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Note

The crystal and molecular structure of 4-cyanophenyl and 4-nitrophenyl β-D-xylopyranosides

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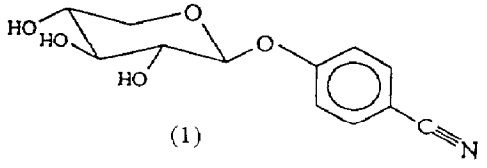
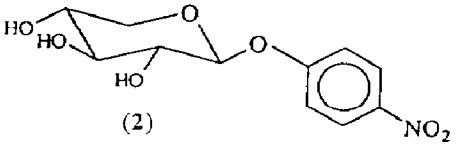
The synthesis of glycosaminoglycans may be induced by exogeneous primers such as β-D-xylopyranosyl derivatives. Although the biological process associated with such a synthesis have not been completely deciphered, there is some interest in elucidating the three-dimensional features that characterize these inducers. Actually some of them displaying antithrombotic activity have been already evaluated in an animal model [1]. The present note describes the crystal and molecular structure of 4-cyanophenyl (**1**) and 4-nitrophenyl β-D-xylopyranosides (**2**) which were respectively crystallized in methanol and a mixture of methanol and water at 20°C.



(1)



(2)

The positional and isotropic thermal parameters of **1** and **2** for the nonhydrogen atoms are given in Tables 1A and 1B, and bond lengths and angles appear in Table 2. Views of **1** and **2**, along with the numbering of the atoms, are shown in Fig. 1. The mean C–H distances for **1** and **2** are, respectively, 0.94 Å (range 0.93 to 1.02 Å), and

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Table 1A
Atomic positional parameters and equivalent thermal parameters for 4-cyanophenyl β-D-xylopyranoside (1)

Atom	x	y	z	B (Å^2)
O-1	0.5331(3)	0.7968(2)	0.8548(7)	2.97(3)
O-2	0.6984(3)	0.7180(2)	0.7423(7)	2.63(3)
O-3	1.0095(4)	0.4594(2)	0.7446(8)	3.40(3)
O-4	0.7692(3)	0.2205(2)	0.8108(7)	3.10(3)
O-5	0.5995(3)	0.5618(2)	0.8887(7)	2.93(3)
N	0.3571(5)	1.0888(3)	1.0200(1)	4.59(5)
C-1	0.5435(4)	0.6474(2)	0.8383(1)	2.51(4)
C-2	0.7493(4)	0.6349(2)	0.7943(1)	2.34(4)
C-3	0.7862(4)	0.4756(3)	0.7763(1)	2.43(4)
C-4	0.7933(4)	0.3709(2)	0.8288(1)	2.51(4)
C-5	0.5991(5)	0.4080(3)	0.8737(1)	2.96(5)
C-6	0.3381(5)	0.8461(2)	0.8872(1)	2.63(5)
C-7	0.1651(5)	0.7562(2)	0.9129(1)	2.76(5)
C-8	−0.0182(5)	0.8189(3)	0.9459(1)	3.04(5)
C-9	−0.0276(5)	0.9718(3)	0.9532(1)	3.05(5)
C-10	0.1439(5)	1.0609(3)	0.9264(1)	3.51(5)
C-11	0.3260(5)	0.9985(3)	0.8934(1)	3.33(5)
C-12	−0.2140(5)	1.0367(3)	0.9901(1)	3.44(5)

1.13 Å (range 1.06 to 1.19 Å), whereas the mean O–H distances are 0.78 Å (range 0.73 to 0.82 Å) and 0.97 Å (range 0.92 to 1.01 Å). The mean C–C distance in the phenyl group is for both structures 1.38 Å.

Table 1B
Atomic positional parameters and equivalent thermal parameters for 4-nitrophenyl β-D-xylopyranoside (2).

Atom	x	y	z	B (Å^2)
O-1	0.0328(5)	0.1309(3)	0.6423(1)	3.14(5)
O-2	0.2024(4)	0.2013(7)	0.7546(1)	2.72(5)
O-3	0.5180(5)	0.4569(3)	0.7541(1)	3.43(5)
O-4	0.2665(5)	0.6987(3)	0.6933(1)	3.27(5)
O-5	0.1052(5)	0.3665(3)	0.6119(1)	3.17(6)
O-6	−0.8487(6)	−0.0161(4)	0.4798(1)	5.15(7)
O-7	−0.8265(5)	−0.2127(3)	0.5317(1)	4.10(6)
N	−0.7563(6)	−0.0895(3)	0.5189(1)	3.42(7)
C-1	0.0475(7)	0.2784(4)	0.6603(2)	2.66(7)
C-2	0.2546(7)	0.2863(4)	0.7040(1)	2.44(4)
C-3	0.2893(4)	0.4436(3)	0.7232(1)	2.67(7)
C-4	0.2943(4)	0.5521(2)	0.6732(2)	2.68(7)
C-5	0.0987(8)	0.5171(4)	0.6283(2)	3.34(8)
C-6	−0.1710(7)	0.0862(4)	0.6120(2)	2.63(8)
C-7	−0.3168(7)	0.1792(2)	0.5802(2)	2.98(8)
C-8	−0.5111(7)	0.1210(4)	0.5488(2)	3.10(5)
C-9	−0.5527(7)	−0.0274(3)	0.5515(1)	2.85(8)
C-10	−0.4083(8)	−0.1213(4)	0.5840(2)	3.08(8)
C-11	−0.2133(8)	−0.0639(4)	0.6140(2)	3.02(8)
C-12	−0.2140(5)	1.0367(3)	0.9901(1)	3.44(5)

Table 2
Bond lengths (Å) and angles (°) of 4-cyanophenyl (**1**) and 4-nitrophenyl (**2**) β-D-xylopyranosides

Atom 1	Atom 2	Distance (**1**)	(**2**)
C-1	C-2	1.512(3)	1.519(5)
C-2	C-3	1.512(3)	1.513(5)
C-3	C-4	1.521(3)	1.514(5)
C-4	C-5	1.512(4)	1.523(5)
C-1	O-1	1.404(3)	1.410(4)
C-1	O-5	1.413(3)	1.406(4)
C-2	O-2	1.424(3)	1.424(4)
C-3	O-3	1.431(3)	1.450(5)
C-4	O-4	1.427(3)	1.423(4)
C-5	O-5	1.433(3)	1.425(4)

Atom 1	Atom 2	Atom 3	Angle (**1**)	(**2**)
C-1	O-1	C-6	119.1(2)	118.4(3)
O-1	C-1	C-2	106.2(2)	106.3(3)
O-1	C-1	O-5	108.8(2)	109.2(3)
C-2	C-1	O-5	109.0(2)	108.8(3)
C-1	C-2	C-3	110.5(2)	109.4(3)
C-1	C-2	O-2	110.9(2)	111.0(3)
C-3	C-2	O-2	107.9(2)	107.8(3)
C-2	C-3	C-4	112.8(2)	113.8(3)
C-2	C-3	O-3	110.4(2)	109.3(3)
C-4	C-3	O-3	107.8(2)	107.4(3)
C-3	C-4	C-5	111.6(2)	111.1(3)
C-3	C-4	O-4	111.6(2)	111.6(3)
C-5	C-4	O-4	109.7(2)	109.9(3)
C-4	C-5	O-5	111.9(2)	111.3(3)
C-1	O-5	C-5	110.0(2)	109.7(3)

The geometric characteristics of the xylopyranose rings are in agreement with the ones reported for carbohydrate structures [2,3]. The xylopyranose residues have the expected $^4C_1$ conformation. The internal C–C–C pyranose ring angles exhibit a

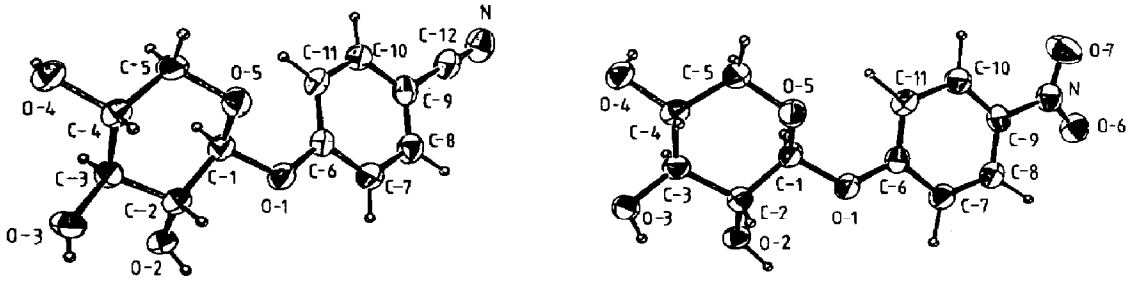

Fig. 1. ORTEP plots of 4-cyanophenyl β-D-xylopyranoside (**1**) and 4-nitrophenyl β-D-xylopyranoside (**2**) in the crystal. Thermal ellipsoids at 50% probability.

significant opening: **1**: range 110.5–112.8°, mean 111.6°; **2**: range 109.4–113.8°, mean 111.4°. The endocyclic C–C–O angles in **1** and **2** have, respectively, an average of 110.4° and 110.0°. In both structures the exocyclic C–C–O bond angles show a wide variation from 107.8° to 111.6°, with an average of 109.7° for **1**; and from 107.4° to 111.6°, with an average of 109.5° for **2**. The endocyclic C-1–O-5–C-5 angle is 110° in **1** and 109.7° in **2**. These results agree with the standard molecular dimensions adopted for pyranosides [2,3].

The geometry around the glycosidic linkage shows the structural features associated with the anomeric effect [4]. However, the C-1–O-1 and C-1–O-5 bond distances are respectively larger (**1**: 1.404 Å; **2**: 1.410 Å) and smaller (**1**: 1.413 Å; **2**: 1.425 Å) than the standard values of 1.385 and 1.428 Å generally shown by β-glycosides [2,3].

The present results illustrate how the geometry at the anomeric center is influenced by an aromatic ring. The magnitude of valence angles τ C-1–O-1–C-6 (**1**: 119.1°; **2**: 118.4°) falls in the range of 117 and 120° reported so far for aryl pyranosides [6], and it is greater than the mean value of 116° reported for alkyl glucosides and disaccharides [4,5].

The orientation of the phenyl substituent with respect to the xylopyranose residue is described by the torsion angles Φ (O-5–C-1–O-1–C-6) and Ψ (C-1–O-1–C-6–C-7). These angles have respective values of $-73.3°$ and $-170.5°$ for **1** and $-76.2°$ and $-158.31°$ for **2** and fall within the respective ranges of $-65°$ to $-85°$ and $-180° \pm 20°$ observed in aryl pyranoside structures [6]. In **1** and **2** the orientation of the aromatic ring is nearly coplanar with respect to the anomeric C-1 carbon atoms. This conformation favors the delocalization of the electrons from the lone-pair orbitals of the glycosidic O atom to the $p\pi$ orbitals of the phenyl ring. This may explain the significant widening of the τ valence angle. Another relevant geometric parameter is the O-1–C-6 bond length of 1.375 (3) Å for **1** and 1.381 Å for **2**. This value is intermediate between those taken, respectively, by a O–C single (1.42 Å) and a double bond (1.22 Å). Such a partial double-bond character reflects the resonance of the glycosidic oxygen lone pairs with the aromatic ring. In **1** the C-9–C-12 distance of 1.448 (3) Å is similarly intermediate between that of a single C–C (1.54 Å) and that of a double bond (1.335 Å), and the C-12–N bond length of 1.141 Å is intermediate between that of a double C–N (1.21 Å) and that of a triple bond (1.158 Å). This is not the case for **2**, in which the C-9–N distance of 1.461 Å has the expected value of a single C–N bond. These data confirm the conjugation of the glycosidic oxygen lone pairs with the aromatic ring. For **1**, the resonance could also involve the C-12 and N atoms of the nitrile group, the phenyl ring being a transmitter of electronic effects.

Two orthogonal views of the packing of the molecules in the unit cell are displayed in Figs. 2a and 2b (**1**) and Figs. 3a and 3b (**2**). They help in illustrating the respective roles of hydrogen-bond and hydrophobic interactions in the three-dimensional arrangements. There are no intramolecular hydrogen bonds. The geometric characteristics of intermolecular hydrogen bonds for **1** and **2** are, respectively, given in Tables 3A and 3B. All secondary hydroxyl groups are involved in hydrogen bonding with neighboring secondary hydroxyl groups; each acts both as a donor and an acceptor. However, the hydrogen-acceptor capacities of the ring oxygens and bridged oxygens are not utilised in this structure.

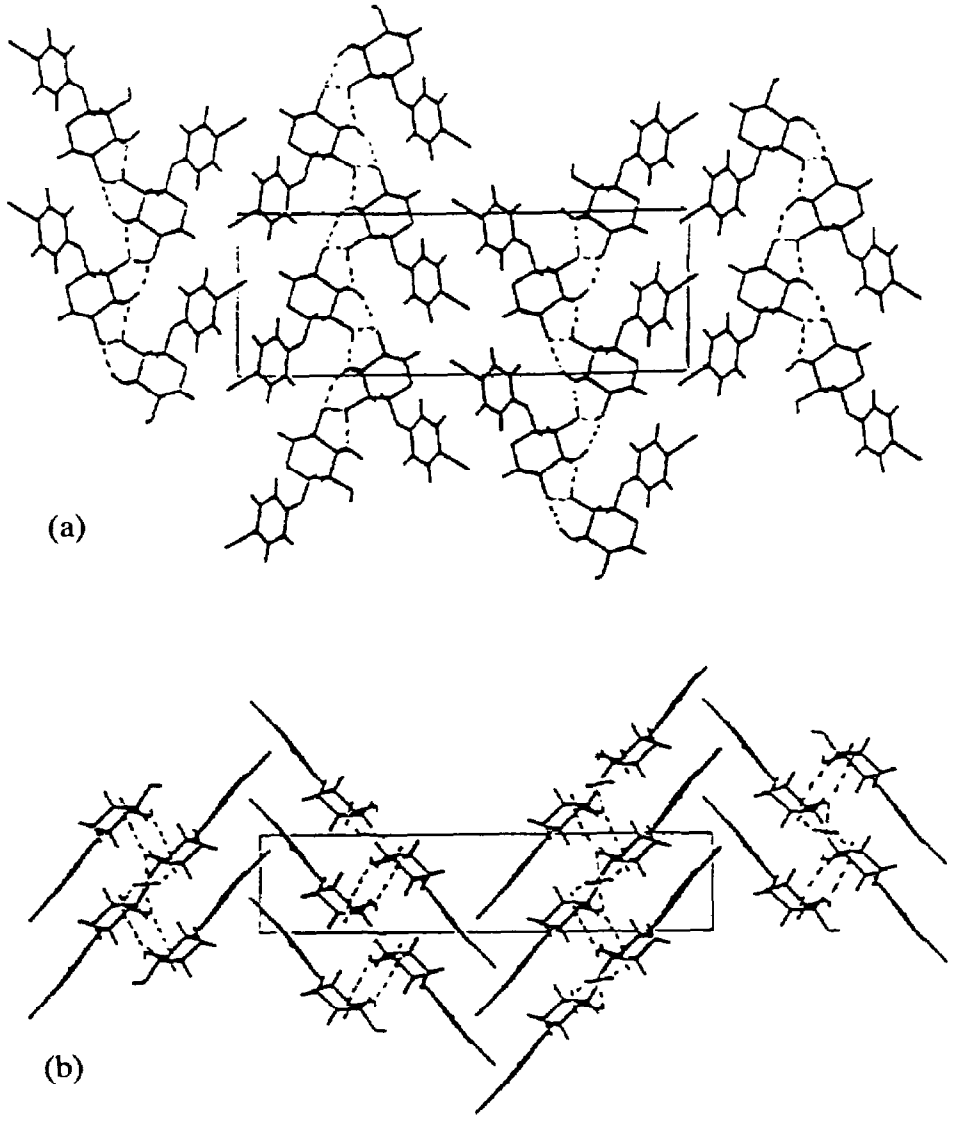

Fig. 2. Packing of the molecules of 4-cyanophenyl β-D-xylopyranoside (**1**) in the crystal. Hydrogen bonds are shown by dashed lines. (a) View down the *a* axis; (b) view down the *b* axis.

The crystal packing is characterised by an alternation of hydrophilic and hydrophobic zones (Figs. 2a, b and 3a, b). The neighboring 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 axis. Then, they stack in columns in which hydrophobic contacts between the aromatic rings are favored; these contacts also involve the most hydrophobic moiety of xylopyranose, around C-6 and O-5. These hydrophobic interactions occur along the longest axis (*c*) of the crystalline unit cell.

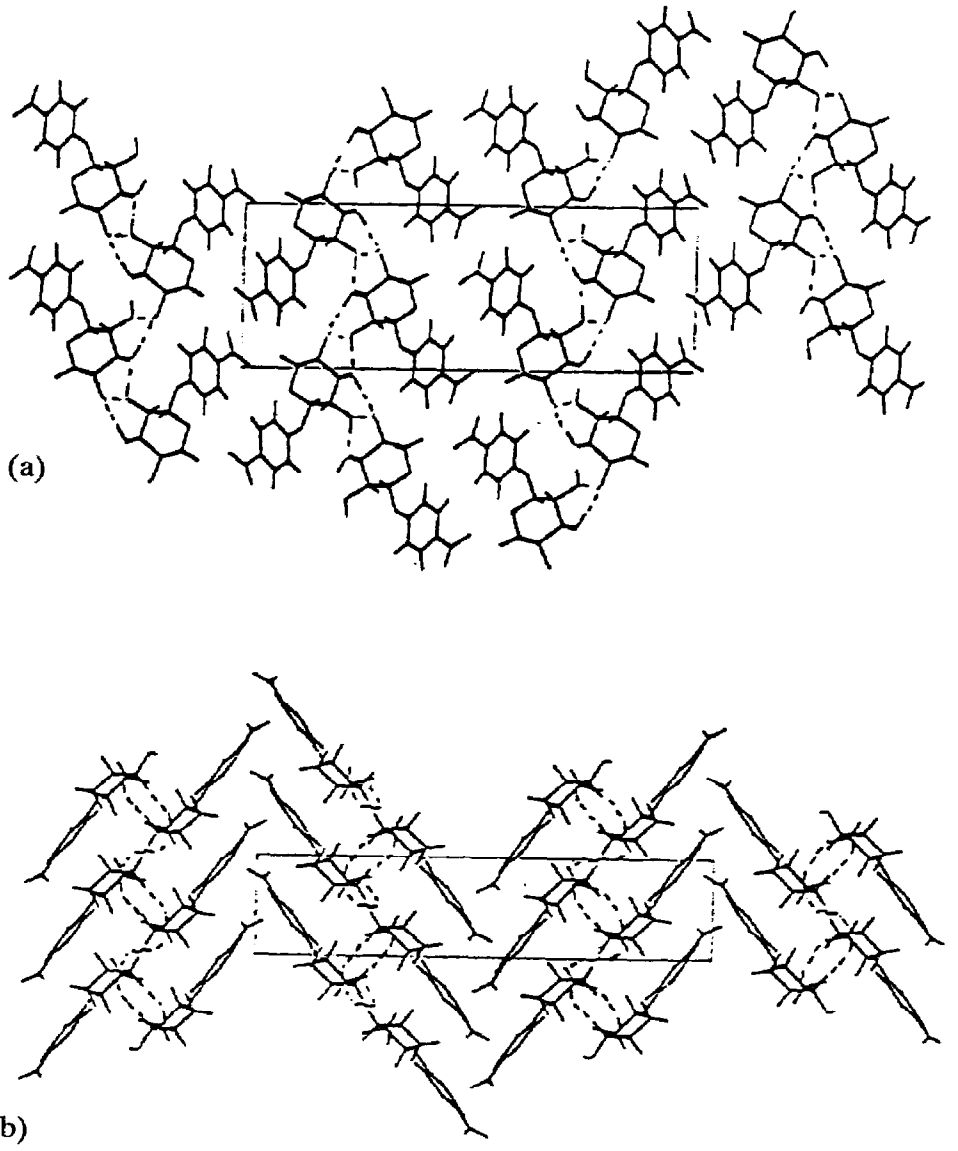

Fig. 3. Packing of the molecules of 4-nitrophenyl β-D-xylopyranoside (2) in the crystal. Hydrogen bonds are shown by dashed lines. (a) View down the *a* axis; (b) view down the *b* axis.

1. Experimental

Single crystals of dimensions $0.20 \times 0.20 \times 0.40$ mm and $0.10 \times 0.10 \times 0.50$ mm were repectively used for **1** and **2**. Accurate unit-cell parameters were determined by a least-squares fit of the setting angles at high 2θ values. Lorentz and polarisation

Table 3A
Hydrogen bonding in 4-cyanophenyl β-D-xylopyranoside (1)

Donor-H · · · acceptor [a]	D · · · A (Å)	D–H (Å)	H · · · A (Å)	D–H · · · A (°)
O-2–H-O-2 · · · O-3 III (2a + c)	2.730	0.778	1.956	172.86
O-3–H-O-3 · · · O-4 III (2a + c)	2.939	0.825	2.244	142.25
O-4–H-O-4 · · · O-2 III (a − b + c)	2.841	0.729	2.127	166.66

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

Table 3B
Hydrogen bonding in 4-nitrophenyl β-D-xylopyranoside (2)

Donor-H · · · acceptor [a]	D · · · A (Å)	D–H (Å)	H · · · A (Å)	D–H · · · A (°)
O-2–H-O-2 · · · O-3 III (a − b + c)	2.718	0.986	1.921	135.87
O-3–H-O-3 · · · O-4 III (a − b + c)	2.900	0.918	2.151	138.19
O-4–H-O-4 · · · O-2 III (c)	2.845	1.013	1.906	152.92

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

corrections were applied, but no correction was made for absorption. The unit-cell parameters and crystallographic data of interest for **1** and **2** are given in Table 4 [1].

For **1** and **2**, the intensities of 1212 and 1401 independent reflections, respectively 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% for **1** and by 0.2% for **2** during the data collection time. All the intensities were corrected from the background noise. From 1212 (**1**) and 1401 (**2**) measured reflections, 1008 and 791 such as $I/\sigma(I) > 2\sigma$ were respectively considered as observed. No absorption correction has been made given the crystal dimensions and the small value of the absorption coefficients at the wavelength used. Scattering factors were taken from the International Tables of Crystallography [7]. The structures were solved by direct methods [8,9] allowing the location of all C, O, and N atoms. The H atoms were located by successive difference Fourier maps and isotropic refinement, leading to R values of 0.076 for **1** and 0.075 for **2**. 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 values were 0.024 for **1** and 0.029 for **2**. During the refinement, each reflection was assigned a weight $w = 1/\sigma(F_o)^2$ derived by $\sigma(I)$. Final electron-density maps showed

[1] Tables of observed and calculated structure-amplitudes and general displacement parameter expressions have been deposited with the Cambridge Crystallographic Data Centre and may be obtained from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

Table 4
Crystal data and structure determination and refinement data for 4-cyanophenyl (**1**) and 4-nitrophenyl β-D-xylopyranose (**2**).

	1	**2**
Molecular formula	$C_{12}H_{13}NO_5$	$C_{11}H_{13}NO_7$
Molecular weight	251.24	271.23
Crystal system	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions		
a (Å)	5.508 (1)	5.508 (1)
b (Å)	9.052 (2)	9.126 (2)
c (Å)	22.616 (6)	22.896 (6)
Cell volume (Å^3)	1127.6 (5)	1150 (1)
Z	4	4
F (000) (e)	528	568
μ(Mo$K\alpha$) cm^{-1}	1.089	1.240
D_c (kg·dm^{-3})	1.480	1.565

no significant residual density, the extreme fluctuations being -0.08 and 0.15 e.Å^{-3} for **1** and -0.17 and 0.16 e.Å^{-3} for **2**.

Acknowledgments

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