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Note

A summary of the structural and conformational data for five methyl thio-D-ribopyranosides in the crystalline state

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The crystal structures of five methyl thio-D-ribopyranosides* have been determined by single-crystal, X-ray structure analysis. The compounds are methyl 1-thio-α-D-ribopyranoside (**1**), methyl 5-thio-α-D-ribopyranoside (**2**), methyl 5-thio-β-D-ribopyranoside (**3**), methyl 1,5-dithio-α-D-ribopyranoside quarter hydrate (**4**), and methyl 1,5-dithio-β-D-ribopyranoside (**5**).

TABLE I

STRUCTURAL AND CONFORMATIONAL DATA[a] FOR THE THIO-D-RIBOPYRANOSIDES

Compound	*Conformation*	*C-1 torsion angles*[b]		Syn-*axial* *H···O and O···O distances*	*C–S distances and angles*		*Mean (spread)*	
		φ	*ψ*		*C-5–S-5–C-1*	*C-1–S-1–C-6*	*C–C*	*C–O*
1	$^1C_4$	+180	+75	2.11 O-2–H···O-4 2.71		1.796 1.809 99.1	1.524 (.022)	1.423 (.010)
2	$^4C_1$	+74	+71	O-1···O-3 2.99	1.812 1.822 98.4		1.516 (0.007)	1.434[c] (.029)
3	$^4C_1$	−178	−69		1.81 97		1.49 (.04)	1.40 (0.8)
4	$^1C_4$	−177	−159	2.34 O-2–H···O-4 2.88	1.772 1.807 99.9	1.777 1.756 101.6	1.531 (0.04)	1.414 (0.16)
		+180	−81	2.24 O-2···H–O-4 2.72	1.806 1.847 95.1	1.803 1.848 98.3	1.522 (.032)	1.433 (.024)
5	$^4C_1$	−177	+67		1.81 99	1.79 102	1.52 (.05)	1.42 (.02)
		−175	+66		1.81 102	1.79 103	1.53 (.09)	1.43 (.02)

[a]All distances are in Å, and angles in degrees. [b]C-1 torsion angles: C-5–$\left\{\begin{matrix}\text{O-5}\\\text{S-5}\end{matrix}\right\}^{\varphi}$C-1$^{\psi}\left\{\begin{matrix}\text{O-1}\\\text{S-1}\end{matrix}\right\}$–C-6. [c]Excluding C-1–O-1 = 1.407 Å.

*The compounds were provided by Professor N. A. Hughes of the University of Newcastle on Tyne, England.

The conformational and structural data on these compounds are summarized in Tables I and II, and Fig. 1. A preliminary report on the geometry of the intramolecular, *syn*-axial hydrogen-bonding in compounds **1** and **4** has been published by Girling and Jeffrey[1]. The crystallographic data and details of the analysis and of the crystal structures will be published elsewhere[2].

Table I gives, in successive columns, the conformations, the torsion angles involving the anomeric carbon atom, the distances between *syn*-axial oxygen atoms [including intramolecular, hydrogen-bond distances where they occur (the shorter distance is H···O and the longer O···O)], the C–S bond-lengths and C–S–C bond-angles, and the mean values for the C–C and C–O bond-lengths, with the spread of these observations in parentheses. For compounds **4** and **5**, there are two symmetry-independent molecules in the crystal unit-cell, and both observations are reported. Compounds **3** and **5** could only be obtained in very fine needles having one of the cross-sections less than 0.05 mm in width, and, in consequence, the structural data for these are less accurate by a factor of 10 than for the other compounds.

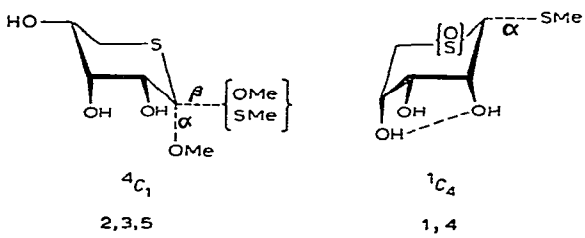

Fig. 1. Conformations of methyl thio-D-ribopyranosides in the crystalline state.

The relationship between the conformation and the anomeric configuration is illustrated in Fig. 1. All of the β-D anomers are in the $^4C_1$(D) conformation, which is consistent with the hypothesis that the most-stable conformation for the ribopyranosides is that having the least number of axial substituents. This rule does not apply to the α anomers, as both chair conformations have two axially attached groups. Of the various factors that determine the conformation in the crystalline state, intramolecular hydrogen-bonding and the anomeric effect appear to have opposing influences. In compounds **1** and **4**, an intramolecular hydrogen-bond between the axially attached hydroxyl groups on C-2 and C-4 stabilizes the $^1C_4$ conformation. The alternative of stabilization of the $^4C_1$ conformer by formation of an intramolecular hydrogen-bond between O-3–H···O-1–CH_3 or O-3–H···S-1–CH_3 appears to be less favorable, because, in compound **2**, these possibilities are rejected in favor of intramolecular hydrogen-bond formation from O-3 to an adjacent molecule in the crystal lattice. In contrast to the intramolecular hydrogen-bond observed in **1** and **4**, there is, in compound **2**, a *syn*-axial repulsion between O-3 and O-1 similar to that observed between the axial hydroxyl groups in the crystal structure of *epi*-inositol[3]. This repulsion is accompanied by a small distortion of the pyranose ring and, intuitively, the $^4C_1$(D)

conformation observed might seem less favorable than $^1C_4$ having a *syn*-axial, intramolecular bond between O-2–H and O-4–H. The conformational energy factor that favors the $^4C_1$(D) conformer for α-D anomers is the *anomeric effect*[4]. These results therefore suggest that the *anomeric effect* may be greater for the 5-thio derivative than for the 1-thio or 1,5-dithio compounds, and that it overrides the conformational stability that could be gained by the intramolecular hydrogen-bond formation.

In the pyranoses and pyranosides, the *anomeric effect* is associated with a variation in C–O bond-lengths, and the C-1–O-1 bond, particularly, is shortened[5,6]. The data on these thio derivatives provide no evidence that the same is true for C–S bonds. There is, however, in compound **4**, a significant difference in the C-1–S-1 bond-lengths in the two symmetry-independent molecules in the crystal structure, and these are associated with a different disposition about the C-1–S-1 bonds. The *ap-ap* or *trans-trans* conformer has shorter C–S bonds than the *ap-sc* or *trans-gauche*, by 0.024, 0.040, 0.026, and 0.092 Å in the four bonds shown in Table I. These difference correspond to about three times the estimated standard deviations, and are significant to better than the 90 percent level.

The fact that these two orientations of the methyl group occur in the same crystal structure suggests that the *exo*-anomeric effect[7] is also weaker in the 1,5-dithio derivatives, and that it can be more readily overridden by intermolecular forces than in the methyl pyranosides, where the *ap-ap* conformer has not been observed in the crystalline state[6].

The mean valence-angle at the sulfur atoms in the thio derivatives is smaller than for the oxygen atoms in comparable pyranosides, as would be expected. The mean values are 97.8° in the ring, and 99.9° external to the ring (excluding the poor

TABLE II

TORSION ANGLES IN THIO-D-RIBOPYRANOSIDES

Methyl D-*ribopyranoside*		C—S—C (*degrees*)	C—C—C (*degrees*)	C—C—S (*degrees*)
5-Thio-α-		55	57	61
5-Thio-β-		53	54	58
1,5-Dithio-α-		53	62	61
		55	63	62
1,5-Dithio-β-		54	63	60
		52	62	58
	Mean	54.7	59.4	59.3
1-Thio-α-		61	55	55
Pyranoses (oxy)	Mean	60.0	53.9	56.1

data from compounds **3** and **5**). More interesting is the comparison of the ring torsion-angles, given in Table II. There is a well-defined difference in the shape of the ring in the 5-thio-D-ribopyranosides compared to that of the 1-thio derivative and to the mean value from the best data for other pyranosides[8,9]. The ring torsion-angles about the hetero-bonds are about 5° greater than those about the C–C bonds, whereas, with oxygen, the reverse trend is observed[9]. This observation can be simply interpreted as being the geometrical consequence of the longer C–S bonds in the ring of the thio compounds.

EXPERIMENTAL

The compounds[10,11] were recrystallized from the following solvents: compound **1**, from ethanol–ethyl acetate; **2** and **3**, from ethanol, ethanol–benzene, and benzene; **4**, ethanol; and **5**, ethanol–benzene. Polymorphism was not observed.

The X-ray diffraction data were measured on Picker FACS-1 and Nonius CAD-3 automatic diffractometers, using CuKα radiation. The parameters were refined by full-matrix least-squares, to give final disagreement indices $R = \sum||F_{obs}| - |F_{calc}|/\sum|F_{calc}||$ of 0.03, 0.03, 0.04, 0.03, and 0.05 for **1**, **2**, **3**, **4**, and **5**, respectively

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REFERENCES

1 R. L. GIRLING AND G. A. JEFFREY, *Carbohyd. Res.*, 18 (1971) 339.
2 R. L. GIRLING AND G. A. JEFFREY, *Acta Crystallogr.*, in press.
3 G. A. JEFFREY AND H. S. KIM, *Carbohyd. Res.*, 15 (1970) 310.
4 R. U. LEMIEUX, in P. DE MAYO (Ed.), *Molecular Rearrangements*, Pt. 2, Interscience, New York, 1964.
5 H. M. BERMAN, S. S. C. CHU, AND G. A. JEFFREY, *Science*, 157 (1967) 1576.
6 G. A. JEFFREY, J. A. POPLE, AND L. RADOM, *Carbohyd. Res.*, 25 (1972) 117.
7 R. U. LEMIEUX, *Pure Appl. Chem.*, 25 (1971) 534.
8 G. A. JEFFREY, Chemistry of Carbohydrates in Solution, *Advan. Chem. Ser.* in press.
9 S. ARNOTT AND W. E. SCOTT, *J. Chem. Soc., Perkin Trans., II*, (1972) 324.
10 C. J. CLAYTON AND N. A. HUGHES, *Carbohyd. Res.*, 4 (1967) 32.
11 C. J. CLAYTON, N. A. HUGHES, AND S. A. SAFED, *J. Chem. Soc. (C)*, (1967) 644.