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X-RAY AND CONFORMATIONAL INVESTIGATIONS OF METHYL 2,3-ANHYDRO-2,3,4-TRIDEOXY-β-D-*lyxo*-HEXOPYRANOSIDE

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ABSTRACT

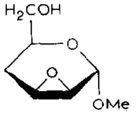
The crystals of methyl 2,3-anhydro-2,3,4-trideoxy-β-D-*lyxo*-hexopyranoside are orthorhombic, space group $P2_12_12_1$ ($Z = 4$) with cell dimensions $a = 4.380(1)$, $b = 12.211(2)$, $c = 14.899(3)$ Å. A hybrid conformation $^{o}E + {}^{o}H_5$ was found for the anhydrohexopyranoside ring. Relatively strong intermolecular hydrogen bonds were observed in the crystal structure, involving the epoxide oxygen as acceptor.

INTRODUCTION

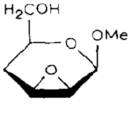
The utility of sugar epoxides for chemical transformations has prompted studies of their ground-state conformations[1], and 2,3-anhydropyranosides were considered to adopt $^{o}H_5$ conformations[1]. Recent findings based on ^{1}H- and ^{13}C-n.m.r. data have modified this general view[2,3]. For example, the sofa conformation (E) was determined by ^{1}H-n.m.r. spectroscopy and by X-ray analysis for 4-substituted methyl 2,3-anhydro-6-bromo-6-deoxy-α-D-allopyranoside[3].

We have reported that 2,3-anhydro-4-deoxy-α-*lyxo*-hexopyranosides of type **1** adopt a half-chair conformation in the crystalline state[4–6], whereas the α-*ribo* isomers of type **3** crystallise in hybrid $^{o}E + {}^{o}H_5$ form[4,7], even though the $^{o}H_5$ form proponderates in solution for both isomers[8,9].

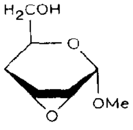
We now report an X-ray structure analysis of β-D-*lyxo* isomer **2**. Within these series, the greatest deviation of **2** from the $^{o}H_5$ conformation towards the $^{5}H_0$ form in solution was observed. Therefore, it was of interest to ascertain whether these conformational forms exist also in the crystal.



1 α-*lyxo*



2 β-*lyxo*



3 α-*ribo*

EXPERIMENTAL

Compound **2** was prepared as described[10], and a well-shaped colourless crystal (0.15 × 0.23 × 0.35 mm) was obtained from ether–acetone. The cell constants were obtained from a least-squares refinement on the setting angles of 25 reflections measured by an Enraf–Nonius CAD-4 diffractometer, using graphite-

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TABLE I

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

Atom	x/a	y/b	z/c	B_{eq}[b]
C-1	2136(11)	7572(4)	1703(4)	4.4(1)
C-2	1534(13)	8791(4)	1777(4)	4.9(2)
C-3	1530(12)	9284(3)	2667(4)	4.8(1)
C-4	2097(14)	8605(4)	3461(4)	5.1(2)
C-5	3112(10)	7445(4)	3247(4)	4.3(1)
C-6	2615(15)	6659(4)	4024(4)	5.4(2)
C-7	1588(24)	6211(5)	634(5)	7.2(2)
O-1	324(10)	7159(3)	1024(3)	5.9(1)
O-2	−1315(8)	9087(3)	2209(3)	5.2(1)
O-5	1404(7)	7037(2)	2503(2)	4.2(1)
O-6	4068(12)	5685(3)	3928(3)	6.9(1)
H(O-6)[c]	266(9)	506(3)	349(4)	8(1)

[a] In this and subsequent Tables, figures 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_{ij} matrix. [c] Coordinates ($\times 10^3$) and temperature factor refined in the isotropic mode.

monochromated CuK_α radiation (1.54178 Å). The data were collected with the $\omega/2\theta$ scan technique.

Crystal data: $C_7H_{12}O_4$, M_r = 160.16, $F(000)$ = 344, orthorhombic, space group $P2_12_12_1$; a = 4.380(1), b = 12.211(2), c = 14.899(3) Å; V = 796.9(3) $Å^3$, Z = 4, D_x = 1.33 Mg m^{-3}, $\mu(\mathrm{Cu}K_\alpha)$ = 8.34 cm^{-1}.

A total of 1016 unique reflections were collected, of which 650 were found to have $I > 2\sigma(I)$. Lorentz and polarisation corrections were applied to the data. No absorption correction was performed at the intensity collection stage.

The phase problem was solved by direct methods using the SHELX-86 program[11]. A total of 11 atoms were found in the E-map. During the isotropic refinement of non-hydrogen parameters, an empirical spherical absorption correction (program DIFABS[12]) was applied. Relative transmission coefficients were in the range from 0.500–1.666, with an average value of 0.988.

Hydrogen atoms bonded to carbon were generated from assumed geometries, and that of the hydroxyl group was found in an E-map. Their positions and isotropic thermal parameters were then refined.

The refinement of atomic positional and anisotropic thermal parameters was performed by the full-matrix, least-squares procedure (program SHELX-76[13]). Only the reflections with $I > 2\sigma(I)$ regarded as observed were used in the refinement process. The final reliability factor was R = 0.061. The highest peak in the final difference map was 0.2 e/$Å^3$.

The refined positional parameters* for the non-hydrogen atoms together with their B_{eq} values are given in Table I.

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*Lists of structure factors, hydrogen co-ordinates, 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/418/*Carbohydr. Res.*, 194 (1989) 31–36.

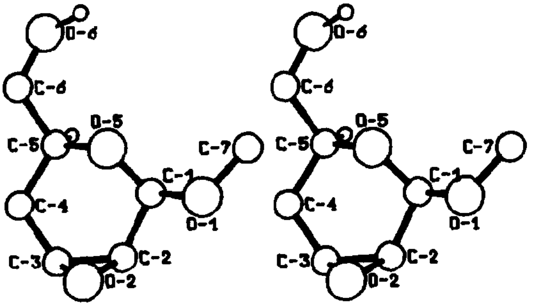


Fig. 1. A stereo-view of **2** with crystallographic numbering. For clarity, the only hydrogen atoms shown are H-5 and HO-6.

RESULTS AND DISCUSSION

The bond lengths, valence angles, and torsion angles for **2** are given in Tables II–IV, and a stereo-view with the crystallographic numbering of the atoms is shown in Fig. 1.

As in the other derivatives of 2,3-anhydro-4-deoxyhexopyranoside[4–7], a shortening of the C-2–C-3 bond in **2** (which is common to both oxirane and pyranose rings) was observed (Table II). The pyranose endocyclic valence angles at C-2 and C-3 (Table III) have values 118.2(5) and 120.1(4)°, respectively, thus making the C-2–C-3 bond similar to a double bond.

Conformational analysis of the 2,3-anhydropyranoside ring in **2**, based on asymmetry[14] and puckering[15] parameters, indicated a hybrid $^{\circ}E$ + $^{\circ}H_5$ conformation.

Comparison of the X-ray data for **1**–**3** shows that they adopt different conformations. The pyranose ring in **1** is an almost "pure" $^{\circ}H_5$ (half-chair), whereas those for **2** and **3** are the hybrids $^{\circ}E$ + $^{\circ}H_5$ and E_5 + $^{\circ}H_5$, respectively, which approximate to sofa (*E*) conformations (see Table V and Figs. 1 and 2).

The analysis of calculated data (Table V) leads to the conclusion that the

TABLE II

BOND DISTANCES (Å) FOR **2**

Bond	*Distance*	*Bond*	*Distance*
C-2–C-1	1.516(7)	C-5–C-4	1.518(7)
O-1–C-1	1.381(7)	C-6–C-5	1.519(8)
O-5–C-1	1.397(6)	O-5–C-5	1.427(6)
C-3–C-2	1.456(8)	O-6–C-6	1.356(7)
O-2–C-2	1.450(7)	O-1–C-7	1.409(8)
C-4–C-3	1.466(8)	H(O-6)–O-6	1.19(5)
O-2–C-3	1.441(7)		

TABLE III

BOND ANGLES (°) FOR **2**

Bonds	*Angle (°)*	*Bonds*	*Angle (°)*
C-1–C-2–C-3	118.2(5)	C-3–C-2–O-2	59.5(4)
C-1–C-2–O-2	115.3(4)	C-2–O-2–C-3	60.5(4)
C-2–C-1–O-1	108.2(4)	C-3–C-4–C-5	114.1(5)
C-2–C-1–O-5	110.9(4)	C-4–C-3–O-2	115.7(4)
C-1–O-1–C-7	112.1(5)	C-4–C-5–C-6	112.8(5)
O-1–C-1–O-5	108.8(4)	C-4–C-5–O-5	109.6(4)
C-1–O-5–C-5	112.3(4)	C-5–C-6–O-6	114.0(5)
C-2–C-3–C-4	120.1(4)	C-6–C-5–O-5	107.2(4)
C-2–C-3–O-2	60.1(4)	C-6–O-6–H(O-6)	112(2)

TABLE IV

TORSION ANGLES (°) FOR **2**

C-3–C-2–C-1–O-1	143.1(5)	C-3–O-2–C-2–C-1	109.2(5)
O-2–C-2–C-1–O-1	75.8(6)	C-5–C-4–C-3–C-2	8.6(7)
C-3–C-2–C-1–O-5	23.9(6)	C-5–C-4–C-3–O-2	77.4(6)
O-2–C-2–C-1–O-5	−43.5(6)	C-2–O-2–C-3–C-4	−111.3(5)
C-7–O-1–C-1–C-2	153.5(5)	C-6–C-5–C-4–C-3	−159.8(5)
C-7–O-1–C-1–O-5	−85.9(6)	O-5–C-5–C-4–C-3	−40.4(6)
C-5–O-5–C-1–C-2	−59.1(5)	O-6–C-6–C-5–C-4	−166.8(5)
C-5–O-5–C-1–O-1	−178.0(4)	O-6–C-6–C-5–O-5	72.5(6)
C-4–C-3–C-2–C-1	0.0(7)	C-1–O-5–C-5–C-4	68.7(5)
O-2–C-3–C-2–C-1	−104.2(5)	C-1–O-5–C-5–C-6	−168.6(4)
C-4–C-3–C-2–O-2	104.2(5)		

conformation of the pyranose ring in **1–3** probably depends on the magnitudes and directions of the interactions of O-2 and O-1 with the atoms in the pyranose ring. For **1**, O-2 and O-1 are on opposite sides of the plane of the ring, and C-5 and O-5 adopt positions with a two-fold axis symmetry characteristic of a half-chair conformation. The 2,3-oxirane group, in a manner similar to that of a double bond, contributes sufficient energy to create a four-atom plane (C-1–4) characteristic of the conformation $^{\mathrm{o}}H_5$.

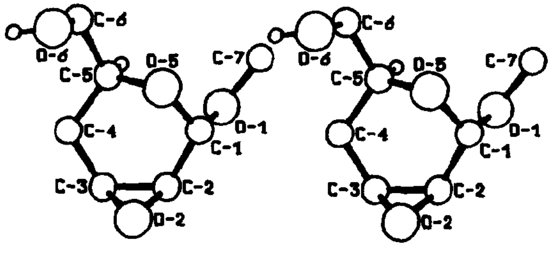
In the stereoisomers **2** and **3**, there is a non-symmetrical interaction of O-1 and O-2 (Figs. 1 and 2) which are situated on the same side of the plane of the ring. The influence of MeO-1 is synergistic with that of O-2 and, enhanced by strong intermolecular hydrogen bonds involving O-2 and O-6, increases the internal energy contribution to the pyranose ring. This energy contribution creates five-atom planes in the rings, characteristic for sofa (E) conformations. However, the calculated puckering parameters indicate that, in **2** and **3**, the rings do not adopt "pure" sofa conformations, but hybrid conformations sofa + half-chair, *i.e.*, $^{\mathrm{o}}E$ + $^{\mathrm{o}}H_5$ and E_{o} + $^{\mathrm{o}}H_5$, respectively.

TABLE V

CONFORMATIONAL PARAMETERS OF THE PYRANOSE RINGS FOR **1–3**

	1 α-lyxo[a]	**2** β-lyxo	**3** α-ribo[a]
Puckering parameters			
Q (Å)	0.491	0.501	0.504
ϕ (°)	93.3	104.3	75.7
θ (°)	128.0	128.5	126.6
q_2 (Å)	0.387	0.392	0.400
Endocyclic torsion angles (°)			
C-1–C-2	17.1	23.9	7.6
C-2–C-3	1.6	0.0	2.3
C-3–C-4	12.4	8.6	20.4
C-4–C-5	−44.8	−40.4	−53.1
C-5–O-5	67.9	68.7	67.8
O-5–C-1	−51.9	−59.1	−43.4
Deviations from least-squares planes (Å)			
	4-atom	*5-atom*	*5-atom*
O-1	1.299	−0.811	1.298
O-2	−1.210	−1.159	1.196
O-5	0.410	0.651	0.027[b]
C-5	−0.330	−0.054[b]	−0.701
Asymmetry parameters (°)			
ΔC_2	6.0	17.1	11.3
ΔC_s	—	12.1	16.8
Conformation	$^{O}H_5$	$^{O}E + {}^{O}H_5$	$E_5 + {}^{O}H_5$

[a] Calculated for the D forms. [b] One of atoms defining the least-squares plane (see text).



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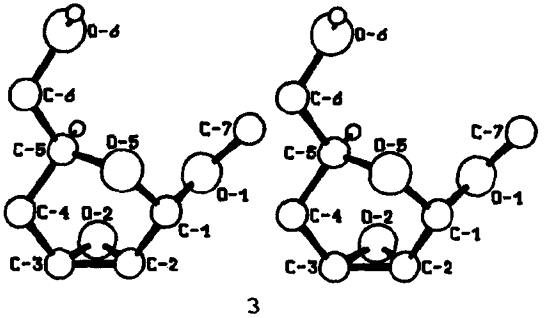

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Fig. 2. Stereo-views of compounds **1** and **3**. The chosen D-enantiomorphs conform to that of **2**.

A strong intermolecular hydrogen bond involving HO-6 and O-2 was observed in the crystal; the symmetry of the O-2 acceptor was $-x$, $-\frac{1}{2} + y$, $\frac{1}{2} - z$. The calculated geometry of the hydrogen bond is: O–H 1.19(5), O-6 · · · O-2 2.852(6), H · · · O-2 1.68(5) Å, angle D–H · · · A 169(2)°. In **1** and **3**, hydrogen bonds of similar strength have been observed[4], but involving other acceptors, namely, O-6 in **1** and O-5 in **3**. For **2** and **3**, where the ring oxygens are involved as acceptors, the strong hydrogen bonds may be reponsible in part for the deviations of the conformations from half-chair.

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