C5—O1—N2	106.08 (8)	N7—C4—C3	110.78 (9)
C3—N2—O1	108.42 (9)	C5—C4—C3	99.81 (9)
O6—C3—N2	125.21 (10)	O1—C5—C8	108.37 (10)
O6—C3—C4	123.05 (10)	O1—C5—C4	103.43 (8)
N2—C3—C4	111.73 (9)	C8—C5—C4	119.25 (10)
N7—C4—C5	114.16 (9)		

Table 3. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N7—H71···O6^{i}	0.921 (17)	1.838 (17)	2.742 (1)	167 (2)
N7—H72···O6^{ii}	0.94 (2)	2.26 (2)	2.798 (1)	116 (2)
N7—H72···O9	0.94 (2)	2.48 (2)	3.003 (1)	115 (1)
N7—H73···N2^{iii}	0.954 (17)	1.929 (18)	2.839 (1)	159 (2)
O9—H9···O6^{iv}	0.87 (2)	1.99 (2)	2.823 (1)	160 (2)
C4—H4···O1^{v}	0.92 (2)	2.52 (2)	3.338 (2)	148 (1)

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

Since the molecule is optically active, the choice of a non-centrosymmetric space group is obvious. The absolute structure determined by means of the anomalous scattering contribution is in agreement with the known chirality of the molecule. At the time of data collection, an absorption correction was deemed unnecessary. Afterwards, when a water molecule was detected in the structure, increasing the absorption coefficient, the crystal had deteriorated so that corrections by ψ scans or numerical integration could not be made.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *DREADD* (Blessing, 1987). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL96* (Sheldrick, 1996). Molecular graphics: *ORTEPII* (Johnson, 1976).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: AB1493). Services for accessing these data are described at the back of the journal.

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6α-Chloro-3α-hydroxymethyl-2,2-dimethylpenam 1,1-Dioxide

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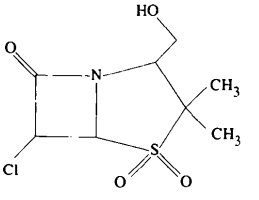
Abstract

In the title compound (6-chloro-3-hydroxymethyl-2,2-dimethyl-5-oxo-2,3,6,6a-tetrahydro-5*H*-azeto[2,1-*b*]thiazole 1,1-dioxide, $C_8H_{12}ClNO_4S$), the 2-azetidinone ring is non-planar. The thiazolidine ring has a conformation that can be classified as *C*3, with 2α-CH_3 pseudo-equatorial, 2β-CH_3 axial and 3α-*R* axial. The N atom has a pyramidal bonding arrangement. The structure is stabilized by O—H···O hydrogen bonds along the direction of the *c* axis.

Comment

As a first step towards the study of structure–activity relationships of β-lactam derivatives as elastase inhibitors, the structure of (1), an intermediate in the synthesis of the active compounds (Boschetti, Mascaretti *et al.*, 1995; Boschetti, Mata *et al.*, 1995), has been determined.



(1)

Analysis of the molecular geometry (Table 1) shows that the 2-azetidinone (β-lactam) ring is non-planar and that the N(4) atom has a pyramidal bonding arrangement, being out of the plane defined by its substituents (Fig. 1). The value of the out-of-plane distance, 0.387 (2) Å, and the sum of the angles around N(4), 338.3°, compare well with the reported values for

other penicillanates (Sweet, 1972). The non-planarity of the 2-azetidinone ring can also be estimated by considering the dihedral angle [Γ = 3.8 (2)°] between the N(4)—C(5)—C(6) and N(4)—C(7)—C(6) planes. This departure from planarity is smaller than in other penicilline derivatives, where Γ is between 8 and 20° (Domiano *et al.*, 1979). Domiano *et al.* (1979) classified the thiazolidine rings as *C*3-, *C*5- or *S*-type by considering which atom is out of the best mean ring plane. Moreover, they found that irrespective of the type, the thiazolidine ring exhibits a conformation near to the *E* (envelope) conformation. In (1), the best plane (in the χ^2 sense) is formed by atoms S(1), C(2), N(4) and C(5), the C(3) atom being displaced by 0.543 (3) Å from this plane. The α-CH_3 group is pseudo-equatorial, β-CH_3 is axial and the α-hydroxymethyl substituent is axial. Therefore, the thiazolidine conformation can be classified as *C*3-type. A similar conformation has been reported by Gibon *et al.* (1988) for the sodium salt of penicillanic acid. In contrast to the findings of Domiano *et al.* (1979) for *C*3-type rings, the ring puckering analysis of (1) [q_2 = 0.372 (3) and Φ_2 = −122.1 (4)°; Cremer & Pople, 1975] shows that it can be better described as having a *T* (half-chair) conformation. This is also different from the conformation found in the penicillanic acid sulfone (Brenner & Knowles, 1981), which exhibits an *S*-type *E*-shape conformation. This *S*-type *E*-shape conformation has also been observed for other penicillin sulfone derivatives, such as pivaloyloxymethyl (3*S*,5*R*,6*S*)-6-bromopenicillanate 1,1-dioxide (Alzari, Ronco *et al.*, 1986) and pivaloyloxymethyl (3*S*,5*R*,6*S*)-6,6-dibromopenicillanate 1,1-dioxide (Alzari, Rivero *et al.*, 1986).

Most of the geometrical features of the thiazolidine ring confirm its *C*3 character. The value of the endocyclic bond angle at S(1), 96.6 (1)°, is in agreement with the expected value for the *C*3-type conformation, 96.1 (2)° (Blanpain *et al.*, 1980). The S(1)—C(2) distance of 1.845 (3) Å is longer than generally expected for a C_{sp^3}—S single bond (1.81 Å), but is of the same order as those reported for *C*3-type derivatives. The dihedral angle formed by the best thiazolidine and β-lactam least-squares planes, 64.3 (1)°, is in accordance with the expected values, 59–65°, for *C*3-type derivatives (Domiano *et al.*, 1979). The configurations at the three chiral C atoms [C(6), C(3) and C(5)] are known from the configuration of the starting material.

A crystal-packing analysis using the contact radii of Bondi (1964) shows that the OH groups are linked by O—H···O hydrogen bonds [O(10)—H(101)···O(10^i): O(10)—H(101) 0.73 (4), H(101)···O(10^i) 1.98 (5), O(10)···O(10^i) 2.712 (3) Å and O(10)—H(101)···O(10^i) 173 (5)°; symmetry code: (i) $\frac{2}{3}-y$, $\frac{1}{3}+x-y$, $\frac{1}{3}+z$]. These interactions induce infinite one-dimensional chains along [001]. No other short intermolecular contacts are observed.

The flexibility and easy interconvertibility between the different conformations of the thiazolidine ring (Cohen, 1983; Joshi *et al.*, 1978) allow us to infer that the *T*-shape *C*3-type conformation observed in the title compound might be induced by the hydrogen bond involving the C(3) substituent.

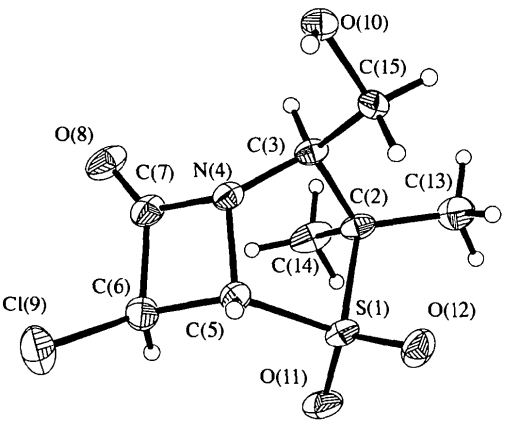


Fig. 1. The molecular structure of (1) showing 50% probability displacement ellipsoids for non-H atoms. H atoms are drawn as small spheres of arbitrary radii.

Experimental

Crystals were obtained from 6α-chloropenicillanic acid sulfone (Cartwright & Coulson, 1979) by the following procedure. At room temperature, borane–methyl sulfide was added dropwise to a solution of 6α-chloropenicillanic acid sulfone (781 mg, 2.91 mmol) in dry THF (10 ml) (2 *M* solution in THF, 2.34 ml, 4.68 mmol). After stirring the resulting solution for 45 h, the solvent was removed and the residue was diluted with ethyl acetate (10 ml), and washed with aqueous sodium hydrogen carbonate (2 × 5 ml) and brine (2 × 5 ml). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*, and the residue was chromatographed [eluent: ethyl acetate–hexane (4:6)] to give the title compound (420 mg, 57%) as white crystals (m.p. 112–114 K). Recrystallization from hexane–dichloromethane afforded crystals suitable for diffraction studies. IR: ν_{max}(film) 3566 (OH), 1792 (β-lactam), 1320 and 1122 cm^{-1} (sulfone). ^{1}H NMR: δ_H (200 MHz, $CDCl_3$, Me_4Si standard) 1.49 (3H, *s*, 8-Me), 1.50 (3H, *s*, 9-Me), 2.33 (1H, broad *s*, 10-OH), 3.78 (2H, *m*, 10-CH_2), 3.92 (1H, *m*, 3-H), 4.56 (1H, *d*, *J* = 1.53 Hz, 5-H) and 5.16 p.p.m. (1H, *d*, *J* = 1.53 Hz, 6-H). ^{13}C NMR: δ_C (50 MHz, $CDCl_3$, $CDCl_3$ as standard) 167.46 (C-7), 68.72 (C-5), 63.33 (C-2), 62.68 (C-3), 60.23 (C-10), 54.84 (C-6), 18.71 (C-9) and 18.04 p.p.m. (C-8). LRMS (CI, methane) 256 (36%), 254 (M^+ + 1, 100), 178 (47), 122 (18), 120 (56), 85 (8). HRMS calculated for $C_8H_{13}ClO_4NS$ 254.0254; found 254.0242. IR spectra were recorded on a Bruker IFS 25 FT–IR spectrometer. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Bruker AC 200 spectrometer. Melting points were obtained on an Ernst Leitz melting-point apparatus and are uncorrected. Analytical thin-layer chromatography (TLC) was carried out with silica gel 60 F_{254} pre-coated aluminium sheets (Merck); column chromatography was performed on silica gel grade 60 (Merck).

Crystal data

$C_8H_{12}ClNO_4S$
M_r = 253.70
Trigonal
$R\bar{3}$
a = 21.511 (5) Å
c = 6.369 (9) Å
V = 2552 (4) Å^3
Z = 9
D_x = 1.486 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 24 reflections
θ = 8–11°
μ = 0.515 mm^{-1}
T = 150 (2) K
Prism
0.30 × 0.20 × 0.20 mm
Colourless

Data collection

Rigaku AFC-6S four-circle diffractometer
$2\theta/\omega$ scans
Absorption correction: none
1400 measured reflections
1347 independent reflections
1246 reflections with $I > 2\sigma(I)$

R_{int} = 0.015
θ_{max} = 27°
$h = -23 \rightarrow 23$
$k = 0 \rightarrow 27$
$l = 0 \rightarrow 8$
3 standard reflections
every 100 reflections
intensity variation: ±0.5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.023
$wR(F^2)$ = 0.060
S = 1.062
1347 reflections
143 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.032P)^2 + 0.663P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = 0.18 (12)

Table 1. *Selected geometric parameters (Å, °)*

S(1)—O(12)	1.440 (2)	C(3)—C(15)	1.518 (3)
S(1)—O(11)	1.442 (2)	N(4)—C(7)	1.392 (3)
S(1)—C(5)	1.824 (2)	N(4)—C(5)	1.478 (4)
S(1)—C(2)	1.845 (3)	C(5)—C(6)	1.547 (3)
C(2)—C(13)	1.529 (4)	C(6)—C(7)	1.544 (4)
C(2)—C(14)	1.535 (3)	C(6)—Cl(9)	1.768 (3)
C(2)—C(3)	1.565 (3)	C(7)—O(8)	1.202 (4)
C(3)—N(4)	1.474 (3)	O(10)—C(15)	1.434 (3)
O(12)—S(1)—O(11)	118.52 (14)	C(15)—C(3)—C(2)	115.2 (2)
O(12)—S(1)—C(5)	106.78 (11)	C(7)—N(4)—C(3)	126.7 (2)
O(11)—S(1)—C(5)	111.77 (12)	C(7)—N(4)—C(5)	93.8 (2)
O(12)—S(1)—C(2)	109.55 (13)	C(3)—N(4)—C(5)	117.8 (2)
O(11)—S(1)—C(2)	111.36 (12)	N(4)—C(5)—C(6)	88.6 (2)
C(5)—S(1)—C(2)	96.58 (12)	N(4)—C(5)—S(1)	103.4 (2)
C(13)—C(2)—C(14)	111.5 (2)	C(6)—C(5)—S(1)	119.0 (2)
C(13)—C(2)—C(3)	114.4 (2)	C(7)—C(6)—C(5)	85.4 (2)
C(14)—C(2)—C(3)	110.7 (2)	C(7)—C(6)—Cl(9)	115.4 (2)
C(13)—C(2)—S(1)	108.6 (2)	C(5)—C(6)—Cl(9)	116.7 (2)
C(14)—C(2)—S(1)	107.9 (2)	O(8)—C(7)—N(4)	131.5 (3)
C(3)—C(2)—S(1)	103.1 (2)	O(8)—C(7)—C(6)	136.5 (2)
N(4)—C(3)—C(15)	110.8 (2)	N(4)—C(7)—C(6)	92.0 (2)
N(4)—C(3)—C(2)	105.2 (2)	O(10)—C(15)—C(3)	110.3 (2)

The low-temperature experiment was carried out using an Oxford Cryosystems Cryostream open-flow gas cryostat (Cosier & Glazer, 1986). H atoms were allowed to ride on their parent C atoms with $U_{iso}(H) = xU_{eq}(C)$; x = 1.5 for methyl H atoms and x = 1.2 for others. C—H distances were fixed at 1.00, 0.99 and 0.98 Å for idealized tertiary CH, CH_2 and CH_3 groups, respectively. Idealized CH_3 groups were allowed to rotate about the X—C bond. The H atom bonded to the O atom of the hydroxymethyl group was located from a difference Fourier map. The coordinates and isotropic displacement parameter of this H atom were refined.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1991). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1989). Program(s) used to solve structure: *SHELXTL* (Sheldrick, 1995). Program(s) used to refine structure: *SHELXTL*. Molecular graphics: *SHELXTL*. Software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1175). Services for accessing these data are described at the back of the journal.

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