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Chemical Synthesis of β-L-Rhamnose Containing the Pentasaccharide Repeating Unit of the *O*-Specific Polysaccharide from a Halophilic Bacterium *Halomonas ventosae* RU5S2EL in the Form of Its 2-Aminoethyl Glycoside

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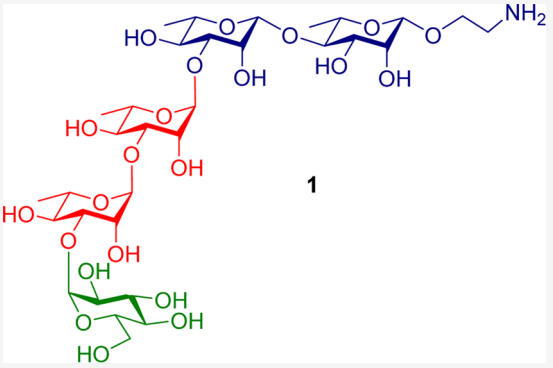
ABSTRACT: Total synthesis of the pentasaccharide repeating unit of the OPS from *Halomonas ventosae* RU5S2EL is accomplished through a [3+2] block strategy. Picoloyl-induced hydrogen-bond-assisted aglycon delivery (HAD) is used for two consecutive 1,2-*cis*-L-rhamnosylations, and remote participation is used for α-selective glucosylation. The choice of 2-aminoethyl glycoside at the reducing end is opted for, leaving the scope for further glycoconjugate formation without hampering the reducing-end stereochemistry.



INTRODUCTION

The genus Halomonas was identified in 1980 with the halophilic and halotolerant Gram-negative aerobic bacteria normally found in saline environments.[1] Ever since, the genus has been growing steadily, with a number of species being added to it. Due to their adaptive physiology in unusual environments,[2] Halomonas species are attractive for industrial uses toward bioremediation and the maintenance of normal physiology of microorganisms in saline environments. The biotechnological importance of Halomonas species triggered the interest of researchers toward extracellular polysaccharides of these bacteria as promising biopolymers that protect the normal physiology of microorganisms in adverse environments. Although detailed pathogenic characterization of these species is yet to be established, diseases caused by Halomonas species in algae, animals, and humans[3] have been reported. Their unique adaptability and increased uses in the industry will undoubtedly allow these species to contaminate environments used by humans in a short time.

Bacterial *O*-polysaccharides are an important class of biomolecules that are responsible for bacterial infections and their adherence to host cells. They are diverse in their structure having different sugar units with varied glycosidic linkages. Since they are immunogenic and decorated in the outermost part of the bacterial cell wall, *O*-polysaccharides offer potential scope for vaccine designing against specific bacteria. To evaluate the potential of a vaccine candidate, chemical synthesis of the complex *O*-polysaccharides becomes necessary, and often the synthesis of these complex structures is challenging even with the development of newer chemical methods. Recently, Sigida et al. reported the pentasaccharide repeating unit of the *O*-specific polysaccharide from *Halomonas ventosae* RU5S2EL.[4] The Gram-negative halophilic bacterium *H. ventosae* RU5S2EL is a marine member[5] isolated from salt samples collected from lake Elton (Russia). Herein, we report the total chemical synthesis of the repeating unit of the *O*-polysaccharide from *H. ventosae* RU5S2EL in the form of its 2-aminoethyl glycoside (**1**, Figure 1).

The presence of two consecutive 1,2-*cis* linked rhamnose and a 1,2-*cis* linked glucose is the prominent synthetic challenge[6] toward this particular total synthesis. For the 1,2-*cis* linked rhamnose units, picoloyl-induced hydrogen-bond-assisted aglycon delivery (HAD)[7−9] was used successfully, whereas for the 1,2-*cis* linked glucose moiety, remote participation of the carbonyl functional group was utilized.[10] 2-Aminoethyl glycoside was chosen, leaving the scope of further glycoconjugate formation using the terminal free amine without hampering the stereochemistry at the reducing end. The synthetic pentasaccharide will pave the path to further

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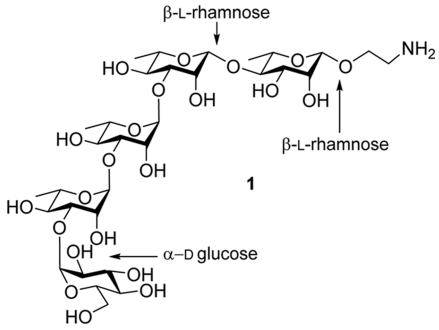

Figure 1. Structure of the target pentasaccharide repeating unit in the form of its 2-aminoethyl glycoside.

understanding of the role of OPS toward the adaptability of Halomonas species in saline environments.

Careful retrosynthetic analysis revealed that the target pentasaccharide **1** may be constructed by a [3+2] block synthesis strategy. Therefore, the protected pentasaccharide **2** was disconnected from the trisaccharide acceptor **3** and the disaccharide donor **4**. The trisaccharide **3** could be accessed from the glycosylation between the disaccharide acceptor **5** and the monosaccharide donor **6**. Glycosylation of the 3-picoloyl donor **7** with the acceptor **8** furnishes the disaccharide **5** with the desired 1,2-*cis* rhamnosidic linkage. Both monosaccharide derivatives **7** and **8** may be prepared from commercially available L-rhamnose. On the other hand, the trichloroacetimidate donor **9** glycosylates with the acceptor **10**

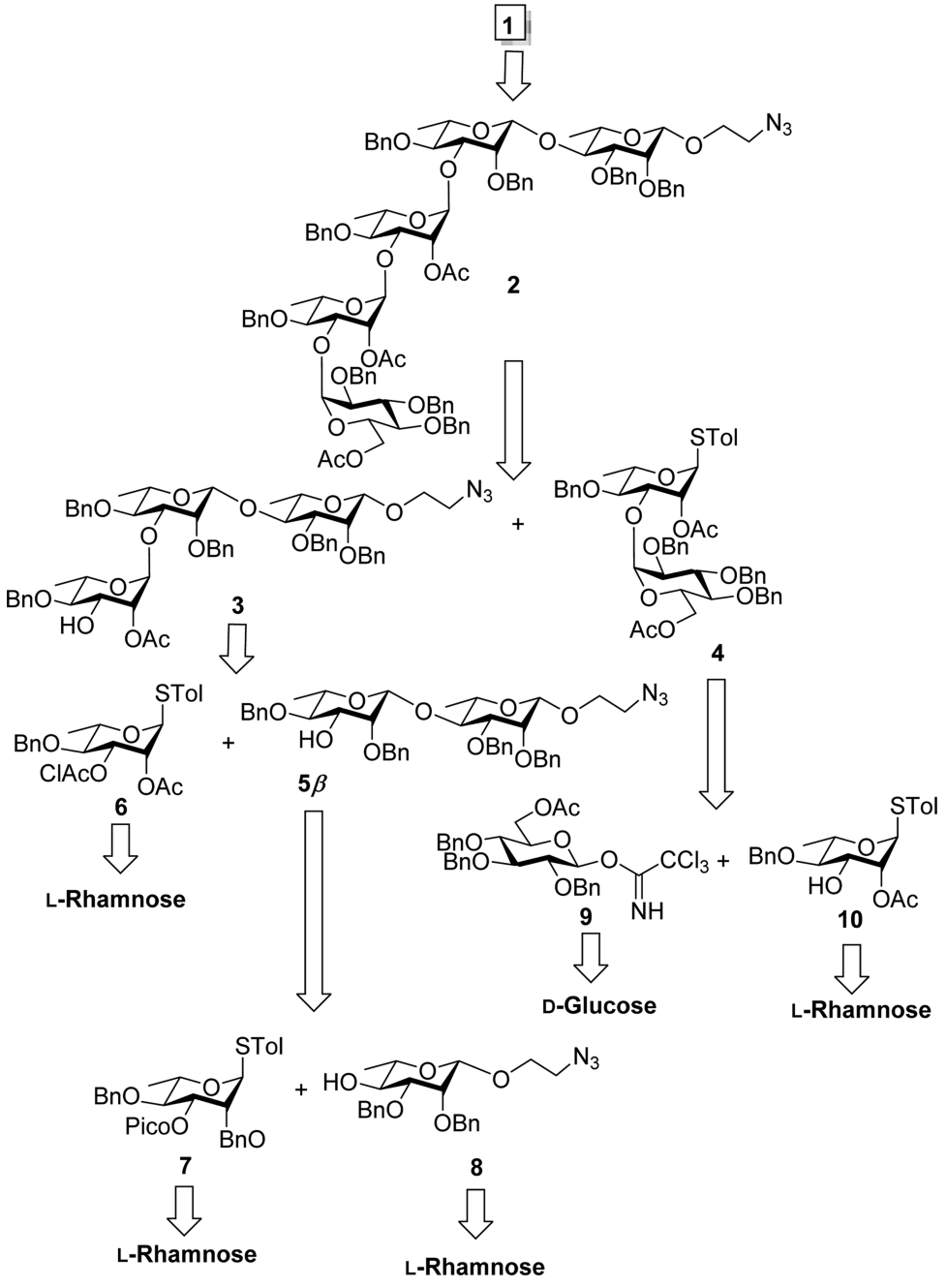

Figure 2. Retrosynthetic analysis.

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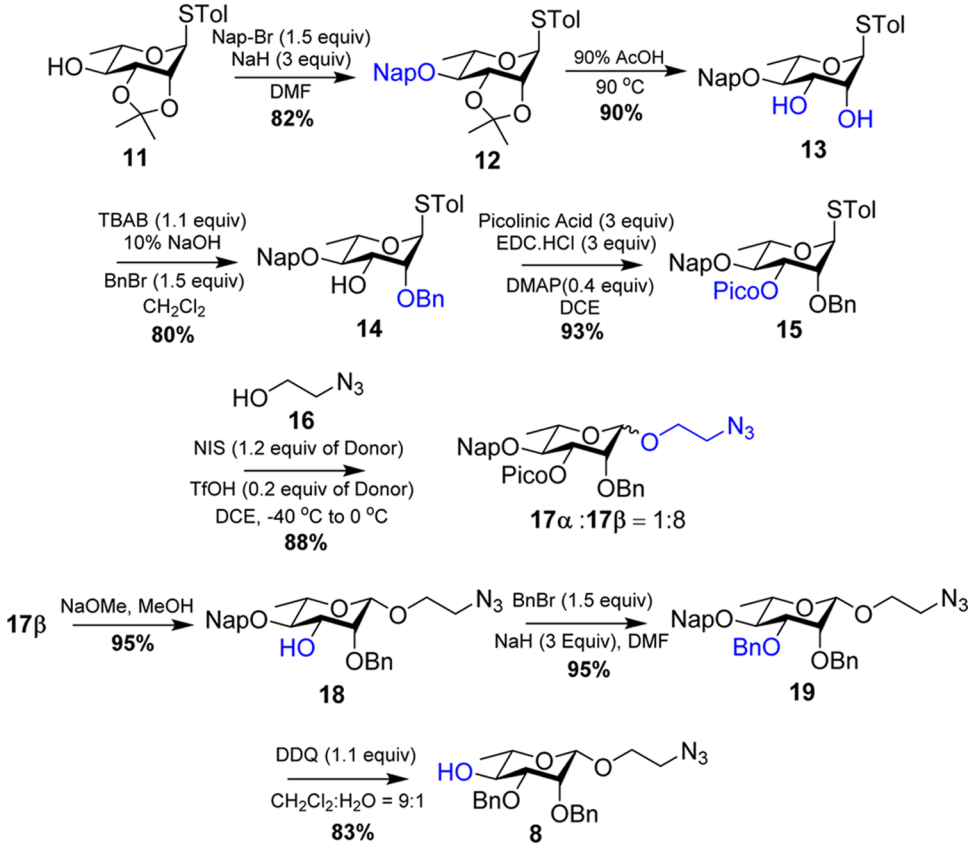
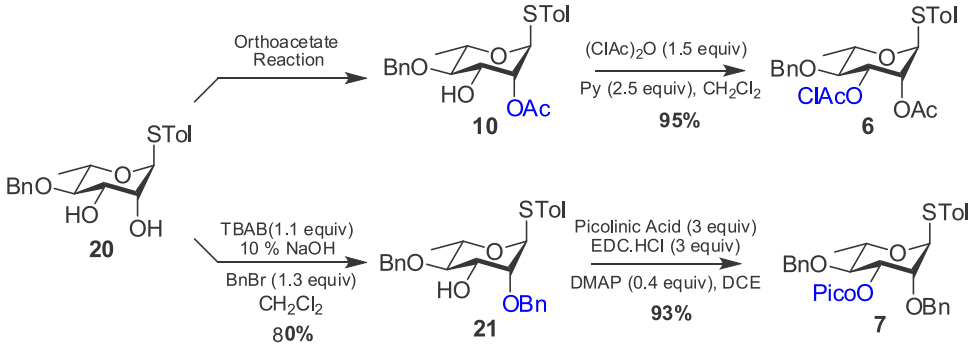
Scheme 1. Picoloyl-Induced β-L-Rhamnosylation with Azido Ethanol Utilizing the HAD Strategy and Synthesis of the Rhamnosyl Acceptor 8



Scheme 2. Synthesis of the Monosaccharide Building Blocks 6 and 7



to afford the required disaccharide donor **4**. Compounds **9** and **10** can be prepared from commercially available D-glucose and L-rhamnose, respectively (Figure 2).

RESULTS AND DISCUSSION

Following the retrosynthetic analysis, synthesis of the trisaccharide acceptor **3** commenced with the preparation of 2-aminoethyl β-L-rhamnoside. The known compound **11**[11] was treated with 2-naphthylmethyl bromide (NapBr) in the presence of NaH[12] to afford the corresponding 2-naphthylmethyl derivative **12** in 82% yield. Further, di-ol **13** was obtained from the hydrolysis of the isopropylidene derivative using 90% AcOH at 90 °C. Next, selective benzylation of the 2-OH position using the phase transfer reaction (PTR)[13] gave compound **14**. Finally, the free 3-OH group in compound **14** was protected with the picoloyl group via an ethylene dichloride (EDC)·HCl-mediated coupling with 2-picolinic acid[14] to obtain donor **15** in 93% yield (Scheme 1).

Recently, Demchenko and co-workers established the remote 3-*O*-picoloyl-group-induced HAD[7,15] method to facilitate direct 1,2-*cis* rhamnosylation. The method worked perfectly for the glycosylation of the rhamnosyl donor **15** with 2-azidoethanol **16** through the activation of thioglycoside using *N*-iodosuccinimide (NIS) in the presence of TfOH in dichloroethane (DCE) at −40 to 0 °C in 88% yield with high stereoselectivity[16−18] (**17*α*:17*β*** = 1:8). The anomeric mixture was successfully separated by flash chromatography, and the newly formed 1,2-*cis* rhamnosidic linkage was confirmed by the peaks at 4.63 ppm (s, 1H, H-1) in the ^{1}H nuclear magnetic resonance (NMR) and at 100.9 (C-1) in the ^{13}C NMR with J_{CH} = 154 Hz. The presence of the azido group was also confirmed by its IR signal at 2075 cm^{-1}. The β-L-

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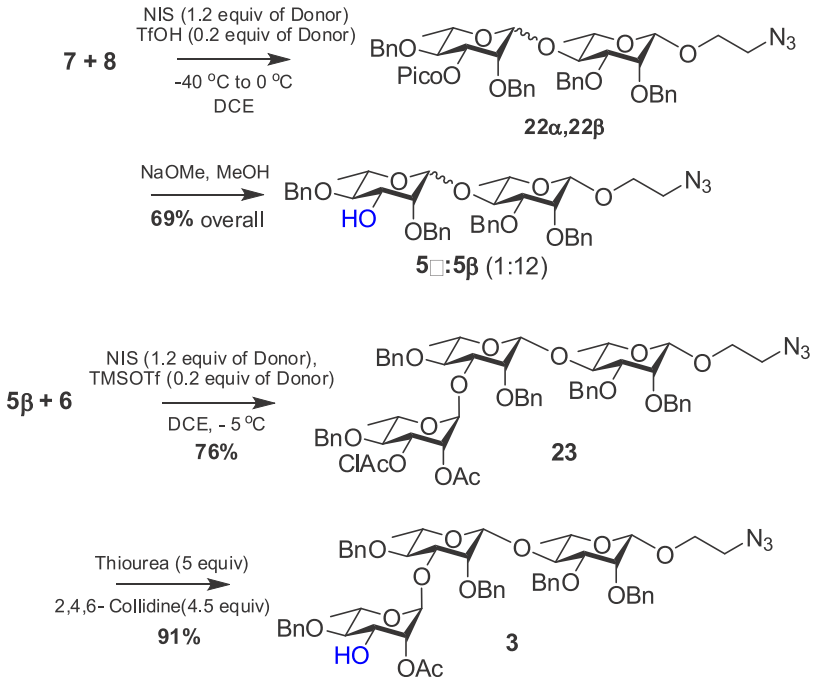
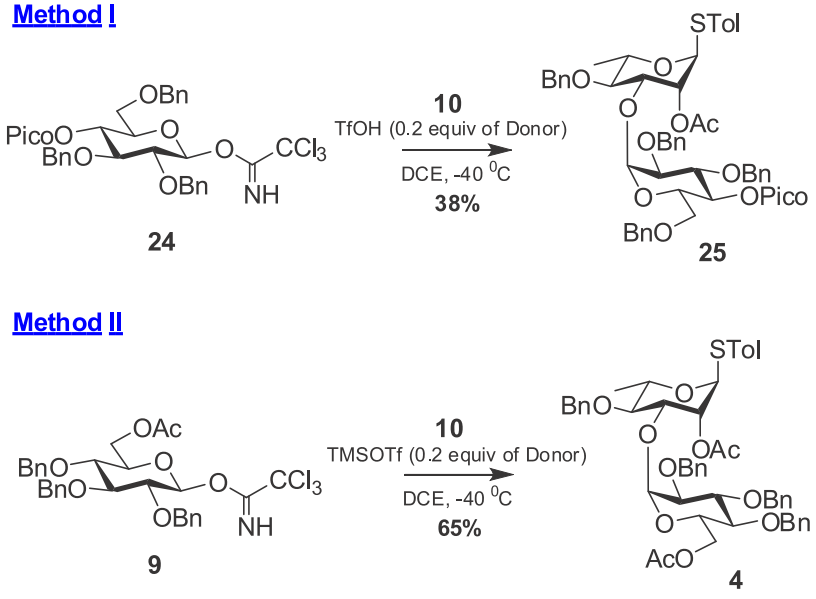
Scheme 3. Picoloyl-Induced β-L-Rhamnosylation and Synthesis of Trisaccharide Acceptor 3



Scheme 4. Synthesis of the Disaccharide Donor 4



rhamnoside **17β** was treated with NaOMe in MeOH to remove the picoloyl group, and subsequently the free OH group of **18** was benzylated using BnBr in the presence of NaH to give the derivative **19**. Finally, oxidative removal of the 2-methylnapthyl group using 1,2-dichloro 4,5-dicyanoquinone (DDQ)[19] in CH_2Cl_2-H_2O (9:1) afforded the desired rhamnosyl acceptor **8** in 83% yield (Scheme 1).

In a separate experiment, a known compound *p*-tolyl 4-*O*-benzyl-1-thio-α-L-rhamnopyranoside **20**[20] was selectively benzylated at the 2-OH position using the phase transfer reaction (PTR)[13] followed by picoloyl group incorporation at the 3-OH position via an EDC·HCl-mediated coupling with 2-picolinic acid;[14] compound **7** was obtained in 93% yield. Next, the known compound **10**[21] was prepared from compound **20** through formation of the orthoester followed by rearrangement. Next, the free 3-OH group was protected with the chloroacetate group using chloroacetic anhydride in the presence of pyridine in 95% yield (Scheme 2).

Glycosylation of the rhamnosyl donor **7** with the acceptor **8** through NIS-mediated activation of thioglycoside afforded the disaccharides **22α** and **22β**. However, complete separation of the anomeric mixture was unsuccessful at this stage. We could only separate the significantly pure β-variant as confirmed by NMR. After removal of the picoloyl group from the mixed disaccharides using NaOMe in MeOH, the anomers were successfully purified, revealing the ratio of **5α**:**5β** to be 1:12 (Scheme 3). Thus, the picoloyl-induced HAD worked perfectly for this 1,2-*cis* rhamnosylation too. Signals in the ^{1}H NMR at δ

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Scheme 5. Synthesis of the Target Pentasaccharide 1

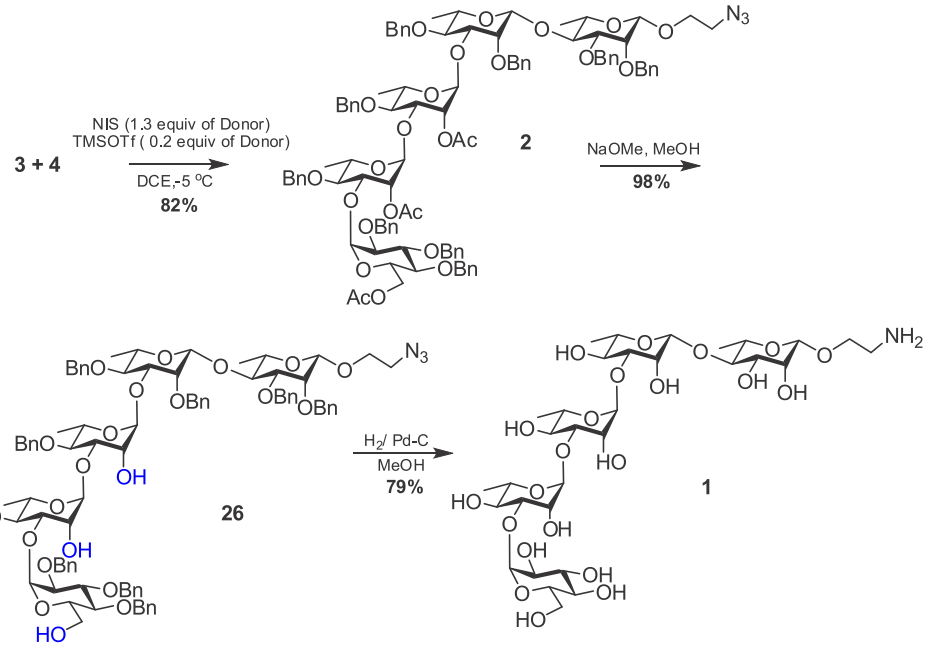

Table 1. Comparison of the ^{1}H and ^{13}C{^{1}H} NMR Signals for the Anomeric Protons and Carbons, Respectively

	H-1	C-1	H-1′	C-1′	H-1″	C-1″	H-1‴	C-1‴	H-1⁗	C-1⁗
1	4.94	101.3	4.70	99.3	4.98	102.3	5.03	101.9	5.08	95.6
lit.	4.74	101.8	4.75	101.4	5.02	103.3	5.11	102.9	5.13	95.3

4.64 (H-1) and 4.43 (H-1′) as well as in the ^{13}C NMR at δ 101.1 ppm (C-1) with J_{CH} 152.5 Hz and at 100.9 ppm (C-1′) with J_{CH} 153.8 Hz confirmed the formation of the desired disaccharide acceptor **5*β***. Glycosylation reaction of the rhamnosyl donor **6** with the disaccharide acceptor **5*β*** using NIS in the presence of TMSOTf at −5 °C afforded the trisaccharide **23** in 76% yield. The rhamnosyl donor containing the participating acetate group at the 2-position ensured the formation of the desired 1,2-*trans* glycoside exclusively.[22] The newly formed glycosidic linkage was further confirmed by the ^{1}H NMR signal at δ 5.02 (H-1″) and by the ^{13}C NMR signal at δ 99.2 (C-1″) with J_{CH} value 174.4 Hz. Subsequently, the chloroacetyl group was hydrolyzed in the presence of thiourea and 2,4,6-collidine[23] to furnish the trisaccharide acceptor **3** in 91% yield (Scheme 3).

The successful application of HAD for the *β*-rhamnosylations inspired us to use the same picoloyl-induced HAD to accomplish the 1,2-*cis* glucosylation for the preparation of the nonreducing-end disaccharide.[14] Thus, the known picoloyl trichloroacetimidate derivative **24**[14] was reacted with the rhamnosyl acceptor **10**[21] in the presence of TfOH at −40 °C. The reaction resulted in the formation of the desired sole *α*-linked disaccharide **25** in 38% yield only (Method I, Scheme 4), and the acceptor and hemiacetal of the donor were recovered by flash chromatography. Considering the low yield with the picoloyl-induced HAD, we explored the remote participation of the 6-*O*-acyl group for *α*-selectivity.[24] When the known trichloroacetimidate derivative **9**[25] was reacted with the same rhamnosyl acceptor **10**[21] in the presence of TMSOTf, the sole *α*-linked disaccharide **4** was obtained in 65% yield (Method II, Scheme 4). Therefore, the remote participation of the 6-*O*-acyl group[26] was found to be more effective for the *α*-selective glucosylation in this particular case. The 1,2-*cis* linkage was confirmed by the ^{1}H NMR signal at δ 5.27 (H-1′) and the ^{13}C NMR signal at δ 92.3 (C-1′) with J_{CH} 167.5 Hz. However, due to the high reactivity[27] of the trichloroacetimidate donor, formation of hemiacetal in a significant amount resulted in a low yield[28] of the disaccharide, but the 1,2-*cis* linkage was formed exclusively.

Having the trisaccharide acceptor **3** and the disaccharide donor **4**, the final glycosylation in the presence of NIS and TMSOTf furnished the protected pentasaccharide **2** in 82% yield. Subsequently, Zemplén de-*O*-acetylation using NaOMe in MeOH gave the partially protected derivative **26** in 98% yield. Finally, hydrogenolysis using a 10% Pd-C cartridge in a ThalesNano continuous-flow hydrogenation assembly[29,30] afforded the target pentasaccharide **1** in 79% yield after six cycles (Scheme 5).

The ^{1}H and ^{13}C anomeric signals of the target structure **1** were compared with those reported in the structure elucidation. The data is given in Table 1.

CONCLUSIONS

We have accomplished the synthesis of the target pentasaccharide through a convergent [3+2] strategy with satisfactory yield throughout. The challenging 1,2-*cis* rhamnosylations were achieved through picoloyl-induced HAD. However, for 1,2-*cis* glucosylation, remote participation of the 6-*O*-acyl group was found to be more beneficial over the HAD strategy if the yield is concerned. The target pentasaccharide in the form of its aminoethyl group leaves the scope of further glycoconjugate formation without disturbing the anomeric stereochemistry at the reducing end. Further exploration of the biological roles of

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this oligosaccharide repeating unit will be facilitated to obtain the same in the purest possible form by chemical means.

EXPERIMENTAL SECTION

General Methods. All solvents and reagents were dried prior to use according to literature methods.[31] 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. 2-Azido ethanol (**16**) was procured from Biosynth Carbosynth, U.K. (CAS No. 1517-05-1). All reactions were monitored by thin-layer chromatography (TLC) on silica gel 60-F254 with detection via fluorescence and by charring after immersion in 10% ethanolic solution of sulfuric acid. Flash chromatography was performed with a silica gel 230−400 mesh. Optical rotations were measured on sodium D-line at ambient temperature. ^{1}H and ^{13}C{^{1}H} NMR were recorded on a Bruker Avance spectrometer at 500 and 126 MHz, respectively, unless otherwise stated. Structural assignments were made with additional information from gCOSY and gHSQC experiments.

*p-Tolyl 2,3-O-Isopropylidene-4-O-(2-naphthylmethyl)-1-thio-α-L-rhamnopyranoside (**12**).* To a solution of *p*-tolyl 2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (**11**)[11] (3.6 g, 11.4 mmol) in dry DMF (30 mL) that was cooled to 0 °C, NaH in 50% mineral oil (830 mg, 35 mmol) was added followed by 2-naphthylmethyl bromide (Nap-Br) (3.7 g, 16.8 mmol), and the mixture was allowed to stir at room temperature for 1 h when TLC (*n*-hexane−EtOAc; 6:1, R_f = 0.7) showed complete conversion of the starting material to a faster moving spot. Excess NaH was neutralized by the careful addition of MeOH, and cold H_2O (100 mL) was added. Stirring was continued for another 40 min. Then, it was extracted with EtOAc (2 × 25 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated *in vacuo*. The crude mixture thus obtained was purified by flash chromatography using *n*-hexane−EtOAc (16:1 → 12:1 → 8:1) as the eluent to afford pure compound **12** (4.3 g, 82%) as a yellowish syrup.

$[\alpha]_D^{25} = -185$ (*c*1.1, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$). δ 7.83−7.07 (m, 11H, Ar*H*), 5.66 (s, 1H, H-1), 5.06 (d, J_{AB} 12.0 Hz, 1H, CH_2Ar), 4.80 (d, J_{AB}12.0 Hz, 1H, CH_2Ar), 4.38−4.33 (m, 2H, H-2, H-3), 4.18 (m, 1H, H-5), 3.96 (t, 1H, $J_{2,3}$ 9.0 Hz, $J_{4,3}$ 9.0 Hz, H-4), 2.31 (s, 3H, $SC_6H_4CH_3$), 1.49 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.25 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$). δ 137.7, 135.7, 135.6, 133.2, 132.9, 129.6, 128.2, 128.0, 127.8, 127.6, 126.7, 126.4, 126.0, 125.9, 125.8, 123.2 (Ar*C*), 109.3, 84.1 (C-1), 81.4 (C-4), 78.4 (C-3), 76.6 (C-2), 73.0 (CH_2Ar), 66.0 (C-5), 28.0 (CH_3), 26.4 (CH_3), 21.1 ($SC_6H_4CH_3$), 17.7 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{27}H_{30}O_4SNa$ (M + Na)$^+$: 473.1762; found: 473.1769.

*p-Tolyl 4-O-(2-Naphthylmethyl)-1-thio-α-L-rhamnopyranoside (**13**).* Compound **12** (4.2 g, 7.5 mmol) was dissolved in 90% aq AcOH (30 mL), and the solution was stirred at 90 °C in an oil bath for 1 h when TLC (*n*-hexane−EtOAc; 1:2, R_f = 0.25) showed complete conversion of the starting material to a slower moving spot. After that, aq AcOH was evaporated *in vacuo* with the help of coevaporation of toluene to afford the di-ol compound **13**. The crude mixture was obtained, which was purified by flash chromatography using *n*-hexane−EtOAc (1:3) as the eluent to afford pure compound **13** (3.63 g, 95%) as a white powder.

$[\alpha]_D^{25}$ − 87 (*c*0.9, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$). δ 7.85−7.09 (m, 11H, Ar*H*), 5.38 (d, 1H, $J_{1,2}$ 1.0 Hz, H-1), 4.89 (bs, 2H, CH_2Ar), 4.25 (m, 1H, H-5), 4.16 (bs, 1H, H-2), 3.96 (dd, 1H, $J_{2,3}$ 3.0 Hz, $J_{4,3}$ 9.0 Hz, H-3), 3.45 (t, 1H, $J_{5,4}$ 9.0 Hz, $J_{3,4}$ 9.0 Hz, H-4), 2.65 (bs, 1H, 2-O*H*), 2.50 (d, 1H, $J_{3,OH}$ 4.5 Hz, 3-O*H*), 2.31 (s, 3H, $SC_6H_4CH_3$), 1.35 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$). δ 137.6, 135.6, 133.3, 133.0, 132.1, 130.2, 129.8,128.5, 127.9, 127.7, 126.7, 126.3, 126.1, 125.7 (Ar*C*), 87.8 (C-1), 81.9 (C-4), 75.1 (CH_2Ar), 72.6 (C-2), 71.9 (C-3), 68.5 (C-5), 21.1 ($SC_6H_4CH_3$), 17.9 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{24}H_{26}O_4SNa$ (M + Na)$^+$: 433.1444; found: 433.1450.

*p-Tolyl 2-O-Benzyl-4-O-(2-naphthylmethyl)-1-thio-α-L-rhamnopyranoside (**14**).* To a solution of diol **13** (3.5 g, 8.5 mmol) in CH_2Cl_2 (30 mL), Bu_4NBr (3 g, 9.4 mmol), 10% aq NaOH (10 mL), and BnBr (1.53 mL, 12.8 mmol) were added, and the mixture was stirred at room temperature for 12 h when TLC (*n*-hexane−EtOAc; 3:1, R_f = 0.65) showed complete conversion of the starting di-ol to a faster moving spot. The mixture was diluted with CH_2Cl_2 (10 mL) and washed with H_2O (30 mL) and brine solution (30 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated *in vacuo*. The crude material thus obtained was purified by flash chromatography using *n*-hexane−EtOAc (4:1) as the eluent to afford pure compound **14** (3.4 g, 80%) as a white foam.

$[\alpha]_D^{25}$ − 39 (*c*1.1, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$). δ 7.88−7.15 (m, 16H, Ar*H*), 5.54 (s, 1H, H-1), 5.12 (d, J_{AB} 12.0 Hz, 1H, CH_2Ar), 4.87 (d, J_{AB} 12.0 Hz, 1H, CH_2Ar), 4.77 (d, J_{AB} 12.0 Hz, 1H, CH_2Ar), 4.56 (d, J_{AB} 12.0 Hz, 1H, CH_2Ar), 4.26 (m, 1H, H-5), 4.11−4.06 (m, 2H, H-2, H-3), 3.50 (t, 1H, $J_{5,4}$ 9.0 Hz, $J_{3,4}$ 10.0 Hz, H-4), 2.47 (bs, 1H, 3-O*H*), 2.37 (s, 3H, $SC_6H_4CH_3$), 1.41 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$). δ 137.7, 137.4, 135.9, 133.3, 133.0, 132.1, 130.2, 129.8, 128.6, 128.1, 128.0, 127.9, 127.7, 126.7, 126.0, 125.9, 125.8 (Ar*C*), 85.3 (C-1), 82.5 (C-4), 80.0 (C-3), 75.1 (CH_2Ar), 72.3 (CH_2Ar), 72.1 (C-2), 68.5 (C-5), 21.1 ($SC_6H_4CH_3$), 17.9 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{31}H_{32}O_4SNa$ (M + Na)$^+$: 523.1914; found: 523.1917.

*p-Tolyl 2-O-Benzyl-4-O-(2-naphthylmethyl)-3-O-picoloyl-1-thio-α-L-rhamnopyranoside (**15**).* It is worth noting that following the recently reported preparation of the picoloyl derivative of a similar synthon,[16] we ended up with 52% yield only. That triggered us to modify the reaction condition. Switching from CH_2Cl_2 to DCE as the solvent and reducing the amount of 2-picolinic acid to 3 equiv only gave us an excellent yield of 93% for the desired picoloyl derivative. It significantly reduced the time of the reaction as complete conversion was obtained within 30 min. Thus, to a stirred solution of **14** (3.3 g, 6.6 mmol) in DCE (30 mL), EDC-HCl (3.8g, 19.8 mmol) and 4-dimethylaminopyridine (DMAP) (324 mg, 2.6 mmol) were added at 25 °C; 2-picolinic acid (2.4 g, 19.8 mmol) was added when the mixture turned canary yellow, which slowly turned to dark yellow with time. The mixture was stirred at 25 °C for 30 min when TLC (*n*-hexane−EtOAc; 3:1, R_f = 0.4) showed complete conversion of the starting compound to a slower moving spot. The mixture was diluted with CH_2Cl_2 (20 mL) and washed with brine (40 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated *in vacuo*; the crude material thus obtained was purified by flash chromatography using *n*-hexane−EtOAc (1:1) as the eluent to afford pure compound **15** (3.7 g, 93%) as a yellowish syrup.

$[\alpha]_D^{25}$ − 49 (*c*0.8, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$). δ 8.75−7.06 (m, 20H, Ar*H*), 5.53 (dd, 1H, $J_{4,3}$ 10.0 Hz, $J_{3,2}$ 3.0 Hz, H-3), 5.44 (d, 1H, $J_{1,2}$ 1.5 Hz, H-1), 4.95 (d, 1H, J_{AB} 12.5 Hz, CH_2Ar), 4.88 (d, 1H, J_{AB} 12.5 Hz, CH_2Ar), 4.65 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.50 (d, 1H, J_{AB} 12.5 Hz, CH_2Ar), 4.32 (m, 1H, H-5), 4.22 (dd, 1H, $J_{1,2}$ 1.5 Hz, $J_{2,3}$ 3.0 Hz, H-2), 3.97 (t, 1H, $J_{5,4}$ 9.0 Hz, $J_{3,4}$ 10.0 Hz, H-4), 2.35 (s, 3H, $SC_6H_4CH_3$), 1.40 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$). δ 164.1 (C_5H_4NCO), 149.8, 147.6, 137.6, 137.4, 136.7, 135.7, 133.1, 132.8, 132.3, 130.4, 129.8, 128.2, 127.9, 127.8, 127.7, 127.6, 126.8, 126.4, 125.9, 125.8, 125.7, 125.1 (Ar*C*), 85.7 (C-1), 79.3 (C-4), 77.1 (C-2), 75.1 (C-3), 75.0 (CH_2Ar), 72.3 (CH_2Ar), 69.2 (C-5), 21.1 ($SC_6H_4CH_3$), 18.0 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{37}H_{36}O_5SN$ (M + H)$^+$: 606.2309; found: 606.2319.

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*2-Azidoethyl 2-O-Benzyl-4-O-(2-naphthylmethyl)-3-O-picoloyl-β-L-rhamnopyranoside (**17β**).* MS 4 Å (2.0 g) in dry DCE (25 mL) activated by glycosyl donor **15** (2.44 g, 4.0 mmol) and azido ethanol acceptor **16** (350 mg, 4.0 mmol) was stirred under a nitrogen atmosphere for 1 h at 25 °C. Then, NIS (1.08 g, 4.84 mmol) was added and stirred under a nitrogen atmosphere for 5 min. After that, the mixture was cooled to −30 °C. TfOH (71 μL, 0.81 mmol) was added after 10 min at −30 °C, and the temperature was allowed to rise up to 0 °C in about 1 h. TLC (*n*-hexane−EtOAc; 2:1, double run, R_f = 0.5) showed complete consumption of the acceptor. The mixture was filtered through a pad of Celite, and the filtrate was washed successively with aq $Na_2S_2O_3$ (2 × 30 mL), saturated $NaHCO_3$ (2 × 30 mL), and H_2O (30 mL). The organic layer was collected, dried with Na_2SO_4, and filtered. The solvent was evaporated *in vacuo*, and the residue was purified by flash chromatography using *n*-hexane−EtOAc (2.2:1) as the eluent to obtain pure **17β** (1.77 g, 78%) along with the corresponding α-derivative **17α** (223 mg, 10%) as a yellowish syrup.

17β.

$[\alpha]_D^{25}$ + 26 (*c*0.9, $CHCl_3$)

An IR = 2075 cm^{-1} sharp peak was present for the $-N_3$ stretching vibration.

^{1}H NMR (500 MHz, CDCl$_3$). δ 8.73−6.99 (m, 16H, Ar*H*), 5.14 (dd, 1H, $J_{2,3}$ 3.0 Hz, $J_{4,3}$ 9.5 Hz, H-3), 4.93 (d, 2H, J_{AB} 12.0 Hz, CH_2Ar), 4.86 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.64 (d, 1H, J_{AB} 9.5 Hz, CH_2Ar), 4.63 (s, 1H, H-1), 4.16 (bs, 1H, H-2), 4.12 (m, 1H, OCH_2), 3.93 (t, 1H, $J_{5,4}$ 9.5 Hz, $J_{3,4}$ 9.5 Hz, H-4), 3.64 (m, 1H, OCH_2), 3.64 (m, 2H, NCH_2, H-5), 3.29 (m, 1H, NCH_2), 1.45 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$). δ 163.8 (C_5H_4NCO), 149.6, 147.3, 138.0, 136.4, 135.4, 132.9, 132.7, 128.2, 127.9, 127.7, 127.7, 127.4, 127.2, 126.6, 126.4, 125.8, 125.8, 125.6, 124.9 (Ar*C*), 100.9 (C-1), 78.5 (C-4),76.6 (C-3), 74.7 (CH_2Ar), 75.3 (CH_2Ar), 75.1 (C-2), 71.8 (C-5), 68.5 (OCH_2), 50.7 (NCH_2), 17.8 (C-6).

^{1}H coupled ^{13}C spectra revealed J_{CH} = 154.0 Hz for the anomeric carbon.

HR-ESI-MS (*m*/*z*) calcd for $C_{32}H_{32}O_6N_4Na$ (M + Na)$^+$: 591.2214; found: 591.2216.

*2-Azido Ethyl 2-O-Benzyl-4-O-(2-naphthylmethyl)-β-L-rhamnopyranoside (**18**).* To a solution of compound **17β** (1.7 g, 3.0 mmol) in MeOH (20 mL), NaOMe (0.5 M in MeOH, 2 mL) was added, and the solution was stirred at room temperature for 30 min. TLC (*n*-hexane−EtOAc; 2:1, R_f = 0.5) showed complete conversion of the starting material to a faster moving spot. The reaction mixture was quenched with DOWEX 50 W resin and filtered, and the filtrate was evaporated to dryness under reduced pressure to give the crude compound **18**. It was diluted with CH_2Cl_2 (15 mL) and washed with H_2O (30 mL) and brine solution (30 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated *in vacuo*. The crude material thus obtained was purified by flash chromatography using *n*-hexane−EtOAc (3:1) as the eluent to afford pure **18** (1.3 g, 95%) as a white amorphous mass.

$[\alpha]_D^{25}$ + 76 (*c*0.8, $CHCl_3$)

^{1}H NMR (500 MHz, CDCl$_3$). δ 7.79−7.19 (m, 12H, Ar*H*), 5.06 (d, 1H, J_{AB} 12.5 Hz, CH_2Ar), 5.05 (d, 1H, J_{AB} 12.5 Hz, CH_2Ar), 4.75 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.60 (d, 1H, J_{AB} 11.5 Hz, CH_2Ar), 4.44 (s, 1H, H-1), 4.05 (m, 1H, OCH_2), 3.82 (d, 1H,$J_{2,3}$ 3.0 Hz, H-2), 3.61−3.55 (m, 2H, OCH_2, H-4), 3.50−3.45 (m, 1H, NCH_2), 3.32−3.22 (m, 3H, NCH_2, H-5, H-3), 2.44 (d, 1H, $J_{3,OH}$ 8.0 Hz, O*H*), 1.38 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$). δ 138.3, 135.8, 133.1, 132.8, 128.4, 128.1, 127.9, 127.8, 127.5, 126.5, 125.9, 125.7 (Ar*C*), 101.5 (C-1), 81.8 (C-3), 78.1 (C-2), 75.1 (CH_2Ar), 74.9 (CH_2Ar), 73.8 (C-4), 71.4 (C-5), 68.4 (OCH_2), 50.6 (NCH_2), 17.8 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{26}H_{29}O_5N_3Na$ (M + Na)$^+$: 486.1999; found: 486.2013.

*2-Azido Ethyl 2,3-Di-O-benzyl-4-O-(2-naphthylmethyl)-β-L-rhamnopyranoside (**19**).* To a solution of compound **18** (1.23 g, 2.65 mmol) in dry DMF (15 mL) that was cooled to 0 °C, NaH in 50% mineral oil (200 mg, 8.3 mmol) was added followed by BnBr (0.5 mL, 4.0 mmol), and the mixture was allowed to stir at room temperature for 1 h when TLC (*n*-hexane−EtOAc; 3:1, R_f = 0.5) showed complete conversion of the starting material to a faster moving spot. Excess NaH was neutralized by the careful addition of MeOH (5 mL), and the mixture was diluted with cold H_2O (50 mL). Stirring was continued for another 30 min. Then, it was extracted with EtOAc (2 × 15 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated *in vacuo*. The crude mixture thus obtained was purified by flash chromatography using *n*-hexane−EtOAc (12:1 → 7:1 → 4:1) as the eluent to afford a white sticky compound **19** (1.4 g, 95%).

$[\alpha]_D^{25}$ + 35 (*c*1.0, $CHCl_3$)

^{1}H NMR (500 MHz, CDCl$_3$). δ 7.79−7.25 (m, 17H, Ar*H*), 5.10 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 5.00 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.83 (d, 1H, J_{AB} 12.5 Hz, CH_2Ar), 4.79 (d, 1H, J_{AB} 13.0 Hz, CH_2Ar), 4.50 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.43 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.38 (s, 1H, H-1), 4.06 (m, 1H, OCH_2), 3.96 (bs, 1H, H-2), 4.68 (t, 1H, $J_{5,4}$ 9.5 Hz, $J_{3,4}$ 9.5 Hz, H-4), 3.57−3.47 (m, 3H, OCH_2, H-3, NCH_2), 3.33 (m, 1H, H-5), 3.25 (m, 1H, NCH_2), 1.39 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$). δ138.6, 138.0, 135.8, 133.1, 132.8, 128.2, 128.1, 127.9, 127.8, 127.7, 127.5, 127.4, 127.2, 126.6, 126.0, 125.9, 125.7 (Ar*C*), 101.4 (C-1), 81.8 (C-3), 79.8 (C-4), 75.3 (CH_2Ar), 74.2 (CH_2Ar, C-2), 71.9 (C-5), 71.2 (CH_2Ar), 68.2 (OCH_2), 50.7 (NCH_2), 17.9 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{33}H_{35}O_5N_3Na$ (M + Na)$^+$: 576.2469; found: 576.2468.

*2-Azido Ethyl 2,3-Di-O-benzyl-β-L-rhamnopyranoside (**8**).* To a solution of compound **19** (1.32 g, 2.4 mmol) in CH_2Cl_2/H_2O = 9:1 (20 mL), DDQ (600 mg, 2.6 mmol) was added, and the mixture was stirred at 25 °C for 2 h when TLC (*n*-hexane−EtOAc; 1.5:1, R_f = 0.5) showed complete conversion of the starting material to a slower moving spot. Then, the mixture was diluted with CH_2Cl_2 (10 mL) and washed successively with $NaHCO_3$ solution (2 × 25 mL) and brine (20 mL). The organic layer was separated, dried by Na_2SO_4, and filtered. The solvent was evaporated *in vacuo*, and the residue was purified by flash chromatography using *n*-hexane−EtOAc (2:1) as the eluent to afford the pure monosaccharide acceptor **8** (805 mg, 83%) as a white amorphous mass.

$[\alpha]_D^{25}$ + 66 (*c*0.9, $CHCl_3$)

^{1}H NMR (500 MHz, CDCl$_3$). δ 7.44−7.22 (m, 10H, Ar*H*), 4.98 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.74 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.47 (s, 1H, H-1), 4.43 (d, 1H, J_{AB} 12.5 Hz, CH_2Ar), 4.21 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.16−4.12 (m, 1H, OCH_2), 3.99 (d, 1H, $J_{3,2}$ 3.0 Hz, H-2), 3.69 (t, 1H, $J_{5,4}$ 9.0 Hz, $J_{3,4}$ 9.0 Hz, H-4), 3.66−3.62 (m, 1H, OCH_2), 3.60−3.54 (m, 1H, NCH_2), 3.34−3.27 (m, 2H, H-5, NCH_2), 3.24 (dd, 1H, $J_{4,3}$ 9.0 Hz, $J_{2,3}$ 3.0 Hz, H-3), 2.27 (bs, 1H, O*H*), 1.37 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$). δ 138.6, 137.5, 128.5, 128.3, 128.1, 127.8, 127.7, 127.5 (Ar*C*), 101.7 (C-1), 81.3 (C-3), 74.4 (CH_2Ar), 73.5 (C-2), 72.4 (C-5), 71.4 (C-4), 70.8 (CH_2Ar), 68.4 (OCH_2), 50.9 (NCH_2), 17.7 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{22}H_{27}O_5N_3Na$ (M + Na)$^+$: 436.1843; found: 436.1836.

*p-Tolyl 2,4-Di-O-benzyl-1-thio-α-L-rhamnopyranoside (**21**).* To a solution of di-ol **20**[20] (1.60 g, 4.4 mmol) in CH_2Cl_2 (30 mL), Bu_4NBr (1.57 g, 4.88 mmol), 10% aq NaOH (10 mL), and BnBr (0.68 mL, 5.7 mmol) were added, and the mixture was stirred at room temperature for 12 h when TLC (*n*-hexane−EtOAc; 2:1, R_f = 0.68) showed complete conversion of the starting di-ol to a faster moving spot. The mixture was diluted with CH_2Cl_2 (10 mL) and washed with H_2O (2 × 30 mL) and brine solution (25 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated *in vacuo*, and the crude material thus obtained was purified by flash chromatography using *n*-

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hexane−EtOAc (3.5:1) as the eluent to afford a colorless syrup **21** (1.6 g, 80%).

$[\alpha]_D^{25}$ − 54 (*c*0.8, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$). δ 7.46−7.16 (m, 14H, Ar*H*), 5.07(d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.85 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.84 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.77 (s, 1H, H-1), 4.72 (d, 1H, 11.5 Hz, CH_2Ar), 4.08 (d, 1H, $J_{2,3}$ 3.0 Hz, H-2), 3.70 (dd, 1H, $J_{2,3}$3.0 Hz, $J_{4,3}$ 9.0 Hz, H-3), 3.44 (t, 1H, $J_{5,4}$ 9.0 Hz, $J_{3,4}$ 9.0 Hz, H-4), 3.36 (m, 1H, H-5), 2.38 (s, 3H, $SC_6H_4CH_3$), 2.21 (bs, 1H, O*H*), 1.45 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$). δ 138.2, 137.9, 137.4, 131.4, 131.3, 129.6, 128.9, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8 (Ar*C*), 87.9 (C-1), 81.5 (C-4), 80.9 (C-2), 73.2 (*C*H_2Ar), 75.8 (C-5), 75.5 (C-3), 75.0 (*C*H_2Ar), 21.0 ($SC_6H_4CH_3$), 17.9 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{27}H_{30}O_4SNa$ (M + Na)$^+$: 473.1757; found: 473.1753.

p-Tolyl 2,4-Di-O-benzyl-3-O-picoloyl-1-thio-α-L-rhamnopyranoside (7). To a stirred solution of **21** (1.5 g, 3.34 mmol) in dichloroethane (DCE) solvent (30 mL), EDC-HCl (1.9 g. 9.9 mmol) and DMAP (165 mg, 1.34 mmol) were added at 25 °C. After 3 min, 2-picolinic acid (1.2 g, 9.9 mmol) was added and the mixture turned canary yellow in color; it was stirred at 25 °C for 30 min when TLC (*n*-hexane−EtOAc; 2:1, R_f = 0.35) showed complete conversion of the starting compound, to a slower moving spot. The mixture was diluted with CH_2Cl_2 (20 mL) and washed with brine (40 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated *in vacuo*, and the crude material thus obtained was purified by flash chromatography using *n*-hexane−EtOAc (2:1) as the eluent to afford the pure white sticky compound **7** (1.7 g, 93%).

$[\alpha]_D^{25}$ − 32 (*c*1.0, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$). δ 8.77−7.10 (m, 18H, Ar*H*), 5.22 (dd, 1H, $J_{4,3}$ 9.0 Hz, $J_{3,2}$ 3.0 Hz, H-3), 4.86 (s, 1H, H-1), 4.82 (d, 3H, J_{AB} 14.0 Hz, CH_2Ar), 4.68 (d, 1H, J_{AB} 12.5 Hz, CH_2Ar), 4.38 (d, 1H, $J_{2,3}$ 3.0 Hz, H-2), 3.92 (t, 1H, $J_{5,4}$ 9.5 Hz, $J_{3,4}$ 9.0 Hz, H-4), 3.47 (m, 1H, H-5), 2.31 (s, 3H, $SC_6H_4CH_3$), 1.42 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$). δ 164.2 (C_5H_4NCO), 149.9, 147.3, 137.8, 137.6, 137.5, 136.7, 131.8, 130.9, 129.6, 128.3, 128.1, 127.9, 127.8, 127.5, 127.4, 126.9, 125.0 (Ar*C*), 87.8 (C-1), 78.2 (C-3), 78.3 (C-2), 77.9 (C-4), 76.0 (C-5), 75.7 (*C*H_2Ar), 75.1 (*C*H_2Ar), 20.9 ($SC_6H_4CH_3$), 18.1 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{33}H_{33}NO_5SNa$ (M + Na)$^+$: 578.1972; found: 578.1978.

p-Tolyl 2-O-Acetyl-4-O-benzyl-3-O-chloroacetyl-α-L-rhamnopyranoside (6). To a solution of the known compound **10**[21] (2.2 g, 5.5 mmol) in dry CH_2Cl_2 (10 mL), pyridine (1 mL, 13.6 mmol) was added followed by chloroacetic anhydride (1.4 g, 8.2 mmol) in an ice bath, and the solution was stirred at for 30 min when TLC (*n*-hexane−EtOAc, 3:1, R_f = 0.6) showed complete conversion of the starting material to a faster running spot. The reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed successively with 1 N HCl (25 mL) and then with $NaHCO_3$ (25 mL) and brine (25 mL). The organic layer was separated, dried by Na_2SO_4, and filtered. The solvent was evaporated at 40 °C *in vacuo*, and the residue was purified by column chromatography using *n*-hexane−EtOAc = 5:1 as an eluent to afford the pure (2.5 g, 95%) compound as sticky syrup **6**.

$[\alpha]_D^{25}$ − 16 (*c*0.9, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$). δ 7.35−7.09 (m, 9H, Ar*H*), 5.5 (d, 1H, $J_{2,3}$ 3.0 Hz, H-2), 5.35 (dd, 1H, $J_{2,3}$ 3.0 Hz, $J_{4,3}$ 9.0 Hz, H-3), 5.28 (s, 1H, H-1), 4.72 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.68 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.32 (m, 1H, H-5), 3.92 (d, 1H, J_{AB} 10.0 Hz, CH_2Cl), 3.88 (d, 1H, J_{AB} 10.0 Hz, CH_2Cl), 2.31 (s, 3H, $SC_6H_4CH_3$), 2.21 (s, 3H,CH_3CO), 1.35 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$). δ 170.0 (CH_3CO), 166.2 ($ClCH_2CO$), 138.2, 137.8, 132.6, 129.9, 129.4, 128.5, 127.9, 127.7 (Ar*C*), 85.9 (C-1), 78.7 (C-4), 75.2 (*C*H_2Ar), 73.7 (C-3), 71.3 (C-2), 69.1 (C-5), 40.52 ($ClCH_2CO$), 21.1 ($SC_6H_4CH_3$), 20.9 (CH_3CO), 17.8 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{24}H_{27}ClO_6SNa$ (M + Na)$^+$: 501.1109; found: 501.1102.

2-Azidoethyl 2,4-Di-O-benzyl-3-O-picoloyl-α/β-L-rhamnopyranosyl-(1 → 4)-2,3-di-O-benzyl-β-L-rhamnopyranoside (22α/β). Glycosyl acceptor **8** (635 mg, 1.54 mmol), glycosyl donor **7** (1.04 g, 1.84 mmol), and activated MS 4 Å (2.0 g) in dry DCE (20 mL) were stirred under a nitrogen atmosphere for 1 h at 25 °C. Then, NIS (500 mg, 2.2 mmol) was added and stirred under a nitrogen atmosphere for 5 min. After that, the mixture was cooled to −30 °C. After 10 min, the mixture (32 μL, 0.367 mmol) was added at −30 °C TLC, and then, the temperature was slowly raised up to 0 °C. TLC (*n*-hexane−EtOAc, 2:1 double run R_f = 0.5) showed complete consumption of the acceptor. The MS was filtered out using a pad of Celite, and the filtrate was washed successively with aq $Na_2S_2O_3$ (2 × 30 mL), saturated $NaHCO_3$ (2 × 30 mL), and H_2O (30 mL). The organic layer was collected, dried with Na_2SO_4, and filtered. The solvent was evaporated *in vacuo*, and the residue was purified by flash chromatography using *n*-hexane−EtOAc (2.2:1) as the eluent to isolate compound **22** as an anomeric mixture. However, a small amount of **22β** was obtained in the pure form as a white amorphous mass.

^{1}H NMR (500 MHz, $CDCl_3$). δ 8.78−7.05 (m, 24H, Ar*H*), 5.07 (dd, 1H, $J_{2',3'}$ 3.0 Hz, $J_{4',3'}$ 10.0 Hz, H-3′), 4.92 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.86 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.83 (s, 1H, H-1), 4.76 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.74 (d, 1H, J_{AB} 10.0 Hz, CH_2Ar), 4.67 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.65 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.61 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.52 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.44 (s, 1H, H-1′) 4.12−4.09 (m, 2H, H-2′, OCH_2), 3.94 (d, 1H, $J_{2,3}$ 2.5 Hz, H-2), 3.85 (t, 1H, $J_{5,4}$ 10.0 Hz, $J_{3,4}$ 10.0 Hz, H-4), 3.77 (t, 1H, $J_{5',4'}$ 10.0 Hz, $J_{3',4'}$ 10.0 Hz, H-4′), 3.64−3.59 (m, 1H, OCH_2), 3.57−3.50 (m, 2H, NCH_2, H-3), 3.40 (m, 1H, H-5), 3.33−3.30 (m, 1H, NCH_2) 3.32 (m, 1H, H-5′), 1.36 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6), 1.21 (d, 3H, $J_{5',6'}$ 6.0 Hz, H-6′).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$). δ 164.2 (C_5H_4NCO), 150.0, 147.6, 138.7, 138.6, 138.4, 138.1, 136.8, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.3, 127.3, 127.1, 126.8, 125.1 (Ar*C*), 101.4 (C-1), 100.7 (C-1′), 80.6 (C-4), 79.9 (C-3), 78.4 (C-4′), 77.3 (C-3′), 76.7 (C-2′), 74.9 (CH$_2$Ar, C-2), 74.7 (*C*H_2Ar), 74.5 (*C*H_2Ar), 71.6 (C-5), 71.5 (C-5′), 71.4 (*C*H_2Ar), 68.4 (O*C*H_2), 50.83 (N*C*H_2), 18.3 (C-6), 17.9 (C-6′).

^{1}H coupled ^{13}C spectra revealed J_{CH} = 152.5 and $J_{C'H'}$ = 157.5 Hz for the two anomeric carbon atoms.

HR-ESI-MS (*m*/*z*) calcd for $C_{48}H_{53}O_{10}N_4$ (M + H)$^+$: 845.3756; found: 845.3762.

2-Azidoethyl 2,4-Di-O-benzyl-α/β-L-rhamnopyranosyl-(1 → 4)-2,3-di-O-benzyl-β-L-rhamnopy-ranoside (5α and 5β). To a solution of the compound **22α/β** (850 mg, 1.0 mmol) in MeOH (20 mL), NaOMe in MeOH (2 mL, 0.5 M) was added, and the solution was stirred for 2 h at room temperature. TLC (*n*-hexane−EtOAc; 2:1, R_f = 0.6) showed complete conversion of the starting material to a faster moving spot, and the reaction mixture was quenched with DOWEX 50 W resin. The resin was filtered, and the filtrate was evaporated to dryness under reduced pressure to give the crude residue, which was diluted with CH_2Cl_2 (10 mL) and washed with H_2O (2 × 30 mL) and brine solution (20 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated *in vacuo*. The crude material thus obtained was purified by flash chromatography using *n*-hexane−EtOAc (2.5:1) as the eluent to afford pure compounds **5β** (652 mg) and **5α** (55 mg) as white gummy masses (overall yield 69%, **α**/**β** = 1:12).

5β.

$[\alpha]_D^{25}$ + 37 (*c*0.7, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.41−7.21 (m, 20H, Ar*H*), 5.04 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.93 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.81 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.76 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.66 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.64 (s, 1H, H-1), 4.63 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.58 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.50 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.43 (s, 1H, H-1′), 4.11−4.06 (m, 1H, OCH_2), 3.93 (d,

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1H, $J_{2',3'}$ 3.0 Hz, H-2′), 3.85 (t, 1H, $J_{5,4}$ 10.0 Hz, $J_{3,4}$ 10.0 Hz, H-4), 3.78 (d, 1H, $J_{2,3}$ 3.0 Hz, H-2), 3.62−3.58 (m, 1H, OCH_2), 3.57−3.47 (m, 3H, NCH_2, H-3, H-3′), 3.43 (m, 1H, H-5), 3.30−3.26 (m, 1H, NCH_2), 3.21 (t, 1H, $J_{5',4'}$ 10.0 Hz, $J_{3',4'}$ 10.0 Hz, H-4′), 3.10 (m, 1H, H-5′), 2.34 (d, 1H, $J_{3',OH}$ 9.0 Hz, O*H*) 1.40 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6), 1.21 (d, 3H, $J_{5',6'}$ 6.0 Hz, H-6′).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$). δ 138.6, 138.5, 138.4, 138.3, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.2, 127.0 (Ar*C*), 101.3 (C-1′), 101.1 (C-1), 81.8 (C-4′), 80.5 (C-4), 79.5 (C-3′), 79.1 (C-2), 75.1 (CH_2Ar), 74.8 (CH_2Ar), 74.7 (C-2′), 74.4 (CH_2Ar), 73.9 (C-3), 71.6 (C-5), 71.4 (CH_2Ar), 71.2 (C-5′), 68.2 (OCH_2), 50.7 (NCH_2), 18.2 (C-6), 17.9 (C-6′).

^1H coupled ^{13}C spectra revealed J_{CH} = 152.5 and $J_{C'H'}$ = 153.8 Hz for the two anomeric carbon atoms.

HR-ESI-MS (*m*/*z*) calcd for $C_{42}H_{53}O_9N_4Na$ $(M + NH_4)^+$: 757.3807; found: 757.3795.

5α.

$[\alpha]_D^{25}$ − 26 (*c*0.8, $CHCl_3$)

^1H NMR (500 MHz, $CDCl_3$). δ 7.43−7.06 (m, 20H, Ar*H*), 5.27 (s, 1H, H-1′), 5.00 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.86 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.74 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.61 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.47 (d, 1H, J_{AB} 10.0 Hz, CH_2Ar), 4.46 (s, 1H, H-1), 4.22 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.20 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.50 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.13−4.11 (m, 1H, OCH_2), 4.02 (d, 1H, $J_{2,3}$ 2.0 Hz, H-2), 3.82−3.76 (m, 4H, H-4, H-5′, H-3′, CH_2Ar), 3.65−3.62 (m, 2H, H-2′, OCH_2), 3.58−3.53 (m, 1H, NCH_2), 3.41 (dd, 1H, $J_{2,3}$ 2.0 Hz, $J_{3,4}$ 10.0 Hz, H-3), 3.33−3.29 (m, 3H, H-5, H-4′, NCH_2), 2.34 (bs, 1H, −OH), 1.38 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6), 1.28 (d, 3H, $J_{5',6'}$ 6.0 Hz, H-6′).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$). δ 138.6, 138.5, 137.9, 137.7, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 127.5, 127.4, 127.3 (Ar*C*), 101.5 (C-1), 98.7 (C-1′), 82.5 (C-3), 82.0 (C-4′), 79.3 (C-2′), 78.9 (C-3′), 75.1 (CH_2Ar), 74.4 (CH_2Ar), 73.6 (C-2), 71.9 (CH_2Ar), 71.5 (C-5′), 71.4 (C-5), 70.7 (CH_2Ar), 68.4 (OCH_2), 67.8 (C-4), 50.8 (NCH_2), 18.2 (C-6), 17.7 (C-6′).

^1H coupled ^{13}C spectra revealed J_{CH} = 152.5 and $J_{C'H'}$ = 165.6 Hz for the two anomeric carbon atoms.

HR-ESI-MS (*m*/*z*) calcd for $C_{42}H_{49}O_9N_3Na$ $(M + Na)^+$: 762.3361; found: 762.3346.

*2-Azido Ethyl 2-O-Acetyl-4-O-benzyl-3-O-chloroacetyl-α-L-rhamnopyranosyl-(1 → 3)-2,4-di-O-benzyl-β-L-rhamnopyranosyl-(1 → 4)-2,3-di-O-benzyl-β-L-rhamnopyranoside (**23**).* A mixture of disaccharide acceptor ***5β*** (220 mg, 0.30 mmol), donor **6** (184 mg, 0.37 mmol), and activated MS 4 Å (1.0 g) in dry DCE solvent (10 mL) was stirred under nitrogen for 5 min at −5 °C. Then, NIS (104 mg, 0.46 mmol) was added followed by TMSOTf (13 μL, 0.08 mmol) and the mixture was stirred at −5 °C for another 15 min when TLC (*n*-hexane−EtOAc; 2:1, R_f = 0.38) showed complete consumption of the acceptor. The reaction was quenched by Et_3N and filtered through a pad of Celite, and the filtrate was washed successively with aq $Na_2S_2O_3$ (2 × 20 mL), saturated $NaHCO_3$ (2 × 20 mL), and H_2O (20 mL). The organic layer was collected, dried with Na_2SO_4, and filtered. The solvent was evaporated *in vacuo*, and the residue was purified by flash chromatography using *n*-hexane−EtOAc (2:1) as the eluent to afford the pure white sticky trisaccharide compound **23** (247 mg, 76%) as a white gummy mass.

$[\alpha]_D^{25}$ − 15 (*c*0.9, $CHCl_3$)

^1H NMR (500 MHz, $CDCl_3$). δ 7.43−7.17 (m, 25H, Ar*H*), 5.35−4.25 (m, 2H, H-2″, H-3″), 5.02 (s, 1H, H-1″), 4.92 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.90 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.79 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.74 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.68 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.66−4.61 (m, 3H, H-1, CH_2Ar), 4.61−4.56 (m, 2H, CH_2Ar), 4.47 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.42 (s, 1H, H-1′), 4.07 (m, 1H, OCH_2), 3.93 (d, 1H, $J_{2,3}$ 2.5 Hz, H-2), 3.90−3.76 (m, 5H, $ClCH_2CO$, H-5″, H-4, H-3′), 3.61−3.56 (m, 3H, OCH_2, H-4″, H-2′), 3.51−3.47 (m, 3H, NCH_2, H-4′, H-3), 3.41 (m, 1H, H-5), 3.27 (m, 1H, NCH_2), 3.06 (m, 1H, H-5′), 2.00 (s, 3H, CH_3CO), 1.35 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6), 1.25 (d, 3H, $J_{5'',6''}$ 6.0 Hz, H-6″), 1.15 (d, 3H, $J_{5',6'}$ 6.0 Hz, H-6′).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$). δ 169.8 (CH_3CO), 166.2 ($ClCH_2CO$), 138.7, 138.6, 138.5, 137.9, 128.4, 128.3, 128.2, 128.2, 128.0, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.2 (Ar*C*), 101.5 (C-1), 101.2 (C-1′), 99.2 (C-1″), 80.5 (C-3′), 80.4 (H-4′), 80.3 (H-4″), 79.8 (C-2′), 78.9 (C-4), 78.3 (C-3), 75.2 (CH_2Ar), 74.9 (CH_2Ar), 74.8 (CH_2Ar), 74.7 (C-2), 74.5 (CH_2Ar), 73.6 (C-3″), 71.8 (C-5′), 71.7 (C-5), 71.4 (CH_2Ar), 69.8 (C-2″), 68.4 (C-5″), 68.3 (OCH_2), 50.8 (NCH_2), 40.6 ($ClCH_2CO$), 20.7 (CH_3CO), 18.3 (C-6), 17.9 (C-6″), 17.8 (C-6′).

^1H coupled ^{13}C spectra revealed J_{CH} = 155.0 Hz, $J_{C'H'}$ = 153.8 Hz, and $J_{C''H''}$ = 174.5 Hz for the three anomeric carbon atoms.

HR-ESI-MS (*m*/*z*) calcd for $C_{59}H_{68}ClO_{15}N_3Na$ $(M + Na)^+$: 1116.4231; found: 1116.4231.

*2-Azido Ethyl 2-O-Acetyl-4-O-benzyl-α-L-rhamnopyranosyl-(1 → 3)-2,4-di-O-benzyl-β-L-rhamnopyranosyl-(1 → 4)-2,3-di-O-benzyl-β-L-rhamnopyranoside (**3**).* A mixture of trisaccharide **23** (210 mg, 0.19 mmol), thiourea (75 mg, 0.96 mmol), and 2,4,6-collidine (0.12 mL, 0.86 mmol) in 20 mL of CH_2Cl_2/MeOH (3:2 v/v) was allowed to stir at 40 °C in an oil bath for 12 h when TLC (*n*-hexane−EtOAc; 1.5:1, R_f = 0.56) showed complete conversion of the starting material to a slower moving spot. The reaction mixture was dried *in vacuo* and dissolved in CH_2Cl_2 (15 mL). The organic layer was washed with ice-cold dilute HCl (30 mL, 0.25 N) and H_2O (30 mL). The organic layer was collected, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude product thus obtained was further purified by flash chromatography using *n*-hexane−EtOAc (2:1) as the eluent to afford pure trisaccharide acceptor **3** (180 mg, 91%) as a white amorphous mass.

$[\alpha]_D^{25}$ − 21 (*c*0.7, $CHCl_3$)

JEOL: ^1H NMR (400 MHz, $CDCl_3$). δ 7.44−7.22 (m, 25H, Ar*H*), 5.23 (dd, 1H, $J_{1'',2''}$ 1.0 Hz, $J_{2'',3''}$ 3.0 Hz, H-2″), 5.07 (d, 1H $J_{1'',2''}$ 1.0 Hz, H-1″), 4.96 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.94 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.82−4.75 (m, 4H, H-1, CH_2Ar), 4.69 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.65 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.62 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.60 (d, 1H, J_{AB} 11.0 Hz, CH_2Ar), 4.50 (d, 1H, J_{AB} 12.0 Hz, CH_2Ar), 4.45 (s, 1H, H-1′), 4.12 (m, 1H, OCH_2), 4.04 (dd, 1H, $J_{3'',4''}$ 9.0 Hz, $J_{2'',3''}$ 3.0 Hz, H-3″), 3.97 (d, 1H, $J_{2,3}$ 3.0 Hz, H-2), 3.81−3.78 (m, 3H, H-5″, H-3′, H-4), 3.66−3.50 (m, 5H, OCH_2, H-3, H-2′, H-4′, NCH_2), 3.44 (m, 1H, H-5), 3.37−3.30 (m, 2H, NCH_2, H-4″), 3.10 (m, 1H, H-5′), 2.01 (s, 3H, CH_3CO), 1.31 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6), 1.29 (d, 3H, $J_{5'',6''}$ 6.0 Hz, H-6″), 1.17 (d, 3H, $J_{5',6'}$ 6.0 Hz, H-6′).

$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$). δ 170.6 (CH_3CO), 138.8, 138.7, 138.5, 138.3, 138.1, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 127.1 (Ar*C*), 101.5 (C-1′), 101.1 (C-1), 99.2 (C-1″), 81.3 (C-4″), 80.6 (C-3), 80.4 (C-2′), 80.0 (C-4′), 79.8 (C-3′), 79.2 (CH_2Ar), 75.2 (CH_2Ar), 74.9 (CH_2Ar), 74.8 (CH_2Ar), 74.5 (C-2″), 72.6 (C-3″), 71.8 (C-2), 71.6 (CH_2Ar), 71.7 (C-4), 71.4 (C-5″), 70.2 (C-5), 68.4 (OCH_2), 68.2 (C-5′), 50.9 (NCH_2), 20.9 (CH_3CO), 18.2 (C-6), 18.0 (C-6″), 17.9 (C-6′).

HR-ESI-MS (*m*/*z*) calcd for $C_{57}H_{67}O_{14}N_3Na$ $(M + Na)^+$: 1040.4515; found: 1040.4506.

*p-Tolyl 2,3,6-Tri-O-benzyl-4-O-picoloyl-α-D-glucopyranosyl-(1 → 3)-2-O-acetyl-4-O-benzyl-1-thio-α-L-rhamnopyranoside (**25**).* A mixture of known reported trichloroacetimidate donor **24**[14] (460 mg, 0.656 mmol) with known acceptor **10**[21] (220 mg, 0.547 mmol) and activated MS 4 Å (1.0 g) in anhydrous DCE solvent (10 mL) was stirred under N_2 for 15 min. After that, the mixture was cooled to −30 °C. After 10 min, TfOH (15 μL, 0.14 mmol) was added at −30 °C TLC, and then, the temperature was slowly raised up to 0 °C. TLC (*n*-hexane−EtOAc, 2:1 R_f = 0.5 after double run) Then, the reaction was quenched by adding Et_3N and immediately filtered over a bed of Celite. The solvents were evaporated *in vacuo*, and the crude product was purified by flash chromatography using *n*-hexane−EtOAc (2:1) as the eluent to afford the pure white yellowish amorphous disaccharide donor **25** (190 mg, 38%), the unreacted acceptor (100 mg), and the hemiacetal of the donor.

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$[\alpha]_D^{25}$ + 27 (*c*0.8, $CHCl_3$)

^{1}H NMR (500 MHz, CDCl$_3$). δ 8.76−7.07 (m, 28H, Ar*H*), 5.65 (bs, 1H, H-2), 3.48 (t, 1H, $J_{5',4'}$ 9.0 Hz, $J_{3',4'}$ 9.0 Hz, H-4′), 5.37 (s, 1H, H-1), 5.22 (d, 1H, $J_{1',2'}$ 3.0 Hz, H-1′), 5.08 (d, 1H, J_{AB}11.0 Hz, C*H*$_2$Ar), 4.69−4.64 (m, 5H, C*H*$_2$Ar), 4.45 (d, 1H, J_{AB} 11.0 Hz, C*H*$_2$Ar), 4.43 (d, 1H, J_{AB} 11.0 Hz, C*H*$_2$Ar), 4.28−4.20 (m, 3H, H-5, H-3, H-5′), 4.15 (t, 1H, $J_{3',4'}$ 9.0 Hz, $J_{3',2'}$ 9.0 Hz, H-3′), 4.15 (dd, 1H, $J_{1',2'}$ 3.0 Hz, $J_{3',2'}$ 9.0 Hz, H-2′), 3.63 (t, 1H, $J_{3,4}$ 9.0 Hz, $J_{4,5}$ 9.0 Hz, H-4), 3.49 (dd, 1H, $J_{5'6a'}$ 3.0 Hz, $J_{6a'6b'}$ 11.0 Hz, H-6a′), 3.41 (dd, 1H, $J_{5'6b'}$ 3.0 Hz, $J_{6a'6b'}$ 11.0 Hz, H-6b′), 2.35 (s, 3H, $SC_6H_4CH_3$), 1.98 (s, 3H, CH_3CO), 1.37 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$). δ 170.3 ($COCH_3$), 163.6 (COAr), 149.8, 147.7, 138.2, 138.1, 137.9, 137.8, 136.6, 132.3, 130.1, 129.8, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.3, 127.2, 126.6, 125.1, 93.3 (C-1′), 86.3 (C-1), 79.9 (C-4), 79.1 (C-2′), 79.0 (C-3′), 75.6 (*C*H$_2$Ar), 74.9 (*C*H$_2$Ar), 73.3 (*C*H$_2$Ar), 73.2 (C-3), 73.1 (CH$_2$Ar), 71.7 (C-4′), 69.7 (C-2), 69.3 (C-5′), 68.8 (C-5), 68.5 (C-6′), 21.1 ($SC_6H_4CH_3$), 20.8 (CH_3CO), 17.8 (C-6).

HR-ESI-MS (*m*/*z*) calcd for $C_{55}H_{57}NO_{11}SNa$ (M + Na)$^+$: 962.3545; found: 962.3546.

p-Tolyl 6-O-Acetyl-2,3,4-tri-O-benzyl-α-D-glucopyranosyl-(1 → 3)-2-O-acetyl-4-O-benzyl-1-thio-α-L-rhamnopyranoside (4). A mixture of known trichloroacetimidate donor **9**[25] (666 mg, 1.05 mmol) with acceptor **10**[21] (337 mg, 0.84 mmol) and activated MS 4 Å (1.0 g) in anhydrous DCE solvent (10 mL) was stirred under N_2 for 5 min. The reaction mixture was cooled to −40 °C; TMSOTf (40 μL, 0.21 mmol) was added to the reaction mixture, and it was allowed to stir at the same temperature for 4 h when TLC (*n*-hexane−EtOAc; 4:1, R_f = 0.5 double run) showed complete consumption of the donor. Then, the reaction was quenched by adding Et_3N and immediately filtered over a bed of Celite. The solvents were evaporated *in vacuo*, and the crude product was purified by flash chromatography using *n*-hexane−EtOAc (5:1) as the eluent to afford the pure white sticky disaccharide donor **4** (470 mg, 65%), the unreacted acceptor (75 mg), and the hemiacetal of the donor.

$[\alpha]_D^{25}$ + 32 (*c*0.8, $CHCl_3$)

^{1}H NMR (500 MHz, CDCl$_3$). δ 7.27−7.09 (m, 24H, Ar*H*), 5.59 (bs, 1H, H-2), 5.32 (s, 1H, H-1), 5.14 (d, 1H, $J_{1',2'}$ 3.0 Hz, H-1′), 5.00 (d, 1H, J_{AB} 11.0 Hz C*H*$_2$Ar), 4.94 (d, 1H, J_{AB} 11.0 Hz, C*H*$_2$Ar), 4.86−4.82 (m, 2H, H-6a′, C*H*$_2$Ar), 4.71−4.61 (m, 3H, H-6b′, C*H*$_2$Ar), 4.51 (d, 1H, J_{AB} 11.0 Hz, C*H*$_2$Ar), 4.23 (m, 1H, H-5), 4.15−4.05 (m, 5H, H-3, H-3′, H-5′, C*H*$_2$Ar), 3.63−3.57 (m, 2H, H-4, H-2′), 3.50 (t, 1H, $J_{5'4'}$ 9.0 Hz, $J_{3'4'}$ 9.0 Hz, H-4′), 2.31 (s, 3H, $SC_6H_4CH_3$), 2.02 (s, 3H, CH_3CO), 1.92 (s, 3H, CH_3CO), 1.36 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$). δ 170.7 ($COCH_3$), 170.3 ($COCH_3$), 138.4, 138.5, 138.0, 137.9, 137.4, 132.2, 129.9, 129.8, 128.7, 128.4, 128.3, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6 (ArC), 92.3 (C-1′), 86.3 (C-1), 81.9 (C-3), 79.7 (C-2′), 79.2 (C-4), 77.6 (C-4′), 76.1 (CH$_2$Ar), 75.6 (CH$_2$Ar), 74.9 (CH$_2$Ar), 72.8 (C-6′), 72.5 (CH$_2$Ar, C-5′), 69.2 (C-5), 69.1 (C-3′), 68.7 (C-2), 62.9 (CH$_2$Ar), 21.1 ($SC_6H_4CH_3$), 20.8 (CH_3CO), 20.7 (CH_3CO), 17.8 (C-6).

^{1}H coupled ^{13}C spectra revealed $J_{C'H'}$ = 167.5 Hz.

HR-ESI-MS (*m*/*z*) calcd for $C_{51}H_{56}O_{11}SNa$ (M + Na)$^+$: 899.3436; found: 899.3427.

2-Azido Ethyl 6-O-Acetyl-2,3,4-tri-O-benzyl-α-D-glucopyranosyl-(1 → 3)-2-O-acetyl-4-O-benzyl-α-L-rhamnopyranosyl-(1 → 3)-2-O-acetyl-4-O-benzyl-α-L-rhamnopyranosyl-(1 → 3)-2,4-di-O-benzyl-β-L-rhamnopyranosyl-(1 → 4)-2,3-di-O-benzyl-β-L-rhamnopyranoside (2). A mixture of trisaccharide acceptor **3** (81 mg, 0.08 mmol), disaccharide donor **4** (100 mg, 0.11 mmol), and activated MS 4 Å (1.0 g) in dry DCE solvent (10 mL) was stirred under nitrogen for 5 min. Then, NIS (33 mg, 0.14 mmol) was added and it was set at −5 °C. After that, TMSOTf (4 μL, 0.022 mmol) and the mixture were stirred at −5 °C for another 15 min when TLC (*n*-hexane−EtOAc, 1.5:1, double run, R_f = 0.5) showed complete consumption of the acceptor. The reaction mixture was filtered through a pad of Celite, and the filtrate was washed successively with aq $Na_2S_2O_3$ (2 × 20 mL), saturated $NaHCO_3$ (2 × 20 mL), and brine solution (20 mL). The organic layer was collected, dried with Na_2SO_4, and filtered. The solvent was evaporated *in vacuo*, and the residue was purified by flash chromatography using *n*-hexane−EtOAc (1.8:1) as the eluent to afford pure pentasaccharide **2** (115 mg, 82%) as a white amorphous mass.

$[\alpha]_D^{25}$ + 52 (*c*0.8, $CHCl_3$)

^{1}H NMR (500 MHz, CDCl$_3$). δ 7.39−7.07 (m, 45H, Ar*H*), 5.38 (bs, 1H, H-2‴), 5.26 (bs, 1H, H-2″), 5.04 (s, 1H, H-1″), 5.03 (d, 1H, $J_{1''',2'''}$ 3.0 Hz, H-1‴′), 4.98 (d, 1H, J_{AB} 11.0 Hz, C*H*$_2$Ar), 4.94 (d, 1H, J_{AB} 11.0 Hz, C*H*$_2$Ar), 5.95 (s, 1H, H-1‴), 4.93 (d, 1H, J_{AB} 11.0 Hz, CH$_2$Ar), 4.88 (d, 1H, J_{AB} 11.0 Hz, C*H*$_2$Ar), 4.83−4.79 (m, 4H, H-6a‴′, C*H*$_2$Ar), 4.76 (d, 1H, J_{AB} 11.0 Hz, C*H*$_2$Ar), 4.70 (d, 1H, J_{AB} 2.0 Hz, C*H*$_2$Ar), 4.66 (d, 1H, J_{AB} 8.0 Hz, C*H*$_2$Ar), 4.61 (d, 2H, J_{AB} 10.0 Hz, C*H*$_2$Ar), 4.59 (s, 1H, H-1), 4.58−4.49 (m, 4H, H-6b‴′, C*H*$_2$Ar), 4.47 (d, 1H, J_{AB} 12.0 Hz, C*H*$_2$Ar), 4.41 (s, 1H, H-1′), 4.20 (d, 1H, J_{AB} 12.0 Hz, C*H*$_2$Ar), 4.13−4.02 (m, 7H, C*H*$_2$Ar, H-3‴, H-3′, H-4‴, H-3‴′, H-5‴′, H-3″), 3.93 (d, 1H, $J_{1,2}$ 2.5 Hz, H-2), 3.79−3.73 (m, 5H, OC*H*$_2$, H-4, H-2′, H-5″, H-5‴), 3.62−3.59 (m, 1H, OC*H*$_2$), 3.58−3.45 (m, 5H, NC*H*$_2$, H-2‴′, H-4′, H-3, H-4″), 3.43−3.33 (m, 2H, H-5, H-4‴′), 3.31−3.27 (m, 1H, NC*H*$_2$) 3.05 (m, 1H, H-5′), 2.06 (s, 3H, C*H*$_3$CO), 1.93 (s, 3H, C*H*$_3$CO), 1.87 (s, 3H, C*H*$_3$CO), 1.34 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6), 1.23 (d, 3H, $J_{5'',6''}$ 6.0 Hz, H-6″), 1.22 (d, 3H, $J_{5''',6'''}$ 6.5 Hz, H-6‴), 1.10 (d, 3H, $J_{5',6'}$ 6.0 Hz, H-6′).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$). δ 170.5 (CH_3CO), 170.1 (CH_3CO), 169.8 (CH_3CO), 138.7, 138.6, 138.5, 138.2, 138.1, 137.9, 137.7,128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.3, 127.1 (ArC), 101.4 (C-1′), 101.2 (C-1), 99.3 (C-1‴), 98.9 (C-1″), 92.1 (C-1‴′), 82.0 (C-3‴), 80.5 (C-4), 80.3 (C-2‴′, C-4‴′), 79.8 (C-3), 79.3 (C-4″), 79.2 (C-4′), 79.1 (C-4‴), 77.2 (C-3″), 75.8 (CH$_2$Ar), 75.6 (CH$_2$Ar), 75.3 (CH$_2$Ar), 74.9 (C-2, CH$_2$Ar), 74.7 (CH$_2$Ar, C-6‴′), 74.5 (C-5‴′), 72.8 (CH$_2$Ar, C-3′), 71.9 (C-2′), 71.7 (CH$_2$Ar), 71.6 (H-3‴′), 71.4 (C-5, C-5′), 71.3 (C-2″, CH$_2$Ar), 69.0 (C-5‴), 68.5 (C-5″), 68.4 (OCH$_2$), 67.5 (C-2‴), 62.6 (CH$_2$Ar), 50.8 (NCH$_2$), 20.9 (CH_3CO), 20.8 (CH_3CO), 20.7 (CH_3CO), 18.3 (C-6), 17.9 (C-6″), 17.9 (C-6‴), 17.8 (C-6′).

HR-ESI-MS (*m*/*z*) calcd for $C_{101}H_{115}N_3O_{25}Na$ (M + Na)$^+$: 1792.7717; found: 1792.7710.

2-Azido Ethyl 2,3,4-Tri-O-benzyl-α-D-glucopyranosyl-(1 → 3)-4-O-benzyl-α-L-rhamnopyranosyl-(1→3)-4-O-benzyl-α-L-rhamnopyranosyl-(1 → 3)-2,4-di-O-benzyl-β-L-rhamnopyranosyl-(1 → 4)-2,3-di-O-benzyl-β-L-rhamnopyranoside (26). To a solution of the protected pentasaccharide **2** (115 mg, 0.07 mmol) in MeOH (20 mL), NaOMe in MeOH (0.5 M, 2 mL) was added, and the solution was stirred at room temperature for 4 h when TLC (*n*-hexane−EtOAc; 1:2, R_f = 0.56) showed complete conversion of the starting material to a slower moving spot. Then, the solution was neutralized with Dowex 50 W X8 (H^+) resin, filtered, and evaporated *in vaccuo*. The residue thus obtained was purified by column chromatography using *n*-hexane−EtOAc (1:1→ 1:2→1:5) as the eluent to afford pure compound **26** (104 mg, 98%) as a white foam.

$[\alpha]_D^{25}$ + 81 (*c*0.6, $CHCl_3$)

^{1}H NMR (500 MHz, CDCl$_3$). δ 7.40−7.15 (m, 45H, Ar*H*), 5.17 (s, 1H, H-1″), 5.06 (s, 1H, H-1‴), 4.98−4.81 (m, 6H, C*H*$_2$Ar, H-1‴′), 4.86−4.64 (m, 7H, C*H*$_2$Ar), 4.65 (s, 1H, H-1), 4.64−4.53 (m, 6H, H-2‴′), 4.48 (d, 1H, J_{AB} 11.0 Hz, C*H*$_2$Ar), 4.41 (s, 1H, H-1′), 4.09−4.01 (m, 2H, OC*H*$_2$, H-4″), 4.00−3.90 (m, 6H, H-3′, H-6a‴′, H-3‴, H-5″, 6b‴′, H-3‴′), 3.81−3.72 (m, 5H, H-2, H-5‴, H-2‴, H-4‴′, H-2″), 3.62−3.52 (m, 2H, H-4, H-4′), 3.53−3.43 (m, 7H, OC*H*$_2$, H-5, NC*H*$_2$, H-4‴, H-3″, H-5‴′, H-2′, H-3), 3.40−3.27 (m, 2H, NC*H*$_2$, H−), 3.07 (m, 1H, H-5′), 2.5−1.9 (bs, OH X 3), 1.35 (d, 3H, $J_{5,6}$ 6.0 Hz, H-6), 1.24 (d, 3H, $J_{5'',6''}$ 6.0 Hz, H-6″), 1.22 (d, 3H, $J_{5''',6'''}$ 6.5 Hz, H-6‴), 1.15 (d, 3H, $J_{5',6'}$ 6.0 Hz, H-6′).

^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$). δ 138.8, 138.7, 138.5, 138.4, 138.3,138.1,137.9, 137.5, 137.3, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.1 (ArC), 101.4 (C-1″), 101.3 (C-1′), 101.1 (C-1), 100.7 (C-1‴),

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93.7 (C-1‴′), 82.1 (C-4″), 80.6 (C-3′), 80.4 (C-4′), 80.1 (C-4), 79.8 (C-5‴′), 79.4 (C-3‴), 79.0 (C-3‴′), 78.6 (C-3″), 77.1 (C-4‴′), 76.5 (CH_2Ar), 75.7 (C-2″), 75.6 (CH_2Ar), 75.3 (CH_2Ar), 75.1 (CH_2Ar), 74.9 (CH_2Ar), 74.8 (CH_2Ar), 74.7 (CH_2Ar, C-4‴), 74.5 (C-2‴), 74.3 (CH_2Ar, C-2), 71.7 (C-5′), 71.6 (C-5), 71.5 (C-2′), 71.4 (C-3), 71.2 (CH_2Ar, C-2‴′), 68.4 (C-5″), 68.2 (C-5‴), 68.0 (OCH_2), 67.5 (C-6‴′), 50.8 (NCH_2), 18.2 (C-6), 17.9 (C-6″), 17.8 (C-6‴), 17.8 (C-6′).

HR-ESI-MS (m/z) calcd for $C_{95}H_{109}N_3O_{22}Na$ $(M + Na)^+$: 1666.7400; found: 1666.7477.

2-Aminoethyl α-D-Glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1 → 3)-α-L-rhamnopyranosyl-(1 → 3)-β-L-rhamnopyranosyl-(1 → 4)-β-L-rhamnopyranoside (1). The pure compound **27** (104 mg) was dissolved in MeOH (50 mL), and the solution was passed through a 10% Pd/C cartridge in a ThalesNano hydrogenation assembly under a continuous flow of H_2 at atmospheric pressure with a flow rate of 1 mL/min. The hydrogenolysis of the benzyl groups was complete after six such cycles, as is evident from mass spectrometry. During this process, the azido group was also converted to the amino group. MeOH was evaporated *in vaccuo*, and the residue was dissolved in high-performance liquid chromatography (HPLC) water (10 mL). The aqueous solution was washed with CH_2Cl_2 (10 mL) to remove possible organic impurities. The aqueous layer was separated and lyophilized to obtain the pure target compound **1** (52 mg, 79%) as a white foam.

$[\alpha]_D^{25}$ + 12 (*c*0.5, CH_3OH)

^{1}H NMR (500 MHz, D_2O). δ 5.08 (s, 1H, H-1‴′), 5.03 (s, 1H, H-1‴), 4.98 (s, 1H, H-1″), 4.94 (s, 1H, H-1), 4.70 (s, 1H, H-1′), 4.66 (s, 1H, H-2), 4.57−4.20 (m, 3H, H-3, H-3‴, H-2″), 4.14−3.90 (m, 6H, H-2‴, H-2′, H-3‴′, H-5‴′, H-3″, H-5‴), 3.84−3.72 (m, 4H, H-6a‴′,H-6b‴′, H-3′, H-4‴), 3.70−3.66 (m, 2H, OCH_2), 3.58−3.13 (m, 10H, NCH_2, H-5, H-5′, H-4‴′, H-2‴′, H-4, H-4′,H-4″, H-5″), 1.25 (m, 12H, H-6, H-6′, H-6″, H-6‴).

$^{13}C\{^1H\}$ NMR (126 MHz, MeOD). δ 102.3 (C-1″), 101.9(C-1‴), 100.3 (C-1), 99.3(C-1′), 95.6 (C-1‴′), 82.6, 80.4, 78.4, 75.5, 72.9, 72.1, 71.7, 71.5, 71.4, 71.3, 71.1, 70.7, 70.5, 70.2, 69.9, 69.4, 69.3, 67.6, 66.8, 62.6, 60.3, 48.9, 23.3, 16.7(C-6″, C-6‴), 16.6 (C-6, C-6′).

HR-ESI-MS (m/z) calcd for $C_{32}H_{57}NO_{22}Na$ $(M + Na)^+$: 830.3270; found: 830.3256.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00467.

Copies of ^{1}H, ^{13}C, ^{1}H−^{1}H COSY, ^{1}H−^{13}C HSQC, DEPT-135, and ^{1}H−^{13}C coupled spectra (PDF)

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Notes

The authors declare no competing financial interest.

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Schemes 2−5 were replaced on June 18, 2021 to fix the numbering to match the Experimental Section.

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