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КРАТКИЕ СООБЩЕНИЯ

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CRYSTAL STRUCTURE OF LANSOPRAZOLE SULFONE

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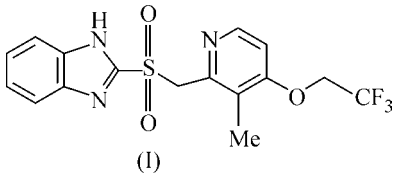
The structure of 2-({[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl}sulfonyl)-1H-1,3-benzimidazole, $C_{16}H_{14}N_3O_3F_3S$, has been solved. The compound belongs to a monoclinic space group ($P2_1/c$) with cell parameters $a = 8.8693(9)$, $b = 23.369(2)$, $c = 8.6141(8)$ Å, $\beta = 104.68(1)°$, $V = 1727.2(3)$ Å^3, $Z = 4$. The final R and $wR(F^2)$ values were 0.070 and 0.147, respectively. The title molecule has a ′Z′ shape in the crystal structure. The fused benzimidazole moiety and the pyridine ring are nearly coplanar. The molecules are linked by N—H…N and C—H…O hydrogen bonds into chains of edge-fused $R_2^2(14)$, $R_2^2(8)$, and $R_2^2(18)$ rings along the c-axis. The crystal lattice is further strengthened by π—π-stacking interactions.

K e y w o r d s: Crystal structure, benzimidazole, X-ray diffraction, hydrogen bonding.

Introduction. The benzimidazole (BI) nucleus is an essential part of many medicinally useful drugs such as omeprazole, lansoprazole, astemizole and emedastine [1, 2]. Further, derivatives of BI have proved to be of considerable value as anthelmintic and antineoplastic [3], antibacterial and antifungal [4] agents. Such compounds are increasingly being studied in the context of modeling biological systems [5, 6]. In continuation of our work [7] on such compounds, we report here the crystal structure of the title compound (I).



(I)

Experimental. The title compound was dissolved in methanol and suitable crystals of X-ray quality were obtained by slow evaporation.

Diffraction data were measured at room temperature with a Bruker SMART CCD area detector [8]. Preliminary lattice parameters and orientation matrix were obtained from three sets of frames. Intensity data were collected using graphite-monochromated MoK_α radiation ($\lambda = 0.71073$ Å).

Integration and scaling of intensity data were accomplished using SAINT [8]. The structure was solved by direct methods and refined by a full matrix least-squares procedure based on F^2 [9]. Non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms were included in calculated positions in the riding model approximation. The details of the data collection and refinement are summarized in Table 1. The geometry and molecular graphics were computed using programs PARST [10], ORTEP-3 [11], and PLATON [12]. Selected bond lengths and angles are listed in Table 2.

Results and Discussion. The title molecule has ′Z′ shaped conformation. The stock of ′Z′ comprises S1—C8 bond. The left arm (top) and the right arm (bottom) are composed of fused BI system

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Table 1

Crystal data and experimental details

Formula	$C_{16}H_{14}N_3O_3F_3S$	Crystal shape and color	Plate, colorless
M	385.36	μ, mm^{-1}	0.0234
Crystal system	Monoclinic	Measured data	16583
Space group	$P2_1/c$	Unique data	3050
Unit cell dimensions		Observed data ($I > 2\sigma(I)$)	2702
a, *b*, *c*, Å	8.8693(9), 23.369(2), 8.6141(8)	Parameters	253
β, deg.	104.68(1)	*R*	0.070
V, $Å^3$	1727.2(3)	$wR(F^2)$	0.147
Z	4	GOF	1.227
Calculated density, g/cm^3	1.482	CCDC deposition number	614305
Crystal dimensions, mm	0.24×0.16×0.11		

Table 2

Selected bond distances d (Å) *and angles* φ (deg.)

Bond	*d*	Bond	*d*	Bond	*d*	Bond	*d*
C(1)—N(2)	1.386(4)	C(9)—N(3)	1.351(4)	C(6)—N(1)	1.388(4)	N(3)—C(10)	1.333(4)
C(7)—N(1)	1.298(4)	C(14)—O(3)	1.415(4)	C(7)—N(2)	1.352(4)	C(15)—F(3)	1.271(5)
C(7)—S(1)	1.773(3)	C(15)—F(2)	1.307(6)	C(8)—S(1)	1.790(3)	C(15)—F(1)	1.313(6)
		O(1)—S(1)	1.422(3)			O(2)—S(1)	1.424(3)

Angle	φ	Angle	φ	Angle	φ
N(2)—C(1)—C(6)	105.8(3)	N(2)—C(1)—C(2)	133.4(3)	N(1)—C(6)—C(5)	128.8(3)
C(1)—C(6)—C(5)	121.1(3)	N(1)—C(7)—N(2)	115.7(3)	N(1)—C(7)—S(1)	119.5(2)
N(2)—C(7)—S(1)	124.8(3)	C(9)—C(8)—S(1)	111.5(2)	N(3)—C(9)—C(13)	124.5(3)
N(3)—C(9)—C(8)	114.6(3)	C(10)—N(3)—C(9)	115.8(3)	N(3)—C(10)—C(11)	125.4(3)
O(3)—C(12)—C(11)	124.7(3)	O(3)—C(12)—C(13)	115.0(3)	O(3)—C(14)—C(15)	106.6(3)
F(3)—C(15)—F(2)	106.0(5)	F(3)—C(15)—F(1)	106.7(5)	F(2)—C(15)—F(1)	106.2(4)
F(3)—C(15)—C(14)	114.5(4)	F(2)—C(15)—C(14)	113.3(4)	F(1)—C(15)—C(14)	109.6(5)
C(7)—N(1)—C(6)	103.5(3)	C(7)—N(2)—C(1)	104.8(3)	C(12)—O(3)—C(14)	118.1(3)
O(1)—S(1)—O(2)	118.8(2)	O(1)—S(1)—C(7)	107.4(2)	O(2)—S(1)—C(7)	108.0(2)
O(1)—S(1)—C(8)	108.5(2)	O(2)—S(1)—C(8)	110.7(2)	C(7)—S(1)—C(8)	102.2(2)

and trifluoroethoxy-2-pyridinyl moiety (Fig. 1). The BI moiety is planar, within maximum deviation of 0.006(2) Å for the N1 atom. The C—N bond lengths of the imidazole ring are in the range 1.300—1.398(4) Å that is shorter than the single bond length of 1.48 Å and longer than the typical C=N distance of 1.28 Å, indicating partial double bond character. The observed lengths can be understood as a result of conjugation in the heterocycle. Further, the exocyclic angles around atom N2 show considerable asymmetry, although the sum of the valent angles around N2 is 360.0°, indicating no significant pyramidalization of this atom. The title molecule (I) adopts a nearly *trans* conformation (C7—S1—C8—C9 angle of 156.2(3)°) which is close to the conformation of omeprazole (179°) [13] but in contrast with a conformation found in lansoprazole (–96.0(2)°) [14]. The pyridine ring is almost coplanar with the BI ring system, with the dihedral angle of 8.1(1)° between their least-squares planes. The plane containing trifluoroethoxy group makes angle of 11.0(2)° with the pyridine ring. The dihedral angle between the sulfonyl moiety and the BI ring system is 54.9(1)°.

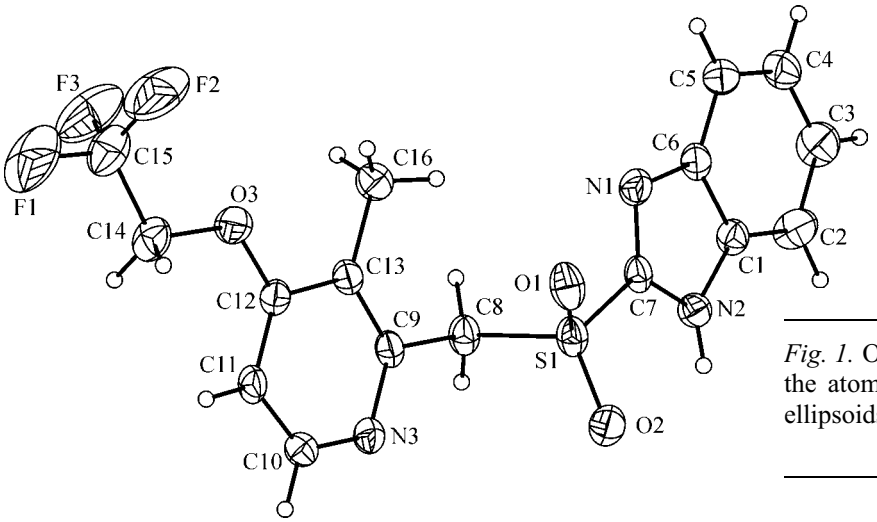

Fig. 1. ORTEP drawing of (I) showing the atom numbering scheme. Thermal ellipsoids are drawn at 30 % probability level

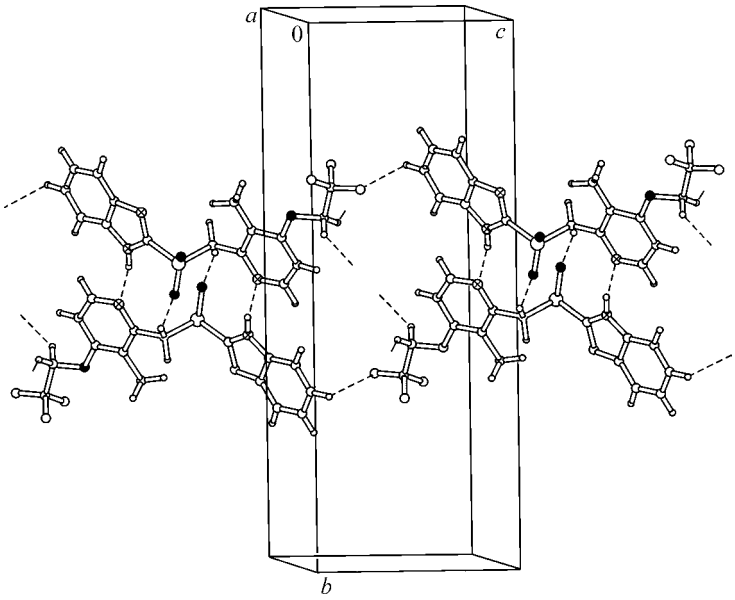

Fig. 2. Fragment of the crystal structure of (I) showing the formation of an edge-fused chain of $R_2^2(14)$, $R_2^2(8)$, and $R_2^2(28)$ rings along the *c*-axis

The sulfonyl oxygen O2 is involved in hydrogen bonding interactions with two types of atoms (C8—H8B…O2 and C14—H14A…O2). While the first interaction generates $R_2^2(8)$ type rings, the second one produces $R_2^2(18)$ rings. Inversion-related pairs of molecules (pseudo dimers) are joined through N—H…N and C—H…O hydrogen bonds, thus forming $R_2^2(14)$ and $R_2^2(8)$ edge-fused rings (Fig. 2) [15]. These pairs are further linked through a C—H…F interaction to form $R_4^4(28)$ rings of hydrogen-bonded tetramers. The aromatic carbon atom C3 in the BI moiety makes a C—H…F contact to one of the fluorine atoms (F1), C(15) type chains being thus formed along the [001] direction. These chains are further connected to the neighboring chains via C—H…N (C(10) type, Table 3) hydrogen bonds.

T a b l e 3

Hydrogen bonding geometry (Å, deg.)

D—H…A	(D—H)	(H…A)	(D…A)	(DHA)
C3—H3…F1^{i}	0.930	2.491	3.285(5)	143
C8—H8B…O2^{ii}	0.970	2.300	3.194(4)	153
N2—H2N…N3^{ii}	0.837(3)	2.226(3)	3.039(4)	164.0(3)
C14—H14A…O2^{iii}	0.970	2.488	3.356(4)	149
C14—H14B…N1^{iv}	0.970	2.614	3.407(5)	139

Symmetry codes: (i) *x*+1, *y*, *z*+2; (ii) –*x*+1, –*y*+1, –*z*+1; (iii) –*x*, –*y*+1, –*z*; (iv) *x*, *y*, *z*–1.

Stacking interactions between the pyridine and the imidazole ring of the BI moiety with a spacing of 3.5 Å provide further stability to the crystal lattice.

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