Crystal structure of 7-chloro-3-isopropylamino-4*H*-1,2,4-benzothiadiazine 1,1-dioxide, $C_{10}H_{12}ClN_3O_2S$

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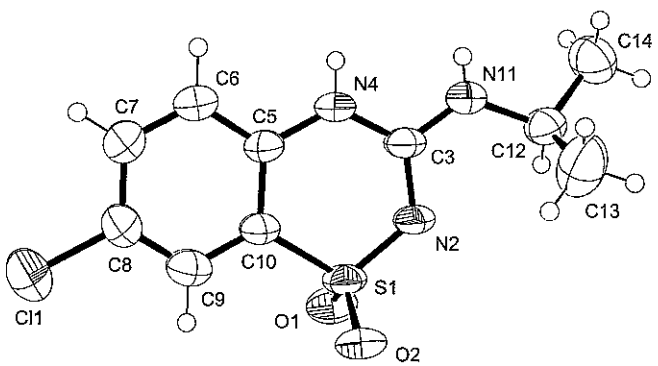
Received April 22 2005 accepted and available on-line July 6 2005; CCDC no 1267/1536



Abstract

$C_{10}H_{12}ClN_3O_2S$, monoclinic, $P12_1/n1$ (no. 14), $a = 5\ 898(1)$ Å, $b = 17.148(3)$ Å, $c = 12\ 506(2)$ Å, $\beta = 94.41(1)°$, $V = 1261.2$ Å^3, $Z = 4$, $R_{gt}(F) = 0\ 043$, $wR_{ref}(F^2) = 0\ 110$, $T = 293$ K.

Source of material

The compound was synthesized by a well described four steps chemical pathway starting from 4-chloroaniline [1]. Crystals were obtained by slow evaporation of a methanol solution.

Experimental details

H atoms were restrained (included as riding atoms) except H(N4) and H(N11) which were refined, with isotropic temperature parameters fixed at 1.2 U_{eq} of the parent atom (1 5 for methyl atoms)

Discussion

7-Chloro-3-isopropylamino-4*H*-1,2,4-benzothiadiazine 1,1-dioxide, namely BPDZ73, was revealed to be one of the most potent and tissue-selective pancreatic B-cells ATP sensitive potassium channel opener [1,2]. Some crystallographic structures of related compounds have been determined such as 7-iodo-3-isopropylamino-4*H*-1,2,4-benzothiadiazine 1,1-dioxide (BPDZ69) [3] which is less powerful and less sensitive at the level of the pancreatic tissue.

X-ray analysis of chloro- and iodo-substituted compounds demonstrated that the N4—C3 distances [1.352(4) Å and 1.367(8) Å] correspond to a single bond type. The 4*H*- rather than the 2*H*- tautomer form is so exhibited in the crystalline state of the two compounds like in many benzothiadiazine 1,1-dioxides previously studied. The presence of N4–H···O hydrogen bond in both structures confirms this scheme. It must be emphasized that all H(N) hydrogen positions were located by Fourier difference synthesis, and included in the refinements. Moreover, there are no significant peaks near N2 in the difference maps. In the crystal structure of BPDZ73, the N2—C3 [1.330(4) Å] and C3—N11 [1.314(4) Å] bond lengths indicate a charge delocalization along the N2–C3–N11–H···O1 bonds network as observed in the structure of BPDZ69 [3]. Although the symmetry in both structures is described by the same space group $P12_1/n1$, the packing modes are quite different. Indeed the hydrogen-bonding scheme in BPDZ73 involves the N4–H4···O2^{i} and N11–H11···O1^{i} bonds [symmetry code (i) ½+x,½−y,½+z)], with distances N4···O2^{i} 2.811(3) Å, N11···O1^{i} 2.976(3) Å, and angles N4–H4–O2^{i} 169(3)°, N11–H11–O1^{i} 177(4) °. The other shortest intermolecular contact is Cl1···O1^{ii} 3.593(4) Å [(ii) −1+x,y,z]. Whereas the stacking of the molecules in the BPDZ69 structure is characterized by three H-bonds N4–H4···O1^{iii}, N4–H4···O1^{iv}, N11–H11···O1^{iv}, and by the other close intermolecular contacts N4···N4^{iii} [3.281(8) Å], O1···O1^{v} [3.172(8) Å] and I1···O2^{vi} [3.258(7) Å] [(iii) 1−x,2−y,−z; (iv) 1+x,y,z; (v): −x,2−y,−z; (vi) −x,2−y,1−z]. The values of the torsion angles inside the heterocycle shows that the BPDZ73 molecule conformation is more plane than that of BPDZ69.

Table 1 Data collection and handling.

Crystal:	colorless prism, size 0.15 × 0.23 × 0.53 mm
Wavelength:	Cu K_α radiation (1.54180 Å)
μ:	42.01 cm^{-1}
Diffractometer, scan mode:	Stoe-Siemens AED 4, ω
$2\theta_{max}$:	135.98°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	2361, 2258
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1062
$N(param)_{refined}$:	163
Programs:	SHELXS-97 [4], SHELXL-97 [5] ORTEP-III [6]

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

Atom	Site	x	y	z	U_{iso}
H(4)	4*e*	0.340(6)	0.266(2)	1.003(3)	0.067
H(6)	4*e*	0.0554	0.3489	1.0683	0.076
H(7)	4*e*	−0.2646	0.4230	1.0270	0.077
H(9)	4*e*	−0.2766	0.3556	0.7212	0.065
H(11)	4*e*	0.584(6)	0.174(2)	0.970(3)	0.065
H(12)	4*e*	0.7043	0.1367	0.7859	0.066
H(13A)	4*e*	0.3785	0.0610	0.7828	0.144
H(13B)	4*e*	0.4647	0.0210	0.8911	0.144
H(13C)	4*e*	0.5909	0.0058	0.7872	0.144
H(14A)	4*e*	0.8455	0.0640	0.9815	0.115
H(14B)	4*e*	0.9707	0.1353	0.9341	0.115
H(14C)	4*e*	0.9659	0.0547	0.8748	0.115

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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*e*	0.1199(2)	0.26178(5)	0.71335(6)	0.0578(5)	0.0659(6)	0.0268(3)	0.0005(5)	−0.0039(3)	0.0006(4)
O(1)	4*e*	0.2184(4)	0.3180(1)	0.6441(2)	0.080(2)	0.082(2)	0.035(1)	−0.011(2)	0.007(1)	0.009(1)
O(2)	4*e*	−0.0480(4)	0.2115(1)	0.6578(2)	0.064(2)	0.074(2)	0.037(1)	−0.007(1)	−0.014(1)	−0.008(1)
N(2)	4*e*	0.3107(4)	0.2093(2)	0.7718(2)	0.059(2)	0.080(2)	0.026(1)	0.017(2)	−0.006(1)	−0.007(1)
C(3)	4*e*	0.3801(6)	0.2164(2)	0.8751(2)	0.053(2)	0.059(2)	0.030(2)	0.002(2)	−0.005(2)	0.000(2)
N(4)	4*e*	0.2851(5)	0.2655(2)	0.9435(2)	0.070(2)	0.065(2)	0.029(1)	0.015(2)	−0.011(1)	−0.003(1)
C(5)	4*e*	0.0898(6)	0.3091(2)	0.9184(2)	0.059(2)	0.050(2)	0.030(2)	0.006(2)	−0.002(2)	0.000(1)
C(6)	4*e*	−0.0088(6)	0.3508(2)	0.9980(3)	0.075(3)	0.077(3)	0.036(2)	0.015(2)	−0.004(2)	−0.005(2)
C(7)	4*e*	−0.2001(6)	0.3946(2)	0.9737(3)	0.070(3)	0.075(3)	0.049(2)	0.016(2)	0.007(2)	−0.004(2)
C(8)	4*e*	−0.2976(6)	0.3965(2)	0.8685(3)	0.059(2)	0.058(2)	0.056(2)	0.012(2)	0.001(2)	0.004(2)
C(9)	4*e*	−0.2074(6)	0.3550(2)	0.7905(3)	0.061(2)	0.058(2)	0.043(2)	−0.002(2)	−0.005(2)	0.007(2)
C(10)	4*e*	−0.0119(5)	0.3116(2)	0.8138(2)	0.050(2)	0.055(2)	0.030(2)	0.004(2)	−0.002(1)	0.001(1)
N(11)	4*e*	0.5474(5)	0.1718(2)	0.9144(2)	0.059(2)	0.065(2)	0.036(1)	0.011(2)	−0.007(1)	−0.004(2)
C(12)	4*e*	0.6645(6)	0.1129(2)	0.8531(3)	0.054(2)	0.070(2)	0.041(2)	0.008(2)	0.004(2)	−0.003(2)
C(13)	4*e*	0.5106(7)	0.0439(2)	0.8261(4)	0.081(3)	0.084(3)	0.124(4)	−0.002(3)	0.009(3)	−0.033(3)
C(14)	4*e*	0.8813(6)	0.0896(2)	0.9167(3)	0.062(3)	0.091(3)	0.076(3)	0.013(2)	0.002(2)	0.004(2)
Cl(1)	4*e*	−0.5363(2)	0.45397(7)	0.83870(9)	0.0738(7)	0.0924(7)	0.0846(7)	0.0297(6)	−0.0007(6)	0.0053(6)

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