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THE X-RAY CRYSTAL STRUCTURE OF 6-DEOXY-α-L-SORBOFURANOSE. CONFORMATIONAL ANALYSIS OF KETOHEXOFURANOSIDES AND THEIR COMPARISON WITH RIBOFURANOSIDES AND ARABINOFURANOSIDES

PANCHANADAM SWAMINATHAN, LAURENS ANDERSON, AND MUTTAIYA SUNDARALINGAM*
Department of Biochemistry, College of Agricultural and Life Sciences, University of Wisconsin, Madison, Wisconsin 53706 (U.S.A.)

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ABSTRACT

The crystal and molecular structure of 6-deoxy-L-sorbose have been determined by the application of multisolution methods and refined to an *R*-index of 0.063 for 560 reflections, using three-dimensional intensity data collected on a Picker automatic diffractometer. The compound crystallizes in the space group $P2_12_12_1$ with unit-cell dimensions a = 18.470 (10), b = 7.636 (10), and c = 5.371 (8) Å; Z = 4. The molecule occurs as the α-furanose form, which is also the preponderant tautomer in solution. The puckering of the furanoid ring is C-3′-*exo*-C-4′-*endo* ($_3T^4$) [equivalent to C-2′-*exo*-C-3′-*endo* ($_2T^3$) in the numbering for D-ribose], with **P** and τ_m angles of −6.5 and 42.7° respectively. Conformational analysis of the known ketofuranosides shows that the $_3T^4$ ($_2T^3$ in D-ribose numbering) puckering mode, which is typical of α-nucleosides, is favored, in contrast to the favored $^3T_2$ or $^2T_3$ puckering mode for the β-D-ribonucleosides and β-D-arabinonucleosides. The conformational differences among furanoid rings are mainly influenced by the configuration at the anomeric carbon atom. The favored orientation about the C-2′–C-1′ bond (O-5′–C-2′–C-1′–O-1′) of the ketofuranosides is −*gauche*. All four hydroxyl groups are involved in donor–acceptor hydrogen bonding, and O-4′···H-8 appears to be involved in a bifurcated hydrogen bond to O-2′ and O-3′ of neighboring molecules.

INTRODUCTION

6-Deoxy-L-sorbose, synthesized by Muller and Reichstein[1] in 1938, is, as far as we are aware, the only crystalline ketohexose unable to form pyranoid ring-structures. This unique attribute makes 6-deoxy-L-sorbose an object of great interest for optical rotatory studies. With it, one should be able to observe mutarotation arising from ketofuranose–ketofuranose interconversion, and determine whether the specific rotations of the anomers obey Hudson's rules[2]. The validity of the rules for keto-

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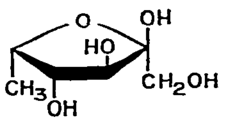
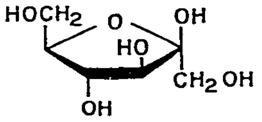
*To whom correspondence should be addressed.



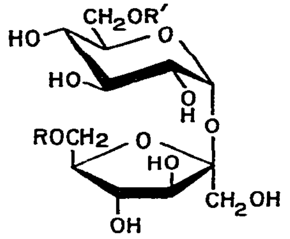
1

6-Deoxy-α-L-sorbofuranose



2

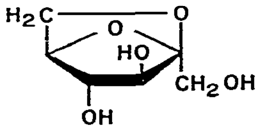
β-D-Fructofuranose



3 R = R′ = H

4 R = H, R′ = α-D-Gal*p*

5 R = α-D-Gal*p*, R=H



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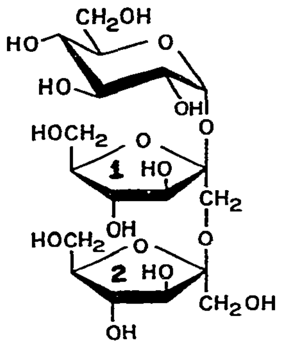

7

1-Kestose

furanoses has not been established, and indications that they may not hold for these anomers is provided by recent observations on the specific rotations of the D-fructofuranoses[3].

Prerequisite to the interpretation of eventual polarimetric data is the identification of the tautomeric form(s) of 6-deoxysorbose present in solution and in the crystalline state. Data (^{13}C-n.m.r.) on the equilibrium composition in aqueous solution have recently been provided by Angyal and Bethell[4]. The present paper describes an X-ray crystallographic analysis of 6-deoxy-L-sorbose, which shows the crystalline material to be the α-furanose (**1**).

EXPERIMENTAL

A crystalline sample of 6-deoxy-L-sorbose was obtained from Prof. T. Reichstein of Basel, Switzerland. The space group, the unit-cell constants, and other pertinent crystal data are presented in Table I. Intensity data were collected on a Picker FACS-I four-circle diffractometer, using θ–2θ scan mode with a scan rate of 2°/min, out to a 2θ limit of 127°. Altogether, 744 reflections were scanned, out of which 560 were greater[5] than 1.5 σ(I), where

$$\sigma(I) = [I_{scan} + I_{bkg} + 0.02\, I^2_{scan}]^{\frac{1}{2}}.$$

STRUCTURE DETERMINATION AND REFINEMENT

The structure was solved by the application of multi-solution methods with the

TABLE I

CRYSTALLOGRAPHIC DATA FOR **1**

Formula	$C_6H_{12}O_5$
Mol. weight	164.257
Cell constants:	
a	18.470(10) Å
b	7.636(10) Å
c	5.371(8) Å
Volume	757.5 Å^3
D_c	1.440 g/cm^3
Z	4
Space group	$P2_12_12_1$
Crystal size	0.4 × 0.1 × 0.8 mm
λ(CuKα)	1.5418 Å
μ_λ (for CuKα)	11.016 cm^{-1}

TABLE II

FRACTIONAL POSITIONAL PARAMETERS OF ALL ATOMS IN 6-DEOXY-L-SORBOFURANOSE (1)[a] (STANDARD DEVIATIONS ARE GIVEN WITHIN PARENTHESES)

Atom	*x*	*y*	*z*
C-1′	2119(3)	2162(8)	−472(13)
C-2′	1505(3)	2915(8)	939(13)
C-3′	785(3)	3007(7)	−365(9)
C-4′	413(3)	4435(8)	1151(9)
C-5′	1030(3)	5754(7)	1457(9)
C-6′	1103(4)	7096(8)	−593(14)
O-1′	2186(3)	3041(7)	−2870(7)
O-2′	1437(2)	1864(6)	3185(8)
O-3′	410(2)	1389(5)	−218(7)
O-4′	−209(2)	5105(5)	−38(7)
O-5′	1681(2)	4680(4)	1555(8)
H-1	245	375	−245
H-2	264	235	58
H-3	194	85	−64
H-4	190	188	411
H-5	76	332	−225
H-6	34	92	−194
H-7	20	394	257
H-8	−64	573	62
H-9	103	650	277
H-10	113	638	−250
H-11	71	796	−97
H-12	145	778	−59

[a] The coordinates of the nonhydrogen atoms are multiplied by 10^4 and those of the hydrogen atoms by 10^3.

program MULTAN[6]. A structure-factor calculation using all of the non-hydrogen atoms gave an initial *R*-index of 0.42. Three cycles of full-matrix, least-squares refinement with isotropic temperature-factors, and unit weights for all the reflections, decreased the *R*-index to 0.10. Further refinement by using anisotropic, thermal parameters for the non-hydrogen atoms decreased the *R*-index to 0.077. From an analysis of $\sqrt{w}*|\Delta F|^2$ *vs* $\langle |F_0| \rangle$, the following weighting scheme was adopted:

for $|F_0| < 48.4$, $w = 1.56/\sigma_F^2$,
for $48.4 < |F_0| < 127.6$, $w = 1/\sigma_F^2$,

and

for $|F_0| < 127.6$, $w = 0.422/\sigma_F^2$.

where σ_F is the standard deviation of the individual reflections. The hydrogen atoms were not refined, but were kept fixed at positions indicated by the difference density-map or at stereochemically plausible positions, and assigned a temperature factor of 4.0 Å^2. Three more cycles of least-squares refinement of the non-hydrogen atoms decreased the *R*-index to 6.3%. The scattering factors used for the non-hydrogen atoms were those given by Cromer and Waber[7], and for the hydrogen atoms those given by Stewart *et al.*[8]. Final positional parameters of the atoms are given in Table II. The anisotropic thermal parameters and the observed and calculated structure-amplitudes are listed in Tables III and IV respectively*.

RESULTS AND DISCUSSION

Although the crystalline anomers of sugars commonly obtained are not necessarily the major tautomers in solution, it could be expected that 6-deoxy-L-sorbose would crystallize in the α-furanoid form because of the great preponderance of this tautomer at equilibrium in water (at 35°, 83% of the total sugar[4]). This expectation is supported by the results of our analysis, as shown in Fig. 1.

The bond lengths and angles observed are given in Fig. 1. The mean standard-deviation in the bond length is 0.006 Å and in the bond angle 0.4°. The C–C bond lengths vary from 1.480 to 1.531 Å, with a mean value of 1.518 Å. The C–O bonds of the molecule vary over the range 1.412–1.457 Å, with a mean of 1.453 Å. As observed in other furanosides, the ring C–O bonds are unequal. The C-2′–O-5′ bond associated with the anomeric carbon atom (C-2′) is significantly shortened in comparison to the C-5′–O-5′ bond, the difference[14,15] being 0.031 Å.

The bond lengths and bond angles in the 6-deoxy-α-L-sorbofuranose molecule are in good agreement with values found in other molecules containing β-D-fructo-

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*Tables III, IV, and V are deposited with, and can be obtained from, Elsevier Scientific Publishing Company, BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/108/*Carbohydr. Res.*, 75 (1979) 1–10.

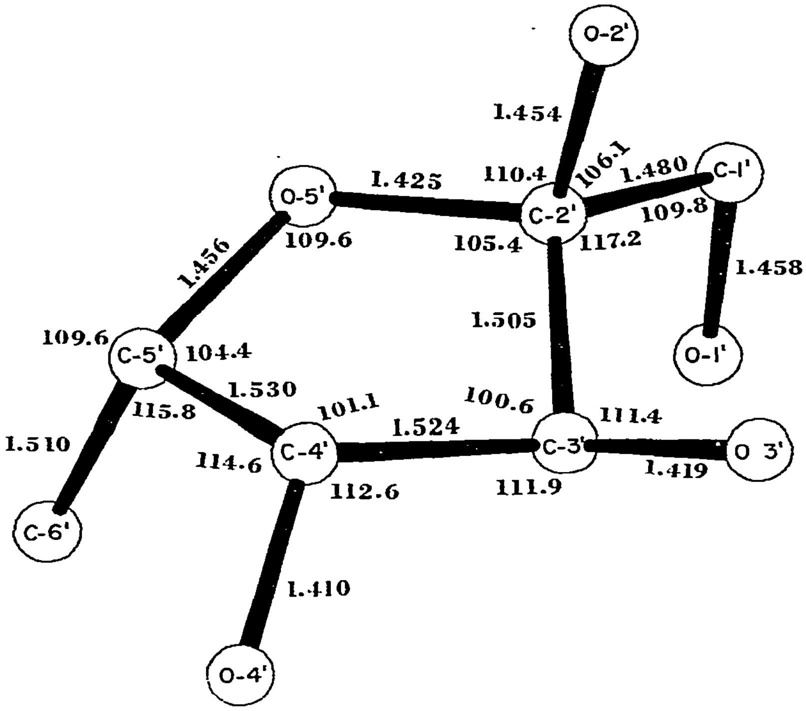

Fig. 1. Bond lengths and bond angles. Angles not shown in the figure are: C-1′–C-2′–O-5′ = 108.1°; and C-3′–C-2′–O-2′ = 109.6°. The mean (see text) bond lengths and bond angles of the furanoid ring averaged over the six ketofuranosides listed in Table V are: C-2′–C-3′ = 1.536(3), C-3′–C-4′ = 1.528(5), C-4′–C-5′ = 1.524(2), C-5′–O-5′ = 1.447(2), and O-5′–C-2′ = 1.409(2) Å; O-5′–C-2′–C-3′ = 104.7(1)°, C-2′–C-3′–C-4′ = 102.5(1), C-3′–C-4′–C-5′ = 101.5(3), C-4′–C-5′–O-5′ = 105.4(4), and C-5′–O-5′–C-2′ = 111.0(2)°.

furanoside groups (Table V)*. A comparison of the internal angles of the fructofuranoside rings indicates that, irrespective of the ring puckering-mode, the angle at C-4′ is the smallest. An analogous feature is observed in ribonucleosides, where the angle at C-2′ is the smallest, whether the ring puckering-mode is C-2′-*endo* or C-3′-*endo*[16].

CONFORMATION

The torsion angles about various bonds in 6-deoxy-α-L-sorbofuranose are shown in Fig. 2. A view of the molecule projected down the C-4′–C-5′ bond is shown in Fig. 3. The pseudorotation[17] amplitude (τ_m) and the phase angle (**P**) of the furanoid ring are 42.7 and —6.5°, respectively. Thus the conformation of the furanoid ring is C-3′-*exo*-C-4′-*endo*, $_3T^4$ (equivalent to C-2′-*exo*-C-3′-*endo*, ($_2T^3$) in the

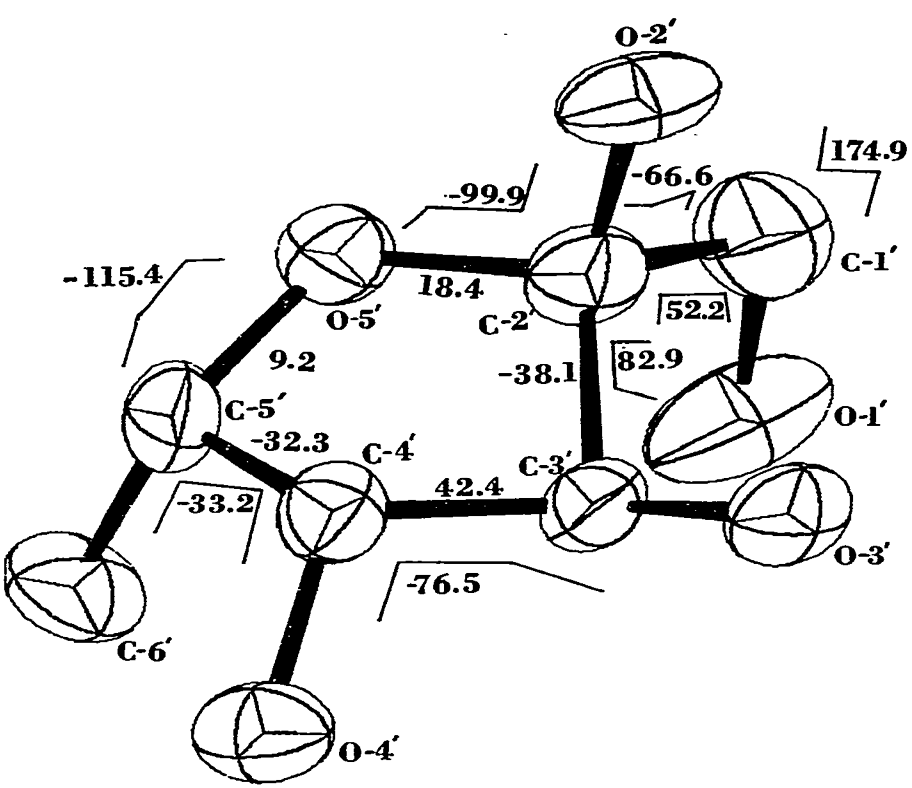

Fig. 2. An ORTEP[20] drawing of 6-deoxy-L-sorbose (1) showing the torsion angles, C-1′–C-2′–O-5′ C-5′ = 144.4°.

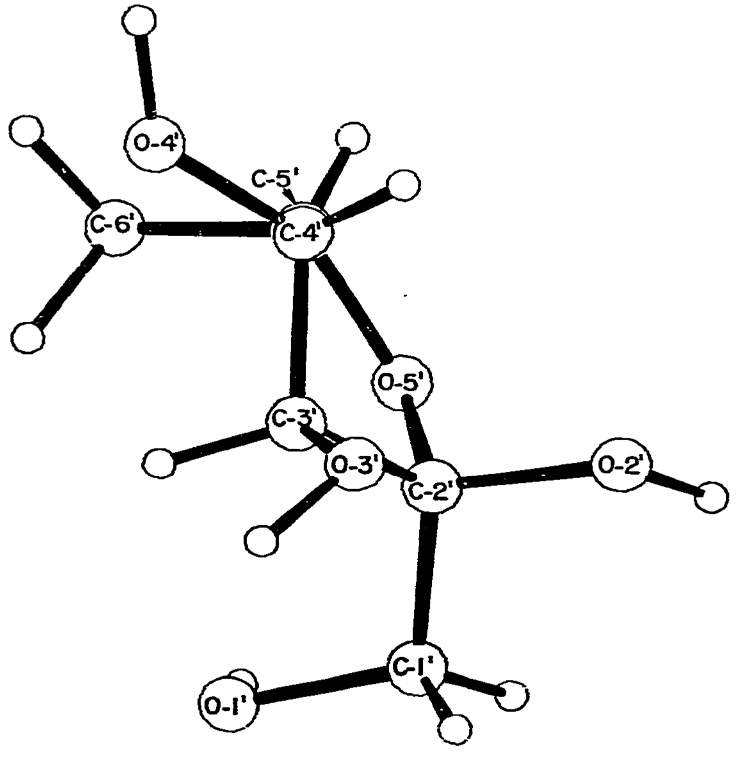

Fig. 3. The conformation of the molecule of **1**, viewed down the C-4′–C-5′ bond.

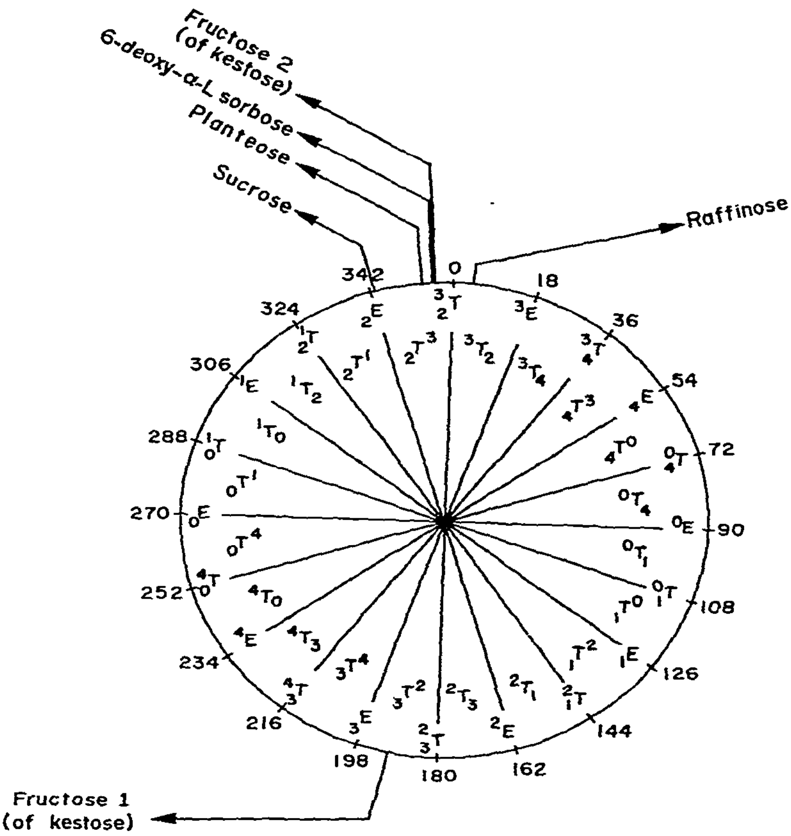

Fig. 4. The pseudorotation circle, illustrating the P-values of various ketofuranoses; with the exception of fructose-1 of 1-ketose, all the other ketofuranosides have P-values clustered around −18° to 9° (see Table VI).

numbering for D-ribose). For comparison, the phase angles (P) of pseudorotation of the fructose residue observed in different oligosaccharide structures are shown on a pseudorotation circle (Fig. 4), and the various torsional parameters are listed in Table VI. It may be seen that the most favored conformation of the fructosyl moiety is $_3T^4$, where C-3′ is puckered most. The puckering of the furanoid ring is mainly influenced by the configuration about the anomeric carbon atom. The orientation of the bulky group attached to C-2′ determines the puckering of C-3′ and C-4′. In the ketofuranosides listed in Table VI, the exocyclic CH_2OH group attached to C-2′ is below the furanoid ring. This factor influences C-3′ to assume *exo*-puckering (equivalent to C-2′-*exo* in the numbering for D-ribose). In α-D-nucleosides, where the base is also below the furanoid ring, a similar puckering feature has been observed, favoring the C-2′-*exo* conformation[18].

The torsion angles O-5′–C-2′–C-1′–O-1′ about the exocyclic C-2′–C-1′ bond observed in the different structures containing a ketofuranose group are represented in the Newman circle (Fig. 5). Of the six structures, four display the −*gauche* dis-

TABLE VI

A. ENDOCYCLIC TORSION-ANGLES OBSERVED IN THE KETOFURANOSE MOIETY OF DIFFERENT CARBOHYDRATE STRUCTURES

Compound	τ_0[a]	τ_1	τ_2	τ_3	τ_4	P[b]	τ_m[c]	*Ref.*
6-Deoxy-α-L-sorbofuranose (1)	18.4	−38.1	42.4	−32.3	9.2	−6.5	42.7	Present work
Sucrose (3)	14.5	−31.2	35.2	−27.5	8.3	−5.2	35.4	9
1-Kestose (7)								
Fructose-1	−3.7	21.1	−29.3	28.0	−15.2	191.5	29.9	10
Fructose-2	24.9	−40.7	40.1	−25.8	0.6	−17.6	42.1	
Raffinose (4)	9.6	−30.9	38.7	−33.7	16.1	4.5	38.8	12
Plantecse (5)	15.9	−34.4	38.8	−29.7	9.1	−5.5	38.9	13

[a] τ_0, τ_1, τ_2, τ_3, and τ_4 denote the endocyclic torsion angles. For details, see ref. 17. [b] P is the phase angle of pseudorotation[17]. [c] τ_m is the amplitude of the pseudorotation[17].

B. EXOCYCLIC TORSION ANGLES OBSERVED IN THE KETOFURANOSE MOIETY OF DIFFERENT CARBOHYDRATE STRUCTURES

Compound	*Torsion angles*[a]								*Ref.*
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	
6-Deoxy-α-L-sorbofuranose (1)	174.9	−67.6	52.2	−38.0	−176.6	−33.3	—	—	Present work
Sucrose (3)	50.6	171.4	−72.0	−39.2	−78.3	91.5	−69.8	48.9	9
1-Kestose (7)									
Fructose-1	56.5	179.2	−64.3	22.4	−148.0	151.3	64.6	−178.0	10
Fructose-2	179.2	−57.9	58.5	−44.5	−75.5	94.2	64.4	−177.2	
Raffinose (4)	−179.3	−59.1	58.4	−32.5	−76.3	82.7	68.9	−173.9	12
Planteose (5)	172.2	−65.7	52.0	−39.6	−78.1	92.9	63.5	−179.8	13

[a] Correspondence between the various numbers and the torsion angles is as follows: *1*, O-2′–C-2′–C-1′–O-1′; *2*, O-5′–C-2′–C-1′–O-1′; *3*, C-3′–C-2′–C-1′–O-1′; *4*, O-2′–C-2′–C-3′–O-3′; *5*, O-3′–C-3′–C-4′–O-4′; *6*, O-4′–C-4′–C-5′–C-6′; *7*, O-5′–C-5′–C-6′–O-6′; and *8*, C-4′–C-5′–C-6′–O-6′.

position, while two have the *trans* arrangement. Thus, it appears that the order of preference for this torsion angle is *−gauche > trans > +gauche.*

MOLECULAR PACKING AND HYDROGEN BONDING

The packing of the 6-deoxy-α-L-sorbofuranose molecule, viewed down the *c*-axis, is given in Fig. 6. The plane of the furanoid ring is approximately perpendicular to the *b*-axis of the unit cell. All four potential hydrogen-bonding protons are involved in hydrogen-bonding interactions. The proton on O-4′ has two oxygen atoms at distances of 1.817 and 2.558 Å, with bond angles O-4′-H-8···*O*-2′ and

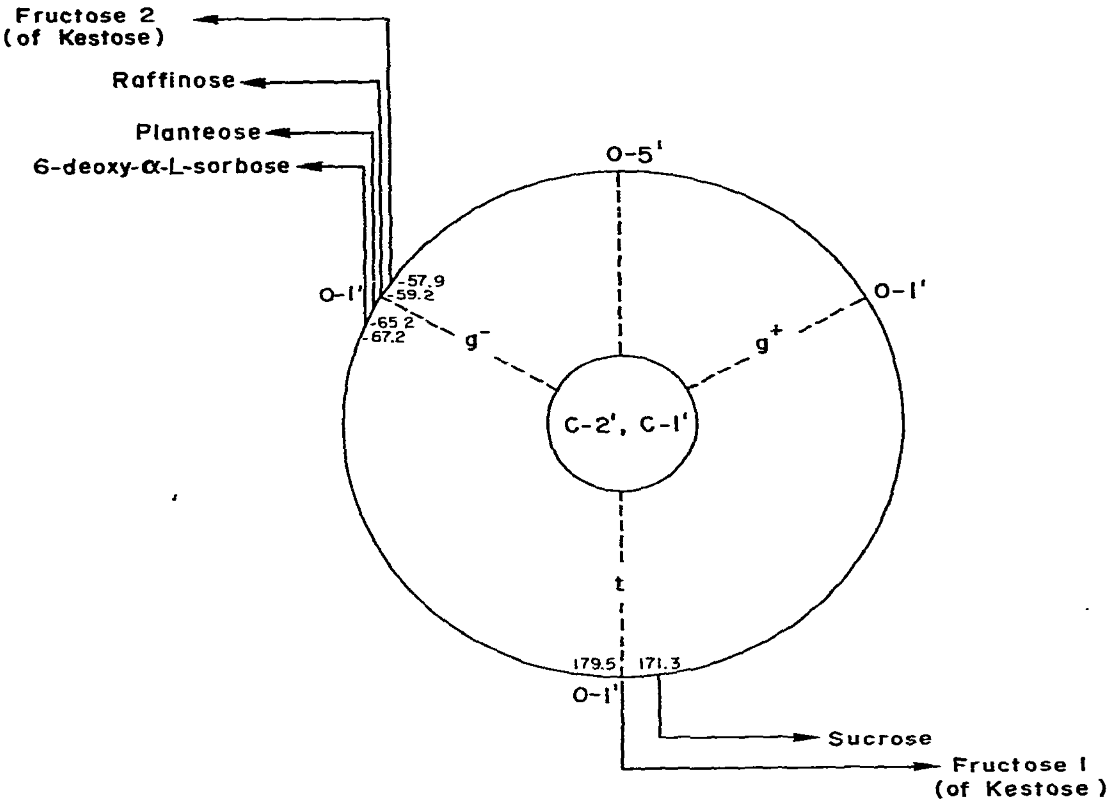

Fig. 5. Projection down the C-1′–C-2′ bond, showing the orientation in different ketofuranosides.

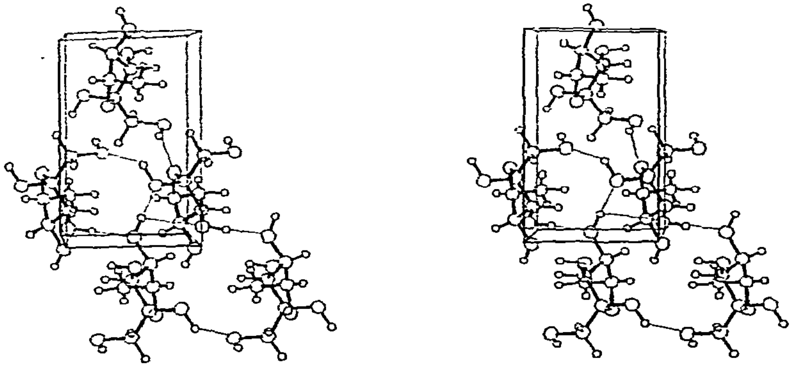

Fig. 6. Stereoview of the packing of the molecule of **1** along the *c*-axis.

O-4′-H-8···*O*-3′ of 180 and 107° respectively (Table VII). Thus the geometry is characteristic of an unsymmetrical, bifurcated hydrogen bond[19]. The hydrogen-bond distances and angles observed in the structure are listed in Table VII.

TABLE VII

HYDROGEN-BOND DISTANCES AND ANGLES

Bond	*Symmetry*	*D-H(Å)*	*D···A(Å)*	*H···A(Å)*	*D-H···A(°)*	*H-D···A(°)*
O-1′-H-1···O-5′	1/2 −x, 1−y, z−1/2	0.76	2.740	2.07	146	25
O-2′-H-2···O-1′	x, y, z+1	0.98	2.685	1.99	132	32
O-4′-H-8···O-2′	−x, 1/2+y, 1/2−z	0.99	2.816	1.82	180	0
O-4′-H-8···O-3′	−x, 1/2+y, −z−1/2	0.99	3.012	2.56	107	54°
O-3′-H-5···O-4′	−x, y−1/2, −z−1/2	1.00	2.754	1.75	180	0

ACKNOWLEDGMENTS

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