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Synthesis of Oligosaccharides of Motifs D and E of Arabinogalactan Present in *Mycobacterium tuberculosis*

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Syntheses of the ethyl glycosides of 5-*O*-(*β*-D-galactofuranosyl)-*β*-D-galactofuranose and 5-*O*-(α-D-arabinofuranosyl)-6-*O*-(*β*-D-galactofuranosyl)-*β*-D-galactofuranose present in motifs D and E of *Mycobacterium tuberculosis* arabinogalactan, respectively, have been presented. The pentenyl-mediated *O*-glycosylation reaction was utilized to obtain the disaccharide of motif D. The first coupling reaction to prepare the inner disaccharide portion of motif E was accomplished by trichloroacetamidate method while the installation of the terminal sugar by pentenyl glycosylation approach was successful.

Introduction

The social and economical burden due to mycobacterial diseases such as leprosy and tuberculosis are of unprecedented nature particularly as it relates to developing countries.[1] In spite of enormous efforts to develop anti-infective drug molecules, tuberculosis still constitutes the leading killer disease.[2] Seven million new cases and three million deaths occur every year due to tuberculosis, and with AIDS becoming epidemic in many developing countries, this mortality figure is bound to increase at an alarming rate.[3]

Mycobacterium (M.) tuberculosis, a causative agent of tuberculosis, contains on its cell wall surface many different groups of oligosaccharides which form the topic of interest for chemists and biochemists alike.[4] However, recent studies on *M. tuberculosis* are targeted toward two major polysaccharides, lipoarabinomannan (LAM) and arabinogalactan (AG). The unique feature of LAM and AG is attributed to arabinose and galactose residues present in the furanose forms.[5] LAM and AG are necessary for the survival of *M. tuberculosis*, and interfering with the biosynthesis of those polysaccharides is an idealistic approach for identifying anti-TB drugs.[6] Ethambutol is a drug of choice for the last 35 years for tuberculosis, but only recently it has been demonstrated that ethambutol exhibits inhibitory power to disrupt the biosynthesis of arabinan portions of LAM and AG.[7]

Five major motifs of AG, namely motifs A−E, have been identified. Synthesis of these motifs provides tremendous opportunities to understand their role in the survival and pathogenicity of these organisms. Motifs A, B, and C are composed of arabinofuranose units having subtle differences between them with respective to *O*-glycosidic linkages.[8] Motif D has solely galactofuranose residues but motif E is unique in that it contains both arabinofuranose and galactofuranose residues. Although motifs A and B oligosaccharides are branched-chain, the branched-chain oligosaccharide of motif E is sterically more demanding because both 5 and 6 positions of the reducing end galactofuranose unit are linked with arabinofuranosyl and galactofuranosyl residues, respectively.

The synthesis of the sugar components of AG of *M. tuberculosis* has been a topic of immense activity.[9−11] The first major contribution appeared from this laboratory and reported the synthesis of the pentaarabinofuranoside of motif A.[9a] Subsequently Lowary and co-workers reported[10] a series of publications on motifs A and B and studied their ring conformation by NMR techniques. Very recently, Prandi et al. also published[11] the synthesis of the pentaarabinofuranosyl structure of motif A. In this report we wish to reveal our recent findings[12] on the stereocontrolled synthesis of ethyl 5-*O*-(α-D-arabinofuranosyl)-6-*O*-(*β*-D-galactofuranosyl)-*β*-D-galactofuranoside (**6**)

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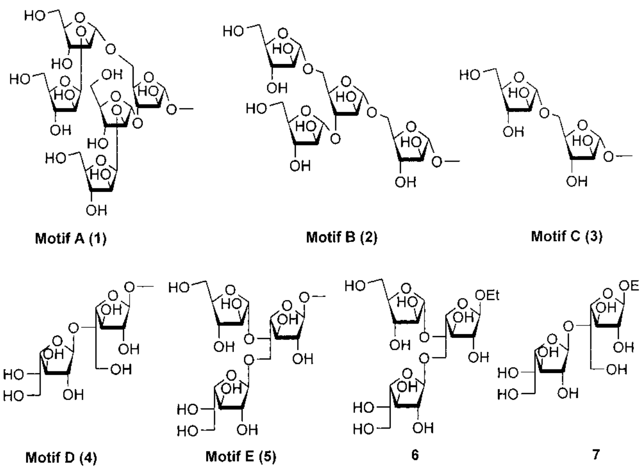
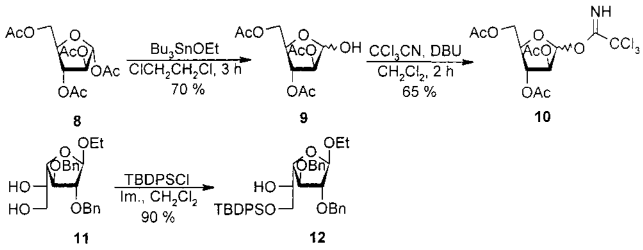


Figure 1.

Scheme 1



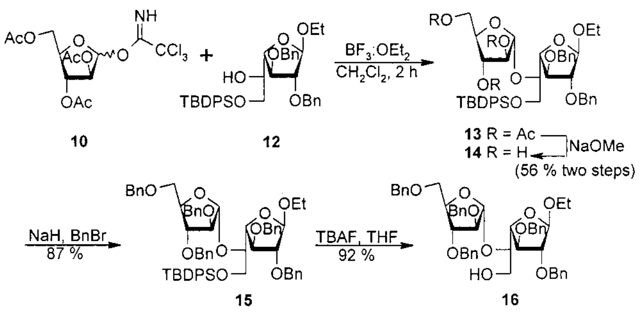
of motif E and ethyl 5-*O*-(β-D-galactofuranosyl)-β-D-galactofuranoside (**7**) of motif D (Figure 1).

Results and Discussion

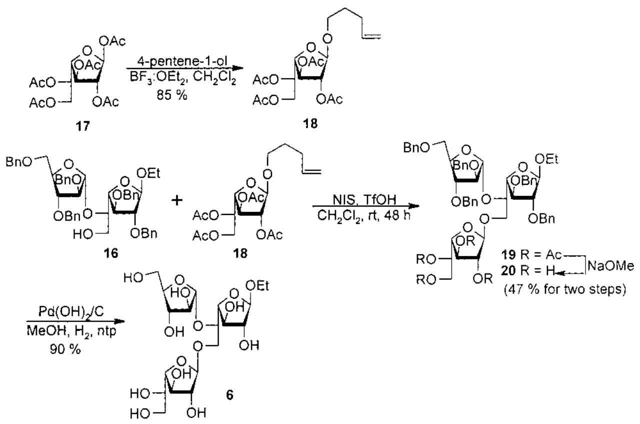
The synthetic strategy utilized for the preparation of ethyl 5-*O*-(α-D-arabinofuranosyl)-6-*O*-(β-D-galactofuranosyl)-β-D-galactofuranoside (**6**) was based on stepwise assembly of three sugar components. The glycosyl donor **10** was synthesized from 1,2,3,5 tetra-*O*-acetyl D-arabinose **8**[13] by selectively deprotecting the 1-*O*-acetyl group by using Bu_3SnOEt in refluxing $ClCH_2CH_2Cl$. The resulting 2,3,5-tri *O*-acetyl D-arabinose **9** was then exposed to $CCl_3CN-DBU-CH_2Cl_2$ at 0 °C to afford the corresponding arabinosyl trichloroimidate derivative **10**. The aglycone segment **12** found its origin[14] from the known ethyl 2,3-di-*O*-benzyl-β-D-galactofuranoside **11** by selective protection of the OH group at C-6 as a sterically hindered *tert*-butyldiphenylsilyl (TBDPS) ether linkage providing the 5-hydroxyl group free for coupling reaction (Scheme 1).

The coupling reaction[15] between **10** and **12** proceeded satisfactorily with $BF_3{\cdot}OEt_2$ as an activator. The resulting disaccharide **13** under Zémplen conditions[16] gave the triol derivative **14**. The structure of **14** was supported by ^1H and ^{13}C NMR data. The characteristic resonances due to anomeric protons H-1 and H-1′ were located at 5.01 and 5.21 ppm as singlets. In the ^{13}C NMR spectrum, the C-1′ carbon was observed at 104.5 ppm.[17] In addition, FAB-MS and satisfactory elemental analysis confirmed the structure of compound **14**. The three hydroxyl groups in **14** were protected as benzyl ethers, and then the TBDPS group was cleaved with 1 M solution of *n*-Bu_4NF in THF (Scheme 2).

Scheme 2



Scheme 3



The installation of third galactofuranose residue at C-6 of **16** was not a straightforward proposition. For instance Schmidt's trichloroimidate method,[15] the classical Helfrich reaction,[18] and SEt-mediated glycosidation[18] did not proceed in our hands. The chemistry that worked for the trisaccharide synthesis was Fraser–Reid's *n*-pentenyl-mediated *O*-glycosidation approach.[19] The synthesis of pent-4-enyl 2,3,5,6-tetra-*O*-acetyl-β-D-galactofuranose **18** was accomplished in one step by treating penta-*O*-acetyl D-galactofuranose **17**[20] and 4-penten-1-ol with a catalytic amount of $BF_3{\cdot}OEt_2$ and 4 Å molecular sieves in CH_2Cl_2 at room temperature. The structure of **18** was confirmed by ^1H and ^{13}C NMR spectral analysis (Scheme 3).

Treatment of **16** and **18** in the presence of *N*-iodosuccinimide (NIS) and cat. triflic acid in CH_2Cl_2 at room temperature gave the crude trisaccharide **19** (contaminated with minor quantity of aglycone **16**) which after Zémplen deacetylation provided the pure penta-*O*-benzylated derivative **20**. The three anomeric proton signals in the ^1H NMR spectrum of **20** were located at 4.84, 4.96, and 5.17 ppm as distinguishable singlets whereas the ^{13}C NMR spectrum revealed[21] anomeric carbons at 105.3, 106.8, and 107.7 ppm. Finally, compound **20** was sub-

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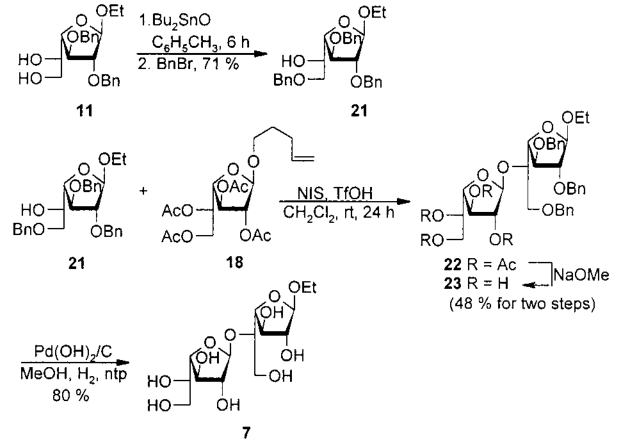
Scheme 4



jected to exhaustive hydrogenolysis over 10% $Pd(OH)_2$/C in methanol to provide the trisaccharide **6** (Scheme 3). The structure was supported by high resolution ^{1}H and ^{13}C NMR spectra. For example, in the ^{1}H NMR spectrum of **6**, resonances typical of anomeric protons (1,2-trans) were identified at 4.88, 4.92, and 5.10 ppm as three clearly distinguishable singlets. The chemical shifts of the anomeric carbons were at 107.6, 108.6, and 109.6 ppm in its ^{13}C NMR spectrum. In addition, FAB-MS and elemental analysis of **6** were in complete agreement with assigned structure. Compound **6** constitutes the oligosaccharide segment of motif E of arabinogalactan segment of *Mycobacterium tuberculosis*.

We also undertook the synthesis of ethyl 5-*O*-(β-D-galactofuranosyl)-β-D-galactofuranoside **7** representing motif D of *M. tuberculosis*. This disaccharide serves as an anchor that couples arabinan and galactan chains of AG. The known precursor **11** was converted into a dibutylstannyl acetal by refluxing with Bu_2SnO in toluene followed by addition of 1.0 equiv of BnBr to give rise[22] to the tribenzyl derivative **21** (Scheme 4).

The coupling reaction between **18** and **21** mediated by NIS and cat. TfOH in CH_2Cl_2 at room temperature gave the disaccharide **22** which was then deacetylated under Zémplen conditions. The ^{1}H and ^{13}C NMR spectra of **23** were in complete agreement with the assigned structure. For example, in the ^{1}H NMR spectrum of **23**, signals due to two anomeric protons (1,2-trans) were observed at 5.00 and 5.34 ppm as singlets. The ^{13}C NMR spectrum showed anomeric carbons at 104.9 and 106.1 ppm. Finally, compound **23** was exhaustively debenzylated by hydrogenolysis over 10% $Pd(OH)_2$/C in methanol to give the disaccharide **7** (Scheme 4). The structure of **7** was fully analyzed by ^{1}H and ^{13}C NMR spectral analysis and gave satisfactory elemental analysis.

Conclusion

With the di- and trisaccharides reported herein, the synthesis of all the oligosaccharides present in motifs A−E of the AG of *M. tuberculosis* are now completed. Arabinogalactan of *M. tuberculosis* has special interest for two fundamental reasons: (1) it is essential for the viability and (2) three out of four sugars—*araf, galf,* and *rhamp*—are not found in human beings.

Experimental Section

The NMR spectra were recorded in $CDCl_3$ with TMS internal standard or D_2O with methanol as standard on AC 200 MHz, MSL 300 MHz, or DRX 500 MHz. Optical rotations were measured with digital polarimeter. FAB mass spectra were recorded on an autospec mass spectrometer. Elemental analyses were done on elemental analyzer model 1108EA. Column chromatography was carried out with silica gel (60−120 mesh). TLC was performed on 0.25 mm precoated silica gel plates (60F-254) with UV or I_2 or anisaldehyde reagent in ethanol. Dry solvents were distilled over CaH_2 and stored over molecular sieves. Light petroleum refers to mixture of hexanes with bp 60−80 °C.

2,3,5-Tri-*O*-acetyl-α,β-D-arabinofuranosyl-trichloroacetamidate (10). A solution of per-*O*-acetyl-D-arabinofuranose **8** (4.0 g, 12.57 mmol) and tri-*n*-butyltin ethoxide (8.4 g, 25.15 mmol) in $ClCH_2CH_2Cl$ (40 mL) was heated under reflux for 3 h and concentrated. The residue was purified on silica gel with light petroleum−ethyl acetate (EtOAc) (3:2) as eluent to give **9** (2.43 g, 70%). The resulting product was immediately treated with CCl_3CN (6.34 g, 44.02 mmol) in the presence of DBU (1.47 g) in CH_2Cl_2 (50 mL) at 0 °C for 2 h. Then solvent was removed, and the residue was purified by flash chromatography on silica gel with light petroleum−EtOAc (3:1) as eluent to give **10** (2.35 g, 65%) which was used without delay.

Ethyl 2,3-Di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactofuranoside (12). A solution of **11** (3.0 g, 7.75 mmol), imidazole (1.1 g, 16.28 mmol), and *tert*-butyldiphenylsilyl chloride (2.13 g, 7.75 mmol) in CH_2Cl_2 (50 mL) was stirred at room temperature for 3 h. The reaction mixture was washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified on silica gel column with light petroleum−EtOAc (10:1) as eluent to give **12** (4.36 g, 90%) as a syrup: $[\alpha]_D$ −53.2 (c = 1, $CHCl_3$); ^{1}H NMR δ (300 MHz, $CDCl_3$): 1.05 (s, 9 H), 1.20 (t, 3 H, J = 7.1 Hz), 3.40−3.48 (m, 1 H), 3.65−3.79 (m, 4 H), 3.96 (dd, 1 H, J = 3.0, 1.3 Hz), 4.03−4.10 (m, 1 H), 4.21 (dd, 1 H, J = 6.65, 2.7 Hz), 4.44−4.58 (m, 4 H), 5.00 (s, 1 H), 7.20−7.40 (m, 15 H), 7.60−7.65 (m, 5 H); ^{13}C NMR δ (50 MHz, $CDCl_3$): 15.0, 19.1, 26.8, 62.9, 64.9, 71.2, 71.8, 72.2, 80.7, 83.4, 87.8, 106.0, 127.5−129.7, 133.0, 134.6−138.0; FAB-MS: 649 (M + 23) Anal. Calcd for $C_{38}H_{46}O_6Si$: C, 72.84; H, 7.34. Found: C, 73.16; H, 7.55.

Ethyl 5-*O*-(α-D-Arabinofuranosyl)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactofuranoside (14). To a stirred solution of **12** (3.0 g, 4.8 mmol), **10** (2.1 g, 5.0 mmol), and 4 Å molecular sieves (MS) powder (0.5 g) in CH_2Cl_2 (50 mL) under nitrogen at −20 °C was added $BF_3{\cdot}OEt_2$ (0.2 mL). After 2 h at room temperature, solid $NaHCO_3$ (0.2 g) was added and then filtered. The filtrate was washed with brine, dried (Na_2SO_4), and concentrated. The residue was passed through a short column of silica gel with light petroleum−EtOAc (9:1) as eluent to obtain the disaccharide **13** (2.96 g) (contaminated with **12** as a minor impurity) and treated with 0.05 M NaOMe in methanol (15 mL) at room temperature for 2 h. The reaction mixture was deionized by the addition of Amberlite IR 120 (H^+) resin (pH 6), filtered, and concentrated. The residue was purified by silica gel column chromatography with light petroleum−EtOAc (1:1) as eluent to obtain **14** (2.03 g, 56%) as a syrup: $[\alpha]_D$ −22.4 (c = 1, $CHCl_3$); ^{1}H NMR δ (200 MHz, $CDCl_3$): 1.07 (s, 9 H), 1.20 (t, 3 H, J = 7.5 Hz), 3.60−3.70 (m, 5 H), 3.90−4.02 (m, 4 H), 4.06−4.17 (m, 4 H), 4.30−4.58 (m, 4 H), 5.01 (s, 1 H), 5.21 (s,1 H), 7.20−7.45 (m,15 H), 7.60−7.75 (m, 5 H); ^{13}C NMR δ (125 MHz, $CDCl_3$): 15.0, 18.0, 25.6, 60.2, 61.7, 62.1, 71.0, 76.8, 77.1, 77.3, 77.4, 79.1, 82.9, 85.8, 86.9, 104.5,106.5,126.1−128.4, 134.0, 136.0; FAB-MS: 781 (M + 23). Anal. Calcd for $C_{43}H_{54}O_{10}Si$: C, 68.07; H, 7.12. Found: C, 68.34; H, 6.93.

Ethyl 5-*O*-(2′,3′,5′-Tri-*O*-benzyl-α-D-arabinofuranosyl)-2,3-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactofuranoside (15). To a stirred solution of **14** (1.5 g, 1.98 mmol) and NaH (60% dispersion in paraffin, 0.35 g, 14.8 mmol) in dry DMF (10 mL) under nitrogen atmosphere was added benzyl bromide (1.11 g, 6.53 mmol). After 3 h at room temperature, the reaction was quenched with methanol (2 mL)

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and partitioned between water and diethyl ether. The ether layer was washed with brine, dried (Na_2SO_4), and concentrated to give a residue which was purified on silica gel with light petroleum−EtOAc (10:1) as eluent to give **15** (1.77 g, 87%) as a syrup; $[\alpha]_D$ −18.4 (c = 1.5, $CHCl_3$); ^1H NMR δ (500 MHz, $CDCl_3$): 1.08 (s, 9 H), 1.20 (t, 3 H, J = 6.25 Hz), 3.45−3.50 (m, 3 H), 3.74−3.80 (m, 2 H), 3.90 (d, 2 H, J = 5.2 Hz), 3.92−4.00 (m, 3 H), 4.05−4.10 (m, 3 H), 4.28−4.60 (m, 10 H), 5.09 (s, 1 H), 5.20 (s, 1 H), 7.18−7.37 (m, 30 H), 7.68−7.72 (m, 5 H); ^{13}C NMR δ (125 MHz, $CDCl_3$): 14.8, 18.9, 26.5, 62.5, 63.0, 68.4, 71.4, 71.6, 71.7, 73.0, 76.4, 76.6, 76.9, 79.5, 79.6, 82.8, 83.4, 88.3, 105.1, 106.6, 127.2−129.2, 133.2, 135.3, 137.6; FAB-MS: 1051 (M + 23). Anal. Calcd for $C_{64}H_{72}O_{10}Si$: C, 74.70; H, 7.00. Found: C, 74.4; H, 7.14.

Pent-4-enyl 2,3,5,6-Tetra-*O*-acetyl-*β*-D-galactofuranoside (18). To a stirred solution of per-*O*-acetyl *β*-D-galactofuranose **17** (2.0 g, 5.13 mmol), 4-pentene-1-ol (1.1 mL, 10.25 mmol), and 4 Å MS powder (0.5 g) in CH_2Cl_2 (20 mL) under nitrogen was added $BF_3{\cdot}OEt_2$ (0.1 mL) at 0 °C. After 2 h, solid $NaHCO_3$ (0.2 g) was added and filtered over Celite. The filtrate was washed with brine, dried (Na_2SO_4), concentrated. The residual syrup was purified by silica gel column chromatography by eluting with light petroleum−EtOAc (4:1) to give **18** (1.81 g, 85%) as a syrup: $[\alpha]_D$ −50.2 (c = 2, $CHCl_3$); ^1H NMR δ (200 MHz, $CDCl_3$): 1.64−1.76 (m, 4 H), 2.06−2.14 (4s, 12 H), 3.40−3.51 (m, 1 H), 3.62−3.74 (m, 1 H), 4.16−4.38 (m, 3 H), 4.96−5.08 (m, 5 H), 5.35−5.42 (m, 1 H), 5.71−5.92 (m, 1 H); ^{13}C NMR δ (50 MHz, $CDCl_3$): 20.3, 28.2, 29.7, 62.2, 66.5, 68.9, 76.2, 79.5, 81.0, 105.1, 114.6, 137.6, 169.6. Anal: Calcd for $C_{19}H_{28}O_{10}$: C, 54.80, H, 6.73. Found: C, 54.65, H, 6.52.

Ethyl 5-*O*-(2′,3′,5′-Tri-*O*-benzyl-α-D-arabinofuranosyl)-6-*O*-(*β*-D-galactofuranosyl)-2,3-di-*O*-benzyl-*β*-D-galactofuranoside (20). Compound **15** (1.5 g, 1.46 mmol) and a 1 M solution of *n*-Bu_4NF (3 mL) in THF (10 mL) were stirred for 30 min at room temperature and then concentrated. The residue was purified on short silica gel column with light petroleum−EtOAc (3:1) to provide **16** (1.06 g, 92%) used as such for subsequent reaction.

To a stirred solution of **16** (1.0 g, 1.26 mmol), **18** (0.63 g, 1.52 mmol), and 4 Å MS powder (0.5 g) in dry CH_2Cl_2 (20 mL) was added NIS (0.7 g, 3.16 mmol) followed by TfOH (0.1 mL in two intervals of 30 min). The reaction was stirred under dark at room temperature for 48 h and filtered through a Celite bed. The filtrate was washed with saturated solutions of $NaHSO_3$ and $NaHCO_3$ followed by brine solution. The organic layer was dried (Na_2SO_4) and concentrated. The residue was subjected column chromatography on silica gel with light petroleum−EtOAc (3:1) as eluent to obtain the crude trisaccharide derivative **19** (0.92 g). The crude **19** was treated with 0.05 M NaOMe in methanol (5 mL) at room temperature for 2 h. After the usual workup as indicated above for Zémplen reaction, the residue was chromatograghed on silica gel with light petroleum−EtOAc (2:3) as eluent to give **20** (0.56 g, 47%) as a syrup: $[\alpha]_D$ −22.6 (c = 0.6, $CHCl_3$); ^1H NMR δ (500 MHz, $CDCl_3$): 1.10 (t, 3 H, J = 7.5 Hz), 3.36−3.65 (m, 8 H), 3.76−3.97 (m, 10 H), 4.00−4.05 (m, 1 H), 4.27−4.51 (m, 10 H), 4.84 (s, 1 H), 4.96 (s, 1 H), 5.17 (s, 1 H), 7.12−7.25 (m, 25 H); ^{13}C NMR δ (125 MHz, $CDCl_3$): 14.8, 62.8, 63.7, 66.6, 69.5, 70.7, 71.5, 71.6, 71.9, 72.0, 73.2, 76.2, 78.3, 78.6, 80.0, 80.6, 83.5, 83.6, 86.9, 87.8, 87.9, 105.3, 106.8, 107.7, 127.4−128.2, 137.1−137.6. Anal. Calcd for $C_{54}H_{64}O_{15}$: C, 68.06, H, 6.72. Found: C, 68.35, H, 6.95.

Ethyl 5-*O*-(α-D-Arabinofuranosyl)-6-*O*-(*β*-D-galactofuranosyl)-*β*-D-galactofuranoside (6). Compound **20** (0.3 g, 0.31 mmol) and 10% $Pd(OH)_2/C$ (50 mg) in methanol (7 mL) were stirred under hydrogen atmosphere at normal temperature and pressure (ntp) for 8 h. The catalyst was filtered and the filtrate concentrated to give **6** (0.14 g, 90%) as a syrup: $[\alpha]_D$ −26.8 (c = 1.1, MeOH); ^1H NMR δ (500 MHz, D_2O): 1.10 (t, 3 H, J = 7.0 Hz), 3.48−3.72 (m, 8 H), 3.78−4.05 (m, 11 H), 4.88 (s, 1 H), 4.92 (s, 1 H), 5.10 (s, 1 H); ^{13}C NMR δ (125 MHz, D_2O): 15.2, 62.1, 63.8, 65.3, 68.2, 71.8, 77.2, 77.3, 77.4, 77.8, 81.9, 82.0, 82.2, 82.9, 83.9, 84.8, 107.6, 108.6, 109.6; FAB-MS: 525 (M + 23). Anal. Calcd for $C_{19}H_{34}O_{15}$: C, 45.42, H, 6.77. Found: C, 46.13, H, 7.0.

Ethyl 2,3,6-Tri-*O*-benzyl-*β*-D-galactofuranoside (21). Compound **11** (1.0 g, 2.1 mmol) and dibutyltin oxide (0.78 g, 3.13 mmol) in dry toluene (20 mL) were heated under reflux for 6 h with azeotropic removal of water, and then Bu_4NBr (0.10 g) and benzyl bromide (0.35 g, 2.1 mmol) were introduced. The reaction was heated under reflux for 24 h, solvent evaporated, and the residue taken up in ethyl acetate. The organic layer was successively washed with 10% aq KF solution and brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography with light petroleum−EtOAc (9:1) as eluent to give **21** (0.87 g, 71%) as a syrup: $[\alpha]_D$ − 48.25 (c = 1.1, $CHCl_3$); ^1H NMR δ (200 MHz, $CDCl_3$): 1.24 (t, 3 H, J = 7.3 Hz), 3.43−3.56 (m, 3 H), 3.72−3.80 (m,1 H), 4.08−4.14 (m, 1 H), 4.54−4.60 (m, 6 H), 5.05 (s, 1 H), 7.28−7.33 (m, 15 H); ^{13}C NMR δ (50 MHz, $CDCl_3$): 14.8, 62.6, 69.6, 71.3, 71.6, 71.9, 72.9, 80.9, 83.0, 87.6, 105.6, 127.2−128.0, 137.1−137.8. Anal. Calcd for $C_{29}H_{34}O_6$: C, 72.8, H, 7.11. Found: C, 72.42, H, 7.01.

Ethyl 5-*O*-(*β*-D-Galactofuranosyl)-2,3,6-tri-*O*-benzyl-*β*-D-galactofuranoside (23). To a stirred solution of **21** (0.5 g, 1.04 mmol), **18** (0.52 g, 1.25 mmol), 4 Å MS powder (0.5 g), and NIS (0.58 g, 2.61 mmol) in CH_2Cl_2 (20 mL) under nitrogen and in the dark was addded TfOH (0.05 mL). The reaction mixture was stirred for 24 h at room temperature and filtered through Celite, and the filtrate washed with saturated solutions of $NaHSO_3$ and $NaHCO_3$ and then with brine, dried (Na_2SO_4), and concentrated. The residual syrup was chromatographed on silica gel with light petroleum−EtOAc (4:1) as eluent to give the crude disaccharide **22** (0.57 g) which was treated with 0.05 M NaOMe in methanol (5 mL) at room temperature. After 2 h and the usual workup as given above for Zémplen reaction, the residue was purified on silica gel with light petroleum−EtOAc (1:4) as eluent to give **23** (0.32 g, 48%) as a syrup: $[\alpha]_D$ −84.12 (c = 1.2, $CHCl_3$); ^1H NMR δ (200 MHz, $CDCl_3$): 1.18 (t, 3 H, J = 7.1 Hz), 3.37−3.72 (m, 6 H), 3.85−3.90 (m, 2 H), 3.93−4.10 (m, 6 H), 4.33−4.61 (m, 6 H), 5.00 (s, 1 H), 5.34 (s, 1 H), 7.27−7.35 (m, 15 H); ^{13}C NMR δ (75 MHz, $CDCl_3$): 14.5, 62.5, 63.5, 69.2, 70.7, 71.5, 71.6, 72.8, 73.0, 78.3, 78.6, 80.2, 83.9, 86.5, 87.0, 104.9, 106.1, 127.1−128.0, 136.6−137.3. Anal. Calcd for $C_{35}H_{44}O_{11}$: C, 65.62, H, 6.87. Found: C, 66.32, H, 6.95.

Ethyl 5-*O*-(*β*-D-Galactofuranosyl)-*β*-D-galactofuranoside (7). A solution of **23** (0.2 g, 0.31 mmol) and 10% $Pd(OH)_2/C$ (50 mg) in methanol (5 mL) was stirred under hydrogen atmosphere at ntp. After 8 h, the catalyst was filtered and the filtrate concentrated to give **7** (0.10 g, 88%) as a thick syrup: $[\alpha]_D$ −105.22 (c = 1.1, MeOH); ^1H NMR δ (500 MHz, D_2O): 0.92 (t, 3 H, J = 6.4 Hz), 3.29−3.32 (m, 1 H), 3.40−3.44 (m, 2 H), 3.46−3.55 (m, 4 H), 3.64 (brs, 1 H), 3.73−3.77 (m, 4 H), 3.81−3.85 (m, 2 H), 4.92 (s, 2 H); ^{13}C NMR δ (125 MHz, D_2O): 15.1, 61.9, 63.6, 65.1, 71.4, 76.7, 77.0, 77.3, 81.7, 82.1, 82.2, 83.5, 107.5, 107.9. Anal. Calcd for $C_{14}H_{26}O_{11}$: C, 45.4, H, 7.02. Found: C, 45.75, H, 7.25.

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Supporting Information Available: ^1H and ^{13}C NMR spectra of **6**, **7**, **12**, **14**, **15**, **18**, **20**, **21**, **23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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