

Table 7. Comparison of the geometries of synthetic antimalarials with the title compound

	O-N	P-N	P-O
Antimalarials other than <i>Cinchona</i> alkaloids (Cheng, 1971)	3.18 ± 0.17 Å	4.98 ± 0.34 Å	3.85 ± 0.27 Å
Cinchoninium cation (this paper)	3.120 (8)	5.195 (10)	3.615 (9)

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The Structure of 1-Deoxy-1-thio-1,6-anhydro-β-D-glucopyranose: Thiolevoglucosan*

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$C_6H_{10}O_4S$, $M_r = 178.21$, orthorhombic, $P2_12_12_1$, $a = 6.654$ (1), $b = 12.235$ (1), $c = 8.893$ (1) Å [$\lambda(Cu K\alpha_1) = 1.54051$ Å], $V = 723.99$ Å³, $Z = 4$, $D_m = 1.639$, $D_x = 1.635$ g cm⁻³. The structure was solved by *MULTAN* and refined to $R(F_o) = 0.026$ and $R_w(F_o) = 0.032$ for 909 reflections measured with graphite-monochromated Cu $K\alpha$ radiation. The conformation is very similar to that of the 1,6-anhydro-β-D-glucopyranose molecule, having a distorted ¹C₄ pyranose ring and an E⁰ anhydro ring. The three axial hydroxyl groups and the ring O and S atoms are all hydrogen-bonded. There is an unsymmetrical bifurcated interaction, involving a strong H...S bond, 2.38 Å, and a weak intramolecular H...O bond, 2.87 Å.

Introduction

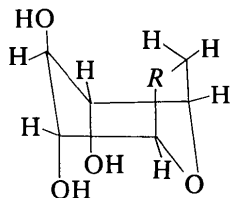
This work is part of a series aimed at studying the effect of substituents and hetero-atoms on the fused-ring conformation and molecular dimensions of anhydro sugars. Other 1,6-anhydro sugar structures which have

been studied are 1,6-anhydro-β-D-glucopyranose (levoglucosan) (Park, Kim & Jeffrey, 1971; Lindberg, 1974), 2,3-di-O-acetyl-1,6-anhydro-β-D-galactopyranose (Foces-Foces, Cano & García-Blanco, 1976), 2,3,4-tri-O-acetyl-1,6-anhydro-β-D-glucopyranose (Leung & Marchessault, 1974), 3-amino-1,6-anhydro-3-deoxy-β-D-glucopyranose (Noordik & Jeffrey, 1977), and 3-ammonio-1,6-anhydro-3-deoxy-β-D-glucopyranose chloride monohydrate (Małuszyńska, Takagi & Jeffrey, 1977).

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Experimental

Transparent crystals of thiolevoglucosan, $C_6H_{10}O_4S$ (I), m.p. $179^\circ C$, were kindly provided by Professor Shafizadeh of the Wood Chemistry Laboratory, University of Montana, Missoula, Montana.

(I) $R = S$ (II) $R = O$

The cell parameters and three-dimensional intensity data were measured on a CAD-4 diffractometer using monochromated $Cu K\alpha$ radiation with a crystal of dimensions $0.28 \times 0.32 \times 0.47$ mm mounted along the diagonal axis $[10\bar{1}]$. The 2983 intensities in the $h\bar{k}l$, hkl and $h\bar{k}\bar{l}$ octants were measured by $\theta-2\theta$ scans to $\theta = 78^\circ$. Absorption corrections were applied using *BNLABS*, a local version of *ORABS* (Busing & Levy, 1957), with $\mu(Cu K\alpha) = 36.52 \text{ cm}^{-1}$. The minimum and maximum corrections to F_o^2 were 0.347 and 0.476 respectively. The agreement between the symmetry-equivalent intensities was $R = 0.029$, thereby confirming the orthorhombic symmetry; these intensities were averaged to give 909 independent structure amplitudes.

The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971), using 150 reflections with $E \geq 1.38$ for the phase generation. The refinement was by full-matrix least squares, using *FLINUS*, a local version of *ORFLS* (Busing, Martin & Levy, 1962), minimizing $\sum w|F_o - kF_c|^2$, with $w^{-1} = [\sigma_c^2(F_o^2) + (0.005F_o^2)^2]/4F_o^2$, where σ_c is from counting statistics.

The H atoms were located from a difference synthesis. The non-hydrogen and H atoms were refined anisotropically and isotropically respectively, with a Zachariasen isotropic extinction parameter (Coppens & Hamilton, 1970) which refined to $0.31(3) \times 10^4$. The final $R = \sum |F_o - kF_c|/\sum |F_o|$, and $R_w = (\sum w|F_o -$

Table 1. Fractional coordinates ($\times 10^4$) for non-hydrogen atoms in thiolevoglucosan

Estimated standard deviations given in parentheses refer to the least significant digits.

	x	y	z
S	388 (1)	5789 (1)	4894 (1)
C(1)	2138 (3)	5688 (2)	6471 (2)
C(2)	2848 (3)	6800 (1)	7055 (2)
C(3)	1125 (3)	7495 (1)	7699 (2)
C(4)	-430 (3)	6805 (2)	8547 (2)
C(5)	-840 (3)	5721 (2)	7762 (2)
C(6)	-1731 (3)	5823 (2)	6178 (2)
O(2)	4351 (2)	6623 (1)	8191 (2)
O(3)	216 (3)	8069 (1)	6472 (2)
O(4)	276 (3)	6535 (1)	10016 (2)
O(5)	1043 (2)	5139 (1)	7620 (2)

Table 2. Fractional coordinates ($\times 10^3$), isotropic thermal parameters (\AA^2) and bond distances (\AA) for the hydrogen atoms in thiolevoglucosan

	x	y	z	B(iso)	C,O-H
H(C1)	337 (4)	514 (2)	616 (3)	3.2 (6)	1.09 (3)
H(C2)	359 (3)	721 (2)	623 (3)	2.0 (4)	1.02 (2)
H(C3)	166 (4)	802 (2)	843 (3)	2.7 (5)	0.98 (3)
H(C4)	163 (4)	724 (2)	855 (3)	2.5 (5)	0.96 (3)
H(C5)	-170 (5)	513 (2)	847 (3)	3.4 (6)	1.12 (3)
H(C61)	-243 (4)	653 (2)	601 (3)	2.8 (5)	0.99 (2)
H(C62)	-257 (5)	520 (2)	594 (4)	3.1 (6)	0.97 (3)
H(O2)	404 (5)	592 (2)	868 (4)	5.2 (7)	0.99 (3)
H(O3)	-39 (6)	874 (3)	684 (5)	7.9 (1.1)	0.97 (4)
H(O4)	1 (5)	701 (3)	1056 (4)	5.2 (8)	0.78 (3)

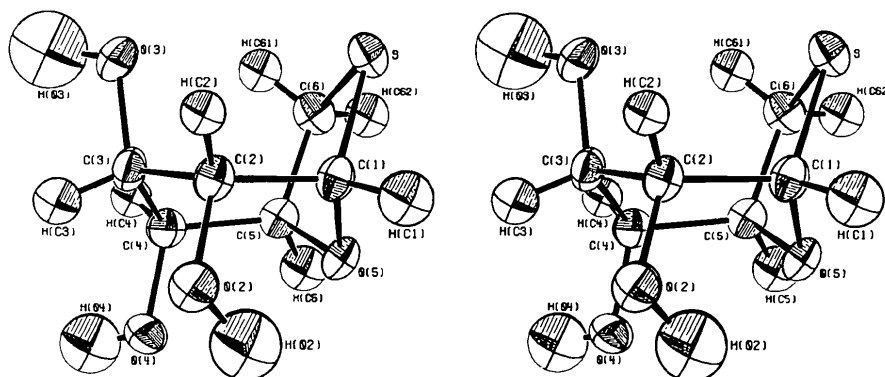


Fig. 1. Thiolevoglucosan. The thermal ellipsoids are at 50% probability (Johnson, 1976).

$kF_c|^{2/\Sigma w|F_o|^{2}})^{1/2}$ for 909 reflections were 0.026 and 0.032 respectively.

The atomic scattering factors for O, C and S were those tabulated by Doyle & Turner (1968) and those of H were given by Stewart, Davidson & Simpson (1965). The final positional parameters for the non-hydrogen atoms are given in Table 1,* and the fractional coordinates, isotropic thermal parameters and bond distances for the H atoms are listed in Table 2. The

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33082 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

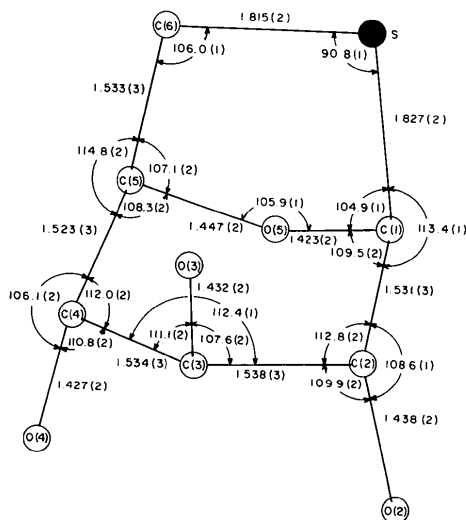


Fig. 2. Bond lengths (Å) and bond angles (°) in thiolevoglucosan.

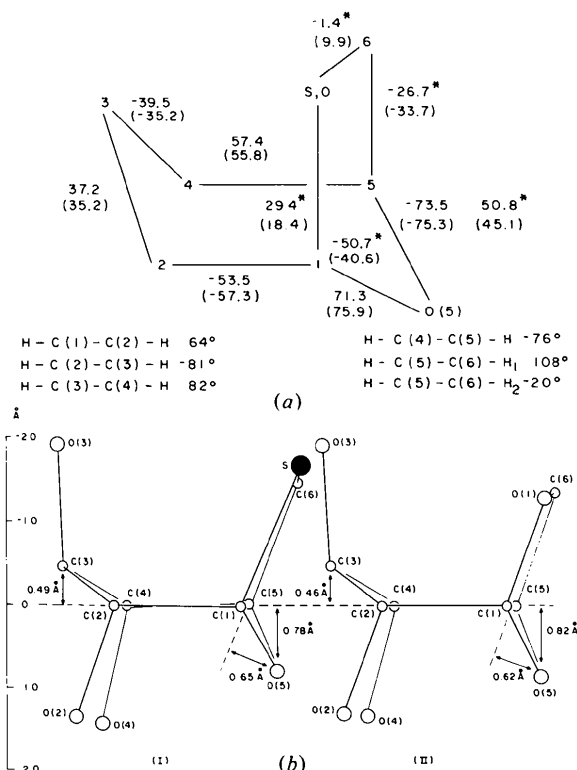


Fig. 3. Conformation of thiolevoglucosan and levoglucosan. (a) Ring torsion angles (values in parentheses are for levoglucosan). Values indicated by an asterisk refer to the anhydro ring. (b) Deviations from the plane C(1), C(2), C(4), C(5) ($A = 2.981$, $B = -5.739$, $C = 6.768$, $|D| = 1.737$) are (for I) 0.016, -0.014, 0.015 and -0.016 Å respectively. Deviations from the plane S, C(1), C(5), C(6) ($A = 0.381$, $B = 12.199$, $C = 0.454$, $|D| = 7.308$) are (for I) -0.009, 0.007, -0.008 and 0.010 Å respectively.

Table 3. Bond lengths (Å) valence angles (°) and torsion angles (°) in the acetal and thio-acetal region of some thiopyranose molecules

Compound	Pyranose ring conformation	Torsion angles (°)				α	β	φ	θ	Reference
		α	β	φ	θ					
Thiolevoglucosan	1C_4	1.815	1.827	1.423	1.447	90.8	105.9	29	-51	(a)
Levoglucosan	1C_4	1.445	1.430	1.402	1.444	106.8	102.0	18	-41	(b)
Methyl thioribosides		C(5) — { S(5) / O(5) } — C(1) — { S(1) / O(1) } — CH ₃								
1-Thio- α	1C_4	1.426	1.435	1.796	1.809	111.4	99.3	180	75	(c)
5-Thio- α	4C_1	1.813	1.821	1.405	1.452	98.5	112.5	74	71	(d)
5-Thio- β^*	4C_1	1.80	1.83	1.40	1.35	97.0	119.0	178	69	(d)
1,5-Thio- α †	1C_4	1.772	1.807	1.777	1.755	99.8	101.6	177	159	(e)
		1.805	1.846	1.802	1.847	95.1	98.3	180	81	
1,5-Thio- β ‡	4C_1	1.813	1.809	1.800	1.780	101.0	102.5	-176	66	(e)

References: (a) This work. (b) Park, Kim & Jeffrey (1971). (c) Girling & Jeffrey (1973a). (d) Girling & Jeffrey (1973b). (e) Girling & Jeffrey (1974).

* Low accuracy due to poor crystals.

† Two molecules in the unit cell with different glycosidic conformations.

‡ Mean of two molecules in the unit cell with the same conformation.

conformation and the atom numbering of thiolevoglucosan are shown in Fig. 1. The molecular dimensions for the non-hydrogen atoms are reported in Fig. 2. The calculations of distances and angles with their estimated standard deviations were made using *FREDFUN*, a local version of *ORFFE* (Busing, Martin & Levy, 1964).

Discussion

The conformation of the thiolevoglucosan molecule (I) is very similar to that of the corresponding molecule with an O atom in the anhydro ring, levoglucosan (II). A comparison of the geometry of the two molecules is given in Fig. 3. The fused-ring conformations are very similar, as also shown in the pyranose ring-puckering parameters (Cremer & Pople, 1975), where the values in parentheses are for (II), *i.e.* $\theta = 158.4$ (154.7°), $\phi_2 = 172.5$ (179.7°), $q_2 = 0.219$ (0.261), $q_3 = -0.552$ (-0.551), and $Q = 0.594$ (0.610 \AA).

Of the seven related 1,6-anhydro pyranose molecules which have now been studied, this molecule is closest to having the anhydro ring in the ideal envelope, E° ,

conformation. The ring torsion angles, corresponding to those in Fig. 3, for the six other 1,6-anhydro compounds which have been studied are given in Table 2 of Noordik & Jeffrey (1977) and in Fig. 2 of Maluszyńska, Takagi & Jeffrey (1977).

The bond distances and angles of particular interest in this molecule are those associated with the anhydro ring, shown in Table 3. In the *oxo* compound (II) there is a disproportionation of the C—O bond lengths, with the outer bonds of the C—O—C—O—C sequence longer than the inner bonds. Similar differences, which are observed in the methyl pyranosides, have been shown to have their origin in the anomeric effect (*cf.* Jeffrey, Pople & Radom, 1972, 1974; Jeffrey, Pople, Binkley & Vishveshwara, 1978). In the *thio* compound (I) the difference in the two C—S bond lengths is of the same magnitude but reversed, with the shorter bond on the outside of the thioacetal sequence. Differences in bond lengths of the same magnitude have been observed in the methyl thioribopyranosides, as shown in Table 3, where the C—S bond lengths vary from 1.755 to 1.846 Å, but the relationship of these differences to the conformations of the molecules is unclear at present.

Table 4. *Hydrogen-bond distances (Å) and angles (°) in thiolevoglucosan*

	H...O	H...O* _{corr}	O...O	O—H...O* _{corr}
O(4)H...O(2)[$x - \frac{1}{2}, \frac{3}{2} - y, 2 - z$]	2.06 (3)	1.86	2.829 (2)	173
O(2)H...S[$\frac{1}{2} - x, 1 - y, \frac{1}{2} + z$]	2.38 (3)	2.40	3.322 (2)	159
O(3)H...O(5)[$-x, \frac{1}{2} + y, \frac{3}{2} - z$]	1.83 (4)	1.83	2.787 (2)	168
O(2)H...O(4)[x, y, z]	2.87 (3)†	2.88	3.162 (2)	98

* Corrected by expanding the covalent O—H bond distances to the neutron diffraction value of 0.97 Å in the direction of the bonds.

† The inclusion of this distance as a hydrogen-bond interaction is based on the suggestion of Allinger (1976) that the van der Waals constant radii for H and O are 1.50 and 1.65 Å respectively.

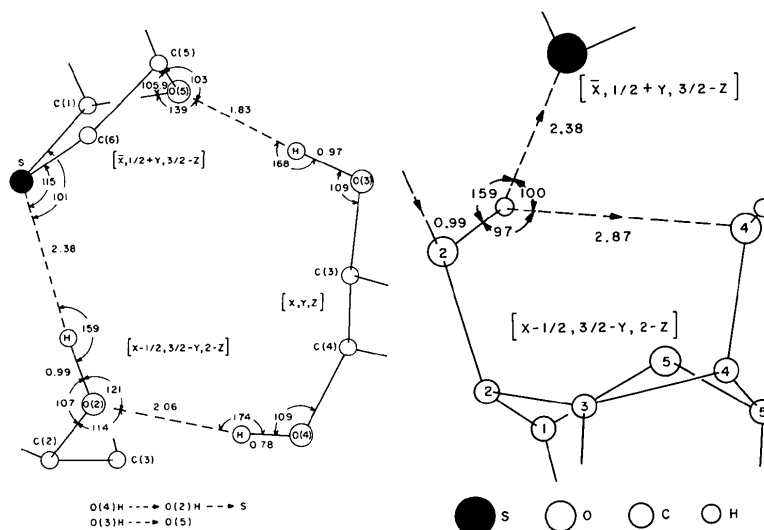


Fig. 4. Hydrogen-bond geometry in the crystal structure of thiolevoglucosan.

The hydrogen bonding in the thiolevoglucosan structure is shown in Table 4. It consists of an infinite chain, which includes a weak intramolecular component of an unsymmetrical bifurcated bond (see Jeffrey & Takagi, 1978); the other component of the bifurcated interaction is a strong hydrogen bond to the S atom. There is also a single link to the pyranose ring O atom. The geometry of the unsymmetrical bifurcated interaction is shown in Fig. 4.

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