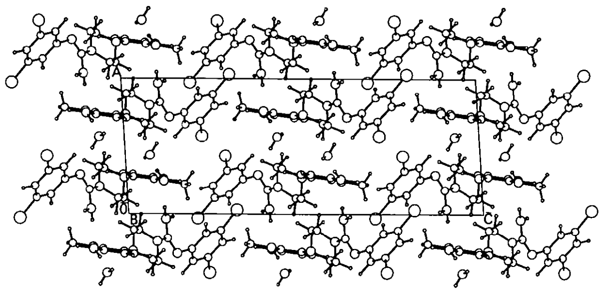


Fig. 2. View of the molecular packing along **b**.

The piperazine ring may be described as a 'half boat', significantly flattened toward N(11), as may be seen by the fact that the in-ring torsion angles involving N(14) but not N(11) average ± 64·8°, while those involving N(11) but not N(14) average ± 48·3°. In terms of the puckering parameters of Cremer & Pople (1975) (starting from either N atom and reducing φ and θ to first quadrant angles): $Q = 0{\cdot}58$ Å, $\varphi = 8{\cdot}8°$ and $\theta = 32{\cdot}4°$.

The molecular packing as viewed along the b axis is shown in Fig. 2. It is dominated by hydrogen bonding and ring stacking. The water molecule is central to the hydrogen bonding, being joined to three different drug molecules. One of its donor bonds appears to be bifurcated, the H atom being equally directed toward N(14) and O(32) of the same molecule. These distances are summarized in Table 2, together with some of the close intermolecular C···C contacts. The main hydrophobic interactions involve atoms of ring 3 interacting with the piperazine ring of the molecules related to it by the inversion centres at $\frac{1}{2}$,1,0 and 0,1,0.

References

Codding, P. W. (1988). *Symposium on the Use of Crystal Structures and Databases in Drug Design*, *21st National Medical Chemistry Symposium*, Minneapolis, USA.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Gould, R. O. & Taylor, P. (1983). *CALC*. Interactive program for molecular geometry. Univ. of Edinburgh, Scotland.

Motherwell, W. D. S. & Clegg, W. (1978). *PLUTO*. Program for plotting molecular and crystal structures. Univ. of Cambridge, England.

Pascal, J. C. (1986). European Patent Application EP204265 (C1.C070295/20).

Sheldrick, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.

Sheldrick, G. M. (1984). *SHELX84*. Program for crystal structure determination. Univ. of Göttingen, Germany.

Vaughan Williams, E. M. (1974). *Adv. Drug. Res.* **9**, 69–101.

Acta Cryst. (1992). C**48**, 873–876

Methyl 4,6-*O*-Benzylidene-2-deoxy-2-*C*-(1,2:3,4-di-*O*-isopropylidene-L-*glycero*-D-*galacto*-hexopyranos-6-yl)-*α*-D-*arabino*-hexopyranosid-3-ulose Monohydrate

By Zbigniew Ciunik

Instytut Chemii, Uniwersytet Wroclawski, ul. Joliot-Curie 14, 50-383 *Wroclaw, Poland*

Peter Luger

Institut für Kristallographie, Freie Universität Berlin, Takustr. 6, *D*-1000 *Berlin* 33, *Germany*

and Kuo-Long Yu

Anti-Infective Chemistry, Bristol-Myers Company, 5 *Research Parkway, PO Box* 5100, *Wallingford,*
CT 06482-7660, *USA*

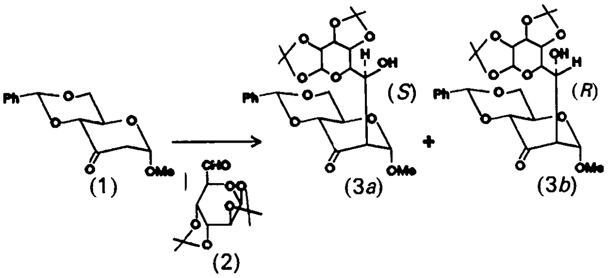
(*Received* 19 *July* 1991; *accepted* 10 *October* 1991)

Abstract. $C_{26}H_{33}O_{11}.H_2O$, $M_r = 539{\cdot}56$, triclinic, $P1$, $a = 8{\cdot}321\ (1)$, $b = 7{\cdot}154\ (1)$, $c = 11{\cdot}727\ (2)$ Å, $\alpha = 76{\cdot}99\ (1)$, $\beta = 78{\cdot}91\ (1)$, $\gamma = 79{\cdot}01\ (1)°$, $V = 659\ (2)$ Å^3, $Z = 1$, $D_x = 1.358\ (4)$ Mg m^{-3}, Cu $K\alpha$, $\lambda = 1.5418$ Å, $\mu = 0.921$ mm^{-1}, room temperature. The refinement of all non-hydrogen-atom parameters yielded $R = 0.041$ for 2144 reflections. The pyranoid rings of the *galacto* and *arabino* subunits have different conformations: twist-boat (^2S_O) and chair ($^4C_1$), respectively. The hydroxyl group at the C(6′) atom is involved in a hydrogen bond with one water molecule.

Introduction. As part of our studies on the conformation of sugars with one sp^2-hybridized C atom in the pyranoid ring by X-ray diffraction methods

0108-2701/92/050873-04$06.00

(Smiatacz, Myszka & Ciunik, 1988; Ciunik, Paulsen, Luger, Smiatacz & Myszka, 1989), we have previously investigated several pyranosides with the oxyimino group in position 2 of the ring. Now we report the crystal structure of the 3-keto derivative which was obtained as a major product of the recently discussed aldol reaction (Kuo-Long & Fraser-Reid, 1989):



The main aim of our studies was the determination of the conformation of the title compound as well as the absolute configuration at the C(6′) atom, a new chiral centre generated during the reaction.

Experimental. The title compound (3*a*) was prepared by the method previously reported (Kuo-Long & Fraser-Reid, 1989). Crystal dimensions 0.33 × 0.38 × 0.55 mm, DEC MicroPDP 11-controlled Stoe–AED diffractometer, Ni-filtered Cu $K\alpha$ radiation. Lattice parameters from 45 reflections ($30 \leq 2\theta \leq 40°$). $\omega/2\theta$ scan, $5 \leq 2\theta \leq 127°$, $0 \leq h \leq 9$, $-7 \leq k \leq 8$, $-12 \leq l \leq 12$, three standard reflections: no variations. 2446 reflections measured [$0.04430 \leq (\sin\theta)/\lambda \leq 0.58089$ Å^{-1}], 2144 with $I > 2\sigma(I)$ considered observed ($R_{\rm int} = 0.016$). No absorption correction.

Structure solved by direct methods and refined (on *F*'s) with anisotropic temperature factors by the full-matrix least-squares method. Some of the H-atom positions were calculated based on standard geometry (C—H = 0.95 Å), the remaining H atoms were found from ΔF syntheses. In the last stage of refinement, the default value of the isotropic extinction correction (Zachariasen, 1963, 1967), $g = 0.03$, was included. Refinement of all 340 non-H-atom parameters converged with $R = 0.041$ and $wR = 0.042$, final $(\Delta/\sigma)_{\max} \leq 0.012$, $-0.318 \leq \Delta\rho \leq 0.344$ e Å^{-3}. The function minimized was $\sum w(|F_o| - |F_c|)^2$ with $w = \sigma^{-2}(F_o)$, where $\sigma(F_o)$ was taken from the counting statistics. The final atomic parameters are given in Table 1.* All crystallographic computations were performed on a VAX/VMS V4.6 computer using programs *SHELXS*90 (Sheldrick, 1990), *XTAL* (Hall & Stewart, 1987) with neutral-atom scattering factors and anomalous-dispersion corrections (O and C atoms) as included in the program, the *XTAL* version of *ORTEP*II (Johnson, 1971), and *PUCK*2 (Luger & Bülow, 1983).

Table 1. *Positional and thermal parameters* ($\times 10^2$) *for non*-H *atoms with e.s.d.'s in parentheses*

$$U_{\rm eq} = \tfrac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$U_{\rm eq}$(Å^2)
O(1)	0.6321 (–)	0.7375 (–)	0.5236 (–)	5.7 (1)
O(3)	0.2127 (6)	0.8345 (7)	0.5032 (4)	5.7 (1)
O(4)	0.1744 (5)	0.4543 (7)	0.5939 (4)	4.9 (1)
O(5)	0.6133 (5)	0.4461 (7)	0.4738 (4)	4.7 (1)
O(6)	0.3248 (6)	0.1765 (7)	0.6910 (4)	5.9 (1)
O(1′)	−0.0365 (6)	0.9185 (7)	0.3153 (4)	5.3 (1)
O(2′)	0.0247 (6)	1.1244 (7)	0.1418 (4)	4.9 (1)
O(3′)	0.1640 (6)	0.7271 (7)	−0.0154 (4)	5.4 (1)
O(4′)	0.4215 (6)	0.6745 (7)	0.0313 (4)	5.9 (1)
O(5′)	0.1957 (5)	0.7096 (7)	0.2529 (4)	4.1 (1)
O(6′)	0.6215 (5)	0.7852 (7)	0.1836 (4)	5.5 (1)
O(*W*)	0.8726 (8)	0.562 (1)	0.0460 (7)	13.3 (3)
C(1)	0.6226 (7)	0.6482 (9)	0.4330 (5)	4.5 (2)
C(2)	0.4696 (7)	0.7570 (8)	0.3780 (5)	4.3 (1)
C(3)	0.3148 (7)	0.7109 (9)	0.4654 (5)	4.5 (2)
C(4)	0.3143 (7)	0.4986 (9)	0.5079 (5)	4.2 (1)
C(5)	0.4732 (7)	0.4143 (9)	0.5629 (5)	4.5 (1)
C(6)	0.4756 (7)	0.2006 (9)	0.6096 (6)	6.1 (2)
C(7)	0.1842 (7)	0.2497 (9)	0.6321 (5)	5.1 (2)
C(71)	0.0339 (7)	0.2042 (9)	0.7221 (5)	5.0 (2)
C(72)	−0.0438 (8)	0.326 (1)	0.7981 (6)	6.1 (2)
C(73)	−0.1818 (8)	0.275 (1)	0.8806 (6)	6.9 (2)
C(74)	−0.2361 (8)	0.108 (1)	0.8861 (6)	7.5 (2)
C(75)	−0.1590 (9)	−0.016 (1)	0.8102 (6)	7.9 (3)
C(76)	−0.0223 (8)	0.035 (1)	0.7274 (6)	6.6 (2)
C(11)	0.7848 (8)	0.672 (1)	0.5718 (6)	7.9 (2)
C(1′)	0.0342 (6)	0.8020 (8)	0.2323 (5)	4.2 (1)
C(2′)	0.0289 (7)	0.9394 (9)	0.1141 (5)	4.5 (2)
C(3′)	0.1810 (7)	0.8992 (9)	0.0203 (5)	4.5 (2)
C(4′)	0.3455 (7)	0.8524 (9)	0.0670 (5)	4.4 (1)
C(5′)	0.3234 (7)	0.8241 (8)	0.2004 (5)	4.0 (1)
C(6′)	0.4757 (7)	0.7175 (9)	0.2532 (5)	4.4 (2)
C(7′)	−0.0652 (7)	1.1194 (9)	0.2591 (5)	5.3 (2)
C(71′)	−0.2529 (8)	1.177 (1)	0.2536 (6)	7.1 (2)
C(72′)	0.0015 (9)	1.238 (1)	0.3211 (7)	7.6 (2)
C(8′)	0.3316 (7)	0.6267 (9)	−0.0439 (6)	5.2 (2)
C(81′)	0.3243 (9)	0.415 (1)	−0.0170 (9)	10.3 (3)
C(82′)	0.3953 (9)	0.699 (1)	−0.1709 (6)	7.9 (3)

Discussion. The numbering scheme and the overall conformation of the compound is shown in Fig. 1. Table 2 lists selected bond distances and angles, and torsion angles.

The compound under investigation is built from two sugar subunits, *arabino* (*A*) and *galacto* (*B*) connected *via* the C(6′)—C(2) bond.

The Cremer & Pople (1975) ring-puckering parameters $Q = 0.584$ (6) Å, $\theta = 6.5$ (6) and $\varphi = 296$ (5)° calculated for the pyranoid *A* ring indicated a small distortion of the $^4C_1$ chair conformation of this ring, and $Q = 0.641$ (6) Å, $\theta = 98.1$ (6) and $\varphi = 141$ (5)° for the pyranoid *B* ring indicated the ^2S_O twist-boat conformation. A small distortion of the chair conformation of the 3-keto pyranoid ring has been

---

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, and bond distances and angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54766 (22 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

observed previously (Arnoux, Pascard, Raynaud & Lumel, 1980). The twist-boat conformation of the pyranoid *B* ring results from the presence of two fused isopropylidene rings and was reported earlier (Boeyens, Nolte & Woolard, 1979). Both isopropylidene rings have the twist conformation. The first ring, fused *via* the C(1′) and C(2′) atoms, has the $^{C(7')}T_{O(2')}$ conformation [$q_2 = 0.299$ (6) Å, $\varphi_2 =$ 86 (1)°], and the second has the $^{O(3')}T_{C(8')}$ conformation [$q_2 = 0.278$ (6) Å, $\varphi_2 = 193$ (1)°]. The conformation of the dioxolane ring with $Q = 0.599$ (6) Å, $\theta =$ 177.1 (6) and $\varphi = 264$ (11)° is close to an ideal chair.

The mutual orientation of both *A* and *B* subunits is described by the C(1)—C(2)—C(6′)—C(5′) and C(2)—C(6′)—C(5′)—O(5′) torsion angles which indicate the *ap*, −*sc* conformation of the compound.

The absolute configuration of the chiral centre at C(6′) was determined as *S* with reference to the known chirality of the *galacto* and *arabino* subunits. In this position the hydroxyl group has the only possible *ap* orientation with regard to the C(5′)—O(5′) bond and the C(2)—C(3) bond, and is directed outwards from the molecule. This orientation of the hydroxyl group is probably a key factor for understanding the high stereospecificity of the mentioned aldol reaction which gave the *S* [the title compound, (3*a*)] and *R* enantiomorphic products (3*b*) in the ratio 10:1. In the case of the *R* enantiomorph (3*b*), the above mentioned mutual orientation of the hydroxyl group is impossible and must be different than in the *S* form. The *ap*, *ap* conformation of both sugar subunits with the hydroxyl group oriented toward the centre of the *A* pyranoid ring seems to be probable for the *R* enantiomorph. Such an orientation of the hydroxyl group, being less favourable compared with the outward orientation of the OH group of the *S* enantiomorph (3*a*), may explain the low amount of the *R* form (3*b*) in products of this reaction. This view agrees well with other experiments presented by Kuo-Long & Fraser-Reid (1989).

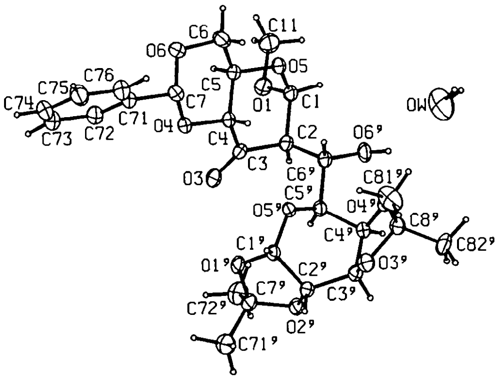


Fig. 1. *ORTEP* drawing showing atom numbering. The non-hydrogen atoms are represented by 30% probability ellipsoids.

Table 2. *Selected bond lengths* (Å), *valency angles* (°) *and torsion angles* (°) *with e.s.d.'s in parentheses*

O(1)—C(1)	1.379 (7)	O(1)—C(11)	1.443 (7)
O(3)—C(3)	1.202 (7)	O(4)—C(4)	1.420 (7)
O(5)—C(1)	1.429 (8)	O(5)—C(5)	1.424 (7)
O(6)—C(6)	1.436 (7)	O(1′)—C(1′)	1.395 (8)
O(2′)—C(2′)	1.424 (9)	O(3′)—C(3′)	1.426 (9)
O(4′)—C(4′)	1.423 (8)	O(5′)—C(1′)	1.420 (7)
O(5′)—C(5′)	1.425 (7)	O(6′)—C(6′)	1.427 (7)
C(1)—C(2)	1.534 (8)	C(2)—C(3)	1.523 (7)
C(2)—C(6′)	1.542 (9)	C(3)—C(4)	1.488 (9)
C(4)—C(5)	1.542 (8)	C(5)—C(6)	1.501 (9)
C(1′)—C(2′)	1.511 (7)	C(2′)—C(3′)	1.537 (7)
C(3′)—C(4′)	1.522 (8)	C(4′)—C(5′)	1.511 (8)
C(5′)—C(6′)	1.515 (8)		
C(1)—O(1)—C(11)	113.3 (4)	C(1)—O(5)—C(5)	111.8 (4)
C(1′)—O(5′)—C(5′)	114.5 (4)	O(1)—C(1)—O(5)	112.0 (4)
O(1)—C(1)—C(2)	106.7 (4)	O(5)—C(1)—C(2)	111.7 (5)
C(1)—C(2)—C(3)	108.7 (4)	C(1)—C(2)—C(6′)	111.6 (4)
C(3)—C(2)—C(6′)	114.9 (5)	O(3)—C(3)—C(2)	122.6 (6)
O(3)—C(3)—C(4)	124.3 (5)	C(2)—C(3)—C(4)	112.8 (5)
O(4)—C(4)—C(3)	113.2 (5)	O(4)—C(4)—C(5)	109.0 (4)
C(3)—C(4)—C(5)	107.4 (5)	O(5)—C(5)—C(4)	108.8 (4)
O(5)—C(5)—C(6)	110.0 (5)	C(4)—C(5)—C(6)	109.2 (5)
O(6)—C(6)—C(5)	107.5 (5)	O(1′)—C(1′)—O(5′)	110.5 (5)
O(1′)—C(1′)—C(2′)	104.2 (4)	O(5′)—C(1′)—C(2′)	114.4 (4)
O(2′)—C(2′)—C(1′)	103.5 (5)	O(2′)—C(2′)—C(3′)	109.3 (5)
C(1′)—C(2′)—C(3′)	114.0 (4)	O(3′)—C(3′)—C(2′)	106.1 (5)
O(3′)—C(3′)—C(4′)	105.2 (5)	C(2′)—C(3′)—C(4′)	114.3 (5)
O(4′)—C(4′)—C(3′)	103.9 (5)	O(4′)—C(4′)—C(5′)	109.5 (4)
C(3′)—C(4′)—C(5′)	112.5 (4)	O(5′)—C(5′)—C(4′)	110.0 (5)
O(5′)—C(5′)—C(6′)	105.6 (4)	C(4′)—C(5′)—C(6′)	114.0 (4)
O(6′)—C(6′)—C(2)	105.9 (5)	O(6′)—C(6′)—C(5′)	110.5 (4)
C(2)—C(6′)—C(5′)	111.1 (5)		
C(1′)—O(5′)—C(5′)—C(6′)	168.7 (5)	O(5′)—C(5′)—C(6′)—O(6′)	163.0 (5)
O(5)—C(1)—C(2)—C(6′)	−75.8 (6)	C(1)—C(2)—C(6′)—O(6′)	−60.6 (6)
C(1)—C(2)—C(6′)—C(5′)	179.5 (5)	O(5′)—C(5′)—C(6′)—C(2)	−79.8 (6)

All bond lengths and valency angles are in the range usually observed in other crystal structures of carbohydrates.

The H atom of the hydroxyl group is involved in a weak intermolecular O(6′)—H(61′)···O(*W*) hydrogen bond with O···O and H···O lengths of 2.848 (9) and 2.12 Å, and with an O—H···O angle of 125°.

This work was performed in Germany during the stay of one of the authors (ZC) on his scholarship from the Alexander von Humboldt Foundation and was funded by the Fonds der Chemischen Industrie.

References

Arnoux, B., Pascard, C., Raynaud, L. & Lumel, J. (1980). *J. Am. Chem. Soc.* **102**, 3605–3608.

Boeyens, J. C. A., Nolte, M. J. & Woolard, G. R. (1979). *Carbohydr. Res.* **70**, 103–115.

Ciunik, Z., Paulsen, H., Luger, P., Smiatacz, Z. & Myszka, H. (1989). *Acta Cryst.* **B45**, 512–518.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Hall, S. R. & Stewart, J. M. (1987). *XTAL2.2 User's Manual.* Univs. of Western Australia, Australia, and Maryland, USA.

Johnson, C. K. (1971). *ORTEP*II. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

KUO-LONG, Y. & FRASER-REID, B. (1989). *J. Chem. Soc. Chem. Commun.* pp. 1442–1445.
LUGER, P. & BÜLOW, R. (1983). *J. Appl. Cryst.* **16**, 431–432.
SHELDRICK, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
SMIATACZ, Z., MYSZKA, H. & CIUNIK, Z. (1988). *Carbohydr. Res.* **172**, 171–182.
ZACHARIASEN, W. H. (1963). *Acta Cryst.* **16**, 1139–1144.
ZACHARIASEN, W. H. (1967). *Acta Cryst.* **23**, 558–564.

Acta Cryst. (1992). C**48**, 876–878

Structures of Sobrerol Enantiomers and Racemates. II. (±)-*trans*-5-Hydroxy-α,α,4-trimethyl-3-cyclohexene-1-methanol (Racemic *trans*-Sobrerol)

BY G. GIUSEPPETTI AND C. TADINI

CNR Centro di Studio per la Cristallografia Strutturale, c/o Dipartimento di Scienze della Terra, Sezione di Mineralogia, Petrografia e Geochimica, Università, Via A. Bassi 4, 27100 *Pavia, Italy*

AND G. P. BETTINETTI

Dipartimento di Scienze Farmaceutiche, Università, Via G. Capponi 9, 50121 *Firenze, Italy*

(*Received* 8 *June* 1991; *accepted* 23 *September* 1991)

Abstract. $C_{10}H_{18}O_2$, $M_r = 170.25$, orthorhombic, $Pna2_1$, $a = 6.570\,(2)$, $b = 19.031\,(4)$, $c = 7.949\,(2)$ Å, $V = 993.9\,(4)$ Å^3, $Z = 4$, $D_m = 1.131$, $D_x = 1.138$ g cm^{-3}, $\lambda(\text{Mo } K\alpha) = 0.7107$ Å, $\mu = 0.720$ cm^{-1}, $F(000) = 376$, $T = 296$ K, $R = 0.021$ for 444 unique reflections with $I > 3\sigma(I)$. The molecular geometry and conformation are substantially the same as for the *trans*-sobrerol enantiomer. Homochiral molecules are linked head-to-tail *via* O—H···O bonds [2.755 (5) Å] forming polymer-like chains joined by O—H···O bonds [2.840 (5) Å] and C—H(sp^3)···O contacts as in *trans*-sobrerol. Paired chains alternate in the crystal with chains of molecules of opposite chiralities, the distance being rather longer than that between paired homochiral chains in the enantiomer. The weaker interchain forces in the racemic structure explain why the crystal is more soluble in water and has a lower melting point than the enantiomer. The same intrachain interactions and hydrogen-bonding pattern account for the analogous spectroscopic properties of the enantiomer and racemic crystals.

Introduction. High structural analogies between the enantiomer and racemic compound of *trans*-sobrerol have been supposed to account for the similarities of their spectroscopic properties and unit-cell parameters (Bettinetti, Giordano, Fronza, Italia, Pellegata, Villa & Ventura, 1990). On the other hand, different intermolecular forces must be responsible for the different physical properties (melting point, solubility) of the two crystalline forms. In the previous study (Giuseppetti, Tadini & Bettinetti, 1992) the crystal structure of the *laevo* enantiomer of *trans*-sobrerol was determined. In this paper we report the crystal structure determination of the racemic compound.

Experimental. Single crystals of the title compound obtained by recrystallization from ethanol, m.p. 404.8 K (Bettinetti *et al.*, 1990). Density measured with a helium pycnometer (Micrometric Instrument Corporation 1302/1303) 1.131 g cm^{-3}. Prismatic crystal (0.58 × 0.18 × 0.18 mm). Philips 1100 four-circle diffractometer, graphite monochromator; 48 reflections ($2 < \theta < 25°$) used for measuring lattice parameters with Philips *LAT* routine. ω–2θ scan mode, scan speed 0.05° s^{-1}, scan width 2.0°, θ range 2–25° (intensities negligible at $\theta > 25°$). Three standard reflections every 180 min, mean intensity variation 2.1%, maximum intensity variation 2.7%. 3516 reflections measured [$-7 \le h \le 7$, $-22 \le k \le 22$, $l \le 9$; maximum $(\sin\theta)/\lambda = 0.59$ Å^{-1}], 720 unique, 444 with $I > 3\sigma(I)$. Corrections for Lorentz–polarization and experimental absorption, between 1.001 and 1.057, following North, Phillips & Mathews (1968). Structure solved by direct methods (*MULTAN*80; Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). Least-squares refinement on F. Coordinates of H atoms calculated by geometrical considerations (*XANADU*; Roberts & Sheldrick, 1975). $\Delta\rho$ maps showed random fluctuations between +0.14 and −0.15 e Å^{-3}; parameters refined: anisotropic thermal parameters for non-H atoms, isotropic for H atoms; scale factor and secondary-extinction parameter [$g = 1.4\,(1) \times 10^{-4}$] calculated

0108-2701/92/050876-03$06.00