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ARTICLE

A versatile approach to the synthesis of glycans containing mannuronic acid residues

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Reported herein is a new method for a highly effective synthesis of β-glycosides from mannuronic acid donors equipped with the 3-*O*-picoloyl group. The stereocontrol of glycosylations was achieved by means of the H-bond-mediated aglycone delivery (HAD). The method was utilized for the synthesis of a tetrasaccharide linked via β-(1→3)-mannuronic linkages. We have also investigated 3,6-lactonized glycosyl donors that provided moderate to high β-manno stereoselectivity in glycosylations. A method to achieve complete α-manno stereoselectivity with mannuronic acid donors equipped with 3-*O*-benzoyl group is also reported.

Introduction

Uronic acid residues are present in many natural polysaccharides and glycoconjugates found in bacteria, animals and plants. Common examples include pectin, heparin, chondroitin, hyaluronan polysaccharides among others.[1] As such, many methods for the synthesis of glycosides of uronic acids have been developed.[2-10] D-Mannuronic acid (ManA) residues (mannuronates) are also commonly found as components in a variety of bacterial glycans[11] and also in alginate, a linear (1→4)-linked co-polymer of β-ManA and its C-5 epimer, α-L-guluronic acid consisting of both homo- and alternating heteromonomeric regions.[12] Mannose-configured sugars have a strong propensity to form α-linkages, and uncontrolled glycosylations typically produce anomeric mixtures. Among methods developed for the synthesis of β-mannosides,[13] Crich's method that relies on low reaction temperatures, powerful promoter systems, and the presence of a 4,6-*O*-benzylidene acetal protecting group is arguably the most effective.[14-18] This method has successfully been used to obtain poly-mannuronates via sequential β-mannosylation followed by oxidation of the 6-OH group.[19,20]

Initially, ManA donors were considered to be very unreactive owing to the C-5 electron-withdrawing group. More recently, their reactivity was found to be similar to that of the respective benzylated (armed) mannosyl donor.[21] This discovery led to the development of effective and robust methodologies for the direct glycosylation with ManA donors. Subsequent studies conducted at Leiden showed that the C-5 carboxylate ester moiety has a stereodirecting role in glycosylations favoring β-mannosides.[22-24] A very instrumental in advancing this chemistry was the development of a chemo- and regioselective oxidation method using TEMPO/BAIB reagent system.[25] The natural abundance, biomedical importance of mannuronates, and a notable improvement in chemical methods have stimulated a notable interest in synthesizing alginates and alginate-like glycan sequences in recent years.[26-38]

Results and discussion

Our group has introduced the H-bond-mediated Aglycone Delivery (HAD) method for stereocontrolled glycosylation.[39-41] We and others have demonstrated that highly stereoselective β-mannosylation reactions could be conducted with glycosyl donors equipped with 3-*O*-picoloyl group.[42-44] Since this method does not rely on the 4,6-*O*-benzylidine protection, it was deemed suitable for the synthesis of ManA glycosides. Reported herein is the investigation of the HAD method and other stereodirecting factors in application to the synthesis of mannuronates. First, we prepared a set of suitable ManA donors including the key donor **5** equipped with the 3-Pico group. As depicted in Scheme 1, the synthesis was initiated from known diol **1**[45] that was obtained via a modified synthetic sequence detailed in the Supporting Information. When compound **1** was subjected to the TEMPO/BAIB oxidation,[25] lactone derivative **2** and the desired carboxylic acid derivative **3** were obtained in a ratio of 3.7:1. Upon separation of the products, the lactone ring in compound **2** was opened under basic conditions (LiOH) to obtain carboxylic acid **3** in 94% yield. Overall, compound **3** was obtained from **1** in a combined yield of 77% yield. Mild benzylation with benzyl bromide in the presence of $NaHCO_3$[46] gave the esterified intermediate **4**. The latter was then picoloylated using standard conditions involving coupling with picolinic acid in the presence of EDC and DMAP.[42] As a result, the desired 3-Pico ManA donor **5** was obtained in 93% yield. For comparison, we also obtained 3-*O*-benzoylated (3-Bz) donor **6**. This was accomplished by reaction of intermediate **4** with benzoyl chloride in the presence of DMAP in pyridine to afford 3-Bz ManA

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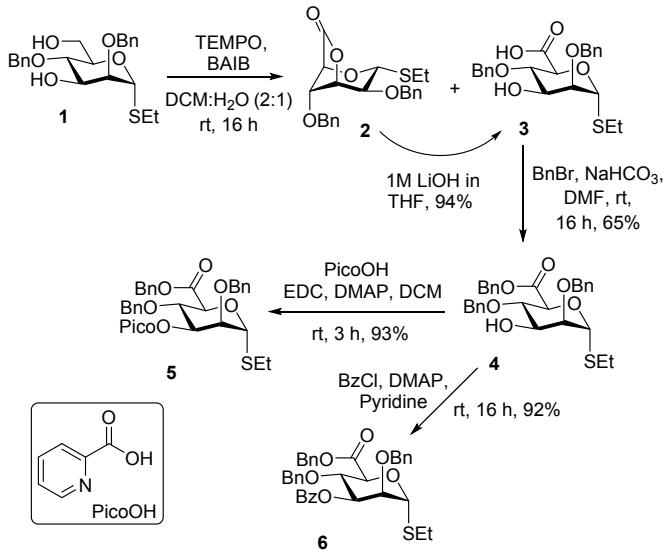
donor **6** in 92% yield. A portion of lactone **2** was also retained to be tested as a glycosyl donor for comparison.

Scheme 1. Synthesis of mannuronic acid donors **2**, **5** and **6**

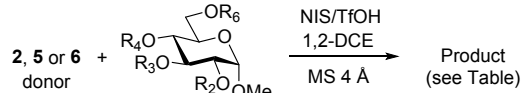


To investigate whether the remote 3-Pico group in donor **5** would act as the hydrogen bond acceptor for the incoming nucleophile and hence lead to the preferential formation of β-ManA glycosides, we set up a series of glycosylations with standard glycosyl acceptors **7-10**[47] (Table 1). When donor **5** was reacted with the primary acceptor **7** in the presence of NIS/TfOH promoter system under regular concentration (50 mM of the donor) in 1,2-DCE, disaccharide **11** was obtained in 91% yield with high stereoselectivity (α/β = 1/12, entry 1, Table 1). This exceeded our initial expectations because the HAD reactions give the highest stereoselectivity under ten-fold dilution conditions (5.0 mM of the donor). However, in this case, the high dilution did not seem to have any effect on the reaction, and disaccharide **11** was produced in a similar yield (88%) and stereoselectivity (α/β = 1/12, entry 1). No difference in the reaction rates was noted either, both glycosylations were completed in 19 h.

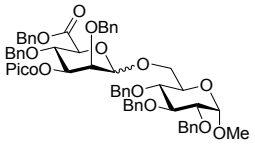
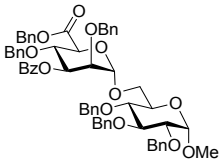
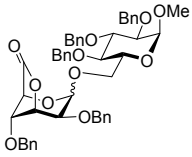
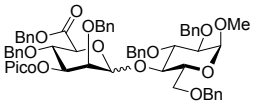
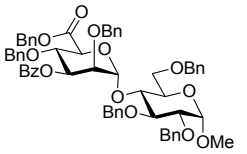
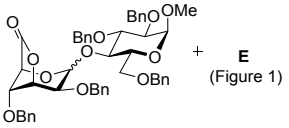
In contrast, exclusive α-ManA stereoselectivity was achieved with mannuronic acid donor equipped with 3-*O*-benzoyl group. Thus, the glycosidation of 3-Bz donor **6** with acceptor **7** yielded the respective α-linked disaccharide **12** (entry 2). Practically the same outcome in terms of yields (92%) and stereoselectivities (α-only) was obtained in both regular concentration and high dilution experiments. Both experiments were relatively swift and completed in 20 min. The lactonized donor **2** provided excellent β-stereoselectivity in reaction with glycosyl acceptor **7**. The corresponding disaccharide **13** was obtained in 57% yield (α/β = 1/25, entry 3).

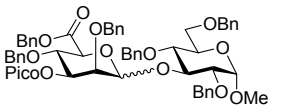
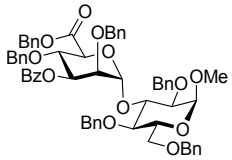
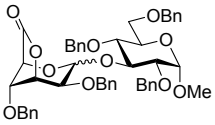
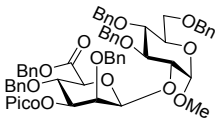
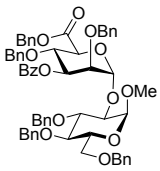
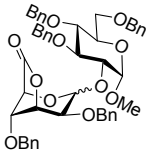
As previously proposed by Codee, van der Marel and co-workers,[21,23] the intermediate ManA oxacarbenium ion **A** adopts the predominantly axial half-chair $^3H_4$ conformation depicted in Figure 1. The axial orientation of the 3-Pico group in donor **5** will favor the HAD pathway as shown for intermediate **B** leading to the formation of the β-linked product. In case of 3-Bz donor **6**, the excellent α-stereoselectivity can be rationalized by the occurrence of a participation of the remote benzoyl group at C-3. This pathway was previously proposed by Crich[48] for regular mannosides and by us for mannosamine glycosides,[43] as well as by Nifantiev[49-52] and Kim[53] for other sugar series. The axial orientation of the 3-Bz group in the $^3H_4$ oxacarbenium ion intermediate **C** will favor the participation pathway as shown in Figure 1. The lactonized donor **2** provided excellent β-stereoselectivity, which could be due to the occurrence of a participation of the remote oxygen at C-4 via intermediate **D** (Figure 1), as previously proposed by Boltje and co-workers.[54,55]

Table 1. Glycosidation of donors **2**, **5** and **6** with glycosyl acceptors **7-10**



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

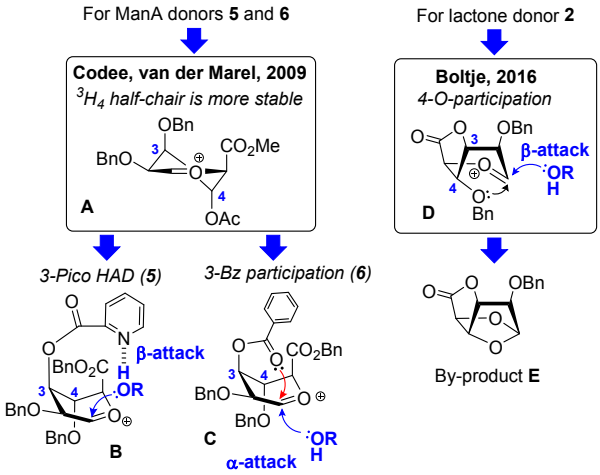
Entry	Reactants (time)	Product: yield, stereoselectivity (concentration of the donor)	$J_{C1',H1'}$ δ H3'
1	**5** + **7** (19 h)	 **11**: 91%, α/β = 1/12 (50 mM) 88%, α/β = 1/12 (5 mM)	157 Hz 4.97 ppm
2	**6** + **7** (20 min)	 **12**: 92%, α/β > 25/1 (50 mM) 92%, α/β > 25/1 (5 mM)	172 Hz 5.52 ppm
3	**2** + **7** (19 h)	 **13**: 57%, α/β = 1/25 (50 mM)	161 Hz 4.68 ppm
4	**5** + **8** (19 h)	 **14**: 79%, α/β = 1/11 (50 mM) 96%, α/β = 1/20 (5 mM)	155 Hz 4.95 ppm
5	**6** + **8** (1.5 h)	 **15**: 85%, α/β > 25/1 (50 mM) 90%, α/β > 25/1 (5 mM)	170 Hz 5.57 ppm
6	**2** + **8** (19 h)	 **E** (Figure 1) **16**: 27%, α/β = 1/11 (50 mM)	172 Hz 4.63 ppm

7	**5** + **9** (19 h)	 **17**: 74%, α/β = 1/1.3 (50 mM) 67%, α/β = 1/1.6 (5 mM)	162 Hz 5.11 ppm
8	**6** + **9** (30 min)	 **18**: 90%, α/β > 25/1 (50 mM) 83%, α/β > 25/1 (5 mM)	171 Hz 5.59 ppm
9	**2** + **9** (19 h)	 **19**: 26%, α/β = 1/2.8 (50 mM)	160 Hz 4.68 ppm
10	**5** + **10** (20 h)	 **20**: 88%, α/β < 1/25 (50 mM) 92%, α/β < 1/25 (5 mM)	160 Hz 5.03 ppm
11	**6** + **10** (40 min)	 **21**: 92%, α/β > 25/1 (50 mM) 91%, α/β > 25/1 (5 mM)	173Hz 5.63 ppm
12	2 + 10 (20 h)	 **22**: 44%, α/β = 1/4.0 (50 mM)	160 Hz 4.59 ppm

To confirm the stereochemical assignment of the products, we conducted a series of NMR experiments. The assignment of the anomeric configuration in sugars of the manno series relies on the measurement of the $J_{C1',H1'}$ coupling constant. The observed values of 157 and 161 Hz for β-ManA glycosides (entries 1 and 3) were in agreement with those reported for conventional β-mannosides (~160 Hz).[56] The $J_{C1',H1'}$ coupling constant of 172 Hz measured for α-ManA glycoside (entry 2) was in line with the previously reported values of 170 Hz or greater.[56] Similarly to our previous studies with mannosamine glycoside,[43] we have also noticed that the chemical shift for H-3' of the α-anomer is always shifted downfield in comparison to that of the β-anomer by $\Delta\delta$ = 0.5-0.6 ppm. Thus, chemical shift for H-3' in β-linked disaccharide **11** was 4.97 ppm, whereas the corresponding signal of disaccharide **12** was 5.52 ppm (entries 1 and 2, Table 1). No such definitive trend was noticed for the lactonized products.

We then continued our studies by glycosylation of a series of secondary glycosyl acceptors. When glycosylation of 4-OH acceptor **8** was performed with 3-Pico donor **5** in the presence of NIS/TfOH under regular concentration (50 mM of the donor) in DCE, disaccharide **14** was obtained in 79% yield with commendable β-manno stereoselectivity (α/β = 1/11, entry 4). The ten-fold dilution experiment (5 mM of donor **5**) produced disaccharide **14** in 96% yield with improved β-manno stereoselectivity (α/β = 1/20, entry 4). It required 19 h for both glycosylations to complete. When glycosylations of acceptor **8** were performed with 3-Bz donor **6**, disaccharide **15** was obtained with exclusive α-stereoselectivity in 1.5 h. High yields (85-90%) and complete α-manno stereoselectivity was achieved for both regular concentration and high dilution experiments (entry 5). Glycosidation of lactone **2** with acceptor **8** yielded disaccharide **16** in 27% yield (α/β = 1/11, entry 6) along with the formation of side product **E** (Figure 1). The formation of this side product, also observed by Boltje and co-workers,[54] supports their hypothesis of the reaction pathway proceeding via the participation of O-4.

Figure 1. Mechanistic rationale for stereoselectivity obtained with lactone donor **2** and ManA donors **5** and **6**



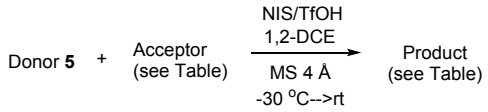
When glycosylation of secondary 3-OH acceptor **9** was performed with donor **5** under regular concentration (50 mM of the donor) in DCE, disaccharide **17** was obtained in 74% yield with a somewhat unexpected poor stereoselectivity (α/β = 1/1.3, entry 7). Also, the ten-fold dilution experiment (5 mM of the donor) produced disaccharide **17** in 67% yield with poor stereoselectivity (α/β = 1/1.6, entry 7). It took 19 h for both glycosylations to complete. When glycosylation of acceptor **9** was performed with 3-Bz donor **6**, disaccharide **18** was obtained with exclusive α-stereoselectivity in 30 min. Good yields (83-90%) and complete α-manno stereoselectivity were achieved for both regular concentration and high dilution conditions (entry 8). Glycosidation of lactone **2** with acceptor **9** yielded disaccharide **19** in 26% yield with preferential, albeit unimpressive β-stereoselectivity (α/β = 1/2.8, entry 9).

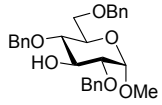
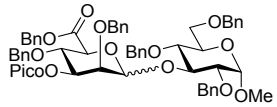
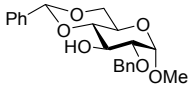
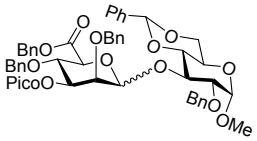
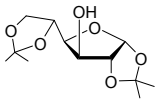
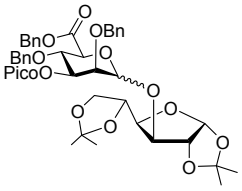
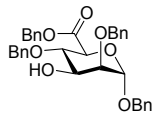
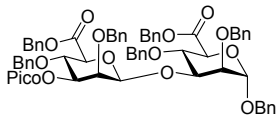
When glycosylation of 2-OH acceptor **10** was performed with 3-Pico donor **5** under regular concentration (50 mM of the donor) in DCE, disaccharide **20** was obtained in 88% yield with practically complete β-manno stereoselectivity (α/β < 1/25, entry 10). The ten-fold dilution experiment (5 mM of donor **5**) produced disaccharide **20** in 92% yield with the same stereoselectivity. It required 20 h for both glycosylations to complete. When glycosylations of acceptor **10** were performed with 3-Bz donor **6**, disaccharide **21** was obtained with

exclusive α-stereoselectivity in 40 min. High yields (91-92%) were achieved for both regular and low concentration experiments (entry 11). Glycosidation of lactone **2** with acceptor **10** yielded disaccharide **22** in 44% yield (α/β = 1/4.0, entry 12).

Being generally satisfied with excellent results achieved for all glycosidations of 3-Pico ManA donor **5** except that with glycosyl acceptor **9**, which gave practically no stereoselectivity (entry 1, Table 2), we endeavored on studying other 3-OH acceptors **23**-**25**. When glycosylation of 4,6-*O*-benzylidene-protected acceptor **23**[57,58] was performed under regular concentration (50 mM of donor **5**) in DCE, disaccharide **26** was obtained in 62% yield with similar β-manno stereoselectivity (α/β = 1/1.3, entry 2). The ten-fold dilution experiment (5 mM of donor **5**) produced disaccharide **26** in 56% yield with only marginally improved stereoselectivity (α/β = 1/1.9, entry 2). When glycosylation of diacetone glucose acceptor **24** was performed under regular concentration (50 mM of donor **5**) in DCE, disaccharide **27** was obtained in 59% yield with enhanced, albeit unimpressive β-manno stereoselectivity (α/β = 1/3.4, entry 3). The ten-fold dilution experiment (5 mM of donor **5**) produced disaccharide **27** in 65% yield (α/β = 1/5.0, entry 3).

Table 2. Glycosidation of 3-Pico donor **5** with various 3-OH glycosyl acceptors **9** and **23-25**

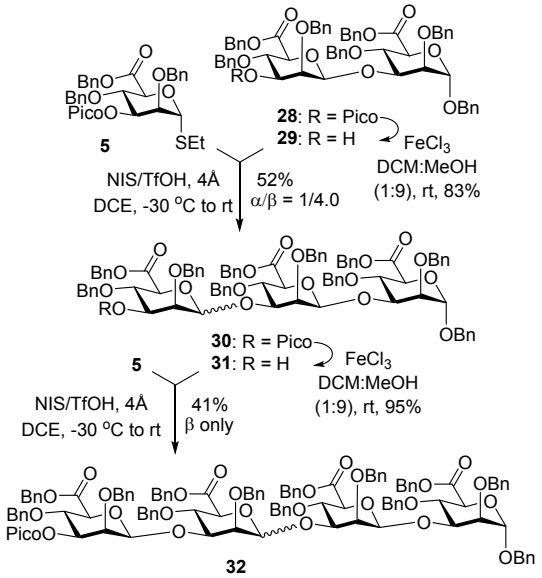


Entry	Acceptor (time)	Product: yield, stereoselectivity (concentration of the donor)
1	 **9** (19 h)	 **17**: 74%, α/β = 1/1.3 (50 mM) 67%, α/β = 1/1.6 (5 mM)
2	 **23** (19 h)	 **26**: 62%, α/β = 1/1.3 (50 mM) 56%, α/β = 1/1.9 (5 mM)
3	 **24** (19 h)	 **27**: 59%, α/β = 1/3.4 (50 mM) 65%, α/β = 1/5.0 (5 mM)
4	 **25** (19 h)	 **28**: 83%, α/β = 1/18 (5 mM)

Still puzzled by this poor reaction outcome with various 3-OH glucosyl acceptors, both in terms of yields and stereoselectivities, we assumed that this is due to a donor-acceptor mismatch.[59] To verify this hypothesis, we synthesized 3-OH mannosyl acceptor **25** (see the Supporting Information for details). To our delight, glycosylation of mannosyl acceptor **25** with 3-Pico donor **5** performed under ten-fold dilution conditions (5 mM of donor **5**) produced disaccharide **28** in 83% yield with excellent β-manno stereoselectivity (α/β = 1/18, entry 4). The $J_{C1',H1'}$ coupling constant of 159 Hz confirmed the β-manno configuration achieved in this reaction. With success in obtaining the ManAβ-(1→3)ManA linkage, we extended this finding to the iterative synthesis of a glycan containing β-(1→3)-linked ManA residues. It is noteworthy that while many efforts have been made to synthesize 1→4 linked ManA glycans found in alginate (vide supra), the synthesis of 1→3 linked oligomers has received a very scarce attention. Previous known syntheses were achieved by trityl-cyanoethylidene polycondensation by Kochetkov[60] and automated solution phase synthesis by Pohl.[31]

To achieve the iterative oligosaccharide assembly, pure β-anomer of disaccharide **28** separated chromatographically was taken forward, and the 3-Pico substituent in was chemoselectively removed with $FeCl_3$ in DCM/MeOH to afford compound **29** as depicted in Scheme 3. Our recent study showed that the Pico group can be removed in a catalytic manner using 30 mol% of iron(III) chloride or copper(II) acetate.[61] In our experience, the reactions performed with $Cu(OAc)_2$ are generally faster, but in general $FeCl_3$-catalyzed reactions provide better yields. Hence, the latter reaction conditions have been used in this study. The resulting disaccharide acceptor **29** was subjected to glycosylation with ManA donor **5** to afford trisaccharide **30** in a good yield of 52% albeit incomplete stereoselectivity. Trisaccharide **30** (α/β = 1/4.0) was then subjected to the Pico group removal using $FeCl_3$ in DCM/MeOH to afford trisaccharide acceptor **31** in 95% yield. The latter was subjected to final glycosylation with ManA donor **5** to obtain tetrasaccharide **32** in 41% yield. The complete β-manno stereoselectivity was achieved in this step.

Scheme 3. Application of 3-Pico donor **5** in the synthesis of ManA tetrasaccharide **32**



Conclusions

In conclusion, a new practical method for the stereoselective synthesis of both α- and β-glycosides of mannuronic acid is reported. The presence of the 3-Pico group on the ManA donor can provide high or complete stereocontrol for β-mannosylation via the HAD pathway. The method was utilized for the synthesis of a tetrasaccharide containing ManA residues linked via β-(1→3) linkages. A mismatch between ManA donor and 3-OH glucosyl acceptors that resulted in poor stereoselectivities and yields was also noticed. In contrast, exclusive α-ManA stereoselectivity was achieved in all glycosylations with the mannuronic acid donor equipped with 3-*O*-benzoyl group. This complete stereoselectivity was rationalized by the occurrence of the remote participation of the 3-Bz substituent. Also investigated was the 6,3-lactonized donor that was generally β-ManA stereoselective, but many reactions gave low yields due to the propensity to form the 1,4-cyclized side product. 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-1020' 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 or 151 MHz. Two-dimensional heteronuclear *J*-resolved spectra (HETERO2DJ)[56] were recorded in $CDCl_3$ at 600 MHz.

Ethyl 2,4-di-*O*-benzyl-1-thio-α-D-mannopyranosidurono-6,3-lactone (2). (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO, 100 mg, 0.636 mmol) and bis(acetoxy)iodobenzene (BAIB, 2.56 g, 7.94 mmol) were added to a mixture of ethyl 2,4-di-*O*-benzyl-1-thio-α-D-mannopyranoside[45] (**1**, 1.29 g, 3.18 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 x 10 mL). The aqueous layer was separated and extracted with EtOAc (2 x 30 mL). The organic extracts were combined, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_3OH-CH_2Cl_2 gradient elution) to give lactone **2** (0.81 g, 2.02 mmol) and acid **3** (0.23 g, 0.55 mmol). Analytical data for **2**: R_f = 0.90 (CH_3OH/CH_2Cl_2, 5/95, v/v), R_f = 0.65 (ethyl acetate/toluene, 1/4, v/v); $[\alpha]_D^{22}$ -6.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38-7.29 (m, 10H, aromatic), 4.72 (d, 1H, $J_{1,2}$ = 8.9 Hz, H-1), 4.69 (dd, 2H, ^2J = 11.7 Hz, CH_2Ph), 4.67-4.58 (m, 2H, $J_{3,4}$ = 5.9 Hz, H-3, C*H*Ph), 4.47 (d, 1H, ^2J = 11.7 Hz, C*H*Ph), 4.25 (br d, 1H, H-5), 4.01 (dd, 1H, $J_{4,5}$ = 3.0 Hz, H-4), 3.87 (dd, 1H, $J_{2,3}$ = 1.5 Hz, H-2), 2.73 (m, 2H, SCH_2CH$_3$), 1.29 (t, 3H, *J* = 7.5 Hz, SCH$_2$CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.1, 137.5, 136.4, 128.9 (x2), 128.7, 128.6 (x2), 128.2 (x5), 82.4, 78.1, 75.1, 74.0, 73.5, 72.0, 71.9, 25.2, 15.2 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{22}H_{24}O_5SNa^+$ 423.1242; found 423.1215.

Ethyl 2,4-di-*O*-benzyl-1-thio-α-D-mannopyranosiduronic acid (3). A 1 M aq. solution of LiOH (5.0 mL) was added to a solution of lactone **2** (0.81 g, 2.02 mmol) in THF (5.0 mL), and the resulting mixture was stirred at rt for 4 h. After that, the reaction mixture was acidified with 1 N aq. HCl to pH ~3 and the volatiles were removed under reduced pressure. The residue was diluted with EtOAc (~20 mL) and washed with water (10 mL). The aqueous layer was extracted with EtOAc (3 x 20 mL). The organic extracts were combined, dried with Na_2SO_4, concentrated under reduced pressure, and dried in *vacuo* for 2 h to give the acid **3** as a colorless syrup in 94% yield (0.80 g, 1.91 mmol), which corresponds to a combined yield of 77% from compound **1**. Analytical data for **3**: R_f = 0.35 (CH_3OH/CH_2Cl_2, 5/95, v/v), R_f = 0.15 (ethyl acetate/toluene, 1/4, v/v); $[\alpha]_D^{22}$ + 68.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.33 (m, 10H, aromatic), 5.54 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.78 (dd, 2H, ^2J = 11.0 Hz, CH_2Ph), 4.66 (dd, 2H, ^2J = 11.5 Hz, CH_2Ph), 4.58 (dd, 1H, $J_{4,5}$ = 7.2 Hz, H-5), 4.08-3.98 (m, 2H, H-3, 4), 3.86 (dd, 1H, $J_{2,3}$ = 3.3 Hz, H-2), 2.81-2.66 (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 173.6, 137.6, 137.3, 128.8 (x2), 128.6 (x2), 128.4, 128.3 (x2), 128.2 (x2), 128.1, 80.4, 77.8, 77.5, 74.2, 72.8, 70.8, 70.7, 25.3, 15.1 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{22}H_{26}O_6SNa^+$ 441.1348; found 441.1375.

Benzyl (ethyl 2,4-di-*O*-benzyl-1-thio-α-D-mannopyranosid)uronate (4). Benzyl bromide (5.4 mL, 45.0 mmol) and $NaHCO_3$ (2.27 g, 27.0 mmol) were added to a solution of **3** (1.88 g, 4.50 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 x 15 mL), and the aqueous layer was extracted with EtOAc (80 mL). The organic extracts were combined, 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 give the title compound as a colorless syrup in 65% yield (1.48 g, 2.91 mmol). Analytical data for **4**: R_f = 0.65 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ +53.7 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37-7.23 (m, 15H, aromatic), 5.46 (d, 1H, $J_{1,2}$ = 4.1 Hz, H-1), 5.18 (s, 2H, CH_2Ph), 4.77 (d, 1H, ^2J = 11.6 Hz, C*H*Ph), 4.68 (d, 1H, ^2J = 11.2 Hz, C*H*Ph), 4.58-4.52 (m, 3H, H-5, 2 x C*H*Ph), 4.05-3.94 (m, 2H, H-3, 4), 3.79 (dd, 1H, $J_{2,3}$ = 3.6 Hz, H-2), 2.65 (m, 2H, SCH_2CH$_3$), 2.40 (d, 1H, *J* = 6.5 Hz, OH), 1.26 (t, 3H, *J* = 7.4 Hz, SCH$_2$CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.5, 138.0, 137.5, 135.4, 128.8 (x2), 128.7 (x2), 128.5 (x5), 128.3, 128.2 (x2), 128.0 (x2), 127.9, 80.6, 78.0, 77.8, 74.1, 72.7, 71.7, 70.7, 67.2, 25.3, 15.1 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{29}H_{32}O_6SNa^+$ 531.1817; found 531.1848.

Benzyl (ethyl 2,4-di-*O*-benzyl-3-*O*-picoloyl-1-thio-α-D-mannopyranosid)uronate (5). Picolinic acid (0.63 g, 5.09 mmol), EDC (0.98 g, 5.09 mmol) and DMAP (83 mg, 0.68 mmol) were added to a solution of compound **4** (1.72 g, 3.39 mmol) in dry CH_2Cl_2 (50 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 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 as a colorless syrup in 93% yield (1.94 g, 3.16 mmol). Analytical data for **5**: R_f = 0.50 (ethyl acetate/hexane, 1/1, v/v); $[\alpha]_D^{22}$ +30.6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.78 (m, 1H, aromatic), 7.98 (m, 1H, aromatic), 7.80 (m, 1H, aromatic), 7.48 (m, 1H, aromatic), 7.32-7.14 (m, 15H, aromatic), 5.56-5.49 (m, 2H, $J_{1,2}$ = 3.2, $J_{3,4}$ = 7.2 Hz, H-1, 3), 5.11 (dd, 2H, ^2J = 12.2 Hz, C*H*$_2$Ph), 4.68 (m, 3H, H-5, 2 x C*H*Ph), 4.59 (m, 2H, 2 x C*H*Ph), 4.44 (dd, 1H, H-4), 4.03 (dd, 1H, $J_{2,3}$ = 4.6 Hz, H-2), 2.69 (m, 2H, SC*H*$_2$CH$_3$), 1.29 (t, 3H, *J* = 7.4 Hz, SCH$_2$C*H*$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 163.9, 150.2, 147.5, 137.7, 137.4, 137.1, 135.1, 128.7 (x3), 128.4 (x5), 128.3 (x2), 128.0, 127.9 (x2), 127.8, 127.2, 125.5, 81.3, 77.4, 75.2, 75.0, 74.1, 72.9, 72.5, 72.4, 67.4, 25.3, 15.0 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{35}H_{35}NO_7SNa^+$ 636.2032; found 636.2043.

Benzyl (ethyl 3-*O*-benzoyl-2,4-di-*O*-benzyl-1-thio-α-D-mannopyranosid)uronate (6). Benzoyl chloride (0.43 mL, 3.68 mmol) and DMAP (45 mg, 0.37 mmol) were added to a solution of compound **4** (0.94 g, 1.84 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 (~30 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 92% yield (1.04 g, 1.70 mmol). Analytical data for **6**: R_f = 0.70 (ethyl acetate/hexane, 2/3, v/v); $[\alpha]_D^{22}$ +24.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02-7.99 (m, 2H, aromatic), 7.61-7.56 (m, 1H, aromatic), 7.47-7.42 (m, 2H, aromatic), 7.29-7.14 (m, 15H, aromatic), 5.52 (d, 1H, $J_{1,2}$ = 4.9 Hz, H-1), 5.49 (dd, 1H, $J_{3,4}$ = 7.4 Hz, H-3), 5.04 (dd, 2H, ^2J = 12.3 Hz, C*H*$_2$Ph), 4.62 (m, 5H, H-5, 2 x C*H*$_2$Ph), 4.41-4.37 (dd, 1H, H-4), 4.01 (dd, 1H, $J_{2,3}$ = 3.2 Hz, H-2), 2.82-2.62 (m, 2H, SC*H*$_2$CH$_3$), 1.31 (t, 3H, *J* = 7.4 Hz, SCH$_2$C*H*$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 165.4, 137.4 (x2), 134.9, 133.4, 129.8 (x2), 129.5, 128.5 (x4), 128.4, 128.3 (x6), 128.0 (x2), 127.8 (x4), 81.1, 75.2, 75.1, 73.9, 72.4 (x2), 71.8, 67.2, 25.1, 14.9 ppm; HR FAB MS $[M+Na]^+$ calcd for $C_{36}H_{36}O_7SNa^+$ 635.2079; found 635.2089.

Synthesis of Disaccharides 11-22, 26 and 27

A general procedure for glycosylation. A mixture of a glycosyl donor (0.06 mmol), glycosyl acceptor (0.05 mmol), 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) and trifluoromethanesulfonic acid (TfOH, 2.0 µL, 0.02 mmol) 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 specified in tables. After that, the solids were filtered off and 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 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 2,4-di-*O*-benzyl-3-*O*-picoloyl-α/β-D-mannopyranosyluronate)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (11). The title compound was obtained as a white amorphous solid from glycosyl donor **5** and acceptor **7**[47] in 91% yield (α/β = 1/12, 50 mM) or 88% yield (α/β = 1/12, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **11**: R_f = 0.45 (ethyl acetate/toluene, 3/7, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.75-8.72 (m, 1H, aromatic), 7.87 (m, 1H, aromatic), 7.75-7.69 (m, 1H, aromatic), 7.45-7.40 (m, 1H, aromatic), 7.28-6.97 (m, 30H, aromatic), 5.12 (dd, 2H, ^2J = 12.0 Hz, C*H*$_2$Ph), 4.99-4.92 (m, 2H, $J_{3',4'}$ = 9.6 Hz, H-3', C*H*Ph), 4.78 (br s, 1H, C*H*Ph), 4.74 (m, 2H, 2 x C*H*Ph), 4.60-4.43 (m, 7H, $J_{1,2}$ = 3.5 Hz, H-1, 6 x C*H*Ph), 4.38 (dd, 1H, $J_{4',5'}$ = 9.4 Hz, H-4'), 4.17 (s, 1H, H-1'), 4.07-4.03 (m, 1H, $J_{6a,6b}$ = 10.0 Hz, H-6a), 3.93 (dd, 1H, H-3), 3.84 (m, 2H, $J_{2',3'}$ = 3.2 Hz, H-2', 5'), 3.72-3.67 (m, 1H, $J_{5,6a}$ = 1.5, $J_{5,6b}$ = 5.3 Hz, H-5), 3.44-3.40 (m, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 3.40-3.36 (m, 1H, H-4), 3.34-3.30 (m, 1H, H-6b), 3.25 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.8, 164.0, 150.2, 147.5, 138.8, 138.2, 138.0, 137.9, 137.0, 135.3, 128.8 (x2), 128.7 (x4), 128.6 (x2), 128.5 (x5), 128.4 (x2), 128.3 (x5), 128.2 (x2), 128.1 (x3), 127.8 (x4), 127.7, 127.6, 127.1, 125.4, 101.9 ($^1J_{C1',H1'}$ = 157.0 Hz, C-1'), 97.8 ($^1J_{C1,H1}$ = 171.0 Hz, C-1), 82.3, 80.0, 77.4, 76.2, 75.9, 75.2, 75.1, 74.9, 74.4, 74.3, 74.1, 73.5, 69.9, 68.8, 67.5, 55.2 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{61}H_{61}NO_{13}Na^+$ 1038.4041; found 1038.4054.

Methyl 6-*O*-(benzyl 3-*O*-benzoyl-2,4-di-*O*-benzyl-α-D-mannopyranosyluronate)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (12). The title compound was obtained as a colorless amorphous solid from glycosyl donor **6** and acceptor **7**[47] in 92% yield (α/β >25/1, 50 mM) and 92% (α/β >25/1, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **12**: R_f = 0.60 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (m, 2H, aromatic), 7.58 (m 1H, aromatic), 7.44 (m, 2H, aromatic), 7.34-7.05 (m, 30H, aromatic), 5.52 (dd, 1H, $J_{3',4'}$ = 7.8 Hz, H-3'), 5.14 (d, 1H, $J_{1',2'}$ = 3.0 Hz, H-1'), 5.06 (dd, 2H, ^2J = 12.3 Hz, C*H*$_2$Ph), 4.90 (dd, 2H, ^2J = 10.9 Hz, C*H*$_2$Ph), 4.75 (dd, 2H, ^2J = 10.9 Hz,

CH_2Ph), 4.67 (dd, 2H, ^2J = 12.1 Hz, CH_2Ph), 4.62 (m, 2H, CH_2Ph), 4.54 (m, 3H, H-1, CH_2Ph), 4.40-4.32 (m, 2H, H-4', 5'), 4.03-3.94 (m, 3H, $J_{2',3'}$ = 3.1 Hz, H-2', 3, 6a), 3.76 (m, 2H, H-4, 6b), 3.54-3.46 (m, 2H, H-2, 5), 3.36 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.3, 165.5, 138.9, 138.3 (x2), 137.9, 137.7, 135.2, 133.4, 129.9 (x2), 129.8, 128.6 (x4), 128.5 (x6), 128.4 (x5), 128.3 (x2), 128.2 (x2), 128.1 (x2), 128.0 (x3), 127.9 (x2), 127.8 (x5), 127.7, 127.6, 98.9 ($^1J_{C1',H1'}$ = 172.0 Hz, C-1'), 98.0 ($^1J_{C1,H1}$ = 173.1 Hz, C-1), 82.2, 80.2, 77.8, 75.8, 75.2, 75.1, 75.0, 74.4, 73.5, 73.1, 72.1, 70.1, 67.2, 67.1, 55.3 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{62}H_{62}O_{13}Na^+$ 1037.4088; found 1037.4099.

Methyl 6-*O*-(2,4-di-*O*-benzyl-α/β-D-mannopyranosid-urono-6,3-lactone)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (13). The title compound was obtained as a colorless amorphous solid from glycosyl donor **2** and acceptor **7**[47] in 57% yield (α/β >1/25, 50 mM). Analytical data for **13**: R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36-7.26 (m, 25H, aromatic), 5.22 (d, 1H, $J_{1',2'}$ = 5.0 Hz, H-1'), 4.95 (d, 1H, ^2J = 10.9 Hz, C*H*Ph), 4.81 (m, 3H, 3 x C*H*Ph), 4.58 (m, 8H, H-1, 3', 6 x C*H*Ph), 4.13 (dd, 1H, H-2'), 4.06-3.95 (m, 4H, H-3, 4', 5', 6a), 3.85 (m, 1H, $J_{5,6b}$ = 9.4 Hz, H-5), 3.62-3.51 (m, 2H, H-2, 4), 3.36 (dd, 1H, H-6b), 3.30 (s, 3H, OCH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.4, 138.9, 138.4 (x2), 137.4, 136.5, 128.9 (x2), 128.7, 128.6 (x3), 128.5 (x6), 128.2 (x2), 128.1 (x6), 128.0 (x2), 127.8 (x2), 127.7, 99.4 ($^1J_{C1',H1'}$ = 160.6 Hz, C-1'), 97.9 ($^1J_{C1,H1}$ = 176.1 Hz, C-1), 82.0, 80.1, 78.3, 77.4, 76.4, 75.8, 74.7, 73.5, 72.2, 71.3, 70.9, 70.2, 68.2, 67.8, 55.3 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{48}H_{50}O_{11}Na^+$ 825.3251; found 825.3267.

Methyl 4-*O*-(benzyl 2,4-di-*O*-benzyl-3-*O*-picoloyl-α/β-D-mannopyranosyluronate)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (14). The title compound was obtained as a colorless amorphous solid from glycosyl donor **5** and acceptor **8**[47] in 79% yield (α/β = 1/11, 50 mM) or 96% yield (α/β = 1/20, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **14**: R_f = 0.35 (ethyl acetate/toluene, 3/7, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.80 (m, 1H, aromatic), 7.90 (m, 1H, aromatic), 7.77 (m, 1H, aromatic), 7.48 (m, 1H, aromatic), 7.45-7.38 (m, 2H, aromatic), 7.33-7.17 (m, 20H, aromatic), 7.15-7.00 (m, 8H, aromatic), 5.16 (d, 1H, ^2J = 10.8 Hz, C*H*Ph), 5.01 (s, 2H, CH_2Ph), 4.95 (dd, 1H, $J_{3',4'}$ = 9.8 Hz, H-3'), 4.79-4.40 (m, 12H, $J_{1,2}$ = 3.7, $J_{4',5'}$ = 9.5 Hz, H-1, 1', 4', 9 x C*H*Ph), 3.94 (m, 3H, $J_{2',3'}$ = 3.1 Hz, H-2', 3, 4), 3.76 (d, 1H, H-5'), 3.66 (m, 1H, H-5), 3.60 (br s, 2H, H-6a, 6b), 3.52 (dd, 1H, $J_{2,3}$ = 9.2 Hz, H-2), 3.38 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.9, 164.0, 150.3, 147.5, 139.5, 138.5, 138.2, 138.0, 137.6, 137.0, 135.3, 128.8 (x2), 128.6 (x4), 128.5 (x2), 128.4, 128.2 (x11), 128.1 (x4), 127.9, 127.7 (x2), 127.6, 127.5, 127.2, 127.1, 125.3, 101.0 ($^1J_{C1',H1'}$ = 155.0 Hz, C-1'), 98.5 ($^1J_{C1,H1}$ = 171.0 Hz, C-1), 80.4, 79.3, 77.7, 76.4, 75.6, 75.5, 75.0, 74.9 (x2), 74.5, 73.8, 73.7, 69.7, 68.5, 67.2, 55.5 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{61}H_{61}NO_{13}Na^+$ 1038.4041; found 1038.4057.

Methyl 4-*O*-(benzyl 3-*O*-benzoyl-2,4-di-*O*-benzyl-α-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 **8**[47] in 85% yield (α/β > 25/1, 50 mM) and 90% (α/β > 25/1, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **15**: R_f = 0.65 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (m, 2H, aromatic), 7.55 (m, 1H, aromatic), 7.40-7.05 (m, 32H, aromatic), 5.82-5.26 (m, 2H, $J_{1',2'}$ = 3.4, $J_{3',4'}$ = 7.3 Hz, H-1', 3'), 5.06-4.90 (m, 3H, 3 x C*H*Ph), 4.83-4.31 (m, 10H, $J_{1,2}$ = 3.3 Hz, H-1, 4', 5', 7 x C*H*Ph), 4.20 (dd, 2H, ^2J = 11.9 Hz, CH_2Ph), 4.05-3.65 (m, 6H, $J_{2,'3'}$ = 2.7 Hz, H-2', 3, 4, 5, 6a, 6b), 3.55 (dd, 1H, $J_{2,3}$ = 9.3 Hz, H-2), 3.39 (s, 3H, OCH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 165.7, 139.0, 138.4, 138.0 (x2), 137.6, 135.0, 133.3, 129.9 (x2), 129.6, 128.6 (x3), 128.5 (x4), 128.4 (x4), 128.2 (x8), 128.0, 127.9 (x2), 127.8, 127.7 (x2), 127.5, 127.4 (x4), 127.3 (x3), 100.2 ($^1J_{C1',H1'}$ = 170.0 Hz, C-1'), 97.9 ($^1J_{C1,H1}$ = 173.1 Hz, C-1), 81.6, 80.0, 77.4, 76.2, 75.3, 75.0, 74.2, 73.3, 72.8, 72.7, 72.5, 69.6, 69.2, 67.2, 55.4 ppm; HR-FAB MS $[M+H]^+$ calcd for $C_{62}H_{62}O_{13}Na^+$ 1037.4088; found 1037.4099.

Methyl 4-*O*-(2,4-di-*O*-benzyl-α/β-D-mannopyranosid-urono-6,3-lactone)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (16). The title compound was obtained as a colorless amorphous solid from glycosyl donor **2** (50 mM) and acceptor **8**[47] in 27% yield. Analytical data for **16** were in agreement with those previously reported.[54]

Methyl 3-*O*-(benzyl 2,4-di-*O*-benzyl-3-*O*-picoloyl-α/β-D-mannopyranosyluronate)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (17). The title compound was obtained as a colorless amorphous solid from glycosyl donor **5** and acceptor **9**[47] in 74% yield (α/β = 1/1.3, 50 mM) or 67% yield (α/β = 1/1.6, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **17**: R_f = 0.30 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.82 (m, 1H, aromatic), 7.95 (m, 1H, aromatic), 7.86-7.77 (m, 1H, aromatic), 7.52-6.99 (m, 51H, aromatic), 5.62 (dd, 1H, $J_{3\alpha',4\alpha'}$ = 8.9 Hz, H-3α'), 5.51 (d, 1H, $J_{1\alpha',2\alpha'}$ = 2.3 Hz, H-1α'), 5.20-4.98 (m, 6H, $J_{1\beta',2\beta'}$ = 3.1 Hz, H-1β', 3β', 2 x CH_2Ph), 4.92-4.81 (m, 2H, H-5α', C*H*Ph), 4.73-4.18 (m, 18H, H-1α, 1β, 3α, 3β, 4α', 4β', 6α^a, 6α^b, 5 x CH_2Ph), 4.10 (dd, H-2β'), 3.98-3.94 (m, 2H, $J_{2\alpha',3\alpha'}$ = 3.0 Hz, H-2α', 5β'), 3.76-3.44 (m, 8H, H-2α, 2β, 4α, 4β, 5α, 5β, 6β^a, 6β^b), 3.35 (s, 3H, OCH_3), 3.26 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.6, 168.1, 164.1, 164.0, 150.2, 150.1, 147.8 (x2), 138.8, 138.5, 138.4 (x2), 138.2, 138.0 (x2), 137.9, 137.5, 136.9 (x2), 135.5 (x2), 129.0 (x2), 128.9 (x2), 128.7 (x2), 128.6 (x2), 128.5 (x7), 128.4 (x4), 128.3 (x3), 128.2 (x4), 128.1 (x3), 128.0, 127.9 (x3), 127.8, 127.7 (x3), 127.6, 127.5 (x3), 127.4, 127.0, 126.9, 126.8, 125.3, 102.0 ($^1J_{C1',H1'}$ = 162.0 Hz, C-1'), 99.0, 98.1 ($^1J_{C1,H1}$ = 173.1 Hz, C-1), 97.4, 80.3, 80.2, 78.9 (x2), 78.1, 76.2, 76.1, 75.5, 75.2 (x2), 75.1 (x2), 74.9, 74.8, 74.1, 73.7 (x2), 73.4, 73.2, 72.6, 72.0, 69.9 (x2), 68.7, 68.6, 67.1, 67.0, 55.2 (x2) ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{61}H_{61}NO_{13}Na^+$ 1038.4041; found 1038.4054.

Methyl 3-*O*-(benzyl 3-*O*-benzoyl-2,4-di-*O*-benzyl-α-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 **9**[47] in 90% yield (α/β > 25/1, 50 mM) and 83% (α/β > 25/1, 5

mM) under regular and high dilution reaction conditions, respectively. Analytical data for **18**: R_f = 0.55 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (m, 2H, aromatic), 7.56 (m, 1H, aromatic), 7.42-7.01 (m, 32H, aromatic), 5.59 (dd, 1H, $J_{3',4'}$ = 8.9 Hz, H-3'), 5.53 (d, 1H, $J_{1',2'}$ = 2.3 Hz, H-1'), 5.07 (dd, 2H, ^2J = 12.4 Hz, CH_2Ph), 4.86 (m, 1H, $J_{4',5'}$ = 8.7 Hz, H-5', C*H*Ph), 4.73 (d, 1H, ^2J = 11.8 Hz, C*H*Ph), 4.60 (d, 1H, ^2J = 5.6 Hz, C*H*Ph), 4.57-4.28 (m, 8H, $J_{1,2}$ = 3.5 Hz, H-1, 4', 6 x C*H*Ph), 4.27-4.11 (m, 2H, H-3, C*H*Ph), 3.93 (dd, 1H, $J_{2',3'}$ = 3.1 Hz, H-2'), 3.82-3.52 (m, 4H, H-4, 5, 6a, 6b), 3.46 (dd, 1H, $J_{2,3}$ = 9.7 Hz, H-2), 3.25 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.7, 165.7, 138.4, 138.3, 137.9 (x2), 137.8, 135.4, 133.2, 129.9 (x2), 128.6 (x2), 128.5 (x6), 128.4 (x2), 128.3 (x3), 128.2 (x5), 128.0 (x2), 127.8 (x4), 127.6, 127.5 (x3), 127.4 (x3), 126.8 (x2), 99.0 ($^1J_{C1',H1'}$ = 171.0 Hz, C-1'), 98.1 ($^1J_{C1,H1}$ = 173.1 Hz, C-1), 78.9, 78.8, 78.2, 76.3, 75.2, 74.4, 74.2, 73.6, 73.5, 73.4, 72.6, 72.0, 69.8, 68.5, 67.0, 55.2 ppm; HR-FAB MS $[M+H]^+$ calcd for $C_{62}H_{62}O_{13}Na^+$ 1037.4088; found 1037.4106.

Methyl 3-*O*-(2,4-di-*O*-benzyl-α/β-D-mannopyranosid-urono-6,3-lactone)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (19). The title compound was obtained as a colorless amorphous solid from glycosyl donor **2** and acceptor **9**[47] in 26% yield (α/β = 1:2.8, 50 mM) under regular dilution reaction conditions. Analytical data for **19**: R_f = 0.45 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33-7.21 (m, 25H, aromatic), 5.67 (d, 1H, $J_{1',2'}$ = 5.3 Hz, H-1'), 4.96 (d, 1H, ^2J = 10.9 Hz, C*H*Ph), 4.76 (br s, 1H, C*H*Ph), 4.73-4.62 (m, 4H, H-3', 3 x C*H*Ph), 4.57 (m, 2H, CH_2Ph), 4.51 (m, 1H, C*H*Ph), 4.48-4.42 (m, 3H, $J_{1,2}$ = 3.8 Hz, H-1, CH_2Ph), 4.14-4.02 (m, 3H, $J_{4',5'}$ = 2.3 Hz, H-2', 3, 4'), 3.94 (d, 1H, H-5'), 3.67 (m, 4H, H-4, 5, 6a, 6b), 3.51 (dd, 1H, $J_{2,3}$ = 9.3 Hz, H-2), 3.30 (s, 3H, OCH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.9, 139.0 (x2), 137.9, 137.8, 136.5, 129.9, 128.8 (x2), 128.6 (x2), 128.5 (x7), 128.3 (x2), 128.2 (x2), 128.1 (x2), 128.0 (x3), 127.8 (x2), 127.7, 127.4, 100.5 ($^1J_{C1',H1'}$ = 160.0 Hz, C-1'), 98.4 ($^1J_{C1,H1}$ = 175.2 Hz, C-1), 83.4, 77.8, 77.4, 76.4, 73.8, 73.7, 73.2, 71.9, 71.5 (x2), 69.8, 69.7, 68.8, 68.2, 55.1 ppm; HR-FAB MS $[M+H]^+$ calcd for $C_{48}H_{50}O_{11}Na^+$ 825.3251; found 825.3274.

Methyl 2-*O*-(benzyl 2,4-di-*O*-benzyl-3-*O*-picoloyl-α/β-D-mannopyranosyluronate)-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (20). The title compound was obtained as a colorless amorphous solid from glycosyl donor **5** and acceptor **10**[47] in 88% yield (α/β = 1/24, 50 mM) or 92% yield (α/β = 1/25, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **20**: R_f = 0.48 (ethyl acetate/toluene, 3/7, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.83 (m, 1H, aromatic), 7.98 (m, 1H, aromatic), 7.82 (m, 1H, aromatic), 7.51 (m, 1H, aromatic), 7.37-7.02 (m, 30H, aromatic), 5.31-5.15 (m, 2H, CH_2Ph), 5.03 (dd, 1H, $J_{3',4'}$ = 9.9 Hz, H-3'), 4.97-4.80 (m, 5H, H-1, 1', 3 x C*H*Ph), 4.70 (m, 3H, 3 x C*H*Ph), 4.58-4.43 (m, 5H, $J_{4',5'}$ = 9.7 Hz, H-4', 2 x CH_2Ph), 4.01 (m, 2H, $J_{2',3'}$ = 3.2 Hz, H-2', 3), 3.91 (d, 1H, H-5'), 3.82-3.66 (m, 5H, H-2, 4, 5, 6a, 6b), 3.38 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.9, 163.9, 150.3, 147.7, 138.3 (x2), 138.2, 138.1, 137.8, 137.0, 135.3, 128.9 (x3), 128.7 (x3), 128.5 (x4), 128.3 (x3), 128.2 (x3), 128.1 (x5), 127.9 (x6), 127.8, 127.7, 127.5, 127.1, 125.4, 102.6 ($^1J_{C1',H1'}$ = 160.0 Hz, C-1'), 99.8 ($^1J_{C1,H1}$ = 171.0 Hz, C-1), 82.1, 78.9, 78.4, 76.4, 76.1, 75.1 (x2), 75.0, 74.4 (x3), 73.7, 70.3, 68.6, 67.4, 55.4 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{61}H_{61}NO_{13}Na^+$ 1038.4041; found 1038.4053.

Methyl 2-*O*-(benzyl 3-*O*-benzoyl-2,4-di-*O*-benzyl-α-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 **10**[47] in 92% yield (α/β > 25/1, 50 mM) and 91% (α/β > 25/1, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **21**: R_f = 0.65 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 (m, 2H, aromatic), 7.58 (m, 1H, aromatic), 7.47-7.00 (m, 32H, aromatic), 5.63 (dd, 1H, $J_{3',4'}$ = 8.0 Hz, H-3'), 5.16 (d, 1H, $J_{1',2'}$ = 3.1 Hz, H-1'), 5.03 (m, 3H, 3 x C*H*Ph), 4.89-4.38 (m, 11H, H-1, 5', 9 x C*H*Ph), 4.36 (dd, 1H, $J_{4',5'}$ = 7.8 Hz, H-4'), 4.13-3.87 (m, 3H, $J_{2',3'}$ = 3.1 Hz, H-2, 2', 3), 3.83-3.56 (m, 4H, H-4, 5, 6a, 6b), 3.30 (s, 3H, OCH_3) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.2, 165.5, 138.5, 138.4, 138.1, 137.9, 137.8, 135.3, 133.4, 129.9 (x2), 129.7, 128.6 (x5), 128.5 (x2), 128.4 (x3), 128.3 (x2), 128.2 (x3), 128.0 (x3), 127.9 (x3), 127.8 (x4), 127.7 (x3), 127.6 (x2), 127.4 (x2), 96.8 ($^1J_{C1',H1'}$ = 173.0 Hz, C-1'), 95.9 ($^1J_{C1,H1}$ = 173.1 Hz, C-1), 80.8, 77.7, 76.1, 76.0, 75.1, 75.0, 74.9, 74.0, 73.6, 73.4, 72.8, 72.2, 70.3, 68.7, 67.1, 55.1 ppm; HR-FAB MS $[M+H]^+$ calcd for $C_{62}H_{62}O_{13}Na^+$ 1037.4088; found 1037.4099.

Methyl 2-*O*-(2,4-di-*O*-benzyl-α/β-D-mannopyranosid-urono-6,3-lactone)-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside (22). The title compound was obtained as a colorless amorphous solid from glycosyl donor **2** and acceptor **10**[47] in 44% yield (α/β = 1/4.0) under regular concentration (50 mM). Analytical data for **22**: R_f = 0.65 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34-7.09 (m, 25H, aromatic), 5.50 (d, 1H, $J_{1',2'}$ = 5.2 Hz, H-1'), 4.90 (m, 3H, ^2J = 12.4 Hz, $J_{1,2}$ = 2.3 Hz, H-1, CH_2Ph), 4.69 (d, 1H, ^2J = 10.3 Hz, C*H*Ph), 4.63-4.43 (m, 7H, H-3', 3 x CH_2Ph), 4.28 (d, 1H, ^2J = 12.4 Hz, C*H*Ph), 4.10-3.99 (m, 3H, H-2', 3, 4'), 3.91 (d, 1H, $J_{4',5'}$ = 2.5 Hz, H-5'), 3.85-3.80 (m, 1H, H-2), 3.77-3.66 (m, 4H, H-4, 5, 6a, 6b), 3.40 (s, 3H, OCH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.4, 139.4, 138.2, 138.1, 137.2, 136.3, 128.9 (x2), 128.6 (x2), 128.5 (x4), 128.4 (x4), 128.2 (x2), 128.1 (x4), 127.9 (x2), 127.8, 127.7, 127.1, 126.7 (x2), 100.4 ($^1J_{C1',H1'}$ = 160.0 Hz, C-1'), 98.8 ($^1J_{C1,H1}$ = 175.2 Hz, C-1), 81.3, 78.9, 78.6, 77.0, 76.3, 75.0, 74.5, 73.6, 72.1, 71.5, 70.3, 70.0, 68.5, 68.1, 55.0 ppm; HR-FAB MS $[M+H]^+$ calcd for $C_{48}H_{50}O_{11}Na^+$ 825.3251; found 825.3276.

Methyl 2-*O*-benzyl-3-*O*-(benzyl 2,4-di-*O*-benzyl-3-*O*-picoloyl-α/β-D-mannopyranosyluronate)-4,6-*O*-benzylidene-α-D-glucopyranoside (26). The title compound was obtained as a colorless amorphous solid from glycosyl donor **5** and acceptor **23**[47,57,58] in 62% yield (α/β = 1/1.3, 50 mM) or 56% yield (α/β = 1/1.9, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for α/β-**26**: R_f = 0.40 (ethyl acetate/toluene, 3/7, v/v); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (m, 1H, aromatic), 7.92-7.88 (m, 1H, aromatic), 7.79-7.74 (m, 1H, aromatic), 7.53-6.82 (m, 26H, aromatic), 5.19-5.03 (m, 3H, H-1', 3', C*H*Ph), 4.94 (d, 1H, C*H*Ph), 4.70-4.32 (m, 9H, H-1, 4', 5', 3x CH_2Ph), 4.27-4.18 (m, 2H, H-3, 6a), 4.16 (dd, 1H, $J_{1',2'}$ = 2.9

Hz, H-2'), 3.87-3.77 (m, 2H, H-5, C*H*Ph), 3.69-3.48 (m, 3H, H-2, 4, 6b), 3.35 (s, 3H, OCH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 168.0, 164.1, 163.9, 150.2, 150.1, 147.8, 147.5, 138.5, 138.1, 137.9, 137.8, 137.7 (x2), 137.4, 137.3, 137.0, 135.5, 135.3, 129.4, 128.9, 128.8 (x4), 128.6 (x3), 128.5 (x2), 128.4 (x3), 128.3 (x2), 128.2 (x4), 128.1 (x2), 128.0 (x2), 127.8 (x2), 127.7 (x2), 127.6, 127.4 (x2), 127.1, 126.3, 126.2 (x2), 125.4, 102.0, 101.6, 101.1, 99.0, 98.5, 98.4, 82.4, 80.1, 79.6, 77.4, 76.6, 75.4, 75.1, 74.9, 74.8, 74.7, 74.3, 73.7, 71.7, 69.0, 67.3, 67.1, 62.4, 61.9, 55.4 (x2) ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{54}H_{53}NO_{13}Na^+$ 946.3415; found 946.3429.

3-*O*-(Benzyl 2,4-di-*O*-benzyl-3-*O*-picoloyl-α/β-D-mannopyranosyluronate)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (27). The title compound was obtained as a colorless amorphous solid from glycosyl donor **5** and commercial acceptor **24** in 59% yield (α/β = 1/3.4, 50 mM) or 65% yield (α/β = 1/5, 5.0 mM) under regular and high dilution reaction conditions, respectively. Analytical data for **27**: R_f = 0.35 (ethyl acetate/toluene, 3/7, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.79 (m, 1H, aromatic), 7.88 (m, 1H, aromatic), 7.78 (m, 1H, aromatic), 7.50 (m, 1H, aromatic), 7.36-7.03 (m, 15H, aromatic), 5.94 (dd, 1H, $J_{1,2}$ =3.7 Hz, H-1), 5.28-5.15 (m, 2H, CH_2Ph), 5.11 (dd, 1H, $J_{3',4'}$ = 9.8 Hz, H-3'), 4.84 (d, 1H, ^2J = 12.2 Hz, C*H*Ph), 4.77 (s, 1H, H-1'), 4.69 (d, 1H, ^2J = 10.8 Hz, C*H*Ph), 4.59-4.44 (m, 5H, H-2, 4', 5', 2 x C*H*Ph), 4.33 (m, 2H, H-3, 6a), 4.17-3.95 (m, 4H, $J_{2',3'}$ = 3.1 Hz, H-2', 4, 5, 6b), 1.41 (3 s, 12H, 2 x CMe_2) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.6, 164.1, 150.2, 147.3, 137.7 (x2), 137.0, 135.2, 128.7 (x4), 128.6, 128.5 (x2), 128.3 (x2), 128.2 (x2), 127.9 (x2), 127.8 (x2), 127.2, 125.4, 112.1, 111.9, 109.7, 108.7, 105.4, 105.1, 100.1, 85.2, 83.0, 81.7, 80.5, 76.4, 75.3, 75.2, 74.9, 74.6, 74.0, 73.3, 67.5, 66.1, 27.0, 26.9, 26.8, 26.7, 26.4, 25.3 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{45}H_{49}NO_{13}Na^+$ 834.3102; found 834.3110.

Synthesis of Mannuronans

Benzyl *O*-(benzyl 2,4-di-*O*-benzyl-3-*O*-picoloyl-β-D-mannopyranosyluronate)-(1→3)-(benzyl 2,4-di-*O*-benzyl-α-D-mannopyranosid)uronate (28). A mixture containing mannosyl donor **5** (47 mg, 0.077 mmol), mannosyl acceptor **25** (39 mg, 0.070 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 (35 mg, 0.154 mmol) and TfOH (3.0 μL, 0.031 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 – toluene gradient elution) to obtain the title compound as a colorless syrup in 83% yield (α/β = 1/18). For the purpose of the glycan synthesis, the mixture was subjected to second purification by column chromatography to afford pure β-anomer of **28**. Analytical data for **28**: R_f = 0.45 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.79 (m, 1H, aromatic), 7.90 (m, 1H, aromatic), 7.77 (m, 1H, aromatic), 7.52-7.44 (m, 1H, aromatic), 7.76-6.86 (m, 35H, aromatic), 5.29-5.00 (m, 6H, $J_{1,2}$ = 3.4 Hz, H-1, 3', 2 x CH_2Ph), 4.86-4.39 (m, 12H, $J_{4',5'}$ = 9.7 Hz, H-1', 4', 5, 9 x C*H*Ph), 4.28 (dd, 1H, $J_{4,5}$ = 6.8 Hz, H-4), 4.15-4.03 (m, 2H, H-3, C*H*Ph), 4.03 (dd, 1H, $J_{2',3'}$ = 2.9 Hz, H-2'), 3.86 (d, 1H, H-5'), 3.75 (dd, 1H, H-2) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.3, 167.8, 163.8, 150.1, 147.4, 138.1, 137.9 (x2), 137.8, 137.1, 136.9, 135.7, 135.2, 128.7 (x2), 128.6 (x8), 128.5 (x6), 128.3 (x7), 128.1, 128.0 (x2), 127.9 (x2), 127.8 (x2), 127.7 (x2), 127.4, 127.1, 125.4, 100.6 ($^1J_{C1',H1'}$ = 159.0 Hz, C-1'), 96.9 ($^1J_{C1,H1}$ = 171.3 Hz, C-1), 78.1, 76.1, 75.1, 75.0, 74.7, 74.5, 74.2, 74.0, 73.9, 72.8, 72.5, 70.0, 67.3, 67.1, 60.5, 21.2, 14.3 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{67}H_{63}NO_{14}Na^+$ 1128.4146; found 1128.4163.

Benzyl *O*-(benzyl 2,4-di-*O*-benzyl-β-D-mannopyranosyluronate)-(1→3)-(benzyl 2,4-di-*O*-benzyl-α-D-mannopyranosid)uronate (29). $FeCl_3$ (1.0 mg, 0.006 mmol) was added to a solution of compound **28** (21 mg, 0.019 mmol) in CH_2Cl_2/MeOH (1.0 mL, 1/9, v/v) and the resulting mixture was stirred for 10 min at rt. The volatiles were removed under reduced pressure. The residue 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 83% yield (15 mg, 0.015 mmol). Analytical data for **29**: R_f = 0.60 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34-7.15 (m, 35H, aromatic), 5.26-5.22 (m, 2H, H-1, C*H*Ph), 5.16-5.03 (m, 3H, 3 x C*H*Ph), 4.93 (d, 1H, ^2J = 11.9 Hz, C*H*Ph), 4.86-4.40 (m, 11H, $J_{1',2'}$ = 2.1 Hz, H-1', 5, 9 x C*H*Ph), 4.28 (dd, 1H, H-4), 4.17 (dd, 1H, $J_{3,4}$ = 6.3 Hz, H-3), 3.92 (dd, 1H, $J_{4',5'}$ = 8.6 Hz, H-4'), 3.79-3.76 (m, 2H, $J_{2,3}$ = 3.1 Hz, H-2, 5'), 3.63-3.51 (m, 2H, $J_{2',3'}$ = 3.6 Hz, $J_{3',4'}$ = 8.9 Hz, H-2', 3'), 2.47 (d, 1H, J = 9.6 Hz, OH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.5, 168.4, 138.1 (x3), 137.2, 135.6, 135.3, 128.6 (x6), 128.5 (x9), 128.4 (x4), 128.3 (x7), 128.2 (x2), 128.0 (x5), 127.9, 127.8, 127.7, 100.9, 97.0, 77.8, 77.7, 76.4 (x2), 74.7, 74.6, 74.5, 73.8, 73.1, 72.8, 72.7, 70.1, 67.2 (x2), 60.5 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{61}H_{60}O_{13}Na^+$ 1023.3932; found 1023.3951.

Benzyl *O*-(benzyl 2,4-di-*O*-benzyl-3-*O*-picoloyl-α/β-D-mannopyranosyluronate)-(1→3)-*O*-(benzyl 2,4-di-*O*-benzyl-β-D-mannopyranosyluronate)-(1→3)-(benzyl 2,4-di-*O*-benzyl-α-D-mannopyranosid)uronate (30). A mixture containing mannosyl donor **5** (22 mg, 0.036 mmol), disaccharide acceptor **29** (33 mg, 0.033 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 (16 mg, 0.072 mmol) and TfOH (1.3 μL, 0.014 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 – toluene gradient elution) to obtain the title compound as a colorless syrup in 52% yield (14 mg, 0.010 mmol, α/β = 1/4.0). Analytical data for **30**: R_f = 0.60 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.80 (m, 1H, aromatic), 7.90 (m, 1H, aromatic), 7.77-7.75 (m, 1H, aromatic), 7.47 (m, 1H, aromatic), 7.36-6.89 (m, 50H, aromatic), 5.30 (d, 1H, $J_{1,2}$ = 4.7 Hz, H-1), 5.24 (d, 1H, ^2J = 12.3 Hz, C*H*Ph), 5.12-4.98 (m, 6H, H-3'', 5 x C*H*Ph), 4.89-4.77 (m, 4H, 2 x CH_2Ph), 4.69-4.16 (m, 18H, H-1', 1'', 2', 3', 4, 4', 4'', 5, 5 x CH_2Ph), 4.03 (m, 1H, H-3), 3.83-3.68 (m, 4H, H-2, 2'', 5', 5'') ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.3, 168.2, 167.7, 163.8, 150.2, 147.4, 138.4, 138.2, 138.1, 137.9 (x2), 137.8, 137.3, 137.0, 135.8, 135.4, 135.1, 129.2, 128.8 (x2), 128.7 (x8), 128.6 (x7), 128.5 (x6), 128.4 (x6), 128.3 (x9), 128.2 (x2), 128.1, 128.0 (x6), 127.9 (x2), 127.8 (x2), 127.6 (x2), 127.5, 125.4 (x2), 102.0 ($^1J_{C1',H1'}$ = 159.2 Hz, C-1'), 97.6 ($^1J_{C1'',H1''}$ = 163.3 Hz, C-1''), 96.9 ($^1J_{C1,H1}$ = 170.1 Hz, C-1), 78.6, 78.2, 77.4, 76.1, 75.2, 75.1, 74.9, 74.6, 74.4, 74.2, 73.7, 72.9, 72.0, 70.2, 67.4, 67.2, 67.1 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{94}H_{89}NO_{20}Na^+$ 1575.5909; found 1575.5932.

Benzyl *O*-(benzyl 2,4-di-*O*-benzyl-α/β-D-mannopyranosyluronate)-(1→3)-*O*-(benzyl 2,4-di-*O*-benzyl-β-D-mannopyranosyluronate)-(1→3)-(benzyl 2,4-di-*O*-benzyl-α-D-mannopyranosid)uronate (31). $FeCl_3$ (0.4 mg, 0.003 mmol) was added to a solution of compound **30** (14 mg, 0.01 mmol) in CH_2Cl_2/MeOH (1 mL, 1/9, v/v) and the resulting mixture was stirred for 15 min at rt. The volatiles were removed under reduced pressure. The residue 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 95% yield (13 mg, 0.01 mmol). Analytical data for **31**: R_f = 0.60 (ethyl acetate/hexane, 2/3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37-7.10 (m, 50H, aromatic), 5.31-3.85 (m, 28H, H-1, 1', 1'', 3, 4, 4', 4'', 5, 10 x CH_2Ph), 3.79-3.63 (m, 5H, H-2, 2', 3', 5', 5''), 3.43-3.33 (m, 2H, H-2'', 3''), 2.33 (d, 1H, *J* = 10.1 Hz, OH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.4, 168.2, 168.1, 138.3, 138.2 (x3), 138.1 (x2), 137.3, 135.7, 135.3, 135.2, 128.8 (x2), 128.7 (x5), 128.6 (x13), 128.5 (x4), 128.4 (x6), 128.3 (x5), 128.1 (x2), 128.0 (x3), 127.9 (x4), 127.8 (x2), 127.7 (x2), 127.3, 127.0, 102.0, 98.1, 96.8, 78.6, 78.2, 77.8, 77.4, 75.2, 75.1, 75.0 (x2), 74.9, 74.6 (x2), 74.4, 73.7, 73.4, 72.9, 72.8, 72.4, 72.3, 70.2, 67.3 (x2), 67.1 ppm. HR-FAB MS $[M+Na]^+$ calcd for $C_{88}H_{86}O_{19}Na^+$ 1469.5661; found 1469.5680.

Benzyl *O*-(benzyl 2,4-di-*O*-benzyl-3-*O*-picoloyl-β-D-mannopyranosyluronate)-(1→3)-*O*-(benzyl 2,4-di-*O*-benzyl-α/β-D-mannopyranosyluronate)-(1→3)-*O*-(benzyl 2,4-di-*O*-benzyl-β-D-mannopyranosyluronate)-(1→3)-(benzyl 2,4-di-*O*-benzyl-α-D-mannopyranosid) uronate (32). A mixture containing mannosyl donor **5** (153 mg, 0.249 mmol), disaccharide acceptor **31** (55 mg, 0.038 mmol), and molec. sieves (4 Å, 450 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 (370 mg, 1.646 mmol) and TfOH (14.6 µL, 0.164 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 – toluene gradient elution) to obtain the title compound as a colorless syrup in 41% yield (31 mg, 0.015 mmol). Analytical data for **32**: R_f = 0.55 (ethyl acetate/toluene, 1/4, v/v); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.80 (m, 1H, aromatic), 7.92 (m, 1H, aromatic), 7.77 (m, 1H, aromatic), 7.47 (m, 1H, aromatic), 7.35-6.79 (m, 65H, aromatic), 5.29-4.96 (m, 12H, H-1, 1', 5 x CH_2Ph), 4.90-4.54 (m, 12H, H-1''', 3', 3''', 9 x C*H*Ph), 4.51-4.33 (m, 7H, H-2''', 4''', 5, 2 x CH_2Ph), 4.29-4.17 (m, 4H, H-4, 3 x C*H*Ph), 4.02-3.85 (m, 4H, H-1'', 2', 3, 4'), 3.80-3.61 (m, 6H, H-2, 3'', 4'', 5', 5'', 5'''), 3.50 (dd, 1H, $J_{1'',2''}$ = 2.9 Hz, H-2'') ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.4, 168.2, 168.0, 167.7, 163.8, 150.3, 147.5, 138.4, 138.3, 138.2, 138.1, 137.9 (x2), 137.8, 137.6, 137.3, 137.0, 135.8, 135.4, 135.3, 135.1, 129.2, 128.9, 128.8, 128.7 (x6), 128.6 (x20), 128.5 (x3), 128.4 (x4), 128.3 (x8), 128.2 (x2), 128.1 (x4), 128.0 (x5), 127.9 (x5), 127.8 (x2), 127.7, 127.6, 127.5, 126.9, 125.4, 102.0 ($^1J_{C1',H1'}$ = 159.2 Hz, C-1'), 97.9 ($^1J_{C1''',H1'''}$ = 159.2 Hz, C-1'''), 97.9 ($^1J_{C1'',H1''}$ = 163.3 Hz, C-1''), 96.9 ($^1J_{C1,H1}$ = 170.1 Hz, C-1), 78.5, 78.3, 77.9, 77.4, 76.1, 75.3, 75.2, 75.1 (x2), 74.9, 74.8 (x2), 74.6, 74.5 (x2), 74.4, 74.2, 74.1, 73.7, 72.9 (x2), 72.8, 72.7, 72.3, 70.2, 67.5, 67.3, 67.2, 67.1 ppm; HR-FAB MS $[M+Na]^+$ calcd for $C_{121}H_{115}NO_{26}Na^+$ 2021.7639; found 2021.7686.

Conflicts of interest

There are no conflicts to declare.

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