Structure of Sulfazecin–Methanol (1/1)

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Abstract. $C_{12}H_{20}N_4O_9S.CH_3OH$, $M_r = 428.4$, orthorhombic, $P2_12_12_1$, $a = 9.457$ (2), $b = 24.403$ (7), $c = 8.414$ (2) Å, $V = 1941.9$ (8) Å^3, $Z = 4$, $D_c = 1.47$ Mg m^{-3}. The compound is a novel antibiotic produced by a new species of *Pseudomonas*. The structure was solved by the heavy-atom method and refined to $R = 0.046$ for 1782 observed reflections. The bond distances of the amide group in the β-lactam ring are 1.347 (7) and 1.210 (7) Å for C—N and C=O, respectively.

Introduction. A novel antibiotic, sulfazecin, is produced by *Pseudomonas acidophila* G-6302. It is active against Gram-negative bacteria and weakly active against Gram-positive bacteria (Imada, Asai, Kitano, Kintaka & Muroi, 1981). The structural study of this compound by physicochemical methods clarified partial structures of the β-lactam, sulfo, methoxy and peptide groups. The identification followed by acid hydrolyses proved the presence of D-glutamyl and D-alanyl residues in the peptide moiety (Muroi, Haibara Asai, Kasahara & Kishi, 1981). In conjunction with that study, we undertook an X-ray analysis of the compound.

A colourless prismatic crystal of dimensions $0.3 \times 0.2 \times 0.2$ mm crystallized from an aqueous methanol solution was used for X-ray experiments. Data from

elemental analysis and PMR showed the existence of one molar equivalent of methanol of crystallization. X-ray measurements were carried out on a Rigaku automated four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0.71069$ Å). The space group was uniquely determined from systematic absences. The unit-cell dimensions were determined by the least-squares treatment of 25 reflections for which 2θ values ranged from 30 to 37°. A total of 1973 unique reflections up to $2\theta = 50°$ were measured, of which 1782 with $F_o \geq 3\sigma(F_o)$ were used
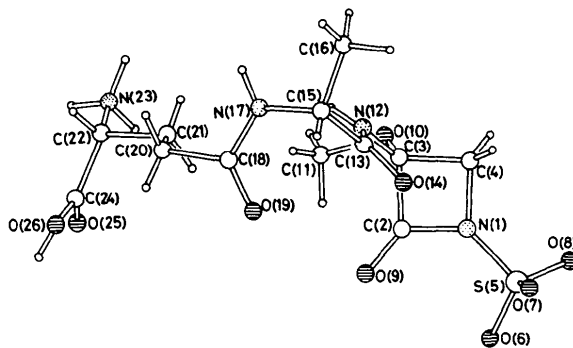

Fig. 1. Perspective view of the molecule. The numbering scheme is also shown.

Table 1. *Positional parameters* ($\times 10^4$) *and* U_{eq} (Å$^2 \times 10^3$) *for nonhydrogen atoms, with e.s.d.'s*

$$U_{eq} = (U_{11} + U_{22} + U_{33})/3.$$

	x	y	z	U_{eq} (Å^2)		x	y	z	U_{eq} (Å^2)
N(1)	5655 (5)	3799 (2)	5986 (6)	33 (2)	C(15)	4377 (6)	3219 (2)	11726 (6)	28 (3)
C(2)	5812 (6)	3300 (2)	6725 (6)	29 (3)	C(16)	3044 (7)	3497 (3)	12326 (7)	47 (3)
C(3)	4228 (6)	3302 (2)	7213 (6)	28 (3)	N(17)	4204 (5)	2622 (2)	11829 (5)	30 (2)
C(4)	4215 (6)	3903 (2)	6594 (7)	36 (3)	C(18)	5261 (6)	2283 (2)	11389 (6)	31 (3)
S(5)	6826 (2)	4232 (1)	5166 (2)	35 (1)	O(19)	6378 (4)	2464 (2)	10834 (5)	41 (2)
O(6)	7853 (5)	3881 (2)	4438 (6)	53 (3)	C(20)	4947 (6)	1675 (2)	11548 (7)	37 (3)
O(7)	7378 (5)	4554 (2)	6460 (5)	51 (2)	C(21)	4149 (6)	1478 (2)	10088 (7)	31 (3)
O(8)	5993 (5)	4550 (2)	4083 (5)	49 (3)	C(22)	3975 (6)	846 (2)	10030 (7)	30 (3)
O(9)	6798 (5)	2988 (2)	6864 (5)	44 (2)	N(23)	2867 (5)	712 (2)	8846 (6)	33 (2)
O(10)	3367 (5)	2981 (2)	6247 (5)	41 (2)	C(24)	5325 (6)	566 (2)	9565 (7)	37 (3)
C(11)	3727 (8)	2404 (2)	6238 (8)	53 (4)	O(25)	5502 (5)	384 (2)	8274 (6)	54 (3)
N(12)	3927 (5)	3183 (2)	8856 (5)	29 (2)	O(26)	6249 (5)	552 (2)	10707 (6)	57 (3)
C(13)	4713 (5)	3403 (2)	10021 (6)	27 (3)	C(27)	704 (11)	4878 (5)	5668 (13)	106 (8)
O(14)	5624 (4)	3750 (2)	9759 (5)	35 (2)	O(28)	1724 (6)	4890 (3)	4523 (8)	96 (4)

for the following calculations. Lorentz and polarization corrections were applied but no correction was made for absorption.

The structure was solved by the heavy-atom method and refined with the method of block-diagonal least squares, in which the function minimized was $\sum (F_o - F_c)^2$. A difference map clearly indicated the positions of the H atoms. Individual anisotropic temperature factors were used for C, N, O and S, with isotropic terms for H. The R factors were 0·046 and 0·048 for 1782 observed and for all 1973 reflections, respectively. Table 1 gives the fractional atomic coordinates for non-hydrogen atoms.* Crystallographic calculations were carried out with an IBM 3031 computer with the XRAY 76 system of programs (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976). Figs. 1, 2

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36045 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.
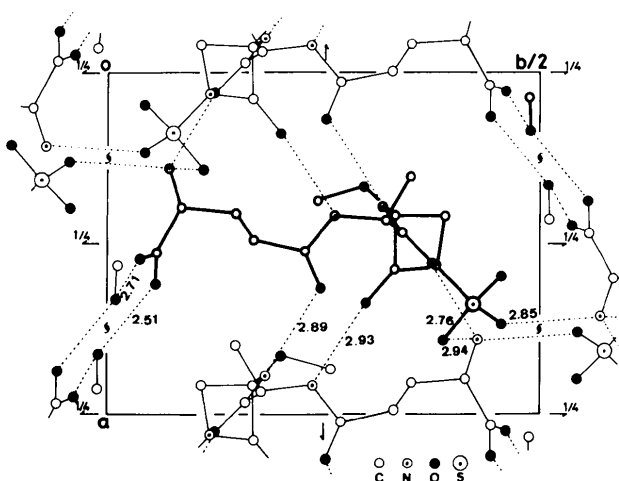

Fig. 2. Packing diagram. Dotted lines show hydrogen bonds and numbers are distances (Å) between donors and acceptors. The average e.s.d. is 0·007 Å.
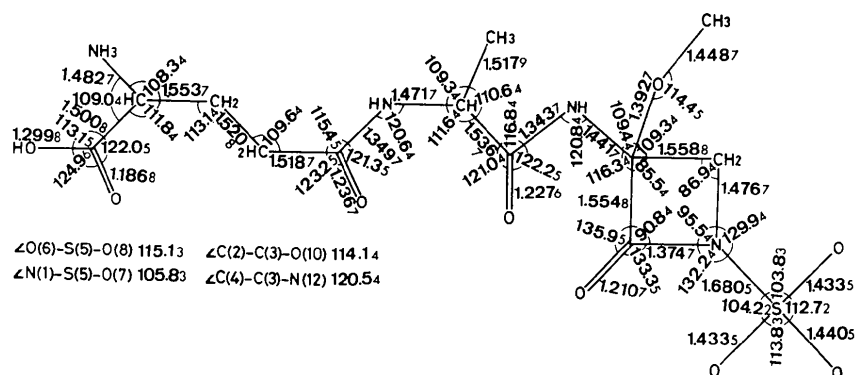
and 3 show perspective views of the molecule with the numbering scheme used in this study, the molecular arrangement in the crystal, and bond lengths and angles, respectively.

Discussion. Sulfazecin is composed of a β-lactam ring, with methoxy and γ-glutamyl-alanylamino groups attached to the ring carbon C(3) and a sulfo group directly linked to N(1) in the ring. Because acid hydrolysis gave D-alanine and D-glutamic acid, the (R) configuration was deduced for the asymmetric carbon C(3). The structure of sulfazecin was thus established to be (3R)-3-(γ-D-glutamyl-D-alanylamino)-3-methoxy-2-oxoazetidine-1-sulfonic acid.

Three H atoms bonded to the amino N(23) were detected clearly on the difference map, and there was no evidence of any positive electron density attributable to H atoms in the vicinity of the SO_3 group. The three bond lengths S(5)–O(6), S(5)–O(7) and S(5)–O(8) are 1·433 (5), 1·440(5) and 1·433 (5) Å, respectively. We conclude that the sulfazecin molecule exists as a zwitterion with positive $N(23)H_3^+$ and negative SO_3^- groups.

The endocyclic amide bond of length 1·374 (7) Å is longer than the exocyclic amide bonds of lengths 1·343 (7) and 1·349 (7) Å while, for the carbonyl bonds adjacent to each of them, the distance C(2)=O(9) is shorter than C(13)=O(14) and C(18)=O(19). The deviations of C(3), C(4) and S(5) from the plane passing through N(1), C(2) and O(9) are 0·06 (2), 0·18 (2) and 0·21 (2) Å, respectively. These bond lengths and relatively large deviations of the two atoms directly bonded to N(1) show that less amide resonance occurs in the β-lactam.

Sweet & Dahl (1970) suggested that decreased amide resonance in antibiotic β-lactams correlated with biological activity. Table 2 shows a comparison of bond lengths in amide groups. The values obtained for sulfazecin resemble those of unstrained β-lactam, penicillins and cephalosporins. The similarity between sulfazecin and biologically active β-lactam antibiotics

∠O(6)–S(5)–O(8) 115.13   ∠C(2)–C(3)–O(10) 114.14
∠N(1)–S(5)–O(7) 105.83   ∠C(4)–C(3)–N(12) 120.54

Fig. 3. Bond lengths (Å) and angles (°). Small digits are e.s.d.'s.

Table 2. *Comparison of bond lengths in amide groups*

| | Distance (Å) | |
Substance	C–N	C=O
Sulfazecin[a]	1·374 (7)	1·210 (7)
Unstrained β-lactam[b]	1·367 (4)	1·210 (4)
Penicillins[c]	1·392 (4)	1·194 (4)
Cephalosporins[d]	1·38 (1)	1·21 (1)
Δ²-Cephalosporins[e]	1·339 (7)	1·223 (7)
	1·36	1·20
	1·334	1·228
Free amide[f]	1·32₅	1·24

References: (*a*) Present work; (*b*) Parthasarathy (1970); (*c*) Domiano, Nardelli, Balsamo, Macchia & Macchia (1979); (*d*) Sweet (1972); (*e*) Sweet & Dahl (1970); Kobelt & Paulus (1974*a*); Kobelt & Paulus (1974*b*); (*f*) Marsh & Donohue (1967).

demonstrates that Sweet & Dahl's concept is also applicable to the present antibiotic.

The crystal packing involves seven independent intermolecular hydrogen bonds, five of which are between sulfazecin molecules with the remaining two between sulfazecin and the methanol of crystallization. The amino N(23) donates three hydrogens to the carbonyl O(14), and the sulfo O(6) and O(7) of the symmetry-related molecules. Two amide nitrogens N(12) and N(17) donate hydrogens to the carbonyl O(19) and O(9) atoms, respectively. As for the oxygens of the carbonyl group, O(25) accepts a hydrogen from the hydroxyl group of methanol, and O(26) donates its hydrogen to the hydroxyl oxygen of the methanol. The sulfo O(8) does not participate in hydrogen bonding.

These hydrogen bonds connect molecules of sulfazecin and methanol of crystallization with each other and form a three-dimensional network in the crystal.

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The Structure of 6-(6-Aminohexanamido)hexanoic Acid Hydrate*

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Abstract. $C_{12}H_{24}N_2O_3 \cdot H_2O$, $M_r = 262 \cdot 3$, monoclinic, $P2_1/c$, $a = 17 \cdot 649$ (2), $b = 4 \cdot 915$ (1), $c = 17 \cdot 516$ (2) Å, $\beta = 107 \cdot 26$ (1)°, $V = 1451 \cdot 1$ (3) Å³, $D_c = 1 \cdot 200$ Mg m⁻³, for $Z = 4$, $\mu(\text{Cu } K\alpha) = 0 \cdot 741$ mm⁻¹. The structure was solved by the direct method and refined anisotropically by the block-diagonal least-squares procedure; $R = 0 \cdot 051$ for 1710 non-zero reflections. The molecules are present in the crystal as zwitterions. Each zwitterion forms four N–H···O bonds with adjacent molecules to form a three-dimensional network. The water of crystallization also engages in the N–H···O and O–H···O hydrogen