It has been proposed that the open form of penam is the active one from the consideration of the relative three-dimensional orientation of the β-lactam carbonyl and 3α-carboxyl groups (Cohen, 1983). Penam molecules can assume either an open or a closed conformation in the crystalline state which may be interconvertable in solution, while the sulfoxide derivatives assume only the open conformation. Therefore, the oxygen functionality on S(1) and/or the intramolecular N(9)—H···O(1) hydrogen bond which limits the flexibility of the 6β side chain seems to be the major factor for the loss of activity in penam sulfoxide derivatives.

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Structure of Diphenylmethyl 7β-Amino-7α-methoxy-3-[(1-methyl-1*H*-tetrazol-5-ylthio)methyl]-3-cephem-4-carboxylate

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Abstract. Diphenylmethyl 7β-amino-7α-methoxy-3-[(1-methyl-1*H*-tetrazol-5-ylthio)methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate, $C_{24}H_{24}N_6O_4S_2$, $M_r = 524.61$, orthorhombic, $P2_12_12_1$, $a = 9.829$ (1), $b = 13.290$ (2), $c = 18.864$ (3) Å, $V = 2464.2$ (6) Å^3, $Z = 4$, $D_x = 1.414$ g cm^{-3}, λ(Cu $K\alpha$) = 1.5418 Å, $\mu = 22.8$ cm^{-1}, $F(000) = 1096$, $T = 295$ K, $R = 0.048$ for 1654 reflections with $I \geq 2\sigma(I)$. The S(1)—C(2) bond is similar to the S(1)—C(6) bond in cephamycin while the former bond is always longer by *ca* 0.02 Å in cephalosporin. The orientation of the carboxyl group with respect to the 3-cephem nucleus is not affected by the presence of the bulky diphenylmethyl group. The 7α-methoxy group assumes the same conformation in cephamycin and oxacephalosporin. The (1-methyl-1*H*-tetrazol-5-ylthio)methyl moiety is perpendicular to the dihydrothiazine ring. Crystal packing consists only of van der Waals interactions.

Introduction. Cephamycins are derivatives of cephalosporin which contain a methoxy group at the 7α position. The 7α-methoxy group contributes to protection of the β-lactam ring against enzymatic inactivation by β-lactamase with little reduction in intrinsic activity (Hoover, 1983). The title compound (DPMCEP) is an intermediate for syntheses of cephamycin analogues with various 7β side chains. Its structure is compared with related compounds.

Experimental. Pale-yellow needles were obtained from a dichloromethane–methanol solution; crystal *ca* 0.5 × 0.2 × 0.2 mm. A Rigaku AFC diffractometer with graphite-monochromated Cu $K\alpha$ radiation was used for data collection; $2\theta \leq 120°$, ω–2θ scan; scan speed 2° min^{-1} in 2θ, ω-scan width $(2.0 + 0.1\tan\theta)°$; background measured for 10 s on either side of the peak. Cell parameters were determined by least-squares fit to observed 2θ values for 20 centred reflections with $22 \leq 2\theta \leq 51°$. Intensity checks for three standard reflections showed little (±1.0%) variation. 2114 independent reflections were measured (h 0 to 11, k −14 to 0, l −21 to 0), of which 1654 (78.2%) were observed with $I \geq 2\sigma(I)$ and used in the refinement. Lp corrections, but no absorption or extinction corrections were applied. The structure

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was solved by direct methods using *SHELXS*86 (Sheldrick, 1986) and refined by full-matrix least squares on F with anisotropic thermal parameters. Positional parameters of H atoms on the C(20) and C(23) methyl and N(21) amino groups, initially identified in the difference map, were refined with distance constraints (1.08 Å) and isotropic thermal parameters fixed with values of 1.3 times those of the bonded atoms; other H atoms were identified in the difference map and refined isotropically. Function $\sum w(|F_o| - |F_c|)^2$ was minimized, with $w = k/[\sigma^2(F_o) + gF_o^2]$, $\sigma(F)$ from counting statistics, k and g optimized in the least-squares procedure ($k = 0.70$, $g = 0.0042$); $wR = 0.049$ for 1654 observed reflections, 408 variables, $R = 0.098$ for all data, $S = 0.39$, $(\Delta/\sigma)_{max} = 0.923$ [y coordinate of H(33)] in the final refinement cycle; maximum and minimum heights in the final difference map were 0.36 and -0.29 e Å^{-3}, respectively. All calculations were performed with *SHELX*76 (Sheldrick, 1976) on an IBM 3090 computer. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV, p. 99).

Discussion. Final atomic parameters are listed in Table 1.* An *ORTEP*II (Johnson, 1976) view of the DPMCEP molecule with the atomic numbering scheme is presented in Fig. 1. Bond distances and angles are listed in Table 2.

Bond distances of the 3-cephem moiety agree well (within 3σ) with those in other cephamycin molecules (Kodama, Yamada, Sato, Kobayashi, Nishio & Murata, 1983). In 7αH-3-cephem, the S(1)—C(2) bond is invariably longer by *ca* 0.02 Å than the S(1)—C(6) bond (Shin & Cho, 1992). However, these two bonds become similar within 1σ in cephamycin. Otherwise, no significant variations in the bond distances of cephamycin and cephalosporin have been observed. Bond distances of the (1-methyl-1H-tetrazol-5-ylthio)methyl moiety are in good agreement (within 2σ) with those in other cephamycin and oxacephalosporin molecules (Kodama *et al.*, 1983; Shiro, Nakai, Onoue & Narisada, 1980; Shiro, Nakai, Matsubara & Kikkawa, 1982).

The dihydrothiazine ring assumes an envelope conformation. S(1) deviates by 0.918 (2) Å from the plane formed by the remaining five atoms which has a maximum deviation of 0.024 (7) Å for C(6). The β-lactam ring is planar with a maximum deviation of

* Lists of structure factors, anisotropic thermal parameters, coordinates of H atoms, molecular dimensions of the phenyl rings and dimensions involving the H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55030 (13 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: HH0557]

Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* (Å$^2 \times 10^3$)

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

	x	y	z	U_{eq}
S(1)	2349 (2)	4373 (1)	1543 (1)	64
C(2)	2043 (7)	3067 (5)	1375 (3)	56
C(3)	1441 (6)	2846 (5)	656 (3)	48
C(4)	1723 (6)	3391 (4)	81 (3)	47
N(5)	2610 (5)	4224 (3)	114 (2)	47
C(6)	3356 (7)	4538 (5)	756 (3)	54
C(7)	3415 (7)	5613 (5)	432 (3)	56
C(8)	2569 (7)	5156 (5)	−181 (3)	61
O(9)	2062 (6)	5452 (4)	−730 (3)	85
C(10)	1171 (6)	3105 (5)	−638 (3)	47
O(11)	37 (4)	2812 (4)	−747 (2)	68
O(12)	2130 (4)	3172 (3)	−1142 (2)	45
C(13)	536 (8)	1940 (6)	647 (4)	67
S(14)	1354 (2)	815 (1)	984 (1)	76
C(15)	2378 (8)	528 (5)	260 (3)	62
N(16)	2354 (7)	932 (4)	−384 (3)	70
N(17)	3327 (8)	429 (5)	−744 (3)	79
N(18)	3917 (8)	−248 (5)	−351 (3)	83
N(19)	3324 (7)	−186 (5)	288 (3)	67
C(20)	3735 (11)	−831 (7)	873 (5)	97
N(21)	2713 (8)	6420 (4)	778 (4)	88
O(22)	4786 (5)	5849 (3)	302 (2)	74
C(23)	4996 (11)	6680 (6)	−120 (5)	110
C(24)	1834 (5)	2586 (4)	−1791 (2)	45
C(25)	3146 (6)	2580 (4)	−2209 (2)	46
C(26)	3792 (6)	3457 (5)	−2410 (3)	56
C(27)	4893 (8)	3446 (7)	−2852 (4)	75
C(28)	5357 (7)	2539 (8)	−3101 (4)	82
C(29)	4771 (8)	1650 (7)	−2912 (4)	82
C(30)	3640 (7)	1652 (5)	−2450 (3)	67
C(31)	696 (6)	3014 (4)	−2229 (3)	44
C(32)	417 (8)	4022 (5)	−2280 (4)	68
C(33)	−575 (8)	4360 (5)	−2742 (5)	83
C(34)	−1269 (8)	3690 (7)	−3153 (4)	78
C(35)	−1004 (7)	2682 (6)	−3118 (3)	71
C(36)	−37 (7)	2351 (5)	−2645 (3)	57

Table 2. *Selected bond distances* (Å) *and angles* (°)

S(1)—C(2)	1.790 (7)	S(1)—C(6)	1.797 (6)
C(2)—C(3)	1.509 (8)	C(3)—C(4)	1.334 (8)
C(3)—C(13)	1.497 (10)	C(4)—N(5)	1.410 (7)
C(4)—C(10)	1.509 (8)	N(5)—C(6)	1.476 (7)
N(5)—C(8)	1.360 (8)	C(6)—C(7)	1.555 (9)
C(7)—C(8)	1.549 (9)	C(7)—N(21)	1.433 (9)
C(7)—O(22)	1.405 (8)	C(8)—O(9)	1.214 (8)
C(10)—O(11)	1.199 (7)	C(10)—O(12)	1.342 (7)
O(12)—C(24)	1.479 (6)	C(13)—S(14)	1.813 (8)
S(14)—C(15)	1.739 (7)	C(15)—N(16)	1.329 (8)
C(15)—N(19)	1.329 (10)	N(16)—N(17)	1.350 (9)
N(17)—N(18)	1.303 (9)	N(18)—N(19)	1.342 (9)
N(19)—C(20)	1.455 (11)	O(22)—C(23)	1.376 (9)
C(24)—C(25)	1.512 (7)	C(24)—C(31)	1.503 (7)

C(3)—C(2)—S(1)	114.4 (5)	C(4)—C(3)—C(2)	122.9 (6)
N(5)—C(4)—C(3)	121.2 (5)	N(5)—C(6)—S(1)	111.7 (4)
C(6)—S(1)—C(2)	93.7 (3)	C(6)—N(5)—C(4)	124.5 (4)
C(7)—C(6)—S(1)	117.3 (4)	C(7)—C(6)—N(5)	87.5 (4)
C(7)—C(8)—N(5)	92.0 (5)	C(8)—N(5)—C(4)	132.7 (5)
C(8)—N(5)—C(6)	95.3 (4)	C(8)—C(7)—C(6)	85.1 (5)
O(9)—C(8)—N(5)	131.1 (6)	O(9)—C(8)—C(7)	136.9 (6)
C(10)—C(4)—C(3)	121.3 (5)	C(10)—C(4)—N(5)	117.4 (5)
O(11)—C(10)—C(4)	124.8 (5)	O(12)—C(10)—C(4)	111.6 (5)
O(12)—C(10)—O(11)	123.5 (5)	C(13)—C(3)—C(2)	113.6 (5)
C(13)—C(3)—C(4)	123.4 (6)	S(14)—C(13)—C(3)	113.3 (5)
C(15)—S(14)—C(13)	99.3 (3)	N(16)—C(15)—S(14)	128.2 (6)
N(17)—N(16)—C(15)	104.3 (6)	N(18)—N(17)—N(16)	111.8 (6)
N(18)—N(19)—C(15)	108.2 (6)	N(19)—C(15)—S(14)	122.0 (5)
N(19)—C(15)—N(16)	109.8 (6)	N(19)—N(18)—N(17)	106.0 (6)
C(20)—N(19)—C(15)	130.2 (6)	C(20)—N(19)—N(18)	121.6 (7)
N(21)—C(7)—C(6)	119.3 (5)	N(21)—C(7)—C(8)	112.0 (6)
O(22)—C(7)—C(6)	108.1 (5)	O(22)—C(7)—C(8)	118.1 (5)
O(22)—C(7)—N(21)	112.0 (6)	C(23)—O(22)—C(7)	115.2 (6)
C(24)—O(12)—C(10)	114.4 (4)	C(25)—C(24)—O(12)	105.5 (4)
C(31)—C(24)—O(12)	113.7 (4)	C(31)—C(24)—C(25)	110.4 (4)
C(26)—C(25)—C(24)	122.1 (5)	C(32)—C(31)—C(24)	123.9 (5)
C(30)—C(25)—C(24)	118.0 (5)	C(36)—C(31)—C(24)	117.3 (5)

0.022 (7) Å and O(9) deviates by 0.044 (6) Å from this plane toward S(1). The dihedral angle between these two planar groups is 28.1 (6)°. N(5) deviates by 0.217 (5) Å toward S(1) from the plane formed by the three bonded C atoms and the sum of the valence angles around N(5) is 354.5°. These indicate diminished pyramidal character of N(5) compared to that of penam, as observed in other cephalosporins (Sweet, 1972). The dihedral angle between the 3α-carboxyl group and the dihydrothiazine ring is 41.0 (7)° [the C(3)—C(4)—C(10)—O(11) torsion angle = 41.3 (7)°], while it is 47° in cefadroxil with an ionized carboxyl group (Shin & Cho, 1992). These values indicate that the bulky diphenylmethyl group does not exert any significant influence on the relative orientation of the carboxyl group with respect to the 3-cephem nucleus. Two phenyl groups are planar with maximum deviations of 0.011 (8) Å, making a dihedral angle of 81.3 (8)°. The tetrazole ring forms a good plane with a maximum deviation of 0.003 (7) Å. S(14) and C(20) deviate by 0.036 (2) and 0.011 (10) Å, respectively, from this plane.

The conformation of the 7α-methoxy group is nearly constant in cephamycin and oxacephalosporin molecules containing this side chain, and the C(6)—C(7)—O(22)—C(23) torsion angle ranges from 167.1 to 171.5° (Kodama *et al.*, 1983; Shiro *et al.*, 1980, 1982). In DPMCEP the methoxy groups assume the same conformation [166.9 (8)°] despite the absence of a bulky substituent on the 7β-amino group. Various values of the torsion angle defining the conformation of the (1-methyl-1*H*-tetrazol-5-ylthio)methyl moiety have been reported for many compounds, showing that this side chain is flexible. It is perpendicular to the dihydrothiazine ring in DPMCEP [dihedral angle = 87.8 (8)°].

A stereoscopic packing diagram is shown in Fig. 2. Diphenylmethyl groups form pleated molecular sheets parallel to the *ab* plane at *ca* $\frac{1}{4}c$. The amino H atoms are not involved in any hydrogen bonds and crystal packing consists only of the normal van der Waals interactions.

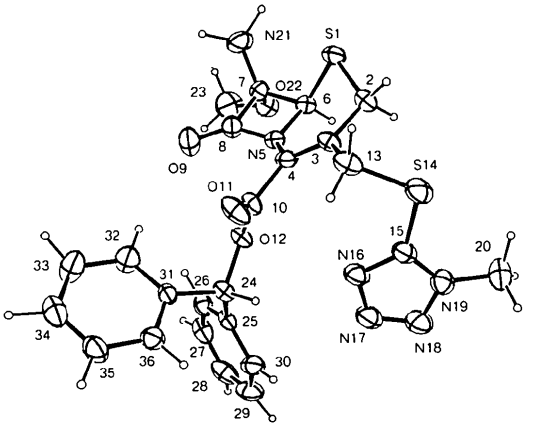

Fig. 1. *ORTEP*II (Johnson, 1976) drawing of the DPMCEP molecule with atomic numbering scheme. Thermal ellipsoids are drawn at the 30% probability level.

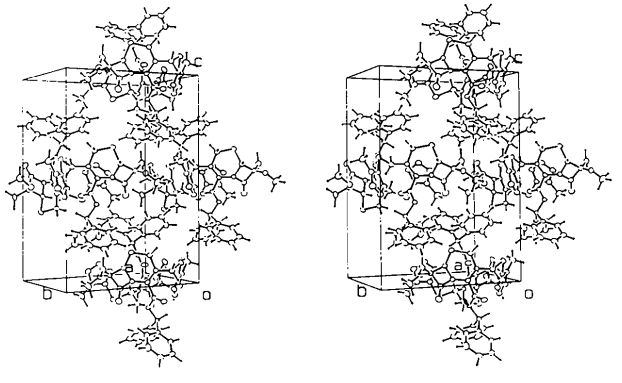

Fig. 2. Stereoscopic *ORTEP*II (Johnson, 1976) packing drawing of DPMCEP.

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