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Structure of (3*R*,4*S*)-1-(*p*-Bromobenzoyl)-3-[(*R*)-1-hydroxyethyl]-4-trimethylsilylethynyl-2-azetidinone

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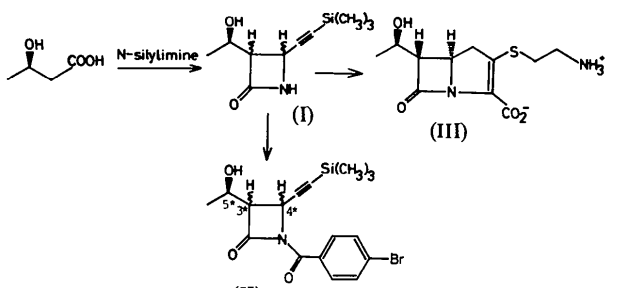
Abstract. $C_{17}H_{20}BrNO_3Si$, $M_r = 394{\cdot}3$, orthorhombic, $P2_12_12_1$, $a = 23{\cdot}833\ (1)$, $b = 12{\cdot}924\ (1)$, $c = 6{\cdot}501\ (1)$ Å, $V = 2003$ Å^3, $Z = 4$, $D_x = 1{\cdot}31$ g cm^{-3}, Cu $K\alpha$, graphite monochromator, $\lambda = 1{\cdot}54178$ Å, $\mu = 36{\cdot}33$ cm^{-1}, $F(000) = 808$, room temperature, final $R = 0{\cdot}086$ for 1693 $[F_o \geq 3\sigma(F)]$ reflections. The absolute configuration at C(3) and C(4) in the lactam ring is *R* and *S*, respectively. The bond lengths and angles are normal except for C(4)–C(7) 1·56 (2) Å and C(7)–C(8) 1·11 (2) Å. Packing of the molecules is governed by normal van der Waals contacts.

Introduction. In the course of a program to synthesize thienamycin (III), one of the carbapenem antibiotics having excellent antimicrobial and β-lactamase inhibitory potency, the title compound is the *p*-bromobenzoate (II) of a key intermediate (I) (Chiba, Nagatsuma & Nakai, 1984; Chiba & Nakai, 1985). The present X-ray analysis was undertaken to establish the absolute configuration of (II), and to confirm the stereochemical selectivity of the reaction.



Experimental. To a solution of (3*R*,4*S*)-3-[(*R*)-1-hydroxyethyl]-4-trimethylsilylethynyl-2-azetidinone (I) (0·1 g) in dry tetrahydrofuran (5 ml) were added *p*-bromobenzoyl chloride (0·15 g) and triethylamine (0·15 ml) at 278 K. The mixture was stirred for 15 h at ambient temperature, diluted with ethyl acetate (50 ml), washed with saturated NaCl solution, dried over magnesium sulfate and evaporated under reduced pressure. The residue was subjected to silica gel column chromatography (eluent: 10% ethyl acetate – 90% hexane) to give 0·12 g of the title compound. $[\alpha]_D^{22°C}$ −192·5° (*c* 0·800, EtOH); IR (Nujol) 3550, 1780, 1680 cm^{-1}; NMR ($CDCl_3$, p.p.m.) 0·10 (9H, *s*), 1·37 (3H, *d*, $J = 6{\cdot}6$ Hz), 2·80 (1H, *m*), 3·33 (1H, *d*, *d*, $J = 6{\cdot}6$, 6·6 Hz), 4·30 (1H, *m*), 4·83 (1H, *d*, $J = 6{\cdot}6$ Hz), 7·53 (2H, *d*, $J = 9$ Hz), 7·90 (2H, *d*, $J = 9$ Hz).

Colorless needle crystals (II), recrystallized from a mixture of hexane–ethyl acetate with dimensions 0·25 × 0·14 × 0·11 mm, Rigaku AFC-5 diffractometer. Cell parameters determined with 25 reflections in the range $51 < 2\theta < 62°$ by least-squares method. Intensities up to $2\theta = 130°$, ω–2θ scan method with scan speed 4° min^{-1}. Scan range ($\Delta\omega$): $1{\cdot}1° + 0{\cdot}5° \tan\theta$, graphite-monochromated Cu $K\alpha$ ($\lambda = 1{\cdot}5418$ Å), 50 kV, 170 mA rotating anode, background measured for 8 s on either side of the peak. Three reference reflections showed no intensity decrease. Lorentz and polarization corrections; no absorption correction. 1693 independent reflections ($h = 0$ to 28, $k = 0$ to 15, $l = 0$ to 7) with $F_o \geq 3\sigma(F)$ used in the refinement.

Structure solved by *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), and refined by block-diagonal least squares, H atoms identified on a difference Fourier map except for three methyl groups bonded to Si. 253 parameters refined. Absolute configuration determined by comparing 24

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Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å²) *with e.s.d.'s in parentheses*

$B_{eq} = \frac{4}{3}\sum_i\sum_j B_{ij}(\mathbf{a}_i.\mathbf{a}_j)$.

	x	y	z	B_{eq}
Br	0·16746 (8)	0·9644 (1)	0·9634 (3)	7·7
Si	0·0117 (2)	0·3218 (5)	0·0110 (10)	10·3
O(1)	0·2044 (3)	0·4605 (6)	0·7802 (11)	4·9
O(2)	0·1718 (4)	0·2261 (6)	0·7742 (14)	6·7
O(3)	0·1691 (5)	0·6113 (6)	0·1961 (13)	7·2
N(1)	0·1757 (3)	0·4918 (6)	0·4364 (12)	4·1
C(2)	0·1961 (4)	0·4366 (9)	0·6097 (18)	4·6
C(3)	0·1979 (4)	0·3396 (8)	0·4909 (18)	4·5
C(4)	0·1789 (4)	0·4038 (9)	0·2971 (18)	4·1
C(5)	0·1583 (5)	0·2521 (9)	0·5644 (21)	5·5
C(6)	0·1615 (7)	0·1533 (10)	0·4312 (21)	7·0
C(7)	0·1211 (5)	0·3753 (10)	0·2001 (19)	4·8
C(8)	0·0813 (5)	0·3567 (12)	0·1212 (21)	6·4
C(9)	−0·0453 (7)	0·3838 (20)	0·1710 (35)	12·9
C(10)	0·0065 (9)	0·3757 (23)	−0·2649 (37)	14·6
C(11)	0·0097 (9)	0·1859 (17)	−0·0155 (50)	20·7
C(12)	0·1724 (5)	0·5939 (9)	0·3802 (17)	4·7
C(13)	0·1728 (4)	0·6758 (8)	0·5282 (17)	4·3
C(14)	0·1490 (4)	0·6716 (8)	0·7229 (18)	4·1
C(15)	0·1457 (5)	0·7558 (10)	0·8452 (19)	5·2
C(16)	0·1717 (6)	0·8483 (9)	0·7771 (20)	5·8
C(17)	0·1960 (5)	0·8600 (10)	0·5904 (21)	5·6
C(18)	0·1971 (5)	0·7735 (9)	0·4692 (21)	5·5

Bijvoet pairs. $R(F) = 0{\cdot}086$ for the structure of $3R$, $4S$, $5R$ configurations ($R = 0{\cdot}090$ for that of the opposite configurations) at a significance level $\geqslant 0{\cdot}995$ by Hamilton's (1965) R-factor-ratio test based on the conventional R values, $wR = 0{\cdot}076$ [$w = 1/\sigma^2(F)$], $S = 1{\cdot}97$, $(\Delta/\sigma)_{max}$ in the final refinement cycle for non-H and H atoms 0·6 and 0·3, respectively.* $-1{\cdot}4 < \Delta\rho < 0{\cdot}6$ e Å^{-3}. Atomic scattering factors and dispersion corrections from *International Tables for X-ray Crystallography* (1974). Computation carried out at the computer center of our laboratories using *MULTAN*78 (Main *et al.*, 1978), *HBLS*-IV (Ashida, 1967) and *ORTEP*II (Johnson, 1976).

Discussion. Final atomic parameters are shown in Table 1,† and bond lengths and angles in Table 2. The bond lengths and angles are normal except for C(4)–C(7) 1·56 and C(7)–C(8) 1·11 Å. The thermal ellipsoids of the molecules with the atomic numbering are shown in Fig. 1. The C atoms of the methyl groups bonded to Si had relatively large temperature factors. The electron densities on the Fourier map were broadened around the Si atom. There are three optically active carbon atoms in the molecule, and the absolute configurations at C(3), C(4) and C(5) were determined as R, S and R, respectively. Thus, the conformation around C(3)–C(4) in the lactam ring was *cis*. It is interesting that these two bulky groups have been selectively arranged in the course of the synthesis. The lactam is approximately planar. The dihedral angle between the plane of N(1), C(3) and C(4) and the plane of N(1), C(3) and C(2) is only 5°. The length of the C(4)–C(7) single bond in the presence of the C(7)–C(8) triple bond is longer than those reported in previous works, 1·46 Å on the average (Albinati, Meille, Arnoldi & Galli, 1985; Toffoli, Khodadad,

Table 2. *Bond lengths* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

Br–C(16)	1·93 (1)	Si–C(8)	1·86 (2)
Si–C(9)	1·89 (3)	Si–C(10)	1·93 (3)
Si–C(11)	1·77 (5)	O(1)–C(2)	1·17 (1)
O(2)–C(5)	1·44 (2)	O(3)–C(12)	1·22 (2)
N(1)–C(2)	1·42 (1)	N(1)–C(4)	1·46 (1)
N(1)–C(12)	1·37 (2)	C(2)–C(3)	1·47 (2)
C(3)–C(4)	1·58 (2)	C(3)–C(5)	1·55 (2)
C(4)–C(7)	1·56 (2)	C(5)–C(6)	1·54 (2)
C(7)–C(8)	1·11 (2)	C(12)–C(13)	1·43 (2)
C(13)–C(14)	1·39 (2)	C(13)–C(18)	1·44 (2)
C(14)–C(15)	1·35 (2)	C(15)–C(16)	1·42 (2)
C(16)–C(17)	1·35 (2)	C(17)–C(18)	1·37 (2)

C(8)–Si–C(9)	109 (1)	C(8)–Si–C(10)	109 (1)
C(8)–Si–C(11)	108 (2)	C(9)–Si–C(10)	108 (1)
C(9)–Si–C(11)	117 (2)	C(10)–Si–C(11)	106 (2)
C(2)–N(1)–C(4)	95 (1)	C(2)–N(1)–C(12)	136 (1)
C(4)–N(1)–C(12)	126 (1)	O(1)–C(2)–N(1)	133 (1)
O(1)–C(2)–C(3)	136 (1)	N(1)–C(2)–C(3)	91 (1)
C(2)–C(3)–C(4)	88 (1)	C(2)–C(3)–C(5)	116 (1)
C(4)–C(3)–C(5)	117 (1)	N(1)–C(4)–C(3)	86 (1)
N(1)–C(4)–C(7)	113 (1)	C(3)–C(4)–C(7)	117 (1)
O(2)–C(5)–C(3)	109 (1)	O(2)–C(5)–C(6)	109 (1)
C(3)–C(5)–C(6)	114 (1)	C(4)–C(7)–C(8)	176 (1)
Si–C(8)–C(7)	175 (1)	O(3)–C(12)–N(1)	116 (1)
O(3)–C(12)–C(13)	122 (1)	N(1)–C(12)–C(13)	122 (1)
C(12)–C(13)–C(14)	126 (1)	C(12)–C(13)–C(18)	118 (1)
C(14)–C(13)–C(18)	116 (1)	C(13)–C(14)–C(15)	122 (1)
C(14)–C(15)–C(16)	118 (1)	Br–C(16)–C(15)	116 (1)
Br–C(16)–C(17)	120 (1)	C(15)–C(16)–C(17)	124 (1)
C(16)–C(17)–C(18)	116 (1)	C(13)–C(18)–C(17)	124 (1)

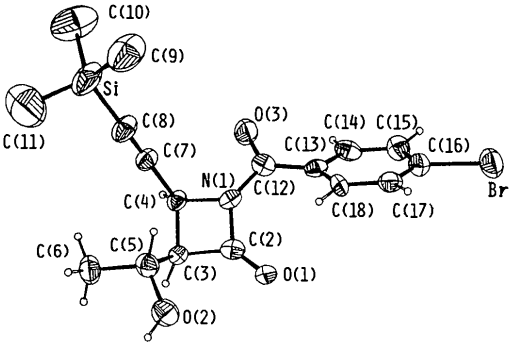

Fig. 1. Molecular structure and atomic numbering. The thermal ellipsoids are drawn at the 30% probability level, except for the H atoms (radius 0·05 Å).

* The rather high R value is due to the large thermal motion of the trimethylsilyl moiety, as described in the *Discussion*.

† Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43304 (5 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Rodier, Céolin & Astoin, 1985; Werninck, Blair, Milburn, Ando, Bloor, Motevalli & Hursthouse, 1985), and seems to have single-bond character. It may be considered that the bond has been lengthened because of two bulky groups arranged *cis* to each other or a conjugation could not extend to C(4)—C(7) due to the heterocyclic four-membered ring containing C(4). No shorter contact than van der Waals radii was found between molecules in the crystal structure.

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Structure of Thiamin Naphthalene-1,5-disulfonate Monohydrate

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Abstract. 3-[(4-Amino-2-methyl-5-pyrimidinio)-methyl]-5-(2-hydroxyethyl)-4-methylthiazolium naphthalene-1,5-disulfonate monohydrate, $C_{12}H_{18}N_4OS^{2+}.C_{10}H_6(SO_3^-)_2.H_2O$, $M_r = 570{\cdot}65$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}887\ (2)$, $b = 15{\cdot}754\ (3)$, $c = 20{\cdot}101\ (4)$ Å, $V = 2498\ (1)$ Å^3, $Z = 4$, $D_x = 1{\cdot}517$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 30{\cdot}54$ cm^{-1}, $F(000) = 1192$, $T = 295$ K, $R = 0{\cdot}040$ for 1798 observed reflections. Thiamin maintains a characteristic *F* conformation, even though it forms a molecular complex with a large molecular anion. The structure shows a partial ring-stacking interaction between the thiazolium ring of thiamin and the naphthalene ring, which has not been observed previously. S(1) is the principal site for interaction. The crystal packing is dominated by an extensive hydrogen-bonding network.

Introduction. Thiamin (vitamin B_1), in the form of pyrophosphate ester, is a coenzyme for enzyme systems catalyzing the transfer of aldehyde or acyl groups such as pyruvate decarboxylase and transketolase (Krampitz, 1969; Gallo, Mieyal & Sable, 1978). Although the nature of the enzyme catalytic site is not completely known, it is generally believed that the ring-stacking interaction between thiamin and tryptophan may play an important role in coenzyme binding. Accordingly, numerous attempts have been made to obtain crystalline complexes between thiamin and tryptophan or indole compounds, the crystal structures of which may show the detailed interaction mode at the atomic level, but these have so far failed. However, we obtained crystals of the molecular complex (thiamin 1,5-salt) between thiamin and naphthalene-1,5-disulfonate (NDS) anion. Its structure may provide an insight into the interaction mode of thiamin with a large π-electron system.

Experimental. Thiamin 1,5-salt prepared by mixing 10% aqueous solution of thiamin chloride hydrochloride and naphthalene-1,5-disulfonic acid disodium salt. Colorless tabular crystals obtained from an aqueous solution of 1,5-salt by slow evaporation at room temperature; crystal *ca* 0·2 × 0·3 × 0·5 mm, Rigaku AFC diffractometer, graphite-monochromated Cu $K\alpha$ radiation, $2\theta < 120°$, ω–2θ scan, scan speed 4° min^{-1} in 2θ, ω-scan width $(1{\cdot}3 + 0{\cdot}5\tan\theta)°$, background measured for 12 s on either side of the peak; cell parameters by least-squares fit to observed 2θ values

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