

THE ALKALOIDS

Chemistry and Physiology

R. H. F. Manske

Edited by
R. G. A. Rodrigo

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Founding Editor
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PREFACE

This volume is largely devoted to a review of the bisindole type and includes all alkaloids containing two tryptophan-derived nuclei. Various aspects of the chemistry of such indole alkaloids have been covered in several earlier volumes up to and including Volume XI of this series. All structural types are included in the present review and the remarkable advances of recent years in our knowledge of these very complex compounds are discussed and evaluated. A smaller chapter reviews the eburnamine-vincamine group of indole alkaloids which has not received any attention in this series since Volume XI.

The editor wishes to thank the authors for their cooperation.

R. G. A. Rodrigo

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—CHAPTER 1—

BISINDOLE ALKALOIDS

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I. Introduction

In previous volumes of this series there has been some discussion of various bisindole alkaloids (1-12). However, this coverage was somewhat sporadic and diffuse because it was part of the broader discussion of alkaloids of a particular genus or of a limited structure type. The remarkable progress made in this area during the past few years indicated that a more unified approach to these alkaloids would be appropriate. Gorman *et al.* have used a similar system in a previous review of this field (13).

Fundamentally, this chapter deals with those alkaloids which contain two nuclei derived from tryptophan, and is organized approximately along the lines of a progressing biosynthetic pathway. Because of the divergence from previous organizational alignments, it appears necessary to mention the prior notations of some of the alkaloids and also to indicate the volumes in this series in which certain of these alkaloids have been described earlier.

At the outset it should be said, as Gorman *et al.* have pointed out, that very few of these alkaloids are "dimeric" in the strict sense of the word, i.e., comprised of two identical units. Rather, it is more common that the two (or more) units differ; indeed, these differences are usually not minor but typically involve quite dissimilar skeleta. The problems associated with the structure elucidation of natural products of this complexity are manifold, and this area was almost unexplored before the structures of vincalcalco-blastine (14) and voacamine (15) were solved. Since then, many new bisindole alkaloids of divergent structure have been isolated, and their characterization has been greatly facilitated by the critical application of spectroscopic techniques. Particularly in the recent past, ^{13}C -NMR spectroscopy has contributed substantially to the solution of structural problems in this area.

In the organization of this chapter the simplest alkaloids derived from tryptophan are considered first. These are followed by a group formed from a monoterpenoid indole alkaloid and tryptophan, and finally by the groups formed by the union of two monoterpenoid indole alkaloid types arranged biogenetically. Besides annual reviews of this field (13, 16–21), there have been several other reviews of various of the alkaloid groups discussed here (15, 22–30).

II. Tryptamine–Tryptamine Type

A. STAUROSPORINE (1)

Staurosporine, $[\alpha]_{\text{D}} + 35.0^\circ$, was obtained from the fungus *Streptomyces staurosporeus* (31), and preliminary data indicated that the alkaloid probably contained two indole nuclei. Structure 1 was deduced by X-ray crystallographic analysis (32) of the methanol solvate which crystallized in the monoclinic space group C2. The final *R* value from analysis of 2352 independent reflections was 4.7%. No biosynthetic studies have been conducted, but one can imagine a derivation from indole-3-acetic acid and tryptamine. The oxidative coupling of two C-2 carbons on indole nuclei is a unique feature of the structure. The alkaloid showed hypotensive activity and antimicrobial activity against both fungi and yeasts (31).

With the structure defined, a brief discussion of the spectral data is warranted. Staurosporine displayed principal absorption maxima at 243