C7	0.5774 (3)	0.2572 (2)	1.0810 (4)	0.0520 (7)
C7*a*	0.3688 (5)	0.3401 (3)	1.2234 (7)	0.081 (1)
C7*b*	0.4928 (6)	0.2102 (4)	1.3414 (8)	0.095 (1)
C8	0.5794 (3)	0.3218 (2)	0.9750 (4)	0.0498 (7)
C8*a*	0.6795 (3)	0.3112 (2)	0.8478 (4)	0.0465 (6)
C11	0.8993 (3)	0.1598 (2)	0.5522 (4)	0.0466 (6)
C13	1.0210 (3)	0.0919 (2)	0.2802 (4)	0.0507 (7)
C14	1.1094 (3)	0.1141 (2)	0.1484 (4)	0.0546 (8)
O1*S*	0.7711 (3)	−0.0426 (2)	0.3052 (4)	0.0938 (10)
C1*S*	0.6581 (5)	−0.0591 (3)	0.3788 (7)	0.094 (1)
C2*S*	0.5669 (6)	−0.1010 (5)	0.2389 (9)	0.129 (2)

Table 2. *Selected geometric parameters (Å, °)*

S9—C4*a*	1.773 (3)	N12—C13	1.436 (3)
S9—C8*a*	1.771 (3)	C1*a*—C1	1.380 (4)
O11—C11	1.225 (3)	C1*a*—C4*a*	1.393 (3)
O14—C14	1.192 (4)	C1—C2	1.385 (4)
O15—C14	1.306 (4)	C2—C3	1.408 (4)
N3—C3*b*	1.434 (4)	C3—C4	1.400 (4)
N3—C3	1.374 (3)	C4—C4*a*	1.384 (4)
N3—C3*a*	1.447 (4)	C5—C5*a*	1.378 (4)
N7—C7	1.383 (4)	C5—C6	1.374 (4)
N7—C7*a*	1.423 (5)	C5*a*—C8*a*	1.392 (4)
N7—C7*b*	1.428 (5)	C6—C7	1.408 (4)
N10—C1*a*	1.432 (3)	C7—C8	1.393 (4)
N10—C5*a*	1.432 (4)	C8—C8*a*	1.396 (4)
N10—C11	1.376 (3)	C13—C14	1.493 (4)
N12—C11	1.352 (4)		
C4*a*—S9—C8*a*	98.5 (1)	S9—C4*a*—C1*a*	118.8 (2)
C3*b*—N3—C3	120.9 (3)	S9—C4*a*—C4	120.5 (2)
C3*b*—N3—C3*a*	118.7 (3)	N10—C5*a*—C5	122.7 (2)
C3—N3—C3*a*	120.4 (3)	N10—C5*a*—C8*a*	118.5 (2)
C7—N7—C7*a*	121.0 (3)	N7—C7—C6	121.1 (3)
C7—N7—C7*b*	121.1 (3)	N7—C7—C8	121.6 (3)
C7*a*—N7—C7*b*	117.0 (3)	S9—C8*a*—C5*a*	119.3 (2)
C1*a*—N10—C5*a*	115.8 (2)	S9—C8*a*—C8	120.1 (2)
C1*a*—N10—C11	123.4 (2)	O11—C11—N10	121.5 (3)
C5*a*—N10—C11	120.2 (2)	O11—C11—N12	122.1 (2)
C11—N12—C13	120.5 (2)	N10—C11—N12	116.4 (2)
N10—C1*a*—C1	122.3 (2)	N12—C13—C14	111.0 (2)
N10—C1*a*—C4*a*	118.9 (2)	O14—C14—O15	124.7 (3)
N3—C3—C2	120.7 (3)	O14—C14—C13	124.8 (3)
N3—C3—C4	121.7 (2)	O15—C14—C13	110.5 (2)
N10—C1*a*—C4*a*—S9	0.7 (3)	C1*a*—N10—C11—N12	0.8 (4)
C3*b*—N3—C3—C2	7.0 (4)	C5*a*—N10—C11—O11	−9.2 (4)
C3*a*—N3—C3—C4	5.4 (4)	O11—C11—N12—C13	−5.9 (4)
N10—C5*a*—C8*a*—S9	−0.1 (3)	C11—N12—C13—C14	176.3 (3)
C7*b*—N7—C7—C6	14.8 (6)	N12—C13—C14—O14	−0.9 (5)
C7*a*—N7—C7—C8	2.8 (5)	N12—C13—C14—O15	−179.5 (3)

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *CAD*-4 *Software*. Program(s) used to solve structure: *SIR*88 (Burla *et al.*, 1989). Program(s) used to refine structure: *TEXSAN LS* (Molecular Structure Corporation, 1992). Molecular graphics: *ORTEP*II (Johnson, 1976).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: MU1269). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Penicillin V Benzhydryl Ester Sulfoxide Monohydrate

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(*Received 22 April 1996; accepted 9 July 1996*)

Abstract

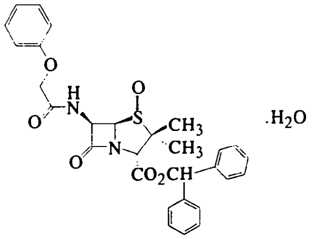
Diphenylmethyl 3,3-dimethyl-7-oxo-6-phenoxyacetamido-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate 4-oxide monohydrate, $C_{29}H_{28}N_2O_6S.H_2O$, assumes an *S* configuration, with the penam moiety (1-azabicyclo-[3.2.0]heptane-7-one) in the open conformation. The conformation of the penam moiety including the 3α-carboxyl and the 6β-acetamido groups is very similar to that of penicillin V benzyl ester sulfoxide [Shin, Kim & Kim (1992). *Acta Cryst.* **C48**, 1449–1451], but the orientations of the terminal phenyl groups at the 6β-position with respect to the central penam moiety are different in the two compounds. The acetamido N9 atom forms an intramolecular three-centred hydrogen bond with the sulfoxide O1 and phenoxy O13 atoms [N9···O1 2.839 (4) and N9···O13 2.554 (4) Å]. The molecules are linked along the *a* axis *via* hydrogen bonds involving water molecules [O1···O*w*···O11].

Comment

Penicillin sulfoxides with protective ester groups are useful as intermediates in the manufacture of therapeutically important cepharosporins and β-lactamase inhibitors (Colvin, 1992). Oxidation of penicillin to its sulfoxide results in the inactive derivative with the *S* configuration. The penam moiety in the sulfoxide derivatives always assumes the open conformation, while that of their parent compounds assumes the closed conformation (Cooper, DeMarco, Cheng & Jones, 1969). An example is the pair, penicillin V benzyl ester

Acta Crystallographica Section C
ISSN 0108-2701 © 1996

(PVBE; Shin & Cho, 1992) and its sulfoxide (PVBS; Shin, Kim & Kim, 1992), in which the conformations of the side chains are also different. We have determined the crystal structure of penicillin V benzhydryl ester sulfoxide (PVHS) as its monohydrate, (I), and compared its structure with those of related compounds.



(I)

The molecular dimensions of PVHS agree well with those of other penicillin sulfoxide compounds. The penam moiety assumes an open conformation in which the S1 atom deviates by 0.940 (5) Å from the plane formed by the remaining four atoms of the thiazolidine ring. The N4 atom retains its pyramidal character, deviating by 0.431 (4) Å from the plane formed by the C3, C5 and C7 atoms. The three phenyl rings are individually planar, with maximum deviations of 0.016 (4), 0.010 (4) and 0.005 (4) Å for atoms C17, C28 and C36, respectively.

It has been suggested that the oxygen functionality on S1 and/or the intramolecular N9—H···O1 hydrogen bond which limits the flexibility of the 6β side chain (Fig. 1) seem to be the major factors in the loss of activity in penicillin sulfoxide derivatives (Shin, Kim & Kim, 1992). The conformation of the penam moiety of PVHS including the 3α-carboxyl and 6β-acetamido groups is very similar to that of PVBS. The orientations of the terminal phenyl groups at the 6β-positions with respect to the central penam moiety, however, are different in the two compounds. The phenoxy and acetamido groups form a plane in PVHS as in PVBE, while the two planar groups are almost perpendicular to one another in PVBS. This indicates that there is conformational flexibility about the C12—O13 bond. The acetamido N9 atom forms an intramolecular three-centred hydrogen bond with the O1 and O13 atoms in PVHS [N9—H 0.92 (5), H···O1 2.21 (5), N9···O1 2.839 (4) Å and N—H···O 126 (4)°; H···O13 2.15 (4), N9···O13 2.554 (4) Å and N—H···O 106 (3)°], while the N9 atom is hydrogen-bonded to only O1 in PVBS and only O13 in PVBE.

The crystal packing is shown in Fig. 2. The molecules are linked along the *a* axis *via* O1···O*w*···O11^{i} hydrogen bonds involving water molecules [O*w*—H*wA* 0.91 (7), H*wA*···O1 2.03 (7), O*w*···O1 2.898 (4) Å and O*w*—H*wA*···O1 158 (6)°; O*w*—H*wB* 1.02 (7), H*wB*···O11^{i} 1.85 (7), O*w*···O11^{i} 2.858 (5) Å and O*w*—H*wB*···O11^{i} 171 (6)°; symmetry code: (i) $1+x$, y, z]. Besides these hydrogen-bonding interactions, there are only van der Waals interactions between the molecules.

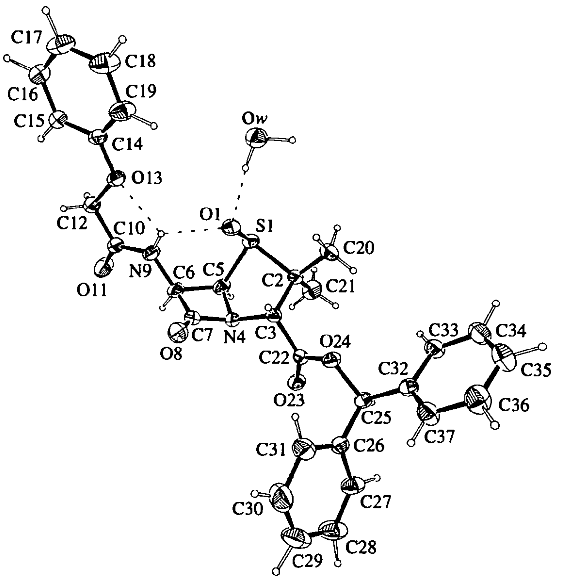


Fig. 1. *ORTEP*II (Johnson, 1976) view of the title compound. Displacement ellipsoids are drawn at the 30% probability level. The dotted lines denote hydrogen bonds.

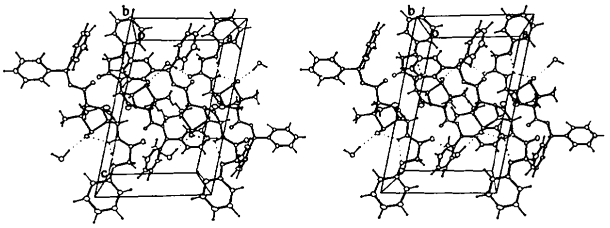


Fig. 2. The packing seen in stereoscopic projection along the *b* axis. The dotted lines denote hydrogen bonds.

Experimental

PVHS was purchased from Sigma (Chemical Abstract Registry Number 10209-09-3) and recrystallized from an aqueous ethanol–dichloromethane solution. The density D_m was measured by flotation in CCl_4/*n*-hexane solution.

Crystal data

$C_{29}H_{28}N_2O_6S.H_2O$
$M_r = 550.625$
Monoclinic
$P2_1$
$a = 9.4140\,(10)$ Å
$b = 10.339\,(2)$ Å
$c = 14.675\,(2)$ Å
$\beta = 102.10\,(2)°$
$V = 1396.6\,(4)$ Å^3
$Z = 2$
$D_x = 1.309$ Mg m^{-3}
$D_m = 1.308\,(9)$ Mg m^{-3}

Cu $K\alpha$ radiation
$\lambda = 1.5418$ Å
Cell parameters from 23 reflections
$\theta = 8.5–25.0°$
$\mu = 1.442$ mm^{-1}
$T = 295\,(2)$ K
Parallelepiped
0.50 × 0.30 × 0.20 mm
Colourless

Data collection

Rigaku AFC-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
2367 measured reflections
2217 independent reflections
1999 observed reflections [$I > 2\sigma(I)$]
$R_{\rm int} = 0.0159$
$\theta_{\rm max} = 59.92°$
$h = -10 \rightarrow 0$
$k = 0 \rightarrow 11$
$l = -16 \rightarrow 16$
3 standard reflections monitored every 50 reflections intensity decay: 3%

Refinement

Refinement on F^2
$R(F) = 0.0341$
$wR(F^2) = 0.0905$
$S = 1.069$
2217 reflections
472 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0657P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = 0.033$
$\Delta\rho_{\rm max} = 0.233$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.185$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0080 (8)
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Absolute configuration: Flack (1983)
Flack parameter = −0.01 (3)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$$U_{\rm eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$U_{\rm eq}$
S1	0.21673 (10)	0	0.33815 (6)	0.0463 (3)
O1	0.2311 (3)	0.1412 (3)	0.3194 (2)	0.0514 (7)
C2	0.3548 (4)	−0.0317 (4)	0.4467 (2)	0.0440 (9)
C3	0.3072 (4)	0.0606 (4)	0.5171 (2)	0.0361 (7)
N4	0.1489 (3)	0.0609 (4)	0.4947 (2)	0.0448 (7)
C5	0.0780 (4)	−0.0064 (5)	0.4084 (3)	0.053 (1)
C6	−0.0366 (4)	0.1033 (5)	0.3921 (3)	0.060 (1)
C7	0.0673 (5)	0.1709 (6)	0.4715 (3)	0.060 (1)
O8	0.0848 (5)	0.2791 (4)	0.5017 (3)	0.089 (1)
N9	−0.0730 (4)	0.1687 (5)	0.3045 (2)	0.059 (1)
C10	−0.2100 (4)	0.1814 (5)	0.2566 (3)	0.052 (1)
O11	−0.3137 (3)	0.1353 (4)	0.2817 (2)	0.083 (1)
C12	−0.2280 (4)	0.2582 (5)	0.1680 (3)	0.052 (1)
O13	−0.0919 (3)	0.2842 (3)	0.1485 (2)	0.0555 (8)
C14	−0.0852 (4)	0.3590 (4)	0.0719 (2)	0.0476 (9)
C15	−0.2056 (5)	0.3962 (5)	0.0068 (3)	0.064 (1)
C16	−0.1873 (6)	0.4731 (5)	−0.0669 (3)	0.074 (2)
C17	−0.0525 (7)	0.5131 (6)	−0.0752 (3)	0.077 (2)
C18	0.0671 (7)	0.4717 (6)	−0.0110 (4)	0.082 (2)
C19	0.0512 (5)	0.3949 (6)	0.0626 (3)	0.071 (1)
C20	0.5032 (5)	0.0011 (8)	0.4280 (3)	0.065 (1)
C21	0.3450 (8)	−0.1745 (5)	0.4720 (4)	0.068 (1)
C22	0.3687 (4)	0.0215 (4)	0.6171 (2)	0.0411 (8)
O23	0.3097 (3)	−0.0457 (3)	0.6640 (2)	0.0534 (7)
O24	0.5003 (3)	0.0750 (3)	0.6442 (2)	0.0450 (6)
C25	0.5789 (4)	0.0462 (4)	0.7397 (2)	0.0413 (9)
C26	0.5159 (4)	0.1201 (4)	0.8092 (3)	0.0482 (9)
C27	0.5189 (5)	0.0643 (6)	0.8952 (3)	0.063 (1)
C28	0.4647 (7)	0.1266 (8)	0.9622 (4)	0.086 (2)
C29	0.4018 (7)	0.2458 (9)	0.9442 (5)	0.098 (2)
C30	0.3978 (8)	0.3028 (9)	0.8606 (6)	0.100 (2)
C31	0.4551 (6)	0.2405 (5)	0.7910 (4)	0.072 (1)
C32	0.7370 (4)	0.0745 (4)	0.7391 (2)	0.0459 (8)
C33	0.8078 (4)	−0.0013 (5)	0.6835 (3)	0.0552 (9)
C34	0.9516 (5)	0.0209 (6)	0.6809 (3)	0.067 (1)
C35	1.0270 (5)	0.1189 (5)	0.7339 (4)	0.073 (1)
C36	0.9588 (5)	0.1924 (6)	0.7887 (4)	0.077 (2)
C37	0.8146 (5)	0.1720 (5)	0.7914 (3)	0.059 (1)
O*w*	0.4064 (4)	0.2283 (4)	0.1909 (2)	0.0678 (8)

Table 2. *Selected geometric parameters (Å, °)*

S1—O1	1.497 (3)	C6—N9	1.430 (5)
S1—C5	1.827 (4)	C6—C7	1.524 (7)
S1—C2	1.862 (4)	C7—O8	1.201 (7)
C2—C20	1.517 (6)	N9—C10	1.340 (5)
C2—C21	1.531 (6)	C10—O11	1.211 (5)
C2—C3	1.541 (5)	C10—C12	1.503 (6)
C3—N4	1.457 (4)	C12—O13	1.396 (5)
C3—C22	1.515 (5)	C22—O23	1.194 (4)
N4—C7	1.375 (6)	C22—O24	1.339 (4)
N4—C5	1.477 (5)	O24—C25	1.472 (4)
C5—C6	1.549 (7)		
O1—S1—C5	104.0 (2)	C3—N4—C5	116.7 (3)
O1—S1—C2	104.8 (2)	N4—C5—C6	87.8 (4)
C5—S1—C2	88.0 (2)	N4—C5—S1	102.6 (2)
C20—C2—C21	111.4 (4)	C6—C5—S1	116.4 (3)
C20—C2—C3	113.0 (4)	N9—C6—C7	117.7 (4)
C21—C2—C3	113.2 (3)	N9—C6—C5	120.8 (3)
C20—C2—S1	108.1 (3)	C7—C6—C5	84.5 (3)
C21—C2—S1	108.1 (3)	O8—C7—N4	130.7 (4)
C3—C2—S1	102.5 (2)	O8—C7—C6	136.5 (4)
N4—C3—C22	112.6 (3)	N4—C7—C6	92.6 (4)
N4—C3—C2	106.1 (3)	O23—C22—O24	125.6 (3)
C22—C3—C2	112.3 (3)	O23—C22—C3	125.8 (3)
C7—N4—C3	123.4 (4)	O24—C22—C3	108.6 (3)
C7—N4—C5	92.8 (3)	C22—O24—C25	116.6 (3)

Data collection, cell refinement and data reduction: local program (Yoon, Kim & Shin, 1994) Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*93.

Financial support from the SNU Daewoo Research Fund (95-05-2055) is gratefully acknowledged.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: CF1116). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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