CHACKO, K. K. & SAENGER, W. (1981). *Z. Naturforsch. Teil B*, **36**, 102–107.

GANTZEL, P. K., SPARKS, R. A. & TRUEBLOOD, K. N. (1961). Program *UCLALS* 1, Univ. of California.

HILGENFELD, R. & SAENGER, W. (1982). *Top. Curr. Chem.* **101**, 1–75.

International Tables for X-ray Crystallography (1962). Vol. III. Birmingham: Kynoch Press.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1980). *MULTAN*80. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

SAENGER, W., BRAND, H., VÖGTLE, F. & WEBER, E. (1977). *Metal Ligand Interactions in Organic Chemistry and Biochemistry*, edited by B. PULLMAN & G. GOLDBLUM, Part I, pp. 363–374. Dordrecht: Reidel.

SAENGER, W., SUH, I.-H. & WEBER, G. (1979). *Isr. J. Chem.* **18**, 253–258.

SUH, I.-H. & SAENGER, W. (1978). *Angew. Chem. Int. Ed. Engl.* **17**, 534.

SUH, I.-H., WEBER, G., KAFTORY, M. & SAENGER, W. (1980). *Z. Naturforsch. Teil B*, **35**, 352–359.

VÖGTLE, F. & WEBER, E. (1979). *Angew. Chem. Int. Ed. Engl.* **18**, 753–776.

Structure and Absolute Configuration of (+)-Doronine–Benzene (1:1), $C_{21}H_{30}ClNO_8.C_6H_6$

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Abstract. $M_r = 538 \cdot 1$, orthorhombic, $P2_12_12_1$, $a = 10 \cdot 873$ (4), $b = 12 \cdot 678$ (3), $c = 20 \cdot 511$ (9) Å, $V = 2827 \cdot 4$ Å^3, $Z = 4$, $D_x = 1 \cdot 26$ g cm^{-3}, Cu $K\alpha$ radiation, $\lambda = 1 \cdot 5418$ Å, $\mu = 16 \cdot 1$ cm^{-1}, $F(000) = 1144$, room temperature, $R = 0 \cdot 08$, 2162 independent reflections. The absolute configuration of the molecule was determined. The X-ray results show the presence of a benzene molecule of crystallization in the crystal structure. An intramolecular transannular interaction is postulated between the N and carbonyl C atoms across the eight-membered ring: the $N \cdots C(8)$ distance is $2 \cdot 231$ Å and the $C(8)=O(23)$ bond length is $1 \cdot 221$ Å. Molecules of (+)-doronine are stabilized in the crystal structure by a single intermolecular hydrogen bond and van der Waals interactions.

Introduction. (+)-Doronine,* a Cl-containing seco-pyrrolizidine alkaloid first isolated by Russian workers from *Doronicum macrophyllum* (Alieva, Abdullaev, Telezhenetskaya & Yunosov, 1976) was isolated from the methanol extract of *Senecio clevelandii* E. L. Greene. The physiological properties of seco-pyrrolizidine alkaloids have not been extensively in-

vestigated (Culvenor, 1976). It has been suggested that the stereochemical disposition of groups attached to C(15) and C(20) can influence toxicological properties such as carcinogenicity (Hirata, 1978). Furthermore, it has been proposed that the intramolecular $N \cdots C=O$ interaction in the structure may be relevant to the physiological activity of pyrrolizidine alkaloids (Bürgi, Dunitz & Shefter, 1973). The structure (I) (empirical formula $C_{21}H_{30}ClNO_8$) based on spectral and chemical data (Alieva *et al.*, 1976) was ascribed to (+)-doronine. The present X-ray analysis was undertaken to determine the configuration at all the chiral centers. The X-ray results confirm the proposed structure and show that a benzene molecule of crystallization is present.

(I)

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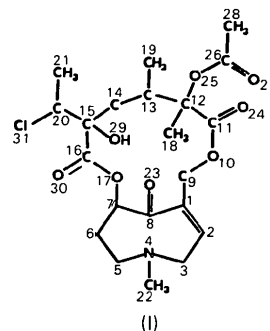
* Systematic name (*Chemical Abstracts*): (15α,20*R*)-12-acet-oxy-20-chloro-15,20-dihydro-15-hydroxy-4-methyl-4,8-secosenecio-nan-8,11,16-trione.

Experimental. Colorless square bipyramidal crystals of the title compound obtained from a benzene solution by slow evaporation; D_m not determined. Crystal dimensions ca $0.4 \times 0.2 \times 0.2$ mm. Nicolet $R3^*$ diffractometer, monochromatic Cu $K\alpha$ radiation, $\theta/2\theta$ scan technique, variable scan speed 8 to 30° min^{-1}. Unit-cell dimensions: least-squares fit to the setting angles of 20 independent reflections. 2302 independent reflections measured ($3° < 2\theta < 114°$), 2162 considered observed ($|F_o| \geq 2\sigma|F_o|$). Two check reflections: statistical fluctuations only. Intensity data corrected for background, Lorentz and polarization effects, but not for absorption. Structure solved by direct-methods program $SHELXTL$ (Sheldrick, 1979). Atomic coordinates, thermal parameters and scale factor refined by means of blocked-cascade least-squares method with $SHELXTL$. $\sum w(|F_o| - |F_c|)^2$ minimized, where $w = [\sigma^2(F_o) + 0.001|F_o|^2]^{-1}$. Scattering factors from $International$ $Tables$ for X-ray $Crystallography$ (1974); those of O and Cl corrected for anomalous dispersion. Positions of all H atoms except those of the solvate molecule calculated. H coordinates of each of the methyl groups calculated geometrically based on a single H position located from a difference Fourier map. In the stucture factor calculations, H atoms allowed to ride on the atom to which they are bonded (C—H 0.96 Å) with a common temperature factor. A formal secondary-extinction correction (0.019) (Larson, 1967) included in the later cycles of refinement to minimize the discrepancy between observed and calculated structure factors of the most intense reflections. Full-matrix refinement of all positional and anisotropic thermal parameters for non-H atoms and H included as constrained estimates converged at $R = 0.081$ and $R_w = 0.089$. Standard deviation of observation of unit weight 3.67; Δ_{av} in the final refinement cycle 0.18σ; final difference Fourier synthesis excursions

within ± 0.5 e Å^{-3}. Absolute configurations of both enantiomers refined; ratio of two final R_w values 1.221; according to Hamilton (1965), the absolute configuration with the lower R_w value is the correct one. All calculations carried out on a Nova-3 computer.

Table 1. *Atom coordinates* ($\times 10^4$) *and temperature factors* (Å$^2 \times 10^3$)

	x	y	z	U^*
C(1)	−145 (6)	4559 (5)	640 (3) .	50 (2)
C(2)	653 (6)	5294 (6)	854 (3)	62 (2)
C(3)	2016 (6)	5122 (5)	773 (3)	59 (2)
N(4)	2194 (5)	4211 (4)	352 (2)	50 (2)
C(5)	2834 (6)	3293 (5)	623 (3)	61 (2)
C(6)	2035 (7)	2329 (6)	512 (3)	65 (2)
C(7)	719 (5)	2630 (5)	708 (2)	47 (2)
C(8)	281 (6)	3580 (4)	307 (3)	48 (2)
C(9)	−1495 (6)	4758 (5)	639 (3)	56 (2)
O(10)	−2125 (4)	4001 (4)	1070 (2)	55 (1)
C(11)	−2399 (5)	4334 (4)	1679 (3)	43 (2)
C(12)	−2922 (5)	3459 (5)	2078 (3)	49 (2)
C(13)	−1870 (5)	2656 (5)	2233 (3)	50 (2)
C(14)	−766 (5)	3233 (5)	2555 (3)	47 (2)
C(15)	475 (5)	2652 (5)	2517 (2)	48 (2)
C(16)	606 (5)	2157 (5)	1840 (3)	48 (2)
O(17)	684 (4)	2933 (3)	1391 (2)	49 (1)
C(18)	−3993 (5)	2902 (6)	1738 (3)	60 (2)
C(19)	−2320 (7)	1713 (6)	2665 (4)	71 (3)
C(20)	1518 (5)	3450 (5)	2639 (3)	49 (2)
C(21)	1515 (8)	3973 (7)	3294 (3)	77 (3)
C(22)	2463 (7)	4455 (8)	−325 (3)	76 (3)
O(23)	6 (4)	3415 (4)	−261 (2)	62 (2)
O(24)	−2179 (4)	5200 (4)	1875 (2)	63 (2)
O(25)	−3270 (4)	3871 (4)	2716 (2)	57 (1)
C(26)	−4154 (7)	4652 (6)	2746 (4)	72 (3)
O(27)	−4742 (6)	4941 (5)	2306 (3)	88 (2)
C(28)	−4237 (10)	5002 (8)	3437 (5)	114 (5)
O(29)	471 (4)	1841 (4)	2989 (2)	66 (2)
O(30)	621 (5)	1237 (4)	1714 (2)	69 (2)
Cl(31)	2959 (2)	2744 (2)	2525 (1)	78 (1)
C(32)	5497 (11)	5320 (10)	242 (7)	146 (6)
C(33)	5867 (14)	5758 (11)	−339 (7)	140 (6)
C(34)	5295 (14)	5831 (16)	828 (10)	189 (9)
C(35)	5537 (23)	6950 (15)	777 (7)	245 (11)
C(36)	6010 (28)	6767 (14)	−347 (7)	295 (17)
C(37)	5915 (41)	7327 (15)	246 (11)	405 (22)

* Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.
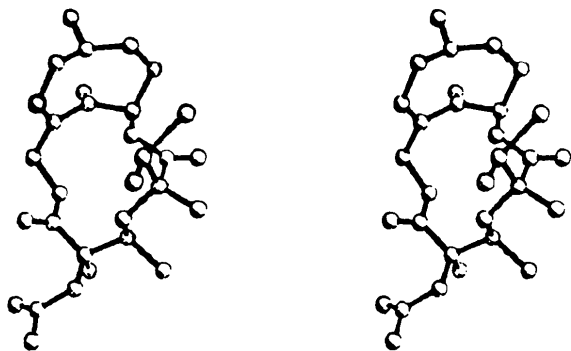
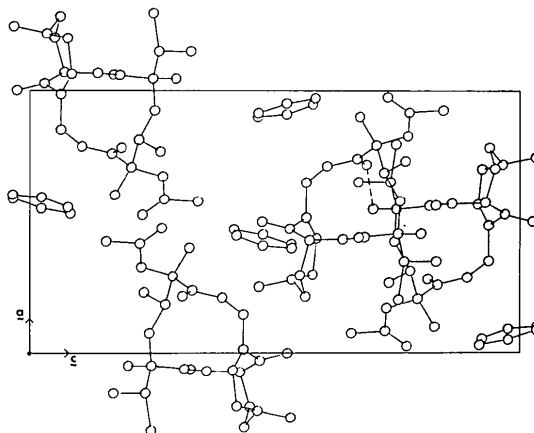Fig. 1. Stereoscopic view of (+)-doronine.

Fig. 2. Perspective packing viewed down **b**. The broken line indicates the intermolecular hydrogen bond. The origin is at the lower-left corner.

Discussion. The structure of (+)-doronine has been determined to be (I). The atom numbering system on the schematic drawing (I) is used in the X-ray investigation. The molecular conformation and absolute configuration are illustrated in the stereoscopic diagram, Fig. 1. The final atomic coordinates, equivalent isotropic thermal parameters and their estimated standard deviations are listed in Table 1.* The orientation of the eight-membered ring in (+)-doronine is very similar to those of senkirkine (Birnbaum, 1974) and clivorine (Birnbaum, Klasek, Sedmera, Snatzke, Johnson & Stantavy, 1971; Birnbaum, 1972). It assumes a conformation in which one half, consisting of C(1), C(2), C(3), N(4) and C(8), is relatively planar (mean e.s.d. ±0·07 Å) with O(23) about 0·88 Å below this mean plane; the other half is envelope-shaped with C(6) below the mean plane of N(4), C(5), C(7) and C(8). The dihedral angle between the two planes is 58·4°. The phenomenon of intramolecular transannular interaction between the tertiary N and carbonyl C atom across the N-heteroring, which has been reported for several other seco-pyrrolizidine alkaloids, is also observed in this structure. The distance N(4)···C(8) across the eight-membered ring is 2·231 Å, which is about 0·76 Å shorter than the sum of the van der Waals radii of these two atoms, and it makes angles of 100·7, 100·0 and 103·0° with the three bonds N(4)—C(3), N(4)—C(5) and N(4)—C(22), respectively. It also makes angles of 88·4, 88·3 and 109·2° with the bonds C(8)—C(1), C(8)—C(7) and C(8)—O(23), respectively. The bond angles involving the three C—N bonds and the short distance N(4)···C(8) are fairly close to the tetrahedral value, and the mean bond angle is 108·8°. The carbonyl double-bond length [C(8)= O(23) = 1·221 Å] is slightly longer than a normal C=O bond length (1·215 ± 0·005 Å) (Sutton, 1965). The three atoms bonded to C(8) and the transannular N are arranged nearly tetrahedrally around the C atom, indicating that hybridization at C(8) is intermediate between sp^2 and sp^3; the mean bond angle at C(8) is 107·2°. The extent of the partial bond N···C=O in the present structure may be compared to those found in clivorine (Birnbaum, 1972) and senkirkine (Birnbaum, 1974): the N···C(=O) distances are 1·993 and 2·292 Å respectively, and the C=O bond lengths are 1·258 and 1·213 Å respectively. The transannular interaction between the carbonyl group and the tertiary amino function in (+)-doronine is significantly weaker than the one in clivorine but slightly stronger than that in senkirkine. Consequently the carbonyl C atom C(8) in the (+)-doronine is much closer to sp^2 hybridization

* Lists of structure factors, anisotropic thermal parameters and assigned H-atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38882 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

and displaced by only 0·13 Å (0·21 Å in clivorine and 0·11 Å in senkirkine) from the mean plane through the three atoms to which it is bonded and towards the transannular N atom. Other observed bond lengths and angles in (+)-doronine are generally compatibile with those values reported for senkirkine and clivorine. The bond lengths and angles involving non-hydrogen atoms are listed in Table 2.

All five asymmetric centers [C(7), C(12), C(13), C(15) and C(20)] on the twelve-membered ring have the R configuration. The methyl C on C(12) is *gauche* to the H on C(13) and *trans* to C(20). The H on C(20) is *trans* to the hydroxyl O on C(15). The crystal structure includes discrete benzene molecules of crystallization in the ratio of 1:1 per formula unit. The closest contact between the solvate benzene molecules and (+)-doronine is at the O-acetyl group [O(27)—C(34) = 3·234 Å]. Mean values of bond lengths and bond angles of the benzene molecule are 1·39 Å and 120·0°, respectively. The benzene C atoms undergo appreciable thermal motion presumably because the solvate molecules are only weakly held in position by van der Waals interactions. Packing of molecules in the unit

Table 2. *Bond lengths (Å) and angles (°), with e.s.d.'s in parentheses*

C(1)—C(2)	1·347 (10)	C(1)—C(8)	1·491 (9)
C(1)—C(9)	1·490 (9)	C(2)—C(3)	1·508 (10)
C(3)—N(4)	1·455 (9)	N(4)—C(5)	1·464 (9)
N(4)—C(22)	1·453 (8)	C(5)—C(6)	1·517 (10)
C(6)—C(7)	1·535 (10)	C(7)—C(8)	1·534 (9)
C(7)—O(17)	1·452 (7)	C(8)—O(23)	1·221 (7)
C(9)—O(10)	1·474 (8)	O(10)—C(11)	1·351 (7)
C(11)—C(12)	1·491 (9)	C(11)—O(24)	1·194 (8)
C(12)—C(13)	1·564 (9)	C(12)—C(18)	1·530 (9)
C(12)—O(25)	1·460 (8)	C(13)—C(14)	1·553 (9)
C(13)—C(19)	1·567 (10)	C(14)—C(15)	1·539 (8)
C(15)—C(16)	1·530 (8)	C(15)—C(20)	1·541 (9)
C(15)—O(29)	1·412 (8)	C(16)—O(17)	1·351 (8)
C(16)—O(30)	1·195 (8)	C(20)—C(21)	1·497 (10)
C(20)—Cl(31)	1·820 (7)	O(25)—C(26)	1·381 (9)
C(26)—O(27)	1·165 (10)	C(26)—C(28)	1·488 (13)
C(32)—C(33)	1·375 (21)	C(32)—C(34)	1·383 (25)
C(33)—C(36)	1·289 (23)	C(34)—C(35)	1·447 (29)
C(35)—C(37)	1·259 (30)	C(36)—C(37)	1·412 (27)
C(2)—C(1)—C(8)	121·7 (6)	C(2)—C(1)—C(9)	121·2 (6)
C(8)—C(1)—C(9)	116·5 (5)	C(1)—C(2)—C(3)	119·9 (6)
C(2)—C(3)—N(4)	108·1 (5)	C(3)—N(4)—C(5)	118·0 (5)
C(3)—N(4)—C(22)	115·1 (6)	C(5)—N(4)—C(22)	115·8 (6)
N(4)—C(5)—C(6)	108·1 (5)	C(5)—C(6)—C(7)	107·1 (6)
C(6)—C(7)—C(8)	110·1 (5)	C(6)—C(7)—O(17)	110·1 (5)
C(8)—C(7)—O(17)	107·5 (5)	C(1)—C(8)—C(7)	120·3 (5)
C(1)—C(8)—O(23)	120·2 (5)	C(7)—C(8)—O(23)	117·0 (5)
C(1)—C(9)—O(10)	110·2 (5)	C(9)—O(10)—C(11)	117·0 (5)
O(10)—C(11)—C(12)	111·0 (5)	O(10)—C(11)—O(24)	123·7 (5)
C(12)—C(11)—O(24)	125·1 (5)	C(11)—C(12)—C(13)	108·5 (5)
C(11)—C(12)—C(18)	112·6 (5)	C(13)—C(12)—C(18)	110·4 (5)
C(11)—C(12)—O(25)	109·0 (5)	C(13)—C(12)—O(25)	103·9 (5)
C(18)—C(12)—O(25)	112·1 (5)	C(12)—C(13)—C(14)	110·2 (5)
C(12)—C(13)—C(19)	112·6 (5)	C(14)—C(13)—C(19)	111·0 (5)
C(13)—C(14)—C(15)	115·5 (5)	C(14)—C(15)—C(16)	108·9 (5)
C(14)—C(15)—C(20)	108·8 (5)	C(16)—C(15)—C(20)	110·4 (5)
C(14)—C(15)—O(29)	108·1 (5)	C(16)—C(15)—O(29)	108·9 (5)
C(20)—C(15)—O(29)	111·6 (5)	C(15)—C(16)—O(17)	109·0 (5)
C(15)—C(16)—O(30)	126·7 (6)	O(17)—C(16)—O(30)	124·3 (6)
C(7)—O(17)—C(16)	117·8 (5)	C(15)—C(20)—C(21)	115·8 (5)
C(15)—C(20)—Cl(31)	106·8 (4)	C(21)—C(20)—Cl(31)	109·6 (5)
C(12)—O(25)—C(26)	118·4 (5)	O(25)—C(26)—O(27)	125·0 (7)
O(25)—C(26)—C(28)	107·3 (7)	O(27)—C(26)—C(28)	127·6 (8)
C(33)—C(32)—C(34)	127·7 (14)	C(32)—C(33)—C(36)	116·6 (14)
C(32)—C(34)—C(35)	111·5 (15)	C(34)—C(35)—C(37)	119·6 (17)
C(33)—C(36)—C(37)	118·6 (16)	C(35)—C(37)—C(36)	125·4 (20)

cell, including solvate molecules and intermolecular hydrogen bonding, as viewed down **b**, with **a** vertical and **c** horizontal, is illustrated in Fig. 2. Besides van der Waals interactions molecules of (+)-doronine are bound together in the crystal structure by a single hydrogen bond (2·802 Å) between O(24) and O(29). There are no other unusually short intermolecular distances.

References

ALIEVA, SH. A., ABDULLAEV, V. A., TELEZHENETSKAYA, M. V. & YUNOSOV, S. YU. (1976). *Khim. Prir. Soedin.* p. 194.

BIRNBAUM, G. I. (1974). *J. Am. Chem. Soc.* **96**, 6165–6168.

BIRNBAUM, K. B. (1972). *Acta Cryst.* B**28**, 2825–2833.

BIRNBAUM, K. B., KLASEK, A., SEDMERA, P., SNATZKE, G., JOHNSON, L. F. & STANTAVY, F. (1971). *Tetrahedron Lett.* **37**, 3421–3424.

BÜRGI, H. B., DUNITZ, J. D. & SHEFTER. E. (1973). *Nature (London), New Biol.* **244**, 186.

CULVENOR, C. C. J. (1976). *Chem. Biol. Interactions,* **12**, 299.

HAMILTON, W. C. (1965). *Acta Cryst.* **18**, 502–510.

HIRATA, Y. (1978). *Pure Appl. Chem.* **50**, 979.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.

LARSON, A. C. (1967). *Acta Cryst.* **23**, 664–665.

SHELDRICK, G. M. (1979). *SHELXTL. An Integrated System for Solving, Refining and Displaying Crystal Structures from Diffraction Data.* Univ. of Göttingen, Federal Republic of Germany.

SUTTON, L. E. (1965). *Tables of Interatomic Distances and Configuration in Molecules and Ions.* Spec. Publ. No. 18. London: The Chemical Society.

Structure of N-Acetyl-DL-phenylalanine p-Nitroanilide, $C_{17}H_{17}N_3O_4$

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Abstract. $M_r = 327·35$, triclinic, $P\bar{1}$, $a = 7·219$ (1), $b = 9·122$ (1), $c = 13·805$ (1) Å, $\alpha = 99·07$ (1), $\beta = 92·55$ (1), $\gamma = 111·41$ (1)°, $Z = 2$, $V = 830·55$ Å^3, $T = 295$ K, $D_m = 1·307$ (3), $D_x = 1·309$ Mg m^{-3}, μ(Cu $K\alpha$) $= 0·7992$ mm^{-1}, $F(000) = 344$, λ(Cu $K\alpha_1$) $= 1·54060$ Å, final $R(F) = 0·054$ for 1903 reflections. The peptide-like groups of this chymotrypsin substrate are non-planar. The N—H···O- and C—H···O-type hydrogen bonds are a stabilizing factor in the molecule that exists in the extended conformation.

Introduction. N-Acetyl-DL-phenylalanine p-nitroanilide (APNA), a chymotrypsin substrate, is a molecule with two aromatic groups. The X-ray analysis of this compound was undertaken as part of the project on the structure of molecules of biological interest. The conformational analysis of APNA may provide useful information towards a better understanding of the conformation of peptides and amino acid derivatives. In this paper the conformation of APNA is compared with those of some other chymotrypsin substrates, such as N-glutaryl-L-phenylalanine p-nitroanilide (GPNA)

(Narasimhan & Pattabhi, 1982), N-acetyl-L-tyrosine p-nitroanilide (ATNA) (Michel & Durant, 1976), and N-acetyl-L-tyrosine ethyl ester (ATEE) (Pieret, Durant, Germain & Koch, 1972).

Experimental. Colourless needles (from an acetone–water mixture), 0·4 × 0·3 × 0·3 mm, Picker four-circle automatic diffractometer, graphite-monochromatized Cu $K\alpha$, $\theta/2\theta$ scan with line profile analysis (Grant & Gabe, 1978); data corrected for direct-beam polarization (Le Page, Gabe & Calvert, 1979) and Lorentz effects; unit-cell parameters determined from least-squares refinement of angles for 40 reflections with $40 < \theta < 50°$; 2474 independent reflections with $\theta < 60°$, 1903 with $I_{net} > 3\sigma(I_{net})$, no absorption correction, *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980), anisotropic full matrix using F_o (Gantzel, Sparks & Trueblood, 1961), H (from ΔF synthesis) isotropic, final $R(F) = 0·054$, $R_w(F) = 0·054$ [Cruickshank's weighting scheme (Cruickshank, Pilling, Bujosa, Lovell & Truter, 1961), $w = 1/(a + F_o + cF_o^2)$ where $a = 10·2$, $c = 0·003$], goodness of fit $= 0·13$; IBM 370/155 computer at the Indian Institute of Technology, Madras, India. Final refinement cycle Δ/σ (max) $= 1·5$, Δ/σ (mean) $= 0·2$, electron density in the final ΔF map $< 0·2$ e Å^{-3},

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† DCB contribution No. 622.
‡ NRC No. 22737.