Assembly of a Series of Malarial Glycosylphosphatidylinositol Anchor Oligosaccharides

Yong-Uk Kwon, Regina L. Soucy, Daniel A. Snyder, and Peter H. Seeberger*[a]

Abstract: We report an efficient and convergent synthesis of a series of oligosaccharides comprised of the malaria GPI glycan (**2a**), a promising anti-malaria vaccine candidate currently in preclinical trials and several related oligosaccharide sequences (**3**–**8**) that are possible biosynthetic precursors of the malarial GPI. A flexible synthetic strategy is disclosed that relies on a late-stage coupling between oligomannosides of varying length and pseudo-disaccharide glycosyl acceptor **11** to readily access various malarial GPI structures. Phosphorylation was accomplished by mild and efficient H-phosphonate chemistry before the final deprotection was carried out by using sodium in ammonia. The direct connection of a thiol group via a phosphate diester linkage to the inositol moiety provides a handle for easy conjugation of the GPI glycan to carrier proteins, immobilization on carbohydrate microarrays and photo-affinity labels identification. These synthetic oligosaccharides will serve as molecular probes.

Keywords: carbohydrates • glycosylation • malaria • oligosaccharides • vaccines

Introduction

Forty percent of the world's population lives with the risk of contracting malaria. While only about 1% of all malaria cases are lethal, malaria continues to claim the lives of over two million people annually. The spread of drug-resistant parasites and insecticide-resistant mosquitoes renders malaria as dangerous as ever.[1] Though more and more infectious diseases are being controlled by the cost-effective and easily administered means of vaccines, no viable vaccine candidate has been developed for malaria.[2] Glycosylphosphatidylinositol (GPI) anchors are a class of naturally occurring glycolipids that link proteins and glycoproteins via their C-terminus to cell membranes. The malarial parasite, *Plasmodium falciparum*, expresses GPI in protein anchored and free form on the cell surface that constitutes the toxin responsible for morbidity and mortality by malaria.[3–9]

We have previously demonstrated that mice vaccinated with a synthetic GPI glycan conjugated to a carrier protein, produced anti-GPI antibodies and had a greatly improved chance of survival upon infection with *P. falciparum*.[10] Between 60–75% of vaccinated mice, compared with 0–9% sham-immunized mice, survived. The parasite levels observed in the blood of the vaccine and control groups did not differ significantly, thus indicating that the synthetic GPI glycan conjugate serves as an anti-toxin vaccine.

Initial efforts focused on the solution phase synthesis of malaria toxin **1a** in order to confirm the structural assignment made by Schofield based on the analysis of isolated material (Figure 1). Conjugation of **1a** to a carrier protein produced the first generation vaccine candidate **1b**. The assembly of **1a** was significantly accelerated by automated solid phase synthesis of the GPI glycan.[11] Still, both routes used to prepare GPI oligosaccharides relied on synthetic paths that allowed no flexibility around the GPI glycan core. In order to determine the minimum structural requirements of GPI glycans to elicit a protective immune response, to map the epitopes of human anti-malarial antibodies, and to study the substrate specificity of GPI biosynthetic enzymes, ready access to a series of GPI glycans is required.

Many GPI structures have been synthesized by using various chemical methodologies and protective group combinations.[12–22] Structural studies on GPIs were the basis for sub-

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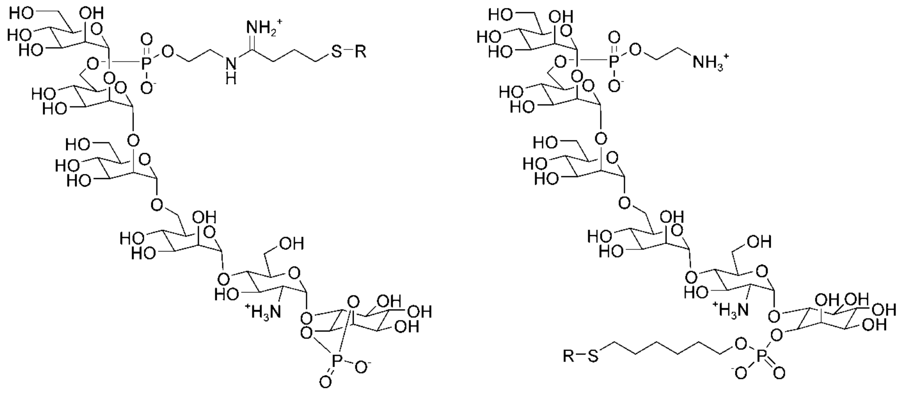


1a: R = H
1b: R = protein

2a: R = H
2b: R = protein

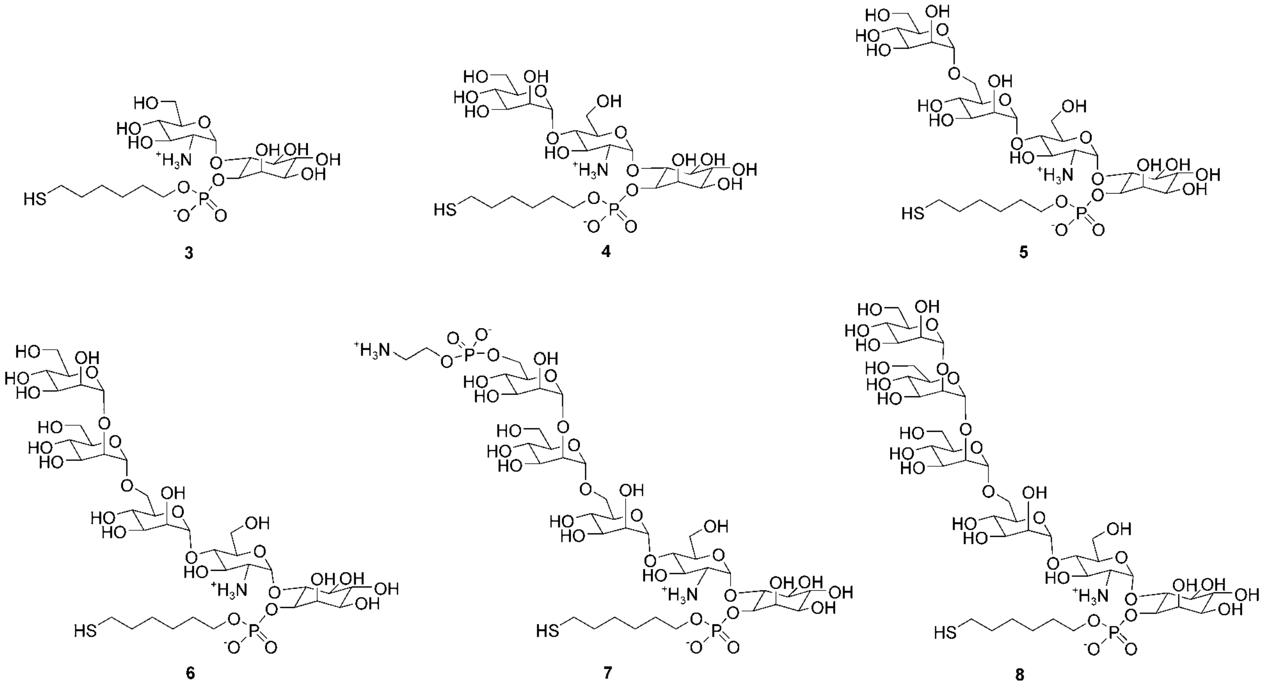
Figure 1. Anti-toxin malaria vaccine candidates.

stantial synthetic work, resulting in total syntheses of the *T. brucei* anchor,[12,13] rat-brain Thy-1 anchor,[14–16] a ceramide-linked yeast anchor,[17] a GPI core structure lacking the phosphoethanolamine,[18] non-lipidated *Toxoplasma gondii* anchor,[19] the sperm CD52 anchor containing an acylated inositol,[20] and a GPI structure containing an acylated inositol ring as well as lipid moieties.[21,22]

In nature, the GPI toxin is anchored in the cell membrane by a lipid portion connected to the inositol ring via a phosphate diester. On this basis, the second-generation malaria GPI vaccine candidate **2a**[23] was designed (Figure 1). Placement of a thiohexanolphosphate group on the inositol moiety provides a point for ready attachment to carrier proteins. Here, we report the synthesis of a series of GPI oligosaccharides that will serve as molecular tools for studies into the biosynthesis, antigenicity and serology of GPIs. These structures will be the basis for the first detailed structure-activity relationships between GPI toxin and anti-malarial antibodies and/or for mapping the specificity of anti-malarial antibodies (Figure 2).

Results and Discussion

Retrosynthetic analysis: The synthesis of a series of GPI oligosaccharides differing in the number of mannoses required us to adopt a synthetic strategy relying on late-stage coupling and modification maneuvers. The retrosynthesis for **2a** may serve as an example for the overall approach. Fully protected oligosaccharide **9** will be the target as it will allow for ready functionalization of the oligosaccharide backbone to create the target molecule. Key to our approach is the n+2 coupling between the mannose oligosaccharides such as **10** and glucosamine-inositol pseudodisaccharide **11**. For the creation of the oligomannosides (e.g. **10**), just three mannose monomers **12–14** would be required (Figure 3). Installation of the phosphate groups was to be effected by use of H-phosphonates. These phosphate ester synthons are very stable and can be purified and stored, but upon activation are highly efficient phosphory-



3
4
5
6
7
8

Figure 2. Target GPI glycan oligosaccharides of different length.

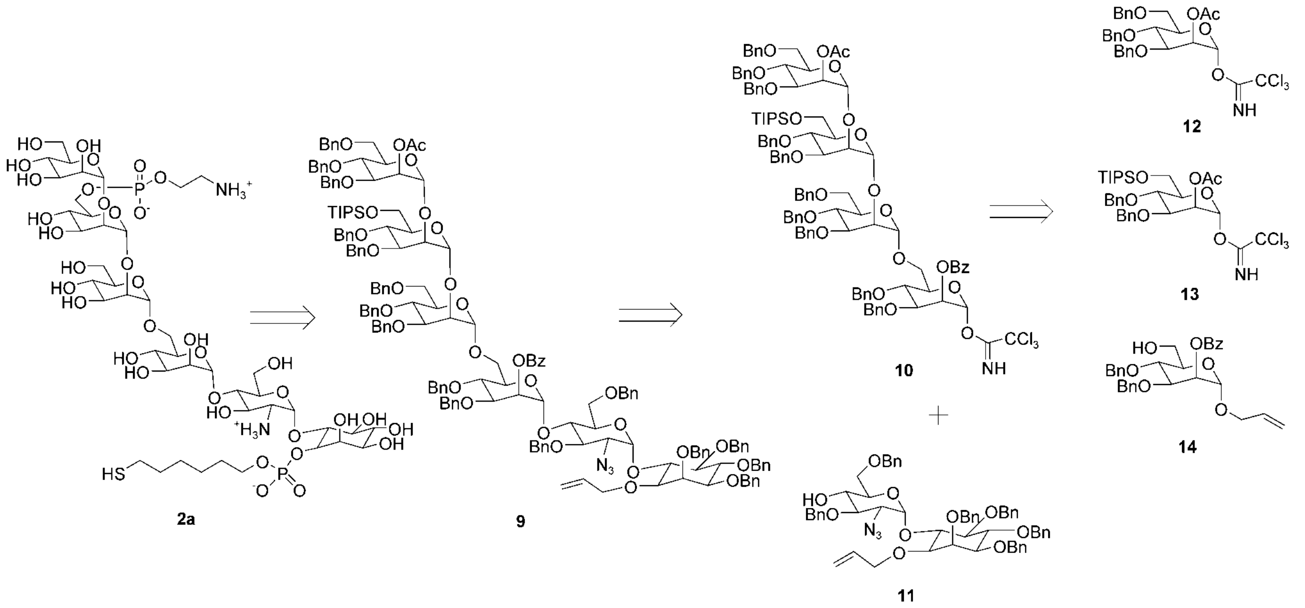
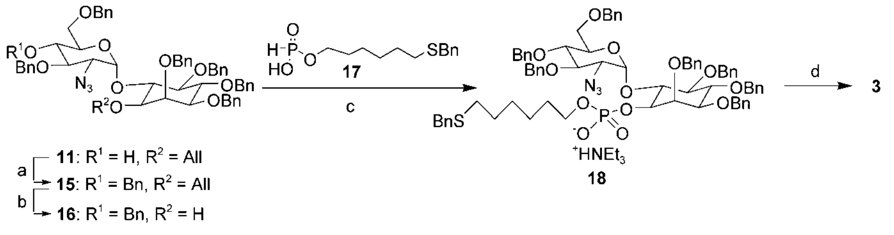


Figure 3. Retrosynthetic analysis for the assembly of GPI oligosaccharides.

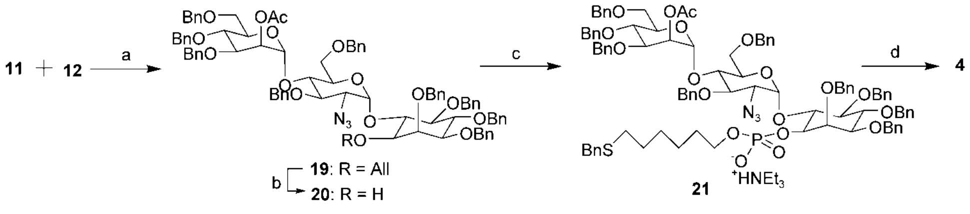
lating agents.[24] The removal of all protective groups at the end of the synthesis was to be achieved by Birch reduction.

Synthesis of GPI glycans of varying length: Disaccharide **3**, the shortest GPI glycan to be prepared, was readily accessible from known pseudo-disaccharide **11**[13] (Scheme 1). Benzylation of **11** to afford disaccharide **15** was followed by removal of the allyl group with palladium(II) chloride in wet acetic acid to provide **16**.[25] H-Phosphonate **17** was prepared by phosphorylation of protected 6-mercapto-1-hexanol.[26] Phosphorylation of **16** by activation of **17** with pivaloyl chloride was directly followed by oxidation of the H-phosphonate diester to the corresponding phosphate diester **18** by treatment with wet iodine. Oxidation with iodine allowed for selective oxidation of the H-phosphonate without oxidation of the thioether present in the molecule.[27] Removal of all protective groups in one step by using sodium in ammonia afforded a mixture of the target compound **3** that was accompanied by the corresponding disulfide.



Scheme 1. Synthesis of GPI disaccharide **3**. a) BnBr, NaH, DMF, 99 %; b) $PdCl_2$, NaOAc, AcOH, H_2O, 60 %; c) 1) **17**, PivCl, pyridine; 2) I_2, H_2O, 97 %; d) Na, NH_3, CH_3OH, THF, 70 %.

Glycosylation of key intermediate **11** with the known mannose trichloroacetimidate **12**[17] in the presence of TMSOTf provided trisaccharide **19** in 90 % yield (Scheme 2). Following the deallylation to produce trisaccharide alcohol **20**, phosphorylation and deprotection protocol established for **3**, the fully protected trisaccharide **21** was prepared. All benzyl ether and ester protective groups present in **21** were readily cleaved under Birch conditions to furnish a mixture of the desired trisaccharide **4** and the corresponding disulfide.



Scheme 2. Synthesis of the GPI glycan trisaccharide **4**. a) TMSOTf, CH_2Cl_2, 90 %; b) $PdCl_2$, NaOAc, AcOH, H_2O, 66 %; c) 1) **17**, PivCl, pyridine; 2) I_2, H_2O, 78 %; d) Na, NH_3, CH_3OH, THF, 63 %.

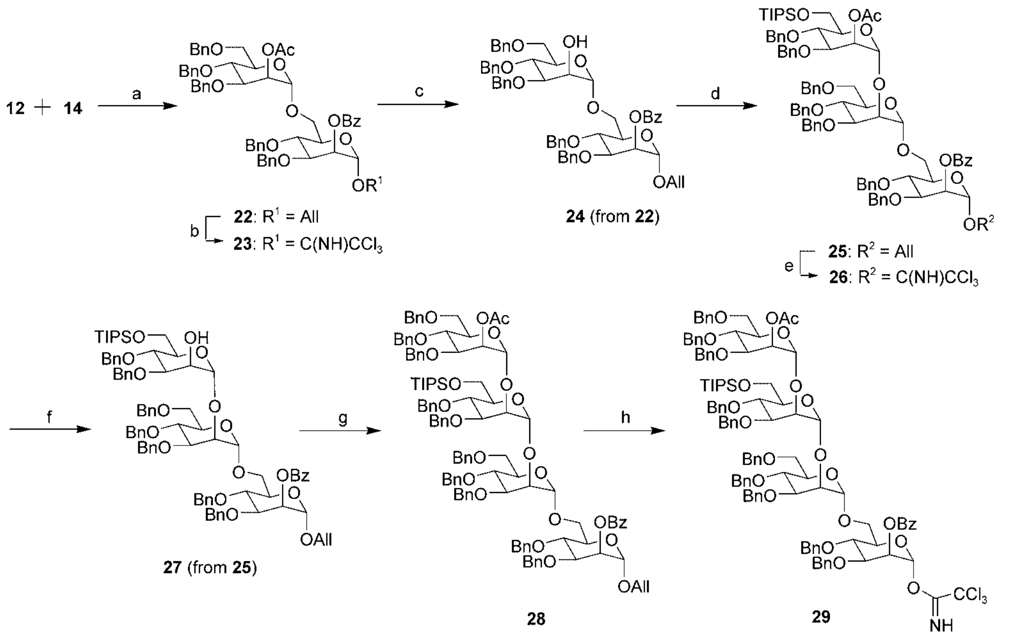
Before the synthesis of longer GPI sequences could be contemplated, a series of oligomannosides to serve as glycosylating agents in the convergent synthesis of the glycan backbone had to be assembled (Scheme 3). Reaction of mannose monomers **12** and **14**[28] yielded dimannoside **22**. Removal of the anomeric allyl group and installation of the trichloroacetimidate leaving group fashioned disaccharide building block **23**. Selective removal of the acetate ester **22** in the presence of benzoate by treatment with hydrogen chloride furnished disaccharide **24**.[29] Glycosylation of **24** with differentially protected mannose **13**[10,11] yielded trimannoside **25** that was readily converted into glycosylating agent **26**. Alternatively, selective deprotection by exposure to magnesium methoxide gave **27**,[30] before mannosylation by using differentially protected mannose **12** resulted in the formation of tetrasaccharide **28**. Deallylation and formation of the glycosyl trichloroacetimidate furnished the tetrasaccharide building block **29**.

With the oligomannoside building blocks (**23**, **26**, and **29**) in hand, the assembly of the GPI glycan backbone was only one step away. Coupling of these oligomannosides with disaccharide **11** afforded the corresponding tetra- (**30**), penta- (**31**) and hexasaccharides (**9**) in excellent yield (Scheme 4).

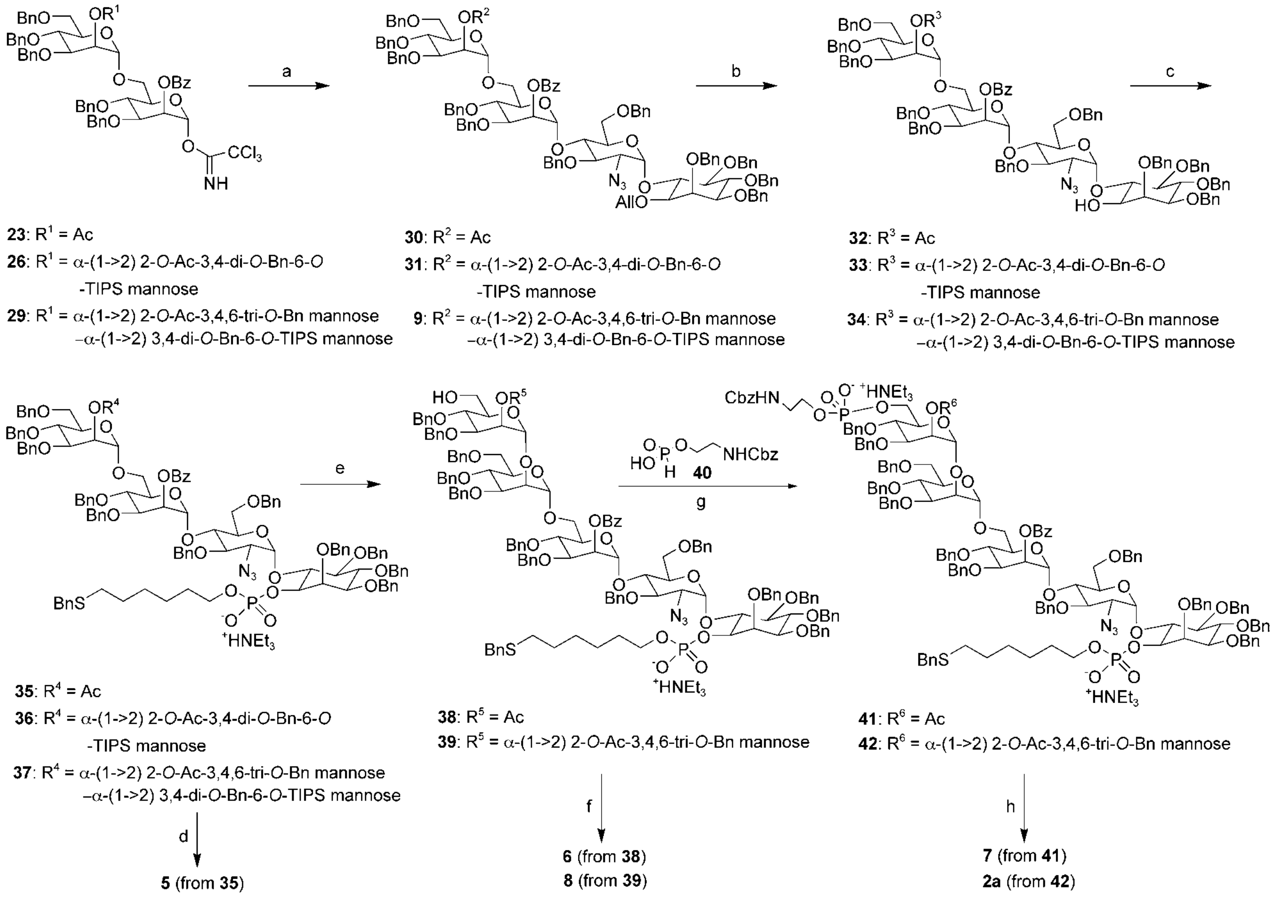
Tetrasaccharide **32** was derived by deallylation of **30** with palladium(II) chloride in wet acetic acid, and was subsequently phosphitylated by the treatment of H-phosphonate **17** and pivaloyl chloride. Successive oxidation with wet iodine afforded the fully protected tetrasaccharide **35**. Birch conditions were applied with the intent to remove all protective groups present in **35**. The ^{1}H NMR of the isolated product revealed small peaks in the region between 7 and 8 ppm. These unexpected resonances did not indicate remaining benzyl groups, instead, more likely, the peaks originated from the partially remaining benzoate group. The benzoate group may be transferred during the Birch reaction to the amine that is obtained by reduction of the azide on glucosamine. Therefore, the global deprotection of **35** was carried using a two-step procedure: removal of the esters by using sodium methoxide in methanol was followed by Birch conditions to afford a mixture of the desired tetrasaccharide **5** and the corresponding disulfide in 58% yield.

The synthesis of the two different pentasaccharide deletion sequences **6** and **7** commenced with the deallylation of **31** by using palladium(II) chloride in aqueous acetic acid. Alcohol **33** was phosphitylated by treatment with H-phosphonate **17** and pivaloyl chloride before oxidation with wet iodine provided the phosphodiester **36** in 95% yield. The TIPS group masking the primary C6 hydroxyl of the terminal mannose of **36** was removed using $Sc(OTf)_3$ in wet acetonitrile at 50°C to afford alcohol **38** in 76% yield.[31] To introduce the second phosphate ester **38** was treated with H-phosphonate **40**[12] and pivaloyl chloride, again followed by oxidation with wet iodine to furnish **41**. The global deprotection of **38** and **41** was accomplished by the removal of the ester groups using sodium methoxide in methanol and subsequent Birch reaction to afford pentasaccharides **6** and **7** in 59% and 56% yield, respectively. In both cases the target compounds were accompanied by the disulfide dimers.

Following the successful preparation of two pentasaccharides, hexasaccharides **2a** and **8** were the next synthetic targets. Deallylation of hexasaccharide **9** by palladium(II) chloride in aqueous acetic acid furnished the alcohol **34** before the previously established (see above) phosphitylation–oxidation sequence yielded phosphate diester **37** in 96% yield. The temporary TIPS group of **37** was removed by using Sc(OTf)$_3$ in wet acetonitrile at 50°C to furnish the alcohol **39** in 79% yield. Installation of the second phosphate diester on **39** by treatment with H-phosphonate **40** and pivaloyl



Scheme 3. Synthesis of the oligomannoside building blocks **23**, **26**, and **29**. a) TMSOTf, CH_2Cl_2, 97%; b) 1) $PdCl_2$, NaOAc, AcOH, H_2O; 2) Cl_3CCN, DBU, CH_2Cl_2 68% (two steps); c) HCl (AcCl, CH_3OH), 91%; d) **13**, TMSOTf, CH_2Cl_2, 93%; e) 1) $PdCl_2$, NaOAc, AcOH, H_2O; 2) Cl_3CCN, DBU, CH_2Cl_2 65% (two steps); f) $Mg(OCH_3)_2$, CH_3OH, THF, 78%; g) **12**, TMSOTf, CH_2Cl_2, 80%; h) 1) $PdCl_2$, NaOAc, AcOH, H_2O; 2) Cl_3CCN, DBU, CH_2Cl_2 62% (two steps).



Scheme 4. Synthesis of GPI oligosaccharides (**5**–**8** and **2a**). a) **11**, TMSOTf, CH_2Cl_2, 82% for **30**, 94% for **31**, 73% for **9**; b) $PdCl_2$, NaOAc, AcOH, H_2O, 58% for **32**, 55% for **33**, 57% for **34**; c) 1) **17**, PivCl, pyridine; 2) I_2, H_2O, 83% for **35**, 95% for **36**, 96% for **37**; d) 1) $NaOCH_3$, CH_3OH, 60°C; 2) Na, NH_3, CH_3OH, THF, 58% (two steps); e) $Sc(OTf)_3$, H_2O, CH_3CN, 76% for **38**, 79% for **39**; f) 1) $NaOCH_3$, CH_3OH, 60°C; 2) Na, NH_3, CH_3OH, THF, 59% for **6**, 61% for **8** (two steps); g) 1) **40**, PivCl, pyridine; 2) I_2, H_2O, 62% for **41**, 72% for **42**; h) 1) $NaOCH_3$, CH_3OH, 60°C; 2) Na, NH_3, CH_3OH, THF, 56% for **7**, 53% for **2a** (two steps).

chloride followed by oxidation afforded **42** in 72% yield. The protective groups of **39** and **42** were completely removed by successive treatment with sodium methoxide in methanol and Birch conditions to provide the two target hexasaccharides **8** and **2a**, respectively.

By developing a highly convergent and reliable synthetic route to the assembly of GPI glycans based on the combination of mannosides with a glucosamine–inositol disaccharide we established the platform for further biological investigations. Although the target compounds were accompanied by the corresponding disulfide dimers, they can be readily reduced to thiol-functionalized GPIs by treatment with tris(carboxyethyl)phosphine hydrochloride (TCEP) before conjugation.[32] The new synthetic GPI glycan **2a** will be conjugated to carrier proteins (**2b**) and will await testing as anti-toxin malaria vaccine candidate. The related shorter GPI oligosaccharides **3**–**8** are readily converted into molecular probes carrying biotin or fluorescent groups by alkylation of the terminal thiol group. Addition of these thiols to appropriately treated surfaces will provide access to GPI microarrays that will be used in epitope mapping and other biological studies including investigations into the biosynthesis of GPIs. Finally, the structures derived via the new synthetic pathway disclosed here, will serve as useful substrates for ELISA tests to detect anti-GPI antibodies in both naturally immune and vaccinated individuals.

Conclusion

We have reported the efficient synthesis of a malaria GPI glycan and a series of related oligosaccharide sequences. Our flexible synthetic strategy, involving late-stage coupling/modification, allows for easy access to various malarial GPI structures ready for biological studies. Direct incorporation of thiol group into inositol moiety of GPI structures provides easy conjugation of GPI glycan to carrier proteins, convenient screening on carbohydrate chips and the potential as photo-affinity labels for receptor/protein identification. The molecules derived during the study reported here, will find use as anti-toxin malaria vaccine candidates, molecular probes for epitope mapping of anti-malarial antibodies and for other biological studies, to reveal the minimal structural requirements that convey protection from malaria.

Experimental Section

General methods: All nonhydrolytic reactions were carried out in oven-dried glassware under dry argon or nitrogen atmosphere. All commercial reagents were used as obtained without further purification. Analytical thin-layer chromatography was performed on Merck silica gel 60 F_{254} glass plates (0.25 mm). Compounds were visualized by dipping the plates in a cerium sulphate/ammonium molybdate solution followed by heating. Flash chromatography was performed using forced flow of the indicated solvent on silica gel (230–400 mesh). NMR spectra were recorded on a Bruker Avance 400, Bruker Avance 500, or Varian Mercury-300 spectrometer; see Supporting Information for selected ^{1}H and ^{13}C NMR spectra. IR spectra were obtained on a Perkin-Elmer 1600 series FT-IR spectrometer. Mass spectra (ESI or MALDI-TOF) were determined on a Bruker Daltonics Apex 3 Telsa FT Spectrometer, an Ionspec Ultima 4.7 Telsa FTICR Spectrometer, or a Bruker FTMS 4.7 Telsa BioAPEX II Spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter.

Preparation of compound 3

(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (15): Benzyl bromide (60 µL, 0.5 mmol) was added at 0 °C to a mixture of compound **11**[13] (118 mg, 0.12 mmol), tetrabutylammonium iodide (5 mg, 0.013 mmol) and NaH (60 %, 30 mg, 0.75 mmol) in DMF (3 mL). The mixture was slowly warmed up to room temperature. After 6 h, CH_3OH was added to quench the reaction, and the solvents were removed. Chromatography (EtOAc/hexane 1:12 → 1:4) of the residue afforded compound **15** (128 mg, 99 %) as a syrup. $R_f=0.42$ (EtOAc/hexane 1:4); $[\alpha]_D^{25}=+54.8$ ($c=4.25$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=3.14$ (dd, $J=2.0$, 8.3 Hz, 1 H), 3.24 (dd, $J=1.6$, 11.0 Hz, 1 H), 3.35 (dd, $J=3.8$, 10.3 Hz, 1 H), 3.40–3.49 (m, 3 H), 3.77 (t, $J=9.5$ Hz, 1 H), 3.99 (dd, $J=9.1$, 10.2 Hz, 1 H), 4.04–4.07 (m, 4 H), 4.19 (t, $J=9.5$ Hz, 1 H), 4.25–4.32 (m, 2 H), 4.42 (d, $J=11.0$ Hz, 1 H), 4.58 (d, $J=12.0$ Hz, 1 H), 4.65–4.77 (m, 4 H), 4.85–4.93 (m, 5 H), 5.03 (d, $J=10.6$ Hz, 1 H), 5.08 (d, $J=10.8$ Hz, 1 H), 5.24 (dd, $J=1.4$, 10.5 Hz, 1 H), 5.33 (dd, $J=1.6$, 17.2 Hz, 1 H), 5.78 (d, $J=3.8$ Hz, 1 H), 5.94–6.03 (m, 1 H), 7.10–7.45 (m, 35 H); ^{13}C NMR ($CDCl_3$): $\delta=63.9$, 68.0, 70.4, 71.3, 73.2, 73.3, 74.5, 75.1, 75.7, 75.9, 76.1, 76.2, 77.7, 80.7, 81.3, 81.8, 82.3, 82.4, 98.1, 117.4, 127.7, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 134.7, 138.4, 138.5, 138.6, 138.7, 138.9, 139.0, 139.3; IR (film): $\tilde{\nu}=3030$, 2866, 2105, 1454, 1359, 1127, 1053 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{64}H_{67}N_3O_{10}Na$ 1060.4719; found 1060.4700 $[M+Na]^+$.

(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (16): Compound **15** (117 mg, 0.11 mmol) was dissolved in AcOH (3 mL). Water (0.15 mL) was added, followed by NaOAc (185 mg, 2.25 mmol) and $PdCl_2$ (196 mg, 1.11 mmol), and the mixture was stirred for 24 h at room temperature. The reaction mixture was diluted with EtOAc and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, concentrated and purified by chromatography (EtOAc/hexane 1:6 → 1:4) to give compound **16** (68 mg, 60 %). $R_f=0.2$ (EtOAc/hexane 1:4); $[\alpha]_D^{25}=+52.0$ ($c=2.90$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=3.10$ (dd, $J=1.5$, 11.0 Hz, 1 H), 3.26–3.30 (m, 2 H), 3.46 (t, $J=13.3$ Hz, 1 H), 3.52–3.58 (m, 2 H), 3.68 (ddd, $J=2.5$, 6.2, 9.1 Hz, 1 H), 3.79 (t, $J=9.9$ Hz, 1 H), 4.00–4.08 (m, 4 H), 4.14–4.21 (m, 2 H), 4.45 (d, $J=10.9$ Hz, 1 H), 4.53 (d, $J=12.0$ Hz, 1 H), 4.68–5.11 (m, 12 H), 5.51 (d, $J=3.6$ Hz, 1 H), 7.21–7.45 (m, 35 H); ^{13}C NMR ($CDCl_3$): $\delta=64.5$, 67.8, 71.3, 73.3, 73.8, 74.0, 75.2, 75.7, 75.9, 76.3, 77.4, 78.5, 80.9, 81.2, 81.4, 81.6, 82.4, 98.8, 127.9, 128.1, 128.2, 128.4, 128.5, 128.7, 128.8, 128.9, 138.2, 138.3, 138.5, 138.7, 138.8, 138.9, 139.0; IR (film): $\tilde{\nu}=3468$, 3030, 2868, 2111, 1454, 1361, 1128, 1049 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{61}H_{63}N_3O_{10}Na$: 1020.4406; found 1020.4429 $[M+Na]^+$.

6-(*S*-Benzyl)thiohexyl *H*-phosphonate (17): Sodium methoxide (25wt %, 4.2 mL, 18.4 mmol) and benzyl chloride (2.12 mL, 18.3 mmol) were added dropwise at 0 °C to a solution of 6-mercapto-1-hexanol (2.5 mL, 18.3 mmol) in EtOH (40 mL). The mixture was heated at reflux for 1 h, cooled, and concentrated. The residue was thoroughly extracted with CH_2Cl_2. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried, filtered, and concentrated. Chromatography (EtOAc/hexane 1:9 → 1:3) of the crude product afforded 6-(*S*-benzyl)thiohexanol. A solution of imidazole (15 g, 220 mmol), triethylamine (38 mL, 273 mmol) and phosphorus trichloride (6.4 mL, 73.3 mmol) in CH_2Cl_2 (700 mL) was stirred for 15 min at 0 °C. To the resulting mixture was added 6-(*S*-benzyl)thiohexanol in CH_2Cl_2 (50 mL) dropwise for 1 h at 0 °C. After being stirred for 1 h at 0 °C, water (30 mL) was added to quench the reaction. The organic layer was washed with 1 N HCl, dried, filtered, and concentrated. The crude product was purified by chromatography (EtOAc/isopropanol/water 5:4:1 with 1 % AcOH) to give 6-(*S*-benzyl)thiohexyl *H*-phosphonate (**17**) (3.8 g, 72 % over two steps). $R_f=0.38$ (CH_3OH/CH_2Cl_2 1:20); ^{1}H NMR ($CDCl_3$): $\delta=1.33$–1.44 (m, 4 H), 1.54–1.61 (m, 2 H), 1.65–1.72 (m, 2 H), 2.41 (t, $J=7.2$ Hz, 2 H), 3.70 (s, 2 H), 3.97–4.06 (m, 2 H), 7.21–7.39 (m, 5 H); ^{13}C NMR ($CDCl_3$): $\delta=28.7$, 29.1, 29.2, 31.3, 31.4, 32.4, 62.7, 126.8, 128.3, 128.7, 138.5; ^{31}P NMR ($CDCl_3$): $\delta=7.47$; HRMS (ESI): *m*/*z*: calcd for $C_{13}H_{20}O_3PS$: 287.0871; found 287.0879 $[M]^-$.

Triethylammonium (2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-1-*O*-(6-(*S*-benzyl)thiohexyl phosphono)-D-*myo*-inositol (18): A mixture of compound **16** (62 mg, 0.062 mmol) and H-phosphonate **17** (179 mg, 0.62 mmol) was coevaporated with pyridine (3×3 mL) and dried in vacuo. To the solution of the residue in pyridine (2 mL) was added pivaloyl chloride (150 µL, 1.22 mmol) at room temperature. After 3 h, water (0.2 mL) and iodine (170 mg, 0.67 mmol) were added. After 1 h, the mixture was diluted with CH_2Cl_2 and washed with 1 M $Na_2S_2O_3$ and water. The organic phase was dried over $MgSO_4$, filtered and concentrated. Chromatography (CH_3OH/CH_2Cl_2 gradient with 1 % Et_3N) afforded phosphodiester **18** (83 mg, 97 %). $R_f=0.3$ (CH_3OH/CH_2Cl_2 1:10); $[\alpha]_D^{25}=+58.2$ ($c=1.77$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=1.21$–1.45 (m, 19 H), 2.39 (t, $J=7.4$ Hz, 2 H), 3.03 (q, $J=7.1$ Hz, 6 H), 3.24 (dd, $J=3.7$, 10.0 Hz, 1 H), 3.38–3.53 (m, 3 H), 3.60 (dd, $J=2.0$, 9.8 Hz, 1 H), 3.68–3.78 (m, 3 H), 3.93–4.18 (m, 4 H), 4.30–4.38 (m, 3 H), 4.47 (d, $J=11.0$ Hz, 1 H), 4.57 (d, $J=12.0$ Hz, 1 H), 4.64 (d, $J=11.6$ Hz, 1 H), 4.66–5.03 (m, 10 H), 5.92 (d, $J=3.6$ Hz, 1 H), 7.02–7.58 (m, 40 H), 12.3 (s, 1 H); ^{13}C NMR ($CDCl_3$): $\delta=8.9$, 25.8, 27.7, 29.1, 29.6, 31.3, 31.7, 36.6, 45.9, 63.6, 66.2, 68.5, 70.4, 72.6, 73.7, 74.6, 74.7, 75.1, 75.2, 75.6, 76.1, 76.5, 77.0, 77.9, 78.0, 78.8, 80.3, 81.4, 82.0, 82.3, 97.1, 127.5, 127.9, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 129.2, 138.5, 138.6, 138.9, 139.0, 139.1, 140.3; ^{31}P NMR ($CDCl_3$): $\delta=0.11$; IR (film): $\tilde{\nu}=3030$, 2931, 2107, 1454, 1360, 1126, 1052 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{80}H_{98}N_4O_{113}PS$: 1385.6521; found 1385.6479 $[M+H]^+$.

(2-Amino-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-(6-thiohexyl phosphono)-D-*myo*-inositol (3): Ammonia (~20 mL) was condensed in a flame-dried three-necked flask at −78 °C. Sodium metal was added portionwise until the solution was dark blue. Phosphodiester **18** (48 mg, 0.035 mmol) in THF (7 mL) was added via cannula, followed by CH_3OH (0.1 mL). The resultant dark blue solution was stirred at −78 °C for 30 min. Following disappearance of the blue color, EtOH (2 mL) and AcOH (~0.5 mL) were added and ammonia was blown off with a stream of Ar. Chromatography of the crude mixture on Sephadex G-25 ($EtOH/H_2O$ 1:1), followed by dialysis and lyophilization afforded a mixture of the target compound **3** and the corresponding disulfide (13 mg, 70 %). ^{1}H NMR (D_2O): $\delta=1.35$–1.83 (m, 10 H), 2.86 (t, $J=7.2$ Hz, 2 H), 3.36–3.48 (m, 1 H), 3.53 (t, $J=9.3$ Hz, 1 H), 3.60–3.65 (m, 2 H), 3.78 (t, $J=9.7$ Hz, 1 H), 3.90–4.04 (m, 4 H), 4.19 (td, $J=3.5$, 10.1 Hz, 1 H), 4.26–4.30 (m, 2 H), 5.61 (d, $J=3.7$ Hz, 1 H); ^{13}C NMR (D_2O): $\delta=24.8$, 27.5, 28.5, 30.0, 38.5, 54.7, 60.4, 66.7, 68.8, 70.8, 71.6, 72.4, 72.5, 73.2, 76.4, 78.0, 97.5; ^{31}P NMR (D_2O): $\delta=1.49$; HRMS (ESI): *m*/*z*: calcd for $C_{36}H_{70}N_2O_{26}P_2S_2Na$: 1095.3026; found 1095.3024 $[M+H]^+$.

Preparation of compound 4

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (19): Disaccharide **11**[13] (200 mg, 0.21 mmol) and mannose donor **12**[17] (150 mg, 0.24 mmol) were coevaporated with toluene (3×3 mL), dried in vacuo and dissolved in CH_2Cl_2 (5 mL). The solution was cooled to 0 °C, followed by the addition of TMSOTf (7 µL, 38 µmol), and stirred for 2 h. The reaction was quenched by the addition of Et_3N (0.1 mL) and the reaction mixture was concentrated. The crude product was purified by chromatography (EtOAc/toluene 1:30 → 1:20) affording trisaccharide **19** (270 mg, 90 %). $R_f=0.36$ (EtOAc/toluene 1:10); $[\alpha]_D^{25}=+59.4$ ($c=0.95$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=1.90$ (s, 3H), 3.21 (d, $J=10.7$ Hz, 1H), 3.27–3.34 (m, 3H), 3.39–3.54 (m, 4H), 3.60 (dd, $J=2.8$, 10.7 Hz, 1H), 3.79 (dd, $J=3.2$, 9.4 Hz, 1H), 3.89–4.07 (m, 7H), 4.16 (t, $J=9.5$ Hz, 1H), 4.22–4.47 (m, 6H), 4.54–5.06 (m, 12H), 5.21 (dd, $J=1.4$, 10.5 Hz, 1H), 5.30 (dd, $J=1.4$, 16.9 Hz, 1H), 5.43 (d, $J=1.4$ Hz, 1H), 5.49 (dd, $J=1.9$, 3.1 Hz, 1H), 5.76 (d, $J=3.7$ Hz, 1H), 5.91–6.01 (m, 1H), 7.01–7.40 (m, 45H); ^{13}C NMR ($CDCl_3$): $\delta=21.4$, 63.8, 68.6, 68.7, 69.1, 70.0, 71.2, 72.2, 72.6, 73.1, 73.2, 73.6, 73.8, 74.1, 74.5, 74.6, 74.9, 75.3, 75.6, 76.0, 76.2, 77.7, 78.7, 81.0, 81.3, 81.6, 82.2, 82.4, 98.1, 99.6, 117.5, 127.4, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 134.6, 138.1, 138.4, 138.6, 138.7, 138.8, 138.9, 139.2, 170.5; IR (film): $\tilde{\nu}=3030$, 2867, 2105, 1741, 1454, 1363, 1236, 1101, 1050 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{86}H_{91}N_3O_{16}Na$: 1444.6292; found 1444.6333 $[M+Na]^+$.

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (20): Compound **19** (110 mg, 0.077 mmol) was dissolved in AcOH (3 mL). Water (0.15 mL) was added, followed by NaOAc (128 mg, 1.56 mmol) and $PdCl_2$ (140 mg, 0.79 mmol), and the mixture was stirred for 24 h at room temperature. The reaction mixture was diluted with EtOAc and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, concentrated and purified by chromatography (EtOAc/toluene 1:20 → 1:10) to give compound **20** (70 mg, 66 %). $R_f=0.17$ (EtOAc/toluene 1:10); $[\alpha]_D^{25}=+57.1$ ($c=2.75$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=2.03$ (s, 3H), 3.10 (d, $J=6.8$ Hz, 1H), 3.25 (d, $J=11.1$ Hz, 1H), 3.34–3.72 (m, 8H), 3.86 (dd, $J=2.8$, 9.4 Hz, 1H), 3.92–4.06 (m, 6H), 4.14 (t, $J=9.4$ Hz, 1H), 4.24–5.08 (m, 19H), 5.44 (s, 1H), 5.53–5.55 (m, 2H), 7.21–7.43 (m, 45H); ^{13}C NMR ($CDCl_3$): δ = 21.4, 64.7, 68.7, 69.1, 70.9, 72.2, 72.7, 73.4, 73.6, 73.8, 73.9, 74.2, 75.0, 75.1, 75.3, 75.4, 75.5, 76.3, 77.6, 78.7, 80.7, 81.3, 81.4, 81.6, 82.3, 98.5, 99.6, 127.6, 127.8, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 137.9, 138.4, 138.5, 138.6, 138.8, 138.9, 139.0, 139.2, 170.5; IR (film): $\tilde{\nu}=3470$, 3030, 2867, 2108, 1742, 1454, 1363, 1235, 1101, 1048 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{83}H_{87}N_3O_{16}Na$: 1404.5979; found 1404.5997 $[M+Na]^+$.

Triethylammonium (2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-1-*O*-(6-(*S*-benzyl)thiohexyl phosphono)-D-*myo*-inositol (21): A mixture of compound **20** (89 mg, 0.089 mmol) and H-phosphonate **17** (186 mg, 0.64 mmol) was coevaporated with pyridine (3× 3 mL) and dried in vacuo. To the solution of the residue in pyridine (1.5 mL) was added pivaloyl chloride (120 µL, 0.97 mmol) at room temperature. After 3 h, water (0.18 mL) and iodine (180 mg, 0.71 mmol) were added. After 1 h, the mixture was diluted with CH_2Cl_2 and washed with 1 M $Na_2S_2O_3$ and water. The organic phase was dried over $MgSO_4$, filtered and concentrated. Chromatography (CH_3OH/CH_2Cl_2 gradient with 1 % Et_3N) afforded phosphodiester **21** (89 mg, 78 %). $R_f=0.35$ (CH_3OH/CH_2Cl_2 1:10); $[\alpha]_D^{25}=+69.0$ ($c=2.10$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=1.21$–1.64 (m, 19H), 2.02 (s, 3H), 2.40 (t, $J=7.4$ Hz, 2H), 2.92 (q, $J=7.3$ Hz, 6H), 3.19 (dd, $J=3.8$, 9.7 Hz, 1H), 3.37–3.70 (m, 8H), 3.76 (dd, $J=3.3$, 9.4 Hz, 1H), 3.88–4.04 (m, 4H), 4.13–4.20 (m, 2H), 4.26–4.49 (m, 7H), 4.58–4.62 (m, 2H), 4.67 (d, $J=11.6$ Hz, 1H), 4.73 (d, $J=10.5$ Hz, 1H), 4.79–5.03 (m, 9H), 5.08 (d, $J=12.0$ Hz, 1H), 5.41 (s, 1H), 5.45 (dd, $J=1.7$, 4.8 Hz, 1H), 5.99 (d, $J=3.7$ Hz, 1H), 7.22–7.59 (m, 50H); ^{13}C NMR ($CDCl_3$): $\delta=8.9$, 21.4, 25.8, 29.1, 29.6, 31.3, 31.7, 36.6, 46.0, 63.5, 68.8, 69.0, 69.2, 69.9, 72.2, 72.6, 73.5, 73.8, 74.2, 75.1, 75.3, 75.4, 76.1, 77.1, 77.6, 77.7, 78.7, 80.6, 81.4, 82.0, 82.3, 97.0, 99.8, 127.3, 127.6, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 128.6, 128.7, 128.9, 129.2, 138.2, 138.4, 138.7, 139.0, 139.1, 139.3, 140.3, 170.4; ^{31}P NMR ($CDCl_3$): $\delta=0.26$; IR (film): $\tilde{\nu}=3030$, 2929, 2862, 2109, 1744, 1454, 1364, 1235, 1099, 1050 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{96}H_{105}N_3O_{19}PS$: 1666.6806; found 1666.6795 $[M]^-$.

(α-D-Mannopyranosyl)-(1→4)-(2-amino-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-(6-thiohexyl phosphono)-D-*myo*-inositol (4): Ammonia (~20 mL) was condensed in a flame-dried three-necked flask at −78 °C. Sodium metal was added portionwise until the solution was dark blue. Phosphodiester **21** (48 mg, 0.027 mmol) in THF (8 mL) was added via cannula, followed by CH_3OH (0.12 mL). The resultant dark blue solution was stirred at −78 °C for 30 min. Following disappearance of the blue color, EtOH (2 mL) and AcOH (~0.5 mL) were added and ammonia was blown off with a stream of Ar. Chromatography of the crude mixture on Sephadex G-25 ($EtOH/H_2O$ 1:1), followed by dialysis and lyophilization afforded a mixture of the target compound **4** and the corresponding disulfide (12 mg, 63 %). ^{1}H NMR (D_2O): $\delta=1.34$–1.83 (m, 10H), 2.86 (t, $J=7.2$ Hz, 2H), 3.45 (dd, $J=3.6$, 10.0 Hz, 1H), 3.50 (t, $J=9.3$ Hz, 1H), 3.62–4.30 (m, 16H), 5.36 (s, 1H), 5.62 (d, $J=3.7$ Hz, 1H); ^{13}C NMR (D_2O): $\delta=24.8$, 27.4, 28.5, 30.0, 38.4, 54.7, 60.4, 61.1, 66.8, 68.9, 70.5, 70.6, 70.9, 71.3, 71.6, 72.5, 73.3, 74.0, 76.2, 76.3, 78.3, 101.8; ^{31}P NMR (D_2O): $\delta=1.53$; HRMS (ESI): m/z: calcd for $C_{48}H_{91}N_2O_{36}P_2S_2$: 1397.4263; found 1397.4284 $[M+H]^+$.

Preparation of compounds 5–8 and 2a

Allyl (2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (22): Trichloroacetimidate **12**[17] (4.3 g, 6.7 mmol) and allyl gylcoside **14**[28] (2.3 g, 4.6 mmol) were coevaporated with toluene (3×3 mL), dried in vacuo and dissolved in CH_2Cl_2 (45 mL). The solution was cooled to 0 °C, followed by the addition of TMSOTf (53 μL, 0.28 mmol), and stirred for 2 h. The reaction was quenched by the addition of Et_3N (1 mL) and the reaction mixture was concentrated. The crude product was purified by chromatography (EtOAc/hexane 1:6 → 1:4) affording disaccharide **22** (4.3 g, 97 %). $R_f=0.5$ (EtOAc/hexane 1:2); $[\alpha]_D^{25}=+33.4$ ($c=3.10$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=2.18$ (s, 3H), 3.61 (dd, $J=1.5$, 10.6 Hz, 1H), 3.71 (dd, $J=3.7$, 10.8 Hz, 1H), 3.76–3.83 (m, 2H), 3.88–4.04 (m, 6H), 4.12–4.21 (m, 2H), 4.42–4.50 (m, 4H), 4.55–4.72 (m, 3H), 4.82–4.91 (m, 3H), 4.98 (d, $J=1.8$ Hz, 1H), 5.03 (d, $J=2.1$ Hz, 1H), 5.18–5.23 (m, 1H), 5.27–5.33 (m, 1H), 5.54 (dd, $J=1.8$, 3.0 Hz, 1H), 5.67 (dd, $J=1.8$, 3.0 Hz, 1H), 5.83–5.96 (m, 1H), 7.11- 7.55 (m, 28H), 8.10–8.14 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta=21.3$, 66.2, 68.2, 68.4, 68.7, 69.0, 70.8, 71.6, 71.7, 73.4, 74.2, 74.3, 75.1, 75.2, 77.9, 78.6, 96.8, 97.9, 118.1, 127.4, 127.5, 127.6, 127.7, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 129.8, 129.9, 133.2, 137.6, 137.8, 138.1, 138.2, 138.4, 165.6, 170.2; IR (film): $\tilde{\nu}=3031$, 2942, 2865, 1731, 1726, 1451, 1268, 1237, 1112, 1059 cm^{-1}; HRMS (MALDI-TOF): m/z: calcd for $C_{59}H_{62}O_{13}Na$: 1001.4082; found 1001.4065 $[M+Na]^+$.

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate (23): Compound **22** (150 mg, 0.15 mmol) was dissolved in AcOH (3 mL). Water (0.15 mL) was added, followed by NaOAc (180 mg, 2.20 mmol) and $PdCl_2$ (190 mg, 1.07 mmol), and the mixture was stirred for 24 h at room temperature. The reaction mixture was diluted with EtOAc and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, concentrated and purified by chromatography (EtOAc/hexane 1:4 → 1:2) to give a lactol. This lactol was dissolved in CH_2Cl_2 (3 mL), and trichloroacetonitrile (0.75 mL) and DBU (5 µL) were added at 0 °C. The mixture was stirred for 1.5 h and concentrated. Chromatography (EtOAc/hexane 1:4) gave compound **23** (113 mg, 68 % from **22**). $R_f=0.50$ (EtOAc/hexane 1:2); $[\alpha]_D^{25}=+41.7$ ($c=2.98$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=2.20$ (s, 3H), 3.63 (dd, $J=1.5$, 10.8 Hz, 1H), 3.76 (dd, $J=3.9$, 10.8 Hz, 1H), 3.84–4.09 (m, 7H), 4.19 (dd, $J=3.2$, 9.0 Hz, 1H), 4.45–4.53 (m, 5H), 4.63–4.73 (m, 3H), 4.86–4.93 (m, 3H), 5.01 (d, $J=1.6$ Hz, 1H), 5.53 (dd, $J=2.0$, 2.7 Hz, 1H), 5.82 (dd, $J=2.1$, 3.0 Hz, 1H), 6.39 (d, $J=1.8$ Hz, 1H), 7.16–8.20 (m, 30H), 8.75 (s, 1H); ^{13}C NMR ($CDCl_3$): $\delta=21.6$, 66.2, 68.1, 68.7, 69.1, 71.9, 72.0, 72.3, 73.7, 73.9, 74.5, 75.5, 75.8, 78.2, 78.4, 91.2, 95.6, 98.2, 128.0, 128.2, 128.3, 128.5, 128.6, 128.7, 128.8, 128.9, 129.1, 129.9, 130.4, 134.0, 137.8, 138.2, 138.4, 138.6, 139.0, 160.1, 165.9, 170.8; IR (film): $\tilde{\nu}=3334$, 3031, 2931, 1730, 1675, 1453, 1366, 1263, 1237, 1096, 1043 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{58}H_{58}Cl_3NO_{13}Na$: 1104.2866; found 1104.2830 $[M+Na]^+$.

Allyl (3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (24): Disaccharide **22** (1.68 g, 1.72 mmol) was dissolved in CH_2Cl_2 (5 mL) and CH_3OH (60 mL). To the reaction mixture was added acetyl choride (0.5 mL, 7.0 mmol) at 0 °C. After being stirred at room temperature for 32 h, Et_3N (1 mL) was added and the reaction mixture was concentrated. The product, **24** (1.46 g, 91 %) was isolated by flash column chromatography (EtOAc/hexane 1:4

→ 1:2) as an oil. $R_f = 0.25$ (EtOAc/hexane 1:2); $[\alpha]_D^{25} = +25.9$ ($c = 1.00$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$): $\delta = 1.68$ (brs, 1H), 3.61–3.71 (m, 2H), 3.82–4.02 (m, 8H), 4.46–4.69 (m, 7H), 4.15 (m, 3H), 4.83 (d, $J = 10.8$ Hz, 2H), 4.90 (d, $J = 10.9$ Hz, 1H), 4.97 (s, 1H), 5.16 (s, 1H), 5.20–5.31 (dd, $J = 17.2$, 10.4 Hz, 2H), 5.65 (m, 1H), 5.84–5.90 (m, 1H), 7.16 (m, 2H), 7.27 (m, 23H), 7.43 (m, 2H), 8.09 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR ($CDCl_3$): $\delta =$ 66.0, 68.4, 68.6, 68.9, 69.2, 71.4, 71.5, 71.8, 72.1, 73.6, 74.4, 74.5, 75.3, 75.5, 78.7, 80.1, 97.0, 99.6, 118.4, 127.8, 127.9, 128.0, 128.1, 128.2, 128.4, 128.5, 128.6, 128.7, 128.8, 130.1, 130.2, 133.5, 133.6, 138.0, 138.2, 138.4, 138.5, 138.6, 165.9; IR (film): $\tilde{\nu} = 3437$, 3031, 2924, 1724, 1602, 1496, 1453, 1269, 1117, 1059 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{57}H_{64}NO_{12}$: 954.4423; found 954.4397 $[M+NH_4]^+$.

Allyl (2-*O*-acetyl-3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (25): Dissacharide acceptor **24** (0.52 g, 0.59 mmol) and mannose donor **13**[10,11] (0.53 g, 0.75 mmol) were coevaporated with toluene (3×3 mL), dried in vacuo and dissolved in CH_2Cl_2 (3 mL). The solution was cooled to 0°C, followed by addition of TMSOTf (7.5 µL, 40 µmol), and stirred for 2 h. The reaction was quenched by addition of Et_3N (0.5 mL) and the reaction mixture was concentrated. The crude product was purified by chromatography (EtOAc/hexane 1:10 → 1:7) affording trisaccharide **25** (0.81 g, 93%). $R_f = 0.56$ (EtOAc/hexane 1:2); $[\alpha]_D^{25} = +13.8$ ($c = 1.00$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$): $\delta = 1.06$ (s, 18H), 2.09 (s, 3H), 3.55–4.18 (m, 19H), 4.40 (s, 1H), 4.43 (d, $J = 2$ Hz, 1H), 4.49–4.67 (m, 8H), 4.77–4.97 (m, 6H), 5.17 (d, $J = 1.3$ Hz, 1H), 5.19 (d, $J = 1.1$ 1H), 5.28 (dd, $J = 17.2$, 1.41, 1H), 5.50 (m, 1H), 5.64 (m, 1H), 5.82–5.90 (m, 1H), 7.14 (m, 3H), 7.20–7.45 (m, 35H), 7.47 (m, 1H), 8.07 (d, $J = 7.1$ Hz, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 12.5$, 18.2, 21.2, 62.9, 66.5, 68.3, 69.0, 69.1, 69.2, 71.0, 71.8, 71.9, 72.1, 72.2, 72.8, 73.0, 73.4, 73.7, 74.1, 74.4, 74.7, 75.3, 75.4, 76.2, 76.3, 78.2, 78.9, 80.1, 96.9, 99.1, 118.4, 127.6, 127.7, 127.8, 127.9, 128.0, 122.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 130.0, 130.1, 133.4, 133.5, 138.7, 139.0, 165.9, 170.3; IR (film): $\tilde{\nu} = 3031$, 2941, 2865, 1732, 1726, 1453, 1268, 1237, 1111, 1053 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{88}H_{108}NO_{18}Si$: 1494.7330; found 1494.7333 $[M+NH_4]^+$.

(2-*O*-Acetyl-3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate (26): Compound **25** (475 mg, 0.32 mmol) was dissolved in AcOH (8 mL). Water (0.4 mL) was added, followed by NaOAc (380 mg, 4.63 mmol) and $PdCl_2$ (400 mg, 2.25 mmol), and the mixture was stirred for 24 h at room temperature. The reaction mixture was diluted with EtOAc and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, concentrated and purified by chromatography (EtOAc/hexane 1:6 → 1:4) to give a lactol. This lactol was dissolved in CH_2Cl_2 (3 mL), and trichloroacetonitrile (1.5 mL) and DBU (12 µL) were added at 0°C. The mixture was stirred for 2 h and concentrated. Chromatography (EtOAc/hexane 1:8) gave compound **26** (330 mg, 65% from **25**). $R_f = 0.47$ (EtOAc/hexane 1:4); $[\alpha]_D^{25} = +25.0$ ($c = 2.82$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 0.95$–1.18 (m, 21H), 2.13 (s, 3H), 3.61 (brd, $J = 9.9$ Hz, 1H), 3.71 (dd, $J = 4.4$, 11.1 Hz, 1H), 3.77–3.79 (m, 2H), 3.85–4.12 (m, 10H), 4.18–4.21 (m, 2H), 4.43–4.48 (m, 2H), 4.56–4.72 (m, 8H), 4.86–4.97 (m, 5H), 5.21 (d, $J = 1.6$ Hz, 1H), 5.54 (s, 1H), 5.80 (t, $J = 2.6$ Hz, 1H), 6.40 (d, $J = 1.8$ Hz, 1H), 7.17–8.15 (m, 40H), 8.76 (s, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 12.5$, 18.4, 18.5, 21.5, 63.0, 66.4, 68.2, 69.4, 72.2, 72.3, 72.4, 73.4, 73.6, 73.9, 74.0, 74.3, 74.9, 75.5, 75.6, 75.7, 78.3, 78.5, 80.5, 91.2, 95.5, 99.3, 99.4, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 129.0, 130.0, 130.3, 133.9, 137.8, 138.4, 138.6, 138.9, 139.0, 139.3, 160.0, 165.9, 170.6; IR (film): $\tilde{\nu} = 3031$, 2941, 1730, 1453, 1368, 1263, 1238, 1096, 1051 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{87}H_{100}Cl_3NO_{18}SiNa$: 1602.5667; found 1602.5601 $[M+Na]^+$.

Allyl (3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (27): Trisaccharide **25** (1.01 g, 0.68 mmol) was dissolved in THF (8 mL) and CH_3OH (34 mL). To the reaction mixture was added magnesium methoxide (7.7 wt%, 9 mL, 6.4 mmol) at room temperature. After 4 h, acetic acid (1 mL) was added and the reaction mixture was concentrated. The desired product, **27** (0.78 g, 78%) was isolated by chromatography (EtOAc/hexane 1:7 → 1:4) as an oil. $R_f = 0.50$ (EtOAc/hexane 1:2); $[\alpha]_D^{25} = +18.3$ ($c = 1.00$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$): $\delta = 1.08$ (s, 18H), 2.34 (d, $J = 3.1$ Hz, 1H), 3.60 (d, $J = 9.9$ Hz, 1H), 3.68–3.71 (dd, $J = 4.1$, 4.3 Hz, 1H), 3.79–4.02 (m, 13H), 4.14–4.19 (m, 3H), 4.24 (t, $J = 2.1$, 2.0 Hz 1H), 4.43–4.59 (m, 9H), 4.66–4.73 (m, 3H), 5.66 (m, 1H), 5.84–5.92 (m, 1H), 7.15–7.43 (m, 37H), 8.09 (d, $J = 7.1$ Hz, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 12.2$, 12.5, 18.2, 18.3, 63.1, 64.9, 66.1, 66.5, 68.2, 68.8, 69.2, 70.9, 71.8, 72.1, 72.2, 72.3, 73.3, 73.4, 74.2, 74.4, 74.8, 75.2, 75.3, 78.9, 80.1, 96.8, 99.2, 100.6, 118.4, 124.6, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.4, 128.5, 128.6, 128.7, 130.0, 130.1, 133.4, 138.0, 138.2, 138.3, 138.7, 138.8, 165.9; IR (film): $\tilde{\nu} = 3413$, 2940, 2865, 1725, 1453, 1363, 1269, 1114, 1050, 737, 697 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{86}H_{106}NO_{17}Si$: 1452.7225; found 1452.7236 $[M+NH_4]^+$.

Allyl (2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (28): Trisacharide acceptor **27** (450 mg, 0.31 mmol) and mannose donor **12**[17] (257 mg, 0.40 mmol) were azeotropically dried with toluene (3×3 mL), dried in vacuo and dissolved in CH_2Cl_2 (5 mL). The solution was cooled to 0°C, followed by the addition of TMSOTf (4 µL, 20 µmol), and stirred for 1.5 h. The reaction was quenched by the addition of Et_3N (0.5 mL) and the reaction mixture was concentrated. The crude product was purified by chromatography (EtOAc/hexane 1:8 → 1:5) affording tetrasaccharide **28** (480 mg, 80%). $R_f = 0.29$ (EtOAc/hexane 1:4); $[\alpha]_D^{25} = +11.7$ ($c = 1.00$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$): $\delta =$ 1.11 (s, 18H), 2.19 (s, 3H), 3.51–4.08 (m, 21H), 4.15–4.22 (m, 4H), 4.31 (d, $J = 12.1$ Hz, 1H), 4.46–4.96 (m, 22H), 4.98 (s, 1H), 5.12 (s, 1H), 5.20 (d, $J = 10.3$ Hz, 1H), 5.28–5.33 (dd, $J = 17.2$, 1.4 Hz, 1H), 5.39 (s, 1H), 5.62–5.69 (m, 2H), 5.85–5.94 (m, 1H), 7.05–7.09 (m, 1H), 7.15–7.49 (m, 52H), 8.11 (d, $J = 7.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 12.3$, 18.3, 18.4, 21.4, 63.1, 66.8, 68.3, 68.9, 69.1, 69.4, 71.0, 71.9, 72.0, 72.1, 72.3, 72.4, 72.5, 73.5, 73.6, 73.7, 73.9, 74.5, 74.7, 75.0, 75.3, 75.4, 75.9, 78.9, 79.0, 79.8, 80.1, 96.9, 99.3, 100.2, 100.4, 118.4, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 130.1, 130.2, 133.5, 133.6, 138.2, 138.3, 138.5, 138.6, 138.8, 138.9, 139.0, 139.1, 166.0, 170.4; IR (film): $\tilde{\nu} =$ 2939, 2865, 17745, 1726, 1497, 1454, 1365, 1269, 1237, 1112, 1055, 1028, 737 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{115}H_{136}NO_{23}Si$: 1926.9267; found 1926.9287 $[M+NH_4]^+$.

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate (29): Tetrasaccharide **28** (600 mg, 0.31 mmol) was dissolved in AcOH (15 mL). Water (0.75 mL) was added, followed by NaOAc (380 mg, 4.63 mmol) and $PdCl_2$ (407 mg, 2.30 mmol), and the mixture was stirred for 18 h at room temperature. The reaction mixture was diluted with EtOAc and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, concentrated and purified by chromatography (EtOAc/hexane 1:5 → 1:3) to give a lactol. The lactol was dissolved in CH_2Cl_2 (5 mL), and trichloroacetonitrile (0.5 mL) and DBU (12 µL) were added at 0°C. The mixture was stirred for 2 h and concentrated. Chromatography (EtOAc/hexane 1:6 → 1:4) gave the imidate donor **29** (392 mg, 62% from **28**). $R_f = 0.57$ (EtOAc/hexane 1:2); $[\alpha]_D^{25} = +21.4$ ($c = 2.80$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 1.07$ (s, 18H), 2.15 (s, 3H), 3.48–3.77 (m, 7H), 3.82–4.18 (m, 18H), 4.27 (d, $J = 12.1$ Hz, 1H), 4.40–4.64 (m, 13H), 4.67–4.92 (m, 9H), 5.33 (s, 1H), 5.58 (m, 1H), 5.76 (m, 1H), 7.05–7.47 (m, 53H), 8.09 (d, $J = 6.8$ Hz, 2H), 8.71 (s, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 12.0$, 18.4, 21.4, 62.4, 63.1, 66.5, 68.2, 69.0, 69.1, 69.4, 72.1, 72.2, 72.3, 72.4, 72.5, 73.5, 73.7, 73.8, 73.9, 74.0, 74.5, 75.0, 75.4, 75.5, 75.9, 77.0, 77.3, 77.5, 77.6, 78.3, 78.9, 79.9, 80.4, 82.4, 83.2, 88.1, 89.8, 91.1, 95.4, 96.4, 97.5, 99.2, 100.2, 100.4, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 129.9, 130.1, 133.7, 137.7, 138.3, 138.4, 138.5, 138.9, 139.0, 139.1, 139.2, 159.9, 165.7, 170.4; IR (film): $\tilde{\nu} = 3339$, 3031, 2940, 2864, 1730, 1676, 1497, 1454, 1365, 1264, 1237, 1093, 1028, 976, 698 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{114}H_{132}Cl_3N_2O_{23}Si$: 2029.8050; found 2029.8121 $[M+NH_4]^+$.

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-

2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (30): Disaccharide **11**[13] (64 mg, 0.067 mmol) and dimannose donor **23** (80 mg, 0.074 mmol) were azeotropically dried with toluene (3× 3 mL), dried in vacuo and dissolved in CH_2Cl_2 (3 mL). The solution was cooled to 0 °C, followed by the addition of TMSOTf (3 μL, 16 μmol), and stirred for 2 h. The reaction was quenched by the addition of Et_3N (0.05 mL) and the reaction mixture was concentrated. The crude product was purified by chromatography (EtOAc/hexane 1:6 → 1:3) affording tetrasaccharide **30** (104 mg, 82 %). $R_f = 0.16$ (EtOAc/hexane 1:4); $[\alpha]_D^{25} = +60.6$ ($c = 2.77$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta = 2.19$ (s, 3 H), 3.24 (dd, $J = 2.2$, 11.2 Hz, 1 H), 3.30 (dd, $J = 3.7$, 10.0 Hz, 1 H), 3.35–3.63 (m, 9 H), 3.77 (dd, $J = 2.5$, 11.3 Hz, 1 H), 3.90–4.10 (m, 10 H), 4.20 (t, $J = 9.5$ Hz, 1 H), 4.32 (t, $J = 9.6$ Hz, 1 H), 4.36–4.48 (m, 7 H), 4.62–5.01 (m, 15 H), 5.10 (d, $J = 11.5$ Hz, 1 H), 5.24 (dd, $J = 1.4$, 10.4 Hz, 1 H), 5.34 (dd, $J = 1.4$, 17.2 Hz, 1 H), 5.53 (d, $J = 1.5$ Hz, 1 H), 5.58 (t, $J = 2.1$ Hz, 1 H), 5.74 (s, 1 H), 5.79 (d, $J = 3.7$ Hz, 1 H), 5.94–6.04 (m, 1 H), 7.07–7.52 (m, 58 H), 8.07–8.10 (m, 2 H); ^{13}C NMR ($CDCl_3$: $\delta = 21.6$, 63.8, 66.3, 68.5, 68.8, 68.9, 69.4, 70.1, 71.2, 71.8, 71.9, 72.0, 73.2, 73.3, 73.8, 74.1, 74.4, 74.5, 74.6, 74.9, 75.3, 75.4, 75.6, 76.0, 76.3, 78.2, 79.0, 80.7, 81.3, 81.7, 82.2, 82.4, 98.1, 98.7, 99.5, 117.5, 127.4, 127.7, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 130.3, 130.4, 133.6, 134.6, 137.8, 138.0, 138.4, 138.6, 138.9, 139.0, 139.2, 139.3, 165.8, 170.6; IR (film): $\tilde{\nu} = 3031$, 2869, 2106, 1746, 1725, 1454, 1362, 1268, 1237, 1100, 1045 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{113}H_{117}N_3O_{22}Na$: 1890.8021; found 1890.8098 $[M+Na]^+$.

(2-*O*-Acetyl-3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (31): Disaccharide **11**[13] (183 mg, 0.19 mmol) and trimannose donor **26** (330 mg, 0.21 mmol) were azeotropically dried with toluene (3×3 mL), dried in vacuo and dissolved in CH_2Cl_2 (6 mL). This solution was cooled to −24 °C, followed by addition of TMSOTf (3.8 μL, 21 μmol), and stirred for 1 h. The reaction was quenched by addition of Et_3N (0.1 mL) and the reaction mixture was concentrated. The crude product was purified by chromatography (EtOAc/toluene 1:30) affording pentasaccharide **31** (430 mg, 94 %). $R_f = 0.22$ (EtOAc/toluene 1:25); $[\alpha]_D^{25} = +39.4$ ($c = 3.73$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta = 0.96$–1.16 (m, 21 H), 2.13 (s, 3 H), 3.24 (dd, $J = 2.6$, 11.3 Hz, 1 H), 3.28–3.37 (m, 3 H), 3.41–3.54 (m, 5 H), 3.63–3.69 (m, 2 H), 3.77 (br d, $J = 8.9$ Hz, 1 H), 3.90–3.95 (m, 6 H), 3.99–4.23 (m, 11 H), 4.31–4.76 (m, 15 H), 4.78–4.88 (m, 6 H), 4.92–5.02 (m, 6 H), 5.11 (d, $J = 11.3$ Hz, 1 H), 5.21 (d, $J = 1.5$ Hz, 1 H), 5.25 (dd, $J = 1.3$, 10.4 Hz, 1 H), 5.35 (dd, $J = 1.5$, 17.2 Hz, 1 H), 5.54 (t, $J = 2.4$ Hz, 1 H), 5.59 (d, $J = 1.5$ Hz, 1 H), 5.74 (s, 1 H), 5.80 (d, $J = 3.7$ Hz, 1 H), 5.97–6.04 (m, 1 H), 7.07–7.48 (m, 68 H), 8.04–8.06 (m, 2 H); ^{13}C NMR ($CDCl_3$): $\delta = 12.5$, 18.4, 18.5, 21.5, 62.9, 64.0, 66.6, 68.8, 69.2, 69.3, 69.4, 70.0, 71.2, 71.6, 71.8, 71.9, 72.0, 72.3, 72.4, 73.1, 73.3, 73.4, 73.6, 73.8, 74.0, 74.1, 74.5, 74.7, 74.8, 74.9, 75.1, 75.5, 75.7, 76.0, 76.3, 76.6, 77.0, 77.7, 78.4, 79.2, 80.4, 80.9, 81.3, 81.7, 82.2, 82.4, 98.1, 99.3, 99.4, 99.5, 117.5, 127.5, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 130.2, 130.4, 133.6, 134.7, 137.8, 138.2, 138.4, 138.6, 138.7, 138.8, 138.9, 139.0, 139.2, 139.3, 139.4, 165.7, 170.6; IR (film): $\tilde{\nu} = 3031$, 2940, 2865, 2106, 1725, 1453, 1361, 1268, 1238, 1099, 1051 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{142}H_{167}N_5O_{27}Si$: 1201.0803; found 1201.0796 $[M+2NH_4]^{2+}$.

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (9): Disaccharide **11**[13] (95 mg, 0.10 mmol) and tetramannose donor **29** (252 mg, 0.13 mmol) were coevaporated with toluene (3×3 mL), dried in vacuo and dissolved in CH_2Cl_2 (5 mL). The solution was cooled to 0 °C, followed by addition of TMSOTf (3.5 μL, 19 μmol), and stirred for 1.5 h. The reaction was quenched by addition of Et_3N (0.1 mL) and the reaction mixture was concentrated. The crude product was purified by chromatography (EtOAc/hexane 1:7 → 1:5) affording hexasaccharide **9** (204 mg, 73 %). $R_f = 0.55$ (EtOAc/hexane 1:2); $[\alpha]_D^{25} = +36.6$ ($c = 4.70$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta = 1.03$–1.11 (m, 21 H), 2.16 (s, 3 H), 3.19–5.01 (m, 68 H), 5.07–5.10 (m, 2 H), 5.24 (dd, $J = 1.5$, 10.5 Hz, 1 H), 5.30–5.37 (m, 2 H), 5.56 (d, $J = 1.5$ Hz, 1 H), 5.62 (br s, 1 H), 5.72 (br s, 1 H), 5.77 (d, $J = 3.6$ Hz, 1 H), 5.92–6.05 (m, 1 H), 6.88–7.49 (m, 83 H), 7.99–8.03 (m, 2 H); ^{13}C NMR ($CDCl_3$): $\delta = 12.2$, 18.4, 21.5, 62.8, 63.8, 66.4, 68.6, 69.0, 69.2, 69.8, 71.1, 71.4, 71.8, 72.1, 72.3, 72.4, 72.8, 73.0, 73.1, 73.5, 73.6, 73.7, 73.8, 74.4, 74.7, 74.8, 75.3, 75.5, 75.6, 75.8, 76.1, 77.5, 79.0, 79.1, 79.8, 80.1, 80.8, 81.2, 81.5, 82.1, 82.3, 97.9, 99.2, 99.3, 100.2, 117.4, 127.2, 127.3, 127.6, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 130.0, 130.2, 133.4, 134.5, 137.7, 138.0, 138.1, 138.4, 138.5, 138.7, 138.8, 138.9, 139.0, 139.1, 139.2, 165.6, 170.4; IR (film): $\tilde{\nu} = 3030$, 2940, 2866, 2106, 1723, 1453, 1360, 1268, 1238, 1098, 1051 cm^{-1}; HRMS (MALDI-TOF): m/z: calcd for $C_{169}H_{187}N_3O_{32}SiNa$: 2823.2822; found 2823.2798 $[M+Na]^+$.

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (32): Compound **30** (115 mg, 0.06 mmol) was dissolved in AcOH (3 mL). Water (0.15 mL) was added, followed by NaOAc (110 mg, 1.34 mmol) and $PdCl_2$ (105 mg, 0.59 mmol), and the mixture was stirred for 24 h at room temperature. The reaction mixture was diluted with EtOAc and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, concentrated and purified by chromatography (EtOAc/hexane 1:5 → 1:3) to give compound **32** (65 mg, 58 %). $R_f = 0.32$ (EtOAc/hexane 1:2); $[\alpha]_D^{25} = +52.6$ ($c = 1.85$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta = 2.18$ (s, 3 H), 3.08 (d, $J = 6.7$ Hz, 1 H), 3.25–3.52 (m, 6 H), 3.54 (dd, $J = 2.2$, 9.9 Hz, 1 H), 3.61–3.70 (m, 4 H), 3.78 (dd, $J = 2.8$, 10.9 Hz, 1 H), 3.89–4.06 (m, 9 H), 4.14 (dd, $J = 9.7$, 10.5 Hz, 1 H), 4.28–4.46 (m, 7 H), 4.61–5.09 (m, 16 H), 5.51–5.55 (m, 3 H),5.73 (t, $J = 2.2$ Hz, 1 H), 7.12–7.38 (m, 58 H), 8.05–8.08 (m, 2 H); ^{13}C NMR ($CDCl_3$): $\delta = 21.6$, 64.6, 66.3, 68.5, 68.8, 68.9, 69.3, 70.9, 71.8, 72.0, 72.1, 72.2, 72.7, 73.4, 73.8, 74.1, 74.4, 74.7, 75.1, 75.3, 75.4, 75.5, 75.6, 76.3, 77.6, 78.2, 78.9, 80.6, 81.2, 81.3, 81.6, 82.3, 98.5, 98.7, 99.4, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 130.3, 133.5, 137.5, 138.0, 138.4, 138.5, 138.6, 138.9, 139.1, 165.8, 170.6; IR (film): $\tilde{\nu} = 3473$, 3031, 2870, 2108, 1746, 1725, 1454, 1362, 1268, 1236, 1099, 1047 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{110}H_{117}N_4O_{22}$: 1845.8154; found 1845.8120 $[M+NH_4]^+$.

(2-*O*-Acetyl-3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (33): Compound **31** (400 mg, 0.17 mmol) was dissolved in AcOH (10 mL). Water (0.5 mL) was added, followed by NaOAc (145 mg, 1.77 mmol) and $PdCl_2$ (150 mg, 0.85 mmol), and the mixture was stirred for 24 h at room temperature. The reaction mixture was diluted with EtOAc and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, concentrated and purified by chromatography (EtOAc/hexane 1:6 → 1:4) to give compound **33** (216 mg, 55 %). $R_f = 0.15$ (EtOAc/hexane 1:4); $[\alpha]_D^{25} = +32.9$ ($c = 1.73$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta = 1.08$–1.14 (m, 21 H), 2.11 (s, 3 H), 3.07 (d, $J = 6.8$ Hz, 1 H), 3.25–3.36 (m, 3 H), 3.40–3.51 (m, 4 H), 3.54 (dd, $J = 2.1$, 9.9 Hz, 1 H), 3.64–3.77 (m, 4 H), 3.89–4.17 (m, 16 H), 4.31–4.85 (m, 21 H), 4.91–5.00 (m, 4 H), 5.05–5.08 (m, 2 H), 5.19 (d, $J = 1.7$ Hz, 1 H), 5.51–5.52 (m, 2 H), 5.55 (d, $J = 1.5$ Hz, 1 H), 5.72 (br s, 1 H), 7.11–7.38 (m, 68 H), 8.04–8.07 (m, 2 H); ^{13}C NMR ($CDCl_3$): $\delta = 12.5$, 18.4, 18.5, 21.5, 62.9, 64.8, 68.8, 69.1, 69.2, 69.3, 70.8, 71.8, 71.9, 72.0, 72.3, 72.4, 73.4, 73.5, 73.6, 73.8, 74.0, 74.1, 74.6, 74.7, 75.1, 75.3, 75.5, 75.6, 75.7, 76.3, 77.6, 78.4, 79.1, 80.4, 80.5, 81.3, 81.4, 81.6, 82.3, 98.4, 99.2, 99.3, 99.4, 127.5, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 130.2, 130.3, 133.6, 137.5, 138.2, 138.4, 138.5, 138.6, 138.9, 139.0, 139.2, 139.3, 165.7, 170.6; IR (film): $\tilde{\nu} = 3031$, 2940, 2865, 2107, 1725, 1453, 1362, 1268, 1238, 1097, 1050 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{139}H_{163}N_5O_{27}Si$: 1181.0647; found 1181.0638 $[M+2NH_4]^{2+}$.

(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol (34): Hexasaccharide **9** (200 mg, 0.07 mmol) was dissolved in AcOH (8 mL). Water (0.4 mL) was added, followed by NaOAc (96 mg, 1.17 mmol) and $PdCl_2$ (100 mg, 0.56 mmol), and the mixture was stirred for 20 h at room temperature.

The reaction mixture was diluted with EtOAc and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, concentrated and purified by chromatography (EtOAc/hexane 1:5) to give compound **34** (112 mg, 57 %). $R_f=0.42$ (EtOAc/hexane 1:2); $[\alpha]_D^{25}=+27.0$ ($c=2.05$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=$ 1.02–1.07 (m, 21 H), 2.12 (s, 3 H), 3.04 (d, $J=6.9$ Hz, 1 H), 3.21–3.46 (m,9 H), 3.50 (dd, $J=2.2$, 10.0 Hz, 1 H), 3.56–5.06 (m, 58 H), 5.32 (br s, 1 H), 5.46 (d, $J=3.6$ Hz, 1 H), 5.51 (d, $J=1.8$ Hz, 1 H), 5.58 (t, $J=2.1$ Hz, 1 H), 5.68 (t, $J=2.4$ Hz, 1 H), 6.85–7.42 (m, 83 H), 7.95–7.99 (m, 2 H); ^{13}C NMR ($CDCl_3$): $\delta=12.2$, 18.4, 21.4, 62.8, 64.6, 66.4, 68.6, 69.0, 69.1, 69.2, 70.6, 71.5, 71.8, 71.9, 72.0, 72.2, 72.4, 72.7, 73.3, 73.4, 73.5, 73.6, 73.8, 74.3, 74.7, 74.8, 75.1, 75.3, 75.4, 75.6, 76.1, 77.5, 78.9, 79.8, 80.2, 80.3, 81.2, 81.4, 82.1, 98.1, 98.9, 99.3, 100.1, 127.3, 127.4, 127.6, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 130.0, 133.4, 137.4, 138.0, 138.2, 138.3, 138.4, 138.7, 138.8, 138.9, 139.0, 139.1, 165.6, 170.4; IR (film): $\tilde{\nu}=3031$, 2940, 2864, 2106, 1725, 1452, 1363, 1268, 1239, 1097, 1051 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{166}H_{183}N_3O_{32}SiNa$: 2783.2509; found 2783.2444 $[M+Na]^+$.

Triethylammonium (2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-1-*O*-(6-(*S*-benzyl)thiohexyl phosphono)-D-*myo*-inositol (35): A mixture of compound **32** (142 mg, 0.08 mmol) and H-phosphonate **17** (200 mg, 0.69 mmol) was coevaporated with pyridine (3 × 3 mL) and dried in vacuo. To the residue in pyridine (2 mL) was added pivaloyl chloride (170 µL, 1.38 mmol) at room temperature. After 3 h, water (0.15 mL) and iodine (190 mg, 0.75 mmol) were added. After 1 h, the mixture was diluted with CH_2Cl_2 and washed with 1 M $Na_2S_2O_3$ and water. The organic phase was dried over $MgSO_4$, filtered and concentrated. Chromatography (CH_3OH/CH_2Cl_2 gradient with 1 % Et_3N) afforded phosphodiester **35** (141 mg, 83 %). $R_f=0.35$ (CH_3OH/CH_2Cl_2 1:10); $[\alpha]_D^{25}=+63.1$ ($c=1.30$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=$ 1.23–1.66 (m, 19 H), 2.18 (s, 3 H), 2.41 (t, $J=7.4$ Hz, 2 H), 2.94 (q, $J=7.2$ Hz, 6 H), 3.21 (dd, $J=3.7$, 10.0 Hz, 1 H), 3.40–3.78 (m, 10 H), 3.86–4.03 (m, 7 H), 4.09 (t, $J=9.4$ Hz, 1 H), 4.15–4.24 (m, 2 H), 4.33–4.52 (m, 9 H), 4.64–4.77 (m, 5 H), 4.81–4.97 (m, 9 H), 5.02–5.12 (m, 3 H), 5.51 (s, 1 H), 5.58 (s, 1 H), 5.69 (s, 1 H), 6.01 (d, $J=3.6$ Hz, 1 H), 7.20–7.51 (m, 63 H), 8.07–8.09 (m, 2 H); ^{13}C NMR ($CDCl_3$): $\delta=9.3$, 21.6, 25.9, 29.2, 29.6, 31.3, 31.4, 31.7, 36.7, 45.8, 63.5, 66.0, 66.1, 66.3, 68.5, 68.9, 69.1, 69.4, 69.9, 71.8, 71.9, 72.0, 72.7, 73.6, 73.8, 74.1, 74.4, 74.5, 74.8, 74.9, 75.1, 75.4, 75.5, 76.1, 76.2, 77.1, 77.7, 77.8, 78.2, 79.0, 80.5, 81.5, 82.1, 82.3, 97.1, 98.8, 99.8, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.5, 128.6, 128.7, 128.8, 128.9, 129.3, 130.3, 130.4, 133.6, 137.9, 138.0, 138.4, 138.6, 138.7, 139.0, 139.1, 139.3, 140.4, 165.8, 170.6; ^{31}P NMR ($CDCl_3$): $\delta=0.33$; IR (film): $\tilde{\nu}=3030$, 2933, 2107, 1745, 1725, 1453, 1362, 1268, 1235, 1098, 1051 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{123}H_{131}N_3O_{25}PS$: 2112.8535; found 2112.8500 $[M]^-$.

Triethylammonium (2-*O*-acetyl-3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-1-*O*-(6-(*S*-benzyl)thiohexyl phosphono)-D-*myo*-inositol (36): A mixture of compound **33** (200 mg, 0.09 mmol) and H-phosphonate **17** (167 mg, 0.58 mmol) was coevaporated with pyridine (3 × 3 mL) and dried in vacuo. To the solution of the residue in pyridine (2.5 mL) was added pivaloyl chloride (140 µL, 1.13 mmol) at room temperature. After 3 h, water (0.2 mL) and iodine (160 mg, 0.63 mmol) were added. After 50 min, the mixture was diluted with CH_2Cl_2 and washed with 1 M $Na_2S_2O_3$ and water. The organic phase was dried over $MgSO_4$, filtered and concentrated. Chromatography (CH_3OH/CH_2Cl_2 gradient with 1 % Et_3N) afforded phosphodiester **36** (222 mg, 95 %). $R_f=0.39$ (CH_3OH/CH_2Cl_2 1:10); $[\alpha]_D^{25}=+41.1$ ($c=2.09$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=$ 1.06–1.10 (m, 21 H), 1.22–1.63 (m, 19 H), 2.09 (s, 3 H), 2.38 (t, $J=7.4$ Hz, 2 H), 2.92 (q, $J=7.2$ Hz, 6 H), 3.16 (dd, $J=3.7$, 9.9 Hz, 1 H), 3.29 (d, $J=9.7$ Hz, 1 H), 3.40–3.60 (m, 8 H), 3.69–3.75 (m, 3 H), 3.87–3.96 (m, 7 H), 4.02–4.17 (m, 6 H), 4.22–4.37 (m, 4 H), 4.40–4.72 (m, 14 H), 4.77–4.93 (m, 10 H), 4.99–5.08 (m, 3 H), 5.16 (br s, 1 H), 5.43 (br s, 2 H), 5.64 (br s, 1 H), 5.98 (d, $J=3.7$ Hz, 1 H), 7.05–7.45 (m, 73 H), 7.99–8.01 (m, 2 H); ^{13}C NMR ($CDCl_3$): $\delta=8.9$, 12.5, 18.5, 18.6, 21.5, 25.9, 29.2, 29.6, 31.7, 36.7, 45.8, 62.9, 63.7, 66.2, 66.3, 66.6, 66.7, 69.2, 69.3, 69.5, 69.9, 71.6, 72.0, 72.3, 72.5, 72.7, 73.5, 73.6, 73.8, 74.0, 74.1, 74.7, 75.1, 75.5, 75.7, 76.2, 77.1, 77.2, 77.6, 77.8, 78.4, 79.2, 80.3, 81.5, 82.1, 82.3, 99.3, 99.5, 99.8, 127.3, 127.5, 127.6, 127.8, 127.9, 128.0, 128.3, 128.5, 128.6, 128.7, 128.8, 128.9, 129.3, 130.2, 130.4, 133.6, 138.0, 138.3, 138.4, 138.7, 138.9, 139.0, 139.1, 139.3, 139.4, 140.3, 139.4, 165.7, 170.6; ^{31}P NMR ($CDCl_3$): $\delta=0.34$; IR (film): $\tilde{\nu}=3030$, 2940, 2865, 2107, 1726, 1453, 1361, 1268, 1237, 1097, 1051 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{152}H_{173}N_3O_{30}PSSi$: 2611.1332; found 2611.1295 $[M]^-$.

Triethylammonium (2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4-di-*O*-benzyl-6-*O*-triisopropylsilyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-1-*O*-(6-(*S*-benzyl)thiohexyl phosphono)-D-*myo*-inositol (37): A mixture of compound **34** (110 mg, 0.04 mmol) and H-phosphonate **17** (115 mg, 0.40 mmol) was coevaporated with pyridine (3 × 3 mL) and dried in vacuo. To the residue in pyridine (2.5 mL) was added pivaloyl chloride (100 µL, 0.81 mmol) at room temperature. After 4 h, water (0.2 mL) and iodine (110 mg, 0.43 mmol) were added. After 40 min, the mixture was diluted with CH_2Cl_2 and washed with 1 M $Na_2S_2O_3$ and water. The organic layer was dried over $MgSO_4$, filtered and concentrated. Chromatography (CH_3OH/CH_2Cl_2 gradient with 1 % Et_3N) afforded phosphodiester **37** (120 mg, 96 %). $R_f=0.35$ (CH_3OH/CH_2Cl_2 1:10); $[\alpha]_D^{25}=+38.7$ ($c=1.35$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta=$ 1.02–1.06 (m, 21 H), 1.21–1.61 (m, 19 H), 2.11 (s, 3 H), 2.36 (t, $J=7.4$ Hz, 2 H), 2.97 (q, $J=7.2$ Hz, 6 H), 3.13 (dd, $J=3.7$, 10.0 Hz, 1 H), 3.25 (d, $J=9.9$ Hz, 1 H), 3.31–5.06 (m, 68 H), 5.32 (br s, 1 H), 5.46 (br s, 1 H), 5.57 (br s, 1 H), 5.62 (br s, 1 H), 5.91 (d, $J=3.9$ Hz, 1 H), 6.81–7.45 (m, 88 H), 7.94–7.98 (m, 2 H); ^{13}C NMR ($CDCl_3$): $\delta=8.6$, 12.1, 18.3, 21.3, 25.5, 28.8, 29.3, 31.4, 36.3, 45.48, 62.6, 63.5, 65.8, 66.1, 68.4, 68.6, 68.7, 69.1, 69.5, 71.1, 71.6, 71.8, 72.0, 72.2, 72.3, 72.4, 73.2, 73.4, 73.5, 74.1, 74.4, 74.5, 74.7, 75.1, 75.3, 75.7, 77.3, 78.7, 78.9, 79.6, 79.8, 80.3, 81.1, 81.6, 81.9, 96.7, 99.1, 99.3, 99.9, 126.8, 126.9, 127.0, 127.1, 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.7, 129.6, 129.9, 133.0, 137.4, 137.5, 137.8, 138.0, 138.1, 138.4, 138.5, 138.7, 138.8, 139.8, 165.1, 169.9; ^{31}P NMR ($CDCl_3$): $\delta=-0.75$; IR (film): $\tilde{\nu}=3030$, 2939, 2865, 2106, 1725, 1453, 1360, 1268, 1237, 1098, 1050 cm^{-1}.

(α-D-Mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→4)-(2-amino-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-(6-thiohexyl phosphono)-D-*myo*-inositol (5): Sodium methoxide (25 wt %, 0.06 mL, 0.26 mmol) was added to a solution of phosphodiester **35** (42 mg, 0.02 mmol) in CH_3OH/CH_2Cl_2 (1.5:0.5, 2 mL). After stirring for 4 h at 60 °C, the mixture was neutralized with Amberlite IR-120, filtered, and evaporated under reduced pressure. The crude product was purified by chromatography (CH_3OH/CH_2Cl_2 gradient with 1 % Et_3N) to give the diol. Ammonia (~20 mL) was condensed in a flame-dried three-necked flask at −78 °C. Sodium metal was added portionwise until the solution was dark blue. The obtained diol in THF (7 mL) was added via cannula, followed by CH_3OH (0.2 mL). The resultant dark blue solution was stirred at −78 °C for 30 min. Following disappearance of the blue color, EtOH (2 mL) and AcOH (~0.5 mL) were added and ammonia was blown off with a stream of Ar. Chromatography of the crude mixture on Sephadex G-25 ($EtOH/H_2O$ 1:1), followed by dialysis and lyophilization afforded a mixture of the target compound **5** and the corresponding disulfide (9.5 mg, 58 %). ^{1}H NMR (D_2O): $\delta=$ 1.31–1.70 (m, 10 H), 2.75 (t, $J=7.2$ Hz, 2 H), 3.32 (dd, $J=3.6$, 10.8 Hz, 1 H), 3.39 (t, $J=9.3$ Hz, 1 H), 3.49–4.22 (m, 22 H), 4.87 (d, $J=1.3$ Hz, 1 H), 5.21 (d, $J=1.5$ Hz, 1 H), 5.49 (d, $J=3.7$ Hz, 1 H); ^{13}C NMR (D_2O): $\delta=24.9$, 27.5, 28.5, 30.0, 38.4, 55.0, 60.6, 61.2, 62.7, 66.3, 66.6, 66.7, 66.8, 67.0, 68.7, 70.2, 70.5, 70.7, 70.8, 71.4, 71.6, 72.4, 72.5, 72.9, 73.5, 76.1, 77.1, 100.0, 102.1; ^{31}P NMR (D_2O): $\delta=1.44$; HRMS (ESI): *m*/*z*: calcd for $C_{60}H_{111}N_2O_{46}P_2S_2$: 1721.5319; found 1721.5348 $[M+H]^+$.

Triethylammonium (2-*O*-acetyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-1-*O*-(6-(*S*-benzyl)thiohexyl phosphono)-D-*myo*-inositol (38): Scandium trifluoromethanesulfonate (50 mg, 0.1 mmol) and water (20 µL) were added to a solution of compound **36** (135 mg, 0.05 mmol) in CH_3CN. After being stirred for 4.5 h at 50 °C, the mixture was diluted with CH_2Cl_2 and washed with brine. The organic phase was dried over $MgSO_4$, filtered and concentrated. Chromatography (CH_3OH/CH_2Cl_2 gradient with 1% Et_3N) afforded compound **38** (97 mg, 76%). $R_f=0.39$ (CH_3OH/CH_2Cl_2 1:10); $[\alpha]_D^{25}=+46.9$ ($c=2.85$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta=1.22$–1.66 (m, 19H), 1.84 (dd, $J=5.0$, 7.4 Hz, 1H), 2.16 (s, 3H), 2.41 (t, $J=7.4$ Hz, 2H), 2.92 (q, $J=7.3$ Hz, 6H), 3.21 (dd, $J=3.7$, 10.0 Hz, 1H), 3.40–3.74 (m, 12H), 3.78–4.01 (m, 10H), 4.06–4.11 (m, 2H), 4.17 (t, $J=9.5$ Hz, 1H), 4.22–4.26 (m, 1H), 4.36–4.48 (m, 8H), 4.57–5.11 (m, 23H), 5.53 (brs, 1H), 5.55 (dd, $J=1.8$, 3.0 Hz, 1H), 5.65 (brs, 1H), 6.01 (d, $J=3.7$ Hz, 1H), 7.06–7.47 (m, 73H), 8.03–8.05 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta=9.3$, 21.6, 25.9, 29.2, 29.6, 31.3, 31.4, 31.7, 36.7, 45.9, 62.1, 63.7, 66.0, 66.1, 66.4, 69.1, 69.2, 69.7, 69.9, 72.0, 72.1, 72.2, 72.3, 72.4, 72.7, 72.8, 73.6, 74.1, 74.5, 74.7, 74.8, 75.1, 75.3, 75.4, 75.5, 75.6, 76.2, 77.1, 77.7, 77.8, 78.4, 79.0, 79.8, 80.7, 81.5, 82.1, 82.3, 97.0, 99.5, 99.6, 99.9, 127.5, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 129.3, 130.2, 130.4, 133.6, 138.0, 138.4, 138.5, 138.8, 138.9, 139.0, 139.1, 139.2, 140.4, 165.7, 170.4; ^{31}P NMR ($CDCl_3$): $\delta=0.30$; IR (film): $\tilde{\nu}=3030$, 2931, 2107, 1734, 1453, 1363, 1268, 1235, 1096, 1050 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{143}H_{153}N_3O_{30}PS$: 2455.0003; found 2454.9915 $[M]^-$.

Triethylammonium (2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-1-*O*-(6-(*S*-benzyl)thiohexyl phosphono)-D-*myo*-inositol (39): Scandium trifluoromethanesulfonate (37 mg, 0.075 mmol) and water (20 μL) were added to a solution of compound **37** (115 mg, 0.037 mmol) in CH_3CN. After being stirred for 5 h at 50°C, the mixture was diluted with CH_2Cl_2 and washed with brine. The organic phase was dried over $MgSO_4$, filtered and concentrated. Chromatography (CH_3OH/CH_2Cl_2 gradient with 1% Et_3N) afforded compound **39** (86 mg, 79%). $R_f=0.35$ (CH_3OH/CH_2Cl_2 1:10); $[\alpha]_D^{25}=+44.8$ ($c=1.02$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta=1.19$–1.61 (m, 19H), 2.12 (s, 3H), 2.36 (t, $J=7.5$ Hz, 2H), 2.95 (q, $J=7.2$ Hz, 6H), 3.14 (dd, $J=3.9$, 9.9 Hz, 1H), 3.26–5.02 (m, 68H), 5.06 (d, $J=1.5$ Hz, 1H), 5.15 (d, $J=1.5$ Hz, 1H), 5.44 (d, $J=1.5$ Hz, 1H), 5.54 (t, $J=2.4$ Hz, 1H), 5.59 (brs, 1H), 5.94 (d, $J=3.9$ Hz, 1H), 6.91–7.45 (m, 88H), 7.94–7.97 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta=8.7$, 21.4, 25.6, 28.9, 29.4, 31.5, 36.5, 45.6, 62.0, 63.5, 68.7, 68.9, 69.0, 69.4, 69.7, 71.6, 71.8, 72.0, 72.3, 72.5, 72.9, 73.5, 73.6, 73.8, 74.3, 74.4, 74.7, 74.9, 75.2, 75.5, 75.9, 77.5, 78.2, 78.9, 79.4, 79.6, 81.2, 81.8, 82.1, 96.9, 99.3, 99.5, 100.4, 127.1, 127.2, 127.4, 127.7, 127.8, 128.0, 128.3, 128.4, 128.5, 129.0, 129.9, 130.2, 133.4, 137.8, 138.1, 138.2, 138.5, 138.6, 138.7, 138.8, 138.9, 139.1, 140.1, 165.5, 170.3; ^{31}P NMR ($CDCl_3$): $\delta=-0.10$; IR (film): $\tilde{\nu}=3030$, 2930, 2107, 1732, 1453, 1361, 1268, 1235, 1095, 1051 cm^{-1}.

(α-D-Mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→4)-(2-amino-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-(6-thiohexyl phosphono)-D-*myo*-inositol (6): Sodium methoxide (25wt%, 0.1 mL, 0.43 mmol) was added to a solution of phosphodiester **38** (57 mg, 0.02 mmol) in CH_3OH/CH_2Cl_2 (1.5:0.5, 2 mL). After stirring for 5 h at 60°C, the mixture was neutralized with Amberlite IR-120, filtered, and evaporated under reduced pressure. The crude product was purified by chromatography (CH_3OH/CH_2Cl_2 gradient with 1% Et_3N) to give the diol. Ammonia (~20 mL) was condensed in a flame-dried three-necked flask at −78°C. Sodium metal was added portionwise until the solution was dark blue. The obtained diol in THF (8 mL) was added via cannula, followed by CH_3OH (0.15 mL). The resultant dark blue solution was stirred at −78°C for 30 min. Following disappearance of the blue color, EtOH (2 mL) and AcOH (~0.5 mL) were added and ammonia was blown off with a stream of Ar. Chromatography of the crude mixture on Sephadex G-25 ($EtOH/H_2O$ 1:1), followed by dialysis and lyophilization afforded a mixture of the target compound **6** and the corresponding disulfide (13.5 mg, 59%). ^1H NMR (D_2O): $\delta=1.30$–1.79 (m, 10H), 2.83 (t, $J=7.2$ Hz, 2H), 3.34–4.29 (m, 30H), 5.09 (brs, 1H), 5.19 (brs, 1H), 5.28 (brs, 1H), 5.36 (m, 1H); ^{13}C NMR (D_2O): $\delta=25.0$, 27.5, 28.6, 30.0, 38.4, 55.4, 60.8, 61.2, 61.4, 62.8, 66.5, 66.7, 66.8, 67.1, 67.2, 70.2, 70.4, 70.5, 70.6, 70.7, 70.8, 71.5, 72.4, 72.5, 73.0, 73.5, 76.0, 77.5, 78.9, 98.7, 102.2, 102.5; ^{31}P NMR (D_2O): $\delta=1.25$; HRMS (ESI): m/z: calcd for $C_{36}H_{66}NO_{28}PSNa$: 1046.3122; found 1046.3135 $[M+Na]^+$.

(α-D-Mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→4)-(2-amino-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-(6-thiohexyl phosphono)-D-*myo*-inositol (8): Sodium methoxide (25wt%, 0.1 mL, 0.43 mmol) was added to a solution of phosphodiester **39** (37 mg, 0.01 mmol) in CH_3OH/CH_2Cl_2 (1.5:0.5, 2 mL). After stirring for 5 h at 60°C, the mixture was neutralized with Amberlite IR-120, filtered, and evaporated under reduced pressure. The crude product was purified by chromatography (CH_3OH/CH_2Cl_2 gradient with 1% Et_3N) to give the diol. Ammonia (~20 mL) was condensed in a flame-dried three-necked flask at −78°C. Sodium metal was added portionwise until the solution was dark blue. The obtained diol in THF (8 mL) was added via cannula, followed by CH_3OH (0.15 mL). The resultant dark blue solution was stirred at −78°C for 30 min. Following disappearance of the blue color, EtOH (2 mL) and AcOH (~0.5 mL) were added and ammonia was blown off with a stream of Ar. Chromatography of the crude mixture on Sephadex G-25 ($EtOH/H_2O$ 1:1), followed by dialysis and lyophilization afforded a mixture of the target compound **8** and the corresponding disulfide (9 mg, 61%). ^1H NMR (D_2O): $\delta=1.27$–1.76 (m, 10H), 2.79 (t, $J=6.9$ Hz, 2H), 3.27–4.22 (m, 36H), 5.05 (d, $J=1.8$ Hz, 1H), 5.13 (brs, 1H), 5.24 (brs, 1H), 5.29 (brs, 1H); ^{13}C NMR (D_2O): $\delta=24.9$, 27.5, 28.6, 30.0, 38.4, 61.2, 61.3, 61.4, 62.8, 66.7, 66.8, 67.1, 67.2, 67.3, 70.2, 70.3, 70.5, 70.6, 70.8, 70.9, 71.6, 72.3, 72.5, 72.6, 73.0, 73.5, 76.2, 78.7, 79.0, 98.7, 100.9, 102.5; ^{31}P NMR (D_2O): $\delta=0.77$; HRMS (ESI): m/z: calcd for $C_{84}H_{152}N_2O_{66}P_2S_2$: 1185.3752; found 1185.3751 $[M+2H]^{2+}$.

Bistriethylammonium (2-*O*-acetyl-3,4-di-*O*-benzyl-6-*O*-(2-(*N*-benzyloxycarbonyl)aminoethyl phosphono)-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-1-*O*-(6-(*S*-benzyl)thiohexyl phosphono)-D-*myo*-inositol (41): A mixture of compound **38** (74 mg, 0.03 mmol) and H-phosphonate **40**[17] (150 mg, 0.42 mmol) was coevaporated with pyridine (3×3 mL) and dried in vacuo. To the residue in pyridine (2 mL) was added pivaloyl chloride (110 μL, 0.89 mmol) at room temperature. After 4 h, water (0.2 mL) and iodine (110 mg, 0.43 mmol) were added. After 1 h, the mixture was diluted with CH_2Cl_2 and washed with 1 M $Na_2S_2O_3$ and water. The organic phase was dried over $MgSO_4$, filtered and concentrated. Chromatography (CH_3OH/CH_2Cl_2 gradient with 1% Et_3N) afforded compound **41** (52 mg, 62%). $R_f=0.2$ (CH_3OH/CH_2Cl_2 1:10); $[\alpha]_D^{25}=+34.2$ ($c=1.30$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta=1.23$–1.58 (m, 28H), 2.04 (s, 3H), 2.35 (t, $J=7.4$ Hz, 2H), 2.91 (q, $J=7.3$ Hz, 12H), 3.10 (dd, $J=3.7$, 10.0 Hz, 1H), 3.19–3.64 (m, 14H), 3.81–4.12 (m, 15H), 4.20–4.49 (m, 13H), 4.56–4.88 (m, 15H), 4.93–5.05 (m, 6H), 5.47 (brs, 1H), 5.49 (brs, 1H), 5.55 (s, 1H), 5.60 (brs, 1H), 5.93 (d, $J=3.6$ Hz, 1H), 6.72 (brs, 1H), 7.06–7.32 (m, 78H), 7.96–7.98 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta=8.5$, 9.6, 21.5, 25.8, 29.1, 29.5, 30.1, 31.4, 31.7, 36.6, 46.2, 53.3, 63.7, 64.5, 65.9, 66.6, 69.1, 69.5, 69.8, 71.5, 72.0, 72.1, 72.3, 72.7, 73.5, 73.9, 74.2, 74.7, 74.8, 75.0, 75.2, 75.3, 75.4, 76.1, 77.1, 77.7, 77.8, 79.2, 80.0, 80.7, 81.5, 82.1, 82.3, 96.9, 99.2, 99.5, 99.8, 127.2, 127.3, 127.4, 127.7, 127.8, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 129.2, 130.1, 130.3, 133.6, 137.3, 137.9, 138.2, 138.3, 138.5, 138.6, 138.8, 138.9, 139.0, 139.2, 139.3, 140.3, 156.9, 165.7, 170.4; ^{31}P NMR ($CDCl_3$): $\delta=0.15$, 2.39; IR (film): $\tilde{\nu}=3030$, 2935, 2107, 1718, 1454, 1363, 1234, 1048 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{153}H_{164}N_4O_{35}P_2S$: 1355.5181; found 1355.5192 $[M]^{2-}$.

Bistriethylammonium (2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-(3,4-di-*O*-benzyl-6-*O*-(2-(*N*-benzyloxycarbonyl)aminoethyl phosphono)-α-D-mannopyranosyl)-(1→2)-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-(2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-2,3,4,5-tetra-*O*-benzyl-1-*O*-(6-(*S*-benzyl)thiohexyl phosphono)-D-*myo*-inositol (42): A mixture of compound **39** (47 mg, 0.016 mmol) and H-phosphonate **40**[12] (41 mg, 0.16 mmol) was coevaporated with pyridine (3×3 mL) and dried in vacuo. To the residue in pyridine (2 mL) was added pivaloyl chloride (40 μL, 0.89 mmol) at room temperature. After 5 h, water (0.1 mL) and iodine (43 mg, 0.17 mmol) were added. After 30 min, the mixture was diluted with CH_2Cl_2 and washed with 1 M $Na_2S_2O_3$ and water. The organic phase was dried over $MgSO_4$, filtered and concentrated. Chromatography (CH_3OH/CH_2Cl_2 gradient with 1% Et_3N) afforded compound **42** (38 mg, 72 %). $R_f=0.25$ (CH_3OH/CH_2Cl_2 1:10); $[\alpha]_D^{25}=+19.3$ ($c=1.15$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta=1.20$–1.56 (m, 28H), 2.06 (s, 3H), 2.33 (t, $J=7.4$ Hz, 2H), 3.03 (q, $J=7.3$ Hz, 12H), 3.23–4.98 (m, 75H), 5.06 (brs, 1H), 5.16 (brs, 1H), 5.41 (brs, 1H), 5.53 (brs, 1H), 5.57 (brs, 1H), 5.88 (d, $J=3.7$ Hz, 1H), 6.64 (brs, 1H), 6.94–7.39 (m, 93H), 7.91–7.94 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta=8.3$, 8.8, 20.3, 25.5, 27.7, 29.3, 29.85, 31.4, 36.3, 38.7, 45.7, 53.0, 63.4, 64.1, 64.6, 65.6, 65.7, 66.1, 66.2, 68.4, 68.6, 68.7, 69.0, 69.1, 69.4, 71.1, 71.5, 71.6, 71.7, 72.0, 72.1, 72.3, 73.0, 73.2, 73.3, 73.5, 74.0, 74.2, 74.3, 74.4, 74.6, 74.8, 75.0, 75.2, 75.7, 76.1, 76.3, 77.3, 78.4, 78.8, 79.4, 79.5, 80.3, 81.0, 81.6, 81.8, 96.4, 98.8, 99.0, 99.1, 100.2, 126.7, 126.8, 126.9, 127.2, 127.3, 127.5, 127.6, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.7, 129.6, 129.8, 133.1, 134.7, 136.8, 137.4, 137.7, 137.9, 138.0, 138.3, 138.4, 138.7, 139.7, 156.3, 165.2, 169.9; ^{31}P NMR ($CDCl_3$): $\delta=-0.88$, 1.56; IR (film): $\tilde{\nu}=3031$, 2935, 2106, 1718, 1454, 1362, 1234, 1050 cm^{-1}.

(6-*O*-(2-Aminoethyl phosphono)α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→4)-(2-amino-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-(6-thiohexyl phosphono)-D-*myo*-inositol (7): Sodium methoxide (25wt %, 0.1 mL, 0.43 mmol) was added to a solution of phosphodiester **41** (50 mg, 0.02 mmol) in CH_3OH/CH_2Cl_2 (1.5:0.5, 2 mL). After stirring for 5 h at 60 °C, the mixture was neutralized with Amberlite IR-120, filtered, and evaporated under reduced pressure. The crude product was purified by chromatography (CH_3OH/CH_2Cl_2 gradient with 1 % Et_3N) to give the diol. Ammonia (~20 mL) was condensed in a flame-dried three-necked flask at −78 °C. Sodium metal was added portionwise until the solution was dark blue. The obtained diol in THF (8 mL) was added via cannula, followed by CH_3OH (0.2 mL). The resultant dark blue solution was stirred at −78 °C for 30 min. Following disappearance of the blue color, EtOH (2 mL) and AcOH (~0.5 mL) were added and ammonia was blown off with a stream of Ar. Chromatography of the crude mixture on Sephadex G-25 ($EtOH/H_2O$ 1:1), followed by dialysis and lyophilization afforded a mixture of the target compound **7** and the corresponding disulfide (11 mg, 56 %). ^1H NMR (D_2O): $\delta=1.42$–1.78 (m, 10H), 2.83 (t, $J=7.2$ Hz, 2H), 3.34–3.49 (m, 4H), 3.61 (dd, $J=2.6$, 10.0 Hz, 1H), 3.72–4.22 (m, 29H), 5.09 (brs, 1H), 5.16 (brs, 1H), 5.27 (d, $J=1.3$ Hz, 1H), 5.59 (d, $J=3.8$ Hz, 1H); ^{13}C NMR (D_2O): $\delta=24.8$, 27.4, 28.5, 29.9, 38.5, 40.3, 54.2, 60.4, 61.2, 62.1, 62.2, 62.8, 65.1, 66.6, 66.7, 66.8, 66.9, 67.2, 70.1, 70.4, 70.6, 70.8, 71.4, 71.7, 72.2, 72.3, 72.5, 72.6, 73.0, 76.5, 76.7, 79.1, 95.6, 98.6, 102.1, 102.6; ^{31}P NMR (D_2O): $\delta=1.52$, 1.55; HRMS (ESI): m/z: calcd for $C_{38}H_{73}N_2O_{31}P_2S$: 1147.3388; found 1147.3387 $[M+H]^+$.

(α-D-Mannopyranosyl)-(1→2)-(6-*O*-(2-aminoethyl phosphono)α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→4)-(2-amino-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-(6-thiohexyl phosphono)-D-*myo*-inositol (2a): Sodium methoxide (25 wt %, 0.1 mL, 0.43 mmol) was added to a solution of phosphodiester **42** (36 mg, 0.01 mmol) in CH_3OH/CH_2Cl_2 (1.5:0.5, 2 mL). After stirring for 5 h at 60 °C, the mixture was neutralized with Amberlite IR-120, filtered, and evaporated under reduced pressure. The crude product was purified by chromatography (CH_3OH/CH_2Cl_2 gradient with 1 % Et_3N) to give the diol. Ammonia (~20 mL) was condensed in a flame-dried three-necked flask at −78 °C. Sodium metal was added portionwise until the solution was dark blue. The obtained diol in THF (8 mL) was added via cannula, followed by CH_3OH (0.15 mL). The resultant dark blue solution was stirred at −78 °C for 30 min. Following disappearance of the blue color, EtOH (2 mL) and AcOH (~0.5 mL) were added and ammonia was blown off with a stream of Ar. Chromatography of the crude mixture on Sephadex G-25 ($EtOH/H_2O$ 1:1), followed by dialysis and lyophilization afforded a mixture (7.5 mg, 53 %) of the target compound **2a** and the corresponding disulfide. ^1H NMR (D_2O): $\delta=1.38$–1.72 (m, 10H), 2.74 (t, $J=7.2$ Hz, 2H), 3.34–4.21 (m, 40H), 5.02 (brs, 1H), 5.06 (brs, 1H), 5.20 (brs, 1H), 5.26 (brs, 1H), 5.52 (d, $J=3.9$ Hz, 1H); ^{13}C NMR (D_2O): $\delta=25.0$, 27.5, 28.6, 30.1, 38.5, 61.2, 61.3, 64.9, 66.7, 66.9, 67.1, 67.2, 70.1, 70.3, 70.5, 70.6, 70.8, 71.5, 72.5, 73.1, 73.6, 73.7, 76.0, 78.6, 79.2, 98.7, 101.0, 102.4; ^{31}P NMR (D_2O): $\delta=1.25$, 1.32; MS (ESI): m/z: calcd for $C_{44}H_{83}N_2O_{36}P_2S$: 1309; found 1309 $[M+H]^+$.

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