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CRYSTAL STRUCTURE AND CONFORMATION OF 3-*O*-(2,3-ANHYDRO-4-DEOXY-α-L-*lyxo*-HEXOPYRANOSYL)-1,2:5,6-DI-*O*-ISOPROPYLIDENE-α-D-GLUCOFURANOSE

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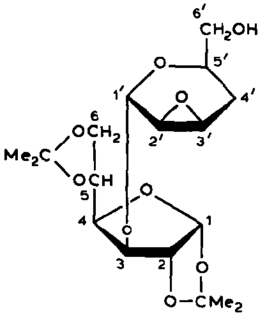
ABSTRACT

A single crystal of 3-*O*-(2,3-anhydro-4-deoxy-α-L-*lyxo*-hexopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**), obtained from its 6-acetate, has been investigated by X-ray diffraction methods. Compound **1** crystallises in the orthorhombic system, space group $P2_12_12_1$, with cell dimensions a = 8.556(1), b = 12.303(1), and c = 18.397(1) Å. An almost ideal half-chair conformation ^5H_o was found for the 2,3-anhydropyranose moiety of **1**.

INTRODUCTION

During our studies of the conformations of 2,3-anhydro-4-deoxyhexopyranosides[1,2], deformed sofa (^5E) conformations were assigned to methyl 2,3-anhydro-4-deoxy-α-DL-*ribo*-hexopyranoside[1] and 3-*O*-(6-*O*-acetyl-2,3-anhydro-4-deoxy-α-L-*ribo*-hexopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[2] (**2**). Previous investigations of conformation by n.m.r. spectroscopy suggested a half-chair form ($^oH_5$) for each compound[3,4]. In contrast, methyl 2,3-anhydro-4-deoxy-α-DL-*lyxo*-hexopyranoside was shown[1] to adopt a half-chair (^5H_o) form.



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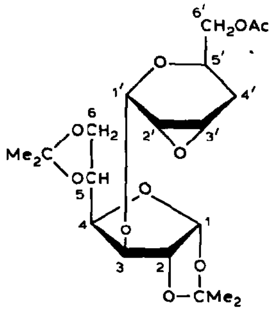

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On the basis of ^{13}C-n.m.r. data[3], the conformations of 2,3-anhydro-4-deoxyhexopyranosides were concluded to be strongly influenced by the configuration of the oxirane ring, *i.e.*, a *trans* relationship of O-5 and O-2(3) with regard to the C-3,4,5 plane in the *ribo*-epoxide, and a *cis* relationship in the *lyxo* isomer.

In exploring further intra- and inter-molecular effects on the conformation of sugar epoxides, we have examined the disaccharide **1** and found it to exist in an almost ideal $^5H_0$ conformation.

EXPERIMENTAL

Compound **1**, prepared by treatment of 3-*O*-(6-*O*-acetyl-2,3-anhydro-4-deoxy-α-L-*lyxo*-hexopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[2] with methanol and potassium carbonate, had m.p. 162° (from methanol–ether), $[\alpha]_D$ −73° (*c* 1.1, dichloromethane); lit.[4] m.p. 160°, $[\alpha]_D$ −72.4°.

A colourless prism (0.20 × 0.20 × 0.35 mm) of **1** was mounted in a random orientation. Cell constants were obtained from least-squares refinement on the setting angles of 25 reflections measured by a computer-controlled Enraf–Nonius CAD-4 diffractometer, using graphite-monochromated Cu*K*α (λ = 1.54184 Å) radiation. The data were collected at ~23°, using an $\omega/2\theta$ scan in the range $1.5 < \theta < 75°$.

Crystal data: $C_{18}H_{28}O_9$, M_r = 388.42, orthorhombic, space group $P2_12_12_1$; a = 8.556(1), b = 12.303(1), c = 18.397(1) Å; V = 1936.6(3) Å^3, Z = 4, $F(000)$ = 832, D_x = 1.33 Mg.m^{-3}, μ(Cu*K*α) = 8.6 cm^{-1}.

A total of 2401 reflections were collected, of which 2123 were unique; 1864 reflections were found to be of $I > 3\sigma_I$. Lorentz and polarisation corrections were applied to the data.

The structure was solved by direct methods using the MULTAN-80 program[5]. A total of 22 atoms were found in the E-map. The remaining atoms were located in subsequent difference Fourier maps. In the course of the isotropic refinement of non-hydrogen positions, an empirical absorption correction using program DIFABS[6] was applied, which reduced R = 0.10 to 0.076. Hydrogen atoms bound to carbon atoms were generated from assumed geometries, whereas that belonging to the OH group was found by $\Delta\rho$ synthesis; their positions and isotropic thermal parameters were refined. A full-matrix least-squares procedure refined $\Sigma w\Delta_F^2$. Anomalous dispersion effects were included[7] in F_c. Only the reflections with $I > 3\sigma_I$ regarded as observed were used in the refinement process. The final reliability factors were R = 0.030 and R_w = 0.027 [$w = 4F_o^2/\sigma(F_o)^2$]. The highest peak in the final difference map was 0.15 e/Å^3.

All calculations were performed on a PDP-11/34 minicomputer with the SDP-34 system provided by Enraf–Nonius (Delft).

RESULTS AND DISCUSSION

The fractional atomic co-ordinates* of **1** are given in Table I. An optimal view of the molecule **1** is shown in Fig. 1. Tables II–IV give the bond lengths, angles, and torsion angles, respectively.

TABLE I

FRACTIONAL CO-ORDINATES (× 10^4)[a] AND EQUIVALENT, ISOTROPIC TEMPERATURE FACTORS ($Å^2$)[b]

Atom	x/a	y/b	z/c	B_{eq}
C-1	7212(2)	−2076(1)	9452(1)	3.4(1)
C-2	5552(2)	−1836(1)	9199(1)	3.0(1)
C-3	5677(2)	−720(1)	8842(1)	2.8(1)
C-4	7355(2)	−726(1)	8570(1)	2.9(1)
C-5	8121(2)	372(1)	8509(1)	3.3(1)
C-6	9826(3)	360(2)	8300(1)	4.1(1)
C-7	6160(2)	−3579(1)	8877(1)	3.1(1)
C-8	6628(3)	−4187(2)	8205(1)	4.9(1)
C-9	5297(3)	−4277(2)	9411(1)	4.4(1)
C-10	8577(3)	1511(2)	7524(1)	3.7(1)
C-11	8198(4)	2703(2)	7515(1)	6.2(1)
C-12	8674(4)	1005(3)	6778(1)	7.3(1)
C-1′	4012(2)	445(1)	9542(1)	3.1(1)
C-2′	4101(3)	942(2)	10291(1)	3.7(1)
C-3′	4013(3)	2109(2)	10372(1)	3.6(1)
C-4′	3843(3)	2816(1)	9712(1)	3.6(1)
C-5′	4263(2)	2215(1)	9021(1)	3.2(1)
C-6′	3818(3)	2808(2)	8338(1)	4.3(1)
O-1	7523(2)	−3145(1)	9222(1)	4.4(1)
O-2	5267(1)	−2652(1)	8670(1)	3.3(1)
O-3	5552(1)	82(1)	9402(1)	3.2(1)
O-4	8207(1)	−1329(1)	9110(1)	3.6(1)
O-5	7403(2)	957(1)	7927(1)	4.4(1)
O-6	9993(2)	1357(1)	7917(1)	3.9(1)
O-2′	2687(2)	1434(1)	10543(1)	4.5(1)
O-5′	3476(1)	1172(1)	9009(1)	3.2(1)
O-6′	2203(2)	3048(1)	8282(1)	4.9(1)

[a]In this and subsequent Tables, the values in parentheses are estimated standard deviations. [b]$B_{eq} = 8\pi^2 \cdot D_u^{1/3}$, where D_u is the determinant of the **U** matrix in orthogonal space.

Conformations of the 2,3-anhydropyranose moieties in **1** *and* **2**. — The results of conformational calculations for the pyranose rings in **1** and **2** are shown in Table V. The 2,3-anhydropyranose moiety in **1** has a half-chair conformation $^5H_0$ which is close to ideal. The small distortion is indicated by the small value of its asymmetry parameter[8] ΔC_2. Also, the pseudorotation angle[9] Φ deviates by only 4° from its

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*Lists of structure factors and anisotropic thermal parameters have been deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/371 *Carbohydr. Res.*, 166 (1987) 19–25.

TABLE II

BOND LENGTHS (Å) FOR **1**

C-1–C-2	1.524(3)	O-6–C-10	1.424(3)
C-2–C-3	1.525(3)	C-10–C-11	1.502(4)
C-3–C-4	1.520(3)	C-10–C-12	1.509(4)
C-4–O-4	1.439(3)	C-3–O-3	1.431(3)
O-4–C-1	1.402(3)	O-3–C-1′	1.415(3)
C-4–C-5	1.506(3)	C-1′–C-2′	1.510(3)
C-5–C-6	1.509(4)	C-2′–C-3′	1.444(4)
C-1–O-1	1.408(3)	C-2′–O-2′	1.430(3)
C-2–O-2	1.419(3)	C-3′–O-2′	1.440(3)
O-1–C-7	1.431(3)	C-3′–C-4′	1.502(3)
O-2–C-7	1.425(3)	C-4′–C-5′	1.513(3)
C-7–C-8	1.499(4)	C-5′–O-5′	1.449(3)
C-7–C-9	1.500(4)	O-5′–C-1′	1.404(3)
C-5–O-5	1.430(3)	C-5′–C-6′	1.502(3)
C-6–O-6	1.422(3)	C-6′–O-6′	1.417(4)
O-5–C-10	1.422(3)		

TABLE III

BOND ANGLES (DEGREES) FOR **1**

C-1–C-2–C-3	103.9(3)	O-5–C-10–C-11	108.7(4)
C-2–C-3–C-4	101.8(3)	O-5–C-10–C-12	108.4(4)
C-3–C-4–O-4	104.7(3)	O-6–C-10–C-11	108.6(4)
C-4–O-4–C-1	109.9(3)	O-6–C-10–C-12	111.1(4)
O-4–C-1–C-2	107.6(3)	C-11–C-10–C-12	113.9(4)
C-1–C-2–O-2	103.4(3)	C-2–C-3–O-3	107.8(3)
C-2–C-1–O-1	105.4(3)	C-4–C-3–O-3	108.1(3)
C-1–O-1–C-7	109.2(3)	C-3–O-3–C-1′	114.8(3)
C-2–O-2–C-7	107.0(3)	C-2′–C-1′–O-3	104.3(3)
O-1–C-7–O-2	104.9(3)	O-5′–C-1′–O-3	112.2(3)
O-1–C-7–C-8	109.5(3)	C-1′–C-2′–C-3′	119.6(4)
O-1–C-7–C-9	108.9(3)	C-2′–C-3′–C-4′	119.8(4)
O-2–C-7–C-8	108.9(3)	C-3′–C-4′–C-5′	111.9(4)
O-2–C-7–C-9	111.7(3)	C-4′–C-5′–O-5′	109.6(3)
C-8–C-7–C-9	112.7(4)	C-5′–O-5′–C-1′	113.6(3)
C-3–C-4–C-5	115.5(3)	C-1′–C-2′–O-2′	115.1(4)
O-4–C-4–C-5	107.0(3)	C-4′–C-3′–O-2′	115.8(4)
C-4–C-5–C-6	115.5(4)	C-2′–C-3′–O-2′	59.4(3)
C-4–C-5–O-5	108.7(3)	C-3′–C-2′–O-2′	60.1(3)
C-5–C-6–O-6	102.4(3)	C-2′–O-2′–C-3′	60.4(3)
C-6–C-5–O-5	103.2(3)	C-4′–C-5′–C-6′	113.8(4)
C-5–O-5–C-10	109.2(3)	O-5′–C-5′–C-6′	107.4(4)
C-6–O-6–C-10	106.3(3)	C-5′–C-6′–O-6′	114.2(4)
O-5–C-10–O-6	105.8(3)		

TABLE IV

COMPARISON OF SOME TORSION ANGLES (DEGREES) IN **1** AND **2**

	1	**2**
2,3-Anhydropyranose ring		
O-5'–C-1'–C-2'–C-3'	−14.4(3)	−5.1(9)
C-1'–C-2'–C-3'–C-4'	−0.3(4)	−2.3(1.4)
C-2'–C-3'–C-4'–C-5'	−17.0(3)	−22.8(1.2)
C-3'–C-4'–C-5'–O-5'	48.4(2)	54.4(9)
C-4'–C-5'–O-5'–C-1'	−67.3(2)	−66.2(8)
C-5'–O-5'–C-1'–C-2'	48.7(2)	40.1(9)
α-D-Glucofuranose ring		
O-4–C-1–C-2–C-3	−13.9(2)	−11.0(8)
C-1–C-2–C-3–C-4	29.2(2)	29.3(7)
C-2–C-3–C-4–O-4	−34.8(2)	−38.2(7)
C-3–C-4–O-4–C-1	27.8(2)	32.9(8)
C-4–O-4–C-1–C-2	−8.6(2)	−13.7(8)
Glycosidic linkage		
H(C-1')–C-1'–O-3–C-3 (ϕ)	40(1)	54(4)
H(C-3)–C-3–O-3–C-1' (ψ)	34(1)	29(4)

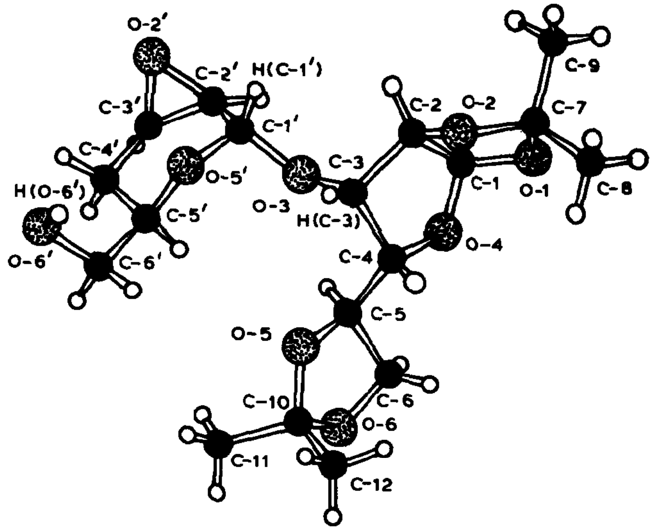

Fig. 1. A parallel projection of **1** oriented at optimal viewing.

ideal value of 270° in the $^{5}H_{6}$ half-chair of cyclohexene[10]. In **1**, C-1',2',3',4' form a four-atom plane characteristic for *H* conformations; C-5' and O-5' deviate from this plane by 0.416 and −0.328 Å, respectively. The asymmetry of these deviations can be understood in terms of the inequality of the lengths of the C–C and C–O bonds.

TABLE V

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

	1	**2**
Atom deviations (Å) from least-squares planes		
C-1′	−0.001(2)[a]	−0.055(8)[a]
C-2′	0.002(3)[a]	0.019(9)[a]
C-3′	−0.002(3)[a]	0.050(11)[a]
C-4′	0.001(3)[a]	−0.045(9)[a]
C-5′	0.416(2)	0.701(8)
O-5′	−0.328(2)	0.025(6)[a]
Asymmetry parameters[9] *(degrees)*		
ΔC_s^5	—	13(1)
$\Delta C_2^{2'-3'}$	1.8(3)	16(1)
Puckering parameters[10]		
Q(Å)	0.381(3)	0.505(9)
ϕ(°)	265.6(4)	250.5(4)
θ(°)	51.0(3)	54.1(3)
q_2(Å)[b]	0.309(3)	0.409(9)
Conformation	$^5H_0$	$^5E \rightarrow {}^5H_0$

[a] Atoms defining the planes. [b] $q_2 = Q \sin \theta$.

A comparison of the 2,3-anhydropyranose moieties in **1** and **2** reveals a difference in their conformations, in that the pyranose ring in **2** has a distorted sofa conformation ($^5E \rightarrow {}^5H_0$). This difference may be due to the configuration of the oxirane ring and the different substituents at C-6′. The nature of the 6′-substituent plays an important role in establishing the ring conformation[3]. Thus, in **1**, HO-6′ forms a strong intermolecular hydrogen-bond to O-6 of the neighbouring molecule (see Table VI). Since **2** is acetylated at position 6′, the intermolecular packing forces in **1** and **2** are completely different in nature, those in **2** being predominantly van der Waals or dipole–dipole forces.

The most important factor which influences the conformational differences is the value of the torsion angle ϕ (Table IV), which is affected by the steric relation of the oxirane ring and glycosidic bond (*trans* in **1**, *cis* in **2**). Different intermolecular interactions also influence the conformations of the rings.

TABLE VI

INTERMOLECULAR HYDROGEN-BONDS

D[a]	*A*[a]	*Acceptor symmetry*	*D····A(Å)*	*D–H(Å)*	*H···A(Å)*	*D–H···A(°)*
O-6′–H(O-6′)···	O-6	−1 + x, y, z	2.891(3)	1.02(4)	1.90(4)	165(3)

[a] D, donor; A, acceptor.

The conformational lability of 2,3-anhydropyranose rings between *H* and *E* forms observed in some monosaccharides[1] was generally supported by molecular mechanics calculations[11] on suitable cyclohexane models, as well as by measurements of mean heat capacities[12] of some sugar units. The *H* and *E* forms were shown to be energetically similar, which implies ease of interchange under the influence of small inter- or intra-molecular forces.

*Conformations of the di-O-isopropylidene-α-*D*-glucofuranose moieties in* **1** *and* **2**. — The α-D-glucofuranose rings in **1** and **2** have similar twist ($^4T_3$) conformations (see Tables IV and VII).

The 1,2-*O*-isopropylidene rings in **1** and **2** adopt *E* and *E* + *T* conformations, respectively. This difference can be due only to intermolecular packing forces. On the other hand, the conformational differences of the 5,6-*O*-isopropylidene rings in **1** and **2** (*E* + *T* and *T*, respectively) may be attributed to the involvement of O-6 in intermolecular hydrogen-bonding, which is not possible in **2**.

TABLE VII

CONFORMATIONAL ASSIGNMENTS FOR 1,2:5,6-DI-*O*-ISOPROPYLIDENE-α-D-GLUCOFURANOSE RINGS IN **1** AND **2**

Compound	*1,2-O-Isopropylidene*	*α-D-Glucofuranose*	*5,6-O-Isopropylidene*
1	E_3	$^4T_3$	$E_2 + {}^2T_3$
2	$E_3 + {}^2T_3$	$^4T_3$	$^2T_3$

ACKNOWLEDGMENT

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