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Block Synthesis of Tetra- and Hexasaccharides (β-D-Glycero-D-manno-Hepp-(1→4)-[α-L-Rhap-(1→3)-β-D-glycero-D-manno-Hepp-(1→4)]$_n$-α-L-Rhap-OMe (n = 1 and 2)) Corresponding to Multiple Repeat Units of the Glycan from the Surface-Layer Glycoprotein from *Bacillus thermoaerophilus*

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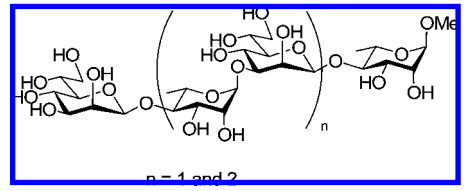

A fully stereocontrolled block synthesis of the title tetra- and hexasaccharides has been achieved taking advantage of the ability of the 4,6-*O*-benzylidene acetal to control the stereochemistry of the β-D-glycero-D-mannoheptopyranoside unit and of a 2,3-*O*-diphenylmethylene acetal to install the α-L-rhamnopyranosidic linkages. Comparison of the spectral data for the hexasaccharide with that of the natural isolate confirms the structure of this very unusual and structurally challenging glycan.

Introduction

In 1995, Kosma and co-workers described the characterization of the surface-layer glycoprotein from *Bacillus thermoaerophilus* and proposed the very unusual disaccharide motif →4)-[α-L-rhamnopyranosyl-(1→3)-β-D-glycero-D-mannoheptopyranosyl-(1→ as the repeating unit of the glycan chain, with the stereochemistry of the β-D-glycero-D-mannoheptopyranoside assigned on the basis of comparison of spectral data with synthetic methyl β-L-glycero-D-mannoheptopyranoside.[1] Having recently described the first stereocontrolled route to β-D-glycero-D-mannoheptopyranosides and their 6-deoxy analogues[2] and applied this chemistry to a linear synthesis of methyl α-L-rhamnopyranosyl-(1→3)-β-D-glycero-D-mannoheptopyranosyl-(1→3)-6-deoxy-β-glycero-D-mannoheptopyranosyl-(1→4)-α-L-rhamnopyranoside, a tetrasaccharide subunit from the *Plesimonas shigelloides* lipopolysaccharide,[3] we selected this oligomer as a proving ground for a block synthesis approach to glycans containing the unusual β-D-glycero-D-mannoheptoside structure.[4,5]

Results and Discussion

Although our previous approach to the synthesis of the key D-glycero-D-mannothioheptopyranoside donor was successful and has subsequently been adopted by others,[6] it suffered from a low yield at the level of the homologation step in which a six-carbon thiomannopyranoside was extended to a seven-carbon system by Swern oxidation and Wittig olefination owing to competing elimination of a benzyloxy group from the 4-position

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(2) Crich, D.; Banerjee, A. *Org. Lett.* **2005**, *7*, 1935–1938.

(3) Crich, D.; Banerjee, A. *J. Am. Chem. Soc.* **2006**, *128*, 8078–8086.

(4) For reviews expounding the difficulties of β-mannoside synthesis and presenting classical and indirect solutions to the problem, see: (a) Barresi, F.; Hindsgaul, O. In *Modern Methods in Carbohydrate Synthesis*; Khan, S. H.; O'Neill, R. A., Eds.; Harwood Academic Publishers: Amsterdam, 1996, pp 251−276. (b) Demchenko, A. V. *Synlett* **2003**, 1225–1240. (c) Pozsgay, V. In *Carbohydrates in Chemistry and Biology*; Ernst, B.; Hart, G. W.; Sinaÿ, P., Eds.; Wiley-VCH: Weinheim, Germany, 2000; Vol. 1, pp 319−343. (d) Gridley, J. J.; Osborn, H. M. I. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1471–1491. (e) Ito, Y.; Ohnishi, Y. In *Glycoscience: Chemistry and Chemical Biology*; Fraser-Reid, B.; Tatsuta, K.; Thiem, J., Eds.; Springer: Berlin, 2001; Vol. 2, pp 1589−1619.

(5) For the direct approach to β-mannopyranoside synthesis and its mechanism, see: (a) Crich, D.; Sun, S. *J. Org. Chem.* **1997**, *62*, 1198–1199. (b) Crich, D.; Sun, S. *Tetrahedron* **1998**, *54*, 8321–8348. (c) Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015–9020. (d) Crich, D.; Banerjee, A.; Li, W.; Yao, Q. *J. Carbohydr. Chem.* **2005**, *24*, 415–424. (e) Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1997**, *119*, 11217–11223. (f) Crich, D.; Chandrasekera, N. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 5386–5389. (g) Jensen, H. H.; Nordstrom, M.; Bols, M. *J. Am. Chem. Soc.* **2004**, *126*, 9205–9213.

(6) Jaipuri, F. A.; Collet, B. Y. M.; Pohl, N. L. *Angew Chem., Int. Ed.* **2008**, *47*, 1707–1710.

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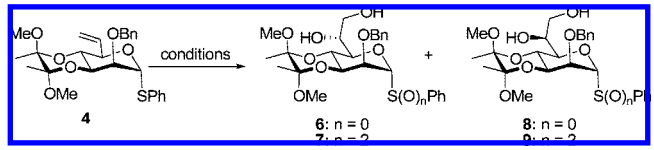
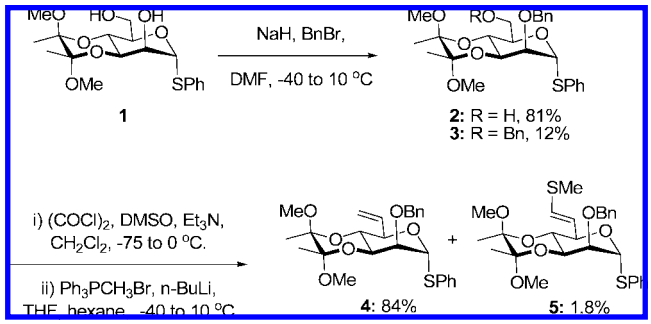
TABLE 1. Osmoylation of Alkene 4



entry	oxidant/ligand	solvent	*T*/°C	**6/8** (yield)	**7/9** (yield)
1	OsO_4/NMO	acetone/H_2O	22	2.2/1 (86%)	1.2/1 (8.40%)
2	AD- β-mix	*t*-BuOH/H_2O	22	1/1.2 (97%)	not detected
3	AD-α-mix	*t*-BuOH/H_2O	0	1.2/1 (93%)	not detected
4	$K_3Fe(CN)_6/OsO_4/(DHQ)_2Pry$	*t*-BuOH/H_2O	22	1.5/1 (96%)	not detected
5	$K_3Fe(CN)_6/OsO_4/(DHQ)_2Pry$	*t*-BuOH/H_2O/$PhCH_3$	0	2.5/1 (96%)	not detected

SCHEME 1. Improved Homologation Procedure



in the course of the Wittig reaction.[2,3] We began, therefore, by seeking to improve the homologation step and were attracted to the use of the Ley bisacetal function[7] for protection of the 3,4-diol functionality on the grounds that elimination would be retarded by the confinement of the putative alkoxide leaving group within a fused bicyclic ring system. Thus, treatment of the bisacetal **1**[8] with sodium hydride and benzyl bromide in DMF from −40 to 10 °C, according to the method described by Ley and others,[9] afforded the 2-*O*-benzyl derivative **2** with good selectivity alongside a minor amount of the 2,6-di-*O*-benzyl system **3**.[10] Swern oxidation followed by standard Wittig homologation then afforded alkene **4** in 84% yield along with a minor amount of a methylthioalkene **5**,[11] representing a distinct improvement over the earlier protocol (Scheme 1).

Catalytic osmoylation of **4** took place with excellent yield but poor selectivity for the formation of **6** and **8**,[12] whatever the conditions employed, in keeping with our previous observations[3] and those of other workers[13] with closely related compounds (Table 1). Some minor overoxidation to the corresponding sulfones **7** and **9** was also observed in these reactions.[14]

Selective monobenzylation with dibutyltin oxide and benzyl bromide[15] of **6** and **8** afforded the corresponding 7-*O*-benzyl-6-ols **10** and **11** in excellent yield. Attempted inversion of the unwanted L,D-alcohol **11** to the desired D,D-isomer **10** by the Mitsunobu protocol[16] was stymied by poor yields, but the desired effect was achieved by recourse to displacement of the 6-*O*-triflate with potassium nitrite with in situ hydrolysis of the corresponding nitroso ester.[17] Hydrolysis of the biacetal function in **10** to give a triol was followed by selective benzylidene acetal formation across the 1,3-diol functionality and introduction of a naphthylmethyl ether[18] onto the remaining alcohol, thereby providing the known glycosyl donor **13**[3] and, incidentally, confirming the D,D-stereochemistry of **6** (Scheme 2).

Two L-rhamnopyranosyl acceptors **16** and **17** were prepared by protection of the corresponding triols as the benzophenone acetals[19] in moderate yield (Scheme 3). Somewhat better yields of **16** and **17** have been reported in the literature for alkylation of **14** and **15** with dichlorodiphenylmethane in pyridine.[19a]

A first glycosidic bond forming reaction involved activation of donor **13** with 4-nitrophenylsulfenyl chloride and silver triflate

(7) Ley, S. V.; Baeschlin, D. K.; Dixon, D. J.; Foster, A. C.; Ince, S. J.; Priepke, H. W. M.; Reynolds, D. J. *Chem. Rev.* **2001**, *101*, 53–80.

(8) Crich, D.; Cai, W.; Dai, Z. *J. Org. Chem.* **2000**, *65*, 1291–1297.

(9) Regioselective monobenzylation of the 2-methoxyphenyl thioglycoside analogue of: Ley, S. V.; Humphries, A. C.; Eick, H.; Downham, R.; Ross, A. R.; Boyce, R. J.; Pavey, J. B. J.; Pietruszka, J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3907–3912.

(10) The regioselectivity of the benzylation reaction was assigned according to the work of Ley with a direct analogue[9] and was confirmed by the subsequent reaction sequence.

(11) Shi, M.; Shen, Y.-M. J. *J. Chem. Res. (S)* **2002**, 422–427.

(12) The stereochemistry of diols **6** and **8** can be determined based on comparison of the double doublet representing H5 with literature values Thus, the L,D-series (**8**) has a the smaller $^3J_{5,6}$ of 2.0 Hz when compared to the $^3J_{5,6}$ coupling of 6.0 Hz observed in the D,D-series (**6**). In addition the 6- and 7-OH signals for **6** resonate downfield (δ 3.16 and 2.20, respectively) relative to those for **8** (δ 2.66 and 1.85, respectively). Read, J. A.; Ahmed, R. A.; Tanner, M. E. *Org. Lett.* **2005**, *7*, 2457–2460.

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(15) (a) David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643–663. (b) David, S. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Dekker: New York, 1997; pp 69−86.

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(17) Adapted from (a) Crich, D.; Vinogradova, O. *J. Am. Chem. Soc.* **2007**, *129*, 11756–11765. (b) Lattrell, R.; Lohaus, G. *Liebigs Ann. Chem.* **1974**, 901–920. (c) Moriarty, R. M.; Zhuang, H.; Penmasta, R.; Liu, K.; Awasthi, A. K.; Tuladhar, S. M.; Rao, M. S. C.; Singh, V. K. *Tetrahedron Lett.* **1993**, *34*, 8029–8032. (d) Binkley, R. W. *J. Org. Chem.* **1991**, *56*, 3892–3896. (e) Binkley, R. W. *J. Carbohydr. Chem.* **1994**, *13*, 111–123. (f) Dong, H.; Pei, Z.; Ramstroem, O. *J. Org. Chem.* **2006**, *71*, 3306–3309. (g) Albert, R.; Dax, K.; Link, R. W.; Stuetz, A. E. *Carbohydr. Res.* **1983**, *118*, C5–C6.

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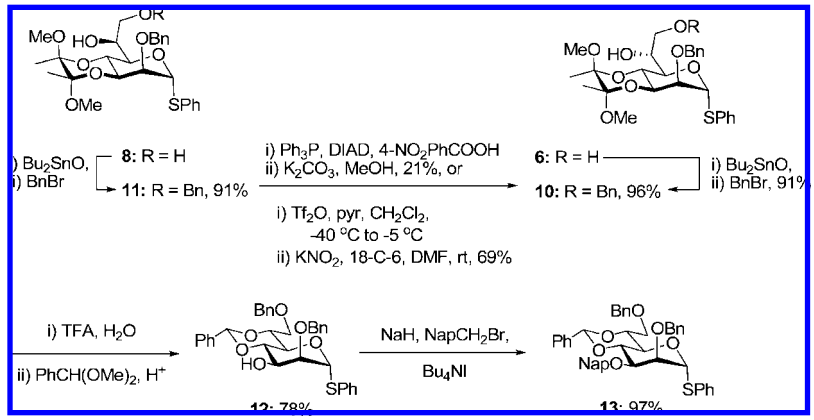
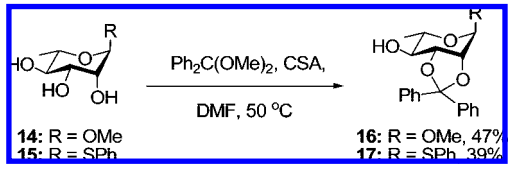
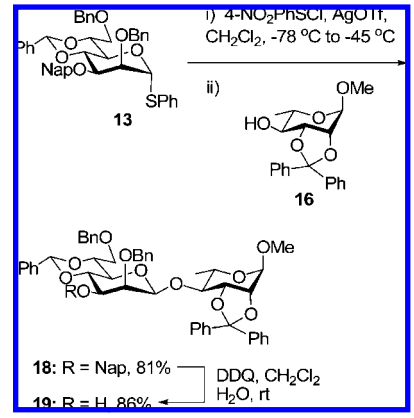
SCHEME 2. Synthesis of Heptosyl Donor 13



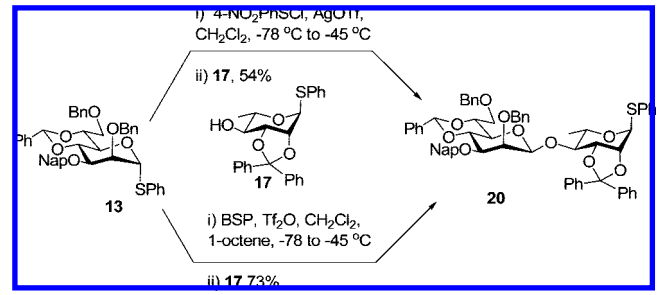
SCHEME 3. Rhamnosyl Acceptor Preparation



SCHEME 4. Upstream Disaccharide Synthesis



SCHEME 5. Disaccharide Donor Synthesis



in dichloromethane at −78 °C to give the corresponding glycosyl triflate followed by addition of the acceptor **16** when disaccharide **18** was obtained in 81% yield and exquisite β-selectivity, in keeping with our previous observations in the benzylidene protected D-glycero-D-mannoheptoside series. The 4-nitrophenylsulfenyl chloride/silver triflate protocol[20] is a convenient variant on benzenesulfenyl triflate activation protocol[21] that employs a commercial, stable sulfenyl chloride. The anomeric stereochemistry of the newly formed glycosidic bond is readily assigned on the basis of the shielded, upfield nature of the heptoside H5 resonance (δ 2.63), something that is highly characteristic of 4,6-*O*-benzylidene-protected β-mannosides and which carries over to corresponding benzylidene acetals of the β-D-glycero-D-mannoheptosides. Confirmation of this anomeric stereochemistry derives from the anomeric 159.7 Hz $^1J_{H1,C1}$ coupling constant.[22] Removal of the naphthylmethyl ether with dichlorodicyanoquinone in wet dichloromethane gave the glycosyl acceptor **19** in good yield (Scheme 4).

An analogous protocol was then applied to the coupling of donor **13** with the thioglycoside-containing acceptor **17** to give the thiodisaccharide **20**, again with exquisite β-selectivity (for the heptopyranoside: δ_{H5} 2.60, $^1J_{H1,C1}$ 159.0 Hz). Unfortunately, yields were lower with acceptor **17** than with the corresponding methyl glycoside **16**, maximizing at 54% when 1.2 equiv of the sulfenyl chloride was employed. However, the 1-benzenesulfinyl piperidine (BSP)/trifluoromethanesulfonic anhydride protocol proved superior when the activation was conducted in the presence of 1-octene as a sacrificial olefin, resulting in a 73% yield of the desired disaccharide (Scheme 5).

The tetrasaccharide **21**, comprising two iterations of the *Bacillus thermoaerophilus* glycan repeating unit was then assembled by coupling of the disaccharide acceptor **19** with the disaccharide donor **20** on activation with *N*-iodosuccinimide and silver triflate in excellent yield and α-selectivity. The 4-nitrophenylsulfenyl chloride/silver triflate protocol was also attempted but only gave the target compound in 26% yield. In addition to the two anomeric resonances characterizing the preinstalled β-mannoheptoside linkages, the ^{13}C NMR spectrum of the tetrasaccharide contained resonances at δ 93.9 and 98.1 with $^1J_{CH}$ of 168.7 and 172.3 Hz, indicative of the α-nature for the two rhamnoside linkages. Finally, global deprotection of **21** was achieved cleanly by hydrogenolysis over palladium on charcoal leading to the isolation of the target tetrasaccharide **22** in 85% yield (Scheme 6).

The synthesis of the hexasaccharide **25** began with removal of the naphthylmethyl protecting group from tetrasaccharide **21** to give the acceptor **23** and was followed by NIS/AgOTf-mediated coupling with the disaccharide donor **20** to give the hexasaccharide **24** in 64% yield as a single anomer. The α-nature of the rhamnopyranosidic linkage formed in this glycosylation again rested on the one-bond CH coupling constant

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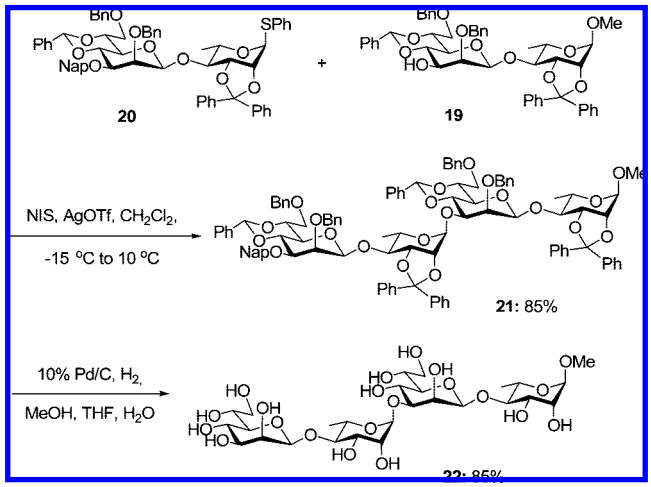
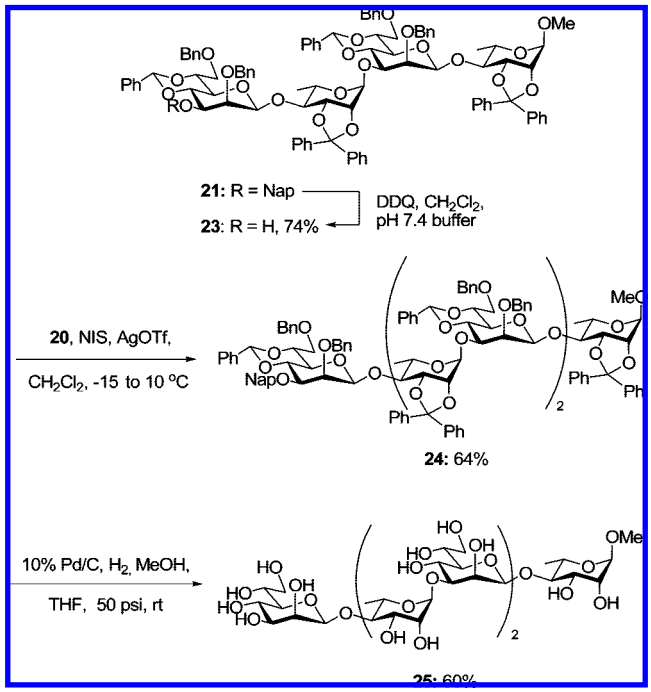
SCHEME 6. Tetrasaccharide Synthesis



SCHEME 7. Hexasaccharide Synthesis



at the anomeric center of the newly formed glycosidic bond (167 Hz). Global deprotection was again achieved by hydrogenolysis, affording the target hexasaccharide in 60% yield (Scheme 7).

The spectral data for the central residues in hexasaccharide **25** were compared to those reported for the natural isolate and were found to show a very high degree of concordance (Supporting Information), thereby confirming the structure proposed by Kosma and co-workers.

Conclusion

A block synthesis of the target hexasaccharide has been achieved and confirms the very rare β-D-glycero-D-mannoheptopyranoside linkage at the heart of this glycan.

Experimental Section

General Experimental. Peak assignments in the NMR spectra were made in the usual manner with the assistance of phase-sensitive COSY-45 and phase-sensitive NOESY experiments.

Phenyl 2-*O*-Benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannopyranoside (2) and Phenyl 2,6-Di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannopyranoside (3). To a cooled (−40 °C) solution of diol **1**[8] (12.24 g, 31.67 mmol) in dry DMF (140 mL) was added benzyl bromide (4.20 mL, 35.4 mmol) followed by 60% NaH in mineral oil (2.57 g, 64.3 mmol). The resultant mixture was stirred for 1 h at −40 °C, then for 16 h at −10 °C. The reaction mixture was poured into water and extracted with CH_2Cl_2. The collected organic phase was further washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel chromatography (AcOEt/hexane = 1/4 to 1/3, then AcOEt/CH_2Cl_2 = 1/3 to 1/2) to afford the monobenzylated ether **2** (12.21 g, 25.6 mmol, 81%): $[\alpha]^{24}_D = +221.3$ (*c* 1.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43−7.41 (m, 4 H), 7.35−7.26 (m, 6 H), 5.48 (s, 1 H), 4.93 (d, 1 H, J = 11.5 Hz), 4.68 (d, 1 H, J = 11.5 Hz), 4.29 (t, 1 H, J = 10.0 Hz), 4.25−4.22 (m, 1 H), 4.08 (dd, 1 H, J = 2.5, 9.5 Hz), 3.99 (br s, 1 H), 3.85−3.77 (m, 2 H), 3.33 (s, 3 H), 3.30 (s, 3 H), 1.90 (br s, 1 H), 1.37 (s, 3 H), 1.34 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 134.2, 132.0, 129.3, 128.5, 128.2, 127.8, 100.3, 99.9, 87.8, 77.7, 73.4, 72.2, 69.6, 64.1, 61.7, 48.3, 48.1, 18.0; HRMS *m*/*z* calcd for $C_{25}H_{32}O_7NaS$, 499.1766 [M + Na^+]; found $C_{25}H_{32}O_7NaS$, 499.1761; and **3**[8] (1.51 g, 3.90 mmol, 12%): $[\alpha]^{23}_D = +172.2$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51−7.46 (m, 4 H), 7.36−7.24 (m, 11 H), 5.59 (s, 1 H), 4.94 (d, 1 H, J = 12.5 Hz), 4.74 (d, 1 H, J = 12.0 Hz), 4.66 (d, 1 H, J = 11.5 Hz), 4.55 (d, 1 H, J = 11.5 Hz), 4.50−4.48 (m, 1 H), 4.36−4.32 (m, 1 H), 4.13−4.10 (m, 1 H), 4.03 (s, 1 H), 3.88−3.84 (m, 2 H), 3.58 (s, 3 H), 3.25 (s, 3 H), 1.40 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.83, 138.81, 134.6, 132.0, 129.2, 128.5, 128.4, 128.0, 127.74, 127.71, 127.67, 127.5, 100.3, 99.9, 87.6, 77.9, 73.6, 73.0, 72.0, 69.8, 69.0, 64.2, 48.3, 48.2, 18.12, 18.09; HRMS *m*/*z* calcd for $C_{32}H_{42}NO_7NaS$, 584.2682 [M + NH_4^+]; found $C_{32}H_{42}NO_7NaS$, 584.2674; calcd for $C_{32}H_{38}O_7NaS$, 589.2236 [M + Na^+]; found $C_{32}H_{38}O_7NaS$, 589.2238.

Phenyl 2-*O*-Benzyl-6,7-dideoxy-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannohepto-6-enopyranoside (4) and Phenyl 2-*O*-Benzyl-6,7-dideoxy-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-1-thia-α-D-mannohepto-(*E*)-7-methylthio-6-enopyranoside (5). To a cooled (−75 °C) solution of oxalyl chloride (1.07 mL, 12.46 mmol) in dry CH_2Cl_2 (30 mL) was added a solution of DMSO (1.80 mL, 25.34 mmol) in dry CH_2Cl_2 (3 mL). After stirring for 10 min at −75 °C, a solution of alcohol **2** (2.95 g, 6.19 mmol) in CH_2Cl_2 (10 mL + 1 mL rinse) was added dropwise. The mixture was stirred for 15 min at −75 °C, then for 45 min at −60 °C, and then for 45 min at −45 °C. At this stage, Et_3N (6.80 mL, 48.92 mmol) was added dropwise, after which stirring was continued for 45 min at −45 °C, before the reaction mixture was allowed to warm to 0 °C over 2 h. The reaction mixture was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated, and the residue was dried for 12 h at −20 °C in vacuum before it was taken up in THF (9 mL + 2 mL rinse) and added to a −40 °C stirred solution of the Wittig reagent formed by addition of *n*-BuLi in hexane (1.80 M, 7.5 mL, 13.50 mmol) at 0 °C to a suspension of Ph_3PCH_3Br (5.00 g, 14.00 mmol) in THF (30 mL) and cooling to −40 °C. The resulting mixture was stirred for 1.5 at −40 °C, then warmed to 10 °C over 2.5 h before it was poured into water and extracted with CH_2Cl_2. The collected organic phase was further washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel chromatography (AcOEt/hexane = 1/15) to furnish alkene **4** (2.45 g, 5.17 mmol, 84%): $[\alpha]^{24}_D = +251.7$ (*c* 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45−7.41 (m, 4 H), 7.35−7.25 (m, 6 H), 6.02−5.95 (m, 1 H), 5.52 (s, 1 H), 5.45−5.42 (m, 1 H), 5.27−5.24 (m, 1 H), 4.91 (d, 1 H, J = 12.0 Hz), 4.71 (d, 1 H, J = 12.0 Hz), 4.63 (t, 1 H, J = 7.5 Hz), 4.09−4.03 (m, 2 H), 3.99 (m, 1 H), 3.33 (s, 3 H), 3.26 (s, 3 H), 1.38 (s, 3 H), 1.34 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 134.8, 134.0, 131.6, 129.2, 128.5, 128.2, 127.8, 127.6, 118.1, 100.2,

100.0, 87.6, 77.8, 73.2, 72.3, 69.8, 67.8, 48.2, 48.1, 18.1, 18.0; HR-ESI *m/z* calcd for $C_{26}H_{32}O_6NaS$, 495.1817 [M + Na^+]; found $C_{26}H_{32}O_6NaS$, 495.1826; and alkene **5** (58.1 mg, 112 μmol, 1.8%): $[\alpha]^{23}_D$ = +218.3 (*c* 0.97, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43−7.38 (m, 4 H), 7.34−7.24 (m, 6 H), 6.45 (dd, 1 H, *J* = 1.0, 15.0 Hz), 5.47 (s, 1 H), 5.45 (dd, 1 H, *J* = 6.5, 15.5 Hz), 4.89 (d, 1 H, *J* = 12.5 Hz), 4.70 (d, 1 H, *J* = 12.0 Hz), 4.65 (t, 1 H, *J* = 7.5 Hz), 4.05−4.00 (m, 2 H), 3.96 (m, 1 H), 3.32 (s, 3 H), 3.25 (s, 3 H), 2.24 (s, 3 H), 1.36 (s, 3 H), 1.33 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 134.8, 131.6, 129.8, 129.3, 128.5, 128.2, 127.8, 127.6, 120.4, 100.2, 100.0, 87.7, 77.8, 73.3, 72.4, 69.7, 68.0, 48.2, 48.0, 18.1, 18.0, 14.6; HR-ESI *m/z* calcd for $C_{27}H_{34}O_6NaS_2$, 541.1695 [M + Na^+]; found $C_{27}H_{34}O_6NaS_2$, 541.1675.

Phenyl 2-*O*-Benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-1-thia-α-D-mannoheptopyranoside (6), Phenyl 2-*O*-Benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-1-sulfonyl-α-D-mannoheptopyranoside (7), Phenyl 2-*O*-Benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-L-glycero-1-thia-α-D-mannoheptopyranoside (8), and Phenyl 2-*O*-Benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-L-glycero-1-sulfonyl-α-D-mannoheptopyranoside (9). Method 1: To a solution of alkene **4** (345 mg, 730 μmol) in 8/1 acetone/H_2O (9 mL), chilled in an ice−water bath, were added NMO (139 mg, 1.2 mmol) and OsO_4 (13.0 mg, 5 μmol). After stirring for 7 h, the reaction was quenched with a solution of sodium sulfite and extracted with AcOEt. The collected organic phase was further washed with brine, dried over Na_2SO_4, and concentrated. The residue was subjected to silica gel chromatography (AcOEt/CH_2Cl_2 = 1/4, then AcOEt/hexane = 1/1 and AcOEt/CH_2Cl_2 = 2/5) to afford **6** (219.3 mg, 433 μmol, 59%): $[\alpha]^{24}_D$ = +240.3 (*c* 0.94, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43−7.40 (m, 4 H), 7.35−7.26 (m, 6 H), 5.43 (s, 1 H), 4.91 (d, 1 H, *J* = 12.0 Hz), 4.67 (d, 1 H, *J* = 12.0 Hz), 4.37 (t, 1 H, *J* = 10.0 Hz), 4.26 (dd, 1 H, *J* = 6.0, 10.0 Hz), 4.07 (dd, 1 H, *J* = 3.0, 10.0 Hz), 3.96−3.93 (m, 2 H), 3.70−3.63 (m, 2 H), 3.33 (s, 3 H), 3.31 (s, 3 H), 3.16 (d, 1 H, OH, *J* = 3.0 Hz), 2.20 (t, 1 H, OH, *J* = 6.5 Hz), 1.36 (s, 3 H), 1.33 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 133.7, 132.2, 129.4, 128.5, 128.2, 128.1, 127.9, 100.3, 100.2, 87.8, 77.5, 73.5, 73.4, 71.2, 69.4, 67.1, 63.2, 48.6, 48.3, 18.1, 18.0; HR-ESI *m/z* calcd for $C_{26}H_{34}O_8NaS$, 529.1872 [M + Na^+]; found $C_{26}H_{34}O_8NaS$, 529.1859; **7** (18.3 mg, 34 μmol, 4.6%): $[\alpha]^{23}_D$ = +148.7 (*c* 0.78, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, 2 H, *J* = 7.5 Hz), 7.69 (t, 1 H, *J* = 7.5 Hz), 7.58 (t, 2 H, *J* = 7.5 Hz), 7.44 (d, 2 H, *J* = 7.0 Hz), 7.37−7.31 (m, 3 H), 5.00 (d, 1 H, *J* = 11.5 Hz), 4.72 (s, 1 H), 4.67 (d, 1 H, *J* = 11.0 Hz), 4.61 (d, 1 H, *J* = 3.0 Hz), 4.52−4.49 (m, 2 H), 4.35 (t, 1 H, *J* = 9.0 Hz), 3.79−3.75 (m, 1 H), 3.57−3.52 (m, 2 H), 3.35 (s, 3 H), 3.33 (s, 3 H), 3.27 (br s, 1 H, OH), 2.23 (br s, 1 H, OH), 1.37 (s, 3 H), 1.35 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 136.7, 134.6, 129.5, 129.3, 128.6, 128.4, 128.1, 100.3, 100.1, 93.0, 74.7, 74.1, 73.9, 71.9, 69.1, 66.1, 62.4, 48.6, 48.4, 18.0, 17.9; HR-ESI *m/z* calcd for $C_{26}H_{34}O_{10}NaS$, 561.1770 [M + Na^+]; found $C_{26}H_{34}O_{10}NaS$, 561.1748; **8** (101.0 mg, 199 μmol, 27%): $[\alpha]^{24}_D$ = +232.2 (*c* 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, 2 H, *J* = 7.5 Hz), 7.38−7.28 (m, 8 H), 5.52 (s, 1 H), 4.95 (d, 1 H, *J* = 12.0 Hz), 4.67 (d, 1 H, *J* = 11.5 Hz), 4.42 (t, 1 H, *J* = 10.0 Hz), 4.14 (dd, 1 H, *J* = 2.0, 10.0 Hz), 4.08 (dd, 1 H, *J* = 3.0, 10.0 Hz), 3.97−3.95 (m, 1 H), 3.94−3.90 (m, 1 H), 3.50 (br s, 2 H), 3.33 (s, 3 H), 3.32 (s, 3 H), 2.66 (d, 1 H, OH, *J* = 6.0 Hz), 1.85 (br s, 1 H, OH), 1.36 (s, 3 H), 1.33 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 133.3, 132.1, 129.5, 128.6, 128.2, 127.9, 100.3, 100.0, 87.6, 77.3, 73.5, 72.9, 69.7, 68.8, 65.1, 63.4, 48.3, 18.1, 18.0; HR-ESI *m/z* calcd for $C_{26}H_{34}O_8NaS$, 529.1872 [M + Na^+]; found $C_{26}H_{34}O_{10}NaS$, 529.1874; **9** (15.1 mg, 28 μmol, 3.8%): $[\alpha]^{23}_D$ = +135.8 (*c* 0.67, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, 2 H, *J* = 8.0 Hz), 7.70 (t, 1 H, *J* = 7.5 Hz), 7.59 (t, 2 H, *J* = 8.0 Hz), 7.44 (d, 2 H, *J* = 7.0 Hz), 7.37−7.30 (m, 3 H), 5.03 (d, 1 H, *J* = 11.0 Hz), 4.81 (s, 1 H), 4.67 (d, 1 H, *J* = 11.0 Hz), 4.60 (d, 1 H, *J*= 3.0 Hz), 4.49−4.45 (m, 1 H), 4.41−4.37(m, 2 H), 3.89 (m, 1 H), 3.51−3.44 (m, 2 H), 3.35 (s, 3 H), 3.32 (s, 3 H), 2.10 (br s, 1 H, OH), 1.72 (br s, 1 H, OH), 1.37 (s, 3 H), 1.33 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 136.9, 134.7, 129.6, 128.9, 128.6, 128.5, 128.1, 100.1, 100.0, 93.2, 76.8, 74.7, 71.9, 69.2, 68.9, 64.6, 62.0, 48.4, 48.3, 17.9; HR-ESI *m/z* calcd for $C_{26}H_{34}O_{10}NaS$, 561.1770 [M + Na^+]; found $C_{26}H_{34}O_{10}NaS$, 561.1746.

Method 2: To a mixture of alkene **4** (1.52 g, 3.2 mmol) in 1/1 *t*-BuOH/H_2O (32 mL) were added toluene (2.5 mL), K_2CO_3 (1.31 g, 9.7 mmol), and $K_3Fe(CN)_6$ (3.29 g, 10.0 mmol). After stirring for 10 min, the mixture was cooled to 0 °C followed by addition of $(DHQ)_2Pyr$ (29.1 mg, 0.033 mmol) and a solution of OsO_4 in *t*-BuOH (2.5 wt %, 161 μL). After the mixture was stirred for 24 h, additional *t*-BuOH/H_2O (8 mL, 1/1), K_2CO_3 (344 mg, 2.5 mmol), and $K_3Fe(CN)_6$ (832 mg, 2.5 mmol) were added. Stirring was continued for another 24 h before the reaction mixture was diluted with CH_2Cl_2, washed with saturated aqueous $NaSO_3$, and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was subjected to silica gel chromatography (AcOEt/CH_2Cl_2 = 1/4) to give **6** (1.12 g, 2.2 mmol, 68%) and **8** (455 mg, 0.9 mmol, 28%).

Phenyl 2,7-Di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-1-thia-α-D-mannoheptopyranoside (10). To a solution of diol **6** (1.69 g, 3.33 mmol) in anhydrous toluene (80 mL) was added Bu_2SnO (957 mg, 3.84 mmol) after which the reaction mixture was heated to reflux in a Dean−Stark apparatus. After 2 h, the resulting clear solution was cooled to room temperature and concentrated under reduced pressure. The residue was dissolved in DMF (30 mL) under N_2, and benzyl bromide (0.48 mL, 4.04 mmol) and CsF (1.07 g, 7.06 mmol) were added. The resulting mixture was stirred for 16 h at room temperature under N_2, diluted with CH_2Cl_2, and washed with aqueous KF and brine. The organic phase was collected, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (AcOEt/hexane = 1/6) to yield ether **10** (1.90 g, 3.19 mmol, 96%): $[\alpha]^{24}_D$ = +186.5 (*c* 1.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41−7.36 (m, 4 H), 7.34−7.23 (m, 11 H), 5.47 (s, 1 H), 4.89 (d, 1 H, *J* = 12.5 Hz), 4.67 (d, 1 H, *J* = 12.0 Hz), 4.53 (d, 1 H, *J* = 12.0 Hz), 4.48 (d, 1 H, *J* = 12.5 Hz), 4.36 (t, 1 H, *J* = 10.0 Hz), 4.20 (dd, 1 H, *J* = 5.0, 10.0 Hz), 4.13−4.10 (m, 1 H), 4.03 (dd, 1 H, *J* = 3.0, 10.5 Hz), 3.93−3.92 (m, 1 H), 3.57 (d, 2 H, *J* = 5.0 Hz), 3.30 (s, 3 H), 3.23 (s, 3 H), 2.84 (d, 1 H, OH, *J* = 2.5 Hz), 1.33 (s, 3 H), 1.28 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 138.5, 134.3, 131.6, 129.3, 128.6, 128.2, 128.1, 127.9, 127.8, 127.7, 100.3, 100.0, 87.5, 77.5, 73.6, 73.3, 72.8, 71.0, 69.6, 65.9, 48.5, 48.3, 18.1, 18.0; HR-ESI *m/z* calcd for $C_{33}H_{40}O_8NaS$, 619.2342 [M + Na^+]; found $C_{33}H_{40}O_8NaS$, 619.2323.

Phenyl 2,7-Di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-L-glycero-1-thia-α-D-mannoheptopyranoside (11). Following the protocol for **10**, diol **8** (1.16 g, 2.29 mmol) gave rise to ether **11** (1.24 g, 2.08 mmol, 91%): $[\alpha]^{24}_D$ = +198.7 (*c* 0.97, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, 2 H, *J* = 7.5 Hz), 7.36−7.22 (m, 13 H), 5.56 (s, 1 H), 4.92 (d, 1 H, *J* = 12.0 Hz), 4.69 (d, 1 H, *J* = 11.5 Hz), 4.48−4.40 (m, 3 H), 4.15−4.13 (m, 2 H), 4.06 (dd, 1 H, *J* = 2.5, 10.0 Hz), 3.95 (br s, 1 H), 3.38 (t, 1 H, *J* = 10.5 Hz), 3.31−3.29 (m, 7 H), 2.15 (br s, 1 H, OH), 1.36 (s, 3 H), 1.31 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 138.3, 134.1, 131.5, 129.2, 128.6, 128.5, 128.2, 127.9, 127.8, 127.6, 100.3, 99.9, 87.3, 77.3, 73.5, 73.3, 71.8, 71.3, 69.9, 67.6, 63.1, 48.2, 18.0; HR-ESI *m/z* calcd for $C_{33}H_{40}O_8NaS$, 619.2342 [M + Na^+]; found $C_{33}H_{40}O_8NaS$, 619.2333.

Formation of Phenyl 2,7-Di-*O*-benzyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-D-glycero-1-thia-α-D-mannoheptopyranoside (10) by Stereochemical Inversion of 11. Method 1: To a solution of alcohol **11** (267.9 mg, 450 μmol), 4-nitrobenzoic acid (155 mg, 924 μmol), and triphenylphosphine (238 mg, 910 μmol), cooled at 0 °C, in THF (125 mL) was added diisopropyl azodicarboxylate (177 μL, 899 μmol). The reaction mixture was allowed to reach ambient temperature and was stirred for 12 h before it was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ and brine. The residue was subjected to silica gel

chromatography to give ester (73.1 mg, 98 μmol, 22%), which was treated with K_2CO_3 (45.8 mg, 331 μmol) in 2/1 MeOH/THF (3 mL). The resulting mixture was stirred for 16 h at ambient temperature under N_2, then concentrated under reduced pressure. The solid was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, filtered, concentrated, and purified by silica gel chromatography (AcOEt/hexane = 1/5) to afford **10** (55.4 mg, 93 μmol, 95%).

Method 2: To a chilled (−40 °C) solution of alcohol **11** (478.7 mg, 802 μmol) in CH_2Cl_2 (12 mL) were added anhydrous pyridine (163 μL, 2.0 mmol) and Tf_2O (240 μL, 1.45 mmol, 1.8 equiv) after which the reaction mixture was stirred for 10 min at −40 °C, then warmed to −5 °C over 80 min, then was poured into cold 0.2 N HCl and extracted with CH_2Cl_2. The collected organic phase was further washed with cold aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The resulting residue was dissolved in dry DMF (10 mL), and 18-C-6 (57 mg, 0.22 mmol) and KNO_2 (460 mg, 5.4 mmol) were added. After stirring for 13 h, more 18-C-6 (256.3 mg, 0.97 mmol) and KNO_2 (324 mg, 3.8 mmol) were added. Stirring was continued for 71 h before the reaction mixture was poured into 1 N aqueous K_2CO_3 and stirred for 2 h and extracted with CH_2Cl_2. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel chromatography (AcOEt/hexane = 1/5) to afford alcohol **10** (331 mg, 556 μmol, 69%).

Phenyl 2,7-Di-*O*-benzyl-4,6-*O*-benzylindene-D-glycero-1-thia-α-D-mannoheptopyranoside (12). To a solution of 1,2-diacetal **10** (2.21 g, 3.7 mmol) in CH_2Cl_2 (30 mL) was added a 10/1 mixture of TFA/H_2O (15 mL). The resulting mixture was stirred for 40 min at ambient temperature under N_2 before the volatiles were removed under reduced pressure and residue was purified by silica gel chromatography (AcOEt/CH_2Cl_2 = 1/1 to 3/2) to give triol (1.60 g, 3.3 mmol, 89%), which was dissolved in dry CH_2Cl_2 (36 mL) and treated with camphorsulfonic acid (52.2 mg, 0.23 mmol) and benzaldehyde dimethyl acetal (2.4 mL, 16 mmol). After stirring for 14 h at room temperature under N_2, the mixture was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was subjected to flash chromatography on silica gel to afford benzylidene **12** (1.64 g, 2.9 mmol, 87%): $[\alpha]^{23}_D$ = +144.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54−7.53 (m, 2 H), 7.41−7.24 (m, 18 H), 5.68 (s, 1 H), 5.62 (s, 1 H), 4.77 (d, 1 H, *J* = 11.5 Hz), 4.66 (d, 1 H, *J* = 11.5 Hz), 4.53 (d, 1 H, *J* = 12.5 Hz), 4.48 (d, 1 H, *J* = 12.0 Hz), 4.14−4.01 (m, 5 H), 3.58−3.51 (m, 2 H), 2.44 (d, 1 H, *OH*, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 137.5, 137.4, 133.7, 131.9, 129.3, 128.9, 128.5, 128.4, 128.3, 127.8, 127.7, 126.7, 101.9, 86.0, 79.9, 78.8, 78.7, 73.7, 73.5, 69.4, 65.7; HRMS *m/z* calcd for $C_{34}H_{34}O_6NaS$, 593.1974 [M + Na^+]; found $C_{34}H_{34}O_6NaS$, 593.1962.

Phenyl 2,7-Di-*O*-benzyl-4,6-*O*-benzylindene-3-*O*-(2-naphthalenylmethyl)-D-glycero-1-thia-α-D-mannoheptopyranoside (13). To a solution of alcohol **12** (1.60 g, 2.8 mmol) in dry DMF (24 mL), cooled in an ice−water bath, was added 60% NaH in mineral oil (230 mg, 5.8 mmol). After stirring for 20 min, tetrabutylammonium iodide (106 mg, 0.29 mmol) and 2-(bromomethyl)naphthalylene (843 mg, 3.7 mmol) were added, and the resulting mixture was stirred for 12.5 h in the dark at room temperature under N_2. At this point, MeOH (2.0 mL) was added, followed by neutralization with acidic resin to pH 6.0. The solid was filtered off, and the filtrate was concentrated under vacuum. The residue was dissolved in CH_2Cl_2 and washed with aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (AcOEt/hexane = 1/8 to 1/6) to yield ether **13**[3] (1.94 g, 2.7 mmol, 91%): $[\alpha]^{24}_D$ = +110.0 (*c* 0.80, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87−7.82 (m, 3 H), 7.76−7.74 (m, 1 H), 7.62−7.60 (m, 2 H), 7.49−7.46 (m, 3 H), 7.44−7.22 (m, 18 H), 5.80 (s, 1 H), 5.60 (s, 1 H), 4.98 (d, 1 H, *J* = 12.0 Hz), 4.84 (d, 1 H, *J* = 12.5 Hz), 4.80 (d, 1 H, *J* = 12.5 Hz), 4.76 (d, 1 H, *J* = 12.5 Hz), 4.57 (d, 1 H, *J* = 12.5 Hz), 4.51 (d, 1 H, *J* = 13.0 Hz), 4.42 (t, 1 H, *J* = 8.5 Hz), 4.19−4.12 (m, 2 H), 4.09−4.04 (m, 2 H), 3.63 (d, 1 H, *J* = 11.0 Hz), 3.57 (dd, 1 H, *J* = 5.5, 12.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 137.9, 136.1, 133.8, 133.6, 133.2, 131.8, 129.3, 129.1, 128.7, 128.5, 128.4, 128.2, 127.9, 127.8, 127.7, 126.6, 126.3, 126.1, 125.9, 101.4, 86.8, 78.8, 78.4, 77.9, 76.7, 73.7, 73.4, 73.3, 69.5, 66.4; HR-ESI *m/z*: calcd for $C_{45}H_{42}O_6NaS$, 733.2600 [M+Na^+]; Found $C_{45}H_{42}O_6NaS$, 733.2561.

Methyl 2,3-*O*-Diphenylmethylene-α-L-rhamnopyranoside (16). Triol **14**[23] (1.43 g, 8.0 mmol), benzophenone dimethyl acetal[24] (3.65 g, 16.0 mmol), and camphorsulfonic acid (308.4 mg, 1.39 mmol) were dissolved in dry DMF (20 mL). The mixture was stirred in a 50 °C water bath in a rotary evaporator for 8 h under the reduced pressure (27 mmHg) to remove methanol formed during the reaction, then was poured into a saturated solution of $NaHCO_3$ in H_2O, and extracted with AcOEt. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by flash chromatography on silica gel (AcOEt/hexane = 1/5to1/4) to afford **16**[19a] (1.29 g, 3.8 mmol, 47%): $[\alpha]^{24}_D$ = −71.6 (*c* 0.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53−7.51 (m, 4 H), 7.34−7.27 (m, 6 H), 5.02 (s, 1 H), 4.28 (t, 1 H, *J* = 6.5 Hz), 4.06 (d, 1 H, *J* = 5.5 Hz), 3.71−3.66 (m, 1 H), 3.42−3.39 (m, 1 H), 3.38 (s, 3 H), 2.28 (br s, 1 H, *OH*), 1.27 (d, 3 H, *J* = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 142.7, 128.4, 128.3, 126.3, 126.2, 109.8, 98.3, 79.1, 76.1, 74.1, 66.2, 55.2, 17.3; HR-ESI *m/z* calcd for $C_{20}H_{22}O_5Na$, 365.1365 [M + Na^+]; found $C_{20}H_{22}O_5Na$, 365.1353.

Phenyl 2,3-*O*-Diphenylmethylene-1-thia-α-L-rhamnopyranoside (17). Following the protocol for **16**, treatment of thioglycoside **15**[25] (1.60 g, 6.2 mmol) with benzophenone dimethyl acetal[24] (2.84 g, 12.5 mmol) and camphorsulfonic acid (81 mg, 0.35 mmol) furnished alcohol **17**[19a] (1.03 g, 2.4 mmol, 39%): $[\alpha]^{24}_D$ = −191.0 (*c* 1.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54−7.47 (m, 6 H), 7.46−7.25 (m, 9 H), 5.91 (s, 1 H), 4.34 (dd, 1 H, *J* = 5.5, 7.0 Hz), 4.29 (d, 1 H, *J* = 6.0 Hz), 4.14−4.09 (m, 1 H), 3.45−3.40 (m, 1 H), 2.14 (br s, 1 H), 1.19 (d, 3 H, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.2, 142.9, 133.6, 132.3, 129.3, 128.5, 128.4, 127.9, 126.2, 126.0, 109.8, 83.8, 79.3, 77.1, 74.9, 67.2, 17.3; HR-ESI *m/z* calcd for $C_{25}H_{24}O_4NaS$, 443.1293 [M + Na^+]; found $C_{25}H_{24}O_4NaS$, 443.1277.

Methyl 2,7-Di-*O*-benzyl-4,6-*O*-benzylindene-3-*O*-(2-naphthalenylmethyl)-D-glycero-β-D-mannoheptopyranosyl-(1→4)-2,3-*O*-(diphenylmethylene)-α-L-rhamnopyranoside (18). A flask, charged with thioheptoside **13** (206.4 mg, 290 μmol), TTBP (240.1 mg, 967 μmol), silver triflate (232 mg, 903 μmol), and 4 Å molecular sieves (500 mg), was dried under vacuum for 1 h with the exclusion of light. Then dry CH_2Cl_2 (7 mL) was added, and the resulting mixture was stirred for 0.5 h at −78 °C before 4-nitrobenzenesulfenyl chloride (112.0 mg, 591 μmol) was added in one portion as a solid. After stirring for 10 min at −78 °C, the mixture was warmed to −45 °C, and stirring continued for 15 min before the reaction mixture was recooled to −78 °C. A solution of methyl rhamnoside **16** (130 mg, 380 μmol) in CH_2Cl_2 (1 mL + 0.5 mL rinse) then was added dropwise. The reaction mixture was stirred for 30 min at −78 °C, then warmed to −45 °C, and stirring continued for 3 h. Saturated aqueous $NaHCO_3$ was added, and after filtration of the solid, the filtrate was further washed with aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (AcOEt/$PhCH_3$ = 1/40 to 1/30) to afford disaccharide **18** (221.1 mg, 234 μmol, 81%) as a white foam: $[\alpha]^{24}_D$ = −59.5

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(*c* 0.63, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.80−7.78 (m, 3 H), 7.68−7.56 (m, 1 H), 7.52−7.27 (m, 25 H), 7.07−7.05 (m, 3 H), 5.71 (s, 1 H), 5.02 (s, 1 H), 4.97 (d, 1 H, J = 12.5 Hz), 4.88 (d, 1 H, J = 12.0 Hz), 4.85 (d, 1 H, J = 13.0 Hz), 4.78 (d, 1 H, J = 13.0 Hz), 4.54 (d, 1 H, J = 12.5 Hz), 4.50 (d, 1 H, J = 12.0 Hz), 4.38 (s, 1 H), 4.23 (dd, 1 H, J = 6.0, 7.5 Hz), 4.18 (t, 1 H, J = 9.5 Hz), 4.10 (t, 1 H, J = 8.0 Hz), 4.03−4.02 (m, 2 H), 3.65−3.60 (m, 1 H), 3.53−3.50 (m, 2 H), 3.39 (s, 3 H), 3.34 (dd, 1 H, J = 7.5, 11.5 Hz), 3.27 (dd, 1 H, J = 7.5, 10.0 Hz), 2.63 (t, 1 H, J = 9.5 Hz), 1.19 (d, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.2, 143.1, 138.8, 138.5, 137.9, 133.5, 133.2, 129.0, 128.9, 128.7, 128.6, 128.4, 128.1, 127.9, 127.8, 126.6, 126.4, 126.3, 126.2, 126.1, 125.8, 109.4, 102.3 (J_{C1-H1} = 159.7 Hz), 101.2, 98.0 (J_{C1-H1} = 174.6 Hz), 80.8, 79.1, 78.9, 78.0, 77.8, 76.5, 76.2, 75.0, 73.6, 72.5, 69.5, 68.7, 64.6, 55.2, 17.8; HR-ESI *m*/*z* calcd for $C_{59}H_{58}O_{11}Na$, 965.3877 [M + Na^+]; found $C_{59}H_{58}O_{11}Na$, 965.3904.

Methyl 2,7-Di-*O*-benzyl-4,6-O-benzylindene-D-glycero-*β*-D-mannoheptopyranosyl-(1→4)-2,3-*O*-(diphenylmethylene)-α-L-rhamnopyranoside (19). To a heterogenerous mixture of **18** (252.2 mg, 267 μmol) in 9/1 CH_2Cl_2/H_2O (6.6 mL) was added DDQ (96.0 mg, 423 μmol). The reaction mixture was stirred for 3 h at ambient temperature under N_2, diluted with CH_2Cl_2, and washed with aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (AcOEt/hexane = 1/4 to 1/3) to furnish alcohol **19** (185.2 mg, 231 μmol, 86%) as a white foam: $[\alpha]^{24}_D$ = −88.1 (*c* 0.1.1, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.52−7.48 (m, 6 H), 7.41−7.22 (m, 18 H), 7.15 (t, 1 H, J = 7.5 Hz), 5.60 (s, 1 H), 5.05 (s, 1 H), 5.02 (d, 1 H, J = 11.5 Hz), 4.68 (d, 1 H, J = 12.0 Hz), 4.58 (s, 1 H), 4.55 (d, 1 H, J = 12.5 Hz), 4.52 (d, 1 H, J = 12.5 Hz), 4.35 (dd, 1 H, J = 6.0, 7.5 Hz), 4.06−3.99 (m, 3 H), 3.77 (t, 1 H, J = 9.5 Hz), 3.68−3.62 (m, 2 H), 3.49 (dd, 1 H, J = 1.5, 11.5 Hz), 3.39 (s, 3 H), 3.72−3.32 (m, 2 H), 2.60 (t, 1 H, J = 9.0 Hz), 2.37 (br s, 1 H, *OH*), 1.21 (d, 3 H, J = 6.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.2, 138.5, 138.4, 137.5, 129.2, 128.7, 128.6, 128.5, 128.4, 128.2, 127.9, 126.6, 126.2, 126.1, 125.9, 109.5, 102.1, 101.6, 98.0, 80.6, 79.2, 79.0, 78.6, 78.5, 76.5, 75.8, 73.6, 71.1, 69.5, 68.3, 64.5, 55.2, 17.9; HR-ESI *m*/*z* calcd for $C_{48}H_{50}O_{11}Na$, 825.3251 [M + Na^+]; found $C_{48}H_{50}O_{11}Na$, 825.3207.

2,7-Di-*O*-benzyl-4,6-*O*-benzylindene-3-*O*-(2-naphthalenylmethyl)-D-glycero-*β*-D-mannoheptopyranosyl-(1→4)-2,3-*O*-diphenylmethylene-1-thia-α-L-rhamnopyranoside (20). Method 1: A mixture of thioheptoside **13** (90.1 mg, 127 μmol), TTBP (70.9 mg, 285 μmol), and AgOTf (81.6 mg, 318 μmol) in CH_2Cl_2 (3 mL) in the presence of 4 Å molecular sieves (290 mg) was stirred for 0.5 h at −78 °C before 4-nitrobenzenesulfenyl chloride (29.6 mg, 156 μmol) was added as a solid. After stirring for 10 min, the reaction mixture was warmed to −45 °C and stirred for 10 min before it was recooled to −78 °C followed by the addition of a solution of thiorhamnoside **17** (64.8 mg, 154 μmol) in CH_2Cl_2 (1 mL + 0.5 mL rinse). The resulting mixture was stirred for 4 h at −78 °C, and then saturated aqueous $NaHCO_3$ was added to quench the reaction, and the solid was filtered off. The filtrate was washed with saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (AcOEt/$PhCH_3$ = 1/40) to afford disaccharide **20** (70.1 mg, 69 μmol, 54%): $[\alpha]^{23}_D$ = −115.5 (*c* 0.74, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.83−7.80 (m, 3 H), 7.73−7.70 (m, 1 H), 7.54−7.28 (m, 30 H), 7.06−7.04 (m, 3 H), 5.89 (s, 1 H), 5.72 (s, 1 H), 4.99 (d, 1 H, J = 12.5 Hz), 4.94 (d, 1 H, J = 12.5 Hz), 4.90 (d, 1 H, J = 13.0 Hz), 4.83 (d, 1 H, J = 12.5 Hz), 4.54 (d, 1 H, J = 12.0 Hz), 4.50 (d, 1 H, J = 12.5 Hz), 4.31 (s, 1 H), 4.26 (d, 1 H, J = 5.5 Hz), 4.22−4.18 (m, 2 H), 4.11−4.04 (m, 2 H), 4.04 (d, 1 H, J = 2.5 Hz), 3.52 (dd, 1 H, J = 3.0, 10.0 Hz), 3.49 (d, 1 H, J = 10.0 Hz), 3.59−3.29 (m, 2 H), 2.60 (t, 1 H, J = 10.0 Hz), 1.14 (d, 3 H, J = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.12, 143.07, 138.8, 138.5, 137.9, 136.1, 133.5, 133.2, 132.3, 129.4, 129.1, 128.6, 128.5, 128.4, 128.13, 128.07, 127.96, 127.90, 127.86, 126.6, 126.5, 126.4, 126.1, 125.8, 125.6, 109.4, 102.3 (J_{C1-H1} = 159.0 Hz), 101.2, 83.9 (J_{C1-H1} = 167.2 Hz), 81.2, 78.9, 78.8, 78.0, 77.9, 77.0, 76.1, 75.0, 73.6, 72.6, 69.5, 68.6, 66.3, 17.6; HR-ESI *m*/*z* calcd for $C_{64}H_{60}O_{10}NaS$, 1043.3805 [M + Na^+]; found $C_{64}H_{60}O_{10}NaS$, 1043.3755.

Method 2: A mixture of thioheptoside **13** (535.6 mg, 753 μmol), TTBP (298.1 mg, 1.2 mmol), and BSP (168.5 mg, 805 μmol) in CH_2Cl_2 (15 mL) in the presence of 4 Å molecular sieves (500 mg) was stirred for 0.5 h at ambient temperature. Then the mixture was cooled to −60 °C, and Tf_2O (156 μL, 940 μmol) was added dropwise. After stirring for 6 min at −78 °C, 1-octene (2.0 mL, 12.7 mmol) was added, and stirring continued for 5 min. The reaction mixture was cooled to −78 °C followed by the addition of a solution of thiorhamnoside **17** (480.0 mg, 1.1 mmol) in CH_2Cl_2 (3 mL + 0.5 mL rinse). The resulting mixture was stirred for 1 h at −78 °C before saturated aqueous $NaHCO_3$ was added to quench the reaction, and the solid was filtered off. The filtrate was washed with saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (AcOEt/$PhCH_3$ = 1/50) to afford disaccharide **20** (561.0 mg, 549 μmol, 73%).

Methyl 2,7-Di-*O*-benzyl-4,6-*O*-benzylindene-3-*O*-(2-naphthalenylmethyl)-D-glycero-*β*-D-mannoheptopyranosyl-(1→4)-2,3-*O*-(diphenylmethylene)-α-L-rhamnopyranosyl-(1→3)-2,7-di-*O*-benzyl-4,6-*O*-benzylindene-D-glycero-*β*-D-mannoheptopyranosyl-(1→4)-2,3-*O*-(diphenylmethylene)-α-L-rhamnopyranoside (21). A mixture of alcohol **19** (90.0 mg, 112 μmol) and thioheptoside **20** (135.3 mg, 132 μmol) in CH_2Cl_2 (6 mL) in the presence of 4 Å molecular sieves (320 mg) was stirred for 50 min at ambient temperature under N_2 atmosphere. Then the mixture was cooled to −15 °C, and NIS (38.4 mg, 170 μmol) and AgOTf (16.9 mg, 66 μmol) were subsequently added. The reaction mixture was stirred for 2.5 h, while the reaction temperature was increased to 5 °C. The solids were filtered off, and the filtrate was washed with saturated aqueous $Na_2S_2O_3$ containing $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (AcOEt/$PhCH_3$ = 1/20 to 1/15) to afford tetrasaccharide **21** (164.2 mg, 96 μmol, 85%): $[\alpha]^{23}_D$ = −86.6 (*c* 1.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.80−7.76 (m, 3 H), 7.68−7.66 (m, 1 H), 7.57−7.19 (m, 46 H), 7.15−7.01 (m, 7 H), 5.70 (s, 1 H), 5.60 (s, 1 H), 5.07 (s, 1 H), 5.01 (s, 1 H), 4.85 (d, 1 H, J = 12.0 Hz), 4.83 (d, 1 H, J = 12.0 Hz), 4.77−4.64 (m, 4 H), 4.56−4.48 (m, 5 H), 4.34 (dd, 1 H, J = 5.5, 7.0 Hz), 4.30 (t, 2 H, J = 6.5 Hz), 4.14 (t, 1 H, J = 9.5 Hz), 4.11−4.04 (m, 3 H), 4.02−3.92 (m, 4 H), 3.91−3.86 (m, 1 H), 3.83 (dd, 1 H, J = 6.0, 9.5 Hz), 3.70−3.66 (m, 1 H), 3.52 (d, 1 H, J = 9.5 Hz), 3.47 (d, 1 H, J = 10.0 Hz), 3.43−3.41 (m, 4 H), 3.37−3.33 (m, 2 H), 3.28 (dd, 1 H, J = 7.5, 11.0 Hz), 3.23 (dd, 1 H, J = 7.5, 10.0 Hz), 2.67 (t, 1 H, J = 9.5 Hz), 2.46 (t, 1 H, J = 9.5 Hz), 1.23 (d, 1 H, J = 6.5 Hz), 1.03 (d, 1 H, J = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.19, 143.15, 143.11, 143.04, 143.07, 138.5, 138.4, 138.1, 138.0, 137.6, 136.1, 133.5, 133.1, 129.2, 129.0, 128.66, 128.63, 128.6, 128.5, 128.45, 128.41, 128.39, 128.35, 128.2, 128.12, 128.09, 127.98, 127.90, 127.8, 126.6, 126.44, 126.38, 126.3, 126.0, 125.9, 125.82, 125.77, 109.6, 109.3, 102.5 (J_{C1-H1} = 161.8 Hz), 102.4 (J_{C1-H1} = 160.5 Hz), 101.6, 101.1, 98.1 (J_{C1-H1} = 172.3 Hz), 93.9 (J_{C1-H1} = 168.7 Hz) 81.0, 80.3, 79.2, 79.1, 78.96, 78.92, 77.9, 77.7, 76.5, 76.4, 75.6, 75.1, 74.9, 74.5, 74.0, 73.9, 73.5, 72.2, 69.6, 69.4, 69.1, 68.7, 65.0, 64.6, 55.2, 17.9, 17.5; ESI-HRMS *m*/*z* calcd for $C_{106}H_{104}O_{21}Na$, 1735.6968 [M + Na^+]; found 1735.7017.

Methyl D-Glycero-*β*-D-mannoheptopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)-D-glycero-*β*-D-mannoheptopyranosyl-(1→4)-α-L-rhamnopyranoside (22). To a solution of tetrasaccharide **21** (37.5 mg, 22 μmol) in 4/4/1 MeOH/THF/H_2O (4.5 mL) were added AcOH (13.0 μL, 227 μmol) and 10% Pd/C (84.6 mg). The mixture was purged with H_2 six times and stirred for 84 h at ambient temperature under 1 atm of H_2. The catalyst was filtered off, and the filtrate was concentrated. The residue was dissolved in H_2O and washed with AcOEt. The aqueous layer was concentrated to

give tetrasaccharide **22** (13.2 mg, 19 μmol, 85%): $[\alpha]^{23}_D = -104.0$ (*c* 0.45, MeOH); ^{1}H NMR (500 MHz, D_2O) δ 4.83 (d, 1 H, *J* = 1.5 Hz), 4.72 (s, 1 H), 4.71 (s, 1 H), 4.55 (d, 1 H, *J* = 1.5 Hz), 4.13 (d, 1 H, *J* = 1.8 Hz), 3.94−3.83 (m, 5 H), 3.78 (dd, 1 H, *J* = 2.0, 4.0 Hz), 3.71−3.47 (m, 13 H), 3.30 (dd, 1 H, *J* = 3.0, 9.5 Hz), 3.26−3.24 (m, 4 H), 1.22 (d, 3 H, *J* = 6.0 Hz), 1.18 (d, 3 H, *J* = 6.0 Hz); ^{13}C NMR (125 MHz, D_2O) δ 100.98 (J_{C1-H1} = 172.1 Hz), 100.86 (J_{C1-H1} = 161.5 Hz), 100.78 (J_{C1-H1} = 161.3 Hz), 96.3 (J_{C1-H1} = 173.0 Hz),, 79.5, 79.2, 77.1, 76.2, 76.1, 73.4, 72.5, 70.8, 70.6, 70.5, 70.4, 68.3, 67.7, 67.3, 66.4, 66.2, 62.2, 54.9, 17.1; ESI-HRMS *m*/*z* calcd for $C_{27}H_{48}O_{21}Na$, 731.2586 [M + Na^+]; found $C_{27}H_{48}O_{21}Na$, 731.2585.

Methyl 2,7-Di-*O*-benzyl-4,6-*O*-benzylindene-D-glycero-β-D-mannoheptopyranosyl-(1→4)-2,3-*O*-(diphenylmethylene)-α-L-rhamnopyranosyl-(1→3)-2,7-di-*O*-benzyl-4,6-*O*-benzylindene-D-glycero-β-D-mannoheptopyranosyl-(1→4)-2,3-*O*-(diphenylmethylene)-α-L-rhamnopyranoside (23). To a mixture of tetrasaccharide **21** (180.1 mg, 106 μmol) in 15/3/5 CH_2Cl_2/H_2O/phosphate buffer (pH = 7.4) (9.2 mL) was added DDQ (38.6 mg, 170 μmol). The mixture was stirred for 2.5 h at ambient temperature under N_2, before another portion of DDQ (34.5 mg, 152 μmol) was added. After the mixture was stirred for another 2 h, it was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$ and brine. The collected organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was subjected to silica gel chromatography to furnish alcohol **23** (123.6 mg, 79 μmol, 74%) as white foam: $[\alpha]^{23}_D = -96.5$ (*c* 0.71, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53−7.45 (m, 10 H), 7.40−7.02 (m, 40 H), 5.59 (s, 1 H), 5.58 (s, 1 H), 5.07 (s, 1 H), 5.02 (s, 1 H), 4.85 (d, 1 H, *J* = 12.0 Hz), 4.84 (d, 1 H, *J* = 12.0 Hz), 4.68 (d, 1 H, *J* = 12.0 Hz), 4.53−4.44 (m, 7 H), 4.41 (dd, 1 H, *J* = 5.5, 7.5 Hz), 4.35 (dd, 1 H, *J* = 5.5, 7.0 Hz), 4.09−3.99 (m, 5 H), 3.95 (t, 1 H, *J* = 10.0 Hz), 3.92−3.88 (m, 2 H), 3.83 (dd, 1 H, *J* = 3.5, 10.5 Hz), 3.81−3.64 (m, 2 H), 3.60−3.56 (m, 1 H), 3.52 (dd, 1 H, *J* = 1.5, 11.0 Hz), 3.44 (dd, 1 H, *J* = 1.5, 11.0 Hz), 3.41 (s, 3 H), 3.37−3.26 (m, 4 H), 2.67 (t, 1 H, *J* = 9.5 Hz), 2.44 (t, 1 H, 9.5 Hz), 2.30 (d, 1 H, *J* = 9.0 Hz, *OH*), 1.23 (d, 1 H, *J* = 6.5 Hz), 1.03 (d, 1 H, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.23, 143.19, 143.15, 143.13, 138.5, 138.4, 138.3, 138.1, 137.6, 129.2, 129.1, 128.8, 128.7, 128.62, 128.59, 128.56, 128.52, 128.49, 128.45, 128.41, 128.2, 128.1, 128.0, 127.94, 127.89, 126.7, 126.5, 126.4, 126.3, 126.0, 109.6, 109.4, 102.6, 102.2, 101.6, 98.1, 93.9, 81.1, 80.2, 79.2, 79.1, 79.03, 78.96, 78.6, 78.0, 76.6, 76.4, 75.6, 75.3, 74.9, 73.9, 73.8, 73.64, 73.60, 71.0, 69.7, 69.4, 69.1, 68.4, 64.9, 64.6, 55.3, 17.9, 17.6; ESI-HRMS *m*/*z* calcd for $C_{95}H_{96}O_{21}Na$, 1595.6342 [M + Na^+]; found 1595.6427.

Methyl 2,7-Di-*O*-benzyl-4,6-*O*-benzylindene-3-*O*-naphthalenylmethyl)-D-glycero-β-D-mannoheptopyranosyl-(1→4)-2,3-*O*-(diphenylmethylene)-α-L-rhamnopyranosyl-(1→3)-2,7-di-*O*-benzyl-4,6-*O*-benzylindene-D-glycero-β-D-mannoheptopyranosyl-(1→4)-2,3-*O*-(diphenylmethylene)-α-L-rhamnopyranosyl-(1→3)-2,7-di-*O*-benzyl-4,6-*O*-benzylindene-D-glycero-β-D-mannoheptopyranosyl-(1→4)-2,3-*O*-(diphenylmethylene)-α-L-rhamnopyranoside (24). A solution of thioglycoside **20** (106.2 mg, 104 μmol) and alcohol **23** (121.6 mg, 77 μmol) in CH_2Cl_2 (8 mL) was stirred for 30 min in the presence of 4 Å molecular sieves at ambient temperature under N_2 before it was cooled to −15 °C and treated with NIS (29.9 mg, 133 μmol) and AgOTf (27.4 mg, 106 μmol). The resulting mixture was stirred for 1.5 h, while the temperature was increased to 10 °C. The solid was filtered off, and the filtrate was washed with saturated aqueous $Na_2S_2O_3$ containing $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (AcOEt/$PhCH_3$ = 1/18) to afford hexasaccharide **24** (124.2 mg, 50 μmol, 64%): $[\alpha]^{23}_D = -92.0$ (*c* 0.44, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80−7.75 (m, 3 H), 7.68−7.66 (m, 1 H), 7.57−7.09 (m, 76 H), 6.93 (t, 2 H, *J* = 8.0 Hz), 5.69 (s, 1 H), 5.58 (s, 2 H), 5.07 (s, 1 H), 5.01 (s, 1 H), 4.88−4.81 (m, 3 H), 4.76−4.62 (m, 5 H), 4.55−4.42 (m, 8 H), 4.38−4.34 (m 3 H), 4.30−4.26 (m, 2 H), 4.15−4.01 (m, 7 H), 3.98−3.82 (m, 8 H), 3.74−3.65 (m, 2 H), 3.51−3.33 (m, 9 H), 3.30−3.25 (m, 3 H), 3.18 (dd, 1 H, *J* = 7.5, 10.0 Hz), 2.67 (t, 1 H, *J* = 9.5 Hz), 2.48 (t, 1 H, *J* = 9.0 Hz), 2.42 (t, 1 H, *J* = 9.5 Hz), 1.23 (d, 3 H, *J* = 6.5 Hz), 1.04 (d, 3 H, *J* = 6.5 Hz), 1.00 (d, 3 H, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.22, 143.18, 143.12, 143.08, 138.6, 138.5, 138.4, 138.06, 137.98, 137.8, 137.63, 137.60, 136.1, 133.5, 133.2, 129.2, 129.1, 129.0, 128.7, 128.65, 128.60, 128.53, 128.5, 128.45, 128.41, 128.4, 128.33, 128.30, 128.27, 128.2, 128.1, 128.0, 127.9, 127.86, 127.84, 126.6, 126.5, 126.4, 126.3, 126.04, 125.98, 125.83, 125.79, 109.6, 109.5, 109.3, 102.6, 102.5, 102.4, 101.7, 101.6, 101.1, 98.1 (J_{C1-H1} = 169.5 Hz), 93.86 (J_{C1-H1} = 168.5 Hz), 93.79 (J_{C1-H1} = 167.0 Hz), 81.2, 80.5, 80.3, 79.2, 79.1, 79.0, 78.9, 77.9, 77.7, 76.6, 76.5, 76.4, 75.6, 75.1, 74.9, 74.5, 74.3, 73.9, 73.8, 73.7, 73.65, 73.62, 73.55, 72.9, 72.2, 69.7, 69.6, 69.4, 69.2, 69.1, 68.8, 64.9, 64.6, 55.3, 17.9, 17.5; ESI-HRMS *m*/*z* calcd for $C_{153}H_{150}O_{31}Na$, 2506.0059 [M + Na^+]; found 2506.0273.

Methyl D-Glycero-β-D-mannoheptopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)-D-glycero-β-D-mannoheptopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)-D-glycero-β-D-mannoheptopyranosyl-(1→4)-α-L-rhamnopyranoside (25). To a solution of hexasaccharide **24** (58.3 mg, 23 μmol) in 3/1 MeOH/THF (6 mL) was added AcOH (100 μL, 1.7 mmol) and 10% Pd/C (100 mg). The mixture was purged with H_2 six times and stirred for 24 h under H_2 at 50 psi. The solid was filtered off, and the filtrate was concentrated to dryness. The resulting residue was dissolved in water and washed with $CHCl_3$ (5 mL × 3). The aqueous phase was concentrated under reduced pressure and dried under vacuum to afford hexamer **25** (14.9 mg, 14 μmol, 60%): $[\alpha]^{23}_D = -84.6$ (*c* 0.71, H_2O); ^{1}H NMR (500 MHz, D_2O, 330 K, referenced to an external standard sodium 3-trimethylsilyl-(2,2,3,3-^{2}H) propionate (δ = 0.00) in D_2O) δ 4.96 (s, 2 H), 4.84 (s, 2 H), 4.83 (s, 1 H), 4.68 (s, 1 H), 4.24 (br. s, 2 H), 4.05−3.96 (m, 8 H), 3.92−3.90 (m, 1 H), 3.83−3.60 (m, 19 H), 3.44−3.41 (m, 2 H), 3.38−3.35 (m, 4 H), 1.33 (d, 3 H, *J* = 6.5 Hz), 1.31 (d, 6 H, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, D_2O, 330 K, referenced to an external standard 1,4-dioxane (δ = 67.40) in D_2O) δ 101.63 (J_{C1-H1} = 174.5 Hz), 101.48 (J_{C1-H1} = 160.5 Hz), 101.36 (J_{C1-H1} = 161.4 Hz), 97.09 (J_{C1-H1} = 170.2 Hz), 80.27, 80.10, 77.99, 76.84, 76.71, 74.08, 73.29, 73.25, 71.52, 71.28, 71.17, 69.10, 68.34, 67.92, 67.29, 67.14, 63.03, 62.98, 55.59, 17.78; ESI-HRMS *m*/*z* calcd for $C_{40}H_{70}O_{31}Na$, 1069.3799 [M + Na^+]; found 1069.3762; calcd for $C_{40}H_{70}O_{31}Na_2$, 546.1848 [M + 2Na]$^{2+}$; found, 546.1837.

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Supporting Information Available: Comparison of spectral data of glycan **25** with that of the natural isolate, and copies of spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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