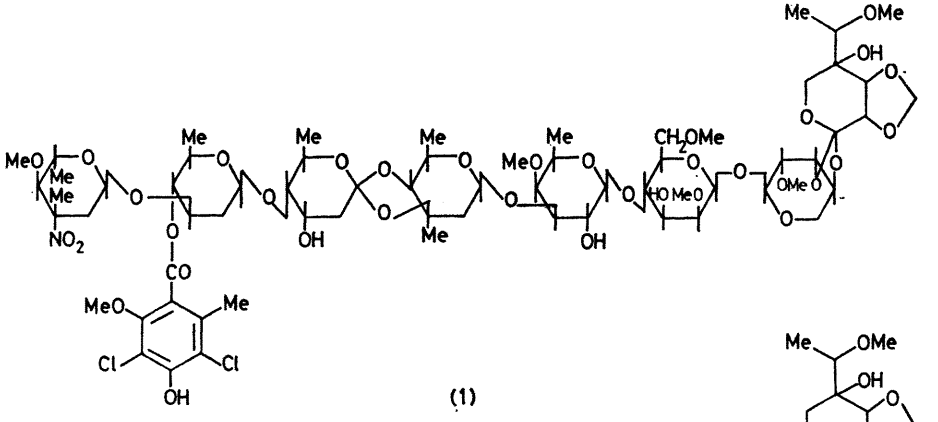
X-Ray Crystal and Molecular Structure of Olgose, a Major Degradation Product of the Oligosaccharide Antibiotic Everninomicin D

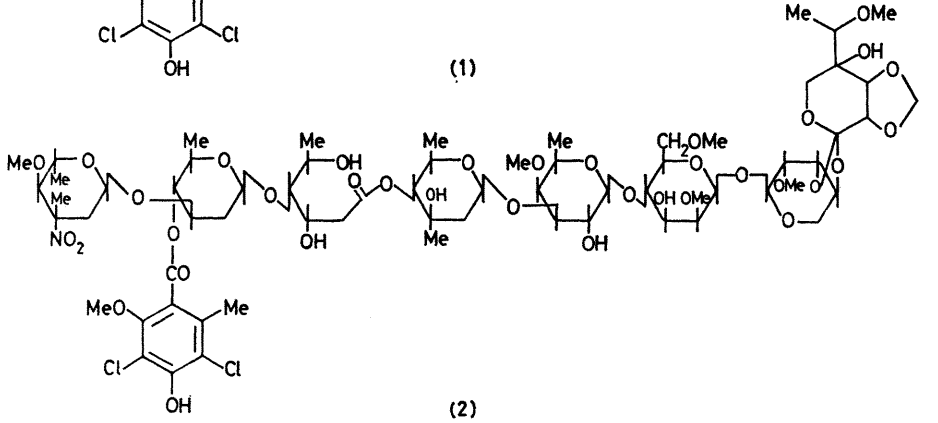
By ASHIT K. GANGULY* and OLGAR Z. SARRE
(*Chemical Research Department, Schering Corporation, Bloomfield, New Jersey* 07003)
and ANDREW T. MCPHAIL* and RICHARD W. MILLER
(*Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina* 27706)

Summary Single crystal *X*-ray analysis of olgose (**4**) unequivocally confirms all the structural features reported earlier[1] and defines stereochemistry at C(4), (C6), and the orthoester carbon atom.

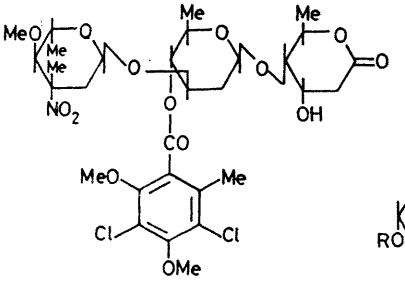
EVERNINOMICIN D[1] (**1**), produced by *Micromonospora Carbonaceae*, displays high activity against gram positive bacteria and Neisseria including strains resistant to β-lactams, tetracycline, lincomycin, rifampicin, macrolides, and chloramphenicols. On mild acidic hydrolysis everninomicin D yielded everninomicin D_1 (**2**) which on treatment with diazomethane underwent smooth cleavage to (**3**) and olgose[1] (**4**). We previously reported on the determination of the structure of olgose as (**4**) based on extensive chemical degradations and spectroscopic data but these studies left undefined the stereochemistries at C(4), C(6), and the orthoester carbon atom.



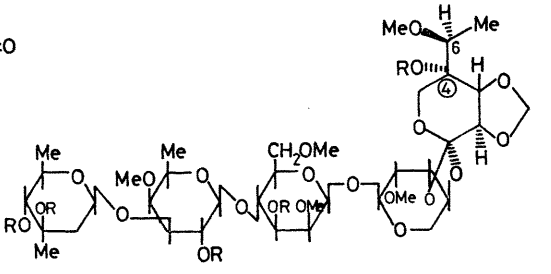
(1)



(2)

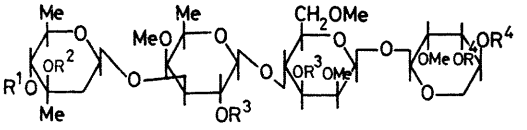


(3)

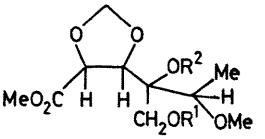


(4) R = H
(7) R = Me

Olgose (**4**) on treatment with methanolic toluene-*p*-sulphonic acid yields evertetrose[2] (**5**) and an ester[1] (**6**). The linkage of (**5**) to (**6**) in the structure of (**4**) was demonstrated by solvolysis of permethylated olgose (**7**) with methanolic toluene *p*-sulphonic acid to produce (**8**) and (**9**).



(5) $R^1 = R^2 = R^3 = R^4 = H$
(9) $R^1 = R^2 = R^3 = Me$; $R^4 = H$



(6) $R^1 = R^2 = H$
(8) $R^1 = H$; $R^2 = Me$

As compound (**7**) had no carbonyl i.r. absorption and on hydrolysis also yielded (**8**) and (**9**), it was evident that the primary hydroxy group and the ester function of (**8**) must be linked to the hydroxy groups in (**9**) in the structure of permethylated olgose (**7**). To explain these observations we proposed[1] structures (**4**) and (**7**), without definition of stereochemistry at C(4), C(6), and the orthoester carbon atom, for olgose and its permethylated derivative, respectively. The ^{13}C n.m.r. spectrum of (**4**) showed a signal at δ 119·8 p.p.m. confirming the presence of an orthoester carbon. We here report the results of an *X*-ray single-crystal structure analysis of olgose monohydrate which not only unequivocally confirm all the structural features deduced earlier but also complete the stereochemical assignments at the asymmetric centres.

Crystals of olgose monohydrate, $C_{37}H_{62}O_{22}.H_2O$, belong to the orthorhombic system, space group $P2_12_12$, $a = 24{\cdot}150(10)$, $b = 24{\cdot}383(10)$, $c = 7{\cdot}748(3)$ Å, $U = 4562{\cdot}2$ Å^3, $Z = 4$, $D_c = 1{\cdot}277$ g cm^{-3}. The structure was solved by direct methods using the MULTAN 76[3] programme package modified to include the magic integer approach.[4] Least-squares refinement of atomic positional and thermal parameters (anisotropic C, O; fixed H contributions) has reduced R to 0·059 over 3587 statistically significant [$I > 2{\cdot}0\sigma(I)$] reflections measured on an Enraf–Nonius CAD-3 automated diffractometer (Ni-filtered Cu–K_α radiation; θ—2θ scans). A view of the solid-state conformation is shown in the Figure.† All the six-membered rings approximate to chair forms and the olgose molecule has an extended conformation with one intramolecular O–H · · · O hydrogen bond; all the other hydroxy groups are involved in intermolecular O–H · · · O hydrogen bonds.

Everninomicins represent a growing class of antibiotics which contain two orthoester linkages. Extensive chemical degradations and spectroscopic evidence have led to the structural elucidation of everninomicin B[5], C[6], and D[1], the first amongst this class of antibiotics whose structures have been determined. Recently the structure of a related antibiotic, flambamycin,[7] has been reported. Here the stereochemistry of one of the two orthoester carbon atoms in everninomicin D has been determined by *X*-ray analysis which we believe is the only unambiguous way of defining

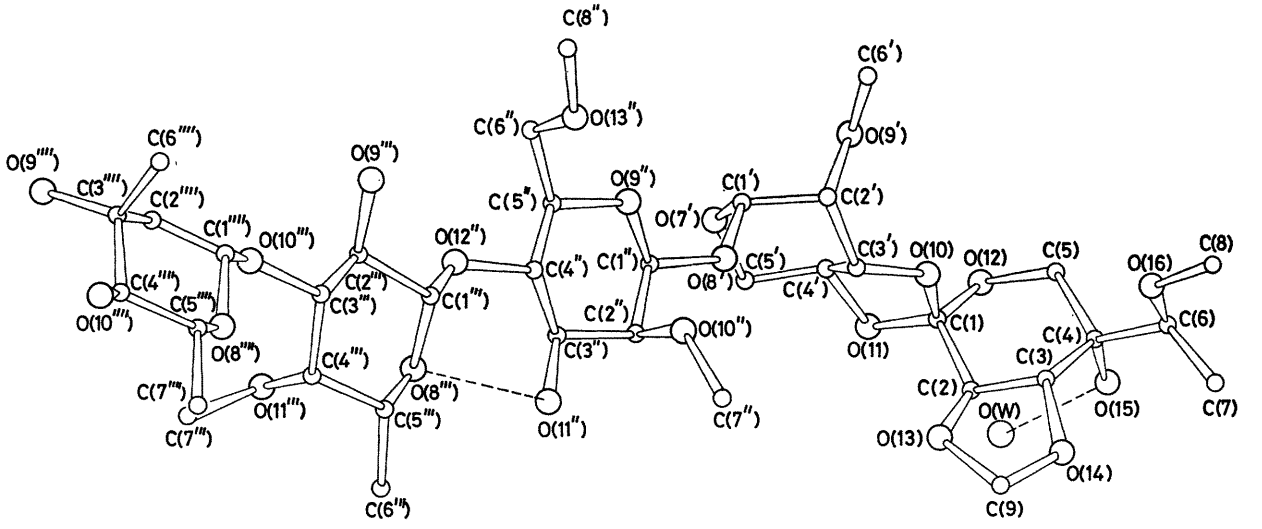


FIGURE. Atomic arrangement in the asymmetric crystal unit of olgose monohydrate; broken lines denote hydrogen bonds.

† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

stereochemistry of such a chiral centre. From the similarity of structure and stereochemistry of everninomicin B, C, D, and flambamycin, it would be fair to assume that the chirality of one of the orthoester carbons (belonging to the olgose portion of the molecule) in all these structures would be as represented in olgose (**4**).

(*Received*, 30*th August* 1978; *Com.* 941.)

[1] A. K. Ganguly, O. Z. Sarre, D. Greeves, and J. Morton, *J. Amer. Chem. Soc.*, 1975, **97**, 1982.
[2] A. K. Ganguly, O. Z. Sarre, and S. Szmulewicz, *Chem. Comm.*, 1971, 746.
[3] P. Main, L. Lessinger, M. M. Woolfson, G. Germain, and J.-P. Declercq, 'MULTAN 76, a System of Computer Programmes for the Automatic Solution of Crystal Structures,' Universities of York and Louvain, 1976.
[4] L. Lessinger and T. N. Margulis, *Acta Cryst.*, 1978, **B34**, 578.
[5] A. K. Ganguly and A. K. Saksena, *J. Antibiotics*, 1975, **28**, 707.
[6] A. K. Ganguly and S. Szmulewicz, *J. Antibiotics*, 1975, **28**, 710.
[7] W. D. Ollis, C. Smith, I. O. Sutherland, and D. E. Wright, *J.C.S. Chem. Comm.*, 1976, 350.