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Crystal and molecular structure of methyl α-D-galactopyranoside 3-(sodium sulfate) monohydrate

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Abstract

The crystal and molecular structure of methyl α-D-galactopyranoside 3-(sodium sulfate) monohydrate has been determined by X-ray diffraction. The molecular structure has a distorted chair conformation ${}^4C_1$. The conformation of the hydroxymethyl group is *gauche–cis* and the methyl group is *gauche–trans* with respect to the pyranoid ring. The distorted sodium ion environment has seven closest oxygens of two different molecules. Coordination with (O-5, O-4, O-6) and (O-1, O-2), related by translational symmetry along the *a* axis, together with water oxygen O-1W and O-9 of the sulfate group, completes the first coordination sphere of sodium. A complex hydrogen-bond pattern involves all oxygens of the sulfate group as acceptors, linking molecules in [100] through O-7. The hydroxyl groups on C-2 and C-4 also participate in the bonding pattern. The complex packing by hydrogen bonds and ion coordination results in relevant differences with respect to the structure of other sulfate pyranosides.

1. Introduction

Synthetic monosulfated methyl glycosides are suitable reference compounds for comparison purposes in NMR and FABMS studies of the structural analysis of sulfated carbohydrate chains derived from N,O-glycoproteins and of sulfated polysacharides [1–4].

In fact, the ${}^1H$ NMR data of synthetic monosulfated methyl α-D-galactopyranosides were useful in the structural elucidation of the carbohydrate chains of

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Table 1

Crystal data for methyl α-D-galactopyranoside 3-(sodium sulfate) monohydrate (1)

Molecular formula	$(C_7H_{13}O_9S)^-$ $Na^+ \cdot H_2O$
Formula weight	314.2
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Cell dimensions	$a = 6.896(10)$ Å
	$b = 12.916(3)$ Å
	$c = 13.654(3)$ Å
Cell volume	1216.1(4) Å^3
Z	4
Density (calcd.)	1.716 g·cm^{-3}
μ (Mo-K_α)	0.333 mm^{-1}
$F(000)$	656
Temperature (K)	293

porcine thyroglobulin, which contain N-linked carbohydrate chains with 3-sulfated galactose residues [5].

X-ray crystallographic studies of these model compounds can provide important stereochemical information about the role of the sulfate group in the conformation of the pyranoside ring, and also the hydrogen-bond patterns. As a continuation of X-ray crystallographic studies of the sulfates of methyl α-D-galactopyranoside, the crystal and molecular structure of the 3-(sodium sulfate) monohydrate **1** is reported, and compared with the structure of methyl α-D-galactopyranoside 4-(sodium sulfate) dihydrate (**2**) [6].

2. Experimental

Methyl α-D-galactopyranoside 3-(sodium sulfate) monohydrate (**1**), synthesised by Ruiz Contreras et al. [1], had mp 166–167°C and $[\alpha]_D$ +146° (c 1.1, H_2O). Suitable crystals were grown by the vapour-phase diffusion method with MeOH as solvent and CH_2Cl_2 as precipitant.

A prismatic crystal (0.6 × 0.9 × 0.2 mm) was studied (Table 1) in a Stoe-Siemens AED 2 four-circle diffractometer operating at 40 kV/35 mA, with highly oriented graphite-monochromated Mo-$K\alpha$ radiation ($\lambda = 0.71069$ Å). Accurate cell parameters were determined by least-squares fit for 25 reflections measured by a $-\omega$ and $+\omega$ scan in the range $12 < 2\Theta < 30$.

Intensity data collection was carried out at 293 K, with a minimum and maximum measuring time of 0.45 and 1.8 s, respectively, and a scan range of 1° plus $K\alpha$ separation.

With the $2\Theta/\omega$ scan method, 6623 independent reflections ($R_{int} = 0.02$) were measured in the whole reflection sphere up to $2\Theta_{max} = 60°$, into an index range ($-9 < h < 9$, $-16 < k < 16$, $-17 < l < 17$), and 3481 unique reflections with $F_0 > 5\sigma(F_0)$ were observed. Four standard reflections (211, 600, 400, 200) were used to

Table 2
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement coefficients ($Å^2 \times 10^4$)

Atom	x/a	y/b	z/c	U_{eq} [a]
S	−42 (2)	7978 (1)	2024 (1)	312 (3)
Na	−1869 (3)	9745 (2)	201 (2)	465 (7)
O-1	−336 (4)	4359 (2)	135 (3)	358 (11)
O-2	414 (4)	6312 (2)	−413 (2)	313 (10)
O-3	−1222 (5)	7485 (3)	1130 (3)	331 (11)
O-4	−4946 (5)	6590 (3)	1076 (2)	379 (10)
O-5	−3649 (4)	4673 (3)	356 (2)	295 (10)
O-6	−7023 (5)	4681 (3)	1478 (3)	537 (14)
O-7	1859 (4)	7498 (3)	2005 (3)	477 (12)
O-8	−1098 (5)	7735 (3)	2907 (3)	513 (13)
O-9	−39 (6)	9040 (2)	1769 (3)	503 (13)
O-1W	−2048 (8)	1.0935 (4)	1479 (4)	1127 (25)
C-1	−1938 (6)	4952 (5)	−159 (4)	281 (14)
C-2	−1417 (6)	6111 (3)	5 (3)	274 (14)
C-3	−1484 (7)	6366 (4)	1092 (3)	283 (16)
C-4	−3379 (7)	6035 (4)	1552 (4)	314 (16)
C-5	−3531 (7)	4858 (4)	1386 (3)	313 (16)
C-6	−5196 (7)	4314 (4)	1862 (4)	437 (17)
C-7	−551 (8)	3288 (3)	−110 (5)	535 (21)

[a] Equivalent isotropic U defined as one-third of the trace of the orthogonalised U_{ij} tensor.

monitor, every 120 min, the intensity variations during exposure to X-rays, and showed no crystal movement or decay.

Intensities were corrected for Lorentz-polarization and absorption effects with the Ψ data collection method (6 reflections, $\Delta\Psi$ 10°).

The structure was solved by direct methods with the SHELXTL PLUS software [7]. Atomic scattering factors used were those in the program, and the calculations were performed on a Microvax II computer. By use of the full-matrix least-squares method, the non-hydrogen atoms were refined. The difference synthesis revealed the position of the H atoms in the hydroxyl groups and the water molecule. However, the positional refinement for the H atoms resulted in unrealistic geometries and, therefore, these atoms were constrained during refinement at the maxima of the Fourier map.

The final refinement gave $R = 0.051$ and $R_\omega = 0.053$ with a weighting scheme $\omega^{-1} = \sigma^2[(F) + 0.002F^2]$, S = 1.99, and maximum $\Delta/\sigma = 0.3$. The final difference map showed minimum and maximum peaks of -1.29 and 1.23 $eÅ^{-3}$, respectively, surrounding the S atoms, indicating disorder in the environment of the sulfur coordination polyhedra. Crystal data are shown in Table 1.

Final atomic parameters for the non-H atoms are listed in Table 2. In Table 3 are shown the bond lengths, angles, and torsion angles *.

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* Observed and calculated structure factors have been deposited with the Cambridge Crystallographic Data Centre. They may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Table 3
Molecular geometry of **1**

Bond lengths (Å)			
S–O-3	1.594 (4)	O-5–C-5	1.428 (6)
S–O-7	1.445 (3)	O-5–C-1	1.421 (5)
S–O-8	1.439 (4)	O-6–C-6	1.443 (5)
S–O-9	1.428 (3)	C-1–C-2	1.556 (3)
O-1–C-1	1.403 (5)	C-2–C-3	1.521 (7)
O-1–C-7	1.431 (5)	C-3–C-4	1.512 (7)
O-2–C-2	1.410 (5)	C-4–C-5	1.542 (7)
O-3–C-3	1.455 (5)	C-6–C-5	1.495 (7)
O-4–C-4	1.451 (4)		

Bond angles (°)			
O-3–S–O-7	106.6 (2)	O-3–C-3–C-2	104.7 (5)
O-3–S–O-8	107.5 (2)	O-3–C-3–C-4	111.8 (3)
O-3–S–O-9	101.2 (2)	C-2–C-3–C-4	111.2 (4)
O-7–S–O-8	112.7 (2)	C-3–C-2–O-2	111.4 (7)
O-9–S–O-7	113.6 (2)	C-5–C-6–O-6	111.5 (4)
O-9–S–O-8	114.0 (2)	O-5–C-5–C-6	108.5 (5)
C-5–O-5–C-1	113.5 (3)	O-5–C-5–C-4	108.0 (7)
C-2–C-3–C-4	111.8 (4)	C-6–C-5–C-4	116.8 (8)
C-3–C-2–O-2	112.5 (4)	O-4–C-4–C-3	107.6 (9)
O-5–C-5–C-6	107.9 (4)	O-4–C-4–C-5	112.3 (5)
O-5–C-1–O-1	111.9 (4)	C-3–C-4–C-5	106.5 (4)
C-2–C-1–O-1	107.7 (4)		

Torsion angles (°)			
Endocyclic			
C-1–O-5–C-5–C-4	65.7 (3)		
C-2–C-1–O-5–C-5	−57.4 (4)		
C-3–C-2–C-1–O-5	48.6 (7)		
C-3–C-4–C-5–O-5	−64.0 (5)		
C-1–C-2–C-3–C-4	−51.9 (7)		
C-2–C-3–C-4–C-5	59.1 (5)		
Exocyclic		Exocyclic (cont.)	
C-3–O-3–S–O-9	177.4 (3)	C-2–C-1–O-1–C-7	−171.9 (9)
C-3–O-3–S–O-7	58.4 (5)	O-3–C-3–C-4–O-4	55.4 (6)
C-3–O-3–S–O-8	−62.7 (7)	O-3–C-3–C-4–C-5	175.6 (4)
S–O-3–C-3–C-2	−145.2 (6)	C-2–C-3–C-4–O-4	−61.1 (5)
S–O-3–C-3–C-4	93.9 (5)	O-4–C-4–C-5–O-5	54.1 (6)
C-1–O-5–C-5–C-6	−167.0 (8)	O-4–C-4–C-5–C-6	−67.8 (7)
O-2–C-2–C-3–O-3	65.3 (5)	C-3–C-4–C-5–C-6	174.1 (9)
O-2–C-2–C-3–C-4	−173.6 (8)	O-2–C-2–C-1–O-1	49.4 (4)
O-1–C-1–O-5–C-5	63.1 (4)	O-5–C-1–O-1–C-7	65.5 (5)
		C-1–C-2–C-3–O-3	−172.9 (7)
		O-5–C-5–C-6–O-6	−58.6 (8)
		C-4–C-5–C-6–O-6	63.5 (4)
		C-3–C-2–C-1–O-1	−74.4 (7)
		O-2–C-2–C-1–O-5	172.4 (7)

3. Results and discussion

Molecular geometry.—The molecular geometry shown in a perspective view (Fig. 1) corresponds to the positional parameters of atoms referenced in Tables 2 and 3.

The bond lengths of the bridging S–O-3 [1.594(4) Å] and C-3–O-3 [1.455(5) Å] are respectively longer and shorter than the corresponding S–O-4 (1.572 Å) and C-4–O-4 (1.467 Å) distances in compound **2**.

The bond angles in the sulfate group range from 106.6° to 114.0°, which is smaller than in other sulfated pyranoses [6,8,9].

The mean distances for C–C (1.522 Å) and C–O (1.424 Å) bonds reported for carbohydrates [10,11] agree well with mean values of 1.525 and 1.430 Å found in **1** (Table 3). The values of C–C bonds range from 1.495(7) to 1.556(3) Å, and of C–O bonds from 1.403(5) to 1.455(5) Å, wider than the equivalents found in **2**.

No meaningful difference between the endocyclic C-1–O-5 [1.421(5) Å] and C-5–O-5 [1.428(3) Å] bond lengths exists; the shortening of C-1–O-1 [1.403(5) Å] is in accord with the reported [11] mean value of 1.409 Å in pyranoses.

Conformation angles in the pyranoid ring range from 48.6° to 65.7° (Table 4), and the ring adopts a moderately distorted $^4C_1$ chair conformation according to the Cremer and Pople [12] puckering parameter ($\Theta = 9.9°$). This parameter is close to the distortion in **2** ($\Theta = 11.9°$).

The position of the *O*-methyl group originates a *gauche–trans* conformation which is the most frequent for this group in methyl α-D-galactopyranosides. The C-7–O-1 bond is *gauche* with respect to O-5 and trans to C-2 in accord with the general conformation.

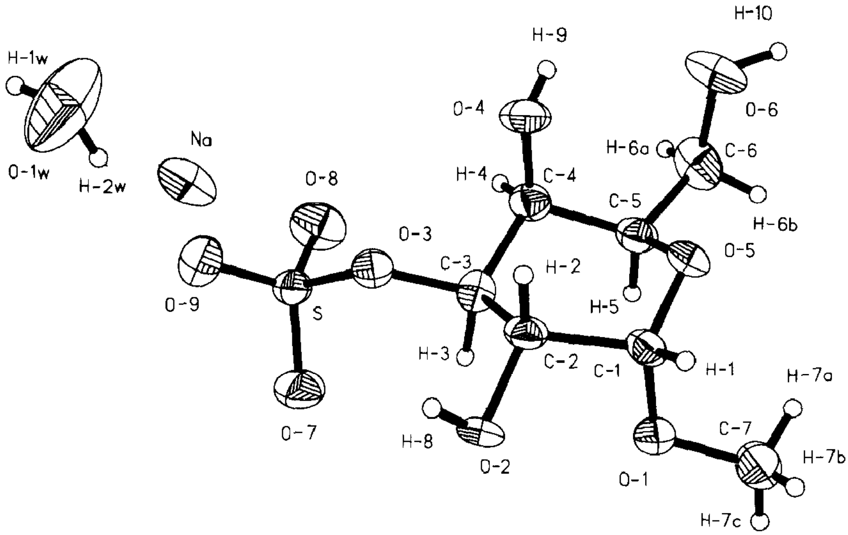

Fig. 1. Molecular view and atom labeling of methyl α-D-galactopyranoside 3-(sodium sulfate) monohydrate (**1**).

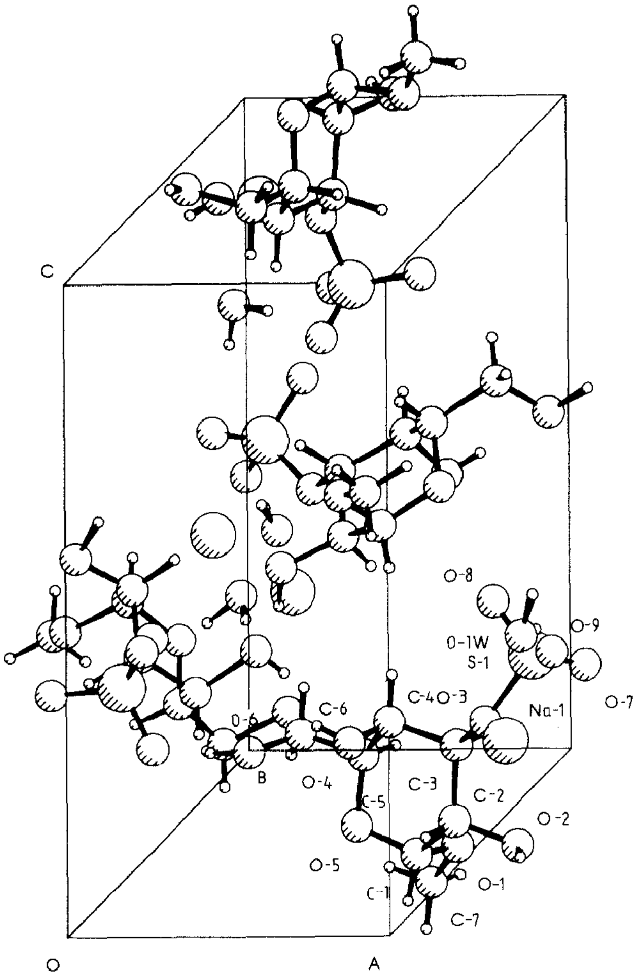

Fig. 2. Crystal packing of compound **1**.

The S–O-3 bridging bond is eclipsed with the C-3–H-3 bond and avoids steric repulsion with O-2–H-8 and O-4–H-9 groups. The O-4–H-9 bond is oriented to donate an intramolecular hydrogen bond to O-6, and the observed conformation of the hydroxymethyl group is *gauche–cis* (Fig. 1) and is the result of the steric response of the molecule to the sulfate substitution on C-3. The *gauche–cis* conformation of the hydroxymethyl group in compound **1** is different from the *gauche–trans* conformation found in other methyl α-D-galactopyranosides [6,13], and could be a consequence of the steric impact of the sulfate group on the O-4–H-9 bond.

Coordination of sodium ions.—The crystal packing is shown in a perspective view of the cell in Fig. 2. Seven oxygen atoms coordinate Na^+ with variable distances ranging from 2.79 Å (Na–O-4) to 2.327 Å (Na–O-1W), see Table 4. The oxygen atoms that participate in the coordination sphere belong to two different

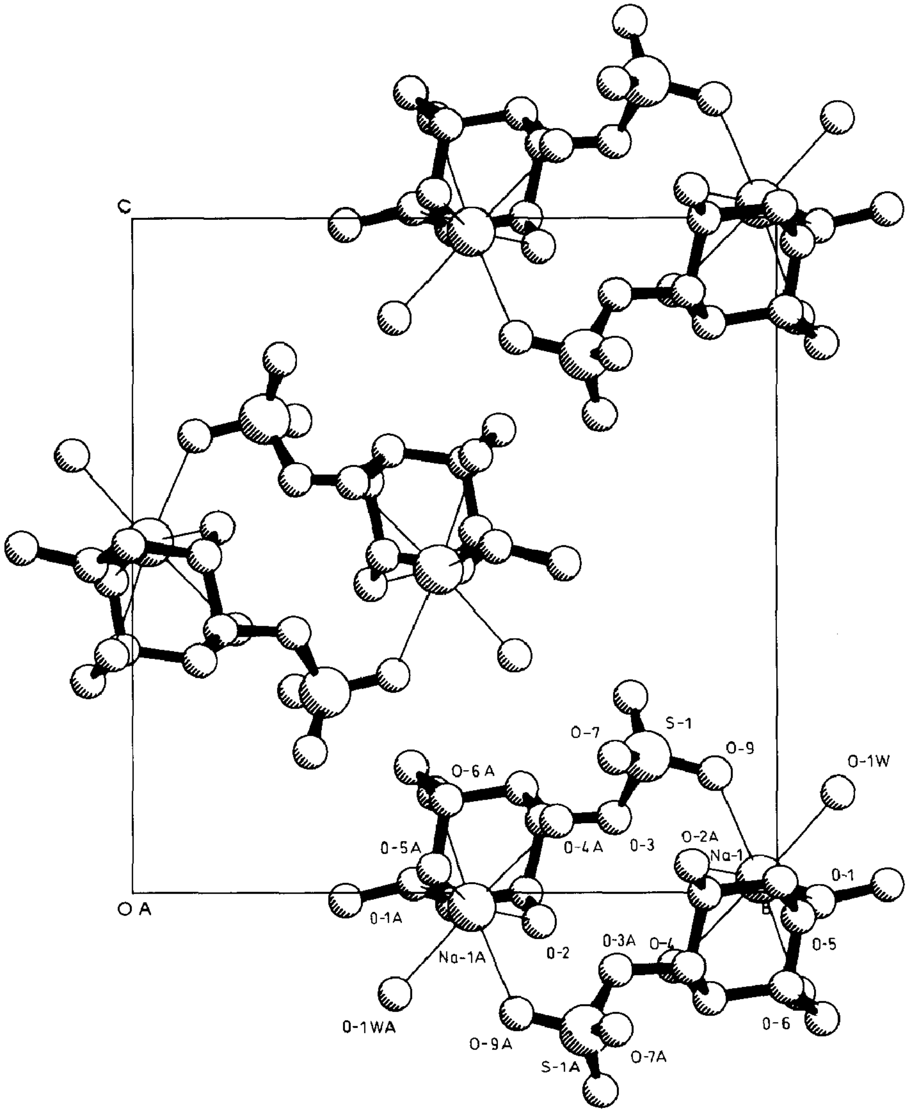

Fig. 3. View along [100] of the sodium coordination.

residues of the pyranoside molecule. The Na ion coordinates to O-9 and O-1W of the sulfate group and water of the same molecule. As can be seen in Fig. 3, oxygen atoms O-4, O-5, and O-6 belong to a different pyranoside molecule, and O-2 and O-1 to a translation equivalent molecule parallel to [100]. The view along the *a* axis (Fig. 4) shows the ring-coordinated molecules following a helical structure that runs parallel to [100].

Hydrogen bonds.—A complex hydrogen-bond pattern involves all of the oxygens of the sulfate group (O-7, O-8, O-9) and also O-4 as acceptors (Table 5).

Table 4
Geometry of the Na^{+} coordination

Symmetry code							
a	x	y	z	d	$x-1$	y	z
b	$x+1/2$	$-y+1/2+1$	$-z$	e	$-x-1$	$y-1/2$	$-z+1/2$
c	$x-1/2$	$-y+1/2+1$	$-z$	f	$-x$	$y+1/2$	$-z+1/2$

Bond length (Å)	
Na···O-4^{b}	2.789 (5)
Na···O-5^{b}	2.464 (6)
Na···O-9^{a}	2.646 (8)
Na···O-2^{c}	2.337 (2)
Na···O-6^{b}	2.412 (7)
Na···O-1W^{a}	2.327 (6)
Na···O-1^{c}	2.695 (3)

Bond angle (°)	
O-4^{b}···Na···O-5^{b}	64.31 (11)
O-4^{b}···Na···O-9^{a}	93.83 (13)
O-4^{b}···Na···O-2^{c}	95.56 (10)
O-4^{b}···Na···O-6^{b}	67.40 (11)
O-4^{b}···Na···O-1W^{a}	154.47 (7)
O-4^{b}···Na···O-1^{c}	125.46 (15)
O-5^{b}···Na···O-9^{a}	85.72 (12)
O-5^{b}···Na···O-2^{c}	159.81 (11)
O-5^{b}···Na···O-6^{b}	69.64 (7)
O-5^{b}···Na···O-1W^{a}	94.51 (9)
O-5^{b}···Na···O-1^{c}	128.02 (15)
O-9^{a}···Na···O-2^{c}	94.63 (12)
O-9^{a}···Na···O-6^{b}	153.58 (17)
O-9^{a}···Na···O-1W^{a}	69.28 (10)
O-9^{a}···Na···O-1^{c}	135.11 (11)
O-2^{c}···Na···O-6^{b}	105.20 (15)
O-2^{c}···Na···O-1W^{a}	104.52 (14)
O-2^{c}···Na···O-1^{c}	63.95 (11)
O-6^{b}···Na···O-1W^{a}	120.49 (9)
O-6^{b}···Na···O-1^{c}	70.56 (10)
O-1W^{a}···Na···O-1^{c}	78.33 (13)

Two molecules inside the unit cell are linked through a water molecule with O-9 and O-7 of symmetry-related sulfate groups following a helical axis parallel to the *b* axis. Also, the sulfate oxygen O-8 accepts bonding with O-6–H-10 and connects molecules in the same [010] direction.

Another complex bonding through O-4–H-9 can be observed (Fig. 4) in which O-4 acts as a single acceptor and also as donor of a bifurcated hydrogen bond. As acceptor of O-2–H-8, O-4 generates a helical symmetry bonding parallel to [100]. The participation of O-4 as donor in the bonding with O-7 connects molecules related by translational symmetry along the *a* axis. The intramolecular bonding O-4–H-9 ··· O-6 completes the bonding pattern.

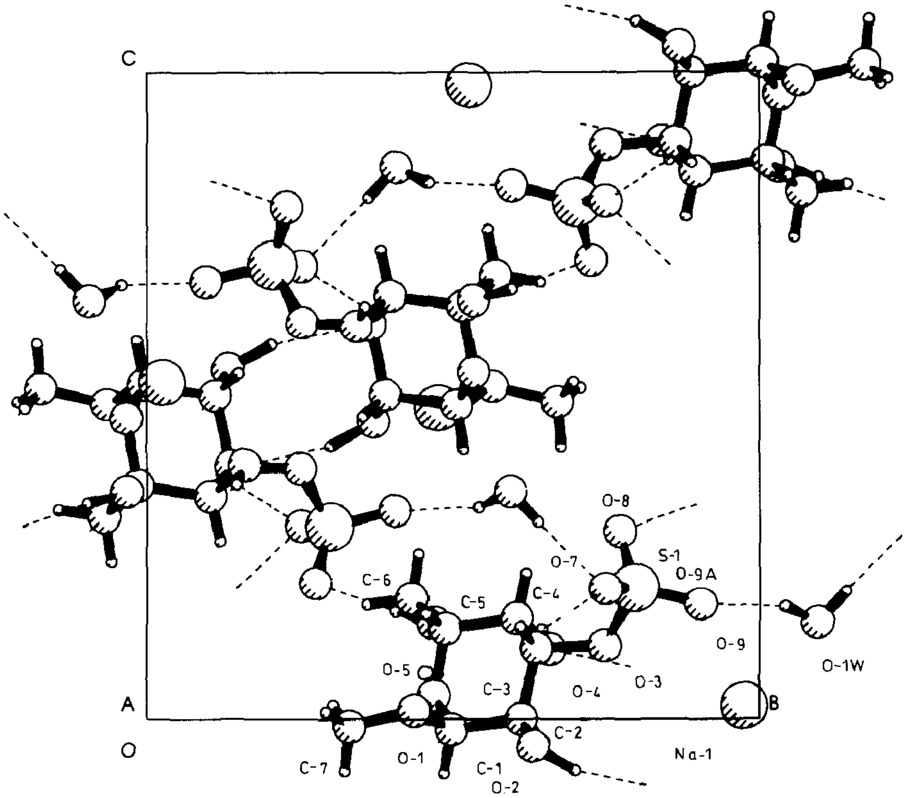

Fig. 4. Hydrogen-bonding pattern shown in (100) projection.

All hydroxyl groups of the molecule donate hydrogen bonding to the sulfate group oxygens; no participation of the ring O-5 or the sulfate linking O-3 in the hydrogen-bond network has been found.

All potential donors are involved in intermolecular hydrogen bonds (Table 5). Acceptors of hydrogen bonds are all of the oxygens of the sulfate group and O-4.

Table 5
Geometry of the hydrogen bonds [a]

Donor-H ··· acceptor	O–H (Å)	D ··· A (Å)	H ··· O (Å)	O–H ··· O (°)
O-W1-H-2W ··· O-9 [a]	0.914	2.840 (6)	1.973	157.70
O-2-H-8 ··· O-4 [b]	1.053	2.867 (7)	1.856	159.51
O-4-H-9 ··· O-7 [d]	0.784	2.800 (5)	2.224	130.75
O-6-H-10 ··· O-8 [e]	1.035	2.949 (4)	1.930	167.19
O-W1-H-1W ··· O-7 [f]	0.881	2.894 (9)	2.015	175.80

[a] The symmetry codes are in Table 4.

As could be expected, important differences from compound **2** in molecular conformation, packing, hydrogen bonds, and sodium ion coordination have been found, as a consequence of substitution of the sulfate group on C-3 of the pyranosid ring.

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