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## Structure of *N*<sup>2</sup>-(3,5-Dichlorophenyl)-4-(4-hydroxy-2-methoxyphenyl)-1-piperazine-carboxamide Monohydrate

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**Abstract.** C<sub>18</sub>H<sub>20</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>2</sub>·H<sub>2</sub>O, *M*<sub>r</sub> = 413.31, monoclinic, *P*2<sub>1</sub>/*c*, *a* = 9.055 (3), *b* = 9.078 (8), *c* = 23.945 (8) Å, β = 93.72 (2)°, *V* = 1964.2 Å<sup>3</sup>, *Z* = 4, *D*<sub>x</sub> = 1.40 g cm<sup>-3</sup>, λ(Mo *K*α) = 0.71069 Å, μ = 3.55 cm<sup>-1</sup>, *F*(000) = 864, *T* = 290 K, *R* = 0.047 for 1536 observed reflections. The trisubstituted guanidine group is shown unambiguously to exist in the solid as the amine tautomeric form.

**Introduction.** The title compound was synthesized by Pascal (1986) as a potential anti-arrhythmic agent with class I and class III activities as proposed by Vaughan Williams (1974). The crystal structure was undertaken to study the molecular geometry and possible intermolecular interactions of relevance to its therapeutic properties (Coddling, 1988).

**Experimental.** Small colourless rods were obtained from 50% aqueous acetone and one with dimensions 0.34 × 0.19 × 0.10 mm was selected for structure determination. Stoë STADI-2 diffractometer, Mo *K*α radiation, graphite monochromator. Lattice parameters refined from the setting angles for 18 reflections with θ between 8.8 and 11.0°. 2584 independent data collected, 2 < θ < 25°, with crystal mounted about *b*. -10 ≤ *h* ≤ 10, 0 ≤ *k* ≤ 9, 0 ≤ *l* ≤ 28. Intensities of two standard reflections were measured after each layer, and no significant decay was observed. No absorption correction was applied. 1536 data with *I* ≥ 2.5σ(*I*) were used to solve and refine the structure. Scattering factors and anomalous corrections from *International Tables for X-ray Crystallography* (1974, Vol. IV). Structure solution

by direct methods (*SHELX84*; Sheldrick, 1984), most non-H atoms being located in the first *E* map, and the rest in the first difference Fourier synthesis. Non-H atoms refined anisotropically, H atoms bonded to C atoms included in calculated positions and allowed to ride (C—H 1.08 Å, geometry constrained to trigonal or tetrahedral as appropriate; methyl group allowed to rotate as a rigid group). Positions of other H atoms refined. All H atoms assigned a fixed isotropic thermal parameter (*U*) of 0.05 Å<sup>2</sup>. Full-matrix least-squares refinement on *F* (*SHELX76*; Sheldrick, 1976) with *w*<sup>-1</sup> = σ<sup>2</sup>(*F*) + 0.00023*F*<sup>2</sup>. Final *R* = 0.047, *wR* = 0.046, *S* = 1.14 based on 262 parameters. Maximum Δ/σ in last cycle 0.06, max. and min. ripple in difference electron density map: 0.33 and -0.38 e Å<sup>-3</sup>. Final atomic coordinates are given in Table 1, derived distances and angles in Table 2 (*CALC*; Gould & Taylor, 1983).\*

**Discussion.** A drawing of the molecular structure, projected into the plane of the guanidine group [C(1), N(2), N(3) and N(11)], together with the numbering system, is given in Fig. 1 (*PLUTO*; Motherwell & Clegg, 1978). In each ring, the last digit of the name corresponds to the chemical ring position. The two aromatic rings are planar, the

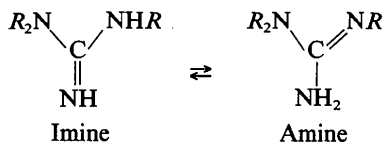
\* Lists of structure factors, anisotropic thermal parameters, torsion angles and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53378 (14 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Fractional coordinates and equivalent isotropic thermal parameters with e.s.d.'s in parentheses

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$$

	x	y	z	$U_{eq}(\text{\AA}^2)$
C(1)	-0.1772 (6)	0.4780 (5)	0.10601 (20)	0.027 (3)
N(2)	-0.0369 (5)	0.4194 (5)	0.10414 (18)	0.034 (3)
N(3)	-0.2865 (4)	0.4156 (4)	0.13016 (16)	0.0311 (25)
N(11)	-0.1992 (4)	0.6068 (4)	0.07663 (15)	0.0260 (23)
C(12)	-0.1154 (5)	0.6362 (5)	0.02702 (20)	0.031 (3)
C(13)	-0.1147 (5)	0.7999 (5)	0.01274 (21)	0.030 (3)
N(14)	-0.2682 (4)	0.8547 (4)	0.00660 (16)	0.0276 (24)
C(15)	-0.3343 (5)	0.8419 (5)	0.06096 (19)	0.030 (3)
C(16)	-0.3454 (5)	0.6789 (5)	0.07559 (20)	0.030 (3)
C(21)	-0.2542 (5)	0.3101 (5)	0.17275 (20)	0.031 (3)
C(22)	-0.3428 (6)	0.1846 (6)	0.17430 (22)	0.039 (3)
C(23)	-0.3159 (6)	0.0820 (6)	0.21658 (23)	0.045 (4)
Cl(23)	-0.42595 (19)	-0.07601 (18)	0.21875 (8)	0.0811 (13)
C(24)	-0.2036 (6)	0.1000 (6)	0.25873 (23)	0.044 (4)
C(25)	-0.1178 (5)	0.2247 (6)	0.25591 (20)	0.039 (3)
Cl(25)	0.03077 (17)	0.24906 (17)	0.30557 (6)	0.0554 (9)
C(26)	-0.1415 (6)	0.3310 (5)	0.21504 (19)	0.032 (3)
C(31)	-0.2732 (5)	0.9985 (5)	-0.01910 (21)	0.027 (3)
C(32)	-0.2543 (5)	1.0064 (5)	-0.07703 (21)	0.029 (3)
O(32)	-0.2422 (4)	0.8734 (4)	-0.10421 (14)	0.0473 (24)
C(3M)	-0.2165 (7)	0.8741 (6)	-0.16209 (22)	0.054 (4)
C(33)	-0.2520 (5)	1.1415 (5)	-0.10443 (21)	0.032 (3)
C(34)	-0.2680 (5)	1.2710 (5)	-0.07466 (22)	0.032 (3)
O(34)	-0.2553 (4)	1.4026 (4)	-0.10297 (15)	0.0412 (24)
C(35)	-0.2904 (5)	1.2673 (5)	-0.01818 (21)	0.032 (3)
C(36)	-0.2923 (5)	1.1300 (5)	0.00937 (20)	0.031 (3)
O(1W)	0.4307 (5)	0.3921 (4)	0.06999 (19)	0.051 (3)

r.m.s. deviations from the mean plane being 0.007 Å for ring 2 and 0.008 Å for ring 3; these planes are inclined at 58.7° to one another. The central guanidine group is also essentially planar, the r.m.s. deviation from the plane defined by C(1), N(2), N(3) and N(11) being 0.012 Å. This plane makes an angle of 55.5° with the planes of ring 2, cf. the torsion angle C(1)—N(3)—C(21)—C(26) of 43.6 (7)°. Coplanarity between ring 2 and the guanidine group would be prevented by the collision of H(2B) with H(26) (2.44 Å in the conformation found). A trisubstituted guanidine group can exist in two tautomeric forms:



the second is shown unambiguously by the structure. Two H atoms were located and refined on N(2): N(2)—H(2A) = 1.00 (5), N(2)—H(2B) = 0.83 (5) Å, and C(1)—N(3) is significantly shorter than C(1)—N(2) by 0.072 (8) Å. That this tautomer is also prevalent in solution is indicated by the fact that the <sup>1</sup>H NMR spectrum in *d*<sup>6</sup>-dimethyl sulfoxide solution shows a single broad resonance at δ = 5.8 p.p.m. That this single resonance is not the result of rapid exchange of the NH protons of the imine structure is suggested by the fact that other exchangeable protons present (phenolic OH, solvent water) give sepa-

Table 2. Selected distances (Å) and angles (°)

C(1)—N(2)	1.380 (6)	C(23)—Cl(23)	1.749 (6)
C(1)—N(3)	1.308 (6)	C(23)—C(24)	1.395 (8)
C(1)—N(11)	1.372 (6)	C(24)—C(25)	1.377 (8)
N(3)—C(21)	1.415 (6)	C(25)—Cl(25)	1.751 (5)
N(11)—C(12)	1.475 (6)	C(25)—C(26)	1.381 (7)
N(11)—C(16)	1.476 (6)	C(31)—C(32)	1.411 (7)
C(15)—N(14)	1.472 (6)	C(31)—C(36)	1.392 (7)
C(15)—C(16)	1.526 (7)	C(32)—O(32)	1.380 (6)
C(13)—N(14)	1.474 (6)	C(32)—C(33)	1.391 (7)
C(13)—C(12)	1.525 (7)	O(32)—C(3M)	1.420 (7)
N(14)—C(31)	1.443 (6)	C(33)—C(34)	1.388 (7)
C(21)—C(22)	1.396 (7)	C(34)—O(34)	1.382 (6)
C(21)—C(26)	1.403 (7)	C(34)—C(35)	1.381 (7)
C(22)—C(23)	1.386 (7)	C(35)—C(36)	1.411 (7)
N(2)—C(1)—N(3)	124.9 (4)	Cl(23)—C(23)—C(24)	117.7 (4)
N(2)—C(1)—N(11)	114.5 (4)	C(23)—C(24)—C(25)	116.6 (5)
N(3)—C(1)—N(11)	120.5 (4)	C(24)—C(25)—Cl(25)	118.8 (4)
C(1)—N(3)—C(21)	119.0 (4)	C(24)—C(25)—C(26)	123.1 (5)
C(1)—N(11)—C(12)	120.2 (4)	Cl(25)—C(25)—C(26)	118.1 (4)
C(1)—N(11)—C(16)	119.1 (4)	C(21)—C(26)—C(25)	119.3 (4)
C(12)—N(11)—C(16)	114.4 (4)	N(14)—C(31)—C(32)	117.6 (4)
N(14)—C(15)—C(16)	108.4 (4)	N(14)—C(31)—C(36)	124.7 (4)
N(14)—C(13)—C(12)	109.5 (4)	C(32)—C(31)—C(36)	117.7 (4)
C(15)—N(14)—C(13)	108.7 (3)	C(31)—C(32)—O(32)	115.9 (4)
C(15)—N(14)—C(31)	116.4 (4)	C(31)—C(32)—C(33)	121.0 (4)
C(13)—N(14)—C(31)	110.5 (4)	O(32)—C(32)—C(33)	123.0 (4)
N(11)—C(12)—C(13)	111.5 (4)	C(32)—O(32)—C(3M)	118.7 (4)
N(11)—C(16)—C(15)	111.2 (4)	C(32)—C(33)—C(34)	120.0 (4)
N(3)—C(21)—C(22)	118.6 (4)	C(33)—C(34)—O(34)	117.8 (4)
N(3)—C(21)—C(26)	122.4 (4)	C(33)—C(34)—C(35)	120.6 (4)
C(22)—C(21)—C(26)	118.9 (4)	O(34)—C(34)—C(35)	121.6 (4)
C(21)—C(22)—C(23)	119.6 (5)	C(34)—C(35)—C(36)	119.1 (4)
C(22)—C(23)—Cl(23)	120.0 (4)	C(31)—C(36)—C(35)	121.6 (4)
C(22)—C(23)—C(24)	122.4 (5)		

## Hydrogen-bond geometry

D	A	Symmetry	D—H	H...A	D...A
N(2)—H(2A)...O(34)		-x, 2-y, -z	1.00 (5)	2.12 (5)	3.102 (6)
N(2)—H(2B)...	(none)		0.83 (5)		
O(34)—H(34)...O(1W)		-x, 2-y, -z	0.95 (5)	1.67 (5)	2.605 (5)
O(1W)—H(1W)...N(14)		-x, 1-y, -z	0.74 (6)	2.49 (6)	3.193 (5)
	...O(32)	-x, 1-y, -z		2.65 (6)	3.094 (5)
O(1W)—H(2W)...N(3)		1+x, y, z	0.89 (5)	1.99 (5)	2.863 (6)

## C...C contacts shorter than 3.75 Å

C(16)...C(35)	-1-x, 2-y, -z	3.523 (7)
C(16)...C(34)	-1-x, 2-y, -z	3.529 (7)
C(15)...C(15)	-x, 1-y, -z	3.537 (7)
C(12)...C(35)	-1-x, 2-y, -z	3.623 (7)
C(1)...C(35)	x, -1+y, z	3.627 (7)
C(15)...C(34)	-x, 2-y, -z	3.681 (7)
C(12)...C(36)	-1-x, 2-y, -z	3.687 (7)
C(13)...C(35)	-x, 2-y, -z	3.713 (7)
C(13)...C(34)	-x, 2-y, -z	3.736 (7)

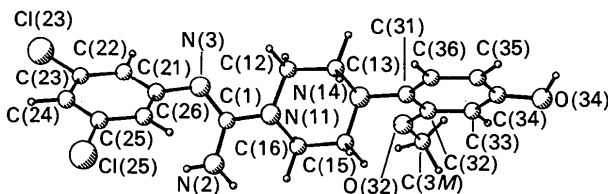


Fig. 1. View of the molecule, projected into the plane of the guanidine group, showing the numbering scheme.

rate discrete signals, implying slow exchange. The 5.8 p.p.m. peak is thus most likely due to the two NH<sub>2</sub> protons of the amine structure.

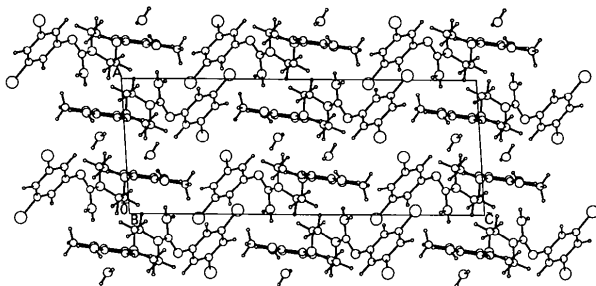


Fig. 2. View of the molecular packing along *b*.

The piperazine ring may be described as a 'half boat', significantly flattened toward N(11), as may be seen by the fact that the in-ring torsion angles involving N(14) but not N(11) average  $\pm 64.8^\circ$ , while those involving N(11) but not N(14) average  $\pm 48.3^\circ$ . In terms of the puckering parameters of Cremer & Pople (1975) (starting from either N atom and reducing  $\varphi$  and  $\theta$  to first quadrant angles):  $Q = 0.58 \text{ \AA}$ ,  $\varphi = 8.8^\circ$  and  $\theta = 32.4^\circ$ .

The molecular packing as viewed along the *b* axis is shown in Fig. 2. It is dominated by hydrogen bonding and ring stacking. The water molecule is central to the hydrogen bonding, being joined to

three different drug molecules. One of its donor bonds appears to be bifurcated, the H atom being equally directed toward N(14) and O(32) of the same molecule. These distances are summarized in Table 2, together with some of the close intermolecular C...C contacts. The main hydrophobic interactions involve atoms of ring 3 interacting with the piperazine ring of the molecules related to it by the inversion centres at  $\frac{1}{2}, 1, 0$  and  $0, 1, 0$ .

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## Methyl 4,6-*O*-Benzylidene-2-deoxy-2-*C*-(1,2:3,4-di-*O*-isopropylidene-*L*-glycero-*D*-galacto-hexopyranos-6-yl)- $\alpha$ -*D*-arabino-hexopyranosid-3-ulose Monohydrate

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**Abstract.**  $C_{26}H_{33}O_{11} \cdot H_2O$ ,  $M_r = 539.56$ , triclinic,  $P1$ ,  $a = 8.321(1)$ ,  $b = 7.154(1)$ ,  $c = 11.727(2) \text{ \AA}$ ,  $\alpha = 76.99(1)$ ,  $\beta = 78.91(1)$ ,  $\gamma = 79.01(1)^\circ$ ,  $V = 659(2) \text{ \AA}^3$ ,  $Z = 1$ ,  $D_x = 1.358(4) \text{ Mg m}^{-3}$ ,  $Cu K\alpha$ ,  $\lambda = 1.5418 \text{ \AA}$ ,  $\mu = 0.921 \text{ mm}^{-1}$ , room temperature. The refinement of all non-hydrogen-atom parameters yielded  $R = 0.041$  for 2144 reflections. The pyranoid rings of the *galacto* and *arabino* subunits have differ-

ent conformations: twist-boat ( ${}^2S_0$ ) and chair ( ${}^4C_1$ ), respectively. The hydroxyl group at the C(6') atom is involved in a hydrogen bond with one water molecule.

**Introduction.** As part of our studies on the conformation of sugars with one  $sp^2$ -hybridized C atom in the pyranoid ring by X-ray diffraction methods