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The Dimethoxyphenylbenzyl Protecting Group: An Alternative to the PMB Group for Protection of Carbohydrates

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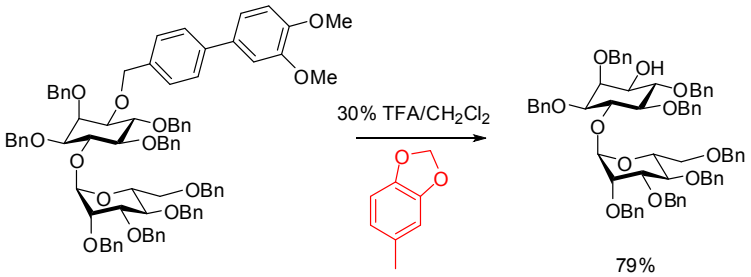


Four further examples are reported with yields ranging from 75 to 87%

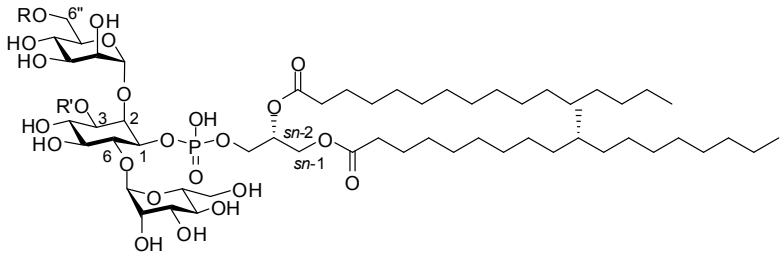
Graphical Abstract

ABSTRACT

A reliable reagent system for the cleavage of 4-(3,4-dimethoxyphenyl)benzyl (DMPBn) ethers under acidic conditions has been established. Treatment of DMPBn-protected mono- and pseudo-di-saccharides with TFA in anhydrous CH_2Cl_2 and 3,4-methylenedioxytoluene as a cation scavenger resulted in the selective cleavage of the DMPBn ether giving the corresponding deprotected products in moderate to high yields. Examples are reported which show that allyl, benzyl and *p*-bromobenzyl ethers, esters, and glycosidic linkages are stable to these reaction conditions. The selective cleavage of allyl, *p*-bromobenzyl, and PMB ethers in protected carbohydrates containing DMPBn ethers are also demonstrated. This work establishes the 4-(3,4-dimethoxyphenyl)benzyl ether as an effective and robust alternative to *p*-methoxybenzyl as a protecting group for alcohols.

INTRODUCTION

Phosphatidylinositol mannosides (PIMs), compounds that are found in the cell wall of mycobacteria, have received much attention due to their immune regulatory properties. In a programme of research aimed at utilising synthetic PIMs for the treatment of diseases such as asthma and also for natural product structural elucidation we have developed syntheses of the major PIM species found in the cell wall as well as simplified analogues that retain some aspects of their biological activities.[1-8] More recently, we have reported the first total synthesis of a fully lipidated PIM, Ac_2PIM_2 **1**[9] that contains four fatty acid residues (Figure 1).



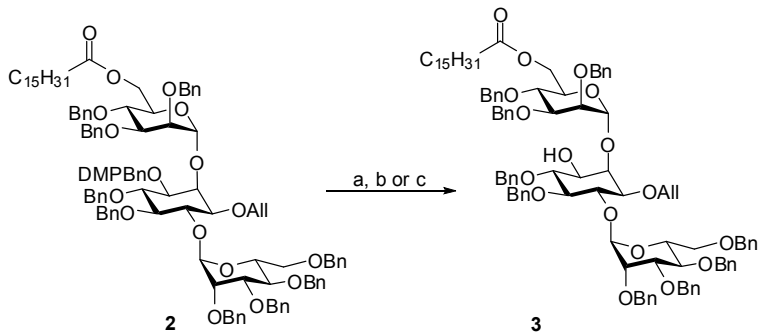
1 (16:0,18:0)(19:0/16:0)-PIM_2 R = $C_{15}H_{31}CO$, R' = $C_{17}H_{35}CO$

Figure 1. Ac_2PIM_2 **1**.

The synthesis of **1** required orthogonal protection of a *myo*-inositol intermediate that allowed sequential introduction of each of the mannose residues, the *O*-6" fatty ester, the *O*-3 fatty ester and finally the *O*-1 phosphatidyl group. The choice of protecting groups proved crucial. In the course of our work we found that the lability of *p*-methoxybenzyl (PMB) ethers was problematic; conditions required for glycosylation reactions resulted in the undesired removal of the PMB group. A similar hydrolysis has been observed by Seeberger et al., who used it to their advantage, in the synthesis of a fully lipidated GPI anchor of *T. gondii*.[10] Our results prompted us to explore the use of the 4-(3,4-dimethoxyphenyl)benzyl (DMPBn) group,

developed by the Seeberger group,[11] as a robust alternative to the PMB group for the protection of alcohols. They found that DMPBn ethers were as labile as PMB ethers when treated with DDQ but were more resistant to acid hydrolysis. Furthermore, oxidative removal of this group could be carried out selectively in the presence of ester, TBS, benzyl and allyl protecting groups as exemplified using protected mono- and di-saccharides.

Our strategy for the synthesis of Ac_2PIM_2 relied on the intermediacy of protected pseudo-trisaccharide **2**.[9] Unfortunately, removal of the DMPBn protecting group proved problematic. Using the reported reaction conditions of three equivalents of DDQ in a 10 to 1 mixture of CH_2Cl_2 and water for three hours, a complex mixture of products was formed (Scheme 1, TLC provided in supporting information). Mass spectral analyses of column fractions revealed that they contained **3** and compounds where the DMPBn group had been removed along with loss of some of the benzyl protecting groups. Seeberger et al. had noted that the DDQ-labile DMPBn group could not be removed selectively when operating on a hexasaccharide intermediate for the synthesis of a fully lipidated GPI anchor of *P. falciparum*.[12] Given our investment in preparing late stage intermediate **2** we investigated developing reaction conditions for the selective deprotection of DMPBn ethers, thereby increasing the scope and utility of this protecting group.

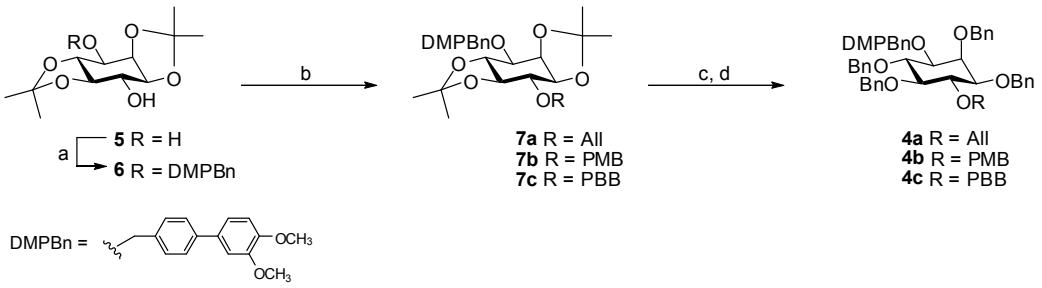


Reagents and conditions: (a) DDQ (3 eq.), CH_2Cl_2/H_2O, 3 h; (b) DDQ (1.2 eq.) CH_2Cl_2/H_2O, 1 h; (c) DDQ (3 eq.), $Mn(OAc)_3.H_2O$ (3 eq.), CH_2Cl_2/H_2O, 12 h.

Scheme 1. Deprotection of pseudo-trisaccharide **2** using DDQ.

RESULTS AND DISCUSSION

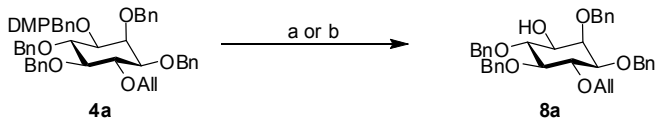
We proposed to optimise the conditions required for the selective removal of the DMPBn protecting group using inositols **4a-c**, prepared from bis-isopropylidene-*myo*-inositol **5**[13-15] (Scheme 2). DMPBn protected inositol **6** was prepared by the selective alkylation of **5** with 4-(3,4-dimethoxyphenyl)benzyl bromide in 85% yield. Allylation of DMPBn alcohol **6** furnished allyl ether **7a** in 91% yield. Acidic cleavage of the isopropylidene groups and subsequent benzylation afforded model inositol **4a**. PMB and PBB inositol ethers **4b** and **4c** were prepared using the same approach. Given literature precedence for the successful hydrolysis of DMPBn protected monosaccharides,[11] **4a** should undergo oxidative deprotection with minimal side reactions occurring.



Reagents and conditions: (a) DMPBnBr, NaH, THF, 85%; (b) for **7a** AllBr, NaH, DMF, 91%; for **7b**, PMBCl, NaH, THF, 86%; for **7c**, PBBBr, NaH, THF, 89%; (c) TFA, MeOH, CH_2Cl_2; (d) BnBr, NaH, DMF, for **7a,** 45%; for 7b, 24%, for **7c**, 74% (2 steps) .

Scheme 2. Synthesis of model protected inositols **4a-c**.

Unexpectedly, reaction of **4a** with 3 equivalents of DDQ in a 10 to 1 mixture of CH_2Cl_2 and water for 3 hours gave a complex mixture of products as determined by TLC and NMR analysis (Scheme 3a). Loss of benzyl groups was evident from the mass spectrum of the crude product. None of the starting material **4a** remained and the desired product **8a** was isolated in 11% yield. Reducing the reaction time to 1 hour showed an improvement giving a 2.5:1 inseparable mixture of product to starting material along with decomposition products. Reducing the amount of DDQ to 1.2 equivalents gave the best result with a 50% conversion of **4a** into **8a** with no evidence of decomposition products. Column chromatography of this reaction gave an 80% recovery of material containing a 1:1 inseparable mixture of **4a** and **8a** along with 4-(3,4-dimethoxyphenyl)benzaldehyde. Given the latter result these reaction conditions were trialled with pseudo-trisaccharide **2**, but unexpectedly no reaction occurred.

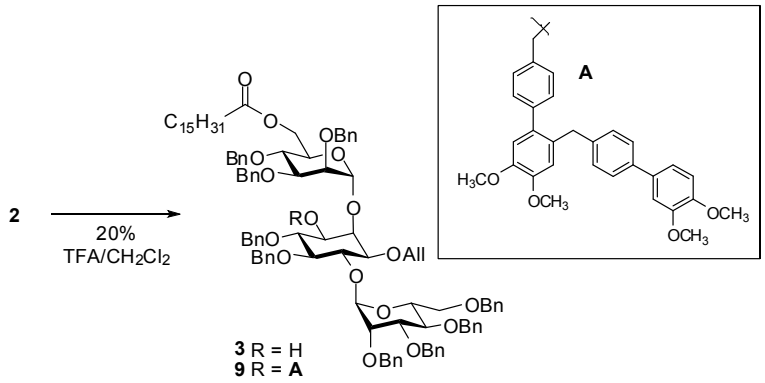


Reagents and conditions: (a) DDQ, CH_2Cl_2/H_2O, 11%; (b) DDQ, $Mn(OAc)_3.H_2O$, CH_2Cl_2/H_2O.

Scheme 3. Deprotection of model DMPBn protected inositol **4a**.

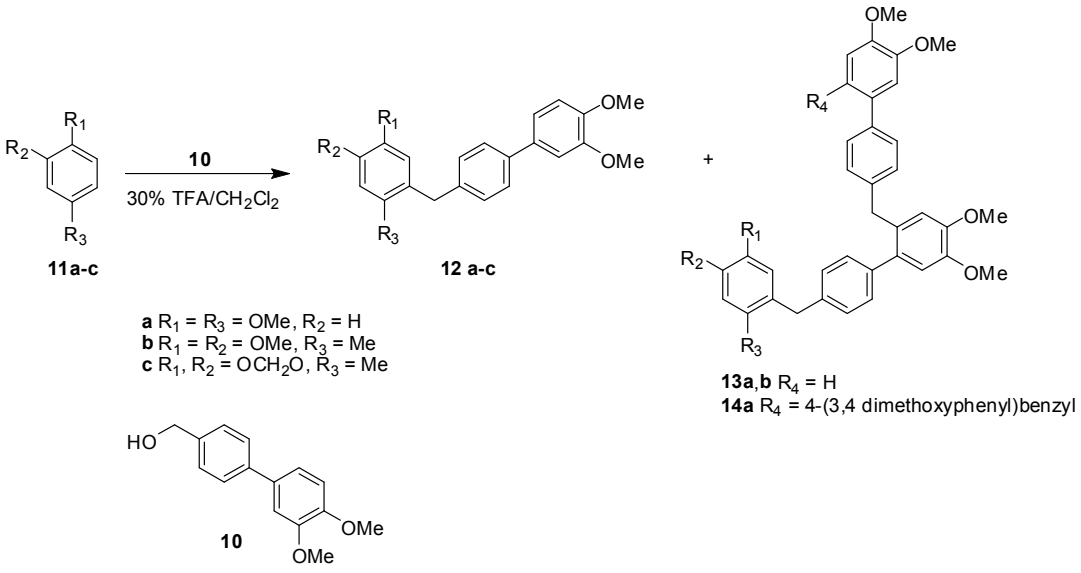
Sharma et al.[16] have reported that $Mn(OAc)_3$ is a mild and efficient reagent for regenerating DDQ for the deprotection of PMB ethers. The use of this as a co-oxidant would minimise the amount of $DDQH_2$ present. Treatment of **4a** with 0.1 equivalents of DDQ and 3 equivalents of $Mn(OAc)_3$ for 12 hours resulted in a 30% conversion into **8a** with no sign of byproduct formation (Scheme 3 reagents b). Increasing the amount of DDQ to 1 equivalent cleanly gave an 80% conversion into **8a**. Unfortunately, reaction of pseudo-trisaccharide **2** under these conditions gave a complex mixture of products along with starting material.

Given the disappointing results using DDQ to deprotect DMPBn ethers our attention turned to exploiting its acid lability. Treatment of **2** with 20% TFA in CH_2Cl_2 at room temperature for 1 h gave a mixture of products as shown by TLC (Scheme 4, TLC provided in supporting information) and after column chromatography gave returned starting material **2** (18%), the target pseudo-trisaccharide **3** (58%), along with 10% of a higher molecular weight product **9** that resulted from the electrophilic addition of the released benzylic cation to the substituted dimethoxyphenyl moiety of **2** (Scheme 4). Mass spectra of the trace amounts of lower R_f products indicated that further substitution of the dimethoxyphenyl moiety had also occurred.



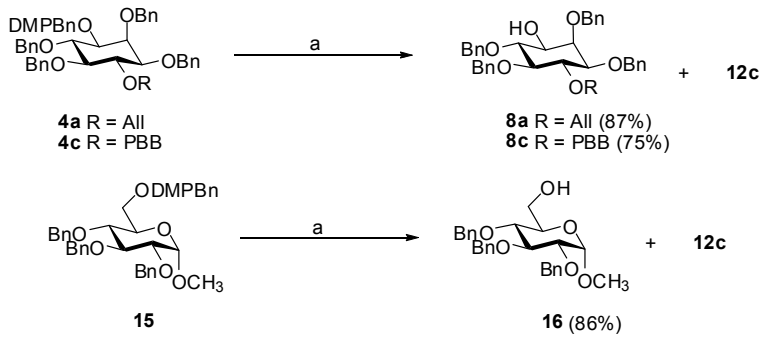
Scheme 4. Deprotection of **2** using 20% TFA for 1 h.

The use of a cation scavenger such as anisole might circumvent this problem. However, we believed that the electron rich benzyl substituted dimethoxyphenyl moiety of the protecting group might still be a more effective cation trap. To test this, anisole was treated with five equivalents of 4-(3,4-dimethoxyphenyl)benzyl alcohol (**10**)[11] in 30% TFA in CH_2Cl_2. A complex mixture of products was produced where further substitution of the activated rings had occurred. Using the more electron rich scavenger 1,4-dimethoxybenzene (**11a**) also gave a mixture of products from which **12a** (21%), **13a** (13%) and **14a** (3%) were isolated (Scheme 5). Given these results scavengers with similar structural features to the activated ring of the DMPBn group were investigated. Under the same reaction conditions 3,4-dimethoxytoluene (**11b**)[17] gave mainly the mono-substituted adduct **12b** (85%) along with a small amount of the further substituted species **13b**. 3,4-Methylenedioxytoluene (**11c**)[17] gave a single scavenged product **12c** in 93% yield.



Scheme 5. Reactions of **10** with cation scavengers **11a-c** in 30% TFA in CH_2Cl_2.

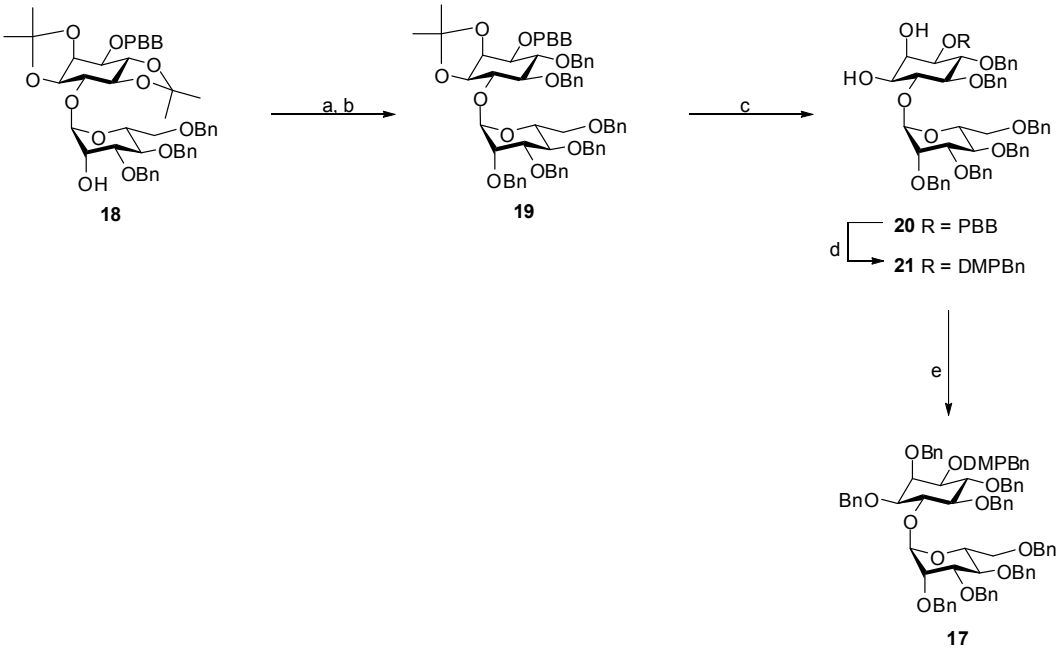
The latter two results were pleasing and the fact that only one product was formed when **11c** was used as the cation trap would facilitate isolation of deprotected DMPBn ethers. Reaction of **4a** with 30% TFA in CH_2Cl_2 and 5 equivalents of **11c** cleanly afforded the deprotected material **8a** in 87% yield (Scheme 6). The scavenged product **12c** was isolated in near quantitative yield. In a similar fashion, PBB ether **4c** gave **8c** in 75% yield. Further examples were investigated and subjected to these reaction conditions. DMPBn glucoside **15**[11] gave the desired deprotected derivative **16** (86%) and the scavenged product **12c** in quantitative yield.



Reagents and conditions: (a) **11c** (5 eq.), 30% TFA/CH_2Cl_2.

Scheme 6. Deprotection of DMPBn inositols **4a** and **4c**, and glucoside **15** using 30% TFA for 1 h.

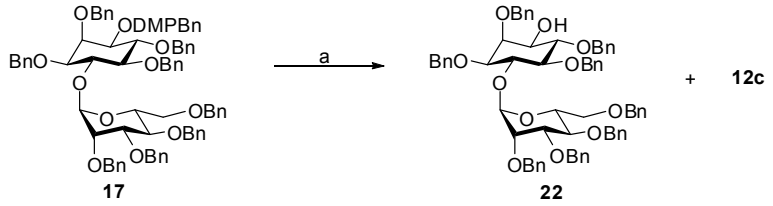
DMPBn protected pseudo-disaccharide **17** was prepared in five steps using standard chemical transformations from **18**[9] (Scheme 7). Selective hydrolysis of the trans-fused isopropylidene group and benzylation afforded **19**. Hydrolysis of the cis-fused isopropylidene group giving **20**, a Suzuki-Miyaura coupling of the PBB group with 3,4-dimethoxyphenylboronic acid to **21** and benzylation of the remaining hydroxyl group gave the target compound **17**.



Reagents and conditions: (a) TFA, H_2O, CH_2Cl_2, 0 °C, 2.5 h; (b) BnBr, NaH, DMF, 74% 2 steps; (c) TFA, MeOH, CH_2Cl_2, 12 h, 85%; (d) K_3PO_4, Bu_4NBr, $Pd(OAc)_2$, 3,4-dimethoxyphenyl boronic acid, EtOH, 69%; (e) BnBr, NaH, DMF, 80%.

Scheme 7. Synthesis of DMPBn pseudo-disaccharide **17**.

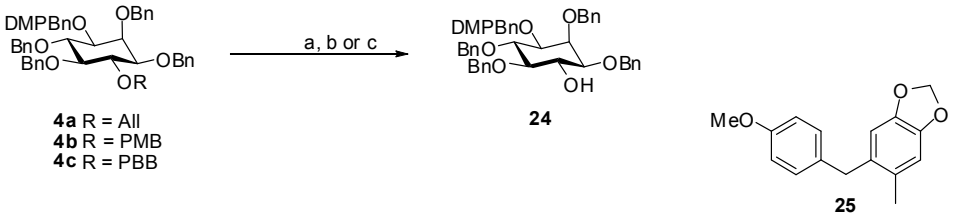
The reaction of pseudo-disaccharide **17** with 30% TFA and scavenger **11c** in CH_2Cl_2 cleanly gave the selectively deprotected product **22** in 79% yield (Scheme 8).



Reagents and conditions: (a) **11c** (5 eq.), 30% TFA/CH_2Cl_2, **22** 79%, **12c** quant.

Scheme 8. Deprotection of DMPBn pseudo-disaccharide **17** using 30% TFA for 1 h.

The compatibility of the DMPBn protecting group with allyl, PMB and PBB ethers was examined (Scheme 9). The allyl protecting group of **4a** was selectively removed by treatment with hydrogen activated iridium(I) catalyst **23** and subsequent treatment with methanolic HCl to give **24** in 63% yield. The PMB ether of **4b** was selectively hydrolysed upon treatment with 1% TFA in CH_2Cl_2 and scavenger **11c** providing inositol **24** in 77% yield and scavenged product **25** in quantitative yield. Deprotection of the PBB ether of **4c** was achieved using a palladium(0) catalysed amination with *N*-methylaniline followed by treatment with methanolic HCl which provided **24** in an unoptimized yield of 52%.



Reagents and conditions: (a) for **4a**, $(COD)(MePh_2P)_2Ir^+PF_6^-$ (**23**), H_2, THF then AcCl, $MeOH/CH_2Cl_2$ (63%); (b) for **4b**, 1% TFA in CH_2Cl_2, **11c**, 1 h (77%); (c) for **4c**, $MeNHC_5H_4N$, (*o*-biphenyl)P(*t*-Bu)$_2$, Pd_2dba_3, NaO*t*-Bu, tol (52%)

Scheme 9. Selective deprotections of **4a-c** in the presence of a DMPBn ether.

The ultimate test of this reagent system was for the removal of the DMPBn group on **2**. As reported in our earlier paper[9] this reaction cleanly afforded the pseudo-trisaccharide **3** in 74% yield.

CONCLUSION

In conclusion, we have developed an alternative method for the deprotection of DMPBn ethers, using anhydrous TFA in CH_2Cl_2, in the presence of either 3,4-dimethoxy- or 3,4 methylenedioxy-toluene as a cation scavenger. Allyl and benzyl ethers, esters, and glycosidic bonds were unaffected by this reagent system. Furthermore, we have demonstrated that allyl, PMB and PBB ethers can be selectively removed in the presence of the DMPBn group. This method, along with the use of either DDQ or a combination of DDQ and $Mn(OAc)_3$, increases the scope of the DMPBn protecting group in organic synthesis by providing an alternative to the acid-labile PMB protecting group.

EXPERIMENTAL SECTION

^1H NMR spectra were obtained at 400 or 500 MHz and referenced to the residual solvent peak (^1H $CHCl_3$ δ 7.26 ppm). ^{13}C NMR spectra were recorded at 125 MHz and referenced to

the internal solvent ($CDCl_3$, δ 77.0 ppm). Electro-spray ionization (ESI) mass spectra were recorded on a microTOF$_Q$ mass spectrometer. Anhydrous solvents were sourced either commercially or from a solvent purification system and used without further treatment unless stated. Powdered molecular sieves were flame dried under vacuum immediately prior to use. Flash column chromatography was carried out using 40–63 μm silica gel unless otherwise stated. All flash chromatography solvents were LR-grade. Petroleum ether with a bp range 60–80°C was used. All compounds were isolated after silica-gel column chromatography and fractions collected were one spot by TLC. Thin layer chromatography (TLC) plates were visualised under an UV lamp and/or with a spray consisting of 5% w/v dodecamolybdophosphoric acid in ethanol with subsequent heating.

(±)-3-*O*-(4-(3,4-Dimethoxyphenyl)benzyl)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol (6)

To a solution of diol **5**[13-15] (3.05 g, 11.7 mmol) in dry THF (150 mL) was added NaH (60% dispersion in oil, 0.558 g, 23.26 mmol) and 4-(3,4-dimethoxyphenyl)benzyl bromide[11] (1.79 g, 5.81 mmol) and refluxed overnight under an atmosphere of nitrogen. The reaction mixture was quenched with H_2O (5 mL) and extracted into EtOAc (3 × 100 mL), washed with H_2O (100 mL) and brine (100 mL). The organic extract was dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 2:3 to 1:1) to give the *title compound* **6** as a white solid (2.41 g, 85%). m.p. 143-146 °C (EtOAc/PE); ν_{max} (ATR-IR) 3519, 2985, 2934, 2888, 2832, 1603, 1590, 1525, 1464, 1465, 1399, 1371, 1242, 1215, 1168, 1140, 1120, 1073, 1046 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.36 (s, 3H), 1.47 (s, 3H), 1.50 (s, 3H), 1.55 (s, 3H), 2.55 (d, *J* = 2.6 Hz, 1H), 3.28 (dd, *J* = 9.4, 10.5 Hz, 1H), 3.83 (dd, *J* = 4.2, 10.1 Hz, 1H), 3.88-3.96 (m, 2H), 3.92 (s, 3H), 3.95 (s, 3H), 4.06 (t, *J* = 9.7 Hz, 1H), 4.35 (t, *J* = 4.5 Hz, 1H), 4.83 (d, *J* = 12.6 Hz, 1H), 4.93 (d, *J* = 12.5 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 7.10 (d, *J* = 2.1 Hz, 1H),

7.15 (dd, *J* = 2.1, 8.3 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.0, 27.02, 27.06, 28.3, 56.02, 56.06, 71.6, 74.4, 74.6, 76.7, 77.4, 78.4, 81.7, 110.3, 110.5, 111.6, 112.6, 119.4, 126.9, 128.9, 133.9, 136.4, 140.8, 148.8, 149.3; HRMS-ESI $[M+Na]^+$ Calcd for $C_{27}H_{34}NaO_8$: 509.2146. Found: 509.2163; Anal. Calcd for $C_{27}H_{34}O_8$: C, 66.65; H, 7.04. Found: C, 66.41; H, 7.22.

(±)-6-*O*-Allyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol (7a)

To a solution of alcohol **6** (1.400 g, 2.87 mmol) in anhydrous DMF (20 mL) was added NaH (60% dispersion in oil, 0.138 g, 5.75 mmol) and allyl bromide (0.50 mL, 5.75 mmol) at 0 °C and the reaction mixture was left to stir overnight. The reaction was quenched with H_2O and extracted into CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2) to give the *title compound* **7a** (1.38 g, 91%) as a white solid. m.p. 123-126 °C (EtOAc/PE); ν_{max} (ATR-IR) 2991, 2932, 2882, 2837, 1603, 1590, 1525, 1504, 1455, 1417, 1397, 1374, 1329, 1279, 1239, 1214, 1168, 1157, 1138, 1122, 1085, 1070, 1055 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, 3H), 1.46 (s, 3H), 1.49 (s, 3H), 1.55 (s, 3H), 3.30 (dd, *J* = 9.4, 10.6 Hz, 1H), 3.66 (dd, *J* = 6.5, 10.7 Hz, 1H), 3.78 (dd, *J* = 4.2, 10.1 Hz, 1H), 3.93 (s, 3H), 3.95 (s, 3H), 4.01-4.08 (m, 2H), 4.27 (dt, *J* = 1.4, 5.7 Hz, 2H), 4.34 (t, *J* = 4.6 Hz, 1H), 4.83 (d, *J* = 12.6 Hz, 1H), 4.93 (d, *J* = 12.7 Hz, 1H), 5.18 (dq, *J* = 10.4, 1.4 Hz, 1H), 5.31 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.94 (dddd, *J* = 5.7, 5.7, 10.4, 17.3 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 7.10 (d, *J* = 2.1 Hz, 1H), 7.15 (dd, *J* = 2.2, 8.2 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.0, 27.09, 27.13, 28.1, 56.02, 56.06, 71.3, 71.6, 74.4, 76.9, 77.2, 78.7, 80.1, 81.4, 110.0, 110.5, 111.6, 112.2, 117.4, 119.4, 126.9, 128.9, 133.9,

134.8, 136.5, 140.7, 148.8, 149.2; HRMS-ESI $[M+Na]^+$ Calcd for $C_{30}H_{38}NaO_8$: 549.2459. Found: 549.2491.

(±)-6-*O*-Allyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol (4a)

To a solution of allyl ether **7a** (0.708 g, 1.34 mmol) in CH_2Cl_2 (10 mL) was added MeOH (0.136 mL, 3.36 mmol) and TFA (0.518 mL, 6.72 mmol) and the reaction mixture was stirred at rt overnight. The solvent was evaporated under reduced pressure to afford (±)-6-*O*-allyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-*myo*-inositol (0.60 g) as a white foam which was used without further purification. HRMS-ESI $[M+Na]^+$ Calcd for $C_{24}H_{30}O_8Na$: 469.1833. Found: 469.1826. NaH (0.322 g, 60% dispersion in oil, 13.4 mmol) was added to a stirred solution of crude tetraol (0.60 g, 1.34 mmol) and BnBr (1.28 mL, 10.8 mmol) in dry DMF (10 mL) at 0 °C. The reaction was left to warm to rt and stirred overnight. Excess NaH was quenched with MeOH (2 mL) and the solvent was removed *in vacuo*. The residue was extracted into CH_2Cl_2 (3 × 50 mL) and the combined organic layers were washed with H_2O (3 × 25 mL), brine (25 mL) and dried ($MgSO_4$). The solution was filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:2) to give the *title compound* **4a** (0.492 g, 45%) as a white solid. m.p. 132-136 °C (EtOAc/PE); ν_{max} (ATR-IR) 3087, 3062, 3028, 2923, 2882, 1603, 1589, 1566, 1504, 1453, 1396, 1359, 1326, 1275, 1256, 1217, 1172, 1134, 1086, 1066, 1024 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.31 (dd, J = 2.2, 9.9 Hz, 1H), 3.37 (dd, J = 2.3, 9.8 Hz, 1H), 3.44 (t, J = 9.3 Hz, 1H), 3.93-3.98 (m, 1H), 3.94 (s, 3H), 3.96 (s, 3H), 4.04-4.08 (m, 2H), 4.33 (ddt, J = 1.1, 5.7, 12.3 Hz, 1H), 4.41 (ddt, J = 1.3, 5.9, 12.2 Hz, 1H), 4.60 (d, J = 11.8 Hz, 1H), 4.62-4.71 (m, 3H), 4.81-4.90 (m, 5H), 4.93 (d, J = 10.8 Hz, 1H), 5.15 (dq, J = 10.3, 1.4 Hz, 1H), 5.27 (dq, J = 17.2, 1.6 Hz, 1H), 5.98 (dddd, J = 5.8, 5.8, 10.4, 17.1 Hz, 1H), 6.95 (d, J = 8.3 Hz,

1H), 7.11 (d, *J* = 2.1 Hz, 1H), 7.16 (dd, *J* = 2.1, 8.3 Hz, 1H), 7.26-7.38 (m, 20H), 7.40-7.42 (m, 2H), 7.49-7.52 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.04, 56.08, 72.5, 72.9, 74.2, 74.6, 74.7, 75.9, 76.0, 80.90, 80.94, 81.5, 81.7, 83.8, 110.5, 111.6, 116.7, 119.4, 126.9, 127.0, 127.4, 127.54, 127.55, 127.58, 127.62, 127.8, 128.0, 128.10, 128.12, 128.2, 128.37, 128.39, 128.4, 128.6, 134.0, 135.5, 137.1, 138.6, 138.9, 139.0, 139.1, 140.42, 148.7, 149.3; HRMS-ESI $[M+Na]^+$ Calcd for $C_{52}H_{54}NaO_8$: 829.3711. Found: 829.3680.

(±)-6-*O*-*para*-Methoxybenzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol (7b)

To a solution of alcohol **6** (134 mg, 0.275 mmol) and 4-methoxybenzyl chloride (110 μL, 0.811 mmol) in anhydrous THF (5 mL) was added NaH (60% dispersion in oil, 33 mg, 0.826 mmol) and the mixture refluxed for 1 h, then stirred at rt overnight. The reaction was quenched with water (30 mL), and the product extracted into CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 3:7) to give the *title compound* **7b** (144 mg, 86%) as a white solid. m.p. 122-124 (EtOAc/PE); ν_{max} (ATR-IR) 2982, 2931, 2904, 2836, 1611, 1588, 1566, 1504, 1455, 1399, 1372, 1327, 1302, 1242, 1216, 1170, 1142, 1082, 1055, 1023; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (s, 3H), 1.41 (s, 3H), 1.47 (s, 3H), 1.51 (s, 3H), 3.34 (dd, *J* = 9.5, 10.4 Hz, 1H), 3.67 (dd, *J* = 6.5, 10.6 Hz, 1H), 3.79 (s, 3H), 3.77-3.81 (m, 1H), 3.92 (s, 3H), 3.95 (s, 3H), 4.03 (t, *J* = 9.8 Hz, 1H), 4.05 (dd, *J* = 5.1, 6.4 Hz, 1H), 4.33 (t, *J* = 4.6 H, 1H), 4.74 (app. s, 2H), 4.85 (d, *J* = 12.6 Hz, 1H), 4.92 (d, *J* = 12.6 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.3 Hz, 1H), 7.10 (d, *J* = 2.0 Hz, 1H), 7.14 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.9, 27.0, 27.1, 27.9, 55.2, 55.92, 55.96, 71.5, 71.6, 74.3, 76.7, 77.2, 78.8, 79.5,

81.12, 109.9, 110.4, 111.5, 112.1, 113.6, 119.3, 126.8, 128.8, 129.6, 130.3, 133.8, 138.5, 140.6, 148.7, 149.2, 159.1; HRMS-ESI $[M+Na]^+$ Calcd for $C_{35}H_{42}O_9Na$: 629.2721. Found: 629.2730.

(±)-6-*O*-*para*-Methoxybenzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol (4b)

Methanol (40 μL, 0.988 mmol) and TFA (26 μL, 0.337 mmol) were added to a solution of the para-methoxybenzyl ether **7b** (148 mg, 0.244 mmol) in CH_2Cl_2 (8 mL) and the mixture was stirred at rt for 7 days. The solvent was removed *in vacuo*, and the residue dissolved in CH_2Cl_2 (30 mL), and washed with water (30 mL), $NaHCO_3$ (30 mL), brine (30 mL), dried ($MgSO_4$), filtered, and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (MeOH/$CHCl_3$ = 1:9) to give (±)-6-*O*-para-methoxybenzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-*myo*-inositol (53 mg) as a slightly impure white solid. HRMS-ESI $[M+Na]^+$ Calcd for $C_{29}H_{34}O_8Na$: 549.2095. Found: 549.2114. Anhydrous DMF (5 mL) and BnBr (230 μL, 1.95 mmol) were added and the mixture cooled to 0 °C under argon. NaH (98 mg, 2.44 mmol, 60% dispersion in oil) was added with stirring and the reaction was warmed to rt overnight. Excess NaH was quenched by the addition of H_2O (30 mL) and the mixture extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with $NaHCO_3$ (30 mL), brine (30 mL), dried ($MgSO_4$), filtered, and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 3:7) to give the *title compound* **4b** (51 mg, 24%) as a white solid. m.p. 129-133 °C (EtOAc/PE); ν_{max} (ATR-IR) 3025, 2932, 1730, 1611, 1588, 1503, 1454, 1400, 1360, 1327, 1302, 1247, 1217, 1171, 1141, 1071, 1027; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.28-3.33 (m, 2H), 3.41 (t, J = 9.3 Hz, 1H), 3.71 (s, 3H), 3.87 (s, 3H), 3.89 (s, 3H),

3.99-4.05 (m, 3H), 4.54-4.63 (m, 4H), 4.70 (d, J = 10.3 Hz, 1H), 4.76-4.88 (m, 7H), 6.73 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.3 Hz, 1H), 7.04 (d, J = 2.0 Hz, 1H), 7.08 (d, J = 2.1 Hz, 1H), 7.10 (d, J = 1.7 Hz, 1H), 7.13 (d, J = 8.5 Hz, 2H), 7.19-7.38 (m, 21H), 7.44 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.2, 55.95, 55.99, 72.4, 72.8, 74.1, 74.4, 75.5, 75.9, 80.9, 81.0, 81.7, 83.7, 110.4, 110.5, 113.7, 119.3, 126.8, 127.4, 127.5, 127.7, 127.8, 128.01, 128.07, 128.14, 128.29, 128.31, 128.35, 129.7, 131.0, 133.9, 137.0, 138.4, 138.85, 138.9, 140.0, 140.4, 148.7, 149.2, 150.1; HRMS-ESI $[M+Na]^+$ Calcd for $C_{57}H_{58}O_9Na$: 909.3973. Found: 909.3943.

(±)-6-*O*-*para*-Bromobenzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol (7c)

NaH (60% dispersion in oil, 49 mg, 1.23 mmol) was added to a stirred solution of inositol **6** (155 mg, 0.319 mmol) and 4-bromobenzyl bromide (159 mg, 0.637 mmol) in anhydrous THF (5 mL) under argon. The reaction mixture was allowed to warm to rt, then heated at reflux for 30 min. The reaction was quenched with water (30 mL), and the product extracted into CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 3:7) to give the *title compound* **7c** (186 mg, 89%) as a white solid. m.p. 140-143 °C (EtOAc/PE); ν_{max} (ATR-IR) 2987, 2933, 1590, 1566, 1527, 1503, 1488, 1454, 1399, 1372, 1327, 1302, 1421, 1216, 1169, 1141, 1083, 1056, 1025, 1011; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (s, 3H), 1.42 (s, 3H), 1.47 (s, 3H), 1.49 (s, 3H), 3.34 (dd, J = 10.5, 9.5 Hz, 1H), 3.64 (dd, J = 10.6, 6.5 Hz, 1H), 3.79 (dd, J = 10.2, 4.2 Hz, 1H), 3.93 (s, 3H), 3.95 (s, 3H), 4.01-4.07 (m, 2H), 4.34 (dd, J = 4.8, 4.3 Hz, 1H), 4.76 (app. s, 2H), 4.83 (d, J = 12.6 Hz, 1H), 4.92 (d, J = 12.6 Hz, 1H), 6.95 (d, J = 8.3 Hz, 1H),

7.10 (d, *J* = 2.1 Hz, 1H), 7.15 (dd, *J* = 9.0, 2.9 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.9, 27.0, 27.1, 28.0, 55.95, 55.99, 71.2, 71.5, 74.2, 76.8, 77.2, 78.7, 80.2, 81.1, 110.0, 110.4, 111.5, 112.2, 119.4, 121.3, 126.8, 128.8, 129.5, 131.3, 133.8, 136.4, 137.3, 140.7, 148.7, 149.2; HRMS-ESI $[M+Na]^+$ Calcd for $C_{34}H_{39}{}^{81}BrO_8Na$: 679.1670. Found: 679.1702.

(±)-6-*O*-*para*-Bromobenzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol (4c)

MeOH (24 μL, 0.60 mmol) and TFA (56 μL, 0.73 mmol) were added to a solution of inositol **7c** (157 mg, 0.239 mmol) in CH_2Cl_2 (4 mL) and the reaction mixture was stirred at rt overnight. The solvent was removed *in vacuo* to give (±)-6-*O*-para-bromobenzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-myo-inositol as a white solid which was used without further purification. HRMS-ESI $[M+Na]^+$ Calcd for $C_{28}H_{31}{}^{79}BrO_8Na$: 597.1095. Found: 597.1093. Anhydrous DMF (5 mL) and BnBr (230 μL, 1.93 mmol) were added and the solution cooled to 0 °C under argon. NaH (60% dispersion in oil, 96 mg, 2.40 mmol) was added and the reaction was left to warm to rt overnight with stirring. Excess NaH was quenched by the addition of water (50 mL). The reaction mixture was extracted into CH_2Cl_2 (3 × 30 mL) and the combined organic layers were washed with brine (50 mL), dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 3:7) to give the *title compound* **4c** (166 mg, 74%) as a white solid. m.p. 154-157 °C (EtOAc/PE); ν_{max} (ATR-IR) 3029, 2918, 1590, 1529, 1505, 1453, 1395, 1359, 1328, 1275, 1256, 1217, 1172, 1134, 1088, 1067, 1036, 1024; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.38 (dd, *J* = 9.9, 2.2 Hz, 1H), 3.41 (dd, *J* = 9.8, 2.2 Hz, 1H), 3.49 (t, *J* = 9.3 Hz, 1H), 3.95 (s, 3H), 3.97 (s, 3H), 4.06-4.14 (m, 3H), 4.62 (app. s, 2H), 4.67 (d, *J* = 11.8 Hz,

1H), 4.71 (d, J = 11.8 Hz, 1H), 4.77 (d, J = 11.2 Hz, 1H), 4.83-4.94 (m, 6H), 4.97 (d, J = 10.7 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.13-7.15 (m, 3H), 7.18 (dd, J = 8.3, 2.1 Hz, 1H), 7.27-7.45 (m, 24H), 7.53 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.9, 56.0, 72.5, 72.7, 74.16, 74.22, 74.8, 75.83, 75.84, 80.85, 80.88, 81.5, 81.7, 83.6, 110.4, 111.5, 119.3, 121.3, 126.8, 127.4, 127.5, 127.6, 127.7, 128.0, 128.2, 128.29, 128.32, 128.36, 129.6, 131.3, 133.8, 136.9, 137.9, 138.2, 138.7, 138.78, 138.89, , 140.9, 148.7, 149.2; HRMS-ESI $[M+Na]^+$ Calcd for $C_{56}H_{55}{}^{81}BrO_8Na$: 959.2924. Found: 959.2957.

(±)-6-*O*-Allyl-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol (8a)

Method 1: DDQ (0.042 g, 0.186 mmol) was added to a solution of **4a** (0.05 g, 0.062 mmol) in CH_2Cl_2/H_2O (10:1, 1.1 mL) at rt. After 3 h the reaction mixture was diluted with CH_2Cl_2 (40 mL) and washed with a freshly prepared aqueous solution of sodium ascorbate (1 mol L^{-1}, 20 mL) to remove excess DDQ. The aqueous solution was re-extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic fractions were washed with $NaHCO_3$ (30 mL), brine (30 mL) and dried ($MgSO_4$). The solution was filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2 to 1:1) to give the *title compound* **8a** (4 mg, 11%) as a colourless oil.

Method 2: To a solution of **4a** (0.030 g, 0.037 mmol) and scavenger **11c** (0.025 g, 0.186 mmol) in CH_2Cl_2 (3.5 mL) was added TFA (1.5 mL) and the reaction was stirred at rt for 1 h. The reaction was diluted with H_2O (40 mL) and extracted into CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with $NaHCO_3$ (20 mL), H_2O (20 mL), brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4) to give 6-(4-(3,4-

dimethoxyphenyl)benzyl)-3,4-(methylenedioxy)toluene (**12c**) (0.016 g, quant, R_f = 0.60, EtOAc/petroleum ether 1:2) and the *title compound* **8a** (0.019 g, 87%, R_f = 0.55, EtOAc/petroleum ether 1:2) both as colourless oils. Data for **8a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.19 (brs, 1H), 3.38-3.46 (m, 2H), 3.48 (dd, *J* = 2.1, 9.7 Hz, 1H), 3.77 (t, *J* = 9.4 Hz, 1H), 3.92 (t, *J* = 9.5 Hz, 1H), 4.01 (t, *J* = 2.4 Hz, 1H), 4.34 (ddt, *J* = 1.3, 5.7, 12.1 Hz, 1H), 4.43 (ddt, *J* = 1.3, 5.8, 12.2 Hz, 1H), 4.66-4.78 (m, 4H), 4.82 (d, *J* = 10.6 Hz, 1H), 4.89 (d, *J* = 11.2 Hz, 1H), 4.92 (d, *J* = 10.7 Hz, 1H), 4.97 (d, *J* = 11.5 Hz, 1H), 5.16 (dq, *J* = 10.5, 1.2 Hz, 1H), 5.29 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.99 (dddd, *J* = 5.7, 5.7, 10.5, 16.2 Hz, 1H), 7.28-7.38 (m, 20H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 72.4, 73.1, 74.7, 74.8, 75.6, 75.9, 77.3, 81.0, 81.7, 82.2, 83.6, 116.7, 127.61, 127.63, 127.69, 127.7, 127.8, 128.07, 128.1, 128.4, 128.45, 128.47, 128.5, 135.4, 138.4, 138.68, 138.69, 138.8; HRMS-ESI $[M+Na]^+$ Calcd for $C_{37}H_{40}NaO_6$: 603.2723. Found: 603.2724.

Data for **12c**: ν_{max} (ATR-IR) 2997, 2920, 2850, 1601, 1588, 1530, 1500, 1485, 1467, 1399, 1353, 1312, 1274, 1252, 1217, 1195, 1170, 1148, 1122 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 3H), 3.92 (s, 5H), 3.94 (s, 3H), 5.90 (s, 2H), 6.64 (s, 1H), 6.68 (s, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 7.09 (d, *J* = 2.0 Hz, 1H), 7.12 (dd, *J* = 2.1, 8.3 Hz, 1H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.7, 38.8, 55.98, 56.03, 100.7, 110.3, 110.4, 110.5, 111.5, 119.3, 126.9, 129.0, 129.5, 131.8, 134.1, 138.8, 139.3, 145.7, 145.9, 148.5, 149.2; HRMS-ESI $[M+Na]^+$ Calcd for $C_{23}H_{22}NaO_4$: 385.1416. Found: 385.1414.

(±)-6-*O*-*para*-Bromobenzyl-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol (8c)

TFA (1.5 mL) was added to a solution of **4c** (30 mg, 0.032 mmol) and **11c** (43 mg, 0.316 mmol) in CH_2Cl_2 (3.5 mL) and the mixture was stirred at rt for 1 hour. The solvent was removed *in vacuo* and the residue was redissolved in CH_2Cl_2 (30 mL), washed with water (30

mL), $NaHCO_3$ (30 mL), and brine (30 mL), dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:3) to give **12c** (10 mg, 86%, R_f = 0.60, EtOAc/petroleum ether 1:2) and the *title compound* **8c** (17 mg, 75%, R_f = 0.55 EtOAc/petroleum ether 1:2) both as colourless oils. Data for **8c**: ν_{max} (ATR-IR) 3553, 2918, 2868, 1496, 1488, 1454, 1392, 1360, 1307, 1208, 1129, 1069, 1027, 1012; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.20 (d, *J* = 6.3 Hz, 1H), 3.43-3.51 (m, 3H), 3.80 (t, *J* = 9.5 Hz, 1H), 4.02 (t, *J* = 9.6 Hz, 1H), 4.04 (t, *J* = 2.6 Hz, 1H), 4.64 (d, *J* = 11.7 Hz, 1H), 4.68 (d, *J* = 11.7 Hz, 1H), 4.72 (d, *J* = 11.5 Hz, 1H), 4.76 (d, *J* = 11.1 Hz, 1H), 4.76 (d, *J* = 11.1 Hz, 1H), 4.85 (app. s, 2H), 4.86 (d, *J* = 11.4 Hz, 1H), 4.88 (d, *J* = 11.1 Hz, 1H), 4.97 (d, *J* = 11.5 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.26-7.36 (m, 23H), 7.38 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 72.4, 72.9, 74.8, 74.9, 75.5, 75.7, 81.0, 81.7, 82.1, 83.5, 121.4, 121.57, 127.61, 127.64, 127.68, 127.76, 127.77, 127.81, 128.1, 128.35, 128.4, 128.45, 128.5, 129.6, 131.4, 137.7, 138.1, 138.51, 138.53, 138.6; HRMS-ESI $[M+Na]^+$ Calcd for $C_{41}H_{41}{}^{79}BrO_6Na$: 731.1979. Found: 731.1928.

1-*O*-Allyl-4,5-di-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-palmitoyl-α-D-mannopyranosyl)-D-*myo*-inositol (3)[9] and 1-*O*-Allyl-4,5-di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxy-(6-(4-(3,4-dimethoxyphenyl)benzyl))-phenyl)benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-palmitoyl-α-D-mannopyranosyl)-D-*myo*-inositol (9)

To a solution of **2**[9] (0.085 g, 0.047 mmol) in CH_2Cl_2 (2.4 mL) was added TFA (0.6 mL) and the reaction was stirred at rt for 1 h. The reaction was diluted with H_2O (50 mL) and extracted into CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with $NaHCO_3$ (20 mL), H_2O (20 mL), brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum

ether = 1:9 to 1:2) to give the title compound **3**[9] (0.043 g, 58%, R_f = 0.52, EtOAc/petroleum ether 1:2) and the *title compound* **9** (0.009 g, 10%, R_f = 0.37, EtOAc/petroleum ether 1:2) both as colourless oils. Data for **9**: $[\alpha]_D^{30}$ +25.4 (*c* = 0.95, $CHCl_3$); ν_{max} (ATR-IR) 3063, 3029, 2922, 2852, 1732, 1604, 1587, 1524, 1453, 1358, 1248, 1210, 1071, 1090, 1026 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.9 Hz, 3H), 1.17-1.27 (m, 24H), 1.51-1.59 (m, 2H), 2.22 (t, *J* = 7.6 Hz, 2H), 3.19 (dd, *J* = 1.5, 9.7 Hz, 1H), 3.24-3.29 (m, 2H), 3.33 (dd, *J* = 2.3, 10.0 Hz, 1H), 3.38 (dd, *J* = 2.7, 11.1 Hz, 1H), 3.78-4.05 (m, 13H), 3.84 (s, 3H), 3.88 (s, 3H), 3.898 (s, 3H), 3.905 (s, 3H), 4.15-4.23 (m, 3H), 4.33-4.34 (m, 1H), 4.45-4.93 (m, 20H), 5.09 (dd, *J* = 10.4, 1.1 Hz, 1H), 5.21 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.21 (d, *J* = 0.9 Hz, 1H), 5.53 (d, *J* = 1.3 Hz, 1H), 5.72 (dddd, *J* = 5.5, 5.5, 10.7, 17.1 Hz, 1H), 6.73 (s, 1H), 6.84 (s, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 7.04-7.42 (m, 55H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 22.8, 24.9, 29.3, 29.35, 29.43, 29.6, 29.7, 29.73, 29.74, 29.8, 32.0, 34.2, 38.2, 55.98, 56.04, 56.07, 56.09, 62.9, 68.6, 70.2, 71.2, 71.3, 71.5, 71.97, 72.01, 72.3, 72.5, 73.3, 74.0, 74.5, 74.8, 75.0, 75.3, 75.7, 75.8, 75.9, 76.1, 78.76, 78.84, 80.3, 81.4, 81.5, 81.8, 98.75, 98.83, 110.4, 111.5, 113.3, 113.4, 117.9, 119.2, 126.8, 127.0, 127.30, 127.32, 127.4, 127.48, 127.5, 127.51, 127.56, 127.6, 127.63, 127.72, 127.76, 127.77, 127.9, 128.0, 128.09, 128.14, 128.17, 128.22, 128.25, 128.26, 128.31, 128.34, 128.37, 128.41, 128.6, 129.1, 129.6, 130.1, 133.9, 134.1, 134.4, 136.3, 138.0, 138.2, 138.3, 138.4, 138.5, 138.6, 138.76, 138.82, 139.1, 140.6, 141.0, 147.3, 148.4, 148.5, 149.2, 173.6; HRMS-ESI $[M+Na]^+$ Calcd for $C_{130}H_{148}NaO_{21}$: 2068.0405. Found: 2068.0367.

Reaction of 4-(3,4-dimethoxyphenyl)benzyl alcohol (10) with 1,4-dimethoxybenzene (11a)

To a solution of alcohol **10**[11] (0.050 g, 0.205 mmol) and 1,4-dimethoxybenzene (**11a**) (0.141 g, 1.023 mmol) in CH_2Cl_2 (3.5 mL) was added TFA (1.5 mL) and the reaction was stirred at

rt for 1 h. The reaction was diluted with H_2O (40 mL) and extracted into CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with $NaHCO_3$ (20 mL), H_2O (20 mL), brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:2) to give 3-(4-(3,4-dimethoxyphenyl)benzyl)-1,4-dimethoxybenzene (**12a**) (0.015 g, 21%, R_f = 0.76, EtOAc/petroleum ether 1:1), 3-(4-(3,4-dimethoxy-(6-(4-(3,4-dimethoxyphenyl)benzyl))-phenyl)benzyl)-1,4-dimethoxybenzene (**13a**) (0.016 g, 13%, R_f = 0.63, EtOAc/petroleum ether 1:1) and 3-(4-(3,4-dimethoxy-(6-(4-(3,4-dimethoxy-(6-(4-(3,4-dimethoxyphenyl)benzyl))-phenyl)benzyl))-phenyl)benzyl)-1,4-dimethoxybenzene (**14a**) (0.005 g, 3%, R_f = 0.34, EtOAc/petroleum ether 1:1) all as colourless oils. Data for **12a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74 (s, 3H), 3.80 (s, 3H), 3.92 (s, 3H), 3.94 (s, 3H), 3.98 (s, 2H), 6.70 (d, *J* = 3.0 Hz, 1H), 6.73 (dd, *J* = 3.1, 8.7 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 1H), 6.93 (d, *J* = 8.3 Hz, 1H), 7.09 (d, *J* = 2.1 Hz, 1H), 7.12 (dd, *J* = 2.1, 8.3 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.7, 55.7, 55.97, 56.0, 56.1, 110.5, 111.3, 111.48, 111.52, 117.0, 119.3, 126.8, 129.4, 130.9, 134.3, 138.7, 139.5, 148.5, 149.1, 151.7, 153.6; HRMS-ESI $[M+H]^+$ Calcd for $C_{23}H_{25}O_4$: 365.1753. Found: 365.1756.

Data for **13a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (s, 3H), 3.79 (s, 3H), 3.84 (s, 3H), 3.87 (s, 3H), 3.92 (s, 3H), 3.94 (s, 3H), 3.95 (s, 2H), 3.98 (s, 2H), 6.70-6.74 (m, 3H), 6.79-6.83 (m, 2H), 6.93 (d, *J* = 8.3 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 1.8 Hz, 1H), 7.11 (dd, *J* = 1.8, 8.2 Hz, 1H), 7.18-7.23 (m, 4H), 7.41 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.7, 38.2, 55.7, 55.99, 56.0, 56.05, 56.07, 56.13, 110.4, 111.2, 111.49, 111.54, 113.3, 113.4, 117.1, 119.2, 126.7, 128.7, 129.1, 129.4, 130.2, 131.0, 134.1, 134.7, 138.5, 139.1, 139.4, 140.7, 147.2, 148.2, 148.5, 149.2, 151.8, 153.6; HRMS-ESI $[M+Na]^+$ Calcd for $C_{38}H_{38}NaO_6$: 613.2566. Found: 613.2565.

Data for **14a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70 (s, 3H), 3.77 (s, 3H), 3.82 (s, 3H), 3.83 (s, 3H), 3.86 (s, 3H), 3.87 (s, 3H), 3.91-3.98 (m, 12H), 6.68-7.47 (m, 22H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.7, 38.2, 38.4, 55.7, 55.99, 56.01, 56.02, 56.06, 56.07, 56.1, 56.11, 110.36, 110.4, 111.1, 111.5, 111.6, 113.3, 113.33, 113.38, 113.4, 117.1, 119.2, 126.7, 126.8, 128.5, 128.6, 128.7, 129.0, 129.1, 129.2, 129.38, 129.43, 129.45, 130.1, 130.2, 131.0, 134.1, 134.6, 134.8, 138.5, 139.0, 139.1, 139.4, 140.6, 140.7, 147.2, 148.17, 148.24, 148.25, 148.5, 149.2, 151.7, 153.6; HRMS-ESI $[M+Na]^+$ Calcd for $C_{53}H_{52}NaO_8$: 839.3560. Found: 839.3563.

Reaction of 4-(3,4-dimethoxyphenyl)benzyl alcohol (10) with 3,4-dimethoxytoluene (11b)

To a solution of alcohol **10**[11] (0.020 g, 0.082 mmol) and 3,4-dimethoxytoluene (**11b**)[17] (0.062 g, 0.409 mmol) in CH_2Cl_2 (3.5 mL) was added TFA (1.5 mL) and the reaction was stirred at rt for 1 h. The reaction was diluted with H_2O (40 mL) and extracted into CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ (20 mL), H_2O (20 mL), brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:2) to give 6-(4-(3,4-dimethoxyphenyl)benzyl)-3,4-dimethoxytoluene (**12b**) (0.026 g, 85%, R_f = 0.59, EtOAc/petroleum ether 1:1) and 6-(4-(3,4-dimethoxy-(6-(4-(3,4-dimethoxyphenyl)benzyl))-phenyl)benzyl)-3,4-dimethoxytoluene (**13b**) (0.004 g, 8%, R_f = 0.43, EtOAc/petroleum ether 1:1) both as colourless oils. Data for **12b**: ν_{max} (ATR-IR) 3017, 3000, 2920, 2851, 1605, 1588, 1562, 1517, 1503, 1451, 1397, 1332, 1319, 1301, 1270, 1250, 1219, 1198, 1170, 1144, 1095, 1070, 1050 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.22 (s, 3H), 3.83 (s, 3H), 3.88 (s, 3H), 3.92 (s, 3H), 3.94 (s, 3H), 3.96 (s, 2H), 6.70 (s, 1H), 6.72 (s, 1H), 6.93 (d, J = 8.3 Hz, 1H), 7.09 (d, J = 2.0 Hz, 1H), 7.13 (dd, J = 2.1, 8.2 Hz, 1H), 7.17 (d, J = 8.1 Hz, 2H), 7.47 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.3, 38.7, 55.97,

55.99, 56.03, 56.1, 110.4, 111.5, 113.8, 119.2, 126.9, 128.6, 128.9, 130.6, 134.1, 138.7, 139.5, 147.0, 147.4, 148.5, 149.2; HRMS-ESI $[M+Na]^+$ Calcd for $C_{24}H_{26}NaO_4$: 401.1729. Found: 401.1738.

Data for **13b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.22 (s, 3H), 3.81 (s, 3H), 3.83 (s, 3H), 3.86 (s, 3H), 3.87 (s, 3H), 3.91 (s, 3H), 3.93 (s, 5H), 3.96 (s, 2H), 6.69 (s, 1H), 6.71 (s, 1H), 6.73 (s, 1H), 6.79 (s, 1H), 6.93 (d, J = 8.3 Hz, 1H), 7.04 (d, J = 8.2 Hz, 2H), 7.07 (d, J = 2.0 Hz, 1H), 7.09-7.12 (m, 3H), 7.20 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.3, 38.2, 38.8, 56.0, 56.01, 56.02, 56.06, 56.08, 56.14, 110.4, 111.6, 113.3, 113.34, 113.8, 113.9, 119.2, 126.7, 128.3, 128.7, 129.0, 129.5, 130.1, 130.7, 134.1, 134.6, 138.6, 139.2, 139.4, 140.7, 147.0, 147.2, 147.4, 148.3, 148.5, 149.2; HRMS-ESI $[M+Na]^+$ Calcd for $C_{39}H_{40}NaO_6$: 627.2723. Found: 627.2726.

6-(4-(3,4-Dimethoxyphenyl)benzyl)-3,4-(methylenedioxy)toluene (12c)

To a solution of alcohol **10**[11] (0.020 g, 0.082 mmol) and 3,4-(methylenedioxy)toluene (**11c**)[17] (0.056 g, 0.409 mmol) in CH_2Cl_2 (3.5 mL) was added TFA (1.5 mL) and the reaction was stirred at rt for 1 h. The reaction was diluted with H_2O (40 mL) and extracted into CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with $NaHCO_3$ (20 mL), H_2O (20 mL), brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:2) to give the *title compound* **12c** (0.028 g, 93%) as a colourless oil.

2,3,4-Tri-*O*-benzyl-6-α-D-glucopyranoside (16)[18]

To a solution of methyl 2,3,4-tri-*O*-benzyl-6-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-α-D-glucopyranoside (**15**)[11] (0.040 g, 0.058 mmol) and 3,4-(methylenedioxy)toluene (**11c**)[17] (0.039 g, 0.290 mmol) in CH_2Cl_2 (3.5 mL) was added TFA (1.5 mL) and the reaction was

stirred at rt for 1 h. The reaction was diluted with H_2O (50 mL) and extracted into CH_2Cl_2 (3 × 25 mL). The combined organic layers were washed with $NaHCO_3$ (20 mL), brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:2) to give 6-(4-(3,4-dimethoxyphenyl)benzyl)-3,4-(methylenedioxy)toluene (**12c**) (0.021 g, quant, R_f = 0.60, EtOAc/petroleum ether 1:2) and the title compound **16** (0.023 g, 86%, R_f = 0.32, EtOAc/petroleum ether 1:2) both as colourless oils. Data for **16**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.57-1.63 (m, 1H), 3.37 (s, 3H), 3.48-3.45 (m, 2H), 3.63-3.72 (m, 2H), 3.74-3.79 (m, 1H), 4.01 (t, *J* = 8.9 Hz, 1H), 4.57 (d, *J* = 3.5 Hz, 1H), 4.62-4.68 (m, 2H), 4.80 (d, *J* = 12.0 Hz, 1H), 4.84 (d, *J* = 10.9 Hz, 1H), 4.88 (d, *J* = 11.1 Hz, 1H), 4.99 (d, *J* = 10.9 Hz, 1H), 7.27-7.38 (m, 15H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 62.0, 70.7, 73.5, 75.1, 75.8, 77.5, 80.0, 82.0, 98.3, 127.7, 127.9, 128.00, 128.02, 128.1, 128.2, 128.46, 128.53, 128.54, 138.17, 138.19, 138.8; HRMS-ESI $[M+Na]^+$ Calcd for $C_{28}H_{32}NaO_6$: 487.2091. Found: 487.2117.

3-*O*-(4-Bromobenzyl)-4,5-di-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-1,2-di-*O*-isopropylidene-L-*myo*-inositol (19)

To a solution of **18**[9] (2.06 g, 2.44 mmol) in CH_2Cl_2 (25 mL) was added H_2O (44 μL, 2.44 mmol) and TFA (0.376 mL, 4.88 mmol) at 0 °C. The solution was stirred for 2.5 h, then diluted with CH_2Cl_2 (100 mL) and washed with saturated $NaHCO_3$ (50 mL) and saturated NaCl (50 mL). The organic phase was dried ($MgSO_4$), filtered and the solvent was evaporated under reduced pressure to give 3-*O*-(4-bromobenzyl)-6-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-1,2-di-*O*-isopropylidene-L-*myo*-inositol (1.97 g) as a white foam. To a solution of crude triol (1.97 g, 2.40 mmol) in dry DMF (20 mL) was added NaH (60% dispersion in oil, (0.517 g, 21.6 mmol) and benzyl bromide (1.71 mL, 14.4 mmol) at 0 °C and the reaction mixture was stirred overnight. The reaction was quenched by careful addition of

H_2O (5 mL) and then extracted into EtOAc (3 × 100 mL). The combined organic layers were washed with H_2O (100 mL) and saturated NaCl (100 mL), then dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:2) to give the *title compound* **19** (1.88 g, 72%) as a colourless oil. $[\alpha]_D^{26}$ +24.2 (*c* = 1.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.29 (s, 3H), 1.52 (s, 3H), 3.31 (t, *J* = 8.6 Hz, 1H), 3.61-3.64 (m, 2H), 3.67 (dd, *J* = 1.9, 10.8 Hz, 1H), 3.85-3.98 (m, 5H), 4.03 (dt, *J* = 2.5, 10.0 Hz, 1H), 4.17 (t, *J* = 9.8 Hz, 1H), 4.26 (t, *J* = 4.5 Hz, 1H), 4.29 (d, *J* = 12.4 Hz, 1H), 4.32 (d, *J* = 12.4 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.54 (d, *J* = 10.8 Hz, 1H), 4.57 (d, *J* = 11.8 Hz, 1H), 4.58 (d, *J* = 11.8 Hz, 1H), 4.64 (d, *J* = 11.8 Hz, 1H), 4.69-4.75 (m, 4H), 4.78 (d, *J* = 10.8 Hz, 1H), 4.85 (d, *J* = 11.7 Hz, 1H), 4.86 (d, *J* = 10.7 Hz, 1H), 5.31 (d, *J* = 1.8 Hz, 1H), 7.14-7.36 (m, 32H), 7.41-7.45 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.8, 27.9, 68.9, 72.0, 72.1, 72.2, 72.4, 73.5, 74.1, 74.6, 74.9, 75.2, 75.3, 75.7, 77.2, 77.5, 78.9, 80.2, 81.0, 82.6, 98.7, 109.8, 121.8, 127.0, 127.1, 127.3, 127.4, 127.5, 127.57, 127.61, 127.82, 127.83, 128.07, 128.19, 128.26, 128.32, 128.44, 128.45, 129.6, 131.6, 137.2, 138.2, 138.4, 138.66, 138.68, 138.8, 138.9; HRMS-ESI $[M+Na]^+$ Calcd for $C_{64}H_{67}{}^{79}BrNaO_{11}$: 1113.3759. Found: 1113.3718.

3-*O*-(4-Bromobenzyl)-4,5-di-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-L-*myo*-inositol (20)

To a solution of **19** (1.48 g, 1.36 mmol) in CH_2Cl_2 (50 mL) was added MeOH (0.084 mL, 2.03 mmol) and TFA (0.522 mL, 6.78 mmol) and the reaction mixture was stirred at rt overnight. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with saturated $NaHCO_3$ (50 mL) and saturated NaCl (50 mL). The organic phase was dried ($MgSO_4$), filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:2 to 1:1) to give the *title*

compound **20** (1.21 g, 85%) as a white foam. $[\alpha]_D^{26}$ +13.3 (c = 1.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.53 (brs, 1H), 3.31 (t, J = 9.4 Hz, 1H), 3.36-3.41 (m, 2H), 3.63 (dd, J = 7.2, 10.2 Hz, 1H), 3.73 (dd, J = 1.9, 10.3 Hz, 1H), 3.77 (t, J = 2.3 Hz, 1H), 3.82-3.91 (m, 3H), 4.00 (t, J = 9.5 Hz, 1H), 4.06-4.11 (m, 1H), 4.14-4.16 (m, 1H), 4.26 (d, J = 3.7 Hz, 1H), 4.43-4.51 (m, 5H), 4.53-4.60 (m, 3H), 4.63 (d, J = 12.1 Hz, 1H), 4.68 (d, J = 12.2 Hz, 1H), 4.77 (d, J = 10.7 Hz, 1H), 4.82 (d, J = 11.3 Hz, 1H), 4.84 (d, J = 10.8 Hz, 1H), 4.85 (d, J = 10.9 Hz, 1H), 5.10 (d, J = 2.1 Hz, 1H), 7.16-7.35 (m, 32H), 7.41-7.44 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 69.4, 69.9, 71.1, 71.8, 72.0, 72.65, 72.71, 73.5, 75.04, 75.08, 75.70, 75.73, 75.9, 79.51, 79.54, 80.8, 82.3, 85.4, 100.5, 121.7, 127.0, 127.55, 127.56, 127.59, 127.65, 127.66, 127.69, 127.77, 127.84, 128.0, 128.02, 128.3, 128.38, 128.41, 128.42, 128.5, 129.5, 131.6, 137.1, 138.0, 138.2, 138.3, 138.6, 138.7; HRMS-ESI $[M+Na]^+$ Calcd for $C_{61}H_{63}{}^{79}BrNaO_{11}$: 1073.3446. Found: 1073.3415.

4,5-Di-*O*-benzyl-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-L-*myo*-inositol (21)

To an oven dried Schlenk flask was added diol **20** (1.04 g, 0.98 mmol), 3,4-dimethoxyphenyl boronic acid (0.215 g, 1.18 mmol), tetrabutylammonium bromide (0.032 g, 0.10 mmol), potassium phosphate (K_3PO_4) (0.626 g, 2.95 mmol) and EtOH (25 mL). The resulting mixture was subjected to the freeze-pump-thaw cycle for three times to exclude air. $Pd(OAc)_2$ (11 mg, 0.05 mmol) was then added under a flow of argon and the reaction mixture was stirred at rt for 3 h. Once the reaction was complete the solution was filtered through a plug of Celite® and washed with EtOAc (100 mL). The reaction mixture was washed with saturated aq. $NaHCO_3$ (100 mL) and the aqueous layer was back-extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with H_2O (50 mL), saturated NaCl (50 mL), dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by

column chromatography on silica gel (EtOAc/petroleum ether = 1:2 to 2:3) to give the *title compound* **21** (0.753 g, 69%) as a white foam. $[\alpha]_D^{27}$ +19.8 (*c* = 1.00, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 2.54 (brs, 1H), 3.33 (t, *J* = 9.4 Hz, 1H), 3.38-3.42 (m, 1H), 3.44 (dd, *J* = 2.6, 9.6 Hz, 1H), 3.63 (dd, *J* = 7.1, 10.3 Hz, 1H), 3.73 (dd, *J* = 2.0, 10.3 Hz, 1H), 3.76 (t, *J* = 2.3 Hz, 1H), 3.82-3.87 (m, 2H), 3.91 (t, *J* = 9.3 Hz, 1H), 3.93 (s, 3H), 3.95 (s, 3H), 4.01 (t, *J* = 9.5 Hz, 1H), 4.07-4.12 (m, 1H), 4.18-4.20 (m, 1H), 4.21 (d, *J* = 3.9 Hz, 1H), 4.23-4.51 (m, 5H), 4.52-4.61 (m, 3H), 4.73-4.79 (m, 3H), 4.83 (d, *J* = 10.9 Hz, 1H), 4.85 (d, *J* = 10.6 Hz, 1H), 4.92 (d, *J* = 10.7 Hz, 1H), 5.12 (d, *J* = 2.0 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 7.10 (d, *J* = 2.1 Hz, 1H), 7.14 (dd, *J* = 2.1, 8.3 Hz, 1H), 7.16-7.18 (m, 2H), 7.20-7.34 (m, 28H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.02, 56.06, 69.4, 70.0, 71.1, 72.0, 72.3, 72.6, 72.7, 73.5, 75.03, 75.07, 75.7, 76.0, 79.48, 79.54, 81.0, 82.4, 85.2, 100.5, 110.5, 111.6, 119.4, 126.95, 126.97, 127.54, 127.56, 127.63, 127.64, 127.65, 127.75, 127.83, 128.01, 128.13, 128.33, 128.37, 128.39, 128.40, 128.44, 128.46, 133.9, 136.6, 138.1, 138.2, 138.3, 138.69, 138.74, 140.7, 148.7; HRMS-ESI $[M+Na]^+$ Calcd for $C_{69}H_{72}NaO_{13}$: 1131.4865. Found: 1131.4820.

3-*O*-(4-(3,4-Dimethoxyphenyl)benzyl)-1,2,4,5-tetra-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-L-*myo*-inositol (17)

To a solution of diol **21** (0.300 g, 0.270 mmol) in dry DMF (15 mL) was added NaH (60% dispersion in oil, 0.039 g, 1.62 mmol) and benzyl bromide (0.161 mL, 1.35 mmol) at 0 °C and the reaction mixture was stirred overnight. The reaction was quenched by careful addition of H_2O (2 mL) and then extracted into EtOAc (3 × 50 mL). The combined organic layers were washed with H_2O (50 mL) and saturated NaCl (50 mL), then dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 1:2) to give the *title compound*

17 (0.279 g, 80%) as a colourless oil. $[\alpha]_D^{27}$ +4.0 (*c* = 1.70, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 3.13 (dd, *J* = 2.2, 10.0 Hz, 1H), 3.36 (dd, *J* = 2.4, 9.8 Hz, 1H), 3.40 (t, *J* = 9.3 Hz, 1H), 3.44 (dd, *J* = 1.9, 11.1 Hz, 1H), 3.50 (dd, *J* = 3.6, 11.1 Hz, 1H), 3.70 (dd, *J* = 1.9, 3.1 Hz, 1H), 3.88 (dd, *J* = 3.0, 9.5 Hz, 1H), 3.93 (s, 3H), 3.95 (s, 3H), 4.03-4.13 (m, 3H), 4.17-4.27 (m, 3H), 4.34 (d, *J* = 12.1 Hz, 1H), 4.36 (t, *J* = 9.6 Hz, 1H), 4.45-4.52 (m, 3H), 4.54-4.72 (m, 7H), 4.80-4.92 (m, 4H), 5.02 (d, *J* = 11.8 Hz, 1H), 5.50 (d, *J* = 1.8 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 7.07-7.33 (m, 40H), 7.36-7.41 (m, 4H), 7.52 (d, *J* =8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.02, 56.06, 68.9, 71.8, 71.9, 72.0, 72.4, 72.8, 73.2, 74.2, 74.3, 74.86, 74.91, 75.0, 75.85, 75.87, 75.91, 79.3, 80.2, 80.7, 81.9, 84.4, 98.5, 110.5, 111.6, 119.4, 126.4, 126.9, 127.0, 127.2, 127.3, 127.36, 127.39, 127.5, 127.6, 127.7, 127.77, 127.83, 128.0, 128.11, 128.14, 128.17, 128.21, 128.22, 128.26, 128.34, 128.4, 128.5, 133.9, 137.0, 137.6, 138.6, 138.74, 138.77, 138.8, 138.95, 139.05, 139.2, 140.5, 148.8, 149.3; HRMS-ESI $[M+Na]^+$ Calcd for $C_{83}H_{84}NaO_{13}$: 1311.5804. Found: 1311.5805.

1,2,4,5-Tetra-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-L-*myo*-inositol (22)

To a solution of DMPBn pseudo-disaccharide **17** (0.020 g, 0.016 mmol) and 3,4-(methylenedioxy)toluene (**11c**)[17] (0.011 g, 0.081 mmol) in CH_2Cl_2 (3.5 mL) was added TFA (1.5 mL) and the reaction was stirred at rt for 1 h. The reaction was diluted with H_2O (50 mL) and extracted into CH_2Cl_2 (3 × 25 mL). The combined organic layers were washed with $NaHCO_3$ (20 mL), brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:4 to 1:2) to give 6-(4-(3,4-dimethoxyphenyl)benzyl)-3,4-(methylenedioxy)toluene (**12c**) (0.006 g, quant, R_f = 0.60, EtOAc/petroleum ether 1:2) and the *title compound* **22** (0.013 g,

79%, R_f = 0.30, EtOAc/petroleum ether 1:2) both as colourless oils. $[\alpha]_D^{28}$ +2.6 (*c* = 0.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (d, *J* = 7.5 Hz, 1H), 3.30 (dd, *J* = 2.2, 10.0 Hz, 1H), 3.39 (t, *J* = 9.3 Hz, 1H), 3.45 (dd, *J* = 1.9, 11.1 Hz, 1H), 3.46-3.53 (m, 2H), 3.71 (dd, *J* = 1.9, 3.0 Hz, 1H), 3.78 (t, *J* = 9.4 Hz, 1H), 3.89 (dd, *J* = 3.0, 9.5 Hz, 1H), 4.03 (t, *J* = 2.7 Hz, 1H), 4.05 (t, *J* = 9.8 Hz, 1H), 4.18-4.25 (m, 3H), 4.32 (d, *J* = 12.5 Hz, 1H), 4.34 (d, *J* = 9.6 Hz, 1H), 4.47 (d, *J* = 11.1 Hz, 1H), 4.53-4.76 (m, 9H), 4.85 (d, *J* = 11.1 Hz, 1H), 4.93-4.99 (m, 2H), 5.52 (d, *J* = 1.8 Hz, 1H), 7.07-7.34 (m, 40H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 69.0, 71.8, 72.0, 72.5, 73.2, 73.3, 74.8, 74.87, 74.9, 75.0, 75.5, 75.6, 75.8, 79.6, 80.2, 82.7, 84.2, 98.5, 126.5, 127.0, 127.24, 127.26, 127.27, 127.4, 127.5, 127.6, 127.76, 127.81, 127.85, 127.9, 128.0, 128.14, 128.19, 128.2, 128.3, 128.46, 128.49, 128.6, 137.4, 138.4, 138.6, 138.65, 138.7, 138.8, 138.9, 139.2; HRMS-ESI $[M+Na]^+$ Calcd for $C_{68}H_{70}NaO_{11}$: 1085.4810. Found: 1085.4774.

(±)-3-*O*-(4-(3,4-Dimethoxyphenyl)benzyl)-1,2,4,5-tetra-*O*-benzyl-*myo*-inositol (24)

Method 1: Deallylation of **4a**

The argon atmosphere of a solution of (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I)hexafluorophosphate (**23**) (7 mg, 8.4 μmol) and **4a** (45 mg, 0.056 mmol) in anhydrous THF (10 mL) was replaced with hydrogen for ca. 1 min then the reaction flask was flushed with argon. The reaction mixture was left to stir for 2.5 h and the volatiles removed *in vacuo*. The residue was redissolved in MeOH/CH_2Cl_2 (1:2, 15 mL). Acetyl chloride (120 μL, 1.67 mmol) was added, and the reaction stirred overnight. The reaction mixture was quenched with sat. aq. $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic fractions were dried ($MgSO_4$), and the solvent

removed under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 3:7) to give the *title compound* **24** (27 mg, 63%) as a colourless oil. ν_{max} (ATR-IR) 3465, 3029, 2922, 1604, 1589, 1526, 1502, 1453, 1399, 1359, 1327, 1307, 1249, 1216, 1171, 1141, 1052, 1025; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.16 (dd, *J* = 9.9, 9.2 Hz, 1H), 3.34 (t, *J* = 9.0 Hz, 1H), 3.36 (dd, *J* = 9.7, 2.5 Hz, 1H), 3.88 (s, 3H), 3.90 (s, 3H), 4.01-4.04 (m, 2H), 4.13 (dd, *J* = 9.7, 9.3 Hz, 1H), 4.50 (d, *J* = 11.8 Hz, 1H), 4.55 (d, *J* = 11.8 Hz, 1H), 4.61 (d, *J* = 11.8 Hz, 1H), 4.65 (d, *J* = 11.8 Hz, 1H), 4.75-4.86 (m, 5H), 4.89 (d, *J* = 10.7 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 7.06 (d, *J* = 2.1 Hz, 1H), 7.10 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.20-7.36 (m, 22H), 7.46 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.95, 55.99, 72.3, 72.5, 72.9, 73.7, 74.1, 75.4, 75.8, 80.1, 81.1, 81.4, 83.5, 110.4, 111.5, 119.3, 126.8, 127.4, 127.5, 127.6, 127.68, 127.73, 127.8, 128.03, 128.05, 128.2, 128.3, 128.4, 128.5, 133.8, 136.9, 137.9, 138.8, 140.4, 148.7, 149.2; HRMS-ESI $[M+Na]^+$ Calcd for $C_{49}H_{50}O_8Na$: 789.3398. Found: 789.3412.

Method 2: Selective hydrolysis of the PMB group of **4b**

Trifluoroacetic acid (50 μL, 0.65 mmol) was added to a solution of the PMB-ether **4b** (18 mg, 0.020 mmol) and **11c** (30 mg, 0.220 mmol) in CH_2Cl_2 (4.95 mL), and the reaction mixture was stirred at rt for 1 h. The reaction was quenched by the addition of aq. $NaHCO_3$ (30 mL) and the aqueous layer extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 2:3) to give the *title compound* **24** (12 mg, 77%, R_f = 0.3 EtOAc/petroleum ether 1:3) and 6-(4-methoxybenzyl)-3,4-(methylenedioxy)toluene (**25)** (7 mg, quant., R_f = 0.75 EtOAc/petroleum ether 1:3). Data for **25**: ν_{max} (ATR-IR) 2925, 1611, 1583, 1509, 1485, 1464, 1442, 1360, 1301, 1245, 1175, 1163, 1105, 1038; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17 (s, 3H), 3.78 (s, 3H), 3.82 (s, 2H), 5.89

(s, 2H), 6.58 (s, 1H), 6.65 (s, 1H), 6.81 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 8.75 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 38.2, 55.3, 100.3, 110.1, 110.4, 113.8, 129.4, 129.5, 132.3, 132.6, 145.6, 145.7, 157.9; HRMS-ESI $[M+Na]^+$ Calcd for $C_{16}H_{16}O_3Na$: 279.0991. Found: 279.1031.

Method 3: Selective removal of the PBB group of **4c**.

Freshly distilled *N*-methylaniline (8 μL, 0.069 mmol) was added to a solution of the PBB ether **4c** (54 mg, 0.058 mmol) in anhydrous toluene (1 mL) under argon. In another flask, (*o*-biphenyl)P(*t*-Bu)$_2$ (1 mg, 3.37 μmol), tris(dibenzylideneacetone)dipalladium(0) (1.2 mg, 1.3 μmol) and NaO*t*-Bu (6 mg, 0.063 mmol) were dissolved in anhydrous toluene (1 mL) under argon. The solution of **4c** was then added to this mixture via cannular under argon. The reaction mixture was heated to 80 °C and left to stir for 2 h. The reaction mixture was cooled to rt, diluted with Et_2O, filtered through a pad of Celite®, and the solvent removed *in vacuo*. Acetyl chloride (10 μL, 0.14 mmol) was added to a solution of the residue in CH_2Cl_2/MeOH (8:2, 10 mL) and the reaction stirred for 30 min. The reaction was quenched by the addition of aq. $NaHCO_3$ (30 mL), extracted with CH_2Cl_2 (2 × 30 mL), dried ($MgSO_4$), and the solvent removed *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc/petroleum ether = 1:9 to 3:7) to give the *title compound* **24** (23 mg, 52%) as a colourless oil.

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SUPPORTING INFORMATION

Copies of ^{1}H and ^{13}C NMR spectra for all novel compounds are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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