The Structure of 2-{3-[4-(*m*-Chlorophenyl)-1-piperazinyl]propyl}-*s*-triazolo-[4,3-*a*]pyridin-3(2*H*)-one Hydrochloride, Trazodone Hydrochloride

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Abstract. $C_{19}H_{22}ClN_5O \cdot HCl$, $M_r = 408 \cdot 33$, monoclinic, $P2_1/c$, $a = 16 \cdot 866$ (3), $b = 10 \cdot 660$ (2), $c = 11 \cdot 230$ (2) Å, $\beta = 93 \cdot 04$ (1)°, $D_m = 1 \cdot 344$, $D_c = 1 \cdot 345$ Mg m^{-3}, $Z = 4$, $T = 298$ (1) K, Mo $K\alpha_1$ ($\lambda = 0 \cdot 70926$ Å). Intensities of 3017 reflections were measured on an Oak Ridge computer-controlled diffractometer and the structure was solved by direct methods. Full-matrix and block-diagonal least-squares refinement yielded an R value of $0 \cdot 042$. The propylene side chain of the molecule is nearly fully extended while the protonated N of the piperazine ring is hydrogen-bonded to the Cl ion ($N \cdots Cl = 3 \cdot 05$ Å).

Introduction. Trazodone hydrochloride is a psychoactive drug showing a therapeutic effect in several pathological conditions, including anxiety and endogenous depression (Antonelli, DeGregorio & Dionisio, 1973). It shares with the phenothiazines a strong antiserotonin effect and the capacity to inhibit the response to painful and unpleasant stimuli (Silvestrini & Quadri, 1970). Trazodone has also been found to stimulate dopamine synthesis, while not producing any cataleptogenic effects characteristic of other neuroleptics (Stefanini, Fadda, Porceddu & Gessa, 1976). Therefore, it is of interest to compare the three-dimensional conformation of trazodone with other neuroleptic drugs.

A sample of trazodone.HCl was supplied by Angelini Francesco, ACR, Italy and recrystallized from methanol. A clear rectangular plate of dimensions $0 \cdot 65 \times 0 \cdot 35 \times 0 \cdot 15$ mm was used in the diffraction study. Weissenberg and precession photographs indicated the space group to be $P2_1/c$. Accurate cell dimensions (see *Abstract*) were obtained by least-squares refinement of the observed setting angles for ten Mo $K\alpha_1$ reflections ($\lambda = 0 \cdot 70926$ Å) (Busing, Ellison, Levy, King & Roseberry, 1968). The intensities of 4625 unique reflections with $\sin \theta / \lambda < 0 \cdot 6$ Å^{-1} were measured with the θ–2θ scan technique on an Oak Ridge computer-controlled diffractometer using Nb-filtered Mo $K\alpha$ ($\lambda = 0 \cdot 71069$ Å) radiation. Of these, 3017 reflections had intensities greater than $3 \cdot 0\sigma(I)$. Absorption corrections were not applied ($\mu = 0 \cdot 343$ mm^{-1}), while an isotropic extinction correction was

applied during refinement (Larson, 1967). Each intensity was assigned a variance $\sigma^2(I)$ based on counting statistics plus a term $(0 \cdot 04I)^2$, where I is the net intensity.

The structure was solved by *MULTAN* (Germain, Main & Woolfson, 1971) using 499 normalized structure factors ($|E| > 1 \cdot 60$). The largest absolute figure of merit ($1 \cdot 15$) indicated the correct solution. Full-matrix and block-diagonal least-squares refinement of the positional parameters, anisotropic thermal parameters for the non-hydrogen atoms and isotropic for the H atoms gave a final R value of $0 \cdot 042$. The standard deviation of an observation of unit weight, defined as $[\sum w|\Delta F|^2/(n-p)]^{1/2}$, where n is the number of observations and p is the number of adjusted parameters, was $1 \cdot 75$. The largest parameter shift during the last cycle of refinement was less than 30% of the estimated standard deviation, and the largest peak, $0 \cdot 46$ e Å^{-3}, in the final difference map was associated with Cl(1).

Scattering factors for the non-hydrogen atoms were taken from Cromer & Mann (1968) and for the H atoms from Stewart, Davidson & Simpson (1965). Values for the real and imaginary parts of the dispersion correction of the atomic scattering factor for Cl were taken from Cromer (1965). All refinement was done with the XRAY system (Stewart, Kruger, Ammon, Dickinson & Hall, 1972). The final atomic parameters for the non-hydrogen atoms along with their standard deviations estimated from the inverse of the normal-equations matrix are given in Table 1.*

Discussion. A perspective drawing of the molecule, including bond distances and angles, is shown in Fig. 1. Least-squares planes were calculated through the triazolo–pyridinone (TPN) nucleus, the C atoms of the

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Table 1. *Fractional atomic coordinates for non-hydrogen atoms* (× 10⁴)

|	x	y	z
C(1)	2253 (1)	8241 (2)	6267 (2)
N(2)	1893 (1)	7587 (2)	5362 (2)
N(3)	2033 (1)	6307 (2)	5411 (2)
C(4)	2830 (2)	5075 (2)	6912 (3)
C(5)	3282 (1)	5190 (3)	7928 (3)
C(6)	3418 (1)	6375 (3)	8480 (2)
C(7)	3110 (2)	7421 (3)	7987 (2)
N(8)	2651 (1)	7310 (2)	6934 (2)
C(9)	2493 (1)	6172 (2)	6378 (2)
C(10)	1359 (1)	8123 (2)	4442 (2)
C(11)	534 (1)	8374 (2)	4865 (2)
C(12)	123 (1)	7170 (2)	5187 (2)
N(13)	−695 (1)	7374 (1)	5601 (1)
C(14)	−1031 (1)	6151 (2)	5977 (2)
C(15)	−1846 (1)	6300 (2)	6427 (2)
N(16)	−2385 (1)	6887 (2)	5539 (2)
C(17)	−2074 (1)	8092 (2)	5152 (2)
C(18)	−1258 (1)	7949 (2)	4683 (2)
C(19)	−3203 (1)	6791 (2)	5713 (2)
C(20)	−3761 (2)	7367 (3)	4933 (3)
C(21)	−4561 (2)	7178 (4)	5054 (4)
C(22)	−4844 (2)	6442 (4)	5949 (4)
C(23)	−4294 (2)	5895 (3)	6716 (3)
C(24)	−3486 (1)	6061 (2)	6625 (2)
O(1)	2244 (1)	9367 (2)	6468 (2)
Cl(1)	9382 (0)	9406 (1)	7519 (0)
Cl(2)	−4610 (0)	4930 (1)	7855 (1)
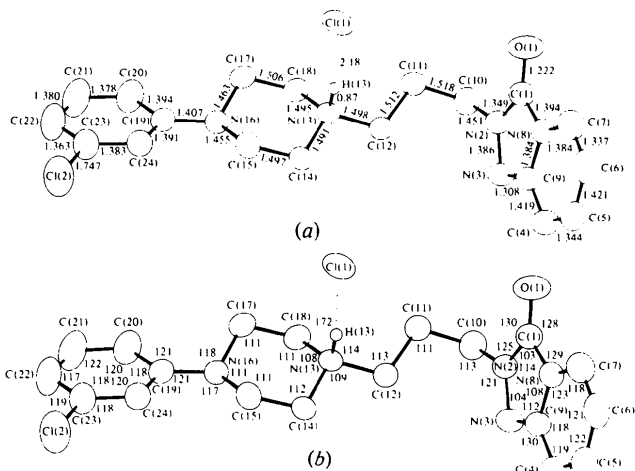
Fig. 1. (*a*) Bond distances (Å) and (*b*) angles (°) for trazodone hydrochloride. The average estimated standard deviations in the structure are 0·003 Å in bond lengths and 0·2° in bond angles. Atoms are shown with 50% probability thermal ellipsoids (*ORTEP*; Johnson, 1965).

piperazine ring, and the chlorophenyl group. The TPN nucleus is planar to within ±0·009 Å, with C(10) deviating 0·10 Å from this plane. The piperazine ring is in the normal chair conformation with N(13) and N(16) deviating from the piperazinyl carbon plane by 0·67 and −0·64 Å, respectively. The chlorophenyl moiety is planar to within ±0·006 Å.

The bond lengths associated with N(8) of the TPN nucleus and the aromatic N of pyridine are similar. The average bond length about N(8) is 1·387 (3) Å while that for pyridine is 1·392 (1) Å (Sørensen, Mahler & Rastrup-Andersen, 1974). The bond lengths associated with the five-membered ring are similar to other 1*H*-1,2,3-triazolo structures (Párkányi, Kálmán, Argay & Schawartz, 1977, and references therein). The bond lengths and angles associated with N(13) are characteristic of tertiary protonated amines while those for N(16) show some sp^2 character due to the attachment of the chlorophenyl moiety.

The torsional angle about N(2)—C(10), which relates C(11) to the TPN nucleus, is 93·2°. The torsional angle about C(11)—C(12) is 178·2°, indicating that the propylene side chain is nearly fully extended. The only hydrogen bond occurring in the molecule is between the protonated amino N(13) atom and the Cl anion; the distance N(13)···Cl(1) is 3·052 Å and the N—H···Cl angle is 172·1°.

One parameter which may be of importance to neuroleptic activity is the relationship of the protonated tertiary amino group to the aromatic ring system (Horn, 1974). Caution must be taken, however, when considering molecules that are not conformationally rigid. The general requirements are an out-of-plane distance for the tertiary N of at least 1·5 Å and a distance of 5·0 to 7·5 Å to the center of the aromatic group. Considering only the protonated amine N(13) and the TPN nucleus, the out-of-plane distance of N(13) is 3·856 Å and it is at a distance of 6·27 Å from the center of the TPN nucleus.

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Bis(triphenylmethyl) Peroxide

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Abstract. $C_{38}H_{30}O_2$, triclinic, $P\bar{1}$, $a = 10\cdot809$ (3), $b = 9\cdot062$ (2), $c = 8\cdot852$ (2) Å, $\alpha = 115\cdot47$ (1), $\beta = 91\cdot50$ (1), $\gamma = 112\cdot98$ (1)°, $M_r = 518\cdot62$, $V = 700\cdot75$ Å^3, $D_c = 1\cdot229$ Mg m^{-3}, $Z = 1$, μ(Mo $K\alpha$) = 0·04 mm^{-1}. The final R for 2220 reflections is 0·0638. The central COOC fragment is *trans*-planar with C—O = 1·461 (2), O—O = 1·480 (2) Å, and a COO angle of 107·5 (2)°.

Introduction. The compound was prepared by the reaction of Ph_3CCl with Zn amalgam in the presence of air; crystals were grown from benzene, and a crystal 0·20 × 0·15 × 0·10 mm was used for data collection on a Philips PW 1100 four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation. The intensities of 2374 unique reflections in the hemisphere $\pm h$, $\pm k$, $+l$ having $3 \le \theta \le 30°$ were measured with the ω–2θ scan technique. Lorentz and polarization corrections were applied, but no correction was made for absorption.

The E statistics suggested space group $P\bar{1}$, but attempts to solve the structure by direct methods with *SHELX* failed in both $P1$ and $P\bar{1}$: the structure was eventually solved in $P1$ with negative quartets (Sheldrick, 1978). The structure was refined by full-matrix least squares with complex neutral-atom scattering factors (Cromer & Mann, 1968) and weights $w = 1/\sigma^2(F)$ for 2220 unique reflections having $F_o \ge 6\sigma(F_o)$. Anisotropic temperature factors were employed for the O and C atoms; H atom coordinates

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Table 1. *Atom coordinates* ($\times 10^4$, *for* H $\times 10^3$)

	x	y	z
O	4737 (1)	4170 (2)	4150 (2)
C(1)	3309 (2)	3722 (3)	3509 (2)
C(11)	3251 (2)	5244 (3)	3200 (3)
C(12)	3472 (2)	6906 (3)	4592 (3)
C(13)	3400 (2)	8272 (3)	4332 (3)
C(14)	3109 (3)	8027 (3)	2694 (4)
C(15)	2875 (3)	6395 (4)	1318 (4)
C(16)	2951 (3)	5013 (3)	1561 (3)
C(21)	2940 (2)	1959 (3)	1819 (2)
C(22)	1636 (2)	491 (3)	1239 (3)
C(23)	1304 (3)	−1089 (3)	−300 (3)
C(24)	2269 (3)	−1221 (3)	−1261 (3)
C(25)	3561 (3)	219 (4)	−711 (3)
C(26)	3899 (2)	1810 (3)	823 (3)
C(31)	2437 (2)	3353 (3)	4745 (2)
C(32)	2768 (3)	2624 (3)	5708 (3)
C(33)	1925 (3)	2170 (3)	6742 (3)
C(34)	746 (3)	2437 (4)	6845 (4)
C(35)	409 (3)	3144 (3)	5897 (4)
C(36)	1234 (2)	3592 (3)	4846 (3)
H(12)	362 (2)	707 (3)	579 (3)
H(13)	357 (2)	940 (3)	531 (3)
H(14)	310 (2)	903 (3)	255 (3)
H(15)	273 (3)	621 (3)	17 (3)
H(16)	284 (2)	388 (3)	56 (3)
H(22)	95 (2)	57 (3)	190 (3)
H(23)	36 (3)	−214 (3)	−67 (3)
H(24)	204 (2)	−234 (3)	−234 (3)
H(25)	423 (2)	17 (3)	−139 (3)
H(26)	484 (3)	289 (3)	125 (3)
H(32)	364 (3)	250 (3)	566 (3)
H(33)	219 (2)	166 (3)	739 (3)
H(34)	16 (2)	216 (3)	761 (3)
H(35)	−43 (2)	330 (3)	595 (3)
H(36)	100 (3)	411 (3)	416 (3)