

Isolation and Structure of Nanaomycin D, an Enantiomer of the Antibiotic Kalafungin

By SATOSHI ŌMURA,* HARUO TANAKA, YUKIO OKADA, and HIROFUTO MARUMO

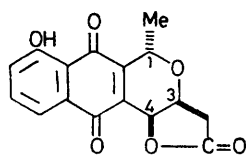
(*Kitasato University and The Kitasato Institute, 5-9-1 Shirokane, Minato-ku, Tokyo 108, Japan*)

Summary The absolute configuration of nanaomycin D, the fourth antibiotic isolated from *Streptomyces rosa* var. *notoensis* which is also obtained from nanaomycin A by air oxidation in methanol, has been determined; it has been found to be the enantiomer (**1**) of kalafungin (**2**).

THE isolation, characterization, and structural determination of nanaomycins A, B, and C, new antifungal antibiotics from *Streptomyces rosa* var. *notoensis* have been reported.¹ We now report the isolation of a new component

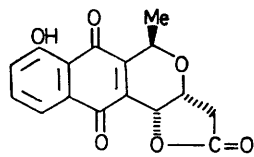
nanaomycin D (**1**), and the conversion of nanaomycin A into nanaomycin D. Evidence is presented that nanaomycin D is the enantiomer of kalafungin (**2**),² obtained from *Streptomyces tanashiensis*.³

From the crude extract, nanaomycin D was isolated by silica gel chromatography (CHCl₃-MeOH, 100:1), m.p. 170–173 °C, λ_{max} (MeOH) 213 (ε 41,700), 257 (11,600), and 426 (4450) nm; ν_{max} (KBr) 1775, 1665, 1650, and 1622 cm⁻¹. The formula C₁₆H₁₂O₈ was deduced from the elemental analysis and mass spectrometry [*m/e* 300.061 (*M*⁺)]. These



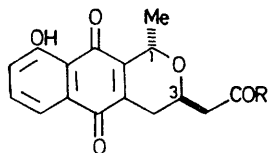
(1S, 3S, 4S)

(1)



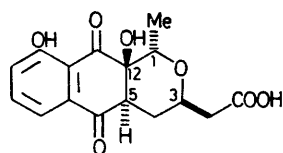
(1R, 3R, 4R)

(2)



(1S, 3R)

(3) R = OH

(5) R = NH₂

(1S, 3R, 5R, 12R)

(4)

properties coincided with those of kalafungin but the direction of the specific rotation of (1), $[\alpha]_D^{20} -278^\circ$ (*c* 0.44,

MeOH), was opposite to that of kalafungin which was reported to be $[\alpha]_D^{25} +159^\circ$ (*c* 1, CHCl₃).³

The o.r.d. curve of (1) shows a negative Cotton effect with a trough, $[\phi] -450$, at 355 nm and a peak, $[\phi] +640$, at, 292 nm (*c* 0.1, MeOH). The o.r.d. curve of (2) is the exact reverse of this, with a peak at 355 nm and a trough at 292 nm, suggesting that the absolute configuration of nanaomycin D is as in (1), the enantiomer of kalafungin (2)²

During t.l.c. comparison of the nanaomycin components, we found that nanaomycin A was converted into nanaomycin D by air oxidation in methanolic solution. When the methanolic solution (1 mg/ml) was kept in the dark at room temperature for three weeks, nanaomycin A was completely oxidized to nanaomycin D. This leads to assignment of the absolute configurations (3), (4), and (5) to nanaomycins A, B, and C, respectively.

The production of two enantiomers by the genus *Streptomyces* is of interest in the biosynthesis of a series of these antibiotics.

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² A. Zeeck, H. Zährer, and M. Mardin, *Annalen*, 1974, 1101.

³ M. E. Bergy, *J. Antibiotics*, 1968, **21**, 454.