Tetrahedron Vol. 35, pp. 1893–1898
© Pergamon Press Ltd., 1979. Printed in Great Britain

0040-4020/79/0801-1893/$02.00/0

THE CRYSTAL AND MOLECULAR STRUCTURE OF DL-BI-(*O*-TRIMETHYL-*cis*-BRAZILANE)

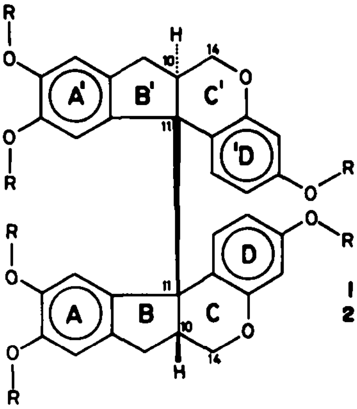
M. F. MACKAY* and N. W. ISAACS†
Laboratory of Molecular Biophysics, Department of Zoology, South Parks Road, Oxford OX1 3PS, England

and

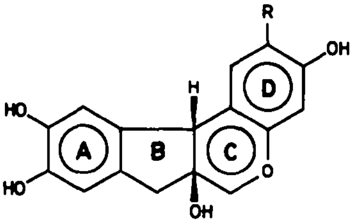
*Department of Physical Chemistry, La Trobe University, Bundoora, Victoria 3083, Australia

(*Received in the UK* 13 *February* 1979)

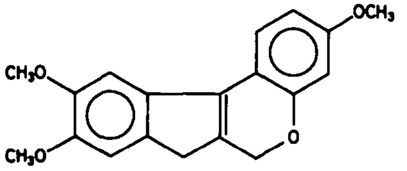
Abstract—X-ray crystallographic analysis has established the crystal and molecular structure of the title compound, $C_{38}H_{38}O_8$. The monoclinic crystals belong to the centrosymmetric space group $P2_1/c$, with $a = 16.701(5)$, $b = 8.037(2)$, $c = 23.600(9)$ Å, $\beta = 93.10(2)°$ and $Z = 4$. The structure was solved by direct methods from diffractometer data measured with CuKα radiation, and refined to a final R index of 0.081 for the 2088 observed terms. The dimeric molecule has approximate two-fold symmetry and its presence in the unit cell in both chiralities forms a racemic structure. The three central bonds, C(10)–C(11), C(11)–C′(11), C′(11)–C′(10), are significantly elongated with a mean value 1.59 Å.



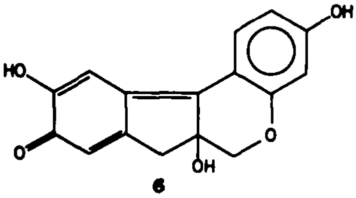
1: R = CH_3
2: R = CH_3CO



3: R = H
4: R = OH



5



6

INTRODUCTION

Bi(*O*-trimethyl-*cis*-brazilane), $C_{38}H_{38}O_8$, shown as **1**, is a derivative of the natural product *d*-brazilin, $C_{16}H_{14}O_5$. The latter was first isolated in crystalline form by Chevreul in 1808[1] from Brazil-wood, a tree occurring in various species of *Caesalpinia*. Together with the related substance *d*-haematoxylin, $C_{16}H_{14}O_6$, isolated by Chevreul[2] from Logwood, which occurs in *Haematoxylon campechianum* (family *Caesalpiniaceae*), brazilin has been the subject of extensive chemical study over the past hundred years.[3] The structures of brazilin and haematoxylin as polyhydroxybenzindenopyrans, shown as **3** and **4** respectively, have been known as a result of almost 50 years work by Perkin and Robinson.[3,4] More recently, however, NMR spectral studies have established the *cis*-fusion[5] of rings B and C.

A recent synthesis of DL-brazilin by way of *O*-trimethyldeoxybrazilone (**5**), also known as anhydro-*O*-trimethylbrazilin, by Robinson *et al.*[6] involved the synthesis of *O*-trimethylbrazilane as an intermediate. As the latter is optically inactive and dimeric,[7] bi-*O*-trimethyl-*cis*-brazilane (**1**) could either form a racemic mixture or a *meso* compound in which the *O*-trimethylbrazilanyl monomers comprising the molecule are of opposite chirality. The reduction product of brazilein (**6**) reported by Herzig and Pollak[8] early this century, now is established to be the dimeric hexacetyl derivative (**2**) which results from reductive coupling of two molecules of brazilein.[7]

The X-ray analysis of crystals of **1** was undertaken to define the structural and conformational detail in the dimeric molecule. The essential features of the structure have been presented earlier.[9]

EXPERIMENTAL

Bi(*O*-trimethyl-*cis*-brazilane) formed colourless, monoclinic lath-shaped crystals from an ethanol/methanol mixture. Weis-

---

†Present address: St. Vincent's School of Medical Research, Victoria Parade, Fitzroy, Victoria, Australia, 3065.

senberg photographs showed that they belonged to the space group $P2_1/c$, and accurate unit cell parameters were determined by a least-squares fit of 2θ values, measured for fifteen strong reflections on a four-circle diffractometer with CuK_α radiation. The crystal density was determined by flotation in a xylene/carbon tetrachloride mixture.

Crystal data. Bi(*O*-trimethyl-*cis*-brazilane), $C_{38}H_{38}O_8$. F.W. = 622.68, monoclinic space group $P2_1/c$, $a = 16.701(6)$, $b = 8.037(2)$, $c = 23.600(9)$ Å, $\beta = 93.10°$, $U = 3163.1$ Å^3, F(000) = 1320, D_m = 1.31(2), $D_c = 1.31$ g cm^{-3}, $Z = 4$; $\mu(CuK_\alpha) = 6.56$ cm^{-1}, λ = 1.5418 Å.

Three-dimensional intensity data were measured with Ni-filtered CuK_α radiation on a Hilger and Watts four-circle diffractometer. The intensities were recorded by the $\omega - 2\theta$ scan technique to a 2θ maximum of 140°, and 2355 non-equivalent terms for which $I_0 > 4\sigma I_0$ were used in the initial analysis. No absorption corrections were applied.

For refinement purposes the initial data set did not prove wholly satisfactory. Accordingly, a further set of intensity data was measured with CuK_α radiation (graphite crystal monochromator) on a Rigaku-*AFC* four-circle diffractometer. A crystal with approximate dimensions 0.05 × 0.125 × 0.10 mm was aligned with the *b* axis, the longest crystal axis, approximately parallel to the ϕ axis of the diffractometer. The intensities were recorded by the $\omega - 2\theta$ scan technique with a scan rate of 2° min^{-1} and 10 sec stationary background counts. Three reference reflections were monitored every 50 reflections and showed no significant variation in intensity over the data collection period. Of the 4566 non-equivalent terms measured to a 2θ maximum of 126°, 2088 terms for which $|F_0| > 3\sigma|F_0|$ were used for the refinement. No corrections for absorption or extinction were applied to the measured intensities. Scattering factors used in the analysis were those given by Cromer and Mann[10] for C and O and by Stewart *et al.*[11] for H.

The structure was solved by direct methods. Phases for 295 $|E|$ terms with values greater than 1.80 were derived by application of the tangent formula.[12] The final phased set of reflections had an R (Karle)[12] of 0.21 and scale factor $\langle|E_0|\rangle/\langle|E_c|\rangle = 1.00$. The subsequent E-map clearly revealed the sites of all the C and O atoms in asymmetric unit comprising the molecular skeleton. Isotropic refinement yielded a reliability index, $R = \Sigma\|F_0| - |F_c\|/\Sigma|F_0|$, of 0.17, and when anisotropic temperature factors were given to all the non-hydrogen atoms and their parameters refined in blocks of 9 × 9, R was reduced to 0.10 for the 2355 terms.

For the final refinement cycles, the second data set of 2088 terms was used. Anisotropic refinement in which the atomic parameters were refined in two blocks, each block including parameters for one monomeric molecular unit, converged at $R = R_\omega = 0.081$ where $R_\omega = (\Sigma\omega\|F_0| - |F_c\|^2/\Sigma|F_0|^2)^{1/2}$. The function minimized was $\omega(|F_0| - |F_c|)^2$ with $\omega = n/(\sigma^2|F_0| + m \times 10^{-2}|F_0|^2)$ for which the appropriate values of n and m were found to be 0.87 and 0.37 respectively. The H atom coordinates were included at idealized positions but were not refined. The methyl H atoms were given an isotropic temperature factor, U = 0.12 Å^2, and all the others were assigned the value 0.07 Å^2.

The program used for the direct methods solution is described in detail by Kennard *et al.*,[13] and is similar to the procedure of Germain and Woolfson.[14] The final least-squares refinements were made with *SHELX*76 program.[15] Final atomic coordinates for the non-hydrogen atoms together with their estimated standard deviations are given in Table 1, and the calculated H atom coordinates are given in Table 2. Bond lengths and angles appear in Fig. 2 while the shortest intermolecular distances are listed in Table 3(a)—see also Fig. 4 which illustrates the molecular packing viewed down the *b* axis. Tables of calculated and observed structure amplitudes and anisotropic thermal parameters for the non-hydrogen atoms are available on request from the authors.

DESCRIPTION OF STRUCTURE

A stereoscopic view of the molecular skeleton is given in Fig. 1 while a conventional representation is shown as 1. The molecule consists of two brazilanyl groups, which are of the same chirality, linked by the bond C(11)–C′(11) into a dimer. Apart from small differences in the relative orientation of the methyl groups in each monomeric unit, the molecule has a non-crystallographic two-fold rotation axis perpendicular to the C(11)–C′(11) bond. Viewed down the latter the configuration is staggered—see Fig. 3. The molecular skeleton of each brazilanyl group consists of four ring systems fused together to form a rigid framework, the only mobile atoms being those of the three methyl groups. All the methoxy carbon atoms are *pseudo* coplanar with the banzene ring planes (mean deviation 0.26 Å, maximum deviation 0.46 Å), and those of the *ortho*-substituted methoxy groups lie on opposite sides of their respective benzene ring planes as noted in other *o*-dimethoxy phenyl moities.[16,17]

The dimensions derived for both brazilanyl ring systems are in reasonable agreement, so that the numerical values given below refer to mean values for the two systems. The benzene ring and associated atoms lie close to two planes with the benzene rings mutually inclined at

Table 1. Final atomic coordinates of the non-hydrogen atoms with their estimated standard deviations in parentheses. All values have been multiplied by 10^4

	x	*y*	*z*		*x*	*y*	*z*
C(1)	4378(7)	1666(16)	1988(5)	C′(1)	3162(5)	−3108(10)	−444(3)
C(2)	3643(7)	2043(13)	2185(4)	C′(2)	2426(4)	−2346(9)	−559(3)
C(3)	2961(6)	1880(12)	1816(4)	C′(3)	2042(4)	−1646(10)	−112(3)
C(4)	3014(5)	1370(10)	1269(4)	C′(4)	2382(4)	−1639(10)	436(3)
C(5)	3775(5)	995(11)	1072(4)	C′(5)	3108(5)	−2466(10)	548(3)
C(6)	4442(6)	1098(14)	1425(4)	C′(6)	3480(5)	−3230(11)	109(3)
C(7)	5306(6)	270(15)	714(4)	C′(7)	4457(7)	−4654(16)	698(4)
C(8)	5065(7)	2108(23)	2883(5)	C′(8)	3369(6)	−3544(14)	−1431(4)
C(9)	2105(6)	2128(13)	1967(4)	C′(9)	1220(4)	−833(11)	−141(3)
C(10)	1622(5)	2062(11)	1392(3)	C′(10)	1049(4)	−565(10)	487(3)
C(11)	2183(5)	1251(10)	948(3)	C′(11)	1883(4)	−636(9)	848(3)
C(12)	2120(5)	2198(11)	386(4)	C′(12)	1802(4)	−1539(9)	1412(3)
C(13)	1494(6)	3303(11)	254(4)	C′(13)	1074(5)	−2038(10)	1604(4)
C(14)	1375(6)	3799(12)	1218(4)	C′(14)	493(5)	−1925(11)	674(4)
C(15)	1347(6)	3966(12)	−286(4)	C′(15)	990(6)	−2773(11)	2137(4)
C(16)	1832(6)	3529(13)	−712(4)	C′(16)	1663(6)	−3129(11)	2471(4)
C(17)	2500(6)	2553(13)	−596(4)	C′(17)	2411(5)	−2699(12)	2296(4)
C(18)	2637(5)	1893(12)	−55(3)	C′(18)	2469(5)	−1915(10)	1780(3)
C(19)	1012(7)	4993(14)	−1408(5)	C′(19)	930(8)	−4675(16)	3145(5)
O(1)	5091(5)	1745(11)	2303(3)	O′(1)	3613(3)	−3824(8)	−852(2)
O(2)	5201(4)	705(10)	1283(3)	O′(2)	4198(3)	−4065(9)	173(2)
O(3)	981(4)	3796(8)	656(3)	O′(3)	371(3)	−1822(7)	1271(3)
O(4)	1731(4)	4082(9)	−1263(3)	O′(4)	1646(4)	−3895(9)	2986(3)

Table 2. Calculated hydrogen atom coordinates multiplied by 10^3. The atoms have been given the same numbering as the carbon to which they are bonded

	x	y	z		x	y	z
H(2)	359	245	262	H'(2)	216	-230	-99
H(5)	383	62	64	H'(5)	337	-251	97
H(7A)	593	-9	74	H'(7A)	503	-528	68
H(7B)	522	132	43	H'(7B)	402	-549	87
H(7C)	495	-76	58	H'(7C)	452	-356	96
H(8A)	566	217.	309	H'(8A)	383	-397	-170
H(8B)	471	118	309	H'(8B)	333	-220	-145
H(8C)	478	331	291	H'(8C)	280	-409	-157
H(9A)	192	114	224	H'(9A)	123	33	-37
H(9B)	203	331	218	H'(9B)	78	-165	-35
H(10)	108	134	142	H(10)	77	63	55
H(14A)	190	459	122	H'(14A)	76	-312	58
H(14B)	96	427	152	H'(14B)	-8	-181	44
H(15)	85	480	-38	H'(15)	40	-304	228
H(17)	292	233	-92	H'(17)	294	-297	256
H(18)	316	111	3	H'(18)	306	-157	165
H(19A)	73	570	-108	H'(19A)	68	-549	282
H(19B)	115	583	-175	H'(19B)	100	-535	354
H(19C)	61	404	-157	H'(19C)	53	-363	320

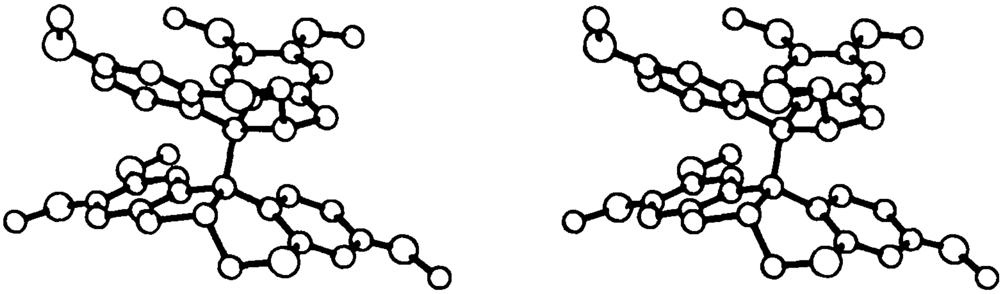


Fig. 1. A stereo view of the molecule.

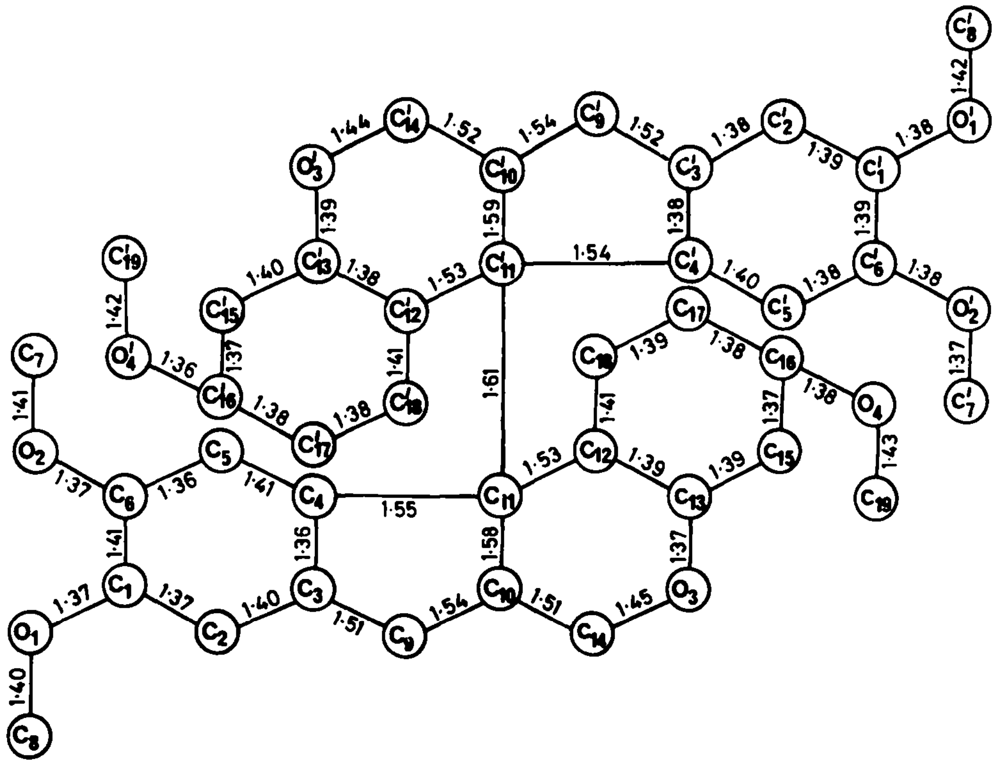


Fig. 2(a).

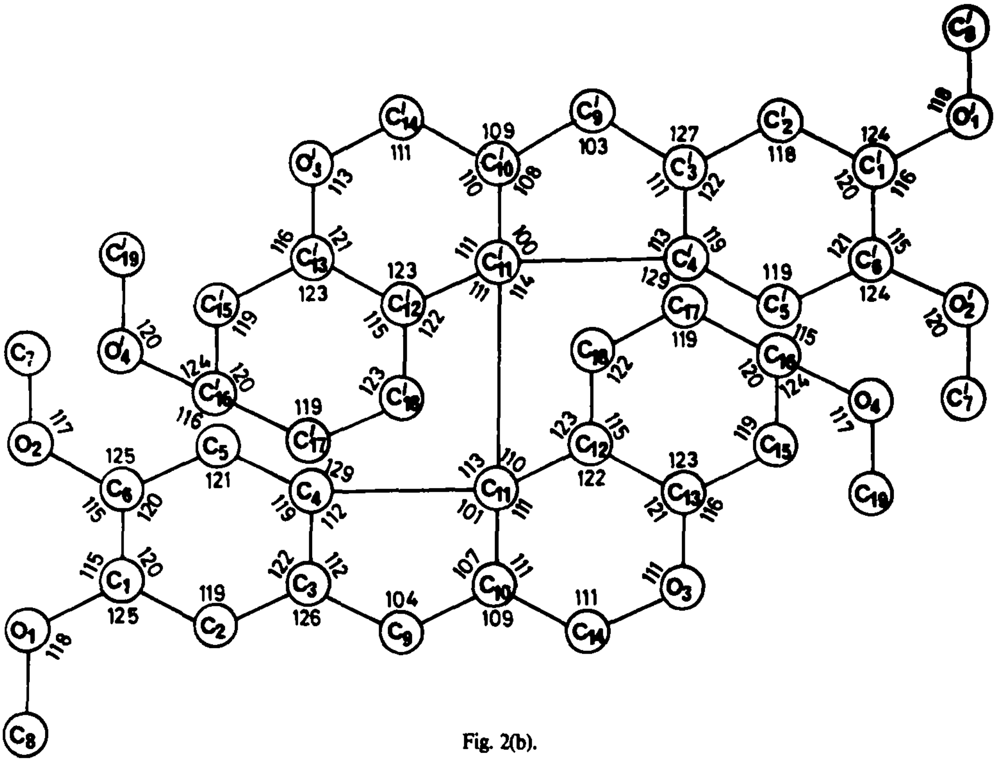


Fig. 2(b).

Fig. 2. (a) Bond lengths. The estimated standard deviations are 0.01 Å. (b) Bond angles. The estimated standard deviations are 0.05°.

Table 3. (a) Intermolecular contact distances less than 3.50 Å. The estimated standard deviations range from 0.01 to 0.02 Å. (b) Selected intramolecular contacts between atoms of different brazilanyl groups

(a)	C(7).....O'(1)$^{\mathrm{I}}$	3.39 Å
	O(2).....C'(8)$^{\mathrm{I}}$	3.31
	O(2).....O'(1)$^{\mathrm{I}}$	3.39
	C(16)....C'(2)$^{\mathrm{II}}$	3.47
	O(4).....C'(2)$^{\mathrm{II}}$	3.48
	O(4).....C'(8)$^{\mathrm{II}}$	3.38
	C(19)....O'(3)$^{\mathrm{III}}$	3.47
	C'(8)....C'(17)$^{\mathrm{IV}}$	3.47
	O'(7)....C'(7)$^{\mathrm{V}}$	3.45

Symmetry Code

I	:	1 - x	- y	- z
II	:	x	1 + y	z
III	:	- x	- y	- z
IV	:	x	-½ - y	-½ + z
V	:	1 - x	-1 - y	- z

(b)	H(10).....H'(10)	2.17 Å	C(12).....C'(4)	3.12 Å
	H(10).....C'(12)	2.61	C(15).....H'(9A)	2.94
	H(10).....C'(13)	2.75	H(5) .....H'(5)	2.75
	O(3) .....H'(10)	2.58	H(5) .....C'(5)	2.76
	C(13).....H'(10)	2.58	C(5) .....H'(5)	2.90

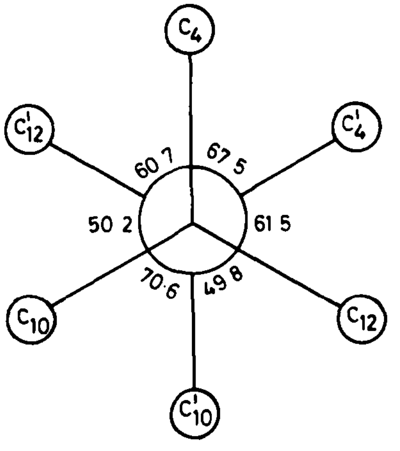


Fig. 3. A Newman projection along the C(11)–C'(11) bond.

45.7° to render the brazilanyl moiety an approximate butterfly shape. The benzene ring atoms are planar within ±0.04 Å. The conformation of the dihydroindeneobenzopyran ring system with the *cis* B/C ring junction is staggered, and the torsion angle, O(3)[C(14), C(10)]C(11) is 56.5°. Ring B is envelope with four atoms planar within ±0.04 Å and C(10) lying 0.31 Å above the plane, whereas ring C assumes a severely distorted boat conformation with atoms C(11), C(12), C(13) and O(3) planar within ±0.05 Å and C(10) and C(14) lying 0.17 and 0.79 Å respectively below the plane. The conformation of the benzopyran system is different from its conformation in the X-ray structure of the pterocarpan derivative phaseollin.[18] In the latter, ring C adopts a skewed conformation, that is the two out-of-plane atoms lie above and below the plane of the other four. Consequently, the phaseollin molecule is an approximate propeller shape.

The aromatic C–C bonds have the usual mean value 1.39 Å (mean deviation 0.02 Å). The C(aromatic)–O and $C(sp^3)$–O mean bond lengths of 1.37 and 1.42 Å respectively, agree satisfactorily with the corresponding mean values found in the two alkaloid structures, 1.371 and 1.426 Å in cryptopine[19] and 1.362 and 1.411 Å in sceletium.[16] The three central bonds, C(10)–C(11), C(11)–C'(11) and C'(11)–C'(10), however, have lengths significantly longer than the usual length of 1.537(5) Å[20] for saturated C–C bonds; their values range from 1.58 to 1.61 Å, with the bond linking the two brazilanyl monomers, C(11)–C'(11), the longest. This elongation could be a consequence of steric interaction involving the two hydrogen atoms bonded to C(10) and C'(10) respectively. Some intramolecular distances involving atoms in the different brazilanyl groups have been included in Table 3(b).

About the exocyclic attachments of the methoxy groups, the angle enclosed by the methyl group is larger than the other, these values being 124.4(0.5) and 115.5(0.5)° respectively. Similar results have been noted in numerous comparable structures, for example in the alkaloid structures of cryptostyline *I*[17] and sceletium.[16] There also is significant distortion from trigonal geometry about C(3) and C(4). The exocyclic angles, C(2)–C(3)–C(9) and C(5)–C(4)–C(11), have the respective values 126.4(0.2) and 128.7(0.1)°, while the endocyclic angles C(3)–C(4)–C(11) and C(4)–C(3)–C(9) have values 111.8(0.4) and 112.4(0.1)°. The angles C(4)–C(11)–C(10)

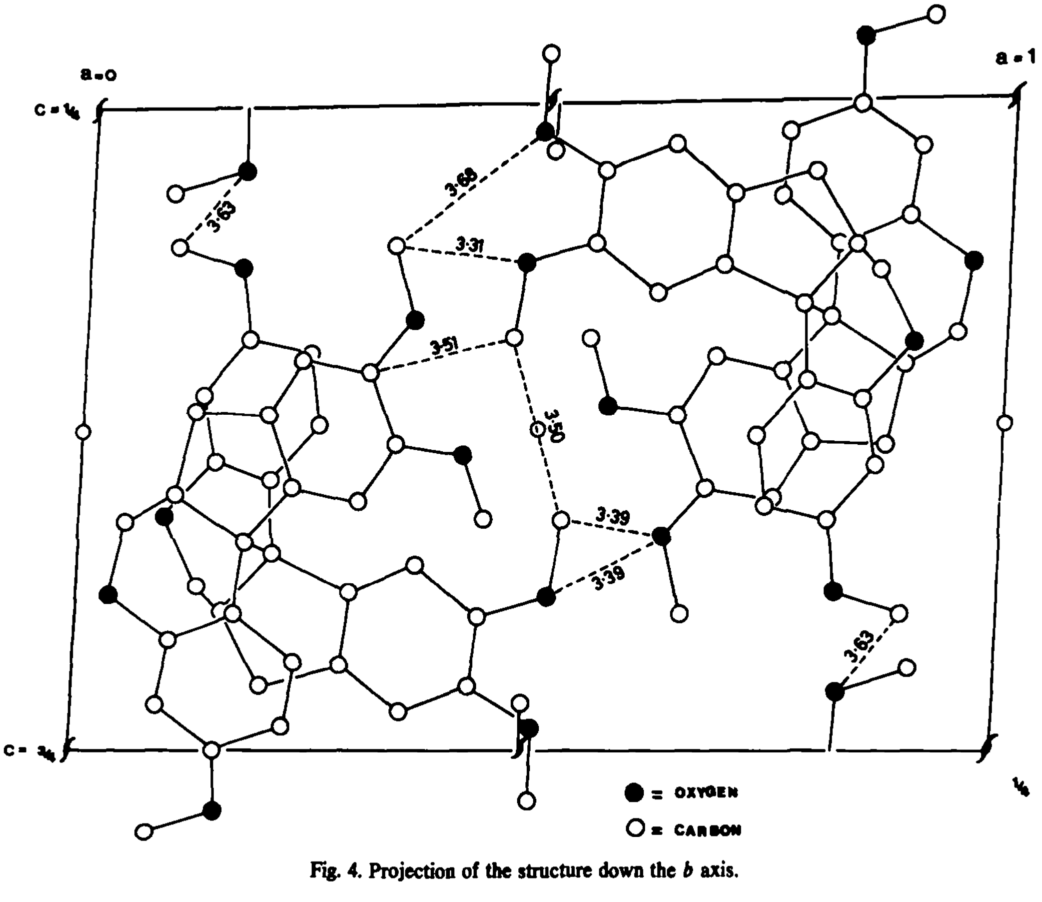


Fig. 4. Projection of the structure down the *b* axis.

are significantly distorted from the standard tetrahedral value, and have a mean of 100.6(0.9)°.

The molecular packing in the crystal is illustrated in Fig. 4. The molecules are held together by van der Waals interactions and are present in the crystal in both D and L configurations to form a racemic mixture. The intermolecular approach distances are normal—see Table 3(a) and Fig. 4.

Acknowledgements—We are grateful to the late Sir Robert Robinson for suggesting this interesting problem and we thank Dr. R. H. Jaeger who kindly prepared the crystals.

REFERENCES

[1] M. E. Chevreul, *Ann. Chim.* **66**, 225 (1808).

[2] M. E. Chevreul, *Ann. Chim. Phys.* **82**, 54, 126 (1810).

[3] R. Robinson, *Bull. Chim. Soc.* (*France*) **1**, 125 (1958).

[4] W. H. Perkin and R. Robinson, *J. Chem. Soc.* 1073 (1907); R. Robinson, *Rodd's Chemistry of Carbon Compounds* (Edited by S. Coffey), Vol. IV, Part E, Chap. 22. Elsevier, New York (1977).

[5] J. C. Craig, A. R. Naik, R. Pratt, E. Johnson and N. S. Bhacca, *J. Org. Chem.* **30**, 1573 (1965).

[6] F. Morsingh and R. Robinson, *Tetrahedron* **26**, 281 (1970); J. N. Chatterjea, R. Robinson and M. L. Tomlinson, *Ibid.* **30**, 507 (1974).

[7] R. H. Jaeger, P. M. E. Lewis and R. Robinson, *Ibid.* **30**, 1295 (1974).

[8] J. Herzig and J. Pollak, *Monatsh* **22**, 207 (1901); with Galitzenstein, *Ibid.* **25**, 871 (1904).

[9] N. L. Isaacs and M. F. Mackay, *Tetrahedron Letters* 1921 (1976).

[10] D. T. Cromer and J. B. Mann, *Acta Cryst.* **A24**, 321 (1968).

[11] R. F. Stewart, E. R. Davidson and W. T. Simpson, *J. Chem. Phys.* **42**, 3175 (1965).

[12] I. L. Karle and J. Karle, *Acta Cryst.* **21**, 849 (1966).

[13] O. Kennard, N. W. Isaacs, W. D. S. Motherwell, J. C. Coppola, D. L. Wampler, A. C. Larson and D. G. Watson, *Proc. R. Soc. Lond. A* **325**, 401 (1971).

[14] G. Germain and M. M. Woolfson, *Acta Cryst.* **B24**, 91 (1968).

[15] G. M. Sheldrick, *SHELX76. Program for Crystal Structure Determination* (1976).

[16] P. A. Luhan and A. T. Mcphail, *J. Chem. Soc. Perkin II* 2006 (1972).

[17] L. Westin, *Acta Chem. Scand.* **26**, 2305 (1972).

[18] C. DeMartinis, M. F. Mackay, D. R. Perrin and B. J. Poppleton, *Tetrahedron Letters* 2981 (1977); C. Demartinis, M. F. Mackay and B. J. Poppleton, *Tetrahedron* **34**, 1849 (1978).

[19] S. R. Hall and F. R. Ahmed, *Acta Cryst.* **B24**, 346 (1968).

[20] *Tables of Interatomic Distances and Configurations in Molecules and Ions.* (Supplement 1956–59). Special Publication No. 11. The Chemistry Society, London (1965).