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X-Ray structure of the (2,2,6,6-tetramethylpiperidin-1-oxyl-4-yl) 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside

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ABSTRACT

The crystal structure of (2,2,6,6-tetramethylpiperidin-1-oxyl-4-yl) 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside, $C_{23}H_{36}NO_{11}$, is orthorhombic, $P2_12_12_1$, with Z 4, a 6.207(1), b 14.219(1), and c 30.986(2) Å. It was solved by use of the MULTAN program and refined to a R_w value 0.044, for 2874 observed reflections. It has a head to tail arrangement, each piperidine heterocycle being located between the carbohydrate residues of each neighboring molecule.

INTRODUCTION

Nitroxide spin-label compounds have been frequently employed as tracers to study biological, medical, and chemical problems and particularly molecular motions in macromolecules. The structure of nitroxides themselves has been studied by X-ray crystallography[1], but to the best of our knowledge the molecular structure described herein, namely that of a spin-labeled carbohydrate, is the first one to be reported. This glucopyranoside was prepared in the natural abundance and in ^{13}C-enriched forms at C-1 and C-6 of the sugar residue for T_1 measurements[3]. The purpose was to test the possible use of the paramagnetic perturbation of ^{13}C-relaxation time to evaluate intramolecular distances in solution[4]. It is reasonable to consider that minimum-energy conformations in solution would not be completly different from conformations in the crystal, at least when solute–solvent interactions by hydrogen bonding are not involved. Consequently, internuclear distances and dihedral angles in the solid state could be taken as a first approximation for solution studies.

RESULTS AND DISCUSSION

The structure of (2,2,6,6-tetramethylpiperidin-1-oxyl-4-yl) 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**1**; for numbering of atoms, see Scheme 1) was solved by direct methods with the MULTAN program[5] which allowed the location of all the non-hydrogen atoms. The structure was refined by use of the XFLSN program with

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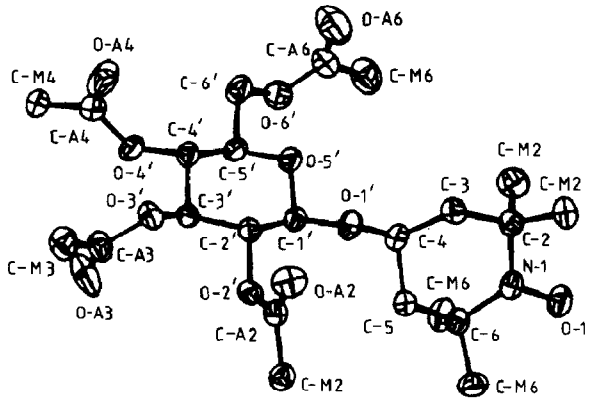

Scheme 1. Atomic notation and thermal ellipsoids.

TABLE I

Crystal and refinement data for (2,2,6,6-tetramethylpiperidin-1-oxyl-4-yl) 2,3,4,6-tetra-*O*-acetyl-*β*-D-gluco-pyranoside (1)

Formula	$C_{23}H_{36}NO_{11}$
Molecular weight	502.549
Space group	$P2_12_12_1$
a (Å)	6.207(1)
b (Å)	14.219(1)
c (Å)	30.986(2)
Cell volume (Å^3)	2736.61(2)
Z (molecules/cell)	4
Density $D_{calc.}$ (g·cm^{-3})	1.224
Crystal color and shape	orange, parallelepipedic
Radiation	Cukα (Ge monochromator)
Diffractometer	Enraf-Nonius CAD4
Scan speed (deg·min^{-1})	1.1
2*θ* Scan range (deg.)	$2<2\theta<60$
Scan mode	*θ*/2*θ*
Data collected	h, k, l (total = 2874)
Scan width (deg.)	1.1
Number of unique data	2874
Number of unique data with Fo > 2.5σ(Fo)	1989
Standard reflections	1 6 -4; -1 -1 -14 ; 1 0 -16
LS parameters	313
Data/parameters	7
R (Fo) (%)	6.6
R_w (Fo) (%)	4.4
R (F^2) (%)	6.9

anisotropic factors for C, N, and O atoms. At this level of refinement, Fourier difference maps showed significant electron densities in the positions of hydrogen atoms. They were introduced in the refinement (B = 1.5 B of adjacent carbon) but not refined. The final R_w [$R_w = \Sigma\omega(Fo-Fc)^2 / \Sigma_\omega Fo^2$] and R ($R = \Sigma|Fo-Fc|/\Sigma Fo$) values reached 0.044 and 0.066, respectively. The main crystal data and refinement parameters are shown in Table I, the final atomic positional and thermal parameters are listed in Table II (with e.s.d. in parentheses), and the thermal ellipsoids are shown in Scheme 1. Bond lengths and angles are reported in Tables III and IV, respectively.

In the crystal, the molecules are arranged antiparallel in the BC plan with a head-to-tail packing along the C direction (see Fig. 1). This arrangement is probably due to the overall shape of the molecule consisting of a big component (the acetylated sugar residue) and a small component (the tetramethylated piperidine ring). The glucopyranosyl ring is in the classical $^4C_1$ (D) chair form, but slightly distorted (Tables V and VI) with the acetate ester groups in the usual conformation, the carbonyl group eclipsing the geminal C–H bond[6]. The torsional angle C-4′–C-5′–C-6′–O-6′ (– 171.25°) corresponds to the usually more stable conformation of the hydroxymethyl group, also designated by *gt* (for O-5′–C-5′–C-6′–O-6′ and C-4′–C-5′–C-6′–O-6′)[7].

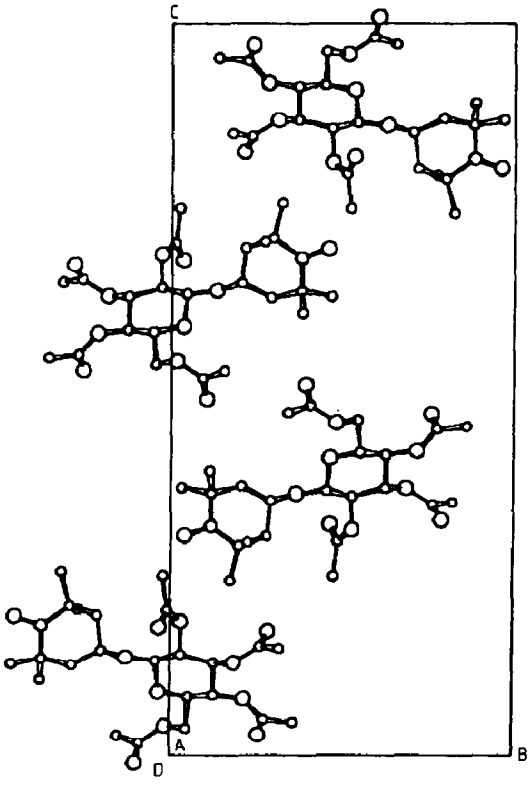

Fig. 1. Molecular packing in the crystal viewed down the *a* axis.

TABLE II

Atomic parameters and equivalent isotropic thermal parameters for **1**[a]

Atom	*x/a*	*y/b*	*z/c*	$B_{eq}(Å^2)$
N-1	5272(0)	6173(0)	1823(0)	6.17
O-1	4366(8)	5394(2)	1947(1)	8.79
C-2	5947(11)	6188(4)	1363(2)	6.12
C-3	7269(10)	7072(4)	1274(1)	6.08
C-4	6375(9)	7949(3)	1470(1)	5.40
C-5	6208(9)	7818(3)	1955(1)	5.22
C-6	4774(11)	7003(4)	2092(2)	6.00
C-M2A	3952(13)	6147(5)	1070(2)	9.30
C-M2B	7387(12)	5314(3)	1291(2)	8.37
C-M6A	2408(11)	7250(4)	2044(2)	7.90
C-M6B	5279(13)	6759(4)	2566(2)	7.80
O-1′	7887(6)	8683(2)	1376(1)	6.26
C-1′	6923(10)	9564(3)	1331(2)	5.34
C-2′	8704(9)	10300(3)	1412(1)	5.19
C-3′	7896(10)	11277(3)	1297(2)	5.22
C-4′	6970(11)	11279(4)	848(2)	5.83
C-5′	5216(11)	10527(4)	821(1)	5.86
O-5′	6216(7)	9647(2)	893(1)	5.97
O-2′	9040(6)	10291(2)	1872(1)	5.81
O-3′	9796(7)	11873(2)	1299(1)	6.50
O-4′	5855(7)	12173(2)	795(1)	6.79
C-6′	4163(13)	10472(4)	379(2)	8.47
C-A2′	10903(12)	9881(4)	2024(2)	6.30
O-A2′	12313(7)	9656(4)	1794(1)	9.37
C-M2′	10779(10)	9766(4)	2501(2)	7.16
C-A3′	9769(14)	12650(5)	1525(2)	7.88
C-M3′	11804(12)	13219(4)	1496(2)	9.39
O-A3′	8283(10)	12880(3)	1735(2)	12.79
C-A4′	6723(16)	12766(6)	502(2)	8.74
O-A4′	8200(13)	12610(4)	292(1)	15.13
C-M4′	5201(17)	13630(4)	465(2)	9.87
O-6′	2325(8)	9845(3)	415(1)	8.09
C-A6′	2278(20)	9085(6)	181(2)	9.92
C-M6′	455(15)	8446(5)	282(2)	10.92
O-A6′	3606(13)	8956(5)	−96(2)	15.01
H-3A	748	715	93	
H-3B	889	696	141	
H-4	473	805	134	
H-5A	536	844	211	
H-5B	780	771	209	
H-CM2A	280	565	120	
H-CM2A	311	682	108	
H-CM2A	425	597	73	
H-CM2B	669	471	145	
H-CM2B	788	528	95	
H-CM2B	899	545	143	
H-CM6A	201	753	168	
H-CM6A	202	782	227	
H-CM6A	141	663	211	
H-CM6B	715	666	260	
H-CM6B	474	727	281	
H-CM6B	435	610	265	
H-1′	556	973	155	

TABLE II (continued)

H-2′	1028	1000	125
H-3′	686	1148	160
H-4′	825	1124	61
H-5′	402	1065	115
H-CM2′	999	1038	267
H-CM2′	989	915	259
H-CM2′	1240	972	263
H-CM3′	1317	1272	149
H-CM3′	1191	1366	179
H-CM3′	1176	1363	120
H-CM4′	392	1347	24
H-CM4′	453	1377	79
H-CM4′	614	1423	35
H-C6′	374	1119	27
H-C6′	546	1015	16
H-CM6′	−17	863	60
H-CM6′	97	771	28
H-CM6′	−88	847	6

[a] $\times 10^4$ for N-1–O-A6′ and $\times 10^3$ for H-3A to H-CM6′. E.s.d. values in parentheses.

The piperidin ring has a chair-like conformation with a plane of symmetry. The only observed perturbation, as compared to a free nitroxide structure[8], seems to be a decreased C–N–C endocyclic angle (126 *vs.* 134°) and a small lenghtening of the N–O bond (1.30 *vs.* 1.26 Å). It is noteworthy that the α angle between the N–O bond and the plane defined by the three atoms C–N–C is not significantly modified (22.04 *vs.* 21°), the oxygen atom being 0.48 Å under this plane, and C-3 and C-5 above.

TABLE III

Bond lengths (Å) for **1**[a]

N-1–O-1	1.300 (3)	N-1–C-2	1.486 (6)
C-4–O-1′	1.434 (6)	N-1–C-6	1.477 (6)
O-1′–C-1′	1.395 (6)	C-2–C-3	1.526 (7)
C-1′–O-5′	1.431 (6)	C-2–C-M2	1.538 (8)
C-2′–O-2′	1.443 (5)	C-3–C-4	1.493 (6)
C-3′–O-3′	1.452 (6)	C-4–C-5	1.519 (7)
C-4′–O-4′	1.456 (6)	C-5–C-6	1.522 (7)
C-5′–O-5′	1.414 (6)	C-6–C-M6	1.517 (8)
O-2′–C-A2	1.378 (7)	C-1′–C-2′	1.543 (7)
O-3′–C-A3	1.308 (6)	C-2′–C-3′	1.520 (7)
O-4′–C-A4	1.352 (8)	C-3′–C-4′	1.507 (7)
C-6′–O-6′	1.452 (7)	C-4′–C-5′	1.528 (7)
C-A2–O-A2	1.174 (6)	C-5′–C-6′	1.521 (8)
C-A3–O-A3	1.175 (7)	C-A2–C-M2	1.489 (7)
C-A4–O-A4	1.146 (9)	C-A3–C-M3	1.503 (9)
O-6′–C-A6	1.302 (8)	C-A4–C-M4	1.554 (10)
C-A6–O-A6	1.205 (9)	C-A6–C-M6	1.484 (11)

[a] E.s.d. values in parentheses.

TABLE IV

Bond angles (degrees) for 1 [a]

O-1–N-1–C-2	114.6 (3)	C-4′–C-3′–O-3′	108.3 (5)
O-1–N-1–C-6	115.1 (3)	C-3′–C-4′–C-5′	108.6 (5)
C-2–N-1–C-6	126.1 (3)	C-3′–C-4′–O-4′	106.6 (4)
N-1–C-2–C-3	109.7 (4)	C-5′–C-4′–O-4′	105.4 (5)
N-1–C-2–C-M2	109.9 (4)	C-3–C-4	1.493 (6)
C-3–C-2–C-M2	110.9 (5)	C-4′–C-5′–C-6′	113.0 (5)
C-M2–C-2–C-M2	110.4 (5)	O-5′–C-5′–C-6′	106.5 (5)
C-2–C-3–C-4	114.5 (5)	C-1′–O-5′–C-5′	110.9 (4)
C-3–C-4–C-5	109.0 (49	C-2′–O-2′–C-A2	117.5 (4)
C-3–C-4–O-1′	106.4 (5)	C-3′–O-3′–C-A3	119.0 (5)
C-5–C-4–O-1′	109.6 (5)	C-4′–O-4′–C-A4	115.5 (5)
C-4–C-5–C-6	114.1 (5)	C-5′–C-6′–O-6′	107.5 (5)
N-1–C-6–C-5	109.2 (4)	O-2′–C-A2–O-A2	122.3 (6)
N-1–C-6–C-M6	108.4 (4)	O-2′–C-A2–C-M2	110.0 (6)
N-1–C-6–C-M6	109.3 (5)	O-A2–C-A2–C-M2	127.7 (7)
C-5–C-6–C-M6	111.3 (5)	O-3′–C-A3–C-M3	114.3 (6)
C-M6–C-6–C-M6	110.1 (6)	O-3′–C-A3–O-A3	122.8 (8)
C-4–O-1′–C-1′	113.2 (4)	C-M3–C-A3–O-A3	123.0 (7)
O-1′–C-1′–C-2′	106.6 (4)	O-4′–C-A4–O-A4	125.4 (9)
O-1′–C-1′–O-5′	107.5 (4)	O-4′–C-A4–C-M4	107.6 (7)
C-2′–C-1′–O-5′	108.5 (4)	O-A4–C-A4–C-M4	126.6 (9)
C-1′–C-2′–C-3′	110.2 (5)	C-6′–O-6′–C-A6	119.0 (8)
C-1′–C-2′–O-2′	105.0 (4)	O-6′–C-A6–C-M6	114.1 (9)
C-3′–C-2′–O-2′	106.6 (4)	O-6′–C-A6–O-A6	120.5 (11)
C-2′–C-3′–C-4′	110.1 (4)	C-M6–C-A6–O-A6	125.4 (9)
C-2′–C-3′–O-3′	105.3 (5)		

[a] E.s.d. values in parentheses.

The most interesting part of the structure from a carbohydrate chemist's point of view is certainly the conformation around the glycoside bond, *i.e.*, the values of the φ (H-1′–C-1′–O-1′–C-4) and ψ (C-1′–O-1′–C-4–H-4) torsional angles that correspond to the most flexible part of the molecule. The values of 37.48 and 29.71°, respectively, are to be compared to those reported for cellobiose octaacetate[6], 44.1 and 15.7°, respectively. These results are not very different and it is interesting to underline that, when dealing with such hydrophobic entities, it seems reasonable to consider this labeled sugar as a disaccharide model. This is of importance when this type of structure is used as molecular probe.

EXPERIMENTAL

The nitroxide-labeled carbohydrate crystallizes very easily and good crystals have been obtained from diethyl ether–petroleum ether mixtures (9/1, v/v) at room temperature or in the refrigerator (0–5°). They are deep orange parallelepipedes whose section range from 0.1 to 3 mm^2. Preliminary unit cell dimension and orthorhombic symmetry

TABLE V

Selected torsion angles[a]

H-1′–C-1′–O-1′–C-4	37.48
C-1′–O-1′–C-4–H-4	29.71
O-A2′–C-A2′–O-2′–C-2′	10.01
C-A2′–O-2′–C-2′–H-2′	−5.81
O-A3′–C-A3′–O-3′–C-3′	1.70
C-A3′–O-3′–C-3′–H-3′	−19.49
O-A4′–C-A4′–O-4′–C-4′	1.79
C-A4′–O-4′–C-4′–H-4′	−5.25
O-A6′–C-A6′–O-6′–C-6′	−8.56
C-A6′–O-6′–C-6′-H-6′a	120.36
C-A6′–O-6′–C-6′-H-6′b	−5.69
C-5′–O-5′–C-1′–C-2′	−65.09
O-5′–C-1′–C-2′–C-3′	55.19
C-1′–C-2′–C-3′–C-4′	−52.16
C-2′–C-3′–C-4′–C-5′	55.65
C-3′–C-4′–C-5′–O-5′	−63.07
C-4′–C-5′–O-5′–C-1′	69.16
O-5′–C-5′–C-6′–O-6′	71.13
C-4′–C-5′–C-6′–O-6′	−171.25
N-1–C-6–C-5–C-4	44.97
C-6–C-5–C-4–C-3	−59.45
C-5–C-4–C-3–C-2	58.37
C-4–C-3–C-2-N-1	−43.43
C-3–C-2–N-1–C-6	32.52
C-2–N-1–C-6–C-5	−33.46

[a] In degrees

(D_2^4) were determined by Weissenberg and Precession photographs. Cell parameters have been refined by least squares from angular positions of 25 reflections. The intensities of reflections ($2° < \theta < 60°$) (crystal size, 0.2 × 0.2 × 0.25 mm) were determined and periodically checked. No decrease in the intensity was observed during the data collection. The data were corrected for Lorentz and polarization factors, but not for absorption and extinction. Among the independent reflections, [$F_o > 2.5\sigma(F_o)$] were used for refinement of the structure parameters.

TABLE VI

Cremer–Pople puckering parameters

	α-D-*Glucopyranose ring*	*Piperidine ring*
Q	0.030 Å	0.035 Å
θ	173.11°	156.50°
ψ	81.00°	3.74°

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