127 parameters
H-atom parameters obtained from difference map and not refined
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}
O	0.5649 (5)	0.1874 (3)	0.9878 (5)	5.0 (3)
N1	0.7836 (6)	0.2628 (3)	1.1743 (6)	4.3 (3)
N2	0.7359 (7)	−0.0834 (3)	1.5767 (7)	4.1 (3)
N3	0.8149 (7)	−0.0679 (3)	1.7329 (7)	4.8 (3)
N4	0.8235 (7)	−0.1328 (3)	1.8319 (7)	5.1 (4)
C1	0.7012 (8)	0.1236 (4)	1.2536 (7)	3.4 (3)
C2	0.5933 (8)	0.0532 (4)	1.2050 (7)	4.0 (4)
C3	0.6072 (8)	−0.0146 (4)	1.3125 (8)	4.4 (4)
C4	0.7307 (8)	−0.0103 (4)	1.4747 (7)	3.4 (4)
C5	0.8394 (8)	0.0600 (4)	1.5266 (7)	3.7 (4)
C6	0.8278 (8)	0.1267 (4)	1.4177 (7)	3.9 (4)
C7	0.6789 (8)	0.1936 (4)	1.1287 (8)	3.9 (4)
C8	0.9029 (10)	−0.1171 (4)	2.0130 (9)	7.2 (5)
C9	0.7426 (9)	−0.2156 (4)	1.7716 (8)	5.7 (4)

Table 2. *Selected geometric parameters* (Å, °)

O—C7	1.232 (7)	C1—C2	1.376 (9)
N1—C7	1.345 (8)	C1—C6	1.412 (8)
N2—N3	1.282 (8)	C1—C7	1.498 (8)
N2—C4	1.433 (8)	C2—C3	1.385 (9)
N3—N4	1.312 (8)	C3—C4	1.392 (8)
N4—C8	1.470 (9)	C4—C5	1.380 (9)
N4—C9	1.466 (8)	C5—C6	1.383 (9)
N3—N2—C4	112.1 (5)	C2—C3—C4	119.0 (6)
N2—N3—N4	114.6 (5)	N2—C4—C3	115.1 (6)
N3—N4—C8	116.7 (5)	N2—C4—C5	124.5 (5)
N3—N4—C9	123.4 (5)	C3—C4—C5	120.4 (6)
C8—N4—C9	119.6 (5)	C4—C5—C6	120.3 (5)
C2—C1—C6	118.9 (5)	C1—C6—C5	119.8 (5)
C2—C1—C7	118.1 (5)	O—C7—N1	121.3 (6)
C6—C1—C7	123.0 (6)	O—C7—C1	120.0 (6)
C1—C2—C3	121.6 (5)	N1—C7—C1	118.8 (5)

D—H···*A*	H···*A*	*D*···*A*	*D*—H···*A*
N1—HN1*A*···O^{i}	1.93	2.935 (6)	150
N1—HN1*B*···N2^{ii}	2.10	3.197 (7)	169

Symmetry codes: (i) $\frac{1}{2}+x, \frac{1}{2}-y, \frac{1}{2}+z$; (ii) $\frac{3}{2}-x, \frac{1}{2}+y, \frac{5}{2}-z$.

Table 3. *Comparison of bond lengths* (Å) *of selected triazenes*

	(2)	(3)[a]	(4)[b]	(5)[c]	(6)[a]	(7)[d]
C4—N2	1.433 (8)	1.415 (2)	1.418 (1)	1.422 (3)	1.48 (2)	1.429 (8)
N2—N3	1.282 (8)	1.282 (2)	1.270 (1)	1.275 (3)	1.29 (2)	1.281 (7)
N3—N4	1.312 (8)	1.307 (2)	1.316 (1)	1.319 (3)	1.344 (15)	1.309 (7)
N4—C8	1.470 (9)	1.454 (2)	1.445 (2)	1.451 (4)	1.46 (2)	1.45 (1)

References: (*a*) Neidle & Wilman (1992); (*b*) Fronczek, Hansch & Watkins (1988); (*c*) Randall, Schwalbe & Vaughan (1984); (*d*) Edwards, Chapuis, Templeton & Zalkin (1977).

All crystallographic calculations were conducted with the PC version of the *NRCVAX* program package (Gabe, Le Page, Charland, Lee & White, 1989) locally implemented on an IBM compatible 80486 computer.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: FG1045). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Ondansetron Hydrochloride: a Competitive Serotonin 5-HT$_3$ Receptor Blocker

K. Chandra Mohan and K. Ravikumar

Laboratory of Crystallography, Indian Institute of Chemical Technology, Hyderabad 500 007, India

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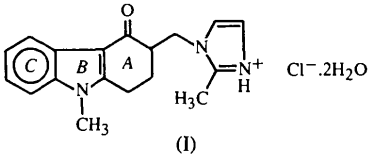
Abstract

The methyl substituted imidazole ring in the title compound, 2-methyl-1-(9-methyl-4-oxo-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl)imidazol-3-ium chloride dihydrate, $C_{18}H_{20}N_3O^+.Cl^-.2H_2O$, is approximately perpendicular to the carbazole plane [dihedral angle 87.0 (1)°]. The water molecules are involved in an elaborate network of hydrogen bonds that reinforce the stability of the dihydrate and the cohesion of the structure.

Comment

Ondansetron hydrochloride dihydrate, (I), is a structurally novel competitive serotonin 5-HT_3 receptor blocker that has proved useful in the prevention of emesis caused by cisplatin and other cancer chemotherapeutic agents (Bozigian, Pritchard, Gooding & Pakes, 1994). The crystal structure analysis of this compound was undertaken to ascertain the conformation of the imidazole side chain with respect to the carbazole moiety of the molecule. Furthermore, the forces responsible for crystal-packing cohesion were examined to find out which functional groups of the title molecule are likely to interact at the receptor site.



(I)

A perspective view of the molecule showing the atom-numbering scheme is shown in Fig. 1. The three-fused-ring fragment, carbazole, is planar with an average deviation of 0.023 Å from the 12-atom least-square plane when C6 [deviation of 0.538 (6) Å] is excluded. At the *A/B* ring junction the torsion angles C1—C2—C3—C4 and N1—C2—C3—C7 are 1.0 (6) and 0.7 (4)°, respectively, and at the *B/C* junction N1—C12—C7—C3 and C11—C12—C7—C8 are −0.1 (4) and −1.0 (6)°, respectively. The angles between the best planes of the rings are: *A*^*B* 5.0 (1), *B*^*C* 1.8 (1) and *C*^*A* 6.8 (1)°.

The imidazole ring is planar, with no atom deviating from the least-square plane through the five atoms by more than 0.007 (5) Å. The angle between the plane of the carbazole ring system and that of the imidazole ring is 87.0 (1)°. The torsional rotations about the C5—C13 and C13—N2 bonds are 40.1 (6) and 74.0 (5)°, respectively.

Crystal cohesion (Fig. 2.) is due, in part, to an intermolecular network of hydrogen bonds involving water molecules and Cl^- ions, which form bridges between water molecules. The protonated N3 atom of the imidazole ring participates in an N—H···O(water) hydrogen bond connecting the $C_{18}H_{20}N_3O^+$ cation to the Cl^- anion *via* a water molecule. By analogy, the imidazole ring may well anchor carbazole to specific amino acids in the binding site of the receptor.

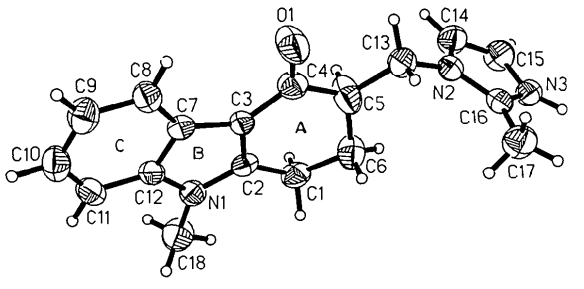


Fig. 1. The molecular structure (*SHELXTL-Plus*, Sheldrick, 1991) of the ondansetron cation showing 50% probability ellipsoids.

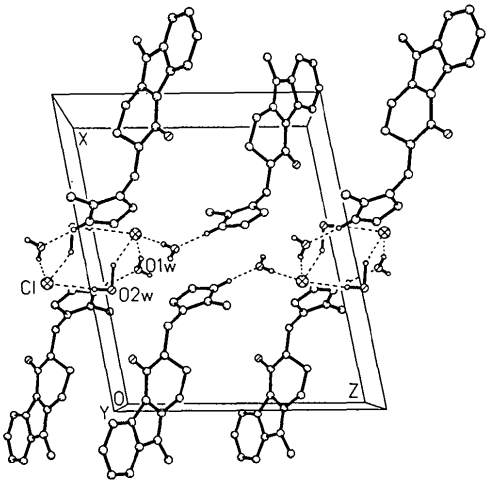


Fig. 2. The crystal structure of ondansetron hydrochloride dihydrate viewed down the *b* axis. Hydrogen bonds are represented by dashed lines. Only H atoms attached to O and N atoms are shown.

Experimental

Crystals of the title compound were obtained from an aqueous methanol solution of the drug (from NATCO Laboratories, Hyderabad, India).

Crystal data

$C_{18}H_{20}N_3O^+.Cl^-.2H_2O$
M_r = 365.86
Monoclinic
$P2_1/c$
a = 15.185 (2) Å
b = 9.810 (1) Å
c = 12.823 (2) Å
β = 100.89 (2)°
V = 1875.8 (4) Å^3
Z = 4
D_x = 1.295 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 25 reflections
θ = 5–18°
μ = 0.23 mm^{-1}
T = 293 K
Cubic
0.20 × 0.18 × 0.15 mm
Transparent colourless

Data collection

Siemens *R3m/V* diffractometer
$\omega/2\theta$ scans
Absorption correction: none
2860 measured reflections
2800 independent reflections
1918 observed reflections [$I \geq 3\sigma(I)$]
R_{int} = 0.043
θ_{max} = 22.5°
h = 0 → 16
k = 0 → 10
l = −13 → 13
2 standard reflections monitored every 98 reflections
intensity decay: ≤1%

Refinement

Refinement on F
R = 0.051
wR = 0.062
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

$S = 1.20$
1918 reflections
226 parameters
$w = 1/[\sigma^2(F) + 0.0046F^2]$
Extinction correction: none
Atomic scattering factors from *SHELXTL-Plus* (Sheldrick, 1991)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

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

	x	y	z	U_{eq}
Cl	0.5860 (1)	0.0743 (1)	0.6893 (1)	0.063 (1)
N1	1.1076 (2)	0.0459 (3)	0.3806 (2)	0.040 (1)
N2	0.6772 (2)	0.0015 (3)	0.1805 (2)	0.039 (1)
N3	0.6020 (2)	−0.0989 (3)	0.0418 (2)	0.043 (1)
O1	0.8395 (2)	0.2511 (3)	0.4049 (3)	0.068 (1)
C1	0.9709 (3)	−0.0616 (4)	0.2646 (3)	0.045 (1)
C2	1.0173 (3)	0.0369 (4)	0.3436 (3)	0.035 (1)
C3	0.9739 (2)	0.1411 (4)	0.3900 (3)	0.033 (1)
C4	0.8785 (3)	0.1600 (4)	0.3654 (3)	0.042 (2)
C5	0.8265 (3)	0.0565 (5)	0.2875 (4)	0.063 (2)
C6	0.8775 (3)	−0.0118 (7)	0.2143 (5)	0.052 (2)
C7	1.0430 (2)	0.2184 (4)	0.4584 (3)	0.034 (1)
C8	1.0434 (3)	0.3321 (4)	0.5235 (3)	0.043 (1)
C9	1.1246 (3)	0.3829 (4)	0.5761 (3)	0.051 (2)
C10	1.2058 (3)	0.3218 (4)	0.5665 (3)	0.050 (2)
C11	1.2082 (2)	0.2060 (4)	0.5047 (3)	0.045 (1)
C12	1.1254 (2)	0.1559 (4)	0.4504 (3)	0.035 (1)
C13	0.7307 (3)	0.0995 (4)	0.2505 (3)	0.047 (1)
C14	0.6461 (3)	−0.1222 (5)	0.2134 (3)	0.051 (1)
C15	0.5999 (3)	−0.1843 (5)	0.1275 (3)	0.053 (2)
C16	0.6487 (2)	0.0127 (4)	0.0746 (3)	0.038 (1)
C17	0.6649 (3)	0.1293 (5)	0.0053 (4)	0.057 (2)
C18	1.1769 (3)	−0.0492 (5)	0.3564 (4)	0.062 (2)
O1*W*	0.4759 (2)	0.1486 (4)	0.1618 (2)	0.076 (1)
O2*W*	0.3919 (2)	0.5064 (5)	0.0536 (3)	0.094 (2)

Table 2. *Hydrogen-bonding geometry* (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1*W*—H1*W*1···Cl^{i}	0.862 (5)	2.299 (4)	3.160 (4)	177.2 (4)
O1*W*—H2*W*1···Cl^{ii}	0.965 (5)	2.243 (4)	3.176 (4)	162.4 (3)
O2*W*—H1*W*2···Cl^{ii}	1.269 (5)	2.135 (4)	3.226 (4)	141.4 (3)
O2*W*—H2*W*2···Cl^{iii}	0.872 (6)	2.402 (4)	3.264 (4)	170.3 (5)
N3—H3···O1*W*^{iv}	0.900 (4)	1.800 (4)	2.699 (4)	178.7 (4)

Symmetry codes: (i) $1-x, -y, 1-z$; (ii) $x, \frac{1}{2}-y, z-\frac{1}{2}$; (iii) $1-x, \frac{1}{2}+y, \frac{1}{2}-z$; (iv) $1-x, -y, -z$.

H-atoms were located from difference Fourier maps and included as riding atoms with fixed isotropic displacement parameters in the structure-factor calculations.

Data collection: Siemens (1994) *P3 Software*. Cell refinement: *P3 Software*. Data reduction: *SHELXTL-Plus* (Sheldrick, 1991). Program(s) used to solve structure: *SHELXTL-Plus*. Program(s) used to refine structure: *SHELXTL-Plus*. Molecular graphics: *SHELXTL-Plus*. Software used to prepare material for publication: *PARST* (Nardelli, 1983).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: VJ1025). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Molecular Co-Crystals of Carboxylic Acids. 22.† The Adducts of Pyrazine-2,3-dicarboxylic Acid with 2-Aminobenzoic Acid (1:2) and 3-Aminobenzoic Acid (1:1 Dihydrate)

GRAHAM SMITH* AND DANIEL E. LYNCH

School of Chemistry, Queensland University of Technology, PO Box 2434, Brisbane 4001, Australia

KARL A. BYRIEL AND COLIN H. L. KENNARD

Department of Chemistry, The University of Queensland, Brisbane 4072, Australia

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Abstract

The structures of two molecular adducts of pyrazine-2,3-dicarboxylic acid (PDCA) with the carboxylic acids 2-aminobenzoic acid (2-ABA), *i.e.* bis(2-carboxyphenylammonium) 2,3-pyrazinedicarboxylate, [(PDCA)$^{2-}$(2-ABA$^+$)$_2$], (1), and 3-aminobenzoic acid (3-ABA), *i.e.* 3-carboxyphenylammonium hydrogen 2,3-pyrazinedicarboxylate dihydrate, [(PDCA)(3-ABA)$^+$.2H$_2$O], (2), have been determined by X-ray diffraction. In adduct (1), each carboxylic acid group of PDCA protonates an amino group of a two 2-ABA molecule. The ion pairs then associate *via* hydrogen bonding giving a three-dimensional network structure. In (2), a single proton transfer occurs. The protonated amine group of 3-ABA then forms hydrogen bonds with the carboxylate O atoms and the hetero N atom of PDCA as well as with the water molecules. The two 3-ABA molecules also associate to form a cyclic hydrogen-bonded dimer. This results in a three-dimensional network structure.

Comment

The aromatic heterocyclic dicarboxylic acid pyrazine-2,3-dicarboxylic (PDCA) provides an example of a proton-donor molecule which has the potential to give

† Part 21: Smith, Gentner, Lynch, Byriel & Kennard (1995).