performed for the free organic ion. The results are similar to those obtained for the protonated clonidine (Byre *et al.*, 1976), the main part of the positive charge (+0·44) being situated on the central C atom of the guanidine function and on the two H atoms of the N—H groups (+0·17). The net charge on C(14) is +0·26 and on O(16) −0·25. Identical results were found for both molecules.

In order to see if the crystalline conformation is also found in vacuum, PCILO calculations (Pullman, 1971) were performed for the free-base state. The two possible tautomeric forms were considered: imino form (with the C=N double bond exocyclic) and amino form (with the C=N double bond endocyclic). The study consisted of constructing the conformational-energy curve (i) by varying the torsion angle C(6)–C(1)–N(7)–C(8) and (ii) by varying at the same time the torsion angles C(6)–C(1)–N(7)–C(8) and C(1)–N(7)–C(8)–C(9). In the first case, two energy minima were found. The first one corresponds to a conformation close to the crystal conformation (angle variation $\simeq -20°$) and the energy was taken as zero; the second one corresponds to an angle variation of $-300°$ with $E = 3{\cdot}3$ kJ mol^{-1}, the related arrangement of the rings being nearly planar: C(6)–C(1)–N(7)–C(8) = −8 (1)°. In the second case, a strong barrier of energy impedes the rotation of the two torsion angles at the same time.

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Structure of *cis*-*N*-(1-Benzyl-2-methyl-3-pyrrolidinyl)-5-chloro-2-methoxybenzamide*

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Abstract. $C_{20}H_{23}ClN_2O_2$, $M_r = 358{\cdot}87$, monoclinic, $P2_1/n$, $a = 16{\cdot}68$ (1), $b = 11{\cdot}94$ (2), $c = 9{\cdot}324$ (5) Å, $\beta = 92{\cdot}82$ (5)°, $V = 1855$ (3) Å^3, $Z = 4$, $D_x = 1{\cdot}285$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, $\mu = 3{\cdot}35$ cm^{-1}, $F(000) = 760$, $T = 298$ K, $R = 0{\cdot}055$ for 3042 observed reflections with $|F_o| > 3\sigma(|F_o|)$. An intramolecular H bond between the amide N and the methoxy O is observed. The torsion angles of the title compound, a weak dopamine antagonist, are almost identical to those of its potent analogue, YM-09151-2, except for the angle around the N(amide) and C(pyrrolidine) bonds. Furthermore, two geometrical parameters relevant to the estimation of the neuroleptic activity are almost the same as those of YM-09151-2. The significant structural difference is the lack of contribution from the quinonoidal resonance form, owing to the absence of the amino group in the benzamide moiety.

Introduction. The crystal-structure determination of the title compound (1) was undertaken as part of serial studies for finding new potent neuroleptic drugs in

* New Potent Neuroleptic Drugs of Benzamide Derivatives. Part IV.

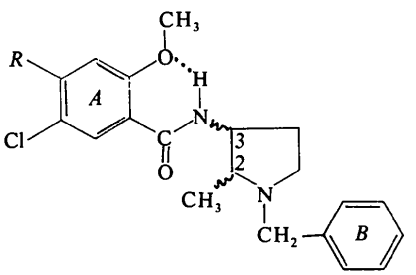
0108-2701/86/081071-03$01.50

Table 1. *Fractional coordinates and isotropic temperature factors*

The B_{eq} values accompanied by ⟨⟩ are the equivalent isotropic temperature factors calculated from anisotropic thermal parameters using the equation $B_{eq} = 8\pi^2(U_1 + U_2 + U_3)/3$, where U_1, U_2, and U_3 are principal components of the mean-square displacement matrix **U**. Values in ⟨⟩ are anisotropicity defined by $[\sum(B_{eq} - 8\pi^2U_i)^2/3]^{1/2}$ and those in () are e.s.d.'s; they refer to last decimal places.

	x	y	z	B_{eq}(Å^2)
Cl	0·84266 (3)	0·20316 (5)	0·71380 (6)	7·38 ⟨270⟩
O(1)	1·16172 (7)	0·0698 (1)	0·5360 (1)	5·25 ⟨164⟩
O(2)	1·09274 (9)	0·0067 (1)	0·9500 (2)	5·52 ⟨210⟩
N(1)	1·18535 (9)	−0·0290 (1)	0·7913 (2)	4·35 ⟨111⟩
N(2)	1·35694 (9)	−0·0407 (1)	0·7898 (2)	4·24 ⟨34⟩
C(1)	0·95738 (7)	0·1837 (1)	0·5217 (1)	5·22 ⟨127⟩
C(2)	0·9365 (1)	0·1609 (1)	0·6592 (2)	4·77 ⟨93⟩
C(3)	0·9888 (1)	0·1064 (2)	0·7544 (2)	4·21 ⟨42⟩
C(4)	1·0645 (1)	0·0746 (1)	0·7132 (2)	3·71 ⟨44⟩
C(5)	1·08637 (9)	0·0997 (1)	0·5735 (2)	4·03 ⟨31⟩
C(6)	1·03208 (8)	0·1531 (1)	0·4787 (1)	4·89 ⟨71⟩
C(7)	1·1873 (1)	0·0998 (1)	0·3970 (2)	6·49 ⟨218⟩
C(8)	1·11579 (7)	0·0153 (1)	0·8277 (1)	3·91 ⟨60⟩
C(9)	1·2393 (1)	−0·0860 (2)	0·8940 (2)	4·6 ⟨12⟩
C(10)	1·3073 (1)	−0·1387 (2)	0·8160 (2)	4·75 ⟨82⟩
C(11)	1·2834 (1)	−0·2046 (2)	0·6831 (2)	6·0 ⟨15⟩
C(12)	1·3633 (1)	0·0178 (2)	0·9289 (2)	5·97 ⟨157⟩
C(13)	1·2838 (1)	−0·0022 (1)	0·9970 (2)	5·42 ⟨123⟩
C(14)	1·4352 (1)	−0·0639 (1)	0·7330 (2)	4·90 ⟨87⟩
C(15)	1·4780 (1)	0·0416 (2)	0·6912 (2)	4·4 ⟨4⟩
C(16)	1·4364 (1)	0·1356 (2)	0·6418 (2)	5·5 ⟨11⟩
C(17)	1·4764 (1)	0·2313 (2)	0·6017 (2)	6·3 ⟨20⟩
C(18)	1·5582 (1)	0·2342 (2)	0·6096 (2)	6·4 ⟨27⟩
C(19)	1·6006 (1)	0·1414 (2)	0·6578 (2)	6·4 ⟨24⟩
C(20)	1·5607 (1)	0·0459 (2)	0·6987 (2)	5·1 ⟨11⟩

benzamide derivatives. In the previous reports (Furuya, Iwanami, Takenaka & Sasada, 1982, 1985, 1986), the crystal structures of both active and inactive compounds having the amino or methylamino group in the *para* position of benzamide have been determined. The present compound lacks an amino group in that position and has weak neuroleptic activity.



(2*R*,3*R*) and (2*S*,3*S*)

(1) (*R* = H)
YM-09151-2 (*R* = $NHCH_3$)

Experimental. Colorless plates obtained from a methanol solution; crystal size, 0·5 × 0·3 × 0·4 mm; Rigaku automated four-circle diffractometer AFC-5R, graphite-monochromated Mo $K\alpha$ radiation (λ = 0·71073 Å). Accurate cell constants determined using 20 high-angle reflections in range $20 < 2\theta < 30°$. Intensities measured for $2 < 2\theta < 55°$, $-21 \le h \le 21$, $0 \le k \le 15$, $0 \le l \le 12$, θ–2θ scan mode, scanning rate 8° (2θ) min^{-1}. Five reference reflections showed no significant intensity deterioration. 3878 independent reflections, 836 reflections with $|F_o| < 3\sigma(|F_o|)$ considered unobserved. Corrections for Lorentz and polarization factors, but not for absorption and secondary extinction. Standard deviations $\sigma^2(|F_o|) = \sigma_p^2(|F_o|) + q^2|F_o|^2$, where $\sigma_p(|F_o|)$ evaluated by counting statistics and q (4·13 × 10^{-3}) derived from variations of monitored reflections (McCandlish, Stout & Andrews, 1975).

Structure solved by direct methods, *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), and block-diagonal least squares. All H atoms found on a difference map, refined isotropically. $\sum w(|F_o| - |F_c|)^2$ minimized, with $w = 1/\sigma(|F_o|)$. Final $R = 0·055$ ($wR = 0·043$); maximum shifts of parameters 0·02σ for C, 0·03σ for N, 0·003σ for O, 0·001σ for Cl and 0·1σ for H atoms. $\Delta\rho_{max} = 0·32$, $\Delta\rho_{min} = -0·33$ e Å^{-3}. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974). Computations performed on a Digital VAX-11/785 computer.

Discussion. Final atomic parameters for non-H atoms are given in Table 1.* The molecular and crystal structures are shown in Figs. 1 and 2, respectively. The bond lengths and angles are listed in Table 2. The C(4)–C(8) length [1·511 (2) Å] is appreciably longer than the corresponding one in previously reported active compounds, YM-09151-2 [1·488 (4) Å] (Furuya *et al.*, 1982), YM-09151-1 [1·489 (12) and 1·494 (10) Å] (Furuya *et al.*, 1986). There are no unusual bond lengths in benzene ring *A* [C(1)–C(6)]. Ring *A* is almost planar with a maximum atomic deviation of 0·009 Å. The methoxy and carbamoyl groups also lie in the plane.

An intramolecular H bond between the amide N(1) and methoxy O(1) results in a six-membered ring fused with benzene ring *A*. This type of H bond is also observed in the benzamide neuroleptics. The N(1)···O(1) length, 2·668 (2) Å, is shorter than in YM-09151-2 [2·680 (3) Å] (Furuya *et al.*, 1982), and metoclopramide [2·683 (6) Å] (Cesario, Pascard, Moukhtari & Jung, 1981). Thus, the benzamide moiety constitutes a rigid part of the molecule as a result of this strong H bond. Benzene ring *B* [C(15)–C(20)] is planar

* Lists of structure factors, anisotropic thermal parameters of non-H atoms, parameters of H atoms, bond lengths and angles involving H atoms, and least-squares planes for the two benzene rings *A* and *B* have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42875 (27 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

with a maximum atomic deviation of 0·003 Å. The bond lengths in ring *B* are shorter than 1·395 Å, the standard C–C bond length in aromatic compounds, probably due to the rather large thermal motions.

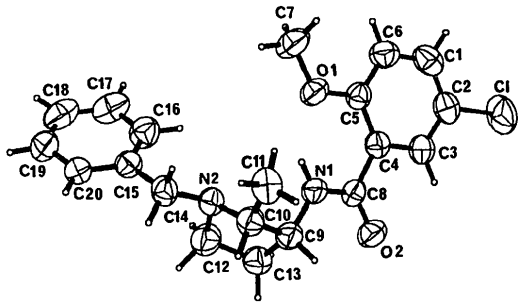


Fig. 1. Molecular structure and atom numbering.

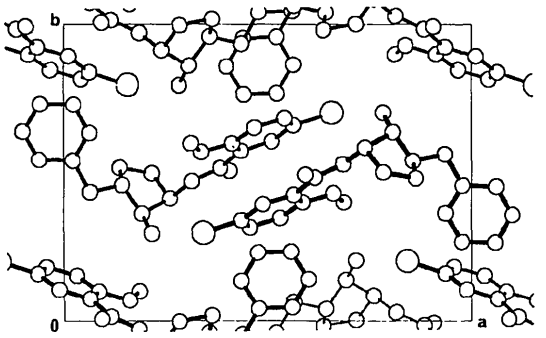


Fig. 2. Projection of the structure on the *ab* plane.

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

Standard deviations are given in parentheses.

Cl–C(2)	1·743 (2)	O(1)–C(5)	1·368 (2)	O(1)–C(7)	1·431 (2)
O(2)–C(8)	1·226 (2)	N(1)–C(8)	1·334 (2)	N(1)–C(9)	1·450 (2)
N(2)–C(10)	1·461 (2)	N(2)–C(12)	1·473 (2)	N(2)–C(14)	1·459 (2)
C(1)–C(2)	1·373 (2)	C(1)–C(6)	1·377 (3)	C(2)–C(3)	1·377 (2)
C(3)–C(4)	1·390 (2)	C(4)–C(5)	1·402 (2)	C(4)–C(8)	1·511 (2)
C(5)–C(6)	1·389 (2)	C(9)–C(10)	1·514 (2)	C(9)–C(13)	1·550 (2)
C(10)–C(11)	1·506 (3)	C(12)–C(13)	1·517 (3)	C(14)–C(15)	1·509 (2)
C(15)–C(16)	1·387 (2)	C(15)–C(20)	1·377 (2)	C(16)–C(17)	1·384 (3)
C(17)–C(18)	1·362 (3)	C(18)–C(19)	1·378 (3)	C(19)–C(20)	1·384 (3)

C(5)–O(1)–C(7)	119·0 (1)	C(8)–N(1)–C(9)	122·5 (1)
C(10)–N(2)–C(12)	104·4 (1)	C(10)–N(2)–C(14)	115·6 (1)
C(12)–N(2)–C(14)	112·5 (1)	C(2)–C(1)–C(6)	119·6 (2)
Cl–C(2)–C(1)	119·2 (1)	Cl–C(2)–C(3)	119·9 (1)
C(1)–C(2)–C(3)	120·9 (2)	C(2)–C(3)–C(4)	120·4 (1)
C(3)–C(4)–C(5)	118·7 (1)	C(3)–C(4)–C(8)	115·0 (1)
C(5)–C(4)–C(8)	126·3 (1)	O(1)–C(5)–C(4)	117·7 (1)
O(1)–C(5)–C(6)	122·4 (1)	C(4)–C(5)–C(6)	119·9 (1)
C(1)–C(6)–C(5)	120·5 (2)	O(2)–C(8)–N(1)	121·4 (1)
O(2)–C(8)–C(4)	120·3 (1)	N(1)–C(8)–C(4)	118·4 (1)
N(1)–C(9)–C(10)	109·5 (1)	N(1)–C(9)–C(13)	111·7 (1)
C(10)–C(9)–C(13)	102·6 (1)	N(2)–C(10)–C(9)	101·0 (1)
N(2)–C(10)–C(11)	114·2 (1)	C(9)–C(10)–C(11)	115·9 (1)
N(2)–C(12)–C(13)	105·5 (1)	C(9)–C(13)–C(12)	104·1 (1)
N(2)–C(14)–C(15)	112·2 (1)	C(14)–C(15)–C(16)	121·7 (2)
C(14)–C(15)–C(20)	120·2 (2)	C(16)–C(15)–C(20)	118·1 (2)
C(15)–C(16)–C(17)	121·1 (2)	C(16)–C(17)–C(18)	120·1 (2)
C(17)–C(18)–C(19)	119·6 (2)	C(18)–C(19)–C(20)	120·4 (2)
C(15)–C(20)–C(19)	120·7 (2)		

Table 3. *Selected torsion angles* (°)

	Present molecule	YM-09151-2
C(7)–O(1)–C(5)–C(4)	183·4 (2)	176·4 (2)
C(7)–O(1)–C(5)–C(6)	3·5 (2)	357·5 (4)
C(3)–C(4)–C(8)–N(1)	172·4 (1)	181·9 (2)
C(5)–C(4)–C(8)–N(1)	352·3 (2)	0·2 (4)
C(4)–C(8)–N(1)–C(9)	179·0 (1)	174·8 (4)
C(8)–N(1)–C(9)–C(10)	173·1 (2)	111·1 (3)
C(8)–N(1)–C(9)–C(13)	286·0 (2)	225·3 (3)
N(1)–C(9)–C(10)–N(2)	76·7 (2)	75·7 (3)
N(1)–C(9)–C(10)–C(11)	312·7 (2)	312·5 (3)
N(1)–C(9)–C(13)–C(12)	264·5 (2)	264·1 (2)
C(9)–C(10)–N(2)–C(12)	47·3 (2)	48·3 (3)
C(9)–C(10)–N(2)–C(14)	171·5 (1)	172·7 (2)
C(9)–C(13)–C(12)–N(2)	6·4 (2)	6·0 (3)
C(10)–N(2)–C(12)–C(13)	326·4 (2)	326·5 (3)
C(10)–N(2)–C(14)–C(15)	172·7 (1)	172·0 (2)
C(11)–C(10)–N(2)–C(14)	296·7 (2)	297·1 (3)
N(2)–C(14)–C(15)–C(16)	329·0 (2)	325·6 (4)
N(2)–C(14)–C(15)–C(20)	150·3 (2)	150·3 (3)
C(12)–N(2)–C(10)–C(11)	172·5 (2)	172·7 (3)
C(12)–C(13)–C(9)–C(10)	21·6 (2)	22·3 (3)
C(12)–N(2)–C(14)–C(15)	292·5 (2)	292·7 (3)
C(13)–C(9)–C(10)–C(11)	194·0 (2)	193·8 (3)
C(13)–C(9)–C(10)–N(2)	318·0 (2)	317·0 (3)
C(13)–C(12)–N(2)–C(14)	200·2 (1)	200·0 (2)

Table 3 shows selected torsion angles of the present molecule and YM-09151-2 (Furuya *et al.*, 1982). They are almost identical to each other except for those around N(1)–C(9). This suggests that the two molecules are approximately superimposable on each other if the torsion angle C(8)–N(1)–C(9)–C(10) is altered from 173 to 111°. Furthermore, two geometrical parameters, the distance between the center of benzene ring *A* and the tertiary amino N atom and the deviation of this N atom from the ring *A* plane (6·25 and 0·07 Å, respectively), are almost the same as those of YM-09151-2 (6·26 and 0·09 Å, respectively). The significant difference is the lack of contribution from the quinonoidal form, owing to the absence of the amino group. Therefore, the resonance structure of the benzamide moiety might have some relation to the neuroleptic activity.

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