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A practical synthesis of β-D-GlcA-(1→3)-β-D-Gal-(1→3)-β-D-Gal-(1→4)-D-Xyl, a part of the common linkage region of a glycosaminoglycan

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Abstract

A practical synthesis of β-D-GlcA-(1→3)-β-D-Gal-(1→3)-β-D-Gal-(1→4)-β-D-Xyl-(1→OMe) was achieved by coupling of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosyluronate trichloroacetimidate with a trisaccharide acceptor. The trisaccharide acceptor was obtained by condensation of 3-*O*-allyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-galactopyranosyl trichloroacetimidate with methyl 2,3-di-*O*-benzoyl-β-D-xylopyranoside, followed by deallylation. The β-(1→3)-linked disaccharide was prepared readily with *p*-methoxyphenyl 3-*O*-allyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside as the key synthon. The α-(1→3)-linkage was formed in considerable amount with galactose mono- and disaccharide trichloroacetimidate donors with C-2 neighboring group participation.

Keywords: Oligosaccharide; Proteoglycan; Trichloroacetimidate

1. Introduction

Proteoglycans are biologically ubiquitous glycosylated glycoprotein conjugates with widely varying roles[1] such as in lubrication,[2] blood anticoagulation,[3] and light transmission.[4] Several different proteoglycans have in common a highly conserved tetrasaccharide linkage region joining a glycosaminoglycan to a core protein. The tetrasaccharide is considered to be a biosynthetic intermediate of an immature glycosaminoglycan chain.[5] For a study of structure–function relationship of oligosaccharides, we present herein a practical method for the synthesis of the linkage region tetrasaccharide.

2. Results and discussion

Recently, the tetrasaccharide serine conjugate was synthesized by Allen and Fraser-Reid[6] with pentenyl glycosyl orthoester as the intermediates. Earlier, synthesis of some complex oligosaccharides containing the tetrasaccharide moiety was also reported.[7] In these syntheses, orthogonal masking groups and multiple steps were needed. We tried to find a practical method for the synthesis of the tetrasaccharide. As outlined in Scheme 1, our synthesis started from *p*-methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**1**), which was obtained by the method used for the preparation of the corresponding mannose analogue.[8] Deacetylation of **1**, 3-selective allylation through a dibutyltin complex,[9] followed by benzoylation, afforded *p*-methoxyphenyl 3-*O*-allyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (**2**). Compound **2** was easily converted to either a donor or an acceptor. Its deallylation with $PdCl_2$[10] gave the acceptor **4**, while its oxidative cleavage of 1-OMP with CAN followed by trichloroacetimidation[11] furnished the donor **3**. Glycosylation of **4** with **3** in the presence of catalytic TMSOTf gave the required β-linked disaccharide **5** as the major product (54%) together with the α-linked isomer **6** as the minor one (31%). Since the α-linkage product was produced in a considerable amount, this coupling was abnormal and contradictory

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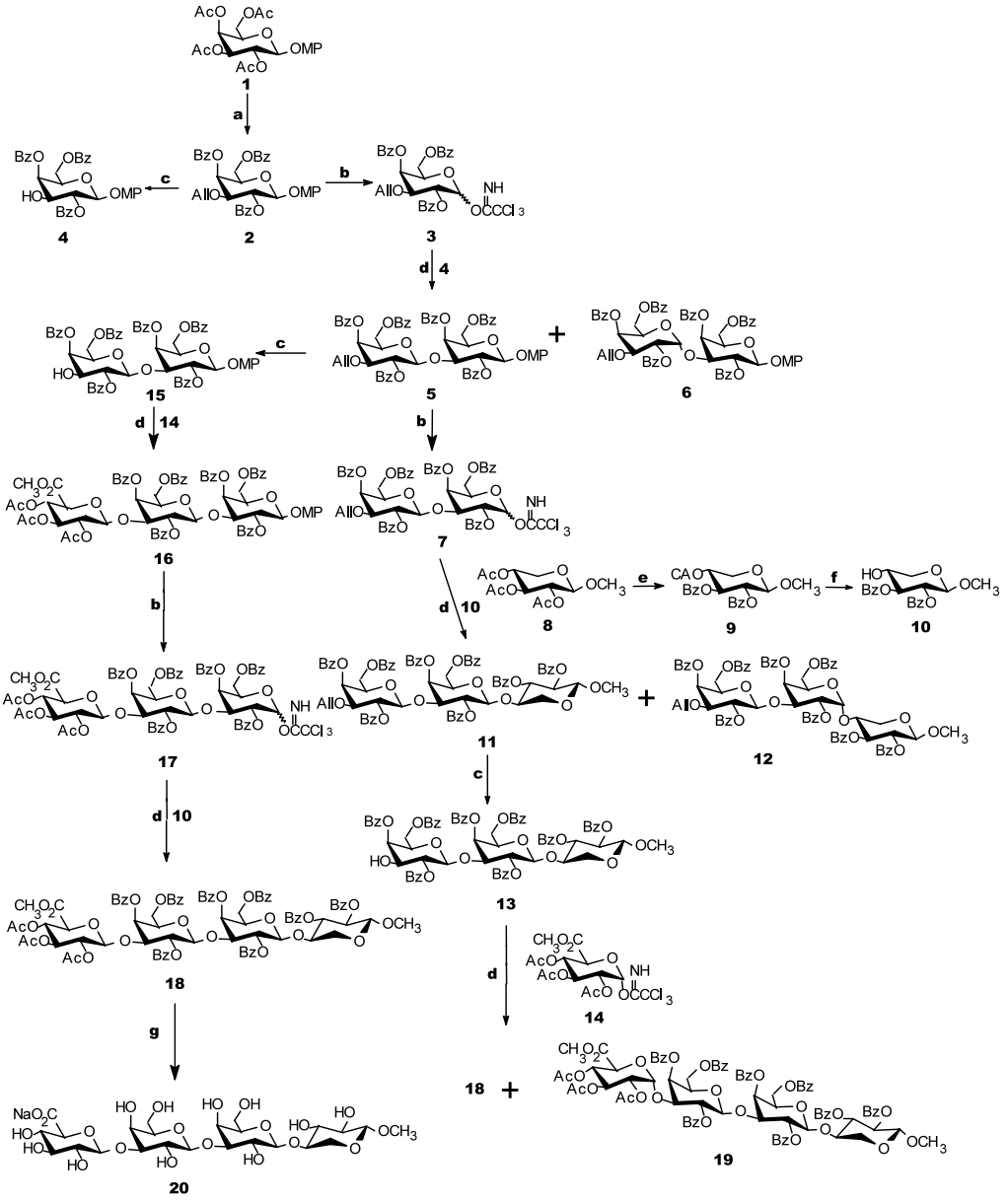
to the conventional rule that a 1,2-*trans* linkage can be obtained solely with the donor with C-2 neighboring group participation.[12] This abnormality was similar to that in the coupling of the corresponding glucose donor and acceptor analogues that gave predominant α-(1→3)-linkages.[13] The disaccharide **5**, as the inner moiety of the target tetrasaccharide, was readily transformed to the disaccharide donor **7** by oxidative cleavage of 1-OMP, followed by trichloroacetimidation. The xyloside acceptor **10** was prepared by deacetylation of **8**, then selective chloroacetylation[14] of the resultant methyl β-D-xylopyranoside, and subsequent benzoylation, followed by dechloroacetylation. Condensation of **7** with **10** yielded equivalent β-linked trisaccharide **11** (40%) and α-linked trisaccharide **12** (40%). Here, it gave abnormal coupling again with the β-(1→3)-linked disaccharide as the donor with a C-2 ester group, and this result was also similar to that in the coupling with β-(1→3)-linked glucodisaccharide donor analogue.[13] Deallylation of **11** produced the trisaccharide acceptor **13**, and subsequent coupling with **14** gave the required tetrasaccharide **18** (31%), together with the α-linked isomer **19** (31%). Alternatively, the nonreducing trisaccharide was built first, then transformed to a donor,



Scheme 1. Reagents and conditions: (a) i. MeONa–MeOH; ii. MeOH, Bu_2SnO, then AllBr, Bu_4NI, toluene; iii. PhCOCl, pyr, rt. (b) i. CH_3CN–H_2O, CAN; ii. CCl_3CN, CH_2Cl_2, K_2CO_3, rt; (c) $PdCl_2$, CH_3OH, 40 °C; (d) TMSOTf, CH_2Cl_2, −25 °C to rt; (e) i. MeONa–MeOH; ii. benzene, Bu_2SnO, then $ClCH_2COCl$; iii. PhCOCl, Pyr, rt; (f) thiourea, EtOH, CH_2Cl_2, reflux; (g) NaOH–CH_3OH–H_2O, rt.

and coupled with **10**. Thus, the disaccharide acceptor **15** was obtained by deallylation of **5**, and subsequent condensation of **15** with **14** furnished **16** as the major product (55%). Oxidative cleavage of 1-OMP of **16**, and subsequent trichloroacetimidation gave the trisaccharide donor **17**, and then condensation with **10** gave **18** as the major product (40%). The latter route was more effective since it minimized the α-isomer formation. Finally, conventional deprotection offered the tetrasaccharide as its methyl glycoside sodium salt. Although some coupling reactions described above gave anomeric mixtures, the anomers were readily separated in sufficient quantities to complete the synthetic sequences.

In summary, we present herein a practical synthesis of β-D-GlcA-(1→3)-β-D-Gal-(1→3)-β-D-Gal-(1→4)-D-Xyl. It should be possible to carry out a large-scale preparation of the tetraose by employing this method. In the preparation of (1→3)-linked galactobiose with a galactose donor or in the preparation of trisaccharides with β-(1→3)-linked galactobiose as the donor, the α-linkage can be produced even with C-2 neighboring group participation.

3. Experimental

General methods.—Melting points were determined with a 'Mel-Temp' apparatus. Optical rotations were determined with a Perkin–Elmer model 241-MC automatic polarimeter for solutions in a 1-dm, jacketed cell. ^{1}H NMR spectra were recorded with Varian XL-400 and Varian XL-200 spectrometers, for solutions in $CDCl_3$ with tetramethylsilane (Me_4Si) as the internal standard or for solutions in D_2O with acetone as the internal standard. Mass spectra were recorded with a Shimadzu LCMS-2010 mass spectrometer using the negative-ion electrospray-ionization mode. The progress of all reactions was followed by thin-layer chromatography (TLC) that was performed on silica gel HF with detection by charring with 30% (v/v) sulfuric acid in methanol or by UV detection. Column chromatography was conducted by elution of a column (8 × 100 mm, 16 × 240 mm, 18 × 300 mm, 35 × 400 mm) of silica gel (100–200 mesh) and EtOAc–petroleum ether (bp 60–90 °C) as the eluent. Analytical LC was performed with a Gilson HPLC consisting of a pump (model 306), stainless steel column packed with silica gel (Spherisorb SiO_2, 10 × 300 mm or 4.6 × 250 mm), differential refractometer (132-RI Detector) and UV/vis detector (model 118). EtOAc–petroleum ether (bp 60–90 °C) was used as the eluent at a flow rate of 1–4 mL/min. Solutions were concentrated at a temperature < 60 °C under diminished pressure.

p-*Methoxyphenyl 3*-O-*allyl-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranoside* (**2**).—To a solution of *p*-methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**1**) (9.08 g, 20.0 mmol) in MeOH (100 mL) was added 4.0 M NaOMe–MeOH solution dropwise to pH 10. After stirring the mixture at rt for 5 h, TLC (EtOAc) indicated that the reaction was complete. The reaction mixture was neutralized with 1:10 HOAc–MeOH, then the mixture was concentrated, and the residue was purified by column chromatography (3:1 EtOH–MeOH) to give a solid. To a solution of the solid in MeOH (200 mL) was added Bu_2SnO (5.22 g, 21.0 mmol), and the mixture was heated under reflux for 2 h, then concentrated to dryness. The residue was diluted with toluene (200 mL), and then allyl bromide (17.1 mL, 200 mmol), Bu_4NI (7.38 g, 20.0 mmol) were added to the mixture. The reaction was carried out at 60 °C for 24 h, at which time TLC (EtOAc) indicated that the reaction was complete. The reaction mixture was concentrated, and the residue was diluted with CH_2Cl_2 (20 mL). To the mixture were added pyridine (8 mL) and BzCl (7.18 mL, 62.0 mmol). The mixture was stirred overnight at rt, at which time TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was diluted with CH_2Cl_2 and washed with 1 N HCl, water, and satd aq $NaHCO_3$. The organic layer was combined, dried, and concentrated. Purification of the crude product by column chromatography (3:1 petroleum ether–EtOAc) gave **2** as a syrup (9.19 g, 72%): $[\alpha]_D$ +69.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.19–7.45 (m, 15 H, PhH), 6.94 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$–), 6.64 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$–), 5.87 (dd, 1 H, $J_{3,4}$ 3.5 Hz, H-4), 5.76 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 5.66 (m, 1 H, CH_2=C*H*–CH_2O), 5.21–5.05 (m, 2 H, CH_2=CH–CH_2O), 5.09 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 4.62–4.54 (m, 2 H, H-6, H-6′), 4.25 (m, 1 H, H-5), 4.19–3.98 (m, 2 H, CH_2=CH–CH_2O), 3.91 (dd, 1 H, H-3), 3.71 (s, 3 H, CH_3O). Anal. Calcd for $C_{37}H_{34}O_{10}$: C, 69.59; H, 5.33. Found: C, 69.89; H, 5.31

3-O-*Allyl-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl trichloroacetimidate* (**3β**) *and 3*-O-*allyl-2,4,6-tri*-O-*benzoyl-α*-D-*galactopyranosyl trichloroacetimidate* (**3α**).—To a solution of **2** (12.76 g, 20.0 mmol) in 4:1 CH_3CN–H_2O (250 mL) was added CAN [$(NH_4)_2Ce(NO_3)_6$, 43.86 g, 80.0 mmol], and the mixture was stirred at rt for 30 min, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was extracted with EtOAc and washed with water. The organic layer was concentrated under reduced pressure, and the crude product was purified by column chromatography (2:1 petroleum ether–EtOAc) to afford a solid. To a solution of the solid in CH_2Cl_2 (100 mL) were added trichloroacetonitrile (3.5 mL) and anhyd potassium carbonate (11.50 g). The reaction mixture was stirred overnight at rt and then filtered, and the filtrate was concentrated in vacuo. The residue was purified by

column chromatography (3:1 petroleum ether–EtOAc) to give **3β** (8.25 g, 61%) and **3α** (2.03 g, 15%), respectively, as syrups: **3β**: $[\alpha]_D$ +192.4° (*c* 0.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.65 (s, 1 H, NH), 8.18–7.43 (m, 15 H, PhH), 6.06 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 5.92 (dd, 1 H, $J_{3,4}$ 3.4 Hz, $J_{4,5}$ 1.3 Hz, H-4), 5.79 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-2), 5.68 (m, 1 H, CH_2=CH–CH_2O), 5.21–5.06 (m, 2 H, CH_2=CH–CH_2O), 4.67 (dd, 1 H, $J_{5,6}$ 6.8 Hz, H-6), 4.46 (dd, 1 H, $J_{5,6'}$ 6.3 Hz, $J_{6,6'}$ 11.4 Hz, H-6′), 4.35 (m, 1 H, H-5), 4.20–4.00 (m, 2 H, CH_2=CH–CH_2O), 3.96 (dd, 1 H, H-3). Anal. Calcd for $C_{32}H_{28}Cl_3NO_9$: C, 56.76; H, 4.14. Found: C, 56.49; H, 4.15. **3α**: $[\alpha]_D$ +124.7° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.57 (s, 1 H, NH), 8.15–7.42 (m, 15 H, PhH), 6.81 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 6.01 (dd, 1 H, $J_{3,4}$ 3.3 Hz, $J_{4,5}$ 1.1 Hz,H-4), 5.79 (m, 1 H, CH_2=CH–CH_2O), 5.70 (dd, 1 H, $J_{2,3}$ 10.4 Hz, H-2), 5.27–5.10 (m, 2 H, CH_2=CH–CH_2O), 4.68 (m, 1 H, H-5), 4.54 (dd, 1 H, $J_{5,6}$ 7.1 Hz, H-6), 4.45 (dd, 1 H, $J_{5,6'}$ 5.5 Hz, $J_{6,6'}$ 11.5 Hz, H-6′), 4.30 (dd, 1 H, H-3), 4.26–4.07 (m, 2 H, CH_2=CH–CH_2O). Anal. Calcd for $C_{32}H_{28}Cl_3NO_9$: C, 56.76; H, 4.14. Found: C, 56.51; H, 4.25.

p-*Methoxyphenyl 2,4,6-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**4**).—To a solution of **2** (6.38 g, 10.0 mmol) in anhyd CH_3OH (150 mL) was added $PdCl_2$ (0.6 g), and the mixture was stirred at 40 °C for 4 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was filtered, and the filtrate was concentrated. The residue was passed through a silica gel column with 2:1 petroleum ether–EtOAc as the eluent to give **4** as a solid (4.78 g, 80%): $[\alpha]_D$ +19.4° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.20–7.43 (m, 15 H, PhH), 6.97 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$–), 6.67 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$–), 5.80 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4), 5.61 (dd, 1 H, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.0 Hz, H-2), 5.14 (d, 1 H, H-1), 4.61–4.52 (m, 2 H, H-6, H-6′), 4.28 (m, 1 H, H-5), 4.21 (dd, 1 H, H-3). Anal. Calcd for $C_{34}H_{30}O_{10}$: C, 68.23; H, 5.02. Found: C, 67.92; H, 5.04.

p-*Methoxyphenyl 3*-O-*allyl-2,4,6-tri*-O-*benzoyl*-β-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**5**) *and* p-*methoxyphenyl 3*-O-*allyl-2,4,6-tri*-O-*benzoyl*-α-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**6**).—A mixture of **3α**, **3β** (1.35 g, 2.0 mmol) and **4** (1.20 g, 2.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (30 mL). TMSOTf (30 μL, 0.08 equiv) was added dropwise at −25 °C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the mixture was gradually warmed to ambient temperature. Then the mixture was neutralized with Et_3N, concentrated and purified by column chromatography (2:1 petroleum ether–EtOAc) to afford **5** (1.20 g, 54%) and **6** (0.69 g, 31%), respectively, as foamy solids: **5**: $[\alpha]_D$ +52.3° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.19–7.15 (m, 30 H, PhH), 6.81 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$–), 6.53 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$–), 5.98 (d, 1 H, $J_{3,4}$ 3.7 Hz, H-4^{II}), 5.82 (dd, 1 H, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 9.8 Hz, H-2^{II}), 5.71 (d, 1 H, $J_{3,4}$ = 3.0 Hz, H-4^{I}), 5.47 (m, 1 H, CH_2=CH–CH_2O), 5.28 (dd, 1 H, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ = 8.1 Hz, H-2^{I}), 5.02–4.89 (m, 2 H, CH_2=CH–CH_2O), 4.97 (d, 1 H, H-1^{II}), 4.89 (d, 1 H, H-1^{I}), 4.65–4.60 (m, 2 H), 4.47 (dd, 1 H, $J_{5,6}$ 8.5 Hz, $J_{6,6'}$ 11.8 Hz, H-6), 4.30 (dd, 1 H, $J_{5,6}$ 6.3 Hz, $J_{6,6'}$ 11.5 Hz, H-6), 4.25 (dd, 1 H, H-3^{II}), 4.16 (dd, 1 H), 4.08 (m, 1 H, H-5), 4.02–3.78 (m, 2 H, CH_2=CH–CH_2O), 3.67 (dd, 1 H, H-3^{I}) 3.65 (s, 3 H, CH_3O). ^{13}C NMR ($CDCl_3$): δ 165.71, 165.57, 165.57, 165.22, 164.11, 164.06 (PhCO), 155.00, 150.79 ($CH_3OC_6H_4O$–), 133.49, 132.88, 132.75, 132.43, 132.02, 129.80, 129.56, 129.34, 129.20, 129.04, 128.97, 128.85, 128.78, 128.22, 128.12, 128.07, 128.04, 127.97, 127.78, 127.55, 118.27 ($CH_3OC_6H_4O$–), 117.13 (CH_2=CH–CH_2O), 113.81 ($CH_3OC_6H_4O$–), 101.31, 100.57 (C-1), 77.15, 75.83, 71.78, 70.78, 70.86, 70.70, 70.11, 69.75, 66.10, 62.78, 61.87, 55.06 (CH_3O). Anal. Calcd for $C_{64}H_{56}O_{18}$: C, 69.06; H, 5.04. Found: C, 69.37; H, 5.08. **6**: $[\alpha]_D$ +124.7° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.13–7.09 (m, 30 H, PhH), 6.87 (d, 2 H, *J* 9.0 Hz, $CH_3OC_6H_4O$–), 6.69 (d, 2 H, *J* 9.0 Hz, $CH_3OC_6H_4O$–), 5.92 (dd, 1 H, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.3 Hz, H-2^{I}), 5.81 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4^{II}), 5.74 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1^{II}), 5.52 (m, 1 H, CH_2=CH–CH_2O), 5.46 (dd, 1 H, $J_{2,3}$ 10.4 Hz, H-2^{II}), 5.21 (dd, 1 H, H-4^{I}), 4.93–4.86 (m, 2 H, CH_2=CH–CH_2O), 4.71 (d, 1 H, H-1), 4.49 (dd, 1 H, $J_{5,6}$ 7.6 Hz, $J_{6,6'}$ 11.4 Hz, H-6), 4.43–4.28 (m, 4 H), 4.21 (dd, 1 H, H-3^{II}), 3.84 (m, 1 H, H-5^{I}), 3.81–3.63 (m, 2 H, CH_2=CH–CH_2O), 3.75 (s, 3 H, CH_3O), 3.68 (dd, 1 H, $J_{3,4}$ 3.2 Hz, H-3^{I}). ^{13}C NMR ($CDCl_3$): δ 165.44, 165.28, 165.28, 165.21, 164.73, 164.50 (PhCO), 155.29, 150.74 ($CH_3OC_6H_4O$–), 133.43, 133.36, 132.96, 132.59, 132.21, 129.50, 129.35, 129.21, 129.12, 128.87, 128.68, 128.38, 128.23, 128.09, 127.73, 127.60, 118.50 ($CH_3OC_6H_4O$–), 116.88 (CH_2=CH–CH_2O), 113.95 ($CH_3OC_6H_4O$–), 100.71, 91.94 (C-1), 72.13, 71.57, 71.29, 70.38, 69.53, 68.71, 67.67, 67.35, 64.58, 62.60, 61.85, 55.19 (CH_3O). Anal. Calcd for $C_{64}H_{56}O_{18}$: C, 69.06; H, 5.04. Found: C, 69.41; H, 5.11.

3-O-*Allyl-2,4,6-tri*-O-*benzoyl*-β-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl*-β-D-*galactopyranosyl trichloroacetimidate* (**7β**) *and 3*-O-*allyl-2,4,6-tri*-O-*benzoyl*-β-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl*-α-D-*galactopyranosyl trichloroacetimidate* (**7α**).—To a solution of **5** (11.12 g, 10.0 mmol) in 4:1 CH_3CN–H_2O (250 mL) was added CAN (43.86 g, 80.0 mmol), and the mixture was stirred at rt for 30 min, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was extracted with EtOAc, and the extract was washed with water. The organic layer was concentrated and purified by column chromatography (2:1 petroleum ether–

EtOAc) to afford a solid. To a solution of the solid in CH_2Cl_2 (80 mL) were added trichloroacetonitrile (3.0 mL) and anhyd potassium carbonate (10.0 g). The reaction mixture was stirred overnight at rt and then filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (2:1 petroleum ether–EtOAc) to give **7β** (5.52 g, 48%) and **7α** (2.76 g, 24%), respectively, as syrups: **7β**: $[\alpha]_D$ + 66.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.56 (s, 1 H, NH), 8.18–7.10 (m, 30 H, PhH), 6.05 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4^{II}), 5.96 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1^{I}), 5.86 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-2^{I}), 5.72 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4^{I}), 5.49 (m, 1 H, CH_2=CH–CH_2O), 5.27 (dd, 1 H, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.1 Hz, H-2^{II}), 5.03–4.88 (m, 2 H, CH_2=CH–CH_2O), 4.89 (d, 1 H, H-1^{II}), 4.62 (dd, 1 H, $J_{5,6}$ 6.8 Hz, $J_{6,6'}$ 11.5 Hz, H-6), 4.51 (m, 2 H), 4.35–4.28 (m, 2 H), 4.23 (m, 1 H, H-5^{II}), 4.08 (m, 1 H, H-5^{I}), 4.02–3.78 (m, 2 H, CH_2=CH–CH_2O), 3.66 (dd, 1 H, H-3^{II}). Anal. Calcd for $C_{59}H_{50}Cl_3NO_{17}$: C, 61.54; H, 4.35. Found: C, 61.31; H, 4.39. **7α**: $[\alpha]_D$ + 61.7° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.47 (s, 1 H, NH), 8.15–7.06 (m, 30 H, PhH), 6.70 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1^{I}), 6.14 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4^{II}), 5.76–5.73 (m, 2 H, H-4^{I}, H-2^{I}), 5.50 (m, 1 H, CH_2=CH–CH_2O), 5.29 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.0 Hz, H-2^{II}), 5.03–4.91 (m, 2 H, CH_2=CH–CH_2O), 5.02 (d, 1 H, H-1^{II}), 4.65 (dd, 1 H, H-6), 4.59 (m, 1 H, H-5^{II}), 4.55–4.35 (m, 4 H), 4.19 (m, 1 H, H-5^{I}), 4.06–3.81 (m, 2 H, CH_2=CH–CH_2O), 3.72 (dd, 1 H, H-3^{II}). Anal. Calcd for $C_{59}H_{50}Cl_3NO_{17}$: C, 61.54; H, 4.35. Found: C, 61.29; H, 4.41.

Methyl 2,3-di-O-*benzoyl-4*-O-*chloroacetyl-β*-D-*xylopyranoside* (**9**).—To a solution of methyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside (**8**, 5.80 g, 20.0 mmol) in MeOH (80 mL) was added 4.0 M NaOMe–MeOH solution dropwise to pH 10. After stirring the mixture at rt for 5 h, TLC (EtOAc) indicated that the reaction was complete. The reaction mixture was directly passed through a silica gel column with 3:1 EtOH–MeOH as the eluent to give a solid. The solid was dispersed in benzene (150 mL), and Bu_2SnO (5.23 g, 21.0 mmol) was added. The mixture was heated under reflux for 2 h, then cooled to rt, at which time $ClCH_2COCl$ (1.59 mL, 20.0 mol) was added to the mixture. The reaction was carried out at rt for 1 h. To the solution were added pyridine (8 mL), BzCl (4.87 mL, 42.0 mmol), and the mixture was stirred overnight at rt. TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was diluted with CH_2Cl_2, washed with 1 N HCl, water, and satd aq $NaHCO_3$. The organic layer was combined, dried, and concentrated. Purification by column chromatography (3:1 petroleum ether–EtOAc) gave **9** (6.46 g, 72%) as a syrup: $[\alpha]_D$ + 63.0° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.99–7.36 (m, 10 H, PhH), 5.59 (dd, 1 H, $J_{2,3} = J_{3,4} = 7.8$ Hz, H-3), 5.32 (dd, 1 H, $J_{1,2}$ 5.8 Hz, H-2), 5.21 (m, 1 H, $J_{4,5}$ 4.6 Hz, $J_{4,5'}$ 7.5 Hz, H-4), 4.66 (d, 1 H, H-1), 4.28 (dd, 1 H, $J_{5,5'}$ 12.2 Hz, H-5), 4.00 (ABq, 2 H, *J* 14.9 Hz, $ClCH_2CO$), 3.63 (dd, 1 H, H-5′), 3.49 (s, 3 H, CH_3O). Anal. Calcd for $C_{22}H_{21}ClO_8$: C, 58.86; H, 4.68. Found: C, 58.69; H, 4.73.

Methyl 2,3-di-O-*benzoyl-β*-D-*xylopyranoside* (**10**).—To a solution of **9** (4.49 g, 10.0 mmol) in EtOH (350 mL)–CH_2Cl_2 (50 mL) was added thiourea (0.94 g, 13.0 mmol), and the mixture was refluxed for 16 h, at the end of which time TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was concentrated, and the residue was passed through a silica gel column with 3:1 petroleum ether–EtOAc as the eluent to give **10** as foamy solid (2.98 g, 80%); $[\alpha]_D$ + 54.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.00–7.37 (m, 10 H, PhH), 5.38–5.28 (m, 2 H, H-3, H-2), 4.61 (d, 1 H, $J_{1,2}$ 6.3 Hz, H-1), 4.21 (dd, 1 H, $J_{4,5}$ 4.8 Hz, $J_{5,5'}$ 11.9 Hz, H-5), 4.01 (m, 1 H, H-4), 3.53 (dd, 1 H, $J_{4,5'}$ 8.4 Hz, H-5′), 3.51 (s, 3 H, CH_3O), 2.80 (br, 1 H, OH). Anal. Calcd for $C_{20}H_{20}O_7$: C, 64.52; H, 5.38. Found: C, 64.33; H, 5.40.

Methyl 3-O-*allyl-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→4)-2,3-di*-O-*benzoyl-β*-D-*xylopyranoside* (**11**) *and methyl 3*-O-*allyl-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl-α*-D-*galactopyranosyl-(1→4)-2,3-di*-O-*benzoyl-β*-D-*xylopyranoside* (**12**).—A mixture of **7α**, **7β** (1.15 g, 1.0 mmol) and **10** (0.37 g, 1.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (20 mL). TMSOTf (30 μL, 0.16 equiv) was added dropwise at −25 °C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the mixture was gradually warmed to ambient temperature. Then the mixture was neutralized with Et_3N and concentrated, and the crude product was purified by flash chromatography (2:1 petroleum ether–EtOAc) to afford **11** (0.54 g, 40%), and **12** (0.54 g, 40%), respectively, as foamy solids: **11**: $[\alpha]_D$ + 24.1° (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.05–7.12 (m, 40 H, PhH), 5.82 (d, 1 H, $J_{3,4}$ 3.4 Hz, H-4^{III}), 5.68 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4^{II}), 5.55 (dd, 1 H, $J_{2,3} = J_{3,4} = 7.5$ Hz, H-3^{I}), 5.49 (m, 1 H, CH_2=CH–CH_2O), 5.48 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.0 Hz, H-2^{III}), 5.22 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.1 Hz, H-2^{II}), 5.18 (dd, 1 H, $J_{1,2}$ 6.1 Hz, H-2^{I}), 5.01–4.87 (m, 2 H, CH_2=CH–CH_2O), 4.80 (d, 1 H, H-1^{III}), 4.71 (d, 1 H, H-1^{II}), 4.56 (dd, 1 H), 4.45 (d, 1 H, H-1^{I}), 4.28 (dd, 1 H), 4.16–4.09 (m, 2 H), 4.01 (m, 1 H, H-5), 4.00–3.75 (m, 2 H, CH_2=CH–CH_2O), 3.94–3.84 (m, 3 H), 3.67 (dd, 1 H), 3.62 (dd, 1 H, H-3^{III}) 3.38 (s, 3 H, CH_3O), 3.25 (m, 1 H, H-4^{I}). ^{13}C NMR ($CDCl_3$): δ 165.66, 165.49, 165.23, 165.19, 164.94, 164.85, 163.98, 163.76 (PhCO), 133.49, 132.87, 132.71, 132.64, 132.60, 132.55, 132.51, 132.40, 131.97, 129.71, 129.57, 129.49, 129.42, 129.40, 129.31, 129.27, 129.21, 129.18, 129.09, 129.06,

129.06, 129.03, 128.97, 128.89, 128.83, 128.79, 128.11, 128.07, 128.01, 127.98, 127.91, 127.83, 127.78, 127.74, 127.70, 127.64, 127.52, 117.08 (CH_2=CH–CH_2O), 101.17, 101.06, 100.83 (C-$1^{III, II, I}$), 77.07, 75.79, 75.24, 71.53, 71.16, 70.80, 70.74, 70.06, 69.73, 66.08, 62.08, 61.81, 61.72, 56.20 (CH_3O). Anal. Calcd for $C_{77}H_{68}O_{23}$: C, 67.94; H, 5.00. Found: C, 67.87; H, 5.07. **12**: $[\alpha]_D$ +74.0° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.09–6.99 (m, 40 H, PhH), 5.98 (d, 1 H, $J_{3,4}$ = 3.3 Hz, H-4^{III}), 5.74 (d, 1 H, $J_{3,4}$ = 3.2 Hz, H-4^{II}), 5.53 (dd, 1 H, $J_{2,3}$ = $J_{3,4}$ = 8.9 Hz, H-3^{I}), 5.51–5.39 (m, 1 H, CH_2=CH–CH_2O), 5.42–5.40 (m, 2 H), 5.19 (dd, 1 H, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.0 Hz, H-2^{III}), 5.12 (dd, 1 H, $J_{1,2}$ 7.2 Hz, $J_{2,3}$ 9.2 Hz, H-2^{I}), 5.01–4.87 (m, 2 H, CH_2=CH–CH_2O), 4.86 (d, 1 H, H-1^{III}), 4.74 (dd, 1 H), 4.54–4.41 (m, 4 H), 4.33 (dd, 1 H), 4.27 (dd, 1 H), 4.16–4.01 (m, 3 H), 4.01–3.76 (m, 2 H, CH_2=CH–CH_2O), 3.61 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-3^{III}), 3.42 (dd, 1 H), 3.38 (s, 3 H, CH_3O); ^{13}C NMR ($CDCl_3$): δ 165.74, 165.67, 165.44, 165.27, 164.72, 164.72, 1645.63, 163.92 (PhCO), 133.49, 132.76, 132.63, 132.37, 132.32, 131.87, 129.73, 129.64, 129.57, 129.44, 129.32, 129.21, 128.99, 128.96, 128.92, 128.80, 128.73, 128.20, 128.12, 128.04, 127.94, 127.89, 127.86, 127.82, 127.60, 127.47, 117.05 (CH_2=CH–CH_2O), 101.41, 101.13, 97.60 (C-1), 75.93, 74.78, 72.70, 72.39, 71.38, 70.98, 70.85, 70.74, 70.09, 69.59, 67.89, 66.17, 63.59, 63.41, 61.92, 56.10 (CH_3O). Anal. Calcd for $C_{77}H_{68}O_{23}$: C, 67.94; H, 5.00. Found: C, 67.78; H, 5.02.

Methyl 2,4,6-tri-O-*benzoyl-β*-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→4)-2,3-di*-O-*benzoyl-β*-D-*xylopyranoside* (**13**).—To a solution of **11** (1.36 g, 1.0 mmol) in anhyd CH_3OH (50 mL) was added $PdCl_2$ (0.1 g), and the mixture was stirred at 40 °C for 4 h, at the end of which time TLC (1:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was filtered, and the filtrate was concentrated. The residue was passed through a silica gel column with 1.5:1 petroleum ether–EtOAc as the eluent to give **13** as a syrup (1.19 g, 90%): $[\alpha]_D$ +9.1° (c 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.04–7.13 (m, 40 H, PhH), 5.81 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4^{III}), 5.62 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4^{II}), 5.57 (dd, 1 H, $J_{2,3}$ = $J_{3,4}$ = 7.5 Hz, H-3^{I}), 5.51 (dd, 1 H, $J_{1,2}$ 7.6 Hz, $J_{2,3}$ 10.0 Hz, H-2^{III}), 5.19 (dd, 1 H, $J_{1,2}$ 6.1 Hz, $J_{2,3}$ 7.8 Hz, H-2^{I}), 5.10 (dd, 1 H, $J_{1,2}$ 7.7 Hz, $J_{2,3}$ 10.0 Hz, H-2^{II}), 4.83 (d, 1 H, H-1^{III}), 4.69 (d, 1 H, H-1^{II}), 4.55 (dd, 1 H, H-3^{II}), 4.47 (d, 1 H, H-1^{I}), 4.28 (dd, 1 H), 4.21 (dd, 1 H, H-3^{III}), 4.07 (dd, 1 H, $J_{5,6}$ 4.7 Hz, $J_{6,6'}$ 11.8 Hz, H-6), 4.02 (m, 1 H, H-5^{III}), 3.94–3.85 (m, 4 H), 3.70 (dd, 1 H, $J_{4,5}$ 7.5 Hz, $J_{5,5'}$ 11.5 Hz, H-5^{I}), 3.39 (s, 3 H, CH_3O), 3.27 (m, 1 H, H-4^{I}); ^{13}C NMR ($CDCl_3$): δ 166.27, 166.01, 165.89, 165.80, 165.43, 165.29, 165.19, 164.26 (PhCO), 133.36, 133.23, 133.02, 132.94, 132.91, 132.89, 132.86, 130.00, 129.93, 129.82, 129.63, 129.53, 129.46, 129.28, 129.21, 128.80, 128.77, 128.47, 128.43, 128.38, 128.12, 127.99, 101.48, 101.18, 100.78 (C-1), 76.74, 75.69, 73.49, 71.80, 71.61, 71.59, 71.24, 71.11, 70.42, 70.03, 69.87, 62.27, 62.06, 61.95, 56.56 (CH_3O). Anal. Calcd for $C_{74}H_{64}O_{23}$: C, 67.27; H, 4.85. Found: C, 66.99; H, 4.82.

p-*Methoxyphenyl 2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranoside* (**15**).—To a solution of **5** (2.22 g, 2.0 mmol) in anhyd CH_3OH (50 mL) was added $PdCl_2$ (0.1 g), and the mixture was stirred at 40 °C for 4 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was filtered, and the filtrate was concentrated. The residue was passed through a silica gel column with 2:1 petroleum ether–EtOAc as the eluent to give **15** as a syrup (1.93 g, 90%): $[\alpha]_D$ +72.9° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.07–7.15 (m, 30 H, PhH), 6.82 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$–), 6.55 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$–), 5.98 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4^{II}), 5.85 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 9.8 Hz, H-2^{II}), 5.65 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4^{I}), 5.16 (dd, 1 H, $J_{1,2}$ 7.7 Hz, $J_{2,3}$ 9.8 Hz, H-2^{I}), 4.95 (d, 1 H, H-1^{II}), 4.92 (d, 1 H, H-1^{I}), 4.65–4.56 (m, 2 H), 4.47 (dd, 1 H), 4.34–4.30(m, 2 H), 4.16–4.07 (m, 2 H), 3.92 (m, 1 H), 3.67 (s, 3 H, CH_3O); Anal. Calcd for $C_{61}H_{52}O_{18}$: C, 68.28; H, 4.85. Found: C, 68.50; H, 4.89.

p-*Methoxyphenyl (methyl 2,3,4-tri*-O-*acetyl-β*-D-*glucopyranosyluronate)-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranoside* (**16**).—A mixture of **14** (0.96 g, 2.0 mmol) and **15** (2.14 g, 2.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (40 mL). TMSOTf (60 μL, 0.16 equiv) was added dropwise at −25 °C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the mixture was gradually warmed to ambient temperature. Then the mixture was neutralized with Et_3N, concentrated and purified by column chromatography (1:1 petroleum ether–EtOAc) to afford **16** (1.53 g, 55%) as foamy solid: $[\alpha]_D$ +43.6° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.11–7.15 (m, 30 H, PhH), 6.77 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$), 6.52 (d, 2 H, *J* 9.1 Hz, $CH_3OC_6H_4O$), 5.92 (d, 1 H, $J_{3,4}$ 3.6 Hz, H-4^{II}), 5.78 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 9.7 Hz, H-2^{II}), 5.72 (d, 1 H, $J_{3,4}$ 3.4 Hz, H-4^{I}), 5.41 (dd, 1 H, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 9.9 Hz, H-2^{I}), 5.07 (dd, 1 H, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz, H-4^{III}), 4.88 (d, 1 H, H-1^{II}), 4.84 (d, 1 H, H-1^{I}), 4.82 (dd, 1 H, H-3^{III}), 4.65 (dd, 1 H, $J_{1,2}$ 7.5 Hz, $J_{2,3}$ 9.5 Hz, H-2^{III}), 4.58–4.35 (m, 4 H), 4.50 (d, 1 H, H-1^{III}), 4.24 (dd, 1 H, H-3^{II}), 4.10–4.03 (m, 3 H), 3.80 (d, 1 H, H-5^{III}), 3.65 (s, 3 H, CH_3O), 3.63 (s, 3 H, CH_3O), 1.91 (s, 3 H, CH_3CO), 1.80 (s, 3 H, CH_3CO), 1.34 (s, 3 H, CH_3CO); ^{13}C NMR ($CDCl_3$): δ 169.43, 168.48, 168.09 ($3CH_3CO$), 166.28 (–CO_2CH_3), 165.63, 165.51, 165.32, 164.93, 164.03, 163.56 (PhCO), 155.09, 150.81

($CH_3OC_6H_4O$–), 132.71, 132.63, 132.58, 132.53, 132.51, 132.35, 129.70, 129.65, 129.41, 129.38, 129.18, 129.07, 128.96, 128.93, 128.78, 128.05, 127.91, 127.87, 127.77, 118.29, 113.86 ($CH_3OC_6H_4O$–), 100.85, 100.62, 100.19 (C-$1^{III,\ II,\ I}$), 72.10, 71.77, 71.48, 71.42, 71.15, 70.97, 70.31, 69.65, 69.05, 68.60, 62.65, 61.99, 55.05, 52.23 (2 CH_3O), 19.86, 19.86, 19.06 (3 CH_3CO). Anal. Calcd for $C_{74}H_{68}O_{27}$: C, 63.98; H, 4.90. Found: C, 63.79; H, 4.95.

(Methyl 2,3,4-tri-O-*acetyl-β*-D-*glucopyranosyluronate)-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl-α*-D-*galactopyranosyl trichloroacetimidate* (**17α**) *and (methyl 2,3,4-tri*-O-*acetyl-β*-D-*glucopyranosyluronate)-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl trichloroacetimidate* (**17β**).—To a solution of **16** (1.39 g, 1.0 mmol) in 4:1 CH_3CN–H_2O (50 mL) was added CAN (4.39 g, 8.0 mmol), and the mixture was stirred at rt for 30 min, at the end of which time TLC (1:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was extracted with EtOAc, and the extract was washed with water. The organic layer was concentrated under reduced pressure, and the crude product was purified by column chromatography (1:1 petroleum ether–EtOAc) to afford a solid. To a solution of the solid in CH_2Cl_2 (20 mL) were added trichloroacetonitrile (0.5 mL) and anhyd potassium carbonate (1.0 g). The reaction mixture was stirred overnight at rt and then filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (1:1 petroleum ether–EtOAc) to give **17α** (0.29 g, 20%) and **17β** (0.71 g, 50%), respectively, as syrups: **17α**: $[\alpha]_D$ +65.4° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.44 (s, 1 H, NH), 8.11–7.07 (m, 30 H, PhH), 6.66 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1^I); Anal. Calcd for $C_{69}H_{62}Cl_3NO_{26}$: C, 58.04; H, 4.35. Found: C, 57.83; H, 4.36. **17β**: $[\alpha]_D$ +49.3° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.54 (s, 1 H, NH), 8.08–7.15 (m, 30 H, PhH), 5.89 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1^I); Anal. Calcd for $C_{69}H_{62}Cl_3NO_{26}$: C, 58.04; H, 4.35. Found: C, 57.78; H, 4.39.

Methyl (methyl 2,3,4-tri-O-*acetyl-β*-D-*glucopyranosyluronate)-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→4)-2,3-di*-O-*benzoyl-β*-D-*xylopyranoside* (**18**) *and methyl (methyl 2,3,4-tri*-O-*acetyl-α*-D-*glucopyranosyluronate)-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→3)-2,4,6-tri*-O-*benzoyl-β*-D-*galactopyranosyl-(1→4)-2,3-di*-O-*benzoyl-β*-D-*xylopyranoside* (**19**).—A mixture of **14** (0.24 g, 0.5 mmol) and **13** (0.66 g, 0.5 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (20 mL). TMSOTf (30 μL, 0.31 equiv) was added dropwise at −25 °C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the mixture was gradually warmed to ambient temperature. Then the mixture was neutralized with Et_3N, concentrated and purified by column chromatography (1:1 petroleum ether–EtOAc) to afford **18** (0.25 g, 31%), and **19** (0.25 g, 31%), respectively, as foamy solids. Alternatively, donor **17** (0.71 g, 0.5 mmol) and acceptor **10** (0.19 g, 0.5 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (20 mL). TMSOTf (30 μL, 0.31 equiv) was added dropwise at −25 °C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the mixture was gradually warmed to ambient temperature. Then the mixture was neutralized with triethylamine, concentrated and purified by column chromatography (1:1 petroleum ether–EtOAc) to afford **18** (0.33 g, 40%) as foamy solid: **18**: $[\alpha]_D$ +23.7° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.05–7.11 (m, 40 H, PhH), 5.76 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4^{III}), 5.69 (d, 1 H, $J_{3,4}$ 3.4 Hz, H-4^{II}), 5.53 (dd, 1 H, $J_{2,3} = J_{3,4} = 7.7$ Hz, H-3^I), 5.45 (dd, 1 H, $J_{1,2}$ 8.2 Hz, H-2^{III}), 5.35 (dd, 1 H, $J_{1,2}$ 7.5 Hz, H-2^{II}), 5.16 (dd, 1 H, $J_{1,2}$ 6.1 Hz, H-2^I), 5.06 (dd, 1 H, $J_{2,3} = J_{3,4} =$ 9.4 Hz, H-3^{IV}), 4.81 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.4$ Hz, H-4^{IV}), 4.75 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1^{IV}), 4.63 (dd, 1 H, H-2^{IV}), 4.62 (d, 1 H, H-1^{III}), 4.48 (d, 1 H, H-1^{II}), 4.44 (d, 1 H, H-1^I), 4.44 (m, 1 H), 4.34 (m, 1 H), 4.14–3.98 (m, 4 H), 3.88–3.79 (m, 3 H), 3.79 (d, 1 H, H-5^{IV}), 3.65 (dd, 1 H), 3.62 (s, 3 H, CH_3O), 3.38 (s, 3 H, CH_3O), 3.21 (m, 1 H), 1.91 (s, 3 H, CH_3CO), 1.80 (s, 3 H, CH_3CO), 1.32 (s, 3 H, CH_3CO); ^{13}C NMR ($CDCl_3$): δ 169.89, 168.93, 168.51, 166.64, 165.97, 165.79, 165.36, 165.25, 165.25, 165.17, 164.05, 163.85 (–CO–), 133.15, 132.98, 132.90, 132.72, 129.99, 129.81, 129.67, 129.59, 129.53, 129.25, 129.14, 128.74, 128.70, 128.42, 128.29, 128.25, 128.12, 127.97, 101.41, 101.16, 101.09, 100.51 (C-1), 75.60, 72.34, 71.82, 71.74, 71.69, 71.59, 71.33, 71.08, 70.54, 70.37, 69.91, 69.29, 68.84, 68.05, 62.27, 62.21, 62.02, 56.54, 52.65 (CH_3O), 20.30, 20.30, 19.42 (CH_3CO). Anal. Calcd for $C_{87}H_{80}O_{32}$: C, 63.81; H, 4.89. Found: C, 63.52; H, 4.91. **19**: $[\alpha]_D$ +22.8° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.02–7.11 (m, 40 H, PhH), 5.79 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4^{III}), 5.71 (dd, 1 H, $J_{3,4}$ 3.4 Hz, H-4^{II}), 5.54 (dd, 1 H, $J_{2,3} = J_{3,4} = 7.6$ Hz, H-3^I), 5.48–5.43 (m, 3 H), 5.39 (dd, 1 H, $J_{1,2}$ 8.0 Hz, H-2^{II}), 5.26 (s, 1 H, H-4^{IV}), 5.17 (dd, 1 H, $J_{1,2}$ 6.1 Hz, $J_{2,3}$ 7.9 Hz, H-2^I), 4.81 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1^{III}), 4.68 (d, 1 H, H-1^{II}), 4.55 (dd, 1 H), 4.44 (d, 1 H, H-1^I), 4.21–4.16 (m, 3 H), 4.11–4.05 (dd, 1 H), 4.09 (m, 1 H, H-5), 3.94–3.73 (m, 5 H), 3.66 (dd, 1 H), 3.62 (s, 3 H, CH_3O), 3.38 (s, 3 H, CH_3O), 3.23 (dd, 1 H), 1.74 (s, 3 H, CH_3CO), 1.61 (s, 6 H, CH_3CO); ^{13}C NMR ($CDCl_3$): δ 169.44, 168.24, 168.18, 165.80, 165.80, 165.80, 165.47, 165.47, 165.27, 165.17, 164.10, 163.95 (–CO–), 133.32, 133.24, 133.00, 132.94, 132.86, 132.32, 130.01, 129.95, 129.81, 129.65, 129.62, 129.53, 129.47, 129.31, 129.26, 129.15, 129.02, 128.77, 128.70, 128.48, 128.42, 128.31, 128.11, 127.98, 127.78, 101.40, 101.40, 101.17, 89.66 (C-1), 75.60, 73.12, 71.77, 71.52, 71.12, 71.01, 70.40, 70.03, 69.92, 67.39, 65.23, 65.06, 62.30, 62.05, 61.64,

56.54, 52.27 (CH_3O), 20.46, 20.46, 20.28 (CH_3CO). Anal. Calcd for $C_{87}H_{80}O_{32}$: C, 63.81; H, 4.89. Found: C, 63.70; H, 4.92.

Methyl (β-D-glucopyranosyluronic acid)-(1→3)-β-D-galactopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-β-D-xylopyranoside, sodium salt (**20**).—Compound **18** (0.20 g, 0.12 mmol) was treated with NaOH (3 mL, 3 M, aq in methanol–water (5:1, 6 mL)) overnight at rt. The reaction mixture was neutralized with Dowex 50 (H^+) and concentrated. The residue was dissolved in water and passed through a column of Dowex 50 (Na^+). The elute was concentrated, and purified on a BioGel P2 column, using water as eluent, affording compound **20** as a foam (66 mg, 80%): $[\alpha]_D$ +4.6° (*c* 1.1, H_2O): ^1H NMR (D_2O): δ 4.56 (m, 2 H, H-1^{IV}, H-1^{III}), 4.41 (m, 2 H, H-1^{II}, H-1^{I}), 4.23–3.98 (m, 5 H), 3.78–3.40 (m, 13 H), 3.43 (s, 3 H, CH_3O), 3.34–3.19 (m, 3 H); ^{13}C NMR (D_2O): δ 175.35 (–CO_2Na), 103.81, 103.75, 103.35, 101.43 (C-$1^{IV,\ III,\ II,\ I}$), 82.84, 81.98, 76.57, 75.90, 75.41, 74.85, 74.71, 73.93, 73.22, 72.73, 71.72, 70.20, 69.79, 68.39, 68.02, 62.90, 60.97, 60.93, 57.03 (CH_3O). ESIMS (negative-ion): Calcd for $C_{24}H_{39}O_{21}Na$, [M] 686.2; Found: [M + Na] 663.1.

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