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Crystal and molecular structure of methyl 3,4-anhydro-*α*-DL-allopyranoside: ring conformations in the 3,4-anhydropyranose system

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ABSTRACT

X-Ray diffractometry of methyl 3,4-anhydro-*α*-DL-allopyranoside (**3**) revealed the crystals to be monoclinic, space group *Cc*, with cell dimensions $a = 6.242(1)$, $b = 16.987(2)$, $c = 7.739(1)$ Å; $\beta = 106.09(1)°$, $Z = 4$. The 3,4-anhydropyranose ring adopts a hybrid $^{1}E + {}^{1}H_{0}$ conformation. Relatively strong intermolecular hydrogen bonds were observed.

INTRODUCTION

Epoxides of carbohydrates are key intermediates in many syntheses. Stereo- and regio-selective opening of the oxirane ring with nucleophiles can be affected variously by the anomeric effect, neighbouring-group participation, or 1,3-diaxial interaction with the incoming nucleophile in the transition state[1]. Thus, conformational factors play an important role in the reactions of sugar epoxides[2].

Studies of the ground-state conformation by n.m.r. spectroscopy led to the general view that 2,3- and 3,4-anhydro sugars exist in half-chair conformations[3]. In contrast, a transitional "skew-boat like" conformation was invoked[2] to explain "anomalous" *trans*-diequatorial ring opening of some 3,4-anhydro sugars.

Our studies[4] of the ring opening of the title epoxide **3** confirmed the exclusive attack of the nucleophile at C-4, leading to the *gulo* product. This result was explained in terms of conformational control involving the most favourable arrangement of a pseudo-axial MeO-1 and a pseudo-equatorial 5-substituent as well as interactions with the incoming nucleophile in the $^{o}H_{1}$ conformation **1** (only one 1,3-diaxial interaction); the alternative $^{1}H_{0}$ conformation **2**, which could yield the *gluco* product, would be destabilized by two 1,3-diaxial interactions involving the pseudo-equatorial MeO-1 and pseudo-axial 5-substituent.

In order to elucidate unambiguously the ground-state conformation of **3**, an X-ray investigation was undertaken. On the basis of similar investigations of the isomeric 2,3-anhydro-4-deoxy-pyranosides, a half-chair form was assigned to the *α-lyxo* epoxide[5] and a slightly distorted sofa conformation to the *α-ribo* isomer[5]. The latter conformation was also assigned to the *talo* isomer **5** of the 3,4-anhydropyranoside[6],

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suggesting considerable steric and electrostatic contribution of the axial HO-2 to the conformational equilibria.

We now report that the distance between oxirane oxygen and other oxygens on the pyranoid ring provide additional criteria of conformational equilibria.

EXPERIMENTAL

A well-shaped colourless crystal (0.20 × 0.15 × 0.45 mm) of **3** (DL-form, m.p. 103–104°), obtained from ethyl ether–acetone, was used with an Enraf–Nonius CAD-4 diffractometer and graphite-monochromated Cu-K_a radiation (λ = 1.54178 Å). The monoclinic cell constants (for a *C*-centered cell) were refined using setting angles of 20 reflections. The data were collected with the $\theta/2\theta$ scan technique in the range $1.5 < \theta < 70°$. A total of 943 reflections was collected, of which 888 unique reflections were of $I > 2\sigma(I)$. Lorentz and polarisation corrections, but no absorption correction, were applied to all reflections.

The analysis of absences in the reflection set indicated space groups either *Cm* or *C2* and, less probably, space group *Cc*. Nevertheless, attempts at direct-method solutions (program SHELXS[7]) gave a satisfactory result only for the *Cc* space group. The assumption of this space group resulted in the removal of 8 relatively weak reflections. All non-hydrogen atoms were found from the *E*-map.

Crystal data: $C_7H_{12}O_5$, M_r = 176.17, $F(000)$ = 376, monoclinic, space group *Cc* (No. 9); a = 6.242(1), b = 16.987(2), c = 7.739(1) Å; β = 106.09(1)°; V = 788.4(3) Å^3, Z = 4, D_x = 1.48 Mg.m^{-3}, μ (Cu-K_a) = 10.5 cm^{-1}.

The refinement of isotropic and then anisotropic atomic parameters was performed in the *Cc* space group against 880 observed reflections, by a full-matrix, least-squares procedure (program SHELX76[8]). An almost "flat" variance analysis of the reflections indicated the unit weights to be used at the refinement. All hydrogen coordinates were then found from difference Fourier maps and added to the set of atomic parameters with isotropic temperature factors equal to B_{eq} of the adjacent atom + 1 Å^2. The final refinement step involved all atomic parameters and resulted in R = 0.0287 at shift/error values of <0.1. A check of the final Fourier difference map revealed no residual electron density peaks >0.13 e/Å^3.

An IBM-PC/AT microcomputer monitored by the DOS 3.10 System was used for all calculations.

The refined positional parameters* for non-hydrogen atoms of **3**, associated by their B_{eq} values are given in Table I.

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* Lists of structure factors, hydrogen coordinates, 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/437/*Carbohydr. Res.*, 203 (1990) 195–203.

TABLE I

Fractional coordinates (× 10^4)[a] and equivalent, isotropic temperature factors ($Å^2$)[b] for 3

Atom	x/a	y/b	z/c	B_{eq}
C-1	−461(6)	8288(2)	2147(5)	2.09(8)
C-2	1953(6)	8012(2)	2543(4)	2.10(8)
C-3	3594(6)	8557(2)	3745(5)	2.32(8)
C-4	2811(6)	9082(2)	4933(5)	2.47(8)
C-5	358(7)	9103(2)	4865(5)	2.36(9)
C-6	66(7)	8994(2)	6735(5)	2.69(11)
C-7	−3183(7)	9112(3)	310(6)	3.15(10)
O-1	−855(5)	8918(1)	922(4)	2.32(6)
O-2	2477(5)	7875(1)	886(4)	2.71(6)
O-3	3371(5)	9388(1)	3356(4)	2.69(8)
O-5	−917[c]	8480(1)	3795[c]	2.28(7)
O-6	836(6)	8226(2)	7332(4)	2.96(7)
H(O-2)[d]	348(6)	751(2)	108(5)	4(1)
H(O-6)[d]	120(9)	815(4)	819(7)	9(2)

[a] In this and subsequent Tables, figures in parentheses are estimated standard deviations. [b] Calculated from anisotropic thermal parameters as $B_{eq} = 8\pi^2 . D_u^{1/3}$, where D_u is the determinant of the U_{ij} matrix in orthogonal space. [c] Fixed coordinate. [d] Coordinates (× 10^3) refined in isotropic mode.

RESULTS AND DISCUSSION

Fig. 1 presents the stereo-view of 3 with the crystallographic numbering of the atoms, and Tables II and III contain the calculated bond lengths and valence angles, respectively.

The bond lengths and valence angles of the 3,4-anhydropyranose ring in 3 do not deviate significantly from those of other 2,3-[5,9] and 3,4-anhydropyranoses 4 and 5 (refs. 6,10) (Fig. 2) as well as of 3,4-epoxypyrans[14]. The shortening of the C-3–C-4 bond and the valence angles at these atoms, characteristic for the epoxide group, may be seen clearly.

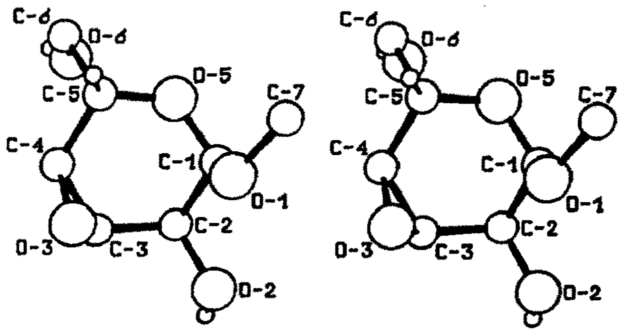

Fig. 1. A stereo-view of 3 with the crystallographic numbering. For clarity, the only hydrogen atoms shown are H-5 and those of hydroxyl groups. The orientation is at optimal viewing.

TABLE II

Bond distances (Å) for **3**

Bond	*Distance*	*Bond*	*Distance*
C-2–C-1	1.526(5)	C-5–C-4	1.517(6)
O-1–C-1	1.405(4)	O-3–C-4	1.455(5)
O-5–C-1	1.420(4)	C-6–C-5	1.519(6)
C-3–C-2	1.498(5)	O-5–C-5	1.440(4)
O-2–C-2	1.428(5)	O-6–C-6	1.422(5)
C-4–C-3	1.459(6)	O-1–C-7	1.436(5)
O-3–C-3	1.442(4)		

TABLE III

Bond angles (°) for **3**

Bonds	*Angle*	*Bonds*	*Angle*
C-1–C-2–C-3	113.7(3)	C-3–C-4–C-5	120.2(3)
C-1–C-2–O-2	109.2(3)	C-3–C-4–O-3	59.3(2)
C-2–C-1–O-1	110.4(3)	C-4–C-3–O-3	60.2(2)
C-2–C-1–O-5	108.8(2)	C-3–O-3–C-4	60.5(2)
C-1–O-1–C-7	111.7(3)	C-4–C-5–C-6	110.5(3)
O-1–C-1–O-5	112.9(3)	C-4–C-5–O-5	113.2(3)
C-1–O-5–C-5	118.0(2)	C-5–C-4–O-3	115.9(3)
C-2–C-3–C-4	118.6(3)	C-5–C-6–O-6	107.6(3)
C-2–C-3–O-3	117.7(3)	C-6–C-5–O-5	105.3(3)
C-3–C-2–O-2	111.8(3)		

Conformations of 3,4-anhydropyranose rings. — Conformational analysis of the 3,4-anhydropyranose ring in **3**, based on calculations of puckering[11] and asymmetry[12] parameters (see Table IV), and torsion angles (Table V), suggests a hybrid $^1E + {}^1H_0$ conformation*, which differs from that found in **4** where an almost "pure" half-chair ($^1H_0$) form was observed (see Table IV). Thus, of the three 3,4-anhydropyranoses discussed, only **4** corresponds with the rule which postulates that the influence of an epoxide ring is similar to that of a double bond in forcing the pyranose ring to adopt a half-chair conformation.

These differences in conformations of **3**–**5** supplement and, in some instances, modify the earlier assumption of electrostatic interactions of the oxygen atoms of 3,4-anhydropyranosides[13] as well as the model compound 3,4-epoxytetrahydropyran[14]. According to earlier suggestions, polar interactions of the epoxide oxygen and either O-1 or O-5 cause the greatest destabilization of the $^1H_0$ conformation, the influence of the pseudo-axial hydroxy group being less pronounced. However, despite the repulsions

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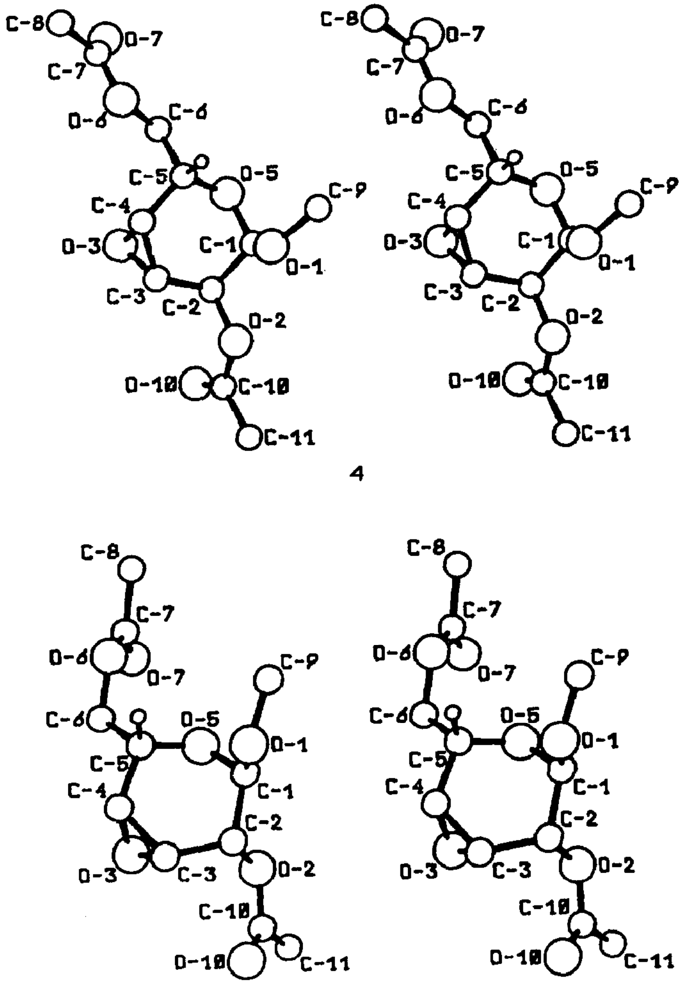
* Although all epoxides discussed represent the racemic forms, only the L forms are depicted.



4

5

Fig. 2. Stereo-views of **4** and **5**. The chosen L enantiomorph conforms to that of **3**.

between the oxirane oxygen and O-5 in **5**, the compound exists in an almost perfect $^1H_0$ form. Analogous polar interactions are present in the *talo* isomer **5**, but the additional effect of the vicinal pseudo-axial 2-substituent causes appreciable departure from the $^1H_0$ towards the ^1E conformation.

A similar effect of vicinal substituents on conformational equilibria was observed[15,16] for the 2,3-anhydropyranosides. This effect was shown by enhancement of the $^1J_{C,H}$ values in epoxides in which axial H-4 is *cis* to the oxirane rings (*manno* series) compared to those (*allo* series) in which it is *trans*. Such an effect of the oxirane oxygen was claimed[15] to be due to the close proximity of the lone-pairs of the epoxide oxygen to the axial protons, thus facilitating delocalisation into the C–H bonds. It is possible that the effect of an oxirane function on the vicinal substituents outweighs the effect on O-5 which is reflected in the adoption of an almost ideal $^1H_0$ conformation by **4** and a hybrid $^1H_0 + E_0$ by **5**.

TABLE IV

Conformational parameters of 3,4-anhydropyranose rings for **3**–**5**

	3	**4**	**5**
Puckering parameters			
Q (Å)	0.450	0.501	0.461
Φ (°)	346.7	336.8	316.9
Θ (°)	48.7	50.4	50.7
q_2 (Å)	0.338	0.386	0.357
Endocyclic torsion angles (degrees)			
C-1–C-2	−50.0	−51.0	−39.0
C-2–C-3	23.3	19.0	9.0
C-3–C-4	−3.4	−0.6	−0.9
C-4–C-5	10.1	13.6	21.9
C-5–O-5	−41.2	−49.1	−54.2
O-5–C-1	61.5	69.5	64.2
Deviations from least-squares planes (Å)			
	5-atom	*4-atom*	*5-atom*
O-5	—	−0.304	−0.602
C-1	0.644	0.449	—
O-1	−2.035	1.819	1.428
O-2	0.760	0.902	−1.361
O-3	1.140	−1.208	−1.147
Asymmetry parameters (degrees)			
ΔC_2	11.2	4.1	14.0
ΔC_s	12.9	—	12.4
Conformation	$^1E + {}^1H_o$	^1H_o	$E_o + {}^1H_o$

TABLE V

Torsional angles (°) for **3**

Bonds	*Angle*	*Bonds*	*Angle*
C-3–C-2–C-1–O-1	74.5(4)	O-3–C-4–C-3–C-2	−107.4(3)
O-2–C-2–C-1–O-1	−51.1(3)	C-5–C-4–C-3–O-3	104.0(3)
C-3–C-2–C-1–O-5	−50.0(4)	C-4–O-3–C-3–C-2	108.8(4)
O-2–C-2–C-1–O-5	−175.6(2)	C-6–C-5–C-4–C-3	128.1(3)
C-7–O-1–C-1–C-2	171.1(3)	O-5–C-5–C-4–C-3	10.1(5)
C-7–O-1–C-1–O-5	−66.8(4)	C-6–C-5–C-4–O-3	−163.9(3)
C-5–O-5–C-1–C-2	61.5(3)	O-5–C-5–C-4–O-3	78.2(3)
C-5–O-5–C-1–O-1	−61.4(3)	C-3–O-3–C-4–C-5	−111.3(3)
C-4–C-3–C-2–C-1	23.3(5)	O-6–C-6–C-5–C-4	−64.4(4)
O-3–C-3–C-2–C-1	−46.0(5)	O-6–C-6–C-5–O-5	58.2(4)
C-4–C-3–C-2–O-2	147.6(3)	C-1–O-5–C-5–C-4	−41.2(4)
O-3–C-3–C-2–O-2	78.2(4)	C-1–O-5–C-5–C-6	−162.1(3)
C-5–C-4–C-3–C-2	−3.4(5)		

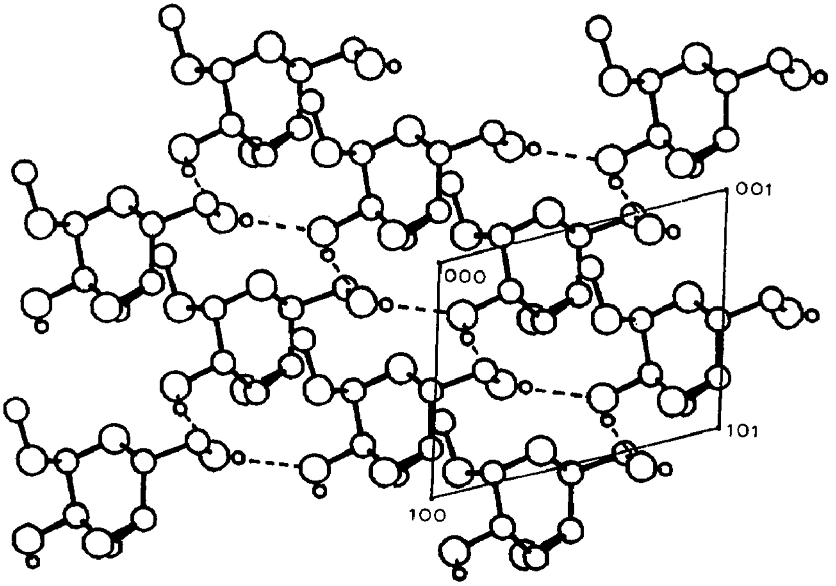
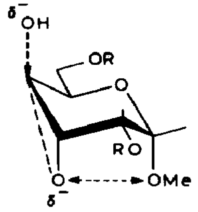


Fig. 3. A projection of the crystal structure of 3 down the *b*-axis. The original cell edges are drawn by light lines. Potential hydrogen bonds are shown as dashed lines. For clarity, only bridging hydrogen atoms are shown.



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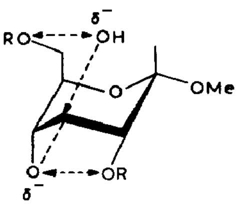

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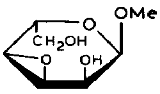

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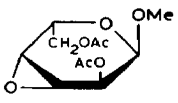

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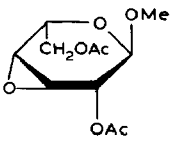

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TABLE VI

Selected non-bonding distances (Å) between oxygen atoms in 3–5

Molecule	*O-1–O-2*	*O-2–O-3*	*O-2–O-5*	*O-3–O-5*
3	2.90	3.16	3.64	3.19
4	4.02	3.67	3.62	2.92
5	4.08	2.82	3.02	2.86

The deviation of the ${}^{1}H_{0}$ conformation in the *allo* epoxide **3**, which leads to a hybrid with a significant contribution of conformer ${}^{1}E$, agrees well with the previously established unfavourable effect of the 1,3-interaction of O-1 and O-3. These interactions could contribute internal energy sufficient to create the five-atom planes in the pyranose rings, characteristic of sofa (E) conformations which have internal energy higher than that of a half-chair form. In the *a-galacto* isomer[10] **4**, the above interactions are much weaker than in **3** or **5**; thus, the pyranose ring adopts the energetically lower H conformation.

The above stereoelectronic factors, which reflect the conformational lability of the epoxides **3**–**5**, are supported further by the distances between the interacting oxygen atoms (see Table VI); they are greater in **4** than in **3** and **5**. Similar conformational effects were observed in some 2,3-anhydropyranoses[5,9].

Intermolecular hydrogen bonding. — Two relatively strong intermolecular hydrogen bonds are found in the crystal lattice of **3** [hydrogen bond, (symmetry of acceptor), donor···acceptor distance, hydrogen···acceptor distance, angle at H]: O-2–H(O-2)···O-6, $(-1/2 + x, 3/2 - y, -1/2 + z)$, 2.801 Å, 1.96 Å, 161°; O-6–H(O-6)···O-2, $(x, y, -1 + z)$, 2.722 Å, 2.07 Å, 177°. The hydrogen bonds link the molecules in the crystal to form the planes parallel to the *ac*-plane and separated by the $1/2\,b$ distance. Fig. 3 shows a projection of the crystal structure on to the *ac*-plane.

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