Sheldrick, G. M. (1985). *SHELXS86. Crystallographic Computing* 3, edited by G. M. Sheldrick, C. Krüger & R. Goddard, pp. 175–189. Oxford Univ. Press.
Stewart, R. F., Davidson, E. R. & Simpson, W. T. (1965). *J. Chem. Phys.* **42**, 3174–3187.
Thompson, H. W., Lalancette, R. A. & Vanderhoff, P. A. (1992). *Acta Cryst.* C**48**, 66–70.
Trotter, J. (1960). *Acta Cryst.* **13**, 732–736.
Trotter, J. (1961). *Acta Cryst.* **14**, 101–105.
Zachariasen, W. H. (1963). *Acta Cryst.* **16**, 1139–1144.
Zachariasen, W. H. (1968). *Acta Cryst.* A**24**, 212–216.

Acta Cryst. (1993). C**49**, 1958–1961

Structure and Absolute Configuration of (+)-6-[(4-Chlorophenyl)(1*H*-1,2,4-triazol-1-yl)methyl]-1-methyl-1*H*-benzotriazole (Vorozole) and its Hydrobromide Monohydrate†

O. M. Peeters, G. S. Schuerman, N. M. Blaton and C. J. De Ranter

Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Instituut voor Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium

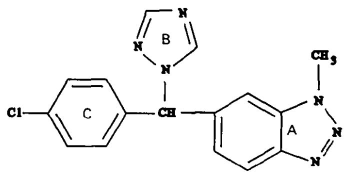
(*Received* 11 *March* 1993; *accepted* 12 *May* 1993)

Abstract

The (+)-6-[(4-chlorophenyl)(1*H*-1,2,4-triazol-1-yl)methyl]-1-methyl-1*H*-benzotriazole base (I) and its hydrobromide salt (II) show similar bond angles except for the C—N—C angle of the 1,2,4-triazolyl moiety, which is smaller in (I) than in (II) because of the presence of the lone-pair electrons on the N atom of (I). The molecular conformation of both structures is different, the dihedral angles between the planar moieties are 105.3 (2), 84.6 (1) and 81.3 (1)° in (I) and 110.4 (2), 79.2 (2) and 108.8 (2)° in (II). The absolute configuration at the central chiral C atom of both molecules is *S*.

Comment

The cytochrome P450 (P450)-dependent aromatization of androgens into oestrogens is one of the most important reactions involved in steroid hormone biosynthesis (Van den Bossche *et al.*, 1990). So, an aromatase inhibitor might be of help in the treatment of oestrogen-dependent disorders such as breast cancer, gynaecomastia and endometriosis. The title compound is a potent and selective inhibitor of the human placental aromatase by forming a stable complex with microsomal P450 from human placenta. For a better understanding of this complexation the crystal structure and the absolute configuration of the molecule were determined.



(I)

Perspective views showing the atomic numbering scheme for (I) and (II) are given in Figs. 1 and 2, respectively. Bond lengths and bond angles of the base and its salt are similar, except for the ring angle C14—N15—C16 which is smaller in the base because the lone-pair electrons on N15 occupy more space in the valence shell and thus decrease the C—N—C bond angle. In both structures the triazolyl ring *B* and the *p*-chlorophenyl ring *C* are planar within their respective experimental error. The benzotriazolyl ring *A* is also essentially planar. However, the molecular conformation of both structures is different. The dihedral angles between the rings *A* and *B*, *B* and *C*, and *A* and *C* are 84.6 (1), 105.3 (2) and 81.3 (1)° for (I) and 79.2 (2), 110.4 (2) and 108.8 (2)° for (II), respectively. As in previous reports (Nowell, Walker & Anderson, 1982; Branch & Nowell, 1985, 1986; Bruno, Foti, Grassi, Caruso & Risitano, 1988) the exocyclic angles around the N12 atom show considerable asymmetry with C11—N12—C16 being much larger than C11—N12—N13. This asymmetry is also usual in 1,2,3-triazoles (Nagawa, Goto, Honda & Nakanishi, 1987) and is visible in benzotriazole, where C10—N1—C9 is much larger than C10—N1—N2. As described previously (Brisse & Sygusch, 1974; Domenicano & Murray-Rust, 1979) the Cl atom of the *p*-chlorophenyl group causes an increase of the ring angle C19—C20—C21 and a decrease of the ring angles C18—C19—C20 and C20—C21—C22 from the sp^2 value of 120.0°. The deviation of the Cl atom out of the mean ring plane *C* is in agreement with the mean deviation of 0.05 Å given by Brisse & Sygusch (1974).

In both crystals the molecules are held together by C—H···N hydrogen bonds (Taylor & Kennard, 1982). In the hydrobromide salt (II), which crystallizes as a monohydrate, Br is strongly hydrogen bonded to N15 but the water O atom is only weakly hydrogen bonded to C16. The contacts between the water H atoms and Br are all greater than the sum of the van der Waals radii.

For both structures the absolute configuration is *S* at C11 and was determined by calculating the Bijvoet coefficient according to the selection procedure of Beurskens, Noordik & Beurskens (1980).

---

† Internal codes of Janssen Research Foundation: R83842 and R86636.

Acta Crystallographica Section C
ISSN 0108-2701 © 1993

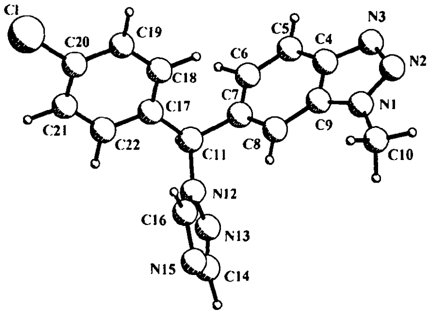


Fig. 1. A perspective view of molecule (I) with atomic numbering scheme.

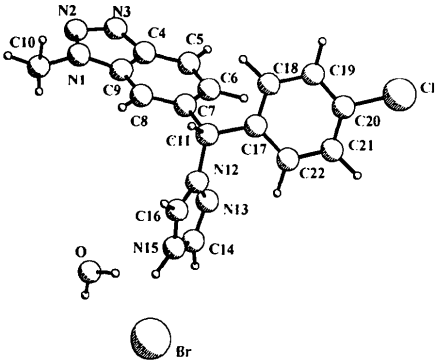


Fig. 2. A perspective view of molecule (II) with atomic numbering scheme.

Experimental

Compound (I)

Crystal data

$C_{16}H_{13}ClN_6$
$M_r = 324.77$
Orthorhombic
$P2_12_12_1$
$a = 5.116$ (1) Å
$b = 10.572$ (2) Å
$c = 28.87$ (1) Å
$V = 1561.5$ (7) Å^3
$Z = 4$
$D_x = 1.381$ Mg m^{-3}
$D_m = 1.377$ Mg m^{-3}
Density measured by flotation in CCl_4/*n*-heptane
Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 24 reflections
$\theta = 30$-$50°$
$\mu = 2.2492$ mm^{-1}
$T = 293$ K
Parallelepiped
0.22 × 0.15 × 0.15 mm
Colourless
Crystal source: grown from 2-propanol solution

Data collection

Siemens *P*4 four-circle diffractometer
$\omega/2\theta$ scans (4.88-29.3° min^{-1})
Absorption correction: empirical (*XEMP*; Siemens, 1989*c*)
$T_{min} = 0.209$, $T_{max} = 0.932$
5305 measured reflections
2138 independent reflections
1599 observed reflections $[I > 3.0\sigma(I)]$
$R_{int} = 0.0400$
$\theta_{max} = 57.27°$
$h = 0 \rightarrow 5$
$k = 0 \rightarrow 11$
$l = -31 \rightarrow 31$
3 standard reflections monitored every 50 reflections
intensity variation: < 3.0%

Refinement

Refinement on F
Final $R = 0.0500$
$wR = 0.0628$
$S = 1.44$
1599 reflections
208 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F) + 0.00100F^2]$
$(\Delta/\sigma)_{max} = 0.003$
$\Delta\rho_{max} = 0.29$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Tables 2.2B, 2.3.1)
Absolute configuration: the Bijvoet coefficient was between 0.843(4) and exactly 1 for the 188 and 42 most significant Bijvoet pairs, respectively.

The structure was solved by direct methods and refined by full-matrix least squares. Data collection: *P*3/*PC Diffractometer Program* (Siemens, 1989*a*). Cell refinement: *P*3/*PC Diffractometer Program*. Data reduction: *XDISK* (Siemens, 1989*b*). Program(s) used to solve structure: *NRCVAX* (Gabe, Le Page, Charland, Lee & White, 1989). Program(s) used to refine structure: *NRCVAX*. Molecular graphics: *PLUTO* (Motherwell & Clegg, 1978). Software used to prepare material for publication: *PARST* (Nardelli, 1983).

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2) *for* (I)

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

	x	y	z	U_{eq}
Cl	−0.2430 (4)	1.3187 (1)	0.07492 (6)	0.1046 (8)
N1	−0.4771 (9)	0.5167 (4)	0.2109 (2)	0.061 (2)
N2	−0.511 (1)	0.5080 (5)	0.2580 (2)	0.087 (2)
N3	−0.340 (1)	0.5813 (6)	0.2780 (2)	0.086 (2)
C4	−0.197 (1)	0.6424 (5)	0.2442 (2)	0.060 (2)
C5	0.010 (1)	0.7259 (5)	0.2480 (2)	0.062 (2)
C6	0.116 (1)	0.7700 (4)	0.2075 (2)	0.052 (2)
C7	0.018 (1)	0.7325 (4)	0.1632 (1)	0.040 (2)
C8	−0.1808 (9)	0.6465 (4)	0.1590 (1)	0.039 (2)
C9	−0.2850 (9)	0.6016 (4)	0.2015 (2)	0.047 (2)
C10	−0.630 (1)	0.4404 (5)	0.1803 (2)	0.075 (2)
C11	0.1435 (9)	0.7944 (4)	0.1214 (1)	0.039 (2)
N12	0.1328 (7)	0.7126 (3)	0.0808 (1)	0.034 (1)
N13	0.3129 (8)	0.6197 (4)	0.0753 (1)	0.049 (1)
C14	0.235 (1)	0.5644 (4)	0.0369 (2)	0.054 (2)
N15	0.0182 (8)	0.6129 (4)	0.0174 (1)	0.053 (1)
C16	−0.0421 (9)	0.7076 (4)	0.0461 (2)	0.043 (2)
C17	0.0346 (9)	0.9260 (4)	0.1105 (1)	0.038 (1)
C18	−0.164 (1)	0.9802 (4)	0.1348 (1)	0.042 (2)
C19	−0.256 (1)	1.1019 (4)	0.1248 (2)	0.055 (2)
C20	−0.132 (1)	1.1667 (4)	0.0889 (2)	0.058 (2)
C21	0.066 (1)	1.1149 (5)	0.0637 (2)	0.059 (2)
C22	0.151 (1)	0.9942 (4)	0.0747 (2)	0.055 (2)

Table 2. *Geometric parameters* (Å, °) *for* (I)

Cl—C20	1.751 (4)	C11—N12	1.458 (5)
N1—N2	1.375 (7)	C11—C17	1.531 (5)
N1—C9	1.358 (6)	N12—N13	1.356 (5)
N1—C10	1.428 (7)	N12—C16	1.344 (5)
N2—N3	1.302 (8)	N13—C14	1.316 (5)
N3—C4	1.380 (7)	C14—N15	1.343 (6)
C4—C5	1.385 (8)	N15—C16	1.335 (5)
C4—C9	1.379 (6)	C17—C18	1.362 (6)
C5—C6	1.373 (7)	C17—C22	1.394 (6)
C6—C7	1.429 (6)	C18—C19	1.401 (6)
C7—C8	1.368 (6)	C19—C20	1.393 (6)
C7—C11	1.518 (5)	C20—C21	1.365 (7)
C8—C9	1.421 (6)	C21—C22	1.385 (6)

C9—N1—C10	130.3 (5)	N12—C11—C17	111.1 (3)
N2—N1—C10	120.3 (5)	C11—N12—C16	130.4 (4)
N2—N1—C9	109.4 (4)	C11—N12—N13	119.8 (3)
N1—N2—N3	108.3 (5)	N13—N12—C16	109.7 (3)
N2—N3—C4	108.7 (5)	N12—N13—C14	102.3 (4)
N3—C4—C9	108.2 (5)	N13—C14—N15	115.7 (4)
N3—C4—C5	130.4 (5)	C14—N15—C16	102.6 (4)
C5—C4—C9	121.4 (5)	N12—C16—N15	109.7 (4)
C4—C5—C6	116.8 (5)	C11—C17—C22	117.8 (4)
C5—C6—C7	122.0 (5)	C11—C17—C18	123.2 (4)
C6—C7—C11	116.2 (4)	C18—C17—C22	119.0 (4)
C6—C7—C8	121.8 (4)	C17—C18—C19	122.0 (4)
C8—C7—C11	122.0 (4)	C18—C19—C20	116.9 (4)
C7—C8—C9	115.0 (4)	Cl—C20—C19	118.4 (4)
C4—C9—C8	123.0 (4)	C19—C20—C21	122.5 (4)
N1—C9—C8	131.6 (4)	Cl—C20—C21	119.1 (3)
N1—C9—C4	105.4 (4)	C20—C21—C22	118.7 (4)
C7—C11—C17	113.6 (3)	C17—C22—C21	120.8 (5)
C7—C11—N12	111.6 (3)		
C6—C7—C11—N12	151.6 (4)	C7—C11—N12—N13	−81.8 (4)
C6—C7—C11—C17	−81.8 (5)	C7—C11—N12—C16	94.4 (5)
C8—C7—C11—N12	−29.0 (6)	N12—C11—C17—C18	124.3 (4)
C8—C7—C11—C17	97.6 (5)	N12—C11—C17—C22	−57.7 (5)
C7—C11—C17—C18	−2.6 (6)	C17—C11—N12—C16	−33.6 (6)
C7—C11—C17—C22	175.4 (4)	C17—C11—N12—N13	150.2 (3)

Table 3. *Hydrogen-bonding geometry* (Å, °) *for* (I)

D	H	*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C6	H6	$N2^{i}$	1.108	2.356	3.377 (8)	152.4
C16	H16	$N15^{ii}$	1.094	2.543	3.467 (6)	141.5
C19	H19	$N3^{iii}$	1.096	2.650	3.493 (7)	133.2
C22	H22	$N15^{iv}$	1.084	2.446	3.447 (6)	153.0

Symmetry codes: (i) $-x, \frac{1}{2}+y, \frac{1}{2}-z$; (ii) $-\frac{1}{2}+x, \frac{3}{2}-y, -z$; (iii) $-x-1, \frac{1}{2}+y, \frac{1}{2}-z$; (iv) $\frac{1}{2}+x, \frac{3}{2}-y, -z$.

Compound (II)

Crystal data

$C_{16}H_{14}ClN_6^+.Br^-.H_2O$
$M_r = 423.70$
Orthorhombic
$P2_12_12_1$
$a = 6.008$ (3) Å
$b = 8.401$ (4) Å
$c = 35.92$ (2) Å
$V = 1813$ (2) Å^3
$Z = 4$
$D_x = 1.552$ Mg m^{-3}
$D_m = 1.53$ Mg m^{-3}
Density measured by flotation in CCl_4/*n*-heptane

Mo *Kα* radiation
$\lambda = 0.71073$ Å
Cell parameters from 36 reflections
$\theta = 16$-$24°$
$\mu = 2.4088$ mm^{-1}
$T = 293$ K
Parallelepiped
0.55 × 0.25 × 0.20 mm
Colourless
Crystal source: grown from acetone/amyl acetate solution

Data collection

Stoe Stadi-4 four-circle diffractometer
ω scans (0.9-3.6° min^{-1})
Absorption correction: empirical (*EMPIR*; Stoe & Cie, 1988*c*)
$T_{\min} = 0.104$, $T_{\max} = 0.130$
7547 measured reflections
3183 independent reflections

2269 observed reflections [$I > 2.0\sigma(I)$]
$R_{\rm int} = 0.0228$
$\theta_{\max} = 24.95°$
$h = 0 \rightarrow 7$
$k = 0 \rightarrow 9$
$l = -42 \rightarrow 42$
3 standard reflections
frequency: 60 min
intensity variation: 4.1%

Refinement

Refinement on *F*
Final $R = 0.0360$
$wR = 0.0451$
$S = 1.57$
2269 reflections
226 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F) + 0.00040F^2]$
$(\Delta/\sigma)_{\max} = 0.002$
$\Delta\rho_{\max} = 0.26$ e Å^{-3}
$\Delta\rho_{\min} = -0.38$ e Å^{-3}

Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV Tables 2.2B, 2.3.1)
Absolute configuration: the Bijvoet coefficient was between 0.958(1) and 0.9924(1) for the 261 and 68 most significant Bijvoet pairs, respectively.

The structure was solved by a combination of Patterson and direct methods, and refined by full-matrix least squares. Data collection: *DIF*4 (Stoe & Cie, 1988*a*). Cell refinement: *DIF*4. Data reduction: locally adapted *REDU*4 (Stoe & Cie, 1988*b*). Program(s) used to solve structure: *DIRDIF*92 (Beurskens *et al.*, 1992). Program(s) used to refine structure: *NRCVAX*. Molecular graphics: *PLUTO*. Software used to prepare material for publication: *PARST*.

Table 4. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2) *for* (II)

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

	x	*y*	*z*	$U_{\rm eq}$
Br	0.1144 (1)	0.00073 (8)	0.02326 (1)	0.0574 (2)
Cl	0.0467 (4)	0.0962 (3)	−0.27864 (5)	0.0935 (8)
N1	0.9526 (8)	0.7849 (5)	−0.1013 (1)	0.044 (2)
N2	0.928 (1)	0.9387 (6)	−0.1098 (2)	0.061 (2)
N3	0.752 (1)	0.9535 (5)	−0.1319 (1)	0.053 (2)
C4	0.661 (1)	0.8067 (7)	−0.1371 (1)	0.044 (2)
C5	0.471 (1)	0.7578 (7)	−0.1560 (2)	0.049 (2)
C6	0.419 (1)	0.5967 (7)	−0.1561 (1)	0.044 (2)
C7	0.5590 (8)	0.4853 (7)	−0.1376 (1)	0.036 (2)
C8	0.7433 (9)	0.5331 (6)	−0.1181 (1)	0.038 (2)
C9	0.7893 (9)	0.6967 (6)	−0.1179 (1)	0.037 (2)
C10	1.119 (1)	0.7354 (7)	−0.0737 (2)	0.056 (2)
C11	0.5040 (9)	0.3073 (6)	−0.1377 (1)	0.034 (2)
N12	0.3874 (7)	0.2640 (4)	−0.1029 (1)	0.035 (1)
N13	0.1933 (8)	0.3369 (5)	−0.0925 (1)	0.047 (2)
C14	0.144 (1)	0.2683 (8)	−0.0608 (2)	0.055 (2)
N15	0.2989 (9)	0.1594 (5)	−0.0509 (1)	0.046 (2)
C16	0.4499 (9)	0.1592 (6)	−0.0775 (1)	0.042 (2)
C17	0.385 (1)	0.2514 (6)	−0.1723 (1)	0.039 (2)
C18	0.482 (1)	0.2779 (9)	−0.2065 (2)	0.060 (2)
C19	0.379 (1)	0.2289 (9)	−0.2392 (2)	0.068 (2)
C20	0.179 (1)	0.1543 (8)	−0.2372 (2)	0.058 (2)
C21	0.075 (1)	0.1221 (7)	−0.2039 (2)	0.055 (2)
C22	0.179 (1)	0.1721 (7)	−0.1714 (1)	0.050 (2)
O	0.1558 (9)	0.5894 (6)	0.0300 (1)	0.077 (2)

Table 5. *Geometric parameters* (Å, °) *for* (II)

Cl—C20	1.758 (6)	C11—N12	1.479 (6)
N1—N2	1.337 (6)	C11—C17	1.509 (7)
N1—C9	1.367 (6)	N12—N13	1.369 (6)
N1—C10	1.467 (8)	N12—C16	1.321 (6)
N2—N3	1.324 (8)	N13—C14	1.311 (7)
N3—C4	1.362 (7)	C14—N15	1.353 (8)
C4—C5	1.391 (8)	N15—C16	1.318 (7)
C4—C9	1.386 (7)	C17—C18	1.377 (7)
C5—C6	1.390 (8)	C17—C22	1.405 (8)
C6—C7	1.424 (7)	C18—C19	1.388 (8)
C7—C8	1.370 (6)	C19—C20	1.36 (1)
C7—C11	1.531 (7)	C20—C21	1.375 (8)
C8—C9	1.402 (7)	C21—C22	1.389 (8)

C9—N1—C10	129.1 (4)	N12—C11—C17	113.3 (4)
N2—N1—C10	120.3 (5)	C11—N12—C16	127.8 (4)
N2—N1—C9	110.0 (4)	C11—N12—N13	121.6 (4)
N1—N2—N3	108.5 (4)	N13—N12—C16	110.7 (4)
N2—N3—C4	108.5 (5)	N12—N13—C14	103.5 (5)
N3—C4—C9	108.2 (5)	N13—C14—N15	111.6 (6)
N3—C4—C5	131.6 (5)	C14—N15—C16	106.6 (5)
C5—C4—C9	120.1 (5)	N12—C16—N15	107.6 (5)
C4—C5—C6	118.3 (6)	C11—C17—C22	123.0 (5)
C5—C6—C7	120.3 (5)	C11—C17—C18	118.9 (5)
C6—C7—C11	120.8 (4)	C18—C17—C22	118.0 (5)
C6—C7—C8	121.6 (5)	C17—C18—C19	121.3 (6)
C8—C7—C11	117.5 (4)	C18—C19—C20	118.9 (5)
C7—C8—C9	116.7 (5)	Cl—C20—C19	118.9 (4)
C4—C9—C8	122.8 (5)	C19—C20—C21	122.6 (6)
N1—C9—C8	132.4 (5)	Cl—C20—C21	118.4 (5)
N1—C9—C4	104.8 (4)	C20—C21—C22	117.8 (6)
C7—C11—C17	114.1 (4)	C17—C22—C21	121.3 (5)
C7—C11—N12	109.9 (4)		
C6—C7—C11—N12	−97.4 (6)	C7—C11—N12—N13	57.4 (6)
C6—C7—C11—C17	31.2 (7)	C7—C11—N12—C16	−120.7 (5)
C8—C7—C11—N12	80.8 (6)	N12—C11—C17—C18	−177.0 (5)
C8—C7—C11—C17	−150.7 (5)	N12—C11—C17—C22	2.6 (7)
C7—C11—C17—C18	56.2 (7)	C17—C11—N12—C16	110.4 (6)
C7—C11—C17—C22	−124.2 (6)	C17—C11—N12—N13	−71.6 (6)

Table 6. *Hydrogen-bonding geometry* (Å, °) *for* (II)

D	H	*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N15	H15	Br	1.027	2.289	3.179 (5)	144.1
C10	H10*A*	N13^{i}	1.120	2.587	3.444 (7)	132.5
C8	H8	N13^{i}	1.084	2.299	3.298 (7)	152.3
C11	H11	N3^{ii}	1.098	2.518	3.333 (7)	130.1
C16	H16	N3^{ii}	1.100	2.400	3.178 (7)	126.4
C22	H22	N2^{iii}	1.100	2.406	3.320 (8)	139.5
C22	H22	N3^{iii}	1.100	2.705	3.458 (8)	125.2
O	H1*W*	Br^{iv}	1.084	3.398	3.849 (5)	106.5
O	H1*W*	Br^{v}	1.084	3.139	3.439 (5)	96.7
O	H2*W*	Br^{vi}	1.083	3.250	3.473 (5)	92.7
C16	H16	O	1.100	2.296	2.966 (7)	117.3

Symmetry codes: (i) $x + 1, y, z$; (ii) $x, y - 1, z$; (iii) $x - 1, y - 1, z$; (iv) $\frac{1}{2} + x, -\frac{1}{2} - y, -z$; (v) $\frac{1}{2} + x, \frac{1}{2} - y, -z$; (vi) $x, y + 1, z$.

The authors thank Professor Dr P. Janssen of Janssen Research Foundation (Beerse, Belgium) for providing the title compounds.

Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71325 (39 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: NA1038]

References

Beurskens, G., Noordik, J. H. & Beurskens, P. T. (1980). *Cryst. Struct. Commun.* **9**, 23-28.

Beurskens, P. T., Admiraal, G., Beurskens, G., Bosman, W. P., Garcia-Granda, S., Gould, R. O., Smits, J. M. M. & Smykalla, C. (1992). *The DIRDIF Program System*. Technical Report. Crystallography Laboratory, Univ. of Nijmegen, The Netherlands.

Branch, S. K. & Nowell, I. W. (1985). *Acta Cryst.* C**41**, 594-597.

Branch, S. K. & Nowell, I. W. (1986). *Acta Cryst.* C**42**, 440-442.

Brisse, F. & Sygusch, J. (1974). *Acta Cryst.* B**30**, 480-486.

Bruno, G., Foti, F., Grassi, G., Caruso, F. & Risitano, F. (1988). *Acta Cryst.* C**45**, 653-656.

Domenicano, A. & Murray-Rust, P. (1979). *Tetrahedron Lett.* **24**, 2283-2286.

Gabe, E. J., Le Page, Y., Charland, J.-P., Lee, F. L. & White, P. S. (1989). *J. Appl. Cryst.* **22**, 384-387.

Motherwell, W. D. S. & Clegg, W. (1978). *PLUTO. Program for Plotting Molecular and Crystal Structures.* Univ. of Cambridge, England.

Nagawa, Y., Goto, M., Honda, K. & Nakanishi, H. (1987). *Acta Cryst.* C**43**, 147-149.

Nardelli, M. (1983). *Comput. Chem.* **7**, 95-98.

Nowell, I. W., Walker, P. E. & Anderson, N. H. (1982). *Acta Cryst.* B**38**, 1857-1859.

Siemens (1989*a*). *P3/PC Diffractometer Program.* Version 3.13. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Siemens (1989*b*). *XDISK. Data Reduction Program.* Version 3.11. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Siemens (1989*c*). *XEMP. Empirical Absorption Correction Program.* Version 4.0. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Stoe & Cie (1988*a*). *DIF4. Diffractometer Control Program.* Version 6.2. Stoe & Cie, Darmstadt, Germany.

Stoe & Cie (1988*b*). *REDU4. Data Reduction Program.* Version 6.2. Stoe & Cie, Darmstadt, Germany.

Stoe & Cie (1988*c*). *EMPIR. Empirical Absorption Correction Program.* Version 1.2. Stoe & Cie, Darmstadt, Germany.

Taylor, R. & Kennard, O. (1982). *J. Am. Chem. Soc.* **104**, 5063-5070.

Van den Bossche, H., Willemsens, G., Roels, I., Bellens, D., Moereels, H., Coene, M., Le Jeune, L., Lauwers, W. & Janssen, P. A. J. (1990). *Biochem. Pharmacol.* **40**, 1707-1718.

Acta Cryst. (1993). C**49**, 1961-1963

Structure and Absolute Configuration of (−)-α-[(2-Acetyl-5-methylphenyl)amino]-2,6-dichlorobenzeneacetamide†

O. M. Peeters, N. M. Blaton and C. J. De Ranter

Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Instituut voor Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium

(*Received* 23 *March* 1993; *accepted* 12 *May* 1993)

Abstract

The title compound is a potent and highly selective human immunodeficiency virus type 1 (HIV-1) inhibitor. The two rings in the molecule are planar with a dihedral angle between their least-squares planes of 108.29 (8)°. An intramolecular N—H···O hydrogen bond forms a pseudo ring and contributes to the near coplanarity of the acetyl group with the methylphenyl moiety. The molecules are linked together in the **a** direction by N—H···O hydrogen bonds. The absolute configuration at the central asymmetric C atom is *S*.

---

† Internal code of Janssen Research Foundation: R90385.