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Stereoselectivity of glycosylations of conformationally restricted mannuronate esters

Jeroen D.C. Codée *, Ana R. de Jong, Jasper Dinkelaar, Herman S. Overkleeft, Gijsbert A. van der Marel *

Leiden Institute of Chemistry, Leiden University, PO Box 9502, 2300 RA Leiden, The Netherlands

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ABSTRACT

Glycosidation of conformationally unrestricted mannuronate ester donors proceeds in a highly β-selective fashion, whereas condensations of mannuronate ester donors, which are conformationally constrained by a 3,4-butanedimethylacetal or a 2,3-isopropylidene function, provide α-selective products. We hypothesize that the difference in stereochemical outcome of these condensations results from the different conformations of the product forming oxacarbenium intermediate. The formation of the β-linked products from the flexible mannuronates is thought to originate from the most favorable $^{3}H_{4}$ oxacarbenium ion, which is not accessible from the conformationally restrained donors. Although an α-triflate intermediate is formed upon activation of the 3,4-butanedimethylacetal protected mannuronate ester thio donor, this is not the product forming intermediate. The anomeric triflate serves as a reservoir for the $^{4}H_{3}$ oxacarbenium ion, which is glycosidated to provide the α-linked mannuronates.

1. Introduction

Recently we reported that glycosidations of mannuronate esters proceed in a highly stereoselective fashion to provide the 1,2-cis linked products.[1,2] This stereochemical outcome stands in contrast to the common perception that mannopyranoside donors are generally α-selective,[3] and that the β-mannosidic linkage is one of the most difficult glycosidic linkages to construct.[4] The stereoselectivity of the mannuronate esters in glycosylations was found to be independent of the type and anomeric configuration of the donor used, and did not rely on the activation protocol employed.[2] Nucleophiles of varying nature and reactivity all provided the β-linked adducts. We have postulated that the counterintuitive selectivity of the mannuronate esters originates from the oxacarbenium ion intermediate **4b** (Scheme 1), having a $^{3}H_{4}$ conformation. The intermediate oxacarbenium ion prefers to adopt this configuration because in this constellation all substituents on the mannose core adopt their preferred orientation:[5] the C2-alkoxy is equatorial, and the alkoxy groups at C3 and C4 and the carboxylate ester at C5 are positioned in an axial fashion.[6,7] The axial orientation of the latter three substituents allows the through space stabilization of the positive charge of the oxacarbenium ion, which is impossible in the alternative $^{4}H_{3}$ half chair conformer.[6,8] Nucleophilic attack on oxacarbenium ion **4b** occurs in a *pseudo* axial fashion to allow the formation of the lower energy chair product, as opposed to a twist boat adduct, which would result from α-attack on **4b**.[9]

This mechanistic rationale requires that, upon activation, mannuronate ester **1** undergoes a conformational change from its ground state $^{4}C_{1}$ chair to reach the $^{3}H_{4}$ half chair intermediate **4b**.[10] We were therefore interested to find out to what extent the stereoselectivity of mannuronate ester **1** is influenced by restriction of its conformational freedom. We here describe the glycosylation properties of conformationally restricted[11] mannuronates **7** and **8** (Fig. 1), and show that locking of the oxacarbenium ion in the $^{4}H_{3}$ conformation reverses the stereoselectivity, leading to the stereoselective formation of α-mannuronic acid bond.[12]

2. Results and discussion

To explore the influence of conformational constraints on the stereoselectivity of mannuronate ester **1** we investigated the glycosylation behavior of the set of mannuronate donors **6**–**8**, which were synthesized from β-*S*-phenyl mannoside **13**[13,14] as depicted in Scheme 2. Donor **6** was synthesized from **13** as reported previously.[2] Mannuronate (**7**) was prepared by first locking the C3- and C4-hydroxyls in a butanedimethylacetal (BDA) function.[15] Next, the C6-alcohol was liberated following a silylation–benzylation–desilylation sequence to give mannoside **15**. The primary alcohol was transformed into methyl ester **7** using 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and bis(acetoxy)iodobenzene (BAIB) and ensuing methylation of the intermediate uronic acid.[16] Mannuronate (**8**) was synthesized by selective silylation of the primary alcohol in **13**, followed by installation of the 2,3-*O*-isopropylidene

* Corresponding authors.
E-mail addresses: jcodee@chem.leidenuniv.nl (J.D.C. Codée), marel_g@chem.leidenuniv.nl (G.A. van der Marel).

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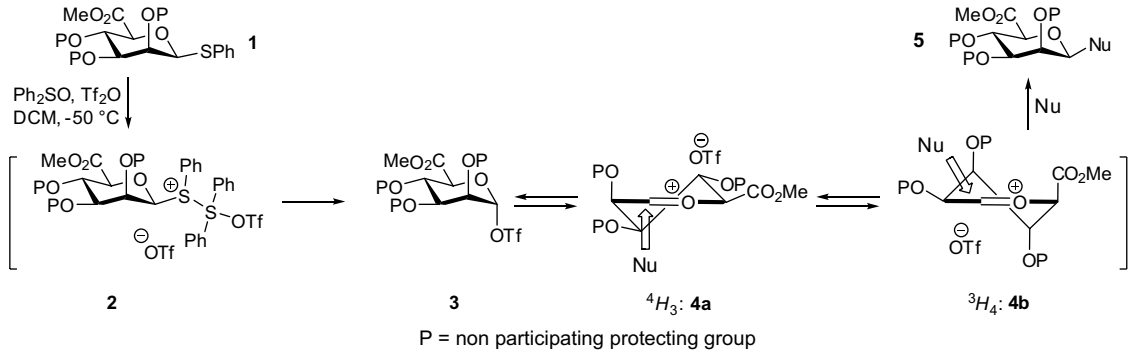


Scheme 1. Intermediates in the glycosylation of mannuronate ester **1**.

moiety. Benzylation and desilylation released the primary alcohol, which was oxidized and esterified to give fully protected **8**.

The glycosylation behavior of mannuronate esters **6**–**8** was assessed in the diphenylsulfoxide (Ph_2SO)–triflic anhydride (Tf_2O) mediated condensations[17] using a set of four acceptors (**9**–**12**, Fig. 1). To detect possible (triflate) intermediates, the pre-activation step of mannuronates **6**, **8**, and **9** by the sulfonium triflate activator was monitored by NMR spectroscopy,[18] and a different behavior for the three thioglycosides was observed. Addition of Tf_2O to a mixture of **6**, Ph_2SO, and tri-*tert*-butylpyrimidine (TTBP) in CD_2Cl_2 at −50 °C led to a complex mixture of products as revealed by the appearance of several sets of resonances in the ^1H NMR spectrum. The species did not converge into a single product on time or upon gradual warming of the probe. In contrast, BDA-locked mannuronate **7** was instantaneously transformed into a single new species (Fig. 2). Based on the singlet at δ=5.95 ppm in the ^1H NMR spectrum, and the signal at δ=105.2 ppm in the ^{13}C NMR spectrum, having a heteronuclear coupling constant (J_{C1-H1}=176 Hz) indicative of an axially oriented substituent, we determined this product to be α-triflate **7a**. This triflate proved to be stable up to −10 °C.[19] Interestingly, the non-oxidized counterpart of **7a**, 2,6-di-*O*-benzyl-3,4-BDA-α-mannopyranyl triflate, has previously been shown by Crich and co-workers to be stable up to +5 °C.[20] The presence of the C-5 carboxylate apparently does not contribute favorably to the stability of the anomeric triflate intermediate, as would be expected based on its electron withdrawing properties. Analogous to unrestricted mannuronate **6**, activation of isopropylidene mannuronate **8** led to a complex NMR spectrum, with several apparent anomeric resonances. Again no single species evolved in time and upon warming.

The results of the condensations of donors **6**, **7**, and **8** with acceptors **9**–**12** are summarized in Table 1. The flexible mannuronate **6** reliably provides the β-linked products, whereas 3,4-BDA-mannoside **7** and 2,3-*O*-isopropylidene mannuronate **8** preferentially form the α-linked products. Based on the fact that no single triflate intermediate could be detected upon activation of mannuronate donor **6**, and that the conformational freedom of this mannoside readily allows flattening of the ring, we have postulated that the oxacarbenium ion intermediate is at the basis for the β-selectivity of **6**. As described above the oxacarbenium ion preferentially takes up the $^3H_4$ half chair conformation, which is substituted from the β-face leading to the 1,2-cis products.[21] This postulate is further supported by the results obtained with the conformationally constrained BDA-donor **7**. In this case a single α-anomeric triflate was observed upon activation, but this species obviously is not the source of the α-products **20**–**23**. The α-selectivity of the BDA-donor **8** is likely to arise from the oxacarbenium ion intermediate, approximating the $^4H_3$ half chair conformer (**4a** in Fig. 1). The anomeric triflate thus serves as a reservoir for the solvent separated oxacarbenium ion intermediate, which is attacked by the incoming nucleophile in an axial fashion to provide the α-linked products. When a reactive nucleophile, such as the primary alcohol **9**, is involved in the condensation reaction, direct S_N2-like substitution of the anomeric α-triflate (or tight ion pair) emerges as a competing reaction pathway, leading to the formation of the β-product. It is of interest to note that the 'non-oxidized' congener of **7**, *S*-phenyl-2,6-di-*O*-benzyl-3,4-BDA-mannopyranoside has also been shown to be highly α-selective.[20,22] As already indicated by the decomposition temperature of triflate **7a** and 2,6-di-*O*-benzyl-3,4-BDA-α-mannopyranyl triflate, the electron withdrawing effect of the carboxylate does not make the intermediate triflate more stable and therefore a similar α-selectivity is observed. The conformational constraint of the 2,3-*O*-isopropylidene group in mannuronate **8** is not large enough to allow the formation of a stable single triflate species reservoir. In analogy with the condensations of **6** and **7**, glycosidations of **8** most likely proceed via an oxacarbenium ion intermediate. Because of the ring strain introduced in the system by the 2,3-ketal function,[23] this oxacarbenium ion cannot access the

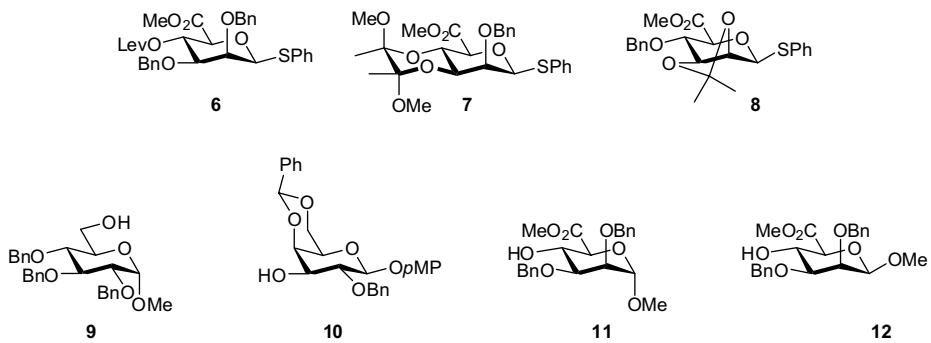
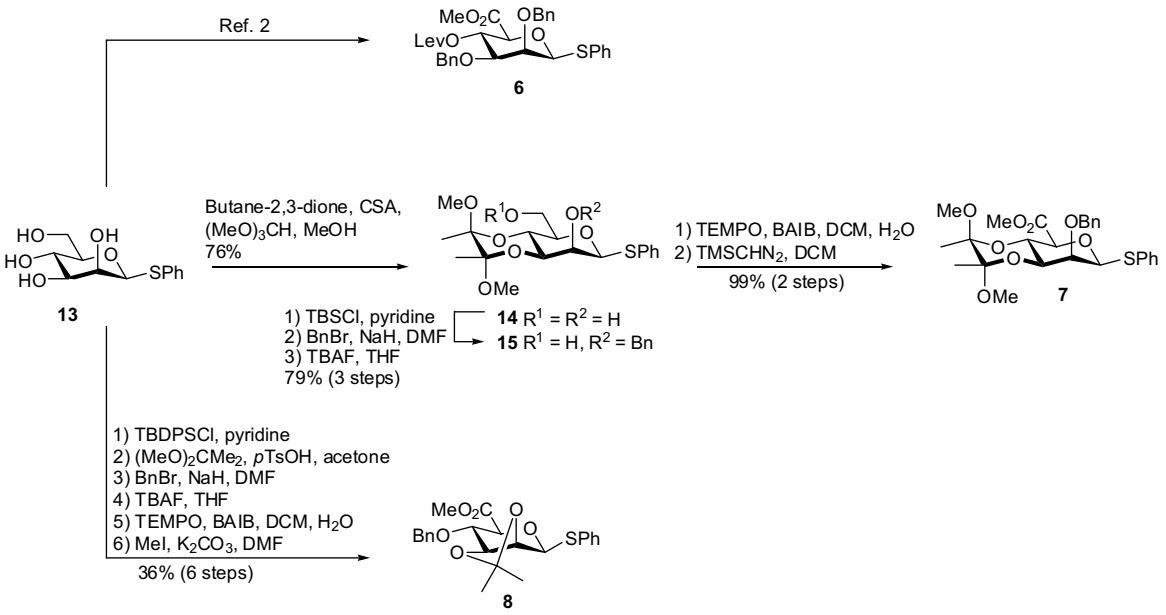


Figure 1. Donors and acceptors used in this study.



Scheme 2. Synthesis of the mannuronate esters.

half chair conformation, and more likely occupies an envelope conformation (^4E or E_4-like). Shielding of the β-face by the *endo*-methyl group of the isopropylidene moiety facilitates nucleophilic attack on the α-face of the mannuronate, leading to the formation of the 1,2-trans products.

Besides the difference in stereoselectivity between the different mannuronate donors, Table 1 also reveals a disparity between the efficiency of the coupling involving α-configured mannuronate acceptor **11** and its anomeric epimer **12**. Although the stereoselectivity of the glycosylations involving these acceptors is comparable, the β-epimer shows a significantly higher yield. A similar difference in reactivity has previously been observed in the glycosylation of the C4–OH of galacturonate ester acceptors and to a lesser extent the C4–OH of glucuronate esters.[24] In acceptors **11** and **12**, the nucleophilicity of the C4–OH is compromised due to the presence of the proximal electron withdrawing carboxylate function. Furthermore the electronegative ring oxygen also withdraws electron density from the C4–OH. Because of the (n→σ*) delocalization of the non-bonding electrons of the ring oxygen into the α-C1–O1 bond the ring oxygen in **11** will be more electron-poor and more electron withdrawing than its counterpart in β-oriented **12**, which lacks this *endo*-anomeric effect. As a consequence the C4–OH in **12** is slightly more nucleophilic than the C4–OH in **11**, leading to improved coupling yields for this anomer.[25]

In conclusion, the stereoselectivity of mannuronate donors has been shown to depend on the nature of the protecting groups on

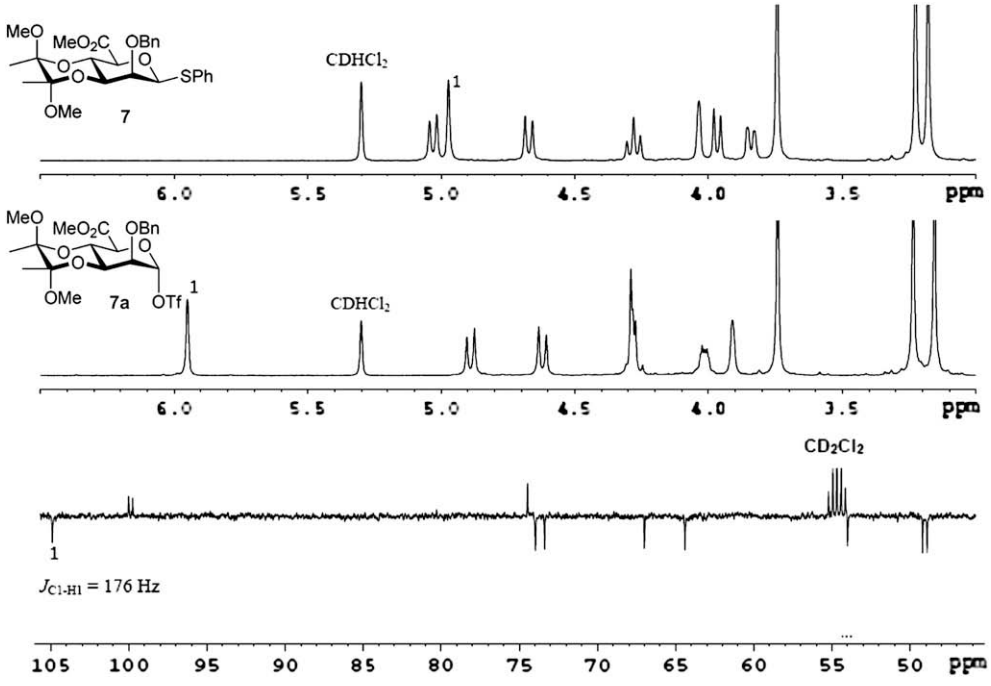
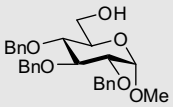
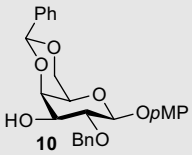
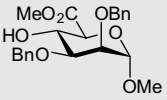
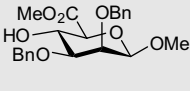
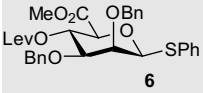
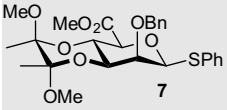
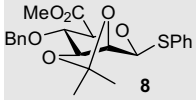


Figure 2. Treatment of mannuronate **7** with Ph_2O and Tf_2O at −50 °C leads to the clean formation of α-triflate **7a**.

Table 1
Condensations of mannuronates **6**, **7**, and **8** with acceptors **9**–**12**[a]

Ph_2SO, Tf_2O, TTBP, DCM, −60 °C to rt, yield (α/β)[a]	 **9**	 **10**	 **11**	 **12**
 **6**	**16**, 93% (0:1)	**17**, 73% (0:1)	**18**, 31% (0:1)	**19**, 55% (0:1)
 **7**	**20**, 56% (2:1)	**21**, 56% (1:0)	**22**, 24% (1:0)	**23**, 49% (3:1)
 **8**	**24**, 67% (5:1)	**25**, 57% (1:0)	**26**, 20% (1:0)	**27**, 50% (1:0)

[a] The stereochemistry of the newly formed mannosidic bonds was assigned based on the value of the $^1J_{C-H}$ coupling constant of H-1′ and C-1′. The isopropylidene function in mannuronates **26** and **27** was hydrolyzed to re-establish the $^4C_1$-conformation of the non-reducing end mannuronate, having a $^1J_{C1'-H1'}$ of 170 Hz for both disaccharides.

the mannose core. The flexible mannuronate donor **6** provides excellent β-selectivity, whereas conformationally constrained systems **7** and **8** lead to the predominant formation of the α-linkage. Although α-triflates have been shown to be intermediates in the condensations of **7**, these triflates have been excluded as product forming intermediates given the α-selectivity of this donor. These results provide support for the postulate that the stereoselectivity of the mannuronate donors originates from the oxacarbenium ion intermediate.

3. Experimental

3.1. General procedure for glycosylations

The mannuronate donor glycoside (1 equiv), Ph_2SO (1.1 equiv), and TTBP (2.5 equiv) were dissolved in DCM (0.05 M) and stirred over molecular sieves 3 Å for $^1/_2$ h. At −60 °C, Tf_2O (1.1 equiv) was added and the resulting mixture was allowed to warm to −45 °C over $^1/_4$ h. Subsequently, the acceptor glycoside (1.5 equiv), dissolved in DCM (0.05 M), was added at −60 °C and the reaction mixture was allowed to warm to rt. The reaction mixture was quenched by addition of Et_3N (5 equiv), diluted, washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. After column chromatography and/or size exclusion chromatography (Sephadex LH-20, eluent: MeOH/DCM 1/1) the corresponding disaccharides were obtained.

3.2. Methyl (phenyl 2-*O*-benzyl-3,4-*O*-[2′,3′-dimethoxybutan-2′,3′-diyl]-1-thio-β-D-mannopyranosyluronate) (7)

Phenyl 2-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutan-2′,3′-diyl)-1-thio-β-D-mannopyranoside **15** (356 mg, 0.75 mmol) was dissolved in DCM (3.7 mL, 0.2 M) and H_2O (1.9 mL), TEMPO (23 mg, 0.15 mmol, 0.2 equiv) and BAIB (515 mg, 1.88 mmol, 2.5 equiv) were added. The resulting mixture was vigorously stirred. After 1 h, TLC analysis showed total conversion into a lower running product and the reaction mixture was quenched by addition of aqueous 10% $Na_2S_2O_3$. The layers were separated and the aqueous layer was extracted with EtOAc (3×). The combined organic phases were dried over $MgSO_4$, filtered, concentrated, and co-evaporated with toluene. The obtained yellow oil was dissolved in DCM (3.7 mL, 0.2 M) and a solution of TMS diazomethane (1.13 mL, 2 M in hexane, 3 equiv) was added. After 5 min, TLC analysis showed conversion into a higher running spot (R_f: 0.78, PE/EtOAc 1/1+1% AcOH) and the reaction was quenched by addition of AcOH (1 mL). Toluene was added and the resulting mixture was concentrated. Column chromatography (PE/EtOAc 19/1 to 17/3) yielded the title compound as a clear oil in 99% yield over two steps (374 mg, 0.74 mmol). $[\alpha]_D$ −3.1 (*c* 0.5, DCM). IR (neat): 733, 849, 887, 934, 1049, 1134, 1211, 1285, 1354, 1377, 1439, 1582, 1751, 2835, 2897, 2951, 2993. ^{1}H NMR (400 MHz): 1.28 (s, 3H, CH_3 BDA), 1.32 (s, 3H, CH_3 BDA), 3.24 (s, 3H, OCH_3 BDA), 3.28 (s, 3H, OCH_3 BDA), 3.78 (s, 3H, CH_3 CO_2Me), 3.81 (dd, 1H, *J*=2.8, 6.0 Hz, H-3), 3.97 (d, 1H, *J*=10.0 Hz, H-5), 4.0 (d, 1H, *J*=0.8 Hz, H-2), 4.51 (t, 1H, *J*=10.0 Hz, H-4), 4.82 (d, 1H, *J*=11.6 Hz, C*H*HPh), 4.87 (s, 1H, H-1), 5.05 (d, 1H, *J*=11.2 Hz, CH*H*Ph), 7.23–7.37 (m, 6H, 6×H_{arom}), 7.46 (d, 2H, *J*=6.8 Hz, 2×H_{arom}), 7.5 (d, 2H, *J*=7.5 Hz, 2×H_{arom}). ^{13}C NMR (100 MHz): 17.6 (CH_3 BDA), 17.7 (CH_3 BDA), 47.8 (OCH_3 BDA), 47.9 (OCH_3 BDA), 52.2 (CH_3 CO_2Me), 64.6 (C-4), 72.3 (C-3), 74.5 (CH_2Ph), 76.7 (C-2), 77.6 (C-5), 89.3 (C-1), 99.7 (C_q BDA), 100.0 (C_q BDA), 127.3–128.9 (CH_{arom}), 135.0 (C_q SPh), 138.1 (C_q Ph), 167.5 (C=O, CO_2Me). ^{13}C GATED NMR (100 MHz): 89.4 ($J_{C\text{-}1,\ H\text{-}1}$=154 Hz). HRMS: $[M+NH_4]^+$ calcd for $C_{26}H_{36}O_8NS$: 522.2156, found 522.2155.

3.3. Methyl (phenyl 4-*O*-benzyl-2,3-*O*-isopropylidene-1-thio-β-D-mannopyranosyluronate) (8)

Phenyl 1-thio-β-D-mannospyranoside **13** (1.0 g, 3.67 mmol) was dissolved in pyridine (18.4 mL, 0.2 M) and TBDPSCl (1.04 mL, 4.04 mmol, 1.1 equiv) was added. After 1 h, TLC analysis (EtOAc/MeOH 9/1) showed total conversion into a higher running spot. The reaction was quenched by addition of MeOH at 0 °C. Water was added and the mixture was extracted with EtOAc (3×). The combined organic layers were dried over $MgSO_4$, filtered, concentrated, and co-evaporated with toluene. The obtained yellow oil was dissolved in acetone (4 mL, 0.92 M), and 2,2-dimethoxypropane (7.7 mL, 62.39 mmol, 17 equiv) and a catalytic amount of pTsOH were added. After 15 min., TLC analysis (PE/EtOAc 1/1) showed total conversion into a higher running spot. The reaction

mixture was neutralized with Et_3N and concentrated. Water was added and the mixture was extracted with $CHCl_3$ (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated, which afforded a yellow oil. The partially protected mannopyranoside was dissolved in DMF (19 mL, 0.2 M) and cooled down to 0 °C. Benzyl bromide (0.52 mL, 4.40 mmol, 1.2 equiv) and NaH (161 mg, 60% dispersion in mineral oil, 4.04 mmol, 1.1 equiv) were added and the reaction mixture was allowed to warm to rt. The mixture turned from yellow to orange to brown to black. After $^1/_2$ h, TLC analysis showed total conversion into a higher running spot. The reaction mixture was quenched with MeOH at 0 °C, diluted with water, and extracted with Et_2O (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. A dark brown residue was obtained, which was dissolved in THF (7.34 mL, 0.5 M) and TBAF (4.04 mL, 1 M in THF, 4.04 mmol, 1.1 equiv) was added. The reaction mixture was stirred overnight and diluted with EtOAc. Water was added, followed by separation of the layers. The aqueous layer was extracted with EtOAc (2×) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated, which gave a yellow oil. The yellow oil was dissolved in DCM (18.4 mL, 0.2 M) and H_2O (9.2 mL), BAIB (2.5 g, 9.18 mmol, 2.5 equiv) and TEMPO (115 mg, 0.73 mmol, 0.2 equiv) were added. After 3 h, TLC analysis (PE/EtOAc 1/1+1% AcOH) showed total conversion into a lower running spot (R_f=0.44) and the reaction mixture was quenched by addition of aqueous $Na_2S_2O_3$ (10%) followed by separation of the layers. The aqueous layer was extracted with EtOAc (3×) and the combined organic layers were dried over $MgSO_4$, filtered, concentrated, and co-evaporated with toluene. A yellow oil was obtained, which was dissolved in DMF (18.4 mL, 0.2 M) and MeI (0.80 mL, 12.85 mmol, 3.5 equiv) and K_2CO_3 (1.52 g, 11.01 mmol, 3 equiv) were added. After $^1/_2$ h, TLC analysis (PE/EtOAc 1/1) showed total conversion into a higher running spot. MeOH and H_2O were added at 0 °C and the mixture was extracted with with Et_2O (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography (PE/EtOAc 1/0 to 8/2) gave the title compound as a yellow oil in 32% yield over six steps (508 mg, 1.18 mmol). $[\alpha]_D$ −62.0 (*c* 3.4, DCM). IR (neat): 737, 802, 833, 872, 957, 1026, 1069, 1219, 1242, 1292, 1381, 1439, 1481, 1585, 1747, 2885, 2936, 2990. ^{1}H NMR (400 MHz): 1.39 (s, 3H, CH_3 isopropylidene), 1.57 (s, 3H, CH_3 isopropylidene), 3.74 (s, 3H, CH_3 CO_2Me), 4.07 (t, 1H, *J*=5.6 Hz, H-4), 4.18 (d, 1H, *J*=6.0 Hz, H-5), 4.38 (t, 1H, *J*=5.6 Hz, H-3), 4.48 (dd, 1H, *J*=6.4, 2.0 Hz, H-2), 4.68 (d, 1H, *J*=11.6 Hz, C*H*HPh), 4.74 (d, 1H, *J*=11.6 Hz, CH*H*Ph), 5.19 (d, 1H, *J*=2.0 Hz, H-1), 7.23–7.31 (m, 8H, 8×H_{arom}), 7.49 (d, 2H, *J*=7.5 Hz, 2×H_{arom}). ^{13}C NMR (100 MHz): 25.9 (CH_3 isopropylidene), 26.9 (CH_3 isopropylidene), 51.4 (CH_3 CO_2Me), 72.8 (CH_2Ph), 75.3 (C-4), 75.4 (C-2), 75.6 (C-5), 76.9 (C-3), 84.5 (C-1), 111.1 (C_q isopropylidene), 127.3–131.2 (CH_{arom}), 135.1 (C_q Ph), 137.4 (C_q Ph), 169.1 (C=O CO_2Me). ^{13}C GATED NMR (125 MHz): 84.6 ($J_{C\text{-}1,\ H\text{-}1}$= 156 Hz). HRMS: $[M+H]^+$ calcd for $C_{23}H_{27}O_6S$: 431.1523, found 431.1521.

3.4. Methyl (methyl 2,3-di-*O*-benzyl-α-D-mannopyranosyluronate) (11)

Methyl 2,3-di-*O*-benzyl-α-D-mannopyranoside (1.34 g, 3.57 mmol) was dissolved in DCM (17.9 mL, 0.2 M) and H_2O (9.0 mL), BAIB (2.45, 8.93 mmol, 2.5 equiv) and TEMPO (111 mg, 0.71 mmol, 0.2 equiv) were added. The resulting orange mixture was vigorously stirred for 2 h at rt. The reaction mixture was quenched with aqueous 10% NaS_2O_3 and the layers were separated. The aqueous layer was extracted with EtOAc (2×) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated, which afforded a yellow oily residue. Column chromatography (1/0 PE/EtOAc, +1% Et_3N to 4/6 PE/EtOAc, +1% Et_3N, then 7/3 PE/EtOAc, +1% AcOH to 1/1 PE/EtOAc, +1% AcOH) gave methyl 2,3-di-*O*-benzyl-α-D-mannopyranosyluronic acid as clear oil. The uronic acid was dissolved in DMF (18 mL, 0.2 M) and MeI (1.11 mL, 17.85 mmol, 5 equiv) and K_2CO_3 (1.48 g, 10.71 mmol, 3 equiv) were added. The resulting mixture was stirred for $^3/_4$ h. TLC analysis showed total conversion into a higher running spot (R_f: 0.78, 1/1 PE/EtOAc, +1% AcOH). The reaction mixture was quenched with MeOH, diluted with EtOAc, and washed with H_2O. The aqueous layer was extracted with EtOAc (2×) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography (9/1 to 7/3 PE/EtOAc) afforded the title compound as a colorless oil in 50% yield over two steps (723 mg, 1.80 mmol). $[\alpha]_D$ +7.7 (*c* 4.4, DCM). IR (neat): 733, 814, 895, 964, 1061, 1130, 1204, 1265, 1358, 1454, 1497, 1747, 2882, 2932. ^{1}H NMR (400 MHz): 2.97 (br s, 1H, C4–OH), 3.80 (s, 3H, CH_3 CO_2Me), 3.73 (m, 2H, H-2, H-3), 3.81 (s, 3H, CH_3 C1–OMe), 4.09 (d, 1H, *J*=9.2 Hz, H-5), 4.30 (t, 1H, *J*=9.2 Hz, H-4), 4.61 (d, 1H, *J*=12 Hz, C*H*HPh), 4.64 (d, 1H, *J*=12 Hz, CH*H*Ph), 4.69 (s, 2H, CH_2Ph), 4.82 (s, 1H, H-1), 7.25–7.35 (m, 10H, 10×H_{arom}). ^{13}C NMR (100 MHz): 52.6 (CH_3 CO_2Me), 55.4 (CH_3 C1–OMe), 68.4 (C-4), 71.6 (C-5), 72.4 (CH_2Ph), 72.9 (CH_2Ph), 74.0 (C-2), 78.5 (C-3), 99.8 (C-1), 127.6–128.4 (CH_{arom}), 138.0 (C_q Ph), 138.2 (C_q Ph), 170.6 (C=O CO_2Me). ^{13}C GATED NMR: 99.8 ($J_{C\text{-}1,\ H\text{-}1}$= 169 Hz). HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_7Na$: 425.1571, found 425.1542.

3.5. Methyl (methyl 2,3-di-*O*-*benzyl*-β-D-mannopyranosyluronate) (12)

Methyl (methyl 2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannopyranosyluronate) was synthesized by coupling of **6** with methanol at −80 °C as described by the general procedure for glycosylations (70% yield, α/β=1/3). This compound (370 mg, 0.74 mmol) was dissolved in pyridine/AcOH (10.6 mL, 4/1, 0.07 M), cooled down to 0 °C, and hydrazine monohydrate (183 μL, 3.77 mmol, 5.1 equiv) was added. After 10 min, TLC analysis showed total conversion into a slightly higher running spot (R_f: 0.34, 1/1 PE/EtOAc). The reaction mixture was quenched with acetone, diluted, washed with aqueous 2 M HCl, satutated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. Column chromatography (9/1 PE/EtOAc to 6/4 PE/EtOAc) gave the title product as an amorphous white solid in 89% yield (264 mg, 0.66 mmol). $[\alpha]_D$ −134.8 (*c* 1.2, DCM). IR (neat): 737, 799, 860, 882, 914, 980, 1026, 1061, 1173, 1207, 1242, 1285, 1362, 1454, 1497, 1747, 2889, 3441. ^{1}H NMR (400 MHz): 3.07 (br s, 1H, C4–OH), 3.34 (dd, 1H, *J*=9.6, 3.2 Hz, H-3), 3.54 (s, 3H, CH_3 CO_2Me), 3.76–3.78 (m, 4H, CH_3 C1–OMe, H-5), 3.86 (d, 1H, *J*=2.8 Hz, H-2), 4.29 (t, 1H, *J*=9.6 Hz, H-4), 4.33 (s, 1H, H-1), 4.46 (d, 1H, *J*=12.0 Hz, CH*H*Ph), 4.52 (d, 1H, *J*=12.0 Hz, CH*H*Ph), 4.74 (d, 1H, *J*=12.4 Hz, CH*H*Ph), 4.95 (d, 1H, *J*=12.4 Hz, CH*H*Ph), 7.22–7.30 (m, 8H, 8×H_{arom}), 7.32 (d, 2H, *J*=2.4 Hz, 2×H_{arom}). ^{13}C NMR (100 MHz): 52.5 (CH_3 CO_2Me), 57.3 (CH_3 C1–OMe), 68.1 (C-4), 71.5 (CH_2Ph), 73.5 (C-2), 75.1 (C-5), 80.1 (C-3), 103.1 (C-1), 127.3–128.3 (CH_{arom}), 137.8 (C_q Ph), 138.4 (C_q Ph), 169.7 (C=O CO_2Me). ^{13}C GATED NMR (100 MHz): 103.1 ($J_{C\text{-}1,\ H\text{-}1}$= 151 Hz). HRMS: $[M+Na]^+$ calcd for $C_{22}H_{26}O_7Na$: 425.1571, found 425.1569.

3.6. Phenyl 2-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutan-2′,3′-diyl)-1-thio-β-D-mannopyranoside (15)

1-Thio-β-D-mannopyranoside **13** (1.0 g, 3.67 mmol) was dissolved in MeOH (18.4 mL, 0.2 M) and butane-2,3-dione (355 μL, 4.04 mmol, 1.1 equiv), trimethyl orthoformate (2.21 mL, 20.19 mmol, 5.5 equiv) and a catalytic amount of CSA were added. The resulting mixture was heated to reflux and stirred for 2 days. TLC analysis showed conversion into a higher running spot (R_f: 0.33, PE/EtOAc 1/1). The reaction mixture was quenched with Et_3N and concentrated. Column chromatography (PE/EtOAc 8/2 to 6/4) yielded phenyl 3,4-*O*-(2′,3′-dimethoxybutan-2′,3′-diyl)-1-thio-β-D-mannopyranoside **14** as a transparent oil in 76% yield (1.10 g,

2.80 mmol). ^{1}H NMR (400 MHz): 1.29 (s, 3H, CH_3 BDA), 1.34 (s, 3H, CH_3 BDA), 2.69 (br s, 1H, OH), 3.25 (s, 3H, OCH_3 BDA), 3.26 (s, 3H, OCH_3 BDA), 3.52 (m, 1H, H-5), 3.78 (m, 2H, H-3, H-6^a), 3.90 (dd, 1H, J=12.0, 2.8 Hz, H-6^b), 4.14 (t, 1H, J=10.0 Hz, H-4), 4.20 (d, 1H, J=2.4 Hz, H-2), 4.94 (d, 1H, J=0.8 Hz, H-1), 7.25–7.34 (m, 3H, 3×H_{arom}), 7.47–7.50 (m, 2H, 2×H_{arom}). Phenyl 3,4-*O*-(2′,3′-dimethoxybutan-2′,3′-diyl)-1-thio-β-D-mannopyranoside **14** (790 mg, 2.04 mmol) was dissolved in pyridine (9.3 mL, 0.22 M) and TBDMSCl (338 mg, 2.24 mmol, 1.1 equiv) was added. The reaction mixture was stirred for 3 h. TLC analysis showed total conversion into a higher running spot (R_f: 0.82, Tol/EtOAc 2/1). The reaction was quenched by addition of MeOH, diluted with Et_2O, and H_2O was added. The aqueous layer was extracted with Et_2O (2×) and the combined organic layers were dried over $MgSO_4$, filtered, concentrated, and co-evaporated with toluene (2×). The obtained yellow oil was dissolved in DMF (10.2 mL, 0.2 M) and benzyl bromide (290 μL, 2.45 mmol, 1.2 equiv) was added. NaH (90 mg, 60% dispersion in mineral oil, 2.24 mmol, 1.1 equiv) was added after cooling to 0 °C and the reaction mixture was allowed to warm to rt. After $^1/_2$ h the reaction was quenched by addition of MeOH at 0 °C, water was added, and the mixture was extracted with Et_2O (3×). The combined organic layers were dried over $MgSO_4$, filtered, concentrated, and co-evaporated with toluene. The obtained yellow oil was dissolved in THF (7.85 mL, 0.26 M) and a solution of TBAF in THF (2.24 mL, 1 M in THF, 2.24 mmol, 1.1 equiv) was added. After 2 h, TLC analysis showed total conversion into a lower running product (R_f: 0.6, PE/EtOAc 2/1) and the reaction was quenched by addition of water and extracted with EtOAc (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography (PE/EtOAc 9/1 to 7/3) gave the title compound as an amorphous white solid in 79% yield over three steps (771 mg, 1.62 mmol). $[\alpha]_D$ +53.7 (*c* 1.8, DCM). IR (neat): 737, 849, 883, 926, 1038, 1107, 1123, 1207, 1281, 1377, 1454, 1585, 2835, 2889, 2947, 3456. ^{1}H NMR (400 MHz): 1.29 (s, 3H, CH_3 BDA), 1.34 (s, 3H, CH_3 BDA), 2.17 (br s, 1H, C6–OH), 3.26 (s, 6H, 2×OCH_3 BDA), 3.51 (m, 1H, H-5), 3.78 (dd, 1H, J=12.0, 5.6 Hz, H-6^a), 3.83 (dd, 1H, J=2.8, 10.4 Hz, H-3), 3.89 (dd, 1H, J=12.0, 2.8 Hz, H-6^b), 4.0 (s, 1H, H-2), 4.23 (t, 1H, J=10.0 Hz), 4.78 (d, 1H, J=10.8 Hz, C*H*HPh), 4.90 (s, 1H, H-1), 5.04 (d, 1H, J=11.6 Hz, CH*H*Ph), 7.22–7.37 (m, 6H, 6×H_{arom}), 7.44 (d, 2H, J=7.2 Hz, 2×H_{arom}), 7.53 (d, 2H, J=7.2 Hz, 2×H_{arom}). ^{13}C NMR (100 MHz): 17.6 (CH_3 BDA), 17.7 (CH_3 BDA), 47.8 (OCH_3 BDA), 47.9 (OCH_3 BDA), 61.8 (C-6), 63.8 (C-4), 72.6 (C-3), 74.6 (CH_2Ph), 77.3 (C-2), 78.5 (C-5), 88.0 (C-1), 99.4 (C_q BDA), 99.8 (C_q BDA), 127.1–130.6 (CH_{arom}), 135.0 (C_q SPh), 138.1 (C_q Ph). ^{13}C GATED NMR (100 MHz): 88.0 ($J_{C\text{-}1,\ H\text{-}1}$=154 Hz). HRMS: $[M+H]^+$ calcd for $C_{25}H_{33}O_8S$: 493.1891, found 493.1890.

3.7. Methyl 2,3,4-tri-*O*-benzyl-6-*O*-[methyl (2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannopyranosyluronate)]-α-D-glucopyranoside (16)

Mannuronate **6** (98 mg, 0.17 mmol) was condensed with glucoside **9** (118 mg, 0.26 mmol, 1.5 equiv) following the general procedure for glycosylations. Column chromatography (Tol/EtOAc 19/1 to 8/2) provided β-linked disaccharide **16** as an amorphous white solid in 93% yield (147 mg, 0.158 mmol). $[\alpha]_D$ +10.2 (*c* 1.9, DCM). IR (neat): 737, 868, 910, 1007, 1061, 1103, 1157, 1211, 1246, 1312, 1358, 1454, 1497, 1713, 1744, 2885, 3032. ^{1}H NMR (400 MHz): 2.15 (s, 3H, CH_3 Lev), 2.53 (m, 2H, CH_2 Lev), 2.71 (t, 2H, J=6.8 Hz, CH_2 Lev), 3.31 (s, 3H, OCH_3), 3.40 (m, 3H, H-3′, H-6^a, H-4), 3.50 (dd, 1H, J=3.6, 6 Hz, H-2), 3.70 (m, 4H, CO_2CH_3, H-2′), 3.77 (m, 2H, H-5, H-5′), 4.01 (t, 1H, J=6 Hz, H-3), 4.13 (m, 2H, H-6^b, H-1′), 4.29 (d, 1H, J=12.4 Hz, CH*H*Ph), 4.49 (d, 2H, J=11.6 Hz, 2×CH*H*Ph), 4.57 (d, 1H, J=3.2 Hz, H-1), 4.66 (d, 1H, J=12.0 Hz, CH*H*Ph), 4.74–4.89 (m, 4H, 4×CH*H*Ph), 4.91 (d, 1H, J=8.0 Hz, CH*H*Ph), 5.02 (d, 1H, J=10.8 Hz, CH*H*Ph), 5.51 (t, 1H, J=9.6 Hz, H-4′), 7.17–7.39 (m, 25H, 25×CH_{arom}). ^{13}C NMR (100 MHz): 27.8 (CH_2 Lev), 29.8 (CH_3 Lev), 37.7 (CH_2 Lev), 52.5 (CO_2CH_3), 55.0 (C-1–OCH_3), 68.6 (C-6), 69.1 (C-4′), 69.7 (C-5), 71.6 (CH_2Ph), 72.9 (C-2′), 73.2 (CH_2Ph), 73.5 (C-5′), 73.5 (CH_2Ph), 74.6 (CH_2Ph), 75.6 (CH_2Ph), 77.5 (C-4), 78.1 (C-3′), 79.8 (C-2), 82.1 (C-3), 97.7 (C-1), 101.5 (C-1′), 127.4–128.4 (CH_{arom}), 137.7 (C_q Ph), 138.0 (C_q Ph), 138.2 (C_q Ph), 138.7 (C_q Ph), 167.8 (C=O CO_2Me or CO_2 Lev), 171.4 (C=O CO_2Me or CO_2 Lev), 206.1 (C=O Lev). ^{13}C GATED NMR (100 MHz): 97.7 ($J_{C\text{-}1,\ H\text{-}1}$=163 Hz), 101.5 ($J_{C\text{-}1',\ H\text{-}1'}$=156 Hz). HRMS: $[M+Na]^+$ calcd for $C_{54}H_{60}O_{14}Na$: 955.3875, found 955.3882.

3.8. *para*-Methoxyphenyl 2-*O*-benzyl-4,6-benzylidene-3-*O*-[methyl (2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannopyranosyluronate)]-β-D-galactopyranoside (17)

Mannuronate **6** (87 mg, 0.15 mmol) was condensed with galactoside **10** (105 mg, 0.225 mmol, 1.5 equiv) following the general procedure for glycosylations. Column chromatography (Tol/EtOAc 9/1 to 8/2), followed by size exclusion chromatography gave β-linked disaccharide **17** as an amorphous white solid in 73% yield (78 mg, 0.11 mmol). $[\alpha]_D$ −31.5 (*c* 1.6, DCM). IR (neat): 729, 799, 826, 907, 999, 1057, 1096, 1153, 1215, 1265, 1366, 1454, 1504, 1717, 1755, 2874. ^{1}H NMR (400 MHz): 2.16 (s, 3H, CH_3 Lev), 2.52 (m, 2H, CH_2 Lev), 2.67 (m, 2H, CH_2 Lev), 3.11 (dd, 1H, J=2.8, 9.6 Hz, H-3′), 3.53 (s, 1H, H-5), 3.64 (d, 1H, J=2.0 Hz, H-2′), 3.71 (m, 4H, H-5′, CH_3 CO_2CH_3), 3.77 (s, 3H, OCH_3 *p*MP), 3.82 (dd, 1H, J=3.6, 10.0 Hz, H-3), 4.08 (m, 2H, H-2, H^{6a}), 4.21 (d, 1H, J=12.0 Hz, CH*H*Ph), 4.28 (d, 1H, J=11.2 Hz, CH*H*Ph), 4.36 (m, 2H, 2×CH*H*Ph), 4.41 (d, 1H, J=3.2 Hz, H-4), 4.69 (s, 1H, H-1′), 4.88 (m, 3H, H-1, 2×CH*H*Ph), 4.95 (d, 1H, J=11.2 Hz), 5.46 (t, 1H, J=9.6 Hz, H-4′), 5.63 (s, 1H, C*H*Ph benzylidene), 6.38 (m, 2H, 2×H_{arom} *p*MP), 7.03–7.39 (m, 20H, 20×H_{arom}), 7.62 (m, 2H, 2×H_{arom} *p*MP). ^{13}C NMR (100 MHz): 27.7 (CH_2 Lev), 29.7 (CH_3 Lev), 37.7 (CH_2 Lev), 52.6 (CH_3 CO_2CH_3), 55.6 (CH_3 *p*MP), 66.6 (C-5), 68.8 (C-6), 68.9 (C-4′), 71.6 (C-2′), 71.7 (CH_2Ph), 73.3 (CH_2Ph), 73.4 (C-5′), 75.2 (CH_2Ph), 75.7 (C-4), 77.7 (C-3), 79.0 (C-3′), 79.1 (C-2), 100.8 (CHPh benzylidene), 102.5 (C-1′), 103.1 (C-1), 114.5 (CH_{arom} *p*MP), 118.8 (CH_{arom} *p*MP), 126.3–128.8 (CH_{arom}), 137.7 (C_q Ph), 137.9 (C_q Ph), 138.1 (C_q Ph), 138.4 (C_q Ph), 151.4 (C_q *p*MP), 155.4 (C_q *p*MP), 167.8 (C=O CO_2CH_3 or CO_2R Lev), 171.4 (C=O CO_2CH_3), 206.1 (C=O Lev). ^{13}C GATED NMR (100 MHz): 102.5 ($J_{C\text{-}1',\ H\text{-}1'}$= 164 Hz), 103.2 ($J_{C\text{-}1,\ H\text{-}1}$=158 Hz). HRMS: $[M+Na]^+$ calcd for $C_{53}H_{56}O_{15}Na$: 955.3514, found 955.3515.

3.9. Methyl 2,3-di-*O*-benzyl-4-*O*-[methyl (2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannopyranosyluronate)]-α-D-mannopyranosyluronate (18)

Mannuronate acid **6** (86 mg, 0.15 mmol) was condensed with mannuronate **11** (90 mg, 0.225 mmol, 1.5 equiv) following the general procedure for glycosylations. Column chromatography (PE/EtOAc 9/1 to 7/3) gave β-linked disaccharide **18** as a clear oil in 31% yield (40 mg, 0.046 mmol). $[\alpha]_D$ −7.3 (*c* 0.8, DCM). IR (neat): 733, 910, 1053, 1096, 1207, 1242, 1265, 1362, 1454, 1497, 1720, 1747, 2855, 2924. ^{1}H NMR (400 MHz): 2.16 (s, 3H, CH_3 Lev), 2.56 (m, 2H, CH_2 Lev), 2.70 (m, 2H, CH_2 Lev), 3.46 (dd, 1H, J=3.2, 10.0 Hz, H-3′), 3.51 (s, 3H, CH_3, CO_2CH_3 or C1–O-CH_3), 3.58 (s, 3H, CH_3, CO_2CH_3 or C1–O-CH_3), 3.61 (s, 3H, CH_3, CO_2CH_3 or C1–O-CH_3), 3.66 (m, 1H, H-2), 3.80 (d, 1H, J=9.2 Hz, H-5), 3.86 (d, 1H, J=2.4 Hz, H-2′), 4.05 (m, 1H, H-3), 4.26 (d, 1H, J=5.2 Hz, H-5′), 4.38–4.45 (m, 2H, H-4, CH*H*Ph), 4.50 (d, 1H, J=12.4 Hz, CH*H*Ph), 4.54–4.64 (m, 5H, 4×CH*H*Ph, H-1′), 4.67–4.73 (m, 2H, 2×CH*H*Ph), 4.82 (d, 1H, J=12.4 Hz, CH*H*Ph), 5.02 (s, 1H, H-1), 5.48 (t, 1H, J=9.6 Hz, H-4′), 7.21–7.32 (m, 20H, 20×H_{arom}). ^{13}C NMR (100 MHz): 27.9 (CH_2 Lev), 29.6 (CH_3 Lev), 37.8 (CH_2 Lev), 52.2 (CH_3 CO_2CH_3), 52.5 (CH_3 CO_2CH_3), 56.1 (CH_3 C-1–OCH_3), 69.0 (C-4′), 71.6 (CH_2Ph), 71.9 (C-5), 72.8 (CH_2Ph), 73.0 (CH_2Ph), 73.5 (C-5′), 74.2 (C-2′), 74.2 (CH_2Ph), 75.2 (C-2), 76.5 (C-5), 76.7 (C-3),

78.2 (C-3′), 99.7 (C-1), 101.0 (C-1′), 127.4–128.2 (CH_{arom}), 138.5 (C_q Ph), 167.7 (C=O CO_2CH_3 or Lev), 169.7 (C=O CO_2CH_3 or Lev), 171.5 (C=O CO_2CH_3 or Lev), 206.1 (C=O Lev). ^{13}C GATED NMR (100 MHz): 99.7 ($J_{C\text{-}1,\ H\text{-}1}$=174 Hz), 101.0 ($J_{C\text{-}1',\ H\text{-}1'}$=161 Hz). HRMS: $[M+Na]^+$ calcd for $C_{48}H_{54}O_{15}Na$: 893.3355, found 893.3359.

3.10. Methyl (methyl 2,3-di-*O*-benzyl-4-*O*-[methyl (2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannopyranosyluronate)]-β-D-mannopyranosyluronate) (19)

Disaccharide **19** was obtained from donor **6** (87 mg, 0.15 mmol) and acceptor **12** (91 mg, 0.225 mmol, 1.5 equiv) according to the general procedure for glycosylations. Disaccharide **19** was isolated as an oily residue in 55% yield (72 mg, 0.083 mmol). $[\alpha]_D$ −41.5 (*c* 1.7, DCM). IR (neat): 729, 806, 895, 1049, 1103, 1153, 1207, 1265, 1362, 1454, 1497, 1720, 1747, 2885. ^{1}H NMR (400 MHz): 2.15 (s, 3H, CH_3 Lev), 2.50–2.55 (m, 2H, CH_2 Lev), 2.66–2.69 (m, 2H, CH_2 Lev), 3.44 (dd, 1H, *J*=2.8, 9.6 Hz, H-3′), 3.53 (s, 3H, CH_3 CO_2CH_3), 3.55 (s, 3H, CH_3 CO_2CH_3), 3.63 (m, 4H, CH_3 C-1–OCH_3, H-3), 3.68 (d, 1H, *J*=8.0 Hz, H-5′), 3.82 (m, 2H, H-2, H-2′), 3.90 (d, 1H, *J*=8.4 Hz, H-5), 4.38–4.43 (m, 3H, CH*H*Ph, H-1, H-4), 4.50 (d, 1H, *J*=12.8 Hz, CH*H*Ph), 4.53 (d, 1H, *J*=12.0 Hz, CH*H*Ph), 4.69 (m, 2H, H-1′, CH*H*Ph), 4.72–4.85 (m, 4H, 4×CHHPh), 5.42 (t, 1H, *J*=9.6 Hz, H-4′), 7.18–7.32 (m, 20H, 20×H_{arom}). ^{13}C NMR (100 MHz): 27.8 (CH_2 Lev), 29.8 (CH_3 Lev), 37.7 (CH_2 Lev), 52.3 (2×CO_2CH_3), 57.4 (C-1–OCH_3), 68.9 (C-4), 71.7 (CH_2Ph), 72.0 (CH_2Ph), 73.2 (C-5′), 73.7 (CH_2Ph), 73.8 (C-2 or C-2′), 74.2 (C-5), 74.3 (CH_2Ph), 74.8 (C-2′ or C-2′), 73.4 (C-4), 78.4 (C-3′), 78.7 (C-3), 102.2 (C-1′), 102.8 (C-1), 127.2–128.3 (CH_{arom}), 137.8 (C_q Ph), 138.3 (C_q Ph), 138.5 (C_q Ph), 138.6 (C_q Ph), 167.7 (C=O CO_2CH_3 or Lev), 168.7 (C=O CO_2CH_3 or Lev), 171.5 (C=O CO_2CH_3 or Lev), 206.2 (C=O Lev). ^{13}C GATED NMR (100 MHz): 102.2 ($J_{C\text{-}1',\ H\text{-}1'}$= 154 Hz), 102.9 ($J_{C\text{-}1,\ H\text{-}1}$=156 Hz). HRMS: $[M+Na]^+$ calcd for $C_{48}H_{54}O_{15}Na$: 893.3355, found 893.3360.

3.11. Methyl 2,3,4-tri-*O*-benzyl-6-*O*-[methyl (ethyl 2-*O*-benzyl-3,4-*O*-[2′,3′-dimethoxybutan-2′,3′-diyl]-α/β-D-mannopyranosyluronate)]-α-D-glucopyranoside (20)

Mannuronic acid **7** (135 mg, 0.27 mmol) was condensed with glucoside **9** (186 mg, 0.40 mmol, 1.5 equiv) following the general procedure for glycosylations. Column chromatography (Tol/EtOAc 1/0 to 7/1) gave **20**α and **20**β as clear oils (129 mg, 0.15 mmol, 56%). α-Isomer: $[\alpha]_D$ +99.4 (*c* 1.8, DCM). IR (neat): 733, 822, 849, 887, 1026, 1111, 1134, 1207, 1265, 1377, 1454, 1497, 1751, 2835, 2924. ^{1}H NMR (400 MHz): 1.34 (s, 3H, CH_3 BDA), 1.38 (s, 3H, CH_3 BDA), 3.20 (s, 3H, OCH_3 BDA), 3.25 (s, 3H, OCH_3 BDA), 3.33 (s, 3H, CO_2CH_3), 3.38 (t, 1H, *J*=9.2 Hz, H-4), 3.45 (dd, 1H, *J*=9.6 , 3.6 Hz, H-2), 3.68–3.71 (m, 6H, H-6^a, H-2′, H-5, CH_3 C-1–OCH_3), 3.78 (m, 1H, H-6^b), 3.97 (t, 1H, *J*=9.6 Hz, H-3), 4.05 (dd, 1H, *J*=2.8, 10.1 Hz, H-3′), 4.24 (d, 1H, *J*=10.4 Hz, H-5′), 4.40 (t, 1H, *J*=10.4 Hz, H-4′), 4.54–4.58 (m, 2H, H-1, CH*H*Ph), 4.65–4.68 (m, 2H, 2×CH*H*Ph), 4.75–4.82 (m, 2H, 2×CH*H*Ph), 4.89–4.91 (m, 2H, 2×CH*H*Ph), 4.93–4.99 (m, 2H, H-1′, CH*H*Ph), 7.13–7.67 (m, 20H, 20×H_{arom}). ^{13}C NMR (100 MHz): 17.6 (CH_3 BDA), 17.7 (CH_3 BDA), 47.8 (OCH_3 BDA), 52.1 (CO_2CH_3), 54.9 (C-1–OCH_3), 64.9 (C-4′), 66.2 (C-6), 68.4 (C-3′), 69.8 (C-2′), 70.6 (C-5′), 73.0 (CH_2Ph), 73.2 (CH_2Ph), 75.0 (C-5), 75.1 (CH_2Ph), 75.8 (CH_2Ph), 77.9 (C-4), 80.0 (C-2′), 82.0 (C-3), 97.7 (C-1), 99.6 (C_q BDA), 100.0 (C_q BDA), 100.2 (C-1′), 124.7–131.0 (CH_{arom}), 138.0 (C_q Ph), 138.1 (C_q Ph), 138.6 (C_q Ph), 169.1 (C=O CO_2CH_3). ^{13}C GATED NMR (100 MHz): 97.6 ($J_{C\text{-}1,\ H\text{-}1}$=167 Hz), 100.12 ($J_{C\text{-}1',\ H\text{-}1'}$=170 Hz). HRMS: $[M+Na]^+$ calcd for $C_{48}H_{58}O_{14}Na$: 881.3719, found 881.3719. β Isomer: $[\alpha]_D$ +77.2 (*c* 0.8, DCM). IR: 733, 799, 849, 895, 1038, 1111, 1134, 1265, 1362, 1454, 1497, 1751, 2928. ^{1}H NMR (400 MHz): 1.27 (s, 3H, CH_3 BDA), 1.32 (s, 3H, CH_3 BDA), 3.26 (s, 6H, 2×OCH_3 BDA), 3.32 (s, 3H, CH_3 CO_2CH_3), 3.37–3.45 (m, 2H, H-4, H-5), 3.50–3.59 (m, 3H, H-2, H-3′, H-2′), 3.72 (m, 4H, C-1–OCH_3, H-6^b), 3.82 (d, 1H, *J*=10 Hz, H-5′), 4.00 (t, 1H, *J*=8.8 Hz, H-3), 4.09 (dd, 1H, *J*=10.4, 1.6 Hz, H-6^a), 4.13 (s, 1H, H-1′), 4.40 (t, 1H, *J*=10.0 Hz, H-4′), 4.45 (d, 1H, *J*=11.6 Hz, CH*H*Ph), 4.57 (d, 1H, *J*=3.6 Hz, H-1), 4.68 (d, 1H, *J*=12.0 Hz, CH*H*Ph), 4.76–4.89 (m, 5H, 5×CH*H*Ph), 5.02 (d, 1H, J_{gem}=10.8 Hz, CH*H*Ph), 7.13–7.38 (m, 20H, 20×H_{arom}). ^{13}C NMR (100 MHz): 17.7 (CH_3 BBA), 47.8 (OCH_3 BBA), 47.9 (OCH_3 BBA), 52.1 (CH_3 CO_2CH_3), 55.0 (C-1–OCH_3), 61.9 (C-6), 64.7 (C-4′), 68.3 (CH_2Ph), 69.5 (C-3′), 70.6 (C-2′), 73.3 (CH_2Ph), 74.0 (C-5′), 74.2 (C-4), 74.6 (CH_2Ph), 75.6 (CH_2Ph), 77.4 (C-4), 79.7 (C-2), 82.1 (C-3), 97.7 (C-1), 99.6 (C_q BBA), 99.9 (C_q BBA), 101.8 (C-1′), 127.2–128.4 (CH_{arom}), 138.4 (C_q Ph), 138.7 (C_q Ph), 138.9 (C_q Ph). ^{13}C GATED NMR (100 MHz): 97.7 ($J_{C\text{-}1,\ H\text{-}1}$=168 Hz), 100.8 ($J_{C\text{-}1',\ H\text{-}1'}$=156 Hz). HRMS: $[M+Na]^+$ calcd for $C_{48}H_{58}O_{14}Na$: 881.3719, found 881.3718.

3.12. *para*-Methoxyphenyl 2-*O*-benzyl-4,6-benzylidene-4-*O*-[methyl (ethyl 2-*O*-benzyl-3,4-*O*-[2′,3′-dimethoxybutan-2′,3′-diyl]-α-D-mannopyranosyluronate)]-β-D-galactopyranoside (21)

Disaccharide **21** was obtained from donor **7** (89 mg, 0.18 mmol) and acceptor **10** (125 mg, 0.27 mmol, 1.5 equiv) according to the general procedure for glycosylations. Disaccharide **21** was isolated as a white amorphous solid in 56% yield (86 mg, 0.10 mmol). $[\alpha]_D$ +26.0 (*c* 0.2, DCM). IR (neat): 733, 826, 887, 999, 1034, 1061, 1080, 1111, 1134, 1180, 1219, 1265, 1369, 1454, 1508, 1751, 2835, 2951. ^{1}H NMR (400 MHz): 1.34 (s, 6H, 2×CH_3 BDA), 3.17 (s, 3H, OCH_3 BDA), 3.27 (s, 3H, OCH_3 BDA), 3.44 (s, 1H, H-5), 3.66 (s, 3H, OCH_3 *p*MP), 3.75 (m, 4H, H-2′, CO_2CH_3), 3.93 (m, 2H, H-2, H-3), 4.03 (d, 1H, *J*=11.2 Hz, H-6^a), 4.22 (d, 1H, *J*=2.4 Hz, H-4), 4.27 (d, 1H, *J*=8 Hz, H-3′), 4.33–4.42 (m, 3H, H-6^b, H-4′, H-5′), 4.68 (d, 1H, J_{gem}=12.4 Hz, CH*H*Ph), 4.78 (d, 1H, *J*=10.0 Hz, CH*H*Ph), 4.89 (m, 2H, H-1, CH*H*Ph), 4.95 (d, 1H, *J*=12.4 Hz, CH*H*Ph), 5.10 (s, 1H, H-1′), 5.43 (s, 1H, C*H*Ph benzylidene), 6.81 (d, 2H, *J*=8.8 Hz, H_{arom} *p*MP), 7.05 (d, 2H, *J*=8.8 Hz, 2H_{arom} *p*MP), 7.23–7.38 (m, 15H, 15×H_{arom}). ^{13}C NMR (100 MHz): 17.8 (CH_3 BDA), 17.8 (CH_3 BDA), 47.8 (OCH_3 BDA), 52.1 (OCH_3 CO_2CH_3), 55.6 (OCH_3 *p*MP), 64.9 (C-5′), 66.2 (C-5), 68.4 (C-3′), 68.4 (C-6), 70.6 (C-4′), 70.9 (C-4), 73.2 (CH_2Ph), 73.9 (C-3), 75.0 (CH_2Ph), 76.0 (C-2), 95.3 (C-1′), 99.7 (C_q BDA), 100.0 (C_q BDA), 100.9 (C*H*Ph benzylidene), 102.8 (C-1), 114.4 (CH_{arom} *p*MP), 118.8 (CH_{arom} *p*MP), 126.3–129.0 (CH_{arom}), 137.6 (C_q Ph), 137.8 (C_q Ph), 138.6 (C_q Ph), 151.6 (C_q *p*MP), 155.3 (C_q *p*MP), 169.3 (C=O CO_2CH_3). ^{13}C GATED NMR (100 MHz): 95.2 ($J_{C\text{-}1',\ H\text{-}1'}$=171 Hz, C-1′), 102.8 ($J_{C\text{-}1,\ H\text{-}1}$= 164 Hz, C-1). HRMS: $[M+Na]^+$ calcd for $C_{47}H_{54}O_{15}Na$: 881.3355, found 881.3358.

3.13. Methyl 2,3-di-*O*-benzyl-4-*O*-[methyl (ethyl 2-*O*-benzyl-3,4-*O*-[2′,3′-dimethoxybutan-2′,3′-diyl]-α-D-mannopyranosyluronate)]-α-D-mannopyranosyluronate (22)

Mannuronic acid **7** (117 mg, 0.23 mmol) was condensed with mannuronic acid **11** (139 mg, 0.35 mmol, 1.5 equiv) according to the general procedure for glycosylations. Column chromatography gave α-linked disaccharide **22** as a clear oil in 24% yield (44 mg, 0.055 mmol). $[\alpha]_D$ +123.8 (*c* 0.8, DCM). IR (neat): 733, 910, 1053, 1096, 1207, 1242, 1265, 1362, 1454, 1497, 1720, 1747, 2870, 2924. ^{1}H NMR (400 MHz): 1.25 (s, 3H, CH_3 BDA), 1.28 (s, 3H, CH_3 BDA), 3.21 (s, 3H, OCH_3 BDA), 3.24 (s, 3H, OCH_3 BDA), 3.41 (s, 3H, OCH_3), 3.58 (t, 1H, *J*=2.4 Hz, H-2′), 3.66 (t, 1H, *J*=3.2 Hz, H-2), 3.75 (m, 7H, H-3, 2×CO_2CH_3), 3.95 (dd, 1H, *J*=2.4, 10 Hz, H-3′), 4.12 (d, 1H, *J*=9.6 Hz, H-5), 4.17 (d, 1H, *J*=8.4 Hz, H-5′), 4.33 (t, 1H, *J*=10.4 Hz, H-4), 4.36–4.43 (m, 3H, H-4′, 2×CH*H*Ph), 4.61 (d, 1H, *J*=12.4 Hz, CH*H*Ph), 4.67 (m, 2H, 2×CH*H*Ph), 4.86 (d, 1H, *J*=2.8 Hz, H-1), 5.24 (s, 1H, H-1′), 7.19–7.31 (m, 15H, 15×H_{arom}). ^{13}C NMR (100 MHz): 17.7 (CH_3 BDA), 17.8 (CH_3 BDA), 47.7 (OCH_3 BDA), 47.9 (OCH_3 BDA), 52.1 (CH_3 CO_2CH_3), 52.6 (CH_3 CO_2CH_3), 55.7 (C-1–OCH_3), 64.9 (C-4′), 68.0

(C-3′), 71.1 (C-5′), 71.8 (CH_2Ph), 72.3 (C-5), 72.7 (CH_2Ph), 72.8 (CH_2Ph), 73.7 (C-2′), 74.5 (C-4), 75.6 (C-2), 78.6 (C-3), 99.5 (C-1), 99.6 (C_q BDA), 99.9 (C_q BDA), 100.8 (C-1′), 127.2–128.4 (CH_{arom}), 137.7 (C_q Ph), 138.0 (C_q Ph), 138.6 (C_q Ph), 129. 1 (2×C=O CO_2CH_3). ^{13}C GATED NMR (100 MHz): 99.3 ($J_{C\text{-}1,\ H\text{-}1}$=171 Hz, C-1), 101.4 ($J_{C\text{-}1',\ H\text{-}1'}$=173 Hz, C-1′). HRMS: $[M+K]^+$ calcd for $C_{42}H_{52}O_{15}K$: 835.2938, found 835.2937.

3.14. Methyl (methyl 2,3-di-*O*-benzyl-4-*O*-[(ethyl 2-*O*-benzyl-3,4-*O*-[2′,3′-dimethoxybutan-2′,3′-diyl]-α/β-D-manno-pyranosyluronate)]-β-D-mannopyranosyluronate) (23)

Disaccharide **23** was obtained as an anomeric mixture (α/β: 3/1) from donor **7** (76 mg, 0.15 mmol) and acceptor **12** (91 mg, 0.225 mmol, 1.5 equiv) according to the general procedure for glycosylations. Disaccharide **23** was isolated as a clear oil in 49% yield (58 mg, 0.073 mmol). IR (neat): 735, 862, 1053, 1078, 1207, 1246, 1265, 1383, 1439, 1454, 1751, 2916. α-Anomer: ^{1}H NMR (400 MHz): 1.25 (s, 3H, CH_3 BDA), 1.34 (s, 3H, CH_3 BDA), 3.20 (s, 3H, OCH_3 BDA), 3.23 (s, 3H, OCH_3 BDA), 3.38 (dd, 1H, *J*=8.8, 2.2 Hz, H-3), 3.52 (s, 3H, C-1–OCH_3), 3.61 (m, 1H, H-2′), 3.76 (s, 3H, CO_2CH_3), 3.79 (s, 3H, CO_2CH_3), 3.85–3.88 (m, 2H, H-2, H-5), 3.92 (dd, 1H, *J*=7.6, 2.4 Hz, H-3′), 4.10 (d, 1H, *J*=10.4 Hz, H-5′), 4.25 (d, 1H, *J*=12.0 Hz, CH*H*Ph), 4.30–4.40 (3H, H-4, H-1, H-4′), 4.63 (d, 1H, *J*=13.2 Hz, CH*H*Ph), 4.68–4.73 (m, 2H, *J*=12.8 Hz, CH*H*Ph), 4.80 (d, 1H, *J*=9.6 Hz, CH*H*Ph), 4.92 (d, 1H, *J*=12.4 Hz, CH*H*Ph), 5.31 (s, 1H, H-1′), 7.17–4.19 (m, 15H, 3×H_{arom}). ^{13}C NMR (100 MHz): 29.7 (CH_3 BDA), 47.7 (OCH_3 BDA), 47.8 (OCH_3 BDA), 52.0 (CH_3 CO_2CH_3), 52.6 (CH_3 CO_2CH_3), 57.4 (CH_3 C-1–OCH_3), 64.9 (C-4′), 68.0 (C-3′), 72.1 (CH_2Ph), 72.1 (C-5′), 72.7 (CH_2Ph), 73.3 (C-5), 73.7 (CH_2Ph), 75.1 (C-4), 75.6 (C-2, C-2′), 80.6 (C-3), 99.5 (C_q BDA), 100.1 (C_q BDA), 101.3 (C-1′), 102.9 (C-1), 127.0–128.4 (CH_{arom}), 137.4 (C_q Ph), 138.4 (C_q Ph), 138.5 (C_q Ph), 138.6 (C_q Ph), 168.1 (C=O CO_2CH_3), 168.7 (C=O CO_2CH_3). ^{13}C GATED NMR (100 MHz): 101.3 ($J_{C\text{-}1',\ H\text{-}1'}$=174 Hz, C-1′), 102.9 ($J_{C\text{-}1,\ H\text{-}1}$=156 Hz, C-1). β-Anomer: diagnostic peaks: ^{13}C NMR (100 MHz): 51.9 (CO_2CH_3), 52.3 (CO_2CH_3), 102.6 (C-1′), 102.8 (C-1). HRMS: $[M+Na]^+$ calcd for $C_{42}H_{52}O_{15}Na$: 819.3198, found 819.3201.

3.15. Methyl 2,3,4-tri-*O*-benzyl-6-*O*-[methyl (4-*O*-benzyl-2,3-*O*-isopropylidene-α/β-D-mannopyranosyluronate)]-α-D-glucopyranoside (24)

Disaccharide **24** was obtained from donor **8** (78 mg, 0.18 mmol) and acceptor **9** (125 mg, 0.27 mmol, 1.5 equiv) according to the general procedure for glycosylations. Disaccharide **24** was isolated as a clear oil, as a mixture of anomers in 67% yield (95 mg, 121 mmol, α/β=5/1). IR (neat): 741, 864, 910, 1088, 1207, 1369, 1454, 1497, 1751, 2041, 2156, 2187, 278, 2924. α-Isomer: ^{1}H NMR (400 MHz): 1.35 (s, 3H, CH_3 isopropylidene), 1.51 (s, 3H, CH_3 isopropylidene), 3.36 (s, 3H, CH_3 CO_2CH_3), 3.50 (m, 2H, H-2, H-4), 3.61 (s, 3H, CH_3 C-1–OCH_3), 3.72 (m, 3H, H-4′, H-5, H-6^a), 3.91 (m, 1H, H-6^b), 3.99 (t, 1H, *J*=9.2 Hz, H-3), 4.15 (d, 1H, *J*=6.0 Hz, H-2′), 4.16 (d, 1H, *J*=10.0 Hz, H-5′), 4.30 (t, 1H, *J*=6.4 Hz, H-3′), 4.58–4.62 (m, 3H, H-1, 2×CH*H*Ph), 4.68 (d, 2H, *J*=6.8 Hz, 2×CH*H*Ph), 4.80 (m, 2H, 2×CH*H*Ph), 4.89 (d, 1H, *J*=10.8 Hz, CH*H*Ph), 4.99 (d, 1H, *J*=10.8 Hz, CH*H*Ph), 5.16 (s, 1H, H-1′), 7.25–7.37 (m, 20H, 4×H_{arom}). ^{13}C NMR (100 MHz): 26.3 (CH_3 isopropylidene), 27.8 (CH_3 isopropylidene), 52.3 (CH_3 CO_2CH_3), 55.2 (C-1–OCH_3), 66.5 (C-6), 68.8 (C-2′), 69.8 (C-4′), 73.0 (CH_2Ph), 73.3 (CH_2Ph), 75.0 (CH_2Ph), 75.3 (C-5′), 75.8 (CH_2Ph), 76.7 (C-5), 77.4 (C-4), 78.0 (C-3′), 79.9 (C-2), 82.1 (C-3), 97.9 (C-1), 98.2 (C-1′), 109.7 (C_q isopropylidene), 127.6–128.5 (CH_{arom}), 137.8 (C_q Ph), 138.1 (C_q Ph), 138.1 (C_q Ph), 138.6 (C_q Ph), 169.7 (C=O CO_2CH_3). ^{13}C GATED NMR (100 MHz): 97.9 ($J_{C\text{-}1,\ H\text{-}1}$= 167 Hz, C-1), 98.2 ($J_{C\text{-}1',\ H\text{-}1'}$=172 Hz, C-1′). β-Anomer: diagnostic peaks: ^{13}C NMR (100 MHz): 99.8 (C-1′). HRMS: $[M+Na]^+$ calcd for $C_{45}H_{52}O_{12}Na$: 807.3351, found 807.3353.

3.16. *para*-Methoxyphenyl 2-*O*-benzyl-4,6-benzylidene-3-*O*-[methyl (4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-manno-pyranosyluronate)]-β-D-galactopyranoside (25)

Disaccharide **25** was obtained from donor **8** (73 mg, 0.17 mmol) and acceptor **10** (118 mg, 0.255 mmol, 1.5 equiv) according to the general procedure for glycosylations. Disaccharide **25** was isolated as an amorphous white solid in 57% yield (76 mg, 0.097 mmol). $[\alpha]_D$ +26.0 (*c* 0.2, DCM). IR (neat): 733, 826, 861, 899, 995, 1030, 1080, 1180, 1219, 1265, 1381, 1454, 1508, 1747, 2858, 2932, 3055. ^{1}H NMR (400 MHz): 1.36 (s, 3H, CH_3 isopropylidene), 1.50 (s, 3H, CH_3 isopropylidene), 3.48 (s, 1H, H-5), 3.61 (s, 3H, CH_3 CH_3CO_2), 3.73 (m, 1H, H-4′), 3.76 (s, 3H, CH_3 *p*MP), 3.97 (m, 2H, H-2, H-3), 4.07 (d, 1H, *J*=11.2 Hz, H-6^b), 4.19 (d, 1H, *J*=6.4 Hz, H-2′), 4.31 (t, 1H, *J*=6.4 Hz, H-3′), 4.36 (m, 2H, H-4, H-6^b), 4.30 (d, 1H, *J*=9.6 Hz, H-5′), 4.58 (d, 1H, *J*=11.6 Hz, CH*H*Ph), 4.81 (m, 2H, 2×CH*H*Ph), 4.95 (m, 2H, CH*H*Ph, H-1), 5.36 (s, 1H, H-1′), 5.53 (s, 1H, C*H*Ph benzylidene), 6.80 (d, 2H, *J*=9.2 Hz, H_{pMP}), 7.03 (d, 2H, *J*=9.2 Hz, 2×H_{pMP}), 7.16–7.40 (m, 13H, 13×H_{arom}), 7.50–7.52 (m, 2H, 2×H_{arom}). ^{13}C NMR (100 MHz): 26.3 (CH_3 isopropylidene), 27.9 (CH_3 isopropylidene), 52.2 (CH_3 CO_2CH_3), 55.6 (CH_3 *p*MP), 66.2 (C-5), 68.6 (C-5′), 69.2 (C-6), 71.0 (C-4), 72.9 (CH_2Ph), 73.9 (C-2), 75.3 (C-2′), 75.4 (CH_2Ph), 76.5 (C-3), 76.8 (C-4′), 78.0 (C-3′), 93.1 (C-1′), 101.1 (CHPh benzylidene), 103.1 (C-1), 109.8 (C_q isopropylidene), 114.4 (CH_{arom} *p*MP), 118.8 (CH_{arom} *p*MP), 126.4–129.0 (CH_{arom}), 137.6 (C_q Ph), 138.0 (C_q Ph), 138.2 (C_q Ph), 151.5 (C_q *p*MP), 155.3 (C_q *p*MP), 170.1 (C=O CO_2CH_3). ^{13}C GATED NMR (100 MHz): 93.1 ($J_{C\text{-}1',\ H\text{-}1'}$=169 Hz, C-1′), 103.0 ($J_{C\text{-}1,\ H\text{-}1}$= 160 Hz, C-1). HRMS: $[M+Na]^+$ calcd for $C_{44}H_{48}O_{13}Na$: 807.2987, found 807.2989.

3.17. Methyl 2,3-di-*O*-benzyl-4-*O*-[methyl (4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-mannopyranosyluronate)]-α-D-mannopyranosyluronate (26)

Disaccharide **26** was obtained from donor **8** (78 mg, 0.18 mmol) and acceptor **11** (125 mg, 0.27 mmol, 1.5 equiv) according to the general procedure for glycosylations. Disaccharide **26** was isolated as an oily residue in 20% yield (22 mg, 0.030 mmol). $[\alpha]^D$ +5.3 (*c* 0.2, DCM). IR (neat): 733, 800, 849, 885, 980, 1047, 1113, 1132, 1205, 1265, 1362, 1377, 1439, 1454, 1497, 1749, 2835, 2903, 2949. ^{1}H NMR (400 MHz): 1.28 (s, 3H, CH_3 isopropylidene), 1.44 (s, 3H, isopropylidene), 3.42 (s, 3H, C-1–OCH_3), 3.68–3.73 (m, 8H, H-2, H-4′, 2×CO_2CH_3), 3.80 (dd, 1H, *J*=2.8, 8.0 Hz, H-3), 4.06–4.11 (m, 2H, H-2′, H-5′), 4.19 (d, 1H, *J*=7.6 Hz, H-5), 4.25 (t, 1H, *J*=*J*=6.0 Hz, H-3′), 4.43–4.46 (m, 2H, CH*H*Ph, H-4), 4.54 (d, 1H, *J*=11.6 Hz, CH*H*Ph), 4.58–4.65 (m, 2H, 2×CH*H*Ph), 4.73 (d, 1H, *J*=12.4 Hz, CH*H*Ph), 4.79 (d, 1H, *J*=11.6 Hz, CH*H*Ph), 4.90 (d, 1H, *J*=2.8 Hz, H-1), 5.43 (s, 1H, H-1′), 7.24–7.34 (m, 15H, 15×H_{arom}). ^{13}C NMR (100 MHz): 26.1 (CH_3 isopropylidene), 27.7 (CH_3 isopropylidene), 52.2 (CH_3 CO_2CH_3), 52.5 (CH_3 CO_2CH_3), 55.7 (CH_3 C-1–OCH_3), 69.6 (C-5′), 71.9 (CH_2Ph), 72.5 (C-5), 72.9 (CH_2Ph), 73.0 (CH_2Ph), 73.7 (C-2), 74.5 (C-4), 75.6 (C-2′), 76.6 (C-4′), 77.8 (C-3+C-3′), 98.8 (C-1′), 99.5 (C-1), 109.5 (C_q isopropylidene), 127.5–129.2 (CH_{arom}), 137.6 (C_q Ph), 137.8 (C_q Ph), 138.1 (C_q Ph), 169.0 (C=O CO_2CH_3), 169.7 (C=O CO_2CH_3). ^{13}C GATED NMR (100 MHz): 98.8 ($J_{C\text{-}1',\ H\text{-}1'}$=177 Hz, C-1′), 99.5 ($J_{C\text{-}1,\ H\text{-}1}$=166 Hz, C-1). HRMS: $[M+Na]^+$ calcd for $C_{39}H_{46}O_{13}Na$: 745.2831, found 745.2827.

3.18. Methyl (methyl 2,3-di-*O*-benzyl-4-*O*-[methyl (4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-mannopyranosyluronate)]-β-D-mannopyranosyluronate) (27)

Disaccharide **27** was obtained from donor **8** (65 mg, 0.15 mmol) and acceptor **12** (91 mg, 0.225 mmol, 1.5 equiv) according to the general procedure for glycosylations. Disaccharide **27** was isolated as an oil in 50% yield (54 mg, 0.075 mmol). $[\alpha]_D$ +6.7 (*c* 2, DCM). IR (neat): 737, 800, 849, 885, 980, 1045, 1113, 1175, 1205, 1252, 1286,

1371, 1377, 1439, 1454, 1497, 1749, 2835, 2949. ^{1}H NMR (400 MHz): 1.25 (s, 3H, CH_3 isopropylidene), 1.44 (s, 3H, isopropylidene), 3.42 (dd, 1H, J=6.0, 3.2 Hz, H-3), 3.51 (s, 3H, C-1–OCH_3), 3.67 (dd, 1H, J=6.0, 8.0 Hz, H-4′), 3.73 (s, 3H, CO_2CH_3), 3.77 (s, 3H, CO_2CH_3), 3.81 (d, 1H, J=8.8 Hz, H-5), 3.89 (d, 1H, J=2.8 Hz, H-2), 3.97 (d, 1H, J=8.4 Hz, H-5′), 4.09 (dd, 1H, J=6, 1.6 Hz, H-2′), 4.23 (t, 1H, J=6.4 Hz, H-3′), 4.31 (d, 1H, J=8.8 Hz, CH*H*Ph), 4.32 (s, 1H, H-1), 4.42–4.49 (m, 2H, H-4, CH*H*Ph), 4.58 (d, 1H, J=12.0 Hz, CH*H*Ph), 4.75 (d, 1H, J=12.8 Hz, CH*H*Ph), 4.81 (d, 1H, J=9.6 Hz, CH*H*Ph), 4.93 (d, 1H, J=12.4 Hz, CH*H*Ph), 5.52 (s, 1H, H-1′), 7.20–7.32 (m, 14H, 14×H_{arom}), 7.35–7.40 (m, 1H, H_{arom}). ^{13}C NMR (100 MHz): 26.1 (CH_3 isopropylidene), 27.7 (CH_3 isopropylidene), 52.2 (CH_3 CO_2CH_3), 52.6 (CH_3 CO_2CH_3), 57.5 (CH_3 C-1–OCH_3), 69.7 (C-5′), 70.9 (CH_2Ph), 72.9 (C-2), 73.0 (CH_2Ph), 73.9 (CH_2Ph), 74.9 (C-4), 75.7 (C-2, C-5), 76.7 (C-4′), 77.9 (C-3′), 80.3 (C-3), 99.2 (C-1′), 102.9 (C-1), 109.5 (C_q isopropylidene), 127.5–128.4 (CH_{arom}), 137.5 (C_q Ph), 168.1 (C=O CO_2CH_3), 168.8 (C=O CO_2CH_3). ^{13}C GATED NMR (125 MHz): 99.2 ($J_{C\text{-}1',\ H\text{-}1'}$=167 Hz, C-1′), 102.9 ($J_{C\text{-}1,\ H\text{-}1}$=156 Hz, C-1). HRMS: $[M+Na]^+$ calcd for $C_{39}H_{46}O_{13}Na$: 745.2831, found 745.2826.

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