Structure of Rosamicin†, a New Macrolide from *Micromonospora rosaria*

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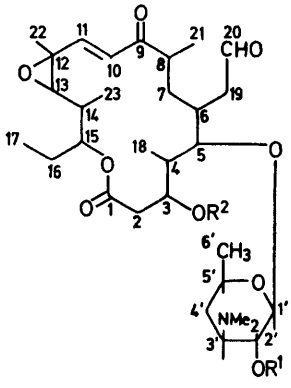
Summary Gross structure (**1**) has been assigned to the new macrolide antibiotic, rosamicin, on the basis of chemical and spectroscopic evidence.

FERMENTATIONS of *Micromonospora rosaria* sp. n. produce a new macrolide antibiotic, named rosamicin.[1] On the basis of chemical and spectroscopic data, structure (**1**), has been assigned to the new antibiotic.



(1) $R^1 = R^2 = H$
(2) $R^1 = COCH_3, R^2 = H$
(3) $R^1 = R^2 = COCH_3$

Compound (**1**) was isolated by extraction[1] and was purified by crystallization from chloroform, m.p. 119—122°, $[\alpha]_D^{26}$ — 35° (ethanol), λ_{max} (MeOH) 240 nm (ϵ 14,600), and analysed for $C_{31}H_{51}NO_9$. The i.r. spectrum indicated hydroxy (2·83 μm), *N*-methyl (*ca.* 3·59 μm), aldehyde (3·68 and 5·78 μm), lactone (5·78 and 8·5 μm) and conjugated ketone (5·90 and 6·15 μm,) while the n.m.r. spectrum (60 MHz, $CDCl_3$) exhibited bands at δ 0·9 (t, *J* 7 Hz, $-CH_2CH_3$), 1·45 (s, C–CH_3), 2·30 [s, 2(N–CH_3)], 4·25 [d, J 7 Hz, O-CH-(CH)O], 4·9 (ddd, >CH–OC=O), 6·54 [s, 2(C=CH)] and 9·72 p.p.m. (broad s, C–CH=O). In $(CD_3)_2CO$ the vinyl proton signal was resolved to an *AB* quartet, δ 6·43 and 6·87 p.p.m., *J* 16 Hz. The m.s. showed a molecular ion peak at *m/e* 581 consistent with the empirical formula, and major fragmentations at *m/e* 563 (*M* — 18), 553 (*M* — 28), 407 (*M* — 174), 389 (*M* — 174 – 18), 174 and 158 (base peak). The latter two fragments are ascribed to a D-desosamine moiety in the molecule; hydrolysis of (**1**) with 6N hydrochloric acid afforded D-desosamine,[2] m.p. 85—87°, $[\alpha]_D$ +15 → + 50° (water, 24 h), identical with an authentic sample (n.m.r., m.s.).

In view of the similarity of the physical properties of (**1**) and those of the macrolide antibiotic cirramycin A_1,[3] a direct comparison of the mass spectra of the two compounds was carried out. Cirramycin A_1 showed a molecular ion peak at *m/e* 597 and fragmentations at *m/e* 579 (*M* — 18), 569 (*M* — 28), 407 (*M* — 190), 389 (*M* — 190 — 18), 190 and 174. The fragmentation patterns indicate that the aglycone in both compounds is the same, the difference being a desosamine moiety in (**1**) corresponding to a mycaminose moiety in cirramycin A_1.‡

Additional support for the structure of (**1**) was provided by its conversion into the 2′-monoacetate (**2**) [m.p. 116—121°, $[\alpha]_D$ — 25° (ethanol), λ_{max} (MeOH) 240 nm (ϵ 14,000)] with one equivalent of acetic anhydride in acetone and into the 3,2′-diacetate (**3**) {m.p. 104—7°, [α] — 24° (ethanol), λ_{max} (MeOH) 240 nm (ϵ 12,700), no residual hydroxy in the i.r.} with excess of acetic anhydride in pyridine. In the m.s., compound (**2**) had M^+ 623, with fragments at *m/e* 407 and 389 for the aglycone and at *m/e* 216 and 200 for 2-acetyldesosamine, while compound (**3**) showed M^+ 665 and fragments at *m/e* 449 (acetyl aglycone) and 389 (449 — acetic acid) as well as at *m/e* 216 and 200.

Examination of the n.m.r. spectra of compounds (**1**), (**2**), and (**3**) [in $(CD_3)_2CO$] permitted assignment of the β configuration to the glycosidic linkage of desosamine ($J_{1',2'}$ 7 Hz).[2b] The point of attachment of the sugar moiety on the aglycone as C-5 followed from the acylation shifts and splitting patterns of H-3, H-5, and H-2′.

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† Formerly named rosaramicin.

‡ The structure of cirramycin A_1 is well founded on degradative studies.[3]

[1] G. H. Wagman, J. A. Waitz, J. Marquez, A. Murawski, E. M. Oden, R. T. Testa, and M. J. Weinstein, *J. Antibiotics*, in the press.
[2] (a) E. H. Flynn, M. V. Sigal, jun., P. F. Wiley, and K. Gerzon, *J. Amer. Chem. Soc.*, 1954, **76**, 3121; (b) P. W. K. Woo, H. W. Dion, L. Durham, and H. S. Mosher, *Tetrahedron Letters*, 1962, **735**.
[3] H. Tsukiura, M. Konishi, M. Saka, T. Naito, and H. Kawaguchi, *J. Antibiotics*, 1969, **22**, 89.