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Note

Conformation of 1,6-anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose and its 2-*O*-acetyl derivative

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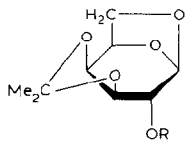
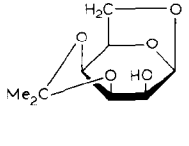
The conformation of 1,6-anhydro-β-D-hexopyranoses and their derivatives has been investigated[1]. ^{1}H-N.m.r. data indicate that the $^1C_4$(D) conformation is generally preferred[2,3]; only in a few cases have the alternative $B_{o,3}$(D) or E_o(D) conformations been proposed[4–7]. X-Ray crystallographic studies[8–19] also demonstrate that the $^1C_4$ conformation is preferred in the crystalline solid. Most derivatives studied by X-ray analysis have been examined by empirical force-field calculations, and the theoretical and observed results have been compared[19,20].

We now report the molecular structure in crystalline 1,6-anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose (**1**), the 2-*O*-acetyl derivative (**2**) of which has been previously reported to exist in solution in the $B_{o,3}$ conformation on the basis of ^{1}H-n.m.r. data[4]. We have analysed the ^{1}H-n.m.r. spectrum of **2** by using a computer programme, and the calculated best values of the vicinal coupling constants have been used with several Karplus-type equations to estimate the torsion angles for vicinal protons.

A view of compound **1** is given in Fig. 1. Table I contains the final fractional atomic co-ordinates, and Table II contains the endocyclic torsion angles compared with those found in 1,6-anhydro-3,4-*O*-isopropylidene-β-D-talopyranose[13] (**3**) and 1,6-anhydro-β-D-galactopyranose[19] (**4**). The conformations of the rings are de-



1 R = H
2 R = Ac



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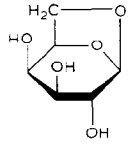

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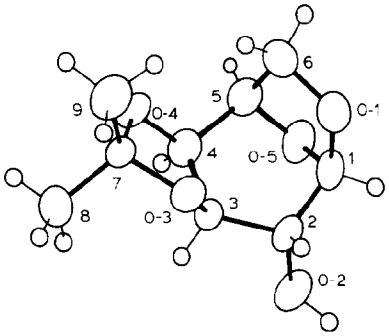

Fig. 1. Perspective ORTEP[32] view of 1,6-anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose (**1**), showing the atomic numbering.

TABLE I

FINAL FRACTIONAL ATOMIC CO-ORDINATES

Atom	*x/a*	*y/b*	*z/c*
C-1	0.0191(2)	−0.2169(7)	0.5498(4)
O-1	0.0323(1)	−0.3456(5)	0.4281(3)
C-2	0.0780(2)	−0.2715(6)	0.6571(3)
O-2	0.0561(1)	−0.1625(6)	0.7839(3)
C-3	0.1555(2)	−0.1694(6)	0.6193(3)
O-3	0.2004(1)	−0.3552(4)	0.5571(2)
C-4	0.1566(2)	0.0352(6)	0.5112(3)
O-4	0.2212(1)	0.0199(4)	0.4279(2)
C-5	0.0855(2)	0.0409(7)	0.4224(4)
O-5	0.0217(1)	0.0339(5)	0.5150(3)
C-6	0.0725(2)	−0.1859(9)	0.3367(4)
C-7	0.2582(2)	−0.2283(6)	0.4840(3)
C-8	0.3213(2)	−0.1480(11)	0.5791(4)
C-9	0.2860(2)	−0.3899(8)	0.3701(4)
H-1	−0.031(2)	−0.256(7)	0.584(4)
H-2	0.084(2)	−0.444(6)	0.663(3)
H-O2	0.028(3)	−0.279(10)	0.834(5)
H-3	0.179(2)	−0.111(7)	0.700(4)
H-4	0.165(2)	0.193(7)	0.552(3)
H-5	0.084(3)	0.188(8)	0.370(4)
H-6A	0.039(2)	−0.148(7)	0.259(4)
H-6B	0.121(2)	−0.250(7)	0.302(4)
H-8A	0.350(3)	−0.275(10)	0.616(5)
H-8B	0.303(2)	−0.037(8)	0.659(4)
H-8C	0.354(2)	−0.035(7)	0.532(4)
H-9A	0.243(2)	−0.435(7)	0.314(4)
H-9B	0.311(3)	−0.564(12)	0.413(6)
H-9C	0.323(2)	−0.315(9)	0.310(4)

TABLE II

EXPERIMENTAL TORSION ANGLES (DEGREES) FOR THE PYRANOID, 1,6-ANHYDRO, AND DIOXOLANE RINGS

Bonds	*Compound*				
	1	**3**[13]	**4**[19a]		
Pyranoid ring					
O-5–C-1–C-2–C-3 (ϕ_0)	−49.0(4)	−50.7(4)	−58.6(5)	−55.3(5)	−58.3(5)
C-1–C-2–C-3–C-4 (ϕ_1)	19.6(4)	25.2(4)	37.1(5)	36.1(5)	36.7(5)
C-2–C-3–C-4–C-5 (ϕ_2)	−20.9(4)	−27.9(4)	−39.2(5)	−39.9(5)	−38.9(5)
C-3–C-4–C-5–O-5 (ϕ_3)	49.7(4)	55.0(4)	59.1(5)	61.3(5)	59.7(5)
C-4–C-5–O-5–C-1 (ϕ_4)	−78.5(4)	−79.7(4)	−77.0(5)	−77.2(5)	−77.4(5)
C-5–O-5–C-1–C-2 (ϕ_5)	79.3(4)	77.8(4)	78.2(5)	74.4(5)	77.3(5)
1,6-Anhydro ring					
O-5–C-1–O-1–C-6 (ϕ_{10})	23.4(4)	25.4(4)	19.5(5)	25.0(5)	24.0(5)
C-1–O-1–C-6–O-5 (ϕ_{11})	3.7(4)	2.0(4)	9.3(5)	2.8(5)	4.5(5)
O-1–C-6–C-5–O-5 (ϕ_{12})	−28.5(4)	−27.6(4)	−33.2(5)	−28.5(5)	−29.8(5)
C-6–C-5–O-5–C-1 (ϕ_{13})	42.2(4)	42.3(4)	45.2(5)	43.9(5)	44.1(5)
C-5–O-5–C-1–O-1 (ϕ_{14})	41.7(4)	−43.2(4)	−41.0(5)	−43.5(5)	−42.9(5)
Dioxolane ring					
C-3–O-3–C-7–O-4 (ϕ_{10})	−38.4(4)	−38.4(4)			
O-3–C-7–O-4–C-4 (ϕ_{11})	21.4(4)	20.4(4)			
C-7–O-4–C-4–O-3 (ϕ_{12})	−3.0(4)	4.2(4)			
O-4–C-4–C-3–O-3 (ϕ_{13})	−19.9(4)	−27.0(4)			
C-4–C-3–O-3–C-7 (ϕ_{14})	35.6(4)	39.9(4)			

[a]Three crystallographically independent molecules

TABLE III

CONFORMATIONAL PARAMETERS FOR THE PYRANOID[21], 1,6-ANHYDRO[22], AND DIOXOLANE[22] RINGS (ALL VALUES IN DEGREES, Σ AND Δ BEING MODULUS 4π)

Parameter	*Compound*				
	1	**3**[13]	**4**[19a]		
Pyranoid ring					
τ_m	−49.5(2)	−52.7(2)	−58.3(3)	−57.4(3)	−58.1(3)
q	33.9(2)	30.2(2)	22.8(3)	22.0(3)	22.9(3)
Σ	178.9(8)	171.6(8)	178.4(14)	163.8(15)	175.7(14)
1,6-Anhydro ring					
ϕ_m	44.2(3)	45.0(3)	46.0(3)	45.9(3)	45.9(3)
Δ	−116.3(6)	−111.6(6)	−129.7(8)	−113.8(8)	−117.6(8)
Dioxolane ring					
ϕ_m	38.9(3)	41.1(3)			
Δ	333.5(7)	312.8(7)			

[a]Three crystallographically independent molecules.

TABLE IV

TORSION ANGLES (DEGREES) FOR VICINAL PROTONS FROM X-RAY ANALYSIS

Bonds	*Compound*				
	1	**3**[13]	**4**[19] [a]		
H-1–C-1–C-2–H-2	74(3)	−59(3)	61(3)	89(4)	48(3)
H-2–C-2–C-3–H-3	−99(3)	29(3)	−88(3)	−78(3)	−80(3)
H-3–C-3–C-4–H-4	−18(3)	−27(3)	−45(3)	−45(4)	−36(3)
H-4–C-4–C-5–H-5	42(3)	49(3)	48(3)	58(4)	66(3)
H-5–C-5–C-6–H-6*endo*	90(3)	102(3)	84(3)	101(4)	100(3)
H-5–C-5–C-6–H-6*exo*	−30.(3)	−32(3)	−54(3)	−28(4)	−39(3)

[a]Three crystallographically independent molecules.

scribed in Table III, and the proton–proton torsion angles from X-ray data are given in Table IV. A hydrogen bond is present in the crystal packing: O-2-H (O-2) = 0.95(2) Å, O-2 · · · O-5i = 2.916(4) Å, H (O-2) · · · O-5i =1.991(5) Å, and O-2-H(O-2) · · · O-5i = 164(5)°, i being the symmetry operation $-x, y-\frac{1}{2}, -z+\frac{3}{2}$.

The pyranoid ring has a $^1C_4$ conformation distorted towards an envelope at O-5 (E_o), flattened at C-3, and almost maintaining the mirror plane through both atoms as in **3** and **4**. The three compounds show the same overall degree of puckering, as measured by $(\tau_m^2 + q^2)^{1/2}$, but the dioxolane rings in **1** and **3** seem to cause more flattening of the pyranoid ring, as indicated by the higher values of q for these compounds. The 1,6-anhydro ring of **1** shows the same degree of puckering as those of **3** and **4**, and almost the same distorted envelope (at O-5) conformation. The conformation of the dioxolane ring of both **1** and **3** is an envelope at O-3.

The 90-MHz ^{1}H-n.m.r. spectrum of **2** has been analysed and the computed best values are given in Table V. Table VI shows the torsion angles for the vicinal protons of the pyranoid ring, calculated from the vicinal coupling constants by using some of the Karplus-type equations proposed for carbohydrates[2,23,24], the general equation of Altona[25], the equation of Forrest[26], and the additivity rule for pyranoid rings[27]. Inspection of molecular models indicates that the values of $\phi_{1,2}$, $\phi_{2,3}$, and $\phi_{4,5}$ could be used to distinguish between the $^1C_4$, $B_{o,3}$, and E_o conformations; $\phi_{3,4}$ has similar values for the $^1C_4$ and $B_{o,3}$ forms. Although the torsion angles determined from vicinal couplings are only approximate, all equations account for an average $^1C_4$ conformation in solution distorted towards an E_o conformation, as found for **1** in the crystalline state; on this basis, the previously reported[4] $B_{o,3}$ conformation of **2** can be discarded.

Because of errors in the determination of the H co-ordinates, due to crystal packing effects and hydrogen bonding, the vicinal-proton torsion angles determined from X-ray crystallographic data cannot be directly compared with the values obtained from n.m.r. studies. However, almost all angles calculated from vicinal couplings for **2** agree reasonably well with those determined by X-ray methods for **1**, the best agreement being found when an equation specifically parameterised for 1,6-anhydrohexoses[2] is used.

TABLE V

^{1}H-N M R. SPECTRAL PARAMETERS[a] FOR COMPOUND **2**

ν_1	483.00	$J_{1,2}$	1.2	$J_{3,4}$	7.0
ν_2	444.00	$J_{1,3}$	1.0	$J_{3,5}$	0.8
ν_3	376.48	$J_{1,4}$	−0.2	$J_{3,6endo}$	0.0
ν_4	403.00	$J_{1,5}$	0.4	$J_{3,6exo}$	−0.2
ν_5	411.12	$J_{1,6endo}$	−0.1	$J_{4,5}$	5.6
ν_{6endo}	378.00	$J_{1,6exo}$	−0.5	$J_{4,6endo}$	−0.4
ν_{6exo}	324.00	$J_{2,3}$	0.7	$J_{4,6exo}$	0.9
		$J_{2,4}$	0.6	$J_{5,6endo}$	0.8
		$J_{2,5}$	0.4	$J_{5,6exo}$	5.2
		$J_{2,6endo}$	−0.1	$J_{6endo,6exo}$	−7.5
		$J_{2,6exo}$	0.0		

[a]At 90 MHz; coupling constants in Hz.

TABLE VI

TORSION ANGLES (DEGREES) FOR VICINAL PROTONS FOR COMPOUND **2** FROM ^{1}H-N M R DATA

Equation (ref.)	*Angle*					
	$\phi_{1,2}$	$\phi_{2,3}$	$\phi_{3,4}$	$\phi_{4,5}$	$\phi_{5,6endo}$	$\nu_{5,6exo}$
2	74	98	34	43	97	46
23	64	108	22	34	109	36
24	74	94	29	39	98	45
25	83	91	22	48	93	43
26	67	104	28	55	118	39
27	65	105	43	59	—	—

EXPERIMENTAL

Materials. — Compounds **1** and **2** were prepared from1,6-anhydro-β-D-galactopyranose (**4**) as previously reported[28].

X-Ray. — Crystal and experimental data, and refinement parameters, are given in Table VII.

^{1}H-N.m.r. spectroscopy. — The spectrum of **2** was recorded for a solution in $CDCl_3$ with Me_4Si as internal standard, using a Varian EM-390 spectrometer in the frequency-sweep mode. A spectral width of 45 Hz was used for the measurements. Analysis was performed by an ASPECT 2.000 data system, using a PANIC program. The experimental and calculated spectra from the resulting best values matched satisfactorily.

Supplementary material. — Bond distances, bond angles, fractional co-ordinates, thermal parameters, and a list of observed and calculated structure factors are 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/275/*Carbohydr. Res.*, 127 (1984) 338–344.

TABLE VII

CRYSTAL ANALYSIS PARAMETERS AT ROOM TEMPERATURE

Crystal data	
Formula	$C_9H_{14}O_5$
Crystal habit	Prismatic
Size (mm)	0.31 × 0.08 × 0.11
Symmetry	Orthorhombic $P2_12_12_1$
Unit-cell dimensions (Å)	17.7022(4), 5.4882(1), 9.7295(5)
Packing: V(Å^3), Z, D (g.cm^{-3}), M, F000	945.25(3), 4, 1.422, 202.2, 432
Experimental data	
Radiation and technique	CuKα. Four-circle PW1100 Philips diffractometer
Monochromator	Graphite oriented
Collection mode ($\omega/2\theta$)	$\theta < 65°$
Total data recorded, independent data	1862, 966
Observed data: $I > 2\sigma(I)$	860
Stability	(Crystal inside capillary) Two reflections every 90 min; no variation.
Solution and refinement	X-Ray 70 system[29]. Univac 1100
Solution mode	Multan 80[30]
Refinement mode	Least-squares on F's. Observed reflections only. Full matrix.
Final maximum shift/error in final cycle	0.013
Parameters	C and O atoms refined anisotropically, and H atoms isotropically.
w-Scheme	Empirical, to give no trends in $\langle w\Delta^2 \rangle$ us. F_o or sin θ/x.
Maximum density in final ΔF insp.	0.15 e Å^{-3}
Max. thermal values	U_{11}(C8) = 0.099 Å^2
R, R_w	0.040, 0.039
Atomic scattering factors	International Tables for X-Ray Crystallography[31].

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