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Bismuth(III) triflate as a novel and efficient activator for glycosyl halides[†]

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Presented herein is the discovery that bismuth(III) trifluoromethanesulfonate (Bi(OTf)₃) is an effective catalyst for the activation of glycosyl bromides and glycosyl chlorides. The key objective for the development of this methodology is to employ only one promoter in the lowest possible amount and to avoid using any additive/co-catalyst/acid scavenger except molecular sieves. Bi(OTf)₃ works well in promoting the glycosidation of differentially protected glucosyl, galactosyl, and mannosyl halides with many classes of glycosyl acceptors. Most reactions complete within 1 h in the presence of only 35% of green and lightstable Bi(OTf)₃ catalyst.

The first chemical glycosylations performed by Michael, Fischer, and Koenigs/Knorr¹⁻³ helped pave the path to modern glycosciences that now encompass many chemical, biomedical, and industrial aspects of carbohydrates. Glycosyl halides, once the glycosyl donors of choice to perform both single-stage glycosylations and multi-step glycan assembly, started losing dominance due to their instability and somewhat sluggish activation profile. To address the issues related to the activation of halides, many promoters have been introduced. Traditionally used silver salt³⁻⁸ and mercury⁹⁻¹⁴ saltbased promoters have been expanded to other metal salts including cadmium,^{11,15-17} zinc,^{11,18-21} tin,^{22,23} indium,²⁴⁻²⁶ and iron.²⁷ The activity of metal salt activators is defined by their halophilicity; however, the rate of glycosylation can be greatly influenced by many other factors.²⁸

Many metal salt-based promoters for the activation of glycosyl halides experience limitations related to their inherent toxicity, light/air/moisture sensitivity, cost, excess requirement, and/or substrate compatibility. As a result, there has been a notable interest in studying non-metallic promoters including organic modulators,^{29–34} halogens,^{35–43} diarylborinic acid,⁴⁴ organocatalysts,^{45,46} supercritical CO₂,⁴⁷ and blue light.⁴⁸ Most of the non-metallic activators function with an associative additive. Recent approaches introduced by Taylor,⁴⁹ Ye,⁴⁵ Jacobsen,⁴⁶ and Nguyen³⁴ have largely changed the way glycosyl halides have been activated by providing a catalytic means to their activation. However, these methods also have certain limitations related to multistep catalyst synthesis, long reaction time (even at high temperatures), requirement of additives that are commonly used in excess, substrate limitations, and, in some cases, a complex reaction set up is needed.

In an ongoing effort to develop new glycosylation reactions suitable for traditional manual and automated synthetic approaches, we have recently developed a cooperative concept for the activation of glycosyl halides. Over the course of this study, we achieved a dramatic acceleration of a silver(I)-promoted glycosylation reaction in the presence of catalytic Lewis or Brønsted acid additive.⁵⁰⁻⁵² As an extension of this effort of identifying suitable activators, reported herein is our first dedicated study to implement promoters based on other metal salts. The substrates of choice for the initial screening were common 2,3,4,6-tetra-O-benzoyl- α -D-glucopyranosyl bromide donor 1⁵³ and methyl 2,3,4-tri-O-benzyl- α -D-glucopyranoside acceptor 2.⁵⁴ After preliminary screening of several halophilic metal salts as potential promoters for the activation of the bromide leaving group, we chose bismuth(m) trifluoromethanesulfonate, Bi $(OTf)_3$, as a promising candidate for further investigation. Other activators considered included Cu₂O, CuO, CaO, ZnCO₃, Ni $(acac)_2$, $(BiO)_2CO_3$, $Fe(OAc)_3$, and $Fe(OTf)_3$, but unfortunately all these reagents were practically ineffective as the desired disaccharide was produced in less than 5% under the tested reaction conditions. Good reaction rates and minimal side products were achieved in the presence of as little as 35 mol% of Bi $(OTf)_3$ in CH₂Cl₂ at rt. These, along with the moderate cost, low hygroscopicity, high stability, and greenness of Bi(OTf)₃, were all important traits of this reaction.

For comparison, silver triflate, arguably the most frequently used metallic promoter for the activation of glycosyl halides, has a very high reactivity profile. However, it has to be preactivated and dried directly prior to each application. AgOTf is highly sensitive towards moisture and light, it must be used in excess (2 equiv. or higher), and it frequently requires an associ-

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ative acid scavenger and low temperature conditions. In contrast, glycosidation of bromide 1 with acceptor 2 in the presence of 35 mol% of Bi(OTf)₃ in CH₂Cl₂ in the absence of molecular sieves produced the desired disaccharide 3 (entry 1, Table 1).⁵⁵ The reaction performed at 0 °C was completed in 1.25 h. The isolated yield of disaccharide 3 was rather modest under these conditions (52%) even though donor 1 has been completely consumed. When the crude reaction mixture was subjected to mass spectrometry analysis, several side products were identified. Along with a variety of the hydrolysis products, one of the major side products was identified as methyl 2,3,4,6-tetra-O-benzovl-p-glucopyranoside. The formation of this compound could be rationalized by the direct intermolecular acceptor-to-donor aglycone transfer.⁵⁶ Alternatively, methyl glycoside hydrolysis followed by glycosylation of the liberated MeOH could not be excluded due to a relatively high acidity (TfOH) of the reaction medium. Indeed, along with glycosylation, TfOH is constantly being produced from Bi(OTf)₃. These observations led us to investigating the means for suppressing the formation of side products.

Practically all chemical glycosylation reactions in modern times rely on molecular sieves as a desiccant (and acid scavenger) to suppress the formation of hydrolyzed by-products. When the aforementioned glycosylation (entry 1) was repeated in the presence of molecular sieves (3 Å, 30 mg, 1/1, w/w to donor 1) we noted a slight increase of the yield of disaccharide 3 to 57% (entry 2). This result was indicative of the reactiondependence on the presence of molecular sieves. To further investigate the role of the desiccant, we performed glycosyla-

Table 1 Glycosylation of donor 1 (30 mg) and acceptor 2 with varying the amount of molecular sieves 3 Å and solvent



2 (0.8 equiv)

Entry	MS 3 Å (mg)	Solvent	Time (h)	Yield of 3
1	_	CH_2Cl_2	1.25	52%
2	30	CH_2Cl_2	2	57%
3	90	CH_2Cl_2	20	84%
4	120	CH ₂ Cl ₂	20	92%
5	150	CH_2Cl_2	20	93%
6	300	CH_2Cl_2	20	98%
7	120	Toluene	20	67%
8	120	Et ₂ O	1	45%
9	120	MeCN	1	50%
10	120	MeNO ₂	1	95%
11	_	MeNO ₂	1	55%
12	120	$MeNO_{2}/CH_{2}Cl_{2}, 1/4, v/v$	20	96%
13	120	$MeNO_2/CH_2Cl_2, 1/1, v/v$	20	98%
14	120	MeNO ₂ /CH ₂ Cl ₂ , 7/3, v/v	1	98%

tion in the presence of 90 mg of molecular sieves under otherwise identical reaction conditions. As a result, disaccharide **3** was obtained in a significantly improved yield of 84% (entry 3). We have also noted a significant increase in the reaction time to 20 h. Further increase of the amount of molecular sieves to 120, 150, and 300 mg led to the formation of disaccharide **3** in excellent yields of 92, 93, and 98%, respectively (entries 4–6). At the conclusion of this series of experiments, we chose to perform subsequent glycosylation reactions in the presence of 120 mg of molecular sieves (4/1, w/w to the donor). In our opinion, these reaction conditions offer the best combination between efficiency, sieve amount, and yield. Since this reaction required 20 h to complete, we turned our attention to investigating other factors with the primary purpose of enhancing the reaction rates.

Keeping all other parameters constant, replacing CH₂Cl₂ with toluene showed no noticeable improvement in the rate of reaction between compounds 1 and 2, but the yield of disaccharide 3 was reduced to 67% (entry 7). A notable enhancement rate was observed for reactions performed in diethyl ether or acetonitrile, reaction solvents known for their ability to affect the stereoselectivity of glycosylation via participation at the anomeric center. While rapid at the beginning, these reactions stalled after about 1 h and failed to proceed past this time point. As a result, disaccharide 3 was obtained in 45-50% yield (entries 8 and 9). In contrast, freshly distilled nitromethane (MeNO₂) was very effective in enhancing the rate of the reaction without having any detrimental effect on the reaction yield. Thus, the glycosylation reaction in MeNO₂ smoothly completed within 1 h and disaccharide 3 was isolated in 95% yield (entry 10). Reaction in MeNO2 without molecular sieves produced disaccharide 3 in 55% yield (entry 11). Only side products resulted from donor hydrolysis have been observed in this reaction.

Over the course of the subsequent experiments, we investigated how modulating the ratios between the reaction solvents CH₂Cl₂ and MeNO₂ would affect the reaction time and product yields (entries 12-14). From this experimentation, we concluded that dichloromethane is a suitable reaction solvent. However, the rate of the reaction was low and 18-24 h were still needed for complete consumption of the glycosyl bromide. In terms of reactivity, yield of glycosides, and suppressing sides products, nitromethane seems a better choice among the investigated solvents. However, nitromethane alone is often a poor solvent for sugars. To develop a universal solvent system that would be suitable for most donor acceptor combinations, we concluded that MeNO₂/CH₂Cl₂ (7/3, v/v) offers an optimal balance between solubility, rates, and yields. Therefore, this solvent combination was chosen as the standard reaction solvent system for future experimentations.

Having optimized the basic reaction conditions, we extended $Bi(OTf)_3$ -promoted reactions to glycosidation of donor **1** with various glycosyl acceptors **4–14** depicted in Fig. 1. Glycosylation reactions of less reactive standard secondary glycosyl acceptors **4–6**⁵⁴ with glucosyl bromide **1** were rapid and efficient affording the respective disaccharides **15–17**^{54,55} in



40-60 min in 92-94% (entries 1-3, Table 2). These and following reactions were exclusively 1,2-trans-stereoselective due to the participatory effect of the benzovl ester group at C-2 of donor 1.

Further, the compatibility of the reaction conditions towards the acid-labile protecting groups was investigated by performing glycosylation reactions with benzylidene-protected acceptor 7⁵⁷ and isopropylidene-protected acceptor 8. The glycosylations proceeded smoothly and produced the respective disaccharides 18⁵⁸⁻⁶⁰ and 19⁶¹ in 1-2 h in 85-86% yield (entries 4 and 5). Glycosylation of electronically deactivated benzoylated glycosyl acceptor 9⁶² was also swift and efficient, but only if carried out in the presence of the increased amount of Bi(OTf)₃ (0.5 equiv.) and in neat MeNO₂. As a result, the corresponding disaccharide 20⁶³ was obtained in 85% yield in 15 min (entry 6).

A selective activation approach⁶⁴ was then undertaken to activate glycosyl bromide 1 over thioglycoside acceptors 10⁶⁵ and 11.66 These efforts still need improvement, and the respective disaccharides 21⁶⁷ and 22⁶⁸ were isolated in 16-42% yield (entries 7 and 8). It should be noted that these disaccharides equipped with the anomeric leaving group can be used as glycosyl donors for subsequent chain elongation directly. A lower efficiency of these reactions in comparison to that of glycosylation of standard acceptors was attributed to the competing aglycone transfer.⁵⁶ Presumably, this side reaction is accelerated due to interaction of the thiophilic bismuth cation with the anomeric sulfur atom of the glycosyl acceptor. Aliphatic glycosyl acceptors, secondary alcohol cholesterol 12 and tertiary 1-adamantanol 13 were then studied. These glycosylations produced corresponding glycosides 23⁶⁹ and 24⁷⁰ in 77% and 96% yield, respectively (entries 9 and 10). Note that reaction in neat CH₂Cl₂ was found to be superior for glycosyl acceptor 13. Finally, to execute multiple glycosylations to

Table 2 Glycosidation of donor 1 with acceptors 4-14

1

2

3

4

5

9







Deviations from standard reaction conditions: ^{*a*} Performed in the presence of 0.5 equiv. Bi(OTf)₃ in neat MeNO₂. ^{*b*} Performed in the presence of 0.5 equiv. Bi(OTf)₃. ^{*c*} Performed in the presence of 0.6 equiv. Bi (OTf)₃. ^{*d*} Performed in neat CH₂Cl₂. ^{*e*} Performed with 0.4 equiv. of acceptor at 0 °C for 5 min and then increased to rt.

access branched structures in one pot, we conducted glycosylation of benzylated 4,6-diol acceptor **14**.⁷¹ This reaction produced trisaccharide **25** in 41% yield (entry 11).

After the successful construction of a variety of glycosidic linkages from donor **1**, we explored the glycosylation reaction with other classes of glycosyl donors depicted in Fig. 2. The



Fig. 2 Glycosyl donors used in this study.

purpose of this study was to further explore the scope of this reaction, determine compatibility with other classes of protecting groups, and to access its applicability to the assembly of complex glycans. Benzylated glycosyl acceptor 2 was chosen as a nucleophile for this study. The first series of experiments was conducted with glycosyl bromide donors bearing disarming protection (benzoyl group). Benzoylated glucosyl donor 1 was supplemented with benzovlated galactosyl bromide **26**⁷² and mannosyl bromide **27**.⁷³ In comparison with the benchmark experiment involving bromide 1 and acceptor 2 that produced disaccharide 3 in 45 min in 98% vield (entry 1, Table 3), donors 26 and 27 provided a very similar outcome. Thus, glycosylation of acceptor 2 with donors 26 and 27 swiftly produced disaccharides 37⁷⁴ and 38⁶³ in 30 min in 97% and 92% yield, respectively (entries 2 and 3).

We then moved on to investigating the glycosylation reactions with per-benzylated (armed) glycosyl bromides that were generated from the corresponding ethyl thioglycoside precursors by reaction with bromine directly prior to application after treatment with stoichiometric molecular bromine. Glycosidation of armed glucosyl bromide generated from thioglycoside 28⁷⁵ afforded disaccharide 39⁷⁶ in 71% in 15 min (entry 4). The lower yield of 39 in comparison to those seen for reactions with benzovlated bromides could be attributed to competitive hydrolysis and the formation of the 1,6-anhydro derivative. Galactosyl and mannosyl bromides generated from the respective thioglycoside precursors 29 37,77 and 30 78 gave rise to disaccharides 40⁷⁹ and 41⁸⁰ in 78 and 91% yield, respectively (entries 5 and 6). The armed glycosyl bromide donors generated from thioglycoside precursors 28-30 produced disaccharides in poor stereoselectivity with α/β ratio ranging within 1/1.1-1.5 due to the lack of stereodirecting factors.

Following the efficient glycosylation reactions of various glycosyl bromide donors with the newly discovered metal salt, we investigated glycosyl chloride donors **31**⁸¹ and **32**.⁸² Glycosidation under the standard reaction conditions was also smooth and efficient in producing disaccharides 37 and 40 in 15 min in 93% and 97% yield, respectively (entries 7 and 8). Glycosidation of differentially protected glycosyl bromide donors obtained from thioglycosides 33-35 was then attempted to understand the compatibility of the new activation conditions with various protecting and functional groups. Of particular interest were aminosugars and temporary protecting groups (TBDMS and Lev) that are commonly used in glycan synthesis. These glycosylations were smooth and efficient producing disaccharides 42-44 in 73-93% yield (entries 9-11). Finally, glycosidation of the L-series sugar, rhamnosyl bromide donor 36,83 afforded disaccharide 45 84 in 79% yield (entry 12).

In conclusion, $Bi(OTf)_3$ was found to be an effective metal salt capable of the activation of glycosyl bromides and chlorides. Successful glycosidation of per-benzoylated glucosyl bromide was carried out with a variety of glycosyl acceptors, and these reactions were relatively high yielding with swift

Disaccharides

3, 37-45

(see Table)

BnO| OMe

ÓMe

BnÒ

BnO| OMe

BnO OMe



о́Ме

laboratory.

37, 93%, β only

Table 3 (Contd.)

differentially protected building blocks have been performed with high efficiency. This glycosylation method is favorable due to the low mol % of green and light-stable Bi(OTf)₃ required. One current limitation of this reaction is the use of thioglycoside acceptors that showed propensity to undergo the competing aglycone transfer reaction, which is not uncommon under other reaction conditions. Further investigation of this reaction is currently underway in our

Table 3 Glycosylation of acceptor 2 with various donors

Experimental section

General

Column chromatography was performed on silica gel 60 (70–230 mesh), reactions were monitored by TLC on Kieselgel 60 F_{254} . The compounds were detected by examination under UV light and by charring with 10% sulfuric acid in methanol. Solvents were removed under reduced pressure at <40 °C. CH₂Cl₂ and MeNO₂ were distilled from CaH₂ directly prior to application. Molecular sieves (3 Å) used for reactions were crushed and activated *in vacuo* at 390 °C for 8 h in the first instance and then for 2–3 h at 390 °C directly prior to application. Optical rotations were measured using a Jasco P-1020 polarimeter. ¹H NMR spectra were recorded in CDCl₃ at 300 MHz and ¹³C NMR spectra were recorded in CDCl₃ at 75 MHz. Accurate mass spectrometry determinations were preformed using Agilent 6230 ESI TOF LCMS mass spectrometer.

Synthesis of glycosyl halide donors and thioglycoside precursors. 2,3,4,6-Tetra-O-benzoyl- α -D-glucopyranosyl bromide (1) was obtained from 1,2,3,4,6-penta-O-benzoyl-D-glucopyranose as reported previously.⁸⁵ The analytical data for 1 was in accordance with that previously reported.⁵³

2,3,4,6-Tetra-O-benzoyl- α -D-galactopyranosyl bromide (26) was obtained from 1,2,3,4,6-penta-O-benzoyl-D-galactopyranose as reported previously.⁸⁶ The analytical data for 26 was in accordance with that previously reported.⁷²

2,3,4,6-Tetra-O-benzoyl- α -D-mannopyranosyl bromide (27) was obtained from 1,2,3,4,6-penta-O-benzoyl-D-mannpyranose as reported previously.⁸⁷ The analytical data for 27 was in accordance with that previously reported.⁷³

Ethyl 2,3,4,6-tetra-O-benzyl-1-thio- β -D-glucopyranoside (28) was obtained as reported previously.⁷⁵

Ethyl 2,3,4,6-tetra-O-benzyl-1-thio-β-D-galactopyranoside (29) was obtained as reported previously.^{37,77}

Ethyl 2,3,4,6-tetra-O-benzyl-1-thio- α -D-mannopyranoside (30) was obtained as reported previously.⁷⁸

2,3,4,6-Tetra-O-benzoyl- α -D-galactopyranosyl chloride (31) was obtained from 2,3,4,6-tetra-O-benzoyl-D-galactopyranose⁸⁸ as reported previously.⁵² The analytical data for 31 was in accordance with that previously reported.⁸¹

2,3,4,6-Tetra-*O*-benzyl- α -D-galactopyranosyl chloride (32) was obtained from 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose⁸⁹ as reported previously.²⁷ The analytical data for 32 was in accordance with that previously reported.^{81,82}

Ethyl 2,6-di-O-benzyl-4-O-benzyl-3-O-tert-butyldimethylsilyl-1-thio-β-D-galactopyranoside (33). Benzoyl chloride (3.93 mL, 33.78 mmol) was added to a solution of ethyl 2-O-benzoyl-4-Obenzyl-3-O-tert-butyldimethylsilyl-1-thio-β-D-galactopyranoside⁹⁰ (46, 12.0 g, 22.52 mmol) in pyridine (50 mL) and the resulting mixture was stirred under argon for 4 h at rt. Methanol (~5 mL) was added dropwise, the volatiles were removed under reduced pressure and the residue was co-evaporated with toluene (3 × 40 mL). The resulting residue was diluted with CH_2Cl_2 (~500 mL) and washed with 1 N aq. HCl (50 mL), sat. aq. NaHCO₃ (50 mL), and water (2 × 50 mL). The organic phase was separated, dried over Na₂SO₄, and concentrated

under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate - hexane gradient elution) and crystallization (diethyl ether-hexane) to afford the title compound as white crystals in 86% yield (12.32 g). Analytical data for 33: $R_f = 0.66$ (ethyl acetate/hexane, 1/4, v/v); m. p. 101.7–102.9 °C (diethyl ether-hexane); $[\alpha]_{D}^{20} + 17.4$ (c = 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ 8.05, 7.99 (2 d, 4H, aromatic), 7.20–7.63 (m, 11H, aromatic), 5.67 (dd, 1H, J_{2.3} = 9.6 Hz, H-2), 4.90 (dd, 2H, ${}^{2}J$ = 11.4 Hz, CH₂Ph), 4.45–4.60 (m, 2H, $J_{1,2} = 9.6, J_{6a,6b} = 11.3$ Hz, H-1, 6a), 4.42 (dd, 1H, H-6b), 4.02 (dd, 1H, $J_{3,4}$ = 1.0 Hz, H-3), 3.92 (m, 1H, $J_{5,6a}$ = 6.8, $J_{5,6b}$ = 5.6 Hz, H-5), 3.87 (br d, 1H, $J_{4.5}$ = 1.9 Hz, H-4), 2.72 (m, 2H, SCH₂), 1.22 (t, 3H, SCH₂CH₃), 0.80 (s, 9H, Si^tBu), 0.13, -0.06 (2 s, 6H, SiMe₂) ppm; ¹³C NMR (75 MHz, CDCl₃): δ 166.3, 165.4, 138.4, 133.3, 133.1, 130.3, 129.9 (×2), 129.8, 129.7 (×2), 128.5 (×2), 128.4 (×4), 128.0 (×2), 127.7, 83.9, 77.1, 76.4, 75.7, 75.1 (×2), 71.0, 63.9, 25.6 (×3), 24.1, 15.0, -3.9, -5.0 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{35}H_{44}O_7SSiNa$ 659.2475, found 659.2465.

Ethyl 4,6-di-O-benzyl-2-deoxy-3-O-levulinoyl-2-phthalimido-1-thio-β-D-glucopyranoside (34). Levulinic acid (0.336 g, 2.90 mmol), N,N'-diisopropylcarbodiimide (DIC, 0.449 mL, 2.90 mmol) and dimethylaminopyridine (DMAP, 35.0 mg, 0.29 mmol, 0.20 equiv.) were added to a solution of ethyl 4,6di-O-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside⁹¹ (47, 0.773 g, 1.45 mmol) in dry DCM (1.0 mL) and the resulting mixture was stirred under argon for 3 h at rt. After that, the reaction mixture was diluted with DCM (~100 mL), washed with saturated aq. NaHCO₃ (2×25 mL) and water (2×25 mL). The organic layer was separated, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate-hexane gradient elution) and crystallization (diethyl ether) to afford the title compound as white crystalline solid in 91% yield (0.83 g). Analytical data for 34: $R_f = 0.24$ (ethyl acetate/hexane, 35/65, v/v); m.p. 133.2–133.8 °C (diethyl ether); $[\alpha]_{D}^{20}$ + 17.7 (c = 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ 7.85 (br s, 2H, aromatic), 7.68-7.76 (m, 2H, aromatic), 7.15-7.42 (m, 10H, aromatic), 5.87 (dd, 1H, $J_{3,4}$ = 9.4 Hz, H-3), 5.44 (d, 1H, $J_{1,2}$ = 10.6 Hz, H-1), 4.52–4.72 (m, 4H, 2 × CH_2Ph), 4.32 (dd, 1H, $J_{2,3}$ = 10.4 Hz, H-2), 3.69-3.90 (m, 4H, H-4, 5, 6a, 6b), 2.57-2.80 (m, 2H, SCH₂), 2.15-2.53 (m, 4H, CH₂CH₂), 1.91 (s, 3H, COCH₃), 1.21 (t, 3H, J = 7.4 Hz, SCH₂CH₃) ppm; ¹³C NMR (75 MHz, CDCl₃): *b* 205.6, 171.8, 167.8, 167.5, 138.0, 137.9, 134.0, 133.9, 131.6, 131.5, 128.3 (×4), 127.8 (×2), 127.7 (×2), 127.6 (×2), 123.5, 123.4, 80.8, 79.1, 76.4, 74.5, 74.00, 73.4, 68.6, 54.0, 37.5, 29.4, 27.7, 24.1, 14.9 ppm; HR-FAB MS [M + Na]⁺ calcd for C35H37NO8SNa 654.2138, found 654.2140.

Ethyl 6-O-benzoyl-4-O-benzyl-2-deoxy-3-O-levulinoyl-2-phthalimido-1-thio-β-D-glucopyranoside (35). Benzoyl chloride (3.63 mL, 31.24 mmol) was added to a solution of ethyl 4-Obenzyl-3-O-*tert*-butyldimethylsilyl-2-deoxy-2-phthalimido-1-thioβ-D-glucopyranoside⁹¹ (48, 5.81 g, 10.42 mmol) in pyridine (40 mL) and the resulting mixture was stirred under argon for 12 h at rt. Methanol (~5 mL) was added dropwise, the volatiles were removed under reduced pressure and the residue was coevaporated with toluene (3 × 20 mL). The resulting residue was diluted with CH₂Cl₂ (~300 mL) and washed with 1 N aq. HCl (50 mL), sat. aq. NaHCO₃ (50 mL), and water (2 × 50 mL). The organic phase was separated, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate–CH₂Cl₂–hexane gradient elution) to afford 6-*O*-benzoyl-4-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-phthalimido-1-thio- β -D-gluco-pyranoside (49) as a white foam in 94% yield (6.46 g). Analytical data for 49: $R_{\rm f}$ = 0.54 (ethyl acetate/hexane, 1/3, v/v);

Analytical data for 43. $K_f = 0.34$ (eff)r acetate/frexane, 1/3, 7/9, $[\alpha]_D^{120} + 37.2$ (c = 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ 8.06 (d, 2H, J = 7.3 Hz, aromatic), 7.87 (br s, 2H, aromatic), 7.71–7.79 (m, 2H, aromatic), 7.54–7.63 (m, 1H, aromatic), 7.42–7.52 (m, 2H, aromatic), 7.19–7.34 (m, 5H, aromatic), 5.39 (d, 1H, $J_{1,2} = 10.5$ Hz, H-1), 4.86 (d, 1H, $^2J = 11.4$ Hz, CHPh), 4.49–4.71 (m, 3H, $J_{3,4} = 8.7$ Hz, $J_{6a,6b} = 12$ Hz, H-3, 6a), 4.40 (dd, 1H, H-6b), 4.31 (dd, 1H, $J_{2,3} = 10.2$ Hz, H-2), 3.82–3.91 (m, 1H, $J_{5,6a} = 2.0, J_{5,6b} = 4.7$ Hz, H-5), 3.60 (dd, 1H, $J_{4,5} = 8.7$ Hz, H-4), 2.49–2.73 (m, 2H, SCH₂), 1.15 (t, 3H, J = 7.4 Hz, SCH₂CH₃), 0.75 (s, 9H, Si⁶Bu), -0.20, -0.40 (2 s, 6H, SiMe₂) ppm; ¹³C NMR (75 MHz, CDCl₃): δ , 168.6, 167.6, 166.1, 137.4, 134.2, 133.0, 131.9, 131.5, 129.8, 129.6 (×2), 128.3 (×4), 127.7, 127.3 (×3), 123.6, 123.2, 80.9, 80.1, 77.2, 75.0, 73.4, 63.6, 55.6, 25.6 (×3), 24.1, 17.6, 14.9, -4.2, -4.6 ppm; HR-FAB MS [M + Na]⁺ calcd for C₃₆H₄₃NO₇SSiNa 684.2427, found 684.2434.

BF3-Et2O (1.23 mL, 9.97 mmol) was added to a solution of compound 49 (6.0 g, 9.06 mmol) in dry CH₃CN (50 mL) and the resulting mixture was stirred under argon for 2 h 45 min at 0 °C. Additional CH₃CN (25 mL) and BF₃-Et₂O (0.33 mL, 2.72 mmol) were added, and the reaction mixture was stirred for additional 15 min at 0 °C. After that, the reaction was quenched with sat. aq. NaHCO₃ (5 mL), and the volatiles were removed under reduced pressure. The residue was diluted with CH_2Cl_2 (~300 mL) and washed with brine (2 × 70 mL). The organic phase was separated, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate-hexane gradient elution) to give ethyl 6-O-benzoyl-4-O-benzyl-2-deoxy-2phthalimido-1-thio- β -D-glucopyranoside (50) as a white foam in 86% yield (4.26 g). Analytical data for 50: $R_f = 0.59$ (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_{D}^{20}$ + 10.2 (*c* = 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ 8.07 (d, 2H, J = 7.6 Hz, aromatic), 7.85 (br s, 2H, aromatic), 7.69–7.77 (m, 2H, aromatic), 7.56–7.64 (m, 1H, aromatic), 7.44-7.53 (m, 2H, aromatic), 7.19-7.35 (m, 5H, aromatic), 5.37 (d, 1H, J_{1,2} = 10.4 Hz, H-1), 4.63-4.81 (m, 3H, H-6b, CH_2Ph), 4.49–4.62 (m, 2H, $J_{3,4}$ = 9.3 Hz, H-3, 6a), 4.28 (dd, 1H, J_{2,3} = 10.4 Hz, H-2), 3.81-3.91 (m, 1H, H-5), 3.64 (dd, 1H, J_{4,5} = 9.3 Hz, H-4), 2.54–2.77 (m, 2H, -SCH₂), 2.25 (br s, 1H, OH), 1.18 (t, 3H, J = 7.4 Hz, SCH₂CH₃) ppm; ¹³C NMR (75 MHz, CDCl₃): δ, 168.2, 167.9, 166.2, 137.5, 134.1, 133.1, 131.4 (×2), 129.7, 129.6 (×2), 128.6 (×3), 128.3 (×2), 128.1, 128.0 (×2), 123.7, 123.2, 81.1, 79.0, 77.1 75.0, 72.9, 63.7, 55.7, 24.2, 14.9 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{30}H_{29}NO_7SNa$ 570.1562, found 570.1571.

Levulinic acid (0.424 g, 3.65 mmol), DIC (0.566 mL, 3.65 mmol) and DMAP (44.0 mg, 0.36 mmol) were added to a

solution of compound 50 (1.00 g, 1.83 mmol) in dry DCM (25 mL) and the resulting mixture was stirred under argon for 3 h at rt. The reaction mixture was then diluted with DCM (~100 mL) and washed with saturated aq. NaHCO₃ (2×25 mL) and water (2 \times 25 mL). The organic layer was separated, dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate-hexane gradient elution) to afford the title compound (35) as a white foam in 94% yield (1.11 g). Analytical data for 35: $R_{\rm f} = 0.37$ (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_{\rm D}^{20} + 25.5$ $(c = 1.0, \text{CHCl}_3);$ ¹H NMR (300 MHz, CDCl₃): δ 8.06 (d, 2H, J = 7.6 Hz, aromatic), 7.87 (br s, 2H, aromatic), 7.69-7.78 (m, 2H, aromatic), 7.56-7.65 (m, 1H, aromatic), 7.44-7.53 (m, 2H, aromatic), 7.16-7.32 (m, 5H, aromatic), 5.95 (dd, 1H, J_{3.4} = 9.8 Hz, H-3), 5.52 (d, 1H, J_{1,2} = 10.5 Hz, H-1), 4.59-4.74 (m, 3H, H-6a, CH₂Ph), 4.52 (dd, 1H, J_{6a,6b} = 12.0 Hz, H-6b), 4.35 (dd, 1H, J_{2,3} = 10.4 Hz, H-2), 3.91–4.00 (m, 1H, J_{5.6a} = 4.5 Hz, H-5), 3.83 (dd, 1H, $J_{4.5}$ = 9.0 Hz, H-4), 2.56–2.76 (m, 2H, SCH₂), 2.22–2.55 (m, 4H, CH₂CH₂), 1.91 (s, 3H, COCH₃), 1.18 (t, 3H, J = 7.4 Hz, SCH₂CH₃) ppm; ¹³C NMR (75 MHz, CDCl₃): δ 205.5, 171.9, 167.8, 167.5, 166.1, 137.2, 134.1, 133.9, 133.1, 131.5, 129.7, 129.6 (×2), 128.4 (×3), 128.3 (×2), 127.9 (×3), 123.6, 123.5, 81.0, 77.1, 76.4, 74.6, 74.1, 63.4, 54.0, 37.5, 29.3, 27.7, 24.4, 14.9 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{35}H_{35}NO_9SNa$ 668.1930, found 668.1939.

2,3,4-Tri-O-benzoyl-α-L-**rhamnopyranosyl bromide** (**36**) was obtained from 1,2,3,4-tetra-*O*-benzoyl-L-rhamnopyranose⁹² as reported previously. The analytical data for **36** was in accordance with that previously reported.^{83,92}

Synthesis of oligosaccharides

General method A. A mixture of glycosyl donor (0.046 mmol), glycosyl acceptor (0.036 mmol), and freshly activated molecular sieves (3 Å, 120 mg) in MeNO₂ and CH₂Cl₂ (1.0 mL, 7/3, v/v) was stirred under argon for 1 h at rt. The mixture was cooled to 0 °C, Bi(OTf)₃ (0.016 mmol) was added, and the resulting mixture was stirred for the time specified in Tables at 0 °C. After that, the solids were filtered off through a pad of Celite and rinsed successively with CH2Cl2. The combined filtrate (~40 mL) was washed with water (2×10 mL). The organic phase was separated, dried with MgSO₄, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane or toluene gradient elution) to afford the corresponding glycosides in yields and stereoselectivities listed in Tables and below. Anomeric ratios (or anomeric purity) were determined by comparison of the integral intensities of relevant signals in ¹H NMR spectra.

General method B. A mixture of thioglycoside precursor (0.048–0.051 mmol) and freshly activated molecular sieves (3 Å, 120 mg) in CH_2Cl_2 (1.0 mL) was stirred under argon for 1 h at rt. The mixture was cooled to 0 °C, Br_2 (1.3 equiv.) was added dropwise, and the resulting mixture was stirred for 15 min at 0 °C. The volatiles were then removed under reduced pressure, and the residue was dried *in vacuo* for 1 h. Glycosyl acceptor (0.038–0.041 mmol) was added and the resulting

mixture was dried in vacuo for an additional 30 min. MeNO2 and CH₂Cl₂ (1.0 mL, 7/3, v/v) were added, the resulting mixture was cooled to 0 °C, Bi(OTf)₃ (0.35 equiv. or as indicated in Tables) was added, and the reaction mixture was stirred under argon for the time specified in Tables at 0 °C. After that, the solids were filtered off through a pad of Celite and rinsed successively with CH₂Cl₂. The combined filtrate (~40 mL) was washed with water (2 \times 10 mL). The organic phase was separated, dried with MgSO₄, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate-hexane or toluene gradient elution) to afford the corresponding glycosides in yields and stereoselectivities listed in Tables and below. Anomeric ratios (or anomeric purity) were determined by comparison of the integral intensities of relevant signals in ¹H NMR spectra.

Methyl 6-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-O-benzyl- α -D-glucopyranoside (3) was obtained from donor 1 and acceptor 2⁵⁴ under the general glycosylation method A in 98% yield (β only) as a white amorphous solid. The analytical data for 3 was in accordance with that previously reported.⁵⁵ ¹H NMR (300 MHz, CDCl₃): δ 7.90-7.03 (m, 35H, aromatic), 5.89 (dd, 1H, J_{3',4'} = 9.6 Hz, H-3'), 5.68 (dd, 1H, $J_{4',5'} = 9.7$ Hz, H-4'), 5.60 (dd, 1H, $J_{2',3'} = 9.6$ Hz, H-2'), 4.89 (d, 1H, ${}^{2}J$ = 10.9 Hz, CHPh), 4.82 (d, 1H, $J_{1',2'}$ = 7.8 Hz, H-1'), 4.73 (d, 1H, ${}^{2}J$ = 12.2 Hz, CHPh), 4.67 (d, 1H, ${}^{2}J$ = 11.1 Hz, CHPh), 4.63-4.57 (m, 2H, CH₂Ph), 4.54-4.46 (m, 3H, H-1, 6a', 6b'), 4.27 (d, 1H, ${}^{2}J$ = 11.1 Hz, CHPh), 4.15 (m, 1H, H-5'), 4.11–4.08 (m, 1H, H-6a), 3.88 (dd, 1H, J_{3,4} = 9.3 Hz, H-3), 3.77-3.70 (m, 2H, H-5, 6b), 3.43 (dd, 1H, $J_{2,3}$ = 9.6, $J_{1,2}$ = 3.6 Hz, H-2), 3.36 (dd, 1H, *J*_{4,5} = 9.3 Hz, H-4), 3.20 (s, 3H, OCH₃) ppm.

Methyl 4-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (15) was obtained from donor 1 and acceptor 4⁵⁴ under the general glycosylation method A in 92% yield (β only) as an off-white amorphous solid. The analytical data for 15 was in accordance with that previously reported.^{54,55} ¹H NMR (300 MHz, CDCl₃): δ 7.97–7.17 (m, 35H, aromatic), 5.59 (dd, 1H, *J*_{3',4'} = 9.5 Hz, H-3'), 5.55 (dd, 1H, $J_{2',3'}$ = 9.6 Hz, H-2'), 5.46 (dd, 1H, $J_{4',5'}$ = 8.0 Hz, H-4'), 5.06 (d, 1H, ${}^{2}J$ = 11.2 Hz, CHPh), 4.81–4.75 (m, 3H, 3 × CHPh), 4.75 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.60 (d, 1H, ${}^{2}J$ = 12.2 Hz, CHPh), 4.54 (d, 1H, J_{1,2} = 3.5 Hz, H-1), 4.41 (dd, 1H, J_{6a',6b'} = 12.1 Hz, H-6a'), 4.33 (d, 1H, ${}^{2}J$ = 12.2 Hz, CHPh), 4.27 (dd, 1H, H-6b'), 3.94 (dd, 1H, H-4), 3.88 (dd, 1H, *J*_{3.4} = 9.4 Hz, H-3), 3.71–3.68 (m, 2H, $J_{5',6a'}$ = 3.6, $J_{5',6b'}$ = 5.0 Hz, H-5', 6a), 3.50–3.47 (m, 1H, H-5), 3.46–3.39 (m, 2H, $J_{2,3}$ = 9.1 Hz, H-2, 6b), 3.27 (s, 3H, OCH₃) ppm.

Methyl 3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2,4,6-tri-O-benzyl-α-D-glucopyranoside (16) was obtained from donor 1 and acceptor 5⁵⁴ under the general glycosylation method A in 93% yield (β only) as a white amorphous solid. The analytical data for 16 was in accordance with that previously reported.^{54,55} ¹H NMR (300 MHz, CDCl₃): δ 8.02–7.07 (m, 35H, aromatic), 5.94 (dd, 1H, $J_{3',4'}$ = 9.6 Hz, H-3'), 5.72 (dd, 1H, $J_{4',5'}$ = 9.7 Hz, H-4'), 5.65 (dd, 1H, $J_{2',3'}$ = 9.7 Hz, H-2'), 5.51 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1'), 5.11 (d, 1H, ²J = 10.7 Hz, CHPh), 4.64 (d, 1H, ${}^{2}J$ = 12.2 Hz, *CH*Ph), 4.54–4.32 (m, 6H, $J_{3,4}$ = 9.7 Hz, H-3, H-6a', 6b', 3 × *CH*Ph), 4.26 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 4.14–4.10 (m, 2H, H-5', *CH*Ph), 3.65–3.51 (m, 4H, H-4, 5, 6a, 6b), 3.32 (dd, 1H, $J_{2,3}$ = 9.6 Hz, H-2), 3.22 (s, 3H, OCH₃) ppm.

Methyl 2-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-3,4,6-tri-O-benzyl-α-D-glucopyranoside (17) was obtained from donor 1 and acceptor 6⁵⁴ under the general glycosylation method A in 94% yield (β only) as a white amorphous solid. The analytical data for 17 was in accordance with that previously reported.^{54,55} ¹H NMR (300 MHz, CDCl₃): δ 8.05–6.95 ppm (m, 35H, aromatic), 5.90 (dd, 1H, $J_{3',4'}$ = 9.6 Hz, H-3'), 5.73–5.68 (m, 2H, H-2', 4'), 5.16 (d, 1H, $J_{1',2'}$ = 7.7 Hz, H-1'), 5.05 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 4.74–4.69 (dd, 1H, H-6a'), 4.64–4.55 (m, 3H, 3 × CHPh), 4.50–4.35 (m, 4H, H-6b', 3 × CHPh), 4.16–4.13 (m, 1H, $J_{5',6a'}$ = 1.5, $J_{5',6b'}$ = 4.8 Hz, H-5'), 3.92 (dd, 1H, $J_{3,4}$ = 9.4 Hz, H-3), 3.95–3.88 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2), 3.82–3.58 (m, 4H, H-4, 5, 6a, 6b), 3.35 (s, 3H, OCH₃) ppm.

Methyl 3-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-2-Obenzyl-4,6-O-benzylidene-α-D-glucopyranoside (18) was obtained from donor 1 and acceptor 7⁵⁷ under the general glycosylation method A in 86% yield (β only) as a white amorphous solid. The analytical data for 18 was in accordance with that previously reported.⁵⁸⁻⁶⁰ ¹H NMR (300 MHz, CDCl₃): δ 7.98–7.78 (m, 8H, aromatic), 7.53–7.22 (m, 22H, aromatic), 5.88 (dd, 1H, H-3'), 5.72–5.62 (m, 2H, $J_{2',3'}$ = 9.6 Hz, H-2', 4'), 5.55 (s, 1H, >CHPh), 5.23 (d, 1H, $J_{1',2'}$ = 7.7 Hz, H-1'), 4.58 (d, 1H, ²J = 12.7 Hz, CHPh), 4.49 (dd, 1H, $J_{6a',6b'}$ = 12.3 Hz, H-6a'), 4.32–4.16 (m, 5H, $J_{1,2}$ = 3.6, H-1, 3, 6a, 6b', CHPh), 3.98–3.93 (m, 1H, $J_{5',6b'}$ = 3.4 Hz, H-5'), 3.80–3.57 (m, 3H, H-4, 5, 6b), 3.41 (dd, 1H, $J_{2,3}$ = 9.1 Hz, H-2), 3.26 (s, 3H, OCH₃) ppm.

6-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (19) was obtained from donor 1 and acceptor 8 under the general glycosylation method A in 85% yield (β only) as an off-white amorphous solid. The analytical data for 19 was in accordance with that previously reported.⁶¹ ¹H NMR (300 MHz, CDCl₃): δ 8.04–7.81 (m, 8H, aromatic), 7.57–7.25 (m, 12H, aromatic), 5.90 (dd, 1H, $J_{3',4'} = 9.6$ Hz, H-3'), 5.68 (dd, 1H, H-4'), 5.54 (dd, 1H, $J_{2',3'} = 9.6$ Hz, H-2'), 5.42 (d, 1H, $J_{1,2} = 5.0$ Hz, H-1), 5.05 (d, 1H, $J_{1',2'} = 7.8$ Hz, H-1'), 4.65 (dd, 1H, $J_{6a',6b'} = 12.2$ Hz, H-6a'), 4.51–4.41 (m, 2H, H-3, 6b'), 4.23–4.15 (m, 2H, $J_{5',6b'} = 3.2$ Hz, H-2, 5'), 4.10 (dd, 1H, $J_{4,5} = 8.1$ Hz, H-4), 4.02 (dd, 1H, $J_{6a,6b} = 9.3$ Hz, H-6a), 3.91–3.82 (m, 2H, $J_{5,6b} = 2.4$ Hz, H-5, 6b), 1.37, 1.24, 1.21, 1.19 (4 s, 12H, 4 × CH₃) ppm.

Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-Dglucopyranosyl)-α-D-glucopyranoside (20) was obtained from donor 1 and acceptor 9⁶² under the general glycosylation method A in 85% yield (β only) as a white amorphous solid. The analytical data for 20 was in accordance with that previously reported.^{63 1}H NMR (300 MHz, CDCl₃): δ 8.01–7.78 (m, 14H, aromatic), 7.52–7.26 (m, 21H, aromatic), 6.07 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 5.93 (dd, 1H, $J_{3',4'}$ = 9.6 Hz, H-3'), 5.67 (dd, 1H, $J_{4',5'}$ = 9.7 Hz, H-4'), 5.57 (dd, 1H, $J_{2,3'}$ = 9.5 Hz, H-2'), 5.32 (dd, 1H, $J_{4,5}$ = 9.9 Hz, H-4), 5.09 (dd, 1H, $J_{2,3}$ = 10.2 Hz, H-2), 4.97 (d, 1H, $J_{1',2'}$ = 7.9 Hz, H-1'), 4.93 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.60 (dd, 1H, $J_{6a',6b'}$ = 12.0 Hz, H-6a'), 4.46 (dd, 1H, $J_{5',6a'}$ = 4.9 Hz, H-6b'), 4.22–4.09 (m, 3H, $J_{5',6b'}$ = 2.6 Hz, H-5, 5', 6a), 3.79 (dd, 1H, $J_{6a,6b}$ = 7.8 Hz, $J_{5,6a}$ = 3.4 Hz, H-6b), 2.94 (s, 3H, OCH₃) ppm.

Ethyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (21) was obtained from donor 1 and acceptor 10⁶⁵ under the general glycosylation method A in 16% yield (β only) as an off-white amorphous solid. The analytical data for 21 was in accordance with that previously reported.⁶⁷ ¹H NMR (300 MHz, CDCl₃): δ 8.02–7.23 (m, 35H), 5.88 (dd, 1H, $J_{3,4}$ = 9.6 Hz, H-3), 5.81 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-3'), 5.63 (dd, 1H, $J_{4,5}$ = 9.7 Hz, H-4), 5.51 (dd, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 5.40 (dd, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 4.65 (d, 1H, $J_{1',2'}$ = 10.0 Hz, H-1'), 4.58 (dd, 1H, $J_{6,6b}$ = 12.1 Hz, H-6a), 4.40 (dd, 1H, H-6b), 4.13–3.83 (m, 4H, $J_{5,6a}$ = 3.0, $J_{5,6b}$ = 5.0 Hz, H-5', 6a', 6b'), 2.52 (m, 2H, SCH₂CH₃), 1.10 (t, 3H, SCH₂CH₃) ppm.

p-Tolyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (22) was obtained from donor 1 and acceptor 11 ⁶⁶ under the general glycosylation method A in 42% yield (β only) as a white amorphous solid. The analytical data for 22 was in accordance with that previously reported.⁶⁸ ¹H NMR (300 MHz, CDCl₃): δ 7.93–7.09 (m, 39H, aromatic), 5.84 (dd, 1H, $J_{3',4'}$ = 9.6 Hz, H-3'), 5.67 (dd, 1H, $J_{4',5'}$ = 9.6 Hz, H-4'), 5.58 (dd, 1H, $J_{2',3'}$ = 9.6 Hz, H-2'), 4.93 (d, 1H, $J_{1',2'}$ = 7.8 Hz, H-1'), 4.86–4.80 (m, 2H, 2 × CHPh), 4.74–4.39 (m, 7H, H-1, 6a', 6b', 4 × CHPh), 4.13 (d, 1H, $J_{6a,6b}$ = 11.4 Hz, H-6a), 3.87–3.82 (m, 1H, H-5'), 3.85 (dd, 1H, H-6b), 3.57 (dd, 1H, $J_{3,4}$ = 8.3 Hz, H-3), 3.42–3.33 (m, 3H, $J_{5,6a}$ = 4.2 Hz, H-2, 4, 5), 2.34 (s, 3H, CH₃) ppm.

(3β)-Cholest-5-en-3-yl 2,3,4,6-tetra-O-benzoyl-β-D-glucopyranoside (23) was obtained from donor 1 and acceptor 12 under the general glycosylation method A in 77% yield (β only) as a white solid. The analytical data for 23 was in accordance with that previously reported.⁶⁹ ¹H NMR (300 MHz, CDCl₃): δ 8.01, 7.96, 7.90 and 7.84 (4 d, 8H, aromatic), 7.57–7.26 (m, 12H, aromatic), 5.90 (dd, 1H, $J_{3,4}$ = 9.7 Hz, H-3), 5.63 (dd, 1H, H-4), 5.50 (dd, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 5.22 (d, 1H), 4.94 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), 4.60 (dd, 1H, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.52 (dd, 1H, H-6b), 4.18–4.12 (m, 1H, $J_{5,6a}$ = 3.3, $J_{5,6b}$ = 5.9 Hz, H-5), 3.53 (m, 1H), 2.17–2.16 (m, 2H), 2.02–1.69 (m, 2H), 1.60–1.57 (m, 1H), 0.91 (d, 3H, *J* = 6.5 Hz), 0.89 (s, 3H), 0.87 (d, 3H, *J* = 6.6 Hz), 0.86 (d, 3H, *J* = 6.6 Hz), 0.65 (s, 3H) ppm.

1-Adamantyl 2,3,4,6-tetra-O-benzoyl-β-D-glucopyranoside (24) was obtained from donor 1 and acceptor 13 under the general glycosylation method A in 96% yield (β only) as a white solid. The analytical data for 24 was in accordance with that previously reported.⁷⁰ ¹H NMR (300 MHz, CDCl₃): δ 8.03–7.90 (m, 8H, aromatic), 7.85–7.26 (m, 12H, aromatic), 5.92 (dd, 1H, $J_{3,4}$ = 9.6 Hz, H-3), 5.55 (dd, 1H, $J_{4,5}$ = 10.0 Hz, H-4), 5.49 (dd, 1H, $J_{2,3}$ = 8.0 Hz, H-2), 5.13 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), 4.59 (dd, 1H, $J_{5,6a}$ = 11.9 Hz, H-6a), 4.48 (dd, 1H, H-6b), 4.19 (ddd, 1H, $J_{5,6a}$ = 3.0 Hz, $J_{5,6b}$ = 7.1 Hz, H-5), 2.02 (s, 3H), 1.82 (d, 3H, J = 11.3 Hz), 1.63 (d, 3H, J = 11.4 Hz), 1.50 (dd, 6H) ppm.

Methyl 4,6-di-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-2,3-di-O-benzyl-α-D-glucopyranoside (25) was obtained from donor **1** and acceptor **14**⁷¹ under the general glycosylation method A in 41% yield (β only) as a white amorphous solid. Analytical data for 25: $R_f = 0.36$ (ethyl acetate/hexane, 35/65, v/v); $[\alpha]_{D}^{23}$ + 26.8 (c 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ 8.12-7.77 (m, 16H, aromatic), 7.62-7.21 (m, 34H, aromatic), 5.75 (dd, 1H, J_{3',4'} = 9.5 Hz, H-3'), 5.66 (dd, 1H, J_{3",4"} = 9.7 Hz, H-3"), 5.59–5.53 (m, 2H, H-4', 4"), 5.50–5.43 (m, 2H, J_{2',3'} = 9.5, $J_{2'',3''} = 9.7$ Hz, H-2', 2"), 4.90 (dd, 2H, CH₂Ph), 4.63 (d, 1H, $J_{1',2'}$ = 7.6 Hz, H-1'), 4.59 (d, 1H, ${}^{2}J$ = 10.0 Hz, CHPh), 4.49–4.38 (m, 4H, $J_{1,2}$ = 3.4 Hz, H-1, 6a', 6b', CHPh), 4.32 (d, 1H, $J_{1'',2''}$ = 7.5 Hz, H-1"), 4.07 (dd, 1H, J_{6a",6b"} = 12.7 Hz, H-6a"), 3.99 (dd, 1H, H-6b"), 3.91–3.83 (m, 2H, J_{3.4} = 10.7 Hz, H-3, 6a), 3.66–3.60 (m, 3H, H-5, 5', 6b'), 3.56 (dd, 1H, J_{4,5} = 3.7 Hz, H-4), 3.38 (dd, 1H, $J_{2,3} = 9.4$ Hz, H-2), 3.30 (m, 1H, $J_{5'',6a''} = 2.0$, $J_{5'',6b''} = 3.6$ Hz, H-5"), 3.18 (s, 3H, OCH₃) ppm; 13 C NMR (75 MHz, CDCl₃): δ 166.1 166.0, 165.5 (×2), 165.4, 165.3, 165.2, 164.8, 138.2, 137.9, 133.4, 133.3, 133.2 (×2), 133.0 (×3), 132.9, 130.0, 129.8 (×4), 129.7 (×4), 129.6 (×5), 129.3, 129.2, 129.1 (×2), 128.9, 128.8, 128.5 (×2), 128.4 (×6), 128.3 (×6), 128.2 (×4), 128.1 (×3), 128.0 (×3), 127.9, 127.4 (×3), 127.1, 101.6, 101.5, 97.9, 80.0, 79.6, 79.2, 74.5, 73.6, 73.2, 72.9, 72.6, 72.3, 72.2, 71.8, 69.7, 69.2, 68.9, 68.3, 63.5, 62.4, 55.4 ppm; HR-FAB MS [M + Na]⁺ calcd for C₈₉H₇₈O₂₄Na 1553.4781, found 1553.4755.

Methyl 6-O-(2,3,4,6-tetra-O-benzoyl-β-D-galactopyranosyl)-2,3,4-tri-O-benzyl- α -D-glucopyranoside (37) was obtained from donor 26 and acceptor 2 under the general glycosylation method A in 97% yield (β only) as a white amorphous solid. The analytical data for 37 was in accordance with that previously reported.⁷⁴ ¹H NMR (300 MHz, $CDCl_3$): δ 8.09–7.11 (m, 35H, aromatic), 5.97 (d, 1H, J_{4',5'} = 2.7 Hz, H-4'), 5.85, (dd, 1H, $J_{2',3'}$ = 10.4 Hz, H-2'), 5.60 (dd, 1H, $J_{3',4'}$ = 3.5 Hz, H-3') 4.90 (d, 1H, ${}^{2}J$ = 10.9 Hz, CHPh), 4.76 (d, 1H, $J_{1',2'}$ = 8.0 Hz, H-1'), 4.72 (d, 1H, ${}^{2}J$ = 12.0 Hz, CHPh), 4.69 (d, 1H, ${}^{2}J$ = 10.9 Hz, CHPh), 4.67 (dd, 1H, $J_{6a',6b'}$ = 11.3 Hz, H-6a'), 4.58 (d, 1H, ²J = 12.0 Hz, CHPh), 4.56 (d, 1H, ${}^{2}J$ = 11.2 Hz, CHPh), 4.51 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.40 (dd, 1H, H-6b'), 4.38 (d, 1H, ${}^{2}J$ = 11.2 Hz, CHPh), 4.24–4.19 (m, 1H, $J_{5',6a'}$ = 6.4, $J_{5',6b'}$ = 6.8 Hz, H-5'), 4.21 (dd, 1H, $J_{6a,6b}$ = 12.7 Hz, H-6a), 3.89 (dd, 1H, $J_{3,4}$ = 9.2 Hz, H-3), 3.77-3.74 (m, 2H, J_{5.6a} = 4.2 Hz, H-5, H-6b), 3.40 (dd, 1H, J_{2.3} = 9.6 Hz, H-2), 3.38 (dd, 1H, H-4), 3.20 (s, 3H, OCH₃) ppm.

Methyl 6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (38) was obtained from donor 27 and acceptor 2 under the general glycosylation method A in 92% yield (α only) as a white amorphous solid. The analytical data for 38 was in accordance with that previously reported.^{63 1}H NMR (300 MHz, CDCl₃): δ 8.09–7.25 (m, 35H, aromatic), 6.07 (dd, 1H, $J_{4',5'}$ = 10.0 Hz, H-4'), 5.86 (dd, 1H, $J_{3',4'}$ = 3.1 Hz, H-3'), 5.72 (dd, 1H, $J_{2',3'}$ = 1.7 Hz, H-2'), 5.15 (d, 1H, $J_{1',2'}$ = 1.5 Hz, H-1'), 5.00 (dd, 2H, CH₂Ph), 4.84–4.78 (m, 2H, 2 × CHPh), 4.70–4.61 (m, 4H, $J_{1,2}$ = 3.6 Hz, H-1, 6a', CH₂Ph), 4.40–4.35 (m, 1H, $J_{5',6a'}$ = 4.3 Hz, H-5'), 4.30 (dd, 1H, H-6b'), 4.03 (dd, 1H, $J_{3,4}$ = 9.2 Hz, H-3), 3.96–3.91 (dd, 1H, H-6a), 3.88–3.78 (m, 2H, $J_{5,6a}$ = 4.9 Hz, H-5, 6b), 3.58–3.49 (m, 2H, $J_{4,5}$ = 9.3 Hz, H-2, 4), 3.45 (s, 3H, OCH₃) ppm. Methyl 6-*O*-(2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl)-2,3,4tri-*O*-benzyl- α -D-glucopyranoside (39) was obtained from donor 28 and acceptor 2 under the general glycosylation method B in 71% yield ($\alpha/\beta = 1/1.5$) as a white amorphous solid. The analytical data for 39 was in accordance with that previously reported.^{76 1}H NMR (300 MHz, CDCl₃): δ 7.32–7.16 (m, 35H, aromatic), 4.98–4.35 (m, 15H), 4.34 (d, 1H, $J_{1',2'} = 7.7$ Hz, H-1'), 4.20–3.42 (m, 12H), 3.35–3.32 (2 s, 6H, 2 × OCH₃) ppm.

Methyl 6-O-(2,3,4,6-tetra-O-benzyl-D-galactopyranosyl)-2,3,4tri-O-benzyl-α-D-glucopyranoside (40) was obtained from donor 32 and acceptor 2 under the general glycosylation method A in 97% yield ($\alpha/\beta = 1/1.1$) as a white amorphous solid. The analytical data for 40 was in accordance with that previously reported.⁷⁹ ¹H NMR (300 MHz, CDCl₃): δ 7.33–7.24 (m, 35H, aromatic), 4.99–4.33 (m, 15H), 4.32 (d, 1H, $J_{1',2'} = 7.6$ Hz, H-1'), 4.16–3.41 (m, 12H), 3.28 (2 s, 6H, 3 × OCH₃) ppm.

Methyl 6-O-(2,3,4,6-tetra-O-benzyl-D-mannopyranosyl)-2,3,4tri-O-benzyl- α -D-glucopyranoside (41) was obtained from donor 30 and acceptor 2 under the general glycosylation method B in 91% yield ($\alpha/\beta = 1/1.4$) as an off-white amorphous solid. The analytical data for 41 was in accordance with that previously reported.⁸⁰ ¹H NMR (300 MHz, CDCl₃): δ 7.40–7.12 (m, 35H, aromatic), 5.04–4.41 (m, 16H), 4.18–3.36 (m, 12H), 3.32–3.30 (2 s, 6H, 2 × OCH₃) ppm.

6-O-(2,6-di-O-benzoyl-4-O-benzyl-3-O-tert-butyldi-Methyl methylsilyl-β-D-galactopyranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (42) was obtained from donor 33 and acceptor 2 by general method A in 93% yield (β -only) as a white foam. Analytical data for 42: $R_f = 0.60$ (ethyl acetate/toluene, 12/88, v/v; $[\alpha]_{D}^{23} + 25.3$ (c 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ 7.98 (m, 4H, aromatic), 7.58-7.23 (m, 26H, aromatic), 7.11 (dd, 2H, aromatic), 5.66 (dd, 1H, $J_{2',3'}$ = 8.6 Hz, H-2'), 5.11 (d, 1H, ${}^{2}J$ = 11.3 Hz, CHPh), 4.87 (d, 1H, ${}^{2}J$ = 11.0 Hz, CHPh), 4.71–4.35 (m, 10H, $J_{1,2}$ = 3.3, $J_{1',2'}$ = 8.6 Hz, H-1, 1', 6a', 6b', 3 × CH₂Ph), 4.12 (m, 1H, H-6b), 3.97 (br d, 1H, H-3'), 3.89–3.82 $(m, 3H, J_{2,3} = 10.1 \text{ Hz}, \text{H-3}, 4', 5'), 3.68-3.60 (m, 2H, H-5, 6a),$ 3.39-3.29 (m, 2H, H-2, 4), 3.13 (s, 3H, OCH₃), 0.79 (s, 9H, Si^tBu), 0.12, -0.06 (2 s, 6H, SiMe₂) ppm; ¹³C NMR (75 MHz, CDCl₃): δ 166.3, 165.0, 138.9, 138.3 (×2), 138.2, 133.2, 132.9, 130.2, 129.9, 129.8 (×2), 129.6 (×2), 128.5 (×2), 128.4 (×4), 128.3 (×5), 128.1 (×4), 127.9 (×3), 127.8, 127.7 (×2), 127.6, 127.5, 101.6, 97.7, 82.0, 80.0, 75.5, 75.1, 74.7, 73.3, 72.5, 69.5, 67.8, 63.7, 54.9 (×2), 29.8, 25.6 (×3), 17.9 (×2), -3.9, -5.0 ppm; HRMS $[M + Na]^+$ calcd for $[C_{61}H_{70}O_{13}SiNa]^+$ 1061.4483 found 1061.4500.

Methyl 6-O-(4,6-di-O-benzyl-2-deoxy-3-O-levulinoyl-2-phthalimido-β-D-glucopyranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (43) was obtained from donor 34 and acceptor 2 by general method B in 73% yield (β-only) as a white foam. Analytical data for 43: $R_f = 0.60$ (ethyl acetate/hexane, 1/1, v/v); $[\alpha]_D^{23} + 30.6$ (c 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ 7.75–7.18 (m, 27H, aromatic), 7.01 (dd, 2H, J = 3.2 Hz, aromatic), 5.82 (dd, 1H, $J_{3',4'} = 8.3$ Hz, H-3'), 5.40 (d, 1H, $J_{1',2'} = 8.5$ Hz, H-1'), 4.85 (d, 1H, ²J = 10.8 Hz, CHPh), 4.73–4.53 (m, 7H, 7 × CHPh), 4.42–4.27 (m, 3H, $J_{1,2} = 3.5$, $J_{2',3'} = 9.6$, ²J = 10.6 Hz, H-1, 2', CHPh), 4.15–4.10 (m, 2H, H-6b, CHPh), 3.87–3.74 (m, 5H, $J_{3,4} = 9.2$ Hz, H-3, 4', 5', 6a', 6b'), 3.66–3.62 (m, 2H, H-5, 6a), 3.38 (dd, 1H, $J_{2,3} = 9.7$ Hz, H-2), 3.26 (dd, 1H, $J_{4,5} = 9.2$ Hz, H-4), 3.13 (s, 3H, OCH₃), 2.20–2.45 (m, 4H, CH₂CH₂), 1.91 (s, 3H, COCH₃) ppm; ¹³C NMR (75 MHz, CDCl₃): δ 205.7, 172.0, 168.2, 167.5, 138.7, 138.2 138.1, 137.9, 137.8, 133.8, 131.5, 128.5 (×2), 128.4 (×6), 128.3 (×2), 128.2 (×2), 128.0 (×3), 127.9 (×4), 127.8 (×3), 127.7 (×5), 127.6, 123.4, 98.2, 97.9, 81.9, 79.7, 77.7, 75.8, 75.1, 74.8, 74.6, 73.5 (×2), 73.4, 73.3, 69.3, 68.6 (×2), 54.9, 37.6, 29.8, 29.5, 27.8 ppm; HRMS [M + Na]⁺ calcd for [C₆₁H₆₃NO₁₄Na]⁺ 1056.4146 found 1056.4164.

Methyl 6-O-(6-O-benzoyl-4-O-benzyl-2-deoxy-3-O-levulinoyl-2-phthalimido-β-D-glucopyranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (44) was obtained from donor 35 and acceptor 2 by general method B in 79% yield (β -only) as a white foam. Analytical data for 44: $R_f = 0.60$ (ethyl acetate/hexane, 45/55, v/v); $[\alpha]_{D}^{23}$ + 33.7 (c 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ 8.06 (d, 2H, J = 7.5 Hz, aromatic), 7.77-7.21 (m, 25H, aromatic), 7.01–6.99 (dd, 2H, J = 3.1 Hz, aromatic), 5.89 (dd, 1H, J_{3',4'} = 8.8 Hz, H-3'), 5.46 (d, 1H, $J_{1',2'}$ = 8.5 Hz, H-1'), 4.83 (d, 1H, ${}^{2}J$ = 10.8 Hz, CHPh), 4.72-4.51 (m, 7H, H-6a', 6b', 5 × CHPh), 4.39-4.35 (m, 3H, $J_{1,2}$ = 3.4 Hz, H-1, 2', CHPh), 4.11–4.05 (m, 2H, H-6b, CHPh), 3.93 (m, 1H, H-5'), 3.87–3.78 (m, 2H, J_{3,4} = 8.9 Hz, H-3, 4'), 3.68–3.61 (m, 2H, H-5, 6a), 3.37 (dd, 1H, J_{2,3} = 9.7 Hz, H-2), 3.23 (dd, 1H, J_{4,5} = 9.6 Hz, H-4), 3.11 (s, 3H, OCH₃), 2.48–2.29 (m, 4H, CH₂CH₂), 1.91 (s, 3H, COCH₃) ppm; ¹³C NMR (75 MHz, CDCl₃): δ 205.7 (×2), 172.0 (×2), 166.2, 138.7, 138.1, 137.7, 137.3, 133.9, 133.2, 131.4, 129.8 (×3), 128.5 (×7), 128.4 (×3), 128.3 (×3), 128.1 (×3), 128.0 (×6), 127.9 127.7 (×3), 127.6, 123.4, 98.3, 97.9, 81.9, 79.6, 76.6, 75.7, 74.8, 74.7, 73.4 (×2), 73.2, 69.2, 68.6, 63.4, 54.9, 37.6, 29.5, 27.8 ppm; HRMS [M + Na^{+}_{1} calcd for $[C_{61}H_{61}NO_{15}Na^{+}_{1}$ 1070.3939 found 1070.3954.

Methyl 6-O-(2,3,4-tri-O-benzoyl-α-ι-rhamnopyranosyl)-2,3,4tri-O-benzyl-α-D-glucopyranoside (45) was obtained from donor 36 and acceptor 2 under the general glycosylation method A in 79% yield (α only) as a white foam. The analytical data for 47 was in accordance with that previously reported.⁸⁴ ¹H NMR (300 MHz, CDCl₃): δ 8.08 (d, 2H, *J* = 7.6 Hz, aromatic), 7.97 (d, 2H, *J* = 7.6 Hz, aromatic), 7.81 (d, 2H, *J* = 7.7 Hz, aromatic), 7.61–7.23 (m, 24H, aromatic), 5.80 (dd, 1H, *J*_{3',4'} = 10.1 Hz, H-3'), 5.67–5.60 (m, 2H, *J*_{2',3'} = 3.4 Hz, *J*_{4',5'} = 9.9 Hz, H-2', 4'), 5.05–4.93 (m, 3H, *J*_{1',2'} = 5.3 Hz, H-1', CH₂Ph), 4.87–4.81 (m, 2H, CH₂Ph), 4.72–4.61 (m, 3H, *J*_{1,2} = 2.9 Hz, H-1, CH₂Ph), 4.16 (m, 1H, *J*_{5',6'} = 6.2 Hz, H-5'), 4.05 (dd, 1H, *J*_{3,4} = 9.4 Hz, H-3), 3.97–3.94 (m, 1H, H-6a), 3.86 (m, 1H, H-5), 3.65–3.52 (m, 3H, *J*_{2,3} = 9.2 Hz, *J*_{4,5} = 10.3 Hz, H-2, 4, 6b), 3.46 (s, 3H, OCH₃), 1.31 (d, 3H, H-6') ppm.

Conflicts of interest

There are no conflicts to declare.

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