

The Structure of the Bisbenzylisoquinoline Alkaloid Dimethylwarifteine

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The crystal structure of the bisbenzylisoquinoline alkaloid dimethylwarifteine, $C_{38}H_{40}N_2O_6$, has been determined by direct methods. The compound crystallizes in the orthorhombic space group $P2_12_12_1$, with $a = 14.714(4)$, $b = 14.827(4)$, $c = 15.365(4)$ Å, $Z = 4$. The structure was refined to a final R value of 0.073, for the 1514 non-zero reflections measured by diffractometry. In the isoquinoline groups the phenyls are planar and the nitrogen-containing rings are in different half-chair conformations, with the pseudo twofold axis parallel to the length of the tetrahydroisoquinoline ring and bisecting two C–C bonds of the dihydroisoquinoline ring. The benzyltetrahydroisoquinoline residue is in an extended conformation while the benzyl-dihydroisoquinoline residue is folded. The two halves of the molecule thus formed are joined by an ether linkage on one side and a methoxy linkage on the other side. The dihedral angle between the two benzyl groups is 53.1° .

Introduction

Dimethylwarifteine, $C_{38}H_{40}N_2O_6$, Fig. 1, (hereinafter denoted DMW) is one of the bisbenzylisoquinoline alkaloids isolated from the dried rhizomes of the plant *Cissampelos ovalifolia* D.C. (Gorinsky, Colyer & Walker, 1970). Chemical and mass spectral studies (Snedden, Parker & Gorinsky, 1970) have shown DMW to be identical with *O*-methylcissampereine, extracted from the related plant *Cissampelos pareira* Linn. (Kupchan, Patel & Fujita, 1965). Chemical analysis has shown that the absolute configuration for DMW is as shown in Fig. 1 (Kupchan, Kubota, Fujita, Kobayashi, Block & Telang, 1966). The curari-form activity of DMW is under investigation (Gorinsky & Willman, 1970).

Experimental

DMW crystallizes from a 1:1 mixture of benzene and diethyl ether plus a drop of dimethylformamide per

2 cm³ of mixture, as colourless needles elongated along **b** (Reynolds, 1974). The orthorhombic symmetry and space group were determined from rotation and Weissenberg photographs (Reynolds, 1974). The unit-cell dimensions and their estimated standard deviations (Table 1) were determined by the least-squares refinement of the θ values of 20 reflections measured on a four-circle diffractometer.

Intensities were collected on a Hilger & Watts Y290 computer-controlled four-circle diffractometer, using Cu $K\alpha$ radiation and the ω - 2θ scanning technique. The counts were recorded in 80 steps at intervals of $\theta = 0.01^\circ$, the count time per step being 2s. The background on each side was estimated in a single step count of 16s. The unusually long counting time was necessary because of the small crystal size (Table 1). Even so only 1514 reflections with significant intensities were recorded. Larger crystals were not available.

Reflections were measured out to a maximum θ value of 70° . 4732 reflections were measured, including 805 symmetry-related pairs. Of the 3927 unique reflections, 2413 with $I \leq 3\sigma(I)$ were classified as unobserved.

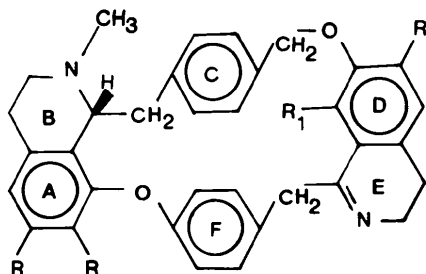


Fig. 1. The structural formula of DMW.

Table 1. Crystal data for DMW

Molecular formula: $C_{38}H_{40}N_2O_6$	Crystal size: 0.2×0.2 $\times 0.1$ mm
Crystal system: orthorhombic	ω axis: b
Space group: $P2_12_12_1$	$a = 14.714(4)$ Å
FW 620.751	$b = 14.827(4)$
$V = 3351$ Å ³	$c = 15.365(4)$
$Z = 4$	Systematic absences
$D_c = 1.229$ g cm ⁻³	$h00: h = 2n + 1$
$F(000) = 1320$	$0k0: k = 2n + 1$
$\lambda(\text{Cu } K\alpha_1) = 1.5405$ Å	$00l: l = 2n + 1$
$\mu(\text{Cu } K\alpha) = 5.5$ cm ⁻¹	

Table 2. Starting set (A), using E values from Wilson plot

Reflection $h\ k\ l$	E	Phase ($^{\circ}$)
0 3 1	2.62	90
3 6 0	2.35	90
2 11 0	2.19	360
2 8 13	2.88	45, 135, 225, 315
2 3 14	2.45	45, 135, 225, 315
3 0 2	3.44	360 Enantiomorph

Periodic checks on three reference reflections showed no significant change over a 10d period of data collection. Lorentz and polarization corrections were applied but no absorption correction was made [$\mu(\text{Cu } K\alpha) = 5.5 \text{ cm}^{-1}$].

Structure determination and refinement

The structure was solved with difficulty by direct methods, using the program *MULTAN 74* (Germain, Main & Woolfson, 1971). Solution of the phase problem proved unusually difficult and the phase determination had to be supplemented by the application of the recycling procedure of Karle (1968), for complete structure determination. Several starting sets had to be tried, using different numbers of E values for the various sets. After many attempts the starting set of phases given in Table 2 was expanded, using 145 E values with $E \geq 1.87$ and 579 Σ_2 relationships, to give 16 phase sets. Several phase sets with high FOM (1.1 to 1.0) and low R_{Karle} (22.4 to 28.8) were used in the calculation of E maps, but this failed to reveal any semblance of the structure. Finally an E map (A) was calculated with phase set 3 (FOM = 0.95 and $R_{\text{Karle}} = 31.7$); this showed six peaks in a fairly sensible chemical configuration. Phases were computed for these six positions but the extension of this information by the tangent formula did not reveal any more of the structure.

E values were then recalculated, using molecular scattering factors (Debye curve, Fig. 2) for the six peaks located from E map (A). Using 145 E values with $E \geq 1.86$ and 521 Σ_2 relationships, 64 phase sets were generated. The starting set (Table 3), having the highest FOM (1.28) and $R_{\text{Karle}} = 23.6\%$, gave E map (B), from which 12 peaks separated by reasonable distances and angles could be chosen for use in the recycling procedure; two of these 12 also appeared in E map (A). Structure factors were calculated from these 12 initial positions, employing an overall temperature factor of $B = 3.60 \text{ \AA}^2$. The criterion for accepting a phase was $|F_{\text{h}}^{\text{calc}}| \geq 0.29 |F_{\text{h}}^{\text{obs}}|$, where $|F_{\text{h}}^{\text{obs}}|$ was associated with an $|E|_{\text{obs}} \geq 1.95$. In this way 100 phases were obtained, which were expanded

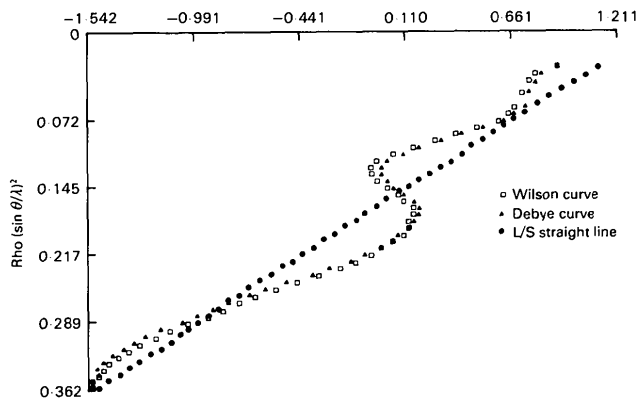


Fig. 2. Plot of the Debye (six-atom fragment) and Wilson curves and least-squares straight line through Debye points. The effect on the E values resulting from the use of partial molecular scattering (Debye) may be seen in Tables 2 and 3.

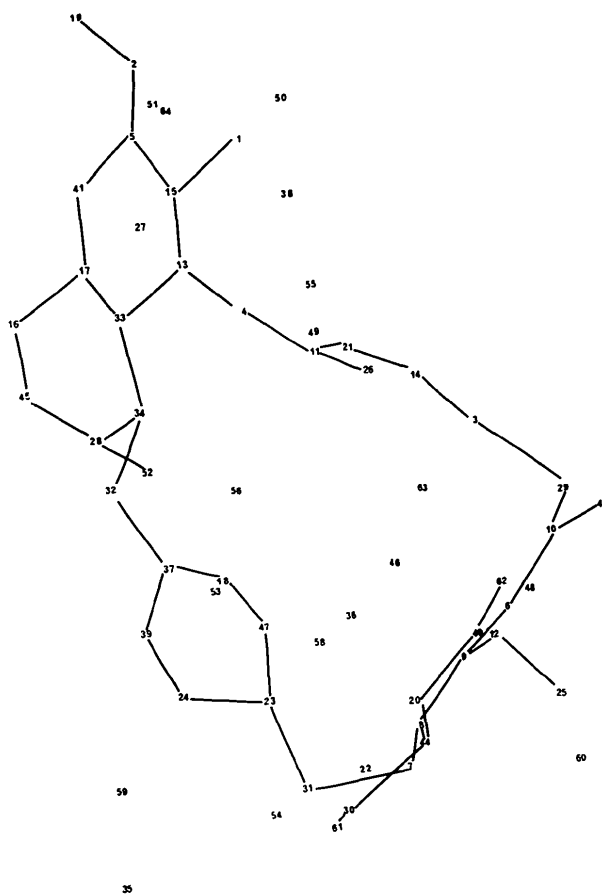


Fig. 3. A representation of the computer output produced by the *SFCALC* routine of *MULTAN 74*. Peaks in atomic positions are shown connected, other peaks are spurious.

Table 3. Starting set (B), using E values from Debye curve

Reflection h k l	E	Phase (°)	
5 0 5	2.68	90	} Origin
0 11 2	2.65	90	
0 3 1	2.25	90	
2 3 14	2.42	45, 135, 225, 315	
7 2 12	2.62	45, 135, 225, 315	
3 3 1	2.43	45, 135, 225, 315	
3 0 2	3.11	360 Enantiomorph	

Table 4 (cont.)

	x	y	z
C(35)	0.9460(10)	0.3879(11)	0.1606(9)
C(36)	0.9960(10)	0.3682(14)	0.0840(11)
C(37)	0.8245(10)	0.4732(9)	0.2388(8)
C(38)	1.3052(8)	0.4178(9)	0.0190(9)
N(1)	0.7904(10)	0.6345(8)	0.2121(6)
N(2)	1.3203(9)	0.7103(9)	0.1258(7)
O(1)	0.8618(6)	0.6549(6)	0.6235(5)
O(2)	0.9816(5)	0.5409(7)	0.5567(6)
O(3)	0.9727(6)	0.4915(5)	0.3861(5)
O(4)	1.2289(5)	0.4531(6)	0.0629(5)
O(5)	1.0393(9)	0.5635(9)	-0.1603(6)
O(6)	1.1166(6)	0.4244(7)	-0.0776(6)

Table 4. Final atomic parameters

E.s.d.'s for heavy-atom coordinates are shown in parentheses. The coordinates for the H atoms marked with an asterisk were calculated. The remaining H atoms were located from a difference Fourier synthesis. U^2 is the mean-square amplitude of atomic vibration (\AA^2).

	x	y	z	U^2
C(1)	0.9150(7)	0.5778(7)	0.5017(5)	0.045
C(2)	0.8546(8)	0.6394(9)	0.5377(7)	0.035
C(3)	0.7913(9)	0.6745(8)	0.4848(7)	0.065
C(4)	0.7855(7)	0.6543(9)	0.3943(6)	0.065
C(5)	0.8472(8)	0.5912(6)	0.3602(6)	0.048
C(6)	0.9104(8)	0.5539(7)	0.4173(8)	0.046
C(7)	0.8451(9)	0.5727(9)	0.2620(8)	0.042
C(8)	0.7034(11)	0.6515(11)	0.2545(8)	0.047
C(9)	0.7169(9)	0.6980(9)	0.3384(8)	0.078
C(10)	0.8396(13)	0.7160(16)	0.1923(8)	0.078
C(11)	0.9615(15)	0.4560(12)	0.5925(15)	0.084
C(12)	0.8045(9)	0.7219(9)	0.6621(7)	0.084
C(13)	1.0499(8)	0.5192(7)	0.3420(6)	0.049
C(14)	1.0505(7)	0.4493(9)	0.3258(9)	0.060
C(15)	1.1891(10)	0.4657(11)	0.2770(11)	0.060
C(16)	1.2074(7)	0.5515(8)	0.2472(6)	0.043
C(17)	1.1484(8)	0.6207(11)	0.2700(6)	0.050
C(18)	1.0669(8)	0.6059(7)	0.3187(7)	0.058
C(19)	1.2942(8)	0.5725(8)	0.1964(7)	0.071
C(20)	1.2762(9)	0.6366(9)	0.1204(8)	0.043
C(21)	1.2996(15)	0.7732(9)	0.0573(12)	0.079
C(22)	1.2053(19)	0.7814(12)	0.0286(12)	0.079
C(23)	1.1710(10)	0.6850(10)	0.0007(9)	0.079
C(24)	1.2131(8)	0.6137(8)	0.0487(8)	0.089
C(25)	1.1899(7)	0.5260(9)	0.0230(6)	0.089
C(26)	1.1322(9)	0.5105(10)	-0.0454(7)	0.089
C(27)	1.0935(9)	0.5850(12)	-0.0909(8)	0.045
C(28)	1.1162(12)	0.6693(11)	-0.0650(9)	0.045
C(29)	1.0069(13)	0.6326(17)	-0.2151(11)	0.087
C(30)	1.0291(9)	0.3902(11)	-0.0802(11)	0.087
C(31)	0.9736(8)	0.4058(8)	0.0052(9)	0.087
C(32)	0.9002(9)	0.4663(8)	0.0028(9)	0.060
C(33)	0.8489(10)	0.4848(8)	0.0760(9)	0.060
C(34)	0.8766(9)	0.4466(8)	0.1570(7)	0.060
H(3)	0.7421	0.7277	0.5021	0.045
H(7)	0.9122	0.5842	0.2407	0.035
H(8)	0.6613	0.6888	0.2130	0.065
H(82)	0.6694	0.5886	0.2654	0.065
H(91)*	0.6544	0.7004	0.3726	0.055
H(92)	0.7362	0.7646	0.3260	0.055
H(14)	1.0951	0.3844	0.3494	0.056
H(15)	1.2129	0.4089	0.2664	0.048
H(17)	1.1649	0.6754	0.2480	0.046
H(18)	1.0220	0.6577	0.3353	0.042
H(19)	1.3384	0.5969	0.2415	0.047
H(192)	1.3215	0.3124	0.1730	0.047
H(21)	1.3231	0.8368	0.0784	0.078
H(212)*	1.3402	0.7542	0.0041	0.078
H(22)	1.2024	0.8262	-0.0248	0.084
H(222)*	1.1659	0.8079	0.0782	0.084
H(28)*	1.0879	0.7246	0.0986	0.049
H(30)*	0.9962	0.4219	-0.1325	0.060
H(302)*	1.0327	0.3211	-0.0941	0.060
H(32)	0.8837	0.4970	-0.0560	0.043
H(33)	0.7923	0.5093	0.0795	0.050
H(35)	0.9640	0.3571	0.2202	0.058
H(36)	1.0682	0.3373	0.0897	0.071
H(37)	0.8411	0.4361	0.3015	0.043
H(372)*	0.7554	0.4649	0.2279	0.043
H(10)	0.8520	0.7529	0.2499	0.079
H(102)*	0.9013	0.6999	0.1639	0.079
H(103)	0.8021	0.7569	0.1507	0.079
H(111)*	0.9497	0.4086	0.5433	0.089
H(112)	1.0127	0.4345	0.6326	0.089
H(113)*	0.9001	0.4603	0.6294	0.089
H(121)*	0.7364	0.7054	0.6531	0.045
H(122)	0.8183	0.7262	0.7286	0.045
H(123)*	0.8165	0.7848	0.6334	0.045
H(29)	1.0638	0.6674	-0.2442	0.087
H(292)	0.9689	0.6058	-0.2659	0.087
H(293)*	0.9699	0.6803	-0.1816	0.087
H(38)	1.2865	0.3970	-0.0404	0.060
H(382)*	1.3297	0.3656	0.0527	0.060
H(383)*	1.3531	0.4652	0.0128	0.060

to 1535 relationships by the tangent formula. The minimum E value associated with the expanded set was $E \geq 1.70$. From the E map computed with these phases, it was possible to locate 43 of the 46 non-hydrogen atoms in the structure (Fig. 3). The remaining five atoms were located from a weighted electron density map. The R factor using this trial structure, with $\bar{U}^2 = 0.04 \text{ \AA}^2$ for all atoms, was 0.36.

The procedure adopted in this analysis appears to be somewhat arbitrary but nevertheless possesses the virtue of having worked. Innumerable attempts to solve the structure by both direct methods and vector verification (Reynolds, 1974) failed, presumably from the combined effects of relatively few data (34 reflections per atom) and the complexity of the structure. E map (A) was the first to show a closed-ring fragment and this was felt to be a major breakthrough. However, it eventually transpired that two of these six atoms were in fact misplaced. The coordinates of the other four were at worst 1 \AA from their final positions. The rational use of molecular scattering factors (Lessinger, 1976) sometimes enables a correct tangent formula expansion to be obtained. However, in the present case it seems that the key to the success was that the small changes in E values (*cf.* Tables 2 and 3) induced by the use of partial molecular scattering forced the expansion onto a correct pathway which had not previously been encountered. More complete molecular scattering using the geometry of the whole molecule failed to reveal this pathway, whereas the six-atom fragment somewhat fortuitously did.

Four cycles of isotropic full-matrix least-squares refinement converged at $R = 0.19$. Anisotropic temperature factors were then employed for limited refinement cycles, using eight selected atoms per cycle. After five complete passes the R value had converged at 0.093. A difference electron density synthesis revealed the positions of 31 possible H atoms, with peak heights in the range 0.3 to 0.6 $e \text{ \AA}^{-3}$. The coordinates of the 15 H atoms not found on this map were calculated from the known positions of the other C and H atoms, with C-H distances of 1.04 \AA , and C-C-H angles of 109.5°. H atom contributions were included in the final refinement cycles but their parameters were not refined. Relative weights were assigned with the function

$$w = [1 - \exp(-a \sin^2 \theta / \lambda^2)](1 + b|F_o| + c|F_o|^2)^{-1},$$

where $a = 20$, $b = 40$, $c = 0.01$. Using this weighting scheme the average of $w(|F_o| - |F_c|)^2$ was approximately constant for the various ranges of $\sin \theta / \lambda$ and $|F_o|$ in the final cycles of refinement.

Final values of the residuals were $R = 0.073$ and $R' = 0.11$ for the 1514 observed reflections. Final positional parameters are given in Table 4. Figs. 4 and 5 show the bond distances and angles for the non-

Table 5. Bond lengths (\AA) and angles ($^\circ$) involving H

C(3)-H(3)	1.10	C(19)-H(192)	1.15
C(7)-H(7)	1.05	C(21)-H(211)	1.07
C(8)-H(81)	1.04	C(21)-H(212)	1.04
C(8)-H(82)	1.07	C(22)-H(221)	1.06
C(9)-H(91)	1.06	C(22)-H(222)	1.06
C(9)-H(92)	0.99	C(28)-H(28)	1.05
C(10)-H(101)	1.05	C(29)-H(291)	1.08
C(10)-H(102)	1.03	C(29)-H(292)	1.04
C(10)-H(103)	1.04	C(29)-H(293)	1.03
C(11)-H(111)	1.05	C(30)-H(301)	1.05
C(11)-H(112)	1.02	C(30)-H(302)	1.02
C(11)-H(113)	1.06	C(32)-H(32)	1.04
C(12)-H(121)	1.04	C(33)-H(33)	0.91
C(12)-H(122)	1.04	C(35)-H(36)	1.06
C(12)-H(123)	1.04	C(36)-H(36)	1.15
C(14)-H(14)	1.04	C(37)-H(371)	1.14
C(15)-H(15)	1.05	C(37)-H(372)	1.04
C(17)-H(17)	0.99	C(38)-H(381)	1.00
C(18)-H(18)	1.04	C(38)-H(382)	0.99
C(19)-H(191)	1.01	C(38)-H(383)	0.99
C(2)-C(3)-H(3)	125.3	C(20)-C(119)-H(191)	114.2
C(4)-C(3)-H(3)	110.3	C(20)-C(10)-H(192)	122.1
C(5)-C(7)-H(7)	105.5	H(191)-C(19)-H(192)	107.1
C(37)-C(7)-H(7)	105.5	C(22)-C(21)-H(211)	109.4
N(1)-C(7)-H(7)	105.2	C(22)-C(21)-H(212)	108.9
C(9)-C(8)-C(81)	111.3	N(2)-C(21)-H(211)	106.5
C(9)-C(8)-H(82)	109.7	N(2)-C(21)-H(212)	105.9
N(1)-C(8)-H(81)	109.9	C(21)-C(22)-H(221)	109.0
N(1)-C(8)-H(82)	108.8	C(21)-C(22)-H(222)	109.9
H(81)-C(8)-H(82)	106.6	H(23)-C(22)-H(221)	110.3
C(4)-C(9)-H(91)	108.5	H(22)-C(22)-H(222)	108.1
C(4)-C(9)-H(92)	109.2	C(23)-C(28)-H(28)	118.8
C(8)-C(9)-H(91)	109.4	C(27)-C(28)-H(28)	118.4
C(8)-C(9)-H(92)	120.7	O(5)-C(29)-H(292)	110.9
H(91)-C(9)-H(92)	109.2	O(5)-C(29)-H(293)	112.2
N(1)-C(10)-H(101)	109.6	O(5)-C(29)-H(291)	112.2
N(1)-C(10)-H(102)	110.2	H(29)-C(29)-H(293)	110.7
N(1)-C(10)-H(103)	110.6	H(292)-C(29)-H(291)	106.9
H(102)-C(10)-H(103)	110.1	H(293)-C(29)-H(291)	106.8
H(102)-C(10)-H(101)	108.7	C(31)-C(30)-H(301)	109.5
H(102)-C(10)-H(101)	107.6	C(31)-C(30)-H(302)	98.3
O(2)-C(11)-H(111)	110.2	O(6)-C(30)-H(301)	110.1
O(2)-C(11)-H(112)	111.3	O(6)-C(30)-H(302)	110.6
O(2)-C(11)-H(113)	109.4	H(301)-C(30)-H(302)	109.3
H(112)-C(11)-H(113)	109.2	C(31)-C(32)-H(32)	119.5
H(112)-C(11)-H(111)	110.1	C(33)-C(32)-H(32)	111.5
O(1)-C(12)-H(121)	110.1	C(32)-C(33)-H(33)	128.8
O(1)-C(12)-H(122)	109.6	C(34)-C(33)-H(33)	111.5
O(1)-C(12)-H(123)	109.9	C(34)-C(35)-H(35)	120.4
H(122)-C(12)-H(123)	109.4	C(36)-C(35)-H(35)	119.9
H(122)-C(12)-H(121)	109.4	C(7)-C(37)-H(371)	102.4
H(123)-C(12)-H(121)	108.4	C(7)-C(37)-H(372)	110.3
C(13)-C(14)-H(14)	119.4	C(34)-C(37)-H(371)	117.8
C(15)-C(14)-H(14)	120.7	C(34)-C(37)-H(372)	109.4
C(14)-C(15)-H(15)	104.4	H(371)-C(37)-H(372)	106.6
C(16)-C(15)-H(15)	134.9	O(4)-C(38)-H(382)	109.2
C(16)-C(17)-H(17)	113.4	O(4)-C(38)-H(383)	109.8
C(18)-C(17)-H(17)	123.6	O(4)-C(38)-H(381)	109.7
C(13)-C(18)-H(18)	121.4	H(382)-C(38)-H(383)	109.8
C(17)-C(18)-H(18)	123.0	H(382)-C(38)-H(381)	109.4
C(16)-C(19)-H(191)	104.9	H(383)-C(38)-H(381)	108.8
C(16)-C(19)-H(192)	112.1		

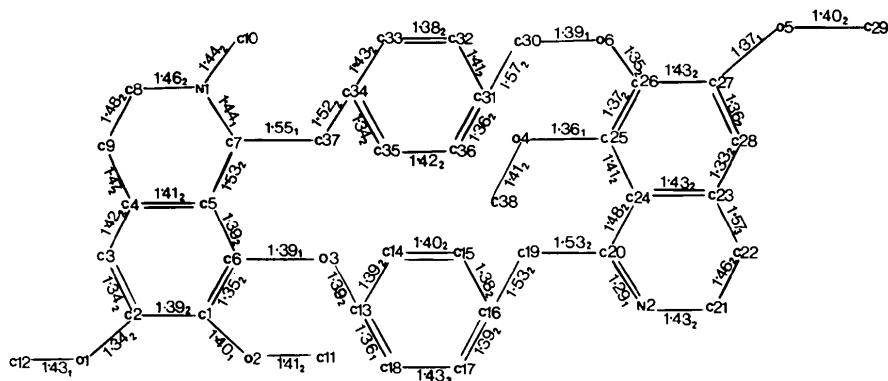


Fig. 4. Bond distances (Å). E.s.d.'s are shown subscripted.

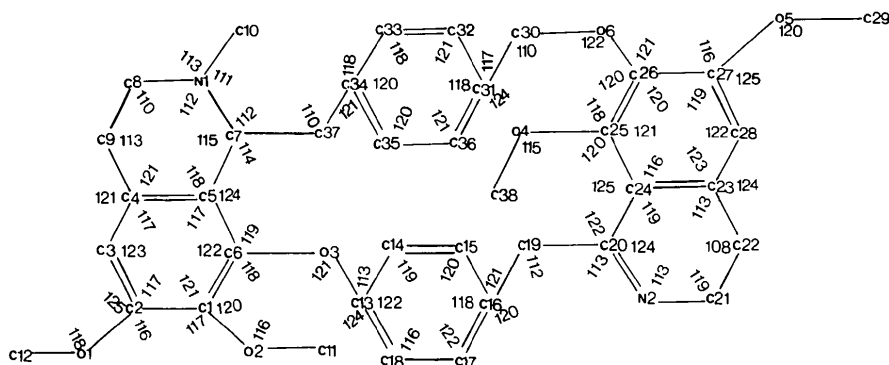


Fig. 5. Bond angles ($^{\circ}$). E.s.d.'s are all about 1° .

hydrogen atoms. Table 5 contains bond distances and angles involving the hydrogen atoms.*

Results and discussion

The overall shape of the molecule is illustrated in Fig. 6 which is a stereoscopic view of the molecule along **a**. The average C—C bond distances in the phenyl rings *A*, *C*, *D*, *F* are 1.383, 1.388, 1.385 and 1.390 Å respectively, with average C—C—C angles of 119.9° in all four rings. The heterocyclic rings *B* and *E* have average C—C single bonds of 1.493 and 1.504 Å respectively. In ring *E*, C(23)—C(24) has a value 1.428 (19) Å, which is lower than the average length by 4σ . The three C—N distances in ring *B* range from 1.441 to 1.458 Å. The average value of 1.447 Å for the C—N bond is smaller than the corresponding values found in other alkaloids; for example 1.52 Å in deoxynapharidine hydrobromide (Oda & Koyama, 1970)

and 1.51 Å in (+)-tubocurarine dibromide (Reynolds & Palmer, 1976). The C=N double bond in the 3,4-dihydroisoquinoline ring *E* is 1.288 (13) Å, in good agreement with the value of 1.292 (7) Å found in methylwarifteine (Borkakoti & Palmer, 1978). The average N—C—C angle for ring *B* is 112.5° , which compares well with the value 111.4° obtained for tetrandrine (Gilmore, Bryan & Kupchan, 1976), and 110.3° found in (+)-tubocurarine dibromide. The C—C single bonds in the methylene linkages vary from 1.519 to 1.548 Å, mean 1.531 Å. For the methoxy linkage between rings *C* and *E* the C—C distance is 1.574 (19) Å and the average C—O bond length is 1.371 Å. The $C_{\text{arom}}\text{—O}$ bond lengths have a mean value of 1.372 Å. The $C(sp^3)\text{—O}$ bond lengths in the methoxy groups attached to rings *A* and *D* are in the range 1.404 to 1.430 Å. The mean value of 1.408 Å for these four bonds is smaller than the average values of 1.452 and 1.467 Å, found for similar bonds in (+)-tubocurarine dibromide and tetrandrine respectively.

Selected torsion angles are given in Fig. 7. Fig. 8 is a stereoview of the molecule seen perpendicular to ring *A*. The C(10) methyl group at N(1) of the tetrahydroisoquinoline group is axial. Details of the planes through the phenyl rings *A*, *C*, *D*, *F* are given in

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33019 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

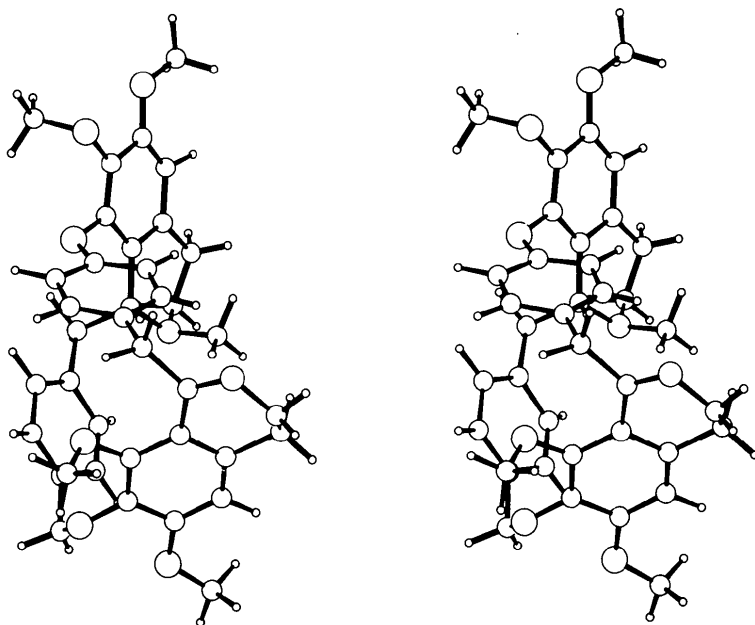


Fig. 6. Stereoscopic view of the molecule looking along *a*; the circles, in increasing order of size, represent H, C, N and O.

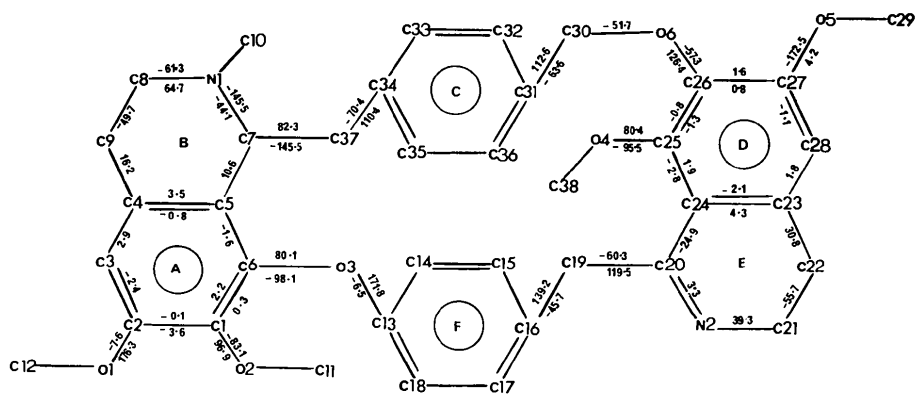


Fig. 7. Selected torsion angles ($^{\circ}$).

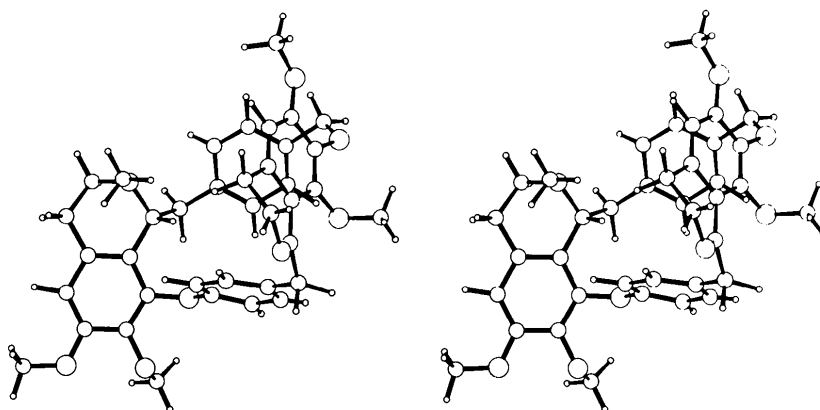


Fig. 8. Stereoscopic diagram of the molecule viewed perpendicular to ring *A*.

Table 6. *Least-squares planes*

Atoms marked with an asterisk have not been included in the calculation of the plane.

(A) EQUATIONS OF THE LEAST-SQUARES PLANES

THE EQUATIONS FOR THE LEAST SQUARES ARE
IN THE FORM $PX + QY + RZ = S$.

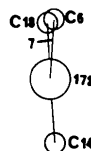
PLANE	P	Q	R	S
A	0.6314	0.7439	-0.2191	13.1706
B	0.7754	-0.0021	-0.6314	13.3381
C	0.6130	0.7673	0.1879	13.4141
D	0.5001	0.1741	0.8488	13.5521

X', Y', Z' ARE THE COORDINATES IN Å REFERRED TO THE AXES *a*, *b*, *c*.

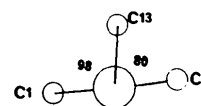
(B) DISTANCES (IN Å) OF THE ATOMS FROM THE LEAST-SQUARES PLANES

PLANE A		PLANE B	
ATOM	DEVIATION	ATOM	DEVIATION
C(1)	0.0091	C(23)	-0.0081
C(2)	0.0067	C(24)	0.0089
C(3)	-0.0167	C(25)	-0.0063
C(4)	0.0114	C(26)	0.0024
C(5)	0.0033	C(27)	-0.0010
C(6)	-0.0137	C(28)	0.0042
C(7)*	0.1112	C(29)*	0.2149
C(8)*	-0.3114	C(30)*	-0.8324
C(9)*	0.0446	O(6)*	0.0912
N(1)*	0.4511	O(5)*	0.0547
O(1)*	-0.0455	O(4)*	0.0570
O(2)*	0.0348	C(38)*	1.3526
O(3)*	-0.0171	C(19)*	-0.4971
C(10)*	1.8741	N(2)*	0.4809
C(11)*	-1.2082	C(20)*	0.0325
C(12)*	0.0317	C(21)*	0.9064
C(13)*	-1.0973	C(22)*	0.1098

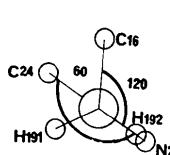
PLANE C		PLANE D	
ATOM	DEVIATION	ATOM	DEVIATION
C(31)	-0.0005	C(13)	-0.0320
C(32)	0.0150	C(14)	0.0214
C(33)	-0.0262	C(15)	0.0073
C(34)	0.0228	C(16)	-0.0256
C(35)	-0.0081	C(17)	0.0162
C(36)	-0.0035	C(18)	0.0127
O(6)*	1.2735	O(3)*	-0.0975
C(30)*	0.0731	C(19)*	0.0042
C(37)*	0.0935		



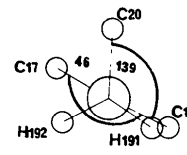
(a)



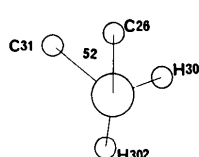
(b)



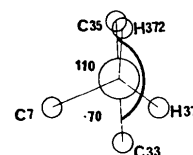
(c)



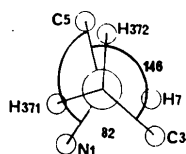
(d)



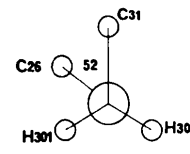
(e)



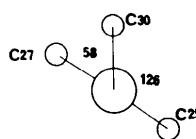
(f)



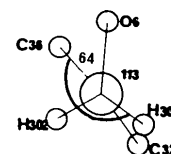
(g)



(h)



(i)



(j)

Fig. 9. Newman projection along bonds (a) O(3)–C(13); (b) O(3)–C(6); (c) C(19)–C(20); (d) C(19)–C(16); (e) O(6)–C(30); (f) C(37)–C(34); (g) C(37)–C(7); (h) C(30)–O(6); (i) O(6)–C(26); (j) C(30)–C(31) in DMW.

Table 6. The phenyl ring units *C* and *F* are rigorously planar, the maximum deviation of the atoms from the plane being 0.02 Å for *C* and -0.03 Å for *F*. Both the rings *B* and *E* are in the half-chair conformation, the pseudo twofold axis bisecting bond N(1)–C(8) in ring *B* and C(21)–C(22) in ring *E*. The asymmetry parameters are $\Delta C_2^{N1,8} = 5.6^\circ$ and $\Delta C_2^{21,22} = 6.4^\circ$ (Duax & Norton, 1975). Of the four methoxy groups, those at O(1) and O(5) have the C atoms close to the ring plane, while the methyl groups at O(2) and O(4) are out of the plane of the aromatic residue.

The conformations about the methylene, ether and methoxy linkages are shown in the Newman projections in Fig. 9. The conformations about the C(37)–C(7) and C(19)–C(20) single bonds differ considerably, the torsion angles C(34)–C(37)–C(7)–C(5) and C(16)–C(19)–C(20)–C(24) being -145° and -60° respectively. This describes the relative orientation of the phenyl rings *C* and *F* with respect to the isoquinoline rings *AB* and *DE* respectively.

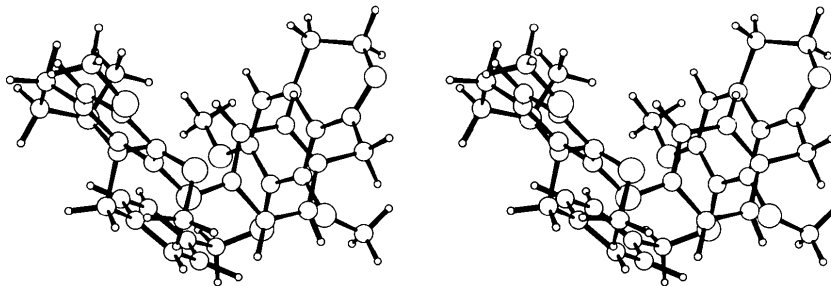
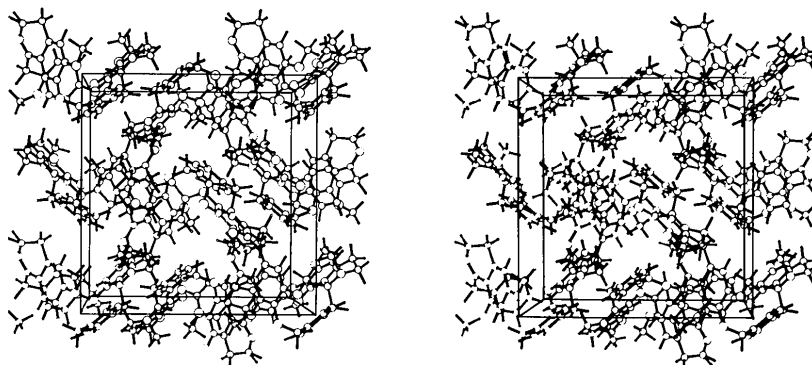
Fig. 10. Stereoscopic view of the molecule along *c*.Fig. 11. Stereoscopic diagram showing the packing of the DMW molecules in the unit cell viewed along *c*.

Table 7. Selected short intermolecular contacts in DMW (Å)

C(2)—H(33 ^l)	3.15	C(9)—H(291 ^{ll})	3.38
C(3)—C(33 ^l)	3.43	C(10)—H(211 ^{ll})	3.34
C(3)—H(32 ^l)	3.42	C(12)—N(2 ^l)	3.41
C(8)—H(28 ^{ll})	3.46	C(17)—H(121 ^{lv})	3.11
C(8)—H(111 ^{lll})	2.98	C(23)—H(100 ^v)	3.15
C(8)—H(291 ^{ll})	3.38	C(29)—O(1 ^{vl})	3.28
C(9)—H(301 ^l)	3.19		

Symmetry code

None	<i>x</i> ,	<i>y</i> ,	<i>z</i>	(iv)	$\frac{1}{2} + x,$	$\frac{3}{2} - y,$	$1 - z$
(i)	$\frac{3}{2} - x,$	$1 - y,$	$\frac{1}{2} + z$	(v)	$\frac{1}{2} + x,$	$\frac{1}{2} - y,$	$-z$
(ii)	$-\frac{1}{2} + z,$	$\frac{3}{2} - y,$	$-z$	(vi)	<i>x</i> ,	<i>y</i> ,	$z - 1$
(iii)	$-\frac{3}{2} - x,$	$1 - y,$	$-\frac{1}{2} + z$				

If the molecule is viewed in the orientation shown in Fig. 10, a stereoscopic diagram along the *c* axis, the molecule appears to show a convex face, with three O atoms [O(3),O(4),O(6)] on the outer (lower right) region of the molecule and three other O atoms [O(1),O(2),O(5)] in the inner region. A stereoscopic diagram illustrating the packing is given in Fig. 11. Short intermolecular contacts are listed in Table 7.

All calculations were carried out on the London University CDC6600 computer, with programs from the Birkbeck College Crystallography Library.

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