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Glycosylamines of 4,6-*O*-butylidene-α-D-glucopyranose: synthesis and characterization of glycosylamines, and the crystal structure of 4,6-*O*-butylidene-*N*-(*o*-chlorophenyl)-β-D-glucopyranosylamine

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Abstract

A total of nine glycosylamines of 4,6-*O*-butylidene-α-D-glucopyranose were synthesized using primary amines having various groups in their ortho- or para-positions. Among these, six are monoglycosylamines, including one primary glycosylamine, and three are bis-glycosylamines. All these compounds were characterized by ^{1}H, ^{1}H–^{1}H COSY, ^{1}H–^{13}C COSY and ^{13}C NMR spectroscopy and FTIR spectra. The FAB mass spectra provided the molecular weights of the products by exhibiting the corresponding molecular ion peaks. The crystal structure of 4,6-*O*-butylidene-*N*-(*o*-chlorophenyl)-β-D-glucopyranosylamine revealed the C-1 glycosylation, the β-anomeric nature, and the $^{4}C_{1}$ chair conformation of the saccharide unit in the product. In the lattice two types of dimers exist. While one type of dimer is formed through O–H···O type of interactions, the other type is formed via C–H···O type of interactions. In the direction of these C–H···O type of interactions, the dimeric units are connected to form a chain. © 2002 Published by Elsevier Science Ltd.

Keywords: Glycosylamines; 4,6-*O*-Butylidene-α-D-glucopyranose; 4,6-*O*-Butylidene-*N*-(*o*-chlorophenyl)-β-D-glucopyranosylamine; Single-crystal X-ray diffraction

1. Introduction

Glycosylamines are important in carbohydrate enzymology. Some of these are considered to be inhibitors of glycosidases.[1] Reactions that occur between the sugars and the amines under physiological conditions have been reviewed.[2] X-ray crystal structures in the literature reveal that glycosylamines can exist as Schiff bases (open-chain imino compounds)[3,6,8–10] or as glycosylamines (cyclic structures).[3–7,11] Our group recently reported 4,6-*O*-ethylidene-α-D-glucopyranose-based monoglycosylamines and the complexing ability of one of these with alkali, alkaline earth and some post-transition metal ions[12,13] and also those based on 4,6-*O*-benzylidene-α-D-glucopyranose[14,15] and thereby demonstrated for the first time that the glycosylamines derived using substituted aromatic amines can enhance the metal-ion binding characteristics of the corresponding saccharide. Further, our group recently reported the structures of the products of cis-VO_2^+, cis-MoO_2^{2+}, and trans-UO_2^{2+} with glycosyl imines[16] possessing the saccharide –C-1–N=C– moiety. Therefore, in continuation with our ongoing efforts, we report here the synthesis and characterization of a series of 4,6-*O*-butylidene-α-D-glucopyranose-based mono- and bis-glycosylamines and the crystal structure of 4,6-*O*-butylidene-*N*-(*o*-chlorophenyl)-β-D-glucopyranosylamine.

2. Experimental

D-Glucose was procured from Aldrich Chemical Co., amines from Lancaster Synthesis Ltd., 1,2-dibro-

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moethane from Spectrochem Pvt. Ltd, and butyraldehyde from Fluka Chemical Co. 4,6-*O*-Butylidene-α-D-glucopyranose and 2,2′-[1,2-ethanediylbis(thio)]bisbenzeneamine were synthesized as per the reported procedures.[17,18] All solvents were purified and dried immediately before use. Elemental analysis was carried out on a CE instruments Flash EA 1112 series, and FTIR spectra were recorded on Nicolet Magna IR 550. The FAB mass spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer data system using argon/xenon (6 Kv, 10 mA) as the FAB gas. The accelerating voltage was 10 kV, and the spectra were recorded at rt with *m*-nitrobenzyl alcohol (NBA) as the matrix. ^{1}H NMR spectra were recorded on a Varian VXR 300S. ^{13}C, $^{1}H-^{1}H$, and $^{1}H-^{13}C$ COSY spectra were recorded on a Bruker Avance DRX 500 spectrometer. 'BUY' refers to the butylidene moiety of the 4,6-*O*-protection.

*General method for the preparation of glycosylamines of 4,6-*O*-butylidene-α-D-glucopyranose.*—To an ethanolic solution of 4,6-*O*-butylidene-α-D-glucopyranose (**1**) (10 mL, 0.48 g, 2.051 mmol) a corresponding amine was added and refluxed for a required period of time. As reported in Table 1, in some of the reactions the product was separated out as a solid, and in some reactions the product was obtained after concentrating the reaction mixture. In either case the product was separated by filtration and purified by necessary solvents as given in Table 1. A catalytic amount of anhyd $ZnCl_2$ (0.006 g, 0.004 mmol) was used in the case of reactions leading to the products **2**–**5** and **7**. Some relevant reaction parameters of the syntheses are given in Table 1.

4,6-O-Butylidene-N-(o-carboxyphenyl)-β-D-glucopyranosylamine (**2**).—(0.410 g, 57%); mp 132–134 °C; IR (KBr); 3347 (b) ν(O–H) and ν(N–H), 2962 (s) and 2878 (s) ν(C–H), 1685 (s) ν(C=O), 1586 (s) δ(N–H), 1523 (s) ν(C=C), 1388 (s) ν(C–O), 1086 (s) δ(C–O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 0.881 (t, 3 H, CH_3 of BUY), 1.306–1.559 (m, 4 H, 2 CH_2 of BUY), 3.186–3.205 (m, 2 H, H-2, H-3), 3.386–3.449 (m, 3 H, H-4, H-6), 4.004–4.022 (m, H, H-5), 4.556 (t, H, CH of BUY), 4.705 (d, H, $^{3}J_{H\text{-}1-H\text{-}2}$ 8.4 Hz, H-1), 5.289 (d, H, 3-OH), 5.475 (d, H, 2-OH), 6.660–7.945 (m, 4 H, Ar-H), 8.392 (d, H, NH), 12.775 (b, H, COOH); ^{13}C NMR (DMSO-d_6): δ 84.2 (C-1), 74.5 (C-2), 80.4 (C-3), 73.8 (C-4), 67.7 (C-5), 66.9 (C-6), 101.4 (CH unit of BUY), 36.0 (CH_2 unit of BUY), 17.1 (CH_2 unit of BUY), 13.9 (CH_3 unit of BUY), 111.4–149.5 (Ar-6 C), 169.8 (COOH); FABMS: m/z 353 $[M]^+$; Anal. Calcd for $C_{17}H_{23}NO_7$: C, 57.78; H, 6.56; N, 3.96. Found: C, 57.26; H, 6.89; N, 4.19.

4,6-O-Butylidene-N-(p-carboxyphenyl)-β-D-glucopyranosylamine (**3**).—(0.51 g, 70%); mp 138–140 °C; IR (KBr); 3354 (b) ν(O–H) and ν(N–H), 2963 (s) and 2878 (s) ν(C–H), 1689 (s) ν(C=O), 1611 (s) δ(N–H), 1537 (s) ν(C=C), 1393 (s) ν(C–O), 1078 (s) δ(C–O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 0.879 (t, 3 H, CH_3 of BUY), 1.305–1.426 (m, 2 H, CH_2 of BUY), 1.490–1.555 (m, 2 H, CH_2 of BUY), 3.102–3.473 (m, 5 H, H-2, H-3, H-4, H-6), 3.961–4.014 (m, H, H-5), 4.552 (t, H, CH of BUY), 4.649 (d, H, $^{3}J_{H\text{-}1-H\text{-}2}$ 8.8 Hz, H-1), 5.00–5.400 (b, 3 H, 2-OH, 3-OH, COOH), 6.73 (d, 2 H, Ar-H), 7.02 (d, H, NH), 7.691 (d, 2 H, Ar-H); ^{13}C NMR (DMSO-d_6): δ 84.6 (C-1), 62.1–82.1 (C-2–C-6), 101.4 (CH unit of BUY), 36.0 (CH_2 unit of BUY), 17.1 (CH_2 unit of BUY), 13.9 (CH_3 unit of BUY), 112.4, 112.6 (Ar-2 C), 131.0, 131.2 (Ar-2 C), 151.1, 119.0 (Ar-2 C), 167.5 (COOH); FABMS: m/z: 353 $[M]^+$; Anal. Calcd for $C_{17}H_{23}NO_7$: C, 57.78; H, 6.56; N, 3.96. Found: C, 57.98; H, 6.62; N, 4.04.

Table 1
Reaction conditions employed for the synthesis of compounds **2**–**10**

Compound	Reaction time (h)	Molar ratio (4,6-*O*-butylidene-α-D-glucopyranose–corresponding amine)	Solvent system for purification	Yield (%)
2	2	1:1	[a]	57
3	0.5	1:1	[a]	70
4	3	1:1	[a]	33
5	3	1:1	[a]	40
6 [b]	48	atm. of ammonia	[c]	53
7	3.5	1:1	[a]	66
8 [d]	1.5	1:0.5	[c]	70
9 [d]	1.5	1:0.5	[c]	54
10 [d]	3	1:0.5	[c]	80

[a] Cold ethanol–diethyl ether.
[b] The product is separated out in the atmosphere of NH_3 at 0–5 °C.
[c] Ethanol–diethyl ether.
[d] The product is separated out in the reaction mixture under hot conditions.

4,6-O-Butylidene-N-(o-fluorophenyl)-β-D-glucopyranosylamine (**4**).—(0.21 g, 33%); mp 164–166 °C; IR (KBr); 3465 (b) ν(O–H) and ν(N–H), 2967 (s) and 2878 (s) ν(C–H), 1624 (s) δ(N–H), 1531 (s) ν(C=C), 1394 (s) ν(C–O), 1092 (s) δ(C–O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 0.880 (t, 3 H, CH_3 of BUY), 1.306–1.429 (m, 2 H, CH_2 of BUY), 1.445–1.558 (m, 2 H, CH_2 of BUY), 3.115–3.460 (m, 5 H, H-2, H-3, H-4, H-6), 3.996–4.053 (m, H, H-5), 4.537–4.588 (m, 2 H, CH of BUY and H-1), 5.172 (d, H, 2-OH), 5.255 (d, H, 3-OH), 5.930 (d, H, NH), 6.616–7.072 (m, 4 H, Ar-H); ^{13}C NMR (DMSO-d_6): δ 85.3 (C-1), 73.52, 73.46 (C-2, C-3), 80.5 (C-4), 67.7 (C-5), 66.8 (C-6), 101.3 (CH unit of BUY), 36.0 (CH_2 unit of BUY), 17.1 (CH_2 unit of BUY), 13.8 (CH_3 unit of BUY), 114.0–151.8 (Ar-6 C); FABMS: *m/z:* 327 $[M]^+$; Anal. Calcd for $C_{16}H_{22}FNO_5$: C, 58.71; H, 6.77; N, 4.28. Found: C, 57.71; H, 7.10; N, 3.79.

4,6-O-Butylidene-N-(o-chlorophenyl)-β-D-glucopyranosylamine (**5**).—Single crystals suitable for X-ray diffraction were grown by slow evaporation of the saturated ethanolic solution of the product at 4 °C (0.27 g, 40%); mp 170–172 °C; IR (KBr); 3492 (b) ν(O–H) and ν(N–H), 2969 (s) and 2874 (s) ν(C–H), 1600 (s) δ(N–H), 1515 (s) ν(C=C), 1379 (s) ν(C–O), 1097 (s) δ(C–O) cm^{-1}; ^1H NMR (DMSO-d_6): 0.870 (t, 3 H, CH_3 of BUY), 1.291–1.429 (m, 2 H, CH_2 of BUY), 1.472–1.558 (m, 2 H, CH_2 of BUY), 3.033–3.491 (m, 5 H, H-2, H-3, H-4, H-6), 3.87–4.00 (m, H, H-5), 4.508–4.557 (m, H, CH of BUY), 4.600 (d, H, $^3J_{H\text{-}1\text{–}H\text{-}2}$ 8.4 Hz, H-1), 5.293 (d, H, 2-OH), 5.370 (d, H, 3-OH), 5.589 (d, H, NH), 6.704 (t, H, Ar-H), 6.926 (d, H, Ar-H), 7.152 (t, H, Ar-H), 7.263 (d, H, Ar-H); ^{13}C NMR (DMSO-d_6): δ 85.1 (C-1), 73.5–81.3 (C-2, C-3, C-4), 67.6 (C-5), 66.0 (C-6), 101.4 (CH unit of BUY), 36.0 (CH_2 unit of BUY), 17.1 (CH_2 unit of BUY), 13.8 (CH_3 unit of BUY), 113.5–142.4 (Ar-6 C); FABMS: *m/z*: 344 $[M]^+$; Anal. Calcd for $C_{16}H_{22}ClNO_5$: C, 55.90; H, 6.45; N, 4.07. Found: C, 56.17; H, 6.75; N, 3.96.

4,6-O-Butylidene-β-D-glucopyranosylamine (**6**).—(0.25 g, 53%); mp 148–150 °C; IR (KBr); 3343 (b) ν(O–H) and ν(N–H), 2971 (s) and 2877 (s) ν(C–H), 1627 (s) δ(N–H), 1395 (s) ν(C–O), 1091 (s) δ(C–O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 0.864 (t, 3 H, CH_3 of BUY), 1.285–1.408 (m, 2 H, CH_2 of BUY), 1.465–1.530 (m, 2 H, CH_2 of BUY), 2.357 (s, 2 H, NH_2), 2.864–2.907 (m, H, H-2), 3.034–3.308 (m, 4 H, H-3, H-4, H-6), 3.88 (d, H, $^3J_{H\text{-}1\text{–}H\text{-}2}$ 8.4 Hz, H-1), 3.949–3.998 (m, H, H-5), 4.520 (t, H, CH of BUY), 4.726 (d, H, 2-OH), δ 5.068 (d, H, 3-OH); ^{13}C NMR (DMSO-d_6): δ 87.2 (C-1), 76.1 (C-2), 73.4 (C-3), 80.7 (C-4), 67.7 (C-5), 67.2 (C-6), 101.3 (CH unit of BUY), 36.0 (CH_2 unit of BUY), 17.1 (CH_2 unit of BUY), 13.8 (CH_3 unit of BUY); FABMS: *m/z*: 233 $[M]^+$; Anal. Calcd for $C_{10}H_{19}NO_5$: C, 51.50; H, 8.21; N, 6.01. Found: C, 51.31; H, 8.05; N, 5.80.

4,6-O-Butylidene-N-(o-pyridyl)-β-D-glucopyranosylamine (**7**).—(0.41 g, 66%); mp 198–200 °C; IR (KBr); 3317 (b) ν(O–H) and ν(N–H), 2965 (s) and 2880 (s) ν(C–H), 1609 (s) δ(N–H), 1540 (s) ν(C=C), 1336 (s) ν(C–O), 1089 (s) δ(C–O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 0.877 (t, 3 H, CH_3 of BUY), 1.323–1.423 (m, 2 H, CH_2 of BUY), 1.488–1.554 (m, 2 H, CH_2 of BUY), 3.119–3.468 (m, 5 H, H-2, H-3, H-4, H-6), 3.965–4.013 (m, H, H-5), 4.546 (t, H, CH of BUY), 5.009 (d, H, $^3J_{H\text{-}1\text{–}H\text{-}2}$ 9.16 Hz, H-1), 5.084 (d, H, 2-OH), 5.230 (d, H, 3-OH), 6.536–6.614 (m, 2 H, Ar-H), 7.018 (d, H, NH), 7.438 (t, H, Ar-H), 8.015 (d, H, Ar-H); ^{13}C NMR (DMSO-d_6): δ 83.2 (C-1), 67.9–80.7 (C-2, C-3, C-4, C-6), 67.3 (C-5), 101.6 (CH unit of BUY), 36.2 (CH_2 unit of BUY), 17.3 (CH_2 unit of BUY), 14.0 (CH_3 unit of BUY), 108.8–157.8 (5 Ar-C); FABMS: *m/z*: 311 $[M]^+$; Anal. Calcd for $C_{15}H_{22}N_2O_5$: C, 58.05; H, 7.15; N, 9.03. Found: C, 58.15; H, 6.91; N, 8.85.

N,N′-Bis(4,6-O-butylidene-β-D-glucopyranosyl)-1,2-benzenediamine (**8**).—(0.38 g, 70%); mp 182–184 °C, IR (KBr); 3405 (b) ν(O–H) and ν(N–H), 2960 (s) and 2877 (s) ν(C–H), 1603 (s) δ(N–H), 1526 (s) ν(C=C), 1263 (s) ν(C–O), 1081 (s) δ(C–O) cm^{-1}; ^1H NMR (DMSO-d_6): 0.883 δ (t, 6 H, CH_3 of BUY), 1.334–1.542 (m, 8 H, CH_2 of BUY), 3.170–3.470 (m, 10, H-2, H-3, H-4, H-6), 3.994–4.079 (m, 2 H, H-5), 4.558 (t, 2 H, CH of BUY), 4.446 (d, 2 H, $^3J_{H\text{-}1\text{–}H\text{-}2}$ 8.4 Hz, H-1), 5.099 (d, 2 H, NH), 5.228–5.286 (m, 4 H, 2-OH, 3-OH), 6.614–6.684 (m, 4 H, Ar-H); ^{13}C NMR (DMSO-d_6): δ 86.3 (C-1), 74.2 (C-2), 73.0 (C-3), 80.1 (C-4), 67.8 (C-5), 66.7 (C-6), 101.3 (CH unit of BUY), 36.0 (CH_2 unit of BUY), 17.1 (CH_2 unit of BUY), 13.8 (CH_3 unit of BUY), 113.4, 119.1, 134.8 (3 Ar-C); FABMS: *m/z*: 541 $[M]^+$; Anal. Calcd for $C_{26}H_{40}N_2O_{10}$: C, 57.77; H, 7.46; N, 5.18. Found: C, 57.41; H, 7.35; N, 4.25.

4,4′-Methylenebis(4,6-O-butylidene-β-D-glucopyranosyl)benzeneamine (**9**).—(0.34 g, 54%); mp 132–34 °C; IR (KBr); 3434 (b) ν(O–H) and ν(N–H), 2962 (s) and 2874 (s) ν(C–H), 1618 (s) δ(N–H), 1522 (s) ν(C=C), 1269 (s) ν(C–O), 1090 (s) δ(C–O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 0.871 (t, 6 H, CH_3 of BUY), 1.318–1.368 (m, 4 H, CH_2 of BUY), 1.392–1.495 (m, 4 H, CH_2 of BUY), 3.105–3.424 (m, 10 H, H-2, H-3, H-4, H-6), 3.620 (s, 2 H, bridging CH_2), 3.981 (m, 2 H, H-5), 4.484–4.534 (m, 4 H, H-1 and CH of BUY), 5.035 (d, 2 H, 2-OH), 5.208 (d, 2 H, 3-OH), 6.078 (d, 2 H, NH), 6.585 (d, 4 H, Ar-H), 6.886 (d, 4 H, Ar-H); ^{13}C NMR (DMSO-d_6): δ 85.8 (C-1), 74.0 (C-2), 73.7 (C-3), 80.6 (C-4), 67.8 (C-5), 66.6 (C-6), 101.3 (CH unit of BUY), 36.0 (CH_2 unit of BUY), 17.1 (CH_2 unit of BUY), 13.8 (CH_3 unit of BUY), 113.3–144.8 (Ar-C); FABMS: *m/z*: 631 $[M]^+$; Anal. Calcd for $C_{33}H_{46}N_2O_{10}$: C, 62.84; H, 7.35; N, 4.44. Found: C, 62.34; H, 7.28, N, 4.00.

Bis(4,6-O-butylidene-β-D-glucopyranosyl)-2,2′-[1,2-ethanediylbis(thio)]bisbenzeneamine (**10**).—(0.57 g, 80%); mp 190–192 °C; IR (KBr); 3345 (b) ν(O–H) and

Table 2
Summary of crystallographic data and structure refinement for **5**

Empirical formula	$C_{16}H_{22}ClNO_5$
Formula weight	343.80
Crystal system	monoclinic
Space group	$P2_1$ (no. 4)
Unit cell dimensions	
a (Å)	10.373(1)
b (Å)	7.128(1)
c (Å)	11.682(1)
β (°)	110.56(1)
D_{calcd} (Mg/m^3)	1.412
V (Å^3)	808.74(15)
Z	2
Reflections collected	4170
Independent reflections	2550 [$R_{int} = 0.0353$]
Final R indices [$I > 2\sigma(I)$]	$R = 0.0404$, $wR = 0.0811$
R indices (all data)	$R = 0.0569$, $wR = 0.0883$
Crystal size (mm)	$0.30 \times 0.30 \times 0.05$
Absorption correction	none
Goodness-of-fit on F^2	1.047
Absorption coefficient (mm^{-1})	0.262
Completeness to theta (24.99°)	99.3%
$F(000)$	364
θ Range for data collection (°)	3.26–24.99

ν(N–H), 2962 (s) and 2873 (s) ν(C–H), 1591 (s) δ(N–H), 1514 (s) ν(C=C), 1310 (s) ν(C–O), 1083 (s) δ(C–O) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 0.880 (t, 6 H, CH_3 of BUY), 1.332–1.430 (m, 4 H, CH_2 of BUY), 1.494–1.539 (m, 4 H, CH_2 of BUY), 2.716–2.841 (m, 4 H, bridging CH_2), 3.139–3.508 (m, 10 H, H-2, H-3, H-4, H-6), 3.980–4.027 (m, 2 H, H-5), 4.538–4.607 (m, 4 H, H-1 and CH of BUY), 5.306 (d, 2 H, 3-OH), 5.453 (d, 2 H, 2-OH), 5.843 (d, 2 H, NH), 6.671 (t, 2 H, Ar-H), 6.847 (d, 2 H, Ar-H), 7.192 (t, 2 H, Ar-H), 7.307 (d, 2 H, Ar-H); ^{13}C NMR (DMSO-d_6): δ 85.5 (C-1), 73.9 (C-2), 73.5 (C-3), 80.4 (C-4), 67.6 (C-5), 66.8 (C-6), 101.3 (CH unit of BUY), 35.9 (CH_2 unit of BUY), 17.0 (CH_2 unit of BUY), 13.8 (CH_3 unit of BUY), 112.3–147.4 (Ar-C), 34.0 (bridging CH_2); FABMS: m/z: 709 [M]$^+$; Anal. Calcd for $C_{34}H_{48}N_2O_{10}S_2$: C, 57.61; H, 6.83; N, 3.95; S, 9.05. Found: C, 57.01; H, 6.69; N, 4.42; S, 9.34.

X-ray crystallography.—The diffraction data were collected for **5** on a Nonius Kappa CCD diffractometer in the ϕ scan + ω scan mode using Mo K_α radiation at 152(2) K. The structure was solved and refined using the SHELXS-97[19] program package. The diagrams were generated using ORTEP3[20] program. Full-matrix least-squares refinement with anisotropic thermal parameters for all non-hydrogen atoms was used. The hydrogen atoms were treated as riding atoms with fixed thermal parameters. Other details of data collection and structure refinement are provided in Table 2. The OH hydrogens of 2-OH and 3-OH were obtained from difference Fourier maps.

3. Results and discussion

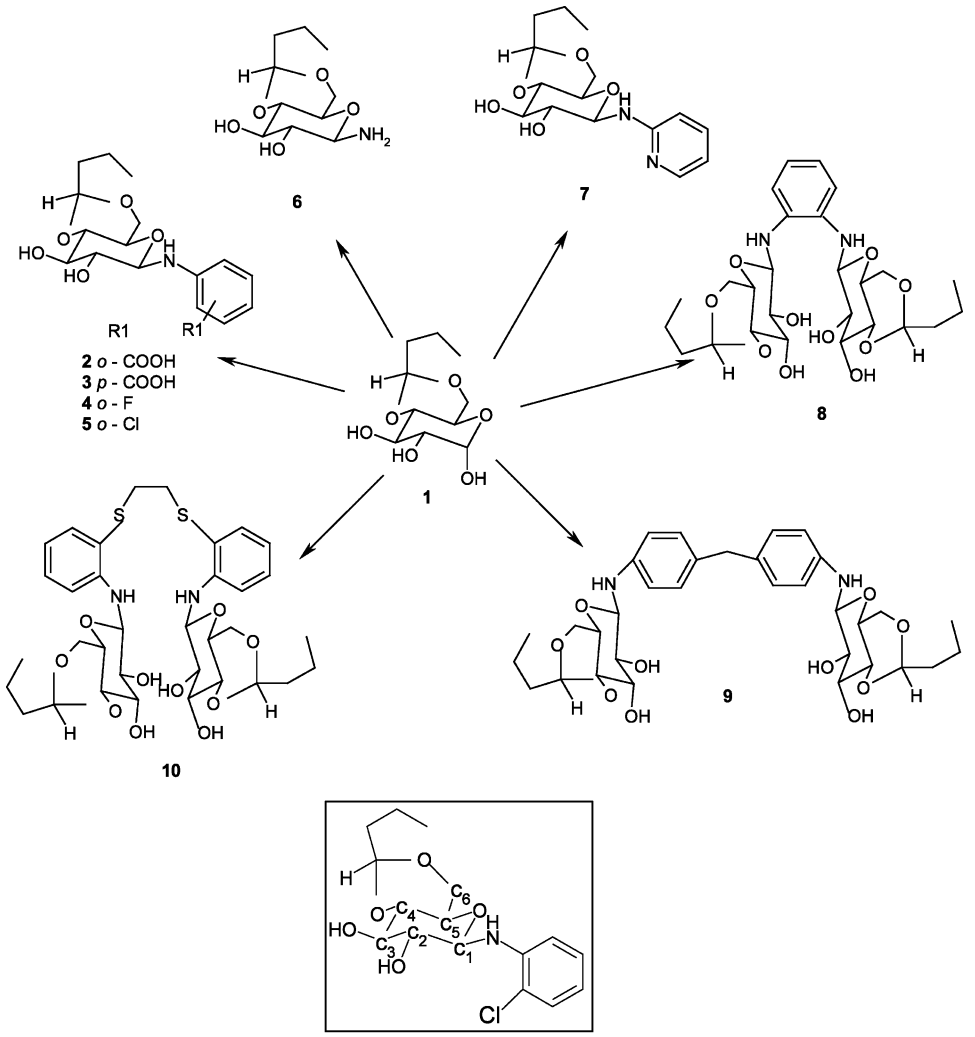
^{1}H NMR studies.—Exchangeable protons such as COOH, OH and NH were further cross checked by measuring the spectra after D_2O addition. The positions of H-1, H-5 and the CH unit of the butylidene moiety were assigned based on ^{1}H–^{1}H COSY spectra.

Formation of the glycosylamines mainly involves the condensation of the saccharide at the C-1 center with NH_2 group of an amine. The spectra of the corresponding glycosylamine products **2**–**10** were devoid of the 1-OH resonance, which was otherwise present in the corresponding precursor saccharide spectrum of **1** (6.45 ppm), indicating that the glycosylation occurred at the C-1 position. Signals corresponding to the two –OH groups, 2-OH and 3-OH, of the saccharide moiety were identified from the spectra of **2**–**10**.

The glycosylamine bond formation was also noted through observing the glycosyl–NH peak in the spectra of the products. The large variation observed in the chemical shift of the –NH groups (5.0–8.4 ppm) may be attributed to the nature of the amine counterpart. In all cases, this resonance was observed as a doublet except in the case of **6**, since **6** is a primary amine product (1-NH_2, 2.35 ppm). Upon going from **2** ($\delta_{o\text{-COOH}}$ 12.8 ppm)) to **3** ($\delta_{p\text{-COOH}}$ 5.2 ppm), the spectra are indicative of the involvement of this NH (δ_{NH} 8.39 ppm in **2** and 7.02 ppm in **3**) group in intramolecular hydrogen bonding with the o-COOH function in the case of **2**, whereas **3** cannot show such interaction. On the other hand, the spectral changes observed from **4** (5.930 ppm, o-fluoro) to **5** (5.589 ppm, o-chloro) are indicative of the inductive effect displayed by the corresponding o-substituents.

In the precursor saccharide **1**, H-1 was found at 4.92 ppm with a coupling constant $^3J_{H\text{-}1\text{–}H\text{-}2}$ of 3.7 Hz, a value that supports the α anomer. In **2**–**10**, both the chemical shift (3.88–5.09 ppm) and the $^3J_{H\text{-}1\text{–}H\text{-}2}$ (8.4–9.2 Hz) value for H-1 support the β-anomeric form. Further, the skeletal proton resonances are not much influenced even after glycosylation. In the ^{1}H NMR spectrum of bis-glycosylamines **8**–**10**, only the resonances of half of the molecule are observed due to the presence of molecular symmetry.

^{13}C NMR studies.—The ^{13}C NMR peaks were assigned on the basis of ^{1}H–^{13}C COSY spectra. The C-1 of **1** was found at 93.1 ppm, supporting the presence of the α anomer. This was shifted to 84.2–87.2 ppm in all the glycosylamines **2**–**10**. In the bis-glycosylamines **8**–**10**, only the peaks of one-half of the molecule were



Scheme 1. 4,6-*O*-Butylidene-α-D-glucopyranose (**1**) and its monoglycosylamines **2**–**7** and bis-glycosylamines **8**–**10**.

observed. Thus the conclusions based on the ^{1}H spectra are also further supported by the ^{13}C spectra.

FTIR studies.—Formation of the glycosylamine was indicated by FTIR spectra where the sharp band originating from the 1-OH stretching vibration, which is otherwise present around 3494 cm^{-1} in the precursor saccharide **1**, disappeared. Formation of the glycosylated product was further revealed by the presence of sharp δ_{NH} band in the range 1514–1540 cm^{-1}. In the case of **6,** δ_{NH_2} appeared around 1627 cm^{-1}. Comparison of the spectra, both in the functional group region and in the fingerprint regions with respect to the precursor, suggested the C-1–N-glycosylation having taken place in all the products.

FABMS studies.—In all the cases, the molecular-ion peaks were observed, confirming the molecular weight of the product structures shown in Scheme 1.

Molecular and crystal structure of **5**.—Glycosylamine **5** crystallized in the monoclinic space group $P2_1$ and is shown in Fig. 1 as an ORTEP structure. The structure of **5** revealed the presence of C-1 glycosylation of the saccharide moiety with *ortho*-chloroaniline to result in 4,6-*O*-butylidene-*N*-(*o*-chlorophenyl)-β-D-glucopyranosylamine. The Cremer–Pople and asymmetry parameters[21–24] (Table 3) were obtained using the program PLATON 94[25] for both of the six-membered rings. Bond lengths and bond angles present in **5** are quite normal, and selected examples are given in Table 4. The β-anomeric form and the $^{4}C_{1}$ chair conformation of the

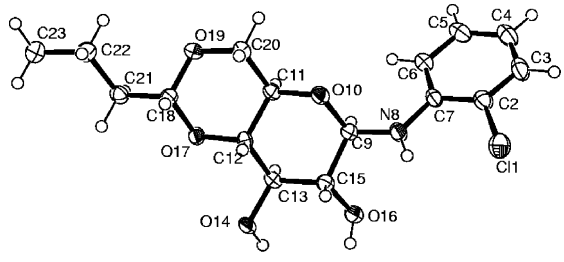


Fig. 1. Molecular structure of 4,6-*O*-butylidene-*N*-(*o*-chlorophenyl)-β-D-glucopyranosylamine (**5**), showing (50%) probability thermal ellipsoids using ORTEP.

Table 3
Cremer–Pople puckering parameters and asymmetry parameters for **5**

O-10–C-9–C-15–C-13–C-12–C-11	
ΔCs (C-9–C-12) [a]	0
ΔCs (C-15–C-11) [a]	0
ΔCs (C-13–O-10) [a]	0
Q (Å), θ (°), ϕ (°) [b]	0.602, 3.1, 292.34
O-17–C-12–C-11–C-20–O-19–C-18	
ΔCs (C-12–O-19) [a]	0
ΔCs (C-11–C-18) [a]	0
ΔCs (C-20–O-17) [a]	0
Q (Å), θ (°), ϕ (°) [b]	0.587, 1.9, 214.65

[a] Cs(I–J): asymmetry parameters for bond I–J.
[b] Q (Å), θ (°), ϕ (°): Cremer–Pople puckering parameters.

saccharide are evidenced through the stereoview shown in Fig. 2 and also through the corresponding torsion angles provided in Table 4. Based on the torsion angles, it was noted that the C-7–N-8 bond is oriented anti- with respect to the C-9–C-15 and gauche- with respect to the C-9–O-10 bonds. The glycosylation clearly resulted in a change in the state of the anomeric form from α to β. With the existing conformation of **5** in the solid state, the arrangement of atoms O-16, N-8 and Cl-1 is not well suited to form a bis-chelate with the metal ions. However, a rotation about C-9–N-8 can bring these three atoms spacially such that the glycosylamine could act as a bis-chelate. Presence of the functional and/or the binding groups in place of the chlorine center (ortho to the amine center) can cause this rotation as the system gains energy during the formation of a bis-chelate with the incoming metal ion.

Each molecule in the lattice (Fig. 3) is connected with one neighboring molecule to result in the formation of a head-to-tail type of dimer through four O–H···O interactions. In the process, the 2-OH extends one donor type of H-bond, the 3-OH extends two H-bond interactions (one donor type and another acceptor), and the 4-O extends one H-bond interaction as acceptor. These dimers are further interconnected through C–H···O type of H-bond interactions between the C–H of the phenyl moiety and 2-O of the neighboring dimer to result in a chain of dimers. This arrangement also resulted in the formation of another type of dimer in the lattice through overlap of the phenyl moieties. However, no interactions were observed between two such chains. The hydrogen-bond data is listed in Table 5.

4. Supplementary material

Full crystallographic details, excluding structure factors, have been deposited with the Cambridge Crystallographic Data Centre for structure **5** (CCDC 173857). These data may be obtained, on request, from The Director, CCDC, 12 Union Road, Cambridge CBZ 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).

Table 4
Selected bond lengths (Å), bond angles (°) and torsion angles (°) for **5**

Bond lengths			
C-7–N-8	1.391(3)	O-10–C-11	1.432(3)
N-8–C-9	1.422(4)	C-11–C-12	1.518(3)
C-9–O-10	1.445(3)	C-12–C-13	1.504(4)
C-9–C-15	1.533(3)	C-13–C-15	1.526(4)
Bond angles			
C-6–C-7–N-8	123.1(3)	C-11–O-10–C-9	111.12(19)
N-8–C-7–C-2	120.0(3)	O-10–C-11–C-12	108.7(2)
C-7–N-8–C-9	122.5(3)	C-13–C-12–C-11	109.7(2)
N-8–C-9–O-10	108.30(18)	C-12–C-13–C-15	108.7(2)
N-8–C-9–C-15	111.1(3)	C-13–C-15–C-9	109.7(2)
O-10–C-9–C-15	110.22(18)		
Torsion angles			
Cl-1–C-2–C-7–C-6	177.7(2)	O-10–C-11–C-12–C-13	−62.1(3)
Cl-1–C-2–C-7–N-8	−3.7(3)	C-11–C-12–C-13–C-15	58.0(3)
C-6–C-7–N-8–C-9	−0.7(4)	O-14–C-13–C-15–O-16	66.9(3)
C-2–C-7–N-8–C-9	−179.2(2)	C-12–C-13–C-15–O-16	−172.4(2)
C-7–N-8–C-9–O-10	−82.4(3)	O-14–C-13–C-15–C-9	−175.52(19)
C-7–N-8–C-9–C-15	156.4(2)	C-12–C-13–C-15–C-9	−54.9(3)
N-8–C-9–O-10–C-11	176.9(2)	N-8–C-9–C-15–O-16	−63.5(3)
C-15–C-9–O-10–C-11	−61.4(3)		

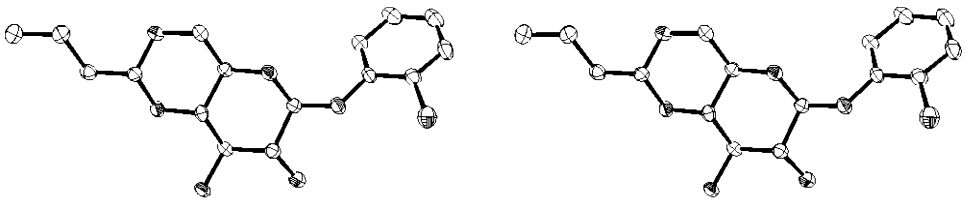


Fig. 2. Stereoview of 4,6-*O*-butylidene-*N*-(*o*-chlorophenyl)-β-D-glucopyranosylamine (**5**).

Table 5
Hydrogen bond data for **5**

D–H···A	d(D···H) (Å)	d(H···A) (Å)	d(D···A) (Å)	<(DHA) (°)	Symmetry
N-8–H-8···Cl-1	0.8800	2.5215	2.9590	111.46	
O-14–H-14···O-17	0.8391	1.9599	2.7931	171.87	$1-x, -1/2+y, -z$
O-16–H-16···O-14	0.8328	2.1701	3.0003	174.69	$1-x, -1/2+y, -z$
C-5–H-5···O-16	0.9500	2.5836	3.4295	148.47	$2-x, 1/2+y, 1-z$
C-6–H-6···Cl-1	0.9500	2.7947	3.5246	134.32	$x, 1+y, z$

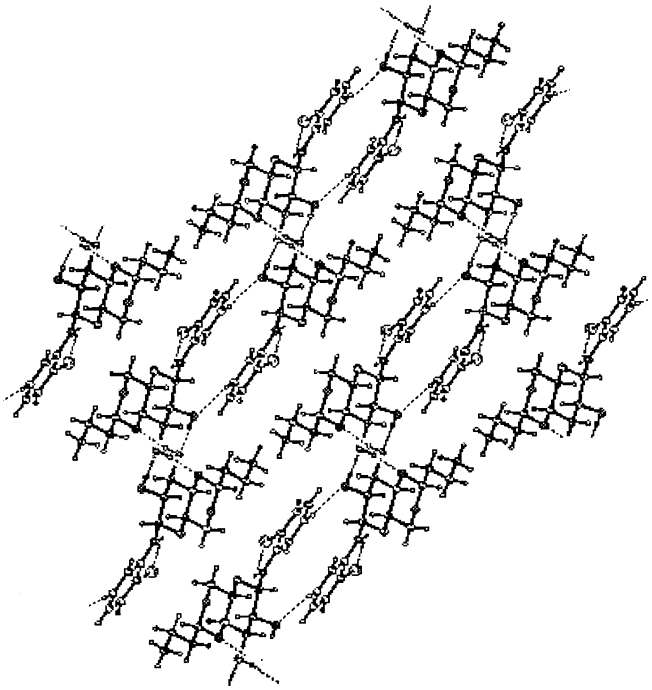


Fig. 3. Lattice structure of **5**.

Acknowledgements

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References

1. (a) Kaneki, H.; Tanaka, M. *Chem. Pharm. Bull.* **1982**, *30*, 1753–1759;
   (b) Lai, H. Y. L.; Axelrod, B. *Biochem. Biophys. Res. Commun.* **1973**, *54*, 463–468;
   (c) Lalegerie, P.; Legler, G.; Yon, J. *Biochimie* **1982**, *64*, 977–1000;
   (d) Walker, D. E.; Axelrod, B. *Arch. Biochem. Biophys.* **1978**, *187*, 102–107;
   (e) Halvorson, H. *Methods Enzymol.* **1966**, *8*, 559–562;
   (f) Kolarovaa, N.; Trgina, R.; Linek, K.; Farkas, V. *Carbohydr. Res.* **1995**, *273*, 109–113;
   (g) Monsigny, M.; Quétard, C.; Bourgerie, S.; Delay, D.; Pichon, C.; Midoux, P.; Mayer, R.; Roche, A. C. *Biochimie* **1998**, *80*, 99–108.
2. Njoroge, F. G.; Monnier, V. M. *Prog. Clin. Biol. Res.* **1989**, *304*, 85–107.
3. Bjamer, K.; Dahm, S.; Furberg, S.; Petersen, C. *Acta Chem. Scand.* **1963**, *17*, 559–561.
4. Dukefos, T.; Mostad, A. *Acta Chem. Scand.* **1965**, *19*, 685–696.
5. Ojala, W. H.; Ojala, C. R.; Gleason, W. B. *J. Chem. Crystallogr.* **1999**, *29*, 19–26.
6. Mostad, A. *Acta Chem. Scand. B* **1978**, *32*, 733–742.
7. Furberg, S.; Petersen, C. *Acta Chem. Scand.* **1962**, *16*, 1539–1548.
8. Ojala, W. H.; Gleason, W. B. *Acta Crystallogr., Sect. C* **1996**, *52*, 3188–3190.
9. Furberg, S.; Solbakk, J. *Acta Chem. Scand.* **1969**, *23*, 3248–3256.
10. Bjamer, K.; Furberg, S.; Petersen, C. *Acta Chem. Scand.* **1964**, *18*, 587–595.
11. Ojala, C. R.; Ostman, J. M.; Ojala, W. H.; Hanson, S. E. *Carbohydr. Res.* **2001**, *331*, 319–325.
12. Sah, A. K.; Rao, C. P.; Saarenketo, P. K.; Wegelius, E. K.; Rissanen, K.; Kolehmainen, E. *J. Chem. Soc., Dalton Trans.* **2000**, 3681–3687.
13. Sah, A. K.; Rao, C. P.; Saarenketo, P. K.; Kolehmainen, E.; Rissanen, K. *Carbohydr. Res.* **2001**, *335*, 33–43.

14. Mohan Das, T.; Rao, C. P.; Kolehmainen, E. *Carbohydr. Res.* **2001**, *334*, 261–269.
15. Mohan Das, T.; Rao, C. P.; Kolehmainen, E. *Carbohydr. Res.* **2001**, *335*, 151–158.
16. Sah, A. K.; Rao, C. P.; Saarenketo, P. K.; Wegelius, E. K.; Kolehmainen, E.; Rissanen, K. *Eur. J. Inorg. Chem.* **2001**, 2773–2781.
17. Mellies, R. L.; Mehltretter, C. L.; Rist, C. E. *J. Am. Chem. Soc.* **1951**, *73*, 294–296.
18. Hay, R. W.; Gidney, P. M.; Lawrance, G. A. *J. Chem. Soc., Dalton Trans.* **1975**, 779–783.
19. Sheldrick, G. M. *SHELX*97: *Programs for Crystal Structure Analysis* (*Release* 97-2); Institute fur Anorganische chemie der university: Gottingen, Germany, 1998.
20. Farugia, L. J. *J. Appl. Crystallogr.* **1997**, *30*, 565.
21. Boeyens, J. C. A. *J. Cryst. Mol. Struct.* **1979**, *8*, 317–320.
22. Cremer, D. *Acta Crystallogr., Sect. B* **1984**, *40*, 498–500.
23. Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354–1358.
24. Koll, P.; Saak, W.; Pohl, S.; Steiner, B.; Koos, M. *Carbohydr. Res.* **1994**, *265*, 237–248.
25. Spek, A. L. *Acta Crystallogr., Sect. A.* **1990**, *46*, C34.