

Structure of Lythranine–Dimethyl Sulphoxide Monohydrate

BY PHILIP J. COX

School of Pharmacy, Robert Gordon's Institute of Technology, Schoolhill, Aberdeen AB9 1FR, Scotland

AND GEORGE A. SIM

Chemistry Department, University of Glasgow, Glasgow G12 8QQ, Scotland

(Received 23 March 1981; accepted 15 June 1981)

Abstract. $C_{28}H_{37}NO_5 \cdot C_2H_6OS \cdot H_2O$, $P2_1$, $a = 12.227(1)$, $b = 9.969(6)$, $c = 12.528(2)$ Å, $\beta = 92.00(1)^\circ$, $Z = 2$, $D_c = 1.23$ Mg m $^{-3}$, $\mu(\text{Cu } K\alpha) = 1.3$ mm $^{-1}$. The structure was refined to $R = 0.044$ for 2895 reflexions. The lythranine, dimethyl sulphoxide and water molecules are linked together by hydrogen bonds: O(1)H...O(W) 2.67, O(W)H...O(DMS) 2.82, O(W)H...N 2.74 Å. The dihedral angle between the benzene planes in the biphenyl system of the alkaloid is 66°.

Introduction. Lythranine was isolated as one of several biphenyl alkaloids from *Lythrum anceps* Makino (Fujita, Bessho, Fuji & Sumi, 1970). Its absolute stereochemistry was established by X-ray analysis of bromolythranine hydrobromide ethanol solvate (McClure & Sim, 1972). Crystallization of lythranine from aqueous dimethyl sulphoxide led to the formation of an adduct. We undertook a crystal structure analysis of the substance to determine the nature of the adduct and to obtain the conformation of lythranine without a heavy-atom substituent.

The X-ray intensities were collected on an Enraf–Nonius CAD-4 diffractometer with Cu $K\alpha$ radiation. Integrated relative intensities for 3325 independent reflexions were measured as 2θ – ω scans in the range $\theta < 72^\circ$; 2895 reflexions had $I > 2.5\sigma(I)$. The structure was elucidated by direct methods with *MULTAN* (Germain, Main & Woolfson, 1971). The H atoms were located in difference electron density distributions calculated at intermediate stages of structure refinement. The coordinates for all atoms, anisotropic thermal parameters for C, N, S and O and isotropic thermal parameters for the H atoms were varied in least-squares calculations. The parameters were refined in two blocks during the final calculations and convergence was reached at $R = 0.044$.* The weighting

scheme adopted was $w^{-1} = \sigma^2(F_o) + 0.007|F_o|^2$. Calculations were performed with *SHELX* (Sheldrick, 1976).

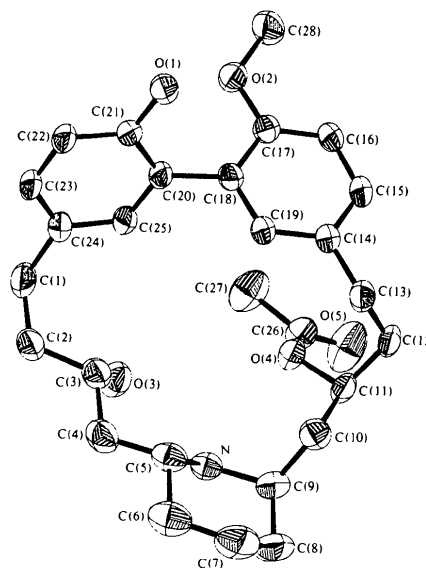


Fig. 1. The atomic arrangement in lythranine.

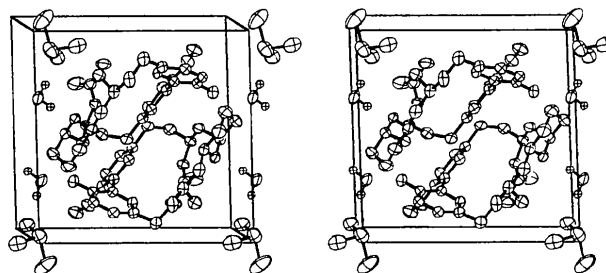


Fig. 2. A stereoscopic view of the crystal structure. **a** is up the page and **c** is to the right.

* Lists of thermal parameters, bond lengths involving hydrogen atoms and structure factors have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36286 (23 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional coordinates* ($\times 10^4$) and *isotropic thermal parameters* ($\text{\AA}^2 \times 10^3$), with *e.s.d.'s* in parentheses

For non-hydrogen atoms $U_{\text{eq}} = \frac{1}{3}(U_{11} + U_{22} + U_{33} + 2U_{13} \cos \beta)$.

	<i>x</i>	<i>y</i>	<i>z</i>	U_{eq}/U
O(1)	2718 (2)	7224 (2)	1961 (1)	47 (1)
O(2)	1427 (2)	4834 (2)	2862 (2)	49 (1)
O(3)	1818 (2)	8683 (2)	7416 (2)	56 (1)
O(4)	3382 (1)	5404 (2)	7277 (1)	40 (1)
O(5)	2552 (2)	3593 (3)	7929 (3)	86 (2)
O(W)	2863 (2)	8868 (3)	294 (2)	63 (1)
N	3890 (2)	8020 (2)	8502 (2)	41 (1)
C(1)	952 (3)	10036 (3)	5456 (2)	57 (2)
C(2)	1868 (3)	10593 (3)	6199 (2)	60 (1)
C(3)	2527 (2)	9523 (3)	6810 (2)	49 (1)
C(4)	3447 (3)	10108 (3)	7518 (2)	54 (1)
C(5)	4346 (2)	9128 (3)	7863 (2)	48 (1)
C(6)	5243 (3)	9821 (4)	8524 (3)	68 (2)
C(7)	6110 (3)	8824 (5)	8937 (3)	71 (2)
C(8)	5593 (3)	7683 (4)	9543 (2)	63 (1)
C(9)	4686 (2)	6988 (3)	8868 (2)	46 (1)
C(10)	5148 (2)	6121 (3)	7970 (2)	48 (1)
C(11)	4444 (2)	4910 (3)	7679 (2)	41 (1)
C(12)	4934 (2)	3985 (3)	6855 (2)	45 (1)
C(13)	5126 (2)	4601 (3)	5758 (2)	43 (1)
C(14)	4124 (2)	4658 (2)	5008 (2)	37 (1)
C(15)	3677 (2)	3483 (3)	4598 (2)	44 (1)
C(16)	2772 (2)	3509 (2)	3881 (2)	43 (1)
C(17)	2309 (2)	4719 (3)	3560 (2)	40 (1)
C(18)	2722 (2)	5929 (2)	3990 (2)	36 (1)
C(19)	3626 (2)	5861 (2)	4707 (2)	37 (1)
C(20)	2216 (2)	7266 (2)	3771 (2)	35 (1)
C(21)	2261 (2)	7892 (2)	2773 (1)	35 (1)
C(22)	1870 (2)	9211 (2)	2657 (2)	38 (1)
C(23)	1436 (2)	9875 (2)	3515 (2)	40 (1)
C(24)	1375 (2)	9276 (2)	4508 (2)	41 (1)
C(25)	1752 (2)	7963 (2)	4607 (2)	39 (1)
C(26)	2517 (2)	4605 (3)	7407 (2)	48 (1)
C(27)	1527 (2)	5134 (4)	6812 (3)	70 (2)
C(28)	1001 (2)	3619 (3)	2416 (3)	59 (1)
S	437 (1)	11215 (1)	-108 (1)	82 (2)
O(DMS)	871 (2)	9913 (3)	-536 (2)	72 (2)
C(29)	164 (3)	12237 (4)	-1248 (3)	82 (2)
C(30)	-962 (5)	10929 (7)	171 (5)	139 (4)
H(O(1))	2714 (28)	7727 (38)	1279 (20)	59 (9)
H(O(3))	1361 (35)	9197 (49)	7897 (32)	90 (14)
H[O(W(1))]	3262 (28)	8560 (42)	-327 (22)	68 (10)
H[O(W(2))]	2241 (27)	9419 (47)	37 (31)	86 (14)
H(N)	3265 (21)	7592 (39)	8088 (24)	55 (9)
H(1A)	452 (36)	10757 (45)	5173 (38)	93 (15)
H(1B)	473 (29)	9428 (38)	5897 (28)	65 (10)
H(2A)	2455 (32)	11058 (52)	5763 (32)	79 (12)
H(2B)	1587 (38)	11073 (52)	6823 (29)	86 (13)
H(3)	2920 (30)	8936 (41)	6283 (26)	66 (10)
H(4A)	3832 (33)	10748 (38)	7064 (30)	74 (12)
H(4B)	3172 (36)	10577 (47)	8168 (27)	81 (13)
H(5)	4633 (22)	8758 (30)	7225 (19)	35 (6)
H(6A)	5496 (50)	10544 (49)	8047 (42)	116 (20)
H(6B)	4929 (28)	10175 (42)	9188 (23)	58 (9)
H(7A)	6605 (33)	9337 (51)	9460 (32)	90 (14)
H(7B)	6461 (28)	8510 (41)	8257 (22)	58 (9)
H(8A)	6173 (35)	7031 (49)	9755 (38)	94 (15)
H(8B)	5286 (27)	8072 (42)	10201 (23)	60 (9)
H(9)	4256 (27)	6386 (36)	9348 (25)	55 (9)
H(10A)	5889 (21)	5789 (39)	8194 (25)	58 (9)
H(10B)	5140 (26)	6690 (33)	7336 (21)	46 (8)
H(11)	4331 (28)	4359 (36)	8325 (23)	55 (9)

Table 1 (cont.)

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i>
H(12A)	4423 (29)	3172 (34)	6863 (31)	69 (11)
H(12B)	5627 (22)	3665 (41)	7201 (25)	56 (9)
H(13A)	5496 (33)	5508 (32)	5857 (32)	72 (11)
H(13B)	5706 (21)	4085 (32)	5412 (21)	39 (7)
H(15)	3929 (26)	2578 (27)	4835 (27)	51 (8)
H(16)	2437 (30)	2681 (33)	3560 (29)	66 (10)
H(19)	3902 (31)	6716 (32)	5084 (29)	66 (11)
H(22)	1882 (25)	9561 (36)	1917 (19)	54 (8)
H(23)	1199 (27)	10817 (25)	3422 (24)	60 (8)
H(25)	1787 (24)	7599 (33)	5309 (18)	51 (7)
H(27A)	1676 (35)	5077 (50)	6040 (17)	94 (5)
H(27B)	909 (28)	4529 (38)	7009 (32)	94 (5)
H(27C)	1356 (38)	6090 (24)	7031 (35)	94 (5)
H(28A)	438 (26)	3957 (52)	1895 (25)	94 (5)
H(28B)	1602 (28)	3186 (48)	2004 (30)	94 (5)
H(28C)	720 (34)	3022 (40)	2987 (26)	94 (5)
H(29A)	-129 (3)	13123 (4)	-1017 (3)	134 (9)
H(29B)	-389 (3)	11785 (4)	-1733 (3)	134 (9)
H(29C)	855 (3)	12378 (4)	-1637 (3)	134 (9)
H(30A)	-1008 (5)	10345 (7)	817 (5)	134 (9)
H(30B)	-1335 (5)	10475 (7)	-454 (5)	134 (9)
H(30C)	-1329 (5)	11806 (7)	307 (5)	134 (9)

Table 2. *Bond lengths* (\AA) with *e.s.d.'s*

O(1)—C(21)	1.353 (3)	C(11)—C(12)	1.523 (4)
O(2)—C(17)	1.369 (3)	C(12)—C(13)	1.531 (4)
O(2)—C(28)	1.425 (3)	C(13)—C(14)	1.519 (3)
O(3)—C(3)	1.441 (3)	C(14)—C(15)	1.384 (3)
O(4)—C(11)	1.462 (3)	C(14)—C(19)	1.391 (3)
O(4)—C(26)	1.339 (3)	C(15)—C(16)	1.401 (4)
O(5)—C(26)	1.202 (4)	C(16)—C(17)	1.386 (4)
N—C(5)	1.484 (4)	C(17)—C(18)	1.408 (3)
N—C(9)	1.478 (3)	C(18)—C(19)	1.401 (3)
C(1)—C(2)	1.535 (5)	C(18)—C(20)	1.491 (3)
C(1)—C(24)	1.515 (4)	C(20)—C(21)	1.400 (3)
C(2)—C(3)	1.526 (4)	C(20)—C(25)	1.394 (3)
C(3)—C(4)	1.524 (4)	C(21)—C(22)	1.405 (3)
C(4)—C(5)	1.522 (4)	C(22)—C(23)	1.384 (3)
C(5)—C(6)	1.517 (5)	C(23)—C(24)	1.384 (3)
C(6)—C(7)	1.530 (5)	C(24)—C(25)	1.392 (3)
C(7)—C(8)	1.518 (6)	C(26)—C(27)	1.495 (4)
C(8)—C(9)	1.536 (4)	S—O(DMS)	1.508 (3)
C(9)—C(10)	1.541 (4)	S—C(29)	1.776 (4)
C(10)—C(11)	1.520 (4)	S—C(30)	1.781 (7)

Table 3. *Non-bonded distances* ($< 3.600 \text{\AA}$)

O(1)⋯O(W)	2.666 (3) \text{\AA}	O(1)⋯O(2)	3.093 (3) \text{\AA}
O(W)⋯H(O(1))	1.69 (3)	O(W)⋯C(21)	3.361 (3)
O(W)⋯O(DMS)	2.815 (3)	O(W)⋯C(22)	3.257 (3)
O(DMS)⋯H[O(W(2))]	1.87 (3)	C(17)⋯C(25)	3.564 (3)
O(3)⋯N	2.910 (3)	C(19)⋯C(21)	3.532 (3)
O(3)⋯H(N)	2.22 (3)	O(1)⋯C(6 ^{III})	3.526 (4)
O(4)⋯N	3.078 (3)	O(3)⋯C(28 ^{IV})	3.461 (3)
O(4)⋯H(N)	2.41 (4)	O(5)⋯C(29 ^V)	3.410 (5)
O(W)⋯N ^I	2.744 (3)	O(W)⋯C(9 ^I)	3.457 (4)
N⋯H[O(W(1 ^{II}))]	1.76 (3)	C(21)⋯C(29 ^{VI})	3.532 (4)
O(3)⋯O(DMS ^{II})	3.104 (3)	C(22)⋯C(29 ^{VI})	3.587 (5)
O(DMS)⋯H(O(3 ^{II}))	2.19 (4)		

The superscripts refer to the following transformations of the atomic coordinates

(I)	$x, y, -1 + z$	(IV)	$-x, \frac{1}{2} + y, 1 - z$
(II)	$x, y, 1 + z$	(V)	$x, -1 + y, z$
(III)	$1 - x, -\frac{1}{2} + y, 1 - z$	(VI)	$-x, -\frac{1}{2} + y, -z$

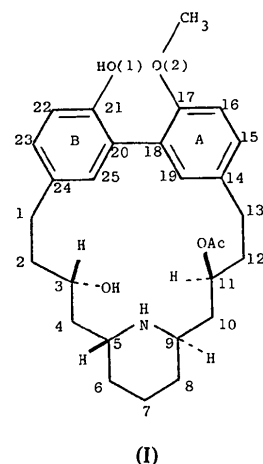
Table 4. Valency angles ($^{\circ}$) with *e.s.d.*'s

C(20)–C(21)–O(1)	118.8 (2)	C(22)–C(21)–O(1)	122.1 (2)
C(28)–O(2)–C(17)	116.6 (2)	C(16)–C(17)–O(2)	124.2 (2)
C(18)–C(17)–O(2)	115.9 (2)	C(2)–C(3)–O(3)	110.7 (2)
C(4)–C(3)–O(3)	111.2 (2)	C(26)–O(4)–C(11)	117.0 (2)
C(10)–C(11)–O(4)	107.7 (2)	C(12)–C(11)–O(4)	109.7 (2)
O(5)–C(26)–O(4)	123.5 (2)	C(27)–C(26)–O(4)	111.0 (2)
C(27)–C(26)–O(5)	125.4 (3)	C(9)–N–C(5)	115.4 (2)
C(4)–C(5)–N	110.5 (2)	C(6)–C(5)–N	108.8 (2)
C(8)–C(9)–N	108.2 (3)	C(10)–C(9)–N	114.7 (2)
C(24)–C(1)–C(2)	113.2 (2)	C(3)–C(2)–C(1)	114.4 (2)
C(23)–C(24)–C(1)	121.3 (2)	C(25)–C(24)–C(1)	121.4 (2)
C(4)–C(3)–C(2)	113.0 (2)	C(5)–C(4)–C(3)	115.5 (2)
C(6)–C(5)–C(4)	111.3 (3)	C(7)–C(6)–C(5)	111.6 (3)
C(8)–C(7)–C(6)	111.1 (3)	C(9)–C(8)–C(7)	111.6 (3)
C(10)–C(9)–C(8)	112.3 (2)	C(11)–C(10)–C(9)	113.7 (2)
C(12)–C(11)–C(10)	114.3 (2)	C(13)–C(12)–C(11)	116.2 (2)
C(14)–C(13)–C(12)	115.1 (2)	C(15)–C(14)–C(13)	119.8 (2)
C(19)–C(14)–C(13)	122.4 (2)	C(19)–C(14)–C(15)	117.8 (2)
C(16)–C(15)–C(14)	121.0 (2)	C(18)–C(19)–C(14)	122.9 (2)
C(17)–C(16)–C(15)	120.5 (2)	C(18)–C(17)–C(16)	119.8 (2)
C(19)–C(18)–C(17)	117.9 (2)	C(20)–C(18)–C(17)	123.7 (2)
C(20)–C(18)–C(19)	118.3 (2)	C(21)–C(20)–C(18)	122.3 (2)
C(25)–C(20)–C(18)	119.0 (2)	C(25)–C(20)–C(21)	118.6 (2)
C(22)–C(21)–C(20)	119.1 (2)	C(24)–C(25)–C(20)	123.0 (2)
C(23)–C(22)–C(21)	120.4 (2)	C(24)–C(23)–C(22)	121.7 (2)
C(25)–C(24)–C(23)	117.2 (2)	C(29)–S–O(DMS)	105.4 (2)
C(30)–S–O(DMS)	106.5 (2)	C(30)–S–C(29)	95.4 (3)

Table 5. Torsion angles ($^{\circ}$) with *e.s.d.*'s

C(28)–O(2)–C(17)–C(16)	–2.6 (3)	C(28)–O(2)–C(17)–C(18)	179.8 (2)
C(26)–O(4)–C(11)–C(10)	–151.9 (2)	C(26)–O(4)–C(11)–C(12)	83.2 (2)
C(11)–O(4)–C(26)–O(5)	8.3 (4)	C(11)–O(4)–C(26)–C(27)	–171.1 (2)
C(9)–N–C(5)–C(4)	179.0 (2)	C(9)–N–C(5)–C(6)	–58.5 (3)
C(5)–N–C(9)–C(8)	58.3 (3)	C(5)–N–C(9)–C(10)	67.8 (3)
C(24)–C(1)–C(2)–C(3)	–68.4 (3)	C(2)–C(1)–C(24)–C(23)	–99.0 (3)
C(2)–C(1)–C(24)–C(25)	78.8 (3)	C(1)–C(2)–C(3)–O(3)	–56.0 (3)
C(1)–C(2)–C(3)–C(4)	178.5 (2)	O(3)–C(3)–C(4)–C(5)	73.7 (3)
C(2)–C(3)–C(4)–C(5)	–161.1 (2)	C(3)–C(4)–C(5)–N	–61.4 (3)
C(3)–C(4)–C(5)–C(6)	177.6 (3)	N–C(5)–C(6)–C(7)	54.1 (3)
C(4)–C(5)–C(6)–C(7)	176.1 (3)	C(5)–C(6)–C(7)–C(8)	–54.3 (4)
C(6)–C(7)–C(8)–C(9)	54.5 (4)	C(7)–C(8)–C(9)–N	–54.7 (3)
C(7)–C(8)–C(9)–C(10)	72.8 (3)	N–C(9)–C(10)–C(11)	–86.5 (3)
C(8)–C(9)–C(10)–C(11)	149.5 (2)	C(9)–C(10)–C(11)–O(4)	62.5 (3)
C(9)–C(10)–C(11)–C(12)	–175.5 (2)	O(4)–C(11)–C(12)–C(13)	59.3 (3)
C(10)–C(11)–C(12)–C(13)	–61.7 (3)	C(11)–C(12)–C(13)–C(14)	–81.6 (3)
C(12)–C(13)–C(14)–C(15)	–68.4 (3)	C(12)–C(13)–C(14)–C(19)	111.7 (3)
C(13)–C(14)–C(15)–C(16)	–178.2 (2)	C(19)–C(14)–C(15)–C(16)	1.7 (4)
C(13)–C(14)–C(19)–C(18)	178.0 (2)	C(15)–C(14)–C(19)–C(18)	–1.9 (3)
C(14)–C(15)–C(16)–C(17)	0.5 (4)	C(15)–C(16)–C(17)–O(2)	179.9 (2)
C(15)–C(16)–C(17)–C(18)	–2.6 (4)	O(2)–C(17)–C(18)–C(19)	–179.9 (2)
O(2)–C(17)–C(18)–C(20)	3.5 (3)	C(16)–C(17)–C(18)–C(19)	2.4 (3)
C(16)–C(17)–C(18)–C(20)	–174.2 (2)	C(17)–C(18)–C(19)–C(14)	–0.1 (3)
C(20)–C(18)–C(19)–C(14)	176.7 (2)	C(17)–C(18)–C(20)–C(21)	–70.8 (3)
C(17)–C(18)–C(20)–C(25)	114.0 (2)	C(19)–C(18)–C(20)–C(21)	112.6 (2)
C(19)–C(18)–C(20)–C(25)	–62.6 (3)	C(18)–C(20)–C(21)–O(1)	4.3 (3)
C(18)–C(20)–C(21)–C(22)	–173.2 (2)	C(25)–C(20)–C(21)–O(1)	179.5 (2)
C(25)–C(20)–C(21)–C(22)	2.0 (3)	C(18)–C(20)–C(25)–C(24)	172.4 (2)
C(21)–C(20)–C(25)–C(24)	–2.9 (3)	O(1)–C(21)–C(22)–C(23)	–178.2 (2)
C(20)–C(21)–C(22)–C(23)	–0.7 (3)	C(21)–C(22)–C(23)–C(24)	0.3 (3)
C(22)–C(23)–C(24)–C(1)	176.8 (2)	C(22)–C(23)–C(24)–C(25)	–1.1 (3)
C(1)–C(24)–C(25)–C(20)	–175.4 (2)	C(23)–C(24)–C(25)–C(20)	2.5 (3)

Discussion. Atomic coordinates, bond lengths, short non-bonded distances, valency angles and torsion angles are listed in Tables 1–5. Fig. 1 presents a general view of the molecule and the crystal structure is shown in Fig. 2. The relative stereochemistry found for lythranine (I) is consistent with the results obtained for bromolythranine.



The lythranine, dimethyl sulphoxide and water molecules of the asymmetric unit are linked by hydrogen bonds, O(1)···O(W) 2.67 and O(W)···O(DMS) 2.82 Å; the corresponding angles are O(1)–H[O(1)]···O(W) 166 (3) and O(W)–H[O(W2)]···O(DMS) 161 (4) $^{\circ}$. A further intermolecular hydrogen bond links the lythranine and water molecules in adjacent asymmetric units O(W)···N^I 2.74 Å, O(W)–H[O(W1)]···N^I 176 (3) $^{\circ}$. The intermolecular separation O(3)···O(DMS)ⁱⁱ = 3.10 Å is also short.

The biphenyl moiety is considerably skewed about the C(18)–C(20) bond to relieve unfavourable steric interaction between O(1) and O(2). The dihedral angle between the mean planes of the benzene rings is 66 $^{\circ}$ and the O(1)···O(2) distance is 3.09 Å; in bromolythranine hydrobromide, where Br is attached to C(22), the corresponding results are 75 $^{\circ}$ and 3.39 Å. The central C(18)–C(20) bond is bent from the plane of ring B, since C(18) and C(15) are displaced to the same side of that ring by 0.16 and 0.52 Å; the displacement of the C(18)–C(20) bond from the plane of ring A is smaller, with C(20) and C(23) deviating by only 0.11 and 0.30 Å from that plane. Similar features were observed in bromolythranine. The biphenyl systems in lythranine IV (Barrow, Cradwick & Sim, 1974) and bromomyricanol (Begley, Campbell, Crombie, Tuck & Whiting, 1971) have shorter *meta,meta*' bridges and show evidence of greater strain.

The molecular conformation of (I) is very similar to that reported for bromolythranine. Within the macrocycle many of the corresponding torsion angles in the C(20)···N and C(18)···N branches are alike. The pair C(1)–C(2)–C(3)–C(4) 179 $^{\circ}$ and C(10)–C(11)–C(12)–C(13) –62 $^{\circ}$ provides an exception, indicating a departure from C₂ symmetry. The short O(3)···N = 2.91 and O(4)···N = 3.08 Å separations indicate possible intramolecular hydrogen bonding but the O(3)···H(N) = 2.22 and O(4)···H(N) = 2.41 Å separations are long.

The piperidine ring has a chair conformation, $\Delta C_s(N) = 0.4^\circ$, with torsion angles about the C—C bonds in the range $54.1 - 54.7^\circ$ and those about the C—N bonds a little larger, 58.3 and 58.5° .

The dimethyl sulphoxide molecule is nonplanar, with the S atom displaced 0.72 \AA from the plane through the O and C atoms.

References

BARROW, M. J., CRADWICK, P. D. & SIM, G. A. (1974). *J. Chem. Soc. Perkin Trans. 2*, pp. 1812–1818.

BEGLEY, M. J., CAMPBELL, R. V. M., CROMBIE, L., TUCK, B. & WHITING, D. A. (1971). *J. Chem. Soc. C*, pp. 3634–3642.

FUJITA, E., BESSHO, K., FUJI, K. & SUMI, A. (1970). *Chem. Pharm. Bull.* **18**, 2216–2223.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst. A* **27**, 368–376.

MCCLURE, R. J. & SIM, G. A. (1972). *J. Chem. Soc. Perkin Trans. 2*, pp. 2073–2076.

SHELDRIK, G. M. (1976). *SHELX 76*. A program for crystal structure determination. Univ. of Cambridge, England.

Acta Cryst. (1982). **B38**, 306–308

(S)- α -Methyl-N-(phenylmethyl)benzenepropanamine Hydrochloride [(S)-N-Benzyl-1-methyl-3-phenylpropylamine Hydrochloride]: Determination of Absolute Configuration

BY PETER MURRAY-RUST AND JUDITH MURRAY-RUST

Department of Chemistry, University of Stirling, Stirling FK9 4LA, Scotland

AND DAVID HARTLEY AND JIM CLIFTON

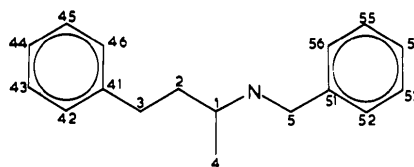
Glaxo Group Research Ltd, Ware, Hertfordshire SG12 0DG, England

(Received 29 April 1981; accepted 18 June 1981)

Abstract. $C_{17}H_{22}N^+.Cl^-$, $M_r = 275.82$, monoclinic, $P2_1$, $a = 5.56$ (3), $b = 9.97$ (3), $c = 14.41$ (5) \AA , $\beta = 80.42$ (2) $^\circ$ from diffractometer measurements (Cu $K\alpha$ radiation), $V = 787.8 \text{ \AA}^3$, $Z = 2$, $D_c = 1.16 \text{ Mg m}^{-3}$, $F(000) = 320$, $\mu = 2.023 \text{ mm}^{-1}$, approximate crystal dimensions $0.6 \times 0.5 \times 0.4 \text{ mm}$. Final $R = 0.044$ for 2289 observed reflexions. The absolute configuration is confirmed as *S*.

Introduction. The resolution of racemic 1-methyl-3-phenylpropylamine has been reported on three occasions by Dutch (van Dijk, Keizer & Moed, 1963), Russian (Potapov, Dem'yanovitch & Terent'ev, 1964), and Czech (Cervinka, Kroupova & Belovsky, 1968) workers. The Dutch and Czech groups attempted to establish the absolute configuration of the (+)-enantiomer by degradation to compounds with known absolute configuration but they arrived at opposite conclusions. The Russians, by studying the optical rotatory dispersion curves of (+)-1-methyl-3-phenylpropylamine and its *N*-benzyl derivative, came to the same conclusion as the Dutch group that the (+)-enantiomer has an *S* configuration.

In order to provide unequivocal evidence for this assignment the title compound (I) was prepared from (+)-1-methyl-3-phenylisopropylamine, by reductive alkylation with benzaldehyde in the presence of hydrogen and a platinum-on-carbon catalyst, followed by conversion into the hydrochloride. Recrystallization from ether–methylene chloride provided a crystal suitable for X-ray crystallography, m.p. $459\text{--}460.5 \text{ K}$, $[\alpha]_D^{21^\circ C} = -7.4^\circ$ (c 5.7 g dm^{-3} , MeOH). [The change in the sign of rotation occurred on forming the hydrochloride in an analogous manner to that observed in converting (+)-1-methyl-3-phenylisopropylamine $\{[\alpha]_D +2.7^\circ$ (c 9.5 g dm^{-3} EtOH) $\}$ into (–)-1-methyl-3-phenylpropylamine hydrochloride $\{m.p. 386\text{--}387 \text{ K}$, $[\alpha]_D -7.2^\circ$ (c 5.8 g dm^{-3} , H_2O) (van Dijk *et al.*, 1963)}].



(I)