Two pseudo-enantiomeric forms of N -benzyl-4-hydroxy-1-methyl-2,2-dioxo-1 H -2λ 6...

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Two pseudo-enantiomeric forms of *N*-benzyl-4-hydroxy-1-methyl-2,2-dioxo-1*H*-2λ^6,1-benzothiazine-3-carboxamide and their analgesic properties

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Two pseudo-enantiomeric forms of *N*-benzyl-4-hydroxy-1-methyl-2,2-dioxo-1*H*-2λ^6,1-benzothiazine-3-carboxamide and their analgesic properties

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CCDC references: 1471701; 1471700

Supporting information: this article has supporting information at journals.iucr.org/c

The fact that molecular crystals exist as different polymorphic modifications and the identification of as many polymorphs as possible are important considerations for the pharmaceutic industry. The molecule of *N*-benzyl-4-hydroxy-1-methyl-2,2-dioxo-1*H*-2λ^6,1-benzothiazine-3-carboxamide, $C_{17}H_{16}N_2O_4S$, does not contain a stereogenic atom, but intramolecular hydrogen-bonding interactions engender enantiomeric chiral conformations as a labile racemic mixture. The title compound crystallized in a solvent-dependent single chiral conformation within one of two conformationally polymorphic $P2_12_12_1$ orthorhombic chiral crystals (denoted forms *A* and *B*). Each of these pseudo-enantiomorphic crystals contains one of two pseudo-enantiomeric diastereomers. Form *A* was obtained from methylene chloride and form *B* can be crystallized from *N*,*N*-dimethylformamide, ethanol, ethyl acetate or xylene. Pharmacological studies with solid–particulate suspensions have shown that crystalline form *A* exhibits an almost fourfold higher antinociceptive activity compared to form *B*.

1. Introduction

The possibility of molecular crystals existing as different polymorphic modifications is very important for the pharmaceutic industry. Significant differences in the properties of drug substances from different manufacturers, such as a sharp decline in biological activity, rapid loss of storage stability, increased water absorption, the sudden appearance of chemical incompatibility of the ingredients in multicomponent dosage forms, the deterioration of solubility and changes of flow ability are just some of the considerable pharmaceutical, pharmacological and technological problems caused mainly by polymorphism (Brittain, 1999; Brüning & Schmidt, 2015; Gunn *et al.*, 2012; Luźnik *et al.*, 2014; Nyström *et al.*, 2015; Saurabh & Kaushal, 2011) that producers have to face. Therefore, the activity of the pharmaceutical companies in detecting and describing as many polymorphs as possible has increased sharply in addition to purely scientific interest, and such research is patented for intellectual property protection (Brittain, 1999; Bernstein, 2002; Hilfiker, 2006).

Taking into account the observed biological activity of *N*-benzyl-4-hydroxy-1-methyl-2,2-dioxo-1*H*-2λ^6,1-benzothiazine-3-carboxamide, (1), in aqueous suspensions of the crystals, we studied the possibility to their forming different crystal structures depending on the nature of the solvent.

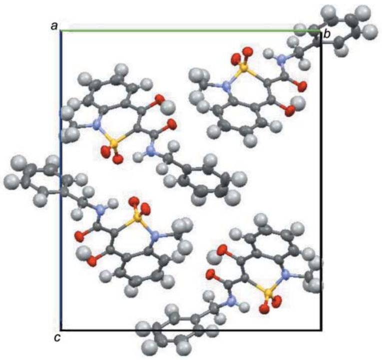


Table 1
Experimental details.

	(1*a*) (existing as polymorph *A*)	(1*b*) (existing as polymorph *B*)
Crystal data		
Chemical formula	$C_{17}H_{16}N_2O_4S$	$C_{17}H_{16}N_2O_4S$
M_r	344.39	344.39
Crystal system, space group	Orthorhombic, $P2_12_12_1$	Orthorhombic, $P2_12_12_1$
Temperature (K)	293	293
a, b, c (Å)	5.4764 (3), 15.9117 (8), 18.3228 (10)	5.4469 (3), 15.8455 (10), 18.2412 (9)
V (Å^3)	1596.63 (15)	1574.38 (15)
Z	4	4
Radiation type	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.23	0.23
Crystal size (mm)	0.20 × 0.02 × 0.02	0.20 × 0.02 × 0.02
Data collection		
Diffractometer	Agilent Xcalibur Sapphire3	Agilent Xcalibur Sapphire3
Absorption correction	Multi-scan (*CrysAlis RED*; Agilent, 2012)	Multi-scan (*CrysAlis RED*; Agilent, 2012)
T_{min}, T_{max}	0.979, 1.000	0.775, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	16369, 4658, 3004	16325, 2777, 2296
R_{int}	0.055	0.068
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.703	0.595
Refinement		
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.051, 0.094, 0.99	0.040, 0.124, 0.84
No. of reflections	4658	2777
No. of parameters	226	225
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.22, −0.28	0.20, −0.22
Absolute structure	Flack x determined using 910 quotients $[(I^+) - (I^-)]/[(I^+) + (I^-)]$ (Parsons *et al.*, 2013)	Flack x determined using 839 quotients $[(I^+) - (I^-)]/[(I^+) + (I^-)]$ (Parsons *et al.*, 2013)
Absolute structure parameter	0.09 (5)	−0.16 (9)

Computer programs: *CrysAlis CCD* (Agilent, 2012), *CrysAlis RED* (Agilent, 2012), *SHELXS97* (Sheldrick, 2008), *SHELXL2014* (Sheldrick, 2015*a*), *SHELXT* (Sheldrick, 2015*b*), *olex2.refine* (Bourhis *et al.*, 2015) and *OLEX2* (Dolomanov *et al.*, 2009).

2. Experimental

2.1. Synthesis and crystallization

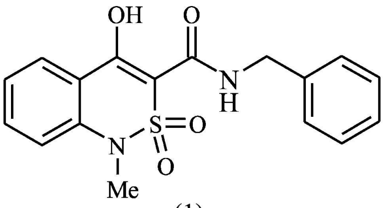
The title compounds were synthesized according to the known methodology of Ukrainets *et al.* (2015). Compound (1*a*) was crystallized from methylene chloride and compound (1*b*) was crystallized from *N*,*N*-dimethylformamide.

2.2. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1. The positions of the H atoms were located from electron-density difference maps and were refined using a riding model, with $U_{iso}(H) = nU_{eq}$(carrier atom), with $n = 1.5$ for the methyl group and 1.2 otherwise. The H atoms of the hydroxy and amide groups were refined using isotropic approximation.

2.3. Pharmacological tests

The antinociceptive activity of benzylamides (1*a*)–(1*e*) [compound (1) recrystallized from methylene chloride is (1*a*), from *N*,*N*-dimethylformamide is (1*b*), from ethanol is (1*c*), from ethyl acetate is (1*d*) and from xylene is (1*e*)], which is the animal parallel of analgesic activity in humans, has been studied using the standard model of thermal irritation of the tail tip (Tail Immersion Test) in 12 adult white male rats weighing 190–200 g. All biological experiments were carried out in full accordance with the European Convention on the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Vogel, 2008) and Ukrainian Law No. 3447-IV ‘On protection of animals from severe treatment’ (2006). The tail tip of the experimental animal was immersed in a water bath heated to 327 K, and the initial length of the latent period of immersion (withdrawal) of the tail expressed in seconds was determined. The antinociceptive effect (in %) was assessed by changing the duration of the latent period 1 h after introduction of the substances studied. All tested substances and the reference drug (Piroxicam) were introduced orally in the form of fine aqueous suspensions stabilized with Tween-80 in a dose of 20 mg kg^{-1}. The animals of the control group received an equivalent amount of water with Tween-80. The results of the biological tests can be significantly affected by the particle size of the substances under



(1)

Table 2
The antinociceptive activity of benzylamides (1*a*)–(1*e*) and Pyroxicam.

Compound	The latent period 1 h after introduction of the compound (s)	Change of the latent period compared to the control (%)
(1*a*)	16.07±0.95	+113.1
(1*b*)	9.92±0.73	+31.6
(1*c*)	9.46±0.77	+25.5
(1*d*)	9.40±0.80	+24.7
(1*e*)	9.67±0.74	+25.3
Pyroxicam	9.45±0.74	+25.3
Control	7.54±0.82	

Table 3
Hydrogen-bond geometry (Å, °) for (I).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
Compound (1*a*) (form *A*)				
N2—H2$\cdots$O3	0.88 (3)	2.15 (3)	2.883 (3)	140 (3)
O1—H1$\cdots$O2	0.96	1.55 (4)	2.463 (3)	158 (4)
C17—H17$a\cdots$O2$^{\rm i}$	0.96	2.45	3.324 (4)	152
C17—H17$c\cdots$C12$^{\rm ii}$ (π)	0.96	2.86	3.614 (5)	136
C17—H17$c\cdots$C13$^{\rm ii}$ (π)	0.96	2.75	3.679 (5)	164
Compound (1*b*) (form *B*)				
N2—H2$\cdots$O4	0.90 (3)	2.14 (3)	2.874 (3)	138 (3)
O1—H1$\cdots$O2	0.92 (4)	1.56 (4)	2.447 (3)	162 (4)
C17—H17$c\cdots$O2$^{\rm iii}$	0.96	2.44	3.306 (4)	150
C17—H17$b\cdots$C12$^{\rm ii}$ (π)	0.96	2.84	3.601 (5)	137
C17—H17$b\cdots$C13$^{\rm ii}$ (π)	0.96	2.73	3.666 (6)	165

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

study (Lin *et al.*, 2014; Alvarez, 2014). Therefore, all five samples of benzylamides (1*a*)–(1*e*) were studied in the form of powder fractions with a particle size of 0.211–0.178 mm selected using the corresponding sieves. Seven experimental animals were used to obtain statistically reliable results (the significance level of the confidence interval accepted in this work was $p \leq 0.05$) in testing each of benzylamides (1*a*)–(1*e*), the reference drug and the control.

3. Results and discussion

The reason for choosing benzylamide (1) as the object of study was its high analgesic activity and accompanying low toxicity (Ukrainets *et al.*, 2015). In this case, the fact that benzylamide (1) had undergone biological testing as a water suspension and, hence, the drug form was applied as the solid dispersed phase, is very important.

We tried to obtain different crystal forms of benzylamide (1) by simple crystallization from solvents that are widely used and necessarily pharmaceutically acceptable (European Pharmacopoeia, 2007): methylene chloride, (1*a*), *N*,*N*-dimethylformamide, (1*b*), ethanol, (1*c*), ethyl acetate, (1*d*), and xylene, (1*e*). The crystals of both forms were not distinguishable by their colour, habit *etc.*, and passed the pharmacological tests (see *Experimental*, §2.3). The results obtained proved to be unexpected (Table 2).

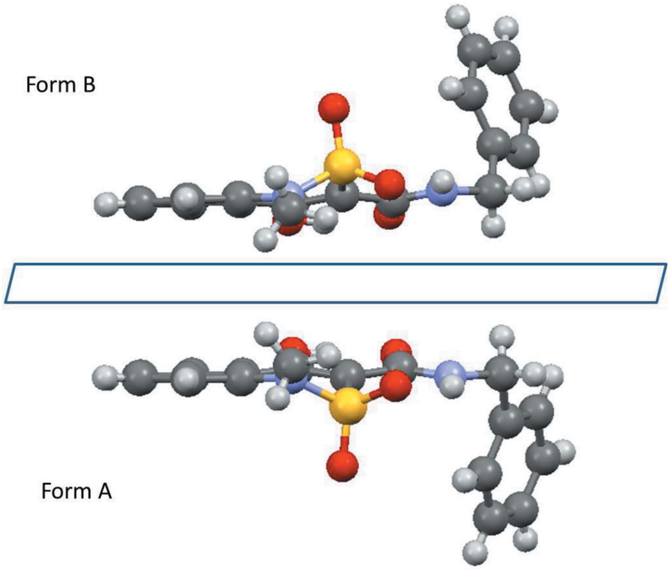
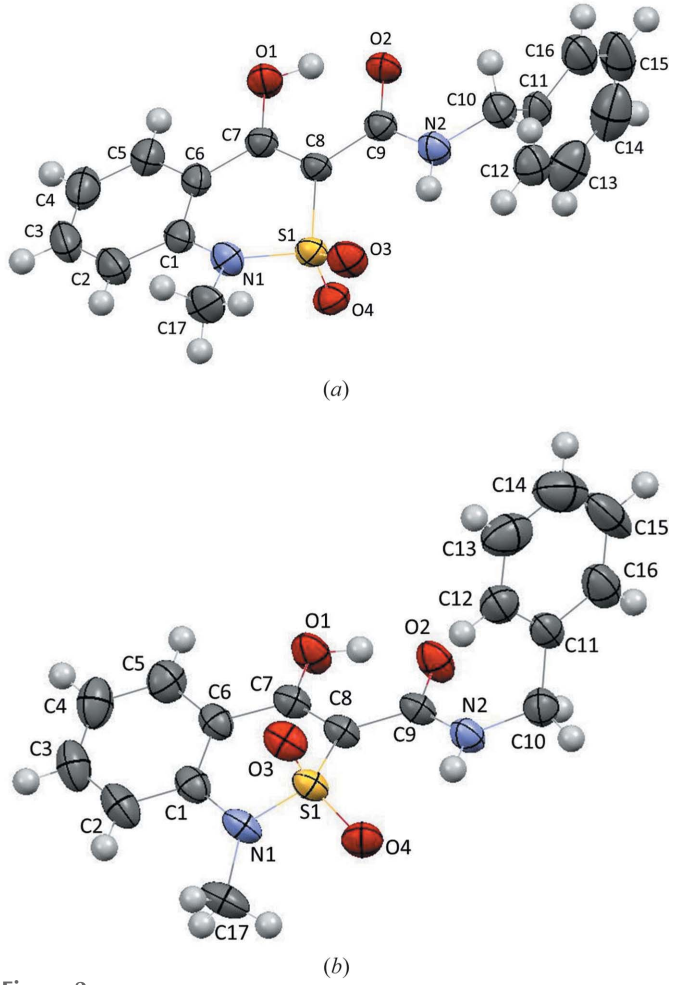


Figure 1
The molecular structures of the two pseudo-enantiomers of benzylamide (1), with form *A* at the bottom and form *B* at the top.



(*a*)

(*b*)

Figure 2
The molecular structures of (*a*) pseudo-enantiomer (1*a*) and (*b*) pseudo-enantiomer (1*b*), showing the atom-labelling schemes. In each case, displacement ellipsoids are drawn at the 50% probability level.

For some incomprehensible reason, only one sample of *N*-benzyl-4-hydroxy-1-methyl-2,2-dioxo-1*H*-2λ^6,1-benzothiazine-3-carboxamide, (1), *i.e.* that crystallized from methylene chloride, (1*a*), revealed high antinociceptive activity. The activities of the samples crystallized from the other four solvents, (1*b*)–(1*e*), proved to be about four times lower.

To study the reason for this, X-ray diffraction measurements were carried out for all five crystal samples of the benzylamide, *i.e.* (1*a*)–(1*e*), taking into account the application of this compound in the solid state. The results have shown that the benzylamide crystallized in the $P2_12_12_1$ orthorhombic chiral space group from all solvents used in our study. This indicates the existence of one enantiomer in the crystal phase. The presence of the S atom in the molecule of (1) has allowed the use of the Flack parameter (Table 1) to determine the molecule types (*A* and *B*) in the crystals, which are mirror reflections of each other (Fig. 1). The molecule of (1) does not contain any stereogenic chirotopic atom. It can be assumed to some degree that the S atom can be considered as asymmetric due to the formation of an N2—H2···O3 intramolecular hydrogen bond in (1*a*) and an N2—H2···O4 intramolecular hydrogen bond in (1*b*) with the participation of one O atom of the sulfonyl group (Table 3). On the other hand, chirality relative to a plane is known (Flack, 2003) and the planar fragment of the benzothiazine bicycle can be such a plane.

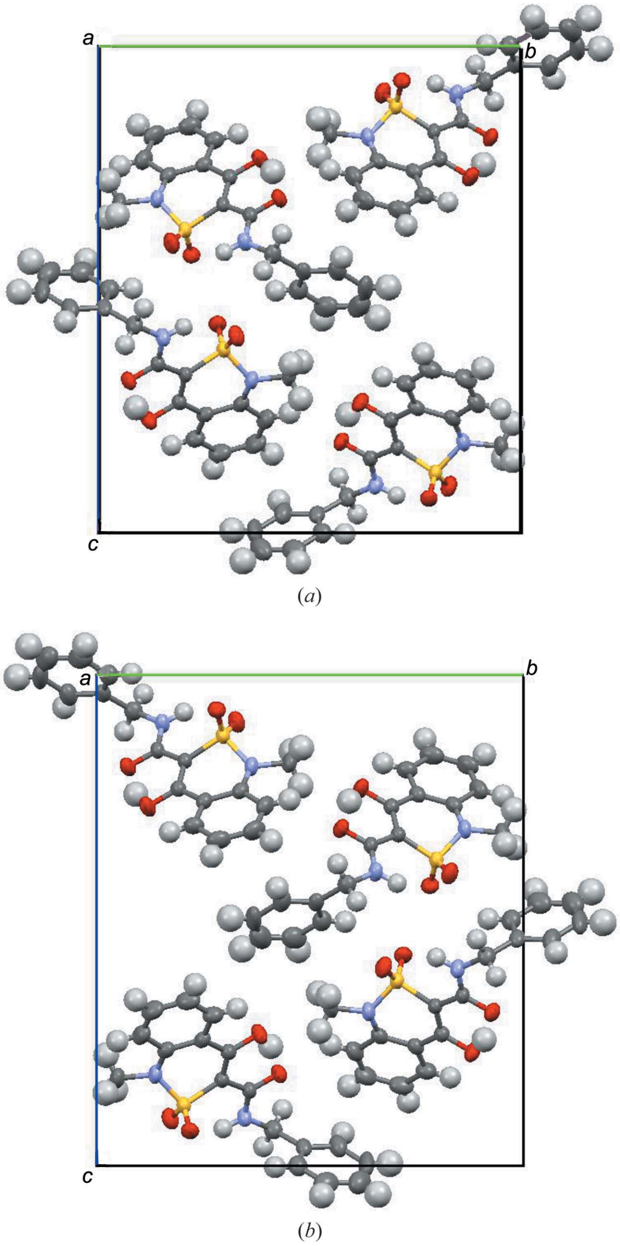


Figure 3
The crystal packing of pseudo-enantiomeric molecules (*a*) (1*a*) (in form *A*) and (*b*) (1*b*) (in form *B*).

Table 4
Selected geometric parameters (Å, °) for (1*a*) (in polymorphic form *A*) and (1*b*) (in polymorphic form *B*).

Ring-puckering parameters (Zefirov *et al.*, 1990)	(1*a*)	(1*b*)
S	0.59	0.59
Θ	50.5	50.9
Ψ	20.6	20.2
Bond lengths		
C9—O2	1.263 (3)	1.261 (4)
O1—C7	1.331 (3)	1.323 (4)
C7—C8	1.374 (4)	1.373 (4)
N1—C1	1.404 (4)	1.400 (4)
Torsion angles		
C1—N1—S1—C8	47.4 (2)	−47.1 (3)
N1—S1—C8—C7	−35.7 (3)	36.0 (3)
C9—N2—C10—C11	−67.5 (4)	67.7 (4)
N2—C10—C11—C12	−31.2 (4)	30.8 (4)
C7—C8—C9—O2	−0.7 (4)	0.8 (4)
C10—N2—C9—C8	174.0 (3)	−173.9 (3)

It was determined also that the crystals obtained from methylene chloride, (1*a*), contain only molecules of pseudo-enantiomeric form *A*, and the crystals obtained from all other solvents, (1*b*)–(1*e*), consist of molecules of pseudo-enantiomeric form *B*. This was confirmed by the single-crystal X-ray studies of benzylamides (1*a*) and (1*b*) (Fig. 2), crystals of which were chosen randomly from the total mass. Moreover, dissolution of crystals of (1*a*) in *N*,*N*-dimethylformamide and recrystallization from this solvent did not change the pseudo-enantiomeric form *A* of the benzylamide molecule, and neither did a similar experiment with crystals of (1*b*) dissolved in methylene chloride. On this basis, it can be argued that we observed the formation of two crystal phases which have to be formed in a spontaneous resolution of a conglomerate of pseudo-enantiomeric chiral molecules.

The unit-cell parameters for the studied crystal structures are similar. The values of the Flack parameter (Parsons *et al.*, 2013) [0.09 (5) for (1*a*) and −0.16 (9) for (1*b*)] have determined unambiguously the pseudo-enantiomeric type of molecule in these crystals. In both pseudo-enantiomers, the dihydrothiazine ring adopts a conformation intermediate between a twist-boat and a sofa (the puckering parameters are given in Table 4). The deviations of atoms S1 and C8 from the mean plane of the remaining atoms of the ring are −0.81 and −0.23 Å, respectively, in (1*a*), and 0.81 and 0.23 Å, respectively, in (1*b*). The ring N atom has an almost planar configuration, with the sum of the bond angles centred at this atom being 358° in both compounds. The carboxamide group at the C8 atom is coplanar with the C7═C8 endocyclic double bond (see the C7—C8—C9—O2 torsion angle in Table 4). Such a conformation is stabilized by the formation of an intramolecular O1—H1···O2 hydrogen bond (Table 3). Additionally, the formation of this fairly strong hydrogen bond causes the redistribution of the electron density within this fragment: the C9—O2 and C7—C8 bonds are elongated (Table 4) compared to the mean values (Burgi & Dunitz, 1994) for such bond types (1.210 and 1.326 Å, respectively) and the C7—O1 bond is shortened (mean value = 1.362 Å). The benzyl substituent has an antiperiplanar conformation relative to the C8—C9 bond (see the C10—N2—C9—C8 torsion angle in Table 4) and its aromatic ring is located in a –*sc* position relative to the C9—N2 bond and is turned due to rotation around the N2—C10 bond (see the C9—N2—C10—C11 and N2—C10—C11—C12 torsion angles in Table 4). A short intramolecular H12···N2 contact [the distance is 2.60 Å in both molecules compared to the van der Waals radii sum (Zefirov, 1997) of 2.67 Å] is observed. Steric repulsion between the methyl substituent and the bicyclic fragment [the shortened intramolecular contacts are: H2*A*···C17 = 2.58 Å in (1*a*) and 2.57 Å in (1*b*) (the van der Waals radii sum is 2.87 Å), H17*a*···C2 = 2.75 Å in (1*a*) and H17*c*···C2 = 2.71 Å in (1*b*) (2.87 Å), H2*A*···H17*a* = 2.33 Å in (1*a*) and H2*A*···H17*c* = 2.30 Å in (1*b*) (2.34 Å), and H17*b*···O3 = 2.38 Å in (1*a*) and H17*a*···O4 = 2.37 Å in (1*b*) (2.46 Å)] causes an elongation of the C1—N1 bond (Table 4) compared to its mean value of 1.371 Å.

The crystal packing of the two pseudo-enantiomeric molecules is of a very similar type and differs from each other as a mirror reflection (Fig. 3).

In the crystal phase, molecules (1*a*) and (1*b*) form a network of weak intermolecular hydrogen bonds (Table 3). Hydrogen bonds of the same type have very close geometric characteristics and inverse-symmetry operations. Thus, the two pseudo-enantiomeric crystal structures are mirror images of each other. Taking into account the almost complete coincidence of all factors except for this one, it could be argued that such an inequality for the two structures is the reason for the different antinociceptive activities.

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Two pseudo-enantiomeric forms of *N*-benzyl-4-hydroxy-1-methyl-2,2-dioxo-1*H*-2λ^6,1-benzothiazine-3-carboxamide and their analgesic properties

Igor V. Ukrainets, Svitlana V. Shishkina, Vyacheslav N. Baumer, Olga V. Gorokhova, Lidiya A. Petrushova and Galina Sim

Computing details

For both compounds, data collection: *CrysAlis CCD* (Agilent, 2012); cell refinement: *CrysAlis RED* (Agilent, 2012); data reduction: *CrysAlis RED* (Agilent, 2012). Program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008) for (I); SHELXT (Sheldrick, 2015b) for (II). Program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015a) for (I); olex2.refine (Bourhis *et al.*, 2015) for (II). Molecular graphics: Olex2 (Dolomanov *et al.*, 2009) for (I); OLEX2 (Dolomanov *et al.*, 2009) for (II). Software used to prepare material for publication: Olex2 (Dolomanov *et al.*, 2009) for (I); OLEX2 (Dolomanov *et al.*, 2009) for (II).

(I) *N*-Benzyl-4-hydroxy-1-methyl-2,2-dioxo-1*H*-2λ6,1-benzothiazine-3-carboxamide

Crystal data

$C_{17}H_{16}N_2O_4S$
M_r = 344.39
Orthorhombic, $P2_12_12_1$
a = 5.4764 (3) Å
b = 15.9117 (8) Å
c = 18.3228 (10) Å
V = 1596.63 (15) Å^3
Z = 4
F(000) = 720
D_x = 1.433 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 3040 reflections
θ = 3.6–30.6°
μ = 0.23 mm^{-1}
T = 293 K
, colourless
0.2 × 0.02 × 0.02 mm

Data collection

Xcalibur, Sapphire3 diffractometer
Radiation source: Enhance (Mo) X-ray Source
Graphite monochromator
Detector resolution: 16.1827 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (*CrysAlis RED*; Agilent, 2012)
$T_{\min}$ = 0.979, $T_{\max}$ = 1.000
16369 measured reflections
4658 independent reflections
3004 reflections with $I > 2\sigma(I)$
R_{int} = 0.055
$\theta_{\max}$ = 30.0°, $\theta_{\min}$ = 3.4°
$h = -5 \rightarrow 7$
$k = -20 \rightarrow 22$
$l = -25 \rightarrow 25$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.051
$wR(F^2)$ = 0.094
S = 0.99
4658 reflections
226 parameters
0 restraints
Hydrogen site location: mixed

H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.035P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.22$ e Å^{-3}
$\Delta\rho_{min} = -0.28$ e Å^{-3}
Absolute structure: Flack x determined using 910 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons *et al.*, 2013)
Absolute structure parameter: 0.09 (5)

Special details

Experimental. Absorption correction: CrysAlis RED, Agilent Technologies, Version 1.171.36.24 (release 03-12-2012 CrysAlis171 .NET) (compiled Dec 3 2012,18:21:49) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.
Intensities of 15460 reflections (4595 independent, $R_{int} = 0.039$) for structure (1*a*) and 15538 reflections (4583 independent, $R_{int} = 0.066$) for structure (1*b*) have been measured on the «Xcalibur-3» diffractometer (graphite monochromated MoK$_\alpha$ radiation, CCD detector, ω-scans, $2\Theta_{max} = 60?$). The structures were solved by direct method using SHELXTL package [Sheldrick, 2015]. Positions of the hydrogen atoms were located from electron density difference maps and refined by ?riding? model with $U_{iso} = nU_{eq}$ of the carrier atom (n = 1.5 for methyl group and 1.2 for other atoms). Hydrogen atoms of hydroxyl and amide groups were refined using isotropic approximation. Full-matrix least-squares refinement of the structures against F^2 in anisotropic approximation for non-hydrogen atoms using 4552 ((1*a*)), 4533 ((1*b*)) reflections was converged to: $wR_2 = 0.096$ ($R_1 = 0.040$ for 3608 reflections with $F>4\sigma(F)$, S = 0.992) for structure (1*a*) and $wR_2 = 0.097$ ($R_1 = 0.050$ for 2816 reflections with $F>4\sigma(F)$, S = 0.957) for structure (1*b*). The final atomic coordinates, and crystallographic data for molecules (1*a*) and (1*b*) have been deposited to with the Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk) and are available on request quoting the deposition numbers CCDC 1430997 for (1*a*) and CCDC 1430998 for (1*b*)).

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
S1	0.30167 (14)	0.70373 (4)	0.12320 (4)	0.04040 (18)
O1	0.1936 (5)	0.88090 (14)	0.26834 (12)	0.0575 (6)
H1	0.319 (7)	0.911 (3)	0.243 (2)	0.096 (14)*
O2	0.5263 (4)	0.92725 (13)	0.18735 (11)	0.0532 (6)
O3	0.5295 (4)	0.67251 (13)	0.09536 (12)	0.0556 (6)
O4	0.1137 (4)	0.71866 (14)	0.07081 (11)	0.0521 (6)
N1	0.2068 (5)	0.63746 (15)	0.18639 (13)	0.0485 (6)
N2	0.6795 (5)	0.84615 (17)	0.09810 (14)	0.0463 (6)
H2	0.671 (5)	0.797 (2)	0.0768 (16)	0.048 (8)*
C1	0.0244 (6)	0.6630 (2)	0.23545 (16)	0.0454 (7)
C2	−0.1351 (6)	0.6048 (2)	0.26687 (19)	0.0611 (9)
H2A	−0.1248	0.5485	0.2538	0.073*
C3	−0.3071 (7)	0.6301 (3)	0.31677 (19)	0.0686 (10)
H3	−0.4089	0.5903	0.3381	0.082*
C4	−0.3315 (6)	0.7139 (3)	0.33592 (18)	0.0651 (10)
H4	−0.4536	0.7307	0.3680	0.078*
C5	−0.1721 (6)	0.7720 (2)	0.30673 (16)	0.0539 (8)
H5	−0.1848	0.8282	0.3203	0.065*
C6	0.0088 (5)	0.7477 (2)	0.25688 (15)	0.0424 (7)
C7	0.1879 (6)	0.80883 (18)	0.23153 (14)	0.0419 (6)

C8	0.3466 (5)	0.79382 (18)	0.17493 (14)	0.0380 (6)
C9	0.5262 (5)	0.85844 (19)	0.15301 (15)	0.0410 (7)
C10	0.8384 (5)	0.91339 (19)	0.07288 (18)	0.0501 (8)
H10A	0.9541	0.8905	0.0381	0.060*
H10B	0.9306	0.9348	0.1141	0.060*
C11	0.7033 (6)	0.98542 (19)	0.03742 (16)	0.0474 (7)
C12	0.4874 (6)	0.9725 (2)	−0.00051 (18)	0.0581 (9)
H12	0.4209	0.9188	−0.0025	0.070*
C13	0.3684 (8)	1.0381 (3)	−0.0355 (2)	0.0782 (12)
H13	0.2229	1.0282	−0.0603	0.094*
C14	0.4641 (10)	1.1164 (4)	−0.0337 (2)	0.0904 (15)
H14	0.3851	1.1599	−0.0579	0.108*
C15	0.6761 (10)	1.1322 (3)	0.0035 (2)	0.0859 (13)
H15	0.7404	1.1863	0.0047	0.103*
C16	0.7967 (8)	1.0657 (2)	0.0400 (2)	0.0675 (10)
H16	0.9395	1.0763	0.0659	0.081*
C17	0.2715 (7)	0.54813 (19)	0.17761 (18)	0.0624 (10)
H17A	0.2814	0.5220	0.2247	0.094*
H17B	0.4265	0.5437	0.1534	0.094*
H17C	0.1487	0.5205	0.1489	0.094*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0524 (4)	0.0280 (3)	0.0408 (3)	0.0002 (3)	−0.0009 (4)	−0.0027 (3)
O1	0.0768 (15)	0.0414 (13)	0.0544 (13)	−0.0090 (13)	0.0192 (13)	−0.0139 (10)
O2	0.0731 (14)	0.0353 (13)	0.0513 (13)	−0.0123 (11)	0.0100 (12)	−0.0109 (10)
O3	0.0602 (13)	0.0395 (14)	0.0670 (14)	0.0056 (10)	0.0099 (12)	−0.0113 (10)
O4	0.0684 (14)	0.0469 (15)	0.0409 (11)	−0.0023 (10)	−0.0115 (10)	0.0006 (10)
N1	0.0650 (15)	0.0286 (13)	0.0519 (14)	−0.0022 (13)	−0.0009 (14)	0.0047 (11)
N2	0.0531 (14)	0.0342 (15)	0.0516 (15)	−0.0036 (13)	0.0099 (14)	−0.0048 (12)
C1	0.0535 (18)	0.043 (2)	0.0398 (16)	−0.0064 (15)	−0.0076 (15)	0.0089 (14)
C2	0.072 (2)	0.050 (2)	0.061 (2)	−0.0174 (18)	−0.0059 (18)	0.0107 (17)
C3	0.069 (2)	0.075 (3)	0.061 (2)	−0.029 (2)	0.003 (2)	0.017 (2)
C4	0.060 (2)	0.084 (3)	0.0520 (19)	−0.009 (2)	0.0059 (17)	0.0091 (19)
C5	0.0578 (19)	0.059 (2)	0.0454 (17)	−0.0040 (17)	0.0034 (17)	0.0039 (15)
C6	0.0450 (16)	0.0448 (19)	0.0374 (15)	−0.0061 (14)	−0.0018 (14)	0.0068 (13)
C7	0.0527 (16)	0.0345 (17)	0.0384 (14)	−0.0010 (15)	−0.0025 (15)	−0.0016 (12)
C8	0.0486 (16)	0.0277 (14)	0.0377 (14)	−0.0025 (13)	−0.0030 (12)	−0.0013 (12)
C9	0.0505 (18)	0.0335 (17)	0.0389 (15)	0.0007 (14)	−0.0030 (14)	−0.0012 (13)
C10	0.0486 (18)	0.045 (2)	0.0565 (18)	−0.0043 (15)	0.0084 (15)	0.0005 (15)
C11	0.0558 (18)	0.0400 (18)	0.0464 (16)	−0.0045 (15)	0.0210 (17)	−0.0030 (13)
C12	0.057 (2)	0.056 (2)	0.062 (2)	0.0039 (17)	0.0090 (19)	0.0002 (18)
C13	0.077 (3)	0.091 (4)	0.066 (2)	0.027 (3)	0.014 (2)	0.003 (2)
C14	0.114 (4)	0.078 (4)	0.080 (3)	0.032 (3)	0.031 (3)	0.018 (3)
C15	0.130 (4)	0.038 (2)	0.090 (3)	−0.007 (3)	0.042 (3)	0.005 (2)
C16	0.082 (2)	0.050 (2)	0.071 (2)	−0.011 (2)	0.024 (2)	−0.0060 (18)
C17	0.094 (3)	0.0308 (17)	0.063 (2)	0.0028 (17)	−0.007 (2)	0.0060 (15)

Geometric parameters (Å, º)

S1—O3	1.437 (2)	C5—C6	1.402 (4)
S1—O4	1.427 (2)	C6—C7	1.457 (4)
S1—N1	1.650 (2)	C7—C8	1.374 (4)
S1—C8	1.736 (3)	C8—C9	1.479 (4)
O1—H1	0.95 (4)	C10—H10A	0.9700
O1—C7	1.331 (3)	C10—H10B	0.9700
O2—C9	1.263 (3)	C10—C11	1.511 (4)
N1—C1	1.404 (4)	C11—C12	1.387 (5)
N1—C17	1.474 (4)	C11—C16	1.377 (4)
N2—H2	0.88 (3)	C12—H12	0.9300
N2—C9	1.325 (3)	C12—C13	1.388 (5)
N2—C10	1.454 (4)	C13—H13	0.9300
C1—C2	1.397 (4)	C13—C14	1.351 (6)
C1—C6	1.407 (4)	C14—H14	0.9300
C2—H2A	0.9300	C14—C15	1.369 (6)
C2—C3	1.373 (5)	C15—H15	0.9300
C3—H3	0.9300	C15—C16	1.416 (6)
C3—C4	1.385 (5)	C16—H16	0.9300
C4—H4	0.9300	C17—H17A	0.9600
C4—C5	1.380 (4)	C17—H17B	0.9600
C5—H5	0.9300	C17—H17C	0.9600

O3—S1—N1	107.55 (14)	C7—C8—C9	120.3 (3)
O3—S1—C8	110.87 (13)	C9—C8—S1	121.3 (2)
O4—S1—O3	116.43 (13)	O2—C9—N2	120.4 (3)
O4—S1—N1	110.57 (13)	O2—C9—C8	117.9 (3)
O4—S1—C8	109.38 (13)	N2—C9—C8	121.7 (3)
N1—S1—C8	100.90 (13)	N2—C10—H10A	108.8
C7—O1—H1	102 (2)	N2—C10—H10B	108.8
C1—N1—S1	119.2 (2)	N2—C10—C11	113.7 (3)
C1—N1—C17	121.3 (3)	H10A—C10—H10B	107.7
C17—N1—S1	117.7 (2)	C11—C10—H10A	108.8
C9—N2—H2	116 (2)	C11—C10—H10B	108.8
C9—N2—C10	120.8 (3)	C12—C11—C10	121.4 (3)
C10—N2—H2	123 (2)	C16—C11—C10	120.5 (3)
N1—C1—C6	120.0 (3)	C16—C11—C12	118.1 (3)
C2—C1—N1	121.2 (3)	C11—C12—H12	119.3
C2—C1—C6	118.8 (3)	C11—C12—C13	121.4 (4)
C1—C2—H2A	119.7	C13—C12—H12	119.3
C3—C2—C1	120.7 (4)	C12—C13—H13	120.0
C3—C2—H2A	119.7	C14—C13—C12	119.9 (4)
C2—C3—H3	119.4	C14—C13—H13	120.0
C2—C3—C4	121.1 (3)	C13—C14—H14	119.6
C4—C3—H3	119.4	C13—C14—C15	120.7 (4)
C3—C4—H4	120.5	C15—C14—H14	119.6
C5—C4—C3	119.1 (3)	C14—C15—H15	120.2

C5—C4—H4	120.5	C14—C15—C16	119.5 (4)
C4—C5—H5	119.5	C16—C15—H15	120.2
C4—C5—C6	121.0 (3)	C11—C16—C15	120.3 (4)
C6—C5—H5	119.5	C11—C16—H16	119.9
C1—C6—C7	120.6 (3)	C15—C16—H16	119.9
C5—C6—C1	119.3 (3)	N1—C17—H17A	109.5
C5—C6—C7	120.0 (3)	N1—C17—H17B	109.5
O1—C7—C6	115.4 (3)	N1—C17—H17C	109.5
O1—C7—C8	121.2 (3)	H17A—C17—H17B	109.5
C8—C7—C6	123.4 (3)	H17A—C17—H17C	109.5
C7—C8—S1	117.8 (2)	H17B—C17—H17C	109.5

S1—N1—C1—C2	151.6 (2)	C2—C3—C4—C5	−3.1 (5)
S1—N1—C1—C6	−32.0 (4)	C3—C4—C5—C6	1.6 (5)
S1—C8—C9—O2	170.6 (2)	C4—C5—C6—C1	1.2 (4)
S1—C8—C9—N2	−7.9 (4)	C4—C5—C6—C7	−174.8 (3)
O1—C7—C8—S1	−172.4 (2)	C5—C6—C7—O1	11.9 (4)
O1—C7—C8—C9	−0.8 (4)	C5—C6—C7—C8	−169.8 (3)
O3—S1—N1—C1	163.6 (2)	C6—C1—C2—C3	1.2 (5)
O3—S1—N1—C17	−31.4 (3)	C6—C7—C8—S1	9.4 (4)
O3—S1—C8—C7	−149.4 (2)	C6—C7—C8—C9	−179.0 (3)
O3—S1—C8—C9	39.1 (3)	C7—C8—C9—O2	−0.7 (4)
O4—S1—N1—C1	−68.3 (2)	C7—C8—C9—N2	−179.2 (3)
O4—S1—N1—C17	96.7 (3)	C8—S1—N1—C1	47.4 (2)
O4—S1—C8—C7	80.9 (2)	C8—S1—N1—C17	−147.6 (2)
O4—S1—C8—C9	−90.6 (2)	C9—N2—C10—C11	−67.5 (4)
N1—S1—C8—C7	−35.7 (3)	C10—N2—C9—O2	−4.4 (4)
N1—S1—C8—C9	152.8 (2)	C10—N2—C9—C8	174.0 (3)
N1—C1—C2—C3	177.6 (3)	C10—C11—C12—C13	−177.4 (3)
N1—C1—C6—C5	−179.1 (3)	C10—C11—C16—C15	176.7 (3)
N1—C1—C6—C7	−3.1 (4)	C11—C12—C13—C14	0.6 (5)
N2—C10—C11—C12	−31.2 (4)	C12—C11—C16—C15	−1.3 (5)
N2—C10—C11—C16	151.0 (3)	C12—C13—C14—C15	−1.0 (6)
C1—C2—C3—C4	1.7 (5)	C13—C14—C15—C16	0.3 (6)
C1—C6—C7—O1	−164.0 (3)	C14—C15—C16—C11	0.9 (6)
C1—C6—C7—C8	14.3 (4)	C16—C11—C12—C13	0.5 (5)
C2—C1—C6—C5	−2.5 (4)	C17—N1—C1—C2	−12.9 (4)
C2—C1—C6—C7	173.4 (3)	C17—N1—C1—C6	163.6 (3)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2···O3	0.88 (3)	2.15 (3)	2.883 (3)	140 (3)
O1—H1···O2	0.96	1.55 (4)	2.463 (3)	158 (4)
C17—H17a···O2^{i}	0.96	2.45	3.324 (4)	152

C17—H17c···C12^{ii}	0.96	2.86	3.614 (5)	136
C17—H17c···C13^{ii}	0.96	2.75	3.679 (5)	164

Symmetry codes: (i) $-x+1$, $y-1/2$, $-z+1/2$; (ii) $x-1/2$, $-y+3/2$, $-z$.

(II) *N*-Benzyl-4-hydroxy-1-methyl-2,2-dioxo-1*H*-2λ6,1-benzothiazine-3-carboxamide

Crystal data

$C_{17}H_{16}N_2O_4S$
$M_r = 344.39$
Orthorhombic, $P2_12_12_1$
$a = 5.4469$ (3) Å
$b = 15.8455$ (10) Å
$c = 18.2412$ (9) Å
$V = 1574.38$ (15) Å^3
$Z = 4$
$F(000) = 720.8596$
$D_x = 1.453$ Mg m^{-3}
Mo *Kα* radiation, $\lambda = 0.71073$ Å
Cell parameters from 2803 reflections
$\theta = 3.4$–$28.2°$
$\mu = 0.23$ mm^{-1}
$T = 293$ K
Stick, colourless
0.2 × 0.02 × 0.02 mm

Data collection

Agilent Xcalibur Sapphire3 diffractometer
Radiation source: Enhance (Mo) X-ray Source
Graphite monochromator
Detector resolution: 16.1827 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (*CrysAlis RED*; Agilent, 2012)
$T_{min} = 0.775$, $T_{max} = 1.000$
16325 measured reflections
2777 independent reflections
2296 reflections with $I \geq 2u(I)$
$R_{int} = 0.068$
$\theta_{max} = 25.0°$, $\theta_{min} = 3.4°$
$h = -6 \rightarrow 7$
$k = -23 \rightarrow 22$
$l = -27 \rightarrow 25$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.124$
$S = 0.84$
2777 reflections
225 parameters
0 restraints
25 constraints
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.20$ e Å^{-3}
$\Delta\rho_{min} = -0.21$ e Å^{-3}
Absolute structure: Flack x determined using 839 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons *et al.*, 2013)
Absolute structure parameter: −0.16 (9)

Special details

Experimental. Absorption correction: CrysAlis RED, Agilent Technologies, Version 1.171.36.24 (release 03-12-2012 CrysAlis171 .NET) (compiled Dec 3 2012,18:21:49) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	U_{iso}*/U_{eq}
S1	0.69864 (14)	0.79616 (4)	0.37664 (4)	0.0416 (2)
O1	0.8053 (5)	0.61912 (14)	0.23171 (13)	0.0597 (6)
H1	0.683 (7)	0.592 (3)	0.257 (2)	0.092 (15)*
O2	0.4734 (4)	0.57292 (14)	0.31270 (12)	0.0550 (6)

O3	0.8868 (4)	0.78152 (15)	0.42918 (12)	0.0537 (6)
O4	0.4709 (4)	0.82769 (14)	0.40441 (14)	0.0575 (6)
N1	0.7926 (5)	0.86279 (15)	0.31387 (15)	0.0495 (6)
N2	0.3199 (5)	0.65392 (17)	0.40157 (14)	0.0476 (6)
H2	0.326 (6)	0.704 (2)	0.4243 (19)	0.054 (9)*
C1	0.9743 (6)	0.8371 (2)	0.26440 (17)	0.0466 (8)
C2	1.1358 (7)	0.8951 (2)	0.2331 (2)	0.0624 (10)
H2a	1.1265 (7)	0.9517 (2)	0.2462 (2)	0.0748 (12)*
C3	1.3080 (7)	0.8692 (3)	0.1833 (2)	0.0677 (10)
H3	1.4117 (7)	0.9090 (3)	0.1622 (2)	0.0812 (12)*
C4	1.3316 (7)	0.7859 (3)	0.1636 (2)	0.0676 (11)
H4	1.4533 (7)	0.7692 (3)	0.1310 (2)	0.0811 (13)*
C5	1.1718 (7)	0.7275 (2)	0.19318 (17)	0.0573 (9)
H5	1.1846 (7)	0.6711 (2)	0.17971 (17)	0.0688 (11)*
C6	0.9913 (6)	0.7522 (2)	0.24306 (17)	0.0442 (7)
C7	0.8119 (6)	0.69118 (18)	0.26832 (16)	0.0434 (7)
C8	0.6530 (5)	0.70668 (19)	0.32516 (15)	0.0402 (7)
C9	0.4747 (6)	0.64221 (19)	0.34671 (16)	0.0417 (7)
C10	0.1612 (6)	0.5863 (2)	0.42677 (19)	0.0518 (8)
H10a	0.0438 (6)	0.6092 (2)	0.46145 (19)	0.0621 (10)*
H10b	0.0697 (6)	0.5644 (2)	0.38530 (19)	0.0621 (10)*
C11	0.2976 (6)	0.51444 (19)	0.46283 (17)	0.0482 (7)
C12	0.5141 (7)	0.5282 (2)	0.5008 (2)	0.0587 (9)
H12	0.5805 (7)	0.5822 (2)	0.5029 (2)	0.0705 (11)*
C13	0.6323 (9)	0.4623 (3)	0.5356 (2)	0.0819 (14)
H13	0.7783 (9)	0.4724 (3)	0.5606 (2)	0.0983 (16)*
C14	0.5392 (11)	0.3841 (4)	0.5340 (3)	0.0900 (15)
H14	0.6198 (11)	0.3406 (4)	0.5583 (3)	0.1080 (18)*
C15	0.3267 (12)	0.3678 (3)	0.4968 (3)	0.0900 (15)
H15	0.2635 (12)	0.3133 (3)	0.4956 (3)	0.1080 (18)*
C16	0.2029 (9)	0.4338 (2)	0.4602 (2)	0.0678 (10)
H16	0.0589 (9)	0.4230 (2)	0.4344 (2)	0.0813 (12)*
C17	0.7284 (8)	0.9518 (2)	0.3220 (2)	0.0646 (11)
H17a	0.571 (3)	0.9565 (2)	0.3451 (14)	0.0969 (16)*
H17b	0.850 (3)	0.9794 (4)	0.3517 (13)	0.0969 (16)*
H17c	0.723 (5)	0.9780 (5)	0.2745 (2)	0.0969 (16)*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
S1	0.0541 (4)	0.0299 (4)	0.0407 (4)	−0.0002 (3)	−0.0005 (4)	−0.0021 (3)
O1	0.0801 (16)	0.0392 (13)	0.0598 (14)	−0.0082 (13)	0.0200 (14)	−0.0139 (10)
O2	0.0749 (15)	0.0385 (13)	0.0517 (13)	−0.0132 (11)	0.0090 (12)	−0.0101 (10)
O3	0.0719 (14)	0.0486 (15)	0.0407 (11)	−0.0024 (11)	−0.0109 (10)	−0.0016 (10)
O4	0.0620 (13)	0.0425 (14)	0.0679 (15)	0.0054 (11)	0.0087 (13)	−0.0111 (11)
N1	0.0670 (16)	0.0280 (13)	0.0535 (14)	−0.0032 (13)	−0.0010 (15)	0.0027 (11)
N2	0.0575 (15)	0.0322 (15)	0.0532 (15)	−0.0034 (13)	0.0098 (14)	−0.0032 (11)
C1	0.0541 (18)	0.0446 (19)	0.0413 (16)	−0.0048 (15)	−0.0054 (15)	0.0085 (14)

C2	0.078 (2)	0.050 (2)	0.059 (2)	−0.0199 (18)	−0.0064 (19)	0.0110 (17)
C3	0.071 (2)	0.075 (3)	0.057 (2)	−0.025 (2)	0.005 (2)	0.0142 (19)
C4	0.060 (2)	0.092 (3)	0.051 (2)	−0.014 (2)	0.0073 (17)	0.008 (2)
C5	0.063 (2)	0.065 (2)	0.0437 (17)	−0.0002 (17)	0.0054 (18)	0.0027 (15)
C6	0.0510 (17)	0.0405 (18)	0.0412 (15)	−0.0049 (14)	−0.0041 (14)	0.0063 (14)
C7	0.0542 (16)	0.0364 (16)	0.0394 (15)	0.0017 (15)	−0.0009 (15)	−0.0002 (12)
C8	0.0521 (17)	0.0324 (15)	0.0362 (14)	−0.0009 (13)	−0.0009 (13)	0.0002 (12)
C9	0.0537 (18)	0.0300 (16)	0.0414 (15)	−0.0004 (13)	−0.0012 (15)	−0.0014 (13)
C10	0.0502 (18)	0.050 (2)	0.0547 (18)	−0.0044 (15)	0.0065 (15)	0.0000 (15)
C11	0.0580 (18)	0.0385 (17)	0.0482 (17)	−0.0009 (15)	0.0190 (17)	−0.0038 (13)
C12	0.060 (2)	0.054 (2)	0.063 (2)	0.0032 (17)	0.0113 (19)	−0.0036 (18)
C13	0.082 (3)	0.093 (4)	0.071 (3)	0.027 (3)	0.013 (2)	0.003 (3)
C14	0.113 (4)	0.075 (4)	0.083 (3)	0.029 (3)	0.023 (3)	0.010 (3)
C15	0.140 (4)	0.038 (2)	0.092 (3)	−0.008 (3)	0.050 (3)	0.003 (2)
C16	0.080 (2)	0.050 (2)	0.073 (2)	−0.0096 (19)	0.022 (2)	−0.0078 (18)
C17	0.096 (3)	0.0346 (17)	0.063 (2)	0.0026 (18)	−0.010 (2)	0.0065 (15)

Geometric parameters (Å, º)

S1—O3	1.422 (2)	C5—C6	1.396 (5)
S1—O4	1.430 (2)	C6—C7	1.450 (4)
S1—N1	1.639 (3)	C7—C8	1.373 (4)
S1—C8	1.719 (3)	C8—C9	1.463 (4)
O1—H1	0.92 (4)	C10—H10a	0.9700
O1—C7	1.323 (4)	C10—H10b	0.9700
O2—C9	1.261 (4)	C10—C11	1.510 (5)
N1—C1	1.400 (4)	C11—C12	1.385 (5)
N1—C17	1.461 (4)	C11—C16	1.378 (5)
N2—H2	0.90 (4)	C12—H12	0.9300
N2—C9	1.322 (4)	C12—C13	1.381 (6)
N2—C10	1.451 (4)	C13—H13	0.9300
C1—C2	1.395 (5)	C13—C14	1.340 (7)
C1—C6	1.403 (5)	C14—H14	0.9300
C2—H2a	0.9300	C14—C15	1.366 (7)
C2—C3	1.369 (6)	C15—H15	0.9300
C3—H3	0.9300	C15—C16	1.412 (7)
C3—C4	1.373 (6)	C16—H16	0.9300
C4—H4	0.9300	C17—H17a	0.9600
C4—C5	1.380 (5)	C17—H17b	0.9600
C5—H5	0.9300	C17—H17c	0.9600

O4—S1—O3	116.33 (14)	C9—C8—S1	121.7 (2)
N1—S1—O3	110.54 (15)	C9—C8—C7	119.8 (3)
N1—S1—O4	107.04 (15)	N2—C9—O2	119.4 (3)
C8—S1—O3	109.74 (14)	C8—C9—O2	118.6 (3)
C8—S1—O4	110.88 (14)	C8—C9—N2	121.9 (3)
C8—S1—N1	101.23 (13)	H10a—C10—N2	108.82 (17)
C7—O1—H1	99 (3)	H10b—C10—N2	108.82 (18)

C1—N1—S1	118.9 (2)	H10b—C10—H10a	107.7
C17—N1—S1	118.5 (2)	C11—C10—N2	113.7 (3)
C17—N1—C1	121.0 (3)	C11—C10—H10a	108.82 (17)
C9—N2—H2	117 (2)	C11—C10—H10b	108.82 (18)
C10—N2—H2	122 (2)	C12—C11—C10	121.2 (3)
C10—N2—C9	121.1 (3)	C16—C11—C10	120.0 (3)
C2—C1—N1	121.2 (3)	C16—C11—C12	118.8 (3)
C6—C1—N1	120.3 (3)	H12—C12—C11	119.7 (2)
C6—C1—C2	118.5 (3)	C13—C12—C11	120.5 (4)
H2a—C2—C1	119.8 (2)	C13—C12—H12	119.7 (3)
C3—C2—C1	120.4 (4)	H13—C13—C12	119.6 (3)
C3—C2—H2a	119.8 (2)	C14—C13—C12	120.8 (5)
H3—C3—C2	119.1 (2)	C14—C13—H13	119.6 (3)
C4—C3—C2	121.7 (3)	H14—C14—C13	119.8 (3)
C4—C3—H3	119.1 (2)	C15—C14—C13	120.5 (5)
H4—C4—C3	120.6 (2)	C15—C14—H14	119.8 (3)
C5—C4—C3	118.9 (4)	H15—C15—C14	120.0 (3)
C5—C4—H4	120.6 (2)	C16—C15—C14	120.0 (4)
H5—C5—C4	119.6 (2)	C16—C15—H15	120.0 (3)
C6—C5—C4	120.7 (4)	C15—C16—C11	119.4 (4)
C6—C5—H5	119.6 (2)	H16—C16—C11	120.3 (2)
C5—C6—C1	119.7 (3)	H16—C16—C15	120.3 (3)
C7—C6—C1	120.4 (3)	H17a—C17—N1	109.5
C7—C6—C5	119.7 (3)	H17b—C17—N1	109.5
C6—C7—O1	115.7 (3)	H17b—C17—H17a	109.5
C8—C7—O1	121.2 (3)	H17c—C17—N1	109.5
C8—C7—C6	123.1 (3)	H17c—C17—H17a	109.5
C7—C8—S1	118.0 (2)	H17c—C17—H17b	109.5

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2···O4	0.90 (3)	2.14 (3)	2.874 (3)	138 (3)
O1—H1···O2	0.92 (4)	1.56 (4)	2.447 (3)	162 (4)
C17—H17*c*···O2iii^{i}	0.96	2.44	3.306 (4)	150
C17—H17*b*···C12iv^{ii}	0.96	2.84	3.601 (5)	137
C17—H17*b*···C13iv^{ii}	0.96	2.73	3.666 (6)	165

Symmetry codes: (i) −*x*+1, *y*+1/2, −*z*+1/2; (ii) −*x*+1/2, −*y*+1, *z*+3/2.