the structure consists of individual molecules stabilized in the crystal by van der Waals forces and there are no unusual short intermolecular contacts, the packing interactions do not influence the geometry of the molecule.

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Structure of Isopropyl 2-Chloro-5-(2-methyl-1,4-oxathiin-3-ylcarbonylamino)-benzoate, Oxathiin Carboxanilide

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Abstract. $C_{16}H_{18}ClNO_4S$, $M_r = 355{\cdot}8$, monoclinic, $P2_1/a$, $a = 8{\cdot}784$ (1), $b = 20{\cdot}342$ (1), $c = 9{\cdot}522$ (1) Å, $\beta = 98{\cdot}61$ (1)°, $V = 1682{\cdot}3$ Å^3, $Z = 4$, $D_x = 1{\cdot}404$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, μ = 33·5 cm^{-1}, $F(000) = 744$, $T = 295$ K, final $R = 0{\cdot}044$ for 2156 observed reflections. The crystal structure and conformation are reported for this new potential AIDS drug whose mode of action differs from that of the dideoxynucleosides. The molecules are hydrogen bonded and form infinite chains along the a axis. The crystal packing leads to parallel stacking of the rings of the molecules.

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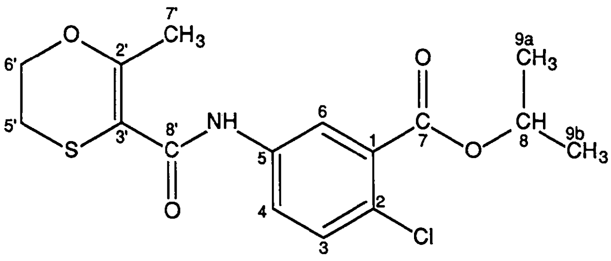
Introduction. This report represents part of a continuing study of the conformational preference of AIDS drugs and compounds having actual or potential antiretroviral activity (first paper in this series: Silverton, Quinn, Haugwitz & Todaro, 1988).



(I)

Oxathiin carboxanilide (NSC 615985) (I) was originally synthesized as a potential fungicide (Harrison, Kulka, Thiara & von Schneling, 1966). Bader, McMahon, Schultz, Narayanan & Boyd (1990) have shown that it is highly active in preventing HIV-induced cytopathicity and has a point of action within the virus reproductive cycle different from that of the known active nucleosides, *e.g.* azidothymidine (AZT) or dideoxycytidine (DDC). The activity was detected in the AIDS antiviral *in vitro* screen of the National Cancer Institute (Weislow, Kiser, Fine, Bader, Shoemaker & Boyd, 1989).

Experimental. Physical data including spectra and analysis are available.* Colorless prismatic needles were obtained from acetonitrile but all samples investigated gave rise to reflected X-ray intensities less than would have been anticipated from the crystal size. However, a crystal 0·4 × 0·1 × 0·1 mm gave measurable reflections out to a θ limit of 74° ($\sin\theta/\lambda_{max} = 0{\cdot}622$ Å^{-1}) with Cu $K\alpha$ radiation and was used for all experimental work. The cell dimensions were determined by least-squares refinement using 20 reflections with $18 \leq \theta \leq 23°$, the Friedel symmetry was $2/m$ and $0k0$ reflections were observed only for $k = 2n$ and $h0l$ only for $h = 2n$ indicating the monoclinic space group $P2_1/a$. The ranges of measured indices were h 0 to 10, k 0 to 25 and l −11 to 11; the diffractometer was an Enraf–Nonius CAD-4, the scan time used had a maximum of 100 s, the counter aperture was 1·4 mm and the scan width was $(1{\cdot}4 + 0{\cdot}35\tan\theta)°$. θ–2θ scans. Three standard reflections ($2\bar{3}8$, $3\bar{3}8$ and 617) were measured every 3 h and any variation was under 3%. Azimuthal scans indicated intensity variations under 3% and Lorentz–polarization corrections were applied but no absorption corrections were made. There were 3403 unique measurements, with 1247 having $I \leq \sigma(I)$. Standard deviations of intensity were calculated following Peterson & Levy (1957) and scattering factors were derived from *International Tables for X-ray Crystallography* (1974, Vol. IV, p. 149). The structure was solved by direct methods using *MITHRIL* (Gilmore, 1983) and refined using the programs of *XTAL*2·4 (Stewart & Hall, 1983). H atoms were found at calculated positions and their positional parameters were refined. Anisotropic temperature factors of the form $\exp-[2\pi^2\sum_i\sum_j(U_{ij}h_ih_ja_i^*a_j^*)]$ were applied to the non-H atoms, an extinction correction of the Zachariesen (1967) type was used and the function minimized was $\sum(w\Delta F)^2$ with $1/\sigma$ weights. Final $R = 4{\cdot}4\%$, $wR = 4{\cdot}4\%$, $R(F^2) = 4{\cdot}8\%$, extinction factor = 0·33 (2) and goodness-of-fit parameter $S = 1{\cdot}79$ (263 parameters and 2156 observations). Final maximum Δ/σ was 0·01 and largest values in a final difference map were ± 0·5 e Å^{-3}. The size of the residual densities and the less-than-optimal crystal quality may indicate the presence of impurities despite respectable chemical analyses. The atomic parameters for non-H atoms are given in Table 1, the molecular dimensions in Table 2 and some selected torsion angles in Table 3.* Calculations were performed with an IBM 3090-300J computer.

Discussion. As may be deduced from Fig. 1, the molecule is fairly flat but the dihedral angles (Table 3) indicate deviations of the order of 30°. The aromatic ring shows deviations from angles of 120° explicable in terms of the short contacts Cl—C7 3·251 (3), Cl—O8 2·888 (2) and C6—C8′ 3·035 (3) Å. It is interesting that the oxathiin ring possesses torsion angles all within 5° of those listed for the low-energy form of cyclohexene by Bucourt (1974).

The most important influence on the packing (Fig. 2) appears to be the N9′···O8′ hydrogen bond [N9′···O8′ 3·030 (3), H9′···O8′ 2·18 (3) Å, N9′—H9′···O8′ 157 (3)°] between molecules related by the glide plane. There are thus infinite chains of molecules along the a axis. Rings in the two molecules joined by the hydrogen bond are nearly parallel and are below others related by the c axis. It is possible that this stacking may be relevant to the as yet unknown mode of action of the drug especially if intercalation into DNA is involved. Intermolecular contacts, other than those in the hydrogen bond, exceed van der Waals distances from Bondi (1964).

* Copies of Report No. A110 of S.R.I. International, Life Sciences Division, prepared under Contract N01-CM-67864, may be obtained from Development Therapeutics Program, Division of Cancer Treatment, NCI, Bethesda, MD 20892, USA.

* Lists of observed structure factors, calculated structure factors, standard deviations, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54042 (24 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Atomic parameters for non-*H *atoms*

The equivalent U values are as given by Fischer & Tillmans (1988) with e.s.d.'s after Schomaker & Marsh (1983).

	x	y	z	U_{eq}
Cl	1·21333 (10)	0·01908 (4)	0·78209 (10)	0·0667 (2)
C1	1·17313 (30)	0·15018 (13)	0·70887 (29)	0·0378 (7)
C2	1·11845 (32)	0·08591 (14)	0·69447 (30)	0·0420 (7)
C3	0·98075 (36)	0·07270 (15)	0·60732 (38)	0·0499 (8)
C4	0·89930 (34)	0·12163 (15)	0·53248 (34)	0·0463 (8)
C5	0·95144 (30)	0·18621 (13)	0·54489 (28)	0·0374 (7)
C6	1·08608 (33)	0·20017 (14)	0·63508 (30)	0·0389 (7)
O7	1·33292 (26)	0·22599 (11)	0·85287 (27)	0·0712 (7)
C7	1·31907 (33)	0·17250 (15)	0·79985 (31)	0·0430 (7)
O8	1·42793 (23)	0·12760 (10)	0·81074 (23)	0·0558 (6)
C8	1·57393 (35)	0·14124 (16)	0·90281 (36)	0·0516 (8)
C9*a*	1·56101 (52)	0·11778 (24)	1·04917 (44)	0·0721 (12)
C9*b*	1·69194 (56)	0·10676 (28)	0·83396 (56)	0·0912 (15)
O1′	0·68451 (26)	0·43168 (10)	0·22728 (24)	0·0630 (6)
C2′	0·78510 (34)	0·39558 (15)	0·32072 (32)	0·0455 (8)
C3′	0·79244 (30)	0·32973 (14)	0·32130 (28)	0·0386 (7)
S4′	0·67119 (11)	0·27897 (4)	0·20362 (9)	0·0609 (2)
C5′	0·52723 (50)	0·33801 (21)	0·14032 (50)	0·0812 (13)
C6′	0·59716 (53)	0·40109 (20)	0·10802 (46)	0·0837 (13)
C7′	0·88066 (47)	0·44074 (18)	0·41978 (46)	0·0650 (11)
O8′	1·03856 (21)	0·31639 (10)	0·46484 (22)	0·0522 (6)
C8′	0·91038 (32)	0·29448 (13)	0·42302 (30)	0·0394 (7)
N9′	0·86250 (27)	0·23452 (12)	0·46378 (26)	0·0419 (6)

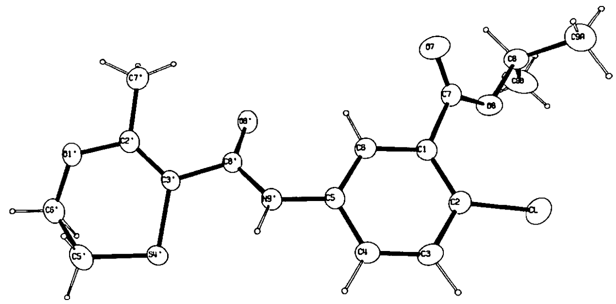


Fig. 1. *ORTEP* (Johnson, 1965) drawing showing crystal conformation.

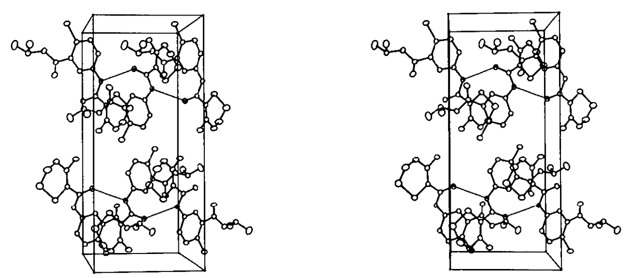


Fig. 2. Packing diagram. Projection down the c axis.

Table 2. *Molecular dimensions* (Å *and* °)

Cl—C2	1·741 (2)	C1—C2	1·392 (3)
C1—C6	1·397 (3)	C1—C7	1·506 (3)
C2—C3	1·387 (4)	C3—C4	1·363 (4)
C4—C5	1·391 (4)	C5—C6	1·383 (3)
C5—N9′	1·411 (3)	O7—C7	1·198 (3)
C7—O8	1·315 (3)	O8—C8	1·468 (3)
C8—C9*b*	1·483 (6)	C8—C9*a*	1·493 (5)
O1′—C2′	1·370 (3)	O1′—C6′	1·416 (4)
C2′—C3′	1·341 (4)	C2′—C7′	1·484 (4)
C3′—C8′	1·492 (3)	C3′—S4′	1·760 (2)
S4′—C5′	1·782 (4)	C5′—C6′	1·475 (6)
O8′—C8′	1·221 (3)	C8′—N9′	1·365 (3)

C2—C1—C6	118·6 (2)	C2—C1—C7	126·2 (2)
C6—C1—C7	115·1 (2)	C3—C2—C1	119·9 (2)
C3—C2—Cl	116·6 (2)	C1—C2—Cl	123·6 (1)
C4—C3—C2	120·9 (2)	C3—C4—C5	120·3 (2)
C6—C5—C4	119·1 (2)	C6—C5—N9′	123·3 (2)
C4—C5—N9′	117·6 (2)	C5—C6—C1	121·1 (2)
O7—C7—O8	124·8 (2)	O7—C7—C1	122·7 (2)
O8—C7—C1	112·5 (2)	C7—O8—C8	118·4 (2)
O8—C8—C9*b*	104·6 (2)	O8—C8—C9*a*	108·4 (2)
C9*b*—C8—C9*a*	114·6 (3)	C2′—O1′—C6′	120·3 (2)
C3′—C2′—O1′	124·3 (2)	C3′—C2′—C7′	126·4 (2)
O1′—C2′—C7′	109·3 (2)	C2′—C3′—C8′	120·7 (2)
C2′—C3′—S4′	124·0 (1)	C8′—C3′—S4′	115·2 (1)
C3′—S4′—C5′	98·7 (1)	C6′—C5′—S4′	111·1 (3)
O1′—C6′—C5′	114·1 (3)	O8′—C8′—N9′	122·8 (2)
O8′—C8′—C3′	123·6 (2)	N9′—C8′—C3′	113·6 (2)
C8′—N9′—C5	127·5 (2)		

Table 3. *Selected torsion angles* (°)

C2′—C3′—C8′—O8′	−32·4 (5)	C7′—C2′—C3′—C8′	−3·5 (5)
O8′—C8′—N9′—C5	−7·0 (5)	C8′—N9′—C5—C6	22·7 (3)
C6—C1—C7—O7	29·2 (5)	C2—C1—C7—O8	31·7 (4)
C6′—O1′—C2′—C3′	−10·6 (5)	O1′—C2′—C3′—S4′	−1·2 (6)
C2′—C3′—S4′—C5′	−14·8 (4)	C3′—S4′—′C5′—C6′	44·0 (3)
S4′—C5′—C6′—O1′	−62·5 (5)	C5′—C6′—O1′—C2′	44·8 (5)

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