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The Crystal Structure of (−)-N-Methyl-Gelsemicine Hydriodide

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N-methyl-gelsemicine hydriodide, $C_{20}H_{26}O_4N_2.CH_3I$, crystallizes in the monoclinic system, space group $C2$,

$$a=16\cdot75,\ b=9\cdot52,\ c=14\cdot06\ \text{Å};\ \beta=90^\circ\ 13',\ Z=4\ .$$

The iodine coordinates were obtained from Patterson projections and the molecular structure was solved by means of three-dimensional Fourier syntheses using the heavy-atom technique. The atomic parameters have been refined by two-dimensional F_o-F_c syntheses and several three-dimensional Fourier series and differential syntheses. The molecule was found to possess a methoxyl group attached to the nitrogen atom of the oxindole nucleus, a seven-membered ring and an intramolecular hydrogen bond. The absolute configuration has been determined using the anomalous-dispersion effects of the Cu $K\alpha$ radiation by the iodine atom.

Introduction

The roots and rhizomes of *Gelsemium sempervirens* have long been known to contain gelsemine, sempervirine and a number of minor alkaloids, one of which is gelsemicine. The skeleton of gelsemine contains a 3,3-disubstituted oxindole nucleus and a very compact, highly stable ring system which resisted intensive chemical degradation studies. Its structure was finally elucidated by the X-ray analysis carried out by Lovell *et al.* (1959). It was of interest to find out how much the skeleton of gelsemicine would differ from that of gelsemine and in view of possible chemical difficulties presented by this compound, a detailed X-ray determination was suggested by Dr Léo Marion. Very little chemistry of gelsemicine was known. Raymond-Hamet (1952) suggested an indole structure for the alkaloid. Schwarz & Marion (1953) established the presence of one C-methyl and two methoxyl groups, one of them being attached to the benzene ring of the indole nucleus. From the study of the infra-red spectra of gelsemicine and its acetyl and benzoyl derivatives, they inferred that one nitrogen is basic and secondary, while the other is neutral and tertiary.

The crystals of gelsemicine hydrobromide hemihydrate and N-methyl-gelsemicine hydrobromide tetrahydrate were examined (Przybylska, 1961), but since both these compounds crystallize with two molecules per asymmetric unit, the iodine derivative was prepared by Dr S. McLean. Two forms of N-methyl-gelsemicine hydriodide were discovered—one of space group $P2_1$ with four molecules per unit cell and the other of space group $C2$. The latter, the only examined derivative with one molecule per asymmetric unit, was chosen for the structural analysis.

Experimental

Crystals of N-methyl-gelsemicine hydriodide, $C_{21}H_{29}O_4N_2I$, m.p. 199–203 °C. were grown from a methanol-ethyl-acetate mixture as monoclinic, colourless plates, elongated along the b axis and with easy cleavage in that direction. They were twinned, but it was possible to split off single-crystal fragments for collecting the data. Chemical analysis gave C = 50·61, H = 5·67; calc. C = 50·40, H = 5·84%. The unit-cell dimensions were determined with a precession instrument using Cu $K\alpha$ radiation. They are:

$$a=16\cdot75\pm0\cdot03,\ b=9\cdot52\pm0\cdot02,\ c=14\cdot06\pm0\cdot03\ \text{Å};$$
$$\beta=90^\circ\ 13'\pm5'.$$

From the absences, hkl with $h+k=2n+1$, three space groups are possible, $C2$, Cm and $C2/m$. Since the compound is optically active the space group can be considered as uniquely determined as $C2$. The optical rotation was measured by Mr J. L. M. Lesage, who found it to be:

$$[\alpha]_D^{25}=-102\cdot60\pm3\cdot47\ (c,\ 1\cdot15\ \text{in abs. ethanol}).$$

The density, calculated for four molecules per unit cell is 1·482 g.cm.$^{-3}$ and the measured value, by flotation in toluene-carbon tetrachloride, 1·488 g.cm.$^{-3}$. The absorption coefficient for Cu $K\alpha$ radiation is 125·9 cm.$^{-1}$.

The intensities of $h0l \ldots h7l$ reflections were estimated from eight multiple-film, equi-inclination Weissenberg photographs. The data for $0kl$, $1kl$, $hk0$ and $hk1$ zones were also collected. Out of a possible 2705 reflections which lie within the range of Cu $K\alpha$ radiation, a total of 1800 were observed. Measurement of the intensities was made by visual comparison with a standard set of reflections. Since the β angle is close to 90°, special care had to be exercised in indexing the Weissenberg films.

All crystals were cylindrical in shape with diameters ranging from 0·10 to 0·16 mm. and therefore absorption corrections were not applied. Overall scale and temperature factor ($B=5{\cdot}0$ Å^2) were evaluated by Wilson's method using the $h0l$ data.

The Fourier and Patterson syntheses were calculated at intervals of 6° along the a and c axes and 12° for the b axis. All the necessary computations were carried out on the IBM 650 using programmes described by Ahmed (1960).

Analysis of the structure

The x and z co-ordinates of the iodine atom derived from Patterson syntheses carried out for the $h0l$, $0kl$ and $hk0$ zones were found to be $x=0{\cdot}296$ and $z=0{\cdot}115$. Having assumed $y=0{\cdot}500$, a three-dimensional Fourier synthesis was then evaluated for sections perpendicular to the b axis, covering $\frac{1}{8}$th of the volume of the unit cell. In this summation, in addition to the real atomic peaks, there were mirror-image peaks related to them by planes of symmetry at $y=0$ and $\frac{1}{2}$. The examination of these electron-density maps with the help of the projection on (010) led to the location of 22 light atoms of the molecule and the oxindole nucleus was readily recognized. The remaining atomic positions were revealed by three ϱ_o cycles using three-dimensional data and one additional cycle using ϱ_o and $\varrho_o-\varrho_c$ projections along the a axis. No effort was made to distinguish between different types of atoms until they were all successfully located and until then only the carbon scattering factors were used in structure-factor calculations. The first recognized oxygen atoms were O_1 and O_2. Their position was substantiated by the calculated C–O and C=O bond lengths. Moreover they were found to be in agreement with the structure of gelsemine (Lovell *et al.*, 1959). Chemical evidence was used in differentiating the two nitrogen atoms from the carbon atoms. It was known that the methyl group was attached to one of them and the other could be considered as established as soon as the oxindole nucleus was recognized. Their placement was also supported by the $\varrho_o-\varrho_c$ maps computed using the $0kl$ and $h0l$ data.

At this stage an F_o differential synthesis, corrected for the finite-summation errors given by the F_c synthesis, was carried out only for those atoms that were expected to lead to completing the solution of the molecular structure. On the basis of a thorough study of the resultant ϱ_o and ϱ_c values and of bond lengths, it was possible to conclude that the remaining two oxygen atoms belong to the methoxyl groups, one attached to the benzene ring and the other to the nitrogen atom of the oxindole nucleus.

Finally, a differential synthesis has been evaluated for all the atoms in the molecule. It was corrected by the back-shift method, but no factor for the lack of

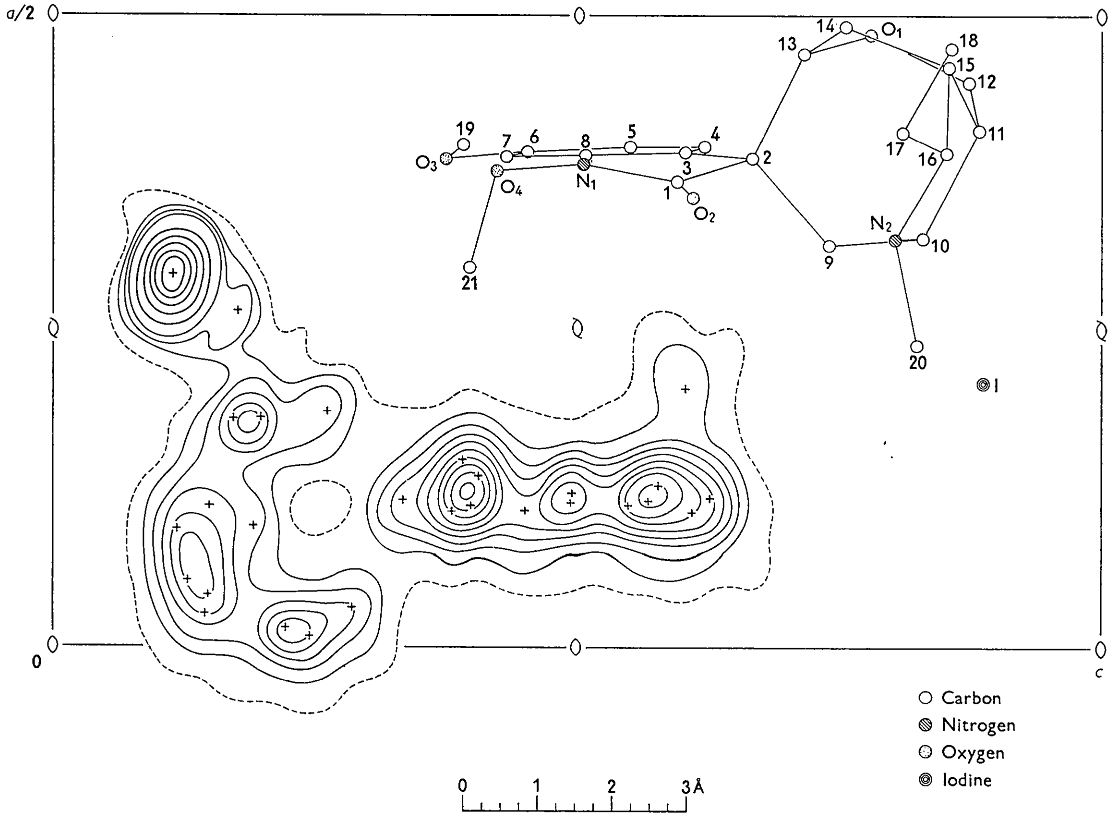

Fig. 1. The (010) Fourier projection of (−)-N-methyl-gelsemicine hydriodide. Contour interval is 2 e.Å^{-2}, except for the iodine atom, which is drawn at intervals of 10 e.Å^{-2}, starting at 10 e.Å^{-2}. The first broken line is at 2 e.Å^{-2}.

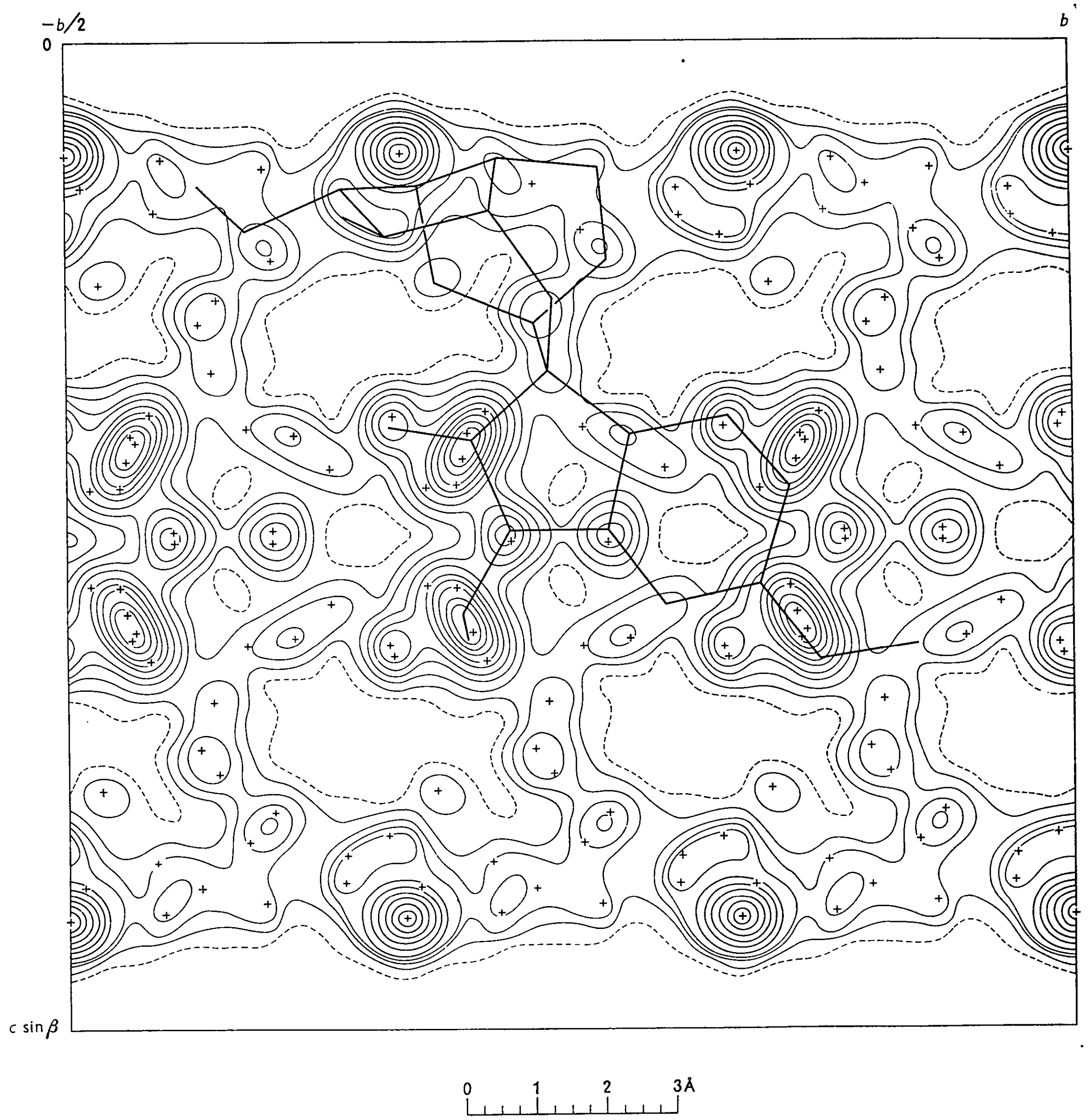

Fig. 2. Final projection up the a axis. The contours are drawn at 2 e.Å^{-2} intervals, starting with a broken line at 4 e.Å^{-2}. The iodine atom contours marked with heavier lines, are at intervals of 10 e.Å^{-2}, starting at 10 e.Å^{-2}.

centre of symmetry was applied, as when this was done the bond length values showed worse agreement with the corresponding nominal values. The average atomic shifts of 0·023, 0·015 and 0·008 Å were obtained in the x, y and z directions respectively and the corresponding maximum shifts were 0·070, 0·044 and 0·021 Å. In this last cycle of refinement, the iodine atom was represented in the structure-factor calculations by four isotropic fractional atoms, placed symmetrically about the atom centre (Kartha & Ahmed, 1960). The use of this method was expedited by assistance from Dr F. R. Ahmed, who calculated the thermal parameters of the iodine atom. They are given in Table 1, as fractions of the axial lengths.

Table 1. *The anisotropic thermal parameters of the iodine atom*

	x	y	z
1.	0·3010	0·5095	0·1148
2.	0·3010	0·4905	0·1148
3.	0·2852	0·5095	0·1114
4.	0·2852	0·4905	0·1114

The correction for the anisotropic motion of the iodine led to the decrease of the reliability factor from 0·20 to 0·16 for the three-dimensional data, having omitted the unobserved reflections. The value of $R(hkl)$ did not decrease when the atomic shifts obtained from the last differential synthesis were applied. The final reliability factors for the three axial zones included the unobserved reflections and were: $R(0kl)=0{\cdot}10$, $R(h0l)=0{\cdot}15$ and $R(hk0)=0{\cdot}11$. The scattering curves of McWeeny were used for carbon, nitrogen and oxygen and that of Thomas & Umeda (1957) for iodine. The temperature factor $B=5{\cdot}0$ Å^2 was employed for the light atoms and $B=5{\cdot}2$ Å^2 for the iodine atom. The contribution made by the hydrogen atoms was not included in structure-factor calculations.

The projection of the structure on (010) is illustrated in Fig. 1. On the projection along the *a* axis (Fig. 2), due to considerable overlapping by neighbouring molecules, only one molecule has been delineated, whereas all other atomic positions are marked by crosses. Fig. 2 shows the molecules arranged in layers parallel to the *b* axis and this explains easy crystal cleavage in that direction.

All the drawings and the final fractional co-ordinates (Table 2) correspond to the absolute configuration of this *leavo*-rotatory compound with a left-handed set of axes. The absolute configuration has been determined having made use of the anomalous dispersion of the Cu $K\alpha$ radiation by the iodine atom. The intensities I_H and $I_{\bar{H}}$ were estimated by visual comparison with an intensity strip, and some observed and calculated ratios are listed in Table 3. The values for the real and imaginary dispersion corrections were those determined by Dauben & Templeton (1955). The hkl and $\bar{h}\bar{k}\bar{l}$ reflections were obtained by inclining the Weissenberg camera in the opposite ways with respect to the X-ray beam, and the films were indexed taking into account all factors described by Peerdeman & Bijvoet (1956).

Table 2. *Fractional atomic co-ordinates*

Atom	x	y	z	ϱ_o (e.Å^{-3})	ϱ_c (e.Å^{-3})
C_1	0·133	0·103	0·405	6·27	5·79
C_2	0·114	0·217	0·334	6·50	6·05
C_3	0·110	0·339	0·398	6·40	6·03
C_4	0·105	0·486	0·379	6·49	6·09
C_5	0·105	0·579	0·450	5·75	6·16
C_6	0·109	0·535	0·548	6·61	6·09
C_7	0·113	0·392	0·568	6·22	6·12
C_8	0·112	0·307	0·493	6·87	6·23
C_9	0·184	0·225	0·260	6·60	6·02
C_{10}	0·178	0·132	0·171	6·50	6·15
C_{11}	0·091	0·144	0·118	6·09	5·97
C_{12}	0·053	0·294	0·128	5·52	5·91
C_{13}	0·031	0·197	0·285	6·41	6·30
C_{14}	0·009	0·050	0·245	5·79	6·10
C_{15}	0·041	0·024	0·147	5·95	6·24
C_{16}	0·110	−0·089	0·149	5·97	6·16
C_{17}	0·093	−0·232	0·191	5·73	6·03
C_{18}	0·026	−0·303	0·145	4·86	5·95
C_{19}	0·103	0·768	0·609	5·29	5·86
C_{20}	0·264	−0·086	0·176	4·84	5·52
C_{21}	0·202	0·096	0·603	5·19	6·04
N_1	0·119	0·161	0·495	7·63	7·62
N_2	0·179	−0·025	0·197	7·19	7·88
O_1	0·015	0·307	0·221	8·75	9·24
O_2	0·146	−0·020	0·390	8·12	9·08
O_3	0·114	0·624	0·625	8·58	9·19
O_4	0·124	0·089	0·577	9·07	9·60
I	0·2931	0·5000	0·1131	77·29	76·82

Table 3. *Ratios* $I_{hkl}/I_{\bar{h}\bar{k}\bar{l}}$ (Cu $K\alpha$)

hkl	Calc.	Obs.
115	1·48	1·62
118	0·69	0·50
$31\bar{7}$	1·32	1·32
711	1·22	1·28
910	2·42	2·30
1,1,11	0·52	0·48

Discussion

The r.m.s. values of the standard deviations of the co-ordinates calculated using Cruickshank's formula (1949) are 0·047 Å for light atoms and 0·003 Å for iodine. These values include a factor of 1·7 to allow for the absence of a centre of symmetry. The e.s.d. of bonds and angles were estimated to be about 0·066 Å and 3·1° respectively. Bond lengths are depicted in Fig. 3 and Table 4 lists the angles. Using Cruickshank & Robertson's (1953) criterion none of the bond lengths are significantly different from their nominal values. The average aromatic C–C bond is 1·38 Å, whereas all other C–C bonds gave the average value of 1·53 Å. The N–O bond was found in good agreement with

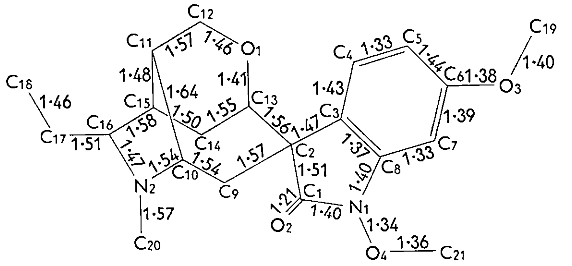

Fig. 3. Intramolecular bond lengths.

Table 4. *Bond angles*

Angle	Value	Angle	Value
C_1–C_2–C_3	100·0°	O_1–C_{13}–C_{14}	113·3°
C_2–C_3–C_8	114·8	O_1–C_{13}–C_2	111·0
C_1–C_2–C_{13}	112·9	C_{12}–O_1–C_{13}	115·3
C_{13}–C_2–C_9	112·3	C_6–O_3–C_{19}	117·9
C_3–C_2–C_9	113·7	N_1–O_4–C_{21}	105·2
C_2–C_9–C_{10}	117·7	C_{16}–N_2–C_{10}	106·6
C_9–C_{10}–C_{11}	112·7	C_{16}–N_2–C_{20}	118·3
C_{10}–C_{11}–C_{12}	112·5	C_{10}–N_2–C_{20}	108·9
C_2–C_{13}–C_{14}	118·7	C_1–N_1–C_8	112·9
C_{13}–C_{14}–C_{15}	113·3	C_1–N_1–O_4	124·3
C_{14}–C_{15}–C_{11}	109·3	C_8–N_1–O_4	122·0
C_{14}–C_{15}–C_{16}	111·1	C_3–C_4–C_5	120·7
C_{11}–C_{15}–C_{16}	96·7	C_4–C_5–C_6	121·5
C_{10}–C_{11}–C_{15}	109·0	C_5–C_6–C_7	118·7
C_{12}–C_{11}–C_{15}	116·7	C_6–C_7–C_8	115·8
C_{15}–C_{16}–C_{17}	118·8	C_7–C_8–C_3	129·7
C_{16}–C_{17}–C_{18}	113·0	C_8–C_3–C_4	113·7
N_1–C_1–C_2	106·2	C_5–C_6–O_3	125·1
C_3–C_8–N_1	104·1	C_7–C_6–O_3	116·1
C_{15}–C_{16}–N_2	107·5	C_2–C_1–O_2	128·2
C_{17}–C_{16}–N_2	110·1	N_1–C_1–O_2	124·7
C_9–C_{10}–N_2	111·4	C_2–C_3–C_4	131·5
C_{11}–C_{10}–N_2	100·6	C_7–C_8–N_1	126·2
C_{11}–C_{12}–O_1	109·6		

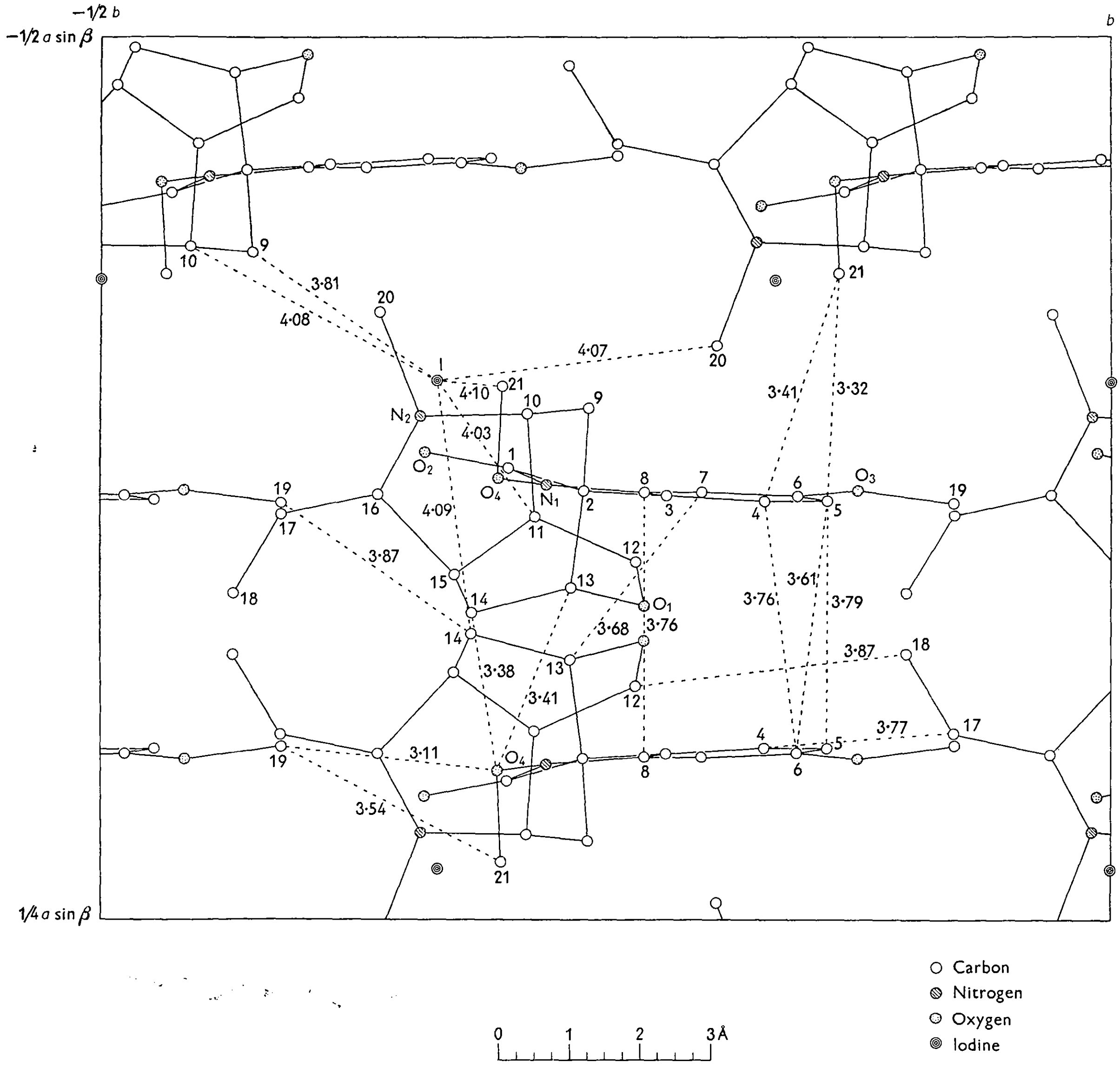

Fig. 4. The projection along the *c* axis showing packing and the closest intermolecular contacts.

the sum of the two covalent radii. It is of interest that the C_{16}–N_2 and C_{10}–N_2 bonds were found to be considerably longer than the C–N bonds of the oxindole group. This is an expected result as the average C–N bond, with a 4-covalent nitrogen, given by *Tables of Interatomic Distances and Configuration in Molecules and Ions* (1958) is 1·48, whereas shortened C–N bonds have been observed whenever a nitrogen atom is attached to a benzene ring.

The only angles that are significantly smaller than the tetrahedral value are those in five-membered rings; they average 105·8°. The angles C_2–C_3–C_4 and N_1–C_8–C_7 are expected to be over 120° as the C_2–C_3 and N_1–C_8 bonds are co-planar with the benzene ring and the angles of the five-membered ring come close to the tetrahedral value. The angles C_2–C_1–O_2 and N_1–C_1–O_2 are 128° and 125° respectively and they agree well with the value 125° for the single-bond: double-bond angle (Pauling, 1960).

The three C–N_2 bonds are arranged approximately tetrahedrally around the nitrogen atom and this supports the conclusion that this atom is quaternary, whereas the bonds about the N_1 atom are nearly planar. It is worth noting that the value of the C_6–O_3–C_{19} bond angle was found to be 118°, whereas the angle C_{16}–C_{17}–C_{18} is closer to the tetrahedral value (113°), and thus confirms the conclusion that it is given by the ethyl group.

The equation of the plane passing through the benzene ring is $0·9986x+0·0410y-0·0329z-1·7769=0$. The average deviation of the benzene ring atoms from this plane is 0·006 Å and the maximum deviation is

Table 5. *Observed and calculated structure factors*

(*a*) *h*0*l* zone

h	*k*	*l*	F_o	F_c
0	0	1	—	−19·3
		2	17·3	−4·3
		3	237·0	−237·5
		4	275·3	−270·4
		5	54·2	−26·2
		6	81·3	−73·7
		7	56·0	+52·4
		8	114·1	+116·7
		9	57·1	+49·3
		10	67·4	+62·4
		11	16·5	−11·2
		12	31·4	−31·6
		13	49·1	−36·5
		14	37·4	−29·7
		15	< 8·7	−4·5
		16	13·0	+11·6
		17	11·6	+7·8
		18	13·9	+15·1
2	0	0	77·3	−75·0
		1	206·5	−195·3
		2	55·2	−43·3
		3	157·7	+149·8
		4	180·3	+177·0
		5	106·6	+105·4
		6	19·6	−18·0
		7	70·8	−72·4
		8	82·0	−74·9
		9	56·6	−56·9
		10	14·8	−18·4
		11	< 9·5	−0·9
		12	49·1	+42·9
		13	38·7	+33·6
		14	42·5	+34·5
		15	< 9·0	−5·1
		16	20·9	−20·3
		17	13·4	−14·2
		18	< 3·7	−9·4
4	0	0	107·7	−112·4
		1	118·5	+121·6
		2	301·9	−318·4
		3	203·3	−191·1
		4	39·2	−25·5
		5	21·8	−23·8
		6	98·1	+111·5
		7	93·1	+104·0
		8	61·1	+64·4
		9	31·9	+32·8
		10	50·3	−51·7
		11	43·8	−46·8
		12	36·8	−33·0
		13	10·0	−10·7
		14	< 9·5	+5·7
		15	8·7	+10·0
		16	12·5	+10·9
		17	15·9	+16·6
6	0	0	18·5	−12·1
		1	113·6	+92·9
		2	30·4	+32·9
		3	129·3	+135·3
		4	84·9	+88·4
		5	53·2	−50·8
		6	74·7	−84·8
		7	83·3	−84·5
		8	34·4	−39·4
		9	< 9·1	+2·0
		10	27·3	+29·6
		11	49·1	+48·4
		12	20·2	+22·5
		13	22·9	+22·0
6	0	14	18·8	−15·7
		15	21·8	−19·2
		16	11·5	−15·5
		17	< 5·1	−7·8
8	0	0	40·7	+31·4
		1	202·6	−243·4
		2	33·1	−43·1
		3	22·0	−41·0
		4	32·4	+41·7
		5	70·0	+94·3
		6	39·5	+51·8
		7	33·7	+50·2
		8	12·9	−11·9
		9	27·3	−35·7
		10	23·0	−35·4
		11	35·1	−39·4
		12	< 9·8	+3·6
		13	13·2	+15·3
		14	17·5	+15·5
		15	< 7·5	+7·5
		16	< 6·0	+5·6
10	0	0	116·4	+137·1
		1	30·4	+43·8
		2	37·4	+48·2
		3	8·1	−6·6
		4	53·0	−64·3
		5	36·8	−45·7
		6	33·6	−45·9
		7	< 9·4	−13·8
		8	25·5	+27·1
		9	25·9	+27·8
		10	20·2	+25·9
		11	< 9·8	+11·6
		12	< 9·4	+9·0
		13	14·4	−13·5
		14	15·4	−17·8
		15	14·6	−14·5
		16	< 3·7	−0·1
12	0	0	70·3	−85·2
		1	23·3	−35·7
		2	21·2	−56·6
		3	34·0	+55·1
		4	42·4	+71·4
		5	22·3	+44·0
		6	< 9·7	+18·4
		7	23·2	−37·3
		8	23·3	−30·7
		9	< 10·0	−22·5
		10	9·7	−12·2
		11	< 9·2	+14·0
		12	< 8·5	+7·5
		13	< 7·5	+10·5
		14	< 6·3	+4·3
		15	< 3·7	−0·1
14	0	0	9·8	−9·5
		1	< 9·8	+8·0
		2	16·2	−12·2
		3	20·1	−21·1
		4	16·5	−17·3
		5	10·0	−22·4
		6	10·0	−9·9
		7	16·4	+19·6
		8	15·9	+24·0
		9	9·2	+21·2
		10	< 8·7	+1·9
		11	< 8·2	−12·7
		12	< 7·0	−10·4
		13	< 5·5	−4·6
16	0	0	< 10·0	−4·7
16	0	1	11·7	+1·1
		2	20·1	+28·0
		3	16·4	+21·7
		4	9·7	+21·5
		5	9·5	−5·7
		6	9·4	−18·6
		7	< 9·0	−13·6
		8	< 8·5	−9·9
		9	< 7·8	−0·7
		10	< 7·0	+3·0
		11	< 6·0	+5·9
		12	< 3·8	+10·5
18	0	0	< 9·0	+6·8
		1	18·2	−20·6
		2	10·4	−8·2
		3	8·7	−5·6
		4	< 8·5	−3·5
		5	< 8·1	+2·4
		6	< 7·7	+8·9
		7	< 7·1	+7·8
		8	< 6·3	+6·6
		9	< 5·4	−1·1
		10	< 3·1	−7·2
20	0	0	< 7·0	+6·7
		1	< 7·0	+8·3
		2	< 6·8	+7·7
		3	< 6·5	+6·9
		4	< 6·1	−8·2
		5	< 5·5	−3·9
		6	8·1	−8·9
		$\bar{7}$	< 1·6	−4·6
2	0	$\bar{1}$	36·5	−30·2
		$\bar{2}$	66·3	−58·5
		$\bar{3}$	42·4	−48·8
		$\bar{4}$	101·5	+89·3
		$\bar{5}$	63·3	+55·7
		$\bar{6}$	97·5	+96·9
		$\bar{7}$	42·5	+46·9
		$\bar{8}$	12·7	−9·4
		$\bar{9}$	45·5	−43·9
		$\overline{10}$	92·3	−87·1
		$\overline{11}$	33·3	−34·4
		$\overline{12}$	23·0	−14·2
		$\overline{13}$	49·5	+42·8
		$\overline{14}$	32·1	+31·5
		$\overline{15}$	21·0	+17·3
		$\overline{16}$	13·2	+7·3
		$\overline{17}$	10·9	−10·6
		$\overline{18}$	< 3·7	−9·9
4	0	$\bar{1}$	349·4	+400·1
		$\bar{2}$	54·6	+64·8
		$\bar{3}$	119·4	+96·2
		$\bar{4}$	62·0	+57·6
		$\bar{5}$	174·5	−174·1
		$\bar{6}$	149·3	−139·4
		$\bar{7}$	83·9	−79·2
		$\bar{8}$	24·7	−14·8
		$\bar{9}$	73·4	+72·7
		$\overline{10}$	62·7	+57·4
		$\overline{11}$	68·7	+53·5
		$\overline{12}$	11·7	+7·7
		$\overline{13}$	11·7	−11·8
		$\overline{14}$	27·4	−22·7
		$\overline{15}$	27·3	−20·4
		$\overline{16}$	21·6	−16·6
		$\overline{17}$	7·1	+5·0
6	0	$\bar{1}$	20·8	−15·2
		$\bar{2}$	168·1	−168·7
		$\bar{3}$	140·5	−128·2

h	k	l	F_o	F_c
6	0	$\bar{4}$	12·5	−13·4
		$\bar{5}$	83·5	+76·1
		$\bar{6}$	50·6	+43·5
		$\bar{7}$	85·7	+77·8
		$\bar{8}$	54·6	+52·2
		$\bar{9}$	10·7	+0·3
		$\bar{10}$	35·3	−30·0
		$\bar{11}$	68·4	−61·8
		$\bar{12}$	20·2	−17·1
		$\bar{13}$	30·3	−20·3
		$\bar{14}$	21·6	+17·5
		$\bar{15}$	27·6	+22·2
		$\bar{16}$	16·4	+9·6
		$\bar{17}$	17·1	+10·9
8	0	$\bar{1}$	30·4	−26·7
		$\bar{2}$	103·2	+106·9
		$\bar{3}$	93·0	+108·9
		$\bar{4}$	47·5	+43·0
		$\bar{5}$	40·7	+40·7
		$\bar{6}$	45·1	−43·0
		$\bar{7}$	83·8	−89·9
		$\bar{8}$	41·4	−32·5
		$\bar{9}$	33·6	−27·5
		$\bar{10}$	10·4	+9·7
		$\bar{11}$	23·3	+22·4
		$\bar{12}$	44·6	+31·0
		$\bar{13}$	24·5	+20·5
		$\bar{14}$	14·4	+7·9
		$\bar{15}$	17·6	−13·3
		$\bar{16}$	17·1	−11·3
10	0	$\bar{1}$	11·1	−2·9
		$\bar{2}$	20·9	−19·9
		$\bar{3}$	65·4	−82·7
		$\bar{4}$	45·1	−47·6
		$\bar{5}$	40·8	−33·6

h	k	l	F_o	F_c
10	0	$\bar{6}$	10·7	−14·8
		$\bar{7}$	19·0	+17·1
		$\bar{8}$	55·7	+51·8
		$\bar{9}$	54·5	+49·6
		$\bar{10}$	20·2	+16·4
		$\bar{11}$	< 9·8	−7·7
		$\bar{12}$	42·7	−38·7
		$\bar{13}$	24·9	−19·6
		$\bar{14}$	17·8	−12·6
		$\bar{15}$	7·4	+7·3
		$\bar{16}$	11·4	+12·7
12	0	$\bar{1}$	10·5	+12·7
		$\bar{2}$	25·9	−10·4
		$\bar{3}$	< 9·1	−9·6
		$\bar{4}$	47·8	+56·3
		$\bar{5}$	44·7	+48·0
		$\bar{6}$	27·9	+22·2
		$\bar{7}$	< 10·0	−4·8
		$\bar{8}$	37·0	−36·9
		$\bar{9}$	28·4	−21·4
		$\bar{10}$	32·0	−23·4
		$\bar{11}$	< 9·2	+1·8
		$\bar{12}$	13·9	+9·7
		$\bar{13}$	24·7	+15·8
		$\bar{14}$	6·1	+5·4
		$\bar{15}$	3·7	+5·6
14	0	$\bar{1}$	47·2	+59·6
		$\bar{2}$	23·0	+22·3
		$\bar{3}$	11·5	+20·0
		$\bar{4}$	20·2	−22·9
		$\bar{5}$	20·2	−25·5
		$\bar{6}$	33·0	−34·0
		$\bar{7}$	11·5	−20·9
		$\bar{8}$	9·7	+7·4

h	k	l	F_o	F_c
14	0	$\bar{9}$	21·8	+21·5
		$\bar{10}$	25·0	+25·1
		$\bar{11}$	8·2	+7·7
		$\bar{12}$	< 7·0	+2·4
		$\bar{13}$	11·5	−10·7
16	0	$\bar{1}$	23·3	−29·0
		$\bar{2}$	20·1	−27·9
		$\bar{3}$	19·9	−16·4
		$\bar{4}$	< 9·7	+5·2
		$\bar{5}$	19·3	+24·7
		$\bar{6}$	18·9	+22·5
		$\bar{7}$	10·5	+7·8
		$\bar{8}$	< 8·5	+1·7
		$\bar{9}$	< 8·0	−8·3
		$\bar{10}$	14·2	−11·3
		$\bar{11}$	15·6	−12·0
		$\bar{12}$	< 3·8	+1·7
18	0	$\bar{1}$	< 9·0	+1·1
		$\bar{2}$	18·1	+19·9
		$\bar{3}$	8·7	+3·6
		$\bar{4}$	< 8·5	+6·1
		$\bar{5}$	< 8·1	+0·9
		$\bar{6}$	< 7·7	−3·9
		$\bar{7}$	11·8	−15·0
		$\bar{8}$	12·9	−8·1
		$\bar{9}$	< 5·4	+1·2
		$\bar{10}$	4·4	+2·7
20	0	$\bar{1}$	< 6·8	−3·0
		$\bar{2}$	< 6·8	−2·1
		$\bar{3}$	< 6·5	−9·5
		$\bar{4}$	< 6·1	−9·8
		$\bar{5}$	< 5·5	−1·4
		$\bar{6}$	< 4·7	+1·9
		$\bar{7}$	< 1·6	+7·4

(*b*) 0*kl* and *hk*0 zones

h	k	l	F_o	F_c	A_c	B_c
0	0	1	—	19·3	−19·3	0
		2	17·3	4·3	−4·3	0
		3	237·0	237·5	−237·5	0
		4	275·3	270·4	−270·4	0
		5	54·2	26·2	−26·2	0
		6	81·3	73·7	−73·7	0
		7	56·0	52·4	+52·4	0
		8	114·1	116·7	+116·7	0
		9	57·1	49·3	+49·3	0
		10	67·4	62·4	+62·4	0
		11	16·5	11·2	−11·2	0
		12	31·4	31·6	−31·6	0
		13	49·1	36·5	−36·5	0
		14	37·4	29·7	−29·7	0
		15	< 8·7	4·5	−4·5	0
		16	13·0	11·6	+11·6	0
		17	11·6	7·8	+7·8	0
		18	13·9	15·1	+15·1	0
0	2	0	192·1	201·3	+180·0	+90·2
		1	124·0	123·0	+104·4	−65·0
		2	74·2	73·1	+67·0	+29·2
		3	90·8	91·8	−89·5	+20·6
		4	177·9	186·2	−185·1	−19·8
		5	58·9	64·5	−62·4	−16·3
		6	73·2	77·2	−75·7	−15·1
		7	44·2	47·1	+43·7	+17·6
		8	59·4	60·0	+58·6	+13·1
		9	86·9	75·4	+75·1	6·6

h	k	l	F_o	F_c	A_c	B_c
0	2	11	16·4	12·9	+12·5	+3·0
		12	41·2	31·4	−31·3	+2·4
		13	31·9	25·3	−25·2	−1·6
		14	36·8	29·6	−29·5	−2·3
		15	10·8	10·1	−10·1	−0·7
		16	7·6	7·7	+7·7	+0·3
		17	14·1	11·6	+11·5	+1·1
0	4	0	129·3	130·0	+128·1	+22·2
		1	123·4	127·4	+121·6	−38·0
		2	43·6	40·6	−28·6	+28·8
		3	46·7	52·5	−51·3	−11·1
		4	92·2	87·0	−86·4	+10·6
		5	105·2	98·9	−94·5	+29·1
		6	39·9	51·2	−33·2	−39·0
		7	10·0	6·4	+5·8	−2·7
		8	56·3	62·6	+62·6	+1·0
		9	61·5	64·0	+61·8	+16·5
		10	35·4	32·3	+32·3	+1·3
		11	19·6	10·8	+5·4	−9·4
		12	34·2	30·4	−30·3	−2·1
		13	34·9	25·1	−24·7	+4·2
		14	26·6	22·2	−22·1	−2·1
		15	< 5·5	1·5	+1·2	+0·9
		16	7·7	6·0	+6·0	−0·1
		17	6·3	6·1	+5·9	+1·4
0	6	0	80·8	83·5	+79·1	−26·6
		1	55·7	67·3	+66·9	+7·3

Table 5 (*cont.*)

(*b*) 0*kl* and *hk*0 zones

h	*k*	*l*	F_o	F_c	A_c	B_c
0	6	4	57·2	65·6	−61·5	+22·8
		5	64·2	79·7	−74·6	−28·1
		6	11·2	12·9	−12·8	−1·7
		7	18·9	22·9	−4·2	+22·5
		8	55·6	56·6	+55·6	−10·8
		9	27·1	35·7	+34·4	+9·7
		10	47·7	38·4	+31·5	−22·0
		11	< 6·8	4·8	−3·6	+3·1
		12	25·7	22·0	−21·1	+6·3
		13	20·4	17·3	−17·3	+1·3
		14	16·9	11·0	−10·6	+2·8
		15	4·1	5·0	−5·0	+0·3
0	8	0	38·1	44·9	+44·9	−1·7
		1	33·6	34·2	+30·2	+16·1
		2	6·8	8·4	+8·3	+1·3
		3	28·7	26·7	−12·2	−23·7
		4	53·5	55·4	−55·1	+5·8
		5	21·0	23·6	−19·9	−12·6
		6	23·1	21·3	−16·1	+14·0
		7	< 6·8	5·9	+5·9	0
		8	21·2	21·8	+21·7	+2·2
		9	14·6	17·5	+17·3	+2·6
		10	19·2	17·5	+16·7	−5·2
		11	5·5	5·4	+5·4	0
		12	9·6	10·0	−10·0	−0·4
		13	9·9	11·1	−11·1	−0·1
0	10	0	26·9	32·8	+32·8	+0·8
		1	9·2	13·8	+12·9	+5·0
		2	< 6·4	5·5	+2·6	−4·8
		3	9·0	11·5	−11·5	−0·6
		4	19·5	23·5	−23·5	−0·4
		5	11·9	13·9	−13·3	−4·1
		6	5·7	8·4	−7·4	+3·9
		7	5·2	8·3	+8·2	+1·3
		8	< 4·8	10·5	+10·3	+1·8
		9	10·3	10·2	+10·2	−0·2
		10	7·3	8·4	+7·0	−4·6
0	12	0	6·1	8·7	+8·2	−2·9
		1	< 3·5	4·9	+4·9	+0·1
		2	< 3·2	4·7	+4·6	+1·0
		3	4·9	5·4	−5·2	+1·5
		4	< 1·7	9·1	−8·7	−2·5
2	0	0	77·3	75·0	−75·0	0
4			107·7	112·4	−112·4	0
6			18·5	12·1	−12·1	0
8			40·7	31·4	+31·4	0
10			116·4	137·1	+137·1	0
12			70·3	85·2	−85·2	0
14			9·8	9·5	−9·5	0
16			< 10·0	4·7	−4·7	0
18			< 9·0	6·8	+6·8	0
20			< 7·0	6·7	+6·7	0
1	1	0	154·3	151·8	+101·8	+112·6
3			180·1	188·3	−185·6	−31·8
5			219·9	217·6	+215·8	+27·8
7			90·4	89·5	−87·6	+18·5
9			31·4	27·9	+25·2	+12·0
11			24·4	18·8	−17·4	−7·2
13			15·8	19·3	−14·7	−12·5
15			37·4	37·7	+37·2	+6·1
17			19·6	25·8	−24·1	+9·3
19			< 6·6	5·5	+4·8	−2·6
21			< 4·3	2·3	−2·0	−1·2
2	2	0	220·5	209·8	−209·7	+7·8
4			71·1	67·9	+49·8	−46·2
6			13·5	30·2	+24·5	+17·6
8			55·6	49·4	−48·8	+7·6
10			53·9	55·4	+54·0	+12·4
12	2	0	42·8	55·7	−53·5	−15·5
14			31·0	35·6	+35·5	−2·7
16			8·2	7·2	−6·5	+3·1
18			< 7·3	4·7	−1·1	−4·6
20			9·3	7·9	+7·3	−3·1
1	3	0	92·2	76·0	+75·8	+5·9
3			77·8	68·1	−68·0	−3·5
5			159·4	163·2	+163·1	+6·1
7			66·7	69·5	−69·3	−5·8
9			38·2	43·2	+41·7	+11·4
11			21·4	20·4	−19·7	−5·4
13			16·3	13·3	−10·5	+8·1
15			25·0	24·1	+23·8	+3·5
17			13·3	15·6	−15·0	−4·2
19			6·0	11·0	+10·4	−3·6
21			< 1·3	3·6	−3·2	+1·6
2	4	0	111·4	93·1	−84·6	+38·9
4			95·5	80·4	+80·3	−3·1
6			33·9	25·3	+24·6	−5·7
8			66·1	67·5	−66·1	+13·7
10			37·1	45·6	+43·4	+14·1
12			28·2	31·7	−31·4	−4·2
14			20·4	22·6	+22·0	+5·3
16			< 7·8	13·6	−13·3	+2·9
18			< 6·5	5·4	−3·2	+4·4
20			< 4·0	8·2	+7·2	+4·0
1	5	0	42·3	30·8	+16·5	+26·0
3			103·3	94·0	−88·0	+33·0
5			76·5	84·3	+78·4	+30·9
7			73·8	72·7	−72·7	+0·1
9			23·1	28·8	+27·9	−7·2
11			14·3	13·0	−6·5	−11·3
13			14·4	9·2	−8·7	+3·1
15			< 7·9	10·2	+7·8	+6·5
17			11·6	11·8	−11·8	+1·0
19			< 4·4	5·8	+5·6	−1·4
2	6	0	62·7	51·8	−50·8	+10·3
4			46·9	47·2	+40·0	+25·0
6			15·0	16·8	+16·7	+1·3
8			28·7	33·3	−33·3	+1·5
10			27·6	28·4	+28·3	−2·0
12			25·0	26·5	−26·2	−3·8
14			11·1	14·5	+14·2	−2·8
16			6·7	7·7	−7·5	−1·6
18			< 4·6	1·5	−1·5	−0·3
1	7	0	17·1	20·9	+15·4	+14·2
3			41·0	42·0	−33·8	+24·9
5			56·4	63·9	+62·7	−12·3
7			39·4	42·1	−42·1	−1·0
9			18·7	14·2	+9·6	+10·4
11			8·2	9·0	−7·9	+4·3
13			< 7·6	2·6	−0·3	−2·6
15			12·8	9·8	+8·6	−4·6
17			< 4·4	8·6	−8·6	+0·3
2	8	0	50·1	51·6	−50·3	+11·5
4			8·2	7·1	+1·0	+7·0
6			20·4	13·7	−2·1	−13·5
8			18·5	21·6	−21·5	+2·3
10			16·0	21·2	+21·2	+1·0
12			12·5	14·7	−14·3	+3·5
14			< 6·0	8·1	+7·9	−1·7
16			< 3·8	3·3	−2·8	−1·7
1	9	0	11·7	13·7	+11·6	−7·2
3			31·0	31·8	−31·1	+6·4
5			20·1	25·4	+25·4	−0·7
7			19·5	22·7	−22·4	−3·6
9			12·8	11·6	+11·2	−3·1
11			< 6·7	3·9	−0·5	+3·9
13			< 5·2	5·5	−5·5	+0·1

Table 5 (*cont.*)

h	k	l	F_o	F_c	A_c	B_c
2	10	0	13·5	16·3	−16·3	−0·4
4			<7·6	10·1	+9·5	+3·5
6			<7·1	2·1	+2·1	+0·2
8			<6·5	4·8	−4·8	+0·2
10			<5·5	8·2	+8·2	+0·2
12			9·5	13·2	−13·2	−0·7
1	11	0	<6·5	2·9	−0·7	+2·8
3			10·8	11·3	−10·9	+2·9
5			10·1	11·1	+11·1	−0·6
7			7·3	9·0	−8·8	−1·7
9			<3·6	4·2	+4·2	0
2	12	0	9·3	11·0	−10·9	+1·2
4			<3·2	2·5	+1·6	+1·9

0·012 Å (atom C_8). The atoms C_2, N_1 and O_4 were found at about +0·06 Å from this plane and can therefore be considered as nearly co-planar with the benzene ring. The five-membered ring of the oxindole group is, however, decidedly puckered at C_1 which was found at +0·30 Å from the above plane. It is of interest that the O_2 atom does not lie in the plane of C_2, C_1 and N_1 atoms, but is displaced from it by 0·17 Å towards the plane of the benzene ring. This may be due to the energy of the intra-molecular hydrogen bond $N_2^+–H \cdots O_2$ which forms a seven-membered chelate ring. The angle $N_2^+ \cdots O_2=C_1$ is 103° and the hydrogen atom attached to N_2 is roughly directed towards O_2. The distance between N_2 and O_2 is 2·77 Å and compares well with the $N^+–H \cdots O$ hydrogen bond lengths listed for a large group of compounds by Pimentel & McClellan (1960). The presence of the hydrogen bond was confirmed by the study of the infra-red absorption spectrum of N-methyl gelsemicine hydriodide (Przybylska & Marion, 1961).

The pyrane ring has the 'boat' form and this can be seen most easily in Fig. 1. A few intra-molecular distances are worth mentioning: $C_4 \cdots O_1$, $C_{11} \cdots C_{16}$ and $C_{21} \cdots O_2$, which are 3·18, 2·28 and 3·32 Å, respectively.

The projection of the structure along the c axis with the closest intermolecular contacts is shown in Fig. 4. The distances between the atoms of the two parallel benzene rings are of the usual order and only those below 3·80 Å are illustrated. The closest approaches of C_{21} to benzene ring atoms are all greater than 3·85 Å with the exception of distances to C_4 and C_5 which are 3·41 and 3·32 Å respectively. All other $C \cdots C$ contacts are greater than 3·5 Å and all those below 4·0 Å are also shown in Fig. 4. Of the $C \cdots O$ intermolecular approaches, all are above 3·75 Å with the exception of three distances to the atom O_4. The shortest of these $C_{19} \cdots O_4$ is 3·11 Å, but it can be considered as normal since the hydrogen atoms attached to C_{19} do not lie along the line joining these two atoms. All the shortest $C \cdots I^-$ distances smaller than 4·11 Å are also depicted in Fig. 4. The $N_2^+ \cdots I^-$ distance was found to be 4·39 Å.

The solution of this hitherto essentially unknown structure revealed a number of unusual features. This is the first compound obtained from natural sources with a methoxyl group attached to the nitrogen atom. It was interesting to find the ethyl group attached to the carbon next to the quaternary nitrogen and in this connection it is worth noting that there is supporting chemical evidence. It has been established that gelsemicine does not form salts of the anhydronium type and therefore this group could not be a methoxyl. The presence of a very compact skeleton of the molecule containing a seven-membered ring contributed also to make this investigation really worth while.

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