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CRYSTAL AND MOLECULAR STRUCTURE OF 6-*C*-(2-FURYL)-1,2:3,4-DI-*O*-ISOPROPYLIDENE-α-D-*glycero*-D-*galacto*-HEXOPYRANOSE

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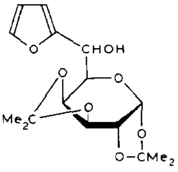
ABSTRACT

6-*C*-(2-Furyl)-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-D-*galacto*-hexopyranose (**1**) has been investigated by X-ray diffraction methods. The crystals obtained from ethyl acetate–light petroleum were monoclinic, space group $P2_1$ ($Z = 2$), with cell dimensions $a = 13.796(2)$, $b = 7.887(1)$, $c = 8.035(1)$ Å, and $\beta = 106.68(3)°$. A four-circle, automatic STOE diffractometer was used for the collection of intensity data. Of 1600 reflection intensities, 1390 were of $I > 2\sigma_I$ and were used for refinement. The structure was solved by direct methods, and the atomic parameters were refined by the full-matrix, least-squares procedure, giving R 0.056. The pyranose ring in **1** adopts a hybrid twist–boat conformation (${}^{\mathrm{O}}T_2 + B_{2,5}$).

INTRODUCTION

The condensation of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose with furan in the presence of trichloroacetic acid yields[1] two stereoisomeric 6-*C*-(2-furyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoses in the ratio 85:15. The major stereoisomer (**1**), isolated by chromatography, had m.p. 173–174°, $[\alpha]_D^{25}$ −53° (*c* 1.5, chloroform), and can be used in the synthesis of higher sugars.

The reasons for undertaking the X-ray structural studies on **1** were to estab-



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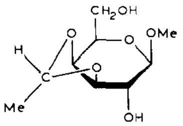

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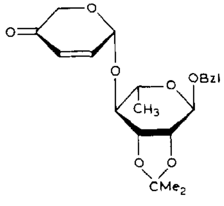

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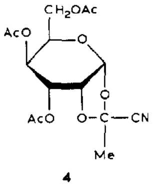

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lish the configuration at C-6, knowledge of which is essential for further synthesis work, and to obtain information on the conformation of the pyranose ring which cannot adopt a chair form.

EXPERIMENTAL

Colourless crystals of **1** were recrystallised from ethyl acetate–light petroleum and had m.p. 174°. Preliminary lattice constants and the space group were established from the oscillation and Weissenberg photographs. The constants were refined during the intensity data collection.

Crystal data for **1** ($C_{16}H_{22}O_7$): monoclinic, space group $P2_1$, $Z = 2$, $a = 13.796(2)$, $b = 7.887(1)$, $c = 8.035(1)$ Å, $\beta = 106.68(2)°$, $V = 837.5(2)$ Å^3, $M_r = 326.34$, F(000) = 348, $D_c = 1.29$ Mg.m^{-3}, $\mu(CuK\alpha) = 0.81$ mm^{-1}.

A well-shaped crystal (0.7 × 0.12 × 0.07 mm) was used for the collection of intensities. Measurement conditions: STOE four-circle, single-crystal automated diffractometer controlled by a DEC-PDP15 minicomputer, CuKα radiation (λ 1.54178 Å), $\omega/2\theta$ scan mode, measurement range up to $2\theta_{max}$ 129° at room temper-

TABLE I

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

Atom	*x/a*	*y/b*	*z/c*	B_{eq}[b]
C-1	−1923(4)	1328(9)	−4177(7)	3.3(2)
C-2	−2835(4)	2120(8)	−3688(8)	3.4(2)
C-3	−3874(4)	1726(7)	−4957(7)	2.9(2)
C-4	−3972(4)	−101(7)	−5718(7)	2.9(2)
C-5	−2987(4)	−1057(7)	−5179(7)	2.7(2)
C-6	−3002(4)	−2647(7)	−6240(7)	3.1(2)
C-7	−1761(4)	988(11)	−1194(8)	4.2(2)
C-8	−1695(6)	−624(11)	−116(10)	5.4(2)
C-9	−1280(6)	2564(12)	−121(10)	5.8(3)
C-10	−4542(5)	1910(8)	−7933(8)	3.7(2)
C-11	−4193(6)	2489(12)	−9435(9)	6.1(3)
C-12	−5664(5)	2165(11)	−8183(9)	4.9(2)
C-13	−2004(4)	−3532(8)	−5738(8)	3.4(2)
C-14	−1526(5)	−3874(9)	−4150(7)	3.4(2)
C-15	−629(8)	−4702(14)	−4201(15)	6.8(4)
C-16	−615(6)	−4862(13)	−5806(17)	5.7(4)
O-1	−1299(3)	703(7)	−2556(5)	4.4(1)
O-2	−2807(3)	1304(7)	−2082(5)	3.8(1)
O-3	−3987(3)	2821(5)	−6404(5)	3.5(1)
O-4	−4258(3)	181(6)	−7556(5)	3.6(1)
O-5	−2184(3)	0[c]	−5379(5)	3.1(1)
O-6	−3800(3)	−3656(6)	−5958(6)	4.0(1)
O-7	−1533(5)	−4151(10)	−6873(9)	8.5(3)

[a] Estimated standard deviations in parentheses. [b] $B_{eq} = 8\pi^2(U_1 \times U_2 \times U_3)^{1/3}$, where U_i are eigenvalues of the U_{ij} matrix. [c] Invariant co-ordinate.

ature. The crystal stability was controlled on two reflections at 25 reflection intervals, no significant decay was observed, and 1600 intensities (1390 of $I > 2\sigma_I$) were collected. The Lorentz and polarisation, but no absorption, correction was aplied. The phase problem for **1** was solved by direct methods using the SHELX-76 programme[2].

The refinement of atomic positional and thermal parameters, initially isotropic and then anisotropic, was performed using the X-RAY 70 System[3] (program CRYLSQ), by the least-squares, full matrix procedure, with the atomic scattering factors taken from the International Tables for X-Ray Crystallography[4]. The positions of the hydrogen atoms were found from a ΔF Fourier synthesis. The final refinement step involved all of the positional and thermal parameters except the H-atomic temperature factors (set as B_{eq} of the adjacent atom + 1 Å^2 and held invariant). The final R value was 0.056 (R_w 0.058, unit weights) at $\Delta/\sigma < 0.1$. The maximum, residual electron-density amplitude on the final $\Delta\rho$ maps was 0.4 e/Å^3. The refined positional parameters and the B_{eq} values for **1** are given in Table I.

RESULTS AND DISCUSSION

The bond lengths, bond angles, and some torsion angles for **1** are given in Tables II–IV. The ORTEP[5] diagram (Fig. 1) shows the view of **1**.

In the fragment of the galactopyranose ring containing C-1/4, a significant bond elongation and increase of the valence angles (>1.55 Å and >114°, respectively) was observed. A similar phenomenon was found in the ring geometry of the 4-*O*-(pentenosylulose)rhamnopyranoside[6] **3** where the valence angles at C-2 and C-3 have particularly increased values. It is reasonable to assume that the observed distortions of the sugar ring in **1** are due to the fusion with two 1,3-dioxolane rings.

Despite the above-mentioned similarities in the structures of the pyranose

TABLE II

BOND DISTANCES (Å) FOR 1[a]

C-1–C-2	1.553(9)	O-3–C-10	1.439(7)
C-2–C-3	1.534(7)	C-10–C-11	1.494(11)
C-3–C-4	1.556(8)	C-10–C-12	1.515(10)
C-4–C-5	1.504(8)	C-10–O-4	1.427(8)
C-5–O-5	1.432(7)	O-4–C-4	1.433(7)
O-5–C-1	1.400(7)	C-5–C-6	1.513(8)
C-1–O-1	1.428(7)	C-6–O-6	1.428(8)
O-1–C-7	1.434(9)	C-6–C-13	1.492(8)
C-7–C-8	1.526(12)	C-13–C-14	1.286(8)
C-7–C-9	1.550(12)	C-14–C-15	1.410(13)
C-7–O-2	1.436(7)	C-15–C-16	1.301(19)
O-2–C-2	1.433(8)	C-16–O-7	1.425(11)
C-3–O-3	1.420(7)	O-7–C-13	1.353(11)

[a] Estimated standard deviations in parentheses.

TABLE III

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

C-2–C-1–O-1	103.2(5)	C-9–C-7–O-1	109.7(6)
C-2–C-1–O-5	114.1(4)	C-9–C-7–O-2	110.2(6)
O-1–C-1–O-5	109.8(5)	O-1–C-7–O-2	104.6(4)
C-1–C-2–C-3	114.9(5)	C-11–C-10–C-12	114.0(6)
C-1–C-2–O-2	103.5(5)	C-11–C-10–O-3	108.7(6)
C-3–C-2–O-2	106.6(5)	C-11–C-10–O-4	109.3(6)
C-2–C-3–C-4	114.0(5)	C-12–C-10–O-3	108.7(6)
C-2–C-3–O-3	106.4(5)	C-12–C-10–O-4	111.3(6)
C-4–C-3–O-3	105.4(4)	O-3–C-10–O-4	104.4(4)
C-3–C-4–C-5	112.5(4)	C-6–C-13–C-14	122.5(7)
C-3–C-4–O-4	103.2(4)	C-6–C-13–O-7	124.8(6)
C-5–C-4–O-4	109.5(5)	C-14–C-13–O-7	112.6(6)
C-4–C-5–C-6	112.9(4)	C-13–C-14–C-15	105.8(7)
C-4–C-5–O-5	109.9(4)	C-14–C-15–C-16	109.7(8)
C-6–C-5–O-5	107.8(5)	C-15–C-16–O-7	107.1(9)
C-5–C-6–C-13	111.9(4)	C-1–O-1–C-7	111.0(5)
C-5–C-6–O-6	105.0(5)	C-2–O-2–C-7	106.8(5)
C-13–C-6–O-6	113.0(5)	C-3–O-3–C-10	107.6(4)
C-8–C-7–C-9	114.0(6)	C-4–O-4–C-10	110 1(5)
C-8–C-7–O-1	109.6(7)	C-1–O-5–C-5	114.4(4)
C-8–C-7–O-2	108.3(6)	C-13–O-7–C-16	104.6(7)

[a] Estimated standard deviations in parentheses.

TABLE IV

SELECTED TORSION ANGLES (DEGREES) FOR **1**[a]

O-5–C-1–C-2–C-3	−17.7(8)	C-2–C-3–O-3–C-10	145.1(5)
C-1–C-2–C-3–C-4	37.3(7)	C-5–C-4–O-4–C-10	−132.3(5)
C-2–C-3–C-4–C-5	−5.5(7)	O-5–C-5–C-6–O-6	178.8(4)
C-3–C-4–C-5–O-5	−45.6(6)	C-4–C-5–C-6–O-6	−59.7(6)
C-4–C-5–O-5–C-1	70.6(5)	O-5–C-5–C-6–C-13	55.9(6)
C-5–O-5–C-1–C-2	−36.1(6)	C-4–C-5–C-6–C-13	177.4(5)
C-1–C-2–O-2–C-7	32.8(6)	C-5–C-6–C-13–O-7	−134.5(7)
C-2–O-2–C-7–O-1	−31 9(7)	C-5–C-6–C-13–C-14	49.8(9)
O-2–C-7–O-1–C-1	17.7(8)	C-6–C-13–O-7–C-16	179.6(7)
C-7–O-1–C-1–C-2	2.1(7)	C-6–C-13–C-14–C-15	179.9(6)
O-1–C-1–C-2–O-2	−21.1(6)	C-13–O-7–C-16–C-15	3.1(10)
O-5–C-1–O-1–C-7	−120.0(6)	O-7–C-16–C-15–C-14	−1.0(12)
C-3–C-2–O-2–C-7	154.3(5)	C-16–C-15–C-14–C-13	−1.6(11)
C-4–C-3–O-3–C-10	23.7(6)	C-15–C-14–C-13–O-7	3.7(9)
C-3–O-3–C-10–O-4	−31.3(6)	C-14–C-13–O-7–C-16	−4.3(9)
O-3–C-10–O-4–C-4	27.0(7)	H-6–C-6–O-6–HO-6	80(5)
C-10–O-4–C-4–C-3	−12.3(6)	C-13–C-6–O-6–HO-6	−46(3)
O-4–C-4–C-3–O-3	−7.1(6)	C-5–C-6–O-6–HO-6	−168(5)

[a] Estimated standard deviations in parentheses.

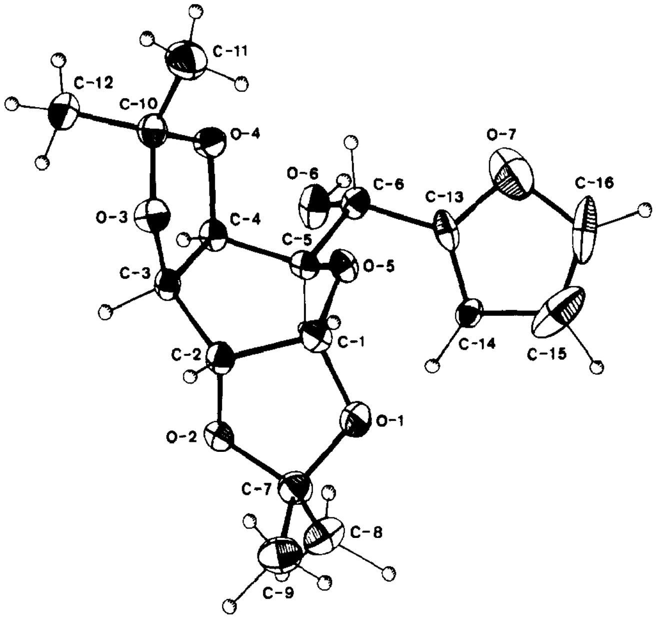


Fig. 1. ORTEP[5] diagram of a single molecule of **1**. Parallel projection oriented at optimal view with the crystallographic labelling of atoms. Thermal motion ellipsoids set at 40% probability level.

rings in **1** and **3**, the bond lengths and angles in these rings differ markedly. Since the conformation of the pyranose ring in 3 deviates significantly from an ideal chair (the conformation assignment was ${}^1C_4 \rightarrow {}^2E$), it could be assumed that the conformation of the pyranose in **1** is not a chair form as suggested by the ^{1}H-n.m.r. data[1].

Analysis of the ring torsion angles (Table V) shows that all the angle values deviate markedly from those characteristic for the chair form of cyclohexane (±56°). Particularly, the torsion angle at the C-3–C-4 bond has a value close to zero [$-5.5(7)$°], which makes the sign sequence in the ring $-+0-+-$. If C-2/5 were nearly coplanar, this might imply the ${}^1H_0$ half-chair conformation. However, this is not so for **1**, since C-2/5 deviate markedly from coplanarity. In order to define the conformation of the pyranose ring in **1**, a least-squares plane through all six atoms of the ring was calculated and the deviations of the atoms were shown graphically (Fig. 2). The deviation values for C-1 and C-4 are close to zero (-0.026 and -0.082 Å, respectively), whereas those for C-2, C-3, C-5, and O-5 are, respectively, 0.279, -0.223, 0.392, and -0.340 Å. This may be interpreted as indicating a deformed twist conformation. The nature of this deformation was analysed by calculation of puckering parameters (program RING[8]) (Table V). The value of the angle ϕ 81°, when located on the Pople diagram[9], indicates a twist conformation deformed towards a boat (${}^oT_2 \rightarrow B_{2,5}$). On the other hand, the value of q_2 (0.63 Å), together with two relatively small values of the torsion angles, indicates some additional flattening of the ring, and thus a small deformation towards the half-chair form may

TABLE V

CONFORMATIONS OF PYRANOSE RINGS IN **1**–**7**[a]

Torsion angle (degrees)	**1**	**2**	**3**	**4**	**5**	**6a**	**6b**	**7**	*Cyclohexane model*
O-5–C-1–C-2–C-3	−17.7(8)	58.7(5)	−41.3(6)	−16.5(5)	−11.5(9)	20.1	20.9	34.2	31.1
C-1–C-2–C-3–C-4	37.3(7)	−40.9(5)	37.4(6)	42.4(6)	52.7(9)	−58.4	−59.0	−64.2	−64.5
C-2–C-3–C-4–C-5	−5.5(7)	34.4(6)	−46.7(6)	−14.9(6)	−38.7(9)	32.1	32.7	28.9	31.1
C-3–C-4–C-5–O-5	−45.6(6)	−43.2(5)	59.0(5)	−38.7(4)	−16.1(9)	28.4	27.9	33.4	31.1
C-4–C-5–O-5–C-1	70.6(5)	61.3(5)	−65.2(5)	69.7(4)	−61.7(9)	−71.7	−70.5	−67.2	−64.5
C-5–O-5–C-1–C-2	−36.1(6)	−70.4(4)	56.4(5)	−39.8(4)	−46.6(9)	43.5	42.6	29.3	31.1
Asymmetry parameters[7] *(degrees)*									
ΔC_s	—	—	18.3(6)	—	—	—	—	4.2[b]	0
ΔC_2	11.2(6)	2.5(5)	5.4(6)	1.4(5)	—	13.6	13.4	4.7[c]	0
Puckering parameters[8]									
q_2 (Å)[d]	0.63	0.20	0.16	0.64	0.68	0.75	0.75	0.77	0.78
ϕ (degrees)	81	150	64	87	106	276	276	266	270
Conformation of pyranose rings	$^{o}T_2 + B_{2,5}$	$^{1}C_4 \rightarrow {}^{3}H_4$	$^{1}C_4 \rightarrow {}^{2}E$	$^{o}T_2$	$^{o}T_2 + {}^{3,o}B$	$^{2}T_o$	$^{2}T_o$	$^{2}T_o$	$^{2}T_6$
Conformation of 1,3-dioxolane rings									
1,2-*O*-Isopropylidene	^{3}E	—	—	$^{3}E + {}^{3}T_4$	—	—	—	—	—
2,3-*O*-Isopropylidene	—	—	^{5}E	—	—	—	—	—	—
3,4-*O*-Isopropylidene	$^{2}T_1 + {}^{2}E$	$^{5}T_1$	—	—	—	—	—	—	—

[a] Estimated standard deviations in parentheses. [b] $\Delta C_2^{1,4}$. [c] $\Delta C_2^{2,3}$. [d] $q_2 = Q \times \sin\theta$.

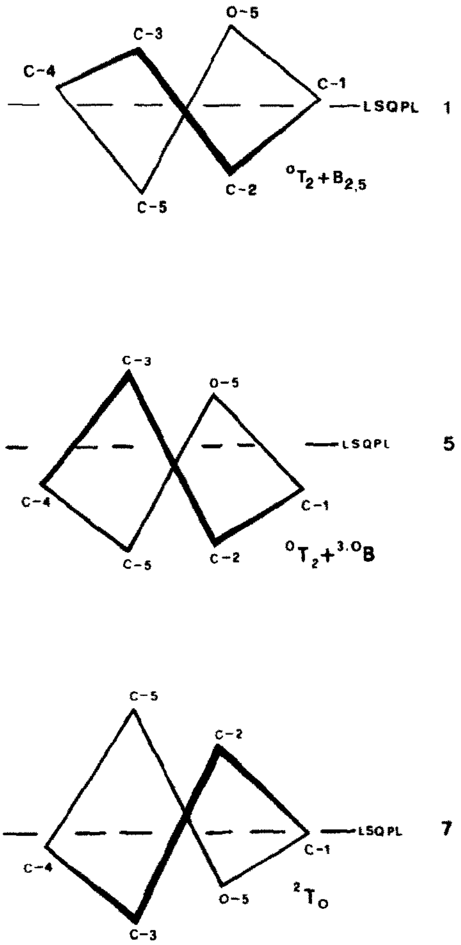


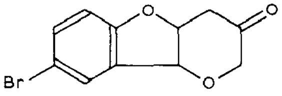
Fig. 2. Projections of pyranose rings for **1**, **5**, and **7** along their least-squares planes defined by all ring atoms. The vertical scale is expanded approximately 5 times. The plane traces are shown as dashed lines.

be also assumed. Thus, the conformation of the pyranose ring in **1** is concluded to be $^{O}T_2 + B_{2,5}$.

The reason why the pyranose ring fused to two 1,3-dioxolane rings in **1** adopts the above conformation in the crystalline state is not known. This conformation is seldom encountered in sugar rings and doubtless is not favoured energetically. An attempt to clarify the situation was made by analysis of the conformational calculations for the rings in **2**[10], **3**[6], and **4**[11].

The pyranose ring in methyl 3,4-*O*-ethylidene-β-D-galactopyranoside (**2**) is fused to a 1,3-dioxolane ring and may be characterised (Table V) as a chair deformed towards a half-chair ($^{1}C_4 \rightarrow {}^{3}H_4$). The pyranose ring in **3**, which is fused similarly at positions 2 and 3, was determined as a chair deformed towards a sofa ($^{1}C_4 \rightarrow {}^{2}E$). Otherwise, the pyranose ring in 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose (**4**), which is fused to a 1,3-dioxolane ring at positions 1 and 2, may be characterised by a twist conformation $^{o}T_2$. The small value of the asymmetry parameter ΔC_2 (1.4°) and the value of the angle ϕ close to 90° for **4** confirm the above assignment. The lowered value of q_2 indicates a small deformation of the $^{o}T_2$ conformation towards $^{2}H_3$.

Thus, the fusion of a pyranose ring to a 1,3-dioxolane ring at the 2,3- or 3,4-positions causes marked deformation of the chair conformations towards the half-chair or sofa forms. A partial change of chair→twist conformation was observed only when the fusion involved positions 1 and 2, as in **1** (which also has a dioxolane ring fused at positions 3 and 4) and in **4**. It seems, therefore, that 1,2-fusion is responsible for this effect and is strengthened by the anomeric effect, which could account for the more marked changes in conformation when there is a 2,3- or 3,4-fusion.



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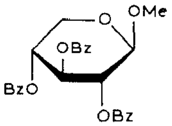

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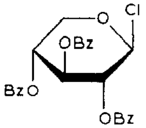

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Other atypical distortions of the $^{1}C_4$ form of a pyranose ring have been found in 6-bromo-1,2,3,4,4a,9a-hexahydro-4,9-dioxafluoren-2-one[12] (**5**) (Fig. 2), methyl 2,3,4-tri-*O*-benzoyl-β-D-xylopyranoside[13] (**6**), and 2,3,4-tri-*O*-benzoyl-β-D-xylopyranosyl chloride[14] (**7**). A hybrid conformation ($^{o}T_2$ + $^{3,o}B$) may be assigned to the pyran ring in **5** which contains the equivalent of a 1,2-fusion. In **6**, the deformed $^{2}T_o$ conformation was assigned to both independent molecules in the asymmetric unit (Table V). In **7**, the pyranose ring has a nearly pure, local D_2 point group symmetry, characteristic of a twist-cyclohexane molecule. Table V and Fig. 2 show the conformational characteristics of the above pyranose rings and of a twist-cyclohexane form. The twist-cyclohexane conformation was established from a model optimised by MM computation (programme MM1[15]) with a D_2 symmetry restriction ($^{2}T_6$ conformation). The values of the torsion angles in **7** are close to those for twist-cyclohexane (the differences are within the range 0.3–3.1°), the asymmetry parameters ΔC_2 differ by less than 5°, and the puckering parameters q_2 and ϕ differ by 0.01 Å and 3°, respectively. Thus, the conformation of **7** should be almost pure $^{2}T_o$.

The conformations of the 1,3-dioxolane rings associated with the 1,2- and 3,4-*O*-isopropylidene groups in **1** differ significantly. The former adopts an envelope ^{3}E conformation, and the latter adopts a hybrid conformation $^{2}T_1$ + ^{2}E.

In the crystal of **1**, there is one strong intermolecular hydrogen-bond between HO-6 and O-3, with the latter translated along the *b* axis, and O-6 · · · O-3 2.804 Å, O-3 · · · HO-6 1.861 Å, O-6–HO-6 · · · O-3 162°. Thus, the molecules in the crystal form infinite chains parallel to the [010] direction.

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