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Structure of 8-Chloro-2-[(3-furoyl)aminomethyl]-1-methyl-5-phenyl-2,3-dihydro-1*H*-1,4-benzodiazepine Hydrochloride

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Abstract. $C_{22}H_{21}ClN_3O_2^+.Cl^-$, $M_r = 430{\cdot}33$, triclinic, $P\bar{1}$, $a = 9{\cdot}302$ (4), $b = 10{\cdot}840$ (3), $c = 11{\cdot}460$ (4) Å, $\alpha = 71{\cdot}99$ (3), $\beta = 78{\cdot}50$ (3), $\gamma = 72{\cdot}08$ (2)°, $V = 1038{\cdot}7$ (7) Å^3, $Z = 2$, $D_m = 1{\cdot}37$, $D_x = 1{\cdot}38$ Mg m^{-3}, graphite-monochromated Cu $K\alpha$ radiation, $\lambda = 1{\cdot}54178$ Å, $\mu = 3{\cdot}044$ mm^{-1}, $F(000) = 448$, $T = 293$ K. Final $R = 0{\cdot}036$ for 2234 unique observed reflections. The structure consists of molecules linked only by van der Waals forces. The seven-membered ring is in a boat conformation. The basic N of this ring and the amidic N form intramolecular hydrogen bonds to the chloride anion.

Introduction. The crystal and molecular structure of the title compound has been determined as part of a study of molecules with μ-opioid agonistic activity.

Experimental. Yellow crystals (from methanol–amyl alcohol), 0·3 × 0·3 × 0·5 mm. Density measured by flotation in *n*-heptane/CCl_4. Siemens AED2 diffractometer, cell parameters by least-squares refinement of the setting angles of 24 reflections with $20 < 2\theta < 25°$, ω/θ scan, $[(\sin\theta)/\lambda]_{\max} = 0{\cdot}5878$ Å^{-1}, $h = -11$ to 11, $k = -13$ to 13, $l = -13$ to 13. Intensities of three standard reflections monitored every hour showed only statistical fluctuations, 6963 reflections measured (3480 unique, $R_{\rm int} = 0{\cdot}053$), 2234 reflections with $I > 3\sigma(I)$, $S = 0{\cdot}106$. Data reduction with the Stoe & Co. (1985) *REDU*4 program, Lp corrections, no absorption correction. Scattering factors from Cromer & Mann (1968) and (for H) Stewart, Davidson & Simpson (1965). The structure was solved with *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) and refined on F with *XRAY*76 programs (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) by full-matrix least squares, first with isotropic temperature factors and finally anisotropically. H atoms were located in a difference synthesis and included in the refinement with the isotropic temperature factors of their parent atoms. The refinement converged to $R = 0{\cdot}036$ ($wR = 0{\cdot}047$). The weighting scheme was $w = (A + F + BF^2)^{-1}$ with $A = 20{\cdot}0$ and $B = 0{\cdot}02$. The average parameter shift during the final cycle was 0·028, the maximum parameter shift 0·13. Difference Fourier synthesis computed at this stage showed no significant features (min. and max. residual electron density −0·27 and 0·24 e Å^{-3}). All calculations performed by the *XRAY*76 system of programs and the program *PARST* (Nardelli, 1983*a*).

Discussion. Atomic coordinates and equivalent isotropic thermal parameters are given in Table 1.† The interatomic distances and angles are summarized in Table 2. The conformation is characterized by the torsion angles given in Table 2. A *PLUTO* plot (Motherwell & Clegg, 1978) of the molecule, with adopted numbering scheme, is shown in Fig. 1.

The seven-membered heterocyclic ring is in a boat conformation. The bow angle between the least-squares plane through N(1)—C(11)—N(9)—C(8) and the plane defined by C(11)—C(10)—N(9) is 60·2 (2)°. The stern angle between the basis plane and the least-squares plane defined by the atoms N(1)—C(2)—C(7)—C(8) is 21·2 (2)°. The two opposite N atoms in the basis plane are slightly twisted with respect to each other. As a consequence the group deviates from planarity [N(1) −0·036 (3), N(9) −0·054 (3) Å]. The ΔC_s displacement asymmetry parameter (Nardelli, 1983*b*) for the C(10) atom is 0·050 (1) indicating a symmetry plane through C(10) and the centre of the C(2)—C(7) bond.

The atoms in the phenyl ring [C(2)···C(7)] are slightly displaced from the least-squares plane. As in nitrazepam (Gilli, Bertolasi, Sacerdoti & Borea, 1977) and oxazepam (Gilli, Bertolasi, Sacerdoti & Borea, 1978*a*), where the atoms corresponding to N(1) and C(8) are in the plane of the chlorophenyl group, the title compound reveals a comparable deviation [N(1) 0·027 and C(8) 0·071 Å *versus* 0·031 and 0·067 Å respectively for oxazepam].

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† Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44767 (23 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters with e.s.d.'s of the refined parameters in parentheses*

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

	x	y	z	U_{eq}(Å^2 × 10^2)
N(1)	1642 (2)	4498 (2)	1665 (2)	4·41 (8)
C(2)	537 (3)	4594 (2)	2646 (2)	3·80 (11)
C(3)	541 (4)	3397 (3)	3621 (3)	4·93 (12)
C(4)	−511 (4)	3361 (3)	4628 (2)	5·17 (13)
C(5)	−1674 (4)	4481 (3)	4774 (3)	5·72 (13)
C(6)	−1730 (3)	5644 (3)	3852 (2)	4·81 (12)
C(7)	−671 (3)	5755 (2)	2778 (2)	3·79 (10)
C(8)	−984 (3)	7070 (2)	1890 (2)	3·50 (10)
N(9)	79 (2)	7539 (2)	1136 (2)	3·94 (8)
C(10)	1694 (3)	6883 (3)	1158 (3)	4·19 (11)
C(11)	2136 (3)	5614 (3)	733 (2)	4·09 (11)
C(12)	2608 (4)	3174 (3)	1565 (4)	5·93 (16)
Cl(13)	−398 (1)	1890·4 (9)	5810·7 (8)	7·62 (3)
C(14)	1566 (3)	5814 (3)	−487 (2)	5·57 (12)
N(15)	2127 (3)	6787 (3)	−1512 (2)	5·09 (11)
C(16)	3468 (3)	6442 (3)	−2195 (2)	4·84 (13)
O(17)	4397 (2)	5347 (2)	−1882 (2)	6·56 (11)
C(18)	3756 (4)	7461 (3)	−3353 (3)	5·46 (15)
C(19)	5125 (6)	7335 (5)	−4155 (4)	8·36 (22)
C(20)	4950 (6)	8389 (5)	−5113 (4)	9·25 (25)
O(21)	3509 (5)	9258 (3)	−4962 (2)	11·08 (18)
C(22)	2809 (5)	8637 (4)	−3873 (3)	7·51 (20)
Cl(23)	−538·1 (9)	9440·7 (8)	−1459·9 (7)	5·43 (2)
C(1′)	−2539 (3)	7963 (2)	1810 (2)	3·77 (10)
C(2′)	−2762 (3)	9343 (3)	1623 (2)	4·69 (12)
C(3′)	−4197 (4)	10202 (3)	1527 (3)	5·78 (15)
C(4′)	−5415 (4)	9719 (4)	1596 (3)	6·36 (16)
C(5′)	−5214 (4)	8363 (4)	1778 (3)	5·94 (16)
C(6′)	−3785 (3)	7483 (3)	1888 (3)	4·86 (13)

Table 2. *Bond lengths* (Å), *bond angles* (°) *and selected torsion angles* (°)

N(1)—C(2)	1·369 (3)	C(14)—N(15)	1·446 (4)
N(1)—C(11)	1·471 (3)	N(15)—C(16)	1·347 (4)
N(1)—C(12)	1·465 (4)	C(16)—O(17)	1·230 (3)
C(2)—C(3)	1·426 (3)	C(16)—C(18)	1·479 (4)
C(2)—C(7)	1·432 (3)	C(18)—C(19)	1·411 (6)
C(3)—C(4)	1·356 (4)	C(18)—C(22)	1·343 (5)
C(4)—C(5)	1·384 (4)	C(19)—C(20)	1·311 (6)
C(4)—Cl(13)	1·734 (3)	C(20)—O(21)	1·394 (6)
C(5)—C(6)	1·367 (4)	C(21)—C(22)	1·364 (5)
C(6)—C(7)	1·414 (4)	C(1′)—C(2′)	1·399 (4)
C(7)—C(8)	1·455 (3)	C(1′)—C(6′)	1·387 (5)
C(8)—N(9)	1·297 (3)	C(2′)—C(3′)	1·375 (4)
C(8)—C(1′)	1·475 (3)	C(3′)—C(4′)	1·367 (6)
N(9)—C(10)	1·452 (3)	C(4′)—C(5′)	1·377 (6)
C(10)—C(11)	1·511 (5)	C(5′)—C(6′)	1·380 (4)
C(11)—C(14)	1·525 (5)		

C(2)—N(1)—C(11)	126·8 (2)	C(10)—C(11)—C(14)	113·4 (2)
C(2)—N(1)—C(12)	119·8 (2)	C(11)—C(14)—N(15)	114·1 (3)
C(11)—N(1)—C(12)	112·9 (2)	C(14)—N(15)—C(16)	121·8 (2)
N(1)—C(2)—C(3)	116·9 (2)	N(15)—C(16)—O(17)	122·3 (2)
N(1)—C(2)—C(7)	127·1 (2)	N(15)—C(16)—C(18)	115·8 (2)
C(3)—C(2)—C(7)	116·0 (2)	O(17)—C(16)—C(18)	121·9 (2)
C(2)—C(3)—C(4)	122·3 (2)	C(16)—C(18)—C(19)	124·7 (3)
C(3)—C(4)—C(5)	122·3 (2)	C(16)—C(18)—C(22)	128·8 (3)
C(3)—C(4)—Cl(13)	120·0 (2)	C(19)—C(18)—C(22)	106·5 (3)
C(5)—C(4)—Cl(13)	117·7 (2)	C(18)—C(19)—C(20)	108·0 (4)
C(4)—C(5)—C(6)	117·2 (2)	C(19)—C(20)—O(21)	109·7 (4)
C(5)—C(6)—C(7)	123·5 (2)	C(20)—O(21)—C(22)	105·7 (3)
C(2)—C(7)—C(6)	118·7 (2)	C(18)—C(22)—O(21)	110·0 (3)
C(2)—C(7)—C(8)	126·9 (2)	C(8)—C(1′)—C(2′)	119·0 (3)
C(6)—C(7)—C(8)	114·4 (2)	C(8)—C(1′)—C(6′)	122·2 (2)
C(7)—C(8)—N(9)	122·5 (2)	C(2′)—C(1′)—C(6′)	118·9 (2)
C(7)—C(8)—C(1′)	121·7 (2)	C(1′)—C(2′)—C(3′)	120·3 (3)
N(9)—C(8)—C(1′)	115·9 (2)	C(2′)—C(3′)—C(4′)	120·3 (3)
C(8)—N(9)—C(10)	124·3 (3)	C(3′)—C(4′)—C(5′)	120·1 (3)
N(9)—C(10)—C(11)	111·7 (3)	C(4′)—C(5′)—C(6′)	120·5 (4)
N(1)—C(11)—C(10)	112·7 (2)	C(1′)—C(6′)—C(5′)	120·0 (3)
N(1)—C(11)—C(14)	109·2 (3)		

C(2)—N(1)—C(11)—C(10)	19·2 (5)	C(2)—N(1)—C(11)—C(14)	−107·7 (4)
C(3)—C(2)—N(1)—C(12)	9·2 (5)	N(1)—C(11)—C(14)—N(15)	−173·4 (3)
C(11)—C(10)—N(9)—C(8)	−70·1 (4)	C(11)—C(14)—N(15)—C(16)	86·4 (4)
N(1)—C(11)—C(10)—N(9)	−74·4 (4)	C(14)—N(15)—C(16)—O(17)	−11·6 (6)
C(10)—N(9)—C(8)—C(7)	−5·8 (5)	C(14)—N(15)—C(16)—C(18)	168·2 (3)
N(9)—C(8)—C(7)—C(2)	−30·1 (5)	C(2)—C(7)—C(8)—C(1′)	151·0 (3)
C(7)—C(2)—N(1)—C(11)	20·7 (6)		

The N(1)—C(2) bond is shorter than the C(sp^2)—N(sp^2) single bond in aromatic amines [*e.g.* dimethylaniline: 1·43 Å (see Vilkov, Mastryukov & Sadova, 1983)] corresponding to an increased electron delocalization between the amine and the chlorophenyl group. The C(7)(sp^2)—C(8)(sp^2) bond is 0·3 Å shorter than that reported by Burke-Laing & Laing (1976) and has a bond order of slightly greater than one. In agreement with the valence-shell electron-pair repulsion (VSEPR) theory (Gillespie, 1972), protonation of the N(9) atom causes a widening of the C(8)—N(9)—C(10) angle to 124·3 (3)° as compared with 116·2 (3)° for the non-protonated form in medazepam (Gilli, Bertolasi, Sacerdoti & Borea, 1978*b*). Other bond lengths are in accordance with the expected normal values. The C(2)···C(7) phenyl group deviates significantly from planarity ($\chi^2_{0.95,3} = 9{\cdot}64$). Atom displacements from the least-squares plane are in the range 0·001 to 0·007 Å for C(2)···C(7). The effect of the substituents on the ring geometry can be explained using the geometrical parameters for benzene derivatives described by Domenicano & Murray-Rust (1979). Superimposing the effect of an NMe_2 group on C(2) with the effect of a CH=N*R* group on C(7) and a Cl at C(4) the following endocyclic angles are calculated: at C(2) 118·6; C(3) 119·6; C(4) 122·8; C(5) 117·3; C(6) 122·4 and C(7) 119·2°. A comparison with the experimental values from Table 2 shows a correspondence in the deviation from 120°, except for the C(3) atom. Exactly matching values are not expected since the diazepine ring determines the rotation about the C—*X* bond at C(2) and C(7), affecting the extent of conjugation and consequently the calculated ring geometry. The averaged values for C—C distances and angles are 1·39 (3) Å and 120 (3)° respectively and are considered normal but the individual values in this part of the molecule are affected by a high vibrational disorder.

The other benzene ring C(1′)···C(6′) does not deviate significantly from planarity ($\chi^2_{0.95,3} = 3{\cdot}67$). The position of the ring is described by the torsion angle C(7)—C(8)—C(1′)—C(6′) which is −41·6 (5)°. The angle between the least-squares planes through C(2)···C(7) and C(1′)···C(6′) is 58·3 (1)°. Bond distances and angles in the aromatic ring C(1′)···C(6′) are comparable [average C—C distance: 1·38 (1) Å; angles: 120 (6)°] with the standard values for substituted benzene. The C(8)(sp^2)—C(1′)(sp^2) bond length is 1·475 (4) Å. Because the torsion angle N(9)—C(8)—C(1′)—C(2′) equals −39·1 (5)°, partial conjugation exists but the bond is mainly a single bond. Owing to substitution the endocyclic angle at C(1′) becomes 1·1° smaller [1·2° predicted for a CH=N*R* substitution (Domenicano & Murray-Rust, 1979)]. For the angles at C(4′) and C(6′) these predictions are rather unsuccessful, as might be expected on account of the large librational motion. The apparent shortening of the bond length in the benzene ring is greatest for the C(3′)—C(4′) bond because these atoms are most affected by thermal motion. The sp^2-hybridized N(15) atom (bond-angle sum 359°) has its smallest angle opposite the N—CO bond. The N(15)—C(14) bond length [1·446 (4) Å] is comparable to the C—N length found in dimethylamine [1·456 (2) Å; Beagley & Hewitt, 1986]. The carbonyl oxygen O(17) is close to the furan ring plane [torsion angle: O(17)—C(16)—C(18)—C(19) = 4·6°]. The C(16)—O(17) bond length [1·230 (3) Å] compares well with the generally accepted double-bond value 1·23 (1) Å (Kennard, 1968). The bond angles around C(16) do not differ from those of other amides of organic acids [*N*-methylacetamide: N—C—C = 114·1 (1), N—C—O = 121·8 (4)°; Kitano & Kuchitsu, 1974]. The C(16)—C(18) distance corresponds to a C(sp^2)—C(sp^2) bond distance (1·48 Å) as described by Burke-Laing & Laing (1976). The furan ring is expected to be planar but deviates significantly from planarity ($\chi^2_{0.95,2} = 11{\cdot}8$). The bond distances are normal compared with the expected values [microwave data (Vilkov, Mastryukov & Sadova, 1983): C—C = 1·361 (1), 1·431 (2); C—O = 1·362 (1) Å, C—O—C = 106·5 (1)°]. The values of the displacement factors in the *xy* plane increase gradually from the atom C(18) towards O(21) reflecting a great deal of librational motion. The non-planarity could be due to this fact.

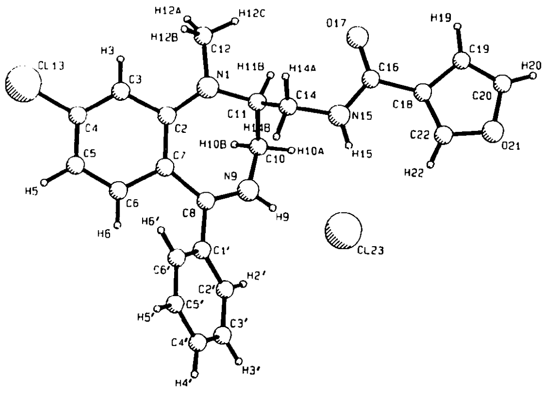

Fig. 1. Perspective view (*PLUTO*78; Motherwell & Clegg, 1978) of the molecule.

The molecules are held together by normal van der Waals forces. The basic N of the diazepine ring and the amidic N form intramolecular hydrogen bonds to the chloride anion with distances and angles: N(9)—Cl(23) 3·096 (3), H(9)—Cl(23) 2·29 (3) Å; N(9)—H(9)—Cl(23) 156 (3)°; N(15)—Cl(23) 3·175 (3), H(15)—Cl(23) 2·35 (3) Å; N(15)—H(15)—Cl(23) 157 (3)°. No intermolecular hydrogen bonds are found. Except for the short H(6′)···O(17) (−*x*, −*y* + 1, −*z*) = 2·45 (4) Å distance, other short molecular contacts conform to normal van der Waals distances.

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