Another interesting feature of the structure is the significant elongation of the C—C double bond [C(2)—C(3) = 1·382 (3) Å] relative to that in ethylene [1·314 (6) Å (van Nes & Vos, 1977)]. This can be attributed to through-conjugation from the electron-donating amino substituent to the electron-withdrawing cyano (and pyridyl) substituent. This is also reflected in the shortening of the N(3)—C(3) bond [1·331 (3) Å] relative to the value [1·452 (2) Å] for a pure $\ddot{N}$—C(sp^2) single bond (Ammon, Mazzocchi, Regan & Colicelli, 1979) and a slight shortening of the C(1)—C(2) bond [1·425 (4) Å] relative to the C(sp^2)—C(sp) bond length [1·437 (2) Å] in ethylenetetracarbonitrile (Little, Pautler & Coppens, 1971), indicating some double-bond character in these bonds, as has been previously observed in other 'push–pull' olefins (Hazell & Mukhopadhyay, 1980; Adhikesavalu & Venkatesan, 1981; Sen & Venkatesan, 1984; Sen, Venkatesan, Acharya & Guru Row, 1984; and references therein). Normally such C—C bond elongation is accompanied by significant bond twisting resulting from a combination of steric and conjugative effects. In the present case, however, there is very little twisting of the double bond as measured by the twist angle [3·6 (3)°] between the mean planes defined by C(2), C(1), C(2′) and by C(3), N(3), C(4). This lack of twisting is attributed to the intramolecular hydrogen bond which maintains one side of the double bond planar. A similar situation was reported for 3-(2-imidazolidinylidene)-2,4-pentanedione (Adhikesavalu & Venkatesan, 1983) wherein bond elongation without twisting was explained by intramolecular hydrogen bonding. The polarization of the double bond observed in the present structure is also reflected in the large difference in ^{13}C NMR chemical shifts of the two olefinic carbons.

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Structure of a Modified Cytosine: An Antiviral Nucleoside Analog

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(*Received* 17 *February* 1986; *accepted* 23 *April* 1987)

Abstract. 5′-Azido-5′-deoxy-1-β-D-arabinofuranosylcytosine sesquihydrate, $C_9H_{12}N_6O_4.\frac{3}{2}H_2O$, $M_r = 295$, monoclinic, $C2$, $a = 15·835$ (7), $b = 7·286$ (4), $c = 12·039$ (6) Å, $\beta = 108·75$ (6)°, $V = 1316·5$ Å^3, $Z = 4$, $D_x = 1·488$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 5·90$ cm^{-1}, $F(000) = 620$, $T = 288$ K, final $R = 0·056$ for 960 observed reflections. Conformational features of the nucleoside include a glycosidic bond conformation in the *anti* range, a ribose moiety in the ^2E [C(2′)-*endo*] form and a C(5′)—N(5′) bond that is *trans*

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0108-2701/87/091731-04$01.50

to C(4′)–O(4′) but *gauche* to C(4′)–C(3′). The crystal contains hydrophobic and hydrophilic zones running alternately, parallel to the *b* axis.

Introduction. Analogs of natural purine and pyrimidine nucleosides have proved to be quite effective as antibacterial, antiviral and anticancer or antitumor agents, due to their roles as enzyme inhibitors and antagonists. However, some effective antiviral nucleosides can also activate C-type viruses, decrease the expression of certain differentiated functions, and show mutagenic and sometimes even carcinogenic activity (Lin & Prusoff, 1975). The marked antiviral activity of 5-iodo-2′-deoxyuridine (IdUrd) and the retention of this activity with low toxicity in its analogs make it of interest to probe into the antiviral functions of other similarly modified nucleosides. 5′-Azido-5′-deoxy-1-β-D-arabinofuranosylcytosine, one of a series of nearly similar analogs of cytosine (received through the courtesy of T. S. Lin and W. H. Prusoff of Yale University, USA), has no antiviral activity against *Herpes simplex* virus type 1 (like the 5′-amino analog of IdUrd), but it possesses inhibitory activity against the replication of sarcoma 180 cells in cultures. These marked changes in the activity of these compounds with modifications are interesting. In this contribution, the X-ray analysis of 5′-azido-5′-deoxy-1-β-D-arabinofuranosylcytosine is reported (hereafter called 5′-N3-AraC).

Table 1. *Final atomic coordinates with e.s.d.'s in parentheses and equivalent isotropic values of the anisotropic thermal parameters for the non-*H *atoms and isotropic thermal parameters for the* H *atoms*

$B_{eq} = \frac{4}{3}\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}/B_{iso}(Å²)
N(1)	0·4617 (3)	−0·1612 (8)	0·7890 (4)	3·21
C(2)	0·4129 (3)	−0·1220 (10)	0·8636 (4)	3·22
N(3)	0·3811 (3)	−0·2604	0·9143 (4)	3·58
C(5)	0·4432 (4)	−0·4804 (10)	0·8102 (5)	4·18
C(6)	0·4754 (3)	−0·3390 (9)	0·7633 (4)	4·26
C(4)	0·3959 (4)	−0·4367 (11)	0·8886 (5)	3·40
O(2)	0·3993 (3)	0·418 (9)	0·8850 (4)	4·20
N(4)	0·3638 (3)	−0·5679 (10)	0·9404 (5)	4·36
O(2′)	0·6446 (2)	−0·1186 (8)	0·8798 (3)	3·78
C(5′)	0·6522 (4)	−0·1519 (13)	0·6146 (5)	5·48
O(3′)	0·6048 (3)	0·3063 (9)	0·7136 (3)	4·51
O(4′)	0·5146 (2)	−0·0654 (9)	0·6395 (3)	4·07
C(1′)	0·5016 (4)	−0·0094 (9)	0·7459 (5)	3·33
C(2′)	0·5949 (3)	0·0410 (11)	0·8291 (4)	3·34
C(3′)	0·6365 (3)	0·1235 (11)	0·7401 (5)	3·56
C(4′)	0·5961 (4)	0·0074 (11)	0·6297 (4)	3·88
N(2′)	0·7292 (6)	−0·0813 (10)	0·4925 (9)	9·84
N(5′)	0·7311 (4)	−0·0764 (17)	0·5885 (7)	9·51
N(3′)	0·7347 (7)	−0·0737 (23)	0·4005 (9)	15·57
*W*1	0·2155 (2)	0·0375 (9)	0·8740 (3)	4·49
*W*2	0·5000	−0·5188 (16)	0·5000	13·65
H(C5)	0·4538 (30)	−0·6156 (90)	0·7923 (40)	4·20
H(O2′)	0·6366 (30)	−0·1289 (90)	0·9643 (40)	3·77
H(C6)	0·4943 (30)	−0·3612 (90)	0·7088 (40)	4·16
H1(N4)	0·3627 (30)	−0·6731 (90)	0·9048 (40)	4·26
H2(N4)	0·3253 (30)	−0·5236 (90)	0·9882 (40)	4·26
H1(C5′)	0·6641 (30)	−0·2178 (90)	0·6953 (40)	5·40
H2(C5′)	0·6220 (30)	−0·2177 (90)	0·5496 (40)	5·40
H(O3′)	0·6560 (30)	0·3813 (90)	0·7696 (40)	4·46
H(C1′)	0·4557 (30)	0·1189 (90)	0·7259 (40)	3·28
H(C2′)	0·5876 (30)	0·1314 (90)	0·9023 (40)	3·26
H(C3′)	0·7031 (30)	0·1356 (90)	0·7670 (40)	3·52
H(C4′)	0·5844 (30)	0·0681 (90)	0·5710 (40)	3·86

Table 2. *Some selected dihedral angles* (°) *describing the molecular conformation with e.s.d.'s in parentheses*

N(5′)–C(5′)–C(4′)–O(4′)	172·6 (6)	C(1′)–C(2′)–C(3′)–O(3′)	79·2 (6)
N(5′)–C(5′)–C(4′)–C(3′)	−69·6 (8)	O(2′)–C(2′)–C(3′)–O(3′)	−164·0 (5)
O(4′)–C(1′)–C(2′)–C(3′)	35·1 (6)	O(2′)–C(2′)–C(3′)–C(4′)	81·7 (6)
C(1′)–C(2′)–C(3′)–C(4′)	−35·1 (6)	C(5′)–C(4′)–C(3′)–C(2′)	−95·3 (6)
C(2′)–C(3′)–C(4′)–O(4′)	23·7 (6)	C(5′)–C(4′)–C(3′)–O(3′)	149·6 (6)
C(3′)–C(4′)–O(4′)–C(1′)	−1·3 (6)	C(5′)–C(4′)–O(4′)–C(1′)	122·8 (6)
C(4′)–O(4′)–C(1′)–C(2′)	−22·0 (6)	O(4′)–C(1′)–N(1)–C(2)	−156·2 (5)
N(1)–C(1′)–C(2′)–C(3′)	152·8 (5)	C(2′)–C(1′)–N(1)–C(2)	87·5 (6)
N(1)–C(1′)–C(2′)–O(2′)	38·4 (7)	O(4′)–C(1′)–N(1)–C(6)	27·6 (7)
N(1)–C(1′)–O(4′)–C(4′)	−142·9 (5)	C(2′)–C(1′)–N(1)–C(6)	−88·6 (6)

Experimental. 5′-N3-AraC crystallizes from a solution of ethanol and water (1:1) in the form of transparent needles at room temperature, dimensions 0·30 × 0·25 × 0·15 mm. Lattice parameters from 15 intermediate sinθ axial reflections in the range $17 < 2\theta < 38°$. 1180 [960 with $I > 3\sigma(I)$] unique reflections collected on an automated Stoe four-circle diffractometer. Ni-filtered Cu $K\alpha$ radiation, θ–2θ step-scan mode, $2\theta \leq 130°$. Range of h, k and l −17 to 17, 0 to 9 and 0 to 13. Three standard reflections, intensity decrease <4%. Data corrected for Lorentz–polarization factors but not for absorption. Structure solved by *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) and refined by full-matrix least squares. All the H atoms have been located from ΔF synthesis and refined isotropically. Final $R = 0{\cdot}056$ and $wR = 0{\cdot}061$; $w = 1/\sigma^2(F_o)$, $\Delta\rho$ peaks are 0·4 to −0·3 e Å^{-3}, $(\Delta/\sigma)_{max} = 0{\cdot}25$. Atomic scattering factors are from *International Tables for X-ray Crystallography* (1974). Programs used from *XRAY ARC* (*World List of Crystallographic Computer Programs*, 1973), modified for the B6700 computer.

Discussion. Final atomic parameters are given in Table 1, some dihedral angles of the molecule in Table 2.* Fig. 1 gives a sketch of 5′-N3-AraC showing the numbering convention with all non-H bond distances and bond angles indicated with intramolecular short contacts. The distances O(2′)···N(1) and O(4′)···C(6) are shorter than the corresponding van der Waals contacts (O···N, 2·9 Å; O···aromatic system, 3·2 Å). Fig. 2 shows a view of the molecule down the *a* axis and Fig. 3 presents a stereoview of the packing of 5′-N3-AraC.

* Lists of structure factors, anisotropic thermal parameters, bond distances and angles involving H, intermolecular short contacts, probable hydrogen-bond distances and least-squares-planes' data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43557 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

The bond distances and bond angles (Fig. 1) in the base moiety are similar to those averaged from cytosine derivatives (Taylor & Kennard, 1982). The atoms of the heterocycle are fairly coplanar with maximum deviations from the mean ring plane of only 0·012 (5) Å. The attached atoms O(2) and N(4) are almost coplanar with the heterocyclic ring, but lie on opposite sides of the mean plane.

Apart from a few exceptions which have half-chair conformations, ribose units in crystalline nucleosides most frequently have an envelope form with four nearly coplanar and one out-of-plane atom. The arabinofuranosyl residue in 5′-N3-AraC is in a similar conformation and puckered in such a way that C(2′) lies 0·58 Å from the best plane through atoms C(4′) O(4′), C(1′), C(3′) on the same side as atom C(5′), thus giving a ^2E conformation. The (2′) and (3′) hydroxyl groups are *trans*, with torsion angle O(2′)–C(2′)–C(3′)–O(3′) −164°.

In 5′-N3-AraC, the torsion angle N(1)–C(1′)–C(2′)–O(2′) is only 38·4° and atoms N(1) and O(2′) are nearly staggered, though in most ribonucleosides this angle is around −140° with a near-*trans* conformation. In 5′-N3-AraC, the proximity of O(2′) to the heterocycle restricts the orientation of the heterocycle with respect to the sugar moiety to *anti* with torsion angle O(4′)–C(1′)–N(1)–C(2) at −156·2°. Spectroscopic investigations using NMR (Cushley, Watnabe & Fox, 1967), ORD and CD methods (Güschlbauer & Garilhe, 1969) suggest that arabinonucleosides generally display *anti* conformations in solution and that the rotation of the heterocycle is inhibited by the O(2′)–H group.

The most common conformation around the C(4′)–C(5′) bond in nucleosides is *gauche–gauche* (Sundaralingam, 1965). However, in 5′-N3-AraC the C(5′)–N(5′) bond is *trans* to C(4′)–O(4′) but *gauche* to C(4′)–C(3′) and the corresponding torsion angles are 172·6 and −69·6° respectively. This feature is probably due to the short contacts between the azido group and the heterocycle that would be produced if the nucleoside were in the *gauche–gauche* conformation (Banerjee & Saenger, 1978; Saenger, 1972). The bond lengths and bond angles of 5′-N3-AraC sugars correspond (within 3σ) to the average ^2E arabinose (Sundaralingam, 1965). While the conformation of N(5′) is normal, the angle N(5′)–N(2′)–N(3′) (172·8°) and the bond lengths N(5′)–N(2′) and N(2′)–N(3′) (about 1·14 Å) indicate a strong double-bond character (Fig. 1). It is interesting that the high thermal vibration we find for the peripheral azido group is similar to that in cytarazid (Głowka, Parthasarathy & Paul, 1982).

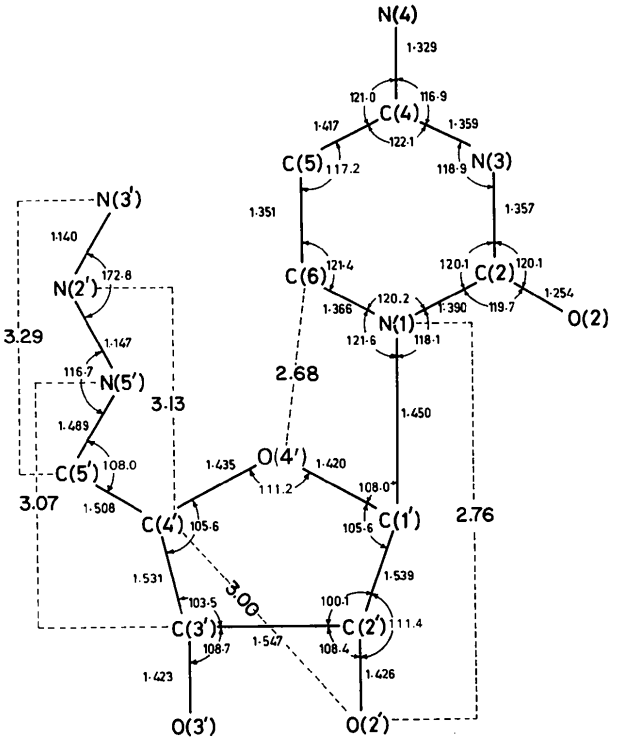

Fig. 1. A sketch of 5′-N3-AraC showing the numbering convention and the bond lengths (Å, e.s.d.'s 0·006–0·016 Å) and bond angles (°, e.s.d.'s 0·4–1·2°) of the non-H atoms with intramolecular short contacts (Å).

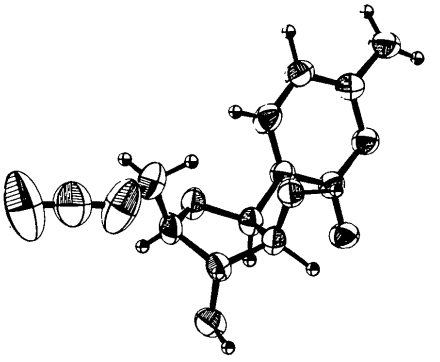

Fig. 2. A view of the molecule down the *a* axis with 50% probability ellipsoids.

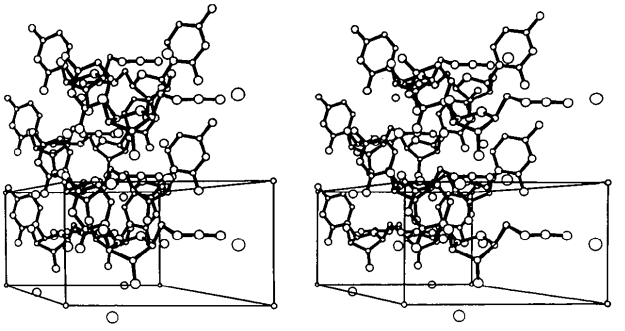

Fig. 3. Stereoview of the molecules in the cell.

The crystal contains hydrophobic and hydrophilic zones running alternately, parallel to the *b* axis. The hydrophobic zones are alternate columns of pyrimidine and azido groups. The hydrophilic zones have hydrogen bonds and short contacts between waters *W*1 and *W*2 and O(2′) and O(3′) of the arabinose. The closest contact from the N(3′) atom of the azido group is to the N(1) and C(2) atoms of the neighboring molecules. No significant short contacts are seen between the azido groups themselves.

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Acta Cryst. (1987). C**43**, 1734–1737

Structure of Dimethyl 1,2-Dihydro-1,2,6-trimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxylate

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(*Received* 23 *February* 1987; *accepted* 10 *April* 1987)

Abstract. $C_{18}H_{20}N_2O_6$, $M_r = 360{\cdot}37$, monoclinic, $P2_1/n$, $a = 9{\cdot}537\ (2)$, $b = 16{\cdot}990\ (4)$, $c = 10{\cdot}909\ (2)$ Å, $\beta = 92{\cdot}48\ (2)°$, $V = 1766$ Å^3, $Z = 4$, $D_x = 1{\cdot}35$ Mg m^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}71073$ Å, $\mu = 0{\cdot}096$ mm^{-1}, $F(000) = 760$, $T = 296$ K, $R = 0{\cdot}049$ for 1738 observed reflections. The structure determination of the title compound was undertaken to compare it to structures of 1,4-dihydropyridine analogues in view of the results from competitive binding studies and measurements of its calcium-channel antagonist activity. The major structural difference is the positioning of the aryl substituent relative to the mean plane of the dihydropyridine ring.

Introduction. The utility of 4-aryl-1,4-dihydropyridines related to nifedipine [dimethyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridinedicarboxylate] as therapeutic agents in cardiovascular disorders (Janis & Triggle, 1983) has stimulated studies to investigate the geometrical requirements at the 1,4-dihydropyridine binding site. The solid-state conformation of several 1,4-dihydropyridine analogues indicated that the nature of the substituents at the C_3, C_4 and C_5 positions altered the conformation of the 1,4-dihydropyridine ring. In the solid state these compounds exist in a boat conformation where the plane of the C_4-substituted-phenyl ring is in a sterically favored orientation axial to the 1,4-dihydropyridine ring. Strain due to non-bonded interactions involving the C_3, C_4 and C_5 substituents is relieved predominantly by puckering of the 1,4-dihydropyridine ring and distortion of the bond angles about C_4 (Fossheim, 1986; Fossheim, Svarteng, Mostad, Romming, Shefter & Triggle, 1982; Triggle, Shefter & Triggle, 1980). Competitive [^{3}H]-nitrendipine [ethyl methyl 1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylate] binding studies indicated that the receptor affinity for the novel 1,2-dihydropyridine compound (1) was much lower than expected from its calcium-channel antagonist activity (Soboleski, Li-Kwong-Ken, Wynn, Triggle,

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0108-2701/87/091734-04$01.50