(amide)N—H···O=C(amide) hydrogen bond (Ramakrishnan & Prasad, 1971; Taylor, Kennard & Versichel, 1984).

To summarize, despite the solution behaviour and solid-state IR absorption spectra, the Piv-L-Pro-NHMe molecules do not fold up in the γ-turn conformation in the crystalline state. Other crystalline amino acid derivatives and linear peptides, promising candidates for adopting such an intramolecularly hydrogen-bonded structure, are currently under scrutiny in our laboratory.

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Structure and Conformation of a Nucleoside Analog 5-Nitro-1-β-D-arabinofuranosyluracil

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Abstract. $C_9H_{11}N_3O_8$, $M_r = 271$, orthorhombic, $P2_12_12_1$, $a = 9{\cdot}241\ (2)$, $b = 20{\cdot}518\ (4)$, $c = 6{\cdot}187\ (1)$ Å, $V = 1173{\cdot}1$ Å^3, $Z = 4$, $D_x = 1{\cdot}29$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}7107$ Å, $\mu = 1{\cdot}57$ cm^{-1}, $F(000) = 600$, $T = 288$ K, final $R = 0{\cdot}051$ for 1078 observed reflections. Conformational features of the nucleoside include a glycosidic bond conformation in the *anti* range, a ribose moiety in the C(2′)-*endo* (^2E) form and the C(5′)—O(5′) bond *gauche* to both C(4′)—O(4′) and C(4′)—C(3′).

Introduction. Pyrimidine nucleosides and nucleotides substituted at the 5 position by various functional groups are very interesting for their antiviral, antitumor

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

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

	x	*y*	*z*	B_{eq}(Å^2)
O(3′)	−0·4617 (4)	−0·2537 (1)	−0·4594 (5)	3·438
O(2)	−0·3407 (3)	−0·4803 (1)	−0·3655 (5)	3·082
O(4′)	−0·6289 (3)	−0·3699 (1)	−0·6853 (5)	2·892
O(4)	−0·6463 (3)	−0·5223 (2)	−1·2226 (5)	3·452
N(5)	−0·5739 (4)	−0·5628 (2)	−1·1237 (6)	2·572
N(3)	−0·3906 (4)	−0·5643 (2)	−0·5907 (5)	2·178
O(2′)	−0·3260 (3)	−0·3631 (1)	−0·8665 (5)	3·431
O(8)	−0·5459 (4)	−0·6172 (1)	−1·1966 (5)	3·541
O(9)	−0·4181 (3)	−0·6494 (1)	−0·8146 (5)	3·320
C(6)	−0·5347 (4)	−0·4823 (2)	−0·8493 (7)	2·253
C(4)	−0·4412 (4)	−0·5916 (2)	−0·7814 (7)	2·217
N(1)	−0·4810 (4)	−0·4611 (1)	−0·6610 (5)	2·075
C(1′)	−0·5009 (5)	−0·3925 (2)	−0·5906 (6)	2·141
C(2)	−0·3981 (4)	−0·5006 (2)	−0·5265 (7)	2·204
C(2′)	−0·3816 (4)	−0·3465 (2)	−0·6622 (7)	2·475
C(4′)	−0·6166 (5)	−0·3012 (2)	−0·7357 (7)	2·545
C(3′)	−0·4638 (5)	−0·2816 (2)	−0·6700 (7)	2·295
C(5)	−0·5173 (4)	−0·5453 (2)	−0·9142 (6)	2·000
O(5′)	−0·5501 (5)	−0·3212 (2)	−1·1053 (5)	5·069
C(5′)	−0·6558 (7)	−0·2917 (2)	−0·9698 (8)	4·213

Table 2. *Bond lengths* (Å) *and selected dihedral angles* (°)

C(4)—N(3)	1·387 (5)	O(4′)—C(4′)	1·448 (5)
N(3)—C(2)	1·368 (5)	C(4′)—C(3′)	1·523 (6)
C(2)—N(1)	1·391 (5)	C(3′)—C(2′)	1·532 (6)
N(1)—C(6)	1·338 (5)	C(2′)—C(1′)	1·518 (6)
C(6)—C(5)	1·364 (5)	C(3′)—O(3′)	1·424 (5)
C(5)—C(4)	1·440 (5)	C(2′)—O(2′)	1·408 (5)
C(4)—O(9)	1·223 (5)	C(4′)—C(5′)	1·506 (6)
C(2)—O(2)	1·204 (5)	C(5′)—O(5′)	1·422 (6)
N(1)—C(1′)	1·483 (5)	C(5)—N(5)	1·443 (5)
C(1′)—O(4′)	1·402 (5)	N(5)—O(8)	1·231 (4)
N(5)—O(4)	1·230 (4)		

O(8)—N(5)—C(5)—C(4)	−5·97 (5)	O(2′)—C(2′)—C(3′)—O(3′)	−155·01 (3)
O(4)—N(5)—C(5)—C(6)	−6·86 (5)	O(2′)—C(2′)—C(3′)—C(4′)	86·68 (4)
N(1)—C(6)—C(5)—N(5)	−177·54 (3)	C(5′)—C(4′)—C(3′)—C(2′)	−100·34 (4)
O(9)—C(4)—C(5)—N(5)	−3·02 (6)	C(5′)—C(4′)—C(3′)—O(3′)	143·49 (4)
C(2)—N(3)—C(4)—C(5)	−4·07 (6)	O(4′)—C(4′)—C(3′)—O(3′)	−96·20 (4)
C(2)—N(3)—C(4)—O(9)	176·42 (4)	C(1′)—O(4′)—C(4′)—C(3′)	1·80 (4)
C(4)—N(3)—C(2)—O(2)	−173·70 (4)	C(1′)—O(4′)—C(4′)—C(5′)	127·32 (4)
C(1′)—N(1)—C(2)—N(3)	175·97 (3)	O(4′)—C(4′)—C(5′)—O(5′)	−67·49 (5)
C(6)—N(1)—C(2)—O(2)	174·22 (4)	C(3′)—C(4′)—C(5′)—O(5′)	51·51 (5)
C(5)—C(6)—N(1)—C(1′)	−179·72 (4)	C(1′)—N(1)—C(2)—O(2)	−2·61 (5)
C(6)—N(1)—C(1′)—O(4′)	27·83 (5)	C(6)—N(1)—C(1′)—C(2′)	−90·20 (4)
C(2)—N(1)—C(1′)—O(4′)	−155·29 (3)	N(1)—C(1′)—C(2′)—C(3′)	152·91 (3)
N(1)—C(1′)—C(2′)—O(2′)	34·50 (4)	C(4′)—O(4′)—C(1′)—N(1)	−146·49 (3)

properties. In contrast to the class of 5-substituted deoxyribonucleosides, which include several compounds with potent antiviral properties, there are only a few examples of arabinofuranosyl 5-substituted pyrimidine nucleosides with remarkable antiviral activity, *viz* the 5-halogenated derivatives of AraC and AraU which are active against *Herpes simplex* virus.

The structure determination of 5-nitro-AraU was undertaken as part of a series of structure determinations of nucleic acid components and their analogs with antitumor, antiviral or anticancer activities to correlate, if possible, their structure–function relation.

Experimental. 5-NO$_2$-AraU crystallizes from a solution of ethanol and water in the form of transparent needles at room temperature, dimensions $0{\cdot}10\times0{\cdot}15\times0{\cdot}25$ mm. 25 reflections (to $\theta=15{\cdot}2°$) for measurement of lattice parameters. 3 standard reflections, no intensity variation. 1585 [1078 with $I>3\sigma(I)$] unique reflections collected on a Syntex *P*3 diffractometer, graphite-monochromatized Mo $K\alpha$ radiation, ω–2θ scan, $2\theta\le50°$, range of *h, k, l* 0 to 12, 0 to 26, 0 to 7, respectively. Data corrected for Lorentz–polarization factors but not for absorption. Structure solved by *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) and full-matrix least-squares refinement on *F* to $R=0{\cdot}068$ with unit weight for F_o. Towards the end of refinement, an analysis of the results of least-squares refinement showed a systematic increase in $w|\Delta F|^2$ with increasing ranges of values of $|F_o|$. With $\sigma(F)\simeq|\Delta F|$ (Seal & Roy, 1981), the following empirical values of $\sigma(F)$ were adopted: for $|F_o|\le4{\cdot}17$, $\sigma(F)=0{\cdot}25|F_o|$; for $4{\cdot}17<|F_o|\le5{\cdot}09$, $\sigma(F)=0{\cdot}18|F_o|$; for $5{\cdot}09<|F_o|\le5{\cdot}84$, $\sigma(F)=0{\cdot}13|F_o|$; for $5{\cdot}84<|F_o|\le7{\cdot}02$, $\sigma(F)=0{\cdot}09|F_o|$; for $7{\cdot}02<|F_o|\le8{\cdot}35$, $\sigma(F)=0{\cdot}7|F_o|$; for $8{\cdot}35<|F_o|\le10{\cdot}69$, $\sigma(F)=0{\cdot}5|F_o|$; for $10{\cdot}69<|F_o|\le13{\cdot}87$, $\sigma(F)=0{\cdot}04|F_o|$; for $|F_o|>13{\cdot}87$, $\sigma(F)=0{\cdot}02|F_o|$. Weights $w=\sigma^{-2}(F)$ with the above empirical values of $\sigma(F)$ were used in subsequent refinements, using only the reflections with $I>3\sigma(I)$. Refinement converged $[(\Delta/\sigma)_{max}=0{\cdot}83]$ at $R=0{\cdot}051$, $wR=0{\cdot}042$ with $S=2{\cdot}742$, and the values of $w|\Delta F|^2$ showed no systematic variation. All the H atoms were located from ΔF syntheses and refined isotropically. Final clean difference Fourier map showed max. and min. peaks of $0{\cdot}2$ to $-0{\cdot}2$ e Å^{-3} respectively. Atomic scattering factors were from *International Tables for X-ray Crystallography* (1974). All calculations carried out on a Burroughs 6700 computer. Programs used from *XRAYARC* (*World List of Crystallographic Computer Programs,* 1973), modified for the B6700 computer.

Discussion. Final atomic parameters are given in Table 1,[*] bond lengths and some dihedral angles of the molecule in Table 2. Fig. 1 gives a sketch of 5-NO$_2$-AraU showing the numbering convention with all non-H-atom bond angles. Fig. 2(*a*) shows a view of the molecular configuration with minimum overlap and Fig. 2(*b*) presents a view of the packing of 5-NO$_2$-AraU.

The bond distances and angles in the base moiety are similar to those averaged from 5-nitro-1-(β-D-ribosyluronic acid)–uracil monohydrate (Srikrishnan &

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[*] Lists of structure factors, anisotropic thermal parameters, H-atom parameters, intermolecular short contacts and least-squares planes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44418 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Parthasarathy, 1978), 1-β-D-arabinofuranosyluracil (Tollin, Wilson & Young, 1973) and 5-hydroxyuridine (Thewalt & Bugg, 1973), but in 5-nitrouridine monohydrate (Egert, Lindner, Hillen & Gassen, 1977) the C(6)—N(1) bond is shorter by 0·05 Å and C(6)—C(5) and N(1)—C(2) are longer by 0·03 Å in the nucleoside. The length of the C(4)—O(9) bond, 1·22 (5) Å, is the same as it is in 5-nitrouracil (Craven, 1967) and the other uridine nucleosides and differs from that of 3-deazauridine (1·34 Å) (Schwalbe, Gassen & Saenger, 1972). The pyrimidine base is almost planar, the maximum deviation of the ring atoms from the mean ring plane being 0·039 (4) Å. The O(2) and O(8) atoms are on the same side of the mean plane with maximum deviations of 0·26 (3) Å while O(9) and O(4) atoms are on the other side of the mean plane with maximum deviations of 0·15 (3) Å. The C(1′)—O(4′) bond is shorter by 0·046 (4) Å than the C(4′)—O(4′) bond, as is usually found in nucleoside structures.

The furanose has the C(2′)-*endo* (^2E) conformation, with C(2′) and C(3′) deviating from the plane of the other three atoms in the sugar moiety by 0·579 and 0·046 Å respectively. The O(2′) atom is displaced 1·592 Å from the mean plane of the furanose ring, but O(3′) is displaced (−1·55 Å) on the side opposite to C(5′). The sugar pucker is similar to that in the related structures 5′-N$_3$-AraC (Biswas, Banerjee & Saenger, 1987), AraU (Tollin, Wilson & Young, 1973), 5-iodouridine (Rahaman & Wilson, 1970), deoxy nucleosides bromodeoxyuridine (Iball, Morgan & Wilson, 1966), iododeoxyuridine (Camerman & Trotter, 1965), chlorodeoxyuridine (Young & Morris, 1973), 5-nitro-1-(β-D-ribosyluronic acid)-uracil monohydrate (Srikrishnan & Parthasarathy, 1978) and differs from that observed in 1-β-D-arabinofuranosyl-4-thiouracil (Saenger, 1972) and 5-nitrouridine monohydrate (Egert, Lindner, Hillen & Gassen, 1977) where the puckering is C(3′)-*endo* (^3E).

The conformation of the C(5′)—O(5′) bond relative to the furanose ring is *gauche* to both the C(4′)—O(4′) and C(4′)—C(3′) bonds. The *gauche–gauche* (Sundaralingam, 1965) conformation is that most commonly found in nucleosides and nucleotides. In 5-NO$_2$-AraU the torsion angle O(5′)—C(5′)—C(4′)—O(4′) is −67·5° and O(5′)—C(5′)—C(4′)—C(3′) is 51·5°. The torsion angles around the sugar and base are listed in Table 2.

The angle between the mean plane of the pyrimidine base and the sugar ring is 57·14°. The conformation about the glycosidic bond is *anti* with a torsion angle C(6)—N(1)—C(1′)—O(4′) of 27·8°. The hydrophilic zones are arranged in channels between stacks of bases. The crystal structure consists of successive layers of sugars and bases, with the layers running parallel to the *bc* plane (Fig. 2) as in the case of 5-hydroxyuridine and 4-thiouridine hydrate (Saenger & Scheit, 1970).

Besides van der Waal repulsive interactions, the crystal structure is stabilized by a series of short

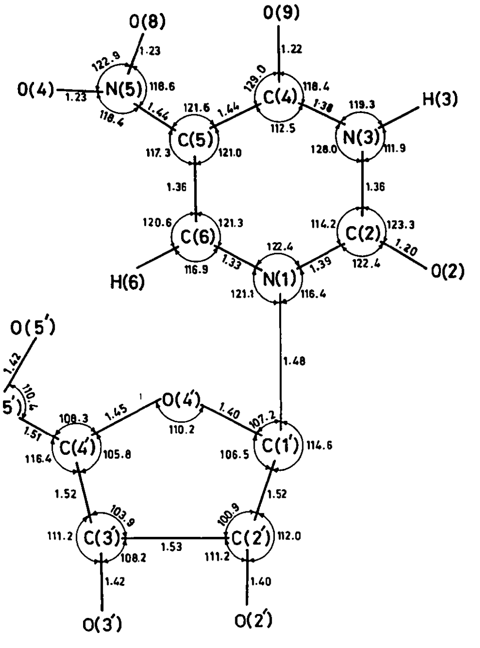

Fig. 1. A sketch of 5-NO$_2$-AraU showing numbering convention and bond angles (°) of non-H atoms. E.s.d.'s are 0·3–0·4°.

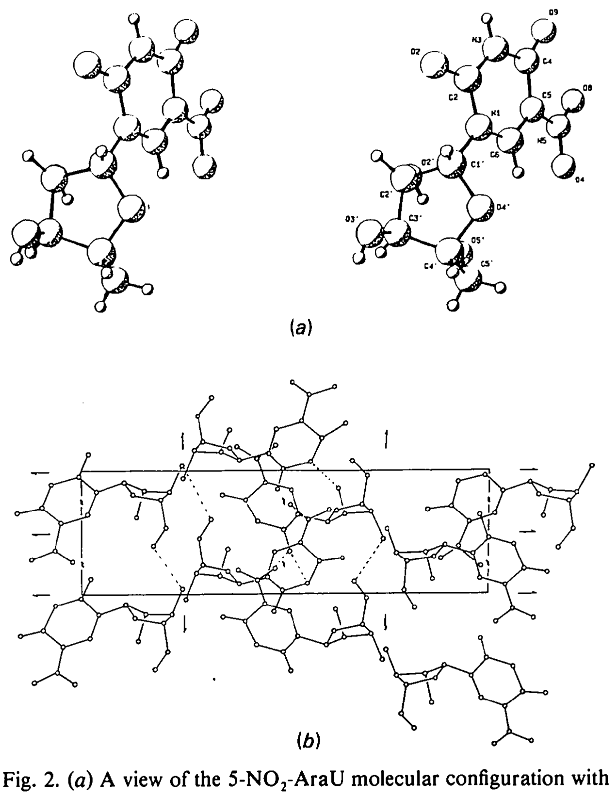

Fig. 2. (*a*) A view of the 5-NO$_2$-AraU molecular configuration with minimum overlap. (*b*) View down **a** of the molecules in the cell.

contacts and hydrogen bonds. Interestingly, a bifurcated hydrogen bond is found between O(2′) and N(3) at $(-x-\frac{1}{2}, -y-1, z-\frac{1}{2})$ of lengths 2·86 Å. Other noted short interactions are between O(3′) and O(5′) at $(x, y, z+1)$ of 2·72 Å; O(2) of the pyrimidine ring with N(3) $(-x-\frac{1}{2}, -y-1, z+\frac{1}{2})$ of 2·88 Å; O(4) with C(2) $(x, y, z-1)$ of 2·99 Å; O(4) with O(2) $(x, y, z-1)$ of 3·08 Å, respectively.

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Structure of the High-Melting Polymorph of the 1/1 Addition Compound Between Benzoic Acid and 2,4-Diamino-5-(3,4,5-trimethoxybenzyl)pyrimidinium Benzoate (Trimethoprim Monobenzoate–Benzoic Acid 1/1 Complex, Form I)*

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Abstract. $C_{14}H_{19}N_4O_3^+.C_7H_5O_2^-.C_7H_6O_2$, $M_r = 534\cdot57$, triclinic, $P\bar{1}$, $a = 14\cdot059\ (2)$, $b = 14\cdot791\ (2)$, $c = 13\cdot262\ (1)$ Å, $\alpha = 96\cdot10\ (1)$, $\beta = 90\cdot50\ (2)$, $\gamma = 93\cdot61\ (2)^\circ$, $V = 2736\cdot4\ (6)$ Å^3, $Z = 4$, $D_m = 1\cdot30$, $D_x = 1\cdot298$ g cm^{-3}, $\lambda(\text{Mo } K\alpha) = 0\cdot7107$ Å, $\mu = 0\cdot883$ cm^{-1}, $F(000) = 1128$, $T = 296$ K, $R = 0\cdot0474$ for 3449 observed reflections. The asymmetric unit of the crystal of the high-melting polymorph (form I) contains two independent systems. The trimethoprim cation shows a bonding pattern to the benzoate anion different from that found in the previously described low-melting polymorph (form II). The benzoic acid molecule in system *A* is linked to the benzoate anion through a strong O—H···O hydrogen bond [2·488 (3) Å] while benzoic acid in system *B* links the two independent systems in the asymmetric unit. Molecular packing is achieved *via* N—H···N and N—H···O hydrogen bonds involving all the amino-pyrimidine N atoms and benzoic acid O atoms not engaged in intraionic and intramolecular bonds. The two crystal forms exhibit conformational polymorphism due to different conformations of trimethoprim cations around the methylene bridge.

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