

A New Type of Anhydronucleoside from the Reaction of a
1,2,6-Thiadiazinone Derivative and Triacetyl-D-glucal

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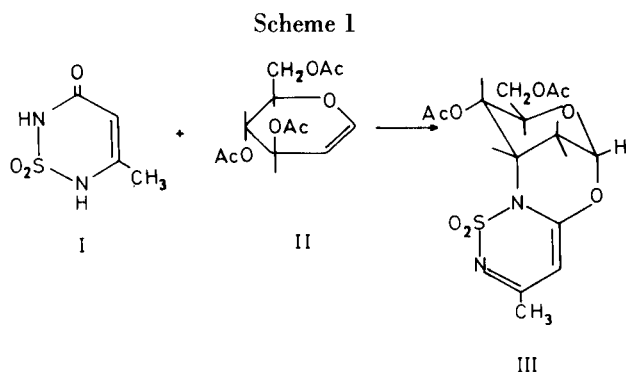
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Sir:

Previously we reported (1) the synthesis of an *S*-dioxo analog of 6-methyluracil, namely 5-methyl-2-*H*-1,2,6-thiadiazin-3-(6*H*)one 1,1-dioxide (I), by the reaction of sulfamide and diketene. When it was attempted to use this compound in nucleoside synthesis by reacting it with an acylated glycal (2), an unexpected anhydronucleoside resulted. We have found that I reacts with 3,4,6-tri-*O*-acetyl-D-glucal to give directly a new type of anhydronucleoside (III) derived from a nucleoside with the base bonded to C-3 of the carbohydrate moiety, and having an oxygen bridge between the base and the anomeric carbon atom.



Condensation of 1.2 g. (7.5 mmoles) of I with 2 g. (7.5 mmoles) of triacetyl-D-glucal (II) in 30 ml. of ethyl acetate containing 4-6 drops of trifluoroacetic acid in a sealed tube under continuous agitation at 90° for 7 hours followed by evaporation of the solvent, afforded a syrup which was chromatographed on a silica gel column (200 g. chloroform as eluent) to give in the first fractions III as a white solid. Crystallization of this product from ethyl acetate-petroleum ether afforded 0.1 g. of pure III (3), m.p. 175-176°; $[\alpha]_D -79.8^\circ$ ($c \sim 1$, chloroform); m/e 374 (M^+), 213 (M -base), 153 (213-AcOH), 111 (153-C₂H₂O); $uv \lambda \max$ (chloroform): 312 nm (ϵ , 7,550); ir

(nujol): 1765, 1743, 1558, 1335 and 1237 cm^{-1} ; nmr (DMSO- d_6 , δ): 5.96 (singlet, anomeric proton), 5.72 (singlet, H-4 thiadiazine ring), 4.91 (quartet, H-4', $J_{3',4'} = 2.9$ Hz, $J_{4',5'} = 10.3$ Hz), 4.76 (broad singlet, H-3'), 4.17 (doublet, 2H-6', $\frac{1}{2}[J_{5',6'_1} + J_{5',6'_2}] = 3.6$ Hz), 3.82 (multiplet, H-5', $J_{4',5'} = 10.3$ Hz, $J_{5',6'_1} + J_{5',6'_2} = 7.0$ Hz), 2.61 (multiplet, H-2'e, $J_{2'a,2'e} = 14, 6$ Hz, $J_{1',2'e} = 2.1$ Hz, $J_{2'e,3'} = 2.1$ Hz), 2.30 (multiplet, H-2'a, $J_{1',2'a} = 2.0$ Hz, $J_{2'a,3'} = 4.3$ Hz), 2.17 (singlet, 3H methyl group thiadiazine ring), 2.01 (singlet, 6H acetoxy groups). The positions for some of the assigned protons were confirmed by decoupling experiments. When the anomeric proton was irradiated the multiplets caused by the H-2' protons at δ 2.61 and δ 2.30 collapsed to quartets. Similarly irradiation of the H-3' signal resulted in collapse of both of the two H-2' signals to quartets. The multiplets at δ 2.61 and δ 2.30 were tentatively assigned to H-2'e and H-2'a, respectively, on the basis of their chemical shifts.

Since these data did not provide definitive evidence to distinguish between structure III and other possible alternative structures, an X-ray crystal structure determination was carried out. Crystals of III are orthorhombic, $a = 19.80(2)$, $b = 10.66(1)$, $c = 7.94(1)$, Å, $D_m = 1.40$ g.

TABLE I

Torsion Angles (deg) Involving the Carbohydrate Moiety

O(1')-C(1')-C(2')-C(3')	-64.60
C(1')-C(2')-C(3')-C(4')	61.39
C(2')-C(3')-C(4')-C(5')	-56.89
C(3')-C(4')-C(5')-O(1')	49.77
C(4')-C(5')-O(1')-C(1')	-60.25
C(5')-O(1')-C(1')-C(2')	60.40

cm^{-3} (flotation), $Z = 4$, $D_c = 1.46 \text{ g. cm}^{-3}$, space group $P2_12_12_1$. The intensities of 1450 reflections were measured on a four-circle Hilger-Watts diffractometer, with $\text{Cu-K}\alpha$ radiation ($\lambda = 1.5418 \text{ \AA}$); of these 75 were reckoned unobserved. The structure was solved by direct methods for phase determination using the MULTAN (4) program and refined by full-matrix least-squares methods. All hydrogen atoms were located from a difference map. The final R-value was 0.083. Figure 1 shows the molecule viewed down the a axis and the crystallographic numbering scheme.

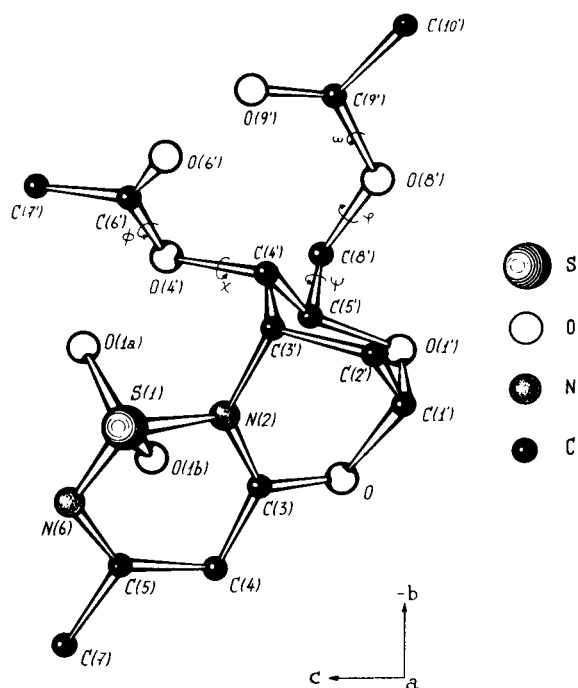


Figure 1

TABLE II

Torsion Angles (deg) in the Thiadiazine Ring

S(1)-N(6)-C(5)-C(4)	-17.45
C(4)-C(3)-N(2)-S(1)	17.33
N(6)-C(5)-C(4)-C(3)	8.55
C(5)-C(4)-C(3)-N(2)	7.84
C(3)-N(2)-S(1)-N(6)	-36.67
N(2)-S(1)-N(6)-C(5)	36.23

Work in this area is currently being done to obtain other anhydronucleosides from suitable thiadiazinone derivatives.

The thiadiazine ring is not planar. The five atoms (excluding the sulfur atom) almost lie on a plane. The deviation for the sulfur atom is 0.569 \AA . The O(1b) atom is on this plane. The short S(1)-O(1b) bond allows apparently the oxygen to approach closer to the straight line joining S(1)-N(2). The repulsion between the two oxygen atoms greater than the repulsion between an oxygen atom and the sulfur atom is shown by the larger magnitude of the O(1a)-S(1)-O(1b) angle (117.6°) versus the O(1b)-S(1)-N(2) (105.8°) angle.

The most interesting twist angles (5) are shown in Tables I and II, which corroborate the found molecular conformation.

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