

## Crystal and Molecular Structure of (3*R*)-3-(3-Methyl-7-phenoxyacetamido-3-cephem-4-yl)-3-hydroxybutanoic Acid

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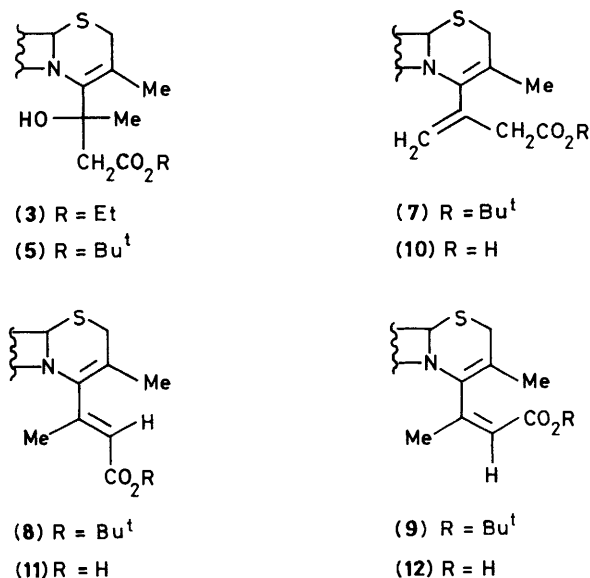
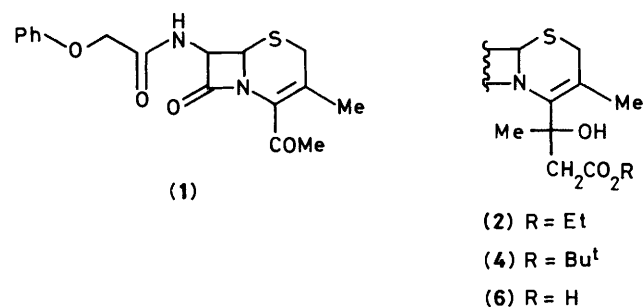
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The *R* configuration of the side-chain linked to the C(4) atom of the  $\Delta^3$ -cephem derivative (**6**) was unequivocally established by means of crystal-structure determination. Crystals are monoclinic, space group *P*2<sub>1</sub>, with *Z* = 4, unit-cell dimensions *a* = 11.293(4), *b* = 20.211(4), *c* = 8.927(3) Å. In the asymmetric unit of (**6**) two independent molecules (**6a** and **b**) are present. The structure was solved by direct methods and refined by least-squares to *R* 0.042. The relevant molecular parameters are compared with the corresponding ones of the ketone (**1**).

For several years we have been interested in structural modifications of  $\beta$ -lactam antibiotics such as penicillins and cephalosporins. Some years ago the synthesis of the  $\Delta^3$ -cephem derivatives (**10**)–(**12**),<sup>1</sup> with an additional double bond conjugated with the  $\Delta^3$ -cephem double bond, was performed. The Reformatsky reaction of the 4-acetyl-3-cephem derivative (**1**) with ethyl  $\alpha$ -bromoacetate gave a mixture of the  $\beta$ -hydroxy esters (**2**) and (**3**) in a ratio of 2:1. The same reaction of (**1**) with the *t*-butyl  $\alpha$ -bromoacetate yielded only the diastereoisomer (**4**), corresponding to (**2**). Dehydration of (**4**) with thionyl chloride and

triethylamine in CH<sub>2</sub>Cl<sub>2</sub> yielded the unsaturated esters (**7**)–(**9**) which were converted into the corresponding acids (**10**)–(**12**).

The structure of the hydroxy esters (**2**) and (**3**), the configurational correspondence between (**2**) and (**4**), and the structures of the esters (**7**)–(**9**), and of the corresponding acids (**10**)–(**12**) were shown by their <sup>1</sup>H n.m.r. spectra. The configurations of the couples (**8**)–(**9**) and (**11**)–(**12**) were established on the basis of the u.v. spectra of acids (**11**) and (**12**). The <sup>1</sup>H n.m.r. spectra did not allow us to assign configurations to esters (**2**)–(**4**). However, they were tentatively assumed on the basis of the usually accepted mechanism of the Reformatsky reaction and of the preferential conformation in the solid state of the carbonyl group of (**1**) with respect to the dihydrothiazine ring plane.<sup>2</sup> Attempts were made to assign unequivocally the configurations of the asymmetric centre of the side-chain linked to C(4) of (**2**)–(**4**) through X-ray crystallographic analysis of acid (**6**), a derivative of ester (**4**). However we were unable to resolve its structure completely.<sup>1</sup> Very recently, however, using a well shaped crystal obtained from a new preparation, affording a significantly greater number of observed reflections, together with MULTAN 80,<sup>3</sup> we successfully performed the crystal analysis of the acid (**6**). The crystal structure of (**6**) was compared with that of the ketone (**1**).



### Results and Discussion

In the asymmetric unit of the title compound (**6**) two independent molecules (**6a** and **b**) are present. Perspective views of the X-ray structures of (**6a** and **b**) showing the crystallographic numbering scheme are given in Figures 1 and 2, respectively. Relevant structural parameters are shown in Tables 1–6.

As can be seen from Figures 1 and 2, the configuration of the asymmetric centre of the side-chain linked to the C(4) of (**6**) is *R*. This configuration is the same as that hypothesized for the corresponding ester (**4**) on the basis only of mechanistic considerations.<sup>1</sup>

From the data shown in Table 2, in which the geometrical parameters of (**6a** and **b**) are compared with those for 4-acetyl-3-methyl-7-phenoxyacetamido- $\Delta^3$ -cephem (**1**),<sup>2</sup> it can be seen that they are in the range usually found in this class of compounds. There are also similarities in the carbacephem system,<sup>4</sup> if sulphur is not taken into account in the six-membered ring. The major differences concern the angles C(2)–C(3)–C(4) and C(3)–C(4)–N(5), and are probably due to

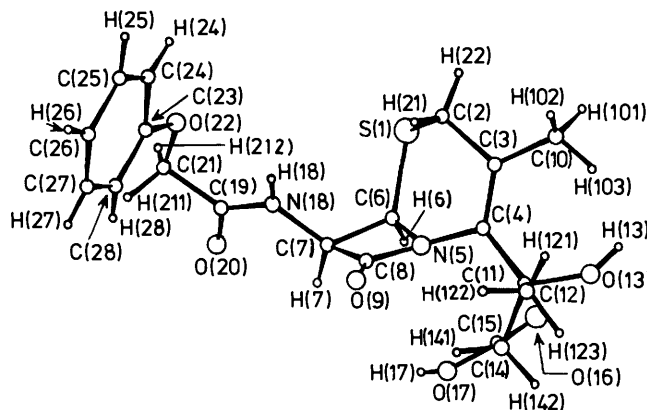


Figure 1. Projection of a molecule of (6a) along the O(9)-C(8) direction with rotation around the *x*, *y* axes to obtain the best view

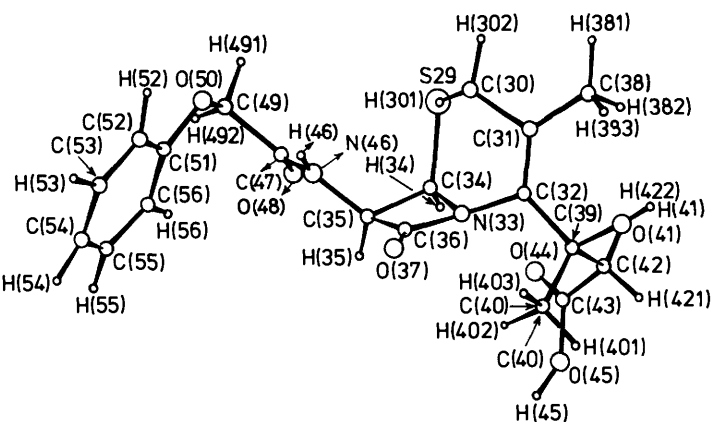


Figure 2. Projection of a molecule of (6b) along the O(37)-C(36) direction with rotation around the *x*, *y* axes

Table 1. Atomic co-ordinates ( $\times 10^4$ )

	X/A	Y/B	Z/C		X/A	Y/B	Z/C
S1	1 518(1)	4 688(0)	1 568(1)	C51	7 304(4)	5 792(2)	364(5)
C2	875(5)	5 427(3)	554(7)	C52	7 083(5)	5 116(3)	136(7)
C3	665(4)	5 382(3)	-1 182(6)	C53	7 599(6)	4 693(3)	1 285(10)
C4	1 576(4)	5 176(2)	-1 805(5)	C54	8 335(6)	4 901(4)	2 624(9)
N5	2 652(3)	4 976(2)	-745(4)	C55	8 535(5)	5 566(4)	2 841(6)
C6	2 741(5)	4 536(2)	604(5)	C56	8 030(5)	6 024(3)	1 733(6)
C7	4 051(4)	4 837(2)	1 191(5)	H21	1 374(43)	5 744(26)	765(56)
C8	3 711(4)	5 307(2)	-176(5)	H22	101(48)	5 523(27)	860(59)
O9	4 137(3)	5 783(2)	-656(4)	H6	2 792(43)	4 044(24)	330(55)
C10	-558(5)	5 596(4)	-2 061(9)	H7	4 632(47)	4 560(26)	1 006(59)
C11	1 618(4)	5 137(2)	-3 487(5)	H101	-1 300(60)	5 245(33)	-1 898(78)
C12	1 740(6)	5 827(3)	-4 175(6)	H102	-689(67)	5 977(43)	-1 917(93)
O13	509(3)	4 861(2)	-4 373(4)	H103	-737(77)	5 472(45)	-3 204(100)
C14	2 696(4)	4 712(2)	-3 739(5)	H121	1 100(50)	6 083(28)	-4 133(68)
C15	2 661(5)	4 029(2)	-3 067(6)	H122	2 419(57)	6 057(35)	-3 469(75)
O16	1 722(3)	3 714(2)	-3 148(5)	H123	1 759(55)	5 776(34)	-5 420(75)
O17	3 708(3)	3 801(2)	-2 365(4)	H13	-233(67)	4 812(38)	-4 444(83)
N18	4 399(4)	5 138(2)	2 675(4)	H141	3 430(24)	4 954(13)	-3 147(30)
C19	5 191(4)	4 860(2)	3 826(5)	H142	2 653(63)	4 679(38)	-4 955(89)
O20	5 626(4)	4 304(2)	3 719(4)	H17	4 074(79)	3 550(47)	-1 711(103)
C21	5 576(6)	5 245(3)	5 293(6)	H18	4 136(43)	5 502(26)	2 831(57)
O22	4 920(3)	5 847(2)	5 289(4)	H211	6 480(46)	5 347(27)	5 454(58)
C23	5 513(4)	6 450(3)	5 322(5)	H212	5 422(48)	4 955(28)	5 951(62)
C24	4 889(5)	6 989(3)	5 706(6)	H24	4 129(45)	6 926(25)	5 900(56)
C25	5 382(7)	7 605(3)	5 781(6)	H25	4 830(89)	7 982(53)	6 050(117)
C26	6 530(8)	7 696(3)	5 423(7)	H26	6 791(41)	8 010(24)	5 639(51)
C27	7 119(6)	7 164(4)	5 028(7)	H27	7 865(63)	7 188(38)	4 777(80)
C28	6 637(5)	6 544(3)	4 944(6)	H28	7 034(37)	6 187(21)	4 784(48)
S29	3 539(1)	7 955(1)	-1 284(2)	H301	2 501(69)	7 012(40)	-1 355(88)
C30	2 219(6)	7 413(3)	-1 705(6)	H302	1 852(78)	7 422(46)	-2 906(105)
C31	1 248(6)	7 620(3)	-886(6)	H34	4 129(43)	8 301(25)	1 230(54)
C32	1 544(4)	7 639(2)	648(5)	H35	5 144(42)	7 501(24)	2 534(54)
N33	2 829(3)	7 532(2)	1 274(4)	H381	-186(62)	7 809(36)	-3 132(76)
C34	3 827(4)	7 876(2)	774(6)	H382	-53(65)	8 345(37)	-1 601(85)
C35	4 671(4)	7 300(2)	1 555(5)	H383	-607(70)	7 516(42)	-1 523(91)
C36	3 495(4)	6 971(2)	1 751(5)	H401	607(57)	7 502(34)	4 028(72)
O37	3 202(3)	6 432(1)	2 166(4)	H402	2 084(75)	7 450(45)	3 784(103)
C38	52(7)	7 833(5)	-1 894(9)	H403	954(83)	6 877(49)	2 945(106)
C39	803(4)	7 828(2)	1 813(6)	H41	-1 114(82)	7 702(46)	632(109)
C40	1 132(6)	7 389(4)	3 269(7)	H421	307(86)	8 602(49)	2 920(111)
O41	-441(3)	7 729(2)	1 118(5)	H422	764(62)	8 848(37)	1 175(80)
C42	961(5)	8 568(3)	2 246(8)	H45	2 637(68)	8 466(41)	5 457(91)
C43	2 202(5)	8 795(3)	3 159(7)	H46	5 190(40)	6 575(22)	627(53)
O44	2 965(4)	9 004(2)	2 590(6)	H491	6 749(55)	7 018(30)	-1 778(70)
O45	2 319(5)	8 740(3)	4 643(6)	H492	7 851(42)	6 982(24)	-342(50)
N46	5 389(3)	6 946(2)	653(4)	H52	6 640(39)	4 958(22)	-997(48)
C47	6 342(4)	7 237(2)	319(5)	H53	7 532(87)	4 137(49)	1 141(111)
O48	6 703(4)	7 798(2)	782(5)	H54	8 677(43)	4 625(26)	3 639(57)
C49	7 046(4)	6 870(2)	-701(5)	H55	9 049(58)	5 683(36)	3 809(80)
O50	6 784(3)	6 188(1)	-841(3)	H56	8 166(39)	6 521(22)	1 933(52)

**Table 2.** Comparison of structural parameters [distances (Å) and angles (°)] of  $\Delta^3$ -cephem derivatives (**6**) and (**1**)

	Molecule ( <b>6a</b> )	Molecule ( <b>6b</b> )*	( <b>1</b> ) <sup>2</sup>
S(1)–C(2)	1.815(6)	1.821(7)	1.813(8)
S(1)–C(6)	1.806(6)	1.802(6)	1.795(7)
C(2)–C(3)	1.520(8)	1.503(10)	1.507(10)
C(3)–C(4)	1.337(7)	1.338(7)	1.337(9)
C(4)–N(5)	1.427(5)	1.453(5)	1.414(7)
N(5)–C(6)	1.484(6)	1.474(7)	1.445(9)
N(5)–C(8)	1.368(5)	1.376(6)	1.396(9)
C(6)–C(7)	1.580(7)	1.568(6)	1.566(10)
C(7)–C(8)	1.529(6)	1.529(7)	1.543(10)
C(8)–C(9)	1.196(6)	1.219(5)	1.210(10)
C(2)–S(1)–C(6)	99.7(2)	96.6(2)	95.5(3)
S(1)–C(2)–C(3)	114.6(4)	112.6(4)	117.7(6)
C(2)–C(3)–C(4)	118.7(5)	117.3(6)	125.7(8)
C(3)–C(4)–N(5)	115.7(4)	113.3(5)	117.8(6)
C(4)–N(5)–C(6)	127.3(4)	125.3(4)	125.8(7)
N(5)–C(6)–S(1)	111.2(3)	111.7(3)	109.8(5)
C(7)–C(6)–S(1)	122.3(3)	118.5(3)	113.0(5)
C(4)–N(5)–C(8)	131.1(4)	132.5(4)	132.6(8)
C(6)–N(5)–C(8)	95.3(4)	94.6(3)	95.1(5)
N(5)–C(6)–C(7)	86.1(3)	86.9(3)	87.5(5)
C(6)–C(7)–C(8)	85.4(3)	85.1(3)	84.8(5)
C(7)–C(8)–N(5)	92.3(3)	92.1(3)	90.2(6)
N(5)–C(8)–O(9)	130.4(4)	131.6(5)	131.0(11)
C(7)–C(8)–O(9)	137.3(4)	136.5(4)	137.8(12)
N(5), C(6), C(7)–N(5), C(7), C(8)	10.2(3)	12.3(4)	16.4
N(5) ... C(4)–C(6)–C(8)	–0.201	–0.222	0.20
S(1) ... C(2)–C(3)–C(4)–N(5)–C(6)	0.505	0.543	–0.751
C(2) ... C(3)–C(4)–N(5)–C(6)–S(1)	–0.760	0.859	0.429
C(3) ... C(4)–N(5)–C(6)–S(1)–C(2)	0.218	0.230	0.086
C(4) ... N(5)–C(6)–S(1)–C(2)–C(3)	0.485	–0.564	–0.289
N(5) ... C(6)–S(1)–C(2)–C(3)–C(4)	–0.479	–0.512	–0.174
C(6) ... S(1)–C(2)–C(3)–C(4)–N(5)	0.063	0.085	0.751

\* Molecule (**6b**) is related to (**6a**) by adding 28 to the numbers attached to the atoms of molecule (**6a**).

the different substituents in the two compounds at C(3) and C(4).

The puckering<sup>5,6</sup> in the two independent molecules of (**6**) shows quite similar values [ $q_2$  0.603(4) and 0.685(4) Å,  $q_3$  –0.113(5) and –0.138(5) Å,  $\Phi_2$  128.4(4) and –127.9(4)° for the dihydrothiazine ring of the molecules (**6a** and **b**), respectively], as can be seen from the distances of each atom from the mean plane of the dihydrothiazine ring (Table 2). Compound (**1**), on the other hand, shows a different trend: only S(1) and C(6) have longer distances with respect to the other ring atoms. The different puckering of compound (**1**) is reflected in the torsion angles of Tables 3 and 4; the most significant differences concern the angles involving S(1)–C(6), S(1)–C(2), and C(2)–C(3). The nitrogen atoms of the  $\beta$ -lactams are displaced by 0.201 and 0.222 Å in molecules (**6a** and **b**), respectively, from the plane of their three bonded carbon atoms [C(4), C(6), C(8); C(32), C(34), C(36)], similar to displacements in cephalosporins;<sup>2,7,8</sup> this shows once again the pyramidal geometry of  $\beta$ -lactams, characteristic of this class of compounds, but does not necessarily imply antibiotic activity.

The edge-deformation of the  $\beta$ -lactams indicated by the dihedral angles N(5)C(6)C(7)–N(5)C(7)C(8) is significantly greater in the two independent molecules of (**6**) than in (**1**), whereas the torsion angles do not differ significantly either in sign or value (see Table 3).

Table 4 shows quite different spatial orientations of the chain departing from the C(4) atom in the two molecules, probably because of the different series of short intermolecular contacts involving oxygen atoms (see Table 6). But the most striking feature of the title compound certainly concerns the phenoxyacetamido group (Figures 1 and 2, Table 5).

Bond distances, bond angles, and planarity of the central

**Table 3.** Comparison of torsion angles (°) of the dihydrothiazine and  $\beta$ -lactam rings of (**6**) and (**1**)

	Molecule ( <b>6a</b> )	Molecule ( <b>6b</b> )*	( <b>1</b> ) <sup>2</sup>
C(2)–S(1)–C(6)–C(7)	90.2(4)	88.8(4)	150.4(5)
C(2)–S(1)–C(6)–N(5)	–8.9(4)	–9.8(4)	54.5(5)
C(6)–S(1)–C(2)–C(3)	47.9(5)	55.0(5)	–38.1(6)
S(1)–C(2)–C(3)–C(4)	–50.4(6)	–59.4(7)	10.6(11)
C(2)–C(3)–C(4)–N(5)	3.9(7)	7.1(7)	6.9(11)
C(3)–C(4)–N(5)–C(6)	46.7(6)	49.5(6)	16.9(9)
C(3)–C(4)–N(5)–C(8)	–98.3(6)	–91.9(6)	–127.3(7)
C(4)–N(5)–C(6)–S(1)	–38.5(6)	–42.0(5)	–53.0(7)
C(4)–N(5)–C(8)–O(9)	–19.8(8)	–21.8(8)	–18.4(13)
C(4)–N(5)–C(8)–C(7)	160.4(4)	158.5(5)	163.8(7)
C(4)–N(5)–C(6)–C(7)	–161.6(4)	–161.5(4)	–166.5(6)
C(8)–N(5)–C(6)–S(1)	115.7(3)	110.5(3)	101.4(5)
C(6)–N(5)–C(8)–O(9)	–172.5(5)	–171.1(5)	–169.9(8)
C(6)–N(5)–C(8)–C(7)	7.7(4)	9.2(4)	12.3(6)
C(8)–N(5)–C(6)–C(7)	–7.4(4)	–9.0(4)	–12.1(5)
N(5)–C(6)–C(7)–C(8)	6.6(3)	8.1(3)	11.0(5)
S(1)–C(6)–C(7)–C(8)	–105.9(4)	–105.1(4)	–99.5(5)
C(6)–C(7)–C(8)–N(5)	–7.2(3)	–8.7(3)	–11.3(5)
C(6)–C(7)–C(8)–O(9)	173.0(6)	171.7(6)	171.1(9)
N(5)–C(6)–C(7)–N(18)	125.0(4)	126.2(4)	134.5(6)
S(1)–C(6)–C(7)–N(18)	12.4(6)	13.1(6)	24.0(8)
N(5)–C(8)–C(7)–N(18)	–123.0(4)	–128.4(4)	–134.9(6)
O(9)–C(8)–C(7)–N(18)	50.2(8)	52.0(7)	47.6(13)

\* See Table 2.

amide bridge compare remarkably well in the two independent molecules (**6a** and **b**) and also with compound (**1**)<sup>2</sup> and values found in literature,<sup>2,7,8</sup> though the orientations of the two groups are completely different; while the orientation of

**Table 4.** Comparison of structural parameters [distances (Å) and angles (°)] for the substituents at C(3) and C(4) of (6) and (1)

	Molecule (6a)	Molecule (6b)*	(1)
C(3)–C(10)	1.498(7)	1.513(10)	1.537(9)
C(4)–C(11)	1.514(7)	1.519(7)	1.489(12)
C(11)–C(12)	1.542(7)	1.551(8)	1.537(14)
C(11)–O(13)	1.441(5)	1.423(5)	
C(11)–C(14)	1.546(7)	1.546(7)	
C(14)–C(15)	1.510(6)	1.531(8)	
C(15)–O(16)	1.225(6)	1.170(8)	
C(15)–O(17)	1.296(6)	1.307(8)	
C(2)–C(3)–C(10)	116.0(5)	116.2(5)	110.6(7)
C(4)–C(3)–C(10)	125.3(5)	126.3(6)	123.7(8)
C(3)–C(4)–C(11)	128.4(4)	131.0(5)	125.1(8)
N(5)–C(4)–C(11)	115.9(4)	115.3(4)	116.4(6)
C(4)–C(11)–C(14)	111.6(4)	111.3(4)	
C(4)–C(11)–O(13)	110.7(4)	107.8(4)	122.6(8)
C(4)–C(11)–C(12)	111.9(4)	111.3(4)	116.4(7)
O(13)–C(11)–C(14)	108.8(4)	107.1(4)	
C(12)–C(11)–C(14)	107.6(4)	110.6(5)	
C(12)–C(11)–O(13)	106.0(4)	108.6(4)	121.0(8)
C(11)–C(14)–C(15)	111.1(4)	117.7(5)	
C(14)–C(15)–O(17)	114.6(4)	113.2(5)	
C(14)–C(15)–O(16)	123.3(4)	123.5(6)	
O(16)–C(15)–O(17)	122.1(4)	123.4(6)	
S(1)–C(2)–C(3)–C(10)	131.4(5)	116.2(6)	–170.5(5)
N(5)–C(4)–C(3)–C(10)	–178.1(5)	–168.1(6)	–172.0(6)
C(2)–C(3)–C(4)–C(11)	–175.2(5)	179.4(5)	176.8(6)
C(8)–N(5)–C(4)–C(11)	80.9(6)	94.5(6)	61.9(9)
C(6)–N(5)–C(4)–C(11)	–134.1(4)	–124.1(5)	–153.9(6)
C(10)–C(3)–C(4)–C(11)	2.8(9)	4.3(10)	–2.0(11)
C(3)–C(4)–C(11)–C(12)	73.8(6)	143.3(6)	–151.3(7)
C(3)–C(4)–C(11)–O(13)	–44.2(7)	24.2(7)	29.1(11)
C(3)–C(4)–C(11)–C(14)	165.6(5)	–92.9(7)	
N(5)–C(4)–C(11)–C(12)	–105.3(5)	–44.6(6)	18.8(9)
N(5)–C(4)–C(11)–O(13)	136.8(4)	–163.6(4)	–160.8(7)
N(5)–C(4)–C(11)–C(14)	15.4(5)	79.3(5)	

\* See Table 2.

molecule (6a) is in agreement with that of compound (1), that of molecule (6b) assumes a more inclined position due to rotation around the C(47)–C(49) bond. The angle between the planes N(5)C(6)C(7)C(8) and C(7)N(18)C(19) is 72.9(4)° and O(22) is 0.124 Å out of the mean plane running through N(18)C(19)O(20)C(21), whereas the angle between the N(33)C(34)C(35)C(36) and C(35)N(46)C(47) planes is 52.8(4)° and O(50) is 0.351 Å out of the N(46)C(47)O(48)C(49) plane.

In both molecules the phenyl ring is nearly at right angles [79.3(2) and 85.0° for molecules (6a and b), respectively (see Table 5)] to the amide chain; in compound (1) this angle is only 20.4°.

As usual the N–C(O) bond in the β-lactams is longer than the N–C(O) in the side-chain amide, whereas the corresponding C–O distances are in a reciprocal relationship, confirming the delocalization in the β-lactam ring.

Possible hydrogen bonds may be involved in the following contacts (see Table 6 for superscripts):

C(2)···O(37)	3.384(6) Å
N(18)···O(37)	2.933(5)
N(46)···O(9)	2.859(5)
C(42) <sup>b</sup> ···O(16)	3.314(7)
C(49) <sup>h</sup> ···O(41)	3.421(5)
C(2)–H(21)···O(37)	160.2(4.5)°
N(18)–H(18)···O(37)	154.9(4.7)
N(46)–H(46)···O(9)	159.8(4.3)
C(42) <sup>b</sup> –H(421)···O(16)	150.9(7.4)
C(49) <sup>h</sup> –H(492)···O(41)	153.3(4.0)

**Table 5.** Comparison of structural parameters [distances (Å) and angles (°)] for the phenoxyacetamido groups of (6) and (1)

	Molecule (6a)	Molecule (6b)*	(1) <sup>2</sup>
C(7)–N(18)	1.432(6)	1.450(6)	1.429(8)
N(18)–C(19)	1.331(5)	1.315(6)	1.348(9)
C(19)–O(20)	1.238(6)	1.245(6)	1.229(9)
C(19)–C(21)	1.504(7)	1.526(7)	1.529(9)
C(21)–O(22)	1.424(7)	1.409(5)	1.398(7)
O(22)–C(23)	1.387(7)	1.367(5)	1.383(8)
Mean C–C phenyl	1.377(9)	1.379(9)	1.380(4)
C(6)–C(7)–N(18)	121.3(4)	118.6(4)	121.2(6)
C(8)–C(7)–N(18)	116.5(4)	117.0(4)	121.2(7)
C(7)–N(18)–C(19)	122.5(4)	119.3(4)	118.4(6)
N(18)–C(19)–O(20)	122.4(4)	123.8(5)	124.4(8)
N(18)–C(19)–C(21)	118.1(4)	118.4(4)	116.6(6)
O(20)–C(19)–C(21)	119.5(4)	117.8(4)	119.0(7)
C(19)–C(21)–O(22)	112.9(4)	113.7(4)	109.5(5)
C(21)–O(22)–C(23)	120.2(4)	117.2(3)	117.2(6)
O(22)–C(23)–C(24)	115.4(5)	115.2(4)	115.1(6)
O(22)–C(23)–C(28)	125.1(5)	124.2(4)	124.2(8)
Mean C–C–C phenyl	120.0(6)	120.0(6)	120.2(4)
O(22)–C(21)–C(19)–N(18)	6.1(7)	–16.0(6)	22.0(8)
O(22)–C(21)–C(19)–O(20)	–174.8(5)	164.4(4)	–158.7(7)
C(6)–C(7)–N(18)–C(19)	109.2(5)	73.5(5)	118.9(7)
C(8)–C(7)–N(18)–C(19)	–149.4(4)	173.2(4)	–137.0(6)
Phenoxy amide	79.3(2)	85.0(2)	20.4

\* See Table 2.

**Table 6.** van der Waals contacts less than 3.5 Å for (6)

O(13)···C(54) <sup>a</sup>	C(54)···O(13) <sup>a</sup>	3.219(8)
O(13)···C(55) <sup>a</sup>	C(55)···O(13) <sup>a</sup>	3.282(7)
C(15)···O(48) <sup>b</sup>	O(48)···C(15) <sup>a</sup>	3.198(6)
O(16)···O(41) <sup>b</sup>	O(41)···O(16) <sup>a</sup>	3.237(6)
O(16)···C(42) <sup>b</sup>		3.314(8)
O(16)···O(48) <sup>c</sup>	O(48)···O(16) <sup>a</sup>	3.068(6)
O(17)···C(26) <sup>c</sup>	C(26)···O(17) <sup>f</sup>	3.492(7)
O(17)···C(34) <sup>c</sup>	C(34)···O(17) <sup>f</sup>	3.398(6)
O(17)···O(48) <sup>c</sup>	O(48)···O(17) <sup>a</sup>	2.571(6)
O(20)···C(43) <sup>d</sup>	C(43)···O(20) <sup>i</sup>	3.445(7)
O(20)···O(44) <sup>d</sup>	O(44)···O(20) <sup>i</sup>	3.388(6)
O(20)···O(45) <sup>d</sup>	O(45)···O(20) <sup>i</sup>	2.710(7)
C(21)···O(44) <sup>d</sup>		3.352(7)
C(23)···O(50) <sup>e</sup>	O(50)···C(23) <sup>m</sup>	3.455(5)
O(41)···O(48) <sup>h</sup>	O(48)···O(41) <sup>i</sup>	3.176(6)
O(41)···C(49) <sup>h</sup>	C(49)···O(41) <sup>i</sup>	3.421(6)
C(42)···C(53) <sup>g</sup>		3.314(8)
O(44)···C(52) <sup>g</sup>	C(52)···O(44) <sup>c</sup>	3.305(8)

Key to the symmetry operations relative to the reference molecule at *x*, *y*, *z*:

<i>a</i>	<i>x</i> – 1, <i>y</i> , <i>z</i> – 1	<i>g</i>	– <i>x</i> , <i>y</i> + $\frac{1}{2}$ , – <i>z</i>
<i>b</i>	<i>x</i> – 1, <i>y</i> – $\frac{1}{2}$ , – <i>z</i>	<i>h</i>	<i>x</i> – 1, <i>y</i> , <i>z</i>
<i>c</i>	1 – <i>x</i> , <i>y</i> – $\frac{1}{2}$ , – <i>z</i>	<i>i</i>	1 – <i>x</i> , <i>y</i> + $\frac{1}{2}$ , 1 – <i>z</i>
<i>d</i>	1 – <i>x</i> , <i>y</i> – $\frac{1}{2}$ , 1 – <i>z</i>	<i>l</i>	1 + <i>x</i> , <i>y</i> , <i>z</i>
<i>e</i>	<i>x</i> , <i>y</i> , 1 + <i>z</i>	<i>m</i>	<i>x</i> , <i>y</i> , <i>z</i> – 1
<i>f</i>	1 – <i>x</i> , <i>y</i> + $\frac{1}{2}$ , – <i>z</i>	<i>n</i>	1 + <i>x</i> , <i>y</i> , 1 + <i>z</i>

The range of bond distances and corresponding e.s.d.s for hydrogen atoms are 0.71–1.13 and 0.04–0.11 Å, respectively.

### Experimental

Crystals of (3*R*)-3-(3-methyl-7-phenoxyacetamido-3-cephem-4-yl)-3-hydroxybutanoic acid (6), m.p. 148–149 °C, were obtained by slow evaporation of a propan-2-ol–CH<sub>2</sub>Cl<sub>2</sub>–Pr<sub>2</sub>O solution.

C<sub>19</sub>H<sub>22</sub>N<sub>2</sub>O<sub>6</sub>S, *M* = 406.5. Monoclinic, *P*2<sub>1</sub>, *a* = 11.293(4), *b* = 20.211(4), *c* = 8.927(3) Å, β = 102.56(3)°, *V* = 1988.8(1.1)

$\text{\AA}^3$ ,  $Z = 4$ ,  $D_c = 1.538 \text{ g cm}^{-3}$ ,  $\lambda(\text{Cu-K}\alpha) = 1.54178 \text{ \AA}$ ,  $\mu(\text{Cu-K}\alpha) = 17.4 \text{ cm}^{-1}$ ,  $F(000) = 856$ .

A prismatic single crystal of approximate size  $0.28 \times 0.33 \times 0.38 \text{ mm}$  was used. The cell parameters and the matrix orientation were obtained from the setting angles of 20 selected high-angle reflections on an AED Siemens diffractometer on line to a General Automatic Jumbo 220 microcomputer.<sup>9</sup> 3790 Independent reflections were collected using the  $\theta$ - $2\theta$  step scan ( $5 < 2\theta < 140^\circ$ ) and the five-point method; one reflection in every 50 was monitored. Only 2803 reflections with  $I > 2\sigma(I)$  [ $\sigma(I)$  based on counting statistics] were considered as observed and used in the analysis; Lorentz and polarization but no absorption corrections were applied. The structure was solved by the direct method with MULTAN 80;<sup>3</sup> of the 56 non-hydrogen atoms in the two crystallographically independent molecules only 10 were not obtained from the  $E$  map calculated with the 500 largest  $E$  values ( $E > 1.4$ ) and the 50 smallest  $E$  values, using a temperature factor of 2.5, a  $\kappa$  value of 0.8, and a probability of 2 for acceptance of phase and sigma 1 relationship respectively. Subsequent calculations were performed with the SHELX-76 program system.<sup>10</sup>

All hydrogen atoms were located from the difference map and theoretical calculations.

In the block least-squares refinement of  $F$ , positional and anisotropic thermal parameters of non-hydrogen atoms were varied separately in subsequent cycles (one independent molecule in one block; 252 parameters); furthermore in the final cycles one block containing the hydrogen atoms (177 parameters) was refined isotropically. The final discrepancy values are  $R = 0.042$  and  $R_w = 0.045$   $\{w = [\sigma^2(F) + 0.007F^2]^{-1}\}$  for all 2803 observed reflections; the final difference electron density synthesis was essentially featureless.

Atomic scattering factors take into account the anomalous scattering effects following ref. 11.

All calculations were carried out on the GOULD-SEL 32/77 of the Centro di Studio per la Strutturistica Diffraattometrica del

CNR (Parma); geometrical calculations were performed with PARST<sup>5</sup> whereas the figures were drawn with PLUTO.<sup>12</sup>

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