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Chemical synthesis of the hexasaccharide related to the repeating unit of the capsular polysaccharide from carbapenem resistant *Klebsiella pneumoniae* 2796 and 3264†

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The total synthesis of the hexasaccharide repeating unit of the CPS from carbapenem resistant *K. pneumoniae* 2796 and 3264 is reported using a sequential glycosylations approach. The total synthesis has been accomplished by glycosylation of rationally protected monosaccharide synthons derived from the commercially available sugars. The required uronic acid on the galactose moiety was successfully installed by a TEMPO-mediated late stage oxidation. The glycosylations were performed by the NIS-mediated activation of thioglycosides using H_2SO_4-silica as the promoter. Chloroacetate group was extensively used as a temporary protecting group to facilitate stereoselective glycosylations.

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Introduction

Bacterial capsular polysaccharides (CPS) and lipopolysaccharides (LPS) are responsible for their virulence factor. CPS and LPS are made up of oligosaccharide repeating units with varied sugar residues. As they remain exposed on the outer surface of the bacterial cell wall, they play pivotal role in infection. Due to the presence of different sugar residues in the oligosaccharide repeats, CPS and LPS demonstrate diverse character and act as the elicitor of innate immune responses. Literature reports suggest that there are potential scope with these bacterial O-antigens as vital candidates for anti-microbial agents and vaccine-targets.[1–3] However, it require tedious isolation and purification processes to harness these complex oligosaccharides in adequate quantity. Thus the chemical synthesis of the required oligosaccharides remains the only way to explore their vivid biological roles and potential as vaccine targets.

Klebsiella pneumoniae (*K. pneumoniae*) is an opportunistic pathogen that is responsible for community or hospital acquired infections. It mostly affects the urinary and respiratory tracts. Both CPS and LPS of the *K. pneumonia* are found to be responsible for the virulence. The CPS antigens are used for K-typing of *K. pneumoniae* whereas LPS antigens are used for O-typing.[4] The capsular antigens are protective against capsular pathogens such as *H. influenza* type b, meningococci and pneumococci.[5] Among large number of *K. pneumoniae* K-antigens only a few are associated with human disease.[6] This is a limiting factor for the development of suitable vaccine against this pathogen. Particularly the carbapenem resistant K-antigens (CRKP) are rarely known in the literature. Only recently, Kubler-Kielb has reported the structures of the CRKP CPS and LPS from clinical isolates collected from the infected patients of a CRKP outbreak in the US.[7] Herein, we report the total synthesis of the hexasaccharide repeating unit of the CPS from *K. pneumoniae* 2796 and 3264 in the form of its *p*-methoxyphenyl glycoside (Fig. 1). The particular aglycon in the reducing end will enable us to form further glycoconjugates

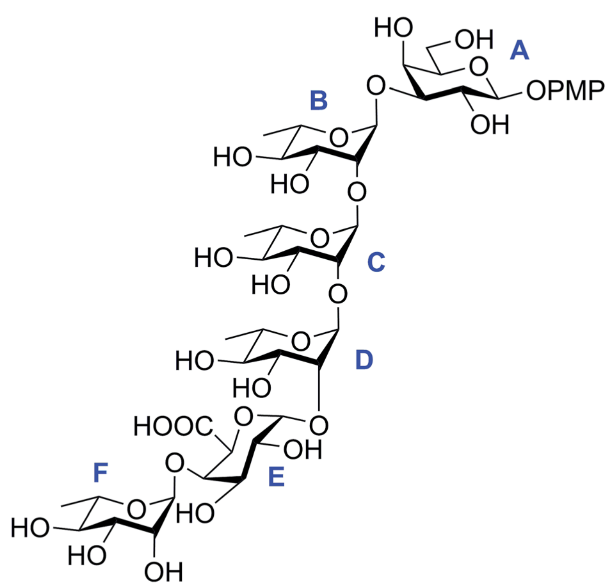

Fig. 1 Structure of the target hexasaccharide in the form of its *p*-methoxyphenyl glycoside.

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after the selective removal of the same from the per-*O*-acetylated derivative of the target oligosaccharide.

Results and discussion

Judicious retro-synthetic analysis indicated that a sequential glycosylations strategy would be the best fit for the successful synthesis of the target hexasaccharide **1**. Thus, three rhamnose moieties were planned to be stitched by using the same synthon **5** with the reducing end galactose moiety **6**. The chloroacetate group was thought to be the perfect choice as a temporary protecting group as it can ensure the required 1,2-*trans* glycosylations as well as can be de-protected selectively to pave the path for introduction of the next sugar unit. Next, a suitably protected galactose synthon **14** having a non-participating group at 2-position thought to be ideal for the required 1,2-*cis* linkage. A per-*O*-acylated rhamnose derivative **17** will complete the target hexasaccharide in its protected form. Finally, a TEMPO mediated oxidation of the primary hydroxyl group of the non-reducing end galactose moiety followed by global de-protection would furnish the required molecule (Fig. 2).

Therefore, the we started our synthesis with known *p*-tolyl 4-*O*-benzoyl-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (**2**).[8] Hydrolysis of the isopropylidene group using 80% AcOH at 80 °C (ref. 9) gave the diol **3** in 91% yield. Next, selective benzylation at the equatorial 3-OH was accomplished by following stannylene chemistry[10] to give the derivative **4** in 85% yield. Finally, protection of the sole 2-OH with chloroacetate[11] group afforded the required donor **5** in 89% yield. Donor **5** was coupled with the known acceptor **6** (ref. 12) by the activation of the thiotolyl using NIS in the presence of H_2SO_4-silica[13] at 0 °C to afford the disaccharide **7** in 91% yield. It is worth noting that the use of H_2SO_4-silica as the promoter for NIS-mediated activation of the thioglycoside donor found to be beneficial compared to the use of toxic, fuming and hygroscopic TfOH or TMSOTf. Further, selective de-protection of the chloroacetate group using thiourea[14] gave the disaccharide acceptor **8** in 87% isolated yield. Subsequently, glycosylations with the same donor **5** followed by de-protection of the chloroacetate group using the same reagent combination and condition was iterated twice to obtain the tetrasaccharide acceptor **12** (Scheme 1). The yields of the individual steps involved are mentioned in the Scheme 1.

In a separate experiment, known *p*-tolyl 2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-1-thio-β-D-galactopyranoside (**13**)[15] was treated with chloroacetic anhydride in the presence of dry pyridine to give the completely protected donor (**14**) in 88% yield. Next, glycosylations of the donor **14** with the tetrasaccharide acceptor **12** using NIS in the presence of H_2SO_4-silica at −50 °C gave the protected pentasaccharide **15** in 82% yield. Presence of the non-participating benzyl group at the 2-position of the galactosyl donor **14** and the reaction at very low temperature assured the formation of the desired 1,2-glycoside as the sole isolated product. Further, selective de-protection of

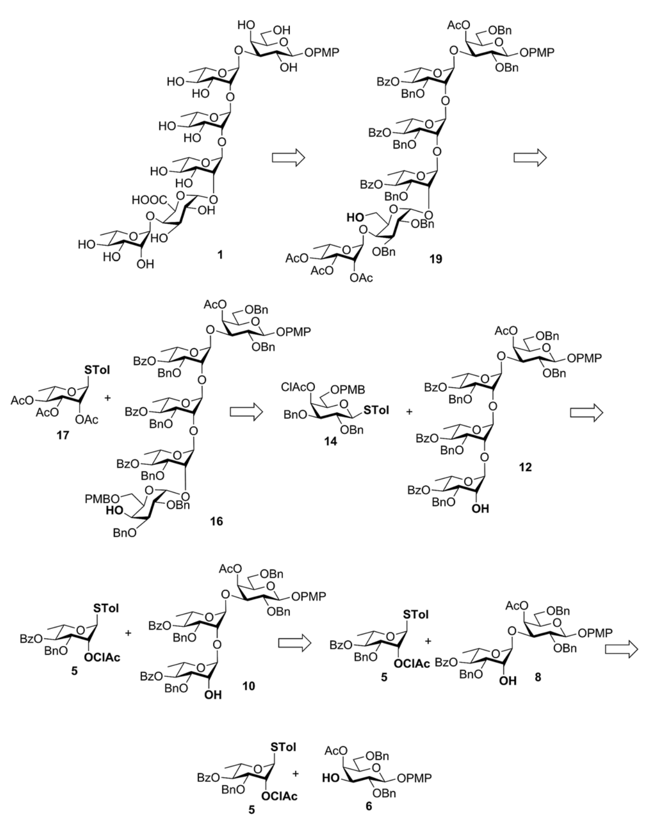
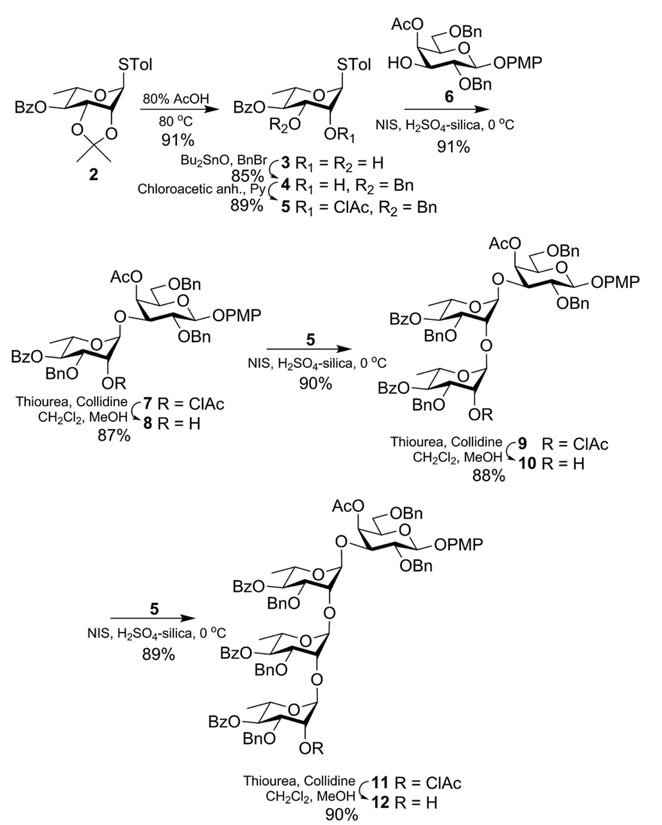


Fig. 2 Retrosynthetic analysis for the total synthesis of the target hexasaccharide 1.



Scheme 1 Synthesis of the tetrasaccharide acceptor 12.

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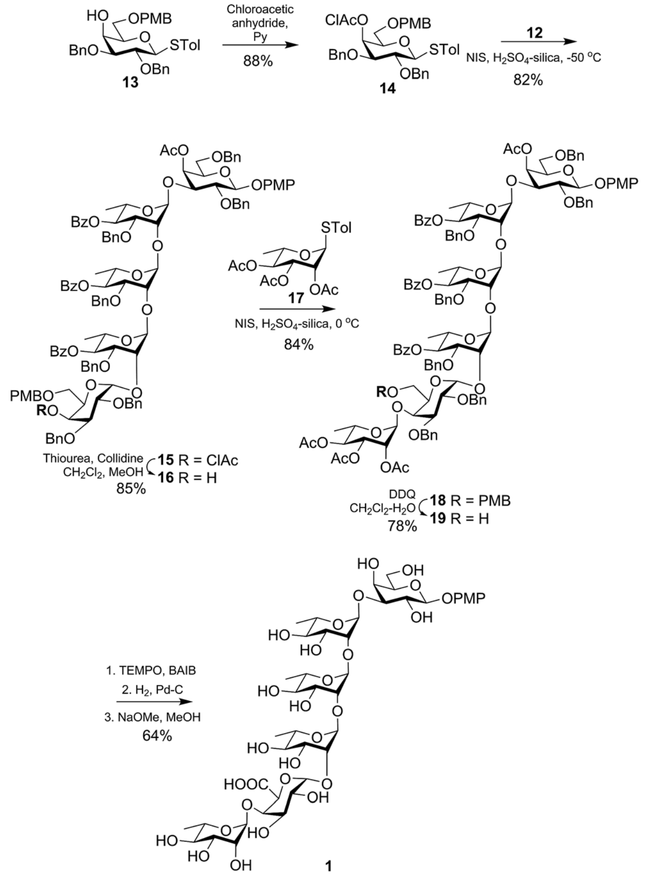

Scheme 2 Synthesis of the target hexasaccharide **1**.

the chloroacetate group using thiourea afforded the pentasaccharide acceptor **16** in 85% yield. Finally, glycosylations of **16** with the known donor **17** (ref. 16) using the same NIS/H_2SO_4-silica at 0 °C furnished the protected hexasaccharide **18** in 84% yield. At this stage, the strategically placed 4-methoxybenzyl group was selectively de-protected by oxidative cleavage using DDQ[17] to afford the hexasaccharide derivative **19** in 78% isolated yield. Oxidation of the primary hydroxyl group using TEMPO in the presence of bis-acetoxy iodobenzene (BAIB)[18] followed by catalytic hydrogenolysis and Zemplen de-*O*-acetylation[19] gave the target hexasaccharide **1** in 64% yield over three steps (Scheme 2). The amorphous white powder of compound **1** was triturated with CH_2Cl_2 and filtered to remove aromatic impurities.

Conclusions

In conclusion, we have successfully accomplished the total synthesis of the hexasaccharide repeating unit of the CPS from *K. pneumoniae* 2796 and 3264 in the form of its *p*-methoxyphenyl glycoside. The practical synthetic strategy used the minimum protecting group manipulations and the chloroacetate group was used extensively as the temporary protecting group to ensure stereoselective glycosylations using rhamnose synthons. A TEMPO-mediated late stage oxidation was used successfully to generate the desired uronic acid moiety. The synthetic will definitely enhance the scope for further biological evaluation of the target oligosaccharide related to the carbopenem resistant *K. pneumoniae* strains and pave the path for a potential vaccine target.

Experimental section

General methods

All solvents and reagents were dried prior to use according to standardized methods.[20] The commercially purchased reagents were used without any further purification unless mentioned otherwise. All reactions were monitored by Thin Layer Chromatography (TLC) on Silica-Gel 60-F_{254} with detection by fluorescence followed by charring after immersion in 10% ethanolic solution of H_2SO_4. Flash chromatography was performed with Silica Gel 230–400 mesh. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance 500 MHz spectrometer (^{1}H NMR at 500 MHz and ^{13}C NMR at 125 MHz). HRMS analysis was performed with Micromass Q-TOF micro (Waters Corporation) instrument by +ve mode electro-spray ionization.

***p*-Tolyl-4-*O*-benzoyl-1-thio-α-L-rhamnopyranoside (3).** Compound **2** (6 g, 14.5 mmol) was dissolved in AcOH–H_2O (8 : 1, 36 mL) and the solution was stirred at 80 °C for 2 h until the starting material was completely converted to a slower moving spot as suggested by TLC (*n*-hexane–EtOAc; 3 : 1). The solvents were evaporated and co-evaporated twice with toluene followed by purification of the crude product by flash chromatography using (*n*-hexane–EtOAc; 3.5 : 1) to afford pure compound **3** (4.9 g, 91%) as colourless syrup. $[\alpha]_D^{25}$ +103° (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.09–7.15 (m, 9H, Ar*H*), 5.51 (d, 1H, $J_{1,2}$ 1.5 Hz, H-1), 5.09 (t, 1H, $J_{3,4}$, $J_{4,5}$ 9.5 Hz, H-4), 4.50 (m, 1H, H-5), 4.26 (bd, 1H, $J_{1,2}$ 1.5 Hz, H-2), 4.07 (dd, 1H, $J_{2,3}$ 3.0 Hz, $J_{3,4}$ 9.5 Hz, H-3), 3.31 (bs, 1H, O*H*), 2.79 (bs, 1H, O*H*), 2.34 (s, 3H, $SC_6H_4CH_3$), 1.31 (d, 3H, $J_{5,6}$ 6.0 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 167.7 (COC_6H_5), 137.9, 133.6 (2), 132.1 (2), 129.9 (4), 129.3, 128.5 (2) (Ar*C*), 87.6 (C-1), 76.6, 72.3, 70.9, 67.0, 21.1 ($SC_6H_4CH_3$), 17.5 (C–CH_3). HRMS calcd for $C_{20}H_{22}O_5SNa$ $(M + Na)^+$: 397.1086, found: 397.1084.

***p*-Tolyl-4-*O*-benzoyl-3-*O*-benzyl-1-thio-α-L-rhamnopyranoside (4).** A mixture of compound **3** (4.8 g, 13 mmol) and Bu_2SnO (4.3 g, 17 mmol) was refluxed for 3 h at 80 °C in dry MeOH (30 mL). The resulting solution was concentrated *in vacuo*. The crude residue was dried under vacuum for 1 h. The residue was then dissolved in dry DMF (20 mL) followed by addition of Bu_4NI (5.3 g, 14.5 mmol) and stirred at room temperature for 10 min. BnBr (2.0 mL, 17 mmol) was added to the mixture and the solution was stirred for 10 h. After evaporating the solvents *in vacuo* the residue was dissolved in CH_2Cl_2 (40 mL) and washed successively with H_2O (50 mL), Na_2SO_3 (50 mL) and brine (50 mL). The organic layer was collected, dried (Na_2SO_4) and evaporated *in vacuo*. The crude product was purified by flash chromatography using *n*-hexane–EtOAc (6 : 1) as eluent to give the pure compound **4** (5.0 g, 85%). $[\alpha]_D^{25}$ +96° (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.03–7.10 (m, 14H, Ar*H*), 5.45 (d, 1H, $J_{1,2}$ < 1.0 Hz, H-1), 5.42 (t, 1H, $J_{3,4}$, $J_{4,5}$ 9.5 Hz, H-4), 4.65, 4.51 (ABq, 2H, J_{A-B} 12.0 Hz, CH_2Ph), 4.37 (m, 1H, H-5), 4.32 (dd, 1H, $J_{1,2}$ < 1.0 Hz, $J_{2,3}$ 3.0 Hz, H-2), 3.90 (dd, 1H, $J_{2,3}$ 3.0 Hz, $J_{3,4}$ 9.5 Hz, H-3),

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3.08 (bs, 1H, O*H*), 2.31 (s, 3H, S–C_6H_4–CH_3), 1.24 (d, 3H, $J_{5,6}$ 6.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 165.9 (*C*OC_6H_5), 137.9, 137.3, 133.3, 132.1 (2), 130.0 (3), 129.9 (2), 128.6 (2), 128.5 (2), 128.1 (4) (Ar*C*), 87.4 (C-1), 77.5, 73.2, 71.7, 69.8, 67.7, 21.2 (SC_6H_4*C*H_3), 17.5 (C–*C*H_3). HRMS calcd for $C_{27}H_{22}O_5SNa$ $(M + Na)^+$: 487.1555, found: 487.1553.

***p*-Tolyl-4-*O*-benzoyl-3-*O*-benzyl-2-*O*-chloroacetyl-1-thio-α-L-rhamnopyranoside (5).** Compound **4** (5.0 g, 11 mmol) and chloroacetic acetic anhydride (4.3 g, 25 mmol) were taken in 20 mL dry CH_2Cl_2 and cooled to 0 °C. Pyridine (3.6 mL, 44 mmol) was then added and after 2 h TLC (*n*-hexane–EtOAc; 7 : 1) showed complete conversion of the reactant to a faster moving spot, the mixture was evaporated *in vacuo* and co-evaporated twice with toluene to obtain a syrupy residue, which was then purified by flash chromatography using *n*-hexane–EtOAc (8 : 1) as eluent to give the pure compound **5** (5.2 g, 89%) as light yellow syrup. $[\alpha]_D^{25}$ +113° (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.04–7.15 (m, 14H, Ar*H*), 5.73 (dd, 1H, $J_{1,2}$, 1.5 Hz, $J_{2,3}$ 3.0 Hz, H-2), 5.45 (d, 1H, $J_{1,2}$ 1.5, H-1), 5.36 (t, 1H, $J_{3,4}$, $J_{4,5}$ 10.0 Hz, H-4), 4.66, 4.45 (ABq, 2H, J_{A-B} 12.5 Hz, CH_2Ph), 4.36 (m, 1H, H-5), 4.25, 4.17 (ABq, 2H, J_{A-B} 15.5 Hz, COCH_2Cl), 3.98 (dd, 1H, $J_{2,3}$ 3.0 Hz, $J_{3,4}$ 10.0 Hz, H-3), 2.35 (s, 3H, S–C_6H_4–CH_3), 1.29 (d, 3H, $J_{5,6}$ 6.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 166.7 (*C*OCH_2Cl), 165.5 (*C*OC_6H_5), 138.3, 136.8, 133.2, 132.4 (2), 129.9 (2), 129.8 (2), 129.5, 129.1, 128.3 (2), 128.2 (2), 128.0 (2), 127.8 (Ar*C*), 86.1 (C-1), 74.2, 72.6, 71.8, 71.3, 67.9, 74.2, 72.6, 71.8, 71.3, 67.9, 40.8 (CO*C*H_2Cl), 21.0 (SC_6H_4*C*H_3), 17.2 (C–*C*H_3). HRMS calcd for $C_{29}H_{29}ClO_6SNa$ $(M + Na)^+$: 563.1271, found: 563.1269.

***p*-Methoxyphenyl 4-*O*-benzoyl-3-*O*-benzyl-2-*O*-chloroacetyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (7).** A mixture of donor **5** (1.9 g, 3.6 mmol), known acceptor **6** (1.4 g, 2.8 mmol) and MS (4 Å) (1.5 g) in dry CH_2Cl_2 (15 mL) was stirred under nitrogen atmosphere for 30 min. NIS (1 g, 4.4 mmol) was added and the mixture was cooled in ice-water bath (~5 °C) before adding H_2SO_4-silica (75 mg). The mixture was stirred at the same temperature for 30 min when TLC (*n*-hexane–EtOAc; 3 : 1) indicated complete consumption of the donor. The reaction mixture was neutralized with Et_3N and the mixture was filtered through a pad of Celite. The filtrate was washed successively with aq. $Na_2S_2O_3$ (2 × 30 mL), aq. $NaHCO_3$ (2 × 30 mL) and brine (30 mL). Organic layer was separated, dried over Na_2SO_4 and evaporated *in vacuo*. The syrupy crude product thus obtained was purified by flash chromatography using *n*-hexane–EtOAc (4 : 1) as eluent to afford pure disaccharide **7** (2.3 g, 91%) as white foam. $[\alpha]_D^{25}$ +86° (*c* 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.07–7.12 (m, 20H, Ar*H*), 7.05, 6.82 (2d, 4H, C_6H_4OCH_3), 5.52 (dd, 1H, $J_{2',3'}$ 1.5 Hz, $J_{1',2'}$ < 1.0 Hz, H-2′), 5.39 (bd, 1H, $J_{3,4}$ 1.5 Hz, H-4), 5.23 (d, 1H, $J_{1',2'}$ < 1.0 Hz, H-1′), 5.22 (t, 1H, $J_{3',4'}$, $J_{4',5'}$ 10.0 Hz, H-4′), 5.06, 4.75 (ABq, 2H, J_{A-B} 11.0 Hz, CH_2Ph), 4.92 (d, 1H, $J_{1,2}$ 7.0 Hz, H-1), 4.61, 4.42 (ABq, 2H, J_{A-B} 12.5 Hz, CH_2Ph), 4.55, 4.48 (ABq, 2H, J_{A-B} 12.0 Hz, CH_2Ph), 4.21, 4.12 (ABq, 2H, J_{A-B} 15.5 Hz, CH_2Cl), 4.13 (m, 1H, H-5′), 3.93 (m, 2H, H-2, H-3), 3.88 (t, 1H, $J_{4,5}$, $J_{5,6a}$, $J_{5,6b}$ 6.5 Hz, H-5), 3.83 (dd, 1H, $J_{2',3'}$ 1.5 Hz, $J_{3',4'}$ 10.0 Hz, H-3′), 3.78 (s, 3H, OC_6H_4OCH_3), 3.58 (m, 2H, H-6a, H-6b), 1.97 (s, 3H, COCH_3), 1.25 (d, 3H, $J_{5',6'}$ 6.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 169.9 (*C*OCH_3), 166.6 (*C*OCH_2Cl), 165.6 (*C*OC_6H_5), 155.4, 151.1, 137.6, 137.5, 137.3, 133.1, 129.9 (2), 129.7, 128.5 (4), 128.3 (4), 128.2 (2), 127.8 (4), 127.7 (2), 127.6, 118.2 (2), 114.6 (2) (Ar*C*), 102.9 (C-1), 98.5 (C-1′), 79.0, 75.1, 74.7, 73.6, 73.5, 72.7, 72.5, 71.1, 69.9, 69.1, 68.2, 67.3, 55.6 (OC_6H_4O*C*H_3), 40.8 (CO*C*H_2Cl), 20.6 (CO*C*H_3), 17.6 (C–*C*H_3). HRMS calcd for $C_{51}H_{53}ClO_{14}Na$ $(M + Na)^+$: 947.3022, found: 947.3019.

***p*-Methoxyphenyl 4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (8).** A mixture of disaccharide **7** (2.2 g, 2.4 mmol), thiourea (900 mg, 12 mmol) and 2,4,6-collidine (1.6 mL, 12 mmol) were refluxed in 20 mL CH_2Cl_2–MeOH (2 : 3) for 10 hours when TLC (*n*-hexane–EtOAc; 2.5 : 1) confirmed the complete conversion of the starting material to a slower moving spot. The solvents were evaporated *in vacuo*, the solid residue was dissolved in CH_2Cl_2 and washed with 1 (N) HCl (2 × 30 mL). The organic layer was collected, filtered, dried (Na_2SO_4) and evaporated *in vacuo*. The crude residue thus obtained was further subjected to flash chromatography using *n*-hexane–EtOAc (3 : 1) as eluent to give the pure disaccharide acceptor **8** (1.8 g, 87%). $[\alpha]_D^{25}$ +121° (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.09–7.17 (m, 20H, Ar*H*), 7.07, 6.83 (2d, 4H, C_6H_4OCH_3), 5.42 (m, 1H, H-4), 5.34 (t, 1H, $J_{3',4'}$, $J_{4',5'}$ 9.5 Hz, H-4′), 5.30 (d, 1H, $J_{1',2'}$ < 1 Hz, H-1′), 5.04, 4.78 (ABq, 2H, J_{A-B} 11.0 Hz, CH_2Ph), 4.93 (d, 1H, $J_{1,2}$ 7.5 Hz, H-1), 4.61, 4.50 (ABq, 2H, J_{A-B} 12.5 Hz, CH_2Ph), 4.56, 4.49 (ABq, 2H, J_{A-B} 11.5 Hz, CH_2Ph), 4.10 (m, 1H, H-5′), 3.97–3.89 (m, 4H, H-2, H-3, H-5, H-2′), 3.78 (s, 3H, OC_6H_4OCH_3), 3.73 (dd, 1H, $J_{2',3'}$ 2.0 Hz, $J_{3',4'}$ 9.5 Hz, H-3′), 3.60 (m, 2H, H-6a, H-6b), 2.60 (bs, 1H, O*H*), 2.03 (s, 3H, COCH_3), 1.26 (d, 3H, $J_{5',6'}$ 6.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 169.8 (*C*OCH_3), 165.7 (*C*OC_6H_5), 155.4, 151.3, 137.8, 137.7, 137.4, 133.0, 129.9, 129.8, 128.4 (2), 128.3 (4), 128.3 (3), 128.2 (2), 127.8, 127.7 (2), 127.7 (2), 127.6 (2), 118.3 (2), 114.5 (2) (Ar*C*), 102.9 (C-1), 100.5 (C-1′), 79.0, 75.8, 75.4, 75.0, 73.6, 72.9, 72.8, 71.3, 69.9, 68.4, 68.2, 66.9, 55.5 (OC_6H_4O*C*H_3), 20.6 (CO*C*H_3), 17.5 (C–*C*H_3). HRMS calcd for $C_{49}H_{52}O_{13}Na$ $(M + Na)^+$: 871.3306, found: 871.3304.

***p*-Methoxyphenyl 4-*O*-benzoyl-3-*O*-benzyl-2-*O*-chloroacetyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (9).** A mixture of disaccharide acceptor **8** (1.6 g, 1.9 mmol), donor **5** (1.3 g, 2.5 mmol) and 4 Å MS (2 g) in dry CH_2Cl_2 (20 mL) was stirred under nitrogen atmosphere for 30 min. NIS (716 mg, 3.2 mmol) was added and cooled to 0 °C. After 15 min H_2SO_4-silica (75 mg) was added and stirring continued for 15 min till TLC (*n*-hexane–EtOAc; 2.5 : 1) confirmed the complete consumption of the donor. Then the reaction mixture was filtered through a pad of Celite. The filtrate was washed successively with aq. $Na_2S_2O_3$ (2 × 30 mL), aq. $NaHCO_3$ (2 × 30 mL) and brine (30 mL). Organic layer was separated, dried (Na_2SO_4) and evaporated *in vacuo*. The crude product thus obtained was subjected to flash chromatography using *n*-hexane–EtOAc (3 : 1) as the eluent to obtain the pure trisaccharide **9** (2.1 g, 90%) as white foam. $[\alpha]_D^{25}$ +87° (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.14–7.12 (m, 30H, Ar*H*), 7.01, 6.79 (2d, 4H, C_6H_4OCH_3), 5.64 (dd, 1H, $J_{2'',3''}$ 2.5 Hz, $J_{1'',2''}$ < 1.0 Hz, H-2″), 5.41 (m, 1H, H-4), 5.36 (t, 1H, $J_{3',4'}$, $J_{4',5'}$ 9.5 Hz, H-4′), 5.22 (d, 1H, $J_{1',2'}$ < 1.0 Hz, H-1′), 5.21 (t, 1H, $J_{3'',4''}$, $J_{4'',5''}$ 10.0 Hz, H-4″), 4.98, 4.82 (ABq, 2H, J_{A-B} 11.5 Hz, CH_2Ph), 4.89 (m, 2H, H-1, H-1″),

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4.65–4.47 (m, 6H, 3 × CH_2Ph), 4.20, 4.12 (ABq, 2H, J_{A-B} 15.0 Hz, COCH_2Cl), 4.08 (m, 1H, H-5′), 4.02 (dd, 1H, $J_{2'',3''}$ 2.5 Hz, $J_{3'',4''}$ 10.0 Hz, H-3″), 3.97 (m, 1H, H-5″), 3.89–3.86 (m, 4H, H-2, H-2′, H-3, H-5), 3.81 (dd, 1H, $J_{2',3'}$ 2.5 Hz, $J_{3',4'}$ 9.5 Hz, H-3′), 3.77 (s, 3H, $OC_6H_4OCH_3$), 3.58 (m, 2H, H-6a, H-6b), 2.03 (s, 3H, COCH_3), 1.30 (d, 3H, $J_{5',6'}$ 7.0 Hz, C–CH_3), 1.07 (d, 3H, $J_{5'',6''}$ 6.0 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 170.0 (COCH$_3$), 166.4 (COCH$_2$Cl), 165.7 (COC$_6$H$_5$), 165.6 (COC$_6$H$_5$), 155.4, 151.2, 137.8, 137.7, 137.3, 133.1, 130.1, 129.9 (2), 129.8, 128.5 (4), 128.4 (5), 128.3 (5), 128.2 (2), 128.1 (2), 127.8 (4), 127.7, 127.6 (3), 118.3 (3), 114.6 (3) (ArC), 103.0 (C-1), 100.4 (C-1′), 99.4 (C-1″), 78.3, 76.5, 76.0, 75.5, 74.6, 74.7, 73.5, 73.3, 72.9, 72.5, 71.0, 71.2, 70.3, 69.6, 68.4, 67.6, 67.4, 55.6 ($OC_6H_4OCH_3$), 40.9 (COCH$_2$Cl), 20.7 (COCH$_3$), 17.8, 17.4 (2 × C–CH$_3$). HRMS calcd for $C_{71}H_{73}ClO_{19}Na$ (M + Na)$^+$: 1287.4332, found: 1287.4330.

***p*-Methoxyphenyl 4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (10).** Pure trisaccharide **9** (2 g), thiourea (600 mg, 7.9 mmol) and collidine (1 mL, 7.9 mmol) were dissolved in 20 mL CH_2Cl_2–MeOH (2 : 3). The mixture was refluxed for 10 h when the complete conversion of the starting material to a slower moving spot was judged by the TLC (*n*-hexane–EtOAc; 2 : 1). The mixture was evaporated *in vacuo*. The solid residue thus obtained was dissolved in CH_2Cl_2 and washed with 1 (N) HCl (2 × 30 mL) and brine (2 × 30 mL). The organic layer was separated, dried (Na_2SO_4) and evaporated *in vacuo* to get the crude product. It was purified by flash chromatography using *n*-hexane–EtOAc (5 : 2) as the eluent to get the pure compound **10** (1.7 g, 88%) as white powder. $[\alpha]_D^{25}$ +78° (*c* 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.08–7.10 (m, 30H, ArH), 6.96, 6.74 (2d, 4H, $C_6H_4OCH_3$), 5.35 (m, 1H, H-4), 5.33 (t, 1H, $J_{3',4'}$, $J_{4',5'}$ 10.0 Hz, H-4′), 5.30 (t, 1H, $J_{3'',4''}$, $J_{4'',5''}$ 10.0 Hz, H-4″), 5.19 (d, 1H, $J_{1',2'}$ 2.0 Hz, H-1′), 5.09 (d, 1H, $J_{1'',2''}$ 2.0 Hz, H-1″), 4.91, 4.82 (ABq, 2H, J_{A-B} 12.5 Hz, CH_2Ph), 4.86 (d, 1H, $J_{1,2}$ 7.5 Hz, H-1), 4.64, 4.52 (ABq, 2H, J_{A-B} 12.0 Hz, CH_2Ph), 4.56–4.42 (m, 4H, 2 × CH_2Ph), 4.31 (dd, 1H, $J_{1'',2''}$ 2.0 Hz, $J_{2'',3''}$ 3.0 Hz, H-2″), 4.03 (m, 1H, H-5′), 3.97 (dd, 1H, $J_{1',2'}$ 2.0 Hz, $J_{2',3'}$ 3.0 Hz, H-2′), 3.93 (m, 1H, H-5″), 3.91 (dd, 1H, $J_{2'',3''}$ 3.0 Hz, $J_{3'',4''}$ 10.0 Hz, H-3″), 3.85–3.82 (m, 3H, H-2, H-3, H-5), 3.75 (dd, 1H, $J_{2',3'}$ 3.0 Hz, $J_{3',4'}$ 10.0 Hz, H-3′), 3.69 (s, 3H, $OC_6H_4OCH_3$), 3.53 (m, 2H, H-6a, H-6b), 2.62 (bs, 1H, OH), 1.93 (s, 3H, COCH_3), 1.23 (d, 3H, $J_{5',6'}$ 6.5 Hz, C–CH_3), 1.03 (d, 3H, $J_{5'',6''}$ 6.5 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 169.9 (COCH$_3$), 165.7, 165.6 (2 × COC$_6$H$_5$), 155.3, 151.1, 137.7 (3), 137.3, 133.0, 132.9, 130.0, 129.9, 129.8 (2), 129.7 (2), 128.4 (4), 128.3 (6), 128.2 (4), 128.1 (2), 127.8, 127.7 (4), 127.6, 127.5 (2), 118.2 (2), 114.5 (2) (ArC), 103.0 (C-1), 101.0 (C-1″), 100.6 (C-1′), 77.8, 75.9 (2), 75.6, 75.2, 74.4, 73.6, 73.2, 72.8 (2), 71.6, 71.3, 69.6, 68.4, 68.0, 67.5, 66.9, 55.5, 20.6 (COCH$_3$), 17.7, 17.3 (2 × C–CH$_3$). HRMS calcd for $C_{69}H_{72}O_{18}Na$ (M + Na)$^+$: 1211.4616, found: 1211.4613.

***p*-Methoxyphenyl 4-*O*-benzoyl-3-*O*-benzyl-2-*O*-chloroacetyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (11).** A mixture of trisaccharide acceptor **10** (1.5 g, 1.3 mmol), donor **5** (890 mg, 1.6 mmol) and 4 Å MS (1.5 g) in dry CH_2Cl_2 (15 mL) was stirred under nitrogen atmosphere for 30 min. NIS (444 mg, 1.9 mmol) was then added and the mixture was cooled to 0 °C. After that H_2SO_4-silica (50 mg) was added to it and allowed to stir for 30 min when TLC (*n*-hexane–EtOAc; 2 : 1) showed complete consumption of the donor. The mixture was filtered through a Celite pad and the filtrate was successively washed with aq. $Na_2S_2O_3$ (2 × 30 mL), aq. $NaHCO_3$ (2 × 30 mL) and brine (30 mL). The organic layer was collected, dried (Na_2SO_4) and evaporated *in vacuo*. Crude product thus obtained was purified by flash chromatography using *n*-hexane–EtOAc (2 : 1) as the eluent. The pure tetrasaccharide **11** (1.8 g, 89%) was obtained as white foam. $[\alpha]_D^{25}$ +142° (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.10–7.10 (m, 40H, ArH), 6.99, 6.78 (2d, 4H, $C_6H_4OCH_3$), 5.65 (dd, 1H, $J_{1''',2'''}$ < 1.0 Hz, $J_{2''',3'''}$ 3.0 Hz, H-2‴), 5.39–5.34 (m, 3H, H-4, H-4′, H-4″), 5.22 (d, 1H, $J_{1',2'}$ 1.5 Hz, H-1′), 5.21 (t, 1H, $J_{3''',4'''}$, $J_{4''',5'''}$ 10.0 Hz, H-4‴), 5.14 (d, 1H, $J_{1'',2''}$ 1.5 Hz, H-1″), 4.96, 4.82 (ABq, 2H, J_{A-B} 12.5 Hz, CH_2Ph), 4.94 (d, 1H, $J_{1''',2'''}$ < 1.0 Hz, H-1‴), 4.88 (d, 1H, $J_{1,2}$ 7.0 Hz, H-1), 4.70–4.42 (m, 8H, 4 × CH_2Ph), 4.29 (dd, 1H, $J_{1'',2''}$ 1.5 Hz, $J_{2'',3''}$ < 1.0 Hz, H-2″), 4.16, 4.09 (ABq, 2H, J_{A-B} 15.5 Hz, COCH_2Cl), 4.07–4.01 (m, 4H, H-3″, H-3‴, H-5′, H-5″), 3.96 (m, 1H, H-5‴), 3.95 (dd, 1H, $J_{1',2'}$ 1.5 Hz, $J_{2',3'}$ 2.5 Hz, H-2′), 3.90–3.84 (m, 3H, H-2, H-3, H-5), 3.78 (dd, 1H, $J_{2',3'}$ 2.5 Hz, $J_{3',4'}$ 9.5 Hz, H-3′), 3.76 (s, 3H, $OC_6H_4OCH_3$), 3.57 (m, 2H, H-6a, H-6b), 1.97 (s, 3H, COCH_3), 1.29 (d, 3H, $J_{5',6'}$ 6.5 Hz, C–CH_3), 1.14 (d, 3H, $J_{5'',6''}$ 6.5 Hz, C–CH_3), 1.09 (d, 3H, $J_{5''',6'''}$ 6.5 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 169.9 (COCH$_3$), 166.4 (COCH$_2$Cl), 165.8, 165.7, 165.6 (3 × COC$_6$H$_5$), 155.5, 151.3, 137.8, 137.7, 137.4, 133.2, 133.1 (2), 130.0 (2), 129.9 (2), 129.8 (2), 128.4 (14), 128.3 (8), 128.2 (2), 128.1 (2), 127.8 (6), 127.7 (2), 127.5 (2), 118.3 (2), 114.6 (2) (ArC), 103.1 (C-1), 101.1 (C-1″), 100.7 (C-1′), 99.2 (C-1‴), 78.2, 76.1, 75.7, 75.4, 74.6, 73.9, 73.7 (2), 73.3, 73.1, 72.9, 72.7, 71.8 (2), 71.3, 70.2, 69.6, 68.4, 67.7, 67.6, 67.3, 55.6, 40.9 (COCH$_2$Cl), 20.6 (COCH$_3$), 17.8, 17.7, 17.5 (3 × C–CH$_3$). HRMS calcd for $C_{91}H_{93}ClO_{24}Na$ (M + Na)$^+$: 1627.5643, found: 1627.5641.

***p*-Methoxyphenyl 4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (12).** To a solution of the tetrasaccharide **11** (1.7 g, 1.1 mmol) and thiourea (400 mg, 5.3 mmol) in 20 mL CH_2Cl_2–MeOH (2 : 3), collidine (0.7 mL, 5.3 mmol) was added and the mixture was refluxed for 12 h till TLC (*n*-hexane–EtOAc; 2 : 1) indicated the complete conversion of the starting material to a slower moving spot. The reaction mixture was evaporated *in vacuo* and the residue was dissolved in CH_2Cl_2. It was further washed with 1 (N) HCl (2 × 30 mL) and brine (2 × 30 mL). Resulting organic layer was collected, dried (Na_2SO_4) and evaporated *in vacuo* to obtain the crude product. It was further purified by flash chromatography using *n*-hexane–EtOAc (2 : 1) as the eluent to obtain the pure tetrasaccharide acceptor **12** (1.5 g, 90%) as white foam. $[\alpha]_D^{25}$ +102° (*c* 0.9, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.11–7.12 (m, 40H, ArH), 6.99, 6.79 (2d, 4H, $C_6H_4OCH_3$), 5.41–5.33 (m, 4H, H-4, H-4′, H-4″, H-4‴), 5.23 (d, 1H, $J_{1',2'}$ 1.5 Hz, H-1′), 5.19 (d, 1H, $J_{1''',2'''}$ 1.5 Hz, H-1‴), 5.12 (d, 1H, $J_{1'',2''}$ 1.5 Hz, H-1″), 4.95, 4.82 (ABq, 2H, J_{A-B} 12.5 Hz, CH_2Ph), 4.88 (d, 1H, $J_{1,2}$ 7.0 Hz, H-1), 4.72–4.44 (m, 8H, 4 × CH_2Ph), 4.37 (dd, 1H, $J_{1''',2'''}$ 1.5 Hz, $J_{2''',3'''}$ < 1.0 Hz, H-2‴), 4.30 (dd, 1H, $J_{1'',2''}$ 1.5 Hz, $J_{2'',3''}$ < 1.0 Hz, H-2″), 4.08–4.02

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(m, 4H, H-3″, H-3‴, H-5′, H-5″), 4.01–3.96 (m, 2H, H-2′, H-5‴), 3.88–3.84 (m, 3H, H-2, H-3, H-5), 3.79 (dd, 1H, $J_{2',3'}$ 3.5 Hz, $J_{3',4'}$ 6.5 Hz, H-3′), 3.77 (s, 3H, $OC_6H_4OCH_3$), 3.58 (m, 2H, H-6a, H-6b), 2.57 (bs, 1H, O*H*), 1.96 (s, 3H, $COCH_3$), 1.28 (d, 3H, $J_{5',6'}$ 6.0 Hz, C–CH_3), 1.16 (d, 3H, $J_{5'',6''}$ 6.0 Hz, C–CH_3), 1.11 (d, 3H, $J_{5''',6'''}$ 6.0 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 169.4 ($COCH_3$), 165.9, 165.8, 165.6 (3 × COC_6H_5), 155.4, 155.2, 127.8, 137.7 (4), 137.5, 133.1 (2), 133.0 (2), 130.6 (6), 129.8 (2), 128.4 (6), 128.3 (4), 128.2 (2), 128.0 (4), 127.8 (6), 127.7 (4), 127.6 (4), 118.3 (2), 114.5 (2) (Ar*C*), 103.0 (C-1), 101.2 (C-1‴), 100.9 (C-1″), 100.6 (C-1′), 78.1, 76.4, 76.2, 76.0, 75.4 (2), 74.8, 74.6, 73.7, 73.2, 73.1, 73.0, 72.9, 71.7, 71.6, 71.5, 69.6, 68.5, 68.2, 67.6 (2), 66.9, 55.6, 20.6 ($COCH_3$), 17.8, 17.7, 17.4 (3 × CH_3). HRMS calcd for $C_{89}H_{92}O_{23}Na$ $(M + Na)^+$: 1551.5927, found: 1551.5925.

4-Tolyl 2,3-di-*O*-benzyl-4-*O*-chloroacetyl-6-*O*-(4-methoxybenzyl)-1-thio-β-D-galactopyranoside (14). The compound **15** (1.3 g, 2.2 mmol) was dissolved in dry CH_2Cl_2 (20 mL) in presence of chloroacetic anhydride (770 mg, 4.5 mmol) and kept at 0 °C for 10 min. Pyridine (0.7 mL, 9.0 mmol) was then added to the reaction mixture and stirred for 2 hours when TLC (*n*-hexane–EtOAc; 4 : 1) showed complete conversion of the starting material to a faster moving spot. The reaction mixture was evaporated *in vacuo* and co-evaporated with toluene. The crude product thus obtained was further subjected to purification by flash chromatography using *n*-hexane–EtOAc (6 : 1) as eluent to get the pure compound **14** (1.3 g, 88%). $[\alpha]_D^{25}$ +139° (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.54–6.96 (m, 18H, Ar*H*), 5.74 (dd, 1H, $J_{3,4}$ 3.0 Hz, $J_{4,5}$ < 1.0 Hz, H-4), 4.83–4.53 (m, 4H, 2 × CH_2Ph), 4.67 (d, 1H, $J_{1,2}$ 9.0 Hz, H-1), 4.55, 4.42 (ABq, 2H, J_{A-B} 12.5 Hz, CH_2PhOMe), 4.10, 4.03 (ABq, 2H, J_{A-B} 15.5 Hz, CH_2Cl), 3.85 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.79 (dd, 1H, $J_{5,6a}$ 6.5 Hz, $J_{6a,6b}$ 9.5 Hz, H-6a), 3.71 (dd, 1H, $J_{2,3}$ 9 Hz, $J_{3,4}$ 3 Hz, H-3), 3.65 (t, 1H, $J_{1,2}$, $J_{2,3}$ 9.0 Hz, H-2), 3.64 (m, 1H, H-5), 3.55 (dd, 1H, $J_{5,6b}$ 7.5 Hz, $J_{6a,6b}$ 9.5 Hz, H-6b), 2.37 (s, 3H, S–C_6H_4–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 166.6 ($COCH_2Cl$), 159.3, 138.0, 137.6, 137.3, 132.6 (2), 129.7 (2), 129.5 (2), 129.4, 129.3, 128.3 (2), 128.2 (4), 128.0 (2), 127.8, 127.7, 113.7 (2) (Ar*C*), 87.8 (C-1), 80.9, 76.5, 75.6, 75.2, 73.1, 72.0, 68.7, 67.0, 55.1, 40.7 ($COCH_2Cl$), 21.0 ($SC_6H_4CH_3$). HRMS calcd for $C_{37}H_{39}ClO_7Na$ $(M + Na)^+$: 685.2001, found: 685.1998.

***p*-Methoxyphenyl 2,3-di-*O*-benzyl-4-*O*-chloroacetyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (15).** A mixture of tetrasaccharide acceptor **12** (1.3 g, 0.85 mmol), donor **14** (740 mg, 1.1 mmol) and MS 4 Å (2.0 g) in dry CH_2Cl_2 (20 mL) was stirred under nitrogen atmosphere for 30 min. NIS (322 mg, 1.4 mmol) was added and the mixture was cooled to −50 °C followed by the addition of H_2SO_4-silica (50 mg) and the mixture was allowed to stir at the same temperature for 15 minutes. As TLC (*n*-hexane–EtOAc; 5 : 2) suggested the full consumption of the donor, the reaction was quenched by Et_3N. It was then followed by filtration of the mixture through a Celite pad. Resulting solution was then successively washed with aq. $Na_2S_2O_3$ (2 × 30 mL), aq. $NaHCO_3$ (2 × 30 mL) and brine (30 mL). It was then dried (Na_2SO_4) and evaporated *in vacuo*. The crude product was then purified by flash chromatography using *n*-hexane–EtOAc (3 : 1) as the eluent. Thus the pure pentasaccharide **15** (1.4 g, 82%) was furnished as white foam. $[\alpha]_D^{25}$ +68° (*c* 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.10–6.99 (m, 55H, Ar*H*), 6.81, 6.79 (2d, 4H, $C_6H_4OCH_3$), 5.69 (bd, 1H, $J_{3,4}$ 1.5 Hz, H-4), 5.42–5.37 (m, 4H, H-4, H-4′, H-4″, H-4‴), 5.21 (d, 1H, $J_{1',2'}$ 1.0 Hz, H-1′), 5.15 (d, 1H, $J_{1''',2'''}$ < 1.0 Hz, H-1‴), 5.11 (d, 1H, $J_{1'',2''}$ 1.0 Hz, H-1″), 4.96, 4.83 (ABq, 2H, J_{A-B} 12.5 Hz, CH_2Ph), 4.88 (d, 1H, $J_{1,2}$ 7.0 Hz, H-1), 4.83, 4.76 (ABq, 2H, J_{A-B} 10.5 Hz, CH_2Ph), 4.79 (d, 1H, $J_{1'''',2''''}$ 3.5 Hz, H-1⁗), 4.70–4.15 (m, 12H, 6 × CH_2Ph), 4.53 (m, 1H, H-5⁗), 4.35 (m, 2H, H-2″, H-2‴), 4.12 (m, 1H, H-3⁗), 4.08–4.01 (m, 3H, H-5′, H-3″, H-3‴), 4.01, 4.90 (ABq, 2H, J_{A-B} 15.0 Hz, $COCH_2Cl$), 3.99–3.94 (m, 3H, H-2′, H-5″, H-5‴), 3.87–3.86 (m, 2H, H-3, H-5), 3.81–3.78 (m, 2H, H-2, H-3′), 3.77 (s, 3H, $OC_6H_4OCH_3$), 3.73 (s, 3H, $OCH_2C_6H_4$-OCH_3), 3.64 (dd, 1H, $J_{1'''',2''''}$ 3.5 Hz, $J_{2'''',3''''}$ 6.5 Hz, H-2⁗), 3.58 (m, 2H, H-6a, H-6b), 3.27 (m, 2H, H-6a⁗, H-6b⁗), 1.95 (s, 3H, $COCH_3$), 1.28 (d, 3H, $J_{5',6'}$ 6.0 Hz, C–CH_3), 1.16 (d, 3H, $J_{5'',6''}$ 6.0 Hz, C–CH_3), 1.09 (d, 3H, $J_{5''',6'''}$ 6.0 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 169.9 ($COCH_3$), 166.7 ($COCH_2Cl$), 165.8, 165.6 (2) (3 × COC_6H_5), 159.1, 155.4, 151.2, 138.8, 138.0, 137.9, 137.7 (2), 137.5, 133.1, 132.9, 130.1, 130.0, 129.9 (2), 129.8, 129.7 (2), 128.4 (10), 128.2 (10), 128.2 (10), 128.1 (4), 127.8 (4), 127.7 (2), 127.6, 127.5 (2), 127.4 (4), 127.3, 118.3 (2), 114.5 (2), 113.6 (2) (Ar*C*), 103.0 (C-1), 101.3 (C-1‴), 100.6 (C-1′), 99.1 (C-1″), 97.2 (C-1⁗), 78.1, 76.0, 75.9, 75.7, 75.5, 75.2, 75.0, 74.7, 74.6, 74.3, 73.7 (2), 73.2, 73.1, 73.0, 72.9, 72.1 (2), 71.6, 71.0, 70.3, 70.0, 68.5, 67.6 (2), 67.4, 67.2, 55.6, 55.1, 41.0 ($COCH_2Cl$), 20.6 ($COCH_3$), 17.8, 17.6 (2) (3 × CH_3). HRMS calcd for $C_{119}H_{123}ClO_{30}Na$ $(M + Na)^+$: 2089.7685, found: 2089.7683.

***p*-Methoxyphenyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (16).** A solution of the pentasaccharide **15** (1.3 g, 0.6 mmol), thiourea (240 mg, 3.2 mmol) and 2,4,6-collidine (0.4 mL, 3.2 mmol) in 20 mL CH_2Cl_2–MeOH (2 : 3) was refluxed for 10 h. When the TLC (*n*-hexane–EtOAc; 2 : 1) suggested the complete conversion of the starting material to a slower moving spot, the reaction mixture was evaporated *in vacuo*. It was then dissolved in CH_2Cl_2 and washed with brine (2 × 30 mL). The organic layer was collected, dried (Na_2SO_4) and evaporated. The crude product thus obtained was purified by flash chromatography using *n*-hexane–EtOAc (2 : 1) to give the pure pentasaccharide acceptor **16** (1.1 g, 85%) as white foam. $[\alpha]_D^{25}$ +108° (*c* 0.7, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.07–6.98 (m, 54H, Ar*H*), 6.78, 6.76 (2d, 4H, $C_6H_4OCH_3$), 5.44–5.34 (m, 4H, H-4, H-4′, H-4″, H-4‴), 5.21 (d, 1H, $J_{1',2'}$ 1.0 Hz, H-1′), 5.15 (d, 1H, $J_{1''',2'''}$ < 1.0 Hz, H-1‴), 5.11 (d, 1H, $J_{1'',2''}$ 1.0 Hz, H-1″), 4.95, 4.81 (ABq, 2H, J_{A-B} 11.5 Hz, CH_2Ph), 4.87 (d, 1H, $J_{1,2}$ 7.0 Hz, H-1), 4.82 (d, 1H, $J_{1'''',2''''}$ 3.0 Hz, H-1⁗), 4.70–4.40 (m, 14H, 7 × CH_2Ph), 4.37–4.36 (m, 3H, H-2″, H-2‴, H-4⁗), 4.13 (m, 1H, H-5⁗), 4.06–3.90 (m, 8H, H-2′, H-3″, H-3‴, H-5′, H-5″, H-5‴, H-6a⁗, H-6b⁗), 3.80–3.79 (m, 4H, H-2, H-3, H-3′, H-5), 3.77 (s, 3H, $OC_6H_4OCH_3$), 3.70 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.58 (m, 3H, H-6a, H-6b, H-2⁗), 3.64 (m, 1H, H-3⁗), 2.82 (br s, 1H, O*H*), 1.94 (s, 3H, $COCH_3$), 1.27 (d, 3H, $J_{5',6'}$ 6.0 Hz, C–CH_3), 1.16 (d, 3H, $J_{5'',6''}$ 6.0 Hz, C–CH_3), 1.09

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(d, 3H, $J_{5''',6'''}$ 6.0 Hz, C–C*H*$_3$). ^{13}C NMR (CDCl$_3$, 125 MHz) δ: 169.9 (*C*OCH$_3$), 165.7 (2), 165.6 (3 × *C*OC$_6$H$_5$), 159.1, 155.5, 151.2, 139.0, 138.0, 137.8 (2), 137.7, 137.6, 133.1, 132.8, 130.2, 130.1 (2), 129.9 (2), 129.8 (4), 129.4 (2), 128.4 (10), 128.3 (4), 128.2 (8), 128.1 (6), 127.9 (4), 127.8 (4), 127.7 (2), 127.6 (2), 127.5 (2), 127.3 (2), 118.3 (2), 114.6 (2), 113.7 (2) (Ar*C*), 103.0 (C-1), 101.3 (C-1‴), 100.7 (C-1′), 99.2 (C-1″), 96.8 (C-1⁗), 78.1, 76.0, 75.5, 74.6, 73.7 (2), 73.3 (4), 73.2 (2), 73.0, 72.7, 72.4, 72.2, 71.6, 70.8, 69.6, 69.4, 68.5, 68.3, 68.2 (2), 67.7, 67.6 (2), 55.6, 55.1, 20.6 (COCH$_3$), 17.8, 17.7, 17.6 (3 × *C*H$_3$). HRMS calcd for C$_{117}$H$_{122}$O$_{29}$Na (M + Na)$^+$: 2013.7969, found: 2013.7967.

***p*-Methoxyphenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (18).** Pentasaccharide acceptor **16** (1.0 g, 0.5 mmol), known donor **17** (260 mg, 0.7 mmol) and 4 Å MS (2 g) were taken in 20 mL of dry CH$_2$Cl$_2$. The mixture was stirred under nitrogen for 45 min followed by the addition of NIS (190 mg, 0.8 mmol). After cooling the reaction mixture to 0 °C H$_2$SO$_4$-silica (75 mg) was added to it. Reaction was continued at the same temperature. After 30 minutes when the TLC (*n*-hexane–EtOAc; 2 : 1) suggested that the whole of the acceptor was consumed, the mixture was neutralised with Et$_3$N and filtered through a Celite pad. The filtrate was successively washed with aq. Na$_2$S$_2$O$_3$ (2 × 30 mL), aq. NaHCO$_3$ (2 × 30 mL) and brine (30 mL). The organic layer was separated, dried (Na$_2$SO$_4$) and evaporated *in vacuo* to get the crude product. It was purified by flash chromatography using *n*-hexane–EtOAc (3 : 2) as eluent to obtain the pure hexasaccharide **18** (960 mg, 84%) as the white foam. $[\alpha]_D^{25}$ +132° (*c* 0.7, CHCl$_3$). ^{1}H NMR (CDCl$_3$, 500 MHz) δ: 8.11–7.00 (m, 54H, Ar*H*), 6.99, 6.79 (2d, 4H, C$_6$H$_4$OC*H*$_3$), 5.50 (s, 1H, H-2′′′′′), 5.44–5.39 (m, 4H, H-4, H-4′, H-4″, H-4‴), 5.37–5.34 (m, 2H, H-3′′′′′, H-5′′′′′), 5.21 (m, 2H, H-1′, H-1′′′′′), 5.09 (m, 2H, H-1″, H-1‴), 5.03 (t, 1H, $J_{3''''',4'''''}$, $J_{4''''',5'''''}$ 10.0 Hz, H-4′′′′′), 4.96, 4.83 (ABq, 2H, J_{A-B} 11.5 Hz, C*H*$_2$Ph), 4.89 (d, 1H, $J_{1,2}$ 6.5 Hz, H-1), 4.78–4.28 (m, 14H, 7 × C*H*$_2$Ph), 4.70 (d, 1H, $J_{1'''',2''''}$ 3.0 Hz, H-1⁗), 4.36–4.34 (m, 2H, H-2‴, H-4⁗), 4.21 (s, 1H, H-2″), 4.08–3.93 (m, 8H, H-2′, H-3″, H-3‴, H-5′, H-5″, H-5⁗, H-6a⁗, H-6b⁗), 3.88–3.78 (m, 5H, H-2, H-3, H-3′, H-5, H-5‴), 3.77 (s, 3H, OC$_6$H$_4$OC*H*$_3$), 3.68 (s, 3H, OCH$_2$C$_6$H$_4$OC*H*$_3$), 3.59–3.53 (m, 3H, H-6a, H-6b, H-2⁗), 3.48 (m, 1H, H-3⁗), 2.09, 2.06, 2.01, 1.96 (4s, 12H, 4 × COC*H*$_3$), 1.29 (d, 3H, $J_{5',6'}$ 6.0 Hz, C–C*H*$_3$), 1.16 (d, 3H, $J_{5'',6''}$ 6.0 Hz, C–C*H*$_3$), 1.13 (d, 3H, $J_{5''''',6'''''}$ 6.0 Hz, C–C*H*$_3$), 1.09 (d, 3H, $J_{5''',6'''}$ 6.0 Hz, C–C*H*$_3$). ^{13}C NMR (CDCl$_3$, 125 MHz) δ: 170.0, 169.9, 169.7, 169.5 (4 × *C*OCH$_3$), 165.7, 165.6, 165.5 (3 × *C*OC$_6$H$_5$), 158.9, 155.4, 151.1, 139.0, 138.5, 137.9, 137.7 (2), 137.6, 137.5, 133.0 (2), 132.8, 131.0, 130.3, 130.1, 130.0 (2), 129.8 (4), 129.2 (2), 128.4 (4), 128.3 (8), 128.2 (8), 128.1 (4), 128.1 (4), 127.8, 127.7 (2), 127.6 (2), 127.5 (4), 127.2 (4), 127.1, 118.2 (2), 114.5 (2), 113.5 (2) (Ar*C*), 102.9 (C-1), 101.3 (C-1‴), 100.6 (C-1′), 99.2 (C-1″), 98.6 (C-1′′′′′), 96.6 (C-1⁗), 81.3, 78.1, 76.1, 76.0 (2), 75.4, 75.1, 74.7, 74.6, 74.2, 73.9 (2), 73.6, 73.2 (2), 73.1, 73.0, 72.9, 72.7, 72.5, 72.2, 71.6, 71.5, 71.1, 70.4, 69.7, 69.5, 69.4, 68.5, 68.1, 67.6, 67.5, 67.5, 66.7, 64.7, 55.5, 55.0, 20.8 (2), 20.7, 20.6 (2) (4 × CO*C*H$_3$), 17.7, 17.6 (2), 17.4 (4 × *C*H$_3$). HRMS calcd for C$_{129}$H$_{138}$O$_{36}$Na (M + Na)$^+$: 2285.8866, found: 2285.8863.

***p*-Methoxyphenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-4-*O*-benzoyl-3-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-4-*O*-acetyl-2,6,-di-*O*-benzyl-β-D-galactopyranoside (19).** To a solution of the pure hexasaccharide **18** (950 mg, 0.4 mmol) in CH$_2$Cl$_2$ (24 mL) water (5 mL) and DDQ (190 mg, 0.8 mmol) were consecutively added and vigorously stirred for 3 h when the TLC (*n*-hexane–EtOAc; 2 : 1) suggested complete conversion of the starting material to a slower moving spot. The reaction mixture was washed successively with H$_2$O and brine. Organic layer was collected, dried (Na$_2$SO$_4$) and evaporated *in vacuo*. The crude product thus obtained was purified by flash chromatography using *n*-hexane–EtOAc (3 : 1) to afford the pure compound **19** (702 mg, 78%) as foam. $[\alpha]_D^{25}$ +172° (*c* 0.7, CHCl$_3$). ^{1}H NMR (CDCl$_3$, 500 MHz) δ: 8.11–7.11 (m, 50H, Ar*H*), 6.99, 6.79 (2d, 4H, C$_6$H$_4$OC*H*$_3$), 5.46–5.38 (m, 6H, H-2′′′′′, H-4, H-4′, H-4″, H-4⁗, H-5′′′′′), 5.28 (dd, 1H, $J_{2''''',3'''''}$ 3.5 Hz, $J_{3''''',4'''''}$ 6.5 Hz, H-3′′′′′), 5.24 (d, 1H, $J_{1',2'}$ < 1.0 Hz, H-1′), 5.16 (d, 1H, $J_{1''''',2'''''}$ < 1.0 Hz, H-1′′′′′), 5.11 (d, 1H, $J_{1'',2''}$ < 1.0 Hz, H-1″), 5.07 (d, 1H, $J_{1''',2'''}$ < 1.0 Hz, H-1‴), 5.02–4.42 (m, 12H, 6 × C*H*$_2$Ph), 4.99 (m, 1H, H-4′′′′′), 4.90 (d, 1H, $J_{1,2}$ 6.5 Hz, H-1), 4.43 (m, 1H, H-2‴), 4.37 (s, 1H, H-2″), 4.18 (t, 1H, $J_{3''',4'''}$, $J_{4''',5'''}$ 6.0 Hz, H-4‴), 4.05–3.95 (m, 8H, H-2′, H-3″, H-3‴, H-5′, H-5″, H-5⁗, H-6a⁗, H-6b⁗), 3.91–3.86 (m, 3H, H-2, H-3, H-3′, H-5, H-5‴), 3.81 (dd, 1H, $J_{2',3'}$ 7.5 Hz, $J_{3',4'}$ 2.5 Hz, H-3′), 3.77 (s, 3H, OC$_6$H$_4$OC*H*$_3$), 3.71–3.58 (m, 3H, H-6a, H-6b, H-2⁗), 3.47 (m, 1H, H-3⁗), 2.06, 1.99, 1.98 (3s, 12H, 4 × COC*H*$_3$), 1.29 (d, 3H, $J_{5',6'}$ 6.0 Hz, C–C*H*$_3$), 1.21 (d, 3H, $J_{5'',6''}$ 6.0 Hz, C–C*H*$_3$), 1.17 (d, 3H, $J_{5''''',6'''''}$ 6.0 Hz, C–C*H*$_3$), 1.09 (d, 3H, $J_{5''',6'''}$ 6.5 Hz, C–C*H*$_3$). ^{13}C NMR (CDCl$_3$, 125 MHz) δ: 170.0, 169.9, 169.7, 169.5 (4 × *C*OCH$_3$), 166.0, 165.8, 165.6 (3 × *C*OC$_6$H$_5$), 155.4, 151.2, 138.9, 138.5, 138.0, 137.8 (2), 137.7, 137.2, 133.3, 133.1, 132.9, 130.1, 130.0 (2), 128.5 (2), 128.4 (8), 128.3 (6), 128.2 (6). 128.1 (8), 128.0, 127.8 (2), 127.7 (2), 127.6 (2), 127.5 (2), 127.4, 127.3, 127.2, 118.3 (2), 114.5 (2) (Ar*C*), 103.3 (C-1), 101.1 (C-1‴), 100.6 (C-1′), 99.2 (C-1″), 98.8 (C-1′′′′′), 95.8 (C-1⁗), 78.2, 77.7, 76.3, 76.1, 76.0, 75.4, 75.3, 75.0, 74.9, 74.6, 73.7, 73.4, 73.2, 72.9, 72.5, 72.2, 71.7, 71.7, 71.0, 70.9, 70.8, 70.7, 70.3, 69.6, 68.9, 68.6, 68.4, 67.7, 67.6, 67.5, 67.0, 62.4, 55.6, 20.8 (2), 20.7, 20.6 (4 × CO*C*H$_3$), 17.8, 17.6 (2), 17.4 (4 × *C*H$_3$). HRMS calcd for C$_{121}$H$_{130}$O$_{35}$Na (M + Na)$^+$: 2165.8290, found: 2165.8287.

***p*-Methoxyphenyl-α-L-rhamnopyranosyl-(1→4)-α-D-galactopyranosyl uronic acid-(1→2)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→3)-β-D-galactopyranoside (1).** Compound **19** (702 mg, 0.3 mmol) was dissolved in CH$_2$Cl$_2$–H$_2$O (1.5 : 1; 20 mL). TEMPO (30 mg, 0.2 mmol) was added followed by iodosobenzene diacetate (480 mg, 1.6 mmol) and the mixture was stirred at 5 °C for 7 h. Aq. saturated Na$_2$S$_2$O$_3$ (5 mL) was added to stop the reaction. After diluting the reaction mixture with CH$_2$Cl$_2$, it was washed with brine (2 × 30 mL). The organic layer was separated, dried (Na$_2$SO$_4$), filtered and evaporated to a syrupy compound. It was then dissolved in MeOH (50 mL) and passed through a 10% Pd–C cartridge in a ThalesNano flow hydrogenation assembly under continuous flow of H$_2$ at atmospheric pressure. The

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hydrogenolysis of the benzyl groups were complete after 3 such cycles as evident from mass spectroscopy. NaOMe in MeOH (0.5 M, 1 mL) was added to the solution and it was stirred at room temperature for 12 h. The solution was neutralized by DOWEX 50W H^+ resin, filtered and evaporated *in vacuo* to afford the final hexasaccharide **1** (257 mg, 75%) as white amorphous mass. $[\alpha]_D^{25}$ +54° (*c* 0.5, MeOH). HRMS calcd for $C_{43}H_{66}O_{29}Na$ $(M + Na)^+$: 1069.3587, found: 1069.3585. ^1H NMR (MeOD, 500 MHz) δ: 6.73, 6.70 (2d, 4H, $C_6H_4OCH_3$), 5.26 (d, 1H, $J_{1',2'} \leq 1.0$ Hz, H-1′), 5.24 (d, 1H, $J_{1''''',2'''''} \leq 1.0$ Hz, H-1′′′′′), 5.21 (d, 1H, $J_{1'''',2''''} \leq 1.0$ Hz, H-1′′′′), 5.11 (d, 1H, $J_{1'',2''} \leq 1.0$ Hz, H-1′′), 5.06 (d, 1H, $J_{1''',2'''} \leq 1.0$ Hz, H-1′′′), 4.77 (d, 1H, $J_{1,2}$ 8.0 Hz, H-1), 3.70 (s, 3H, $C_6H_4OCH_3$), 1.28–1.24 (m, 12H, 4 × CH_3). ^{13}C NMR (125 MHz, MeOD) δ: 173.4 (COOH), 156.5, 152.1, 116.7 (2), 115.7 (2) (aromatic *C*), 103.3 (C-1), 102.7 (C-1′), 102.6 (C-1′′′), 102.4 (C-1′′), 102.3 (C-1′′′′′), 101.2 (C-1′′′′), 80.0, 79.8, 78.2, 77.7, 76.6, 76.4, 74.9, 74.4, 74.2, 73.9, 73.7, 73.5, 72.3, 72.2, 72.1, 72.0, 71.9, 71.8, 70.5, 70.4, 70.3, 70.2, 69.5, 63.9, 63.2, 56.2, 18.1, 18.0, 17.9 (2) (4 × C–CH_3).

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