Acta Cryst. (1986). C**42**, 1233–1235

Structure of *N*-{2-[3-(Dimethylamino)propylthio]phenyl}-3-phenylpropenamide Monohydrochloride (Cinanserin Hydrochloride)

By O. M. Peeters, N. M. Blaton and C. J. De Ranter*

Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Instituut voor Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium

(*Received* 31 *January* 1986; *accepted* 3 *April* 1986)

Abstract. $C_{20}H_{25}N_2OS^+Cl^-$, $M_r = 376{\cdot}94$, monoclinic, $P2_1/n$, $a = 22{\cdot}60\,(1)$, $b = 7{\cdot}672\,(2)$, $c = 11{\cdot}795\,(4)$ Å, $\beta = 94{\cdot}14\,(4)°$, $V = 2040\,(1)$ Å^3, $Z = 4$, $D_m = 1{\cdot}22$, $D_x = 1{\cdot}227$ Mg m^{-3}, $\lambda(\text{Mo}\,K\alpha) = 0{\cdot}71069$ Å, $\mu(\text{Mo}\,K\alpha) = 0{\cdot}293$ mm^{-1}, $F(000) = 800$, room temperature, final $R = 0{\cdot}052$ for 1991 observed reflections. The phenylpropenamide moiety of cinanserin, a serotonin antagonist drug, has a localized double bond [1·322 (3) Å] and a *trans* configuration. A dimer is formed around an inversion center through hydrogen bonds between the chloride ion and the amido and amino nitrogen atoms [$\text{Cl}\cdots\text{N} = 3{\cdot}460\,(3)$ and 3·063 (2) Å, respectively].

Introduction. Since the discovery of ketanserin (Leysen, Awouters, Kennis, Laduron, Vandenberk & Janssen, 1981) and pirenperone (Colpaert & Leysen, 1981) there has been renewed interest in compounds which possess 5-HT (5-hydroxytryptamine, serotonin) antagonist activity. In order to obtain a better understanding of the complex structure–activity relationships of these compounds we started a crystal structure study for some of them. Here we report the results obtained for cinanserin.

Experimental. Crystals obtained at room temperature from an *n*-hexane/$CHCl_3$ solution. Density measured by flotation in KBr solution; crystal ~0·2 × 0·2 × 0·4 mm, Syntex $P2_1$ computer-controlled four-circle diffractometer, graphite-monochromated Mo $K\alpha$ radiation, ω-scan technique ($2\theta_{\max} = 46°$, $0 \le h \le 24$, $0 \le k \le 8$, $-12 \le l \le 12$); cell dimensions by least-squares refinement of the setting angles of 24 reflections with $15° < 2\theta < 25°$; three standard reflections ($2\bar{2}0$, 501, $\bar{4}02$) measured after every 50 reflections showed no significant reduction in intensity (overall e.s.d.'s 3·8, 4·6 and 3·0% respectively); 5683 reflections measured, 2843 unique ($R_{\text{int}} = 0{\cdot}049$), 1991 observed with $I > 2\sigma(I)$; Lp corrections, no absorption corrections; scattering factors from Cromer & Mann (1968) and Stewart, Davidson & Simpson (1965) (for H); scattering factors for Cl and S were corrected for anomalous dispersion (*International Tables for X-ray Crystallography*, 1974).

The structure was partially solved with *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). With the sulfur position of this partial structure as input *DIRDIF* (Beurskens, Bosman, Doesburg, Gould, van den Hark, Prick, Noordik, Beurskens & Parthasarathi, 1981) revealed the complete structure. Initial isotropic and anisotropic refinement on *F* with *SHELX*76 (Sheldrick, 1976). H atoms calculated [except H(15) located in ΔF synthesis] with C—H 1·08 Å, included in the refinement with $U_{\text{iso}} = 0{\cdot}05$ Å^2 and riding on their parent atom. Finally two cycles of full-matrix least squares with *XRAY*76 (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) executed (H-atom positions fixed). Final $R = 0{\cdot}052$, $wR = 0{\cdot}051$ and $S = 1{\cdot}35$, $w = 1$, $(\Delta/\sigma)_{\text{ave}} = 0{\cdot}28$, $(\Delta/\sigma)_{\max} = 2{\cdot}0$ (scale factor), $\Delta\rho = -0{\cdot}33$ to 0·29 e Å^{-3} (rejection ratio = 0·3).

Table 1. *Atomic coordinates and equivalent isotropic thermal parameters with e.s.d.'s of the refined parameters in parentheses*

$$B_{\text{eq}} = \tfrac{4}{3}\textstyle\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}(Å^2)
Cl	0·93998 (3)	0·71067 (8)	0·40534 (5)	4·25 (1)
C(1)	0·8687 (1)	0·2500 (3)	0·7276 (2)	3·42 (7)
C(2)	0·8126 (1)	0·3249 (3)	0·7155 (2)	4·16 (8)
C(3)	0·7969 (1)	0·4567 (4)	0·7880 (2)	4·87 (8)
C(4)	0·8373 (1)	0·5152 (3)	0·8723 (2)	4·99 (9)
C(5)	0·8937 (1)	0·4481 (3)	0·8841 (2)	4·34 (8)
C(6)	0·9102 (1)	0·3155 (3)	0·8121 (2)	3·54 (7)
N(7)	0·96892 (8)	0·2504 (2)	0·8168 (2)	3·84 (6)
C(8)	1·0058 (1)	0·2221 (3)	0·9127 (2)	3·75 (7)
C(9)	0·8467 (1)	0·0830 (3)	0·5151 (2)	4·07 (7)
S(10)	0·88950 (3)	0·06508 (8)	0·65024 (6)	4·34 (2)
O(12)	0·99067 (7)	0·2460 (2)	1·0085 (1)	5·15 (5)
C(13)	0·8656 (1)	0·2310 (3)	0·4391 (2)	4·40 (7)
C(14)	0·9252 (1)	0·1948 (3)	0·3951 (2)	4·10 (7)
N(15)	0·94555 (9)	0·3352 (2)	0·3185 (2)	3·88 (6)
C(16)	1·0080 (1)	0·3027 (3)	0·2925 (2)	5·26 (8)
C(20)	0·9068 (1)	0·3576 (3)	0·2116 (2)	4·78 (8)
C(30)	1·0648 (1)	0·1614 (3)	0·8852 (2)	3·47 (7)
C(31)	1·1051 (1)	0·1010 (3)	0·9622 (2)	3·69 (7)
C(32)	1·1638 (1)	0·0341 (3)	0·9381 (2)	3·57 (7)
C(33)	1·1866 (1)	0·0562 (3)	0·8321 (2)	4·38 (8)
C(34)	1·2408 (1)	−0·0152 (4)	0·8099 (2)	5·14 (9)
C(35)	1·2738 (1)	−0·1074 (4)	0·8928 (3)	5·29 (10)
C(36)	1·2516 (1)	−0·1284 (4)	0·9969 (3)	5·59 (10)
C(37)	1·1975 (1)	−0·0584 (4)	1·0202 (2)	4·65 (8)

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* To whom correspondence should be addressed.

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Table 2. *Bond lengths* (Å) *and angles* (°)

C(1)—C(2)	1·390 (3)	C(2)—C(1)—C(6)	118·7 (2)
C(1)—C(6)	1·410 (3)	C(2)—C(1)—S(10)	123·6 (1)
C(1)—S(10)	1·769 (2)	C(6)—C(1)—S(10)	117·6 (1)
C(2)—C(3)	1·387 (3)	C(1)—C(2)—C(3)	120·6 (2)
C(3)—C(4)	1·375 (3)	C(2)—C(3)—C(4)	119·9 (2)
C(4)—C(5)	1·373 (3)	C(3)—C(4)—C(5)	120·9 (2)
C(5)—C(6)	1·393 (3)	C(4)—C(5)—C(6)	119·9 (2)
C(6)—N(7)	1·416 (3)	C(1)—C(6)—C(5)	119·9 (2)
N(7)—C(8)	1·374 (3)	C(1)—C(6)—N(7)	118·4 (2)
C(8)—O(12)	1·217 (3)	C(5)—C(6)—N(7)	121·6 (2)
C(8)—C(30)	1·471 (3)	C(6)—N(7)—C(8)	126·8 (1)
C(9)—C(13)	1·526 (3)	N(7)—C(8)—O(12)	123·1 (2)
C(13)—C(14)	1·504 (3)	N(7)—C(8)—C(30)	112·0 (2)
C(14)—N(15)	1·499 (3)	O(12)—C(8)—C(30)	124·9 (2)
N(15)—C(16)	1·487 (3)	C(9)—C(13)—C(14)	111·1 (1)
N(15)—C(20)	1·492 (3)	C(13)—C(14)—N(15)	113·4 (1)
C(30)—C(31)	1·322 (3)	C(14)—N(15)—C(16)	110·0 (1)
C(31)—C(32)	1·470 (3)	C(14)—N(15)—C(20)	113·9 (1)
C(32)—C(33)	1·396 (3)	C(16)—N(15)—C(20)	110·6 (1)
C(32)—C(37)	1·384 (3)	C(8)—C(30)—C(31)	123·4 (2)
C(33)—C(34)	1·383 (3)	C(30)—C(31)—C(32)	125·2 (2)
C(34)—C(35)	1·382 (4)	C(31)—C(32)—C(33)	121·8 (2)
C(35)—C(36)	1·369 (4)	C(31)—C(32)—C(37)	120·1 (2)
C(36)—C(37)	1·381 (4)	C(33)—C(32)—C(37)	118·0 (2)
		C(32)—C(33)—C(34)	120·7 (2)
		C(33)—C(34)—C(35)	120·6 (2)
		C(34)—C(35)—C(36)	118·7 (2)
		C(35)—C(36)—C(37)	121·3 (2)
		C(32)—C(37)—C(36)	120·6 (2)

Discussion. The atomic coordinates and equivalent isotropic thermal parameters are given in Table 1.* The structure with the atomic numbering scheme is depicted in Fig. 1. Bond lengths and angles are listed in Table 2. The monosubstituted benzene ring is almost exactly planar [$\Delta = 0{\cdot}005\ (3)$ Å] and the deformations of the internal angles caused by the —CH=CH— substituent are in agreement with the values given by Domenicano & Murray-Rust (1979). The bond lengths in the propene moiety are typical for carbon atoms which have sp^2 hybridization (Burke-Laing & Laing, 1976). The value of 1·322 (3) Å for C(30)—C(31) indicates a localized double bond. The 3-phenylpropenamide moiety has the *trans* form. The disubstituted benzene ring deviates significantly from planarity in the χ^2 test at the 95% significance level with the S and N atoms −0·207 (1) and 0·115 (2) Å out of the mean plane. The dihedral angles between the mean plane of the amide group and the mono- and disubstituted benzene ring are 158·0 (1) and 38·6 (1)° respectively. N(7) is sp^2 hybridized (sum of valence angles = 359·9°) and the sum of the bond orders, taking N—H as 1, is 3·45. The *p* electrons on the N atom are thus delocalized into the C(6)—N(7) and the N(7)—C(8) bond (Burke-Laing & Laing, 1976). The contraction of the C(1)—S(10) bond length [1·769 (2) Å] may be interpreted in terms of some π bonding between a $p\pi$ orbital of the C atom and 3*d* orbitals of the S atom (McDowell, 1975; Hosoya, 1966). The S(10)—C(9) bond distance of 1·809 (2) Å agrees well with the normal S—C(sp^3) distance (Talberg, 1974). The bond-length values in the aminopropyl chain are normal although C(13)—C(14) with distance 1·504 (4) Å is rather short for a C(sp^3)—C(sp^3) bond. A packing diagram for cinanserin hydrochloride is given in Fig. 2. The chloride ion is hydrogen bonded to the amino nitrogen atom [Cl···N(15) = 3·063 (2), Cl···H(15) = 2·13 Å, $\angle$N(15)—H(15)···Cl = 172°] and to the amido nitrogen atom [Cl···N(7^i) = 3·460 (3), Cl···H(7^i) = 2·49 Å, $\angle$N(7^i)—H(7^i)···Cl = 150°; symmetry code (i) $2-x,\ 1-y,\ 1-z$] so that a dimer is formed around the inversion center at $(1, \frac{1}{2}, \frac{1}{2})$. There are no other unusually short intermolecular distances. The short intramolecular contacts of S(10)—H(7), O(12)—H(5) and O(12)—H(31) with distances of 2·65, 2·50 and 2·60 Å respectively can be considered as intramolecular hydrogen bonds (Taylor & Kennard, 1982) and justify the observed conformation of the molecule. The computer program *PARST* (Nardelli, 1982) was used to calculate the molecular parameters.

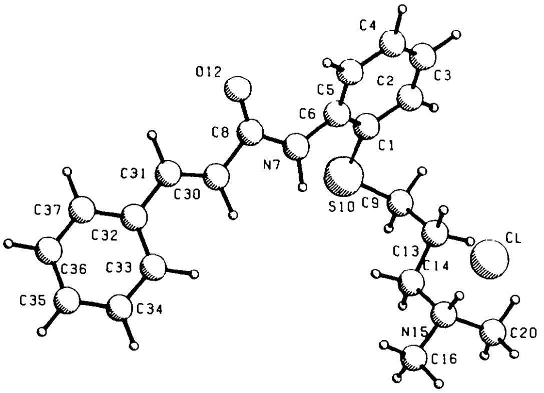

Fig. 1. Perspective view (*PLUTO*78, Motherwell & Clegg, 1978) of the molecule with the atomic numbering scheme.

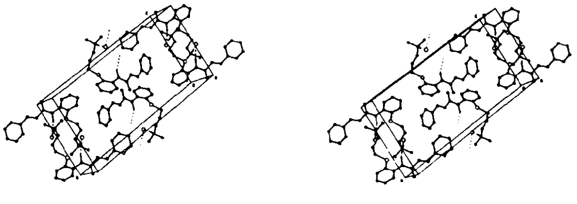

Fig. 2. Stereoscopic packing diagram (*PLUTO*78, Motherwell & Clegg, 1978) with hydrogen bonds shown as broken lines.

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* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, distances and angles involving H atoms and least-squares planes data have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42978 (21 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1986). C**42**, 1235–1237

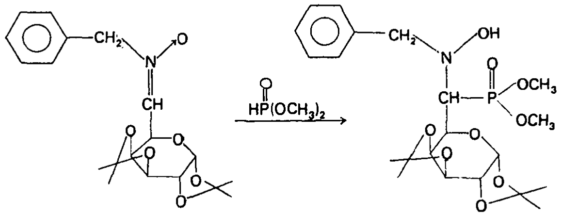
Structural Chirality of an α-Aminophosphonic Acid Derivative

By Michael Dyrbusch and Ernst Egert

Institut für Anorganische Chemie der Universität Göttingen, Tammannstrasse 4, *D*-3400 *Göttingen, Federal Republic of Germany*

(*Received* 3 *July* 1985; *accepted* 28 *July* 1986)

Abstract. (6*R*)-6-(*N*-Benzyl-*N*-hydroxyamino)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-ylphosphonic acid dimethyl ester, $C_{21}H_{32}NO_9P$, $M_r = 473\cdot5$, orthorhombic, $P2_12_12_1$, $a = 9\cdot552$ (1), $b = 14\cdot395$ (1), $c = 17\cdot992$ (1) Å, $V = 2473\cdot9$ (3) Å^3, $Z = 4$, $D_x = 1\cdot271$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0\cdot7107$ Å, $\mu = 0\cdot15$ mm^{-1}, $F(000) = 1008$, room temperature (295 K), $R = 0\cdot049$ for 3584 observed reflections. η refinement was employed to determine the absolute configuration of the molecule. All bond lengths and angles are as expected. The N atom is *trans* to the galactopyranose ring O atom. The molecules pack together with a hydrogen bond between the hydroxyl and phosphate P=O groups.



(I) (II)

Introduction. α-Aminophosphonic acids are of great interest because of their potential biological activity (Horiguchi & Kandatsu, 1959; Kittredge & Roberts, 1969). An important reaction step in the course of their enantioselective synthesis (Hoppe & Schöllkopf, 1985) is the stereospecific addition of dimethyl phosphonate to the α-D-galactose derivative (I). The absolute configuration of the reaction product (II) was confirmed by X-ray structural analysis using the anomalous scattering of the phosphorus atom.

Experimental. Crystals from ethyl acetate/hexane, colourless rectangular prisms, dimensions $0\cdot8 \times 0\cdot2 \times 0\cdot2$ mm; Stoe four-circle diffractometer; lattice parameters measured by centring 60 reflections with $20 < 2\theta < 25°$; data collection with profile-fitting method (Clegg, 1981); $2\theta_{\max} = 50°$ ($-11 \leq h \leq 11$, $k \leq 17$, $l \leq 21$); 4286 unique reflexions including Friedel opposites (measured at -2θ, ω–2θ, χ, φ in order to reduce systematic errors); 3584 with $|F| > 3\sigma(F)$ treated as observed; empirical absorption correction [$R_{\rm int} = 0\cdot036$ for 400 azimuthal scans, transmission factors: $0\cdot85$ (max.), $0\cdot75$ (min.)]; structure solved by Patterson and Fourier techniques; $R = 0\cdot113$ after isotropic refinement with unit weights; all hydrogen

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