

# Synthesis and X-Ray Crystal Structure of a New Potent Pyrethroid Acid, ( $\pm$ )-*cis*-3-[(*Z*)-2-Chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylic Acid

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Single-crystal X-ray analysis of the title compound has established its structure and molecular geometry. Crystals are monoclinic, space group  $P2_1/c$ , with  $a = 9.487(4)$ ,  $b = 8.009(4)$ ,  $c = 16.214(6)$  Å,  $\beta = 119.91(1)^\circ$ ,  $Z = 4$ . The structure was solved by direct methods and refined by full-matrix least-squares calculations to  $R$  0.056 over 1 242 reflections measured by diffractometer. The crystals contain centrosymmetric hydrogen-bonded dimers ( $O \cdots O$  2.65 Å) in which the carboxy and vinyl substituents are in a 'bisecting' orientation, and the C=O group and one of hydrogen atoms on each methyl group point over the cyclopropane ring. The bond lengths in the ring reflect the substitution pattern.

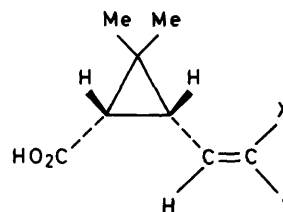
As the agricultural utilization of photostable pyrethroids has rapidly expanded over the past decade, detailed structural analysis of pyrethroids has increased in anticipation of designing new, more effective compounds of this class. Crystallographic investigations of pyrethroids<sup>1,2</sup> and their derivatives<sup>3,4</sup> have formed an essential part of these studies. Information derived in this manner is important for the determination of molecular dimensions, configurations, and conformations, and has potential applications in the development of detailed structure-activity relationships.

Published structural data have thus far been limited to dihalogenovinyl and chrysanthemate esters. Recent reports<sup>5</sup> indicate that certain halogenoalkyl substituted pyrethroid esters are, in some cases, among the most active insecticides known to date. In particular, several esters of *cis*-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid (1) offer potential as wide-spectrum, foliar insecticides.<sup>5,6</sup> Obviously in this acid, in contrast to the earlier reported acid structures, the question of stereochemistry about the exocyclic double bond arose. Although we, as well as others,<sup>5</sup> found that one vinyl isomer predominates using our particular methodology, we were concerned about the security of assigning *E/Z*-stereochemistries to the products solely on the basis of spectral data. Accordingly, a single-crystal X-ray analysis of the major ( $\pm$ )-*cis*-acid product (1a) was undertaken to define unequivocally the configuration at the double bond and to provide details of the overall molecular geometry.

## Results and Discussion

The crystal structure of (1a) was solved by direct methods. Refinement of atomic positional and thermal parameters by full-matrix least-squares calculations converged to  $R$  0.056 over 1 242 reflections. Final fractional atomic co-ordinates are in Table 1. Bond lengths and angles are in Table 2, and displacements of selected atoms from least-squares planes are in Table 3. A view of the structure, which clearly shows that (1a) has a *Z*-configuration about the C(1')=C(2') double bond, is provided in Figure 1. Molecules of (1a) occur in the crystal as typical centrosymmetric hydrogen-bonded dimers<sup>7</sup> ( $O \cdots O$  2.65 Å) separated by normal van der Waals distances as illustrated in Figure 2.

With two electron-withdrawing  $\pi$ -bonding substituents, the mean cyclopropane C-C bond length at 1.520 Å in (1a) is only slightly longer than that in cyclopropane<sup>8</sup> (1.510 Å). Individual bond length and angle variations which reflect the ring



- (1) a; X = Cl, Y = CF<sub>3</sub>  
 b; X = CF<sub>3</sub>, Y = Cl

Table 1. Fractional atomic co-ordinates ( $\times 10^4$ ;  $\times 10^3$  for hydrogen atoms<sup>a</sup>), with standard deviations in parentheses

Atom	x	y	z
C(1)	8 560(3)	8 019(4)	1 428(2)
C(2)	8 983(3)	6 243(4)	1 300(2)
C(3)	8 707(3)	6 624(4)	2 118(2)
C(4)	10 750(3)	6 023(5)	1 561(2)
C(5)	7 812(4)	5 185(4)	485(2)
C(6)	6 989(3)	8 820(4)	797(2)
O(7)	5 686(2)	8 097(3)	406(2)
O(8)	7 156(2)	10 439(3)	702(2)
C(1')	7 282(3)	6 017(4)	2 150(2)
C(2')	7 190(3)	5 772(4)	2 921(2)
C(3')	5 736(4)	5 047(5)	2 924(2)
F(4')	5 179(3)	6 047(6)	3 356(2)
F(5')	4 513(3)	4 784(6)	2 050(2)
F(6')	6 097(4)	3 611(5)	3 400(2)
Cl	8 757(1)	6 190(2)	4 049(1)
H(1)	935(4)	874(4)	166(2)
H(3)	966(4)	660(5)	274(2)
H(4A)	1 143(4)	675(5)	214(3)
H(4B)	1 070(7)	603(8)	96(4)
H(4C)	1 098(6)	479(8)	164(4)
H(5A)	659(5)	544(6)	29(3)
H(5B)	808(8)	372(9)	83(5)
H(5C)	798(9)	508(13)	4(6)
H(8)	621(4)	1 080(5)	37(2)
H(1')	640(4)	571(5)	161(3)

<sup>a</sup> Hydrogen atoms bear the same labels as the atoms to which they are bonded.

**Table 2.** Interatomic distances (Å) and angles (°), with standard deviations in parentheses

## (a) Bond lengths

C(1)–C(2)	1.519(4)	C(6)–O(8)	1.324(4)
C(1)–C(3)	1.537(4)	C(1')–C(2')	1.310(4)
C(1)–C(6)	1.469(4)	C(2')–C(3')	1.500(5)
C(2)–C(3)	1.504(4)	C(3')–F(4')	1.335(5)
C(2)–C(4)	1.521(4)	C(3')–F(5')	1.326(5)
C(2)–C(5)	1.495(5)	C(3')–F(6')	1.332(5)
C(3)–C(1')	1.462(4)	C(2')–Cl	1.720(3)
C(6)–O(7)	1.218(4)		
C(1)–H(1)	0.87(4)	C(5)–H(5A)	1.06(5)
C(3)–H(3)	0.97(3)	C(5)–H(5B)	1.27(8)
C(4)–H(4A)	1.02(4)	C(5)–H(5C)	0.82(9)
C(4)–H(4B)	0.95(7)	O(8)–H(8)	0.83(4)
C(4)–H(4C)	1.01(6)	C(1')–H(1')	0.89(4)

## (b) Bond angles

C(2)–C(1)–C(3)	59.0(2)	C(1)–C(6)–O(8)	111.7(3)
C(3)–C(1)–C(6)	121.1(2)	O(7)–C(6)–O(8)	123.6(3)
C(2)–C(1)–C(6)	124.0(3)	C(1)–C(1')–C(2')	125.9(3)
C(1)–C(2)–C(3)	61.1(2)	C(1')–C(2')–C(3')	124.0(3)
C(1)–C(2)–C(4)	113.6(3)	C(3')–C(2')–Cl	112.4(2)
C(1)–C(2)–C(5)	121.4(3)	C(1')–C(2')–Cl	123.6(2)
C(3)–C(2)–C(4)	115.5(3)	C(2')–C(3')–F(4')	112.0(3)
C(3)–C(2)–C(5)	121.0(3)	C(2')–C(3')–F(5')	112.0(3)
C(4)–C(2)–C(5)	114.2(3)	C(2')–C(3')–F(6')	111.4(3)
C(1)–C(3)–C(2)	59.9(2)	F(4')–C(3')–F(5')	107.0(3)
C(1)–C(3)–C(1')	121.2(2)	F(4')–C(3')–F(6')	105.6(3)
C(2)–C(3)–C(1')	122.3(3)	F(5')–C(3')–F(6')	108.5(4)
C(1)–C(6)–O(7)	124.6(3)		

(c) Torsion angles<sup>a</sup>

C(6)–C(1)–C(2)–C(3)	–108.8(2)	C(5)–C(2)–C(3)–C(1')	–1.3(3)
C(6)–C(1)–C(2)–C(4)	144.0(3)	C(4)–C(2)–C(3)–C(1)	104.0(2)
C(6)–C(1)–C(2)–C(5)	1.9(3)	C(5)–C(2)–C(3)–C(1)	–111.3(3)
C(3)–C(1)–C(2)–C(4)	–107.2(3)	C(1)–C(3)–C(1')–C(2')	–133.2(4)
C(3)–C(1)–C(2)–C(5)	110.6(4)	C(2)–C(3)–C(1')–C(2')	154.9(4)
C(2)–C(1)–C(3)–C(1')	–111.8(3)	C(3)–C(1')–C(2')–C(3')	–176.0(4)
C(6)–C(1)–C(3)–C(1')	1.7(3)	C(3)–C(1')–C(2')–Cl	1.9(3)
C(6)–C(1)–C(3)–C(2)	113.5(2)	C(1')–C(2')–C(3')–F(4')	–124.3(4)
C(2)–C(1)–C(6)–O(7)	34.0(3)	C(1')–C(2')–C(3')–F(5')	–4.1(3)
C(2)–C(1)–C(6)–O(8)	–146.0(3)	C(1')–C(2')–C(3')–F(6')	117.7(4)
C(3)–C(1)–C(6)–O(7)	–37.3(3)	Cl–C(2')–C(3')–F(4')	57.5(3)
C(3)–C(1)–C(6)–O(8)	142.6(3)	Cl–C(2')–C(3')–F(5')	–60.5(3)
C(1)–C(2)–C(3)–C(1')	110.0(3)	Cl–C(2')–C(3')–F(6')	177.7(3)
C(4)–C(2)–C(3)–C(1')	–146.0(3)		

<sup>a</sup> The torsion angle A–B–C–D is defined as positive if, when viewed along the B–C bond, atom A must be rotated clockwise to eclipse atom D.

substitution pattern are quite evident. The C(1)–C(3) bond opposite the carbon atom bearing the methyl groups [1.537(4) Å] is significantly longer than those opposite the other two carbon atoms [C(2)–C(3) 1.504(4), C(1)–C(2) 1.519(4) Å] which carry  $\pi$ -bonding carboxy and vinyl substituents with their planes lying approximately perpendicular to the cyclopropane ring plane [dihedral angles 88.3 and 82.0°, respectively (Table 3)]. These bond length variations and the 'bisecting' orientations adopted by the carboxy and vinyl substituents are in accord with theoretical predictions.<sup>9,10</sup> Thus, the presence of the carboxy group at C(1) leads to a weakening of adjacent bonds C(1)–C(2) and C(1)–C(3) and strengthening of C(2)–C(3) while the C(1)–C(3) and C(2)–C(3) bonds are weakened and the C(1)–C(2) bond is strengthened by the vinyl substituent at C(3), the combined effect being that C(1)–C(3) is significantly longer than either C(1)–C(2) or C(2)–C(3). The smaller, but still significant, difference between the latter pair of bond lengths implies that the

electron-withdrawing character of the carboxy group is greater than that of the vinyl substituent.

In common with the preferred conformation found in other previously studied pyrethroids<sup>1-4</sup> as well as simple cyclopropane carboxylic acids,<sup>11,12</sup> the carboxy group in (1a) is oriented such that the carbonyl oxygen atom O(7) lies over the ring. This conformational preference differs significantly from the synplanar C<sub>β</sub>–C<sub>α</sub>–C=O arrangement normally found in saturated carboxylic acids which has been rationalized by Dunitz and Strickler<sup>13</sup> in terms of interactions arising from a bent-bond description for the C=O double bond in addition to differences in non-bonded steric interactions between C<sub>β</sub>–H and the carbonyl and hydroxy oxygen atoms as suggested earlier by Leiserowitz and Schmidt.<sup>14</sup> With regard to a cyclopropane carboxy substituent, the 'bisecting' orientation required for effective  $\pi$ -bonding clearly precludes adoption of a synplanar conformation involving either of the ring bonds adjacent to the site of substitution. The observed orientation

**Table 3.** Equations of least-squares planes through groups of atoms, in the form  $PX + QY + RZ - S = 0$ ,<sup>a</sup> with, in square brackets, displacements (Å) of selected atoms from these planes

**Plane A:** C(1)–C(3)

$$-0.7888X - 0.2065Y - 0.5789Z + 7.983 = 0$$

[C(1) 0.000, C(2) 0.000, C(3) 0.000, C(4) -1.332, C(5) 1.195, C(6) 1.154, O(7) 2.318, O(8) 0.779, C(1') 1.161, C(2') 1.134, Cl -0.306]

**Plane B:** C(1), C(6)–O(8)

$$0.5886X - 0.1874Y - 0.7864Z - 1.318 = 0$$

[C(1) 0.000, C(2) 0.705, C(3) -0.799, C(4) 1.313, C(5) 1.499, C(6) 0.000, O(7) 0.000, O(8) 0.000, C(1') -1.554]

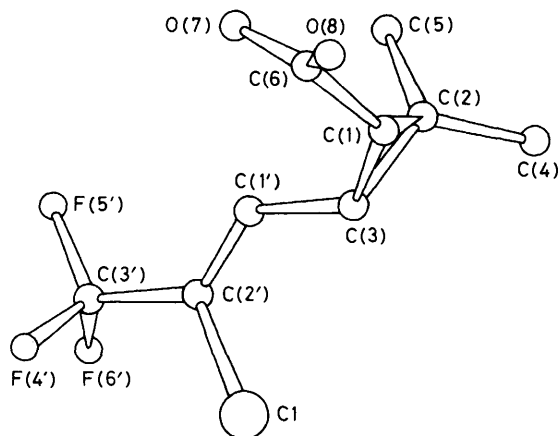
**Plane C:** C(3), C(1')–C(3'), Cl

$$-0.3631X + 0.9287Y - 0.0755Z - 2.346 = 0$$

[C(1) 0.937, C(2) -0.553, C(3) -0.022, C(4) -1.277, C(5) -1.089, C(6) 1.956, O(7) 1.794, C(1') 0.024, C(2') 0.018, C(3') -0.020, Cl 0.001, F(4') 0.997, F(5') 0.042, F(6') -1.124]

Dihedral angles (°) between planes: A/B 88.3, A/C 82.0, B/C 70.8

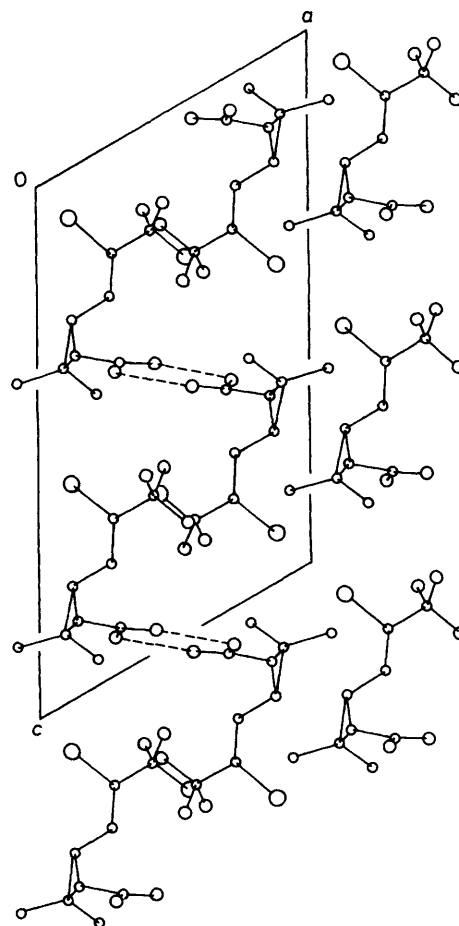
<sup>a</sup> Cartesian co-ordinates ( $X, Y, Z$ ) are related to the fractional atomic co-ordinates ( $x, y, z$ ) in Table 1 by the transformations:  $X = xa + zc \cos \beta$ ,  $Y = yb$ ,  $Z = zc \sin \beta$ .



**Figure 1.** Atom numbering scheme and solid-state conformation of (1a)

in (1a) with the C=O group over the ring rather than the alternative one where it eclipses the cyclopropane ring hydrogen atom at C(1) is at variance with the proposal that non-bonded H/O steric interactions dictate the conformational preference since  $H(1) \cdots O(7)$  would be greater than  $H(1) \cdots O(8)$  by ca. 0.2 Å. However, if the cyclopropane ring is viewed as being constructed from Walsh orbitals<sup>9</sup> and one extends to (1a) the Dunitz and Strickler suggestion that the C=O double bond is considered as being comprised of two bent bonds, then the observed orientation is that which yields an energetically favourable staggered disposition about the C(1)–C(6) bond, whereas the alternative conformation with the C(6)–O(8) bond pointing over the ring would give rise to an unfavourable eclipsed geometry. Thus, H/O steric factors and staggered bond disposition operate in opposite directions with the latter apparently prevailing. Similar considerations are applicable to other cyclopropane acids,<sup>11,12</sup> esters,<sup>1–3</sup> and amides.<sup>4</sup>

Other bond lengths and angles are close to expected values.



**Figure 2.** Crystal structure of (1a), viewed in projection along the  $b$ -axis; O–H  $\cdots$  O hydrogen bonds about crystallographic centres of symmetry are denoted by broken lines

The conformation adopted about the C(3)–C(1') bond [torsion angles C(1)–C(3)–C(1')–C(2') – 133.2° and C(2)–C(3)–C(1')–C(2') 154.9°] is such that it orients the chlorine atom away from the cyclopropane ring. The slight rotation from an exactly eclipsed geometry serves here to increase the  $H(3) \cdots Cl$  separation and occurs in the direction which minimizes interactions between  $H(1')$  and the *syn* ester carbonyl oxygen and methyl hydrogen atoms. One hydrogen atom of each methyl group lies approximately equidistant from both C(1) and C(3), and thus these groups adopt 'bisecting' conformations similar to those found earlier in crystals of *trans*-2,2-*trans*-3-dimethylcyclopropanecarboxylic acid<sup>11</sup> and subsequently concluded from theoretical considerations<sup>13</sup> to be more favourable than the 'straddling' form.

### Experimental

(±)-*cis*-3-[(*Z*)-2-Chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylic Acid (1a).—Ethyl (±)-*cis*, *trans*-3-[(*E,Z*)-2-chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylate<sup>5</sup> (14 mmol) and sodium hydroxide (17 mmol) in ethanol (94 ml)/water (6 ml) was refluxed 6 h. The mixture was concentrated, diluted with water (50 ml) and dilute hydrochloric acid and finally extracted with ether. Removal of the ether from the extract provided a solid (m.p. 95–107 °C) which recrystallized from hexane to give the

product, m.p. 108–110 °C;  $\delta$  (CDCl<sub>3</sub>), 1.32 (6 H, s, CH<sub>3</sub>), 1.9–2.4 (2 H, m, 1-, 3-H), 6.86 (1 H, d, *J* 8 Hz), and 14.2 (1 H, s, OH).

**Crystal Data.**—C<sub>9</sub>H<sub>10</sub>ClF<sub>3</sub>O<sub>2</sub>, *M* = 242.6, Monoclinic, *a* = 9.487(4), *b* = 8.009(4), *c* = 16.214(6) Å,  $\beta$  = 119.91(5)°, *U* = 1 067.9 Å<sup>3</sup>, *D<sub>m</sub>* (flotation) = 1.52 g cm<sup>-3</sup>, *Z* = 4, *D<sub>c</sub>* = 1.509 g cm<sup>-3</sup>. Cu-*K<sub>α</sub>* radiation,  $\lambda$  = 1.5418 Å;  $\mu$ (Cu-*K<sub>α</sub>*) = 34.5 cm<sup>-1</sup>. Space group *P*2<sub>1</sub>/*c*(*C*<sub>2h</sub><sup>5</sup>) uniquely from systematic absences: 0*h*0 when *k* ≠ 2*n*, *h*0*l* when *l* ≠ 2*n*.

**Crystallographic Measurements.**—Space group information and preliminary unit-cell dimensions were obtained from oscillation and Weissenberg photographs taken with Cu-*K<sub>α</sub>* radiation and from precession photographs taken with Mo-*K<sub>α</sub>* radiation ( $\lambda$  = 0.7107 Å). For intensity measurements, a crystal of dimensions ca. 0.50 × 0.40 × 0.60 mm was oriented on an Enraf-Nonius CAD-3 automated diffractometer (Ni-filtered Cu-*K<sub>α</sub>* radiation) where the intensities of all unique reflections with  $\theta < 67^\circ$  were recorded by the  $\theta$ –2 $\theta$  scanning procedure as described in detail elsewhere.<sup>16</sup> Refined unit-cell parameters were derived by least-squares treatment of the diffractometer setting angles for 40 high angle reflections widely separated in reciprocal space. From a total of 1 926 unique intensity measurements, only those 1 242 for which  $I > 2.0\sigma(I)$  [ $\sigma^2(I)$  = scan count + total background count] were retained for the structure analysis. These data were corrected for the usual Lorentz and polarization effects, and for absorption, based on the  $\phi$ -dependence of the intensity of the 040 reflection measured at  $\chi$  90°.

**Structure Analysis.**—The structure was solved by direct methods by use of MULTAN76<sup>17</sup> with the highest 175  $|E|$ -values. An *E*-map evaluated with that set of phases which gave the highest combined figure-of-merit clearly revealed positions for all non-hydrogen atoms. Full-matrix least-squares refinement of the structure model, at first with isotropic and subsequently with anisotropic thermal parameters, reduced *R* smoothly from its initial value of 0.320 to 0.072. With the inclusion of hydrogen atom parameters as variables in the later least-squares iterations, the refinement converged at *R* 0.056. Final positional parameters are in Table 1. Thermal parameters and a list of observed and calculated structure amplitudes are in Supplementary Publication No. SUP 23595 (11 pp). \*

Atomic scattering factors for carbon, chlorine, fluorine, and

oxygen were taken from ref. 18, and for hydrogen from ref. 19; anomalous dispersion corrections<sup>20</sup> were included in the structure-factor calculations. In the least-squares iterations, the function minimized was  $\Sigma w\Delta^2$  ( $\Delta = ||F_o| - |F_c||$ ), with weights assigned according to the scheme:  $\sqrt{w} = 1$  for  $|F_o| \leq 8.5$ , and  $\sqrt{w} = 8.5/|F_o|$  for  $|F_o| > 8.5$ ; this scheme was considered satisfactory as it showed no systematic dependence of  $\langle w\Delta^2 \rangle$  on  $|F_o|$ .

## References

- 1 J. D. Owen, *J. Chem. Soc., Chem. Commun.*, 1974, 859; *J. Chem. Soc., Perkin Trans. 1*, 1975, 1865.
- 2 J. D. Owen, *J. Chem. Soc., Perkin Trans. 1*, 1976, 1231.
- 3 M. S. Begley, L. Crombie, D. J. Simmonds, and D. A. Whiting, *J. Chem. Soc., Chem. Commun.*, 1972, 1276; *J. Chem. Soc., Perkin Trans. 1*, 1974, 1230.
- 4 A. F. Cameron, G. Ferguson, and C. Hannaway, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1567.
- 5 P. D. Bentley, R. Cheetham, R. K. Huff, R. Pascoe, and J. D. Sayle, *Pestic. Sci.*, 1980, 11, 156.
- 6 J. F. Engel, U. S. Patent 4 238 505, 1980; 4 263 319, 1981.
- 7 L. Leiserowitz, *Acta Crystallogr.*, 1976, B32, 775.
- 8 O. Bastiansen, F. N. Fritsch, and K. Hedberg, *Acta Crystallogr.*, 1967, 17, 538.
- 9 A. D. Walsh, *Trans. Faraday Soc.*, 1949, 179.
- 10 R. Hoffmann, *Tetrahedron Lett.*, 1970, 2907; R. Hoffmann, *Pure Appl. Chem.*, 1971, 2, 233.
- 11 P. A. Luhan and A. T. McPhail, *J. Chem. Soc., Perkin Trans. 2*, 1972, 2372.
- 12 C. C. Chiang, C.-T. Lin, A. H.-J. Wang, D. Y. Curtin, and I. C. Paul, *J. Am. Chem. Soc.*, 1977, 99, 6303.
- 13 J. D. Dunitz and P. Strickler in 'Structural Chemistry and Molecular Biology,' ed. A. Rich and N. Davidson, Freeman, San Francisco, 1968, p. 595.
- 14 L. Leiserowitz and G. M. J. Schmidt, *Acta Crystallogr.*, 1965, 18, 1058.
- 15 W. J. Hehre and J. A. Pople, *J. Am. Chem. Soc.*, 1975, 97, 6941; W. J. Hehre, J. A. Pople, and A. J. P. Devaquet, *J. Am. Chem. Soc.*, 1976, 98, 664.
- 16 R. W. Miller and A. T. McPhail, *J. Chem. Soc., Perkin Trans. 2*, 1979, 1527.
- 17 P. Main, L. Lessinger, M. M. Woolfson, G. Germain, and J.-P. Declercq, 'MULTAN76, a System of Computer Programmes for the Automatic Solution of Crystal Structures,' Universities of York and Louvain, 1976.
- 18 D. T. Cromer and J. T. Waber, *Acta Crystallogr.*, 1965, 18, 104.
- 19 R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, 42, 3175.
- 20 'International Tables for X-Ray Crystallography,' Kynoch Press, Birmingham, 1968, vol. III.

\* For details of the Supplementary publications scheme, see 'Instructions for Authors (1983),' *J. Chem. Soc., Perkin Trans. 1*, 1983, Issue 1.

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