

## References

- BATS, J. W. & COPPENS, P. (1977). *Acta Cryst.* **B33**, 1542–1548.
- CARON, A. & DONOHUE, J. (1969). *Acta Cryst.* **B25**, 404.
- COPPENS, P. & HAMILTON, W. C. (1970). *Acta Cryst.* **A26**, 71–83.
- FINGER, L. (1972). A Fortran IV computer program for structure factor calculation and least-squares refinement of crystal structures. Carnegie Inst. of Washington.
- FRITCHIE, C. J. (1966). *Acta Cryst.* **20**, 27–36.
- HAMILTON, W. C. (1965). *Acta Cryst.* **18**, 502–510.
- HELLNER, E. (1977). *Acta Cryst.* **B33**, 3813–3816.
- International Tables for X-ray Crystallography* (1974). Vol. IV. Birmingham: Kynoch Press.
- JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
- MULLEN, D. & HELLNER, E. (1977). *Acta Cryst.* **B33**, 3816–3822.
- PRYOR, A. & SANGER, P. L. (1970). *Acta Cryst.* **A26**, 543–558.
- ZACHARIASEN, W. H. (1967). *Acta Cryst.* **23**, 558–564.

*Acta Cryst.* (1978). **B34**, 1627–1630

## Antiviral Nucleic Acid Derivatives. II.\* Crystal Structure of 5-Vinyl-2'-deoxyuridine

BY T. A. HAMOR, M. K. O'LEARY AND R. T. WALKER

*Chemistry Department, The University, Birmingham B15 2TT, England*

(Received 12 October 1977; accepted 18 November 1977)

$C_{11}H_{14}N_2O_5$  is orthorhombic, space group  $P2_12_12_1$ , with  $a = 4.861$  (5),  $b = 16.70$  (1),  $c = 14.01$  (1) Å,  $Z = 4$ . The structure was refined by least squares calculations to  $R = 5.9\%$  for 748 observed counter amplitudes. The pyrimidine ring is planar with the vinyl group inclined at  $12^\circ$  to it and the glycosidic torsion angle is  $39^\circ$  (*anti* conformation). The sugar ring has the C(3')-*exo* conformation, and the arrangement about C(4')–C(5') is such that O(5') is oriented *gauche-trans* with respect to O(1') and C(3').

### Introduction

The 5-substituted uracils and the corresponding nucleosides have recently attracted attention because of their antiviral activity. 5-Vinyl-2'-deoxyuridine first appeared in the literature in 1975, having been prepared by two different routes (Sharma & Bobek, 1975; Barwölf & Langen, 1975*a*). Since then studies have been made of its antiviral characteristics (Cheng, Domin, Sharma & Bobek, 1976; de Clercq, 1977) and also its mode of action (Barwölf & Langen, 1975*b*).

Interest in the title compound in this laboratory has stemmed not only from its potential antiviral activity, but also from its ability to replace thymidine in the DNA of some organisms (Jones & Walker, 1975).

### Experimental

Suitable crystals were obtained from methanol–water. Cell dimensions and intensities were measured on a Stoe two-circle computer-controlled diffractometer with

graphite-monochromated Mo  $K\alpha$  radiation and a scintillation counter. The  $\omega$ -scan technique was employed with a scan speed of  $0.6^\circ \text{ min}^{-1}$  and 30 s background counts at the beginning and end of each scan. For layers  $0kl$  and  $1kl$ ,  $\Delta\omega$  was  $1.4^\circ$  and for the higher layers it was calculated from  $(A + B \sin \mu / \tan \theta')^\circ$ , where  $\mu$  is the equi-inclination angle,  $2\theta'$  is the azimuth angle, and  $A$  and  $B$  were assigned the values of 1.0 and 0.5. 1644 reflexions were scanned, of which 748 [ $I > 2.5\sigma(I)$ ] were used in the analysis.

### Crystal data

$C_{11}H_{14}N_2O_5$ ,  $M_r = 254.2$ , orthorhombic,  $a = 4.861$  (5),  $b = 16.70$  (1),  $c = 14.01$  (1) Å,  $U = 1137$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.485 \text{ g cm}^{-3}$ ,  $F(000) = 536$ . Systematic absences:  $h00$ ,  $h$  odd;  $0k0$ ,  $k$  odd;  $00l$ ,  $l$  odd. Space group  $P2_12_12_1$ . Mo  $K\alpha$  radiation,  $\lambda = 0.71069$  Å;  $\mu(\text{Mo } K\alpha) = 0.75 \text{ cm}^{-1}$ .

### Structure determination

The structure was solved by direct methods with *SHELX* (Sheldrick, 1975), the  $E$  map revealing the

\* Part I: Hamor, O'Leary & Walker [*Acta Cryst.* (1977), **B33**, 1218–1223].

Table 1. Fractional atomic coordinates ( $\times 10^4$ )

	<i>x</i>	<i>y</i>	<i>z</i>
C(2)	1442 (18)	707 (4)	3114 (5)
C(4)	4807 (17)	1184 (5)	4293 (5)
C(5)	5592 (17)	349 (4)	4493 (5)
C(6)	4199 (16)	-220 (4)	4001 (5)
C(7)	7719 (19)	190 (5)	5188 (6)
C(8)	8398 (25)	-466 (6)	5582 (7)
C(1')	737 (18)	-732 (4)	2828 (5)
C(2')	2334 (19)	-1086 (5)	1995 (6)
C(3')	1464 (16)	-1964 (4)	2028 (5)
C(4')	1260 (17)	-2125 (4)	3094 (5)
C(5')	3925 (18)	-2390 (5)	3523 (6)
N(1)	2213 (13)	-66 (3)	3344 (4)
N(3)	2833 (15)	1282 (3)	3620 (5)
O(2)	-338 (18)	875 (3)	2538 (4)
O(4)	5852 (13)	1767 (3)	4696 (4)
O(1')	278 (10)	-1366 (3)	3497 (3)
O(3')	-1181 (13)	-2077 (3)	1622 (4)
O(5')	3577 (14)	-2387 (5)	4550 (4)
H N(3)	2075 (179)	1699 (46)	3522 (55)
H C(7)	8568 (180)	608 (44)	5444 (56)
H C(8)	7503 (184)	-910 (48)	5483 (57)
H2 C(8)	10079 (194)	-594 (39)	6051 (51)
H C(6)	4660 (184)	-785 (43)	4190 (49)
H C(1')	-841 (209)	-514 (47)	2628 (58)
H1 C(2')	4234 (202)	-1008 (43)	2050 (55)
H2 C(2')	1975 (182)	-798 (43)	1383 (52)
H C(3')	2675 (180)	-2359 (45)	1771 (56)
H C(4')	-216 (198)	-2539 (40)	3193 (53)
H1 C(5')	5532 (179)	-1952 (43)	3372 (51)
H2 C(5')	4492 (173)	-2949 (43)	3277 (51)
H O(3')	-795 (232)	-1936 (48)	1168 (59)
H O(5')	4666 (225)	-2369 (57)	4830 (74)

positions of all C, N and O atoms. Least-squares refinement of atomic parameters, initially with isotropic and finally anisotropic temperature factors, reduced *R* to 8.5%. At this stage H atoms were located from a difference synthesis and in subsequent least-squares calculations their coordinates (but not their temperature factors) were refined. Refinement was terminated when all calculated shifts were  $<0.25\sigma$  and *R* was

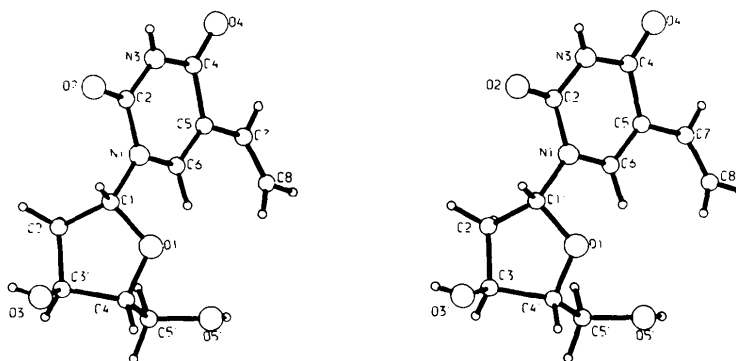


Fig. 1. Stereoscopic view of the nucleoside.

Table 2. Molecular dimensions

## (a) Bond lengths (Å)

N(1)—C(2)	1.38 (1)	N(1)—C(1')	1.51 (1)
C(2)—O(2)	1.22 (1)	C(1')—C(2')	1.52 (2)
C(2)—N(3)	1.37 (1)	C(2')—C(3')	1.53 (2)
N(3)—C(4)	1.36 (1)	C(3')—O(3')	1.42 (1)
C(4)—O(4)	1.23 (1)	C(3')—C(4')	1.52 (1)
C(4)—C(5)	1.47 (1)	C(4')—C(5')	1.50 (2)
C(5)—C(7)	1.44 (2)	C(5')—O(5')	1.45 (1)
C(7)—C(8)	1.27 (2)	C(4')—O(1')	1.47 (1)
C(5)—C(6)	1.36 (1)	O(1')—C(1')	1.43 (1)
C(6)—N(1)	1.36 (1)		
N(3)—H N(3)	0.8 (1)	C(2')—H2 C(2')	1.0 (1)
C(6)—H C(6)	1.0 (1)	C(3')—H C(3')	1.0 (1)
C(7)—H C(7)	0.9 (1)	O(3')—H O(3')	0.7 (1)
C(8)—H C(8)	0.9 (1)	C(4')—H C(4')	1.0 (1)
C(8)—H2 C(8)	1.1 (1)	C(5')—H1 C(5')	1.1 (1)
C(1')—H C(1')	0.9 (1)	C(5')—H2 C(5')	1.0 (1)
C(2')—H1 C(2')	0.9 (1)	O(5')—H O(5')	0.7 (1)

## (b) Bond angles; mean estimated standard deviation 1.0°

C(6)—N(1)—C(2)	121.8	C(5)—C(6)—N(1)	124.6
C(6)—N(1)—C(1')	121.6	N(1)—C(1')—O(1')	107.8
C(2)—N(1)—C(1')	116.6	N(1)—C(1')—C(2')	114.3
N(1)—C(2)—N(3)	113.6	O(1')—C(1')—C(2')	107.1
N(1)—C(2)—O(2)	124.3	C(1')—C(2')—C(3')	102.0
N(3)—C(2)—O(2)	122.1	C(2')—C(3')—C(4')	102.6
C(2)—N(3)—C(4)	128.6	C(2')—C(3')—O(3')	111.6
N(3)—C(4)—C(5)	115.5	O(3')—C(3')—C(4')	108.1
N(3)—C(4)—O(4)	120.9	C(3')—C(4')—C(5')	113.1
O(4)—C(4)—C(5)	123.6	C(3')—C(4')—O(1')	104.3
C(4)—C(5)—C(6)	116.0	O(1')—C(4')—C(5')	112.5
C(4)—C(5)—C(7)	119.2	C(4')—C(5')—O(5')	107.3
C(6)—C(5)—C(7)	124.8	C(4')—O(1')—C(1')	109.6
C(5)—C(7)—C(8)	129.6		

## (c) Selected torsion angles. The sign convention is as defined by Klyne &amp; Prelog (1960).

C(1')—C(2')—C(3')—C(4')	-36.9
C(2')—C(3')—C(4')—O(1')	34.3
C(3')—C(4')—O(1')—C(1')	-18.3
C(4')—O(1')—C(1')—C(2')	-5.5
O(1')—C(1')—C(2')—C(3')	26.7
O(1')—C(4')—C(5')—O(5')	52.4
C(3')—C(4')—C(5')—O(5')	170.2
O(3')—C(3')—C(4')—C(5')	153.9
O(1')—C(1')—N(1)—C(6)	38.7

5.9%. Final atomic coordinates are in Table 1.\* The weighting scheme was  $w = 1/[\sigma^2(F)]$ , where  $\sigma(F)$  is the standard deviation in the observed amplitudes based on counting statistics.

### Results and discussion

The stereochemistry of the molecule is illustrated in Fig. 1, which also shows the numbering of the atoms. Molecular dimensions are in Table 2 and the results of mean-plane calculations in Table 3.

#### Packing and hydrogen bonding

The arrangement of the molecules in the unit cell is shown in Fig. 2, and the shorter intermolecular contact distances are listed in Table 4. All the H atoms linked to N and O take part in hydrogen bonding forming an infinite three-dimensional network.

O(5') of the reference molecule donates a H atom

\* Lists of observed and calculated structure amplitudes and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33254 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. Mean-plane calculations with deviations (Å) of atoms from least-squares planes

Distances marked with an asterisk refer to atoms defining the plane.

	(I)	(II)	(III)	(IV)	(V)
N(1)	0.007*		0.859	1.110	1.116
C(2)	-0.006*				
N(3)	-0.002*				
C(4)	0.009*	0.286			
C(5)	-0.009*	0*			
C(6)	0.001*	-0.236			
O(2)	0.010				
O(4)	0.027				
C(7)	-0.025	0*			
C(8)	0.177	0*			
C(1')	0.027		-0.104*	-0.030*	0*
C(2')			0.207*	0.018*	0.139
C(3')			-0.233*	-0.572	-0.462
C(4')			0.169*	-0.019*	0*
O(1')			-0.038*	0.031*	0*
C(5')			1.573	1.317	1.337
O(5')			1.901	1.827	1.759

Equations of planes ( $x$ ,  $y$  and  $z$  are in Å)

$$\begin{aligned} \text{(I)} & 0.6974x + 0.0335y - 0.7160z = -2.6011 \\ \text{(II)} & 0.6503x - 0.1758y - 0.7390z = -2.9871 \\ \text{(III)} & -0.9401x - 0.0395y - 0.3386z = -1.7343 \\ \text{(IV)} & -0.8739x - 0.1639y - 0.4576z = -1.9555 \\ \text{(V)} & -0.9027x - 0.1624y - 0.3985z = -1.7039 \end{aligned}$$

Interplanar angles

$$\begin{array}{ll} \text{(I)-(II)} & 12.4^\circ \\ \text{(I)-(III)} & 65.5^\circ \end{array}$$

forming a hydrogen bond with O(5') at  $\frac{1}{2} + x$ ,  $-\frac{1}{2} - y$ ,  $1 - z$ , of length 2.76 Å. O(5') also acts as an acceptor in the symmetry-related hydrogen bond with O(5') at  $-\frac{1}{2} + x$ ,  $-\frac{1}{2} - y$ ,  $1 - z$ . The other hydrogen bonds involve interactions O(3')-H...O(4) and N(3)-H...O(3') so that O(3') also acts both as a donor and as an acceptor. All other contacts correspond to normal van der Waals interactions.

#### Stereochemistry and conformation of the molecule

(a) *The pyrimidine base.* The pyrimidine ring is planar to well within the limits of experimental error. The substituents all lie close to the plane of the ring. This is somewhat unusual since C(1') is generally displaced by *ca* 0.1 Å from this plane in other nucleo-

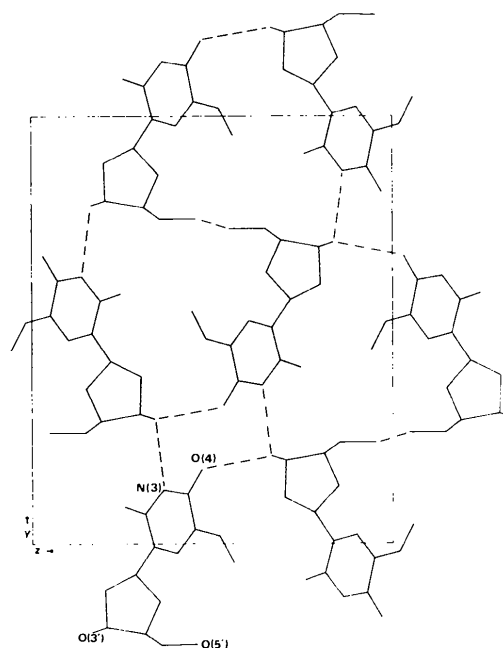


Fig. 2. The contents of the unit cell projected along  $x$ . Hydrogen bonds are shown as dashed lines.

Table 4. The shorter intermolecular contact distances (Å)

For contacts between the heavier atoms distances up to 3.4 Å are listed; for those involving H atoms, distances up to 2.3 Å are shown.

O(3')...O(4')	2.75	N(3)...O(3 <sup>iii</sup> )	2.87
O(5')...O(5 <sup>ii</sup> )	2.76	O(2)...C(8')	3.19
H O(3')...O(4')	2.08	H N(3)...O(3 <sup>iii</sup> )	2.10
H O(5')...O(5 <sup>ii</sup> )	2.13		

Symmetry code

$$\begin{array}{lll} \text{(i)} & \frac{1}{2} - x, & -y, & -\frac{1}{2} + z \\ \text{(ii)} & \frac{1}{2} + x, & -\frac{1}{2} - y, & 1 - z \\ \text{(iii)} & -x, & \frac{1}{2} + y, & \frac{1}{2} - z \end{array}$$

sides (Young & Morris, 1973). The vinyl group is inclined at  $12^\circ$  to the pyrimidine ring.

Bond lengths and angles agree quite well with averaged values for uridines published by Voet & Rich (1970) and with those in thymidine (Young, Tollin & Wilson, 1969), 2'-deoxyuridine (Rahman & Wilson, 1972) and 5-chloro-2'-deoxyuridine (Young & Morris, 1973). Our bond-length and angle measurements are not, however, sufficiently accurate (e.s.d.'s 0.01–0.02 Å for lengths,  $1^\circ$  for angles) to discuss these in detail. In particular it does not seem possible to decide whether there is any conjugation between the vinyl group and the pyrimidine ring, or whether the shortness (1.27 Å) of C(7)–C(8) is significant.

(b) *The deoxyribose residue.* To a good approximation the sugar ring can be described in terms of the envelope conformation. C(1'), C(2'), C(4') and O(1') are coplanar to within  $\pm 0.03$  Å and C(3') is displaced by 0.57 Å from the four-atom plane, on the opposite side to C(5'). The sugar therefore has the C(3')-*exo* conformation,  ${}_3E$  (Sundaralingam, 1975). Alternatively its conformation can be described as a half-chair, C(2') and C(3') being displaced by 0.14 and 0.46 Å on opposite sides of the three-atom plane defined by C(1'), C(4') and O(1'), denoted  ${}_3T^2$  (Sundaralingam, 1975). The  ${}_3E$  pucker is unusual for the sugar rings of 2'-deoxy nucleosides, although thymidine and deoxyadenosine (Watson, Sutor & Tollin, 1965) also have this conformation.

The conformation about C(4')–C(5') is *gauche-trans* as defined by torsion angles O(1')–C(4')–C(5')–O(5') =  $52^\circ$  and C(3')–C(4')–C(5')–O(5') =  $170^\circ$ . A similar conformation occurs in thymidine and 5-chloro- and 5-bromo-2'-deoxyuridine (Iball, Morgan & Wilson, 1966). Bond lengths and angles agree to within the limits of experimental error with those determined for the deoxyribose residues of other nucleosides. As usual, C(1')–O(1') is shorter than C(4')–O(1'), the difference in this case being 0.04 Å.

(c) *The glycosidic link.* The conformation about the glycosidic bond is *anti* (Sundaralingam, 1969), the torsion angle O(1')–C(1')–N(1)–C(6) being  $39^\circ$ . This compares with 26 and  $28^\circ$  for the two independent molecules in the crystal structure of 2'-deoxyuridine,  $39^\circ$  for thymidine and with angles in the range  $42$ – $63^\circ$  for the 5-halogeno-2'-deoxyuridines.

(d) *Overall conformation.* The main conformational parameters which define the shape of the molecule are the torsion angles about the glycosidic bond and C(4')–C(5') of the sugar residue, and the nature of the sugar-ring pucker. In the present case, in standard nomenclature (Sundaralingam, 1975), the conformation is *anti, gauche-trans (t)*, C(3')-*exo* ( ${}_3E$  or  ${}_3T^2$ ). Of related nucleosides only thymidine has this overall conformation.\*

We thank Professor A. S. Jones for his interest and helpful discussions and the Science Research Council for a studentship (to MKO'L).

\* Crystals of thymidine and the title compound are virtually isomorphous. Our atomic coordinates are related to those published for thymidine ( $x_T, y_T, z_T$ ) by  $x \sim \frac{1}{4} - x_T, y \sim \frac{1}{4} - z_T, z \sim \frac{1}{4} - y_T$ .

### References

- BARWÖLFF, D. & LANGEN, P. (1975a). *Nucleic Acids Res. Spec. Publ.* No. 1, pp. S29–S31.
- BARWÖLFF, D. & LANGEN, P. (1975b). *Biochem. Pharmacol.* **24**, 1907–1910.
- CHENG, Y. C., DOMIN, B. A., SHARMA, R. A. & BOBEK, M. (1976). *Antimicrob. Agents Chemother.* **10**, 119–122.
- CLERCQ, E. DE (1977). Personal communication.
- IBALL, J., MORGAN, C. H. & WILSON, H. R. (1966). *Proc. R. Soc. London Ser. A*, **295**, 320–333.
- JONES, A. S. & WALKER, R. T. (1975). *Nucleic Acids Res. Spec. Publ.* No. 1, S1–S4.
- KLYNE, W. & PRELOG, V. (1960). *Experientia*, **16**, 521–523.
- RAHMAN, A. & WILSON, H. R. (1972). *Acta Cryst.* **B28**, 2260–2270.
- SHARMA, R. A. & BOBEK, M. (1975). *J. Org. Chem.* **40**, 2377–2379.
- SHELDRIK, G. M. (1975). *SHELX*. Program for crystal structure determination. Univ. of Cambridge.
- SUNDARALINGAM, M. (1969). *Biopolymers*, **7**, 821–860.
- SUNDARALINGAM, M. (1975). *Ann. NY Acad. Sci.* **255**, 3–42.
- VOET, D. & RICH, A. (1970). *Prog. Nucleic Acid Res. Mol. Biol.* **10**, 183–265.
- WATSON, D. G., SUTOR, D. J. & TOLLIN, P. (1965). *Acta Cryst.* **19**, 111–124.
- YOUNG, D. W. & MORRIS, E. M. (1973). *Acta Cryst.* **B29**, 1259–1264.
- YOUNG, D. W., TOLLIN, P. & WILSON, H. R. (1969). *Acta Cryst.* **B25**, 1423–1432.