Bonafousine, a Novel Dimeric Indole Alkaloid: *X*-Ray Crystal Structure

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Summary The elucidation of the structure of bonafousine, a novel dimeric alkaloid from *Bonafousia tetrastachya*, from its spectral properties (u.v., c.d., i.r., and ^1H and ^{13}C n.m.r.) and *X*-ray crystal structure analysis is reported.

We report the elucidation of the structure of the dimeric indole alkaloid bonafousine (**1**), extracted from leaves of *Bonafousia tetrastachya* (Humboldt, Bonpland, and Kunth) Markgraf (Apocynaceae).[1] This major alkaloid was isolated by standard methods (*ca.* 0·02% yield from dried plant material and 12% of the total alkaloids): m.p. 199—200 °C (methanol), $[\alpha]_D^{20} - 35°$ (c 1, $CHCl_3$). The formula $C_{35}H_{40}N_4O_3$ was established by high-resolution mass spectrometry ($M = 564·3093$) and the molecular peak confirmed by chemical ionization mass spectrometry. Bonafousine, ν_{max} ($CHCl_3$): 2·78, 2·96, 3·05 (OH and NH), and 5·83 μm (CO_2Me) exhibits an indole-type u.v. spectrum, λ_{max} (EtOH): 228 (log ϵ 4·88), 286 (4·09), 294 sh. (4·54), and 300 (3·00) nm, with a bathochromic shift in alkaline solution due to a phenolic group: 228 (4·88), 286 (4·54), 294 (4·54), and 320 (4·49) nm. Its mass spectrum shows fragmentions at m/e 353, 136, 135, 124, and 122, implying the presence of a phenolic ibogane species (A),[2] and m/e 211, 184, 170, 169, and 156, suggesting another indole unit[2,3] typical of a 1′,2′,3′,3a′,4′, 5′-hexahydroindolo[3,2,1-*d,e*]naphthyridine (B^1) or a 1,2,3,4,5,11b-hexahydroindolizino[8,7-*b*]indole (B^2). The ^1H n.m.r. spectrum ($CDCl_3$, Me_4Si) displays signals at δ 0·84 (3H, t, J 6 Hz, 18-Me), 3·54 (3H, s, H_3C–O–CO), 7·08 (1H, d, J 8 Hz, 10-H), and 7·51 (1H, d, J 8 Hz, 9-H). The ^{13}C n.m.r. spectral analysis (see structural formulae)† (31 peaks, 35 carbon atoms) was consistent with the presence of an 11-hydroxy-16-methoxycarbonylibogane unit (A)‡ substituted at C-12 by a methine carbon (bearing a nitrogen atom) of an indole unit (B^1) or (B^2).§

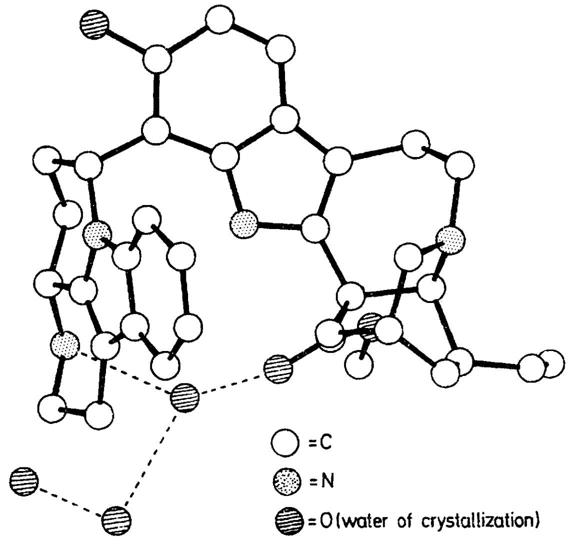
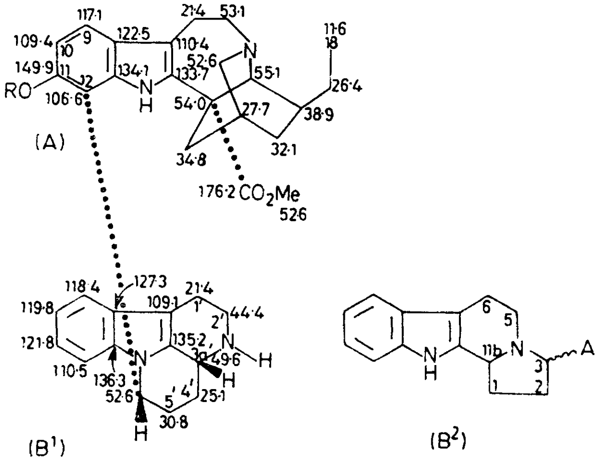


FIGURE. X-ray structure of bonafousine dihydrochloride. Water molecules of crystallization are shaded. Intramolecular hydrogen bonding is also shown.

The complete structure and stereochemistry of (1) were determined by X-ray crystallographic analysis of the dihydrochloride trihydrate, m.p. 235 °C (decomp.) (from H_2O).

Crystal data: bonafousine dihydrochloride trihydrate, $C_{35}H_{42}Cl_2N_4O_3.3H_2O$, $M = 691$, monoclinic, space group $P2_1$, $a = 7·840(4)$, $b = 13·324(6)$, $c = 16·760(8)$ Å, $\beta = 91·9(2)°$, $Z = 2$, $D_m = 1·35$, $D_c = 1·31$ g cm^{-3}. Single-crystal X-ray diffraction data were measured with a Philips PW 1100 diffractometer using θ–2θ scan techniques with graphite-monochromated Mo-K_α radiation. Co-ordinates of the non-hydrogen atoms were determined by conventional Patterson and Fourier methods. A least-squares refinement based on 1380 observed reflections with anisotropic temperature factors for the Cl^- ions and isotropic temperature factors for the C, N, and O atoms resulted in an R factor of 0·114.



(1) R = H
(2) R = Me

^{13}C N.m.r. assignments (δ/p.p.m.)

The c.d. curves of 11-*O*-methyl bonafousine (2): λ_{max} (EtOH) 213 ($\Delta\epsilon$ −3·9), 226 (+13·5), 235 (+17·5), 286 (−4·2), 294 (−4·3), and 307 (−4·0) nm indicate an ibogane unit (A) of the isovoacangine-type.[4] The molecular structure of bonafousine (1), showing its absolute configuration is given in the Figure together with the hydrogen bonding arrangement between the alkaloid and the three water molecules. Both amino nitrogen atoms, N(4) and N(3′), are bonded to the Cl^- ions.

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† The ^{13}C n.m.r. spectra (proton-noise-decoupled, noise-off-resonance-decoupled, and single-frequency, off-resonance-decoupled) were recorded in $CDCl_3$ solutions at 22·63 MHz on a Bruker HX90E Fourier transform spectrometer.

‡ Comparison of chemical shifts for bonafousine and isovoacangine, for instance, afforded evidence for this. A ^{13}C n.m.r. study of iboga-type alkaloids still needs to be carried out.

§ Signal assignments are based on comparison with hexahydrocanthionone-type chemical shifts.

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[2] H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Structure Elucidation of Natural Products by Mass Spectroscopy,' 1964, Vol. 1, Alkaloids, Holden-Day, San Francisco.
[3] G. W. Gribble and R. B. Nelson, *J. Org. Chem.*, 1974, **39**, 1845.
[4] K. Bláha, Z. Koblicová, and J. Trojanek, *Tetrahedron Letters*, 1972, 2763.