# Absolute Configuration of the Most Potent Isomer of the Pyrethroid Insecticide α-Cyano-3-phenoxybenzyl cis-3-(2,2-Dibromovinyl)-2,2-dimethylcyclopropanecarboxylate by Crystal Structure Analysis

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The absolute configuration of the title compound has been determined by X-ray diffraction analysis. Crystals are orthorhombic, space group $P2_12_12_1$, with $Z = 4$ in a unit cell of dimensions: $a = 12.319(10)$, $b = 27.170(26)$, $c = 6.294(5)$ Å. Intensity data were collected on a diffractometer and the structure solved by standard methods and refined to R 0.070 for 616 observed reflections. The absolute configuration about the benzylic α-carbon atom is (S); the conformation of the molecule is discussed.

RECENTLY discovered pyrethroids have a favourable combination of properties, including outstanding insecticidal activity and greater photostability than previous natural and synthetic esters.[1] Considerable progress has been made in relating the structure of

(I)

(II)
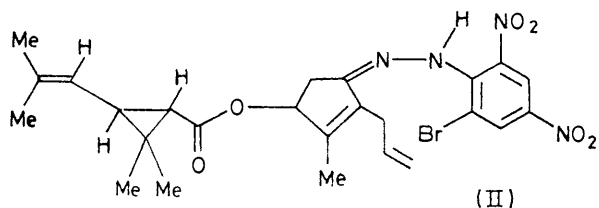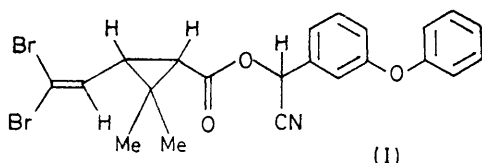
pyrethroids with their biological activity,[2] but refinement of such concepts needs reliable information on molecular shape (including configuration, bond lengths and angles, and conformation).

any class, available at present.[3] The molecule of (I) has three asymmetric centres. The configuration about the cyclopropane ring is known to be cis-$(1R,3R)$ from the method of synthesis and that of the benzylic α-carbon atom was deduced to be (S) by an extended chemical argument.[3] In view of its crystalline nature, (I) forms an excellent subject for X-ray diffraction work, and the results of this are reported here. A preliminary report has appeared.[4] The only previous crystallographic work on a pyrethroid determined the absolute configuration, in doubt at C(4), of the cyclopentene ring of the synthetic 6-bromo-2,4-dinitrophenylhydrazone derivative of $(4S)$-2-(prop-2-enyl)rethron-4-yl $(1R,3R)$-$trans$-chrysanthemate [5] [(S)-bioallethrin] (II). However, the present work on (I) is the first structure determination of an actual insecticide in the pyrethroid group.

The crystal structure of (I) was solved by Patterson and Fourier methods and refined by least-squares techniques. The absolute configuration was obtained by calculating structure factors (using anomalous dispersion coefficients for the bromine atoms) for the hkl and $h\bar{k}l$ Bijvoet pairs. The resulting atomic coordinates are listed in Table 1 and the atom numbering and bond distances in Figure 1.

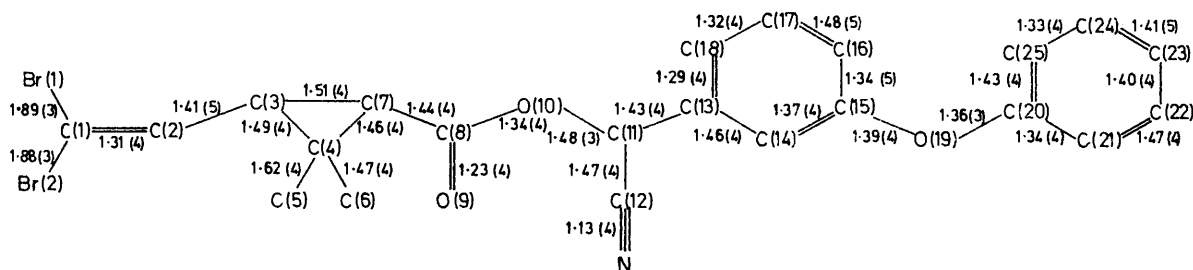
FIGURE 1   Molecule of (I) showing atom numbering system used and bond distances

Recently α-cyano-3-phenoxybenzyl cis-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropane carboxylate (I) was synthesised, and one of the two isomers (designated NRDC 161) was obtained as crystals and shown to be more potent as an insecticide than any compound, of

RESULTS AND DISCUSSION

The crystal structure results from the packing of discrete molecules, the closest intermolecular contacts being between hydrogen atoms and all >2.34 Å (Table 2).

[1] L. Crombie and M. Elliott, *Fortschr. Chem. org. Naturstoffe*, 1961, **19**, 120; M. Elliott and N. F. Janes, ' Pyrethrum, the Natural Insecticide,' ed. J. E. Casida, Academic Press, New York, 1973, p. 55; M. Elliott, A. W. Farnham, N. F. Janes, P. H. Needham, D. A. Pulman, and J. H. Stevenson, *Nature*, 1973, **246**, 169.

[2] M. Elliott, *Chem. and Ind.*, 1969, 776; *Bull. World Health Organisation*, 1971, **44**, 315.

[3] M. Elliott, A. W. Farnham, N. F. Janes, P. H. Needham, and D. A. Pulman, *Nature*, 1974, **248**, 710.

[4] J. D. Owen, *J.C.S. Chem. Comm.*, 1974, 859.

[5] M. J. Begley, L. Crombie, D. J. Simmonds, and D. A. Whiting, *J.C.S. Perkin I*, 1974, 1230.

The packing diagram (Figure 2) shows there are no obvious strong interactions (such as hydrogen bonds) holding the molecules together in the crystal.

TABLE 1

Fractional co-ordinates ($\times 10^4$ for Br, $\times 10^3$ otherwise), and temperature factors ($U \times 10^3$); estimated standard deviations in parentheses; $U = 0.051$ for H atoms

Atom	x/a	y/b	z/c	U
Br(1)	−0 204(4)	7 329(2)	8 877(6)	*
Br(2)	−0 649(3)	8 430(2)	10 350(6)	*
C(1)	−006(2)	801(1)	829(5)	31(8)
C(2)	046(3)	814(1)	655(6)	67(11)
C(3)	089(2)	784(1)	492(6)	45(9)
C(4)	201(2)	763(1)	488(5)	35(8)
C(5)	274(3)	777(1)	693(6)	52(11)
C(6)	213(3)	713(1)	408(7)	59(11)
C(7)	174(2)	802(1)	338(5)	39(9)
C(8)	215(3)	852(1)	336(7)	67(12)
O(9)	235(2)	876(1)	496(5)	68(7)
O(10)	233(2)	870(1)	141(3)	39(6)
C(11)	288(2)	919(1)	131(5)	28(8)
C(12)	227(2)	949(1)	−024(5)	35(8)
N	183(3)	971(1)	−148(7)	89(12)
C(13)	399(2)	912(1)	069(5)	26(8)
C(14)	483(3)	918(1)	230(5)	41(9)
C(15)	590(2)	906(1)	192(4)	17(8)
C(16)	621(3)	889(1)	002(7)	53(10)
C(17)	535(3)	884(1)	−160(5)	38(9)
C(18)	434(3)	897(1)	−114(5)	42(10)
O(19)	661(2)	911(1)	362(4)	70(8)
C(20)	760(2)	932(1)	339(5)	28(9)
C(21)	831(3)	921(1)	495(6)	51(9)
C(22)	940(3)	943(1)	503(5)	45(8)
C(23)	969(3)	973(1)	333(6)	64(11)
C(24)	894(3)	984(1)	171(6)	52(10)
C(25)	790(3)	961(1)	182(6)	51(10)
H(2)	054	848	643	
H(3)	036	764	439	
HA(5)	227	781	811	
HB(5)	324	750	715	
HC(5)	313	806	660	
HA(6)	152	694	435	
HB(6)	273	697	479	
HC(6)	230	714	259	
H(7)	171	794	193	
H(11)	289	933	271	
H(14)	462	932	362	
H(16)	696	880	−027	
H(17)	550	872	−300	
H(18)	381	897	−228	
H(21)	808	900	606	
H(22)	988	936	616	
H(23)	1 039	987	331	
H(24)	914	1 006	057	
H(25)	735	970	077	

* Anisotropic vibration parameters in the form: $\exp[-2\pi^2(U_{11}h^2a^{*2} + 2U_{12}hka^*b^* + U_{22}k^2b^{*2} + 2U_{23}klb^*c^* + 2U_{13}hla^*c^* + U_{33}l^2c^{*2})]$, with parameters

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Br(1)	91(3)	67(3)	47(2)	0(3)	25(2)	15(3)
Br(2)	57(2)	82(3)	39(2)	25(2)	9(2)	−4(3)

The isomer giving the lower R (see Experimental section) also confirmed the configurations about the two asymmetric centres on the cyclopropane ring (Figure 3). Thus establishment of the absolute configuration at the benzylic α-carbon atom in two ways as (S), confirms that derived by chemical arguments.[3]

Bond lengths (Figure 1) and angles (Table 2) show no unusual features. The phenyl groups have a mean bond length of 1.39(2) Å and angle of 120(1)°; the

TABLE 2

Interatomic distances and angles

(a) Bond angles (deg.)

Br(1)–C(1)–Br(2)	115(2)	C(12)–C(11)–C(13)	112(3)
Br(1)–C(1)–C(2)	119(3)	C(11)–C(12)–N	178(3)
Br(2)–C(1)–C(2)	126(3)	C(11)–C(13)–C(14)	118(3)
C(1)–C(2)–C(3)	129(3)	C(11)–C(13)–C(18)	127(3)
C(2)–C(3)–C(4)	125(3)	C(14)–C(13)–C(18)	115(3)
C(2)–C(3)–C(7)	123(3)	C(13)–C(14)–C(15)	122(3)
C(4)–C(3)–C(7)	58(2)	C(14)–C(15)–O(19)	117(3)
C(3)–C(7)–C(4)	62(2)	C(14)–C(15)–C(16)	121(3)
C(3)–C(7)–C(4)	60(2)	C(16)–C(15)–O(19)	123(3)
C(3)–C(4)–C(5)	115(3)	C(15)–C(16)–C(17)	116(3)
C(3)–C(4)–C(6)	117(3)	C(16)–C(17)–C(18)	120(3)
C(5)–C(4)–C(6)	115(3)	C(17)–C(18)–C(13)	126(3)
C(5)–C(4)–C(7)	119(2)	C(15)–O(19)–C(20)	122(3)
C(6)–C(4)–C(7)	119(3)	O(19)–C(20)–C(21)	115(3)
C(3)–C(7)–C(8)	124(3)	O(19)–C(20)–C(25)	125(3)
C(4)–C(7)–C(8)	127(3)	C(21)–C(20)–C(25)	120(3)
C(7)–C(8)–O(9)	125(4)	C(20)–C(21)–C(22)	122(3)
C(7)–C(8)–O(10)	114(4)	C(21)–C(22)–C(23)	116(3)
O(9)–C(8)–O(10)	121(3)	C(22)–C(23)–C(24)	121(3)
C(8)–O(10)–C(11)	116(3)	C(23)–C(24)–C(25)	117(3)
O(10)–C(11)–C(12)	106(2)	C(24)–C(25)–C(20)	123(3)
O(10)–C(11)–C(13)	109(2)		

(b) Selected non-bonded distances (Å)

(i) Intramolecular

Br(1) · · · Br(2)	3.18	O(9) · · · H(11)	2.20
H(2) · · · O(9)	2.53	H(11) · · · H(14)	2.22
HB(5) · · · HB(6)	2.16	H(16) · · · H(25)	2.56

(ii) Intermolecular

Br(1) · · · HB(5^{I})	3.19	O(19) · · · H(24^{V})	2.73
Br(2) · · · H(16^{II})	3.14	H(2) · · · H(22^{VI})	2.52
O(9) · · · H(18^{III})	2.56	HA(5) · · · H(7^{III})	2.53
N · · · H(11^{IV})	2.68	HA(6) · · · H(17^{VII})	2.34
O(19) · · · H(17^{III})	2.74		

Roman numeral superscripts relate the atoms to those at x, y, z by the following operations:

I $x - \frac{1}{2}, \frac{3}{2} - y, 2 - z$ V $\frac{3}{2} - x, 2 - y, \frac{1}{2} + z$
II $x - 1, y, 1 + z$ VI $x - 1, y, z$
III $x, y, 1 + z$ VII $x - \frac{1}{2}, \frac{3}{2} - y, -z$
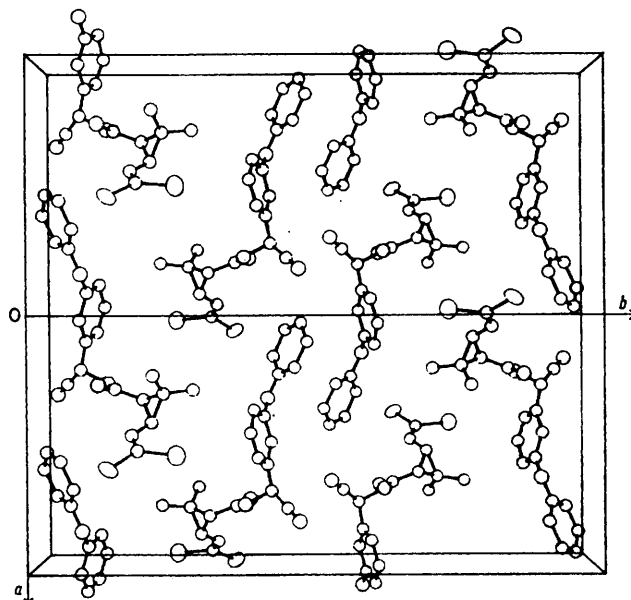IV $\frac{1}{2} - x, 2 - y, z - \frac{1}{2}$

FIGURE 2 The contents of two unit cells. The crystallographic c axis has its positive direction away from the viewer, into the plane of the paper

cyclopropane ring a mean bond length of 1.49(2) Å and internal angle 60(1)°.

Thermal parameters of the bromine atoms show that the major vibration directions are almost perpendicular to the plane of the dibromovinyl group. Isotropic thermal parameters for other non-hydrogen atoms are all reasonable, those atoms with many or heavy neighbours showing smaller vibrations. The nitrogen atom shows the largest motion and probably contains a high degree of anisotropy. This large motion probably explains
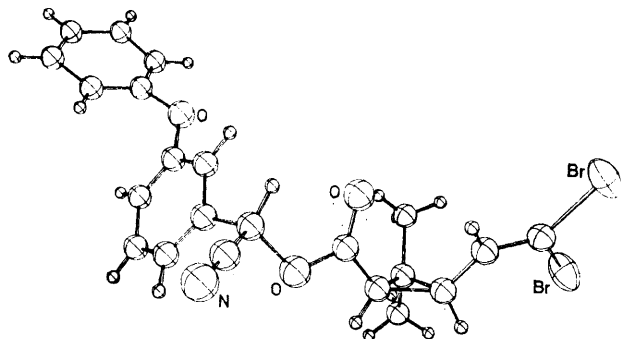

FIGURE 3 One molecule, showing the absolute configuration and the conformation in the crystal; 50% ellipsoids are shown for bromine atoms

the deviation of the C(11)–C(12)–N group from linearity, but the shortening of the C(12)–N bond is not significant in this case.

The conformation of the molecule shows several interesting features (Tables 3 and 4). The plane of the

TABLE 3

Equations of the planes with reference to orthonormal axes.* Deviations from the planes (Å) are shown in square brackets; atoms designated in italics were used to define the planes

Plane (1)

$$-0.8745X - 0.0064Y - 0.4849Z + 2.6141 = 0$$

[*Br(1)* −0.004(4), *Br(2)* 0.006(4), *C(1)* 0.006(30), *C(2)* −0.022(38), *C(3)* 0.014(32), C(4) −1.17(3), C(7) −0.43(3)]

Plane (2)

$$-0.9339X + 0.3571Y + 0.0143Z - 5.7531 = 0$$

[*C(7)* −0.001(30), *C(8)* 0.004(38), *O(9)* −0.002(23), *O(10)* −0.001(20), C(3) 0.79(3), C(4) −0.70(3), C(11) −0.17(3), H(11) −0.04]

Plane (3)

$$0.1444X + 0.9495Y - 0.2785Z - 24.0652 = 0$$

[*C(11)* −0.08(3), *C(13)* 0.05(3), *C(14)* 0.06(3), *C(15)* 0.01(3), *C(16)* −0.03(3), *C(17)* −0.03(3), *C(18)* 0.04(3), O(19) −0.03(2), H(11) 0.05]

Plane (4):

$$0.3345X - 0.7871Y - 0.5181Z + 17.9127 = 0$$

[*O(19)* −0.02(2), *C(20)* 0.02(3), *C(21)* 0.02(3), *C(22)* −0.02(3), *C(23)* 0.01(4), *C(24)* −0.01(4), *C(25)* 0.01(3)]

* Orthonormal axes, X, Y, Z are parallel to crystallographic axes a, b, c

dibromovinyl group does not include the mid-point of the C(4)–C(7) bond; the torsion is such as to move the bromine atoms away from the ester group, which itself

forms a plane which almost includes the mid-point of the C(3)–C(4) bond; H(11) is relatively close (0.04 Å) to this plane, so that H(11) · · · O(9) is 2.20 Å. H(11) is

TABLE 4

Torsion angles (deg.) in (I) and (II)

Angle	(I)	(II) *
C(1)–C(2)–C(3)–C(4)	−90(5)	128(6)
C(1)–C(2)–C(3)–C(7)	−161(4)	−161(6)
C(3)–C(7)–C(8)–O(9)	39(6)	23(7)
C(4)–C(7)–C(8)–O(9)	−36(6)	−61(6)
O(9)–C(8)–O(10)–C(11)	7(5)	−12(5)
C(8)–O(10)–C(11)–H(11)	−13(4)	
H(11)–C(11)–C(13)–C(14)	12(4)	
C(16)–C(15)–O(19)–C(20)	45(4)	
C(15)–O(19)–C(20)–C(25)	21(5)	

* Ref. 5.

also close (0.05 Å) to the plane of the benzyl group and has another fairly close contact of 2.22 Å with H(14). Thus the conformation at this point can be described by two planes intersecting almost along the C(11)–H(11) bond, and making an angle of 78°. The conformation of the terminal phenoxy-group is described by the two torsion angles about the C(15)–O(19) and O(19)–C(20) bonds. These angles [45(4) and 21(5)°] are not close to the 90°,90° angles which is the preferred conformation in diphenyl ether.[6] The observed conformation, with H(16) · · · H(25) 2.56 Å, will be determined by this contact and any intermolecular contacts. However, calculations for diphenyl ether have shown the potential-energy surface is relatively flat, away from the highly strained 0°,0° conformation.[6] Relatively small steric effects could therefore give the conformation observed.

It is interesting to compare the conformation of those parts of the molecules common to both (I) and (II). Values for (II) used in the following discussion were calculated from ref. 5.

In (II), the 2-methylpropenyl chain [corresponding to the dibromovinyl group in (I)] forms a plane which has the two other carbon atoms of the cyclopropane ring at distances −0.10 and 1.14 Å. Although the torsion angle about the C(2)–C(3) bond is not as large as in (I), it is still significant, and is in the same direction, away from the ester group, even though the configuration round the cyclopropane ring is *trans* in (II).

In contrast to (I), the ester group in (II) is not co-planar with the centre of the C(3)–C(4) bond, the distances from the plane being 1.17 and −0.25 Å. However, in both cases, the carbonyl oxygen atom points towards the axis of the cyclopropane ring.

The distance from the ester plane to C(11) is 0.17 for (I) and 0.08 Å for (II). It is uncertain whether these deviations are significant, especially in (II), since the torsion angles about the C(8)–O(10) bond differ insignificantly (Table 4). However, in both cases, C(7) and C(11) are disposed *s-trans* about the C(8)–O(10) bond.

The conformation of (I) at the site of action in the

6 P. A. Kollman, W. J. Murray, M. E. Nuss, E. C. Jorgensen, and S. Rothenberg, *J. Amer. Chem. Soc.*, 1973, **95**, 8518.

insect is not likely to be the same as that in the crystal. However, both (I) and (II) are not strained by close intermolecular contacts in the crystalline state, so features common to (I) and (II) may carry over to the dissolved insecticide molecules. Refinement of structure–activity relationships needs much more conformational data than is currently available.

EXPERIMENTAL

Crystal Data.—$C_{22}H_{19}Br_2NO_3$, $M = 505.22$. Orthorhombic needles, $a = 12.319(10)$, $b = 27.170(26)$, $c = 6.294(5)$ Å, $U = 2\ 107$ Å^3, D_m (flotation) $= 1.59$, $Z = 4$, $D_c = 1.59$ g cm^{-3}, $F(000) = 1\ 008$. Space group $P2_12_12_1$ (D_2^4, No. 19) uniquely determined. No molecular symmetry required. Mo-K_α radiation, Zr filter, $\lambda = 0.7107$ Å, $\mu = 41.03$ cm^{-1}; no absorption correction applied.

Data Collection.—A crystal of dimensions $0.14 \times 0.36 \times 2.74$ mm was mounted on a Hilger and Watts four-circle diffractometer. The orientation matrix and cell dimensions were refined by use of the positions of 12 reflections. Intensity data were collected by scanning through the peaks in steps of $\omega = \theta = 0.01°$ counting for 4 s each step. A symmetric scan of $0.8°$ was used and stationary-crystal–stationary-counter background counts for 60 s were measured before and after the scan. Three standard reflections (180), (05$\bar{3}$), and (211) were measured after every 30 normal reflections. Intensities were collected for the two octants hkl and $h\bar{k}l$ out to a $\theta_{max.}$ 20°. A total of 2 138 reflections were measured, 1 199 of which were in the hkl octant. Towards the end of data collection, the intensities of the two strongest standards, (180) and (211), began to increase and at completion, had done so by an average of 30%. However, the intensity of the weakest (05$\bar{3}$) had fallen by 9%. On repeating measurement of some early reflections, it was found that the behaviour of the strong standards was atypical, and since the strong intensities had been recorded by the time the increase started, all reflections were scaled to the variation of the (05$\bar{3}$) reflection only. Lorentz and polarisation factors (LP) were applied, and the standard deviations were calculated from: $\sigma^2(F) = \sigma^2(I)/4I.\text{LP}$, where $\sigma^2(I) = $ total count $+ (0.25$ background) (scan time/background time)^2. Reflections were considered unobserved if the intensity (I) was <200 counts, in which case it was set to 100, or if the intensity was $<3\sigma(I)$. These criteria gave a total of 1 083 observed reflections, of which 616 were in the hkl octant and were used for the structure solution and refinement initially.

Structure Determination.—A three-dimensional Patterson map located the bromine atoms and a Fourier map phased by these atoms gave the positions of 21 other atoms. These positions were refined and a further Fourier map located the five missing atoms. Refinement of these non-

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* See Notice to Authors No. 7 in *J.C.S. Perkin I*, 1974, Index issue.

[7] 'World List of Crystallographic Computer Programs,' *J. Appl. Cryst.*, 1973, **6**, 309.

[8] ICL 4/70 Programs adapted from IBM 360 versions: NUCLS, R. J. Doedens and J. A. Ibers; ORFFE, W. R. Busing, K. O. Martin, and H. A. Levy; ORTEP, C. K. Johnson.

hydrogen atoms with either unit weights or those obtained from counting statistics gave unsatisfactory interatomic distances and angles. However, use of a weighting scheme giving constant $\langle W\Delta^2 \rangle$ for ranges of F_o gave a satisfactory model. At this stage the bromine atoms were allowed to refine with anisotropic temperature factors, and the refinement gave R 0.0760 for the 616 hkl reflections classed as observed. The agreement between F_o and F_c was poorest for reflections with sin $\theta/\lambda < 0.4$, indicating that the hydrogen atomic scattering was significant, and should be allowed for. The positions of all hydrogen atoms, except those on the two methyl groups, were determined by molecular geometry, so these were calculated and included in the model. Non-hydrogen atoms were refined and a difference-Fourier map using observed reflections with sin $\theta/\lambda < 0.4$ was calculated. This map showed the location of one hydrogen atom on each methyl carbon sufficiently well to enable location of the other two from geometrical consideration. The non-hydrogen atoms were then refined to give R 0.0756.

At this stage the absolute configuration was sought by two structure-factor calculations on the 1 083 observed reflections in both the hkl and $h\bar{k}l$ octants. The isomer used so far gave R 0.0830 whereas that obtained by reversing the signs of all three co-ordinates of each atom gave R 0.0743. The second isomer was thus taken as being the correct one. This was then refined by use of a final weighting scheme: $|F_o| < 27$, $W = 1/21.86$ and $|F_o| > 27$, $W = 1/(65.49 - 2.175|F_o| + 0.02308|F_o|^2)$, giving R 0.0700 and R' 0.0840 for the 616 observed hkl reflections. The maximum change/error on the last cycle was 0.038. A weighting analysis showed no obvious trends against ranges of sin θ/λ or $|F_o|$. The difference map after this refinement showed only peaks due to the inadequate description of the thermal motion of the atoms. Measured and calculated structure factors are listed in Supplementary Publication No. SUP 21354 (6 pp., 1 microfiche).*

Computing.—The orientation matrix was determined and unit-cell parameters refined on the PDP 8 computer attached to the diffractometer. Structure solution and refinement and molecular geometry calculations were for the most part carried out on an IBM 1130 computer by use of the *X*-RAY ARC programs.[7] Final full-matrix least-squares refinement used NUCLS,[8] and bond lengths and angles, with errors from the variance–covariance matrix were calculated by use of ORFFE.[8] Diagrams were drawn by use of ORTEP.[8] Scattering factor curves for bromine, carbon, oxygen, and nitrogen were taken from ref. 9, and for hydrogen from ref. 10; anomalous dispersion coefficients for bromine were taken from ref. 11.

[9] D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.
[10] R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.
[11] D. T. Cromer and D. Liberman, *J. Chem. Phys.*, 1970, **53**, 1891.