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N-(Hydroxymethyl)ibogaine

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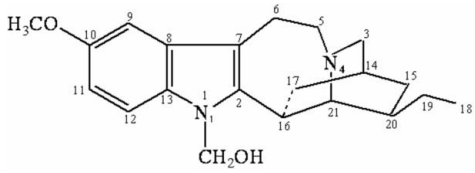
Key indicators: single-crystal X-ray study; T = 293 K; mean σ(C–C) = 0.005 Å; R factor = 0.049; wR factor = 0.123; data-to-parameter ratio = 9.3.

The title compound (systematic name: 16-hydroxymethyl-12-methoxyibogamine), $C_{21}H_{28}N_2O_2$, was prepared by reaction of ibogaine with a formaldehyde–acetic acid solution (pH = 4). The crystal structure of this new product, belonging to the iboga indole family, is stabilized by an intermolecular O—H···N hydrogen bond. The identity of the compound was confirmed by one- and two-dimensional NMR spectroscopic techniques.

Related literature

For related literature on ibogaine and its derivatives, see: Alper *et al.* (2008); Levant & Pazdernik (2004); Maisonneuve *et al.* (1991); Soriano-García (1992).



Experimental

Crystal data

$C_{21}H_{28}N_2O_2$
M_r = 340.45
Orthorhombic, $P2_12_12_1$
a = 8.4990 (10) Å
b = 10.2537 (11) Å
c = 20.676 (3) Å
V = 1801.8 (4) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 293 (2) K
0.47 × 0.33 × 0.26 mm

Data collection

Bruker Kappa APEXII CCD diffractometer
Absorption correction: multi-scan (Coppens *et al.*, 1965)
T_{min} = 0.962, T_{max} = 0.981
9906 measured reflections
2131 independent reflections
1225 reflections with $I > 2\sigma(I)$
R_{int} = 0.079

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.123
S = 1.00
2131 reflections
228 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2···N4^{i}	0.82	2.10	2.825 (3)	148

Symmetry code: (i) $x+1, y, z$.

Data collection: *APEX2* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 1998); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: ZL2132).

References

Alper, K. R., Lotsof, H. S. & Kaplan, C. D. (2008). *J. Ethnopharmacol.* **115**, 9–24.
Bruker (1998). *SAINT*. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruker (2004). *APEX2*. Bruker AXS Inc., Madison, Wisconsin, USA.
Coppens, P., Leiserowitz, L. & Rabinovich, D. (1965). *Acta Cryst.* **18**, 1035–1038.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Levant, B. & Pazdernik, T. L. (2004). *Brain Res.* **1003**, 159–167.
Maisonneuve, I. M., Keller, R. W. Jr & Glick, S. D. (1991). *Eur. J. Pharmacol.* **199**, 35–42.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Soriano-García, M. (1992). *Acta Cryst.* C**48**, 2055–2057.

supplementary materials

Acta Cryst. (2008). E**64**, o1739 [**doi:10.1107/S1600536808025324**]

N-(Hydroxymethyl)ibogaine

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Comment

Ibogaine is the main alkaloid found in the root bark of Tabernanthe iboga (Apocynaceae family), a shrub native to equatorial Africa. Its crystal structure was previously established by *M*. Soriano-García (1992). It is used, at low doses, to produce increased energy, arousal, and appetite and at high doses, for its hallucinogenic properties (Maisonneuve *et al.*, 1991) and it has been claimed to be effective in abolishing drug craving in heroin and cocaine addicts (Levant & Pazdernik, 2004).

Ibogaine is a psychostimulant of interest as an ethnopharmacological prototype for experimental investigation and possible rational pharmaceutical development (Alper *et al.*, 2008). In this context and in order to prepare other substitutes, we realised the reaction of ibogaine with a formaldehyde-acetic acid solution (pH= 4). This reaction led to 47% of the title compound (Fig. 1).

The current study describes the preparation and the structure elucidation of N-hydroxymethylene ibogaine. Its structure was established principally by two-dimensional NMR spectroscopy and its solid state structure was determined through X-ray diffraction analysis (Fig. 2, Fig. 4).

The conformation of this compound is stabilized by an intermolecular hydrogen bond between the hydroxyl O_2—H_2 group and atom N_4 (Fig. 3).

Experimental

The title compound (2) was prepared by reaction of ibogaine (1) (100 mg, 0.3 mmol) with formaldehyde-acetic acid solution (pH= 4) (10 ml). The mixture was stirred at room temperature for 2 h. Then, the mixture was diluted with H_2O, made alkaline with an NH_4OH solution (pH = 9) and immediately extracted with CH_2Cl_2. The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure. The concentrate was then purified by chromatography on silica gel column with dichloromethane as eluent to yield 47% of the title compound.

N-hydroxymethylene ibogaïne (2), white crystals (CH_2Cl_2), $C_{21}H_{28}N_2O_2$: 340, m.p. 436 K, UV: λ_{max}(EtOH) nm = 209, 287, 230. IR: (KBr) ν_{max}(cm^{-1}): 3448, 3101,2935,1617, 1586, 1482, 1456. Spectroscopic analysis, ^{1}H NMR (300 MHz; $CDCl_3$-d_6, p.p.m.): 0.91 (t, J = 7.2 Hz, 3H, Me_{18}); 1.26 (m, 2H, H_{15}); 1.61 (m, 1H, H_{19}); 1.62 (m, 1H, H_{17}); 1.75 (m, 1H, H_{19}); 1.83 (m, 1H, H_{20}); 1.95 (m, 1H, H_{14}); 2.13 (m, 1H, H_{17}); 2.56 (m, 1H, H_6); 2.89 (m, 1H, H_{21}); 2.90 (m, 1H, H_{16}); 2.95 (m, 1H, H_3); 3.12 (m, 1H, H_5); 3.26 (m, 1H, H_3); 3.30 (m, 1H, H_6); 3.31 (m, 1H, H_5); 3.85 (s, 3H, CH_3—O); 5.50 (dd, J= 11.7, 2H, N_1—CH_2OH); 6.83 (dd, J = 8.7, 2.4, 1H, aromatic H, H_{11}); 6.90 (d, J = 2.4, 1H, aromatic H, H_9); 7.25 (d, J = 8.7, 1H, aromatic H, H_{12}). ^{13}C NMR (75 MHz; $CDCl_3$-d_6, p.p.m.): 11.9, C_{18}; 20.2, C_6; 25.7, C_{14}; 27.6, C_{19}; 29.7, C_{15}; 33.4, C_{17}; 41.7, C_{16}; 41.7, C_{20}; 50.3, C_3; 54.6, C_5; 56.1, O—CH_3; 58.2, C_{21}; 66.2, N_1—CH_2OH; 100.9, C_9; 109.7, C_7; 110.2, C_{12}; 111.2, C_{11}; 128.9, C_8; 142.3, C_2; 154.5, C_{10}. Repeated recrystallizations from dichloromethane afforded white crystals suitable for single crystal X-ray diffraction.

Refinement

All H atoms were fixed geometrically and treated as riding with C—H = 0.98 Å (Cmethine), 0.97 Å (Cmethylene), 0.96 Å (Cmethyl), 0.93 Å (CH_2) and O—H = 0.82 Å with U_{iso}(H) = 1.2U_{eq}(Cmethylene, methine, CH_2) or U_{iso}(H) = 1.5U_{eq}(Cmethyl, O).

In the absence of anomalous scattering Friedel pairs were merged and any references to the Flack parameter were removed.

Figures

Fig. 1. Chemical pathway of the formation of the N-hydroxymethylene ibogaine (2).

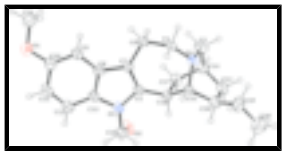


Fig. 2. *ORTEP* drawing of the title compound with the atom-labelling scheme. Ellispsoids are drawn at the 30% probability level. H atoms are represented as small spheres of arbitrary radii.

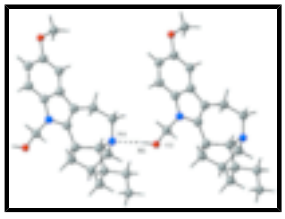


Fig. 3. Partial packing view showing the formation of intermolecular O–H···N hydrogen bonds.

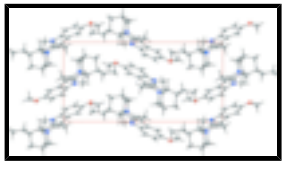


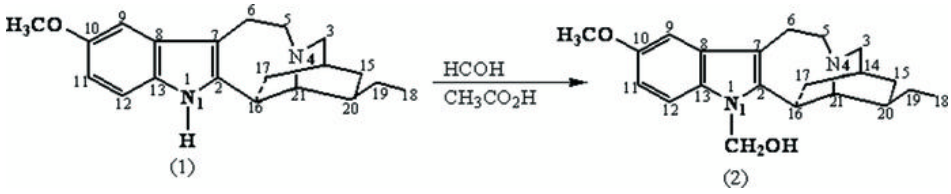
Fig. 4. The crystal paking of the N-hydroxymethylene ibogaine structure along [001].

16-Hydroxymethyl-12-methoxyibogamine

Crystal data

$C_{21}H_{28}N_2O_2$	D_x = 1.255 Mg m^{-3}
M_r = 340.45	Melting point: 436 K
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation λ = 0.71070 Å
Hall symbol: P 2ac 2ab	Cell parameters from 2130 reflections
a = 8.4990 (10) Å	θ = 3.2–24.5º
b = 10.2537 (11) Å	μ = 0.08 mm^{-1}
c = 20.676 (3) Å	T = 293 (2) K
V = 1801.8 (4) Å^3	Prism, colourless
Z = 4	0.47 × 0.33 × 0.26 mm
F_{000} = 736	

Fig. 1



(1) (2)

Fig. 2

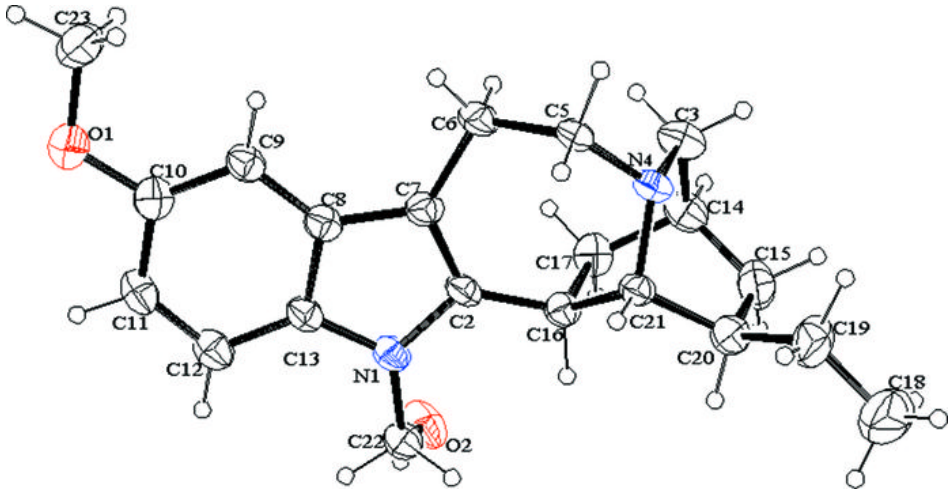

C23
O1
C10
C9
C8
C7
C6
C5
C3
N4
C14
C15
C17
C11
C12
C13
N1
C2
C16
C21
C20
C19
C18
C22
O2

Fig. 3

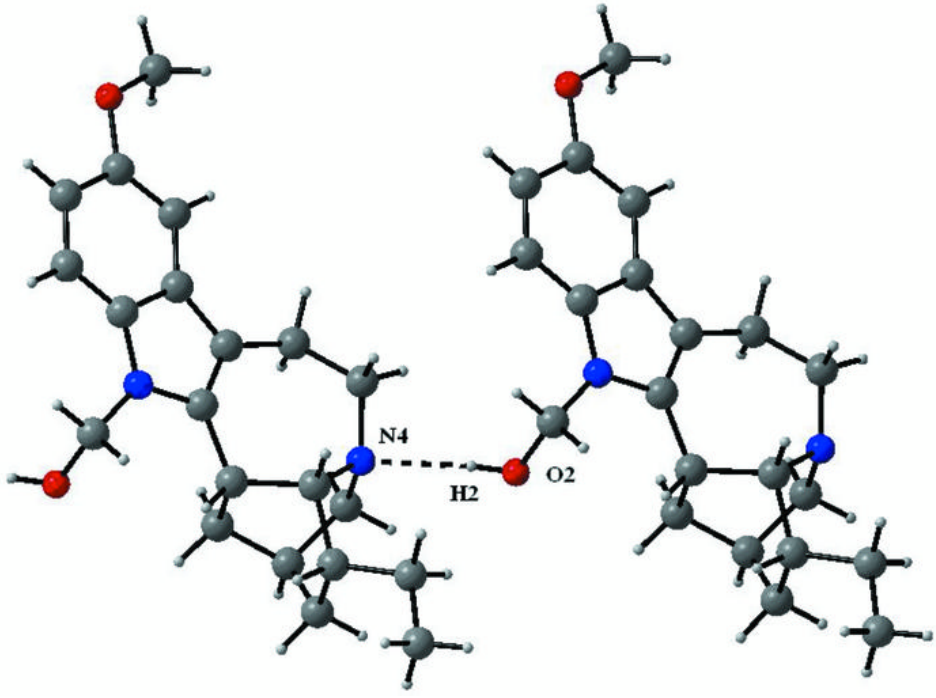


Fig. 4