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Note

X-ray diffraction and high-resolution NMR spectroscopic analysis of 2,4,7,8-tetra-*O*-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosono-1,5-lactone

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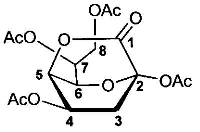
Abstract

The X-ray diffraction and high-resolution ^{1}H and ^{13}C NMR spectral data are reported for 2,4,7,8-tetra-*O*-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosono-1,5-lactone. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Kdo; 2,4,7,8-Tetra-*O*-acetyl-3-deoxy-α-D-manno-2-octulopyranosono-1,5-lactone; X-ray diffraction; ^{1}H and ^{13}C NMR spectroscopy

Kdo (3-deoxy-D-*mannno*-2-octulosonic acid) is a key component of the cell wall lipopolysaccharide (LPS) of Gram-negative bacteria. Kdo residues form the critical linkage between the polysaccharide and lipid A regions of LPS.[1] The syntheses of various Kdo derivatives have been reported for the preparation of Kdo-containing oligosaccharides.[2–5] Ulosonic acids including neuraminic acid, Kdn, and Kdo are known to form lactones in nature contributing to important chemical and biological properties.[6–8]



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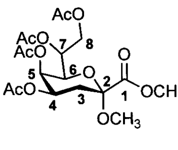

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2,4,7,8-Tetra-*O*-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosono-1,5-lactone (**1**) was synthesized by peracetylation of Kdo using acetic anhydride in pyridine according to general procedures.[9–11] Briefly, the reaction mixture of ammonium Kdo and acetic anhydride in pyridine was stirred at 40° C for 4 h. The mixture was evaporated to dryness, and the residue was purified by flash chromatography on silica gel using 5:1 toluene–diethyl ether. Lactone **1** (1 g) was dissolved in chloroform (5 mL), cyclohexane (6 mL) was added, and crystals (0.61 g) appeared within 12 h at room temperature. The absolute structure of lactone **1** was determined using X-ray diffraction analysis on an Enraf–Nonius CAD-4 diffractometer, and NMR spectroscopy utilized a Varian 500 MHz spectrometer. Structural differences between **1** and the related methyl(methyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosid)onate (**2**)[12] are examined.

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Table 1
Chemical shifts (ppm) and coupling constants (Hz) of the high-resolution ^{1}H NMR (499.7 MHz, CDCl$_3$) and ^{13}C NMR spectra (125.7 MHz, CDCl$_3$) of **1**

Group/atom no.	^{1}H NMR	^{13}C NMR
CH_3	2.08, 2.09, 2.12, 2.17	20.6 (C-2 Ac), 20.7 (C-4 and C-7 Ac), 21.0 (C-8 Ac)
1		165.2
2		93.0
3	2.20 (*J* 2.4, 14.7 Hz), 2.94 (*J* 9.5, 14.7 Hz)	37.7
4	5.21 (*J* 2.4, 9.5 Hz)	67.4
5	4.86	73.5
6	4.30 (*J* 9.3 Hz)	70.9
7	5.14 (*J* 2.4, 2.7, 9.5 Hz)	67.8
8	4.15 (*J* 3.0, 12.5 Hz), 4.64 (*J* 2.7, 12.5 Hz)	60.9
Carbonyl carbons		166.2 (C-2 Ac), 169.1 (C-7 Ac), 170.1 (C-4 Ac), 170.3 (C-8 Ac)

Table 2
Crystal data and structure refinement for compound **1**

Empirical formula	$C_{16}H_{20}O_{11}$
Formula weight	388.32
Crystal color	colorless
Crystal system	trigonal
Space group	$P3_2$
Unit cell dimensions	
a (Å)	8.843(2)
b (Å)	8.843(2)
c (Å)	20.558(6)
α (°)	90
β (°)	90
γ (°)	120
Z	3
D_{calc} (g cm^{-3})	1.389
F(000)	612
Crystal size (mm)	0.58 × 0.27 × 0.22
θ Range for data collection (°)	2.5–30.0
Limiting indices	$-10 \le h \le 10$, $-10 \le k \le 10$, $-28 \le l \le 28$
Reflections collected	10 770
Independent reflections	2688 ($R_{int} = 0.0482$)
Refinement method	full-matrix least-squares on F^2
Number of parameters	248
Goodness of fit on F^2	1.041
Final R indices $[I > 2\sigma(I)]$	$R_1 = 0.0380$, $wR_2 = 0.0973$
R indices (all data)	$R_1 = 0.0599$, $wR_2 = 0.1140$
Largest difference peak and hole	0.365 and -0.282 (e Å^{-3})

Table 3
Atomic coordinates (× 10^4) and equivalent isotropic displacement parameters (Å × 10^3)

Atom[a]	x	y	z	U_{eq}[b]
O(1)	3776(2)	12719(2)	2424(1)	45(1)
C(1)	4189(4)	12127(3)	1885(1)	47(1)
C(2)	2960(4)	10162(3)	1793(1)	42(1)
O(2)	5460(3)	13036(3)	1572(1)	69(1)
C(3)	3267(4)	9283(3)	2370(1)	47(1)
C(4)	2780(4)	9966(3)	2982(1)	44(1)
C(5)	2310(4)	11335(3)	2778(1)	43(1)
C(6)	749(4)	10475(3)	2325(1)	42(1)
O(3)	1179(3)	9716(2)	1788(1)	46(1)
C(7)	226(4)	11747(3)	2039(1)	44(1)
C(8)	−1097(4)	10956(4)	1498(2)	52(1)
O(4)	3311(3)	9573(3)	1210(1)	50(1)
C(9)	3150(5)	10303(4)	638(1)	56(1)
O(5)	2562(4)	11246(3)	607(1)	70(1)
C(10)	3862(7)	9757(6)	87(2)	83(1)
O(6)	4254(3)	10807(2)	3420(1)	49(1)
C(11)	4580(5)	9690(4)	3763(2)	58(1)
O(7)	3646(4)	8140(3)	3719(2)	84(1)
C(12)	6205(6)	10613(5)	4153(2)	75(1)
O(8)	−468(3)	12275(2)	2572(1)	50(1)
C(13)	−2(4)	13972(4)	2592(2)	56(1)
O(9)	907(5)	14976(3)	2192(2)	108(1)
C(14)	−846(6)	14387(5)	3133(2)	76(1)
O(10)	−2569(3)	9357(2)	1730(1)	48(1)
C(15)	−3542(4)	8207(4)	1272(1)	47(1)
O(11)	−3229(4)	8471(4)	703(1)	81(1)
C(16)	−5024(4)	6601(4)	1552(2)	54(1)

[a] Atom numbering corresponds to that of the ORTEP figure of Fig. 1.

[b] U_{eq} is defined as one-third of the trace of the orthogonalized U_{ij} tensor.

The ^{1}H and ^{13}C NMR spectra of **1** were completely assigned by using DQF-COSY, HMQC and HMBC (Table 1). A summary of the crystallographic data, data collection and structure-refinement parameters for **1** is presented in Table 2. The nonhydrogen atom coordinates and the equivalent temperature factors are reported in Table 3. The X-ray diffraction study of **1** clearly showed the crystalline product to contain a lactone ring (Fig. 1). The C–C bonds range from 1.484 to 1.547 Å (mean 1.517 Å), the C–O bonds are in the range 1.337–1.456 Å (mean 1.411 Å) and the C=O double bonds are in the range 1.182–1.199 Å (mean 1.192 Å). The bond lengths of C-3–C-4 and C-4–C-5 of **1** are 1.547 and 1.522 Å, respectively, while those of **2** are 1.52 and 1.49 Å, respectively.[12] The C–C–C angles range from 106.0 to 113.7° (mean 108.7°). The bond angles of O-3–C-2–C-3, C-2–C-3–C-4, C-5–C-4–C-3, C-6–C-5–C-4 and O-3–C-6–C-5 of **1** are 108.7, 106.3, 109.1, 108.2 and 108.5°, respectively, while those of **2** are 112, 110, 111, 108 and 111°, respectively.[12] These smaller bond angles are consistent with the more rigid, compact structure of the bicyclic lactone **1**. The NOESY spectrum of **1** showed an NOE between H-4 and both H-6 and H-3eq. In contrast, the NOESY spectrum of **2**, having no lactone ring, showed a single NOE between H-4 and H-6. The NOE between H-4 and H-3eq in **1** provides strong evidence that **1** contains a lactone ring. These NOE results agree with the proposed structure of **1** and are confirmed by X-ray diffraction analysis (Fig. 1).

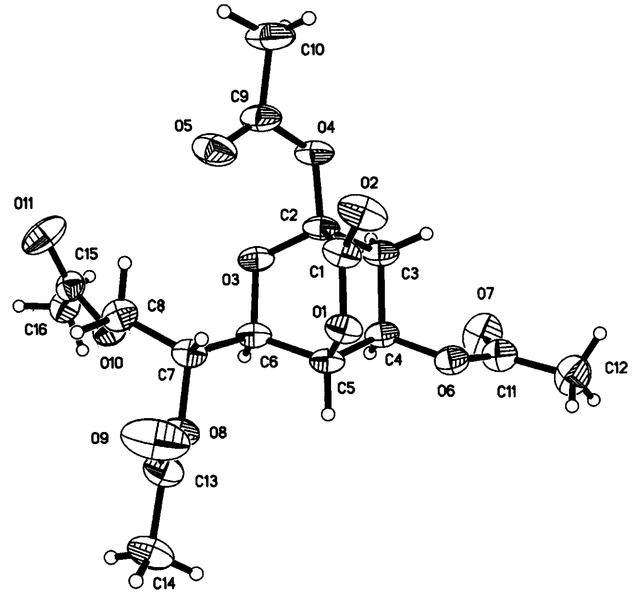

Fig. 1. Molecular structure of 2,4,7,8-tetra-*O*-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosono-1,5-lactone **1**. 50% probability thermal ellipsoids are shown for nonhydrogen atoms.

1. Supplementary material

Full crystallographic details, excluding structure features, have been deposited (Accession No. CCDC 149879) with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Tel.: +44 1223 336408; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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