X-RAY STRUCTURE DETERMINATION

A PRACTICAL GUIDE

Second Edition

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WILEY

A Wiley-Interscience Publication

JOHN WILEY & SONS

New York • Chichester • Brisbane • Toronto • Singapore

Library of Congress Cataloging in Publication Data:

Stout, George H., 1932–
X-ray structure determination

"A Wiley-Interscience publication"
Includes bibliographical references and index
1. X-ray crystallography. I. Jensen, Lyle H
II. Title.
QD945.S8 1989 548'.83 88-27931
ISBN 0-471-60711-8

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

PREFACE

The first edition of this book arose from our belief that X-ray crystallography was a powerful tool which could be applied by scientists whose main interests lay in other fields. This view has been entirely supported by the events since the late 1960s, and has been so widely accepted that there is now a risk that the field of X-ray crystallography of small molecules will be or has been relegated to a minor, service role. It is often felt, or so it seems, that all of the necessary knowledge is contained in various computer programs, and that these will serve by themselves to carry out an analysis to a uniquely correct result. We do not hold to this view and the main thrust of this edition is not merely that one can do the work oneself, but that it is necessary to understand what one is doing in order to be able to have confidence in the results.

The contents and organization of this book come very much out of our own experience and reflect our views of what is important and useful to the practical worker. Much of the material has been rearranged and rewritten from the first edition to reflect changes in the relative importance of various topics and the innovations in the field over the last twenty years. We believe, perhaps more strongly than ever, that "there appears to exist in crystallography, perhaps more than in most fields, a body of practical knowledge widely disseminated among members of the group but nowhere available in print to outsiders." We have continued to try to include as much of this material as possible.

We continue to offer our thanks to our colleagues who helped us with the first edition, and add our gratitude to all those, colleagues and students, who have contributed to our thoughts about crystallography in the intervening

years. As before, our thanks go to our wives for continued understanding and support in what has turned out to be a *very* much longer undertaking than we originally imagined.

Seattle, Washington
March 1989

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INTRODUCTION

The recent explosive growth in the development and distribution of electronic computers has reduced the labor associated with the determination of crystal structures by X-ray diffraction analysis immensely. As a result such analysis may now be used routinely to supply answers to problems arising in many unrelated fields. In the past, the common mode of attack has been for a worker, faced with a problem for which X-ray methods seemed appropriate, to attempt to find a crystallographer who would be willing to undertake the determination. As a result of a growing awareness of the capabilities of the method, however, the number of problems has been increasing at a greater rate than the number of crystallographers.

It is the thesis of this book that the average chemist who is willing to devote some time to study, and who can obtain a suitable set of programs, can learn without great difficulty to perform crystallographic structural analyses for himself. The mathematical requirements are much less formidable than are widely supposed, the techniques of data collection are no more complicated than many other physico-chemical measurements, and the tedium of computation has been very largely removed by computers. Furthermore, no errors, other than the loss of a unique crystal, are irredeemable; one can always return to the point of error and find a new path.[1]

This introduction to the first edition of this book has been entirely justified by the results of the last twenty years. So much so, in fact, that we now feel the need to counterbalance the swing and to provide throughout this volume cautionary statements and evidence that the process of crystal

[1]G. H. Stout and L. H. Jensen, *X-Ray Structure Determination*, Macmillan, New York, 1968, p. 1.

structure determination is *not* as simple as is often supposed. The great advances in computer technology, the advent of automatic data collection systems, and the progress in dealing with the phase problem have all combined to relegate the crystallography of small molecules to a service function, almost comparable to infrared or NMR spectroscopy as yet another tool in the chemist's workbox. To some extent this view is justified, and in many cases structures can, indeed, be solved in a quick and routine fashion. Nevertheless, this process is also being accompanied by an increasing number of published errors and an unknown but significant number of structures which fail to solve by the routine methods but which prove amenable to more thoughtful attack. We hope to provide the readers of this much revised edition with the tools and insight that will enable them to make use of the modern techniques with understanding and judgment.

As before, the pattern of this book follows closely the development of an actual structural determination. After some introductory material on the nature of X-rays, the diffraction process, and the internal geometry of crystals, the selection and preparation of a crystal are considered. The techniques involved in the measurement of raw X-ray data are next taken up, followed by a discussion of the reduction of these data into the form in which they are usually used.

The second part of the book is devoted largely to a discussion of various methods of solving the "phase problem," the principal difficulty on the path from the raw data to the final answer. The past two decades have seen great advances in dealing with this problem, but it is still not a trivial barrier to the successful completion of a structural study. A number of methods are considered to provide the reader with insight into both common and uncommon approaches. Chapter 15 describes the process of completing the structure once the phase problem has been overcome.

The third part considers the processes of refinement by which an attempt is made to obtain the maximum information from the observed data and to evaluate its reliability. Finally, there is a discussion of some of the sources of errors in practice and interpretation, and of further knowledge which can be derived from the basic structure once it is known.

It is assumed without further comment that the reader has access to a modern computer.[2] More than any other factor, it has been the growth and widespread distribution of computers that have turned X-ray crystallography into a commonplace structural tool. Computers require programs, however, and obtaining, understanding, and using these programs often pose a serious problem. The material given here will help supply the background that is needed, but while the general characteristics of the more

[2]For discussion of hand calculations, which form a powerful educational tool, see S. C. Nyburg, *X-Ray Analysis of Organic Structure*, Academic Press, New York, 1961, pp. 77–84, 96–111; M. J. Buerger, *Crystal–Structure Analysis*, Wiley, New York, 1960, pp. 274–279 and references cited there; and H. Lipson and W. Cochran, *The Determination of Crystal Structures*, Bell, London, 1957, pp. 54–65, 76–97.

common sorts of programs are discussed, the wide variation in individual specimens prevents any detailed consideration.

No attempt is made here to cover the general problem of computer use: It is not necessary that the user of a computer know what is happening inside the machine, but some understanding of scientific programming and one of the languages used (commonly FORTRAN, much less often BASIC or C) is very valuable. Operating instructions are often written in the jargon of the programming languages, and unfamiliarity can lead to total frustration. Furthermore, it is often necessary to make changes in preexisting programs or to write small ones for special purposes, especially if one has any wish to progress beyond the "black-box" stage of operation.

The problem of obtaining programs is a real but not insuperable one. Most of the common operations have been programmed, generally repeatedly, for all of the ordinary varieties of computers. Crystallographers are usually very generous in regard to supplying copies within the limitations of their time, so the major difficulty is tracking down what is available. Probably the best single source for new material is the descriptions and abstracts of programs that appear in *Journal of Applied Crystallography*.

When selecting programs, the value of obtaining ones with good "write-ups" can hardly be overstressed. Furthermore, as is discussed in Chapter 7, it is advantageous to obtain the standard core of programs from a single source, so that they are matched and the output of one can serve directly as the input for another. A number of crystallographic "systems," collections of programs linked into a common unit, are available, some provided with diffractometers and others as stand-alone packages for computers of all sizes including PC-class machines.[3]

Since the structural interests of the authors of this work lie in the field of organic compounds, this volume shows a decided bias toward the problems likely to be encountered in the analysis of organic and organometallic structures. This is not to say that much of the material is not more generally applicable, but where there is a choice the discussion is restricted to crystals of low symmetry. This approach is not as unfair as might at first seem, since there are already available a number of works by crystallographers of more classical or mineralogical bent, which deal with the problems more characteristic of purely inorganic systems.

The orientation of this book is heavily toward the practical aspects of structure determination. Some theoretical material has been included where it is needed for intelligent application of the techniques described, but there has been no effort to justify all the statements made. Interested readers can find fuller details in the references given in the bibliographies following the various chapters.

[3]For an extensive survey and listing, see K. Huml in *Crystallographic Computing 3: Data Collection, Structure Determination, Proteins, and Data Bases*, G. H. Sheldrick, C. Krüger, and R. Goddard, Eds., Clarendon Press, Oxford, 1985, pp. 131–145. For a detailed description of one such system see S. R. Hall, J. M. Stewart, and R. J. Munn, *Acta Cryst.*, **A36**, 979 (1980).

Similarly, the choice of literature to be cited has been selective rather than exhaustive. An attempt has been made to provide references that would be illuminating to students with relatively limited crystallographic backgrounds. Little attention has been paid to questions of priority, and much use has been made of the secondary literature.[4] Where a secondary reference has been used repeatedly in a chapter, it appears in the footnotes as a short form and the full citation is given at the end of the chapter.

Many new references have been supplied for this revision, but many old ones have been retained as being more suited for introductory purposes. Unfortunately, many of the classic texts are out of print and have not been adequately replaced, so they need to be searched out in libraries.

Although crystal structures now appear in many journals, particularly those dealing with particular classes of compounds, the bulk of important papers on techniques appear in *Acta Crystallographia* (*Acta Cryst.*), published by the International Union of Crystallography (IUCr). The IUCr has also published four volumes that contain an immense amount of practical information used constantly by crystallographers. We shall cite these works in the shortened form *International Tables, Vol. I–IV, A* corresponding to the full references given in Table A.

We suggest that the novice intending to carry out a structure determination read Chapters 1, 2, 10, and 19 to get a brief introduction to the problems ahead. The actual analysis can be begun with Chapter 4, and carried on in sequence, a chapter or two at a time. Chapters 2 and 3 are vital and will probably require several rereadings at various stages.

TABLE A Full Citations for *International Tables* Volumes

Vol. I	*International Tables for X-Ray Crystallography*, Vol. I, N. F. M. Henry and K. Lonsdale, Eds., Kynoch Press, Birmingham, England, 1952.
Vol. II	*International Tables for X-Ray Crystallography*, Vol. II, J. S Kaspar and K. Lonsdale, Eds., Kynoch Press, Birmingham, England, 1959.
Vol. III	*International Tables for X-Ray Crystallography*, Vol. III, C. H. Macgillavry and G. D. Rieck, Eds., Kynoch Press, Birmingham, England, 1962.
Vol. IV	*International Tables for X-Ray Crystallography*, Vol. IV, J. A. Ibers and W. C. Hamilton, Eds., Kynoch Press, Birmingham, England, 1974.
Vol. A	*International Tables for Crystallography*, Vol. A, T. Hahn, Ed., D. Riedel, Dordrecht, Netherlands, 1983.

[4]Excellent lists of literature references prior to 1959 can be found for many of the topics covered here in M. J. Buerger, *Crystal-Structure Analysis*, Wiley, New York, 1960.

PART I

PRELIMINARY STAGES