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Conformational features of rhamnopyranose derivatives. The molecular structure of methyl 2,3,4-tri-*O*-acetyl-*α*-L-rhamnopyranoside

M. Ashraf Shalaby *, Frank R. Fronczek, Ezzat S. Younathan

Departments of Biochemistry and Chemistry, Louisiana State University, Baton Rouge, LA 70803, USA

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Abstract

Methyl 2,3,4-tri-*O*-acetyl-*α*-L-rhamnopyranoside, $C_{13}H_{20}O_8$, $M_r = 304.3$, is monoclinic, space group C_2, with $a = 23.619(1)$, $b = 8.2168(5)$, $c = 19.093(1)$ Å, $\beta = 118.72(1)°$, $V = 3249.6(8)$ Å^3, $D_c = 1.244$ g cm^{-3}, μ (MoK_α) = 0.97 cm^{-1} and $Z = 8$. The structure was refined to $R = 0.044$ and $R_w = 0.039$ for 1969 observed reflections. There are two independent molecules in the asymmetric unit. The bond lengths and bond angles of the pyranose rings of the two are in good agreement within the limits of error. The molecules have similar conformation except for the orientation of one of the acetoxy groups. Each molecule is a normal $^1C_4$ chair with Cremer–Pople puckering parameters $Q = 0.557(6)$ Å, $\theta = 174.6(2)°$ and $\psi = 144.6(9)°$ for molecule A and 0.564(4) Å, 177.9(1)° and 30.8(8)° for molecule B, respectively. The acetyl groups have the planar, (*S*)-cis conformation most commonly observed. They are oriented with the acetyl planes within ±35° of the C–H bond at the ring carbon atom to which they are attached.

Keywords: X-ray crystal structure; Conformation; *α*-L-Rhamnopyranoside, 2,3,4-tri-*O*-acetyl-

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1. Introduction

Methyl 6-deoxyhexopyranosides are compounds of particular interest. They are suitable starting materials for the synthesis of branched-chain deoxy sugars [1], the essential components of many macrolide antibiotics and constitute a partial structure of several compounds that have been shown to possess significant antimicrobial and potential antitumor activities [2–6]. We have recently reported the structural analysis of methyl *α*-L-rhamno-

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* Corresponding author (present address): Center for Advanced Materials, Lawrence Berkeley Laboratory, One Cyclotron Road, University of California-Berkeley, Berkeley, CA 94720, USA.

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Table 1
Crystallographic data for methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside

Molecular formula	$C_{13}H_{20}O_8$
Molecular weight	304.3
Melting point (°C)	92
Crystal dimensions (mm)	0.12×0.25×0.33
Space group	C_2
Cell dimensions (Å)	
a	23.619(1)
b	8.2168(5)
c	19.093(1)
β(°)	118.72(1)
Volume (Å^3)	3249.6(8)
Z (molecules/cell)	8
F (000)	1296
μ (cm^{-1})	0.97
Radiation (graphite monochromator)	MoK$_\alpha$
Calculated density (g cm^{-3})	1.244
Unique reflections	3068
$I > 1\sigma(I)$	1969
S (379 variables)	1.393
Final residual factors	
R	0.044
R_w	0.039

pyranoside [7], and showed that the compound adopts a similar conformation, $^1C_4$, both in the solid state and in solution. In the present work, we report on the conformation and 3D molecular structure of methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside as determined by X-ray crystallography.

2. Experimental

The sample of methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside was kindly provided by Professor Hassan El Khadem from the late Dr. H.S. Isbell's collection of rare sugars at The American University, Washington DC. Colorless crystals suitable for X-ray were grown from ethyl acetate–ether. The crystal used for data collection was a fragment with dimensions 0.12×0.25×0.33 mm.

Data collection and processing.—Intensity data were collected on an Enraf–Nonius CAD4 diffractometer equipped with graphite-monochromated Mo*K*α radiation at 23°C. Unit-cell parameters were obtained from setting angles of 25 reflections having $20 < 2\theta < 26°$. A total of 5695 reflections was measured by $\omega - 2\theta$ scans (two quadrants having $2 < 2\theta < 50°$) and variable scan rates (1.10–3.30 deg min^{-1}), 3068 unique data were obtained; 1969 reflections with $I > 1\sigma(I)$ were used in the refinement. Crystal stability was monitored by recording three standard reflections every 10 000 s, and a linear decay correction of 4.9% was applied to the intensities. The effects of absorption for this compound were very small, and were neglected in our calculations (Table 1).

Structure analysis.—The structure was solved by direct methods using the program SHELXS [8] which revealed the positions of all nonhydrogen atoms. It was refined by full-matrix least squares based upon F with weights $w = 4F_o^2[\sigma^2(I) + (0.02F_o^2)^2]^{-1}$ using the MolEN programs [9]. Nonhydrogen atoms were refined anisotropically. Most hydrogen atoms were visible in difference maps, but these were placed in calculated positions with C–H distance 0.95 Å. Atomic coordinates and equivalent isotropic thermal parameters, along with their esds, are given in Table 2 [1]. Final $R = 0.044$ for 1934 observed data (0.097 for all 3068 data), $R_w = 0.039$, and $S = 1.393$ for 379 variables. In the final cycle of refinement, the maximum shift was 0.01σ, maximum residual density 0.13, minimum -0.07 eÅ^{-3}, and extinction coefficient $g = 6.7(5) \times 10^{-7}$ where the factor $(1 + gI_c)^{-1}$ was applied to F_c. All calculations were performed on a VAX 3600 computer. Atomic scattering factors were obtained from the International Tables for X-ray Crystallography [10].

3. Results and discussion

The crystal structure of the title compound shows that there are two independent molecules in the asymmetric unit. A perspective drawing (ORTEP [11]) of their structures with the atomic numbering is shown in Fig. 1 and the molecular packing is illustrated in Fig. 2. The bond lengths, bond angles, and selected torsion angles with their estimated standard deviations are given in Tables 3, 4, and 5, respectively. The C–C bonds of the pyranose rings range from 1.499(6) to 1.536(4) Å in molecule **A** and 1.500(5) to 1.516(5) Å in molecule **B**, with mean values of 1.518 and 1.508 Å, respectively. These values are in good agreement with the values reported for carbohydrates [12,13]. The two adjacent endocyclic C–O bonds, C-1–O-5 and O-5–C-5, show small differences, but these are not significant in terms of standard deviations. The exo-anomeric effect [14] was not definitively observed in the present compound, as the average C-1–O-5 and C-1–O-1 bond lengths, 1.405(4) and 1.392(4) Å do not differ by a significant amount. This is presumably due to the presence of the lone-pair electrons of O-5 and O-1 in a synaxial position, causing dipolar repulsion and restraining the back donation of the O-5 lone-pair. The conformation about the anomeric bonds is gauche–gauche, the C-5–O-5–C-1–O-1 and O-5–C-5–O-1–C-7 torsion angles being −61.0(4)° and 63.2(4)° in molecule **A** and −61.5(4)° and −66.4(5)° in molecule **B**, respectively. The methoxy group is so oriented that O-1–C-7 is almost trans to C-1–C-2, with C-7–O-1–C-1–C-2 = 172.4(4)° and 171.1(4)° in molecule **A** and **B**, respectively.

For the side groups, the mean C–O bond length of 1.439 Å between the carboxylic carbon atom of the acetyl group and the carbohydrate oxygen is equivalent to that found in several peracetylated α-hexopyranosides [15–17]. The mean C=O of 1.184 Å is within the range of the expected values for carbonyl group.

The oxygen ring-valence angles [113.3(3)° in **A** and 114.4(3)° in **B**] are normal and nearly identical to that of 112.90(7)° found in methyl α-L-rhamnopyranoside [7]. The

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[1] Lists of observed and calculated structure-amplitudes, anisotropic thermal parameters, hydrogen coordinates and isotropic thermal parameters, and torsion angles for this compound have been deposited with the Cambridge Crystallographic Data Centre and may be obtained on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Table 2
Atomic coordinates and equivalent isotropic thermal parameters of methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside

Atom	x	y	z	B_{eq} (Å^2)	Atom	x	y	z	B_{eq} [a] (Å^2)
O-1A	0.3430(1)	0	−0.1287(1)	5.96(8)	O-1B	0.0995(1)	0.0670(5)	0.5588(1)	6.72(9)
O-2A	0.3922(1)	−0.3709(4)	−0.0178(1)	4.88(7)	O-2B	0.0849(1)	−0.3227(4)	0.4683(2)	5.91(8)
O-3A	0.4528(1)	−0.1580(4)	0.1095(1)	5.50(8)	O-3B	0.0581(1)	−0.1229(4)	0.3348(1)	5.74(8)
O-4A	0.3456(1)	−0.0073(4)	0.1049(1)	5.61(7)	O-4B	0.1802(1)	0.0150(4)	0.3930(1)	5.30(7)
O-5A	0.2784(1)	−0.1685(4)	−0.0981(1)	5.46(8)	O-5B	0.1832(1)	−0.1130(4)	0.5781(1)	5.47(8)
O-6A	0.4331(1)	−0.4319(5)	−0.0978(2)	7.39(9)	O-6B	−0.0209(1)	−0.3702(2)	0.4033(2)	9.3(1)
O-7A	0.5084(2)	0.0598(5)	0.1122(2)	10.4(1)	O-7B	−0.0133(2)	0.0742(6)	0.3034(2)	10.9(1)
O-8A	0.3086(2)	−0.1921(6)	0.1581(2)	12.1(1)	O-8B	0.2231(1)	−0.1932(5)	0.3615(2)	9.6(1)
C-1A	0.3333(2)	−0.1552(6)	−0.1080(2)	5.4(1)	C-1B	0.1174(2)	−0.0936(7)	0.5557(2)	5.9(1)
C-2A	0.3949(2)	−0.1999(5)	−0.0334(2)	4.4(1)	C-2B	0.0747(2)	−0.1503(7)	0.4706(2)	5.3(1)
C-3A	0.3989(2)	−0.1051(6)	0.0359(2)	4.4(1)	C-3B	0.0933(2)	−0.0619(6)	0.4154(2)	4.8(1)
C-4A	0.3386(2)	−0.1177(6)	0.0433(2)	4.8(1)	C-4B	0.1640(2)	−0.0850(6)	0.4430(2)	4.7(1)
C-5A	0.2808(2)	−0.0667(6)	−0.0364(2)	5.1(1)	C-5B	0.2035(2)	−0.0278(6)	0.5284(2)	4.7(1)
C-6A	0.2168(2)	−0.0817(8)	−0.0383(3)	7.4(2)	C-6B	0.2747(2)	−0.0549(7)	0.5623(2)	6.0(1)
C-7A	0.2927(3)	0.0573(9)	−0.2046(3)	10.1(2)	C-7B	0.1275(2)	0.135(1)	0.6370(2)	9.0(2)
C-8A	0.4136(2)	−0.4754(6)	−0.0541(2)	5.5(1)	C-8B	0.0327(2)	−0.4182(7)	0.4331(2)	6.5(1)
C-9A	0.4102(2)	−0.6475(7)	−0.0324(3)	7.0(1)	C-9B	0.0522(2)	−0.5911(8)	0.4368(3)	8.7(2)
C-10A	0.4044(2)	−0.0613(7)	0.1431(2)	6.1(1)	C-10B	0.0069(2)	−0.0374(8)	0.2830(2)	7.1(2)
C-11A	0.5553(2)	−0.128(1)	0.2208(3)	9.1(2)	C-11B	−0.0218(2)	−0.105(1)	0.20005(2)	9.3(2)
C-12A	0.3308(2)	−0.0618(8)	0.1602(2)	7.1(1)	C-12B	0.2074(2)	−0.0560(7)	0.3532(2)	6.0(1)
C-13A	0.3454(2)	0.066(1)	0.2214(2)	9.3(2)	C-13B	0.2177(2)	0.0605(8)	0.3011(2)	8.3(2)

[a] $B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij}a^{i*}a^{j*}a_i \cdot a_j$

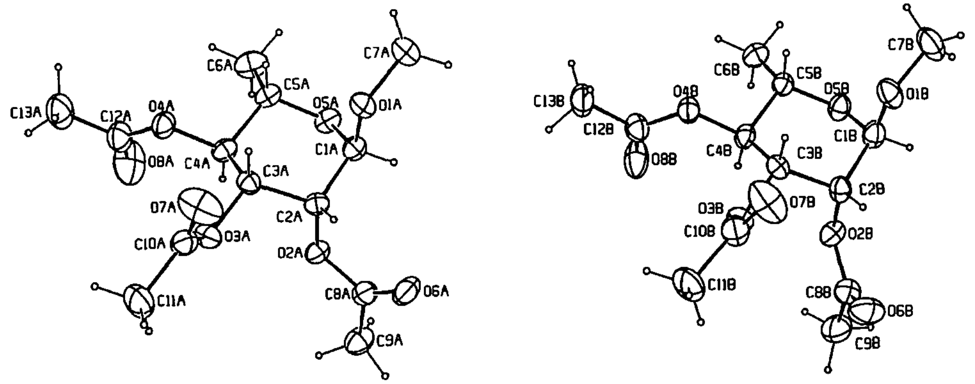

Fig. 1. Molecular structures and atomic numbering of molecules **A** and **B** in the crystal of methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside. Nonhydrogen atoms are represented with 30% ellipsoids and hydrogen atoms with circles of arbitrary radius.

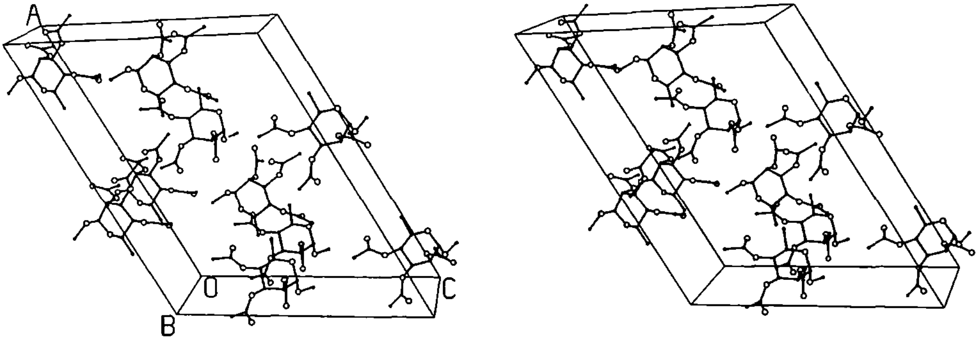

Fig. 2. Molecular packing in the crystal structure of the title compound in stereo.

Table 3
Bond lengths (Å) for methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside

Atoms	Molecule **A**	Molecule **B**	Atoms	Molecule **A**	Molecule **B**
O-1–C-1	1.387(5)	1.396(7)	O-6–C-8	1.185(6)	1.180(5)
O-1–C-7	1.442(5)	1.426(6)	O-7–C-10	1.184(7)	1.182(8)
O-2–C-2	1.444(5)	1.441(6)	O-8–C-12	1.184(8)	1.174(7)
O-2–C-8	1.344(6)	1.338(5)	C-1–C-2	1.512(4)	1.516(5)
O-3–C-3	1.437(4)	1.442(4)	C-2–C-3	1.499(6)	1.509(6)
O-3–C-10	1.333(5)	1.335(5)	C-3–C-4	1.500(6)	1.503(5)
O-4–C-4	1.431(5)	1.443(5)	C-4–C-5	1.536(4)	1.513(5)
O-4–C-12	1.339(6)	1.341(6)	C-5–C-6	1.497(7)	1.500(5)
O-5–C-1	1.402(6)	1.409(5)	C-8–C-9	1.486(8)	1.484(8)
O-5–C-5	1.424(6)	1.435(6)	C-10–C-11	1.493(6)	1.491(7)
C-12–C-13	1.482(8)	1.483(8)			

Table 4
Bond angles (deg) for methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside

Atoms	Molecule A	Molecule B	Atoms	Molecule A	Molecule B
C-1–O-1–C-7	114.7(3)	114.7(4)	O-4–C-4–C-5	109.7(3)	108.3(3)
C-2–O-2–C-8	116.8(3)	117.7(3)	C-3–C-4–C-5	108.7(3)	110.1(4)
C-3–O-3–C-10	117.8(3)	117.4(4)	O-5–C-5–C-4	108.7(3)	109.4(3)
C-4–O-4–C-12	117.8(4)	118.5(4)	O-5–C-5–C-6	107.0(3)	107.7(3)
C-1–O-5–C-5	113.3(3)	114.4(3)	C-4–C-5–C-6	114.2(4)	113.7(4)
O-1–C-1–O-5	113.6(4)	114.0(4)	O-2–C-8–O-6	122.6(5)	124.3(5)
O-1–C-1–C-2	106.0(3)	106.1(3)	O-2–C-8–C-9	112.4(4)	110.3(4)
O-5–C-1–C-2	112.8(4)	111.1(4)	O-6–C-8–C-9	125.0(5)	125.4(5)
O-2–C-2–C-1	108.2(3)	107.5(3)	O-3–C-10–O-7	122.3(3)	121.9(4)
O-2–C-2–C-3	108.3(3)	110.1(4)	O-3–C-10–C-11	111.9(5)	112.1(5)
C-1–C-2–C-3	109.2(3)	109.5(4)	O-7–C-10–C-11	125.8(4)	125.9(4)
O-3–C-3–C-2	110.9(3)	111.5(3)	O-4–C-12–O-8	123.6(5)	123.3(5)
O-3–C-3–C-4	108.8(3)	107.7(3)	O-4–C-12–C-13	109.6(5)	112.1(5)
C-2–C-3–C-4	112.8(3)	110.0(3)	O-8–C-12–C-13	126.9(5)	124.5(5)
O-4–C-4–C-3	107.1(3)	107.4(3)			

endocyclic torsion angle magnitudes of the pyranose ring **A** fall within the range 51.0–61.7°, whereas the corresponding magnitudes in ring **B** 55.2–58.5°. These small deviations can be attributed to the slight flattening of the pyranose ring associated with the orientation of the acetyl group on C-2. The smallest values of the endocyclic torsion angles are observed at the C-2–C-3 and C-2–C-1 bonds [51.0(5)° and 52.0(5)° in molecule **A**, respectively].

The two molecules have similar conformations except for the orientation of one of the acetoxy groups. Each molecule is a normal chair $^{1}C_{4}$, with Cremer–Pople [18] puckering

Table 5
Selected torsion angles (deg) in methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside

Ring angles	Molecule A	Molecule B
C-5–O-5–C-1–C-2	59.7(5)	58.3(5)
C-1–O-5–C-5–C-4	61.7(4)	58.5(5)
O-5–C-1–C-2–C-3	52.0(5)	55.3(6)
C-1–C-2–C-3–C-4	51.0(5)	55.2(5)
C-2–C-3–C-4–C-5	54.6(5)	56.6(5)
C-3–C-4–C-5–O-5	57.7(5)	56.4(5)
Exocyclic angles		
C-7–O-1–C-1–O-5	63.2(4)	66.4(6)
C-7–O-1–C-1–C-2	172.4(4)	171.1(4)
C-12–O-4–C-4–C-5	108.9(4)	117.2(4)
C-12–O-4–C-4–C-3	133.2(4)	124.0(4)
C-10–O-3–C-3–C-2	105.7(4)	99.7(5)
C-10–O-3–C-3–C-4	129.7(4)	139.6(4)
C-8–O-2–C-2–C-1	87.2(4)	131.2(3)
C-8–O-2–C-2–C-3	154.5(3)	109.6(4)
C-3–O-3–C-10–O-7	4.4(7)	7.8(7)
C-5–O-5–C-1–O-1	61.0(4)	61.5(4)

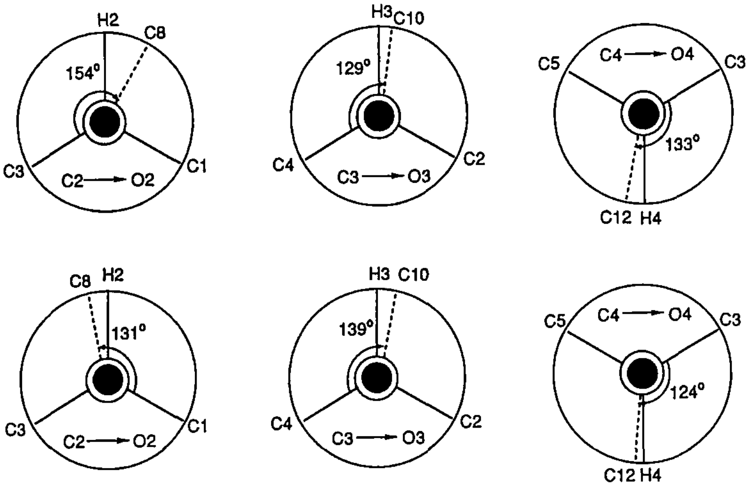

Fig. 3. Orientation of the acetate groups (Newman Projection) of molecule **A** (above) and molecule **B** in the crystal of methyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside.

parameters $Q = 0.557(6)$ Å, $\theta = 174.6(2)°$, and $\psi = 144.6(9)°$ for molecule **A** and 0.564(4) Å, 177.9(1)°, and 30.8(8)° for molecule **B**, respectively. The deviations of C-1 and C-4 from the plane defined by C-2, C-3, C-5, and O-5 are 0.6156(5) Å and 0.685(4) Å, in molecule **A**, and 0.641(6) Å and 0.678(5) Å, in molecule **B**, respectively.

The acetyl groups have the (*S*)-cis conformation with the C–O and C=O bonds eclipsed. This is the conformation most commonly observed in simple esters [19]. The acetyl groups are planar, with the nonhydrogen atoms deviating less than 0.01 Å from their mean plane. The orientation of the acetate groups is similar to that observed in many other peracetylated pyranose molecules, with the C=O groups syndiaxial to the C–H bond at the ring carbon atom to which the group is attached [20–23]. The orientation of the acetate groups with respect to the pyranose ring is shown in the Newman projection of Fig. 3. The carbon (acetate)–oxygen bond makes a dihedral angle of ca. 35° with the carbon (ring)–hydrogen bond. The calculations are based on nonhydrogen positions, the ring hydrogen positions were estimated assuming sp^3 hybridization of the carbon atoms. The acetoxy groups are so oriented that the C=O bond almost eclipses the exocyclic C–H bond, except in molecule **A**, where the acetoxy group on C-2 is midway between the eclipsed and staggered orientations with respect to the exocyclic C–H bond, with C-8–O-2–C-2–C-3 = 154.5(3)°.

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