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Synthesis of a Pentasaccharide Fragment of Varianose, a Cell Wall Polysaccharide from *Penicillium varians*

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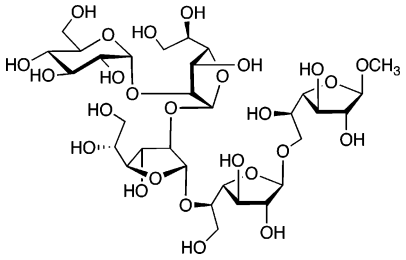

The first synthesis of an oligosaccharide fragment of varianose, a polysaccharide produced by *Penicillium varians*, is reported. The target pentasaccharide features both α- and *β*-galactofuranoside residues and the α-galactofuranoside residue is hindered, being substituted on adjacent oxygens (O1 and O2), both of which are cis to the two-carbon side chain at C4. Key features of the synthesis include a novel method for the selective protection of the C3 hydroxyl group of galactofuranosyl residues via an epoxide formation/opening sequence, the introduction of the α-D-galactofuranosyl residue using a 2,3-anhydrosugar donor, and the use of the 1-benzenesulfinylpiperidine/trifluoromethanesulfonic anhydride activation method for the addition of an α-D-glucopyranosyl residue to a hindered hydroxyl group in an advanced tetrasaccharide intermediate.

Introduction

Varianose, a cell wall polysaccharide produced by *Penicillium varians*, was first described in 1935 by Haworth et al., who demonstrated that this glycan contained D-glucose, D-galactose, and an unidentified sugar suggested to be either L-altrose or D-idose.[1] Subsequent studies by Jansson and Lindberg showed that this unidentified sugar was D-mannose and that the major component of this heterogeneous complex polysaccharide was a glucogalactan.[2] Through the use of methylation analysis, NMR spectroscopy, and degradation studies, the structure of this glucogalactan was established to have a backbone of alternating *β*-(1→5)- and *β*-(1→6)-D-galactofuranose (D-Gal*f*) residues. Attached to the O2 of the *β*-(1→5)-linked residue of this core is a disaccharide side chain consisting of D-glucopyranose (D-Glc*p*) attached α-(1→2) to an α-D-Gal*f* moiety. Thus, the repeating unit is that shown in Figure 1. This polysaccharide has some interesting structural features, for example, the presence of both α- and *β*-Gal*f* residues as well as a hindered α-D-Gal*f* residue that is substituted on adjacent oxygens (O1 and O2), both of which are cis to the two-carbon side chain appended at C4. In the time since this initial structural work, polysaccharides containing this repeating unit have been identified in other fungi including additional penicillium species as well as a number of talaromyces strains.[3]

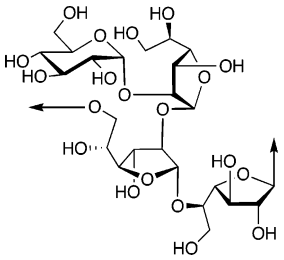

FIGURE 1. Repeating unit of varianose.

Despite the novel structural features present in this glycan and the occurrence of this structural motif in a range of

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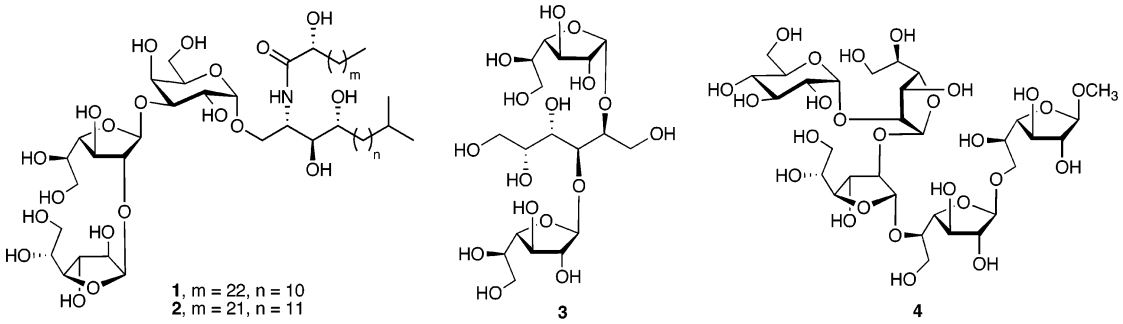
CHART 1

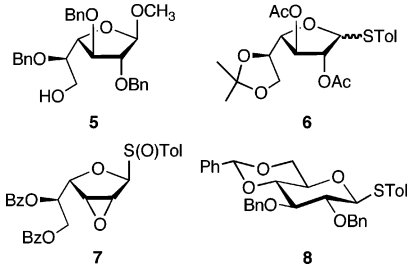


polysaccharides, to date there have been no reports on the synthesis of oligosaccharides related to varianose. The absence of synthetic activity in this area is likely due to the paucity of methods available for the stereoselective synthesis of α-D-Gal*f* bonds. These 1,2-*cis*-furanosides are stereochemically equivalent to *β*-arabinofuranosides[4] but have received far less synthetic attention.[5−7] Indeed, only very recently have reports appeared describing the synthesis of naturally occurring glycoconjugates containing α-D-Gal*f* residues.[8,9] Examples include two immunomodulatory glycolipids (**1** and **2**, Chart 1) that contain single α-D-Gal*f* moieties[8] and a trisaccharide (**3**)[9] produced upon reductive *β*-elimination of *Bacteroides cellulosolvens* glycoproteins. Other recent papers have reported studies on the stereocontrolled synthesis of oligosaccharides containing D-fucofuranose (6-deoxy-D-galactofuranose) residues.[10] In the course of other investigations, we needed to prepare pentasaccharide **4**, which consists of the repeating unit of varianose, plus an additional main-chain Gal*f* residue. We describe here the synthesis of **4** via a route that employs, as a key step, the 2,3-anhydrosugar methodology developed in our laboratory.[11,12]

Results and Discussion

In designing a route to **4**, we envisioned that it could be synthesized in a stepwise manner starting from the four monosaccharides shown in Chart 2. Methyl glycoside **5** would be the precursor to the "reducing" end residue and thioglycoside **6** would serve as the source of the other two *β*-D-Gal*f* residues. The remaining two building blocks, glycosyl sulfoxide **7** and thioglycoside **8**, would provide the α-D-Gal*f* and α-D-Glc*p* residues, respectively.

CHART 2



The preparation of **5** and **6** is shown in Scheme 1; **7** and **8** were synthesized as previously reported.[11,13] Starting from a 1:10 α/*β* mixture of **9**, treatment with sodium methoxide cleaved the acetate esters yielding a tetrol that was first tritylated and then benzylated under conventional conditions to afford **10**, which could be separated from its α-glycoside counterpart. The overall yield for this process was high, giving **10** in 76% yield over the three steps. A subsequent reaction of **10** with *p*-toluenesulfonic acid in a mixture of dichloromethane and methanol gave **5** in 85% yield. Thioglycoside **6** was synthesized in two steps and in 84% overall yield from the known thioglycoside **11**,[11] first by a reaction with dimethoxypropane and *p*-toluenesulfonic acid in acetone, then followed by acetylation.

Once synthesized, the building blocks could be assembled into the pentasaccharide. As illustrated in Scheme 2, reaction of alcohol **5** with thioglycoside **6** in the presence of *N*-iodosuccinimide and silver triflate (NIS/AgOTf)[14] afforded disaccharide **12** in 94% yield. Looking ahead to the eventual need to use a base-promoted opening of a 2,3-anhydrosugar residue (vide infra), the acetate esters in **12** were exchanged with benzyl ethers first by deacylation (sodium methoxide in methanol) and then benzylation (benzyl bromide, sodium hydride in DMF). The product, **13**, was obtained in excellent overall yield, 96%. The acetal in **13** was then hydrolyzed to give **14**, the primary hydroxyl group of which was protected as a benzyl ether using a two-step process involving the formation of a stannylidene acetal and its alkylation with benzyl bromide.[15] The desired product, **15**, was isolated in 78% yield, together with 9% of the 5-*O*-benzyl ether regioisomer. The position of the benzyl group in **15** could be readily discerned from its ^{13}C NMR spectrum. The signal for C6 of the non-reducing end

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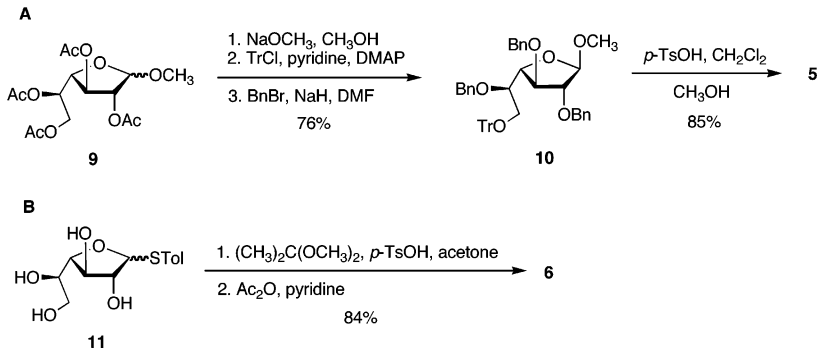
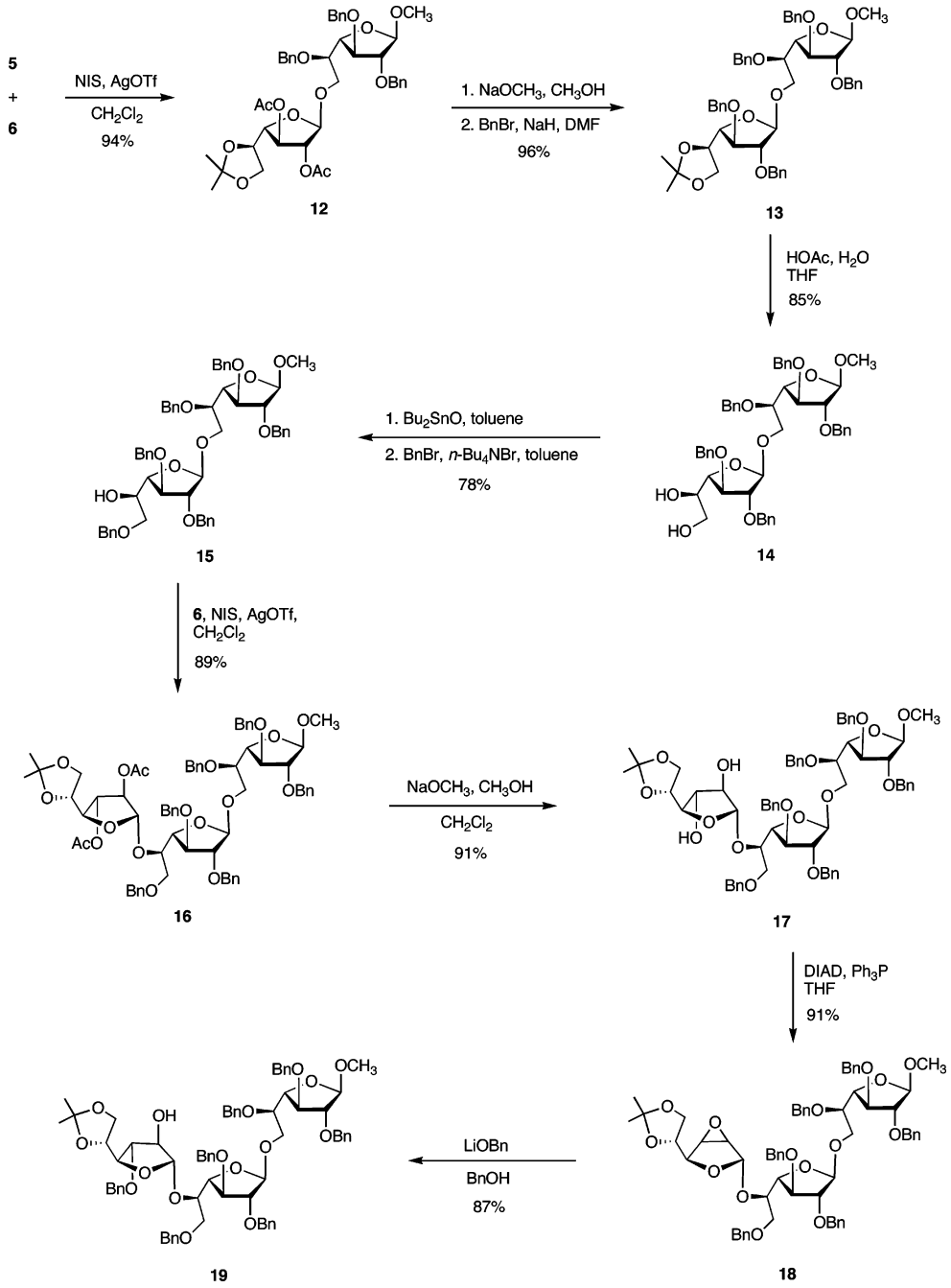
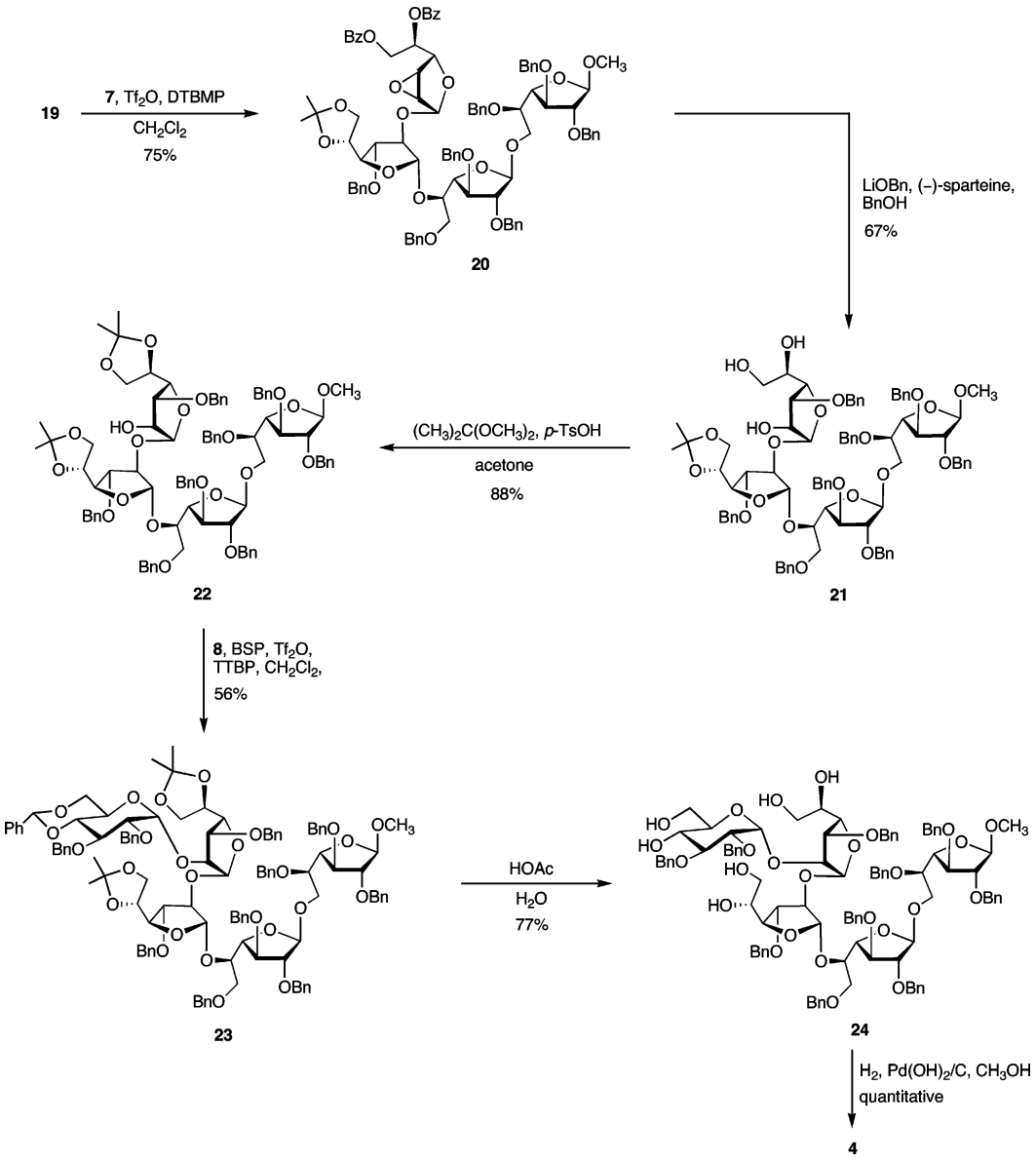
SCHEME 1



SCHEME 2



SCHEME 3



residue was found at 71.5 ppm, which is shifted downfield from this resonance in **14** (64.4 ppm), as would be expected upon alkylation.[16]

With alcohol **15** in hand, its NIS/AgOTf-promoted coupling with thioglycoside **6** afforded trisaccharide **16**, which was subsequently deacylated giving **17** in 81% yield over the two steps. Next, we needed to selectively protect the O3 of the terminal Gal*f* residue in **17**. While protocols for differentiating these hydroxyl groups have been reported,[10] we explored an alternate approach in which the diol was first converted to an epoxide which was, in turn, regioselectively opened with lithium benzylate. Thus, **17** was subjected to a Mitsunobu reaction with DIAD and triphenylphosphine, which afforded the corresponding epoxide **18** in excellent (91%) yield. The presence of the 2,3-anhydrosugar residue in **18** was easily discernible by the presence of two signals in its ^{13}C NMR spectrum, at 55.7 and 53.7 ppm, corresponding to C2 and C3, respectively. The stereochemistry of the epoxide was determined from the $^{1}J_{C1,H1}$ of the 2,3-anhydrosugar residue, which was 176 Hz, clearly indicating the cis orientation of the epoxide and anomeric hydrogen.[11,17] Treatment of **18** with lithium benzylate gave alcohol **19** in 87% yield. The regioselectivity of the epoxide opening was established on the basis of the chemical shift of the anomeric carbon resonance (109.0 ppm) and the $^{3}J_{H1,H2}$ (0 Hz), both of which support the *β*-D-*galacto* configuration of the monosaccharide at the non-reducing end of **19**.[18] The high selectivity in the opening of the epoxide moiety in **18** is presumably due to steric hindrance from the anomeric substituent, which prohibits attack of the nucleophile at C2.[19]

Having in place a robust method for the synthesis of trisaccharide **19**, the introduction of the α-D-Gal*f* residue was achieved in two steps using glycosyl sulfoxide **7** (Scheme 3).

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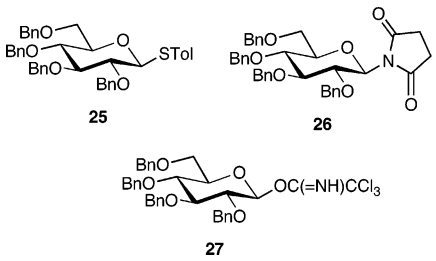
CHART 3



First, glycosylation of **19** with **7** promoted by trifluoromethanesulfonic anhydride (Tf_2O) yielded the expected tetrasaccharide, **20**, in 75% yield. None of the corresponding β-glycoside was detected by TLC. The magnitude of the $^1J_{C1,H1}$ for the 2,3-anhydrosugar was 167 Hz, which establishes the α-stereochemistry of this residue.[11] Opening of the epoxide ring in **20** using lithium benzylate and (−)-sparteine[11,12] proceeded to give a 67% yield of the expected product, **21**, in addition to an 11% yield of the isomer with the D-idofuranose stereochemistry, arising from nucleophilic attack at C2. Protection of O5 and O6 in **21** as an isopropylidene acetal was straightforward, and an 88% yield of tetrasaccharide alcohol **22** was obtained.

While all of the glycosylations leading to **22** could be carried out in good yield and without difficulty, the introduction of the final residue, an α-D-Glc*p* moiety, was more challenging. The C2 hydroxyl group of the α-D-Gal*f* residue in **22** is very hindered, being cis not only to the aglycone on the adjacent carbon but also to the isopropylidene-protected 1,2-dihydroxyethyl side chain attached at C4. Our initial attempts to glycosylate the alcohol in **22** with a fully benzylated thioglycoside donor (**25**,[20] Chart 3) using NIS/AgOTf activation failed, yielding only unreacted **22** and hydrolyzed donor together with the glycosyl-succinimide byproduct **26**.[21] Similar adducts have previously been reported in glycosylations promoted by NIS,[21,22] and these byproducts are usually observed when acceptors of low reactivity are used. We also considered the use of imidate **27**[23] for the introduction of the Glc*p* residue. However, a series of model reactions were not promising, and on the basis of previous studies,[11] we had concerns about the stability of the isopropylidene acetals in **22** to the acidic conditions required for imidate activation. Finally, we explored the 1-benzenesulfinylpiperidine (BSP)/Tf_2O activation method for thioglycosides reported by Crich and Smith.[24] Particularly attractive features of the method are the basic reaction conditions and the potent activating power of this reagent combination. With these considerations in mind, reaction of thioglycoside **8**, which had previously been shown to be a highly α-selective glucosylating agent,[24] with BSP/Tf_2O afforded the desired pentasaccharide **23** in 56% yield. While this is not an exceptional yield, it is respectable considering the highly hindered nature of the acceptor. The α-stereochemistry of the Glc*p* residue was established by the $^3J_{H1,H2}$ which was 3.6 Hz. Deprotection of **23** to provide the target **4** was uneventful and could be achieved in two steps and in 77% overall yield first by cleavage of the acetal-protecting groups under acidic conditions (yielding **24**) and then by hydrogenolysis of the benzyl ethers over Pearlman's catalyst. The NMR data for **4** was in excellent agreement with that reported for the polysaccharide from *Talaromyces flavus*.[3a]

In summary, we describe here the first synthesis of an oligosaccharide fragment of varianose, a polysaccharide produced by *Penicillium varians*; glycans of identical structure have also been identified in a number of other organisms. Key features of the synthesis include a novel method for the selective protection of the C3 hydroxyl group of Gal*f* residues through an epoxide formation/opening sequence, the introduction of the α-D-Gal*f* residue using the 2,3-anhydrosugar methodology, and the use of the BSP/Tf_2O activation method for the addition of an α-D-Glc*p* residue onto a highly hindered hydroxyl group in tetrasaccharide **22**.

Experimental Section

Methyl α-D-Glucopyranosyl-(1→2)-α-D-galactofuranosyl-(1→2)-β-D-galactofuranosyl-(1→5)-β-D-galactofuranosyl-(1→6)-β-D-galactofuranoside (4). To a solution of compound **24** (14 mg, 0.008 mmol) in CH_3OH (2 mL) was added 20% $Pd(OH)_2$ on carbon (5 mg), and the reaction mixture was stirred under a hydrogen atmosphere for 24 h. The mixture was filtered through Celite and then concentrated to yield **4** (6.8 mg, 100%) as a white foam. R_f 0.53 (100% CH_3OH); $[\alpha]_D$ +1.9 (*c* 0.5, H_2O); ^{1}H NMR (600 MHz, D_2O, δ_H) 5.37 (d, 1H, J = 4.3 Hz, H-1D), 5.32 (s, 1H, H-1C), 5.01 (s, 1H, H-1B), 4.99 (d, 1H, J = 3.6 Hz, H-1E), 4.91 (s, 1H, H-1A), 4.36 (dd, 1H, J = 8.0, 7.9 Hz), 4.28−4.22 (m, 3H), 4.13−4.10 (m, 2H), 4.09−4.04 (m, 4H), 3.99−3.93 (m, 3H), 3.88−3.60 (m, 15H), 3.55 (dd, 1H, J = 10.0, 3.7 Hz), 3.44 (dd, 1H, J = 9.6, 9.4 Hz), 3.41 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, D_2O, δ_C) 109.0 (C-1A), 108.6 (C-1B), 106.7 (C-1C), 99.7 (C-1D), 98.2 (C-1E), 87.8, 83.9, 82.7, 82.3, 81.9 (× 2), 81.6, 80.6, 77.6, 77.55, 77.1, 75.6, 73.7, 73.4, 73.3, 72.9, 72.1, 71.0, 70.5, 70.3, 70.0, 63.7, 63.1, 62.3, 61.3, 55.8 (OCH_3). HRMS (ESI): [M + Na] calcd for $C_{31}H_{54}O_{26}Na$, 865.2796; found, 865.2795.

Methyl 2,3-Di-*O*-acetyl-5,6-*O*-isopropylidene-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (12). To a mixture of **5** (790 mg, 1.7 mmol), **6** (770 mg, 1.9 mmol), and 4 Å molecular sieves (0.5 g) in CH_2Cl_2 (50 mL) was added NIS (534 mg, 2.25 mmol) followed by AgOTf (146 mg, 0.56 mmol) at 0 °C. After stirring for 20 min at 0 °C, the solution turned dark red, and Et_3N was added. The mixture was then diluted with CH_2Cl_2 (50 mL) and filtered through Celite. The filtrate was washed with a saturated aq $Na_2S_2O_3$ soln (3 × 50 mL), dried (Na_2SO_4), and concentrated to give a crude residue that was purified by chromatography (3:1 hexanes/EtOAc) to afford **12** (1.24 g, 94%) as a colorless oil. R_f 0.25 (2:1 hexanes/EtOAc); $[\alpha]_D$ −86.2 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.38−7.21 (m, 15H, Ar), 5.08 (s, 1H, H-1B), 5.06 (d, 1H, J = 1.3 Hz, H-2B), 5.02 (dd, 1H, J = 4.8, 1.3 Hz, H-3B), 4.95 (s, 1H, H-1A), 4.69 (d, 1H, J = 11.7 Hz, PhCH_2), 4.56 (d, 1H, J = 11.9 Hz, PhCH_2), 4.51 (d, 1H, J = 11.7 Hz, PhCH_2), 4.47 (d, 1H, J = 11.9 Hz, PhCH_2), 4.46 (d, 1H, J = 11.7 Hz, PhCH_2), 4.33 (ddd, 1H, J = 6.7, 6.1, 6.1 Hz, H-5B), 4.31 (d, 1H, J = 11.7 Hz, PhCH_2), 4.12−4.08 (m, 2H, H-4A, H-4B), 4.04 (dd, 1H, J = 8.6, 6.7 Hz, H-6B), 4.01 (dd, 1H, J = 7.2, 3.3 Hz, H-3A), 3.96−3.94 (m, 1H, H-2A), 3.94 (dd, 1H, J = 10.1, 5.2 Hz, H-6A), 3.85 (dd, 1H, J = 8.6, 6.1 Hz, H-6B), 3.78−3.74 (m, 1H, H-5A), 3.67 (dd, 1H, J = 10.1, 7.0 Hz, H-6A), 3.35 (s, 3H, OCH_3), 2.08 (s, 3H, acyl CH_3), 2.06 (s, 3H, acyl CH_3), 1.43 (s, 3H, isopropylidene CH_3), 1.37 (s, 3H, isopropylidene CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 170.1 (C═O), 169.6 (C═O), 138.3 (Ar), 137.8 (Ar), 137.7 (Ar), 128.4 (Ar), 128.33 (Ar), 128.3 (Ar), 128.27 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.7 (Ar), 109.9

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(isopropylidene C), 107.2 (C-1A), 105.6 (C-1B), 88.4 (C-2A), 82.9 (C-4B), 82.6 (C-3A), 81.3 (C-2B), 80.5 (C-4A), 77.0 (C-3B), 75.9 (C-5A), 75.3 (C-5B), 73.4 (PhCH$_2$), 72.1 (PhCH$_2$), 71.9 (PhCH$_2$), 67.3 (C-6A), 65.5 (C-6B), 54.9 (OCH$_3$), 26.3 (isopropylidene CH$_3$), 25.2 (isopropylidene CH$_3$), 20.8 (acyl CH$_3$ × 2). HRMS (ESI): [M + Na] calcd for $C_{41}H_{50}O_{13}Na$, 773.3144; found, 773.3147.

Methyl 2,3-Di-*O*-benzyl-5,6-*O*-isopropylidene-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (13). To a solution of **12** (1.2 g, 1.6 mmol) in CH$_3$OH (15 mL) and CH$_2$Cl$_2$ (15 mL) was added NaOCH$_3$ until the pH of the solution was ∼10. The mixture was stirred for 12 h, neutralized by the addition of HOAc, and then concentrated. The crude was dissolved in DMF (20 mL), and the solution was cooled to 0 °C before NaH (0.19 g, 4.8 mmol) and BnBr (0.5 mL, 4.0 mmol) were added. The solution was then stirred for 12 h at rt, and then the reaction was quenched by the addition of CH$_3$OH. Dilution of the mixture with CH$_2$Cl$_2$ (50 mL) provided a solution that was then washed with a saturated aq NaHCO$_3$ solution (3 × 30 mL). The organic layer was subsequently dried (Na$_2$SO$_4$) and concentrated, and the residue was purified by chromatography (8:1 hexanes/EtOAc) to give **13** (1.3 g, 96%) as a light yellow oil. R_f 0.29 (8:1 hexanes/EtOAc); $[\alpha]_D$ −63.2 (*c* 1.7, CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$, δ_H) 7.39−7.23 (m, 25H, Ar), 5.13 (s, 1H, H-1B), 4.98 (s, 1H, H-1A), 4.78 (d, 1H, *J* = 11.7 Hz, PhC*H*$_2$), 4.60−4.54 (m, 3H, PhC*H*$_2$), 4.51−4.44 (m, 5H, PhC*H*$_2$), 4.33 (d, 1H, *J* = 11.7 Hz, PhC*H*$_2$), 4.22 (ddd, 1H, *J* = 6.8, 6.8, 6.7 Hz, H-5B), 4.11−4.07 (m, 2H, H-4A, H-4B), 4.06−4.04 (m, 1H, H-2B), 4.04 (dd, 1H, *J* = 7.2, 3.0 Hz, H-3A), 4.00 (dd, 1H, *J* = 10.4, 3.9 Hz, H-6A), 4.00−3.98 (m, 1H, H-2A), 3.90 (dd, 1H, *J* = 8.2, 6.7 Hz, H-6B), 3.87−3.80 (m, 3H, H-6B, H-5A, H-3B), 3.75 (dd, 1H, *J* = 10.4, 7.7 Hz, H-6A), 3.37 (s, 3H, OCH$_3$), 1.44 (s, 3H, isopropylidene CH$_3$), 1.38 (s, 3H, isopropylidene CH$_3$); ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 138.5 (Ar), 137.8 (Ar), 137.7 (Ar), 137.5 (Ar), 137.4 (Ar), 128.6 (Ar), 128.5 (Ar), 128.4 (Ar), 128.38 (Ar), 128.3 (Ar), 128.25 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.85 (Ar), 127.8 (Ar), 127.6 (Ar), 109.7 (isopropylidene C), 107.0 (C-1A), 106.6 (C-1B), 88.3 (C-2A), 87.9 (C-2B), 84.1 (C-3B), 82.9 (C-3A), 82.0 (C-4B), 80.8 (C-4A), 76.4 (C-5B), 76.2 (C-5A), 73.6 (PhCH$_2$), 72.2 (PhCH$_2$ × 2), 72.0 (PhCH$_2$), 71.8 (PhCH$_2$), 68.9 (C-6A), 65.4 (C-6B), 54.8 (OCH$_3$), 26.5 (isopropylidene CH$_3$), 25.4 (isopropylidene CH$_3$). HRMS (ESI): [M + Na] calcd for $C_{51}H_{58}O_{11}Na$, 869.3871; found, 869.3876.

Methyl 2,3-Di-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (14). A solution of compound **13** (190 mg, 0.22 mmol) in 50% HOAc (6 mL, 3:2:1 HOAc/H$_2$O/THF) was stirred for 10 h at 50 °C. The solution was then concentrated, and the product was purified by chromatography (3:2 hexanes/EtOAc) to give **14** (153 mg, 85%) as a colorless syrup. R_f 0.25 (1:1 hexanes/EtOAc); $[\alpha]_D$ −67.5 (*c* 0.9, CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$, δ_H) 7.40−7.25 (m, 25H, Ar), 5.07 (s, 1H, H-1B), 4.97 (s, 1H, H-1A), 4.73 (d, 1H, *J* = 11.7 Hz, PhC*H*$_2$), 4.61−4.45 (m, 8H, PhC*H*$_2$), 4.34 (d, 1H, *J* = 11.7 Hz, PhC*H*$_2$), 4.14−4.10 (m, 2H, H-4A, H-4B), 4.08 (dd, 1H, *J* = 6.6, 2.7 Hz, H-3B), 4.04−4.02 (m, 1H, H-2B), 4.01 (dd, 1H, *J* = 6.9, 3.0 Hz, H-3A), 3.98 (d, 1H, *J* = 3.0, H-2A), 3.89 (dd, 1H, *J* = 10.4, 4.1 Hz, H-6A), 3.81−3.74 (m, 2H, H-5A, H-5B), 3.69 (dd, 1H, *J* = 10.4, 7.5 Hz, H-6A), 3.70−3.61 (m, 2H, H-6B × 2), 3.38 (s, 3H, OCH$_3$); ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 138.4 (Ar), 137.8 (Ar), 137.6 (Ar), 137.5 (Ar), 137.2 (Ar), 128.5 (Ar), 128.48 (Ar), 128.42 (Ar), 128.4 (Ar), 128.3 (Ar), 128.14 (Ar), 128.1 (Ar), 128.0 (Ar), 127.94 (Ar), 127.9 (Ar), 127.83 (Ar), 127.8 (Ar), 127.6 (Ar), 107.1 (C-1A), 106.9 (C-1B), 88.2 (C-2A), 87.5 (C-2B), 83.6 (C-3B), 82.8 (C-3A), 82.3 (C-4B), 80.9 (C-4A), 76.5 (C-5A), 73.5 (PhCH$_2$), 72.4 (PhCH$_2$), 72.1 (PhCH$_2$), 72.0 (PhCH$_2$), 71.9 (PhCH$_2$), 71.2 (C-5B), 68.6 (C-6A), 64.4 (C-6B), 54.9 (OCH$_3$). HRMS (ESI): [M + Na] calcd for $C_{48}H_{54}O_{11}Na$, 829.3558; found, 829.3550.

Methyl 2,3,6-Tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (15). Compound **14** (500 mg, 0.62 mmol) and dibutyltin oxide (236 mg, 0.93 mmol) in dry toluene (15 mL) were heated at reflux for 6 h, and then *n*-Bu$_4$NBr (200 mg, 0.62 mmol) and benzyl bromide (90 μL, 0.74 mmol) were added. The reaction mixture was heated at reflux for another 24 h and then concentrated. The resulting residue was dissolved in ethyl acetate (30 mL) and washed with a 10% aq KF solution (30 mL) and then brine (30 mL) before being dried (Na$_2$SO$_4$) and filtered. The filtrate was concentrated, and the crude product was purified by column chromatography (3:1 hexanes/EtOAc) to give **15** (432 mg, 78%) as a colorless oil. R_f 0.32 (2:1 hexanes/EtOAc); $[\alpha]_D$ −53.5 (*c* 1.3, CH$_2$Cl$_2$); ^{1}H NMR (600 MHz, CDCl$_3$, δ_H) 7.38−7.22 (m, 30H, Ar), 5.09 (br s, 1H, H-1B), 4.94 (br s, 1H, H-1A), 4.73 (d, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.58−4.43 (m, 10H, PhC*H*$_2$), 4.32 (d, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.13 (dd, 1H, *J* = 6.4, 3.5 Hz, H-4B), 4.10−4.07 (m, 2H, H-4A, H-3B), 4.02 (dd, 1H, *J* = 2.7, 1.0 Hz, H-2B), 4.01 (dd, 1H, *J* = 7.0, 3.1 Hz, H-3A), 3.96 (dd, 1H, *J* = 3.1, 1.2 Hz, H-2A), 3.92 (br s, 1H, H-5B), 3.91 (dd, 1H, *J* = 10.4, 4.0 Hz, H-6A), 3.79 (ddd, 1H, *J* = 7.7, 4.0, 3.5 Hz, H-5A), 3.68 (dd, 1H, *J* = 10.4, 7.7 Hz, H-6A), 3.56−3.51 (m, 2H, H-6B × 2), 3.33 (s, 3H, OCH$_3$), 2.40 (br s, 1H, OH); ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 138.5 (Ar), 138.1 (Ar), 137.8 (Ar), 137.78 (Ar), 137.7 (Ar), 137.3 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 128.26 (Ar), 128.2 (Ar), 128.1 (Ar), 128.09 (Ar), 128.0 (Ar), 127.9 (Ar), 127.88 (Ar), 127.84 (Ar), 127.8 (Ar), 127.79 (Ar), 127.76 (Ar), 127.7 (Ar), 127.68 (Ar), 127.6 (Ar), 107.0 (C-1A), 106.8 (C-1B), 88.3 (C-2A), 87.6 (C-2B), 83.4 (C-3B), 82.8 (C-3A), 81.6 (C-4B), 80.9 (C-4A), 76.4 (C-5A), 73.6 (PhCH$_2$), 73.4 (PhCH$_2$), 72.3 (PhCH$_2$), 72.1 (PhCH$_2$), 71.9 (PhCH$_2$), 71.8 (PhCH$_2$), 71.6 (C-6B), 70.1 (C-5B), 68.7 (C-6A), 54.8 (OCH$_3$). HRMS (ESI): [M + Na] calcd for $C_{55}H_{60}O_{11}Na$, 919.4028; found, 919.4022.

Methyl 2,3-Di-*O*-acetyl-5,6-*O*-isopropylidene-β-D-galactofuranosyl-(1→5)-2,3,6-tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (16). To a mixture of **6** (61 mg, 0.15 mmol), **15** (102 mg, 0.11 mmol), and 4 Å molecular sieves (0.2 g) in CH$_2$Cl$_2$ (6 mL) at 0 °C was added NIS (42 mg, 0.18 mmol) followed by AgOTf (12 mg, 0.044 mmol). After stirring for 20 min at 0 °C, the reaction mixture turned dark red, and Et$_3$N was added. The solution was diluted with CH$_2$Cl$_2$ (20 mL) and filtered through Celite. The filtrate was then washed with a saturated aq Na$_2$S$_2$O$_3$ solution (3 × 10 mL), dried (Na$_2$SO$_4$), and concentrated to give a crude residue that was purified by chromatography (3:1 hexanes/EtOAc) yielding **16** (119 mg, 89%) as a colorless syrup. R_f 0.31 (2:1 hexanes/EtOAc); $[\alpha]_D$ −57.8 (*c* 0.8, CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$, δ_H) 7.38−7.21 (m, 30H, Ar), 5.51 (s, 1H, H-1C), 5.20 (d, 1H, *J* = 1.2 Hz, H-2C), 5.09 (d, 1H, *J* = 1.4 Hz, H-1B), 5.02 (dd, 1H, *J* = 4.6, 1.2 Hz, H-3C), 4.94 (s, 1H, H-1A), 4.75 (d, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.60−4.44 (m, 9H, PhC*H*$_2$), 4.41 (d, 1H, *J* = 11.5 Hz, PhC*H*$_2$), 4.31 (d, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.25 (ddd, 1H, *J* = 6.2, 6.2, 6.2 Hz, H-5C), 4.22−4.13 (m, 4H, H-5B, H-3B, H-4B, H-4C), 4.07 (dd, 1H, *J* = 7.1, 3.0 Hz, H-4A), 4.03 (dd, 1H, *J* = 3.4, 1.4 Hz, H-2B), 4.01 (dd, 1H, *J* = 7.1, 3.1 Hz, H-3A), 3.97−3.92 (m, 2H, H-2A, H-6C), 3.90 (dd, 1H, *J* = 10.1, 3.9 Hz, H-6A), 3.81−3.77 (m, 2H, H-6C, H-5A), 3.73 (dd, 1H, *J* = 10.2, 7.5 Hz, H-6B), 3.71−3.67 (m, 1H, H-6A), 3.65 (dd, 1H, *J* = 10.2, 4.2 Hz, H-6B), 3.35 (s, 3H, OCH$_3$), 2.04 (s, 3H, acyl CH$_3$), 1.92 (s, 3H, acyl CH$_3$), 1.35 (s, 3H, isopropylidene CH$_3$), 1.33 (s, 3H, isopropylidene CH$_3$); ^{13}C NMR (125 MHz, CDCl$_3$, δ_C) 170.2 (C═O), 169.3 (C═O), 138.4 (Ar), 138.2 (Ar), 138.0 (Ar), 137.8 (Ar), 137.7 (Ar), 137.4 (Ar), 128.4 (Ar), 128.37 (Ar), 128.34 (Ar), 128.3 (Ar), 128.26 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.83 (Ar), 127.8 (Ar), 127.77 (Ar), 127.7 (Ar), 127.67 (Ar), 127.6 (Ar), 127.5 (Ar), 109.8 (isopropylidene C), 107.0 (C-1A), 106.6 (C-1B), 105.5 (C-1C), 88.6 (C-2B), 88.3 (C-2A), 83.5 (C-3B), 83.2 (C-4C), 82.9 (C-3A), 81.2 (C-2C), 80.9 (C-4A), 80.4 (C-4B), 77.0 (C-3C), 76.3 (C-5A), 75.4 (C-5C), 73.6 (PhCH$_2$), 73.4 (PhCH$_2$), 73.2 (C-5B), 72.3 (PhCH$_2$), 72.2 (PhCH$_2$ × 2), 71.9 (PhCH$_2$), 71.2 (C-6B), 68.8 (C-6A), 65.4 (C-6C), 54.8 (OCH$_3$), 26.3 (isopropylidene CH$_3$), 25.2 (isopropylidene CH$_3$), 20.7 (acyl CH$_3$), 20.6 (acyl CH$_3$). HRMS (ESI): [M + Na] calcd for $C_{68}H_{78}O_{18}Na$, 1205.5086; found, 1205.5093.

Methyl 5,6-*O*-Isopropylidene-β-D-galactofuranosyl-(1→5)-2,3,6-tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (17). To a solution of **16** (635 mg, 0.54 mmol) in CH_3OH (25 mL) and CH_2Cl_2 (25 mL) was added $NaOCH_3$ until the pH of the solution was ~10. The mixture was stirred for 12 h, neutralized by the addition of HOAc, and concentrated. The crude residue was purified by chromatography (3:2 hexanes/EtOAc) to give **17** (535 mg, 91%) as a colorless syrup. R_f 0.36 (1:1 hexanes/EtOAc); $[\alpha]_D$ −55.9 (*c* 1.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.38−7.21 (m, 30H, Ar), 5.36 (s, 1H, H-1C), 5.05 (s, 1H, H-1B), 4.95 (s, 1H, H-1A), 4.73 (dd, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.58−4.44 (m, 8H, PhC*H*$_2$), 4.38 (d, 1H, *J* = 12.1 Hz, PhC*H*$_2$), 4.37 (d, 1H, *J* = 11.9 Hz, PhC*H*$_2$), 4.33 (d, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.22 (dd, 1H, *J* = 7.7, 6.9 Hz, H-5C), 4.16−4.09 (m, 2H, H-4B, H-5B), 4.08 (dd, 1H, *J* = 7.0, 3.2 Hz, H-4A), 4.04−3.84 (m, 10H, H-3A, H-4C, H-3C, H-2B, H-2A, H-2C, H-6C × 2, H-3B, H-6A), 3.77 (ddd, 1H, *J* = 7.7, 3.7, 3.2 Hz, H-5A), 3.75 (br s, 1H, OH), 3.67 (dd, 1H, *J* = 10.3, 7.7 Hz, H-6A), 3.61 (dd, 1H, *J* = 10.3, 4.0 Hz, H-6B), 3.57 (dd, 1H, *J* = 10.3, 6.3 Hz, H-6B), 3.36 (s, 3H, OCH_3), 1.40 (s, 3H, isopropylidene CH_3), 1.38 (s, 3H, isopropylidene CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 138.5 (Ar), 137.9 (Ar), 137.8 (Ar), 137.7 (Ar), 137.5 (Ar), 137.1 (Ar), 128.5 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 128.12 (Ar), 128.1 (Ar), 128.0 (Ar), 127.85 (Ar), 127.8 (Ar), 127.77 (Ar), 127.7 (Ar), 127.68 (Ar), 127.6 (Ar), 127.5 (Ar), 110.0 (isopropylidene C), 107.1 (C-1C), 107.0 (C-1A), 106.1 (C-1B), 88.3 (C-2A), 87.1 (C-2B), 85.4 (C-3A), 84.6 (C-3B), 82.9 (C-4C), 81.4 (C-4B), 80.9 (C-4A), 78.9 (C-2C), 78.6 (C-3C), 76.4 (C-5A), 75.9 (C-5C), 73.6 (C-5B), 73.5 (PhCH$_2$), 73.4 (PhCH$_2$), 72.1 (PhCH$_2$), 72.0 (PhCH$_2$), 71.9 (PhCH$_2$), 71.8 (PhCH$_2$), 69.9 (C-6B), 68.4 (C-6A), 65.7 (C-6C), 54.8 (OCH_3), 25.7 (isopropylidene CH_3), 25.6 (isopropylidene CH_3). HRMS (ESI): [M + Na] calcd for $C_{64}H_{74}O_{16}Na$, 1121.4874; found, 1121.4877.

Methyl 2,3-Anhydro-5,6-*O*-isopropylidene-β-D-gulofuranosyl-(1→5)-2,3,6-tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (18). To a solution of **17** (535 mg, 0.487 mmol) and PPh_3 (383 mg, 1.46 mmol) in THF (25 mL) at 0 °C was added DIAD (0.30 mL, 1.46 mmol) dropwise. The reaction mixture was warmed to rt over 30 min, and then stirred for another 30 min at 40 °C. The resulting mixture was concentrated, and the residue was purified by chromatography (3:1 hexanes/EtOAc) to yield **18** (481 mg, 91%) as a colorless syrup. R_f 0.65 (3:2 hexanes/EtOAc); $[\alpha]_D$ −53.6 (*c* 0.7, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.38−7.20 (m, 30H, Ar), 5.47 (s, 1H, H-1C), 5.13 (s, 1H, H-1B), 4.94 (br s, 1H, H-1A), 4.74 (dd, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.64 (d, 1H, *J* = 11.3 Hz, PhC*H*$_2$), 4.59−4.40 (m, 9H, PhC*H*$_2$), 4.31 (d, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.21 (ddd, 1H, *J* = 6.8, 6.8, 6.8 Hz, H-5C), 4.17 (ddd, 1H, *J* = 8.2, 3.8, 2.1 Hz, H-5B), 4.14 (d, 1H, *J* = 7.2 Hz, H-3B), 4.13 (d, 1H, *J* = 6.8 Hz, H-4C), 4.10−3.99 (m, 5H, H-4A, H-4B, H-6C, H-2B, H-3A), 3.96 (dd, 1H, *J* = 3.1, 1.2 Hz, H-2A), 3.88 (dd, 1H, *J* = 10.4, 4.0 Hz, H-6A), 3.79−3.70 (m, 3H, H-5A, H-6B H-6C), 3.71 (d, 1H, *J* = 2.9 Hz, H-2C), 3.68 (dd, 1H, *J* = 10.4, 7.7 Hz, H-6A), 3.60 (dd, 1H, *J* = 10.1, 3.8 Hz, H-6B), 3.44 (d, 1H, *J* = 2.9 Hz, H-3C), 3.32 (s, 3H, OCH_3), 1.38 (s, 3H, isopropylidene CH_3), 1.34 (s, 3H, isopropylidene CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 138.4 (Ar), 138.1 (Ar), 138.08 (Ar), 137.8 (Ar), 137.7 (Ar), 137.6 (Ar), 128.42 (Ar), 128.4 (Ar), 128.37 (Ar), 128.34 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.84 (Ar), 127.8 (Ar), 127.76 (Ar), 127.7 (Ar), 127.6 (Ar), 127.57 (Ar), 127.5 (Ar), 109.7 (isopropylidene C), 107.0 (C-1A), 106.6 (C-1B), 102.0 (C-1C), 88.2 (C-2A), 88.17 (C-2B), 84.3 (C-3B), 82.9 (C-3A), 81.0 (C-4A), 80.9 (C-4B), 77.3 (C-4C), 76.2 (C-5A), 75.3 (C-5B), 75.1 (C-5C), 73.6 (PhCH$_2$), 73.3 (PhCH$_2$), 72.8 (PhCH$_2$), 72.2 (PhCH$_2$), 71.9 (PhCH$_2$), 71.8 (PhCH$_2$), 71.6 (C-6B), 68.6 (C-6A), 65.6 (C-6C), 55.6 (C-2C), 54.8 (OCH_3), 53.6 (C-3C), 26.6 (isopropylidene CH_3), 25.2 (isopropylidene CH_3). HRMS (ESI): [M + Na] calcd for $C_{64}H_{72}O_{15}Na$, 1103.4769; found. 1103.4770.

Methyl 3-*O*-Benzyl-5,6-*O*-isopropylidene-β-D-galactofuranosyl-(1→5)-2,3,6-tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (19). A prepared solution of lithium benzylate in benzyl alcohol (2 M, 8 mL) was added to **18** (481 mg, 0.445 mmol). The reaction mixture was heated to 75 °C and stirred for 12 h; the solution was cooled and then neutralized with HOAc. The resulting solution was diluted with EtOAc (20 mL) and washed with H_2O (10 mL). The organic layer was dried (Na_2SO_4) and concentrated to give a crude mixture which was purified by column chromatography (3:1 hexanes/EtOAc) to yield **19** (458 mg, 87%) as a colorless oil. R_f 0.47 (2:1 hexanes/EtOAc); $[\alpha]_D$ −76.6 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 7.37−7.20 (m, 35H, Ar), 5.39 (s, 1H, H-1C), 5.08 (d, 1H, *J* = 1.6 Hz, H-1B), 4.94 (s, 1H, H-1A), 4.75 (dd, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.66 (d, 1H, *J* = 12.3 Hz, PhC*H*$_2$), 4.57−4.42 (m, 10H, PhC*H*$_2$), 4.40 (d, 1H, *J* = 12.3 Hz, PhC*H*$_2$), 4.35−4.32 (m, 1H, H-3B), 4.31 (d, 1H, *J* = 11.8 Hz, PhC*H*$_2$), 4.26 (br s, 1H, H-2C), 4.21−4.15 (m, 2H, H-4B, H-5B), 4.10 (dd, 1H, *J* = 3.0, 2.8 Hz, H-4C), 4.06 (dd, 1H, *J* = 7.1, 3.0 Hz, H-4A), 4.05−3.99 (m, 3H, H-2B, H-5C, H-3A), 3.96−3.94 (m, 1H, H-2A), 3.90 (dd, 1H, *J* = 10.5, 4.0 Hz, H-6A), 3.86−3.73 (m, 5H, H-3C, H-6C × 2, H-5A, H-6B), 3.70−3.64 (m, 2H, H-6A, H-6B), 3.33 (s, 3H, OCH_3), 1.35 (s, 3H, isopropylidene CH_3), 1.33 (s, 3H, isopropylidene CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 138.5 (Ar), 138.48 (Ar), 138.2 (Ar), 137.9 (Ar), 137.8 (Ar), 137.7 (Ar), 128.4 (Ar), 128.33 (Ar), 128.3 (Ar), 128.26 (Ar), 128.2 (Ar), 128.17 (Ar), 128.15 (Ar), 128.12 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.79 (Ar), 127.78 (Ar), 127.73 (Ar), 127.7 (Ar), 127.67 (Ar), 127.6 (Ar), 127.55 (Ar), 127.5 (Ar), 127.4 (Ar), 109.7 (isopropylidene C), 109.0 (C-1C), 107.0 (C-1A), 106.7 (C-1B), 88.6 (C-3A), 88.3 (C-2A), 85.5 (C-3C), 82.9 (C-2B, C-3B), 82.4 (C-4C), 81.0 (C-4A), 80.6 (C-4B), 78.0 (C-2C), 76.5 (C-5A), 76.4 (C-5C), 73.5 (PhCH$_2$), 73.4 (PhCH$_2$), 73.1 (C-5B), 72.2 (PhCH$_2$), 72.15 (PhCH$_2$), 71.9 (PhCH$_2$), 71.8 (PhCH$_2$), 71.78 (PhCH$_2$), 71.0 (C-6B), 68.8 (C-6A), 65.5 (C-6C), 54.7 (OCH_3), 25.8 (isopropylidene CH_3), 25.7 (isopropylidene CH_3). HRMS (ESI): [M + Na] calcd for $C_{71}H_{80}O_{16}Na$, 1211.5339; found, 1211.5338.

Methyl 2,3-Anhydro-5,6-di-*O*-benzoyl-α-D-gulofuranosyl-(1→2)-3-*O*-benzyl-5,6-*O*-isopropylidene-β-D-galactofuranosyl-(1→5)-2,3,6-tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (20). The sulfoxide donor **7** (381 mg, 0.77 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (649 mg, 3.1 mmol), and 4 Å molecular sieves (1.0 g) were dried for 3 h under vacuum in the presence of P_2O_5. To this mixture was added CH_2Cl_2 (30 mL), and the solution was cooled to −78 °C. Tf_2O (156 μL, 0.93 mmol) was added, and the mixture was stirred for 10 min. The solution was then warmed to −40 °C and stirred for 20 min, which was then followed by the addition of trisaccharide alcohol **19** (368 mg, 0.31 mmol) in CH_2Cl_2 (10 mL) via a syringe. After 45 min, the reaction mixture was warmed to rt and stirred for 24 h before a saturated aq solution of $NaHCO_3$ (2 mL) was added. The resulting solution was then filtered through Celite, dried (Na_2SO_4), filtered, and concentrated. Column chromatography (3:1 hexane/EtOAc) provided **20** (359 mg, 75%) as a colorless syrup. R_f 0.47 (2:1 hexanes/EtOAc); $[\alpha]_D$ −29.3 (*c* 1.45, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H) 8.20−7.98 (m, 4H, Ar), 7.58−7.50 (m, 2H, Ar), 7.45−7.17 (m, 39H, Ar), 5.72 (ddd, 1H, *J* = 5.8, 5.8, 4.1 Hz, H-5D), 5.42 (s, 1H, H-1C), 5.11 (s, 1H, H-1B), 5.05 (s, 1H, H-1D), 4.94 (s, 1H, H-1A), 4.77−4.65 (m, 5H, PhC*H*$_2$ × 3, H-6D × 2), 4.58−4.38 (m, 11H, PhC*H*$_2$ × 10, H-2C), 4.30 (d, 1H, *J* = 11.7 Hz, PhC*H*$_2$), 4.27 (dd, 1H, *J* = 7.0, 3.2 Hz, H-3B), 4.23 (ddd, 1H, *J* = 9.2, 2.7, 2.7 Hz, H-5B), 4.19 (dd, 1H, *J* = 7.3, 7.3 Hz, H-4C), 4.11−4.04 (m, 4H, H-4B, H-5C, H-4A, H-4D), 4.03−4.00 (m, 2H, H-2B, H-3A), 3.97−3.95 (m, 1H, H-2A), 3.90 (dd, 1H, *J* = 10.3, 4.0 Hz, H-6A), 3.85 (dd, 1H, *J* = 9.8, 9.2 Hz, H-6B), 3.80 (dd, 1H, *J* = 7.3, 3.5 Hz, H-3C), 3.79−3.75 (m, 2H, H-5A, H-6C), 3.71−3.65 (m, 2H, H-6A, H-6C), 3.64 (dd, 1H, *J* = 9.8, 2.7 Hz, H-6B), 3.56 (d, 1H, *J* = 2.9 Hz, H-3D), 3.32 (s, 3H, OCH_3), 3.10 (d, 1H, *J* = 2.9 Hz, H-2D), 1.26 (s, 3H, isopropylidene

CH_3), 1.24 (s, 3H, isopropylidene CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 166.0 (C═O), 165.8 (C═O), 138.4 (Ar × 2), 138.3 (Ar), 137.8 (Ar), 137.7 (Ar), 137.6 (Ar), 137.4 (Ar), 133.2 (Ar), 133.1 (Ar), 129.8 (Ar), 129.7 (Ar), 129.66 (Ar), 128.4 (Ar), 128.39 (Ar), 128.33 (Ar), 128.3 (Ar), 128.25 (Ar), 128.22 (Ar), 128.2 (Ar), 128.0 (Ar), 127.9 (Ar), 127.8 (Ar), 127.76 (Ar), 127.74 (Ar), 127.7 (Ar), 127.6 (Ar), 127.58 (Ar), 127.55 (Ar), 127.5 (Ar), 127.48 (Ar), 109.4 (isopropylidene C), 108.2 (C-1C), 107.0 (C-1A), 106.7 (C-1B), 100.6 (C-1D), 88.3 (C-2A, C-3A), 87.7 (C-2C), 83.9 (C-3B), 83.2 (C-3C), 82.8 (C-2B), 81.8 (C-4C), 81.1 (C-4A), 80.9 (C-4B), 76.2 (C-5A, C-5C), 75.2 (C-4D), 74.9 (C-5B), 73.5 (Ph*C*H_2), 73.3 (Ph*C*H_2), 72.6 (Ph*C*H_2), 72.2 (Ph*C*H_2), 71.8 (Ph*C*H_2), 71.79 (Ph*C*H_2 × 2), 71.7 (C-6B), 71.6 (C-5D), 68.7 (C-6A), 65.3 (C-6C), 63.4 (C-6D), 55.3 (C-2D), 54.7 (OCH_3), 54.3 (C-3D), 26.4 (isopropylidene CH_3), 25.5 (isopropylidene CH_3). HRMS (ESI): [M + Na] calcd for $C_{91}H_{96}O_{22}Na$, 1563.6291; found, 1563.6305.

Methyl 3-*O*-Benzyl-α-D-galactofuranosyl-(1→2)-3-*O*-benzyl-5,6-*O*-isopropylidene-β-D-galactofuranosyl-(1→5)-2,3,6-tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (21). To a solution of **20** (257 mg, 0.167 mmol) in benzyl alcohol (6.0 mL) was added a prepared solution of lithium benzylate in benzyl alcohol (1.5 M, 0.9 mL) and (−)-sparteine (0.05 mL, 0.2 mmol). The resulting mixture was subsequently warmed to 75 °C and stirred until the reaction was complete (∼16 h). After cooling to rt, the solution was neutralized with HOAc and diluted with EtOAc (20 mL). The organic layer was washed with water (15 mL), dried (Na_2SO_4), filtered, and concentrated to give a crude residue that was purified by chromatography (1:1 hexane/EtOAc) to yield **21** (160 mg, 67%) as a colorless syrup and its corresponding D-idofuranoside product (27 mg, 11%). Data for **21**: R_f 0.41 (1:1 hexanes/EtOAc); $[\alpha]_D$ −36.7 (*c* 2.0, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.37−7.20 (m, 40H, Ar), 5.41 (s, 1H, H-1C), 5.11 (d, 1H, J = 4.8 Hz, H-1D), 5.10 (s, 1H-1B), 4.94 (s, 1H, H-1A), 4.79 (d, 1H, J = 11.8 Hz, PhCH_2), 4.73 (d, 1H, J = 11.8 Hz, PhCH_2), 4.67 (d, 1H, J = 11.7 Hz, PhCH_2), 4.60−4.39 (m, 13H, PhCH_2 × 12, H-2C), 4.30 (d, 1H, J = 11.7 Hz, PhCH_2), 4.24 (dd, 1H, J = 7.1, 3.2 Hz, H-3B), 4.19−4.14 (m, 2H, H-4C, H-5B), 4.11−4.07 (m, 2H, H-4B, H-5C), 4.07 (dd, 1H, J = 7.2, 3.3 Hz, H-4A), 4.03 (dd, 1H, J = 6.3, 3.0 Hz, H-3C), 4.02−3.91 (m, 6H, H-3A, H-2B, H-3D, H-4D, H-2A, H-2D), 3.89 (dd, 1H, J = 10.3, 4.2 Hz, H-6A), 3.80−3.74 (m, 4H, H-6C × 2, H-5A, H-6B), 3.67 (dd, 1H, J = 10.3, 7.7 Hz, H-6A), 3.66−3.62 (m, 1H, H-5D), 3.61 (dd, 1H, J = 10.2, 3.2 Hz, H-6B), 3.59−3.57 (m, 2H, H-6D × 2), 3.31 (s, 3H, OCH_3), 2.74 (br s, 1H, OH), 2.56 (br s, 1H, OH), 1.33 (s, 3H, isopropylidene CH_3), 1.31 (s, 3H, isopropylidene CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 138.4 (Ar), 138.2 (Ar), 137.9 (Ar), 137.8 (Ar), 137.7 (Ar), 137.6 (Ar), 128.5 (Ar), 128.46 (Ar), 128.4 (Ar), 128.39 (Ar), 128.33 (Ar), 128.3 (Ar), 128.25 (Ar), 128.1 (Ar), 128.0 (Ar), 127.9 (Ar), 127.84 (Ar), 127.83 (Ar), 127.8 (Ar), 127.77 (Ar), 127.75 (Ar), 127.72 (Ar), 127.7 (Ar), 127.6 (Ar), 127.55 (Ar), 109.6 (isopropylidene C), 107.0 (C-1A), 106.9 (C-1C), 106.6 (C-1B), 101.7 (C-1D), 88.3 (C-2A), 88.2 (C-3A), 86.8 (C-2C), 83.7 (C-3B), 83.65 (C-3C), 82.84 (C-2B), 82.8 (C-3D), 82.3 (C-4A), 81.4 (C-4C), 81.0 (C-4B), 80.9 (C-5C), 77.2 (C-2D), 76.2 (C-5A), 75.8 (C-4D), 74.8 (C-5B), 73.6 (Ph*C*H_2), 73.4 (Ph*C*H_2), 72.4 (Ph*C*H_2), 72.2 (Ph*C*H_2), 72.1 (Ph*C*H_2), 72.05 (C-5D), 72.0 (Ph*C*H_2 × 2), 71.9 (Ph*C*H_2), 71.8 (C-6B), 68.7 (C-6A), 65.4 (C-6C), 64.1 (C-6D), 54.7 (OCH_3), 26.1 (isopropylidene CH_3), 25.4 (isopropylidene CH_3). HRMS (ESI): [M + Na] calcd for $C_{84}H_{96}O_{21}Na$, 1463.6342; found, 1463.6345.

Methyl 3-*O*-Benzyl-5,6-*O*-isopropylidene-α-D-galactofuranosyl-(1→2)-3-*O*-benzyl-5,6-*O*-isopropylidene-β-D-galactofuranosyl-(1→5)-2,3,6-tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (22). To a solution of compound **21** (160 mg, 0.11 mmol) and 2,2-dimethoxypropane (0.11 mL, 0.89 mmol) in acetone (5 mL) was added *p*-TsOH (0.5 mg), and the reaction mixture was stirred at rt for 4 h. Two drops of Et_3N were added, and the solution was concentrated. Column chromatography (3:1 hexanes/EtOAc) of the residue gave **22** (145 mg, 88%) as a colorless oil. R_f 0.51 (2:1 hexanes/EtOAc); $[\alpha]_D$ −36.8 (*c* 0.6, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$, δ_H) 7.40−7.20 (m, 40H, Ar), 5.42 (s, 1H, H-1C), 5.12 (d, 1H, J = 4.8 Hz, H-1D), 5.09 (s, 1H, H-1B), 4.95 (s, 1H, H-1A), 4.80 (d, 1H, J = 11.7 Hz, PhCH_2), 4.79 (d, 1H, J = 11.7 Hz, PhCH_2), 4.74 (d, 1H, J = 11.7 Hz, PhCH_2), 4.61 (d, 1H, J = 11.2 Hz, PhCH_2), 4.60−4.58 (m, 1H, H-2C), 4.58−4.43 (m, 10H, PhCH_2), 4.40 (d, 1H, J = 11.2 Hz, PhCH_2), 4.31 (d, 1H, J = 11.7 Hz, PhCH_2), 4.23 (dd, 1H, J = 6.9, 3.5 Hz, H-3B), 4.20−4.06 (m, 6H, H-4C, H-5B, H-4B, H-5C, H-4A, H-4D), 4.02−3.99 (m, 2H, H-3A, H-2B), 3.97−3.64 (m, 14H, H-3C, H-2A, H-2D, H-3D, H-5A, H-5D, H-6A × 2, H-6C × 2, H-6B × 2, H-6D × 2), 3.33 (s, 3H, OCH_3), 2.60 (br s, 1H, OH), 1.41 (s, 3H, isopropylidene CH_3), 1.31 (s, 3H, isopropylidene CH_3), 1.29 (s, 3H, isopropylidene CH_3), 1.26 (s, 3H, isopropylidene CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 138.5 (Ar), 138.3 (Ar), 138.0 (Ar), 137.8 (Ar), 137.77 (Ar), 137.7 (Ar), 137.65 (Ar), 137.5 (Ar), 128.5 (Ar), 128.43 (Ar), 128.4 (Ar), 128.33 (Ar), 128.3 (Ar), 128.27 (Ar), 128.25 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.95 (Ar), 127.83 (Ar), 127.8 (Ar), 127.77 (Ar), 127.7 (Ar), 127.68 (Ar), 127.66 (Ar), 127.5 (Ar), 109.8 (isopropylidene C), 109.6 (isopropylidene C), 107.3 (C-1C), 107.0 (C-1A), 106.7 (C-1B), 101.9 (C-1D), 88.3 (× 2), 86.3, 84.4, 83.6, 83.3, 82.9, 82.3, 82.0, 81.1, 80.9, 78.4, 76.3, 76.2 (× 2), 74.7, 73.5, 73.4, 72.4, 72.2, 72.15, 72.0 71.8 (× 2), 71.6, 68.8, 65.5, 65.2, 54.7 (OCH_3), 26.7 (isopropylidene CH_3), 26.3 (isopropylidene CH_3), 25.6 (isopropylidene CH_3), 25.5 (isopropylidene CH_3). HRMS (ESI): [M + Na] calcd for $C_{87}H_{100}O_{21}Na$, 1503.6655; found, 1503.6651.

Methyl 4,6-*O*-Benzylidene-2,3-di-*O*-benzyl-α-D-glucopyranosyl-(1→2)-3-*O*-benzyl-5,6-*O*-isopropylidene-α-D-galactofuranosyl-(1→2)-3-*O*-benzyl-5,6-*O*-isopropylidene-β-D-galactofuranosyl-(1→5)-2,3,6-tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (23). Thioglycoside **8** (140 mg, 0.25 mmol), BSP (53 mg, 0.25 mmol), 2,4,6-tri-*tert*-butyl-pyrimidine (130 mg, 0.51 mmol), and 4 Å molecular sieves (500 mg) were dried for 4 h under vacuum in the presence of P_2O_5. To this mixture was added CH_2Cl_2 (8 mL), and the solution was cooled to −60 °C. Tf_2O (47 μL, 0.28 mmol) was added; the mixture was allowed to stir for 10 min and was followed by the addition (via a syringe) of a solution of the vacuum-dried acceptor **22** (75 mg, 0.051 mmol) in CH_2Cl_2 (7 mL). After 40 min, the reaction mixture was warmed to rt and was kept stirring for 48 h. A saturated aq solution of $NaHCO_3$ (2 mL) was added, and the resulting solution was filtered through Celite, dried (Na_2SO_4), filtered, and concentrated. Column chromatography (7:3 hexane/EtOAc) of this residue provided **23** (54 mg, 56%) as a colorless syrup. R_f 0.47 (7:3 hexanes/EtOAc); $[\alpha]_D$ −2.7 (*c* 1.4, CH_2Cl_2); ^1H NMR (600 MHz, CD_2Cl_2, δ_H) 7.50−7.21 (m, 55H, Ar), 5.57 (s, 1H, benzylidene CH), 5.44 (d, 1H, J = 1.2 Hz, H-1C), 5.40 (d, 1H, J = 4.2 Hz, H-1D), 5.11 (d, 1H, J = 3.6 Hz, H-1E), 5.09 (s, 1H, H-1B), 4.89 (s, 1H, H-1A), 4.86−4.79 (m, 4 H), 4.71 (d, 1H, J = 11.5 Hz), 4.69 (d, 1H, J = 11.5 Hz), 4.63−4.34 (m, 15 H), 4.27 (dd, 1H, J = 7.5, 4.2 Hz), 4.21 (dd, 1H, J = 10.2, 4.7 Hz), 4.19 (dd, 1H, J = 7.0, 3.2 Hz), 4.17−4.12 (m, 4 H), 4.05−3.97 (m, 5 H), 3.93−3.92 (m, 1 H), 3.90−3.82 (m, 5 H), 3.81−3.61 (m, 9 H), 3.58−3.54 (m, 2 H), 3.28 (s, 3H, OCH_3), 1.38 (s, 3H, isopropylidene CH_3), 1.19 (s, 3H, isopropylidene CH_3), 1.17 (s, 3H, isopropylidene CH_3), 1.16 (s, 3H, isopropylidene CH_3); ^{13}C NMR (125 MHz, CD_2Cl_2, δ_C) 139.2 (Ar), 139.1 (Ar), 138.9 (Ar), 138.8 (Ar), 138.6 (Ar), 138.4 (Ar), 138.3 (Ar), 138.2 (Ar), 138.1 (Ar), 137.5 (Ar), 129.3 (Ar), 129.2 (Ar), 128.9 (Ar), 128.8 (Ar), 128.75 (Ar), 128.7 (Ar), 128.67 (Ar), 128.6 (Ar), 128.58 (Ar), 128.54 (Ar), 128.5 (Ar), 128.44 (Ar), 128.4 (Ar), 128.35 (Ar), 128.33 (Ar), 128.3 (Ar), 128.26 (Ar), 128.2 (Ar), 128.17 (Ar), 128.12 (Ar), 128.1 (Ar), 128.0 (Ar), 127.96 (Ar), 127.83 (Ar), 127.8 (Ar), 127.77 (Ar), 126.6 (Ar), 110.0 (isopropylidene C), 109.6 (isopropylidene C), 107.3 (C-1A), 107.2 (C-1C), 107.0 (C-1B), 102.0 (benzylidene CH), 99.1 (C-1D), 96.0 (C-1E), 88.7 (× 2), 85.7, 84.7, 84.3, 83.6, 82.1, 81.7, 81.68, 81.6, 81.5, 80.8, 79.1, 79.0 (× 2), 78.0, 77.1, 76.9, 75.5, 75.2, 73.7, 73.6, 73.3, 72.9, 72.8, 72.6, 72.5, 72.2 (× 3), 69.2, 68.6, 65.5, 65.47,

64.0, 54.8 (OCH_3), 27.0 (isopropylidene CH_3), 26.6 (isopropylidene CH_3), 25.7 (isopropylidene CH_3), 25.6 (isopropylidene CH_3). HRMS (ESI): [M + Na] calcd for $C_{114}H_{126}O_{26}Na$, 1933.8435; found, 1933.8449.

Methyl 2,3-Di-*O*-benzyl-α-D-glucopyranosyl-(1→2)-3-*O*-benzyl-α-D-galacto-furanosyl-(1→2)-3-*O*-benzyl-β-D-galactofuranosyl-(1→5)-2,3,6-tri-*O*-benzyl-β-D-galactofuranosyl-(1→6)-2,3,5-tri-*O*-benzyl-β-D-galactofuranoside (24). A solution of **23** (40 mg, 0.02 mmol) in 70% HOAc (7 mL, HOAc/H_2O/THF 5:1:1) was stirred at 50 °C for 16 h. The resulting mixture was concentrated and purified by chromatography (30:1 CH_2Cl_2/CH_3OH) to give **24** (28.1 mg, 77%) as a colorless syrup. R_f 0.36 (20:1 CH_2Cl_2/CH_3OH); $[\alpha]_D$ −5.07 (*c* 0.15, CH_2Cl_2); ^1H NMR (600 MHz, $CDCl_3$, δ_H) 7.39−7.20 (m, 50H, Ar), 5.44 (s, 1H, H-1C), 5.20 (d, 1H, J = 4.3 Hz, H-1D), 5.06 (d, 1H, J = 1.0 Hz, H-1B), 5.00 (d, 1H, J = 3.3 Hz, H-1E), 4.96 (d, 1H, J = 11.3 Hz), 4.92 (br s, 1H, H-1A), 4.74−4.67 (m, 4 H), 4.63 (d, 1H, J = 11.9 Hz), 4.59 (d, 1H, J = 11.3 Hz), 4.55−4.38 (m, 13 H), 4.34 (d, 1H, J = 11.8 Hz), 4.29 (d, 1H, J = 11.8 Hz), 4.22 (dd, 1H, J = 5.9, 2.5 Hz), 4.14 (dd, 1H, J = 5.9, 2.4 Hz), 4.11−4.04 (m, 5H), 4.00−3.98 (m, 2 H), 3.97 (dd, 1H, J = 3.1, 1.0 Hz), 3.90 (dd, 1H, J = 3.2, 1.3 Hz), 3.87 (dd, 1H, J = 10.2, 4.0 Hz), 3.83 (dd, 1H, J = 9.2, 9.2 Hz), 3.78−3.70 (m, 3 H), 3.69−3.46 (m, 10 H), 3.44−3.39 (m, 2 H), 3.28 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C) 138.7 (Ar), 138.4 (Ar), 138.0 (Ar), 137.9 (Ar), 137.8 (Ar), 137.7 (Ar), 137.6 (Ar), 137.5 (Ar), 137.3 (Ar), 128.5 (Ar), 128.45 (Ar), 128.4 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 128.0 (Ar), 127.98 (Ar), 127.8 (Ar), 127.77 (Ar), 127.7 (Ar), 127.65 (Ar), 127.6 (Ar), 107.0 (C-1A), 106.5 (C-1C), 106.4 (C-1B), 99.9 (C-1D), 95.9 (C-1E), 88.2 (× 2), 87.8, 85.3, 83.7, 83.5, 82.9, 82.8, 82.5, 80.8 (× 4), 80.3, 79.0, 76.2 (× 2), 75.4, 75.1, 73.5, 73.4, 73.0, 72.3, 72.1 (× 2), 72.0, 71.9, 71.8, 71.3, 71.0, 70.6, 68.5, 64.4, 64.2, 62.5, 54.7 (OCH_3). HRMS (ESI): [M + Na] calcd for $C_{101}H_{114}O_{26}Na$, 1765.7496; found, 1765.7509.

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Supporting Information Available: Experimental details for the preparation of **5**, **6**, and **10**, as well as associated characterization data and ^1H and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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