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(*R*/*S*)-3-(3-Methyl-2-butylamino)-4*H*-pyrido[4,3-e]-1,2,4-thiadiazine 1,1-dioxide monohydrate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.011 Å
R factor = 0.077
wR factor = 0.251
Data-to-parameter ratio = 11.7

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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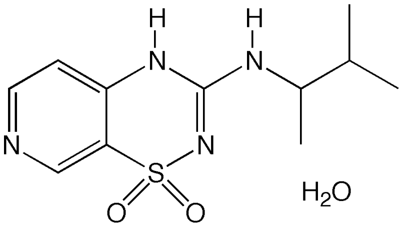
The crystal structure of the title compound, $C_{11}H_{16}N_4O_2S\cdot H_2O$, a pancreatic B-cell selective K_{ATP} channel opener, reveals that that the *N*-alkylsulfonylguanidine moiety of the drug containing the two guanidine NH groups in the same spatial orientation (in parallel) is closely related to the *N*-alkylcyanoguanidine moiety of pinacidil in the solid state. The results confirm that the title drug may be considered as a hybrid compound between pinacidil and diazoxide. The crystal packing involves four hydrogen bonds which link the drug and water molecules.

Comment

The crystal structure of the title compound, (I), was determined in order to confirm that the best representative of pancreatic B-cell selective K_{ATP} channel openers belonging to the class of pyridothiadiazine dioxides is structurally related to both diazoxide (a benzothiadiazine dioxide K_{ATP} channel opener; Bandoli & Nicolini, 1977) and pinacidil (a pyridylalkylcyanoguanidine K_{ATP} channel opener; Pirotte, Dupont *et al.*, 1993).



(I)

The crystal packing of (I) is dominated by four hydrogen bonds (Table 2). The water molecule is an acceptor in two N—H···O bonds and a donor in O—H···N(pyridinic) and O—H···O(sulfoxide) bonds. This scheme confirms the 4*H*-tautomeric form as N4 is involved in a hydrogen bond, whereas N2 is not included in any close intermolecular contact. The orientation of N4—H and N11—H is similar to that of the two guanidine NH groups observed in pinacidil.

Experimental

The synthesis of the title compound, (I), has been described by Pirotte, de Tullio *et al.* (1993). Crystals of (I) were obtained by slow evaporation of a methanol solution.

Crystal data

$C_{11}H_{16}N_4O_2S{\cdot}H_2O$
$M_r = 286.35$
Trigonal, $R\overline{3}$
$a = 26.198\ (5)$ Å
$c = 11.024\ (7)$ Å
$V = 6552\ (4)$ Å^3
$Z = 18$
$D_x = 1.306$ Mg m^{-3}

Cu $K\alpha$ radiation
Cell parameters from 30 reflections
$\theta = 20.7$–$40.7°$
$\mu = 2.08$ mm^{-1}
$T = 293\ (2)$ K
Prism, colourless
0.57 × 0.38 × 0.34 mm

Data collection

Stoe–Siemens AED four-circle diffractometer
ω scans
Absorption correction: ψ scan (*EMPIR*; Stoe & Cie, 1987)
$T_{\min} = 0.351$, $T_{\max} = 0.493$
6653 measured reflections
2166 independent reflections
1429 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.049$
$\theta_{\max} = 60.0°$
$h = -29 \rightarrow 25$
$k = 0 \rightarrow 29$
$l = -12 \rightarrow 12$
2 standard reflections
frequency: 60 min
intensity decay: 5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.077$
$wR(F^2) = 0.251$
$S = 1.05$
2166 reflections
185 parameters
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.1779P)^2 + 0.4536P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.44$ e Å^{-3}
$\Delta\rho_{\min} = -0.27$ e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.00026 (11)

Table 1
Selected geometric parameters (Å, °).

S1—O2	1.386 (5)	C3—N11	1.329 (6)
S1—O1	1.433 (5)	C3—N4	1.343 (6)
S1—N2	1.542 (4)	N11—C12	1.476 (7)
N2—C3	1.330 (6)		
N2—S1—C10	107.0 (2)	N2—C3—N4	124.1 (5)
C3—N2—S1	122.7 (4)	C3—N4—C5	125.1 (4)
N11—C3—N2	119.5 (5)	C3—N11—C12	124.6 (5)
N11—C3—N4	116.4 (4)		
C10—S1—N2—C3	15.4 (6)	N2—S1—C10—C5	−12.4 (5)
S1—N2—C3—N11	173.2 (5)	N2—C3—N11—C12	−4.9 (9)
S1—N2—C3—N4	−7.9 (8)	C3—N11—C12—C13	79.4 (10)
N11—C3—N4—C5	172.6 (5)	C3—N11—C12—C14	−150.1 (7)
N2—C3—N4—C5	−6.3 (9)	N11—C12—C14—C15	168.2 (8)
C3—N4—C5—C10	8.8 (8)	N11—C12—C14—C16	−71.0 (8)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N4—H4$\cdots$O3$^{\rm i}$	0.72 (6)	2.21 (6)	2.872 (6)	154 (6)
N11—H11$\cdots$O3$^{\rm i}$	1.00 (6)	1.99 (6)	2.961 (6)	161 (5)
O3—H31$\cdots$N8$^{\rm ii}$	0.86 (7)	2.27 (7)	2.997 (6)	141 (7)
O3—H31$\cdots$O1	0.86 (7)	2.24 (8)	2.801 (7)	122 (6)
O3—H32$\cdots$O2$^{\rm iii}$	0.68	2.12	2.771 (6)	161

Symmetry codes: (i) $1-x, -y, 1-z$; (ii) $\frac{2}{3}+y, \frac{1}{3}-x+y, \frac{1}{3}-z$; (iii) $\frac{2}{3}-y, x-y-\frac{2}{3}, \frac{1}{3}+z$.

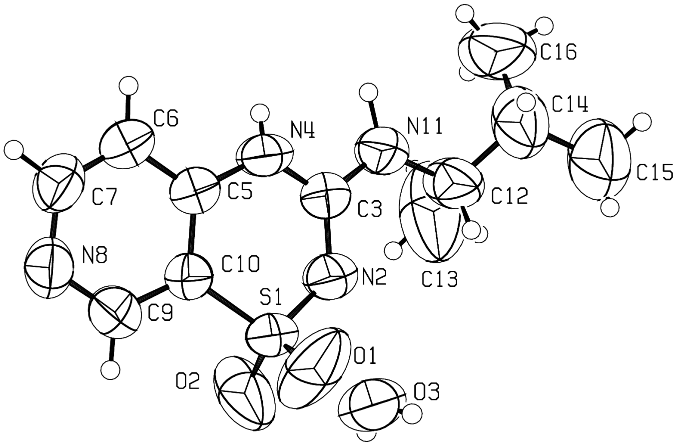


Figure 1
The molecular structure of (I) with the atom-labelling scheme. Displacement ellipsoids are shown at the 50% probability level.

All H atoms (with the exception of the nitrogen-bound atoms H4 and H11, and the water H atoms H31 and H32) were included in the refinement as riding, with isotropic displacement parameters fixed at $1.2U_{\rm eq}$ of the parent atom ($1.5U_{\rm eq}$ for methyl H atoms). Atoms H4, H11, H31 and H32 were refined isotropically, their displacement parameters being fixed at $1.2U_{\rm eq}$ of the N or O atom. H32 was, however, kept fixed in the last cycles of least-squares refinement. The large value (0.25) of wR at the end of the refinement could be related to a slight disorder of the *N*-alkylsulfonylguanidine moiety. Some of its atoms exhibit rather large values of the anisotropic displacement parameters. Various data collections undertaken with Mo $K\alpha$ radiation on different samples mounted on the Stoe four-circle diffractometer and also on a MAR345 image-plate diffractometer yielded similar results.

Data collection: *DIF*4 (Stoe & Cie, 1987); cell refinement: *DIF*4; data reduction: *REDU*4 (Stoe & Cie, 1987); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Burnett & Johnson, 1996); software used to prepare material for publication: *SHELXL*97.

References

Bandoli, G. & Nicolini, M. (1977). *J. Cryst. Mol. Struct.* **7**, 229–240.

Burnett, M. N. & Johnson, C. K. (1996). *ORTEP*III. Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, USA.

Pirotte, B., de Tullio, P., Lebrun, P., Antoine, M.-H., Fontaine, J., Masereel, B., Schynts, M., Dupont, L., Herchuelz, A. & Delarge, J. (1993). *J. Med. Chem.* **36**, 3211–3213.

Pirotte, B., Dupont, L., de Tullio, P., Masereel, B., Schynts, M. & Delarge, J. (1993). *Helv. Chim. Acta*, **76**, 1311–1318.

Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.

Stoe & Cie (1987). *DIF*4, *REDU*4 and *EMPIR*. Version 6.2. Stoe & Cie, Darmstadt, Germany.

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