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Directing/protecting groups mediate highly regioselective glycosylation of monoprotected acceptors

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ABSTRACT

A directing/protecting group designed for regioselective functionalization of partially-protected glucopyrannosides has been successfully used to prepare disaccharides in high yields. Most importantly, it has been demonstrated that highly regioselective and stereoselective glycosylation can be achieved when disarmed donors are employed. This study demonstrates the ability of directing/protecting group to induce regioselective glycosylation of carbohydrates and opens the field to the design of other DPGs for other monosaccharides.

1. Introduction

Carbohydrate derivatives, carbohydrate-based peptidomimetics, carbohydrate mimics, and oligosaccharides are gaining in popularity not only as a means of targeting and delivering therapeutics efficiently, but also as drugs and vaccines.[1–8] However, their challenging synthesis hinders many groups from exploring their true potential. One major issue is that synthetic routes utilizing carbohydrates require numerous, wasteful steps of hydroxyl protection and deprotection. In lieu of these steps, researchers developed various strategies to perform simple, selective reactions on carbohydrates,[9,10] including enzymatic,[11] and catalytic processes.[12] In fact, open glycosylation has been seen as a promising but challenging strategy for effective preparation of oligosaccharides.[13,14]

In the early seventies, efforts were directed by Ferrier[15,16] toward the glycosylation of partially or non-protected donors with simple alcohols. Years later, Hanessian reacted designed unprotected glycosyl donors with simple alcohols[17] or with sugar acceptors (Fig. 1a).[18] Similar efforts have also been reported more recently by Schmidt for unprotected glycosylation.[19] Despite these successful study cases, only a few research groups have dealt with the regioselective glycosylation with partially or non-protected acceptors. Aoyama regioselectively glycosylated a fucose unit using arylboronic acid as a transient activating group[13] (Fig. 1b), an approach further investigated by Kaji.[20]

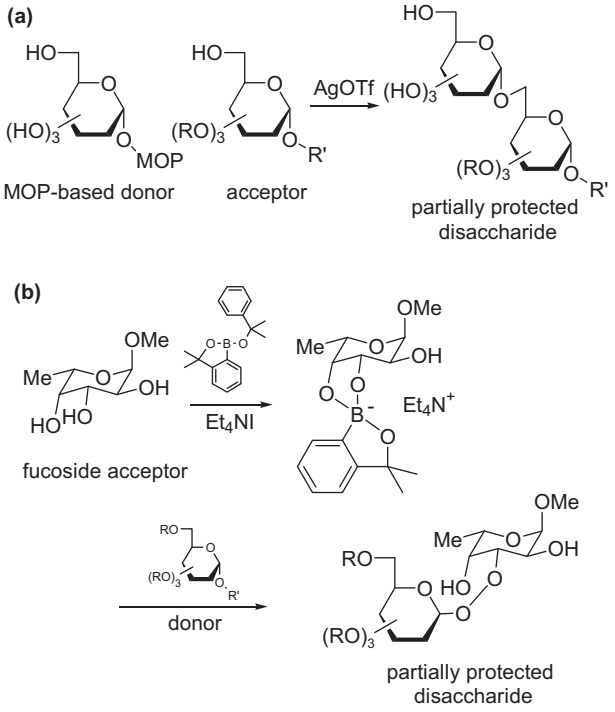

Fig. 1. Selected methods for glycosylation with partially or non-protected donors or acceptors.

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Wang and Kong disclosed the glycosylation of partially or non-protected mannose[21–24] and glucose[25] acceptors with high regioselectivity. Open glycosylation (glycosylation with non-protected acceptors) mediated by stannylene activation was also reported.[14]

In the mid-90s, Vasella has shown that regioselectivity of the glycosylation with glycosylidene carbenes or trichloroacetimidate as donors can be controlled by their relative acidity and nucleophilicity, respectively.[26] The relative reactivity of the secondary hydroxyl groups of monosaccharides can also be modulated by intra- or intermolecular hydrogen bonds.[27–29] Recently, there have been a few new innovative approaches aiming at regioselective manipulation of carbohydrate hydroxyl groups through the control of the surrounding hydrogen bond pattern.[30] Yoshida's seminal work on the relative reactivity of secondary hydroxyl groups revealed the role and potential of the H-bonds in the control of the relative reactivities of the carbohydrate hydroxyl groups.[31] Kawabata et al. followed up on this work with the regioselective acylation of 6-*O*-protected octyl β-D-glucopyranosides using DMAP.[32] The hydrogen bond network has also been proposed to explain the regioselectivity observed with other reactions.[33]

An efficient open glycosylation strategy—a procedure allowing regiocontrolled glycosylation without recourse to protection/deprotection steps—implies the modulation of the rates of glycosylation reactions. Such a strategy would represent an expeditious approach to form a given oligosaccharide or libraries of oligosaccharides (for a report on random glycosylation of unprotected *N*-acetyl glucosamine, see Ref. 34). We reasoned that a protecting group at position 6—the easiest to install—would greatly facilitate our investigations.

Based on these premises, we have designed a hydrogen-bonding protecting group referred to as a directing/protecting group (DPG) that we predicted to hydrogen bond with the hydroxyl groups of glucopyranosides.[29] In the past, Crich and Dudkin have shown that hydrogen-bonding protecting groups influence the rate of glycosylation reaction.[35] In the present work, we demonstrate that glycosyl donors can glycosylate DPG-protected glucosyl acceptors *regioselectively*. By means of NMR spectroscopy and various acceptors (**1**–**4**), we have further investigated the mechanism leading to the observed regioselectivity.

2. Influence of protecting groups on regioselectivity

2.1. Preparation and reaction of monoprotected glucopyranosides

At the outset of this research program, we assessed how different protecting groups at position 6 of monoprotected methyl α-D-glucopyranoside acceptors influenced the regioselectivity of glycosylation reactions. A set of monoprotected methyl α-D-glucopyranoside acceptors (**1b**–**m**) were prepared from methyl α-D-glucopyranoside **1a** following previously described synthetic approaches (Fig. 2).[29] We then reacted each of these partially-protected glycosyl acceptors with 1 equiv of glycosyl donor (**5**) in the presence of TMSOTf. The reactions yielded the six possible isomers **7a**/**b**, **8a**/**b**, and **9a**/**b** after deprotection (Fig. 2 and Table 1). Quick filtration allowed us to isolate the six expected disaccharides in combined yields of 30–55%. Careful analysis of the reaction mixtures confirmed that little to no trisaccharide—resulting from di-glycosylation of the acceptors—was formed and that conversions and isolated yields were equivalent. At this stage, regioselectivity and not yield was investigated.

2.2. Preparation of the 6 possible isomers

In order to evaluate the regioselectivity and stereoselectivity of these glycosylation reactions, the six possible disaccharide products (**7a**/**b**, **8a**/**b**, **9a**/**b**) were prepared individually from **1a** in 5–6 steps, using traditional protection/deprotection strategies (Schemes 1 and 2).

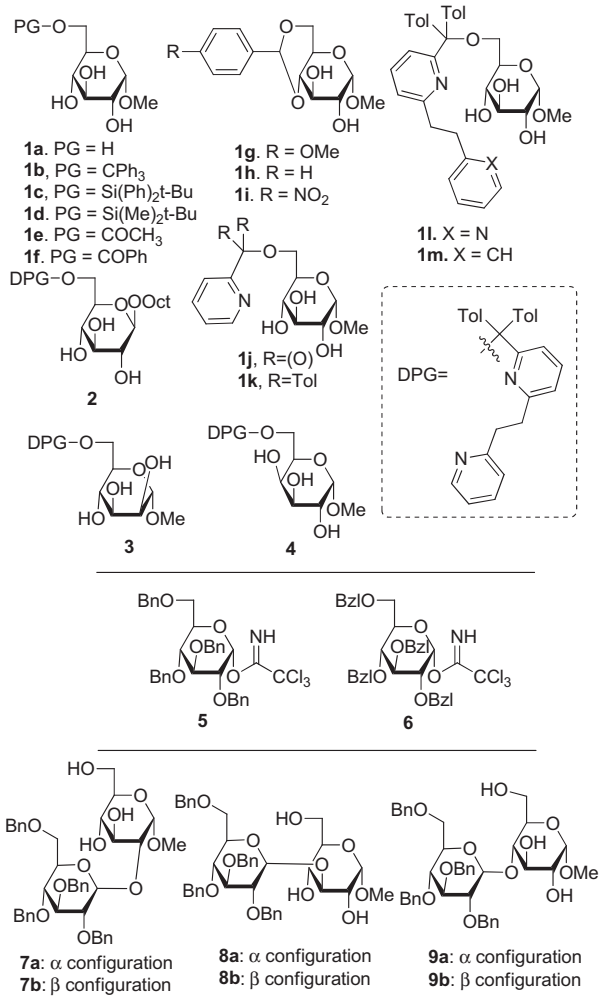


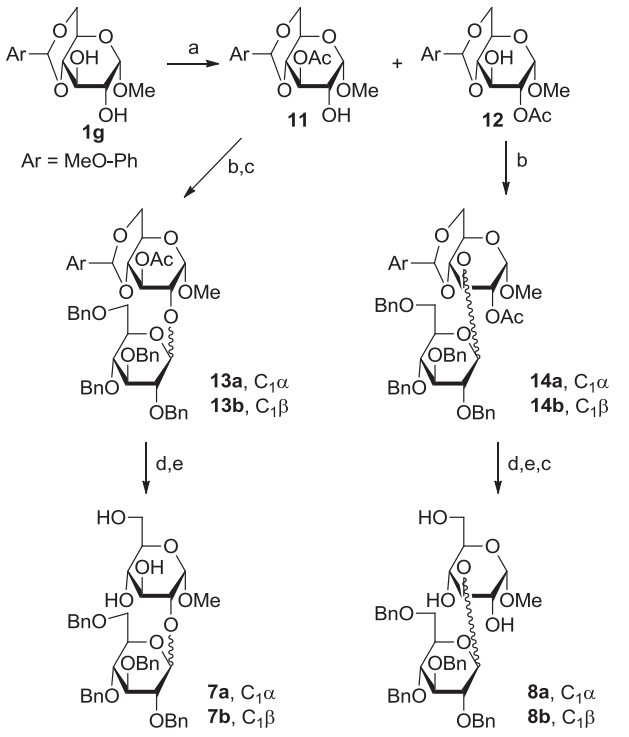
Fig. 2. Selected monoprotected glycosyl acceptors (**1**–**4**) and glycosyl donors (**5**, **6**) and possible regio/stereoisomeric disaccharides (**7a**,**b**–**9a**,**b**).

The synthesis began with the differentiation of the two hydroxyl groups of **1g** (Scheme 1). Monoacetylation of diol **1g** with acetic anhydride led to chromatographically separable regioisomers **11** and **12**.[36] Glycosylation of donor **5**[37] with both alcohols was next carried out. Optimization at this stage eventually led to the use of Schmidt trichloroacetimidate method[38,39] and catalytic trimethylsilyl triflate (TMSOTf) as an activator providing separable disaccharides **13a** and **13b** and non-separable disaccharides **14a** and

Table 1
Initial investigations: regioselectivity versus PG via Scheme 3

Entry	Compd	**7a**/**7b**[a] (%)	**8a**/**8b**[a] (%)	**9a**/**9b**[a] (%)
1	**1b**	39 (1:1.1)	53 (1:4.2)	8
2	**1c**	39 (1.0:1)	57 (1:1.4)	4
3	**1d**	40 (1.3:1)	56 (1.1:1)	4
4	**1e**	24 (1.6:1)	60 (1:1.2)	16
5	**1f**	27 (1.5:1)	69 (1:1.2)	4
6	**1g**	41 (1.4:1)	59 (1:1.6)	—
7	**1h**	45 (1.8:1)	55 (1:7.9)	—
8	**1i**	45 (2.2:1)	55 (1:2.1)	—
9	**1j**	35 (1.1:1)	53 (1:1.2)	12
10	**1k**	40 (1:1.1)	56 (1:1.4)	4
11	**1l**	65 (1.6:1)	33 (1.6:1)	2
12	**1m**	45 (1:1)	51 (2.2:1)	4

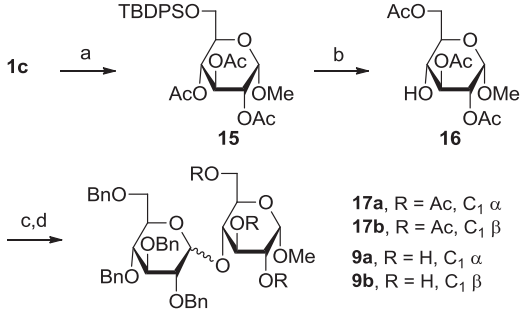
[a] HPLC analysis of the mixtures after filtration on a silica gel pad, α:β ratios are given in brackets.



Scheme 1. (a) Ac_2O (1.1 equiv), DMAP, K_2CO_3, CH_2Cl_2, 47% (**11**), 40% (**12**); (b) 2,3,4,6-tetra-*O*-benzyl glucopyranosyl trichloroacetimidate **5**, TMSOTf, 4 Å MS, CH_2Cl_2, 0 °C, 84% (**13a**/**13b**=2:1), 72% (**14a**/**14b**=2:1); (c) preparative HPLC separation; (d) AcOH/THF/H_2O, 1:1:1, 40 °C; (e) MeONa, MeOH, 90% (**7a**), 93% (**7b**), 93% (**8a**+**8b**).

14b, respectively (Scheme 1). Both anomers **13a** and **13b** were sequentially deprotected by hydrolysis in acidic medium followed by Zemplén deacetylation to give target compounds **7a** and **7b** in good yields. Similarly, compounds **14a** and **14b** were hydrolyzed then methanolized affording the corresponding separable mixture of anomers **8a** and **8b**.

The last two reference compounds **9a** and **9b** were prepared from readily available triacetylated glucopyranoside **16**.[40] As illustrated on Scheme 2, peracetylation of triol **1c** was achieved on treatment with acetic anhydride in presence of DMAP yielding the fully protected saccharide **15**. Triacetylated compound **15** was subsequently reacted with a fluoride source to generate **16** after acetyl migration as reported by Passancatelli et al.[41] Both glycosylation partners (**5** and **16**) were next reacted to give the inseparable mixture of disaccharides **17a** and **17b**. These two fully protected compounds were methanolized into the target disaccharides **9a** and **9b**, which unfortunately remained inseparable



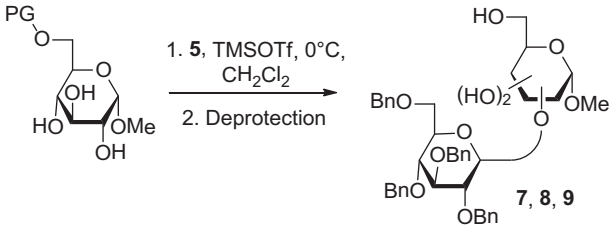
Scheme 2. (a) Ac_2O (10 equiv), DMAP, Et_3N, CH_2Cl_2, 100%; (b) TBAF, THF, 0 °C then rt, 84%; (c) **5**, TMSOTf, 4 Å MS, CH_2Cl_2, 0 °C, 79%; (d) MeONa, MeOH, 91%.

even after extensive chromatographic work.

Analytical HPLC conditions were found where 2, 3, and 4-glycosylated isomers were clearly identified on chromatograms. In addition, the ratios of model mixtures of known composition of **7a**,**b**, **8a**,**b**, and **9a**,**b** were accurately reproduced on chromatograms with an accuracy of 0.5%. However, even if the isomers **7a**, **7b**, **8a**, and **8b** were separated, the epimers **9a** and **9b** came out with identical retention times on silica gel or reversed phase HPLC columns.

2.3. Regioselectivity of the glycosylation reaction

These six individually-prepared disaccharides were used as HPLC references to identify the disaccharides produced in each reaction. As expected, we observed that glycosylation with the bulky armed donor **5** occurred preferentially at position 3 over position 2 with all the traditional protecting groups investigated in this work (Table 1, entries 1–8, Scheme 3). Furthermore, for the reaction of **5** with the bulky TBDPS or trityl group-containing derivatives **1b** and **1c**, we observed low levels (4–8%) of 4-*O*-glycosylated products **9a** and **9b**. On the other hand, the small acetylated derivative **1e** gave larger amounts of **9a**/**b** (16%, entry 4).



Scheme 3. Regioselectivity in the glycosylation.

The higher regioselectivity observed using electron-withdrawing esters (**7a**/**b**:**8a**/**b**: 1:2.5–2.55, entries 4 and 5) over that observed using ethers (1:1.35, entry 1) and silyl ethers (1:1.40 to 1.45, entries 2 and 3) was rationalized by electronic effects. Electronic effects were further investigated using benzylidene protecting groups ranging from electron-poor to electron-rich (entries 6–8). This study revealed that the electronic effects of this series of protecting groups are not strong enough to provide a tool for regioselective transformations.

When comparing the outcome of the glycosylation reactions with **1b** and **1k** differing only by the presence of a nitrogen atom, we were also pleased to observe the influence of the pyridyl ring of **1**, which altered the ratio of 4-*O*-glycosylated products **9a** and **9b** (entries 1 and 10). Although the same amount of 4-*O* regioisomers **9a**/**b** were observed with the pyridyl-containing glucopyrannoside **1k** and TBDPS-containing glucopyrannoside **1c**, we believe that the reduced levels of **9a**/**9b** observed with **1** was due to the effect of the intramolecular hydrogen bond while the low level of **9a**/**9b** observed with **1c** is due to the steric effects induced by this bulky protecting group, which is known to adopt conformations very different to ethers.[42] Even more gratifying was the reversal of selectivity observed when moving from **1k** (**7**/**8**: 1:1.4, entry 10) to **1l** (**7**/**8**: 2.0:1, entry 11). We previously showed that position 3 was the most reactive,[29] and yet we observed glycosylation predominantly at position 2. Although the substitution of a phenyl ring in **1b** to a pyridyl ring in **1k** did not significantly affect the rate of the Lewis acid mediated glycosylation reactions, introduction of the second pyridyl ring in **1l** significantly did. Although one could rationalize this loss of reactivity by a reaction between TMSOTf and the terminal pyridyl group, a similar trend was previously observed with the acetylation reaction carried out in basic media with **1b**, **1k**, and **1l**.[29] Hence this poor reactivity cannot be only attributed to the formation of trimethylsilylpyridinium salts (see below).

In order to further assess the role of the terminal pyridyl ring of **1l**, the terminal phenyl analogue **1m** was reacted under the same

conditions. Once the hydrogen bond between the protecting group and position 3 was removed, the regioselectivity of the glycosylation reverted to a level closer to that of the reaction of the simpler, mono-pyridyl-protected acceptor (entries 10 and 12 vs 11). This observation confirmed the critical role of the nitrogen of the terminal pyridyl group of **1l**, which provides bulk and blocks position 3 from being glycosylated.

3. Optimization for practical applications

At this stage, DPGs were shown to influence the regioselectivity of the investigated reaction, however not with practical levels of regioselectivity. Optimization of the reaction conditions (Lewis acid, temperature, addition time, and amount of donors) significantly increased the efficiency of this method in terms of yields and regioselectivities (Table 2, entry 1). Unlike other reported methods, our strategy significantly favors glycosylation of position 2 over positions 3 and 4. However, we failed to increase the stereoselectivity to practical levels. To address this issue, we turned our attention to the disarmed glycosyl donor **6**. Our set of reference disaccharides **7a**/**b**, **8a**/**b**, **9a**/**b** was no longer valid. Fortunately, products formed with the new donor yielded significantly clearer NMR spectra, no longer cluttered with the benzylic protons, which prevented any possible 2D NMR analysis of the products. Thus, rather than preparing another set of reference compounds, we were able to perform extensive 2D NMR experiments (COSY, HSQC, and HMBC) of each product in order to determine the position of the glycosidic linkage formed and stereochemistry of the anomeric center.

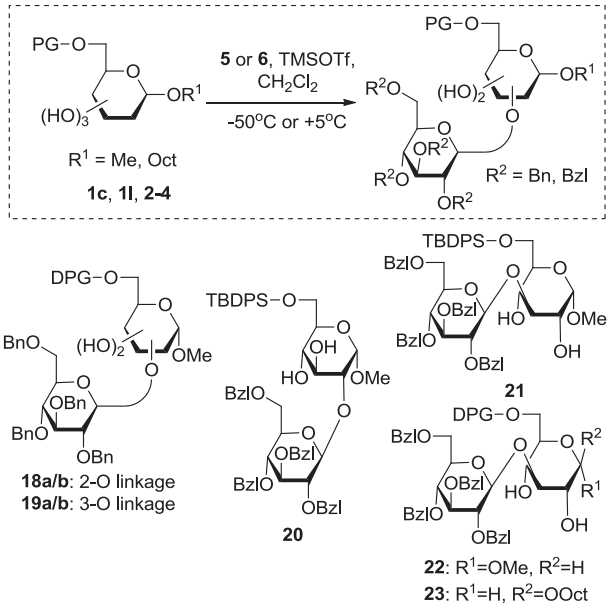
Table 2
Regioselectivity and stereoselectivity

Entry	Reactants	T (°C)	2-O[a] (%)	3-O[a] (%)	SM[a] (%)
1	**1l**–**5**	−50	61 (1:1.8) **18a**,**b**	11 (1:1.9) **19a**,**b**	8
2	**1c**–**6**	−50	18 (0:1), **20**	20 (0:1), **21**	62
3	**1l**–**6**	−50	<5%	80% (0:1), **22**	<5%
4	**1l**–**6**	+5	<5%	90% (0:1), **22**	<5%
5	**2**–**6**	−50	<5%	87% (0:1), **23**	<5%
6	**3**–**6**	−50	<5%	<5%	>90%
7	**3**–**6**	5	Complex mixture[b]		
8	**4**–**6**	−50	<5%	<5%	>90%
9	**4**–**6**	5	Complex mixture[b]		

[a] α:β ratios are given in brackets.
[b] Several products were observed in the reaction mixtures.

Our investigation started with the widely used TBDPS protecting group and confirmed the expected stereoselectivity obtained with the disarmed donor. However, even at low temperature and low conversions, no regioselectivity was observed (Table 2, entry 2) revealing the challenge we were facing. We were very pleased to observe reproducible, high levels of regioselectivity (glycosylation at position 3 almost exclusively) and stereoselectivity (β-anomer formed), low levels of polyglycosylation (very little trisaccharide was observed) and high yields (yields of 90% and 87%, entries 4 and 5, respectively) with the anomers **1l** and **2**.

Although the proposed strategy was successful in producing a single isomer out of the six possible, we were puzzled with the reversal of regioselectivity observed when moving from the armed donor **5** to the disarmed donor **6** (Scheme 4).



Scheme 4. Glycosylation of DPG-functionalized acceptors.

network positions the DPG close to the 3-OH and 4-OH, increasing the steric hindrance at these positions while increasing their nucleophilicity. Armed donors (**5**) are reactive enough to glycosylate the three hydroxyl groups and steric factors will induce regioselective glycosylation at position 2. In contrast, poorly reactive donors (**6**) are not reactive enough to react with non-activated position 2 and proceeds through regioselective glycosylation at position 3.

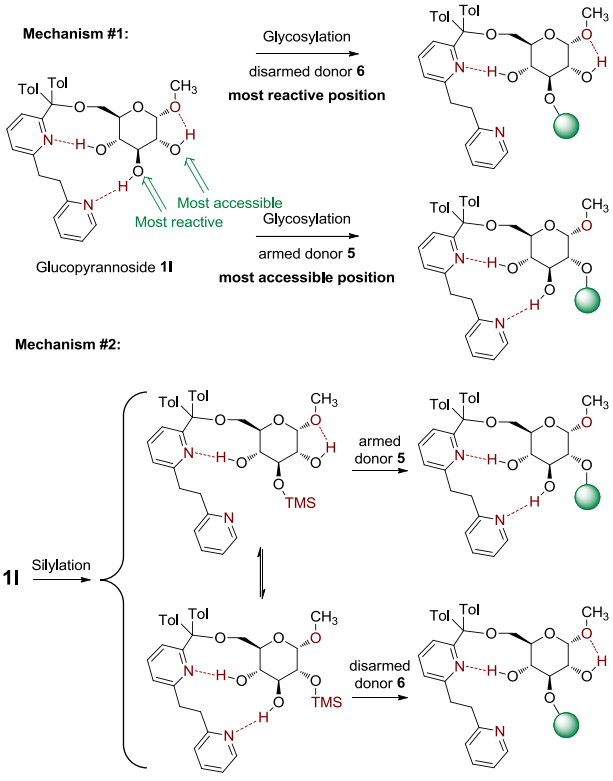


Fig. 3. Proposed alternative mechanisms.

4. Mechanistic study

4.1. Two possible mechanisms

Two mechanisms were proposed to explain this reversal of regioselectivity (Fig. 3). In a first mechanism, the hydrogen bond

As an alternative mechanism, silylation of 3-OH by internal delivery of a TMS group by the terminal pyridyl ring of the DPG blocks this position. This last mechanism is supported by

previously reported carbohydrate silylation using trimethylsilylpyridinium triflate.[43] This fairly labile protecting group would then come off at the deprotection stage and/or during work up. The internal delivery at position 3 is most likely faster than the intermolecular delivery at position 2. Although the 3-*O*-silylated regioisomer is majoritarily formed (kinetic product), equilibrium either by intramolecular or intermolecular migration would lead to the more stable 2-*O*-silylated regioisomer (thermodynamic isomer).

4.2. Mechanism #2

To investigate this second mechanism, an NMR spectroscopy study was carried out. A reversible formation of trimethylsilylpyridinium salts primarily with the terminal pyridyl group was observed by alternative addition of TMSOTf and **1l** in $CDCl_3$. However, this study also revealed that no silylation of the hydroxyl groups took place after 4 h (Fig. 4) and rules out the second mechanism. In addition, during the glycosylation experiments described in Tables 1 and 2, TMSOTf was added over time keeping its levels sub-stoichiometric and leaving hydrogen-bonded **1l** free to react.

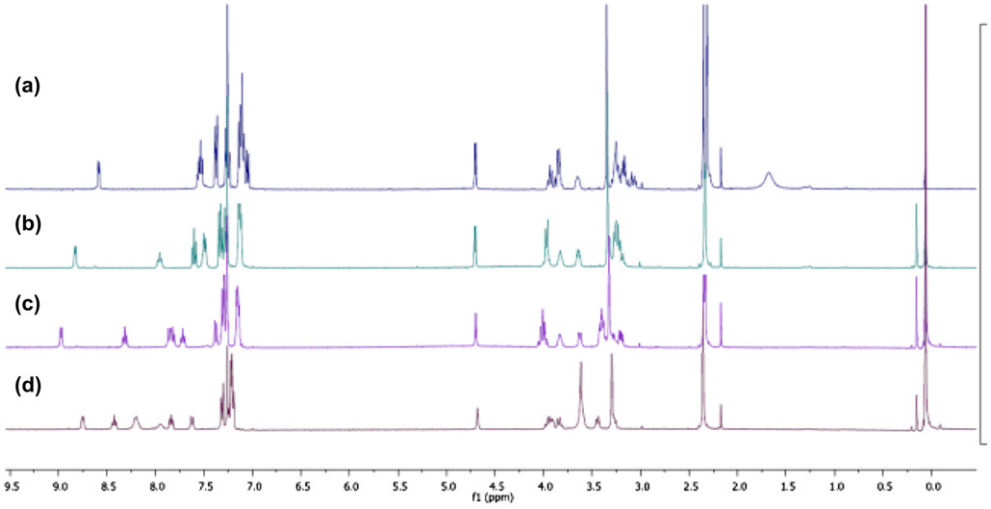


Fig. 4. NMR spectra of **1l** with various amount of TMSOTf—0.0 equiv (a), 0.5 equiv (b), 1.0 equiv (c), 1.5 equiv (d). Addition of **1l** to (c) leads to (b) and vice-versa. No significant changes in the spectra were observed after 4 h.

4.3. Mechanism #1-modulating the hydrogen bond network

To further elucidate the role of hydrogen bonds in the regioselectivity of this reaction and probe the first mechanism (Fig. 3), the derivatives **2**, **3**, and **4** were prepared and their induced hydrogen bond network investigated by NMR following a method reported previously (Fig. 5).[29] In a nutshell, hydroxyl protons when hydrogen-bonded to a pyridyl ring are significantly shifted downfield (δ in the range of 7 ppm) and broad in $CDCl_3$. This makes their observation and identification on ^1H NMR spectra difficult. Using various mixtures of $CDCl_3$ and DMSO-d_6 these proton peaks were shifted and sharpened and extrapolation can be used to evaluate their chemical shift in neat $CDCl_3$.

Based on this data, we proposed hydrogen bond networks shown in Fig. 6. First, both glucopyranosides **1l** and **2** adopted the same hydrogen bond network and their reactivity and regioselectivity in the glycosylation were expected to be highly similar. Although the mannopyrannoside derivative **3** adopted a network similar to **1l**, the postulated hydrogen bond between O-3 and HO-2 shuts down the reactivity of O-3. In contrast, the NMR spectroscopy investigation of the galactopyranoside derivative **4** did not show any pyridyl-hydroxyl group interaction.

The DPG described herein has been specifically designed for glucopyrannosides and is not expected to induce the same levels of selectivity with the mannopyranoside and galactopyrannoside **3** and **4**. Recently, a TBDPS-protected mannose derivative has been shown to be highly selective for glycosylation at position 3 and poorly reactive at position 2 (axial hydroxyl group).[44] In the present work, the additional postulated hydrogen bond between O-H2 and O-3 blocks position 3 (Fig. 6), making this acceptor most likely unreactive. In fact, we observed the expected low conversions and poor regioselectivities with the mannose derivative **3** (Table 2, entries 6 and 7). Similarly, the DPG specifically designed for glucose provided low regioselectivities with the galactose derivative **4** (Table 2, entries 8 and 9). This data provides additional evidences for the role of hydrogen bonds in the DPG-mediated regioselective glycosylation of glucopyranosides.

5. Conclusion

We have established a novel strategy for modulation of the relative reactivity in glycosylation reactions of the 2-, 3-, and 4-OH's, consistent with the experimentally observed hydrogen bonds. Our designed directing/protecting group, which can be selectively installed at position 6, can direct glycosylation with disarmed glycosyl donors to position 3 with great levels of regio- and stereoselectivity and high yields. To our knowledge, this is the first report on the stereo- and regioselective synthesis of Glu-Glu using monoprotected acceptors offering an alternative to the traditional approaches of orthogonal protection. This study also demonstrated that DPGs can be used in different ways, as they enhanced not only the nucleophilicity of hydroxyl groups (i.e., increasing selectivity by directing glycosylation with disarmed donors to position 3) but also the steric hindrance around selected hydroxyls (i.e., increasing selectivity by directing glycosylation with armed donors to position 2). Further design and synthesis are underway to better explore this concept and more specifically to apply it to other carbohydrate acceptors such as galactose and mannose.

6. Experimental section

6.1. General methods

Solvents were distilled and dried by standard methods; THF and ether, from Na/benzophenone; and CH_2Cl_2 from P_2O_5. All

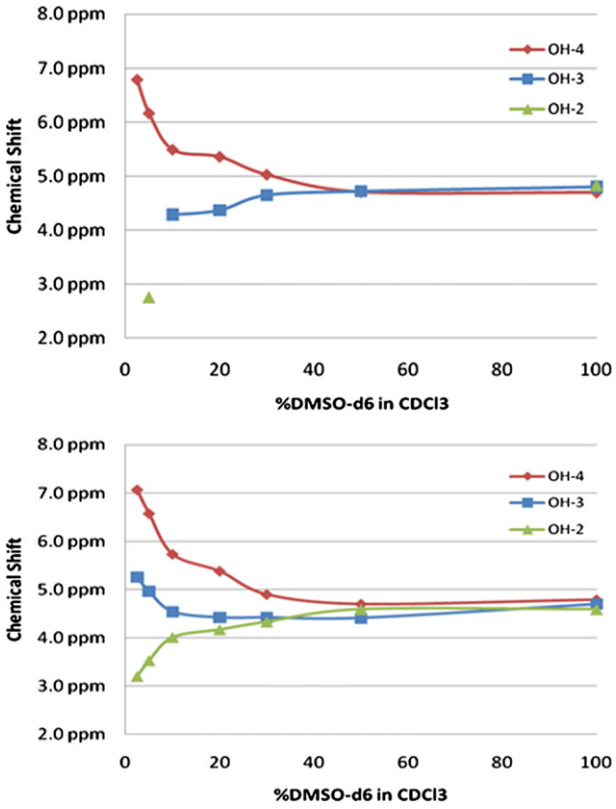


Fig. 5. ^{1}H NMR chemical shift of hydroxyl groups. Top panel: glucopyrannoside **2**. Bottom: mannopyrannoside **3**. When the chemical shift was not ascertained (peaks hidden within the carbohydrate peaks or too broad), values are missing. For galactopyrannoside **4**, the OH peaks were all in the 2.5–5 ppm region indicating no strong hydrogen bonds.

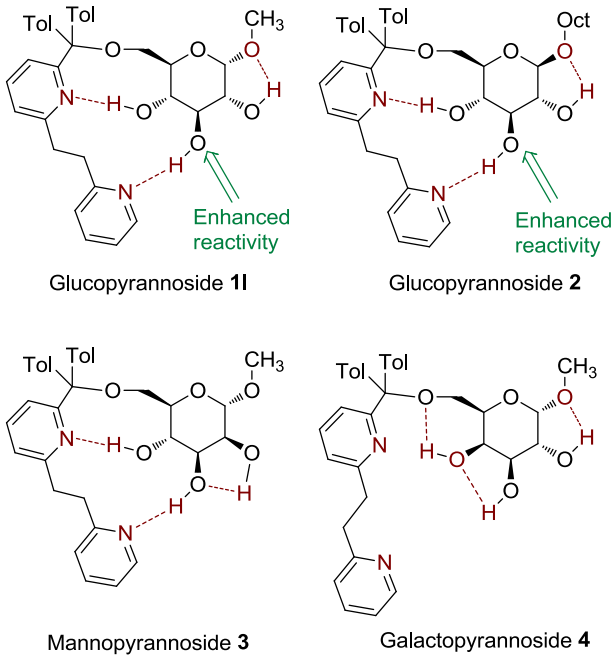


Fig. 6. Hydrogen bond network of DPG-protected gluco-, galacto- and mannopyrannosides.

commercially available reagents were used without further purification. 4 Å molecular sieves were dried at 100 °C prior to use. Melting points are uncorrected and recorded with a Büchi capillary tube melting-point apparatus. Optical rotations were measured on a Perkin–Elmer 141 polarimeter in a 1 dm cell at 20 °C. FTIR spectra were recorded on a Perkin Elmer Spectrum 1000 on NaCl windows or KBr pellets or a Perkin–Elmer Spectrum One FT-IR. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC 250 or DRX 400 spectrometers (250 and 400 MHz, respectively) or on Varian mercury 400 MHz, 300 MHz or Unity 500 spectrometers. Chemical shifts are reported in parts per million using the residual of chloroform as internal standard (7.27 ppm for ^{1}H and 77.0 ppm for ^{13}C, respectively). Mass spectra were recorded on a Trio 1000 Thermo Quest spectrometer in the electron impact mode, a Platform Micromass in the electrospray mode, a Kratos MS25 RFA Double focusing mass spectrometer in electron impact Peak matching (70 eV) mode or on a IonSpec 7.0 t FTMS by electrospray ionization. Elemental analyses were obtained on a Perkin–Elmer 240C microanalyser. Analytical thin-layer chromatography was performed on Merck 60 F_{254} pre-coated silica gel plates or on Silicycle 60 F254 pre-coated silica gel plates. Visualization was performed by UV or by development using $KMnO_4$, H_2SO_4/MeOH or Mo/Ce solutions. Preparative chromatography was performed on silica gel 60 (230–40 mesh ASTM) at increased pressure. Analytic reverse phase HPLC was performed on two C18 columns: Kromasyl C18 10 μm, from A.I.T. Chromato (Le Mesnil le Roi, France) and Platinum C18 10 μm, from Alltech (Laarne, Belgium). A flow rate of 1.0 mL min^{-1} was used with a mobile phase of CH_3CN/H_2O (gradient A: 50%–70% within 45 min, gradient B: 70–90% within 40 min). UV detection was monitored at 254 nm.

6.2. Preparation of the monoprotected glucopyrannosides 1b–m

Synthesis of these compounds has been reported previously.[29]

6.3. Preparation of the reference compounds

*6.3.1. Methyl 2/3-O-acetyl-4,6-O-(p-methoxybenzylidene)-α-D-glucopyranoside (**11**/**12**).* To a suspension of **1g**[29] (2.15 g, 6.9 mmol) and K_2CO_3 (4.4 g, 32 mmol) in CH_2Cl_2 (400 mL) were added acetic anhydride (0.78 mL, 8.3 mmol) and DMAP (77 mg, 1.4 mmol). After stirring for 5 h, the reaction mixture was concentrated and the resulting mono- and diacetylated compounds were separated (silica gel, H/EA, 4:1 then 3:2) to afford isomers **11** (1.15 mg, 47%, white crystals) and **12** (991 mg, 40%, white powder) along with the diacetylated compound (344 mg, 12%).

Data for **11**: R_f=0.24 (H/EA, 1:1); $[\alpha]_D^{20}$ +92.8 (*c* 0.9, $CHCl_3$); mp 175 °C; IR (neat/NaCl) 3474, 1741 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.39 (d, 2H, *J*=8.9 Hz), 6.88 (d, 2H, *J*=8.9 Hz), 5.45 (s, 1H), 5.22 (dd, 1H, *J*=9.5, 9.5 Hz), 4.80 (d, 1H, *J*=3.5 Hz), 4.29 (dd, 1H, *J*=3.5, 9.5 Hz), 3.87 (m, 1H), 3.81 (s, 3H), 3.75 (dd, 1H, *J*=9.5, 9.5 Hz), 3.65 (m, 1H), 3.56 (dd, 1H, *J*=9.5, 9.5 Hz), 3.47 (s, 3H), 2.29 (d, 1H, *J*=11.0 Hz), 2.12 (s, 3H); ^{13}C NMR (65 MHz, $CDCl_3$) δ 170.9, 159.9, 129.4, 127.4, 113.4, 101.3, 100.0, 78.5, 72.1, 71.6, 68.6, 62.6, 55.4, 55.1, 20.9.

Data for **12**: R_f=0.34 (H/EA, 1:1); $[\alpha]_D^{20}$ +93.6 (*c* 0.8, $CHCl_3$); mp 123 °C; IR (neat/NaCl) 3480, 1741 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.43 (d, 2H, *J*=8.9 Hz), 6.90 (d, 2H, *J*=8.9 Hz), 5.51 (s, 1H), 4.96 (d, 1H, *J*=4.5 Hz), 4.81 (dd, 1H, *J*=4.5, 9.5 Hz), 4.29 (dd, 1H, *J*=3.5, 9.5 Hz), 4.18 (ddd, 1H, *J*=2.0, 9.5, 9.5 Hz), 3.82 (m, 1H), 3.81 (s, 3H), 3.75 (dd, 1H, *J*=9.5, 9.5 Hz), 3.54 (dd, 1H, *J*=9.5, 9.5 Hz), 3.41 (s, 3H), 2.57 (br s, 1H), 2.17 (s, 3H); ^{13}C NMR (65 MHz, $CDCl_3$) δ 170.6, 159.9, 129.3, 127.4, 113.4, 101.6, 97.2, 81.0, 73.3, 68.5, 68.1, 61.8, 55.1, 55.0, 20.6.

*6.3.2. Methyl 3-O-acetyl-2-O-(2′,3′,4′,6′-tetra-O-benzyl-α-D-glucopyranosyl)-4,6-O-(p-methoxybenzylidene)-α/β-D-glucopyranoside (**13a**/**13b**).* To a solution of pyranoside **11**[29] (307 mg, 0.87 mmol), glucopyranosyl trichloroacetimidate **5** (652 mg, 0.95 mmol) and 4 Å MS in dry CH_2Cl_2 (25 mL) was added a freshly prepared 0.1 M

solution of TMSOTf in CH_2Cl_2. The resulting mixture was stirred for 1 h at 0 °C then quenched with a drop of Et_3N, diluted with CH_2Cl_2, washed with 1 M $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. The isomers were separated by chromatography (H/EA, 4:1) to afford regioisomers **13a** (425 mg, 56%, colorless oil) and **13b** (215 mg, 28%, white crystals).

Data for **13a**: R_f=0.43 (H/EA, 7:3); $[\alpha]_D^{20}$ +48.5 (*c* 1.1, $CHCl_3$); IR (neat/NaCl) 1755 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.40 (d, 2H, *J*=8.9 Hz), 7.32 (m, 20H), 6.88 (d, 2H, *J*=8.9 Hz), 5.62 (dd, 1H, *J*=9.5, 9.5 Hz), 5.43 (s, 1H), 4.96 (d, 1H, *J*=11.5 Hz), 4.91 (d, 1H, *J*=3.5 Hz), 4.86 (d, 1H, *J*=3.5 Hz), 4.84 (d, 1H, *J*=11.5 Hz), 4.82 (2d, 2H, *J*=11.5 Hz), 4.65 (d, 1H, *J*=11.5 Hz), 4.59 (d, 1H, *J*=11.5 Hz), 4.46 (2d, 2H, *J*=11.5 Hz), 4.28 (dd, 1H, *J*=4.5, 9.5 Hz), 3.96 (dd, 1H, *J*=9.5, 9.5 Hz), 3.92 (m, 1H), 3.88 (m, 1H), 3.81 (s, 3H), 3.79 (dd, 1H, *J*=3.5, 9.5 Hz), 3.74–3.60 (m, 3H), 3.53 (dd, 1H, *J*=9.5, 9.5 Hz), 3.54 (dd, 1H, *J*=3.5, 9.5 Hz), 3.51 (dd, 1H, *J*=9.5, 9.5 Hz), 3.43 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (65 MHz, $CDCl_3$) δ 169.4, 159.9, 138.6, 138.3, 138.2, 137.7, 129.4, 128.3–127.3, 113.4, 101.3, 97.5, 95.8, 81.4, 79.3, 79.2, 77.2, 75.4, 74.7, 74.6, 73.2, 72.9, 70.6, 69.8, 68.7, 68.1, 62.2, 55.1, 55.0, 20.9.

Data for **13b**: R_f=0.30 (H/EA, 7:3); $[\alpha]_D^{20}$ +35.7 (*c* 0.7, $CHCl_3$); IR (neat/NaCl) 1755 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.40 (d, 2H, *J*=8.9 Hz), 7.32 (m, 18H), 7.19 (m, 2H), 6.88 (d, 2H, *J*=8.9 Hz), 5.65 (dd, 1H, *J*=9.5, 9.5 Hz), 5.45 (s, 1H), 5.07 (d, 1H, *J*=3.5 Hz), 4.94 (d, 1H, *J*=11.5 Hz), 4.92 (d, 1H, *J*=11.5 Hz), 4.82 (d, 1H, *J*=11.5 Hz), 4.78 (d, 1H, *J*=11.5 Hz), 4.70 (d, 1H, *J*=11.5 Hz), 4.57 (d, 1H, *J*=11.5 Hz), 4.52 (2d, 2H, *J*=11.5 Hz), 4.50 (d, 1H, *J*=7.5 Hz), 4.30 (dd, 1H, *J*=4.5, 10.0 Hz), 3.95 (dd, 1H, *J*=4.5, 10.0, 10.0 Hz), 3.82 (dd, 1H, *J*=3.5, 9.5 Hz), 3.81 (s, 3H), 3.75–3.58 (m, 4H), 3.58–3.45 (m, 3H), 3.43 (m, 1H), 3.45 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (65 MHz, $CDCl_3$) δ 169.8, 159.9, 138.4, 138.3, 137.82, 137.79, 129.4, 128.3–127.2, 113.4, 105.0, 101.2, 100.3, 84.5, 81.4, 79.7, 78.6, 77.5, 75.5, 74.9, 74.6, 74.3, 73.3, 70.1, 69.0, 68.8, 62.1, 55.3, 55.1, 20.6.

*6.3.3. Methyl 2-O-acetyl-3-O-(2′,3′,4′,6′-tetra-O-benzyl-α/β-D-glucopyranosyl)-4,6-O-(p-methoxybenzylidene)-α-D-glucopyranoside (**14a**/**14b**).* Following the same procedure as for compounds **13a** and **13b**, glucopyranoside **12** (415 mg, 1.17 mmol) and **5** (882 mg, 1.29 mmol) led to an inseparable mixture of regioisomers **14a** and **14b** (740 mg, 72% **14a**/**14b**=2:1).

R_f=0.40 (H/EA, 7:3); IR (neat/NaCl) 1754 cm^{-1}; ^1H NMR (1:1 mixture, 250 MHz, $CDCl_3$) δ 7.38–7.23 (m, 38×0.5H), 7.20–7.08 (m, 5×0.5H), 7.00 (m, 0.5H), 6.86 (d, 2×0.5H, *J*=8.9 Hz), 6.76 (d, 2×0.5H, *J*=8.9 Hz), 5.58 (d, 0.5H, *J*=3.0 Hz), 5.48 (s, 0.5H), 5.48 (s, 0.5H), 5.00 (d, 1H, *J*=3.0 Hz), 4.99 (d, 1H, *J*=3.0 Hz), 4.95 (m, 4×0.5H), 4.88–4.32 (m, 17×0.5H), 4.27 (dd, 0.5H, *J*=5.0, 10.0 Hz), 4.26 (dd, 0.5H, *J*=5.0, 10.0 Hz), 4.05 (m, 0.5H), 3.94–3.82 (m, 4×0.5H), 3.82 (s, 3×0.5H), 3.81–3.70 (m, 5×0.5H), 3.71 (s, 3×0.5H), 3.69–3.55 (m, 5×0.5H), 3.52–3.43 (m, 2×0.5H), 3.42 (s, 3×0.5H), 3.41 (s, 3×0.5H), 3.27 (m, 0.5H), 2.05 (s, 3H), 1.97 (s, 3H); ^{13}C NMR (65 MHz, $CDCl_3$) δ 170.1, 169.9, 160.1, 159.8, 138.6–137.6, 129.6, 129.3, 128.1–127.2, 113.5, 113.2, 102.9, 101.8, 101.3, 97.3, 97.1, 95.7, 84.5, 82.4, 82.0, 81.1, 79.7, 78.4, 77.5, 77.1, 75.3, 75.2, 74.6, 74.5, 73.6, 73.3, 73.2, 71.9, 70.9, 70.3, 70.1, 68.7, 68.6, 68.5, 68.3, 62.3, 61.7, 55.0, 54.8, 20.7, 20.6.

*6.3.4. Methyl 2-O-(2′,3′,4′,6′-tetra-O-benzyl-α-D-glucopyranosyl)-α-D-glucopyranoside (**7a**).* A solution of **13a** (550 mg, 0.63 mmol) in an equimolar mixture of AcOH/THF/H_2O (60 mL) was stirred at 50 °C for 3 h then concentrated in vacuo. Flash purification by chromatography (H/A, 4:1 then 1:4) afforded the diol, pure enough for the next step. Thus, the residue was dissolved in MeOH then a catalytic amount of freshly prepared MeONa/MeOH solution was added. After stirring for 3 h, the mixture was concentrated and purified by chromatography (CH_2Cl_2/MeOH, 19:1) to afford disaccharide **7a** (416 mg, 90%, white crystals).

R_f=0.48 (EA); t_R=24.2 min (gradient A); $[\alpha]_D^{20}$ +95.1 (*c* 0.7, $CHCl_3$); mp 156 °C; IR (neat/NaCl) 3441 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 18H, Ph), 7.18 (m, 2H, Ph), 5.00 (d, 1H, *J*=11.0 Hz, C*H*$_2$Ph), 4.92 (d, 1H, $J_{1'-2'}$=4.5 Hz, *H*-1′), 4.86 (d, 1H, *J*=10.5 Hz, C*H*$_2$Ph), 4.85 (d, 1H, C*H*$_2$Ph), 4.84 (d, 1H, J_{1-2}=3.5 Hz, *H*-1), 4.78 (d, 1H, *J*=12.0 Hz, C*H*$_2$Ph), 4.65 (d, 1H, C*H*$_2$Ph), 4.58 (d, 1H, *J*=11.5 Hz, C*H*$_2$Ph), 4.51 (d, 1H, C*H*$_2$Ph), 4.48 (d, 1H, C*H*$_2$Ph), 4.12 (ddd, 1H, J_{4-5}=10.0, $J_{5'-6'}$=2.0, 5.5 Hz, *H*-5), 4.06 (dd, 1H, $J_{2'-3'}$=9.5, $J_{3'-4'}$=9.5 Hz, *H*-3′), 3.88 (dd, 1H, J_{2-3}=9.5, J_{3-4}=9.5 Hz, *H*-3), 3.82 (m, 2H, *H*-6′, *H*-6′), 3.72–3.64 (m, 3H, *H*-5, *H*-6, *H*-6), 3.60 (dd, 1H, *H*-2′), 3.56 (dd, 1H, *H*-4′), 3.47 (dd, 1H, J_{4-5}=9.5 Hz, *H*-4), 3.45 (dd, 1H, *H*-2), 3.42 (s, 3H, OMe), 2.94 (br s, 1H, OH), 2.28 (br s, 1H, OH), 1.97 (br s, 1H, OH); ^{13}C NMR (65 MHz, $CDCl_3$) δ 138.6, 137.9, 137.8, 137.5 (Ph), 128.2–127.3 (Ph), 97.0 (*C*-1), 94.8 (*C*-1′), 81.4 (*C*-3′), 79.1 (*C*-2′), 77.4 (*C*-4), 76.8 (*C*-4′), 75.3, 74.9, 73.1, 72.5 (*C*H$_2$Ph), 72.0 (*C*-3), 70.7 (*C*-5′), 70.0 (*C*-2), 69.7 (*C*-5), 68.1 (*C*-6′), 61.3 (*C*-6), 54.8 (OMe); LRMS (EI$^+$, *m*/*z*, %): 625 (5) (M−Bn$^+$), 522 (7), 431 (12), 325 (17), 281 (26), 253 (100), 181 (100); Anal. calcd for $C_{41}H_{48}O_{11}$: C, 68.70; H, 6.75; found: C, 68.90; H, 6.78.

*6.3.5. Methyl 2-O-(2′,3′,4′,6′-tetra-O-benzyl-β-D-glucopyranosyl)-α-D-glucopyranoside (**7b**).* Following the same procedure as for disaccharide **7a**, disaccharide **13b** (250 mg, 0.285 mmol) led to disaccharide **7b** (195 mg, 93%, white powder).

R_f=0.52 (EA); t_R=24.6 min (gradient A); $[\alpha]_D^{20}$ +54.7 (*c* 0.8, $CHCl_3$); IR (neat/NaCl) 3422 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.32 (m, 18H, Ph), 7.17 (m, 2H, Ph), 4.93 (d, 1H, *J*=11.0 Hz, C*H*$_2$Ph), 4.92 (d, 1H, J_{1-2}=4.0 Hz, *H*-1), 4.92 (d, 1H, *J*=10.5 Hz, C*H*$_2$Ph), 4.86 (2d, 2H, C*H*$_2$Ph), 4.83 (d, 1H, *J*=10.5 Hz, C*H*$_2$Ph), 4.70 (d, 1H, $J_{1'-2'}$=8.0 Hz, *H*-1′), 4.59 (d, 1H, *J*=12.0 Hz, C*H*$_2$Ph), 4.57 (d, 1H, C*H*$_2$Ph), 4.52 (d, 1H, C*H*$_2$Ph), 3.91 (dd, 1H, J_{2-3}=8.5, J_{3-4}=8.5 Hz, *H*-3), 3.87 (dd, 1H, J_{5-6}=3.5, J_{6-6}=11.5 Hz, *H*-6), 3.80 (dd, 1H, J_{5-6}=4.5 Hz, *H*-6), 3.73–3.61 (m, 4H, *H*-3′, *H*-5′, *H*-6′, *H*-6′), 3.61–3.49 (m, 5H, *H*-2, *H*-2′, *H*-4, *H*-4′, *H*-5), 3.39 (s, 3H, OMe), 3.21 (br s, 1H, OH), 2.71 (br s, 1H, OH), 2.09 (br s, 1H, OH); ^{13}C NMR (65 MHz, $CDCl_3$) δ 138.3, 138.0, 137.9, 137.8 (Ph), 128.4–127.6 (Ph), 103.8 (*C*-1′), 99.5 (*C*-1), 84.8 (*C*-3′), 82.0 (*C*-2′), 80.9 (*C*-4), 77.9 (*C*-4′), 75.6, 75.1, 74.9, 73.4 (*C*H$_2$Ph), 74.6 (*C*-2), 72.4 (*C*-3), 70.5, 70.4 (*C*-5, *C*-5′), 69.0 (*C*-6′), 62.1 (*C*-6), 55.2 (OMe); LRMS (EI$^+$, *m*/*z*, %): 625 (7) (M−Bn$^+$), 593 (5), 522 (7), 431 (49), 325 (55), 313 (61), 253 (75), 181 (78), 91 (100); Anal. calcd for $C_{41}H_{48}O_{11}$: C, 68.70; H, 6.75; found: C, 68.75; H, 6.77.

*6.3.6. Methyl 3-O-(2′,3′,4′,6′-tetra-O-benzyl-α-D-glucopyranosyl)-α-D-glucopyranoside (**8a**).* Following the same procedure as for **7a**, the mixture **14a**/**14b** (309 mg, 0.352 mmol) was deprotected into the separable compounds (HPLC, H/EA, 3:1) **8a** (160 mg, 62%, colorless oil) and **8b** (79 mg, 31%, colorless oil).

Data for **8a**: R_f=0.59 (EA); t_R=27.2 min (gradient A); $[\alpha]_D^{20}$ +80.6 (*c* 0.5, $CHCl_3$); IR (neat/NaCl) 3447 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 18H, Ph), 7.15 (m, 2H, Ph), 4.94 (d, 1H, *J*=11.0 Hz, C*H*$_2$Ph), 4.91 (d, 1H, C*H*$_2$Ph), 4.91 (d, 1H, $J_{1'-2'}$=4.5 Hz, *H*-1′), 4.84 (d, 1H, *J*=11.0 Hz, C*H*$_2$Ph), 4.83 (d, 1H, *J*=10.5 Hz, C*H*$_2$Ph), 4.83 (d, 1H, J_{1-2}=3.5 Hz, *H*-1), 4.71 (d, 1H, C*H*$_2$Ph), 4.58 (d, 1H, *J*=12.0 Hz, C*H*$_2$Ph), 4.51 (d, 1H, C*H*$_2$Ph), 4.50 (d, 1H, C*H*$_2$Ph), 4.10 (m, 1H, *H*-3), 4.03 (dd, 1H, J_{2-3}=9.5, J_{3-4}=9.5 Hz, *H*-3′), 3.89 (dd, 1H, J_{5-6}=3.5, J_{6-6}=11.5 Hz, *H*-6), 3.81 (dd, 1H, J_{5-6}=4.5 Hz, *H*-6), 3.73 (m, 1H, *H*-5), 3.70–3.62 (m, 3H, *H*-5′, *H*-6′, *H*-6′), 3.62–3.49 (m, 4H, *H*-2, *H*-2′, *H*-4, *H*-4′) 3.46 (s, 3H, OMe), 3.22 (br s, 1H, OH), 2.11 (br s, 1H, OH), 1.70 (br s, 1H, OH); ^{13}C NMR (65 MHz, $CDCl_3$) δ 138.3, 137.7, 137.4, 137.1 (Ph), 128.6–127.6 (Ph), 99.7, 99.5 (*C*-1, *C*-1′), 86.9 (*C*-3), 82.3 (*C*-3′), 79.3 (*C*-2′), 77.8 (*C*-4′), 75.6, 74.9, 74.0, 73.4 (*C*H$_2$Ph), 71.0, 70.7, 70.5, 70.1 (*C*-2, *C*-4, *C*-5, *C*-5′), 68.3 (*C*-6′), 62.4 (*C*-6), 55.2 (OMe); LRMS (EI$^+$, *m*/*z*, %): 625 (3) (M−Bn$^+$), 522 (3), 431 (55), 325 (65), 313 (49), 91 (100); Anal. calcd for $C_{41}H_{48}O_{11}$: C, 68.70; H, 6.75; found: C, 68.65; H, 6.77.

Data for **8b**: R_f=0.70 (EA); t_R=31.9 min (gradient A); $[\alpha]_D^{20}$ +68.3 (*c* 1.0, $CHCl_3$); IR (neat/NaCl) 3429 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 18H, Ph), 7.18 (m, 2H, Ph), 5.06 (d, 1H, *J*=11.0 Hz, C*H*$_2$Ph),

4.94 (d, 1H, J=11.0 Hz, CH_2Ph), 4.83 (2d, 2H, J=11.0 Hz, CH_2Ph), 4.80 (d, 1H, $J_{1'-2'}$=4.0 Hz, H-1′), 4.78 (d, 1H, CH_2Ph), 4.58–4.48 (m, 4H, H-1, CH_2Ph), 3.99 (dd, 1H, J_{5-6}=4.0, J_{6-6}=11.5 Hz, H-6), 3.80 (dd, 1H, J_{5-6}=5.0 Hz, H-6), 3.70 (2dd, 2H, J_{2-3}=9.0, J_{3-4}=9.0, $J_{2'-3'}$=9.0, $J_{3'-4'}$=9.0 Hz, H-3, H-3′), 3.68–3.60 (m, 3H, H-2, H-5, H-5′), 3.60–3.51 (m, 5H, H-2′, H-4, H-4′, H-6′, H-6′), 3.44 (s, 3H, OMe), 2.33 (br s, 1H, OH), 2.15 (br s, 1H, OH), 1.77 (br s, 1H, OH); ^{13}C NMR (65 MHz, $CDCl_3$) δ 138.3, 138.0, 137.7, 137.5 (Ph), 128.4–127.7 (Ph), 104.2 (C-1′), 99.0 (C-1), 86.9 (C-3), 84.6 (C-3′), 81.9 (C-2′), 77.7, 74.3 (C-4, C-4′), 75.7, 75.1, 73.5 (CH_2Ph), 71.1, 69.6 (C-2, C-5, C-5′), 68.8 (C-6′), 62.9 (C-6), 55.1 (OMe); LRMS (EI$^+$, m/z, %): 625 (3) (M−Bn$^+$), 593 (2), 522 (3), 431 (30), 325 (35), 281 (65), 253 (100), 181 (96); Anal. calcd for $C_{41}H_{48}O_{11}$: C, 68.70; H, 6.75; found: C, 68.70; H, 6.72.

*6.3.7. Methyl 2,3,6-tri-O-acetyl-4-O-(2′,3′,4′,6′-tetra-O-benzyl-α-D-glucopyranosyl)-α/β-D-glucopyranoside (**17a**/**17b**).* Following the same procedure as for disaccharides **13a** and **13b**, coupling of compounds **16** (351 mg, 1.10 mmol) made following reported procedures[41] and **5** (1.5 g, 2.19 mmol) led to an inseparable mixture of disaccharides **17a** and **17b** (730 mg, 79% **17a**/**17b**=2.4:1).

R_f=0.61 (H/EA, 7:3); IR (neat/NaCl) 1745 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 18H), 7.14 (m, 2H), 5.61 (dd, 0.7H, J=9.5, 9.5 Hz), 5.45 (m, 0.3H), 4.95–4.24 (m, 13H), 3.98–3.41 (m, 8H), 3.40 (s, 3H), 2.11 (s, 3H), 2.04 (s, 3H), 2.03 (s, 0.9H), 1.95 (s, 2.1H); ^{13}C NMR (65 MHz, $CDCl_3$) δ 170.2, 170.1, 169.7, 138.5–137.5, 128.3–127.3, 102.8, 98.9, 96.3, 84.5, 82.3, 81.1, 80.0, 77.2, 76.4, 75.5, 75.4, 75.3, 75.0, 74.7, 74.5, 73.5, 73.3, 73.0, 71.4, 70.9, 70.6, 70.5, 69.4, 68.7, 68.3, 68.0, 62.6, 61.7, 55.1, 55.0, 20.7, 20.7, 20.5.

*6.3.8. Methyl 4-O-(2′,3′,4′,6′-tetra-O-benzyl-α-D-glucopyranosyl)-α/β-D-glucopyranoside (**9a**/**9b**).* A solution of disaccharides **17a** and **17b** (710 mg, 0.84 mmol) in MeOH (10 mL) was treated with a catalytic amount of freshly prepared solution of MeONa/MeOH. After stirring for 3 h and concentration, the residue was purified by chromatography (CH_2Cl_2/MeOH, 19:1) to afford disaccharides **9a**/**9b** (545 mg, 91%, **9a**/**9b**=2.4:1).

R_f=0.48 (EA); t_R=28.1 min (gradient A); IR (neat/NaCl) 3412 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 18H), 7.14 (m, 2H), 5.02–4.71 (m, 6H), 4.61–4.40 (m, 4H), 4.07–3.43 (m, 12H), 3.42 (s, 3H), 2.37 (m, 1H), 2.20 (d, 1H, J=8.0 Hz); ^{13}C NMR (65 MHz, $CDCl_3$) δ 138.1–136.8, 128.4–127.6, 102.9, 100.2, 99.0, 84.4, 81.9, 81.7, 80.2, 80.0, 78.8, 77.7, 77.5, 75.5, 75.4, 75.1, 74.8, 74.2, 73.9, 73.8, 73.3, 73.2, 72.0, 71.7, 71.2, 70.2, 70.0, 68.4, 61.0, 60.6, 55.2, 55.0; LRMS (EI$^+$, m/z, %): 625 (2) (M−Bn$^+$), 522 (2), 431 (33), 325 (20), 281 (30), 253 (93), 181 (100); Anal. calcd for $C_{41}H_{48}O_{11}$: C, 68.70; H, 6.75; found: C, 68.77; H, 6.77.

6.4. Preparation and glycosylation of monoprotected acceptors

6.4.1. Glycosylation-general procedure (Table 1). To a solution of **1b**–**m**[29] (0.25 mmol) and glucopyranosyl trichloroacetimidate **5** (0.25 mmol) in dry CH_2Cl_2 (25 mL) was added a freshly prepared 0.1 M solution of TMSOTf. The resulting mixture was stirred for 1 h then quenched with a drop of Et_3N, diluted with CH_2Cl_2, washed with 1 M $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. For the systematic glycosylation reactions, the residue was deprotected without further purification (Table 1).

6.4.2. Deprotection. Disaccharides made by reacting **5** with either **1b**, **1k**, **1l** or **1m** were stirred in a mixture of TFA/CH_2Cl_2 (1:1, 10 mL) for 5 h. Disaccharides made by reacting **5** with **1c** or **1d** were reacted with TBAF (0.75 mL of a 1 M solution in THF, 0.75 mmol) and AcOH (0.05 mL, 1.0 mmol) in THF (10 mL). Disaccharides made by reacting **5** with **1g**, **1h** or **1i** were heated at 40 °C in a mixture of AcOH/H_2O/THF (1:1:1, 20 mL) for 3 h. Disaccharides made by reacting **5** with **1e**, **1f**, or **1j** were stirred in a MeONa/MeOH solution for 5 h. Standard workup and filtration on a silica gel pad (eluent hexanes/EtOAc 1:1 then 0:1) led to the isolated disaccharides **7a**, **7b**, **8a**, **8b**, **9a**, and **9b** described above.

6.4.3. Glycosylation-optimized procedure. To a solution of **1l** (0.50 mmol) in dry CH_2Cl_2 (50 mL) was added a freshly prepared solution of TMSOTf (2 mL, 0.1 M in CH_2Cl_2) and a freshly prepared solution of glucopyranosyl trichloroacetimidate **5** (2 mL, 0.50 mmol, 0.25 M) at −50 °C. The resulting mixture was stirred for 1 h. This protocol was repeated two to three times (TMSOTf, 2×2 mL, trichloroacetimidate 5, 2×2 mL). After stirring for a further 3 h at −50 °C, the reaction was quenched with a drop of Et_3N. The resulting mixture was diluted with CH_2Cl_2, washed with 1 M $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was filtered on a silica gel pad and analyzed by HPLC and further purified by chromatography (H/EA, gradient from 2:3 to 0:5) to afford **18a** (120 mg, 22%), **18b** (214 mg, 39%), together with another two regioisomers (21 mg, 4% and 39 mg, 7%).

*6.4.4. Methyl 2-O-(2′,3′,4′,6′-tetra-O-benzyl-α-D-glucopyranosyl)-6-O-[6-(2-pyridinylethyl)-pyridin-2-yl]-di-p-tolylmethyl-α-D-glucopyranoside (**18a**).* R_f=0.57 (CH_2Cl_2/MeOH, 9:1); t_R=33.2 min (gradient B); IR (neat/NaCl) 3409 cm^{-1}; $[\alpha]_D^{20}$ +56.2 (c 0.8, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.45 (d, 1H, J=4.5 Hz), 7.54–6.92 (m, 34H), 6.40–5.80 (br s, 1H (OH)), 5.02 (d, 1H, J=11.0 Hz), 4.95 (d, 1H, J=3.5 Hz), 4.85 (2d, 2H, J=11.0 Hz), 4.79 (d, 1H, J=3.5 Hz), 4.77 (d, 1H, J=11.0 Hz), 4.72 (d, 1H, J=11.0 Hz), 4.62 (d, 1H, J=11.0 Hz), 4.52 (d, 1H, J=11.0 Hz), 4.43 (d, 1H, J=11.0 Hz), 4.27 (d, 1H, J=10.0 Hz), 4.13 (dd, 1H, J=9.5, 9.5 Hz), 4.08 (m, 1H), 3.90–3.53 (m, 9H), 3.42 (s, 3H), 3.44–3.06 (m, 4H), 2.36 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (65 MHz, $CDCl_3$) δ 161.9, 160.9, 160.3, 149.0, 140.8, 140.0, 138.9, 138.4, 137.9, 137.1, 136.9, 136.6, 136.4, 129.3, 128.8, 128.5, 128.3, 127.9, 127.7, 127.6, 123.2, 121.8, 121.2, 121.1, 97.5, 95.6, 86.9, 81.8, 79.6, 77.7, 77.2, 75.5, 74.9, 73.5, 73.4, 72.8, 71.4, 70.1, 69.6, 68.4, 66.1, 55.0, 38.7, 38.0, 21.0.

*6.4.5. Methyl 2-O-(2′,3′,4′,6′-tetra-O-benzyl-α-D-glucopyranosyl)-6-O-[6-(2-pyridinylethyl)-pyridin-2-yl]-di-p-tolylmethyl-β-D-glucopyranoside (**18b**).* R_f=0.66 (CH_2Cl_2/MeOH, 9:1); t_R=35.4 min (gradient B); IR (neat/NaCl) 3400 cm^{-1}; $[\alpha]_D^{20}$ +52.3 (c 0.5, $CHCl_3$); mp 74 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.41 (d, 1H, J=3.5 Hz), 7.54–6.98 (m, 34H), 5.28 (d, 1H, J=11.0 Hz), 4.96 (d, 1H, J=11.0 Hz), 4.93 (d, 1H, J=3.5 Hz), 4.83 (2d, 2H, J=11.0 Hz), 4.80 (d, 1H, J=11.0 Hz), 4.70 (d, 1H, J=7.5 Hz), 4.58 (d, 1H, J=11.0 Hz), 4.55 (d, 1H, J=11.0 Hz), 4.50 (d, 1H, J=11.0 Hz), 4.32–4.10 (br s, 1H, OH), 4.19 (dd, 1H, J=9.0, 9.0 Hz), 3.89 (m, 2H), 3.75–3.53 (m, 8H), 3.58 (m, 1H), 3.45 (s, 3H), 3.47–3.05 (m, 4H), 2.37 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (65 MHz, $CDCl_3$) δ 161.8, 160.7, 160.4, 149.3, 141.1, 139.6, 138.9, 138.7, 138.1, 137.4, 136.9, 136.8, 136.5, 129.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.6, 127.5, 123.1, 122.3, 121.3, 121.2, 105.3, 99.8, 87.0, 84.7, 81.9, 81.8, 77.7, 75.6, 75.0, 74.6, 74.5, 74.3, 73.4, 71.6, 69.3, 69.2, 66.7, 55.3, 39.1, 38.2, 21.0.

*6.4.6. Octyl 2,3,4-tri-O-acetyl-6-O-[6-(2-pyridinylethyl)-pyridin-2-yl]-di-p-tolylmethyl-β-D-glucopyranoside (**2a**).* Following the same procedure as for the preparation of **1l**, octyl-β-D-glucopyranoside (3.50 g, 12.0 mmol) and (6-(2-(pyridin-2-yl)ethyl)pyridin-2-yl)di-p-tolylmethanol (1.10 g, 2.79 mmol) led to **2**. Acetylation was carried out to facilitate its purification. Thus a solution of acetic anhydride (6.5 mL, excess) in pyridine (30 mL) in CH_2Cl_2 was added to the crude mixture. After stirring for 16 h, the solution was concentrated to provide, after flash chromatography (H/EA, 4:1 then 3:2), **2a** (1.03 g, 46%).

R_f=0.5 (H/EA, 1:1); IR (neat): 2927, 2856, 1755 cm^{-1}; $[\alpha]_D^{20}$ +25.5 (c 0.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (br d, 1H, J=4 Hz), 7.63 (d, 1H, J=8 Hz), 7.49 (t, 1H, J=8 Hz), 7.43–7.37 (m, 3H), 7.28 (s,

1H), 7.06 (3d, 5H J=7 Hz), 6.85 (d, 1H, J=7.5 Hz), 6.77 (d, 1H, J=7.5 Hz), 5.24 (t, 1H, J=9.5 Hz), 5.15 (t, 1H, J=9.5 Hz), 5.06 (t, 1H, J=8 Hz), 4.50 (d, 1H, J=8 Hz), 3.95–3.89 (ddd, 1H, J=6.5, 9.5 Hz), 3.57–3.51 (m, 2H), 3.33 (dd, 1H, J=2, 11 Hz), 3.12–3.07 (m, 5H), 2.31 (s, 6H), 2.05 (s, 3H), 2.00 (s, 3H), 1.76 (s, 3H), 1.67–1.57 (m, 2H), 1.34–1.26 (m, 10H), 0.89–0.85 (t, 3H, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.62, 169.56, 169.08, 162.92, 161.59, 159.44, 149.07, 140.63, 140.16, 136.54, 136.51, 136.27, 129.49, 129.39, 128.19, 128.14, 123.27, 121.01, 120.73, 118.82, 100.91, 86.63, 73.40, 73.37, 71.68, 69.96, 68.79, 62.21, 37.64, 37.31, 31.94, 29.63, 29.43, 26.08, 22.78, 21.17, 20.85, 20.57, 14.23; HRMS (EI^+) calcd for $[C_{47}H_{59}N_2O_9+H]^+$: 795.42151. Found: 795.42232.

*6.4.7. Octyl 6-O-[6-(2-pyridinylethyl)-pyridin-2-yl]-di-p-tolylmethyl-β-D-glucopyranoside (**2**).* A solution of **2a** (1.03 g, 1.30 mmol) in MeOH (80 mL) was stirred in presence of MeONa (280 mg, 5.2 mmol) for 2 h. The solution was neutralized with IR120H resin, filtered and concentrated to provide pure 2 (light yellow foam, 760 mg, 88%).

R_f=0.30 (DCM/MeOH, 9:1); IR (DCM solution): 3380, 2925, 2856, 1451 cm^{-1}; $[\alpha]_D^{20}$ +11.9 (c 0.16, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (br s, 1H), 7.63, (br s, 1H), 7.59–7.52 (m, 2H), 7.39 (d, 2H, J=7.5 Hz), 7.28 (s, 1H), 7.21 (d, 3H, J=8 Hz), 7.14 (d, 3H, J=8 Hz), 7.08 (d, 3H, J=8 Hz), 4.31 (d, 1H, J=8 Hz), 3.82–3.74 (m, 3H), 3.62–3.59 (m, 1H), 3.49–3.39 (m, 2H), 3.37–3.33 (t, 1H, J=8 Hz), 3. 28–3.26 (m, 1H), 3.20–3.18 (m, 2H), 2.37 (s, 3H), 2.30 (s, 3H), 1.60–1.53 (m, 2H), 1.28–1.23 (m, 10H), 0.87–0.84 (t, 3H, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.82, 160.63, 160.59, 149.43, 142.05, 138.23, 138.14, 137.25, 137.07, 136.90, 130.41, 128.76, 127.87, 123.41,122.80, 121.70, 121.67, 103.00, 87.24, 75.55, 75.21, 74.33, 73.93, 70.34, 67.86, 39.47, 38.58, 31.92, 29.67, 29.50, 29.31, 26.04, 22.77, 21.26, 21.18, 14.24; HRMS (EI^+) calcd for $[C_{41}H_{52}N_2O_6+H]^+$: 669.38981. Found: 669.39095.

*6.4.8. Methyl 6-O-[6-(2-pyridinylethyl)-pyridin-2-yl]-di-p-tolylmethyl-α-D-mannopyranoside (**3**).* Following the same procedure as for the preparation of **1l**, methyl-α-D-mannopyranoside (3.10 g, 16.0 mmol) and (6-(2-(pyridin-2-yl)ethyl)pyridin-2-yl)di-*p*-tolylmethanol (1.60 g, 4.06 mmol) led, after purification by flash chromatography (CH_2Cl_2/MeOH, gradient 98:2 to 9:1), to **3** (brown foam, 1.80 g, 85%).

R_f=0.35 (DCM/MeOH, 9/1); IR ($CDCl_3$ solution): 3372 (broad), 2924, 1451 cm^{-1}; $[\alpha]_D^{20}$ +104.4 (c 0.10, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59–8.58 (d, 1H, J=3.5 Hz), 8.06 (br s, 1H), 7.61–7.55 (m, 2H), 7.43–7.41 (d, 2H, J=8 Hz), 7.30–7.28 (d, 1H, J=8 Hz), 7.23–7.21 (d, 2H, J=8 Hz), 7.18–7.12 (m, 4H), 7.08–7.06 (d, 3H, J=7.5 Hz), 4.68 (d, 1H, J=1 Hz), 4.09–4.07 (m, 2H,), 4.02 (s, 1H), 3.87–3.82 (m, 1H), 3.43–3.39 (t, 1H, J=9 Hz), 3.30 (s, 3H), 3.29–3.20 (m, 2H), 3.15–3.09 (m, 2H), 3.07–3.00 (m, 2H), 2.37 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.99, 160.65, 160.52, 149.29, 142.46, 138.13, 137.88, 137.26, 137.21, 136.76, 130.66, 128.77, 127.62, 123.46, 122.91, 121.74, 121.65, 100.83, 87.43, 72.50, 70.62, 70.05, 69.64, 68.59, 55.25, 39.54, 38.65, 21.25, 21.16; HRMS (EI^+) calcd for $[C_{34}H_{38}N_2O_6+H]^+$: 571.28026. Found: 571.28081.

*6.4.9. Methyl 6-O-[6-(2-pyridinylethyl)-pyridin-2-yl]-di-p-tolylmethyl-α-D-galactopyranoside (**4**).* Following the same procedure as for the preparation of **1l**, methyl-α-D-galactopyranoside (3.10 g, 16.0 mmol) and (6-(2-(pyridin-2-yl)ethyl)pyridin-2-yl)di-*p*-tolylmethanol (1.60 g, 4.06 mmol) led, after purification by flash chromatography (gradient 98:2 to 9:1), to **4** (brown foam, 330 mg, 14%).

R_f=0.35 (DCM/MeOH, 9/1); IR ($CDCl_3$ solution): 3361 (broad), 2924, 1451 cm^{-1}; $[\alpha]_D^{20}$ +99.9 (c 0.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (br s, 1H), 7.58 (br s, 1H), 7.50 (t, 1H, J=7.5 Hz), 7.18 (dd, 2H, J=8, 21 Hz), 7.08 (d, J=8 Hz), 7.03 (d, 1H, J=7.5 Hz), 4.79 (d, 1H, J=2.5 Hz), 4.60 (br s, 1H), 3.98 (dd, 1H, J=6.5, 8 Hz), 3.92 (br s, 2H), 3.47 (t, 1H, 8.5 Hz), 3.33 (s, 3H), 3.31–3.14 (m, 4H), 3.10 (dd, 1H, J=5.5, 8 Hz), 2.37 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 161.72, 160.92, 160.19, 149.18, 142.05, 138.89, 137.53, 136.73, 136.69, 136.44, 130.08, 128.53, 128.44, 128.02, 123.10, 121.89, 121.40, 121.17, 99.99, 86.96, 70.39, 70.17, 69.26, 69.16, 63.26, 55.35, 38.62, 37.93, 21.09, 21.02; HRMS (EI^+) calcd for $[C_{34}H_{38}N_2O_6+H]^+$: 571.28026. Found: 571.28003.

6.5. General procedure

To a solution of the acceptor (0.50 mmol) in dry CH_2Cl_2 (50 mL) was added a freshly prepared solution of TMSOTf (2 mL, 0.1 M) and a freshly prepared solution of glucopyranosyl trichloroacetimidate 5 (2 mL, 0.50 mmol, 0.25 M) at −50 °C. The resulting mixture was stirred for 1 h. This protocol was repeated two to three times (TMSOTf, 2×2 mL, trichloroacetimidate 8, 2×2 mL). After stirring for a further 3 h at −50 °C, the reaction was quenched with a drop of Et_3N. The resulting mixture was diluted with CH_2Cl_2, washed with 1 M $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude mixture was next treated with TBAF in THF to cleave any silyl ethers formed. The solution was concentrated and the residue was purified by column chromatography (H/EA, gradient from 7:3 to 1:1) to afford the corresponding products.

*6.5.1. Methyl 2-O-(2′,3′,4′,6′-tetra-O-benzoyl-β-D-glucopyranosyl)-(6-O-tert-butyldiphenylsilyl)-α-D-glucopyranoside (**20**) and methyl 3-O-(2′,3′,4′,6′-tetra-O-benzoyl-β-D-glucopyranosyl)-6-O-(tert-butyldiphenylsilyl)-α-D-glucopyranoside (**21**).* Following the general glycosylation procedure, **1c** (1 equiv) was reacted with **6** (1 equiv) yielding both **20** and **21** (18%: 20%, **20**/**21**).

Data for **20**: R_f=0.2 (H/EA, 7:3); IR ($CHCl_3$) 3494, 1724 cm^{-1}; $[\alpha]_D^{20}$ +43.4 (c 0.17, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, J=8.2 Hz, 2H), 7.97 (d, J=7.1 Hz, 2H), 7.93 (d, J=7.3 Hz, 2H), 7.83 (d, J=5.8 Hz, 2H), 7.71–7.65 (m, 5H), 7.55–7.49 (m, 4H), 7.45–7.33 (m, 17H), 7.30 (dd, J=8.3 Hz, 16.5, 4H), 5.95 (t, J=9.6 Hz, 1H), 5.67 (t, J=9.7 Hz, 1H), 5.58 (dd, J=7.9, 9.8 Hz, 1H), 5.25 (d, J=7.9 Hz, 1H), 5.05 (d, J=7.9 Hz, 0.3H), 4.77 (d, J=3.2 Hz, 2H), 4.73 (dd, J=3.3, 15.1 Hz, 1H), 4.43 (dd, J=5.8, 12.2 Hz, 1H), 4.40–4.34 (m, J=12.4 Hz, 0.4H), 4.23–4.18 (m, J=6.5 Hz, 0.2H), 4.07 (t, J=6.8 Hz, 0.2H), 3.93 (dd, J=7.1, 16.3 Hz, 1H), 3.85 (t, J=4.8 Hz, 2H), 3.76–3.69 (m, J=9.1 Hz, 0.5H), 3.66–3.61 (m, 1H), 3.58–3.54 (m, 2H), 3.39 (s, 0.8H), 3.27 (s, 3H), 1.04 (s, 11H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.29, 166.24, 165.91, 165.82, 165.55, 165.35, 165.33, 135.81, 135.80, 135.75, 133.83, 133.74, 133.72, 133.68, 133.61, 133.54, 133.44, 133.38, 133.27, 133.26, 130.13, 130.03, 130.00, 129.95, 129.91, 129.90, 129.88, 129.68, 129.67, 129.47, 129.39, 129.15, 128.86, 128.80, 128.66, 128.61, 128.60, 128.46, 128.41, 127.85, 127.84, 127.71, 102.77, 101.39, 99.27, 98.86, 87.86, 81.24, 72.88, 72.76, 72.64, 72.32, 72.28, 72.21, 71.83, 71.66, 71.01, 70.64, 69.53, 68.66, 64.33, 63.42, 63.07, 55.21, 55.00, 36.77, 26.94, 26.92, 24.82, 19.46, 19.37; HRMS (ESI^+) calcd for $[C_{57}H_{58}O_{15}Si+Na]^+$: 1033.34372. Found: 1033.34419.

Data for **21**: R_f=0.3 (H/EA, 7:3); IR ($CHCl_3$) 3494, 1724 cm^{-1}; $[\alpha]_D^{20}$ +54.7 (c 0.12, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J=7.9 Hz, 2H), 7.98 (d, J=7.8 Hz, 2H), 7.93 (d, J=7.7 Hz, 2H), 7.83 (d, J=7.8 Hz, 2H), 7.70 (t, J=7.3 Hz, 4H), 7.51 (dt, J=6.7, 9.4 Hz, 3H), 7.47–7.27 (m, 19H), 5.93 (t, J=9.6 Hz, 1.1H), 5.64 (t, J=9.7 Hz, 1H), 5.61–5.54 (m, 1.2H), 5.35–5.30 (m, 0.2H), 5.25 (d, J=7.8 Hz, 0.2H), 5.05 (d, J=7.9 Hz, 1H), 4.78 (d, J=12.2 Hz, 1.2H), 4.72 (d, J=3.8 Hz, 1H), 4.67–4.63 (m, 0.2H), 4.50–4.41 (m, 0.4H), 4.38 (dd, J=6.7, 12.1 Hz, 1H), 4.26–4.19 (m, 1.2H), 4.14–4.04 (m, 0.2H), 3.96 (d, J=10.7 Hz, 1H), 3.93–3.89 (m, 0.2H), 3.85 (dd, J=5.5, 10.8 Hz, 1.2H), 3.72 (dd, J=8.0, 17.1 Hz, 2H), 3.68–3.63 (m, J=5.4 Hz, 1.2H), 3.59–3.53 (m, J=9.0 Hz, 2H), 3.39 (s, 3H), 3.27 (s, 0.5H), 2.82 (s, 0.2H), 2.64 (s, 0.2H), 1.92 (d, 0.7H), 1.05 (s, 10H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.37, 166.29, 166.24, 165.96, 165.91, 165.82, 165.55, 165.40,

165.35, 165.33, 136.01, 135.81, 135.80, 135.75, 135.64, 133.83, 133.74, 133.72, 133.68, 133.61, 133.58, 133.55, 133.45, 133.38, 133.26, 130.22, 130.13, 130.03, 130.00, 129.96, 129.89, 129.83, 129.68, 129.67, 129.47, 129.39, 129.30, 129.16, 129.10, 129.05, 128.86, 128.81, 128.68, 128.67, 128.61, 128.60, 128.54, 128.52, 128.46, 128.41, 128.16, 127.86, 127.84, 127.71, 102.78, 101.39, 99.27, 98.86, 90.62, 87.86, 81.24, 77.41, 72.88, 72.77, 72.64, 72.35, 72.32, 72.28, 72.21, 71.82, 71.67, 71.01, 70.63, 70.23, 69.59, 69.52, 68.66, 67.97, 64.33, 63.42, 63.05, 55.21, 55.00, 36.77, 27.06, 26.92, 24.82, 19.47, 19.37; HRMS (ESI^+) calcd for $[C_{57}H_{58}O_{15}Si+Na]^+$: 1033.34372. Found: 1033.34436.

*6.5.2. Methyl 3-O-(2′,3′,4′,6′-tetra-O-benzoyl-β-D-glucopyranosyl)-6-O-[6-(2-pyridinylethyl)-pyridin-2-yl]-di-p-tolylmethyl-α-D-glucopyranoside (**21**).* Following the general glycosylation procedure, **1l** was reacted with **6** yielding only **22** (80% yield).

R_f=0.3 (H/EA, 4:6); IR ($CHCl_3$): 3489, 1730 cm^{-1}; $[\alpha]_D^{20}$ +59.8 (*c* 0.11, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J*=4.8 Hz, 1H), 7.99 (dd, *J*=7.3, 12.3 Hz, 5H), 7.92 (d, *J*=7.3 Hz, 3H), 7.83 (d, *J*=7.3 Hz, 2H), 7.59–7.17 (m, 28H), 7.05 (t, *J*=8.5 Hz, 6H), 6.84 (t, *J*=8.3 Hz, 2H), 5.91 (t, *J*=9.7 Hz, 1H), 5.65–5.52 (m, 2H), 5.11 (d, *J*=8.0 Hz, 1H), 4.75 (dd, *J*=3.3, 8.7 Hz, 2H), 4.35 (dd, *J*=6.5, 12.2 Hz, 1H), 4.18 (ddd, *J*=2.7, 6.4, 9.4 Hz, 1H), 4.04 (s, 1H), 3.76 (dd, *J*=7.0, 10.9 Hz, 2H), 3.71–3.57 (m, 2H), 3.43 (s, 3H), 3.33 (dd, *J*=5.8, 10.1 Hz, 1H), 3.13 (s, 4H), 2.32 (s, 6H), 2.00 (d, *J*=7.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.26, 165.83, 165.55, 165.34, 163.10, 161.63, 159.63, 149.20, 141.09, 140.82, 136.55, 136.50, 136.22, 133.71, 133.51, 133.43, 133.27, 130.04, 129.96, 129.89, 129.51, 129.36, 129.27, 129.19, 128.82, 128.70, 128.59, 128.45, 128.40, 128.27, 123.28, 121.04, 120.77, 119.36, 102.52, 87.25, 86.59, 72.80, 72.29, 71.08, 70.94, 69.54, 69.30, 37.62, 21.19; HRMS (ESI^+) calcd for $[C_{68}H_{64}N_2O_{15}+H]^+$: 1149.43795. Found: 1149.43769.

*6.5.3. Octyl 3-O-(2′,3′,4′,6′-tetra-O-benzoyl-β-D-glucopyranosyl)-6-O-[6-(2-pyridinylethyl)-pyridin-2-yl]-di-p-tolylmethyl-β-D-glucopyranoside (**23**).* Following the general glycosylation procedure, **2** was reacted with **6** yielding **23** (87% yield).

R_f=0.3 (H/EA, 1:1); IR ($CHCl_3$) 3494, 1730 cm^{-1}; $[\alpha]_D^{20}$ +21.0 (*c* 0.12, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J*=4.5 Hz, 1H), 8.28–8.23 (m, 1H), 7.98 (t, *J*=8.1 Hz, 6H), 7.93–7.85 (m, 5H), 7.82 (d, *J*=7.4 Hz, 3H), 7.57 (d, *J*=7.9 Hz, 2H), 7.50 (d, *J*=7.2 Hz, 4H), 7.42 (d, *J*=3.0 Hz, 7H), 7.40–7.28 (m, 18H), 7.22 (t, *J*=7.7 Hz, 3H), 7.05 (d, *J*=7.9 Hz, 7H), 6.84 (t, *J*=8.3 Hz, 2H), 5.91 (t, *J*=9.7 Hz, 1H), 5.63–5.52 (m, 2H), 5.10 (d, *J*=8.0 Hz, 1H), 4.73 (d, *J*=10.1 Hz, 1H), 4.37–4.29 (m, 2H), 4.21 (d, *J*=7.9 Hz, 2H), 4.18–4.13 (m, 1H), 4.07 (s, 1H), 3.87 (d, *J*=9.6 Hz, 1H), 3.64 (d, *J*=9.5 Hz, 1H), 3.55–3.50 (m, 2H), 3.48–3.38 (m, 5H), 3.34–3.30 (m, 1H), 3.12 (s, 6H), 2.29 (s, 9H), 1.63–1.57 (m, 5H), 1.28–1.22 (m, 14H), 0.85 (d, *J*=6.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.26, 166.24, 165.82, 165.38, 165.32, 163.07, 161.59, 159.61, 149.16, 141.00, 140.81, 136.50, 136.48, 136.22, 133.67, 133.39, 133.24, 130.00, 129.93, 129.86, 129.47, 129.37, 129.31, 128.82, 128.70, 128.56, 128.51, 128.42, 128.38, 128.23, 123.29, 121.03, 120.75, 119.43, 102.53, 102.49, 88.36, 86.50, 86.35, 75.18, 72.99, 72.72, 72.08, 69.99, 69.61, 64.10, 63.05, 60.51, 37.65, 37.58, 34.78, 31.90, 31.71, 29.82, 29.73, 29.48, 29.35, 26.15, 22.78, 21.18, 14.32, 14.25, 14.21; HRMS (ESI^+) calcd for $[C_{75}H_{78}N_2O_{15}+H]^+$: 1247.54750. Found: 1247.54653.

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