X-Ray Crystal Structure Determination of Furanomycin

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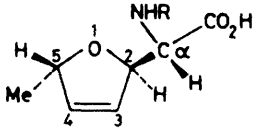
Summary The structure of furanomycin has been established from the *X*-ray crystal structure analysis of its *N*-acetyl-derivative, to be (+)-(α*S*, 5*S*, 2*R*)-α-amino (2,5-dihydro-5-methyl)furan-2-acetic acid.

THE structure of furanomycin (**1**), an isoleucine antagonist and antibiotic isolated from *Streptomyces* L-803 (ATCC 15795), has previously been investigated by ^{1}H n.m.r. and c.d. spectroscopy and by chemical degradation.[1] The most likely configuration in view of the large ^4J(H-2,H-5) value (5·7 Hz) was proposed to be 5*R*,2*R*,α*S* at the respective asymmetric centres;† the protons H-2 and H-5 are *cis* to each other in this structure. However, recent theoretical studies of ^4J(H,H) across a dual path in five-membered rings[2] suggested that these protons might occupy *trans* positions. Our investigations using lanthanide-assisted ^{1}H n.m.r. spectra of (**1**) in [$^2H_2$]O using shift reagents for aqueous solutions‡ seemed to support the *trans* structure.



(**1**) R = H
(**2**) R = COMe

The total stereospecific synthesis of (**1**) also indicated a molecular configuration of 5*S*,2*R*,α*S*.[3] To establish this molecular structure for (**1**), the *X*-ray crystal structure analysis of *N*-acetylfuranomycin (**2**) (m.p. 216 °C; $[\alpha]_D^{20.5}$ +311·3; $[\theta]_{200}$ +143,000 in MeOH) was carried out.

Crystal data: $C_9H_{13}NO_4$, space group $P2_12_12_1$, a = 9·911(1), b = 11·827(2), c = 8·939(1) Å, D_c = 1·262 g cm^{-3}, Z = 4. 1118 independent intensities were collected on a Rigaku diffractometer with graphite-monochromatized Cu-K_α radiation (θ_{max} = 70°). The structure was solved by direct methods and refined by the block-diagonal least-squares technique to an R value of 0·043 for 991 reflections.§

A perspective view of (**2**) is shown in the Figure from which it can be seen that H-5 is *trans* to H-2. The absolute configuration of the molecule was determined assuming the *S* configuration at C-6, assigned from a previous c.d. spectral study.[1] Hence, C-2 and C-5 adopt the *R* and *S* configurations, respectively.

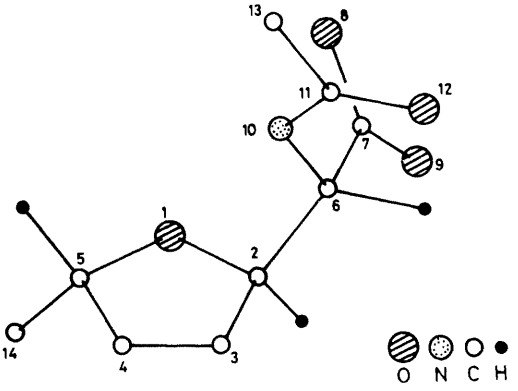


FIGURE. Perspective view of *N*-acetylfuranomycin including the atom numbering systems

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† In ref. 1, this was incorrectly described as 5*R*,2*R*,α*R*.

‡ Lanthanide-induced shift ratios for the H-α, H-2, H-3, H-4, H-5, and CH_3 signals were 1·00, 0·84, 0·32, 0·09, 0·13, and −0·01, using $Pr(NO_3)_3$, and 1·00 (unobservable owing to overlapping of H_2O signals) 0·58, 0·25, 0·30, and 0·07 using $Eu(NO_3)_3$, respectively [corrected by $La(NO_3)_3$]. These shift ratios were obtained according to the method of F. Inagaki, S. Takahashi, M. Tasumi, and T. Miyazawa, *Bull. Chem. Soc. Jpn.*, 1975, **48**, 853, 1590.

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

[1] K. Katagiri, K. Tori, Y. Kimura, T. Yoshida, T. Nagasaki, and H. Minato, *J. Med. Chem.*, 1967, **10**, 1149.
[2] M. Barfield, R. J. Spear, and S. Sternhell, *J. Am. Chem. Soc.*, 1971, **93**, 5322; 1975, **97**, 5160.
[3] M. Joullié, personal communication. The total synthesis of (±)-furanomycin has also been reported (T. Masamune and M. Ono, *Chem. Lett.*, 1975, 625).