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3-Methoxy-1-(4-methoxyphenyl)-4,4-bis(methylsulfoxy)azetidin-2-one

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Key indicators

Single-crystal X-ray study
T = 193 K
Mean σ(C–C) = 0.003 Å
R factor = 0.042
wR factor = 0.115
Data-to-parameter ratio = 11.8

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

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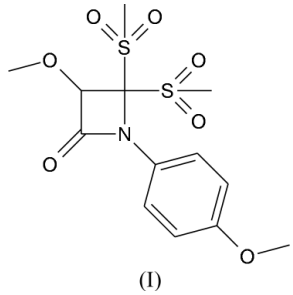
The title compound, $C_{13}H_{17}NO_7S_2$, was designed as a precursor of human leukocyte elastase inhibitors. The title compound belongs to a series of monocyclic C-methylthiolated β-lactam sulfones with different substituents at the ring N atom and the C atom opposite. The compound crystallizes with two independent molecules in the asymmetric unit differing mainly in the orientation of the phenyl ring.

Comment

Since the discovery of β-lactam antibiotics, the β-lactam ring (azetidin-2-one) is considered a general 'lead structure' for the design of new inhibitors of enzymes containing a serine nucleophile in the active site.

Currently, the most important medicinal targets, representatives of serine enzymes, are elastases and β-lactamases. Their inactivation has been recently explored with monocyclic azetidinones. In this new generation of inhibitors, the β-lactam ring is designed to have as substituents, electron-withdrawing groups (EWG), providing chemical activation of the lactam ring toward nucleophilic attack. Another feature of the monocyclic inhibitors is the presence of substituents required for specific enzyme recognition at the C3, C4 and N1 positions (Konaklieva, 2002). The title compound, (I), was synthesized as part of an ongoing program on the synthesis of monocyclic β-lactams as potential inhibitors of human leukocyte elastase.



(I)

The title compound crystallizes in the triclinic space group $P\overline{1}$ with two molecules in the asymmetric unit (Fig. 1). A comparison of the four-membered rings and their adjacent atoms (*i.e.* N1, C1′, C2, O2, C3, O3 and C4 in molecule 1 with their corresponding atoms in molecule 2) yields an r.m.s. deviation of 0.387 Å. The small r.m.s. deviation for these core atoms is also reflected in a small difference in the N1—C2—C3—C4 and N11—C12—C13—C14 torsion angles (Table 1). Much larger deviations are evident in other parts of the structure (Fig. 2), as evidenced by the difference in the C4—N1—C1′—C2′ torsion angles [-110.2 (2) *versus* 110.5 (3)°], and relatively large r.m.s. deviations for the S atoms (0.789 and 0.819).

Experimental

The title compound was prepared using the [2+2] cycloaddition reaction between acyl chloride and dithiocarbonimidate to give 3-methoxy-1-(4-methoxyphenyl)-4,4-bis(methylthio)azetidin-2-one. To a solution of this azetidin-2-one in methylene chloride at room temperature were added 4.5 molar equivalents of *meta*-chloroperoxybenzoic acid (mCPBA). The mixture was stirred overnight and was then treated with 5% of $NaHSO_4$ for 15 min. The organic layer was washed with 5% $NaHCO_3$ solution. The aqueous layer was extracted with methylene chloride, and the combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Flash chromatography yielded 65% of the title sulfone as a white solid.

Crystal data

$C_{13}H_{17}NO_7S_2$
$M_r = 363.40$
Triclinic, $P\overline{1}$
$a = 8.0552$ (1) Å
$b = 11.6680$ (1) Å
$c = 18.3257$ (2) Å
$\alpha = 95.079$ (1)°
$\beta = 102.171$ (1)°
$\gamma = 93.226$ (1)°
$V = 1672.10$ (3) Å^3
$Z = 4$
$D_x = 1.444$ Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 7139 reflections
$\theta = 2.5$–67.1°
$\mu = 3.21$ mm^{-1}
$T = 193$ (2) K
Prism, colorless
0.26 × 0.11 × 0.10 mm

Data collection

Bruker SMART 6000 CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2000)
$T_{min} = 0.452$, $T_{max} = 0.729$
8699 measured reflections
4996 independent reflections
4587 reflections with $I > 2\sigma(I)$
$R_{int} = 0.033$
$\theta_{max} = 67.2°$
$h = -9 \rightarrow 8$
$k = -13 \rightarrow 12$
$l = -21 \rightarrow 21$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.042$
$wR(F^2) = 0.115$
$S = 1.08$
4996 reflections
422 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0656P)^2 + 0.2601P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.25$ e Å^{-3}
$\Delta\rho_{min} = -0.34$ e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0136 (7)

Table 1
Selected torsion angles (°).

N1—C2—C3—C4	−7.08 (15)	N11—C12—C13—C14	8.93 (14)
C2—N1—C1′—C2′	59.6 (3)	C14—N11—C11′—C12′	110.5 (3)
C2—C3—O3—C3*A*	−145.6 (2)	C12—C13—O13—C13*A*	144.5 (2)

The coordinates of atom H3 (and the corresponding atom H13 in the other independent molecule) were refined and the isotropic displacement parameter set at 1.2 times the equivalent isotropic displacement parameter of the parent atom. All other H atoms were refined as riding.

Data collection: *SMART* (Bruker, 1999); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 2000) and *XPREP* (Bruker, 1997); program(s) used to solve structure: *SHELXTL* (Bruker, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

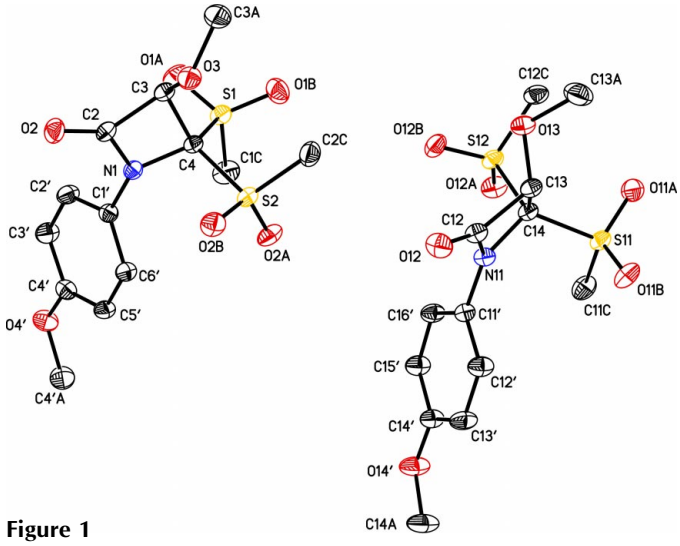


Figure 1
View of (I), showing the labeling of the non-H atoms in the two molecules in the asymmetric unit. Displacement ellipsoids are shown at the 50% probability level. H atoms have been omitted.

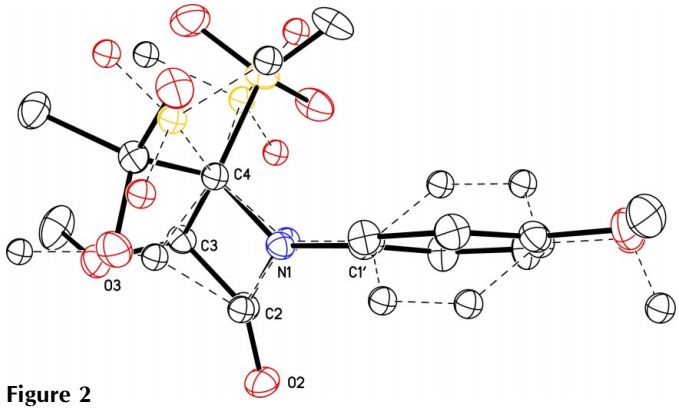


Figure 2
Comparison of molecules 1 and 2. Atoms used for the least-squares fit are labeled.

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