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The Crystal Structure of Methyl α-D-Galactofuranoside

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The crystal structure of methyl α-D-galactofuranoside has been determined from three-dimensional single-crystal X-ray diffraction data. The compound crystallizes in the monoclinic space group $P2_1$ with two molecules in the unit cell of dimensions $a = 6.217(2)$ Å, $b = 14.806(5)$ Å, $c = 4.811(2)$ Å, and $\beta = 105.62(1)°$. The structure was solved by direct methods and refined by full-matrix least-squares technique to an R_w value of 0.037 ($R = 0.048$) for 1394 observed reflections.

The furanose ring has the twist conformation ${}^2_1T$ with the anomeric carbon atom 0.28 Å below and its neighbouring carbon atom 0.33 Å above the plane of the remaining ring atoms. The exocyclic anomeric C−O bond is short [1.395(3) Å]. All oxygen atoms except for the glycosidic one are engaged in intermolecular hydrogen bonds forming a three-dimensional network.

The furanose ring occurs in a variety of important biological molecules, particularly in the nucleic acids. During the last years crystal structures of several complex carbohydrate compounds in which the carbohydrate component is in the furanose form have been determined. Due to their biological interest attention has been concentrated on D-ribofuranose and 2-deoxy-D-ribofuranose derivatives. However, little structure information has appeared in the literature of compounds where the furanose residue constitutes the major part of the molecule.

In several simple carbohydrates containing a pyranose ring the exocyclic anomeric C−O bond is short except in the case of an axial glycosidic group where there is evidence of a distinction between the two ring C−O bonds.[1] The C−O−C−N system of glycofuranosides shows unequal C−O bond lengths, the cyclic anomeric C−O bond being shorter than the other ring C−O bond.[1] Few data, on the other hand, are available for the C−O−C−O system of glycofuranosides.[2-4]

The structure analysis of methyl α-D-galactofuranoside (Me α-D-Gal*f*) has been undertaken in order to supplement our knowledge of the conformation of furanose carbohydrates and to provide data for study of carbon to oxygen distances in such compounds.

EXPERIMENTAL

Me α-D-Gal*f*, m.p. 89 °C, $[\alpha]_D^{20}$ +104 (*c* 0.25, water) was prepared as described by Augestad and Berner.[5] Crystals suitable for X-ray studies were obtained by slow crystallization from ethyl acetate.

Oscillation, Weissenberg, and precession photographs showed the space group to be $P2_1$. Setting angles for 15 reflections (Cu$K\beta$, $\lambda = 1.3922$ Å) determined on a Picker manual four-circle diffractometer were used for calculation of the unit cell dimensions. Intensity data were collected on a Picker automatic four-circle diffractometer using Mo$K\alpha$ radiation (graphite monochromator). A crystal of dimensions $0.15 \times 0.15 \times 0.30$ mm was mounted with the plane $(11\bar{2})$ normal to the ϕ axis of the goniostat. Intensities were measured using the $\omega - 2\theta$ scanning technique with a 2θ scan speed of 1° min^{-1} through the scan range from 0.7° below $2\theta(\alpha_1)$ to 0.7° above $2\theta(\alpha_2)$. Background counts were taken for 30 s at each of the scan range limits. The intensities of three standard reflections, measured at regular intervals throughout the data collection showed no significant fluctuations and were accordingly not used for scaling. Estimated standard deviations $\sigma(I)$ of the intensities were taken as $[\sigma_s^2 + (0.02\ C_N)^2]^{\frac{1}{2}}$ (σ_s is the standard deviation due to counting statistics and C_N is the net count). Of 2171 unique reflections measured with $2\theta < 75°$ 1374 (529 with $2\theta > 55°$) had intensities greater than $2.5\sigma(I)$ and were regarded as observed. The intensities were corrected for Lorentz and polarization effects.

CRYSTAL DATA

Methyl α-D-galactofuranoside, $C_7H_{14}O_6$, M = 194.19 amu. Space group $P2_1$ (No. 4).
$a = 6.217(2)$ Å, $b = 14.806(5)$ Å, $c = 4.811(2)$ Å, $\beta = 105.62(1)°$, $Z = 2$, $D_m = 1.51(1)$ g cm^{-3}, $D_x = 1.51$ g cm^{-3}.

STRUCTURE DETERMINATION

The phase problem was solved by direct methods.[6] The hydrogen atoms were located in difference Fourier maps. Least-squares refinement including all observed reflections and with anisotropic thermal parameters for non-hydrogen atoms gave a final R_w of 0.037 (R = 0.048). The intensity data showed no secondary extinction effects. A final difference Fourier synthesis showed electron density fluctuations not exceeding 0.3 e Å^{-3}.

The atomic scattering factors used were those of Doyle and Turner [7] for carbon and oxygen and of Stewart *et al.*[8] for hydrogen. Except for ORTEP [9] and those for phase determination all programs applied are described in Ref. 10.

RESULTS

Lists of observed and calculated structure factors are available from the authors on request. The final fractional coordinates and thermal parameters with their estimated standard deviations for the non-hydrogen atoms are given in Table 1 and for the hydrogen atoms in Table 2. The eigenvalues of the vibration tensors for the non-hydrogen atoms are also included in Table 1. A stereoscopic illustration of the molecule is shown in Fig. 1 where also the numbering of the atoms is indicated.

Rigid-body analysis of translational, librational, and screw motion [11] gave an r.m.s. difference between observed and calculated U_{ij}'s of 0.0041 Å^2 when all the non-hydrogen atoms were included. The whole molecule can therefore not be regarded as a rigid body. By excluding the terminal atoms except for substituents of the ring an r.m.s. value of 0.0025 Å^2 is obtained, thus indicating that this part of the molecule may be regarded as an oscillating rigid body. The latter description was adopted when correcting the coordinates for libration.

Table 3a contains the bond lengths. For

Table 1. Fractional coordinates (× 10^4), anisotropic thermal parameters U_{ij} (× 10^4), and r.m.s. amplitudes of vibration (× 10^3) for the non-hydrogen atoms. The parameters U_{ij} are terms in the temperature factor expression $\exp[-2\pi^2(U_{11}h^2a^{*2}+\cdots+2U_{23}klb^*c^*)]$. The e.s.d.'s given in parentheses refer to the last figure of respective values.

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}	$u1$	$u2$	$u3$
O1	4124(3)	7504(3)	5876(4)	290(8)	323(9)	392(11)	84(7)	136(8)	68(8)	21	18	15
O2	8383(3)	7189(3)	8655(5)	216(8)	285(9)	787(16)	8(8)	147(9)	99(10)	29	16	14
O3	7530(3)	5090(3)	9778(5)	237(8)	348(10)	413(12)	97(8)	68(8)	68(9)	21	19	13
O4	2936(3)	6528(3)	8990(4)	241(7)	253(8)	376(10)	3(6)	154(7)	−53(7)	20	16	13
O5	−6(3)	5279(3)	5675(5)	179(7)	475(12)	340(11)	15(8)	74(8)	−38(10)	22	18	13
O6	1692(3)	4070(3)	2171(4)	417(11)	235(9)	363(11)	−18(8)	73(8)	−46(8)	21	19	15
C1	4491(4)	7205(3)	8716(6)	243(10)	271(11)	331(14)	−3(9)	98(9)	−21(11)	18	16	15
C2	6724(4)	6719(3)	9598(6)	232(10)	281(12)	343(15)	−23(9)	59(10)	14(11)	19	17	15
C3	6141(3)	5792(3)	8263(6)	172(9)	276(11)	271(12)	32(8)	72(9)	41(10)	18	15	13
C4	3717(3)	5649(3)	8328(5)	220(10)	225(11)	246(12)	8(8)	99(9)	4(9)	16	15	13
C5	2253(3)	5287(3)	5507(5)	172(9)	227(10)	261(12)	20(8)	75(8)	10(9)	16	15	13
C6	2973(4)	4341(3)	4934(6)	275(12)	265(12)	367(16)	41(9)	50(11)	−30(12)	20	17	15
C7	2089(5)	8000( )	4889(8)	299(14)	454(19)	536(22)	98(13)	122(14)	122(17)	25	20	16

Table 2. Fractional coordinates ($\times 10^3$) and isotropic thermal parameters U ($\times 10^3$) for the hydrogen atoms. The temperature factor expression is exp $(-8\pi^2 U \sin^2\theta/\lambda^2)$. The e.s.d.'s given in parentheses refer to the last figure of respective values.

Atom	x	y	z	U
HO2	953(6)	690(2)	880(7)	48(10)
HO3	838(6)	502(3)	905(8)	45(11)
HO5	−62(6)	517(3)	417(8)	43(10)
HO6	178(5)	356(2)	206(7)	40(10)
H1	423(4)	770(2)	996(5)	18(6)
H2	712(4)	670(2)	1168(6)	28(7)
H3	618(4)	581(2)	634(5)	16(6)
H4	364(4)	522(2)	986(6)	24(6)
H5	240(4)	567(2)	401(5)	13(6)
H6A	457(5)	437(2)	510(6)	33(7)
H6B	275(5)	390(2)	635(6)	35(8)
H7A	200(6)	847(2)	620(8)	54(11)
H7B	203(5)	826(3)	303(8)	53(10)
H7C	86(6)	766(3)	491(8)	63(11)

bonds not involving hydrogen atoms corrected bond lengths are also listed. Bond angles and torsion angles involving non-hydrogen atoms are listed in Table 3b and Table 3c, respectively. The hydrogen bonding scheme is shown in Fig. 2 and the corresponding hydrogen bonding data are given in Table 3d. The estimated standard deviations were calculated from the least-squares correlation matrix.

DISCUSSION

The furanose ring in Me α-D-Gal*f* is non-planar. The displacements of C1 and C2 from the plane of C3, C4, and O4 are −0.285 and 0.327 Å, respectively, showing that the ring adopts a twist conformation. Alternatively, the conformation of the furanose ring is conveniently described by the torsion angles τ_j ($j=0,4$) about the five ring bonds.[12,13] Starting

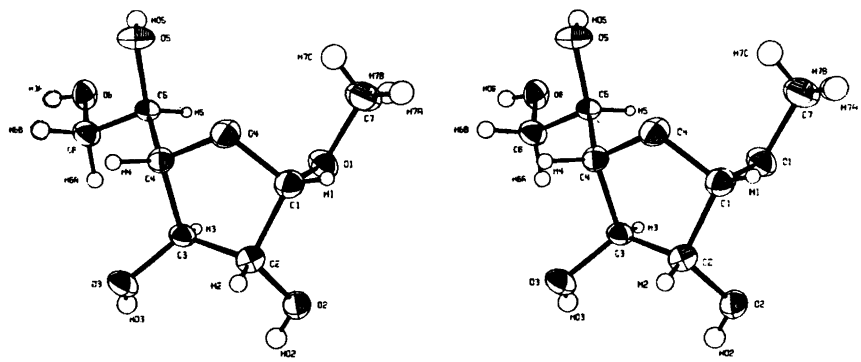

Fig. 1. Stereoscopic drawing of the methyl α-D-galactofuranoside molecule with atom numbering. The hydrogen atoms are assigned isotropic thermal parameters corresponding to one third of the values listed in Table 2. The thermal ellipsoids are scaled to 50 % probability.

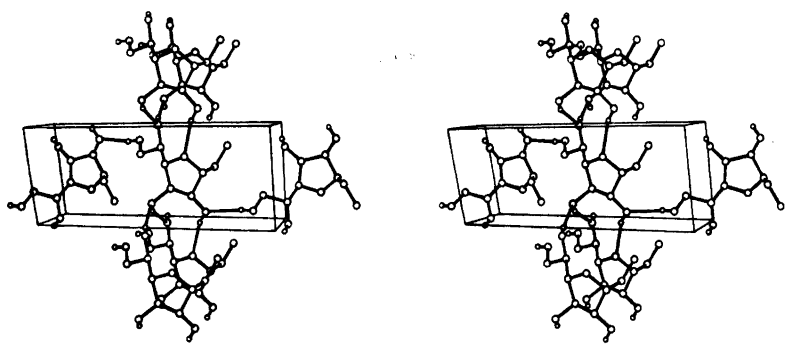

Fig. 2. Stereoscopic drawing showing the hydrogen bonding scheme. Hydrogen atoms not involved in hydrogen bonds are omitted for clarity.

Table 3. (a) Bond lengths. For bonds between non-hydrogen atoms bond lengths corrected for libration are also listed. (b) Bond angles involving non-hydrogen atoms. (c) Torsion angles involving non-hydrogen atoms. (d) Hydrogen bond parameters.
The e.s.d.'s given in parentheses refer to the last figure of respective values.

(a) Bond lengths (Å)

O1–C1	1.395(3)	1.401	O6–C6	1.412(3)	1.414	O2–HO2	0.81(3)	C4–H4	0.99(3)
O1–C7	1.429(3)	1.431	C1–C2	1.520(3)	1.524	O3–HO3	0.72(3)	C5–H5	0.94(2)
O2–C2	1.416(3)	1.420	C2–C3	1.517(4)	1.520	O5–HO5	0.74(4)	C6–H6A	0.98(3)
O3–C3	1.420(3)	1.423	C3–C4	1.530(3)	1.536	O6–HO6	0.75(3)	C6–H6B	0.98(3)
O4–C1	1.424(3)	1.428	C4–C5	1.514(3)	1.519	C1–H1	0.98(3)	C7–H7A	0.95(4)
O4–C4	1.454(3)	1.457	C5–C6	1.518(3)	1.520	C2–H2	0.96(3)	C7–H7B	0.97(4)
O5–C5	1.428(3)	1.431				C3–H3	0.93(2)	C7–H7C	0.92(4)

(b) Bond angles (°)

C1–O1–C7	112.6(2)	O2–C2–C1	111.5(2)	C2–C3–C4	103.9(2)	O5–C5–C4	108.4(2)
C1–O4–C4	109.6(2)	O2–C2–C3	114.9(2)	O4–C4–C3	105.7(2)	O5–C5–C6	110.1(2)
O1–C1–O4	112.2(2)	C1–C2–C3	102.4(2)	O4–C4–C5	110.9(2)	C4–C5–C6	110.7(2)
O1–C1–C2	108.7(2)	O3–C3–C2	113.7(2)	C3–C4–C5	112.9(2)	O6–C6–C5	108.3(2)
O4–C1–C2	103.4(2)	O3–C3–C4	110.8(2)				

(c) Torsion angles (°)

C7–O1–C1–O4	68.3(3)	O1–C1–C2–O2	42.9(3)	C1–C2–C3–O3	−151.7(2)	O4–C4–C5–O5	−54.9(2)
C7–O1–C1–C2	−177.9(2)	O1–C1–C2–C3	−80.4(2)	C1–C2–C3–C4	−31.2(2)	O4–C4–C5–C6	−175.9(2)
C4–O4–C1–O1	84.7(2)	O4–C1–C2–O2	162.3(2)	O3–C3–C4–O4	135.2(2)	C3–C4–C5–O5	−173.3(2)
C4–O4–C1–C2	−32.2(3)	O4–C1–C2–C3	39.0(2)	O3–C3–C4–C5	−103.4(2)	C3–C4–C5–C6	65.8(3)
C1–O4–C4–C3	12.3(3)	O2–C2–C3–O3	87.3(3)	C2–C3–C4–O4	12.8(3)	O5–C5–C6–O6	65.3(3)
C1–O4–C4–C5	−110.4(2)	O2–C2–C3–C4	−152.2(2)	C2–C3–C4–C5	134.2(2)	C4–C5–C6–O6	−174.8(2)

(d) Hydrogen bond distances (Å) and angles (°)

O2···O4^{i}	2.958(2)	HO2···O4^{i}	2.17(3)	O2–HO2···O4^{i}	163(3)	(i) $1+x,y,z$
O3···O5^{i}	2.819(3)	HO3···O5^{i}	2.16(4)	O3–HO3···O5^{i}	153(4)	(ii) $1-x,-\frac{1}{2}+y,1-z$
O5···O3^{iii}	2.852(3)	HO5···O3^{iii}	2.12(4)	O5–HO5···O3^{iii}	171(4)	(iii) $-1+x,y,-1+z$
O5···O2^{ii}	2.812(3)	HO6···O2^{ii}	2.06(4)	O6–HO6···O2^{ii}	172(3)	

at the O4−C1 bond ($j=0$), the values along the ring are −32.2, 39.0, −31.2, 12.8, and 12.3°. These torsion angles correspond to a phase angle of pseudorotation P and an amplitude of pucker τ_m of 143.6 and 38.7°, respectively.[14] In terms of the formalism suggested by Altona and Sundaralingam[14] the Me α-D-Gal*f* ring has approximately the twist conformation ${}^{3}_{1}T$. This conformation is different from those of a variety of other furanose rings in which either C2 or C3 (or both) have been shown to be the out-of-plane ring atoms.[15] The puckering in Me α-D-Gal*f* may be related to eclipsed interaction between the substituents at C1 and C2. For the five-membered ring in methyl β-D-arabinofuranoside, which is configurationally related to Me α-D-Gal*f*, a ${}_{2}E$ conformation has been proposed from a consideration of non-bonded interaction.[16]

In view of the puckering observed in the furanose ring the substituents cannot exhibit a "true" *cis* or *trans* relation. This affects mainly the C1 and C2 substituents, a fact which is reflected in the torsion angle about the C1−C2 bond between O1 and O2 of 42.9°. The orientation of the methyl group relative to the furanose ring oxygen is +*sc*[12] (*gauche*). When relating O4 to O5 about the C4−C5 bond and O5 to O6 about C5−C6, the conformations are −*sc* (*gauche*) and +*sc*, respectively.

The C−C bond lengths in Me α-D-Gal*f* average to 1.520 Å. None of the C−C bond lengths in the ring are significantly different from this mean or from the value of 1.523 Å reported by Sundaralingam as an average value for furanose rings.[15] The C−O bonds lengths in the molecule average to 1.422 Å. The values for O1−C1 (1.395 Å) and O4−C4 (1.454 Å) both deviate significantly from this mean. It may be pointed out that a short exocyclic anomeric bond [1.382(11) Å] is also found in methyl α-D-lyxofuranoside.[4] The two ring C−O bond lengths in Me α-D-Gal*f* (1.428 and 1.454 Å) agree well with those reported as average values for such bonds (1.427 and 1.450 Å).[15]

Except for the bond angle at O4 (109.6°) all the internal angles in the furanose ring are significantly less than the tetrahedral angle. The internal C−C−C bond angle (102.4°) at the out-of-plane carbon atom C2 is less than the C−C−C bond angle (103.9°) at the in-plane carbon atom C3. Other characteristic features of bond angles in furanosides described by Sundaralingam[15] do not fit well for this structure. This may be related to the different mode of puckering in the present structure.

The Me α-D-Gal*f* molecules are linked through hydrogen bonding and except for O1 all oxygen atoms participate in the three-dimensional hydrogen bond network (Fig. 2 and Table 3d). Each of the oxygen atoms O2, O3, and O5 donate as well as accept protons, O6 acts as a donor only, and O4 as an acceptor. The O2···O4^{i} separation of 2.958 Å is somewhat longer than the other O···O distances of Table 3c. However, the position of the hydrogen atom HO2 (O−H···O angle of 163°) indicates the presence of a hydrogen bond. The molecules pack with the ring planes (five-atom least-squares planes) nearly parallel to the *ab* plane.

The present structure shows two short intermolecular contacts involving non-hydrogen atoms, one oxygen oxygen contact (O6···O3^{iii}) of 2.949(3) Å and one carbon oxygen contact (C3···O5^{i}) of 3.077(3) Å.

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