Acta Cryst. (1978). B**34**, 3830–3832

8-[1-(4-Methylphenyl)ethyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one ½ Methanol: R 6372*

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(*Received* 29 *July* 1978; *accepted* 1 *September* 1978)

Abstract. $C_{22}H_{27}N_3O.\frac{1}{2}CH_3OH$, triclinic, $P\bar{1}$, a = 17·435 (5), b = 15·390 (5), c = 13·642 (5) Å, α = 129·62 (5), β = 99·27 (5), γ = 114·5 (5)°; D_m = 1·20, D_c = 1·19 g cm^{-3}, Z = 4. The packing is governed by hydrogen bonds.

Introduction. The structure of this compound was investigated as part of a study on the structure–activity relationship of narcotic analgesics. The title compound is 186 times more potent than morphine.

The prismatic crystals were obtained from methanol. The space group was determined from photographs. The cell dimensions and intensities were measured on a Nonius CAD-4 automatic diffractometer. The experimental conditions are given in Table 1.

The intensities were corrected for Lorentz and polarization effects but not for absorption. Scattering factors were from Cromer & Mann (1968) for non-hydrogen atoms and from Stewart, Davidson & Simpson (1965) for H. The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971). The most probable computed phase set permitted the location of 16 of the 26 non-hydrogen atoms for each of the two molecules in the asymmetric unit. The others were found by application of the tangent refinement procedure included in *MULTAN*. The structure was refined with XRAY 72 (Stewart, Kruger, Ammon, Dickinson & Hall, 1972). A difference map revealed the presence of four methanol molecules in the cell. However, from the distance between the C atoms of two neighbouring methanol molecules in the asymmetric unit (which is too short) and from the calculated density, we have supposed only one methanol per asymmetric unit alternately hydrogen-bonded to one of each analgesic molecule. Therefore, the population factor of 0·5 was used for the four methanol molecules in the cell. The positions of 16 H atoms were located on a difference map, those of the others were calculated, but not refined. The final R obtained by a block-diagonal least-squares method is 0·087 for the observed reflexions. The final positional parameters are given in Table 2.†

Table 1. *Experimental conditions*

Source: Cu $K\bar{\alpha}$, λ = 1·5418 Å
Graphite monochromator
Scan: ω–2θ
Confidence level: 2·5σ with $\sigma^2(I) = S + B + (0{\cdot}03S)^2$ (S being the scan and B the background count)
Scanning angle: 0·6 + 0·3 tan θ (°)
$\theta_{\min}$ = 2°; $\theta_{\max}$ = 72°
Aperture: 2·5 + 0·5 tan θ (mm)
Total number of independent reflexions: 6901
Total observed: 3479

Discussion. The packing is essentially due to the following hydrogen bonds: N(18)···O(42) 2·881 Å [O(42): $\bar{x},\bar{y},\bar{z}$] and N(44)···O(20) 2·892 Å [O(20): $\bar{x},\bar{y},\bar{z}$].

In the position x,y,z one molecule of methanol is hydrogen bonded to N(10) and in the position $\bar{x},\bar{y},\bar{z}$, another is hydrogen bonded to N(36): N(10)···O(53)–C(55) 2·979 Å, N(36)···O(54)–C(56) 2·912 Å.

The atomic numbering, the bond distances and angles for non-hydrogen atoms are given in Fig. 1(*a*)–(*d*); for the H atoms, they are included in Table 3. The two molecules of the asymmetric unit are rather similar as can be seen from their main torsion angles in Table 4. Their conformation is shown in Fig. 2. Fig. 3 shows a stereoscopic view of the cell. The five-membered and the 1-phenyl groups are nearly coplanar (4·3°) and perpendicular to the mean plane of the piperidine ring.

This structure is similar to the analogous 8-[(4-methylphenyl)methyl]-1-phenyl-1,3,8-triazaspiro[4.5]-decan-4-one, which is twenty times weaker than the title compound (Humblet, Durant & Evrard, 1976). The conformation difference lies in the orientation of the substituent of the piperidine N atom: the position of the

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* Janssen Pharmaceutica internal code number.

† Lists of structure factors, thermal parameters and positional parameters for H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33853 (70 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Final positional parameters with e.s.d.'s in parentheses*

	x	*y*	*z*		*x*	*y*	*z*
C(1)	0·4726 (10)	−0·1050 (12)	0·1242 (10)	C(29)	0·6061 (7)	0·0193 (10)	−0·4176 (11)
C(2)	0·5404 (8)	0·0581 (10)	0·2217 (13)	C(30)	0·6691 (8)	0·1722 (10)	−0·3272 (11)
C(3)	0·6418 (10)	0·1673 (13)	0·3599 (11)	C(31)	0·7572 (7)	0·2941 (9)	−0·1685 (11)
C(4)	0·7098 (8)	0·3210 (11)	0·4547 (12)	C(32)	0·7819 (8)	0·2585 (11)	−0·1042 (12)
C(5)	0·6765 (7)	0·3686 (9)	0·4144 (10)	C(33)	0·7204 (8)	0·1092 (11)	−0·1924 (12)
C(6)	0·5737 (7)	0·2556 (9)	0·2747 (10)	C(34)	0·8273 (8)	0·4606 (10)	−0·0687 (12)
C(7)	0·5084 (8)	0·1042 (10)	0·1831 (12)	C(35)	0·8504 (17)	0·4895 (19)	−0·1423 (24)
C(8)	0·7539 (8)	0·5354 (10)	0·5165 (11)	N(36)	0·7958 (5)	0·5426 (6)	0·0215 (7)
C(9)	0·7692 (14)	0·5577 (16)	0·4352 (18)	C(37)	0·6881 (6)	0·4708 (8)	−0·0746 (9)
N(10)	0·7486 (5)	0·6403 (7)	0·6436 (7)	C(38)	0·6757 (6)	0·5852 (8)	0·0237 (8)
C(11)	0·7736 (6)	0·6517 (9)	0·7613 (9)	C(39)	0·7147 (5)	0·6624 (7)	0·1893 (8)
C(12)	0·7938 (6)	0·7874 (9)	0·9101 (9)	C(40)	0·8155 (6)	0·6993 (8)	0·2704 (9)
C(13)	0·7060 (6)	0·7848 (7)	0·8738 (8)	C(41)	0·8162 (6)	0·5745 (9)	0·1540 (9)
C(14)	0·6619 (6)	0·7355 (7)	0·7242 (8)	O(42)	0·5849 (4)	0·4240 (6)	0·0836 (8)
C(15)	0·6476 (6)	0·6016 (8)	0·5859 (8)	C(43)	0·6254 (6)	0·5550 (8)	0·1681 (9)
N(16)	0·7355 (5)	0·9307 (6)	1·0127 (7)	N(44)	0·6018 (5)	0·6291 (7)	0·2604 (8)
C(17)	0·6695 (6)	0·9106 (8)	1·0618 (9)	C(45)	0·6566 (6)	0·7799 (8)	0·3396 (10)
N(18)	0·5990 (5)	0·7487 (7)	0·9534 (7)	N(46)	0·7275 (5)	0·7984 (6)	0·2964 (8)
C(19)	0·6132 (6)	0·6727 (8)	0·8462 (9)	C(47)	0·7962 (6)	0·9346 (8)	0·3556 (8)
O(20)	0·5611 (4)	0·5334 (5)	0·7402 (6)	C(48)	0·7979 (6)	1·0518 (8)	0·4594 (9)
C(21)	0·8090 (6)	1·0732 (8)	1·0861 (9)	C(49)	0·8655 (7)	1·1895 (9)	0·5205 (10)
C(22)	0·8773 (6)	1·1039 (8)	1·0468 (9)	C(50)	0·9325 (7)	1·2129 (9)	0·4797 (11)
C(23)	0·9493 (7)	1·2491 (10)	1·1246 (12)	C(51)	0·9306 (7)	1·0973 (9)	0·3768 (10)
C(24)	0·9559 (8)	1·3658 (10)	1·2401 (12)	C(52)	0·8654 (6)	0·9613 (8)	0·3176 (8)
C(25)	0·8917 (8)	1·3381 (10)	1·2825 (12)	O(53)	0·9084 (8)	0·9291 (12)	0·7704 (13)
C(26)	0·8183 (7)	1·1943 (9)	1·2068 (10)	O(54)	1·0433 (11)	1·1852 (16)	0·8670 (7)
C(27)	0·5589 (8)	−0·1791 (10)	−0·4499 (13)	C(55)	0·8594 (10)	0·9439 (15)	0·6933 (15)
C(28)	0·6293 (7)	−0·0133 (9)	−0·3519 (11)	C(56)	0·9339 (9)	1·0658 (13)	0·7231 (14)

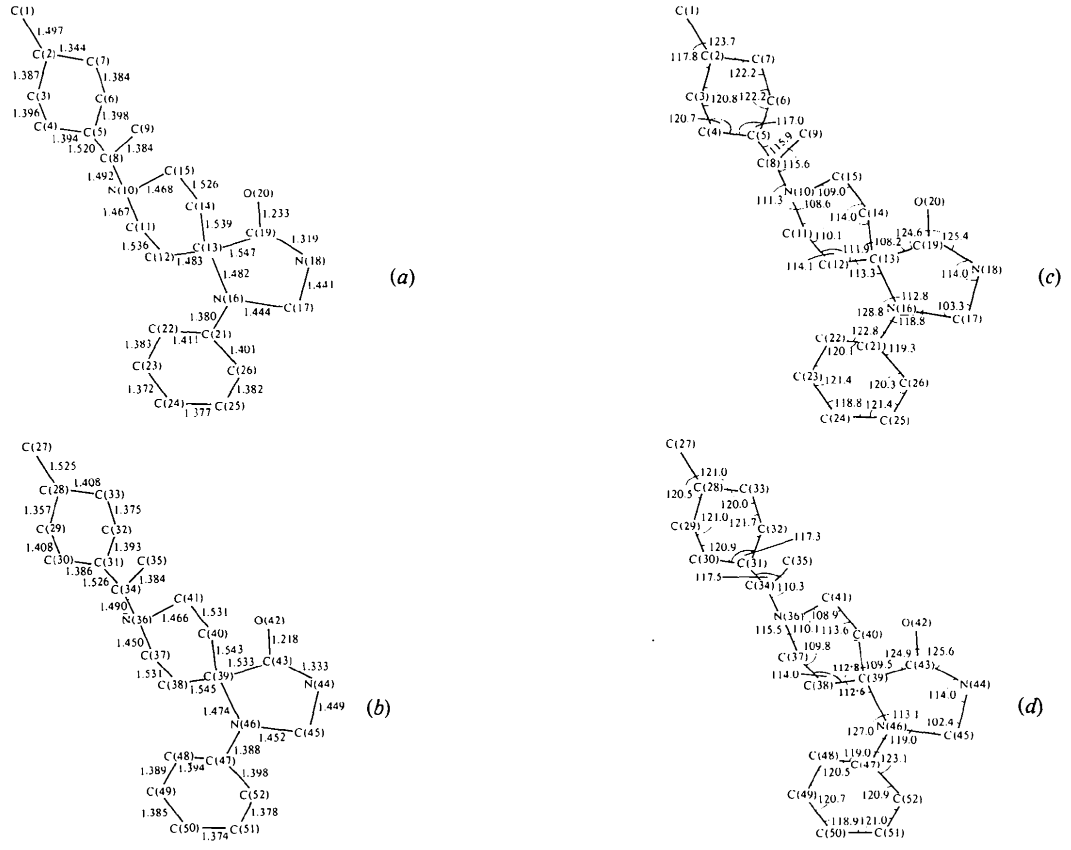

Fig. 1. Bond distances (Å) and angles (°) for non-hydrogen atoms. The e.s.d.'s for the bond lengths are in the range 0·002–0·005 Å and for the angles 0·1–0·3°.

Table 3. *Bond distances* (Å) *and angles* (°) *involving* H *atoms*

The e.s.d.'s for the bond lengths are 0·03 Å and 3° for the angles.

C(1)–H(11)	1·148	C(26)–H(261)	1·171
C(1)–H(12)	1·029	C(29)–H(291)	1·080
C(1)–H(13)	1·030	C(30)–H(301)	1·049
C(3)–H(31)	1·105	C(32)–H(321)	1·067
C(4)–H(41)	1·053	C(37)–H(371)	1·041
C(6)–H(61)	0·947	C(37)–H(372)	1·036
C(7)–H(71)	1·073	C(38)–H(381)	1·042
C(11)–H(111)	1·038	C(38)–H(382)	1·053
C(11)–H(112)	1·045	C(40)–H(401)	1·028
C(12)–H(121)	1·043	C(40)–H(402)	1·032
C(12)–H(122)	1·054	C(41)–H(411)	1·033
C(15)–H(151)	1·027	C(41)–H(412)	1·041
C(15)–H(152)	1·042	N(44)–H(441)	1·058
N(18)–H(181)	0·977	C(45)–H(451)	0·905
C(17)–H(171)	1·093	C(45)–H(452)	1·068
C(17)–H(172)	1·164	C(48)–H(481)	1·040
C(22)–H(221)	1·031	C(49)–H(491)	1·033
C(23)–H(231)	1·054	C(50)–H(501)	1·047
C(24)–H(241)	1·053	C(51)–H(511)	1·043
C(25)–H(251)	1·089	C(52)–H(521)	1·037
H(251)–C(25)–C(26)	117·1	H(11)–C(1)–C(2)	116·1
H(261)–C(26)–C(21)	118·3	H(12)–C(1)–C(2)	112·7
H(291)–C(29)–C(28)	112·1	H(31)–C(3)–C(4)	117·4
H(301)–C(30)–C(29)	148·0	H(41)–C(4)–C(5)	118·5
H(321)–C(32)–C(31)	118·6	H(61)–C(6)–C(7)	115·5
H(331)–C(33)–C(32)	121·2	H(71)–C(7)–C(2)	118·9
H(371)–C(37)–N(36)	109·7	H(111)–C(11)–C(12)	110·9
H(372)–C(37)–N(36)	110·2	H(112)–C(11)–C(12)	109·1
H(381)–C(38)–C(37)	109·2	H(121)–C(12)–C(13)	109·8
H(382)–C(38)–C(37)	109·2	H(122)–C(12)–C(13)	109·2
H(401)–C(40)–C(39)	108·3	H(141)–C(14)–C(15)	109·1
H(402)–C(40)–C(39)	107·5	H(142)–C(14)–C(15)	108·2
H(441)–N(44)–C(43)	119·2	H(151)–C(15)–N(10)	109·5
H(451)–C(45)–N(44)	102·2	H(152)–C(15)–N(10)	108·9
H(452)–C(45)–N(44)	108·8	H(171)–C(17)–C(16)	107·7
H(481)–C(48)–C(47)	119·7	H(172)–C(17)–C(16)	106·7
H(491)–C(49)–C(48)	120·9	H(181)–N(18)–C(19)	115·5
H(501)–C(50)–C(49)	120·3	H(221)–C(22)–C(23)	115·6
H(511)–C(51)–C(50)	118·7	H(231)–C(23)–C(24)	119·0
H(521)–C(52)–C(51)	120·0	H(241)–C(24)–C(25)	121·5

Table 4. *Main torsion angles* (°)

Molecule (1)	
C(4)–C(5)–C(8)–N(10)	−95·7
C(6)–C(5)–C(8)–N(10)	88·0
C(6)–C(5)–C(8)–C(9)	−52·0
C(9)–C(8)–N(10)–C(11)	−158·0
C(9)–C(8)–N(10)–C(15)	77·5
C(14)–C(13)–C(19)–O(20)	62·8
C(12)–C(13)–N(16)–C(21)	67·7
C(13)–N(16)–C(21)–C(22)	−7·2
C(13)–N(16)–C(21)–C(26)	173·9
Molecule (2)	
C(32)–C(31)–C(34)–N(36)	−91·3
C(30)–C(31)–C(34)–N(36)	90·9
C(30)–C(31)–C(34)–C(35)	−41·1
C(35)–C(34)–N(36)–C(41)	−154·5
C(35)–C(34)–N(36)–C(37)	78·3
C(38)–C(39)–C(43)–O(42)	65·2
C(40)–C(39)–C(46)–C(47)	65·4
C(39)–N(46)–C(47)–C(52)	0·8
C(39)–N(46)–C(47)–C(48)	−178·4

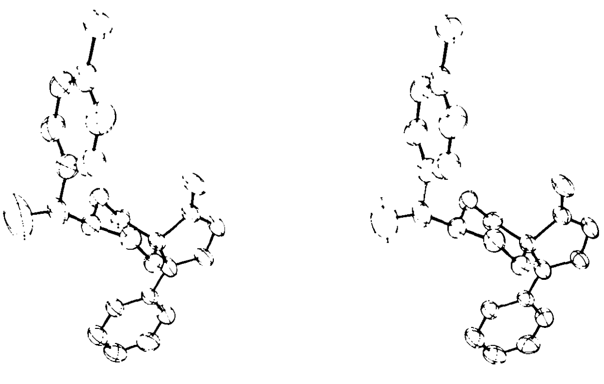

Fig. 2. Stereoscopic view of one molecule with 50% probability ellipsoids.

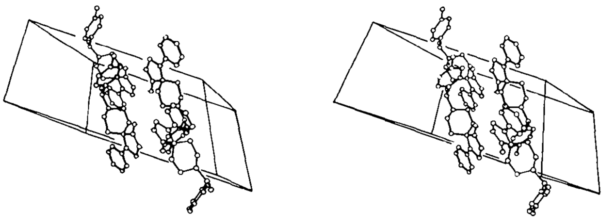

Fig. 3. Stereoscopic view of the packing. The N(18)···O(42) and N(44)···O(20) hydrogen bonds are indicated by dotted lines (methanol molecules are not drawn).

phenyl in the title compound is oriented to the upper part of the piperidine plane. This position seems favourable for activity in this kind of analgesic.

We thank Dr P. A. J. Janssen (Janssen Pharmaceutica, B-2340 Beerse, Belgium) and Dr M. H. J. Koch for providing the sample. One of the authors (CH) would like to thank the Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture (IRSIA) for the award of a doctoral fellowship.

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