

- BÜRGI, H. B., DUNITZ, J. D. & SHEFTER, E. (1974). *Acta Cryst.* **B30**, 1517–1527.
- BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1971). *ORXFLS* 3. Report ORNL-59-4-37. Oak Ridge National Laboratory, Tennessee.
- CRUICKSHANK, D. W. J. (1969). *Crystallographic Computing*, p. 195, édité par F. AHMED. Copenhagen: Munksgaard.
- EVANS, D. L. & ROBINSON, W. T. (1977). *Acta Cryst.* **B33**, 2891–2893.
- FOSTER, R. (1973). *Molecular Complexes*, Tome I, p. 191. London: Elck Science.
- FYFE, C. A., HAROLD-SMITH, D. & RIPMEESTER, J. (1976). *J. Chem. Soc. Faraday Trans. 2*, **72**, 2269–2282.
- GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* **A27**, 368–376.
- HERBSTEIN, F. H. (1971). *Perspect. Struct. Chem.* **4**, 166–395.
- International Tables for X-ray Crystallography* (1974). Tome IV. Birmingham: Kynoch Press.
- KUMAKURA, S., IWASAKI, F. & SAITO, Y. (1967). *Bull. Chem. Soc. Jpn*, **40**, 1826–1833.
- MACFARLANE, R. M. & USHIODA, S. (1977). *J. Chem. Phys.* **67**, 3214–3220.
- MARSH, R. E., UBELL, E. & WILCOX, H. E. (1962). *Acta Cryst.* **15**, 35–41.
- PAULING, L. (1960). *The Nature of the Chemical Bond*, 3ème éd. Ithaca: Cornell Univ. Press.
- PONOMAREV, V. I., FILIPENKO, O. S. & ATOVMIAN, L. O. (1976). *Kristallografiya*, **21**, 392–394.
- SHMUELI, U. & GOLDBERG, I. (1973). *Acta Cryst.* **B29**, 2466–2471.
- SHMUELI, U. & GOLDBERG, I. (1974). *Acta Cryst.* **B30**, 573–578.
- STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
- TSUCHIYA, M., MARUMO, F. & SAITO, Y. (1972). *Acta Cryst.* **B28**, 1935–1941.

*Acta Cryst.* (1979). **B35**, 920–923

## U:U Base-Pairs – Crystal Structure and Conformation of 5-Dimethylaminouridine

BY ERNST EGERT AND HANS JÖRG LINDNER

*Fachgebiet Organische Chemie I, Technische Hochschule Darmstadt, Petersenstrasse 22, D-6100 Darmstadt, Federal Republic of Germany*

AND WOLFGANG HILLEN AND HANS GÜNTER GASSEN

*Fachgebiet Biochemie, Technische Hochschule Darmstadt, Petersenstrasse 22, D-6100 Darmstadt, Federal Republic of Germany*

(Received 1 November 1978; accepted 4 January 1979)

### Abstract

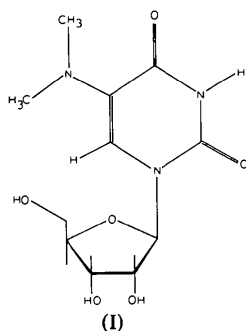
$C_{11}H_{17}N_3O_6$  is monoclinic, space group  $C2$ , with  $a = 16.224$  (6),  $b = 8.349$  (3),  $c = 10.347$  (4) Å,  $\beta = 111.18$  (2)°,  $Z = 4$ . The structure, which was refined to  $R = 0.058$  for 1245 counter reflections, exhibits the influence of an electron-donating 5-substituent on the nucleoside conformation, supporting the results from the structure of 5-aminouridine. The orientation of the base is *anti* ( $\chi = 51.0^\circ$ ); the ribosyl moiety shows a  $C(2')$ -*endo* conformation and a *gauche-trans* arrangement of the  $C(5')$ – $O(5')$  bond. There is no base stacking between adjacent layers parallel to the *ac* plane. Two molecules are connected to each other by their 2-keto and 3-imino groups. These U:U base-pairs are discussed with respect to other nucleosides like 5-

methoxyuridine which amplify the wobble recognition in tRNA's.

### Introduction

In our attempt to clarify the influence of 5-substitution on the structure and function of modified pyrimidine nucleosides, some of which occur in the wobble position of tRNA's, we studied the conformation of crystalline 5-dimethylaminouridine (I). It should demonstrate the influence of an electron-donating substituent on the conformation of the nucleoside, especially on the  $N(1)$ – $C(1')$  and  $C(1')$ – $O(1')$  lengths, to confirm the results obtained from the crystal structure determination of 5-aminouridine (Egert, Lindner,

Hillen & Gassen, 1978). Furthermore, the steric hindrance by one methyl group protecting the adjacent carbonyl O atom must be seen in comparison with 5-methoxyuridine which amplifies the wobble recognition by the formation of U:U base-pairs.



### Experimental

1- $\beta$ -D-Ribofuranosyl-5-dimethylaminouracil was synthesized from 5-bromouridine and dimethylamine (Visser, 1968). Crystals were grown from water as colourless monoclinic blocks. The space group is  $C2$ , as determined by the systematic absences of reflections with  $h + k$  odd. Crystal data are summarized in Table 1. Intensities were collected on a Stoe four-circle diffractometer (Mo  $K\alpha$  radiation) equipped with a graphite monochromator. 2389 reflections with  $\theta < 25^\circ$  were measured in the  $\theta$ - $2\theta$  scan mode. The data were corrected for background and for Lorentz and polarization factors, but not for absorption.

### Structure determination and refinement

The structure was solved with *SHELX 76* (Sheldrick, 1976) which uses scattering factors from *International Tables for X-ray Crystallography* (1974).

Isotropic refinement with unit weights, including 1245 symmetry-independent reflections having  $|F| > 3\sigma_F$ , reduced  $R$  to 0.142; this dropped to 0.081 with the inclusion of anisotropic temperature factors. At this stage 12 of the 17 H atoms were located by a difference synthesis. Weights  $w = 1/\sigma(|F|)^2$  were introduced, and further refinement with fixed H atom temperature factors yielded the positions of the five

remaining H atoms and finally converged at  $R = 0.058$ . None of the positional parameters of the heavy atoms (Table 2) shifted more than  $0.04\sigma$  in the last cycle.\*

### Results and discussion

#### Structure of the base

The pyrimidine ring is not quite planar (Table 3), showing a standard deviation of the ring atoms of  $\sigma = 0.039$  Å with noticeable deviations of the adjacent N(3) (0.054 Å) and C(4) (-0.063 Å) in opposite directions. Of the substituents, O(2) and N(5) lie in the plane whereas C(1') (-0.210 Å) and O(4) (-0.237 Å)

\* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34143 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Positional parameters ( $\times 10^4$ , for H  $\times 10^3$ ) and their *e.s.d.*'s

	<i>x</i>	<i>y</i>	<i>z</i>
N(1)	3376 (2)	760	1889 (3)
C(2)	4049 (3)	1108 (8)	3113 (4)
O(2)	4787 (2)	1480 (7)	3190 (3)
N(3)	3814 (2)	993 (8)	4254 (4)
C(4)	3042 (3)	426 (8)	4337 (4)
O(4)	3006 (2)	134 (7)	5477 (3)
C(5)	2323 (3)	214 (8)	2991 (4)
N(5)	1491 (3)	-260 (7)	2981 (4)
C(51)	1106 (4)	761 (9)	3765 (6)
C(52)	835 (3)	-608 (9)	1620 (5)
C(6)	2525 (3)	371 (7)	1847 (4)
C(1')	3572 (3)	712 (7)	616 (4)
C(2')	3525 (3)	-959 (7)	-4 (4)
C(3')	3361 (3)	-570 (7)	-1506 (4)
C(4')	2729 (3)	840 (8)	-1772 (4)
O(1')	2919 (2)	1613 (6)	-424 (3)
O(2')	4247 (2)	-1953 (6)	707 (3)
O(3')	4185 (2)	-135 (6)	-1595 (3)
C(5')	1769 (3)	351 (9)	-2380 (5)
O(5')	1186 (3)	1605 (9)	-2793 (5)
H(N3)	415 (3)	121 (5)	497 (4)
H(C51)	147 (3)	124 (6)	457 (5)
H'(C51)	62 (3)	15 (6)	390 (5)
H''(C51)	70 (3)	190 (7)	293 (5)
H(C52)	28 (3)	-114 (7)	168 (5)
H'(C52)	98 (3)	-146 (6)	99 (5)
H''(C52)	66 (3)	57 (7)	106 (5)
H(C6)	207 (3)	23 (5)	84 (4)
H(C1')	418 (3)	116 (5)	84 (4)
H(C2')	301 (3)	-160 (5)	-5 (4)
H(C3')	310 (3)	-150 (6)	-211 (4)
H(C4')	289 (3)	157 (6)	-237 (5)
H(O2')	463 (3)	-149 (5)	94 (4)
H(O3')	408 (3)	17 (6)	-236 (5)
H(C5')	163 (4)	14 (7)	-154 (5)
H'(C5')	165 (4)	-22 (7)	-345 (5)
H(O5')	108 (4)	208 (9)	-191 (7)

Table 1. Crystal data

Molecular formula: $C_{11}H_{17}N_3O_6$	
$M_r = 287$	
Space group: $C2$	$V = 1306.9$ Å <sup>3</sup>
$a = 16.224$ (6) Å	$Z = 4$
$b = 8.349$ (3)	$\rho_o = 1.47$ Mg m <sup>-3</sup> (floatation)
$c = 10.347$ (4)	$\rho_c = 1.459$
$\beta = 111.18$ (2)°	$\mu = 0.08$ mm <sup>-1</sup>

deviate considerably. N(5) is not planar trigonal but pyramidal; C(52) of the dimethylamino group is situated exactly in the base plane, unlike C(51) which deviates by 1.026 Å (Fig. 1). Thus, the 5-substituent is twisted by nearly 30° relative to the  $\pi$  system, resulting in a reduced  $\pi$ -electron-donating ability. This can be seen from the C(5)—N(5) distance which is longer by 0.038 Å than that in 5-aminouridine. The reason for this distortion is the steric hindrance between the 4-carbonyl and one methyl group which is evident from the short O(4)···H(C51) distance of 2.50 Å and the increased C(5)—C(4)—O(4) angle (Fig. 1).

Table 3. Least-squares planes through the base and ribose moieties, and deviations (Å) of atoms from them

The plane equations in crystal space are of the form  $lx + my + nz = p$ . Atoms which define the planes are marked by an asterisk.

Base				
$l = -0.2728$	N(1)*	-0.036 (6)	C(5)*	0.027 (7)
$m = 0.9613$	C(2)*	-0.001 (7)	N(5)	0.008 (6)
$n = 0.0380$	O(2)	-0.021 (6)	C(51)	1.026 (9)
$p = -0.7481$	N(3)*	0.054 (7)	C(52)	-0.040 (8)
	C(4)*	-0.063 (7)	C(6)*	0.020 (6)
	O(4)	-0.237 (6)	C(1')	-0.210 (6)
Ribose				
$l = 0.7012$	C(1')*	-0.012 (6)		
$m = 0.5776$	C(2')	-0.612 (6)		
$n = -0.4180$	C(3')*	0.011 (6)		
$p = 4.7539$	C(4')*	-0.019 (7)		
	O(1')*	0.020 (5)		

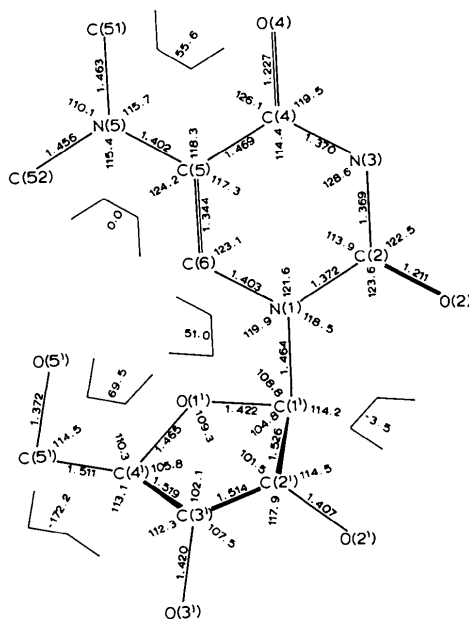


Fig. 1. Bond lengths (Å) and bond and dihedral angles (°) in 5-dimethylaminouridine ( $\sigma_{XX} = 0.006$  Å,  $\sigma_{XXX} = 0.4^\circ$ ; X = C, O, N).

That part of the base [N(1)—C(2)—N(3)—C(4)] which should not be influenced by the 5-substitution correlates well with the base geometry of uridine (Green, Rosenstein, Shiono, Abraham, Trus & Marsh, 1975) whereas the other part deviates noticeably from it with N(1)—C(6) and C(5)—C(4) longer by 0.034 and 0.048 Å respectively. The tendency of these bond-length alterations is the same as that in 5-aminouridine, but the amount is greater for C(4)—C(5) owing to the steric influence of the methyl group and smaller for N(1)—C(6) because of the reduced electronic influence of the 5-substituent.

### Conformation of the ribose

The ribose has a C(2')-endo conformation (Fig. 2) with C(1'), C(3'), C(4') and O(1') in the plane ( $\sigma = 0.016$  Å), while C(2') deviates by 0.61 Å. The orientation at N(1)—C(1') is *anti* with a dihedral angle C(6)—N(1)—C(1')—O(1') of  $\chi = 51.0^\circ$ , supporting the common relation between the puckering of the ribose and the orientation of the base (Sundaralingam, 1969; Egert, Lindner, Hillen & Gassen, 1977).

As is normally found in nucleoside structures, C(1')—O(1') is shorter than C(4')—O(1') but longer (+0.009 Å) than in uridine and accompanied by a shortened N(1)—C(1') distance (-0.026 Å). These bond-length alterations are typical for an electron-donating 5-substituent (Egert, Lindner, Hillen & Gassen, 1978) but are less pronounced than that in 5-aminouridine (+0.019 and -0.063 Å respectively). C(5')—O(5') is *gauche* to O(1')—C(4') and *trans* to C(3')—C(4') with dihedral angles of 69.5 and  $-172.2^\circ$  (Figs. 1 and 2).

### Packing of the molecules

A view down **b** (Fig. 3) illustrates the crystal structure, which is determined by twofold rotation axes parallel to **b** with a centred C face. There are four

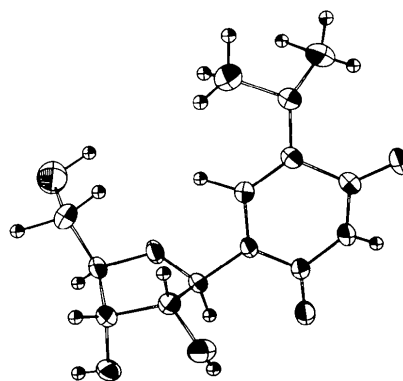


Fig. 2. Structural representation of 5-dimethylaminouridine with the thermal ellipsoids of the heavy atoms.

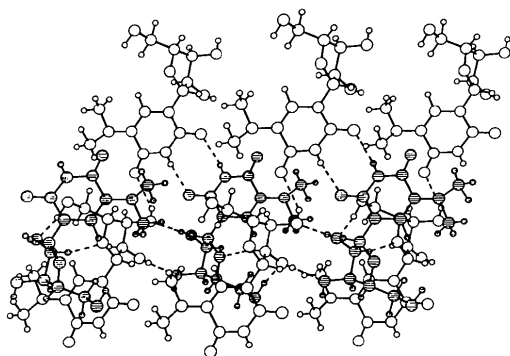


Fig. 3. A view down *b* with *a* horizontal and *c* approximately vertical. The molecules formed by the twofold rotation axes are hatched and the hydrogen bonds are shown as broken lines.

hydrogen bonds (Table 4) formed with participation of all possible donor groups. Three are approximately parallel to the *ac* plane, connecting the molecules in layers which are held together only by the strong O(5')—H...O(2') hydrogen bond supported by a C(2')—H...O(1') interaction. There is no base overlap between adjacent layers, which have a separation of *b*/2, but the bases lying in the *ac* plane are located above the ribosyl moieties of the next layer and *vice versa* (Fig. 3).

By the twofold rotation axes, uridine–uridine base-pairs are formed with the aid of a N(3)—H...O(2) hydrogen bond (Figs. 3 and 4). U:U base-pairs are postulated to occur during the codon–anticodon interaction when modified uridines like 5-methoxyuridine (Hillen, Egert, Lindner, Gassen & Vorbrüggen, 1978) or uridine-5-oxycetic acid (Morikawa, Torii, Iitaka, Tsuboi & Nishimura, 1974) are in the wobble position of tRNA's. This U:U base-pairing represents an amplification of the wobble recognition. Although the orientation of the riboses of U:U base-pairs in the anticodon loop must be different from that found in 5-dimethylaminouridine crystals, the ability of uridine to form non-Watson–Crick base-pairs is demonstrated.

Table 4. List of intermolecular hydrogen bonds (including a C—H...O interaction)

( $\sigma_{X-H} = 0.05 \text{ \AA}$ ,  $\sigma_{H...Y} = 0.07 \text{ \AA}$ ,  $\sigma_{X...Y} = 0.008 \text{ \AA}$ ,  $\sigma_{XH...Y} = 4^\circ$ )

<i>X</i> —H... <i>Y</i>	<i>X</i> —H	H... <i>Y</i>	<i>X</i> ... <i>Y</i>	$\angle X-H...Y$
N(3)—H...O(2)	0.77 Å	2.07 Å	2.824 Å	169°
O(2')—H...O(3')	0.70	2.12	2.815	177
O(3')—H...O(4)	0.79	2.29	2.950	143
O(5')—H...O(2')	1.07	1.72	2.775	169
C(2')—H...O(1')	0.98	2.30	3.248	164

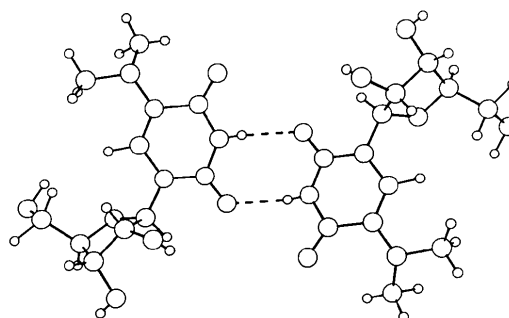


Fig. 4. A uridine–uridine base-pair with the N(3)—H...O(2) bonds shown as broken lines.

Since O(4) is protected sterically by one methyl group the participation of O(2) in base-pairing may be favoured. This may give additional support to the structural explanation of the unusual base-pairing properties of 5-methoxyuridine, O(4) of which is also protected (Hillen, Egert, Lindner & Gassen, 1978).

We thank Dr H. Paulus for the data collection and Mrs E. Rönfeldt for her help in preparing the manuscript. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

#### References

- EGERT, E., LINDNER, H. J., HILLEN, W. & GASSEN, H. G. (1977). *Acta Cryst.* B33, 3704–3707.
- EGERT, E., LINDNER, H. J., HILLEN, W. & GASSEN, H. G. (1978). *Acta Cryst.* B34, 2204–2208.
- GREEN, E. A., ROSENSTEIN, R. D., SHONO, R., ABRAHAM, D. J., TRUS, B. L. & MARSH, R. E. (1975). *Acta Cryst.* B31, 102–107.
- HILLEN, W., EGERT, E., LINDNER, H. J. & GASSEN, H. G. (1978). *FEBS Lett.* 94, 361–364.
- HILLEN, W., EGERT, E., LINDNER, H. J., GASSEN, H. G. & VORBRÜGGEN, H. (1978). *J. Carbohydr. Nucleosides Nucleotides*, 5, 23–32.
- International Tables for X-ray Crystallography* (1974). Vol. IV, pp. 99–102. Birmingham: Kynoch Press.
- MORIKAWA, K., TORII, K., IITAKA, Y., TSUBOI, M. & NISHIMURA, S. (1974). *FEBS Lett.* 48, 279–282.
- SHELDRICK, G. M. (1976). *SHELX 76*. Program for crystal structure determination. Univ. of Cambridge, England.
- SUNDARALINGAM, M. (1969). *Biopolymers*, 7, 821–860.
- VISSER, D. W. (1968). *Synthetic Procedures in Nucleic Acid Chemistry*, Vol. 1, edited by W. W. ZORBACH & R. S. TIPSON, pp. 407–408. New York: Interscience.