

**Structural Studies of Pyrimidine Cyclonucleoside Derivatives. VIII.\* Structure of  
6,3'-Anhydro-1-(4'-O-acetyl-2'-deoxy- $\beta$ -D-xylopyranosyl)-6-methyluracil Hemimethanol,  
 $C_{12}H_{14}N_2O_5 \cdot \frac{1}{2}CH_3OH$**

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**Abstract.**  $M_r = 282.3$ , monoclinic,  $C2$ ,  $a = 14.050$  (2),  $b = 7.066$  (1),  $c = 13.211$  (5) Å,  $\beta = 93.18$  (3)°,  $V = 1309.5$  (6) Å<sup>3</sup>,  $Z = 4$ ,  $D_m = 1.430$  (1),  $D_x = 1.432$  Mg m<sup>-3</sup>,  $\lambda(\text{Cu } K\alpha) = 1.5418$  Å,  $\mu(\text{Cu } K\alpha) = 0.89$  mm<sup>-1</sup>,  $F(000) = 680$ ,  $T = 290$  K,  $R = 0.052$  for 1108 independent reflections. The torsion angle O(5')–C(1')–N(1)–C(6) is 99.1 (4)°, corresponding to the *anti* range in nucleosides. The pyranose moiety shows a chair form.

**Introduction.** Cyclonucleosides, in which base and sugar moieties are cyclized through an O or S atom, have been used to investigate the relationships between the sign and magnitude of Cotton effects and glycosyl torsion angles (Rogers & Ulbricht, 1970; Ikehara, Kaneko, Nakahara, Yamada & Uesugi, 1971; Ueda & Shibuya, 1974) and also to check the validity of the Karplus equation applied to coupling constants of furanose protons (Manor, Saenger, Davies, Jankowski & Rabczenko, 1974; Yamagata, Fujii, Fujiwara, Tomita & Ueda, 1981). Cyclonucleosides cyclized through a C atom, however, are much better model nucleosides for such investigations because the bridged C atom has less effect on the physicochemical properties of the base or the sugar moiety. Therefore, we tried to synthesize several new types of carbon-bridged pyrimidine cyclonucleosides and, in the course of the synthesis of 6,3'-anhydro-1-(2'-deoxy- $\beta$ -D-xylofuranosyl)-6-methyluracil by the radical cyclization of (3'R)-5'-O-benzoyl-5-chloro-3'-iodomethyl-2',3'-dideoxyuridine, an unexpected by-product was obtained whose structure we have determined by X-ray diffraction. The analysis reveals that the title by-product forms a novel pyranose ring instead of the original furanoside.

**Experimental.** Title compound synthesized as described in the previous paper (Ueda, Shuto, Sano, Usui &

Inoue, 1982) and crystallized from methanol solution as colorless plates; density by flotation in  $C_6H_6$ – $CCl_4$  mixture; crystal  $0.2 \times 0.15 \times 0.07$  mm, Rigaku automatic four-circle diffractometer,  $\omega$ – $2\theta$  scanning technique,  $2\theta_{\max} = 125^\circ$ , graphite-monochromatized Cu  $K\alpha$  radiation, unit-cell dimensions by least-squares procedure based on the  $2\theta$  values ( $28^\circ < 2\theta < 48^\circ$ ) of 17 reflections, intensity fluctuation monitored periodically by three reflections (800, 440 and 005): average 0.8%, 1135 independent reflections ( $0 \leq h \leq 16$ ,  $0 \leq k \leq 8$ ,  $-15 \leq l \leq 15$ ), 1109 observed with  $I > 2\sigma(I)$ , Lorentz and polarization but no absorption corrections; structure solved by direct interpretation of the three-dimensional Patterson function: the peaks around the origin indicated the orientations of the uracil ring and the six-membered ring formed by the cyclization (11 atoms), and the positions determined by the  $R$ -map method; using the coordinates with the minimum  $R$  value (0.54), an electron density map revealed the positions of the remaining non-hydrogen atoms; structure refined by full-matrix least squares with anisotropic temperature factors for all non-hydrogen atoms; all H atoms except those of the methanol solvent located from a difference Fourier map; the final refinement including H atoms with isotropic temperature factors reduced  $R$  to 0.052 ( $R_w = 0.078$ ,  $S = 1.26$ );† one intense low-angle reflection (020) influenced by secondary extinction was not included in the refinement; function minimized  $\sum w(|F_o| - k|F_c|)^2$ , where  $w = 1/[\sigma^2(F_o) + 0.02|F_o| + 0.0019|F_o|^2]$  and  $k$  is the scale factor; largest peaks in final difference map:  $0.6 e \text{ \AA}^{-3}$  (about  $1.0 \text{ \AA}$  from methanol molecule),  $(\Delta/\sigma)_{\text{ave}} = 0.08$

† Lists of structure factors, anisotropic thermal parameters, H-atom coordinates, selected torsion angles and the results of the mean-plane calculations have been deposited with the British Library Lending Division as Supplementary Publication No SUP 39035 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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and  $(\Delta/\sigma)_{\max} = 0.25$ , for nonhydrogen atoms; scattering factors from *International Tables for X-ray Crystallography* (1974); program system UNICS (1979) on the ACOS 700 computer of the Crystallographic Research Center, Institute for Protein Research, Osaka University.

Table 1. Final atomic coordinates of non-H atoms ( $\times 10^4$ ) and equivalent isotropic thermal parameters with their estimated standard deviations in parentheses

$$B_{eq} = \frac{1}{3} \sum_i \sum_j \beta_{ij} a_i \cdot a_j$$

	x	y	z	$B_{eq}(\text{\AA}^2)$
O(4)	1013 (2)	9990 (6)	5753 (2)	4.19 (13)
O(2)	912 (2)	9751 (7)	2337 (2)	4.77 (15)
N(1)	2370 (2)	10105 (6)	3165 (2)	3.08 (13)
C(2)	1394 (3)	9883 (8)	3122 (3)	3.58 (17)
N(3)	987 (2)	9830 (6)	4051 (2)	3.42 (14)
C(4)	1469 (3)	9983 (7)	4989 (3)	3.22 (16)
C(5)	2479 (3)	10075 (8)	4965 (3)	3.47 (16)
C(6)	2909 (3)	10153 (7)	4070 (3)	3.00 (15)
C(6')	3975 (3)	10270 (8)	4071 (3)	3.56 (18)
C(1')	2806 (3)	10519 (7)	2180 (3)	3.38 (17)
O(5')	3022 (2)	8832 (5)	1668 (2)	3.89 (13)
C(5')	3749 (3)	7703 (8)	2179 (4)	4.11 (20)
C(4')	4624 (3)	8792 (8)	2511 (3)	3.84 (19)
O(4')	5133 (2)	9228 (6)	1611 (2)	4.25 (14)
C(7')	6085 (3)	9522 (9)	1744 (4)	4.34 (21)
O(7')	6499 (2)	9413 (8)	2563 (3)	5.83 (19)
C(8')	6522 (4)	9922 (13)	780 (4)	6.31 (30)
C(3')	4395 (3)	10649 (8)	3032 (3)	3.44 (17)
C(2')	3668 (3)	11738 (7)	2363 (3)	3.53 (18)
O(Me)	0	9737 (32)	0	13.00 (94)
C(Me)	893 (14)	9628 (34)	142 (11)	12.3 (10)

Table 2. Bond distances ( $\text{\AA}$ ) and angles ( $^\circ$ ) for the nonhydrogen atoms

N(1)—C(2)	1.379 (6)	C(1')—C(2')	1.495 (6)
N(1)—C(6)	1.379 (5)	C(2')—C(3')	1.522 (6)
C(2)—N(3)	1.383 (6)	C(3')—C(4')	1.525 (6)
N(3)—C(4)	1.383 (5)	C(4')—C(5')	1.495 (7)
C(4)—C(5)	1.422 (6)	C(5')—O(5')	1.435 (6)
C(5)—C(6)	1.358 (6)	C(3')—C(6')	1.548 (6)
C(2)—O(2)	1.211 (6)	C(4')—O(4')	1.455 (6)
N(1)—C(1')	1.497 (6)	O(4')—C(7')	1.354 (6)
C(4)—O(4)	1.226 (5)	C(7')—C(8')	1.472 (8)
C(6)—C(6')	1.500 (6)	C(7')—O(7')	1.203 (6)
C(1')—O(5')	1.412 (5)	C(Me)—O(Me)	1.26 (3)
C(2)—N(1)—C(6)	122.4 (4)	O(5')—C(1')—C(2')	111.7 (4)
C(2)—N(1)—C(1')	116.1 (3)	C(1')—C(2')—C(3')	108.3 (4)
C(6)—N(1)—C(1')	121.2 (3)	C(2')—C(3')—C(4')	109.0 (4)
N(1)—C(2)—N(3)	115.2 (4)	C(2')—C(3')—C(6')	109.0 (4)
N(1)—C(2)—O(2)	123.5 (4)	C(4')—C(3')—C(6')	110.6 (4)
N(3)—C(2)—O(2)	121.2 (4)	C(3')—C(4')—C(5')	112.6 (4)
C(2)—N(3)—C(4)	125.9 (4)	C(3')—C(4')—O(4')	108.2 (4)
N(3)—C(4)—C(5)	115.1 (4)	C(5')—C(4')—O(4')	107.6 (4)
N(3)—C(4)—O(4)	119.0 (4)	C(4')—C(5')—O(5')	113.8 (4)
C(5)—C(4)—O(4)	125.9 (4)	C(1')—O(5')—C(5')	114.3 (3)
C(4)—C(5)—C(6)	120.9 (4)	C(6)—C(6')—C(3')	116.0 (4)
N(1)—C(6)—C(5)	120.3 (4)	C(4')—O(4')—C(7')	117.0 (4)
N(1)—C(6)—C(6')	120.1 (4)	O(4')—C(7')—O(7')	122.1 (5)
C(5)—C(6)—C(6')	119.6 (4)	O(4')—C(7')—C(8')	112.0 (4)
N(1)—C(1')—O(5')	111.1 (3)	O(7')—C(7')—C(8')	125.9 (5)
N(1)—C(1')—C(2')	109.8 (4)		

**Discussion.** Tables 1 and 2 give the final atomic parameters and the bond distances and angles, respectively. Fig. 1 is an ORTEPII (Johnson, 1976) stereodrawing of the molecular conformation and Fig. 2 shows the molecular packing projected along the  $b$  axis.

The bond distances and angles of the base moiety agree very well with standard values (Taylor & Kennard, 1982). The pyrimidine ring is essentially planar and the maximum atom deviation from the mean plane is 0.032 (6)  $\text{\AA}$  for C(4). The orientation of the base moiety is *anti*, with the torsion angle O(5')—C(1')—N(1)—C(6) 99.1 (4) $^\circ$ . The pyranose ring shows a chair conformation, which is slightly distorted from the typical chair form found in sucrose; *i.e.* the mean deviation from the average absolute endocyclic torsion angle (55.6 $^\circ$ ) in sucrose (Brown & Levy, 1973) is 5 $^\circ$ , reflecting the strain caused by the cyclization between C(6) in the uracil moiety and C(3') in the pyranose ring. The newly formed six-membered heterocycle has an envelope conformation with C(2') displaced 0.772 (6)  $\text{\AA}$  from the plane through the remaining five atoms.

In this crystal no base stacking is observed, but one N(3)—H...O(4) hydrogen bond of length 2.838 (5)  $\text{\AA}$  forms a dimer between adjacent molecules related by a twofold rotation axis. This kind of hydrogen-bonded pairing between uracil residues has been found in several uracil derivatives (Voet & Rich, 1970).

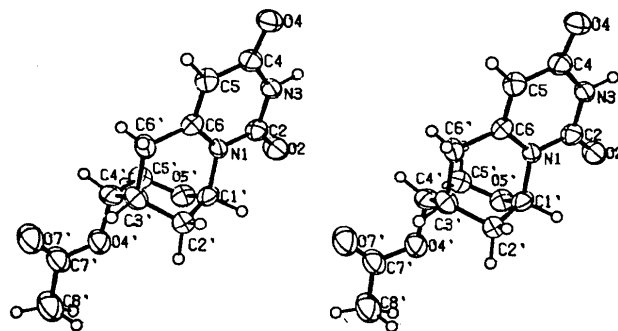


Fig. 1. Stereoview of the molecular conformation and atom numbering.

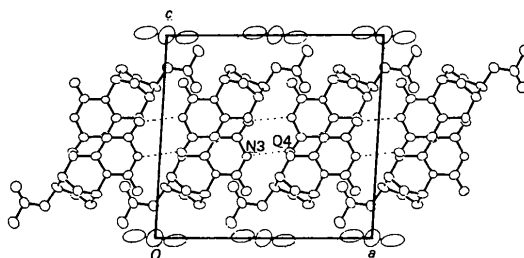


Fig. 2. Molecular packing viewed down the  $b$  axis. Dotted lines indicate the hydrogen bonds.

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## 2-Methoxymethoxybenzoic Acid, C<sub>9</sub>H<sub>10</sub>O<sub>4</sub>\*

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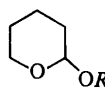
**Abstract.**  $M_r = 182.18$ , triclinic,  $P\bar{1}$ ,  $a = 4.964$  (1),  $b = 7.918$  (2),  $c = 11.777$  (3) Å,  $\alpha = 99.99$  (2),  $\beta = 91.61$  (2),  $\gamma = 106.15$  (2)°,  $U = 436.5$  Å<sup>3</sup>,  $Z = 2$ ,  $D_x = 1.39$  g cm<sup>-3</sup>,  $M_o K\alpha$ ,  $\lambda = 0.71069$  Å,  $\mu = 0.1$  mm<sup>-1</sup>,  $F(000) = 192$ ,  $T = 293$  K,  $R = 0.062$  for 1532 unique reflections. The carboxylic acid groups are paired by hydrogen bonding, as is usual. The crystal structure does not reflect the unusual reactivity of the compound towards acetal hydrolysis.

**Introduction.** We are interested in correlations between bond length and reactivity. In both axial and equatorial series of tetrahydropyranyl acetals (1) the length of the exocyclic C–OR bond increases with increasing electron withdrawal in the R group (Jones & Kirby, 1979, 1984), and we find a simple linear correlation between the length of the bond and the ease with which it is broken in hydrolysis.

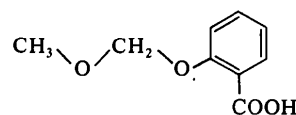
We are currently examining a large number of different systems, and have so far found evidence for variable (C–O and P–O) bond lengths and similar correlations with reactivity in nine out of ten series of compounds (Allen & Kirby, 1984; Jones & Kirby, 1984). Another system of interest is the simplest series of acetals, MeOCH<sub>2</sub>OR: we recently reported the crystal structure of methoxymethoxy-2,4-dinitro-

benzene (Jones, Sheldrick, Glenn & Kirby, 1983), and are working on other compounds in this series.

If we can establish relationships between bond length and normal reactivity, it becomes of interest to look at compounds which show abnormal reactivity. One class of particular interest is that of compounds which undergo intramolecular reactions, and we have found linear relationships between reactivity and interatomic distances in two series of sulphonamides and carboxylic esters, which undergo intramolecular nucleophilic and general base catalysis, respectively (Jager, Graafland, Schenk, Kirby & Engberts, 1983). We examine here an acetal which is known to be hydrolysed with intramolecular general acid catalysis. This mode of catalysis is very efficient for derivatives of salicylic acid (Kirby, 1980) – so much so that acetal (1, R = 2-carboxyphenyl) is too reactive to prepare and crystallize (Glenn, 1982). We have therefore examined the more stable acetal (2) (Craze & Kirby, 1974). Colourless rectangular blocks of (2), extremely sensitive to X-rays, were grown by liquid diffusion of hexane into a chloroform solution.



(1)



(2)

\* Crystal Structures of Acetals. 23. Part 22: Jones, Sheldrick, Kirby & Briggs (1983).