Fig. 2. Stereoscopic view of diethylmalonic acid drawn with PLUTO78 (Motherwell & Clegg, 1978).

The C—O and C—OH bond lengths and O—C—O angles are in good agreement with values found in a previous study on carboxylic acids (Leiserowitz, 1976). The two independent molecules in the asymmetric unit are linked by two hydrogen bonds (Table 2) and form a dimer via a ring of six atoms (Fig. 1). Each dimer is bonded with two others by the second carboxylic group and the hydrogen bonds form dihedral angles of 147 and 152 (1)°. So, as in malonic acid (Goedkoop & MacGillavry, 1957), methylmalonic acid (Derissen, 1970) and dimethylmalonic acid (Haas & Brenner, 1966; Sheng-Zhi & Mak, 1986), the diethylmalonic acid molecules are arranged in infinite chains along the c axis (Fig. 2). The two carboxylic groups of one molecule are not coplanar as in even-number dicarboxylic acids but are rotated in opposite directions, the angle between the C(2)—O(1)—O(2) and C(3)—

O(3)—O(4) planes being 79 (1)° (XANADU; Roberts & Sheldrick, 1975). The chains are zigzag. The values of the O—C—C—C torsion angles (Table 2) give a twist conformation about the α-C atom. As in the odd-member malonic derivatives there is nearly a twofold symmetry axis through the α-C atom. All the results agree well with the spectroscopic study.

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Evidence for Rotational Isomerism of the Fluorophenyl Ring in the Crystal Structure of 5-(2-Fluorophenyl)-1,3-dihydro-1,6,8-trimethyl-2H-1,4-benzodiazepin-2-one*

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Abstract. $C_{18}H_{17}FN_2O$, $M_r = 296.3$, monoclinic, $P2_1/c$, $a = 14.215$ (3), $b = 8.135$ (1), $c = 13.449$ (3) Å, $\beta = 98.12$ (2)°, $V = 1539.6$ Å^3, $Z = 4$, $D_x = 1.278$ Mg m^{-3}, $\lambda(Mo K\alpha) = 0.71069$ Å, $\mu = 0.05$ mm^{-1}, $F(000) = 624$, $T = 293$ K, $R = 0.046$ for 1939 observed reflections. The seven-membered ring adopts a moderately distorted cycloheptatriene-like boat conformation with bow and stern angles of 59.6 (5) and 41.3 (5)° respectively. The N—C amide bond length is 1.367 (3) Å. The angle between the 5-phenyl ring and the fused benzo moiety is 76.6 (5)°.

Introduction. The title compound, described by Finner, Zeugner & Milkowski (1984), differs from the clinically used psychoactive benzodiazepines, such as diazepam,† in the nature of the substitution of the fused benzene

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† 7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one, marketed as Valium (Roche).

$C_{18}H_{17}FN_2O$

ring. It has been observed that an electron-withdrawing substituent at C(7) is necessary for good *in vivo* activity (Sternbach, 1973; Randall, Schallek, Sternbach & Ning, 1974); however, these findings are not paralleled by *in vitro* binding assays. The title compound, which possesses methyl substituents at C(6) and C(8), but no substituent at C(7), binds moderately well to the benzodiazepine receptor, its affinity being about twice that of chlordiazepoxide* (Braestrup & Squires, 1978).

Experimental. Crystals were grown from butanone. A crystal of size $0.7 \times 0.7 \times 0.2$ mm was mounted on an Enraf–Nonius CAD-4 diffractometer. Lattice parameters from 24 reflections having $17 < \theta < 26°$. Intensity data were measured with ω–2θ scans in the range $2 < \theta < 26°$. Two standard reflections measured every 2 h showed no significant variation over the period of data collection. 6041 reflections were scanned of which 3017 were unique, $R_{int} = 0.031$, and 1939 were considered observed $[I > 2.5\sigma(I)]$ and were used in the analysis. These covered the index range $h \pm 17$, $k\,0$ to 10, $l\,0$ to 16. No absorption correction was applied. The structure was solved by direct methods using *SHELX*76 (Sheldrick, 1976); all non-hydrogen atoms could be located from the E map with the highest figure of merit. The H atoms were located in a subsequent difference Fourier synthesis and refined with isotropic thermal parameters. Non-hydrogen atoms were refined anisotropically. The refinement was carried out by least squares in two blocks on F values with weights $w = 1/[\sigma^2(F) + 0.001F^2]$. NMR spectroscopic studies by Finner *et al.* (1984) indicated that in solution at 198 K two rotational isomers are in equilibrium, with the fluorophenyl ring oriented such that in the major conformer the electronegative fluorine points away from the electronegative N(4), and towards the fused benzene moiety. The less stable conformer has the 5-aryl ring rotated through *ca* 180°. Finner *et al.* (1984) estimate the major:minor conformer ratio to be 3:1.

At first sight our results indicate only the Finner major conformer (see Fig. 1), which corresponds to the normal orientation of an *ortho*-halo-substituted phenyl

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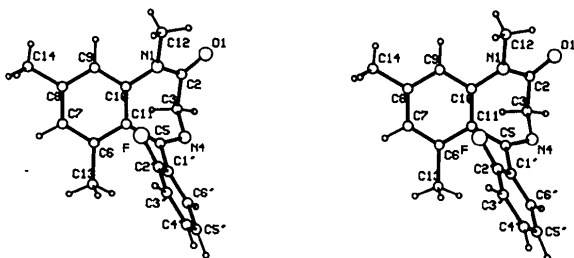* 7-Chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide, marketed as Librium (Roche).

Fig. 1. Stereoscopic view of the molecule in a direction perpendicular to the mean plane of atom C(6)–C(11).

Table 1. *Fractional atomic coordinates* $(\times 10^4)$ *with e.s.d.'s in parentheses and equivalent isotropic temperature factors* $(\text{Å}^2 \times 10^3)$

U_{eq} is one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
F(2')*	3044 (1)	4171 (3)	−1322 (1)	87
F(6')†	505 (23)	6695 (44)	−128 (19)	66 (13)
O(2)	3781 (1)	5829 (2)	2789 (1)	63
N(1)	3823 (1)	3938 (2)	1562 (1)	42
N(4)	1906 (1)	5297 (2)	1095 (1)	42
C(2)	3361 (2)	4844 (3)	2200 (2)	44
C(3)	2297 (2)	4632 (3)	2080 (2)	46
C(5)	2017 (1)	4397 (2)	338 (1)	36
C(6)	2057 (2)	1384 (3)	−89 (1)	40
C(7)	2559 (2)	−72 (3)	−57 (2)	44
C(8)	3476 (2)	−211 (2)	447 (2)	43
C(9)	3877 (2)	1129 (3)	980 (2)	43
C(10)	3381 (1)	2597 (2)	988 (1)	36
C(11)	2483 (1)	2768 (2)	417 (1)	37
C(12)	4844 (2)	4191 (3)	1589 (2)	56
C(13)	1057 (2)	1429 (3)	−637 (2)	58
C(14)	4011 (2)	−1802 (3)	440 (2)	64
C(1')	1692 (2)	5104 (3)	−673 (2)	40
C(2')	2215 (2)	4968 (3)	−1462 (2)	55
C(3')	1936 (2)	5672 (4)	−2389 (2)	72
C(4')	1104 (2)	6543 (4)	−2545 (2)	78
C(5')	566 (2)	6716 (4)	−1788 (2)	72
C(6')	860 (2)	6017 (3)	−859 (2)	54

* Site occupation 0·955 (5).

† Site occupation 0·045 (5).

ring in this class of compounds (Hamor & Martin, 1983). A closer inspection, however, showed that the temperature factor of the H atom [H(6')] at the other *ortho* position had refined to an unusually low value (0.017 Å^2) and a small residual peak (0.2 e Å^{-3}) in the difference map at a distance of 1·34 Å from C(6') corresponded to the position that the F atom would occupy in the minor conformer postulated by Finner *et al.* (1984). For a 180° rotation the ring C atoms would, of course, coincide in the two conformations.

This peak was designated as fluorine, F(6'), and its coordinates [with restraints $C(6')-F(6') = 1.34$ (3), $C(5')-F(6') = C(1')-F(6') = 2.36$ (3) Å], site occupation factor and isotropic thermal parameter included in the refinement. The occupation factor converged to a value of 0·045 (5).

The X-ray results thus indicate the presence in the solid state of *ca* 4·5% of the Finner minor conformer. The final value of the temperature factor of H(6') is 0·03 (1) Å². The refined position of F(6') lies 0·46 Å from the mean plane of the phenyl ring indicating that the two conformers are related by a rotation of 170 rather than precisely 180°. As would be expected, the parameters of the ring carbon atoms are insensitive to this effect. Atomic coordinates are listed in Table 1.* In

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Table 2. *Bond lengths* (Å) *and bond angles* (°) *with e.s.d.'s in parentheses and selected torsion angles* (°), *for which e.s.d.'s are ca* 0·5°

F(2')–C(2')	1·335 (3)	C(6)–C(13)	1·506 (3)
F(6')–C(6')	1·290 (31)	C(7)–C(8)	1·387 (3)
O(2)–C(2)	1·222 (3)	C(8)–C(9)	1·383 (3)
N(1)–C(2)	1·367 (3)	C(8)–C(14)	1·501 (3)
N(1)–C(10)	1·429 (2)	C(9)–C(10)	1·388 (3)
N(1)–C(12)	1·463 (3)	C(10)–C(11)	1·401 (3)
N(4)–C(3)	1·466 (3)	C(1')–C(2')	1·382 (3)
N(4)–C(5)	1·282 (3)	C(1')–C(6')	1·390 (3)
C(2)–C(3)	1·508 (3)	C(2')–C(3')	1·379 (4)
C(5)–C(11)	1·479 (3)	C(3')–C(4')	1·368 (5)
C(5)–C(1')	1·489 (3)	C(4')–C(5')	1·365 (5)
C(6)–C(7)	1·380 (3)	C(5')–C(6')	1·382 (4)
C(6)–C(11)	1·407 (3)		

C(2)–N(1)–C(10)	122·5 (2)	N(1)–C(10)–C(9)	118·4 (2)
C(2)–N(1)–C(12)	118·1 (2)	N(1)–C(10)–C(11)	121·2 (2)
C(10)–N(1)–C(12)	118·7 (2)	C(9)–C(10)–C(11)	120·4 (2)
C(3)–N(4)–C(5)	115·7 (2)	C(5)–C(11)–C(6)	121·7 (2)
O(2)–C(2)–N(1)	121·8 (2)	C(5)–C(11)–C(10)	119·5 (2)
O(2)–C(2)–C(3)	122·3 (2)	C(6)–C(11)–C(10)	118·8 (2)
N(1)–C(2)–C(3)	115·7 (2)	C(5)–C(1')–C(2')	122·6 (2)
N(4)–C(3)–C(2)	107·5 (2)	C(5)–C(1')–C(6')	121·1 (2)
N(4)–C(5)–C(11)	124·0 (2)	C(2')–C(1')–C(6')	116·2 (2)
N(4)–C(5)–C(1')	116·6 (2)	F(2')–C(2')–C(1')	119·4 (2)
C(11)–C(5)–C(1')	119·3 (2)	F(2')–C(2')–C(3')	117·7 (2)
C(7)–C(6)–C(11)	119·1 (2)	C(1')–C(2')–C(3')	122·9 (2)
C(7)–C(6)–C(13)	119·0 (2)	C(2')–C(3')–C(4')	119·1 (3)
C(11)–C(6)–C(13)	121·9 (2)	C(3')–C(4')–C(5')	120·1 (3)
C(6)–C(7)–C(8)	122·1 (2)	C(4')–C(5')–C(6')	120·2 (3)
C(7)–C(8)–C(9)	118·6 (2)	F(6')–C(6')–C(1')	120·4 (13)
C(7)–C(8)–C(14)	120·6 (2)	F(6')–C(6')–C(5')	114·4 (14)
C(9)–C(8)–C(14)	120·7 (2)	C(1')–C(6')–C(5')	121·5 (3)
C(8)–C(9)–C(10)	120·6 (2)		

C(10)–N(1)–C(2)–C(3)	−14·5	C(5)–C(11)–C(10)–N(1)	5·0
N(1)–C(2)–C(3)–N(4)	−66·4	C(11)–C(10)–N(1)–C(2)	49·6
C(2)–C(3)–N(4)–C(5)	75·5	N(4)–C(5)–C(1')–C(6')	−39·4
C(3)–N(4)–C(5)–C(11)	1·5	C(11)–C(5)–C(1')–C(2')	−39·8
N(4)–C(5)–C(11)–C(10)	−51·4	N(4)–C(5)–C(1')–C(2')	137·3

the final cycle of least-squares refinement max. shift/ e.s.d. = 0·16. The residual electron density in a final difference synthesis was within $\pm 0·24$ e Å^{-3}. Final $R = 0·046$, $wR = 0·061$. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). Computations were performed with *SHELX*76 (Sheldrick, 1976) and *PLUTO* (Motherwell & Clegg, 1978).

Discussion. Fig. 1 shows a stereoscopic view of the molecule and also indicates the atom numbering. Bond lengths, bond angles and selected torsion angles are listed in Table 2.

The bond lengths and angles agree with those found in other benzodiazepines, and the overall conformation is similar (Hamor & Martin, 1983). The N(1)–C(2) amide bond is shortened from the single-bond length, with a near-planar disposition of bonds at N(1) and C(2), due to N→O electron delocalization. The seven-membered ring adopts a cycloheptatriene-like boat conformation, C(2), C(3), N(4) forming the bow and C(5), C(11), C(10), N(1) the stern. The bow and stern angles of 59·6 (5) and 41·3 (5)° compare with values of 58–64 and 32–40° found in a selection of 5-phenyl-

1,4-benzodiazepin-2-ones (Hamor & Martin, 1983). The deviation parameter (Hamor & Martin, 1983; Butcher & Hamor, 1985), which is a measure of the deviation of the seven-membered ring from an ideal cycloheptatriene with mirror symmetry and zero torsion angles about the three double bonds, is 8·0°. This value is typical of N(1)-methyl substituted compounds which tend to show a somewhat greater distortion than the N(1)–H analogues. The C(2)–N(1)–C(10) angle of 122·5 (2)° is in good agreement with those found in other N(1)-methyl substituted benzodiazepines but is some 3–5° smaller than in the N(1)–H analogues.

The angle between the 5-phenyl ring and the fused benzo moiety, 76·6 (5)°, falls within the range of values in 7-substituted 5-phenyl-1,4-benzodiazepines where the 5-phenyl ring carries an *ortho* substituent. The methyl group at C(6) thus has little or no effect on the orientation of the 5-phenyl ring. The C(5)–C(1') bond length of 1·489 (3) Å corresponds to that of a single bond between sp^2-hybridized C atoms.

Intermolecular contacts correspond to normal van der Waals interactions, apart from a short contact of 2·01 (4) Å between the F atom of the minor conformer and one of the C(13) methyl H atoms of a centrosymmetrically related molecule. Presumably in molecules related in this way to the minor conformer, the C(13) methyl group is rotated in such a way as to increase the F(6')···H distance.

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