Carbohydrate Research, 93 (1981) 135–140
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Note

Extended zigzag conformation of 1-*O*-D-α-glucopyranosyl-D-mannitol

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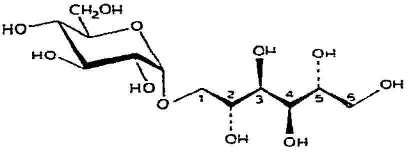
(Received October 20th, 1980; accepted for publication, December 18th, 1980)

The wealth of conformational information on acyclic sugar chains[1,2] and on pyranoid sugars[1,3] contrasts with the scarce knowledge of systems in which both of these structural features are combined. Thus, for the large variety of glycosylalditols[4], conformational data are only available—in the form of X-ray analyses—for two β-(1→4)-linked compounds[5]. There is intrinsic interest in such compounds, in particular in relation to the extent to which the alditol conformation is influenced by the attached pyranoid ring, and to whether conformation can be correlated with sweetness. 1-*O*-α-D-Glucopyranosyl-D-mannitol (**1**) and its C-5-epimer isomaltitol* have been developed as low-nutritive[6], non-cariogenic[7] sugar substitutes having about half the sweetness of sucrose[8]. Compound **1** is readily available from sucrose *via* microbial 2→6-transglucosylation to give palatinose (isomaltulose)[9] and subsequent hydrogenation[10] to give a mixture of **1** and isomaltitol*: both reactions can be performed on an industrial scale. The convenient crystallisation of **1** as a dihydrate provided the opportunity to examine its conformational features by a crystal structure analysis, ^{1}H- (270 MHz) and ^{13}C-n.m.r. data[11] having failed to provide any information utilisable in this respect. The conformation of **1**, using an adaptation of the graphic presentation with tapered bonds[12], is shown in **1a**.



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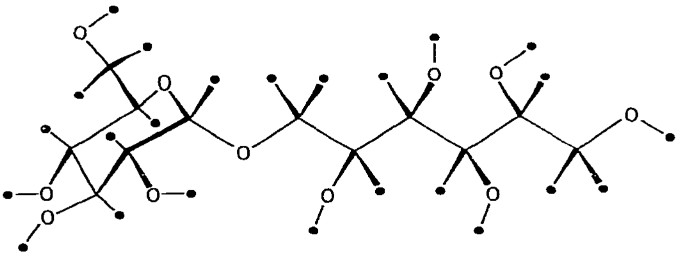

1a

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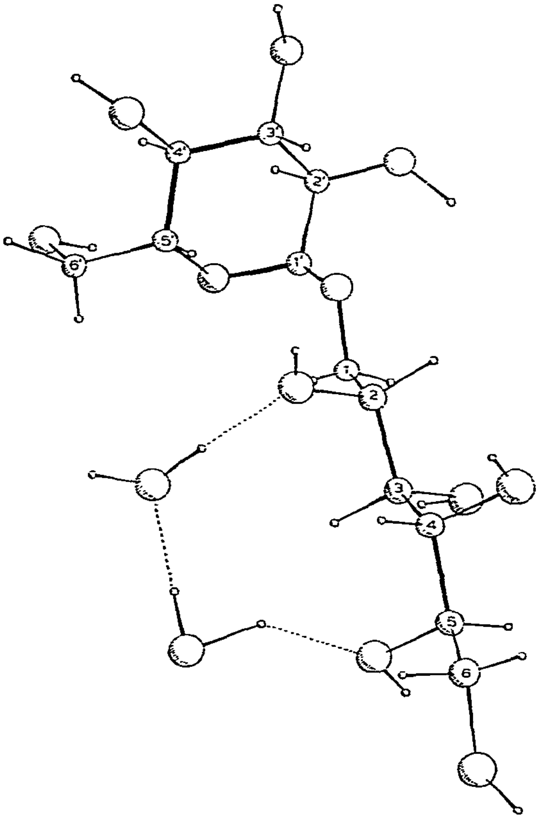
*An equimolar mixture of **1** and isomaltitol is designated Palatinit®, a registered trade name of Süddeutsche Zucker AG, Mannheim.



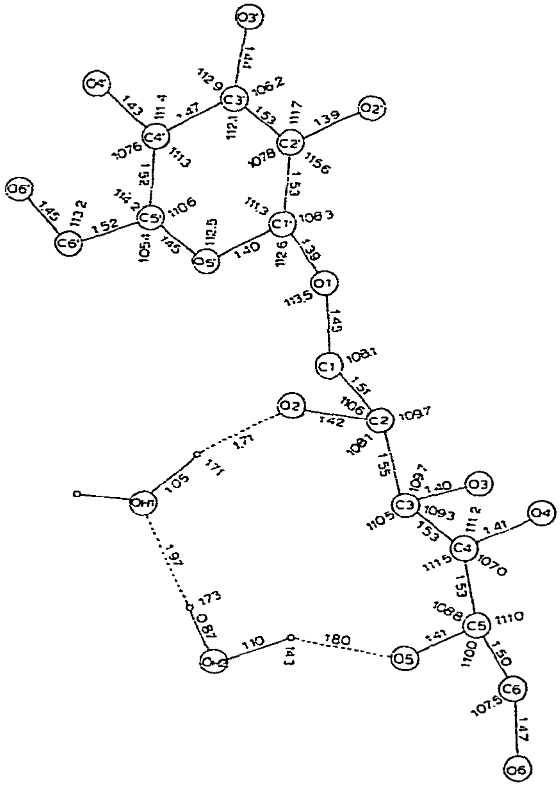


Fig. 1. Perspective view[15] of the molecular structure of 1-*O*-α-D-glucopyranosyl-D-mannitol dihydrate (**1** · $2H_2O$), the two molecules of crystal water forming a double bridge between O-2 and O-5 of the mannitol portion. Carbon atoms have been numbered; for complete numbering, see Fig. 2.

Fig. 2. Bond distances (Å) and bond angles (degrees) in the dihydrate of **1**. Standard deviations are $\sigma_{xx} = 0.01$ Å, $\sigma_{xxx} = 0.8°$ (x = C,O), $\sigma_{OH} = 0.06$ Å, and $\sigma_{OHO} = 4°$.

Fig. 1 depicts the molecular geometry of **1** dihydrate, whereby the two molecules of crystal water are fixed *via* hydrogen bonds to the mannitol portion, forming a "double water bridge" of the unusual type $\text{-}\underset{H}{O}(\text{-}2)\cdots\underset{H}{HO}\cdots\underset{H}{HOH}\cdots O(\text{-}5)$, *i.e.*, between two oxygen atoms that are five bonds apart. The mannitol chain adopts a nearly planar, zigzag conformation, the deviation from 180° torsional angles along the carbon chain being within the same range (±5°) as those observed[13,14] for the polymorphic forms of D-mannitol (**2**), as is revealed by the juxtaposition of the respective data (Table I); only the C-3–C-4–C-5–C-6 dihedral angle exhibits a somewhat larger (11.7°) divergence. The terminal 6-hydroxyl group, unlike those in **2**, is in an extended orientation, so that the oxygen atom is in the same plane as the carbon atoms. The same holds true for the glycosidically linked O-1. Since, in addition, the torsion angles of the glycosidic linkage, *i.e.*, C-1′–O-1–C-1–C-2 and C-2′–C-1′–O-1–C-1, deviate

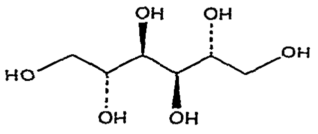
TABLE I

COMPARISON OF TORSIONAL ANGLES (DEGREES) IN **1**, MANNITOL[13,14] (**2**), METHYL α-D-GLUCOPYRANOSIDE[16] (**3**), AND DECYL α-D-GLUCOPYRANOSIDE[17] (**4**)

Mannitol chain	**1**	**2**	
		B-form[13]	*K-form*[14]
O-1–C-1/C-2–C-3	−171.9	55.5	62.9
C-1–C-2/C-3–C-4	178.9	−179.8	−176.6
C-2–C-3/C-4–C-5	176.4	175.8	175.8
C-3–C-4/C-5–C-6	−168.3	−175.3	−174.8
C-4–C-5/C-6–O-6	175.8	56.2	65.4
O-1–C-1/C-2–O-2	68.9	−64.9	−60.5
O-2–C-2/C-3–O-3	179.1	176.5	−173.9
O-3–C-3/C-4–O-4	56.0	59.0	58.9
O-4–C-4/C-5–O-5	−168.4	−176.8	−175.3
O-5–C-5/C-6–O-6	55.3	−64.5	−58.0
Pyranoid ring[a]	**1**	**3**[16]	**4**[17]
C-1′–C-2′/C-3′–C-4′	−53.5	−55.6	−52.8
C-2′–C-3′/C-4′–C-5′	52.8	−54.2	53.8
C-3′–C-4′/C-5′–O-5′	−53.4	−54.1	−54.1
C-4′–C-5′/O-5′–C-1′	58.4	58.0	58.3
C-5′–O-5′/C-1′–C-2′	−61.7	−60.1	−60.7
O-5′–C-1′/C-2′–C-3′	57.4	58.2	56.5
O-1–C-1′/C-2′–O-2′	58.7	61.5	56.5
O-2′–C-2′/C-3′–O-3′	54.8	58.7	62.0
O-3′–C-3′/C-4′–O-4′	−67.4	−67.7	−69.1
O-4′–C-4′/C-5′–C-6′	65.6	64.3	68.7
O-5′–C-5′/C-6′–O-6′	−65.6	−73.5	−66.2
Glycosidic link[a]			
O-5′–C-1′/O-1–C-1	74.6	63.0	66.2
C-2′–C-1′/O-1–C-1	−161.9	−175.6	−171.0
C-1′–O-1/C-1–C-2	−167.1	—	−164.5

[a] For comparative reasons, atoms of the pyranoid ring in **3** and **4** are prime-numbered; O-1 refers to the interglycosidic oxygen atom, and C-1 to the carbon atom of the acyclic residue directly linked to O-1.

from the perfect antiparallel arrangement by only 13 and 18°, respectively, the conformation of **1** is best described as having a nearly planar, zigzag chain from the terminal O-6 to C-2′ in the pyranoid ring, comprising a total of 10 atoms.



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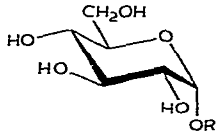

3 R = Me

4 R = $H_3C(CH_2)_9$

The pyranoid ring in **1**-dihydrate has the expected chair conformation ($^4C_1$-D), as evidenced by ring torsion-angles of 53–62° (Table I) that are very similar to those observed for methyl and decyl α-D-glucopyranosides (**3** and **4**) (*cf.* Table I). Similarly, ring valence angles and bond lengths (Fig. 2) are within the normal[2] limits, the anomeric O-5′–C-1′ bond expectedly being shorter (1.40 Å) than the O-5′–C-5′ distance (1.45 Å). In the pyranoid hydroxymethyl group, O-6′ is in a *gauche–gauche* relationship towards the ring, which is the expected[3] conformational preference. Thus, on the basis of the close correspondence of the ring conformations of **1**, **3**, and **4**, no influence is exerted by the mannitol portion on the ring conformation or *vice versa*, inasmuch as intramolecular hydrogen-bonds between OH groups of the cyclic and acyclic portions of the molecule are also distinctly absent.

Notwithstanding, the glycosidic torsion-angle O-5′–C-1′–O-1–C-1 in **1** is somewhat larger (75°) than that observed for **3** and **4** (63 and 66°, respectively), and

TABLE II

POSITIONAL PARAMETERS FOR 6-*O*-α-D-GLUCOPYRANOSYL-D-MANNITOL DIHYDRATE (**1** · $2H_2O$)[a]

Atom	*x/a*	*y/b*	*z/c*	*Atom*	*x/a*	*y/b*	*z/c*
C-1	0.8702(4)	0.5099(11)	0.7430(14)	H(C-1′)	0.933(4)	0.322(9)	0.715(11)
O-1	0.9333(3)	0.5120(7)	0.7097(8)	H(C-11)	0.866(4)	0.444(9)	0.827(12)
C-2	0.8513(4)	0.6490(10)	0.7949(12)	H(C-12)	0.851(4)	0.494(9)	0.626(12)
O-2	0.8555(3)	0.7376(7)	0.6492(9)	H(C-2)	0.882(4)	0.679(9)	0.891(11)
C-3	0.7860(4)	0.6471(10)	0.8577(13)	H(O-2)	0.879(4)	0.781(9)	0.646(13)
O-3	0.7800(3)	0.5592(8)	0.9996(10)	H(C-3)	0.760(3)	0.616(9)	0.733(9)
C-4	0.7664(4)	0.7869(10)	0.9144(13)	H(O-3)	0.773(4)	0.497(8)	0.921(10)
O-4	0.7983(3)	0.8306(8)	1.0626(10)	H(C-4)	0.769(4)	0.849(9)	0.807(12)
C-5	0.7009(4)	0.7868(10)	0.9652(14)	H(O-4)	0.821(4)	0.871(10)	1.014(12)
O-5	0.6686(3)	0.7193(8)	0.8345(9)	H(C-5)	0.699(4)	0.728(9)	1.078(12)
C-6	0.6780(5)	0.9267(13)	0.9850(20)	H(O-5)	0.640(4)	0.698(9)	0.895(12)
O-6	0.6143(3)	0.9180(9)	0.0203(10)	H(C-6′)	0.693(4)	0.959(10)	0.088(12)
C-1′	0.9535(4)	0.3972(10)	0.6252(12)	H(C-6′)	0.680(4)	0.972(9)	0.901(13)
C-2′	1.0208(4)	0.3888(10)	0.6499(13)	H(O-6)	0.598(4)	0.987(8)	0.094(10)
O-2′	1.0403(3)	0.3847(7)	0.8233(9)	H(C-2′)	1.032(4)	0.309(8)	0.551(10)
C-3′	1.0487(4)	0.5045(11)	0.5487(12)	H(O-2′)	1.009(4)	0.391(9)	0.913(12)
O-3′	1.1119(3)	0.4895(8)	0.5677(9)	H(C-3′)	1.036(4)	0.587(9)	0.623(11)
C-4′	1.0295(4)	0.5076(11)	0.3643(13)	H(O-3′)	1.130(4)	0.568(8)	0.542(11)
O-4′	1.0500(3)	0.6253(7)	0.2772(10)	H(C-4′)	1.040(4)	0.447(8)	0.279(10)
C-5′	0.9623(4)	0.5052(11)	0.3498(13)	H(O-4′)	1.071(4)	0.608(9)	0.172(12)
O-5′	0.9381(3)	0.3939(7)	0.4467(8)	H(C-5′)	0.952(4)	0.586(9)	0.434(11)
C-6′	0.9393(4)	0.4893(12)	0.1635(15)	H(C-6′1)	0.950(4)	0.560(8)	0.042(10)
O-6′	0.9619(3)	0.3714(8)	0.0761(10)	H(C-6′2)	0.899(4)	0.485(9)	0.181(11)
OH-1	0.7794(3)	0.6678(9)	0.3822(12)	H(O-6′)	0.958(4)	0.294(9)	0.156(11)
OH-2	0.6708(4)	0.7883(9)	0.4807(11)	H(OH-11)	0.810(4)	0.701(9)	0.478(10)
				H(OH-12)	0.785(4)	0.717(8)	0.279(10)
				H(OH-21)	0.688(4)	0.765(9)	0.613(10)
				H(OH-22)	0.702(3)	0.749(9)	0.440(11)

[a] Standard deviations in parentheses.

TABLE III

THERMAL PARAMETERS[a] FOR THE HEAVY ATOMS[b] IN **1** · $2H_2O$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C-1	0.009(5)	0.025(5)	0.017(2)	−0.007(5)	0.003(4)	0.000(5)
O-1	0.004(3)	0.025(4)	0.015(2)	−0.002(3)	−0.001(3)	0.000(3)
C-2	0.005(4)	0.016(4)	0.010(2)	0.000(4)	0.001(4)	0.000(4)
O-2	0.009(3)	0.028(4)	0.018(2)	0.007(4)	0.006(3)	−0.009(3)
C-3	0.007(4)	0.020(5)	0.013(2)	0.003(5)	0.003(4)	−0.002(4)
O-3	0.028(4)	0.026(4)	0.027(2)	0.013(4)	0.018(4)	0.004(4)
C-4	0.011(5)	0.013(5)	0.012(2)	0.000(4)	0.002(4)	−0.002(4)
O-4	0.015(4)	0.037(5)	0.026(2)	−0.004(4)	−0.002(3)	−0.010(4)
C-5	0.010(5)	0.021(5)	0.016(2)	−0.010(5)	0.002(4)	0.000(4)
O-5	0.011(3)	0.036(4)	0.023(2)	−0.010(4)	0.004(3)	−0.002(4)
C-6	0.026(6)	0.038(7)	0.032(3)	−0.006(7)	0.000(5)	0.006(6)
O-6	0.013(4)	0.054(5)	0.033(2)	−0.014(4)	0.010(3)	0.017(4)
C-1′	0.004(4)	0.021(5)	0.013(2)	−0.001(5)	−0.002(4)	−0.003(4)
C-2′	0.007(4)	0.023(5)	0.015(2)	−0.004(5)	−0.002(4)	0.004(4)
O-2′	0.013(3)	0.031(4)	0.022(2)	0.001(4)	0.000(3)	0.008(3)
C-3′	0.006(4)	0.027(5)	0.016(2)	−0.001(5)	0.001(4)	0.003(5)
O-3′	0.011(4)	0.045(5)	0.029(2)	0.011(4)	−0.004(3)	0.001(4)
C-4′	0.011(4)	0.019(5)	0.015(2)	0.004(5)	0.007(4)	0.002(4)
O-4′	0.035(4)	0.023(4)	0.029(2)	0.013(4)	0.013(4)	−0.011(4)
C-5′	0.012(4)	0.024(5)	0.018(2)	0.004(5)	0.001(4)	−0.003(5)
O-5′	0.009(3)	0.022(4)	0.015(2)	0.002(3)	0.000(3)	0.000(3)
O-6′	0.015(5)	0.030(7)	0.023(3)	0.001(6)	−0.001(4)	−0.002(5)
C-6′	0.033(4)	0.028(4)	0.031(2)	0.001(4)	0.000(4)	−0.004(4)
OH-1	0.030(4)	0.058(6)	0.044(3)	0.003(5)	−0.001(4)	−0.010(5)
OH-2	0.036(5)	0.053(5)	0.044(3)	0.009(5)	0.006(4)	0.025(5)

[a] The form of the anisotropic temperature factor is $T = \exp[-2\pi^2(U_{11}a^{*2}h^2 + U_{22}b^{*2}k^2 + U_{33}c^{*}{}_{2}l^2 + 2U_{12}a^{*}b^{*}hk + 2U_{13}a^{*}c^{*}hl + 2U_{23}b^{*}c^{*}kl)]$; standard deviations in parentheses. [b] Isotropic temperature factor for all H atoms: $U = 0.038$ Å^2.

more closely corresponds to those observed for such (1→6)-α-D-linked disaccharides as isomaltulose[18] (77°) and α-melibiose[19] (76°), which both have either direct or indirect hydrogen-bonding between the glycosyl portions. This clearly indicates that intermolecular forces are operating, which indeed are observed, since all hydroxyl groups are involved in a complex system of hydrogen bonds between different molecules*.

EXPERIMENTAL

Crystals of **1**-dihydrate, prepared from Palatinit[8,10], and grown from aqueous solution, were orthorhombic needles, space group $P2_12_12_1$, with cell constants of $a = 22.59$ (2), $b = 10.02$ (1), and $c = 7.61$ (1) Å; $V = 1722.1$ Å^3, $Z = 4$, $D_x =$

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*Figures on packing of the molecules in the crystal are available from the authors.

1.467 g.cm^{-3}, D_0 = 1.47 (1) g.cm^{-3} (flotation). Intensities of 1515 symmetry-independent reflections hk0 to hk6 with 4° < δ < 60° were measured on a STOE two-circle-diffractometer (CuKα radiation) equipped with a graphite monochromator; 1272 reflections with $|F| \geqslant 3\sigma_F$ were used for structure determination and refinement. The structure was solved by direct methods and refined by least-squares calculations and difference maps[20]. With anisotropic temperature factors for the C and O atoms and a constant isotropic temperature factor for all H atoms, R was reduced to 0.070. The final parameters are listed in Tables II and III. All C–C and C–O bond-distances and bond-angles are summarised in Fig. 2.

ACKNOWLEDGMENTS

The authors thank Drs. H. Schiweck and M. Munir (Süddeutsche Zucker AG, Obrigheim) for kindly providing crystals of **1**, Dr. K.-H. Fasol (Südzucker Mannheim) for computer-time funds, and Dr. J. Stegemann for expert technical assistance.

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