Crystal structure of 7-chloro-3-isopropoxy-4*H*-1,2,4-benzothiadiazine 1,1-dioxide monohydrate, $C_{10}H_{11}ClN_2O_3S \cdot H_2O$

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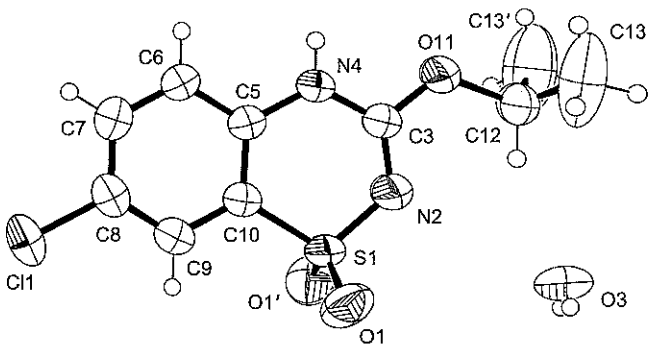

Abstract

$C_{10}H_{13}ClN_2O_4S$, monoclinic, *C*12/*m*1 (no. 12), a = 16.6352(6) Å, b = 6.8145(7) Å, c = 12.2805(6) Å, β = 107.921(3)°, V = 1324.6 Å^3, Z = 4, $R_{gt}(F)$ = 0.043, $wR_{ref}(F^2)$ = 0.126, T = 293 K

Source of material

The compound was synthesized by alkylation of 7-chloro-3-oxo-3,4-dihydro-4*H*-1,2,4-benzothiadiazine 1,1-dioxide, a well known synthetic intermediate [1,2] with isopropyl iodide. Crystals were obtained by slow evaporation of a methanol solution.

Experimental details

The space group *C*2/*m*, the highest symmetry compatible with the statistics of the reflections, seemed to be the most appropriate to describe the structure according to the criteria formulated in [3]. The refinements of the title crystal structure in the space groups *Cm* and *C*2 were nevertheless investigated (private unpublished data). In both of them large correlation matrix elements are observed mainly between parameters of atoms which are out of the molecular mean plane in *C*2 or out of the mirror plane in *Cm*, like the oxygen atoms of SO_2 and the terminal carbon atoms of the side chain. Unusually large e.s.ds. are also obtained for some parameters of these atoms. The refinement in the group *Cm* exhibits no significantly better results than in *C*2/*m*. Quite the opposite some anisotropic displacement parameters of C12 and C13 have less satisfactory values. Moreover, a disorder of the positions of the hydrogen atoms around the water molecule cannot be resolved. The final *R* indices are slightly better in *Cm* (for instance wR = 0.114 for all data to be compared to 0.126 in *C*2/*m*) but the ratio number of data/number of parameters (1360/217) is smaller than that in *C*2/*m* (1298/111). The refinement in the space group *C*2 brings to a final wR index (for all data) equal to 0.113. The ratio data/parameters is 1299/175. The values of the anisotropic displacement parameters of C12 and C13 are not better than in the *C*2/*m* refinement. The deviations of the bond lengths and angles in the non-centrosymmetric refinement from their corresponding values in the *C*2/*m* refinement are not significant (less than 1σ) except when the highly correlated parameters are included.

Discussion

7-Chloro-3-isopropoxy-4*H*-1,2,4-benzothiadiazine 1,1-dioxide (BPDZ229), is a putative ATP sensitive potassium channel opener (K_{ATP} PCO), structurally related to BPDZ73 (7-chloro-3-isopropylamino-4*H*-1,2,4-benzothiadiazine 1,1-dioxide), a reference pancreatic K_{ATP} opener [1,4]. The isosteric change of the 3-isopropylamino chain of BPDZ73 by a 3-isopropoxyl side chain led to an important change in the pharmacological profile of the drug. The crystal structure may also be compared to that of the 3-isopropylsulfanyl derivative BPDZ209 [5].

All the atoms are in the mirror plane of the *C*2/*m* space group, except O1 (linked to the atom S), C13 of the isopropoxyl group and H3 of the water molecule. The N2=C3 double bond character and the N4—C3 single bond character are well defined with distances 1.289(4) Å and 1.339(4) Å, respectively. The 4*H*- rather than the 2*H*-tautomer form is so exhibited in the cristalline state of BPDZ229 like in BPDZ73 and BPDZ209 previously studied [4,5]. The presence of an N4–H···O hydrogen bond and the absence of a significant peak near N2 in the Fourier difference map of the crystal structure of BPDZ229 monohydrate confirm this scheme. There are two hydrogen bonds in the structure. They both include the water molecule. The main characteristics are: N4–H4···O3, d(N4···O3) = 2.780(3) Å, ∠N4–H4···O3 167(4)°; O3–H3···O1^i (symmetry code (i) –½+x,–½+y,z)), d(O3···O1^i) = 2.844(2) Å and ∠O3–H3···O1^i 175(4)°. Concerning the torsion angles, the largest deviation observed from the two space groups refinements (see Experimental details) is 1.7(2)° inside the phenyl ring, and 4.6(2)° (N4–C5–C10–S1) inside the thiadiazine ring. The values of N2–C3–O11–C12 and C3–O11–C12–C13 torsion angles are respectively 4.4(2)° and –111.3(2)° in *C*2, 0° and –120.7(3)° in *C*2/*m*. The corresponding values are –0.9(5)° and –70.7(4)° in BPDZ73 [4], and –4.5(4)° and –72.3(4) ° in BPDZ209 [5].

Table 1 Data collection and handling

Crystal:	colorless prism, size 0.30 × 0.46 × 0.46 mm
Wavelength:	Cu K_α radiation (1.54180 Å)
μ:	41.31 cm^{-1}
Diffractometer, scan mode:	Stoe-Siemens AED4 ω
$2\theta_{max}$:	136°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	1361, 1298
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$ 1043
$N(param)_{refined}$:	111
Programs:	SHELXS-97 [6], SHELXL-97 [7], ORTEP [8]

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Table 2. Atomic coordinates and displacement parameters (in $Å^2$).

Atom	Site	x	y	z	U_{iso}
H(4)	4*i*	0 126(3)	0	0 814(3)	0 06(1)
H(6)	4*i*	0 1438	0	1 0155	0 057
H(7)	4*i*	0 2358	0	1 1978	0 065
H(9)	4*i*	0 4337	0	1 0757	0 062
H(12)	4*i*	0 2150	0	0 5322	0 110
H(13A)	8*j*	0 0552	0 1846	0 4581	0 238
H(13B)	8*j*	0 1166	0 1797	0 3836	0 238
H(13C)	8*j*	0 1420	0 2947	0 4998	0 238
H(3)	8*j*	−0 014(2)	−0 087(4)	0 832(3)	0 092

Table 3. Atomic coordinates and displacement parameters (in $Å^2$)

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
S(1)	4*i*	0 35917(4)	0	0 83659(6)	0 0353(4)	0 0604(5)	0 0538(5)	0	0 0161(3)	0
O(1)	8*j*	0 4058(1)	0 1766(3)	0 8396(2)	0 081(1)	0 087(1)	0 084(1)	−0 034(1)	0 041(1)	−0 005(1)
N(2)	4*i*	0 2785(2)	0	0 7259(2)	0 045(1)	0 116(3)	0 050(2)	0	0 017(1)	0
C(3)	4*i*	0 2016(2)	0	0 7284(2)	0 040(1)	0 064(2)	0 046(2)	0	0 012(1)	0
N(4)	4*i*	0 1767(2)	0	0 8223(2)	0 035(1)	0 053(1)	0 047(1)	0	0 011(1)	0
C(5)	4*i*	0 2326(2)	0	0 9329(2)	0 041(1)	0 038(1)	0 048(2)	0	0 016(1)	0
C(6)	4*i*	0 2018(2)	0	1 0271(3)	0 047(2)	0 046(2)	0 052(2)	0	0 020(1)	0
C(7)	4*i*	0 2565(2)	0	1 1356(3)	0 066(2)	0 049(2)	0 051(2)	0	0 023(2)	0
C(8)	4*i*	0 3437(2)	0	1 1536(3)	0 060(2)	0 048(2)	0 047(2)	0	0 007(1)	0
C(9)	4*i*	0 3756(2)	0	1 0634(3)	0 045(2)	0 051(2)	0 055(2)	0	0 010(1)	0
C(10)	4*i*	0 3196(2)	0	0 9533(2)	0 040(1)	0 041(1)	0 049(2)	0	0 013(1)	0
O(11)	4*i*	0 1377(1)	0	0 6333(2)	0 045(1)	0 114(2)	0 043(1)	0	0 0121(9)	0
C(12)	4*i*	0 1541(2)	0	0 5217(3)	0 058(2)	0 179(5)	0 040(2)	0	0 016(1)	0
C(13)	8*j*	0 1133(4)	0 1809(7)	0 4603(3)	0 285(7)	0 122(4)	0 081(2)	−0 009(4)	0 075(4)	0 021(2)
Cl(1)	4*i*	0 41254(7)	0	1 29202(8)	0 0816(7)	0 1043(8)	0 0481(5)	0	−0 0017(4)	0
O(3)	4*i*	0 0124(2)	0	0 8335(3)	0 045(1)	0 069(2)	0 120(2)	0	0 032(2)	0

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