Table 3. *Observed values for the ring torsion angles* (°) *compared with the calculated values of Geise, Altona & Romers* (1967) *for rings A and C, and with the average for a selection of other steroids* (*Duax & Norton,* 1975) *for rings B and D*

	Observed	Calculated	
Ring *A*			
10–1–2–3	−57·7 (4)	−57	
1–2–3–4	53·1 (4)	55	
2–3–4–5	−49·6 (4)	−56	
3–4–5–10	50·7 (3)	58	
1–10–5–4	−49·9 (4)	−58	
5–10–1–2	53·2 (4)	58	
Ring *C*		With *D*	Without *D*
13–12–11–9	−56·0 (4)	−56	−56
12–11–9–8	51·1 (4)	57·3	56
11–9–8–14	−49·7 (3)	−58	−58
9–8–14–13	57·4 (3)	58	58
8–14–13–12	−60·9 (3)	−58	−59
14–13–12–11	57·4 (3)	58	58
Ring *B*			
6–5–10–9	15·4 (5)	13·5	
10–5–6–7	1·2 (5)	2·3	
5–6–7–8	12·8 (5)	14·2	
6–7–8–9	−42·6 (4)	−44·7	
7–8–9–10	60·7 (3)	63·1	
8–9–10–5	−45·9 (3)	−45·8	
Ring *D*			
17–13–14–15	45·2 (3)	47·7	
13–14–15–16	−34·6 (3)	−38·2	
14–15–16–17	9·7 (3)	13·4	
15–16–17–13	18·2 (3)	16·2	
16–17–13–14	−38·1 (3)	−38·3	

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Structure of an Analogue of the Triazolobenzodiazepine Alprazolam*

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Abstract. 1-Methyl-6-phenyl-8-(trifluoromethyl)-4*H*-*s*-triazolo[4,3-*a*][1,4]benzodiazepine sesquihydrate, $C_{18}H_{13}F_3N_4.1{\cdot}5H_2O$, $M_r = 369{\cdot}3$, monoclinic, $C2/c$, $a = 13{\cdot}115$ (4), $b = 9{\cdot}673$ (3), $c = 27{\cdot}007$ (7) Å, $\beta = 96{\cdot}79$ (3)°, $V = 3402{\cdot}1$ Å^3, $Z = 8$, $D_x = 1{\cdot}442$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 1{\cdot}16$ cm^{-1}, $F(000) = 1528$, $T = 294$ K, $R = 0{\cdot}049$ for 1544 observed reflections. The seven-membered ring is in a cycloheptatriene-like boat conformation with bow and stern angles of 55·5 (8) and 36·2 (8)°, respectively. The angle between the 6-phenyl ring and the fused benzo moiety is 63·5 (8)°. The triazolo ring and the two aromatic rings are each planar to within the limits of experimental error.

Introduction. The title compound (Hester, Rudzik & Kamdar, 1971) belongs to the class of triazolobenzodiazepines, exemplified by alprazolam† and triazolam,‡ which have found use in clinical practice as anxiolytics and hypnotics. It differs from alprazolam only in that the substituent at C8 is a trifluoromethyl group, rather than a chlorine atom. However, its affinity for the benzodiazepine receptor *in vitro* is about 12 times less strong.

Experimental. Crystals were grown from amyl acetate. A crystal of size 0·15 × 0·4 × 0·4 mm was mounted on

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* Contribution from the Crystallography Unit, Universities of Aston and Birmingham.

† 8-Chloro-1-methyl-6-phenyl-4*H*-*s*-triazolo[4,3-*a*][1,4]-benzodiazepine. Marketed as Xanax (Upjohn).

‡ 8-Chloro-6-(2-chlorophenyl)-1-methyl-4*H*-*s*-triazolo[4,3-*a*]-[1,4]benzodiazepine. Marketed as Halcion (Upjohn).

0108-2701/88/101823-03$03.00

Table 1. *Fractional atomic coordinates* ($\times 10^4$) *for the heavier atoms with e.s.d.'s in parentheses, and equivalent isotropic temperature factors* ($Å^2 \times 10^3$)

$$U_{eq} = \tfrac{1}{3}(U_{11} + U_{22} + U_{23} + 2U_{13}\cos\beta).$$

	x	y	z	U_{eq}
F(1)	108 (3)	−2805 (3)	3137 (2)	106
F(2)	−1079 (3)	−1993 (5)	3517 (1)	121
F(3)	−838 (2)	−1234 (3)	2815 (1)	73
N(1)	2432 (2)	2223 (4)	4231 (1)	39
N(2)	3698 (3)	3195 (5)	4698 (1)	62
N(3)	2978 (3)	4215 (5)	4547 (1)	62
N(5)	1401 (3)	4131 (4)	3452 (1)	45
C(1)	3361 (3)	2024 (5)	4504 (1)	47
C(3)	2233 (3)	3603 (5)	4269 (1)	46
C(4)	1310 (4)	4197 (6)	3989 (2)	52
C(6)	1382 (3)	2948 (4)	3243 (1)	34
C(7)	547 (3)	625 (4)	3273 (1)	38
C(8)	382 (3)	−611 (5)	3494 (1)	40
C(9)	886 (3)	−923 (5)	3956 (2)	48
C(10)	1568 (3)	−4 (5)	4198 (2)	46
C(11)	1743 (3)	1256 (4)	3972 (1)	36
C(12)	1238 (3)	1604 (4)	3502 (1)	34
C(13)	3926 (5)	706 (7)	4556 (2)	66
C(14)	−357 (4)	−1658 (5)	3245 (2)	55
C(1′)	1504 (3)	2893 (4)	2704 (1)	33
C(2′)	1943 (3)	1773 (5)	2494 (2)	42
C(3′)	2080 (4)	1767 (5)	1995 (2)	54
C(4′)	1777 (4)	2896 (6)	1701 (2)	56
C(5′)	1353 (4)	4013 (5)	1907 (2)	53
C(6′)	1221 (3)	4034 (5)	2402 (2)	43
O(1)	743 (5)	1889 (6)	323 (2)	136
O(2)	2048 (14)	2974 (13)	−188 (6)	213*

* Disordered water oxygen; s.o.f. 0·5.

an Enraf–Nonius CAD-4 diffractometer. Lattice parameters from 25 reflections having $11 < \theta < 20°$. Data collected using ω–2θ scans, $2 < \theta < 25°$; two standard reflections measured every 2 h showed no significant variation over period of data collection; 3121 reflections scanned, 2983 unique, $R_{\text{int}} = 0{\cdot}022$; of these 1544 having $I > 2{\cdot}5\sigma(I)$ were used in the analysis, index range h −14 to 15, k 0 to 11, l 0 to 31; no absorption corrections applied; structure solved by direct methods; non-H atoms refined with anisotropic temperature factors, H atoms refined isotropically; full-matrix least-squares refinement on F magnitudes. $R = 0{\cdot}049$, $wR = 0{\cdot}065$, $w = 1/[\sigma^2(F) + 0{\cdot}001F^2]$, max. $\Delta/\sigma < 0{\cdot}1$; residual electron density in final difference Fourier map within $\pm 0{\cdot}3$ e Å^{-3}; atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). Computations were carried out with *SHELX* (Sheldrick, 1978) on the University of Birmingham Honeywell computer.

In agreement with analytical data (Hester, Rudzik & Kamdar, 1971) a molecule of water of hydration was found to be present. In addition, a fairly large peak in the difference map, near a centre of symmetry, was interpreted as a disordered water molecule which could occupy one of the two symmetry-related positions. It was included in the calculations with site-occupation factor of 0·5. The H atoms of this disordered water molecule were not located.

Table 2. *Molecular dimensions*

(*a*) Bond lengths (Å) with e.s.d.'s in parentheses

F(1)—C(14)	1·316 (6)	C(7)—C(8)	1·366 (6)
F(2)—C(14)	1·305 (5)	C(7)—C(12)	1·402 (5)
F(3)—C(14)	1·320 (5)	C(8)—C(9)	1·375 (6)
N(1)—C(1)	1·361 (5)	C(8)—C(14)	1·504 (6)
N(1)—C(3)	1·367 (5)	C(9)—C(10)	1·370 (6)
N(1)—C(11)	1·425 (5)	C(10)—C(11)	1·395 (6)
N(2)—N(3)	1·392 (6)	C(11)—C(12)	1·401 (5)
N(2)—C(1)	1·303 (6)	C(1′)—C(2′)	1·381 (5)
N(3)—C(3)	1·303 (5)	C(1′)—C(6′)	1·396 (5)
N(5)—C(4)	1·470 (6)	C(2′)—C(3′)	1·380 (6)
N(5)—C(6)	1·275 (5)	C(3′)—C(4′)	1·380 (7)
C(1)—C(13)	1·473 (7)	C(4′)—C(5′)	1·363 (7)
C(3)—C(4)	1·465 (6)	C(5′)—C(6′)	1·369 (6)
C(6)—C(12)	1·498 (5)	C(6)—C(1′)	1·484 (5)

(*b*) Bond angles (°) with e.s.d.'s in parentheses

C(1)—N(1)—C(3)	105·3 (4)	C(9)—C(10)—C(11)	119·3 (4)
C(1)—N(1)—C(11)	130·5 (4)	N(1)—C(11)—C(10)	119·1 (3)
C(3)—N(1)—C(11)	124·2 (4)	N(1)—C(11)—C(12)	119·4 (3)
N(3)—N(2)—C(1)	108·2 (4)	C(10)—C(11)—C(12)	121·5 (4)
N(2)—N(3)—C(3)	106·4 (4)	C(6)—C(12)—C(7)	119·4 (3)
C(4)—N(5)—C(6)	118·4 (4)	C(6)—C(12)—C(11)	123·9 (3)
N(1)—C(1)—N(2)	109·5 (4)	C(7)—C(12)—C(11)	116·6 (4)
N(1)—C(1)—C(13)	125·6 (4)	F(1)—C(14)—F(2)	107·6 (4)
N(2)—C(1)—C(13)	124·9 (4)	F(1)—C(14)—F(3)	104·6 (4)
N(1)—C(3)—N(3)	110·5 (4)	F(2)—C(14)—F(3)	105·6 (4)
N(1)—C(3)—C(4)	119·9 (4)	F(1)—C(14)—C(8)	112·1 (4)
N(3)—C(3)—C(4)	129·5 (5)	F(2)—C(14)—C(8)	112·8 (4)
N(5)—C(4)—C(3)	109·4 (4)	F(3)—C(14)—C(8)	113·5 (4)
N(5)—C(6)—C(12)	124·7 (3)	C(6)—C(1′)—C(2′)	122·0 (4)
N(5)—C(6)—C(1′)	117·9 (3)	C(6)—C(1′)—C(6′)	119·5 (4)
C(12)—C(6)—C(1′)	117·4 (3)	C(2′)—C(1′)—C(6′)	118·4 (4)
C(8)—C(7)—C(12)	121·8 (4)	C(1′)—C(2′)—C(3′)	120·9 (4)
C(7)—C(8)—C(9)	120·3 (4)	C(2′)—C(3′)—C(4′)	119·7 (5)
C(7)—C(8)—C(14)	121·4 (4)	C(3′)—C(4′)—C(5′)	119·8 (5)
C(9)—C(8)—C(14)	118·2 (4)	C(4′)—C(5′)—C(6′)	121·0 (5)
C(8)—C(9)—C(10)	120·5 (4)	C(1′)—C(6′)—C(5′)	120·2 (4)

(*c*) Selected torsion angles (°); e.s.d.'s are *ca* 0·8°

C(11)—N(1)—C(3)—C(4)	−6·7	C(12)—C(11)—N(1)—C(3)	44·2
N(1)—C(3)—C(4)—N(5)	−67·0	N(5)—C(6)—C(1′)—C(2′)	150·4
C(3)—C(4)—N(5)—C(6)	68·0	C(12)—C(6)—C(1′)—C(2′)	−30·1
C(4)—N(5)—C(6)—C(12)	2·3	C(7)—C(8)—C(14)—F(1)	115·8
N(5)—C(6)—C(12)—C(11)	−44·7	C(7)—C(8)—C(14)—F(2)	−122·6
C(6)—C(12)—C(11)—N(1)	0·6	C(7)—C(8)—C(14)—F(3)	−2·5

Discussion. Final atomic parameters 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 in the triazolo ring are in good agreement with those found in brotizolam (Butcher & Hamor, 1985). The N(1)—C(3) formal single bond is shortened to 1·367 (5) Å, about half-way between the C—N single- and double-bond lengths, and the dispositions of valencies about N(1) and C(3) are near planar, torsion angle C(11)—N(1)—C(3)—C(4) = −6·7°. The geometry of this bond thus resembles that of a double bond, as has been observed in benzodiazepin-2-ones (Hamor & Martin, 1983), and is

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* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51143 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

indicative of the participation of this bond in the electron delocalization of the triazolo ring. The triazolo ring is planar to within ±0·0025 Å.

The seven-membered ring thus contains three 'double' bonds and adopts a cycloheptatriene-like boat conformation, with C(3), C(4) and N(5) forming the bow and N(1), C(11), C(12) and C(6) forming the stern plane. The bow and stern angles which these planar groupings of atoms make with the central plane of the boat, atoms N(1), C(3), N(5), C(6), are 55·5 (8) and 36·2 (8)°, respectively. The values are similar to those found in other triazolobenzodiazepines (Hester, Duchamp & Chidester, 1971; Kamiya, Wada & Nishikawa, 1973). The bow angle is, however, slightly smaller than is commonly found in 1,4-benzodiazepin-2-ones (range 58–64°) (Hamor & Martin, 1983). The deviation parameter (Hamor & Martin, 1983), which is a measure of the deviation of the seven-membered ring from mirror symmetry and zero torsion angles about the three double bonds of the ideal cycloheptatriene boat conformation, is 3·2°, typical for this class of compounds.

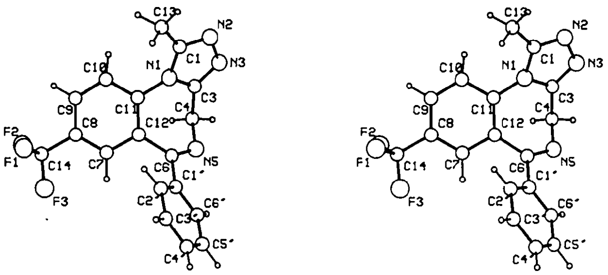

Fig. 1. Stereoscopic view of the molecule in a direction perpendicular to the mean plane through atoms C(7)–C(12) drawn with *PLUTO* (Motherwell & Clegg, 1978).

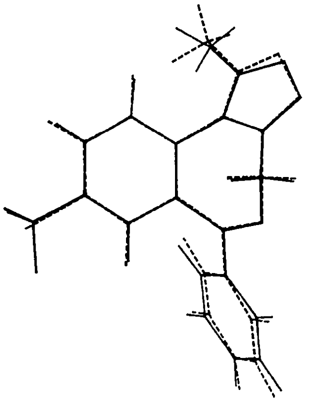

Fig. 2. Superposition of drawings of the title compound (full lines) and alprazolam (dashed lines).

The angle between the mean planes of the 6-phenyl ring and the fused benzene ring is 63·5 (8)°, well within the range 54–75° observed in other benzodiazepines containing unsubstituted phenyl rings. The corresponding angle in alprazolam is 69°. The close geometrical similarity between alprazolam and the title compound is illustrated in Fig. 2. The C(6)–C(1') bond length, 1·484 (5) Å, corresponds to that of a single bond between sp^2-hybridized carbon atoms, and the C(6)–N(5) bond length, 1·275 (5) Å, to that of a C=N double bond.

The complete water molecule is involved in two hydrogen bonds to the benzodiazepine. One is to N(3) of the symmetry-related molecule at $\frac{1}{2}-x, -\frac{1}{2}+y, \frac{1}{2}-z$ and the other is to N(2) of the molecule at $-\frac{1}{2}+x, \frac{1}{2}-y, -\frac{1}{2}+z$. Distances and angles involved are O(1)···N(3) = 3·081 (7), H(O1*A*)···N(3) = 2·12 (6) Å, O(1)–H(O1*A*)···N(3) = 143 (2)° and O(1)···N(2) = 2·997 (7), H(O1*B*)···N(2) = 2·20 (6) Å, with angle at H(O1*B*) = 155 (2)°. There are also two possible hydrogen bonds involving the disordered water molecule, O(2)···O(1) = 2·55 (2) Å and O(2)···N(3) = 3·10 (2) Å. Other intermolecular contacts correspond to van der Waals interactions.

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