

= 2.15 (6) Å, N—H...Cl = 171 (6)°. The water molecule is hydrogen bounded with the Cl<sup>-</sup> anion: Cl(17)...O(18)(x, 1 + y, z) = 3.206 (5), O(18)—H(180) = 1.01 (6), Cl(17)...H(180) = 2.20 (6) Å, Cl...H—O = 173 (5)°; O(18)...Cl(17)(x, 1 - y, z) = 3.206 (5), O(18)—H(181) = 1.03 (7), H(181)...Cl(17) = 2.20 (7) Å, O—H...Cl = 167 (6)°.

The sample was kindly provided by ICI, Pharmaceuticals Division (Macclesfield, England).

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## Structure of 5,6-Dimethoxy-2-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]-1H-indole (Oxypertine) Dihydrate, C<sub>23</sub>H<sub>29</sub>N<sub>3</sub>O<sub>2</sub>.2H<sub>2</sub>O

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**Abstract.**  $M_r = 415.5$ , monoclinic,  $P2_1/n$ ,  $a = 10.936$  (1),  $b = 13.640$  (1),  $c = 15.502$  (2) Å,  $\beta = 92.66$  (1)°,  $V = 2309.9$  (3) Å<sup>3</sup>,  $Z = 4$ ,  $D_x = 1.20$  Mg m<sup>-3</sup>,  $Cu K\alpha$ ,  $\lambda = 1.54178$  Å,  $\mu = 2.69$  mm<sup>-1</sup>,  $F(000) = 896$ , room temperature, final  $R = 0.044$  for 2112 reflections. The title compound is a tranquilizer and  $\alpha$ -adrenoceptor antagonist. The solid-state conformation differs somewhat from that of AR-C 239, a well known specific  $\alpha_1$ -antagonist.

**Introduction.** Among a series of (indolylalkyl)(phenyl)-piperazines synthesized some twenty years ago in Sterling–Winthrop Research Institute, New York (Archer, Wylie, Harris, Lewis, Schulenberg, Bell, Kullnig & Arnold, 1962), oxypertine has been found to possess a potent central depressant activity. This compound is used in therapeutics as a tranquilizer.

Like other groups of potent tranquilizers, oxypertine exhibits some adrenergic blocking activity (Wylie & Archer, 1962; Campbell, 1981). For this reason, we included oxypertine in a research program on the conformational requirements of  $\alpha$ -adrenoceptor antagonists.

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

$$B_{eq} = \frac{4}{3} \sum_i \beta_{ii} a_i \cdot a_i$$

	x	y	z	$B_{eq}(\text{Å}^2)$
C(1)	7284 (3)	7384 (2)	9369 (2)	3.2 (1)
C(2)	8435 (3)	7698 (2)	9134 (2)	3.8 (1)
C(3)	9073 (3)	8395 (3)	9608 (2)	4.4 (2)
C(4)	8589 (3)	8803 (3)	10332 (2)	4.7 (2)
C(5)	7454 (3)	8503 (2)	10566 (2)	4.5 (2)
C(6)	6800 (3)	7804 (2)	10097 (2)	3.9 (1)
N(7)	6647 (2)	6675 (2)	8854 (2)	3.4 (1)
C(8)	5453 (3)	6354 (2)	9146 (2)	4.3 (2)
C(9)	4780 (3)	5727 (2)	8470 (2)	4.3 (2)
N(10)	5503 (2)	4865 (2)	8247 (2)	3.3 (1)
C(11)	6680 (3)	5206 (2)	7950 (2)	4.1 (2)
C(12)	7358 (3)	5808 (2)	8630 (2)	4.2 (2)
C(13)	4894 (3)	4273 (2)	7567 (2)	3.7 (1)
C(14)	3714 (3)	3768 (2)	7809 (2)	3.8 (1)
C(15)	3383 (3)	2982 (2)	7163 (2)	3.4 (1)
C(16)	2645 (3)	3065 (2)	6431 (2)	3.7 (1)
N(17)	2673 (2)	2204 (2)	5968 (2)	3.7 (1)
C(18)	3440 (3)	1553 (2)	6405 (2)	3.1 (1)
C(19)	3897 (3)	2011 (2)	7156 (2)	3.1 (1)
C(20)	4702 (3)	1495 (2)	7723 (2)	3.1 (1)
C(21)	5002 (3)	546 (2)	7528 (2)	3.2 (1)
C(22)	4533 (3)	101 (2)	6756 (2)	3.4 (1)
C(23)	3747 (3)	592 (2)	6194 (2)	3.5 (1)
O(24)	5768 (2)	-51 (2)	8022 (1)	4.1 (1)
C(25)	6226 (4)	331 (3)	8826 (2)	5.2 (2)
O(26)	4942 (2)	-839 (2)	6630 (2)	4.9 (1)
C(27)	4503 (4)	-1330 (3)	5869 (3)	6.4 (2)
C(28)	1872 (4)	3884 (3)	6108 (3)	5.7 (2)
O(29)	1581 (2)	1838 (2)	4232 (1)	5.4 (1)
O(30)	3199 (2)	2191 (2)	2843 (2)	5.6 (1)

**Experimental.** Small white block (from ethanol),  $0.17 \times 0.10 \times 0.06$  mm,  $D_m$  not measured, Enraf-Nonius CAD-4 diffractometer, 25 reflections used for measuring lattice parameters ( $5 < \theta < 35^\circ$ ),  $3437 \pm hkl$  independent reflections with  $\theta < 60^\circ$ , 2112 with  $I \geq 3\sigma(I)$ , Lp correction, absorption ignored; two standard reflections ( $202, 1\bar{1}2$ ) every 5400s: no unusual variations. Direct methods (MULTAN, Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), anisotropic diagonal-matrix, refinement on  $F$ ; weighting scheme;  $w = 1$  if  $|F_o| < P$ ,  $P = (F_o^2 \max / 10)^{1/2}$ ,  $w = (P/F_o)^2$  if  $|F_o| > P$ ; water molecules and H from  $\Delta F$  synthesis, H isotropic, final  $R = 0.044$ ,  $wR = 0.0426$ ,  $S = 0.565$ ; final maximum shift to error  $0.5$ , max. and min. heights in final difference Fourier map  $\pm 0.4 e \text{ \AA}^{-3}$ ; no correction for secondary extinction;  $f_i$  of non-hydrogen atoms from *International Tables for X-ray Crystallography* (1974),  $f_i$  for H atoms from Stewart, Davidson & Simpson (1965); IRIS 80, CII, computer of the 'Centre Interuniversitaire de Calcul' (Talence).

Table 2. Bond distances (Å) and angles ( $^\circ$ )

C(1)–C(2)	1.394 (4)	C(15)–C(16)	1.366 (4)
C(1)–C(6)	1.393 (4)	C(15)–C(19)	1.439 (4)
C(1)–N(7)	1.416 (4)	C(16)–N(17)	1.379 (4)
C(2)–C(3)	1.372 (5)	C(16)–C(28)	1.474 (5)
C(3)–C(4)	1.381 (5)	N(17)–C(18)	1.377 (4)
C(4)–C(5)	1.372 (5)	C(18)–C(19)	1.393 (4)
C(5)–C(6)	1.379 (5)	C(18)–C(23)	1.396 (4)
N(7)–C(8)	1.468 (4)	C(19)–C(20)	1.404 (4)
N(7)–C(12)	1.466 (4)	C(20)–C(21)	1.372 (4)
C(8)–C(9)	1.516 (5)	C(21)–C(22)	1.417 (4)
C(9)–N(10)	1.467 (4)	C(21)–O(24)	1.374 (4)
N(10)–C(11)	1.463 (4)	C(22)–C(23)	1.370 (4)
N(10)–C(13)	1.464 (4)	C(22)–O(26)	1.374 (4)
C(11)–C(12)	1.504 (5)	O(24)–C(25)	1.422 (4)
C(13)–C(14)	1.525 (5)	O(26)–C(27)	1.421 (5)
C(14)–C(15)	1.500 (4)		
C(2)–C(1)–C(6)	117.9 (3)	C(16)–C(15)–C(19)	106.6 (3)
C(2)–C(1)–N(7)	119.3 (3)	C(15)–C(16)–N(17)	109.6 (3)
C(6)–C(1)–N(7)	122.8 (3)	C(15)–C(16)–C(28)	130.7 (3)
C(1)–C(2)–C(3)	121.1 (3)	N(17)–C(16)–C(28)	119.7 (3)
C(2)–C(3)–C(4)	120.7 (3)	C(16)–N(17)–C(18)	108.7 (3)
C(3)–C(4)–C(5)	118.7 (3)	N(17)–C(18)–C(19)	108.0 (3)
C(4)–C(5)–C(6)	121.4 (3)	N(17)–C(18)–C(23)	129.6 (3)
C(1)–C(6)–C(5)	120.3 (3)	C(19)–C(18)–C(23)	122.4 (3)
C(1)–N(7)–C(8)	116.8 (2)	C(15)–C(19)–C(18)	107.0 (3)
C(1)–N(7)–C(12)	115.6 (2)	C(15)–C(19)–C(20)	133.7 (3)
C(8)–N(7)–C(12)	108.8 (2)	C(18)–C(19)–C(20)	119.3 (3)
N(7)–C(8)–C(9)	111.5 (3)	C(19)–C(20)–C(21)	119.0 (3)
C(8)–C(9)–N(10)	111.4 (3)	C(20)–C(21)–C(22)	120.6 (3)
C(9)–N(10)–C(11)	108.1 (2)	C(20)–C(21)–O(24)	125.6 (3)
C(9)–N(10)–C(13)	112.4 (2)	C(22)–C(21)–O(24)	113.8 (3)
C(11)–N(10)–C(13)	109.0 (2)	C(21)–C(22)–C(23)	121.3 (3)
N(10)–C(11)–C(12)	111.4 (3)	C(21)–C(22)–O(26)	114.3 (3)
N(7)–C(12)–C(11)	110.9 (3)	C(23)–C(22)–O(26)	124.4 (3)
N(10)–C(13)–C(14)	115.7 (3)	C(18)–C(23)–C(22)	117.5 (3)
C(13)–C(14)–C(15)	109.8 (3)	C(21)–O(24)–C(25)	116.9 (3)
C(14)–C(15)–C(16)	127.6 (3)	C(22)–O(26)–C(27)	117.3 (3)
C(14)–C(15)–C(19)	125.5 (3)		

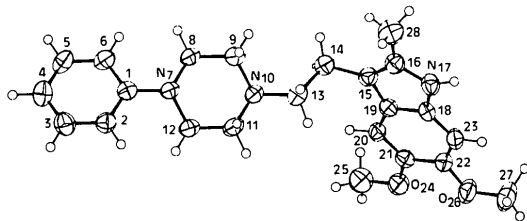


Fig. 1. Perspective view of the molecule showing the numbering of the atoms.

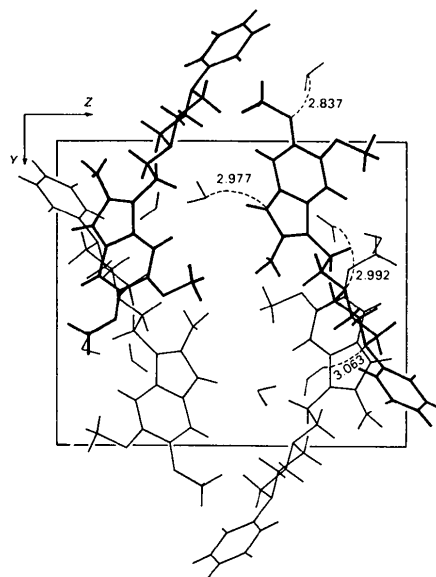


Fig. 2. Packing of the molecules projected on (100); projection axis  $Ox$ . (Distances in Å.)

**Discussion.** Atomic parameters are given in Table 1, bond distances and angles in Table 2.\* Fig. 1 shows the numbering and Fig. 2 the packing. The piperazine ring adopts a chair conformation, N(7) and N(10) being on opposite sides of the plane containing C(8), C(9), C(11) and C(12) (plane II). If we call the plane of the phenyl ring plane I and that of the indolyl ring plane III, the respective positions of the three planes are defined by the following angles: plane I/plane II =  $25 (1)^\circ$ , plane II/plane III =  $54 (1)^\circ$  and plane I/plane III =  $78 (1)^\circ$ . One can also define the respective positions of the rings by the values of the torsion angles ( $\pm 1^\circ$ ): C(2)–C(1)–N(7)–C(8)  $178$ , C(11)–N(10)–C(13)–C(14)  $174$ , N(10)–C(13)–C(14)–C(15)  $196$ , C(13)–C(14)–C(15)–C(16)  $268$ . These values are comparable with those found in 2-[2-[4-(*o*-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-2*H*,4*H*-1,3-isoquinoline-dione (AR-C239) a well known specific  $\alpha_1$ -antagonist (Carpy, Goursolle & Léger, 1983).

When oxypertine is protonated, the protonation occurs on N(10). The centers implicated in the interaction of  $\alpha$ -ligands with their receptor are the quaternary N and the aromatic rings (Pullman, Coubeils, Courrière & Gervois, 1972). The distance N(10)– $\pi_3$  [ $\pi_3$  is the middle of C(18)–C(21)] is  $5.72 (2) \text{ \AA}$ ; N(10)– $\pi_1$  ( $\pi_1$  is the center of the phenyl

\* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates, and least-squares planes have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38625 (25 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

ring) is 5.67 (2) Å. The distances N(10)–plane III and N(10)–plane I are, respectively, 1.832 (3) and 0.736 (2) Å. Neither of these pairs of values agrees with our model of  $\alpha$ -ligands (Carpy, Léger, Leclerc, Decker, Rouot & Wermuth, 1982).

The crystalline cohesion is strengthened by hydrogen bonds involving the two water molecules: N(17)···O(29) = 2.977 (4), N(17)–H(170) = 0.98 (3), H(170)···O(29) = 1.96 (3) Å, N–H···O = 173 (3)°; N(10)···O(29)( $\frac{1}{2}+x$ ,  $\frac{1}{2}-y$ ,  $\frac{1}{2}+z$ ) = 2.992 (4), O(29)–H(290) = 1.00 (3), N(10)···H(290) = 2.04 (3) Å, N···H–O = 158 (3)°; N(7)···O(30)(1– $x$ , 1– $y$ , 1– $z$ ) = 3.063 (4), O(30)–H(301) = 0.93 (3), N(7)···H(301) = 2.16 (3) Å, N···H–O = 163 (3)°; O(26)···O(30)(1– $x$ ,  $\bar{y}$ , 1– $z$ ) = 2.837 (4), O(30)–H(300) = 0.96 (3), O(26)···H(300) = 1.92 (3) Å, O···H–O = 159 (3)°.

The sample was kindly provided by Winthrop, France.

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### Structure of 3-{*N*–[(4,5-Dihydro-2-imidazolyl)methyl]-*p*-toluidino}phenol (Phentolamine) Hydrochloride, C<sub>17</sub>H<sub>20</sub>N<sub>3</sub>O<sup>+</sup>.Cl<sup>–</sup>

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**Abstract.**  $\alpha$ -Adrenoceptor antagonist. Antihypertensive drug.  $M_r = 317.7$ , monoclinic,  $P2_1/c$ ,  $a = 12.201$  (1),  $b = 10.321$  (1),  $c = 13.292$  (3) Å,  $\beta = 97.89$  (1)°,  $V = 1658.0$  (3) Å<sup>3</sup>,  $Z = 4$ ,  $D_x = 1.27$  g cm<sup>–3</sup>,  $\lambda(\text{Cu } K\alpha) = 1.54178$  Å,  $\mu = 20.84$  cm<sup>–1</sup>,  $F(000) = 746$ , room temperature. Final  $R = 0.037$  for 1168 reflections. The imidazoline ring is perpendicular to the 3-hydroxyphenyl ring. Both nitrogens of the guanidine function are involved in hydrogen bonds with the Cl<sup>–</sup> ions.

**Introduction.** Phentolamine is a classical  $\alpha$ -adrenoceptor antagonist, blocking both pre- ( $\alpha_2$ ) and postsynaptic ( $\alpha_1$ ) adrenoceptors (Langer, 1977; Starke, 1977; Westfall, 1977). It is used for its antihypertensive and vasodilating properties, specially for the diagnosis of the pheochromocytoma.

The crystal structure determination of this drug has been undertaken in order to compare its conformation with those of 2-imidazoline antihypertensive  $\alpha_2$ -

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adrenoceptor agonists related to clonidine (Carpy, Léger, Leclerc, Decker, Rouot & Wermuth, 1982, and references therein).

**Experimental.** Small white plates (from ethanol), 0.13 × 0.13 × 0.08 mm, Enraf–Nonius CAD-4 diffractometer, lattice parameters from 22 reflections ( $3 < \theta < 36^\circ$ ), 1419 independent  $\pm hkl$  with  $\theta < 45^\circ$  ( $-11 \leq h \leq 11$ ,  $0 \leq k \leq 9$ ,  $0 \leq l \leq 12$ ), 1168 with  $I \geq 3\sigma(I)$ ,  $L_p$  correction, absorption ignored; direct methods (*MULTAN*; Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), anisotropic diagonal-matrix refinement on  $F$ , H from  $\Delta F$  synthesis, isotropic, final  $R = 0.037$ ,  $wR = 0.032$ ,  $S = 0.782$ ;  $w = 1$  if  $|F_o| < P$ ,  $P = (F_o^2 \max./10)^{1/2}$ ;  $w = (P/F_o)^2$  if  $|F_o| > P$ ;  $(\Delta/\sigma)_{\max} = 0.4$ , in final difference map  $\Delta\rho = \pm 0.3$  e Å<sup>–3</sup>;  $f_i$  of non-hydrogen atoms (*International Tables for X-ray Crystallography*, 1974),  $f_i$  of H atoms (Stewart, Davidson & Simpson, 1965), IRIS 80, CII, computer of the 'Centre Interuniversitaire de Calcul' (Talence).