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CRYSTAL STRUCTURE OF 2,8-BIS(BROMOMETHYL)-1,7-DIOXASPIRO[5,5]UNDECANE, AN INTERMEDIATE IN THE SYNTHESIS OF ANALOGUES OF A23187

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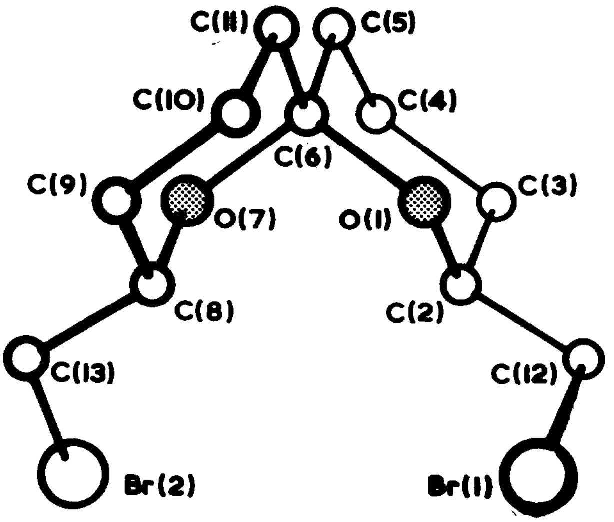
The synthesis of two stereoisomers of a key intermediate in the preparation of ionophoric analogues of the antibiotic A23187 has been described in the preceding paper.[1] To establish the stereochemistry of these products, a sample of one (compound **7** of that paper) was analysed by X-ray diffraction methods.

Crystals were clear and colourless. A square prism 0.12 x 0.12 x 0.24 mm was mounted on a Picker four-circle diffractometer.

Crystal data: $C_{11}H_{18}Br_2O_2$, *M* = 342.1. Triclinic, space group P$\bar{1}$, *a* = 7.422(4), *b* = 11.431(6), *c* = 8.964(10)Å, *α* = 79.82(6), *β* = 112.91(6), *γ* = 108.69(3)°, *U* = 662.4 Å^3. *Z* = 2, F(000) = 340. μ(Mo-K_α) = 60.4 cm^{-1}, (no absorption corrections applied). λ(Mo-$K_{\bar{\alpha}}$) = 0.71069 Å (with Zr filter).

Intensities of 1240 unique reflections, to θ = 20 °, were raised to a common scale to allow for the steady fall of the intensity of a control reflection to 79 % of its original value; the crystal also turned brown.



Projection of the molecule, showing the atomic numbering scheme.
The enantiomer shown is that with the configuration found in A23187.

Location of two bromine atoms from the Patterson map indicated the space group (centrosymmetric, $P\bar{1}$) and an electron density map phased by these atoms showed the remaining non-hydrogen atoms, and thus confirmed the symmetry. Coordinates of hydrogen atoms were calculated. Refinement of the atomic parameters by the program SHELX[2] is at R = 0.074 for 931 planes having $I > \sigma_I$. Tables of atomic parameters, molecular dimensions and structure factors may be obtained from the author.

RESULTS

In this crystal, the molecule displays a pseudo two-fold axis of symmetry (Figure). The tetrahydropyran rings are chair-shaped and the bromomethyl substituents lie in equatorial positions. This (racemic) product is thus shown to have the same configuration and conformation as the dioxaspiro[5,5]undecane group in A23187[3]: the structure determination of this compound therefore enables preparation of analogues with the required and established stereochemistry to proceed. Identical arrangements of dioxaspiro[5,5]undecane groups are found also in the milbemycins[4], in the antibiotics rutamycin[5] and oligomycin[6], and perhaps in aplysiatoxin.[7]

In the preparation of our sample (see preceding paper) the product might have had any of three configurations (each with an enantiomer); there are three possible chair-chair conformations for each configuration. Examination of Dreiding models suggests that, of the nine, only the form found in the X-ray analysis is relatively free from close intramolecular contacts; the shortest contact in this molecule appears to be that between the secondary hydrogen atoms on C(2) and C(8), 2.57 Å.

Two conformers of structure **6**[1] have C_2 symmetry. In one of these forms, and in one form of structure **8**[1], there are H...H contacts of ca. 1.8 Å which might be lengthened by distortion from the Dreiding conformation. It is more probable, of course, that alternative boat or skew conformations would be adopted by these isomers.

All intermolecular contacts in our sample are of the van der Waals' type, although some appear short, e.g. $C(10)\ldots C(10^{I})$ 3.65, $C(11)\ldots C(11^{II})$ 3.66, and $Br(1)\ldots Br(1^{III})$ 3.70 Å.

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