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N,N-Dimethylspiro[5*H*-dibenzo[*a,d*]cycloheptene-5,1′-cyclohexane]-4′-amine

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Abstract. *N,N*-Dimethylspiro[5*H*-dibenzo[*a,d*]cycloheptene-5,1′-cyclohexane]-4′-amine, $C_{22}H_{25}N$, $M=303$, monoclinic, *Cc*, $a=6{\cdot}649$ (5), $b=30{\cdot}90$ (2), $c=8{\cdot}477$ (8) Å, $\beta=102{\cdot}41°$, $D_x=1{\cdot}21$, $D_m=1{\cdot}25$ g cm^{-3}, $Z=4$.

Introduction. Prismatic crystals of the free base, grown from diethyl ether, were supplied by Dr N. Stjernstrom of Astra Lakemedel Pharmaceuticals, Sweden. Space group and preliminary cell dimensions were determined photographically. Systematic absences indicated that the space group was *Cc* or *C*2/*c*. Intensity statistics confirmed *Cc*. The intensities were measured up to $2\theta=120°$ on a Picker, card-controlled, 4-circle diffractometer with graphite-monochromated Cu $K\alpha$ radiation ($\lambda=1{\cdot}54178$ Å) in the θ–2θ scan mode at a speed of 2° min^{-1}. 1556 reflexions were recorded of which 623 were $\leq 2\sigma(I)$. These were treated as unobserved. The remaining 933 reflexions were scaled and Lorentz and polarization factors applied.

The structure was solved with reflexions with $E\geq 1{\cdot}2$, by a non-centrosymmetric direct-methods technique involving the use of magic integers (White & Woolfson, 1975) and programmed by G.M.S. 24 *E* maps were generated but only one gave the major part of the molecular structure. Four atoms were poorly defined or absent and were located from a difference map.

The structure was refined by isotropic full-matrix least squares to $R=14{\cdot}0\%$. Further anisotropic refinement gave $R=10{\cdot}2\%$. At this stage a difference map gave the positions of 14 H atoms from which the average C–H distance was determined as 1·05 Å. This value was used to calculate the position of all 25 H atoms, with standard geometry. The H atoms were then included in the refinement with the methyls treated as rigid groups and all other C–H vectors constrained in both magnitude (to 1·05 Å) and direction. Further refinement gave an *R* of 8·9% for 933 reflexions. At this stage a weighting scheme was introduced. The function minimized was $\sum w\{||F_o|-|F_c||\}^2$ where $w=2{\cdot}4585/\sigma^2(F_o)$. The refinement was terminated at $R=8{\cdot}0\%$ and $R_w=8{\cdot}0\%$. Final positional and thermal parameters are given in Tables 1–3†.

Table 1. *Final fractional coordinates for non-hydrogen atoms* ($\times 10^4$), *with estimated standard deviations in parentheses*

	x	*y*	*z*
C(1)	3471 (28)	1532 (4)	7593 (22)
C(2)	3107 (32)	1984 (4)	6833 (23)
C(3)	1487 (30)	2232 (4)	7479 (23)
C(4)	−471 (30)	1959 (4)	7207 (25)
C(5)	−48 (29)	1517 (4)	8030 (21)
C(6)	1517 (31)	1241 (4)	7326 (21)
C(7)	720 (30)	1123 (4)	5525 (22)
C(8)	1991 (30)	1191 (4)	4433 (23)
C(9)	1206 (34)	1098 (4)	2767 (24)
C(10)	−735 (38)	961 (5)	2228 (26)
C(11)	−1993 (33)	878 (5)	3268 (24)
C(12)	−1185 (29)	934 (4)	4979 (23)
C(13)	−2418 (30)	733 (4)	6002 (23)
C(14)	−1739 (29)	561 (4)	7442 (24)
C(15)	348 (32)	526 (4)	8380 (23)
C(16)	818 (33)	156 (4)	9400 (24)
C(17)	2797 (35)	68 (5)	10283 (23)
C(18)	4360 (32)	341 (5)	10084 (22)
C(19)	3979 (30)	720 (4)	9174 (21)
C(20)	1962 (28)	819 (4)	8275 (19)
N(1)	1010 (0)	2665 (3)	6600 (0)
C(21)	2931 (38)	2909 (5)	6595 (31)
C(22)	−355 (37)	2925 (5)	7331 (27)

Discussion. *N,N*-Dimethylspiro[5*H*-dibenzo[*a,d*]cycloheptene-5,1′-cyclohexane]-4′-amine (Fig. 1) a tricyclic antidepressant, is a potent competitive inhibitor of noradrenaline uptake at nerve endings (Carnmalm, Jacupovic, Johansson, De Paulis, Ramsby, Stjernstrom, Renyi, Ross & Ogren, 1974). The analysis reported here is part of a series of investigations in which we attempted to correlate, by a combination of X-ray and pharmacological techniques, the conformational characteristics of tricyclic antidepressants with drug activity (Rodgers, Horn & Kennard, 1975, and references therein). Since most of the antidepressants have

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† A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31577 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. *Anisotropic temperature factors* ($Å^2 \times 10^4$), *with estimated standard deviations in parentheses*

Coefficients in the temperature factor expression:

$$\exp[-2\pi^2(U_{11}h^2a^{*2}+U_{22}k^2b^{*2}+U_{33}l^2c^{*2}+2U_{12}hka^*b^*+2U_{13}hla^*c^*+2U_{23}klb^*c^*)].$$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	44 (8)	44 (8)	47 (8)	6 (6)	7 (6)	−1 (7)
C(2)	52 (9)	42 (8)	63 (10)	6 (7)	14 (7)	−2 (8)
C(3)	61 (9)	44 (8)	49 (9)	−4 (6)	13 (7)	1 (7)
C(4)	49 (9)	36 (7)	77 (11)	2 (7)	21 (8)	−1 (7)
C(5)	52 (9)	26 (7)	61 (9)	−4 (6)	20 (7)	−2 (6)
C(6)	39 (8)	42 (8)	45 (8)	−2 (6)	8 (6)	−8 (6)
C(7)	43 (9)	39 (8)	52 (9)	−6 (6)	7 (7)	3 (7)
C(8)	48 (8)	36 (7)	61 (10)	−6 (7)	5 (7)	0 (6)
C(9)	73 (12)	46 (9)	75 (12)	5 (8)	20 (10)	15 (8)
C(10)	99 (15)	50 (9)	66 (12)	−13 (8)	3 (11)	10 (9)
C(11)	57 (10)	58 (10)	72 (12)	−24 (8)	−1 (9)	9 (8)
C(12)	28 (7)	33 (7)	66 (9)	−9 (6)	1 (6)	2 (6)
C(13)	43 (9)	40 (8)	69 (10)	−27 (7)	14 (7)	−2 (7)
C(14)	41 (9)	43 (8)	80 (11)	−17 (8)	33 (8)	−6 (7)
C(15)	61 (9)	42 (8)	56 (9)	−7 (7)	25 (8)	−2 (8)
C(16)	79 (12)	36 (7)	74 (11)	4 (7)	29 (9)	−8 (8)
C(17)	99 (14)	47 (9)	54 (10)	15 (7)	14 (9)	5 (9)
C(18)	61 (11)	59 (10)	50 (9)	3 (7)	6 (8)	6 (8)
C(19)	63 (10)	41 (8)	42 (8)	−3 (6)	0 (7)	−4 (7)
C(20)	53 (8)	43 (7)	31 (7)	3 (6)	8 (6)	0 (7)
N(1)	85 (9)	32 (6)	84 (9)	17 (6)	27 (8)	8 (7)
C(21)	126 (17)	38 (10)	119 (18)	0 (10)	54 (14)	−9 (11)
C(22)	109 (16)	44 (9)	101 (14)	15 (10)	39 (12)	21 (11)

Table 3. *Final fractional coordinates* ($\times 10^4$) *and isotropic temperature factors* ($Å^2 \times 10^4$) *for the* H *atoms* (*estimated standard deviations are given in parentheses*)

	x	y	z	U
H(011)	4604 (28)	1372 (4)	7077 (22)	2 (20)
H(012)	4040 (28)	1568 (4)	8865 (22)	3 (21)
H(021)	2608 (32)	1952 (4)	5552 (23)	59 (40)
H(022)	4524 (32)	2161 (4)	7105 (23)	111 (56)
H(031)	2051 (30)	2297 (4)	8737 (23)	0 (21)
H(041)	−1612 (30)	2125 (4)	7697 (25)	25 (28)
H(042)	−1029 (30)	1912 (4)	5938 (25)	46 (36)
H(051)	564 (29)	1567 (4)	9291 (21)	11 (24)
H(052)	−1468 (29)	1343 (4)	7871 (21)	21 (26)
H(081)	3526 (30)	1310 (4)	4840 (23)	42 (31)
H(091)	2188 (34)	1138 (4)	1929 (24)	94 (59)
H(101)	−1308 (38)	917 (5)	959 (26)	56 (42)
H(111)	−3546 (33)	773 (5)	2826 (24)	111 (58)
H(131)	−4047 (30)	724 (4)	5539 (23)	59 (40)
H(141)	−2898 (29)	428 (4)	8001 (24)	45 (35)
H(161)	−399 (33)	−62 (4)	9494 (24)	231 (31)
H(171)	3091 (35)	−203 (5)	11086 (23)	56 (36)
H(181)	5914 (32)	259 (5)	10641 (22)	93 (55)
H(191)	5217 (30)	940 (4)	9158 (21)	233 (28)
H(211)	3937 (38)	2729 (5)	6011 (31)	26 (26)
H(212)	3699 (38)	2977 (5)	7813 (31)	38 (38)
H(213)	2514 (38)	3206 (5)	5961 (31)	199 (35)
H(221)	−1828 (37)	2783 (5)	7318 (27)	50 (45)
H(222)	−559 (37)	3230 (5)	6726 (27)	223 (31)
H(223)	456 (37)	2970 (5)	8554 (27)	40 (34)

a highly flexible side chain attached to the flexible tricyclic nucleus, the present comparatively rigid structure is of particular interest.

The molecule is shown in Fig. 2 and bond lengths and angles are given in Tables 4 and 5. The tricyclic nucleus is rigid and the cyclohexane ring takes up a chair conformation. The terminal N is pyramidal, displaced 0·47 Å from the plane of C(3)–C(21)–C(22).

The angle between the mean planes of the benzene rings is 121° and the angle between the mean plane through ring *A* and C(6), C(13) and that through ring

Table 4. *Bond lengths* (Å), *with estimated standard deviations in parentheses*

C(2)—C(1)	1·54 (1)	C(6)—C(1)	1·56 (1)
C(3)—C(2)	1·52 (2)	C(4)—C(3)	1·53 (2)
C(5)—C(4)	1·53 (2)	C(6)—C(5)	1·56 (1)
C(7)—C(6)	1·55 (2)	C(20)–C(6)	1·53 (2)
C(8)—C(7)	1·39 (1)	C(12)–C(7)	1·38 (2)
C(9)—C(8)	1·43 (2)	C(10)–C(9)	1·34 (2)
C(11)–C(10)	1·36 (1)	C(12)–C(11)	1·45 (2)
C(13)–C(12)	1·46 (2)	C(14)–C(13)	1·32 (2)
C(15)–C(14)	1·45 (2)	C(16)–C(15)	1·43 (2)
C(20)–C(15)	1·42 (2)	C(17)–C(16)	1·39 (2)
C(18)–C(17)	1·38 (2)	C(19)–C(18)	1·39 (1)
C(20)–C(19)	1·43 (2)	C(21)–N(1)	1·48 (2)
C(22)–N(1)	1·45 (2)		

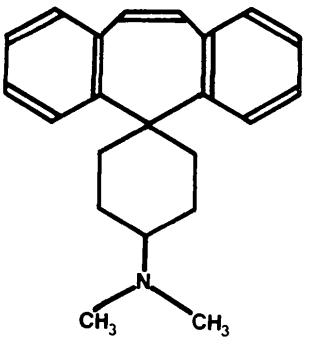

Fig. 1. Chemical formula for *N*,*N*-dimethylspiro[5*H*-dibenzo-[*a*,*d*]cycloheptene-5,1′-cyclohexane]-4′-amine.

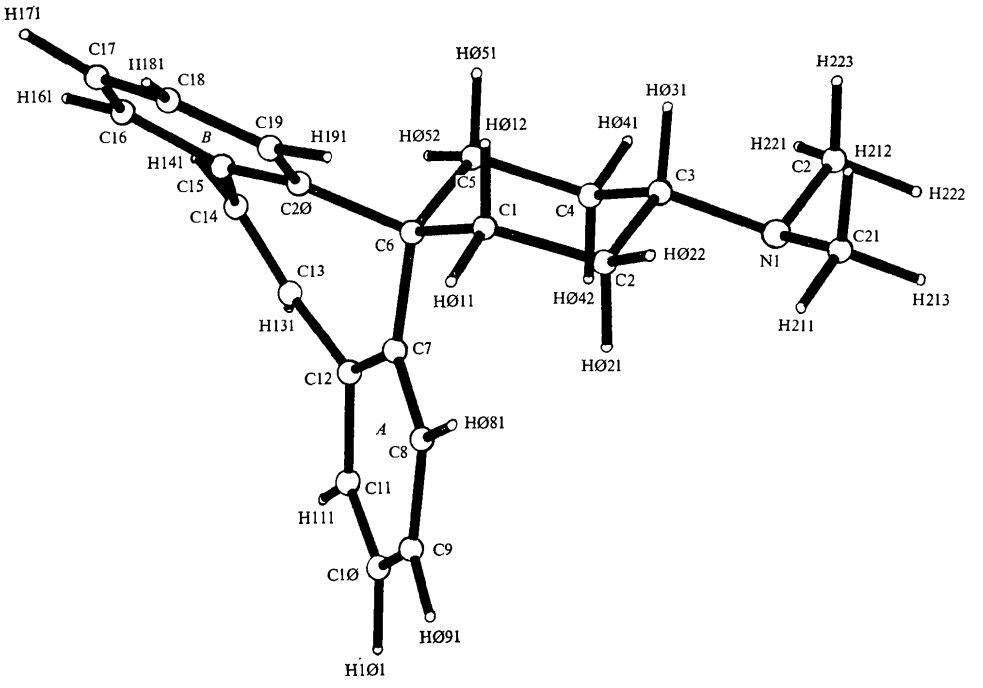

Fig. 2. A general view of *N*,*N*-dimethylspiro[5*H*-dibenzo[*a*,*d*]cycloheptene-5,1′-cyclohexane]-4′-amine.

B and C(6), C(14) is 123°. The deviations of the atoms from these mean planes are given in Table 6. There are no unusually close van der Waals intermolecular contacts.

Table 5. *Valency angles* (°) *with estimated standard deviations in parentheses*

C(6)—C(1)—C(2)	114·4 (1)	C(3)—C(2)—C(1)	111·6 (1)
C(4)—C(3)—C(2)	108·4 (1)	N(1)—C(3)—C(2)	110·7 (1)
N(1)—C(3)—C(4)	109·2 (1)	C(5)—C(4)—C(3)	110·9 (1)
C(6)—C(5)—C(4)	112·7 (1)	C(5)—C(6)—C(1)	103·5 (1)
C(7)—C(6)—C(1)	112·2 (1)	C(7)—C(6)—C(5)	113·0 (1)
C(20)-C(6)—C(1)	110·8 (1)	C(20)-C(6)—C(5)	109·6 (1)
C(20)-C(6)—C(7)	107·8 (1)	C(8)—C(7)—C(6)	119·4 (1)
C(12)-C(7)—C(6)	121·6 (1)	C(12)-C(7)—C(8)	118·9 (1)
C(9)—C(8)—C(7)	118·8 (1)	C(11)-C(10)-C(9)	121·2 (2)
C(12)-C(11)-C(10)	118·6 (2)	C(11)-C(12)-C(7)	120·3 (1)
C(13)-C(12)-C(7)	125·0 (1)	C(13)-C(12)-C(11)	114·3 (1)
C(14)-C(13)-C(12)	126·8 (1)	C(15)-C(14)-C(13)	129·5 (1)
C(16)-C(15)-C(14)	116·9 (2)	C(20)-C(15)-C(14)	124·3 (1)
C(20)-C(15)-C(16)	118·6 (1)	C(17)-C(16)-C(15)	122·7 (2)
C(18)-C(17)-C(16)	117·7 (1)	C(19)-C(18)-C(17)	122·0 (2)
C(20)-C(19)-C(18)	120·9 (1)	C(15)-C(20)-C(6)	120·9 (1)
C(19)-C(20)-C(6)	121·2 (1)	C(19)-C(20)-C(15)	117·7 (1)
C(21)-N(1)—C(3)	110·9 (1)	C(22)-N(1)—C(3)	111·0 (1)

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Table 6. *Distances of atoms from mean planes*

Plane through ring *A* and C(6), C(13)

Equation of plane: $-2{\cdot}76x+27{\cdot}89y-0{\cdot}20z=2{\cdot}79$

Deviations from mean plane (Å)

C(6)	0·11	C(10)	0·05
C(7)	0·04	C(11)	0·12
C(8)	−0·10	C(12)	0·01
C(9)	−0·11	C(13)	0·15

r.m.s. deviation = 0·11 Å

Plane through ring *B* and C(6), C(14)

Equation of plane: $-2{\cdot}52x+15{\cdot}41y+7{\cdot}15z=6{\cdot}7$

Deviations from mean plane (Å)

C(14)	−0·08	C(18)	−0·06
C(15)	0·01	C(19)	−0·03
C(16)	0·05	C(20)	−0·02
C(17)	0·05	C(6)	0·07

r.m.s. deviation = 0·05 Å

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