X-Ray Determination of the Structure of the Polyether Antibiotic K-41

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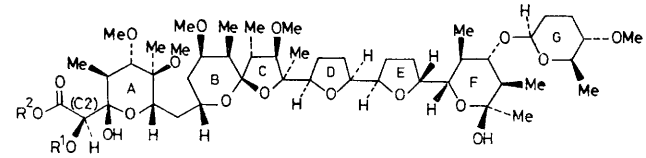
Summary The molecular structure and absolute configuration of the antibiotic K-41 has been established by *X*-ray crystal structure analyses of the sodium salts of its *p*-iodo- and *p*-bromo-benzoates.

ANTIBIOTIC K-41, from *Streptomyces hygroscopicus*, has an interesting pesticidal effect[1] besides antibacterial activity. It was characterized as a polycyclic polyether monocarboxylic acid antibiotic by preliminary examination.[2] The formula of its sodium salt was proposed to be $C_{48}H_{81}O_{19}Na$ based on microanalytical data; no loss in weight up to the decomposition point was observed. *X*-Ray crystal structure analyses of the sodium salts of the *p*-iodo- and *p*-bromo-benzoate of K-41, recrystallized as solvates from their respective water-saturated n-hexane solutions,



K-41, $R^1=H$, $R^2=H$
(I), $R^1=COC_6H_4I$, $R^2=Na$
(II), $R^1=COC_6H_4Br$, $R^2=Na$

were undertaken to establish the structure of the antibiotic. The results indicate the correct molecular formula of the sodium salt to be $C_{48}H_{81}O_{18}Na.H_2O$, the presence of water of crystallization being confirmed by the Karl Fischer reagent.

Crystal data: (I) $C_{55}H_{84}O_{19}NaI\cdot H_2O\cdot C_6H_{14}$, space group $P2_12_12$, $a = 36{\cdot}330(4)$, $b = 15{\cdot}321(4)$, $c = 12{\cdot}790(1)$ Å, $D_C = 1{\cdot}23$ g cm^{-3}, $Z = 4$; (II) $C_{55}H_{84}O_{19}NaBr.H_2O\cdot C_6H_{14}$, space group $P2_12_12_1$, $a = 33{\cdot}963(3)$, $b = 15{\cdot}407(2)$, $c = 12{\cdot}943(1)$ Å, $D_C = 1{\cdot}23$ g cm^{-3}, $Z = 4$. The intensity data were collected on a Hilger and Watts Y-290 diffractometer by use of nickel-filtered Cu-K_α radiation ($\theta_{max} = 38°$).

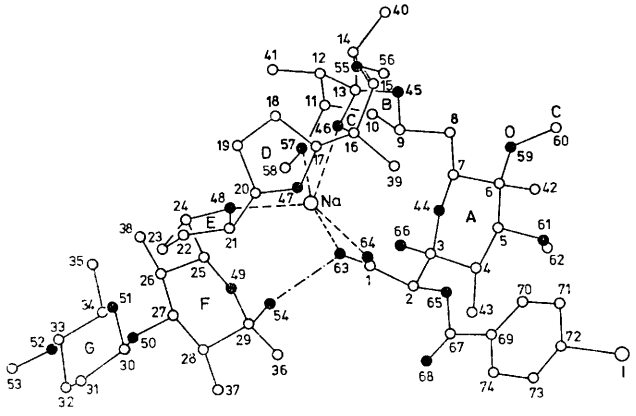


FIGURE. Perspective view of (I). The sodium atom is surrounded by six oxygen atoms (– – – –), and the polycyclic chain is bridged by a hydrogen bond (–·–·–). The solvate molecules are not shown.

The structures were solved by direct methods and refined to R values of 0·093 (1862 reflections) and 0·107 (1684) for (I) and (II), respectively, by block-diagonal least-squares using anisotropic temperature factors for iodine, bromine, and sodium atoms. The solvate molecules, disordered in the crystals, and all the hydrogen atoms have not as yet been located. The absolute configuration of (I) was determined by the anomalous scattering method.†

The structure of (I) (Figure) is almost the same as that of (II). The molecular structure of K-41 deduced from (I) and (II) is very similar, except for a hydroxy-group at C(2), to those of the polyether antibiotics such as A204A, A28695 (septamycin), and carriomycin.[3] The ^{1}H n.m.r. spectrum (in $CDCl_3$) of (II) shows a sharp singlet (1H) at σ 5·33 due to a >CH–OCO– unit. Further, the C(2)–C(3) bond is easily cleaved by $Pb(OAc)_4$ to give a lactone which has lost two carbon atoms. The results clearly support the presence of the α-hydroxycarboxylic acid function which has never been found in the family of nigericin.

The accompanying communication[4] describes the independent determination of the structure of an antibiotic (A32887) identical to K-41 using mainly mass spectrometric methods.

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† The atomic co-ordinate 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.

[1] T. Ishiguro, unpublished work.
[2] N. Tsuji, K. Nagashima, M. Kobayashi, Y. Wakisaka, Y. Kawamura, S. Kozuki, and M. Mayama, *J. Antibiotics*, 1976, **29**, 10.
[3] Carriomycin: N. Otake, H. Nakayama, H. Miyamae, S. Sato, and Y. Saito, *J. C. S. Chem. Comm.*, 1977, 590, and reference therein for work on other polyether antibiotics.
[4] J. L. Occolowitz, D. E. Dorman, and R. L. Hamill, *J. C. S. Chem. Comm.*, following communication.