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THE X-RAY CRYSTAL STRUCTURE OF 2,3:4,5-DI-*O*-ISOPROPYLIDENE-1-*O*-METHYL-β-D-FRUCTOPYRANOSE

S. F. WATKINS, S. J. KIM, F. R. FRONCZEK, R. J. VOLL, AND E. S. YOUNATHAN
Departments of Chemistry and Biochemistry, Louisiana State University, Baton Rouge, Louisiana 70803 (U.S.A.)

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ABSTRACT

2,3:4,5-Di-*O*-isopropylidene-1-*O*-methyl-β-D-fructopyranose, $C_{13}H_{22}O_6$, M_r = 274.3, orthorhombic, $P2_12_12_1$, a = 12.388 (2), b = 13.307 (5), c = 8.660 (1) Å, V = 1427.4 (9) Å^3, Z = 4, D_m = 1.24 g.cm^{-3}, D_x = 1.276 g.cm^{-3}, CuK_α, λ = 1.54184 Å, μ = 8.0 cm^{-1}, $F(000)$ = 592, T = 295 (1) K, R = 0.032 for 1586 observations (of 1693 unique data). The molecule is a derivative of the naturally occurring carbohydrate D-fructose. The data reported here indicate that the ketose six-membered ring is constrained by the presence of two fused five-membered rings into the ^3S_O conformation. These findings agree with the n.m.r.-spectroscopic results for 2,3:4,5-di-*O*-benzylidene-β-D-fructopyranose. As a result of crystal packing forces, the exocyclic side-chain has a C–C–O–C torsion angle of −102°, quite different from the expected value of 180°.

INTRODUCTION

Emil Fischer reported the reaction of D-fructose with acetone under acid conditions[1]. He was able to isolate two crystalline compounds which have proved to be isomeric, namely, 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**2**) and 2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**3**). This reaction has more recently been reinvestigated, and conditions for the preparation of each pure isomer have been reported[2]. These compounds are useful in the synthesis of physiologically important derivatives of D-fructose[3] and as chiral intermediates in organic chemistry. The crystal structure of the first of these compounds (**2**) has been reported[4] and the crystal structure of the second (**3**) was reported[5] while this work was in progress. During this same time period, we obtained a more precise refinement of the structure of **3**, results of which are included in the discussion. Crystal data and coordinates for **3** are included in the supplementary data*.

The title compound, 2,3:4,5-di-*O*-isopropylidene-1-*O*-methyl-β-D-fructopyranose (**1**), was studied as a simple derivative (of the second isomer) that cannot form hydrogen bonds due to the conversion of the primary hydroxyl group into a methyl ether. We had studied[6] a compound with the same arrangement of rings,

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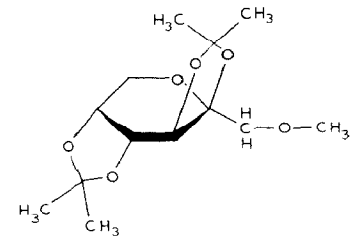

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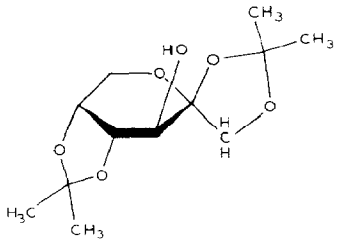

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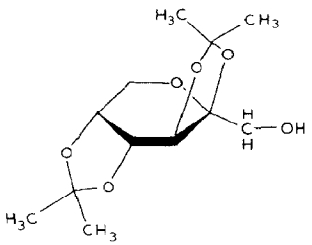

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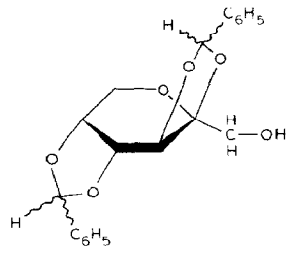

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namely, 2,3:4,5-di-*O*-benzylidene-β-D-fructopyranose (**4**), by n.m.r. spectroscopy and shown that it exists in a skew conformation in solution[6]. This paper is one in a series from our group studying the structure of compounds having interesting biological properties[7–9].

EXPERIMENTAL

2,3:4,5-Di-*O*-isopropylidene-1-*O*-methyl-β-D-fructopyranose (**1**) was prepared from D-fructose[2,10]. The compound crystallized from methanol, m.p. 48–49°, density 1.24 g.cm^{-3} by flotation in aqueous KBr solution. A clear, rectangular prism was sealed in a capillary on an Enraf-Nonius CAD-4 diffractometer with graphite monochromator; cell dimensions were obtained from setting angles of 25 reflections having $25° < \theta < 28°$. The unit-cell constants are shown in Table I. Data collection was by $\omega - 2\theta$ scans; reflections having $2 < \theta < 75°$, $h = 0$–15, $k = 0$–16, and $l = 0$–10 were measured, and corrected for background, Lorentz, and polarization effects. A linear decay correction of 2.6% was applied, using standard reflections 600, 040, 004. The space group was determined from systematic absences.

The structure was solved by using direct methods, and refined by full-matrix least squares based on F with weights $w = [\sigma^2(F) + 0.02\,F^2]^{-1}$. The atomic scattering factors were taken from the International Tables[11]. Non-hydrogen atoms were refined anisotropically, and H-atom positions were calculated and then refined isotropically. The largest Δ/σ was 0.10 on the final cycle, and the maximum residual electron density was 0.14 e/Å^3, extinction coefficient 9.9(2) × 10^{-6}. The programs

TABLE I

CRYSTAL DATA FOR 2,3:4,5-DI-*O*-ISOPROPYLIDENE-1-*O*-METHYL-β-D-FRUCTOPYRANOSE

Formula	$C_{13}H_{22}O_6$
Formula weight	274.3
Cell constants	
a (Å)	12.388 (2)
b (Å)	13.307 (5)
c (Å)	8.660 (1)
Volume (Å)^3	1427.4 (9)
Z (molecules/cell)	4
Density measured (g/cm^3)	1.24
Density calculated (g/cm^3)	1.276
Space group	$P2_12_12_1$
Crystal size (mm)	0.40 × 0.40 × 0.60
λ (CuKα) (Å)	1.54184
Minimum transmission	0.94
Reflections measured	1693
$I > 3\sigma(I)$	1586
R	0.032
R_w	0.043
S (261 variables)	2.84

TABLE II

ATOMIC COORDINATES AND EQUIVALENT ISOTROPIC THERMAL PARAMETERS FOR 2,3:4,5-DI-*O*-ISOPROPYLIDENE-1-*O*-METHYL-β-D-FRUCTOPYRANOSE

Atom	x	y	z	B(Å^2)[a]
O-1	1.0218(1)	−0.0432(1)	0.4088(2)	5.06(3)
O-2	0.83093(9)	0.05407(9)	0.5347(1)	3.68(2)
O-3	0.90815(9)	0.20625(9)	0.5795(1)	3.73(2)
O-4	1.13332(9)	0.0998(1)	0.7853(1)	3.87(2)
O-5	1.0411(1)	0.0870(1)	1.0091(2)	5.21(3)
O-6	0.8954(1)	0.00436(9)	0.7739(1)	3.92(2)
C-1	0.98841(2)	−0.0571(2)	0.5617(2)	4.35(4)
C-2	0.9247(1)	0.0337(1)	0.6233(2)	3.27(3)
C-3	0.9876(1)	0.1325(1)	0.6159(2)	3.18(3)
C-4	1.0420(1)	0.1630(1)	0.7654(2)	3.30(3)
C-5	0.9732(1)	0.1447(1)	0.9105(2)	3.61(3)
C-6	0.8719(1)	0.0856(1)	0.8760(2)	3.84(3)
C-7	0.9579(2)	−0.0909(2)	0.2940(3)	5.74(5)
C-8	0.8295(1)	0.1572(1)	0.4851(2)	3.75(3)
C-9	0.8595(2)	0.1631(2)	0.3154(2)	5.22(4)
C-10	0.7202(2)	0.2021(2)	0.5168(3)	4.94(4)
C-11	1.1471(1)	0.0829(2)	0.9467(2)	3.94(3)
C-12	1.1927(2)	−0.0213(2)	0.9686(3)	5.85(5)
C-13	1.2177(2)	0.1633(2)	1.0163(3)	5.35(5)

[a]The equivalent isotropic thermal parameter, for atoms refined anisotropically, is defined by the expression $^4/_3[a^2\beta_{11} + b^2\beta_{22} + c^2\beta_{33} + ab\beta_{12}\cos\gamma + ac\beta_{13}\cos\beta + bc\beta_{23}\cos\alpha]$.

used were MULTAN-80[12], SDP/VAX[13], SHELX76[14], and ORTEP[15]. Atomic coordinates and equivalent isotropic thermal parameters are given in Table II*.

DISCUSSION

The molecular structure and atomic numbering of 2,3:4,5-di-*O*-isopropylidene-1-*O*-methyl-β-D-fructopyranose (**1**) are illustrated in Fig. 1. The D form of this compound was assumed, based on the configuration of the starting material. The crystal structure determination confirmed that the molecule has the *arabino* configuration and that the anomeric carbon atom has the β configuration. It should be noted that this anomeric configuration is dictated by the orientation of O-3 and by the presence of the five-membered ring defined by C-2–C-3–O-3–C-8–O-2 in the thermodynamically more stable *cis*-fusion to the six-membered ring defined by C-2–C-3–C-4–C-5–C-6–O-6. Bond lengths are given in Table III and bond angles are listed in Table IV. Selected torsion angles are listed in Table V.

Compound **1** should have a six-membered ring conformation similar to that of its unmethylated parent compound **3**. This is in view of the fact that the predominant force determining the conformation of the central ring is the two fused side-rings and not the functionality on the exocyclic group. In contrast, **1** should be different from compound **2** which has the anomeric ring *spiro, i.e.*, not fused to the central ring.

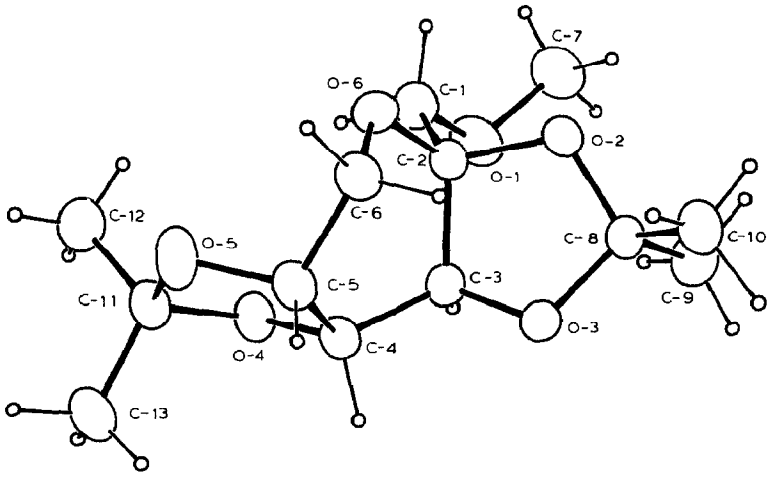

Fig. 1. Molecular structure and atomic numbering of 2,3:4,5-di-*O*-isopropylidene-1-*O*-methyl-β-D-fructopyranose (**1**).

*Lists of observed and calculated structure-amplitudes, anisotropic thermal parameters, hydrogen coordinates, and isotropic thermal parameters for **1**, as well as the crystal data, and atomic coordinates and equivalent isotropic thermal parameters for **3**, 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/422/*Carbohydr. Res.*, 197 (1990) 33–40.

TABLE III

BOND LENGTHS FOR 2,3:4,5-DI-*O*-ISOPROPYLIDENE-1-*O*-METHYL-β-D-FRUCTOPYRANOSE

Atom 1	*Atom 2*	*Distance (Å)*	*Atom 1*	*Atom 2*	*Distance (Å)*
O-1	C-1	1.416(2)	O-6	C-6	1.426(2)
O-1	C-7	1.421(2)	C-1	C-2	1.512(2)
O-2	C-2	1.418(1)	C-2	C-3	1.530(2)
O-2	C-8	1.438(1)	C-3	C-4	1.515(2)
O-3	C-3	1.425(1)	C-4	C-5	1.537(2)
O-3	C-8	1.429(1)	C-5	C-6	1.511(2)
O-4	C-4	1.420(1)	C-8	C-9	1.517(2)
O-4	C-11	1.426(1)	C-8	C-10	1.505(2)
O-5	C-5	1.423(2)	C-11	C-12	1.509(2)
O-5	C-11	1.422(2)	C-11	C-13	1.508(2)
O-6	C-2	1.409(1)			

TABLE IV

BOND ANGLES FOR 2,3:4,5-DI-*O*-ISOPROPYLIDENE-1-*O*-METHYL-β-D-FRUCTOPYRANOSE

Atom 1	*Atom 2*	*Atom 3*	*Angle (°)*	*Atom 1*	*Atom 2*	*Atom 3*	*Angle (°)*
C-1	O-1	C-7	114.4(1)	O-3	C-3	C-4	108.17(9)
C-2	O-2	C-8	110.73(8)	C-2	C-3	C-4	114.88(9)
C-3	O-3	C-8	106.45(9)	O-4	C-4	C-3	107.39(9)
C-4	O-4	C-11	107.91(9)	O-4	C-4	C-5	104.38(9)
C-5	O-5	C-11	109.8(1)	C-3	C-4	C-5	114.17(9)
C-2	O-6	C-6	114.61(9)	O-5	C-5	C-4	104.40(9)
O-1	C-1	C-2	112.7(1)	O-5	C-5	C-6	109.2(1)
O-2	C-2	O-6	110.01(9)	C-4	C-5	C-6	112.4(1)
O-2	C-2	C-1	111.1(1)	O-6	C-6	C-5	110.37(9)
O-2	C-2	C-3	103.31(8)	O-2	C-8	O-3	104.85(9)
O-6	C-2	C-1	103.4(1)	O-2	C-8	C-9	109.6(1)
O-6	C-2	C-3	114.11(9)	O-2	C-8	C-10	109.6(1)
C-1	C-2	C-3	115.1(1)	O-3	C-8	C-9	111.3(1)
O-3	C-3	C-2	104.42(8)	O-3	C-8	C-10	109.1(1)
C-9	C-8	C-10	112.1(1)	O-5	C-11	C-12	109.5(1)
O-4	C-11	O-5	104.8(1)	O-5	C-11	C-13	110.9(1)
O-4	C-11	C-12	108.3(1)	C-12	C-11	C-13	112.6(1)
O-4	C-11	C-13	110.5(1)				

Because the solution structure of a similar compound (**4**) has been reported[6], those results will be utilized for comparison. In **4**, the ring conformation is indicated by the magnitude of the proton–proton coupling-constants. These values indicate a torsion angle between H-3 and H-4 of ~60° and between H-4 and H-5 of <20°. These values fit the skew conformation ^3S_O (which is equivalent to the S_4^6 conformation discussed in reference). Compound **3** was reported[5] to exist in two crystallographically independent molecules (A and B), and this was confirmed in our study. Our torsion-angle values for crystalline **3** are 69° and 10° (for molecule A), and 65° and 16° (for molecule B). These values are in marked contrast to the values of 164°

TABLE V

SELECTED TORSION ANGLES FOR 2,3:4,5-DI-*O*-ISOPROPYLIDENE-1-*O*-METHYL-β-D-FRUCTOPYRANOSE

Atom 1	*Atom 2*	*Atom 3*	*Atom 4*	*Angle (°)*
C-7	O-1	C-1	C-2	−101.89(20)
C-8	O-2	C-2	O-6	118.30(14)
C-8	O-2	C-2	C-1	−127.86(15)
C-8	O-2	C-2	C-3	−3.90(16)
C-2	O-2	C-8	O-3	−15.51(17)
C-2	O-2	C-8	C-9	104.10(17)
C-2	O-2	C-8	C-10	−132.50(15)
C-8	O-3	C-3	C-2	−32.22(16)
C-8	O-3	C-3	C-4	−155.01(13)
C-3	O-3	C-8	O-2	29.88(16)
C-3	O-3	C-8	C-9	−88.56(17)
C-3	O-3	C-8	C-10	147.21(15)
C-11	O-4	C-4	C-3	−146.48(14)
C-11	O-4	C-4	C-5	−24.93(17)
C-4	O-4	C-11	O-5	30.63(18)
C-4	O-4	C-11	C-12	147.44(15)
C-4	O-4	C-11	C-13	−88.85(17)
C-11	O-5	C-5	C-4	8.71(19)
C-11	O-5	C-5	C-6	129.11(16)
C-5	O-5	C-11	O-4	−24.03(19)
C-5	O-5	C-11	C-12	−139.99(17)
C-5	O-5	C-11	C-13	95.19(18)
C-6	O-6	C-2	O-2	−82.02(16)
C-6	O-6	C-2	C-1	159.26(14)
C-6	O-6	C-2	C-3	33.53(19)
C-2	O-6	C-6	C-5	−67.90(18)
O-1	C-1	C-2	O-2	62.32(19)
O-1	C-1	C-2	O-6	−179.74(15)
O-1	C-1	C-2	C-3	−54.65(20)
O-2	C-2	C-3	O-3	21.93(16)
O-2	C-2	C-3	C-4	140.23(13)
O-6	C-2	C-3	O-3	−97.48(15)
O-6	C-2	C-3	C-4	20.82(19)
C-1	C-2	C-3	O-3	143.23(14)
C-1	C-2	C-3	C-4	−98.46(17)
O-3	C-3	C-4	O-4	−169.56(12)
O-3	C-3	C-4	C-5	75.23(17)
C-2	C-3	C-4	O-4	74.26(16)
C-2	C-3	C-4	C-5	−40.94(19)
O-4	C-4	C-5	O-5	9.87(17)
O-4	C-4	C-5	C-6	−108.34(16)
C-3	C-4	C-5	O-5	126.81(15)
C-3	C-4	C-5	C-6	8.61(21)
O-5	C-5	C-6	O-6	−72.18(17)
C-4	C-5	C-6	O-6	43.17(20)

and 26° in **2**, the conformation of which is a chair ($^2C_5$) but are somewhat distorted toward a half-chair (^2H_O). These same angles in **1** are 78° and 9° and are, as expected, similar to the values for **3**, which indicates that **1** is also in the ^3S_O conformation.

Because this compound is in a skew conformation, a bond-length intercomparison of **1** to our data for **3** to the literature data[5] for **3** was of interest. The C–O bond lengths of the pyranose ring for all the data sets show the usual shortening of the bond to the anomeric carbon atom, even though the compound is in a skew, not a chair, conformation. The C–O bond lengths in the 2,3-*O*-isopropylidene ring do not show a significant pattern between the compounds, even though C-2 and C-3 differ in degree of substitution. The C–O bond lengths in the 4,5-*O*-isopropylidene ring do not show significant differences, even though C-4 and C-5 have the same degree of substitution.

The exocyclic side-chain of **1** would be expected to have a different orientation from that found in **3**, due to the lack of a hydrogen atom on O-1 and the resulting loss of hydrogen-bond donor ability. The torsion angle about the C-1–C-2 bond has similar values in **1** and **3**. The torsion angle C-7–O-1–C-1–C-2 in **1** is −102°, in contrast to **3**, where this angle is −75° in molecule A and −69° in molecule B. Thus, the presence of hydrogen bonds in **3** decreases this value by ~30°. Another factor to consider is the steric interaction between the methyl group protons on C-7 and C-9, which would cause an increase in this value towards the expected 180°. Crystal packing forces are the probable cause of the difference between the expected and observed values for this torsion angle.

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