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Paniculine Hydrobromide

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Abstract. $C_{18}H_{30}BrNO_3$, $M_r = 388{\cdot}3$, triclinic, $P\bar{1}$, $a = 7{\cdot}999$ (2), $b = 15{\cdot}549$ (7), $c = 7{\cdot}929$ (2) Å, $\alpha = 103{\cdot}52$ (3), $\beta = 105{\cdot}57$ (2), $\gamma = 86{\cdot}89$ (3)°, $V = 923{\cdot}7$ (6) Å^3, $Z = 2$, $D_x = 1{\cdot}396$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 22{\cdot}15$ cm^{-1}, $F(000) = 408$, $T = 293$ K, final $R = 0{\cdot}049$ for 4066 observed reflections. The structure deduced by chemical and spectroscopic methods for this alkaloid is confirmed and consists of four fused six-membered rings in chair conformation. Two independent molecules in the asymmetric unit are the result of different intermolecular hydrogen bonds.

Introduction. Paniculine was isolated from the Chilean *Lycopodium paniculatum* and its structure was first deduced as 5α-acetoxy-7α-hydroxylicopodane (Morales, Loyola & Castillo, 1979). Later, a detailed study by high-frequency ^{1}H and ^{13}C NMR spectroscopy of paniculine and of other closely related alkaloids led to a revision of the structure to 5β-acetoxy-10α-hydroxylycopodane (Muñóz & Castillo, 1982). An alternative structure, namely 5β-acetoxy-1α-hydroxylycopodane, was discarded on the basis of the observed J_{gem} values for the axial and equatorial methylene protons next to the N atom. This X-ray crystallographic study was undertaken in order to verify the validity of this empirical correlation and its usefulness in future structural studies on this group of compounds.

Experimental. Needle-shaped single crystal, 0·1 × 0·1 × 0·6 mm; Syntex *P*3 four-circle diffractometer, graphite-monochromated Mo $K\alpha$ radiation; lattice parameters and orientation matrix from 15 reflections, $15 < 2\theta < 25°$. ψ-scan absorption correction applied using only reflections with χ between 40 and 90° as well as θ between 3 and 25°; $(\sin\theta)/\lambda \leq 0{\cdot}65$ Å^{-1}. Data collection of half the reciprocal sphere, index range $h = 0 \rightarrow 10$, $k = -19 \rightarrow 20$, $l = -10 \rightarrow 9$; 4252 unique reflections measured, 4068 observed reflections with $F > 3\sigma(F)$ were used for structure determination; intensity of standard reflection 240 varied 4·1%. The structure was solved by direct-phase determination using *SHELXTL* (Sheldrick, 1985) on an Eclipse S/250; phases of 403 strong reflections determined and on the resulting *E* map approximate positions of all non-hydrogen atoms could be determined; positional and thermal parameters refined by anisotropic least-squares cycles using F^2 magnitudes to $R = 0{\cdot}049$, $wR = 0{\cdot}049$, $w = 1/\sigma^2$, $S = 3{\cdot}544$. The H-atom positions of the NH and OH groups were taken from the difference Fourier map, all other positions of H atoms were calculated geometrically and considered isotropically in all refinements. $(\Delta/\sigma)_{max} = 3{\cdot}68$ for *y* of H(1*B*). Max. and min. height in final difference synthesis +0·62 and −0·58 e Å^{-3}. Scattering factors from *International Tables for X-ray Crystallography* (1974).

Discussion. Table 1 contains final atomic parameters for all non-hydrogen atoms including the four positionally refined H atoms of the OH and NH groups.† A perspective molecular drawing is shown in Fig. 1 with atom labels corresponding to the standard numbering system for these alkaloids (MacLean, 1986). The molecular structure of the title compound consists of four fused six-membered rings in chair conformation with methyl, acetyl and hydroxyl substituents at C(15), C(5) and C(10), respectively. Rings *A* and *C* are in near-perfect chair conformation. However, the chair form of ring *B* shows C(5) as the flap −0·385 Å out of the mean plane defined by C(4), C(6), C(13) and C(7) compared with 0·762 Å for C(12) (see Table 2). This flattening of ring *B*, due to the close proximity between C(15) and O(1) (3·069 Å), had been deduced previously on the basis of NMR-spectroscopy data on

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† Lists of structure factors, bond lengths, bond angles and anisotropic thermal parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44400 (33 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($Å^2 \times 10^3$)

	x	*y*	*z*	U_{eq}*
Br(1)	4315	1665	122	59 (1)
Br(2)	5673 (1)	8347 (1)	−81 (1)	60 (1)
O(11)	1977 (5)	3400 (3)	7105 (5)	43 (1)
N(11)	−2647 (6)	1509 (3)	3682 (6)	31 (2)
C(11)	−3347 (8)	1630 (4)	5339 (8)	41 (2)
O(12)	4904 (6)	3468 (4)	7716 (7)	66 (2)
C(12)	−1880 (8)	1577 (5)	6990 (8)	47 (2)
O(13)	−863 (6)	−491 (3)	1127 (7)	55 (2)
C(13)	−379 (8)	2228 (5)	7280 (8)	44 (2)
C(14)	248 (7)	2070 (4)	5580 (7)	34 (2)
C(15)	1960 (7)	2561 (4)	5831 (7)	33 (2)
C(16)	2314 (7)	2642 (4)	4071 (8)	38 (2)
C(17)	772 (7)	2694 (4)	2466 (8)	37 (2)
C(18)	−104 (8)	3586 (4)	2532 (8)	43 (2)
C(19)	−2185 (8)	556 (4)	3052 (8)	40 (2)
C(110)	−1496 (7)	399 (4)	1401 (8)	39 (2)
C(111)	−6 (7)	1025 (4)	1701 (8)	40 (2)
C(112)	−595 (7)	1992 (4)	2235 (7)	33 (2)
C(113)	−1220 (6)	2194 (4)	3952 (7)	29 (2)
C(114)	−2119 (7)	3096 (4)	4096 (8)	37 (2)
C(115)	−974 (8)	3857 (4)	4066 (8)	39 (2)
C(116)	−2096 (10)	4683 (5)	3891 (10)	56 (3)
C(117)	3571 (9)	3752 (5)	8028 (9)	53 (2)
C(118)	3398 (12)	4513 (7)	9477 (12)	84 (4)
O(21)	−279 (5)	−3500 (3)	1417 (5)	44 (2)
N(21)	1973 (6)	−1517 (3)	6952 (6)	34 (2)
C(21)	362 (8)	−1668 (5)	7519 (9)	46 (2)
O(22)	−842 (8)	−3538 (4)	−1536 (7)	70 (2)
C(22)	−1289 (8)	−1657 (5)	6016 (10)	55 (3)
O(23)	3599 (7)	502 (3)	6091 (7)	56 (2)
C(23)	−1180 (8)	−2314 (5)	4271 (9)	48 (2)
C(24)	444 (7)	−2127 (4)	3736 (7)	36 (2)
C(25)	508 (7)	−2630 (4)	1828 (8)	37 (2)
C(26)	2312 (8)	−2662 (4)	1501 (8)	43 (2)
C(27)	3891 (7)	−2667 (4)	3112 (8)	37 (2)
C(28)	4280 (8)	−3559 (4)	3636 (9)	45 (2)
C(29)	2104 (8)	−563 (4)	6874 (8)	41 (2)
C(210)	3704 (8)	−384 (4)	6321 (8)	40 (2)
C(211)	3776 (7)	−1019 (4)	4561 (8)	38 (2)
C(212)	3732 (7)	−1972 (4)	4752 (7)	32 (2)
C(213)	2112 (7)	−2205 (4)	5234 (7)	31 (2)
C(214)	2395 (7)	−3107 (4)	5770 (8)	39 (2)
C(215)	2909 (8)	−3856 (4)	4379 (8)	42 (2)
C(216)	3525 (10)	−4640 (5)	5224 (11)	58 (3)
C(217)	−935 (9)	−3864 (5)	−322 (9)	53 (3)
C(218)	−1786 (14)	−4735 (7)	−597 (12)	92 (4)
H(1*A*)	−3598 (87)	1585 (48)	3102 (95)	60
H(1*B*)	−1837 (87)	−821 (48)	939 (93)	60
H(2*A*)	3197 (88)	−1879 (48)	7160 (93)	60
H(2*B*)	3731 (86)	802 (47)	7069 (92)	60

* Equivalent isotropic U defined as one-third of the trace of the orthogonalized U_{ij} tensor.

Table 2. *Distances of atoms from the mean plane through the four atoms of the six-membered rings, with e.s.d.'s in parentheses*

Rings	Mean plane	Axial atom	Distance (Å)
A	N(1)C(9)C(11)C(12)	C(10)	0·653 (6)
		C(13)	−0·649 (5)
B	C(4)C(6)C(7)C(13)	C(12)	0·762 (6)
		C(5)	−0·385 (6)
C	C(1)C(2)C(4)C(13)	N(1)	0·695 (5)
		C(3)	−0·691 (8)
D	C(7)C(8)C(13)C(14)	C(12)	0·779 (5)
		C(15)	−0·594 (6)

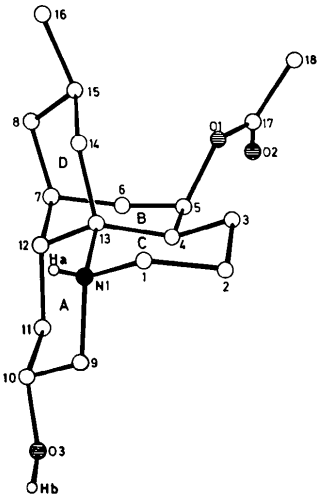

Fig. 1. Perspective drawing of paniculine hydrobromide with atom labels corresponding to Table 1 and plane labels corresponding to Table 2.

alkaloids of this type (Nakashima, Singer, Browne & Ayer, 1975). The secondary hydroxyl group at C(10) is equatorial, in agreement with the revised structure proposed by Muñóz & Castillo (1982). Thus, paniculine corresponds to 5β-acetoxy-10α-hydroxylycopodane. The absolute configuration is the same for both molecules in the unit cell and was previously determined by chemical means. It corresponds to that shown in Fig. 1, in agreement with the molecular chirality of lycopodium alkaloids of well established absolute configuration (Morales *et al.*, 1979).

All bond lengths are within the expected ranges. Despite the rather centrosymmetric positions of the bromine atoms the two paniculine molecules result in the noncentrosymmetric space group.

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