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Synthesis of the *C*-glycoside of α-D-mannose-(1 → 6)-D-*myo*-inositol†

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The dimannosylatedinositol pseudotrisaccharide phospholipid of the lipoarabinomannan (LAM) component of the mycobacterial cell wall has attracted interest as a therapeutic target because of its uniqueness to mycobacteria, its assembly at an early stage in LAM biosynthesis and the immunological activity of oligosaccharides containing this subunit. Accordingly, analogues of this pseudotrisaccharide, α-D-mannose-(1 → 2)-α-D-mannose-(1 → 6)-D-*myo*-inositol are of interest as mechanistic probes and drug leads. *C*-glycosides are of special interest because of their hydrolytic stability and conformational differences compared to *O*-glycosides. Herein, as a prelude to *C*-glycoside analogues of this pseudotrisaccharide, we describe the synthesis of the *C*-glycoside of α-D-mannose-(1 → 6)-D-*myo*-inositol. The synthetic strategy centers on the elaboration of a C1-linked glycal-inositol, the glycone segment of which is assembled *via* an oxocarbenium ion cyclization on a thioacetal-enol ether precursor that originates from "glycone" and "aglycone" components.

Introduction

The resurgence of mycobacterial infections (*M. tuberculosis* and AIDS-associated *M. avium*) has been associated with increasing populations of immunocompromised and homeless individuals.[1,2] Of particular concern is the emergence of *M. tuberculosis* strains that are resistant to many of the drugs that are used to treat tuberculosis.[3] Consequently the development of new antimycobacterial agents is an active area of research.[4,5] The mycobacterial cell wall contains numerous components that are believed to be necessary for survival in the host and is the site of action of established antimycobacterial agents.[6] The LAM subunit is composed of an outermost arabinomannan segment linked to a phosphotidylinositol mannoside (PIM) region. In addition to maintaining the structural integrity of the cell wall LAM has been implicated in the suppression of immune responses thereby contributing to pathogenesis and many of the clinical manifestations of tuberculosis.[7] Accordingly, inhibition of the biosynthesis of LAM is a potential therapeutic strategy and the pseudotrisaccharide PIM_2 **2** an early stage intermediate is an attractive target because it is unique to mycobacteria (Fig. 1).[8] An α-mannose transferase that catalyzes the synthesis of **2** from GDP-mannose and the pseudodisaccharide **1** has recently been isolated, and this presents and opportunity for rational drug design.[9] *C*-glycoside analogues such as **3** that may act as hydrolytically stable, bi-substrate mimetics of the transition state leading to **2**, are of interest as pharmaceutical leads and for enzyme studies.[10–12] Small PIM fragments have also shown interesting immunomodulatory activities and their *C*-glycosides may also find applications as probes of the underlying mechanisms.[13–16] However, while the synthesis of *O*-glycoside analogues is well documented, studies on *C*-glycosides thereof,

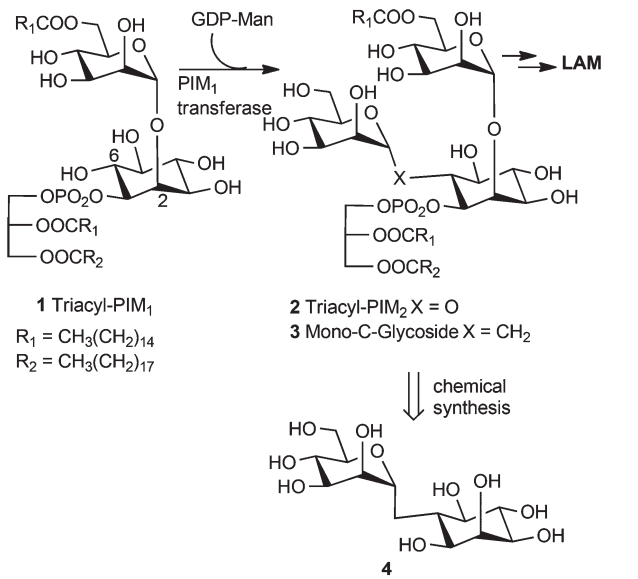

Fig. 1 Biosynthesis and *C*-glycoside analogues of PIM_2.

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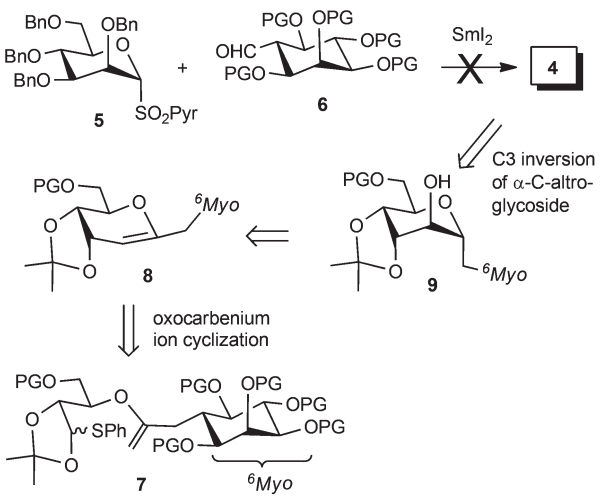
are not.[17–20] Herein, *en route* to structures like **3**, we describe the synthesis of **4**, the *C*-glycoside of the core pseudodisaccharide, α-D-mannose-(1 → 6)-D-*myo*-inositol.

Results and discussion

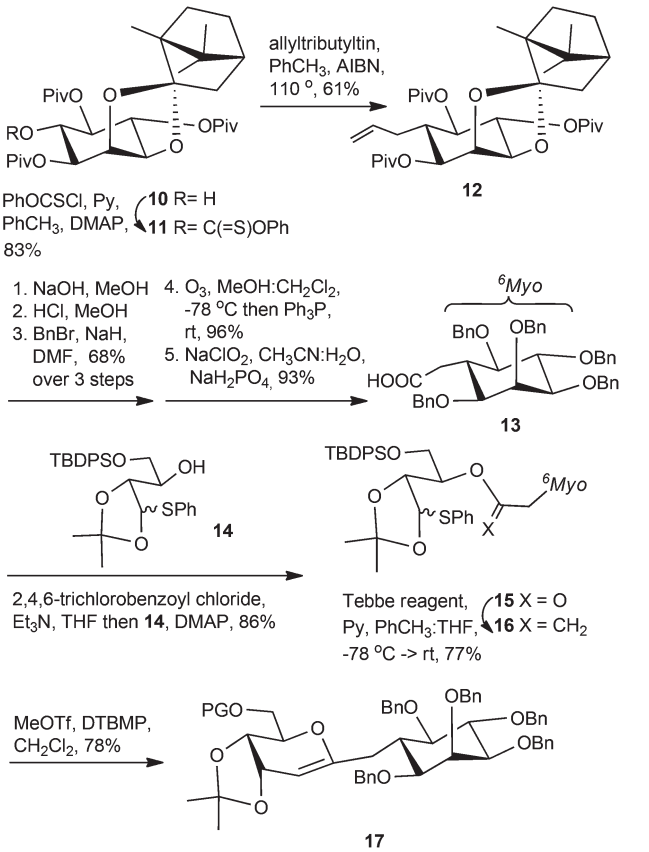
Our first approach to **4** followed the Beau α-*C*-*manno*-glycosidation protocol of coupling the mannosyl sulfone **5** and 6-*C*-formyl-*myo*-inositols like **6** (Scheme 1).[21] Unfortunately this approach was not successful, possibly because of the highly hindered nature of the aldehyde partner. We therefore adopted a *C*-glycosidation strategy that is based on *de novo* synthesis of the glycone segment, and which we have used for *C*-disaccharides.[22–25] Thus, we envisaged that **4** could be fabricated by elaboration of a *C*-linked glycal-inositol **8**, which is available *via* an oxocarbenium ion cyclization on thioacetal-enol ether **7**.

The synthesis of the requisite *C*-linked glycal-inositol **17** started from the known 1-phenylthio-1,2-*O*-isopropylidene alcohol **14**[23] and the 6-*C*-branched *myo*-inositol acid **13** (Scheme 2). The latter was prepared from the known D-*myo*-inositol derivative **10**[26] using the Keck *C*-radical allylation methodology.[27] Thus, alcohol **10** was converted to the thiocarbonate **11** and treatment of **11** with allyltributyltin in the presence of AIBN gave the *C*-allyl derivative **12**. Removal of ester and ketal protecting groups in **12** provided the pentaol derivative, which was protected as the penta-*O*-benzyl ether. Standard oxidative processing of the alkene in the latter gave acid **13**. With acid **13** and alcohol **14** in hand DCC mediated esterification was next attempted. However, **15** was obtained in low yield. The Yamaguchi protocol was more successful, providing **15** in 86% yield.[28] Reaction of **15** with the Tebbe reagent yielded **16** in 77% yield. The oxocarbenium ion cyclization on **16** was promoted by methyl triflate to give **17** in 78% yield.

Elaboration of *C*-glycal **17** to the desired α-*C*-mannoside motif started with a hydroboration–borane oxidation sequence

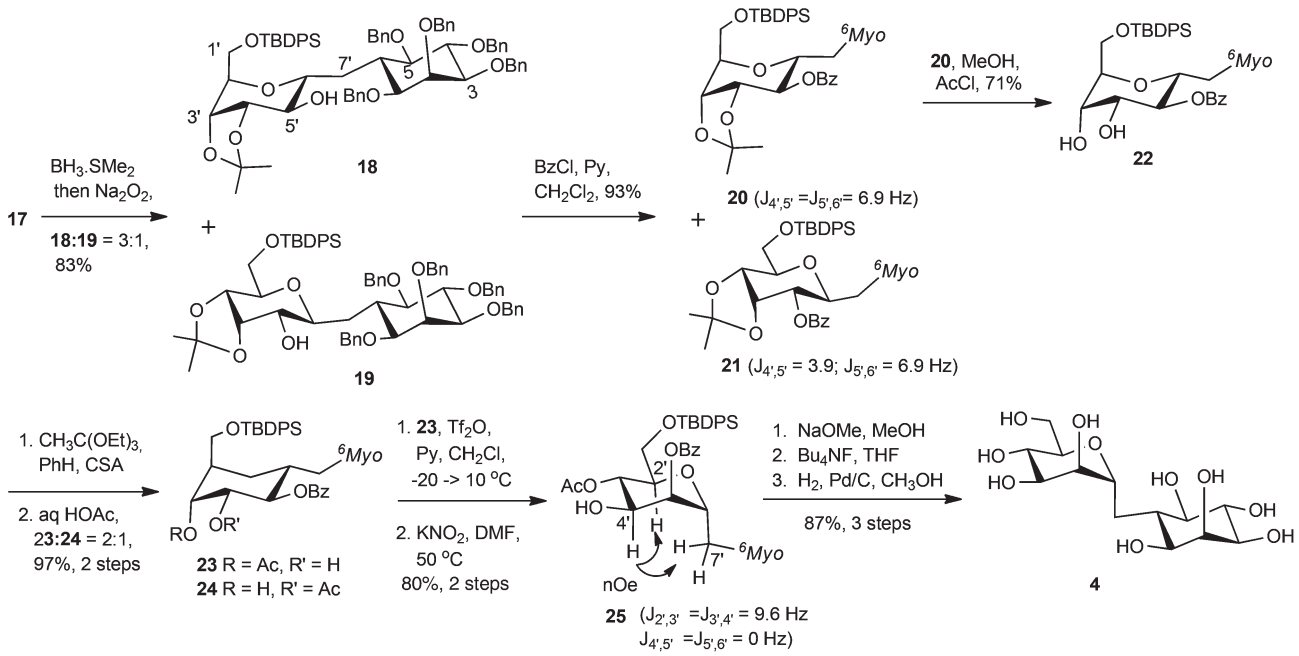


Scheme 1 Strategies for α-*C*-*manno*-pseudodisaccharides.



Scheme 2 Synthesis of *C*-linked glycal-inositol.

on **17** (Scheme 3). This led to a 3 : 1 mixture of **18** : **19**, which was more easily separated as the respective benzoates **20** and **21**. ^{1}H NMR analysis suggested that **20** was the α-*C*-*altro*-isomer in predominantly the $^{6'}C_{3'}$ conformation ($J_{4',5'}$ = $J_{5',6'}$ = 6.9 Hz), and **21** was the β-*C*-*allo*-favoring the $^{3'}C_{6'}$ ($J_{4',5'}$ = 3.9 Hz; $J_{5',6'}$ = 6.9 Hz).[29,30] We envisaged that the desired α-*C*-*manno* motif could be obtained through configurational inversion at the C4′ position in **20** and towards this end **20** was next transformed to alcohol **23**. Thus, acetonide cleavage in **20** provided diol **22**, which was converted *via* the derived orthoacetate to a 2 : 1 mixture of **23** and its regioisomer **24**.[31] As for the precursor **20**, the desired isomer **23** was also found to favor the $^{6'}C_{3'}$ conformation ($J_{2',3'}$ = $J_{3',4'}$ = 3.8 Hz; $J_{4',5'}$ = $J_{5',6'}$ = 7.5 Hz). Reaction of **23** with trifluoromethanesulfonic anhydride and dry dichloromethane at −20 to 10 °C afforded the triflate derivative. The crude product was treated with potassium nitrite in DMF at 50 °C to give the desired alcohol **25** in 80% yield over two steps.[32] The *manno* configuration and the $^{3'}C_{6'}$ conformation of **25** was supported by *J* values ($J_{2',3'}$ = $J_{3',4'}$ = 9.6 Hz; $J_{4',5'}$ = $J_{5',6'}$ = 0 Hz) and H-2′/H-4′ and H-4′/H-7′ nOe's. Straightforward removal of alcohol protecting groups in **25** provided the target α-*C*-*manno*-pyranosyl-*myo*-inositol **4**. By starting with a *myo*-inositol precursor with orthogonal protecting groups on the C1 and C2 alcohols, this synthesis can be easily adapted to produce *C*-disaccharide derivatives of **25**,



Scheme 3 Transformation of *C*-linked glycal to α-*C*-mannos.

that are primed for incorporation into pseudo-trisaccharide mimetics of **3**.

Conclusions

In summary the *C*-glycoside of α-D-mannose-(1 → 6)-D-*myo*-inositol **4** was prepared *via* a *de novo* synthesis of the "glycone" segment, over ten steps from thioacetal **13** and the *C*-branched inositol **14**. This synthesis illustrates the feasibility of this strategy for synthetically challenging α-*C*-mannosides. The method is currently being applied to higher order saccharide mimetics of PIM and to stereochemically diverse *C*-glycoinositols. These results will be reported in due course.

Experimental

Solvents were purified by standard procedures or used from commercial sources as appropriate. Petroleum ether refers to the fraction of petroleum ether boiling between 40 and 60 °C. Ether refers to diethyl ether. Unless otherwise stated thin layer chromatography (TLC) was done on 0.25 mm thick precoated silica gel 60 (HF-254, Whatman) aluminium sheets and flash column chromatography (FCC) was performed using Kieselgel 60 (32–63 mesh, Scientific Adsorbents). Elution for FCC usually employed a stepwise solvent polarity gradient, correlated with TLC mobility. Chromatograms were observed under UV (short and long wavelength) light, and/or were visualized by heating plates that were dipped in a solution of ammonium(VI) molybdate tetrahydrate (12.5 g) and cerium(IV) sulfate tetrahydrate (5.0 g) in 10% aqueous sulphuric acid (500 mL), or a solution of 20% sulfuric acid in ethanol. Optical rotations ($[\alpha]_D$ were recorded using a Rudolph Autopol III or Jasco P-1020 polarimeters with 10 or 5 cm cells (path lengths of 1 or 0.5 dm) respectively, and are given in units of 10^{-1} deg cm^2 g at 589 nm (sodium D-line). Infra-red spectra were obtained using a Thermo Scientific Nicolet IS5 spectrometer as thin film liquid samples between sodium chloride plates. Only selected absorbances (ν_{max}) are reported. NMR spectra were recorded using either Varian Unity Plus 500, Bruker Ultra Shield and Bruker Ultra Shield Plus instruments. Unless otherwise noted, ^{1}H and ^{13}C spectra were recorded at 500 and 125 MHz respectively in $CDCl_3$ or C_6D_6 solutions with residual $CHCl_3$ or C_6H_6 as internal standard (δ_H 7.27, 7.16 and δ_C 77.2, 128.4 ppm). Chemical shifts are quoted in ppm relative to tetramethylsilane (δ_H 0.00) and coupling constants (J) are given in hertz. First order approximations are employed throughout. High resolution mass spectrometry was performed on an Ultima Micromass Q-TOF or Waters Micromass LCT Premier mass spectrometers.

6-*O*-Phenylcarbonothioyl-2,3-*O*-(D-1′,7′,7′-trimethyl-[2.2.1]-bicyclohept-2′-ylidene)-1,4,5-tris-*O*-pivaloyl-D-*myo*-inositol (11)

Phenyl chlorothionoformate (0.10 mL, 0.77 mmol) was added dropwise to a suspension of the alcohol **10** (196 mg, 0.35 mmol) and DMAP (4 mg, 0.04 mmol), in dry toluene 10 mL at rt. Pyridine (0.14 mL, 1.75 mmol) was then added and the resulting suspension was stirred for 2 h at rt. The reaction mixture was then washed with 0.1 M HCl and saturated aqueous $NaHCO_3$, and the organic extract dried (Na_2SO_4) and concentrated *in vacuo*. FCC of the residue gave **11** (0.20 g, 83%). R_f = 0.50 (10% ethyl acetate–petroleum ether); ^{1}H NMR ($CDCl_3$) δ ^{1}H NMR ($CDCl_3$) δ 0.88 (s, 3H), 0.98 (s, 3H), 1.09 (s, 3H), 1.25 (m, 28H), 1.45 (m, 2H), 1.74 (m, 2H), 1.91 (m, 2H),

4.10 (t, 1H, J = 6.0 Hz, H-2/3), 4.65 (dd, 1H, J = 4.3, 6.4 Hz, H-2/3), 5.25 (m, 3H, H-1, 4, 5), 6.31 (dd, 1H, J = 7.7, 10.7 Hz, H-6), 7.00 (d, 2H, J = 8.0 Hz), 7.30 (t, 1H, J = 8.0 Hz), 7.42 (t, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 9.93, 20.2 (two signals), 26.9, 27.0, 27.0, 27.1, 29.3, 38.8, 44.0, 45.1, 48.0, 69.4, 71.8, 72.1, 72.2, 72.9, 79.0, 118.7, 121.7, 126.6, 129.5, 153.4, 176.5, 177.0, 177.6, 194.5. HRMS (EI) m/z calcd for $C_{38}H_{54}O_{10}NaS$ $(M + Na)^+$ 725.3334, found 725.3334.

6-Deoxy-6-*C*-(3′-propenyl)-2,3-*O*-(D-1′,7′,7′-trimethyl-[2.2.1]-bicyclohept-2′-ylidene)-1,4,5-tris-*O*-pivaloyl-D-*myo*-inositol (12)

A solution of **11** (167 mg, 0.24 mmol), allyltributyltin (0.22 mL, 0.72 mmol), AIBN (7.88 mg, 0.05 mmol) and toluene (3.5 mL) was heated at reflux for 18 h. The mixture was then evaporated under reduced pressure. FCC of the residue afforded **12** (0.85 g, 61%). R_f = 0.69 (10% ethyl acetate–petroleum ether); IR ν 1734 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (s, 3H), 1.00 (s, 3H), 1.05 (s, 3H), 1.22 (s, 18H), 1.22 (m, 1H, buried under singlet), 1.28 (s, 9H), 1.44 (m, 2H), 1.70 (m, 2H), 1.90 (m, 2H), 2.25 (m, 2H, H-6′), 2.57 (m, 1H, H-6), 3.97 (t, 1H, J = 6.2 Hz, H-3), 4.45 (dd, 1H, J = 4.4, 5.3 Hz, H-2), 4.95 (m, 3H, H-1, 5, =CH), 5.08 (m, 2H, H-4, =CH), 5.65 (m, 1H, =CH); ^{13}C NMR ($CDCl_3$) δ 9.6, 20.2, 20.3, 26.9, 27.0, 27.1, 27.2, 29.2, 30.6, 38.1, 38.7, 38.8, 38.9, 45.0, 45.1, 48.0, 51.7, 68.7, 69.7, 72.8, 73.7, 74.5, 118.1, 119.0, 132.6, 177.0, 177.0, 177.5. HRMS (EI) m/z calcd for $C_{34}H_{54}O_8Na$ $(M + Na)^+$ 613.3710, found 613.3712.

6-Deoxy-6-*C*-(2′-ethanoic acid)-1,2,3,4,5-*O*-penta-*O*-benzyl-D-*myo*-inositol (13)

Sodium hydroxide (5.5 g, 0.14 mol) was added to the solution of **12** (2.0 g, 3.4 mmol) in dry methanol (30 mL). The reaction mixture was heated at reflux for 3 h. Most of the volatiles were then removed under reduced pressure. The residue was diluted with water, neutralized with 1 M HCl and extracted with ethyl acetate. The organic phase was dried (Na_2SO_4) and concentrated *in vacuo*. An approximately 2 M solution of HCl in methanol (200 mL) was added to the residue, the mixture stirred for 16 h, then neutralized with methanolic NaOH and evaporated *in vacuo*. The product was taken up in a mixture of 20% MeOH in $CHCl_3$ and filtered through a short column of silica gel. The filtrate was evaporated *in vacuo*. To a solution of the residue in dry DMF (15 mL) at 0 °C under an argon atmosphere, was added NaH (2.1 g, 60% in mineral oil, 52 mmol) and Bu_4NI (0.54 g, 1.5 mmol). After 10 min BnBr (5.7 mL, 48 mmol) was introduced and stirring continued for an additional 0.5 h at rt. The reaction mixture was then diluted with water, and extracted with ether. The organic layer was washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by FCC to give the penta-*O*-benzyl derivative (1.5 g, 68%): clear oil; R_f = 0.75 (10% ethyl acetate–petroleum ether); IR ν 3433 (br), 1729, 1644 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.60 (m, 3H, H-6, 6′), 3.15 (dd, 1H, J = 1.7, 11.1 Hz, H-1), 3.25–3.40 (m, 2H, H-3/4, 5), 4.10–4.25 (m, 2H, H-2, 3/4), 4.46 (ABq, 2H, $\Delta\delta$ = 0.02 ppm, J = 11.4 Hz, $PhCH_2$), 4.68 (m, 3H, PhCH), 4.85 (m, 3H, PhCH), 5.05 (m, 4H, =CH_2, PhCH), 5.74 (m, 1H, =CH), 7.18–7.48 (m, 25H, ArH); ^{13}C NMR ($CDCl_3$) δ 30.3, 41.2, 71.4, 72.7, 73.1, 73.7, 74.5, 75.6, 77.2, 79.5, 81.5, 83.6, 117.6, 127.0–128.5 (several lines), 135.0, 138.1, 138.5, 138.9, 139.2. HRMS (EI) m/z calcd for $C_{44}H_{47}O_5$ $(M + H)^+$ 655.3418, found 655.3421.

A solution of the material from the previous step (1.53 g, 2.34 mmol) in 5 : 1 CH_2Cl_2–MeOH (72 mL) was cooled to −78 °C. A stream of O_3 in O_2 was bubbled through the solution until the starting material was not detectable by TLC. The mixture was flushed with argon and then triphenylphosphine (1.22 g, 4.68 mmol) was added. The mixture was warmed to rt, stirred for 2 h, and concentrated *in vacuo*. The residue was purified by FCC to provide the derived aldehyde (1.47 g, 96%): clear oil; R_f = 0.79 (30% ethyl acetate–petroleum ether); ^{1}H NMR ($CDCl_3$) δ 2.40–2.56 (m, 2H), 2.80–3.00 (m, 1H), 3.07 (dd, 1H, J = 2.0, 11.2 Hz), 3.20 (dd, 1H, J = 9.0, 10.7 Hz), 3.37 (dd, 1H, J = 2.2, 9.85 Hz), 4.07 (bt, 1H, J = 2.0 Hz), 4.08–4.19 (m, 2H), 4.30 (d, 1H, J = 11.5 Hz), 4.50 (dd, 2H, J = 2.0, 10.7 Hz), 4.75 (ABq, $\Delta\delta$ = 0.08, J = 11.8 Hz), 4.82 (d, 2H, J = 10.9 Hz), 8.87 (d, 1H, J = 11.9 Hz), 8.88 (d, 1H, J = 10.7 Hz), 5.01 (d, 1H, J = 10.8 Hz), 7.20–7.50 (m, 25H), 9.55 (t, 1H, J = 2.6 Hz); ^{13}C NMR ($CDCl_3$) δ 38.8, 44.2, 71.6, 72.8, 73.0, 74.0, 74.9, 75.6, 78.4, 81.2, 81.4, 83.3, 127.4, 127.5, 127.7, 127.7, 127.9, 128.0, 128.1, 128.2, 128.2, 128.4, 128.4, 128.5, 128.5, 137.2, 138.0, 138.2, 138.8, 138.9, 202.0.

A solution of aldehyde from the previous step (1.47 g, 2.23 mmol), in THF (22.3 mL) was cooled to 0 °C. Solutions of 2,3-dimethyl-2-butene (1.1 mL, 2 M in THF), aqueous 1 M sodium biphosphate (2.20 mL, 2.20 mmol), and aqueous 1 M sodium chlorate (2.20 mL, 2.20 mmol) were then sequentially added. The reaction mixture was warmed to rt, stirred for 2 h, then extracted with ethyl acetate. The organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by FCC to give **13** (1.37 g, 93%); R_f = 0.48 (30% ethyl acetate–petroleum ether); ^{1}H NMR ($CDCl_3$) δ 2.68 (d, 2H, J = 4.9 Hz), 2.70–2.78 (m, 1H), 3.30–3.34 (dd, 1H, J = 1.9, 11.4 Hz), 3.38 (dd, 1H, J = 2.3, 9.8 Hz), 3.40 (dd, 1H, J = 8.9, 10.9 Hz), 3.70–4.02 (m, 1H), 4.03–4.20 (m, 2H), 4.37 (d, 1H, J = 11.4 Hz), 4.52 (d, 1H, J = 11.4 Hz), 4.60 (d, 1H, J = 11.0 Hz), 4.61 (ABq, $\Delta\delta$ = 0.08, J = 8.3 Hz), 4.75–4.90 (m, 3H), 5.00 (t, 2H, J = 10.9 Hz), 7.20–7.49 (m, 25H); ^{13}C NMR ($CDCl_3$) δ 23.9, 29.1, 32.0, 39.2, 67.7, 71.6, 72.8, 72.9, 73.8, 75.0, 75.6, 77.8, 80.2, 81.3, 83.4, 108.0, 127.3, 127.5, 127.6, 127.7, 127.7, 127.9, 127.9, 127.9, 128.0, 128.2, 128.4, 128.4, 128.4, 128.4, 128.5, 137.6, 138.4, 138.4, 138.8, 139.0. HRMS (ES) m/z calcd for $C_{43}H_{44}O_7Na$ $(M + Na)^+$ 695.2985, found 695.2963.

Thioacetal ester (15)

A mixture of acid **13** (0.38 g, 0.56 mmol), 2,4,6-trichlorobenzoyl chloride (0.09 mL, 0.56 mmol) and triethylamine (0.16 mL, 1.13 mmol) in THF (30 mL) was stirred for 3.5 h at 0 °C. A mixture of alcohol **14** (0.29 g, 0.56 mmol) and DMAP (89 mg, 0.73 mmol) in toluene (15 mL) were added, and stirring continued for 1 h. The mixture was then diluted with ether, washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, and evaporated under reduced pressure.

The residue was purified by FCC to give ester **15** (0.57 g, 86%): colorless oil; R_f = 0.58 (15% ethyl acetate–petroleum ether); IR ν 1727 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (s, 9H), 1.37 (s, 3H), 1.44 (s, 3H), 2.68–2.85 (m, 3H), 3.38 (dd, 1H, J = 2.3, 9.9 Hz), 3.45–3.55 (m, 2H), 3.70–3.83 (m, 2H), 4.03–4.15 (m, 2H), 4.33 (dd, 1H, J = 4.5, 6.7 Hz), 4.40 (d, 1H, J = 11.4 Hz), 4.48 (d, 1H, J = 11.4 Hz), 4.52 (d, 1H, J = 10.9 Hz), 4.64 (d, 2H, J = 4.2 Hz), 4.75–4.85 (m, 3H), 4.90 (d, 1H, J = 10.8 Hz), 5.01 (d, 1H, J = 10.9 Hz), 5.23 (q, 1H, J = 5.0 Hz), 5.50 (d, 1H, J = 6.7 Hz), 7.15–7.73 (m, 40H); ^{13}C NMR ($CDCl_3$) δ 19.1, 26.0, 26.8, 27.3, 31.5, 39.4, 62.1, 62.1, 71.7, 72.6, 72.8, 73.2, 73.7, 75.0, 75.4, 77.6, 79.4, 80.1, 81.3, 83.5, 84.9, 111.5, 127.6, 127.7, 127.7, 127.7, 127.8, 127.9, 127.9, 128.1, 128.3, 128.3, 128.4, 128.4, 128.4, 129.0, 132.0, 135.6, 135.6, 139.1, 172.0. HRMS (EI) m/z calcd for $C_{72}H_{78}O_{10}NaSiS$ $(M + Na)^+$ 1185.4977, found 1185.4977.

Thioacetal enol ether (16)

To a mixture of ester **15** (1.35 g, 1.16 mmol), and pyridine (0.10 mL) in anhydrous 3 : 1 toluene–THF (30 mL), was added, under an argon atmosphere and at −78 °C, Tebbe reagent (5.71 mL, 0.5 M in THF). The reaction mixture was warmed to rt, stirred at this temperature for 1 h, then slowly poured into 1 N aqueous NaOH at 0 °C. The resulting suspension was extracted with ether and the organic phase was washed with brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. FCC of the residue on basic alumina provided enol ether **16** (0.70 g, 77% based on recovered starting material) as a light yellow oil: R_f (basic alumina) = 0.45 (10% ethyl acetate–petroleum ether); ^1H NMR (C_6D_6) δ 1.16 (s, 9H), 1.40 (s, 3H), 1.51 (s, 3H), 2.61–3.00 (m, 3H), 3.47 (dd, 1H, J = 2.1, 10.0 Hz), 3.60 (dd, 1H, J = 1.8, 11.3 Hz), 3.77 (t, 1H, J = 9.1 Hz), 4.06 (dd, 1H, J = 4.8, 10.8 Hz), 4.10–4.20 (m, 2H), 4.20–4.26 (m, 3H), 4.40 (t, 1H, J = 9.5 Hz), 4.45–4.55 (m, 6H), 4.56 (q, 1H, J = 4.6 Hz), 4.61–4.77 (m, 2H), 4.80–5.11 (m, 5H), 5.26 (d, 1H, J = 11.4 Hz), 5.53 (s, 1H), 5.90 (d, 1H, J = 6.3 Hz), 6.87–7.85 (m, 40H); ^{13}C NMR (C_6D_6) δ 19.7, 23.1, 26.5, 27.4, 27.5, 28.0, 30.4, 32.2, 34.8, 41.9, 62.7, 71.9, 73.2, 74.7, 74.9, 74.9, 75.9, 76.8, 79.1, 80.6, 80.7, 82.5, 85.0, 86.0, 86.4, 112.5, 112.6, 127.9, 127.9, 128.0, 128.1, 128.1, 128.1, 128.3, 128.5, 128.7, 128.7, 128.8, 128.8, 128.9, 129.0, 129.0, 129.6, 130.6, 130.6, 132.0, 133.8, 135.4, 136.4, 139.6, 139.7, 140.3, 140.3, 140.8, 160.8. HRMS (EI) m/z calcd for $C_{73}H_{80}O_9NaSiS$ $(M + Na)^+$ 1183.4184, found 1183.5188.

6-Deoxy-1,2,3,4,5-penta-*O*-benzyl-6-*C*-(2′,6′-anhydro-5′,7′-dideoxy-3,4-*O*-isopropylidene-1′-*O*-*tert*-butyldiphenylsilyl-L-*ribo*-hept-5-enitol-7′-*C*-yl)-D-*myo*-inositol (17)

A mixture of enol ether **16** (0.49 g, 0.42 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (1.02 g, 5.0 mmol), and freshly activated, powdered 4 Å molecular sieves (1.47 g) in anhydrous CH_2Cl_2 (20 mL), was stirred for 15 min, at rt, under an atmosphere of argon, then cooled to 0 °C. Methyl triflate (0.47 mL, 4.2 mmol) was then introduced, and the mixture warmed to rt, and stirred for an additional 18 h, at which time, triethylamine (1 mL) was added. The mixture was diluted with ether, washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), filtered and evaporated *in vacuo*. FCC of the residue provided **17** (0.35 g, 78%) as a light yellow oil. R_f (basic alumina) = 0.35 (10% ethyl acetate–petroleum ether); ^1H NMR (C_6D_6) δ 1.16 (s, 9H, *t*Bu), 1.23 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 2.70 (dd, 1H, J = 5.0, 14.3 Hz, H-7′a), 2.91 (dd, 1H, J = 3.1, J = 14.3 Hz, H-7′b), 2.97 (m, 1H, H-6), 3.39 (dd, 1H, J = 1.7, 12.0 Hz, H-1), 3.42 (dd, 1H, J = 2.0, 10.4 Hz, H-3), 3.64 (m, 1H, bdd, J = 2.5, 10.0 Hz, H-2′), 3.69 (dd, 1H, J = 9.1, 10.0 Hz, H-5), 3.99 (dd, 1H, J = 4.2, 11.0 Hz, H-1′a), 4.04 (dd, 1H, J = 5.5, 10.0 Hz, H-3′), 4.08 (bd, 1H, J = 11.0 Hz), 4.21 (bt, 1H, J = 1.9 Hz, H-2), 4.24 (t, 1H, J = 5.5 Hz, H-4′), 4.41 (t, 1H, J = 9.5 Hz, H-4), 4.46 (ABq, 2H, $\Delta\delta$ = 0.04 ppm, J = 11.1 Hz, $PhCH_2$), 4.55 (ABq, 2H, $\Delta\delta$ = 0.04 ppm, J = 11.9 Hz, $PhCH_2$), 4.80 (apparent d, 1H, J = 10.9 Hz, PhCH), 4.92 (ABq, 2H, $\Delta\delta$ = 0.03 ppm, J = 12.1 Hz, $PhCH_2$), 5.05 (m, 3H, H-5′, $PhCH_2$), 5.30 (apparent d, 1H, J = 11.3 Hz, PhCH), 7.00–7.28 (m, 21H, ArH), 7.31 (d, 2H, J = 1.2 Hz, ArH), 7.38 (d, 2H, J = 7.5 Hz, ArH), 7.46 (d, 4H, J = 7.5 Hz, ArH), 7.52 (d, 2H, J = 7.3 Hz, ArH), 7.84 (dt, 4H, J = 1.4, 7.9 Hz, ArH); ^{13}C NMR (C_6D_6) δ 21.0, 27.2, 28.6, 30.2, 32.8, 42.6, 64.7, 70.7, 71.2, 72.9, 74.2, 75.4, 76.0, 76.1, 77.2, 78.7, 80.4, 82.3, 83.5, 85.8, 98.9 (C-5′), 109.5, 128.9–130.0 (several lines buried under C_6D_6), 131.4, 135.0, 135.1, 137.4, 137.5, 140.6, 140.7, 141.2, 141.6, 160.0 (C-6′). HRMS (EI) m/z calcd for $C_{67}H_{75}O_9Si$ $(M + H)^+$ 1051.5174, found 1051.5159.

6-Deoxy-1,2,3,4,5-penta-*O*-benzyl-6-*C*-(2′,6′-anhydro-3′,4′-*O*-isopropylidene-1′-*O*-*tert*-butyldiphenylsilyl-7′-deoxy-D-*glycero*-D-*talo*-heptitol-7′-*C*-yl)-D-*myo*-inositol (18) and 6-deoxy-1,2,3,4,5-penta-*O*-benzyl-6-*C*-(2′,6′-anhydro-3′,4′-*O*-isopropylidene-1′-*O*-*tert*-butyldiphenylsilyl-7′-deoxy-L-*glycero*-L-*allo*-heptitol-7′-*C*-yl)-D-*myo*-inositol (19)

$BH_3{\cdot}Me_2S$ (1.3 mL, 1 M solution, 1.3 mmol) was added at 0 °C to a solution of **17** (0.35 g, 0.33 mmol) in anhydrous THF (15 mL) under an atmosphere of argon. The mixture was warmed to rt and stirred for an additional 1 h, then recooled to 0 °C and treated with a mixture of 3 N NaOH (2.4 mL) and 30% aqueous H_2O_2 (2.4 mL) for 30 min. The mixture was then diluted with ether and washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), filtered and evaporated under reduced pressure. FCC of the residue provided an unseparated mixture of 18 : 19 (0.30 g, *ca*. ratio 3 : 1, 83%). Repeated FCC on the mixture provided samples of separated **18** and **19**.

For **18**: R_f = 0.25 (20% ethyl acetate–petroleum ether); $[\alpha]_D^{23}$ −13.3 (c 1.02, $CHCl_3$); IR ν 3411 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (s, 9H, *t*-Bu), 1.34 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.75 (m, 1H, H-7′), 1.87 (m, 1H, H-7′), 2.65 (m, 1H, H-6), 3.15 (m, 3H, H-1, H-5, OH), 3.30 (dd, 1H, J = 2.1, 9.9 Hz, H-3), 3.44 (m, 1H, H-5′), 3.57 (m, 1H, H-6′), 3.71 (dd, 1H, J = 4.8, 10.5 Hz, H-1′a), 3.78 (dd, 1H, J = 6.7, 10.6 Hz, H-1′b), 3.89 (m, 2H, H-2′, H-4′), 4.05 (bs, 1H, H-2), 4.09 (t, 1H, J = 9.2 Hz, H-4), 4.26 (apparent d, 1H, J = 11.3 Hz, PhCH), 4.31 (dd, 1H, J = 3.6, 6.10 Hz, H-3′), 4.48 (apparent d, 1H, J = 11.2 Hz, PhCH), 4.64 (m, 3H, PhCH × 3), 4.72–4.89 (m, 3H, PhCH × 3), 4.94 (apparent d, 1H, J = 12.0 Hz, PhCH), 4.96 (apparent d, 1H, J = 12.0 Hz, PhCH), 7.11 (m, 3H, ArH), 7.20–7.50 (m, 28H, ArH), 7.65 (m, 4H, ArH); ^{13}C NMR ($CDCl_3$) δ 19.2, 25.8, 26.9, 28.0, 33.2, 37.7, 64.1, 71.9,

72.6, 72.8, 73.5, 73.5, 73.6, 73.7, 74.8, 74.8, 75.4, 76.8, 80.3, 81.5, 82.4, 83.3, 108.8, 127.3–128.6 (several signals), 129.8 (two signals), 133.3, 135.6, 137.1, 138.5, 138.6, 138.9, 138.9. HRMS (EI) *m*/*z* calcd for $C_{67}H_{77}O_{10}Si$ (M + H)$^+$ 1069.5280, found 1069.5266.

For **19**: R_f = 0.23 (20% ethyl acetate–petroleum ether); IR ν 3455 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (s, 9H, *t*-Bu), 1.25 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.88 (m, 2H, H-7′), 2.58 (d, *J* = 8.3 Hz, OH), 2.50 (m, 1H, H-6), 3.09 (d, *J* = 10.9 Hz, H-1), 3.27 (m, 3H, H-2′, 3′, 3), 3.40 (t, *J* = 9.3 Hz, H-5), 3.60 (m, 2H, H-1′, 6′), 3.73 (bd, *J* = 11.2 Hz, H-1′), 3.87 (dd, *J* = 4.9, 9.3 Hz, H-3′), 4.00 (t, *J* = 9.6 Hz, H-4), 4.07 (bs, 1H, H-2), 4.26 (apparent d, *J* = 11.3 Hz, PhCH), 4.29 (t, *J* = 4.5 Hz, H-4′), 4.49 (m, 3H, PhCH × 3), 4.73 (m, 4H, PhCH × 4), 4.88 (apparent d, *J* = 10.8, PhCH), 4.94 (apparent d, *J* = 11.3, PhCH), 7.10–7.30 (m, 28H, ArH), 7.60 (m, 4H, ArH); ^{13}C NMR ($CDCl_3$) δ 19.5, 26.6, 27.1, 28.4, 22.1, 38.4, 64.5, 71.8 (2C), 72.8, 72.9 (two signals), 73.7, 75.0, 75.3 (2C), 75.8, 78.8, 79.9, 81.8, 82.7, 83.7, 110.0, 127.4–128.6 (several signals), 129.7 (two signals), 133.7, 133.8, 135.8, 135.9, 138.1, 138.8, 138.9, 139.1, 139.3. HRMS (EI) *m*/*z* calcd for $C_{67}H_{76}O_{10}NaSi$ (M + Na)$^+$ 1091.5105, found 1091.5076.

6-Deoxy-1,2,3,4,5-penta-*O*-benzyl-6-*C*-(2′,6′-anhydro-5-*O*-benzoyl-3′,4′-*O*-isopropylidene-1′-*O*-*tert*-butyldiphenylsilyl-7′-deoxy-D-*glycero*-D-*talo*-heptitol-7′-*C*-yl)-D-*myo*-inositol (20) and 6-deoxy-1,2,3,4,5-penta-*O*-benzyl-6-*C*-(2′,6′-anhydro-5-*O*-benzoyl-3′,4′-*O*-isopropylidene-1′-*O*-*tert*-butyl-diphenylsilyl-7′-deoxy-L-*glycero*-L-*allo*-heptitol-7′-*C*-yl)-D-*myo*-inositol (21)

A mixture of **18** and **19** (244 mg, 0.229 mmol) was dissolved in CH_2Cl_2 (20 mL), and pyridine (0.055 mL, 0.675 mmol) and benzoyl chloride (0.034 mL, 0.296 mmol) were added to the reaction mixture. The reaction was monitored by TLC. The mixture was diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), filtered and evaporated *in vacuo*. FCC of the residue provided recovered **19** (30 mg, 12%), **20** (94 mg, 40% brsm), **21** (77 mg, 33% brsm), and unseparated **20**/**21** (38 mg, 16% brsm).

For **20**: R_f = 0.63 (20% ethyl acetate–petroleum ether); IR ν 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.11 (s, 9H, *t*-Bu), 1.28 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.62 (ddd, *J* = 2.1, 7.4, 12.8 Hz, 1H, H-7′a), 2.18 (dt, *J* = 1.8, 12.8 Hz, 1H, H-7′b), 2.67 (apparent q, *J* = 11.1 Hz, 1H, H-6), 3.19 (m, 2H, H-1, H-5), 3.26 (dd, 1H, *J* = 2.2, 9.9 Hz, H-3), 3.82 (dd, 1H, *J* = 4.1, 10.9 Hz, H-1′a), 3.89 (dd, 1H, *J* = 4.7, *J* = 10.9 Hz, H-1′b), 4.00 (q, 1H, *J* = 4.5 Hz, H-2′), 4.03 (bt, 1H, *J* = 2.0 Hz, H-2), 4.15 (t, 1H, *J* = 9.3 Hz, H-4), 4.23 (t, 1H, *J* = 6.1 Hz, H-4′), 4.29 (m, 2H, H-6′, PhCH × 2), 4.35 (t, 1H, *J* = 5.1 Hz, H-3′), 4.46 (apparent d, 1H, *J* = 11.6 Hz, PhCH), 4.60 (m, 3H, PhCH × 3), 4.75 (apparent d, 1H, *J* = 10.7 Hz, PhCH), 4.81 (s, 2H, $PhCH_2$), 4.97 (apparent t, 2H, *J* = 9.6 Hz, PhCH × 2), 5.22 (t, 1H, *J* = 6.9 Hz, H-5′), 7.09–7.40 (m, 33H, ArH), 7.60 (t, 1H, *J* = 7.5 Hz, ArH), 7.75 (m, 4H, ArH), 7.95 (d, 2H, *J* = 8.0 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 19.5, 26.4, 27.2, 27.9, 30.4, 37.8, 64.7, 71.5, 72.4, 72.5, 72.8, 72.9, 73.1, 73.5, 74.3, 75.6, 81.0, 81.1, 81.6, 83.4, 109.5, 127.6–130.4 (several signals), 133.2, 133.6, 133.8, 135.9, 136.0, 138.2, 138.7, 138.9, 139.2, 139.4, 165.8. HRMS (EI) *m*/*z* calcd for $C_{74}H_{81}O_{11}Si$ (M + H)$^+$ 1173.5542, found 1173.5525.

For **21**: R_f = 0.55 (20% ethyl acetate–petroleum ether); ^{1}H NMR ($CDCl_3$) δ 0.96 (s, 9H, *t*-Bu), 1.20 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.82 (m, 1H, H-7′a), 1.94 (m, 1H, H-7′b), 2.58 (m, 1H, H-6), 3.18 (dd, 1H, *J* = 0.7, 11.5 Hz, H-1), 3.23 (dd, 1H, *J* = 2.1, 10.0 Hz, H-3), 3.44 (dd, 1H, *J* = 6.3, 7.8 Hz, H-2′), 3.52 (t, 1H, *J* = 10.0 Hz, H-5), 3.64 (dd, 1H, *J* = 5.9, 11.3 Hz, H-1′a), 3.78 (bd, 1H, *J* = 10.0 Hz, H-1′b), 3.91 (t, 1H, *J* = 11.0 Hz, H-4), 3.95 (dd, 1H, *J* = 4.8, 9.4 Hz, H-3′), 4.12 (bs, 1H, H-2), 4.17 (dt, 1H, *J* = 2.9, 9.8 Hz, H-6′), 4.30 (apparent d, 1H, *J* = 11.0, PhCH), 4.42 (ABq, 2H, *J* = 11.8 Hz, $\Delta\delta$ = 0.06 ppm, $PhCH_2$), 4.54 (apparent d, 1H, *J* = 10.9 Hz, PhCH), 4.58 (t, 1H, *J* = 4.3 Hz, H-4′), 4.63 (apparent d, 1H, *J* = 10.8 Hz, PhCH), 4.72 (apparent d, 1H, *J* = 11.0 Hz, PhCH), (s, 2H, $PhCH_2$), 4.79 (m, 3H, PhCH × 3), 4.85 (partially buried dd, 1H, *J* = 3.9, 9.7 Hz, H-5′), 4.88 (apparent d, 1H, *J* = 10.8, PhCH), 7.05–7.40 (m, 33H, ArH), 7.45 (t, 1H, *J* = 7.5, ArH), 7.62 (m, 4H, ArH); 7.78 (d, 2H, *J* = 7.8 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 19.5, 26.5, 27.2, 28.3, 29.8, 38.4, 64.5, 71.9, 72.8, 72.9 (two signals), 73.0, 73.2, 73.9, 74.7, 75.8, 79.0, 79.4, 81.1, 81.8, 81.9, 84.0, 110.4, 127.4–128.7 (several signals), 129.8, 130.1, 130.2, 133.2, 133.6, 133.8, 135.8 (two signals), 138.0, 139.0, 139.2, 139.3, 139.4, 166.0. HRMS (ES) *m*/*z* calcd for $C_{74}H_{80}O_{11}NaSi$ (M + Na)$^+$ 1195.5368, found 1195.5410.

6-Deoxy-1,2,3,4,5-penta-*O*-benzyl-6-*C*-(2′,6′-anhydro-5-*O*-benzoyl-1′-*O*-*tert* butyldiphenylsilyl-7′-deoxy-L-*glycero*-L-*allo*-heptitol-7′-*C*-yl)-D-*myo*-inositol (22)

5% Acetyl chloride in methanol (0.1 mL) was added to a solution of **20** (206 mg, 0.176 mmol) in dry CH_2Cl_2 (15 mL). The reaction mixture was stirred at rt for 20 min. The mixture was neutralized by addition of sodium methoxide. Removal of the volatiles under reduced pressure and FCC of the residue provided **22** (142 mg, 71%): IR ν 3443 cm^{-1}; R_f = 0.54 (40% ethyl acetate–petroleum ether); ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 9H, *t*-Bu), 1.54 (m, 1H, H-7′a), 2.56 (m, 2H, H-6, 7′b), 2.67 (d, 1H, *J* = 3.1 Hz, OH), 2.93 (d, 1H, *J* = 4.0 Hz, OH), 3.17 (m, 2H, H-1, 5), 3.33 (dd, 1H, *J* = 2.3, *J* = 9.9 Hz, H-3), 3.80 (dd, 1H, *J* = 6.8, 10.5 Hz, H-1′a), 3.83 (dd, 1H, *J* = 4.3, *J* = 10.5 Hz, H-1′b), 3.92 (m, 1H, H-2′), 4.02 (m, 1H, H-4′), 4.07 (m, 2H, H-2, 3′), 4.18 (t, 1H, *J* = 9.3 Hz, H-4), 4.32 (m, 2H, H-6′, PhCH), 4.51 (apparent d, 1H, *J* = 11.5 Hz, PhCH), 4.62 (m, 3H, PhCH × 3), 4.80 (m, 3H, PhCH × 3), 5.03 (apparent d, 1H, *J* = 11.5 Hz, PhCH), 5.04 (apparent d, 1H, *J* = 11.5 Hz, PhCH), 5.15 (dd, 1H, *J* = 3.7, *J* = 4.8 Hz, H-5′), 7.20–7.41 (m, 33H, ArH), 7.54 (t, 1H, *J* = 6.5 Hz, ArH), 7.68 (m, 4H, ArH), 7.95 (d, 2H, *J* = 7.0 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 19.2, 27.0, 30.0, 37.2, 65.1, 69.0, 69.2, 69.3, 71.4, 72.6 (two signals), 73.3, 73.5, 74.0, 75.4, 75.5, 81.4, 81.5, 81.8, 83.6, 127.5, 127.5, 127.7, 127.9, 128.0, 128.0, 128.1, 128.3, 128.3, 128.3, 128.4, 128.4, 129.9, 130.0, 132.8, 133.0 135.6, 135.7, 135.7, 137.7, 138.5, 138.6, 138.7, 139.2, 166.0. HRMS (EI) *m*/*z* calcd for $C_{71}H_{77}O_{11}Si$ (M + H)$^+$ 1133.5229, found 1133.5215.

6-Deoxy-1,2,3,4,5-penta-*O*-benzyl-6-*C*-(3′-*O*-acetyl-2′,6′-anhydro-5-*O*-benzoyl-1′-*O*-*tert*-butyldiphenylsilyl-7′-deoxy-L-*glycero*-L-*allo*-heptitol-7′-*C*-yl)-D-*myo*-inositol (23) and 6-deoxy-1,2,3,4,5-penta-*O*-benzyl-6-*C*-(4′-*O*-acetyl-2′,6′-anhydro-5-*O*-benzoyl-1′-*O*-*tert*-butyldiphenylsilyl-7′-deoxy-L-*glycero*-L-*allo*-heptitol-7′-*C*-yl)-D-*myo*-inositol (24)

A solution of **22** (0.041 g, 0.036 mmol) in dry benzene (6 mL) and triethyl orthoacetate (6 mL) was treated with CSA (1.1 mg) at rt for 1 h. Triethylamine (3 mL) was then added and the mixture diluted with water and extracted with ethyl acetate. The organic phase was washed with saturated aqueous $NaHCO_3$, water and brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) and treated with 80% aqueous acetic acid (20 mL). The mixture was stirred at rt for 35 min, then diluted with toluene and evaporated under reduced pressure. FCC of the residue afforded **23** (0.027 g, 64%) and **24** (0.014 g, 33%).

For **23**: R_f = 0.17 (20% ethyl acetate–petroleum ether); IR ν 3443, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (s, 9H, *t*-Bu), 1.66 (m, 1H, H-7′a), 2.00 (s, 3H, CH_3CO), 2.20 (dd, 1H, J = 6.4, 10.4 Hz, H-7′b), 2.63 (m, 1H, H-6), 3.18 (m, 2H, H-1, 5), 3.26 (dd, 1H, J = 2.2, 9.9 Hz, H-3), 3.76 (dd, 1H, J = 4.7, 10.9 Hz, H-1′b), 3.81 (dd, 1H, J = 6.0, 10.9 Hz, H-1′a), 3.99–4.17 (m, 4H, H-2, 4, 2′, 4′), 4.7 (m, 1H, PhCH, H-6′), 4.48 (apparent d, 1H, J = 11.4 Hz), 4.60 (m, 3H, PhCH), 4.7 (m, 3H, PhCH), 4.90 (m, 2H, PhCH), 5.13 (t, 1H, J = 7.5 Hz, H-5′), 5.43 (t, 1H, J = 3.8 Hz, H-3′), 7.18–7.46 (m, 33H, ArH), 7.51 (t, J = 7.5 Hz, 1H, ArH), 7.68 (m, 4H, ArH), 7.86 (d, 2H, J = J = 7.8 Hz, ArH); ^{13}C NMR (500 MHz, $CDCl_3$) δ 19.2, 21.1, 26.8, 30.6, 37.3, 62.4, 68.9, 71.1, 71.4, 72.6, 72.7, 72.8, 73.2, 73.3, 74.5, 74.7, 75.5, 81.0, 81.2, 81.4, 83.3, 127.2, 127.5, 127.6, 127.7, 127.7, 127.8, 127.8, 128.0, 128.1, 128.2, 128.3, 128.4, 129.8, 129.9, 133.2, 135.6, 135.7, 138.0, 139.1, 166.5, 170.2. HRMS (ES) m/z calcd for $C_{73}H_{78}O_{12}NaSi$ $(M + Na)^+$ 1197.5160, found 1197.5205.

For **24**: R_f = 0.20 (20% ethyl acetate–petroleum ether); IR ν 3452, 1726 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (s, 9H, *t*-Bu), 1.45 (m, 1H, H-7′a), 1.86 (s, 3H, CH_3CO), 2.06 (bs, 1H, OH), 2.32 (t, 1H, J = 12.2 Hz, H-7′b), 2.50 (m, 1H, H-6), 3.07 (m, 2H, H-1, 5), 3.17 (dd, 1H, J = 2.2, 9.9 Hz, H-3), 3.72 (m, 1H, CH_2-1′), 3.88 (m, 1H, H-2′), 3.94 (bs, 1H, H-2), 4.02 (t, 1H, J = 9.3 Hz, H-4), 4.14 (apparent d, 1H, J = 11.4 Hz, 1H, PhCH), 4.22 (m, 1H, H-3′), 4.27 (m, 1H, H-6′), 4.35 (apparent d, 1H, J = 11.4 Hz, PhCH), 4.50 (m, 3H, PhCH), 4.68 (m, 3H, PhCH), 4.91 (m, 2H, PhCH), 5.13, (t, 1H, J = 5.10, H5′), 5.30 (dd, 1H, J = 3.6, 6.3 Hz, H-4′), 7.10–7.30 (m, 33H, ArH), 7.46 (t, 1H, J = 7.5 Hz, ArH), 7.62 (m, 4H, ArH), 7.80 (d, 2H, J = 7.8 Hz, ArH); ^{13}C NMR (500 MHz, $CDCl_3$) δ 19.4, 21.1, 27.1, 29.8, 37.7, 63.9, 67.1, 71.1, 71.5, 72.2, 72.6, 72.7, 72.8, 73.5, 75.0, 75.6, 81.1, 81.2, 81.6, 83.6, 127.8–128.6 (several lines), 129.8, 129.9, 130.0, 130.1, 133.1, 133.2, 133.4, 135.8, 135.9, 138.0, 138.7, 138.8, 139.1, 139.3, 166.5, 170.2. HRMS (ES) m/z calcd for $C_{73}H_{78}O_{12}NaSi$ $(M + Na)^+$ 1197.5160, found 1197.5188.

6-Deoxy-1,2,3,4,5-penta-*O*-benzyl-6-*C*-(3′-*O*-acetyl-2′,6′-anhydro-5-*O*-benzoyl-1′-*O*-*tert*-butyldiphenylsilyl-7′-deoxy-D-*glycero*-D-*manno*-heptitol-7′-*C*-yl)-D-*myo*-inositol (25)

To a solution of **23** (0.025 g, 0.021 mmol), in CH_2Cl_2 (0.3 mL) was added pyridine (0.03 mL) at −20 °C. Trifluoromethanesulfonic anhydride (0.007 mL, 0.021 mmol) in CH_2Cl_2 (0.5 mL) was then added dropwise, and the mixture warmed to 10 °C over 2 h. The solution was then diluted with CH_2Cl_2 and washed with 1 M HCl, saturated aqueous $NaHCO_3$, water and brine. The organic phase was dried (Na_2SO_4) and concentrated *in vacuo* at rt. KNO_2 (0.020 g, 0.24 mmol) was added to a solution of the crude product in dry DMF (1 mL). After stirring at 50 °C for 6 h, the mixture was diluted with CH_2Cl_2 and washed with brine. The organic phase was dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the residue by FCC afforded **25** (0.020 g, 80%): R_f = 0.10 (20% ethyl acetate–petroleum ether); $[\alpha]_D^{23}$ −23 (*c* 1.0, $CHCl_3$); IR ν 3468, 1717 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (s, 9H, *t*-Bu), 1.41 (m, 1H, H-7′a), 2.00 (s, 3H, CH_3CO), 2.08 (m, 1H, H-7′b), 2.30 (d, 1H, J = 9.9 Hz, OH), 2.54 (m, 1H, H-6), 3.12 (m, 2H, H-1, 5), 3.31 (dd, 1H, J = 2.1, 9.9 Hz, H-3), 3.51 (dd, 1H, J = 3.5, 11.3 Hz, H-1′a, 2′), 3.68 (m, 2H, H-1′b, 2), 3.86 (m, 1H, H-4′), 4.15 (m, 2H, H-2, 4), 4.26 (apparent d, 1H, J = 11.6 Hz, PhCH), 4.65 (m, 5H, H-6′, PhCH × 4), 4.77 (apparent d, 1H, 10.7 Hz, PhCH), 4.82 (s, 2H, $PhCH_2$), 5.01 (apparent d, 1H, J = 10.7 Hz, PhCH), 5.03 (apparent d, 1H, J = 11.2 Hz, PhCH), 5.28 (bs, 1H, H-5′), 5.49 (t, 1H, J = 9.6 Hz, H-3′), 7.16–7.48 (m, 33H, ArH), 7.55 (t, 1H, J = 7.41, ArH), 7.69 (dd, 2H, J = 1.1, 7.7 Hz, ArH), 7.71 (dd, 2H, J = 1.2, 7.8 Hz, ArH), 8.09 (d, 2H, J = 7.3 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 19.3 (C-Si), 21.0 (CH_3), 26.7 [$(CH_3)_3C$], 28.1 (C-7′), 37.2 (C-6), 62.7 (C-1′), 69.7 (C-4′), 70.2 (C-3′), 71.0 (PhC), 71.2 (C-2′), 72.4 (C-2), 72.6 (PhC), 73.4 (PhC), 74.5 (PhC), 75.2 (C-5′, 6′), 75.4 (PhC), 80.6 (C-1), 81.3 (C-3, 5), 83.7 (C-4), 127.2–128.5 (several signals), 129.4, 129.5, 130.2, 133.0, 133.3, 133.5, 135.7, 135.8, 137.5, 138.5, 138.6, 138.9, 139.2 (all Ar), 166.0 (C═O), 171.4 (C═O). HRMS (ES) m/z calcd for $C_{73}H_{78}O_{12}NaSi$ $(M + Na)^+$ 1197.5160, found 1197.5167.

6-Deoxy-6-*C*-(2′,6′-anhydro-7′-deoxy-D-*glycero*-D-*manno*-heptitol-7′-*C*-yl)-D-*myo*-inositol [*C*-glycoside of α-D-mannose-(1 → 6)-D-*myo*-inositol] (4)

A mixture of **25** (0.008 g, 0.01 mmol) and NaOMe (*ca*. 5 mg, 0.01 mmol) in methanol (5 mL) was stirred at rt for 30 min. The solvent was then removed under reduced pressure and THF (1 mL) and TBAF (0.012 mL of a 1 M solution in THF, 0.012 mmol) were added to the residue. The mixture was stirred for 5 h at rt, then diluted with saturated aqueous $NaHCO_3$ and extracted with ether. The organic phase was dried (Na_2SO_4) and concentrated *in vacuo*. FCC of the residue afforded a homogeneous material (0.0040 g) as a colorless oil: R_f = 0.21 (2% methanol–ethyl acetate). A mixture of this product, 20% Pd on carbon (0.0123 g), and methanol (1 mL) was stirred under an atmosphere of hydrogen (balloon), for 12 h. The mixture was then purged with argon and filtered through Celite. The filtrate was concentrated *in vacuo*, and the

residue purified by FCC to give **4** (0.002 g, 87%); R_f = 0.12 (40% methanol–CH_2Cl_2); $[\alpha]_D^{19}$ 6 (*c* 0.2, H_2O); ^{1}H NMR (600 MHz, D_2O, external standard: Me_4NBr) δ 1.70 (m, 1H, H-7′a), 1.90 (m, 1H, H-6), 2.18, (bt, 1H, *J* = 13.8 Hz, H-7′b), 3.20 (t, 1H, *J* = 9.1 Hz, H-5), 3.46 (bd, 1H, *J* = 10.0 Hz, H-3), 3.55–3.78 (m, 5H), 3.83 (m, 2H), 3.92 (bd, 1H, *J* = 1.5 Hz), 3.99 (bd, 1H, *J* = 2.4 Hz), 4.25 (bd, 1H, *J* = 8.4 Hz, H-6′); ^{13}C NMR (150 MHz, D_2O) δ 29.1 (C-7′), 41.7 (C-6), 63.8 (C-1′), 69.9, 73.1, 73.5, 73.6, 74.4, 75.2 (C-5), 75.7, 76.0, 76.5 (C-3), 79.3; HRMS (ES) *m*/*z* calcd for $C_{13}H_{24}O_{10}Na$ $(M + Na)^+$ 363.1267, found 363.1267.

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