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References

BRUTKIEWICZ, R. R. & SUZUKI, F. (1987). *In Vivo*, **1**, 189–204.
CHIANG, H.-C., LIN, S.-M. & UENG, C.-H. (1992). *Acta Cryst.* C**48**, 991–993.
CLARK, E. R. (1959). *Nature (London)*, **183**, 536–537.
Enraf–Nonius (1979). *Structure Determination Package*. Enraf–Nonius, Delft, The Netherlands.
JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
LARSON, A. C., LEE, F. L., LE PAGE, Y., WEBSTER, M., CHARLAND, J.-P. & GABE, E. J. (1990). *NRCVAX Crystal Structure System*. Chemistry Division, NRC, Ottawa, Canada K1A 0R6.
MIKANOVA, E. & BARTUSEK, M. (1981). *Scr. Fac. Sci. Nat. Univ. Purkynianae Brun.* **11**, 439–449.
STERLING, C. (1967). *J. Inorg. Nucl. Chem.* **29**, 1211–1215.

Acta Cryst. (1993). C**49**, 246–250

Structure of (+)-(5*R*,6*R*)-5-Chloro-6-methoxy-5,6-dihydro-1-(2′,3′-didehydro-2′,3′-dideoxy-β-D-*glycero*-2-enopentofuranosyl)thymine

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Abstract. $C_{11}H_{15}ClN_2O_5$, $M_r = 290.70$, m.p. 411–412 K, $[\alpha]_D$ (296 K) = 75.44° (c = 0.42% in MeOH), monoclinic, $P2_1$, $a = 9.901$ (5), $b = 12.659$ (10), $c = 10.998$ (5) Å, $\beta = 100.06$ (5)°, $V = 1357.23$ (9) Å^3, $Z = 4$, $D_x = 1.42$ g cm^{-3}, Cu $K\alpha_1$ radiation (Ni filtered), $\lambda = 1.5405$ Å, $\mu = 26.99$ cm^{-1}, $F(000) = 608$, $T = 293$ K, $R = 0.046$, GOF = 2.02, for 1612 unique observed reflections. Two molecules are present in the asymmetric unit. Conformational differences are exemplified by χ values of −154.4 (5) and −124.2 (6)° for molecules A and B, respectively; and further by the exocyclic C(4′)—C(5′) torsion angles γ (molecule A) = 62.2 (7)° and γ (molecule B) = 49.5 (9)°. This analysis establishes the absolute configuration of the two asymmetric C atoms of the derivatized pyrimidine ring as 5*R*,6*R*.

Introduction. Acquired immunodeficiency syndrome (AIDS) is a degenerative disease of the immune and central nervous systems for which there is no known cure. The pyrimidine analogue 2′,3′-didehydro-2′,3′-dideoxythymidine has demonstrated activity against the causative agent, human immunodeficiency virus type-1 (HIV-1) in some patients with AIDS and AIDS-related complex (ARC) during phase 1 clinical trials (Lin, Schinazi & Prusoff, 1987; Mansuri, Starrett, Ghazzouli, Hitchcock, Sterzychi, Brankovan, Lin, August, Prusoff, Sommadossi & Martin, 1989). HIV in the central nervous system (CNS) may replicate more actively than in other tissues, and the CNS may serve as a principal reservoir of the virus in the whole body (Gartner, Markovits, Markovits, Kaplan, Gallo & Popovic, 1986; Koenig, Gendelman, Orenstein, Dal Canto, Pezeshkpour, Yungbluth, Janotta, Aksamit, Martin & Fauci, 1986; Watkins, Dorn, Kelly, Armstrong, Potts, Michaels, Kufta & Dubois-Dalcq, 1990). Thus, the ability of antiretroviral agents to penetrate the CNS may constitute an important feature for treatment of HIV infection. 5-Halo-6-methoxy-5,6-dihydro-1-(2′,3′-didehydro-2′,3′-dideoxy-β-D-*glycero*-2-enopentofuranosyl)thymines could serve as a new class of lipophilic masked prodrugs to 1-(2′,3′-didehydro-2′,3′-dideoxy-β-D-*glycero*-2-enopentofuranosyl)thymines (Duschinsky, Gabriel, Tautz, Nussbaum, Hoffer, Grunberg, Burchenal & Fox, 1967).

We now describe the X-ray analysis of (+)-5-chloro-6-methoxy-5,6-dihydro-1-(2′,3′-didehydro-2′,3′-dideoxy-β-D-*glycero*-2-enopentofuranosyl)thymine that may penetrate the CNS more effectively, for which the absolute configuration of the substituents in the derivatized pyrimidine ring were unknown.

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Experimental. The title compound (R. Kumar, L. I. Wiebe & E. E. Knaus, unpublished synthesis) crystallized from ethyl acetate–hexane (70/30 *v/v*) as colourless needles. The crystal chosen for data collection exhibited good morphology and had dimensions of $0.24 \times 0.09 \times 0.07$ mm. Least-squares refinement of 25 high-order reflections ($30 \le \theta \le 35°$) gave the unit-cell dimensions as reported in the *Abstract*. A hemisphere of data ($-10 \le h \le 10$, $-11 \le k \le 11$, $0 \le l \le 13$) corresponding to $2 < \theta < 55°$ ($\sin\theta_{max}/\lambda = 0.53$ Å^{-1}) was collected on an Enraf–Nonius CAD-4 diffractometer using Ni-filtered Cu $K\bar{\alpha}$ radiation. Two intensity controls ($0\bar{2}0$, $1\bar{3}0$) were measured every 5 h of data collection with I showing only statistical fluctuations.

All data processing and crystallographic calculations were undertaken with *Xtal*3.0 (Hall & Stewart, 1990). Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV). Diagrams were constructed with *PLUTO* (Motherwell & Clegg, 1978). During data processing, counting statistics were used in the calculation of $\sigma(I)$. No corrections were made for absorption effects in this analysis. The initial F_{rel} scale factor and overall thermal parameters were derived from a Wilson plot. The 3690 collected reflections were merged to 1800 unique, $R_1 = 0.0363$, $R_2 = 0.0433$ where $R_1 = \sum|I_j - I|/\sum I_j$, $R_2 = \sum\sigma I_j/\sum I_j$. Examination of the $|E|$ statistics revealed a non-centrosymmetric distribution. This, along with information regarding the cell and systematic absences, allowed the designation of the space group as $P2_1$. Consideration of the cell volume and molecular weight of the compound suggested two independent molecules in the asymmetric unit.

Direct methods (*Xtal*3.0; Hall & Stewart, 1990) were employed to solve the structure; examination of the E map provided the Cl-atom positions. These were used as an initial phasing model to generate an F_{obs} map ($R = 0.492$) which facilitated the identification of 11 of the non-H atoms. Full-matrix least-squares refinement (on F) minimized $\sum w(|F_o| - |F_c|)^2$, where $w = 1/\sigma^2(F)$. The remaining non-H atoms and a total of 23 out of the expected 30 H atoms were located by examination of subsequent difference Fourier maps. The remaining H-atom positions were calculated using an initial C—H distance of 0.95 Å. All H atoms were assigned temperature factors 20% greater than that of their parent atom and incorporated into the phasing model, but the parameters were not refined. Corrections were made for dispersion and extinction, the latter based on the formalism of Zachariasen incorporated into the expressions of Larson (Larson, 1970), and a $\bar{T}$ (mean path length) value of 0.03 cm.

The structure was solved initially with both molecules exhibiting an S configuration for C(1′). The refinement of the coordinates for this enantiomer converged at $R = 0.050$, $wR = 0.045$ [$w = \sigma(F)^{-2}$], GOF = 2.25 [343 parameters, 1612 independent observations having $I > 2\sigma(I)$]. Using the same set of data, the refinement of the R enantiomer converged at $R = 0.046$, $wR = 0.041$ [$w = \sigma(F)^{-2}$], GOF = 2.02. The Hamilton R-factor ratio test (Hamilton, 1965) gives $R' = 1.0976$, where $R' = wR(S \text{ config.})/wR(R \text{ config.})$. According to Hamilton's tables $R'_{1,1269,0.01} = 1.0022$ for the one-dimensional hypothesis with 1269 degrees of freedom. Thus, the enantiomer exhibiting R configuration at C(1′) is shown to have the correct configuration at the 0.01 significance level. This agrees with the knowledge that the chiral synthesis incorporated β-D-ribose. In the final refinement $(\Delta/\sigma)_{max} = 0.0035$, and on the final difference map $\Delta\rho_{max} = 0.3$, $\Delta\rho_{min} = -0.3$ e Å^{-3}. The two largest peaks in the ΔF map correspond to density close to the Cl atoms, 0.27 e Å^{-3}, approximately 1.26 Å from Cl(1)*A*, and 0.35 e Å^{-3}, at a position 1.11 Å from Cl(1)*B*. These features are presumed to be the result of not taking into account the effects of absorption in this analysis.

Discussion. The atomic coordinates of the non-H atoms, and equivalent isotropic Gaussian parameters (U_{eq}) with e.s.d.'s are given in Table 1.*

The asymmetric unit consists of two molecules identified by suffix *A* or *B*. The atom-labelling scheme is illustrated in Fig. 1, and a stereoview of the two molecules in the asymmetric unit is given in Fig. 2. The hydrogen-bonding network involved in the molecular packing is depicted in Fig. 3.

This crystallographic analysis affords the assignment of the absolute configurations of the derivatized thymine ring substituents as *R*. A comparison of the bond lengths and bond angles (Table 2) exhibited by the two molecules reveals a high degree of similarity within the accuracy of this experiment, and shows agreement with equivalent parameters expected for other derivatized pyrimidine nucleosides. A tabulation of the torsion angles commonly used to describe nucleosides (Table 2) exemplifies the conformational differences between the two molecules.

The root mean square (r.m.s.) deviation between fragments of molecules *A* and *B* consisting of the 2′,3′-didehydro-2′,3′-dideoxyfuranose ring with C(5′) and N(1′), is 0.037 Å. Comparison between the derivatized thymine rings, excluding the methyl of

* Lists of structure factors, anisotropic thermal parameters, bond lengths involving H atoms and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55316 (10 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: CD0082]

Table 1. *Non*-H *atomic fractional coordinates and equivalent isotropic thermal parameters* ($Å^2$)

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

	x	y	z	U_{eq}
Cl(1)*A*	0.9508 (2)	0.63038	0.7859 (1)	0.0668 (6)
Cl(1)*B*	0.7112 (2)	0.8035 (2)	0.5674 (2)	0.0741 (7)
C(1')*A*	0.8298 (6)	0.6148 (6)	1.1027 (5)	0.055 (2)
C(2')*A*	0.7249 (7)	0.6702 (6)	1.0106 (7)	0.067 (3)
C(3')*A*	0.6153 (7)	0.6097 (7)	0.9809 (6)	0.064 (3)
C(4')*A*	0.6334 (6)	0.5090 (7)	1.0513 (6)	0.059 (3)
O(4')*A*	0.7745 (4)	0.5139 (4)	1.1123 (4)	0.062 (2)
C(5')*A*	0.6015 (6)	0.4098 (6)	0.9831 (6)	0.060 (3)
O(5')*A*	0.6868 (4)	0.3910 (4)	0.8918 (4)	0.060 (2)
N(1)*A*	0.9646 (5)	0.6097 (4)	1.0651 (4)	0.043 (2)
C(2)*A*	1.0486 (6)	0.6907 (6)	1.0988 (5)	0.046 (2)
O(2)*A*	1.0292 (5)	0.7591 (4)	1.1725 (4)	0.064 (2)
N(3)*A*	1.1648 (5)	0.6991 (4)	1.0441 (4)	0.049 (2)
C(4)*A*	1.1874 (6)	0.6425 (6)	0.9428 (5)	0.053 (3)
O(4)*A*	1.2890 (4)	0.6585 (5)	0.8985 (4)	0.074 (2)
C(5)*A*	1.0783 (6)	0.5601 (5)	0.8930 (5)	0.046 (2)
C(6)*A*	1.0071 (6)	0.5225 (5)	0.9949 (5)	0.045 (2)
O(6)*A*	1.1082 (4)	0.4593 (4)	1.0714 (4)	0.063 (2)
C(7)*A*	1.1387 (7)	0.4760 (7)	0.8220 (7)	0.074 (3)
C(8)*A*	1.0600 (8)	0.4058 (8)	1.1663 (8)	0.091 (4)
C(1')*B*	0.3837 (7)	0.6769 (6)	0.6388 (5)	0.060 (3)
C(2')*B*	0.3993 (8)	0.7900 (7)	0.6795 (5)	0.069 (3)
C(3')*B*	0.2834 (8)	0.8424 (6)	0.6517 (6)	0.062 (3)
C(4')*B*	0.1768 (7)	0.7677 (7)	0.5876 (6)	0.065 (3)
O(4')*B*	0.2495 (4)	0.6723 (4)	0.5682 (4)	0.063 (2)
C(5')*B*	0.0958 (6)	0.8071 (7)	0.4654 (6)	0.066 (3)
O(5')*B*	0.1845 (4)	0.8456 (4)	0.3883 (4)	0.058 (2)
N(1)*B*	0.4826 (5)	0.6411 (5)	0.5637 (3)	0.045 (2)
C(2)*B*	0.5680 (6)	0.5602 (6)	0.6062 (5)	0.048 (2)
O(2)*B*	0.5541 (4)	0.5025 (4)	0.6912 (4)	0.061 (2)
N(3)*B*	0.6811 (5)	0.5461 (5)	0.5463 (4)	0.050 (2)
C(4)*B*	0.7267 (6)	0.6153 (6)	0.4666 (5)	0.052 (2)
O(4)*B*	0.8281 (5)	0.5967 (5)	0.4205 (4)	0.070 (2)
C(5)*B*	0.6427 (6)	0.7164 (5)	0.4416 (5)	0.046 (2)
C(6)*B*	0.4952 (6)	0.6928 (4)	0.4480 (4)	0.046 (2)
O(6)*B*	0.4577 (4)	0.6239 (6)	0.3466 (3)	0.061 (2)
C(7)*B*	0.6562 (8)	0.7682 (6)	0.3200 (6)	0.072 (3)
C(8)*B*	0.3222 (8)	0.5863 (7)	0.3241 (7)	0.075 (3)

the methoxy group, gives an r.m.s. deviation of 0.064 Å. These results are indicative of the great similarity of these fragments in the two molecules. Differences arise in regard to the orientation of the derivatized pyrimidine ring with respect to the 2′,3′-didehydro-2′,3′-dideoxyfuranose ring. This orientation, which is *anti* [pyrimidine nucleosides are considered to exhibit an *anti* conformation when the criteria $90 \le \chi \le 180°$ or $-90° \le \chi \le -180°$ are satisfied (Saenger, 1984)] is apparent in both molecules, and correlates with the C(1′)—N(1) bond lengths of 1.465 (8) and 1.459 (8) Å for molecules *A* and *B*, respectively. The actual extent of twist about C(1′)—N(1) is significantly different for the two molecules: $\chi = -154.4\ (5)°$ for molecule *A*, and $\chi = -124.2\ (6)°$ for molecule *B*.

Another important feature associated with nucleosides is the orientation of the (4′)-hydroxymethyl group with respect to the 2′,3′-didehydro-2′,3′-dideoxyfuranose ring. This is specified by γ, the exocyclic C(4′)—C(5′) torsion angle. The preferred mode in pyrimidine nucleosides is *gauche–gauche*, in accord with the values here. However, it is interesting to note the difference between the angles: γ(molecule *A*) = 62.2 (7), γ(molecule *B*) = 49.5 (9)°.

It is considered here that the differences observed for the χ and γ values associated with each molecule are related somewhat to the effects of the hydrogen bonds detected between the two molecules, specifically those involving O(2) to the H atom bound to O(5′) (Table 2). The twisting of the derivatized pyrimidine ring about the glycosyl bond will also have implications for the final orientation of the —CH_2OH group with respect to the 2′,3′-didehydro-2′,3′-dideoxyfuranose ring. It is apparent that the orientation of the derivatized thymine ring in molecule *B* brings the methoxy substituent closer to the

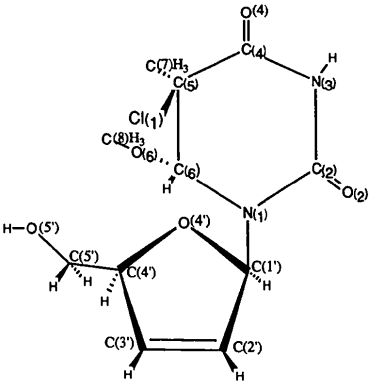

Fig. 1. Diagram illustrating the atom-labelling scheme for (+)-5-chloro-6-methoxy-5,6-dihydro-1-(2′,3′-didehydro-2′,3′-dideoxy-β-D-*glycero*-2-enopentofuranosyl)thymine.

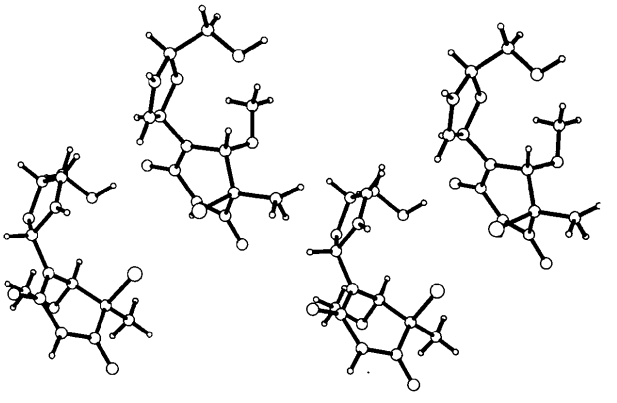

Fig. 2. Stereoscopic view of the two molecules in the asymmetric unit.

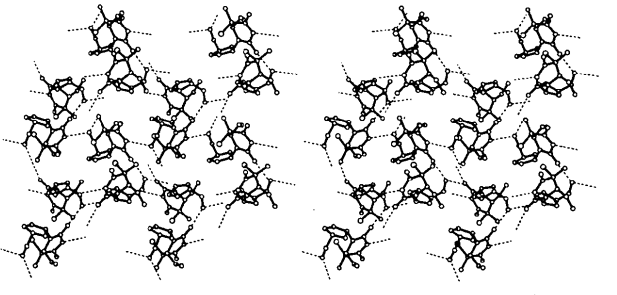

Fig. 3. Molecular packing diagram illustrating the hydrogen-bonding network.

Table 2. *Bond lengths* (Å), *bond angles* (°), *characteristic torsion angles* (°) *and hydrogen-bond lengths* (Å)

		Molecule *A*	Molecule *B*
	Cl(1)—C(5)	1.804 (6)	1.806 (6)
	N(1)—C(2)	1.332 (8)	1.358 (8)
	N(1)—C(6)	1.450 (8)	1.454 (7)
	C(2)—O(2)	1.224 (8)	1.214 (8)
	C(2)—N(3)	1.393 (8)	1.406 (8)
	N(3)—C(4)	1.375 (8)	1.370 (9)
	C(4)—O(4)	1.210 (9)	1.224 (8)
	C(4)—C(5)	1.532 (9)	1.524 (9)
	C(5)—C(6)	1.502 (9)	1.504 (9)
	C(5)—C(7)	1.50 (1)	1.517 (9)
	C(6)—O(6)	1.435 (7)	1.413 (7)
	O(6)—C(8)	1.40 (1)	1.404 (9)
	C(1′)—C(2′)	1.494 (9)	1.50 (1)
	C(1′)—O(4′)	1.401 (9)	1.418 (7)
	C(1′)—N(1)	1.465 (8)	1.459 (8)
	C(2′)—C(3′)	1.32 (1)	1.31 (1)
	C(3′)—C(4′)	1.49 (1)	1.50 (1)
	C(4′)—O(4′)	1.442 (7)	1.44 (1)
	C(4′)—C(5′)	1.47 (1)	1.525 (9)
	C(5′)—O(5′)	1.440 (8)	1.409 (8)
	C(2′)—C(1′)—N(1)	112.9 (5)	114.9 (6)
	C(2)—N(1)—C(6)	120.6 (5)	119.8 (5)
	N(1)—C(2)—O(2)	124.5 (6)	124.8 (6)
	N(1)—C(2)—N(3)	117.5 (5)	115.7 (5)
	O(2)—C(2)—N(3)	117.9 (6)	119.5 (6)
	C(2)—N(3)—C(4)	125.0 (5)	126.7 (6)
	N(3)—C(4)—O(4)	118.0 (5)	121.8 (6)
	N(3)—C(4)—C(5)	116.1 (5)	114.9 (5)
	O(4)—C(4)—C(5)	123.7 (4)	123.2 (6)
	Cl—C(5)—C(4)	105.5 (4)	104.7 (4)
	Cl—C(5)—C(6)	106.1 (4)	108.8 (4)
	Cl—C(5)—C(7)	107.9 (4)	109.4 (5)
	C(4)—C(5)—C(6)	110.0 (5)	109.2 (5)
	C(4)—C(5)—C(7)	110.3 (5)	113.2 (5)
	C(6)—C(5)—C(7)	116.4 (6)	111.3 (5)
	N(1)—C(6)—C(5)	112.4 (5)	111.2 (4)
	N(1)—C(6)—O(6)	110.4 (4)	111.3 (5)
	C(5)—C(6)—O(6)	104.1 (5)	102.0 (5)
	C(6)—O(6)—C(8)	114.5 (5)	117.3 (5)
	C(1′)—N(1)—C(2)	116.3 (5)	118.6 (5)
	C(1′)—N(1)—C(6)	123.3 (5)	121.6 (5)
	C(2′)—C(1′)—O(4′)	104.2 (5)	103.9 (6)
	O(4′)—C(1′)—N(1)	111.6 (6)	109.6 (5)
	C(1′)—C(2′)—C(3′)	109.8 (7)	111.8 (6)
	C(2′)—C(3′)—C(4′)	110.5 (6)	107.8 (7)
	C(3′)—C(4′)—O(4′)	103.0 (6)	105.6 (5)
	C(3′)—C(4′)—C(5′)	118.2 (5)	115.3 (7)
	O(4′)—C(4′)—C(5′)	112.3 (6)	110.1 (6)
	C(1′)—O(4′)—C(4′)	111.4 (5)	109.2 (5)
	C(4′)—C(5′)—O(5′)	113.4 (6)	110.9 (5)
χ	O(4′)—C(1′)—N(1)—C(2)	−154.4 (5)	−124.2 (6)
γ	O(5′)—C(5′)—C(4′)—C(3′)	62.2 (7)	49.5 (9)
ν_0	C(4′)—O(4′)—C(1′)—C(2′)	−10.8 (7)	−12.4 (7)
ν_1	O(4′)—C(1′)—C(2′)—C(3′)	5.8 (8)	7.9 (7)
ν_2	C(1′)—C(2′)—C(3′)—C(4′)	1.2 (9)	−0.3 (8)
ν_3	C(2′)—C(3′)—C(4′)—O(4′)	−7.5 (8)	−7.4 (7)
ν_4	C(3′)—C(4′)—O(4′)—C(1′)	11.4 (7)	12.5 (7)

*D*H	*A*′	*DH*···*A*′	Symmetry operator on *A*′
O(5′)*A*···O(2)*B*		2.752 (6)	
O(5′)*B*···O(2)*A*		2.813 (6)	
N(3)*B*···O(5′)*B*		2.899 (7)	$-x, \frac{1}{2}+y, -z$
N(3)*A*···O(5′)*A*		2.863 (7)	$-x, \frac{1}{2}+y, -z$

(4′)-hydroxymethyl group. Thus, it would be expected that the latter moiety would move to a position associated with a smaller γ angle in order to relieve any unacceptable increase in steric energy. Indeed, a smaller γ angle was observed for molecule *B*.

The six-membered rings of both molecules in the asymmetric unit adopt what might be loosely termed a half-chair conformation, with atoms C(6)*A* and C(6)*B*, respectively, 0.56 (1) and 0.60 (1) Å from the best least-squares plane of the other five atoms. The atoms comprising the conjugated portion of the six-membered rings of molecules *A* and *B* [N(1), C(2), O(2), N(3), C(4) and O(4)] are coplanar within 0.11 (1) Å, whereas C(5) and C(6) are on opposite sides of this plane by 0.30 (1) and 0.34 (1) Å in molecule *A*, and by 0.38 (1) and 0.33 (1) Å in molecule *B*. The Cl atom as well as the methoxy group are in axial positions on C(5) and C(6) of each six-membered ring, and the C(5) methyl group is quasi-equatorial. The methoxy and methyl groups bonded to atoms C(5) and C(6) exhibit a staggered conformation; the O(6)*A*—C(6)*A*—C(5)*A*—C(7)*A* dihedral angle is 55.0 (6)°, and O(6)*B*—C(6)*B*—C(5)*B*—C(7)*B* is 60.2 (6)°.

Five-membered β-D-ribofuranose rings are generally non-planar since puckering reduces steric interactions among substituents on adjacent atoms, thereby lowering the energy of the system. Consequently, the low-energy states are associated with C(2′)-*endo* and C(3′)-*endo* puckering modes. In this structure the only substituents at the 2′ and 3′ ring atoms are H atoms which are in the plane, thus reducing the steric contacts. Both molecules exhibit O(4′)-*endo* puckering; O(4′)*A* and O(4′)*B* are 0.16 (1) and 0.18 (1) Å, respectively, out of the 2′,3′-didehydro-2′,3′-dideoxyfuranose plane as defined by C(1′), C(2′), C(3′) and C(4′). This is further supported by the pseudorotation phase angles and phase signs of the endocyclic torsion angles (Saenger, 1984): *P*(molecule *A*) = 84.1°, *P*(molecule *B*) = 91.3°. The ring-pucker amplitudes for molecule *A* and molecule *B* (τ_m) are 11.62 and 13.22°, respectively, implying a high degree of planarity. The distance between the N(1) (base) and C(5′) exocyclic substituent, N(1)*A*—C(5′)*A* = 4.34 (5) and N(1)*B*—C(5′)*B* = 4.36 (4) Å, is indicative of their equatorial orientation, as expected in the O(4′)-*endo* puckering mode.

Nucleosides are often shown to exhibit a close intramolecular contact between C(6) and O(5′); for example, that in 1-(2-deoxy-β-D-ribofuranosyl)-5-[(1*S*)-2,2-dibromocyclopropyl]uracil (Moore, Santarsiero, Lin, James, Tandon, Wiebe & Knaus, 1989). In the structure presented here the relevant distances are 3.585 (7) and 3.596 (7) Å for molecules *A* and *B*, respectively; they are not considered to be significantly different from the sum of the van der Waals radii of the contributing atoms.

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References

DUSCHINSKY, R., GABRIEL, T., TAUTZ, W., NUSSBAUM, M., HOFFER, M., GRUNBERG, E., BURCHENAL, J. H. & FOX, J. J. (1967). *J. Med. Chem.* **10**, 47–58.

GARTNER, S., MARKOVITS, P., MARKOVITS, D. M., KAPLAN, M. H., GALLO, R. C. & POPOVIC, M. (1986). *Science*, **233**, 215–219.
HALL, S. R. & STEWART, J. M. (1990). Editors. *Xtal3.0 User's Manual*. Univs. of Western Australia, Australia, and Maryland, USA.
HAMILTON, W. C. (1965). *Acta Cryst.* **18**, 502–510.
KOENIG, S., GENDELMAN, H. E., ORENSTEIN, J. M., DAL CANTO, M. C., PEZESHKPOUR, G. H., YUNGBLUTH, M., JANOTTA, F., AKSAMIT, A., MARTIN, M. A. & FAUCI, A. S. (1986). *Science*, **233**, 1089–1093.
LARSON, A. C. (1970). *Crystallographic Computing*, edited by F. R. AHMED, S. R. HALL & C. P. HUBER, pp. 291–294. Copenhagen: Munksgaard.
LIN, T. S., SCHINAZI, R. F. & PRUSOFF, W. H. (1987). *Biochem. Pharmacol.* **36**, 2713–2718.
MANSURI, M. M., STARRETT, J. E., GHAZZOULI, I., HITCHCOCK, M. J. M., STERZYCHI, R. Z., BRANKOVAN, V., LIN, T. S., AUGUST, E. M., PRUSOFF, W. H., SOMMADOSSI, J.-P. & MARTIN, J. C. (1989). *J. Med. Chem.* **32**, 461–466.
MOORE, S. A., SANTARSIERO, B. D., LIN, T., JAMES, M. N. G., TANDON, M., WIEBE, L. I. & KNAUS, E. E. (1989). *Acta Cryst.* C**45**, 647–650.
MOTHERWELL, W. D. S. & CLEGG, W. (1978). *PLUTO*. Program for plotting molecular and crystal structures. Univ. of Cambridge, England.
SAENGER, W. (1984). *Principles of Nucleic Acid Structure*, pp. 21–25, 69–71. New York: Springer-Verlag.
WATKINS, B. A., DORN, H. H., KELLY, W. B., ARMSTRONG, R. C., POTTS, B. J., MICHAELS, F., KUFTA, C. V. & DUBOIS-DALCQ, M. (1990). *Science*, **249**, 549–553.

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Structure of the Anthracycline Antibiotic Aranciamycin

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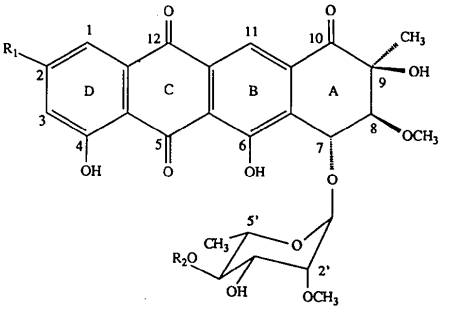
Abstract. 4-[(6-Deoxy-2-*O*-methyl-α-L-mannopyranosyl)oxy]-3,4-dihydro-2,5,7-trihydroxy-3-methoxy-2-methyl-1,6,11(2*H*)-naphthacenetrione, $C_{27}H_{28}O_{12}$, $M_r = 544.5$, orthorhombic, $P2_12_12_1$, $a = 8.029$ (1), $b = 8.224$ (1), $c = 37.261$ (6) Å, $V = 2460.4$ (6) Å^3, $Z = 4$, $D_x = 1.470$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.7107 Å, $\mu = 0.11$ mm^{-1}, $F(000) = 1144$, $T = 293$ K, $R = 0.069$ for 3186 observed reflections. The absolute configuration of this α-glycoside is 7*R*,8*S*,9*S*. Ring *A* adopts a half-chair conformation without an extra stabilizing intramolecular hydrogen bond from O(9) to O(7). The overall conformation is very similar to that found for the related antibiotic steffimycin B.

Introduction. The anthracycline antibiotic aranciamycin is produced by *Streptomyces echinatus* and consists of the aglycone aranciamycinone and the sugar 2-*O*-methyl-L-rhamnose. Aranciamycin shows weak antitumour activity and is closely related to steffimycin B. These antibiotics differ from the very well known anthracyclines (*e.g.* daunomycin, adriamycin, carminomycin) with respect to the substitution of ring *A* and the sugar moiety, which does not carry an amino group. The X-ray crystal-structure analysis confirms the structure elucidation by chemical and spectroscopic methods (Keller-Schierlein, Sauerbier, Vogler & Zähner, 1970; Keller-Schierlein & Müller, 1970; Zeeck, Schröder, Krone & Frobel, 1978).



Aranciamycin: R_1 = H; R_2 = H
Steffimycin B: R_1 = OCH_3; R_2 = CH_3

Experimental. Crystals grown from methanol were orange plates. A crystal 0.9 × 0.4 × 0.2 mm was mounted in a glass capillary and used to register 6292 profile-fitted intensities (Clegg, 1981) with $2\theta \leq 50°$ (h −9→9, k 0→9, l 0→44; $\sin\theta/\lambda = 0.59$ Å^{-1}) on a Stoe–Siemens four-circle diffractometer (ω-scan

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