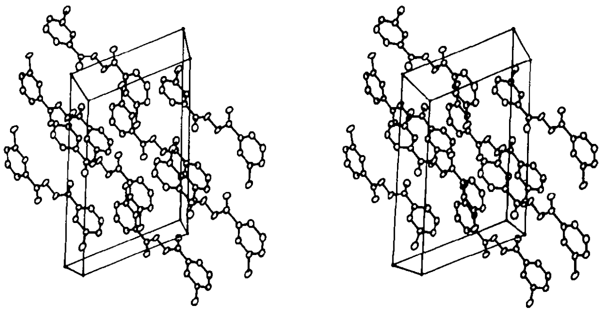

Fig. 2. Stereoview of the molecular packing in the unit cell along the *b* axis, with *c* axis approximately horizontal and *a* axis vertical.

Fig. 2 represents the stereopacking of the molecules. The shortest intermolecular contacts between non-hydrogen atoms are 3·279 (2) Å for Cl–O(2) and 3·285 (3) Å for O(2)–O(2). The molecules are held together by usual van der Waals forces to form parallel chains.

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Structure and Stereochemistry of 2-Methylthio-7-(*p*-bromophenyl)-8-phenoxy-4,5-benzo-3-aza-2-nonem,* $C_{24}H_{19}BrN_2O_2S$†

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Abstract. $M_r = 479·4$, monoclinic, $P2_1/n$, $a = 16·577\,(5)$, $b = 7·838\,(1)$, $c = 16·771\,(4)$ Å, $\beta = 95·66\,(2)°$, $V = 2168\,(3)$ Å^3, $Z = 4$, $D_x = 1·47$ Mg m^{-3}, Cu $K\alpha$, $\lambda = 1·5418$ Å, $\mu = 3·66$ mm^{-1}, $F(000) = 976$, $T = 293$ K, final $R = 0·043$ for 2451 reflections. The conformation of the molecule (RML-5) is governed by the steric and electrostatic interactions of the substituents. The diazepine ring adopts a boat conformation. The four-membered β-lactam ring is planar with phenyl substituents in the eclipsed conformation. Bond lengths and angles are normal.

Introduction. A great number of studies have been devoted to the search for structural analogues of cephalosporin and penicillin with specific activity (Guthikonda, Cama & Christensen, 1974; Bose, Ram, Hoffman, Hutchinson & Manhas, 1979; Itil, Saletu & Marasa, 1974). It appeared of interest to us to combine the two functionalities of cephalosporin and penicillin by preparing compounds in which the β-lactam moiety is integrated into the benzodiazepine system and to investigate their pharmacological profile. Synthesis of the title compound (1) was accomplished by cycloaddition of phenoxyacetyl chloride onto 2-*p*-bromophenyl)-4-methylthio-3*H*-1,5-benzodiazepine (Cortés & Martinez, 1983). The structure determination was undertaken to elucidate the stereochemistry of the product.

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* 2a-(*p*-Bromophenyl)-4-methylthio-2-phenoxy-1,2,2a,3-tetrahydroazeto[1,2-*a*][1,5]benzodiazepin-1-one.

† Contribution No. 678 of the Instituto de Química, UNAM.

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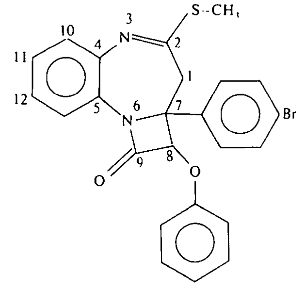

(1)

Experimental. RML-5 prepared and crystallized by Cortés & Martínez (1983). Prismatic crystal, 0·09 × 0·12 × 0·22 mm, Nicolet *R*3 four-circle diffractometer, lattice parameters from 25 machine-centred reflections with $10{\cdot}6 < 2\theta < 28{\cdot}7^\circ$, 2923 reflections with $3 < 2\theta < 115^\circ$, 2451 independent with $I > 2{\cdot}5\sigma(I)$, $R_{\text{int}} = 0{\cdot}0291$, index range *h* 0–±17, *k* 0–8, *l* 0–18, ω-scan mode, variable scan speed, scan width 1·0 (°θ), two standard reflections ($\bar{1}10$, $\bar{2}1\bar{1}$) monitored every 50 measurements, Lp correction, absorption ignored; structure solved by combination of direct methods and partial structure expansion by an iterative *E*–Fourier procedure using *SHELXTL* (Sheldrick, 1981); least-squares anisotropic refinement of all non-H atoms; H atoms riding on bonded C with fixed isotropic temperature factor, $U = 0{\cdot}06$ Å^2; function minimized $\sum w(\Delta F)^2$, $w = \{\sigma^2(F_o) + G(F_o)^2\}^{-1}$, where σ is standard deviation of observed amplitudes, based on counting statistics, *G* a variable adjusted after each cycle, final $G = 0{\cdot}00121$; isotropic extinction parameter $x = 0{\cdot}00161$; $(\Delta/\sigma)_{\max} < 0{\cdot}02$; $\Delta\rho$ −0·3 to +0·5 e Å^{-3}; final *R* 0·043, *wR* 0·056; scattering factors from *International Tables for X-ray Crystallography* (1974).

Discussion. The final atomic coordinates are listed in Table 1.* Fig. 1 shows the molecular conformation for one of the molecules of the racemate of the title compound, RML-5; bond distances and angles for the non-H atoms are given in Table 2. Calculations of the least-squares planes passing through the diazepine, benzo, four-membered β-lactam and the two phenyl rings, and the methylthio group, and the deviations of individual atoms from the planes and interplanar angles have been deposited.*

The molecule consists of a benzodiazepine ring with a methylthio group and a four-membered β-lactam ring with two phenyl substituents with different orientations. The three benzene rings and the four-membered ring are

Table 1. *Atomic coordinates* (×10^4) *and equivalent isotropic temperature factors* (Å^2 × 10^3)

$$U_{\text{eq}} = (U_{11}U_{22}U_{33})^{1/3}.$$

	x	*y*	*z*	U_{eq}
Br	−2097 (1)	3148 (1)	4622 (1)	73 (1)
S	−210 (1)	8695 (1)	2466 (1)	74 (1)
N(3)	626 (2)	6081 (4)	2024 (2)	50 (1)
N(6)	−448 (2)	3580 (4)	998 (2)	42 (1)
O(1)	−882 (2)	1866 (4)	−113 (2)	77 (1)
O(2)	−2369 (1)	3598 (3)	780 (1)	48 (1)
C(1)	−709 (2)	6625 (5)	1227 (2)	49 (1)
C(2)	−26 (2)	6916 (4)	1871 (2)	50 (1)
C(4)	873 (2)	4574 (5)	1647 (2)	43 (1)
C(5)	392 (2)	3367 (4)	1199 (2)	42 (1)
C(7)	−1034 (2)	4804 (4)	1279 (2)	42 (1)
C(8)	−1622 (2)	4225 (5)	554 (2)	45 (1)
C(9)	−965 (2)	2949 (5)	378 (2)	51 (1)
C(10)	1698 (2)	4223 (5)	1793 (2)	54 (1)
C(11)	2042 (2)	2761 (6)	1517 (3)	59 (1)
C(12)	1558 (2)	1569 (5)	1106 (2)	55 (1)
C(13)	741 (2)	1866 (5)	948 (2)	49 (1)
C(14)	−1295 (2)	4381 (4)	2098 (2)	37 (1)
C(15)	−980 (2)	2993 (5)	2531 (2)	48 (1)
C(16)	−1219 (2)	2620 (5)	3278 (2)	53 (1)
C(17)	−1783 (2)	3633 (5)	3592 (2)	45 (1)
C(18)	−2120 (2)	4993 (5)	3164 (2)	55 (1)
C(19)	−1876 (2)	5357 (5)	2421 (2)	50 (1)
C(20)	−2951 (2)	3062 (5)	185 (2)	48 (1)
C(21)	−3709 (2)	2812 (5)	426 (3)	61 (2)
C(22)	−4318 (3)	2158 (7)	−111 (4)	79 (2)
C(23)	−4163 (3)	1752 (7)	−877 (4)	88 (2)
C(24)	−3411 (3)	2028 (6)	−1113 (3)	77 (2)
C(25)	−2794 (3)	2684 (5)	−584 (2)	58 (1)
C(26)	674 (3)	8790 (8)	3153 (4)	118 (3)

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

Br–C(17)	1·891 (4)	S–C(2)	1·760 (4)
S–C(26)	1·774 (6)	N(3)–C(2)	1·266 (5)
N(3)–C(4)	1·419 (5)	N(6)–C(5)	1·410 (4)
N(6)–C(7)	1·475 (4)	N(6)–C(9)	1·371 (4)
O(1)–C(9)	1·200 (5)	O(2)–C(8)	1·417 (4)
O(2)–C(20)	1·384 (4)	C(1)–C(2)	1·503 (5)
C(1)–C(7)	1·531 (5)	C(4)–C(5)	1·406 (5)
C(4)–C(10)	1·392 (5)	C(5)–C(13)	1·394 (5)
C(7)–C(8)	1·550 (5)	C(7)–C(14)	1·516 (5)
C(8)–C(9)	1·529 (5)	C(10)–C(11)	1·380 (6)
C(11)–C(12)	1·371 (6)	C(12)–C(13)	1·374 (5)
C(14)–C(15)	1·381 (5)	C(14)–C(19)	1·381 (5)
C(15)–C(16)	1·382 (6)	C(16)–C(17)	1·371 (5)
C(17)–C(18)	1·373 (5)	C(18)–C(19)	1·378 (5)
C(20)–C(21)	1·370 (6)	C(20)–C(25)	1·374 (5)
C(21)–C(22)	1·383 (6)	C(22)–C(23)	1·373 (8)
C(23)–C(24)	1·362 (8)	C(24)–C(25)	1·384 (6)
C(2)–S–C(26)	102·8 (2)	C(2)–N(3)–C(4)	128·2 (3)
C(5)–N(6)–C(7)	131·7 (3)	C(5)–N(6)–C(9)	131·9 (3)
C(7)–N(6)–C(9)	95·5 (3)	C(8)–O(2)–C(20)	118·5 (3)
C(2)–C(1)–C(7)	110·2 (3)	S–C(2)–N(3)	119·1 (3)
S–C(2)–C(1)	111·5 (3)	N(3)–C(2)–C(1)	129·3 (3)
N(3)–C(4)–C(5)	128·6 (3)	N(3)–C(4)–C(10)	114·1 (3)
C(5)–C(4)–C(10)	117·1 (3)	N(6)–C(5)–C(4)	122·9 (3)
N(6)–C(5)–C(13)	117·1 (3)	C(4)–C(5)–C(13)	119·9 (3)
N(6)–C(7)–C(1)	110·0 (3)	N(6)–C(7)–C(8)	86·6 (2)
C(1)–C(7)–C(8)	115·2 (3)	N(6)–C(7)–C(14)	113·8 (3)
C(1)–C(7)–C(14)	112·9 (3)	C(8)–C(7)–C(14)	115·7 (3)
O(2)–C(8)–C(7)	112·9 (3)	O(2)–C(8)–C(9)	118·8 (3)
C(7)–C(8)–C(9)	86·4 (3)	N(6)–C(9)–O(1)	132·0 (4)
N(6)–C(9)–C(8)	91·3 (3)	O(1)–C(9)–C(8)	136·6 (3)
C(4)–C(10)–C(11)	122·4 (4)	C(10)–C(11)–C(12)	119·6 (4)
C(11)–C(12)–C(13)	119·9 (4)	C(5)–C(13)–C(12)	121·0 (3)
C(7)–C(14)–C(15)	121·4 (3)	C(7)–C(14)–C(19)	120·5 (3)
C(15)–C(14)–C(19)	118·1 (3)	C(14)–C(15)–C(16)	121·1 (3)
C(15)–C(16)–C(17)	119·5 (4)	Br–C(17)–C(16)	119·6 (3)
Br–C(17)–C(18)	119·9 (3)	C(16)–C(17)–C(18)	120·4 (3)
C(17)–C(18)–C(19)	119·5 (4)	C(14)–C(19)–C(18)	121·3 (3)
O(2)–C(20)–C(21)	115·1 (3)	O(2)–C(20)–C(25)	124·0 (3)
C(21)–C(20)–C(25)	120·7 (4)	C(20)–C(21)–C(22)	119·4 (4)
C(21)–C(22)–C(23)	120·3 (5)	C(22)–C(23)–C(24)	119·8 (5)
C(23)–C(24)–C(25)	120·8 (5)	C(20)–C(25)–C(24)	119·0 (4)

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* Lists of structure amplitudes, anisotropic thermal parameters, H-atom coordinates, the results of mean-plane calculations and selected intra- and intermolecular distances have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39413 (20 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

planar to a good approximation. The diazepine ring deviates considerably from planarity – maximum deviations from the plane are 0·428 (4) and −0·367 (4) Å for C(1) and C(7), respectively – adopting a boat conformation with C(1) as the bow and C(4) and C(5) forming the stern as in the case of 7-chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepin-3-ol (Chananont, Hamor & Martin, 1980). The angle between the mean planes of phenyl rings C(5)–C(4)–C(10)–C(11)–C(12)–C(13) and C(14) through C(19) is 85·9 (4)°. Similar interplanar angles occur in clonazepam (Chananont, Hamor & Martin, 1979), where the halogen substituent is in the *ortho* position, with values of 83·7 and 77·8° for the two independent molecules.

There is no conjugation between the seven-membered diazepine ring and the phenyl substituent at C(7). Owing to steric inhibition, caused by the neighbouring O(2) of the phenoxy ring and the S atom of the methylthio substituent at C(2), the *p*-bromophenyl ring is rotated by an angle of 85·4 (4)° from the mean plane of the diazepine ring. The planes formed by the atoms of the methylthio substituent and the *p*-bromophenyl ring are almost parallel to each other; the dihedral angle is 7·4 (4)°.

The four-membered ring with surrounding substituents is clearly shown in Fig. 1. The substituents at C(7) and C(8) are synperiplanar to one another, whereas the substituents at C(8) and C(9) are in synclinal conformation. The torsion angles C(14)–C(7)–C(8)–O(2) and O(2)–C(8)–C(9)–O(1) are 8·3 (4) and 65·5 (6)°, respectively.

The Br atom lies in the plane of the phenyl ring [deviation 0·053 (4) Å]. The Br–C_{ar} bond length, 1·891 (4) Å, compares well with the value of 1·87 Å cited for a C_{ar}–Br bond by Sutton (1965), and the corresponding endocyclic angle is 120·4 (3)°.

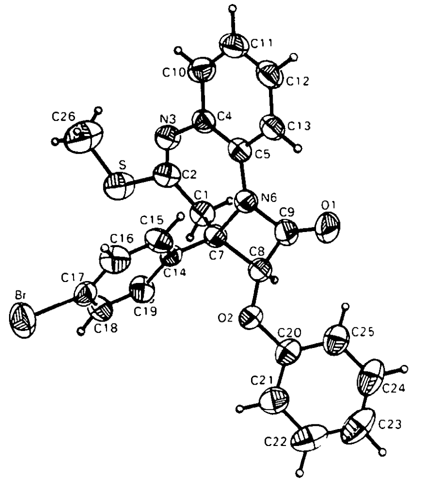

Fig. 1. The molecular conformation of RML-5, showing atom numbering. The thermal ellipsoids are drawn at the 50% probability level.

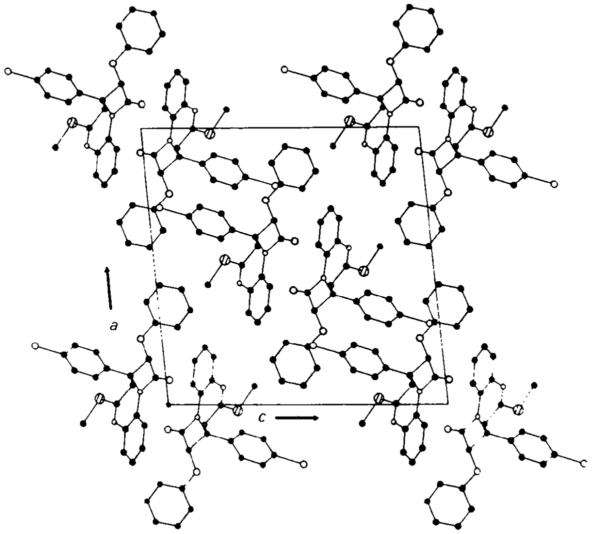

Fig. 2. Packing arrangement of the RML-5 molecules as viewed along **b**.

The arrangement of the molecules in the unit cell is shown in Fig. 2. Selected intra- and intermolecular distances have been deposited.* They compare well with the sum of the van der Waals radii of the given atoms (Bondi, 1964).

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* See deposition footnote.

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