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Direct Synthesis of Glycans Containing Challenging ManNAcA Residues

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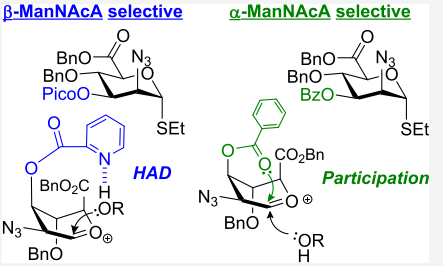
ABSTRACT: A method for direct, highly stereoselective synthesis of glycans containing β-linked D-mannosaminuronic acid (ManNAcA) residues is reported herein, among which is the capsular polysaccharide of *Staphylococcus aureus* type 8. Previous chemical syntheses of this glycan relied on indirect methods comprising glucosylation followed by a multistep epimerization and oxidation sequence. The high β-stereocontrol with direct glycosidation of 3-*O*-picoloylated ManNAcA donors was achieved using the H-bond-mediated aglycone delivery (HAD) reaction. A method to achieve complete α-ManNAcA stereoselectivity with 3-*O*-benzoylated donors is also reported.



INTRODUCTION

With the development of the H-bond-mediated aglycone delivery (HAD) reaction, many linkages have become more accessible.[1−3] Among these, mannosyl donors containing 3-*O*-picoloyl (3-Pico) group are capable of providing highly stereoselective β-mannosylation reactions.[4] This methodology was already applied to the synthesis of glycans containing β-mannosamine (ManNAc)[5] and β-mannuronic acid (ManA),[6] common residues in bacteria. Our discovery that the HAD reaction also works well in the synthesis of oligosaccharides containing D-mannosaminuronic acid (ManNAcA) residues is reported herein. We adopted common abbreviations that refer to the naturally occurring *N*-acetylated residues, which are commonly found in bacterial glycans. Among these are capsular polysaccharides of *Staphylococcus aureus*, a Gram-positive, opportunistic pathogenic bacteria, which is a causative agent for community and health-care-associated infections.[7,8] Methicillin-resistant *S. aureus* is one of the greatest current health concerns due to its limited treatment options. While the development of new antibiotics is not economically feasible, immunotherapies based on capsular polysaccharides have come forward as promising treatment options. The *S. aureus* capsular polysaccharide type 8 (CP8) comprises the trisaccharide repeating unit consisting of uncommon monosaccharides, all linked via 1,2-*cis* glycosidic bonds: ManNAcA, L-fucosamine (L-FucNAc), and D-fucosamine (D-FucNAc) to C-3 of D-FucNAc.[7] There have only been a few reports for the total synthesis of CP8 disaccharides,[9,10] a trisaccharide,[11] and a hexasaccharide[12] sequence. All previous syntheses of *S. aureus* CP8 fragments containing the ManNAcA residue were approached indirectly via glucosylation followed by epimerization to the mannosamine residue and subsequent oxidation. With the development of the HAD reaction, the direct synthesis of a trisaccharide derived from *S. aureus* CP8 became a reality and is reported herein. A method for the direct β-glycosidation of ManNAcA has been previously reported, but somewhat relaxed stereoselectivity was observed in a number of reactions.[13]

RESULTS AND DISCUSSION

To initiate the study of the HAD reaction in the context of ManNAcA linkages, we synthesized ManNAcA building blocks that included donor **6** containing the 3-Pico group. As shown in Scheme 1, a known ManNAc derivative **1**[5,14] was used as the starting material, which was subjected to regioselective reductive ring opening using $Cu(OTf)_2$ to obtain diol **2** in an 84% yield. TEMPO/BAIB oxidation[15] of diol **2** resulted in a mixture of lactone **3** and the desired compound **4** in a ratio of 1.6:1.

The products were separated by column chromatography, and compound **3** was subjected to the lactone opening in the presence of LiOH to obtain compound **4** in a 98% yield. Altogether, carboxylic acid derivative **4** was synthesized from precursor **2** in a 91% overall yield. Benzylation of the carboxyl group in compound **4** with benzyl bromide in the presence of $NaHCO_3$[6,11] afforded ester derivative **5**. The latter compound was subjected to picoloylation with PicoOH (picolinic acid) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC) and DMAP.[16] As a result, ManNAcA donor **6** was obtained in a 96% yield. For the purpose of creating a comparison point in glycosylation, we also benzoylated intermediate **5**. This reaction was conducted

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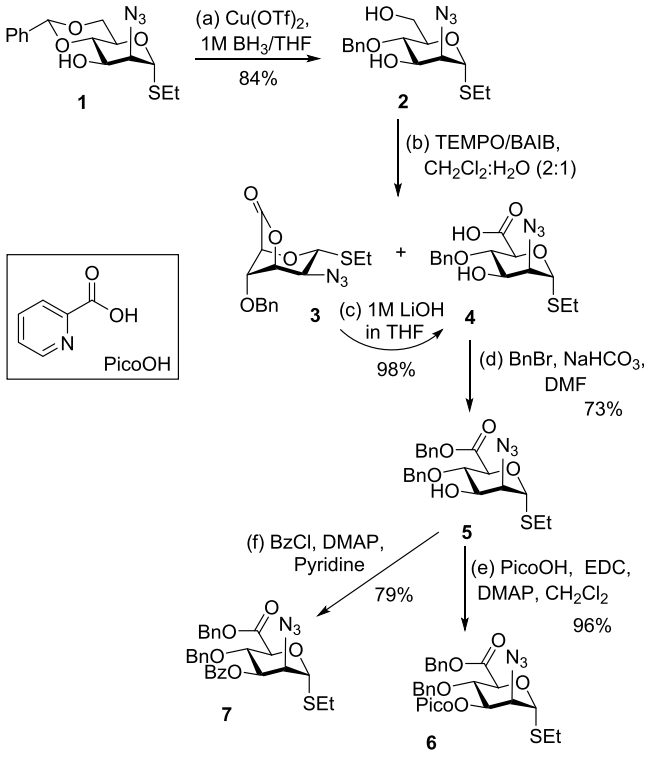
Scheme 1. Synthesis of ManNAcA Donors 3, 6, and 7

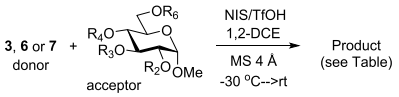


with benzoyl chloride in the presence of DMAP in pyridine to obtain 3-*O*-benzoylated (3-Bz) ManNAcA donor **7** in a 79% yield. Also for comparison, a part of lactone derivative **3** was preserved to be investigated as a glycosyl donor.

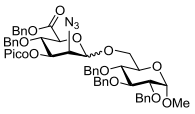
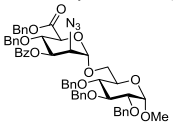
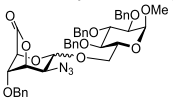
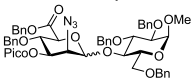
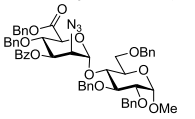
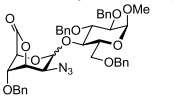
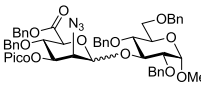
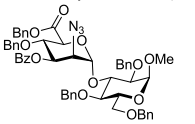
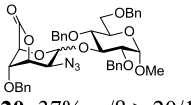
To study the formation of β-ManNAcA glycosides with 3-Pico donor **6**, we performed a series of glycosylations with common acceptors **8**−**11**[17] (Table 1). When glycosyl donor **6** was glycosidated with the primary glycosyl acceptor **8** in the presence of NIS/TfOH in 1,2-DCE under regular concentration (50 mM of donor **6**), product **12** was isolated in a 79% yield with excellent stereoselectivity (α/β = 1/24). The HAD reactions typically provide the best results in terms of the stereoselectivity in high dilution experiments (5.0 mM of the donor).[1] Also, in this case, 10-fold dilution conditions led to compound **12** in a 93% yield (α/β = 1/24; Table 1, entry 1), and both reactions required 3 h to go to completion. We believe that the high stereoselectivity observed herein can be rationalized using the analogy of ManA donors that react via the intermediacy of the axial-rich half-chair oxacarbenium ion.[6,18,19] Also, in the case of the ManNAcA series, such conformation will favor the HAD reaction pathway, thereby favoring the β-glycosides (intermediate **A**; Figure 1).

Conversely, complete α-ManNAcA stereoselectivity was accomplished in the reaction of 3-Bz ManNAcA donor **7** with acceptor **8**. These glycosylations produced glycoside **13** in 91 and 96% yields under 50 and 5 mM conditions, respectively (entry 2). Both glycosylations were completed within 50 min. We believe that the high stereoselectivity observed in this case is due to participation of the 3-Bz group, as shown in Figure 1 for intermediate **B**. The analogy for this phenomenon is found in the work by Crich with regular mannosides,[20] our studies with ManNAc[5] and ManA glycosyl donors,[6] as well as observations by Nifantiev[21−24] and Kim[25] made with other sugar series.

Table 1. Glycosidation of Glycosyl Donors 3, 6, and 7 with Glycosyl Acceptors 8−11



8: R_2 = R_3 = R_4 = Bn, R_6 = H (6-OH)
9: R_2 = R_3 = R_6 = Bn, R_4 = H (4-OH)
10: R_2 = R_4 = R_6 = Bn, R_3 = H (3-OH)
11: R_2 = H, R_3 = R_4 = R_6 = Bn (2-OH)

Entry	Reactants (time)	Product: yield, stereoselectivity (concentration of the donor)	$J_{C1',H1'}$, δ H3'
1	**6** + **8** (3 h)	 **12**: 79%, α/β = 1/24 (50 mM) 93%, α/β = 1/24 (5.0 mM)	165 Hz 5.15 ppm
2	**7** + **8** (0.8 h)	 **13**: 91%, α/β > 25/1 (50 mM) 96%, α/β > 25/1 (5.0 mM)	172 Hz 5.58 ppm
3	**3** + **8** (19 h)	 **14**: 26%, α/β > 25/1 (50 mM)	177 Hz 4.82 ppm
4	**6** + **9** (19 h)	 **15**: 43%, α/β = 1/6.0 (50 mM) 29%, α/β = 1/20 (5.0 mM)	162 Hz 5.02 ppm
5	**7** + **9** (3 h)	 **16**: 92%, α/β > 25/1 (50 mM) 88%, α/β > 25/1 (5.0 mM)	174 Hz 5.58 ppm
6	**3** + **9** (19 h)	 **17**: 27%, α/β = 6.0/1 (50 mM)	178 Hz 4.71 ppm
7	**6** + **10** (19 h)	 **18**: 37%, α/β = 1/9.0 (50 mM) 97%, α/β = 1/25 (5.0 mM)	164 Hz 5.16 ppm
8	**7** + **10** (4 h)	 **19**: 98%, α/β > 25/1 (50 mM) 94%, α/β > 25/1 (5.0 mM)	175 Hz 5.65 ppm
9	**3** + **10** (19 h)	 **20**: 37%, α/β > 20/1 (50 mM)	178 Hz 4.81 ppm

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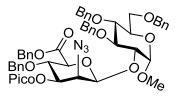
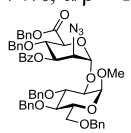
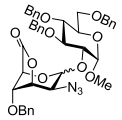
J. Org. Chem. 2022, 87, 271−280

Table 1. continued

10	**6** + **11** (5 h)	 **21**: 64%, α/β = 1/13 (50 mM) 74%, α/β < 1/25 (5.0 mM)	162 Hz 5.10 ppm
11	**7** + **11** (1 h)	 **22**: 90%, α/β = 10/1 (50 mM) 90%, α/β = 10/1 (5.0 mM)	169 Hz 5.68 ppm
12	**3** + **11** (20 h)	 **23**: 40%, α/β > 20/1 (50 mM)	178 Hz 4.85 ppm

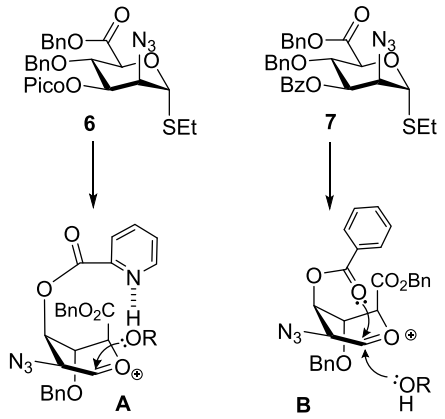


Figure 1. Rationalization of the stereoselectivity observed.

The lactonized donor **3** also provided high α-stereoselectivity in the glycosylation of acceptor **8**. The corresponding glycoside **14** was obtained in a 26% yield (α/β > 25/1, entry 3). This result somewhat contradicts β-stereoselective reactions with lactones performed by Boltje and co-workers[26,27] and our own studies with ManA donors.[6] It is possible that the opposite stereoselectivity could be due to the 2-azide group.

A series of comparative NMR experiments were performed to con rm the stereochemical assignment of all products. Mannose anomeric assignment often relies on the $J_{C1'-H1'}$ coupling constant value. Conventional β-mannosides have the coupling constant value around 160 Hz[28] and the observed value of 165 Hz for β-ManNAcA glycoside **12** (entry 1) con rms its assignment. The $J_{C1',H1'}$ coupling constants of 172 and 177 Hz measured for α-ManNAcA glycosides **13** and **14** (entries 2 and 3), respectively, were in accordance with the standard values (170 Hz or greater) for α-mannosides.[28] Similar to our previous observations with ManNAc and ManA glycosides,[5,6] we have observed that the H-3′ signal of the α-anomer in ^{1}H NMR spectra always appears shifted down eld by Δ = 0.4−0.6 ppm in respect to that of the β-anomer. While β-linked disaccharide **12** showed the H-3′ signal at 5.15 ppm, the H-3′ signal of α-linked counterpart **13** appeared at 5.58 ppm (entries 1 and 2, Table 1). However, we have not observed such a trend with the lactonized products.

Secondary glycosyl acceptors were also included in the glycosylation studies. The glycosidation of 3-Pico donor **6** with 4-OH acceptor **9** was conducted in the presence of the NIS/TfOH promoter system in 1,2-DCE. Under regular (50 mM of the donor) concentration, disaccharide **15** was obtained in a 43% yield with moderate β-stereoselectivity (α/β = 1/6.0, entry 4). When 5.0 mM of donor **6** conditions were applied, glycoside **15** was obtained in a modest yield of 29% albeit with excellent β-stereoselectivity (α/β = 1/20, entry 4). Both glycosylations required 19 h to complete, and the modest yields can be attributed to a low reactivity of both counterparts: the hindered glycosyl acceptor and the electronically deactivated glycosyl donor. Glycosidations of 3-Bz donor **7** with glycosyl acceptor **9** yielded α-linked compound **16** in 3 h. High yields (88−92%) and exclusive α-stereoselectivity were achieved for both regular and high dilution experiments (entry 5). A reaction between lactone **3** and glycosyl acceptor **9** afforded glycoside **17** in a 27% yield (α/β = 6.0/1) in 19 h (entry 6).

The secondary 3-OH glycosyl acceptor **10** was then reacted with donor **6** in 1,2-DCE. Regular concentration (50 mM of the donor) experiment led to the formation of disaccharide **18** in a 37% yield with a moderate stereoselectivity (α/β = 1/9.0, entry 7). The high dilution (5.0 mM of donor **6**) reaction afforded glycoside **18** in a 97% yield with excellent stereoselectivity (α/β = 1/25, entry 7). Both glycosylations required 19 h to complete. The reaction between 3-Bz donor **7** and glycosyl acceptor **10** was α-stereoselective in both regular concentration and high dilution experiments (entry 8). The corresponding disaccharide **19** was obtained in very high yields of 94−98%. A reaction between lactone derivative **3** and glycosyl acceptor **10** gave product **20** in a 37% yield in 19 h with α/β > 20/1 stereoselectivity (entry 9).

A coupling between 3-Pico glycosyl donor **6** and 2-OH glycosyl acceptor **11** under regular (50 mM of donor **6**) concentration in 1,2-DCE afforded glycoside **21** in a 64% yield with good β-stereoselectivity (α/β = 1/13, entry 10). High dilution (5.0 mM of the donor) reaction led to the formation of compound **21** with an improved yield and stereoselectivity (74%, α/β < 1/25, entry 10). These glycosylations required 5 h to go to completion. The glycosidation of 3-Bz donor **7** with glycosyl acceptor **11** smoothly produced product **22** in 1 h, but the reaction proceeded with moderate α-stereoselectivity (α/β = 10/1, entry 11). Both regular and high dilution reactions produced disaccharide 22 in a 90% yield. A coupling between lactone derivative **3** and glycosyl acceptor **11** afforded product **23** in a 40% yield (α/β > 20/1, entry 12).

Upon re ning basic parameters for the synthesis of 1,2-*cis* β-ManNAcA linkages, we decided to extend this methodology to the synthesis of compound **28** corresponding to the trisaccharide repeating unit of *S. aureus* capsular polysaccharide type 8 (CP8). A reaction between ManNAcA donor **6** and fucosyl acceptor **24**[7] was performed in the presence of NIS/TfOH in 1,2-DCE (5.0 mM concentration of donor **6**) at −30 °C to rt to afford the desired disaccharide **26** in a 61% yield with complete β-stereoselectivity (Scheme 2). The β-manno con guration of disaccharide **26** was con rmed by measuring the $J_{C1',H1'}$ coupling constant (158 Hz). The 3-Pico group in compound **26** was then removed by reaction with $Cu(OAc)_2$-H_2O in CH_2Cl_2/MeOH[16] to obtain disaccharide acceptor **27** in a 93% yield. The latter was then reacted with D-fucosyl donor **25** to produce the target repeating unit **28** in a 41% yield (α/β = 18/1).

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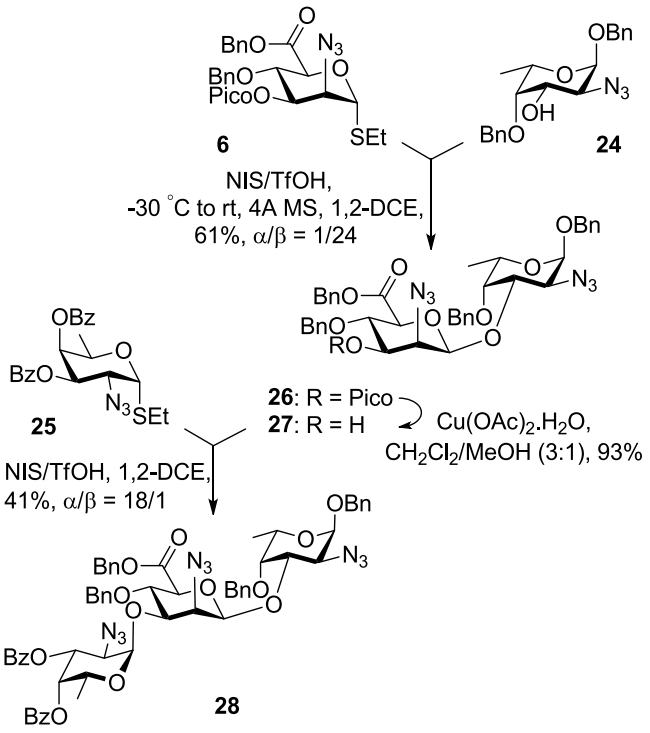
J. Org. Chem. 2022, 87, 271−280

Scheme 2. Application of Glycosyl Donor 6 in the Assembly of Trisaccharide 28 Representing the Repeating Unit of *S. aureus* CP8



CONCLUSIONS

E cient reactions for a highly stereocontrolled formation of either α- or β-glycosides of ManNAcA are described. The ManNAcA donor equipped with the 3-*O*-picoloyl group is capable of achieving high or even exclusive stereoselectivity in β-mannosylation by means of the HAD reaction. The developed method was utilized for the synthesis of a trisaccharide sequence containing ManNAcA residues linked via β-(1→3) linkages found in the capsular polysaccharide of *S. aureus* type 8. Excellent α-stereoselectivity was achieved in all glycosidations of the ManNAcA donor functionalized with 3-*O*-benzoyl ester. This entire stereocontrol was credited to the participation of the remote 3-benzoyl group. Also studied was the 6,3-lactone donor that was less effective in terms of both the reaction yields and stereoselectivity.

EXPERIMENTAL SECTION

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 or 4 Å), used for reactions, were crushed and activated *in vacuo* at 390 °C for 8 h in the rst instance and then for 2−3 h at 390 °C directly prior to application. Optical rotations were measured at a "Jasco P-1020" polarimeter. Unless noted otherwise, ^{1}H NMR spectra were recorded in $CDCl_3$ at 300 or 600 MHz, and ^{13}C NMR spectra were recorded in $CDCl_3$ at 75 or 151 MHz. Two-dimensional heteronuclear *J*-resolved spectra (HETERO2DJ)[28] were recorded in $CDCl_3$ at 600 MHz. Structural assignments were made, with additional information from gCOSY experiments. Accurate mass spectrometry determinations were performed using an Agilent 6230 ESI TOF LCMS spectrometer.

Synthesis of ManNAcA Donors. *Ethyl 2-Azido-4-O-benzyl-2-deoxy-1-thio-α-D-mannopyranoside (**2**).* A 1.0 M solution of the borane−THF complex in tetrahydrofuran (21.8 mL, 21.8 mmol) and copper(II) tri uoromethanesulfonate (158 mg, 0.436 mmol) was added to a ask containing ethyl 2-azido-4,6-*O*-benzylidene-2-deoxy-1-thio-α-D-mannopyranoside[5,14] (**1**, 1.47 g, 4.36 mmol), and the resulting mixture was stirred under argon for 2.5 h at rt. The reaction mixture was then cooled to 0 °C, and triethylamine (3 mL) was added until neutral pH. After that, CH_3OH (10 mL) was added dropwise, and the volatiles were removed under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to give the title compound as a colorless syrup in an 84% yield (1.24 g, 3.65 mmol). Analytical data for **2**: R_f = 0.45 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{21}$ +110.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 7.37−7.30 (m, 5H, aromatic), 5.26 (br. s, 1H, H-1), 4.76 (dd, 2H, ^2J = 11.3 Hz, CH_2Ph), 4.12−4.05 (m, 1H, H-3), 4.00−3.94 (m, 2H, H-2, 5), 3.82−3.73 (m, 3H, H-4, 6a, 6b), 2.81 (d, 1H, 3-OH), 2.66−2.53 (m, 2H, SCH_2CH$_3$), 2.42 (t, 1H, 6-OH), 1.27 (t, 3H, *J* = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 138.0, 128.7 (×2), 128.2, 128.0 (×2), 82.5, 75.7, 75.1, 72.3, 72.0, 65.4, 61.7, 25.5, 14.8 ppm; HR-FAB MS [M + Na]$^+$ calcd for $C_{15}H_{21}N_3O_4SNa^+$ 362.1145; found 362.1157.

*Ethyl 2-Azido-4-O-benzyl-2-deoxy-1-thio-α-D-mannopyranosi-durono-6,3-lactone (**3**).* (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO, 113 mg, 0.722 mmol) and bis(acetoxy)iodobenzene (BAIB, 2.91 g, 9.02 mmol) were added to a mixture of compound **2** (1.22 g, 3.61 mmol) in CH_2Cl_2/H_2O (30 mL, 2/1, v/v), and the resulting mixture was stirred for 16 h at rt. The reaction was quenched with aq. $Na_2S_2O_3$ (3 mL), and the volatiles were removed under reduced pressure. The residue was diluted with EtOAc (30 mL) and washed with water (2 × 10 mL). The aqueous layer was then separated and extracted with EtOAc (2 × 30 mL). The organic layers were combined, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (CH_3OH−CH_2Cl_2 gradient elution) to give lactone **3** as a colorless solid (0.71 g, 2.02 mmol) and acid **4** (0.45 g, 1.27 mmol). Analytical data for **3**: R_f = 0.80 (CH_3OH/CH_2Cl_2, 1/9, v/v), R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); $[\alpha]_D^{21}$ +42.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) 7.43−7.34 (m, 5H, aromatic), 4.73 (d, 1H, $J_{3,4}$ = 5.8 Hz, H-3), 4.68 (d, 1H, $J_{1,2}$ = 9.5 Hz, H-1), 4.67 (dd, 2H,^2J = 11.6 Hz, CH_2Ph), 4.29 (d, 1H, H-5), 4.05 (dd, 1H, $J_{4,5}$ = 2.8 Hz, H-4), 3.96 (dd, 1H, H-2), 2.86−2.72 (m, 2H, SCH_2CH$_3$), 1.33 (t, 3H, *J* = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$) 169.3, 136.0, 128.8 (×3), 128.2 (×2), 82.0, 78.2, 74.4, 72.2, 71.7, 58.7, 25.1, 15.2 ppm; HR-FAB MS [M + Na]$^+$ calcd for $C_{15}H_{17}N_3O_4SNa^+$ 358.0832; found 358.0841.

*Ethyl 2-Azido-4-O-benzyl-2-deoxy-1-thio-α-D-mannopyranosi-duronic Acid (**4**).* A 1 M aq. solution of LiOH (5.0 mL) was added to a solution of lactone **3** (0.71 g, 2.02 mmol) in THF (10.0 mL), and the resulting mixture was stirred for 2 h at rt. After that, 1 N aq. HCl was added to the reaction mixture to acidify to pH 3 (5 mL), and the volatiles were removed under reduced pressure. The residue was diluted with EtOAc (25 mL) and washed with water (10 mL). The aqueous layer was extracted with EtOAc (3 × 25 mL). The combined organic phase was dried with Na_2SO_4 and concentrated under reduced pressure. The residue was dried in *vacuo* for 2 h to give the title compound as a colorless syrup in a 98% yield (0.71 g, 2.01 mmol), which corresponds to a combined yield of 91% from compound **2**. Analytical data for **4**: R_f = 0.15 (CH_3OH/CH_2Cl_2, 1/9, v/v), R_f = 0.20 (ethyl acetate/toluene, 1/4, v/v); $[\alpha]_D^{21}$ +48.8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): 7.34−7.27 (m, 5H, aromatic), 5.41 (d, 1H, $J_{1,2}$ = 6.8 Hz, H-1), 4.65 (dd, 2H, ^2J = 11.4 Hz, CH_2Ph), 4.53 (d, 1H, H-5), 4.14 (dd, 1H, $J_{3,4}$ = 5.3 Hz, H-3), 4.03 (dd, 1H, $J_{4,5}$ = 4.7 Hz, H-4), 3.81 (dd, 1H, $J_{2,3}$ = 2.8 Hz, H-2), 2.73 (m, 2H, SCH_2CH$_3$), 1.31 (t, 3H, *J* = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C{H} NMR (151 MHz, $CDCl_3$): 176.1, 140.1, 131.2 (×2), 130.7, 130.5 (×2), 82.3, 75.7, 74.8, 72.7, 69.1, 64.3, 27.5, 17.6 ppm; HR-FAB MS [M + Na]$^+$ calcd for $C_{15}H_{19}N_3O_5SNa^+$ 376.0938; found 376.0967.

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J. Org. Chem. 2022, 87, 271−280

*Benzyl (Ethyl 2-Azido-4-O-benzyl-2-deoxy-1-thio-α-D-mannopyranosid)uronate (**5**).* Benzyl bromide (4.5 mL, 37.9 mmol) and $NaHCO_3$ (1.91 g, 22.7 mmol) were added to a solution of compound **4** (1.34 g, 3.79 mmol) in *N,N*-dimethylformamide (DMF, 15 mL), and the resulting mixture was stirred for 16 h at rt. The reaction mixture was diluted with EtOAc (100 mL), washed with water (2 × 15 mL), and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to give the title compound as a colorless syrup in a 73% yield (1.23 g, 2.77 mmol). Analytical data for **5**: R_f = 0.55 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ +53.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 7.34−7.25 (m, 10H, aromatic), 5.38 (d, 1H, $J_{1,2}$ = 5.7 Hz, H-1), 5.18 (dd, 2H, ^2J = 12.2 Hz, CH_2Ph), 4.63−4.51 (m, 3H, $J_{4,5}$ = 5.9 Hz, H-5, CH_2Ph), 4.05 (m, 2H, $J_{3,4}$ = 12.4 Hz, H-3, 4), 3.88 (dd, 1H, $J_{2,3}$ = 3.2 Hz, H-2), 2.69 (m, 2H, SCH_2CH$_3$), 2.24 (d, 1H, J = 3.8 Hz, 3-OH), 1.29 (t, 3H, J = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 169.1, 137.3, 135.1, 128.6 (×4), 128.5 (×3), 128.1, 127.9 (×2), 80.7, 76.8, 73.5, 71.9, 70.4, 67.3, 62.6, 25.4, 15.0 ppm; HR-FAB MS [M + Na]$^+$ calcd for $C_{22}H_{25}N_3O_5SNa^+$ 466.1408; found 466.1422.

*Benzyl (Ethyl 2-Azido-4-O-benzyl-2-deoxy-3-O-picoloyl-1-thio-α-D-mannopyranosid) uronate (**6**).* Picolinic acid (0.51 g, 4.15 mmol), EDC (0.80 g, 4.15 mmol), and DMAP (68 mg, 0.55 mmol) were added to a solution of compound **5** (1.23 g, 2.77 mmol) in dry CH_2Cl_2 (30 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 (50 mL) and washed with water (15 mL), sat. aq. $NaHCO_3$ (15 mL), and water (2 × 15 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to give the title compound as a colorless syrup in a 96% yield (1.46 g, 2.66 mmol). Analytical data for **6**: R_f = 0.50 (ethyl acetate/hexane, 1/1, v/v); $[\alpha]_D^{22}$ +83.5 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 8.77 (m, 1H, aromatic), 8.03 (m, 1H, aromatic), 7.84 (m, 1H, aromatic), 7.49 (m, 1H, aromatic), 7.31−7.21 (m, 10H, aromatic), 5.60 (dd, 1H, $J_{3,4}$ = 6.6 Hz, H-3), 5.53 (d, 1H, $J_{1,2}$ = 6.2 Hz, H-1), 5.02 (dd, 2H, ^2J = 12.1 Hz, CH_2Ph), 4.70 (m, 3H, J = 8.3 Hz, H-5, CH_2Ph), 4.40−4.35 (dd, 1H, H-4), 4.10 (m, 1H, $J_{2,3}$ = 3.3 Hz, H-2), 2.81−2.66 (m, 2H, SCH_2CH$_3$), 1.32 (t, 3H, J = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 168.7, 163.7, 146.9, 137.2, 134.9, 128.7 (×3), 128.6, 128.5 (×2), 128.4 (×3), 128.1, 128.0 (×3), 125.6, 80.7, 77.3, 74.1, 73.9, 72.7, 72.6, 67.5, 25.3, 15.0 ppm; HR-FAB MS [M + Na]$^+$ calcd for $C_{28}H_{28}N_4O_6SNa^+$ 571.1622; found 571.1639.

*Benzyl (Ethyl 2-Azido-3-O-benzoyl-4-O-benzyl-2-deoxy-1-thio-α-D-mannopyranosid) uronate (**7**).* Benzoyl chloride (0.23 mL, 1.96 mmol) and DMAP (24 mg, 0.20 mmol) were added to a solution of compound **5** (0.43 g, 0.98 mmol) in pyridine (10 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 coevaporated with toluene. The resulting residue was diluted with CH_2Cl_2 (20 mL) and washed with water (8 mL), 1 N aq. HCl (8 mL), and water (2 × 8 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to give the title compound as a colorless syrup in a 79% yield (0.43 g, 0.79 mmol). Analytical data for **7**: R_f = 0.40 (ethyl acetate/hexane, 1/4, v/v); $[\alpha]_D^{22}$ +77.3 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 8.01 (m, 2H, aromatic), 7.61 (m, 1H, aromatic), 7.50−7.44 (m, 2H, aromatic), 7.29−7.21 (m, 8H, aromatic), 7.10 (m, 2H, aromatic), 5.59−5.53 (m, 2H, $J_{1,2}$ = 6.9, $J_{3,4}$ = 6.1, H-1, 3), 4.89 (dd, 2H, ^2J = 12.2 Hz, CH_2Ph), 4.66 (m, 3H, H-5, CH_2Ph), 4.33 (dd, 1H, $J_{4,5}$ = 1.1 Hz, H-4), 4.03 (dd, 1H, $J_{2,3}$ = 3.2 Hz, H-2), 2.88−2.72 (m, 2H, SCH_2CH$_3$), 1.37 (t, 3H, J = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 168.6, 165.0, 137.0, 134.6, 133.8, 129.9 (×2), 128.7 (×2), 128.5 (×6), 128.2 (×2), 128.1, 127.9 (×2), 80.2, 77.2, 74.2, 73.6, 72.7, 71.6, 67.3, 25.1, 15.0 ppm; HR-FAB MS [M + Na]$^+$ calcd for $C_{29}H_{29}N_3O_6SNa^+$ 570.1670; found 570.1691.

Synthesis of Disaccharides 12−23. *General Procedure for Glycosylation.* A mixture of a glycosyl donor (0.06 mmol, 1.2 equiv), glycosyl acceptor (0.05 mmol, 1.0 equiv), and freshly activated molecular sieves (4 Å, 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, 2.2 equiv) and tri uoromethanesulfonic acid (TfOH, 2.0 L, 0.02 mmol, 0.22 equiv) were added, and the external cooling was removed. The resulting mixture was allowed to warm to ambient temperature and stirred at rt for the time speci ed in Table 1. After that, the solids were ltered off and washed successively with CH_2Cl_2. The combined ltrate (30−40 mL) was washed with water (10 mL), 10% sodium thiosulfate ($Na_2S_2O_3$, 10 mL), and water (2 × 10 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane or ethyl acetate−toluene 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 the ^{1}H NMR spectra.

*Methyl 6-O-(Benzyl-2-azido-4-O-benzyl-2-deoxy-3-O-picoloyl-α/β-D-mannopyranosyluronate)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (**12**).* The title compound was obtained as a white amorphous solid from glycosyl donor **6** and acceptor **8**[17] in a 79% yield (α/β = 1/24, 50 mM) or 93% yield (α/β = 1/24, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **12**: R_f = 0.40 (acetone/toluene, 3/17, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 8.81 (m, 1H, aromatic), 8.07 (m, 1H, aromatic), 7.83 (m, 1H, aromatic), 7.50 (m, 1H, aromatic), 7.36−7.27 (m, 20H, aromatic), 7.15−7.11 (m, 3H, aromatic), 7.01 (m, 2H, aromatic), 5.24−5.12 (m, 3H, $J_{3',4'}$ = 9.5, ^2J = 12.2 Hz, H-3′, CH_2Ph), 5.00 (d, 1H, J = 10.9 Hz, CHPh), 4.89−4.75 (m, 3H, 3 × CHPh), 4.65−4.48 (m, 5H, $J_{1,2}$ = 3.3 Hz, H-1, 4 × CHPh), 4.35 (br. s, 1H, H-1′), 4.32−4.25 (dd, 1H, $J_{4',5'}$ = 9.4 Hz, H-4′), 4.10−4.06 (m, 2H, H-2′, 6a), 4.01 (dd, 1H, $J_{3,4}$ = 9.2 Hz, H-3), 3.87 (d, 1H, H-5′), 3.80−3.75 (m, 1H, H-5), 3.51−3.46 (m, 2H, H-2, 6b), 3.41 (dd, 1H, H-4), 3.35 (s, 3H, OCH$_3$) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 167.3, 164.0, 150.3, 146.9, 138.6, 138.2, 138.0, 137.4, 137.1, 134.9, 128.7 (×2), 128.6 (×4), 128.5 (×2), 128.4 (×2), 128.3 (×2), 128.2 (×5), 128.1 (×2), 128.0 (×2), 127.8 (×2), 127.7 (×2), 127.4, 125.5, 100.3 ($^1J_{C1',H1'}$ = 165.0 Hz, C-1′), 97.8 ($^1J_{C1,H1}$ = 173.0 Hz, C-1), 82.1, 79.8, 77.2, 75.8, 75.1, 74.9, 74.7, 74.5, 73.7, 73.4, 69.5, 68.6, 67.5, 61.4, 55.2 ppm; HR-FAB MS [M + Na]$^+$ calcd for $C_{54}H_{54}N_4O_{12}Na^+$ 973.3631; found 973.3663.

*Methyl 6-O-(Benzyl-2-azido-3-O-benzoyl-4-O-benzyl-2-deoxy-α-D-mannopyranosyluronate)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (**13**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **7** and acceptor **8**[17] in 91% (α/β > 25/1, 50 mM) and 96% (α/β > 25/1, 5.0 mM) yields under regular and high dilution reaction conditions, respectively. Analytical data for **13**: R_f = 0.65 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 8.00 (m, 2H, aromatic), 7.59 (m, 1H, aromatic), 7.45 (m, 2H, aromatic), 7.35−7.12 (m, 25H, aromatic), 5.59 (dd, 1H, $J_{3',4'}$ = 6.9 Hz, H-3′), 5.23 (d, 1H, $J_{1',2'}$ = 4.6 Hz, H-1′), 5.05−4.58 (m, 11H, H-1, 5 × CH_2Ph), 4.45 (d, 1H, H-5′), 4.26 (dd, 1H, $J_{4',5'}$ = 6.2 Hz, H-4′), 4.12−4.04 (m, 2H, $J_{2',3'}$ = 3.3 Hz, H-2′, 6a), 4.04−3.96 (m, 1H, $J_{3,4}$ = 9.2 Hz, H-3), 3.84−3.76 (m, 2H, H-5, 6b), 3.59−3.51 (m, 2H, H-2, 4), 3.38 (s, 3H, OCH$_3$) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 168.7, 165.1, 138.8, 138.2, 138.1, 137.1, 134.8, 133.8, 130.0, 128.9, 128.7, 128.6 (×2), 128.5 (x11), 128.4 (×2), 128.3 (×2), 128.2 (×2), 128.1 (×2), 128.0 (×3), 127.9 (×2), 127.8, 127.7, 98.2 ($^1J_{C1',H1'}$ = 172.0 Hz, C-1′), 98.0 ($^1J_{C1,H1}$ = 168.0 Hz, C-1), 82.1, 80.0, 75.8, 75.2, 74.3, 73.9, 73.5, 72.4, 71.9, 69.9, 67.5, 67.3, 60.3, 55.3 ppm; HR-FAB MS [M + Na]$^+$ calcd for $C_{55}H_{55}N_3O_{12}Na^+$ 972.3678; found 972.3692.

*Methyl 6-O-(2-Azido-4-O-benzyl-2-deoxy-α/β-D-mannopyranosid-urono-6,3-lactone)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (**14**).* The title compound was obtained as a colorless amorphous solid

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from glycosyl donor **3** and acceptor **8**[17] in a 26% yield (50 mM). Analytical data for **14**: R_f = 0.50 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 7.41−7.27 (m, 20H, aromatic), 5.12 (d, 1H, $J_{1',2'}$ = 5.0 Hz, H-1′), 4.98 (d, 1H, ^2J = 10.8 Hz, C*H*Ph), 4.90 (d, 1H, ^2J = 11.1 Hz, C*H*Ph), 4.84−4.80 (m, 2H, H-3′, C*H*Ph), 4.77−4.72 (m, 1H, C*H*Ph), 4.69−4.52 (m, 5H, H-1, 4 × C*H*Ph), 4.08−4.00 (m, 4H, H-4′, 5, 5′, 6a), 3.85 (dd, 1H, $J_{3,4}$ = 9.4 Hz, H-3), 3.62−3.49 (m, 3H, $J_{2,3}$ = 7.2 Hz, H-2, 2′, 6b), 3.40 (s, 3H, OCH_3), 3.35 (dd, 1H, H-4) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 170.7, 138.7, 138.1 (×2), 136.1, 128.8 (×2), 128.7, 128.4 (×5), 128.1 (×2), 128.0 (×4), 127.9 (×4), 127.7, 127.6, 100.2 ($^1J_{C1',H1'}$ = 177.0 Hz, C-1′), 97.8 ($^1J_{C1,H1}$ = 168.0 Hz, C-1), 81.8, 79.9, 78.6, 78.1, 77.2, 75.7, 75.4, 74.7, 73.3, 72.2, 69.8, 68.1, 67.2, 55.2 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{41}H_{43}N_3O_{10}Na^+$ 760.2841; found 760.2850.

*Methyl 4-O-(Benzyl-2-azido-4-O-benzyl-2-deoxy-3-O-picoloyl-α/β-D-mannopyranosyluronate)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**15**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **6** and acceptor **9**[17] in 43% yield (α/β = 1/6.0, 50 mM) or 29% yield (α/β = 1/20, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **15**: R_f = 0.25 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 8.82 (m, 1H, aromatic), 8.03 (m, 1H, aromatic), 7.84 (m, 1H, aromatic), 7.51 (m, 1H, aromatic), 7.41−7.22 (m, 20H, aromatic), 7.11 (m, 3H, aromatic), 6.99 (m, 2H, aromatic), 5.07−4.99 (m, 4H, $J_{3',4'}$ = 9.7 Hz, H-3′, 3 × C*H*Ph), 4.83−4.70 (m, 4H, H-1′, 3 × C*H*Ph), 4.61−4.54 (m, 3H, $J_{1,2}$ = 3.2 Hz, H-1, 2 × C*H*Ph), 4.47−4.41 (m, 2H, 2 × C*H*Ph), 4.25 (dd, 1H, H-4′), 4.02−3.92 (m, 3H, H-2′, 3, 4), 3.76−3.61 (m, 4H, H-5, 5′, 6a, 6b), 3.52 (dd, 1H, $J_{2,3}$ = 8.8 Hz, H-2), 3.36 (s, 3H, OCH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$) 167.3, 163.8, 150.3, 146.9, 139.1, 138.1, 137.5, 137.3, 137.1, 135.0, 128.7 (×2), 128.6 (×2), 128.5 (×2), 128.4 (×2), 128.2 (×8), 128.1 (×2), 127.9 (×3), 127.6 (×3), 127.3, 127.2, 125.4, 99.7 ($^1J_{C1',H1'}$ = 162.0 Hz, C-1′), 98.2 ($^1J_{C1,H1}$ = 170.0 Hz, C-1), 80.1, 79.4, 77.2, 75.2, 75.0, 74.8, 74.5, 73.9, 73.7, 73.5, 69.1, 68.1, 67.3, 62.1, 55.4 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{54}H_{54}N_4O_{12}Na^+$ 973.3631; found 973.3675.

*Methyl 4-O-(Benzyl-2-azido-3-O-benzoyl-4-O-benzyl-2-deoxy-α-D-mannopyranosyluronate)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**16**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **7** and acceptor **9**[17] in 92% yield (α/β > 25/1, 50 mM) and 88% yield (α/β > 25/1, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **16**: R_f = 0.70 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$) 7.94 (m, 2H, aromatic), 7.56 (m, 1H, aromatic), 7.39−7.12 (m, 27H, aromatic), 5.59 (dd, 1H, $J_{3',4'}$ = 7.0 Hz, H-3′), 5.50 (d, 1H, $J_{1',2'}$ = 4.4 Hz, H-1′), 4.92 (dd, 2H, ^2J = 11.1 Hz, CH_2Ph), 4.85 (dd, 2H, ^2J = 12.2 Hz, CH_2Ph), 4.75 (d, 1H, C*H*Ph), 4.62−4.36 (m, 7H, $J_{1,2}$ = 3.3 Hz, H-1, 5′, 5 × C*H*Ph), 4.23 (dd, 1H, H-4′), 4.02 (dd, 1H, $J_{3,4}$ = 9.0 Hz, H-3), 3.92 (dd, 1H, H-4), 3.86−3.84 (dd, 1H, $J_{2',3'}$ = 3.1 Hz, H-2′), 3.75 (m, 3H, H-5, 6a, 6b), 3.56 (dd, 1H, $J_{2,3}$ = 9.3 Hz, H-2), 3.38 (s, 3H, OCH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 168.5, 165.2, 138.7, 138.3, 138.0, 137.2, 134.8, 133.6, 129.9, 128.9, 128.7, 128.6 (×4), 128.5, 128.4 (×8), 128.3 (×2), 128.2 (×2), 128.1, 128.0, 127.9 (×2), 127.7 (×2), 127.6 (×2), 127.5, 127.4, 99.7 ($^1J_{C1',H1'}$ = 174.0 Hz, C-1′), 97.8 ($^1J_{C1,H1}$ = 169.0 Hz, C-1), 81.4, 80.4, 77.3, 75.5, 74.3, 74.0, 73.4, 73.3, 72.9, 71.7, 69.4, 69.0, 67.3, 60.8, 55.4 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{55}H_{55}N_3O_{12}Na^+$ 972.3678; found 972.3729.

*Methyl 4-O-(2-Azido-4-O-benzyl-2-deoxy-α/β-D-mannopyranosid-urono-6,3-lactone)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (**17**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **3** and acceptor **9**[17] in a 27% yield (50 mM). Analytical data for **17**: R_f = 0.50 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 7.45−7.30 (m, 20H, aromatic), 5.20 (d, 1H, $J_{1',2'}$ = 5.7 Hz, H-1′), 5.04 (dd, 2H, ^2J = 11.2 Hz, CH_2Ph), 4.75−4.55 (m, 6H, $J_{1,2}$ = 2.6 Hz, H-1, 3′, 4 × C*H*Ph), 4.47−4.42 (m, 2H, 2 × C*H*Ph), 3.99−3.90 (m, 3H, H-3, 4′, 6a), 3.83−3.76 (m, 3H, H-4, 5, 6b), 3.66 (d, 1H, $J_{4',5'}$ = 8.0 Hz, H-5′), 3.59−3.52 (m, 2H, $J_{2,3}$ = 8.8 Hz, H-2, 2′), 3.35 (s, 3H, OCH_3) ppm; ^{13}C{H} NMR (151 MHz, $CDCl_3$): 167.5, 129.0 (×2), 128.9, 128.6 (×3), 128.5 (×3), 128.4 (×3), 128.3 (×6), 128.2 (×2), 128.1, 127.8, 127.5 (×2), 127.1, 100.6 ($^1J_{C1',H1'}$ = 177.8 Hz, C-1′), 97.8 ($^1J_{C1,H1}$ = 168.0 Hz, C-1), 81.6, 80.2, 78.8, 77.8, 75.5, 74.0, 73.7, 73.2, 72.1, 69.4, 68.4, 67.3, 55.5 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{41}H_{43}N_3O_{10}Na^+$ 760.2841; found 760.2864.

*Methyl 3-O-(Benzyl-2-azido-4-O-benzyl-2-deoxy-3-O-picoloyl-α/β-D-mannopyranosyluronate)-2,4,6-tri-O-benzyl-α-D-glucopyranoside (**18**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **6** and acceptor **10**[17] in 37% yield (α/β = 1/9, 50 mM) or 97% yield (α/β = 1/25, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **18**: R_f = 0.35 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 8.84−8.83 (m, 1H, aromatic), 8.08 (m, 1H, aromatic), 7.89−7.83 (m, 1H, aromatic), 7.55−7.51 (m, 1H, aromatic), 7.44−7.19 (m, 20H, aromatic), 7.11−7.05 (m, 3H, aromatic), 7.02−6.94 (m, 2H, aromatic), 5.23 (s, 1H, $J_{1',2'}$ = 3.6 Hz, H-1′), 5.19−5.08 (m, 3H, $J_{3',4'}$ = 9.8 Hz, H-3′, 2 × CHPh), 5.01 (d, 1H, ^2J = 12.2 Hz, C*H*Ph), 4.72 (d, 1H, $J_{1,2}$ = 3.3 Hz, H-1), 4.67−4.59 (m, 4H, 4 × C*H*Ph), 4.52−4.47 (m, 2H, 2 × C*H*Ph), 4.39−4.22 (m, 3H, $J_{3,4}$ = 8.8, $J_{4',5'}$ = 9.7 Hz, H-3, 4′, C*H*Ph), 4.10 (dd, 1H, $J_{2',3'}$ = 3.8 Hz, H-2′), 3.93 (d, 1H, H-5′), 3.74−3.59 (m, 5H, H-2, 4, 5, 6a, 6b), 3.35 (s, 3H, OCH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 167.5, 163.8, 150.3, 147.1, 138.3, 137.8, 137.4, 137.3, 137.1, 135.0, 128.9 (×4), 128.6 (×2), 128.5 (×3), 128.4 (×5), 128.3 (×2), 128.2 (×2), 128.1 (×2), 127.8 (×3), 127.7, 127.6, 127.3, 125.4, 100.8 ($^1J_{C1,H1}$ = 167.0 Hz, C-1), 97.1 ($^1J_{C1',H1'}$ = 164.1 Hz, C-1′), 80.5, 80.1, 75.7, 75.2, 74.9, 74.8, 74.7, 74.1, 73.5, 73.2, 69.8, 68.2, 67.2, 62.2, 55.1 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{54}H_{54}N_4O_{12}Na^+$ 973.3631; found 973.3670.

*Methyl 3-O-(Benzyl-2-azido-3-O-benzoyl-4-O-benzyl-2-deoxy-α-D-mannopyranosyluronate)-2,4,6-tri-O-benzyl-α-D-glucopyranoside (**19**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **7** and acceptor **10**[17] in 98% yield (α/β > 25/1, 50 mM) and 94% yield (α/β > 25/1, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **19**: R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 7.99 (m, 2H, aromatic), 7.58 (m, 1H, aromatic), 7.43−7.04 (m, 27H, aromatic), 5.66 (dd, 1H, $J_{3',4'}$ = 8.3 Hz, H-3′), 5.38 (d, 1H, H-1′), 5.02 (dd, 2H, ^2J = 12.3 Hz, CH_2Ph), 4.86−4.79 (m, 2H, H-5′, C*H*Ph), 4.66−4.62 (m, 2H, 2 × C*H*Ph), 4.54−4.47 (m, 6H, $J_{1,2}$ = 3.3 Hz, H-1, 5 × C*H*Ph), 4.22 (dd, 1H, H-4′), 4.16 (dd, 1H, $J_{3,4}$ = 10.2 Hz, H-3), 3.83 (dd, 1H, $J_{2',3'}$ = 3.2 Hz, H-2′), 3.74−3.62 (m, 4H, H-4, 5, 6a, 6b), 3.45 (dd, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 3.25 (s, 3H, OCH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 169.1, 165.4, 138.2, 137.8, 137.6, 137.4, 135.1, 133.6, 129.9, 129.0, 128.6, 128.5 (x10), 128.4 (×5), 128.3 (×3), 128.2 (×2), 127.9 (×2), 127.8 (×3), 127.6 (×2), 98.9 ($^1J_{C1',H1'}$ = 175.3 Hz, C-1′), 98.0 ($^1J_{C1,H1}$ = 168.3 Hz, C-1), 79.1, 78.8, 77.8, 74.8, 74.6, 74.4, 73.7, 73.4, 72.6, 71.9, 69.7, 68.3, 67.1, 61.6, 55.1 ppm; HR-FAB MS $[M + H]^+$ calcd for $C_{55}H_{55}N_3O_{12}Na^+$ 972.3678; found 972.3703.

*Methyl 3-O-(2-Azido-4-O-benzyl-2-deoxy-α/β-D-mannopyranosid-urono-6,3-lactone)-2,4,6-tri-O-benzyl-α-D-glucopyranoside (**20**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **3** and acceptor **10**[17] in a 37% yield (50 mM) under regular dilution reaction conditions. Analytical data for **20**: R_f = 0.55 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 7.42−7.26 (m, 20H, aromatic), 5.76 (d, 1H, $J_{1',2'}$ = 5.7 Hz, H-1′), 4.83−4.80 (m, 2H, H-3′, C*H*Ph), 4.67 (dd, 2H, ^2J = 11.2 Hz, CH_2Ph), 4.66−4.57 (m, 4H, H-1, 3 × C*H*Ph), 4.51−4.47 (m, 2H, 2 × C*H*Ph), 4.13 (dd, 1H, $J_{3,4}$ = 8.7 Hz, H-3), 4.06−4.03 (m, 1H, H-4′), 3.93 (d, 1H, H-5′), 3.77−3.61 (m, 6H, H-2, 2′, 4, 5, 6a, 6b), 3.26 (s, 3H, OCH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$) 170.7, 139.0, 138.2, 137.7, 136.1, 128.8 (×2), 128.6, 128.4 (×4), 128.2 (×2), 128.1 (×6), 127.9, 127.7, 127.4 (×2), 127.1, 101.1 ($^1J_{C1',H1'}$ = 177.6 Hz, C-1′), 97.2 ($^1J_{C1,H1}$ = 168.0 Hz, C-1), 82.6, 80.1, 78.4, 77.2, 76.2, 75.2, 73.5, 72.9, 72.8, 71.9, 69.6, 68.7, 67.4, 55.0 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{41}H_{43}N_3O_{10}Na^+$ 760.2841; found 760.2864.

*Methyl 2-O-(Benzyl-2-azido-4-O-benzyl-2-deoxy-3-O-picoloyl-α/β-D-mannopyranosyluronate)-3,4,6-tri-O-benzyl-α-D-glucopyranoside (**21**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **6** and acceptor **11**[17] in 64% yield (α/β = 1/13, 50 mM) or 74% yield (α/β = 1/24, 5.0 mM) under regular and

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J. Org. Chem. 2022, 87, 271−280

high dilution reaction conditions, respectively. Analytical data for **21**: R_f = 0.40 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 8.82 (m, 1H, aromatic), 8.07 (m, 1H, aromatic), 7.87−7.82 (m, 1H, aromatic), 7.51 (m, 1H, aromatic), 7.42−7.12 (m, 24H, aromatic), 6.99 (m, 1H, aromatic), 5.21 (dd, 2H, ^2J =12.2 Hz, CH_2Ph), 5.10 (dd, 1H, $J_{3',4'}$ = 9.6 Hz, H-3′), 4.94−4.82 (m, 4H, $J_{1,2}$ = 3.5 Hz, H-1, 1′, 2 × CHPh), 4.69−4.48 (m, 6H, 6 × CHPh), 4.30 (dd, 1H, $J_{4',5'}$ = 9.7 Hz, H-4′), 4.06−3.97 (m, 2H, $J_{2',3'}$ = 3.5 Hz, H-2′, 3), 3.88 (d, 1H, H-5′), 3.83−3.65 (m, 5H, H-2, 4, 5, 6a, 6b), 3.37 (s, 3H, OCH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 167.3, 163.8, 150.3, 147.0, 138.2, 138.1, 137.8, 137.3, 137.1, 134.9, 128.9 (×2), 128.6 (×4), 128.5, 128.4 (×5), 128.2 (×2), 128.1 (×3), 128.0 (×2), 127.9 (×2), 127.8 (×4), 127.3, 125.5, 100.7 ($^1J_{C1',H1'}$ = 162.0 Hz, C-1′), 99.3 ($^1J_{C1,H1}$ = 171.4 Hz, C-1), 81.9, 78.4, 78.3, 77.2, 76.0, 75.1, 74.9 (×2), 73.9, 73.5, 70.1, 68.2, 67.5, 61.1, 55.4 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{54}H_{54}N_4O_{12}Na^+$ 973.3631; found 973.3676.

*Methyl 2-O-(Benzyl-2-azido-3-O-benzoyl-4-O-benzyl-2-deoxy-α-D-mannopyranosyluronate)-3,4,6-tri-O-benzyl-α-D-glucopyranoside (**22**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **7** and acceptor **11**[17] in a 90% yield (α/β =10/1, 50 mM) under both regular and high dilution reaction conditions. Analytical data for **22**: R_f = 0.65 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 7.99 (m, 2H, aromatic), 7.59 (m, 1H, aromatic), 7.48−7.07 (m, 27H, aromatic), 5.68 (dd, 1H, $J_{3',4'}$ = 6.2 Hz, H-3′), 5.40 (d, 1H, $J_{1',2'}$ = 5.3 Hz, H-1′), 5.06−4.98 (m, 3H, H-1, 2 × CHPh), 4.86 (d, 1H, ^2J = 10.7 Hz, CHPh), 4.78−4.73 (m, 2H, 2 × CHPh), 4.65−4.60 (m, 4H, H-5′, 3 × CHPh), 4.53−4.46 (m, 2H, 2 × CHPh), 4.26 (dd, 1H, H-4′), 4.12−3.99 (m, 3H, $J_{2',3'}$ = 3.3 Hz, H-2, 2′, 3), 3.82−3.65 (m, 4H, H-4, 5, 6a, 6b), 3.44 (s, 3H, OCH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 168.6, 165.0, 138.5, 138.4, 138.0, 137.2, 134.8, 133.8, 130.0, 128.8, 128.7, 128.6 (×2), 128.5 (×5), 128.4 (×6), 128.3 (×2), 128.2 (×2), 128.0 (×2), 127.9 (×3), 127.8 (×2), 127.7 (×2), 127.5, 96.9 ($^1J_{C1',H1'}$ = 169.0 Hz, C-1′), 94.9 ($^1J_{C1,H1}$ = 170.0 Hz, C-1), 80.7, 77.3, 76.9, 76.0, 75.1, 74.2, 73.5 (×2), 72.6, 71.7, 70.2, 68.5, 67.1, 59.9, 55.1 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{55}H_{55}N_3O_{12}Na^+$ 972.3678; found 972.3711.

*Methyl 2-O-(2-Azido-4-O-benzyl-2-deoxy-α/β-D-mannopyranosid-urono-6,3-lactone)-3,4,6-tri-O-benzyl-α-D-glucopyranoside (**23**).* The title compound was obtained as a colorless amorphous solid from glycosyl donor **3** and acceptor **11**[17] in a 40% yield under regular concentration (50 mM). Analytical data for **23**: R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 7.39−7.26 (m, 18H, aromatic), 7.14 (m, 2H, aromatic), 5.61 (d,1H, $J_{1',2'}$ = 5.5 Hz, H-1′), 4.92−4.78 (m, 5H, H-1, 3′, 3 × CHPh), 4.71−4.48 (m, 5H, 5 × CHPh), 4.14−4.06 (m, 2H, $J_{4',5'}$ = 1.8 Hz, H-3, 4′), 3.97 (d, 1H, H-5′), 3.89−3.60 (m, 6H, H-2, 2′, 4, 5, 6a, 6b), 3.41 (s, 3H, OCH_3) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 171.0, 138.6, 138.2, 138.0, 136.1, 128.9 (×2), 128.8, 128.5 (×2), 128.4 (×4), 128.2 (×2), 128.0 (×2), 127.9 (×2), 127.7 (×3), 127.6 (×2), 100.4 ($^1J_{C1',H1'}$ = 178.2 Hz, C-1′), 98.5 ($^1J_{C1,H1}$ = 171.5 Hz, C-1), 82.0, 78.7 (×2), 77.3, 75.3, 74.9, 74.4, 73.5, 72.3, 70.1, 68.4, 67.3, 55.3, 54.4 ppm; HR-FAB MS $[M + H]^+$ calcd for $C_{41}H_{43}N_3O_{10}Na^+$ 760.2841; found 760.2854.

Synthesis of CP8 Glycan 28. *Benzyl-2-azido-3-O-(benzyl-2-azido-4-O-benzyl-2-deoxy-3-O-picoloyl-β-D-mannopyranosyluronate)-4-O-benzyl-2,6-dideoxy-α-L-fucopyranoside (**26**).* A mixture containing mannosyl donor **6** (44mg, 0.081 mmol), L-fucosamine acceptor **24**[5] (27 mg, 0.073 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 then cooled to −30 °C, NIS (36 mg, 0.161 mmol) and TfOH (3.0 L, 0.032 mmol) were added, the external cooling was removed, and the resulting mixture was stirred for 16 h at rt. After that, the solids were ltered off through a pad of celite, rinsed successively with CH_2Cl_2, and the combined ltrate 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 ×8 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to obtain the title compound as a colorless syrup in a 61% yield (α/β = 1/24). Analytical data for **26**: R_f = 0.35 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (600 MHz, $CDCl_3$): 8.81 (m, 1H, aromatic), 8.04 (m, 1H, aromatic), 7.85−7.83 (m, 1H, aromatic), 7.51 (m, 1H, aromatic), 7.39−7.25 (m, 15H, aromatic), 7.13−7.12 (m, 3H, aromatic), 7.01 (m, 2H, aromatic), 5.22−5.14 (m, 3H, $J_{3',4'}$ = 9.8, ^2J = 12.2 Hz, H-3′, CH_2Ph), 5.03 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 4.76 (br. s, 1H, H-1′), 4.73 (d, 1H, ^2J = 11.5 Hz, CHPh), 4.70−4.67 (m, 2H, 2 × CHPh), 4.63−4.60 (m, 2H, 2 × CHPh), 4.52 (d, 1H, ^2J = 10.8 Hz, CHPh), 4.40−4.36 (m, 2H, H-3, 4′), 3.96−3.92 (m, 3H, $J_{2',3'}$ = 3.5 Hz, H-2′, 5, 5′), 3.71 (dd, 1H, $J_{4,5}$ = 1.6 Hz, H-4), 3.64 (dd, 1H, $J_{2,3}$ = 10.8 Hz, H-2), 1.25 (d, 3H, J = 6.5 Hz, H-6) ppm; ^{13}C{H} NMR (151 MHz, $CDCl_3$): 166.9, 163.9, 150.3, 146.9, 137.7, 137.3, 137.1, 137.0, 135.0, 128.6 (×2), 128.5 (×4), 128.4 (×3), 128.2 (×4), 128.1 (×3), 127.8 (×3), 127.7, 127.3, 125.4, 97.8 ($^1J_{C1,H1}$ = 171.1 Hz, C-1), 97.5 ($^1J_{C1',H1'}$ = 158.5 Hz, C-1′), 76.2, 75.8, 75.4, 75.2 (×2), 74.7, 73.6, 69.8, 67.6, 66.6, 61.7, 57.9, 16.7 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{46}H_{45}N_7O_{10}Na^+$ 878.3121; found 878.3156.

*Benzyl-2-azido-3-O-(benzyl-2-azido-4-O-benzyl-2-deoxy-β-D-mannopyranosyluronate)-4-O-benzyl-2,6-dideoxy-α-L-fucopyranoside (**27**).* $Cu(OAc)_2$-H_2O (36 mg, 0.196 mmol) was added to a solution of compound **26** (112 mg, 0.131 mmol) in CH_2Cl_2/MeOH (4.0 mL, 3/1, v/v), and the resulting mixture was stirred for 20 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 puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to obtain the title compound in a 93% yield (91 mg, 0.121 mmol). Analytical data for **27**: R_f = 0.45 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): 7.39−7.25 (m, 18H, aromatic), 7.18−7.16 (m, 2H, aromatic), 5.17 (dd, 2H, ^2J = 12.1 Hz, CH_2Ph), 5.02 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.73−4.60 (m, 6H, H-1′, 5 × CHPh), 4.47 (d, 1H, ^2J = 10.9 Hz, CHPh), 4.36 (dd, 1H, $J_{3,4}$ = 10.9 Hz, H-3), 3.97−3.83 (m, 2H, $J_{4',5'}$ = 9.4, $J_{5,6}$ = 6.5 Hz, H-4′, 5), 3.76 (d, 1H, H-5′), 3.70−3.58 (m, 4H, $J_{2,3}$ = 2.8 Hz, H-2, 2′, 3′, 4), 2.34 (d, 1H, J = 7.4 Hz, OH), 1.23 (d, 3H, H-6) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 167.6, 138.0, 137.7, 137.0, 135.1, 128.8 (×2), 128.7 (×2), 128.6 (×7), 128.3 (×2), 128.2 (×3), 128.1 (×3), 128.0, 97.9 (×2), 77.1, 76.9, 76.0, 75.2, 75.1 (×2), 72.5, 69.9, 67.6, 66.6, 63.8, 58.0, 16.8 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{40}H_{42}N_6O_9Na^+$ 773.2906; found 773.2939.

*Benzyl O-(2-Azido-3,4-di-O-benzoyl-2,6-di-deoxy-α/β-D-fucopyranosyl)-(1→3)-O-(benzyl-2-azido-4-O-benzyl-2-deoxy-β-D-mannopyranosyluronate)-(1→3)-2-azido-4-O-benzyl-2,6-dideoxy-α-L-fucopyranoside (**28**).* A mixture containing D-fucosamine donor **25** (23 mg, 0.052 mmol), disaccharide acceptor **27** (22 mg, 0.029 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 then cooled to −30 °C, NIS (26 mg, 0.114 mmol) and TfOH (1.0 L, 0.011 mmol) were added, the external cooling was removed, and the resulting mixture was stirred for 16 h at rt. After that, the solids were ltered off through a pad of celite, rinsed successively with CH_2Cl_2, and the combined ltrate 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 × 8 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−toluene gradient elution) to obtain the title compound as a colorless syrup in a 41% yield (11.3 mg, 0.010 mmol, α/β = 18/1). Analytical data for **28**: R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); 1H NMR (300 MHz, $CDCl_3$): 8.01 (m, 2H, aromatic), 7.89 (m, 2H, aromatic), 7.60 (m, 1H, aromatic), 7.55−7.45 (m, 3H, aromatic), 7.41−7.22 (m, 20H, aromatic), 7.16−7.14 (m, 2H, aromatic), 5.78−5.70 (m, 2H, H-3″, 4″), 5.26 (d, 1H, $J_{1'',2''}$ = 3.7 Hz, H-1″), 5.16 (dd, 2H, ^2J = 12.2 Hz, CH_2Ph), 5.04 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.96 (d, 1H, ^2J = 10.3 Hz, CHPh), 4.77−4.54 (m, 6H, $J_{5'',6''}$ = 6.5 Hz, H-1′, 5″, 4 × CHPh), 4.45-4.38 (m, 2H, H-3, CHPh), 4.17−4.11 (m, 2H, $J_{4',5'}$ = 9.8 Hz, H-2″, 4′), 3.99−3.92 (m, 1H, $J_{5,6}$ = 6.3 Hz, H-5), 3.88 (dd, 1H, $J_{1',2'}$ = 3.4 Hz, H-2′), 3.83 (d, 1H, H-5′), 3.72−3.62 (m, 3H, H-2, 3′, 4), 1.25 (d, 3H, H-6), 1.16 (d, 3H, H-6″) ppm; ^{13}C{H} NMR (151 MHz, $CDCl_3$): 167.0, 165.6, 165.3, 137.8,

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J. Org. Chem. 2022, 87, 271−280

137.0, 135.1, 133.5, 133.3, 129.8 (×4), 129.7, 129.3, 129.1, 128.6 (×6), 128.5 (×2), 128.4 (×4), 128.3 (×3), 128.1 (×3), 127.9 (×5), 127.7, 100.3 ($J_{C1'',H1''}$ = 171.1 Hz, C-1″), 97.9 ($J_{C1,H1}$ = 171.1 Hz, C-1), 97.6 ($J_{C1',H1'}$ = 158.0 Hz, C-1′), 81.6, 76.9, 75.8, 75.6, 75.2, 74.8, 74.5, 71.0, 70.0, 69.9, 67.5, 66.5, 66.4, 63.6, 58.9, 58.0, 16.7, 16.3 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{60}H_{59}N_9O_{14}Na^+$ 1152.4074; found 1152.4099.

Synthesis of D-Fucosyl Donor 25. *3,4-Di-O-acetyl-1,5-anhydro-6-bromo-2,6-dideoxy-D-lyxo-hex-1-enitol (**30**).* NaBr (0.54 g, 5.26 mmol) and $NaHCO_3$ (0.177 g, 2.11 mmol) were added to a solution of 3,4-di-*O*-acetyl-1,5-anhydro-2-deoxy-6-*O*-toluenesulfonyl-D-*lyxo*-hex-1-enitol[29] (**29**, 0.40 g, 1.05 mmol) in anhydrous dimethylformamide (DMF, 8 mL) at rt, and the resulting mixture was stirred under argon for 16 h at 65 °C. After that, the reaction mixture was allowed to cool to rt, and the volatiles were removed under reduced pressure. The residue was diluted with ethyl acetate (40 mL) and washed with water (3 × 10 mL) and sat. aq. NaCl (8 mL). The resulting aqueous layer (40 mL) was additionally extracted with ethyl acetate (80 mL). The combined organic phase was dried with Na_2SO_4 and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to give the title compound as a colorless syrup in a 75% yield (0.23 g, 2.89 mmol). Analytical data for **30**: R_f = 0.55 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ −32.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 6.48 (d, 1H, $J_{1,2}$ = 6.3 Hz, H-1), 5.60−5.54 (m, 2H, H-3, 4), 4.73 (dd, 1H, $J_{2,3}$ = 2.4 Hz, H-2), 4.34−4.28 (m, 1H, $J_{5,6a}$ = 7.7 Hz, $J_{5,6b}$ = 3.3 Hz, H-5), 3.55 (dd, 1H, $J_{6a,6b}$ = 10.8 Hz, H-6a), 3.42 (dd, 1H, H-6b), 2.15, 2.03 (2 s, 6H, 2 × $OCOCH_3$) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): 170.4, 170.2, 145.6, 99.0, 75.2, 64.5, 64.4, 28.9, 21.0, 20.8 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{10}H_{13}O_5BrNa^+$ 314.9839; found 314.9844.

*3,4-Di-O-acetyl-1,5-anhydro-2,6-dideoxy-D-lyxo-hex-1-enitol (**31**).* Recrystallized azobisisobutyronitrile (AIBN, 115 mg, 0.702 mmol) and tributyltin hydride (Bu_3SnH, 850 L, 3.16 mmol) were added to a solution of compound **30** (1.03 g, 3.51 mmol) in benzene (20 mL), and the resulting mixture was re uxed for 3 h at 80 °C. After that, the reaction mixture was allowed to cool to rt and the volatiles were removed under reduced pressure. The residue was diluted with CH_2Cl_2 (50 mL) and washed with water (2 × 20 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−toluene gradient elution) to give the title compound as a colorless syrup in a 77% yield (0.62 g, 2.89 mmol). Analytical data for **31**: R_f = 0.45 (ethyl acetate/toluene, 1/4, v/v); $[\alpha]_D^{22}$ +4.7 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): 6.47 (d, 1H, $J_{1,2}$ = 6.3 Hz, H-1), 5.60−5.57 (dd, 1H, H-3), 5.31−5.28 (dd, 1H, H-4), 4.65 (dd, 1H, H-2), 4.21 (dd, 1H, $J_{5,6}$ = 6.6 Hz, H-5), 2.17, 2.03 (2 s, 6H, 2 × $OCOCH_3$), 1.28 (d, 3H, H-6) ppm; ^{13}C{H} NMR (151 MHz, $CDCl_3$): 170.7, 170.4, 146.1, 98.3, 71.5, 66.3, 65.1, 20.9, 20.7, 16.5 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{10}H_{14}O_5Na^+$ 237.0734; found 237.0752.

*1,3,4-Tri-O-acetyl-2-azido-2-deoxy-α/β-D-fucopyranose (**32**).* A mixture containing compound **31** (0.43 g, 2.0 mmol) and freshly activated molec. sieves (3 Å, 1.0 g) in anhydrous MeCN (20 mL) was stirred under argon for 40 min at rt. The mixture was then cooled to −15 °C, ceric ammonium nitrate (CAN, 3.51 g, 6.40 mmol) and sodium azide (0.31 g, 4.80 mmol) were added, and the resulting mixture was stirred under argon for 2 h at −15 °C. After that, the solids were ltered off, rinsed successively with CH_2Cl_2, and the combined ltrate was concentrated under reduced pressure. The resulting residue was diluted with CH_2Cl_2 (50 mL) and washed with water (2 × 20 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure and dried in *vacuo* for 2 h. The resulting crude glycosyl nitrate (0.57 g, 1.80 mmol) was dissolved in acetic acid (AcOH, 12 mL), sodium acetate (NaOAc, 0.30 g, 3.60 mmol) was added, and the resulting mixture was stirred under argon for 2 h at 100 °C. After that, the reaction mixture was allowed to cool to rt, diluted with CH_2Cl_2 (20 mL), and washed with cold water (8 mL), sat. aq. $NaHCO_3$ (2 × 8 mL), and water (8 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to give the title compound as a colorless syrup in a 63% yield (0.36 g, 1.14 mmol, α/β = 2.3/1). Analytical data for **32**: R_f = 0.55 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): ***α*-32**: 6.29 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 5.35−5.30 (m, 2H, H-3, 4), 4.21 (q, 1H, $J_{4,5}$ = 6.4 Hz, H-5), 3.91 (dd, 1H, $J_{2,3}$ = 7.4 Hz, H-2), 2.20, 2.17, 2.08 (3 s, 9H, 3 × $OCOCH_3$), 1.15 (d, 3H, J = 6.5 Hz, H-6) ppm; ***β*-32**: 5.53 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1), 5.23 (dd, 1H, $J_{3,4}$ = 3.3 Hz, H-4), 4.88 (dd, 1H, $J_{2,3}$ = 10.8 Hz, H-3), 3.91 (dd, 1H, H-5), 3.82 (dd, 1H, H-2), 1.22 (d, 3H, J = 6.4 Hz, H-6) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): ***α*-32**: 170.4, 170.0, 169.0, 90.7, 70.0, 69.1, 67.2, 56.7, 21.0, 20.7, 20.6, 16.0 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{12}H_{17}N_3O_7Na^+$ 338.0959; found 338.0985.

*Ethyl 3,4-Di-O-acetyl-2-azido-2-deoxy-1-thio-α/β-D-fucopyranoside (**33**).* Ethanethiol (124 L, 1.36 mmol) and boron tri uoride diethyl etherate (BF_3-Et_2O, 432 L, 3.41 mmol) were added to a solution of compound **32** (0.36 g, 1.14 mmol) in anhydrous CH_2Cl_2 (10 mL) under argon at 0 °C. The resulting mixture was allowed to warm to rt and stirred under argon for 4 h. After that, the reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with water (10 mL), sat. aq. $NaHCO_3$ (2 × 10 mL), and water (10 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to give the title compound as a colorless syrup in a 65% yield (0.236 g, 0.744 mmol, α/β = 1/1.8). Analytical data for α/β-**33**: R_f = 0.62 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): ***β*-33**: 5.28 (dd, 1H, $J_{3,4}$ = 3.2 Hz, H-4), 4.88 (dd, 1H, $J_{2,3}$ = 10.2 Hz, H-3), 4.37 (d, 1H, $J_{1,2}$ = 10.1 Hz, H-1), 3.77 (q, 1H, $J_{4,5}$ = 6.5 Hz, H-5), 3.68 (dd, 1H, H-2), 2.88−2.74 (m, 2H, SCH_2CH_3), 2.18, 2.07 (2 s, 6H, 2 × $OCOCH_3$), 1.34 (t, 3H, J = 7.4 Hz, SCH_2CH_3), 1.21 (d, 3H, J = 6.4 Hz, H-6) ppm; ***α*-33**: 5.46 (d, 1H, $J_{1,2}$ = 5.6 Hz, H-1), 5.24 (dd, 1H, $J_{3,4}$ = 3.2 Hz, H-4), 5.13 (dd, 1H, $J_{2,3}$ = 11.0 Hz, H-3), 4.49 (q, 1H, $J_{4,5}$ = 6.4 Hz, H-5), 4.23 (dd, 1H, H-2), 2.68-2.54 (m, 2H, SCH_2CH_3), 1.31 (t, 3H, J = 7.4 Hz, SCH_2CH_3), 1.16 (d, 3H, J = 6.5 Hz, H-6) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): ***β*-33**: 170.6, 169.9, 83.2, 73.4, 69.7, 60.3, 57.9, 25.0, 20.7 (×2), 16.5, 14.9 ppm; ***α*-33**: 170.4, 169.7, 84.3, 73.0, 70.7, 70.4, 65.1, 60.3, 57.9, 24.7, 15.9, 14.7 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{12}H_{19}N_3O_5SNa^+$ 340.0938; found 340.0964.

*Ethyl 2-Azido-2-deoxy-1-thio-α/β-D-fucopyranoside (**34**).* A freshly prepared 1 N solution of NaOMe in MeOH (0.5 mL) was added to a solution of **33** (0.17 g, 0.54 mmol) in MeOH (5 mL) until pH 9, and the resulting mixture was stirred for 10 min at rt. After that, the reaction mixture was neutralized with Dowex (H^+), the resin was ltered off, rinsed successively with MeOH (7 × 5 mL), and the combined ltrate was concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (MeOH-CH_2Cl_2 gradient elution) to give the title compound as a colorless syrup in a 98% yield (0.123 g, 0.53 mmol, α/β = 1/2.0). Analytical data for **34**: R_f = 0.50 (MeOH/CH_2Cl_2, 1/9, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): ***β*-34**: 4.28 (d, 1H, $J_{1,2}$ = 9.8 Hz, H-1), 3.77−3.75 (m, 1H, H-4), 3.63 (q, 1H, H-5), 3.56−3.43 (m, 2H, H-2, 3), 2.84−2.69 (m, 2H, SCH_2CH_3), 2.78 (d, 1H, 3-OH), 2.25 (d, 1H, J = 6.0 Hz, 4-OH), 1.32 (t, 3H, SCH_2CH_3), 1.30 (d, 3H, H-6) ppm; ***α*-34**: 5.42 (d, 1H, $J_{1,2}$ = 5.5 Hz, H-1), 4.36 (q, 1H, H-5), 4.03 (dd, 1H, H-2), 3.86−3.80 (m, 1H, H-3), 2.64−2.58 (m, 1H, H-4), 2.64−2.58 (m, 2H, SCH_2CH_3), 2.33 (d, 1H, 3-OH), 1.30 (t, 3H, SCH_2CH_3), 1.29 (d, 3H, H-6), 1.25 (d, 1H, 4-OH) ppm; ^{13}C{H} NMR (151 MHz, $CDCl_3$): ***β*-34**: 84.2, 74.6, 74.4, 71.2, 63.8, 24.8, 16.6, 15.0 ppm; ***α*-34**: 83.2, 71.6, 70.5, 66.2, 61.0, 24.8, 16.1, 14.8 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_8H_{15}N_3O_3SNa^+$ 256.0727; found 256.0731.

*Ethyl 2-Azido-3,4-di-O-benzoyl-2-deoxy-1-thio-α/β-D-fucopyranoside (**25**).* Benzoyl chloride (256 L, 2.20 mmol) was added to a solution of compound **34** (0.13 g, 0.55 mmol) in anhydrous pyridine (10 mL), and the resulting mixture was stirred under argon for 16 h at rt. After that, the reaction was quenched with MeOH (3 mL), the volatiles were removed under reduced pressure, and the residue was coevaporated with toluene. The resulting residue was diluted with

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J. Org. Chem. 2022, 87, 271−280

CH_2Cl_2 (20 mL) and washed with water (8 mL), sat. aq. $NaHCO_3$ (8 mL), water (8 mL), 1 N aq. HCl (5 mL), and water (8 mL). The organic phase was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was puri ed by column chromatography on silica gel (ethyl acetate−hexane gradient elution) to give the title compound as a colorless syrup in a 63% yield (0.153 g, 0.35 mmol, α/β = 1/3). Analytical data for **25**: R_f = 0.70 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): **β-25**: 8.04 (m, 2H, aromatic), 7.89 (m, 2H, aromatic), 7.63 (m, 1H, aromatic), 7.49 (m, 3H, aromatic), 7.35 (m, 2H, aromatic), 5.66 (d, 1H, $J_{3,4}$ = 3.1 Hz, H-4), 5.25 (dd, 1H, H-3), 4.52 (d, 1H, $J_{1,2}$ = 10.1 Hz, H-1), 4.01−3.91 (m, 2H, H-2, 5), 2.97−2.81 (m, 2H, SCH_2CH_3), 1.40 (t, 3H, J = 7.4 Hz, SCH_2CH_3), 1.31 (d, 3H, J = 6.4 Hz, H-6) ppm; **α-25**: 5.70 (dd, 1H, $J_{3,4}$ = 3.2 Hz, H-4), 5.62 (d, 1H, $J_{1,2}$ = 5.6 Hz, H-1), 5.50 (dd, 1H, $J_{2,3}$ = 11.0 Hz, H-3), 4.69 (m, 1H, H-5), 4.50 (m, 1H, H-2), 2.73-2.61 (m, 2H, SCH_2CH_3), 1.37 (t, 3H, J = 7.4 Hz, SCH_2CH_3), 1.26 (d, 3H, J = 6.4 Hz, H-6) ppm; ^{13}C{H} NMR (75 MHz, $CDCl_3$): **β-25**: 165.8, 165.4, 133.5, 133.4, 129.9 (×2), 129.8 (×3), 128.6 (×3), 128.4 (×2), 84.4, 74.0, 73.5, 70.4, 61.0, 24.9, 16.7, 15.0 ppm; **α-25**: 165.7, 165.3, 129.3, 129.2, 129.0, 83.4, 71.4, 71.0, 65.54, 58.7, 24.8, 16.1, 14.8 ppm; HR-FAB MS $[M + Na]^+$ calcd for $C_{22}H_{23}N_3O_5SNa^+$ 464.1251; found 464.1282.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c02351.

NMR spectra for all new compounds (PDF)

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The manuscript was written through contributions of all authors. All authors have given approval to the nal version of the manuscript.

Notes

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