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CRYSTAL AND MOLECULAR STRUCTURES OF METHYL 2,3-ANHYDRO-4-DEOXY-α-DL-*ribo*- AND -α-DL-*lyxo*-HEXOPYRANOSIDES

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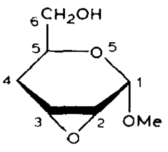
ABSTRACT

Single crystals of methyl 2,3-anhydro-4-deoxy-α-DL-*ribo*- (**1**) and -α-DL-*lyxo*-hexopyranoside (**2**) have been investigated by X-ray diffraction methods. Compound **1** crystallises in the monoclinic system, space group $P2_1/c$, with cell dimensions a = 7.694(1), b = 12.954(1), c = 8.415(1) Å, and β = 110.34(1)°. Compound **2** crystallises in the tetragonal system, space group $I4_1/a$ (No. 88, origin at $\bar{1}$), with cell dimensions a = 22.995(2) and c = 6.086(1) Å. The intensity data were collected in a four-circle CAD-4D automatic diffractometer, with 1623 reflections for **1**, and 2421 for **2**. The structures were solved by direct methods. The atomic parameters were refined in an anisotropic mode by the full-matrix, least-squares procedure against 1456 and 1109 observed reflections for **1** and **2**, respectively, resulting in $R = 0.049$ for **1**, and $R = 0.042$ for **2**.

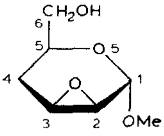
A hybrid conformation $^5E + {}^5H_0$ was found for the anhydrohexopyranose ring in **1**, whereas a slightly deformed $^5H_0$ conformation was assigned to that in **2**. Relatively strong intermolecular hydrogen-bonds were observed in each compound. In **1** (acceptor atom O-5), they result in dimers of pairs of enantiomeric molecules; in **2** (acceptor atom O-6), the molecules form helices around the four-fold screw axes in the crystal.

INTRODUCTION

As a part of our studies on the conformation of sugars by X-ray diffraction methods, we have investigated[1] 3-*O*-(6-*O*-acetyl-2,3-anhydro-4-deoxy-α-L-*ribo*-hexopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**3**). A deformed sofa (*E*) conformation was assigned to the 2,3-anhydrohexopyranosyl moiety in contrast to the half-chair (*H*) conformation assigned[2,3] to 2,3-anhydro-4-deoxyhexopyranosides. This result prompted us to determine whether the *E* conformation is exceptional for **3**. We now report X-ray studies aimed at determining the effect of the C-1 substituent on the conformation of 2,3-anhydrohexopyranosyl



1



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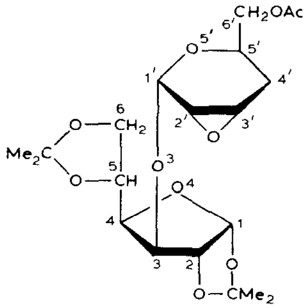

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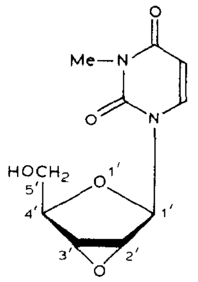

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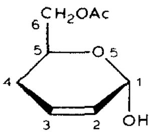

5

rings. Such an influence has been observed for the 2,3-unsaturated analogue of **3**, and its analogue **5** unsubstituted at C-1 (analogue of **2**)[4].

EXPERIMENTAL

Colourless crystals of **1** (0.08 × 0.40 × 0.50 mm) and **2** (0.12 × 0.12 × 0.30 mm) were obtained[5] from ether–acetone. The reflection intensities were collected for **1** and **2** on an Enraf–Nonius CAD-4D automated diffractometer controlled by a PDP8/11 computer (Central Research Institute for Chemistry, Hungarian Academy of Sciences, Budapest). The graphite-monochromated CuKα radiation was applied with the $\omega/2\theta$ scan technique up to $2\theta_{max} = 150°$. Crystal stability was controlled on two reflections at 50 reflection intervals, and intensities were corrected automatically. Lattice parameters were refined against 25 reflections. No absorption correction was performed at the intensity collection stage.

For **1**, 1623 intensities were collected (1456 of $F^2 > 3\sigma_{F^2}$), 13.7% loss of control reflection intensities (13.5-h period).

For **2**, 2421 intensities were collected (1109 of $F^2 > 2.5\sigma_{F^2}$), 49.5% loss of control reflection intensities (25.5-h period, decay due to sublimation).

TABLE I

FRACTIONAL CO-ORDINATES ($\times 10^4$) AND EQUIVALENT, ISOTROPIC TEMPERATURE FACTORS[a] ($Å^2$) FOR **1** AND **2**[b]

Atom	**1**				**2**			
	x/a	y/b	z/c	B_{eq}	x/a	y/b	z/c	B_{eq}
C-1	1489(2)	1864(1)	9436(2)	3.59(5)	−4634(1)	−780(1)	566(4)	3.24(5)
C-2	−577(2)	1854(1)	8558(2)	4.19(6)	−4681(1)	−531(1)	2835(4)	3.82(5)
C-3	−1483(2)	966(2)	7552(2)	4.29(6)	−4163(1)	−476(1)	4187(4)	3.81(5)
C-4	−334(2)	84(1)	7349(2)	4.16(5)	−3587(1)	−682(1)	3339(4)	3.63(5)
C-5	1661(2)	416(1)	7716(2)	3.33(5)	−3652(1)	−1047(1)	1290(4)	2.99(5)
C-6	2904(3)	−484(1)	7753(2)	4.36(5)	−3090(1)	−1135(1)	55(4)	3.70(5)
C-7	4106(3)	2884(2)	9685(3)	5.41(5)	−4933(2)	−1616(1)	−1359(6)	6.29(11)
O-1	2214(2)	2669(1)	8742(1)	4.12(4)	−4873(1)	−1341(1)	704(3)	4.25(5)
O-2	−1264(2)	1910(1)	6738(1)	4.61(5)	−4410(1)	27(1)	3100(3)	4.36(5)
O-5	2334(1)	903(1)	9345(1)	3.48(3)	−4057(1)	−780(1)	−217(2)	2.87(3)
O-6	4705(2)	−148(1)	7879(1)	4.89(4)	−2817(1)	−602(1)	−535(3)	4.34(4)
HO-6	5699(32)	−448(19)	8961(30)	—	−2534(10)	−548(10)	316(41)	—

[a] $B_{eq} = 8\pi^2 \times D_U^{1/3}$, where D_U is the determinant of the U matrix. [b] Estimated standard deviations in parentheses.

Crystal data for **1**: $C_7H_{12}O_4$, $M_r = 160.17$, monoclinic, space group $P2_1/c$, $Z = 4$, $a = 7.694(1)$, $b = 12.954(1)$, $c = 8.415(1)$ Å, $\beta = 110.34(1)°$, $V = 786.4(3)$ $Å^3$, $F(000) = 344$, $D_c = 1.35$ $Mg.m^{-3}$, $\mu(CuK\alpha) = 8.99$ cm^{-1}.

Crystal data for **2**: $C_7H_{12}O_4$, $M_r = 160.17$, tetragonal, space group $I4_1/a$ (No. 88, origin at $\bar{1}$), $Z = 16$, $a = 22.995(2)$, $c = 6.086(1)$ Å, $V = 3218(1)$ $Å^3$, $F(000) = 1376$, $D_c = 1.32$ $Mg.m^{-3}$, $\mu(CuK\alpha) = 8.80$ cm^{-1}.

The phase problem for each structure was solved by direct methods using the MULTAN-80 programme[6].

The refinement of atomic positional and thermal parameters was performed for **1** and **2** by the full-matrix, least-squares procedure included in the standard SDP System provided by Enraf–Nonius (1978), using atomic scattering factors implemented there. After completion of isotropic refinement, a spherical empirical absorption correction was calculated by program DIFABS[7] and applied to both data sets (with minor effects). Further refinement was performed with anisotropic atomic thermal parameters. The refinement was accomplished for each structure by locating all positional H-parameters from ΔF maps and adding them (as isotropic) for the last refinement step to the whole parameter set. The final reliability factors were for **1**, $R = 0.049$, $R_w = 0.051$, $w = 1/\{1 + [(F - \bar{F})/(0.33 \times F_{max})]^2\}$; for **2**, $R = 0.042$, $R_w = 0.054$ (unit weights).

The refined positional parameters for the non-H atoms of **1** and **2**, together with their B_{eq} values are given in Table I.

RESULTS AND DISCUSSION

The stereoisomeric molecules of **1** and **2** are shown as ORTEP[8] diagrams in Fig. 1, and Tables II and III contain the bond lengths and valence angles.

Table IV shows a comparison of bond lengths and angles, involving C-2 and C-3 in **1** and **2**, with those in 3-*O*-(6-*O*-acetyl-2,3-anhydro-4-deoxy-α-L-*ribo*-hexopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[1] (**3**), 3-methyl-2′,3′-anhydrouridine[9] (**4**), and the unsaturated ring of 6-*O*-acetyl-2,3,4-trideoxy-α-DL-*glycero*-hex-2-enopyranose[4] (**5**). The C-2–C-3 bond lengths are similar in **1**–**3** and different (~0.15 Å) from that in **5**. In the anhydropyranoses, the bond lengths discussed are intermediate of the usual bond lengths $C_{sp}2$–$C_{sp}2$ and $C_{sp}3$–$C_{sp}3$. The same situation is observed for the C-2′–C-3′ bond in the five-membered ring of **4**.

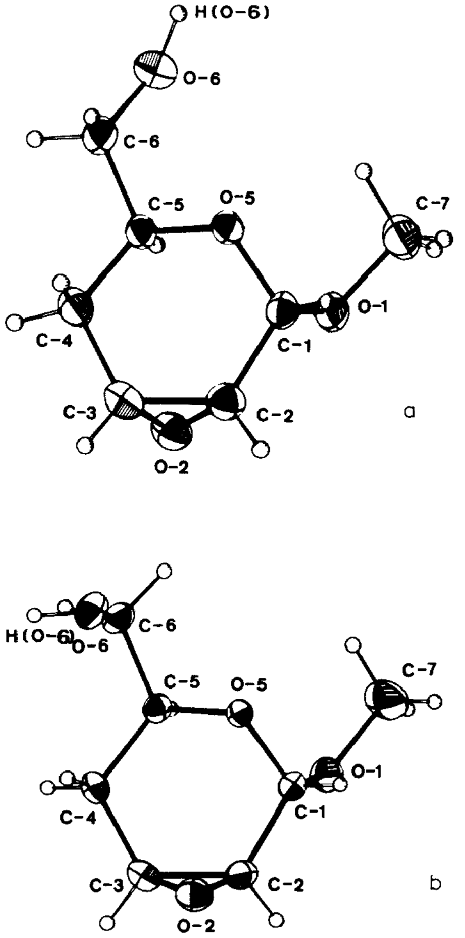

Fig. 1. ORTEP[7] diagrams of single molecules. Projections onto the least-squares planes defined by the six atoms of the pyranoid rings. Thermal motion ellipsoids set at 40% probability level. *a*, **1**; *b*, **2**.

TABLE II

BOND LENGTHS (Å)[a] FOR **1** AND **2**

	1	**2**		**1**	**2**
C-1–C-2	1.502(2)	1.499(3)	O-1–C-7	1.422(2)	1.412(4)
C-2–C-3	1.454(3)	1.453(3)	C-2–O-2	1.438(2)	1.437(3)
C-3–C-4	1.490(3)	1.499(3)	C-3–O-2	1.440(2)	1.449(3)
C-4–C-5	1.519(2)	1.510(3)	C-5–C-6	1.501(2)	1.507(3)
C-5–O-5	1.432(2)	1.444(2)	C-6–O-6	1.421(3)	1.422(3)
O-5–C-1	1.419(2)	1.409(2)	O-6–HO-6	1.04(1)	0.84(2)
C-1–O-1	1.402(2)	1.404(3)			

[a] Estimated standard deviations in parentheses.

TABLE III

BOND ANGLES (DEGREES)[a] FOR **1** AND **2**

	1	**2**		**1**	**2**
O-5–C-1–C-2	113.1(1)	112.4(2)	C-1–O-1–C-7	113.0(1)	113.3(2)
C-1–C-2–C-3	120.3(1)	119.7(2)	C-2–O-2–C-3	60.7(1)	60.5(2)
C-2–C-3–C-4	119.3(1)	120.2(2)	C-3–C-2–O-2	59.7(1)	60.2(2)
C-3–C-4–C-5	110.9(1)	111.8(2)	C-2–C-3–O-2	59.6(1)	59.4(2)
C-4–C-5–O-5	108.8(1)	110.6(2)	C-4–C-5–C-6	112.1(1)	113.6(2)
C-5–O-5–C-1	114.7(1)	113.1(2)	O-5–C-5–C-6	107.8(1)	107.1(2)
O-5–C-1–O-1	112.0(1)	112.9(2)	C-5–C-6–O-6	111.2(1)	112.9(2)
C-2–C-1–O-1	107.9(1)	105.5(2)			

[a] Estimated standard deviations in parentheses.

TABLE IV

COMPARISON OF BOND LENGTHS (Å) AND ANGLES (DEGREES) INVOLVING C-2 AND C-3 IN THE RINGS OF THE ANHYDROPYRANOSES **1–3**, THE ANHYDROFURANOSE **4**, AND THE DIHYDROPYRAN **5**[a]

	1	**2**	**3**	**4**	**5**
C-1–C-2	1.520(2)	1.499(3)	1.503(11)	1.499(2)	1.497(6)
C-2–C-3	1.454(3)	1.453(3)	1.446(12)	1.457(2)	1.308(6)
C-3–C-4	1.490(3)	1.499(3)	1.505(12)	1.502(3)	1.505(6)
C-1–C-2–C-3	120.3(1)	119.7(2)	120.5(7)	108.0(2)	122.5(4)
C-2–C-3–C-4	119.3(1)	120.2(2)	118.3(7)	108.1(2)	122.0(4)
C-1–C-2–HC-2	111(1)	109(1)	117(4)	—	—
C-3–C-2–HC-2	122(1)	124(1)	117(4)	—	—
C-4–C-3–HC-3	111(1)	110(1)	114(5)	—	—
C-2–C-3–HC-3	124(1)	122(1)	120(5)	—	—
C-1–C-2–C-3–HC-3	148(1)	−149(2)	145(6)	—	
C-5–C-4–C-3–HC-3	−175(1)	139(2)	−172(5)	—	
C-4–C-3–C-2–HC-2	−150(1)	147(2)	−149(5)	—	
O-5–C-1–C-2–HC-2	143(1)	−170(1)	142(5)	—	
HC-2–C-2–C-3–HC-3	0.4(1)	−1(2)	−1(6)	—	

[a] Estimated standard deviations in parentheses.

The valence angles at C-2 and C-3 in **1**–**3** resemble those characteristic of $C_{sp}2$ atoms (~120°). Even in **4**, they are larger than those usually observed for $C_{sp}3$.

Conformation of the 2,3-anhydrohexopyranose ring. — The conformation of the 2,3-anhydrohexopyranose ring has been investigated[1] for **3** and found to deviate from a half-chair. It may be described as a hybrid conformation $^5E + {}^5H_0$. Tables V and VI give the data essential for conformational analysis, from which it is concluded that there are remarkable differences in the conformations of the anhydrohexopyranose rings.

The endocyclic torsion angles for the C-1–C-2 and C-2–C-3 bonds in **1** and **3** are close to zero (Table V). This situation implies that five atoms of these rings (O-5, C-1,2,3,4) are approximately coplanar, which is characteristic for a sofa (E) conformation (see Table VI). However, the high values of the asymmetry parameters ΔC_s and ΔC_2 for **1** indicate a remarkable deformation of the sofa conformation, which is hybridised in some way. The puckering parameters (program RING[11]) for the ring in **1** localise the corresponding point on a Cremer and Pople diagram[12] between the positions of the ^5E and $^5H_0$ conformations (closer to ^5E). Therefore, the conformation of the 2,3-anhydrohexopyranose ring in **1** may be defined as a hybrid $^5E + {}^5H_0$ which is similar to that assigned to **3**.

Similar analysis for **2** identifies a four-atom (C-1/C-4) plane. The small value of the ΔC_2 asymmetry parameter implies a slightly deformed half-chair ($^5H_0$), which is confirmed by the puckering parameters (Table VI).

TABLE V

COMPARISON OF SOME TORSION ANGLES (DEGREES)[a]

	1	**2**	**3**	**5**	A^b	B^b
2,3-Anhydropyranose ring						
O-5–C-1–C-2–C-3	−7.6(2)	−17.1(2)	−5.1(1.2)	−10.3(5)	−15.4	−12.6
C-1–C-2–C-3–C-4	−2.3(3)	−1.6(3)	−2.3(1.4)	−3.0(7)	−2.2	−0.8
C-2–C-3–C-4–C-5	−20.4(2)	−12.4(3)	−22.8(1.2)	−15.3(6)	−20.6	−19.3
C-3–C-4–C-5–O-5	53.1(2)	44.7(2)	54.4(9)	46.2(4)	54.1	55.0
C-4–C-5–O-5–C-1	−67.8(2)	−67.8(2)	−66.2(8)	−63.5(3)	−72.6	−73.9
C-5–O-5–C-1–C-2	43.4(2)	51.9(2)	40.1(9)	44.0(3)	51.2	49.9
Other angles						
O-5–C-1–O-1–C-7	−66.3(2)	−64.6(3)	—	—	−63.4	−62.0
C-2–C-1–O-1–C-7	168.7(2)	172.3(2)	—	—	170.9	173.6
C-1–C-2–O-2–C-3	110 9(2)	−111.5(2)	111.2(8)	—	110.2	−110.3
C-4–C-3–O-2–C-2	−110 6(2)	111.1(2)	−109.4(8)	—	−106.6	106.8
C-3–C-4–C-5–C-6	172.3(1)	165.2(2)	170.0(8)	163.7(3)	172.6	175.1
C-1–O-5–C-5–C-6	170 4(1)	167.8(2)	169.9(6)	175.8(2)	165.8	163.3
C-4–C-5–C-6–O-6	172.5(1)	−56.2(3)	63.9(9)	167.2(3)	178.7	−60.0
O-5–C-5–C-6–O-6	−67.8(2)	66.2(2)	−177.5(6)	−73.3(3)	−61.6	60.9

[a] Estimated standard deviations in parentheses. [b] Models of 2,3-anhydropyranoses obtained by MM calculations (see text) (A, *ribo*; B, *lyxo*).

TABLE VI

RING CONFORMATIONS IN THE 2,3-ANHYDROPYRANOSES **1**–**3**, AND THE DIHYDROPYRAN **5**

	1	**2**	**3**	**5**	*A*[a]	*B*[a]
Atom deviations (Å)[b] *from least-squares planes*						
C-1	0.087(2)[c]	0.004(2)[c]	−0.05(1)[c]	0.003(3)[c]	0.005[c]	0.002[c]
C-2	−0.024(2)[c]	−0.007(2)[c]	0.02(1)[c]	−0.011(4)[c]	−0.010[c]	−0.004[c]
C-3	−0.061(2)[c]	0.007(2)[c]	0.05(1)[c]	0.014(4)[c]	0.010[c]	0.004[c]
C-4	0.064(2)[c]	−0.004(2)[c]	−0.05(1)[c]	−0.006(5)[c]	−0.005[c]	−0.002[c]
C-5	0.701(2)	0.331(2)	0.70(1)	0.430(3)	0.463	0.488
O-5	−0.027(1)[c]	−0.409(1)	0.02(1)[c]	−0.285(2)	−0.308	−0.297
O-2	1.124(1)	−1.212(2)	1.142(7)	—	1.184	−1.182
Asymmetry parameters[10] *(degrees)*[b]						
ΔC_s	16.8(2)	—	13(1)	—	—	—
ΔC_2	11.3(2)	6.0(2)	16(1)	3.9(5)	4.2	5.9
Puckering parameters[11]						
Q (Å)	0.503	0.490	0.505	0.472	0.515	0.526
ϕ (°)	255.7	273.2	250.5	263.4	262.6	261.2
θ (°)	53.4	52.0	54.1	52.1	49.3	51.8
q_2 (Å)[d]	0.404	0.386	0.409	0.372	0.390	0.414
Conformation						
	$^5E + {}^5H_0$	$^5H_0$	$^5E + {}^5H_0$	$^5H_0$	$^5H_0$	$^5H_0$

[a] Models of 2,3-anhydropyranoses obtained by MM calculations (A, *ribo*; B, *lyxo*). [b] Estimated standard deviations in parentheses. [c] Atoms defining the planes. [d] $q_2 = Q\sin\theta$.

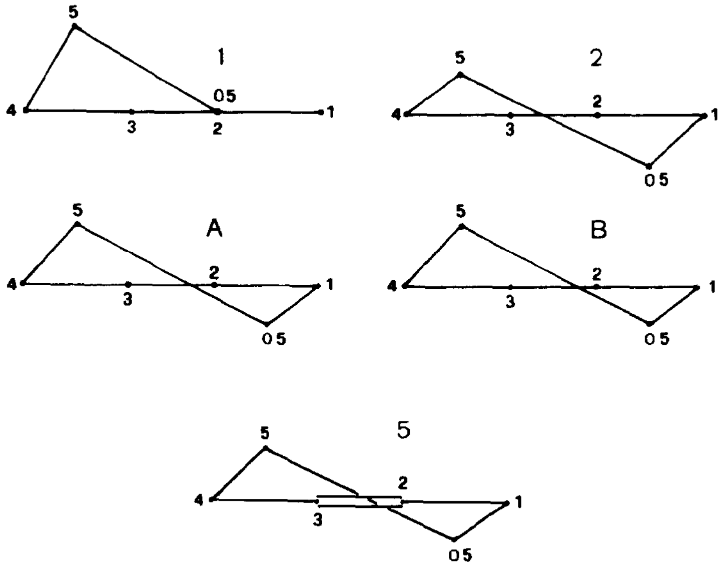

Fig. 2. Schematic conformational views of pyranoid rings along the four-atom C-1/C-4 least-squares planes. A and B refer to model molecules (see text and Tables V and VI).

TABLE VII

INTERMOLECULAR HYDROGEN-BONDS IN **1** AND **2**[a]

	D[b]	*A*	*Acceptor symmetry*	*D* · · · · *A* (Å)	*D-H* (Å)	*H* · · · · *A* (Å)	*D-H* · · · · *A* (°)
1	O-6–HO-6 · · · ·	O-5	1 − x, − y, 2 − z	2.811(3)	1.04(2)	1.78(2)	171(1)
2	O-6–HO-6 · · · ·	O-6	− 1/4 − y, 1/4 + x, 1/4 + z	2.686(3)	0.84(3)	1.85(3)	171(1)

[a] Estimated standard deviations in parentheses. [b] D, donor; A, acceptor.

In **4**, the presence of an oxirane ring forces the furanose ring to be planar, an unusual feature for ribofuranoses.

If the influence of an oxirane ring or a C=C bond on the conformation of pyranoid rings is similar or even equivalent, the problem cannot be solved at the present stage of our X-ray investigations of the crystalline state. There are no indications at present of effects which could cause the conformations of the *ribo* (**1**) and *lyxo* (**2**) stereoisomers to be different. ^{1}H-N.m.r. investigations of solutions[2,3], where the intermolecular interactions are markedly weakened, indicate half-chair

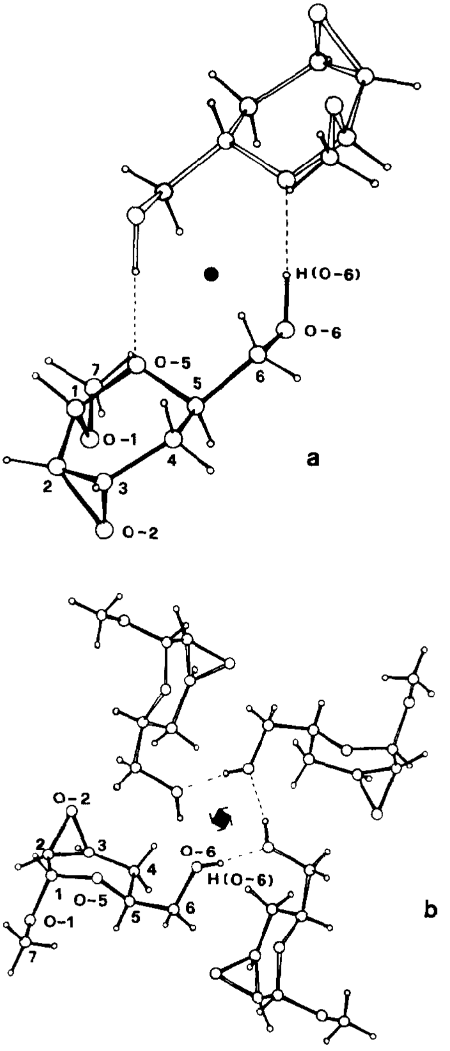

Fig. 3. Projections showing the intermolecular hydrogen-bonding scheme. a–**1**, projection onto least-squares plane through four donor/acceptor atoms; b–**2**, projection along the four-fold screw axis of the crystal.

conformations for 2,3-anhydro-*ribo*- and -*lyxo*-hexopyranoses. The results of model calculations of minimal intramolecular strain energies (MM) for **1** and **2** as isolated molecules (program MM1[13], parametrised additionally for oxirane C and O atoms) are included in Tables V and VI (columns A and B) and presented in Fig. 2. Typical half-chair conformations result from the calculations, indicating that the differences found from X-ray investigations may be due to intermolecular interactions in the crystalline state.

Intermolecular hydrogen-bonds. — The high symmetry found for the crystal of **2** ($I4_1/a$ space group) contrasts with the monoclinic space group ($P2_1/c$) of **1**, which is usually observed for racemic monosaccharides.

There is one possibility for forming strong intermolecular hydrogen-bonds in **1** and **2** (Table VII, Fig. 3). For **1**, the hydrogen bonds form dimers from two enantiomeric molecules. The bonding to the ring oxygen O-5 is relatively unusual in sugars[14]. For **2**, the hydrogen bonds involve O-6 acting as donor and acceptor simultaneously. The chains of molecules form helices around the four-fold screw axes in the crystal, the helices around neighbouring axes consisting of opposite enantiomers.

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