The Structures of Methyl 5-Thio-β-D-ribopyranoside (S)-S-Oxide and Methyl 5-Thio-β-D-ribopyranoside (R)-S-Oxide

By E. Miler-Srenger* and C. Stora

Laboratoire de Cristallochimie, Faculté des Sciences, Tour 44, 11 quai Saint Bernard, Paris 75005, France

and N. A. Hughes

Department of Organic Chemistry, The University, Newcastle upon Tyne NE 1 7RU, England

Abstract

Crystals of methyl 5-thio-β-D-ribopyranoside (S)-S-oxide (I) and of methyl 5-thio-β-D-ribopyranoside (R)-S-oxide (II), $C_6H_{12}O_5S$, are orthorhombic, space group $P2_12_12_1$. The unit-cell dimensions are $a = 8.483$ (5), $b = 14.578$ (5), $c = 6.921$ (6) Å, $V = 855.9$ Å^3 for (I) and $a = 8.249$ (9), $b = 8.698$ (7), $c = 11.435$ (9) Å, $V = 820.5$ Å^3 for (II). The crystal structures have been determined from Cu Kα data and refined to R values of 0.044 for (I) and 0.031 for (II). Both molecules have the $^4C_1$ ring conformation. The bond lengths in the O(S)–S(5)–C(1)–O(1) chain as well as the C(5)–S(5)–C(1) bond angle in (I) are significantly different from the corresponding values observed in (II). In each structure the molecules are hydrogen bonded into a network of infinite helical chains.

Introduction

Sugars and their derivatives containing sulphur in place of the ring oxygen give rise to a new type of carbohydrate by oxidation of the sulphur to the sulphoxide or sulphone levels. Oxidation of methyl 5-thio-β-D-ribopyranoside gave a mixture of equatorial and axial sulphoxides, with the axial derivative preponderant (Clayton, Hughes & Inch, 1975).

Crystal-structure analyses of methyl 5-thio-β-D-ribopyranoside (S)-S-oxide (I) and of methyl 5-thio-β-D-ribopyranoside (R)-S-oxide (II) have been undertaken in order to determine the influence of the sulphoxide-group orientation on the molecular geometry and conformation of methyl 5-thio-β-D-ribopyranoside.

---

* Present address: Laboratoire de Chimie des Métaux de Transition, Université Pierre et Marie Curie, 4 place Jussieu, 75230 Paris CEDEX 05, France.

Experimental

The cell constants were calculated from a least-squares fit to 2θ values ($2\theta \geq 95°$) of nine reflexions measured manually on a diffractometer with Cu Kα radiation ($\lambda = 1.54051$ Å).

Weissenberg photographs confirmed the orthorhombic cell and the systematic extinctions for reflexions $h00$ with h odd, $0k0$ with k odd and $00l$ with l odd defined the space group as $P2_12_12_1$. The crystal data are given in Table 1.

The crystals used for data collection were $0.14 \times 0.11 \times 0.3$ mm and $0.32 \times 0.28 \times 0.23$ mm for (I) and (II) respectively. The intensities for hkl and $\bar{h}kl$ were measured on a Nonius CAD-3 automatic diffractometer by the θ–2θ scan method up to $2\theta = 133.2°$ (Cu Kα radiation). Two check reflexions were monitored every 40 reflexions. Their intensity fluctuations were random with a maximum variation of 5%. Each intensity was assigned an observational variance based on the following equation: $\sigma^2(I) = S + B_1 + B_2 + (pI)^2$, where S, B_1 and B_2 are the total integrated and background counts, I the net intensity, and p is taken to be 0.05.

The equivalent intensities were averaged when both values, I_{hkl} and $I_{\bar{h}kl}$, satisfied the condition $I \geq 3\sigma(I)$. From 1849 measured reflexions for (I) and 1722 measured reflexions for (II), 851 and 844 independent average intensities were obtained respectively. The net counts were corrected for Lorentz and polarization effects, but no correction was applied for absorption.

Table 1. *Crystal data for* (I) *and* (II)

$C_6H_{12}O_5S$	$M_r = 196.2$	$Z = 4$
(I)		(II)
$a = 8.483$ (5) Å		$a = 8.249$ (9) Å
$b = 14.578$ (5)		$b = 8.698$ (7)
$c = 6.921$ (6)		$c = 11.435$ (9)
$V = 855.9$ Å^3		$V = 820.5$ Å^3
$D_c = 1.52$ Mg m^{-3}		$D_c = 1.59$ Mg m^{-3}
$\mu = 3.19$ mm^{-1}		$\mu = 3.33$ mm^{-1}

Structure determination and refinement

The initial attempts to solve the phase problems were based on 162 reflexions for (I) and 254 reflexions for (II) with $E > 1.3$ using *MULTAN* (Germain, Main & Woolfson, 1971). The solutions that produced the highest figures of merit each yielded an E map in which all the 12 non-hydrogen atoms of the structures could be recognized.

Anisotropic full-matrix least-squares heavy-atom refinement gave an agreement index of 0·098 for (I) and 0·079 for (II). The hydrogen atoms were located from difference maps. Anomalous-dispersion corrections for sulphur and oxygen atoms were added (Cromer & Liberman, 1970). The weighting scheme was chosen so that the averages of $w(\Delta F)^2$ were constant for different ranges of $|F_o|$. A full-matrix least-squares refinement of all the heavy atoms anisotropically and the hydrogen atoms isotropically yielded a final $R = (\sum ||F_o| - |F_c||)/\sum |F_o|$ of 0·044 for (I) and 0·031 for (II). The weighted residuals $R_w = \{[\sum w(|F_o| - |F_c|)^2]/\sum wF_o^2\}^{1/2}$ are 0·065 and 0·051 respectively. The 040 reflexion, affected by errors of measurement,

was not included in the final refinement of (I). The final parameter shifts were less than 0.1σ and the standard deviation of an observation of unit weight, $S = [(\sum w||F_o| - |F_c||)^2/(m - n)]^{1/2}$ was 1·07 for 144 refined parameters and 851 observed reflexions for (I) and 0·92 for 144 refined parameters and 844 observed reflexions for (II). The absolute configurations were confirmed at the 99·9% confidence level by the method of Ibers & Hamilton (1964). The scattering factors for the heavy atoms were from Cromer & Waber (1965) and for H from Stewart, Davidson & Simpson (1965). The hydrogen-atom positions were checked on a final difference-Fourier synthesis, computed with contributions from all the non-hydrogen atoms. The final atomic parameters with their e.s.d.'s are given in Table 2 for the heavy atoms and in Table 3 for the H atoms.*

---

* Lists of structure factors, anisotropic thermal parameters and torsional angles involving hydrogen atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35506 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Fractional atomic coordinates* $(\times 10^4)$ *and equivalent isotropic thermal parameters* (Å^2)

The B_{eq} values were calculated with Hamilton's (1959) formula.   The e.s.d.'s in parentheses apply to the last significant digit.

	(I)				(II)			
	x	y	z	B_{eq}	x	y	z	B_{eq}
S(5)	6249 (1)	414 (1)	7656 (1)	3·58	363 (1)	4569 (1)	4536 (1)	1·87
C(1)	5320 (4)	1148 (2)	9494 (5)	3·19	9610 (4)	5510 (3)	5889 (3)	1·89
C(2)	6241 (5)	2044 (2)	9722 (5)	2·89	8008 (4)	6298 (3)	5665 (3)	1·83
C(3)	6351 (4)	2603 (2)	7870 (5)	2·61	6662 (4)	5156 (4)	5340 (3)	1·94
C(4)	7138 (4)	2082 (2)	6243 (5)	2·88	7080 (4)	4337 (4)	4198 (3)	1·83
C(5)	6213 (4)	1225 (2)	5711 (5)	3·18	8608 (4)	3379 (3)	4326 (3)	1·91
O(1)	5334 (4)	683 (2)	11243 (4)	5·19	768 (3)	6588 (2)	6249 (2)	2·64
O(2)	5499 (4)	2611 (2)	11133 (5)	4·51	7583 (3)	7073 (3)	6721 (2)	2·91
O(3)	4825 (3)	2903 (1)	7288 (4)	3·34	6436 (3)	4038 (3)	6237 (2)	2·65
O(4)	7248 (4)	2665 (2)	4585 (4)	4·10	5763 (3)	3397 (3)	3852 (2)	2·66
O(S)	5074 (5)	−312 (2)	7109 (6)	5·90	275 (3)	5778 (3)	3574 (2)	2·74
C(6)	4113 (8)	44 (4)	11603 (10)	5·94	2115 (5)	5927 (5)	6857 (4)	2·83

Table 3. *Fractional coordinates* $(\times 10^3)$ *and isotropic temperature factors* (Å^2) *for the hydrogen atoms*

	(I)				(II)			
	x	y	z	B	x	y	z	B
H(5)	411 (4)	128 (3)	897 (6)	2·9 (0·7)	939 (5)	467 (4)	645 (3)	1·9 (0·8)
H(2)	524 (7)	220 (4)	1156 (10)	4·4 (1·8)	672 (5)	788 (6)	641 (5)	6·3 (1·3)
H(6)	710 (4)	188 (2)	1020 (5)	1·8 (0·6)	811 (5)	706 (4)	504 (3)	2·6 (0·9)
H(3)	459 (5)	360 (3)	751 (6)	3·6 (0·8)	621 (6)	456 (6)	676 (5)	4·3 (1·2)
H(7)	675 (4)	315 (3)	820 (6)	2·6 (0·7)	573 (5)	567 (4)	520 (3)	1·3 (0·7)
H(4)	778 (7)	234 (4)	400 (8)	4·4 (2·0)	619 (5)	296 (5)	304 (4)	3·3 (1·0)
H(8)	810 (4)	191 (2)	682 (5)	1·7 (0·6)	735 (4)	491 (4)	365 (3)	1·3 (0·6)
H(9)	513 (6)	140 (4)	552 (7)	4·8 (1·1)	862 (4)	280 (3)	500 (3)	4·4 (1·0)
H(10)	643 (6)	100 (3)	459 (7)	4·1 (0·9)	862 (6)	291 (6)	347 (4)	4·4 (1·1)
H(11)	446 (7)	−54 (4)	1103 (9)	6·2 (1·8)	193 (5)	535 (5)	748 (4)	3·0 (0·9)
H(12)	311 (7)	19 (4)	1092 (9)	6·2 (1·3)	278 (5)	657 (5)	708 (4)	3·3 (0·9)
H(13)	403 (7)	−11 (4)	1309 (9)	6·2 (2·3)	268 (6)	527 (6)	636 (4)	4·0 (1·1)

Results and discussion

A perspective view of the molecules with atomic numbering is shown in Fig. 1(a). The bond lengths are given in Fig. 1(b) and the bond angles in Fig. 1(c). The bond angles involving hydrogen atoms are listed in Table 4 and the torsional angles of the molecule in Table 5.

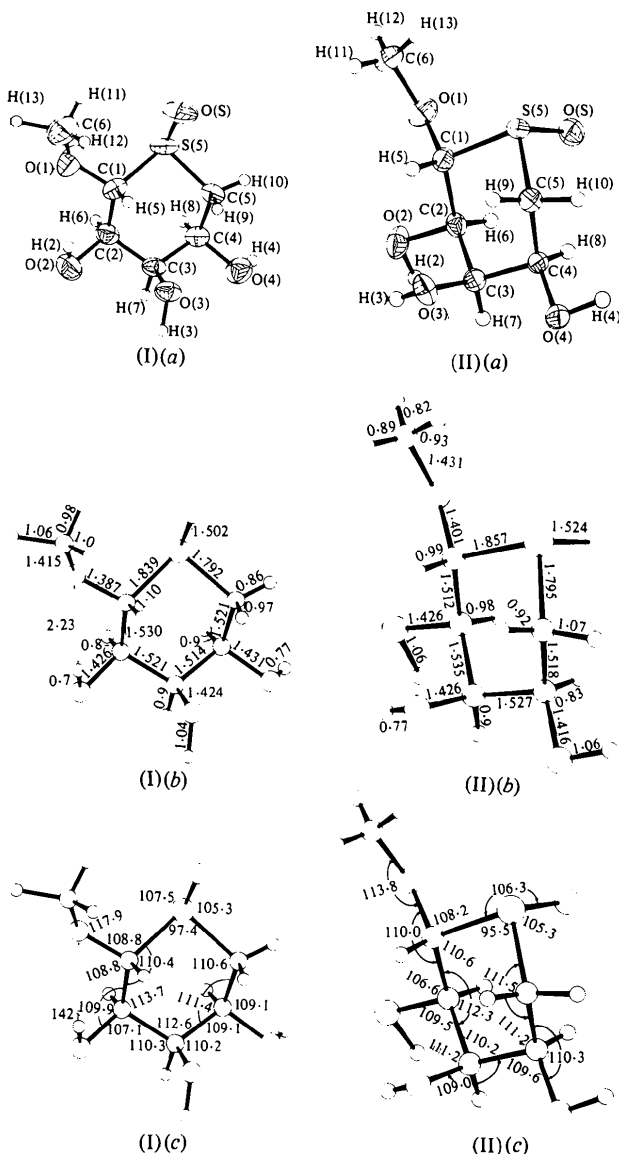Both molecules have the normal $^4C_1$ conformation. An intramolecular vicinal hydrogen bond of 2·23 (5) Å

(I)(a)

(II)(a)

(I)(b)

(II)(b)

(I)(c)

(II)(c)

Fig. 1. (a) Perspective view and atomic numbering of methyl 5-thio-β-D-ribopyranoside (S)-S-oxide (I) and of methyl 5-thio-β-D-ribopyranoside (R)-S-oxide (II). (b) Bond lengths (Å). The e.s.d.'s are in (I): 0·004 Å for S–C and S–O; 0·005 Å for C–C and C–O; 0·05 Å for C–H and O–H; and in (II): 0·003 Å for S–C and S–O; 0·004 Å for C–C and C–O; 0·05 Å for C–H and O–H. (c) Bond angles (°). The e.s.d.'s in both structures are: 0·2° for C–S–C and C–S–O and 0·3° for C–C–C and C–C–O.

Table 4. Bond angles (°) involving hydrogen atoms

The e.s.d.'s are in parentheses.

	(I)	(II)
H(5)–C(1)–S(5)	106 (2)	106 (2)
H(5)–C(1)–O(1)	112 (2)	115 (2)
H(5)–C(1)–C(2)	111 (2)	106 (2)
H(6)–C(2)–C(1)	104 (2)	111 (2)
H(6)–C(2)–C(3)	116 (2)	109 (2)
H(6)–C(2)–O(2)	106 (2)	109 (2)
H(7)–C(3)–C(2)	107 (2·5)	110 (3)
H(7)–C(3)–C(4)	118 (2·5)	105 (3)
H(7)–C(3)–O(3)	98 (2·5)	111 (3)
H(8)–C(4)–C(3)	101 (2)	114 (3)
H(8)–C(4)–C(5)	109 (2)	100 (3)
H(8)–C(4)–O(4)	116 (2)	111 (3)
H(9)–C(5)–C(4)	108 (3)	113 (3)
H(9)–C(5)–S(5)	107 (3)	101 (3)
H(9)–C(5)–H(10)	100 (4)	124 (4)
H(10)–C(5)–C(4)	115 (3)	97 (2)
H(10)–C(5)–S(5)	115 (3)	110 (2)
H(2)–O(2)–C(2)	86 (5)	101 (2)
H(3)–O(3)–C(3)	116 (2)	102 (3)
H(4)–O(4)–C(4)	96 (4)	102 (2)
H(11)–C(6)–O(1)	113 (3)	119 (3)
H(12)–C(6)–O(1)	106 (4)	113 (3)
H(13)–C(6)–O(1)	111 (3)	110 (3)
H(11)–C(6)–H(12)	104 (5)	105 (5)
H(11)–C(6)–H(13)	103 (5)	103 (4)
H(12)–C(6)–H(13)	116 (5)	105 (5)

Table 5. Torsional angles (°)

The e.s.d.'s are 0·3° for O/C–S/O, O/C–S/C and C/C–S/C; 0·35° for S/C–C/O, S/C–C/C and S/C–O/C; 0·4° for O/C–C/O and O/C–C/C.

	(I)	(II)
Ring angles		
S(5)–C(1)–C(2)–C(3)	59·4	64·1
C(1)–C(2)–C(3)–C(4)	−59·1	−62·8
C(2)–C(3)–C(4)–C(5)	61·7	63·3
C(3)–C(4)–C(5)–S(5)	−66·4	−67·4
C(4)–C(5)–S(5)–C(1)	59·6	59·2
C(5)–S(5)–C(1)–C(2)	−55·8	−57·5
Exocyclic angles		
O(1)–C(1)–C(2)–C(3)	178·2	−176·5
O(1)–C(1)–S(5)–C(5)	−174·9	−178·1
O(1)–C(1)–S(5)–O(S)	76·4	−70·4
O(2)–C(2)–C(3)–C(4)	179·4	179·0
O(2)–C(2)–C(1)–S(5)	179·3	−176·1
O(2)–C(2)–C(1)–O(1)	−61·8	−56·6
O(3)–C(3)–C(4)–C(5)	−62·0	−59·1
O(3)–C(3)–C(2)–C(1)	64·4	58·2
O(3)–C(3)–C(2)–O(2)	−57·1	−60·0
O(4)–C(4)–C(5)–S(5)	173·1	170·8
O(4)–C(4)–C(3)–C(2)	−177·9	−174·5
O(4)–C(4)–C(3)–O(3)	58·5	63·2
O(S)–S(5)–C(5)–C(4)	170·1	−49·5
O(S)–S(5)–C(1)–C(2)	−164·5	50·1
C(6)–O(1)–C(1)–S(5)	−83·5	−79·6
C(6)–O(1)–C(1)–C(2)	156·4	159·5

is observed between H(2) and O(1) in (I). The O(2)–H(2)···O(1) angle is 142 (6)°. Intramolecular hydrogen bonding between vicinal hydroxyls has been observed in the crystal structure of methyl α-D-altropyranoside (Gatehouse & Poppleton, 1971) where the O(3)–H(3)···O(4) distance is 2·22 Å and the O(3)–H(3)···O(4) angle 119°.

The conformation about the glycosidic bond is $-sc$ (*gauche*) with respect to the ring S atom with a C(6)–O(1)–C(1)–S(5) torsional angle of $-83\cdot5\,(0\cdot35)°$ in (I) and $-79\cdot6\,(0\cdot35)°$ in (II). An increase of the glycosidic bond torsional angle with respect to the normal value of 60° (Jeffrey, Pople & Radom, 1972) is observed, and in (I) an additional widening of the C(1)–O(1)–C(6) angle [117·9 (4)°] with respect to 113·4°, the mean observation in methyl-substituted monosaccharides (Arnott & Scott, 1972). Both effects are in the direction to establish normal non-bonding distances between the methyl group and O(S) and O(2) atoms.

The smallest endocyclic torsional angle is about the S(5)–C(1) bond [$-55\cdot8\,(0\cdot3)°$ in (I) and $-57\cdot5\,(0\cdot3)°$ in II)] as observed by Girling & Jeffrey (1973, 1974) in methyl 5-thioribopyranosides.

The mean C–C distance of 1·522 (5) Å and the mean C–O bond length [excluding the C(1)–O(1) bond] of 1·425 (2) Å are in good agreement with the values of 1·525 and 1·430 Å given by Berman & Kim (1968) for an ideal pyranose ring. None of the C–C and C–O distances is significantly different from the corresponding mean value, except C(1)–O(1), which is 0·037 Å (7·4σ) shorter in (I) and 0·023 Å (5·7σ) shorter in (II).

The C–H bond lengths range between 0·80 (5) and 1·10 (5) Å in (I) and between 0·82 (5) and 1·07 (5) Å in (II). The corresponding mean values are 0·95 and 0·93 Å respectively. The average O–H distances are 0·84 Å in (I), with a range of 0·70 (5) to 1·04 (5) Å, and 0·96 Å in (II), with a range of 0·77 (5) to 1·06 (5) Å.

The bond-length distribution in the C(5)–S(5)–C(1)–O(1) sequence does not follow the predicted and observed bond-length trends in methyl β-pyranosides (Jeffrey, Pople & Radom, 1972). The C(5)–S(5) bonds are significantly shorter [1·792 (4) and 1·795 (3) Å] than the S(5)–C(1) distances [1·839 (4) and 1·857 (3) Å].

The S–O bond in (I) [1·502 (4) Å] is shorter than the corresponding bond in (II) [1·524 (3) Å].

If we admit that increased opposite charges across a link have shortening effects on the bond, the significant difference observed in the S–O bond length in (I) and (II) [$\Delta(\sigma_1^2 + \sigma_2^2)^{1/2} = 4\cdot4$] could be attributed to different amounts of positive net charge on the S atoms. In (I) the axial lone pair of electrons is suitably oriented for delocalization and is of higher energy than the equatorial lone pair of electrons in (II). Consequently,

in (I) a competitive back-donation process could take place between the axial lone pair of electrons of S(5) and O(1), while in (II) only the O(1) lone pair of electrons would be delocalized in the σ framework of the molecule. Thus, in (I) the same molecular geometry is observed as in methyl 5-thio-β-D-ribopyranoside [S(5)–C(1) bond is 1·839 (4) and 1·83 Å and the C(5)–S(5)–C(1) bond angle is 97·4 (2) and 97° respectively]. In (II) the S(5)–C(1) bond [1·857 (3) Å] is significantly longer and the C(5)–S(5)–C(1) bond angle [95·5 (2)°] is significantly smaller.

The hydrogen-bond lengths and angles are given in Table 6, and the molecular packing is illustrated in Figs. 2 and 3. In both structures two of the three hydroxyls are involved in hydrogen–oxygen inter-actions which form a network of infinite helical chains of molecules. In (I) they extend through the O(3)–H(3)···O(S) bond in the **b** direction and through the O(3)···H(4)–O(4) bond in the **a** direction, the O(3) atom being hydrogen donor and acceptor. The third hydroxyl, O(2)–H(2), forms an intramolecular hydrogen bond with O(1) and has a short contact with O(4) of an equivalent molecule, translated one unit cell in the **c** direction. The geometry of this weak asymmetrical bifurcated interaction is described in Table 6.

Table 6. *Hydrogen-bond geometry*

	O–H (Å)	H···O (Å)	O···O (Å)	$\angle$O–H···O (°)
Hydrogen bond in (I)				
O(4)–H(4)···O(3^i)	0·77 (6)	1·98 (6)	2·674 (4)	150 (6)
O(3)–H(3)···O(S^{ii})	1·04 (4)	1·64 (4)	2·636 (4)	159 (4)
···O(1)		2·23 (5)	2·814 (4)	142 (6)
O(2)–H(2)⟨	0·70 (6)			
···O(4^{iii})		2·78 (6)	2·813 (5)	86 (5)*
Hydrogen bond in (II)				
O(4)–H(4)···O(2^{ii})	1·08 (4)	1·82 (4)	2·821 (4)	156 (4)
O(2)–H(2)···O(S^i)	1·06 (5)	1·67 (6)	2·690 (3)	160 (4)
···O(S^{ii})		2·42 (5)	3·026 (4)	137 (4)
O(3)–H(3)⟨	0·76 (5)			
···O(2)		2·49 (5)	2·859 (4)	112 (4)*

	C···O (Å)	$\angle$C–H···O (°)
Short intermolecular contacts in (II)		
C(5)–H(9)···O(4^i)	0·92 (4)	2·44 (4)	3·145 (5)	134 (4)
C(5)–H(10)···O(2^{ii})	1·05 (4)	2·24 (4)	3·160 (5)	145 (3)
O(4)···S(5^i)	3·188 (3) Å			

* Angle O···H···O is 107 (2) in (I) and 110 (2) in (II).

Symmetry code

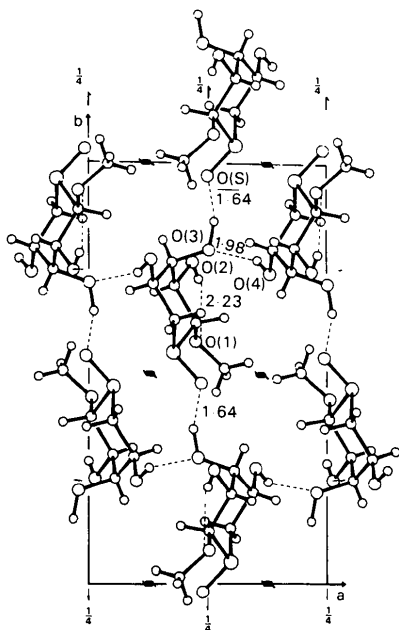|	(I)			(II)		
none	x,	y,	z	x,	y,	z
(i)	$\frac{1}{2}+x$,	$\frac{1}{2}-y$,	$-z$	$\frac{1}{2}+x$,	$\frac{1}{2}-y$,	$-z$
(ii)	$-x$,	$\frac{1}{2}+y$,	$\frac{1}{2}-z$	$\frac{1}{2}-x$,	$-y$,	$\frac{1}{2}+z$.
(iii)	x,	y,	$1+z$			

Fig. 2. Molecular packing of methyl 5-thio-β-D-ribopyranoside (S)-S-oxide viewed along the c axis. Hydrogen bonds are represented by dashed lines.

Fig. 3. Molecular packing of methyl 5-thio-β-D-ribopyranoside (R)-S-oxide viewed along the b axis. Hydrogen bonds are represented by dashed lines and short contacts by dotted lines.

In (II) the helical chains of molecules extend through the O(S)···H(2)—O(2) bond in the **a** direction and through the O(2)···H(4)—O(4) bond in the **c** direction, the O(2) atom being the hydrogen donor and acceptor. The O(3)—H(3) hydroxyl is involved in a weak bifurcated electrostatic interaction with an intramolecular component to O(2) and an intermolecular one to O(S). Further short contacts are observed between O(2) and H(10), O(4) and H(9) as well as between the S(5) and O(4) atoms.

References

Arnott, S. & Scott, W. E. (1972). *J. Chem. Soc. Perkin Trans.* 2, pp. 324–335.

Berman, H. M. & Kim, S. H. (1968). *Acta Cryst.* B**24**, 897–904.

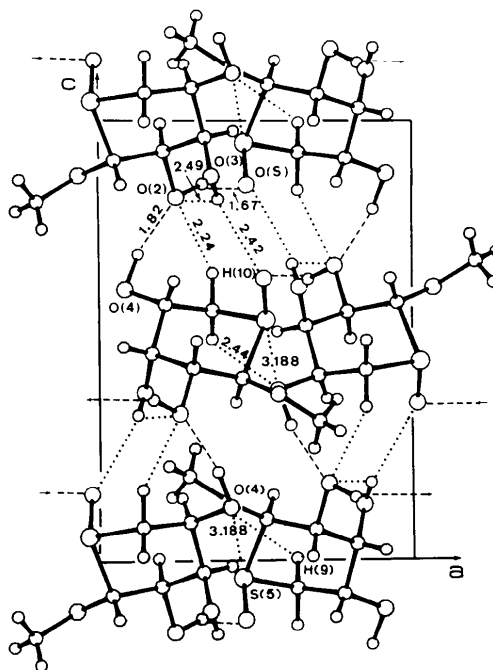Clayton, C. J., Hughes, N. A. & Inch, T. D. (1975). *Carbohydr. Res.* **45**, 54–64.

Cromer, D. T. & Liberman, D. (1970). *J. Chem. Phys.* **53**, 1891–1896.

Cromer, D. T. & Waber, J. T. (1965). *Acta Cryst.* **18**, 104–109.

Gatehouse, B. M. & Poppleton, B. J. (1971). *Acta Cryst.* B**27**, 871–876.

Germain, G., Main, P. & Woolfson, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

Girling, R. L. & Jeffrey, G. A. (1973). *Acta Cryst.* B**29**, 1006–1011.

Girling, R. L. & Jeffrey, G. A. (1974). *Acta Cryst.* B**30**, 327–333.

Hamilton, W. C. (1959). *Acta Cryst.* **12**, 609–610.

Ibers, J. A. & Hamilton, W. C. (1964). *Acta Cryst.* **17**, 781–782.

Jeffrey, G. A., Pople, J. A. & Radom, L. (1972). *Carbohydr. Res.* **25**, 117–131.

Stewart, R. F., Davidson, E. R. & Simpson, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.