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Improved methods for the stereoselective synthesis of mannoheptosyl donors and their glycosides: toward the synthesis of the trisaccharide repeating unit of the *Campylobacter jejuni* RM1221 capsular polysaccharide

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ABSTRACT

In view of the importance of 6-deoxymannoheptosides as structural units in the *Campylobacter jejuni* RM1221 capsular polysaccharide, the development of effective synthetic protocols for 4-*O*-6-*S*-α-cyanobenzylidene thio-D-mannoheptapyranoside donors carrying either 3-*O*-naphthylmethyl or 3-*O*-acetyl groups is described starting from D-mannose. In particular, tris(phenylthio)methyllithium is found to undergo highly stereoselective addition to a mannose-6-aldehyde in sharp contrast to the vinyl Grignard reagent whose reactions were essentially devoid of selectivity. A brief survey of coupling reactions with the two donors indicted the 3-*O*-acetyl system to be highly α-selective whereas the 3-*O*-naphthylmethyl congener was highly β-selective indicating that the presence of the seventh carbon atom in these donors is not detrimental to coupling selectivity in either instance.

1. Introduction

The synthesis of the higher carbon sugars and their glycosides, particularly the β-D-*glycero*-D-*manno*- and the β-L-*glycero*-D-*manno*-heptosides and their 6-deoxy congeners has been an area of interest in our laboratory for some time with the emphasis on the control of anomeric stereochemistry as influenced by the functionality and stereochemistry at the 6-position.[1,2] The 6-deoxy-β-D-mannoheptosides are of particular interest owing to the problems posed by the need for a 4,6-*O*-benzylidene acetal or related function to control the anomeric stereochemistry[3,4] and the need for subsequent selective reductive cleavage of the C6–O6 bond, which is closely related to the problem of the synthesis of the β-D- and β-L-rhamnopyranosides.[2,5] A secondary but none the less important problem from the practical standpoint in the development of an efficient synthetic route is that of the introduction of the seventh carbon with high levels of stereocontrol at the 6-position.[1b,6] Our current focus is on the glycosyl phosphosugars, which are present in the cell walls and capsules of numerous bacteria,[7] and in particular on the capsular polysaccharide **1** from *Campylobacter jejuni* RM1221 (Fig. 1), the leading cause of human gastroenteritis, identified by Vinogradov et al.[8] This polysaccharide has a linear main chain comprised of a trisaccharide repeating unit that is made up of two α- and one β-6-deoxy-D-*manno*-hepto-pyrannose residues, which are joined through a phosphodiester linkage. Having established a method for the highly stereocontrolled synthesis of the phosphodiester linkage,[9] we turned our attention to the development of improved methods for the preparation of the mannoheptose unit, which we describe here.

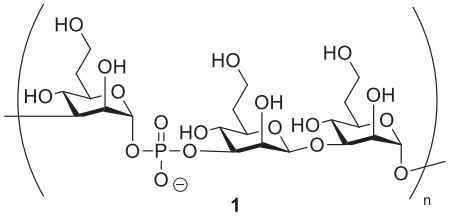

Fig. 1. Structure of capsular polysaccharide **1** from *Campylobacter jejuni* RM1221.

2. Results and discussion

For the introduction of the seventh carbon we first investigated a modification of a strategy developed earlier in the laboratory in

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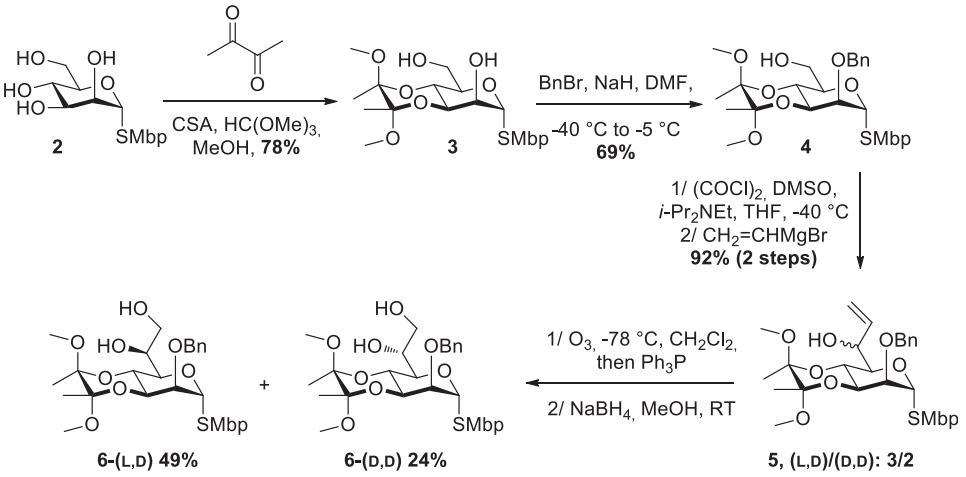
the course of a block synthesis of multiple repeating units of the glycan from the Surface-Layer Glycoprotein from *Bacillus thermoaerophilus*.[1c] Thus, starting from α-D-mannose pentaacetate, the tetraol **2** was prepared in two steps using the commercially available odorless 2-methyl-5-*tert*-butylthiophenol (MbpSH) recommended by Mallet et al.[10,11] Subsequently, the tetraol **2** was protected at the 3,4-*O*-position with butane-2,3-dione followed by the highly regioselective benzylation at the 2-*O*-position using Ley's methodologies (Scheme 1) to give the thioglycoside **4**.[12]

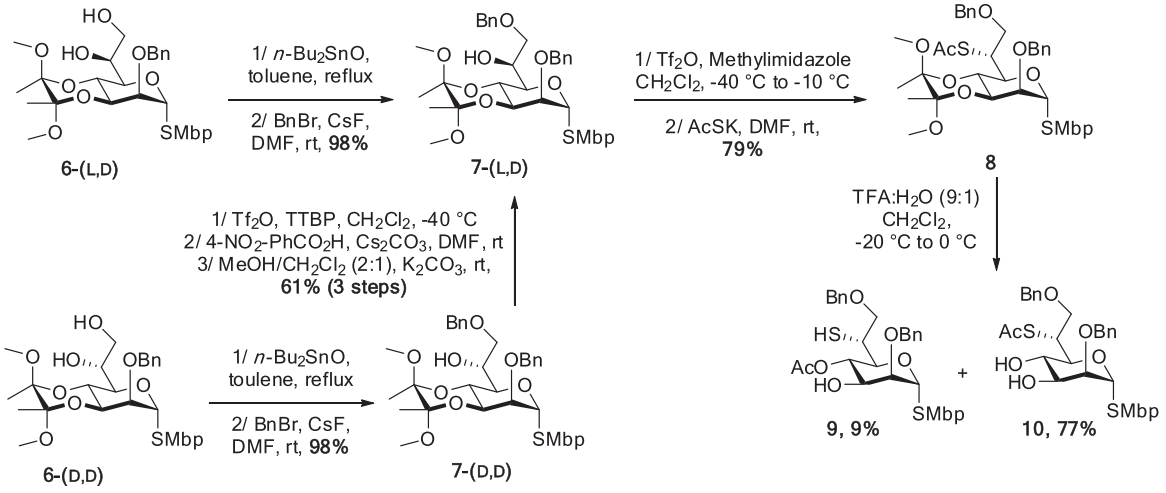
Subsequent exposure of the reaction mixture to sodium borohydride afforded the diols **6**, which were separated by silica gel chromatography resulting in the isolation of **6**-(L,D) and **6**-(D,D) in 49% and 24% yield, respectively (Scheme 1).

Selective monobenzylation using dibutyltin oxide and benzyl bromide of both isomers of **6** afforded the expected 7-*O*-benzyl-6-ols **7** with excellent yield (Scheme 2).[14] The unwanted **7**-(D,D) diastereoisomer was salvaged by conversion to the **7**-(L,D) isomer in 61% overall yield by triflation, displacement with 4-nitrobenzoate



Scheme 1. Synthesis of *manno-hepto*-pyrannosides **6**-(L,D) and **6**-(D,D).

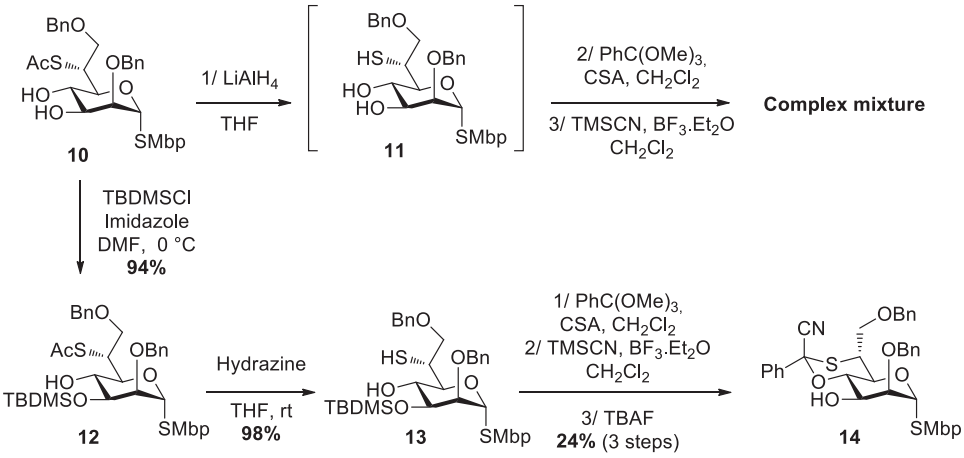
A Swern oxidation on glycoside **4**, followed by the addition in situ of the vinyl Grignard reagent afforded the adduct **5** as an inseparable 3:2 mixture of diastereoisomers **5**-(L,D) and **5**-(D,D) in 92% yield. Despite previous reports of very high selectivity for the formation of the L,D isomer in the closely related additions to the corresponding methyl mannoside,[6i] we were unable to improve the selectivity of this reaction thereby highlighting its susceptibility to substituent effects and especially to the anomeric functionality and hydrolysis; the Mitsunobu protocol was not effective for this conversion. Subsequently, a thioacetyl group was introduced at the 6-position with inversion of configuration also by a triflation and displacement sequence in 79% yield. Hydrolysis of the bisacetal function in the thioacetate **8** with aqueous TFA afforded the expected diol **10** in 77% yield and 9% of byproduct **9**, resulting from concomitant *S*- to *O*-acetyl migration, which we were unable to suppress (Scheme 2).



Scheme 2. Synthesis of the 6-deoxy-6-mercapto D,D-mannoheptoside **10**.

(α-SMbp vs α-OMe). Continuing with the synthesis, the mixed diastereomers of **5** were subjected to ozone at −78 °C and quenched with triphenylphosphine at that temperature, thereby enabling cleavage of the alkene without oxidation of the thioglycoside.[13]

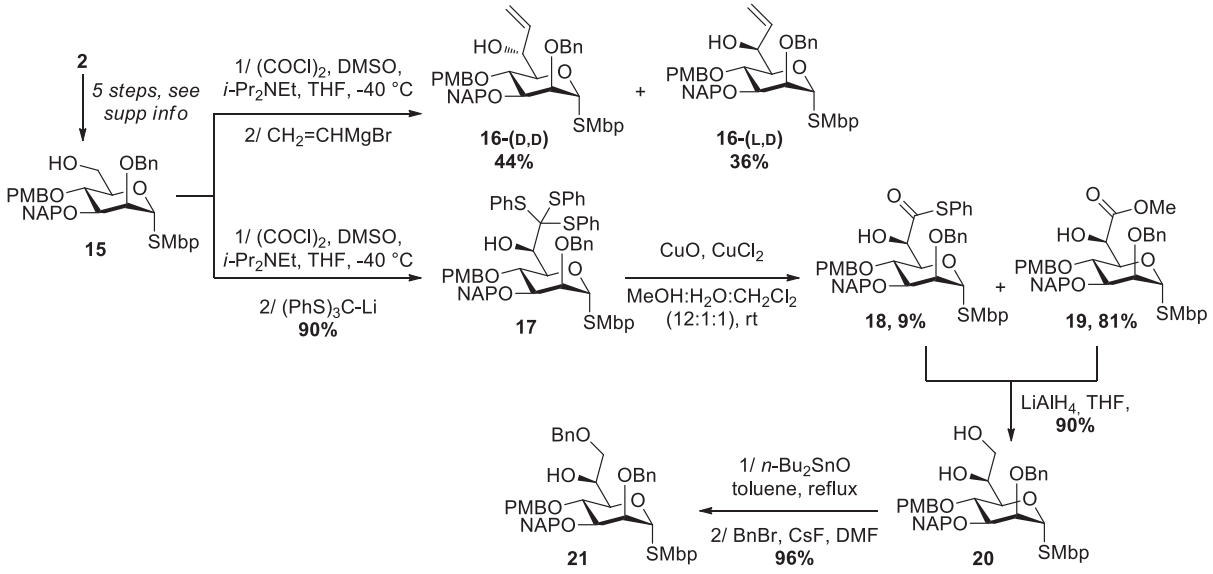
Deacetylation of **10** followed by attempted installation of the α-cyanobenzylidene acetal spanning O4 and S6, under conditions previously optimized in the 6-deoxy-6-mercaptorhamnopyranoside series,[5] gave a complex mixture of unidentified products (Scheme 3).



Scheme 3. Synthesis of the cyanobenzylidene protected mannoheptoside **14**.

Therefore **10** was selectively silylated at the 3-position by a TBDMS group as reported by Yamasaki et al. in a cognate series,[15] and the acetyl removed with hydrazine to afford **13** in good yield. Finally, the requisite 4-*O*-6-*S*-α-cyanobenzylidene system was built from **13** by the standard two-step procedure involving orthoester exchange and cyanation; after removal of the TBDMS group compound **14** was obtained in 24% yield (Scheme 3), with the low yield apparently the result of the instability of the silyl ether toward the conditions employed for introduction of the cyanoacetal.

The poor selectivity in the transformation of **8** to **9** and the overall inefficiency of this first synthesis of the thioglycoside **14** prompted the exploration and development of an alternative strategy for the preparation of suitably protected 6-deoxy-6-mercapto-D,D-mannoheptoside donors. Accordingly, tetraol **2** was converted to the thioglycoside **15** (Scheme 4) by adaptation addition to methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyrannoside, and further reinforces above-mentioned dependence of the stereoselectivity of additions to mannose-6-aldehydes on the protecting group array and anomeric functionality.[6o] Fortunately, it was discovered that treatment of the aldehyde obtained on oxidation of **15** with the sterically hindered tris(phenylthio) methyllithium reagent gave the (L,D)-isomer of the adduct **17** exclusively and in excellent yield (Scheme 4).[17] No evidence for the formation of the (D,D) diastereoisomer was observed in the ^{1}H NMR spectrum of the crude reaction mixture. The excess organolithium reagent employed in order to achieve the high yield of the adduct was readily recyclable in the form of tris(phenylthio) methane following work-up and chromatographic purification. Treatment of the tris(phenylthio)orthoester moiety in **17** with a mixture of CuO and $CuCl_2$ afforded the thiophenyl ester **18** and



Scheme 4. Stereoselective synthesis of the mannoheptoside **21**.

of a standard protocol described in detail in the Supplementary data.[1b,16] Swern oxidation of **15** followed by the addition of the vinyl Grignard reagent afforded **16** as an approximately 1:1 mixture of diastereoisomers, which contrasts with the 9:1 (L,D):(D,D) ratio obtained by Oscarson et al. for the parallel the methyl ester **19** in excellent combined yield, both of which were reduced to the primary alcohol **20** without event. Selective monobenzylation of **20** with dibutyltin oxide and benzyl bromide then gave the expected 7-*O*-benzyl-6-ol **21** with excellent yield (Scheme 4).[14]

Attempted inversion of the 6-position of **21** by the thio-Mitsunobu protocol[18] failed, but triflation followed displacement with an appropriate nucleophile proved adequate for the task. The choice of conditions for this inversion was nevertheless critical. Thus, triflation followed by exposure to NH_4SCN or AcSH/*i*-Pr_2NEt afforded the 3,6-dianhydro glycoside **22** in good yield with no indication of the formation of the desired product **23** (Scheme 5). The structure of **22** was confirmed by NOE correlations between H-1 and H-6. The formation of related 3,6-anhydrosugars has been previously observed by Kováč et al. and more recently by Lowary et al. under DAST conditions.[19] The use of Comin's reagent for triflation followed by treatment with potassium thioacetate afforded the expected thioester **23** with a moderate 40% yield together with 7% of the elimination product **24**. To avoid the formation of **24** the final displacement was conducted with a mixture of potassium thioacetate and thioacetic acid, when **23** was isolated in 76% yield (Scheme 5).

removing the naphthylmethyl group with dichlorodicyanoquinone in wet dichloromethane followed by acetylation (Scheme 6).

With an effective synthesis of the donors **27** and **28** in hand model glycosylation reactions were conducted in order to determine that the effectiveness of the cyanobenzylidene thioacetal moiety as a stereocontrol agent in the mannoheptose series. Thus, preactivation of the donor **28** with Ph_2SO/Tf_2O[20] combination in the presence of TTBP (Fig. 2) in dichloromethane at −78 °C was

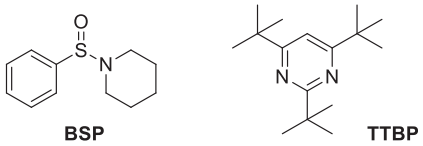
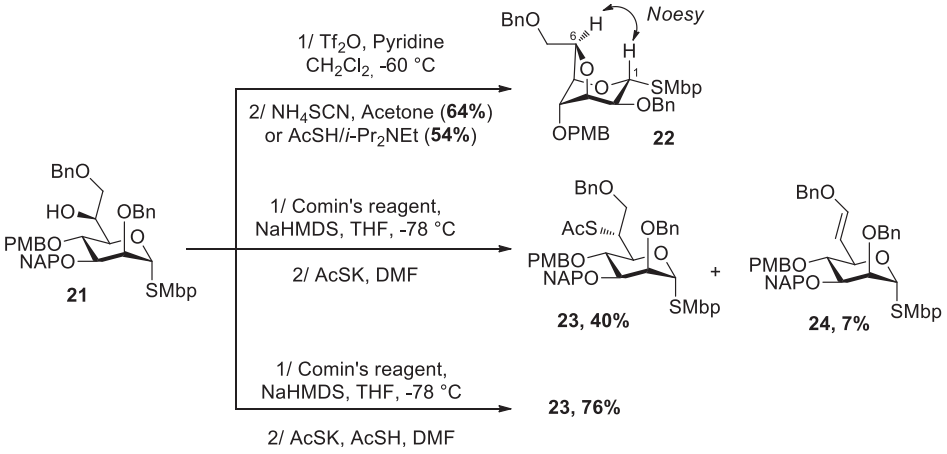


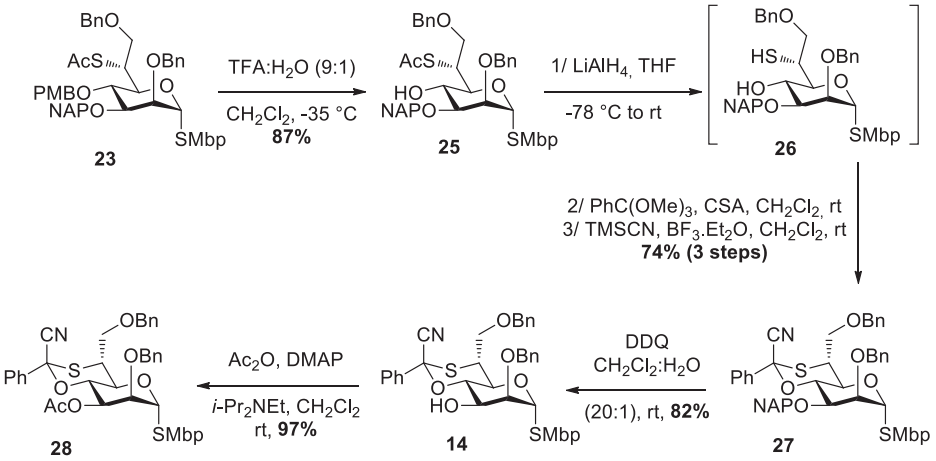
Fig. 2. Structure of BSP and TTBP.



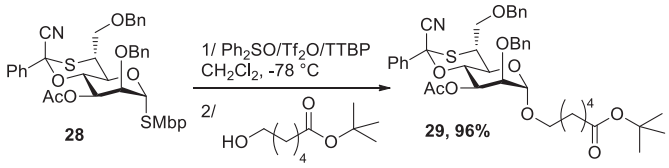
Scheme 5. Substitution of the heptanol **21**.

The PMB group was selectively removed from **23** under acidic condition at low temperature so as to prevent acetyl transfer, resulting in the formation of **25** in 87% yield (Scheme 6). The intermediate thiol **26** was obtained by reduction of the thioester using $LiAlH_4$, and the 4-*O*-6-*S*-α-cyanobenzylidene system was introduced in good yield by the usual two-step procedure of orthoester exchange and cyanation.[5] The 3-*O*-acetyl protected donor **28** was obtained by

followed by addition of *tert*-butyl 6-hydroxyhexanoate,[21] resulting in the isolation of glycoside **29** in 96% yield with complete α-selectivity (Scheme 7). The very high degree of α-selectivity observed in this coupling process is consistent with that seen previously for the 3-*O*-acyl-4,6-*O*-benzylidene protected mannosyl donors[9,22] and indicates that neither the presence of the seventh carbon nor of the longer C–S bond is detrimental to stereoselectivity.

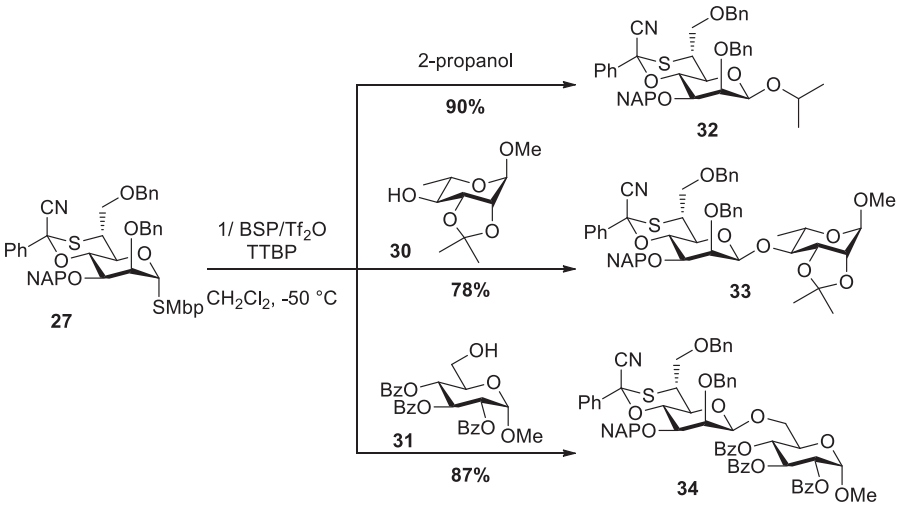


Scheme 6. Synthesis of differentially protected mannoheptosyl donors **27** and **28**.



Scheme 7. α-Selective glycosylation with donor **28**.

The 3-*O*-naphthylmethyl protected donor **27** was glycosylated following preactivation with the BSP/Tf_2O (Fig. 2) combination[23] in the presence of TTBP in dichloromethane at −50 °C with three model acceptors: 2-propanol, methyl rhamnoside **30**, and methyl glucoside **31**. In each case completely β-selective couplings were observed and the pure β-mannoheptosides **32**, **33**, and **34** were isolated in good yield, again indicating the lack of influence of the seventh carbon on the glycosylation stereoselectivity (Scheme 8).



Scheme 8. β-Selective glycosylation with donor **27**.

3. Conclusion

The use of tris(phenylthiomethyl)lithium as nucleophile affords extremely high stereoselectivity on addition to a mannopyranosyl 6-aldehyde in sharp contrast to the mixtures obtained with the less hindered vinyl Grignard reagent. This high selectivity, coupled with the use of the 3-*O*-naphthylmethyl protecting system enables the efficient synthesis of the α- and β-selective mannoheptosyl **27** and **28**. Model coupling reactions to donors **27** and **28** proceed with very high levels of α- and β-selectivity, respectively, indicating in both cases that the presence of the seventh carbon in the donors is not in any way detrimental to the yield or selectivity of the coupling reactions. Further progress on the synthesis of the *C. jejuni* capsular polysaccharide will be reported in due course.

4. Experimental section

4.1. General experimental

All reactions were performed using oven dried glassware under an atmosphere of argon. All purifications were performed on prepacked silica gel columns (50 μm). Reactions were monitored by thin-layer chromatography on alumina backed silica gel plates (60 F_{254} aluminum) visualized by UV light and/or spraying with vanillin (15%)+sulfuric acid (2.5%) in EtOH followed by heating. Solvents were freshly distilled before use over CaH_2 for CH_2Cl_2 or benzophenone/Na for THF. Commercial ExtraDry Acroseal® quality toluene, MeOH and DMF, were used without further purification. ^{1}H NMR (500 and 300 MHz) and ^{13}C NMR (125 and 75 MHz) spectra were recorded at 298 K unless otherwise stated. Chemical shifts are given in parts per million (δ) and are referenced to the internal solvent signal or to TMS used as an internal standard. Multiplicities are given as follows: s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quadruplet), dd (doublet of doublet), ddd (doublet of doublet of doublet), dt (doublet of triplet), m (multiplet). Coupling constants *J* are given in Hertz. Carbon multiplicities were determined by DEPT135 experiments. Diagnostic correlations were obtained by two-dimensional COSY, HSQC. Specific rotations were measured at 589 nm; $[\alpha]_D^C$ is expressed in deg cm^3 g^{-1} dm^{-1} and *c* in g/100 cm^3. Melting points were recorded in open capillary tubes and are uncorrected. High resolution mass spectra (HMRS) were recorded using electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI).

*4.1.1. (2-Methyl-5-tert-butylphenyl) 3,4-O-(2′,3′-dimethoxybutane-2′-3′-diyl)-1-thia-α-D-mannopyranoside (**3**).* To a solution of tetraol **2** (4 g, 11.67 mmol), in dry methanol (120 mL), was added butane-2,3-dione (1.23 mL, 14 mmol), $HC(OMe)_3$ (7.1 mL, 64.2 mmol), and CSA (272 mg, 1.17 mmol). The reaction mixture was heated at reflux for 8 h before being cooled to room temperature and quenched with 20 mL of Et_3N. The reaction mixture was concentrated under reduced pressure and the crude product was purified on silica gel (20% EtOAc in toluene) to give **3** (4.16 g, 78%) as a white powder. $[\alpha]_D^{24}$ +292.0 (*c* 1.0, $CHCl_3$); mp 65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.29 (s, 9H), 1.32 (s, 3H), 1.34 (s, 3H), 2.39 (s, 3H), 3.26 (s, 3H), 3.33 (s, 3H), 3.78 (d, *J*=3.5 Hz, 2H), 4.11 (d, *J*=10.0 Hz, 1H), 4.18 (t, *J*=10.0 Hz, 1H), 4.22–4.25 (m, 1H), 4.26–4.31 (m, 1H), 5.50 (s, 1H), 7.14 (d, *J*=8.0 Hz, 1H), 7.22 (d, *J*=8.0 Hz, 1H), 7.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.7, 17.8, 20.2, 31.1, 34.4, 47.9, 48.2, 61.2, 63.2, 68.7, 71.4, 71.6, 97.4, 99.9, 100.5, 125.2, 130.0, 130.1, 131.9, 136.9, 136.9, 149.7; ESIHRMS $C_{23}H_{36}O_7S$ calcd for $[M+Na]^+$: 479.2079, found 479.2093.

*4.1.2. (2-Methyl-5-tert-butylphenyl) 2-O-benzyl-3,4-O-(2′,3′-dimethoxybutane-2′-3′-diyl)-1-thia-α-D-mannopyranoside (**4**).* To a chilled (−40 °C) solution of **3** (7.42 g, 16.3 mmol) in dry DMF (160 mL) was added benzyl bromide (2.13 mL, 17.9 mmol) followed by 60% NaH in mineral oil (1.31 g, 32.6 mmol). The reaction mixture was stirred 2 h at −40 °C and 24 h at −5 °C before it was quenched with saturated aqueous $NaHCO_3$ and then extracted with dichloromethane. The

combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified on silica gel (10% EtOAc in heptane to 20% EtOAc in heptane) to give **4** (6.1 g, 69%) as a white powder: $[\alpha]_D^{24}$ +189.0 (*c* 1.0, $CHCl_3$); mp 56 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.28 (s, 9H), 1.34 (s, 3H), 1.37 (s, 3H), 2.33 (s, 3H), 3.31 (s, 3H), 3.34 (s, 3H), 3.72–3.90 (m, 2H), 3.95–4.10 (m, 1H), 4.13 (dd, *J*=9.5, 2.5 Hz, 1H), 4.24–4.33 (m, 2H), 4.68 (d, *J*=12.0 Hz, 1H), 4.94 (d, *J*=12.0 Hz, 1H), 5.42 (s, 1H), 7.13 (d, *J*=8.0 Hz, 1H), 7.21 (d, *J*=8.0 Hz, 1H), 7.28 (d, *J*=7.5 Hz, 1H), 7.33 (t, *J*=7.5 Hz, 2H), 7.43 (d, *J*=7.5 Hz, 2H), 7.49 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.8, 20.2, 31.2, 31.3, 34.4, 47.9, 48.0, 61.6, 63.9, 69.4, 72.0, 73.1, 77.6, 87.1, 99.6, 100.0, 125.0, 127.6, 127.9, 128.3, 129.8, 130.1, 132.3, 136.6, 138.4, 149.7; ESIHRMS $C_{30}H_{42}O_7S$ calcd for $[M+Na]^+$: 569.2549, found 569.2546.

*4.1.3. (2-Methyl-5-tert-butylphenyl) 2-O-benzyl-3,4-O-(2′,3′-dimethoxybutane-2′-3′-diyl)-D-glycero-1-thia-α-D-mannoheptopyranoside (**6**-(D,D)) and (2-methyl-5-tert-butylphenyl) 2-O-benzyl-3,4-O-(2′,3′-dimethoxybutane-2′-3′-diyl)-L-glycero-1-thia-α-D-mannoheptopyranoside (**6**-(L,D)).* To a chilled (−60 °C) solution of oxalyl chloride (2.64 mL, 30.75 mmol) in dry THF (25 mL) was added a solution of DMSO (4.4 mL, 61.7 mmol) in dry THF (25 mL). The reaction mixture was stirred 30 min at −60 °C and then a solution of **4** (6.7 g, 12.3 mmol) in dry THF (50 mL) was added. The reaction mixture was stirred 5 h at −40 °C and *i*-Pr_2NEt was slowly added (21.9 mL, 123 mmol). The reaction mixture was warmed to room temperature and stirred 2 h at room temperature. The reaction mixture was cooled at −78 °C and a solution of vinyl magnesium bromide (0.7 M in THF, 88.2 mL, 61.7 mmol) was slowly added. The reaction mixture was stirred 2 h at −78 °C, quenched with ethanol (20 mL) and warmed to room temperature. Then, saturated aqueous NH_4Cl was added, and then extracted with EtOAc. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (10% EtOAc in heptane) to give **5** (6.5 g, 92%) as a 3:2 mixture of diastereoisomers (L,D) and (D,D). This mixture was dissolved in dry CH_2Cl_2 (600 mL), cooled to −78 °C, and ozone was bubbled until see a blue color persisted. The reaction mixture was purged with argon and Ph_3P (16.1 g, 61.5 mmol) was added. The reaction mixture was stirred 4 h at −78 °C, warmed slowly to room temperature and stirred overnight at room temperature. CH_2Cl_2 was removed under reduced pressure and the residue was dissolved in a mixture of dry CH_2Cl_2/MeOH (1:2, 210 mL), cooled at −78 °C and $NaBH_4$ (2.33 g, 61.5 mmol) was added. The reaction was stirred 1 h at −78 °C, warmed to room temperature, stirred overnight at room temperature, quenched with saturated aqueous $NaHCO_3$, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (Gradient: 5%–20% EtOAc in toluene) to give **6**-(D,D) (1.5 g, 24%) as a white powder: $[\alpha]_D^{27}$ +195.5 (*c* 1.0, $CHCl_3$); mp 51 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.29 (s, 9H), 1.34 (s, 3H), 1.37 (s, 3H), 2.11 (t, *J*=6.0 Hz, 1H), 2.31 (s, 3H), 3.02 (d, *J*=3.0 Hz, 1H), 3.31 (s, 3H), 3.34 (s, 3H), 3.63–3.74 (m, 2H), 3.92–3.99 (m, 2H), 4.11 (d, *J*=10.0 Hz, 1H), 4.25 (d, *J*=9.5, 5.5 Hz, 1H), 4.38 (t, *J*=10.0 Hz, 1H), 4.67 (t, *J*=12.0 Hz, 1H), 4.97 (d, *J*=12.0 Hz, 1H), 5.40 (s, 1H), 7.12 (d, *J*=8.0 Hz, 1H), 7.21 (d, *J*=8.0 Hz, 1H), 7.28 (d, *J*=7.0 Hz, 1H), 7.34 (t, *J*=7.0 Hz, 2H), 7.42 (d, *J*=7.5 Hz, 2H), 7.47 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.8, 17.9, 20.2, 31.3, 34.5, 48.1, 48.4, 63.2, 66.6, 69.3, 71.7, 73.2, 73.3, 77.6, 87.1, 100.0, 100.1, 125.1, 127.7, 127.9, 128.3, 129.2, 130.2, 132.5, 136.4, 138.3, 149.9. ESIHRMS $C_{31}H_{44}O_8S$ calcd for $[M+Na]^+$: 599.2655, found 599.2649; and **6**-(L,D) (3.1 g, 44%) as a white powder: $[\alpha]_D^{25}$ +212.7 (*c* 1.0, $CHCl_3$); mp 53 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.29 (s, 9H), 1.34 (s, 3H), 1.37 (s, 3H), 1.82 (dd, *J*=7.0, 4.5 Hz, 1H), 2.32 (s, 3H), 2.33–2.34 (m, 1H), 3.34 (s, 3H), 3.35 (s, 3H), 3.53–3.61 (m, 2H), 3.92–4.02 (m, 2H), 4.11–4.17 (m, 2H), 4.44 (t, *J*=10.0 Hz, 1H), 4.68 (t, *J*=12.0 Hz, 1H), 4.97 (d, *J*=12.0 Hz, 1H), 5.47 (s, 1H), 7.14 (d, *J*=8.0 Hz, 1H), 7.23 (d, *J*=8.0 Hz, 1H), 7.28 (d, *J*=7.0 Hz, 1H), 7.34 (t, *J*=7.0 Hz, 2H), 7.39 (d, *J*=7.5 Hz, 2H), 7.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.8, 20.2, 31.3, 34.5, 48.1, 63.3, 65.1, 68.7, 69.5, 73.1, 73.3, 77.2, 86.9, 99.8, 100.0, 125.3, 127.7, 128.0, 128.3, 129.0, 130.3, 131.9, 136.5, 138.4, 149.9. ESIHRMS $C_{31}H_{44}O_8S$ calcd for $[M+Na]^+$: 599.2655, found 599.2660.

*4.1.4. (2-Methyl-5-tert-butylphenyl) 2,7-di-O-benzyl-3,4-O-(2′,3′-dimethoxybutane-2′-3′-diyl)-L-glycero-1-thia-α-D-mannoheptopyranoside **7**-(L,D).* A mixture of **6**-(L,D) (2.8 g, 4.8 mmol) and *n*-Bu_2SnO (1.45 g, 5.8 mmol) in dry toluene (50 mL) was heated 4 h at reflux. The resulting clear solution was cooled to room temperature and concentrated under reduced pressure. The residue was dissolved in dry DMF (25 mL) and benzyl bromide (690 μL, 5.8 mmol) was added followed by the addition of CsF (1.46 g, 9.6 mmol). The reaction mixture was stirred overnight at room temperature, diluted with CH_2Cl_2, and filtrated through Celite®. The filtrate was concentrated under reduced pressure and the crude was purified on silica gel (10% EtOAc in heptane) to give **7**-(L,D) (3.14 g, 98%) as a clear viscous oil: $[\alpha]_D^{24}$ +212.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.30 (s, 9H), 1.34 (s, 3H), 1.39 (s, 3H), 2.18 (d, *J*=7.5 Hz, 1H), 2.29 (s, 3H), 3.34 (s, 3H), 3.35 (s, 3H), 3.42 (dd, *J*=9.5, 4.0 Hz, 1H), 3.51 (t, *J*=9.0 Hz, 1H), 4.01 (s, 1H), 4.10–4.21 (m, 3H), 4.38 (d, *J*=12.0 Hz, 1H), 4.44 (t, *J*=12.0 Hz, 1H), 4.51 (d, *J*=10.5 Hz, 1H), 4.72 (d, *J*=12.5 Hz, 1H), 4.96 (d, *J*=12.5 Hz, 1H), 5.57 (s, 1H), 7.10 (d, *J*=8.0 Hz, 1H), 7.19 (d, *J*=8.0 Hz, 1H), 7.22–7.37 (m, 8H), 7.43 (d, *J*=7.0 Hz, 2H), 7.46 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.8, 20.1, 31.4, 34.5, 48.0, 48.1, 62.9, 67.6, 69.7, 71.5, 72.0, 73.1, 73.2, 77.6, 86.7, 99.7, 100.0, 124.3, 127.3, 127.5, 127.6, 128.0, 128.2, 128.3, 130.0, 133.3, 135.4, 138.1, 138.4, 149.8. ESIHRMS $C_{38}H_{50}O_8S$ calcd for $[M+Na]^+$: 689.3124, found 689.3121.

*4.1.5. (2-Methyl-5-tert-butylphenyl) 6-S-acetyl-2,7-di-O-benzyl-3,4-O-(2′,3′-dimethoxybutane-2′-3′-diyl)-D-glycero-1,6-dithio-α-D-mannoheptopyranoside (**8**).* To a chilled (−40 °C) solution of **7**-(L,D) (134 mg, 0.2 mmol) and methylimidazole (40 μL, 0.503 mmol) was added Tf_2O (freshly distilled over P_2O_5, 64 μL, 0.4 mmol). The reaction mixture was stirred 10 min at −40 °C, warmed at −10 °C, and stirred 10 min at −10 °C before to be poured into cold 0.1 N HCl and extracted with CH_2Cl_2. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was dissolved in dry DMF (2 mL) and then AcSK (91.4 mg, 0.8 mmol) was added. The reaction mixture was stirred 6 h at room temperature, quenched with saturated aqueous $NaHCO_3$, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (10% EtOAc in heptane) to give **8** (114 mg, 79%) as yellow viscous oil: $[\alpha]_D^{24}$ +162.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.33 (s, 3H), 1.34 (s, 9H), 1.36 (s, 3H), 2.29 (s, 3H), 2.32 (s, 3H), 3.19 (s, 3H), 3.32 (s, 3H), 3.56 (dd, *J*=10.0, 7.5 Hz, 1H), 3.91 (dd, *J*=10.0, 7.0 Hz 1H), 3.98–4.02 (m, 2H), 4.37 (t, *J*=7.0 Hz, 1H), 4.40–4.49 (m, 2H), 4.50 (d, *J*=12.5 Hz, 1H), 4.56 (d, *J*=12.5 Hz, 1H), 4.69 (d, *J*=12.0 Hz, 1H), 4.91 (d, *J*=12.0 Hz, 1H), 5.43 (s, 1H), 7.12 (d, *J*=8.0 Hz, 1H), 7.22 (dd, *J*=8.0, 2.0 Hz, 1H), 7.24–7.34 (m, 8H), 7.43 (d, *J*=7.5 Hz, 2H), 7.59 (d, *J*=2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.8, 20.1, 30.6, 31.3, 34.6, 43.4, 48.0, 48.3, 65.3, 69.0, 69.8, 72.7, 72.9, 73.6, 78.2, 87.4, 99.8, 100.1, 124.5, 127.4, 127.5, 127.7, 127.8, 128.2, 128.9, 129.8, 133.6, 135.8, 138.3, 149.8, 194.2. ESIHRMS $C_{40}H_{52}O_8S_2$ calcd for $[M+Na]^+$: 747.3001, found 747.3008.

*4.1.6. (2-Methyl-5-tert-butylphenyl) 4-O-acetyl-2,7-di-O-benzyl-D-glycero-1,6-dithio-α-D-mannoheptopyranoside (**9**) and (2-methyl-5-tert-butylphenyl) 6-S-acetyl-2,7-di-O-benzyl-D-glycero-1,6-dithio-α-D-mannoheptapyranoside (**10**).* To a chilled (−20 °C) solution of **8**

(1.55 g, 2.14 mmol) was added a mixture of TFA/H_2O (9:1, 4 mL). The reaction mixture was stirred 10 min at −20 °C, warmed at 0 °C, and stirred 2 h at 0 °C. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (30% EtOAc in heptane) to give **9** (118.2 mg, 9%) as a clear viscous oil: $[\alpha]_D^{24}$ +93.3 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 1.31 (s, 9H), 1.87 (d, *J*=8.5 Hz, 1H), 2.11 (s, 3H), 2.36 (s, 3H), 2.46 (d, *J*=10.0 Hz, 1H), 3.25–3.29 (m, 1H), 3.50 (dd, *J*=9.5, 7.5 Hz, 1H), 3.81 (dd, *J*=9.5, 6.0 Hz, 1H), 3.88–3.91 (m, 1H), 4.02–4.07 (m, 1H), 4.42–4.46 (m, 1H), 4.48 (d, *J*=12.5 Hz, 1H), 4.54 (d, *J*=12.5 Hz, 1H), 4.64 (d, *J*=12.0 Hz, 1H), 4.73 (d, *J*=12.0 Hz, 1H), 5.39 (t, *J*=9.5 Hz, 1H), 5.56 (s, 1H), 7.15 (d, *J*=8.0 Hz, 1H), 7.23 (d, *J*=8.0 Hz, 1H), 7.24–7.36 (m, 10H), 7.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.2, 21.0, 31.3, 34.5, 39.9, 71.0, 71.4, 71.6, 72.5, 73.1, 73.6, 80.0, 84.6, 125.0, 127.5, 127.6, 127.7, 127.8, 128.1, 128.3, 128.6, 129.4, 130.2, 132.3, 136.4, 137.3, 138.0, 149.8, 170.9; ESIHRMS $C_{34}H_{42}O_6S_2$ calcd for $[M+Na]^+$: 633.2321, found 633.2341; and **10** (1.01 g, 77%) as a clear viscous oil: $[\alpha]_D^{26}$ +108.9 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 1.36 (s, 9H), 2.29 (s, 3H), 2.34 (s, 3H), 2.45 (d, *J*=8.0 Hz, 1H), 3.08 (d, *J*=3.5 Hz, 1H), 3.56 (dd, *J*=10.0, 4.0 Hz, 1H), 3.82–3.88 (m, 1H), 3.95 (dd, *J*=10.5, 8.5 Hz, 1H), 4.03–4.10 (m, 2H), 4.27–4.33 (m, 2H), 4.58 (d, *J*=12.0 Hz, 1H), 4.62 (d, *J*=12.0 Hz, 1H), 4.63 (d, *J*=12.0 Hz, 1H), 4.73 (d, *J*=12.0 Hz, 1H), 5.53 (s, 1H), 7.15 (d, *J*=8.0 Hz, 1H), 7.23 (dd, *J*=8.0, 2.0 Hz, 1H), 7.28–7.36 (m, 10H), 7.58 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.2, 30.5, 31.4, 34.6, 44.0, 69.8, 70.0, 71.7, 72.2, 73.4, 74.5, 79.9, 85.6, 124.6, 127.7, 127.8, 128.0, 128.5, 128.7, 129.9, 133.3, 135.9, 137.5, 137.6, 149.8, 194.6; ESIHRMS $C_{34}H_{42}O_6S_2$ calcd for $[M+Na]^+$: 633.2321, found 633.2321.

*4.1.7. (2-Methyl-5-tert-butylphenyl) 6-S-acetyl-2,7-di-O-benzyl-3-O-tert-butyldimethylsilyl-D-glycero-1,6-dithio-α-D-mannoheptopyranoside (**12**).* To a cooled (0 °C) solution of **10** (240 mg, 0.4 mmol) and imidazole (69 mg, 1.0 mmol) in dry DMF (4 mL) was added TBDMSCl (122 mg, 0.8 mmol). The reaction mixture was stirred overnight at room temperature, quenched with saturated aqueous $NaHCO_3$, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (10% EtOAc in heptane) to give **12** (271 mg, 94%) as a clear viscous oil: $[\alpha]_D^{24}$ +113.8 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 0.16 (s, 3H), 0.17 (s, 3H), 0.97 (s, 9H), 1.36 (s, 9H), 2.29 (s, 3H), 2.34 (s, 3H), 2.55 (d, *J*=3.5 Hz, 1H), 3.55 (dd, *J*=10.0, 5.0 Hz, 1H), 3.89–3.93 (m, 2H), 3.97 (t, *J*=8.5 Hz, 1H), 4.17–4.30 (m, 2H), 4.35–4.39 (m, 1H), 4.57 (s, 2H), 4.67 (d, *J*=12.0 Hz, 1H), 4.78 (d, *J*=12.0 Hz, 1H), 5.45 (s, 1H), 7.14 (d, *J*=8.0 Hz, 1H), 7.22 (d, *J*=8.0 Hz, 1H), 7.24–7.34 (m, 10H), 7.60 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: −4.5, 18.3, 20.2, 25.9, 30.5, 31.4, 34.6, 43.9, 69.3, 69.4, 73.0, 73.1, 73.6, 75.2, 81.0, 86.8, 124.6, 127.5, 127.6, 127.7, 128.3, 128.4, 129.1, 129.8, 133.6, 136.0, 137.9, 138.3, 149.7, 194.7; ESIHRMS $C_{40}H_{56}O_6S_2Si$ calcd for $[M+Na]^+$: 747.3185, found 747.3205.

*4.1.8. (2-Methyl-5-tert-butylphenyl) 2,7-di-O-benzyl-3-O-tert-butyldimethylsilyl-D-glycero-1,6-dithio-α-D-mannohepto-pyranoside (**13**).* To a cooled (0 °C) solution of **12** (153 mg, 0.21 mmol) in dry THF (2 mL) was added hydrazine (28.7 mg, 0.32 mmol). The reaction mixture was stirred 3 h at room temperature, diluted with EtOAc, and washed with water. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The crude was purified on silica gel (10% EtOAc in heptane) to give **13** (140 mg, 98%) as a clear viscous oil: $[\alpha]_D^{24}$ +84.4 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 0.17 (s, 3H), 0.18 (s, 3H), 0.97 (s, 9H), 1.31 (s, 9H), 1.90 (d, *J*=9.0 Hz, 1H), 2.36 (s, 3H), 2.55 (s, 1H), 3.49–3.51 (m, 1H), 3.64 (dd, *J*=9.5, 5.0 Hz, 1H), 3.92 (s, 1H), 3.96 (d, *J*=8.0 Hz, 1H), 4.20–4.30 (m, 2H), 4.50–4.55 (m, 2H), 4.68 (d, *J*=11.5 Hz, 1H), 4.79 (d, *J*=11.5 Hz, 1H), 5.50 (s, 1H), 7.14 (d, *J*=8.0 Hz, 1H), 7.21 (d, *J*=8.0 Hz, 1H), 7.24–7.34 (m, 10H), 7.57 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: −4.6, −4.5, 18.2, 20.2, 25.9, 31.4, 34.5, 40.5, 69.2, 72.3, 72.9, 73.2, 73.7, 75.7, 80.5, 86.3, 124.9, 127.6, 127.7, 127.8, 128.3, 128.4, 129.5, 130.0, 132.8, 136.4, 137.8, 138.2, 149.7. ESIHRMS $C_{38}H_{54}O_5S_2Si$ calcd for $[M+Na]^+$: 705.3080, found 705.3089.

*4.1.9. (2-Methyl-5-tert-butylphenyl) 2,7-di-O-benzyl-4-O-6-S-(1-cyano)benzylidene-D-glycero-1,6-dithio-α-D-mannohepto-pyranoside (**14**).* To a room temperature solution of **13** (130 mg, 0.19 mmol) in dry CH_2Cl_2 (0.2 mL) was added CSA (9 mg, 38 μmol) followed by the addition of $PhC(OMe)_3$ (116 μL, 0.95 mmol). The reaction mixture was stirred overnight at room temperature, quenched with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was dissolved in dry CH_2Cl_2 (2 mL), cold at 0 °C, and TMSCN (191 μL, 1.52 mmol) was added followed by the addition of BF_3–Et_2O (24 μL, 0.19 mmol). The reaction mixture was stirred 1 h at 0 °C, warmed to room temperature, stirred 2 h at room temperature, quenched with saturated aqueous $NaHCO_3$, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was dissolved in dry THF (2 mL) and TBAF (1 M in THF, 380 μL, 0.38 mmol) was added. The mixture was stirred 1 h at room temperature, quenched with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (20% EtOAc in heptane) to give **14** (32 mg, 24%) as a clear viscous oil: $[\alpha]_D^{24}$ +147.6 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 1.30 (s, 9H), 2.28 (s, 3H), 2.39 (d, *J*=9.0 Hz, 1H), 3.43 (dd, *J*=10.0, 7.5 Hz, 1H), 3.73 (dd, *J*=10.0, 3.0 Hz, 1H), 3.98–4.03 (m, 1H), 4.09–4.12 (m, 1H), 4.16 (td, *J*=9.0, 3.5 Hz, 1H), 4.22–4.37 (m, 4H), 4.69 (d, *J*=12.0 Hz, 1H), 4.77 (d, *J*=12.0 Hz, 1H), 5.60 (s, 1H), 7.08 (d, *J*=8.0 Hz, 1H), 7.12 (d, *J*=6.5 Hz, 1H), 7.19 (dd, *J*=8.0, 2.0 Hz, 1H), 7.23–7.28 (m, 4H), 7.30–7.33 (m, 1H), 7.35–7.38 (m, 4H), 7.40 (d, *J*=1.5 Hz, 1H), 7.42–7.44 (m, 3H), 7.74–7.76 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.0, 31.4, 34.6, 45.5, 67.6, 68.4, 69.1, 73.0, 73.3, 77.2, 78.1, 79.5, 79.7, 84.1, 115.9, 124.4, 125.7, 126.8, 127.3, 127.6, 128.1, 128.3, 128.7, 130.2, 132.4, 135.0, 135.5, 137.0, 137.5, 149.8. ESIHRMS $C_{40}H_{43}NO_5S_2$ calcd for $[M+Na]^+$: 704.2480, found 704.2495.

*4.1.10. (2-Methyl-5-tert-butylphenyl) 2-O-benzyl-4-O-(p-methoxybenzyl)-3-O-(2-naphtalenyl-methyl)-7-S-tris(thiophenol)-l-glycero-1-thia-α-D-thiomannoheptopyranoside (**17**).* To a chilled (−60 °C) solution of oxalyl chloride (820 μL, 9.5 mmol) in dry THF (8 mL) was added a solution of DMSO (1.3 mL, 19 mmol) in dry THF (5 mL). The reaction mixture was stirred 30 min at −60 °C and then a solution of **15** (2.63 g, 3.8 mmol) in dry THF (30 mL) was slowly added. The reaction mixture was stirred 5 h at −40 °C and *i*-Pr_2NEt was slowly added (5.4 mL, 30.4 mmol) at −60 °C. The reaction mixture was slowly warmed to room temperature and stirred 2 h at room temperature. In another flask, to a cooled (−78 °C) solution of tris(thiophenol)methane (12.9 g, 38 mmol), in dry THF (40 mL), was dropwise added a solution of *n*-BuLi (1.6 M in hexane, 23.8 mL, 38 mmol). The yellow suspension was stirred 90 min at −78 °C and the previous mixture from Swern reaction was slowly added by cannula at −78 °C. The reaction mixture was stirred, warmed slowly to room temperature and stirred overnight at room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl and then extracted with EtOAc. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (5%–20% *t*-BuOMe in heptane) to give **17** (3.5 g, 90%) as a clear viscous oil: $[\alpha]_D^{24}$ +116.0 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 1.15 (s, 9H), 2.24 (s, 3H), 3.28 (d, *J*=11.0 Hz, 1H); 3.79 (s, 3H), 3.92

(dd, J=9.5, 2.0 Hz, 1H), 3.99–4.02 (m, 1H), 4.08 (t, J=9.5 Hz, 1H), 4.18 (d, J=11.0 Hz, 1H), 4.21 (d, J=10.0 Hz, 1H), 4.67–4.85 (m, 6H), 5.54 (s, 1H), 6.73 (d, J=8.0 Hz, 2H), 6.87 (d, J=8.0 Hz, 2H), 7.07 (d, J=7.5 Hz, 1H), 7.11–7.16 (m, 7H), 7.22–7.30 (m, 6H), 7.32–7.35 (m, 2H), 7.43–7.55 (m, 9H), 7.60 (s, 1H), 7.71–7.75 (m, 1H), 7.77–7.85 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.4, 31.3, 34.5, 55.3, 72.2, 72.3, 73.0, 75.1, 75.2, 77.2, 79.7, 80.1, 85.9, 113.5, 124.4, 125.9, 126.0, 126.5, 127.7, 127.8, 127.9, 128.2, 128.4, 129.1, 129.6, 129.8, 130.5, 131.6, 133.0, 133.3, 133.7, 135.7, 135.8, 137.0, 137.2, 138.2, 149.8, 159.3. ESIHRMS $C_{62}H_{62}O_6S_4$ calcd for $[M+Na]^+$: 1053.3327, found 1053.3340.

*4.1.11. S-Phenyl [(2-methyl-5-tert-butylphenyl) 2-O-benzyl-4-O-(p-methoxybenzyl)-3-O-(2-naphtalenylmethyl)-L-glycero-1-thia-α-D-mannoheptopyranosyl urinate] (**18**) and methyl [(2-methyl-5-tert-butylphenyl) 2-O-benzyl-4-O-(p-methoxybenzyl)-3-O-(2-naphtalenylmethyl)-L-glycero-1-thia-α-D-mannoheptopyranosyl urinate] (**19**).* To a solution of **17** (3.7 g, 3.6 mmol), in MeOH/H_2O/CH_2Cl_2 mixture (42 mL, 12:1:1), was added CuO (331 mg, 3.6 mmol) and $CuCl_2$ (1.94 g, 14.4 mmol). The reaction mixture was stirred 4 h at room temperature, quenched with saturated aqueous NH_4Cl, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (20% EtOAc in petroleum ether) to give **18** (243 mg, 9%) as a yellow viscous oil: $[\alpha]_D^{24}$ +32.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.16 (s, 9H), 2.21 (s, 3H), 3.18 (d, J=10.5 Hz, 1H); 3.79 (s, 3H), 4.01 (dd, J=9.5, 2.0 Hz, 1H), 4.05–4.07 (m, 1H), 4.27 (d, J=9.5 Hz, 1H), 4.53 (d, J=9.5 Hz, 1H), 4.62 (d, J=10.5 Hz, 1H), 4.68 (d, J=10.5 Hz, 1H), 4.72 (s, 2H), 4.79 (d, J=12.0 Hz, 1H), 4.83 (d, J=12.0 Hz, 1H), 4.96 (d, J=12.0 Hz, 1H), 5.52 (s, 1H), 6.84 (d, J=8.0 Hz, 2H), 7.04–7.09 (m, 3H), 7.16 (d, J=8.0 Hz, 1H), 7.23–7.37 (m, 11H), 7.46–7.51 (m, 3H), 7.78–7.80 (m, 1H), 7.81–7.87 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.2, 31.2, 34.4, 55.3, 72.4 (×2), 74.0, 74.2, 75.2, 76.3, 76.9, 80.3, 85.9, 113.5, 124.5, 125.8, 126.0, 126.2, 126.6, 127.0, 127.6, 127.7, 127.9, 128.0, 128.2, 128.5, 129.0, 129.1, 129.6, 129.9, 130.4, 132.9, 133.0, 133.3, 134.6, 135.5, 135.9, 137.8, 149.9, 159.3, 199.3. ESIHRMS $C_{50}H_{52}O_7S_2$ calcd for $[M+Na]^+$: 851.3052, found 851.3097; and **19** (2.18 g, 81%) as a clear viscous oil: $[\alpha]_D^{25}$ +52.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.28 (s, 9H), 2.21 (s, 3H), 2.95 (d, J=9.0 Hz, 1H); 3.34 (s, 3H), 3.78 (s, 3H), 4.00 (dd, J=7.5, 1.0 Hz, 1H), 4.02–4.03 (m, 1H), 4.26–4.32 (m, 2H), 4.53 (d, J=9.0 Hz, 1H), 4.64–4.82 (m, 5H), 4.95 (d, J=10.0 Hz, 1H), 5.59 (s, 1H), 6.82 (d, J=8.5 Hz, 2H), 7.05 (d, J=7.5 Hz, 1H), 7.13 (d, J=7.5 Hz, 1H), 7.22–7.30 (m, 7H), 7.34–7.37 (m, 2H), 7.46–7.49 (m, 3H), 7.75–7.78 (m, 1H), 7.81–7.86 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 19.9, 31.3, 34.5, 52.0, 55.2, 69.4, 72.3, 72.4, 74.1, 74.2, 75.2, 76.8, 80.3, 84.7, 113.8, 123.9, 125.6, 125.8, 125.9, 126.1, 126.5, 127.7, 127.8, 127.9, 128.1, 128.4, 129.6, 129.8, 130.6, 133.0, 133.1, 133.3, 134.7, 135.6, 137.8, 149.9, 159.2, 172.8. ESIHRMS $C_{45}H_{50}O_8S$ calcd for $[M+Na]^+$: 773.3124, found 773.3153.

*4.1.12. (2-Methyl-5-tert-butylphenyl) 2-O-benzyl-4-O-(p-methoxybenzyl)-3-O-(2-naphtalenyl-methyl)-L-glycero-1-thia-α-D-mannoheptopyranoside (**20**).* To a cooled (−78 °C) solution of **19** (2.1 g, 2.8 mmol), in dry THF (30 mL), was added $LiAlH_4$ (213 mg, 5.6 mmol). The reaction mixture was stirred 10 min at −78 °C, warmed to room temperature, and stirred 4 h at room temperature. The reaction mixture was quenched with a Rochelle's salt solution, stirred 4 h at room temperature, and then extracted with EtOAc. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (40% EtOAc in heptane) to give **20** (1.82 g, 90%) as a clear viscous oil: $[\alpha]_D^{24}$ +58.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.29 (s, 9H), 1.76 (dd, J=10.0, 6.0 Hz, 1H), 2.26 (s, 3H), 2.32 (d, J=9.5 Hz, 1H), 3.50–3.61 (m, 3H), 3.78 (s, 3H), 3.95–4.04 (m, 4H), 4.24 (d, J=9.5 Hz, 1H); 4.68 (d, J=10.5 Hz, 1H), 4.71 (d, J=12.5 Hz, 1H), 4.74 (d, J=12.5 Hz, 1H), 4.79 (d, J=12.0 Hz, 1H), 4.83 (d, J=12.0 Hz, 1H), 4.72 (s, 2H), 4.93 (d, J=10.5 Hz, 1H), 5.47 (s, 1H), 6.82 (d, J=8.5 Hz, 2H), 7.12 (d, J=8.0 Hz, 1H), 7.23–7.37 (m, 9H), 7.46–7.51 (m, 3H), 7.76–7.79 (m, 1H), 7.81–7.86 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.1, 31.3, 34.4, 55.2, 65.1, 69.3, 72.3, 72.4, 74.1, 74.2, 75.1, 76.3, 84.1, 85.4, 113.8, 125.3, 125.8, 125.9, 126.0, 126.1, 126.5, 127.7, 127.9, 128.2, 128.4, 128.9, 129.7, 129.9, 130.3, 130.4, 132.0, 133.0, 133.3, 133.5, 134.6, 136.5, 137.8, 149.9, 159.3, 199.3. ESIHRMS $C_{44}H_{50}O_7S$ calcd for $[M+Na]^+$: 745.3175, found 745.3178.

*4.1.13. (2-Methyl-5-tert-butylphenyl) 2,7-di-O-benzyl-4-O-(p-methoxybenzyl)-3-O-(2-naphtalenylmethyl)-L-glycero-1-thia-α-D-mannoheptopyranoside (**21**).* A mixture of **20** (1.40 g, 1.9 mmol) and *n*-Bu_2SnO (570 mg, 2.28 mmol), in dry toluene (20 mL), was heated overnight at reflux. The resulting clear solution was cooled to room temperature and then concentrated under reduced pressure. The residue was dissolved in dry DMF (10 mL) and then CsF (578 mg, 3.8 mmol) and benzyl bromide (340 μL, 2.85 mmol) were added. The reaction mixture was stirred 20 h at room temperature, diluted with CH_2Cl_2, and filtrated through Celite®. The filtrate was concentrated under reduced pressure. The crude was purified on silica gel (20% EtOAc in heptane) to give **21** (1.5 g, 96%) as a clear viscous oil: $[\alpha]_D^{24}$ +51.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.29 (s, 9H), 2.26 (s, 3H), 2.25 (d, J=7.0 Hz, 1H), 3.40 (dd, J=10.0, 4.5 Hz, 1H), 3.55 (t, J=9.5 Hz, 1H), 3.78 (s, 3H), 3.97 (dd, J=9.5, 2.5 Hz, 1H), 4.01–4.05 (m, 2H), 4.20–4.25 (m, 1H), 4.31 (t, J=9.5 Hz, 1H); 4.38 (d, J=12.0 Hz, 1H), 4.44 (d, J=12.0 Hz, 1H), 4.68–4.82 (m, 5H), 4.94 (d, J=10.5 Hz, 1H), 5.57 (s, 1H), 6.82 (d, J=8.5 Hz, 2H), 7.08 (d, J=8.0 Hz, 1H), 7.17 (dd, J=8.0, 1.5 Hz, 1H), 7.21–7.32 (m, 10H), 7.36–7.42 (m, 3H), 7.46–7.7.51 (m, 3H), 7.76–7.79 (m, 1H), 7.81–7.86 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.0, 31.4, 34.5, 55.2, 68.3, 72.2, 72.3 (×2), 72.8, 73.2, 74.0, 75.1, 76.5, 80.4, 85.2, 113.8, 124.3, 125.8, 125.9, 126.0, 126.4, 127.5, 127.6, 127.7, 127.9, 128.1, 128.3, 128.4, 129.7, 129.9, 130.6, 132.9, 133.2, 133.3, 133.6, 135.7, 137.9, 138.0, 149.7, 159.2, 199.3. ESIHRMS $C_{51}H_{56}O_7S$ calcd for $[M+Na]^+$: 835.3644, found 835.3654.

*4.1.14. (2-Methyl-5-tert-butylphenyl) 6-S-acetyl-2,7-di-O-benzyl-4-O-(p-methoxybenzyl)-3-O-(2-naphtalenylmethyl)-D-glycero-1,6-dithio-α-D-mannoheptopyranoside (**23**).* To a cooled (−78 °C) solution of **21** (1.40 g, 1.7 mmol) and Comin's reagent (1.35 g, 3.45 mmol), in dry THF (17 mL), was slowly added a solution of NaHMDS (1 M in THF, 3.5 mL, 3.45 mmol). The reaction mixture was stirred at −78 °C until TLC showed completed reaction (~2 h) and then AcSH (1.2 mL, 17 mmol) was added followed by the addition of a solution of AcSK (1.94 g, 17 mmol) in dry DMF (17 mL). The reaction mixture was stirred overnight at room temperature, quenched with saturated aqueous $NaHCO_3$, and then extracted with *t*-BuOMe. The combined organic layer was washed with water, brine, dried ($MgSO_4$), and then concentrated under reduced pressure (water bath at room temperature). The crude was purified on silica gel (10%–20% *t*-BuOMe in heptane) to give **23** (1.12 g, 76%) as a yellow viscous oil: $[\alpha]_D^{25}$ +71.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.33 (s, 9H), 2.25 (s, 3H), 2.27 (s, 3H), 3.52 (dd, J=10.5 H, J=6.5 Hz, 1H), 3.76 (s, 3H), 3.85 (dd, J=8.0, 2.5 Hz, 1H), 3.55 (dd, J=10.0, 7.5 Hz, 1H), 3.99–4.02 (m, 1H), 4.26–4.33 (m, 2H), 4.45–4.54 (m, 3H), 4.64–4.85 (m, 6H), 5.43 (s, 1H), 6.84 (d, J=8.5 Hz, 2H), 7.09 (d, J=8.0 Hz, 1H), 7.18–7.36 (m, 13H), 7.45–7.49 (m, 3H), 7.56 (s, 1H), 7.75–7.79 (m, 1H), 7.80–7.86 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.3, 30.6, 31.4, 34.6, 43.6, 55.3, 69.7, 72.0, 72.3, 73.0, 74.5, 75.3, 75.6, 77.2, 80.7, 86.0, 113.8, 124.6, 125.9, 126.1, 126.6, 127.4, 127.6, 127.7, 128.0, 128.1, 128.3, 128.4, 129.2, 129.8, 129.9, 130.8, 133.0, 133.3, 133.7, 135.7, 136.0, 138.1, 149.8, 159.2, 194.4. ESIHRMS $C_{53}H_{58}O_7S_2$ calcd for $[M+Na]^+$: 893.3522, found 893.3546.

*4.1.15. (2-Methyl-5-tert-butylphenyl) 6-S-acetyl-2,7-di-O-benzyl-3-O-(2-naphtalenylmethyl)-D-glycero-1,6-dithio-α-D-mannoheptopyranoside (**25**).* To a chilled (−35 °C) solution of **23** (1.10 g, 1.26 mmol), in CH_2Cl_2 (25 mL), was slowly added a mixture of TFA/H_2O (9:1,

2.5 mL). The reaction mixture was stirred 2 h at −35 °C and 1 h at −25 °C. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and then concentrated under reduced pressure (water bath at room temperature). The crude was purified on silica gel (20% EtOAc in heptane) to give **25** (822 mg, 87%) as a clear viscous oil: $[\alpha]_D^{26}$ +62.0 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 1.33 (s, 9H), 2.26 (s, 3H), 2.27 (s, 3H), 2.81 (d, *J*=3.5 Hz, 1H), 3.54 (dd, *J*=10.0, 5.0 Hz, 1H), 3.73 (dd, *J*=9.0, 3.0 Hz, 1H), 3.94 (dd, *J*=10.5, 8.0 Hz, 1H), 4.02–4.04 (m, 1H), 4.30 (dd, *J*=10.0, 2.5 Hz, 1H), 4.34–4.40 (m, 2H), 4.57 (s, 2H), 4.59 (d, *J*=12.5 Hz, 1H), 4.67 (d, *J*=12.5 Hz, 1H), 4.76 (d, *J*=12.0 Hz, 1H), 4.79 (d, *J*=12.0 Hz, 1H), 5.46 (d, *J*=1.0 Hz, 1H), 7.10 (d, *J*=8.0 Hz, 1H), 7.20 (dd, *J*=8.0, 2.0 Hz, 1H), 7.23–7.34 (m, 10H), 7.44–7.49 (m, 3H), 7.56 (d, *J*=2.0 Hz, 1H), 7.79–7.85 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.2, 30.5, 31.4, 34.6, 43.9, 68.4, 69.3, 72.0, 72.4, 73.0, 75.2, 76.8, 79.6, 86.1, 124.5, 125.7, 125.9, 126.1, 126.6, 127.5, 127.6, 127.9, 128.2, 128.3, 128.8, 129.8, 133.0, 133.2, 133.5, 135.4, 135.8, 137.8, 137.9, 149.8, 194.6. ESIHRMS $C_{45}H_{50}O_6S_2$ calcd for $[M+Na]^+$: 773.2947, found 773.2972.

*4.1.16. (2-Methyl-5-tert-butylphenyl) 2,7-di-O-benzyl-4-O,6-S-(1-cyano)benzylidene-3-O-(2-naphtalenyl-methyl)-D-glycero-1,6-dithio-α-D-mannoheptopyranoside (**27**).* To a cooled (−78 °C) solution of **25** (200 mg, 0.26 mmol), in dry THF (2.6 mL), was slowly added a solution of $LiAlH_4$ (2 M in THF, 130 μL, 0.26 mmol). The reaction mixture was stirred 30 min at −78 °C, warmed to room temperature, and stirred 1 h at room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl and then extracted with *t*-BuOMe. The combined organic layer was washed with brine, dried (Na_2SO_4), and then concentrated under reduced pressure (water bath at room temperature). The residue was dissolved in dry CH_2Cl_2 (1 mL) and CSA (6 mg, 0.026 mmol) and $PhC(OMe)_3$ (160 μL, 1.3 mmol) were added. The reaction mixture was stirred overnight at room temperature, quenched with aqueous saturated $NaHCO_3$, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried (Na_2SO_4), and then concentrated under reduced pressure (water bath at room temperature) and dried under strong vacuum. The residue was dissolved in dry CH_2Cl_2 (3 mL), cooled at 0 °C, and then TMSCN (326 μL, 2.6 mmol) was added followed by the addition of BF_3–Et_2O (27 μL, 0.26 mmol). The reaction mixture was stirred 2 h at 0 °C, warmed to room temperature and stirred 2 h at room temperature. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and then concentrated under reduced pressure. The crude was purified on silica gel (10% *t*-BuOMe in heptane) to give **4** (160 mg, 74%) as a clear viscous oil: $[\alpha]_D^{26}$ +113.5 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 1.28 (s, 9H), 2.19 (s, 3H), 3.46 (dd, *J*=10.0, 7.5 Hz, 1H), 3.76 (dd, *J*=10.0 H, *J*=3.5 Hz, 1H), 4.03–4.11 (m, 3H), 4.23–4.32 (m, 3H), 4.71–4.84 (m, 5H), 5.54 (s, 1H), 7.05 (d, *J*=8.0 Hz, 1H), 7.10–7.13 (m, 2H), 7.16 (dd, *J*=8.0, 2.0 Hz, 1H), 7.20–7.32 (m, 6H), 7.35–7.47 (m, 6H), 7.35–7.47 (m, 9H), 7.68–7.74 (m, 5H), 7.79–7.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.2, 31.4, 34.5, 45.5, 67.7, 69.3, 73.0, 73.2, 73.3, 76.5, 77.3, 77.5, 79.2, 85.5, 116.1, 124.4, 125.6, 125.8, 125.9, 126.0, 126.5, 126.9, 127.3, 127.5, 127.6, 127.9, 128.1, 128.2, 128.3, 128.5, 128.7, 130.0, 130.1, 132.6, 133.0, 133.2, 135.4, 135.5, 137.5, 137.6, 149.8. ESIHRMS $C_{51}H_{51}NO_5S_2$ calcd for $[M+Na]^+$: 844.3106, found 844.3110.

*4.1.17. (2-Methyl-5-tert-butylphenyl) 3-O-acetyl-2,7-di-O-benzyl-4-O,6-S-(1-cyano)benzylidene-D-glycero-1,6-dithio-α-D-mannoheptopyranoside (**28**).* To a solution of **27** (300 mg, 0.365 mmol), in a mixture of CH_2Cl_2/H_2O (20:1, 4.2 mL), was added DDQ (100 mg, 0.44 mmol). The reaction mixture was stirred overnight at room temperature, quenched with saturated aqueous $NaHCO_3$, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (20% EtOAc in heptane) to give **14** (204.1 mg, 82%). To a solution of **14** in dry CH_2Cl_2 (4 mL), DMAP (4.5 mg, 36.5 μmol), *i*-Pr_2NEt (127 μL, 0.73 mmol), and Ac_2O (70 μL, 0.73 mmol) were added. The reaction mixture was stirred 4 h at room temperature, quenched with saturated aqueous $NaHCO_3$, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and then concentrated under reduced pressure. The crude was purified on silica gel (10% EtOAc in heptane) to give **28** (210 mg, 97%) as a clear viscous oil: $[\alpha]_D^{26}$ +132.3 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 1.29 (s, 9H), 2.00 (s, 3H), 2.28 (s, 3H), 3.43 (dd, *J*=9.5, 7.5 Hz, 1H), 3.75 (dd, *J*=10.5 H, *J*=3.5 Hz, 1H), 4.03–4.11 (m, 1H), 4.10–4.14 (m, 1H), 4.25 (dd, *J*=12.0 Hz, 1H), 4.29 (dd, *J*=12.0 Hz, 1H), 4.39 (t, *J*=10.0 Hz, 1H), 4.59–4.65 (m, 2H), 4.72 (d, *J*=12.5 Hz, 1H), 5.47 (dd, *J*=10.0, 3.0 Hz, 1H), 5.57 (s, 1H), 7.08 (d, *J*=8.0 Hz, 1H), 7.11–7.14 (m, 2H), 7.19 (dd, *J*=8.0, 1.5 Hz, 1H), 7.23–7.35 (m, 8H), 7.40–7.43 (m, 4H), 7.64–7.67 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.0, 20.9, 31.4, 34.5, 45.5, 67.5, 69.0, 69.9, 73.0, 73.1, 74.8, 77.2, 79.0, 84.6, 116.1, 124.5, 125.4, 126.9, 127.3, 127.6, 128.2, 128.3, 128.5, 128.8, 130.0, 130.2, 132.3, 135.1, 135.6, 137.1, 137.4, 149.8, 170.2. ESIHRMS $C_{42}H_{45}NO_6S_2$ calcd for $[M+Na]^+$: 746.2586, found 746.2582.

*4.1.18. 5-tert-Butyloxycarbonylpentyl 3-O-acetyl-2,7-di-O-benzyl-4-O,6-S-(1-cyano)benzylidene-D-glycero-1-thia-α-D-mannoheptopyranoside (**29**).* To a cooled (−78 °C) solution of **28** (140 mg, 0.19 mmol), TTBP (125 mg, 0.5 mmol), and Ph_2SO (47 mg, 0.23 mmol) in dry CH_2Cl_2 (4.0 mL), was added Tf_2O (freshly distilled over P_2O_5, 39 μL, 0.23 mmol). The orange mixture was stirred 1 h at −78 °C and a solution of *tert*-butyl 6-hydroxyhexanoate (57 mg, 0.3 mmol) in dry CH_2Cl_2 (1.0 mL) was added. The reaction mixture was stirred 1 h at −78 °C, warmed to room temperature, and stirred 1 h at room temperature. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude was purified on silica gel (10% EtOAc in heptane) to give **29** (140 mg, 96%) as a clear viscous oil: $[\alpha]_D^{26}$ +61.8 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 1.22–1.28 (m, 2H), 1.44 (s, 9H), 1.46–1.52 (m, 4H), 2.00 (s, 3H), 2.16 (t, *J*=7.0 Hz, 2H), 3.29 (dt, *J*=9.0, 6.5 Hz, 1H), 3.60 (dt, *J*=9.0, 6.5 Hz, 1H), 3.76 (dd, *J*=10.0 H, *J*=3.0 Hz, 1H), 3.82–3.87 (m, 2H), 3.94–3.98 (m, 1H), 4.04 (t, *J*=10.0 Hz, 1H), 4.47–4.55 (m, 3H), 4.65 (d, *J*=12.5 Hz, 1H), 4.68 (d, *J*=12.5 Hz, 1H), 4.76 (d, *J*=1.0 Hz, 1H), 5.41 (dd, *J*=10.0, 3.0 Hz, 1H), 7.24–7.36 (m, 10H), 7.39–7.44 (m, 3H), 7.63–7.66 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.0, 24.8, 25.5, 28.1, 28.9, 35.4, 45.8, 66.8, 67.2, 67.7, 70.1, 73.3, 73.6, 75.2, 76.2, 78.9, 80.0, 98.4 ($^1J_{CH}$=168.5 Hz), 116.2, 125.3, 127.4, 127.7, 127.9, 128.0, 128.3, 128.4, 128.7, 129.9, 135.3, 137.4, 137.5, 170.1, 173.0. ESIHRMS $C_{41}H_{59}NO_9S$ calcd for $[M+Na]^+$: 754.3026, found 754.3012.

4.1.19. General β-glycosylation procedure. Into a Schlenk flask, to a chilled (−50 °C) solution of **27** (1.0 equiv), TTBP (5 equiv), and BSP (1.1 equiv) in dry CH_2Cl_2 (0.5 M), was added Tf_2O (freshly distilled over P_2O_5, 1.2 equiv). The orange mixture was stirred 1 h at −50 °C and a solution of alcohol (1.5 equiv) in dry CH_2Cl_2 was added. The reaction mixture was stirred 8 h at −50 °C, quenched with saturated aqueous $NaHCO_3$, and then extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified on silica gel (eluent: EtOAc/heptane).

*4.1.19.1. i-Propyl 2,7-di-O-benzyl-4-O,6-S-(1-cyano)benzylidene-3-O-(2-naphtalenylmethyl)-D-glycero-6-thia-β-D-mannoheptopyranoside (**32**).* Prepared by the general procedure with a yield of 90% as a clear viscous oil: $[\alpha]_D^{26}$ +12.9 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ: 1.13 (d, *J*=6.0 Hz, 1H), 1.23 (d, *J*=6.0 Hz, 1H), 3.53 (t, *J*=10.0 Hz, 1H), 3.60 (dd, *J*=9.5, 3.0 Hz, 1H), 3.72 (dd, *J*=10.0, 3.0 Hz,

1H), 3.80–3.86 (m, 2H), 3.92 (dd, *J*=10.0, 5.0 Hz, 1H), 4.02–4.06 (m, 1H), 4.43 (s, 1H), 4.45 (d, *J*=12.5 Hz, 1H), 4.50 (d, *J*=12.5 Hz, 1H), 4.60–4.68 (m, 3H), 4.92 (d, *J*=12.5 Hz, 1H), 5.01 (d, *J*=12.5 Hz, 1H), 7.23–7.34 (m, 9H), 7.40–7.51 (m, 7H), 7.62 (s, 1H), 7.66–7.72 (m, 4H), 7.79–7.82 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 21.7, 23.4, 45.5, 67.2, 70.4, 71.8, 72.2, 73.4, 74.4, 75.4, 77.2, 77.9, 79.5, 99.8 ($^1J_{CH}$=154.7 Hz), 116.0, 125.6, 125.8, 125.9, 126.0, 126.4, 127.5, 127.7, 127.8, 127.9, 128.0, 128.1, 128.4, 128.7, 128.8, 130.1, 133.0, 133.1, 135.5, 135.6, 137.5, 138.4. ESIHRMS $C_{43}H_{43}NO_6S$ calcd for $[M+Na]^+$: 724.2709, found 724.2689.

*4.1.19.2. Methyl 2,7-di-O-benzyl-4-O,6-S-(1-cyano)benzylidene-3-O-(2-naphtalenylmethyl)-D-glycero-6-thia-β-D-mannoheptopyranoside-(1→4)-2,3-isopropylidene-α-L-rhamnopyranoside (**33**).* Prepared by the general procedure with a yield of 78% as a clear viscous oil: $[\alpha]_D^{24}$ −11.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.28 (s, 3H), 1.32 (d, *J*=6.0 Hz, 3H), 1.35 (s, 3H), 3.41 (s, 3H), 3.44–3.51 (m, 2H), 3.61–3.65 (m, 2H), 3.76 (dd, *J*=10.0, 6.5 Hz, 1H), 3.84 (dd, *J*=10.0, 3.0 Hz, 1H), 3.98 (d, *J*=2.5 Hz, 1H), 4.06–4.11 (m, 3H), 4.49 (m, 2H), 4.58 (t, *J*=9.5 Hz, 1H), 4.63 (d, *J*=12.5 Hz, 1H), 4.68 (d, *J*=12.5 Hz, 1H), 4.83–4.86 (m, 3H), 4.91 (d, *J*=12.0 Hz, 1H), 7.23–7.35 (m, 9H), 7.39–7.47 (m, 7H), 7.65–7.72 (m, 5H), 7.79–7.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.8, 26.2, 28.0, 45.7, 54.9, 64.0, 67.4, 71.1, 72.0, 73.3, 74.6, 75.5, 76.0, 77.2, 77.8, 78.4, 79.5, 97.9 ($^1J_{CH}$=167.6 Hz), 100.4 ($^1J_{CH}$=157.7 Hz), 109.3, 116.1, 125.6, 125.7, 125.8, 126.0, 126.3, 127.5, 127.6, 127.8, 127.9, 128.1, 128.4, 128.7, 130.1, 132.9, 133.1, 135.4, 135.5, 137.3, 138.4. ESIHRMS $C_{50}H_{53}NO_{10}S$ calcd for $[M+NH_4]^+$: 877.3734, found 877.3740.

*4.1.19.3. Methyl 2,7-di-O-benzyl-4-O,6-S-(1-cyano)benzylidene-3-O-(2-naphtalenylmethyl)-D-glycero-6-thia-β-D-mannoheptopyranoside-(1→6)-2,3,4-tri-O-benzoyl-α-D-glucopyranoside (**34**).* Prepared by the general procedure with a yield of 87% as a clear viscous oil: $[\alpha]_D^{26}$ +31.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.47 (s, 3H), 3.50–3.55 (m, 2H), 3.59–3.64 (m, 2H), 3.78 (dd, *J*=10.0, 5.5 Hz, 1H), 3.96–4.01 (m, 1H), 4.04–4.11 (m, 2H), 4.36 (d, *J*=12.0 Hz, 1H), 4.40 (s, 1H), 4.62 (t, *J*=9.5 Hz, 1H), 4.64 (d, *J*=12.5 Hz, 1H), 4.68 (d, *J*=12.5 Hz, 1H), 4.98 (d, *J*=12.5 Hz, 1H), 5.06 (d, *J*=12.5 Hz, 1H), 5.24–5.30 (m, 2H), 5.49 (t, *J*=10.0 Hz, 1H), 6.20 (t, *J*=9.5 Hz, 1H), 7.20–7.56 (m, 25H), 7.65–7.74 (m, 5H), 7.81–7.85 (m, 1H), 7.89 (d, *J*=7.5 Hz, 2H), 7.93 (d, *J*=7.5 Hz, 2H), 8.01 (d, *J*=7.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 45.5, 55.5, 67.0, 68.3, 68.7, 69.5, 70.4, 70.5, 72.1, 72.2, 73.2, 74.8, 75.0, 76.8, 77.6, 79.5, 96.9 ($^1J_{CH}$=171.9 Hz), 101.9 ($^1J_{CH}$=156.1 Hz), 115.9, 125.6, 125.8, 125.9, 126.0, 126.5, 127.7, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.1, 129.3, 129.7, 129.8, 129.9, 130.1, 133.0, 133.1, 133.4, 133.6, 135.4, 137.6, 138.2, 165.4, 165.7, 165.8. ESIHRMS $C_{68}H_{61}NO_{14}S$ calcd for $[M+NH_4]^+$: 1165.4157, found 1165.4111.

Supplementary data

Preparation and characterization of **2**, **7**-(L,D), **15**, **16**, **22**, **24**, ^{1}H and ^{13}C NMR spectra of all new compounds are available free of charge. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.04.094.

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