managing editor: *Kathleen Schiaparelli*
Director of production and manufacturing: *David W. Riccardi*
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COVER ART: BioGrafx
A computer-generated representation of a tripeptide, glycylcysteylalanine. In this representation, carbon is green, hydrogen is white, nitrogen is blue, oxygen is red, and sulfur is yellow.

Printed in the United States of America

10 9 8 7 6 5 4 3

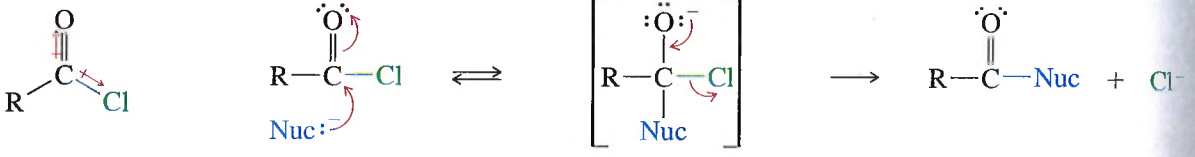
ISBN 0-13-0301631-5

Prentice-Hall International (UK) Limited, *London*
Prentice-Hall of Australia Pty. Limited, *Sydney*
Prentice-Hall Canada, Inc., *Toronto*
Prentice-Hall Hispanoamericana, S.A., *Mexico*
Prentice-Hall of India Private Limited, *New Delhi*
Prentice-Hall of Japan, Inc., *Tokyo*
Simon & Schuster Asia Pte. Ltd., *Singapore*
Editora Prentice-Hall do Brasil, Ltda., *Rio de Janeiro*

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]

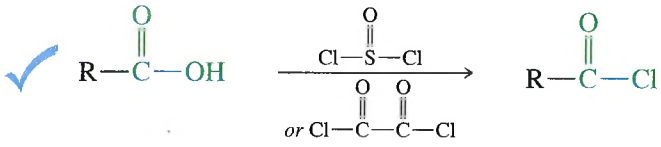
20-10 Synthesis and Use of Acid Chlorides

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.

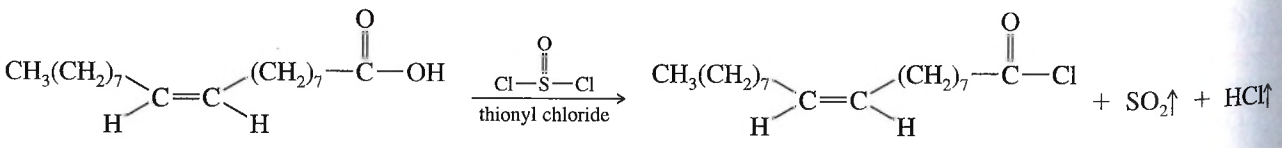


an acid chloride (acyl chloride) | acid chloride | tetrahedral intermediate | acid derivative

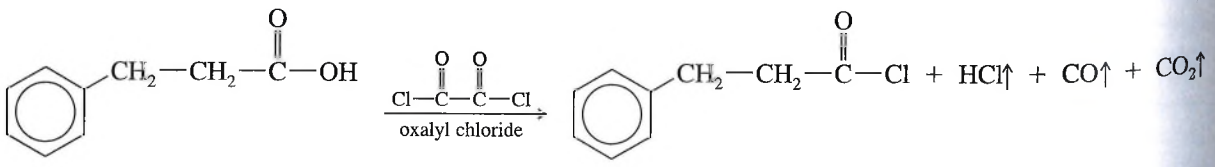
The best reagents for converting carboxylic acids to acid chlorides are thionyl chloride ($SOCl_2$) and oxalyl chloride ($(COCl)_2$), because they form gaseous byproducts that do not contaminate the product. Oxalyl chloride is particularly easy to use because it boils at 62°C and is easily evaporated from the reaction mixture.



Examples



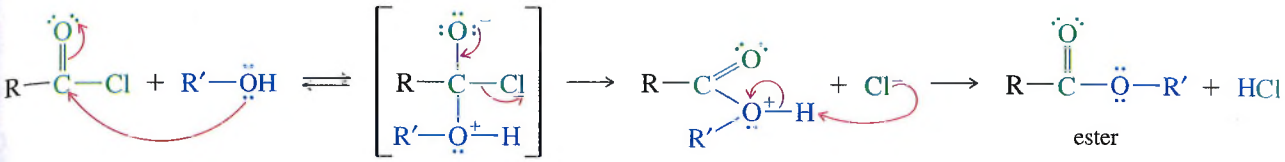
oleic acid | thionyl chloride | oleoyl chloride (95%)



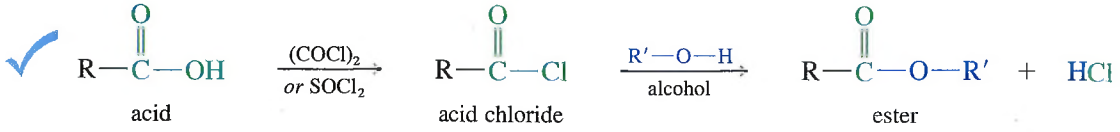
3-phenylpropanoic acid | oxalyl chloride | 3-phenylpropanoyl chloride (95%)

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

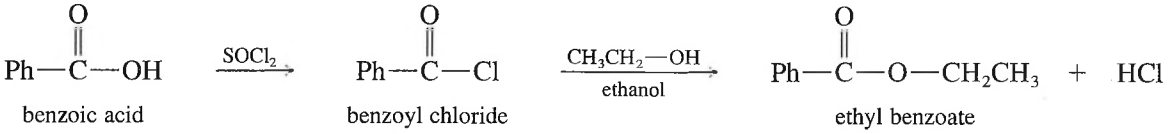
the alcohol at the electrophilic carbonyl group gives a tetrahedral intermediate. Loss of chloride and deprotonation give the ester.



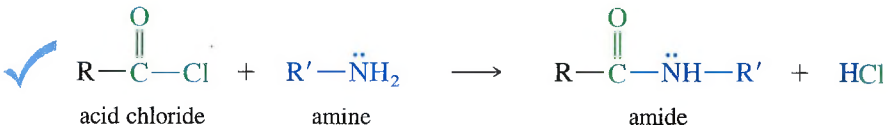
This reaction provides an efficient two-step method for converting a carboxylic acid to an ester. The acid is converted to the acid chloride, which reacts with an alcohol to give the ester.



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

(a) *N*-phenylbenzamide (PhCONHPh) from benzoic acid and aniline.
(b) Phenyl propionate (CH_3CH_2COOPh) from propionic acid and phenol.

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