Table 3. *Torsion angles* (°)

C(1)–C(2)–C(3)–C(3a)	+7 (1)
C(2)–C(3)–C(3a)–C(4)	+95 (1)
C(3)–C(3a)–C(4)–C(5)	−98 (1)
C(3a)–C(4)–C(5)–C(6)	−9 (1)
C(4)–C(5)–C(6)–C(7)	−35 (1)
C(5)–C(6)–C(7)–C(6a)	+69 (1)
C(6)–C(7)–C(6a)–C(1)	+45 (1)
C(7)–C(6a)–C(1)–C(2)	−146 (1)
C(6a)–C(1)–C(2)–C(3)	+13 (1)
C(8)–C(1)–C(2)–C(3)	−99 (1)
C(2)–C(3)–C(3a)–C(6a)	−24 (1)
C(3)–C(3a)–C(6a)–C(1)	+30 (1)
C(3a)–C(6a)–C(1)–C(2)	−27 (1)
C(4)–C(5)–C(6)–C(8)	+74 (1)
C(5)–C(6)–C(8)–C(1)	−81 (1)
C(6)–C(8)–C(1)–C(6a)	−4 (1)
C(6)–C(8)–C(1)–C(2)	+107 (1)
C(8)–C(1)–C(6a)–C(3a)	+94 (1)
C(8)–C(1)–C(6a)–C(7)	−26 (1)
C(5)–C(4)–C(3a)–C(6a)	+14 (1)
C(4)–C(3a)–C(6a)–C(7)	+27 (1)
C(3a)–C(6a)–C(7)–C(6)	−67 (1)
C(8)–C(6)–C(7)–C(6a)	−46 (1)
C(7)–C(6)–C(8)–C(1)	+31 (1)
C(4)–C(3a)–C(6a)–C(1)	−86 (1)
C(3)–C(3a)–C(6a)–C(7)	+144 (1)

Fig. 2 shows the packing arrangement for the racemate in the crystal. Short intermolecular distances across centres of symmetry $(-x,\ 1-y,\ -z)$ are Cl(2)–Cl(3) 3·552 (2), Cl(2)–Cl(4) 3·335 (2), Cl(2)–Cl(5) 3·467 (2); and $(-x,\ 1-y,\ 1-z)$ Cl(3)–Cl(3a) 3·484 (2) Å. These distances are of the same order as for (2).

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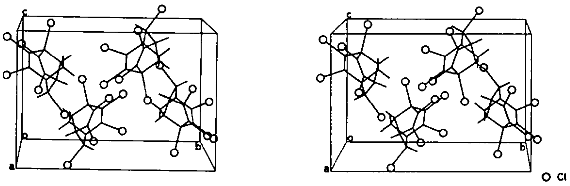

Fig. 2. Stereoview perpendicular to the *bc* plane.

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Structure of 7-Chloro-1-methyl-5-phenyl-1*H*-1,5-benzodiazepine-2,4(3*H*,5*H*)-dione (Clobazam), $C_{16}H_{13}ClN_2O_2$

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Abstract. $M_r = 300{\cdot}74$, trigonal, $R\bar{3}$, $a = 14{\cdot}656\ (5)$ Å, $\alpha = 111{\cdot}75\ (4)°$, $V = 2195{\cdot}3$ Å^3, $Z = 6$, $D_x = 1{\cdot}365$ Mg m^{-3}, μ(Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å) = $0{\cdot}22$ mm^{-1}, $F(000) = 936$, room temperature, $R = 0{\cdot}043$ for 1588 observed reflections. The seven-membered ring adopts a slightly distorted cycloheptatriene-like boat conformation, the C—N amide bonds of length 1·361 (3) and 1·360 (3) Å acting geometrically as double bonds. The angle between the phenyl ring and the fused benzene moiety is 85·2 (4)°.

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Bond lengths and angles are normal and the overall geometry of the molecule is similar to that of the psychoactive 5-phenyl-1,4-benzodiazepin-2-ones.

Introduction. Clobazam (Rossi, Pirola & Maggi, 1969; Weber, Bauer & Hauptmann, 1972) is a benzodiazepine psychotropic drug in which the nitrogen atoms in the heterocyclic ring are in the 1,5- rather than in the more common 1,4-positions. It has found use in clinical practice as an anxiolytic.* We now report its crystal structure as part of a study of structure–activity relationships for this class of compounds.

Experimental. Clobazam (Hoechst) recrystallized from amyl acetate, crystal size 0·3 × 0·5 × 0·7 mm. Enraf–Nonius CAD-4 diffractometer, cell dimensions from setting angles of 25 reflections, graphite-monochromated Mo *K*α, no absorption corrections, 3800 reflections scanned, 2028 unique, $R_{\text{int}} = 0{\cdot}021$, 1591 considered observed $[I > 2{\cdot}5\sigma(I)]$, index range $h = -13$ to 8, k −12 to 8, l 1 to 16, $2\theta_{\max} = 50°$. Two standard reflections, measured every 2 h; no significant intensity variation. Structure solved by direct methods; H atoms located from Fourier difference map; least-squares refinement, $\sum w(\Delta F)^2$ minimized, non-H atoms refined anisotropically, H-atom coordinates fixed, isotropic temperature factors refined; final calculated shifts all $< 0{\cdot}1\,\sigma$; $R = 0{\cdot}043$, $wR = 0{\cdot}07$; $w = 1/[\sigma^2(F) + 0{\cdot}005\,F^2]$; residual electron density in final difference map within $\pm 0{\cdot}5$ e Å^{-3}; no correction for secondary extinction, but three strong reflections affected by extinction discarded.

Computations performed with *SHELX*78 (Sheldrick, 1978) using complex neutral-atom scattering factors (*International Tables for X-ray Crystallography*, 1974) and *PLUTO*78 (Motherwell & Clegg, 1978).

Discussion. Atomic coordinates are listed in Table 1† bond lengths, bond angles and selected torsion angles are in Table 2. The atomic-numbering scheme is illustrated in Fig. 1.

Bond lengths and angles generally agree well with those found in the 1,4-benzodiazepin-2-ones (Hamor & Martin, 1983, and references cited therein). The N(1)—C(2) and C(4)—N(5) formal single bonds are shortened to 1·361 (3) and 1·360 (3) Å. The disposition of bonds at N(1), C(2), C(4) and N(5) is near-planar (sum of valence angles 358·9, 359·9, 359·9, 359·9°, respectively) so that the geometry of the N(1)—C(2) and C(4)—N(5) bonds resembles that of a normal

Table 1. *Fractional atomic coordinates* (×10^4) *with e.s.d.'s in parentheses and equivalent isotropic temperature factors* (Å^2 ×10^3) *for non-hydrogen atoms*

$$U_{\text{eq}} = \tfrac{1}{3}[U_{11} + U_{22} + U_{33} + 2\cos\alpha(U_{23} + U_{13} + U_{12})].$$

	x	*y*	*z*	U_{eq}
Cl	−4993 (1)	608 (1)	−6004 (1)	31
O(2)	−1033 (2)	−1489 (2)	−7216 (2)	37
O(4)	−2882 (2)	−3155 (2)	−6334 (2)	38
N(1)	−1423 (2)	−219 (2)	−6317 (2)	22
N(5)	−2923 (2)	−1520 (2)	−5754 (2)	24
C(2)	−1728 (3)	−1347 (2)	−7033 (3)	25
C(3)	−2945 (3)	−2397 (3)	−7530 (3)	29
C(4)	−2931 (2)	−2420 (2)	−6501 (3)	27
C(6)	−3861 (2)	−482 (2)	−5909 (2)	22
C(7)	−3926 (2)	377 (2)	−6048 (2)	21
C(8)	−3173 (3)	1054 (2)	−6241 (2)	25
C(9)	−2365 (2)	832 (2)	−6335 (3)	24
C(10)	−2279 (2)	−29 (2)	−6209 (2)	20
C(11)	−3012 (2)	−670 (2)	−5972 (2)	20
C(12)	−257 (3)	822 (3)	−5839 (3)	32
C(1′)	−2904 (3)	−1438 (3)	−4732 (3)	29
C(2′)	−1950 (4)	−379 (4)	−3587 (3)	38
C(3′)	−1933 (5)	−272 (5)	−2586 (4)	53
C(4′)	−2847 (7)	−1221 (7)	−2775 (7)	62
C(5′)	−3791 (6)	−2254 (7)	−3911 (7)	59
C(6′)	−3841 (4)	−2390 (4)	−4923 (4)	44

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

Cl—C(7)	1·736 (2)	C(6)—C(11)	1·397 (4)
O(2)—C(2)	1·213 (3)	C(7)—C(8)	1·382 (4)
O(4)—C(4)	1·210 (3)	C(8)—C(9)	1·380 (4)
N(1)—C(2)	1·361 (3)	C(9)—C(10)	1·384 (4)
N(1)—C(10)	1·432 (3)	C(10)—C(11)	1·389 (3)
N(1)—C(12)	1·459 (4)	C(1′)—C(2′)	1·379 (5)
N(5)—C(4)	1·360 (3)	C(1′)—C(6′)	1·385 (5)
N(5)—C(11)	1·433 (3)	C(2′)—C(3′)	1·407 (5)
N(5)—C(1′)	1·446 (4)	C(3′)—C(4′)	1·365 (8)
C(2)—C(3)	1·501 (4)	C(4′)—C(5′)	1·360 (8)
C(3)—C(4)	1·513 (4)	C(5′)—C(6′)	1·390 (7)
C(6)—C(7)	1·378 (3)		

C(2)—N(1)—C(10)	122·4 (2)	C(7)—C(8)—C(9)	118·7 (2)
C(2)—N(1)—C(12)	117·6 (2)	C(8)—C(9)—C(10)	121·1 (2)
C(10)—N(1)—C(12)	118·9 (2)	N(1)—C(10)—C(9)	118·5 (2)
C(4)—N(5)—C(11)	122·8 (2)	N(1)—C(10)—C(11)	122·2 (2)
C(4)—N(5)—C(1′)	120·1 (2)	C(9)—C(10)—C(11)	119·3 (2)
C(11)—N(5)—C(1′)	117·0 (2)	N(5)—C(11)—C(6)	117·1 (2)
O(2)—C(2)—N(1)	121·6 (3)	N(5)—C(11)—C(10)	122·6 (2)
O(2)—C(2)—C(3)	122·2 (2)	C(6)—C(11)—C(10)	120·3 (2)
N(1)—C(2)—C(3)	116·1 (2)	N(5)—C(1′)—C(2′)	117·8 (3)
C(2)—C(3)—C(4)	109·5 (2)	N(5)—C(1′)—C(6′)	120·0 (3)
O(4)—C(4)—N(5)	122·9 (3)	C(2′)—C(1′)—C(6′)	122·1 (3)
O(4)—C(4)—C(3)	122·3 (3)	C(1′)—C(2′)—C(3′)	118·6 (4)
N(5)—C(4)—C(3)	114·7 (2)	C(2′)—C(3′)—C(4′)	119·1 (5)
C(7)—C(6)—C(11)	118·7 (2)	C(3′)—C(4′)—C(5′)	121·6 (4)
Cl—C(7)—C(6)	119·6 (2)	C(4′)—C(5′)—C(6′)	120·8 (5)
Cl—C(7)—C(8)	118·6 (2)	C(1′)—C(6′)—C(5′)	117·7 (5)
C(6)—C(7)—C(8)	121·8 (2)		

C(10)—N(1)—C(2)—C(3)	−10·0*	N(5)—C(11)—C(10)—N(10)	3·0
N(1)—C(2)—C(3)—C(4)	−67·0	C(11)—C(10)—N(1)—C(2)	49·0
C(2)—C(3)—C(4)—N(5)	71·0	C(4)—N(5)—C(1′)—C(2′)	121·0
C(3)—C(4)—N(5)—C(11)	4·0	C(11)—N(5)—C(1′)—C(2′)	−62·0
C(4)—N(5)—C(11)—C(10)	−50·0	C(12)—N(1)—C(10)—C(11)	−142·0

* E.s.d.'s *ca* 0·6°.

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* Marketed as Frisium (Hoechst).

† Lists of structure factors, anisotropic thermal parameters, H-atom parameters and the results of mean-plane calculations have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42125 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

double bond (apart from a 0·08 Å increase in length). For comparison, in 1,4-benzodiazepin-2-ones, the C(1)—N(2) amide bond is typically 1·35–1·37 Å and the N(4)—C(5) double bond, 1·27–1·29 Å (Hamor & Martin, 1983). The seven-membered ring of the title compound accordingly adopts a cycloheptatriene-like boat conformation, with C(10) and C(11) as stern and C(3) as bow, similar to that in the 1,4-benzodiazepin-2-ones. The bow and stern angles, 59·4 (5) and 40·7 (5)°, compare with values 58–64 and 32–40° found in a selection of 1,4-benzodiazepin-2-ones (Hamor & Martin, 1983).

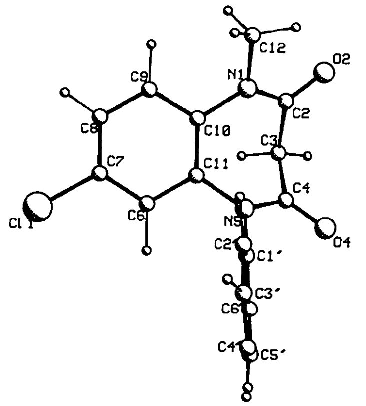

Fig. 1. View of the molecule in a direction perpendicular to the mean plane through atoms C(6)–(11).

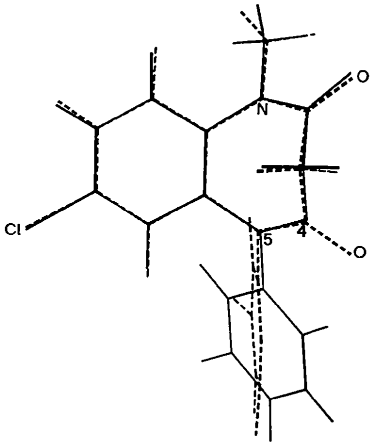

Fig. 2. Superposition of clobazam (dashed lines) and 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one (diazepam) (full lines). Clobazam has C at position 4 and N at 5; diazepam has N at 4 and C at position 5.

In an ideal cycloheptatriene 'boat' with mirror symmetry, the ring torsion angles about N(1)—C(2), C(4)—N(5) and C(10)—C(11), here designated $\tau1$, $\tau4$ and $\tau6$ are zero and the other four torsion angles taken in pairs [about C(2)—C(3), $\tau2$ and C(3)—C(4), $\tau3$ and about N(5)—C(11), $\tau5$ and C(10)—N(1), $\tau7$] are equal in magnitude but of opposite sign. A quantitative measure of distortion given by

$$\Delta = \{\tfrac{1}{5}[\tau1^2 + \tau4^2 + \tau6^2 + (\tau2 + \tau3)^2 + (\tau5 + \tau7)^2]\}^{1/2}$$

based on the asymmetry parameter of Duax, Weeks & Rohrer (1976), is 5·7° for the title compound, a value well within the range found in 1,4-benzodiazepin-2-ones.

The angle between the 5-phenyl ring and the 'benzo' plane [atoms C(6)–(11)] is 85·2 (4)°, the phenyl ring being more steeply inclined than is generally the case for 2'-unsubstituted phenyl rings in 5-phenyl-1,4-benzodiazepines (range 54–74°). Angles of 75–86° are, however, normal for highly active compounds where the 5-phenyl ring is substituted with chlorine in the 2'-position.

The overall geometry of the clobazam molecule is thus consistent with its high benzodiazepine-like psychotropic activity; its potential for hydrogen bonding with a receptor at the 4-position (C=O rather than N) is, however, clearly different. This is illustrated in Fig. 2, which shows a superposition of clobazam (dashed lines) and the potent 5-phenyl-1,4-benzodiazepine, diazepam (full lines), whose crystal structure has been determined by Camerman & Camerman (1972).

There are no abnormally close intermolecular contacts in the crystal structure.

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