Tetrahedron Vol. 36, pp. 1269 to 1273
Pergamon Press Ltd., 1980. Printed in Great Britain

THE SYNTHESIS AND CRYSTAL STRUCTURE OF 5-ACETYL-2'-DEOXYURIDINE

P. J. BARR, PONGCHAN CHANANONT, T. A. HAMOR, A. S. JONES, M. K. O'LEARY and R. T. WALKER
Department of Chemistry, University of Birmingham, Birmingham B15 2TT, England

(*Received in UK* 21 *June* 1979)

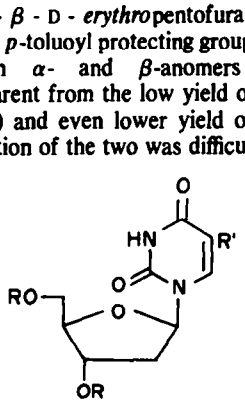
Abstract—5 - Acetyl - 2' - deoxyuridine (1) has been synthesised by treating 2' - deoxy - 5 - ethynyluridine with dilute sulphuric acid. Condensation of the trimethylsilyl derivative of 5-acetyluracil with 2-deox-3, 5-di-*O*-*p*-toluoyl-α-D-*erythro*pentofuranosyl chloride gave a mixture of α- and β-anomeric blocked nucleosides from which the α-anomer was isolated and the *p*-toluoyl groups removed to give 5 - acetyl - 1 - (α - D - 2- deoxy*erythro*pentofuranosyl) uracil. Only a poor yield of the β-anomer (1) was obtained by this procedure. The UV spectra and m.p. obtained for 1 differed from the values quoted in the literature. The crystals of 1 are monoclinic, space group $P2_1$, with $a = 9.525$, $b = 12.16$, $c = 5.22$ Å, $\beta = 92.03°$ and two molecules in the unit cell. The structure was refined by least-squares calculations to R 3.4% for 1426 observed counter amplitudes. The pyrimidine ring is essentially planar with the acetyl group inclined at 6° to it. The sugar ring has the highly unusual C(4')-*exo* conformation and the arrangement about C(4')–C(5') is such that O(5') is oriented *gauche* with respect to both O(1') and C(3'). The glycosidic torsion angle O(1')–C(1')–N(1)–C(6) is 56° (*anti* conformation).

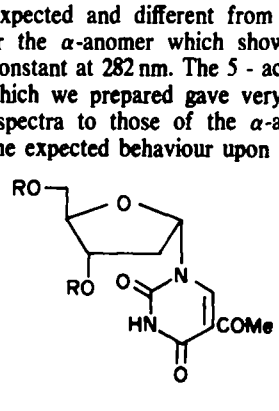
5 - Substituted - 2' - deoxyuridines are currently of great interest because many of them are antiviral agents. A large number of substituents at the 5-position will confer on 2'-deoxyuridine activity against herpes viruses. Thus bromo-, iodo-, nitro-, ethyl-, propyl-, vinyl-, trifluoromethyl-, propynyloxy-, ethynyl-, *E*-(2-bromovinyl)- and a number of other groups are all effective in this respect to a greater or lesser extent.[1] We have been concerned with the synthesis of some of these compounds, particularly the vinyl-, ethynyl- and *E*-(2-bromovinyl)- derivatives.[2] Our route to these has been via 5-acetyluracil, so that we have been engaged also in the synthesis of 5-acetyl-2'-deoxyuridine. It is noteworthy that this compound shows no activity against herpes viruses[3] so that we thought that it would be of interest to determine the crystal structure of this compound and to compare it with the structures of the antiviral vinyl- and ethynyl-derivatives which we have already published[4,5] and with other 5-substituted 2'-deoxyuridines whose crystal structures are known.

A synthesis of 5 - acetyl - 2' - deoxyuridine (1) has been reported by Kampf *et al.*[6] They obtained the compound by the standard procedure of condensing the trimethylsilyl derivative of 5-acetyluracil with 2 - deoxy - 3,5 - di - *O* - *p* - toluoyl - β - D - *erythro*pentofuranosyl chloride and removing the *p*-toluoyl protecting groups. In the condensation, both α- and β-anomers are produced and it was apparent from the low yield of the β-anomer obtained (20%) and even lower yield of the α-anomer that the separation of the two was difficult.

We have carried out this condensation but under slightly different conditions and have found that the compound most easily obtained was the α-anomer (2, R = *p*-toluoyl). The blocking groups were removed from this to give 5 - acetyl - 1 - (2 - deoxy - α - D - *erythro*pentofuranosyl) uracil (2, R = H), the structure of which has already been established by X-ray crystallography.[7] Only a low yield of the protected β-anomer (3) was obtained and this was deprotected in the usual way to give a small amount of the required product (1), which was characterised by comparison with material prepared by an alternative and more satisfactory route. This was to treat 2' - deoxy - 5 - ethynyluridine (4) with dilute aqueous sulphuric acid to give the required compound in 98% yield. We have already reported the synthesis of 2' - deoxy - 5 - ethynyluridine[8] and although this also involves the separation of the α- and β-anomers of the blocked nucleosides, in this case it is much easier to obtain a satisfactory yield of the required β-anomer.

In their report on the synthesis of 5 - acetyl - 2' - deoxyuridine, Kampf *et al.*[6] give results on the UV absorption spectrum of this compound which are difficult to explain. They report that the λ_{max} shifts from 282 nm to 274 nm when a neutral solution is made alkaline. This is quite unexpected and different from the results they report for the α-anomer which shows that the λ_{max} remains constant at 282 nm. The 5 - acetyl - 2' - deoxyuridine which we prepared gave very similar UV absorption spectra to those of the α-anomer and both showed the expected behaviour upon changing the pH.





2

1 R' = —COMe, R = H
3 R' = —COMe, R = *p*-toluoyl-
4 R' = —C≡CH, R = H

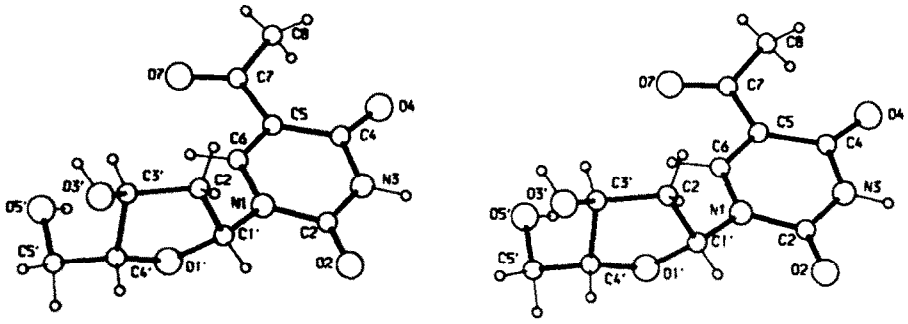


Fig. 1. Stereoscopic view of the nucleoside (1).

These results and the fact that the melting point of our product is different from that reported by Kampf *et al.* makes it questionable whether these workers obtained the correct compound.

The solid state conformation of 1 and the atom numbering are shown in Fig. 1. Atomic positional and thermal parameters are in Table 1, and molecular dimensions, and the results of mean-plane calculations are in Tables 2 and 3. Estimated standard deviations are 0.003–0.004 Å for bond lengths and 0.2° for bond angles.

The pyrimidine ring is planar to within ±0.02 Å. The substituents O(2), O(4) and C(7) all lie within 0.1 Å of the ring plane but C(1') is displaced by a greater amount (0.21 Å). Deviations of up to 0.15 Å for C(1') have, however, been reported[4] for other 5-substituted 2'-deoxyuridines. The acetyl group is accurately planar and is inclined at 6° to the pyrimidine ring.

Bond lengths and angles in the pyrimidine ring system generally agree closely with those found[7] for the α-anomer. In the latter structure, comparison of bond lengths with averaged values for uridines published by Voet and Rich[9] indicated possible π-electron conjugation between O(7) of the acetyl group and N(1). The evidence for such conjugation is less marked in 1, the formal double bond C(5)–C(6) being 0.010 Å shorter, and N(1)–C(6) 0.015 Å longer than in the α-anomer, and closer to the averaged values of Voet and Rich. The largest bond length differences between the α- and β-anomers, however, occur in the other two bonds involving N(1). N(1)–C(2) is longer by 0.025 Å and N(1)–C(1') is shorter by 0.042 Å than in the α-anomer. The length of the glycosidic bond agrees closely with the expected value,[9] but N(1)–C(2) is longer by 0.032 Å.

Comparison with 2' - deoxy - 5 - ethynyluridine[5] shows that only two bonds in the base residue differ by > 0.010 Å. These are N(1)–C(2) and N(3)–C(4), which are both significantly (by 0.019 and 0.026 Å) longer in 1. Detailed comparison of bond lengths with the 5 - vinyl - derivative is not possible as sufficiently accurate measurements could not be obtained.[4] Endocyclic bond angles deviate by a maximum of 1.3° from those in the 5 - ethynyl - derivative.

The sugar ring can be described in terms of the envelope conformation. C(1'), C(2'), C(3') and O(1') are coplanar to within ±0.025 Å and C(4') is displaced by 0.51 Å from the plane of these four atoms. Alternatively

Table 1. Fractional atomic coordinates and thermal parameters (both × 10^4). Estimated standard deviations are in parentheses. Isotropic temperature factors are in the form $\exp[-2\pi^2 U(2\sin\theta/\lambda)^2]$. Anisotropic temperature factors are in the form $\exp[-2\pi^2(U_{11}h^2a^{*2}+\ldots+2U_{12}hka^*b^*)]$.

	x	y	z	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N(1)	-1476(2)	2070	5244(4)	201(8)	297(9)	426(10)	-83(8)	47(7)	-7(7)
C(2)	-52(2)	2070(2)	4620(4)	194(8)	291(11)	380(11)	-1(9)	24(8)	7(7)
O(2)	393(2)	1500(2)	2919(4)	298(8)	525(11)	526(10)	-187(9)	93(8)	8(8)
N(3)	780(2)	2754(2)	6095(4)	206(8)	312(10)	453(10)	-39(9)	53(7)	-14(7)
C(4)	367(2)	3458(2)	8052(5)	308(11)	267(10)	361(11)	-6(9)	9(9)	-22(9)
O(4)	1269(2)	3993(2)	9218(4)	338(9)	488(11)	636(12)	-159(10)	-29(8)	-91(9)
C(5)	-1142(2)	3464(3)	8456(4)	261(10)	295(11)	339(10)	18(9)	48(8)	16(9)
C(6)	-1970(2)	2758(3)	7063(5)	249(10)	288(11)	388(11)	-12(9)	78(8)	1(8)
C(7)	-1862(3)	4185(3)	10318(4)	492(13)	268(11)	310(10)	18(9)	86(9)	33(10)
O(7)	-3153(2)	4164(2)	10354(4)	417(10)	534(12)	552(11)	-116(10)	145(8)	115(9)
C(8)	-1027(4)	4917(3)	12063(6)	655(20)	442(16)	402(15)	-106(13)	74(14)	-36(15)
C(1')	-2414(2)	1245(3)	4034(5)	219(10)	304(12)	521(14)	-91(11)	-16(9)	8(9)
O(1')	-3599(2)	1820(2)	2970(3)	234(7)	315(8)	444(8)	71(7)	7(6)	-27(6)
C(2')	-2985(3)	396(3)	5889(9)	350(13)	347(14)	919(24)	196(16)	-217(15)	-66(12)
C(3')	-4575(2)	476(3)	5632(4)	337(11)	265(11)	312(10)	5(9)	42(8)	3(9)
O(3')	-5235(2)	-578(2)	5505(4)	397(10)	327(9)	517(11)	44(8)	150(8)	-66(8)
C(4')	-4793(2)	1098(2)	3094(4)	257(10)	267(10)	285(10)	-16(8)	27(8)	-23(8)
C(5')	-6119(3)	1783(3)	2833(6)	271(11)	377(13)	541(14)	3(13)	-49(9)	12(10)
O(5')	-6324(2)	2482(2)	4959(4)	287(8)	314(9)	756(14)	-65(9)	116(8)	15(7)

	x	y	z	U		x	y	z	U
H[N(3)]	1750(42)	2797(33)	5728(83)	668(108)	H2[C(2')]	-2694(44)	-306(39)	5685(92)	724(124)
H[C(6)]	-3025(32)	2702(27)	7244(60)	391(75)	H[C(3')]	-4855(29)	953(27)	7009(64)	378(74)
H1[C(8)]	-564(54)	5552(43)	11167(113)	923(146)	H[O(3')]	-5728(43)	-577(36)	6814(91)	678(116)
H2[C(8)]	-1573(60)	5262(49)	13016(110)	964(172)	H[C(4')]	-4770(26)	572(23)	1750(54)	256(62)
H3[C(8)]	-270(54)	4532(45)	12729(117)	922(162)	H1[C(5')]	-6829(33)	1281(28)	2552(63)	403(78)
H[C(1')]	-1961(33)	932(31)	2760(71)	432(82)	H2[C(5')]	-6074(34)	2211(32)	1121(73)	544(93)
H1[C(2')]	-2642(53)	517(42)	7546(114)	899(151)	H[O(5')]	-5734(39)	3025(33)	4995(70)	529(95)

Table 2. Molecular dimensions

(a) Bond lengths (Å)

N(1)-C(2)	1.406(2)	C(6)-N(1)	1.362(3)
C(2)-O(2)	1.214(3)	N(1)-C(1')	1.471(3)
C(2)-N(3)	1.368(3)	C(1')-C(2')	1.529(4)
N(3)-C(4)	1.400(3)	C(2')-C(3')	1.519(4)
C(4)-O(4)	1.222(3)	C(3')-O(3')	1.427(3)
C(4)-C(5)	1.460(3)	C(3')-C(4')	1.533(3)
C(5)-C(7)	1.493(3)	C(4')-C(5')	1.515(3)
C(7)-O(7)	1.231(3)	C(5')-O(5')	1.417(4)
C(7)-C(8)	1.484(4)	C(4')-O(1')	1.441(3)
C(5)-C(6)	1.359(3)	O(1')-C(1')	1.424(3)
N(3)-H[N(3)]	0.95(4)	C(4')-H[C(4')]	0.95(3)
C(6)-H[C(6)]	1.02(3)	C(5')-H1[C(5')]	0.92(3)
C(1')-H[C(1')]	0.89(4)	C(5')-H2[C(5')]	1.04(4)
C(2')-H1[C(2')]	0.93(6)	O(5')-H[O(5')]	0.87(4)
C(2')-H2[C(2')]	0.91(5)	C(8)-H1[C(8)]	1.01(6)
C(3')-H[C(3')]	0.97(3)	C(8)-H2[C(8)]	0.84(7)
O(3')-H[O(3')]	0.84(5)	C(8)-H3[C(8)]	0.92(6)

(b) Bond angles (deg.); estimated standard deviations are 0.2°

C(6)-N(1)-C(2)	121.4	C(8)-C(7)-O(7)	121.1
C(6)-N(1)-C(1')	119.9	C(5)-C(6)-N(1)	123.6
C(2)-N(1)-C(1')	118.5	N(1)-C(1')-O(1')	107.0
N(1)-C(2)-N(3)	114.5	N(1)-C(1')-C(2')	114.4
N(1)-C(2)-O(2)	122.3	C(2')-C(1')-O(1')	106.5
N(3)-C(2)-O(2)	123.3	C(1')-C(2')-C(3')	106.1
C(2)-N(3)-C(4)	127.6	C(2')-C(3')-O(3')	112.5
N(3)-C(4)-C(5)	114.3	C(2')-C(3')-C(4')	102.2
N(3)-C(4)-O(4)	118.6	O(3')-C(3')-C(4')	110.9
O(4)-C(4)-C(5)	127.1	C(3')-C(4')-C(5')	115.8
C(4)-C(5)-C(7)	125.0	C(3')-C(4')-O(1')	104.9
C(4)-C(5)-C(6)	118.3	O(1')-C(4')-C(5')	108.5
C(6)-C(5)-C(7)	116.6	C(4')-C(5')-O(5')	113.4
C(5)-C(7)-O(7)	118.6	C(4')-O(1')-C(1')	107.4
C(5)-C(7)-C(8)	120.2		

(c) Selected torsion angles (deg.); mean estimated standard deviation 0.4°

C(1')-C(2')-C(3')-C(4')	16.8
C(2')-C(3')-C(4')-O(1')	-32.3
C(3')-C(4')-O(1')-C(1')	36.9
C(4')-O(1')-C(1')-C(2')	-25.6
O(1')-C(1')-C(2')-C(3')	4.3
O(1')-C(4')-C(5')-O(5')	-68.0
C(3')-C(4')-C(5')-O(5')	49.6
O(3')-C(3')-C(4')-C(5')	87.9
O(3')-C(3')-C(4')-O(1')	-152.5
O(1')-C(1')-N(1)-C(6)	55.9
O(7)-C(7)-C(5)-C(4)	175.2
O(7)-C(7)-C(5)-C(6)	-5.4
N(1)-C(1')-O(1')-C(4')	-148.5

it can be described as a half-chair, C(4') and O(1') being displaced by 0.43 and 0.10 Å on opposite sides of the three-atom plane defined by C(1'), C(2') and C(3'). In either case, C(4') is displaced from the reference plane on the opposite side to N(1). The sugar, therefore, has the C(4')-*exo* pucker, ${}_4E$, or ${}_4T^{\circ}$. In this conformation, C(5') lies quite close to the reference plane (Table 3). The ${}_4T^{\circ}$ sugar conformation is very unusual and does not occur in any of the nucleoside or nucleotide crystal structures listed in the comprehensive tabulations of Sundaralingam.[10] The related ${}^{\circ}T_4$ conformation has, however, been found in the crystal structure of disodium deoxyguanosine monophosphate tetrahydrate, and the ${}_4T^3$ conformation in a number of 3', 5'-cyclic nucleotides.[10] The arrangement about C(4')–C(5') is *gauche-gauche* (g^+), torsion angle C(3')–C(4')–C(5')–O(5') being 50°.

Bond lengths in the sugar residue are generally in good agreement with those determined in other nucleosides. As usual C(4')–O(1') is longer than O(1')–C(1'), the difference in this structure being 0.017 Å. Bond angles, apart from C(1')–C(2')–C(3'), also agree well with those determined in other nucleosides. This angle is some 4–6° greater than is generally found with deoxyribose rings in nucleosides, which, although also adopting envelope conformations, have C(2') or C(3') as the out-of-plane atom. The difference in C(1')–C(2')–C(3') angle is probably related to the difference in ring pucker.[11]

The glycosidic torsion angle O(1')–C(1')–N(1)–C(6) is 56°, so that the conformation is *anti*. This conformation predominates in nucleoside and nucleotide crystal structures.[12] It is adopted by all the 5 - substituted - 2' - deoxyuridines whose crystal structures are known.[5] In these nucleosides the glycosidic torsion angles vary from 19 to 63° and the present value of 56° falls within this range. In the ethynyl- and vinyl-derivatives, however, the glycosidic torsion angles, at 19 and 39°, respectively, are at the lower end of the range.

The arrangement of the molecules in the crystal is shown in Fig. 2. All three H atoms linked to N or O take

Table 3. Mean-plane calculations. 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)	0.023*		0.936	1.112	1.131
C(2)	−0.023*				
N(3)	0.000*				
C(4)	0.023*				
C(5)	−0.024*	−0.001*			
C(6)	0.001*				
O(2)	−0.069				
O(4)	0.076				
C(7)	−0.088	0.003*			
O(7)	−0.214	−0.001*			
C(8)	−0.011	−0.001*			
C(1')	0.205		−0.079*	−0.025*	0*
C(2')			−0.048*	0.023*	0*
C(3')			0.151*	−0.015*	0*
C(4')			−0.214*	−0.514	−0.434
O(1')			0.190*	0.016*	0.102
C(5')			0.463	−0.070	0.066
O(5')			1.867	1.324	1.460

Equations of planes (x, y and z are fractional coordinates relative to the cell axes)

(I) $-1.2221x + 8.7666y - 3.5293z = 0.1675$
(II) $-0.2775x + 8.8655y - 3.5622z = 0.0894$
(III) $1.4070x - 8.5518y - 3.6553z = -2.9584$
(IV) $-0.0110x - 8.0006y - 3.9283z = -2.6029$
(V) $0.1886x - 8.3810y - 3.7821z = -2.6150$

Interplanar angles

(I) - (II) 5.7° (I) - (III) 87.0°

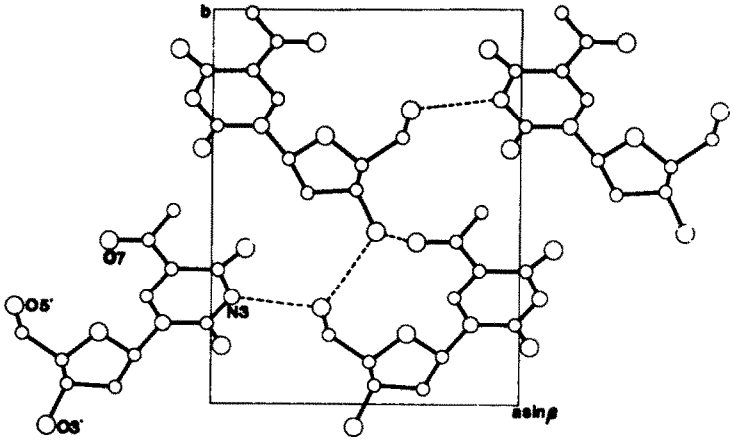


Fig. 2. The contents of the unit cell viewed in projection along z. Hydrogen bonds are shown as dashed lines.

part in intermolecular H-bonding. O(3') of the reference molecule donates a H atom forming a H-bond with the carbonyl O(7) of the acetyl group of the molecule at $-1-x, -(1/2)+y, 2-z$, of length 2.71 Å. O(3') also acts as acceptor in a H-bond with O(5'), of the molecule at $-1-x, -(1/2)+y, 1-z$, of length 2.80 Å. The third H-bond involves N(3) as donor and O(5') of the molecule at $1+x, y, z$ as acceptor, the N···O distance being 2.86 Å. In each case the H-atom lies close to the donor-acceptor line.

Compound 1 differs from many other 5 - substituted - 2' - deoxyuridines in its lack of antiviral activity.[3] The structural features which distinguish it from the other eight 5 - substituted - 2' - deoxy - β - uridines whose

crystal structures are known, are the slightly greater lengths of bonds N(1)–C(2) and N(3)–C(4), and the unusual conformation of the sugar residue. We do not, however, consider it possible to postulate any structure-activity relationship on the basis of the data available at this time.

EXPERIMENTAL

The condensation of 5-acetyluracil with 2 - deoxy - 3, 5 - di - O - p - toluoyl - β - D - erythropentofuranosyl chloride. 5-Acetyluracil (6.4 g)[13] was added to hexamethyldisilazane (30 ml) and the mixture boiled under reflux until a clear soln was obtained (24 hr). The excess of hexamethyldisilazane was distilled off and the residual oil dissolved in dry acetonitrile (100 ml). To this soln there was added a suspension of 2 - deoxy - 3, 5 - di - *O* - *p* - toluoyl - α - D - *erythro*pentosyl chloride (16 g)[14] in dry acetonitrile (100 ml). The mixture was stirred for 2–5 days at room temp after which time a ppt had formed. This was filtered off to give 3.8 g of material (shown as described below to be the blocked α-nucleoside). Work up of the acetonitrile soln gave a further quantity (11 g) of material which was a mixture of blocked α and β-nucleosides. Several attempts to separate the anomers by chromatography in various solvent systems failed. Subsequent separation of the unblocked anomers as described below made it possible to ascertain that in this condensation reaction the blocked anomers had been produced in ratio α/β of 3.7:1. Later experiments using $HgBr_2$ as a catalyst improved the amount of the β-anomer produced, but the best ratio was α/β of 1.7:1.

A portion of the ppt (blocked α-anomer) was dissolved in dry MeOH (150 ml) containing NaOMe (520 mg) and the soln boiled under reflux for 2 hr. It was then neutralised by the addition of Dowex 50 (H^+) ion exchange resin, the resin was removed and well washed with MeOH-water (1:1) until no more UV-absorbing material was removed. The combined soln and washings was evaporated to a small volume and allowed to stand. The crystalline material which separated out was filtered off to give 5 - *acetyl* - 1 - (2 - *deoxy* - α - D - erythro*pentofuranosyl*-)*uracil* (Found: C, 48.7; H, 5.2; N, 10.2. Calc for $C_{11}H_{14}N_2O_6$: C, 48.9; H, 5.2; N, 10.4%); λ_{max} 229 nm (ε, 11,280), 288 nm (ε, 13,300), λ_{min} 250 nm (ε, 1543) in ethanol; λ_{max} 230 nm (ε, 10,200), 283 nm (ε, 13,000), λ_{min} 249 nm (ε, 2250) at pH 1; λ_{max} 235 nm (ε, 11,000), 288 nm (ε, 9500), λ_{min} 261 nm at pH 14. δ(d⁶DMSO) 1.70–2.10 (2H, m, H–2'), 2.50 (singlet partly obscured by solvent,–$COCH_3$), 3.38 (2H, t, H-5'), 4.20 (2H, t, H-3', H-4'), 5.21 (1H, t, 5'–OH), 4.80 (1H, d, 3'–OH), 6.05 (1H, d, H-1'), 8.58 (1H, s, H-6), 11.5 ppm (1H, s, –NH).

A portion of the mixture of blocked α- and β-anomers was treated with NaOMe in MeOH as described for the α-anomer. The resulting mixture of anomers was separated on silica gel plates by development five times with EtOAc–MeOH (94:6). The anomers were eluted from the silica and shown to be present in the ratio of α/β of 18:7. The slower running component was identical by chromatography and by UV spectroscopy with the crystalline α-anomer and the faster component was similarly identical with 5-acetyl-2'-deoxyuridine prepared by the method described below.

5 - Acetyl - 2' - deoxyuridine. 2' - Deoxy - 5 - ethynyluridine (200 mg) was dissolved in 0.1 M H_2SO_4 (10 ml) and the soln allowed to stand at room temp for 7 days. The soln was brought to pH6 by the use of a strongly basic ion exchange resin. The resin was filtered off, well washed with aqueous MeOH (50 ml) and the filtrate and washings evaporated to give a white powder of almost pure 5' - acetyl - 2' - deoxyuridine (209 mg, 98% yield) which upon crystallisation from EtOH water gave white prisms, m.p. 156–158° (*cf* 160–170°[6]) (Found: C, 48.7; H, 5.5; N, 10.1. Calc. for $C_{11}H_{14}N_2O_6$: C, 48.9; H, 5.2; N, 10.4%); λ_{max} 232 nm (ε, 10,170), 284 nm (ε, 13,450), λ_{min} 251 nm (ε, 2450) at pH 1; λ_{max} 235 nm (sh) (ε, 9500), 287 nm (ε, 9950), λ_{min} 260 nm (ε, 3,750) at pH 13. δ(d⁶DMSO) 2.18 (2–H, m, H–2'), 2.45 (3–H, s, –CH_3), 3.58 (2H, m, H–5'), 3.87 (1H, m, H–4'), 4.25 (1H, m, H – 3'), 5.08 (1H, bs, 5'-OH), 5.35 (1H, bs, 3'–OH), 6.10 (1H, t, H – 1'), 8.37 ppm (1H, s, H–6).

X-Ray analysis of 5 - acetyl - 2' - deoxyuridine. A crystal of dimensions 0.2 × 0.3 × 0.1 mm^3 mounted about *z* was used for all X-ray measurements. After preliminary examination by oscillation and Weissenberg photographs, final unit-cell dimensions and intensities were measured on a Stoe two-circle diffractometer with graphite-monochromated Mo-K_α radiation. The ω-scan technique was employed with a scan speed of 0.6° min^{-1} and 30 s stationary background measurements at each end of the scan. For layers *hk*0 and *hk*1 the scan-width was 1.4° and for the higher layers it was calculated from (0.9 + 0.8 sin μ/tan θ')° where μ is the equi-inclination angle and 2θ' is the azimuth angle. Reflections were scanned within the range $0.1 < \sin\theta/\lambda < 0.65$, and of these 1426 ($I > 2.5\sigma(I)$) were considered to be observed. The intensities of three zero-layer reflections, checked after each layer of data collection to monitor the stability of the system, showed no significant variation with time.

The structure was solved by direct methods with SHELX.[15] An E map based on the 301 highest E values revealed the positions of all 19 C, N and O atoms. Hydrogen atoms were located from a subsequent difference Fourier synthesis. Refinement was carried out by full-matrix least-squares calculations and in the final cycles of refinement coordinates and anisotropic thermal parameters were refined for the heavier atoms and coordinates and isotropic temp. factors for the H-atoms. The calculations were terminated when all calculated shifts were $< 0.1\sigma$ and *R* was 3.4% for the 1426 observed amplitudes. The weighting scheme was $w = 1/[\sigma^2(F)]$, where σ(F) is the standard deviation in the observed amplitudes based on counting statistics.

Crystal data for 5 - acetyl - 2' - deoxyuridine. Monoclinic, $a = 9.525(10)$, $b = 12.16(1)$, $c = 5.22(1)$ Å, $\beta = 92.03(5)°$, $U = 604.2$ Å^3, $Z = 2$, $D_c = 1.486$ g cm^{-3}. $F(000) = 284$. Mo-*K*α radiation, $\lambda = 0.71069$ Å. Absorption coefficient = 0.8 cm^{-1}. Space group $P2_1$ or $P2_{1/m}$ from systematic absences, 0*k*0 when *k* is odd. $P2_1$ established as a result of the analysis.

Acknowledgements—We thank the University of Birmingham and the British Council for financial support (to P.C.) and the Science Research Council for the award of studentships (to P.J.B. and M.K.O'L.). Computations were carried out on the University of Birmingham ICL 1906A computer, and we thank the staff of the Computer Centre for their assistance.

REFERENCES

[1]E. De Clercq and P. F. Torrence, *J. Carbohydrates, Nucleosides, Nucleotides* **5**, 187 (1978).
[2]R. T. Walker, P. J. Barr, E. De Clercq, J. Descampes, A. S. Jones and P. Serafinowski, *Nucleic Acides Research*, Special Publication No. 4, 5103 (1978).
[3]E. De Clercq, Personal communication.
[4]T. A. Hamor, M. K. O'Leary and R. T. Walker, *Acta Cryst.* **B34**, 1627 (1978).
[5]P. J. Barr, T. A. Hamor and R. T. Walker, *Ibid.* **B34**, 2799 (1978), and refs cited.
[6]A. Kampf, C. J. Pillar, W. J. Woodford and M. P. Mertes, *J. Med. Chem.* **19**, 909 (1976).
[7]T. A. Hamor, M. K. O'Leary and R. T. Walker, *Acta Cryst.* **B33**, 1218 (1977).
[8]P. J. Barr, A. S. Jones, P. Serafinowski and R. T. Walker, *J. Chem. Soc.* Perkin Transactions I, 1263 (1978).
[9]D. Voet and A. Rich, *Progr. Nucleic Acid Res. Mol. Biol.* **10**, 183 (1970).
[10]M. Sundaralingam, *Ann. N.Y. Acad. Sci.* **255**, 3 (1975).
[11]M. Sundaralingam, *J. Am. Chem. Soc.* **87**, 599 (1965).
[12]A. Lo, E. Shefter and T. G. Cochran, *J. Pharm. Sci.* **64**, 1707 (1975).
[13]R. K. Ralph, G. Shaw and R. N. Naylor, *J. Chem. Soc.* 1169 (1959); J. H. Dewar and G. Shaw, *Ibid.* 3254 (1961).
[14]C. C. Bhat, *Synthetic Procedures in Nucleic Acid Chemistry* (Edited by W. W. Zorbach and R. S. Tipson), p. 521. Interscience, New York (1968).
[15]G. M. Sheldrick, SHELX. *Program for crystal structure determination.* University of Cambridge, England (1975).