

C8—C9—C10	123.8 (2)	124.2 (2)
C4—C10—C5	126.0 (2)	125.5 (2)
C4—C10—C9	117.8 (2)	118.5 (2)
C5—C10—C9	116.2 (2)	116.0 (2)
C2—C3—C1'—C2'	−50.5 (3)	−56.2 (2)
O2—C2—C3—C4	172.7 (2)	174.6 (2)
O2—C2—C3—C1'	−4.2 (3)	−4.2 (3)

All non-H atoms were located by direct methods using *SIR88* (Burla *et al.*, 1989) and refined anisotropically. All H atoms were found from difference Fourier maps and refined isotropically.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *CAD-4 Software*. Program(s) used to refine structure: *TEXSAN* (Molecular Structure Corporation, 1992). Molecular graphics: *ORTEPII* (Johnson, 1976).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry and torsion angles have been deposited with the IUCr (Reference: NA1203). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Absolute Configuration of D-Brompheniramine Maleate

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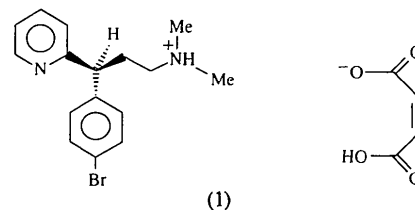
Abstract

The crystal structure and absolute configuration of the title compound, 3-(4-bromophenyl)-*N,N*-dimethyl-3-(2-pyridyl)propylammonium hydrogen maleate, $C_{16}H_{20}BrN_2^+ \cdot C_4H_3O_4^-$, a potent anti-allergic agent, has been determined. The crystals are composed of two independent brompheniraminium cations, which differ

significantly in their conformations, hydrogen bonded to maleate anions, with $N \cdots O$ distances of 2.673 (9) and 2.664 (9) Å. The anions form seven-membered rings through strong intramolecular $O—H \cdots O$ hydrogen bonds, with $O \cdots O$ distances of 2.418 (10) and 2.430 (8) Å.

Comment

As a continuation of our studies (Parvez, 1990) on the anti-allergic drugs effective on H1 receptors, we have determined the crystal structure and absolute configuration of D-brompheniramine hydrogen maleate, (1).



ORTEPII drawings (Johnson, 1976) of the two independent molecules, *A* and *B*, found in the crystal of (1), with the atomic numbering schemes, are shown in Fig. 1. The molecular dimensions in both molecules are unexceptional, with mean bond distances $Br—C_{sp^2}$ 1.92 (1), $N—C_{sp^3}$ 1.48 (2), $N—C_{sp^2}$ 1.34 (1), $C_{sp^3}—C_{sp^3}$ 1.52 (1), $C_{sp^3}—C_{sp^2}$ 1.52 (3) and $C—C_{aromatic}$ 1.37 (3) Å in the cations, and $C_{sp^2}—C_{sp^2}$ 1.49 (1), $C=C$ 1.34 (1), $C—O$ 1.29 (1), $C—O^-$ 1.27 (1) and $C=O$ 1.22 (1) Å in the anions. The angles at the C13A and C13B atoms [111.8 (9) and 118.3 (8)°, respectively] are significantly different in the two molecules, showing more strain in molecule *B*. The six-membered rings in the two molecules are essentially planar, with the maximum deviation from the least-squares planes being 0.03 (2) Å for atom C2A.

The maleate anions are hydrogen bonded to the dimethylamino groups of the brompheniraminium cations via normal $N—H \cdots O$ interactions (Table 3) and show typically strong intramolecular hydrogen bonding.

The two molecules show significant differences in their conformations. For instance, the mean-planes angles between the pyridyl and phenyl rings (A1), the pyridyl ring and C6—C13—C14 chain (A2), and the phenyl ring and C6—C13—C14 chain (A3) in molecule *A* are 72.5 (5), 82.9 (6) and 70.5 (7)°, respectively, compared with values of 79.6 (5), 79.3 (5) and 14.4 (9)°, respectively, in molecule *B*. The corresponding angles in the crystal structure of DL-pheniramine hydrogen maleate, (2) (Parvez & Rusiewicz, 1996), with values of 87.1 (3), 86.6 (3) and 6.9 (6)°, respectively, show it to have a conformation similar to that of molecule *B*. The conformation of neither of the

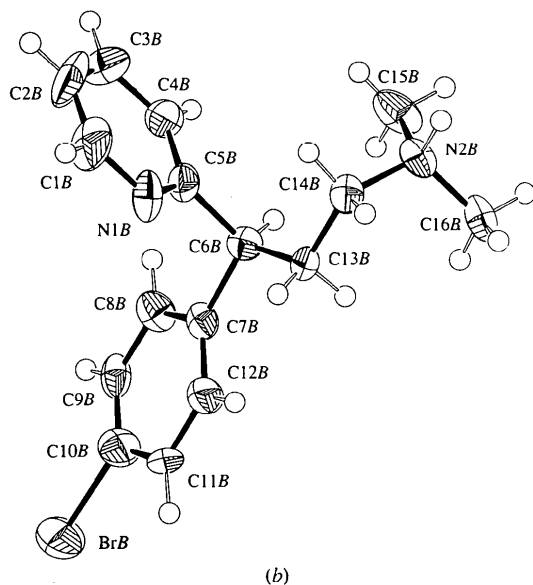
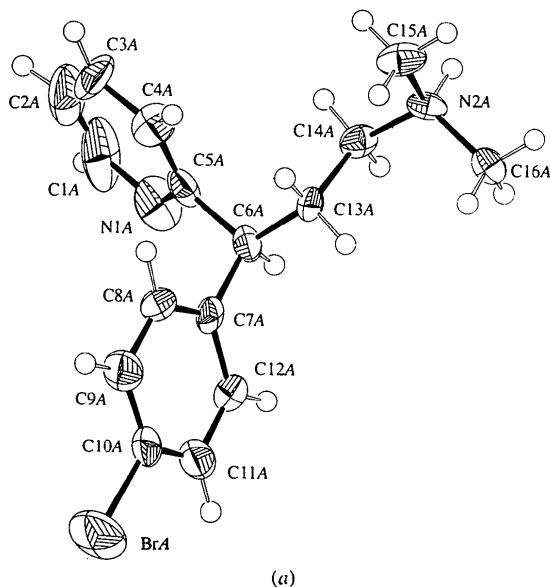


Fig. 1. ORTEP representations (Johnson, 1976) of (a) molecule A and (b) molecule B of the title compound with the atomic numbering schemes. Displacement ellipsoids are plotted at the 50% probability level and H atoms have been assigned arbitrary radii.

molecules of compound (1) resembles the conformation of the structure of D-chlorpheniramine, (3) (James & Williams, 1974), with angles A1, A2 and A3 of 113.6 (2), 96.1 (2) and 51.9 (3)°, respectively. It is interesting to note that the structures of DL-chlorpheniramine, (4) (Parvez, 1990), and DL-brompheniramine, (5) (James & Williams, 1971), adopt more or less identical conformations with A1, A2 and A3 angles of 105.1 (1), 33.5 (2) and 82.5 (1)°, respectively, for compound (4) and 103.7 (2), 30.9 (3) and 81.8 (2)° for compound (5);

the conformations of molecules A or B do not match either of these structures.

There are notable differences in the conformations of the side chains of the two molecules in compound (1). In molecule A, a fully extended side chain is composed of atoms C7A, C6A, C13A, C14A, N2A and H1N2A, with atoms C15A and C16A lying on opposite sides of the chain. On the other hand, a fully extended side chain in molecule B is comprised of only the C7B, C6B, C13B and C14B atoms, with the dimethylamino group and the pyridyl ring on opposite sides of the plane of this group of atoms. The conformations of the side chains in none of the above mentioned molecules, (2)–(5), match those of the side chains of either of the molecules of compound (1).

Experimental

Crystals of the title compound (Sigma Inc.) were grown from an ethanol solution by slow evaporation at room temperature.

Crystal data

$C_{16}H_{20}BrN_2^+ \cdot C_4H_3O_4^-$

$M_r = 435.32$

Triclinic

$P1$

$a = 9.796 (4) \text{ \AA}$

$b = 17.725 (7) \text{ \AA}$

$c = 6.042 (1) \text{ \AA}$

$\alpha = 97.22 (2)^\circ$

$\beta = 95.70 (2)^\circ$

$\gamma = 104.65 (3)^\circ$

$V = 997.5 (6) \text{ \AA}^3$

$Z = 2$

$D_x = 1.449 \text{ Mg m}^{-3}$

Mo $K\alpha$ radiation

$\lambda = 0.71069 \text{ \AA}$

Cell parameters from 25 reflections

$\theta = 10.0\text{--}20.0^\circ$

$\mu = 2.094 \text{ mm}^{-1}$

$T = 200 \text{ K}$

Prism

$0.40 \times 0.20 \times 0.20 \text{ mm}$

Colourless

Data collection

Rigaku AFC-6S diffractometer

$\omega/2\theta$ scans

Absorption correction:

ψ scans (North, Phillips & Mathews, 1968)

$T_{\min} = 0.910$, $T_{\max} =$

0.996

4872 measured reflections

4604 independent reflections

1649 observed reflections [$I > 3\sigma(I)$]

$R_{\text{int}} = 0.057$

$\theta_{\max} = 27.5^\circ$

$h = 0 \rightarrow 12$

$k = -23 \rightarrow 22$

$l = -7 \rightarrow 7$

3 standard reflections

monitored every 200 reflections

intensity decay: 1.53%

Refinement

Refinement on F

$R = 0.035$

$wR = 0.039$

$S = 1.262$

1649 reflections

484 parameters

H atoms riding with C—H,

N—H and O—H 0.95 \AA

$w = 1/[\sigma^2(F_o) + 0.033(F_o^2)]$

$(\Delta/\sigma)_{\max} = 0.1330$

$\Delta\rho_{\max} = 0.28 \text{ e \AA}^{-3}$

$\Delta\rho_{\min} = -0.25 \text{ e \AA}^{-3}$

Extinction correction: none

Atomic scattering factors

from *International Tables*

for *X-ray Crystallography*

(1974, Vol. IV)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (\AA^2)
$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{eq}
BrA	0.0101	0.0094	-0.0018	0.090 (1)
O1A	0.5346 (6)	0.2601 (4)	-0.1013 (10)	0.048 (2)
O2A	0.7043 (6)	0.2761 (4)	0.1839 (11)	0.048 (2)
O3A	0.2814 (6)	0.2506 (4)	-0.1498 (11)	0.050 (2)
O4A	0.1177 (6)	0.2614 (4)	0.0691 (10)	0.050 (2)
N1A	0.5845 (12)	-0.0410 (7)	0.7857 (18)	0.062 (4)
N2A	0.9277 (7)	0.2471 (5)	0.7065 (12)	0.031 (2)
C1A	0.627 (2)	-0.1073 (10)	0.793 (3)	0.086 (6)
C2A	0.705 (2)	-0.1337 (10)	0.646 (3)	0.087 (7)
C3A	0.755 (2)	-0.0899 (9)	0.495 (2)	0.072 (5)
C4A	0.716 (1)	-0.0203 (8)	0.478 (2)	0.051 (4)
C5A	0.631 (1)	0.0019 (7)	0.628 (2)	0.038 (3)
C6A	0.581 (1)	0.0762 (6)	0.621 (2)	0.034 (3)
C7A	0.441 (1)	0.0591 (7)	0.467 (2)	0.031 (3)
C8A	0.427 (1)	0.0267 (7)	0.244 (2)	0.037 (3)
C9A	0.297 (1)	0.0104 (8)	0.101 (2)	0.048 (4)
C10A	0.186 (1)	0.0328 (8)	0.194 (2)	0.050 (4)
C11A	0.196 (1)	0.0652 (8)	0.407 (2)	0.052 (4)
C12A	0.325 (1)	0.0796 (7)	0.552 (2)	0.041 (4)
C13A	0.6897 (9)	0.1464 (5)	0.564 (2)	0.034 (3)
C14A	0.8227 (9)	0.1736 (6)	0.742 (2)	0.036 (3)
C15A	0.9905 (10)	0.2379 (6)	0.494 (2)	0.046 (3)
C16A	0.8696 (9)	0.3159 (5)	0.731 (1)	0.032 (3)
C17A	0.5806 (10)	0.2687 (6)	0.109 (2)	0.033 (2)
C18A	0.481 (1)	0.2718 (6)	0.283 (2)	0.033 (3)
C19A	0.3397 (9)	0.2654 (6)	0.253 (1)	0.035 (3)
C20A	0.238 (1)	0.2578 (7)	0.043 (2)	0.030 (3)
BrB	0.8732 (1)	0.7230 (1)	1.1786 (3)	0.073 (1)
O1B	0.3753 (7)	0.4566 (5)	1.0819 (13)	0.052 (2)
O2B	0.2092 (6)	0.4484 (4)	0.8014 (11)	0.051 (2)
O3B	0.6286 (8)	0.4695 (5)	1.1347 (13)	0.050 (3)
O4B	0.8001 (6)	0.4815 (4)	0.9202 (11)	0.052 (2)
N1B	0.2990 (12)	0.7552 (6)	0.4261 (18)	0.051 (3)
N2B	-0.0037 (7)	0.5046 (5)	0.2783 (12)	0.037 (2)
C1B	0.271 (2)	0.8240 (9)	0.398 (3)	0.071 (5)
C2B	0.186 (2)	0.8547 (9)	0.525 (3)	0.077 (6)
C3B	0.127 (2)	0.8157 (9)	0.686 (3)	0.073 (6)
C4B	0.153 (1)	0.7441 (8)	0.711 (2)	0.053 (4)
C5B	0.239 (1)	0.7155 (7)	0.579 (2)	0.039 (3)
C6B	0.275 (1)	0.6393 (7)	0.608 (2)	0.033 (3)
C7B	0.427 (1)	0.6565 (7)	0.744 (2)	0.033 (3)
C8B	0.447 (1)	0.6942 (8)	0.965 (2)	0.042 (3)
C9B	0.577 (1)	0.7118 (7)	1.094 (2)	0.039 (3)
C10B	0.688 (1)	0.6953 (8)	1.004 (2)	0.050 (4)
C11B	0.674 (1)	0.6570 (7)	0.785 (2)	0.044 (4)
C12B	0.541 (1)	0.6398 (7)	0.655 (2)	0.044 (4)
C13B	0.2579 (9)	0.5855 (5)	0.387 (2)	0.034 (3)
C14B	0.1191 (9)	0.5682 (5)	0.229 (1)	0.037 (3)
C15B	-0.063 (1)	0.5265 (8)	0.484 (2)	0.058 (4)
C16B	0.0313 (10)	0.4291 (6)	0.274 (2)	0.046 (3)
C17B	0.329 (1)	0.4480 (7)	0.869 (2)	0.039 (2)
C18B	0.4298 (9)	0.4383 (6)	0.708 (1)	0.037 (3)
C19B	0.5697 (9)	0.4463 (6)	0.736 (1)	0.038 (3)
C20B	0.6726 (10)	0.4682 (6)	0.946 (2)	0.039 (2)

Table 2. Selected geometric parameters (\AA , $^\circ$)

BrA—C10A	1.91 (1)	BrB—C10B	1.92 (1)
N1A—C1A	1.35 (2)	N1B—C1B	1.34 (2)
N1A—C5A	1.33 (1)	N1B—C5B	1.32 (1)
N2A—C14A	1.50 (1)	N2B—C14B	1.51 (1)
N2A—C15A	1.49 (1)	N2B—C15B	1.48 (1)
N2A—C16A	1.47 (1)	N2B—C16B	1.46 (1)
C5A—C6A	1.52 (2)	C5B—C6B	1.50 (2)
C6A—C7A	1.52 (2)	C6B—C7B	1.57 (2)
C6A—C13A	1.52 (1)	C6B—C13B	1.51 (2)
C13A—C14A	1.53 (1)	C13B—C14B	1.52 (1)
C1A—N1A—C5A	116 (1)	C1B—N1B—C5B	119 (1)
C14A—N2A—C15A	113.5 (8)	C14B—N2B—C15B	114.3 (8)
C14A—N2A—C16A	112.1 (7)	C14B—N2B—C16B	111.7 (8)
C15A—N2A—C16A	112.4 (8)	C15B—N2B—C16B	112.1 (9)

C5A—C6A—C7A	111.1 (9)	C5B—C6B—C7B	110 (1)
C5A—C6A—C13A	115.0 (9)	C5B—C6B—C13B	112.3 (10)
C7A—C6A—C13A	110.9 (10)	C7B—C6B—C13B	112.2 (9)
C6A—C13A—C14A	111.8 (9)	C6B—C13B—C14B	118.3 (8)
N2A—C14A—C13A	114.2 (8)	N2B—C14B—C13B	116.4 (8)

Table 3. Hydrogen-bonding geometry (\AA , $^\circ$)

<i>D</i> — <i>H</i> ... <i>A</i>	<i>D</i> — <i>H</i>	<i>H</i> ... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> — <i>H</i> ... <i>A</i>
N2A—H1N2A...O4A'	0.95	1.74	2.673 (9)	167
N2B—H1N2B...O4B''	0.95	1.72	2.664 (9)	174
O1A—H1O1A...O3A	0.95	1.48	2.430 (8)	180
O1B—H1O1B...O3B	0.95	1.48	2.418 (10)	168

Symmetry codes: (i) $1 + x, y, 1 + z$; (ii) $x - 1, y, z - 1$.

The space group, *P1*, was determined from a statistical analysis of intensity distribution and successful solution and refinement of the structure. In the final stages of refinement, parallel and independent rounds of calculations on the two opposite enantiomers of the structure converged with *R* = 0.035 and 0.043, and *wR* = 0.39 and 0.050. A statistical test on the *wR*-factor ratio (Hamilton, 1965) indicated that the latter stereoisomer could be rejected at the 0.005 significance level as being the configuration present in the crystal. The coordinates reported in this paper refer to the statistically favoured configuration. The configuration determined by the analysis is in accord with that anticipated.

Data collection: *MSCIAFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSCIAFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1994). Program(s) used to solve structure: *PATY* in *DIRDIF92* (Beurskens *et al.*, 1992). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

The authors thank the Natural Sciences and Engineering Research Council (Canada) for providing the diffractometer through an equipment grant to the University of Calgary.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: FG1126). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1996). **C52**, 904–905

Clemizole Hydrochloride

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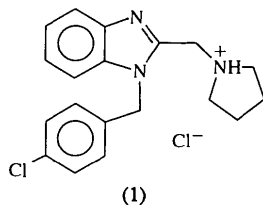
(Received 19 September 1995; accepted 2 November 1995)

Abstract

The crystal structure of the title compound, 1-[1-(*p*-chlorobenzyl)-2-benzimidazolylmethyl]pyrrolidinium chloride, C₁₉H₂₁ClN₃⁺·Cl⁻, a potent anti-allergic agent, has been determined. The crystals are composed of independent cations which are hydrogen bonded to chloride ions, with an N···Cl distance of 3.021 (6) Å and an N—H···Cl angle of 173°.

Comment

As a continuation of studies on the anti-allergic drugs [5-methoxy-3-(1-methylethoxy)-1-phenyl-*N*-(1*H*-tetrazol-5-yl)-1*H*-indole-2-carboxamide-diethylamine (Parvez, Unangst, Connor & Mullican, 1991*a*) and 3-(1-methyl-ethoxy)-7-phenyl-*N*-(1*H*-tetrazol-5-yl)-2-benzofuran-carboxamide (Parvez, Unangst, Connor & Mullican, 1991*b*)] effective on H1 receptors, the crystal structure of clemizole hydrochloride, (1), has been determined and is described herein.



An ORTEP drawing (Johnson, 1976) of (1) with the atomic numbering scheme is shown in Fig. 1. The molecular dimensions in the cation are unexceptional, with mean bond distances Cl—C_{sp²} 1.722 (9), N—C_{sp³} 1.50 (3), N—C_{sp²} 1.37 (1), C_{sp³}—C_{sp³} (in the pyrrolidinium ring) 1.49 (3), C_{sp³}—C_{sp²} 1.50 (1), C—C_{aromatic} 1.38 (1) and C=N 1.325 (8) Å, and normal angles. The benzimidazole moiety and the six-membered phenyl ring are essentially planar, with maximum deviations from the respective least-squares planes of 0.006 (9) and

0.016 (9) Å; the planes are inclined at almost right angles to one another [82.8 (9)°]. The pyrrolidinium ring has an N3-envelope conformation, with the N3 atom 0.537 (6) Å out of the plane of the remaining four C atoms of the ring [maximum deviation of 0.04 (1) Å for the C17 atom].

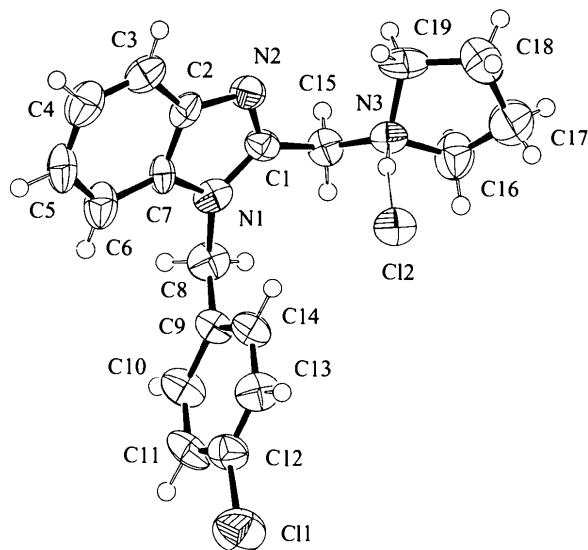


Fig. 1. An ORTEP drawing (Johnson, 1976) of the title compound with the atomic numbering scheme. Displacement ellipsoids are plotted at the 50% probability level and H atoms have been assigned arbitrary radii.

The clemizole cation is hydrogen bonded to the chloride ion *via* normal N—H···Cl interactions (Table 2).

Experimental

Colourless prismatic crystals of the title compound (Sigma Inc.) were grown from a mixture of CH₃OH/CH₃CN (1:1) by slow evaporation at room temperature.

Crystal data

C₁₉H₂₁ClN₃⁺·Cl⁻

M_r = 362.30

Monoclinic

*P*2₁/*n*

a = 5.525 (2) Å

b = 10.968 (3) Å

c = 30.003 (5) Å

β = 91.01 (3)°

V = 1817.8 (7) Å³

Z = 4

D_x = 1.324 Mg m⁻³

D_m not measured

Mo *K*α radiation

λ = 0.71069 Å

Cell parameters from 17 reflections

θ = 18.4–24.4°

μ = 0.362 mm⁻¹

T = 296 K

Needle

0.50 × 0.40 × 0.30 mm

Colourless

Data collection

Rigaku AFC-6S diffractometer

ω/2θ scans

1488 observed reflections

[*I* > 3σ(*I*)]

*R*_{int} = 0.044