Structures of New Antibiotic Substances, Sakyomicin A, B, C, and D; *X*-Ray Crystal and Molecular Structure of Sakyomicin A

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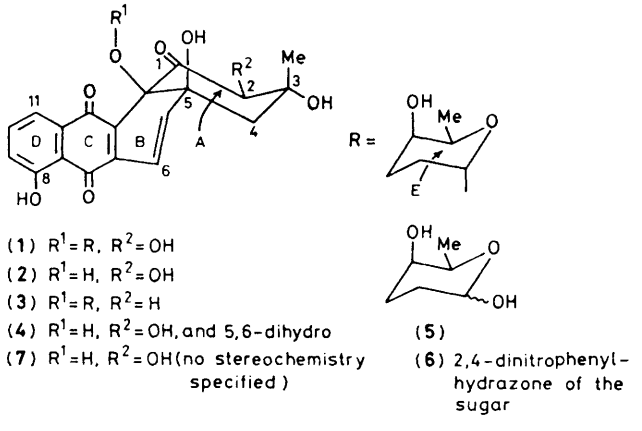
The structure of a new antibiotic substance, sakyomicin A has been elucidated by *X*-ray crystallographic analysis and structures for its congeners, sakyomicin B, C, and D have been proposed from their spectroscopic properties.

Investigation of cultures of Nocardia sp. No. 53 resulted in the isolation of four new antibiotic substances, sakyomicin A (**1**), B (**2**), C (**3**), and D (**4**) effective to Gram-positive bacteria. We report here the structure elucidation of these metabolites.

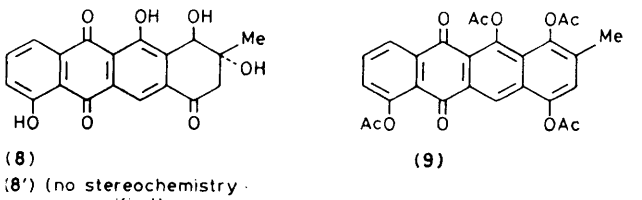
Compound (**1**), $C_{25}H_{26}O_{10}$, m.p. 205—207 °C (from n-hexane–acetone), $[\alpha]_D^{20}$ −99.4° (*c* 0.8, EtOH), λ_{max} (EtOH) (ε) 216, 238, 310, and 415 nm (28,500, 15,900, 5,300, and 4,500), ν_{max} (KBr) 3490, 3200, 1720, and 1638 cm^{-1}, and δ_H(CD_3OD, 360 MHz) 0.56 (3H, d, *J* 6.6 Hz, 6′-Me) (see Figure 1 for numbering scheme used), 1.25 (3H, s, 13-Me), 1.63 and 1.93 [1H each, m, C(2′)-H_2], 1.84 and 2.10 [1H each, broad d and m, C(3′)-H_2], 2.00 and 2.12 [1H each, d, *J* 14.9 Hz, C(4)-H_2], 3.42 [1H, br. s, C(4′)-H], 3.70 [1H, q, *J* 6.6 Hz, C(5′)-H], 4.23 [1H, s, C(2)-H], 5.37 [1H, diffused d, *J* 2.8 Hz, C(1′)-H], 6.46 [1H, d, *J* 10.0 Hz, C(5)-H], 6.93 [1H, d, *J* 10.0 Hz, C(6)-H], 7.37 [1H, d, *J* 7.9 Hz, C(9)-H], 7.65 [1H, d, *J* 7.9 Hz, C(11)-H], and 7.77 [1H, t, *J* 7.9 Hz, C(10)-H] gave (**2**) and a hexose (**5**) by hydrolysis with 2 M HCl at room temp. for 1 h. The latter was characterised as its 2,4-dinitrophenylhydrazone (**6**) (M^+ = 312.1097: $C_{12}H_{16}N_4O_6$ requires 312.1070), m.p. 117—118 °C, $[\alpha]_D^{26}$ +14.8° (*c* 0.5, pyridine), δ_H(CD_3OD, 200 MHz) 1.18 (3H, d, *J* 6.2 Hz), 1.78 (2H, m), 2.56 (2H, m), 3.43 (1H, d-t, *J* 4.6 and 9.2 Hz), 3.64 (1H, d-q, *J* 4.6 and 6.2 Hz), 7.32 (1H, s), 7.79 (1H, t, *J* 5.2 Hz), 7.96 (1H, d, *J* 9.6 Hz), 8.31 (1H, d-d, *J* 9.6 and 2.8 Hz), and 9.01 (1H, d, *J* 2.8 Hz), and was proposed to be the enantiomer of (−)-rhodinose (2,3,6-trideoxy-L-*threo*-hexose).[1] A single-crystal *X*-ray analysis of (**1**) was carried out.



(**1**) R^1 = R, R^2 = OH
(**2**) R^1 = H, R^2 = OH
(**3**) R^1 = R, R^2 = H
(**4**) R^1 = H, R^2 = OH, and 5,6-dihydro
(**7**) R^1 = H, R^2 = OH (no stereochemistry specified)

(**5**)

(**6**) 2,4-dinitrophenylhydrazone of the sugar



(**8**)
(8′) (no stereochemistry specified)

(**9**)

Crystal data: orthorhombic, $P2_12_12_1$, a = 15.901(5), b = 12.771(9), c = 11.232(3) Å, U = 2280.9 Å^3, Z = 4, D_x = 1.416 g/cm^3. The structure was determined on a FACOM M200 computer, using 1845 reflection data collected on a Rigaku AFC-5 diffractometer with graphite-monochromated Mo-K_α radiation; current R = 0.054.† Figure 1 shows the structure of (**1**). The sugar group is located above the B- and C-rings, and the methyl group in the sugar moiety has a short contact with one of the keto-functions on the C-ring.

Based on the absolute configuration of the sugar (**5**), the absolute configuration of (**1**) was elucidated. Recently Ohta, Okazaki, and Kishi reported the structure of P-1894B (rineomycin A_1) based on the configuration of the sugar obtained from its hydrolysate.[1] The aglycone part of (**1**) is enantiomeric to that of P-1894B and, to our knowledge, (**1**) is the first naturally occurring compound containing (+)-rhodinose.

The structure of (**2**), aglycone of (**1**), is similar to that of of yoronomycin (**7**),[2] but not identical since they differ in their $[\alpha]_D$ values [(**2**), 31.6°; yoronomycin, 73.5° in dioxan].

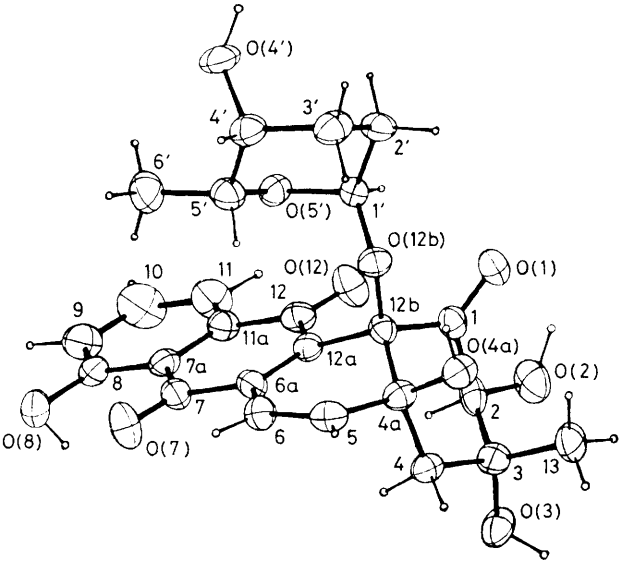


Figure 1. Structure of sakyomicin A (**1**) showing the crystallographic numbering system used.

† 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.

In addition, the ^{1}H n.m.r. spectrum of yoronomycin in $(CD_3)_2SO$ was measurable but no spectrum of (**2**) could be obtained in $(CD_3)_2SO$ owing to line broadening. Irradiation of (**2**) with sunlight in methanol resulted in formation of the tetracyclinone (**8**) in 67% yield by electrocyclic ring opening of the B-ring followed by tautomerisation and recyclisation. In 1977, the transformation of yoronomycin into the tetracyclinone (**8′**) (no stereochemistry indicated) was reported[3] but its ^{1}H n.m.r. spectrum was not identical with that of (**8**) by direct comparison.‡ Acetylation of (**8**) (acetic anhydride–pyridine) gave the acetate (**9**), the i.r. spectrum of which was identical with that of the acetate obtained from (**8′**);[3] this suggests that yoronomycin is in fact a diastereoisomer of (**2**) at C(2) and/or C(3).

Sakyomicin C, $C_{25}H_{26}O_9$, m.p. 143—145 °C, $[\alpha]_D^{21}$ −82.7° (*c* 0.8, MeOH), λ_{max} (EtOH) (ε), 216, 240, 310, and 415 nm (20,000, 11,500, 3,500, and 4,400), ν_{max} (KBr) 3400, 1722, and 1635 cm^{-1}, showed signals at δ 2.46 [1H, d, *J* 11.8 Hz, C(2)-H] and 2.75 [1H, d-d, *J* 11.8 and 2.3 Hz, C(2)-H] in its ^{1}H n.m.r. spectrum and its ^{13}C n.m.r. ($CDCl_3$) spectrum exhibited a signal at 55.78 p.p.m. (t). Based on its molecular formula and spectroscopic properties, the structure was proposed as (**3**).

‡ We have, to date, been unable to obtain an authentic specimen for direct comparison.

The structure of sakyomicin D, $C_{19}H_{18}O_8$, m.p. 161—163 °C (benzene solvate) $[\alpha]_D^{20}$ −140° (*c* 0.8, MeOH), λ_{max} (EtOH), (ε) 213, 249, 273, and 425 nm (37,000, 8,400, 8,800, and 3,600), ν_{max} (KBr) 3400, 1728, and 1640 cm^{-1} was proposed to be (**4**), since hydrogenation of (**2**) (5% Pd–carbon) gave (**4**) in good yield.

We thank Prof. N. Morimoto and Dr. K. Tomita, Institute of Geology and Mineralogy, Faculty of Sciences, Kyoto University for use of the AFC-5 *X*-ray diffractometer and Drs. H. Naoki and T. Iwashita, Suntory Institute for Bio-organic Research for measurement of the 360 MHz ^{1}H and ^{13}C n.m.r. spectra.

Received, 20th September 1982; Com. 1111

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