which produces a dimer (Fig. 1). There is also a longer bond O(2)···H(14) of 2·21 (1) Å. Similar dimeric arrangements are frequently observed, for example in the structure of the ammonium picrate complex with 1,10-phenanthroline (Jones, Milburn, Sawyer & Hughes, 1981). The 1,3,2-dioxaphosphorinane ring is a slightly distorted chair (Fig. 2). The asymmetry parameters (Duax & Norton, 1975) are: C_s(P) = 0·7 (5)° and C_2[O(1),C(6)] = 5·7 (5)°. The S=P bond is situated axially to the ring and the P—O bond equatorially. The C(7) methyl group and the exocyclic oxygen atom are in a *cis* configuration, as expected by Mikołajczyk & Łuczak (1972). The geometry of the ring closely resembles those in similar structures of the dicyclohexylammonium salt of the title compound (Bartczak, 1983) and in 4-methyl-1,3,2-dioxaphosphorinane 2-oxide (Saenger & Mikołajczyk, 1972).

Table 2. *Bond lengths* (Å) *and angles* (°)

P—S	1·957 (2)	O(2)—P	1·499 (3)
O(1)—P	1·600 (3)	O(3)—P	1·599 (3)
C(6)—O(1)	1·463 (7)	C(4)—O(3)	1·470 (6)
C(5)—O(4)	1·509 (8)	C(7)—C(4)	1·504 (9)
C(6)—C(5)	1·520 (9)		
O(2)—P—S	116·5 (2)	O(1)—P—S	112·6 (2)
O(1)—P—O(2)	106·2 (2)	O(3)—P—S	110·7 (1)
O(3)—P—O(2)	106·9 (2)	O(3)—P—O(1)	102·8 (2)
C(6)—O(1)—P	115·5 (3)	C(4)—O(3)—P	116·8 (3)
C(5)—C(4)—O(3)	108·7 (4)	C(7)—C(4)—O(3)	106·0 (4)
C(7)—C(4)—C(5)	114·4 (5)	C(6)—C(5)—C(4)	111·9 (4)
C(5)—C(6)—O(1)	110·2 (4)		

All bonds and angles have typical values for this class of compounds and will not be discussed in detail.

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Structures of 7-Bromo-1,3-dihydro-5-(2-pyridyl)-2*H*-1,4-benzodiazepin-2-one (Bromazepam, $C_{14}H_{10}BrN_3O$) and 5-(2-Fluorophenyl)-1,3-dihydro-1-methyl-7-nitro-2*H*-1,4-benzodiazepin-2-one (Flunitrazepam, $C_{16}H_{12}FN_3O_3$)*

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Abstract. Bromazepam: $M_r = 316·2$, monoclinic, $P2_1/c$, $a = 10·304$ (4), $b = 15·897$ (5), $c = 8·122$ (3) Å, $\beta = 106·8$ (3)°, $U = 1273·6$ Å^3, $Z = 4$, $D_x = 1·649$ Mg m^{-3}, μ(Mo $K\alpha$, $\lambda = 0·71069$ Å) = 3·13 mm^{-1}, $F(000) = 632$, room temperature, $R = 0·040$ for 1470 observed reflections. Flunitrazepam: $M_r = 313·3$, monoclinic, $P2_1/n$, $a = 7·321$ (1), $b = 13·668$ (5), $c = 14·356$ (5) Å, $\beta = 96·68$ (2)°, $U = 1426·8$ Å^3, $Z = 4$, $D_x = 1·459$ Mg m^{-3}, μ(Mo $K\alpha$, $\lambda = 0·71069$ Å) = 0·07 mm^{-1}, $F(000) = 648$, room temperature, $R = 0·054$ for 1017 observed reflections. In both molecules the seven-membered ring is in a boat conformation. The angle between the benzo moiety of

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the 1,4-benzodiazepine system and the aromatic ring in the 5-position is 60·3 (6)° in bromazepam and 75·5 (9)° in flunitrazepam. Otherwise their overall geometries are similar.

Introduction. Bromazepam (Fryer, Schmidt & Sternbach, 1964) and flunitrazepam (Sternbach, Fryer, Keller, Metlesics, Sach & Steiger, 1963) exhibit to a marked degree the psychotropic properties typical of many 5-phenyl-1,4-benzodiazepines (Sternbach, 1978) and have found use in clinical practice, bromazepam as an anxiolytic and flunitrazepam as a hypnotic.* Their affinities for the benzodiazepine receptor *in vitro* are comparable to that of diazepam† (Braestrup & Squires, 1978). We now report the crystal structures of the title compounds as part of a study of structure–activity relationships for this class of compounds. Bromazepam differs from the majority of clinically useful 1,4-benzodiazepines in being a 5-pyridyl rather than a 5-phenyl derivative.

Experimental. Bromazepam: crystals from amyl acetate/ethanol, Enraf–Nonius CAD-4 diffractometer, crystal size 0·3 × 0·25 × 0·2 mm, cell dimensions from setting angles of 25 reflections, graphite-monochromated Mo $K\alpha$ radiation, no absorption correction, 2364 reflections scanned by ω–2θ scans up to $\theta = 25°$, 1470 considered observed [$I > 2{\cdot}5\sigma(I)$], index range h −12 to 11, k 0 to 18, l 0 to 9. Two standard reflections, measured every 2 h: no significant variation in intensity. Structure solved by Patterson and Fourier methods; all H atoms located from difference Fourier map, least-squares refinement, $\sum w(\Delta F)^2$ minimized, H isotropic, non-H anisotropic; final calculated shifts all $< 0{\cdot}25\sigma$; $R = 0{\cdot}040$, $wR = 0{\cdot}051$; weighting scheme, $w = 1/[\sigma^2(F) + 0{\cdot}001F^2]$; residual electron density in final difference map ± 0·5 e Å^{-3}; no correction for secondary extinction.

Flunitrazepam: crystals from butanone, diffractometer and measurement parameters as for bromazepam, crystal size 0·4 × 0·3 × 0·2 mm, no absorption correction, 2514 reflections scanned, 1017 considered observed, index range $h \pm 8$, k 0 to 13, l 0 to 16. No crystal deterioration. Structure solved by direct methods, refined by least squares, $\sum w(\Delta F)^2$ minimized, H atoms apart from those of *N*-methyl group located from difference map; methyl group refined as rigid group, other H atoms refined isotropically in initial cycles; in final cycles H-atom parameters fixed, coordinates and anisotropic thermal factors refined for non-H atoms; final LS shifts $< 0{\cdot}1\sigma$, apart from methyl group ($<0{\cdot}3\sigma$); $R = 0{\cdot}054$, $wR = 0{\cdot}072$; $w = 1/[\sigma^2(F) + 0{\cdot}001F^2]$; residual electron density in difference map ± 0·2 e Å^{-3}; no correction for secondary extinction.

Computations were carried out with *SHELX* (Sheldrick, 1978) using complex neutral-atom scattering factors (*International Tables for X-ray Crystallography*, 1974).

Considerable difficulty was experienced in obtaining untwinned single crystals of flunitrazepam. Photographs of the crystal used in the analysis showed no sign of twinning. However, generally large U_{22} values [maximum 0·23 and 0·26 Å^2 for C(8) and C(9), respectively] might be indicative of some residual twinning effect. A difference Fourier synthesis computed with F_c values from which these two atoms had been excluded showed maxima elongated in the y direction, but no evidence of any peak splitting.

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

$$U_{eq} = \tfrac{1}{3}(U_{11} + U_{22} + U_{33} + 2U_{13}\cos\beta).$$

	x	y	z	U_{eq}
Bromazepam				
Br	−1601 (1)	617 (1)	1023 (1)	184
O(2)	−8156 (3)	−1404 (3)	−6128 (5)	177
N(1)	−6566 (4)	−528 (2)	−4561 (5)	94
N(4)	−5071 (3)	−2169 (2)	−4171 (5)	102
N(2′)	−2083 (3)	−1209 (2)	−4314 (5)	95
C(2)	−7119 (4)	−1298 (3)	−4969 (6)	110
C(3)	−6361 (5)	−2004 (3)	−3843 (8)	163
C(5)	−4128 (4)	−1626 (5)	−3632 (5)	86
C(6)	−3115 (5)	−520 (3)	−1495 (6)	101
C(7)	−3149 (4)	237 (3)	−701 (6)	104
C(8)	−4299 (5)	726 (3)	−1165 (6)	108
C(9)	−5411 (5)	449 (3)	−2404 (6)	119
C(10)	−5406 (4)	−324 (3)	−3221 (5)	78
C(11)	−4240 (4)	−821 (2)	−2761 (5)	75
C(1′)	−2782 (4)	−1841 (3)	−3875 (5)	79
C(3′)	−885 (4)	−1400 (3)	−4510 (6)	110
C(4′)	−308 (5)	−2190 (3)	−4251 (6)	126
C(5′)	−1025 (5)	−2820 (4)	−3779 (6)	125
C(6′)	−2287 (5)	−2650 (3)	−3622 (6)	99
Flunitrazepam				
F	−11817 (5)	−3754 (3)	−5491 (2)	98
O(2)	−10101 (6)	−3375 (4)	−1642 (3)	98
O(7*A*)	−12972 (7)	439 (4)	−6175 (3)	120
O(7*B*)	−10835 (7)	−409 (4)	−6692 (3)	109
N(1)	−11580 (6)	−2613 (4)	−2894 (3)	82
N(4)	−7928 (5)	−3153 (4)	−3487 (3)	66
N(7)	−11853 (9)	−224 (5)	−6102 (4)	100
C(2)	−10022 (7)	−2892 (6)	−2332 (4)	78
C(3)	−8249 (7)	−2584 (5)	−2671 (3)	74
C(5)	−8944 (6)	−2950 (5)	−4255 (3)	61
C(6)	−10468 (7)	−1586 (5)	−5158 (3)	76
C(7)	−11726 (8)	−836 (6)	−5261 (4)	91
C(8)	−12903 (9)	−661 (7)	−4604 (4)	122
C(9)	−12830 (9)	−1260 (8)	−3839 (4)	121
C(10)	−11554 (7)	−2002 (6)	−3687 (3)	83
C(11)	−10346 (7)	−2166 (5)	−4358 (3)	66
C(1′)	−8634 (7)	−3543 (4)	−5087 (3)	59
C(2′)	−10070 (8)	−3947 (5)	−5675 (4)	68
C(3′)	−9853 (11)	−4533 (5)	−6418 (4)	79
C(4′)	−8094 (14)	−4740 (5)	−6595 (5)	91
C(5′)	−6621 (10)	−4357 (6)	−6043 (5)	88
C(6′)	−6883 (8)	−3768 (5)	−5288 (4)	71
C(12)	−13362 (8)	−2848 (6)	−2575 (5)	93

* Bromazepam marketed as Lexotanil (Roche); flunitrazepam as Rohypnol (Roche).

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

Discussion. Final atomic parameters for both compounds 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 values found in analogous molecules (Chananont, Hamor & Martin, 1979, 1981; Gilli, Bertolasi, Sacerdoti & Borea, 1977). The N(1)–C(2) formal single bond is shortened to 1·351 (5) Å in bromazepam and 1·372 (7) Å in flunitrazepam and the disposition of bonds at N(1) is near planar so that the geometry of the bond resembles that of a normal double bond (*cf.* torsion angles in Table 2*c*). The ring angle at N(1) is, however, 3·8° smaller in the N(1)-Me-substituted flunitrazepam; similar differences between N(1)-Me and N(1)-H benzodiazepines have been noted previously (Chananont *et al.*, 1981). The N(4)–C(5) length in both molecules corresponds to that of a C=N double bond and the C(5)–C(1′) and C(5)–C(11) lengths are within the accepted range (1·48–1·50 Å) for a C(sp^2)–C(sp^2) single bond. There is, therefore, no evidence for any electron delocalization between the 5-pyridyl ring in bromazepam or the 5-phenyl ring in flunitrazepam and the 1,4-benzodiazepine system.

The seven-membered ring is in a cycloheptatriene-like boat conformation, C(10) and C(11) forming the 'stern' and C(3) the 'bow'. The bow angles, 60·3 (8)° in bromazepam, 61·0 (12)° in flunitrazepam, do not differ significantly, but the stern angles, 30·8 (8) and

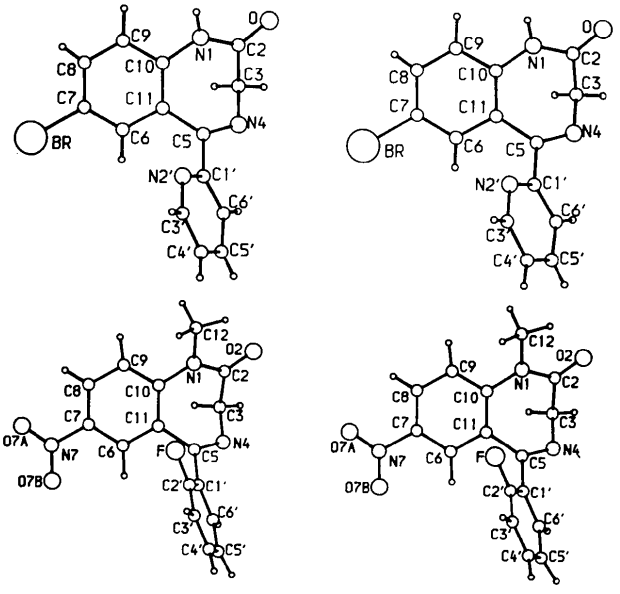

Fig. 1. The molecules of bromazepam (upper diagram) and flunitrazepam (lower diagram) viewed in a direction perpendicular to the mean plane through C(6)–(11).

* 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 38712 (21 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Molecular dimensions*

	Broma-zepam	Flunitra-zepam		Broma-zepam	Flunitra-zepam		Broma-zepam	Flunitra-zepam
(*a*) Bond lengths (Å)								
N(1)–C(2)	1·351 (5)	1·372 (7)	C(9)–C(10)	1·397 (6)	1·379 (9)	C(5)–C(1′)	1·495 (6)	1·483 (7)
C(2)–O(2)	1·214 (5)	1·199 (7)	C(10)–C(11)	1·395 (6)	1·400 (7)	C(1′)–N(2′)	1·343 (5)	—
C(2)–C(3)	1·514 (7)	1·498 (8)	C(10)–N(1)	1·402 (5)	1·414 (8)	C(1′)–C(2′)	—	1·384 (7)
C(3)–N(4)	1·453 (6)	1·448 (7)	Br–C(7)	1·892 (4)	—	N(2′)–C(3′)	1·325 (6)	—
N(4)–C(5)	1·278 (5)	1·286 (5)	N(7)–C(7)	—	1·464 (9)	C(2′)–C(3′)	—	1·359 (8)
C(5)–C(11)	1·483 (5)	1·479 (8)	N(7)–O(7*A*)	—	1·217 (7)	C(3′)–C(4′)	1·380 (7)	1·370 (10)
C(6)–C(11)	1·394 (6)	1·391 (8)	N(7)–O(7*B*)	—	1·217 (6)	C(4′)–C(5′)	1·363 (7)	1·366 (10)
C(6)–C(7)	1·371 (6)	1·374 (8)	C(12)–N(1)	—	1·468 (7)	C(5′)–C(6′)	1·370 (7)	1·381 (8)
C(7)–C(8)	1·376 (7)	1·371 (8)	H(1)–N(1)	0·88 (5)	—	C(1′)–C(6′)	1·378 (6)	1·381 (7)
C(8)–C(9)	1·362 (6)	1·366 (11)				F–C(2′)	—	1·362 (6)
(*b*) Bond angles (°)								
C(12)–N(1)–C(2)	—	117·7 (5)	C(6)–C(7)–Br	119·8 (4)	—	C(5)–C(1′)–N(2′)	117·0 (4)	—
C(12)–N(1)–C(10)	—	118·4 (5)	C(8)–C(7)–Br	119·8 (3)	—	C(5)–C(1′)–C(2′)	—	122·2 (5)
H(1)–N(1)–C(2)	119 (3)	—	C(6)–C(7)–N(7)	—	119·5 (6)	C(5)–C(1′)–C(6′)	120·7 (4)	121·5 (5)
H(1)–N(1)–C(10)	113 (3)	—	C(8)–C(7)–N(7)	—	118·9 (6)	C(2′)–C(1′)–C(6′)	—	116·2 (5)
C(10)–N(1)–C(2)	127·1 (4)	123·3 (5)	C(7)–N(7)–O(7*A*)	—	118·2 (6)	N(2′)–C(1′)–C(6′)	122·3 (4)	—
N(1)–C(2)–O(2)	122·1 (5)	121·5 (5)	C(7)–N(7)–O(7*B*)	—	118·0 (6)	C(1′)–N(2′)–C(3′)	116·8 (4)	—
N(1)–C(2)–C(3)	114·6 (4)	115·1 (5)	O(7*A*)–N(7)–O(7*B*)	—	123·8 (6)	C(1′)–C(2′)–C(3′)	—	124·4 (6)
C(3)–C(2)–O(2)	123·3 (4)	123·4 (6)	C(7)–C(8)–C(9)	119·5 (4)	118·6 (7)	C(1′)–C(2′)–F	—	117·9 (5)
C(2)–C(3)–N(4)	111·3 (4)	109·9 (5)	C(8)–C(9)–C(10)	121·2 (4)	122·1 (6)	C(3′)–C(2′)–F	—	117·7 (6)
C(3)–N(4)–C(5)	117·4 (4)	116·4 (5)	C(9)–C(10)–C(11)	119·5 (4)	118·6 (6)	C(2′)–C(3′)–C(4′)	—	117·7 (7)
N(4)–C(5)–C(11)	126·1 (4)	124·6 (5)	C(9)–C(10)–N(1)	116·9 (4)	119·3 (5)	N(2′)–C(3′)–C(4′)	124·4 (5)	—
N(4)–C(5)–C(1′)	116·3 (4)	116·4 (5)	C(11)–C(10)–N(1)	123·5 (4)	121·9 (6)	C(3′)–C(4′)–C(5′)	117·8 (5)	120·5 (6)
C(11)–C(5)–C(1′)	117·6 (3)	119·0 (4)	C(10)–C(11)–C(6)	118·1 (4)	119·5 (6)	C(4′) C(5′)–C(6′)	119·2 (5)	120·5 (6)
C(11)–C(6)–C(7)	121·3 (4)	119·5 (5)	C(10)–C(11)–C(5)	122·8 (4)	122·3 (5)	C(5′)–C(6′)–C(1′)	119·4 (5)	120·7 (6)
C(6)–C(7)–C(8)	120·3 (4)	121·6 (6)	C(6)–C(11)–C(5)	119·0 (4)	118·3 (4)			

(*c*) Selected torsion angles (°); e.s.d.'s *ca* 0·6° for bromazepam, 0·8° for flunitrazepam

C(10)–N(1)–C(2)–C(3)	−1·1	−5·8	N(4)–C(5)–C(11)–C(10)	−37·6	−43·0	N(4)–C(5)–C(1′)–C(2′)	—	133·5
N(1)–C(2)–C(3)–N(4)	−70·3	−71·1	C(5)–C(11)–C(10)–N(1)	−1·2	−3·8	C(11)–C(5)–C(1′)–N(2′)	−39·8	—
C(2)–C(3)–N(4)–C(5)	72·3	72·8	C(11)–C(10)–N(1)–C(2)	39·8	47·6	C(11)–C(5)–C(1′)–C(2′)	—	47·6
C(3)–N(4)–C(5)–C(11)	−2·7	2·1	N(4)–C(5)–C(1′)–N(2′)	141·6	—			

36·9 (12)°, respectively, show that in the N(1)-methyl-substituted molecule there is a greater degree of twist out of the benzo plane as noted previously (Chananont *et al.*, 1981). In the methyl-substituted molecule the boat conformation is also distorted to a slightly greater extent from the ideal cycloheptatriene-like shape.

The major conformational difference between the title compounds is in the orientation of the 5-aryl ring. The angle between the mean plane of the 5-aryl ring and the 'benzo' plane is 60·3 (6)° in bromazepam and 75·5 (9)° in flunitrazepam. The latter value falls within the range of angles found in 5-phenyl-1,4-benzodiazepines where the 5-phenyl ring carries an *ortho* substituent and the former is typical of structures containing an unsubstituted 5-phenyl ring (Chananont, Hamor & Martin, 1980).

NMR studies of bromazepam in solution by Sarrazin, Faure, Aubert & Vincent (1980) have led these authors to suggest that the 5-(2-pyridyl) ring is involved in an intramolecular hydrogen bond C(6)—H···N(2′) at room temperature. The present study indicates that in the solid state any such interaction can only be very weak. The pertinent lengths are C(6)···N(2′) 2·996 (7), H(6)···N(2′) 2·65 (5) Å and the H(6)—C(6)···N(2′) angle is 59 (3)° with H(6) displaced by 2·30 (5) Å from the plane of the pyridyl ring. In the solid state N(2′) prefers to form an intermolecular hydrogen bond with N(1) of a centrosymmetrically related molecule, N(1)···N(2′) 3·108 (5), H(1)···N(2′) 2·24 (5) Å, angle H(1)—N(1)···N(2′) 9 (3)°.

Other intermolecular contact distances in this structure, and those in flunitrazepam, correspond to normal van der Waals interactions.

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