

*Les chaînes latérales*

Les longueurs de liaison et angles valentiels des groupes carboxylate d'éthyle sont identiques dans les trois composés. Il est intéressant de remarquer que ces deux motifs en principe mobiles autour des carbones C(4a) ou C(5a) adoptent la même orientation dans les trois dérivés d'empilements moléculaires différents.

L'examen des distances entre l'atome d'oxygène O(1) et les protons H1(C4) et HC(3b) [dérivé (2)], 2,74 (8) et 2,36 (8) Å et entre l'oxygène O(4) et les protons H1C(6) et HC(6a), 2,70 (7) et 2,63 (8) Å, montre que les atomes d'oxygène O(1) et O(4) sont bloqués. La rotation des chaînes latérales est ainsi inhibée. Le plan de la chaîne contenant O(1) et O(2) forme de ce fait un angle de 83,0 (7)° avec le cycle à trois chaînons C(3b), C(3a) et C(4) et la chaîne contenant O(4) et O(5) un angle de 92,9 (8)° avec le motif cyclopropanique C(5a), C(6a) et C(6). Chaque chaîne latérale est donc sensiblement perpendiculaire à l'un des cycles à trois chaînons. La disposition relative des groupes carboxylates d'éthyle et des motifs cyclopropanique, vis à vis du cycle à sept chaînons n'est donc pas indépendante.

Des études spectroscopiques (RMN et IR) n'ont pas permis de préciser l'origine de cet empêchement. La morphologie des spectres de RMN (<sup>1</sup>H et <sup>13</sup>C) n'est pas modifiée par variation de température et les spectres IR

(phases solide et liquide) à diverses concentrations ne présentent pas une évolution significative.

**Conclusion**

L'ensemble des données précédentes montre à l'évidence une profonde rigidité moléculaire dans les trois dérivés étudiés. En effet, l'orientation des chaînes latérales, la disposition relative du motif cyclopropanique et du cycle à sept chaînons sont étroitement liées. Cet état conformationnel privilégié se retrouve quelque soit l'empilement moléculaire dans l'édifice cristallin.

**Références**

- BUSING, W. R., MARTIN, K. O., LEVY, H. A., ELLISON, R. D., HAMILTON, W. C., IBERS, J. A., JOHNSON, C. K. & THIESSEN, W. E. (1971). *ORXFLS3*. Oak Ridge National Laboratory, Tennessee.
- GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* **A27**, 368–376.
- HANQUET, B. & GUILARD, R. (1978). *C.R. Acad. Sci.* **287**, 515.
- HANQUET, B., GUILARD, R. & FOURNARI, P. (1977). *Bull. Soc. Chim. Fr.* pp. 571–577.
- SUGIMURA, Y., SOMA, N. & KISHIDA, Y. (1967). *Tetrahedron Lett.* pp. 241–244.

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## The Structures of 7-Chloro-5-(2-chlorophenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one and 7-Chloro-5-(2-chlorophenyl)-1,3-dihydro-1-methyl-2H-1,4-benzodiazepin-2-one

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**Abstract**

The structures of 7-chloro-5-(2-chlorophenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one (I) and of the 1-methyl derivative (II) have been refined to  $R = 0.065$  (I) for 713 amplitudes [ $I > 3.5\sigma(I)$ ] and  $R = 0.049$

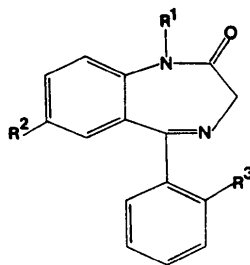
(II) for 2612 amplitudes [ $I > 2.5\sigma(I)$ ]. (I),  $C_{15}H_{10}Cl_2N_2O$ ,  $M_r = 305.2$ , is monoclinic, space group  $P2_1/c$ , with  $a = 12.23$  (1),  $b = 9.87$  (1),  $c = 15.29$  (1) Å,  $\beta = 127.37$  (5)°,  $U = 1467$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.382$  Mg m<sup>-3</sup>,  $F(000) = 624$ ,  $\mu(\text{Mo } K\alpha) = 0.386$  mm<sup>-1</sup>. (II),  $C_{16}H_{12}Cl_2N_2O$ ,  $M_r = 319.2$ , is orthorhombic, space group  $Pbca$ , with  $a = 10.70$  (1),  $b = 26.26$  (2),  $c = 10.52$  (1) Å,  $U = 2956$  Å<sup>3</sup>,  $Z = 8$ ,  $D_c = 1.434$  Mg m<sup>-3</sup>,  $F(000) = 1312$ ,  $\mu(\text{Mo } K\alpha) = 0.384$  mm<sup>-1</sup>. E.s.d.'s average 0.02 Å (I) and 0.005 Å (II) for bond lengths

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and  $1^\circ$  (I) and  $0.3^\circ$  (II) for bond angles. The angle between the 5-phenyl ring and the phenyl moiety of the 1,4-benzodiazepine system is  $80(2)^\circ$  in (I) and  $85.7(4)^\circ$  in (II). The overall geometries of the 1,4-benzodiazepine residues of (I) and (II) are similar. However, small but significant differences in the ring bond angle at N(1) and in the conformations about the ring bonds involving N(1) occur.

### Introduction

The title compounds (I) and (II) exhibit to a marked degree the muscle relaxant, anticonvulsant and anxiolytic effects typical of many 5-phenyl-1,4-benzodiazepines. They have anticonvulsant and muscle-relaxant activities similar to the closely related diazepam (III),\* but are 10–20 times more potent in their anti-anxiety efficacies (Randall, Schallek, Sternbach & Ning, 1974). As part of a study of structure–activity relationships for this class of compound, we report the crystal structures of (I) and (II) to provide a comparison with diazepam (Camerman & Camerman, 1972) and other related compounds.



- (I)  $R^1 = H, R^2 = Cl, R^3 = Cl$   
 (II)  $R^1 = Me, R^2 = Cl, R^3 = Cl$   
 (III)  $R^1 = Me, R^2 = Cl, R^3 = H$   
 (IV)  $R^1 = H, R^2 = NO_2, R^3 = Cl$

### Experimental

After initial examination by photographic methods, final cell dimensions and intensities were measured on a Stoe STADI-2 two-circle diffractometer with graphite-monochromated  $Mo K\alpha$  radiation and a scintillation counter. The  $\omega$ -scan technique was employed with a variable scan range for the upper layers (equi-inclination angle  $>5^\circ$ ) calculated from  $\Delta\omega = A + (B \sin \mu / \tan \theta')$  where  $\mu$  is the equi-inclination angle and  $2\theta'$  the azimuth angle. The intensities of four zero-layer

Table 1. *Experimental parameters*

	(I)	(II)
Crystal size (mm)	$0.1 \times 0.1 \times 0.05$	$0.2 \times 0.2 \times 0.05$
Scan speed ( $^\circ \text{ min}^{-1}$ )	0.6	0.8
Background count time (s)	30	20
Scan range:		
(a) lower layers ( $^\circ$ )	3.8	1.4
(b) upper layers (see text)	$A = 2.7, B = 1.35$	$A = 1.0, B = 0.5$
$\sin \theta / \lambda$ range ( $\text{\AA}^{-1}$ )	0.1–0.54	0.1–0.65
Significant reflexions		
$I > n\sigma(I)$	713 ( $n = 3.5$ )	2612 ( $n = 2.5$ )

reflexions were remeasured periodically; there was no significant variation in their intensities. Only relatively poor data could be obtained for (I). Reflexion occurred over a considerable range of angle, and intensities fell off rapidly with increasing Bragg angle. Details of the experimental procedure are shown in Table 1. Crystal data are shown in the *Abstract*. The space groups  $P2_1/c$  (I) and  $Pbca$  (II) were assigned from the systematic absences  $h0l, l$  odd;  $0k0, k$  odd, and  $0kl, k$  odd;  $h0l, l$  odd;  $hk0, h$  odd respectively.

### Determination of the structure

Both structures were solved by direct methods with *SHELX* (Sheldrick, 1978) and refined by least squares, first with isotropic temperature factors and finally anisotropically. For (I), H atoms, except for H[N(1)], were included in the calculations in theoretical positions but their coordinates were not refined. H[N(1)] was located from a difference synthesis and its coordinates and isotropic temperature factor refined to define the disposition of bonds from N(1). One overall isotropic temperature factor for all the other H atoms refined to  $U = 0.067 \text{ \AA}^2$ . For (II), all H atoms were located from a difference synthesis but their coordinates were not refined. One overall isotropic temperature factor for the H atoms refined to  $U = 0.061 \text{ \AA}^2$ . The reflexion 060 which appeared to be affected by extinction was omitted from the final cycles.

Refinement was terminated when all calculated shifts were  $<0.1\sigma$ , and  $R$  was 0.065 and 0.049 for (I) and (II), respectively. Difference syntheses computed at this stage showed no significant features. Final atomic coordinates are in Table 2.\* The weighting scheme was  $w = 1/[\sigma^2(F)]$  where  $\sigma(F)$  is the standard deviation in the observed amplitudes based on counting statistics.

\* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35991 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. Equivalent isotropic temperature factors  $U_{eq}$  calculated from the anisotropic values by the method of Willis & Pryor (1975) are given in Table 2.

\* Marketed as Valium (Roche).

Table 2. Fractional atomic coordinates ( $\times 10^4$ ) with e.s.d.'s in parentheses and equivalent isotropic temperature factors ( $\text{\AA}^2 \times 10^3$ )

	(I)				(II)			
	x	y	z	$U_{eq}$	x	y	z	$U_{eq}$
Cl(7)	-1454 (3)	3494 (4)	4042 (3)	81	-8053 (1)	-1031 (0)	1534 (1)	56
Cl(2')	2728 (4)	6202 (4)	4323 (4)	87	-3480 (1)	-2132 (0)	158 (1)	58
N(1)	425 (14)	4357 (14)	1320 (12)	60	-3081 (3)	-685 (1)	-807 (3)	38
N(4)	2836 (10)	2708 (10)	3062 (11)	56	-4235 (3)	-1292 (1)	-2889 (3)	40
O(2)	1495 (8)	3925 (8)	557 (7)	65	-1938 (2)	-427 (1)	-2501 (2)	52
C(2)	1276 (13)	3620 (14)	1232 (11)	50	-2916 (3)	-601 (1)	-2083 (3)	37
C(3)	1833 (15)	2341 (13)	1892 (12)	59	-3997 (3)	-741 (1)	-2934 (3)	39
C(5)	2364 (14)	3258 (12)	3541 (12)	53	-4739 (3)	-1466 (1)	-1875 (3)	35
C(6)	428 (12)	3359 (11)	3654 (10)	45	-6243 (3)	-1229 (1)	-184 (3)	35
C(7)	-923 (15)	3681 (13)	3208 (13)	54	-6582 (3)	-943 (1)	853 (3)	36
C(8)	-1807 (15)	4243 (12)	2183 (14)	62	-5777 (3)	-591 (1)	1381 (3)	39
C(9)	-1359 (15)	4430 (13)	1555 (12)	55	-4627 (3)	-512 (1)	824 (3)	38
C(10)	-26 (14)	4077 (11)	1936 (11)	46	-4274 (3)	-780 (1)	-254 (3)	33
C(11)	858 (15)	3549 (12)	2998 (13)	54	-5079 (3)	-1152 (1)	-756 (3)	32
*R <sup>1</sup>	72 (113)	4862 (108)	955 (94)	†	-2030 (4)	-562 (2)	42 (4)	61
C(1')	3386 (14)	3516 (18)	4734 (12)	55	-5075 (3)	-2022 (1)	-1831 (3)	36
C(2')	3558 (17)	4823 (19)	5113 (16)	61	-4580 (3)	-2347 (1)	-940 (3)	41
C(3')	4538 (24)	5118 (18)	6227 (26)	90	-4891 (4)	-2862 (1)	-914 (4)	52
C(4')	5279 (20)	4085 (30)	6964 (18)	98	-5744 (4)	-3042 (1)	-1804 (4)	58
C(5')	5104 (19)	2767 (28)	6600 (20)	99	-6242 (4)	-2727 (2)	-2677 (4)	56
C(6')	4177 (17)	2449 (19)	5499 (19)	77	-5923 (4)	-2209 (1)	-2704 (3)	46
H <sup>1</sup> (3)	2322	1739	1629		-3650	-660	-3792	
H <sup>2</sup> (3)	1002	1770	1778		-4720	-545	-2675	
H(6)	1131	2969	4481		-6830	-1498	-476	
H(8)	-2833	4541	1878		-6001	-403	2117	
H(9)	-2061	4853	739		-4010	-276	1200	
H(3')	4702	6153	6511		-4494	-3092	-225	
H(4')	6020	4322	7827		-5977	-3430	-1803	
H(5')	5702	1982	7205		-6866	-2888	-3250	
H(6)	4064	1413	5227		-6405	-1987	-3272	
H <sup>1</sup> (12)					-1270	-670	-349	
H <sup>2</sup> (12)					-2046	-766	862	
H <sup>3</sup> (12)					-1928	-131	7	

\* R<sup>1</sup> is H[N(1)] in (I) and C(12) in (II).† Isotropic temperature factor refined to 0.021 (41)  $\text{\AA}^2$ .

Computations were carried out on the Birmingham University ICL 1906A computer and on the CDC 7600 at the University of Manchester Regional Computer Centre, mainly with *SHELX*.

### Results and discussion

Fig. 1 shows stereoscopic views of (I) and (II), and the atom numbering. Molecular dimensions are in Table 3 and the results of mean-plane calculations in Table 4.

Bond lengths and angles generally agree well with values found in analogous molecules (Camerman & Camerman, 1972; Chananont, Hamor & Martin, 1979). As was noted previously, the N(1)–C(2) single bond [length 1.34 (2)  $\text{\AA}$  in (I), 1.371 (4)  $\text{\AA}$  in (II)] is shortened and the C(2)–O(2) carbonyl bond [length 1.25 (1)  $\text{\AA}$  in (I), 1.225 (4)  $\text{\AA}$  in (II)] is slightly

lengthened in comparison with standard values, indicative of electron delocalization. The disposition of bonds at N(1) is near planar in both molecules and the geometry of the N(1)–C(2) bond resembles that of a normal double bond [*cf.* torsion angles in Table 3(*d*)]. The ring angle at N(1) is, however, 5° greater in (I) than in (II), 128 (1)° compared with 122.9 (3)°. This difference is probably significant and parallels a somewhat smaller difference of 3½° between the angles at N(1) in clonazepam (IV) (Chananont, Hamor & Martin, 1979) and diazepam (III) (Camerman & Camerman, 1972). It appears, therefore, that substitution of the H atom linked to N(1) by a methyl group causes a decrease in the C(10)–N(1)–C(2) angle of some 3–5°. The N(4)–C(5) length, 1.30 (1)  $\text{\AA}$  in (I), 1.280 (4)  $\text{\AA}$  in (II), is in good agreement with accepted values for the length of a C=N double bond. C(5)–C(11), 1.52 (2)  $\text{\AA}$  in (I), 1.483 (4)  $\text{\AA}$  in (II), and C(1')–C(5) 1.48 (2)  $\text{\AA}$  in (I), 1.505 (4)  $\text{\AA}$  in (II), do

not differ significantly from the accepted range (1.48–1.50 Å) for the length of a C(sp<sup>2</sup>)–C(sp<sup>2</sup>) single bond.

The overall conformations of (I) and (II) are quite similar. The angles between the mean planes of phenyl

Table 3. *Molecular dimensions*

## (a) Bond lengths (Å)

	(I)	(II)
N(1)–C(2)	1.34 (2)	1.371 (4)
C(2)–O(2)	1.25 (1)	1.225 (4)
C(2)–C(3)	1.50 (2)	1.507 (5)
C(3)–N(4)	1.47 (2)	1.469 (4)
N(4)–C(5)	1.30 (1)	1.280 (4)
C(5)–C(11)	1.52 (2)	1.483 (4)
C(6)–C(11)	1.40 (2)	1.399 (4)
C(6)–C(7)	1.39 (1)	1.372 (4)
C(7)–Cl(7)	1.76 (1)	1.744 (3)
C(7)–C(8)	1.37 (2)	1.381 (4)
C(8)–C(9)	1.38 (2)	1.378 (5)
C(9)–C(10)	1.40 (2)	1.387 (4)
C(10)–N(1)	1.38 (2)	1.425 (4)
C(10)–C(11)	1.39 (2)	1.404 (4)
*R <sup>1</sup> –N(1)	0.67 (10)	1.472 (4)
C(1')–C(5)	1.48 (2)	1.505 (4)
C(1')–C(2')	1.38 (2)	1.374 (5)
C(2')–Cl(2')	1.69 (2)	1.743 (4)
C(2')–C(3')	1.40 (2)	1.393 (5)
C(3')–C(4')	1.37 (2)	1.390 (6)
C(4')–C(5')	1.38 (2)	1.346 (6)
C(5')–C(6')	1.38 (2)	1.403 (5)
C(6')–C(1')	1.43 (2)	1.381 (5)

## (b) Bond angles (°)

	(I)	(II)
C(10)–N(1)–C(2)	128 (1)	122.9 (3)
*R <sup>1</sup> –N(1)–C(2)	118 (11)	117.4 (3)
*R <sup>1</sup> –N(1)–C(10)	113 (11)	118.3 (3)
N(1)–C(2)–O(2)	121 (1)	121.5 (3)
N(1)–C(2)–C(3)	117 (1)	116.3 (3)
O(2)–C(2)–C(3)	121 (1)	122.2 (3)
C(2)–C(3)–N(4)	108 (1)	110.7 (3)
C(3)–N(4)–C(5)	117 (1)	116.8 (3)
N(4)–C(5)–C(11)	125 (1)	124.6 (3)
N(4)–C(5)–C(1')	116 (1)	118.2 (3)
C(11)–C(5)–C(1')	119 (1)	117.2 (3)
C(11)–C(6)–C(7)	118 (1)	119.9 (3)
C(6)–C(7)–Cl(7)	118 (1)	119.5 (3)
C(6)–C(7)–C(8)	122 (1)	121.4 (3)
Cl(7)–C(7)–C(8)	119 (1)	119.1 (2)
C(7)–C(8)–C(9)	119 (1)	119.1 (3)
C(8)–C(9)–C(10)	122 (1)	120.9 (3)
C(9)–C(10)–C(11)	118 (1)	119.6 (3)
C(9)–C(10)–N(1)	121 (1)	119.3 (3)
C(11)–C(10)–N(1)	121 (1)	121.1 (3)
C(10)–C(11)–C(5)	122 (1)	122.3 (3)
C(5)–C(11)–C(6)	116 (1)	118.6 (3)
C(6)–C(11)–C(10)	121 (1)	119.0 (3)
C(5)–C(1')–C(2')	119 (2)	122.1 (3)
C(5)–C(1')–C(6')	122 (2)	118.8 (3)
C(6')–C(1')–C(2')	119 (1)	119.1 (3)
C(1')–C(2')–Cl(2')	126 (1)	120.8 (3)
Cl(2')–C(2')–C(3')	114 (2)	117.5 (3)
C(1')–C(2')–C(3')	120 (2)	121.6 (3)
C(2')–C(3')–C(4')	120 (2)	118.3 (4)
C(3')–C(4')–C(5')	120 (2)	120.7 (3)
C(4')–C(5')–C(6')	121 (2)	120.9 (4)
C(5')–C(6')–C(1')	119 (2)	119.4 (4)

Table 3 (cont.)

(c) Selected non-bonded distances (Å); e.s.d.'s are ca 0.02 Å in (I) and 0.005 Å in (II). *A* is the centre of phenyl ring C(6)–(11); *B* is the centre of phenyl ring C(1')–(6').

	(I)	(II)	(I)	(II)
Cl(7)···N(1)	5.91	5.93	N(4)··· <i>A</i>	3.83 3.77
Cl(7)···N(4)	6.32	6.23	N(4)··· <i>B</i>	3.64 3.67
Cl(7)···O(2)	8.06	7.96	O(2)··· <i>A</i>	4.95 4.90
N(4)···O(2)	3.34	3.37	O(2)··· <i>B</i>	6.60 6.70
Cl(7)··· <i>B</i>	5.84	6.00	<i>A</i> ··· <i>B</i>	4.89 4.91
N(1)··· <i>B</i>	5.57	5.56		

(d) Selected torsion angles (°). E.s.d.'s average 2.5° (I) and 0.5° (II). E.s.d.'s involving H[N(1)] are ca 15°.

	(I)	(II)
C(10)–N(1)–C(2)–C(3)	–1	–14.8
N(1)–C(2)–C(3)–N(4)	–71	–63.9
C(2)–C(3)–N(4)–C(5)	70	73.0
C(3)–N(4)–C(5)–C(11)	0	–0.7
N(4)–C(5)–C(11)–C(10)	–42	–44.5
C(5)–C(11)–C(10)–N(1)	0	0.3
C(11)–C(10)–N(1)–C(2)	41	50.4
N(4)–C(5)–C(1')–C(2')	122	120.3
C(11)–C(5)–C(1')–C(2')	–63	–62.8
C(9)–C(10)–N(1)–C(2)	–145	–131.7
C(6)–C(11)–C(5)–N(4)	143	135.4
N(4)–C(3)–C(2)–O(2)	115	115.3
*R <sup>1</sup> –N(1)–C(2)–C(3)	–168	178.7
*R <sup>1</sup> –N(1)–C(2)–O(2)	6	–0.5
*R <sup>1</sup> –N(1)–C(10)–C(11)	–152	–143.3

\* R<sup>1</sup> denotes H[N(1)] in (I) and C(12) in (II).

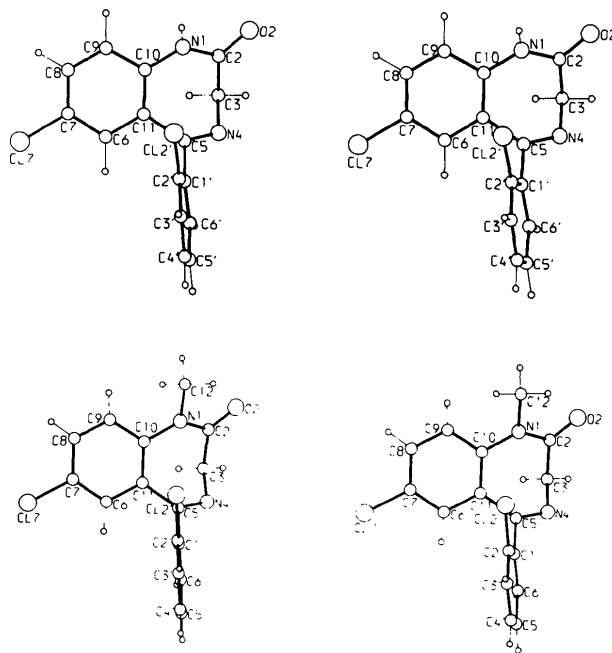


Fig. 1. The molecules (I) and (II) viewed in a direction perpendicular to the mean plane through C(5)–(11),N(1). Upper diagram molecule (I), lower diagram molecule (II).

Table 4. Mean-plane calculations

(a) Deviations of atoms from planes ( $\text{\AA} \times 100$ ). Distances marked with an asterisk refer to atoms defining the plane. E.s.d.'s are *ca* 0.02  $\text{\AA}$  for (I) and 0.006  $\text{\AA}$  for (II).

Plane	(1)		(2)		(3)		(4)	(5)	
Compound	(I)	(II)	(I)	(II)	(I)	(II)	(I) & (II)	(I)	(II)
N(1)	7	-2			-1*	3*		0*	0*
$\dagger R^1$	36	73							
C(2)	-52	-90			1*	-4*	0*		
O(2)	-46	106							
C(3)	-138	-164			-74	-71	0*		
N(4)	-50	-70	101	-99	-1*	4*	0*		
C(5)	12	4	-1	1	1*	-3*		0*	0*
C(6)	1*	1*							
C(7)	2*	-2*							
C(8)	1*	1*							
C(9)	1*	1*							
C(10)	-1*	-2*			-65	-75		0*	0*
C(11)	0*	1*	119	117	-68	-80		0*	0*
Cl(7)	5	-6							
C(1')	91	94	1*	-1*					
C(2')	226	230	2*	1*					
C(3')	305	313	-2*	0*					
C(4')	247	255	1*	0*					
C(5')	112	121	1*	0*					
C(6')	32	38	1*	0*					
Cl(2')	312	306	0	-4					

(b) Interplanar angles ( $^\circ$ )

	(I)	(II)
Plane (1)–plane (2)	80 (2)	85.7 (4)
Plane (3)–plane (4)	59 (2)	57.5 (5)
Plane (3)–plane (5)	33 (2)	38.8 (5)

$\dagger R^1 = \text{H}[\text{N}(1)] \text{ (I) or C}(2) \text{ (II)}.$

rings C(6)–(11) and C(1')–(6') are  $80 (2)^\circ$  in (I) and  $85.7 (4)^\circ$  in (II), typical of the interplanar angles in 5-phenyl-1,4-benzodiazepines where the 5-phenyl ring carries an *o*-chloro substituent (Chananont, Hamor & Martin, 1980). The seven-membered ring is in the expected boat conformation with C(10) and C(11) forming the stern and C(3) the bow (Table 4, planes 3–5).

Small, but significant differences do, however, occur in the conformations about C(10)–N(1) and N(1)–C(2). Torsion angles C(9)–C(10)–N(1)–C(2) and C(11)–C(10)–N(1)–C(2) are respectively  $-145$  and  $41^\circ$  in (I), compared with  $-132$  and  $50^\circ$  in (II), and C(10)–N(1)–C(2)–C(3) is  $-1^\circ$  in (I) compared with  $-15^\circ$  in (II). With respect to these torsion angles, clonazepam (IV) closely resembles (I), and diazepam (III) closely resembles (II). Hence the greater degree of twist in (II) and (III) can probably be attributed to the presence of the larger methyl substituent at N(1) in these compounds.

Intermolecular contact distances are listed in Table 5. In the crystal structure of (I), molecules related by the centre of symmetry at  $(0, \frac{1}{2}, 0)$  are linked by hydrogen bonds N(1)–H[N(1)] $\cdots$ O(2). The H atom lies close to the N(1) $\cdots$ O(2) line, the angle H[N(1)]–N(1) $\cdots$ O(2) being  $11^\circ$ . Other contact distances in this

Table 5. Intermolecular contacts ( $\text{\AA}$ )

Distances involving only C, N and O atoms are listed up to 3.5  $\text{\AA}$  and those involving Cl up to 3.7  $\text{\AA}$ . H atom contacts are not included.

Structure (I); e.s.d.'s are *ca* 0.03  $\text{\AA}$

N(1) $\cdots$ O(2')	2.91	Cl(2') $\cdots$ C(9 <sup>III</sup> )	3.47
O(2) $\cdots$ C(6 <sup>II</sup> )	3.26	Cl(2') $\cdots$ C(8 <sup>III</sup> )	3.53
C(8) $\cdots$ C(3 <sup>III</sup> )	3.38	C(2) $\cdots$ Cl(7 <sup>II</sup> )	3.63
C(3') $\cdots$ N(4 <sup>IV</sup> )	3.45	Cl(2') $\cdots$ Cl(7 <sup>V</sup> )	3.67

Superscripts refer to the following equivalent positions:

(i)	$-x, 1-y, -z$	(iv)	$1-x, 1-y, 1-z$
(ii)	$x, \frac{1}{2}-y, -\frac{1}{2}+z$	(v)	$-x, 1-y, 1-z$
(iii)	$-x, \frac{1}{2}+y, \frac{1}{2}-z$		

Structure (II); e.s.d.'s are *ca* 0.007  $\text{\AA}$

O(2) $\cdots$ C(3')	3.29	O(2) $\cdots$ C(9 <sup>IV</sup> )	3.46
C(9) $\cdots$ C(9 <sup>II</sup> )	3.30	C(9) $\cdots$ Cl(7 <sup>V</sup> )	3.52
O(2) $\cdots$ C(6')	3.31	Cl(7) $\cdots$ C(3 <sup>III</sup> )	3.57
O(2) $\cdots$ C(11')	3.31	C(5') $\cdots$ Cl(2 <sup>III</sup> )	3.59
C(4') $\cdots$ Cl(2 <sup>III</sup> )	3.43		

Superscripts refer to the following equivalent positions:

(i)	$\frac{1}{2}+x, y, -\frac{1}{2}-z$	(iv)	$-\frac{1}{2}-x, -y, -\frac{1}{2}+z$
(ii)	$-1-x, -y, -z$	(v)	$\frac{1}{2}+x, y, \frac{1}{2}-z$
(iii)	$-\frac{1}{2}+x, -\frac{1}{2}-y, -z$		

structure, and those in (II), correspond to normal van der Waals interactions.

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## References

- CAMERMAN, A. & CAMERMAN, N. (1972). *J. Am. Chem. Soc.* **94**, 268–272.
- CHANANONT, P., HAMOR, T. A. & MARTIN, I. L. (1979). *Cryst. Struct. Commun.* **8**, 393–400.
- CHANANONT, P., HAMOR, T. A. & MARTIN, I. L. (1980). *Acta Cryst.* **B36**, 1690–1692.
- RANDALL, L. O., SCHALLEK, W., STERNBACH, L. H. & NING, R. Y. (1974). *Psychopharmacological Agents*, Vol. 3, edited by M. GORDON, pp. 175–281. New York: Academic Press.
- SHELDRICK, G. M. (1978). *SHELX*. Program for crystal structure determination. Univ. of Cambridge, England.
- WILLIS, B. T. M. & PRYOR, A. W. (1975). *Thermal Vibrations in Crystallography*, pp. 101–102. Cambridge Univ. Press.