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Crystal Structure and Absolute Configuration of a Hydrogen Maleate of a Potentially Neuroleptic Rigid Spiro Amine: (1*S*,4*R*)-3′-Chloro-10′,11′-dihydro-*N*,*N*-dimethylspiro-[2-cyclohexene-1,5′-[5*H*]dibenzo[*a*,*d*]cyclohepten]-4-amine

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Abstract

The crystal structure and absolute configuration of a neuroleptic rigid spiro amine, A23887, have been determined. The compound, $C_{22}H_{24}ClN$, crystallizes as a hydrogen maleate ($C_4H_4O_4$) in space group $P2_1$ with two formula units in the asymmetric unit. The cell dimensions are a = 10·857 (1), b = 21·696 (3), c = 11·234 (1) Å and β = 117·14 (1)°. The structure was solved by direct methods and refined to an R value of 0·059. The e.s.d.'s in bond lengths are about 0·01 Å. The compound is two to three times more potent than chlorpromazine as regards the dopamine-receptor blocking efficiency. Half-normal probability plots show that there are small differences in conformation between the two cations in the asymmetric unit, but rather large ones between the two separate formula units.

Introduction

The present investigation has been undertaken as part of a study of dopamine-receptor blocking rigid spiro amines (Carnmalm, Johansson, Rämsby, Stjernström, Ross & Ögren, 1976). The isomer mixture of 3′-chloro-10′,11′-dihydro-*N*,*N*-dimethylspiro[2-cyclohexene-1,5′-[5*H*]dibenzo[*a*,*d*]cyclohepten]-4-amine has been resolved into its four possible enantiomers and tested for neuroleptic activity (Carnmalm *et al.*, 1976; Ögren, Hall & Köhler, 1978). It was shown that only the β-isomer was potent. Further, most of the activity resides in the $\beta(-)$ enantiomer, A23887,* being two to three times more potent than chlorpromazine.

The operating mechanism at the molecular level is being debated, but it has been proposed that the blocking capability of several neuroleptics on the dopamine receptor arises from similarities between certain portions of their structures and that of dopamine (Horn & Snyder, 1971).

Most of the active compounds so far studied in the solid state are relatively flexible and may adopt several conformations in solution. It was therefore thought of interest to determine the crystal structure of a more rigid compound showing a neuroleptic effect. Thus, a structure determination as well as a determination of the absolute configuration of A23887 were undertaken. Its structure has been determined in the form of a maleate salt.

Experimental

Crystals were grown from a solution in EtOH. A large needle crystal was cut to approximate dimensions 0·25 × 0·25 × 0·25 mm. This was used for both the data collection and measurements of the Bijvoet differences. Data were collected with a Philips PW1100 diffractometer using graphite-monochromatized Cu $K\alpha$ radiation. Cell dimensions were determined by least-squares refinement of the setting angles of 25 accurately centred reflections. Crystal data are given in Table 1. A total of 3465 reflections were collected up to $2\theta = 120°$ with θ–2θ scans using a scan width of 1·60° and a speed of 0·025° s^{-1}. Backgrounds were measured by stationary counts on each side of the peaks. 2697 reflections had $I_{net} \geq 3\sigma(I)$ and these were used in the subsequent calculations. Lorentz and polarization factors were applied. No corrections for absorption or extinction effects were made (μ = 1·70 mm^{-1}).

Table 1. *Crystal data*

$C_{22}H_{25}ClN^+.C_4H_3O_4^-$, M_r = 453·96
Monoclinic, space group $P2_1$
a = 10·857 (1) Å
b = 21·696 (3)
c = 11·234 (1)
β = 117·14 (1)°
Systematic absence
$0k0$ for $k = 2n + 1$

Z = 4
$F(000)$ = 840
D_c = 1·28 Mg m^{-3}
λ = 1·5418 Å for Cu $K\alpha$
μ = 1·70 mm^{-1}
V = 2354·8 Å^3

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* Internal code number. Astra Pharmaceuticals AB, Sweden.

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Table 2. *Positional parameters* ($\times 10^4$) *for the non-hydrogen atoms*

E.s.d.'s are in parentheses.

	Molecule *A*			Molecule *B*		
	x	*y*	*z*	*x*	*y*	*z*
Cl(1)	8004 (2)	7635 (1)	7274 (2)	10490 (2)	1226 (1)	4668 (2)
C(1)	8881 (7)	7546 (3)	9021 (7)	8711 (8)	1344 (3)	3801 (7)
C(2)	8583 (8)	7923 (4)	9807 (10)	7793 (10)	977 (4)	4061 (9)
C(3)	9308 (9)	7841 (4)	11164 (10)	6404 (10)	1100 (4)	3339 (9)
C(4)	10290 (8)	7374 (3)	11742 (8)	5889 (8)	1556 (3)	2403 (8)
C(5)	11104 (11)	7331 (5)	13233 (8)	4360 (8)	1614 (5)	1596 (11)
C(6)	12613 (10)	7493 (5)	13691 (10)	3945 (10)	1460 (5)	147 (12)
C(7)	13479 (9)	6958 (4)	13615 (7)	4114 (7)	1972 (4)	−678 (8)
C(8)	14849 (11)	6931 (5)	14638 (8)	3086 (10)	1988 (5)	−2050 (11)
C(9)	15741 (9)	6463 (6)	14751 (10)	3067 (10)	2432 (5)	−2919 (11)
C(10)	15292 (10)	6011 (5)	13819 (10)	4043 (11)	2911 (5)	−2438 (9)
C(11)	13944 (8)	6029 (4)	12791 (9)	5033 (9)	2905 (4)	−1095 (8)
C(12)	13002 (7)	6495 (3)	12648 (7)	5104 (7)	2443 (3)	−211 (8)
C(13)	11539 (7)	6406 (3)	11434 (6)	6318 (6)	2521 (3)	1254 (7)
C(14)	10591 (6)	6980 (3)	10901 (6)	6812 (7)	1940 (3)	2162 (7)
C(15)	9828 (7)	7070 (3)	9529 (6)	8195 (6)	1816 (3)	2861 (6)
C(16)	10777 (7)	5908 (3)	11828 (7)	5889 (6)	3023 (3)	1989 (7)
C(17)	9648 (7)	5566 (3)	10600 (7)	7166 (6)	3314 (3)	3151 (7)
C(18)	10355 (6)	5242 (3)	9890 (6)	7976 (6)	3665 (3)	2576 (6)
C(19)	11255 (6)	5661 (3)	9597 (6)	8263 (6)	3270 (3)	1654 (6)
C(20)	11787 (6)	6171 (3)	10287 (6)	7548 (6)	2767 (3)	1053 (6)
C(21)	8329 (9)	5350 (5)	7597 (8)	10180 (8)	3508 (4)	4692 (8)
C(22)	8685 (8)	4371 (4)	8896 (8)	9018 (8)	4520 (4)	4196 (8)
N(1)	9363 (5)	4909 (3)	8626 (5)	9276 (5)	3941 (3)	3616 (5)
C(23)	2212 (7)	4418 (3)	8412 (7)	2116 (7)	4337 (3)	3330 (6)
C(24)	3271 (8)	4522 (4)	7914 (7)	3171 (7)	4319 (3)	2845 (6)
C(25)	4606 (7)	4650 (4)	8578 (7)	4558 (7)	4321 (3)	3569 (6)
C(26)	5523 (7)	4713 (3)	10046 (7)	5479 (7)	4321 (4)	5023 (7)
O(1)	985 (5)	4445 (3)	7553 (5)	891 (4)	4263 (2)	2448 (4)
O(2)	2606 (5)	4330 (3)	9637 (5)	2445 (5)	4435 (4)	4536 (5)
O(3)	5050 (5)	4605 (3)	10882 (5)	4940 (6)	4434 (5)	5829 (5)
O(4)	6723 (6)	4867 (3)	10411 (6)	6708 (5)	4246 (4)	5436 (5)

Structure determination and refinement

The structure was solved by multisolution tangent refinement of the phases of 399 E values ($|E| \geq 1{\cdot}4$) using *SHELX* (Sheldrick, 1976). A23887 crystallizes with two cations and two anions in the asymmetric unit (*i.e.* two positively charged spiro amines and two negatively charged hydrogen maleates). With the exception of three non-hydrogen atoms, the complete structure could be derived from an E map. After three cycles of isotropic full-matrix least-squares refinement, the three remaining atoms could be located on a difference Fourier map. Another three cycles of refinement yielded an R value of 0·128. Anisotropic thermal parameters were then assigned and further blocked full-matrix least-squares refinement using *SHELX* lowered R to 0·073. At this stage all H positions, except those belonging to the hydroxyl groups in the two hydrogen maleate molecules, were calculated from geometrical considerations assuming a hydrogen-bond distance of 1·08 Å. The H atoms were then included in the final refinement cycles, with a fixed isotropic overall temperature factor of 0·05 Å^2, and allowed to ride on their respective bonded atoms.

The refinement was terminated at $R = 0{\cdot}059$.* During the last refinement cycles, weights were assigned as $w = 0{\cdot}2091/[\sigma^2(F) + 0{\cdot}0353F^2]$. The function minimized was $\sum w(|F_o| - |F_c|)^2$. The weighted R value defined by the equation $R_w = \sum w^{1/2}||F_o| - |F_c||/\sum w^{1/2}|F_o|$ was 0·066.

The largest shift/e.s.d. in the final refinement cycle was 0·20 in the positional parameters and 0·50 in the thermal parameters. Atomic scattering factors for the non-hydrogen atoms were taken from Cromer & Mann (1968) and those for the H atoms from Stewart, Davidson & Simpson (1965). Final atomic coordinates for the non-hydrogen atoms* are given in Table 2.

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* Lists of structure factors, anisotropic thermal parameters and H atomic positions have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34885 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *Calculated* (X_c) *and observed* (X_o) *Bijvoet ratios* ($\times 10^2$)

Cu *Ka* radiation was used.

h k l	X_o	X_c	θ	F_c
1 1 0	9·2	7·4	5·0	78·7
0 2 1	−11·9	−28·5	6·0	15·3
1 2 0	−32·7	−43·2	6·1	9·9
0 3 1	10·0	6·4	7·6	65·0
0 1 2	9·2	6·5	9·1	50·4
−2 2 1	−6·3	−7·5	9·1	64·3
2 1 0	23·4	39·9	9·4	14·4
1 1 2	7·0	5·7	11·9	52·1
2 4 0	37·2	32·9	12·3	20·3
−3 1 1	−5·2	−6·4	12·6	46·1
−2 5 1	10·9	4·8	13·1	86·2
0 6 1	−4·7	−14·6	13·1	27·8
1 6 0	−3·6	−7·2	13·2	61·1
3 2 0	15·9	10·3	14·5	47·1
1 7 0	13·0	5·8	15·1	86·7
0 7 1	19·5	11·9	15·1	36·4
−4 1 1	−27·3	−44·0	17·1	8·6
3 1 2	−2·6	−4·5	19·9	63·4

Absolute configuration

The absolute configuration has been determined by measuring Bijvoet differences using Cu *Ka* radiation. Reflections up to $\theta = 45°$ were generated using the program *BYFOT* written by Karlsson (1976) which calculates $|F|$, the Bijvoet differences and the Bijvoet ratios. Reflections which exhibited large Bijvoet differences and large Bijvoet ratios $2(I_{\rm h} - I_{\bar{\rm h}})/(I_{\rm h} + I_{\bar{\rm h}})$ were selected for measurement. For each of the 18 selected reflections, the intensities of hkl, $\bar{h}k\bar{l}$, $\bar{h}\bar{k}\bar{l}$ and $h\bar{k}l$ were measured. The averages of the pairs hkl, $\bar{h}k\bar{l}$ and $\bar{h}\bar{k}\bar{l}$, $h\bar{k}l$ were used in the subsequent calculations. The anomalous scattering of the Cl, N, O and C atoms was used and the f' and f'' values were taken from *International Tables for X-ray Crystallography* (1974). Table 3 lists the calculated (X_c) and observed (X_o) Bijvoet ratios. From this table it can be seen that the signs of the corresponding calculated and observed Bijvoet ratios are all identical and that the numerical values are of approximately the same magnitude. Thus, the absolute configuration corresponds to the coordinates given in Table 2.

Results and discussion

A23887 was found to have an (*S*) configuration at the spiro carbon atom (1,5′) and an (*R*) configuration at the carbon atom (4) bearing the amino group. The absolute configuration of A23887 is shown in Fig. 1. As expected, the two cations in the asymmetric unit have the same absolute configuration. Therefore, only one of them (molecule *A*) is shown in Fig. 1. Atomic numbering and notation of rings are given in Fig. 2. Bond distances and bond angles are listed in Table 4 and torsion angles are listed in Table 5.

Half-normal probability plots

To comparè the two formula units in the asymmetric unit, half-normal probability plots for interatomic distances were calculated (Abrahams & Keve, 1971; De Camp, 1973; Abrahams, 1974). The normalized δp_i is defined as $\delta p_i = |p(1)_i - p(2)_i| / [\sigma^2 p(1)_i + \sigma^2 p(2)_i]^{1/2}$ where $p(1)_i$ and $p(2)_i$ denote corresponding distances in molecules 1 and 2 and $\sigma p(1)_i$ and $\sigma p(2)_i$ their respective e.s.d.'s. The plots indicate that the two sets of bond

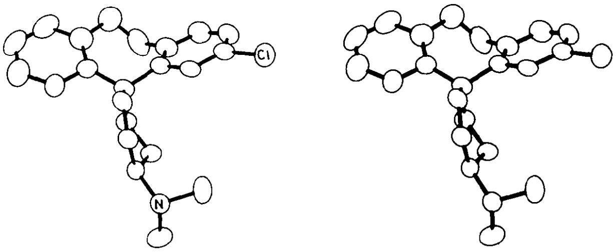


Fig. 1. Absolute configuration of A23887. Only one of the molecules in the asymmetric unit is shown (molecule *A*).

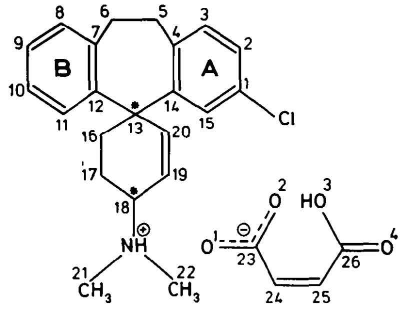


Fig. 2. Atomic numbering of the non-hydrogen atoms and notation of rings.

Table 4. *Bond distances* (Å) *and bond angles* (°)

E.s.d.'s are in parentheses.

	A	*B*		*A*	*B*
Cl–C(1)	1·758 (7)	1·740 (8)	C(13)–C(16)	1·543 (9)	1·561 (9)
C(1)–C(2)	1·347 (12)	1·407 (12)	C(16)–C(17)	1·553 (10)	1·541 (9)
C(2)–C(3)	1·371 (14)	1·374 (14)	C(17)–C(18)	1·509 (9)	1·513 (9)
C(3)–C(4)	1·398 (11)	1·364 (11)	C(18)–C(19)	1·477 (9)	1·483 (9)
C(4)–C(5)	1·498 (11)	1·490 (11)	C(19)–C(20)	1·323 (9)	1·331 (9)
C(5)–C(6)	1·518 (15)	1·515 (16)	C(20)–C(13)	1·520 (9)	1·547 (8)
C(6)–C(7)	1·520 (14)	1·510 (14)	C(18)–N	1·518 (8)	1·487 (8)
C(7)–C(8)	1·406 (13)	1·434 (13)	N–C(21)	1·526 (11)	1·491 (10)
C(8)–C(9)	1·369 (16)	1·366 (15)	N–C(22)	1·483 (10)	1·499 (10)
C(9)–C(10)	1·353 (16)	1·404 (15)	O(1)–C(23)	1·240 (8)	1·255 (8)
C(10)–C(11)	1·391 (13)	1·397 (12)	O(2)–C(23)	1·255 (9)	1·252 (8)
C(11)–C(12)	1·394 (8)	1·388 (11)	C(23)–C(24)	1·508 (10)	1·476 (9)
C(12)–C(13)	1·563 (9)	1·580 (10)	C(24)–C(25)	1·322 (10)	1·346 (10)
C(13)–C(14)	1·551 (9)	1·555 (9)	C(25)–C(26)	1·494 (10)	1·476 (9)
C(14)–C(4)	1·418 (10)	1·421 (10)	C(26)–O(3)	1·281 (9)	1·306 (9)
C(14)–C(15)	1·391 (9)	1·367 (9)	C(26)–O(4)	1·221 (9)	1·207 (8)
C(15)–C(1)	1·383 (9)	1·392 (9)			

Table 4 (*cont.*)

	A	*B*		*A*	*B*		*A*	*B*
Cl–C(1)–C(2)	119·7 (6)	120·7 (6)	C(10)–C(11)–C(12)	123·7 (8)	122·9 (8)	C(17)–C(18)–C(19)	112·2 (5)	110·8 (5)
Cl–C(1)–C(15)	117·5 (5)	119·5 (5)	C(11)–C(12)–C(7)	116·1 (7)	118·5 (7)	C(17)–C(18)–N	113·7 (5)	113·3 (5)
C(15)–C(1)–C(2)	122·6 (7)	119·7 (7)	C(7)–C(12)–C(13)	129·6 (6)	127·0 (7)	C(19)–C(18)–N	110·1 (5)	110·8 (5)
C(1)–C(2)–C(3)	117·5 (8)	117·3 (8)	C(11)–C(12)–C(13)	114·3 (6)	114·6 (6)	C(18)–C(19)–C(20)	122·7 (6)	124·6 (6)
C(2)–C(3)–C(4)	122·7 (8)	123·3 (8)	C(12)–C(13)–C(14)	118·0 (5)	118·1 (5)	C(19)–C(20)–C(13)	125·4 (6)	123·5 (6)
C(3)–C(4)–C(5)	120·0 (8)	118·8 (8)	C(12)–C(13)–C(16)	107·5 (5)	108·5 (5)	C(21)–N–C(18)	111·9 (6)	114·9 (6)
C(3)–C(4)–C(14)	119·1 (7)	119·7 (7)	C(12)–C(13)–C(20)	106·2 (5)	104·5 (5)	C(21)–N–C(22)	112·7 (6)	111·1 (6)
C(5)–C(4)–C(14)	120·6 (7)	121·4 (7)	C(14)–C(13)–C(16)	108·9 (5)	108·4 (6)	C(22)–N–C(18)	113·0 (5)	112·4 (5)
C(4)–C(5)–C(6)	111·1 (8)	109·8 (8)	C(14)–C(13)–C(20)	106·6 (5)	108·2 (5)	O(1)–C(23)–O(2)	124·6 (6)	123·6 (6)
C(5)–C(6)–C(7)	113·8 (9)	115·9 (8)	C(16)–C(13)–C(20)	109·5 (5)	108·8 (5)	O(1)–C(23)–C(24)	115·8 (6)	115·3 (5)
C(6)–C(7)–C(8)	115·9 (8)	115·1 (8)	C(13)–C(14)–C(15)	119·7 (6)	119·8 (6)	O(2)–C(23)–C(24)	119·6 (6)	121·2 (6)
C(6)–C(7)–C(12)	125·1 (8)	126·5 (8)	C(13)–C(14)–C(4)	122·7 (6)	122·6 (6)	C(23)–C(24)–C(25)	130·4 (7)	128·3 (6)
C(8)–C(7)–C(12)	119·0 (8)	118·3 (8)	C(4)–C(14)–C(15)	116·9 (6)	117·4 (6)	C(24)–C(25)–C(26)	130·5 (7)	132·5 (6)
C(7)–C(8)–C(9)	123·1 (9)	122·4 (9)	C(14)–C(15)–C(1)	121·1 (6)	122·5 (6)	C(25)–C(26)–O(3)	120·3 (6)	118·4 (6)
C(8)–C(9)–C(10)	118·4 (9)	119·0 (10)	C(13)–C(16)–C(17)	112·9 (6)	111·3 (5)	C(25)–C(26)–O(4)	117·9 (6)	119·8 (6)
C(9)–C(10)–C(11)	119·6 (9)	118·8 (9)	C(16)–C(17)–C(18)	107·9 (5)	108·6 (6)	O(3)–C(26)–O(4)	121·8 (7)	121·7 (7)

Table 5. *Torsion angles* (°)

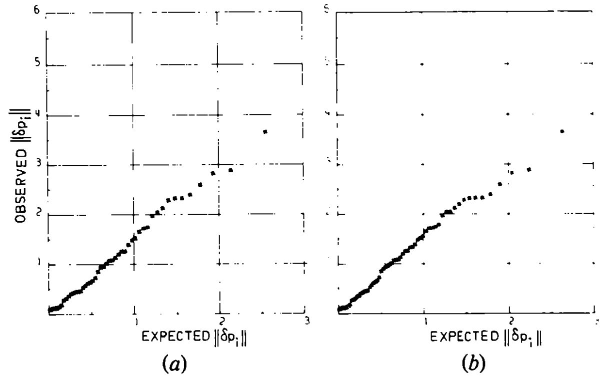
E.s.d.'s are in parentheses.

	Molecule *A*	Molecule *B*
C(15)–C(1)–C(2)–C(3)	3·3 (13)	1·1 (13)
C(1)–C(2)–C(3)–C(4)	−2·3 (14)	−0·3 (15)
C(2)–C(3)–C(4)–C(14)	2·2 (14)	−1·4 (14)
C(3)–C(4)–C(14)–C(15)	−2·8 (11)	2·3 (12)
C(4)–C(14)–C(15)–C(1)	3·7 (10)	−1·6 (11)
C(14)–C(15)–C(1)–C(2)	−4·1 (12)	0·0 (12)
C(14)–C(4)–C(5)–C(6)	63·5 (11)	63·2 (11)
C(4)–C(5)–C(6)–C(7)	−83·6 (11)	−81·5 (11)
C(5)–C(6)–C(7)–C(12)	33·7 (13)	30·4 (14)
C(12)–C(7)–C(8)–C(9)	−1·3 (15)	2·0 (15)
C(7)–C(8)–C(9)–C(10)	1·3 (17)	−3·4 (17)
C(8)–C(9)–C(10)–C(11)	−0·8 (16)	2·1 (16)
C(9)–C(10)–C(11)–C(12)	0·4 (16)	0·5 (15)
C(10)–C(11)–C(12)–C(7)	−0·4 (13)	−2·0 (13)
C(11)–C(12)–C(7)–C(8)	0·7 (12)	0·7 (12)
C(7)–C(12)–C(13)–C(14)	22·0 (11)	22·1 (11)
C(12)–C(13)–C(14)–C(4)	−51·9 (9)	−53·4 (10)
C(14)–C(13)–C(16)–C(17)	76·7 (7)	73·8 (7)
C(13)–C(16)–C(17)–C(18)	61·9 (8)	65·8 (7)
C(16)–C(17)–C(18)–C(19)	−51·7 (7)	−51·9 (7)
C(17)–C(18)–C(19)–C(20)	23·8 (9)	21·3 (9)
C(18)–C(19)–C(20)–C(13)	−1·4 (11)	−0·8 (11)
C(19)–C(20)–C(13)–C(12)	125·2 (9)	127·7 (8)
C(19)–C(18)–N–C(22)	165·3 (8)	156·5 (8)
O(2)–C(23)–C(24)–C(25)	−14·1 (13)	8·9 (12)
C(23)–C(24)–C(25)–C(26)	2·6 (15)	2·6 (13)
C(24)–C(25)–C(26)–O(3)	4·0 (13)	−12·9 (13)

lengths agree with each other within a few e.s.d.'s but there is a difference in the molecular conformation between the formula units.

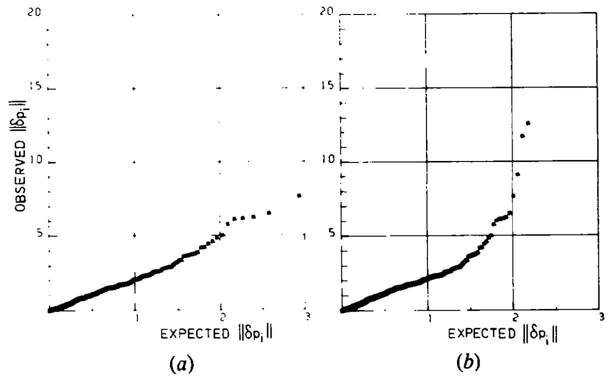
A half-normal probability plot, calculated for the intramolecular distances shorter than 2·5 Å between the 24 non-hydrogen atoms in the cations, shows a normal error distribution (*cf.* Fig. 3*a*). A least-squares line through the 37 points (of a total of 47) with $\delta p \le 2{\cdot}0$ has a slope of 1·53 (3), an intercept of −0·03 (2) and a correlation coefficient of 0·9951. A similar calculation was done for the complete formula unit (32 atoms) as well (*cf.* Fig. 3*b*). In this case, the least-squares line was fitted to 48 points of a total of 61. The slope, the intercept and the correlation coefficient were 1·58 (2), −0·01 (1) and 0·9972 respectively. From the slopes one may conclude that the e.s.d.'s are underestimated by a factor of approximately 1·5.

Half-normal probability plots for distances less than 4·65 Å were also calculated. While the 24-atom plot



(*a*) (*b*)

Fig. 3. (*a*) Half-normal probability plot comparing interatomic distances < 2·5 Å for the 24 non-hydrogen atoms in the cations. (*b*) Half-normal probability plot comparing interatomic distances < 2·5 Å for the 32 non-hydrogen atoms in the formula units.



(*a*) (*b*)

Fig. 4. (*a*) Half-normal probability plot comparing interatomic distances < 4·65 Å for the 24 non-hydrogen atoms in the cations. (*b*) Half-normal probability plot comparing interatomic distances < 4·65 Å for the 32 non-hydrogen atoms in the formula units.

Table 6. *Some selected distances* (Å) *and angles* (°)

E.s.d.'s are in parentheses. The first of the two values in each column refers to molecule *A*, the second to molecule *B*.

D	H	*A*	*D*···*A*	H···*A*	∠*D*–H–*A*
N	H(N)	O(1)	2·739 (7), 2·717 (6)	1·660 (7), 1·642 (6)	177·9 (6), 172·7 (6)
C(24)	H(24)	O(2)	3·483 (9), 3·368 (8)	2·416 (6), 2·320 (5)	169·1 (1), 163·3 (4)
C(25)	H(25)	O(3)	3·303 (9), 3·354 (8)	2·393 (6), 2·398 (7)	140·9 (5), 146·8 (6)
O(2)	–	O(3)	2·443 (7), 2·420 (8)		

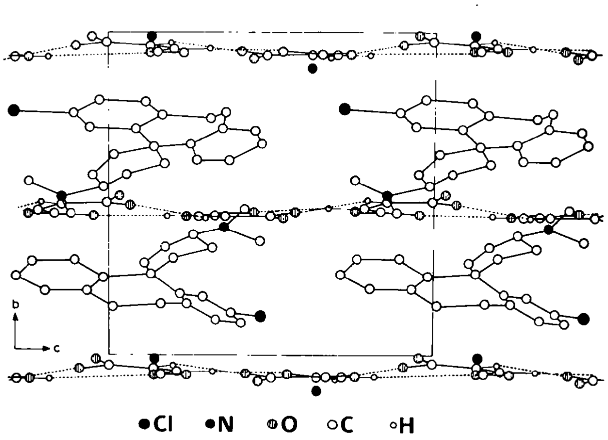


Fig. 5. Projection of the packing arrangement viewed along the *a* axis.

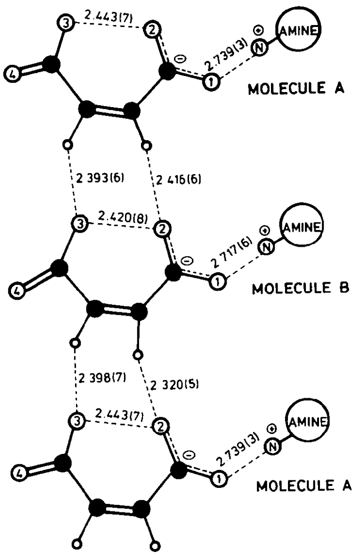


Fig. 6. The hydrogen-bond network.

indicates only a slight difference in conformation between the two cations (*cf.* Fig. 4*a*), a large difference between the two formula units is indicated by the 32-atom plot (*cf.* Fig. 4*b*). Thus, it may be assumed that the cation–anion relation is responsible for the major part of the discrepancy between the formula units.

In analysing Fig. 4, one should note that random errors in interatomic distances should be normally distributed and result in a linear plot. Conversely, non-linearity reflects a difference in conformation between the two molecules. Almost 30% of the points in both the 24-atom plot (50 of 152) and 32-atom plot (67 of 192) have $\delta p \geq 2{\cdot}0$. Several extreme points have $\delta p \geq 6{\cdot}0$. The slopes of the least-squares lines are 2·06 (2) and 2·19 (2) respectively.

Hydrogen bonding and molecular packing.

The packing arrangement in this structure is of the same type as that found in the crystal structure of the hydrogen maleate salt of another neuroleptic compound, methoxypromazine (Marsau & Gauthier, 1973). Parallel chains are formed by hydrogen bonds between the oxygen and ethylene hydrogens in the hydrogen maleate molecules. These chains are in contact with the two cations by means of hydrogen bonds between O(1*A*)···N(*A*) and O(1*B*)···N(*B*) at distances of 2·739 (7) and 2·717 (6) Å, respectively. Fig. 5 shows a projection along the *a* axis of the packing arrangement of the hydrogen maleate chains and the cations. Since C(26)–O(3) is longer than C(23)–O(2), the H atom in the hydrogen maleate group is assumed to be located at O(3). This is supported by a small peak found in the difference Fourier map between O(2) and O(3), somewhat closer to O(3). Further, the distance between O(2) and O(3) is characteristic of a hydrogen bond. Therefore, an intramolecular hydrogen bond O(3)–H··· O(2) should exist (*cf.* Fig. 6). Some selected contacts and angles are listed in Table 6.

Geometry of the molecule A23887

The tricyclic system may be described in terms of three parameters: a bend angle, a twist angle and a skew distance (Corey, Corey & Glick, 1975). The bend angle is the dihedral angle between the two benzene rings. For A23887 this has been calculated to be 139·1 (9)° in molecule *A* and 143·5 (5)° in molecule *B*. The twist angle is the average of the torsion angles about the non-bonded vectors across the seven-membered ring that involve the benzo C atoms [*e.g.*

Table 7. *Some molecular parameters for* A23887

E.s.d.'s are in parentheses.

	Molecule *A*	Molecule *B*
Bend angle	139·1 (9)°	143·5 (5)°
Twist angle	23·1 (5)	23·9 (5)
Skew distance	0·59 (1) Å	0·54 (1) Å
Distance between aromatic ring centres	5·29 (1)	5·25 (1)
Distance to N from ring centre *A*	5·83 (1)	5·73 (1)
Distance to N from ring centre *B*	6·75 (1)	6·81 (1)
Distance from N to the plane through the four benzo C atoms	−1·96 (1)	−1·94 (1)

Equations for the planes through the four benzo C atoms and deviations in Å; e.s.d.'s are given in parentheses

Molecule *A* $0{\cdot}4\,(1)x + 0{\cdot}7\,(1)y - 0{\cdot}7\,(4)z - 9{\cdot}0 = 0$

Molecule *B* $0{\cdot}4\,(4)x - 0{\cdot}7\,(7)y - 0{\cdot}6\,(6)z - 0{\cdot}48 = 0$

Molecule *A*		Molecule *B*	
C(7)	0·12 (1)	C(7)	0·13 (1)
C(14)	0·15 (1)	C(14)	0·15 (1)
C(4)	−0·12 (1)	C(4)	−0·13 (1)
C(12)	−0·15 (1)	C(12)	−0·15 (1)
N	−1·96 (1)	N	−1·94 (1)

C(14)–C(4)···C(7)–C(12) and C(4)–C(14)··· C(12)–C(7)].

The two benzene rings are twisted out of the plane in opposite directions by an angle of approximately 23° in molecule *A* and 24° in molecule *B*. The skew distance is defined as the difference between the non-bonding distances C(4)···C(7) and C(14)···C(12). For A23887 this is calculated to be 0·59 Å in molecule *A* and 0·54 Å in molecule *B*, the C(14)···C(12) atoms being closer to each other than the C(4)···C(7) atoms.

Some molecular parameters of possible significance for the neuroleptic effect and the dopamine-receptor blocking capability (Horn, Post & Kennard, 1975) have also been calculated. These are (1) the distance between the centres of gravity in the benzene rings, (2) the distance between these centres and the N atom and (3) the distance from the N atom to a mean plane through the four benzo C atoms in the seven-membered ring. These distances, including the above-mentioned parameters, are listed in Table 7. A comparison between A23887 and some other related rigid compounds resulting in a topographical model of the neuroleptic receptor is presented by Carnmalm, Johansson, Rämsby, Stjernström & Wägner (1979). A discussion of the neuroleptic activity and stereoselective effect of A23887 and related compounds in the dopaminergic system will be published elsewhere (Wägner, 1980).

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