Communications to the editor

STRUCTURE OF ANTIBIOTIC A 25822B, A NOVEL NITROGEN-CONTAINING C28-STEROL WITH ANTIFUNGAL PROPERTIES

Sir:

The mold Geotrichum flavo-brunneum was found to produce a complex of closely related compounds with broad-spectrum antifungal activity (K. Michel et al., to be published).

The principal active component, A 25822B (m.p. 115–118°C, [α]D 0° [c 0.775, MeOH], pKa’ 8.4 [66% DMF], λmax [EtOH] 238 nm [ε 12,300], vmax [CHCl3] 3571, 1618 cm⁻¹), has the molecular formula C28H45NO (M⁺ 411.3497; required, 411.3501). A shift of the maximum to 277 nm (s 13,400) in acidic solution suggested that u.v. absorption was due to the presence of a conjugated imine group; i.e., C=C–C=\overset{\text{N}}{\text{N}}. This was supported by the observation that A 25822B reacted with KBH4 in CH₃OH to give an amorphous dihydro derivative (M⁺ 413; no u.v. λmax at 238 nm). The latter formed a crystalline diacetate (m.p. 130–132°C; M⁺ 497.3869; required for C32H51NO₃, 497.3869; vmax [CHCl₃] 1706 [ester C=O] 1639 [amide C=O] cm⁻¹). The nmr spectrum (Fig. 1) revealed the presence of several methyl groups and exhibited a broad envelope of absorption due to methine and methylene protons. Two olefinic protons (δ 4.67 [J<1.0], 4.75 [J<1.0]) were assigned to an exomethylene group because of the characteristic small, vinyl geminal coupling (<1.0 Hz).

On the basis of the foregoing information, together with additional spectroscopic and chemical data that will be reported at a later time, two possible structures, 1a and 2, were considered for A 25822B. Conclusive evidence for structure 1a was obtained by X-ray crystallographic analysis of its methiodide derivative. The latter crystallized from CH₃OH–H₂O solu-

Fig. 1. NMR spectrum of A25822B (100 MHz, CDCl₃)
tion as yellow plates. The crystals belong to the noncentrosymmetric space group P2₁2₁2₁, with four molecules in a unit cell having the dimensions $a=8.248±0.002$ Å, $b=7.804±0.002$ and $c=46.33±0.02$. The crystal density measured by flotation is 1.230 g cm$^{-3}$, compared to a calculated density of 1.233 g cm$^{-3}$ for C$_{28}$H$_{45}$NO·CH$_3$I. Intensities for 1454 unique reflections were measured on an automated diffractometer using copper X-radiation. The position of the iodide ion was determined from a sharpened Patterson map. Calculation of a three-dimensional electron density map phased on the iodide revealed all of the non-hydrogen atoms except six on the end of the side chain. The structure was partially refined by least-squares and a difference map calculated to find the remaining non-hydrogen atoms. Further refinement brought the R value down to 0.16. Complete details of the refined crystal structure will be published elsewhere.

A related minor factor, A 25822 A (m. p. 147°C, $[\alpha]_D^{25} -72^\circ$ [c 1.15, MeOH], pKa’ 8.0 [66 % DMF], $\lambda_{max}$ 239 nm [ε 12,600], $\gamma_{max}$ 3584 [OH], 1621 [C=C—C=N] cm$^{-1}$), was shown to be the 4,4-dimethyl analog of A 25822 B (lb). It has the molecular formula C$_{30}$H$_{49}$NO (M$^{+}$ 439.3776; required, 439.3814).

Compounds la and lb are thus members of a new family of mold metabolites. To the best of our knowledge, they are the first reported examples of naturally-occurring homo-aza sterols. Details of their isolation and properties and, also, other factors of the complex will be reported in subsequent papers from these laboratories.

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