ELSEVIER

www.elsevier.nl/locate/carres

Carbohydrate Research 331 (2001) 343–346

CARBOHYDRATE RESEARCH

Note

Preparation, single-crystal X-ray diffraction and high-resolution NMR spectroscopic analyses of *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) trimethylammonium bromide

Eugenia Skorupowa,[a] Maria Kurszewska,[a] Antoni Konitz,[a,b] Wiesław Wojnowski,[b] Andrzej Wiśniewski[a,*]

[a]*Department of Chemistry, Sugar Chemistry Group, Gdańsk University, Sobieskiego 18, 80-952 Gdańsk, Poland*
[b]*Technical University, Narutowicza 11/12, 80-952 Gdańsk, Poland*

Received 21 November 2000; accepted 22 January 2001

Dedicated to the memory of Professor Janusz Sokołowski

Abstract

Preparation of *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)trimethylammonium bromide as the unique N-glycosylated quaternary salt derived from trialkylamine is described. The structure of the compound was elucidated by ^{1}H and ^{13}C NMR spectroscopy and by single-crystal X-ray analysis as well. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Trialkylammonium salt; ^{1}H NMR spectroscopy; ^{13}C NMR spectroscopy, X-ray crystallography

Quaternary ammonium salts are interesting compounds with a broad spectrum of antimicrobial activity, including anti-bacterial, fungicidal and virucidal activities.[1–7] Their practical use as essential components for many commercial products of daily use is well known and described.[8] Only one *N*-glycosylammonium salt derived from trialkylamine was isolated in small yield and insufficiently identified (on the basis of physical properties only) by Karrer and Smirnoff.[9] Extending our studies on the synthesis,[10] transformation with sodium methoxide[11] and crystallographic study of *N*-D-glycopyranosylpyridinium and related compounds,[12,13] we now describe the preparation and crystal structure of *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-trimethylammonium bromide.

Reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with a 30% ethanolic solution of trimethylamine carried out under the procedure of Karrer and Smirnoff[9] afforded inter alia *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)trimethylammonium bromide. The compound obtained (see Section

* Corresponding author: Tel.: +48-58-3415271; fax: +48-58-3410357.
E-mail address: andrzejw@chemik.chem.univ.gda.pl (A. Wiśniewski).

PII: S0008-6215(01)00037-4

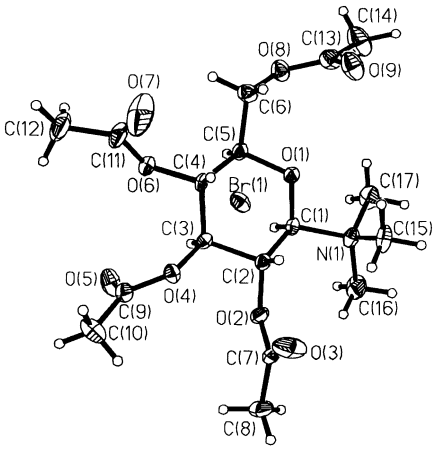

Fig. 1. The X-ray structure of *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)trimethylammonium bromide showing 50% probability displacement for ellipsoids.

Table 1
Crystal data and structure refinement for *N*-(tri-*O*-acetyl-D-glucopyranosyl)trimethylammonium bromide

Empirical formula	$C_{17}H_{28}BrNO_9$
Formula weight	470.31
Temperature (K)	293(2)
Wavelength (Å)	0.71073
Crystal system, space group	orthorhombic, $P2_12_12_1$
Unit cell dimensions	
a (Å)	8.476 (2)
b (Å)	10.945 (3)
c (Å)	24.370 (5)
V (Å^3)	2260.8 (9)
Z	4
D_{calc} (Mg/m^3)	1.382
Absorption coefficient (mm^{-1})	1.862
F(000)	976
Crystal size (mm)	$0.3\times0.4\times0.4$
Theta range for data collection (°)	1.67–30.06
Index ranges	$0\le h\le11$, $0\le k\le15$, $0\le l\le34$
Reflections collected/unique	3673/3673
Reflections [$I>2\sigma>(I)$]	963
Completeness to $\theta=30.06$	98.1%
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	3673/0/253
Goodness-of-fit on F^2	1.008
Final *R* indices [$I>2\sigma(I)$]	$R_1=0.0342$, $wR_2=0.0764$
R indices (all data)	$R_1=0.3127$, $wR_2=0.1469$
Absolute structure parameter	−0.02 (2)
Largest difference peak and hole (e Å^{-3})	0.387 and −0.622

Table 2
Atomic coordinates ($\times10^4$) and equivalent isotropic displacement parameters (Å$^2\times10^3$) for *N*-2,3,4,6-(tetra-*O*-acetyl-β-D-glucopyranosyl)trimethylammonium bromide [a]

	x	*y*	*z*	U_{eq}
Br(1)	−2128(1)	−2306(1)	2670(1)	70(1)
O(1)	−3967(6)	−1141(5)	1228(2)	45(2)
O(2)	−6913(7)	−3296(5)	1713(2)	52(2)
O(3)	−8830(9)	−3102(8)	1099(4)	119(4)
O(4)	−5393(6)	−4591(5)	908(2)	46(2)
O(5)	−4102(10)	−5960(6)	1427(3)	82(2)
O(6)	−2186(7)	−3961(4)	742(2)	49(2)
O(7)	−1975(15)	−3573(9)	−135(3)	168(5)
O(8)	−1013(8)	−178(6)	1006(3)	66(2)
O(9)	−2620(10)	1135(6)	581(3)	89(2)
N(1)	−5954(9)	−547(6)	1827(3)	51(2)
C(1)	−4985(9)	−1639(6)	1622(3)	37(2)
C(2)	−5862(8)	−2672(7)	1355(3)	40(2)
C(3)	−4618(9)	−3612(7)	1177(3)	36(2)
C(4)	−3383(9)	−3056(6)	812(3)	40(2)
C(5)	−2690(10)	−1916(6)	1084(3)	45(2)
C(6)	−1631(11)	−1178(8)	713(4)	57(3)
C(7)	−8408(12)	−3529(8)	1512(5)	66(3)
C(8)	−9324(11)	−4271(9)	1904(4)	87(3)
C(9)	−5023(12)	−5736(9)	1082(4)	57(3)
C(10)	−5990(14)	−6669(9)	774(5)	90(4)
C(11)	−1639(13)	−4201(10)	240(5)	82(4)
C(12)	−522(14)	−5245(10)	239(5)	110(4)
C(13)	−1595(12)	921(10)	908(4)	67(3)
C(14)	−936(15)	1878(9)	1292(5)	108(4)
C(15)	−6949(12)	−25(7)	1388(3)	70(3)
C(16)	−6972(13)	−927(8)	2303(4)	86(3)
C(17)	−4816(11)	376(8)	2039(4)	78(3)

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

1) was investigated by ^{1}H and ^{13}C NMR spectroscopy. The high-resolution ^{1}H NMR spectroscopy of this compound indicates the β configuration at the anomeric carbon atom ($J_{1,2}$) and the $^4C_1$-D conformation of the sugar moiety ($J_{2,3}$, $J_{3,4}$, $J_{4,5}$). X-ray crystallography (Fig. 1) confirmed this proposed structure.

A summary of the crystallographic data, data collection and structure refinement are given in Table 1. Positional parameters of nonhydrogen atoms and their equivalent isotropic temperature factors are given in Table 2.

The value of bond lengths and angles determined in this work agree well with those expected.[14] In the crystal, the six-membered pyranoid ring occurs in the $^4C_1$-D conformation with all substituents equatorial (pucker-

ing parameters: $Q = 0.596$ (8), $\Theta = 6.4$ (7)[15]). The C-1–N-1 bond length of the title compound is longer (Table 3) than the mean value [1.485(9) Å] given in the International Tables for X-ray Crystallography (1993). Selected torsion angles describing the chair conformation of the sugar moiety and spatial orientation of aglycon for this compound are collected in Table 4.

Table 3
Selected bond lengths (Å) for *N*-2,3,4,6-(tetra-*O*-acetyl-β-D-glucopyranosyl)-trimethylammonium bromide

Bond length	
N-1–C-1	1.534(9)
C-1–C-2	1.501(10)
C-2–C-3	1.535(10)
C-3–C-4	1.502(10)
C-4–C-5	1.530(10)
O-1–C-1	1.402(9)
O-2–C-2	1.421(9)
O-4–C-3	1.418(9)
O-6–C-4	1.428(8)

Table 4
Selected torsion angles (°) for *N*-2,3,4,6-(tetra-*O*-acetyl-β-D-glucopyranosyl)trimethylammonium bromide

Torsion angles	
C-5–O-1–C-1–N-1	164.6(6)
O-1–C-1–C-2–O-2	178.2(6)
N-1–C-1–C-2–C-3	178.5(6)
C-1–C-2–C-3–C-4	−55.7(8)
C-1–O-1–C-5–C-6	−173.4(6)
C-1–O-1–C-5–C-4	64.2(8)
C-2–C-3–C-4–C-5	52.4(8)
C-3–C-4–C-5–C-6	−170.7(7)
O-6–C-4–C-5–C-6	72.2(8)

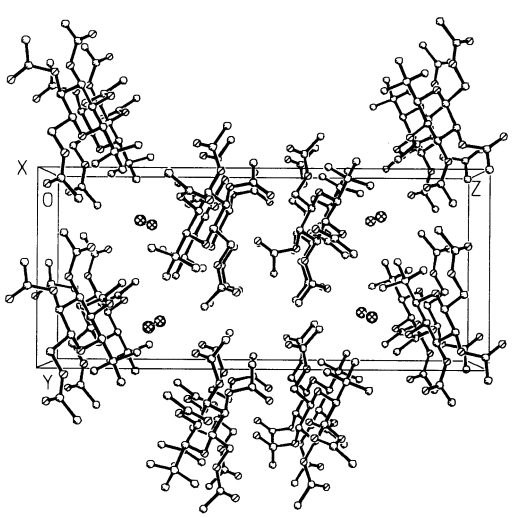

Fig. 2. View of cell packing along the *b*-direction of *N*-2,3,4,6-(tetra - *O* - acetyl - β - D - glucopyranosyl)trimethylammonium bromide.

A view of the cell packing along the *b*-direction is demonstrated in Fig. 2.

The shortest contacts (in Å) of the neighboring *N*-2,3,4,6-(tetra-*O*-acetyl-β-D-glucopyranosyl)trimethylammonium cations to bromine anion (Br-1) are as follows (the symmetry operation for transformation of given atoms are in parentheses): H-1A, 2.670; H-5A, 3.097: H-8B $(1+x,\ y,\ z)$, 3.092; H-17C $(-1-x,\ -0.5+y,\ 0.5-z)$, 2.769; H-8C $(-1-x,\ 0.5+y,\ 0.5+z)$, 2.773; N-1, 4.293(7); N-1 $(-1-x,\ -0.5+y,\ 0.5-z)$, 4.091(7); and O-1, 4.050(6).

1. Experimental

General procedures.—^{1}H 400 MHz and ^{13}C 100 MHz were recorded on an a Mercury-400BB spectrometer with D_2O as a solvent and acetone as the external standard.

X-ray crystallography.—X-ray measurements were carried out on a KUMA KM-4 four circle diffractometer. The structures were solved by direct methods with the SHELXS program[16] and refined employing full-matrix least-squares method implemented in the SHELXL program.[17] Anisotropic displacement coefficients were applied to all nonhydrogen atoms. Hydrogen atoms of sugar moiety were refined in idealized positions with isotropic factors 1.2 times the equivalent isotropic temperature factor of adjacent C atoms. Water molecules were refined as rigid bodies with an H–O distance of 0.82 and H–H distance of 1.3 Å. The atomic scattering factors were taken from the International Tables for X-ray Crystallography (1993). Molecular illustrations were drawn using the ORTEP program.[18]

Preparation of N-*2,3,4,6-(tetra*-O-*Acetyl-β*-D-*glucopyranosyl)trimethylammonium bromide.*—2,3,4-Tri-*O*-acetyl-α-D-glucopyranosyl bromide (2.4 g, 5.8 mmol) was dissolved in a 30% ethanolic solution of trimethylamine (5 mL), and the reaction mixture was kept at rt according to the procedure of Karrer and Smirnoff.[9] *N*-2,3,4,6-(tetra-*O*-Acetyl-β-D-glucopyranosyl)trimethylammonium bromide was isolated by careful crystallization from the

multicomponent mixture thus obtained. Recrystallization from EtOH delivered the title compound (0.83 g, 30%): mp (dec) 173 °C, (lit.[9], 192 °C); $[\alpha]_D^{20}$ + 8.7° (*c*. 1.5, water), (lit.[9], $[\alpha]_D^{18}$ + 10.2°, (*c*. 3.19, water)); ^{1}H NMR (D_2O): δ 3.23 (s, 9 H, 3 × CH_3 of aglycone), 5.20 (d, 1 H, H-1, $J_{1,2}$ 8.8 Hz), 5.66 (t, 1 H, H-2, $J_{2,3}$ 8.8 Hz), 5.49 (t, 1 H, H-3, $J_{3,4}$ 8.4 Hz), 5.27 (t, 1 H, H-4, $J_{4,5}$ 8.8 Hz), 4.31 (ddd, 2 H, H-5, $J_{5,6a}$ 2.8, $J_{5,6b}$ 3.2 Hz), 4.32 (dd, 1 H, H-6a, $J_{6a,6b}$ 6.0 Hz), 4.34 (dd, 1 H, H-6b), 2.11–2.19)12 H, 4 × *O*Ac); ^{13}C NMR (D_2O, 100 MHz): δ 93.45 (C-1), 68.12 (C-2), 73.97 (C-3), 67.27 (C-4), 74.89 (C-5), 61.77 (C-6), 20.61, 20.49, 20.40, 20.35 (4 × CH_3 of *O*Ac), 173.66, 172.74, 172.53, 171.72 (4 × C=O of *O*Ac). Anal. Calcd for $C_{17}H_{28}BrNO_9$ (470.31): C, 43.41; H, 6.00; N, 3.00. Found: C, 43.42; H, 6.07; N, 3.00.

2. Supplementary material

Full crystallographic details, excluding structure features, have been deposited (deposition no. CCDC 152349) with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from The Director, 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).

Acknowledgements

This work was partially financed by grant DS /8361-4-0134-0.

References

1. Jones, G. In *Pyridines and their Benzo Derivatives in Comprehensive Heterocyclic Chemistry*, *Part 2A*; Katrizky, A. R.; Rees, Ch., Eds.; Pergamon: Oxford, 1984; Vol. 2, pp. 395–510.
2. Śliwa, W. *N-Substituted Salts of Pyridine and Related Compounds*; WSP: Czestochowa, Poland, 1996; pp. 3–427 ISBN 83-7098-198-4, and references cited therein.
3. Pernak, J. *Ind. J. Heterocycl. Chem.* **1997**, *7*, 97–100.
4. Pernak, J.; Arndt, A.; Brycki, B. *Arch. Pharm. Med. Chem.* **1997**, *330*, 253–258 and references cited therein.
5. Urbanik, E.; Zabielska-Matejuk, J.; Skrzypczak, A.; Pernak, J. *Mater. Org.* **1997**, *31*, 247–263 and references cited therein.
6. Skrzypczak, A.; Brycki, B.; Mirska, I.; Pernak, J. *Eur. J. Med. Chem.* **1997**, *32*, 661–668.
7. Pernak, J.; Zabielska-Matejuk, J.; Urbanik, E. *Holzforschung* **1998**, *52*, 249–254 and references cited therein.
8. Yates, F. S. In *Comprehensive Heterocyclic Chemistry*, *Part 2A*; Katrizky, A. R.; Rees, Ch., Eds. Pyridines and their benzoderivatives: Applications. Pergamon: Oxford, 1984; Vol. 2, pp. 511–524.
9. Karrer, P.; Smirnoff, A. P. *Helv. Chim. Acta* **1921**, *4*, 817–820.
10. Dmochowska, B. *Ph.D. Thesis*; University of Gdansk: Poland, 1999.
11. Skorupowa, E.; Dmochowska, B.; Madaj, J.; Kasprzykowski, F.; Sokołowski, J.; Wiśniewski, A. *J. Carbohydr. Chem.* **1998**, *17*, 49–59.
12. Dmochowska, B.; Bednarczyk, D.; Nowacki, A.; Konitz, A.; Wojnowski, W.; Wiśniewski, A. *Carbohydr. Res.* **2000**, *329*, 703–707.
13. Wojnowski, W.; Konitz, A.; Dmochowska, B.; Nowacki, A.; Wiśniewski, A. *Carbohydr. Res.* (submitted).
14. Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, S1–S19.
15. Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358.
16. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467–473.
17. Sheldrick, G. M. *SHELXL; Program for the Refinement of Crystal Structures*; University of Göttingen: Germany, 1997.
18. Johnson, C. K. *ORTEP; Report ORNL-5138*; Oak Ridge National Laboratory: Oak Ridge, TN, USA, 1976.