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Note

The crystal and molecular structure of 4-cyanophenyl 5-thio-β-D-xylopyranoside

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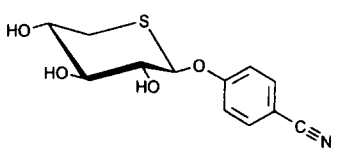
The synthesis of glycosaminoglycans may be induced by exogeneous primers such as β-D-xylopyranosyl derivatives. Although the biological process associated with such syntheses are not completely understood, there is some interest in elucidating the three-dimensional features that characterize these inducers. Actually some of them displaying antithrombotic activity have already been evaluated in an animal model [1]. The doses required for biological activity are however high. In order to design compounds that are active at lower doses, the heteroatom of these derivatives has been changed, and thioanalogues have in particular been synthesised [2]. The present note describes the crystal and molecular structure of 4-cyanophenyl 5-thio-β-D-xylopyranoside [3] (**1**) which was crystallized in methanol at 20°C.



The positional and isotropic thermal parameters of **1** for the nonhydrogen atoms are given in Table 1, whereas bond lengths and angles are reported in Table 2. A view of **1**, along with the numbering of the atoms, is shown in Fig. 1. The mean C–H distance for

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Table 1
Atomic positional parameters and equivalent thermal parameters for 4-cyanophenyl 5-thio-β-D-xylopyranoside

Atom	x	y	z	B (Å^2)
S	0.6092(9)	0.6790	0.7743(6)	3.59(2)
O-1	0.8145(2)	0.6018(9)	0.7688(1)	3.77(8)
O-2	0.8522(2)	0.4377(9)	0.8942(2)	3.57(7)
O-3	0.6953(2)	0.5197(9)	0.9784(1)	3.16(7)
O-4	0.4879(3)	0.402(1)	0.9335(2)	6.5(1)
N	0.8775(4)	0.151(2)	0.4710(2)	7.6(2)
C-1	0.7312(3)	0.494(1)	0.8034(2)	2.9(1)
C-2	0.7550(3)	0.569(1)	0.8726(2)	2.53(9)
C-3	0.6702(3)	0.449(1)	0.9140(2)	2.61(9)
C-4	0.5587(3)	0.560(1)	0.8963(2)	3.4(1)
C-5	0.5243(3)	0.503(1)	0.8282(2)	3.5(1)
C-6	0.8241(4)	0.491(1)	0.7084(2)	3.3(1)
C-7	0.7578(4)	0.289(1)	0.6790(2)	4.2(1)
C-8	0.7729(4)	0.195(2)	0.6184(2)	4.7(1)
C-9	0.8564(4)	0.306(2)	0.5868(2)	4.6(1)
C-10	0.9253(4)	0.507(2)	0.6164(2)	4.8(1)
C-11	0.9107(4)	0.597(1)	0.6778(2)	4.2(1)
C-12	0.8686(5)	0.221(2)	0.5221(3)	5.9(2)

1 is 1.00 Å (range 0.91 to 1.09 Å), whereas the mean O–H distance is 0.93 Å (range 0.79 to 1.05 Å). The mean C–C distance in the phenyl groups is 1.38 Å.

The geometric characteristics of the xylopyranose ring are in agreement with those reported for carbohydrate structures in which the intracyclic oxygen atom has been substituted by a sulfur atom [4–7]. The xylopyranose residue has the expected $^4C_1$ conformation. The internal C–C–C pyranose ring angles exhibit a significant opening (range 111.6–114.6°, mean 113.0°). The endocyclic C–C–S angles have an average of 108.8°. The exocyclic C–C–O bond angles show a wide variation: from 106.8° to 110.2°, with an average of 108.2°. The endocyclic C-1–S–C-5 angle of 96.4° is more acute than for a cyclic oxygen, this value being in agreement with those already reported for 5-thiopyranosides [4–7].

The torsion angles around the pyranose ring and the glycosidic linkage are given in Table 3. As observed by Girling and Jeffrey [4,5] and Miler-Srenger et al. [7], the angles about the C–S ring bonds are among the smallest torsion angles in the ring, whereas in the pyranose sugars, the coresponding C–O torsion angles are the largest.

The glycosidic linkage represents a molecular segment where two electronegative atoms bearing lone pairs of electrons are linked to the anomeric C atom. The electronic structure of this arrangement affects the geometry and conformation of the molecule, the resulting consequences being termed the anomeric and exo-anomeric effect [8]. If their influence on molecular geometry is well described for the C–O–C–O–C sequence, this is not the case when oxygen(s) atom(s) are substitued by sulfur(s) atom(s). This work illustrates the geometry of the C–S–C–O–C sequence.

The C-1–O-1 bond distance of 1.413 Å is larger than the standard value of 1.385 Å taken by β glycosides [9] but shorter than the standard value of 1.430 Å for a single

Table 2
Bond lengths (Å) and angles (°) of **1**

Atom 1	Atom 2	Distance	
C-1	C-2	1.517 (7)	
C-2	C-3	1.532 (8)	
C-3	C-4	1.529 (7)	
C-4	C-5	1.504 (8)	
C-1	O-1	1.413 (6)	
C-1	S	1.836 (5)	
C-2	O-2	1.421 (7)	
C-3	O-3	1.418 (6)	
C-4	O-4	1.426 (8)	
C-5	S	1.803 (6)	
Atom 1	Atom 2	Atom 3	Angle
C-1	O-1	C-6	117.6 (4)
O-1	C-1	C-2	108.2 (4)
O-1	C-1	S	108.1 (4)
C-2	C-1	S	109.5 (4)
C-1	C-2	C-3	111.6 (4)
C-1	C-2	O-2	109.5 (4)
C-3	C-2	O-2	107.2 (4)
C-2	C-3	C-4	114.6 (4)
C-2	C-3	O-3	110.2 (4)
C-4	C-3	O-3	108.1 (4)
C-3	C-4	C-5	112.8 (5)
C-3	C-4	O-4	107.7 (5)
C-5	C-4	O-4	106.8 (5)
C-4	C-5	S	112.4 (4)
C-1	S	C-5	96.4(2)

C–O bond. The bond-length distribution in the C-5–S–C-1–O-1 sequence does not follow the predicted and observed bond trends in methyl pyranosides [10]. As reported by Miler-Srenger et al. [7], the C-5–S bond is significantly shorter [1.803 (6) Å] than the S–C-1 distance [1.836 (5) Å].

The following results illustrate how the geometry at the anomeric center is influenced by an aromatic ring. The valence angle τ C-1–O-1–C-6: 117.6° falls in the range of 117° and 120° reported for aryl pyranosides [11], which is greater than the mean value of 116° reported for alkyl glucosides and disaccharides [9,12].

The orientation of the phenyl substituent with respect to the xylopyranose residue is described by the torsion angles Φ (S–C-1–O-1–C-6) and Ψ (C-1–O-1–C-6–C-7). These angles have respective values of $-78.6°$, $-177.3°$ and fall within the respective ranges of $-65°$ to $-85°$ and $180 \pm 20°$ observed in aryl pyranoside structures [11]. The orientation of the aromatic ring is nearly coplanar with respect to the anomeric carbon atom C-1. This conformation favors the delocalization of the electrons from the lone-pair orbitals of the glycosidic O atoms to the $p\pi$ orbitals of the phenyl ring. This may explain the significant opening of the τ valence angle. Another relevant geometric parameter is the O-1–C-6 bond length of 1.387 (6) Å. This value is intermediate

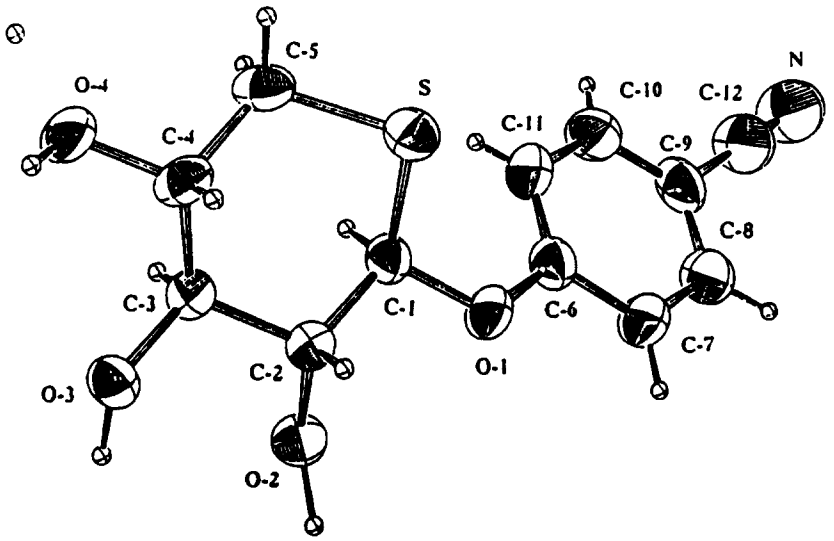

Fig. 1. A single molecule of 4-cyanophenyl 5-thio-β-D-xylopyranoside in the crystal. Thermal ellipsoids at 50% probability.

between those taken respectively by an O–C single (1.42 Å) and double bond (1.22 Å). Such partial double-bond character reflects the resonance of the glycosidic oxygen lone pairs with the aromatic ring. In this structure, the C-9–C-12 distance of 1.441 (5) Å is similarly intermediate between that of a single C–C (1.54 Å) and that of a double bond (1.33 Å). This is not the case for the C-12–N bond length, (1.140 Å), which is typical of a triple bond (1.16 Å). These data confirm the conjugation of the glycosidic oxygen lone pairs with the aromatic ring.

Two orthogonal views of the packing of the molecules in the unit cell are displayed in Fig. 2. These help to illustrate the respective roles of hydrogen-bond and hydrophobic

Table 3
Torsion angles (°) of **1**

Atom 1	Atom 2	Atom 3	Atom 4	Angle
S	C-1	O-1	C-6	−78.6(5)
C-1	O-1	C-6	C-7	−177.3(4)
S	C-1	C-2	C-3	64.4(5)
C-1	C-2	C-3	C-4	−58.4(5)
C-2	C-3	C-4	C-5	55.3(6)
C-3	C-4	C-5	S	−59.8(6)
C-4	C-5	S	C-1	59.0(4)
C-5	S	C-1	C-2	−60.8(4)
C-5	S	C-1	O-1	−178.5(3)
O-1	C-1	C-2	O-2	−59.3(5)
O-2	C-2	C-3	O-3	59.6(5)
O-3	C-3	C-4	O-4	−63.7(5)

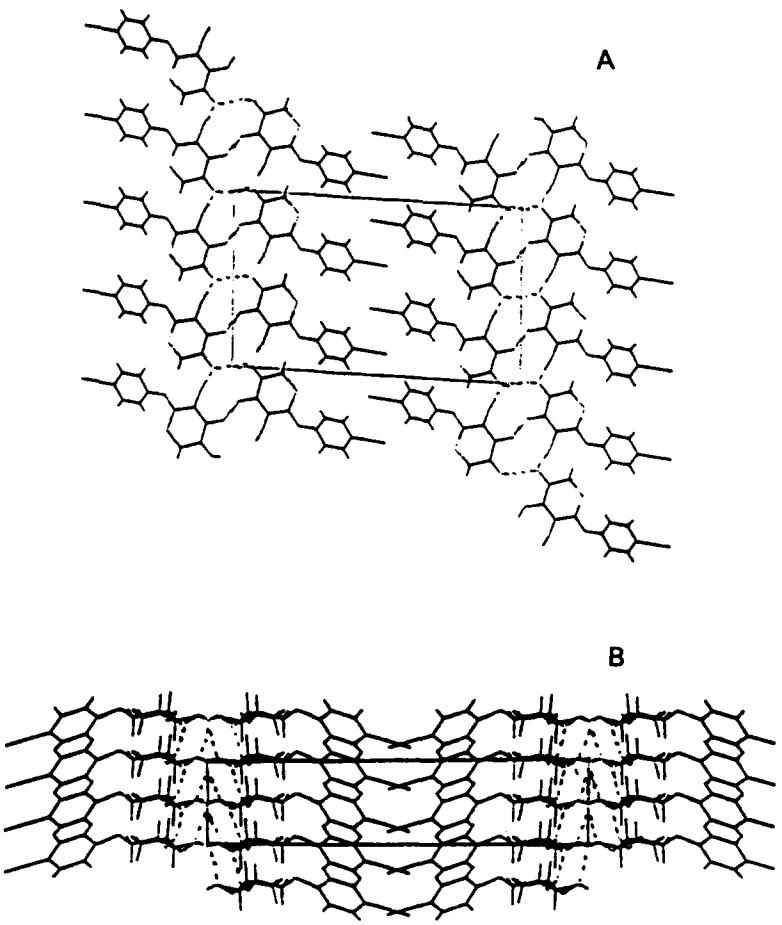

Fig. 2. Packing of the molecules of 4-cyanophenyl 5-thio-β-D-xylopyranoside in the crystal. Hydrogen bonds are shown by dashed lines. (A) View down the *a*-axis; (B) view down the *b*-axis.

interactions in the three-dimensional arrangement. There are no intramolecular hydrogen bonds. The geometrical characteristics of intermolecular hydrogen bonds of **1** are given in Table 4. It is worth noticing that all secondary hydroxyl groups are involved in

Table 4
Hydrogen bonding [a] in 4-cyanophenyl 5-thio-β-D-xylopyranoside

Donor-H · · · acceptor	D · · · A	D–H	H · · · A	D–H · · · A
	(Å)	(Å)	(Å)	(°)
O-2–H–O-2 · · · O-4 III	2.816	1.047	1.839	153.5
O-3–H–O-3 · · · O-3IV (a − b + 2c)	2.793	0.955	2.123	125.6
O-3–H–O-3 · · · O-3IV (a + 2c)	2.793	0.955	2.640	89.0
O-4–H–O-4 · · · O-4II (a + 2c)	2.835	0.800	2.232	133.0

[a] Equivalent positions: (I) x, y, z (II) $-x, y, -z$ (III) $x+1/2, 1/2+y, z$ (IV) $1/2-x, 1/2+y, -z$.

hydrogen bonding with neighbouring secondary hydroxyl groups; each acts both as a donor and an acceptor except O-2–H–O-2 which is only involved as a donor. The hydrogen-acceptor capacity of the bridged oxygen is not utilized in this structure.

The crystal packing, which is characterized by an alternation of hydrophilic and hydrophobic zones (Fig. 2), is very similar to the one reported by Girling et al. for methyl 5-thio-α- and β-D-ribopyranosides [4]. The neighbouring molecules are first arranged so as to maximize their hydrophylic interactions through the network of hydrogen-bond interactions. These arrangements occur preferentially along the *a* and *b* crystallographic axes. Then, they stack in columns in which hydrophobic contacts between the aromatic rings are favoured. These contacts also involve the most hydrophobic regions of the xylopyranose moiety, around C-6 and S. These hydrophobic interactions occur along the longest axis (*c*) of the crystalline unit cell.

1. Experimental

A single crystal of dimensions $0.28 \times 0.40 \times 0.42$ mm was used. Accurate unit-cell parameters were determined by a least-squares fit of the setting angles at high 2θ values. Lorentz and polarisation corrections were applied, but no correction was made for absorption. The unit-cell parameters and crystallographic data of interest are given in Table 5.

The intensities of 1487 independent reflections were measured inside the sphere limited by $2\theta < 50°$ at the Mo wavelength using the $\omega - 2\theta$ technique. The average of three reference reflections monitored each hour decreased by 0.1% during the data collection time. All the intensities were corrected from the background noise. From 1487 measured reflections, 1086 such as $I/\sigma(I) > 2\sigma$ were considered as observed. No absorption correction has been made being given the crystal dimensions and the small value of the absorption coefficient at the wavelength used. Scattering factors were taken

Table 5
Crystal data of 4-cyanophenyl 5-thio-β-D-xylopyranose

Molecular formula	$C_{12}H_{13}NO_4S$
Molecular weight	267.31
Crystal system	Monoclinic
Space group	C_2
Cell dimensions	
a (Å)	12.707(8)
b (Å)	4.543(3)
c (Å)	21.575(9)
β	93.57(7)
Cell volume (Å^3)	1220(1)
Z	4
F (000) (e)	560
μ (Mo$K\alpha$) cm^{-1}	2.59
D_c (kg dm^{-3})	1.455

from the International Tables of Crystallography [13]. The structure was solved by direct methods [14,15] allowing the location of all C, O, S, and N atoms. The H atoms were located by successive difference Fourier maps and isotropic refinement, leading to an R-value of 0.075. The last refinement cycles were performed using an anisotropic thermal temperature factor for the nonhydrogen atoms, whereas the hydrogen atoms were assigned an isotropic temperature factor. The final R-value was 0.029. During the refinement, each reflection was assigned a weight $w = 1/\sigma(F_o)^2$ derived by $\sigma(I)$. A final electron density map showed no significant residual density, the extreme fluctuations being -0.17 and 0.80 e A^3.

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