X-Ray Crystal Structure of Staurosporine: a New Alkaloid from a *Streptomyces* Strain

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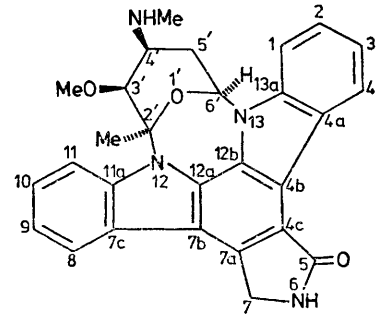
Summary The structure of staurosporine (**1**), a new alkaloid from a *Streptomyces* strain, has been established by *X*-ray crystallography.

PREVIOUSLY, we reported the isolation and preliminary characterization of the alkaloid staurosporine, formerly referred to as AM-2282, from *Streptomyces staurosporeus* Awaya, Takahashi, and Ōmura, nov. sp.[1] The alkaloid showed strong hypotensive activity as well as antimicrobial activity against fungi and yeast. We now report the elucidation of the structure of staurosporine (**1**).

The complete structure and stereochemistry of staurosporine was elucidated by an *X*-ray crystallographic study of its methanol solvate, m.p. 270 °C (decomp.). *Crystal data:* $C_{28}H_{26}N_4O_3$·MeOH, monoclinic, space group *C*2,



(1)

Staurosporine, showing the crystallographic numbering.

$a = 23{\cdot}487(6)$, $b = 7{\cdot}636(3)$, $c = 15{\cdot}638(4)$ Å, $\beta = 116{\cdot}71(5)°$, $Z = 4$, $D_c = 1{\cdot}322$ g cm^{-3}. Intensity data for $2\theta \leqslant 140°$ were collected on an automatic, four-circle diffractometer using Cu-K_α radiation monochromatized with an LiF crystal. 2532 independent structure factor amplitudes greater than their estimated standard deviations were selected for the structural study. Although various attempts were made to solve the structure by conventional direct methods, none was successful. The structure was finally solved by a new Monte Carlo method† on the basis of 487 E-values above 1·30. An E-map calculated with 458 phases yielded 33 out of the 37 independent non-hydrogen atoms. The remaining four atoms were located in a difference Fourier map. After several cycles least-squares refinement using atomic scattering factors for carbon for all the non-hydrogen atoms, the nitrogen and oxygen atoms were located by taking account of isotropic temperature factors as well as interatomic distances. The structure thus obtained was refined by block-diagonal least-squares, using anisotropic thermal motions assumed for all the non-hydrogen atoms. After the 25 hydrogen atoms had been located in a second difference Fourier map, several cycles of the least-squares refinement were repeated including these hydrogen atoms. The final R-value was 4·7%. The molecular structure obtained is shown in the Figure and the structure of staurosporine has thus been established as (**1**).‡

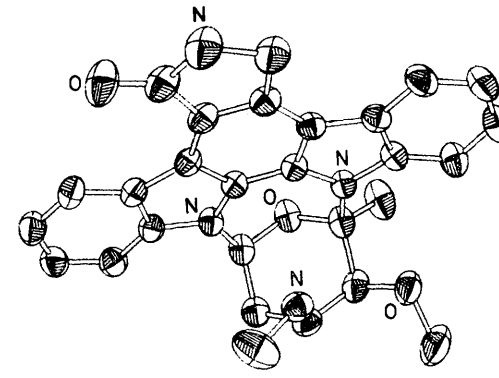


FIGURE. A perspective view of the staurosporine molecule.

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† Details of this method will be published elsewhere.

‡ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

[1] S. Ōmura, Y. Iwai, A. Hirano, A. Nakagawa, J. Awaya, H. Tsuchiya, Y. Takahashi, and R. Masuma, *J. Antibiotics*, 1977, **30**, 275.