Structures of Two Stereoisomers of a New Type of Indoloditerpene Related to the Tremorgenic Mycotoxin Paxilline, from *Emericella desertorum* and *Emericella striata*

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The structure elucidation of emindoles DA (**1**) and SA (**2**), indoloditerpenes from the mycelial extract of *Emericella desortorum* and *Emericella striata*, respectively, is reported, based on their ^1H and ^{13}C n.m.r. spectra and an *X*-ray crystallographic study of emindole DA monoacetate (**4**); these are novel proto-type indoloditerpenes biologically related to paxilline (**3**).

Recently we reported the isolation of paxilline (**3**),[1] a tremorgenic mycotoxin from the mycelial extract of *Emericella striata* (Rai, Tewari & Mukerji) Malloch & Cain, strain 80-NE-22,[1] as a major metabolite, and *Emericella desertorum* Samson & Mouchacca, strain CBS 653.73,[2] as a minor component. During our search for compounds related to (**3**), two new compounds designated as emindole DA (**1**), prisms (from benzene–hexane), m.p. 146—147 °C, $[\alpha]_D$ −30.7° (*c* 2.32, methanol), and emindole SA (**2**), amorphous powder, m.p. 58—60 °C, $[\alpha]_D$ +32.0° (*c* 0.79, methanol), were isolated from the mycelial hexane extract of *E. desertorum* and from the mycelial acetone extract of *E. striata*, respectively.

Electron-impact (e.i.) mass spectrometry [*m/z* 405 (M^+)] and elemental analysis of (**1**) and (**2**) confirmed their empirical formula as $C_{28}H_{39}NO$. A positive colouration with the Ehrlich reagent (green to greenish red)[3] and the strong fragment ion at

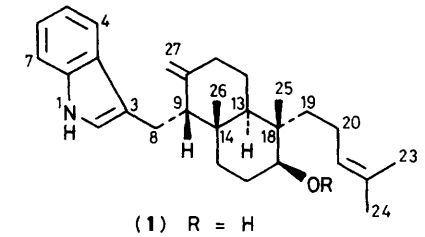
m/z 130 $[(C_9H_8N)^+]$ in the e.i. mass spectra of (**1**) and (**2**) suggested the presence of an (indol-3-yl)methyl group in both compounds.†

^1H and ^{13}C N.m.r. data indicate structure (**1**) for emindole DA, and this was confirmed by an *X*-ray crystal structure determination of its monoacetate (**4**), needles from hexane, m.p. 142.5—143.5 °C, which was derived from (**1**) by acetylation with acetic anhydride in pyridine.‡

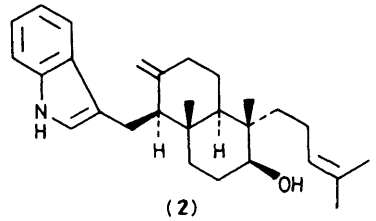
The structure of the acetate (**4**), showing the relative configuration, is shown in Figure 1. The absolute configuration was not determined; we assume that the structure of emindole DA is as shown in (**1**), in view of the co-occurrence with (**3**) from *E. desertorum*.

Emindole SA (**2**) showed similar spectral data (u.v., i.r., ^1H and ^{13}C n.m.r.) to those of emindole DA (**1**). Homonuclear ^1H–{^1H} decoupling experiments, and homonuclear ^1H–^1H and heteronuclear ^1H–^{13}C correlation spectra were in accordance with emindole SA having structure (**1**), including relative stereochemistry.

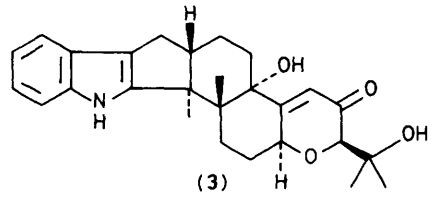
Acklin *et al.*[5] reported that indoloditerpenes such as paspaline (**5**) and paspalicine (**6**) were derived from tryptophan and geranylgeraniol in *Claviceps paspali* Stevens & Hall



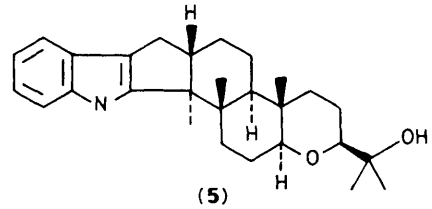
(**1**) R = H
(**4**) R = Ac



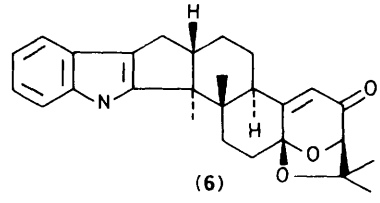
(**2**)



(**3**)



(**5**)



(**6**)

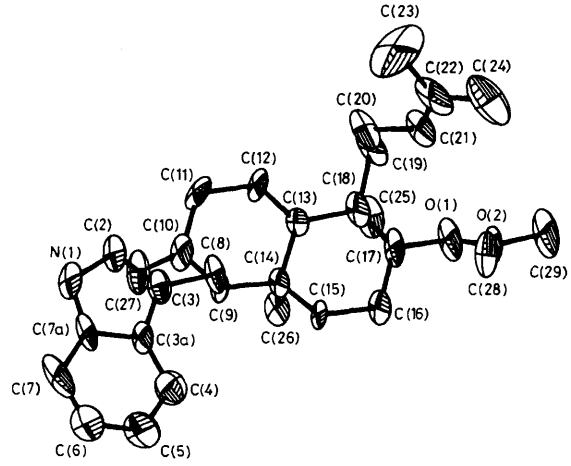


Figure 1. Perspective view of the crystal structure of one of the independent molecules of the acetate (**4**), with 50% probability thermal ellipsoids.

† *Spectral data* for (**1**): $\lambda_{max.}$ (MeOH) 224 (log ε 4.22), 277 sh (3.75), 283 (3.79), and 291 nm (3.75); $\nu_{max.}$ (KBr) 3550, 3400, 3280, 1450, 1430 and 740 cm^{-1}; $\delta_H(CDCl_3)$ 0.827 (3H, s), 0.984 (3H, s), 1.28—1.50 (3H, m), 1.50—1.66 (3H, m), 1.671 (3H, br.s), 1.715 (3H, br.s), 1.73—1.80 (3H, m), 1.93—2.10 (4H, m), 2.180 (1H, dd, *J* 12.7 and 3.2 Hz), 2.284 (1H, ddd, *J* 13.4, 13.1, and 5.4 Hz), 2.700 (1H, dd, *J* 14.4 and 10.3 Hz), 3.132 (1H, dd, *J* 14.4 and 3.7 Hz), 3.618 (1H, dd, *J* 8.6 and 6.9 Hz, CH_2CHOH), 4.156 (1H, br.s, C=CH_2), 4.510 (1H, br.s, C=CH_2), 5.162 (1H, br.t, *J* 7.1 Hz, CH_2CH=C), 6.887 (1H, d, *J* 2.0 Hz), 7.087 (1H, br.t, *J* 7.8 Hz), 7.162 (1H, br.dd, *J* 8.1 and 7.8 Hz), 7.325 (1H, br.d, *J* 8.1 Hz), 7.563 (1H, br.d, *J* 7.8 Hz), and 7.866 (1H, br.s, NH); $\delta(^{13}C)$ ($CDCl_3$) 16.91 (C-25), 17.70 (C-23), 21.89 (C-20), 23.03 (C-12), 23.18 (C-26), 23.27 (C-8), 25.74 (C-24), 27.75 (C-16), 30.83 (C-11), 34.58 (C-15), 37.54 (C-19), 37.92 (C-14), 39.07 (C-13), 41.12 (C-18), 58.61 (C-9), 73.95 (C-17), 110.20 (C-27), 111.10 (C-7), 115.57 (C-3), 118.88 (C-4), 118.94 (C-5), 121.63 (C-6), 121.90 (C-2), 124.94 (C-21), 127.64 (C-3a), 131.21 (C-22), 136.25 (C-10), and 148.10 (C-7a).

N.m.r. data for (**2**): $\delta_H(CDCl_3)$ 0.812 (3H, s), 0.873 (3H, s), 1.25—1.75 (6H, m), 1.606 (3H, br.s), 1.677 (3H, br.s), 1.75—2.10 (7H, m), 2.196 (1H, br.d, *J* 10.7 Hz) 2.389 (1H, ddd, *J* 13.9, 2.5, and 2.5 Hz), 2.817 (1H, dd, *J* 15.4 and 10.7 Hz), 2.983 (1H, br.d, *J* 15.4 Hz), 3.597 (1H, dd, *J* 11.4 and 4.8 Hz, CH_2CHOH), 4.719 (1H, br.s, C=CH_2), 4.840 (1H, br.s, C=CH_2), 5.094 (1H, br.t, *J* 6.9 Hz, CH_2CH=C), 6.893 (1H, d, *J* 2.2 Hz), 7.113 (1H, br.dd, *J* 8.1 and 7.4 Hz), 7.167 (1H, br.dd, *J* 8.1 and 7.4 Hz), 7.313 (1H, br.d, *J* 8.1 Hz), 7.620 (1H, br.d, *J* 8.1 Hz), and 7.882 (1H, br.s, NH); $\delta(^{13}C)$ 14.98 (C-26), 16.94 (C-25), 17.65 (C-23), 19.63 (C-8), 21.59 (C-20), 23.74 (C-12), 25.70 (C-24), 27.98 (C-16), 37.39 (C-15), 37.52 (C-19), 37.92 (C-11), 39.63 (C-14), 41.36 (C-18), 48.94 (C-13), 56.79 (C-9), 73.27 (C-17), 107.94 (C-27), 111.02 (C-7), 116.23 (C-3), 118.70 (C-4), 119.06 (C-5), 121.69 (C-2), 121.78 (C-6), 124.76 (C-21), 127.66 (C-3a), 131.18 (C-22), 136.13 (C-10), and 147.94 (C-7a).

‡ *Crystal data:* $[(C_{30}H_{41}NO_2)_2]$, prisms from MeOH, monoclinic, space group $P2_1$, a = 18.155(25), b = 12.137(13), c = 13.097(12) Å, β = 113.07(9)°, Z = 2, D_c = 1.12 g cm^{-3}. Intensity measurements were made with Cu-K_α radiation (λ = 1.5405 Å; graphite monochromator) on a Rigaku AFC-5 FOS diffractometer in the ω–2θ mode with θ ≤ 60°. A total of 4166 unique reflections were measured, of which 3784 were considered observed, $F > 3\sigma(F)$. The measured reflections were corrected for Lorenz–polarization only. The structure was solved using MULTAN 80[4] and refined by block-diagonal least-squares. Convergence, with anisotropic thermal parameters for all non-hydrogen atoms, was reached at R = 0.089 (R_w = 0.090) using all the observed reflections. The difference electron density map based on the final atomic parameters showed no maxima greater than 0.37 e $Å^{-3}$. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

and that migration of the carbon skeleton in the diterpene moiety occurred during the biosynthesis. It is interesting in considering the biogenesis of indoloditerpenes that the stereoisomers (**1**) and (**2**) were isolated, along with (**3**), from two fungi, *E. desertorum* and *E. striata*, repectively, There seem to be two pathways for cyclization of the diterpene moiety in *E. desertorum* and *E. striata* at the earlier stages of biosynthesis: one will give paxilline (**3**) which is biosynthesized by migration of the carbon skeleton after cyclization, and the other may give the new type of indoloditerpenes, emindoles DA (**1**) and SA (**2**), by partial cyclization only.

Received, 30th March 1987; Com. 403

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