C(4B)	0.578 (1)	−0.065 (1)	0.3746 (9)	0.078 (7)
C(5B)	0.686 (1)	0.058 (1)	0.3743 (9)	0.072 (6)
C(6B)	0.682 (1)	0.063 (1)	0.259 (1)	0.075 (6)
C(7B)	0.797 (1)	0.172 (1)	0.491 (1)	0.089 (7)
N(8B)	0.363 (1)	−0.2833 (9)	0.0471 (8)	0.096 (6)
C(10B)	0.359 (1)	−0.281 (1)	−0.072 (1)	0.099 (7)
C(12B)	0.465 (2)	−0.319 (1)	−0.122 (1)	0.128 (9)
C(9B)	0.908 (1)	0.287 (1)	0.503 (1)	0.100 (8)
N(14B)	1.014 (1)	0.393 (1)	0.624 (1)	0.113 (8)
O(15B)	1.126 (1)	0.493 (1)	0.6241 (8)	0.145 (7)
O(16B)	0.989 (1)	0.380 (1)	0.7152 (9)	0.143 (7)
C(11B)†	0.236 (2)	−0.421 (2)	0.041 (2)	0.130 (9)
C(13B)†	0.311 (3)	−0.503 (2)	0.047 (2)	0.121 (9)
C(21B)‡	0.288 (5)	−0.417 (4)	0.054 (3)	
C(23B)‡	0.123 (5)	−0.476 (4)	0.065 (4)	

† Occupancy 0.6.
‡ Occupancy 0.4.

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

C(1A)—C(2A)	1.43 (2)	C(1B)—C(2B)	1.42 (1)
C(1A)—C(6A)	1.39 (1)	C(1B)—C(6B)	1.35 (1)
C(2A)—C(3A)	1.42 (2)	C(2B)—C(3B)	1.41 (2)
C(2A)—N(8A)	1.356 (9)	C(2B)—N(8B)	1.38 (1)
C(3A)—C(4A)	1.36 (1)	C(3B)—C(4B)	1.37 (1)
C(4A)—C(5A)	1.39 (2)	C(4B)—C(5B)	1.40 (2)
C(5A)—C(6A)	1.41 (2)	C(5B)—C(6B)	1.42 (2)
C(5A)—C(7A)	1.46 (1)	C(5B)—C(7B)	1.47 (1)
C(7A)—C(9A)	1.31 (2)	C(7B)—C(9B)	1.29 (2)
N(8A)—C(10A)	1.48 (2)	N(8B)—C(10B)	1.47 (2)
N(8A)—C(11A)	1.45 (1)	N(8B)—C(11B)	1.55 (2)
C(9A)—N(14A)	1.44 (1)	N(8B)—C(21B)	1.47 (1)
C(10A)—C(12A)	1.49 (2)	C(9B)—N(14B)	1.47 (1)
C(11A)—C(13A)	1.50 (2)	C(10B)—C(12B)	1.50 (2)
N(14A)—O(15A)	1.21 (1)	C(11B)—C(13B)	1.49 (4)
N(14A)—O(16A)	1.23 (2)	C(11B)—C(21B)	0.52 (2)
		C(21B)—C(23B)	1.59 (2)
		N(14B)—O(15B)	1.25 (2)
		N(14B)—O(16B)	1.22 (2)

C(2A)—C(1A)—C(6A)	121 (1)	C(2B)—C(1B)—C(6B)	121 (1)
C(1A)—C(2A)—C(3A)	116.4 (7)	C(1B)—C(2B)—C(3B)	117.2 (7)
C(1A)—C(2A)—N(8A)	120 (1)	C(1B)—C(2B)—N(8B)	121 (1)
C(3A)—C(2A)—N(8A)	124 (1)	C(3B)—C(2B)—N(8B)	121.8 (9)
C(2A)—C(3A)—C(4A)	122 (1)	C(2B)—C(3B)—C(4B)	122 (1)
C(3A)—C(4A)—C(5A)	121 (1)	C(3B)—C(4B)—C(5B)	121 (1)
C(4A)—C(5A)—C(6A)	118.6 (7)	C(4B)—C(5B)—C(6B)	117.2 (7)
C(4A)—C(5A)—C(7A)	120 (1)	C(4B)—C(5B)—C(7B)	118 (1)
C(6A)—C(5A)—C(7A)	122 (1)	C(6B)—C(5B)—C(7B)	124.7 (9)
C(1A)—C(6A)—C(5A)	121 (1)	C(1B)—C(6B)—C(5B)	122 (1)
C(5A)—C(7A)—C(9A)	126 (1)	C(5B)—C(7B)—C(9B)	124 (1)
C(2A)—N(8A)—C(10A)	122.5 (9)	C(2B)—N(8B)—C(10B)	122.4 (9)
C(2A)—N(8A)—C(11A)	121 (1)	C(2B)—N(8B)—C(11B)	123 (1)
C(9A)—N(14A)—O(15A)	117 (1)	C(2B)—N(8B)—C(21B)	114.9 (9)
C(9A)—N(14A)—O(16A)	120 (1)	C(9B)—N(14B)—O(15B)	114 (1)
C(10A)—N(8A)—C(11A)	115.9 (7)	C(9B)—N(14B)—O(16B)	121 (1)
N(8A)—C(10A)—C(12A)	112 (1)	C(10B)—N(8B)—C(11B)	114.1 (9)
N(8A)—C(11A)—C(13A)	114 (1)	C(10B)—N(8B)—C(21B)	119.6 (6)
C(7A)—C(9A)—N(14A)	121 (1)	N(8B)—C(10B)—C(12B)	113 (1)
O(15A)—N(14A)—O(16A)	123.4 (8)	N(8B)—C(11B)—C(13B)	104 (2)
		N(8B)—C(21B)—C(23B)	119 (4)
		C(7B)—C(9B)—N(14B)	120 (1)
		O(15B)—N(14B)—O(16B)	125.2 (9)

In the disordered branch, the pairs [C(11B), C(13B)] and [C21(B), C23(B)] were refined alternatively because of correlations. Isotropic displacement parameters for [C21(B), C(23B)] were not refined.

The structure was solved using *PATSEE* (*Xtal*; Hall & Stewart, 1990).

Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the IUCr (Reference: PA1096). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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9-(4-Methyl-1-piperazinyl)-9,10-dihydro-9,10-ethanoanthracene Hydrochloride Dihydrate (Trazitilin)

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Abstract

The title compound, trazitilin, $C_{21}H_{24}N_2 \cdot HCl \cdot 2H_2O$, is an antagonist of histamine H1 receptors. Steric hindrance of the two components of the molecule (the piperazinyl radical and 9,10-dihydro-9,10-ethanoanthracene) causes a slight distortion of substituents and allows the structure very little flexibility.

Comment

As part of our conformational studies on antihistamine drugs, we investigated the X-ray structure of trazitilin. This compound as a whole is quite rigid and can be used therefore as a basis for the modeling of histamine H1 receptors (Brouant & Barbe, 1992).

(I)
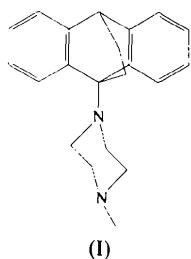
Trazitilin crystallizes with two water molecules and one hydrochloride molecule. An intermolecular bonding search reveals that some interactions occur between trazitilin and these molecules. The chloride ion is located at the center of a very flattened tetrahedral complex comprising the two water molecules, the atom N2 from an adjacent cell and one water molecule from a third cell (Fig. 2). The water molecules are themselves connected to atoms of adjacent cells and generate an endless lattice of hydrogen bonds surrounding the molecules of trazitilin. Characteristic contact parameters are reported in Table 3.

The interaction between N2 and the chloride ion is probably the result of the protonation of the N atom; the values of the three angles C1—N2^i—C21^i [98.9 (3)°], C1—N2^i—C19^i [103.7 (2)°] and C1—N2^i—C18^i [120.8 (2)°] (see Fig. 2) lead to this interpretation. No interactions are observed between N1 and other atoms. These results agree with the general observations found for polycyclic compounds substituted by piperazinyl radicals, where the distant N atom is protonated preferentially by acids in solution.

The bonding of the piperazinyl radical to 9,10-dihydro-9,10-ethanoanthracene involves slight dis-

tortions of the latter. These deformations can be described easily in terms of two geometrical features and may be compared to those of similar compounds substituted with smaller components such as methylaminomethyl in benzoctamin (Brouant, Pierrot, Baldy, Soyfer & Barbe, 1984). The ethylene bridge torsion angle C7—C11—C12—C10 is −3.7 (3)° in trazitilin and 1.2 (3)° in benzoctamin, while the angle between the directions C4···C1 and C13···C16 is 4.0 (3)° in trazitilin and 0.5 (2)° in benzoctamin.

Conformational analysis shows that the rotating bond between the polycyclic fragment and the piperazinyl group allows only weak oscillations (±7° within an energy range of 6 kcal mol^{-1}; 1 cal = 4.184 J) around the observed value of −158.0 (2)° for C6—C10—N1—C17.
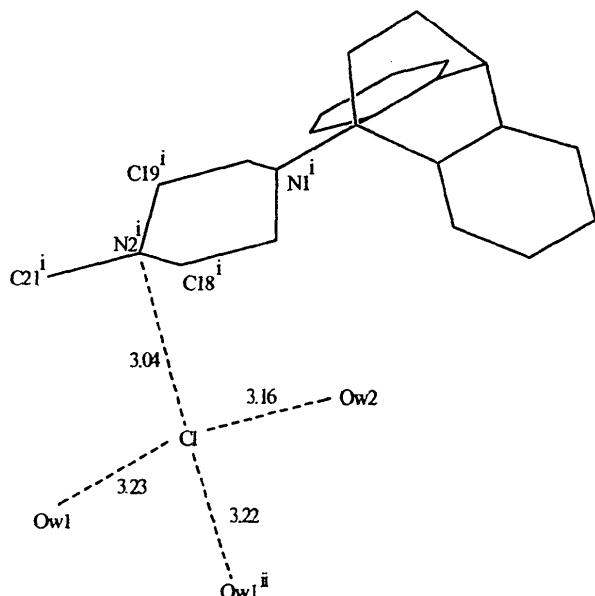

Fig. 2. Intermolecular interactions in the title compound. Symmetry codes: (i) x, y, $1 + z$; (ii) $1 - x$, $1 - y$, $1 - z$.

Experimental

Crystal data
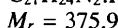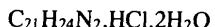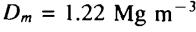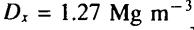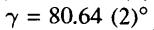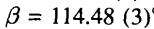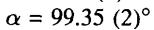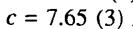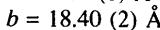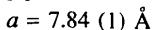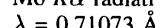
Fig. 1. ORTEPII view (Johnson, 1976) of the title compound. Displacement ellipsoids are drawn at the 50% probability level.
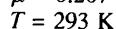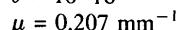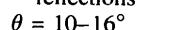
$C_{21}H_{24}N_2.HCl.2H_2O$	Mo $K\alpha$ radiation
$M_r = 375.9$	$\lambda = 0.71073$ Å
Triclinic	Cell parameters from 25
$P\bar{1}$	reflections
$a = 7.84$ (1) Å	$\theta = 10–16°$
$b = 18.40$ (2) Å	$\mu = 0.207$ mm^{-1}
$c = 7.65$ (3) Å	$T = 293$ K
$\alpha = 99.35$ (2)°	Orthorhombic
$\beta = 114.48$ (3)°	0.5 × 0.3 × 0.3 mm
$\gamma = 80.64$ (2)°	Transparent
$V = 987.2$ (6) Å^3	Crystal source: evaporation
$Z = 2$	of a saturated 50/50%
$D_x = 1.27$ Mg m^{-3}	H$_2$O/ethanol solution
$D_m = 1.22$ Mg m^{-3}	

Data collection

Enraf–Nonius CAD-4 diffractometer	$R_{int} = 0.022$
	$\theta_{max} = 24°$
θ–2θ scans	$h = -8 \rightarrow 8$
Absorption correction: none	$k = 0 \rightarrow 21$
	$l = -8 \rightarrow 8$
3187 measured reflections	2 standard reflections
3078 independent reflections	frequency: 60 min
2064 observed reflections	intensity decay: 2.4%
$[F > 3\sigma(F)]$	

Refinement

Refinement on F	$(\Delta/\sigma)_{max} = 0.02$
$R = 0.051$	$\Delta\rho_{max} = 0.44$ (2) e Å^{-3}
$wR = 0.054$	$\Delta\rho_{min} = -0.26$ (2) e Å^{-3}
$S = 0.854$	Extinction correction: none
2064 reflections	Atomic scattering factors
235 parameters	from *International Tables*
H-atom parameters not refined	*for X-ray Crystallography* (1974, Vol. IV)
Unit weights applied	

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

$$B_{eq} = (4/3)\Sigma_i\Sigma_j\beta_{ij}a_i.a_j.$$

	x	y	z	B_{eq}
C1	0.7057 (5)	0.1129 (2)	0.2381 (5)	2.56 (8)
C2	0.7976 (5)	0.0427 (2)	0.2784 (5)	2.99 (9)
C3	0.7064 (5)	−0.0121 (2)	0.2941 (5)	3.03 (9)
C4	0.5214 (5)	0.0035 (2)	0.2767 (5)	2.86 (8)
C5	0.4295 (4)	0.0735 (2)	0.2369 (5)	2.38 (8)
C6	0.5187 (4)	0.1282 (2)	0.2128 (4)	2.24 (8)
C7	0.2347 (4)	0.1000 (2)	0.2292 (5)	2.69 (8)
C8	0.1224 (4)	0.1310 (2)	0.0402 (5)	2.46 (8)
C9	0.2052 (4)	0.1863 (2)	0.0072 (5)	2.37 (8)
C10	0.3957 (4)	0.2025 (2)	0.1720 (5)	2.35 (8)
C11	0.2599 (5)	0.1647 (2)	0.3911 (5)	3.04 (9)
C12	0.3484 (5)	0.2270 (2)	0.3541 (5)	2.84 (8)
C13	−0.0492 (5)	0.1099 (2)	−0.0936 (5)	3.02 (9)
C14	−0.1386 (5)	0.1431 (2)	−0.2634 (5)	3.38 (9)
C15	−0.0597 (5)	0.1988 (2)	−0.2951 (5)	3.35 (9)
C16	0.1118 (5)	0.2213 (2)	−0.1598 (5)	2.88 (9)
C17	0.4388 (5)	0.3359 (2)	0.1777 (5)	3.38 (9)
C18	0.6030 (6)	0.3794 (2)	0.2262 (6)	4.0 (1)
C19	0.7228 (5)	0.2834 (2)	0.0309 (6)	3.74 (9)
C20	0.5500 (5)	0.2441 (2)	−0.0173 (5)	3.06 (8)
C21	0.8458 (6)	0.4053 (3)	0.1244 (7)	5.7 (1)
N1	0.4987 (4)	0.2571 (2)	0.1482 (4)	2.61 (7)
N2	0.6776 (4)	0.3645 (2)	0.0713 (5)	3.69 (8)
Cl	0.4433 (2)	0.41486 (7)	0.6735 (2)	5.55 (3)
Ow1	0.7949 (5)	0.4884 (2)	0.6824 (6)	8.1 (1)
Ow2	0.0506 (6)	0.3676 (2)	0.6113 (7)	10.4 (2)

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

C1—C2	1.388 (5)	C10—C12	1.567 (5)
C1—C6	1.384 (5)	C10—N1	1.464 (5)
C2—C3	1.375 (6)	C11—C12	1.550 (6)
C3—C4	1.386 (5)	C13—C14	1.385 (5)
C4—C5	1.383 (5)	C14—C15	1.380 (7)
C5—C6	1.390 (6)	C15—C16	1.393 (5)
C5—C7	1.507 (5)	C17—C18	1.510 (6)
C6—C10	1.536 (6)	C17—N1	1.461 (4)
C7—C8	1.498 (5)	C18—N2	1.497 (6)
C7—C11	1.545 (5)	C19—C20	1.521 (6)
C8—C9	1.399 (6)	C19—N2	1.489 (5)
C8—C13	1.382 (4)	C20—N1	1.456 (5)
C9—C10	1.541 (4)	C21—N2	1.500 (6)
C9—C16	1.387 (5)		

C2—C1—C6	119.6 (4)	C6—C10—N1	110.8 (3)
C1—C2—C3	121.2 (3)	C9—C10—C12	104.5 (3)
C2—C3—C4	119.5 (3)	C9—C10—N1	117.8 (3)
C3—C4—C5	119.3 (4)	C12—C10—N1	110.7 (3)
C4—C5—C6	121.3 (3)	C7—C11—C12	109.8 (3)
C4—C5—C7	125.1 (4)	C10—C12—C11	110.2 (3)
C6—C5—C7	113.5 (3)	C8—C13—C14	119.6 (4)
C1—C6—C5	118.9 (3)	C13—C14—C15	120.0 (3)
C1—C6—C10	127.0 (3)	C14—C15—C16	120.7 (3)
C5—C6—C10	114.0 (3)	C9—C16—C15	119.4 (4)
C5—C7—C8	107.5 (3)	C18—C17—N1	109.0 (3)
C5—C7—C11	105.7 (3)	C17—C18—N2	111.4 (3)
C8—C7—C11	107.8 (3)	C20—C19—N2	109.5 (3)
C7—C8—C9	113.9 (3)	C19—C20—N1	108.7 (3)
C7—C8—C13	125.4 (4)	C10—N1—C17	119.3 (3)
C9—C8—C13	120.7 (3)	C10—N1—C20	118.1 (3)
C8—C9—C10	113.3 (3)	C17—N1—C20	108.9 (3)
C8—C9—C16	119.5 (3)	C18—N2—C19	110.3 (3)
C10—C9—C16	127.1 (4)	C18—N2—C21	111.1 (3)
C6—C10—C9	107.4 (3)	C19—N2—C21	111.3 (3)
C6—C10—C12	104.6 (3)		

Table 3. *Intermolecular contact parameters* (Å)

Cl$\cdots$N2^i	3.040 (3)	Cl$\cdots$Ow2	3.160 (5)
Cl$\cdots$Ow1	3.235 (5)	Ow1$\cdots$Ow2^{iii}	2.885 (6)
Cl$\cdots$Ow1^{ii}	3.219 (4)		
N2$^i\cdots$Cl$\cdots$Ow1	91.1 (1)	Ow1$\cdots$Cl$\cdots$Ow1^{ii}	83.3 (1)
N2$^i\cdots$Cl$\cdots$Ow1^{ii}	164.5 (1)	Ow1$\cdots$Cl$\cdots$Ow2	168.6 (1)
N2$^i\cdots$Cl$\cdots$Ow2	98.9 (1)	Ow1$^{ii}\cdots$Cl$\cdots$Ow2	85.6 (1)

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

The H atoms of the water molecules and the N2 proton were not introduced or found by difference Fourier methods. Data collection: CAD-4 software. Data reduction and structure resolution: *SDP* software package (Frenz, 1978) and direct methods *MULTAN*80 (Main *et al.*, 1980), completed by Fourier synthesis. H atoms were introduced at idealized positions in the calculation before the last refinement cycle but were not refined. Conformational analysis was performed using *SYBYL* (TRIPOS, 1993).

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