

compounds have already been reported (Lynch, Daniel, Martin & Davis, 1989, 1990).

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Structure of a Novel Bisindole Derivative

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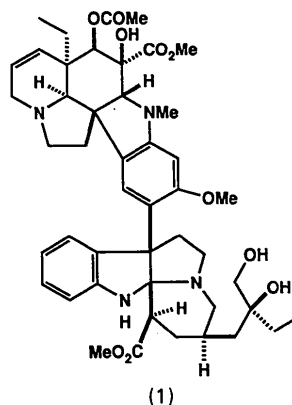
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Abstract. (3a*R*-{3a α ,4 β ,5a β ,9[1*R*,3*R*(2*S*),5*R*,7a*S*,12a*S*],10b*R*,13a α })-Methyl-4-(acetyloxy)-3a-ethyl-3a,4,5,5a,6,11,12,13a-octahydro-9-[1,2,3,4,6,7,7a,12-octahydro-3-(2-hydroxy-2-hydroxymethylbutyl)-1-(methoxycarbonyl)indolizino[1,2-*b*]indol-7a-yl]-5-hydroxy-8-methoxy-6-methyl-1*H*-indolizino[8,1-*c,d*]-carbazole-5-carboxylate methanol hydrate solvate, C₄₆H₆₀N₄O₁₀.CH₃OH.H₂O, $M_r = 879.06$, monoclinic, $P2_1$, $a = 8.2878$ (8), $b = 31.018$ (4), $c = 9.2267$ (7) Å, $\beta = 105.211$ (7)°, $V = 2288.8$ (4) Å³, $Z = 2$, $D_x = 1.28$ g cm⁻³, $\mu = 0.8580$ cm⁻¹, Mo $K\alpha$ radiation, $\lambda = 0.7107$ Å, $F(000) = 944$, $T = 198$ K, $R = 0.0382$ for 2931 reflections [$F_o \geq 4\sigma(F_o)$]. A very short intramolecular hydrogen-bonding interaction is observed between the hydroxyl group and N9 of the vindoline portion of the molecule. The relevant parameters are: O3—H3O···N9, O···N 2.598 (4), H···N 1.68 (5) Å, O—H···N 164 (5)°. Molecules related by the 2₁ screw operation are hydrogen bonded into columns parallel to **b**. The relevant hydrogen-bonding parameters are: O18'—H18O'···O3 (−*x*, 0.5 + *y*, 1 + *z*), O···O 2.925 (4), H···O 2.36 (6) Å, O—H···O 119 (5)°; O18'—H18O'···O23 (−*x*, 0.5 + *y*, 1 − *z*), O···O 3.089 (4), H···O 2.17 (6) Å, O—H···O 168 (5)°; O19'—H19O'···O3 (−*x*, 0.5 + *y*, 1 − *z*), O···O 2.801 (4), H···O 1.88 (6) Å, O—H···O 169 (5)°. The hydrogen bonding at H18O' is bifurcated and the O3···H···O23 angle is 70 (2)°. The solvent methanol molecule

(C1A, O1A) and water molecule (O1B) are also involved in hydrogen-bonding interactions with the following parameters: O1A—H1A···O19' (1 + *x*, *y*, *z*), O···O 2.711 (5), H···O 1.77 (9) Å, O—H···O 156 (7)°; O1B—H1B···O18', O···O 2.932 (5), H···O 1.86 (12) Å, O—H···O 161 (9)°; O1B—H2B···O1A, O···O 2.777 (6), H···O 1.98 (7) Å, O—H···O 178 (7)°.

Experimental. (1) was obtained in two steps from the product of a novel coupling reaction between the *Aspidosperma* alkaloid vindoline and a substituted indolizino[8,7-*b*]indole derivative (Magnus, Ladow, Elliot & Kim, 1989; Magnus, Stamford & Ladlow, 1990). The absolute configuration of (1) was assigned



on the basis of internal comparison to the vindoline moiety (Moncrief & Lipscomb, 1966). Colorless crystals were obtained by slow evaporation of a methanol–water solution. The data crystal was a long needle of approximate dimensions $0.2 \times 0.2 \times 0.6$ mm. The data were collected at 198 K on a Nicolet R3 diffractometer using a graphite monochromator and equipped with a Nicolet LT-2 low-temperature delivery system. The lattice parameters were obtained by the least-squares refinement of 40 reflections with $18.7 < 2\theta < 24.5^\circ$. The data were collected from 4.0 to 47.5° in 2θ using the ω -scan technique, with a 1.2° scan range in ω at $3-6^\circ \text{ min}^{-1}$. 7418 reflections were measured, of which 3687 were unique (the R for averaging symmetry equivalent reflections was 0.0188), where h ranged from $-9 \rightarrow 9$, k ranged from $0 \rightarrow 36$ and l ranged from $-10 \rightarrow 10$. Four reflections ($243, 2.11\bar{2}, 11\bar{4}, \bar{3}41$) were remeasured every 96 reflections to monitor instrument and crystal stability. A smoothed curve of the intensities of these check reflections was used to scale the data. The scaling factor ranged from $0.990-1.03$. The data were also corrected for Lp effects but not for absorption ($\mu = 0.8580 \text{ cm}^{-1}$). 756 reflections having $F_o < 4\sigma(F_o)$ were considered unobserved. Data reduction and decay correction were performed using the *SHELXTL-Plus* software package (Sheldrick, 1988). The structure was solved by direct methods and refined by full-matrix least squares (Sheldrick, 1988) with anisotropic thermal parameters for the non-H atoms. All H atoms were located from a ΔF map and refined with isotropic thermal parameters. However, in the latter stages of refinement the geometry of the methyl H atoms on C25, C26, C23' and C2A was idealized (C—H 0.96 \AA). The function $\sum w(|F_o| - |F_c|)^2$ was minimized, where $w = 1/[\sigma(F_o)]^2$ and $\sigma(F_o) = (0.5kI)^{-1/2} \{[\sigma(I)]^2 + (0.02I)^2\}^{1/2}$. The intensity, I , is given by $(I_{\text{peak}} - I_{\text{background}}) \times (\text{scan rate})$; where 0.02 is a factor to downweight intense reflections and to account for instrument instability and k is the correction due to Lp effects and decay. $\sigma(I)$ was

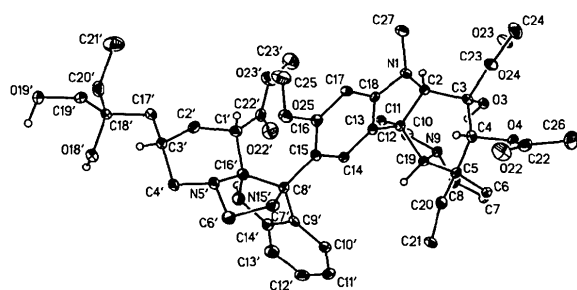


Fig. 1. View of (1) showing the atom-labeling scheme. Thermal ellipsoids are scaled to the 30% probability level. Most H atoms were removed for clarity. H atoms are represented as spheres of arbitrary size. The solvent MeOH and H_2O molecules are not shown.

Table 1. Fractional coordinates and equivalent isotropic thermal parameters (\AA^2) for the non-H atoms of (1)

$$U_{\text{eq}} = (1/3) \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j.$$

	x	y	z	U_{eq}
N1	0.0931 (4)	-0.07455 (10)	0.4832 (3)	0.0221 (12)
C2	0.1031 (5)	-0.09005 (12)	0.6368 (4)	0.0193 (14)
C3	0.2386 (5)	-0.12571 (12)	0.6887 (4)	0.0202 (14)
O3	0.2070 (3)	-0.14802 (9)	0.8138 (3)	0.0230 (10)
C4	0.4095 (5)	-0.10476 (13)	0.7270 (5)	0.0226 (15)
O4	0.5327 (3)	-0.13915 (9)	0.7470 (3)	0.0287 (10)
C5	0.4468 (5)	-0.07522 (13)	0.8673 (4)	0.0229 (14)
C6	0.5302 (5)	-0.09905 (13)	1.0106 (5)	0.027 (2)
C7	0.4707 (6)	-0.10103 (14)	1.1301 (5)	0.030 (2)
C8	0.3026 (6)	-0.0842 (2)	1.1321 (5)	0.030 (2)
N9	0.2020 (4)	-0.08005 (10)	0.9770 (3)	0.0218 (12)
C10	0.0313 (6)	-0.06251 (15)	0.9581 (5)	0.026 (2)
C11	-0.0076 (6)	-0.03836 (14)	0.8077 (5)	0.024 (2)
C12	0.1395 (5)	-0.04874 (13)	0.7402 (4)	0.0211 (14)
C13	0.1641 (5)	-0.01459 (12)	0.6323 (4)	0.0200 (14)
C14	0.2028 (5)	0.02862 (13)	0.6599 (5)	0.0211 (15)
C15	0.2070 (5)	0.05737 (12)	0.5453 (4)	0.0210 (14)
C16	0.1595 (5)	0.04058 (13)	0.3969 (4)	0.0229 (15)
C17	0.1179 (5)	-0.00263 (13)	0.3673 (5)	0.0237 (15)
C18	0.1233 (5)	-0.03047 (12)	0.4872 (4)	0.0188 (13)
C19	0.2828 (5)	-0.05428 (14)	0.8823 (4)	0.0209 (14)
C20	0.5692 (6)	-0.04006 (15)	0.8426 (5)	0.030 (2)
C21	0.6429 (7)	-0.0109 (2)	0.9774 (6)	0.037 (2)
C22	0.6433 (5)	-0.1387 (2)	0.6616 (5)	0.036 (2)
O22	0.6641 (4)	-0.10842 (12)	0.5880 (4)	0.0499 (14)
C23	0.2190 (5)	-0.16108 (13)	0.5692 (5)	0.0235 (15)
O23	0.1373 (4)	-0.19317 (10)	0.5677 (3)	0.0382 (12)
C24	0.2971 (8)	-0.1858 (2)	0.3549 (6)	0.040 (2)
O24	0.3036 (4)	-0.15260 (6)	0.4683 (3)	0.0297 (10)
C25	0.0836 (9)	0.0560 (2)	0.1328 (5)	0.062 (3)
O25	0.1522 (4)	0.07005 (9)	0.2833 (3)	0.0329 (11)
C26	0.7325 (7)	-0.1808 (2)	0.6729 (8)	0.059 (3)
C27	-0.0392 (5)	-0.09268 (13)	0.3598 (5)	0.030 (2)
C1'	-0.0795 (5)	0.12126 (14)	0.4539 (5)	0.027 (2)
C2'	-0.2005 (6)	0.16018 (14)	0.4219 (5)	0.030 (2)
C3'	-0.1367 (6)	0.19931 (14)	0.3504 (5)	0.027 (2)
C4'	0.0454 (6)	0.20888 (14)	0.4352 (6)	0.033 (2)
N5'	0.1424 (5)	0.16949 (11)	0.4495 (4)	0.0273 (13)
C6'	0.3234 (6)	0.17298 (15)	0.4931 (6)	0.033 (2)
C7'	0.3748 (6)	0.12581 (15)	0.5035 (5)	0.029 (2)
C8'	0.2505 (5)	0.10483 (13)	0.5831 (4)	0.0234 (14)
C9'	0.3205 (5)	0.11184 (13)	0.7516 (5)	0.0254 (15)
C10'	0.4654 (6)	0.09525 (14)	0.8459 (5)	0.032 (2)
C11'	0.5014 (7)	0.10478 (15)	0.9986 (6)	0.039 (2)
C12'	0.3970 (6)	0.1316 (2)	1.0517 (5)	0.039 (2)
C13'	0.2538 (6)	0.1494 (2)	0.9582 (5)	0.037 (2)
C14'	0.2185 (5)	0.13911 (14)	0.8058 (5)	0.030 (2)
N15'	0.0832 (5)	0.15448 (12)	0.6920 (4)	0.0324 (14)
C16'	0.0943 (5)	0.13719 (13)	0.5447 (4)	0.0238 (14)
C17'	-0.1561 (7)	0.19323 (15)	0.1818 (5)	0.029 (2)
C18'	-0.1933 (5)	0.23401 (13)	0.0870 (5)	0.0247 (15)
O18'	-0.0697 (4)	0.26723 (9)	0.1467 (3)	0.0291 (11)
C19'	-0.3664 (6)	0.25176 (15)	0.0829 (5)	0.030 (2)
O19'	-0.4058 (4)	0.29047 (10)	-0.0009 (4)	0.0355 (12)
C20'	-0.1752 (7)	0.2264 (2)	-0.0721 (5)	0.034 (2)
C21'	-0.2812 (9)	0.1902 (2)	-0.1589 (7)	0.056 (3)
C22'	-0.1589 (5)	0.08607 (14)	0.5232 (6)	0.033 (2)
O22'	-0.1620 (4)	0.08385 (12)	0.6525 (4)	0.0505 (15)
C23'	-0.3314 (8)	0.0241 (2)	0.4685 (9)	0.070 (3)
O23'	-0.2396 (4)	0.05818 (11)	0.4179 (4)	0.0459 (13)
O1A	0.2745 (5)	0.30992 (13)	-0.1484 (5)	0.067 (2)
C2A	0.2329 (9)	0.2757 (2)	-0.2477 (8)	0.074 (3)
O1B	0.0101 (6)	0.33684 (13)	-0.0378 (5)	0.054 (2)

estimated from counting statistics; $\sigma(I) = [(I_{\text{peak}} + I_{\text{background}})^{1/2} \times \text{scan rate}]$. 796 independent parameters were refined in blocks of 383 and 414 parameters (the scale factor was refined in each block) to a final $R = 0.0382$, with $wR = 0.0352$ and goodness of fit = 1.061 . The origin along the 2_1 screw axis was defined by the atoms in the block not being refined. For all data $R = 0.0549$, with $wR = 0.0391$. The maximum $|\Delta F/\sigma| < 0.1$ in the final refinement cycle and

Table 2. Bond lengths (Å) and angles (°) for the non-hydrogen atoms of (1)

1	2	3	1-2	1-2-3
C2	N1	C18	1.479 (5)	109.2 (3)
C18	N1	C27	1.389 (5)	119.4 (3)
C27	N1	C2	1.469 (5)	117.5 (3)
C3	C2	C12	1.559 (5)	112.5 (3)
C3	C2	N1		112.3 (3)
C12	C2	N1	1.579 (5)	105.6 (3)
O3	C3	C4	1.427 (5)	112.2 (3)
O3	C3	C23		103.1 (3)
O3	C3	C2		108.8 (3)
C4	C3	C23	1.514 (6)	113.0 (4)
C4	C3	C2		108.8 (3)
C23	C3	C2	1.534 (6)	110.8 (3)
O4	C4	C5	1.454 (5)	110.4 (3)
O4	C4	C3		107.3 (3)
C5	C4	C3	1.549 (6)	114.7 (4)
C22	O4	C4	1.357 (6)	118.6 (3)
C6	C5	C19	1.514 (6)	109.7 (4)
C6	C5	C20		107.8 (3)
C6	C5	C4		112.7 (3)
C19	C5	C20	1.545 (6)	110.1 (3)
C19	C5	C4		109.6 (3)
C20	C5	C4	1.546 (6)	106.8 (4)
C7	C6	C5	1.323 (7)	124.5 (4)
C8	C7	C6	1.492 (7)	123.2 (4)
N9	C8	C7	1.461 (5)	108.3 (4)
C10	N9	C19	1.483 (6)	107.5 (3)
C10	N9	C8		115.5 (4)
C19	N9	C8	1.469 (6)	113.5 (3)
C11	C10	N9	1.535 (6)	104.7 (4)
C12	C11	C10	1.541 (7)	105.2 (3)
C13	C12	C19	1.504 (6)	115.9 (3)
C13	C12	C2		102.1 (3)
C13	C12	C11		112.3 (3)
C19	C12	C2	1.530 (5)	114.1 (3)
C19	C12	C11		101.3 (3)
C2	C12	C11		111.6 (3)
C14	C13	C18	1.386 (5)	120.6 (4)
C14	C13	C12		128.6 (4)
C18	C13	C12	1.382 (5)	110.4 (3)
C15	C14	C13	1.390 (6)	122.1 (4)
C16	C15	C8'	1.421 (5)	124.1 (3)
C16	C15	C14		116.2 (3)
C8'	C15	C14	1.534 (5)	119.6 (3)
C17	C16	O25	1.393 (6)	121.9 (3)
C17	C16	C15		122.3 (4)
O25	C16	C15	1.380 (5)	115.8 (3)
C18	C17	C16	1.395 (6)	119.0 (4)
N1	C18	C13		112.0 (3)
N1	C18	C17		128.3 (3)
C13	C18	C17		119.8 (4)
C5	C19	N9		112.0 (3)
C5	C19	C12		118.3 (3)
N9	C19	C12		101.4 (3)
C21	C20	C5	1.529 (7)	115.7 (4)
O22	C22	C26	1.198 (7)	125.8 (5)
O22	C22	O4		123.8 (5)
C26	C22	O4	1.491 (8)	110.4 (5)
O23	C23	O24	1.202 (5)	123.7 (4)
O23	C23	C3		123.6 (4)
O24	C23	C3	1.330 (6)	112.7 (3)
O24	C24		1.460 (6)	
C23	O24	C24		115.8 (4)
O25	C25		1.424 (5)	
C16	O25	C25		117.7 (3)
C2'	C1'	C16'	1.548 (6)	108.6 (3)
C16'	C1'	C22'	1.545 (6)	116.9 (3)
C22'	C1'	C2'	1.502 (7)	108.3 (4)
C3'	C2'	C1'	1.539 (7)	114.8 (4)
C4'	C3'	C17'	1.535 (6)	111.6 (4)
C4'	C3'	C2'		109.7 (3)
C17'	C3'	C2'	1.533 (6)	112.4 (4)
N5'	C4'	C3'	1.449 (6)	109.3 (3)
C6'	N5'	C16'	1.452 (6)	108.1 (3)
C6'	N5'	C4'		118.1 (4)
C16'	N5'	C4'	1.455 (6)	113.7 (4)
C7'	C6'	N5'	1.520 (7)	101.4 (4)
C8'	C7'	C6'	1.556 (7)	102.9 (4)
C9'	C8'	C16'	1.525 (6)	101.9 (3)
C9'	C8'	C15		111.9 (3)
C9'	C8'	C7'		107.4 (3)
C16'	C8'	C15	1.602 (6)	115.0 (3)
C16'	C8'	C7'		103.3 (3)
C15'	C8'	C7'		116.0 (4)
C10'	C9'	C14'	1.384 (6)	120.9 (4)

Table 2 (cont.)

1	2	3	1-2	1-2-3
C10'	C9'	C8'		128.6 (4)
C14'	C9'	C8'	1.380 (7)	110.6 (3)
C11'	C10'	C9'	1.393 (7)	118.5 (5)
C12'	C11'	C10'	1.380 (8)	120.0 (4)
C13'	C12'	C11'	1.385 (6)	122.2 (4)
C14'	C13'	C12'	1.396 (6)	117.1 (5)
N15'	C14'	C9'	1.403 (5)	112.5 (4)
N15'	C14'	C13'		126.3 (4)
C9'	C14'	C13'		121.3 (4)
C16'	N15'	C14'	1.486 (6)	109.4 (4)
C1'	C16'	N5'		104.9 (3)
C1'	C16'	C8'		120.2 (3)
C1'	C16'	N15'		109.8 (4)
N5'	C16'	C8'		103.4 (3)
N5'	C16'	N15'		113.3 (3)
C8'	C16'	N15'		105.3 (3)
C18'	C17'	C3'	1.523 (6)	115.6 (4)
O18'	C18'	C19'	1.455 (5)	108.5 (3)
O18'	C18'	C20'		103.6 (4)
O18'	C18'	C17'		110.7 (3)
C19'	C18'	C20'	1.528 (7)	111.0 (3)
C19'	C18'	C17'		111.1 (4)
C20'	C18'	C17'	1.532 (7)	111.5 (4)
O19'	C19'	C18'	1.419 (6)	113.5 (4)
C21'	C20'	C18'	1.519 (8)	115.5 (5)
O22'	C22'	O23'	1.202 (7)	123.1 (4)
O22'	C22'	C1'		126.2 (4)
O23'	C22'	C1'	1.341 (5)	110.6 (4)
O23'	C23'		1.450 (8)	
C22'	O23'	C23'		116.2 (4)
C24	O14		1.386 (8)	

the minimum and maximum peaks in the difference electron density map were -0.17 and 0.18 e \AA^{-3} , respectively. Neutral atom scattering factors for the non-H atoms were taken from Cromer & Mann (1968), with the anomalous-dispersion corrections taken from Cromer & Liberman (1970). Scattering factors for the H atoms were obtained from Stewart, Davidson & Simpson (1965). Values used to calculate the linear absorption coefficient are from *International Tables for X-ray Crystallography* (1974, Vol. IV, p. 55). Figures were generated using *SHELXTL-Plus* (Sheldrick, 1988). The positional and thermal parameters for the non-H atoms are listed in Table 1.* The bond lengths and angles are listed in Table 2. The atom-labeling scheme is shown in Fig. 1. Other computer programs used in this work are listed elsewhere (Gadol & Davis, 1982).

Related literature. Much effort has been directed toward the coupling reaction of vindoline with a variety of indolo-fused aza-heterocycles to synthesize reagents analogous to the clinically active antitumor agents vinblastine and vincristine (Magnus, Ladlow, Elliot & Kim, 1989; Kuehne & Marko, 1990). The crystal structure of 18'-epivinblastine has been

* Tables of anisotropic thermal parameters, H-atom positional parameters, bond distances and angles involving the H atoms, torsion angles, H-bonding interactions, observed and calculated structure factors and a unit-cell packing diagram have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53771 (31 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

recently reported (Lynch, Stamford, Magnus & Davis, 1991).

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Determination of the Absolute Configuration of a Novel Dipeptide Isostere

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Abstract. {1*R*-[1*α*(1*R**,2*R**,3*S**)],2*β*,5*α*]-2-(4-Morpholinocarbonyl)-3-phenylcyclopropane 2-(1-methyl-ethyl)-5-methylcyclohexyl ester, C₂₅H₃₅NO₄, *M_r* = 413.56, orthorhombic, *P*2₁2₁, *a* = 9.359 (2), *b* = 10.1172 (14), *c* = 24.710 (4) Å, *V* = 2339.8 (6) Å³, *Z* = 4, *D_x* = 1.17 g cm⁻³, *μ* = 0.7332 cm⁻¹, Mo *Kα* radiation, *λ* = 0.7107 Å, *F*(000) = 896, *T* = 198 K, *R* = 0.0475 for 2460 reflections [*F_o* ≥ 4*σ*(*F_o*)]. The assignment of the absolute configuration was based on internal comparison to the (–)-menthol moiety. The morpholenyl and cyclohexyl rings are in the chair conformation. The amide group is essentially planar [max. deviation 0.025 (2) Å for N19] resulting in a close non-bonded contact between the amide oxygen, O18, and H24*a* of 2.24 (4) Å.

Experimental. (1) was synthesized by the dicyclohexylcarbodiimide/4-dimethylaminopyridine mediated esterification of the corresponding optically

active carboxylic acid with (–)-menthol (Doyle, Pieters, Martin, Austin, Oalman & Muller, 1991; Martin, Austin & Oalman, 1990). Crystals of (1) were obtained by slow evaporation from a carbon tetrachloride–diethyl ether solution. The data crystal was a large block of approximate dimensions 0.56 × 0.70 × 0.76 mm. Data were collected on a Nicolet R3 diffractometer using a graphite monochromator and a Nicolet LT-2 low-temperature delivery system. Lattice parameters were obtained from the least-squares refinement of 40 reflections with 25.2 < 2*θ* < 27.8°. Data were collected using the *ω*-scan technique, with a 1.2° *ω* scan at 4–8° min⁻¹ and a 2*θ* range from 4.0–55.0° (*h* = 0 → 11, *k* = 0 → 12, *l* = 0 → 32). 3068 reflections were collected. Four reflections (354, $\bar{3}, \bar{2}, \bar{1}4$, $\bar{3}, 2, 14$, 354) were remeasured every 96 reflections to monitor instrument and crystal stability. A smoothed curve of the intensities of these check reflections was used to scale the data. The scaling factor ranged from 0.995–1.01. Data were also corrected for *Lp* effects but not absorption. 608 reflections were considered unobserved, *F_o* < 4*σ*(*F_o*). Data reduction and decay correction were performed using the Nicolet XRD *SHELXTL-Plus* software package (Sheldrick, 1988). The structure was solved by direct methods and refined by full-matrix least squares (Sheldrick, 1988). In all, 399 parameters were refined. The non-H atoms were refined with anisotropic thermal parameters. All H-atom positions were obtained from a *ΔF* map and refined with isotropic thermal parameters. The bond lengths

