

X-Ray Structure of Alborixin, a New Antibiotic Ionophore

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Summary The structure of a new antibiotic, alborixin, has been determined by X-ray and chemical methods.

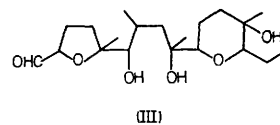
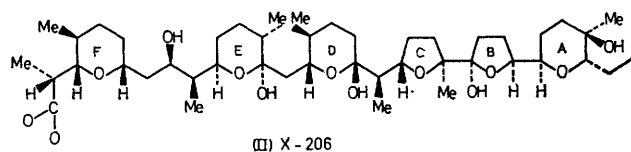
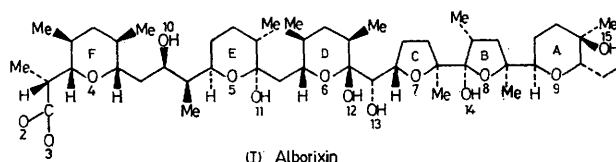
FROM cultures of a strain of *Streptomyces albus*, we have isolated a biologically active compound we named alborixin. It shows activity against gram-positive bacteria and antifungal properties which will be described elsewhere.

Alborixin (I) is a monocarboxylic acid, pK_a 10.02 (MeOH). Its potassium salt, $C_{48}H_{83}O_{14}K$,¶ is a crystalline solid, m.p. 209–210 °C; ν_{max} (KBr) 3700–3100 (OH) and 1560 cm^{-1} (CO_2^-); m/e 922 (M^+). The free acid (I), $C_{48}H_{84}O_{14}$, is an amorphous solid, m.p. 100–115 °C; $[\alpha]_{D}^{20} -7^\circ$ (c 4, acetone). Treatment of (I) by conventional methods afforded the methyl ester $C_{48}H_{86}O_{14}$, m.p. 67–68 °C, a triacetate, $C_{54}H_{90}O_{17}$, m.p. 70–75 °C, and a tetrasilylated compound. The presence of 6 OH groups (alcohols and hemiacetals) was confirmed by the mass spectra of these derivatives. A derivative corresponding to the reduction of 3 hemiacetal rings was obtained by treatment of (I) with $NaBH_4$. It was oxidised by KIO_4 to give a product with m.p. 55–56 °C, to which we assign structure (III).

The structure of alborixin potassium salt was established by X-ray diffraction analysis on crystals obtained from aqueous EtOH.

Crystal data: $C_{48}H_{83}O_{14}^-K^+$, $M = 922$; monoclinic, $a = 12.202$ (4), $b = 16.087$ (5), $c = 13.471$ (5) Å, $\beta = 102.43^\circ$,

$D_m = 1.5$; $D_c = 1.55$ g cm^{-3} ; $Z = 2$; space group $P2_1$. 5334 independent reflections were collected on a Siemens



computer-controlled automatic diffractometer, with Ni-filtered $Cu-K_\alpha$ radiation. 4414 non-zero reflections were

¶ Satisfactory elementary analyses have been obtained for all compounds whose molecular formulae are given.

used in the Fourier synthesis and least-squares refinement. The potassium was found from a Patterson synthesis. However, the well known pseudo-mirror problem related to the $P2_1$ space group, the heavy atom, and the high symmetry of the molecule led to the failure of the multiresolution direct method generally used for such structures. A method, based on enantiomorph discrimination by the quartets,¹ and a modified tangent formula for phase refinement was then developed.** The structure was refined by least squares to an R value of 0.067.

Alborixin is very similar to X-206 (II). [The addition of 4 methyl groups (on rings B, D, and F) and the exchange of an Me by an OH group do not modify the conformation and the absolute configuration of the backbone]. The backbone 'describes a path similar to that of the seam of a tennis ball,' but the hydrogen bonding and the cation co-ordination are slightly different in alborixin and X-206.

** Details of the method and its application will be published elsewhere.

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⁶ T. J. Petcher and H. P. Wezer, *J.C.S. Chem. Comm.*, 1974, 697.

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Three intramolecular hydrogen bonds stabilize the conformation: O(2) \cdots O(15), 2.64; O(3) \cdots O(12), 2.58; and O(11) \cdots O(14) 2.78 Å. The potassium is co-ordinated to 8 oxygen atoms in a distorted cubic arrangement. The distances are: K \cdots O(2), 2.89; K \cdots O(7), 3.07; K \cdots O(8), 2.81; K \cdots O(9), 2.76; K \cdots O(10), 2.71; K \cdots O(11), 2.98; K \cdots O(12), 2.69; K \cdots O(15), 2.76 Å.

Alborixin is a new member of the family of polycyclic polyether monocarboxylic acid antibiotics which now includes monensin, nigericin, X-537A (lasalocid), grisorixin, dianemycin, X-206, A-204A,³ salinomycin,⁴ A-23187,⁵ septamycin,⁶ and lysocellin.⁷

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