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ARTICLE

A versatile approach to the synthesis of mannosamine glycosides

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O-Picoloyl protecting groups at remote positions can affect the stereoselectivity of glycosylation by means of the H-bond-mediated aglycone delivery (HAD) pathway. A new practical method for the stereoselective synthesis of β-glycosides of mannosamine is reported. The presence of the *O*-picoloyl group at the C-3 position of a mannosamine donor can provide high or complete stereocontrol. The method was also utilized for the synthesis of a biologically relevant trisaccharide related to the capsular polysaccharide *of Streptococcus pneumoniae* serotype 4. Also reported herein is a method to achieve complete α-manno stereoselectivity with mannosamine donors equipped with 3-*O*-benzoyl group.

Introduction

While understanding the roles and composition of carbohydrates is difficult, their synthesis has been particularly challenging. Among reactions employed in glycosciences, chemical glycosylation remains cumbersome even with the aid of modern methods. The formation of many glycosidic bonds can now be achieved, and the highest levels of stereocontrol is typically reached by means of the neighboring group participation. It is well established that the neighboring group participation can be achieved with esters,[1] but more recent methodologies introduced participation by means of thioether auxiliaries[2-9] and picolinyl (Pic) or similar ether groups.[10-16] Glycosylations in the absence of the neighboring group participation that proceed with complete stereoselectivity are still rare.[17] Although a concept of switchable stereoselectivity has been explored in a variety of ways,[18-24] there is no universal method that would work for the synthesis of all types of glycosidic linkages.

We have previously reported that 3, 4, or 6-*O*-picolinyl or picoloyl (Pico) remote protecting groups can provide high *syn*-selectivities.[25] This result implied a unique mode of action by which the remote Pic/Pico substituents influence the stereoselectivity as opposed to 2-Pic donors that provide exclusive *anti*- (1,2-*trans*) selectivity via direct participation. To explain this result, we acquired experimental evidence consistent with a reaction pathway that we named H-bond-mediated Aglycone Delivery (HAD). For this pathway to occur, the glycosyl acceptor should establish hydrogen bonding with the Pic/Pico nitrogen of the donor. Upon activation of the donor, the acceptor is delivered to form the glycosidic linkage from the *syn*-face with respect to the Pic/Pico group. Among a number of targets, the HAD reaction has been applied to α-glucosylation via 4-Pico donor,[25] and its utility was demonstrated by the synthesis of α-glucans.[26]

Mannose has a strong propensity to form 1,2-trans or α-linkages due to the anomeric effect that is particularly strong in this sugar series.[27] Nevertheless, some uncontrolled reactions can lead to anomeric mixtures. In contrast, α-mannosides are best obtained from glycosyl donors equipped with the neighboring participating ester group at C-2. A few methods for the synthesis of β-mannosides have also been developed. Besides indirect methods involving intramolecular glycosylations[28] or epimerization,[29] Crich's method remains a very powerful tool for the direct formation of 1,2-cis or β-mannosides. In accordance with the Crich method, the successful formation of β-mannosides typically requires low reaction temperatures, powerful promoter systems, and the presence of a 4,6-*O*-benzylidene acetal protecting group.[30-34] We have previously investigated the effect of a remote 3-*O*-picoloyl group and demonstrated that direct β-mannosylation reactions could be conducted with high facial *syn* selectivity for attack of the glycosyl acceptor.[35] In this application of the HAD method, high β-manno stereoselectivity could be achieved even at the ambient temperature with or without 4,6-*O*-benzylidene group. The mechanism through which the HAD pathway takes place is still unclear as the all-axial oxacarbenium conformation, that was deemed necessary for the D-gluco-configured donors, is not possible herein. That is due to the conformational strain attributed to the benzylidene protecting group. The utility of this approach was applied in the synthesis of a mannan containing both primary and secondary β-mannosidic linkages.[35] More recently, the HAD mannosylation was applied to the synthesis of the N-glycan core structure using both conventional and automated solid phase synthesis approaches.[36]

N-Acetylmannosamine or 2-acetamido-2-deoxy-mannopyranose (ManNAc) residue is a commonly found component in bacterial polysaccharides.[37] ManNAc is also the key intermediate in the biosynthesis of *N*-acetylneuraminic

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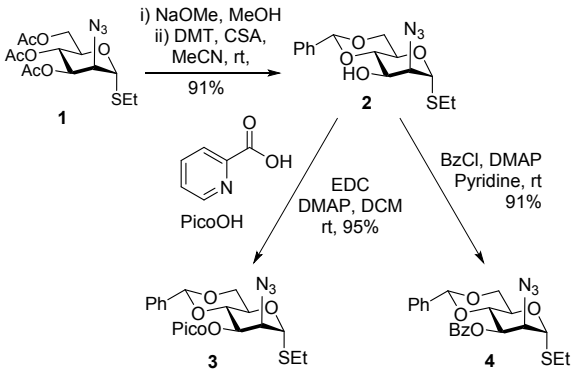
acid.[38] The occurrence of ManNAc residues in biologically relevant oligosaccharides and asparagine-linked glycopeptides[28] makes it an interesting candidate of study. A few pathways for the synthesis of β-glycosides of ManNAc have also been developed. However, early studies showed that the direct application of Crich's method that gives excellent stereoselectivity in β-mannosylation does not really work that well for mannosamine. Various labs reported the relaxed stereoselectivity in glycosidation of 2-azidomannosyl donors.[39, 40] As a consequence, only a handful of articles dealing with the synthesis β-mannosamine glycosides have been published in the last decade, whereas hundreds of examples have been published on the synthesis of neutral β-mannosides. A vast majority of recent protocols involve indirect methods,[41] including those wherein β-glucosides are formed first followed by post-glycosylational inversion of configuration at C-2.[42-44] Yu and coworkers reported a comparison data showed a significant decline in β-manno stereoselectivity from α/β = 1/10 achieved with 2-O-benzyl donors to α/β = 1/4.9 with 2-azido donors under the same reaction conditions.[45] Very recently, Boons and co-workers managed to achieve the desired target by direct β-mannosylation. Although these reactions proceeded with commendable yields of 71-74%, the stereoselectivity was poor α/β = 1/1.1-1.2). However, the authors have managed to separate the diastereomers and the desired β-mannoside was carried forward.[46] Reported herein is our preliminary investigation of the HAD glycosidation of mannosamine donors.

Results and discussion

Having anticipated that the synthesis of 1,2-cis ManNAc containing sugar derivatives will follow similar principles to those established for the HAD synthesis of neutral β-mannosides,[35] we endeavored to prepare mannosamine donor **3** equipped with the Pico group at C-3 position along with the 4,6-*O*-benzylidene acetal tether. Mannosamine derivative **1** equipped with the 2-azido group was selected as a convenient starting material. The synthesis of this building block was recently developed by our group,[47] but there are other methods that can be used to obtain ManNAc from D-arabinose,[48] D-glucosamine under alkaline conditions,[49] or by means of diazotransfer reaction from mannosamine.[50, 51] As depicted in Scheme 1, building block **1** was deacetylated with NaOMe in MeOH followed by benzylidene introduction with dimethoxytoluene (DMT) in the presence of camphorsulfonic acid (CSA) to afford 3-OH derivative **2** in 91% yield. Compound **2** was then picoloylated with picolinic acid in the presence of EDC and DMAP to afford the desired 3-Pico glycosyl donor **3**. With the main intention to acquire a neutral glycosyl donor for comparison, we also benzoylated intermediate **2** with benzoyl chloride in the presence of DMAP and pyridine. 3-*O*-Benzoylated (3-Bz) donor **4** was obtained in 91% yield.

Scheme 1. Synthesis of mannosamine donors 3 and 4

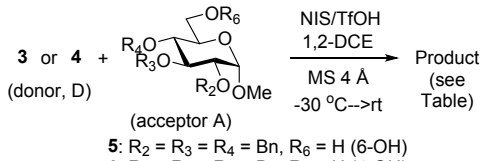


With the anticipation that the remote Pico group in donor **3** will act as the hydrogen bond acceptor for the incoming nucleophile and hence lead to the preferential formation of β-mannosides, we set up a series of glycosylations with standard glycosyl acceptors **5**-**8**[52] (Table 1). When donor **3** was reacted with the primary acceptor **5** in the presence of NIS/TfOH promoter system under regular concentration (50 mM of the donor) in 1,2-DCE, disaccharide **9** was obtained in a high yield of 82% albeit unremarkable stereoselectivity of α/β = 1/5.0 (entry 1, Table 1). This was not entirely unexpected because the HAD reactions are best performed under ten-fold dilution conditions (5.0 mM of the donor). To our delight, the high dilution experiment produced disaccharide **9** in a high yield of 91% and excellent β-manno stereoselectivity (α/β = 1/21, entry 1). The high dilution did not seem to have any effect on the reaction rate, a common observation for HAD reactions, and both glycosylations were completed in 20 h. The HAD pathway is absent in the 3-Bz (control) donor **4** that was expected to provide no stereoselectivity. To our surprise, reactions between 3-Bz donor **4** and acceptor **5** yielded the respective disaccharide **10** with exclusive α-stereoselectivity. Practically the same outcome in terms of yields (82-89%) and stereoselectivities (α-only) was obtained in both regular concentration and high dilution experiments (entry 2). Both experiments were relatively swift and completed in 1 h. While somewhat unexpected, the precedent for completely α-stereoselective synthesis of manno-[53] and mannosamine glycosides in the absence of the neighboring groups participation exists.[54]

When glycosylation of secondary 4-OH acceptor **6** was performed with donor **3** in the presence of NIS/TfOH promoter system under regular concentration (50 mM of the donor) in DCE, disaccharide **11** was obtained in 81% yield with commendable β-manno stereoselectivity (α/β = 1/11, entry 3). The high ten-fold dilution experiment (5 mM of the donor) produced disaccharide **11** in 69% yield and further improved β-manno stereoselectivity (α/β = 1/14, entry 3). It required 19 h for both glycosylations to complete. When the glycosylations were performed with 3-Bz donor **4** and acceptor **6**, disaccharide **12** was obtained with exclusive α-stereoselectivity in 1 h. Good yields (75-79%) and complete α-manno stereoselectivity was achieved for both regular concentration and high dilution conditions (entry 4). Very similar trends were achieved in

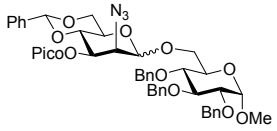
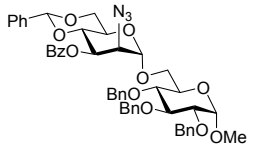
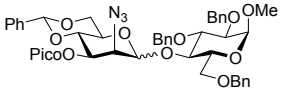
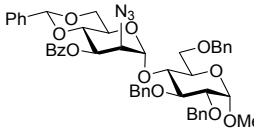
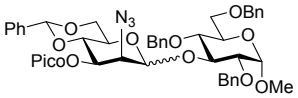
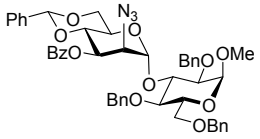
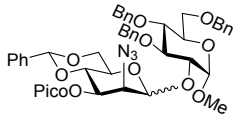
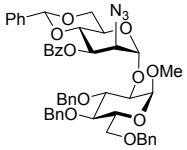
glycosylations of secondary 3-OH acceptor **7** and 2-OH acceptor **8** with donors **3** and **4** in the presence of NIS/TfOH promoter system. The corresponding disaccharides **13-16** were achieved in commendable yields and high or even complete stereoselectivities, either α- or β- depending on the type of the protecting group at C-3 used (entries 5-8). disaccharide **14** was formed in 70% yield under regular 50 mM concentration and in 57% yield in high dilution conditions with exclusive α-stereoselectivity within 4 h (entry 6).

Table 1. Glycosidation of donors 3 and 4 with glycosyl acceptors 5-8



(acceptor A)

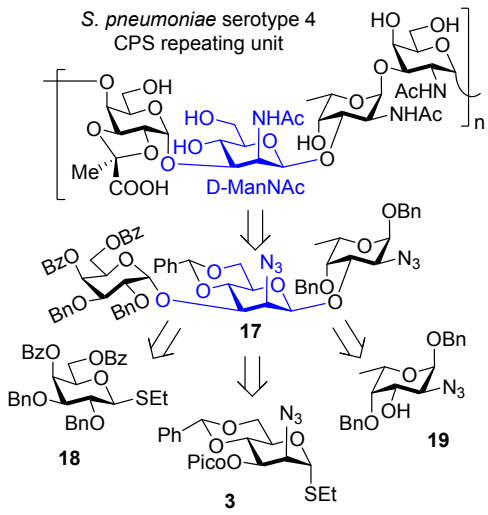
5: $R_2 = R_3 = R_4$ = Bn, R_6 = H (6-OH)
6: $R_2 = R_3 = R_6$ = Bn, R_4 = H (4-OH)
7: $R_2 = R_4 = R_6$ = Bn, R_3 = H (3-OH)
8: R_2 = H, $R_3 = R_4 = R_6$ = Bn (2-OH)

Entry	D + A (time)	Product: yield, stereoselectivity (concentration of D)	$J_{C1',H1'}$ δ H3'
1	**3** + **5** (20 h)	 **9**: 82%, α/β = 1/5.0 (50 mM) 97%, α/β = 1/21 (5 mM)	160 Hz 5.32 ppm
2	**4** + **5** (1 h)	 **10**: 82%, α/β > 25/1 (50 mM) 89%, α/β > 25/1 (5 mM)	208 Hz 5.72 ppm
3	**3** + **6** (19 h)	 **11**: 81%, α/β = 1/11 (50 mM) 69%, α/β = 1/14 (5 mM)	159 Hz 5.10 ppm
4	**4** + **6** (1 h)	 **12**: 79%, α/β > 25/1 (50 mM) 75%, α/β > 25/1 (5 mM)	220 Hz 5.70 ppm
5	**3** + **7** (18 h)	 **13**: 76%, α/β = 1/6.0 (50 mM) 61%, α/β = 1/11 (5 mM)	162 Hz 5.30 ppm
6	**4** + **7** (4 h)	 **14**: 70%, α/β > 25/1 (50 mM) 57%, α/β > 25/1 (5 mM)	230 Hz 5.72 ppm
7	**3** + **8** (19 h)	 **15**: 86%, α/β = 1/9.0 (50 mM) 87%, α/β < 1/25 (5 mM)	161 Hz 5.25 ppm
8	**4** + **8** (2 h)	 **16**: 78%, α/β > 25/1 (50 mM) 82%, α/β > 25/1 (5 mM)	227 Hz 5.87 ppm

This reversible stereoselectivity was a useful outcome, and to acquire ultimate proof for the stereoselectivity observed, we conducted a series of structural studies using NMR spectroscopy. The assignment of the anomeric configuration was conducted by measuring the $J_{C1',H1'}$ coupling constant. We detected that $J_{C1',H1'}$ coupling constants for all synthesized β-mannosides were in agreement with those reported for neutral, 2-oxygenated β-mannosides (~160 Hz).[55, 56] Observed herein are $J_{C1',H1'}$ coupling constants within 159-162 Hz range for all β-mannosamine glycosides (Table 1). The previously reported $J_{C1',H1'}$ coupling constants for α-mannosides were typically at least 10 Hz higher than those of the corresponding β-mannosides (170 Hz or greater).[56] Observed herein were $J_{C1',H1'}$ coupling constants in the range of 208-230 Hz. Although these experiments ultimately confirmed α-mannosamine configuration of glycosides obtained with 3-Bz donor **4**, these values were considerably higher than those expected for 2-oxygenated α-mannosides. This might be attributed by the protecting groups present in the donor or reasons yet unknown. In this context, we have also noticed another useful trend that was very instrumental and reliable in assessing the anomeric configuration based on standard proton NMR experiments. Thus, while chemical shift δ for H-3′ of β-anomers was about or below 5.30 ppm, the corresponding signal in α-anomer always appeared shifted downfield by at least 0.4 ppm. This, δ for H-3′ for α-anomers was at or above 5.70 ppm (Table 1).

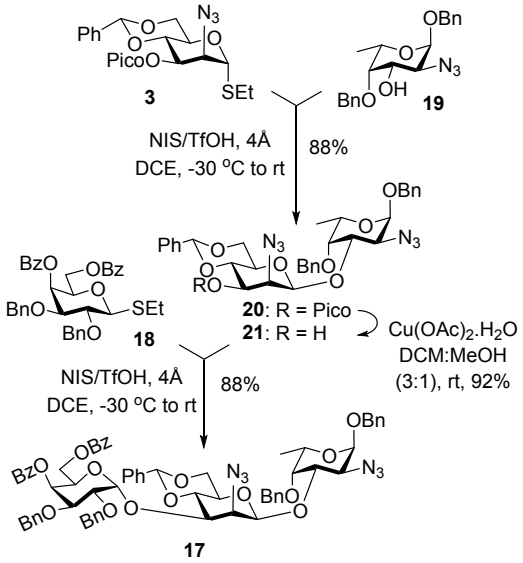
With success in obtaining challenging 1,2-cis β-glycosides of mannosamine, we applied this finding to the synthesis of trisaccharide sequence **17** corresponding to *Streptococcus pneumoniae* serotype 4 capsular polysaccharide. We anticipated that this sequence could be obtained from building blocks **3**, **18** and **19** in accordance with the retrosynthetic analysis depicted in Scheme 2. The synthesis of D-galactose donor **18** and L-fucosamine acceptor **19** is detailed in the supporting information. To address the anticipated challenge of stereoselective 1,2-*cis* galactosylation, we strategically placed benzoyl ester groups at C-4 and C-6 of the galactosyl donor **18** that are often beneficial for enhancing α-stereoselectivity.[57, 58]

Scheme 2. Repeating unit of CPS *S. pneumoniae* serotype 4 and retrosynthetic analysis of trisaccharide 17



As depicted in Scheme 3, glycosidation of mannosamine donor **3** (5 mM) with fucosyl acceptor **19** was carried in the presence of NIS/TfOH promoter system at -30 °C to rt in DCE. This coupling gave the desired disaccharide **20** in 88% yield with exclusive β-manno stereoselectivity. The $J_{C1',H1'}$ coupling constant of 159 Hz confirmed the β-manno configuration achieved in this reaction. It should be noted that glycosylation of **19** with control donor **4** produced the corresponding disaccharide **22** with exclusive α-stereoselectivity. The Pico substituent in **20** was selectively removed with $Cu(OAc)_2$-H_2O in DCM/MeOH.[35] The resulting disaccharide acceptor **21** was subjected to glycosylation with galactosyl donor **18** to afford the target trisaccharide **17** in a good yield of 88% and excellent stereoselectivity (α/β > 20/1).

Scheme 3. Application of donor 3 in the synthesis of pneumococcal trisaccharide 17



Conclusions

A new practical method for the stereoselective synthesis of both α- and β-glycosides of mannosamine is reported. The presence of the 3-Pico of a mannosamine donor can provide high or complete stereocontrol for β-mannosylation. High or even complete facial stereoselectivity was attributed to the intermediacy of the H-bonding *via* the nitrogen atom of the Pico substituent. The method was also utilized for the synthesis of biologically relevant trisaccharide related to the capsular polysaccharide *of Streptococcus pneumoniae* serotype 4. In contrast, exclusive α-manno stereoselectivity was achieved with mannosamine donors equipped with 3-*O*-benzoyl group. This complete reversal of stereoselectivity could be a result of the remote participation of 3-Bz substituent, as proposed by Crich[53] for regular mannosides, Nifantiev[59-62] and Kim[63] for other sugar series, or alternate forces. To verify the direct effect of the 3-Bz group on stereoselectivity, we glycosidated analogous 3-*O*-benzylated donor[39] with glycosyl acceptor **5** using standard high dilution reaction (50 mM) conditions. This reaction was non-stereoselective, and the corresponding disaccharide was isolated in a good yield of 85% albeit poor stereoselectivity (α/β = 1/1.6). Further investigation of the mechanisms and the kinetic profile of these reactions is currently underway in our laboratory.

Experimental

General. Column chromatography was performed on silica gel 60 (70-230 mesh), reactions were monitored by TLC on Kieselgel 60 F254. 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. CH_2Cl_2 and $ClCH_2CH_2Cl$ (1,2-DCE) were distilled from CaH_2 directly prior to application. Anhydrous DMF was used as is. Molecular sieves (3 Å or 4 Å), used for reactions, were crushed and activated *in vacuo* at 390 °C during 8 h in the first instance and then for 2-3 h at 390 °C directly prior to application. Optical rotations were measured at 'Jasco P-2000' polarimeter. Unless noted otherwise, ^{1}H-NMR spectra were recorded in $CDCl_3$ at 300 or 600 MHz, ^{13}C-NMR spectra were recorded in $CDCl_3$ at 75 MHz. Two-dimensional heteronuclear *J*-resolved spectra (HETERO2DJ)[56] were recorded in $CDCl_3$ at 600 MHz.

Synthesis of Glycosyl Donors 3 and 4

Ethyl 2-azido-4,6-*O*-benzylidene-2-deoxy-1-thio-α-D-mannopyranoside (2). A freshly prepared 1 N solution of NaOMe in MeOH (~2 mL) was added to a solution of ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-1-thio-α-D-mannopyranoside[47] (**1**, 1.70 g, 4.64 mmol) in MeOH (20 mL) until pH ~ 9 and the resulting mixture was stirred at rt for 30 min. After that, the reaction mixture was neutralized with Dowex (H^+), the resin was filtered-off and rinsed successively with MeOH (7 x 5 mL). The combined filtrate (~75 mL) was concentrated under reduced pressure and dried *in vacuo*. The crude residue containing deacetylated mannosyl derivative (1.20 g, 4.81 mmol) was

dissolved in MeCN (60 mL), benzaldehyde dimethyl acetal (DMT, 1.4 mL, 9.24 mmol) and camphorsulfonic acid (CSA, 54 mg, 0.231 mmol) were added, and the resulting mixture was stirred at rt for 1 h. After that, the reaction mixture was neutralized with triethylamine (~ 5 mL) and the volatiles were removed under reduced pressure. The residue was diluted with CH_2Cl_2 (~50 mL) and washed with water (10 mL), sat. aq. $NaHCO_3$ (10 mL) and water (2 x 10 mL). The organic layer was separated, dried with Na_2SO_4, 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 as a pale-yellow syrup in 91% yield (1.42 g, 4.36 mmol). Analytical data for **2**: R_f = 0.70 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ +38.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52-7.46 (m, 2H, aromatic), 7.41-7.36 (m, 3H, aromatic), 5.57 (s, 1H, C*H*Ph), 5.29 (d, 1H, $J_{1,2}$ = 1.0 Hz, H-1), 4.24-4.16 (m, 3H, H-3, 5, 6a), 4.05 (dd, 1H, $J_{2,3}$ = 3.9 Hz, H-2), 3.92 (dd, 1H, $J_{3,4}$ = 9.4 Hz, H-4), 3.87-3.78 (m, 1H, H-6b), 2.74-2.55 (m, 3H, SC*H*$_2$CH$_3$, OH), 1.31 (t, 3H, *J* = 7.4 Hz, SCH$_2$C*H*$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.1, 129.5, 128.6 (x2), 126.4 (x2), 102.0, 83.4, 79.4, 69.4, 68.6, 65.2, 63.9, 25.7, 15.0 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{15}H_{20}N_3O_4S$ 338.1166; found 338.1169.

Ethyl 2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-picoloyl-1-thio-α-D-mannopyranoside (3). Picolinic acid (0.60 g, 4.71 mmol), EDC (0.90 g, 4.71 mmol) and DMAP (77 mg, 0.63 mmol) were added to a solution of compound **2** (1.10 g, 3.26 mmol) in dry CH_2Cl_2 (15 mL), and the resulting mixture was stirred under argon for 3 h at rt. After that, the reaction mixture was diluted with CH_2Cl_2 (~ 20 mL) and washed with water (10 mL), sat. aq. $NaHCO_3$ (10 mL), and water (2 x 10 mL). The organic phase was separated, dried with Na_2SO_4, 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 as a white amorphous solid in 95% yield (1.32 g, 2.98 mmol). Analytical data for **3**: R_f = 0.50 (ethyl acetate/hexane, 1/1, v/v); $[\alpha]_D^{22}$ + 29.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.81-8.79 (m, 1H, aromatic), 8.17-8.14 (m, 1H, aromatic), 7.87-7.81 (m, 1H, aromatic), 7.50-7.41 (m, 3H, aromatic), 7.35-7.29 (m, 3H, aromatic), 5.74 (dd, 1H, $J_{3,4}$ = 9.9 Hz, H-3), 5.61 (s, 1H, C*H*Ph), 5.38 (d, 1H, $J_{1,2}$ = 0.9 Hz, H-1), 4.43 (m, 1H, $J_{5,6a}$ = 4.7 Hz, $J_{5,6b}$ = 10.1 Hz, H-5), 4.39 (dd, 1H, $J_{2,3}$ = 3.9 Hz, H-2), 4.34 (dd, 1H, $J_{4,5}$ = 9.7 Hz, H-4), 4.26 (dd, 1H, $J_{6a,6b}$ = 10.4 Hz, H-6a), 3.90 (dd, 1H, H-6b), 2.69 (m, 2H, SC*H*$_2$CH$_3$), 1.34 (t, 3H, *J* = 7.4 Hz, SCH$_2$C*H*$_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.1, 150.3, 147.2, 137.1 (x2), 129.2, 128.3 (x2), 127.3, 126.3 (x2), 125.7, 102.1, 83.4, 76.4, 71.5, 68.6, 64.7, 63.6, 25.6, 14.9 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{21}H_{23}N_4O_5S$ 443.1395; found 443.1384.

Ethyl 2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-1-thio-α-D-mannopyranoside (4). Benzoyl chloride (0.55 mL, 4.77 mmol) and DMAP (58 mg, 0.48 mmol) were added to a solution of compound **2** (0.80 g, 2.38 mmol) in pyridine (20 mL), and the resulting mixture was stirred under argon for 2 h at rt. After that, the reaction was quenched with MeOH (~5 mL), the volatiles were removed under reduced pressure, and the residue was co-evaporated with toluene. The resulting residue was diluted with CH_2Cl_2 (~20 mL) and washed with water (10 mL), 1 N aq. HCl (10 mL) and water (2 x 10 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate - hexane gradient elution) to give the title compound as a colorless amorphous solid in 91% yield (0.96 g, 2.26 mmol). Analytical data for **4**: R_f = 0.80 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ +118.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12-8.08 (m, 2H, aromatic), 7.62-7.54 (m, 1H, aromatic), 7.49-7.40 (m, 4H, aromatic), 7.35-7.30 (m, 3H, aromatic), 5.68 (dd, 1H, $J_{3,4}$ = 10.1 Hz, H-3), 5.62 (s, 1H, C*H*Ph), 5.36 (d, 1H, *J* = 0.7 Hz, H-1), 4.46-4.37 (m, 2H, $J_{2,3}$ = 3.8 Hz, $J_{5,6a}$ = $J_{5,6b}$ = 5.0 Hz, H-2, 5), 4.29-4.22 (m, 2H, $J_{4,5}$ = 9.8 Hz, $J_{6a,6b}$ = 4.4 Hz, H-4, 6a), 3.91 (dd, 1H, H-6b), 2.79-2.57 (m, 2H, SC*H*$_2$CH$_3$), 1.33 (t, 3H, *J* = 7.4 Hz, SCH$_2$C*H*$_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.7, 137.1, 133.6, 130.1 (x2), 129.2 (x2), 128.6 (x2), 128.4 (x2), 126.3 (x2), 102.0, 83.5, 76.7, 70.8, 68.6, 64.7, 63.9, 25.6, 14.9 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{22}H_{24}N_3O_5S$ 442.1436; found 442.1431.

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A general procedure for glycosylation in the presence of NIS/TfOH. A mixture of a glycosyl donor (0.06 mmol), glycosyl acceptor (0.05 mmol), and freshly activated molecular sieves (4Å, 100 mg for 50 mM or 200 mg for 5.0 mM reactions) in 1,2-DCE (1.0 mL for 50 mM or 10 mL for 5.0 mM reactions) was stirred under argon for 1 h at rt. The mixture was then cooled to -30 °C, *N*-iodosuccinimide (NIS, 0.12 mmol) and trifluoromethanesulfonic acid (TfOH, 2.0 µL, 0.02 mmol) were added, and the resulting mixture was allowed to warm to ambient temperature and stirred for 16 h at rt. After that, the solids were filtered off and was washed sucessively with CH_2Cl_2. The combined filtrate (~30-40 mL) was washed with water (10 mL), 10% sodium thiosulfate ($Na_2S_2O_3$, 10 mL) and water (2 x 10 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate - hexane gradient elution) to afford respective disaccharide derivatives. Anomeric ratios (or anomeric purity) were determined by comparison of the integral intensities of the relevant signals in ^{1}H NMR spectra.

Methyl 6-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-picoloyl-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (9). The title compound was obtained as a colorless amorphous solid from glycosyl donor **3** and acceptor **5**[52] in 82% yield (α/β = 1/5.0, 50 mM) or 97% yield (α/β = 1/21, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for β-**9**: R_f = 0.40 (ethyl acetate/toluene, 3/7, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.88-7.34 (m, 24H, aromatic), 5.61 (s, 1H, C*H*Ph), 5.32 (dd, 1H, $J_{3',4'}$ = 10.2 Hz, H-3'), 4.90 (dd, 2H, ^2J = 10.8 Hz, C*H*$_2$Ph), 4.75 (dd, 2H, ^2J = 10.8 Hz, C*H*$_2$Ph), 4.70 (dd, 2H, ^2J = 10.8 Hz, C*H*$_2$Ph), 4.57 (d, 1H, $J_{1,2}$ = 3.0 Hz, H-1), 4.44 (d, 1H, $J_{1',2'}$ = 1.0 Hz, H-1'), 4.35 (dd, 1H, $J_{6a',6b'}$ = 10.5 Hz, H-6a'), 4.23-4.05 (m, 4H, $J_{2',3'}$ = 3.8 Hz, $J_{3,4}$ = 9.0 Hz, H-2', 3, 4', 6a), 3.95 (dd, 1H,

H-6b'), 3.83 (m, 1H, $J_{5,6a}$ = 7.0 Hz, $J_{5,6b}$ = 3.5 Hz, H-5), 3.64-3.44 (m, 4H, $J_{2,3}$ = 9.0 Hz, $J_{5',6a'}$ = 4.8 Hz, $J_{5',6b'}$ = 10.5 Hz, H-2, 4, 5', 6b), 3.42 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.2, 150.4, 147.2, 138.8, 138.5, 138.2, 137.0, 129.2, 129.1, 128.7 (x2), 128.6 (x2), 128.5 (x2), 128.4 (x2), 128.3 (x4), 128.2 (x2), 128.1 (x2), 127.8, 127.4, 126.2 (x2), 125.8, 101.9, 100.5 ($^1J_{C1',H1'}$ = 160.0 Hz, C-1'), 98.0 ($^1J_{C1,H1}$ = 171.0 Hz, C-1), 82.3, 79.9, 77.1, 75.9, 75.3, 74.8, 73.6, 71.8, 69.6, 68.7, 68.4, 67.5, 62.5, 55.3 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{47}H_{48}N_4O_{11}Na$ 867.3238; found 867.3212.

Methyl 6-*O*-(2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (10). The title compound was obtained as a colorless amorphous solid from glycosyl donor **4** and acceptor **5** in 82% yield (α/β >25/1, 50 mM) and 89% (α/β >25/1, 5 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **10**: R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11-7.25 (m, 25H, aromatic), 5.72 (dd, 1H, $J_{3',4'}$ = 10.2 Hz, H-3'), 5.59 (s, 1H, C*H*Ph), 5.00 (dd, 2H, ^2J = 11.0 Hz, CH_2Ph), 4.91 (s, 1H, H-1'), 4.82 (dd, 2H, ^2J = 11.4 Hz, CH_2Ph), 4.67 (dd, 2H, ^2J = 11.6 Hz, CH_2Ph), 4.62 (d, 1H, $J_{1,2}$ = 3.0 Hz, H-1), 4.29 (d, 1H, $J_{2',3'}$ = 3.4 Hz, H-2'), 4.22-4.19 (m, 2H, H-4', 6a'), 4.04-3.96 (m, 2H, H-3, 5'), 3.86-3.78 (m, 3H, H-5, 6a, 6b'), 3.68 (d, 1H, $J_{6a,6b}$ = 11.1 Hz, H-6b), 3.57 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2), 3.52 (dd, 1H, $J_{3,4}$ = 9.4 Hz, H-4), 3.41 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.6, 138.8, 138.2, 138.2, 137.2, 133.5, 130.1 (x2), 129.3, 129.1, 128.6 (x6), 128.5 (x2), 128.3 (x2), 128.2 (x2), 128.1 (x3), 128.0 (x3), 127.7, 126.2 (x2), 101.9, 99.4 ($^1J_{C1',H1'}$ = 207.8 Hz), 98.1 ($^1J_{C1,H1}$ = 173.1 Hz), 82.2, 80.2, 77.6, 76.4, 75.9, 75.2, 73.5, 70.5, 69.9, 68.7, 66.7, 64.2, 62.5, 55.4 ppm; HR-FAB MS $[M+H]^+$ calcd for $C_{48}H_{50}O_{11}N_3$ 844.3443; found 844.3440.

Methyl 4-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-picoloyl-D-mannopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (11). The title compound was obtained as a colorless syrup from glycosyl donor **3** and acceptor **6**[52] in 81% (α/β = 1/11, 50 mM) and 69% yield (α/β = 1/14, 5 mM) under regular and high dilution reaction conditions, respectively. Analytical data for β-**11**: R_f = 0.35 (ethyl acetate/hexane, 1/1, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.83-7.28 (m, 24H, aromatic), 5.47 (s, 1H, C*H*Ph), 5.10 (dd, 1H, $J_{3',4'}$ = 10.1 Hz, H-3'), 4.93 (dd, 2H, ^2J = 10.8 Hz, CH_2Ph), 4.82-4.75 (m, 2H, 2 x C*H*Ph), 4.70 (d, 1H, $J_{1',2'}$ = 1.0 Hz, H-1'), 4.66-4.61 (m, 2H, H-1, C*H*Ph), 4.43 (d, 1H, ^2J = 12.0 Hz, C*H*Ph), 4.07-3.92 (m, 5H, $J_{2',3'}$ = 3.8 Hz, $J_{4',5'}$ = 4.8 Hz, H-2', 3, 4, 4', 6a'), 3.76-3.64 (m, 3H, H-5, 6a, 6b), 3.59-3.52 (m, 2H, H-2, 6b'), 3.39 (s, 3H, OCH_3), 3.09 (dd, 1H, $J_{5',6a'}$ = 9.7, H-5') ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.1, 150.4, 147.2, 139.3, 138.3, 137.5, 137.2, 137.0, 129.2, 128.9 (x2), 128.5 (x6), 128.4 (x2), 128.3 (x2), 128.2 (x2), 128.0, 127.6 (x2), 127.5, 127.4, 126.3 (x2), 101.9, 100.1 ($^1J_{C1',H1'}$ = 159.0 Hz), 98.5 ($^1J_{C1,H1}$ = 171.0 Hz), 80.3, 79.3, 77.5, 75.4 (x2), 73.8, 73.7, 72.0, 69.4, 68.4, 68.1, 67.2, 62.9, 55.6 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{47}H_{48}N_4O_{11}Na$ 867.3238; found 867.3212.

Methyl 4-*O*-(2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (12). The title compound was obtained as a colorless syrup from glycosyl donor **4** and acceptor **6** in 79% (α/β >25/1, 50 mM) and 75% yield (α/β >25/1, 5 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **12**: R_f = 0.65 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09-7.16 (m, 25H, aromatic), 5.69 (dd, 1H, $J_{3',4'}$ = 9.8 Hz, H-3'), 5.54 (s, 1H, C*H*Ph), 5.21 (br. s, 1H, H-1'), 4.93 (dd, 2H, ^2J = 11.4 Hz, CH_2Ph), 4.70 (dd, 2H, ^2J = 12.1 Hz, CH_2Ph), 4.65 (d, 1H, $J_{1,2}$ = 3.3 Hz, H-1), 4.57 (dd, 2H, ^2J = 11.9 Hz, CH_2Ph), 4.15 (dd, 1H, H-4'), 4.07-3.95 (m, 3H, H-3, 5', 6a'), 3.88-3.68 (m, 6H, $J_{2',3'}$ = 3.5 Hz, H-2', 4, 5, 6a, 6b, 6b'), 3.57 (dd, 1H, $J_{2,3}$ = 9.5 Hz, H-2), 3.41 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.6, 138.3, 138.0, 137.9, 137.2, 133.5, 130.1 (x2), 129.3, 129.1, 128.6 (x6), 128.5 (x2), 128.3 (x4), 128.2, 127.9, 127.7 (x6), 126.2 (x2), 101.9, 101.1 ($^1J_{C1',H1'}$ = 220.0 Hz), 97.9 ($^1J_{C1,H1}$ = 170.0 Hz), 81.5, 80.4, 76.4, 75.6, 73.8, 73.3, 70.4, 69.5, 68.9, 68.6, 65.1, 62.8, 55.5 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{48}H_{49}N_3O_{11}Na$ 866.3263; found 866.3259.

Methyl 3-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-picoloyl-D-mannopyranosyl)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (13). The title compound was obtained as a colorless syrup from glycosyl donor **3** and acceptor **7**[52] in 76% (α/β = 1/6.0, 50 mM) and 61% yield (α/β = 1/11, 5 mM) under regular and high dilution reaction conditions, respectively. Analytical data for β-**13**: R_f = 0.25 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.84-7.26 (m, 24H, aromatic), 5.54 (s, 1H, C*H*Ph), 5.30 (dd, 1H, $J_{2',3'}$ = 3.9 Hz, H-3'), 5.22 (d, 1H, $J_{1',2'}$ = 1.1 Hz, H-1'), 4.72 (dd, 2H, ^2J = 10.0 Hz, CH_2Ph), 4.73 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 4.57 (dd, 2H, ^2J = 12.2 Hz, CH_2Ph), 4.63 (dd, 2H, ^2J = 6.3 Hz, CH_2Ph), 4.27-4.11 (m, 4H, $J_{3',4'}$ = 10.1 Hz, H-2', 4', 6a, 6a'), 3.76-3.60 (m, 6H, H-2, 3, 4, 5, 6b, 6b'), 3.42 (dd, 1H, $J_{5',6a'}$ = 4.9 Hz, H-5'), 3.36 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.1, 150.4, 147.3, 138.5, 138.0, 137.5, 137.2, 137.0, 129.2, 129.1 (x2), 128.8 (x2), 128.7, 128.6 (x4), 128.3 (x4), 128.2 (x2), 127.9, 127.8, 127.4, 126.3 (x2), 125.7, 101.9, 101.1 ($^1J_{C1',H1'}$ = 162.0 Hz), 97.4 ($^1J_{C1,H1}$ = 170.1 Hz), 80.8, 80.1, 75.9, 75.7, 74.9, 73.7, 73.4, 72.1, 70.0, 68.6, 68.3, 67.2, 62.9, 55.3 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{47}H_{48}N_4O_{11}Na$ 867.3229, found 867.3212.

Methyl 3-*O*-(2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranosyl)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (14). The title compound was obtained as a colorless syrup from glycosyl donor **4** and acceptor **7** in 70% (α/β >25/1, 50 mM) and 57% yield (α/β >25/1, 5 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **14**: R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.11-7.16 (m, 25H, aromatic), 5.72 (dd, 1H, $J_{3',4'}$ = 10.2 Hz, H-3'), 5.55 (s, 1H, C*H*Ph), 5.16 (d, 1H, $J_{1',2'}$ = 1.4 Hz, H-1'), 4.69 (dd, 2H, ^2J = 12.1 Hz, CH_2Ph), 4.59 (dd, 2H, ^2J = 12.0 Hz, CH_2Ph), 4.58 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.56 (s, 2H, CH_2Ph), 4.40 (dd, 1H, $J_{5',6a'}$ = 9.9 Hz, H-5'), 4.20-4.15 (m, 2H, $J_{4',5'}$ = 4.8 Hz, H-4', 6a'), 4.03 (dd, 1H, $J_{3,4}$ = 8.7 Hz, H-3), 3.89 (dd, 1H, $J_{2',3'}$ = 3.6 Hz, H-2'), 3.76-3.66 (m, 5H, H-4, 5, 6a, 6b, 6b'), 3.48 (dd, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 3.30 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ

165.8, 137.7 (x3), 137.5, 133.5, 130.1 (x2), 129.4, 129.0, 128.8 (x3), 128.7 (x3), 128.6 (x3), 128.3, 128.2 (x5), 128.0 (x2), 127.6 (x2), 126.3 (x2), 101.8, 100.0 ($^1J_{C1',H1'}$ = 230.0 Hz), 97.8 ($^1J_{C1,H1}$ = 173.0 Hz), 79.0, 78.6, 77.8, 76.5, 74.8, 73.8, 73.3, 70.9, 69.8, 68.7, 68.4, 64.1, 62.7, 55.3 ppm; HR-FAB MS $[M+H]^+$ calcd for $C_{48}H_{50}N_3O_{11}$ 844.3367; found 844.3440.

Methyl 2-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-picoloyl-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (15). The title compound was obtained as a colorless amorphous solid from glycosyl donor **3** and acceptor **8**[52] in 86% yield (α/β = 1/9.0, 50 mM) and 87% (α/β < 1/25, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for β-**15**: R_f = 0.50 (ethyl acetate/toluene, 3/7, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.82-7.17 (m, 24H, aromatic), 5.55 (s, 1H, C*H*Ph), 5.25 (dd, 1H, $J_{3',4'}$ = 9.7 Hz, H-3'), 4.99 (br. s, 1H, H-1'), 4.81 (dd, 2H, ^2J = 11.0 Hz, CH_2Ph), 4.87-4.84 (m, 2H, H-1, C*H*Ph), 4.58 (dd, 2H, ^2J = 9.6 Hz, CH_2Ph), 4.53 (d, 1H, J = 8.3 Hz, C*H*Ph), 4.30 (dd, 1H, $J_{6a',6b'}$ = 10.5 Hz, H-6a'), 4.18 (dd, 1H, H-4'), 4.08-4.02 (m, 2H, $J_{2',3'}$ = 3.7 Hz, H-2', 3), 3.91-3.65 (m, 6H, H-2, 4, 5, 6a, 6b, 6b'), 3.42 (m, 4H, $J_{5',6a'}$ = 4.9 Hz, H-5', OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.0, 150.4, 147.2, 138.3, 138.2, 137.9, 137.2, 136.9, 129.2, 129.1 (x2), 128.6 (x2), 128.5 (x2), 128.3 (x5), 128.1 (x2), 127. 9 (x4), 127.4, 126.2 (x2), 125.8, 101.9, 101.0 ($^1J_{C1',H1'}$ = 161.0 Hz), 99.5 ($^1J_{C1,H1}$ = 171.0 Hz), 82.1, 78.5 (x2), 76.2, 75.6, 75.1, 73.7, 72.3, 70.2, 68.4, 68.3, 67.6, 62.0, 55.5 ppm; HR-FAB MS $[M+H]^+$ calcd for $C_{47}H_{49}N_4O_{11}$ 845.3425; found 845.3392.

Methyl 2-*O*-(2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (16). The title compound was obtained as a colorless syrup from glycosyl donor **4** and acceptor **8** in 78% (α/β = 24/1, 50 mM) and 82% yield (α/β >25/1, 5 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **16**: R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.11-7.11 (m, 25H, aromatic), 5.86 (dd, 1H, $J_{3',4'}$ = 9.9 Hz, H-3'), 5.58 (s, 1H, C*H*Ph), 4.95 (dd, 2H, ^2J = 10.5 Hz, CH_2Ph), 5.00 (s, 1H, H-1'), 4.96 (d, 1H, $J_{1,2}$ = 3.1 Hz, H-1), 4.68 (dd, 2H, ^2J = 10.9 Hz, CH_2Ph), 4.56 (dd, 2H, ^2J = 12.1 Hz, CH_2Ph), 4.38 (dd, 1H, $J_{2',3'}$ = 3.6 Hz, H-2'), 4.28-4.18 (m, 3H, H-4', 5', 6a'), 4.00 (dd, 1H, $J_{3,4}$ = 9.3 Hz, H-3), 3.89 (dd, 1H, H-2), 3.82 (dd, 1H, $J_{6a',6b'}$ = 10.0 Hz, H-6b'), 3.78-3.67 (m, 4H, H-4, 5, 6a, 6b), 3.43 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 165.5, 138.3, 138.0, 137.9, 137.3, 133.5, 130.2 (x2), 129.1, 128.6 (x6), 128.5 (x5), 128.2 (x2), 128.1 (x2), 127.9 (x3), 127.8 (x2), 126.5 (x2), 102.0, 96.0 ($^1J_{C1',H1'}$ = 233.2 Hz), 95.5 ($^1J_{C1,H1}$ = 173.5 Hz), 80.7, 77.8, 76.6, 76.2, 75.2, 74.4, 73.7, 70.5, 70.3, 68.6, 68.4, 64.4, 62.6, 55.2 ppm; HR-FAB MS $[M+H]^+$ calcd for $C_{48}H_{50}N_3O_{11}$ 844.3449; found 844.3440.

Methyl 6-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-benzyl-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (35). The title compound was obtained as a colorless amorphous solid from ethyl 2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-benzyl-1-thio-α-D-mannopyranoside **34**[39] and acceptor **5**[52] in 85% yield (α/β = 1/1.6, 50 mM) under regular dilution reaction condition. The anomers were partially separated by column chromatography on silica gel. Selected analytical data for α-**35**: R_f = 0.70 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47-7.19 (m, 25H), 5.60 (s, 1H, C*H*Ph), 5.01 (d, 1H, ^2J = 10.7 Hz, C*H*Ph), 4.92-4.78 (m, 5H, H-1', 2 x CH_2Ph), 4.74-4.67 (m, 2H, CH_2Ph), 4.60 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.50 (d, 1H, ^2J = 11.0 Hz, C*H*Ph), 4.14 (br. dd, 1H, $J_{5',6a'}$ = 5.5 Hz, H-6a'), 4.11-3.99 (m, 3H, $J_{3,4}$ = 12.8 Hz, H-3, 3', 4'), 3.95 (br. dd, 1H, H-2'), 3.82-3.76 (m, 3H, H-5', 6a, 6b'), 3.70 (br. dd, 1H, H-5), 3.59 (dd, 1H, $J_{6a,6b}$ = 11.0 Hz, H-6b), 3.50 (dd, 1H, $J_{2,3}$ = 9.6 Hz, H-2), 3.39 (dd, 1H, $J_{4,5}$ = 6.0 Hz, H-4), 3.32 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 138.7, 138.2, 138.0, 136.7, 129.1, 128.7 (x2), 128.6 (x6), 128.3 (x2), 128.2 (x4), 128.1 (x2), 128.0 (x2), 127.9 (x3), 127.8 (x2), 126.2 (x2), 101.8, 99.6 ($^1J_{C1',H1'}$ = 173.1 Hz, C-1'), 98.0, 82.2, 80.1, 79.2, 77.6, 76.0, 75.2, 75.2, 73.4, 73.4, 69.8, 68.7, 66.5, 64.1, 62.8, 55.3 ppm; Selected analytical data for β-**36**: R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50-7.18 (m, 25H), 5.56 (s, 1H, C*H*Ph), 5.00 (d, 1H, ^2J = 10.8 Hz, C*H*Ph), 4.89-4.71 (m, 5H, 5 x C*H*Ph), 4.66-4.54 (m, 3H, H-1, CH_2Ph), 4.24 (dd, 1H, $J_{6a',6b'}$ = 10.5 Hz, H-6a'), 4.17 (s, 1H, H-1'), 4.04-3.93 (m, 3H, $J_{4',5'}$ = 9.7 Hz, H-3, 4', 6a), 3.85 (dd, 1H, H-6b'), 3.76 (dd, 1H, $J_{5,6a}$ = 9.8 Hz, H-5), 3.70 (dd, 1H, $J_{2',3'}$ = 3.5 Hz, H-2'), 3.59 (dd, 1H, $J_{3',4'}$ = 9.6 Hz, H-3'), 3.52-3.39 (m, 3H, $J_{4,5}$ = 3.8 Hz, H-2, 4, 6b), 3.34 (s, 3H, OCH_3), 3.19 (dd, 1H, $J_{5',6a'}$ = 4.8 Hz, H-5') ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 138.7, 138.4, 138.1, 137.8, 137.3, 129.0, 128.5 (x4), 128.4 (x4), 128.2 (x4), 128.0 (x7), 127.8 (x2), 127.7 (x2), 126.0 (x2), 101.5, 100.3 ($^1J_{C1',H1'}$ = 162.0 Hz, C-1'), 97.9, 82.1, 79.8, 78.5, 75.8, 75.7, 74.6, 73.4, 72.9, 69.5, 68.4, 68.3, 67.2, 63.5, 55.2 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{48}H_{51}N_3O_{10}Na$ 852.3467; found 852.3466.

Synthesis of fucosyl acceptor 19

Benzyl 3,4-di-*O*-acetyl-2-azido-2-deoxy-L-fucopyranoside (24). A mixture containing 3,4-di-*O*-acetyl-1,5-anhydro-2-deoxy-L-*lyxo*-hex-l-enitol[64] (**23**, 7.90 g, 36.7 mmol) and freshly activated molecular sieves (MS 3Å, 8.0 g) in anhydrous MeCN (150 mL) was stirred under argon for 40 min at rt. The mixture was then cooled to -15 ˚C, cerium(IV) ammonium nitrate (64.4 g, 117.5 mmol) and sodium azide (5.73 g, 88.1 mmol) were added, and the resulting mixture was stirred under argon for 2 h at -15 ˚C. After that, the solids were filtered off and rinsed successively with CH_2Cl_2, and the combined filtrate was concentrated under reduced pressure. The residue was diluted with CH_2Cl_2 (~150 mL) and washed with water (2 x 20 mL). The organic phase was separated, dried with Na_2SO_4, concentrated under reduced pressure, and dried *in vacuo* for 2 h. The resulting pale-yellow residue containing crude glycosyl nitrate was subjected to glycosylation with BnOH using the following methods.

Method A. MS 3Å (0.35 g) and benzyl alcohol (35 µL, 0.334 mmol) were added to a solution of crude glycosyl nitrate (0.12 g) in anhydrous MeCN (10 mL), and the resulting mixture was stirred under argon for 1 h at rt. Ytterbium(IV) trifluoromethanesulfonate (0.31 g, 0.501 mmol) was added, and the reaction mixture was stirred under argon for 18 h at rt. After that, the solids were filtered off and rinsed successively

with CH_2Cl_2. The combined filtrate (~20 mL) was concentrated under reduced pressure. The residue was diluted with CH_2Cl_2 (~20 mL) and washed with water (5 mL), sat. aq. $NaHCO_3$ (5 mL) and water (2 x 5 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (acetone - toluene gradient elution) to give the title compound in 59% yield (0.121 g, 0.334 mmol, α/β = 1/4.0).

Method B. A solution of crude glycosyl nitrate (6.03 g) in AcOH (60 mL) was heated to 100 ˚C, NaOAc (3.11g, 37.9 mmol) was added, and the resulting mixture was stirred under argon for 2 h at 100 ˚C. The reaction mixture was then allowed to cool to rt, diluted in CH_2Cl_2 (~150 mL) and washed with water (50 mL), sat. aq. $NaHCO_3$ (2x 50 mL) and water (50 mL). The organic phase was separated, dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to give the intermediate glycosyl acetate (4.9 g, 15.5 mmol). A portion of glycosyl acetate (1.34 g, 4.25 mmol) was dissolved in dry CH_2Cl_2 (20 mL), BnOH (0.53 mL, 5.10 mmol) was added, and the resulting mixture was stirred under argon for 15 min at rt. After that, BF_3-Et_2O (1.62 mL, 12.7 mmol) was added dropwise, the mixture was allowed to warm to rt, and the resulting mixture was stirred for 16 h at rt. The reaction mixture was diluted with CH_2Cl_2 (~40 mL) and washed with water (15 mL), sat. aq. $NaHCO_3$ (2 x 15 mL), and water (2 x 15 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to give the title compound in 68% yield (1.1 g, 2.91 mmol, α/β = 1.5/1). Analytical data for β-**24**: R_f = 0.50 (acetone/toluene, 1/9, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44-7.32 (m, 5H, aromatic), 5.19 (dd, 1H, $J_{4,5}$ = 3.3 Hz, H-4), 4.85 (dd, 2H, ^2J = 11.9 Hz, CH_2Ph), 4.77 (dd, 1H, $J_{3,4}$ = 3.4 Hz, H-3), 4.41 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1), 3.78-3.71 (m, 2H, $J_{2,3}$ = 10.9 Hz, H-2, $J_{5,6}$ = 6.4 Hz, H-5), 2.19, 2.06 (2 s, 6H, 2 x $COCH_3$), 1.26 (d, 3H, H-6) ppm; ^{13}C NMR for α/β-**24** (151 MHz, $CDCl_3$): δ 170.5, 170.4, 169.9, 136.6, 136.5, 128.6, 128.5 (x2), 128.2, 128.1, 128.0 (x2), 100.5, 97.1, 71.5, 71.1, 70.7, 70.0, 69.6, 69.1, 68.7, 66.6, 64.9, 60.8, 57.4, 20.7 (x2), 16.1, 15.8 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{17}H_{21}N_3O_6Na$ 386.1334; found 386.1323.

Benzyl 2-azido-2-deoxy-α- and β-L-fucopyranosides (25 and 26). A freshly prepared 1 N solution of NaOMe in MeOH (~2 mL) was added to a solution of compound **24** (1.10 g, 3.03 mmol) in MeOH (30 mL) until pH ~ 9 and the resulting mixture was stirred for 1 h at rt. After that, the reaction mixture was neutralized with Dowex (H^+), the resin was filtered-off, and rinsed successively with MeOH (7 x 5 mL). The combined filtrate (~70 mL) was concentrated under reduced pressure. The residue was separated by column chromatography in silica gel (ethyl acetate – hexane gradient elution) to give compound **25** as a white amorphous solid (0.424 g, 1.52 mmol) and **26** as a colorless amorphous solid (0.261 g, 0.93 mmol). Analytical data for **25**: R_f = 0.55 (ethyl acetate/hexane, 7/3, v/v); $[\alpha]_D^{22}$ -141.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40-7.30 (m, 5H, aromatic), 5.00 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.66 (dd, 2H, ^2J = 12.0 Hz, CH_2Ph), 4.10 (m, 1H, $J_{3,4}$ = 3.3 Hz, H-3), 4.02 (dd, 1H, $J_{5,6}$ = 6.7 Hz, H-5), 3.81 (dd, 1H, H-4), 3.46 (dd, 1H, $J_{2,3}$ = 10.5 Hz, H-2), 2.60 (d, 1H, *J* = 6.7 Hz, 3-OH), 2.34 (d, 1H, *J* = 4.2 Hz, 4-OH), 1.27 (d, 3H, H-6) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 137.0, 128.6 (x2), 128.1, 128.1 (x2), 97.2, 71.9, 69.9, 68.8, 66.1, 60.4, 16.2 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{13}H_{18}N_3O_4$ 280.1293; found 280.1292.

Analytical data for **26**: R_f = 0.50 (ethyl acetate/hexane, 7/3, v/v); $[\alpha]_D^{22}$ -28.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42-7.28 (m, 5H, aromatic), 4.82 (dd, 2H, ^2J = 80.8, 12.0 Hz, CH_2Ph), 4.32 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), 3.69 (dd, 1H, $J_{3,4}$ = 3.3 Hz, $J_{4,5}$ = 5.1, H-4), 3.61-3.51 (m, 2H, H-5, H-2), 3.41 (m, 1H, H-3), 2.72 (d, 1H, *J* = 6.5 Hz, 3-OH), 2.37 (d, 1H, *J* = 5.8 Hz, 4-OH), 1.37 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.4, 136.8, 128.6 (x2), 128.1 (x2), 100.7, 72.7, 70.1 (x2), 70.6, 64.3, 16.4 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{13}H_{18}N_3O_4$ 280.1294; found 280.1292.

Benzyl 2-azido-2-deoxy-3-*O*-*p*-methoxybenzyl-α-L-fucopyranoside (27). Dibutyl tin(IV) oxide (0.44 g, 1.75 mmol) was added to a solution of compound **25** (0.41 g, 1.46 mmol) in dry toluene (50 mL), and the resulting mixture was heated for 3 h at reflux (110 ˚C) using Dean-Stark apparatus. After that, *p*-methoxybenzyl chloride (0.24 mL, 1.75 mmol) and tetrabutylammonium bromide (0.704 g, 2.18 mmol) were added, and the resulting mixture was stirred for 16 h at 110 ˚C. The reaction mixture was then allowed to cool to rt and the volatiles were removed under reduced pressure. The residue was diluted in CH_2Cl_2 (~20 mL) and washed with water (2 x 8 mL). The organic layer was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to obtain the title compound as a colorless syrup in 98% yield (0.572 g, 1.43 mmol). Analytical data for **27**: R_f = 0.45 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ -85.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38-6.89 (m, 9H, aromatic), 4.95 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.66 (dd, 2H, ^2J = 12.2 Hz, CH_2Ph), 4.61 (dd, 2H, ^2J = 10.9 Hz, CH_2Ph), 3.97-3.90 (m, 2H, $J_{5,6}$ = 6.6 Hz, H-3, 5), 3.85 (br. s, 1H, H-4), 3.81 (s, 3H, OCH_3), 3.66 (dd, 1H, $J_{2,3}$ = 10.4 Hz, H-2), 2.36 (s, 1H, 4-OH), 1.28 (d, 3H, H-6) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.8, 137.2, 129.9 (x2), 129.4, 128.6 (x2), 128.1 (x2), 128.1, 114.2 (x2), 97.3, 76.4, 71.8, 69.8, 69.0, 65.9, 59.0, 55.4, 16.3 ppm. HR FAB MS $[M+Na]^+$ calcd for $C_{21}H_{25}N_3O_5Na$ 422.1700; found 422.1686.

Benzyl 2-azido-4-*O*-benzyl-2-deoxy-3-*O*-*p*-methoxybenzyl-α-L-fucopyranoside (28). NaH (60% in mineral oil, 0.17 g, 4.31 mmol) and benzyl bromide (0.34 mL, 2.88 mmol) were added to a solution of compound **27** (0.575 g, 1.44 mmol) in dimethylformamide (5.0 mL) and the resulting mixture was stirred under argon for 2.5 h at 0 ˚C. After that, the reaction mixture was poured into ice-water (15 mL), stirred for 30 min, and extracted with diethyl ether (3 × 10 mL). The combined organic extract (~30 mL) was washed with cold water (3 × 10 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to give the title compound as a colorless liquid

in 94% yield (0.66 g, 1.35 mmol). Analytical data for **28**: R_f = 0.80 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ -90.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41-6.91 (m, 14H, aromatic), 4.97 (dd, 2H, $J_{1,2}$ = 3.6 Hz, H-1, C*H*Ph), 4.73-4.58 (m, 5H, 5 x C*H*Ph), 4.03 (dd, 1H, $J_{3,4}$ = 2.6 Hz, H-3), 3.94-3.87 (m, 2H, $J_{2,3}$ = 10.7 Hz, $J_{5,6}$ = 6.5 Hz, H-2, 5), 3.83 (s, 3H, OCH_3), 3.71 (br. d, 1H, H-4), 1.17 (d, 3H, H-6) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.5, 138.4, 137.3, 129.9, 129.7 (x2), 128.6 (x2), 128.5 (x2), 128.4 (x2), 128.0 (x2), 128.0, 127.9, 114.1 (x2), 97.5, 77.7, 76.2, 75.0, 72.2, 69.7, 66.9, 59.7, 55.4, 16.8 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{28}H_{31}N_3O_5Na$ 512.2174; found 512.2156.

Benzyl 2-azido-4-*O*-benzyl-2-deoxy-α-L-fucopyranoside (19). 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 0.45 g, 1.98 mmol) and water (5 drops) were added to a solution of compound **28** (0.65 g, 1.32 mmol) in CH_2Cl_2 (10 mL), and the resulting mixture was stirred for 3 h at rt. After that, the reaction mixture was diluted with CH_2Cl_2 (~20 mL) and washed with water (10 mL), sat. aq. $NaHCO_3$ (10 mL) and water (2 x 10 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to obtain the title compound as a white amorphous solid in 84% yield (0.41 g, 1.12 mmol). Analytical data for **19**: R_f = 0.70 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ -22.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39-7.31 (m, 10H, aromatic), 4.98 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.82 (d, 1H, ^2J = 11.5 Hz, *CH*Ph), 4.70 (dd, 2H, ^2J = 11.5 Hz, CH_2Ph), 4.69 (d, 1H, ^2J = 12.0 Hz, C*H*Ph), 4.11 (ddd, 1H, $J_{3,4}$ = 3.4 Hz H-3), 3.99 (m, 1H, $J_{5,6}$ = 6.6 Hz, H-5), 3.67 (d, 1H, H-4), 3.46 (dd, 1H, $J_{2,3}$ = 10.7 Hz, H-2), 2.09 (d, 1H, *J* = 9.4 Hz, 3-OH), 1.26 (d, 3H, H-6) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 137.9, 137.2, 128.8 (x2), 128.6 (x2), 128.3 (x3), 128.0 (x3), 97.4, 80.3, 76.3, 69.8, 68.9, 66.8, 61.1, 16.9 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{20}H_{23}N_3O_4Na$ 392.1591; found 392.1581.

Synthesis of galactosyl donor 18

Ethyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (30). EtSH (1.14 mL, 15.58 mmol) was added followed by a dropwise addition of BF_3-Et_2O (6.6 mL, 51.92 mmol) to a solution of 1,2,3,4,6-penta-*O*-acetyl-β-D-galactopyranoside (**29**, 5.1 g, 12.98 mmol) in dry CH_2Cl_2 (50 mL), and the resulting mixture was stirred under argon for 15 min at 0 ˚C. After that, the reaction mixture was diluted with CH_2Cl_2 (~50 mL) and washed with water (20 mL), sat. aq. $NaHCO_3$ (20 mL) and water (2 x 20 mL). The organic phase was separated, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to obatin the title compound as a white amorphous solid in 98% yield. Analytical data for **30**: R_f = 0.70 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ -1.50 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.44 (d, 1H, H-4), 5.25 (dd, 1H, $J_{2,3}$ = 10.0 Hz, H-2), 5.05 (dd, 1H, $J_{3,4}$ = 3.3 Hz, H-3), 4.50 (d, 1H, $J_{1,2}$ = 9.9 Hz, H-1), 4.14 (m, 2H, $J_{6a,6b}$ = 11.3, H-6a, 6b), 3.94 (dd, 1H, $J_{5,6a}$ = 6.6 Hz, H-5), 2.83-2.64 (m, 2H, SCH_2CH$_3$), 2.16, 2.08, 2.05, 1.99 (4 s, 12H, 4 x COCH_3), 1.29 (t, 3H, *J* = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.4, 170.3, 169.8, 84.2, 74.5, 72.0, 67.4, 67.3, 61.6, 24.5, 21.0, 20.8 (x3), 15.0 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{16}H_{24}O_9SNa$ 415.1051; found 415.1033.

Ethyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (31). Freshly prepared 1 N NaOMe in MeOH (~ 5 mL) was added to a solution of **30** (5.0 g, 12.75 mmol) in MeOH (50 mL) and CH_2Cl_2 (10 mL) until pH ~9 and the reaction mixture was stirred for 30 min at rt. The reaction mixture was neutralized with Dowex (H^+), the resin was filtered off and rinsed successively with MeOH (7 x 10 mL). The combined filtrate was concentrated under reduced pressure and dried *in vacuo* for 16 h to afford ethyl 1-thio-β-D-galactopyranoside (2.79 g, 12.46 mmol). A portion of ethyl 1-thio-β-D-galactopyranoside (1.51 g, 6.72 mmol) was dissolved in MeCN (30 mL), dimethoxytoluene (DMT, 2.02 mL, 13.43 mmol) and camphorsulfonic acid (CSA, 78 mg, 0.34 mmol) were added, and the resulting mixture was stirred under argon for 15 min at rt. After that, triethylamine (~4 mL) was added and the volatiles were removed under reduced pressure. The residue was diluted with CH_2Cl_2 (~40 mL) and washed with water (10 mL), sat. aq. $NaHCO_3$ (10 mL), and water (2 x 10 mL). The organic phase was separated, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was dissolved in minimum amount of CH_2Cl_2 and precipitated with hexane to afford the title compound as a white amorphous solid in 85% yield (1.8 g, 5.68 mmol). Analytical data for **31**: R_f = 0.50 (methanol/dichloromethane, 1/9, v/v); $[\alpha]_D^{22}$ -8.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52-7.36 (m, 5H, aromatic), 5.55 (s, 1H, C*H*Ph), 4.38-4.33 (m, 2H, $J_{1,2}$ = 9.6 Hz, H-1, H-6a), 4.27 (d, 1H, $J_{3,4}$ = 2.9 Hz, H-4), 4.05 (dd, 1H, $J_{6a,6b}$ = 12.6 Hz, H-6b), 3.82 (dd, 1H, $J_{2,3}$ = 1.4 Hz, H-2), 3.70 (dd, 1H, $J_{3,4}$ = 3.7 Hz, H-3), 3.54 (d, 1H, $J_{5,6a}$ = 1.2 Hz, $J_{5,6b}$ = 1.8 Hz, H-5), 2.88-2.73 (m, 2H, SCH_2CH$_3$), 2.63-2.59 (m, 2H, 2-OH, 3-OH), 1.35 (t, 3H, *J* = 7.5 Hz, SCH$_2$CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.6, 129.5, 128.5 (x2), 126.5 (x2), 101.7, 85.5, 75.7, 74.0, 70.3, 69.9, 69.5, 23.6, 15.4 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{15}H_{20}O_5SNa$ 335.0931; found 335.0924.

Ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (32). NaH (60% in mineral oil, 0.62 g, 15.44 mmol) and benzyl bromide (1.2 mL, 10.30 mmol) were added to a solution of compound **31** (0.80 g, 2.57 mmol) in dimethylformamide (10.0 mL), and the resulting mixture was stirred under argon for 2.5 h at 0 ˚C. After that, the reaction mixture was poured into ice-water (10 mL), stirred for 30 min, and extracted with diethyl ether (3 × 30 mL). The combined organic extract (~90 mL) was washed with cold water (3 × 15 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to give the title compound as a colorless syrup in 93% yield (1.18 g, 2.39 mmol). Analytical data for **32**: R_f = 0.50 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ +1.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58-7.28 (m, 15H, aromatic), 5.48 (s, 1H, C*H*Ph), 4.87 (dd, 2H, ^2J = 10.1 Hz, CH_2Ph), 4.76 (s, 2H, CH_2Ph), 4.44 (d, 1H, $J_{1,2}$ = 9.6 Hz, H-1), 4.31 (dd, 1H, $J_{6a,\ 6b}$ = 12.3 Hz, H-

6a), 4.16 (dd, 1H, $J_{4,5}$ = 0.6 Hz, H-4), 3.96 (dd, 1H, $J_{5,6b}$ = 1.7 Hz, H-6b), 3.89 (dd, 1H, $J_{2,3}$ = 9.2 Hz, H-2), 3.60 (dd, 1H, $J_{3,4}$ = 3.5, H-3), 3.36 (d, 1H, $J_{5,6a}$ = 1.5 Hz, H-5), 2.92-2.69 (m, 2H, SCH_2CH$_3$), 1.33 (t, 3H, J = 7.5 Hz, SCH$_2$CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.3, 138.2, 137.9, 129.0, 128.4 (x4), 128.3 (x2), 128.2 (x2), 127.8 (x3), 126.5 (x3), 101.5, 84.3, 81.0, 76.8, 75.7, 73.9, 71.7, 69.7, 69.4, 23.8, 15.1 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{29}H_{33}O_5S$ 493.2065; found 493.2043.

Ethyl 2,3-di-*O*-benzyl-1-thio-β-D-galactopyranoside (33). *p*-TsOH-H_2O (0.14 g, 0.75 mmol) and EtSH (0.50 mL, 8.95 mmol) were added to a solution of compound **32** (0.73 g, 1.50 mmol) in CH_2Cl_2 and the resulting mixture was stirred under argon for 30 min at rt. After that, triethylamine (~1 mL) was added and the volatiles were removed under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to give the title compound in 97% yield (0.58 g, 1.44 mmol). Analytical data for **33**: R_f = 0.15 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ -6.1 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42-7.30 (m, 10H, aromatic), 4.83 (dd, 2H, ^2J = 16.1 Hz, CH_2Ph), 4.73 (s, 2H, CH_2Ph), 4.44 (d, 1H, $J_{1,2}$ = 9.6 Hz, H-1), 4.06 (br. s, 1H, H-4), 4.00-3.92 (m, 1H, H-6a), 3.84-3.76 (m, 1H, H-6b), 3.67 (dd, 1H, $J_{2,3}$ = 8.9 Hz, H-2), 3.56 (dd, 1H, $J_{3,4}$ = 3.2 Hz, H-3), 3.48 (dd, 1H, H-5), 2.86-2.70 (m, 2H, SCH_2CH$_3$), 2.68 (s, 1H, 4-OH), 2.22 (br. s, 1H, 6-OH), 1.32 (t, 3H, J = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.2, 137.7, 128.7 (x2), 128.5 (x4), 128.2, 128.0 (x3), 85.3, 82.3, 77.9 (x2), 76.0, 72.4, 67.6, 62.9, 25.0, 15.3 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{22}H_{29}O_5S$ 405.1737; found 405.1730.

Ethyl 4,6-di-*O*-benzoyl-2,3-di-*O*-benzyl-1-thio-β-D-galactopyranoside (18). Benzoyl chloride (0.67 mL, 5.74 mmol) and DMAP (35 mg, 0.29 mmol) were added to a solution of compound **33** (0.58 g, 1.44 mmol) in pyridine (15 mL), and the resulting mixture was stirred under argon for 2 h at rt. After that, the reaction was quenched with MeOH (5 mL), the volatiles were removed under reduced pressure, and the residue was co-evaporated with toluene. The resulting residue was diluted with CH_2Cl_2 (~20 mL) and washed with water (10 mL), 1 N aq. HCl (10 mL), and water (2 x 10 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to give the title compound as a colorless syrup in 97% yield (0.86 g, 1.39 mmol). Analytical data for **18**: R_f = 0.80 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ +3.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15-7.23 (m, 20H, aromatic), 5.90 (d, 1H, H-4), 4.88-4.74 (m, 3H, 3 x CHPh), 4.60-4.54 (m, 3H, H-1, 6a, CHPh), 4.36 (dd, 1H, $J_{6a,6b}$ = 11.4 Hz, H-6b), 4.02 (dd, 1H, $J_{5,6b}$ = 5.9 Hz, H-5), 3.79-3.70 (m, 2H, $J_{3,4}$ = 2.6 Hz, H-2, 3), 2.89-2.70 (m, 2H, SCH_2CH$_3$), 1.34 (t, 3H, J = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.3, 165.9, 138.1, 137.7, 133.5, 133.4, 130.2 (x2), 129.9 (x2), 129.7 (x2), 128.6 (x7), 128.4 (x3), 128.2 (x2), 128.0, 127.9, 85.6, 81.1, 77.8, 76.1, 74.8, 72.1, 67.5, 62.9, 25.2, 15.3 ppm; HR FAB MS $[M+H]^+$ calcd for $C_{36}H_{37}O_7S$ 613.2275; found 613.2255.

Synthesis of trisaccharide 17 and disaccharide 22

Benzyl 2-azido-3-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-3-*O*-picoloyl-β-D-mannopyranosyl)-4-*O*-benzyl-2,6-dideoxy-α-L-fucopyranoside (20). A mixture containing mannosyl donor **3** (45 mg, 0.101 mmol), fucosyl acceptor **19** (34 mg, 0.092 mmol), and molec. sieves (4 Å, 200 mg) in 1,2-DCE (5.0 mL) was stirred under argon for 1 h at rt. The mixture was cooled to -30 °C, NIS (45 mg, 0.201 mmol) and TfOH (3.6 µL, 0.0403 mmol) were added, the external cooling was removed, and the resulting mixture was stirred for 16 h at rt. After that, the solids were filtered off through a pad of Celite, rinsed successively with CH_2Cl_2, and the combined filtrate was concentrated under reduced pressure. The residue was redissolved in CH_2Cl_2 (~20 mL) and washed with water (8 mL), 10% aq. $Na_2S_2O_3$ (8 mL) and water (2 x 8 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to obtain the title compound as a colorless syrup in 88% yield (α/β < 1/25). Analytical data for **20**: R_f = 0.30 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.82-7.25 (m, 19H, aromatic), 5.58 (s, 1H, CHPh), 5.35 (dd, 1H, $J_{3',4'}$ = 9.7 Hz, H-3'), 5.04 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.84 (d, 1H, $J_{1',2'}$ = 1.1 Hz, H-1'), 4.70 (dd, 2H, ^2J = 11.4 Hz, CH_2Ph), 4.69 (dd, 2H, ^2J = 11.9 Hz, CH_2Ph), 4.40-4.33 (m, 2H, H-3, 6a'), 4.23 (dd, 1H, H-4'), 4.02 (dd, 1H, $J_{2',3'}$ = 3.8 Hz, H-2'), 3.98-3.90 (m, 2H, H-5, 6b'), 3.74 (dd, 1H, $J_{4,5}$ = 2.5 Hz, H-4), 3.67 (dd, 1H, $J_{2,3}$ = 10.9 Hz, H-2), 3.48 (dd, 1H, $J_{5',6a'}$ = 9.8 Hz, $J_{5',6b'}$ = 4.9 Hz, H-5'), 1.26 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 164.2, 150.4, 147.1, 137.8, 137.2, 137.0, 136.9, 129.2, 128.7 (x2), 128.6 (x2), 128.4 (x2), 128.3 (x5), 128.2, 128.1, 127.4, 126.2 (x2), 125.8, 101.9, 98.1 ($^1J_{C1',H1'}$ = 159 Hz), 97.9 ($^1J_{C1,H1}$ = 171.3 Hz), 76.0, 75.7, 75.3, 72.0, 70.0, 68.5, 67.8, 66.7, 62.5, 58.2, 16.8 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{39}H_{39}N_7O_9Na$ 772.2726; found 772.2701.

Benzyl 2-azido-3-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-mannopyranosyl)-4-*O*-benzyl-2,6-dideoxy-α-L-fucopyranoside (21). $Cu(OAc)_2$-H_2O (16 mg, 0.090 mmol) was added to a solution of compound **20** (45 mg, 0.060 mmol) in CH_2Cl_2/MeOH (4.0 mL, 3/1, v/v) and the resulting mixture was stirred for 10 min at rt. After that, the reaction mixture was diluted with CH_2Cl_2 (~10 mL) and washed with water (5 mL), sat. aq. $NaHCO_3$ (5 mL) and water (5 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to obtain the title compound in 92% yield (36 mg, 0.056 mmol). Analytical data for **21**: R_f = 0.50 (ethyl acetate/toluene, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49-7.28 (m, 15H, aromatic), 5.53 (s, 1H, CHPh), 5.03 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.73 (dd, 2H, ^2J = 11.4 Hz, CH_2Ph), 4.70 (s, 1H, H-1'), 4.65 (dd, 2H, ^2J = 12.0 Hz, CH_2Ph), 4.36-4.31 (m, 2H, H-3, 6a'), 3.95 (dd, 1H, $J_{4,5}$ = 6.5 Hz, H-5), 3.89-3.64 (m, 6H, $J_{4',5'}$ = 4.9 Hz, H-2, 2', 3', 4, 4', 6b'), 3.29 (dd, 1H, $J_{5',6a'}$ = 9.8 Hz, $J_{5',6b'}$ = 7.9 Hz, H-5'), 2.55 (d, 1H, J = 5.5 Hz, 3-OH), 1.24 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.9, 137.0 (x2), 129.4, 128.7 (x2), 128.6 (x2), 128.5 (x2), 128.3 (x5),

128.2, 128.1, 126.3 (x2), 102.2, 98.1, 97.9, 78.4, 76.1, 75.4, 70.2, 70.0, 68.5, 67.4, 66.6, 64.4, 58.1, 16.8 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{33}H_{36}N_6O_8Na$ 667.2509; found 667.2487.

Benzyl *O*-(4,6-di-*O*-benzoyl-2,3-di-*O*-benzyl-α/β-D-galactopyranosyl)-(1→3)-*O*-(2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-mannopyranosyl)-(1→3)-2-azido-4-*O*-benzyl-2,6-dideoxy-α-L-fucopyranoside (17). A mixture containing glycosyl donor **18** (34 mg, 0.056 mmol), disaccharide acceptor **21** (33 mg, 0.051 mmol), and molec. sieves (4 Å, 200 mg) in 1,2-DCE (5.0 mL) was stirred under argon for 30 min at rt. The mixture was cooled to -30 ˚C, NIS (25 mg, 0.112 mmol) and TfOH (1.0 µL, 0.0112 mmol) were added, the external cooling was removed, and the resulting mixture was stirred for 2 h at rt. After that, the solids were filtered off through a pad of Celite, rinsed successively with CH_2Cl_2, and the combined filtrate was concentrated under reduced pressure. The residue was redissolved in CH_2Cl_2 (~20 mL) and washed with water (8 mL), 10% aq. $Na_2S_2O_3$ (8 mL) and water (2 x 8 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to obtain the title compound as a colorless syrup in 88% yield (54 mg, 0.045 mmol, α/β >20/1). Analytical data for **17**: R_f = 0.55 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98-7.01 (m, 35H, aromatic), 5.85 (dd, 1H, $J_{4'',5''}$ = 2.4 Hz, H-4''), 5.52 (d, 1H, $J_{1'',2''}$ = 3.0 Hz, H-1''), 5.49 (s, 1H, C*H*Ph), 5.05 (d, 1H, $J_{1,2}$ = 3.0 Hz, H-1), 4.72 (dd, 2H, ^2J = 11.4 Hz, CH_2Ph), 4.70 (dd, 2H, ^2J = 11.5 Hz, CH_2Ph), 4.64 (br. s, 1H, H-1'), 4.63 (s, 2H, CH_2Ph), 4.61 (dd, 2H, ^2J = 11.7 Hz, CH_2Ph), 4.43-4.40 (m, 1H, H-6a''), 4.38-4.34 (m, 3H, H-5'', 6a', 6b''), 4.21-4.12 (m, 4H, $J_{4',5'}$ = 5.0 Hz, H-3, 3', 3'', 4'), 3.97 (dd, 1H, $J_{2',3'}$ = 2.4 Hz, H-2'), 3.93-3.88 (m, 3H, H-2'', 5, 6b'), 3.67 (dd, 1H, $J_{2,3}$ = 10.6 Hz, H-2), 3.54 (br. s, 1H, H-4), 3.34 (dd, 1H, $J_{5',6a'}$ = 9.4, H-5'), 1.22 (d, 3H, $J_{5,6}$ = 6.3 Hz, H-6) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.3, 165.9, 138.2, 138.2, 138.1, 137.2, 137.1, 133.5, 133.3, 130.0 (x2), 129.8 (x3), 129.4, 128.7, 128.6 (x3), 128.5 (x2), 128.5 (x3), 128.3 (x2), 128.3 (x3), 128.2 (x3), 128.2, 127.9 (x3), 127.9 (x2), 127.5, 127.5 (x3), 127.4, 126.4 (x2), 102.3, 99.2, 98.4, 98.1, 78.5, 78.3, 76.1, 75.2, 74.5, 74.0, 72.5, 71.6, 70.0, 68.6, 68.4, 67.7, 67.2, 66.7, 64.8, 62.7, 58.4, 16.7 ppm. HR-FAB MS $[M+Na]^+$ calcd for $C_{67}H_{66}N_6O_{15}Na$ 1217.4488; found 1217.4478.

Benzyl 2-azido-3-*O*-(2-azido-3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranosyl)-4-*O*-benzyl-2,6-dideoxy-α-L-fucopyranoside (22). A mixture containing mannosyl donor **4** (29 mg, 0.066 mmol), fucosyl acceptor **19** (22 mg, 0.060 mmol), and molec. sieves (4 Å, 200 mg) in 1,2-DCE (5.0 mL) was stirred under argon for 1 h at rt. The mixture was cooled to -30 ˚C, NIS (30 mg, 0.131 mmol) and TfOH (2.3 µL, 0.026 mmol) were added, the external cooling was removed, and the resulting mixture was stirred for 16 h at rt. After that, the solids were filtered off through a pad of Celite, rinsed successively with CH_2Cl_2, and the combined filtrate was concentrated under reduced pressure. The residue was redissolved in CH_2Cl_2 (~20 mL) and washed with water (8 mL), 10% aq. $Na_2S_2O_3$ (8 mL) and water (2 x 8 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate – hexane gradient elution) to obtain the title compound **22** as a colorless syrup in 88% (α/β > 25/1). Analytical data for **22**: R_f = 0.70 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.12-7.25 (m, 20H, aromatic), 5.83 (dd, 1H, $J_{3',4'}$ = 10.2 Hz, H-3'), 5.63 (s, 1H, C*H*Ph), 5.26 (br. s, 1H, $J_{1',2'}$ = 1.2 Hz, H-1'), 5.04 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.91 (dd, 2H, ^2J = 11.3 Hz, CH_2Ph), 4.65 (dd, 2H, ^2J = 11.9 Hz, CH_2Ph), 4.45 (dd, 1H, $J_{2',3'}$ = 3.7 Hz, H-2'), 4.31-4.28 (m, 2H, H-4', 6a'), 4.19 (dd, 1H, $J_{3,4}$ = 2.6 Hz, H-3), 4.12-4.08 (m, 1H, H-5'), 4.02 (dd, 1H, $J_{2,3}$ = 10.6 Hz, H-2), 3.97 (dd, 1H, H-5), 3.91 (dd, 1H, $J_{6a',6b'}$ = 10.4 Hz, H-6b'), 3.66 (dd, 1H, $J_{4,5}$ = 1.5 Hz, H-4), 1.21 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.5, 137.9, 137.0, 136.9, 133.6, 130.1 (x2), 129.3, 129.2, 128.6 (x2), 128.6 (x2), 128.6 (x2), 128.4 (x2), 128.3 (x2), 128.3 (x2), 128.2, 128.1, 126.2 (x2), 102.0, 100.3 ($^1J_{C1',H1'}$ = 241.0 Hz), 96.9 ($^1J_{C1,H1}$ = 154.1 Hz), 79.2, 76.3, 76.0, 75.7, 70.1, 70.0, 68.7, 67.3, 65.5, 62.6, 60.3, 16.8 ppm. HR-FAB MS $[M+H]^+$ calcd for $C_{40}H_{41}N_6O_9$ 749.2924; found 749.2930.

Conflicts of interest

There are no conflicts to declare.

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