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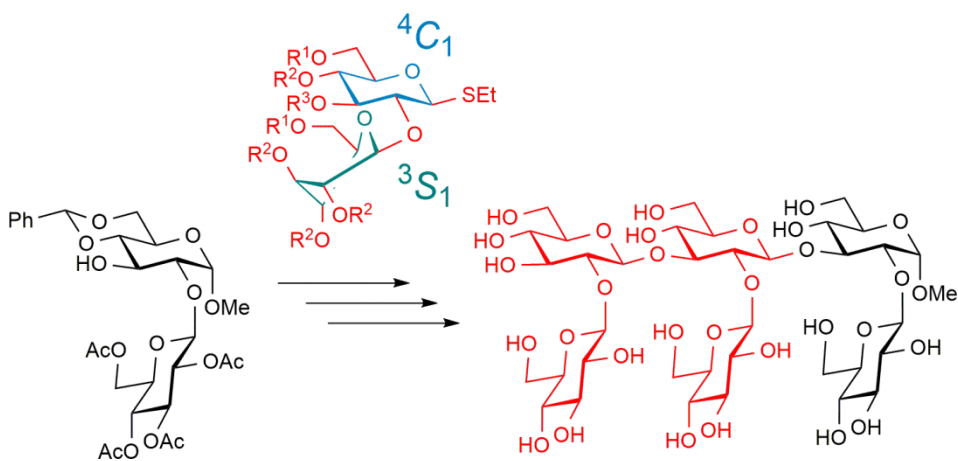
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Structure-Reactivity Relationships of Conformationally Armed Disaccharide Donors and Their Use in Synthesis of a Hexasaccharide Related to the Capsular Polysaccharide from *Streptococcus pneumoniae* type 37

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ABSTRACT

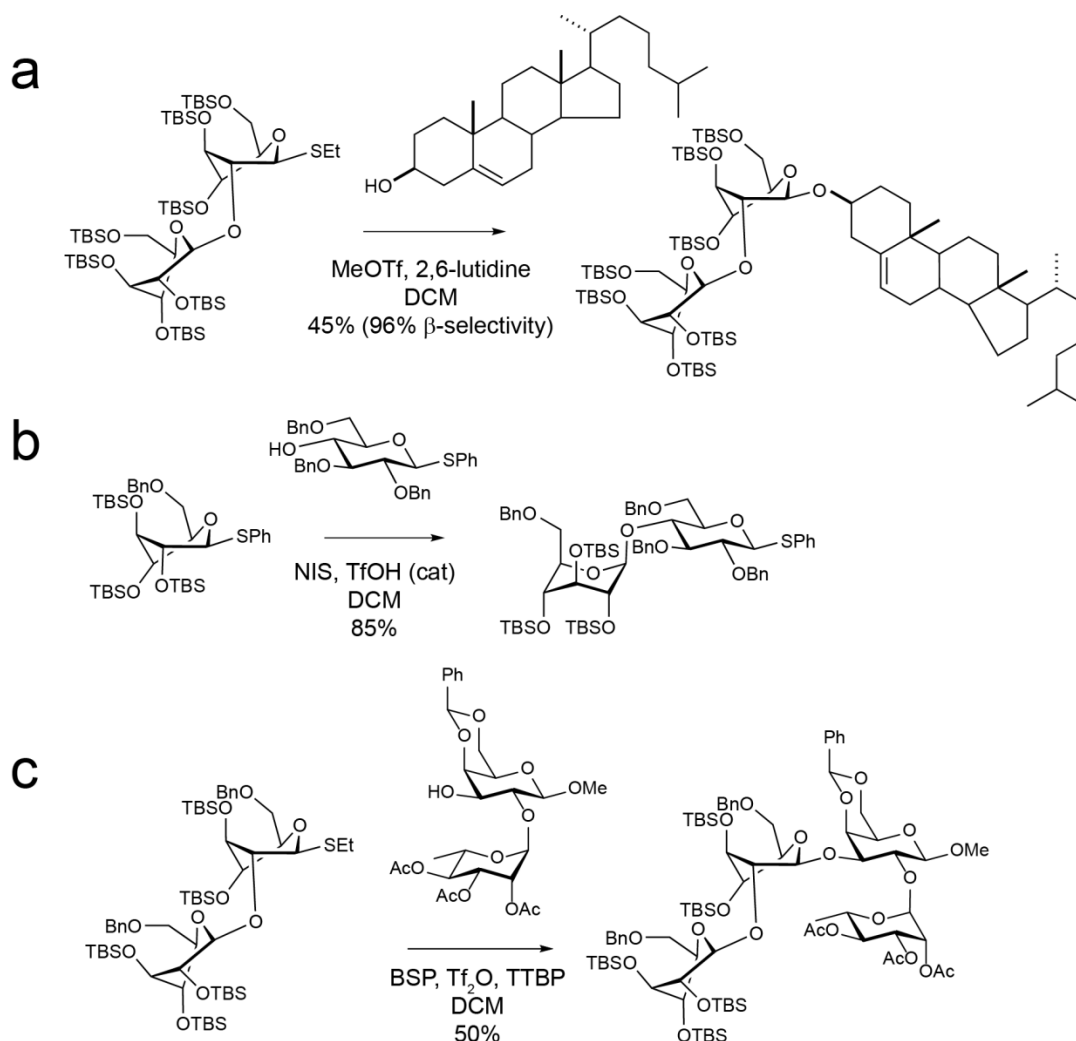
To advance the field of glycobiology efficient synthesis methods of oligosaccharides and glycoconjugates are a requisite. In glycosylation reactions using super-armed donors both selectivity and reactivity issues must be considered, and we herein investigate these aspects for differently protected β -linked 2-*O*-glycosylated glucosyl donors carrying bulky *tert*-butyldimethylsilyl groups to different extent. The acceptors in reactions being secondary alcohols present a challenging situation with respect to steric crowding. Conformational pyranose ring equilibria of the super-armed disaccharide donors with axial-rich substituents contained skew and boat conformations and three-state models were generally assumed. With NIS/TfOH as promotor, 2,6-di-*tert*-butyl-4-methylpyridine as base and a dichloromethane:toluene solvent mixture ethyl 1-thio- β -D-glucosyl disaccharide donors having 6-*O*-benzyl group(s) besides *tert*-butyldimethylsilyl groups were efficiently coupled at $-40\text{ }^{\circ}\text{C}$ to the hydroxyl group at position three of glucopyranosyl acceptors to form β -(1 \rightarrow 2), β -(1 \rightarrow 3)-linked trisaccharides, isolated in excellent 95% yield. The more axial-rich donors in skew and boat conformations are thus pre-organized closer to the assumed transition state in these glycosylation reactions. The developed methodology was subsequently applied in synthesis of a multi-branched hexasaccharide related to the capsular polysaccharide from *Streptococcus pneumoniae* type 37, which consists of a β -(1 \rightarrow 3)-linked backbone and a β -(1 \rightarrow 2)-linked side-chain of D-glucosyl residues in disaccharide repeating units.

KEY WORDS: super-armed donors, convergent carbohydrate synthesis, glycan building-blocks, preorganization, conformational analysis, NMR spin-simulation, transition state conformation, ring puckering

INTRODUCTION

In the present era of functional glycomics, light is increasingly shed on the vast number of important functions of carbohydrates in biological processes.¹⁻³ Glycans act as receptors for, *inter alia*, cells, hormones and pathogens and they govern immune reactions. This is valid to the extent that there is essentially no vital process in mammals, including pathogenicity, not intervened by carbohydrates.⁴ The advancement of efficient protocols for synthesis of these molecules is therefore of great importance. Chemical synthesis in general, and carbohydrate synthesis in particular, require control over selectivity, protective group orthogonality and substrate reactivity.⁵⁻⁹ Due to their manifestation of numerous hydroxyl groups and the special nature of the anomeric center, the preparation of homologous oligosaccharides with minor structural modifications generally involve multi-step procedures. The herein presented study aims at systematically introducing functional glycan building blocks for the application in convergent syntheses of challenging targets.

2-*O*-Glycosylated glucosyl donors introduce selectivity issues as well as steric bulk, impeding acceptor accessibility in glycosylation reactions.¹⁰ If a participating group is not present at O2 and if the β -anomeric configuration is desired, other means of directing selectivity have to be employed. Yamada and co-workers have proposed the introduction of bulky protective groups, particularly at position 2 of an aldohexose, to induce a ring-flip into a skew conformation and thus sterically hinder access to the α -face of the donor.¹¹ This approach resulted in excellent *selectivity* but moderate yields for various targets (Scheme 1a).¹² Changes in ring conformation into axial-rich arrangements bring about additional benefits to glycosyl donors, *i.e.*, the reactivity increases. A decade ago, Bols and co-workers introduced the notion of conformational arming,^{13,14} thereby extending the established armed-disarmed concept¹⁵ to comprise super-armed glycosyl donors.¹⁶ In subsequent studies various 1-thio-glycoside donors were investigated, showing a 20-fold reactivity enhancement¹⁷ (Scheme 1b) and more recently a 100-fold higher reactivity¹⁸ compared to non-axial-rich analogues. Conformationally super-armed thio-ethyl glycosyl donors have also been used in one-pot synthesis of trisaccharides.¹⁹ Furthermore, for alkoxy substituents, axial arrangements will be less destabilizing for the charged transition state through an amplified charge-dipole interaction.^{20,21} Coupling reactions with 2-*O*-glucosylated glucosyl donors are intrinsically challenging due to potential steric crowding as was noted in the synthesis of the four anomeric combinations of D-Glcp-(1 \rightarrow 2)-D-Glcp-(1 \rightarrow 3)- α -D-Glcp-OMe,¹⁰ a structural arrangement that we will refer to as (1 \rightarrow 2),(1 \rightarrow 3)-linked trisaccharides. In targeting tetra- and pentasaccharides containing β -D-Glcp residues at these types of linkages, glucosyl monosaccharide donors were employed.²²



Scheme 1. Examples of axial-rich donors with the purposes of attaining stereoselectivity (a), enhanced reactivity (b), or stereoselectivity as well as enhanced reactivity (c) by work of Yamada and co-workers, Bols and co-workers, and Angles d'Ortoli and Widmalm, respectively.^{12,13,23}

To utilize disaccharides efficiently in such syntheses very potent donors would be necessary. We recently showed that by employing a super-armed donor, glycosylation of a disaccharide acceptor was possible (Scheme 1c) resulting, after deprotection, in the tetrasaccharide glycoside moiety of the glycoalkaloid Solaradixine.²³ By using different super-armed disaccharide donors and exploring their scope in glycosylation reactions we herein show that not only can excellent selectivity in the formation of β -linked trisaccharides products¹¹ be obtained but also excellent yields for challenging situations, in which the hydroxyl group is attached to a secondary carbon atom. Tetrasaccharides were also synthesized from the same donors using a convergent approach employing a disaccharide acceptor, and the reaction conditions were investigated to shed light on the influence of steric crowding. With this acquired knowledge we apply the developed methodology in the synthesis of a hexasaccharide (Figure 1) corresponding to three repeating units of the capsular polysaccharide (CPS) from *Streptococcus pneumoniae* type 37 and the exopolysaccharide from *Propionibacterium freudenreichii* ssp. *shermanii* JS.^{24,25}

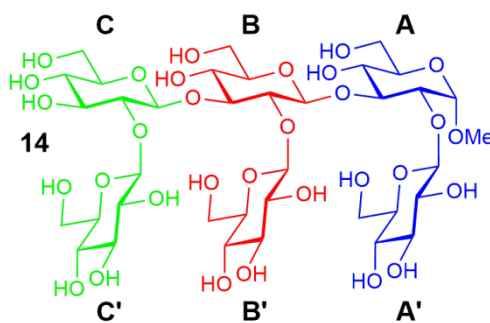
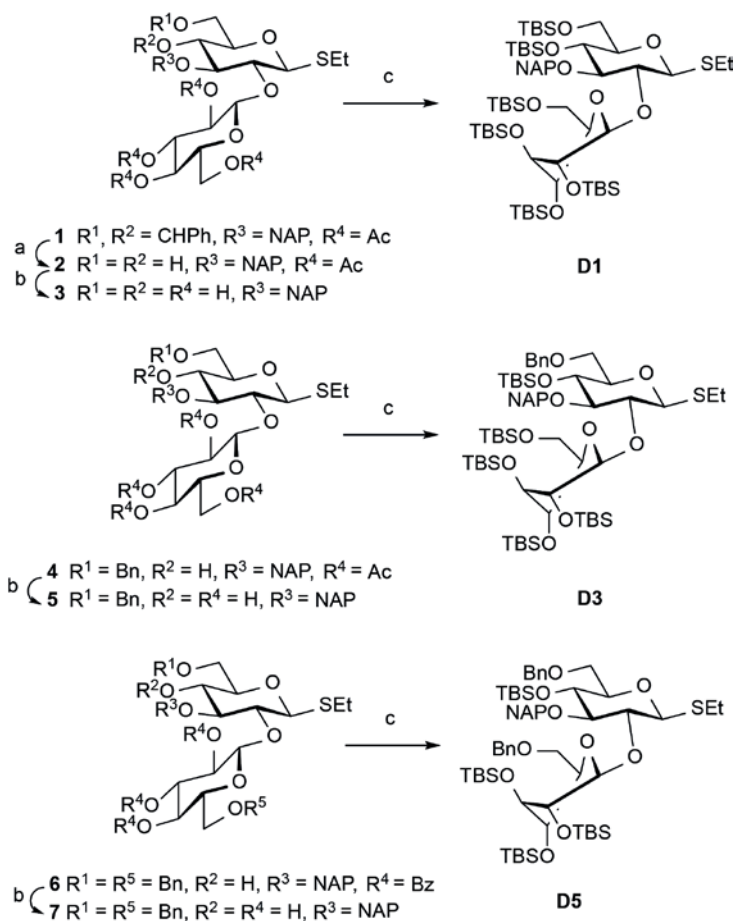


Figure 1. Schematic of a glucosyl-containing hexasaccharide (**14**) corresponding to three repeating units of the CPS from *S. pneumoniae* type 37. The oligosaccharide is colored to highlight its repetitive disaccharide structural elements. The sugar residues are denoted by capital letters in the β -(1 \rightarrow 3)-linked backbone and by primed capital letters in the β -(1 \rightarrow 2)-linked side-chains.

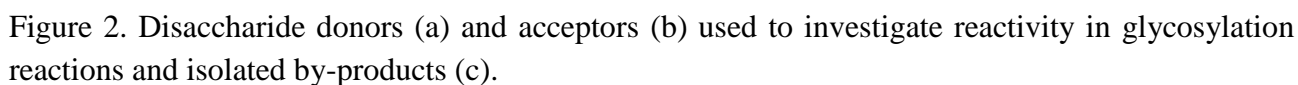
RESULTS AND DISCUSSION

Synthesis of glycosyl donors.

Synthesis of armed donors **D1**, **D3** and **D5** (Scheme 2) having a 2-naphthylmethyl (NAP or just naphthyl) group²⁶ at O3 of the reducing end residue started from previously described disaccharides **1**, **4** and **6**.²³ Acetal **1** was hydrolyzed at 80 °C for 2 h²⁷ using a solution of 80% AcOH (aq), which gave diol **2** in 82% yield. Compounds **2**, **4** and **6** had their O-acyl groups removed under standard conditions employing a solution of 1 M NaOMe in MeOH and the resulting hexaol **3**, pentaol **5** and tetraol **7** were obtained in 90 – 92% yield. In separate experiments, alcohols **3**, **5** and **7**, respectively, together with 4-dimethylaminopyridine (DMAP), were dissolved in pyridine; TBDMSOTf was added at 0 °C and the mixture was stirred overnight at 80 °C. Fully protected super-armed donors **D1**, **D3** and **D5** were isolated after flash column chromatography in 85 – 88% yield. The syntheses of the super-armed donors **D2**, **D4** and **D6** have been described previously.^{11,23} In total, six donors, **D1** – **D6**, armed to different extent (Figure 2a) are thus available for subsequent glycosylation reactions.



Scheme 2. Synthesis of armed donors **D1**, **D3** and **D5**. Reagents and conditions: (a) 80% AcOH (aq), 80 °C, 4 h, 82%; (b) 1 M NaOMe, MeOH, 16 h, 90 – 92%; (c) TBDMSOTf, DMAP, Pyr, 80 °C, 24 h, 85 – 88%.



The differently functionalized β -(1 \rightarrow 2)-linked disaccharide donors **D1** – **D6** all have *tert*-butyldimethylsilyl substituents (TBS), which are bulky protective groups known to induce distortions to the pyranose chair conformation (Scheme 1a). It has been shown that TBS-group insertion at positions 2 and 3 on β -D-glucopyranose forces the ring into a 1C_4 conformation,²⁸ whereas the same substituents at positions 3 and 4 do not change the ring puckering; to alter the ring conformation in the latter case requires an even bulkier protecting group, viz., *tert*-butyldiphenylsilyl (TBDPS) group at O3 and at O4.²⁹ Furthermore, full TBS-protection yields a 3S_1 ring conformation in β -D-glucopyranoside donors^{12,14,30} and this conformation has also been observed for 2-*O*-glycosylated¹² (Scheme 1a) and 6-*O*-benzylated^{12,14} (Scheme 1b) derivatives of 1-thio- β -D-glucose.

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a group was introduced in compounds **D3** – **D6**. Given the fact that the terminal glucose units of the donors also reside in distorted conformations, computer modeling suggested that protective groups at O6 of these residues, may explore three-dimensional space to different extent (Figure S1). The insertion of a benzyl group, instead of a TBS group, might thus impede steric hindrance, as in **D5** and **D6**.

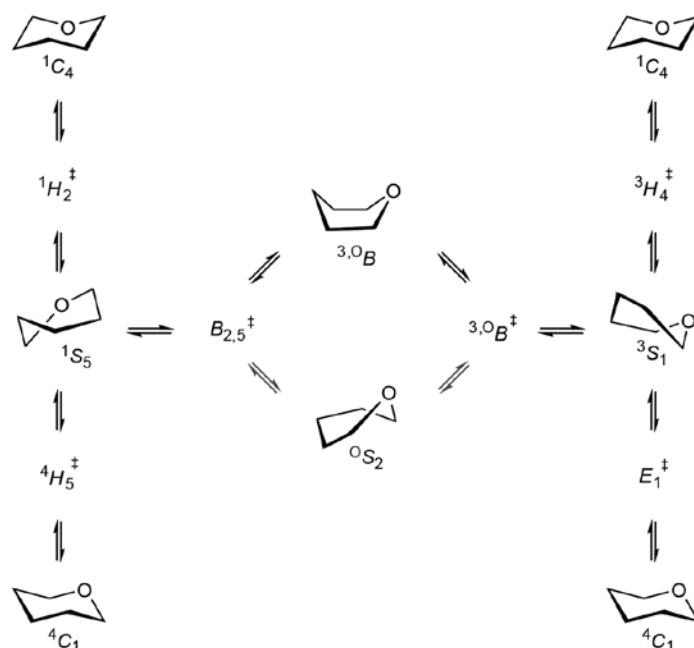
By means of NMR spectroscopy, the donor ring protons were exploited to relate their J couplings to torsion angles and thereby ring conformations by Karplus-type relationships. Initially, ^1H resonances were assigned using 1D and 2D NMR experiments suitable for carbohydrates³¹ and the chemical shifts and scalar coupling constants were refined by NMR spin-simulation using an iterative total-lineshape analysis approach (Figure S2 and Table S1).³² Observed J couplings will reflect population-weighted averages and by fitting experimental data to models, a distribution can be obtained. Built structures of relevant canonical ring puckers³³ were energy minimized and with the generalized Haasnoot-Altona equation³⁴ their ring-defining $^3J_{\text{HH}}$ couplings were calculated. These computed $^3J_{\text{HH}}$ values were compared by a root-mean-square deviation (RMSD) to those experimentally determined. The RMSD was minimized with the generalized reducing gradient algorithm,³⁵ by altering the populations of the different conformations and a weighted population distribution was thus achieved for both residues of donors **D1** – **D6** (Table 1a). For the residues populating axial-rich conformations, significant long-range $^4J_{\text{HH}}$ couplings were observed for the H2-H4 and H3-H5 proton pairs typically being around -1 Hz and -0.7 Hz, respectively (Table S1), which supported the presence of the conformational equilibria established. It should be noted that the conformational equilibria for each donor correspond to similar or adjacent conformers with puckering geometries that readily interconvert in-between each other for itineraries on the conformational sphere as described for β -D-glucose by Mayes et al.³³

Table 1. Populations (%) of donors **D1** – **D6** (a) and products **P3b** and **P4** (b) at 25 °C in CDCl_3 .

a	Residue B'				Residue B							
	$^1\text{S}_5$	$^3,0\text{B}$	$^3\text{S}_1$	RMSD	$^4\text{C}_1$	$^3\text{S}_1$	$^1\text{C}_4$	RMSD	$^1\text{S}_5$	$^3,0\text{B}$	$^3\text{S}_1$	RMSD
D1	4	8	88	0.05	85	15	0	0.10				
D2	0	28	72	0.10					23	12	65	0.16
D3	0	13	87	0.12	84	12	4	0.13				
D4	5	11	84	0.07					30	47	23	0.19
D5	8	31	61	0.08	85	13	2	0.12				
D6	5	37	57	0.07					32	33	35	0.19

b	Residue B'				Residue B				Residue A	
	$^4\text{C}_1$	$^3\text{S}_1$	$^1\text{C}_4$	RMSD	$^4\text{C}_1$	$^1\text{S}_5$	$^1\text{C}_4$	RMSD	$^4\text{C}_1$	RMSD
P3b	0	73	27	0.09	12	88	0	0.19	100	0.25
P4	0	70	29	0.08	3	94	3	0.17	100	0.23

The results of the conformational analysis indicated interconversion pathways somewhat extending from the geometry itineraries of cyclohexane proposed by Stoddart³⁶ to include transformations between stable energy minimum puckers for β -glucose (Scheme 3), investigated by Beckham and co-workers in a recent study.³³ The terminal residues (**B'** in Table 1a), not directly affecting the reactivity, were all shown to reside in a major 3S_1 conformation as would be expected from previous studies (*vide supra*). However, this single conformer was not sufficient to describe the conformational space and an equilibrium with the axial-rich arrangements $^3S_1 \rightleftharpoons ^{3,0}B \rightleftharpoons ^1S_5$ was considered. Upon benzylation at the O6 position, as in **D5** and **D6**, a slight shift toward a higher population of $^{3,0}B$ was observed. Conformational changes were also investigated by analysis of $^3J_{H5,H6}$ coupling constants for the terminal residue **B'**, which in **D4** had $^3J_{H5,H6pro-R} = 5.63$ Hz and $^3J_{H5,H6pro-S} = 8.15$ Hz; in **D6** these were $^3J_{H5,H6pro-R} = 6.30$ Hz and $^3J_{H5,H6pro-S} = 6.34$ Hz. Based on these spin-spin coupling constants the rotamer populations at the ω torsion angle were estimated.³⁷ In **D4** a relative distribution of 0.24:0.04:0.72 was deduced for the *gt:gg:tg* conformational states and in **D6** the corresponding distribution was 0.39:0.09:0.52. Given the fact that the *J* couplings and thus rotamer distribution do differ, besides the 3D shape of the protecting group *per se*, these data suggest an increased flexibility upon exchanging the TBS group for the benzyl group. The corresponding effect was not observed for **D3** vs **D5** (cf. Figure S1). For these compounds the inter-residual strain is likely to be lower due to the difference in conformations between the two rings. Thus, each conformational equilibrium of donors in Table 1 is present with a major 3S_1 skew conformation and adjacent ones that are populated via interconversion between states.



Scheme 3. Selected ring conformational interconversion pathways of β -D-glucose adapted from Beckham and co-workers,³³ including local minima and transition states between them. Only the pyranoid ring is shown for simplicity.

For the reducing end moieties (**B** in Table 1a) it is evident that donors with a large naphthyl group at O3 (**D1**, **D3** and **D5**) instead of a TBS group, do not undergo any major interconversion from 4C_1 , despite the bulkiness of the bicyclic aromatic group. Nevertheless, a slight perturbation of the equilibrium, involving also the 3S_1 conformer, was detected; changes in conformation upon benzylation at O6 were not detected. For the reducing end residue of **D2**, **D4** and **D6**, a more equal population distribution along the pathway ${}^3S_1 \rightleftharpoons {}^3,0B \rightleftharpoons {}^1S_5$ was observed, where benzylation of O6 (**D4** and **D6**) shifted the equilibrium toward the 1S_5 conformer. Since the subsequent glycosylation reactions were all performed at temperatures between -80 and -20 °C, an investigation of the 1H NMR temperature dependence was conducted for donor **D4** at temperatures between -30 and 25 °C (Figure S3). The results indicated that residue **B'** does not change conformation with temperature whereas for residue **B** the conformational equilibrium shifts as a consequence of temperature changes. The resonances of residue **B** are successively broadened as a result of lower temperature, further supporting the presence of a dynamic conformational equilibrium.

Glycosylations.

Trisaccharides. – The glycosylation reactions were first investigated using donors **D1** and **D2**; it was anticipated that product formation would be difficult since previous attempts with similar but monosaccharide donor substrates only gave 1,6-anhydro products.¹⁴ As a matter of fact, using different kind of promoter systems, several attempts were made to couple donors **D1** and **D2** with acceptor **A1** (Figure 2b), which all resulted in the formation of the intramolecularly glycosylated by-products **B1** and **B2** (Figure 2c). The use of reaction conditions developed by Okada *et al.*^{11,12} to couple donor **D1** and acceptor **A1**, MeOTf and 2,6-lutidine as base in DCM as such, only resulted to traces amount of trisaccharide product **P1** with the major formation of compound **B2**. It is to be noted that 1,6-anhydro by-product formation was higher employing donor **D2** as opposed to **D1**, 65% and 48%, respectively, with NIS/TfOH as the activator system (Scheme 4). From these results it was concluded that **D2** is more reactive than **D1**, which carries a NAP group at O3. Nevertheless, the latter compound still undergoes the internal cyclization, which is a strong indication that it readily experiences a ring-flip toward an axial-rich conformation, which the conformational analysis revealed (Table 1a).

Subsequently, suitable glycosylation procedures for donors **D3** – **D6** were elaborated. Donor **D4** represented the potentially most acid labile compound and was therefore selected as a model for optimizations of the reaction conditions in glycosylations with acceptor **A2** (Figure 2b). At an activation temperature of -78 °C, a wide range of relevant promoter systems were tested (Table 2) including MeOTf and NIS/TfOH, previously described to be suitable for related reactions.^{11,12,14} NIS/TfOH appeared to give the best results and gave rise to the least by-product formation; it was consequently chosen in further optimizations. The reactions were all monitored by MS analyses, which revealed that cleavage of the silyl ether protective groups were major side-reactions. Also hydrolysis reactions were repeatedly observed. To minimize the loss of the acid-labile silyl ethers, different sterically hindered bases were tested during the glycosylation reactions. The bulky base 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) gave the best results for neutralizing acidic species in the reaction solution. Interestingly, it was only when dry toluene was added in equal proportions to dry dichloromethane, that hydrolysis reactions could be suppressed yielding the desired product as the major one. Allowing the temperature to reach -40 °C and employing the optimized conditions permitted isolation of trisaccharide **P4** in an excellent 95% yield (Scheme 4).

Table 2. Glycosylation of **D4** with **A2**.

Entry	Activator	Amount TfO ⁻ /Tf ₂ O	Base	Solvent	Activation temp. (°C)	Yield (%)	By-products <i>i:ii</i> (%) ^a
1	MeOTf	cat	2,6-Lutidine	CH ₂ Cl ₂	-78 → RT	traces	major:minor
2	NIS/AgOTf	cat	2,6-Lutidine	CH ₂ Cl ₂	-78	25	minor:minor
3	NIS/TMSOTf	cat	2,6-Lutidine	CH ₂ Cl ₂	-78	20	minor:minor
4	NIS/TfOH	cat	2,6-Lutidine	CH ₂ Cl ₂	-78	25	minor:minor
5	Tf ₂ O-DMDS	1.1 eq	DTBMP	CH ₂ Cl ₂	-78	29	major:minor
6	Tf ₂ O-DPSO	1.25 eq	TTBP	CH ₂ Cl ₂	-78	17	minor:51
7	Tf ₂ O-BSP	1.25 eq	TTBP	CH ₂ Cl ₂	-78	20	minor:48
8	NIS/TfOH	cat	DTBMP	CH ₂ Cl ₂	-78	40	minor:55
9	NIS/TfOH	cat	DTBMP	CH ₂ Cl ₂ /Tol 1:1	-78 → -40	95	traces:traces

^a *i* and *ii* refer to hydrolysis- or elimination by-products and de-*O*-silylated by-products, respectively. Entries devoid of values infer by-product detected with MS, otherwise isolated yield.

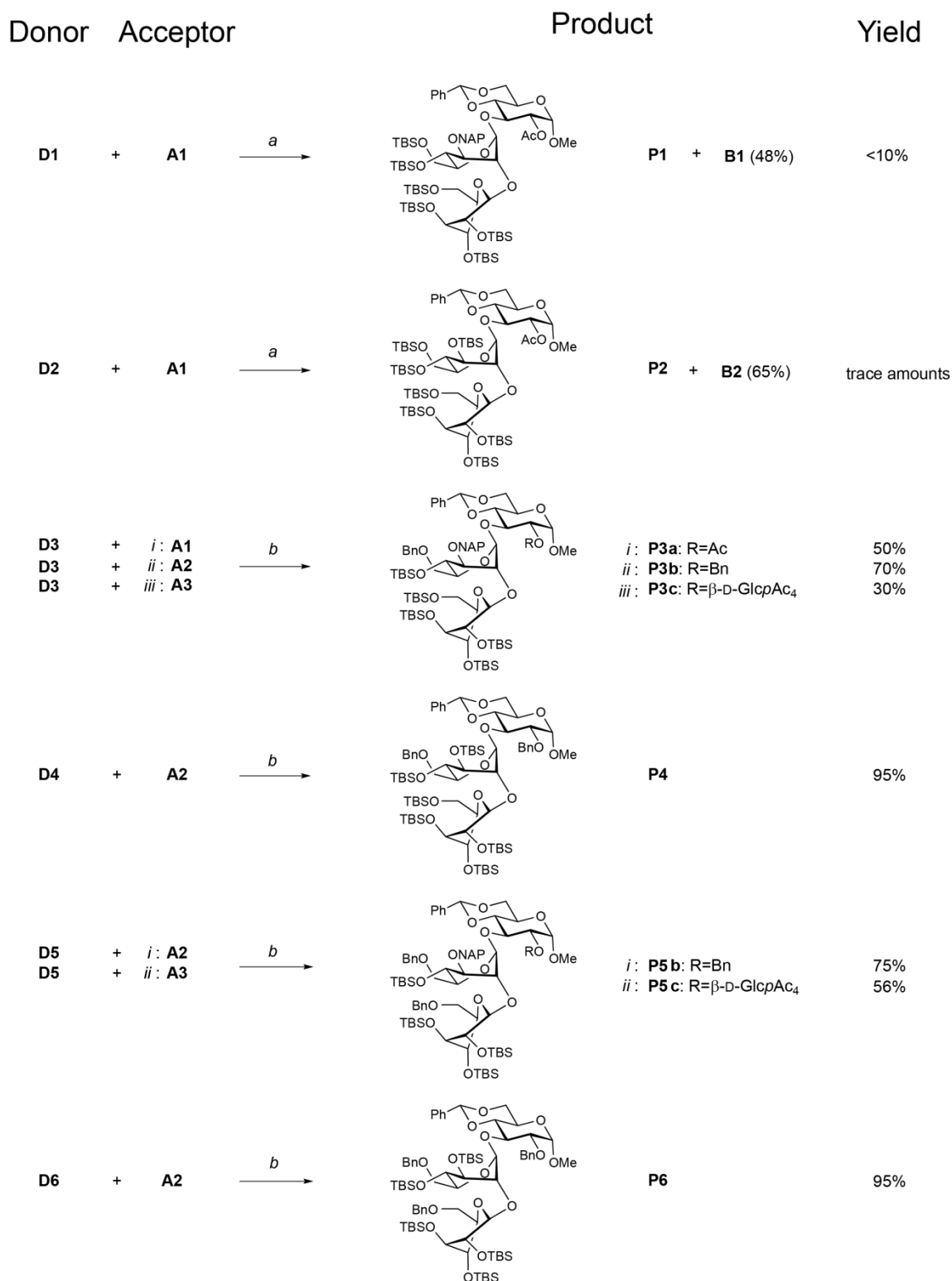
DMDS: Dimethyl disulfide;

DPSO: Diphenyl sulfoxide;

BSP: Benzenesulfinylpiperidine;

DTBMP: 2,6-Di-*tert*-butyl-4-methylpyridine;

TTBP: 2,4,6-Tri-*tert*-butylpyrimidine.



Scheme 4. Glycosylation reactions using different donors and acceptors, products formed and the respective yields. Reagents and conditions: (a) NIS, TfOH, 4 Å MS, DCM. (b) NIS, TfOH, DTBMP, 4 Å MS, DCM/Tol 1:1.

The subsequent glycosylations with donors **D3** – **D6** were performed using the improved conditions stated by entry 9 in Table 2 though the reactions temperature was set to –60 °C to increase solubility of the acceptors (**A1** and **A3** in particular) in the toluene-containing solvent mixture. These changes

had limited or no effect on reaction yields. Donor **D6** was reacted with acceptor **A2** to give product **P6** in 95% yield also (Scheme 4). NAP-protected donor **D3** was reacted with **A1** and **A2** yielding products **P3a** and **P3b**, respectively, in moderate to good isolated yields. Compound **P3b** was obtained in a better yield than for **P3a** due to the fact that **A2** is a more electron-rich nucleophile than acceptor **A1**, but steric aspects may also influence the yield. Furthermore, donor **D5** was coupled with acceptors **A2** whereafter product **P5b** was isolated in a good yield of 75%.

In the previous synthesis of a β -(1 \rightarrow 2), β -(1 \rightarrow 3)-linked glucosyl trisaccharide (cf. compounds **P4**, **P5b** and **P6**) a disaccharide acceptor corresponding to residues **B** and **A** was used employing a monosaccharide donor, corresponding to residue **A'**, in the silver triflate promoted glycosylation reaction to furnish the target trisaccharide in a good 75% yield.¹⁰ These glycosylations utilized monosaccharide donors thereby 'capping' the acceptor in syntheses whose directionality can be described as 'toward the nonreducing end'. The developments of the super-armed disaccharide donors facilitate chemical synthesis in a direction 'toward the reducing end' of an oligosaccharide. Importantly, and in contrast to our previous synthesis protocols, we have herein shown that it is possible to carry out glycosidic bond formation with complete stereoselectivity in an excellent yield of 95% using a *disaccharide donor* and an acceptor where the substitution takes place at a secondary alcohol, i.e., resulting in that the C3 atom of a glucose residue becomes glycosyloxyated in the present case.

Tetrasaccharides. – The highly *O*-acetylated, disarmed, as well as sterically crowded acceptor **A3** (Figure 2b), which was synthesized in a two-step procedure by glycosylation of 2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl trichloroacetimidate with methyl 3-*p*-methoxybenzyl-4,6-*O*-benzylidene- α -D-glucopyranoside followed by removal of the *p*-methoxybenzyl group by DDQ, was coupled with donor **D3** in a 2+2 fashion,^{23,38} to form tetrasaccharide **P3c**, but only in 30% yield. Additionally, donor **D5** was coupled with acceptor **A3**, whereafter product **P5c** was isolated in a moderate 56% yield. All glycosylation reactions gave excellent anomeric selectivity for the formation of the β -(1 \rightarrow 3)-linkages as would be expected from the work of Yamada and co-workers.¹¹ (*vide supra*). Indeed, none or only supposedly trace amounts of oligosaccharides having the α -configuration at this glycosidic linkage could be observed in ¹H NMR spectra of isolated products. In the earlier synthesis of the tetrasaccharide corresponding to compound **P5c** a β -(1 \rightarrow 3)-linked disaccharide acceptor was used and condensed with two monosaccharides as donors to produce the tetrasaccharide in a very good yield of 84%.²²

Conformational aspects related to product formation.

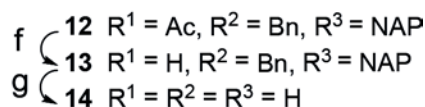
The results from the glycosylations clearly show that the conformationally distorted **D2**, **D4** and **D6** donors were significantly more reactive compared with **D1**, **D3** and **D5**. The still reasonable yields when donors **D3** and **D5** were used, given the hindered system, may be explained by the existence of a minor population of the ³S₁ conformation for the reacting residues, thus implying a slight conformational arming effect (Table 1a). This reasoning is supported by the substantial intramolecular by-product formation to **B1** over an intermolecular reaction when glycosylation was carried out with **D1**, not likely to occur under the employed conditions if the donor was not in an axial-rich conformation. Also, two of the products, namely trisaccharides **P3b** and **P4** were subjected to conformational analyses (Table 1b) and clearly, the increased level of steric bulk had an impact on the conformational preferences. Interestingly, both these products showed similar conformations where all three residues had distinctly different shapes. The terminal residue **B'** was

still adopting mainly a 3S_1 conformation but now in equilibrium with the 1C_4 chair conformation. Residue **B** populates mainly a 1S_5 conformation, also for **P3b**, bearing a less bulky naphthyl group. The conformationally constrained residue **A** resided in the expected 4C_1 chair conformation. 1H NMR spectra and resonance assignments of products **P5b** and **P6** showed that they were highly comparable to those of **P3b** and **P4**, thus indicating the same type of conformational behavior of all isolated trisaccharides products.

The glycosylation reactions of the type studied herein have been proposed to proceed via an S_N1 -like mechanism with an oxocarbenium like transition state (TS).¹² Thus, the bulky nature of the protective groups in the glycosyl donors **D1** – **D6** imply that axial arrangements of exocyclic substituents on the pyranose sugar ring should be adopted also in the transient oxocarbenium intermediate. The influence of conformational preorganization could constitute an additional basis for the reactivity enhancements of **D2**, **D4** and **D6** as well as similar conformationally armed donors. The pyranose rings of these compounds have puckered to adopt conformations on the equator of the pseudorotational hemisphere³³ and the energy penalty for leaving the low energy well of the 4C_1 conformation is already paid. Consequently, the prearranged axially oriented dipoles can stabilize the buildup of positive charge in the course of oxocarbenium ion formation. Donors **D1**, **D3** and **D5** reside mainly in 4C_1 conformations but the small presence of 3S_1 might be sufficient to drive the reaction via this conformer and therefore proceed via a charge-dipole stabilized TS, which is supported by the significant 1,6-anhydro formation (**B1**) when **D1** is used. The difference in reactivity compared to **D2**, **D4** and **D6** may thus be explained by the altered level of conformational preorganization.

Synthesis of a multi-branched hexasaccharide and comparison to polysaccharide NMR data.

In order to avoid potential and superfluous steric clashes during the 2+4 glycosylation step, it was decided to first remove all bulky silyl ether groups on compound **P5c** (Scheme 5) and subsequently replace them by smaller *O*-acetyl protective groups. A 1 M solution of tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF) was employed to cleave *tert*-butyldimethylsilyl ether groups and then directly after a simple workup, the obtained tetraol **7** was *O*-acetylated using acetic anhydride (Ac₂O) in pyridine in presence of a catalytic amount of DMAP. Thus, compound **8** was obtained in 92% yield over two steps. An excess of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in the solvent mixture DCM/MeOH 4:1 removed the NAP protecting group as well as the labile benzylidene acetal and triol **9** was furnished in 85% yield. Subsequently, position 6 on sugar residue **A** was selectively *O*-silylated³⁹ at $-20\text{ }^{\circ}\text{C}$ using *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBDMSOTf) and 2,6-lutidine in DCM to form diol acceptor **10** in 95% yield. The hydroxyl group at position 4 of residue **A** was judged to be less reactive than that at position 3 of residue **B** in **10** and a glycosylation that should be selective was therefore tried out. Sugars were dissolved as described above in a mixture of dry DCM/Tol 1:1; reagents and reaction temperature employed were the same as for the formation of tetrasaccharides. The regioselective glycosylation was accomplished using 3 eq of donor **D5** which was reacted with tetrasaccharide acceptor **10** to give hexasaccharide **11**, isolated in 65% yield (Scheme 5). The subsequent *O*-desilylation step was carried out by treatment with a 1 M solution of TBAF in THF followed by *O*-acetylation using pyridine and acetic anhydride; compound **12** was isolated in 79% yield over two steps. All *O*-acetyl groups were then removed using 1 M NaOMe in MeOH and compound **13** was obtained in 82% yield. Hydrogenolysis employing Palladium on carbon (loading 10 – 20%) as a catalyst furnished the hexasaccharide target compound **14** in 73% yield.



The structure of the synthesized hexasaccharide **14** was corroborated by high resolution mass spectrometry data in which the pseudomolecular ion from an ESI-MS spectrum showed $[M + Na]^+ m/z$ 1027.3326, in excellent agreement with that calculated for $C_{37}H_{64}O_{31}Na$, viz., m/z 1027.3329. The 1H and ^{13}C NMR resonances of **14** were fully assigned using 1D and 2D experiments (Table 3); all transglycosidic $^3J_{CH}$ -based correlations anticipated in the 1H , ^{13}C -HMBC NMR spectrum were observed, thereby leading further credence to the synthesized hexasaccharide structure. 1H NMR chemical shifts and $^nJ_{HH}$ coupling constants were refined by simulation of the 1H NMR spectrum using an iterative total line-shape analysis,³² the result of which was in excellent agreement with the experimental 1H NMR spectrum (Figure 3). The structures of the repeating units of the CPS from *S. pneumoniae* type 37 and that the EPS from *P. freudenreichii* ssp. *shermanii* JS are the same^{24,25} and for the latter 1H and ^{13}C NMR chemical shift assignments have been reported. A comparison of the

chemical shifts of the central disaccharide entity (**B** and **B'**) of the hexasaccharide (cf. Figure 1) and those of the EPS shows full agreement (Figure 4), in contrast to a pentasaccharide²² in which the terminal **C'** residue is missing and key chemical shifts deviate from those of the polysaccharide. Thus, a hexasaccharide model containing three repeating units is required to obtain agreement of NMR data; consequently, the local environment at **B** and **B'** residues should represent the 3D structure of the polysaccharide.

Table 3. ¹H and ¹³C NMR chemical shifts (ppm), ⁿJ_{HH} and ¹J_{H1,C1} (Hz) of hexasaccharide **14** at 9 °C.

Residue		1	2	3	4	5		6	
β-D-Glcp-(1→ C'	¹ H	4.838	3.461	3.531	3.369	3.471		3.739 ^a	3.944 ^b
	³ J _{HH}	7.95 (164) ^c	9.46	9.18	9.99	6.82 ^a	1.96 ^b	-12.35 ^d	
	¹³ C	104.42	74.49	76.54	70.64	77.13		61.90	
→2)-β-D-Glcp-(1→3) C	¹ H	5.113	3.636	3.772	3.460	3.494		3.741 ^a	3.935 ^b
	³ J _{HH}	7.87 (~165) ^c	9.19	9.09	10.14	6.06 ^a	2.14 ^b	-12.31 ^d	
	¹³ C	100.29	82.32	77.01	70.34	76.82		61.40	
β-D-Glcp-(1→ B'	¹ H	5.053	3.379	3.549	3.392	3.492		3.742 ^a	3.928 ^b
	³ J _{HH}	7.94 (165) ^c	9.52	9.02	10.00	6.18 ^a	1.32 ^b	-12.44 ^d	
	¹³ C	102.60	74.86	76.28	70.73	77.21		61.75	
→2,3)-β-D-Glcp-(1→3) B	¹ H	5.147	3.895	4.056	3.552	3.486		3.751 ^a	3.927 ^b
	³ J _{HH}	7.88 (~165) ^c	9.01	9.12	9.96	5.57 ^a	2.28 ^b	-12.51 ^d	
	¹³ C	100.23	79.81	82.36	68.65	76.23		61.43	
β-D-Glcp-(1→ A'	¹ H	4.775	3.342	3.522	3.426	3.446		3.757 ^a	3.920 ^b
	³ J _{HH}	7.96 (163) ^c	9.45	8.77	9.97	4.80 ^a	2.03 ^b	-12.26 ^d	
	¹³ C	103.81	74.15	76.65	70.31	76.71		61.40	
→2,3)-α-D-Glcp-OMe ^e A	¹ H	5.015	4.068	4.089	3.585	3.689		3.782 ^a	3.886 ^b
	³ J _{HH}	3.77 (175) ^c	9.62	9.10	10.14	5.24 ^a	2.22 ^b	-12.38 ^d	
	¹³ C	99.87	80.19	78.22	68.31	71.63		61.28	

^a H6_{pro-R}; ^b H6_{pro-S}; ^c ¹J_{H1,C1} at 21 °C; ^d ²J_{HH}; ^e OMe: δ_H 3.402, δ_C 55.46.

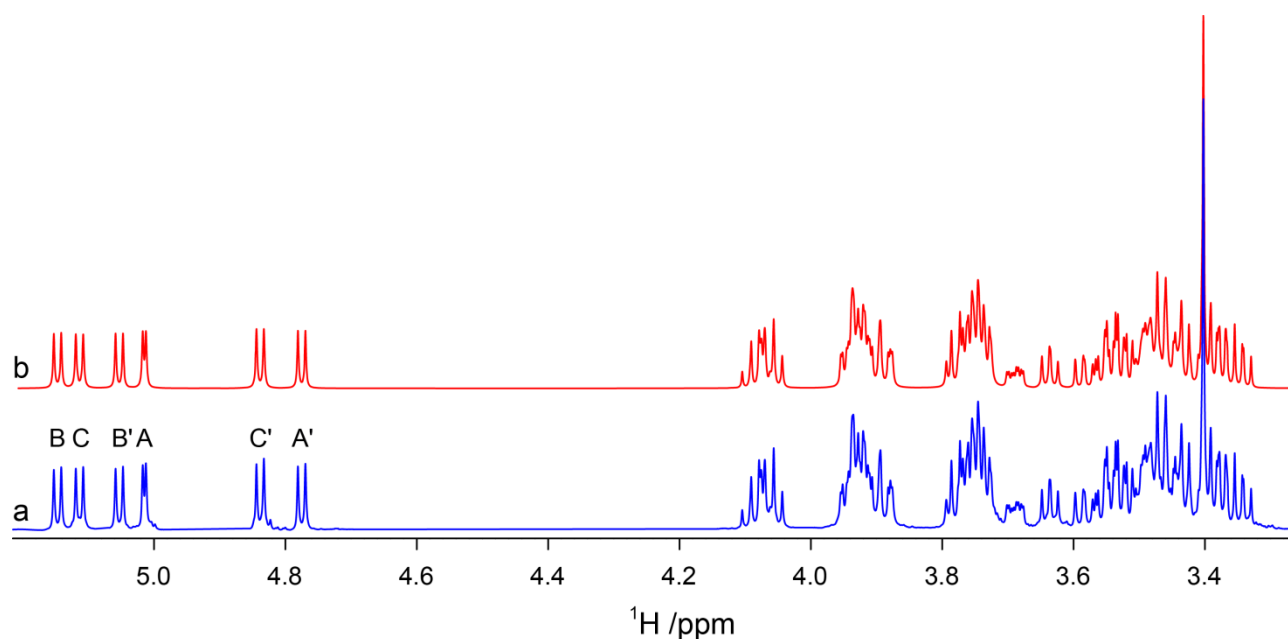


Figure 3. ¹H NMR spectrum at 700 MHz of hexasaccharide **14** at 9 °C (a) and the corresponding spectrum simulated by total-lineshape analysis using the PERCH NMR software (b). The HDO resonance in the experimental spectrum (δ_{H} 4.93) was removed prior to the lineshape fitting procedure. Anomeric proton resonances are annotated according to residue.

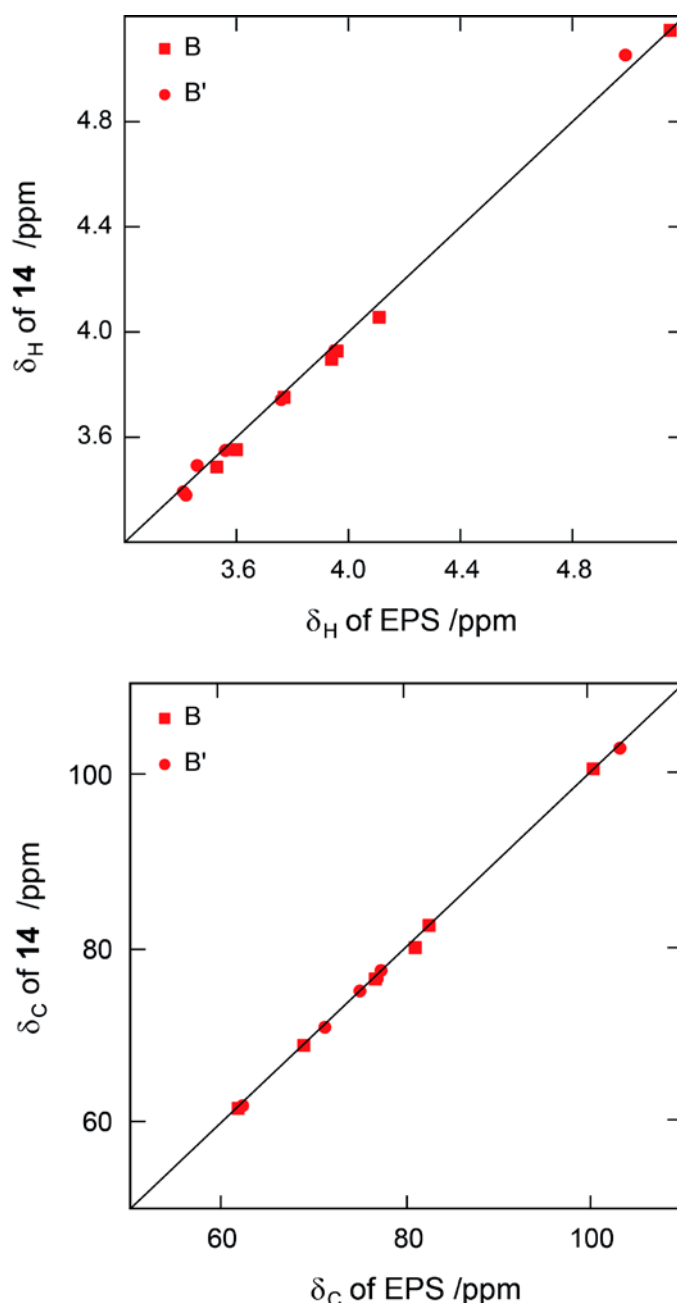


Figure 4. Comparison of ^1H and ^{13}C NMR chemical shifts (*top* and *bottom*, respectively) between residues **B** and **B'** from hexasaccharide **14** and EPS from *P. freudenreichii* ssp. *shermanii* JS,²⁵ which has the same polysaccharide structure as that of the CPS from *S. pneumoniae* type 37.²⁴

CONCLUSIONS

In conclusion, a number of conformationally armed glycan building blocks have been introduced and employed in convergent syntheses of tri- and tetrasaccharides. For some of these glucosyl donors, excellent yields were obtained in the formation of trisaccharides. Due to the crowded nature of the substrates, the reactions studied represent challenging systems and suitable reactions were investigated. Orthogonal protective groups were used allowing selective functionalization of the donors. The developed methodology was subsequently successfully applied in the synthesis of a hexasaccharide representing three repeating units of CPS and EPS with β -(1 \rightarrow 2)-linked side-chains and a β -(1 \rightarrow 3)-linked backbone. Notably, an NMR chemical shift analysis showed that a

hexasaccharide is the smallest structure for which the central disaccharide entity (**B** and **B'**) represents a model for the above bacterial polysaccharides.

A conformational and structure-reactivity analysis was performed with the six disaccharide donors **D1** – **D6** as well as the glycosylation products **P3b** and **P4**. This analysis rendered high quality data through NMR spin-simulations of very complex ^1H NMR spectra and population-weighted averages could be produced when a single conformer was not sufficient to describe the conformational space. The explored conformations deviate somewhat from those presented in the literature for similar compounds, which have been designated as single conformers.^{11,14,30} The present study indicates that a more elaborate description is necessary to structurally assign these species; we foresee that by the use of low-temperature NMR studies one should be able to unravel conformational preferences and elucidate dynamic equilibria between different ring conformations,⁴⁰ indicated to take place *e.g.* in donor **D4**. A correlation affirming that the more axial-rich donors had a higher reactivity was clearly found, *i.e.*, **D2**, **D4** and **D6** vs. **D1**, **D3** and **D5**. Furthermore, we hypothesize that the axial-rich skew and boat conformations for the particularly reactive donors are pre-organized close to the anticipated transition states in the glycosylation reactions. The structures and the corresponding structure-reactivity information obtained in this study of super-armed disaccharide donors, in conjunction with previously established glycosylation methodology, should be possible to apply efficiently in future challenging oligo- or polysaccharide syntheses.

EXPERIMENTAL SECTION

General methods

Dry solvents, including toluene (Tol), dichloromethane (DCM), tetrahydrofuran (THF) and acetonitrile (ACN) were obtained from a VAC solvent purifier (Hawthorne, CA, USA). Dry *N,N*-dimethylformamide (DMF) was purchased from Acros Organics (New Jersey, USA) and used as received. Pyridine (Pyr) was distilled over CaH_2 and dried with molecular sieves (4 Å). Methanol (MeOH) was dried over molecular sieve (4 Å). All reagents were used as received. A nitrogen gas flow was used for reactions requiring inert atmosphere. Powdered molecular sieves (4 Å) were activated by heating under high vacuum. Column chromatography was performed on a Biotage Isolera flash chromatography system (Uppsala, Sweden) using KP-Sil or HP-Sil snap silica gel cartridges and purification on t-C18 Sep-pak[®] cartridges. TLC was carried out on silica gel 60 F₂₅₄ plates (20 × 20 cm, 0.2 mm thickness) and monitored with UV light 254 – 360 nm or by a staining solution prepared from Ceric Ammonium Sulfate (2 g) in ethanol (40 mL) and 2 M sulfuric acid (40 mL).

NMR spectra for characterization of all isolated compounds were recorded at 25 °C, unless otherwise stated, on spectrometers operating at ^1H frequencies of 400, 500, 600 or 700 MHz. The NMR chemical shifts (δ) are reported in ppm and referenced to TMS as an internal standard, $\delta_{\text{H}} = 0.0$, or the residual solvent peaks for CDCl_3 , $\delta_{\text{H}} = 7.26$, or $\text{MeOH-}d_4$, $\delta_{\text{H}} = 3.31$. ^{13}C chemical shifts were referenced to external 1,4-dioxane in D_2O , $\delta_{\text{C}} = 67.40$, or internally to the CDCl_3 residual solvent peak $\delta_{\text{C}} = 77.16$ or to the $\text{MeOH-}d_4$ -residual solvent peak $\delta_{\text{C}} = 49.00$. *J* coupling constants are reported in Hertz (Hz). All new compounds synthesized were fully characterized using 1D ^1H , 1D ^1H -decoupled ^{13}C , 2D ^1H , ^1H -DQF-COSY, 2D ^1H , ^{13}C -multiplicity-edited-HSQC and 2D ^1H , ^{13}C -HMBC NMR experiments. If required, 1D ^1H , ^1H -TOCSY, 1D ^1H , ^1H -NOESY, 2D ^1H , ^1H -TOCSY,

2D ^1H , ^{13}C -H2BC, 2D ^{13}C , ^1H -HETCOR or 2D ^1H , ^{13}C -HSQC-TOCSY experiments were acquired. High-resolution mass spectra were recorded in positive mode on spectrometers using electrospray ionization (ESI) equipped with time-of-flight (TOF) analyzers. Samples of $1\text{ mg}\cdot\text{mL}^{-1}$ were prepared using a solution of 1:1 ACN/ H_2O containing 0.1% formic acid.

Abbreviations for NMR resonances: br (broad), s (singlet), d (doublet), t (triplet), dd (doublet of doublet), q (quadruplet), dt (doublet of triplet), dq (doublet of quadruplet), ddd (doublet of doublet of doublet), m (multiplet). Of the two protons constituting the hydroxymethyl group, the one resonating at lower chemical shift is denoted H-6a, and the one at higher chemical shift is denoted H-6b.

General procedure for O-deacylation

The saccharide (x g, y mmol) was dissolved in MeOH (0.1 M) and NaOMe in MeOH was added (2 eq per acyl group using a 1 M solution) and the mixture was stirred at room temperature overnight. When TLC (DCM/MeOH 9:1) indicated completion of the reaction, the solution was stirred for 30 min with Dowex[®] 50W X8- H^+ resin until pH 6 was reached. The resin was filtered off and washed with methanol after which solvents were evaporated to yield O-deacylated products.

General procedure for per-O-silylation

The saccharide (x g, y mmol) was dissolved in dry Pyr to a concentration of $\sim 0.03\text{ mM}$ and DMAP (0.2 eq) was added to the mixture whereafter 3 molar equivalents of TBDMSOTf per alcohol group to be protected were added dropwise at $0\text{ }^\circ\text{C}$. The reaction mixture was heated to $80\text{ }^\circ\text{C}$ and stirred overnight after which it was left to cool and subsequently quenched by addition of MeOH. The mixture was extracted with DCM and successively washed with 1 M HCl, saturated aqueous NaHCO_3 and brine. The solution was dried over anhydrous Na_2SO_4 prior to solvent evaporation under vacuum. The resulting residue was purified by flash chromatography to afford the respective O-silylated disaccharide donor as colorless syrup.

General procedure for glycosylation

Donor (50 mg, y mmol), acceptor (3 eq) and base DTBMP (1.5 eq) were dissolved in dry solvents (DCM/Tol 1:1) at room temperature to a concentration of $\sim 0.04\text{ mM}$ with respect to the donor and stirred with 4 \AA molecular sieves under N_2 flow. The temperature was decreased to $-60\text{ }^\circ\text{C}$ and NIS (1.2 eq), previously dissolved in dry DCM, was added. TfOH ($1.5\text{ }\mu\text{L}$, cat amount) was subsequently added at the same temperature. The mixture was allowed to reach $-30\text{ }^\circ\text{C}$ and stirred for 30 min, while monitored by mass spectrometry analysis. The reaction was then quenched by the addition of NEt_3 ($50\text{ }\mu\text{L}$). Once room temperature was attained, the mixture was filtered through a Celite pad and subsequently diluted into DCM. The resulting organic phase was washed with a 10% $\text{Na}_2\text{S}_2\text{O}_3$ solution and then with brine. The acquired mixture was dried over $\text{Na}_2\text{S}_2\text{O}_4$ after which solvents were evaporated. The obtained residue was purified by flash column chromatography (Pentane/EtOAc 3:1) to yield tri- or tetrasaccharides as colorless oils.

Ethyl 2,3,4,6-tetra-O-acetyl- β -D-glucopyranosyl-(1 \rightarrow 2)-3-O-(2-naphthyl)methyl-1-thio- β -D-glucopyranoside (2).

Disaccharide **1**²³ (0.3 g, 0.38 mmol) was dissolved in AcOH/ H_2O , 8:2 (5 mL). The reaction mixture was heated at $80\text{ }^\circ\text{C}$ during 4 h, monitored by TLC ($R_f = 0.6$ Tol/EtOAc 1:4). At completion, the mixture was left to reach room temperature and then the reaction was quenched by NEt_3 (0.5 mL).

The solvents were evaporated and co-evaporated with toluene. The product was purified by flash chromatography to yield the desired product **2**, 220 mg (82% yield) as a colorless oil. ¹H NMR (CDCl₃, 25 °C, 400 MHz): Residue **B**: δ 7.95-7.44 (m, 7H, H-Ar), 5.05 (d, *J*_{gem} -11.05, 1H, NapCH₂), 4.90 (d, *J*_{gem} -11.05, 1H, NapCH₂), 4.47 (d, *J*_{H1,H2} 9.64, 1H, H-1), 3.86 (dd, *J*_{H5,H6b} 3.72, *J*_{gem} -11.95, 1H, H-6b), 3.76 (dd, *J*_{H5,H6a} 4.78, *J*_{gem} -11.95, 1H, H-6a), 3.74 (dd, *J*_{H1,H2} 9.64, *J*_{H2,H3} 8.66, 1H, H-2), 3.66 (dd, *J*_{H3,H4} 9.06, *J*_{H4,H5} 9.28, 1H, H-4), 3.57 (dd, *J*_{H2,H3} 8.66, *J*_{H3,H4} 9.06, 1H, H-3), 3.32 (ddd, *J*_{H4,H5} 9.28, *J*_{H5,H6a} 4.78, *J*_{H5,H6b} 3.72, 1H, H-5), 2.70 (2q, 2H, SCH₂CH₃), 1.27 (t, 3H, SCH₂CH₃). Residue **B'**: 5.24-5.10 (m, 4H, H-1, H-2, H-3, H-4), 4.23 (dd, *J*_{H5,H6b} 4.98, *J*_{gem} -12.37, 1H, H-6b), 4.13 (dd, *J*_{H5,H6a} 2.56, *J*_{gem} -12.37, 1H, H-6a), 3.63 (ddd, *J*_{H4,H5} 9.31, *J*_{H5,H6a} 2.56, *J*_{H5,H6b} 4.98, 1H, H-5), 2.08, 2.07, 2.02, 2.01 (4 s, 12H, CH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): Residue **B**: 135.5, 133.5, 133.2 (3 C-*ipso*), 128.9, 128.1, 127.8, 127.3, 126.5, 126.4, 126.1 (7 C-Ar), 86.7 (C-2), 83.7 (C-1), 79.2 (C-5), 77.2 (C-3), 75.9 (NapCH₂), 71.2 (C-4), 62.4 (C-6), 24.1 (SCH₂CH₃), 14.7 (SCH₂CH₃). Residue **B'**: 170.8, 170.4, 169.5, 169.3 (4 C=O), 99.9 (C-1), 73.3 (C-2), 72.1 (C-4), 71.8 (C-5), 68.5 (C-3), 62.1 (C-6), 21.0, 20.9, 20.7, 20.6 (4 CH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₃₃H₄₂O₁₄SNa 717.2193, found 717.2191.

Ethyl β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-1-thio-β-D-glucopyranoside (**3**).

General procedure for *O*-deacylation: 2 eq per *O*-acyl group to be cleaved using a 1 M solution of NaOMe in MeOH were added. Starting from ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthyl)methyl-1-thio-β-D-glucopyranoside **2** (320 mg) the procedure yielded compound **3** (TLC: R_f = 0.35 DCM/MeOH 9:1) in 91% yield (220 mg) as a colorless syrup. ¹H NMR (CD₃OD, 25 °C, 400 MHz): Residue **B**: δ 7.99-7.42 (m, 7H, H-Ar), 5.12 (s, 2H, NapCH₂), 4.52 (d, *J*_{H1,H2} 9.46, 1H, H-1), 3.88 (dd, *J*_{H5,H6b} 2.26, *J*_{gem} -12.16, 1H, H-6b), 3.79 (dd, *J*_{H1,H2} 9.46, *J*_{H2,H3} 8.62, 1H, H-2), 3.72 (dd, *J*_{H2,H3} 8.62, *J*_{H3,H4} 9.10, 1H, H-3), 3.67 (dd, *J*_{H5,H6a} 6.03, *J*_{gem} -12.16, 1H, H-6a), 3.54 (dd, *J*_{H3,H4} 9.10, *J*_{H4,H5} 9.82, 1H, H-4), 3.34 (ddd, *J*_{H4,H5} 9.82, *J*_{H5,H6a} 6.03, *J*_{H5,H6b} 2.26, 1H, H-5), 2.77 (2q, 2H, SCH₂CH₃), 1.27 (t, 3H, SCH₂CH₃). Residue **B'**: 4.86 (d, *J*_{H1,H2} 7.65, 1H, H-1), 3.81 (dd, *J*_{H5,H6b} 2.49, *J*_{gem} -11.77, 1H, H-6b), 3.63 (dd, *J*_{H5,H6a} 5.89, *J*_{gem} -11.77, 1H, H-6a), 3.29-3.28 (m, 3H, H-3, H-4, H-2), 3.11 (ddd, *J*_{H4,H5} 8.75, *J*_{H5,H6a} 5.89, *J*_{H5,H6b} 2.49, 1H, H-5). ¹³C NMR (CD₃OD, 25 °C, 100 MHz): Residue **B**: δ 137.6, 134.9, 134.5 (3 C-*ipso*), 129.0, 128.8, 128.6, 128.1, 127.8, 127.0, 126.8 (7 C-Ar), 88.1 (C-3), 84.6 (C-1), 82.2 (C-5), 77.4 (C-2), 76.3 (NapCH₂), 72.3 (C-4), 62.8 (C-6), 24.4 (SCH₂CH₃), 14.9 (SCH₂CH₃). Residue **B'**: 103.6 (C-1), 78.0 (C-3), 78.0 (C-5), 75.4 (C-2), 71.8 (C-4), 63.0 (C-6). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₂₅H₃₄O₁₀SNa 549.1770, found 549.1772.

Ethyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-4,6-di-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranoside (**D1**).

General procedure for *per-O*-silylation: to hexaol **3** (92 mg) were added slowly, DMAP (0.2 eq) and TBDMSOTf (3 eq per alcohol group to be protected) at 0 °C under N₂ atmosphere and the mixture was heated to 80 °C overnight. The product was purified by chromatography (TLC: R_f = 0.5 Pentane/DCM 1:1) to afford thioglycoside donor **D1** in 85% yield (180 mg) as a colorless oil. ¹H NMR (CDCl₃, 25 °C, 400 MHz): Residue **B**: δ 7.84-7.13 (m, 7H, H-Ar), 5.25 (d, *J*_{gem} -11.81, 1H, NapCH₂), 4.76 (d, *J*_{gem} -11.81, 1H, NapCH₂), 4.69 (d, *J*_{H1,H2} 9.19, 1H, H-1), 3.94 (dd, *J*_{H1,H2} 9.19, *J*_{H2,H3} 7.99, 1H, H-2), 3.87 (dd, *J*_{gem} -11.14, 1H, H-6b), 3.80 (dd, *J*_{H2,H3} 7.99, *J*_{H3,H4} 8.24, 1H, H-3), 3.72 (dd, *J*_{gem} -11.14, 1H, H-6a), 3.66 (dd, *J*_{H3,H4} 8.24, *J*_{H4,H5} 9.29, 1H, H-4), 3.32 (ddd, *J*_{H4,H5} 9.29, 1H, H-5), 2.70 (2q, 2H, SCH₂CH₃), 1.26 (t, 3H, SCH₂CH₃). Residue **B'**: 5.25 (d, *J*_{H1,H2} 5.95, 1H, H-

1), 3.81 (ddd, $J_{\text{H4,H5}}$ 1.70, 1H, H-5), 3.80 (dd, J_{gem} -9.94, 1H, H-6b), 3.80 (dd, $J_{\text{H3,H4}}$ 3.47, $J_{\text{H4,H5}}$ 1.70, 1H, H-4), 3.72 (dd, J_{gem} -9.94, 1H, H-6a), 3.66 (dd, $J_{\text{H2,H3}}$ 0.58, $J_{\text{H3,H4}}$ 3.47, 1H, H-3), 3.62 (dd, $J_{\text{H1,H2}}$ 5.95, $J_{\text{H2,H3}}$ 0.58, 1H, H-2); 0.92, 0.90, 0.84, 0.83, 0.80, 0.78 (6 s, 54H, C(CH₃)₃), 0.11, 0.10, 0.08, 0.06, 3 × 0.02, 0.01, 2 × -0.02, -0.03, -0.10 (12 s, 36H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): Residue **B**: δ 137.7, 134.3, 133.7 (3 C-*ipso*), 128.8, 2 × 128.4, 126.4, 126.3, 126.2, 126.1 (7 C-Ar), 87.5 (C-3), 83.2 (C-1), 81.7 (C-5), 77.7 (C-2), 71.6 (C-4), 74.8 (NapCH₂), 63.7 (C-6), 25.1 (SCH₂CH₃), 15.7 (SCH₂CH₃). Residue **B'**: 99.6 (C-1), 83.0 (C-5), 79.4 (C-3), 79.1 (C-2), 71.6 (C-4), 65.8 (C-6); 26.2, 3 × 26.1, 2 × 25.9 (6 C(CH₃)₃), 2 × 18.6, 2 × 18.2, 2 × 17.9 (6 C(CH₃)₃), -2.9, -3.0, -3.1, -3.5, 3 × -3.6, -3.9, -4.0, -4.1, -4.2, -4.4 (12 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₆₁H₁₁₈O₁₀SSi₆Na 1233.6959, found 1233.6956.

Ethyl β-D-glucopyranosyl-(1→2)-3-O-(2-naphthylmethyl)-6-O-benzyl-1-thio-β-D-glucopyranoside (5).

General procedure for *O*-deacylation: 2 eq per *O*-acyl group to be cleaved using a 1 M solution of NaOMe in MeOH were added. Starting from ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-6-*O*-benzyl-1-thio-β-D-glucopyranoside²³ **4** (250 mg) yielded compound **5** (*R_f* = 0.45 DCM/MeOH 9:1) in 92% yield (181 mg) as a colorless syrup. ¹H NMR (CD₃OD, 25 °C, 400 MHz): Residue **B**: δ 7.99-7.23 (m, 12H, H-Ar), 5.12 (s, 2H, NapCH₂), 4.59 (s, 2H, PhCH₂), 4.54 (d, $J_{\text{H1,H2}}$ 9.46, 1H, H-1), 3.84 (dd, $J_{\text{H5,H6b}}$ 1.95, J_{gem} -11.10, 1H, H-6b), 3.80 (dd, $J_{\text{H1,H2}}$ 9.46, $J_{\text{H2,H3}}$ 8.78, 1H, H-2), 3.73 (dd, $J_{\text{H2,H3}}$ 8.78, $J_{\text{H3,H4}}$ 8.60, 1H, H-3), 3.67 (dd, $J_{\text{H5,H6a}}$ 5.83, J_{gem} -11.10, 1H, H-6a), 3.59 (dd, $J_{\text{H3,H4}}$ 8.60, $J_{\text{H4,H5}}$ 9.94, 1H, H-4), 3.50 (ddd, $J_{\text{H4,H5}}$ 9.94, $J_{\text{H5,H6a}}$ 5.83, $J_{\text{H5,H6b}}$ 1.95, 1H, H-5), 2.74 (2q, 2H, SCH₂CH₃), 1.27 (t, 3H, SCH₂CH₃). Residue **B'**: 4.85 (d, 1H, H-1), 3.81 (dd, $J_{\text{H5,H6b}}$ 2.56, J_{gem} -11.82, 1H, H-6b), 3.64 (dd, $J_{\text{H5,H6a}}$ 5.81, J_{gem} -11.82, 1H, H-6a), 3.32-3.28 (m, 3H, H-3, H-4, H-2), 3.12 (ddd, $J_{\text{H4,H5}}$ 8.86, $J_{\text{H5,H6a}}$ 5.81, $J_{\text{H5,H6b}}$ 2.56, 1H, H-5). ¹³C NMR (CD₃OD, 25 °C, 100 MHz): Residue **B**: δ 139.7, 137.6, 134.8, 134.4 (4 C-*ipso*), 2 × 129.3, 129.0, 3 × 128.8, 2 × 128.6, 128.1, 127.7, 127.0, 126.8 (12 C-Ar), 88.0 (C-3), 84.6 (C-1), 81.0 (C-5), 77.5 (C-2), 76.3 (NapCH₂), 74.4 (PhCH₂), 72.4 (C-4), 70.8 (C-6), 24.6 (SCH₂CH₃), 15.2 (SCH₂CH₃). Residue **B'**: 103.5 (C-1), 78.0 (C-3), 78.0 (C-5), 75.4 (C-2), 71.8 (C-4), 63.0 (C-6). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₃₂H₄₀O₁₀SNa 639.2240, found 639.2238.

Ethyl 2,3,4,6-tetra-*O*-tert-butyldimethylsilyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-4-*O*-tert-butyldimethylsilyl-6-*O*-benzyl-1-thio-β-D-glucopyranoside (D3).

General procedure for *per-O*-silylation: to pentaol **5** (85 mg) were added slowly, DMAP (0.2 eq) and TBDMSOTf (3 eq per alcohol group to be protected) at 0 °C under N₂ atmosphere and the mixture was heated to 80 °C overnight. The product was purified by chromatography (TLC: *R_f* = 0.8 Pentane/DCM 2:1) to afford thioglycoside donor **D3** in 86% yield (141 mg) as a colorless oil. ¹H NMR (CDCl₃, 25 °C, 400 MHz): Residue **B**: δ 7.82-7.24 (m, 12H, H-Ar), 5.23 (d, J_{gem} -11.44, 1H, NapCH₂), 4.76 (d, J_{gem} -11.44, 1H, NapCH₂), 4.76 (d, $J_{\text{H1,H2}}$ 8.92, 1H, H-1), 4.65 (d, J_{gem} -12.20, 1H, PhCH₂), 4.52 (d, J_{gem} -12.20, 1H, PhCH₂), 4.01 (dd, $J_{\text{H1,H2}}$ 8.92, $J_{\text{H2,H3}}$ 7.73, 1H, H-2), 3.82 (dd, $J_{\text{H2,H3}}$ 7.73, $J_{\text{H3,H4}}$ 8.18, 1H, H-3), 3.77 (dd, J_{gem} -10.47, 1H, H-6b), 3.69 (dd, $J_{\text{H3,H4}}$ 8.18, $J_{\text{H4,H5}}$ 9.46, 1H, H-4), 3.57 (dd, J_{gem} -10.47, 1H, H-6a), 3.57 (ddd, $J_{\text{H4,H5}}$ 9.46, 1H, H-5), 2.76 (q, 2H, SCH₂CH₃), 1.30 (t, 3H, SCH₂CH₃). Residue **B'**: 5.24 (d, $J_{\text{H1,H2}}$ 6.00, 1H, H-1), 3.81 (dd, $J_{\text{H3,H4}}$ 3.40, $J_{\text{H4,H5}}$ 1.55, 1H, H-4), 3.81 (ddd, $J_{\text{H4,H5}}$ 1.55, 1H, H-5), 3.81 (dd, J_{gem} -9.96, 1H, H-6b), 3.73 (dd, J_{gem} -9.96, 1H, H-6a), 3.67 (dd, $J_{\text{H2,H3}}$ 0.54, $J_{\text{H3,H4}}$ 3.40, 1H, H-3), 3.63 (dd, $J_{\text{H1,H2}}$ 6.00,

J_{H_2,H_3} 0.54, 1H, H-2); 0.93, 0.85, 0.81, 0.80, 0.78 (5 s, 45H, $C(CH_3)_3$), 0.12, 0.11, 0.05, 0.03, 0.01, -0.005, -0.02, -0.03, -0.05, -0.12 (10 s, 30H, $SiCH_3$). ^{13}C NMR ($CDCl_3$, 25 °C, 100 MHz): Residue **B**: δ 138.7, 136.8, 133.5, 132.9 (4 C-*ipso*), 2×128.4 , 128.1, 127.8, 3×127.7 , 127.5, 125.8, 125.6, 125.5, 125.4 (12 C-Ar), 86.4 (C-3), 82.8 (C-1), 79.7 (C-5), 76.7 (C-2), 73.9 (NapCH₂), 73.4 (PhCH₂), 71.4 (C-4), 70.1 (C-6), 24.6 (SCH₂CH₃), 15.0 (SCH₂CH₃). Residue **B'**: 98.8 (C-1), 82.3 (C-5), 78.6 (C-3), 78.4 (C-2), 70.7 (C-4), 64.9 (C-6); 26.2, 26.1, 26.0, 2×25.9 (5 $C(CH_3)_3$), 18.6, 2×18.2 , 2×17.9 (5 $C(CH_3)_3$), -3.7, -3.8, -3.9, -4.4, 2×-4.6 , 2×-4.7 , -4.9, -5.1 (10 $SiCH_3$). ESI-HRMS: $[M + Na]^+$ m/z calc for $C_{62}H_{110}O_{10}SSi_5Na$ 1209.6564, found 1209.6567.

Ethyl 6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 2)-3-*O*-(2-naphthylmethyl)-6-*O*-benzyl-1-thio- β -D-glucopyranoside (7).

General procedure for *O*-deacylation: 2 eq per acyl group to be cleaved using a 1 M solution of NaOMe in MeOH were added. Starting from ethyl 2,3,4-tri-*O*-benzoyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 2)-3-*O*-(2-naphthylmethyl)-6-*O*-benzyl-1-thio- β -D-glucopyranoside **6**²³ (210 mg) yielded compound **7** (R_f = 0.55 DCM/MeOH 9:1) in 92% yield (134 mg) as a colorless syrup. 1H NMR (CD_3OD , 25 °C, 400 MHz): δ 8.00-7.17 (m, 17H, H-Ar); Residue **B**: 5.12 (s, 2H, NapCH₂), 4.59 (s, 2H, PhCH₂), 4.53 (d, J_{H_1,H_2} 9.45, 1H, H-1), 3.84 (dd, J_{H_5,H_6b} 1.93, J_{gem} -11.11, 1H, H-6b), 3.80 (dd, J_{H_1,H_2} 9.45, J_{H_2,H_3} 8.74, 1H, H-2), 3.74 (dd, J_{H_2,H_3} 8.74, J_{H_3,H_4} 8.57, 1H, H-3), 3.67 (dd, J_{H_5,H_6a} 5.93, J_{gem} -11.11, 1H, H-6a), 3.58 (dd, J_{H_3,H_4} 8.57, J_{H_4,H_5} 9.88, 1H, H-4), 3.49 (ddd, J_{H_4,H_5} 9.88, J_{H_5,H_6a} 5.93, J_{H_5,H_6b} 1.93, 1H, H-5), 2.71 (2q, 2H, SCH₂CH₃), 1.22 (t, 3H, SCH₂CH₃). Residue **B'**: 4.88 (d, 1H, H-1), 4.60 (2d, J_{gem} -11.97, 2H, PhCH₂), 3.81 (dd, J_{H_5,H_6b} 2.00, J_{gem} -11.29, 1H, H-6b), 3.64 (dd, J_{H_5,H_6a} 5.93, J_{gem} -11.29, 1H, H-6a), 3.36-3.29 (m, 3H, H-3, H-4, H-2), 3.23 (ddd, J_{H_4,H_5} 9.31, J_{H_5,H_6a} 5.93, J_{H_5,H_6b} 2.00, 1H, H-5). ^{13}C NMR (CD_3OD , 25 °C, 100 MHz): δ 139.9, 139.7, 137.6, 134.8, 134.4 (5 C-*ipso*), 130.4, 129.6, 4×129.3 , 129.0, 4×128.8 , 2×128.6 , 128.4, 128.1, 127.7, 127.0 (17 C-Ar); Residue **B**: 88.2 (C-3), 84.8 (C-1), 81.0 (C-5), 77.2 (C-2), 76.3 (NapCH₂), 74.4 (PhCH₂), 72.4 (C-4), 70.8 (C-6), 24.5 (SCH₂CH₃), 15.3 (SCH₂CH₃). Residue **B'**: 103.5 (C-1), 78.1 (C-3), 77.4 (C-5), 75.3 (C-2), 71.8 (C-4), 70.8 (C-6). ESI-HRMS: $[M + Na]^+$ m/z calc for $C_{39}H_{46}O_{10}SNa$ 729.2709, found 729.2706.

Ethyl 2,3,4-tri-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 2)-3-*O*-(2-naphthylmethyl)-4-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl-1-thio- β -D-glucopyranoside (D5).

General procedure for *per-O*-silylation: to tetraol **7** (105 mg) were added slowly, DMAP (0.2 eq) and TBDMSOTf (3 eq per alcohol group to be protected) at 0 °C under N₂ atmosphere and the mixture was heated to 80 °C overnight. The product was purified by chromatography (TLC: R_f = 0.75 Pentane/DCM 2:1) to afford thioglycoside donor **D5** in 88% yield (152 mg) as a colorless oil. 1H NMR ($CDCl_3$, 25 °C, 400 MHz): δ 7.82-7.24 (m, 17H, H-Ar); Residue **B**: 5.22 (d, J_{gem} -11.89, 1H, NapCH₂), 4.77 (d, J_{gem} -11.89, 1H, NapCH₂), 4.70 (d, J_{H_1,H_2} 9.02, 1H, H-1), 4.64 (d, J_{gem} -12.16, 1H, PhCH₂), 4.53 (d, J_{gem} -12.16, 1H, PhCH₂), 4.00 (dd, J_{H_1,H_2} 9.02, J_{H_2,H_3} 7.98, 1H, H-2), 3.78 (dd, J_{H_2,H_3} 7.98, J_{H_3,H_4} 8.23, 1H, H-3), 3.76 (dd, J_{gem} -10.60, 1H, H-6b), 3.66 (dd, J_{H_3,H_4} 8.23, J_{H_4,H_5} 9.50, 1H, H-4), 3.57 (dd, J_{gem} -10.60, 1H, H-6a), 3.53 (ddd, J_{H_4,H_5} 9.50, 1H, H-5), 2.75 (2q, 2H, SCH₂CH₃), 1.30 (t, 3H, SCH₂CH₃). Residue **B'**: 5.24 (d, J_{H_1,H_2} 5.43, 1H, H-1), 4.65 (d, J_{gem} -12.08, 1H, PhCH₂), 4.55 (d, J_{gem} -12.08, 1H, PhCH₂), 3.99 (ddd, J_{H_4,H_5} 2.95, 1H, H-5), 3.85 (dd, J_{H_3,H_4} 3.41, J_{H_4,H_5} 2.95, 1H, H-4), 3.70 (dd, J_{gem} -9.67, 1H, H-6b), 3.65 (dd, J_{H_1,H_2} 5.43, J_{H_2,H_3} 0.73, 1H, H-2), 3.65 (dd, J_{H_2,H_3} 0.73, J_{H_3,H_4} 3.41, 1H, H-3), 3.64 (dd, J_{gem} -9.67, 1H, H-6a); 0.81, 0.79,

0.77, 0.75 (4 s, 36H, C(CH₃)₃), 0.07, -0.01, -0.04, 2 × -0.05, -0.06, -0.07, -0.14 (8 s, 24H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): δ 2 × 138.7, 136.7, 133.5, 132.9 (5 C-*ipso*), 4 × 128.4, 128.1, 3 × 127.8, 3 × 127.7, 2 × 127.6, 125.8, 125.5, 2 × 125.4 (17 C-Ar); Residue **B**: 86.8 (C-3), 83.1 (C-1), 80.0 (C-5), 76.6 (C-2), 74.0 (NapCH₂), 73.5 (PhCH₂), 71.4 (C-4), 70.1 (C-6), 24.7 (SCH₂CH₃), 15.1 (SCH₂CH₃). Residue **B'**: 99.2 (C-1), 79.4 (C-5), 78.6 (C-3), 77.6 (C-2), 73.4 (PhCH₂), 71.9 (C-6), 71.5 (C-4); 26.1, 26.0, 2 × 25.9 (4 C(CH₃)₃), 2 × 18.1, 2 × 17.9 (4 C(CH₃)₃), -3.7, 2 × -4.0, -4.3, -4.4, -4.6, 2 × -4.7 (8 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₆₃H₁₀₂O₁₀SSi₄Na 1185.6168, found 1185.6164.

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)-4,6-*O*-benzylidene-α-D-glucopyranoside (A3).

A solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl trichloroacetimidate⁴¹ (245 mg, 2 eq) and methyl 3-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-glucopyranoside⁴² (100 mg) in dry CH₂Cl₂ (4 mL) was stirred for 20 min in the presence of 4 Å molecular sieves. TMSOTf (0.08 eq) was added at -40 °C. The reaction was monitored by TLC (pentane/EtOAc 1:2) and allowed to warm up to room temperature. NEt₃ was added to quench the reaction and the mixture was filtered through a pad of Celite. It was then diluted with CH₂Cl₂ and washed successively with solutions of saturated NaHCO₃ and brine and dried over Na₂SO₄. The solvent was removed in vacuo, and the residue obtained was purified by flash chromatography (TLC: R_f = 0.79 Pentane/EtOAc 1:2) to yield the precursor disaccharide methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)-3-*O*-*p*-methoxybenzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**A3p**) in 92% yield (168 mg) as a white powder. ¹H NMR (CDCl₃, 25 °C, 400 MHz): Residue **A**: δ 7.48-6.83 (m, 9H, H-Ar), 5.54 (s, 1H, CHPh), 4.83 (d, *J*_{H1,H2} 3.66, 1H, H-1), 4.73 (d, *J*_{gem} -10.58, 1H, CH₃OArCH₂), 4.64 (d, *J*_{gem} -10.58, 1H, CH₃OArCH₂), 4.28 (dd, *J*_{H5,H6a} 10.26, *J*_{H5,H6b} 4.68, *J*_{gem} -10.01, 1H, H-6b), 3.98 (dd, *J*_{H2,H3} 9.43, *J*_{H3,H4} 9.29, 1H, H-3), 3.84 (ddd, *J*_{H4,H5} 9.36, *J*_{H5,H6a} 5.86, *J*_{H5,H6b} 4.68, 1H, H-5), 3.79 (s, 3H, CH₃OArCH₂), 3.73 (dd, *J*_{H5,H6a} 10.26, *J*_{gem} -10.01, 1H, H-6a), 3.71 (dd, *J*_{H1,H2} 3.66, *J*_{H2,H3} 9.43, 1H, H-2), 3.66 (dd, *J*_{H3,H4} 9.29, *J*_{H4,H5} 9.36, 1H, H-4), 3.42 (s, 3H, OMe). **A'**: 5.20 (dd, *J*_{H2,H3} 9.36, *J*_{H3,H4} 9.30, 1H, H-3), 5.12 (dd, *J*_{H1,H2} 7.80, *J*_{H2,H3} 9.36, 1H, H-2), 5.10 (dd, *J*_{H3,H4} 9.30, *J*_{H4,H5} 9.92, 1H, H-4), 4.87 (d, *J*_{H1,H2} 7.80, 1H, H-1), 4.18 (m, 2H, H-6b, H-6a), 3.67 (ddd, 1H, H-5), 2.08, 2.03, 2.00, 1.91 (4s, 12H, CH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): Residue **A**: δ 158.5 (C-*para*), 137.5, 130.6 (2 C-*ipso*), 2 × 129.7, 129.1, 2 × 128.4, 2 × 126.2, (7 C-Ar), 114.0 (2 C-Ar), 101.5 (CHPh), 100.2 (C-1), 82.4 (C-4), 80.2 (C-2), 77.3 (C-3), 75.0 (CH₃OArCH₂), 69.3 (C-6), 62.4 (C-5), 55.6 (OMe), 55.4 (CH₃OArCH₂). **A'**: 170.7, 170.5, 169.5, 169.3 (4 C=O), 101.8 (C-1), 73.3 (C-3), 72.1 (C-5), 71.7 (C-2), 68.6 (C-4), 62.2 (C-6), 20.9, 2 × 20.8, 20.7 (4 CH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₃₆H₄₄O₁₆Na 755.2527, found 755.2525.

To a solution of **A3p** (163 mg) in CH₂Cl₂ (3 ml) was added water (0.3 ml) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 76 mg, 1.5 eq).⁴³ The reaction mixture was stirred at room temperature for 2 h. The mixture was diluted with CH₂Cl₂ and washed twice with a solution of saturated NaHCO₃ and then dried over Na₂SO₄. The solvent was evaporated, and the oil obtained was purified by flash chromatography (TLC: R_f = 0.65 Pentane/EtOAc 1:2) to yield the acceptor methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)-4,6-*O*-benzylidene-α-D-glucopyranoside **A3** in 88% yield (120 mg) as a white powder. ¹H NMR (CDCl₃, 25 °C, 400 MHz): Residue **A**: δ 7.51-7.33 (m, 5H, H-Ar), 5.53 (s, 1H, CHPh), 4.82 (d, *J*_{H1,H2} 3.69, 1H, H-1), 4.29 (dd, *J*_{H5,H6b} 4.70, *J*_{gem} -10.10, 1H, H-6b), 4.13 (ddd, *J*_{H2,H3} 9.42, *J*_{H3,H4} 9.20, *J*_{H3,OH3} 1.67, 1H, H-3), 3.85 (ddd, *J*_{H4,H5}

9.40, $J_{H5,H6a}$ 10.35, $J_{H5,H6b}$ 4.70, 1H, H-5), 3.73 (dd, $J_{H5,H6a}$ 10.35, J_{gem} -10.10, 1H, H-6a), 3.61 (dd, $J_{H1,H2}$ 3.69, $J_{H2,H3}$ 9.42, 1H, H-2), 3.51 (dd, $J_{H3,H4}$ 9.20, $J_{H4,H5}$ 9.40, 1H, H-4), 3.42 (s, 3H, OMe), 2.83 (d, $J_{H3,OH3}$ 1.67, 1H, OH-3). **A'**: 5.23 (dd, $J_{H2,H3}$ 9.60, $J_{H3,H4}$ 9.48, 1H, H-3), 5.05 (dd, $J_{H1,H2}$ 7.98, $J_{H2,H3}$ 9.60, 1H, H-2), 5.05 (dd, $J_{H3,H4}$ 9.48, $J_{H4,H5}$ 10.05, 1H, H-4), 4.84 (d, $J_{H1,H2}$ 7.98, 1H, H-1), 4.21 (dd, $J_{H5,H6b}$ 2.68, J_{gem} -12.27, 1H, H-6b), 4.15 (dd, $J_{H5,H6a}$ 5.64, J_{gem} -12.27, 1H, H-6a), 3.72 (ddd, $J_{H4,H5}$ 10.05, $J_{H5,H6a}$ 5.64, $J_{H5,H6b}$ 2.68, 1H, H-5), 2.08, 2 × 2.03, 2.00 (4 s, 12H, CH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): Residue **A**: δ 137.2 (C-*ipso*), 129.3, 2 × 128.4, 2 × 126.4, (5 C-Ar), 102.0 (CHPh), 100.0 (C-1), 81.8 (C-2), 81.3 (C-4), 69.2 (C-3), 69.1 (C-6), 62.2 (C-5), 55.7 (OMe). **A'**: 170.7, 170.3, 169.6, 169.5 (4 C=O), 101.7 (C-1), 72.7 (C-3), 72.0 (C-5), 71.6 (C-2), 68.6 (C-4), 62.2 (C-6), 2 × 20.8, 2 × 20.7 (4 CH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₂₈H₃₆O₁₅Na 635.1952, found 635.1948.

2,3,4,6-tetra-*O*-tert-butyltrimethylsilyl-β-D-glucopyranosyl-(1→2)-1,6-anhydro-3-*O*-(2-naphthylmethyl)-4-*O*-tert-butyltrimethylsilyl-β-D-glucopyranose (B1**).**

General procedure for Glycosylation: from Donor **D1** (50 mg) and acceptor **A1** (40 mg). The obtained mixture was purified by flash column chromatography (*R_f* = 0.85 Pentane/DCM 2:1) to yield disaccharide **B1** in 48% yield (21 mg) as a colorless oil. ¹H NMR (CDCl₃, 25 °C, 400 MHz): Residue **B**: δ 7.85-7.41 (m, 7H, H-Ar), 5.72 (d, $J_{H1,H2}$ 1.92, 1H, H-1), 4.83 (d, J_{gem} -11.71, 1H, NapCH₂), 4.68 (d, J_{gem} -11.71, 1H, NapCH₂), 4.39 (ddd, $J_{H5,H6b}$ 1.00, 1H, H-5), 3.95 (dd, $J_{H5,H6b}$ 1.00, J_{gem} -7.11, 1H, H-6b), 3.77 (dd, 1H, H-3), 3.73 (dd, 1H, H-4), 3.67 (dd, J_{gem} -7.11, 1H, H-6a), 3.64 (dd, $J_{H1,H2}$ 1.92, 1H, H-2). Residue **B'**: 4.89 (d, $J_{H1,H2}$ 5.34, 1H, H-1), 3.92 (dd, 1H, H-4), 3.76 (dd, 1H, H-3), 3.76 (dd, 1H, H-6b), 3.73 (dd, 1H, H-6a), 3.66 (dd, 1H, H-2), 3.63 (ddd, 1H, H-5); 2 × 0.89, 0.88, 0.87, 0.82 (5 s, 45H, C(CH₃)₃), 0.10, 0.08, 0.07, 2 × 0.06, 3 × 0.05, 0.04, -0.08 (10 s, 30H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): Residue **B**: δ 135.7, 133.4, 133.1 (3 C-*ipso*), 128.3, 128.0, 127.8, 2 × 126.2, 125.9, 125.6 (7 C-Ar), 102.3 (C-1), 81.2 (C-3), 77.6 (C-2), 77.4 (C-5), 72.7 (C-4), 72.3 (NapCH₂), 65.5 (C-6). Residue **B'**: 103.2 (C-1), 81.2 (C-5), 78.8 (C-3), 77.2 (C-2), 70.1 (C-4), 63.9 (C-6); 3 × 26.1, 2 × 26.0 (5 C(CH₃)₃), 2 × 18.5, 18.1, 2 × 18.0 (5 C(CH₃)₃), -3.6, -4.0, 2 × -4.3, 2 × -4.5, 2 × -4.6, 2 × -5.2 (10 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₅₃H₉₈O₁₀Si₅Na 1057.5904, found 1057.5908.

2,3,4,6-tetra-*O*-tert-butyltrimethylsilyl-β-D-glucopyranosyl-(1→2)-1,6-anhydro-3,4-di-*O*-tert-butyltrimethylsilyl-β-D-glucopyranose (B2**).**

General procedure for Glycosylation: from Donor **D2** (50 mg) and acceptor **A1** (41 mg). The obtained mixture was purified by flash column chromatography (*R_f* = 0.55 Pentane/DCM 2:1) to yield disaccharide **B2** in 65% yield (28 mg) as a colorless oil. ¹H NMR (CDCl₃, 25 °C, 400 MHz): Residue **B**: δ 5.72 (d, $J_{H1,H2}$ 1.55, 1H, H-1), 4.38 (ddd, $J_{H4,H5}$ 1.47, $J_{H5,H6a}$ 6.10, $J_{H5,H6b}$ 1.20, 1H, H-5), 4.04 (dd, $J_{H5,H6b}$ 1.20, J_{gem} -6.80, 1H, H-6b), 3.81 (dd, $J_{H2,H3}$ 0.66, $J_{H3,H4}$ 1.05, 1H, H-3), 3.66 (dd, $J_{H5,H6a}$ 6.10, J_{gem} -6.80, 1H, H-6a), 3.52 (dd, $J_{H3,H4}$ 1.05, $J_{H4,H5}$ 1.47, 1H, H-4), 3.33 (dd, $J_{H1,H2}$ 1.55, $J_{H2,H3}$ 0.66, 1H, H-2). Residue **B'**: 4.82 (d, $J_{H1,H2}$ 5.88, 1H, H-1), 3.92 (dd, $J_{H3,H4}$ 2.91, $J_{H4,H5}$ 1.47, 1H, H-4), 3.76 (dd, $J_{H2,H3}$ 0.71, $J_{H3,H4}$ 2.91, 1H, H-3), 3.75 (ddd, $J_{H4,H5}$ 1.47, $J_{H5,H6a}$ 5.31, $J_{H5,H6b}$ 8.59, 1H, H-5), 3.71 (dd, $J_{H5,H6b}$ 8.59, J_{gem} -9.93, 1H, H-6b), 3.67 (dd, $J_{H1,H2}$ 5.88, $J_{H2,H3}$ 0.71, 1H, H-2), 3.66 (dd, $J_{H5,H6a}$ 5.31, J_{gem} -9.93, 1H, H-6a); 0.93, 2 × 0.89, 3 × 0.88, (6s, 54H, C(CH₃)₃), 0.12, 0.11, 3 × 0.10, 0.09, 2 × 0.08, 2 × 0.07, 2 × 0.04 (12s, 36H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): Residue **B**: δ 102.2 (C-1), 79.7 (C-2), 76.4 (C-5), 73.9 (C-3), 73.7 (C-4), 64.5 (C-6). Residue **B'**: 104.4 (C-1), 81.6 (C-5), 79.4 (C-3), 77.0 (C-2), 70.0 (C-4), 63.9 (C-6); 26.4, 2 × 26.1, 2

× 26.0, 25.8 (6 C(CH₃)₃), 18.7, 18.5, 18.1, 18.0, 2 × 17.9 (6 C(CH₃)₃), -2.9, -3.9, -4.0, -4.3, 2 × -4.4, -4.5, 2 × -4.6, -4.8, 2 × -5.1 (12 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₄₈H₁₀₄O₁₀Si₆Na 1031.6143, found 1031.6146.

Methyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-4-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→3)-4,6-*O*-benzylidene-2-*O*-acetyl-α-D-glucopyranoside (P3a).

General procedure for Glycosylation: from Donor **D3** (50 mg) and acceptor **A1** (41 mg). The obtained product was purified by flash column chromatography (R_f = 0.55 Pentane/EtOAc 9:1) to yield trisaccharide **P3a** in 50% yield (31 mg) as a colorless oil. ¹H NMR (CDCl₃, 25 °C, 400 MHz): δ 7.85-7.21 (m, 17H, H-Ar); Residue **B'**: 5.02 (d, *J*_{H1,H2} 6.29, 1H, H-1), 3.96 (dd, 1H, H-3), 3.78 (dd, 1H, H-4), 3.76 (ddd, 1H, H-5), 3.71 (dd, 1H, H-6b), 3.67 (dd, 1H, H-6a), 3.62 (dd, *J*_{H1,H2} 6.29, 1H, H-2); Residue **B**: 5.24 (d, *J*_{H1,H2} 2.75, 1H, H-1), 4.86 (d, *J*_{gem} -11.71, 1H, NapCH₂), 4.55 (d, *J*_{gem} -12.40, 1H, PhCH₂), 4.54 (d, *J*_{gem} -11.71, 1H, NapCH₂), 4.31 (d, *J*_{gem} -12.40, 1H, PhCH₂), 4.09 (dd, *J*_{H1,H2} 2.75, 1H, H-2), 4.02 (dd, 1H, H-4), 3.81 (ddd, 1H, H-5), 3.48 (dd, 1H, H-3), 3.48 (dd, 1H, H-6b), 3.41 (dd, 1H, H-6a); Residue **A**: 5.43 (s, 1H, CHPh), 4.88 (d, *J*_{H1,H2} 3.71, 1H, H-1), 4.84 (dd, *J*_{H1,H2} 3.71, *J*_{H2,H3} 9.39, 1H, H-2), 4.40 (dd, *J*_{H2,H3} 9.39, *J*_{H3,H4} 9.32, 1H, H-3), 4.21 (dd, *J*_{H5,H6b} 4.71, *J*_{gem} -10.20, 1H, H-6b), 3.84 (ddd, *J*_{H5,H6b} 4.71, 1H, H-5), 3.62 (dd, *J*_{gem} -10.20, 1H, H-6a), 3.61 (dd, *J*_{H3,H4} 9.32, 1H, H-4), 3.37 (s, 3H, OMe), 1.99 (s, 1H, CH₃); 0.88, 0.87, 0.86, 0.83, 0.66 (5 s, 45H, C(CH₃)₃), 2 × 0.12, 0.09, 0.08, 0.05, 0.01, -0.01, -0.02, -0.15, -0.32 (10 s, 30H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): δ 139.2, 137.6, 136.0, 133.4, 133.0 (5 C-*ipso*), 129.2, 2 × 128.4, 2 × 128.3, 128.1, 127.9, 127.8, 2 × 127.6, 127.3, 2 × 126.8, 2 × 126.0, 2 × 125.7 (17 C-Ar); Residue **B'**: 98.8 (C-1), 82.6 (C-5), 78.9 (C-4), 77.8 (C-2), 69.8 (C-3), 64.0 (C-6); Residue **B**: 99.7 (C-1), 84.6 (C-3), 74.7 (C-2), 74.3 (C-5), 72.9 (PhCH₂), 71.0 (NapCH₂), 71.3 (C-6), 70.0 (C-4); Residue **A**: 170.4 (C=O), 102.3 (CHPh), 97.8 (C-1), 80.3 (C-4), 74.6 (C-2), 72.8 (C-3), 69.1 (C-6), 62.7 (C-5), 55.4 (OMe), 21.1 (CH₃).; 26.2, 26.1, 26.0, 2 × 25.9 (5 C(CH₃)₃), 18.4, 18.2, 18.1, 2 × 18.0, (5 C(CH₃)₃), -3.7, -3.8, -4.1, -4.3, -4.4, -4.6, -4.7, 3 × -5.2 (10 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₇₆H₁₂₄O₁₇Si₅Na 1471.7583, found 1471.7582.

Methyl 2,3,4,6-tetra-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-4-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→3)-4,6-*O*-benzylidene-2-*O*-benzyl-α-D-glucopyranoside (P3b).

General procedure for Glycosylation: from Donor **D3** (50 mg) and acceptor **A2** (47 mg). The obtained product was purified by flash column chromatography (R_f = 0.75 Pentane/EtOAc 9:1) to yield trisaccharide **P3b** in 70% yield (45 mg) as a white powder. ¹H NMR (CDCl₃, 25 °C, 400 MHz): δ 7.84-7.13 (m, 22H, H-Ar); Residue **B'**: 5.13 (d, *J*_{H1,H2} 6.60, 1H, H-1), 4.02 (dd, 1H, H-3), 3.84 (ddd, 1H, H-5), 3.80 (dd, 1H, H-4), 3.71 (dd, 1H, H-6b), 3.67 (dd, *J*_{H1,H2} 6.60, 1H, H-2), 3.60 (dd, 1H, H-6a); Residue **B**: 5.42 (d, *J*_{H1,H2} 2.95, 1H, H-1), 4.91 (d, *J*_{gem} -11.66, 1H, NapCH₂), 4.66 (d, *J*_{gem} -11.66, 1H, NapCH₂), 4.58 (d, *J*_{gem} -12.56, 1H, PhCH₂), 4.35 (d, *J*_{gem} -12.56, 1H, PhCH₂), 4.24 (dd, *J*_{H1,H2} 2.95, 1H, H-2), 4.22 (dd, 1H, H-4), 3.84 (ddd, 1H, H-5), 3.56 (dd, 1H, H-3), 3.49 (dd, 1H, H-6b), 3.48 (dd, 1H, H-6a); Residue **A**: 5.39 (s, 1H, CHPh), 4.61 (d, *J*_{gem} -12.49, 1H, PhCH₂), 4.48 (d, *J*_{gem} -12.49, 1H, PhCH₂), 4.34 (d, *J*_{H1,H2} 3.66, 1H, H-1), 4.28 (dd, 1H, H-3), 4.14 (dd, 1H, H-6b), 3.75 (ddd, 1H, H-5), 3.52 (dd, 1H, H-4), 3.47 (dd, 1H, H-6a), 3.38 (dd, *J*_{H1,H2} 3.66, 1H, H-2), 3.32 (s, 3H, OMe); 2 × 0.89, 0.85, 0.79, 0.70 (5 s, 45H, C(CH₃)₃), 0.15, 0.12, 0.11, 0.09, 0.04, 0.01, -0.06, -0.08, -0.11, -0.21 (10 s, 30H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): δ

139.1, 138.1, 137.6, 136.1, 133.3, 132.8 (6 C-*ipso*), 129.0, 2 × 128.6, 2 × 128.4, 2 × 128.3, 128.1, 127.9, 2 × 127.8, 127.7, 3 × 127.4, 127.3, 2 × 126.7, 126.0, 2 × 125.7, 125.4 (22 C-Ar); Residue **B'**: 98.7 (C-1), 82.5 (C-5), 79.3 (C-4), 77.7 (C-2), 69.6 (C-3), 63.6 (C-6); Residue **B**: 99.8 (C-1), 84.8 (C-3), 74.8 (C-2), 73.9 (C-5), 72.7 (PhCH₂), 70.7 (NapCH₂), 70.7 (C-6), 70.0 (C-4); Residue **A**: 101.9 (CHPh), 99.2 (C-1), 80.7 (C-4), 79.0 (C-2), 75.4 (C-3), 73.8 (PhCH₂), 69.1 (C-6), 62.4 (C-5), 55.3 (OMe); 26.2, 26.0, 3 × 25.9 (5 C(CH₃)₃), 18.3, 3 × 18.1, 17.9 (5 C(CH₃)₃), -3.6, -3.8, -4.1, -4.3, -4.5, -4.6, -4.8, -5.2, 2 × -5.3 (10 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₈₁H₁₂₈O₁₆Si₅Na 1519.7946, found 1519.7948.

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)[2,3,4,6-tetra-*O*-tert-butyltrimethylsilyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-4-*O*-tert-butyltrimethylsilyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→3)]-4,6-*O*-benzylidene-α-D-glucopyranoside (P3c).

General procedure for Glycosylation: from Donor **D3** (50 mg) and acceptor **A3** (77 mg). The obtained product was purified by flash column chromatography (R_f = 0.40 Pentane/EtOAc 3:1) to yield tetrasaccharide **P3c** in 30% yield (22 mg) as a white solid. ¹H NMR (CDCl₃, 25 °C, 400 MHz): δ 7.89-7.21 (m, 17H, H-Ar); Residue **B'**: 5.15 (d, *J*_{H1,H2} 6.91, 1H, H-1), 4.10 (dd, 1H, H-3), 3.88 (ddd, 1H, H-5), 3.84 (dd, 1H, H-4), 3.78 (dd, 1H, H-6b), 3.67 (dd, 1H, H-6a), 3.57 (dd, *J*_{H1,H2} 6.91, 1H, H-2); Residue **B**: 5.22 (d, *J*_{H1,H2} 1.86, 1H, H-1), 4.85 (d, *J*_{gem} -13.12, 1H, NapCH₂), 4.77 (d, *J*_{gem} -13.12, 1H, NapCH₂), 4.58 (d, *J*_{gem} -12.46, 1H, PhCH₂), 4.27 (d, *J*_{gem} -12.46, 1H, PhCH₂), 4.18 (dd, *J*_{H1,H2} 1.86, 1H, H-2), 4.14 (dd, 1H, H-4), 3.90 (ddd, 1H, H-5), 3.54 (dd, 1H, H-3), 3.38 (2 dd, 2H, H-6b, H-6a); Residue **A**: 5.49 (s, 1H, CHPh), 4.70 (d, *J*_{H1,H2} 3.69, 1H, H-1), 4.38 (dd, *J*_{H2,H3} 9.21, *J*_{H3,H4} 9.11, 1H, H-3), 4.23 (dd, 1H, H-6b), 3.90 (ddd, 1H, H-5), 3.69 (dd, 1H, H-6a), 3.55 (dd, *J*_{H1,H2} 3.69, *J*_{H2,H3} 9.21, 1H, H-2), 3.52 (dd, *J*_{H3,H4} 9.11, 1H, H-4), 3.37 (s, 3H, OMe); Residue **A'**: 5.00 (dd, *J*_{H3,H4} 9.42, *J*_{H4,H5} 10.04, 1H, H-4), 4.95 (dd, *J*_{H1,H2} 7.89, *J*_{H2,H3} 9.60, 1H, H-2), 4.77 (dd, *J*_{H2,H3} 9.60, *J*_{H3,H4} 9.42, 1H, H-3), 4.25 (d, *J*_{H1,H2} 7.89, 1H, H-1), 4.00 (2 dd, 2H, H-6b, H-6a), 2.99 (ddd, *J*_{H4,H5} 10.04, 1H, H-5), 2.12, 2.05, 1.94, 1.87 (4 s, 12H, CH₃); 0.92, 0.88, 2 × 0.86, 0.60 (5 s, 45H, C(CH₃)₃), 2 × 0.12, 0.11, 0.09, 0.08, 0.07, 0.06, 0.05, -0.12, -0.36 (10 s, 30H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): δ 139.7, 137.7, 137.2, 133.4, 132.8 (5 C-*ipso*), 129.5, 2 × 128.5, 3 × 128.2, 3 × 127.9, 3 × 127.7, 127.3, 126.4, 125.8, 124.8, 124.6 (17 C-Ar); Residue **B'**: 97.2 (C-1), 83.3 (C-5), 79.6 (C-4), 77.4 (C-2), 69.8 (C-3), 63.9 (C-6); Residue **B**: 98.4 (C-1), 83.4 (C-3), 73.6 (C-5), 72.9 (PhCH₂), 72.4 (C-2), 71.4 (C-6), 70.6 (C-4), 69.3 (NapCH₂); Residue **A**: 102.9 (CHPh), 100.7 (C-1), 81.1 (C-4), 81.0 (C-2), 72.8 (C-3), 69.5 (C-6), 62.3 (C-5), 55.8 (OMe); Residue **A'**: 170.6, 170.1, 169.4, 169.1 (4 C=O), 101.1 (C-1), 73.4 (C-3), 71.5 (C-5), 71.2 (C-2), 68.3 (C-4), 61.5 (C-6), 21.6, 20.9, 20.8, 20.6 (4 CH₃); 26.3, 26.1, 26.0, 2 × 25.9 (5 C(CH₃)₃), 18.4, 18.2, 3 × 18.0 (5 C(CH₃)₃), -3.3, -4.1, -4.2, -4.3, 2 × -4.4, -4.9, -5.0, 2 × -5.4 (10 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₈₈H₁₄₀O₂₅Si₅Na 1759.8428, found 1759.8430.

Methyl 2,3,4,6-tetra-*O*-tert-butyltrimethylsilyl-β-D-glucopyranosyl-(1→2)-3,4-*O*-di-tert-butyltrimethylsilyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→3)-4,6-*O*-benzylidene-2-*O*-benzyl-α-D-glucopyranoside (P4).

General procedure for Glycosylation: from Donor **D4** (50 mg) and acceptor **A2** (48 mg). The obtained product was purified by flash column chromatography (R_f = 0.55 Tol/EtOAc 12:1) to yield trisaccharide **P4** (60 mg) in 95% yield as a colorless oil. ¹H NMR (CDCl₃, 25 °C, 400 MHz): δ 7.40-7.20 (m, 15H, H-Ar); Residue **B'**: 4.97 (d, *J*_{H1,H2} 6.41, 1H, H-1), 4.01 (dd, 1H, H-3), 3.82 (ddd,

1H, H-5), 3.79 (dd, 1H, H-4), 3.67 (dd, 1H, H-6b), 3.63 (dd, $J_{H1,H2}$ 6.41, 1H, H-2), 3.58 (dd, 1H, H-6a); Residue **B**: 5.57 (d, $J_{H1,H2}$ 2.89, 1H, H-1), 4.58 (d, J_{gem} -12.76, 1H, PhCH₂), 4.44 (d, J_{gem} -12.76, 1H, PhCH₂), 4.03 (dd, $J_{H1,H2}$ 2.89, 1H, H-2), 3.90 (ddd, 1H, H-5), 3.86 (dd, 1H, H-3), 3.77 (dd, 1H, H-4), 3.45 (dd, 1H, H-6b), 3.32 (dd, 1H, H-6a); Residue **A**: 5.35 (s, 1H, CHPh), 4.84 (d, J_{gem} -12.56, 1H, PhCH₂), 4.53 (d, J_{gem} -12.56, 1H, PhCH₂), 4.36 (dd, $J_{H2,H3}$ 9.17, $J_{H3,H4}$ 9.40, 1H, H-3), 4.33 (d, $J_{H1,H2}$ 3.62, 1H, H-1), 4.15 (dd, J_{gem} -10.21, 1H, H-6b), 3.79 (ddd, $J_{H5,H6b}$ 4.78, 1H, H-5), 3.58 (dd, J_{gem} -10.21, 1H, H-6a), 3.42 (dd, $J_{H1,H2}$ 3.62, $J_{H2,H3}$ 9.17, 1H, H-2), 3.39 (dd, $J_{H3,H4}$ 9.40, 1H, H-4), 3.34 (s, 3H, OMe); 0.93, 3 × 0.88, 0.77, 0.67 (6 s, 54H, C(CH₃)₃), 0.22, 3 × 0.10, 0.09, 0.08, 0.06, 0.05, 0.01, -0.11, -0.13, -0.14 (12 s, 36H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): δ 139.3, 138.4, 137.8 (3 C-*ipso*), 129.2, 2 × 128.6, 2 × 128.5, 2 × 128.4, 2 × 128.3, 128.0, 2 × 127.6, 127.3, 2 × 126.9 (15 C-Ar); Residue **B'**: 102.6 (C-1), 82.3 (C-5), 79.7 (C-4), 77.9 (C-2), 69.9 (C-3), 64.0 (C-6); Residue **B**: 99.0 (C-1), 79.1 (C-2), 77.8 (C-3), 74.0 (C-5), 73.4 (C-4), 72.9 (PhCH₂), 72.1 (C-6); Residue **A**: 102.6 (CHPh), 99.4 (C-1), 80.7 (C-4), 80.6 (C-2), 73.7 (PhCH₂), 73.4 (C-3), 69.3 (C-6), 62.7 (C-5), 55.4 (OMe); 26.4, 26.3, 2 × 26.1, 2 × 26.0 (6 C(CH₃)₃), 18.4, 18.3, 3 × 18.1, 18.0 (6 C(CH₃)₃), -2.6, -3.2, -3.5, 2 × -3.6, 2 × -4.3, -4.4, -4.7, -4.8, -5.3, -5.4 (12 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₇₆H₁₃₄O₁₆Si₆Na 1493.8185, found 1493.8189.

Methyl 2,3,4-tri-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-4-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→3)-4,6-*O*-benzylidene-2-*O*-benzyl-α-D-glucopyranoside (P5b).

General procedure for Glycosylation: from Donor **D5** (50 mg) and acceptor **A2** (48 mg). The obtained product was purified by flash column chromatography (*R_f* = 0.65 Pentane/EtOAc 9:1) to yield trisaccharide **P5b** (48 mg) in 75% yield as a white solid. ¹H NMR (CDCl₃, 25 °C, 400 MHz): δ 7.82-7.14 (m, 27H, H-Ar); Residue **B'**: 5.10 (d, $J_{H1,H2}$ 6.04, 1H, H-1), 4.35 (d, 1H, PhCH₂), 3.99 (dd, 1H, H-4), 3.89 (dd, 1H, H-3), 3.78 (ddd, 1H, H-5), 3.69 (dd, $J_{H1,H2}$ 6.04, 1H, H-2), 3.59 (dd, 1H, H-6b), 3.49 (dd, 1H, H-6a); Residue **B**: 5.42 (d, $J_{H1,H2}$ 3.18, 1H, H-1), 4.94 (d, J_{gem} -11.73, 1H, NapCH₂), 4.65 (d, J_{gem} -11.73, 1H, NapCH₂), 4.56 (d, J_{gem} -12.47, 1H, PhCH₂), 4.34 (d, J_{gem} -12.47, 1H, PhCH₂), 4.22 (dd, $J_{H1,H2}$ 3.18, 1H, H-2), 4.14 (dd, 1H, H-4), 3.79 (ddd, 1H, H-5), 3.58 (dd, 1H, H-3), 3.49 (2 dd, 2H, H-6b, H-6a); Residue **A**: 5.37 (s, 1H, CHPh), 4.68 (d, J_{gem} -12.38, 1H, PhCH₂), 4.42 (d, J_{gem} -12.38, 1H, PhCH₂), 4.37 (d, $J_{H1,H2}$ 3.55, 1H, H-1), 4.30 (dd, $J_{H2,H3}$ 9.19, $J_{H3,H4}$ 9.14, 1H, H-3), 4.15 (dd, 1H, H-6b), 3.77 (ddd, 1H, H-5), 3.52 (dd, $J_{H3,H4}$ 9.14, 1H, H-4), 3.52 (dd, 1H, H-6a), 3.42 (dd, $J_{H1,H2}$ 3.55, $J_{H2,H3}$ 9.19, 1H, H-2), 3.31 (s, 3H, OMe); 0.88, 0.87, 0.83, 0.70 (4 s, 36H, C(CH₃)₃), 0.13, 2 × 0.09, 0.04, 0.01, -0.02, -0.09, -0.22 (8 s, 24H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): δ 139.2, 138.5, 138.4, 137.8, 136.4, 133.4, 132.9 (7 C-*ipso*), 129.1, 2 × 128.5, 2 × 128.4, 5 × 128.3, 128.0, 127.9, 2 × 127.8, 5 × 127.6, 127.4, 127.3, 2 × 126.8, 126.0, 125.8, 125.7, 125.6 (27 C-Ar); Residue **B'**: 99.7 (C-1), 80.6 (C-4), 78.9 (C-5), 77.4 (C-2), 73.2 (PhCH₂), 71.4 (C-6), 70.8 (C-3); Residue **B**: 99.8 (C-1), 85.0 (C-3), 75.5 (C-2), 74.2 (C-5), 72.9 (PhCH₂), 71.0 (C-6), 70.9 (NapCH₂), 70.3 (C-4); Residue **A**: 102.1 (CHPh), 99.2 (C-1), 80.8 (C-4), 79.9 (C-2), 75.2 (C-3), 73.8 (PhCH₂), 69.2 (C-6), 62.6 (C-5), 55.3 (OMe); 26.2, 3 × 26.0 (4 C(CH₃)₃), 18.2, 2 × 18.1, 18.0 (4 C(CH₃)₃), -3.7, -3.8, -4.0, -4.3, -4.4, -4.6, -4.8, -5.0 (8 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₈₂H₁₂₀O₁₆Si₄Na 1495.7551, found 1495.7549.

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)[2,3,4-tri-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-4-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→3)]-4,6-*O*-benzylidene-α-D-glucopyranoside (P5c).

General procedure for Glycosylation: from Donor **D5** (50 mg) and acceptor **A3** (79 mg). The obtained product was purified by flash column chromatography (R_f = 0.45 Pentane/EtOAc 3:1) to yield tetrasaccharide **P5c** (41 mg) in 56% yield as a white powder. ^1H NMR (CDCl_3 , 25 °C, 400 MHz): δ 7.87-7.16 (m, 22H, H-Ar); Residue **B'**: 5.11 (d, $J_{\text{H1,H2}}$ 6.70, 1H, H-1), 4.64 (d, J_{gem} -11.76, 1H, PhCH_2), 4.55 (d, J_{gem} -11.76, 1H, PhCH_2), 4.10 (ddd, 1H, H-5), 3.92 (dd, 1H, H-3), 3.80 (dd, 1H, H-4), 3.69 (2 dd, 2H, H-6b, H-6a), 3.60 (dd, $J_{\text{H1,H2}}$ 6.70, 1H, H-2); Residue **B**: 5.23 (d, $J_{\text{H1,H2}}$ 1.91, 1H, H-1), 4.87 (d, J_{gem} -12.76, 1H, NapCH_2), 4.71 (d, J_{gem} -12.76, 1H, NapCH_2), 4.60 (d, J_{gem} -12.59, 1H, PhCH_2), 4.30 (d, J_{gem} -12.59, 1H, PhCH_2), 4.23 (dd, $J_{\text{H1,H2}}$ 1.91, 1H, H-2), 4.10 (dd, 1H, H-4), 3.91 (ddd, 1H, H-5), 3.51 (dd, 1H, H-3), 3.39 (2 dd, 2H, H-6b, H-6a); Residue **A**: 5.48 (s, 1H, CHPh), 4.71 (d, $J_{\text{H1,H2}}$ 3.67, 1H, H-1), 4.39 (dd, $J_{\text{H2,H3}}$ 9.07, $J_{\text{H3,H4}}$ 9.10, 1H, H-3), 4.21 (dd, 1H, H-6b), 3.89 (ddd, 1H, H-5), 3.69 (dd, 1H, H-6a), 3.48 (dd, $J_{\text{H1,H2}}$ 3.67, $J_{\text{H2,H3}}$ 9.07, 1H, H-2), 3.52 (dd, $J_{\text{H3,H4}}$ 9.10, 1H, H-4), 3.36 (s, 3H, OMe); Residue **A'**: 4.95 (dd, $J_{\text{H1,H2}}$ 7.83, $J_{\text{H2,H3}}$ 9.68, 1H, H-2), 4.93 (dd, $J_{\text{H3,H4}}$ 9.47, $J_{\text{H4,H5}}$ 9.88, 1H, H-4), 4.82 (dd, $J_{\text{H2,H3}}$ 9.68, $J_{\text{H3,H4}}$ 9.47, 1H, H-3), 4.17 (d, $J_{\text{H1,H2}}$ 7.83, 1H, H-1), 3.94 (2dd, 2H, H-6b, H-6a), 2.76 (ddd, $J_{\text{H4,H5}}$ 9.88, 1H, H-5), 2.17, 2.04, 1.96, 1.91 (4s, 12H, CH_3); 0.91, 0.87, 0.86, 0.59 (4 s, 36H, $\text{C}(\text{CH}_3)_3$), 2×0.09 , 0.08, 3×0.07 , -0.14, -0.42 (8 s, 24H, SiCH_3). ^{13}C NMR (CDCl_3 , 25 °C, 100 MHz): δ 139.2, 138.9, 137.7, 136.9, 133.4, 132.9 (6 C-*ipso*), 129.5, 2×128.5 , 3×128.4 , 3×128.3 , 4×127.9 , 3×127.7 , 127.5, 127.3, 2×127.1 , 126.3, 125.1 (22 C-Ar); Residue **B'**: 97.9 (C-1), 82.1 (C-5), 79.1 (C-4), 77.0 (C-2), 73.2 (PhCH_2), 71.9 (C-6), 70.6 (C-3); Residue **B**: 98.2 (C-1), 83.5 (C-3), 73.5 (C-5), 72.8 (PhCH_2), 72.4 (C-2), 71.3 (C-6), 70.6 (C-4), 69.5 (NapCH_2); Residue **A**: 102.9 (CHPh), 100.7 (C-1), 81.3 (C-2), 81.1 (C-4), 72.4 (C-3), 69.4 (C-6), 62.1 (C-5), 55.8 (OMe); Residue **A'**: 170.6, 170.1, 169.7, 169.4 (4 C=O), 101.0 (C-1), 73.0 (C-3), 71.1 (C-5), 71.0 (C-2), 68.5 (C-4), 61.4 (C-6), 21.7, 20.8, 2×20.7 (4 CH_3); 26.2, 26.0, 2×25.9 (4 $\text{C}(\text{CH}_3)_3$), 2×18.1 , 2×18.0 (4 $\text{C}(\text{CH}_3)_3$), -3.7, -4.0, -4.2, 2×-4.5 , -4.7, -4.8, -5.5 (8 SiCH_3). ESI-HRMS: $[\text{M} + \text{Na}]^+ m/z$ calc for $\text{C}_{89}\text{H}_{132}\text{O}_{25}\text{Si}_4\text{Na}$ 1735.8032, found 1735.8036.

Methyl 2,3,4-tri-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 2)-3,4-*O*-di-*tert*-butyldimethylsilyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 3)-4,6-*O*-benzylidene-2-*O*-benzyl- α -D-glucopyranoside (P6**).**

General procedure for Glycosylation: from Donor **D6** (50 mg) and acceptor **A2** (49 mg). The obtained product was purified by flash column chromatography (R_f = 0.45 Tol/EtOAc 12:1) to yield trisaccharide **P6** (64 mg) in 95% yield as a colorless oil. ^1H NMR (CDCl_3 , 25 °C, 400 MHz): δ 7.38-7.14 (m, 20H, H-Ar); Residue **B'**: 4.94 (d, $J_{\text{H1,H2}}$ 5.89, 1H, H-1), 4.28 (2d, 2H, PhCH_2), 3.95 (ddd, 1H, H-5), 3.90 (dd, 1H, H-3), 3.74 (dd, 1H, H-4), 3.62 (dd, $J_{\text{H1,H2}}$ 5.89, 1H, H-2), 3.56 (dd, 1H, H-6b), 3.42 (dd, 1H, H-6a); Residue **B**: 5.58 (d, $J_{\text{H1,H2}}$ 2.61, 1H, H-1), 4.57 (d, J_{gem} -12.82, 1H, PhCH_2), 4.45 (d, J_{gem} -12.82, 1H, PhCH_2), 3.96 (dd, $J_{\text{H1,H2}}$ 2.61, 1H, H-2), 3.88 (ddd, 1H, H-5), 3.82 (dd, 1H, H-3), 3.74 (dd, 1H, H-4), 3.42 (dd, 1H, H-6b), 3.28 (dd, 1H, H-6a); Residue **A**: 5.34 (s, 1H, CHPh), 4.85 (d, J_{gem} -12.73, 1H, PhCH_2), 4.47 (d, J_{gem} -12.73, 1H, PhCH_2), 4.37 (dd, $J_{\text{H2,H3}}$ 9.30, $J_{\text{H3,H4}}$ 9.15, 1H, H-3), 4.35 (d, $J_{\text{H1,H2}}$ 3.60, 1H, H-1), 4.14 (dd, $J_{\text{H5,H6b}}$ 4.71, J_{gem} -10.13, 1H, H-6b), 3.79 (ddd, $J_{\text{H5,H6b}}$ 4.71, 1H, H-5), 3.57 (dd, J_{gem} -10.13, 1H, H-6a), 3.42 (dd, $J_{\text{H1,H2}}$ 3.60, $J_{\text{H2,H3}}$ 9.30, 1H, H-2), 3.36 (dd, $J_{\text{H3,H4}}$ 9.15, 1H, H-4), 3.32 (s, 3H, OMe); 0.93, 2×0.87 , 0.86, 0.67 (5 s, 45H, $\text{C}(\text{CH}_3)_3$), 0.21, 0.10, 2×0.09 , 0.08, 2×0.03 , 0.001, -0.14, -0.53, (10 s, 30H, SiCH_3). ^{13}C NMR (CDCl_3 , 25 °C, 100 MHz): δ 139.2, 2×138.6 , 137.7 (4 C-*ipso*), 129.3, 128.6, 128.5, 3×128.3 , 4×128.2 , 127.9, 3×127.6 , 3×127.4 , 2×127.3 , 126.9 (20 C-Ar); Residue **B'**: 101.9 (C-1),

80.1 (C-5), 79.2 (C-4), 77.1 (C-2), 73.1 (PhCH₂), 71.4 (C-6), 70.6 (C-3); Residue **B**: 98.7 (C-1), 79.7 (C-2), 78.3 (C-3), 73.6 (C-5), 73.3 (C-4), 72.8 (PhCH₂), 72.0 (C-6); Residue **A**: 102.7 (CHPh), 99.2 (C-1), 80.9 (C-2), 80.6 (C-4), 73.6 (PhCH₂), 73.0 (C-3), 69.3 (C-6), 62.5 (C-5), 55.4 (OMe); 26.3, 26.1, 3 × 26.0 (5 C(CH₃)₃), 18.3, 18.1, 2 × 18.0, 17.9 (5 C(CH₃)₃), -2.6, -3.4, -3.5, -3.7, -3.8, -4.3, -4.4, -4.7, 2 × -4.8 (10 SiCH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₇₇H₁₂₆O₁₆Si₅Na 1469.7790, found 1469.7786.

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)[2,3,4-tri-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→2)-3-*O*-(2-naphthylmethyl)-4-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→3)]-4,6-*O*-benzylidene-α-D-glucopyranoside (8).

Compound **P5c** (75 mg) was dissolved in dry THF and a 1 M solution of TBAF in THF (15 eq) was added dropwise at room temperature. At completion, the mixture was taken into CH₂Cl₂ and washed with water. The organic phase was dried over Na₂SO₄, filtered and concentrated to dryness. The protected tetraol obtained was dissolved in dry Pyr (2 mL). Acetic anhydride (10 eq) and DMAP were added and the reaction was left to stir overnight. The reaction was stopped by adding a few drops of MeOH and the yellow oil was diluted with EtOAc and was washed with NaHCO₃, brine, 1 M HCl and brine before being dried over Na₂SO₄, filtered and concentrated. Purification by flash chromatography (R_f = 0.45 EtOAc/Petroleum ether 2:1) gave 57 mg of **8** as a white powder (92% yield over two steps). ¹H NMR (CDCl₃, 25 °C, 400 MHz): δ 7.87-7.20 (m, 22H, H-Ar); Residue **B'**: 5.21 (dd, *J*_{H2,H3} 9.69, *J*_{H3,H4} 9.28, 1H, H-3), 5.19 (dd, *J*_{H3,H4} 9.28, *J*_{H4,H5} 9.58, 1H, H-4), 5.06 (dd, *J*_{H1,H2} 7.81, *J*_{H2,H3} 9.69, 1H, H-2), 4.97 (d, *J*_{H1,H2} 7.81, 1H, H-1), 4.58 (d, *J*_{gem} -12.08, 1H, PhCH₂), 4.54 (d, *J*_{gem} -12.08, 1H, PhCH₂), 3.65 (ddd, *J*_{H4,H5} 9.58, 1H, H-5), 3.62 (dd, 1H, H-6b), 3.55 (dd, 1H, H-6a); Residue **B**: 5.03 (dd, *J*_{H3,H4} 9.30, *J*_{H4,H5} 9.79, 1H, H-4), 4.88 (d, *J*_{H1,H2} 7.34, 1H, H-1), 4.90 (d, *J*_{gem} -11.76, 1H, NapCH₂), 4.65 (d, *J*_{gem} -11.76, 1H, NapCH₂), 4.48 (d, *J*_{gem} -11.63, 1H, PhCH₂), 4.39 (d, *J*_{gem} -11.63, 1H, PhCH₂), 3.69 (dd, *J*_{H1,H2} 7.34, *J*_{H2,H3} 8.94, 1H, H-2), 3.63 (dd, *J*_{H2,H3} 8.94, *J*_{H3,H4} 9.30, 1H, H-3), 3.47 (2 dd, 2H, H-6b, H-6a), 3.35 (ddd, *J*_{H4,H5} 9.79, 1H, H-5); Residue **A**: 5.35 (s, 1H, CHPh), 4.84 (d, *J*_{H1,H2} 3.67, 1H, H-1), 4.36 (dd, *J*_{H2,H3} 9.07, *J*_{H3,H4} 9.30, 1H, H-3), 4.18 (dd, 1H, H-6b), 3.88 (dd, *J*_{H1,H2} 3.67, *J*_{H2,H3} 9.20, 1H, H-2), 3.79 (ddd, 1H, H-5), 3.54 (dd, *J*_{H3,H4} 9.30, 1H, H-4), 3.52 (dd, 1H, H-6a), 3.33 (s, 3H, OMe); Residue **A'**: 5.41 (dd, *J*_{H2,H3} 8.79, *J*_{H3,H4} 9.08, 1H, H-3), 5.12 (dd, *J*_{H3,H4} 9.08, *J*_{H4,H5} 10.06, 1H, H-4), 5.02 (dd, *J*_{H1,H2} 7.76, *J*_{H2,H3} 8.79, 1H, H-2), 4.97 (d, *J*_{H1,H2} 7.76, 1H, H-1), 4.19 (2dd, 2H, H-6b, H-6a), 3.80 (ddd, *J*_{H4,H5} 10.06, 1H, H-5); 2.11, 2.08, 2.06, 2.02, 1.99, 1.91, 1.87, 1.84 (8s, 24H, CH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): δ 170.6, 170.4, 170.3, 170.0, 2 × 169.7, 2 × 169.6 (8 C=O), 138.1, 137.8, 137.5, 135.7, 133.4, 133.0 (6 C-*ipso*), 128.9, 2 × 128.6, 2 × 128.4, 128.3, 2 × 128.2, 3 × 128.1, 2 × 128.0, 127.9, 2 × 127.7, 126.4, 2 × 126.3, 126.2, 126.0, 125.7 (22 C-Ar); Residue **B'**: 100.4 (C-1), 73.7 (PhCH₂), 73.5 (C-3), 73.5 (C-5), 72.5 (C-2), 69.0 (C-4), 68.4 (C-6); Residue **B**: 99.9 (C-1), 82.3 (C-3), 80.6 (C-2), 75.5 (NapCH₂), 73.9 (PhCH₂), 73.5 (C-5), 71.5 (C-4), 69.9 (C-6); Residue **A**: 101.4 (CHPh), 100.1 (C-1), 81.1 (C-2), 79.9 (C-4), 73.8 (C-3), 69.1 (C-6), 62.1 (C-5), 55.4 (OMe); Residue **A'**: 100.8 (C-1), 73.2 (C-3), 73.0 (C-2), 71.5 (C-5), 68.5 (C-4), 62.2 (C-6); 21.5, 2 × 20.9, 3 × 20.8, 2 × 20.7 (8 CH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₇₃H₈₄O₂₉Na 1447.1996, found 1447.2001.

Methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→2)[2,3,4-tri-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→2)-4-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1→3)]-α-D-glucopyranoside (9).

Compound **8** (50 mg) was dissolved at room temperature in a mixture of DCM/MeOH 4/1 and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 36 mg, 4.5 eq) was added whereafter the reaction mixture was stirred until completion, monitored by TLC (R_f = 0.45 Petroleum ether/EtOAc 1:5). Once complete, the reaction mixture was diluted with DCM and 1 mL of satd NaHCO_3 was added. The two phases were separated and the organic phase was washed three times with a solution of satd NaHCO_3 and then dried over Na_2SO_4 . The residue was purified by flash chromatography (R_f = 0.55 EtOAc/Petroleum ether 9:1) to yield compound **9** as a white solid in 85% yield (36 mg). ^1H NMR (CDCl_3 , 25 °C, 400 MHz): δ 7.38-7.27 (m, 10H, H-Ar); Residue **B'**: 5.20 (dd, $J_{\text{H}_2,\text{H}_3}$ 9.14, $J_{\text{H}_3,\text{H}_4}$ 9.38, 1H, H-3), 5.14 (dd, $J_{\text{H}_3,\text{H}_4}$ 9.38, $J_{\text{H}_4,\text{H}_5}$ 9.56, 1H, H-4), 5.06 (dd, $J_{\text{H}_1,\text{H}_2}$ 8.05, $J_{\text{H}_2,\text{H}_3}$ 9.14, 1H, H-2), 4.93 (d, $J_{\text{H}_1,\text{H}_2}$ 8.05, 1H, H-1), 4.56 (d, J_{gem} -12.33, 1H, PhCH_2), 4.51 (d, J_{gem} -12.33, 1H, PhCH_2), 3.71 (ddd, $J_{\text{H}_4,\text{H}_5}$ 9.56, 1H, H-5), 3.56 (dd, 1H, H-6b), 3.55 (dd, 1H, H-6a); Residue **B**: 4.94 (dd, $J_{\text{H}_3,\text{H}_4}$ 9.03, $J_{\text{H}_4,\text{H}_5}$ 9.62, 1H, H-4), 4.62 (d, $J_{\text{H}_1,\text{H}_2}$ 7.19, 1H, H-1), 4.54 (d, J_{gem} -11.88, 1H, PhCH_2), 4.47 (d, J_{gem} -11.88, 1H, PhCH_2), 3.66 (ddd, $J_{\text{H}_3,\text{H}_4}$ 9.03, $J_{\text{H}_3,\text{OH}_3}$ 3.45, 1H, H-3), 3.58 (dd, $J_{\text{H}_1,\text{H}_2}$ 7.19, 1H, H-2), 3.57 (ddd, $J_{\text{H}_4,\text{H}_5}$ 9.62, 1H, H-5), 3.56 (dd, 1H, H-6b), 3.55 (dd, 1H, H-6a), 3.11 (d, $J_{\text{H}_3,\text{OH}_3}$ 3.45, 1H, OH3); Residue **A**: 4.80 (d, $J_{\text{H}_1,\text{H}_2}$ 3.69, 1H, H-1), 3.95 (dd, $J_{\text{H}_2,\text{H}_3}$ 9.11, $J_{\text{H}_3,\text{H}_4}$ 9.20, 1H, H-3), 3.83 (br dd, 1H, H-6b), 3.75 (dd, 1H, H-6a), 3.72 (dd, $J_{\text{H}_1,\text{H}_2}$ 3.69, $J_{\text{H}_2,\text{H}_3}$ 9.11, 1H, H-2), 3.63 (ddd, $J_{\text{H}_4,\text{H}_5}$ 9.34, 1H, H-5), 3.48 (dd, $J_{\text{H}_3,\text{H}_4}$ 9.20, $J_{\text{H}_4,\text{H}_5}$ 9.34, 1H, H-4), 3.36 (s, 3H, OMe); Residue **A'**: 5.23 (dd, $J_{\text{H}_2,\text{H}_3}$ 9.08, $J_{\text{H}_3,\text{H}_4}$ 9.13, 1H, H-3), 5.10 (dd, $J_{\text{H}_3,\text{H}_4}$ 9.39, $J_{\text{H}_4,\text{H}_5}$ 9.90, 1H, H-4), 5.02 (dd, $J_{\text{H}_1,\text{H}_2}$ 7.83, $J_{\text{H}_2,\text{H}_3}$ 9.08, 1H, H-2), 4.97 (d, $J_{\text{H}_1,\text{H}_2}$ 7.83, 1H, H-1), 4.14 (dd, $J_{\text{H}_5,\text{H}_6\text{b}}$ 4.65, J_{gem} -12.37, 1H, H-6b), 4.09 (dd, $J_{\text{H}_5,\text{H}_6\text{a}}$ 2.65, J_{gem} -12.37, 1H, H-6a), 3.65 (ddd, $J_{\text{H}_5,\text{H}_6\text{a}}$ 2.65, $J_{\text{H}_5,\text{H}_6\text{b}}$ 4.65, $J_{\text{H}_4,\text{H}_5}$ 9.90, 1H, H-5); 2.07, 3 \times 2.04, 2 \times 1.99, 1.99, 1.90 (8s, 24H, CH_3). ^{13}C NMR (CDCl_3 , 25 °C, 100 MHz): δ 170.9, 170.6, 170.4, 170.2, 2 \times 169.7, 169.6, 169.5 (8 C=O), 137.6, 137.5 (2 C-*ipso*), 2 \times 128.7, 2 \times 128.6, 3 \times 128.1, 3 \times 128.0 (10 C-Ar); Residue **B'**: 101.7 (C-1), 73.6 (PhCH_2), 73.5 (C-5), 73.3 (C-3), 72.1 (C-2), 69.8 (C-4), 68.3 (C-6); Residue **B**: 99.4 (C-1), 82.4 (C-2), 74.8 (C-3), 73.6 (PhCH_2), 72.9 (C-5), 71.3 (C-4), 68.6 (C-6); Residue **A**: 99.5 (C-1), 80.8 (C-3), 78.1 (C-2), 70.5 (C-5), 69.4 (C-4), 63.0 (C-6), 55.4 (OMe); Residue **A'**: 100.6 (C-1), 73.3 (C-3), 72.0 (C-2), 71.5 (C-5), 68.5 (C-4), 62.2 (C-6); 21.3, 21.0, 2 \times 20.9, 2 \times 20.8, 2 \times 20.7 (8 CH_3). ESI-HRMS: $[\text{M} + \text{Na}]^+ m/z$ calc for $\text{C}_{55}\text{H}_{72}\text{O}_{29}\text{Na}$ 1219.4057, found 1219.4061.

Methyl 2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl-(1 \rightarrow 2)[2,3,4-tri-*O*-acetyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 2)-4-*O*-acetyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 3)]-6-*O*-tert-butyltrimethylsilyl- α -D-glucopyranoside (10).

Triol **9** (30 mg) was dissolved in dry DCM (2 mL), 2,6-lutidine (9 μL , 3 eq) was added and the solution was cooled down to -20 °C. TBDMSOTf (9 μL , 1.5 eq) was added dropwise at the same temperature under N_2 atmosphere and the mixture was stirred at room temperature overnight. The reaction was stopped by adding a few drops of MeOH and the oil was diluted with DCM and washed with 1 M HCl, brine, NaHCO_3 , and brine before being dried over Na_2SO_4 , filtered and concentrated. The product was purified by chromatography (TLC: R_f = 0.55 Petroleum ether/EtOAc 1:5) to afford diol acceptor **10** in 95% yield (31 mg) as a colorless oil. ^1H NMR (CDCl_3 , 25 °C, 400 MHz): δ 7.38-7.25 (m, 10H, H-Ar); Residue **B'**: 5.21 (dd, $J_{\text{H}_2,\text{H}_3}$ 9.17, $J_{\text{H}_3,\text{H}_4}$ 9.23, 1H, H-3), 5.14 (dd, $J_{\text{H}_3,\text{H}_4}$ 9.23, $J_{\text{H}_4,\text{H}_5}$ 9.45, 1H, H-4), 5.02 (dd, $J_{\text{H}_1,\text{H}_2}$ 8.10, $J_{\text{H}_2,\text{H}_3}$ 9.17, 1H, H-2), 4.92 (d, $J_{\text{H}_1,\text{H}_2}$ 8.10, 1H, H-1), 4.54 (d, J_{gem} -12.08, 1H, PhCH_2), 4.45 (d, J_{gem} -12.08, 1H, PhCH_2), 3.70 (ddd, $J_{\text{H}_4,\text{H}_5}$ 9.45, 1H, H-5), 3.54 (2 dd, 2H, H-6b, H-6a); Residue **B**: 4.94 (dd, $J_{\text{H}_3,\text{H}_4}$ 9.30, $J_{\text{H}_4,\text{H}_5}$ 9.79, 1H, H-4), 4.62 (d, $J_{\text{H}_1,\text{H}_2}$ 7.35, 1H, H-1), 4.58 (d, J_{gem} -11.63, 1H, PhCH_2), 4.49 (d, J_{gem} -11.63, 1H, PhCH_2), 3.66 (dd, 1H, H-3), 3.55 (dd, $J_{\text{H}_1,\text{H}_2}$ 7.35, 1H, H-2), 3.55 (2 dd, 2H, H-6b, H-6a), 3.55 (ddd,

1H, H-5), 3.07 (br d, 1H, OH-3); Residue A: 4.80 (d, $J_{H1,H2}$ 3.67, 1H, H-1), 3.97 (dd, $J_{H2,H3}$ 9.05, $J_{H3,H4}$ 9.14, 1H, H-3), 3.92 (dd, 1H, H-6b), 3.76 (dd, 1H, H-6a), 3.74 (dd, $J_{H1,H2}$ 3.67, $J_{H2,H3}$ 9.05, 1H, H-2), 3.59 (ddd, $J_{H4,H5}$ 9.27, 1H, H-5), 3.47 (br d, 1H, OH-4), 3.43 (dd, $J_{H3,H4}$ 9.14, $J_{H4,H5}$ 9.27, 1H, H-4), 3.35 (s, 3H, OMe); Residue A': 5.20 (dd, $J_{H2,H3}$ 9.22, $J_{H3,H4}$ 9.06, 1H, H-3), 5.08 (dd, $J_{H3,H4}$ 9.06, $J_{H4,H5}$ 9.94, 1H, H-4), 5.06 (dd, $J_{H1,H2}$ 7.77, $J_{H2,H3}$ 9.22, 1H, H-2), 4.94 (d, $J_{H1,H2}$ 7.77, 1H, H-1), 4.14 (dd, 1H, H-6b), 4.01 (dd, 1H, H-6a), 3.61 (ddd, $J_{H4,H5}$ 9.94, 1H, H-5); 2.06, 2.04, 2×2.03 , 3×1.99 , 1.89 (8s, 24H, CH₃), 0.91 (s, 9H, C(CH₃)₃), 2×0.08 (2s, 6H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 100 MHz): δ 170.7, 170.6, 170.4, 170.1, 2×169.7 , 169.5, 169.4 (8 C=O), 137.7, 137.5 (2 C-*ipso*), 2×128.7 , 2×128.5 , 3×128.0 , 3×127.9 (10 C-Ar); Residue B': 101.8 (C-1), 73.6 (PhCH₂), 73.5 (C-5), 73.4 (C-3), 72.0 (C-2), 68.7 (C-4), 68.7 (C-6); Residue B: 99.6 (C-1), 82.8 (C-2), 74.6 (C-3), 73.5 (PhCH₂), 72.9 (C-5), 71.2 (C-4), 68.3 (C-6); Residue A: 99.2 (C-1), 80.8 (C-3), 78.5 (C-2), 71.7 (C-5), 68.6 (C-4), 63.0 (C-6), 55.0 (OMe); Residue A': 100.6 (C-1), 73.4 (C-3), 72.1 (C-2), 71.5 (C-5), 68.5 (C-4), 62.3 (C-6); 26.1 (C(CH₃)₃), 21.4, 21.0, 20.9, 20.8, 4×20.7 (8 CH₃), 18.6 (C(CH₃)₃), 2×-5.1 (2 SiCH₃). ESI-HRMS: [M + Na]⁺ m/z calc for C₆₁H₈₆O₂₉SiNa 1333.4922, found 1333.4927.

Methyl 2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl-(1 \rightarrow 2)[2,3,4-tri-*O*-acetyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 2){2,3,4-tri-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 2)-3-*O*-(2-naphthylmethyl)-4-*O*-*tert*-butyldimethylsilyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 3)}-4-*O*-acetyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 3)]-6-*O*-*tert*-butyldimethylsilyl- α -D-glucopyranoside (11).

Donor **D5** (48 mg, 3 eq), diol acceptor **10** (18 mg, 1 eq), base DTBMP (4 eq) and NIS (1.2 eq) were dissolved in dry solvents, DCM/Tol 1:1, at room temperature and stirred with 4 Å molecular sieves under N₂ flow. The temperature was decreased to -60 °C and TfOH (1.0 μ L, cat amount) was added. The mixture was allowed to reach -30 °C and stirred for 30 min, while monitored by mass spectrometry analysis. The reaction was then quenched by the addition of NEt₃ (50 μ L). Once room temperature was reached, the mixture was filtered through a Celite pad and subsequently diluted into DCM. The resulting organic phase was washed with a 10% Na₂S₂O₃ solution and then with brine. The acquired mixture was dried over Na₂S₂O₄ after which solvents were evaporated. The obtained residue was purified by flash column chromatography (R_f = 0.45 Pentane/EtOAc 2:1) to yield hexasaccharide **11** (22 mg) in 65% yield as a white solid. ¹H NMR (CDCl₃, 25 °C, 600 MHz): δ 7.91-7.16 (m, 27H, H-Ar); Residue C': 5.15 (d, $J_{H1,H2}$ 5.96, 1H, H-1), 4.63 (d, J_{gem} -11.63, 1H, PhCH₂), 4.51 (d, J_{gem} -11.63, 1H, PhCH₂), 4.10 (ddd, 1H, H-5), 3.98 (dd, 1H, H-3), 3.79 (dd, 1H, H-4), 3.72 (dd, 1H, H-6b), 3.68 (dd, 1H, H-6a), 3.62 (dd, $J_{H1,H2}$ 5.96, 1H, H-2); Residue C: 5.05 (d, $J_{H1,H2}$ 1.92, 1H, H-1), 5.21 (d, J_{gem} -12.79, 1H, NapCH₂), 4.63 (d, J_{gem} -12.79, 1H, NapCH₂), 4.60 (d, J_{gem} -12.00, 1H, PhCH₂), 4.50 (d, J_{gem} -12.00, 1H, PhCH₂), 4.31 (dd, $J_{H1,H2}$ 1.92, 1H, H-2), 4.20 (dd, $J_{H4,H5}$ 10.51, 1H, H-4), 3.85 (ddd, $J_{H4,H5}$ 10.51, $J_{H5,H6a}$ 6.21, 1H, H-5), 3.71 (dd, 1H, H-3), 3.65 (dd, 1H, H-6b), 3.54 (dd, $J_{H5,H6a}$ 6.21, 1H, H-6a); Residue B': 5.02 (dd, $J_{H1,H2}$ 7.81, $J_{H2,H3}$ 9.31, 1H, H-2), 4.96 (dd, $J_{H3,H4}$ 9.80, $J_{H4,H5}$ 9.86, 1H, H-4), 4.67 (d, $J_{H1,H2}$ 7.89, 1H, H-1), 4.62 (dd, $J_{H2,H3}$ 9.31, $J_{H3,H4}$ 9.80, 1H, H-3), 4.54 (d, J_{gem} -12.30, 1H, PhCH₂), 4.19 (d, J_{gem} -12.30, 1H, PhCH₂), 3.05 (dd, $J_{H5,H6b}$ 3.03, J_{gem} -10.90, 1H, H-6b), 2.72 (dd, $J_{H5,H6a}$ 2.25, J_{gem} -10.90, 1H, H-6a), 2.58 (ddd, $J_{H4,H5}$ 9.86, $J_{H5,H6a}$ 2.25, $J_{H5,H6b}$ 3.03, 1H, H-5); Residue B: 4.93 (dd, 1H, H-4), 4.40 (d, $J_{H1,H2}$ 7.35, 1H, H-1), 4.40 (d, J_{gem} -11.55, 1H, PhCH₂), 4.34 (d, J_{gem} -11.55, 1H, PhCH₂), 3.75 (dd, 1H, H-3), 3.70 (dd, $J_{H1,H2}$ 7.35, 1H, H-2), 3.47 (dd, 1H, H-6b), 3.38 (ddd, 1H, H-5), 3.37 (dd, 1H, H-6a); Residue A: 4.78 (d, $J_{H1,H2}$ 3.86, 1H, H-1), 3.97 (dd, 1H, H-6b), 3.81 (dd, $J_{H2,H3}$ 8.99, $J_{H3,H4}$ 9.10, 1H, H-3),

3.77 (dd, $J_{H5,H6b}$ 1.82, 1H, H-6a), 3.70 (dd, $J_{H1,H2}$ 3.86, $J_{H2,H3}$ 8.99, 1H, H-2), 3.59 (ddd, $J_{H5,H6b}$ 1.82, 1H, H-5), 3.36 (dd, $J_{H3,H4}$ 9.10, 1H, H-4), 3.34 (s, 3H, OMe); Residue A': 5.22 (dd, $J_{H2,H3}$ 9.34, $J_{H3,H4}$ 9.22, 1H, H-3), 5.08 (dd, $J_{H3,H4}$ 9.22, $J_{H4,H5}$ 9.77, 1H, H-4), 5.04 (dd, $J_{H1,H2}$ 7.82, $J_{H2,H3}$ 9.34, 1H, H-2), 4.94 (d, $J_{H1,H2}$ 7.82, 1H, H-1), 4.14 (dd, $J_{H5,H6b}$ 4.49, J_{gem} -12.29, 1H, H-6b), 3.94 (dd, $J_{H5,H6a}$ 2.07, J_{gem} -12.29, 1H, H-6a), 3.80 (ddd, $J_{H4,H5}$ 9.77, $J_{H5,H6a}$ 2.07, $J_{H5,H6b}$ 4.49, 1H, H-5); 2.09, 1.99, 1.98, 2×1.95 , 1.94, 1.85, 1.63 (8s, 24H, CH₃), 0.92, 0.88, 0.86, 0.84, 0.73 (5 s, 45H, C(CH₃)₃), 2×0.10 , 2×0.09 , 0.08, 0.06, 0.04, 0.03, 0.01, -0.04 (10 s, 30H, SiCH₃). ¹³C NMR (CDCl₃, 25 °C, 176 MHz): δ 170.7, 170.4, 170.3, 170.0, 169.7, 169.6, 169.3, 169.0 (8 C=O), 138.9, 138.6, 138.1, 137.6, 136.1, 133.4, 132.8 (7 C-*ipso*), 2×128.5 , 6×128.4 , 128.3, 2×128.2 , 128.1, 2×128.0 , 127.9, 2×127.7 , 3×127.6 , 2×127.5 , 127.4, 126.1, 125.7, 124.7, 124.5 (27 C-Ar); Residue C': 98.7 (C-1), 80.5 (C-5), 78.8 (C-4), 77.6 (C-2), 73.2 (PhCH₂), 71.1 (C-6), 70.5 (C-3); Residue C: 99.9 (C-1), 82.8 (C-3), 73.8 (C-2), 73.3 (C-5), 72.7 (PhCH₂), 70.6 (NapCH₂), 70.5 (C-4), 70.2 (C-6); Residue B': 100.9 (C-1), 73.9 (C-3), 73.5 (PhCH₂), 72.7 (C-2), 71.6 (C-5), 68.0 (C-4), 67.1 (C-6); Residue B: 100.3 (C-1), 82.4 (C-3), 80.4 (C-2), 73.7 (C-5), 73.6 (PhCH₂), 71.5 (C-4), 70.2 (C-6); Residue A: 99.7 (C-1), 81.2 (C-3), 77.8 (C-2), 71.7 (C-5), 69.0 (C-4), 63.2 (C-6), 55.1 (OMe); Residue A': 100.4 (C-1), 73.7 (C-3), 71.8 (C-2), 71.0 (C-5), 68.9 (C-4), 62.2 (C-6); 26.2, 26.1, 26.0, 2×25.9 (5 C(CH₃)₃), 21.3, 21.2, 21.0, 3×20.8 , 20.7, 20.6 (8 CH₃), 18.6, 2×18.1 , 18.0, 17.9 (5 C(CH₃)₃), -3.7, 2×-4.0 , -4.3, -4.4, 2×-4.8 , -4.9, 2×-5.0 (10 SiCH₃). ESI-HRMS: $[M + Na]^+$ m/z calc for C₁₂₂H₁₈₂O₃₉Si₅Na 2434.1002, found 2434.0996.

Methyl 2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl-(1 \rightarrow 2)[2,3,4-tri-*O*-acetyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 2){2,3,4-tri-*O*-acetyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 2)-3-*O*-(2-naphthylmethyl)-4-*O*-acetyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 3)}-4-*O*-acetyl-6-*O*-benzyl- β -D-glucopyranosyl-(1 \rightarrow 3)]-4,6-di-*O*-acetyl- α -D-glucopyranoside (12).

Compound **11** (22 mg) was dissolved in dry THF and a 1 M solution of TBAF in THF (15 eq) was added dropwise at room temperature. At completion, the mixture was taken into CH₂Cl₂ and washed with water. The organic phase was dried over Na₂SO₄, filtered and concentrated to dryness. The protected tetraol obtained was dissolved in dry Pyr (2 mL). Acetic anhydride (10 eq) and DMAP were added and the reaction was left to stir overnight. The reaction was stopped by adding a few drops of MeOH and the yellow oil was diluted with EtOAc and was washed with NaHCO₃, brine, 1 M HCl and brine before being dried over Na₂SO₄, filtered and concentrated. Purification by flash chromatography (R_f = 0.50 EtOAc/Petroleum ether 5:1) gave 15 mg of **12** as a white powder (79% yield over two steps). ¹H NMR (CDCl₃, 25 °C, 600 MHz): δ 7.91-7.13 (m, 27H, H-Ar); Residue C': 5.13 (dd, 1H, H-3), 5.13 (dd, 1H, H-4), 5.10 (dd, $J_{H1,H2}$ 7.73, 1H, H-2), 4.88 (d, $J_{H1,H2}$ 7.73, 1H, H-1), 4.57 (d, J_{gem} -12.22, 1H, PhCH₂), 4.47 (d, J_{gem} -12.22, 1H, PhCH₂), 3.60 (ddd, 1H, H-5), 3.56 (dd, 1H, H-6b), 3.49 (dd, 1H, H-6a); Residue C: 5.01 (dd, 1H, H-4), 4.98 (d, J_{gem} -11.98, 1H, NapCH₂), 4.76 (d, $J_{H1,H2}$ 7.57, 1H, H-1), 4.68 (d, J_{gem} -11.98, 1H, NapCH₂), 4.42 (d, J_{gem} -12.03, 1H, PhCH₂), 4.38 (d, J_{gem} -12.03, 1H, PhCH₂), 3.71 (dd, 1H, H-3), 3.60 (dd, $J_{H1,H2}$ 7.57, 1H, H-2), 3.36 (2 dd, 2H, H-6b, H-6a), 3.35 (ddd, 1H, H-5); Residue B': 5.43 (dd, $J_{H3,H4}$ 9.32, $J_{H4,H5}$ 9.53, 1H, H-4), 5.35 (dd, $J_{H2,H3}$ 9.21, $J_{H3,H4}$ 9.32, 1H, H-3), 5.21 (d, $J_{H1,H2}$ 7.93, 1H, H-1), 5.11 (dd, $J_{H1,H2}$ 7.93, $J_{H2,H3}$ 9.21, 1H, H-2), 4.81 (d, J_{gem} -11.81, 1H, PhCH₂), 4.56 (d, J_{gem} -11.81, 1H, PhCH₂), 3.93 (ddd, 1H, H-5), 3.83 (dd, 1H, H-6b), 3.74 (dd, 1H, H-6a); Residue B: 5.01 (dd, 1H, H-4), 4.47 (d, J_{gem} -11.95, 1H, PhCH₂), 4.43 (d, $J_{H1,H2}$ 7.56, 1H, H-1), 4.42 (d, J_{gem} -11.95, 1H, PhCH₂), 3.93 (dd, $J_{H1,H2}$ 7.35, 1H, H-2), 3.86 (dd, 1H, H-3), 3.58 (dd, 1H, H-6b), 3.46 (dd, 1H, H-6a), 3.41 (ddd, 1H, H-5); Residue A: 4.85 (d, $J_{H1,H2}$ 3.67, 1H, H-1), 4.82 (dd, 1H, H-4), 4.05 (dd,

1H, H-3), 4.04 (dd, 1H, H-6b), 3.98 (dd, 1H, H-6a), 3.87 (ddd, 1H, H-5), 3.82 (dd, $J_{H1,H2}$ 3.69, 1H, H-2), 3.37 (s, 3H, OMe); Residue A': 5.43 (dd, $J_{H2,H3}$ 9.56, $J_{H3,H4}$ 9.62, 1H, H-3), 5.14 (dd, $J_{H3,H4}$ 9.62, 1H, H-4), 5.00 (dd, $J_{H1,H2}$ 7.75, $J_{H2,H3}$ 9.56, 1H, H-2), 4.86 (d, $J_{H1,H2}$ 7.75, 1H, H-1), 4.32 (dd, $J_{H5,H6b}$ 4.19, J_{gem} -12.22, 1H, H-6b), 4.17 (dd, $J_{H5,H6a}$ 1.87, J_{gem} -12.22, 1H, H-6a), 3.99 (ddd, $J_{H5,H6a}$ 1.87, $J_{H5,H6b}$ 4.19, 1H, H-5); 2.11, 2.08, 2.07, 2.04, 1.99, 1.95, 1.94, 1.93, 1.91, 1.88, 1.84, 1.78, 1.75, 1.58 (14s, 42H, CH₃). ¹³C NMR (CDCl₃, 25 °C, 150 MHz): δ 2 × 170.8, 170.4, 2 × 170.3, 169.9, 2 × 169.8, 2 × 169.7, 2 × 169.5, 169.4, 169.3 (14 C=O), 138.3, 138.1, 138.0, 137.6, 135.7, 133.4, 133.1 (7 C-*ipso*), 8 × 128.5, 5 × 128.4, 2 × 128.3, 2 × 128.0, 3 × 127.9, 2 × 127.8, 127.7, 126.7, 126.3, 2 × 126.1 (27 C-Ar); Residue C': 102.3 (C-1), 74.0 (C-3), 73.8 (C-5), 73.2 (PhCH₂), 72.6 (C-2), 69.0 (C-4), 67.8 (C-6); Residue C: 100.1 (C-1), 81.7 (C-3), 81.7 (C-2), 75.6 (NapCH₂), 73.6 (C-5), 73.6 (PhCH₂), 71.1 (C-4), 69.4 (C-6); Residue B': 98.8 (C-1), 74.3 (C-3), 74.0 (PhCH₂), 73.0 (C-5), 72.8 (C-2), 69.1 (C-4), 68.5 (C-6); Residue B: 100.4 (C-1), 78.7 (C-3), 78.2 (C-2), 73.6 (PhCH₂), 72.9 (C-5), 69.1 (C-6), 68.9 (C-4); Residue A: 100.0 (C-1), 79.4 (C-2), 75.4 (C-3), 68.9 (C-4), 66.8 (C-5), 63.3 (C-6), 55.7 (OMe); Residue A': 100.2 (C-1), 73.6 (C-3), 73.1 (C-2), 71.2 (C-5), 68.3 (C-4), 61.8 (C-6); 2 × 21.3, 2 × 21.0, 3 × 20.9, 3 × 20.8, 2 × 20.8, 20.7, 20.6 (14 CH₃). ESI-HRMS: [M + Na]⁺ *m/z* calc for C₁₀₄H₁₂₄O₄₅Na 2115.7312, found 2115.7319.

Methyl β-D-glucopyranosyl-(1→2)[6-O-benzyl-β-D-glucopyranosyl-(1→2){6-O-benzyl-β-D-glucopyranosyl-(1→2)-3-O-(2-naphthylmethyl)-6-O-benzyl-β-D-glucopyranosyl-(1→3)}-6-O-benzyl-β-D-glucopyranosyl-(1→3)]-α-D-glucopyranoside (13).

General procedure for *O*-deacylation: 2 eq per *O*-acyl group to be cleaved using a 1 M solution of NaOMe in MeOH were added. Starting from compound 12 (21 mg) the procedure yielded, after purification on Sep-Pak[®] t-C18 using a H₂O/ACN solvents gradient from 100:0 to 0:100, compound 13 (TLC: R_f = 0.75 EtOAc/MeOH/H₂O 7:2:1) in 82% yield (12 mg) as a colorless syrup. ¹H NMR (CD₃OD, 25 °C, 700 MHz): δ 7.91-7.13 (m, 27H, H-Ar); Residue C': 4.81 (d, $J_{H1,H2}$ 7.92, 1H, H-1), 4.61 (d, J_{gem} -12.15, 1H, PhCH₂), 4.53 (d, J_{gem} -12.15, 1H, PhCH₂), 3.76 (dd, 1H, H-6b), 3.62 (dd, 1H, H-6a), 3.44 (dd, $J_{H1,H2}$ 7.73, 1H, H-2), 3.31 (m, 3H, H-3, H-4, H-5); Residue C: 5.14 (br s, 2H, NapCH₂), 5.01 (d, $J_{H1,H2}$ 7.61, 1H, H-1), 4.56 (br s, 2H, PhCH₂), 3.83 (dd, 1H, H-3), 3.82 (dd, 1H, H-6b), 3.76 (dd, $J_{H1,H2}$ 7.61, 1H, H-2), 3.66 (dd, 1H, H-6a), 3.66 (dd, 1H, H-4), 3.60 (ddd, 1H, H-5); Residue B': 4.98 (d, $J_{H1,H2}$ 7.94, 1H, H-1), 4.63 (br s, 2H, PhCH₂), 3.75 (dd, 1H, H-6b), 3.65 (dd, 1H, H-6a), 3.54 (dd, 1H, H-3), 3.48 (ddd, 1H, H-5), 3.45 (dd, $J_{H1,H2}$ 7.94, 1H, H-2), 3.41 (dd, 1H, H-4); Residue B: 4.86 (d, $J_{H1,H2}$ 7.76, 1H, H-1), 4.51 (br s, 2H, PhCH₂), 3.87 (dd, $J_{H2,H3}$ 8.74, $J_{H3,H4}$ 8.84, 1H, H-3), 3.81 (dd, $J_{H1,H2}$ 7.76, $J_{H2,H3}$ 8.74, 1H, H-2), 3.74 (dd, 1H, H-6b), 3.47 (ddd, 1H, H-5), 3.46 (dd, 1H, H-6a), 3.30 (dd, $J_{H3,H4}$ 8.84, 1H, H-4); Residue A: 4.87 (d, $J_{H1,H2}$ 3.43, 1H, H-1), 3.94 (dd, $J_{H2,H3}$ 9.04, $J_{H3,H4}$ 9.35, 1H, H-3), 3.82 (dd, 1H, H-6b), 3.80 (dd, $J_{H1,H2}$ 3.43, $J_{H2,H3}$ 9.04, 1H, H-2), 3.57 (dd, $J_{H3,H4}$ 9.35, 1H, H-4), 3.54 (dd, 1H, H-6a), 3.39 (s, 3H, OMe), 3.32 (ddd, 1H, H-5); Residue A': 4.72 (d, $J_{H1,H2}$ 7.84, 1H, H-1), 3.75 (dd, 1H, H-6b), 3.66 (dd, 1H, H-6a), 3.47 (dd, $J_{H2,H3}$ 9.35, 1H, H-3), 3.34 (dd, 1H, H-4), 3.29 (ddd, 1H, H-5), 3.24 (dd, $J_{H1,H2}$ 7.84, $J_{H2,H3}$ 9.35, 1H, H-2). ¹³C NMR (CD₃OD, 25 °C, 176 MHz): δ 2 × 139.9, 139.5, 139.4, 137.7, 134.8, 134.5 (7 C-*ipso*), 2 × 129.5, 6 × 129.4, 7 × 129.0, 2 × 128.9, 128.8, 128.7, 3 × 128.6, 128.5, 128.0, 127.7, 126.9, 126.8 (27 C-Ar); Residue C': 104.7 (C-1), 78.2 (C-3), 77.8 (C-5), 75.2 (C-2), 74.9 (PhCH₂), 71.9 (C-4), 70.9 (C-6); Residue C: 101.5 (C-1), 86.2 (C-3), 80.8 (C-2), 76.5 (C-5), 75.9 (NapCH₂), 74.6 (PhCH₂), 72.7 (C-4), 70.5 (C-6); Residue B': 104.1 (C-1), 77.7 (C-3), 77.3 (C-5), 75.7 (C-2), 74.8 (PhCH₂), 72.2 (C-4), 70.6 (C-6); Residue B: 101.9 (C-1), 85.6 (C-3), 80.3 (C-2), 76.3 (C-5), 74.5 (PhCH₂), 70.6 (C-6), 70.3 (C-4); Residue A: 100.8 (C-1), 81.2 (C-3), 79.9 (C-2),

73.2 (C-4), 70.3 (C-5), 63.0 (C-6), 55.3 (OMe); Residue A': 104.6 (C-1), 77.8 (C-3), 77.8 (C-5), 75.6 (C-2), 71.6 (C-4), 62.6 (C-6). ESI-HRMS: $[M + Na]^+$ m/z calc for $C_{76}H_{96}O_{31}Na$ 1527.5833, found 1527.5829.

Methyl β -D-glucopyranosyl-(1 \rightarrow 2)[β -D-glucopyranosyl-(1 \rightarrow 2){ β -D-glucopyranosyl-(1 \rightarrow 2)- β -D-glucopyranosyl-(1 \rightarrow 3)}- β -D-glucopyranosyl-(1 \rightarrow 3)]- α -D-glucopyranoside (14).

Compound **13** (8 mg, 5.32 μ mol) was dissolved in MeOH (1.5 mL) and 10 – 20% Pd/C catalyst (15 mg) was added in a small pierced vial, which was left to stir overnight at room temperature under 10 atmospheres of H_2 . Once TLC analysis indicated full conversion (R_f = 0.2 EtOAc/MeOH/ H_2O /AcOH 13:3:3:1), the mixture was filtered through a Celite pad, washed with water and concentrated to dryness. Purification by Sep-Pak[®] t-C18 using a H_2O /ACN solvents gradient from 100:0 to 90:10, followed with an ÄKTA[™] system equipped with a Superdex[™] column gave 4 mg of compound **14** as a white powder (73%). 1H and ^{13}C NMR data: see Table 3. ESI-HRMS: $[M + Na]^+$ m/z calc. for $C_{37}H_{64}O_{31}Na$ 1027.3329, found 1027.3326.

Conformational analysis

For conformational analysis, NMR samples of donors **D1** – **D6** as well as products **P3b** and **P4** were prepared by dissolving 5 – 10 mg of the compounds in $CDCl_3$ with the addition of TMS as an internal reference. Accurate 1H NMR chemical shifts and $^nJ_{HH}$ coupling constants were determined with the aid of PERCH NMR spin-simulation software (PERCH Solutions Ltd., Kuopio, Finland). In this approach we utilize 1D 1H NMR spectra processed with an applied Gaussian function for resolution enhancement as input. Chemical shifts and couplings were altered iteratively until a simulated and the experimental spectra appeared most similar according to visual inspection and the total root-mean-square value was below 0.1%; $^2J_{HH}$ and $^4J_{HH}$ were assumed to have negative signs.

Three-dimensional models of the studied compounds as different canonical conformers were built with CarbBuilder⁴⁴ as an add-in to the CASPER software⁴⁵ and subsequent modifications were made using the VEGA ZZ software.⁴⁶ The molecular structures were subsequently energy minimized using algorithms implemented in the VEGA ZZ software in consecutive order: (i) steepest descent, (ii) conjugate gradient and (iii) truncated Newton. For all modeled conformers, the ring-defining $^3J_{HH}$ (H1-H2, H2-H3, H3-H4 and H4-H5) were calculated with the generalized Haasnoot-Altona equation,³⁴ including β -effects, as implemented in the MSpin software.⁴⁷

Calculations of the weighted population distributions of the ring conformational states were performed using the Solver function in Microsoft Excel[®] together with the calculated coupling constants of canonical representations of different conformers. Based on $^3J_{HH}$ values the root-mean-square deviation (RMSD) was minimized employing the general reducing agent algorithm³⁵ by altering the populations of the conformational states of the sugar rings. Three-state models were generally assumed and all such possibilities for pyranoid and β -D-glucose ring interconversion pathways according to Stoddart³⁶ and Mayes et al.,³³ respectively, were tested. The models and population distributions therefrom, with the lowest average RMSD, were regarded as the most probable population distributions. The determined populations were estimated to be accurate to within 5%.

ASSOCIATED CONTENT

Supporting Information: Molecular models, Table of NMR data related to conformational analysis, ^1H and ^{13}C NMR spectra of synthesized compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interests.

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