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Chemical synthesis of the pentasaccharide related to the repeating unit of the *O*-antigen of *Enterobacter cloacae* G2277

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ABSTRACT

A practical and highly efficient total synthesis of the pentasaccharide related to the *O*-antigen of *Enterobacter cloacae* G2277, the causative agent of nosocomial infection, has been accomplished in the form of its 4-methoxyphenyl glycoside. The unique pentasaccharide, →2)-α-L-Rha*p*-(1→2)-α-L-Rha*p*-(1→2)-α-L-Rha*p*-(1→4)-α-D-Gal*p*A-(1→3)-α-D-Glc*p*NAc-(1→, was assembled by a [3+2] convergent approach as well as a sequential assembly of five rationally protected monosaccharide building blocks. In the convergent approach, α-D-Gal*p*-(1→3)-α-D-Glc*p*NAc disaccharide was synthesized with a potential site for the uronic acid and the α-L-Rha*p*-(1→2)-α-L-Rha*p*-(1→2)-α-L-Rha*p* trisaccharide trichloroacetimidate was glycosylated to form the protected pentasaccharide in good yield. A TEMPO-mediated late stage oxidation of 6-OH of the galactose moiety resulted the characteristic uronic acid. Finally, global deprotection gave the target pentasaccharide. Both strategies were found to be equally efficient in respect to the yield of the target pentasaccharide derivative.

1. Introduction

Enterobacter cloacae are the causative agent for various nosocomial infections.[1] It is further complicated by the emergence of multidrug resistant strains.[2] Although the serotyping scheme for *E. cloacae* based on *O*-antigens has been established in 1983, only a few *O*-polysaccharide structures have been reported so far.[3] Recently, Perepelov et al.[4] reported the structure of the *O*-polysaccharide from *E. cloacae* G2277. Herein, we report the total chemical synthesis of that pentasaccharide repeating unit of the *O*-polysaccharide from *E. cloacae* in the form of its 4-methoxyphenyl glycoside (**1**, Fig. 1). Establishment of the chemical pathway for the synthesis of the target pentasaccharide will pave the path for making pure material in quantity and help further biological studies. Moreover, the selective removal of the 4-methoxyphenyl group will allow the formation of suitable glycoconjugate with aglycons using trichloroacetimidate chemistry.

2. Results and discussion

Critical evaluation of the retrosynthetic analysis revealed that a convergent [3+2] approach will suit best for the synthesis of the linear pentasaccharide. Therefore, it was first disconnected to a disaccharide, α-D-Gal*p*-(1→3)-α-D-Glc*p*NAc and a trisaccharide, α-L-Rha*p*-(1→2)-α-L-Rha*p*-(1→2)-α-L-Rha*p*. The disaccharide was further disconnected to two monosaccharides that can be derived from commercially available D-GlcNH$_2$ and D-Gal. On the otherhand,

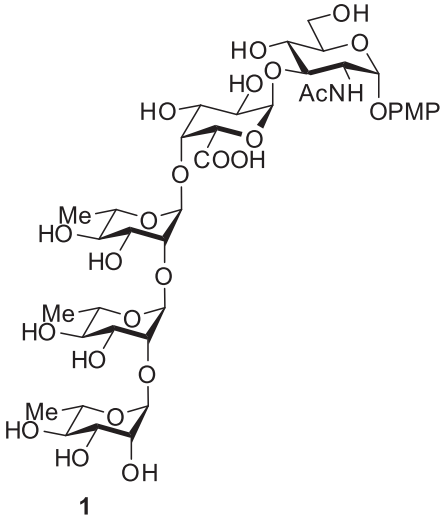

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Fig. 1. Structure of the target pentasaccharide **1**.

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the trisaccharide can be prepared from three suitably protected rhamnose derivatives through sequential glycosylations. These rhamnose derivatives may be obtained from commercially available L-rhamnose through rational protecting group manipulations (Fig. 2).

The known galactose derivative **2**[5] was treated with *p*-anisaldehydedimethylacetal in the presence of 10-camphorsulfonic acid (CSA)[6] to afford the 4,6-*O*-(4-methoxy benzylidene) derivative **3** in 89% yield. The remaining hydroxyl groups were further benzylated using BnBr in the presence of NaH[7] to give the fully protected derivative **4** in 94% yield. Regioselective opening of the 4-methoxybenzylidene acetal using $NaCNBH_3$ and TFA[6] followed by acetylation using Ac_2O in pyridine[8] furnished the desired donor **6** in 96% yield. Next, the donor **6** was coupled to the known acceptor **7**[9] through activation of the thioglycoside using NIS in the presence of H_2SO_4-silica[10] at −50 °C to form the disaccharide **8** in 85% isolated yield. Only the desired 1,2-*cis* disaccharide was formed as evident by the ^1H signal at δ 5.69 (d, 1H, $J_{1',2'}$ 4.0 Hz) and the ^{13}C signal at δ 97.4 assigned to the newly formed linkage. The 4-*O*-acetate group of the galactose donor **6** is the key for the exclusive formation of the 1,2-*cis* linkage.[11] Finally, Zemplen de-O-acetylation[12] of the disaccharide **8** gave the disaccharide acceptor **9** in 95% yield (Scheme 1).

In a separate experiment, the disaccharide acceptor **10** was prepared from suitably protected L-rhamnose derivatives derived from commercially available L-rhamnose following the reported literature procedure.[13] The structure of the disaccharide acceptor was satisfactorily characterized by NMR and mass spectrometry and matched satisfactorily with the data available in the literature.

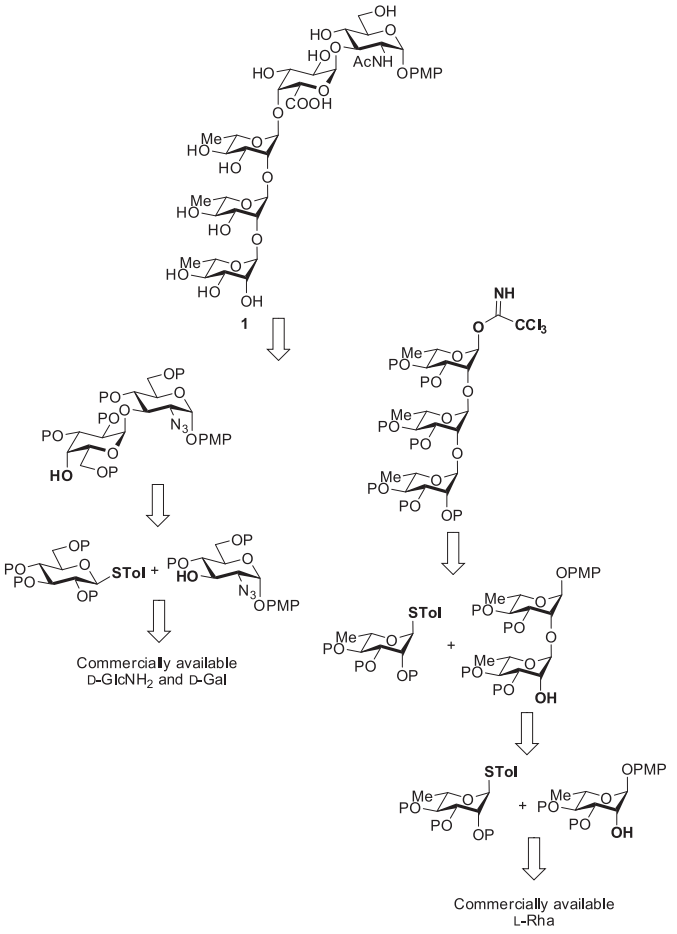
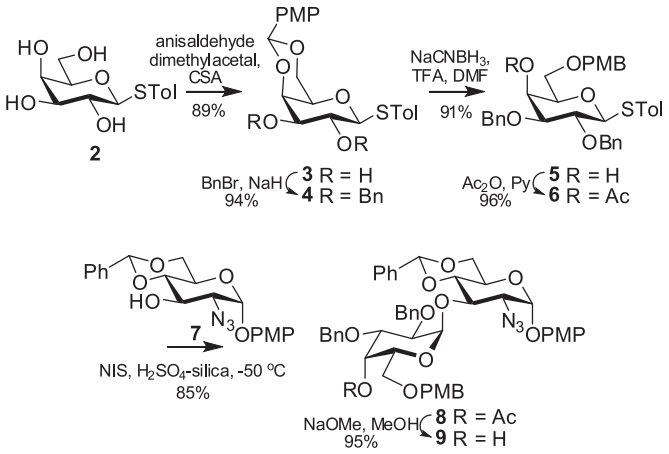
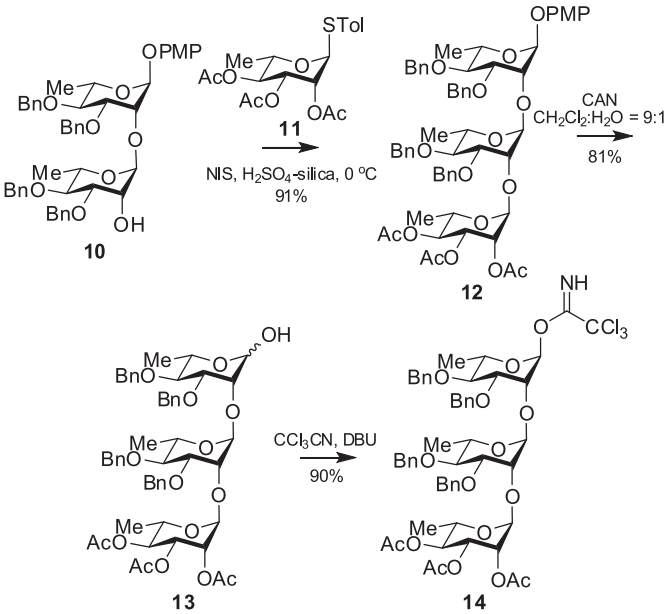


Fig. 2. Retrosynthetic analysis for the synthesis of the target pentasaccharide **1**.



Scheme 1. Synthesis of the disaccharide acceptor **9.**

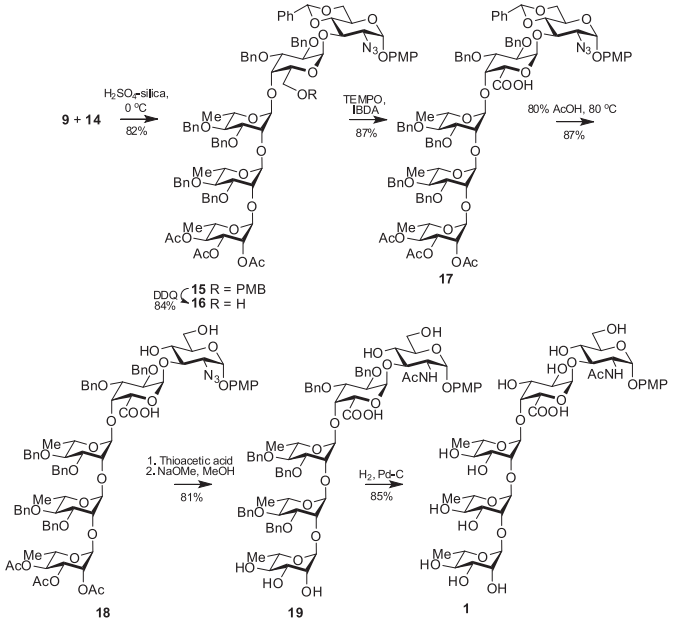
Further, the known thiotolyl L-rhamnose derivative **11**[14] was coupled with the disaccharide acceptor **10** using NIS and H_2SO_4-silica to afford the protected trisaccharide **12** in 91% yield. The newly formed 1,2-*trans*glycosidic linkage was confirmed by the ^1H signal at δ 4.99 (d, 1H, $J_{1'',2''}$ 1.5 Hz) and the ^{13}C signal at δ 99.0. CAN-mediated[15] oxidative cleavage of the 4-methoxyphenyl group resulted the corresponding hemiacetal **13** in 81% yield, which was subsequently treated with trichloroacetonitrile in the presence of DBU[16] to furnish the trisaccharide trichloroacetimidate **14** in 90% yield (Scheme 2). Considering the reactivity of the trichloroacetimidate derivative, it was directly used for glycosylation without further characterization.



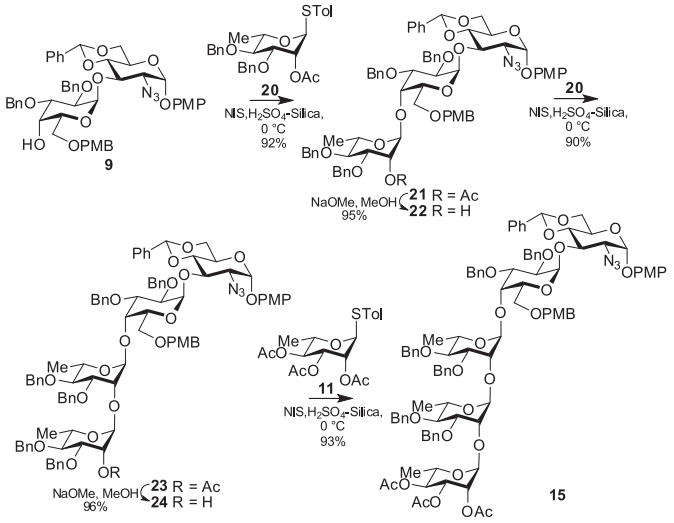
Scheme 2. Synthesis of the trisaccharide trichloroacetimidate donor **14**.

The disaccharide acceptor **9** was coupled with the trisaccharide donor **14** through the activation of the trichloroacetimidate by H_2SO_4-silica[17] to furnish the protected pentasaccharide **15** in 82% isolated yield. Once the protected pentasaccharide was obtained, the 4-methoxybenzyl group was selectively deprotected through DDQ[18] mediated oxidative cleavage. The primary OH group thus obtained, was oxidized to the corresponding uronic acid **17** using TEMPO in the presence of iodosobenzene diacetate.[19] It is worth

noting that the 4-methoxyphenyl group at the reducing end of the protected pentasaccharide remained unaffected by the TEMPO-mediated oxidation. Next, the benzylidene group was hydrolysed by 80% AcOH at 80 °C[20] to afford the pentasaccharidediol **18** in 87% yield. At this point the azido functionality was converted to the required acetamido moiety by the treatment of thioacetic acid.[21] Subsequently, Zemplen de-O-acetylation using NaOMe in MeOH gave the pentasaccharide derivative **19** in 81% yield. Finally, hydrogenolysis using 10% Pd–C cartridge in a continuous flow hydrogenation assembly furnished the target pentasaccharide **1** in 85% yield (Schemes 3 and 4).



Scheme 3. Synthesis of the target pentasaccharide **1**.



Scheme 4. Synthesis of the protected pentasaccharide **15** through sequential glycosylations.

After successful completion of the total synthesis of the target pentasaccharide via (2+3) strategy, we wanted to compare the efficiency of the sequential glycosylation strategy. Therefore, the disaccharide acceptor **9** was reacted with the known donor **20**[22] using NIS in the presence of H_2SO_4-silica to afford the trisaccharide **21** in 92% isolated yield. De-O-acetylation using NaOMe in MeOH gave the trisaccharide acceptor **22** in 95% yield. Further glycosylation of the same donor **20** with the acceptor **22** resulted the tetrasaccharide **23** in 90% yield. Zemplen de-O-acetylation using NaOMe in MeOH afforded the tetrasaccharide acceptor **24** in 96% yield. Final glycosylation of the tetrasaccharide acceptor **24** with the known donor **11** through activation of the thioglycoside using NIS in the presence of H_2SO_4-silica furnished the protected pentasaccharide **15** in 93% yield. The protected pentasaccharide **15** was converted to the target pentasaccharide **1** by the strategy depicted in Scheme 3.

3. Conclusions

In conclusion, we have accomplished the total synthesis of the pentasaccharide repeating unit of *Enterobacter cloacae* G2277 in the form of its 4-methoxyphenyl glycoside starting from commercially available sugars. The total synthesis has been achieved through a convergent [3+2] strategy as well as the sequential approach. Both strategies found to be almost equally efficient in terms of the overall yield. H_2SO_4-silica alone or in conjunction with NIS was proved to be a better alternative to classical acids such as TfOH or TMSOTf for the activation of trichloroacetimidate and thioglycosides, respectively. The 4-methoxyphenyl group at the reducing end may be deprotected selectively from the per-*O*-acetyl derivative of the target pentasaccharide and further coupled to suitable aglycon using trichloroacetimidate chemistry.

4. Experimental

4.1. General

All solvents and reagents were dried prior to use according to standardized methods.[23] The commercially purchased reagents were used without any further purification unless mentioned otherwise. Dichloromethane was dried and distilled over P_2O_5 to make it anhydrous and moisture-free. 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. Optical rotations were measured on sodium-line at ambient temperature. ^1H and ^{13}C NMR were recorded on Bruker 500 MHz spectrometer.^1H NMR values were denoted as H for the reducing end glucosamine unit, H′ for the galacturonic acid unit, H″ for the rhamnose unit connected to the 4-*O*-position of the galacturonic acid unit, H‴ for the fourth rhamnose unit from the reducing end and H⁗ for the non-reducing end rhamnose unit.

4.2. Preparation of H_2SO_4-silica:[24]

To a slurry of silica gel (10 g, 200–400 mesh) in dry diethyl ether (50 mL) was added commercially available concentrated H_2SO_4 (1 mL), and the slurry was shaken for 5 min. The solvent was evaporated under reduced pressure, resulting in free flowing H_2SO_4-silica, which was dried at 110 °C for 3 h and used for the reactions.

4.3. 4-Tolyl 4,6-*O*-(4-methoxybenzylidene)-1-thio-β-D-galactopyranoside (3)

A mixture of known 4-tolyl-1-thio-β-D-galactopyranoside **2** (3.0 g, 10.5 mmol), 4-anisaldehyde dimethyl acetal (2.7 mL, 15.7 mmol) and CSA (50 mg) in anhydrous CH_3CN (20 mL) was stirred at room temperature for 3 h when TLC (EtOAc) showed complete conversion of starting material. Et_3N was added to neutralize the solution. After evaporating the solvents in vacuo, the crude product was purified by flash chromatography using *n*-

hexane-EtOAc (1:2) as eluent to furnish pure compound **3** (3.8 g, 89%) as amorphous white mass. $[\alpha]_D^{25}+102$ (*c* 1.0, $CHCl_3$); Rf (*n*-hexane-EtOAc, 1:2) 0.45; IR (neat): 1742, 1628, 1565, 1539, 1434, 1363, 1181, 1043, 761 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.56, 7.10 (2d, 4H, *J* 8.0 Hz, $C_6H_4OCH_3$), 7.30, 6.85 (2d, 4H, *J* 8.5 Hz, $SC_6H_4CH_3$), 5.42 (s, 1H, $CHC_6H_4OCH_3$), 4.41 (d, 1H, $J_{1,2}$ 9.0 Hz, H-1), 4.31 (dd, 1H, $J_{5,6a}$ 1.0 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.11 (d, 1H, $J_{3,4}$ 1.5 Hz, *H*-4), 3.95 (dd, 1H, $J_{5,6b}$ 1.0 Hz, $J_{6a,6b}$ 12.5 Hz, H-6b), 3.8 (s, 3H, $CHC_6H_4OCH_3$), 3.61 (m, 2H, H-2, H-3), 3.45 (d, 1H, H-5), 2.35 (s, 3H, $SC_6H_4CH_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 160.2, 138.3, 134.2(2), 130.2, 129.6(2), 127.9(2), 126.9, 113.4(2) (Ar*C*), 101.1 ($CHC_6H_4OCH_3$), 87.0 (*C*-1), 75.3, 73.6, 69.8, 69.2, 68.6, 55.2 ($CHC_6H_4OCH_3$), 21.2 ($SC_6H_4CH_3$). HRMS (ESI): $(M+Na)^+$, found 427.1189. $C_{21}H_{24}O_6SNa$ requires 427.1191.

4.4. 4-Tolyl 2,3-di-*O*-benzyl-4,6-*O*-(4-methoxybenzylidene)-1-thio-β-D-galactopyranoside (4)

To the solution of compound **3** (3.8 g, 9.4 mmol) in DMF (30 mL), sodium hydride (0.9 g, 37.6 mmol, 60% in mineral oil) followed by benzyl bromide (3.4 mL, 28.2 mmol) were added. The reaction was completed after 2 h as judged by TLC (*n*-hexane-EtOAc; 2:1). MeOH (5 mL) was added to quench the reaction. The solvents were evaporated and the residue was dissolved in CH_2Cl_2 (30 mL) and washed with brine solution (2×50 mL). The organic layer was separated, dried over Na_2SO_4, evaporated in vacuo and finally purified by flash chromatography using *n*-hexane-EtOAc (3:1) to afford the pure product **4** (5.1 g, 94%) as colourless syrup. $[\alpha]_D^{25}+112$ (*c* 1.1, $CHCl_3$). Rf (*n*-hexane-EtOAc, 3:1) 0.42; IR (neat): 1753, 1621, 1587, 1533, 1428, 1353, 1178, 1039, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.62, 7.04 (2d, 4H, *J* 8.0 Hz, $SC_6H_4CH_3$), 7.47–7.28 (m, 12H, Ar*H*), 6.93 (m, 2H, $C_6H_4OCH_3$), 5.45 (s, 1H, $CHC_6H_4OCH_3$), 4.74, 4.72 (2s, 4H, CH_2Ph), 4.58 (d, 1H, $J_{1,2}$ 9.5 Hz, H-1), 4.36 (dd, 1H, $J_{5,6a}$ 1.5 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.13 (d, 1H, $J_{3,4}$ 3.0 Hz, H-4), 3.97 (dd, 1H, $J_{5,6b}$ 1.5 Hz, $J_{6a,6b}$ 12.5 Hz, H-6b), 3.85 (m, 4H, H-2, $CHC_6H_4OCH_3$), 3.62 (dd, 1H, $J_{2,3}$ 9.0 Hz, $J_{3,4}$ 3.0 Hz, H-3), 3.39 (d, 1H, $J_{4,5}$ 0.5 Hz, H-5), 2.33 (s, 3H, $SC_6H_4CH_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 160.1, 138.6, 138.1, 137.6, 133.4(2), 130.6, 129.6(2), 128.7, 128.4(2), 128.3(2), 128.2(2), 128.0(2), 127.8(2), 127.7, 127.6, 113.4(2) (Ar*C*), 101.2 ($CHC_6H_4OCH_3$), 86.6 (C-1), 81.4, 75.4, 75.3, 73.6, 71.7, 69.7, 69.4, 55.3 ($CHC_6H_4OCH_3$), 21.1 ($SC_6H_4CH_3$). HRMS (ESI): $(M+Na)^+$, found 607.2127. $C_{35}H_{36}O_6SNa$ requires 607.2130.

4.5. 4-Tolyl 2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-1-thio-β-D-galactopyranoside (5)

A solution of the acetal **4** (5.1 g, 8.7 mmol) in anhydrous DMF (50 mL) was cooled to 0 °C followed by addition of solid $NaCNBH_3$ (2.7 g, 43.6 mmol). The mixture was stirred under nitrogen for 30 min. A solution of TFA (6.7 mL, 87.3 mmol) in dry DMF (50 mL) was added dropwise to the reaction mixture. The resulting suspension was stirred for 2 h at 0 °C and then 10 h at room temperature. Solid $NaHCO_3$ was added to neutralize the mixture. DMF was evaporated and the residue was diluted with EtOAc (50 mL). The solution was filtered over Celite pad and washed successively with $NaHCO_3$ (2×50 mL) and brine (50 mL). The organic phase was collected, dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography using *n*-hexane-EtOAc (2:1) to afford pure compound **5** (4.7 g, 91%) as colourless syrup. $[\alpha]_D^{25}+134$ (*c* 1.0, $CHCl_3$); Rf (*n*-hexane-EtOAc, 2:1) 0.41; IR (neat): 1738, 1614, 1591, 1527, 1431, 1363, 1228, 1175, 1037, 857, 748 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.47–7.24 (m, 14H, Ar*H*), 7.05 (d, 2H, *J* 8.0 Hz, $SC_6H_4CH_3$), 6.87 (m, 2H, $C_6H_4OCH_3$), 4.83, 4.74 (2d, 2H, *J* 10.5 Hz, CH_2Ph), 4.72, 4.67 (2d, 2H, *J* 11.5 Hz, CH_2Ph), 4.57 (d, 1H, $J_{1,2}$ 9.5 Hz, H-1), 4.51, 4.48 (2d, 2H, *J* 11.5 Hz, $CH_2C_6H_4OCH_3$), 4.09 (s, 1H, H-4), 3.81 (s, 3H, $CH_2C_6H_4OCH_3$), 3.75 (m, 2H, H-5, H-6a), 3.70 (t, 1H, $J_{1,2}$, $J_{2,3}$ 9.5 Hz, H-2), 3.55 (m, 2H, H-3, H-6b), 2.51 (d, 1H, *J* 1.5 Hz, O*H*), 2.3 (s, 3H, $SC_6H_4CH_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 159.3, 138.2, 137.7, 137.6, 132.6(2), 130.1, 129.9, 129.6(2), 129.5(2), 128.5(2), 128.4(2), 128.3(2), 128.0, 127.9(2), 127.8, 113.8(2) (Ar*C*), 88.0 (*C*-1), 82.6, 77.6, 75.7, 73.4, 72.1, 69.1, 66.9, 67.2, 55.3 ($CH_2C_6H_4OCH_3$), 21.1 ($SC_6H_4CH_3$). HRMS (ESI): $(M+Na)^+$, found 609.2286. $C_{35}H_{38}O_6SNa$ requires 609.2287.

4.6. 4-Tolyl 4-*O*-acetyl-2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-1-thio-β-D-galactopyranoside (6)

Compound **5** (4.0 g, 6.8 mmol) was treated with Ac_2O (15 mL) and pyridine (15 mL). The reaction was stirred at room temperature for 2 h when TLC (*n*-hexane-EtOAc; 2:1) showed complete conversion of the starting material to a faster moving spot. Solvents were evaporated in vacuo and co-evaporated with toluene. The crude product was purified by flash chromatography (*n*-hexane-EtOAc, 2:1) to give the pure donor **6** (4.1 g, 96%) as white foam. $[\alpha]_D^{25}+98$ (*c* 1.1); Rf (*n*-hexane-EtOAc, 2:1) 0.54; IR (neat): 1742, 1604, 1580, 1521, 1445, 1358, 1232, 1170, 1030, 833, 754, 682 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.47, 7.06 (2d, 4H, *J* 8.0 Hz, $SC_6H_4CH_3$), 7.41–7.24 (m, 12H, Ar*H*), 6.89 (m, 2H, $C_6H_4OCH_3$), 5.62 (s, 1H, H-4), 4.76 (d, 2H, *J* 11.0 Hz, CH_2Ph), 4.72 (d, 1H, *J* 10.0 Hz, CH_2Ph), 4.62 (d, 1H, $J_{1,2}$ 9.5 Hz, H-1), 4.48 (d, 2H, *J* 12.0 Hz, CH_2Ph), 4.38 (d, 1H, *J* 11.5 Hz, CH_2Ph), 3.81 (s, 3H, $CH_2C_6H_4OCH_3$), 3.71 (t, 1H, $J_{5,6a}$, $J_{5,6b}$ 6.5 Hz, H-5), 3.62 (m, 2H, H-3, H-6a), 3.59 (dd, 1H, $J_{1,2}$ 9.5 Hz, $J_{2,3}$ 6.0 Hz, H-2), 3.49 (dd, 1H, $J_{5,6a}$ 6.5 Hz, $J_{6a,6b}$ 9.5 Hz, H-6b), 2.31 (s, 3H, $COCH_3$), 2.09 (s, 3H, $SC_6H_4CH_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 170.3 ($COCH_3$), 159.4, 138.3, 137.6, 129.9, 129.8, 129.7(2), 129.6(2), 128.4(2), 128.3(2), 128.2(2), 128.2(2), 127.8(2), 127.7, 113.8(2) (Ar*C*), 88.1 (*C*-1), 81.3, 76.8, 75.9, 75.7, 73.3, 71.9, 67.9, 66.9, 55.3 ($CH_2C_6H_4OCH_3$), 21.1 ($SC_6H_4CH_3$), 20.9 ($COCH_3$). HRMS (ESI): $(M+Na)^+$, found 651.2391. $C_{37}H_{40}O_7SNa$ requires 651.2392.

4.7. 4-Methoxyphenyl 4-*O*-acetyl-2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-α-D-galactopyranosyl-(1→3)-2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (8)

A mixture of donor **6** (4.1 g, 6.5 mmol), known acceptor **7** (2.0 g, 5 mmol) and MS 4 Å (2.0 g) in dry CH_2Cl_2 (30 mL) was stirred under nitrogen for 1 h. NIS (1.9 g, 8.5 mmol) was added to it and the mixture was cooled to −50 °C followed by addition of H_2SO_4-silica (150 mg). The mixture was allowed to stir at the same temperature for 30 min when TLC (*n*-hexane-EtOAc; 2:1) revealed that entire acceptor **4** was consumed. Et_3N was added to neutralize the reaction. The reaction mixture was immediately filtered through a pad of Celite. The filtrate was successively washed with $Na_2S_2O_3$ (2×50 mL), $NaHCO_3$ (2×50 mL) and brine (50 mL). The organic layer was collected, dried (Na_2SO_4) and evaporated in vacuo. The crude product thus obtained, was purified by flash chromatography using *n*-hexane-EtOAc (4:1) to give the pure disaccharide **8** (3.8 g, 85%) as a white foam. $[\alpha]_D^{25}+98$ (*c* 1.0, $CHCl_3$); Rf (*n*-hexane-EtOAc, 4:1) 0.34; IR (KBr): 2110, 1746, 1719, 1634, 1613, 1368, 1215, 1040 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.38–6.85 (m, 23H, Ar*H*), 5.74 (dd, 1H, $J_{3',4'}$ 3.5 Hz, $J_{4',5'}$ 1.0 Hz, H-4′), 5.69 (d, 1H, $J_{1',2'}$ 4.0 Hz, H-1′), 5.53 (d, 1H, $J_{1,2}$ 4.0 Hz, H-1), 5.45 (s, 1H, $CHPh$), 4.78 (d, 1H, *J* 10.5 Hz, CH_2Ph), 4.58 (m, 3H, H-5′, CH_2Ph), 4.50 (m, 2H, CH_2Ph), 4.46 (t, 1H, $J_{2,3}$, $J_{3,4}$ 6.5 Hz, H-3), 4.41 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.23 (dd. 1H, $J_{5,6a}$ 5.0 Hz, $J_{6a,6b}$ 10.0 Hz, H-6a), 4.12 (m, 1H, H-5), 4.02 (dd, 1H, $J_{2',3'}$ 10.0 Hz, $J_{3',4'}$ 3.5 Hz, H-3′), 3.88 (t, 1H, $J_{3,4}$, $J_{4,5}$ 9.5 Hz, H-4), 3.79 (s, 3H, $C_6H_4OCH_3$), 3.77 (m, 4H, H-2′, $CH_2C_6H_4OCH_3$), 3.74 (t, 1H, $J_{5,6b}$, $J_{6a,6b}$ 9.5 Hz, H-6b), 3.63 (dd, 1H, $J_{5,6a'}$ 5.0 Hz, $J_{6a',6b'}$ 9.5 Hz, H-6a′), 3.49 (m, 2H, H-2, H-6b′), 2.0 (s, 3H, $COCH_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 170.1 ($COCH_3$), 159.2, 155.6, 150.1, 138.3, 138.2, 129.9, 129.6(2), 129.4, 128.4(2), 128.2(2), 128.1(2), 128.0(2), 127.4, 127.3, 127.2(2), 126.2(2), 118.2(2), 114.7(2), 113.8(2) (Ar*C*), 102.1 (*CH*Ph), 98.3 (*C*-1), 97.4 (*C*-1′), 82.8, 75.6, 74.6, 73.1, 72.2, 72.0, 71.6, 68.8, 68.0, 67.9, 67.8, 62.8,

61.8, 55.6 ($C_6H_4OCH_3$), 55.2 ($CH_2C_6H_4OCH_3$), 20.9 ($COCH_3$). HRMS (ESI) $(M+Na)^+$, found 926.3472. $C_{50}H_{53}N_3O_{13}Na$ requires 926.3476.

4.8. 4-Methoxyphenyl 2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-α-D-galactopyranosyl-(1→3)-2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (9)

Compound **8** (3.8 g, 4.2 mmol) was dissolved in MeOH (20 mL) and NaOMe in MeOH (0.5M, 2 mL) was added to it. The solution was stirred at room temperature for 12 h. The solution was neutralized with DOWEX 50W H^+ resin, filtered and the solvents were evaporated under reduced pressure. The residue was purified by flash chromatography using *n*-hexane-EtOAc (2:1) to afford the desired disaccharide acceptor **9** (3.5 g, 95%) as white foam. $[\alpha]_D^{25}+84$ (*c* 0.8, $CHCl_3$); Rf (*n*-hexane-EtOAc, 2:1) 0.31; IR (KBr): 2075, 1782, 1730, 1650, 1621, 1378, 1225, 970 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.38–6.87 (m, 23H, Ar*H*), 5.76 (d, 1H, $J_{1',2'}$ 3.5 Hz, H-1′), 5.55 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.47 (s, 1H, C*H*Ph), 4.8, 4.73 (2d, 2H, *J* 11.5 Hz, CH_2Ph), 4.66 (t, 1H, $J_{2,3}$, $J_{3,4}$ 9.5 Hz, H-3), 4.58 (m, 3H, CH_2Ph), 4.48 (d, 1H, *J* 12.0 Hz, CH_2Ph), 4.31 (t, 1H, $J_{5',6a'}$, $J_{5',6b'}$ 5.0 Hz, H-5′), 4.24 (m, 2H, H-4′, H-6a), 4.14 (m, 1H, H-5), 3.91 (m, 4H, H-2′, H-3′, H-4, H-6a′), 3.82 (m, 1H, H-6b′), 3.80 (s, 3H, $C_6H_4OCH_3$), 3.78 (s, 3H, $CH_2C_6H_4OCH_3$), 3.73 (t, 1H, $J_{5,6b}$, $J_{6a,6b}$ 9.5 Hz, H-6b), 3.51 (dd, 1H, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 10.0 Hz, H-2). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 159.1, 155.5, 150.0, 138.2, 138.1, 136.7, 130, 129.4(2), 129.3, 128.3(2), 128.2(2), 128.1(2), 127.7(2), 127.6, 127.3, 127.1(2), 126.2(2), 118.1(2), 114.7(2), 113.7(2) (Ar*C*), 102.0 (*C*HPh), 98.2 (*C*-1), 97.1 (*C*-1′), 82.8, 76.9, 74.6, 73.2, 72.5, 71.8, 71.3, 69.1, 68.7, 68.6, 67.8, 62.8, 61.8, 55.6 ($C_6H_4OCH_3$), 55.1 ($CH_2C_6H_4OCH_3$). HRMS (ESI) $(M+Na)^+$, found 884.3366. $C_{48}H_{51}N_3O_{12}Na$ requires 884.3370.

4.9. 4-Methoxyphenyl 3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (10)

The compound was prepared by following the reported literature procedure.[13] The NMR data of the disaccharide matched satisfactorily with the reported data. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.41–7.29 (m, 20H, Ar*H*), 6.95, 6.84 (2d, 4H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.38 (d, 1H, $J_{1,2}$ 1.5 Hz, H-1), 5.14 (s, 1H, H-1′), 4.91 (AB_q, 2H, *J* 11.0 Hz, CH_2Ph), 4.76 (m, 4H, CH_2Ph), 4.68 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.65 (d, 1H, *J* 10.5 Hz, CH_2Ph), 4.19 (m, 2H, H-2, H-2′), 4.08 (dd, 1H, $J_{2,3}$ 3 Hz, $J_{3,4}$ 9.5 Hz, H-3), 3.93 (dd, 1H, $J_{2',3'}$ 3.0 Hz, $J_{3',4'}$ 9.5 Hz, H-3′), 3.89 (m, 1H, H-5), 3.83 (m, 1H, H-5′), 3.78 (s, 3H, $C_6H_4OCH_3$), 3.54 (t, 1H, $J_{3,4}$, $J_{4,5}$ 9.5 Hz, H-4), 3.48 (t, 1H, $J_{3',4'}$, $J_{4',5'}$ 9.5 Hz, H-4′), 1.32 (d, 3H, $J_{5,6}$ 6 Hz, C–CH_3), 1.29 (d, 3H, $J_{5',6'}$ 6 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 154.8, 150.2, 138.4, 138.3, 138.2, 138, 128.6, 128.5 (2), 128.4(4), 128.3(3), 128(2), 127.9(4), 127.8, 127.7(2), 127.6, 117.4(2), 114.6(2) (Ar*C*), 100.8 (*C*-1′), 97.7 (*C*-1), 80.2, 79.9, 79.5 (2), 75.4, 75.3, 74.5, 72.4, 72.2, 68.7, 68.5, 68, 55.6 ($C_6H_4OCH_3$), 18, 17.9 (2× C–CH_3). HRMS (ESI) calcd for $C_{47}H_{52}O_{10}Na$ $(M+Na)^+$: 799.3458, found: 799.3455.

4.10. 4-Methoxyphenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (12)

A mixture of disaccharide acceptor **10** (2.0 g, 2.6 mmol), known donor **11** (1.3 g, 3.3 mmol) and MS 4 Å (2.0 g) in dry CH_2Cl_2 (30 mL) was stirred under nitrogen atmosphere for 1 h. NIS (980 mg, 4.4 mmol) was added to the reaction mixture and it was cooled to 0 °C. H_2SO_4-silica (50 mg) was added to the reaction mixture and it was stirred for 10 min till TLC (*n*-hexane-EtOAc; 3:1) indicated complete consumption of acceptor **10**. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and filtered through a pad of Celite. The filtrate was successively washed with aq $Na_2S_2O_3$ (2×50 mL), satd aq $NaHCO_3$ (2×50 mL) and brine (50 mL). The organic layer was separated, dried (Na_2SO_4) and evaporated in vacuo. The crude product thus obtained, was purified by flash chromatography using *n* hexane-EtOAc (3:1) as eluent to afford pure trisaccharide **12** (2.4 g, 91%) as white foam. $[\alpha]_D^{25}+74$ (*c* 0.9, $CHCl_3$); Rf (*n*-hexane-EtOAc, 3:1) 0.35; IR (Neat): 2108, 1772, 1723, 1626, 1607, 1372, 1218, 1015 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.39–7.28 (m, 20H, Ar*H*), 6.93, 6.82 (2d, 4H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.49 (dd, 1H, $J_{1'',2''}$ 1.5 Hz, $J_{2'',3''}$ 3.5 Hz H-2″), 5.38 (dd, 1H, $J_{2'',3''}$ 3.5 Hz, $J_{3'',4''}$ 10 Hz, H-3″), 5.34 (d, 1H, $J_{1,2}$ 1.5 Hz, H-1), 5.16 (d, 1H, $J_{1',2'}$ 1.5 Hz, H-1′), 5.05 (t, 1H, $J_{3'',4''}$, $J_{4'',5''}$ 10.0 Hz, H-4″), 4.99 (d, 1H, $J_{1'',2''}$ 1.5 Hz, H-1″), 4.91 (AB_q, 2H, *J* 11.0 Hz, CH_2Ph), 4.71 (m, 6H, CH_2Ph), 4.16 (t, 1H, $J_{1,2}$, $J_{2,3}$ 2.0 Hz, H-2), 4.12 (t, 1H, $J_{1',2'}$, $J_{2',3'}$ 2.5 Hz, H-2′), 4.05 (dd, 1H, $J_{2',3'}$ 3.0 Hz, $J_{3',4'}$ 9.5 Hz, H-3′), 3.92 (m, 2H, H-3, H-5″), 3.81 (m, 2H, H-5, H-5′), 3.78 (s, 3H, $C_6H_4OCH_3$), 3.6 (t, 1H, $J_{3,4}$, $J_{4,5}$ 9.5 Hz, H-4), 3.44 (t, 1H, $J_{3',4'}$, $J_{4',5'}$ 9.5 Hz, H-4′), 2.13, 2.05, 2.02 (3s, 9H, 3× $COCH_3$)1.34 (d, 3H, $J_{5,6}$ 6.0 Hz, C–CH_3), 1.27 (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: 170, 169.9, 169.7 (3× *C*OCH_3), 154.8, 150.1, 138.4(2), 138.3, 138.2, 128.5(2), 128.4(4), 128.3(3), 128.2(2), 127.9(2), 127.8(3), 127.7, 127.6, 127.5(2), 117.4(2), 114.6(2) (Ar*C*), 100.3 (*C*-1′), 99 (*C*-1″), 97.7 (*C*-1), 80.3, 80.2, 79.5, 79.1, 75.7, 75.5, 75.3, 74.2, 72.5 (2), 71.1, 69.7, 69.1, 68.8, 68.6, 66.8, 55.6 ($C_6H_4OCH_3$), 20.9, 20.8, 20.7 (3× $COCH_3$), 18, 17.9, 17.3 (3×C–CH_3). HRMS (ESI) $(M+Na)^+$, found 1071.4351. $C_{59}H_{68}O_{17}Na$ requires 1071.4354.

4.11. 2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl trichloroacetimidate (14)

The trisaccharide **12** (2.4 g, 2.3 mmol) was treated with CAN (3.7 g, 6.9 mmol) in CH_3CN–H_2O (30 mL, 9:1). The reaction was continued for 30 min till TLC (*n*-hexane-EtOAc 2:1) showed complete conversion of the starting material to a slower running spot. The solvents were evaporated and the crude material was subjected to flash chromatography using *n*-hexane-EtOAc (2:1) to afford the desired trisaccharide hemiacetal **13** (1.7 g, 81%). Rf (*n*-hexane-EtOAc, 2:1) 0.26. Compound **13** (1.7 g, 1.8 mmol) was dissolved in dry CH_2Cl_2, DBU (0.3 mL, 2.3 mmol) was added followed by trichloroacetonitrile (1.8 mL, 18 mmol) and the solution was stirred under nitrogen for 20 min when TLC (*n*-hexane-EtOAc: 3:2) indicated complete conversion of the starting material to a faster running spot. The solvents were evaporated in vacuo and the crude product, thus obtained, was subjected to flash chromatography using *n*-hexane-EtOAc (3:1) to afford the desired trichloroacetamidate donor **14** (1.8 g, 90%). Rf (*n*-hexane-EtOAc, 3:1) 0.39. The material was used for the next reaction without any further characterization.

4.12. 4-Methoxyphenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-α-D-galactopyranosyl-(1→3)-2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (15)

A mixture of disaccharide acceptor **9** (1.0 g, 1.2 mmol), trichloroacetamidate donor **14** (1.8 g, 1.6 mmol) and freshly activated MS 4 Å (1.0 g) in dry CH_2Cl_2 (20 mL) was stirred under nitrogen for 1 h at room temperature. After cooling the reaction mixture to 0 °C, H_2SO_4-silica (50 mg) was added and the mixture was allowed to stir at the same temperature for 10 min when TLC (*n*-hexane-EtOAc; 3:2) showed complete consumption of acceptor **9**. The reaction mixture was neutralized with Et_3N and filtered through a pad of Celite. The filtrate was diluted with CH_2Cl_2 and was successively washed with $NaHCO_3$ (2×50 mL) and brine (50 mL). The organic layer was separated, dried (Na_2SO_4) and evaporated in vacuo. The crude product thus obtained was purified by flash chromatography

using *n*-hexane-EtOAc (1.5:1) to give the pure pentasaccharide **15** (1.7 g, 82%). $[\alpha]_D^{25}$ + 78 (*c* 0.8, $CHCl_3$); Rf (*n*-hexane-EtOAc, 1.5:1) 0.44; IR (Neat): 2107, 1758, 1731, 1645, 1613, 1375, 1219, 1033 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.37–6.85 (m, 43H, Ar*H*), 5.59 (d, 1H, $J_{1',2'}$ 3.0 Hz, H-1′), 5.52 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.45 (m, 2H, H-2‴′, C*H*Ph), 5.36 (dd, 1H, $J_{2''',3'''}$ 3.0 Hz, $J_{3''',4'''}$ 8.0 Hz, H-3‴′), 5.24 (d, 1H, $J_{1'',2''}$ 1.5 Hz, H-1″), 4.99 (m, 3H, H-1‴, H-1⁗, H-4⁗′), 4.87 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.85 (d, 1H, *J* 11.5 Hz, CH_2Ph), 4.79 (d, 1H, *J* 11.5 Hz, CH_2Ph), 4.74 (d, 1H, *J* 12.0 Hz, CH_2Ph), 4.68 (d, 1H, *J* 11.5 Hz, CH_2Ph), 4.64 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.63 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.59 (m, 3H, H-3, CH_2Ph), 4.39 (m, 5H, CH_2Ph), 4.23 (m, 3H, H-3′, H-5′, *H*-6a), 4.12 (m, 1H, H-5⁗′), 4.09 (m, 2H, H-2″, H-5), 3.94 (t, 1H, $J_{3',4'}$, $J_{4',5'}$ 3.5 Hz, H-4′), 3.86 (m, 3H, H-2‴, H-4, H-5″), 3.82–3.73 (m, 11.0H, H-2′, H-3″, H-5‴, H-6b, H-6a′, $C_6H_4OCH_3$, $CH_2C_6H_4OCH_3$), 3.61 (m, 2H, H-3‴′, H-6b′), 3.53 (t, 1H, $J_{3'',4''}$, $J_{4'',5''}$ 9.5 Hz, H-4″), 3.44 (dd, 1H, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 10.0 Hz, H-2), 3.35 (t, 1H, $J_{3''',4'''}$, $J_{4''',5'''}$ 9.5 Hz, H-4‴), 2.10, 2.04, 2.00 (3s, 9H, 3× $COCH_3$), 1.22 (d, 3H, $J_{5'''',6''''}$ 6.5 Hz, 6.5 Hz, C–CH_3), 1.15 (d, 3H, $J_{5''',6'''}$ 6.5 Hz, C–CH_3), 1.01 (d, 3H, $J_{5'',6''}$ 6 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 170 (2), 169.8 (3× *C*OCH_3), 159.2, 155.6(2), 150.0(2), 139.0, 138.6, 138.5(2), 138.4(2), 138.3(3), 138.2(3), 136.9, 129.5, 129.4, 128.4(3), 128.3(3), 128.2(3), 128.1(2), 128.0(2), 127.9(2), 127.8(2), 127.6, 127.5(3), 127.3, 127.0(2), 126.3(2), 118.2(2), 118.1(2), 114.7(3), 113.7, 110.7 (Ar*C*), 102.2 (*C*HPh), 100.2 (*C*-1‴), 100.1 (*C*-1″), 98.9 (*C*-1⁗′), 98.4 (*C*-1), 97.3 (*C*-1′), 82.9, 80.4, 80.2, 79.5, 79.3, 77.6, 75.6, 75.4, 75.2, 75.1, 73.1, 73, 72.8, 72.4, 72, 71.9, 71.8, 71.4, 71.2, 71.1, 66.7, 62.9, 61.8, 60.4, 56.3, 55.6 ($C_6H_4OCH_3$), 55.2 ($CH_2C_6H_4OCH_3$), 69.7, 69.4, 68.8, 68.6, 20.9, 20.8, 20.7 (3× $COCH_3$), 18.2, 17.8, 17.2 (3×C–CH_3). HRMS (ESI) $(M+Na)^+$, found 1808.7302. $C_{100}H_{111}N_3O_{27}Na$ requires 1808.7303.

4.13. 4-Methoxyphenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl (1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→3)-2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (16)

To a solution of the pentasaccharide **15** (1.7 g, 0.9 mmol) in CH_2Cl_2–H_2O (4:1; 25 mL), DDQ (432 mg, 1.9 mmol) was added and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was then washed with H_2O (2×50 mL). The organic layer was collected, dried over Na_2SO_4, filtered and evaporated in vacuo. The product thus obtained, was purified using flash chromatography using *n*-hexane-EtOAc (2:1) as eluent to furnish the pentasaccharide derivative **16** (1.3 g, 84%) as white foam. $[\alpha]_D^{25}$ + 112 (*c* 0.9, $CHCl_3$); Rf (*n*-hexane-EtOAc, 2:1) 0.28; IR (Neat): 2101, 1762, 1719, 1638, 1603, 1368, 1213, 1035 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.38–7.01 (m, 35H, Ar*H*), 7.04, 6.85 (2d, 4H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.58 (d, 1H, $J_{1',2'}$ 3.5 Hz, H-1′), 5.50 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.45 (dd, 1H, $J_{1'''',2''''}$ 1.5 Hz, $J_{2'''',3''''}$ 3.5 Hz, H-2⁗′), 5.42 (s, 1H, C*H*Ph), 5.36 (dd, 1H, $J_{2'''',3''''}$ 3.5 Hz, $J_{3'''',4''''}$ 10.0 Hz, H-3⁗′), 5.06 (d, 1H, $J_{1'',2''}$ 1.5 Hz, H-1″), 5.02 (t, 1H, $J_{3'''',4''''}$, $J_{4'''',5''''}$ 10.0 Hz, H-4⁗′), 4.98 (d, 1H, $J_{1''',2'''}$ 1.5 Hz, H-1‴), 4.95 (d, 1H, $J_{1'''',2''''}$ 1.5 Hz, H-1⁗′), 4.87, 4.81 (2d, 2H, *J* 11.0 Hz, CH_2Ph), 4.74 (m, 3H, CH_2Ph), 4.64 (d, 1H, *J* 10.5 Hz, CH_2Ph), 4.62 (d, 1H, *J* 11.5 Hz, CH_2Ph), 4.56 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.53 (m, 2H, H-3, CH_2Ph), 4.43 (d, 1H, *J* 11.5 Hz, CH_2Ph), 4.38 (d, 1H, *J* 13.0 Hz, CH_2Ph), 4.34 (d, 1H, *J* 12.0 Hz, CH_2Ph), 4.22 (dd, 1H, $J_{5',6a'}$ 5.0 Hz, $J_{6a',6b'}$ 10.5 Hz, H-6a′), 4.12 (m, 3H, H-5,H-3′, H-5′), 4.09 (t, 1H, $J_{1'',2''}$, $J_{2'',3''}$ 2.5 Hz, H-2″), 4.04 (t, 1H, $J_{1''',2'''}$, $J_{2''',3'''}$ 2.5 Hz, H-2‴), 3.92 (dd, 1H, $J_{5,6a}$ 3.0 Hz, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.84 (m, 5H, H-2′, H-4, H-4′, H-5‴, H-5⁗′), 3.78 (s, 3H, H-5″, $C_6H_4OCH_3$), 3.76 (m, 1H, H-5″), 3.71 (m, 3H, H-3″, H-3‴, H-6b), 3.63 (t, 1H, $J_{5',6a'}$, $J_{6a',6b'}$ 9.5 Hz, *H*-6a′), 3.54 (t, 1H, $J_{3'',4''}J_{4'',5''}$ 9.5 Hz, H-4″), 3.45 (dd, 1H, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 10.5 Hz, H-2), 3.34 (t, 1H, $J_{3''',4'''}$, $J_{4''',5'''}$ 9.5 Hz, H-4‴), 2.09, 2.04, 2 (3s, 9H, 3× $COCH_3$), 1.28 (d, 3H, $J_{5'',6''}$ 5.5 Hz, C–CH_3), 1.24 (d, 3H, $J_{5''',6'''}$ 6.5 Hz, C–CH_3), 0.99 (d, 3H, $J_{5'''',6''''}$ 6.0 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 170.0(2), 169.8 (3× *C*OCH_3), 155.6, 150.2, 138.5, 138.4(3), 138.3, 138.2(2), 136.9, 129.5, 128.5(2), 128.4(4), 128.3(4), 128.2(2), 128.1(2), 128(2), 127.9(2), 127.8(2), 127.6(3), 127.5(3), 127.3, 127.0(2), 126.4(2), 118.2(3), 114.8(3) (Ar*C*), 100.3 (*C*HPh), 102.1 (*C*-1″), 100.2 (*C*-1‴), 99.1 (*C*-1⁗′), 98.4 (*C*-1), 97.1 (*C*-1′), 82.9, 80.3, 79.8, 79.3(2), 77.6, 76.3, 75.6, 75.5, 75.3, 75.2, 74.4, 73, 72.5, 72.1, 71.5(2), 71.2, 70.4, 69.7 (2), 69.2, 68.9, 68.8, 66.8, 62.9, 62.0, 61.5, 55.7 ($C_6H_4OCH_3$), 20.9(2), 20.8 (3× *C*OCH_3), 18.1, 18.0, 17.2 (3×C–CH_3). HRMS (ESI) $(M+Na)^+$, found 1688.6727. $C_{92}H_{103}N_3O_{26}Na$ requires 1688.6728.

4.14. 4-Methoxyphenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranosyluronic acid-(1→3)-2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (17)

To a solution of the pentasaccharide derivative **16** (1.3 g, 0.8 mmol) in CH_2Cl_2–H_2O (2:1, 20 mL), TEMPO (20 mg, 0.12 mmol) was added followed by [bis-(acetoxy)-iodo]benzene (BAIB) (480 mg, 1.5 mmol) and the mixture was vigorously stirred at room temperature for 2 h till TLC (EtOAc) indicated complete conversion of the starting material to a lower running spot. $Na_2S_2O_3$ solution (10% in H_2O, 10 mL) was added to quench the reaction. The mixture was then extracted with CH_2Cl_2 (2×30 mL). The combined organic layer was dried over Na_2SO_4, filtered and evaporated in vacuo. The crude product was purified by flash chromatography using *n*-hexane-EtOAc (1:1) as eluent to furnish the uronic acid derivative **17** (1.1 g, 87%) as white amorphous mass. $[\alpha]_D^{25}$ + 108 (*c* 0.8, $CHCl_3$); Rf (*n*-hexane-EtOAc, 1:1) 0.24; IR (KBr): 2350, 2095, 1683, 1194, 782 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.38–7.00 (m, 35H, Ar*H*), 7.05, 6.85 (2d, 4H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.66 (d, 1H, $J_{1',2'}$ 3.5 Hz, H-1′), 5.5 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.45 (m, 2H, C*H*Ph, H-2⁗′), 5.36 (dd, 1H, $J_{2'''',3''''}$ 3.0 Hz, $J_{3'''',4''''}$ 10.0 Hz, H-3⁗′), 5.12 (s, 1H, H-1″), 5.06 (s, 1H, H-1‴), 5.01 (t, 1H, $J_{3'''',4''''}J_{4'''',5''''}$ 10.0 Hz, H-4⁗′), 4.95 (s, 1H, H-1⁗′), 4.86 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.79 (d, 1H, *J* 11.5 Hz, CH_2Ph), 4.72 (m, 3H, CH_2Ph), 4.62 (m, 2H, H-3, CH_2Ph), 4.56 (m, 2H, CH_2Ph), 4.49 (d, 1H, *J* 11.5 Hz, CH_2Ph), 4.44 (d, 1H, *J* 10.5 Hz, CH_2Ph), 4.39 (d, 2H, *J* 11.5 Hz, CH_2Ph), 4.24 (dd, 1H, $J_{5,6a}$ 5.0 Hz, $J_{6a,6b}$ 20.0 Hz, H-6a), 4.14 (m, 1H, H-5), 4.04 (s, 1H, H-2‴), 3.95 (s, 1H, H-2″), 3.86 (m, 5H, H-3′, H-4, H-4′, H-5′, H-5⁗′), 3.78 (m, 4H, H-2′, $C_6H_4OCH_3$), 3.72 (m, 3H, H-3‴, H-5‴, H-6b), 3.62 (dd, 1H, $J_{2'',3''}$ 2.5 Hz, $J_{3'',4''}$ 9.5 Hz, H-3″), 3.52 (t, 1H, $J_{3''',4'''}$, $J_{4''',5'''}$ 9.5 Hz, H-4‴), 3.45 (m, 1H, H-5″), 3.34 (m, 2H, H-2, H-4″), 2.09, 2.04, 2.00 (3s, 9H, 3× $COCH_3$), 1.25 (d, 3H, $J_{5'',6''}$ 6.5 Hz, C–CH_3), 1.20 (d, 3H, $J_{5''',6'''}$ 6.5 Hz, C–CH_3), 1.01 (d, 3H, $J_{5'''',6''''}$ 6.0 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 172.6 (*C*OOH), 170 (2), 169.7 (3× *C*OCH_3), 155.6, 150.1, 138.6, 138.4(2), 138.2(2), 138.0, 137.9, 136.8, 129.5, 128.5(2), 128.3(5), 128.2(2), 128.1(2), 128.0(2), 127.9(4), 127.7(4), 127.6, 127.5, 127.4(3), 127.3, 127.0(2), 126.4(2), 118.1(2), 114.8(2), 114.1 (Ar*C*), 102.4 (*C*HPh), 100.1 (*C*-1″), 100 (*C*-1‴), 99 (*C*-1⁗′), 98.4 (*C*-1), 97.6 (*C*-1′), 82.5, 80.3, 79.9, 79.2, 76.4, 75.7, 75.6, 75.5, 75.3, 75.1, 74.5, 74.4, 74, 72.9, 72.4, 72.2 (2), 72, 71.7, 71.1, 69.7, 69.2, 68.8, 68.7, 66.7, 62.9, 61.5, 55.6 ($C_6H_4OCH_3$), 20.9, 20.8, 20.7 (3× *C*OCH_3), 17.9, 17.6, 17.2 (3×C–CH_3). HRMS (ESI) $(M+Na)^+$, found 1702.6521. $C_{92}H_{101}N_3O_{27}Na$ requires 1702.6520.

4.15. 4-Methoxyphenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranosyluronicacid-(1→3)-2-azido-2-deoxy-α-D-glucopyranoside (18)

The acid derivative **17** (1.1 g, 0.65 mmol) was treated with 80% AcOH (10 mL) at 80 °C for 2 h resulting in the hydrolysis of the benzylidene ring. The solvents were evaporated and co-evaporated with toluene. The crude product was purified by flash chromatography using *n*-hexane-EtOAc (1:2) as eluent to furnish pure

derivative **18** (906 mg, 87%). $[\alpha]_D^{25}$ + 132 (*c* 0.8, $CHCl_3$); Rf (*n*-hexane-EtOAc, 1:2) 0.21; IR (Neat): 2362, 2105, 1690, 1187, 764 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.42–7.27 (m, 30H, Ar*H*), 7.05, 6.84 (2d, 4H, $C_6H_4OCH_3$), 5.47 (dd, 1H, $J_{1''',2'''}$ 2.0 Hz, $J_{2''',3'''}$ 3.5 Hz, H-2‴), 5.45 (d, 1H, $J_{1,2}$ 3 Hz, H-1), 5.38 (dd, 1H, $J_{2'''',3''''}$ 3.5 Hz, $J_{3''',4''''}$ 10.0 Hz, H-3‴′), 5.19 (d, 1H, $J_{1'',2''}$ 1.5 Hz, H-1″), 5.1 (d, 1H, $J_{1''',2'''}$ 1.0 Hz, H-1‴), 5.06 (m, 2H, H-1′, H-4‴′), 4.98 (d, 1H, $J_{1''',2''''}$ 1.5 Hz, H-1‴′), 4.9 (d, 1H, *J* 11.0 Hz, C*H*$_2$Ph), 4.89 (d, 1H, *J* 11.5 Hz, C*H*$_2$Ph), 4.83 (d, 1H, *J* 11.0 Hz, C*H*$_2$Ph), 4.82 (d, 1H, *J* 11.5 Hz, C*H*$_2$Ph), 4.73 (m, 2H, C*H*$_2$Ph), 4.67 (m, 3H, C*H*$_2$Ph), 4.63, 4.62 (2d, 2H, *J* 11.5 Hz, C*H*$_2$Ph), 4.58 (d, 1H, *J* 10.5 Hz, C*H*$_2$Ph), 4.16 (m, 2H, H-2″, H-3′), 4.09 (m, 1H, H-2‴), 4.01 (m, 3H, H-3, H-5′, H-6a), 3.89 (m, 3H, H-4′, H-5, H-5‴′), 3.81 (m, 3H, H-2′, H-5″, H-5‴), 3.78 (m, 5H, H-3″, H-3‴, $C_6H_4OCH_3$), 3.74 (m, 1H, H-6b), 3.67 (t, 1H, $J_{3,4}$, $J_{4,5}$ 10.0 Hz, H-4), 3.58 (t, 1H, $J_{3'',4''}$, $J_{4'',5''}$ 9.5 Hz, H-4″), 3.39 (t, 1H, $J_{3''',4'''}$, $J_{4''',5'''}$ 9.5 Hz, H-4‴), 3.05 (dd, 1H, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 9.5 Hz, H-2), 2.11, 2.05, 2.02 (3s, 9H, 3× *C*O*C*H$_3$), 1.31 (m, 6H, 2× C–*C*H$_3$), 1.04 (d, 3H, $J_{5''',6'''}$ 6.5 Hz, C–*C*H$_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 172.2 (*C*OOH), 170.0, 169.9, 169.8 (3× *C*OCH$_3$), 155.6, 150.3, 139.2, 138.4, 138.3, 138.2, 138.1, 137.7, 136.9, 128.7(2), 128.6(2), 128.5(2), 128.4(4), 128.3(5), 128.1(2), 127.9(3), 127.8(2), 127.7, 127.6(3), 127.5(2), 118.2(2), 114.7(2), 114.0 (Ar*C*), 101.9 (*C*-1″), 101.0 (*C*-1‴), 100.1 (*C*-1′), 99.0 (*C*-1‴′), 98.9 (*C*-1), 82.2, 80.3, 79.9, 79.2, 78.4, 75.9, 75.5(2), 75.1, 74.8, 74.4, 74.3, 72.4, 72.3, 72.2, 71.6, 71.5(2), 71.1, 69.7, 69.5, 69.2, 68.8, 66.8, 62.3, 61.6, 61.3, 55.6 ($C_6H_4OCH_3$), 20.9, 20.8, 20.7 (3× *C*OCH$_3$), 18.1, 18, 17.2 (3×C–*C*H$_3$). HRMS (ESI) $(M+Na)^+$, found 1614.6206. $C_{85}H_{97}N_3O_{27}Na$ requires 1614.6207.

4.16. 4-Methoxyphenyl α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranosyluronicacid-(1→3)-2-acetamido-2-deoxy-α-D-glucopyranoside (19)

Compound **18** (906 mg, 0.6 mmol) was dissolved in thioacetic acid (10 mL) and the mixture was stirred at room temperature in dark for 3 days, until TLC (CH_2Cl_2–MeOH 6:1) confirmed complete conversion of the starting material. The solvents were evaporated and co-evaporated with toluene. The crude residue was dissolved in MeOH (10 mL). NaOMe in MeOH (2 mL, 0.5 M) was added to the solution and stirred for 12 h. DOWEX 50W H^+ resin was added to neutralize the solution. It was then filtered through a cotton plug and the filtrate was evaporated in vacuo and the residue was purified by a short flash column using CH_2Cl_2–MeOH (6:1) to afford the pentasaccharide **19** (680 mg, 81%) as white compound. $[\alpha]_D^{25}$ + 82 (*c* 0.7, $CHCl_3$); Rf (CH_2Cl_2–MeOH, 6:1) 0.31; IR (Neat): 2365, 2090, 1688, 1178, 784 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.39–7.25 (m, 30H, Ar*H*), 6.96, 6.83 (2d, 4H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.92 (d, 1H, $J_{NH,2}$ 9.0 Hz, N*H*COCH$_3$), 5.41 (d, 1H, $J_{1,2}$ 4 Hz, H-1), 5.19 (d, 1H, $J_{1'',2''}$ 1.5 Hz, H-1″), 5.11 (d, 1H, $J_{1''',2'''}$ 1.5 Hz, H-1‴), 5.02 (d, 1H, $J_{1,2}$ 1.5 Hz, H-1‴′), 4.86 (m, 2H, H-1′, C*H*$_2$Ph), 4.81 (d, 1H, *J* 12 Hz, C*H*$_2$Ph), 4.78 (d, 1H, *J* 11.5 Hz, C*H*$_2$Ph), 4.67 (m, 3H, C*H*$_2$Ph), 4.62 (d, 1H, *J* 11.5 Hz, C*H*$_2$Ph), 4.59 (m, 3H, C*H*$_2$Ph), 4.52 (d, 1H, *J* 11.5 Hz, C*H*$_2$Ph), 4.26 (m, 1H, H-2), 4.12 (dd, 1H, $J_{1'',2''}$ 2.0 Hz, $J_{2'',3''}$ 5.0 Hz, H-2″), 4.08 (s, 1H, H-2‴), 4.04 (d, 1H, $J_{1''',2'''}$ 1.5 Hz, H-2‴′), 3.96 (dd, 1H, $J_{2',3'}$ 2.5 Hz, $J_{3',4'}$ 10.0 Hz, H-3′), 3.89 (m, 2H, H-3″, H-3‴), 3.81 (m, 5H, H-2′, H-4, H-5, H-5‴′, H-6a), 3.77 (s, 3H, $C_6H_4OCH_3$), 3.68 (m, 6H, H-3, H-3‴′, H-4′, H-5′, H-5″, H-5‴), 3.58 (dd, 1H, $J_{5,6b}$ 5.5 Hz, $J_{6a,6b}$ 11.5 Hz, H-6b), 3.42 (m, 2H, H-4″, H-4‴), 3.38 (t, 1H, $J_{3''',4''''}$, $J_{3''',4''''}$ 9.5 Hz, H-4‴′), 2.02 (s, 3H, NHCOC*H*$_3$), 1.29 (d, 3H, $J_{5'',6''}$ 6.5 Hz, C–C*H*$_3$), 1.21 (d, 3H, $J_{5''',6'''}$ 6.5 Hz, C–C*H*$_3$), 1.18 (d, 3H, $J_{5''',6''''}$ 6.0 Hz, C–C*H*$_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 171.1 (NH*C*OCH$_3$), 170.7 (*C*OOH), 155.5, 150, 139.3, 138.4, 138.3, 138.2(2), 137.6, 137.0, 128.7(2), 128.6(3), 128.5(4), 128.4(5), 128.3(2), 128.1(3), 127.9(2), 127.8(5), 127.7(2), 127.6, 123.5, 118.2(2), 114.8(2), 114.0 (Ar*C*), 101.8 (*C*-1′), 100.8 (*C*-1‴′), 100.7 (*C*-1″), 100.3 (*C*-1‴), 97.5 (*C*-1), 84.1, 80.5, 80, 79.3, 79.2, 78.2, 76, 75.3, 75.2, 74.7, 74.6, 74.5, 74.4, 73.5, 72.5, 72.4, 72.2 (2), 71.8, 71.7, 71.6, 70.8, 69.3, 68.6, 68.4, 62.6, 62.2, 55.6 ($C_6H_4OCH_3$), 22.7 (NHCO*C*H$_3$), 18.2, 18.1, 17.5 (3× C–*C*H$_3$). HRMS (ESI) $(M+Na)^+$, found 1504.6091. $C_{81}H_{95}NO_{25}Na$ requires 1504.6091.

4.17. 4-Methoxyphenyl α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→4)-α-D-galactopyranosyluronicacid-(1→3)-2-acetamido-2-deoxy-α-D-glucopyranoside (1)

The solution of the compound **19** (680 mg, 0.45 mmol) in MeOH (10 mL) and AcOH (1 mL) was passed through flow hydrogenation assembly fitted with a Pd–C cartridge at 50 °C at normal atmospheric pressure of hydrogen. The reaction was found to be complete after three cycles as judged by TLC (CH_2Cl_2–MeOH; 5:1). The solvents were evaporated in vacuo and the residue was purified by HPLC using C18 column; CH_3CN–H_2O mixture was used as eluent to furnish the desired pentasaccharide **1** (370 mg, 85%) as white amorphous mass. $[\alpha]_D^{25}$ + 48 (*c* 0.7, MeOH); IR (KBr): 2375, 1760, 1618, 1386, 1232, 1057, 744 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.06, 6.84 (2d, 4H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.32 (m, 2H, H-1, H-1″), 5.29 (s, 1H, H-1‴), 5.13 (s, 1H, H-1‴′), 4.92 (s, 1H, H-1′), 4.17 (m, 1H, H-2), 4.03 (m, 8H, H-2′, H-2″, H-2‴′, H-3, H-3′, H-3″, H-3‴, H-3‴′), 3.86 (m, 3H, H-2‴, H-4, H-4′), 3.77–3.6 (m, 13H, H-4″, H-4‴, H-4‴′, H-5, H-5′, H-5″, H-5‴, H-5‴′, H-6, $C_6H_4OCH_3$),2.06 (s, 3H, NHCOC*H*$_3$), 1.26 (bd, 9H, *J* 6.0 Hz, (3×C–C*H*$_3$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 175.2 (*C*OOH), 171.1 (NH*C*OCH$_3$), 156.9, 152.4, 119.6(2), 115.6(2) (Ar*C*), 103.4 (*C*-1′), 102.4 (*C*-1‴), 102.2 (*C*-1‴′), 102.1 (*C*-1″), 99.2 (*C*-1), 81.6, 79.9, 79.3, 78.2, 74.5, 74.4, 74.3, 74.1, 74, 73.4, 72.3, 72.2, 72, 71.9, 71.8, 71.1, 70.6, 70.3, 63.2, 62.2, 56.1 ($C_6H_4OCH_3$), 53.9, 22.8 (NHCO*C*H$_3$), 18.1, 18, 17.9 (3×C–*C*H$_3$). HRMS (ESI) $(M+Na)^+$, found 964.3273. $C_{39}H_{59}NO_{25}Na$ requires 964.3274.

4.18. 4-Methoxyphenyl 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-α-D-galactopyranosyl (1→3)-2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (21)

To a mixture of disaccharide acceptor **9** (1.5 g, 1.7 mmol) and known donor 4-tolyl 2-*O*-acetyl-3,4-di-*O*-benzyl-1-thio-α-L-rhamnopyranoside **20** (1.1 g, 2.3 mmol) in dry CH_2Cl_2 (20 mL), 4 Å powdered molecular sieves (1.0 g) was added and the mixture was stirred under nitrogen atmosphere for 1 h. NIS (662 mg, 2.9 mmol) was added to the mixture and it was cooled to 0 °C. H_2SO_4-silica (50 mg) was added to the reaction mixture and it was stirred for 10 min when TLC (hexane-EtOAc; 3:1) showed complete consumption of acceptor **9**. Et_3N was added to neutralize the reaction. The reaction mixture was diluted and filtered through a pad of Celite. The filtrate was then successively washed with aq $Na_2S_2O_3$ (2×50 mL), satd aq $NaHCO_3$ (2×50 mL) and brine (50 mL). The organic layer was separated, dried (Na_2SO_4) and evaporated in vacuo. The crude trisaccharide thus obtained, was purified by flash chromatography using *n*-hexane-EtOAc (3:1) as eluent to afford pure trisaccharide **21** (1.9 g, 92%). $[\alpha]_D^{25}$ + 132 (*c* 1.0, $CHCl_3$); Rf (*n*-hexane-EtOAc, 3:1) 0.34; IR (neat): 2367, 1751, 1594, 1382, 1227, 1050 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.43–6.82 (m, 33H, Ar*H*), 5.61 (d, 1H, $J_{1',2'}$ 4.0 Hz, H-1′), 5.54 (d, 1H, $J_{1,2}$ 2.5 Hz, H-1), 5.51 (s, 1H, C*H*Ph), 5.48 (d, 1H, $J_{2'',3''}$ 2.0 Hz, H-2″), 5.2 (s, 1H, H-1″), 4.89 (d, 1H, *J* 10.5 Hz, C*H*$_2$Ph), 4.81 (d, 1H, *J* 11.5 Hz, C*H*$_2$Ph), 4.74 (d, 1H, *J* 11.0 Hz, C*H*$_2$Ph), 4.56 (m, 4H, H-3, H-3′, C*H*$_2$Ph), 4.45 (m, 3H, C*H*$_2$Ph), 4.33 (t, 1H, $J_{5',6'}$, $J_{6a',6b'}$ 6.5 Hz, H-6a′), 4.29 (s, 2H, C*H*$_2$Ph), 4.24 (m, 1H, *H*-6a), 4.14 (m, 1H, H-5), 3.98 (d, 1H, $J_{3',4'}$ 9.5 Hz, H-4′), 3.94 (d, 1H, $J_{1',2'}$ 4.0 Hz, H-2′), 3.88 (m, 2H, H-3″, H-5″), 3.80 (s, 3H, $C_6H_4OCH_3$), 3.76 (m, 4H, $CH_2C_6H_4OCH_3$, H-4), 3.71 (m, 2H, H-5′, H-6b), 3.67 (d, 1H, $J_{5',6'}$ 6 Hz, H-6′), 3.49 (dd, 1H, $J_{1,2}$ 3.0 Hz, $J_{2,3}$ 10.0 Hz,

H-2), 3.38 (t, 1H, $J_{3'',4''}$, $J_{4'',5''}$ 9 Hz, H-4″), 2.06 (s, 3H, COCH_3), 1.27 (d, 3H, $J_{5'',6''}$ 6.5 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 169.7 (*C*OCH$_3$), 159.2, 155.6, 150.2, 138.7, 138.4, 138.1, 138, 136.9, 130.3, 129.5, 129.4 (2), 128.5 (3), 128.2 (4), 128, 127.9(3), 127.7, 127.5(3), 127.4, 127.3, 127.2(2), 127.1, 127, 126.4, 126.3(3), 118.2(2), 114.8(2), 113.7(2) (Ar*C*), 102.3 (*C*HPh), 99.1 (*C*-1″), 98.4 (*C*-1), 97.3 (*C*-1′), 82.9, 79.8, 78, 77.9, 75.2, 74.4, 73.6, 73.1, 73, 71.7, 71.5 (2), 69.4, 68.8, 68.7, 68.6, 68.4, 62.9, 61.9, 55.6 ($C_6H_4OCH_3$), 55.2 ($CH_2C_6H_4OCH_3$), 21.1 (*C*OCH$_3$), 18.1 (C–*C*H$_3$). HRMS (ESI) $(M+Na)^+$, found 1252.4993. $C_{70}H_{75}N_3O_{17}Na$ requires 1252.4994.

4.19. 4-Methoxyphenyl 3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-α-D-galactopyranosyl-(1→3)-2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (22)

To the methanolic solution of trisaccharide **21** (1.9 g, 1.5 mmol) in MeOH (20 mL), NaOMe (10 mL, 0.5M) was added. The reaction was stirred for 12 h, as monitored by TLC (*n*-hexane-EtOAc 2:1). DOWEX 50W H^+ resin was added to neutralize the reaction. The solution was filtered and the solvents were evaporated under reduced pressure and the residue was purified by a flash column using *n*-hexane-EtOAc (2:1) to afford the desired trisaccharide acceptor **22** (1.74 g, 95%). $[\alpha]_D^{25}$ + 64 (*c* 0.8, $CHCl_3$); Rf (*n*-hexane-EtOAc, 2:1) 0.32; IR (neat): 2373, 1762, 1579, 1373, 1241, 1057, 710 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.43–6.82 (m, 33H, Ar*H*), 5.64 (d, 1H, $J_{1',2'}$ 2.5 Hz, H-1′), 5.54 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.51 (s, 1H, C*H*Ph), 5.28 (s, 1H, H-1″), 4.86, 4.78, 4.74 (3d, 3H, *J* 11.0 Hz, CH_2Ph), 4.61 (d, 2H, *J* 11.0 Hz, CH_2Ph), 4.58 (d, 1H, $J_{2,3}$ 3.5 Hz, H-3), 4.52 (m, 2H, CH_2Ph), 4.46 (d, 2H, *J* 11.0 Hz, CH_2Ph), 4.42 (d, 1H, *J* 12.5 Hz, CH_2Ph), 4.33 (t, 1H, $J_{5',56a'}$, $J_{6a',6b'}$ 6.0 Hz, H-6a′), 4.3 (s, 1H, H-3′), 4.24 (dd, 1H, $J_{5,6a}$ 4.5 Hz, $J_{6a,\ 6b}$ 10.0 Hz, H-6a), 4.15 (m, 1H, H-5), 4.09 (s, 1H, H-2″), 3.98 (d, 1H, $J_{2',3'}$ 10.5 Hz, H-4′), 3.91 (m, 2H, H-4, H-5″), 3.8 (m, 4H, H-2′, $C_6H_4OCH_3$), 3.76 (s, 3H, $CH_2C_6H_4OCH_3$), 3.72 (m, 2H, H-3″, H-6b), 3.69 (m, 2H, H-5′, H-6b′),3.49 (dd, 1H, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 10 Hz, H-2), 3.45 (t, 1H, $J_{3'',4''}$, $J_{4'',5''}$ 9.0 Hz, H-4″), 1.27 (d, 3H, $J_{5'',6''}$ 6.5 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 159.2, 155.6, 150.2, 138.5, 138.3, 138.1, 138.0, 136.9, 130.3, 129.5(2), 129.4, 128.4(2), 128.4(2), 128.3(3), 128.1(2), 127.9(2), 127.8(3), 127.7, 127.7(2), 127.6, 127.5, 127.3, 127.1(2), 126.4(2), 118.2(2), 114.7(2), 113.7(2) (Ar*C*), 102.3 (*C*HPh), 100.7 (*C*-1″), 98.4 (*C*-1), 97.2 (*C*-1′), 82.9, 79.9, 79.6, 77.8, 75.1, 74.9, 74, 73.1, 73, 71.7, 71.6, 71.5, 69.5, 68.8, 68.7, 68.5, 68.1, 62.9, 61.9, 55.6 ($C_6H_4OCH_3$), 55.2 ($CH_2C_6H_4OCH_3$), 18 (C–CH_3). HRMS (ESI) $(M+Na)^+$, found 1210.4888. $C_{68}H_{73}N_3O_{16}Na$ requires 1210.4889.

4.20. 4-Methoxyphenyl 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl (1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-α-D-galactopyranosyl-(1→3)-2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (23)

A mixture of acceptor **22** (1.74 g, 1.5 mmol), and another equivalent of known donor **20** (937 mg, 1.9 mmol) and MS 4 Å (1.0 g) in dry CH_2Cl_2 (20 mL) was stirred under nitrogen for one hour. To the reaction mixture, NIS (557 mg, 2.5 mmol) was added and the mixture was cooled to 0 °C followed by addition of H_2SO_4-silica (25 mg). The mixture was allowed to stir at the same temperature for 10 min when TLC (*n*-hexane-EtOAc; 3:2) showed complete consumption of acceptor **22**. Et_3N was added to neutralize the reaction. The reaction mixture was immediately filtered through a pad of Celite. The filtrate was diluted with CH_2Cl_2 and was successively washed with $Na_2S_2O_3$ (2×50 mL), $NaHCO_3$ (2×50 mL) and brine (50 mL). The organic layers were together collected, dried (Na_2SO_4) and evaporated in vacuo. The crude product thus obtained, was purified by flash chromatography using *n*-hexane-EtOAc (2.5:1) to give the pure tetrasaccharide **23** (2.0 g, 90%). $[\alpha]_D^{25}$ + 76 (*c* 0.9, $CHCl_3$); Rf (*n*-hexane-EtOAc, 2.5:1) 0.31; IR (neat): 2380, 1764, 1603, 1372, 1237, 1035 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.4–6.86 (m, 43H, Ar*H*), 5.62 (d, 1H, $J_{1',2'}$ 3.5 Hz, H-1′), 5.53 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.51 (s, 1H, H-2‴), 5.47 (s, 1H, C*H*Ph), 5.3 (d, 1H, $J_{1'',2''}$ 3.5 Hz, H-1″), 4.9 (d, 2H, *J* 11.0 Hz, CH_2Ph), 4.84 (s, 1H, H-1‴), 4.75 (2d, 2H, *J* 11.0 Hz, CH_2Ph), 4.7 (d, 1H, *J* 11.5 Hz, CH_2Ph), 4.64 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.58 (m, 5H, H-3, 2× CH_2Ph), 4.45 (m, 4H, 2× CH_2Ph), 4.25 (m, 3H, H-3′, H-5, H-6), 4.15 (t, 1H, $J_{5',6a'}$, $J_{6a',6b'}$ 7.0 Hz, H-6a′), 4.08 (s, 1H, H-2″), 3.96 (m, 2H, H-3″, H-4′), 3.9 (t, 1H, $J_{3,4}$, $J_{4,5}$ 9.0 Hz, H-4), 3.8 (br s, 6H, $C_6H_4OCH_3$, $CH_2C_6H_4OCH_3$),3.76 (m, 3H, H-2′, H-3″, H-5‴), 3.71 (m, 1H, H-6′), 3.65 (m, 2H, H-5′, H-6), 3.47 (dd, 1H, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 10.5 Hz, H-2), 3.42 (t, 1H, $J_{3'',4''}$, $J_{4'',5''}$ 9.5 Hz, H-4″), 3.41 (t, 1H, $J_{3''',4'''}$, $J_{4''',5'''}$ 9.5 Hz, H-4‴), 2.14 (s, 3H, COCH_3), 1.26 (d, 3H, $J_{5''',6'''}$ 6.0 Hz, C–CH_3), 1.15 (d, 3H, $J_{5'',6''}$ 5.5 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 169.9 (*C*OCH$_3$), 159.1, 157.6, 155.6, 150.1, 139.0(2), 138.7, 138.6(3), 138.4(2), 138.3(2), 138.2(2), 138.1(2), 136.9(2), 129.5, 129.4, 128.4(2), 128.3(3), 128.2(3), 128.1(3), 128.1, 127.9(2), 127.8, 127.7, 127.6(2), 127.5, 127.4(2), 127.3, 127.1(2), 126.3(2), 118.2(2), 114.8(2), 113.7, 110.7 (Ar*C*), 102.2 (*C*HPh), 100 (*C*-1″), 99.3 (*C*-1‴), 98.4 (*C*-1), 97.3 (*C*-1′), 82.9, 80.1, 77.8, 75.3, 75.2, 73, 72.9, 72.8, 72, 71.9, 71.7, 71.6, 71.4, 69, 68.8(2), 68.5, 68.2, 69, 68.8(2), 68.5, 68.2, 62.9, 61.8, 56.3 ($C_6H_4OCH_3$), 55.2 ($CH_2C_6H_4OCH_3$), 21.1 (*C*OCH$_3$), 18.2, 18.1 (2× C–*C*H$_3$). HRMS (ESI) $(M+Na)^+$, found 1578.6512. $C_{90}H_{97}N_3O_{21}Na$ requires 1578.6512.

4.21. 4-Methoxyphenyl 3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzyl-α-L-rhamnopyranosyl-(1→4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-α-D-galactopyranosyl-(1→3)-2-azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (24)

To a solution of the tetrasaccharide derivative **23** (2.0 g, 1.3 mmol) in MeOH (20 mL), NaOMe (2 mL, 1M) was added and the solution was stirred at room temperature for 12 h. After neutralization with DOWEX 50W H^+ resin, the solution was filtered and the solvents were evaporated under reduced pressure. The residue thus obtained was purified by flash chromatography using *n*-hexane-EtOAc (2:1) as eluent to afford the desired tetrasaccharide acceptor **24** (1.86 g, 96%). $[\alpha]_D^{25}$ + 104 (*c* 0.8, $CHCl_3$); Rf (*n*-hexane-EtOAc, 2:1) 0.31; IR (neat): 2356, 1731, 1587, 1378, 1233, 1025 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38–6.85 (m, 43H, Ar*H*), 5.6 (d, 1H, $J_{1',2'}$ 3.5 Hz, H-1′), 5.52 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.47 (s, 1H, C*H*Ph), 5.3 (d, 1H, $J_{1'',2''}$ 2.5 Hz, H-1″), 4.96 (d, 1H, $J_{1''',2'''}$ 3.5 Hz, H-1‴), 4.87 (d, 1H, *J* 10.5 Hz, CH_2Ph), 4.86 (d, 1H, *J* 10.5 Hz, CH_2Ph), 4.7 (m, 3H, CH_2Ph), 4.59 (m, 5H, H-3, CH_2Ph), 4.5 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.43 (m, 2H, CH_2Ph), 4.36 (d, 1H, *J* 11.0 Hz, CH_2Ph), 4.25 (m, H-3′, H-5, H-6), 4.09 (br s, 2H, H-2″, H-2‴), 3.95 (t, 1H, $J_{3',4'}$, $J_{4',5'}$ 5.0 Hz, H-4′), 3.87 (m, 2H, H-3″, H-4), 3.79, 3.78 (2s, 6H, $C_6H_4OCH_3$, $CH_2C_6H_4OCH_3$), 3.77 (m, 4H, H-2′, H-5′, H-5″, H-5‴), 3.73 (m, 2H, H-3‴, H-6′), 3.63 (m, 2H, H-6, H-6′), 3.44 (m, 2H, H-2, H-4″), 3.38 (t, 1H, $J_{3''',4'''}$, $J_{4''',5'''}$ 9.5 Hz, H-4‴), 1.26 (d, 3H, $J_{5'',6''}$ 5.5 Hz $J_{5''',6'''}$ 6.5 Hz, C–CH_3), 1.12 (d, 3H, $J_{5''',6'''}$ 6.0 Hz, C–CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 159.1, 157.6, 155.6, 150.2, 139, 138.7(2), 138.5, 138.4, 138.3 (2), 138.2, 138.1, 136.9, 129.5, 129.4(2), 128.5(2), 128.4(4), 128.3(4), 128.2(2), 128.0(2), 127.9(3), 127.8(3), 127.6(2), 127.5, 127.3, 127.1(2), 126.3(2), 118.2(4), 114.8(2), 113.7(2), 110.7 (Ar*C*), 100.2 (*C*HPh), 100.7 (*C*-1‴), 100 (*C*-1″), 98.4 (*C*-1), 97.3 (*C*-1′), 85.7, 82.9, 80.2, 80.1, 79.7, 79.4, 75.3, 75.2, 75.1, 75, 73.2, 73, 72.8, 72.1(2), 72, 71.9, 71.8, 71.4, 69.4, 68.8, 68.5, 67.8, 62.9, 61.9, 56.3 ($C_6H_4OCH_3$), 55.2 ($CH_2C_6H_4OCH_3$), 18.2 (2× C–*C*H$_3$). HRMS (ESI) $(M+Na)^+$, found 1536.6406. $C_{88}H_{95}N_3O_{20}Na$ requires 1536.6407.

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Supplementary data

Supplementary data (Copies of the ^{1}H and ^{13}C NMR spectra of new compounds) associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.tet.2015.06.095.

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