Preliminary communication

The intramolecular hydrogen-bonding and conformation of methyl 1-thio-α-D-ribopyranoside and methyl 1,5-dithio-α-D-ribopyranoside hemihydrate in the crystalline state

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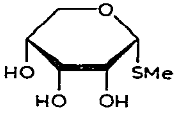
The determination of the crystal structure of two 1-thioglycosides, namely, methyl 1-thio-α-D-ribopyranoside (**1**), and methyl 1,5-dithio-α-D-ribopyranoside hemihydrate (**2**), has been completed★. The only previous crystal-structure determinations of thio monosaccharides are those of methyl 1-thio-β-D-xylopyranoside[1] and of ethyl 1-thio-α-D-glucofuranoside[2]. In both structures, the molecules had the expected conformation, namely, the $^4C_1$ for the pyranoside and the E^3 for the furanoside; all of the hydrogen bonding was intermolecular.



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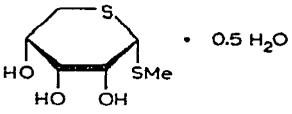

2

The crystal data for **1** and **2** are given in Table I. The crystal structures were solved by direct methods that used diffraction data measured on an automatic diffractometer with Ni-filtered CuKα X-radiation. For **1**, 833 intensities were measured, and the structure was refined to a final agreement index of R = 0.028. For **2**, the corresponding figures are 1563 and 0.029. That each compound had the absolute D configuration was confirmed by use of the anomalous scattering factors of the sulfur and oxygen atoms.

Both molecules have the supposedly rare $^1C_4$ conformation[3] (*1C* in the Reeves notation). Axial 1,3 or 2,4 interactions can only be avoided for the α-D-ribopyranosides by their adopting a boat or skew conformation. In the $^4C_1$ conformation, the axial interaction is between substituents at C-1 and C-3, whereas, in these structures, it occurs between O-2 and O-4, and is associated with an intramolecular hydrogen-bond between the hydroxyl groups. The relevant conformational geometry of these molecules is shown in Fig.1. In the asymmetric unit of the crystal structure of compound **2** are two independent

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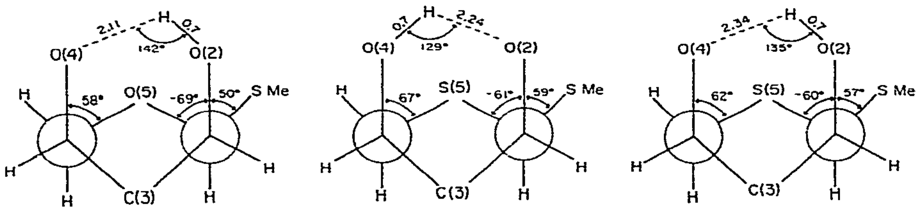
★These are two of a series of thio-D-ribopyranosides supplied by Dr. N. A. Hughes of the University of Newcastle-on-Tyne, who is conducting complementary studies by n.m.r. methods on these compounds in solution.

molecules, and therefore the molecule is observed twice, as 2A and 2B, in the same crystal, but in different intermolecular environments. It is interesting that, although the same intramolecular hydrogen-bonding occurs in the two symmetry-independent molecules, the donor–acceptor direction is different, *i.e.*, O-4-H–O-2 in 2A, and O-2-H–O-4 in 2B. The ring geometry of these two molecules and that of 1 are very similar. Even in the absence of the intramolecular bonding, the $^1C_4$ conformation would be favored for these molecules, because of the greater Van der Waals repulsion between an axial sulfur atom and an oxygen atom *vis-a-vis* two axial oxygen atoms.

TABLE I

CRYSTAL DATA FOR COMPOUNDS 1 AND 2

Property	*Compound* 1	*Compound* 2
Molecular formula	$C_6H_{12}O_4S$	$C_6H_{12}O_3S_2 \cdot 0.5\ H_2O$
Molecular weight	180	205
M.p. (degrees)	155–156	63–65
Space group	$P2_12_12_1$	$C2$
Lattice constants		
a (Å)	8.696(2)	29.8
b	12.829(3)	5.60
c	7.335(2)	11.4
β (degrees)		107.7
Z	4	8
Density (g/ml)		
Obs.	1.476	1.485
Calc.	1.472	1.490



1 2A 2B

Fig. 1. Diagram of the intramolecular hydrogen-bonding in methyl 1-thio-α-D-ribopyranoside (1) and methyl 1,5-dithio-α-D-ribopyranoside (2). The molecules are viewed in the direction of the C-2–C-1, C-4–C-5 bonds. The O–H distances have estimated standard deviations of ±0.1 Å. The O-4–O-2 distances are 2.71, 2.72, 2.88 Å in 1, 2A, and 2B, respectively, with standard deviations of ±0.02 Å.

Intramolecular hydrogen-bonding has not previously been reported in the crystal structure of a cyclic monosaccharide. It has been found to occur between hydroxyl groups of the different monosaccharide units of a disaccharide, as in sucrose[4], and in the gluconate ion[5], where it stabilizes an otherwise unfavorable acyclic conformation.

The orientation of the methyl groups is different in the two dithio molecules. In 2A, the S-1–C-6 is *syn*(–) with respect to C-1–C-2, whereas, in 2B it is *anti*, these being the two staggered conformations of lowest energy. The third alternative, *syn*(+) with respect to C-1—C-2, would incur a 1,3 (or *peri*) interaction between the methyl group and O-2. The fact that these two conformers occur in the same crystal structure implies that their energy difference is small; and that, in solution, the rotamers having both staggered orientations of the methyl group would populate to an almost equal extent. In **1**, the S-1—C-6 bond is *anti* with respect to C-1—C-2.

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