# X-Ray Crystal and Molecular Structure of Antibiotic X-206

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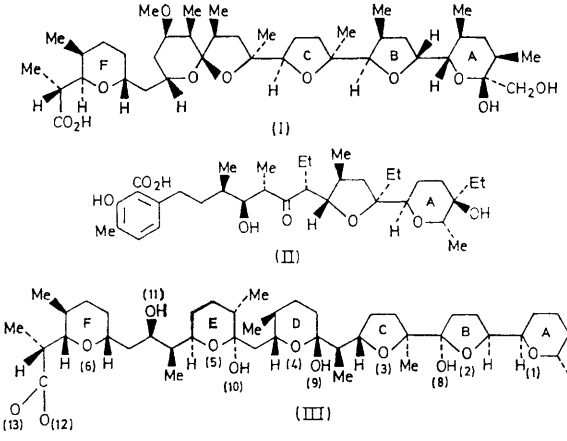
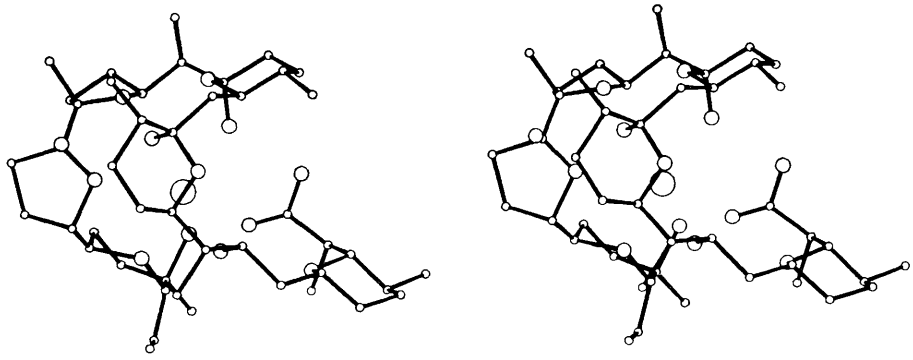
*Summary* The molecular structure and absolute configuration of the polyether antibiotic X-206 has been established from an *X*-ray crystallographic analysis of its silver salt, $C_{45}H_{77}AgO_{13}$.

THE structures of several antibiotics of the polyether type have recently been elucidated by *X*-ray crystallographic studies of their salts, *e.g.* monensin[1] and nigericin[2] (I) which were shown to have similar structures. The isolation of three polyether antibiotics has been reported[3] and the first was identical[4] with nigericin.[2] The structure[5] and biosynthesis[6] of the second (II) were reported recently as was grisorixin.[7]

The third (III), antibiotic X-206, $(C_{45}H_{78}O_{13}\cdot H_2O)$,[8] m.p. 133—145°, is a monocarboxylic acid, $\nu_{max}$ ($CHCl_3$) 1725 $cm^{-1}$, p$K_a$ 8·1 (70% dimethylformamide) and forms a typical organic soluble, water-insoluble sodium salt, m.p. 189—190°, $\nu_{max}$ ($CHCl_3$) 1570 $cm^{-1}$ ($CO_2^-$).

The structure of X-206 was established as (III) from a three-dimensional *X*-ray diffraction analysis of its silver salt.[3] *Crystal data:* $C_{45}H_{77}AgO_{13}$ $a = 22{\cdot}90$, $c = 17{\cdot}44$ Å, $D_m = 1{\cdot}24$ (flotation in aqueous KI), $Z = 6$, $D_c = 1{\cdot}19$, space group $P6_3$. 1392 Reflections were measured on a Hilger and Watts Y290 four-circle diffractometer with Ni-filtered Cu-$K_\alpha$ radiation. Absorption corrections were applied ($\mu = 37$ $cm^{-1}$). The structure was solved by the heavy-atom method and refined by block-diagonal least-squares. The absolute configuration of the molecule was established by calculating structure factors for both enantiomers. The results ($R = 8{\cdot}9$ and 10·2%) show the molecule to have the configuration depicted in (III) and the Figure.

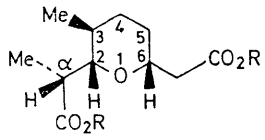


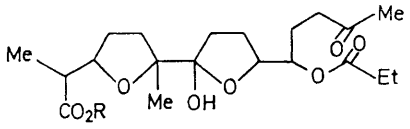
FIGURE

The manner in which the antibiotic ion complexes with the silver ion is similar to that found for other salts of this type.[1,2,5,7] Here the anion is wrapped around the silver in such a way that its backbone describes a path similar to

that of the seam on a tennis ball. This "seam" is completed by an intramolecular hydrogen bond (2·69 Å) from O(7) to O(13). The silver is co-ordinated unsymmetrically to 6 oxygen atoms [O(1), O(13), O(9), O(11), O(2), and O(10)] with Ag–O distances in the range 2·5—2·8 Å.




(IVa), R = H
(IVb), R = Me




(Va), R = H
(Vb), R = Me

Jones oxidation of (III) gave *inter alia*, the acids (IVa) and (Va). Compound (IVa), m.p. **193°**, is an isomer of the dicarboxylic acid isolated[2b] from nigericin. N.m.r. spectra showed all three ring substituents in (IVa) to be equatorial, δ ($CDCl_3$) 0·83 (3H, d, *J* 6 Hz, 3-Me), 1·08 (3H, d, *J* 7 Hz, α-Me), 1·00—2·00 (5H, m, ·CH·$CH_2$·$CH_2$·), 2·35 (2H, d, *J* 7 Hz, ·$CH_2$·$CO_2$), 2·69 (1H, dq, *J* 3 and 7 Hz, α-H), 3·57 (1H, d, *J* 9·5 and 3 Hz, 2-H), and 3·79 p.p.m. (1H,m, *J* 7 Hz, 6-H). This difference in chemical shift (0·22 p.p.m.) between 2-H and 6-H in both (IVa) and (IVb) is in agreement with the configuration (calc.[9] 0·28 p.p.m.) given by *X*-ray rather than the α-C-epimer (calc. 0·94 p.p.m.).

The second oxidation product was isolated as its methyl ester (Vb) after treatment with diazomethane. High resolution mass spectrometry gave a molecular ion at *m/e* 414·2300 consistent with $C_{21}H_{34}O_8$ and fragment ions at *m/e* 356 ($M - C_3H_6O$) and 355 ($M - C_2H_3O_2$) supporting a methyl ketone and methyl ester respectively.

The two oxidation products were compatible with the structure assigned by *X*-ray for rings A, B, C, and F. The absolute configuration of (III) shows similarities to the absolute stereochemistry of (II)[5] and nigericin[2] (I). After interchanging the methyl and ethyl groups in (III), ring A has the structure identical to the tetrahydropyranyl ring in (II). Three of the four asymmetric centres in ring F [C(2) of (IVa) is the exception] have the same absolute configuration as the analogous centres in nigericin.

Antibiotic X-206 contains twenty asymmetric centres and is the largest polyether antibiotic for which a molecular structure has been established. The molecule is unusual in possessing three lactol functions.

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