Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

'Segmented' crystals solved using synchrotron radiation: (2*S*,3*R*,4*S*,5*R*)-4-(10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]decan-4-ylcarbonyl)-2,6-diphenylperhydropyrrolo[3,4-*c*]pyrrole-1,3-dione

Graeme J. Gainsford,* Simon P. H. Mee and Andreas Luxenburger

Industrial Research Limited, PO Box 31-310, Lower Hutt, New Zealand
Correspondence e-mail: g.gainsford@irl.cri.nz

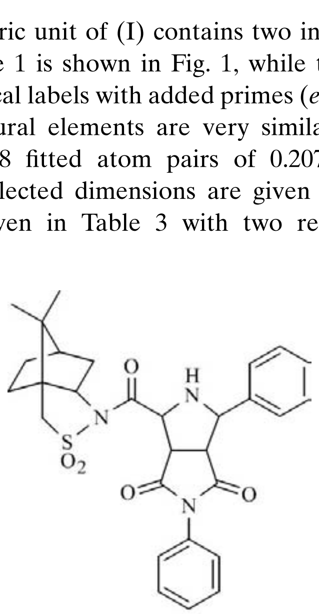
Received 19 May 2009
Accepted 28 May 2009
Online 13 June 2009

The title compound, $C_{29}H_{31}N_3O_5S$, forms needle-shaped 'segmented' crystals, thereby inhibiting successful single-crystal data collection using conventional laboratory facilities. One crystallite of dimensions 0.15 × 0.03 × 0.01 mm yielded sufficent single-crystal diffraction data on the Australian Synchrotron PX1 beamline. The two independent molecules in the asymmetric unit are nearly superimposable and show only minor conformational deviations from closely related compounds. The molecules pack using one N—H···O hydrogen bond and several phenyl C—H···O(=S), phenyl C—H···O(=C) and methylene C—H···O(=C) hydrogen bonds and weak C—H···π interactions.

Comment

The title compound, (I), originated from a continuing research programme designed to explore preparative routes to chiral pyrrolidine scaffolds. The previously used synthetic route to (I) was employed (Gainsford *et al.*, 2009), with the 1,3-dipolar cycloaddition carried out with *N*-phenylmaleimide and benzaldehyde in the presence of silver acetate. This structural study was undertaken to confirm the stereochemistry. Two conventional laboratory data collections failed, possibly because of the crystal morphology: the single acicular crystals are almost invariably multiple crystals, 'segmented' along the needle axis. Eventually, a fragment 0.15 × 0.03 × 0.01 mm in size was obtained that proved to be a single crystal, and data were collected from it using the Australian Synchrotron PX1 beamline (McPhillips *et al.*, 2002). The known absolute configuration of the independent molecules was confirmed by the observed X-ray anomalous dispersion effects [3909 Bijvoet pairs, Flack *x* parameter = 0.03 (4) (Flack, 1983); Hooft *y* parameter = 0.04 (3) (Hooft *et al.*, 2008)].

The asymmetric unit of (I) contains two independent molecules; molecule 1 is shown in Fig. 1, while the second molecule has identical labels with added primes (*e.g.* S1′ instead of S1). The structural elements are very similar, with a mean deviation for 38 fitted atom pairs of 0.207 Å (*PLATON*; Spek, 2009). Selected dimensions are given in Table 1, and comparisons given in Table 3 with two related structures isomorphous by addition, *viz.* the diethyl and dimethyl ester analogues (II) [Cambridge Structural Database (CSD, Version 5.30, with May 2009 updates; Allen, 2002) refcode MOLGAW; Gainsford *et al.*, 2009] and (III) (CSD refcode MIPPOQ; Garner *et al.*, 2001), respectively. The bond length internal self-consistency raised an issue when it was observed that the S=O bond distances [average 1.440 (3) Å] are significantly longer than those in other reported 4-(10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-4-carbonyl structures, where the mean for 24 values in the CSD is 1.421 (1) Å. However, the other structural parameters in this entity are normal (Tables 1 and 3). Specifically, the S—N average and ranges for the 12 previously reported compounds



(I)

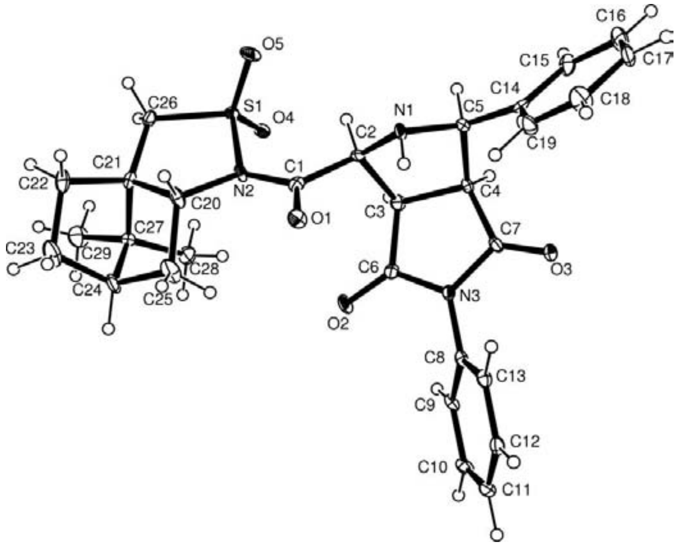


Figure 1
The structure of one of the independent molecules in the asymmetric unit of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

doi:10.1107/S0108270109020435

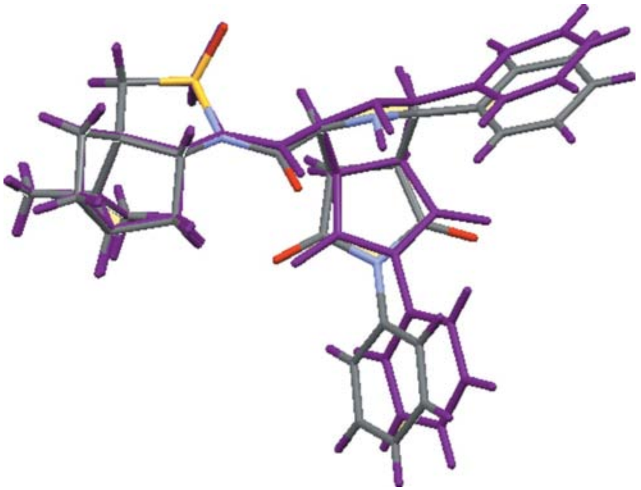


Figure 2
Overlap view of the two independent molecules of (I). Differently coloured bonds denote the primed molecule 2, and the single colour denotes molecule 1.

are 1.689 (1) and 1.657–1.706 Å, respectively, and the corresponding S—C values are 1.779 (2) and 1.771–1.795 Å.

Conformational differences between the two molecules of (I) are shown in the overlap view in Fig. 2, and are quantified by the different torsion angles involving the S1—N2 (S1′—N2′) bond (Table 1) and the dihedral φ angles between the mean planes through selected ring atoms (Table 3). The five-membered pyrrole-1,3-dione rings (C3/C4/C6/C7/N3) are effectively planar [maximum out-of-plane deviation for atom C4 = 0.025 (3) Å], with the maximum dione O-atom deviation being 0.067 (2) Å for atom O2′. The two pyrrolidine rings (N1/C2–C5) are very similar, being midway between envelope and twist conformations: Cremer & Pople (1975) Q_2 and φ_2 parameters are 0.399 (3)/0.382 (3) Å and 171.9 (4)/168.8 (5)°, respectively. The mean planes through the two fused five-membered rings subtend angles of 68.81 (16) and 68.70 (16)° to each other in the unprimed and primed molecules, respectively, compared with 73.93 (16)° in *endo*-methyl 3-(*R*,*S*)-[*cis*-3-benzyloxy-1-(4-methoxyphenyl)-4-oxoazetidin-2-(*S*,*R*)-yl]-5-methyl-4,6-dioxooctahydropyrrolo[3,4-*c*]pyrrole-1-carboxylate (CSD refcode VEMJOM; Grigg *et al.*, 1999). The few structural differences between (I) and closely related structures (II) and (III) are shown in the torsion angles (last four entries, Table 3).

As in both previously reported structures (II) and (III), there are a plethora of intermolecular contacts in (I) involving ‘nonconventional’ C—H interactions with O-atom acceptors; acceptor atoms are the sultam O atoms (O4 and O4′) and the carbonyl O atoms (O1, O2 and O3) (Table 2). In Table 2, entries 13 and 14 refer to C—H$\cdots\pi$ interactions (*Cg*1 and *Cg*2 are the ring centres of phenyl groups C8′–C13′ and C14′–C19′, respectively). For molecule 1 (unprimed labels), a conventional hydrogen bond (entry 1, Table 2) exists between the amine H atom on N1 and sultam atom O4. For completeness, the last two entries in Table 2 indicate the close intramolecular interaction between the amine H atoms on N1 and N1′ and atoms O1 and O1′, respectively.

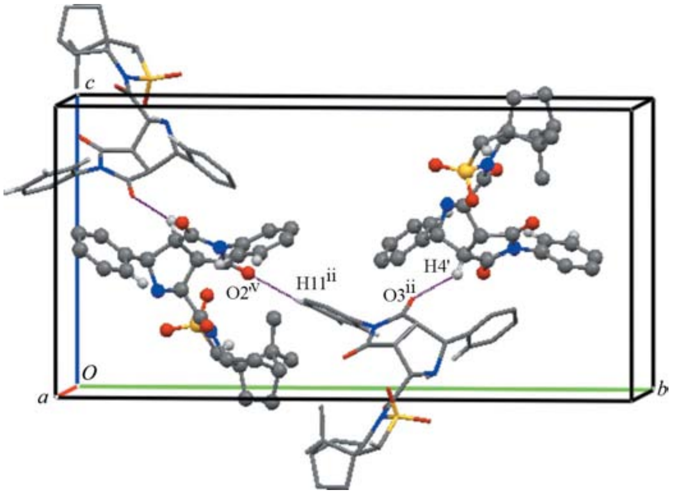


Figure 3
A view of the packing of the cell of (I) down the *a* axis. Primed (molecule 1) and unprimed (molecule 2) molecules are shown in stick and ball modes, respectively. Two representative C—H$\cdots$O interactions are shown. Only H atoms involved in interactions (Table 2) are shown for clarity. [Symmetry codes: (ii) $x + 1, y, z$; (v) $-x + 1, y - \frac{1}{2}, -z + 1$.]

There are four comments worth making about the intermolecular binding interactions in (I). Firstly, most involve atoms of symmetry-related molecules rather than being between the two independent molecules (the exceptions being entries 2, 3 and 10 in Table 2). Secondly, sultam atom O4 is trifurcated, utilizing interactions with the closest symmetry-related molecule along the *a* axis (entries 1, 6 and 8). Thirdly, all the interactions except one have been observed in closely related structures as follows [where the type, H$\cdots$O distance in Å, C (or N)—H$\cdots$O angle in degrees (°) and CSD refcode are given in the order listed in Table 2]: entry 1, N—H$\cdots$O═S, 2.23, 158 (YEXTUQ; von Wangelin *et al.*, 2001); entry 2, tertiary C—H$\cdots$O═C (pyrrole-1,3-dione), 2.41, 136 (SALYEJ; Grigg *et al.*, 1989); entry 3, *N*-phenyl C—H(*para*)$\cdots$O═C (pyrrole-1,3-dione), 2.52, 146 (PICXOO; Harwood *et al.*, 1993); entries 4 and 5, *N*-phenyl C—H(*meta*)$\cdots$O═C (pyrrole-1,3-dione), 2.41, 141 (XOKFEI; Petrovskaia *et al.*, 2001); entries 6–9, phenyl C—H(*ortho*)$\cdots$O═S, 2.39, 156 (GASSOJ; Yong *et al.*, 2005); entries 11 and 12, *S*-methylene C—H$\cdots$O═C, 2.26, 156 (ISOGUS; Miyabe *et al.*, 2004). Finally, the C—H$\cdots\pi$ interactions (entries 13 and 14) appear to ‘combine’ with C—H$\cdots$O interactions; in Table 2, the linked entries are 3 and 13, and 10 and 14. Entry 10, involving a C—H interaction with a three-coordinate N atom (N1′), has not been observed before (according to a CSD search). Thus, apart from this latter interaction, it has not been possible to assign a relative significance to these ‘nonclassical’ interactions. A packing diagram to illustrate all these interactions is not feasible. Fig. 3 illustrates how the two independent chiral molecules are packed in the cell.

Finally, we note that even with on-site scrutiny, admittedly without the benefit of a microscope fitted with crossed polarizing light capacity, it was almost impossible to identify a ‘clean’ single crystal from the crystal batch. In the end, although the observed initial diffraction images gave some indication, it took six different crystal mountings using the intense (synchrotron) X-ray source before a succesful unique data set was collected. We have since observed the segmentation pattern in the larger needles under high magnification using polarized light.

Experimental

2-Amino-1-(10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo-[5.2.1.0^{1,5}]dec-4-yl)ethanone (185 mg, 680 µmol) was treated with benzaldehyde (69.0 µl, 680 µmol), *N*-phenylmaleimide (353 µl, 2.04 mmol) and silver acetate (5.70 mg, 34.0 µmol) in tetrahydrofuran (2.00 ml), as described previously by Gainsford *et al.* (2009), to give the title compound (250 mg, 69%) as an off-white solid (m.p. 537–539 K). $[\alpha]_D^{21} = -17.9°$ (*c* 1.09, $CHCl_3$). The spectroscopic data were consistent with those previously reported by Garner *et al.* (2001) {compound (39*a*) in section 3.6.3, which has the alternative name [1*R*-[1α(3a*R**,6*S**,7a*S**),3α,3aβ,6aβ]]-hexahydro-8,8-dimethyl-1-[(hexahydro-4,6-dioxo-3,5-diphenylpyrrolo[3,4-*c*]pyrrol-1-yl)carbonyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide}. The crystallization solvent was dichloromethane and crystals of (I) formed from the diffusion of ether into the solution.

Crystal data

$C_{29}H_{31}N_3O_5S$
$M_r = 533.63$
Monoclinic, $P2_1$
$a = 7.3990\ (15)$ Å
$b = 26.328\ (5)$ Å
$c = 13.214\ (3)$ Å
$\beta = 91.17\ (3)°$
$V = 2573.6\ (9)$ Å^3
$Z = 4$
Synchrotron radiation
$\lambda = 0.77300$ Å
$\mu = 0.17$ mm^{-1}
$T = 100$ K
0.15 × 0.03 × 0.01 mm

Data collection

ADSC Quantum 210r CCD area-detector diffractometer
29004 measured reflections
8071 independent reflections
7637 reflections with $I > 2\sigma(I)$
$R_{int} = 0.092$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.044$
$wR(F^2) = 0.111$
$S = 1.03$
8071 reflections
693 parameters
1 restraint
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max} = 0.32$ e Å^{-3}
$\Delta\rho_{min} = -0.39$ e Å^{-3}
Absolute structure: Flack (1983), with 3898 Friedel pairs
Flack parameter: 0.03 (4)

Table 1
Selected geometric parameters (Å, °).

N1—H1N	0.95 (3)	N1′—H1′N	0.89 (4)
N3—C6	1.381 (4)	N3′—C6′	1.386 (4)
N3—C7	1.414 (4)	N3′—C7′	1.414 (4)
N3—C8	1.439 (4)	N3′—C8′	1.437 (3)
C8—C9	1.377 (4)	C8′—C9′	1.395 (4)
C1—N2—C20	120.8 (2)	C1′—N2′—C20′	122.2 (2)
C1—N2—S1	123.81 (19)	C1′—N2′—S1′	123.6 (2)
O4—S1—N2—C1	78.6 (2)	O4′—S1′—N2′—C1′	69.4 (2)
O5—S1—N2—C1	−50.1 (2)	O5′—S1′—N2′—C1′	−58.9 (2)

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

*Cg*1 and *Cg*2 are the centroids of the C8′–C13′ and C14′–C19′ rings, respectively.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1N···O4^{i}	0.95 (3)	2.55 (4)	3.495 (3)	170 (2)
C4′—H4′···O3^{ii}	1.00	2.41	3.243 (4)	140
C11—H11···O2′^{iii}	0.95	2.55	3.321 (4)	138
C12—H12···O2^{i}	0.95	2.38	3.259 (4)	155
C12′—H12′···O2′^{i}	0.95	2.41	3.280 (4)	151
C13—H13···O4^{i}	0.95	2.51	3.320 (3)	144
C13′—H13′···O4′^{i}	0.95	2.48	3.317 (4)	147
C19—H19···O4^{i}	0.95	2.32	3.245 (4)	165
C19′—H19′···O4′^{i}	0.95	2.36	3.290 (4)	168
C26—H26*A*···N1′^{iv}	0.99	2.52	3.477 (4)	162
C26—H26*B*···O1^{ii}	0.99	2.30	3.243 (3)	160
C26′—H262···O1′^{ii}	0.99	2.36	3.242 (4)	149
C10—H10···*Cg*1^{iii}	0.95	2.69	3.486 (3)	142
C22—H22*B*···*Cg*2^{iv}	0.99	2.84	3.757 (3)	153
N1′—H1N′···O1′	0.89 (4)	2.29 (4)	2.746 (3)	112 (3)
N1—H1N···O1	0.95 (3)	2.43 (3)	2.802 (3)	103 (2)

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

Table 3
Comparison of selected bond lengths and angles (Å, °) in compounds (I), (II) and (III).

φ are interplanar angles.

Bonds/angles	(I), unprimed	(I), primed	(II)	(III)
S1—O4	1.438 (2)	1.439 (2)	1.426 (2)	1.423 (4)
S1—O5	1.440 (3)	1.443 (2)	1.430 (2)	1.428 (4)
S1—N2	1.703 (2)	1.699 (2)	1.6733 (18)	1.687 (3)
S1—C26	1.779 (3)	1.780 (3)	1.791 (2)	1.795 (3)
O1—C1	1.213 (3)	1.215 (4)	1.195 (3)	1.199 (9)
φ†	88.87 (15)	83.23 (15)		
φ‡	57.35 (13)	52.01 (13)		
N2—C1—C2—N1	141.0 (2)	140.7 (2)	148.7 (2)	148.2 (3)
O1—C1—C2—C3	78.7 (3)	79.2 (3)	90.5 (3)	89.2 (5)
S1—N2—C1—O1	161.3 (2)	167.9 (2)	153.6 (2)	151.1 (4)
C2—C3—C6—O2	70.7 (4)	71.3 (4)	−166.8 (2)	−165.2 (3)

† Mean planes through C20/C21/C26/S1/N2 and C2–C5/N1. ‡ Mean planes through phenyl rings C8–C13 and C14–C19.

A total of 18 reflections were omitted, 13 as outliers (mainly at the edge of resolution) and five partially screened by the backstop. The H atoms on N1 and N1′ were located and refined. All C-bound H atoms were constrained to their expected geometries, with C—H = 0.98, 0.99 or 1.00 Å. Methyl H atoms were refined with $U_{iso}(H) = 1.5U_{eq}(C)$, and all other H atoms were refined with $U_{iso}(H) = 1.2U_{eq}(C,N)$.

Data collection: Quantum 210r software (ADSC, 2009); cell refinement: *XDS* (Kabsch, 1993); data reduction: *XDS* (locally modified) and *XPREP* (Bruker, 2001); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXL97* and *PLATON* (Spek, 2009).

The structural study was supported by the New Zealand Synchrotron Group and the Australian Synchrotron, Victoria, Australia. We thank Drs Adams, Huyton and Williamson of the Australian Synchrotron for their assistance, and the New

Zealand Foundation for Research, Science and Technology and New Zealand Pharmaceuticals Ltd for financial support. The diffraction data were collected on the PX1 beamline (McPhillips *et al.*, 2002) at the Australian Synchrotron, Victoria, Australia. The views expressed herein are those of the authors and are not necessarily those of the owner or operator of the Australian Synchrotron.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ3199). Services for accessing these data are described at the back of the journal.

References

ADSC (2009). Quantum 210r software, http://www.adsc-xray.com/.

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.

Bruker (2001). *XPREP for UNIX*. Bruker AXS Inc., Madison, Wisconsin, USA.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Gainsford, G. J., Mee, S. P. H. & Luxenburger, A. (2009). *Acta Cryst.* C**65**, o15–o18.

Garner, P., Dogan, O., Youngs, W. J., Kennedy, V. O., Protasiewicz, J. & Zaniewski, R. (2001). *Tetrahedron*, **57**, 71–85.

Grigg, R., Donegan, G., Gunaratne, H. Q. N., Kennedy, D. A., Malone, J. F., Sridharan, V. & Thianpatanugal, S. (1989). *Tetrahedron*, **45**, 1723–1746.

Grigg, R., Thornton-Pett, M., Xu, J. & Xu, L.-H. (1999). *Tetrahedron*, **55**, 13841–13866.

Harwood, L. M., Manage, A. C., Robin, S., Hopes, S. F. G., Watkin, D. J. & Williams, C. E. (1993). *Synlett*, pp. 777–780.

Hooft, R. W. W., Straver, L. H. & Spek, A. L. (2008). *J. Appl. Cryst.* **41**, 96–103.

Kabsch, W. (1993). *J. Appl. Cryst.* **26**, 795–800.

Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.

McPhillips, T. M., McPhillips, S. E., Chiu, H.-J., Cohen, A. E., Deacon, A. M., Ellis, P. J., Garman, E., Gonzalez, A., Sauter, N. K., Phizackerley, R. P., Soltis, S. M. & Kuhn, P. (2002). *J. Synchrotron Rad.* **9**, 401–406.

Miyabe, H., Yamaoka, Y., Naito, T. & Takemoto, Y. (2004). *J. Org. Chem.* **69**, 1415–1418.

Petrovskaia, O., Taylor, B. M., Hauze, D. B., Carroll, P. J. & Joulli, M. M. (2001). *J. Org. Chem.* **66**, 7666–7675.

Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.

Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.

Wangelin, A. J. von, Neumann, H., Gördes, D., Spannenberg, A. & Beller, M. (2001). *Org. Lett.* **3**, 2895–2898.

Yong, S. R., Williams, M. C., Pyne, S. G., Ung, A. T., Skelton, B. W., White, A. H. & Turner, P. (2005). *Tetrahedron*, **61**, 8120–8129.