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THE MOLECULAR STRUCTURE OF NAPHTHYRIDINOMYCIN- A BROAD SPECTRUM ANTIBIOTIC

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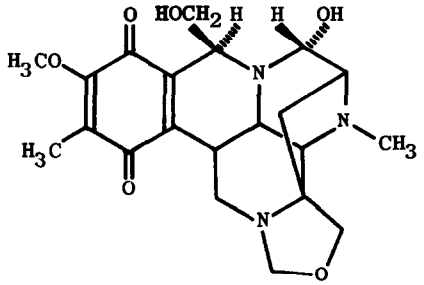
We wish to disclose the structure of the title compound, a broad spectrum antibiotic, isolated from a streptomycete[1]. The pure antibiotic was obtained as ruby red crystals, m.p. 108-110 (dec.); $[\alpha]_D^{25}$ 69.4° (*c* 1, $CHCl_3$); λ_{max} 270mμ; $\varepsilon_{1cm}^{1\%}$ 248.5 (MeOH). The molecular formula of $C_{21}H_{27}N_3O_6$ was obtained by high resolution mass spectrometry and agrees with the empirical formula of $C_7H_9NO_2$ corresponding to the microanalytical data[2]. The compound is soluble in water and most polar organic solvents. It exhibits <u>in vitro</u> inhibition of RNA and protein biosynthesis as well as cell wall formation.



NAPHTHYRIDINOMYCIN

Precession photographs showed the crystal to belong to the orthorhombic system with unit cell dimensions: a=11.038(1), b=19.566(2) and c=9.255(1)Å, space group $P2_12_12_1$. The density, measured by pycnometry, was found to be 1.387 g. cm^{-3}. There are four molecules $C_{21}H_{27}N_3O_6$ per unit cell.

Three dimensional intensity data were collected on a Picker FACS-I diffractometer with monochromatized CuK_α radiation. All reflections with $2\theta \leq 64^\circ$ were collected twice. Of the 1904 possible independent reflections, 1852 were observed. The phases of 195 reflections, with normalized structure factors $E \geq 1.50$, were determined using the TANFOR program[3]. The first 30 peaks from the E-map yielded the entire structure. The atomic and thermal parameters were refined by the least square program NUCLS5[4].

Anisotropic block-diagonal refinement (including anisotropic thermal parameters for all hydrogen atoms) reduced the weighted and unweighted R(|F|) values to 3.2% and 2.9% respectively. The N and O atoms were identified unequivocally from consideration of thermal parameters and intramolecular bond distances. No enantiomorph distinction could be made.

The molecular structure of naphthyridinomycin is shown Fig. 1. It is essentially a substituted quinone ring fused to an unusual alkaloid possessing three tertiary amines. The intramolecular bond distances compare well with the generally accepted values for the different bond types. A novel structural feature is observed in this compound: an intramolecular hydrogen bond between an hydroxyl group and a tertiary amine: O(6b2) -H(6b2)...N(11), with bond distances O(6b2) ...N(11) and H(6b2 ... N(11) of 2.832 (4) and 1.83(3) Å respectively. The O(6b2) -H(6b2) ...N(11) bond angle is 167(2)°.

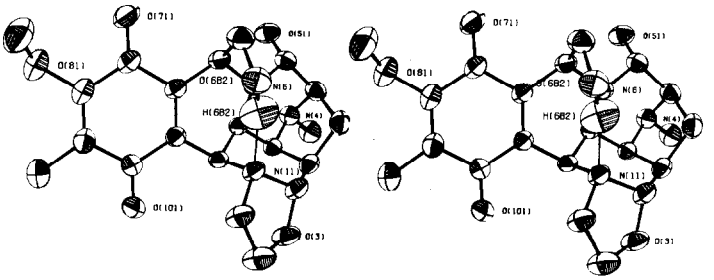


Figure 1

References

1. D. Kluepfel, H.Baker, G. Piattoni, S.N. Sehgal, A. Sidorowicz, K. Singh and C. Vézina: Naphthyridinomycin, a new broad spectrum Antibiotic., in preparation.

2. Found for $C_7H_9NO_2$ (or its multiples); C, 60.29; H. 6.63; N, 9.93; calculated = C, 60.42; H, 6.52; N, 10.07.

3. A tangent formula program by M. Drew, Lawrence Radiation Laboratory, University of California, Berkely, California, extensively modified by A.C. Larson, S. Motherwell, Cambridge University, England, K. Fawcette, University of Toronto, Canada, F. Leung, University of Montreal, Canada.

4. J. Sygusch, F.R. Brisse, S. Hanessian, Acta Cryst., B30, 40(1974).