X-Ray Crystal Structure of a Silver Complex of Antibiotic X-537A; a Structure Enclosing Two Metal Ions

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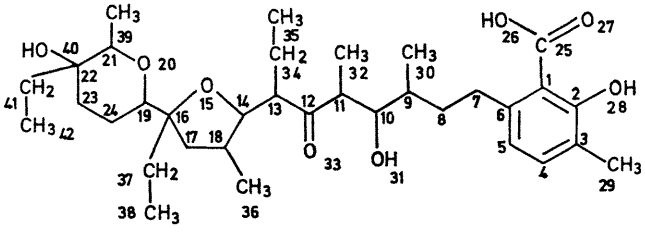
Summary The *X*-ray structure analysis of the Ag^+ salt of the oxygen-containing antibiotic, X-537A, reveals a dimeric cylindrical-like structure for the complex with a hydrophobic exterior and two Ag^+ ions on the inside of the cylinder; each Ag^+ ion complexes to five oxygen atoms and one phenyl ring.

THE antibiotic X-537A,[1] active against coccidial infections in chickens, has been shown to have structure (I) by the results of an *X*-ray crystallographic examination of a barium salt, $(C_{34}H_{53}O_8)_2{-}Ba^{2+}{\cdot}H_2O$.[2] That complex consisted of discrete $(C_{34}H_{53}O_8)_2Ba{\cdot}H_2O$ groups which had a generally circular shape with almost all the oxygen atoms of the two antibiotic anions directed inward to complex the Ba^{2+} ion and the water molecule, and a hydrophobic hydrocarbon exterior.[2] It was structurally similar to the complexes of neutral cyclodepsipeptide antibiotics,[3,4] which complex metal ions in the presence of anions, and which may act as metal carriers through membranes.[5] We have carried out an *X*-ray analysis on the Ag^+ complex of (I) to determine to what extent the above structural features are altered by the presence of a monovalent cation. The Ag^+ salts of two other oxygen-containing antibiotics of similar function have been determined by *X*-ray methods.[6,7]‡

The Ag^+ salt of (I) was prepared by treating an ethereal solution of the Ba^{2+} salt[1] with aqueous Ag_2SO_4, followed by crystallization from aqueous acetone.[8] The crystals of the Ag^+ salt of X-537A are irregularly shaped, approximately equidimensional, transparent prisms. *Crystal data*: monoclinic, $(C_{34}H_{53}O_8)^{-}Ag^{+}{\cdot}CH_3COCH_3$, M 755·7, a = 12·25(3), b = 16·81(3), c = 19·82(4) Å, β = 97°39′(1′), U = 4045 × 10^{-24} cm^3, D_m = 1·25 g cm^{-3}, D_c = 1·24 g cm^{-3}, Z = 4, space group $P2_1$. The structure was determined by the heavy-atom method, and has been refined by full-matrix least-squares methods, employing anisotropic temperature factors for all non-hydrogen atoms, to an R-factor of 0·068 on 5690 independent non-zero reflections collected on a Picker FACS-1 diffractometer (Cu-K_α radiation).



(I)

The structure consists of discrete dimers of two antibiotic anions and two Ag^+ ions (Figure 1). The molecules of acetone could not be located on a difference map and are presumed to be located in a disordered fashion in channels of 8 Å diameter (between atoms) that run parallel to the *a*-axis. The presence of *ca.* one acetone molecule per Ag^+ ion was conclusively demonstrated by n.m.r. spectra of dissolved crystals. The two anions completely enclose the two Ag^+ ions by forming a rather distorted cylinder with virtually all the oxygen atoms directed inward to the central axis of the cylinder and with most of the hydrocarbon side chains on the outside, (Figure 2). There is a pseudo-two-fold rotation axis almost along the crystallographic *a*-direction (perpendicular to the paper in Figure 1) relating the two antibiotic anions.

Each Ag^+ ion is within 3·0 Å of five oxygen atoms [O(15),

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‡ *Added in proof.* Since submission of this paper, the structure of the Ag^+ salt of grisorixin, an antibiotic closely related to nigericin, has been reported; M. Alleaume and D. Hickel, *Chem. Comm.*, 1970, 1422.

O(20), O(31), O(33), and O(40)], with *one* antibiotic anion providing the entire oxygen co-ordination for *one* Ag^+ ion.

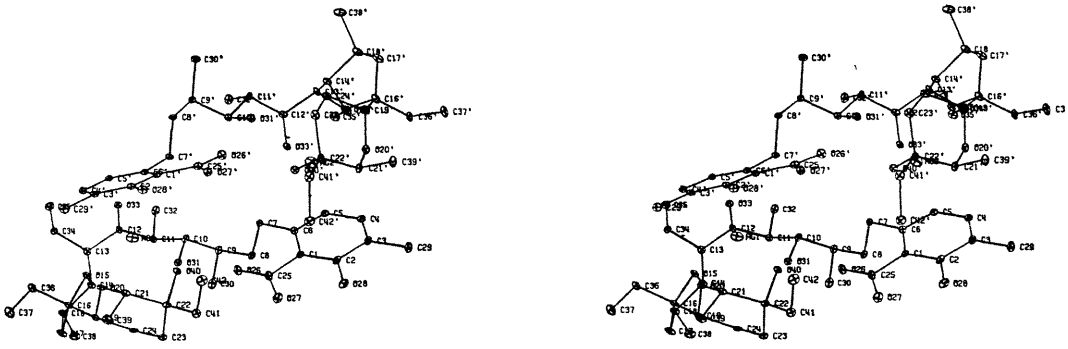

FIGURE 1. *Stereoscopic pair of the complex viewed along the* a-*axis.*

A novel feature of this antibiotic complex when compared to those of monensic acid[6] and nigericin (polyetherin A),[7]

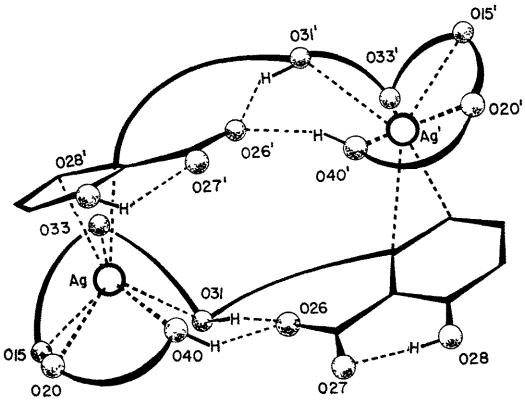

FIGURE 2. *Schematic drawing of the co-ordination of the* Ag^+ *ion. The covalent backbone of the molecule is shown by thick solid lines; the co-ordination bonds by discontinuous lines. Hydrogen-bonding assignments are also shown.*

is that in addition to the oxygen co-ordination, each Ag^+ ion complexes with the phenyl ring of one of the anions. Each Ag^+ ion is closest to C(5) [2·41(1) and 2·46(2) Å], followed by C(6) [2·61(1) and 2·79(2) Å]. The full three-dimensional structures of several Ag^+–aromatic complexes have been reported[9–12] and in these structures the Ag^+ ion is usually found associated unsymmetrically with two carbon atoms of a phenyl ring. In most such structures the shorter $Ag^+ \cdots C$ distance lay in the range 2·45—50 Å, a wider variation being found in the lengths of the longer $Ag^+ \cdots C$ distance.[12] In the present structure, the planes defined by the two groups of atoms Ag, C(5), and C(6), make angles of 93°26′ and 93°34′ with the planes defined by the respective phenyl rings. Corresponding angles of 98° and 94° were found in the $C_6H_6 \cdot AgAlCl_4$[10] and bis-(*m*-xylene) $AgClO_4$[12] structures.

The two antibiotic anions in the complex are held in virtually identical conformations by hydrogen bonding between the same pairs of oxygen atoms. The O(27) · · · O(28), O(31) · · · O(26), O(40) · · · O(26) distances are 2·41(2) and 2·39(2), 2·91(2) and 2·90(2), and 2·60(2) and 2·64(2) Å respectively. Virtually the same hydrogen-bonding pattern was found in the Ba^{2+} salt,[2] the only difference being that O(40) was closer to O(27) than to O(26) in that complex.

As was found in the case of the Ag^+ salt of monensic acid,[6] but unlike the Ba^{2+} salt of X-537A,[2] the oxygen atoms of the carboxyl groups are not involved in co-ordination to the metal ion. In the monensic acid salt,[6] the Ag^+ ion co-ordinated to six oxygen atoms (< 2·7 Å), while in the nigericin salt,[7] the Ag^+ ion co-ordinated to five oxygen atoms (< 2·7 Å). The $Ag^+ \cdots Ag^+$ distance is 7·108(2) Å.

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