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THE CRYSTAL AND MOLECULAR STRUCTURE OF 1,6-ANHYDRO-β-D-MANNOPYRANOSE

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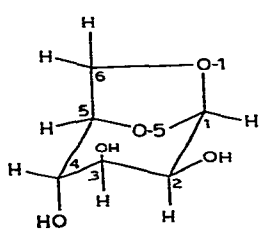
ABSTRACT

The crystal structure of 1,6-anhydro-β-D-mannopyranose, $C_6H_{10}O_5$, is orthorhombic, $P2_12_12_1$, with $a = 10.971(2)$, $b = 13.935(3)$, $c = 9.012(1)$ Å, $V = 1377.76$ Å^3 (MoKα, $\lambda = 0.7107$ Å), $Z = 8$, $D_x = 1.563$ M.gm^{-3}, $D_m = 1.565$ M.gm^{-3}. The structure was solved by MULTAN and refined to $R(F) = 0.043$ for 2355 reflections. The two symmetry-independent molecules in the unit cell have similar conformations, except for the orientation of one of the three hydroxyl groups. The conformation of the pyranose rings is $^1C_4$ distorted towards E_0, and that of the anhydro rings is ^oE. There are significant differences between the two molecules in two of the four C–O bond-lengths. These occur where there are important differences in the hydrogen-bonding environment of the oxygen atoms. The molecules are hydrogen-bonded by three linear and three bifurcated O-H···O interactions which form four-membered loops linked into infinite chains. Empirical force-field calculations with MMI-CARB reproduced the geometry of the molecules within the variations observed experimentally between the two molecules, except for a C–O bond in one of the molecules. The effect of excluding the anomeric effect from the theoretical calculations was not significant. Calculations for an intramolecularly hydrogen-bonded molecule were also carried out as a model for the molecules in a non-polar solvent.

INTRODUCTION

The structure determination of 1,6-anhydro-β-D-mannopyranose (**1**) is the eleventh in a series of 1,6-anhydropyranose molecules studied by X-ray analysis.



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Except for 1,6-anhydro-2,4-deoxy-2,4-difluoro-β-D-glucopyranose[1], all of these molecules have been examined by empirical force-field calculations, and the theoretical and observed results have been compared[2,3].

The presence of two symmetry-independent molecules of **1** in its crystal structure provides a further opportunity to examine the effect of crystal-field forces on the geometry of these fused-ring molecules and compare these results with those from empirical force-field calculations.

EXPERIMENTAL

A crystal of **1** with dimensions 0.3 × 0.3 × 0.5 mm was used to measure 3379 symmetry-independent intensities by θ-2θ scans to $\theta_{max} = 35°$ on a CAD-4 X-ray diffractometer with graphite-monochromated MoKα radiation. No corrections for absorption ($\mu_{MoK\alpha} = 1.481$ cm^{-1}) or extinction were made. The unit-cell parameters were determined by least-squares fit of $\sin^2\theta$ values for 40 reflections with $18° \leqslant \theta \leqslant 22°$. The structure was solved by MULTAN[4], using 300 E-values for phase generation. The first E-map revealed all of the non-hydrogen atoms. The structure was refined by full-matrix, least squares minimizing $\sum_i \omega_i(|F_o| - k|F_c|)^2$, with $\omega_i = (\sigma_{ci})^{-2}$, where σ_{ci} was from counting statistics. The positional parameters for hydrogen atoms were calculated theoretically, except for the hydrogen atoms from hydroxyl groups which were found on the difference Fourier map. The hydrogen-atom para-

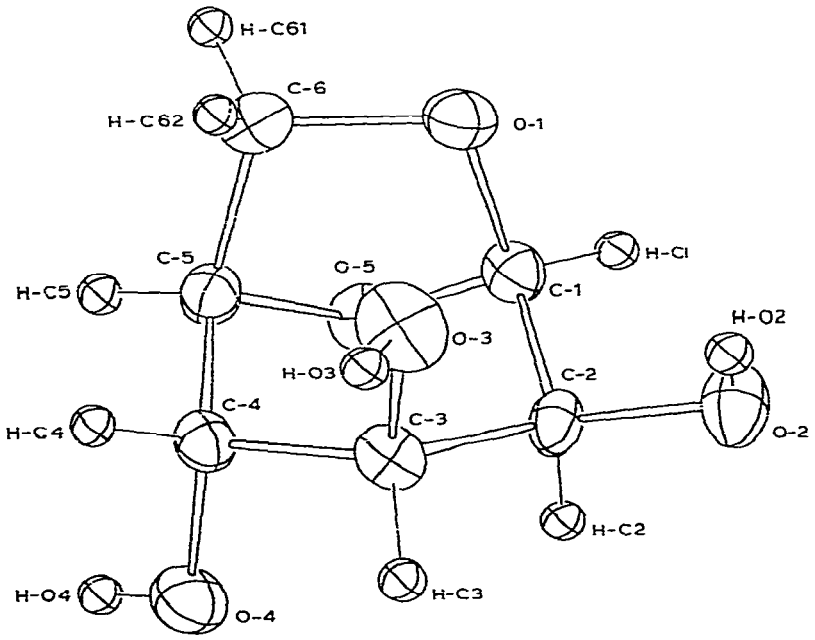


Fig. 1. The atomic notation and thermal ellipsoids (at 50 percent probability)[17] of 1,6-anhydro-β-D-mannopyranose, molecule A.

TABLE I

ATOMIC COORDINATES × 10^4 FOR NON-HYDROGEN ATOMS AND × 10^3 FOR HYDROGEN ATOMS[a]

	x	y	z	B_{eq}	
C-1A	871(1)	780(1)	4177(2)	1.8	
C-2A	1383(1)	1796(1)	3997(2)	1.6	
C-3A	2200(1)	2076(1)	5304(2)	1.8	
C-4A	3039(1)	1228(1)	5711(2)	1.7	
C-5A	2360(1)	270(1)	5650(2)	1.8	
C-6A	1204(2)	257(1)	6582(2)	2.3	
O-1A	279(1)	632(1)	5585(1)	2.3	
O-2A	453(1)	2483(1)	3740(2)	2.6	
O-3A	1426(1)	2344(1)	6518(2)	2.6	
O-4A	4006(1)	1244(1)	4654(2)	2.4	
O-5A	1870(1)	133(1)	4176(1)	2.1	
C-1B	−1715(2)	−1476(1)	5137(2)	2.4	
C-2B	−2033(1)	−735(1)	3955(2)	2.1	
C-3B	−3352(2)	−839(1)	3404(2)	2.1	
C-4B	−4219(2)	−1139(1)	4663(2)	2.0	
C-5B	−3626(2)	−1855(1)	5716(2)	2.4	
C-6B	−3070(2)	−2722(1)	4933(3)	3.1	
O-1B	−1834(1)	−2430(1)	4608(2)	3.0	
O-2B	−1167(1)	−768(1)	2784(2)	3.0	
O-3B	−3367(1)	−1541(1)	2249(2)	3.2	
O-4B	−4637(1)	−328(1)	5480(2)	2.8	
O-5B	−2552(1)	−1393(1)	6339(1)	2.5	
				B_{iso}	C,O-H
H-C-1A	30(1)	61(1)	336(2)	0.6(3)	0.99(1)
H-C-2A	190(1)	180(1)	317(2)	0.9(3)	0.94(2)
H-C-3A	271(1)	264(1)	503(2)	1.6(3)	0.92(2)
H-C-4A	337(2)	132(1)	673(2)	1.9(4)	0.99(2)
H-C-5A	292(1)	−24(1)	589(2)	1.0(3)	0.96(2)
H-C-61A	127(2)	72(1)	742(2)	2.6(5)	1.00(2)
H-C-62A	96(2)	−38(1)	691(2)	2.3(4)	0.98(2)
H-O-2A	20(2)	266(2)	442(2)	3.5(6)	0.72(2)
H-O-3A	171(2)	274(2)	696(3)	2.6(6)	0.75(2)
H-O-4A	446(2)	79(1)	479(2)	2.8(5)	0.81(2)
H-C-1B	−87(2)	141(1)	552(2)	2.6(5)	0.99(2)
H-C-2B	−195(2)	−10(1)	441(2)	2.0(4)	0.98(2)
H-C-3B	−364(2)	−24(1)	305(2)	2.2(4)	0.95(2)
H-C-4B	−496(2)	−146(1)	433(2)	1.9(4)	0.97(2)
H-C-5B	−418(2)	−204(1)	654(3)	3.2(5)	1.00(2)
H-C-61B	−351(2)	−285(2)	398(3)	3.1(5)	1.00(2)
H-C-62B	−308(2)	−325(2)	552(3)	3.6(5)	0.91(2)
H-O-2B	−116(2)	−126(2)	240(3)	3.9(7)	0.77(3)
H-O-3B	−394(3)	−142(2)	177(4)	4.3(9)	0.78(3)
H-O-4B	−417(3)	−10(2)	598(4)	2.8(1.0)	0.76(3)

[a]The temperature expression used for hydrogens is $T = \exp[-(B\sin^2\theta/\lambda^2)]$. B_{eq} is defined as $B_{eq} = \frac{4}{3}\sum_i\sum_j \beta_{ij}\vec{a}_i\vec{a}_j$.

meters were refined isotropically. The final values of $R = \sum_i ||F_o| - k|F_c||/\sum|F_o|$ and $R_\omega = [\sum_\omega(|F_o| - k|F_c|)^2/\sum_\omega|F_o|^2]^{1/2}$ were 0.043 and 0.036, respectively, for 2355 reflections for which $I > 2\sigma(I)$. The goodness of fit, $S = (\sum_\omega(|F_o| - |F_c|)^2/n - m)^{1/2}$, where n is the number of observations and m is the number of parameters, is 1.19. The atomic scattering-factors used for carbon and oxygen were those of Doyle and Turner[5], and for hydrogen those of Stewart *et al.*[6]. The atomic notation and thermal ellipsoids are shown in Fig. 1. The atomic coordinates are given in Table I.*

TABLE II

OBSERVED AND CALCULATED MOLECULAR DIMENSIONS FOR 1,6-ANHYDRO-β-D-MANNOPYRANOSE[a]

	Observed		*Calculated with MMI-CARB*				
			Excluding anomeric effect			*Including anomeric effect*	
	Mol. A	*Mol. B*	*Mol. A*	*Mol. B*	*Mol. B*[b]	*Mol. A*	*Mol. B*
Bond lengths Å							
C-1–C-2	1.531(2)	1.524(3)	1.528	1.528	1.531	1.529	1.529
C-2–C-3	1.531(2)	1.535(2)	1.528	1.528	1.527	1.529	1.530
C-3–C-4	1.541(2)	1.539(2)	1.529	1.528	1.528	1.530	1.529
C-4–C-5	1.530(2)	1.523(3)	1.531	1.529	1.529	1.532	1.530
C-5–C-6	1.522(2)	1.526(3)	1.522	1.522	1.522	1.526	1.525
C-6–O-1	1.452(2)	1.445(3)	1.423	1.423	1.423	1.410	1.409
C-1–O-1	1.440(2)	1.418(2)	1.418	1.417	1.418	1.394	1.394
C-1–O-5	1.419(2)	1.425(2)	1.414	1.414	1.414	1.405	1.405
C-2–O-2	1.419(2)	1.421(2)	1.414	1.413	1.413	1.414	1.413
C-3–O-3	1.434(2)	1.429(2)	1.415	1.415	1.418	1.415	1.415
C-4–O-4	1.426(2)	1.425(2)	1.414	1.416	1.418	1.415	1.416
C-5–O-5	1.445(2)	1.455(2)	1.415	1.415	1.416	1.421	1.421
Valence angles							
C-1–C-2–C-3	111.7	112.2	111.2	110.3	110.3	111.2	110.2
C-2–C-3–C-4	109.7	111.7	109.5	110.4	110.5	109.8	110.9
C-3–C-4–C-5	111.7	111.9	112.4	112.8	112.3	112.5	112.8
C-4–C-5–C-6	113.3	113.6	116.1	116.1	115.7	115.7	115.7
C-2–C-1–O-5	107.7	109.2	108.4	108.0	108.3	107.4	107.0
C-4–C-5–O-5	109.2	107.2	109.1	108.1	108.1	108.3	107.3
C-6–C-5–O-5	101.3	101.8	99.3	99.7	100.1	98.5	98.9
C-2–C-1–O-1	113.0	112.3	110.6	111.0	111.6	109.8	110.3
C-5–C-6–O-1	103.7	104.2	104.1	104.1	104.3	104.3	104.3
C-1–C-2–O-2	112.2	110.1	109.4	109.3	109.1	109.3	109.4
C-3–C-2–O-2	112.0	112.8	112.0	110.1	109.1	112.1	110.1
C-2–C-3–O-3	107.9	108.1	111.0	109.8	109.5	111.0	109.9
C-4–C-3–O-3	111.8	110.1	108.5	108.2	109.9	108.5	108.2

*Tables of structure factors and anisotropic thermal parameters are deposited with, and can be obtained from: Elsevier Scientific Publishing Company, BBA Data Deposition, P. O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/200/*Carbohydr. Res.*, 100 (1982) 17–28.

TABLE II *(continued)*

Valence angles	*Observed*		*Calculated with MMI-CARB*				
			Excluding anomeric effect			*Including anomeric effect*	
	Mol. A	*Mol. B*	*Mol. A*	*Mol. B*	*Mol. B*[b]	*Mol. A*	*Mol. B*
C-3–C-4–O-4	105.9	111.4	107.7	108.8	108.6	107.7	108.7
C-5–C-4–O-4	110.6	109.6	109.3	108.2	107.9	109.3	108.2
C-1–O-1–C-6	106.4	106.4	104.9	104.9	105.2	105.7	105.7
C-1–O-5–C-5	101.7	101.1	101.0	101.1	101.2	101.8	101.9
O-1–C-1–O-5	104.9	105.8	107.1	107.7	107.1	107.8	108.3
Torsion angles							
C-1–C-2–C-3–C-4	43.1	35.8	41.5	40.4	41.0	41.4	40.2
C-2–C-3–C-4–C-5	−41.0	−37.9	−39.9	−38.6	−40.1	−39.4	−38.2
C-3–C-4–C-5–O-5	58.3	59.7	58.5	57.4	58.6	57.6	56.4
C-4–C-5–O-5–C-1	−74.6	−77.6	−74.8	−75.5	−75.7	−75.5	−76.2
C-5–O-5–C-1–C-2	76.2	76.4	77.1	79.1	78.3	78.1	80.2
O-5–C-1–C-2–C-3	−63.0	−56.9	−62.6	−62.5	−62.1	−62.6	−62.5
C-1–O-5–C-5–C-6	45.2	42.0	47.2	46.2	45.7	45.3	44.4
O-5–C-5–C-6–O-1	−29.8	−25.5	−37.4	−37.4	−35.0	−36.8	−36.8
C-5–C-6–O-1–C-1	3.5	−1.1	12.4	13.2	10.0	13.6	14.3
C-6–O-1–C-1–O-5	25.0	28.3	17.4	16.2	19.0	15.5	14.2
O-1–C-1–O-5–C-5	−44.5	−44.6	−42.3	−40.8	−42.1	−40.2	−38.7
C-2–C-1–O-1–C-6	−92.1	−90.7	−100.5	−101.9	−99.3	−101.3	−102.6
C-3–C-2–C-1–O-1	52.4	60.2	54.6	55.3	55.6	54.4	55.1
C-3–C-4–C-5–C-6	−53.8	−52.1	−52.6	−53.5	−52.5	−51.8	−52.9
C-4–C-5–C-6–O-1	87.0	89.5	79.3	78.3	80.8	78.3	77.3
O-5–C-1–C-2–O-2	170.3	176.6	173.2	176.2	177.6	173.1	176.2
C-1–C-2–C-3–O-3	−78.9	−85.5	−78.2	−79.0	−80.0	−78.6	−79.4
C-2–C-3–C-4–O-4	79.4	85.2	80.6	81.4	79.1	81.1	81.9
C-1–C-2–O-2–H-2	86	61	86[c]	61[c]	168.5	86[c]	61[c]
C-2–C-3–O-3–H-3	−146	−156	−146[c]	−156[c]	14.8	−146[c]	−156[c]
C-3–C-4–O-4–H-4	−177	−73	−177[c]	−73[c]	−82.5	−177[c]	−73[c]

[a]Bond lengths in Å, valence and torsion angles in degrees. E.s.d. values for observed bond-lengths, given in parentheses, refer to the least significant digit. The standard deviations of the valence angles and torsion angles are 0.10–0.15°. [b]Simulated isolated molecule (see text). [c]Fixed at the observed values.

DISCUSSION

The molecular structure

The bond distances, valence angles, and torsion angles of **1** for the two symmetry-independent molecules are given in Table II. The major conformational differences between the two molecules are in the C–C–O–H torsion angles. This is to be expected, since the orientations of the hydroxyl groups are determined by the intermolecular forces in the crystal rather than the intramolecular forces within the

TABLE III

PUCKERING PARAMETERS[a] FOR SOME RELATED 1,6-ANHYDRO-β-D-PYRANOSES (*I, manno*; *II, galacto*[b]; *III, gluco*[c])

	Experimental			*Theoretical MMI-CARB*		
	Q (Å)	*θ (deg)*	*φ (deg)*	*Q (Å)*	*θ (deg)*	*φ (deg)*
Pyranose rings						
I Mol. A	0.64	160	187	0.64	158	187
Mol. B	0.64	155	175	0.64	157	188
Mol. B[d]				0.64	159	185
II Mol. A	0.64	156	176	0.63	155	174
Mol. B	0.63	156	168			
Mol. C	0.64	155	175			
III Mol. A	0.61	155	180			
Anhydro rings						
I Mol. A	0.43		355	0.43		342
Mol. B	0.42		0	0.42		340
Mol. B[d]				0.43		346
II Mol. A	0.42		346	0.45		356
Mol. B	0.42		355			
Mol. C	0.42		353			
III Mol. A	0.42		355			

[a]Ref. 7. [b]Ref. 3. [c]Ref. 9. [d]The intramolecularly hydrogen-bonded molecule.

molecule. The conformations of the rings are described by the puckering parameters[7] given in Table III. The pyranoid ring is $^1C_4$, distorted in the direction of the sofa or half-boat conformation (*i.e.*, towards E_3 for which $\theta = 135°$, $\varphi = 180°$). One of the anhydro rings is exactly ^{O-5}E ($\varphi = 0°$), the other is twisted towards $^{O-5}T_5$ ($\varphi = 342°$).

As shown in Table III, these ring conformations are very similar to those observed in the corresponding *galacto* and *gluco* molecules. There is no evidence that changes in configuration at C-2, C-3, and C-4 introduce any difference in the shape of the fused-ring structure, since the differences between different molecules are comparable to the differences between the same molecules.

The bond lengths and valence angles in the two molecules of **1**, shown in Table II, agree well, with two interesting exceptions in each category. The C-1–O-1 bonds differ by 0.022 Å (8σ), which is highly significant; the C-5–O-5 bonds differ by 0.010 Å (3.5σ). The differences appear to be related to the difference in crystal-field environment of the two molecules. O-1A and O-5B are strong hydrogen-bond acceptors (see below), whereas O-1B and O-5A are the only two oxygen atoms in the structure which are not involved in hydrogen-bonding. It is known, from comparisons of X-ray and neutron-diffraction studies of pyranoses[8], that the X-ray C–O distances are observed to be ~0.010 Å shorter than those derived by neutron diffraction. This finding can be interpreted as being due to a displacement of the peak of the thermally

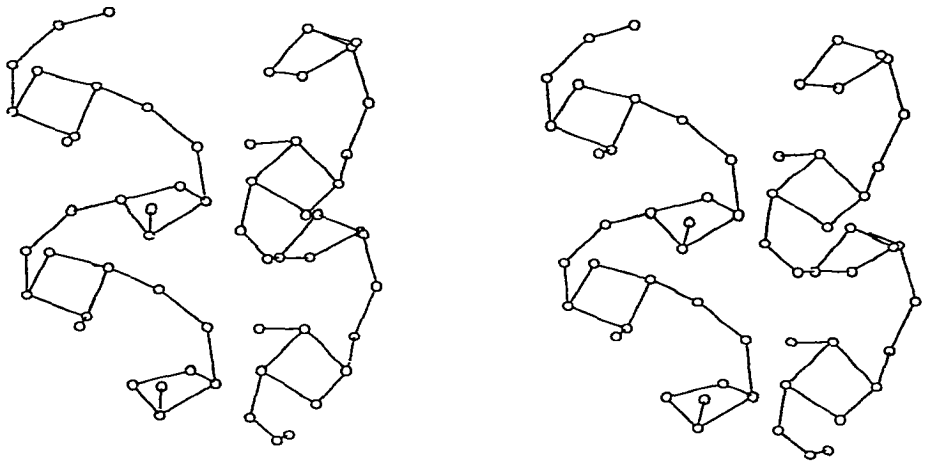


Fig. 2. Stereo-view of the hydrogen-bonding in the crystal structure of 1,6-anhydro-β-D-mannopyranose, viewed in the [001] direction. The circles are oxygen atoms and the lines are hydrogen bonds.

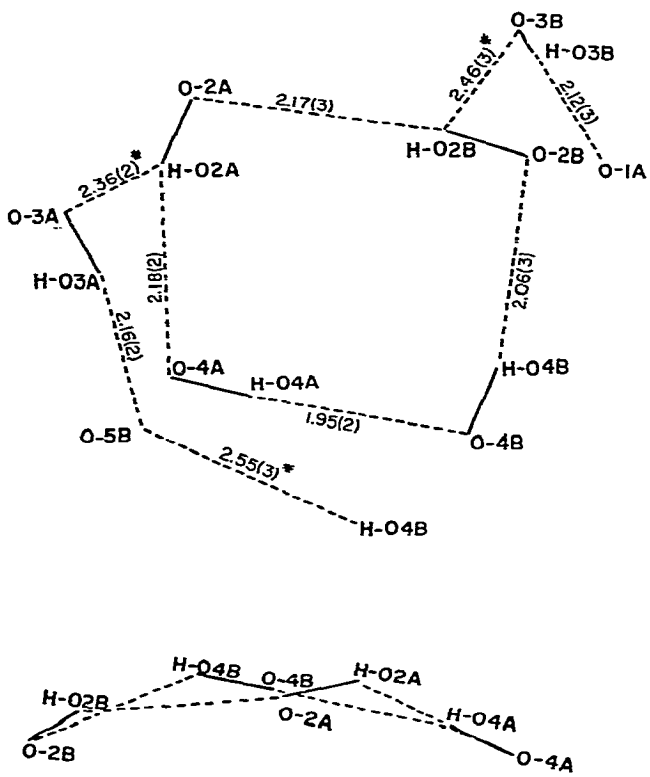
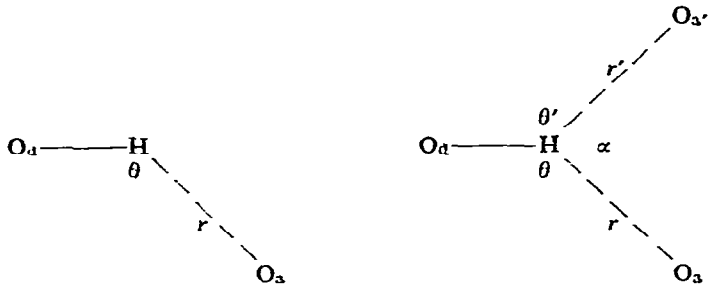


Fig. 3. The geometry of the buckled square of hydrogen bonds, viewed normal to, and in, the mean plane. The distances are the uncorrected H---O values in Å.

TABLE IV

HYDROGEN-BOND GEOMETRY IN THE CRYSTAL STRUCTURES OF 1,6-ANHYDRO-β-D-MANNOPYRANOSE[a] (1) AND 1,6-ANHYDRO-β-D-GLUCOPYRANOSE (2)



	Bonds	*r (Å)*	*r' (Å)*	*θ (deg)*	*θ' (deg)*	*α (deg)*	*Σθ + θ' + α (deg)*
1	O-3A----H-3A - - - O-5B	1.94		164			
	O-4A----H-4A - - - O-4B	1.79		168			
	O-3B----H-O-3B - - - O-1A	1.94		160			
	O-2A----H-O-2A (O-4A, O-3A)	1.98	2.27[b]	139	108	109	356
	O-2B----H-O-2B (O-2A, O-3B)	1.99	2.43[b]	157	94	108	359
	O-4B----H-O-4B (O-2B, O-5B)	1.88	2.50[b]	143	100	108	351
2	O-3----H - - - O-2	1.81		170			
	O-4----H - - - O-1	1.82		168			
	O-2----H (O-4, O-5)	1.84	2.57	157	99	91	347

[a]Covalent O–H distances were normalized to the standard value of 0.97 Å to calculate the H---O distances. The actual, observed H---O distances are given in Fig. 3. [b]Intramolecular.

averaged electron-density distribution away from the nucleus in the direction of the oxygen lone-pairs. Since the lone-pair electron density is involved in hydrogen-bonding, these observed differences in the C–O bond lengths could be a manifestation of a polarization effect induced by hydrogen-bond formation.

The greatest difference in valence angles between the two molecules is for C-3–

C-4–O-4, which is significant, being greater than 40 σ. This is associated with the large difference in C-3–C-4–O-4–H-4 torsion angle.

Hydrogen-bonding

The hydrogen-bonding geometry is described in Table IV and illustrated in Figs. 2 and 3. There are three linear and three bifurcated bonds which involve all the hydroxyl and ring oxygen atoms except the two ring oxygens, O-1B* and O-5A. This is in contrast to the structures of 1,6-anhydro-β-D-galactopyranose[3] and 1,6-anhydro-β-D-glucopyranose[9], where all of the available oxygen atoms have hydrogen-bond interactions. In this structure, the hydrogen-bonding consists of four-membered loops linked by short three-membered sections into infinite chains which extend throughout the crystal in the [001] direction, as shown in Fig. 3. Single links are also attached to the loops at one of the two corners not involved in the infinite chains. The loops, having all the donor–acceptor directions of the bonds in the same direction, belong to the *homodromic* classification of Saenger[10], thereby maximizing the *cooperative effect*[11]. The four oxygen atoms form buckled squares, with O---O distances of O-2A---→O-4A = 2.786 Å, O-4A---→O-4B = 2.750 Å, O-4B---→O-2B = 2.724 Å, and O-2B---→O-2A = 2.905 Å. The buckling is quite symmetrical, as shown by the lateral view of the squares in Fig. 3. The displacements from the least-squares plane are O-2A, O-2B ±0.23 Å, and O-4A, O-4B ±0.24 Å. The hydrogen-bond chains connecting the loops include the ring-oxygen O-5B as a double acceptor. These linking chains are therefore *antidromic*, as defined by Saenger[10]. As with the 1,6-anhydro-β-D-galactopyranose structure[3], this is an arrangement that attempts to maximize the number of hydrogen-bond interactions so as to include as many as possible of the ring oxygens and, at the same time, allow the cooperative effect[11,12] to operate. All of the three bifurcated bonds involve intramolecular interactions, *i.e.*, H-O-4B···O-5B, H-O-2B···O-3B, and H-O-2A···O-3A. As pointed out elsewhere[11], ring oxygens, which have no hydrogens, act as chain-stoppers, breaking the cooperative effect unless they interact through bifurcated bonds. They therefore tend to be excluded from the hydrogen-bonding scheme, unless they can be included in this way.

The hydrogen-bond distances and angles, using normalized, covalent O–H bond-lengths[8] of 0.97 Å, are given in Table IV. The two shortest hydrogen-bonds are those in the *homodromic* "squares". That involved in only one interaction, H-O-4A···O-4B, has a length which agrees well with the mean bond-length of 1.805(9) Å for cooperative hydrogen-bonds deduced from the analysis of neutron diffraction data from carbohydrate crystal structures[12]. The H-O-4B···O-2B bond is longer, because the hydrogen is shared by the bifurcated interaction to the ring-oxygen O-5B.

*Using O–H covalent distances normalized to the neutron-diffraction value of 0.97 Å, the H-O-2B to O-1B distance is 2.64 Å. This was not considered to be a hydrogen-bonding interaction, because O-1B lies out of the plane of the bifurcated bond involving O-2B, H-O-2B, O-2A, and O-3B (see Table IV).

The linear hydrogen-bonds in the short (less cooperative) chains, H-3A···O-5B and H-3B···O-1A, are longer than the mean neutron-diffraction value of 1.869 Å for all types of non-cooperative bonds[13]. This supports the view that hydrogen bonds to ether oxygens are longer and weaker than those to hydroxyl oxygens, even when these are not involved in cooperative arrangements[11].

All of the bifurcated bonds fulfil the criterion that the hydrogen atom be close to the plane of the one donor and two acceptor oxygens, as shown by $\theta + \theta' + \sigma \sim 360°$. They are unsymmetrical with $r' - r$ in the range between 0.29 and 0.62 Å. This is consistent with the results of the study of 25 bifurcated interactions where the positions of the hydrogen atoms were known accurately from neutron data[12]. In that analysis, in only four cases was $r' - r < 0.11$ Å. In the other 21 examples, $r' - r$ ranged from 0.38 to 0.78 Å.

For comparison, Table IV also gives the hydrogen-bonding data for the crystal structure of 1,6-anhydro-β-D-glucopyranose[9], which was not previously reported in this way. In that structure, all oxygen atoms are hydrogen-bonded through one bifurcated and two linear bonds which form finite, three-link chains terminating at the anhydro-ring oxygen. The pyranose-ring oxygen is included through the bifurcated bond. The cooperative effect is small in a finite, three-membered chain and both the linear hydrogen-bonds have H···O bond lengths which are longer than the average value[12] of 1.81 Å. With only one molecule in the asymmetric unit, this is a much simpler hydrogen-bonding than that in 1,6-anhydro-β-D-galactopyranose[3], which has three molecules in the asymmetric unit, and this structure which has two.

Empirical force-field calculations

Theoretical calculations on the isolated molecule, **1**, at rest, were carried out with the molecular mechanics program MMI-CARB[13]. The results are shown, with the experimental values, in Table II. Calculations were made including and excluding the two-fold torsional potential for the O–C–O lone-pair sequence, which takes into account the *anomeric effect*[14]. The two molecules differed in the orientations of the three hydroxyl groups, and these orientations were fixed in the calculations, thereby including this aspect of the effect of the crystal field on the molecules. Two of these orientations were significantly different in C–C–O–H torsion angles (by 25 and 104°), but this resulted in very small differences in calculated molecular geometry. The differences in calculated bond lengths and valence angles in the two molecules were much less than the experimental uncertainties in these quantities. The torsion angles are more sensitive, but again the differences in the calculated values for the two molecules were much less than those observed.

The inclusion or exclusion of the anomeric effect also produced very minor differences in molecular geometry, and the comparison with the experimental data gave no basis for distinguishing between them.

As shown in Tables II and III, the calculations reproduced the observed, overall shape of the pyranoid ring and the puckering at O-5, so that the ring torsion-angles C-4–C-5–O-5–C-1 and C-5–O-5–C-1–C-2 are ~75°, and the flattening at C-3, so

that C-1–C-2–C-3–C-4 and C-2–C-3–C-4–C-5 are ~40°. For the anhydro ring, the agreement was better for molecule A than for molecule B. This is probably due to the failure of the calculations to reproduce the observed, *long* C-1–O-1 bond-length in molecule A.

We therefore conclude that the molecular mechanics method, and in particular MMI-CARB, can reproduce the molecular geometry of these fused-ring compounds within the variations that can arise from crystal-field forces. For these molecules in hydrogen-bonding solvents, the application of molecular mechanics gives as good a description of the probable molecular geometry as does a crystal structure analysis. Similar conclusions were reached for simple pyranoses and methyl pyranosides[13], using MMI-CARB, and for more-complex carbohydrate molecules, using a different force field[15].

For the molecules in a non-polar solvent, the intermolecular hydrogen-bonding observed in the crystal will be replaced by intramolecular bonding[16]. This was examined by using MMI-CARB[13], together with a hydrogen-bonding potential which had been tested on simpler pyranose molecules[18]. The function used for the hydrogen bond is

$$E(\text{H-bond}) = \sum D(\exp -2\alpha[r_{H\cdots O} - r_o] - 2\exp -\alpha[r_{H\cdots O} - r_o])\cos^2\delta,$$

where D = 1.3 kcal/mol, $\alpha = 1.7$ Å^{-1}, $r_o = 2.2$ Å, δ is the supplement of the O-H···O angle, and $r_{H\cdots O}$ is the hydrogen-bond distance. This is a Morse function with an attenuation factor $\cos^2\delta$, which expresses the decreasing importance of charge transfer as the hydrogen bond becomes more linear. If the angle O-H···O is <90°, $\cos^2\delta$ is made zero[18].

The starting model used was molecule B (without the anomeric effect) with the C-1–C-2–O-2–H, C-2–C-3–O-3–H, and C-3–C-4–O-4–H torsion angles given values of 86, 40, and −73°. This corresponds to formation of the following intramolecular hydrogen-bonds: O-2-H···O-3, O-3-H···O-1, and O-4-H···O-5. There were no significant changes in the bond lengths and valence angles or the total energy of the molecule, as compared with the other calculated values. However, the orientation of the O-2-H and O-3-H groups did change significantly. These changes were such that H-O-3 made a bifurcated interaction with both O-1 at 2.21 Å and O-2 at 2.26 Å, rather than a linear hydrogen-bond with O-1. This is clearly a sterically reasonable alternative. The O-2-H···O-3 bond became much weaker with an H···O distance of 2.6 Å. The O-4-H···O-5 distance shortened from 2.6 to 2.3 Å. This appears to be a better model for the intramolecularly hydrogen-bonded, "isolated" molecule than the starting model.

SUMMARY

The experimental results show that the conformation of the 1,6-anhydropyranose ring system is insensitive to the configuration of the substituents on C-2 provided they are only hydroxyl groups. Both the ring conformations and the detailed structures are insensitive to the hydrogen-bonding environment, with the exception

of the C–O bond lengths involving oxygens which are strongly hydrogen-bonded in one molecule and not in the other. The molecular-mechanics calculations did not reproduce this effect, suggesting that it is due to a difference in polarization which was not included in the empirical parameters used.

The use of molecular mechanics with a hydrogen-bonding potential gave a reasonable prediction for the intramolecular hydrogen-bonding anticipated for the molecules in a non-polar solvent.

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