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

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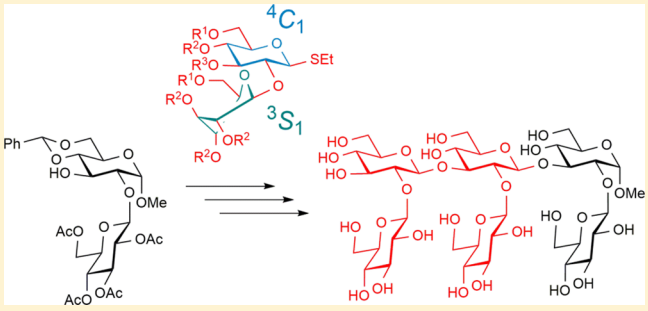
Supporting Information

ABSTRACT: To advance the field of glycobiology, efficient synthesis methods of oligosaccharides and glycoconjugates are a requisite. In glycosylation reactions using superarmed 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 extents. The acceptors in reactions being secondary alcohols presents a challenging situation with respect to steric crowding. Conformational pyranose ring equilibria of the superarmed disaccharide donors with axial-rich substituents contained skew and boat conformations, and three-state models were generally assumed. With NIS/TfOH as the promotor, 2,6-di-*tert*-butyl-4-methylpyridine as the 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 °C to the hydroxyl group at position 3 of glucopyranosyl acceptors to form β-(1 → 2),β-(1 → 3)-linked trisaccharides, isolated in excellent 95% yield. The more axial-rich donors in skew and boat conformations are thus preorganized closer to the assumed transition state in these glycosylation reactions. The developed methodology was subsequently applied in the synthesis of a multibranched hexasaccharide related to the capsular polysaccharide from *Streptococcus pneumoniae* type 37, which consists of a β-(1 → 3)-linked backbone and a β-(1 → 2)-linked side chain of D-glucosyl residues in disaccharide repeating units.



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 mammalians, including pathogenicity, not intervened by carbohydrates.[4] The advancement of efficient protocols for the synthesis of these molecules is therefore of great importance. Chemical synthesis in general, and carbohydrate synthesis in particular, requires 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 involves multistep 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 concept[15] to comprise superarmed glycosyl donors.[16] In subsequent studies, various 1-thioglycoside donors were investigated, showing a 20-fold reactivity enhancement[17] (Scheme 1b) and more recently a 100-fold higher reactivity[18] compared to those of non-axial-rich analogues. Conformationally superarmed ethyl thioglycosyl donors have also been used in the one-pot synthesis of trisaccharides.[19] Furthermore, for

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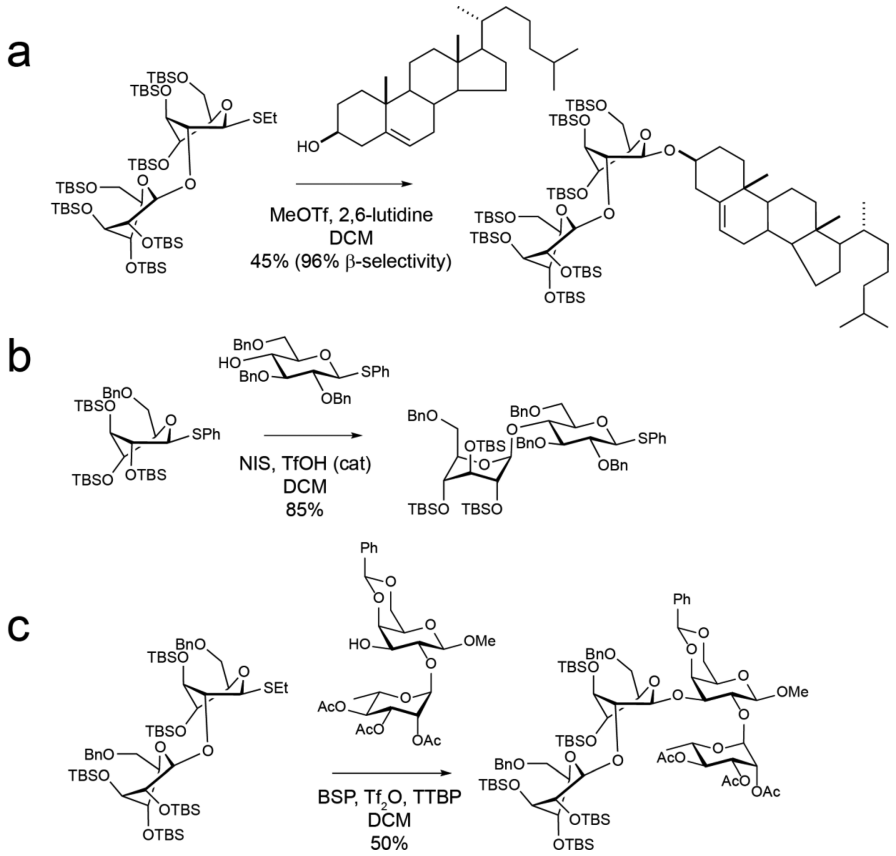
Scheme 1. Examples of Axial-Rich Donors with the Purposes of Attaining Stereoselectivity (a), Enhanced Reactivity (b), or Stereoselectivity as Well as Enhanced Reactivity (c) by the Work of Yamada and Co-Workers, Bols and Co-Workers, and Angles d'Ortoli and Widmalm, Respectively[12,13,23]



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-Glc*p*-(1 → 2)-D-Glc*p*-(1 → 3)-*α*-D-Glc*p*-OMe,[10] a structural arrangement that we will refer to as (1 → 2),(1 → 3)-linked trisaccharides. In targeting tetra- and pentasaccharides containing *β*-D-Glc*p* residues at these types of linkages, glucosyl monosaccharide donors were employed.[22]

To utilize disaccharides efficiently in such syntheses, very potent donors would be necessary. We recently showed that by employing a superarmed 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 superarmed disaccharide donors and exploring their scope in glycosylation reactions, we herein show that not only excellent selectivity in the formation of *β*-linked trisaccharide products[11] but also excellent yields for challenging situations, in which the hydroxyl group is attached to a secondary carbon atom, can be obtained. 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

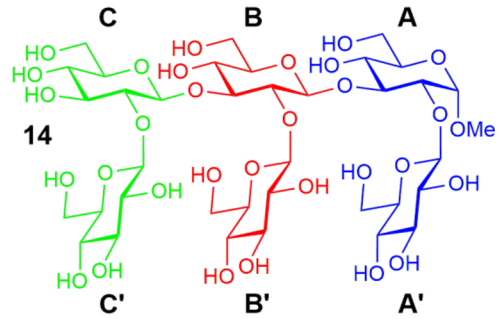


Figure 1. Schematic of a glucosyl-containing hexasaccharide (**14**) corresponding to three repeating units of the CPS from *S. pneumoniae* type 37. The oligosaccharide is colored to highlight its repetitive disaccharide structural elements. The sugar residues are denoted by capital letters in the *β*-(1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

Streptococcus pneumoniae type 37 and the exopolysaccharide from *Propionibacterium freudenreichii* ssp. *shermanii* JS.[24,25]

RESULTS AND DISCUSSION

Synthesis of Glycosyl Donors. The synthesis of armed donors D1, D3, and D5 (Scheme 2) having a 2-naphthylmethyl (NAP or just naphthyl) group[26] 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 h[27] 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

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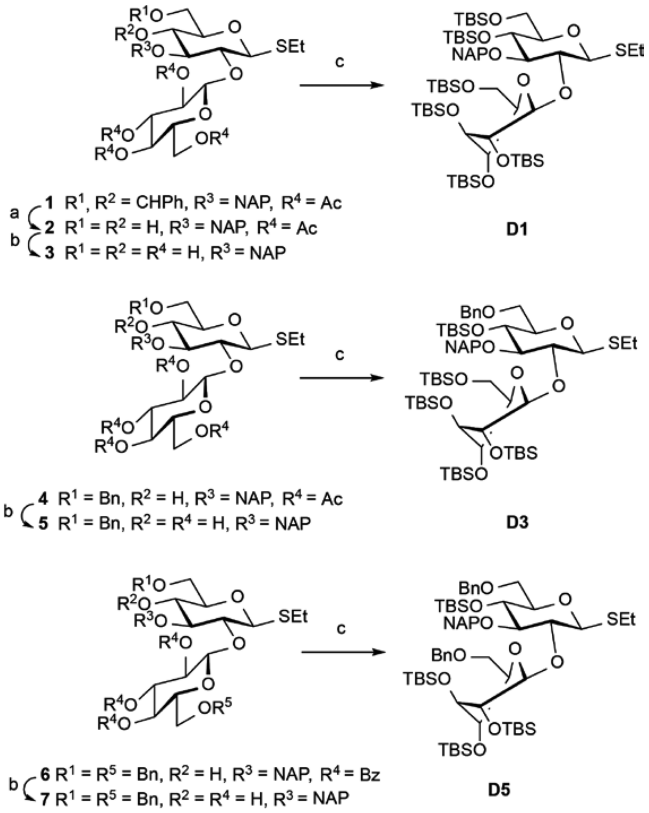
Scheme 2. Synthesis of Armed Donors D1, D3, and D5[a]



[a]Reagents and conditions: (a) 80% AcOH(aq), 80 °C, 4 h, 82%; (b) 1 M NaOMe, MeOH, 16 h, 90–92%; (c) (TBDMS)OTf, DMAP, Pyr, 80 °C, 24 h, 85–88%.

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-(dimethylamino)pyridine (DMAP), were dissolved in pyridine; (TBDMS)OTf was added at 0 °C, and the mixture was stirred overnight at 80 °C. Fully protected superarmed donors D1, D3, and D5 were isolated after flash column chromatography in 85–88% yield. The syntheses of the superarmed donors D2, D4, and D6 have been described previously.[11,23] In total, six donors, D1–D6, armed to different extents (Figure 2a), are thus available for subsequent glycosylation reactions.

Conformational Analysis of Glycosyl Donors. The differently functionalized β-(1 → 2)-linked disaccharide donors D1–D6 all have *tert*-butyldimethylsilyl (TBS) substituents, 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, an even bulkier protecting group, viz., a *tert*-butyldiphenylsilyl (TBDPS) group, at O3 and at O4 is required.[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*-glycosylated[12] (Scheme 1a) and 6-*O*-benzylated[12,14] (Scheme 1b) derivatives of 1-thio-β-D-glucose.

To this end, we set out to investigate how various types of protective groups would affect the conformation and consequently the reactivity of 1-thio-β-D-glucosyl donors. The introduction of an NAP group, orthogonal to silyl and benzyl ethers as well as to ester protective groups, would enable selective deprotection. It is known that glycosylation with an axial-rich donor equipped with an acid-labile group at position 6 at the reducing end (e.g., D1 and D2 in Figure 2a) could afford internally cyclized byproducts, viz., 1,6-anhydrohexopyranose derivatives.[14] The exchange for a more robust protective group, such as a benzyl ether, has been shown to prevent this byproduct formation,[14] and such 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 extents (Figure S1, Supporting Information). 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, ^{1}H resonances were assigned using 1D and 2D NMR experiments suitable for carbohydrates,[31] and the chemical shifts and scalar coupling constants were refined by NMR spin simulation using an iterative total-line-shape analysis approach (Figure S2 and Table S1, Supporting Information).[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 puckers[33] were energy minimized, and with the generalized Haasnoot–Altona equation,[34] their ring-defining $^3J_{HH}$ couplings were calculated. These computed $^3J_{HH}$ 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 $^4J_{HH}$ couplings were observed for the H2–H4 and H3–H5 proton pairs, typically being around −1 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 between each other for itineraries on the conformational sphere as described for β-D-glucose by Mayes et al.[33]

The results of the conformational analysis indicated interconversion pathways somewhat extending from the geometry itineraries of cyclohexane proposed by Stoddart[36] 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, $^3S_1 \rightleftharpoons {}^{3,O}B \rightleftharpoons {}^1S_5$, was considered. Upon benzylation at the O6 position, as in D5 and D6, a slight shift toward a higher population of $^{3,O}B$ was observed. Conformational changes were also investigated by analysis of $^3J_{HS,H6}$ coupling constants for the terminal residue

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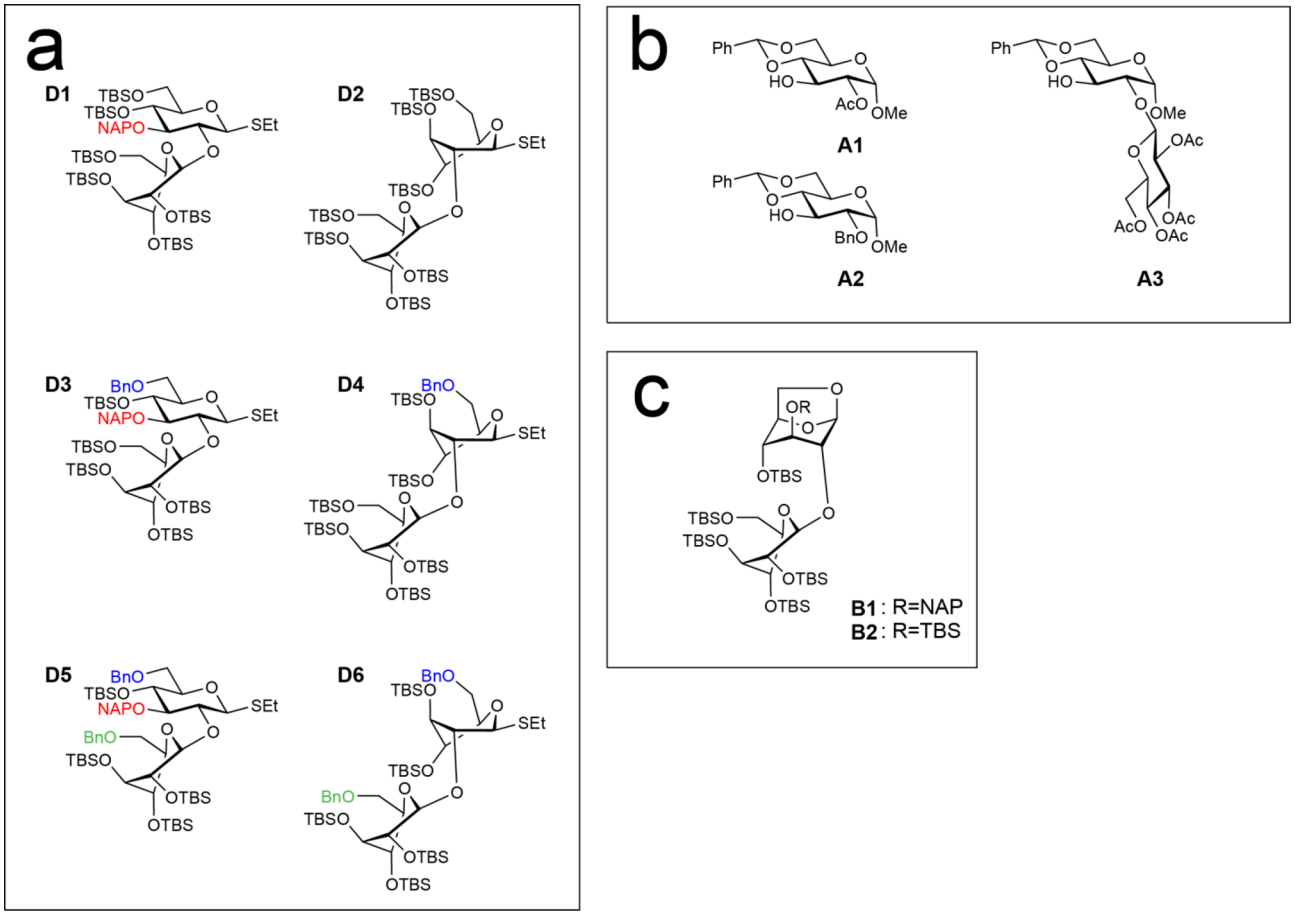

Figure 2. Disaccharide donors (a) and acceptors (b) used to investigate reactivity in glycosylation reactions and isolated byproducts (c).

Table 1. Populations (%) of Donors D1–D6 and Products P3b and P4 at 25 °C in $CDCl_3$

(a) Populations of D1–D6

	residue B′				residue B							
	$^1S_5$	$^{3,O}B$	$^3S_1$	RMSD	$^4C_1$	$^3S_1$	$^1C_4$	RMSD	$^1S_5$	$^{3,O}B$	$^3S_1$	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) Populations of P3b and P4

	residue B′				residue B				residue A	
	$^4C_1$	$^3S_1$	$^1C_4$	RMSD	$^4C_1$	$^1S_5$	$^1C_4$	RMSD	$^4C_1$	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

B′, which in D4 had $^3J_{H5,H6pro\text{-}R}$ = 5.63 Hz and $^3J_{H5,H6pro\text{-}S}$ = 8.15 Hz; in D6, these were $^3J_{H5,H6pro\text{-}R}$ = 6.30 Hz and $^3J_{H5,H6pro\text{-}S}$ = 6.34 Hz. On the basis of 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 the rotamer distributions 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.

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

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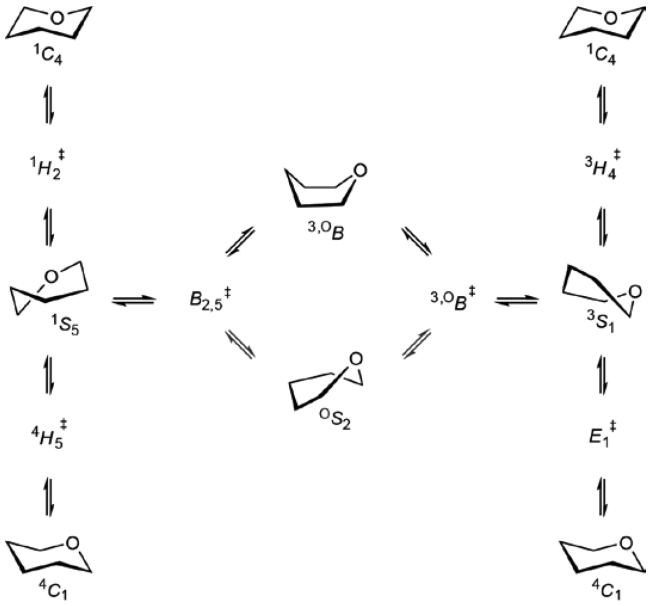
Scheme 3. Selected Ring Conformational Interconversion Pathways of β-D-Glucose Adapted from Beckham and Co-workers,[33] Including Local Minima and Transition States between Them[a]



[a]Only the pyranoid ring is shown for simplicity.

equilibrium, also involving 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 $^3S_1 \rightleftharpoons {}^{3,O}B \rightleftharpoons {}^1S_5$ 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 ^{1}H NMR temperature dependence was conducted for donor D4 at temperatures between −30 and +25 °C (Figure S3, Supporting Information). 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 kinds 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 byproducts 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 the base in DCM as such, only resulted in trace amounts of trisaccharide product P1 with the major formation of compound B2. It is to be noted that 1,6-anhydro byproduct 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 an 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 byproduct formation; it was consequently chosen in further optimizations. The reactions were all monitored by MS analyses, which revealed that cleavages 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).

The subsequent glycosylations with donors D3−D6 were performed using the improved conditions stated by entry 9 in Table 2, though the reaction temperature was set to −60 °C to increase the solubility of the acceptors (A1 and A3 in particular) in the toluene-containing solvent mixture. These changes had limited or no effect on the 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 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 acceptor A2, whereafter product P5b was isolated in a good yield of 75%.

In the previous synthesis of a β-(1 → 2),β-(1 → 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 B′, 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 superarmed 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 the C3 atom of a glucose residue becoming glycosyloxylated in the present case.

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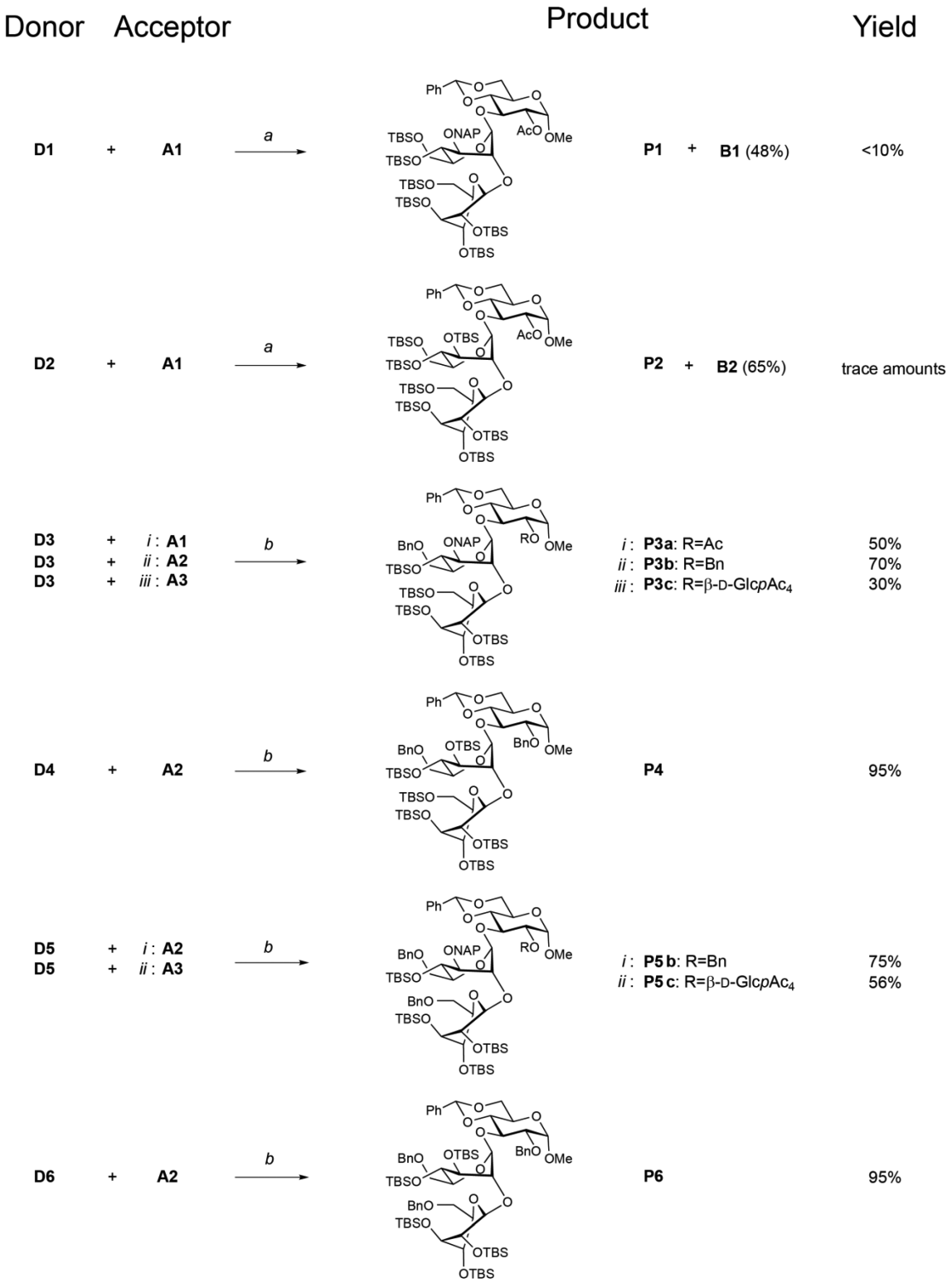
Scheme 4. Glycosylation Reactions Using Different Donors and Acceptors, Showing the Products Formed and the Respective Yields[a]



[a]Reagents and conditions: (a) NIS, TfOH, 4 Å molecular sieves, DCM; (b) NIS, TfOH, DTBMP, 4 Å molecular sieves, DCM/Tol (1:1).

Tetrasaccharides. The highly *O*-acetylated, disarmed, and 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.

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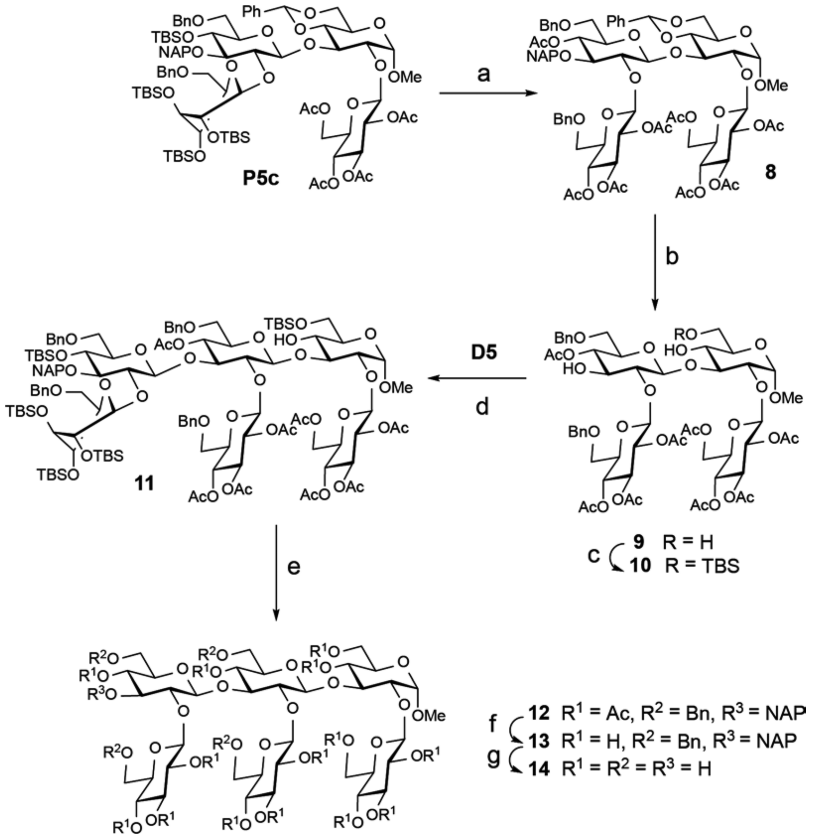
Table 2. Glycosylation of D4 with A2[a]

entry	activator	amt of TfO^-/Tf_2O	base	solvent	activation temp (°C)	yield (%)	yield of byproducts i:ii[b] (%)
1	MeOTf	cat	2,6-lutidine	CH_2Cl_2	−78 → rt	trace	major:minor
2	NIS/AgOTf	cat	2,6-lutidine	CH_2Cl_2	−78	25	minor:major
3	NIS/(TMS)OTf	cat	2,6-lutidine	CH_2Cl_2	−78	20	minor:major
4	NIS/TfOH	cat	2,6-lutidine	CH_2Cl_2	−78	25	minor:major
5	Tf_2O−DMDS	1.1 equiv	DTBMP	CH_2Cl_2	−78	29	major:minor
6	Tf_2O−DPSO	1.25 equiv	TTBP	CH_2Cl_2	−78	17	minor:51
7	Tf_2O−BSP	1.25 equiv	TTBP	CH_2Cl_2	−78	20	minor:48
8	NIS/TfOH	cat	DTBMP	CH_2Cl_2	−78	40	minor:55
9	NIS/TfOH	cat	DTBMP	CH_2Cl_2/Tol (1:1)	−78 → − 40	95	trace:trace

[a]DMDS = dimethyl disulfide, DPSO = diphenyl sulfoxide, BSP = benzenesulfinylpiperidine, DTBMP = 2,6-di-*tert*-butyl-4-methylpyridine, and TTBP = 2,4,6-tri-*tert*-butylpyrimidine. [b]i and ii refer to hydrolysis or elimination byproducts and de-*O*-silylated byproducts, respectively. Entries devoid of values infer byproduct detected with MS, otherwise isolated yield.

Scheme 5. Formation of Hexasaccharide 14[a]



[a]Reagents and conditions: (a) (i) 1 M TBAF, THF, 5 h, (ii) Ac_2O, DMAP, Pyr, 16 h, 92% over two steps; (b) DDQ, DCM/MeOH (4:1), 8 h, 85%; (c) (TBDMS)OTf, 2,6-lutidine, DCM, − 20 °C → rt, 16 h, 95%; (d) NIS, TfOH, DTBMP, DCM/Tol (1:1), − 60 °C → − 30 °C, 2 h, 65%; (e) (i) 1 M TBAF, THF, 5 h, (ii) Ac_2O, DMAP, Pyr, 16 h, 79% over two steps; (f) 1 M NaOMe, MeOH, 16 h, 82%; (g) 10−20% Pd/C, H_2 (10 atm), MeOH, 16 h, 73%.

All glycosylation reactions gave excellent anomeric selectivity for the formation of the β-(1 → 3)-linkages as would be expected from the work of Yamada and co-workers[11] (vide supra). Indeed, no or only supposedly trace amounts of oligosaccharides having the α-configuration at this glycosidic linkage could be observed in ^{1}H NMR spectra of isolated products. In the earlier synthesis of the tetrasaccharide corresponding to compound P5c, a β-(1 → 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 $^3S_1$ conformation for the reacting residues, thus implying a slight conformational arming effect (Table 1a). This reasoning is supported by the substantial intramolecular byproduct 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

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Table 3. ^{1}H and ^{13}C NMR Chemical Shifts (ppm) and $^{n}J_{HH}$ and $^{1}J_{H1,C1}$ (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] $H6_{pro\text{-}R}$. [b] $H6_{pro\text{-}S}$. [c] $^{1}J_{H1,C1}$ at 21 °C. [d] $^{2}J_{HH}$. [e] OMe: δ_H 3.402, δ_C 55.46.

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′ still adopted mainly a $^{3}S_1$ conformation but now in equilibrium with the $^{1}C_4$ chair conformation. Residue B populates mainly a $^{1}S_5$ conformation, also for P3b, bearing a less bulky naphthyl group. The conformationally constrained residue A resided in the expected $^{4}C_1$ chair conformation. ^{1}H 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 implies 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 hemisphere,[33] and the energy penalty for leaving the low-energy well of the $^{4}C_1$ 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 the $^{4}C_1$ conformation, but the small presence of $^{3}S_1$ 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 those of D2, D4, and D6 may thus be explained by the altered level of conformational preorganization.

Synthesis of a Multibranched Hexasaccharide and Comparison to Polysaccharide NMR Data. 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 tetrol was *O*-acetylated using acetic anhydride (Ac_2O) in pyridine in the 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*-silylated[39] at −20 °C using *tert*-butyldimethylsilyl trifluoromethanesulfonate ((TBDMS)OTf) 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. Sugars were dissolved as described above in a mixture of dry DCM/Tol (1:1); the reagents and reaction temperature employed were the same as for the formation of tetrasaccharides. The regioselective glycosylation was accomplished using 3 equiv 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

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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 lending 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

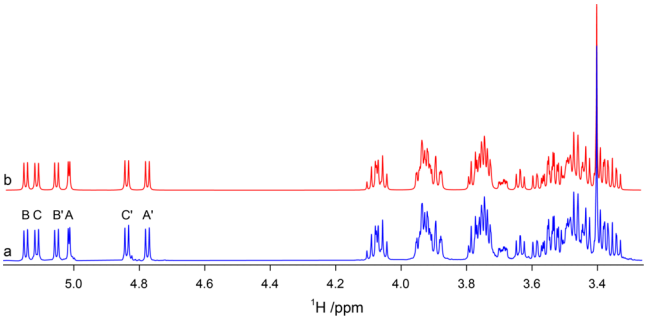

Figure 3. ^1H NMR spectrum at 700 MHz of hexasaccharide **14** at 9 °C (a) and the corresponding spectrum simulated by total-line-shape analysis using the PERCH NMR software (b). The HDO resonance in the experimental spectrum (δ_H 4.93) was removed prior to the line-shape fitting procedure. Anomeric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

the repeating units of the capsular polysaccharide (CPS) from *S. pneumoniae* type 37 and the repeating units of the extracellular polysaccharide (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 pentasaccharide[22] 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 the NMR data; consequently, the local environment at B and B′ residues should represent the 3D structure of the polysaccharide.

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 the CPS and EPS with β-(1 → 2)-linked side chains and a β-(1 → 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.

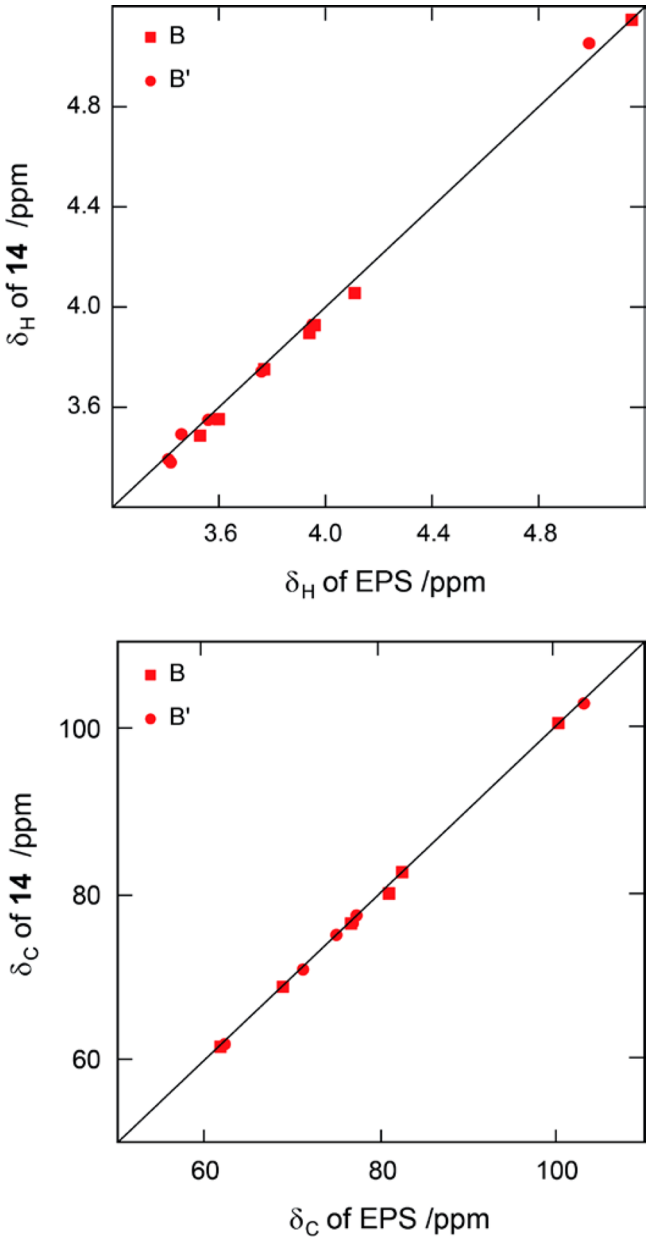

Figure 4. Comparison of ^1H and ^{13}C NMR chemical shifts (top and bottom, respectively) between residues B and B′ from hexasaccharide **14** and the EPS from *P. freudenreichii* ssp. *shermanii* JS,[25] which has the same polysaccharide structure as that of the CPS from *S. pneumoniae* type 37.[24]

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

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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 preorganized close to the anticipated transition states in the glycosylation reactions. The structures and the corresponding structure−reactivity information obtained in this study of superarmed 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). Dry *N*,*N*-dimethylformamide (DMF) was purchased from Acros Organics (New Jersey) and used as received. Pyridine (Pyr) was distilled over CaH_2 and dried with molecular sieves (4 Å). Methanol (MeOH) was dried over molecular sieves (4 Å). All reagents were used as received. A nitrogen gas flow was used for reactions requiring an 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 F_{254} 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 ^{1}H frequencies of 400, 500, 600, or 700 MHz. The NMR chemical shifts (δ) are reported in parts per million and referenced to TMS as an internal standard, δ_H = 0.0, or the residual solvent peaks for $CDCl_3$, δ_H = 7.26, or MeOH-d_4, δ_H = 3.31. ^{13}C chemical shifts were referenced to external 1,4-dioxane in D_2O, δ_C = 67.40, or internally to the $CDCl_3$ residual solvent peak, δ_C = 77.16, or to the MeOH-d_4-residual solvent peak, δ_C = 49.00. *J* coupling constants are reported in hertz. All new compounds synthesized were fully characterized using 1D ^{1}H, 1D ^{1}H-decoupled ^{13}C, 2D ^{1}H,^{1}H DQF-COSY, 2D ^{1}H,^{13}C multiplicity-edited HSQC, and 2D ^{1}H,^{13}C HMBC NMR experiments. If required, 1D ^{1}H,^{1}H TOCSY, 1D ^{1}H,^{1}H NOESY, 2D ^{1}H,^{1}H TOCSY, 2D ^{1}H,^{13}C H2BC, 2D ^{13}C,^{1}H HETCOR, and 2D ^{1}H,^{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 mg·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 doublets), q (quadruplet), dt (doublet of triplets), dq (doublet of quadruplets), ddd (doublet of doublets of doublets), m (multiplet). Of the two protons constituting the hydroxylmethyl 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 mM), and NaOMe in MeOH was added (2 equiv per acyl group using a 1 M solution). 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 the 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 ∼0.03 mM, and DMAP (0.2 equiv) was added to the mixture, whereafter 3 mol equiv of (TBDMS)OTf per alcohol group to be protected was added dropwise at 0 °C. The reaction mixture was heated to 80 °C and stirred overnight, after which it was allowed 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 a colorless syrup.

General Procedure for Glycosylation. The donor (50 mg, *y* mmol), acceptor (3 equiv), and base DTBMP (1.5 equiv) were dissolved in dry solvents (DCM/Tol, 1:1) at room temperature to a concentration of ∼0.04 mM with respect to the donor, and the solution was stirred with 4 Å molecular sieves under a N_2 flow. The temperature was decreased to −60 °C, and NIS (1.2 equiv), previously dissolved in dry DCM, was added. TfOH (1.5 μL, cat amount) was subsequently added at the same temperature. The mixture was allowed to reach −30 °C and stirred for 30 min while being monitored by mass spectrometry analysis. The reaction was then quenched by the addition of NEt_3 (50 μL). 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% $Na_2S_2O_3$ solution and then with brine. The acquired mixture was dried over $Na_2S_2O_4$, after which the 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 → 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 °C for 4 h and monitored by TLC (R_f = 0.6, Tol/EtOAc, 1:4). At completion, the mixture was allowed to reach room temperature, and then the reaction was quenched by NEt_3 (0.5 mL). The solvents were evaporated and coevaporated with toluene. The product was purified by flash chromatography to yield the desired product **2**, 220 mg (82% yield), as a colorless oil. ^{1}H NMR ($CDCl_3$, 25 °C, 400 MHz): δ (residue B) 7.95−7.44 (m, 7H, H−Ar), 5.05 (d, J_{gem} −11.05, 1H, NapCH_2), 4.90 (d, J_{gem} −11.05, 1H, NapCH_2), 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, SCH_2CH$_3$), 1.27 (t, 3H, SCH$_2$CH_3); (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, CH_3). ^{13}C NMR ($CDCl_3$, 25 °C, 100 MHz): δ (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 (NapCH_2), 71.2 (C-4), 62.4 (C-6), 24.1 (SCH_2CH$_3$), 14.7 (SCH$_2$CH_3); (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 CH_3). ESI-HRMS: $[M + Na]^+$ *m*/*z* calcd for $C_{33}H_{42}O_{14}SNa$ 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 equiv per *O*-acyl group to be cleaved using a 1 M solution of NaOMe in MeOH was 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. ^{1}H NMR (CD_3OD, 25 °C, 400 MHz): δ (residue B) 7.99−7.42 (m, 7H, H−Ar), 5.12 (s, 2H, NapCH_2), 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, SCH_2CH$_3$), 1.27 (t, 3H, SCH$_2$CH_3); (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,

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$J_{H5,H6b}$ 2.49, 1H, H-5). ^{13}C NMR (CD_3OD, 25 °C, 100 MHz): δ (residue B) 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 ($NapCH_2$), 72.3 (C-4), 62.8 (C-6), 24.4 (SCH_2CH_3), 14.9 (SCH_2CH_3); (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* calcd for $C_{25}H_{34}O_{10}SNa$ 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 hexol **3** (92 mg) were slowly added DMAP (0.2 equiv) and (TBDMS)OTf (3 equiv per alcohol group to be protected) at 0 °C under a N_2 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. ^{1}H NMR ($CDCl_3$, 25 °C, 400 MHz): δ (residue B) 7.84−7.13 (m, 7H, H−Ar), 5.25 (d, J_{gem} −11.81, 1H, $NapCH_2$), 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, SCH_2CH_3), 1.26 (t, 3H, SCH_2CH_3); (residue B′) 5.25 (d, $J_{H1,H2}$ 5.95, 1H, H-1), 3.81 (ddd, $J_{H4,H5}$ 1.70, 1H, H-5), 3.80 (dd, J_{gem} −9.94, 1H, H-6b), 3.80 (dd, $J_{H3,H4}$ 3.47, $J_{H4,H5}$ 1.70, 1H, H-4), 3.72 (dd, J_{gem} −9.94, 1H, H-6a), 3.66 (dd, $J_{H2,H3}$ 0.58, $J_{H3,H4}$ 3.47, 1H, H-3), 3.62 (dd, $J_{H1,H2}$ 5.95, $J_{H2,H3}$ 0.58, 1H, H-2); 0.92, 0.90, 0.84, 0.83, 0.80, 0.78 (6 s, 54H, $C(CH_3)_3$), 0.11, 0.10, 0.08, 0.06, 3 × 0.02, 0.01, 2 × −0.02, −0.03, −0.10 (12 s, 36H, $SiCH_3$). ^{13}C NMR ($CDCl_3$, 25 °C, 100 MHz): δ (residue B) 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 ($NapCH_2$), 63.7 (C-6), 25.1 (SCH_2CH_3), 15.7 (SCH_2CH_3); (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 $C(CH_3)_3$), 2 × 18.6, 2 × 18.2, 2 × 17.9 (6 $C(CH_3)_3$), −2.9, −3.0, −3.1, −3.5, 3 × −3.6, −3.9, −4.0, −4.1, −4.2, −4.4 (12 $SiCH_3$). ESI-HRMS: $[M + Na]^+$ *m*/*z* calcd for $C_{61}H_{118}O_{10}SSi_6Na$ 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 equiv per *O*-acyl group to be cleaved using a 1 M solution of NaOMe in MeOH was 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-glucopyranoside (**4**)[23] (250 mg) yielded compound **5** (R_f = 0.45, DCM/MeOH, 9:1) in 92% yield (181 mg) as a colorless syrup. ^{1}H NMR (CD_3OD, 25 °C, 400 MHz): δ (residue B) 7.99−7.23 (m, 12H, H−Ar), 5.12 (s, 2H, $NapCH_2$), 4.59 (s, 2H, $PhCH_2$), 4.54 (d, $J_{H1,H2}$ 9.46, 1H, H-1), 3.84 (dd, $J_{H5,H6b}$ 1.95, J_{gem} −11.10, 1H, H-6b), 3.80 (dd, $J_{H1,H2}$ 9.46, $J_{H2,H3}$ 8.78, 1H, H-2), 3.73 (dd, $J_{H2,H3}$ 8.78, $J_{H3,H4}$ 8.60, 1H, H-3), 3.67 (dd, $J_{H5,H6a}$ 5.83, J_{gem} −11.10, 1H, H-6a), 3.59 (dd, $J_{H3,H4}$ 8.60, $J_{H4,H5}$ 9.94, 1H, H-4), 3.50 (ddd, $J_{H4,H5}$ 9.94, $J_{H5,H6a}$ 5.83, $J_{H5,H6b}$ 1.95, 1H, H-5), 2.74 (2q, 2H, SCH_2CH_3), 1.27 (t, 3H, SCH_2CH_3); (residue B′) 4.85 (d, 1H, H-1), 3.81 (dd, $J_{H5,H6b}$ 2.56, J_{gem} −11.82, 1H, H-6b), 3.64 (dd, $J_{H5,H6a}$ 5.81, J_{gem} −11.82, 1H, H-6a), 3.32−3.28 (m, 3H, H-3, H-4, H-2), 3.12 (ddd, $J_{H4,H5}$ 8.86, $J_{H5,H6a}$ 5.81, $J_{H5,H6b}$ 2.56, 1H, H-5). ^{13}C NMR (CD_3OD, 25 °C, 100 MHz): δ (residue B) 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 ($NapCH_2$), 74.4 ($PhCH_2$), 72.4 (C-4), 70.8 (C-6), 24.6 (SCH_2CH_3), 15.2 (SCH_2CH_3); (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* calcd for $C_{32}H_{40}O_{10}SNa$ 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 pentol **5** (85 mg) were slowly added DMAP (0.2 equiv) and (TBDMS)OTf (3 equiv per alcool group to be protected) at 0 °C under a N_2 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. ^{1}H NMR ($CDCl_3$, 25 °C, 400 MHz): δ (residue B) 7.82−7.24 (m, 12H, H−Ar), 5.23 (d, J_{gem} −11.44, 1H, $NapCH_2$), 4.76 (d, J_{gem} −11.44, 1H, $NapCH_2$), 4.76 (d, $J_{H1,H2}$ 8.92, 1H, H-1), 4.65 (d, J_{gem} −12.20, 1H, $PhCH_2$), 4.52 (d, J_{gem} −12.20, 1H, $PhCH_2$), 4.01 (dd, $J_{H1,H2}$ 8.92, $J_{H2,H3}$ 7.73, 1H, H-2), 3.82 (dd, $J_{H2,H3}$ 7.73, $J_{H3,H4}$ 8.18, 1H, H-3), 3.77 (dd, J_{gem} −10.47, 1H, H-6b), 3.69 (dd, $J_{H3,H4}$ 8.18, $J_{H4,H5}$ 9.46, 1H, H-4), 3.57 (dd, J_{gem} −10.47, 1H, H-6a), 3.57 (ddd, $J_{H4,H5}$ 9.46, 1H, H-5), 2.76 (q, 2H, SCH_2CH_3), 1.30 (t, 3H, SCH_2CH_3); (residue B′) 5.24 (d, $J_{H1,H2}$ 6.00, 1H, H-1), 3.81 (dd, $J_{H3,H4}$ 3.40, $J_{H4,H5}$ 1.55, 1H, H-4), 3.81 (ddd, $J_{H4,H5}$ 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, $J_{H2,H3}$ 0.54, $J_{H3,H4}$ 3.40, 1H, H-3), 3.63 (dd, $J_{H1,H2}$ 6.00, $J_{H2,H3}$ 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): δ (residue B) 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 ($NapCH_2$), 73.4 ($PhCH_2$), 71.4 (C-4), 70.1 (C-6), 24.6 (SCH_2CH_3), 15.0 (SCH_2CH_3); (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* calcd for $C_{62}H_{110}O_{10}SSi_5Na$ 1209.6564, found 1209.6567.

Ethyl 6-*O*-Benzyl-β-D-glucopyranosyl-(1 → 2)-3-*O*-(2-naphthylmethyl)-6-*O*-benzyl-1-thio-β-D-glucopyranoside (7). General procedure for *O*-deacylation: 2 equiv per acyl group to be cleaved using a 1 M solution of NaOMe in MeOH was added. Starting from ethyl 2,3,4-tri-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranosyl-(1 → 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. ^{1}H NMR (CD_3OD, 25 °C, 400 MHz): δ 8.00−7.17 (m, 17H, H−Ar); (residue B) 5.12 (s, 2H, $NapCH_2$), 4.59 (s, 2H, $PhCH_2$), 4.53 (d, $J_{H1,H2}$ 9.45, 1H, H-1), 3.84 (dd, $J_{H5,H6b}$ 1.93, J_{gem} −11.11, 1H, H-6b), 3.80 (dd, $J_{H1,H2}$ 9.45, $J_{H2,H3}$ 8.74, 1H, H-2), 3.74 (dd, $J_{H2,H3}$ 8.74, $J_{H3,H4}$ 8.57, 1H, H-3), 3.67 (dd, $J_{H5,H6a}$ 5.93, J_{gem} −11.11, 1H, H-6a), 3.58 (dd, $J_{H3,H4}$ 8.57, $J_{H4,H5}$ 9.88, 1H, H-4), 3.49 (ddd, $J_{H4,H5}$ 9.88, $J_{H5,H6a}$ 5.93, $J_{H5,H6b}$ 1.93, 1H, H-5), 2.71 (2q, 2H, SCH_2CH_3), 1.22 (t, 3H, SCH_2CH_3); (residue B′) 4.88 (d, 1H, H-1), 4.60 (2d, J_{gem} −11.97, 2H, PhCH2), 3.81 (dd, $J_{H5,H6b}$ 2.00, J_{gem} −11.29, 1H, H-6b), 3.64 (dd, $J_{H5,H6a}$ 5.93, J_{gem} −11.29, 1H, H-6a), 3.36−3.29 (m, 3H, H-3, H-4, H-2), 3.23 (ddd, $J_{H4,H5}$ 9.31, $J_{H5,H6a}$ 5.93, $J_{H5,H6b}$ 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 ($NapCH_2$), 74.4 ($PhCH_2$), 72.4 (C-4), 70.8 (C-6), 24.5 (SCH_2CH_3), 15.3 (SCH_2CH_3); (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* calcd 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 → 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 tetrol 7 (105 mg) were slowly added DMAP (0.2 equiv) and (TBDMS)OTf (3 equiv per alcohol group to be protected) at 0 °C under a N_2 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. ^{1}H 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, $NapCH_2$), 4.77 (d, J_{gem} −11.89, 1H, $NapCH_2$), 4.70 (d, $J_{H1,H2}$ 9.02, 1H, H-1), 4.64 (d, J_{gem} −12.16, 1H, $PhCH_2$), 4.53 (d, J_{gem} −12.16, 1H, $PhCH_2$), 4.00 (dd, $J_{H1,H2}$ 9.02, $J_{H2,H3}$ 7.98, 1H, H-2), 3.78 (dd, $J_{H2,H3}$ 7.98, $J_{H3,H4}$ 8.23, 1H, H-3), 3.76 (dd, J_{gem} −10.60, 1H, H-6b), 3.66 (dd, $J_{H3,H4}$ 8.23, $J_{H4,H5}$ 9.50, 1H, H-4), 3.57 (dd, J_{gem} −10.60, 1H, H-6a), 3.53 (ddd, $J_{H4,H5}$ 9.50, 1H, H-5), 2.75 (2q, 2H, SCH_2CH_3), 1.30 (t, 3H, SCH_2CH_3); (residue B′) 5.24 (d, $J_{H1,H2}$ 5.43, 1H, H-1), 4.65 (d, J_{gem} −12.08, 1H, $PhCH_2$), 4.55 (d, J_{gem} −12.08, 1H, $PhCH_2$), 3.99 (ddd, $J_{H4,H5}$ 2.95, 1H, H-5), 3.85 (dd, $J_{H3,H4}$ 3.41, $J_{H4,H5}$ 2.95, 1H, H-4), 3.70 (dd, J_{gem} −9.67, 1H, H-6b), 3.65

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(dd, $J_{H1,H2}$ 5.43, $J_{H2,H3}$ 0.73, 1H, H-2), 3.65 (dd, $J_{H2,H3}$ 0.73, $J_{H3,H4}$ 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(CH_3)$_3$), 0.07, −0.01, −0.04, 2 × −0.05, −0.06, −0.07, −0.14 (8 s, 24H, SiCH_3). ^{13}C NMR ($CDCl_3$, 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 (NapCH$_2$), 73.5 (PhCH$_2$), 71.4 (C-4), 70.1 (C-6), 24.7 (SCH$_2$CH$_3$), 15.1 (SCH$_2$CH$_3$); (residue B′) 99.2 (C-1), 79.4 (C-5), 78.6 (C-3), 77.6 (C-2), 73.4 (PhCH$_2$), 71.9 (C-6), 71.5 (C-4); 26.1, 26.0, 2 × 25.9 (4 C(CH_3)$_3$), 2 × 18.1, 2 × 17.9 (4 C(CH_3)$_3$), −3.7, 2 × −4.0, −4.3, −4.4, −4.6, 2 × −4.7 (8 SiCH_3). ESI-HRMS: [M + Na]$^+$ *m*/*z* calcd for $C_{63}H_{102}O_{10}SSi_4Na$ 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 trichloroacetimidate[41] (245 mg, 2 equiv) and methyl 3-*O*-(*p*-methoxybenzyl)-4,6-*O*-benzylidene-α-D-glucopyranoside[42] (100 mg) in dry CH_2Cl_2 (4 mL) was stirred for 20 min in the presence of 4 Å molecular sieves. (TMS)OTf (0.08 equiv) was added at −40 °C. The reaction was monitored by TLC (pentane/EtOAc, 1:2) and allowed to warm to room temperature. NEt_3 was added to quench the reaction, and the mixture was filtered through a pad of Celite. It was then diluted with CH_2Cl_2, washed successively with solutions of saturated $NaHCO_3$ and brine, and dried over Na_2SO_4. The solvent was removed in vaccuo, 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. ^{1}H NMR ($CDCl_3$, 25 °C, 400 MHz): δ (residue A) 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, CH_3OArCH_2), 4.64 (d, J_{gem} −10.58, 1H, CH_3OArCH_2), 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, CH_3OArCH_2), 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); (residue 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, CH_3). ^{13}C NMR ($CDCl_3$, 25 °C, 100 MHz): δ (residue A) 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 (CH_3OArCH_2), 69.3 (C-6), 62.4 (C-5), 55.6 (OMe), 55.4 (CH_3OArCH_2); (residue 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 CH_3). ESI-HRMS: [M + Na]$^+$ *m*/*z* calcd for $C_{36}H_{44}O_{16}Na$ 755.2527, found 755.2525.

To a solution of A3p (163 mg) in CH_2Cl_2 (3 mL) were added water (0.3 mL) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ; 76 mg, 1.5 equiv).[43] The reaction mixture was stirred at room temperature for 2 h. The mixture was diluted with CH_2Cl_2, washed twice with a solution of saturated $NaHCO_3$, and then dried over Na_2SO_4. 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. ^{1}H NMR ($CDCl_3$, 25 °C, 400 MHz): δ (residue A) 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); (residue 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, CH_3). ^{13}C NMR ($CDCl_3$, 25 °C, 100 MHz): δ (residue A) 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); (residue 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 CH_3). ESI-HRMS: [M + Na]$^+$ *m*/*z* calcd for $C_{28}H_{36}O_{15}Na$ 635.1952, found 635.1948.

2,3,4,6-Tetra-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl-(1 → 2)-1,6-anhydro-3-*O*-(2-naphthylmethyl)-4-*O*-(*tert*-butyldimethylsilyl)-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. ^{1}H NMR ($CDCl_3$, 25 °C, 400 MHz): δ (residue B) 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, NapCH$_2$), 4.68 (d, J_{gem} −11.71, 1H, NapCH$_2$), 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(CH_3)$_3$), 0.10, 0.08, 0.07, 2 × 0.06, 3 × 0.05, 0.04, −0.08 (10 s, 30H, SiCH_3). ^{13}C NMR ($CDCl_3$, 25 °C, 100 MHz): δ (residue B) 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 (NapCH$_2$), 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(CH_3)$_3$), 2 × 18.5, 18.1, 2 × 18.0 (5 C(CH_3)$_3$), −3.6, −4.0, 2 × −4.3, 2 × −4.5, 2 × −4.6, 2 × −5.2 (10 SiCH_3). ESI-HRMS: [M + Na]$^+$ *m*/*z* calcd for $C_{53}H_{98}O_{10}Si_5Na$ 1057.5904, found 1057.5908.

2,3,4,6-Tetra-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl-(1 → 2)-1,6-anhydro-3,4-di-*O*-(*tert*-butyldimethylsilyl)-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. ^{1}H NMR ($CDCl_3$, 25 °C, 400 MHz): δ (residue B) 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(CH_3)$_3$), 0.12, 0.11, 3 × 0.10, 0.09, 2 × 0.08, 2 × 0.07, 2 × 0.04 (12s, 36H, SiCH_3). ^{13}C NMR ($CDCl_3$, 25 °C, 100 MHz): δ (residue B) 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(CH_3)$_3$), 18.7, 18.5, 18.1, 18.0, 2 × 17.9 (6 C(CH_3)$_3$), −2.9, −3.9, −4.0, −4.3, 2 × −4.4, −4.5, 2 × −4.6, −4.8, 2 × −5.1 (12 SiCH_3). ESI-HRMS: [M + Na]$^+$ *m*/*z* calcd for $C_{48}H_{104}O_{10}Si_6Na$ 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. ^{1}H NMR ($CDCl_3$, 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, NapCH$_2$), 4.55 (d, J_{gem} −12.40, 1H, PhCH$_2$), 4.54 (d, J_{gem} −11.71, 1H, NapCH$_2$), 4.31 (d, J_{gem} −12.40, 1H, PhCH$_2$), 4.09

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(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, CH_3); 0.88, 0.87, 0.86, 0.83, 0.66 (5 s, 45H, C(CH_3)$_3$), 2 × 0.12, 0.09, 0.08, 0.05, 0.01, −0.01, −0.02, −0.15, −0.32 (10 s, 30H, SiCH_3). ^{13}C NMR ($CDCl_3$, 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 ($PhCH_2$), 71.0 ($NapCH_2$), 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 (CH_3).; 26.2, 26.1, 26.0, 2 × 25.9 (5 C(CH_3)$_3$), 18.4, 18.2, 18.1, 2 × 18.0, (5 C(CH_3)$_3$), −3.7, −3.8, −4.1, −4.3, −4.4, −4.6, −4.7, 3 × −5.2 (10 SiCH_3). ESI-HRMS: $[M + Na]^+$ *m*/*z* calcd for $C_{76}H_{124}O_{17}Si_5Na$ 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. ^{1}H NMR ($CDCl_3$, 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, $NapCH_2$), 4.66 (d, J_{gem} −11.66, 1H, $NapCH_2$), 4.58 (d, J_{gem} −12.56, 1H, $PhCH_2$), 4.35 (d, J_{gem} −12.56, 1H, $PhCH_2$), 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, $PhCH_2$), 4.48 (d, J_{gem} −12.49, 1H, $PhCH_2$), 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(CH_3)$_3$), 0.15, 0.12, 0.11, 0.09, 0.04, 0.01, −0.06, −0.08, −0.11, −0.21 (10 s, 30H, SiCH_3). ^{13}C NMR ($CDCl_3$, 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 ($PhCH_2$), 70.7 ($NapCH_2$), 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 ($PhCH_2$), 69.1 (C-6), 62.4 (C-5), 55.3 (OMe); 26.2, 26.0, 3 × 25.9 (5 C(CH_3)$_3$), 18.3, 3 × 18.1, 17.9 (5 C(CH_3)$_3$), −3.6, −3.8, −4.1, −4.3, −4.5, −4.6, −4.8, −5.2, 2 × −5.3 (10 SiCH_3). ESI-HRMS: $[M + Na]^+$ *m*/*z* calcd for $C_{81}H_{128}O_{16}Si_5Na$ 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*-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-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. ^{1}H NMR ($CDCl_3$, 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, $NapCH_2$), 4.77 (d, J_{gem} −13.12, 1H, $NapCH_2$), 4.58 (d, J_{gem} −12.46, 1H, $PhCH_2$), 4.27 (d, J_{gem} −12.46, 1H, $PhCH_2$), 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, CH_3); 0.92, 0.88, 2 × 0.86, 0.60 (5 s, 45H, C(CH_3)$_3$), 2 × 0.12, 0.11, 0.09, 0.08, 0.07, 0.06, 0.05, −0.12, −0.36 (10 s, 30H, SiCH_3). ^{13}C NMR ($CDCl_3$, 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 ($PhCH_2$), 72.4 (C-2), 71.4 (C-6), 70.6 (C-4), 69.3 ($NapCH_2$); (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 CH_3); 26.3, 26.1, 26.0, 2 × 25.9 (5 C(CH_3)$_3$), 18.4, 18.2, 3 × 18.0 (5 C(CH_3)$_3$), −3.3, −4.1, −4.2, −4.3, 2 × −4.4, −4.9, −5.0, 2 × −5.4 (10 SiCH_3). ESI-HRMS: $[M + Na]^+$ *m*/*z* calcd for $C_{88}H_{140}O_{25}Si_5Na$ 1759.8428, found 1759.8430.

Methyl 2,3,4,6-Tetra-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl-(1 → 2)-3,4-*O*-di-(*tert*-butyldimethylsilyl)-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. ^{1}H NMR ($CDCl_3$, 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, $PhCH_2$), 4.44 (d, J_{gem} −12.76, 1H, $PhCH_2$), 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, $PhCH_2$), 4.53 (d, J_{gem} −12.56, 1H, $PhCH_2$), 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(CH_3)$_3$), 0.22, 3 × 0.10, 0.09, 0.08, 0.06, 0.05, 0.01, −0.11, −0.13, −0.14 (12 s, 36H, SiCH_3). ^{13}C NMR ($CDCl_3$, 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 ($PhCH_2$), 72.1 (C-6); (residue A) 102.6 (CHPh), 99.4 (C-1), 80.7 (C-4), 80.6 (C-2), 73.7 ($PhCH_2$), 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(CH_3)$_3$), 18.4, 18.3, 3 × 18.1, 18.0 (6 C(CH_3)$_3$), −2.6, −3.2, −3.5, 2 × −3.6, 2 × −4.3, −4.4, −4.7, −4.8, −5.3, −5.4 (12 SiCH_3). ESI-HRMS: $[M + Na]^+$ *m*/*z* calcd for $C_{76}H_{134}O_{16}Si_6Na$ 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. ^{1}H NMR ($CDCl_3$, 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, $PhCH_2$), 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, $NapCH_2$), 4.65 (d, J_{gem} −11.73,

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1H, NapCH$_2$), 4.56 (d, J_{gem} −12.47, 1H, PhCH$_2$), 4.34 (d, J_{gem} −12.47, 1H, PhCH$_2$), 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, PhCH$_2$), 4.42 (d, J_{gem} −12.38, 1H, PhCH$_2$), 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(C*H*$_3$)$_3$), 0.13, 2 × 0.09, 0.04, 0.01, −0.02, −0.09, −0.22 (8 s, 24H, SiC*H*$_3$). ^{13}C NMR (CDCl$_3$, 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 (PhCH$_2$), 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 (PhCH$_2$), 71.0 (C-6), 70.9 (NapCH$_2$), 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 (PhCH$_2$), 69.2 (C-6), 62.6 (C-5), 55.3 (OMe); 26.2, 3 × 26.0 (4 C(*C*H$_3$)$_3$), 18.2, 2 × 18.1, 18.0 (4 *C*(CH$_3$)$_3$), −3.7, −3.8, −4.0, −4.3, −4.4, −4.6, −4.8, −5.0 (8 SiCH$_3$). ESI-HRMS: [M + Na]$^+$ m/z calcd for $C_{82}H_{120}O_{16}Si_4Na$ 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. ^{1}H NMR (CDCl$_3$, 25 °C, 400 MHz): δ 7.87−7.16 (m, 22H, H−Ar); (residue B′) 5.11 (d, $J_{H1,H2}$ 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, $J_{H1,H2}$ 6.70, 1H, H-2); (residue B) 5.23 (d, $J_{H1,H2}$ 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, $J_{H1,H2}$ 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, $J_{H1,H2}$ 3.67, 1H, H-1), 4.39 (dd, $J_{H2,H3}$ 9.07, $J_{H3,H4}$ 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, $J_{H1,H2}$ 3.67, $J_{H2,H3}$ 9.07, 1H, H-2), 3.52 (dd, $J_{H3,H4}$ 9.10, 1H, H-4), 3.36 (s, 3H, OMe); (residue A′) 4.95 (dd, $J_{H1,H2}$ 7.83, $J_{H2,H3}$ 9.68, 1H, H-2), 4.93 (dd, $J_{H3,H4}$ 9.47, $J_{H4,H5}$ 9.88, 1H, H-4), 4.82 (dd, $J_{H2,H3}$ 9.68, $J_{H3,H4}$ 9.47, 1H, H-3), 4.17 (d, $J_{H1,H2}$ 7.83, 1H, H-1), 3.94 (2dd, 2H, H-6b, H-6a), 2.76 (ddd, $J_{H4,H5}$ 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, C(C*H*$_3$)$_3$), 2 × 0.09, 0.08, 3 × 0.07, −0.14, −0.42 (8 s, 24H, SiC*H*$_3$). ^{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 C(CH$_3$)$_3$), 2 × 18.1, 2 × 18.0 (4 *C*(CH$_3$)$_3$), −3.7, −4.0, −4.2, 2 × −4.5, −4.7, −4.8, −5.5 (8 SiCH$_3$). ESI-HRMS: [M + Na]$^+$ m/z calcd for $C_{89}H_{132}O_{25}Si_4Na$ 1735.8032, found 1735.8036.

Methyl 2,3,4-Tri-*O*-(*tert*-butyldimethylsilyl)-6-*O*-benzyl-*β*-D-glucopyranosyl-(1 → 2)-3,4-*O*-di-(*tert*-butyldimethylsilyl)-6-*O*-benzyl-*β*-D-glucopyranosyl-(1 → 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. ^{1}H NMR (CDCl$_3$, 25 °C, 400 MHz): δ 7.38−7.14 (m, 20H, H−Ar); (residue B′) 4.94 (d, $J_{H1,H2}$ 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, $J_{H1,H2}$ 5.89, 1H, H-2), 3.56 (dd, 1H, H-6b), 3.42 (dd, 1H, H-6a); (residue B) 5.58 (d, $J_{H1,H2}$ 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, $J_{H1,H2}$ 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, $J_{H2,H3}$ 9.30, $J_{H3,H4}$ 9.15, 1H, H-3), 4.35 (d, $J_{H1,H2}$ 3.60, 1H, H-1), 4.14 (dd, $J_{H5,H6b}$ 4.71, J_{gem} −10.13, 1H, H-6b), 3.79 (ddd, $J_{H5,H6b}$ 4.71, 1H, H-5), 3.57 (dd, J_{gem} −10.13, 1H, H-6a), 3.42 (dd, $J_{H1,H2}$ 3.60, $J_{H2,H3}$ 9.30, 1H, H-2), 3.36 (dd, $J_{H3,H4}$ 9.15, 1H, H-4), 3.32 (s, 3H, OMe); 0.93, 2 × 0.87, 0.86, 0.67 (5 s, 45H, C(C*H*$_3$)$_3$), 0.21, 0.10, 2 × 0.09, 0.08, 2 × 0.03, 0.001, −0.14, −0.53, (10 s, 30H, SiC*H*$_3$). ^{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 (PhCH$_2$), 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 (PhCH$_2$), 72.0 (C-6); (residue A) 102.7 (CHPh), 99.2 (C-1), 80.9 (C-2), 80.6 (C-4), 73.6 (PhCH$_2$), 73.0 (C-3), 69.3 (C-6), 62.5 (C-5), 55.4 (OMe); 26.3, 26.1, 3 × 26.0 (5 C(*C*H$_3$)$_3$), 18.3, 18.1, 2 × 18.0, 17.9 (5 *C*(CH$_3$)$_3$), −2.6, −3.4, −3.5, −3.7, −3.8, −4.3, −4.4, −4.7, 2 × −4.8 (10 SiCH$_3$). ESI-HRMS: [M + Na]$^+$ m/z calcd for $C_{77}H_{126}O_{16}Si_5Na$ 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 equiv) was added dropwise at room temperature. At completion, the mixture was taken into CH_2Cl_2 and washed with water. The organic phase was dried over Na_2SO_4, filtered, and concentrated to dryness. The protected tetrol obtained was dissolved in dry Pyr (2 mL). Acetic anhydride (10 equiv) and DMAP were added, and the reaction was allowed to stir overnight. The reaction was stopped by adding a few drops of MeOH, and the yellow oil was diluted with EtOAc and washed with $NaHCO_3$, brine, 1 M HCl, and brine before being dried over Na_2SO_4, 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). ^{1}H NMR (CDCl$_3$, 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, PhCH$_2$), 4.54 (d, J_{gem} −12.08, 1H, PhCH$_2$), 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, NapCH$_2$), 4.65 (d, J_{gem} −11.76, 1H, NapCH$_2$), 4.48 (d, J_{gem} −11.63, 1H, PhCH$_2$), 4.39 (d, J_{gem} −11.63, 1H, PhCH$_2$), 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, CH$_3$). ^{13}C NMR (CDCl$_3$, 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 (PhCH$_2$), 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 (NapCH$_2$), 73.9 (PhCH$_2$), 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),

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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 CH_3). ESI-HRMS: $[M + Na]^+$ m/z calcd for $C_{73}H_{84}O_{29}Na$ 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 equiv) 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). ^{1}H NMR ($CDCl_3$, 25 °C, 400 MHz): δ 7.38−7.27 (m, 10H, H−Ar); (residue B′) 5.20 (dd, $J_{H2,H3}$ 9.14, $J_{H3,H4}$ 9.38, 1H, H-3), 5.14 (dd, $J_{H3,H4}$ 9.38, $J_{H4,H5}$ 9.56, 1H, H-4), 5.06 (dd, $J_{H1,H2}$ 8.05, $J_{H2,H3}$ 9.14, 1H, H-2), 4.93 (d, $J_{H1,H2}$ 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, $J_{H4,H5}$ 9.56, 1H, H-5), 3.56 (dd, 1H, H-6b), 3.55 (dd, 1H, H-6a); (residue B) 4.94 (dd, $J_{H3,H4}$ 9.03, $J_{H4,H5}$ 9.62, 1H, H-4), 4.62 (d, $J_{H1,H2}$ 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, $J_{H3,H4}$ 9.03, $J_{H3,OH3}$ 3.45, 1H, H-3), 3.58 (dd, $J_{H1,H2}$ 7.19, 1H, H-2), 3.57 (ddd, $J_{H4,H5}$ 9.62, 1H, H-5), 3.56 (dd, 1H, H-6b), 3.55 (dd, 1H, H-6a), 3.11 (d, $J_{H3,OH3}$ 3.45, 1H, OH3); (residue A) 4.80 (d, $J_{H1,H2}$ 3.69, 1H, H-1), 3.95 (dd, $J_{H2,H3}$ 9.11, $J_{H3,H4}$ 9.20, 1H, H-3), 3.83 (br dd, 1H, H-6b), 3.75 (dd, 1H, H-6a), 3.72 (dd, $J_{H1,H2}$ 3.69, $J_{H2,H3}$ 9.11, 1H, H-2), 3.63 (ddd, $J_{H4,H5}$ 9.34, 1H, H-5), 3.48 (dd, $J_{H3,H4}$ 9.20, $J_{H4,H5}$ 9.34, 1H, H-4), 3.36 (s, 3H, OMe); (residue A′) 5.23 (dd, $J_{H2,H3}$ 9.08, $J_{H3,H4}$ 9.13, 1H, H-3), 5.10 (dd, $J_{H3,H4}$ 9.39, $J_{H4,H5}$ 9.90, 1H, H-4), 5.02 (dd, $J_{H1,H2}$ 7.83, $J_{H2,H3}$ 9.08, 1H, H-2), 4.97 (d, $J_{H1,H2}$ 7.83, 1H, H-1), 4.14 (dd, $J_{H5,H6b}$ 4.65, J_{gem} −12.37, 1H, H-6b), 4.09 (dd, $J_{H5,H6a}$ 2.65, J_{gem} −12.37, 1H, H-6a), 3.65 (ddd, $J_{H5,H6a}$ 2.65, $J_{H5,H6b}$ 4.65, $J_{H4,H5}$ 9.90, 1H, H-5); 2.07, 3 × 2.04, 2 × 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 × 169.7, 169.6, 169.5 (8 C═O), 137.6, 137.5 (2 C-*ipso*), 2 × 128.7, 2 × 128.6, 3 × 128.1, 3 × 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 × 20.9, 2 × 20.8, 2 × 20.7 (8 CH_3). ESI-HRMS: $[M + Na]^+$ m/z calcd for $C_{55}H_{72}O_{29}Na$ 1219.4057, found 1219.4061.

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)]-6-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranoside (10). Triol **9** (30 mg) was dissolved in dry DCM (2 mL), 2,6-lutidine (9 μL, 3 equiv) was added, and the solution was cooled to −20 °C. (TBDMS)OTf (9 μL, 1.5 equiv) was added dropwise at the same temperature under a 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. ^{1}H NMR ($CDCl_3$, 25 °C, 400 MHz): δ 7.38−7.25 (m, 10H, H−Ar); (residue B′) 5.21 (dd, $J_{H2,H3}$ 9.17, $J_{H3,H4}$ 9.23, 1H, H-3), 5.14 (dd, $J_{H3,H4}$ 9.23, $J_{H4,H5}$ 9.45, 1H, H-4), 5.02 (dd, $J_{H1,H2}$ 8.10, $J_{H2,H3}$ 9.17, 1H, H-2), 4.92 (d, $J_{H1,H2}$ 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, $J_{H4,H5}$ 9.45, 1H, H-5), 3.54 (2 dd, 2H, H-6b, H-6a); (residue B) 4.94 (dd, $J_{H3,H4}$ 9.30, $J_{H4,H5}$ 9.79, 1H, H-4), 4.62 (d, $J_{H1,H2}$ 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, $J_{H1,H2}$ 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, CH_3), 0.91 (s, 9H, $C(CH_3)_3$), 2 × 0.08 (2s, 6H, $SiCH_3$). ^{13}C NMR ($CDCl_3$, 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 ($PhCH_2$), 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 ($PhCH_2$), 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 ($C(CH_3)_3$), 21.4, 21.0, 20.9, 20.8, 4 × 20.7 (8 CH_3), 18.6 ($C(CH_3)_3$), 2 × −5.1 (2 $SiCH_3$). ESI-HRMS: $[M + Na]^+$ m/z calcd for $C_{61}H_{86}O_{29}SiNa$ 1333.4922, found 1333.4927.

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)-{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-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1 → 3)]-6-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (11). Donor D5 (48 mg, 3 equiv), diol acceptor **10** (18 mg, 1 equiv), base DTBMP (4 equiv), and NIS (1.2 equiv) were dissolved in dry solvents, DCM/Tol, 1:1, at room temperature and stirred with 4 Å molecular sieves under a N_2 flow. The temperature was decreased to −60 °C, and TfOH (1.0 μL, cat amount) was added. The mixture was allowed to reach −30 °C and stirred for 30 min, while being monitored by mass spectrometry analysis. The reaction was then quenched by the addition of NEt_3 (50 μL). 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% $Na_2S_2O_3$ solution and then with brine. The acquired mixture was dried over $Na_2S_2O_4$, after which the 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. ^{1}H NMR ($CDCl_3$, 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, $PhCH_2$), 4.51 (d, J_{gem} −11.63, 1H, $PhCH_2$), 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, $NapCH_2$), 4.63 (d, J_{gem} −−12.79, 1H, $NapCH_2$), 4.60 (d, J_{gem} −12.00, 1H, $PhCH_2$), 4.50 (d, J_{gem} −12.00, 1H, $PhCH_2$), 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, $PhCH_2$), 4.19 (d, J_{gem} −12.30, 1H, $PhCH_2$), 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, $PhCH_2$), 4.34 (d, J_{gem} −11.55, 1H, $PhCH_2$), 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,

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1.98, 2 × 1.95, 1.94, 1.85, 1.63 (8s, 24H, CH_3), 0.92, 0.88, 0.86, 0.84, 0.73 (5 s, 45H, $C(CH_3)_3$), 2 × 0.10, 2 × 0.09, 0.08, 0.06, 0.04, 0.03, 0.01, −0.04 (10 s, 30H, $SiCH_3$). ^{13}C NMR ($CDCl_3$, 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 ($PhCH_2$), 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 ($PhCH_2$), 70.6 ($NapCH_2$), 70.5 (C-4), 70.2 (C-6); (residue B′) 100.9 (C-1), 73.9 (C-3), 73.5 ($PhCH_2$), 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 ($PhCH_2$), 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 $C(CH_3)_3$), 21.3, 21.2, 21.0, 3 × 20.8, 20.7, 20.6 (8 CH_3), 18.6, 2 × 18.1, 18.0, 17.9 (5 $C(CH_3)_3$), −3.7, 2 × −4.0, −4.3, −4.4, 2 × −4.8, −4.9, 2 × −5.0 (10 $SiCH_3$). ESI-HRMS: $[M + Na]^+$ *m*/*z* calcd for $C_{122}H_{182}O_{39}Si_5Na$ 2434.1002, found 2434.0996.

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)-{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-*O*-acetyl-6-*O*-benzyl-β-D-glucopyranosyl-(1 → 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 equiv) was added dropwise at room temperature. At completion, the mixture was taken into CH_2Cl_2 and washed with water. The organic phase was dried over Na_2SO_4, filtered, and concentrated to dryness. The protected tetrol obtained was dissolved in dry Pyr (2 mL). Acetic anhydride (10 equiv) and DMAP were added, and the reaction was allowed to stir overnight. The reaction was stopped by adding a few drops of MeOH, and the yellow oil was diluted with EtOAc and washed with $NaHCO_3$, brine, 1 M HCl, and brine before being dried over Na_2SO_4, 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). ^{1}H NMR ($CDCl_3$, 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, $PhCH_2$), 4.47 (d, J_{gem} −12.22, 1H, $PhCH_2$), 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, $NapCH_2$), 4.76 (d, $J_{H1,H2}$ 7.57, 1H, H-1), 4.68 (d, J_{gem} −11.98, 1H, $NapCH_2$), 4.42 (d, J_{gem} −12.03, 1H, $PhCH_2$), 4.38 (d, J_{gem} −12.03, 1H, $PhCH_2$), 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, $PhCH_2$), 4.56 (d, J_{gem} −11.81, 1H, $PhCH_2$), 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, $PhCH_2$), 4.43 (d, $J_{H1,H2}$ 7.56, 1H, H-1), 4.42 (d, J_{gem} −11.95, 1H, $PhCH_2$), 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, CH_3). ^{13}C NMR ($CDCl_3$, 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 ($PhCH_2$), 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 ($NapCH_2$), 73.6 (C-5), 73.6 ($PhCH_2$), 71.1 (C-4), 69.4 (C-6); (residue B′) 98.8 (C-1), 74.3 (C-3), 74.0 ($PhCH_2$), 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 ($PhCH_2$), 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 CH_3). ESI-HRMS: $[M + Na]^+$ *m*/*z* calcd for $C_{104}H_{124}O_{45}Na$ 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 equiv per *O*-acyl group to be cleaved using a 1 M solution of NaOMe in MeOH was added. Starting from compound **12** (21 mg), the procedure yielded, after purification on a Sep-Pak t-C18 using a H_2O/ACN solvent gradient from 100:0 to 0:100, compound **13** (TLC: R_f = 0.75, EtOAc/MeOH/H_2O, 7:2:1) in 82% yield (12 mg) as a colorless syrup. ^{1}H NMR (CD_3OD, 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, $PhCH_2$), 4.53 (d, J_{gem} −12.15, 1H, $PhCH_2$), 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, $NapCH_2$), 5.01 (d, $J_{H1,H2}$ 7.61, 1H, H-1), 4.56 (br s, 2H, $PhCH_2$), 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, $PhCH_2$), 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, $PhCH_2$), 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). ^{13}C NMR (CD_3OD, 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 ($PhCH_2$), 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 ($NapCH_2$), 74.6 ($PhCH_2$), 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 ($PhCH_2$), 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 ($PhCH_2$), 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* calcd for $C_{76}H_{96}O_{31}Na$ 1527.5833, found 1527.5829.

Methyl β-D-Glucopyranosyl-(1 → 2)[β-D-glucopyranosyl-(1 → 2){β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 3)}-β-D-glucopyranosyl-(1 → 3)]-α-D-glucopyranoside (14). Compound **13** (8 mg, 5.32 μmol) was dissolved in MeOH (1.5 mL), and 10−20% Pd/C catalyst (15 mg) was added in a small pierced vial, and the resulting solution was allowed to stir overnight at room temperature under 10 atm 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 a Sep-Pak t-C18 using a H_2O/ACN solvent gradient from 100:0 to 90:10, followed by an ÄKTA system equipped with a Superdex column gave 4 mg of compound **14** as a white powder (73%). ^{1}H and ^{13}C NMR data: see Table 3. ESI-HRMS: $[M + Na]^+$ *m*/*z* calcd for $C_{37}H_{64}O_{31}Na$ 1027.3329, found 1027.3326.

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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 spectrum and the experimental spectrum 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 CarbBuilder[44] as an add-in to the CASPER software,[45] 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 $^3J_{HH}$ values (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. On the basis of the $^3J_{HH}$ values, the root-mean-square deviation (RMSD) was minimized employing the general reducing agent algorithm[35] 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 Stoddart[36] and Mayes et al.,[33] respectively, were tested. The models and population distributions therefrom, with the lowest average RMSDs, were regarded as the most probable population distributions. The determined populations were estimated to be accurate to within 5%.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01264.

Stick and space-filling models of D3 and D5, selected regions of the ^1H NMR spectra of donors D1−D6, ^1H NMR spectrum of D4, table of NMR data related to conformational analysis, and ^1H and ^{13}C NMR spectra of the synthesized compounds (PDF)

Molecular model of D3 (PDB)

Molecular model of D5 (PDB)

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Notes

The authors declare no competing financial interest.

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