In the crystal structure, the molecules form an infinite chain along the *b* crystallographic axis held together by O—H···N hydrogen bonds [O···N = 2.821, O—H = 1.02 (4), H···N = 1.83 (4) Å, O—H···N = 163 (3)°] (Fig. 3).

Since MER25 is a proven antiestrogen, and its solid-state conformer resembles the (*E*) isomer of tamoxifen, which is purely estrogenic, one must suspect that the MER25 conformation undergoes transformation from the *anti* [Fig. 4 (I)] to the *gauche* [Fig. 4 (II)] conformation *in vivo* when attaching to the estrogen receptor. Work is in progress to test this hypothesis through the preparation and testing of rigid conformers of MER25. Work is also in progress to investigate the various minimum-energy conformers of MER25 through extensive molecular-mechanics calculations. Preliminary results (Hossain, Magarian, Symersky & van der Helm, 1992) show that a low energy synclinal (*gauche*) conformer (II) of MER25 has energy which is only 1.2 kcal mol^{-1} higher than that of the *anti* conformation observed in the crystal structure. Details of these results will be published later.

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Structure of (−)-β-Hydrastine

BY RAJNIKANT AND K. N. GOSWAMI

Department of Physics, University of Jammu, Jammu Tawi-180 001, *India*

V. S. YADAVA AND V. M. PADMANABHAN

Solid State Physics Division, Modular Laboratories, Bhabha Atomic Research Centre, Trombay, Bombay-400 085, *India*

AND S. K. BANERJEE

Natural Products Chemistry Division, Regional Research Laboratory (CSIR), Jammu Tawi-180 001, *India*

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Abstract. 6,7-Dimethoxy-3-(5,6,7,8-tetrahydro-6-methyl-1,3-dioxolo[4,5-*g*]isoquinolin-5-yl)-1(3*H*)-isobenzofuranone, $C_{21}H_{21}NO_6$, $M_r = 383$, tetragonal, $P4_3$, $a = 7.542$ (2), $c = 33.266$ (2) Å, $V = 1892$ Å^3, $Z = 4$, D_m(flotation) = 1.334, $D_x = 1.344$ Mg m^{-3}, λ(Cu $K\alpha_1$) = 1.5405 Å, $\mu = 0.733$ mm^{-1}, $F(000) = 808$, $R = 0.061$ for 1579 observed reflections with $I > 2.5\sigma(I)$. The N-containing ring has a half-chair con-

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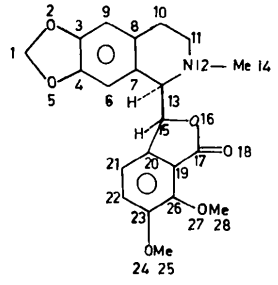
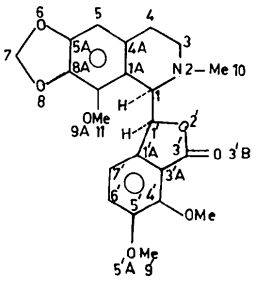
formation. The bond joining the two moieties is axial with respect to the tetrahydropyridine ring. The N—CH_3 bond is equatorial. The five-membered lactone ring is puckered and shows an envelope conformation.

Introduction. Hydrastine is a naturally occurring phthalideisoquinoline alkaloid and is closely related to (−)-α-narcotine and bicuculline. It is used as an antiseptic and as a uterine hemostatic. The aim of the present investigation was to determine the molecular structure of (−)-β-hydrastine (I) and compare some of its structural aspects with those of (−)-α-narcotine (II) and bicuculline (III).



(I)



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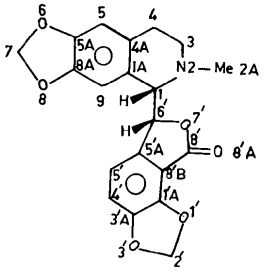

(III)

Experimental. The isolation of β-hydrastine has been reported by various workers (Ohta, Tani & Morozumi, 1963; Ohta, Tani, Morozumi, Kodaira & Kuriyama, 1963). The title compound, isolated from *Fumaria parviflora*, crystallized as transparent prisms from alcohol; m.p. 404–405 K; $[\alpha]_D^{25°C}$ −51.3° (c = 0.3 in absolute alcohol). The identity of the compound is based on m.p., specific rotation, ^1H and ^{13}C NMR data and mass spectra. A crystal of size 0.17 × 0.29 × 0.32 mm was used for intensity-data collection on a CAD-4 diffractometer (Indian Institute of Technology, Madras), with ω–2θ scans at 1.5–6.6° min^{-1}. Unit-cell parameters were refined by least-squares techniques using the 2θ angles measured on the diffractometer from 20 reflections in the range 2–30°. The standard reflections measured every 70 reflections showed no significant variation in intensity. Of 2129 reflections (h 0 to 9, k 0 to 9, l 0 to 40) collected in the range $2 < 2\theta < 70°$, 1579 had net intensities greater than $2.5\sigma(I)$ [where $\sigma(I)$ is the standard deviation from counting statistics], and were regarded as observed. R_{merge} = 0.083. Data were corrected for Lorentz and polarization factors. No absorption correction was applied.

Table 1. *Atomic coordinates and equivalent isotropic temperature factors* (Å^2 × 10^3)

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
C(1)	0.5493 (13)	−0.6042 (13)	−0.1569 (3)	87 (11)
O(2)	0.6059 (9)	−0.4275 (9)	−0.1617 (2)	97 (8)
C(3)	0.5867 (11)	−0.3535 (11)	−0.1245 (3)	72 (9)
C(4)	0.5189 (9)	−0.4760 (10)	−0.0980 (3)	62 (7)
O(5)	0.4881 (9)	−0.6332 (7)	−0.1179 (2)	88 (7)
C(6)	0.4873 (9)	−0.4421 (9)	−0.0586 (3)	59 (7)
C(7)	0.5339 (8)	−0.2689 (8)	−0.0451 (2)	55 (6)
C(8)	0.6037 (9)	−0.1452 (9)	−0.0716 (3)	62 (7)
C(9)	0.6350 (11)	−0.1893 (10)	−0.1117 (3)	75 (9)
C(10)	0.6516 (11)	0.0329 (10)	−0.0554 (3)	81 (10)
C(11)	0.7118 (12)	0.0134 (12)	−0.0144 (4)	102 (12)
N(12)	0.5733 (7)	−0.0605 (8)	0.0132 (2)	66 (6)
C(13)	0.4869 (8)	−0.2195 (9)	−0.0025 (2)	54 (6)
C(14)	0.6516 (13)	−0.0883 (13)	0.0526 (3)	102 (12)
C(15)	0.2864 (8)	−0.1986 (8)	0.0010 (2)	52 (6)
O(16)	0.2426 (6)	−0.1599 (5)	0.0423	57 (4)
C(17)	0.1901 (9)	0.0130 (8)	0.0472 (3)	56 (7)
O(18)	0.1633 (8)	0.0727 (7)	0.0795 (2)	72 (6)
C(19)	0.1740 (8)	0.0910 (8)	0.0069 (2)	47 (6)
C(20)	0.2139 (7)	−0.0399 (8)	−0.0216 (2)	48 (6)
C(21)	0.1917 (8)	−0.0089 (9)	−0.0619 (2)	53 (6)
C(22)	0.1305 (8)	0.1570 (9)	−0.0746 (2)	57 (7)
C(23)	0.0985 (8)	0.2891 (8)	−0.0459 (2)	54 (6)
O(24)	0.0469 (7)	0.4573 (6)	−0.0559 (2)	68 (5)
C(25)	0.0255 (12)	0.4995 (11)	−0.0975 (3)	82 (10)
C(26)	0.1183 (8)	0.2588 (8)	−0.0054 (2)	51 (6)
O(27)	0.1018 (7)	0.3893 (6)	0.0225 (2)	64 (5)
C(28)	−0.0662 (12)	0.4653 (13)	0.0286 (3)	100 (12)

Table 2. *Bond distances* (Å) *and bond angles* (°)

C(1)—O(2)	1.408 (12)	C(1)—O(5)	1.392 (12)
O(2)—C(3)	1.366 (11)	C(4)—C(3)	1.375 (11)
C(3)—C(9)	1.360 (12)	C(4)—O(5)	1.377 (10)
C(4)—C(6)	1.358 (12)	C(7)—C(6)	1.424 (9)
C(7)—C(8)	1.387 (10)	C(8)—C(9)	1.396 (13)
C(7)—C(13)	1.510 (11)	C(8)—C(10)	1.491 (11)
C(10)—C(11)	1.448 (17)	C(11)—N(12)	1.496 (13)
N(12)—C(13)	1.461 (9)	N(12)—C(14)	1.455 (13)
C(13)—C(15)	1.525 (9)	C(15)—O(16)	1.442 (7)
C(15)—C(20)	1.516 (9)	O(16)—C(17)	1.373 (8)
C(17)—O(18)	1.180 (10)	C(17)—C(19)	1.471 (11)
C(19)—C(20)	1.402 (9)	C(19)—C(26)	1.394 (9)
C(20)—C(21)	1.371 (10)	C(21)—C(22)	1.399 (10)
C(22)—C(23)	1.400 (10)	C(23)—O(24)	1.367 (8)
C(23)—C(26)	1.375 (11)	O(24)—C(25)	1.432 (12)
C(26)—O(27)	1.358 (9)		

O(5)—C(1)—O(2)	110.9 (8)	C(3)—O(2)—C(1)	104.5 (7)
C(4)—C(3)—O(2)	110.2 (7)	C(9)—C(3)—O(2)	128.9 (8)
C(9)—C(3)—C(4)	120.8 (8)	O(5)—C(4)—C(3)	109.5 (7)
C(6)—C(4)—C(3)	123.9 (7)	C(6)—C(4)—O(5)	126.7 (7)
C(4)—O(5)—C(1)	104.8 (6)	C(7)—C(6)—C(4)	115.7 (7)
C(8)—C(7)—C(6)	120.8 (7)	C(8)—C(7)—C(13)	121.3 (6)
C(9)—C(8)—C(7)	120.7 (7)	C(7)—C(8)—C(10)	118.0 (8)
C(9)—C(8)—C(10)	121.2 (7)	C(8)—C(9)—C(3)	118.1 (8)
C(8)—C(10)—C(11)	108.9 (7)	C(10)—C(11)—N(12)	113.3 (8)
C(11)—N(12)—C(13)	113.6 (7)	C(11)—N(12)—C(14)	108.8 (7)
C(13)—C(7)—C(6)	117.6 (6)	N(12)—C(13)—C(7)	115.6 (6)
C(13)—N(12)—C(14)	112.5 (6)	C(15)—C(13)—C(7)	109.2 (6)
N(12)—C(13)—C(15)	109.4 (5)	O(16)—C(15)—C(13)	108.6 (6)
C(15)—C(20)—C(21)	132.6 (6)	C(13)—C(15)—C(20)	113.7 (5)
O(16)—C(15)—C(20)	103.3 (5)	O(16)—C(17)—O(18)	121.4 (7)
C(15)—O(16)—C(17)	111.9 (5)	C(19)—C(17)—O(18)	131.5 (6)
O(16)—C(17)—C(19)	107.1 (6)	C(17)—C(19)—C(26)	130.9 (6)
C(17)—C(19)—C(20)	108.6 (5)	C(15)—C(20)—C(19)	107.3 (6)
C(20)—C(19)—C(26)	120.4 (7)	C(20)—C(21)—C(22)	119.1 (6)
C(19)—C(20)—C(21)	121.0 (6)	C(22)—C(23)—O(24)	123.0 (7)
C(21)—C(22)—C(23)	119.2 (7)	O(24)—C(23)—C(26)	115.0 (6)
C(22)—C(23)—C(26)	122.0 (6)	C(19)—C(26)—C(23)	118.1 (6)
C(23)—O(24)—C(25)	118.2 (6)	C(23)—C(26)—O(27)	122.6 (6)
C(19)—C(26)—O(27)	119.0 (7)		
C(26)—O(27)—C(28)	118.5 (6)		

Symmetry and systematic absences ($l \neq 4n$ for $00l$) indicated space group $P4_1$ or the enantiomeric $P4_3$. We have described the structure in $P4_3$. No absolute configuration is implied in this choice.

The structure was solved by direct methods using *SHELXS*86 (Sheldrick, 1986) and refined with unit weights using *SHELX*76 (Sheldrick, 1976). Positional parameters of H atoms were fixed at calculated positions and they were assigned temperature factors of 0.07 Å^2. The z origin was defined by keeping the z coordinate of O(16) fixed. The final R index was 0.061. $(\Delta/\sigma)_{max} = 0.06$ for non-H atoms. $\Delta\rho$ in the final difference map was 0.32 to −0.19 e Å^{-3}. The number of parameters refined was 252. Atomic scattering factors were used as contained in *SHELX*76. All calculations were performed on an ND500 computer.

Discussion. Final atomic coordinates and equivalent isotropic temperature factors are given in Table 1.* Bond distances and bond angles are listed in Table 2. Atomic numbering is shown in the scheme above. The packing of the molecules is shown in Fig. 1.

Hydrastine has a very similar molecular structure to narcotine (Moss & Watson, 1984) and bicuculline (Gorinsky & Moss, 1973), but its configurations at C(13) and C(15) correspond only to those in (−)-α-narcotine. It is of interest to compare the conformation of hydrastine with those of narcotine and bicuculline. In hydrastine, plane 1 [C(1)–O(2)–C(3)–C(9)–C(8)–C(10)–C(11)–N(12)–C(13)–C(7)–C(6)–C(4)–O(5)] is inclined to plane 2 [C(15)–O(16)–C(17)–C(19)–C(26)–C(23)–C(22)–C(21)–C(20)] by 42.9°, with torsion angle N(12)—C(13)—C(15)—O(16) of −55.2°. The planes in the case of narcotine are inclined at angles of 53° (molecule 1) and 50° (molecule 2) with torsion angles of −57.6 and −62.8°, respectively, whereas the planes in bicuculline are approximately parallel, there being a dihedral angle of 14° and a torsion angle of 164.1°.

The bond distances and angles in the N-heterocyclic ring compare well with those reported for other compounds containing a similar ring system (Karle, Estlin & Karle, 1967; Beisler, Silverton, Penttila, Horn & Fales, 1971; Gilardi, 1972; Brown & Trefonas, 1972; Cameron, Hair, Greengrass & Romage, 1974; Bruderer, Metzger, Brossi & Daly, 1976; Shakked & Kennard, 1977; Wong-Ng & Nyburg, 1979; Moss & Watson, 1984). The half-chair conformation ($q_2 = 0.03054$ Å, $q_3 = 0.1250$ Å, $Q = 0.3300$ Å, $\theta = 66.73°$, $\varphi_2 = 160.50°$) of the N-containing ring in hydrastine corresponds to that of bicuculline, whereas the narcotine rings are in a sofa conformation. The lactone ring shows an envelope conformation ($q_2 = 0.1130$ Å, $\varphi_2 = 354.56°$).

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* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, least-squares-planes data and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55644 (13 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: HH0508]

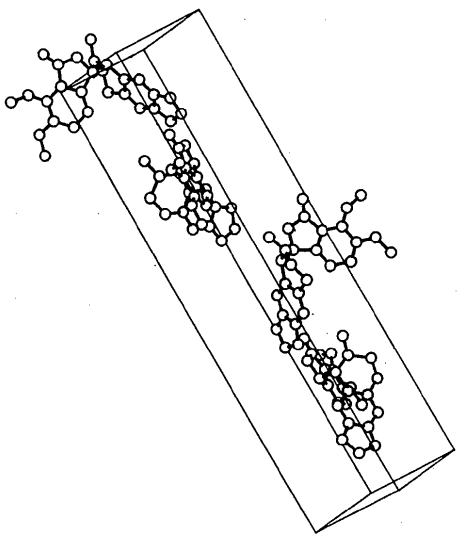

Fig. 1. The packing diagram for hydrastine molecules.

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