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Synthesis of a tetrasaccharide phosphate from the linkage region of the arabinogalactan–peptidoglycan complex in the mycobacterial cell wall

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Abstract—The synthesis of dibenzyl 6-*O*-naphthylmethyl-2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl-(1→5)-2,3-di-*O*-benzoyl-6-*O*-benzyl- β-D-galactofuranosyl-(1→4)-3-*O*-benzyl-2-*O*-pivaloyl-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-benzoyl-α-D-glucopyranosyl phosphate (**1**), a protected form of the tetrasaccharide phosphate of the linkage region of the arabinogalactan–peptidoglycan complex in the mycobacterial cell wall, has been accomplished. Key steps include the coupling of four monosaccharide building blocks with complete stereoselectivity by glycosylations employing thioglycosides, 2′-carboxybenzyl glycosides, and glycosyl fluorides as glycosyl donors. The α-glycosyl phosphate linkage was also stereoselectively elaborated by reaction of a tetrasaccharide hemiacetal with tetrabenzyl pyrophosphate in the presence of a base.

Keywords: Oligosaccharides; Glycosylation; Glycosyl phosphate; CB glycosides; Mycobacterial cell wall

1. Introduction

Mycobacterial infections have attracted a great deal of attention in recent years mainly due to the emergence of multi-drug resistant strains[1] of *Mycobacterium tuberculosis*, the causative agent of tuberculosis, one of the most threatening of human infectious diseases. The resistance of *M. tuberculosis* to many therapeutic agents is partly attributable to its extremely robust and largely impermeable cell wall envelope.[2] One of the major structural components of the cell wall of *M. tuberculosis* is composed of a covalently linked complex of mycolic acid, D-arabinan, D-galactan, and peptidoglycan and is often referred to as the mAGP complex, which plays a crucial role for the survival and pathogenicity of *M. tuberculosis*.[3] Within the mAGP complex, the D-galactan, composed of about 30 alternating β-(1→5)-, and β-(1→6)-galactofuranose units,[3a] is attached to the peptidoglycan via a linkage unit, →4)-α-L-Rha*p*-(1→3)-α-D-GlcNAc-1-P[3b] as shown in Figure 1.

Ethambutol, an effective anti-TB drug, inhibits the polymerization step of D-arabinan biosynthesis[4] while the D-galactan moiety was suggested to be essential for the growth and viability of mycobacteria[5] and the biosynthetic pathway for the linkage unit has been elucidated.[6] Very recently, it has also been reported that the biosynthesis of the D-galactan is catalyzed by two galactofuranosyltransferase enzymes.[7]

Because of their biological importance as substrates for enzymes involved in the biosynthesis of mycobacterial cell wall, as well as their potential as anti-TB agents, several motifs of the mAGP complex have been synthesized. For example, Lowary and co-workers succeeded in the synthesis of a highly complex 22 unit arabinan domain containing the β-D-arabinofuranosyl linkages of D-arabinogalactan.[8] Arabinosyl–galactosyl disaccharides,[9] trisaccharides,[10] and tetrasaccharides[11] have also been synthesized. Galactosyl trisaccharides[12] and linkage di-[13] and oligosaccharides[7] have also been prepared.

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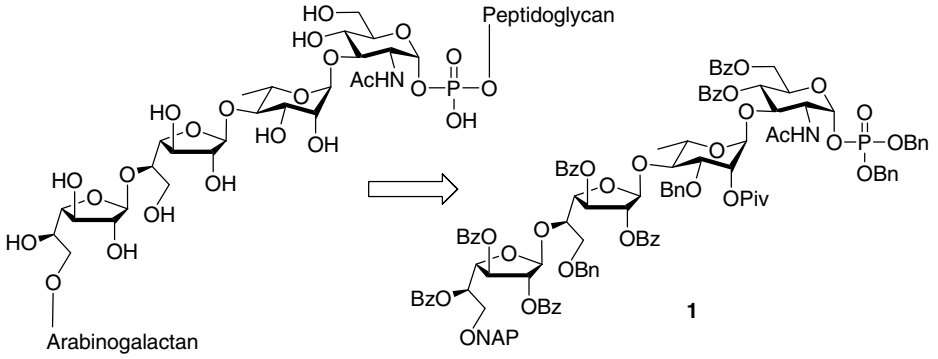


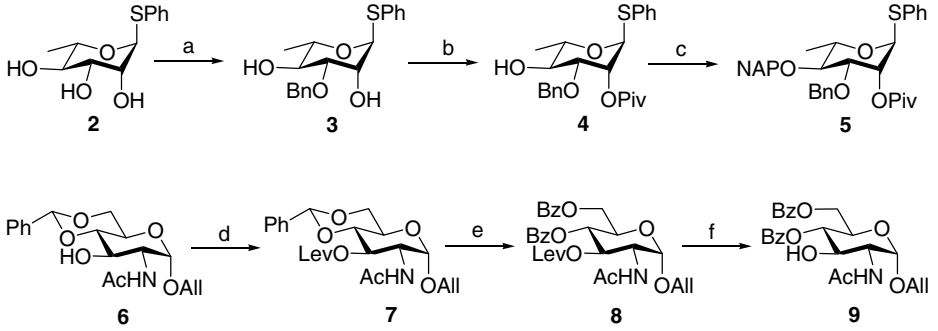
Figure 1. Structure of the linkage region of the arabinogalactan–peptidoglycan complex of the mycobacterial cell wall and target tetrasaccharide phosphate **1**.

Herein we report for the first time the synthesis of compound **1** (Fig. 1) a protected form of the tetrasaccharide phosphate, β-D-Gal*f*-(1→5)-β-D-Gal*f*-(1→4)-α-L-Rha*p*-(1→3)-α-D-GlcNAc-1-P, of the linkage region of mAGP complex in the mycobacterial cell wall. The naphthylmethyl (NAP) protective group of the target molecule **1** was chosen after consideration of the future connection of the linkage region with the arabinogalactan moiety.

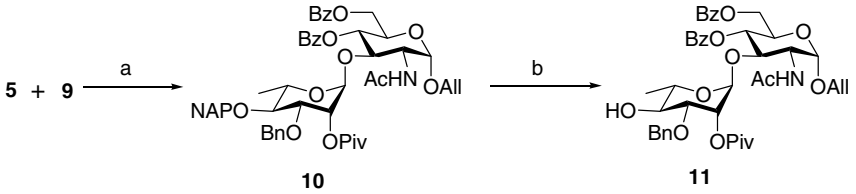
2. Results and discussion

The synthesis of the rhamnose building block started with a selective benzylation of known thio-L-rhamnoside **2**[14] by using the dibutyltin oxide method[15] to afford exclusively monobenzyl ether **3** in 76% yield as shown in Scheme 1. Selective protection of the diol **3** employing bis(tributyltin) oxide[16] and pivaloyl chloride followed by naphthylmethylation of resulting 2-*O*-pivaloyl sugar **4** provided the fully protected rhamnosyl donor **5**. Because the glycosylation of the known glucosamine derivative **6**[17] with donor **5** gave the desired disaccharide in poor yield, compound **6** was converted into a properly protected glycosyl acceptor by the following sequence: (i) protection of **6** with a levulinyl group, (ii) debenzylidenation of resulting **7** with camphorsulfonic acid, (iii) benzoylation of resulting diol to give dibenzoate **8**, and (iv) conversion of levulinyl ester **8** with hydrazine acetate into desired glucosamine derivative **9**.

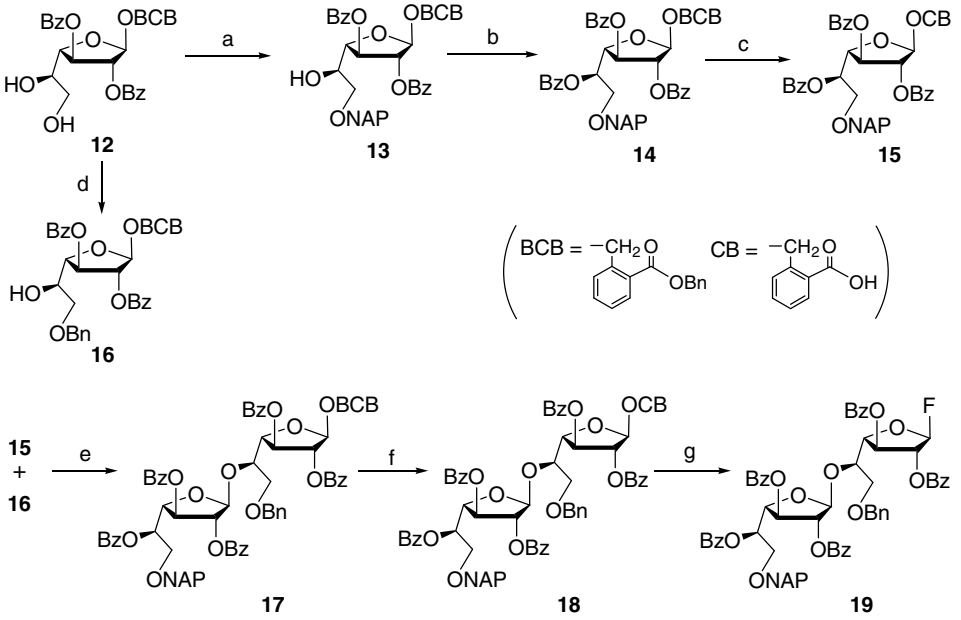
Glycosylation of **9** with **5** was carried out by activation of the donor **5** with 1-benzenesulfinyl piperidine (BSP)[18] and Tf_2O in the presence of tri-*t*-butylpyrimidine (TTBP) at −40 °C followed by addition of the acceptor **9** at −40 °C to afford exclusively the α-L-rhamnosyl disaccharide **10** in 85% yield as shown in Scheme 2. It is worth commenting that the efficiency of the glycosylation was quite sensitive to the protecting groups on the glycosyl donor **5**. Thus, the glycosylation of **9** with a donor having an acetyl or levulinyl group instead of the NAP group at O-4 of the compound **5** provided the desired disaccharide **10** in a much lower yield. The glycosyl donor having a benzoyl group in place of the pivaloyl group at O-2 of **5** was not satisfactory in the glycosylation of **9**. Deprotection of the NAP group of disaccharide **10** with DDQ gave disaccharide acceptor **11** in 84% yield. The stereochemistry of the newly generated anomeric center of the disaccharide was unequivocally determined to be of the α-configuration on the



Scheme 1. Reagents and conditions: (a) (i) *n*-Bu_2SnO, benzene, reflux, 10 h; (ii) BnBr, *n*-Bu_4NI, DMF, 50 °C, 3 h, 76% in two steps; (b) (i) (*n*-$Bu_3Sn)_2O$, benzene, reflux, 10 h; (ii) PivCl, benzene, 60 °C, 3 h, 79% in two steps; (c) NAPBr, NaH, *n*-Bu_4NI, DMF, 0 °C to rt, 2 h, 86%; (d) levulinic acid, EDC, DMAP, CH_2Cl_2, DMF, rt, 3 h, 83%; (e) (i) CSA, CH_2Cl_2, MeOH, rt, 2 h; (ii) BzCl, DMAP, pyridine, rt, 5 h, 62% in two steps; (f) NH_2NH_2, AcOH, THF, MeOH, rt, 30 min, 95%.



Scheme 2. Reagents and conditions: (a) BSP, Tf_2O, TTBP, 4 Å MS, CH_2Cl_2, −40 °C→0 °C, 2 h, 85%; (b) DDQ, CH_2Cl_2, MeOH, rt, 2 h, 84%.

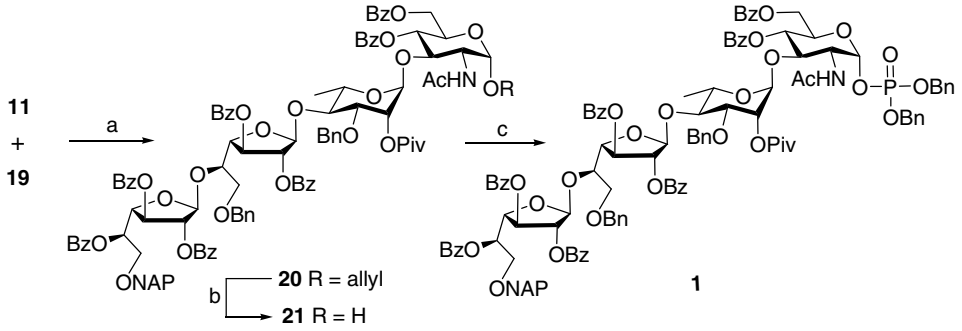


Scheme 3. Reagent and conditions: (a) (i) *n*-Bu_2SnO, benzene, reflux, 10 h; (ii) NAPBr, NaH, *n*-Bu_4NI, DMF, 60 °C, 3 h, 82% in two steps; (b) BzCl, Et_3N, DMAP, CH_2Cl_2, 0 °C to rt, 30 min, 96%; (c) H_2, Pd–C, NH_4OAc, MeOH, EtOAc, rt, 1 h, 89%; (d) (i) *n*-Bu_2SnO, benzene, reflux, 10 h; (ii) BnCl, NaH, *n*-Bu_4NI, DMF, 60 °C, 3 h, 86% in two steps; (e) DTBMP, Tf_2O, CH_2Cl_2, 4 Å MS, −78 °C to 0 °C, 2 h, 88%; (f) H_2, $Pd(OH)_2$, NH_4OAc, MeOH, EtOAc, rt, 5 h, 89%; (g) 4Å MS, DTBMP, Tf_2O, CH_2Cl_2, Deoxofluor, HF–pyridine, 2 h, 84%.

basis of the one-bond C1′-H1′ coupling constant of compound **11**, $J_{C1'-H1'} = 170$ Hz at δ_C 100.4.[19]

The synthesis of a galactose disaccharide started with selective naphthylmethylation of the known 2′-(benzyloxycarbonyl)benzyl (BCB) galactoside **12**[20] using *n*-Bu_2SnO and subsequent benzoylation of the resulting NAP ether **13** to give the fully protected galactoside **14** as shown in Scheme 3. The BCB galactoside **14** was converted into 2′-carboxybenzyl (CB) galactoside **15** by selective hydrogenolysis of the benzyl ester functionality of the BCB moiety of **14** in the presence of ammonium acetate.[21] On the other hand, selective benzylation of **12** afforded compound **16** as a glycosyl acceptor. Glycosylation of **16** with **15** was performed by sequential addition of Tf_2O and the donor **15** to a solution of the acceptor **16** and DTBMP in CH_2Cl_2 at −78 °C to give exclusively the β-D-galactosyl disaccharide **17** in 88% yield.

The BCB disaccharide **17** was transformed to CB disaccharide **18** by selective hydrogenolysis. However, coupling of the disaccharide acceptor **11** and the disaccharide donor **18** did not provide a desired tetrasaccharide because of the generation of an undesired self-condensed ester of the CB glycoside **18**.[22] This result led us to examine another glycosyl donor in place of **18**, such as a glycosyl fluoride. We have previously shown that CB glycosides could be readily converted into glycosyl fluorides by treatment with Tf_2O followed by HF–pyridine[20] or by (diethylamino)sulfur trifluoride (DAST).[23] However, neither HF–pyridine nor DAST with Tf_2O, was quite satisfactory for the conversion of the CB disaccharide **18** into fluoride **19**, but a combination of Tf_2O, bis(2-methoxyethyl)aminosulfur trifluoride (Deoxofluor),[24] and HF–pyridine cleanly converted **18** into **19**. Thus, sequential addition of Tf_2O, Deoxofluor, and HF–pyridine to a solution of **18** in CH_2Cl_2 in the presence of DTBMP at −78 °C provided desired disaccharide fluoride **19** in 84% yield. The anomeric carbon chemical shifts at δ_C 105.3 of **17**, δ_C 105.5 or 105.6 of **18**, and δ_C 105.3 of **19** clearly indicated that the newly generated galactosyl linkage of the disaccharides is in the β-configuration.[20,25]



Scheme 4. Reagents and conditions: (a) $SnCl_2$, $AgClO_4$, Et_2O/CH_2Cl_2, 0 °C to rt, 30 min, 90%; (b) $PdCl_2$, NaOAc, 95% aq AcOH, rt, 12 h, 71%; (c) LDA, $[(BnO)_2P(O)]_2O$, THF, −78 °C to 0 °C, 2 h, 92%.

A proposed mechanism of the conversion of **18** into **19** could be as follows: Addition of Tf_2O to **18** would give a highly reactive mixed anhydride intermediate, a glycosyl acyl triflate. Then, upon addition of Deoxofluor, the triflate would be displaced by the fluoride anion from Deoxofluor to provide a glycosyl acyl fluoride intermediate. Finally, HF–pyridine would facilitate the lactonization of the acyl fluoride to generate a glycosyl oxocarbenium ion, which would readily react with a fluoride ion to afford the glycosyl fluoride **19**. In fact, we were able to isolate the glycosyl acyl fluoride intermediate.

The stage was set now for the construction of the tetrasaccharide by coupling of the pyranose disaccharide acceptor **11** and the furanose disaccharide donor **19**. Glycosylation of **11** with **19** employing $SnCl_2$ and $AgClO_4$ as promoters in Et_2O and CH_2Cl_2 at 0 °C gave exclusively β-tetrasaccharide **20** in 90% yield (see Scheme 4). The anomeric allyl group of **20** was removed by $PdCl_2$ and sodium acetate in aqueous acetic acid to afford tetrasaccharide hemiacetal **21** in 71% yield. Phosphorylation of **21** with tetrabenzyl pyrophosphate in the presence of LDA[26] provided exclusively the α-glycosyl dibenzyl phosphate **1** in 92% yield. The stereochemistry at the newly generated anomeric center of the tetrasaccharide was determined to be the β-configuration on the basis of their anomeric carbon chemical shifts at δ_C 105.2 for all three tetrasaccharides, **20**, **21**, and **1**. The stereochemistry at all other anomeric centers in the tetrasaccharide was confirmed by ^{13}C NMR spectral data. One-bond C1–H1 coupling constants of **1**, $J_{C1-H1} = 179$ Hz and $J_{C1'-H1'} = 172$ Hz, indicated that the anomeric linkages of both pyranose rings of **1** were in α-configuration[26] while the presence of another anomeric carbon chemical shift at δ_C 106.6 of **1** indicated that the galactofuranosyl linkage formed in the coupling of **11** and **19** was also in the β-configuration.[20,25]

In summary, the synthesis of compound **1**, a protected form of the tetrasaccharide phosphate, β-D-Gal*f*-(1→5)-β-D-Gal*f*-(1→4)-α-L-Rha*p*-(1→3)-α-D-GlcNAc-1-P, of the linkage region of the mAGP complex in the mycobacterial cell wall has been accomplished. The synthesis of more complex oligosaccharide phosphates and biological evaluation of their deprotected forms are currently underway.

3. Experimental

3.1. General methods

All reactions were conducted under a positive pressure of dry argon with dry, freshly distilled solvents unless otherwise noted. All reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. Optical rotations were determined at 20 °C with an automatic polarimeter. ^1H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer (400 MHz for ^1H, 100 MHz for ^{13}C). Chemical shifts are given in ppm downfield from internal tetramethylsilane for spectra recorded in $CDCl_3$. Flash column chromatography was performed employing 230–400 mesh silica gel. Thin-layer chromatography was performed using Silica Gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Visualization on TLC was achieved by UV light (254 nm) and a typical TLC indication solution (cerium sulfate–molybdic acid solution). Solutions were concentrated at below 40 °C under reduced pressure.

3.2. Phenyl 3-*O*-benzyl-1-thio-α-L-rhamnopyranose (3)

A solution of phenyl 1-thio-α-L-rhamnopyranose[14] (9.65 g, 37.7 mmol) and *n*-Bu_2SnO (11.25 g, 45.2 mmol) in benzene (100 mL) was stirred under reflux using a Dean–Stark trap for 10 h. After removal of the solvent in vacuo, the residue was dissolved in DMF (50 mL) and then benzyl chloride (5.2 mL, 45.2 mmol) and *n*-Bu_4NI (16.7 g, 45.2 mmol) were added to the DMF solution. After being stirred at 50 °C for 3 h, the reaction mixture was diluted with EtOAc (100 mL). The organic layer was washed with satd aq NH_4Cl (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by silica gel flash

column chromatography (hexane–EtOAc 2:1, v/v) to afford compound **3** (9.91 g, 28.6 mmol, 76%) as a colorless oil, R_f 0.20 (hexane–EtOAc 2:1, v/v); IR ($CHCl_3$ film) 3424, 1103, 1070 cm^{-1}; $[\alpha]_D^{20}$ −184.3 (*c* 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 1.31 (d, $J = 6$ Hz, 3H, CH_3), 2.28 (d, $J = 1.6$ Hz, 1H, OH), 2.60 (d, $J = 2.4$ Hz, 1H, OH), 3.60–3.67 (m, 2H, *H*-3,4), 4.11–4.18 (m, 1H, H-5), 4.25 (d, $J = 1.2$ Hz, 1H, H-2), 4.61 and 4.73 (ABq, $J = 11.2$ Hz, 2H, $PhCH_2$), 5.53 (d, $J = 1.2$ Hz, 1H, H-1), 7.25–7.46 (m, 10H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 17.7, 69.2, 69.6, 71.98, 71.99, 80.0, 87.4 (C-1), 127.5, 128.2, 128.5, 129.0, 129.2, 131.5, 134.2, 137.5. Anal. Calcd for $C_{19}H_{22}O_4S$: C, 65.87; H, 6.40; S, 9.26. Found: C, 65.80; H, 6.39; S, 9.17.

3.3. Phenyl 3-*O*-benzyl-2-*O*-pivaloyl-1-thio-α-L-rhamnopyranose (4)

A solution of diol **3** (5.0 g, 14.43 mmol) and $(n\text{-}Bu_3Sn)_2O$ (3.67 mL, 7.22 mmol) in benzene (50 mL) was stirred under reflux using a Dean–Stark trap for 10 h and cooled to room temperature. After addition of PivCl (1.95 mL, 15.83 mmol) to the above solution, the reaction mixture was stirred at 60 °C for 3 h, cooled to room temperature, and diluted with EtOAc (100 mL). The combined organic layer was washed with brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 7:1, v/v) to afford compound **4** (4.92 g, 11.43 mmol, 79%) as a colorless amorphous solid, R_f 0.60 (hexane–EtOAc 2:1, v/v); IR ($CHCl_3$ film) 3473, 1728, 1483, 1160, 1111, 1074 cm^{-1}; $[\alpha]_D^{20}$ −43.2 (*c* 1.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 1.21 (s, 9H, 3 × CH_3C), 1.34 (d, $J = 6$ Hz, 3H, CH_3), 2.39 (d, $J = 6.8$ Hz, 1H, OH), 3.61 (t, $J = 9.2$ Hz, 1H, H-4), 3.71 (dd, $J = 2.8$, 9.2 Hz, 1H, H-3), 4.18–4.22 (m, 1H, H-5), 4.43 and 4.71 (ABq, $J = 10.8$ Hz, 2H, $PhCH_2$), 5.40 (br s, 1H, H-1), 5.59 (t, $J = 1.4$ Hz, 1H, H-2), 7.25–7.49 (m, 10H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 17.9, 27.3, 39.1, 69.3, 69.4, 71.4, 72.3, 78.2, 86.6 (*C*-1), 127.9, 128.2, 128.4, 128.7, 129.3, 132.1, 134.0, 137.5, 177.7 (CO). Anal. Calcd for $C_{24}H_{30}O_5S$: C, 66.95; H, 7.02; S, 7.45. Found: C, 67.05; H, 7.01; S, 7.33.

3.4. Phenyl 3-*O*-benzyl-4-*O*-naphthylmethyl-2-*O*-pivaloyl-1-thio-α-L-rhamnopyranose (5)

To a solution of compound **4** (2.18 g, 5.06 mmol) in DMF (20 mL) were added NaH (60%, 243 mg, 6.08 mmol) and 2-bromomethyl naphthalene (1.34 g, 6.06 mmol) at 0 °C and then the ice bath was removed. After being stirred at room temperature for 2 h, the reaction mixture was quenched by the addition of water (10 mL) and extracted with EtOAc (2 × 50 mL). The combined organic layer was washed with satd aq NH_4Cl (3 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 9:1, v/v) to afford compound **5** (2.48 g, 4.34 mmol, 86%) as a colorless oil, R_f 0.38 (hexane–EtOAc 9:1, v/v); IR ($CHCl_3$ film) 1728, 1160, 1103 cm^{-1}; $[\alpha]_D^{20}$ −98.3 (*c* 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 1.21 (s, 9H, 3 × CH_3C), 1.34 (d, $J = 6$ Hz, 3H, CH_3), 3.54 (t, $J = 9.2$ Hz, 1H, H-4), 3.97 (dd, $J = 3.2$, 9.2 Hz, 1H, H-3), 4.28–4.32 (m, 1H, H-5), 4.49 and 4.69 (ABq, $J = 11.2$ Hz, 2H, $PhCH_2$), 4.79 and 5.04 (ABq, $J = 11.2$ Hz, 2H, $PhCH_2$), 5.42 (d, $J = 1.6$ Hz, 1H, H-1), 5.67 (dd, $J = 1.6$, 2.8 Hz, 1H, H-2), 7.04–7.76 (m, 17H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 18.1, 27.1, 38.9, 68.9, 70.0, 71.5, 75.3, 78.7, 79.8, 86.2 (*C*-1), 125.9, 126.0, 126.2, 126.9, 127.6, 127.7, 127.9, 128.0, 128.3, 129.0, 131.9, 133.0, 133.2, 133.9, 135.7, 137.9, 177.3 (CO). Anal. Calcd for $C_{35}H_{38}O_5S$: C, 73.65; H, 6.71; S, 5.62. Found: C, 73.61; H, 6.58; S, 5.53.

3.5. Allyl 2-acetamido-2-deoxy-3-*O*-levulinyl-4,6-*O*-benzylidene-α-D-glucopyranoside (7)

A solution of allyl 2-acetamido-2-deoxy-4,6-*O*-benzylidene-α-D-glucopyranoside (**6**)[13] (4.15 g, 11.88 mmol), levulinic acid (2.07 g, 17.83 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (3.42 g, 17.84 mmol), 4-(dimethylamino)pyridine (436 mg, 3.57 mmol) in CH_2Cl_2 (20 mL) and DMF (20 mL) was stirred at room temperature for 3 h. The reaction mixture was diluted with $CHCl_3$ (100 mL) and washed with satd aq NH_4Cl (2 × 50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (CH_2Cl_2–MeOH 9:1, v/v) to afford compound **7** (4.40 g, 9.83 mmol, 83%) as a colorless oil, R_f 0.53 (CH_2Cl_2–MeOH 9:1, v/v); IR ($CHCl_3$ film) 3273, 1740, 1716, 1659, 1548, 1377, 1095 cm^{-1}; $[\alpha]_D^{20}$ +50.5 (*c* 0.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 1.98 (s, 3H, $COCH_3$), 2.09 (s, 3H, $COCH_3$), 2.50–2.68 (m, 4H), 3.68–3.77 (m, 2H), 3.87–3.99 (m, 2H), 4.16 (dd, $J = 5.2$, 12.8 Hz, 1H), 4.25 (dd, $J = 4.4$, 10.0 Hz, 1H), 4.34–4.40 (m, 1H), 4.87 (d, $J = 3.2$ Hz, 1H, H-1), 5.18–5.36 (m, 3H), 5.49 (s, 1H), 5.80–5.90 (m, 1H, allyl CH), 6.13 (d, $J = 9.2$ Hz, 1H), 7.31–7.44 (m, 5H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 22.8, 27.8, 29.4, 37.6, 52.0, 62.8, 68.4, 68.5, 70.1, 78.9, 97.0 (C-1), 101.1 (PhCH), 117.9, 126.0, 127.9, 128.8, 133.2, 136.9, 170.2 (CO), 172.6 (CO), 205.89 (CO). Anal. Calcd for $C_{23}H_{29}NO_8$: C, 61.73; H, 6.53; N, 3.13. Found: C, 61.93; H, 6.50; N, 3.09.

3.6. Allyl 2-acetamido-2-deoxy-4,6-di-*O*-benzoyl-3-*O*-levulinyl-α-D-glucopyranoside (8)

A solution of compound **7** (4.40 g, 9.83 mmol) and camphorsulfonic acid (457 mg, 1.97 mmol) in CH_2Cl_2

(20 mL) and MeOH (20 mL) was stirred at room temperature for 2 h. The reaction mixture was concentrated in vacuo, diluted with CH_2Cl_2, and washed with satd aq $NaHCO_3$ (2 × 50 mL) and brine (50 mL). The organic phase was dried over $MgSO_4$ and concentrated in vacuo. The residue was dissolved in pyridine (20 mL). After addition of BzCl (2.78 mL, 23.93 mmol) and DMAP (293 mg, 2.61 mmol) to the above solution, the reaction mixture was stirred at room temperature for 5 h, diluted with $CHCl_3$ (100 mL), and washed with 1 N HCl (2 × 50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (CH_2Cl_2–MeOH 20:1, v/v) to afford compound **8** (3.45 g, 6.08 mmol, 62% in two steps) as a colorless amorphous solid, R_f 0.53 (CH_2Cl_2–MeOH 20:1, v/v); IR ($CHCl_3$ film) 3371, 1728, 1279, 1034 cm^{-1}; $[\alpha]_D^{20}$ +73.4 (*c* 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 2.02 (s, 3H, $COCH_3$), 2.04 (s, 3H, $COCH_3$), 2.31–2.62 (m, 4H), 4.05 (dd, $J = 6.0$, 12.4 Hz, 1H), 4.22–4.27 (m, 2H), 4.38 (dd, $J = 5.2$, 12.0 Hz, 1H), 4.44–4.50 (m, 1H), 4.53 (dd, $J = 2.4$, 12.0 Hz, 1H), 4.97 (d, $J = 3.6$ Hz, 1H, H-1), 5.23 (d, $J = 10.4$ Hz, 1H), 5.30 (dd, $J = 1.4$, 17.2 Hz, 1H), 5.46–5.53 (m, 2H), 5.83 (d, $J = 9.6$ Hz, 1H), 5.87–5.97 (m, 1H, allyl CH), 7.40–7.58 (m, 6H, Ar), 7.98 (d, $J = 7.6$ Hz, 2H, Ar), 8.02 (d, $J = 7.6$ Hz, 2H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 23.3, 28.2, 29.6, 37.8, 51.9, 63.0, 68.2, 68.9, 69.4, 71.2, 96.6 (C-1), 118.6, 128.5, 128.6, 129.0, 129.7, 129.8, 130.0, 133.19, 133.21, 133.6, 165.2 (CO), 166.2 (CO), 170.5 (CO), 172.9 (CO), 206.0 (CO). HRMS calcd for $[M+Na]^+$: 590.2002. Found: 590.2006.

3.7. Allyl 2-acetamido-2-deoxy-4,6-di-*O*-benzoyl-α-D-glucopyranoside (9)

To a stirred solution of compound **8** (238 mg, 0.42 mmol) in THF–MeOH (10:1 v/v, 10 mL) was added 80% hydrazine–acetic acid (1:2 v/v, 3 mL) in THF–MeOH (5:1 v/v, 2 mL) at room temperature. After being stirred at room temperature for 30 min, the reaction mixture was concentrated in vacuo. The resulting oil was dissolved in $CHCl_3$ (50 mL), washed with sat. $NaHCO_3$ (2 × 50 mL) and brine (50 mL). The organic phase was dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (CH_2Cl_2–MeOH 20:1, v/v) to afford compound **9** (188 mg, 0.40 mmol, 95%) as a colorless amorphous solid, R_f 0.25 (CH_2Cl_2–MeOH 20:1, v/v); IR ($CHCl_3$ film) 3375, 3305, 1728, 1654, 1552, 1274, 1123, 1029 cm^{-1}; $[\alpha]_D^{20}$ +79.6 (*c* 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 2.04 (s, 3H, $COCH_3$), 3.33 (br s, 1H), 3.97–4.07 (m, 2H), 4.20–4.33 (m, 3H), 4.39 (dd, $J = 5.6$, 12.0 Hz, 1H), 4.56 (dd, $J = 2.8$, 12.0 Hz, 1H), 4.95 (d, $J = 4.0$ Hz, 1H), 5.22–5.35 (m, 3H), 5.88–5.96 (m, 2H), 7.39–8.06 (m, 10H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 23.1, 54.1, 63.4, 68.1, 68.7, 71.5, 72.6, 96.5 (C-1), 118.3, 128.4, 128.42, 129.5, 129.7, 129.73, 130.0, 133.1, 133.3, 133.4, 166.0 (CO), 166.3 (CO), 171.7 (CO). Anal. Calcd for $C_{25}H_{27}NO_8$: C, 63.96; H, 5.80; N, 2.98. Found: C, 63.70; H, 5.72; N, 3.23.

3.8. Allyl 3-*O*-benzyl-4-*O*-naphthylmethyl-2-*O*-pivaloyl-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-benzoyl-α-D-glucopyranoside (10)

To a solution of thioglycoside **9** (133 mg, 0.23 mmol), 1-benzenesulfinyl piperidine (73 mg, 0.34 mmol), and tri-*t*-butylpyrimidine (174 mg, 0.70 mmol) in the presence of activated 4 Å powdered molecular sieves in CH_2Cl_2 (10 mL) at −40 °C under an argon atmosphere was added Tf_2O (59 μL, 0.35 mmol). After 5 min, a solution of the glycosyl acceptor **5** (164 mg, 0.35 mmol) in CH_2Cl_2 (2 mL) was added to the above solution at −40 °C. The reaction mixture was stirred for 1 h at −40 °C, then warmed to 0 °C, diluted with CH_2Cl_2 (50 mL), and filtered. The filtrate was washed with satd aq $NaHCO_3$ (50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 2:1, v/v) to afford disaccharide **10** (185 mg, 0.12 mmol, 85%) as a white foam, R_f 0.25 (hexane–EtOAc 2:1, v/v); IR ($CHCl_3$ film) 3264, 1727, 1274, 1122 cm^{-1}; $[\alpha]_D^{20}$ +22.6 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 0.62 (d, $J = 6.0$ Hz, 3H, L-Rha CH_3), 1.15 (s, 9H, Piv $(CH_3)_3C$), 2.12 (s, 3H, acetyl CH_3), 3.26 (t, $J = 9.6$ Hz, 1H), 3.55–3.60 (m, 1H), 3.94 (dd, $J = 3.2$, 9.6 Hz, 1H), 4.00–4.08 (m, 2H), 4.19–4.23 (m, 2H), 4.34 (dd, $J = 4.8$, 12.0 Hz, 1H), 5.00–4.63 (m, 5H), 4.87–4.89 (m, 3H), 5.13 (br s, 1H), 5.22–5.31 (m, 2H), 5.49 (t, $J = 9.6$ Hz, 1H), 5.86–5.96 (m, 2H), 7.22–8.04 (m, 22H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 17.7, 23.6, 27.1, 39.0, 52.9, 63.1, 68.4, 68.6, 68.8, 69.4, 70.2, 71.3, 74.5, 77.6, 79.4, 79.9, 96.9 (C-1), 100.1 (C-1′), 118.7, 125.7, 125.9, 126.1, 126.5, 127.4, 127.7, 127.8, 127.86, 127.9, 128.2, 128.4, 128.44, 129.5, 129.7, 129.8, 130.1, 132.9, 133.2, 133.22, 133.3, 136.1, 138.5, 165.1 (CO), 166.3 (CO), 170.5 (CO), 178.0 (CO). Anal. Calcd for $C_{54}H_{59}NO_{13}$: C, 69.74; H, 6.39; N, 1.51. Found: C, 69.72; H, 6.14; N, 1.49.

3.9. Allyl 3-*O*-benzyl-2-*O*-pivaloyl-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-benzoyl-α-D-glucopyranoside (11)

To a solution of compound **10** (220 mg, 0.24 mmol) was added dichlorodicyanobenzoquinone (161 mg, 0.71 mmol) in CH_2Cl_2 (4.5 mL) and MeOH (0.25 mL) in two portions over 20 min at 0 °C. After being stirred at room temperature for 2 h, the reaction mixture was

diluted with CH_2Cl_2 (50 mL), washed with satd aq $NaHCO_3$ (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 1:1, v/v) to afford compound **11** (156 mg, 0.20 mmol, 84%) as a white foam, R_f 0.43 (hexane–EtOAc, 1:1, v/v); IR ($CHCl_3$ film) 3273, 1728, 1663, 1279, 1140, 1050 cm^{-1}; $[\alpha]_D^{20}$ +55 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 0.62 (d, $J = 6.0$ Hz, 3H, L-Rha CH_3), 1.15 (s, 9H, Piv $(CH_3)_3C$), 2.10 (s, 3H, acetyl CH_3), 2.16 (br s, 1H), 3.37 (t, $J = 9.6$ Hz, 1H), 3.46–3.50 (m, 1H), 3.69 (dd, $J = 3.2$, 9.6 Hz, 1H), 4.01–4.07 (m, 2H), 4.18–4.24 (m, 2H), 4.34 (dd, $J = 4.8$, 12.0 Hz, 1H), 4.39 (d, $J = 11.2$ Hz, 1H), 4.50–4.60 (m, 3H), 4.88–4.89 (m, 2H), 5.09 (d, $J = 2.4$ Hz, 1H), 5.24–5.32 (m, 2H), 5.49 (t, $J = 9.6$ Hz, 1H), 5.86–5.93 (m, 2H), 7.22–8.04 (m, 15H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 17.4, 23.6, 27.1, 38.9, 52.9, 63.1, 68.4, 68.5, 68.7, 69.2, 70.2, 71.1, 71.7, 80.2, 96.9 ($J_{C-H} = 172$ Hz), 100.4 ($J_{C-H} = 170$ Hz), 118.8, 127.8, 128.0, 128.4, 128.43, 128.5, 129.4, 129.7, 129.8, 130.1, 133.1, 133.15, 133.5, 138.0, 165.2 (CO), 166.2 (CO), 170.5 (CO), 177.9 (CO). Anal. Calcd for $C_{43}H_{51}NO_{13}$: C, 65.39; H, 6.51; N, 1.77. Found: C, 65.50; H, 6.46; N, 1.79.

3.10. 2′-(Benzyloxycarbonyl)benzyl 6-*O*-naphthylmethyl-2,3-di-*O*-benzoyl-β-D-galactofuranoside (13)

A solution of compound **12** (1.91 g, 3.12 mmol) and *n*-Bu_2SnO (931 mg, 3.74 mmol) in benzene (100 mL) was stirred under reflux using a Dean–Stark trap for 10 h. After removal of the solvent in vacuo, the residue was dissolved in DMF (50 mL) and then 2-bromomethyl naphthalene (828 mg, 3.74 mmol) and *n*-Bu_4NI (1.38 g, 3.74 mmol) were added to the reaction mixture. After being stirred at 60 °C for 3 h, the reaction mixture was diluted with EtOAc (100 mL), washed with satd aq NH_4Cl (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 2:1, v/v) to afford compound **13** (1.93 g, 2.56 mmol, 82%) as a colorless oil, R_f 0.35 (hexane–EtOAc 2:1, v/v); IR ($CHCl_3$ film) 3501, 1720, 1262, 1115 cm^{-1}; $[\alpha]_D^{20}$ −11.5 (*c* 0.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 2.76 (d, $J = 7.2$ Hz, 1H), 3.64 (dd, $J = 5.2$, 9.6 Hz, 1H), 3.70 (dd, $J = 6.8$, 9.6 Hz, 1H), 4.29–4.31 (m, 1H), 4.42 (t, $J = 3.6$ Hz, 1H), 4.64 and 4.68 (ABq, $J = 12.0$ Hz, 2H), 5.09 and 5.24 (ABq, $J = 14.4$ Hz, 2H), 5.27 (br s, 2H), 5.41 (br s, 1H), 5.64 (br s, 1H), 5.72 (d, $J = 4.4$ Hz, 1H), 7.24–8.11 (m, 26H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 66.7, 67.2, 69.8, 71.4, 73.5, 77.9, 81.6, 83.5, 105.5 (*C*-1), 125.7, 125.8, 126.1, 126.4, 127.1, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.46, 128.5, 128.6, 129.2, 129.3, 129.9, 130.0, 130.7, 132.5, 133.0, 133.2, 133.4, 133.5, 135.4, 135.9, 140.3, 165.4 (CO), 165.9 (CO), 166.5 (CO). Anal. Calcd for $C_{46}H_{40}O_{10}$: C, 73.39; H, 5.36. Found: C, 73.39; H, 5.31.

3.11. 2′-(Benzyloxycarbonyl)benzyl 6-*O*-naphthylmethyl-2,3,5-tri-*O*-benzoyl-β-D-galactofuranoside (14)

A solution of compound **13** (1.57 g, 2.09 mmol), benzoyl chloride (291 μL, 2.51 mmol), and 4-(dimethylamino)pyridine (77 mg, 0.63 mmol) in Et_3N (2 mL) and CH_2Cl_2 (10 mL) was stirred at room temperature for 30 min. The reaction mixture was quenched by the addition of satd aq NH_4Cl (2 mL) and extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layer was washed with brine (30 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 2:1, v/v) to afford compound **14** (1.71 g, 1.99 mmol, 96%) as a colorless oil, R_f 0.5 (hexane–EtOAc, 2:1, v/v); IR ($CHCl_3$ film) 1728, 1270, 1119 cm^{-1}; $[\alpha]_D^{20}$ −22.1 (*c* 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 3.90 (dd, $J = 6.0$, 10.0 Hz, 1H), 3.96 (dd, $J = 6.0$, 10.0 Hz, 1H), 4.67 and 4.72 (ABq, $J = 12.0$ Hz, 2H), 4.79 (t, $J = 4.4$ Hz, 1H), 5.14 and 5.31 (ABq, $J = 14.4$ Hz, 2H), 5.27 (br s, 2H), 5.48 (br s, 1H), 5.64 (br s, 1H), 5.71 (d, $J = 5.2$ Hz, 1H), 5.92–5.94 (m, 1H), 7.24–8.11 (m, 31H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 66.7, 67.1, 68.6, 71.4, 73.4, 77.7, 81.7, 82.2, 105.4 (C-1), 125.6, 125.8, 126.0, 126.4, 127.1, 127.6, 127.7, 127.9, 128.13, 128.15, 128.2, 128.36, 128.4, 128.6, 129.0, 129.2, 129.8, 129.9, 130.0, 130.7, 132.5, 132.9, 133.1, 133.2, 133.3, 133.4, 135.3, 135.9, 140.2, 165.4 (CO), 165.6 (CO), 165.9 (CO), 166.5 (CO). Anal. Calcd for $C_{53}H_{44}O_{11}$: C, 74.29; H, 5.18. Found: C, 74.31; H, 5.05.

3.12. 2′-Carboxybenzyl 6-*O*-naphthylmethyl-2,3,5-tri-*O*-benzoyl-β-D-galactofuranoside (15)

Compound **14** (1.71 g, 1.99 mmol) was stirred under hydrogen atmosphere using a balloon in the presence of Pd–C (10%, 212 mg) and ammonium acetate (154 mg, 2.00 mmol) as an additive in MeOH–EtOAc (1:1 v/v, 20 mL) at room temperature for 1 h. The reaction mixture was filtered through Celite and the filtrate was concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 1:1, v/v) to afford compound **15** (1.35 g, 1.77 mmol, 89%) as a colorless oil, R_f 0.23 (hexane–EtOAc 2:1, v/v); IR ($CHCl_3$ film) 1724, 1691, 1274, 1115 cm^{-1}; $[\alpha]_D^{20}$ −30.6 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 3.89 (dd, $J = 6.0$, 10.0 Hz, 1H), 3.94 (dd, $J = 6.0$, 10.0 Hz, 1H), 4.68 and 4.72 (ABq, $J = 12.0$ Hz, 2H), 4.77 (dd, $J = 1.2$, 3.6 Hz, 1H), 5.08 and 5.28 (ABq, $J = 14.8$ Hz, 2H), 5.49 (br s, 1H), 5.61 (d, $J = 1.2$ Hz, 1H), 5.67 (d, $J = 5.2$ Hz, 1H), 5.87–5.91 (m, 1H), 7.24–8.11 (m, 26H, Ar); ^{13}C NMR

(100 MHz, $CDCl_3$) δ_C 67.4, 68.5, 71.4, 73.5, 77.7, 81.7, 82.4, 105.6 (C-1), 125.7, 125.9, 126.1, 126.5, 126.9, 127.3, 127.7, 128.0, 128.2, 128.4, 128.5, 129.1, 129.3, 129.9, 129.91, 130.0, 130.1, 131.6, 133.0, 133.2, 133.24, 133.4, 133.5, 135.3, 141.0, 165.6 (CO), 165.8 (CO), 166.0 (CO), 172.2 (CO). Anal. Calcd for $C_{46}H_{38}O_{11}$: C, 72.05; H, 5.00. Found: C, 72.04; H, 4.95.

3.13. 2′-(Benzyloxycarbonyl)benzyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-galactofuranoside (16)

A solution of compound **12** (1.74 g, 2.85 mmol) and *n*-Bu_2SnO (851 mg, 3.42 mmol) in benzene (100 mL) was stirred under reflux using a Dean–Stark trap for 10 h. After removal of the solvent in vacuo, the residue was dissolved in DMF (50 mL) and then benzyl chloride (394 μL, 3.42 mmol) and *n*-Bu_4NI (1.26 g, 3.41 mmol) were added to the reaction mixture. After being stirred at 60 °C for 3 h, the reaction mixture was diluted with EtOAc (100 mL), washed with satd aq NH_4Cl (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 2:1, v/v) to afford compound **16** (1.72 g, 2.45 mmol, 86%) as a colorless oil, R_f 0.35 (hexane–EtOAc 2:1, v/v); IR ($CHCl_3$ film), 1106, 1251, 1654, 1718, 3428 cm^{-1}; $[\alpha]_D^{20}$ +5.0 (*c* 0.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 2.53 (d, $J = 7.2$ Hz, 1H, O*H*), 3.60 (dd, $J = 5.2$, 9.6 Hz, 1H, H-6), 3.66 (dd, $J = 6.8$, 9.6 Hz, 1H, H-6′), 4.23–4.26 (m, 1H, *H*-5), 4.38 (dd, $J = 3.2$, 4.4 Hz, 1H, H-4), 4.51 and 4.55 (ABq, $J = 12.0$ Hz, 2H, PhCH_2), 5.08 and 5.23 (ABq, $J = 14.4$ Hz, 2H, PhCH_2), 5.31 (br s, 2H, PhCH_2), 5.41 (br s, 1H, H-1), 5.61 (d, $J = 1.2$ Hz, 1H, H-2), 5.67 (d, $J = 4.8$ Hz, 1H, H-3), 7.28–8.08 (m, 24H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 66.9, 67.3, 69.9, 71.4, 73.6, 78.0, 81.7, 83.5, 105.6 (C-1), 127.2, 127.75, 127.79, 127.9, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 130.0, 130.1, 130.8, 132.6, 133.6, 133.7, 136.1, 138.1, 140.5, 165.5 (CO), 166.0 (CO), 166.8 (CO). Anal. Calcd for $C_{42}H_{38}O_{10}$: C, 71.78; H, 5.45. Found: C, 71.84; H, 5.33.

3.14. 2′-(Benzyloxycarbonyl)benzyl 6-*O*-naphthylmethyl-2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl-(1→5)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-galactofuranoside (17)

A solution of compound **16** (734 mg, 1.04 mmol) and DTBMP (641 mg, 3.12 mmol) in CH_2Cl_2 (40 mL) in the presence of 4 Å molecular sieves was stirred for 10 min at room temperature and cooled to −78 °C. After addition of Tf_2O (350 μL, 2.08 mmol) to the above solution, compound **15** (877 mg, 1.14 mmol) in CH_2Cl_2 (10 mL) was added drop-wise. After being stirred at −78 °C for a further 1 h, the reaction mixture was warmed to 0 °C over 1 h, quenched by the addition of satd aq $NaHCO_3$ (1 mL), and diluted with CH_2Cl_2 (50 mL). The organic phase was washed with satd aq $NaHCO_3$ (2 × 50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (hexanes–EtOAc–CH_2Cl_2 5:1:1, v/v) to afford compound **17** (1.21 g, 0.92 mmol, 88%) as a colorless oil, R_f 0.53 (hexanes–EtOAc–CH_2Cl_2, 3:1:1, v/v); IR ($CHCl_3$ film) 1723, 1270, 1114 cm^{-1}; $[\alpha]_D^{20}$ −23.2 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 3.82–3.85 (m, 1H), 3.91–3.95 (m, 3H), 4.51–4.61 (m, 4H), 4.63 (t, $J = 4.8$ Hz, 1H), 4.67 (d, $J = 12.8$ Hz, 1H), 5.03–5.07 (m, 2H), 5.21–5.29 (m, 3H), 5.38 (br s, 1H), 5.66–5.67 (m, 2H), 5.71 (d, $J = 1.2$ Hz, 1H), 5.81 (br s, 1H), 5.89 (d, $J = 4.0$ Hz, 1H), 5.95–5.99 (m, 1H), 7.14–8.10 (m, 46H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 66.6, 67.1, 68.7, 69.5, 70.2, 71.3, 72.9, 73.4, 74.0, 77.7, 81.5, 81.7, 82.1, 82.5, 105.3 (C-1 × 2), 122.0, 125.39, 125.4, 125.5, 125.6, 125.8,126.1,126.7, 127.4,127.5, 127.6, 127.7, 127.9, 128.07, 128.14, 128.2, 128.23, 128.3, 128.4, 128.5, 128.8, 128.9, 129.0, 129.1, 129.68,129.7, 129.73, 129.8, 129.9, 130.5,132.4, 132.7, 132.95, 133.0,133.04, 133.2, 133.3, 133.8, 135.3, 135.8, 137.8, 140.2, 146.4, 165.2, 165.3, 165.5 (CO × 2), 165.8 (CO), 166.3 (CO). HRMS calcd for $[M+Na]^+$: 1339.4303. Found: 1339.4307.

3.15. 2′-Carboxybenzyl 6-*O*-naphthylmethyl-2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl-(1→5)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-galactofuranoside (18)

Compound **17** (570 mg, 0.43 mmol) was stirred under hydrogen atmosphere using a balloon in the presence of $Pd(OH)_2$ (20%, 30 mg) and ammonium acetate (17 mg, 0.22 mmol) as an additive in MeOH–EtOAc (1:1 v/v, 20 mL) at room temperature for 5 h. The reaction mixture was filtered through Celite and the filtrate was concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 1:1, v/v) to afford compound **18** (473 mg, 0.38 mmol, 89%) as a colorless oil, R_f 0.45 (hexane–EtOAc 1:1, v/v); IR ($CHCl_3$ film) 1724, 1274, 1115 cm^{-1}; $[\alpha]_D^{20}$ −19.2 (*c* 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 3.80–3.88 (m, 4H), 4.49–4.55 (m, 4H), 4.60 (t, $J = 4.8$ Hz, 1H), 4.65 (d, $J = 12.8$ Hz, 1H), 4.90 and 5.20 (ABq, $J = 14.0$ Hz, 2H), 4.97 (t, $J = 4.4$ Hz, 1H), 5.33 (br s, 1H), 5.57–6.00 (m, 2H), 5.62 (br s, 1H), 5.69 (br s, 1H), 5.81 (d, $J = 4.8$ Hz, 1H), 5.85–5.89 (m, 1H), 7.13–8.05 (m, 41H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 67.5, 68.8, 70.1, 71.4, 73.2, 73.6, 74.3, 77.3, 77.8, 81.6, 82.0, 82.4, 82.6, 105.5 (C-1), 105.6 (C-1), 127.0,127.3, 127.59,127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.4, 128.5, 128.54, 129.1, 129.15, 129.2,129.3, 129.86, 129.88, 129.9, 130.0, 130.1, 131.6, 133.0, 133.1, 133.2, 133.22, 133.3, 133.4, 135.4, 138.0, 140.9, 165.4 (CO), 165.55 (CO), 165.66 (CO), 165.7 (CO), 166.0 (CO), 171.4 (CO). Anal. Calcd for $C_{73}H_{62}O_{18}$: C, 71.44; H, 5.09. Found: C, 71.53; H, 4.93.

3.16. 6-*O*-Naphthylmethyl-2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl-(1→5)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-galactofuranosyl fluoride (19)

A solution of compound **18** (304 mg, 0.25 mmol) and DTBMP (153 mg, 0.74 mmol) in CH_2Cl_2 (20 mL) in the presence of 4 Å molecular sieves was stirred for 10 min at room temperature and cooled to −78 °C. After sequential addition of Tf_2O (63 μL, 0.37 mmol), Deoxofluor (69 μL, 0.37 mmol), and hydrogen fluoride (70% in pyridine, 10 μL, 0.385 mmol) to the above solution, the reaction mixture was stirred at −78 °C for further 1 h, allowed to warm to 0 °C over 1 h, quenched by the addition of satd aq $NaHCO_3$ (1 mL), and diluted with CH_2Cl_2 (50 mL). The organic phase was washed with satd aq $NaHCO_3$ (2 × 30 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (hexane–EtOAc 2:1, v/v) to afford compound **19** (228 mg, 0.21 mmol, 84%) as a colorless oil, R_f 0.45 (hexane–EtOAc 2:1, v/v); IR ($CHCl_3$ film) 1724, 1270, 1115 cm^{-1}; $[\alpha]_D^{20}$ −3.5 (*c* 0.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 3.82–3.90 (m, 4H), 4.49–4.55 (m, 3H), 4.58 and 4.68 (ABq, $J = 12.4$ Hz, 2H), 4.78 (t, $J = 4.0$ Hz, 1H), 4.97 (dd, $J = 3.6$, 5.2 Hz, 1H), 5.62–5.63 (m, 3H), 5.72 (br s, 1H), 5.89 (d, $J =$ 58.4 Hz, 1H, H-1), 5.84–5.88 (m, 2H), 7.15–8.08 (m, 37H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 68.6, 69.6, 71.4, 73.3, 73.5, 73.8, 76.0, 77.6, 80.9 (d, $J = 40$ Hz, C-2), 81.5, 82.2, 85.8, 105.1 (C-1′), 112.4 (d, $J = 225$ Hz, C-1), 125.6, 125.8, 126.0, 126.4, 127.6, 127.7, 127.9, 128.1, 128.2, 128.4, 128.5, 128.58, 128.6, 128.9,129.0, 129.1, 129.9, 129.94, 130.0, 132.9, 133.1, 133.19, 133.24, 133.3, 133.6, 133.7, 135.3, 137.8, 165.1 (CO), 165.4 (CO), 165.55 (CO), 165.6 (CO), 165.9 (CO). Anal. Calcd for $C_{65}H_{55}FO_{15}$: C, 71.29; H, 5.06. Found: C, 71.33; H, 5.01.

3.17. Allyl 6-*O*-naphthylmethyl-2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl-(1→5)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-galactofuranosyl-(1→4)-3-*O*-benzyl-2-*O*-pivaloyl-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-benzoyl-α-D-glucopyranoside (20)

A solution of compound **11** (134 mg, 0.17 mmol), $SnCl_2$ (71 mg, 0.37 mmol), and $AgClO_4$ (78 mg, 0.37 mmol) in Et_2O (10 mL) and CH_2Cl_2 (10 mL) in the presence of 4 Å molecular sieves was stirred for 30 min at room temperature and cooled down to 0 °C. After drop-wise addition of a solution of glycosyl fluoride (205 mg, 0.19 mmol) in Et_2O (5 mL) and CH_2Cl_2 (5 mL) to the above solution at 0 °C, the reaction mixture was stirred for a further 30 min and concentrated to half its volume. After dilution of the concentrated solution with CH_2Cl_2 (50 mL), the organic solution was washed with satd aq $NaHCO_3$ (2 × 30 mL) and brine (30 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (hexane–EtOAc 1:1, v/v) to afford compound **20** (286 mg, 0.15 mmol, 90%) as a white foam, R_f 0.3 (hexane–EtOAc 1:1, v/v); IR ($CHCl_3$ film) 3301, 1728, 1458, 1270, 1119 cm^{-1}; $[\alpha]_D^{20}$ +19.8 (*c* 0.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 0.64 (d, $J = 6.0$ Hz, 3H, L-Rha CH_3), 1.11 (s, 9H, Piv $(CH_3)_3C$), 2.12 (s, 3H, acetyl CH_3), 3.55–3.60 (m, 1H), 3.64–3.68 (m, 2H), 3.74–3.80 (m, 3H), 3.98–4.06 (m, 3H), 4.16–4.30 (m, 3H), 4.35–4.47 (m, 5H), 4.50–4.59 (m, 5H), 4.82–4.84 (m, 2H), 4.92 (d, $J = 3.2$ Hz, 1H), 5.11 (m, 1H), 5.25–5.33 (m, 2H), 5.52–5.57 (m, 4H), 5.64 (br s, 1H), 5.69 (br s, 1H), 5.70–5.78 (m, 2H), 5.85 (d, $J = 10.0$ Hz, 1H), 5.87–5.99 (m, 1H, allyl CH), 6.89–8.08 (m, 52H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 17.9, 23.7, 27.2, 39.0, 52.8, 63.1, 68.1,68.4, 68.9, 69.0, 69.1, 70.2, 70.3, 71.47, 71.5, 73.0, 73.5, 73.6, 75.8, 77.4, 77.7, 77.8, 81.5, 81.6, 82.1, 83.0, 97.0 (C-1), 101.0 (C-1′), 105.2, 106.6, 118.9, 125.6, 125.7, 125.9, 126.2, 127.3, 127.5, 127.60, 127.65, 127.7, 127.90, 127.98, 128.00, 128.04, 128.10, 128.13, 128.26, 128.32, 128.35, 128.40, 128.48, 128.5, 128.7, 128.8, 129.10, 129.18, 129.2, 129.4, 129.5, 129.80, 129.84, 129.90, 129.99, 130.1, 132.9, 133.0, 133.18, 133.23, 133.4, 133.5, 135.6, 137.9, 138.0, 165.0 (CO), 165.1 (CO), 165.3 (CO), 165.6 (CO), 165.7 (CO), 165.9 (CO), 166.3 (CO), 170.4 (CO), 178.3 (CO). Anal. Calcd for $C_{108}H_{105}NO_{28}$: C, 69.55; H, 5.67; N, 0.75. Found: C, 69.45; H, 5.64; N, 0.78.

3.18. 6-*O*-Naphthylmethyl-2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl-(1→5)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-galactofuranosyl-(1→4)-3-*O*-benzyl-2-*O*-pivaloyl-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-benzoyl-α-D-glucopyranose (21)

A solution of compound **20** (78 mg, 0.04 mmol), NaOAc (14 mg, 0.17 mmol), and $PdCl_2$ (15 mg, 0.08 mmol) in 95% aq HOAc (1 mL) was stirred for 12 h at room temperature. The reaction mixture was filtrated through a Celite pad, diluted with EtOAc (50 mL), washed with satd aq $NaHCO_3$ (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (CH_2Cl_2–MeOH 20:1, v/v) to afford compound **21** (54 mg, 0.03 mmol, 71%) as a white foam, R_f 0.33 (CH_2Cl_2–MeOH 20:1, v/v); ^1H NMR (400 MHz, $CDCl_3$) δ_H 0.64 (d, $J = 5.6$ Hz, 3H, L-Rha CH_3), 1.11 (s, 9H, Piv $(CH_3)_3C$), 2.06 (s, 3H, acetyl CH_3), 3.57 (t, $J = 9.2$ Hz, 1H), 3.65–3.68 (m, 2H), 3.76–3.82 (m, 3H), 3.93–4.09 (m, 2H), 4.28–4.60 (m, 12H), 4.76–4.87 (m, 3H), 5.12 (br s, 1H), 5.25 (br s, 1H), 5.55–5.75 (m, 8H), 6.10 (d, $J = 9.6$ Hz, 1H), 6.90–8.07 (m, 52H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 18.0, 23.5, 27.2, 39.0, 53.4, 68.0, 68.1, 69.0, 69.1, 70.2, 70.3, 71.5, 71.54, 73.0 (2), 73.5 (2), 73.6, 75.8, 77.7, 77.8, 81.1, 81.6, 81.7,

82.1, 83.0, 92.2 (C-1), 100.9 (C-1′), 105.2, 106.6, 128.0, 128.1, 128.20, 128.28, 128.33, 128.37, 128.4, 128.5, 128.56, 128.7, 129.1, 129.2, 129.4, 129.6, 129.80, 129.88, 129.92, 129.95, 130.0, 130.1, 132.9, 133.0, 133.2, 133.3, 133.5, 135.5, 137.9, 138.0, 165.1(CO × 2), 165.3 (CO), 165.7 (CO × 2), 166.0 (CO), 166.5 (CO), 171.0 (CO). MALDI-TOFMS calcd for $C_{105}H_{101}NNaO_{28}$ $[M+Na]^+$: 1846.6408. Found: 1846.6321.

3.19. Dibenzyl 6-*O*-naphthylmethyl-2,3,5-tri-*O*-benzoyl-β-D-galactofuranosyl-(1→5)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-galactofuranosyl-(1→4)-3-*O*-benzyl-2-*O*-pivaloyl-α-L-rhamnopyranosyl-(1→3)-2-acetamido-2-deoxy-4,6-di-*O*-benzoyl-α-D-glucopyranosyl phosphate (1)

To a stirred solution of compound **21** (100 mg, 0.05 mmol) in THF (3 mL) was added 2.0 M LDA in THF (55 μL, 0.11 mmol) at −78 °C under an argon atmosphere. The solution was stirred for 30 min and then a solution of tetrabenzyl pyrophosphate (35 mg, 0.06 mmol) in THF (1 mL) was added. After being stirred at −78 °C for further 1 h, the reaction mixture was allowed to warm to 0 °C over 30 min, diluted with EtOAc (50 mL), washed with satd aq $NaHCO_3$ (2 × 50 mL) and brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (CH_2Cl_2–MeOH 20:1, v/v) to afford compound **1** (105 mg, 0.05 mmol, 92%) as a white foam, R_f 0.48 (CH_2Cl_2–MeOH 20:1, v/v); IR ($CHCl_3$ film) 3210, 2953, 2923, 2854, 1725, 1688, 1451, 1270, 1109, 1046 cm^{-1} $[\alpha]_D^{20}$ +8.5 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ_H 0.64 (d, J = 5.6 Hz, 3H, L-Rha CH_3), 1.13 (s, 9H, Piv $(CH_3)_3C$), 1.89 (s, 3H, acetyl CH_3), 3.54–3.59 (m, 2H), 3.66–3.69 (m, 1H), 3.72–3.81 (m, 3H), 3.82–3.90 (m, 2H), 4.22–4.29 (m, 3H), 4.36–4.47 (m, 7H), 4.49–4.59 (m, 2H), 4.75 (d, J = 1.6 Hz, 1H), 4.83 (dd, J = 4.0, 4.8 Hz, 1H), 5.02–5.13 (m, 5H), 5.49 (d, J = 1.6 Hz, 1H), 5.53–5.56 (m, 3H), 5.63–5.68 (m, 3H), 5.71–5.77 (m, 3H), 6.89–8.06 (m, 62H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 17.9, 23.2, 27.2, 39.0, 52.8, 52.9, 62.3, 68.2, 68.9, 69.0, 69.3, 70.1, 70.2 (2), 70.3, 71.4, 71.5, 72.0, 73.5, 75.7, 77.4, 77.67, 77.7, 79.7, 81.6, 81.7, 82.1, 82.9, 97.2 (d, J = 6.0 Hz; J_{C-H} = 179 Hz), 100.7 (J_{C-H} = 172 Hz), 105.2 (J_{C-H} = 181 Hz), 106.6 (J_{C-H} = 181 Hz), 125.7, 125.9, 126.2, 127.4, 127.5, 127.64, 127.66, 127.7, 127.9, 128.0, 128.04, 128.06, 128.1, 128.2, 128.3, 128.4, 128.4, 128.5, 128.7, 128.9, 129.10, 129.14, 129.2, 129.3, 129.4, 129.6, 129.7, 129.8, 129.90, 129.99, 130.00, 130.05, 130.1, 132.9, 133.0, 133.2, 133.2, 133.5, 135.3 (d, J = 6.0 Hz), 135.5 (d, J = 6.0 Hz), 135.6, 137.8, 137.9, 164.9 (CO), 165.1 (CO), 165.3 (CO), 165.6 (CO × 2), 166.0 (CO), 166.2 (CO), 170.8 (CO), 178.1 (CO). MALDI-TOFMS calcd for $C_{119}H_{114}NNaO_{31}P$ $[M+Na]^+$: 2106.7010. Found: 2106.6941.

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References

1. (a) Nettleman, M. D. *JAMA* **2005**, *293*, 2788–2790; (b) Long, R. *CMAJ* **2000**, *163*, 425–428; (c) Pablos-Mendez, A.; Raviglione, M. C.; Laszlo, A.; Binkin, N.; Rieder, H. L.; Bustreo, F.; Cohn, D. L.; Weezenbeek, C. S. B. L.; Kim, S. J.; Chaulet, P.; Nunn, P. *N. Eng. J. Med.* **1998**, *338*, 1641–1649.
2. (a) Brennan, P. J. *Tuberculosis* **2003**, *83*, 91–97; (b) Lowary, T. L. In *Glycoscience: Chemistry and Chemical Biology*; Springer: Berlin, 2001; pp 2005–2080; (c) Chatterjee, D. *Curr. Opin. Chem. Biol.* **1997**, *1*, 579–588; (d) Brennan, P. J.; Nikaido, H. *Annu. Rev. Biochem.* **1995**, *64*, 29–63; (e) Jarlier, V.; Nikaido, H. *FEMS Microbiol. Lett.* **1994**, *123*, 11–18.
3. (a) Daffe, M.; Brennan, P. J.; McNeil, M. *J. Biol. Chem.* **1990**, *265*, 6734–6743; (b) McNeil, M.; Daffe, M.; Brennan, P. J. *J. Biol. Chem.* **1990**, *265*, 18200–18206; (c) Bersa, G. S.; Khoo, K.-H.; McNeil, M. R.; Dell, A.; Morris, H. R.; Brennan, P. *J. Biochem.* **1995**, *34*, 4257–4266; (d) Lee, R. E. B.; Li, W.; Chatterjee, D.; Lee, R. E. *Glycobiology* **2005**, *15*, 139–151.
4. (a) Takayama, K.; Kilburn, J. O. *Antimicrob. Agents Chemother.* **1989**, *33*, 1493–1499; (b) Mikusov, K.; Slayden, R. A.; Bersa, G. S.; Brennan, P. *J. Antimicrob. Chemother.* **1995**, *39*, 2484–2489.
5. (a) Kremer, L.; Dover, L. G.; Morehouse, C.; Hitchin, P.; Everett, M.; Morris, H. R.; Dell, A.; Brennan, P. J.; McNeil, M. R.; Flaherty, C.; Ducan, K.; Besra, G. S. *J. Biol. Chem.* **2001**, *276*, 26430–26440; (b) Pan, F.; Jackson, M.; Ma, Y.; McNeil, M. *J. Bacteriol.* **2001**, *183*, 3991–3998.
6. (a) Crick, D. C.; Mahapatra, S.; Brennan, P. *Glycobiology* **2001**, *11*, 107R–118R; (b) Mikusova, K.; Mikus, M.; Besra, G. S.; Hancock, I.; Brennan, P. J. *J. Biol. Chem.* **1996**, *271*, 7820–7828; (c) Mikusova, K.; Yagi, T.; Stern, R.; McNeil, M. R.; Besra, G. S.; Crick, D. C.; Brennan, P. J. *J. Biol. Chem.* **2000**, *275*, 33890–33897.
7. Belanova, M.; Dianiskova, P.; Brennan, P. J.; Completo, G. C.; Rose, N. L.; Lowary, T. L.; Mikusova, K. *J. Bacteriol.* **2008**, *190*, 1141–1145.
8. Joe, M.; Bai, Y.; Nacario, R. C.; Lowary, T. L. *J. Am. Chem. Soc.* **2007**, *129*, 9885–9901.
9. (a) Pathak, A. K.; Pathak, V.; Suling, W. J.; Gurcha, S. S.; Morehouse, C. B.; Besra, G. S.; Maddry, J. A.; Reynolds, R. C. *Bioorg. Med. Chem.* **2002**, *10*, 923–928; (b) Gandolfi-Donadio, L.; Gallo-Rodriguez, C.; de Lederkremer, R. M. *Can. J. Chem.* **2006**, *84*, 486–491.
10. (a) Gurjar, M. K.; Reddy, L. K.; Hotha, S. *J. Org. Chem.* **2001**, *66*, 4657–4660; (b) Wang, H.; Ning, J. *J. Org. Chem.* **2003**, *68*, 2521–2524.
11. Gandolfi-Donadio, L.; Gallo-Rodriguez, C.; de Lederkremer, R. M. *Carbohydr. Res.* doi:10.1016/j.carres.2008.01.024. Available online January 29, 2008.

12. Gandolfi-Donadio, L.; Gallo-Rodriguez, C.; de Lederkremer, R. M. *J. Org. Chem.* **2003**, *68*, 6928–6934.
13. Wen, X.; Crick, D. C.; Brennan, P. J.; Hultin, P. G. *Bioorg. Med. Chem.* **2003**, *11*, 3579–3587.
14. Groneberg, R. D.; Miyazaki, T.; Stylianides, N. A.; Schulze, T. J.; Stahl, W.; Schreiner, E. P.; Suzuki, T.; Iwabuchi, Y.; Smith, A. L.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1993**, *115*, 7593–7611.
15. Grindley, T. B. *Adv. Carbohydr. Chem. Biochem.* **1998**, *53*, 117–142.
16. David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643–663.
17. Feng, F.; Okuyama, K.; Niikura, K.; Ohta, T.; Sadamoto, R.; Monde, K.; Noguchi, T.; Nishimura, S. I. *Org. Biomol. Chem.* **2004**, *2*, 1617–1623.
18. Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015–9020.
19. Bock, K.; Pedersen, C. *J. Chem. Soc., Perkin Trans. 2* **1974**, 293–297.
20. Lee, Y. J.; Lee, B-. Y.; Jeon, H. B.; Kim, K. S. *Org. Lett.* **2006**, *8*, 3971–3974.
21. Kim, K. S.; Kim, J. H.; Lee, Y. J.; Lee, Y. J.; Park, J. *J. Am. Chem. Soc.* **2001**, *123*, 8477–8481.
22. Kim, K. S.; Kang, S. S.; Seo, Y. S.; Kim, H. J.; Lee, Y. J.; Jeong, K.-S. *Synlett* **2003**, 1311–1314.
23. Lee, Y. J.; Baek, J. Y.; Lee, B.-Y.; Kang, S. S.; Park, H.-S.; Jeon, H. B.; Kim, K. S. *Carbohydr. Res.* **2006**, *341*, 1708–1716.
24. Lal, G. S.; Pez, G. P.; Pesaresi, R. J.; Prozonic, F. M.; Cheng, H. *J. Org. Chem.* **1999**, *64*, 7048–7054.
25. Gelin, M.; Ferriéres, V.; Plusquellec, D. *Eur. J. Org. Chem.* **2000**, 1423–1431.
26. (a) Yuko, N.; Tomoharu, N.; Hironobu, H.; Yoshiaki, N. *Biosci. Biotechnol. Biochem.* **2003**, *67*, 1761–1766; (b) Muller, T.; Danac, R.; Ball, L.; Gurr, S. J.; Fairbanks, A. *Tetrahedron: Asymmetry* **2007**, *18*, 1299–1307.