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Synthesis and characterisation of *N*-glycosyl amines from the reaction between 4,6-*O*-benzylidene-D-glucopyranose and substituted aromatic amines and also between 2-(*o*-aminophenyl)benzimidazole and pentoses or hexoses

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Abstract

Twelve *N*-glycosyl amines were synthesised using 4,6-*O*-benzylidene-D-glucopyranose and different substituted aromatic amines, including some diamines that resulted in bis-glycosyl amines. Another set of six *N*-glycosyl amines was synthesised using different hexoses and pentoses and 2-(*o*-aminophenyl)benzimidazole. All compounds were isolated as solid products and purified, their elemental compositions were established, and these were characterised by NMR (^{1}H and ^{13}C), UV–Vis, and FTIR spectroscopy, by FAB mass spectrometry (molecular-ion peaks gave molecular weights), and by their optical rotations. While the protected saccharide, 4,6-*O*-benzylidene-D-glucopyranose, exists as a mixture of β and α anomers in solution, the corresponding *N*-glycosyl amines were of only the β anomeric form as determined by NMR and FTIR spectroscopy. On the other hand, *N*-glycosyl amines synthesised from 2-(*o*-aminophenyl)benzimidazole prefer the α anomeric form, and in two cases a mixture of both the β and the α anomers were observed. The trends observed in the chemical shifts were compared among different products.

Keywords: *N*-Glycosyl amines; α and β anomers; Optical rotation; 4,6-*O*-Benzylidene-D-glucopyranose; 4,6-*O*-Butylidene-D-glucopyranose; 2-(*o*-Aminophenyl)benzimidazole; Hydrogen-bonding interaction

1. Introduction

The finding of insulin-like activity associated with various alkyl and aryl glycosyl amines[1] and their generally wide range of biological activities[2] prompted our study of *N*-glycosyl amines. Glycosyl amines[3] are important because these occur as junctures in glycoproteins.[4] The chemical and structural nature of the derivatives formed from the reaction of a monosaccharide and different nitrogen bases depends upon the reaction conditions and the base used. Thus glycosyl amines exist either in cyclic or acyclic form.[5] Benzimidazole-based non-glycosyl amine derivatives exhibit a range of biological activities.[6] *N*-Glycosyl amines have better advantage in binding to metal ions over their sac-

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charide counter parts, as these compounds provide additional binding centres. Thus in view of such important aspects of *N*-glycosyl amines, herein we report the synthesis and characterisation of different *N*-glycosyl amines of simple and partially protected saccharides using different amines, such as the ortho-substituted aromatic amines and the benzimidazole-based amines.

2. Experimental

All solvents were purified and dried prior to use by adopting routine procedures. Saccharides (Lancaster, UK), ortho-substituted anilines (Lancaster, UK), nitrobenzaldehyde, and Pd–C (10%) (Loba Chimie) were purchased and used without further purification. NMR spectra were measured in Me_2SO-d_6 on a Bruker Avance DRX 500 spectrometer or on a 300 MHz spectrometer. FTIR spectra were recorded on an Impact 400 Nicolet FTIR spectrometer in KBr matrix in the region of 400–4000 cm^{-1}. Microanalyses were performed on a Carlo–Erba elemental analyser. FAB mass spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer using argon as the FAB gas at 6 kV and 10 mA. UV absorption spectra were recorded on a Shimadzu UV-2101 spectrophotometer as 10^{-4} M solutions in *N*,*N*-dimethylformamide (DMF). Optical rotations of *N*-glycosyl amines **1**–**12** were measured in dimethyl sulfoxide (Me_2SO) on a JASCO DIP-370 digital polarimeter, whereas **13**–**18** were measured on an AA-10 automatic polarimeter at the sodium D line (589 nm). While assigning the spectral data several short forms were used and these include, 'Ar' for aromatic, 'Gly'' for glycosidic, 'Sac' for saccharide, 'Ts' for tosyl, 'But' for butylidene, 'Ace' for acetal and 'Imi' for imidazole.

4,6-*O*-Benzylidene-D-glucopyranose,[7] 4,6-*O*-butylidene-D-glucopyranose[8] and *N*-*p*-toluenesulfonyl-1,2-diaminobenzene[9] were synthesised as per the indicated literature procedures, and the compounds were identified based on analytical and spectral data. *N*-Glycosyl amines of 4,6-*O*-benzylidene-D-glucopyranose were synthesised using different mono- and diamines to give products **1**–**12** by adopting the same procedure. 2-(*o*-Nitrophenyl)benzimidazole was synthesised by adopting a literature procedure,[10] but by using *o*-phenylenediamine in our case, the product was subsequently converted to 2-(*o*-aminophenyl)benzimidazole. Benzimidazol-2-yl-phenyl *N*-Glycosyl amines were synthesised using different saccharides and their derivatives, resulting in products **13**–**18**. A typical synthetic procedure for **1** is reported in the following section.

*4,6-*O*-Benzylidene-*N*-(o-carboxyphenyl)-β-D-glucopyranosylamine* (**1**).—4,6-*O*-Benzylidene-D-glucopyranose (4 mmol, 1.072 g) and anthranilic acid (4 mmol, 0.548 g) were dissolved in EtOH (30 mL) and stirred under reflux. The reaction mixture was stirred for 15 min, and the product separated. The solid thus obtained was purified by repeated washings with EtOH, followed by Et_2O, and then it was dried under vacuum. Yield 0.898 g (58%): mp 140–142 °C; $[\alpha]_D^{25}$ −86° (*c* 1.0, Me_2SO); FTIR (KBr): 3351, 2888, 1668, 1587, 1382, 1090 cm^{-1}; ^1H NMR (Me_2SO-d_6): δ 12.86–13.00 (br, 1 H, COO*H*), 8.43 (d, 1 H, $^3J_{H1,NH}$ 7.32 Hz, Gly-N*H*), 7.82 (d, 1 H, Ar-*H*), 7.38–7.47 (m, 6 H, Ar-*H*), 6.99 (d, 1 H, Ar-*H*), 6.705 (t, 1 H, Ar-*H*), 5.59 (s, 1 H, Ace-*H*), 5.53 (d, 1 H, Sac-O*H*), 5.42 (d, 1 H, Sac-O*H*), 4.77 (d, 1 H, $^3J_{H1,H2}$ 8.82 Hz, H-1–*H*), 3.20–4.20 (6 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 169.7 (1 C, *C*OOH), 111.3–149.3 (12 C, Ar-*C*), 100.6 (1 C, Ace-*C*), 66.6–84.2 (6 C, Sac-*C*); FABMS: *m*/*z* 388 $[M+H]^+$; Anal. Calcd for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.43; N, 3.62. Found: C, 61.78; H, 5.39; N, 3.54.

*4,6-*O*-Benzylidene-*N*-(o-hydroxyphenyl)-β-D-glucopyranosylamine* (**2**).—Yield 0.086 g (24%): mp 150–152 °C; $[\alpha]_D^{25}$ −144° (*c* 1.0, Me_2SO); FTIR (KBr); 3485, 3374, 3301, 2929, 2878, 1590, 1381, 1085 cm^{-1}; ^1H NMR (Me_2SO-d_6): δ 9.30 (s, 1 H, Ar-O*H*), 7.41 (d, 5 H, Ar-*H*), 6.64–6.75 (m, 3 H, Ar-*H*), 6.53 (t, 1 H, Ar-*H*), 5.59 (s, 1 H, Ace-*H*), 5.33 (s, 2 H, Gly-N*H* and Sac-O*H*), 5.20 (d, 1 H, Sac-O*H*), 4.57 (t, 1 H, $^3J_{H1,H2}$ 8.30 Hz, H-1), 3.44–4.19 (6 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 111.9–144.1 (12 C, Ar-*C*), 100.6 (1 C, Ace-*C*), 66.5–86.0 (6 C, Sac-*C*); FABMS: *m*/*z* 360 [M+

H]$^+$; Anal. Calcd for $C_{19}H_{21}NO_6$: C, 63.51; H, 5.85; N, 3.90. Found: C, 62.71; H, 5.53; N, 3.55.

4,6-O-Benzylidene-N-(phenyl)-β-D-glucopyranosylamine (**3**).—Yield 0.487 g (71%): mp 120–122 °C; $[\alpha]_D^{25}$ −114° (*c* 1.0, Me_2SO); FTIR (KBr); 3338, 2879, 1604, 1383, 1097 cm^{-1}; ^{1}H NMR (Me_2SO-d_6): δ 7.34–7.51 (m, 5 H, Ar-*H*), 7.11 (t, 2 H, Ar-*H*), 6.72 (d, 2 H, Ar-*H*), 6.62 (t, 1 H, Ar-*H*), 6.33 (d, 1 H, $^3J_{H1,NH}$ 8.42 Hz, Gly-N*H*), 5.59 (s, 1 H, Ace-*H*), 5.35 (d, 1 H, Sac-O*H*), 5.16 (d, 1 H, Sac-O*H*), 4.63 (t, 1 H, $^3J_{H1,H2}$ 8.79 Hz, H-1), 3.24–4.21 (6 H, Sac-*H*); FABMS: *m*/*z* 344 [M + H]$^+$; Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.12; N, 4.08. Found: C, 66.22; H, 5.98; N, 3.94.

4,6-O-Benzylidene-N-(o-fluorophenyl)-β-D-glucopyranosylamine (**4**).—Yield 0.448 g (62%): mp 130–132 °C; $[\alpha]_D^{25}$ −96° (*c* 1.0, Me_2SO); FTIR (KBr); 3369, 2882, 1598, 1383, 1095 cm^{-1}; ^{1}H NMR (Me_2SO-d_6): δ 7.42 (d, 5 H, Ar-*H*), 6.95–7.09 (m, 3 H, Ar-*H*), 6.67 (d, 1 H, Ar-*H*), 5.99 (d, 1 H, $^3J_{H1,NH}$ 6.00 Hz, Gly-N*H*), 5.59 (s, 1 H, Ace-*H*), 5.37 (d, 1 H, Sac-O*H*), 5.22 (d, 1 H, Sac-O*H*), 4.66 (t, 1 H, $^3J_{H1,H2}$ 8.79 Hz, H-1), 3.39–4.16 (6 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 113.5–142.3 (12 C, Ar-*C*), 100.6 (1 C, Ace-*C*), 66.6–85.1 (6 C, Sac-*C*); FABMS: *m*/*z* 362 [M + H]$^+$; Anal. Calcd for $C_{19}H_{20}FNO_5$: C, 63.15; H, 5.54; N, 3.88. Found: C, 63.66; H, 5.34; N, 3.75.

4,6-O-Benzylidene-N-(o-chlorophenyl)-β-D-glucopyranosylamine (**5**).—Yield 0.226 g (60%): mp 138–140 °C; $[\alpha]_D^{25}$ −86° (*c* 1.0, Me_2SO); FTIR (KBr): 3407, 2885, 1624, 1394, 1094 cm^{-1}; ^{1}H NMR (Me_2SO-d_6): δ 7.47 (q, 2 H, Ar-*H*), 7.38–7.40 (m, 3 H, Ar-*H*), 7.29 (dd, 1 H, Ar-*H*), 7.16–7.19 (m, 1 H, Ar-*H*), 6.98 (dd, 1 H, Ar-*H*), 6.71–6.74 (m, 1 H, Ar-*H*), 5.63 (d, 1 H, $^3J_{H1,NH}$ 7.34 Hz, Gly-N*H*), 5.59 (s, 1 H, Ace-*H*), 5.38 (q, 2 H, Sac-O*H*), 4.69 (t, 1 H, $^3J_{H1,H2}$ 8.50 Hz, H-1), 3.42–4.21 (6 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 113.5–142.3 (12 C, Ar-*C*), 100.6 (1 C, Ace-*C*), 66.6–85.1 (6 C, Sac-*C*); FABMS: *m*/*z* 378 [M + H]$^+$; Anal. Calcd for $C_{19}H_{20}ClNO_5$: C, 60.40; H, 5.30; N, 3.71. Found: C, 60.95; H, 5.25; N, 3.84.

4,6-O-Benzylidene-N-[o-(p-toluenesulfonamido)phenyl]-β-D-glucopyranosylamine (**6**).—Yield 0.296 g (58%): mp 168–170 °C; $[\alpha]_D^{25}$ −33° (*c* 1.0, Me_2SO); FTIR (KBr); 3510, 3326, 2873, 1601, 1328 cm^{-1}; ^{1}H NMR (Me_2SO-d_6): δ 9.3 (br, 1 H, Ts-N*H*), 7.65 (d, 2 H, Ar-*H*), 7.47 (d, 2 H, Ar-*H*), 7.34–7.39 (m, 5 H, Ar-*H*), 6.98 (t, 1 H, Ar-*H*), 6.81 (d, 1 H, Ar-*H*), 6.72 (dd, 1 H, Ar-*H*), 6.53 (t, 1 H, Ar-*H*), 5.68 (d, 1 H, $^3J_{H1,NH}$ 7.91 Hz, Gly-N*H*), 5.60 (s, 1 H, Ace-*H*), 5.36 (d, 1 H, Sac-O*H*), 5.24 (d, 1 H, Sac-O*H*), 4.52 (t, 1 H, $^3J_{H1,H2}$ 8.61 Hz, H-1), 3.28–4.20 (6 H, Sac-*H*), 2.37 (s, 3 H, –CH_3 of Ts group); ^{13}C NMR (Me_2SO-d_6): δ 113.6–142.9 (18 C, Ar-*C*), 100.6 (1 C, Ace-*C*), 66.5–85.5 (6 C, Sac-*C*), 20.9 (1 C, *C*H$_3$ of Ts group); Anal. Calcd for $C_{26}H_{28}N_2O_7S$: C, 60.93; H, 5.47; N, 5.47; S, 6.25. Found: C, 61.51; H, 5.73; N, 5.85; S, 6.61.

4,6-O-Benzylidene-N-(1-napthyl)-β-D-glucopyranosylamine (**7**).—Yield 0.239 g (61%): mp 118–120 °C; $[\alpha]_D^{25}$ −94° (*c* 1.0, Me_2SO); FTIR (KBr); 3338, 2885, 1634, 1383, 1077 cm^{-1}; ^{1}H NMR (Me_2SO-d_6): δ 7.61–7.69 (m, 3 H, Ar-*H*), 7.31–7.48 (m, 6 H, Ar-*H*), 7.16 (t, 1 H, Ar-*H*), 7.07 (d, 1 H, Ar-*H*), 7.02 (s, 1 H, Ar-*H*), 6.62 (d, 1 H, $^3J_{H1,NH}$ 8.10 Hz, Gly-N*H*), 5.61 (s, 1 H, Ace-*H*), 5.38 (d, 1 H, Sac-O*H*), 5.19 (d, 1 H, Sac-O*H*), 4.79 (t, 1 H, $^3J_{H1,H2}$ 8.42 Hz, H-1), 3.32–4.22 (6 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 105.4–144.7 (16 C, Ar-*C*), 100.7 (1 C, Ace-*C*), 56.0–85.5 (6 C, Sac-*C*); FABMS: *m*/*z* 394 [M + H]$^+$; Anal. Calcd for $C_{23}H_{23}NO_5$: C, 70.22; H, 5.85; N, 3.56. Found: C, 69.38; H, 5.78; N, 3.63.

4,6-O-Benzylidene-N-[o-(4,6-O-benzylidene-β-D-glucopyranosylamino)phenyl)-β-D-glucopyranosylamine (**8**).—Yield 0.740 g (61%): mp 140–142 °C; $[\alpha]_D^{25}$ −61° (*c* 1.0, Me_2SO); FTIR (KBr); 3569, 3374, 3302, 2883, 1604, 1385, 1093 cm^{-1}; ^{1}H NMR (Me_2SO-d_6): δ 7.47 (s, 2 H, Ar-*H*), 7.38 (d, 3 H, Ar-*H*), 6.76 (t, 1 H, Ar-*H*), 6.66 (dd, 1 H, Ar-*H*), 5.61 (s, 1 H, Ace-*H*), 5.31 (q, 2 H, $^3J_{H1,NH}$ 9.95 Hz, Gly-N*H* and Sac-O*H*), 5.13 (d, 1 H, Sac-O*H*), 4.50 (br, 1 H, H-1), 3.38–4.24 (6 H, Sac-*H*); ^{13}C (Me_2SO-d_6): δ 113.4–137.9 (9 C, Ar-*C*), 100.7 (1 C, Ace-*C*), 68.2–86.4 (6 C, Sac-*C*); Anal. Calcd for $C_{32}H_{36}N_2O_{10}$: C, 63.16; H, 5.92; N, 4.61. Found: C, 62.05; H, 5.74; N, 4.46.

4,6-O-*Benzylidene*-N-*[*p-*(4,6*-O-*benzylidene*-*β*-D-*glucopyranosylamino)*-*benzyl]phenyl*-*β*-D-*glucopyranosylamine* (**9**).—Yield 0.441 g (63%): mp 124–126 °C; $[\alpha]_D^{25}$ −62° (*c* 1.0, Me_2SO); FTIR (KBr): 3372, 3035, 2873, 1618, 1383, 1085 cm^{-1}; ^1H NMR (Me_2SO-d_6): δ 7.46 (t, 2 H, Ar-*H*), 7.37 (d, 3 H, Ar-*H*), 6.92 (d, 2 H, Ar-*H*), 6.64 (d, 2 H, Ar-*H*), 6.11 (d, 1 H, $^3J_{H1,NH}$ 8.5 Hz, Gly-N*H*), 5.58 (s, 1 H, Ace-*H*), 5.29 (d, 1 H, Sac-O*H*), 5.06 (d, 1 H, Sac-O*H*), 4.60 (t, 1 H, $^3J_{H1,H2}$ 7.87 Hz, H-1), 3.37–4.17 (6 H, Sac-*H*), 2.08 (s, 1 H, –CH_2); ^{13}C NMR (Me_2SO-d_6): δ 113.3–144.7 (12 C, Ar-*C*), 100.6 (1 C, Ace-*C*), 66.4–85.9 (6 C, Sac-*C*); FABMS: *m*/*z* 699 $[M+H]^+$; Anal. Calcd for $C_{39}H_{42}N_2O_{10}$: C, 67.05; H, 6.02; N, 4.01. Found: C, 66.61; H, 5.85; N, 3.88.

4,6-O-*Benzylidene*-N-*(*p-*aminophenyl)phenyl*-*β*-D-*glucopyranosylamine* (**10**).—Yield: 0.239 g (55%): mp 128–130 °C; $[\alpha]_D^{25}$ −63° (*c* 1.0, Me_2SO); ^1H NMR (Me_2SO-d_6): δ 7.58 (s, 1 H, Ar-*H*), 7.45 (s, 2 H, Ar-*H*), 7.38 (d, 3 H, Ar-*H*), 7.10 (t, 2 H, Ar-*H*), 6.92 (d, 2 H, Ph-N*H* and Ar-*H*), 6.82 (d, 2 H, Ar-*H*), 6.60–6.71 (m, 3 H, Ar-*H*), 6.08 (d, 1 H, $^3J_{H1,NH}$ 8.10 Hz, Gly-N*H*), 5.59 (s, 1 H, Ace-*H*), 5.34 (d, 1 H, Sac-O*H*), 5.11 (d, 1 H, Sac-O*H*), 4.59 (t, 1 H, $^3J_{H1,H2}$ 8.06 Hz, H-1), 3.24–4.19 (6 H, Sac-*H*); Anal. Calcd for $C_{25}H_{26}N_2O_5$: C, 69.12; H, 5.99; N, 6.45. Found: C, 68.76; H, 5.74; N, 6.30.

4,6-O-*Benzylidene*-N-*(*p-*carboxyphenyl)*-*β*-D-*glucopyranosylamine* (**11**).—Yield 0.230 g (59%): mp 150–152 °C; $[\alpha]_D^{25}$ −96° (*c* 1.0, Me_2SO); ^1H NMR (Me_2SO-d_6): δ 7.72 (d, 2 H, Ar-*H*), 7.46 (q, 2 H, Ar-*H*), 7.38 (t, 3 H, Ar-*H*), 7.07 (d, 1 H, $^3J_{H1,NH}$ 8.40 Hz, Gly-N*H*), 6.77 (d, 2 H, Ar-*H*), 5.59 (s, 1 H, Ace-*H*), 5.39 (br, 1 H, Sac-O*H*), 5.22 (br, 1 H, Sac-O*H*), 4.72 (t, 1 H, $^3J_{H1,H2}$ 8.43 Hz, H-1), 3.29–4.20 (6 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 167.4 (1 C, –*C*OOH), 112.3–151.0 (12 C, Ar-*C*), 100.6 (1 C, Ace-*C*), 66.6–84.6 (6 C, Sac-*C*); Anal. Calcd for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.43; N, 3.62. Found: C, 61.39; H, 5.74; N, 3.81.

4,6-O-*Benzylidene*-N-*(2-pyridyl)*-*β*-D-*glucopyranosylamine* (**12**).—Yield 0.144 g (42%): mp 158–160 °C; $[\alpha]_D^{25}$ −18° (*c* 1.0, Me_2SO); ^1H NMR (Me_2SO-d_6): δ 8.02 (d, 1 H, Ar-*H*), 7.42–7.48 (m, 3 H, Ar-*H*), 7.34–7.40 (m, 3 H, Ar-*H*), 7.08 (d, 1 H, $^3J_{H1,NH}$ 8.91 Hz, Gly-N*H*), 6.56–6.40 (m, 2 H, Ar-*H*), 5.59 (s, 1 H, Ace-*H*), 5.35 (d, 1 H, Sac-O*H*), 5.14 (t, 2 H, $^3J_{H1,H2}$ 9.15 Hz, Sac-O*H* and H-1), 3.27–4.18 (6 H, Sac-*H*); Anal. Calcd for $C_{18}H_{20}N_2O_5$: C, 62.79; H, 5.81; N, 8.14. Found: C, 63.12; H, 5.46; N, 8.52.

N-*[*o-*(Benzimidazol*-*2*-*yl)phenyl]*-*4,6*-O-*benzylidene*-*α*-D-*glucopyranosylamine* (**13**).—Yield 0.326 g (71%): mp 192–194 °C; $[\alpha]_D^{24}$ 20° (*c* 1.0, Me_2SO); FTIR (KBr): 3360, 2920, 2859, 1621, 1459, 1099 cm^{-1}; UV (DMF), λ (nm) (ε (M^{-1} cm^{-1})): 291 (12,660), 360 (10,500); ^1H NMR (Me_2SO-d_6): δ 7.80 (d, 1 H, Ar-*H*), 7.56 (d, 3 H, Ar-*H*), 7.44 (br, 3 H, Ar-*H*), 7.16 (t, 1 H, Ar-*H*), 7.08 (d, 2 H Ar-*H*), 6.82 (d, 1 H, Imi-N*H*), 6.68–6.74 (m, 3 H, Ar-*H*), 6.16 (s, 1 H, H-1), 5.75 (s, 1 H, Ace-*H*), 5.08 (d, 1 H, $^3J_{H1,NH}$ 3.66 Hz, Gly-N*H*), 4.74 (d, 1 H, Sac-O*H*), 4.63 (d, 1 H, Sac-O*H*), 3.55–4.17 (6 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 109.8–147.6 (19 C, Ar-*C*), 100.5 (1 C, Ace-*C*), 60.2–80.9 (6 C, Sac-*C*); FABMS: *m*/*z* 460 $[M+H]^+$; Anal. Calcd for $C_{26}H_{25}N_3O_5$: C, 67.97; H, 5.45; N, 9.15. Found: C, 67.32; H, 5.12; N, 9.65.

N-*[*o-*(Benzimidazol*-*2*-*yl)phenyl]*-*4,6*-O-*butylidene*-*α*-D-*glucopyranosylamine* (**14**).—Yield 0.319 g (75%): mp 162–164 °C; $[\alpha]_D^{24}$ 10° (*c* 1.0, Me_2SO); FTIR (KBr): 3363, 2956, 2926, 2863, 1615, 1382, 1087 cm^{-1}; ^1H NMR (Me_2SO-d_6): δ 7.86 (d, 1 H, Ar-*H*), 7.57 (d, 2 H, Ar-*H*), 7.17–7.40 (m, 3 H, Ar-*H*), 6.79–6.84 (br, 2 H, Ar-*H*), 6.46 (s, 1 H, Imi-N*H*), 5.88 (s, 1 H, H-1), 4.94 (t, 3 H, Sac-O*H*s and Gly-N*H*), 4.56 (br, 1 H, Ace-*H*), 3.59–4.56 (6 H, Sac-*H*), 1.43–1.47 (s, 2 H, –CH_2 of But-*H*), 1.26–1.33 (s, 2 H, –CH_2 of But-*H*) and 0.81–0.84 (s, 3 H, –CH_3 of But-*H*); ^{13}C NMR (Me_2SO-d_6): δ 111.6–145.9 (13 C, Ar-*C*), 100.7 (1 C, Ace-*C*), 60.2–80.4 (6 C, Sac-*C*), 13.7–35.9 (*C*H_3 and *C*H_2s); FABMS: *m*/*z* 426 $[M+H]^+$; Anal. Calcd for $C_{23}H_{27}N_3O_5$: C, 64.94; H, 6.35; N, 9.88. Found: C, 65.32; H, 6.74; N, 10.61.

N-*[*o-*(Benzimidazol*-*2*-*yl)phenyl]*-*α*-D-*mannopyranosylamine* (**15**).—Yield 0.267 g, (72%): mp 164–166 °C; $[\alpha]_D^{24}$ 110° (*c* 1.0, Me_2SO); FTIR (KBr): 3377, 3299, 2922, 1620, 1329, 1085, 1022 cm^{-1}; UV (DMF), λ (nm) (ε (M^{-1} cm^{-1})): 292 (24,600), 366 (20,660); ^1H

NMR (Me_2SO-d_6): δ 7.78 (d, 1 H, Ar-*H*), 7.62 (d, 1 H, Ar-*H*), 7.52 (d, 1 H, Ar-*H*), 7.20 (d, 2 H, Ar-*H*), 7.13 (t, 1 H, Ar-*H*), 6.85 (s, 2 H, Ar-*H* and Imi-N*H*), 6.63 (t, 1 H, Ar-*H*), 6.29 (s, 1 H, H-1), 4.72 (s, 1 H, Gly-N*H*), 4.56 (d, 1 H, Sac-O*H*), 4.40 (s, 2 H, Sac-O*H*), 4.27 (d, 1 H, Sac-O*H*), 3.43–3.89 (6 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 111.8–148.1 (13 C, Ar-*C*), 63.5-71.5 (6 C, Sac-*C*); FABMS: *m*/*z* 372 $[M+H]^+$; Anal. Calcd for $C_{19}H_{21}N_3O_5$: C, 61.46; H, 5.66; N, 11.32. Found: C, 62.23; H, 5.25; N, 10.76.

N-*[o-(Benzimidazol-2-yl)phenyl]*-α-D-*ribofuranosylamine* (**16**).—Yield 0.241 g (71%): mp 204–206 °C; $[\alpha]_D^{24}$ 130° (*c* 1, Me_2SO); FTIR (KBr): 3283, 2908, 2862, 1620, 1327, 1271, 1072 cm^{-1}; UV (DMF): λ (nm) (ε (M^{-1} cm^{-1})) 301 (23,640), 354 (18,030); ^{1}H NMR (Me_2SO-d_6): δ 7.49–7.81 (m, 3 H, Ar-*H*), 6.83–7.22 (m, 4 H, Ar-*H*), 6.64 (t, 2 H, Ar-*H* and Imi-N*H*), 6.22 (s, 1 H, H-1), 5.01 (d, 1 H, $^3J_{H1,NH}$ 6.00 Hz, Gly-N*H*), 4.92 (d, 1 H, Sac-O*H*), 4.86 (d, 1 H, Sac-O*H*), 4.50 (t, 1 H, Sac-O*H*), 3.43–3.94 (5 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 111.1–148.0 (13 C, Ar-*C*), 62.8–73.3 (5 C, Sac-*C*); FABMS: *m*/*z* 342 $[M+H]^+$; Anal. Calcd for $C_{18}H_{19}N_3O_4$: C, 63.34; H, 5.57; N, 12.32. Found: C, 62.83; H, 5.92; N, 13.02.

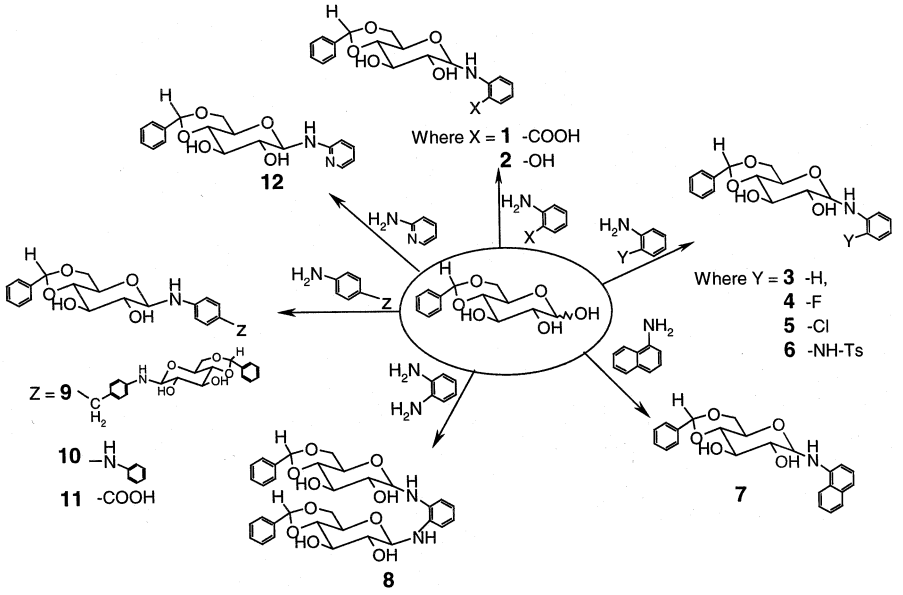
N-*[o-(Benzimidazol-2-yl)phenyl]*-α,β-D-*xylopyranosylamine* (**17**).—Yield 0.235 g (69%): mp 162–164 °C; $[\alpha]_D^{24}$ 30° (*c* 1.0, Me_2SO); ^{1}H NMR (Me_2SO-d_6): δ 7.85 (dd, 1 H, Ar-*H*), 7.56–7.64 (m, 2 H, Ar-*H*), 7.14–7.27 (m, 3 H, Ar-*H*), 6.70–6.92 (m, 3 H, Ar-*H* and Imi-N*H*), 6.04 (d, 0.5 H, $^3J_{H1,H2}$ 4.03 Hz, α, H-1), 5.88 (d, 0.5 H, $^3J_{H1,H2}$ 8.79 Hz, β, H-1), 4.99 (d, 1 H, Sac-O*H*), 4.87 (d, 0.5 H, $^3J_{H1,NH}$ 5.13 Hz, Gly-N*H*), ~4.74 (br, 0.5 H, Gly-N*H*), 4.68 (t, 1 H, Sac-O*H*), 4.49–4.54 (m, 1 H, Sac-O*H*), 3.40–3.86 (5 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 111.6–147.3 (26 C, Ar-*C*), 62.3–73.5 (10 C, Sac-*C*); FABMS: *m*/*z* 342 $[M+H]^+$; Anal. Calcd for $C_{18}H_{19}N_3O_4$: C, 63.33; H, 5.61; N, 12.31. Found: C, 64.22; H, 6.13; N, 12.13.

N-*[o-(Benzimidazol-2-yl)phenyl]*-α,β-D-*arabinopyranosylamine* (**18**).—Yield 0.228 g (67%): mp 160–162 °C; $[\alpha]_D^{24}$ 40° (*c* 1.0, Me_2SO); FTIR (KBr): 3346, 1619, 1406, 1034 cm^{-1}; UV (DMF): λ (nm) (ε (M^{-1} cm^{-1})) 301 (19,940), 352 (15,280); ^{1}H NMR (Me_2SO-d_6): δ 7.86 (t, 1 H, Ar-*H*), 7.58–7.65 (m, 2 H, Ar-*H*), 7.14–7.27 (m, 3 H, Ar-*H*), 6.96 (q, 1 H, Ar-*H*), 6.78–6.86 (m, 2 H, Ar-*H* and Imi-N*H*), 5.86 (d, 0.5 H, $^3J_{H1,H2}$ 6.80 Hz, α, H-1), 5.83 (d, 0.5 H, $^3J_{H1,H2}$ 9.05 Hz, β, H-1), 5.08 (d, 0.5 H, $^3J_{H1,NH}$ 6.95 Hz, Gly-N*H*), 4.80 (d, 0.5 H, $^3J_{H1,NH}$ 6.00 Hz, Gly-N*H*), 4.64 (t, 1 H, Sac-O*H*), 4.45 (d, 1 H, Sac-O*H*), 4.37 (br, 1 H, Sac-O*H*), 3.00–3.93 (5 H, Sac-*H*); ^{13}C NMR (Me_2SO-d_6): δ 110.2–146.9 (26 C, Ar-*C*), 63.3–71.5 (10 C, Sac-*C*); FABMS: *m*/*z* 342 $[M+H]^+$; Anal. Calcd for $C_{18}H_{19}N_3O_4$: C, 63.33; H, 5.61; N, 12.31. Found: C, 63.97; H, 5.34; N, 11.98.

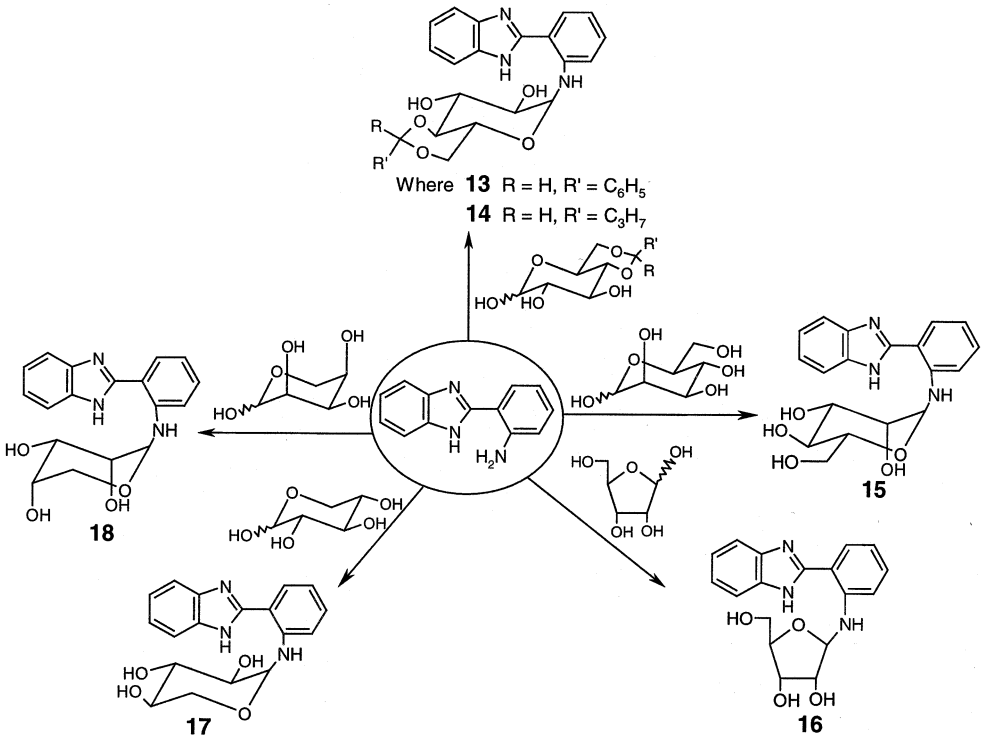
3. Results and discussion

A simple procedure has been adopted to synthesise different *N*-glycosyl amines of the free and the partially protected saccharides with different types of amines. *N*-Glycosyl amines **1**–**12** were synthesised from 4,6-*O*-benzylidene-D-glucopyranose using different ortho-substituted anilines as shown in Scheme 1. Formation of a gel-like product was observed in case of the *N*-glycosyl amines of *o*-fluroaniline (**4**); *o*-chloroaniline (**5**); 1-aminonapthalene (**7**); *o*-phenylenediamine (**8**) and the methylene-linked dianiline (**9**). Saccharides and their derivatives that have hydrogen bond-forming segments are generally prone to form gels.[11,12] Some *p*-nitrophenyl-based saccharides have exhibited gel formation[12,13]. However, the gels formed in the present studies were converted to solid products by repeated washings with ethanol, followed by ether. The syntheses of different *N*-glycosyl amines, **13**–**18** from 2-(*o*-aminophenyl)benzimidazole are outlined in Scheme 2. Compounds **1**–**18** were characterised based on analytical and spectral techniques, and the corresponding data is reported in Section 2. Comparison of melting points of *N*-glycosyl amines **1**–**12** exhibited a trend, $\mathbf{3 \leq 7 < 4 < 5 < 1 < 11 \leq 2}$, which is attributable to their increasing intermolecular interacting abilities.

FAB mass spectral studies.—Mass spectra of the *N*-glycosyl amines reported in this paper exhibited the molecular-ion peaks. Thus the molecular weights of the *N*-glycosyl amines shown in Schemes 1 and 2 were confirmed by these data.



Scheme 1. *N*-Glycosyl amines **1**–**12** derived from the reaction between 4,6-*O*-benzylidene-D-glucopyranose and different aromatic amines.



Scheme 2. *N*-Glycosyl amines **13**–**18** derived from the reaction between 2-(*o*-aminophenyl)benzimidazole and different free and protected saccharides.

Table 1
Chemical shifts (ppm) and coupling constants (Hz) of the anomeric proton (H-1) and glycosyl amine proton (Gly-NH)

Compound no.	δ (H-1), $^3J_{H1,H2}$	δ (N–H), $^3J_{H1,NH}$
1	4.77 (d), 8.82	8.43 (d), 7.30
2	4.57 (t), 8.30	5.33 (s) [a]
3	4.63 (t), 8.79	6.33 (d), 8.42
4	4.66 (t), 8.79	5.99 (d), 6.00
5	4.69 (t), 8.50	5.63 (d), 7.34
6	4.52 (t), 8.61	5.68 (d), 7.91
7	4.79 (t), 8.42	6.62 (d), 8.10
8	4.50 (br)	5.31 [a] (q), 9.95
9	4.60 (t), 7.87	6.11 (d), 8.50
10	4.59 (t), 8.06	6.08 (d), 8.10
11	4.72 (t), 8.43	7.07 (d), 8.40
12	5.14 (t), 9.15	7.08 (d), 8.91
13	6.16 (s)	5.08 (d), 3.66
14	5.88 (s)	4.94 (t) [a]
15	6.29 (s)	4.72 (s)
16	6.22 (s)	5.01 (d), 6.00

[a] Gly-NH peak overlapped with the Sac-OH.

NMR studies.—^{1}H and ^{13}C NMR spectra of the *N*-glycosyl amines **1**–**18** were recorded in Me_2SO-d_6 and were assigned by comparing these with the spectra of the corresponding amine and the saccharide counterparts.

^{1}H NMR studies.—Exchangeable protons, such as, the COOH, OH and NH, were further cross-checked by measuring the spectra after D_2O addition. *N*-Glycosyl amines **1** and **11** exhibited –COOH protons, and **2** exhibited phenolic-OH proton resonances in the corresponding spectra. Products **1**–**18** showed glycosidic-NH protons, and in addition, the products **13**–**18** showed the imidazole-NH proton peaks.

As the glycosylation occurs at the C-1 centre by condensation of the saccharide with the amine, the spectrum of the corresponding *N*-glycosyl amine product is devoid of the C-1–OH resonance that is otherwise present in the corresponding saccharide spectrum (6.49–6.78 ppm). Signals corresponding to the OH groups of the saccharide moiety were identified from the spectra of the *N*-glycosyl amines (5.00–5.55 ppm in case of **1**–**12** and 4.25–5.10 ppm in case of **13**–**18**).

While the precursor saccharide, 4,6-*O*-benzylidene-D-glucopyranose, exists as a mixture of both the α (60%) and β (40%) anomers in Me_2SO, the corresponding *N*-glycosyl amines **1**–**12** exist only in the β form,[14] as judged from the coupling constants $^3J_{H1,H2}$, which were found in the range of 7.87–8.79 Hz. On the other hand, **13**, which was derived from the same saccharide, shows C-1–H at 5.758 ppm as a broad singlet, indicating the presence of some α anomer in the product. In case of **14**, the precursor saccharide, 4,6-*O*-butylidene-D-glucopyranose (4.917 ppm, 3.7 Hz), as well as the product, are found in the α-anomeric form. Similarly, the spectra of **15** and **16** exhibited broad singlet for C-1–H indicating the presence of α anomer. However, in **17** and **18** the C-1–H resonances each appear as two doublets corresponding to the presence of both the α (60%) and the β anomers (40%) having coupling constants of 4.0 and 8.8 Hz, respectively. Correspondingly, two different signals were observed in the case of **17** and **18** for the C-1–NH (glycosyl) indicating the presence of mixture of anomers. *N*-Glycosyl amines formed from D-arabinose and D-ribose with sulfanilamide showed the formation of α anomeric form, whereas D-mannose showed the β anomeric form, indicating that the formation of different anomeric forms depends on the saccharide part as well as on the amine part.[15]

Further, the *N*-glycosyl amine bond formation was noted through observing the glycosyl–NH peak in the spectra of the products. The large variation observed in the chemical shift of the glycosyl amine–NH groups (5.3–8.5 ppm for **1**–**12** and 4.7–6.9 ppm for **13**–**18**) may be attributed to the nature of the saccharide moiety as well as to the amine counterpart. Chemical shifts and coupling constants, $^3J_{H1,NH}$ of all the compounds are provided in Table 1. Comparison of the glycosyl amine–NH chemical shift of **3** (*o*-H, 6.35 ppm) with **1** (*o*-COOH, 8.43 ppm) and **11** (*p*-COOH, 7.07 ppm) suggests the involvement of this –NH in intramolecular hydrogen bonding with the *o*-COOH function in the case of **1** as shown in Fig. 1, whereas **11** cannot show such interaction. On the other hand, the variations observed among **3** (6.35 ppm, *o*-H), **4** (5.99 ppm, *o*-fluoro), **5** (5.63 ppm, *o*-chloro) and **6** (5.68 ppm, *o*-tosyl) are attributable to the inductive effects of the corresponding ortho-substituents.

While the heterocyclic NH of the 2-(*o*-aminophenyl)benzimidazole appeared at 12.63 ppm, the same group in the *N*-glycosyl amine products **13**–**18** experienced a large upfield shift (6.8–7.0 ppm) owing to the breakage of the intramolecular N–H···N hydrogen bond present in the former as shown in Fig. 2.

^{13}C NMR studies.—^{13}C NMR spectra were shown to be consistent with the structures proposed in Schemes 1 and 2. The chemical shifts of the C-1 carbon atoms indicated the presence of β anomers in the case of **1**–**12** and the α anomers in the case of **13**–**16**, and a mixture of these two in the case of **17** and **18**.

Electronic spectra.—Absorption spectra of the *N*-glycosyl amines derived from 4,6-*O*-benzylidene-D-glucopyranose, compounds **1** and **11**, showed doubling of the absorptivity without any change in the position of the $n \rightarrow \pi^*$ transition with respect to the corresponding amine. The *N*-glycosyl amines derived from 2-(*o*-aminolphenyl)benzimidazole showed changes in the position of the absorption peaks when compared with that of the parent amine. Out of the two absorption bands observed in case of the 2-(*o*-aminophenyl)benzimidazole, the 292-nm band did not show any change upon glycosylation, whereas the 351-nm band showed marginal shift in the position.

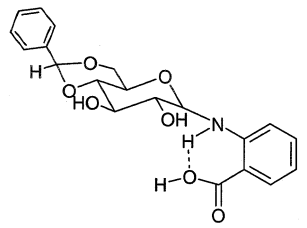


Fig. 1. Intra molecular N–H···O hydrogen bonding in **1**.

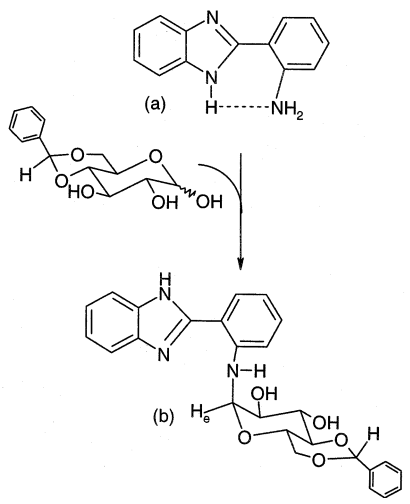


Fig. 2. Presence of H-bond interaction in (a) 2-(*o*-aminophenyl)benzimidazole; and (b) its absence in the corresponding *N*-glycosyl amine.

FTIR spectral studies.—Formation of the *N*-glycosyl amines was observed by comparing the FTIR spectra of the products **1**–**12,** with the spectra of the saccharide, 4,6-*O*-benzylidene-D-glucopyranose and the amine. When 2-(*o*-aminophenyl)benzimidazole reacts with the saccharide, the band corresponding to the primary amine was absent, and that of the secondary amine was shifted to higher frequency in the products **13**–**18** due to the formation of the *N*-glycosyl amine. The difference observed between the $\nu_{C=O}$ vibration of **1** (*o*-COOH, 1668 cm^{-1}) and that of **11** (*p*-COOH, 1692 cm^{-1}) supports the observation made by NMR studies of the involvement of **1** in H-bonding.

Vibrations corresponding to the anomeric properties[16] of these *N*-glycosyl amines were observed in the spectra. Strong bands were observed for **1**–**12** (β anomer, 750–757 and 695–698 cm^{-1}), **13**–**16** (α anomer, 737–745 cm^{-1}), and **17** and **18** (α and β anomers, 740–742, 775, 695 cm^{-1}), indicating the presence of the corresponding anomer(s). This is consistent with the observations made by NMR studies.

Optical rotation studies.—In the case of *N*-glycosyl amines **1**–**12**, both the precursor saccharide and the *N*-glycosyl amines were found to be levorotatory, while the benzimidazole-based glycosyl amines **13**–**18** were dextrorotatory. These results are consistent with those reported in the literature[17] for the corresponding anomer type.

Conclusions.—The present study demonstrates that unprotected and partially protected saccharides are promising building blocks for the synthesis of new glycosyl amines with different characteristic properties, such as gellation, and intra- and intermolecular H-bond formation. These molecules support binding cores, an aspect which is currently under investigation in our laboratory, as shown for **1** and **2** in Fig. 3. Therefore, such molecules are potentially important in the metal-ion binding studies. *N*-Glycosyl

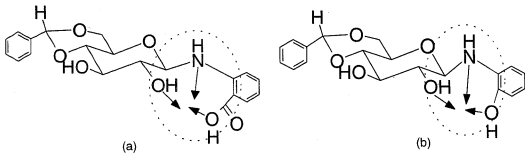


Fig. 3. 'ONO' core present in the *N*-glycosyl amines (a) **1** and (b) **2**.

amines, **1**–**12** are found in the β anomeric form, although their saccharide precursor was in the α anomeric form. Similar types of *N*-glycosyl amines of deoxy monosaccharides are reported in the literature.[18] The effect of different substituents is reflected on the chemical shifts of the glycosyl amine NH protons. Depending upon the nature of the substituent at ortho-position, the presence of a different type, as well as the extent of, H-bondings are observed. The specific rotations of the *N*-glycosyl amines **1**–**12** were negative (levorotatory), whereas the *N*-glycosyl amines **13**–**18** were positive (dextrorotatory), a result which is consistent with the corresponding anomeric assignments.

The imidazole N–H proton in the glycosylic amines **13**–**18** appears at an upfield position relative to that of the corresponding amine. As some of the derivatives of 2-(*o*-aminophenyl)benzimidazoles are shown to have biological activity[6], we believe that the presence of saccharide moiety would serve to enhance the activity in these *N*-glycosyl amine products, and hence, these molecules may act as models for the biological systems.

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