XI

THE X-RAY CRYSTALLOGRAPHIC INVESTIGATION OF THE STRUCTURE OF PENICILLIN

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CONTENTS

Introduction 310
The crystallographic examination of certain degradation products of penicillin 312
Penicillamine group 312
Penilloaldehyde group 314
Penillamines 315
Penillic acids 316
Tables I–IV 319
The X-ray analysis of the structures of sodium, potassium and rubidium benzylpenicillin . 321
The crystallization of the salts of penicillin . 321
Chemical theories of the structure of penicillin and the course of the crystallographic investigation 322
Crystallographic data on the penicillin salts 324
The position of the heavy atoms; the calculation of Patterson series 326
Approximate electron density projections and trial and error analysis for rubidium and potassium benzylpenicillin 327
Trial and error analysis, including the use of the optical diffraction method, in the investigation of sodium benzylpenicillin . 330
The integration of the investigations on sodium and rubidium benzylpenicillin; the curled configuration of the molecule . . . 332
Additional evidence supporting the curled configuration 334
The refinement of the *b* plane projection for the three penicillin salts; the first definite evidence from X-ray analysis on the molecular structure of penicillin 335
The study of projections perpendicular to the *b* axis 338
Calculations involving the atomic coordinates in three dimensions 342
The accuracy of the structure determination. 347
The details of the molecular structure and crystal structure of sodium, potassium and rubidium benzylpenicillin 349
Conclusion 355
Acknowledgments 355
Experimental
Tables XIV–XX 359

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INTRODUCTION

The X-ray crystallographic investigation of the structure of penicillin began at the earliest possible moment in the chemical examination of penicillin, at the time of the isolation of the first crystalline degradation product, penicillamine hydrochloride, in the late summer of 1942. It has led, in the course of the last four years, to the determination in detail of the structure of the molecule as it exists in crystals of sodium, potassium, and rubidium benzylpenicillin. The development of the X-ray crystallographic research, which has made this result possible, has been interesting quite apart from the interest of its final conclusions. In the first place, crystallographic measurements have been far more closely associated than is usual with the whole of the chemical investigation of the structure. X-ray data have been employed in the solution of a variety of problems that arose during the experiments on the chemical degradation and synthesis of penicillin; and, at the same time, the course taken in the X-ray analysis has depended on the close collaboration of workers in other fields and has been influenced by the conclusions that they have reached at different times. In the second place, a large variety of techniques in X-ray crystallography, several of them only recently introduced, have been applied during the examination of the different penicillin products. The final solution of the crystal structure of the penicillin salts has accordingly provided a quite unexpected demonstration of the strength of present X-ray analytical methods.

The use of X-ray diffraction data in problems of structural chemistry is based upon the fact that the intensities of the X-ray reflections from a crystal are related to the positions in space of the atoms within the crystal. The solution of any particular crystal structure depends therefore upon finding a set of atomic positions which will, according to calculation, give intensities of X-ray reflections similar to those observed. It is common in crystal structure analyses of organic compounds to think in this connection of two variables, the arrangement of the atoms within the molecule and the relative arrangement of the molecules within the crystal; but where the molecular structure is itself largely unknown, the distinction ceases to be of value. By