

Structure of Ibogaine*

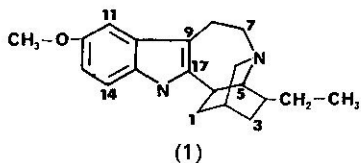
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(Received 3 December 1991; accepted 3 March 1992)

Abstract. 12-Methoxyibogamine, $C_{20}H_{26}N_2O$, $M_r = 310.4$, orthorhombic, $P2_12_12_1$, $a = 10.485$ (5), $b = 16.892$ (8), $c = 19.750$ (6) Å, $V = 3498$ (2) Å³, $Z = 8$, $D_x = 1.18$ Mg m⁻³, $\lambda(\text{Mo } K\alpha) = 0.7107$ Å, $\mu = 0.068$ mm⁻¹, $F(000) = 1344$, $T = 293$ K, $R = 0.073$ for 2002 observed reflections and 422 refined parameters. There are two crystallographically independent molecules. In both molecules *A* and *B* the seven-membered ring has a boat conformation. The mean planes through the C(5)—N(6)—C(19)—C(2) atoms of the central axis of the isoquinuclidine tricyclic structure and the indole ring are inclined to each other at angles of 114.0 (2) and 85.6 (2)° for molecules *A* and *B* respectively. The crystal structure is stabilized by one intramolecular hydrogen bond [N(16*B*)—H...O(14) ($1 + x, y, z$) = 3.150 (8) Å] and by van der Waals forces.

Experimental. Ibogaine (1) is an alkaloid from *Tabernanthe iboga*, a West African shrub (Henry, 1949; Dickel, Holden, Maxfield, Paszek & Taylor, 1958).



The crystal used for data collection was weakly diffracting and had dimensions $0.24 \times 0.40 \times 0.54$ mm. A Nicolet R3 four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation was used to measure intensities. Lattice parameters were determined from 25 machine-centred reflections with $4.3 < 2\theta < 16.7^\circ$. 3476 reflections with $3 < 2\theta < 50^\circ$ were measured for one octant, of which 2002 were independent with $I > 2.8\sigma(I)$ (index range $h\ 0 \rightarrow 12$, $k\ 0 \rightarrow 16$, $l\ 0 \rightarrow 22$; ω -scan mode, variable scan speed). Two standard reflections (210 and 132), monitored every 50 measurements, showed no significant variation. Intensities were corrected for Lorentz-polarization effects but not for absorption. Data

were adjusted to an approximately absolute scale and an overall U value of 0.050 Å². The structure was solved by a combination of direct methods and partial structure expansion by an iterative E -Fourier procedure using *SHELXTL* (Sheldrick, 1985). The absolute molecular structure of ibogaine was assigned from the stereochemistry of ibogaine hydrobromide (Arai, Coppola & Jeffrey, 1960). Blocked-cascade least-squares refinement was performed with all non-H atoms treated anisotropically; H atoms of CH, CH₂ and CH₃ were allowed to ride on their bonded C atoms with a fixed isotropic $U = 0.06$ Å². The H atom bonded to the N atom was located on a difference Fourier map at an advanced stage of anisotropic refinement and its coordinates refined. $\sum w(\Delta F)^2$ was minimized, where $w = |\sigma^2(F_o) + 0.0015(F_o)^2|^{-1}$, in which σ is the standard deviation of observed amplitudes based on counting statistics. An isotropic extinction parameter $X = 0.0007$. In the last cycle $(\Delta/\sigma)_{\max} = 0.12$, $\Delta\rho$ was from -0.25 to 0.27 e Å⁻³, $S = 1.20$, final $R = 0.073$, and $wR = 0.076$, for 422 refined parameters. Scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV). All computations were performed on a Nova 4S computer and plots drawn on a Tektronix plotter with the *SHELXTL* system of programs.

Atomic coordinates are given in Table 1.† A perspective molecular drawing and the atom labelling are displayed in Fig. 1. Bond distances and angles are listed in Table 2. For the seven-membered rings, the ring-puckering parameters (Cremer & Pople, 1975) are $\theta = 93.7$ (5), $\varphi = -113.2$ (5)° and $Q = 0.805$ (8) Å for molecule *A*, and $\theta = 91.4$ (5), $\varphi = -105.9$ (5)° and $Q = 0.807$ (8) Å for molecule *B*.

Related literature. The crystal structure of ibogaine hydrobromide has been published (Arai, Coppola &

† Lists of structure amplitudes, H-atom parameters, least-squares planes and anisotropic thermal parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55271 (18 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AL0529]

* Contribution No. 1130 of the Instituto de Química, UNAM.

Table 1. Atomic coordinates ($\times 10^4$) and equivalent isotropic temperature factors ($\text{\AA}^2 \times 10^3$)
$$U_{eq} = (U_{11}U_{22}U_{33})^{1/3}.$$

	x	y	z	U_{eq}
C(1A)	4834 (7)	11926 (5)	8254 (4)	72 (3)
C(2A)	5012 (9)	12562 (5)	8817 (4)	79 (4)
C(3A)	4280 (8)	13291 (4)	8639 (4)	91 (4)
C(4A)	2865 (8)	13083 (4)	8524 (4)	68 (3)
C(5A)	2680 (7)	12222 (4)	8730 (3)	52 (2)
N(6A)	3153 (6)	12134 (3)	9430 (2)	54 (2)
C(7A)	2638 (6)	11472 (4)	9809 (3)	56 (3)
C(8A)	3094 (7)	10637 (4)	9637 (3)	52 (2)
C(9A)	2969 (6)	10393 (4)	8906 (3)	42 (2)
C(10A)	2686 (5)	9594 (4)	8689 (3)	37 (2)
C(11A)	2434 (6)	8883 (4)	9041 (3)	39 (2)
C(12A)	2163 (6)	8233 (3)	8672 (3)	44 (2)
C(13A)	2189 (7)	8220 (4)	7965 (4)	51 (3)
C(14A)	2477 (7)	8902 (4)	7616 (3)	54 (3)
C(15A)	2706 (6)	9589 (4)	7976 (3)	43 (2)
N(16A)	2976 (5)	10349 (3)	7776 (3)	48 (2)
C(17A)	3138 (6)	10832 (4)	8338 (3)	42 (2)
C(18A)	3390 (7)	11707 (4)	8227 (4)	54 (3)
C(19A)	4527 (7)	12227 (5)	9464 (4)	74 (3)
C(20A)	1911 (11)	13641 (5)	8875 (5)	92 (4)
C(21A)	563 (9)	13579 (5)	8656 (5)	118 (5)
O(1A)	1803 (5)	7503 (3)	8945 (2)	57 (2)
C(22A)	1846 (8)	7428 (4)	9663 (3)	73 (3)
C(1B)	9085 (7)	9326 (4)	9496 (3)	60 (3)
C(2B)	8366 (8)	10106 (5)	9582 (4)	73 (3)
C(3B)	9043 (9)	10746 (5)	9192 (5)	93 (4)
C(4B)	9250 (7)	10469 (4)	8463 (4)	79 (4)
C(5B)	8420 (6)	9747 (4)	8351 (4)	49 (3)
N(6B)	7118 (5)	9960 (3)	8558 (3)	50 (2)
C(7B)	6085 (7)	9532 (4)	8240 (4)	60 (3)
C(8B)	5805 (6)	8703 (4)	8510 (4)	55 (3)
C(9B)	6906 (6)	8152 (4)	8594 (3)	44 (2)
C(10B)	6741 (7)	7317 (4)	8660 (3)	48 (2)
C(11B)	5652 (8)	6830 (4)	8642 (3)	55 (3)
C(12B)	5818 (10)	6034 (5)	8753 (4)	70 (4)
C(13B)	6979 (11)	5706 (4)	8880 (4)	73 (4)
C(14B)	8060 (9)	6174 (4)	8911 (3)	61 (3)
C(15B)	7937 (8)	6983 (4)	8794 (3)	51 (3)
N(16B)	8814 (5)	7597 (3)	8808 (3)	51 (2)
C(17B)	8180 (7)	8309 (4)	8675 (3)	47 (2)
C(18B)	8948 (6)	9057 (4)	8749 (3)	47 (2)
C(19B)	7040 (7)	10031 (5)	9294 (4)	79 (3)
C(20B)	9005 (8)	11137 (5)	7963 (5)	98 (4)
C(21B)	9530 (9)	11041 (6)	7334 (6)	171 (7)
O(1B)	4826 (7)	5481 (3)	8723 (3)	88 (3)
C(22B)	3674 (10)	5759 (5)	8477 (5)	103 (5)

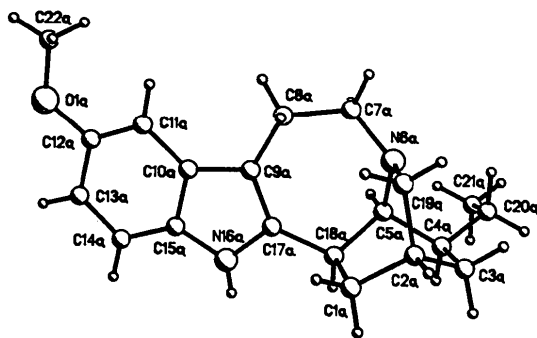


Fig. 1. The molecular structure of ibogaine (molecule A), showing atom numbering.

Jeffrey, 1960). The seven-membered ring for ibogaine hydrobromide, ibogamine (Soriano-García, Walls, Rodríguez & López-Celis, 1988), voacangine (Soriano-García, Rodríguez, Walls & Toscano, 1989) and isovoacangine (Soriano-García, Rodríguez-Romero, Walls, Toscano & Villena Iribe, 1991) has a

Table 2. Bond lengths ($\text{\AA}$) and angles ($^\circ$)

	Molecule A	Molecule B
C(1)—C(2)	1.559 (12)	1.528 (11)
C(1)—C(18)	1.560 (10)	1.549 (9)
C(2)—C(3)	1.492 (12)	1.506 (13)
C(2)—C(19)	1.487 (12)	1.508 (11)
C(3)—C(4)	1.542 (12)	1.529 (13)
C(4)—C(5)	1.521 (9)	1.516 (10)
C(4)—C(20)	1.539 (12)	1.521 (12)
C(5)—N(6)	1.477 (9)	1.470 (8)
C(5)—C(18)	1.516 (9)	1.511 (9)
N(6)—C(7)	1.450 (8)	1.445 (9)
N(6)—C(19)	1.450 (10)	1.460 (10)
C(7)—C(8)	1.527 (9)	1.527 (10)
C(8)—C(9)	1.507 (8)	1.492 (9)
C(9)—C(10)	1.448 (9)	1.427 (9)
C(9)—C(17)	1.356 (9)	1.371 (10)
C(10)—C(11)	1.412 (8)	1.408 (10)
C(10)—C(15)	1.408 (9)	1.401 (11)
C(11)—C(12)	1.348 (9)	1.373 (11)
C(12)—C(13)	1.396 (10)	1.360 (15)
C(12)—O(1)	1.398 (8)	1.398 (11)
C(13)—C(14)	1.376 (10)	1.383 (14)
C(14)—C(15)	1.382 (10)	1.391 (10)
C(15)—N(16)	1.373 (9)	1.387 (9)
N(16)—C(17)	1.388 (8)	1.399 (9)
C(17)—C(18)	1.518 (9)	1.506 (9)
C(20)—C(21)	1.482 (14)	1.369 (14)
O(1)—C(22)	1.425 (8)	1.384 (12)
C(2)—C(1)—C(18)	107.7 (6)	108.3 (6)
C(1)—C(2)—C(3)	109.8 (7)	109.2 (7)
C(1)—C(2)—C(19)	108.0 (7)	109.9 (7)
C(3)—C(2)—C(19)	110.0 (7)	107.6 (7)
C(2)—C(3)—C(4)	110.0 (6)	109.2 (7)
C(3)—C(4)—C(5)	107.5 (6)	107.6 (7)
C(3)—C(4)—C(20)	114.8 (7)	111.2 (7)
C(5)—C(4)—C(20)	112.5 (6)	113.9 (7)
C(4)—C(5)—N(6)	107.7 (5)	107.2 (6)
C(4)—C(5)—C(18)	108.1 (6)	109.5 (6)
N(6)—C(5)—C(18)	113.0 (5)	112.6 (5)
C(5)—N(6)—C(7)	115.9 (5)	116.9 (5)
C(5)—N(6)—C(19)	111.5 (6)	110.5 (5)
C(7)—N(6)—C(19)	115.5 (6)	115.6 (6)
N(6)—C(7)—C(8)	118.7 (5)	116.8 (6)
C(7)—C(8)—C(9)	116.0 (5)	117.5 (5)
C(8)—C(9)—C(10)	123.8 (5)	122.2 (6)
C(8)—C(9)—C(17)	129.2 (6)	130.2 (6)
C(10)—C(9)—C(17)	106.9 (5)	107.4 (6)
C(9)—C(10)—C(11)	133.3 (6)	132.4 (7)
C(9)—C(10)—C(15)	107.4 (5)	107.9 (6)
C(11)—C(10)—C(15)	119.3 (6)	119.6 (6)
C(10)—C(11)—C(12)	117.8 (6)	117.8 (8)
C(11)—C(12)—C(13)	123.3 (6)	122.7 (9)
C(11)—C(12)—O(1)	124.5 (6)	123.5 (8)
C(13)—C(12)—O(1)	112.2 (5)	113.7 (7)
C(12)—C(13)—C(14)	119.5 (6)	120.6 (7)
C(13)—C(14)—C(15)	118.9 (6)	118.6 (8)
C(10)—C(15)—C(14)	121.1 (6)	120.6 (7)
C(10)—C(15)—N(16)	106.5 (5)	107.2 (6)
C(14)—C(15)—N(16)	132.3 (6)	132.1 (7)
C(15)—N(16)—C(17)	110.2 (5)	108.9 (6)
C(9)—C(17)—N(16)	108.9 (5)	108.6 (6)
C(9)—C(17)—C(18)	132.4 (6)	134.0 (6)
N(16)—C(17)—C(18)	118.6 (6)	116.7 (6)
C(1)—C(18)—C(5)	108.6 (6)	107.6 (5)
C(1)—C(18)—C(7)	113.2 (6)	112.8 (5)
C(5)—C(18)—C(7)	112.3 (5)	113.6 (5)
C(2)—C(19)—N(6)	110.0 (7)	109.3 (6)
C(4)—C(20)—C(21)	116.4 (8)	115.7 (8)
C(12)—O(1)—C(22)	117.0 (5)	116.0 (6)

distorted chair conformation. The dihedral angles between the indole ring and the mean plane through the C(5)—N(6)—C(19)—C(2) atoms for ibogaine hydrobromide, for the two independent molecules in ibogamine, for voacangine, and for isovoacangine, are: 74; 78.3 (5) and 83.8 (5); 92.7 (1); and 69.1 (1) $^\circ$, respectively.

I thank Dr F. Walls for providing the crystals of ibogaine and Mr R. Toscano for technical assistance.

References

- ARAI, G., COPPOLA, J. & JEFFREY, G. A. (1960). *Acta Cryst.* **13**, 553–564.
- CREMER, D. & POPLA, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
- DICKEL, D. F., HOLDEN, C. L., MAXFIELD, R. C., PASZEK, L. E. & TAYLOR, W. I. (1958). *J. Am. Chem. Soc.* **80**, 123–125.
- HENRY, T. A. (1949). *The Plant Alkaloids*, pp. 768–769. Philadelphia: Blakiston.
- SHELDICK, G. M. (1985). *SHELXTL. An Integrated System for Solving, Refining and Displaying Crystal Structures from Diffraction Data*. Univ. of Göttingen, Germany.
- SORIANO-GARCÍA, M., RODRÍGUEZ, A., WALLS, F. & TOSCANO, R. (1989). *J. Crystallogr. Spectrosc. Res.* **19**, 725–732.
- SORIANO-GARCÍA, M., RODRÍGUEZ-ROMERO, A., WALLS, F., TOSCANO, R. & VILLENA IRIBE, R. (1991). *J. Crystallogr. Spectrosc. Res.* **21**, 681–685.
- SORIANO-GARCÍA, M., WALLS, F., RODRÍGUEZ, A. & LÓPEZ-CELIS, I. (1988). *J. Crystallogr. Spectrosc. Res.* **18**, 197–206.

Acta Cryst. (1992). **C48**, 2057–2058

Structure of 2-[1-(2-Carboxyethyl)ethylidene]hydrazinecarbothioamide

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(Received 28 October 1991; accepted 26 February 1992)

Abstract. $\text{CH}_3\text{C}(\text{=NNHCSNH}_2)(\text{CH}_2)_2\text{CO}_2\text{H}$, $\text{C}_6\text{H}_{11}\text{N}_3\text{O}_2\text{S}$, $M_r = 189.24$, monoclinic, $P2_1/n$, $a = 7.652$ (2), $b = 10.398$ (1), $c = 11.135$ (2) Å, $\beta = 96.80$ (1)°, $V = 879.7$ (3) Å³, $Z = 4$, $D_x = 1.430$ g cm⁻³, $\lambda(\text{Mo K}\alpha) = 0.71073$ Å, $\mu = 3.18$ cm⁻¹, $T = 298$ K, $F(000) = 400$, $R = 0.047$ for 1047 $I \geq 3\sigma(I)$ reflections. The thiosemicarbazone exists in the tautomeric thione form; the double-bonded S is H-bonded to two adjacent carboxyl O atoms [$\text{S}\cdots\text{O} = 3.085$ (5), 3.280 (5) Å].

Experimental. Equimolar amounts of levulinic acid and thiosemicarbazide were briefly heated together in ethanol; the cooled mixture furnished slightly tan colored crystals of the title compound. A crystal measuring approximately $0.22 \times 0.22 \times 0.22$ mm was used for the diffraction analysis. The diffractometer was an Enraf–Nonius instrument equipped with Mo $K\alpha$ radiation. Accurate cell dimensions were obtained from the 25 most intense reflections in the $13 \leq \theta \leq 15^\circ$ thin shell. Intensity data were collected up to $2\theta_{\text{max}} = 50^\circ$ ($h, k, \pm l, 9, 12, 13$) by using the ω - 2θ scan technique; 1659 reflections collected; 1417 unique reflections, with 1047 data satisfying the $I \geq 3\sigma(I)$ criterion. The data were corrected for decay (min./max. correction = 1.0000/1.0002); three (008, 245, 404) monitor reflections; negligible variation for the 16 h of collection. The data set was corrected for absorption by using the ψ -scan data (min./max. correction = 0.9751, 0.9995). The structure was solved using *MULTAN*11/82 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982). The non-H atoms were refined anisotropically. A difference Fourier synthesis revealed all the H atoms. H atoms

were refined with $B = 5$ Å². The full-matrix least-squares refinement based on F converged with $\Delta/\sigma < 0.01$ at $R = 0.047$, $wR = 0.074$ [$w = [\sigma(F)^2 + (0.02F)^2 + 1]^{-1}$]; $S = 0.830$; 142 variables were refined. The max. $\Delta\rho$ was 0.28 (3) e Å⁻³. Scattering factors were taken from Tables 2.2B and 2.3.1 of *International Tables for X-ray Crystallography* (1974, Vol. IV). Computations were performed using the *MolEN* structure determination package (Fair, 1990) on a DEC MicroVAX minicomputer. Table 1* lists the atomic coordinates and Table 2 bond distances and angles; the structure is shown in Fig. 1.

Related literature. The N–N bond length of 1.382 (7) Å in the thiosemicarbazone, which is shorter than the statistical average of 1.401 Å found for planar $\text{R}_2\text{N}=\text{NR}_2$ compounds but longer than the statistical average of 1.240 Å found for $\text{R}=\text{N}=\text{N}=\text{R}$ compounds (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987), suggests double-bond character in the flat $\text{C}=\text{N}=\text{N}=\text{C}$ [$\text{C}=\text{N}=\text{N}=\text{C} = -178.9$ (5)°] fragment. The compound also possesses a carboxylate unit, but the acid does not form a dimer through hydrogen bonding. Instead, the S atom hydrogen bonds to two adjacent [(i) $x - \frac{1}{2}, \frac{1}{2} - y, z - \frac{1}{2}$; (ii) $\frac{1}{2} - x, y - \frac{1}{2}, \frac{1}{2} - z$] carboxyl O atoms [$\text{S}\cdots\text{O}^{\text{i}} = 3.085$ (5), $\text{S}\cdots\text{O}^{\text{ii}} = 3.280$ (5) Å] to give rise to a hydrogen-bonded network.

* Lists of structure factors, anisotropic thermal parameters and calculated hydrogen positional parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55256 (14 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AS0572]