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X-RAY AND CONFORMATIONAL INVESTIGATIONS OF METHYL 2,6-DI-*O*-ACETYL-3,4-ANHYDRO-α-DL-(6,6-$^2H_2$)GALACTOPYRANOSIDE

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ABSTRACT

The crystals of methyl 2,6-di-*O*-acetyl-3,4-anhydro-α-DL-(6,6-$^2H_2$)galactopyranoside are triclinic, space group $P\bar{1}$ ($Z = 2$) with cell dimensions: $a = 7.346(1)$, $b = 8.122(1)$, $c = 10.860(1)$ Å; $\alpha = 100.39(1)$, $\beta = 94.97(1)$, $\gamma = 100.39(1)°$. The structure was solved by direct methods, and the atomic parameters were refined anisotropically against 2301 observed reflections by a full-matrix least-squares procedure giving $R = 0.050$. The 3,4-anhydropyranose ring has a half-chair (^1H_o) conformation.

INTRODUCTION

Half-chair conformations with the 5-substituent equatorial or pseudo-equatorial have been considered[1] for 2,3- and 3,4-anhydropyranoside derivatives. For α compounds, this preference is reinforced by the anomeric effect. Steric and polar interactions associated with either the ring oxygen or O-1 were shown by n.m.r. studies[2,3] to play a significant role in conformational equilibria. X-Ray studies[4–6] of four 2,3-anhydro-4-deoxyhexopyranosides also supported the predominant role of polar effects in the adoption of deformed sofa (*E*) conformations by the *ribo* compounds and deformed half-chair (^5H_o) conformations by the *lyxo* isomers.

On the basis of the $J_{1,2}$ values, Buchanan *et al.*[7] assigned half-chair (^1H_o) conformations to methyl 3,4-anhydro-α-D-altro- and -galacto-pyranoside in which O-2,3 are *trans*. However, the $J_{1,2}$ values for the *allo* and *talo* isomers (O-2,3 *cis*) are similar for both half-chair conformations. For these compounds, the $J_{4,5}$ values seemed to be more reliable for conformational elucidation and, on this basis, it was suggested[8] that the conformational equilibria were shifted towards the ^1H_o conformations.

In 3,4-anhydrohexopyranosides, the 5-substituent in pseudo-axial orientation does not interact markedly with an axial 1-substituent[2]. Therefore, polar 1,3-interactions involving O-3, the ring oxygen, or O-1 probably govern the conformational

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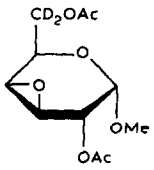

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equilibria of these epoxides. On the other hand, in 3,4-anhydropyranosides, the differences associated with pseudo-axial and pseudo-equatorial 5-substituents are equilibria of these epoxides. On the other hand, in 3,4-anhydropyranosides, the differences associated with pseudo-axial and pseudo-equatorial substituents are smaller than the equatorial–axial difference in 2,3-anhydropyranosides. This is reflected by the "abnormal" reactions of 3,4-epoxides with nucleophiles[2,9], which suggests a considerable conformational flexibility.

We have begun a study of the ground-state conformations of 3,4-anhydropyranosides by X-ray diffraction methods and now report on methyl 2,6-di-*O*-acetyl-3,4-anhydro-α-DL-(6,6-$^2H_2$)galactopyranoside (**1**).

EXPERIMENTAL

A well-shaped colourless crystal (0.13 × 0.21 × 0.50 mm) of **1** (m.p. 49–50°, rac-DL), formerly investigated[8] by ^{1}H-n.m.r. spectroscopy, was obtained from ethyl ether–acetone. The cell constants were obtained from a least-squares refinement on the setting angles of 25 reflections measured by a computer-controlled Enraf–Nonius CAD-4 diffractometer, using graphite-monochromated Cu$K\alpha$ (λ = 1.54184 Å) radiation. The data were collected with the $\omega/2\theta$ scan technique in the range $1.5 < \theta < 75°$.

Crystal data: $C_{11}H_{14}D_2O_7$, M_r = 262.43, $F(000)$ = 276, triclinic, space group $P\bar{1}$; a = 7.346(1), b = 8.122(1), c = 10.860(1) Å; α = 100.39(1), β = 94.97(1), γ = 100.39(1)°; V = 622.1(3) Å^3, Z = 2, D_x = 1.40 Mg.m^{-3}, μ(Cu$K\alpha$) = 9.6 cm^{-1}.

A total of 2760 reflections were collected, of which 2510 were unique; 2301 reflections were found to be of $I > 3\sigma_I$. Lorentz and polarisation corrections were applied to the data.

The phase problem was solved by direct methods using the MULTAN-80 program[10]. A total of 18 atoms were found in an E-map. During the isotropic refinement of non-hydrogen parameters, an empirical, spherical absorption correction (program DIFABS[11]) was applied. Relative transmission coefficients ranged from 0.749 to 1.297, with an average value of 1.002.

Hydrogen atoms bonded to carbon atoms were generated from assumed geometries, and their positions and isotropic thermal parameters were refined.

The refinement of atomic positional and anisotropic thermal parameters was performed for **1** by the full-matrix, least-squares procedure. Anomalous dispersion

TABLE I

FRACTIONAL COORDINATES ($\times 10^4$) AND EQUIVALENT ISOTROPIC TEMPERATURE FACTORS ($Å^2$)[a,b] FOR NON-HYDROGEN ATOMS OF **1**

	x/a	*y/b*	*z/c*	B_{eq}
C-1	10969(3)	2480(2)	7708(2)	3.22(4)
C-2	12160(3)	1377(3)	8251(2)	3.35(4)
C-3	10984(3)	−239(3)	8465(2)	3.54(4)
C-4	9093(3)	−823(3)	7813(2)	3.46(4)
C-5	8329(2)	199(2)	6945(2)	3.08(4)
C-6	7441(3)	−870(3)	5695(2)	3.57(4)
C-7	4628(3)	−2857(2)	4919(2)	3.45(4)
C-8	2845(3)	−3771(3)	5248(2)	4.59(5)
C-9	9009(3)	4436(3)	8304(2)	4.27(5)
C-10	14900(3)	2108(3)	9743(2)	3.51(4)
C-11	15756(4)	3175(3)	10972(3)	5.42(6)
O-1	10009(2)	3184(1)	8653(1)	3.23(3)
O-2	13163(2)	2365(2)	9424(1)	4.01(3)
O-3	10588(2)	−1633(2)	7393(1)	4.31(3)
O-5	9768(2)	1464(1)	6645(1)	3.29(3)
O-6	5715(2)	−1885(2)	5923(1)	4.10(3)
O-7	5061(2)	−2951(2)	3870(1)	5.91(4)
O-10	15600(2)	1110(2)	9085(1)	4.76(4)

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

effects were included[12] in F_c. Only the reflections with $I > 3\sigma_I$ regarded as observed were used in the refinement processes. The final reliability factors were $R = 0.050$, $R_w = 0.050$ ($w = 4F_0^2/\sigma_{F_0}^2$). The highest peak in the final difference map was 0.24(4) e/Å^3.

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

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

RESULTS AND DISCUSSION

The bonding interatomic distances, valence angles, and selected torsion angles for **1** are given in Tables II–IV, respectively. Figure 1 presents a clinographic projection of a molecule of **1**.

As in derivatives of 2,3-anhydropyranoses investigated earlier[4–6], a shortening of the C-3–C-4 bond, common to both oxirane and pyranose rings, is observed (Table II). The pyranose endocyclic valence angles at C-3 and C-4 (Table

*A list of structure factors has 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/370 *Carbohydr. Res.*, 166 (1987) 13–18.

TABLE II

BONDING DISTANCES (Å) FOR NON-HYDROGEN ATOMS OF **1**

O-5–C-1	1.418(2)	C-10–O-10	1.199(3)
C-1–C-2	1.516(3)	C-10–C-11	1.473(4)
C-2–C-3	1.503(3)	C-3–O-3	1.438(3)
C-3–C-4	1.459(3)	O-3–C-4	1.444(2)
C-4–C-5	1.500(3)	C-5–C-6	1.496(3)
C-5–O-5	1.438(2)	C-6–O-6	1.449(2)
C-1–O-1	1.391(2)	O-6–C-7	1.327(3)
O-1–C-9	1.441(2)	C-7–O-7	1.202(3)
C-2–O-2	1.437(3)	C-7–C-8	1.490(3)
O-2–C-10	1.356(2)		

TABLE III

VALENCE ANGLES (DEGREES) INVOLVING NON-HYDROGEN ATOMS OF **1**

O-5–C-1–C-2	108.8(3)	O-10–C-10–C-11	125.9(4)
C-1–C-2–C-3	111.3(3)	C-2–C-3–O-3	115.0(3)
C-2–C-3–C-4	119.6(3)	C-3–C-4–O-3	59.4(2)
C-3–C-4–C-5	119.9(3)	C-3–O-3–C-4	60.8(2)
C-4–C-5–O-5	111.9(3)	C-4–C-3–O-3	59.8(2)
C-5–O-5–C-1	114.3(2)	O-3–C-4–C-5	115.7(3)
C-2–C-1–O-1	108.4(3)	C-4–C-5–C-6	112.8(3)
O-5–C-1–O-1	112.9(3)	O-5–C-5–C-6	104.8(3)
C-1–O-1–C-9	113.8(3)	C-5–C-6–O-6	106.5(3)
C-1–C-2–O-2	107.5(3)	C-6–O-6–C-7	116.7(3)
C-3–C-2–O-2	110.2(3)	O-6–C-7–O-7	122.5(3)
C-2–O-2–C-10	117.3(3)	O-6–C-7–C-8	112.4(3)
O-2–C-10–O-10	122.4(3)	O-7–C-7–C-8	125.1(3)
O-2–C-10–C-11	111.7(3)		

TABLE IV

SOME TORSIONAL ANGLES (DEGREES)

C-1–C-2–C-3–C-4	19.0(3)
C-2–C-3–C-4–C-5	−0.6(3)
C-3–C-4–C-5–O-5	13.6(3)
C-4–C-5–O-5–C-1	−49.1(3)
C-5–O-5–C-1–C-2	69.5(3)
O-5–C-1–C-2–C-3	−51.1(3)
C-2–C-1–O-1–C-9	−67.0(3)
O-5–C-1–O-1–C-9	172.4(3)
O-1–C-1–C-2–O-2	−48.7(2)
O-2–C-2–C-3–O-3	−153.8(3)
C-1–C-2–C-3–O-3	87.1(3)
C-1–C-2–O-2–C-10	−146.3(3)
C-2–O-2–C-10–C-11	−179.0(4)
C-4–C-5–C-6–O-6	71.6(3)
O-5–C-5–C-6–O-6	−166.4(3)
C-5–C-6–O-6–C-7	175.7(3)
C-6–O-6–C-7–C-8	−176.8(4)
C-6–O-6–C-7–O-7	2.4(3)

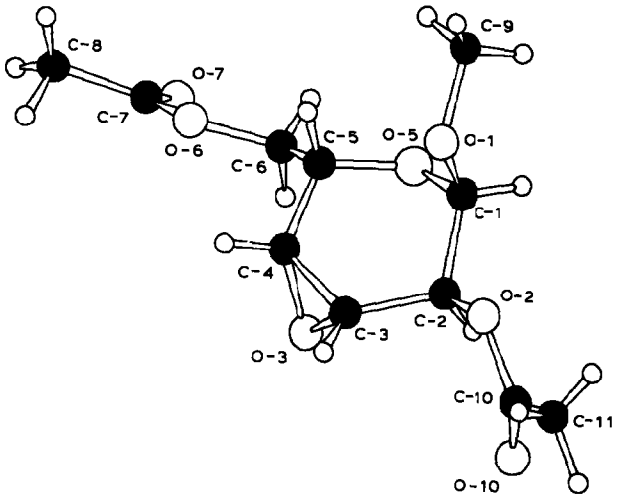

Fig. 1. Calculated projection of a molecule of **1** with the crystallographic labelling of the atoms; orientation at optimal viewing.

III) have values close to 120°, thus making this bond similar to a double bond.

The conformational analysis of the 3,4-anhydropyranose ring, based on calculations of asymmetry[13] and puckering[14] parameters, indicated a ^1H_o conformation close to the ideal. The main puckering parameters are: $\phi = 336.9(4)°$ and $q_2 = 0.386(2)$ Å. The deviations of these parameters from those for a $^1H_6$ cyclohexene conformation[15] are as small as 7° and 0.04 Å, respectively. The asymmetry parameters $\Delta C_2^{3-4} = 4.1(3)°$ indicate a small deviation of the pyranose ring from a two-fold axis symmetry. The above deviations may be fully explained in terms of the deformational influence of the heteroatom O-5 in the pyranose ring.

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