C1—C5—C11	120.6 (6)	C1′—C5′—C11′	120.1 (7)
C4—C5—C11	110.8 (6)	C4′—C5′—C11′	110.5 (7)
O6—C5—C11	105.2 (6)	O6′—C5′—C11′	106.7 (7)
C5—O6—C7	112.6 (4)	C5′—O6′—C7′	113.4 (5)
O6—C7—O7	110.3 (5)	O6′—C7′—O7′	110.4 (5)
O6—C7—C8	106.5 (5)	O6′—C7′—C8′	106.8 (5)
O7—C7—C8	111.2 (5)	O7′—C7′—C8′	109.8 (6)
O6—C7—C12	107.1 (5)	O6′—C7′—C12′	107.1 (7)
O7—C7—C12	107.5 (7)	O7′—C7′—C12′	108.4 (6)
C8—C7—C12	114.1 (6)	C8′—C7′—C12′	114.3 (6)
C1—C8—C7	104.0 (5)	C1′—C8′—C7′	104.1 (6)
C1—C9—F1	109.1 (6)	C1′—C9′—F1′	109.8 (8)
C1—C9—F2	111.8 (6)	C1′—C9′—F2′	113.3 (8)
F1—C9—F2	106.5 (5)	F1′—C9′—F2′	108.3 (8)
C1—C9—F3	113.1 (6)	C1′—C9′—F3′	110.9 (8)
F1—C9—F3	107.3 (7)	F1′—C9′—F3′	106.0 (8)
F2—C9—F3	108.7 (6)	F2′—C9′—F3′	108.2 (8)
C3—C10—F4	111.9 (7)	C3′—C10′—F4′	112.9 (6)
C3—C10—F5	110.9 (6)	C3′—C10′—F5′	112.1 (7)
F4—C10—F5	105.9 (6)	F4′—C10′—F5′	106.7 (7)
C3—C10—F6	111.5 (6)	C3′—C10′—F6′	110.4 (8)
F4—C10—F6	107.7 (7)	F4′—C10′—F6′	106.7 (7)
F5—C10—F6	108.7 (7)	F5′—C10′—F6′	107.7 (7)
C5—C11—F7	111.9 (7)	C5′—C11′—F7′	112.5 (9)
C5—C11—F8	112.0 (6)	C5′—C11′—F8′	111.5 (8)
F7—C11—F8	106.8 (7)	F7′—C11′—F8′	107.5 (9)
C5—C11—F9	111.2 (7)	C5′—C11′—F9′	107.9 (9)
F7—C11—F9	107.4 (6)	F7′—C11′—F9′	109.0 (9)
F8—C11—F9	107.3 (7)	F8′—C11′—F9′	108.3 (10)
C7—C12—F10	111.1 (7)	C7′—C12′—F10′	111.7 (7)
C7—C12—F11	111.3 (7)	C7′—C12′—F11′	112.0 (7)
F10—C12—F11	107.3 (6)	F10′—C12′—F11′	106.3 (8)
C7—C12—F12	110.9 (6)	C7′—C12′—F12′	111.9 (8)
F10—C12—F12	108.1 (8)	F10′—C12′—F12′	107.8 (7)
F11—C12—F12	108.1 (7)	F11′—C12′—F12′	106.9 (7)

Data were corrected for Lorentz and polarization effects. The structure solution, by direct methods, and the full-matrix least-squares refinement used programs in *SHELXTL-Plus* (Sheldrick, 1987). Hydroxyl H-atom coordinates were refined with fixed isotropic displacement parameters.

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Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the IUCr (Reference: CR1114). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Ebrotidine

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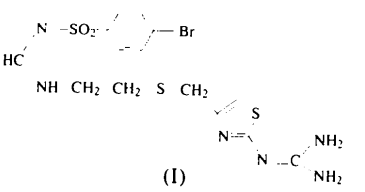
Abstract

The crystal structure of a new histamine H_2-receptor antagonist, 4-bromo-*N*-[2-({2-[(diaminomethylene)-amino]-1,3-thiazol-4-yl}methylthio)ethylaminomethylene]benzenesulfonamide, $C_{14}H_{17}BrN_6O_2S_3$, has been determined. The main difference between the title compound and other related derivatives is in the torsion angles defining the conformation of the side chain. In the present compound the conformation of the C(thiazole)—C—S—C—C—N side chain is given by torsion angles of 74.5 (3), −76.0 (3), −91.5 (3), 72.2 (3) and −89.0 (3)°, this being the first reported derivative having this conformation. Another difference is seen in the intermolecular hydrogen-bonding scheme.

Comment

Ebrotidine is a new histamine H_2-receptor antagonist synthetized by Grupo Ferrer Research Center (Anglada, Márquez, Sacristán & Ortiz, 1988). Structurally, the cyanoguanidine moiety found in cimetidine and the 2-nitro-1,1-ethenediamine moiety found in ranitidine are here replaced by an *N*-sulfonylformamidine group. The crystal structures of several related compounds have been determined (Hadicke, Fickel & Franke, 1978; Kojic-Prodic, Ruzic-Toros, Bresciani-Pahor & Randaccio, 1980; Kojic-Prodic, Ruzic-Toros & Toso, 1982; Yanagisawa, Hirata & Ishii, 1987; Solans, Font-Altaba & Cuevas-Diarte, 1988, 1995; Golic, Djinovic & Florjanic, 1989; Ishida, In, Doi, Inoue & Yanagisawa, 1989) and a structure–activity relationship study was carried out by Ishida *et al.* (1989). In order to obtain geometrical data for the title compound, (I), the present crystal structure determination was carried out.



(I)

The π conjugation between the N(6)H_2 amino group and the N(3) atom of the thiazole group produces the observed planarity of the 2-aminomethyleneaminothiazole moiety. This results in an intramolecular hydrogen bond between the N(6) and N(3) atoms [N(6)···N(3) 2.722 (3), H(N6)···N(3) 2.21 (4) Å, N(6)—H(N6)···N(3) 124 (3)°], which has been observed in the related compound famotidine.

The significant difference between the S(1)—O(1) [1.415 (2) Å] and S(1)—O(2) [1.441 (2) Å] bond lengths is explained by the fact that the O(2) atom is involved in an intermolecular hydrogen bond to N(5) [N(5)···O(2) 2.875 (3), H(N5)···O(2) 2.04 (4) Å, N(5)—H(N5)···O(2) 174 (3)°; symmetry code for O(2): $-x$, $1-y$, $1-z$], while O(1) does not participate in hydrogen bonding.

The torsion about the N(1)—C(7) bond [S(1)—N(1)—C(7)—N(2) −170.4 (2)°] is influenced by the hydrogen bond between the N(1) and N(2) atoms [N(2)···N(1) 2.958 (3), H(N2)···N(1) 1.93 (4) Å, N(2)—H(N2)···N(1) = 169 (3)°; symmetry code for N(1): $-x$, $-y$, $-z$]. The planarity of the N(1)—C(7)—N(2)—C(8) moiety and the lengths of the N(1)—C(7) and C(7)—N(2) bonds [1.326 (3) and 1.319 (3) Å, respectively] are indicative of π delocalization along this moiety.

The torsion angles defining the conformation of the side chain with respect to the thiazole ring are [using ω defined by Ishida *et al.* (1989)] ω_1[N(3)—C(11)—C(10)—S(2)] −74.5 (3), ω_2[C(11)—C(10)—S(2)—C(9)] −76.0 (3), ω_3[C(10)—S(2)—C(9)—C(8)] −91.5 (3), ω_4[S(2)—C(9)—C(8)—N(2)] 72.2 (3) and ω_5[C(9)—C(8)—N(2)—C(7)] −89.0 (3)°. The ω_1 and ω_2 torsion angles show the common synclinal conformations observed in all the previously mentioned compounds, ω_3 is similar to those observed in both phase B of famotidine and its hydrochloride derivative (Solans *et al.*, 1988; Ishida *et al.*, 1989; Golic *et al.*, 1989), ω_4 has the synclinal conformation observed in some derivatives of this family, while the ω_5 torsion angle has a value close to those observed in cimetidine (Kojic-Prodic *et al.*, 1980).

The antagonist activity of this compound agrees with the results found by Ishida *et al.* (1989) on the structure–activity relationship.

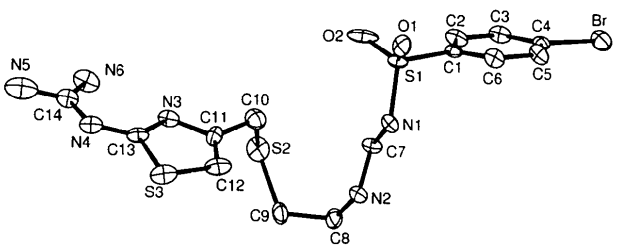


Fig. 1. *ORTEP* (Brueggemann & Schmid, 1990) view of the molecular structure of ebrotidine with the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are not shown for clarity.

Experimental

Crystal data

$C_{14}H_{17}BrN_6O_2S_3$
M_r = 477.41
Triclinic
$P\bar{1}$
a = 10.004 (2) Å
b = 10.611 (2) Å
c = 10.846 (2) Å
α = 96.43 (1)°
β = 105.48 (2)°
γ = 116.58 (2)°
V = 955.9 (4) Å^3
Z = 2
D_x = 1.659 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 25 reflections
θ = 12–21°
μ = 2.465 mm^{-1}
T = 288 K
Prism
0.2 × 0.1 × 0.1 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$2\theta/\omega$ scans
Absorption correction: none
3432 measured reflections
3432 independent reflections
2760 observed reflections [$I \geq 2.5\sigma(I)$]
θ_{max} = 30°
$h = -11 \rightarrow 12$
$k = -14 \rightarrow 13$
$l = 0 \rightarrow 14$
3 standard reflections
frequency: 120 min
intensity decay: not significant

Refinement

Refinement on F
R = 0.031
wR = 0.034
S = 0.952
2760 reflections
281 parameters
$w = 1/[\sigma^2(F_o) + 0.0011|F_o|^2]$
$(\Delta/\sigma)_{max}$ = 0.3
$\Delta\rho_{max}$ = 0.4 e Å^{-3}
$\Delta\rho_{min}$ = −0.4 e Å^{-3}
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}
Br	0.84637 (4)	−0.01105 (4)	0.34124 (3)	4.13 (2)
S(1)	0.22436 (7)	0.03680 (7)	0.30063 (5)	2.44 (2)
S(2)	0.18224 (10)	0.47765 (9)	0.18892 (9)	4.35 (3)
S(3)	−0.42141 (9)	0.21404 (8)	0.06179 (7)	3.80 (3)
O(1)	0.1036 (3)	−0.0974 (2)	0.3057 (2)	3.82 (9)
O(2)	0.2706 (3)	0.1696 (3)	0.3942 (2)	3.87 (9)
N(1)	0.1615 (2)	0.0429 (2)	0.1482 (2)	2.28 (7)
N(2)	0.1700 (3)	0.1922 (3)	0.0086 (2)	2.99 (9)
N(3)	−0.1604 (3)	0.4063 (3)	0.2466 (2)	2.98 (8)
N(4)	−0.3927 (3)	0.4287 (2)	0.2360 (2)	2.94 (8)
N(5)	−0.4089 (4)	0.5995 (4)	0.3669 (3)	4.89 (14)
N(6)	−0.1582 (3)	0.6330 (3)	0.3938 (3)	3.89 (10)
C(1)	0.3963 (3)	0.0221 (3)	0.3222 (2)	2.16 (8)
C(2)	0.5459 (3)	0.1446 (3)	0.3839 (3)	3.04 (11)
C(3)	0.6801 (3)	0.1358 (3)	0.3912 (3)	3.12 (10)
C(4)	0.6647 (3)	0.0020 (3)	0.3377 (2)	2.82 (10)
C(5)	0.5169 (3)	−0.1208 (3)	0.2795 (3)	3.07 (10)
C(6)	0.3798 (4)	−0.1118 (3)	0.2723 (3)	3.09 (10)
C(7)	0.2282 (3)	0.1727 (3)	0.1245 (3)	2.44 (8)
C(8)	0.2261 (4)	0.3344 (4)	−0.0172 (3)	3.70 (13)
C(9)	0.1366 (4)	0.4104 (4)	0.0144 (3)	3.89 (14)
C(10)	0.0338 (4)	0.3271 (4)	0.2266 (3)	4.16 (15)
C(11)	−0.1299 (4)	0.3097 (3)	0.1796 (3)	3.16 (11)
C(12)	−0.2575 (4)	0.2000 (4)	0.0778 (3)	3.89 (14)
C(13)	−0.3118 (3)	0.3691 (3)	0.1961 (2)	2.66 (9)
C(14)	−0.3183 (3)	0.5517 (3)	0.3307 (3)	3.19 (10)

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

C(4)—Br	1.874 (2)	C(13)—N(4)	1.351 (3)
O(1)—S(1)	1.415 (2)	C(14)—N(4)	1.317 (3)
O(2)—S(1)	1.441 (2)	C(14)—N(5)	1.338 (4)
N(1)—S(1)	1.624 (2)	C(14)—N(6)	1.350 (4)
C(1)—S(1)	1.753 (2)	C(2)—C(1)	1.381 (4)
C(9)—S(2)	1.802 (4)	C(6)—C(1)	1.382 (3)
C(10)—S(2)	1.808 (3)	C(3)—C(2)	1.369 (4)
C(12)—S(3)	1.678 (3)	C(4)—C(3)	1.396 (4)
C(13)—S(3)	1.740 (2)	C(5)—C(4)	1.369 (4)
C(7)—N(1)	1.326 (3)	C(6)—C(5)	1.400 (4)
C(7)—N(2)	1.319 (3)	C(9)—C(8)	1.522 (4)
C(8)—N(2)	1.446 (3)	C(11)—C(10)	1.496 (4)
C(11)—N(3)	1.380 (3)	C(12)—C(11)	1.354 (4)
C(13)—N(3)	1.313 (3)		
O(2)—S(1)—O(1)	118.7 (1)	C(5)—C(4)—Br	119.0 (2)
N(1)—S(1)—O(1)	104.5 (1)	C(5)—C(4)—C(3)	120.7 (2)
N(1)—S(1)—O(2)	111.7 (1)	C(6)—C(5)—C(4)	119.7 (2)
C(1)—S(1)—O(1)	107.4 (1)	C(5)—C(6)—C(1)	119.1 (3)
C(1)—S(1)—O(2)	107.3 (1)	N(2)—C(7)—N(1)	121.0 (2)
C(1)—S(1)—N(1)	106.4 (1)	C(9)—C(8)—N(2)	113.3 (2)
C(10)—S(2)—C(9)	103.5 (2)	C(8)—C(9)—S(2)	114.8 (2)
C(13)—S(3)—C(12)	90.5 (1)	C(11)—C(10)—S(2)	114.5 (2)
C(7)—N(1)—S(1)	116.8 (2)	C(10)—C(11)—N(3)	119.4 (3)
C(8)—N(2)—C(7)	123.1 (3)	C(12)—C(11)—N(3)	115.4 (3)
C(13)—N(3)—C(11)	110.8 (2)	C(12)—C(11)—C(10)	125.1 (3)
C(14)—N(4)—C(13)	121.5 (2)	C(11)—C(12)—S(3)	110.5 (2)
C(2)—C(1)—S(1)	120.0 (2)	N(3)—C(13)—S(3)	112.8 (2)
C(6)—C(1)—S(1)	119.1 (2)	N(4)—C(13)—S(3)	117.2 (2)
C(6)—C(1)—C(2)	120.8 (2)	N(4)—C(13)—N(3)	129.9 (2)
C(3)—C(2)—C(1)	120.1 (2)	N(5)—C(14)—N(4)	117.2 (3)
C(4)—C(3)—C(2)	119.6 (2)	N(6)—C(14)—N(4)	125.2 (3)
C(3)—C(4)—Br	120.3 (2)	N(6)—C(14)—N(5)	117.6 (3)

Of the H atoms, 15 were found in the difference synthesis and two were computed. All were refined with an overall temperature factor, a riding model being used for the computed atoms.

The *CFEO* program (Solans, 1978) was used for data reduction. The structure was determined by direct methods using *SHELXS*86 (Sheldrick, 1990) and refined by full-matrix least squares with *SHELX*76 (Sheldrick, 1976). The molecular view was obtained using a PC version of *ORTEP* (Brueggemann & Schmid, 1990).

Lists of structure factors, anisotropic displacement parameters and H-atom coordinates and geometry have been deposited with the IUCr (Reference: NA1081). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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The Diels–Alder Reaction Product of β-Ionone and Maleic Anhydride

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Abstract

The structure of the title compound, 6,7,7-trimethyl-1-(3-oxobutyl)bicyclo[2.2.2]oct-5-ene-2,3-dicarboxylic acid anhydride, $C_{17}H_{22}O_4$, a Diels–Alder reaction product of β-ionone and maleic anhydride, was solved by direct methods. The three six-membered rings of the bicyclo[2.2.2]oct-5-ene cage all slightly deviate from ideal boat conformations. The 3-oxobutyl side chain has an extended configuration.

Comment

Several drimanic terpenes, like polygodial and warburganal, are very active insect antifeedents (Kubo, Lee, Pettei, Pilkiewicz & Nakanishi, 1976). In an effort to synthesize them from freely available β-ionone (1), a Diels–Alder reaction was envisaged with maleic anhydride. Since the carbonyl deactivates the diene it was thought to be protected as an ethylene ketal (2) [^{1}H NMR ($CDCl_3$): δ 0.95 (*s*, 6H, 2 × CH_3), 1.35–1.60 (*m*, 7H, 2 × CH_2 and CH_3), 1.65 (*s*, 3H, C=C—CH_3), 1.97 (*t*, 2H, C=C—CH_2, *J* = 6.0 Hz), 3.90–4.00 (*m*, 4H, 2 × CH_2—O), 5.20 (*d*, 1H, olefinic, *J* = 16.0 Hz), 6.14 (*d*, 1H, olefinic, *J* = 16.0 Hz)] and then subjected to Diels–Alder reaction. The ^{1}H NMR spectrum of the product, which had the molecular formula $C_{17}H_{22}O_4$, corresponding to the anticipated product (3), did not, however, have signals for a tertiary methyl at a ring junction, but instead had an sp^2-methyl proton signal at