ELSEVIER

www.elsevier.nl/locate/carres

Carbohydrate Research 330 (2001) 431–435

CARBOHYDRATE
RESEARCH

Note

Molecular and crystal structures of N-(β-D-galactopyranosyl)pyridinium bromide and its per-O-acetylated derivative

Barbara Dmochowska,[a] Andrzej Nowacki,[a] Wiesław Wojnowski,[b] Antoni Konitz,[a,b]
Andrzej Wiśniewski[a,]*

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

Received 13 July 2000; received in revised form 13 November 2000; accepted 16 November 2000

Dedicated to Professor Gerard Descotes on the occasion of his 70th birthday

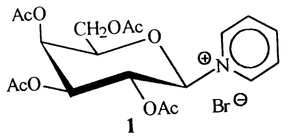
Abstract

^{1}H NMR spectroscopy and X-ray diffraction data are described for N-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)pyridinium bromide and N-(β-D-galactopyranosyl)pyridinium bromide. X-ray crystallography revealed that the O-acetylated salt crystallizes with two molecules of water and one molecule of ethanol. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Pyridinium salt; ^{1}H NMR; X-ray crystallography

Pyridinium salts with N-alkyl, N-aryl or N-acyl substituents belong to a large and important group of organic compounds.[1] The X-ray structures for many of them were determined.[2] It was documented that the pyridinium salts can crystallize as mono-,[3] di-[4] and trihydrates.[5]

N-Glycosylpyridinium salts can be obtained in the reaction of per-O-acetyl-glycopyranosyl bromide with dry pyridine.[6a–c,7] Both anomers are present in the post-reaction mixture. The title compounds represent a special case of molecules with a cationic aglycon in which the reverse anomeric effect is observed. Influence of this effect on conformational equilibria of these compounds in a solution was discovered by Lemieux,[7] and all results obtained before 1995 were summarized by Perrin.[8] These salts undergo hydrolysis independent of pH in the range of 4.4–10.5 pH units,[9] enzymatic hydrolysis,[10] O-glycosidation and intramolecular cyclization (competitive reactions),[11] and photohydration.[12] Crystal structures of these compounds are unknown. In this article we describe the molecular and crystal structures of N-(β-D-galactopyranosyl)pyridinium bromide (**2**) and its per-O-acetylated derivative (**1**).

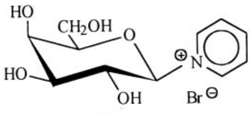


1

---

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

PII: S0008-6215(00)00301-3



2

The reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide with dry pyridine according to Fischer and Raske[6a] affords predominantly the β anomer of the pyridium salt **1**.[10a]

The high resolution ^{1}H NMR spectrum of **1** confirmed the β anomeric configuration and the $^4C_1$-D conformation for the sugar moiety. Unrepeatable results for the elemental analysis for **1** prompted us to an X-ray analysis, despite of the rather poor quality of the crystals. As seen in Fig. 1, **1** crystallizes with two molecules of water and one molecule of ethanol. The summary of crystallographic data, data collection and structure refinement for **1** is given in Table 1. The crystallographic analysis of **1** showed rather short C-5–C-6 bond length [1.44(12) Å]. The poor quality crystal probably explains this striking and incredible value. Bromide ion, ethanol and two water molecules in the crystal of **1** are involved in hydrogen bonds of which only one between the water molecules is rather strong [O-23–O-24 distance 2.635 Å and angle 134° at H atom]. The hydrogen bond parameters are

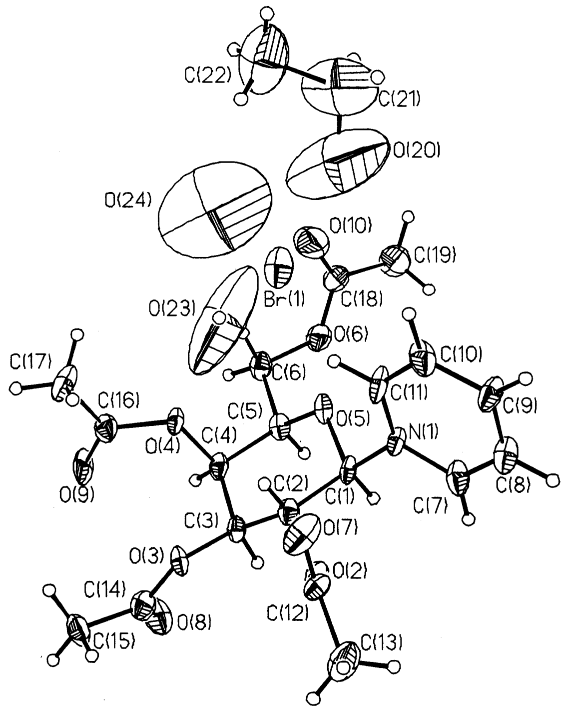


Fig. 1. The X-ray structure of *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)pyridinium bromide (**1**) showing 50% probability displacement for ellipsoids.

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

	1	**2**
Empirical formula	$C_{21}H_{34}BrNO_{12}$ ($C_{19}H_{24}BrNO_9 \cdot 2H_2O + C_2H_5OH$)	$C_{11}H_{16}BrNO_5$
Formula weight	572.40	322.16
Temperature (K)	223(2) (liquid nitrogen)	293(2)
Wavelength (Å)	0.71073	0.71073
Crystal system, space group	monoclinic, $P2_1$	tetragonal, $P4_12_12$
Unit cell dimensions		
a (Å)	10.394(2)	9.9260(10)
b (Å)	12.188(4)	9.9260(10)
c (Å)	10.929(3)	26.146(5)
β (°)	94.22(2)	
V (Å^3)	1380.8(6)	2576.0(6)
Z, D_{calcd} (Mg/m^3)	2, 1.377	8, 1.661
Absorption coefficient (mm^{-1})	1.546	3.204
F(000)	596	1312
Crystal size (mm)	0.2 × 0.3 × 0.5	0.3 × 0.3 × 0.5
Theta Range for data collection (°)	1.87–26.99	2.19–30.06
Index ranges	$-13 \le h \le 13$, $0 \le k \le 15$, $-11 \le l \le 13$	$0 \le h \le 13$, $-9 \le k \le 9$, $0 \le l \le 36$
Reflections collected/unique	5328/3140 [$R_{int} = 0.0613$]	4029/3735 [$R_{int} = 0.1197$]
Completeness to (**1**)$\theta = 26.99$ (%) (**2**)$\theta = 30.06$	99.6	98.3
Refinement method	full-matrix least-squares on F^2	full-matrix least-squares on F^2
Data/restraints/parameters	3140/12/303	3735/12/205
Goodness-of-fit on F^2	0.979	1.007
Final *R* indices [for 1375 (**1**) and 1826 (**2**) reflections with $I > 2\sigma(I)$]	$R_1 = 0.0763$, $wR_2 = 0.1714$	$R_1 = 0.0299$, $wR_2 = 0.0760$
R indices (all data)	$R_1 = 0.2222$, $wR_2 = 0.2227$	$R_1 = 0.1413$, $wR_2 = 0.0979$
Absolute structure parameter	0.03(3)	0.045(10)
Largest difference peak and hole (e Å^{-3})	1.240 and −0.681	0.517 and −0.948

Table 2
Hydrogen bond parameters for **1** and **2** with H···A < r(A) + 2.000 Å and < DHA 110°

Donor (D–H)	Distance (Å) (D–H)	Distance (Å) (H···A)	Angle (°) (D–H–A)	Distance (Å) (D···A)	Acceptor (A)
*Compound **1***					
O-20–H-20	0.82	2.423	161.3	3.21(4)	O-24
O-23–H-23A	0.82	2.623	153.6	3.38(2)	Br-1
O-23–H-23B	0.82	2.04	135.0	2.69(4)	O-24
O-24–H-24A	0.82	2.545	140.0	3.22(3)	O-10
*Compound **2***					
O-2–H-2	0.82	2.39	171.7	3.21(3)	Br-1
O-3–H-4	0.82	2.54	145.8	3.25(3)	Br-1
O-4–H-4	0.82	2.15	151.3	2.90(4)	O-6
O-4–H-4	0.82	2.29	111.5	2.70(4)	O-3
O-6–H-6	0.82	2.48	160.8	3.27(3)	Br-1

given in Table 2. In order to check for the C-5–C-6 bond length value mentioned above, we decided to perform the X-ray analysis on the deacetylated compound. Treatment of *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)pyridinium bromide (**1**) with a 3% aqueous solution of hydrogen bromide afforded the pure β anomer of the *O*-deacetylated salt **2**, which turned out to be the appropriate compound for the purpose. This compound was earlier obtained by Sinnott[10a] under the Lemieux and Morgan procedure[6b] but its ^{1}H NMR spectrum was not described.

The high resolution ^{1}H NMR spectrum of **2** confirmed the β anomeric configuration and the $^4C_1$-D conformation for the sugar moiety. Crystal structure for **2** is presented in Fig. 2 and the summary of crystallographic data, data collection and structure refinement is given in Table 1.

The C-5–C-6 bond length in **2**, for good quality crystals, is 1.517 Å which is a standard value. The C-1–N-1 bond length of **2** (1.482 Å) is between the values of well known analogues i.e. *N*-methylpyridinium iodide [1.46(2) Å][13] and *N*-[3-(adenin-9-yl)propyl]-3-carbamoylpyridinium bromide hydrobromide dihydrate [1.491(9) Å][4] or *N*-[3-(adenin-9-yl)-propyl]-3-carbamoylpyridinium bromide trihydrate [1.496(7) Å].[5] The same bond of **1** (per-*O*-acetylated derivative) is longer [1.521(11) Å] than those cited above.[†] The selected bond lengths for **1** and **2** are summarized in Table 3. The important dihedral angles for **1** and **2** are given in Table 4.

The pyridinium ring in the molecules studied is slanted toward the heterocyclic oxygen atom of the pyranoid ring [torsion angle O-5–C-1–N-1–C-11 is 43.4° for **1** and 39.8° for **2**]. The values of bond lengths and angles

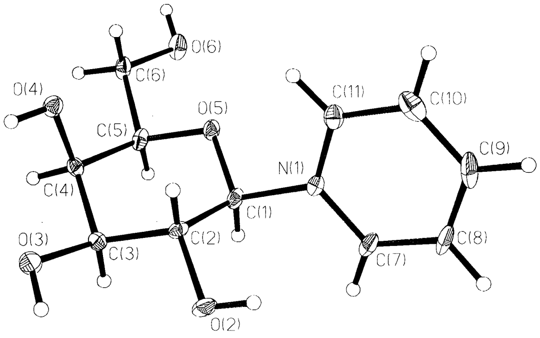


Fig. 2. The X-ray structure of *N*-(β-D-galactopyranosyl)pyridinium bromide (**2**) showing 50% probability displacement for ellipsoids.

Table 3
Selected bond lengths (Å) for **1** and **2**

Bond	Length (Å) for compound	
	1	**2**
C-1–N-1	1.521(11)	1.482(4)
C-1–C-2	1.532(12)	1.527(4)
C-2–C-3	1.531(12)	1.518(5)
C-3–C-4	1.513(12)	1.529(5)
C-4–C-5	1.514(12)	1.516(5)
C-5–C-6	1.441(12)	1.517(5)
O-5–C-1	1.409(10)	1.390(4)
O-5–C-5	1.446(10)	1.456(4)

[†] It is worthy to mention that the mean value of Csp^3–N^+ bond length in substituted pyridinium compounds taken from

Table 4
Torsion angles (°) for **1** and **2**

Dihedral angle	Angle (°) for compound **1**	**2**
O-5–C-1–C-2–O-2	178.8(6)	−179.9(3)
N-1–C-1–C-2–O-2	−68.2(8)	−61.9(3)
N-1–C-1–C-2–C-3	172.0(7)	179.4(3)
O-2–C-2–C-3–O-3	67.8(9)	67.0(4)
C-1–C-2–C-3–O-3	−173.9(7)	−172.8(3)
C-1–C-2–C-3–C-4	−50.3(10)	−54.1(4)
O-3–C-3–C-4–O-4	46.9(9)	53.0(3)
C-2–C-3–C-4–O-4	−71.4(9)	−68.9(4)
C-2–C-3–C-4–C-5	48.7(10)	52.0(4)
C-1–O-5–C-5–C-4	59.8(9)	59.0(3)
O-4–C-4–C-5–C-6	−53.8(9)	−51.1(4)
C-3–C-4–C-5–C-6	−173.4(7)	−172.7(3)
C-3–C-4–C-5–O-5	−52.5(9)	−53.1(4)
C-4–C-5–C-6–O-6	−170.6(7)	−178.4(3)
O-5–C-1–N-1–C-11	43.4(10)	39.8(4)

determined in this work, except for the C-5–C-6 bond length in **1**, agree well with those reported by Allen et al.[14] In the crystal, **1** and **2** show both six-membered pyranoid rings in $^4C_1$-D conformation with one axial substituent at C-4 (puckering parameters: $Q = 0.559(8)$, $\Theta = 6.9(9)°$ and $Q = 0.574(3)$, $\Theta = 4.7(4)°$ for **1** and **2**, respectively).[15]

Previous studies of protonated *N*-glycosylimidazoles and -pyrimidines[6b,16,17] showed that the positive charge on the nitrogen atoms linked to the anomeric center provides a strong driving-force for the aglycon to adopt the equatorial orientation. The same situation occurs with the salts presently studied, where the nitrogen atom formally bears a positive charge. The sugar moieties of **1** and **2** adopt a nearly ideal $^4C_1$-D conformation in solution and in the solid state as well, and the cationic aglycons are in the energetically preferred equatorial orientation.

1. Experimental

General methods.—A Varian Unity Plus 500 MHz and a Mercury-400BB 400 MHz spectrometers were used with D_2O as a solvent and TMS or acetone as an external standard, and 2D COSY technique at temperature of 25 °C.

X-ray crystallography.—X-ray data were measured on a KUMA KM-4 four circle diffractometer. The structures were solved by direct methods with the SHELXS program[18] and refined employing full-matrix least-square methods implemented in the SHELXL program,[19] with anisotropic displacement coefficients for all non-hydrogen atoms. Hydrogen atoms for **2** were refined with individual isotropic temperature factors. Common distances for C(sp^3)–H and C(sp^2)–H to 0.963 and 0.969 Å, respectively were used in refinement. Hydrogen atoms of O–H groups were refined at 0.82 Å from oxygen atoms with tetrahedral angle at the vertex atom. Hydrogen atoms of the sugar moiety for **1** were refined in idealized positions with isotropic factors 1.2 times the equivalent isotropic temperature factor of the adjacent C atom. Ethanol and water molecules were refined as rigid with C–C distance of 1.52 Å, C–O distance of 1.43 Å, H–O distance of 0.82 Å and H–H (not bonded) distance of 1.3 Å. The atomic scattering factors were taken from the International Tables for X-ray Crystallography (1993). Molecular illustrations for two compounds were drawn using the ORTEP program.[20]

N-*(2,3,4,6-Tetra*-O-*acetyl-β*-D-*galactopyranosyl)pyridinium bromide* (**1**).—2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide[21] (10 g, 24.3 mmol) and phenol (3.7 g, 39.3 mmol) were dissolved in dry pyridine (20.6 g, 21.02 mL) and the reaction mixture was kept at rt. After 7 days the solvent was evaporated and the crude product was extracted with water. The aq solution was evaporated under diminished pressure to a dark oil, then decolorized with charcoal in boiling aq solution. Next, the charcoal was filtered off and the solution was concentrated to a thick syrup (8 g), which was crystallized from acetone–CCl_4 system and recrystallized from EtOH giving pure **1** (3 g, 25%), mp 176–178 °C, (lit.,[10a] 187–188 °C), $[\alpha]_D^{20} = +16.7°$ (*c* 1.5, water), (lit.,[10a] $[\alpha]_D^{20} = +25°$ (*c* 2, $CHCl_3$)); ^{1}H NMR (D_2O) δ: 9.04–8.08 (m, 5 H, Py); 6.08 (d, 1 H, $J_{1,2}$ 8.8 Hz, H-1), 5.34 (t, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 5.44 (dd, 1 H, $J_{3,4}$ 1.5 Hz, H-3), 5.56 (t, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 4.52 (t, 1 H, $J_{5,6a}$ 6.1, $J_{5,6b}$ 5.4 Hz, H-5), 4.20 (d, 2 H, H-6a, H-6b), 2.16-1.82 (12 H, 4 × *O*Ac). Anal. Calcd for $C_{19}H_{24}BrNO_9 \cdot 2\ H_2O + EtOH$ (572.40): C, 44.06; H, 5.99; N, 2.45. Found: C, 44.80; H, 5.10; N, 2.56, (lit.,[10a] C, 46.15; H, 4.9; N, 2.95 for $C_{19}H_{24}BrNO_9$).

*N-(β-*D*-Galactopyranosyl)pyridinium bromide* (**2**).—Compound **1** (0.65 g, 1.3 mmol) was dissolved in a 3% aq solution of HBr (65 mL). The mixture was conditioned at 45 °C for 24 h. Next the solution was evaporated to a dense oil. Crystallization from 10:1 EtOH–EtOAc gave the expected compound (0.37 g, 70%), mp 175–176 °C, (lit.,[10a] 164–165 °C) $[\alpha]_D^{20} = +150°$ (c 1.5, water) (lit.,[10a] $[\alpha]_D^{20} = +141°$ (c 2, water)); ^{1}H NMR (D_2O) δ: 9.10–8.12 (m, 5 H, Py); 5.78 (d, 1 H, $J_{1,2}$ 8.8 Hz, H-1), 3.86 (t, 1 H, $J_{2,3}$ 9.2 Hz, H-2), 3.96 (dd, 1 H, $J_{3,4}$ 3.4 Hz, H-3), 4.16 (dd, 1 H, $J_{4,5}$ 0.4 Hz, H-4), 4.14 (dd, 1 H, $J_{5,6a}$ 7.6, $J_{5,6b}$ 4.4 Hz, H-5), 3.95 (dd, 1 H, $J_{6a,6b}$ 12.4 H-6a), 3.88 (dd, 1 H, H-6b), Anal. Calcd for $C_{11}H_{16}BrNO_5$ (322.13): C, 41.01; H, 4.95; N, 4.35. Found: C, 41.00; H, 4.90; N, 4.20, (lit.,[10a] C, 41.4; H, 5.25; N, 4.45).

2. Supplementary material

Full crystallographic details, excluding structure features, have been deposited (deposition no. CCDC 151046 for **1** and CCDC 151047 for **2**) with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from The Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Acknowledgements

This work was partially supported by the Polish Research Council (KBN) under grant DS/8242-4-0096-9.

References

1. Śliwa, W. *N-Substituted Salts of Pyridine and Related Compounds*; WSP: Częstochowa, Poland, 1996 ISBN 83-7098-198-4.
2. (a) Van Havere, W.; Lenstra, A. T. H.; Geise, H. J.; Van den Berg, G. R.; Benschop, H. P. *Acta Crystallogr., Sect. B* **1982**, *38*, 1635–1637. (b) Weber, H.; Pant, J.; Liedigk, M.; Wimderlich, H. *Chem. Ber.* **1981**, *114*, 1455–1463. (c) Buncel, E.; Keum, S. R.; Cygler, M.; Varughese, K. I.; Birnbaum, G. *Can. J. Chem.* **1984**, *62*, 1628–1639. (d) Chweh, A. Y.; DeBernardis, J. F.; Siuda, J. F.; Rondan, N. G.; Abola, J. E.; Abraham, D. J. *J. Med. Chem.* **1984**, *27*, 825–830. (e) Oleksyn, B.; Stadnicka, K. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1985**, *41*, 743–746. (f) Lewinski, K.; Stadnicka, K.; Oleksyn, B. *J. Crystallogr. Spectrosc. Res.* **1990**, *20*, 397–401. (g) Kamenar, B.; Vickovic, I.; Bruvo, M. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1986**, *42*, 1818–1821. (h) Ishida, T.; Itoh, M.; Doi, M.; Inoue, M. *Chem. Pharm. Bull.* **1986**, *34*, 4899–4909. (i) Chen, X. -M.; Mak, T. C. W. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1994**, *50*, 1805–1807.
3. (a) Vongbupnimit, K.; Noguchi, K.; Okuyama, K. *Acta Crystallogr., Sect.C: Cryst. Struct. Commun.* **1995**, *51*, 1940–1941. (b) Miura, M.; Takanohashi, Y.; Habata, Y.; Akabori, S. *J. Chem. Soc., Perkin Trans 1*, **1995**, 719–724; *Tetrahedron Lett.* **1994**, *35*, 8213–8216. (c) Hider, R. C.; Taylor, P. D.; Walkinshaw, M.; Wang, J. L.; Van der Helm, D. *J. Chem. Res. Synop.* **1990**, *10*, 316–317. (d) Paradies, H. H.; Habben, F. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1993**, *49*, 744–747. (e) Chen, X. -M.; Mak, T. C. W. *J. Mol. Struct.* **1990**, *221*, 265–269.
4. Johnson, P. L.; Frank, J. K.; Paul, I. C. *J. Am. Chem. Soc.* **1973**, *95*, 5377–5385.
5. Johnson, P. L.; Maier, C. A.; Paul, I. C. *J. Am. Chem. Soc.* **1973**, *95*, 5370–5377.
6. (a) Fischer, E.; Raske, K. *Chem. Ber.* **1910**, *43*, 1750–1753. (b) Lemieux, R. U.; Morgan, A. *Can. J. Chem.* **1965**, *43*, 2205–2213 and 2214–2221. (c) Hosie, L.; Marshall, P.; Sinnott, M. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1121–1131.
7. Lemieux, R. U.; Morgan, A. *J. Am. Chem. Soc.* **1963**, *85*, 1889–1890.
8. Perrin, Ch. L. *Tetrahedron* **1955**, *51*, 11901–11935.
9. (a) Huang, X.; Surry, C.; Hiebert, T.; Bennet, A. J. *J. Am. Chem. Soc.* **1995**, *117*, 10614–10621. (b) Zhu, J.; Bennet, A. J. *J. Am. Chem. Soc.* **1998**, *120*, 3887–3893.
10. (a) Sinnott, M. L.; Withers, S. G. *Biochem. J.* **1974**, *143*, 751–762. (b) Jones, C. C.; Sinnott, M. L.; Souchard, I. J. L. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1191–1198. (c) Withers, S. G.; Jullien, M.; Sinnot, M. L.; Viratelle, O. M.; Yon, J. M. *Eur. J. Biochem.* **1978**, *87*, 249–256.
11. Skorupowa, E.; Dmochowska, B.; Madaj, J.; Kasprzykowski, F.; Sokołowski, J.; Wiśniewski, A. *J. Carbohydr. Chem.* **1998**, *17*, 49–59.
12. Glarner, F.; Acar, B.; Etter, I.; Damiano, T.; Acar, E. A.; Bernardinelli, G.; Burger, U. *Tetrahedron* **2000**, *56*, 4311–4316.
13. Lalancette, R.; Furey, W.; Costanzo, J.; Hemmes, P.; Jordan, F. *Acta Crystallogr., Sect. B* **1978**, *34*, 2950–2953.
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. Lemieux, R. U. *Pure Appl. Chem.* **1971**, *25*, 527–548.
17. Paulsen, H.; Györgydeák, Z.; Friedmann, M. *Chem. Ber.* **1974**, *107*, 1590–1613.
18. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467–473.
19. Sheldrick, G. M. *SHELXL; Program for the Refinement of Crystal Structures*; University of Göttingen: Germany, 1997.
20. Johnson, C. K. *ORTEP; Report ORNL-5138*; Oak Ridge National Laboratory: Oak Ridge, TN, 1976.
21. Conchie, J.; Levvy, G. A. *Methods Carbohydr. Chem.* **1963**, *2*, 335.