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Note

Synthesis of *n*-octyl 2,6-dideoxy-α-L-*lyxo*-hexopyranosyl-(1→2)-3-amino-3-deoxy-β-D-galactopyranoside, an analog of the H-disaccharide antigen

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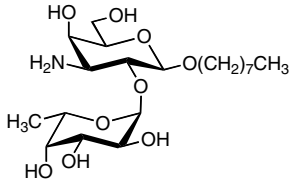
Abstract—The synthesis of an analog of the H-disaccharide antigen (**2**), in which the galactopyranosyl moiety bears an amino group at C-3 and the fucopyranosyl residue is deoxygenated at C-2, is reported. The key reaction in the preparation of **2** was the glycosylation of an appropriately protected *n*-octyl 3-azido-3-deoxy-galactopyranoside derivative with a 2,6-dideoxy thioglycoside promoted by 1-(phenylsulfinyl)piperidine and triflic anhydride. Disaccharide **2** is of interest in studies directed towards understanding the molecular basis of substrate recognition by the blood group A and B glycosyltransferases.

Keywords: H-disaccharide antigen; Blood group; Synthesis; Inhibitor; Molecular recognition

The human A and B blood group antigens are among the most well-known oligosaccharide antigens, and these structural motifs, which are found in both glycolipids and glycoproteins, play critical roles in organ transplants and blood transfusions.[1–3] These trisaccharide antigens are biosynthesized[4] from the H disaccharide antigen by the action of either an *N*-acetylgalactosaminyltransferase (A antigen) or a galactosyltransferase (B antigen), termed GTA and GTB, respectively (Fig. 1). GTA and GTB are highly homologous, differing in only four of the 354 amino acids,[5] and over the past several years a series of X-ray crystallographic and kinetics studies on native and mutant proteins have revealed the molecular basis for substrate discrimination by these enzymes.[6–12]

As part of these studies, the structures of both GTA and GTB in complex with a disaccharide inhibitor (**1**) in which the reactive hydroxyl group had been replaced with an amino group moiety were solved.[11] Disaccharide **1**, first synthesized in 1994,[13] is a potent inhibitor of both enzymes and has been shown to reduce the expression of the A-antigen on cell surfaces.[14] For GTB, **1** is a competitive inhibitor with a K_i of 7.8 μM, while for GTA the mode of inhibition is complex, and the K_i is estimated to be approximately 200 nM.



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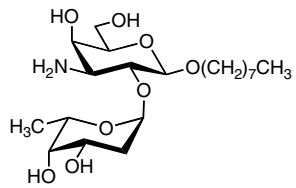

2

In the initial report describing this disaccharide,[13] it was proposed that the strong inhibition resulted from an ionic interaction between the amino group, which is protonated a physiological pH, and an anionic group in the enzyme active site. In the crystal structure of **1** in complex with GTA,[11] the disaccharide adopts a conformation different from the natural substrate, driven by

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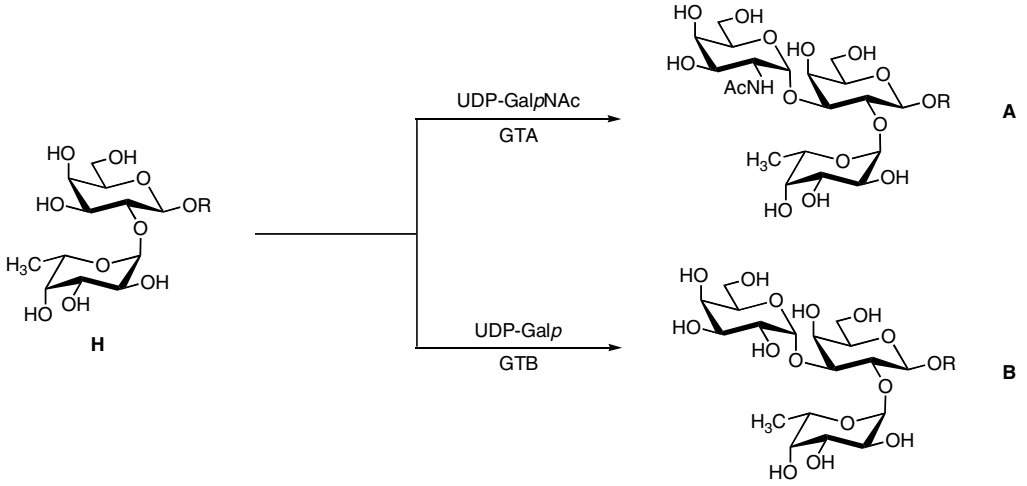
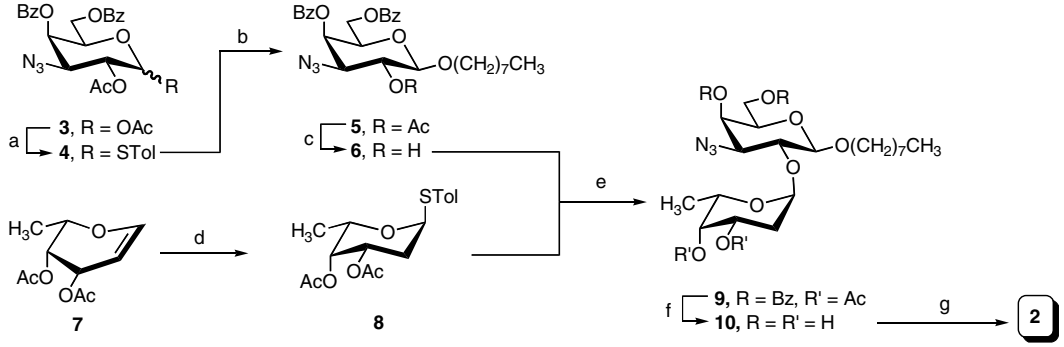


Figure 1. Biosynthesis of the A and B blood group antigens from the H antigen; R = glycoprotein or glycolipid.

the formation of an intramolecular hydrogen bond between the protonated amino group and the hydroxyl group at C-2 of the fucopyranosyl ring. This conformational change substantially reorients the inhibitor in the combining site, forcing the fucopyranose ring into a region normally occupied by the donor, UDP-GalNAc. The competition of **1** and the donor substrate for the same region of the active site is consistent with the complex mode of inhibition observed with this disaccharide. We are interested in further probing the importance of this intramolecular hydrogen bond on the manner by which **1** inhibits GTA. Therefore, we report here the synthesis of an H-disaccharide analog (**2**) in which the hydroxyl group at C-3 of the galactopyranosyl ring is replaced with an amino group, while C-2 of the fucopyranosyl moiety is deoxygenated. This compound, while maintaining the key amino group required for inhibition, lacks the hydrogen bond acceptor that drives the conformational change seen in the complex with GTA.

The synthesis of **2** is shown in Scheme 1 and began with the known[15] 3-azido-3-deoxy-galactopyranose derivative **3**. Thus, reaction of **3** with boron trifluoride etherate and *p*-thiocresol afforded thioglycoside **4** in 90% yield as a 1:3 α:β mixture of anomers. Conversion of **3** into octyl glycoside **5** was achieved in 78% yield upon treatment with *n*-octanol in the presence of *N*-iodosuccinimide and silver triflate.[16] The β-stereochemistry of the newly formed glycosidic bond could be unambiguously determined from the ^{1}H NMR spectrum of **5**; the multiplicity of the resonance for H-1 appeared as a doublet with $J_{1,2}$ 7.9 Hz. We initially investigated the direct conversion of **3** into **5** upon reaction with *n*-octanol and a Lewis acid. However, when boron trifluoride etherate was used, only small amounts of the product were observed, even at extended reaction times. The use of a stronger Lewis acid, tin tetrachloride, provided more of the product; unfortunately, at the extended reaction times required, anomerization of **5** to the corresponding α-glycoside occurred to a significant degree. For this reason, the indirect approach via thioglycoside **4** is preferable. Treatment of **5** with a methanolic solution of hydrogen chloride[17] enabled the selective cleavage of the acetate ester affording alcohol **6** in 92% yield.



Scheme 1. Reagents and conditions: (a) *p*-TolSH, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C, 90%; (b) *n*-octanol, NIS, AgOTf, CH_2Cl_2, 0 °C→rt, 78%; (c) AcCl, CH_3OH, rt, 92%; (d) *p*-TolSH, $(NH_4)_2Ce(NO_3)_6$, CH_3CN, −78 °C→rt, 81%; (e) 1-(phenylsulfinyl)piperidine, Tf_2O, 2,4,6-tri-*tert*-butylpyrimidine, −60 °C→rt, 48%; (f) $NaOCH_3$, CH_3OH, rt, 83%; (g) H_2, $Pd(OH)_2/C$, CH_3OH, rt, 80%.

To synthesize the disaccharide, we chose to couple **6** with thioglycoside **8**, which was readily prepared in one step and in 81% yield from 3,4-di-*O*-acetyl fucal (**7**),[18] by reaction with *p*-thiocresol and ceric ammonium nitrite, a method reported recently by Paul and Jayaraman.[19] With both **6** and **8** in hand, the standard *N*-iodosuccinimide and silver triflate activation method was investigated for the glycosylation reaction. However, under these conditions only low yields of the desired product were produced. We thus chose to use the 1-(phenylsulfinyl)piperidine/triflic anhydride promoter system developed recently by Crich and Smith,[20] which provided disaccharide **9** in a modest 48% yield. The other reaction products were unreacted starting acceptor and hydrolyzed donor. Regardless of the yield, sufficient quantities of **9** were obtained, and treatment under Zemplén transesterification conditions (sodium methoxide in methanol) yielded the expected deacylated azidodisaccharide **10** in 83% yield. This compound was then converted to target **2** in 80% yield upon reaction with hydrogen and palladium hydroxide-on-carbon. The ^{1}H and ^{13}C NMR spectra for **2** were consistent with the proposed structure. Thus, the anomeric hydrogen of the fucopyranosyl residue appeared as a doublet ($J_{1,2ax}$ 3.3 Hz; $J_{1,2eq}$ 0 Hz) at 5.23 ppm, while the anomeric carbon resonated at 100.07 ppm. Both these data support the α-stereochemistry of this residue. In addition, the amino group at C-3 in the galactopyranose residue could be confirmed by the appearance of the resonance for H-3 as a doublet of doublets ($J_{3,4}$ 2.7 Hz; $J_{2,3}$ 9.4 Hz) at 2.87 ppm in the ^{1}H NMR spectrum. In the ^{13}C NMR spectrum, C-3 of the galactopyranose residue appeared at 57.07 ppm, consistent with its attachment to an amino group.

In summary, we describe here the synthesis of an analog of the H-disaccharide in which the galactopyranose moiety is modified by the substitution of the hydroxyl group at C-3 with an amino group and in which the C-2 position of the fucopyranosyl moiety is deoxygenated. X-ray crystallographic and kinetics studies of this compound with GTA and GTB are in progress and will be reported in the future.

1. Experimental

1.1. General methods

Reactions were carried out in oven-dried glassware. Solvents were distilled from appropriate drying agents before use. Unless stated otherwise, all reactions were carried out under a positive pressure of argon and were monitored by TLC on Silica Gel 60 F_{254} (0.25 mm, E. Merck). Spots were detected under UV light or by charring with 10% H_2SO_4, in EtOH. Unless otherwise indicated, all column chromatography was performed on Silica Gel 60 (40–60 mM). Iatrobead refers to a beaded silica gel 6RS–8060, which is manufactured by Iatron Laboratories (Tokyo). The ratio between silica gel and crude product ranged from 100 to 50:1 (w/w). Optical rotations were measured at 22 ± 2 °C and are in units of degrees mL/g dm. ^{1}H NMR spectra were recorded at 500 or 600 MHz and chemical shifts are referenced to either TMS (0.0, $CDCl_3$) or HOD (4.78, D_2O and CD_3OD). ^{13}C NMR spectra were recorded at 125 MHz, and ^{13}C chemical shifts are referenced to internal $CHCl_3$ (77.23, $CDCl_3$), external acetone (31.07 D_2O) or internal CHD_2OD (48.9, CD_3OD). Electrospray-ionization mass spectra (ESIMS) were recorded on samples suspended in mixtures of THF with CH_3OH and added NaCl.

1.2. *n*-Octyl 2,6-dideoxy-α-L-*lyxo*-hexopyranosyl-(1→2)-3-amino-3-deoxy-β-D-galactopyranoside (2)

To a solution of **10** (19 mg, 0.31 mmol) in CH_3OH (2.0 mL), 20% palladium hydroxide-on-carbon was added, and the reaction was stirred under positive pressure of hydrogen for 6 h. The resulting mixture was filtered through Celite and concentrated to give a crude residue that was purified by chromatography on Iatrobeads using CH_3OH as the eluant to yield **2** (14 mg, 80%) as a white foam after freeze drying: R_f 0.51 (CH_3OH); $[\alpha]_D$ −70.1 (*c* 0.2, H_2O); ^{1}H NMR (600 MHz, D_2O, δ_H) 5.23 (d, 1H, *J* 3.3 Hz, H-1′), 4.39 (d, 1H, *J* 7.9 Hz, H-1), 4.23 (q, 1H, *J* 6.6 Hz, H-5′), 4.04–3.98 (m, 1H, H-3′), 3.92–3.87 (m, 2H, H-4, octyl OCH_2), 3.77–3.70 (m, 2H, H-6), 3.68–3.65 (m, 2H, H-5, H-4′), 3.65–3.58 (m, 1H, octyl OCH_2), 3.46 (dd, 1H, *J* 9.4, 7.9 Hz, H-2), 2.87 (dd, 1H, *J* 9.4, 2.7 Hz, H-3), 2.00 (dd, 1H, *J* 13.1, 5.0 Hz, H-2′), 1.90 (ddd, 1H, *J* 13.1, 13.1, 3.3 Hz, H-2′), 1.68–1.58 (m, 2H, octyl CH_2), 1.38–1.35 (m, 10H, octyl CH_2), 1.20 (d, 3H, *J* 6.5 Hz, H-6′), 0.88 (t, 3H, *J* 6.7 Hz, octyl CH_3); ^{13}C NMR (125 MHz, CD_3OD, δ_C) 103.08 (C-1), 100.07 (C-1′), 78.47 (C-2), 77.14 (C-5), 71.40 (C-4′), 71.06 (octyl OCH_2), 69.82 (C-4), 67.89 (C-5′), 66.02 (C-3′), 61.58 (C-6), 57.07 (C-3), 32.29 (C-2′), 32.09 (octyl CH_2), 30.01 (octyl CH_2), 29.81 (octyl CH_2), 29.68 (octyl CH_2), 26.48 (octyl CH_2), 23.14 (octyl CH_2), 17.16 (C-6′), 14.49 (octyl CH_3); ESIMS: *m*/*z* calcd for $[C_{20}H_{40}NO_8]H^+$: 422.2748. Found 422.2745.

1.3. *p*-Tolyl 2-*O*-acetyl-3-azido-4,6-di-*O*-benzoyl-3-deoxy-1-thio-β-D-galactopyranoside (4)

To a solution of *p*-thiocresol (98 mg, 0.77 mmol) and 1,2-di-*O*-acetyl-3-azido-4,6-di-*O*-benzoyl-3-deoxy-β-D-galactopyranoside (**3**)[15] (349 mg, 0.70 mmol) in dry CH_2Cl_2 (15 mL), $BF_3{\cdot}Et_2O$ (0.88 mL, 7.0 mmol) was added at 0 °C. The reaction mixture was stirred at 0 °C for 6 h and then diluted with CH_2Cl_2 (20 mL),

washed with satd aq $NaHCO_3$ (3×20 mL), dried (Na_2SO_4), and concentrated. Chromatography (4:1 hexanes–EtOAc) yielded **4** (354 mg, 90%) in a 1:3 α:β ratio as a colorless syrup. Data for β anomer: R_f 0.67 (2:1 hexanes–EtOAc); $[\alpha]_D$ −2.9 (*c* 2.0, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$, δ_H): 8.04–8.01 (m, 2H, Ar), 7.98–7.95 (m, 2H, Ar), 7.63–7.57 (m, 2H, Ar), 7.48–7.42 (m, 6H, Ar), 7.03 (d, 2H, *J* 8.3 Hz, Ar), 5.79 (d, 1H, *J* 3.2 Hz, H-4), 5.30 (dd, 1H, *J* 9.9, 9.9 Hz, H-2), 4.71 (d, 1H, *J* 9.9 Hz, H-1), 4.51 (dd, 1H, *J* 11.5, 7.1 Hz, H-6), 4.38 (dd, 1H, *J* 11.5, 5.5 Hz, H-6), 4.14 (dd, 1H, *J* 7.1, 5.5 Hz, H-5), 3.82 (dd, 1H, *J* 9.9, 3.2 Hz, H-3), 2.36 (s, 3H, tolyl CH_3), 2.21 (s, 3H, acetyl CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C): 169.31 (CO), 166.02 (CO), 165.34 (CO), 138.52 (Ar), 133.91 (Ar × 2), 133.69 (Ar), 133.28 (Ar), 130.17 (Ar × 2), 129.82 (Ar × 2), 129.62 (Ar × 2), 129.47 (Ar), 128.63 (Ar), 128.53 (Ar × 2), 128.42 (Ar × 2), 127.77 (Ar), 86.47 (C-1), 75.64 (C-5), 68.54 (C-4), 68.52 (C-2), 63.33 (C-3), 62.51 (C-6), 21.26 (tolyl CH_3), 20.94 (acetyl CH_3); IR: 2109 cm^{-1} (N_3); ESIMS: *m*/*z* calcd for $[C_{29}H_{27}N_3O_7S]$-Na^+: 584.1462. Found: 584.1463.

1.4. *n*-Octyl 2-*O*-acetyl-3-azido-4,6-di-*O*-benzoyl-3-deoxy-β-D-galactopyranoside (5)

To a mixture of **4** (262 mg, 0.47 mmol), *n*-octanol (88 μL, 0.56 mmol) and 4 Å molecular sieves (100 mg) in CH_2Cl_2 (15 mL), *N*-iodosuccinimide (332 mg, 1.40 mmol), and silver triflate (120 mg, 0.47 mmol) were added in succession at 0 °C. After stirring for 15 min at 0 °C, the reaction mixture was warmed to room temperature and stirred for 1 h. The reaction mixture turned dark red, and Et_3N was added, diluted with CH_2Cl_2 (25 mL), and filtered through Celite. The filtrate was washed with satd aq $Na_2S_2O_3$ (3×30 mL), dried (Na_2SO_4) and concentrated to give a crude residue that was purified by chromatography (4:1 hexanes–EtOAc) to give **5** (208 mg, 78%) as a colorless oil: R_f 0.58 (3:1 hexanes–EtOAc); $[\alpha]_D$ +14.2 (*c* 0.9, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$, δ_H): 8.14–8.12 (m, 2H, Ar), 8.04–8.02 (m, 2H, Ar), 7.63–7.56 (m, 2H, Ar), 7.50–7.43 (m, 4H, Ar), 5.80 (dd, 1H, *J* 3.4, 1.0 Hz, H-4), 5.31 (dd, 1H, *J* 10.5, 7.9 Hz, H-2), 4.56 (dd, 1H, *J* 11.3, 6.6 Hz, H-6), 4.54 (d, 1H, *J* 7.9 Hz, H-1), 4.33 (dd, 1H, *J* 11.3, 5.6 Hz, H-6), 4.11 (ddd, 1H, *J* 6.6, 5.6, 1.0 Hz, H-5), 3.92 (ddd, 1H, *J* 9.7, 6.2, 6.2 Hz, octyl OCH_2), 3.78 (dd, 1H, *J* 10.5, 3.4 Hz, H-3), 3.52 (ddd, 1H, *J* 9.7, 6.8, 6.8 Hz, octyl OCH_2), 2.14 (s, 3H, acetyl CH_3), 1.65–1.54 (m, 2H, octyl CH_2), 1.37–1.23 (m, 10H, octyl CH_2), 0.89 (t, 3H, *J* 7.0 Hz, octyl CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C): 169.21 (CO), 166.06 (CO), 165.50 (CO), 133.68 (Ar), 133.29 (Ar), 130.20 (Ar × 2), 129.77 (Ar × 2), 129.46 (Ar), 128.75 (Ar), 128.58 (Ar × 2), 128.45 (Ar × 2), 101.58 (C-1), 71.97 (C-5), 70.28 (octyl OCH_2), 70.20 (C-2), 68.35 (C-4), 62.12 (C-3), 62.01 (C-6), 31.80 (octyl CH_2), 29.43 (octyl CH_2), 29.27 (octyl CH_2), 25.84 (octyl CH_2), 22.64 (octyl CH_2), 20.77 (acetyl CH_3), 14.08 (octyl CH_3); IR: 2107 cm^{-1} (N_3); ESIMS: *m*/*z* calcd for $[C_{30}H_{37}N_3O]$-Na^+: 590.2473. Found 590.2472.

1.5. *n*-Octyl 3-azido-4,6-di-*O*-benzoyl-3-deoxy-β-D-galactopyranoside (6)

Compound **5** (152 mg, 0.27 mmol) was dissolved in 50:1 CH_3OH–AcCl (5.1 mL), and the solution was stirred for 24 h. The reaction mixture was quenched by the addition of satd aq $NaHCO_3$ and then diluted with CH_2Cl_2 (20 mL). After being washed with water (20 mL) and a satd NaCl solution (20 mL), the organic layer was dried with Na_2SO_4 and concentrated. Chromatography (4:1 hexanes–EtOAc) gave **6** (130 mg, 92%) as a colorless oil: R_f 0.73 (2:1 hexanes–EtOAc); $[\alpha]_D$ +0.4 (*c* 1.5, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$, δ_H): 8.12–8.09 (m, 2H, Ar), 8.05–8.01 (m, 2H, Ar), 7.62–7.55 (m, 2H, Ar), 7.49–7.42 (m, 4H, Ar), 5.73 (dd, 1H, *J* 3.5, 1.0 Hz, H-4), 4.55 (dd, 1H, *J* 11.3, 6.6 Hz, H-6), 4.42 (d, 1H, *J* 7.7 Hz, H-1), 4.32 (dd, 1H, *J* 11.3, 6.5 Hz, H-6), 4.09 (ddd, 1H, *J* 6.6, 6.5, 1.0 Hz, H-5), 3.99–3.93 (m, 2H, H-2, octyl OCH_2), 3.71 (dd, 1H, *J* 10.3, 3.5 Hz, H-3), 3.59 (ddd, 1H, *J* 9.6, 7.0, 7.0 Hz, octyl OCH_2), 1.72–1.62 (m, 2H, octyl CH_2), 1.40–1.23 (m, 10H, octyl CH_2), 0.89 (t, 3H, *J* 7.0 Hz, octyl CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C): 166.05 (CO), 165.44 (CO), 133.57 (Ar), 133.27 (Ar), 130.11 (Ar × 2), 129.76 (Ar × 2), 129.50 (Ar), 128.99 (Ar), 128.51 (Ar × 2), 128.44 (Ar × 2), 103.38 (C-1), 72.07 (C-5), 70.96 (C-2), 70.67 (octyl OCH_2), 68.30 (C-4), 63.30 (C-3), 62.12 (C-6), 31.79 (octyl CH_2), 29.56 (octyl CH_2), 29.33 (octyl CH_2), 29.22 (octyl CH_2), 25.93 (octyl CH_2), 22.64 (octyl CH_2), 14.08 (octyl CH_3); IR: 2110 cm^{-1} (N_3); ESIMS: *m*/*z* calcd for $[C_{28}H_{35}N_3O_7]Na^+$: 548.2367. Found: 548.2365.

1.6. *p*-Tolyl 3,4-di-*O*-acetyl-2,6-dideoxy-1-thio-α-L-*lyxo*-hexopyranoside (8)

To a solution of 3,4-di-*O*-acetyl-L-fucal (**7**)[18] (0.32 g, 1.49 mmol) in CH_3CN (10 mL), $(NH_4)_2Ce(NO_3)_6$ (0.41 g, 0.75 mmol) and *p*-thiocresol (0.92 g, 7.4 mmol) were added at −78 °C. The mixture was allowed to warm to room temperature slowly over 4 h. The reaction mixture was diluted with CH_2Cl_2 (30 mL) and then washed with satd aq $Na_2S_2O_3$ and satd aq $NaHCO_3$ before being dried over $MgSO_4$. The residue obtained after concentration of the organic layer was purified by chromatography (9:1 hexanes–EtOAc) to give **8** (0.41 g, 81%) as a white solid: R_f 0.24 (6:1 hexanes–EtOAc); $[\alpha]_D$ −304.9 (*c* 1.4, CH_3OH); ^1H NMR (500 MHz, $CDCl_3$, δ_H): 7.34 (d, 2H, *J* 8.2 Hz, Ar), 7.12 (d, 2H, *J* 8.2 Hz, Ar), 5.66 (d, 1H, *J* 5.7 Hz, H-1), 5.31–5.26 (m,

1H, H-3), 5.23 (br s, 1H, H-4), 4.56 (q, 1H, *J* 6.5 Hz, H-5), 2.44 (td, 1H, *J* 12.9, 5.7 Hz, H-2), 2.33 (s, 3H, tolyl CH_3), 2.16 (s, 3H, acetyl CH_3), 2.05 (dd, 1H, *J* 12.9, 5.0 Hz, H-2), 2.01 (s, 3H, acetyl CH_3), 1.15 (d, 3H, *J* 6.5 Hz, H-6); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C): 170.57 (CO), 169.93 (CO × 2), 137.38 (Ar), 131.69 (Ar × 2), 130.80 (Ar) 129.74 (Ar × 2), 84.04 (C-1), 69.76 (C-4), 67.27 (C-3), 65.67 (C-5), 30.51 (C-2), 21.08 (acetyl CH_3), 20.88 (acetyl CH_3), 16.44 (C-6); ESIMS: *m*/*z* calcd for $[C_{17}H_{22}O_5S]Na^+$: 361.1080. Found: 361.1081.

1.7. *n*-Octyl 3,4-di-*O*-acetyl-2,6-dideoxy-α-L-*lyxo*-hexopyranosyl-(1→2)-3-azido-4,6-di-*O*-benzoyl-3-deoxy-β-D-galactopyranoside (9)

Donor **7** (135 mg, 0.40 mmol), 1-(phenylsulfinyl)piperidine (83 mg, 0.4 mmol), 2,4,6-tri-*tert*-butylpyrimidine (200 mg, 0.8 mmol) and 4 Å molecular sieves (150 mg) were dried for 4 h under vacuum in the presence of P_2O_5. To this mixture in CH_2Cl_2 (15 mL), triflic anhydride (72 μL, 0.44 mmol) was added at −60 °C. After stirring for 10 min, a solution of vacuum-dried **6** in CH_2Cl_2 (3 mL) was added via a syringe. After 40 min, the reaction mixture was warmed to room temperature and stirred continuously for 24 h. Satd aq $NaHCO_3$ was added, and the resulting solution was diluted with CH_2Cl_2 (25 mL) and filtered through Celite. The filtrate was washed with satd aq $NaHCO_3$ (30 mL), dried (Na_2SO_4), and concentrated to give a crude residue that was purified by chromatography (5:1 hexanes–EtOAc) to give **9** (71 mg, 48%) as colorless oil: R_f 0.43 (4:1 hexanes–EtOAc); $[\alpha]_D$ −35.2 (*c* 0.8, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, δ_H): 8.12–8.09 (m, 2H, Ar), 8.05–8.02 (m, 2H, Ar), 7.63–7.55 (m, 2H, Ar), 7.49–7.42 (m, 4H, Ar), 5.77 (d, 1H, *J* 3.3 Hz, H-4), 5.33–5.27 (m, 2H, H-1′, H-3′), 5.19 (br s, 1H, H-4′), 4.55 (dd, 1H, *J* 11.3, 6.8 Hz, H-6), 4.48 (q, 1H, *J* 6.6 Hz, H-5′), 4.46 (d, 1H, *J* 7.6 Hz, H-1), 4.32 (dd, 1H, *J* 11.3, 6.5 Hz, H-6), 4.08 (dd, 1H, *J* 6.8, 6.5 Hz, H-5), 3.89 (ddd, 1H, *J* 9.2, 7.9, 7.9 Hz, octyl OCH_2), 3.84 (dd, 1H, *J* 10.1, 7.6 Hz, H-2), 3.75 (dd, 1H, *J* 10.1, 3.3 Hz, H-3), 3.55 (ddd, 1H, *J* 9.2, 7.8, 7.8 Hz, octyl OCH_2), 2.16 (s, 3H, acetyl CH_3), 2.09 (ddd, 1H, *J* 12.8, 12.8, 3.8 Hz, H-2′), 2.00 (s, 3H, acetyl CH_3), 1.97 (m, 1H, H-2′), 1.69–1.61 (m, 2H, octyl CH_2), 1.37–1.23 (m, 10H, octyl CH_2), 1.15 (d, 3H, *J* 6.6 Hz, H-6′), 0.89 (t, 3H, *J* 6.9 Hz, octyl CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ_C): 170.76 (CO), 170.15 (CO), 166.03 (CO), 165.57 (CO), 133.60 (Ar), 133.27 (Ar), 130.14 (Ar × 2), 129.75 (Ar × 2), 129.51 (Ar), 128.91 (Ar), 128.53 (Ar × 2), 128.44 (Ar × 2), 102.30 (C-1), 98.50 (C-1′), 74.48 (C-2), 71.76 (C-5), 70.44 (octyl OCH_2), 69.91 (C-4′), 68.51 (C-4), 66.54 (C-3′), 65.52 (C-3), 65.27 (C-5′), 62.09 (C-6), 31.77 (octyl CH_2), 29.94 (octyl CH_2), 29.61 (octyl CH_2), 29.34 (octyl CH_2), 29.22 (C-2′), 25.93 (octyl CH_2), 22.62 (octyl CH_2), 20.94 (acetyl CH_3), 20.75 (acetyl CH_3), 16.48 (C-6′), 14.08 (octyl CH_3); IR: 2108 cm^{-1} (N_3); ESIMS: *m*/*z* calcd for $[C_{38}H_{49}N_3O_{12}]Na^+$: 762.3208. Found: 762.3206.

1.8. *n*-Octyl 2,6-dideoxy-α-L-*lyxo*-hexopyranosyl-(1→2)-3-azido-3-deoxy-β-D-galactopyranoside (10)

To a solution of **9** (62 mg, 0.08 mmol) in CH_3OH (3 mL) and CH_2Cl_2 (3 mL), solid $NaOCH_3$ was added until the pH was ∼10. The solution was allowed to stir at room temperature for 5 h, followed by neutralization with HOAc. The resulting mixture was concentrated, and the residue was purified by chromatography (10:1 CH_2Cl_2–CH_3OH), to yield **8** (31 mg, 83%) as a colorless semisolid: R_f 0.31 (10:1 CH_2Cl_2–CH_3OH); $[\alpha]_D$ −40.2 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3OD, δ_H): 5.23 (d, 1H, *J* 3.3 Hz, H-1′), 4.34 (d, 1H, *J* 7.7 Hz, H-1), 4.29 (q, 1H, *J* 6.6 Hz, H-5′), 3.98 (d, 1H, *J* 3.1 Hz, H-4), 3.94–3.86 (m, 2H, H-3′, octyl OCH_2), 3.74 (dd, 1H, *J* 10.3, 7.7 Hz, H-2), 3.70 (dd, 2H, *J* 6.6 Hz, H-6), 3.54–3.48 (m, 3H, H-4′, H-5, octyl OCH_2), 3.48 (dd, 1H, *J* 10.3, 3.1 Hz, H-3), 1.91 (ddd, 1H, *J* 12.7, 12.7, 3.3 Hz, H-2′), 1.82 (dd, 1H, *J* 12.7, 5.2 Hz, H-2′), 1.62–1.55 (m, 2H, octyl CH_2), 1.39–1.25 (m, 10H, octyl CH_2), 1.17 (d, 3H, *J* 6.6 Hz, H-6′), 0.90 (dd, 3H, *J* 7.1, 6.8 Hz, octyl CH_3); ^{13}C NMR (125 MHz, CD_3OD, δ_C): 103.79 (C-1), 99.25 (C-1′), 77.11 (C-5), 74.24 (C-2), 72.45 (C-4′), 70.75 (octyl OCH_2), 69.37 (C-4), 68.40 (C-3), 67.90 (C-5′), 66.83 (C-3′), 62.23 (C-6), 33.34 (C-2′), 33.03 (octyl CH_2), 30.97 (octyl CH_2), 30.62 (octyl CH_2), 30.45 (octyl CH_2), 27.37 (octyl CH_2), 23.72 (octyl CH_2), 17.30 (C-6′), 14.43 (octyl CH_3); IR: 2104 cm^{-1} (N_3); ESIMS: *m*/*z* calcd for $[C_{20}H_{37}N_3O_8]Na^+$: 470.2473. Found: 470.2471.

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