

# Reciprocal Donor–Acceptor Selectivity: the Influence of the Donor O-2 Substituent in the Regioselective Mannosylation of *myo*-Inositol Orthopentanoate

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*Dedicated to Prof. Serafin Valverde on the occasion of his 70th birthday*

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The regioselectivity in the glycosylation of *myo*-inositol orthopentanoate with an *n*-pentenyl orthoester (NPOE) and an armed thioglycoside as glycosyl donors has been examined. The NPOE displayed higher regioselectivity and its preferred

site for glycosidation coincided with that for selective acylation with RCOCl/pyridine.

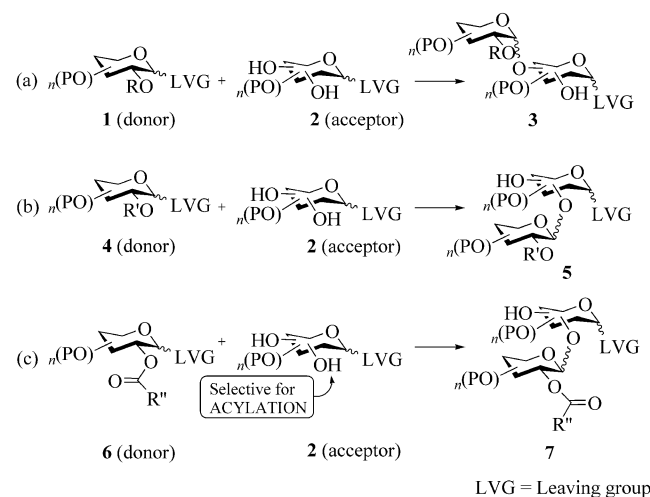
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## Introduction

The seemingly simple operation of linking a donor and acceptor, exemplified by the hypothetical reactions in Scheme 1, is the fundamental process of oligosaccharide synthesis.<sup>[1]</sup> This process is, however, more complex than it appears because it entails, *stereo*-, *chemo*- and *regio*selectivity, three of the four selectivities that according to Trost<sup>[2]</sup> confront organic synthesis in general. The fourth, *enantio*-selectivity,<sup>[3]</sup> is usually not a factor in carbohydrate syntheses because D- or L-designation of the reacting partners is specified by nature.

The issue of *regio*selectivity in glycosylation of diol (or polyol) acceptors brings into question the lengthy protecting-group manipulations in carbohydrate chemistry, because the generally accepted hydroxy preferences of organic structures,<sup>[1,4]</sup> e.g., primary > secondary, and equatorial > axial, have proven to be unreliable with respect to glycosylation. As a consequence, saccharide formation is usually carried out with all hydroxy groups of the glycosyl acceptor protected, except for the targeted one.

We have been recently interested in the study of regioselective strategies that might help to simplify saccharide synthesis.<sup>[5]</sup> We first observed that the substituent at O-2 of the glycosyl donor could have a profound influence on the targeted-OH of the acceptor diol. Thus, the reaction of diol



Scheme 1. Preparation of a disaccharide by glycosylation of a donor with a glycosyl acceptor.

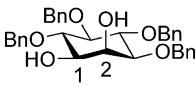
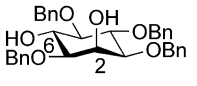
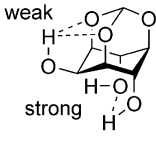
2 with two glycosyl donors, differing in the protecting group at O-2, e.g., 1 and 4 (Scheme 1 a, b), might give rise to regioisomeric disaccharides, e.g., 3 and 5. These O-2 substituent-induced regiopreferences have been found in several pairs of secondary OH acceptors,<sup>[5,6]</sup> and even in primary-secondary-OH pairs.<sup>[7]</sup>

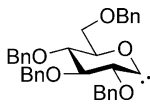
Furthermore, we have noticed several instances where an acceptor-diol displays comparable regioselectivities towards glycosyl donors and protecting reagents. For example the preferred site for acylation of 2 (Scheme 1 c) is also preferred by donor 6 as well as the corresponding *n*-pentenyl orthoester (NPOE), affording disaccharide 7.<sup>[8]</sup>

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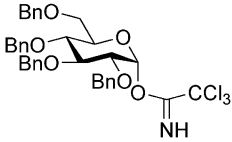
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Table 1. Observed regioselectivity in some reactions of diols **8**, **9**, and triol **10**.

								
entry	reagent	O-1 : O-2 (ratio)	entry	reagent	O-6 : O-2 (ratio)	entry	reagent	eq : ax (ratio)
(i)	TsCl	only --	(v)	BzCl	only --	(x)	TBDMSCl	only --
(ii)	BnBr	1 3	(vi)	BnBr	1 3	(xi)	PhCOCl	23 1
(iii)	NPOE	6 1	(vii)	NPOE	only --	(xii)	BnBr	-- only
(iv)	NPG (2-OAc)	2 1	(viii)	NPG (2-OAc) only	--	(xiii)	carbene ( <b>11</b> )	-- only
			(ix)	NPG (2-OAlk)	1 3	(xiv)	TCA ( <b>12</b> )	1 3



**11**  
glycosylidene carbene  
(non-classical donor)



**12**  
trichloroacetimidate (TCA)  
(classical donor)

Examples of similar selectivities are scattered throughout the literature. Thus, with the vicinal diol **8** (Table 1), Angyal found that tosylation occurred ONLY at O-1, whereas benzylation occurred mainly at O-2. We found subsequently, that O-1 is also the preferred site for glycosylation with an NPOE and, to a lesser extent, a 2-*O*-acyl NPG. Similar preferences were found for diol **9**, where O-6 was the exclusive site for benzylation, and also for glycosidation with NPOE or 2-*O*-acyl NPG. On the other hand, benzyl bromide and a 2-*O*-alkyl NPG favoured O-2 to 3:1 extent.

The foregoing brings to mind the interesting chemistry of Kishi's inositol orthoformate (**10**),<sup>[9,10]</sup> which presents two enantiotopic axial –OH groups involved in strong intramolecular H-bonds, while the equatorial –OH group is weakly H-bonded to the orthoester oxygen atoms.<sup>[11]</sup> Several studies on compound **10** have shown dramatic contrasts in regioselectivities (Table 1). The equatorial OH was found to be the site of exclusive silylation by Kishi,<sup>[9]</sup> and of predominant benzylation by Ozaki.<sup>[12]</sup> Chiara showed that acyl migration was not a factor in the latter result.<sup>[13]</sup>

On the other hand, Billington found that benzylation occurred exclusively at the axial position(s).<sup>[14]</sup>

These results were examined by Vasella in connection with his extensive studies aimed at correlating hydroxy reaction preferences with H-bonding data.<sup>[15]</sup> From the data in Table 1, compound **10** undergoes selective acylation at the site of weak H-bonding (Table 1, Entry xi), whereas alkylation occurs at the site of strong H-bonding (Table 1, Entry xii).

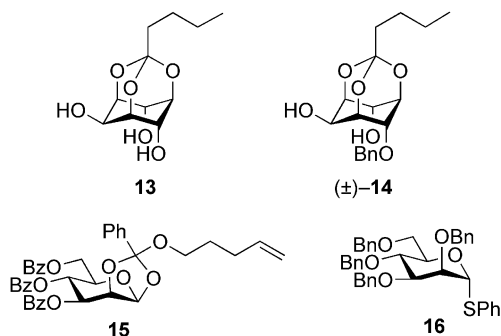
Finally, in glycosylation-related studies, Vasella's group reported that the glycosylidene carbene **11**, termed a "non-classical" donor, went exclusively to the axial OH,<sup>[16]</sup> the same site as that preferred 3:1 by the "classical" donor, tetra-*O*-benzylglucosyl trichloroacetimidate (TCA) **12**.

In light of our observations on acceptor diols **2**, **8** and **9** seen in Scheme 1 c and Table 1 (Entries iii, iv, vii, viii and ix), we decided to evaluate the influence of H-bonding in the acceptor as a *regiodirecting* factor in glycosylation reactions. In this connection it should be noted that Vasella's notion of "non-classical" and "classical" donors, e.g. **11** and **12** respectively, was proposed before the regiopreferences seen in Table 1, Entries (vii), (viii) and (ix) for our "classical" *n*-pentenyl donors were observed.

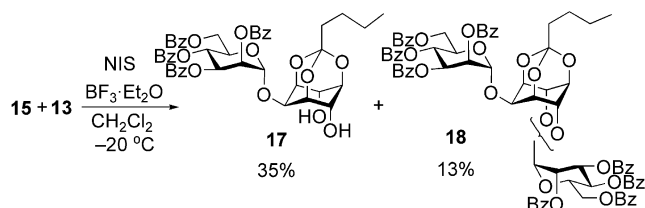
## Results and Discussion

Throughout this study, *myo*-inositol pentan-3-yl orthoester (**13**),<sup>[17]</sup> was used instead of the orthoformate **10**, because of its enhanced solubility in CH<sub>2</sub>Cl<sub>2</sub>. Accordingly compound **13**, and its monobenzyl derivative (±)-**14**, were prepared. As glycosyl donors we selected NPOE **15** (Scheme 2), and phenyl 1-thio-α-D-mannopyranoside **16**. Our previous work has shown that armed and disarmed thioglycosides and NPGs display similar regioselectivities for acceptor diols.<sup>[18]</sup>

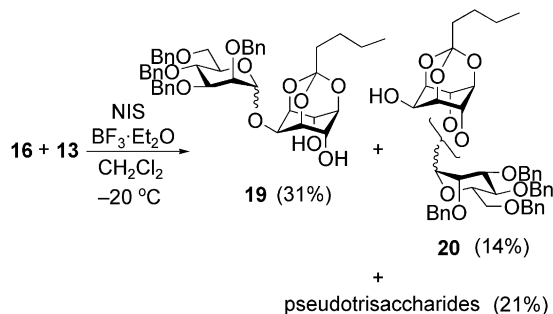
Glycosylation of triol **13** (1.2 equiv.) with NPOE **15** (1.0 equiv.) afforded a single disaccharide **17**, (35% yield) resulting from selective reaction of the equatorial –OH group, and a mixture of two diastereomeric pseudo-trisaccharides **18**, very likely resulting from a subsequent mannosylation of one of the enantiotopic axial –OH groups of **17** (Scheme 3). *n*-Pentenyl 2,3,4,6-tetra-*O*-benzoylmannopyranoside (24% yield), arising from the rearrangement of **15**,<sup>[19]</sup> was also isolated from the crude reaction mixture. Notably absent was a pseudo-disaccharide resulting from glycosidation at one of the axial OH groups of **13**. The identity of compound **17** was established by support studies

Scheme 2. *myo*-Inositol derivatives **13**, **14**, and glycosyl donors **15**, **16**.

that included acetylation,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, HSQC, as well as unequivocal synthetic transformations of the resulting pseudo-saccharides, as will be outlined below.

Scheme 3. Glycosylation of *myo*-inositol **13**, with NPOE **15**.

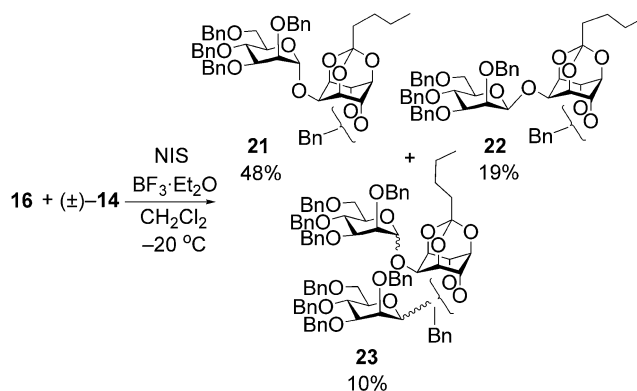
On the other hand, glycosylation of triol **13** (1.2 equiv.) with armed thioglycoside **16** (1.0 equiv.) yielded a complex reaction mixture composed of disaccharides **19** resulting from  $\alpha/\beta$  glycosylation at the equatorial OH, and diastereomeric **20**, ensuing from  $\alpha/\beta$  glycosylation at the enantiotopic axial OH groups (Scheme 4). A complex mixture of trisaccharides (21%) was also isolated.

Scheme 4. Glycosylation of *myo*-inositol **13**, with armed thioglycoside **16**.

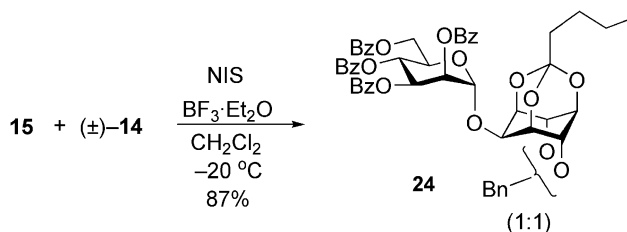
### Glycosylation of Diol (±)-14

In order to gain more insight into the axial vs. equatorial regioselection, we decided to carry out additional glycosylations using (±)-**14** as the glycosyl acceptor. Racemic (±)-**14** possesses only one equatorial and one axial OH, rather than the two axial OH groups present in compound **13**. Accordingly, glycosylation of diol (±)-**14** (1.2 equiv.) with armed donor **16** (1 equiv.), yielded a reaction mixture

that included three sets of pseudo-saccharides, (Scheme 5), which could be separated chromatographically. Two sets proved to be pseudo-disaccharides **21** (48%) and **22** (19%), which arose from  $\alpha$ - and  $\beta$ -glycosylation at the equatorial OH of (±)-**14**, respectively. The third set was the pseudo-trisaccharides **23** (10%), arising from further glycosylation at the axial OH of **21** and **22**.

Scheme 5. Glycosylation of (±)-**14** with armed donor **16**.

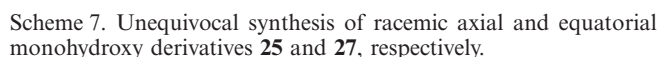
On the contrary, an analogous reaction of racemic diol (±)-**14** (1.2 equiv.) with NPOE **15** (1 equiv.), in  $\text{CH}_2\text{Cl}_2$  mediated by NIS and  $\text{BF}_3 \cdot \text{OEt}_2$  at  $-20^\circ\text{C}$ , resulted in exclusive glycosylation at the equatorial OH to give a 1:1 diastereomeric mixture of disaccharides, **24** (Scheme 6). The absence of a pseudo-trisaccharide corresponding to **23** (Scheme 5), emphasises the reluctance of NPOEs to react at the axial OH.

Scheme 6. Glycosylation of (±)-**14** with armed donor **15**.

### Structural Assignment Studies

The mixture(s) shown in Schemes 3, 4 and 5 arise because of  $\alpha$  vs.  $\beta$  orientation, as well as equatorial vs. axial glycosidation(s). It was now necessary to disentangle these possibilities, and for this task we relied on two secure precedents, the previously mentioned regioselectivities for alkylation<sup>[9]</sup> (e.g. **13**→**14**), and silylation<sup>[9]</sup> (e.g. **14**→**25**) of *myo*-inositol orthoester derivatives (Scheme 7), and the  $\alpha$ -anomeric selectivity induced by NPOEs.

We first secured the equatorial OH in **27** as the site for glycosylation, beginning with racemic mixture (±)-**14** as shown in Scheme 7. Silylation gave (±)-**25** which upon benzylation gave (±)-**26** and desilylation then afforded the desired (±)-**27**. This material was now subjected to transfor-



Accordingly, glycosylation of **27** with armed donor **16** (Scheme 8), afforded a mixture of *pseudodisaccharides*, which upon saponification furnished a diastereomeric mixture of **21** and **22**.

It was now necessary to confirm that the latter compounds were the same as those that had been previously obtained (*as separate structures*) by glycosylation of ( $\pm$ )-**14** with donor **16** in Scheme 5. To that end, the crude mixture of **21** and **22** obtained in Scheme 8 was acetylated, and column chromatography of the resulting material allowed iso-

The foregoing anomeric assignments were confirmed by acetylation of the pure isomers **21** and **22** (obtained in Scheme 5). The former also gave **28**, which was clearly therefore an  $\alpha$ -mixture of diastereomers **28**. Similarly, parallel acetylation of **22** furnished compounds **29** and **30**.

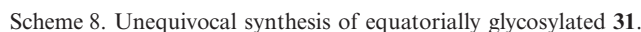
Anomeric configurations of these compounds were rigorously assigned by comparison of their  $^1J_{C,H}$  coupling constants. Thus,  $\alpha$ -anomeric mixture **28**, displayed  $^1J_{C,H}$  coupling constant 168.4 Hz, while corresponding values for the  $\beta$ -isomers **29** and **30** were 155.2, and 153.0 Hz, respectively.

On the other hand, benzylation of the diastomeric/anomeric mixture comprising **21** and **22**, yielded the anomeric  $\alpha/\beta$ -**31** (Scheme 8). This mixture was also obtained in a parallel manner by benzylation of  $\alpha/\beta$ -**19** obtained in Scheme 4.

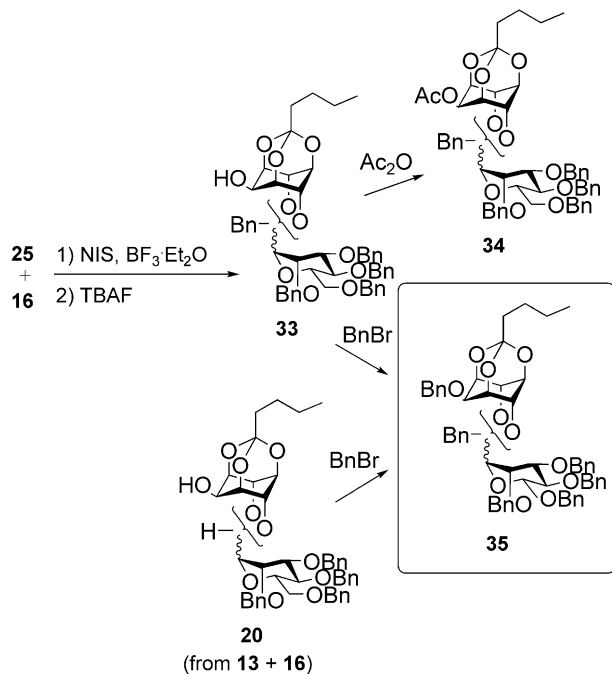
Preparation of the anomerically pure products was now undertaken, as outlined in Scheme 8. Compound **24**, the sole compound arising from the glycosylation of ( $\pm$ )-**14** with NPOE donor **15**, upon acetylation yielded  $\alpha$ -**32**, as a 1:1 diastereomeric mixture. Exhaustive saponification followed by benzoylation granted access to  $\alpha$ -**31**.

The isomeric  $\beta$ -**31** could be obtained by benzylation of **22**.

A comparable strategy was now needed to confirm that the site of glycosylation in **20** in Scheme 4 was an axial-OH. For this task, the silylated derivative **25** was the logical precursor. This analysis is outlined in Scheme 9. Glycosyl-

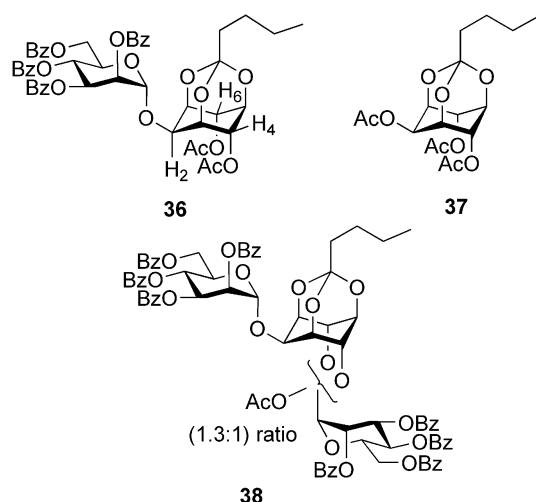


ation of compound **25** with thioglycoside **16** led, after desilylation, to axially glycosylated compound **33**. The latter was acetylated to **34**, and benzylated to give perbenzylated derivative **35**, which proved to be identical with the product obtained by benzylation of **20**, thus confirming its axial site of glycosylation.



Scheme 9. Unequivocal synthesis of axially glycosylated **35**.

In an alternative route compound **17** (obtained in Scheme 3) was acetylated to yield one single product, diacetate **36** (Scheme 10), thus confirming that glycosylation had taken place at the equatorial OH group. Compound **36** ( $^1\text{H}$  NMR: 5.42 and 5.21 ppm for the diastereotopic 4-H and 6-H.  $^{13}\text{C}$  NMR, one signal for C-4 and C-6 at  $\delta = 67.8$  ppm) showed good NMR signal overlapping with triacetate **37**



Scheme 10. Acetylated derivatives **36**–**38**.

( $^1\text{H}$  NMR: 5.46 ppm for 4-H and 6-H.  $^{13}\text{C}$  NMR: 67.9 ppm for C-4 and C-6). Acetylation of pseudo-trisaccharides **18**, yielded a 1.3:1 mixture of diastereomeric monoacetates **38**.

## Regioselectivity

Glycosylation of triol **13** with NPOE (**15**) afforded just one pseudo-disaccharide **17** (Scheme 3), whereas the two possible regioisomeric pseudo-disaccharides, **19** and **20**, were obtained by glycosylation of **13** with armed donor **16** (Scheme 4). The higher regioselectivity displayed by NPOE **15** when compared with armed donor **16** towards triol **13** is in agreement with previous results from our research groups.<sup>[6,7,18]</sup> The observed regioselectivity displayed by NPOE **15** is remarkable because there is just one equatorial OH group compared with two enantiotopic axial OH groups in the acceptor. Blocking of one of the axial OH groups in compound **14** resulted in a considerable enhancement of the glycosylation regioselectivity towards the equatorial OH group. Thus, glycosylation of **14** with NPOE **15** led exclusively to the equatorially glycosylated compound **24** (see Scheme 6) and also induced more equatorial glycosylation when compared with the armed thioglycoside **16** (compare Scheme 6 with 4).

## Conclusions

We have examined the regioselective glycosylation of *myo*-inositol pentanoyl orthoester derivatives **13** and **14**, with NPOE (**15**) and armed thioglycoside **16** as model donors with conflicting regioselectivities.<sup>[5–7]</sup> The NPOE has, yet again, displayed a higher regioselectivity than the armed donor in all couplings. The observed regioselectivity in the coupling of triol **13** with **15**, coincides with that observed in the acylation (RCOCl, pyridine) of orthoester *myo*-inositol derivatives, as reported by Ozaki's<sup>[12]</sup> and Chiara's<sup>[13]</sup> groups. Thus, only one pseudo-disaccharide was obtained arising from glycosylation at the equatorial hydroxy group of **13**. However, the reaction of armed donor **16** with triol **13** generated two pseudo-disaccharides resulting from glycosylation at the equatorial (major isomer) and the axial OH groups. In both cases some pseudo-trisaccharides were also present (see Schemes 3 and 4). On the other hand, the axial benzyl group in ( $\pm$ )-**14**, exerts a significant hindrance over the remaining axial OH group and precludes the incorporation of a second mannose unit when NPOE (**15**) was used as the glycosyl donor (Scheme 6). On the other hand, when donor **16** was used, a second donor unit was incorporated to the *myo*-inositol core, and pseudo-trisaccharide **23** was obtained, albeit in low yield (Scheme 5).

## Experimental Section

**General Remarks:** All reactions were performed in dry flasks fitted with glass stoppers or rubber septa under a positive pressure of Ar, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred by syringe or stainless steel cannula. Op-



tical rotations were determined at 20 °C for solutions in chloroform. Flash-column chromatography was performed using 230–400 mesh silica gel. Thin-layer chromatography was conducted on Kieselgel 60 F254 (Merck). Spots were observed first under UV irradiation (254 nm) then by charring with a solution of 20% aqueous H<sub>2</sub>SO<sub>4</sub> (200 mL) in AcOH (800 mL). Anhydrous MgSO<sub>4</sub> or Na<sub>2</sub>SO<sub>4</sub> were used to dry organic solutions during workup, and evaporation of the solvents was performed under vacuum using a rotary evaporator. Solvents were dried and purified using standard methods. Unless otherwise noted <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> at 300 or 500 MHz and 50 or 125 MHz, respectively. Chemical shifts are expressed in parts per million ( $\delta$  scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (CHCl<sub>3</sub>:  $\delta$  = 7.25 ppm). *N*-Iodosuccinimide was purchased from Aldrich and recrystallized from hot CH<sub>2</sub>Cl<sub>2</sub>.

**General Procedure for Glycosidations:** A solution of the glycosyl acceptor (1.2 equiv.) and the glycosyl donor (1 equiv.) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> and in the presence of 5-Å molecular sieves (200 mg/mmol of donor) was cooled to –20 °C. The mixture was then treated with *N*-iodosuccinimide (3 equiv.) and stirred for 5 min after which BF<sub>3</sub>·OEt<sub>2</sub> (0.3 equiv.) was added. The reaction was warmed to 0 °C and stirred until total disappearance of the starting material. Then, the reaction mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (30 mL) washed with 10% aqueous sodium thiosulfate, saturated sodium hydrogen carbonate and brine. The organic layer was dried with Na<sub>2</sub>SO<sub>4</sub>, concentrated in vacuo and the crude was purified by flash chromatography.

**DL-4-*O*-Benzyl-1,3,5-*O*-pentylidene-*myo*-inositol (14):** A stirred solution of **13**<sup>[15]</sup> (1.6 g, 6.5 mmol) in dry DMF (200 mL), was cooled to 0 °C and then treated portionwise with 60% NaH (187 mg, 7.8 mmol). After 15 min, benzyl bromide (0.93 mL, 7.8 mmol) was added, warmed to room temperature and stirred for 12 h. The solution was carefully quenched with water, diluted with Et<sub>2</sub>O, washed with H<sub>2</sub>O, dried and concentrated. The product was then purified by flash chromatography (20% EtOAc/hexane) to afford ( $\pm$ )-**14** (1.71 g, 78%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.81 (t, *J* = 7.2 Hz, 3 H), 1.15–1.29 (m, 2 H), 1.28–1.38 (m, 2 H), 1.54–1.59 (m, 2 H), 3.93–3.98 (m, 1 H), 4.12–4.20 (m, 3 H), 4.28–4.37 (m, 2 H), 4.57 (d, *J* = 11.6 Hz, 1 H), 4.62 (d, *J* = 11.6 Hz, 1 H), 7.18–7.33 (m, 5 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 15.1, 23.7, 26.0, 38.1, 60.2, 67.6, 68.1, 72.9, 73.2, 74.5, 75.4, 110.7, 129.3, 130.0, 130.1, 137.2 ppm. API-ES<sup>+</sup>: *m/z* = 337.2 [M + H]<sup>+</sup>, 359.2 [M + Na]<sup>+</sup>. C<sub>18</sub>H<sub>24</sub>O<sub>6</sub> (336.16): calcd. C 64.27, H 7.19; found C 64.53, H 6.95.

**2-*O*-(2,3,4,6-Tetra-*O*-benzoyl- $\alpha$ -D-mannopyranosyl)-1,3,5-*O*-pentylidene-*myo*-inositol (17):** Application of the general procedure for the glycosidation reaction to triol **13** (60 mg, 0.24 mmol) and *n*-pentenyl orthoester **15**<sup>[20]</sup> (133 mg, 0.20 mmol) afforded a material that was subjected to flash chromatography (30% EtOAc/hexane) to yield trisaccharide **18** (37 mg, 13%) followed by disaccharide **17** (57 mg, 35%).

**17:** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.83 (t, *J* = 7.2 Hz, 3 H), 1.13–1.30 (m, 2 H), 1.29–1.37 (m, 2 H), 1.54–1.59 (m, 2 H), 4.20 (m, 1 H), 4.28 (m, 1 H), 4.40–4.45 (m, 2 H), 4.51 (dd, *J* = 4.9, 12.0 Hz, 1 H), 4.54 (m, 1 H), 4.64 (dd, *J* = 1.7, 4.2 Hz, 1 H), 4.69 (dd, *J* = 2.6, 12.0 Hz, 1 H), 4.76 (m, 1 H), 5.40 (d, *J* = 1.7 Hz, 1 H), 5.79 (dd, *J* = 1.8, 2.7 Hz, 1 H), 6.03 (dd, *J* = 3.4, 10.0 Hz, 1 H), 6.08 (t, *J* = 10.0 Hz, 1 H), 7.25–8.10 (m, 20 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.1, 22.6, 25.0, 37.0, 63.3, 67.2, 68.2, 68.3, 68.4, 68.8, 69.5, 70.22, 70.9, 72.8, 73.1, 98.1, 109.3, 128.4, 128.6, 128.7, 129.8, 129.9, 133.3, 133.6, 165.6, 165.7, 165.8, 166.5 ppm.

API-ES<sup>+</sup>: *m/z* = 825.5 [M + H]<sup>+</sup>, 847.5 [M + Na]<sup>+</sup>. C<sub>45</sub>H<sub>44</sub>O<sub>15</sub> (824.27): calcd. C 65.53, H 5.38; found C 65.49, H 5.17.

**Glycosidation of Triol 13 with Thioglycoside 16:** Application of the general procedure for the glycosidation reaction to triol **13** (60 mg, 0.24 mmol) and the glycosyl donor **16**<sup>[21]</sup> (126 mg, 0.20 mmol) afforded a material that was subjected to flash chromatography (10% to 20% EtOAc/hexane) to yield three different fractions which were analyzed by mass spectrometry and later assigned to disaccharides **19** (48 mg, 31%, API-ES<sup>+</sup>: *m/z* = 769.5 [M + H]<sup>+</sup>, 786.7 (M+NH<sub>4</sub>)<sup>+</sup>), disaccharides **20** (21 mg, 14%, API-ES<sup>+</sup>: *m/z* = 769.5 [M + H]<sup>+</sup>, 791.5 [M + Na]<sup>+</sup>) and trisaccharides (54 mg, 21%, API-ES<sup>+</sup>: *m/z* = 1292.2 [M + H]<sup>+</sup>).

**Glycosidation Reaction of Diol 14 with Thioglycoside 16:** Application of the general procedure for the glycosidation reaction to diol ( $\pm$ )-**14** (100 mg, 0.30 mmol) and the glycosyl donor **16** (156 mg, 0.25 mmol) afforded a material that was subjected to flash chromatography (10% EtOAc/hexane) to collect three different fractions which were later assigned to  $\alpha$ -disaccharide **21** (102 mg, 48%),  $\beta$ -disaccharide **22** (40 mg, 19%) and trisaccharide **23** (34 mg, 10%).

**DL-4-*O*-Benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzoyl- $\alpha$ -D-mannopyranosyl)-1,3,5-*O*-pentylidene-*myo*-inositol (24):** The diol ( $\pm$ )-**14** (30 mg, 0.09 mmol) and the donor **15** (49.8 mg, 0.075 mmol) were submitted to the general method of the glycosylation reaction. Purification by flash chromatography (20% EtOAc/hexane) afforded a 1:1 diastereomeric mixture of disaccharides **24** (60 mg, 87%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  (selected signals) = 5.16 (d, *J* = 1.7 Hz, 0.5 H, 1'-H), 5.26 (d, *J* = 1.7 Hz, 0.5 H, 1'-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  (selected signal) = 98.0 (C-1') ppm. API-ES<sup>+</sup>: *m/z* = 915.5 [M + H]<sup>+</sup>, 937.5 [M + Na]<sup>+</sup>.

**DL-4-*O*-Benzyl-2-*O*-tert-butylidimethylsilyl-1,3,5-*O*-pentylidene-*myo*-inositol (25):**<sup>[9]</sup> *tert*-Butylidimethylsilyl chloride (466 mg, 3.0 mmol) was added to a stirred solution of diol ( $\pm$ )-**14** (850 mg, 2.52 mmol) and imidazole (429 mg, 6.3 mmol), in DMF (15 mL) at 0 °C. The reaction mixture was stirred at room temperature for 12 h and then concentrated in vacuo to dryness. The crude material was purified by flash chromatography (10% EtOAc/hexane) to afford ( $\pm$ )-**25** (1.1 g, 97%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.12 (s, 3 H), 0.13 (s, 3 H), 0.87 (t, *J* = 7.2 Hz, 3 H), 0.94 (s, 9 H), 1.29 (sext, *J* = 7.4 Hz, 2 H), 1.37–1.47 (m, 2 H), 1.61–1.66 (m, 2 H), 3.63 (d, *J* = 10.1 Hz, 1 H), 4.10–4.15 (m, 3 H), 4.19–4.23 (m, 1 H), 4.65 (m, 2 H), 7.29–7.42 (m, 5 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = –4.7, –4.6, 1.0, 13.9, 18.2, 22.4, 24.8, 25.8, 36.9, 59.9, 67.7, 68.4, 72.9, 73.0, 75.0, 75.3, 109.2, 128.0, 128.7, 128.8, 136.2 ppm. API-ES<sup>+</sup>: *m/z* = 451.5 [M + H]<sup>+</sup>, 473.5 [M + Na]<sup>+</sup>. C<sub>24</sub>H<sub>38</sub>O<sub>6</sub>Si (450.24): calcd. C 63.97, H 8.50; found C 64.09, H 8.17.

**DL-4-*O*-Benzoyl-6-*O*-benzyl-2-*O*-tert-butylidimethylsilyl-1,3,5-*O*-pentylidene-*myo*-inositol (26):** The alcohol ( $\pm$ )-**25** (250 mg, 0.55 mmol) was dissolved in pyridine (10 mL), and benzoyl chloride (128  $\mu$ L, 1.1 mmol) and a catalytic amount of DMAP were added. The reaction was stirred at room temperature for 12 h and then concentrated. The crude was purified by flash chromatography (5% EtOAc/hexane) to afford ( $\pm$ )-**26** (274 mg, 90%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.08 (s, 3 H), 0.12 (s, 3 H), 0.89 (t, *J* = 7.27 Hz, 3 H), 0.93 (s, 9 H), 1.33 (sext, *J* = 7.21, 7.18 Hz, 2 H), 1.42–1.53 (m, 2 H), 1.70–1.75 (m, 2 H), 4.24–4.28 (m, 2 H), 4.32–4.35 (m, 2 H), 4.54 (m, 2 H), 4.58 (m, 1 H), 5.64–5.67 (m, 1 H), 7.13–8.20 (m, 10 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = –4.7, –4.6, 14.0, 18.4, 22.5, 24.8, 25.9, 37.0, 60.9, 67.1, 68.9, 72.1, 72.8, 73.5, 74.3, 109.8, 127.5, 127.8, 128.3, 128.4, 128.9, 129.7, 130.6, 133.2, 137.2, 165.4 ppm. API-ES<sup>+</sup>: *m/z* = 555.5 [M + H]<sup>+</sup>, 577.5 [M + Na]<sup>+</sup>.

**DL-4-*O*-Benzoyl-6-*O*-benzyl-1,3,5-*O*-pentylidene-*myo*-inositol (27):** Tetrabutylammonium fluoride (473 mg, 1.5 mmol) was added to a stirred solution of ( $\pm$ )-**26** (277 mg, 0.5 mmol) in THF and at room temperature (8 mL). After 30 min the reaction was diluted with diethyl ether (50 mL) and washed with brine (2  $\times$  25 mL). The organic layer was then dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. Purification by flash chromatography (10% EtOAc/hexane) afforded ( $\pm$ )-**27** (198 mg, 90%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.91 (t,  $J$  = 7.2 Hz, 3 H, CH<sub>3</sub>), 1.32 (sext,  $J$  = 7.10 Hz, 2 H), 1.47 (m, 2 H), 1.69–1.74 (m, 2 H), 4.19 (bt,  $J$  = 1.8 Hz, 1 H), 4.32–4.39 (m, 3 H), 4.52 (d,  $J$  = 11.4 Hz, 1 H), 4.56 (d,  $J$  = 11.4 Hz, 1 H), 4.61 (m, 1 H), 5.68–5.72 (m, 1 H), 7.12–8.17 (m, 10 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 13.8, 22.4, 24.6, 36.8, 60.7, 66.7, 68.2, 72.0, 72.4, 73.0, 73.6, 110.0, 127.5, 127.7, 128.2, 128.3, 129.7, 129.0, 130.0, 133.1, 136.9, 165.3 ppm. API-ES<sup>+</sup>:  $m/z$  = 441.5 [M + H]<sup>+</sup>, 463.5 [M + Na]<sup>+</sup>.

**Glycosidation of Alcohol 27 with Thioglycoside 16:** Application of the general procedure for the glycosidation reaction to the alcohol **27** (90.7 mg, 0.21 mmol) and the glycosyl donor **16** (156 mg, 0.25 mmol) afforded a material which was purified by flash chromatography (10% EtOAc/hexane) (164 mg, 83%) and subsequently subjected to methanolysis by treatment with a freshly prepared solution of NaOMe (5 mg, 0.1 mmol) in MeOH. The reaction mixture was then neutralized with Amberlite H<sup>+</sup> resin, filtered, and concentrated. Purification by flash chromatography (20% EtOAc/hexane) afforded a 1:1 mixture of disaccharides **21** and **22** (130 mg, 89%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  (selected signals) = 5.08 (d,  $J$  = 1.74 Hz, 1 H, 1'<sub>a</sub>-H), 5.11 (d,  $J$  = 1.69 Hz, 1 H, 1'<sub>a</sub>-H) ppm.

A fraction of this anomeric mixture (60 mg, 0.07 mmol) was acetylated under standard conditions by treatment with pyridine (5 mL) and an excess of acetic anhydride (0.66 mL, 0.7 mmol). Concentration in vacuo and purification by thin-layer chromatography (20% EtOAc/hexane) gave three different compounds which were later assigned as a diastereomeric mixture of  $\alpha$ -disaccharides **28** (25 mg, 40%), and enantiomerically pure  $\beta$ -disaccharides **29** (12 mg, 19%) and **30** (13 mg, 21%).

A different fraction of the **21** and **22** mixture (60 mg, 0.07 mmol) was dissolved in DMF (5 mL), cooled to 0 °C and treated portion-wise with 60% NaH (5.6 mg, 0.14 mmol). After 30 min, benzyl bromide (10  $\mu$ L, 0.084 mmol) was added. The reaction was warmed to room temperature and stirred overnight. The solution was carefully quenched with water, diluted with Et<sub>2</sub>O, washed with H<sub>2</sub>O, dried and concentrated. The product was then purified by flash chromatography (10% EtOAc/hexane) to give a mixture of anomers  $\alpha$ , $\beta$ -**31**.

**DL-4-*O*-Acetyl-6-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl- $\alpha$ -D-mannopyranosyl)-1,3,5-*O*-pentylidene-*myo*-inositol (28):** <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.87 (t,  $J$  = 7.3 Hz, 3 H), 1.26–1.34 (m, 2 H), 1.38–1.46 (m, 2 H), 1.64–1.68 (m, 2 H), 1.82 (s, 3 H, Ac), 3.70 (t,  $J$  = 9.4 Hz, 1 H), 3.76–3.80 (m, 1 H), 3.92 (m, 1 H), 3.99–4.07 (m, 4 H), 4.15–4.19 (m, 1 H), 4.24–4.27 (m, 0.6 H), 4.30 (d,  $J$  = 11.5 Hz, 0.4 H), 4.42–4.57 (m, 0.6 H), 4.64 (dd,  $J$  = 4.8, 12.2 Hz, 1 H), 4.67–4.70 (m, 2 H), 4.73 (dd,  $J$  = 3.6, 12.3 Hz, 1 H), 4.80 (dd,  $J$  = 4.6, 12.3 Hz, 1 H), 4.87 (dd,  $J$  = 2.8, 10.8 Hz, 1 H), 5.11 (d,  $J$  = 2.4 Hz, 0.4 H), 5.12 (d,  $J$  = 2.1 Hz, 0.6 H), 5.24–5.26 (m, 0.6 H), 5.29–5.31 (m, 0.4 H), 7.15–7.40 (m, 25 H) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  (selected signals) = 98.27 (d,  $J$  = 168.4 Hz, C-1'), 98.32 (d,  $J$  = 168.4 Hz, C-1') ppm. API-ES<sup>+</sup>:  $m/z$  = 923.8 [M + Na]<sup>+</sup>.

**D- and L-4-*O*-Acetyl-6-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl- $\beta$ -D-mannopyranosyl)-1,3,5-*O*-pentylidene-*myo*-inositol (29/30). Isomer**

**1:** [ $\alpha$ ]<sub>D</sub> = –29.2 ( $c$  = 0.3, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.85 (t,  $J$  = 7.3 Hz, 3 H), 1.25–1.32 (m, 2 H), 1.42–1.48 (m, 2 H), 1.67–1.70 (m, 2 H), 1.75 (s, 3 H), 3.50 (dd,  $J$  = 3.0, 9.4 Hz, 1 H), 3.46–3.52 (m, 1 H), 3.74–3.75 (m, 2 H), 3.88 (t,  $J$  = 9.6 Hz, 1 H), 3.97 (d,  $J$  = 2.9 Hz, 1 H), 4.24 (m, 1 H), 4.28–4.29 (m, 1 H), 4.32–4.34 (m, 1 H), 4.40 (d,  $J$  = 11.8 Hz, 1 H), 4.49–4.57 (m, 8 H), 4.61 (m, 1 H), 4.93 (d,  $J$  = 10.8 Hz, 1 H), 4.99 (d,  $J$  = 12.4 Hz, 1 H), 5.05 (d,  $J$  = 12.4 Hz, 1 H), 5.33 (m, 1 H, 4-H), 7.19–7.56 (m, 25 H) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 13.9, 20.6, 22.5, 27.7, 37.0, 66.1, 66.6, 68.7, 69.6, 69.9, 71.5, 71.6, 71.7, 72.9, 73.3, 73.7, 74.7, 75.1, 76.1, 81.9, 100.2 (d,  $J$  = 157.2 Hz), 109.8, 127.43, 127.48, 127.49, 127.59, 127.64, 127.67, 128.0, 128.1, 128.32, 128.33, 128.5, 128.8, 137.5, 138.0, 138.30, 138.35, 138.6, 170.11 ppm. API-ES<sup>+</sup>:  $m/z$  = 901.5 [M + H]<sup>+</sup>. C<sub>54</sub>H<sub>60</sub>O<sub>12</sub> (900.41): calcd. C 71.98, H 6.71; found C 72.06, H 6.97.

**Isomer 2:** [ $\alpha$ ]<sub>D</sub> = –12.2 ( $c$  = 0.4, CHCl<sub>3</sub>). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.85 (t,  $J$  = 7.3 Hz, 3 H), 1.25–1.31 (m, 2 H), 1.43–1.49 (m, 2 H), 1.68–1.71 (m, 2 H), 1.76 (s, 3 H, Ac), 3.47 (ddd,  $J$  = 1.9, 6.0, 9.6 Hz, 1 H), 3.51 (dd,  $J$  = 3.0, 9.4 Hz, 1 H), 3.70 (dd,  $J$  = 1.9, 10.7 Hz, 1 H), 3.74 (dd,  $J$  = 6.0, 10.7 Hz, 1 H), 3.90 (t,  $J$  = 9.5 Hz, 1 H), 3.98 (d,  $J$  = 3.0 Hz, 1 H), 4.15 (m, 1 H), 4.23 (dt,  $J$  = 1.6, 3.8 Hz, 1 H), 4.28–4.31 (m, 2 H), 4.41 (d,  $J$  = 11.9 Hz, 1 H), 4.48–4.55 (m, 6 H), 4.66 (br. s, 1 H), 4.70–4.71 (m, 1 H), 4.93 (d,  $J$  = 10.8 Hz, 1 H), 5.02 (d,  $J$  = 12.4 Hz, 1 H), 5.08 (d,  $J$  = 12.4 Hz, 1 H), 5.31 (m, 1 H), 7.19–7.56 (m, 25 H) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 13.9, 20.6, 22.5, 24.7, 37.0, 66.8, 67.3, 68.8, 69.4, 70.2, 71.10, 71.14, 71.7, 72.7, 73.2, 73.4, 73.5, 74.7, 75.2, 75.9, 81.7, 101.4 (d,  $J$  = 153.0 Hz), 109.8, 127.4, 127.5, 127.6, 127.7, 127.9, 128.1, 128.2, 128.3, 128.9, 137.5, 138.0, 138.21, 138.23, 138.5, 170.1 ppm. API-ES<sup>+</sup>:  $m/z$  = 901.8 [M + H]<sup>+</sup>, 923.8 [M + Na]<sup>+</sup>. C<sub>54</sub>H<sub>60</sub>O<sub>12</sub> (900.41): calcd. C 71.98, H 6.71; found C 71.87, H 6.64.

**D-4,6-Di-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl- $\alpha$ -D-mannopyranosyl)-1,3,5-*O*-pentylidene-*myo*-inositol ( $\alpha$ -31):** The pseudodisaccharide  $\alpha$ -**32** (50 mg, 0.052 mmol) was subjected to the usual conditions of deacylation by treatment with a freshly prepared solution of NaOMe (1 mL, 0.1 mmol). The reaction mixture was then neutralized with Amberlite H<sup>+</sup> resin, filtered, and concentrated. The residue was submitted to the standard benzylation conditions by treatment with NaH (4 mg, 0.1 mmol) and BnBr (0.075 mL, 0.06 mmol). Extractive work-up and purification by flash chromatography (20% EtOAc/hexane) gave  $\alpha$ -**31** (29 mg, 60%)-[ $\alpha$ ]<sub>D</sub> = –9.4 (CHCl<sub>3</sub>,  $c$  = 0.52). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.79 (t,  $J$  = 7.2 Hz, 3 H), 1.15–1.25 (m, 2 H), 1.28–1.39 (m, 2 H), 1.49–1.60 (m, 2 H), 3.59 (dd,  $J$  = 10.6, 1.0 Hz, 1 H), 3.68 (dd,  $J$  = 10.6, 4.3 Hz, 1 H), 3.81 (m, 1 H), 3.91–3.99 (m, 3 H), 4.06–4.07 (m, 1 H), 4.10–4.21 (m, 3 H), 4.28–4.36 (m, 3 H), 4.39–4.47 (m, 3 H), 4.49–4.53 (m, 2 H), 4.56–4.59 (m, 3 H), 4.64 (d,  $J$  = 12.9 Hz, 1 H), 4.69 (d,  $J$  = 12.5 Hz, 1 H), 4.79 (d,  $J$  = 10.8 Hz, 1 H), 5.01 (d,  $J$  = 1.8 Hz, 1 H, 1 $\alpha$ -H), 7.07–7.32 (m, 30 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  (selected peak) = 14.0, 22.5, 24.8, 37.0, 66.9, 68.1, 69.3, 71.1, 71.3, 71.4, 72.1, 72.3, 72.7, 73.2, 73.9, 74.1, 74.9, 75.0, 75.3, 80.2, 98.3, 109.7 ppm. API-ES<sup>+</sup>:  $m/z$  = 971.7 [M + Na]<sup>+</sup>. C<sub>59</sub>H<sub>64</sub>O<sub>11</sub> (948.841): calcd. C 74.66, H 6.80; found C 74.26, H 6.71.

**D-4,6-Di-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl- $\beta$ -D-mannopyranosyl)-1,3,5-*O*-pentylidene-*myo*-inositol ( $\beta$ -31):** The pseudodisaccharide  $\beta$ -**22** (30 mg, 0.035 mmol) was subjected to the usual benzylation conditions by treatment with NaH (2.8 mg, 0.07 mmol) and BnBr (0.005 mL, 0.042 mmol). Extractive work-up and purification by flash chromatography (20% EtOAc/hexane) gave  $\beta$ -**31** (30 mg, 90%) [ $\alpha$ ]<sub>D</sub> = +10.1 (CHCl<sub>3</sub>,  $c$  = 1.7). <sup>1</sup>H NMR (300 MHz,

$\text{CDCl}_3$ ):  $\delta$  (selected peaks) = 4.56 (d,  $J$  = 1.9 Hz, 1 H) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  (selected signals) = 13.9, 22.5, 24.8, 37.2, 66.9, 68.2, 69.2, 71.1, 71.4, 71.5, 72.9, 73.2, 74.3, 74.7, 75.1, 75.9, 77.2, 81.8, 101.6, 109.7 ppm. API-ES<sup>+</sup>:  $m/z$  = 971.7 [ $\text{M} + \text{Na}$ ]<sup>+</sup>.  $\text{C}_{59}\text{H}_{64}\text{O}_{11}$  (948.841): calcd. C 74.66, H 6.80; found C 74.82, H 6.67.

**DL-4-*O*-Acetyl-6-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzoyl- $\alpha$ -D-mannopyranosyl)-1,3,5-*O*-pentylidene-myio-inositol (32):** Acetylation of **24** (47 mg, 0.052 mmol) under standard conditions by treatment with pyridine (5 mL) and an excess of acetic anhydride (0.49 mL, 0.52 mmol) gave after solvent evaporation a crude material, which was separated by flash chromatography (10% EtOAc/hexane) to afford **32** (45 mg, 90%) as a 1:1 mixture of diastereomers.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.85 (t,  $J$  = 7.2 Hz, 3 H), 1.16–1.28 (m, 2 H), 1.31–1.35 (m, 2 H), 1.42–1.59 (m, 2 H), 1.74 (s, 1.5 H, Ac), 1.84 (s, 1.5 H, Ac), 4.04–4.06 (m, 1 H), 4.13 (m, 1 H), 4.23 (m, 1 H), 4.31–4.37 (m, 1.5 H), 4.41–4.54 (m, 2.5 H), 4.58 (m, 1 H), 4.63 (m, 1 H), 4.71–4.76 (m, 1 H), 5.10 (m, 0.5 H), 5.20 (m, 0.5 H), 5.28 (m, 0.5 H), 5.29 (m, 0.5 H), 5.70 (m, 0.5 H), 5.72 (m, 0.5 H), 5.96 (dd,  $J$  = 3.2, 10.0 Hz, 1 H), 6.04 (t,  $J$  = 10.0 Hz, 0.5 H), 6.05 (t,  $J$  = 10.0 Hz, 0.5 H), 7.13–8.07 (m, 25 H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 13.9, 20.6, 22.4, 24.8, 36.9, 63.0, 66.3, 66.5, 66.9, 68.5, 69.3, 69.4, 69.6, 69.7, 70.0, 70.4, 70.6, 70.7, 70.8, 70.9, 71.2, 71.9, 72.1, 73.6, 73.7, 98.3, 98.4, 109.9, 127.4, 127.5, 128.0, 128.1, 128.3, 128.4, 128.47, 128.5, 128.6, 128.9, 129.1, 129.6, 129.7, 129.8, 133.1, 133.2, 133.5, 133.6, 137.2, 137.3, 165.4, 165.5, 166.1, 169.9, 170.0 ppm. API-ES<sup>+</sup>:  $m/z$  = 971.7 [ $\text{M} + \text{Na}$ ]<sup>+</sup>.

**Glycosidation of Alcohol 25 with Thioglycoside 16:** Application of the general procedure for the glycosidation reaction to diol ( $\pm$ )-**25** (93 mg, 0.206 mmol) and the glycosyl donor **16** (156 mg, 0.247 mmol) afforded a material that was subjected to flash chromatography (10% EtOAc/hexane) and then dissolved in THF (5 mL) and treated with tetrabutylammonium fluoride (189 mg, 0.6 mmol). Aqueous extraction, concentration and flash chromatography provided disaccharide **33** (130 mg, 90%).

A fraction of this anomeric mixture (30 mg, 0.035 mmol) was acetylated under standard conditions by treatment with pyridine (5 mL) and an excess of acetic anhydride (0.33 mL, 0.35 mmol). Concentration in vacuo and purification by flash chromatography (20% EtOAc/hexane) gave **34** (29 mg, 93%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  (selected signals for  $\alpha$  anomers) = 2.12 (s, 3 H), 2.15 (s, 3 H), 4.92 (d,  $J$  = 1.8 Hz, 1 H), 4.95 (d,  $J$  = 1.8 Hz, 1 H), 5.12 (t,  $J$  = 1.5 Hz, 1 H), 5.18 (t,  $J$  = 1.7 Hz, 1 H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  (selected signals for  $\alpha$  anomers) = 63.09 (d,  $J$  = 152.5 Hz), 96.40 (d,  $J$  = 169.3 Hz), 97.38 (d,  $J$  = 169.5 Hz) ppm. API-ES<sup>+</sup>:  $m/z$  = 902.7 [ $\text{M} + \text{H}$ ]<sup>+</sup>.

A different fraction of the **33** mixture (100 mg, 0.12 mmol) was dissolved in DMF (5 mL), cooled to 0 °C and treated portionwise with 60% NaH (9.6 mg, 0.24 mmol). After 30 min, benzyl bromide (0.172 mL, 0.144 mmol) was added. The reaction was warmed to room temperature and stirred overnight. The solution was carefully quenched with water, diluted with  $\text{Et}_2\text{O}$ , washed with  $\text{H}_2\text{O}$ , dried and concentrated. The product was then purified by flash chromatography (10% EtOAc/hexane) to give a mixture of anomers **35**.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  (selected signals) = 4.84 (d,  $J$  = 1.4 Hz, 1 H), 4.97 (d,  $J$  = 1.8 Hz, 1 H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  (selected signals) = 96.9, 98.0 ppm. API-ES<sup>+</sup>:  $m/z$  = 949.7 [ $\text{M} + \text{H}$ ]<sup>+</sup>, 971.7 [ $\text{M} + \text{Na}$ ]<sup>+</sup>.

**4,6-Di-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-benzoyl- $\alpha$ -D-mannopyranosyl)-1,3,5-*O*-pentylidene-myio-inositol (36):** Acetylation of **17** (50 mg, 0.06 mmol) by treatment with pyridine (3 mL) and an excess of acetic anhydride (0.56 mL, 0.6 mmol) afforded after flash

chromatography (20% EtOAc/hexane) disaccharide **36** (50 mg, 92%).  $[\alpha]_{\text{D}} = -38.3$  ( $\text{CHCl}_3$ ,  $c$  = 1.1).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.86 (t,  $J$  = 7.3 Hz, 1 H), 1.26–1.33 (m, 2 H,  $\text{CH}_2$ ), 1.40–1.51 (m, 2 H,  $\text{CH}_2$ ), 1.66 (t,  $J$  = 8.2 Hz, 2 H), 1.94 (s, 3 H), 2.03 (s, 3 H), 4.04 (pt,  $J$  = 1.8 Hz, 1 H), 4.35–4.36 (m, 1 H), 4.42 (dd,  $J$  = 5.14, 12.0 Hz, 1 H), 4.43–4.45 (m, 1 H), 4.61 (dd,  $J$  = 2.3, 12.1 Hz, 1 H), 4.62–4.64 (m, 1 H), 4.72 (ddd,  $J$  = 2.2, 5.1, 10.1 Hz, 1 H), 5.21 (m, 1 H), 5.33 (d,  $J$  = 1.9, 3.2 Hz, 1 H), 5.95 (dd,  $J$  = 3.3, 10.1 Hz, 1 H), 6.05 (t,  $J$  = 10.1 Hz, 1 H) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 14.0, 20.7, 20.8, 22.4, 24.7, 36.8, 62.9, 66.0, 66.7, 67.9, 69.5, 69.6, 69.9, 69.9, 70.2, 70.9, 98.3 (d,  $J$  = 171.1 Hz), 110.0, 128.3, 128.41, 128.43, 128.6, 128.8, 129.0, 129.1, 129.6, 129.7, 129.8, 133.1, 133.2, 133.5, 133.7, 165.4, 165.5, 165.7, 166.1, 169.0, 169.1 ppm. API-ES<sup>+</sup>:  $m/z$  = 909.5 [ $\text{M} + \text{H}$ ]<sup>+</sup>.

**2,4,6-Tri-*O*-acetyl-1,3,5-*O*-pentylidene-myio-inositol (37):** Acetylation of **13** (100 mg, 0.4 mmol) under standard conditions by treatment with pyridine (5 mL) and an excess of acetic anhydride (3.7 mL, 4 mmol) afforded after flash chromatography (20% EtOAc/hexane) triacetate **37**.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 0.88 (t,  $J$  = 7.2 Hz, 1 H), 1.31 (sext,  $J$  = 7.2 Hz, 2 H), 1.38–1.48 (m, 2 H), 1.68–1.73 (m, 2 H), 2.08 (s, 6 H), 2.19 (s, 3 H), 4.32 (dt,  $J$  = 1.83, 4.52 Hz, 2 H), 4.52 (m), 5.12 (t,  $J$  = 1.8 Hz, 1 H), 5.44 (t,  $J$  = 3.9 Hz, 2 H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 14.0, 20.8, 22.5, 24.6, 36.8, 62.6, 66.4, 67.9, 69.7, 110.1, 169.3, 170.7 ppm. API-ES<sup>+</sup>:  $m/z$  = 373.3 [ $\text{M} + \text{H}$ ]<sup>+</sup>, 395.2 [ $\text{M} + \text{Na}$ ]<sup>+</sup>.

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