Crystal structure of 4,7-di-O-methyl 8,9-O-isopropylidine Neu5Ac methyl ester methyl ketoside, $C_{18}H_{31}NO_9$

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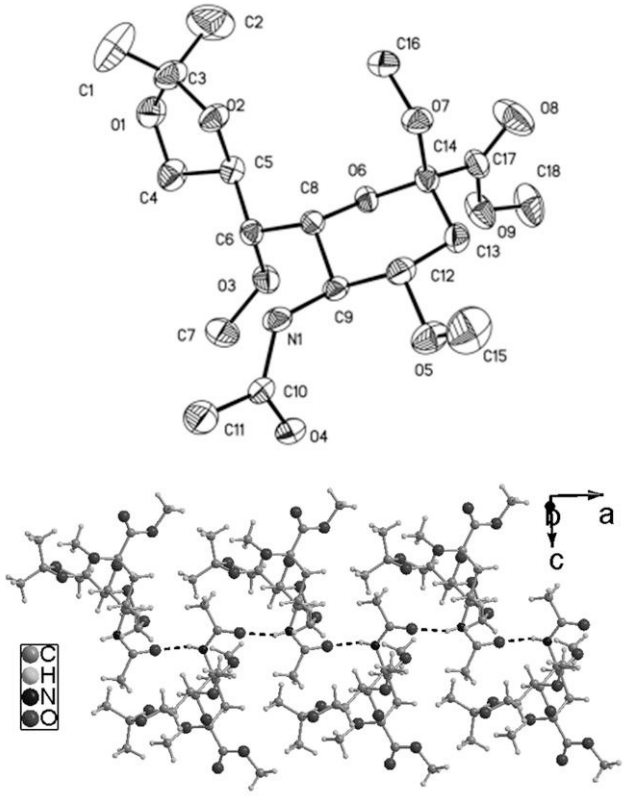

Abstract

$C_{18}H_{31}NO_9$, orthorhombic, $P2_12_12_1$ (no. 19), a = 9.113(2) Å, b = 15.047(3) Å, c = 15.575(3) Å, V = 2135.6 Å^3, Z = 4, $R_{gt}(F)$ = 0.0435, $wR_{ref}(F^2)$ = 0.1189, T = 293 K.

Source of material

Starting materials and solvents for synthesis were purchased commercially, except for 8,9-O-isopropylidine Neu5Ac methyl ester methyl ketoside, which was prepared according to reference [6]. A mixture of 8,9-O-isopropylidine Neu5Ac methyl ester methyl ketoside (4.0 g) was treated with the barium oxide (5.84 g) and barium hydroxide octahydrate (0.69 g) in dry dimethyl formamide (36 mL). After 10 min, methyl iodide (9.8 mL) was added, the reaction suspension was kept stirring for 45 hours at room temperature. The solids were filtered off and washed exhaustively with EtOAc. The filtrate was further extracted with EtOAc (60 mL) and 5 % NaCl solution (30 mL) and evaporated under reduced pressure, giving the product in a yield of 58.4 %. Colourless crystals were obtained by slow evaperation from the methanol solution containing the product.

Table 1. Data collection and handling.

Crystal:	colourless blocks, size 0.12×0.15×0.18 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.01 cm^{-1}
Diffractometer, scan mode:	Bruker APEX II CCD, ω and φ
$2\theta_{max}$:	52°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	11467, 4181
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3129
$N(param)_{refined}$:	267
Programs:	SHELXS-97 [7]

Experimental details

All H atoms on C atoms were generated geometrically and refined as riding atoms with d(C–H) = 0.96-0.98 Å, and U_{iso}(H) = 1.2 U_{eq}(C) for C atoms of CH_2 and CH groups and U_{iso}(H) = 1.5 U_{eq}(C) for C atoms of CH_3 groups. The hydrogen atom of the N1 atom has been added on the basis of the Q peak, the bond H–N has been constrained with 'dfix' command in a distance of 0.82 Å, with a deviation of 0.01. In addition, the 'PART' command has been used to deal the disorder of O1 atom.

Discussion

Sialic acids are a family comprising of over 40 kinds of derivatives of *N*-acetylneuraminic acid (Neu5Ac), with structural diversity generated by substitutions at the carbon positions 4, 5, 7, 8 and 9 [1,2], which can take part in a large variety of biological functions including recognition phenomena [3]. As consequence, they are usually exploited as anti-influenza drugs and substrates of detecting influenza [4,5]. In this work, we present a derivative, namely 4,7-di-O-methyl 8,9-O-isopropylidine Neu5Ac methyl ester methyl ketoside. Crystal structure and spectroscopic characterization are described herein. The unit cell of this compound contains four 4,7-di-O-methyl 8,9-O-isopropylidine Neu5Ac methyl ester methyl ketoside molecules. In this molecular structure, there are two heterocycles, including a five number 1,3-dioxolane ring and a six number pyran cycle. In the crystal structure, there are intermolecular hydrogen bonds between N1 and O4 (symmetry code: x-½, -y+½, -z+1) with the distance N1···O4 = 2.081(13) Å and the angles N1–H99···O4 = 161(3)°, which interlink molecules to form a 1D supramolecular structure. The absorption bands at 2941, 2838, 1750, 1225 cm^{-1} in the IR spectra of this compound are attributed to the characteristic vibrations of the C–H bond of the methyl group, the C–H bond of the methoxyl group, the C=O bond of the carbonyl group, the C–O bond of the ether group. In addition, two strong absorption at 1655 and 1570 cm^{-1} are assigned to the acylamide group.

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Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	*x*	*y*	*z*	U_{iso}
H(1A)	4*a*	–0.2147	0.4359	0.6737	0.204
H(1B)	4*a*	–0.1551	0.4881	0.5938	0.204
H(1C)	4*a*	–0.2468	0.5378	0.6642	0.204
H(2A)	4*a*	–0.1051	0.4681	0.8196	0.198
H(2B)	4*a*	–0.1298	0.5705	0.8077	0.198
H(2C)	4*a*	0.0284	0.5336	0.8248	0.198
H(4A)	4*a*	0.2334	0.6251	0.6597	0.080
H(4B)	4*a*	0.1561	0.5771	0.5815	0.080
H(5)	4*a*	0.2476	0.4973	0.7383	0.059
H(6)	4*a*	0.2703	0.4284	0.5686	0.052
H(7A)	4*a*	0.5739	0.5470	0.5417	0.123
H(7B)	4*a*	0.4067	0.5545	0.5190	0.123
H(7C)	4*a*	0.4921	0.4663	0.4997	0.123
H(8)	4*a*	0.2415	0.3123	0.6679	0.048
H(9)	4*a*	0.5365	0.3108	0.6089	0.050
H(11A)	4*a*	0.3010	0.2435	0.3790	0.109

Table 2. continued.

Atom	Site	*x*	*y*	*z*	U_{iso}
H(11B)	4*a*	0.4520	0.2101	0.3433	0.109
H(11C)	4*a*	0.4063	0.3099	0.3319	0.109
H(12)	4*a*	0.3524	0.1642	0.6507	0.059
H(13A)	4*a*	0.6004	0.2223	0.7456	0.063
H(13B)	4*a*	0.4924	0.1464	0.7734	0.063
H(15A)	4*a*	0.5955	0.0180	0.5757	0.151
H(15B)	4*a*	0.4273	0.0384	0.5832	0.151
H(15C)	4*a*	0.5229	0.0286	0.6663	0.151
H(16A)	4*a*	0.0718	0.2547	0.8544	0.094
H(16B)	4*a*	0.1425	0.3376	0.8096	0.094
H(16C)	4*a*	0.1953	0.3086	0.9012	0.094
H(18A)	4*a*	0.7830	0.3832	0.9274	0.150
H(18B)	4*a*	0.7288	0.2917	0.9637	0.150
H(18C)	4*a*	0.6445	0.3793	0.9870	0.150
H(99)	4*a*	0.305(2)	0.254(2)	0.515(2)	0.054(8)

Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	Occ.	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	4*a*		–0.1760(4)	0.4917(3)	0.6542(4)	0.067(2)	0.134(3)	0.208(6)	0.027(2)	–0.035(3)	–0.011(4)
C(2)	4*a*		–0.0638(5)	0.5220(3)	0.7972(3)	0.157(4)	0.122(3)	0.118(3)	0.034(3)	0.062(3)	–0.012(3)
C(3)	4*a*		–0.0397(3)	0.5122(2)	0.7014(2)	0.058(2)	0.058(2)	0.095(2)	0.017(1)	0.015(2)	0.000(2)
C(4)	4*a*		0.1635(3)	0.5794(2)	0.6436(2)	0.064(2)	0.048(1)	0.088(2)	0.002(1)	–0.004(2)	0.006(1)
C(5)	4*a*		0.2069(2)	0.4895(2)	0.6805(2)	0.046(1)	0.048(1)	0.053(2)	0.002(1)	–0.005(1)	0.001(1)
C(6)	4*a*		0.3110(2)	0.4343(2)	0.6265(2)	0.039(1)	0.048(1)	0.043(1)	–0.005(1)	–0.006(1)	0.007(1)
C(7)	4*a*		0.4826(4)	0.5152(2)	0.5388(2)	0.075(2)	0.088(2)	0.083(2)	–0.009(2)	0.021(2)	0.028(2)
C(8)	4*a*		0.3366(2)	0.3423(2)	0.6633(1)	0.032(1)	0.050(1)	0.038(1)	–0.004(1)	–0.0021(9)	0.004(1)
C(9)	4*a*		0.4386(2)	0.2838(1)	0.6098(1)	0.029(1)	0.052(1)	0.044(1)	–0.0002(9)	0.0005(9)	–0.001(1)
C(10)	4*a*		0.4732(3)	0.2815(2)	0.4534(2)	0.040(1)	0.060(2)	0.049(2)	0.015(1)	0.003(1)	0.001(1)
C(11)	4*a*		0.4017(3)	0.2593(2)	0.3693(2)	0.067(2)	0.095(2)	0.056(2)	0.015(2)	–0.004(2)	–0.013(2)
C(12)	4*a*		0.4488(2)	0.1931(2)	0.6521(2)	0.041(1)	0.046(1)	0.060(2)	0.002(1)	0.005(1)	0.001(1)
C(13)	4*a*		0.4985(3)	0.2036(2)	0.7448(2)	0.048(1)	0.049(1)	0.060(2)	0.005(1)	–0.001(1)	0.016(1)
C(14)	4*a*		0.4063(2)	0.2711(1)	0.7940(1)	0.044(1)	0.043(1)	0.049(1)	–0.004(1)	–0.003(1)	0.011(1)
C(15)	4*a*		0.5221(5)	0.0492(2)	0.6080(3)	0.124(3)	0.058(2)	0.119(3)	0.017(2)	0.005(3)	–0.020(2)
C(16)	4*a*		0.1609(3)	0.2878(2)	0.8466(2)	0.053(1)	0.070(2)	0.066(2)	–0.001(1)	0.014(1)	0.010(1)
C(17)	4*a*		0.4838(3)	0.2919(2)	0.8786(2)	0.057(1)	0.061(1)	0.046(2)	–0.004(1)	–0.006(1)	0.016(1)
C(18)	4*a*		0.6982(4)	0.3489(3)	0.9429(2)	0.104(3)	0.111(3)	0.085(2)	–0.032(2)	–0.053(2)	0.025(2)
N(1)	4*a*		0.3860(2)	0.2755(1)	0.5221(1)	0.028(1)	0.069(1)	0.046(1)	–0.0018(9)	0.0005(9)	–0.006(1)
O(2)	4*a*		0.0684(2)	0.4458(1)	0.6858(1)	0.0465(9)	0.0469(9)	0.076(1)	0.0087(8)	0.0074(8)	0.0002(8)
O(3)	4*a*		0.4458(2)	0.4827(1)	0.6218(1)	0.047(1)	0.071(1)	0.064(1)	–0.0148(8)	–0.0025(9)	0.0238(9)
O(4)	4*a*		0.6025(2)	0.3044(1)	0.4578(1)	0.0366(9)	0.091(1)	0.061(1)	0.0083(9)	0.0090(8)	0.010(1)
O(5)	4*a*		0.5520(2)	0.1402(1)	0.6063(1)	0.061(1)	0.053(1)	0.083(1)	0.0088(9)	0.012(1)	–0.0094(9)
O(6)	4*a*		0.3956(2)	0.35234(9)	0.74825(9)	0.0433(8)	0.0436(8)	0.0387(8)	–0.0027(7)	–0.0056(7)	0.0042(7)
O(7)	4*a*		0.2696(2)	0.2318(1)	0.8086(1)	0.0454(9)	0.053(1)	0.064(1)	–0.0075(8)	0.0079(8)	0.0054(8)
O(8)	4*a*		0.4485(3)	0.2623(2)	0.9461(1)	0.098(2)	0.192(3)	0.057(1)	–0.049(2)	–0.014(1)	0.035(2)
O(9)	4*a*		0.6054(2)	0.3374(1)	0.8684(1)	0.079(1)	0.097(2)	0.060(1)	–0.038(1)	–0.029(1)	0.023(1)
O(1)	4*a*	0.7	0.028(1)	0.5946(4)	0.681(1)	0.073(3)	0.052(3)	0.092(6)	0.025(2)	0.010(3)	0.014(3)
O(1A)	4*a*	0.3	0.006(2)	0.584(2)	0.641(3)	0.064(6)	0.12(1)	0.10(2)	0.027(6)	–0.003(8)	0.06(1)

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