MICRO AND SEMIMICRO METHODS

A. WEISSBERGER

TECHNIQUE OF ORGANIC CHEMISTRY

Volume VI

MICRO AND SEMIMICRO METHODS

NICHOLAS D. CHERONIS
Professor of Chemistry, Brooklyn College

With Contributions by

A. R. RONZIO
Los Alamos Scientific Laboratory
and **T. S. MA**
New York University

1954

INTERSCIENCE PUBLISHERS, INC., NEW YORK

INTERSCIENCE PUBLISHERS LTD., LONDON

To the memory of

FRIEDRICH EMICH

Founder of Modern Microchemistry

LIBRARY OF CONGRESS Catalog Card Number 45-8533

INTERSCIENCE PUBLISHERS, INC., 250 Fifth Avenue, New York 1, N. Y.

For Great Britain and Northern Ireland:
INTERSCIENCE PUBLISHERS LTD., 88/90 Chancery Lane, London, W. C. 2

PRINTED IN THE UNITED STATES OF AMERICA BY MACK PRINTING CO., EASTON, PA.

INTRODUCTION

Organic chemistry, from its very beginning, has used specific tools and techniques for the synthesis, isolation, and purification of compounds, and physical methods for the determination of their properties. Much of the success of the organic chemist depends upon a wise selection and a skillful application of these methods, tools, and techniques, which, with the progress of the science, have become numerous and often intricate.

The present series is devoted to a comprehensive presentation of the techniques which are used in the organic laboratory and which are available for the investigation of organic compounds. The authors give the theoretical background for an understanding of the various methods and operations and describe the techniques and tools, their modifications, their merits and limitations, and their handling. It is hoped that the series will contribute to a better understanding and a more rational and effective application of the respective techniques. The volume at hand deals with methods where minutiae can be important and require description. We hope that it will succeed in transmitting the results of the author's experience in many years of teaching and research and that the procedures will enable the reader to develop his techniques and to evaluate his own problems.

The field is broad and some of it is difficult to survey. Authors and editor hope that the volumes will be found useful and that many of the readers will let them have the benefit of their criticism and of suggestions for improvements.

A. W.

Research Laboratories
Eastman Kodak Company
Rochester, New York

GENERAL PLAN

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Micro and Semimicro Methods

PREFACE

The present volume of *Technique of Organic Chemistry* differs in two respects from those which precede it in the series. First, there is little or no theoretical discussion of micromethods, since the basis for these procedures is identical with that of the macromethods presented earlier in the series. Therefore, except for cases in which the basis of the micromethod differs from that of the macroprocedure, the theoretical discussion is either omitted or kept at a minimum. Second, the description of the microtechniques has been given in considerable detail; this course was deemed essential for reproducible results, since the number of organic chemists who have practical experience with these procedures is still small. In fact, in the opinion of the author, the worker with considerable practical experience in the organic laboratory often requires the same detailed description as the beginner.

The book was designed to give a critical and practical review of the microtechniques of preparative and analytical organic chemistry for the use of the research worker and the advanced student of experimental organic chemistry. Not included are the micromethods used in the elementary analysis of organic substances, which have been developed to a high degree of accuracy and precision, and the special methods of histo- and cytochemistry; both have been admirably covered in other books (listed as General References in the Introduction).

After an introductory chapter dealing with advantages, applications, and historical development of microchemical methods, the first four chapters are devoted to the discussion of microfractionation procedures employed for the purification, and determination of physical constants, of small quantities of material. The merits and limitations of the various tools and apparatus designed for these procedures are reviewed and discussed. In general, of the many types of apparatus which have been described in the literature for a particular purpose, one or two are discussed in detail; the selection was made on the basis of the following criteria: (*a*) suitability for the desired scale, (*b*) precision and accuracy, (*c*) cost and availability, (*d*) ease of repair and replacement of parts. Obviously, complete

objectivity is impossible, and types of apparatus not accorded detailed description may nevertheless be well suited for the purpose for which they were designed. In the case of frequently used operations, for example the determination of melting points, all types of available apparatus were tested and evaluated.

Chapters V through XIII deal with micropreparative methods; their discussion is arranged according to types of organic reactions, with the primary objective of illustrating microsyntheses rather than including examples of all types of organic reactions. A large number of examples of micropreparations are described in detail in order to provide directions for trial runs with small quantities. Most of the preparations described have been tested and checked. In general, once an experienced worker becomes familiar with operations employing small quantities, it is relatively easy to adapt a given preparation from a method designed to give a yield of 1 to 100 grams to a scale of 25 to 100 milligrams. Greater care and exact procedures are required when the scale of preparation is a few milligrams or less. Chapter XIII, which completes the preparative part of the work, was written by Dr. A. R. Ronzio and deals with the special techniques and precautions employed in microsyntheses with tracer elements.

The third part of the book discusses microanalytical procedures and reactions. In Chapter XIV the general aspects of characterization and identification of organic compounds and the special techniques employed with small quantities of material are reviewed. The chromatographic procedures included in this chapter are designed only for qualitative identification. A more extensive treatment seems superfluous since several extensive and detailed treatises on these techniques have been published within the past few years. Chapter XV deals with the applications and limitations of the tests employed to detect functions in organic compounds, while Chapter XVI gives directions for the micropreparation of derivatives of organic compounds useful for characterization. The final chapter, written in collaboration with Professor T. S. Ma, gives a survey of the present status of microprocedures for the quantitative estimation of functional groups in organic compounds.

The author acknowledges his indebtedness to all who assisted in writing this book. Valuable suggestions were made by Professor T. S. Ma, recently of New York University and now at Brooklyn College, who read the complete manuscript, Dr. John B. Entrikin of Centenary College (Chapters XIV and XV), Dr. A. R. Ronzio of the Los Alamos Scientific Laboratory (Chapters V through XII), Professor A. A. Benedetti-Pichler (Introductory Chapter), Professor David Davidson of Brooklyn College (Chapter XIV), and Dr. Herbert Alber of Arthur H. Thomas Co., who read critically Chapters I to IV and gave information on all types of microap-

paratus. Alexander Vavoulis of Davidson College has helped in checking a large number of microprocedures, Richard Kronenthal and Sol Cohen have assisted in the application of chromatographic procedures in the detection of organic compounds, and a great number of my students have, over a period of years, helped in the checking and development of the microprocedures. Miss Barbara Wehringer and Miss Aletha Kowitz assisted in assembling the bibliography of micromethods, and Mrs. Agnete Prottsman, Mrs. Merilyn Wente, and Mrs. Annette Baslaw typed the manuscript.

N. D. C.

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