ORGANIC CHEMISTRY

SECOND EDITION

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THE UNIVERSITY OF MICHIGAN

D. C. HEATH AND COMPANY
LEXINGTON, MASSACHUSETTS TORONTO

ACKNOWLEDGMENTS

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Published simultaneously in Canada.

Printed in the United States of America.

International Standard Book Number: 0-669-18178-1

Library of Congress Catalog Card Number: 88-080264

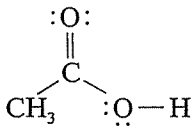
10 9 8 7 6 5 4 3 2 1

14

Carboxylic Acids and Their Derivatives I. Nucleophilic Substitution Reactions at the Carbonyl Group

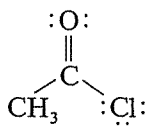
A • LOOK • AHEAD

Carboxylic acids and their derivatives are compounds in which a carbonyl group is bonded to an atom that has at least one pair of nonbonding electrons on it. Acetic acid and its derivatives are examples.



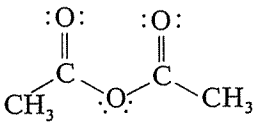
acetic acid

a carboxylic acid



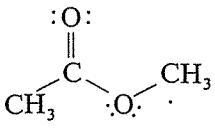
acetyl chloride

an acid chloride



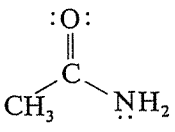
acetic anhydride

an acid anhydride



methyl acetate

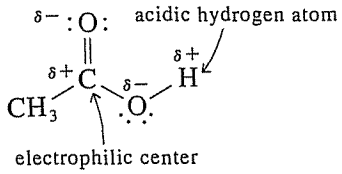
an ester



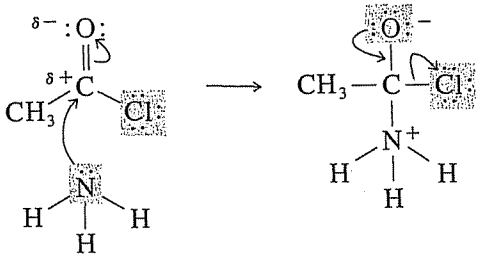
acetamide

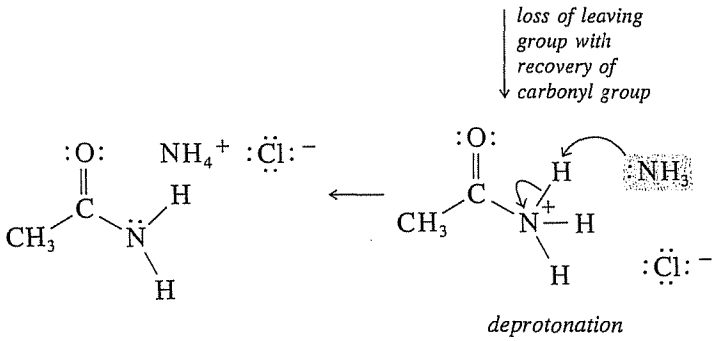
an amide

Carboxylic acids are strong organic acids. Also, the carbon atom of the carbonyl group is electrophilic and reacts with nucleophiles.



An acid derivative may be thought of as having been created from a carboxylic acid by replacement of the hydroxyl group of the carboxyl group by another atom or group. This group either is a good leaving group or may be converted to a good leaving group by protonation. Acids and acid derivatives, therefore, undergo nucleophilic substitution reactions, an example of which is the reaction of acetyl chloride with ammonia.

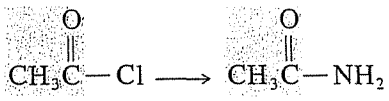




Most nucleophilic substitution reactions of acids and acid derivatives have two steps.

1. Nucleophilic attack on the carbon atom of the carbonyl group, with formation of a tetrahedral intermediate.
2. Loss of a leaving group, with the recovery of the carbonyl group.

In the reaction shown above, the acetyl group, an acyl group, is transferred from a chlorine atom to a nitrogen atom.



These important reactions of acid derivatives are called acylation, or acyl-transfer, reactions.

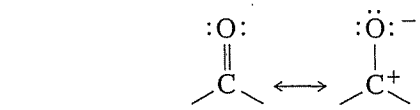
The reactions of acid derivatives differ from those of aldehydes and ketones, which do not have good leaving groups bonded to the carbonyl group. The first step of the reaction with nucleophiles is the same for acid derivatives as it is for aldehydes and ketones (p. 504, for example). Unlike aldehydes and ketones, however, acid derivatives undergo nucleophilic substitution rather than nucleophilic addition.

This chapter will emphasize the interconversions of the different acid derivatives through nucleophilic substitution reactions.

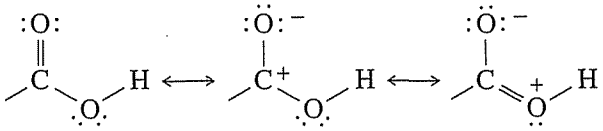
14.1 PROPERTIES OF THE FUNCTIONAL GROUPS IN CARBOXYLIC ACIDS AND THEIR DERIVATIVES

A. The Functional Groups in Carboxylic Acids and Their Derivatives

Carboxylic acids are organic compounds that contain the carboxyl group, a functional group in which a hydroxyl group is directly bonded to the carbon atom of a carbonyl group. Interaction between the carbonyl group and the hydroxyl group affects the properties of both. For example, the carbonyl group in acids is not as electrophilic as the carbonyl group in aldehydes and ketones. A comparison of the resonance contributors possible for a carbonyl group and for a carboxyl group shows why this is so.



resonance contributors for a carbonyl group



resonance contributors for a carboxyl group

The carbon atom of the carbonyl group in an aldehyde or ketone is an electrophilic center that reacts with a variety of nucleophiles, such as alcohols (p. 499), amine derivatives (p. 503), and organometallic reagents (p. 491). In carboxylic acids, the electrophilicity of the carbonyl group is modified by the presence of nonbonding electrons on the oxygen atom of the hydroxyl group. Donation of these electrons to the carbonyl group transfers some of the positive character of the carbonyl carbon atom to that oxygen atom. For that reason, many reagents that react easily with the carbonyl group of aldehydes or ketones react more slowly or only in the presence of powerful catalysts when attacking the carbonyl group of a carboxylic acid or an acid derivative.

The hydroxyl group of a carboxylic acid is unlike the hydroxyl group of an alcohol. The drain of electrons away from the hydroxyl group by the carbonyl group increases the positive character of the hydrogen atom and stabilizes the carboxylate

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