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Synthesis of a Pentasaccharide Corresponding to the Repeating Unit of the Exopolysaccharide from *Cryptococcus neoformans* Serovar D

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Abstract—The assembly of the pentasaccharide repeating unit of the exopolysaccharide from *Cryptococcus neoformans* serovar D (i.e. **1**) is described. The glucuronic acid residue in **1** is introduced as a glucopyranoside and oxidized in a later stage of the synthesis. Thus, iodonium ion-assisted glycosylation of the partially protected methyl mannopyranoside **11** with ethylthio donor **14** gave, after selective deprotection, disaccharide **18**. Elongation of the latter with D-glucopyranoside **35** gave trisaccharide **36**. Subsequent protective group manipulations yielded the acceptor **37**. Condensation of disaccharide donor **31** with trisaccharide acceptor **37** yielded pentasaccharide **38**. Protective group manipulations of **38** afforded **42**, the glucoside of which was oxidized to yield the corresponding glucuronide **44**. Hydrogenolysis of **44** gave the target pentasaccharide **1**. Copyright © 1996 Elsevier Science Ltd

Introduction

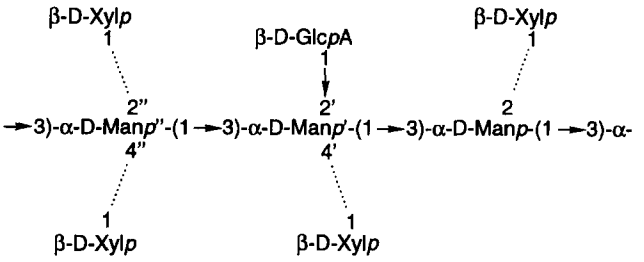
In the last few years it has become apparent that *Cryptococcus neoformans* is a primary cause of opportunistic infections in patients diagnosed with AIDS.[1] The yeast *C. neoformans* is a pulmonary pathogen and can disseminate to the central nervous system causing meningoencephalitis.[2]

The major exopolysaccharide (EPS) of *C. neoformans* is a high molecular weight glucuronoxylomannan (GXM), which is responsible for the serological properties and its prominent virulency. The four specified GXMs (A, B, C and D) comprise a core of repeating units (see Figure 1) containing three mannopyranosides (Man*p*) and one glucuronic acid (Glc*p*A), while xylopyranosides (Xyl*p*) are added in increments of one to four residues.[3–6] Serotypes A and D are substituted with Xyl*p* at *O*-2, whereas serotypes B and C are substituted at *O*-2 and *O*-4.

As part of an ongoing project to synthesize cell-wall components,[7] we here present a stereoselective synthesis of the repeating unit of *C. neoformans* serovar D[6] (i.e. **1** in Fig. 2), the α-(1→3)-linked tri-D-mannopyranan unit of which is substituted at O-2′ and O-2″ with a β-D-Glc*p*A and a β-D-Xyl*p* units, respectively.

Results and Discussion

The synthesis of a spacer-containing tetrasaccharide corresponding to the repeating unit of the EPS of *C. neoformans* serotype A was reported earlier by Garegg et al.[8] A major problem in the assembly of a repeating unit of the EPS of *C. neoformans* entails *inter alia* the introduction of a β-D-glucuronic acid residue at the axially orientated *O*-2 position of a mannopyranoside moiety.[9,10] In order to circumvent this problem, we explored the possibility whether a glucoside could be converted into the required glucuronide in a later stage of the synthesis. To this end, we first examined the outcome of the glycosylation of model acceptor[11]



Manp / serovar	2	2″	4′	4″
A	X	X		
B	X	X	X	
C	X	X	X	X
D		X		

Key to the Xyl*p* (X) substitution pattern.
Dotted lines indicate the position of Xyl*p* substitution.

Figure 1.

methyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**2**) (see Scheme 1) with the readily accessible[12] ethyl 2,3,4-tri-*O*-benzoyl-6-*O*-(*t*-butyldimethylsilyl)-1-thio-β-D-glucopyranoside (**3**). However, coupling of **2** with **3** in the presence of *N*-iodosuccinimide (NIS) and a catalytic amount of triflic acid (TfOH)[13] was not successful. Fortunately, iodonium ion-mediated condensation of **2** with the more reactive donor ethyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**6**) (see Scheme 1) gave the expected β-linked disaccharide **7** in 83% yield. Compound **6** was prepared, in an overall yield of 74%, by regioselective benzylation of the stannylidene derivative[14] of the known[15] ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**4**) followed by benzoylation of **5**.

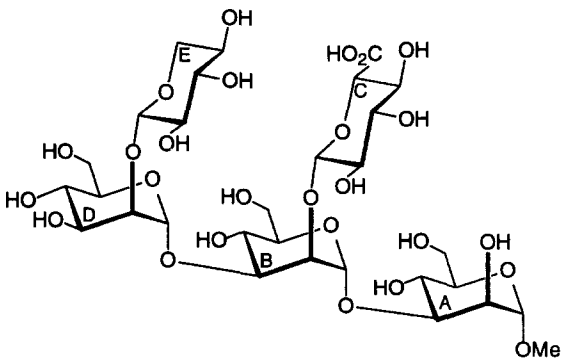
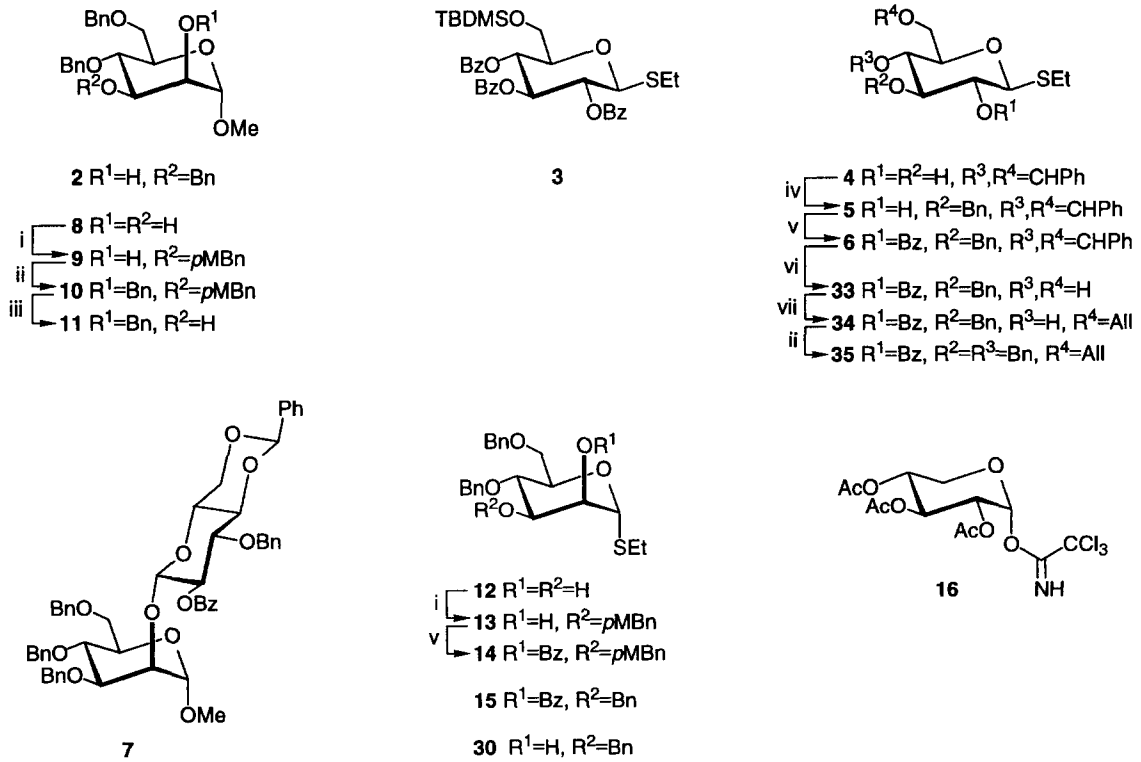


Figure 2.

The favourable outcome of the latter condensation urged us to prepare the partially protected glucoside containing derivative **42** (see Scheme 2) following a sequential glycosylation strategy A→AB→ABC→ABC-D→ABCDE. It was expected that oxidation of the resulting pentasaccharide fragment **42** would afford, after hydrogenation, the target pentasaccharide **1**.[16]

Synthesis of the additional mannopyranosyl building blocks (i.e. **11** and **14**) was carried out as depicted in Scheme 1. Methyl 2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**11**, unit A) was prepared from known[17] methyl 4,6-di-*O*-benzyl-α-D-mannopyranoside (**8**) by the following three-step procedure. *p*-Methoxybenzylation of the stannylidene complex of **8** followed by benzylation of **9** and oxidative removal of the *p*-methoxybenzyl group in **10** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[18] (DDQ) yielded the required building unit **11** in an overall yield of 62%. Donor **14** necessary for the introduction of mannosyl unit B was obtained in a similar fashion from ethyl 4,6-di-*O*-benzyl-1-thio-α-D-mannopyranoside (**12**).[19] Regioselective *p*-methoxybenzylation of **12** and subsequent benzoylation of **13** gave the requisite donor (**14**) in an overall yield of 65% based on **12**. The known[20,21] ethyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (**15**) and 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl imidate (**16**) were used for the introduction of units D and E, respectively.

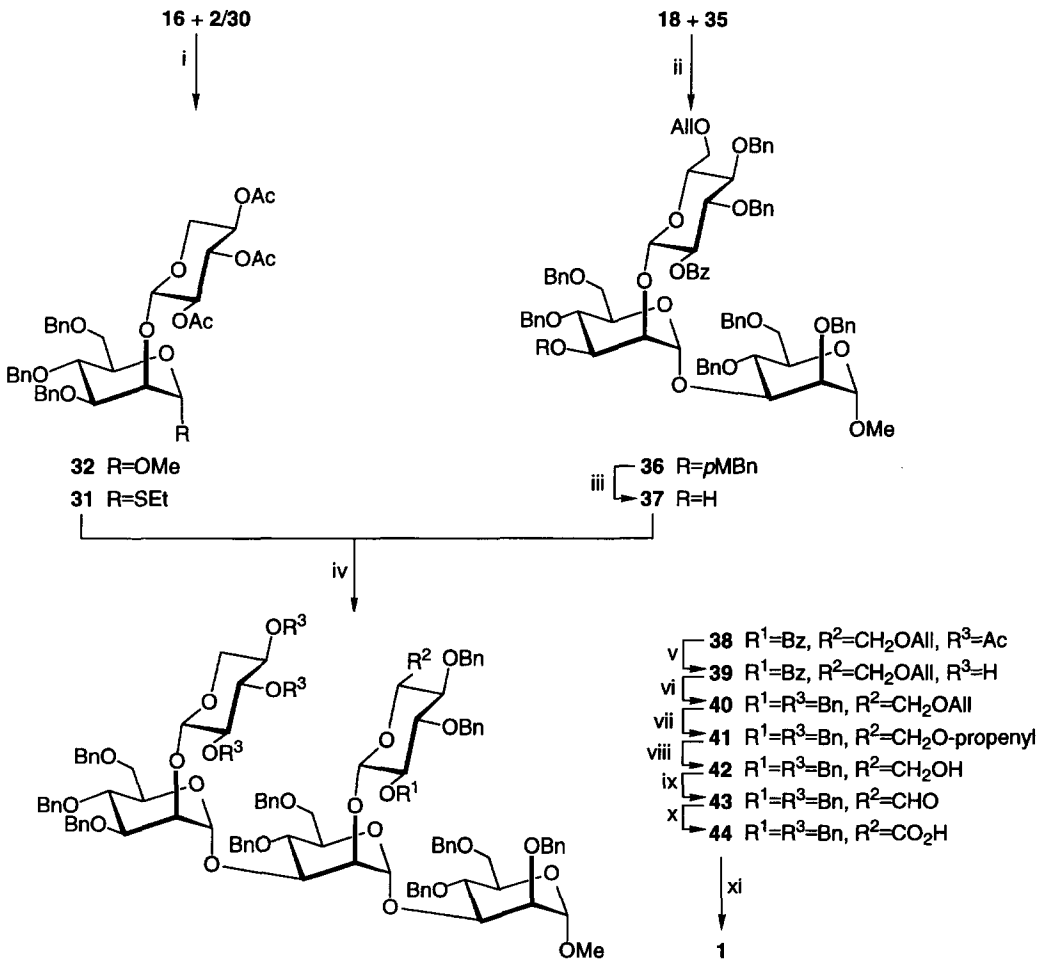
The sequential assembly of the pentasaccharide **1** is outlined in Scheme 3. The terminal acceptor **11** was



Scheme 1. Reagents and conditions: (i) Bu_2SnO, MeOH, reflux, 1.5 h; *p*MBnCl, CsF, NaI, DMF, 17 h, **9** 79%, **13** 75%; (ii) BnBr, NaH, DMF, 1.5 h, **10** 97%, **35** 82%; (iii) DDQ, dichloromethane–water, 1 h, 81%; (iv) Bu_2SnO, MeOH, reflux, 1.5 h; BnBr, CsF, DMF, 17 h, 84%; (v) BzCl, pyridine, 1.5 h, **6** 88%, **14** 87%; (vi) 80% HOAc, 1 h, 85%; (vii) Bu_2SnO, MeOH, reflux, 1.5 h; AllBr, CsF, DMF, 18 h, 78%.

mannosylated with donor **14** in the presence of NIS/TfOH(cat.) to yield disaccharide **17**, as evidenced by NMR spectroscopy (e.g. $\delta_{H\text{-}1'}$ 5.32, $J_{1,2}=1.9$ Hz). Debenzoylation of **17** and subsequent NIS/TfOH(cat.)-mediated glucosylation of the resulting acceptor **18** with donor **6** gave trisaccharide **19**. Prior to the elongation of **19** to give tetrasaccharide **24**, the following protective group manipulations were carried out. Zemplén type debenzoylation of **19** (→**20**) followed by standard benzylation provided the fully protected derivative **21**. Regioselective ring-opening[22] of the benzylidene acetal in **21** with aluminium trichloride and borane-triethylamine complex in toluene was accompanied by concomitant removal of the *p*-methoxybenzyl group resulting in a low recovery of **22**. The latter side-reaction prompted us to perform the reductive ring-opening of the benzylidene acetal at a later stage of the synthesis. Thus, selective removal of the *p*-methoxybenzyl group in **21** with DDQ gave the partially protected trisaccharide **23**, which was condensed with mannopyranoside **15** under the agency of NIS/TfOH(cat.) to yield tetrasaccharide **24**. Unfortunately, regioselective reductive ring-opening of the benzylidene acetal in **24**, under the above described conditions (**21**→**22**), led to an intractable mixture of products. On the other hand, removal of the benzylidene function in **24** by acid hydrolysis at high temperature afforded diol **25** in 83% yield. Regioselective silylation of **25** with *t*-butyldimethylsilyl chloride (TBDMS-Cl) as well as subsequent introduction of the benzyloxymethyl (BOM) group (**26**→**27**) proceeded rather sluggishly. Debenzoylation of **27** gave the partially protected tetrasaccharide fragment **28** in an overall yield of 59% based on **25**. Glycosylation of **28** with xylopyranosyl imidate **16** in the presence of trimethylsilyl triflate (TMSOTf) was unsuccessful and resulted in the isolation of the desilylated tetrasaccharide **29**.

The outcome of the latter glycosylation urged us to pursue an alternative strategy towards the construction of pentasaccharide **1**. Earlier studies[23] revealed that condensation of a 2-*O*-glycosylated mannopyranoside donor with an acceptor may proceed with a high

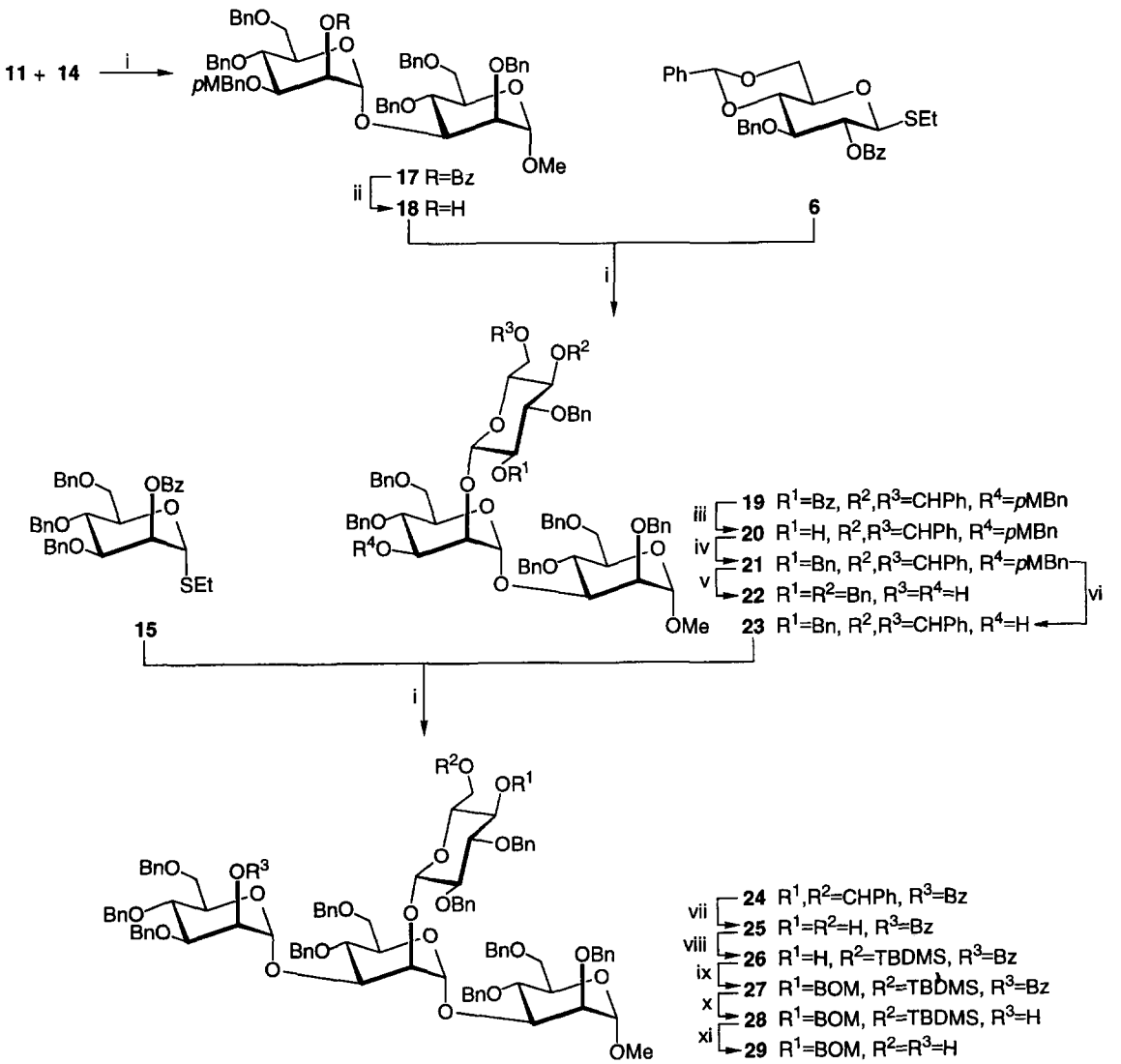


Scheme 2. Reagents and conditions: (i) TMSOTf, 1,2-dichloroethane, −40 °C→20 °C, **31** 5 h, 38%, **32** 1 h, 68%; (ii) NIS/TfOH (cat.), 1,2-dichloroethane-Et_2O, −30 °C, 15 min, 81%; (iii) DDQ, dichloromethane–water, 1 h, 82%; (iv) see ii, 0 °C, 67%; (v) KO*t*-Bu, MeOH, 20 h, 73%; (vi) BnBr, NaH, DMF, 3 h, 88%; (vii) $Ir(COD)[PCH_3(Ph)_2]_2PF_6$, 1,2-dichloroethane, 70 h; (viii) HCl-MeOH (0.5 M), 22 h, 78% (over 2 steps); (ix) ClCOCOCl, DMSO, 1.5 h; (x) $NaClO_2$, 2-Me-2-butene, NaH_2PO_4, *t*-BuOH, water, 20 h; (xi) Pd(C), H_2, *t*-BuOH-water, 38 h, 57% (over 3 steps).

degree of α-stereoselectively. On the basis of above information, the block-coupling of trisaccharide acceptor **37** (ABC) with disaccharide donor **31** (DE) was explored. In addition, the more stabile allyl group, instead of the TBDMS group, was selected as a temporary hydroxyl protecting group at HO-6 of the glucopyranoside in **37**.

The route of synthesis to donor **31** (DE) is depicted in Scheme 2 and entails TMSOTf-mediated glycosylation of known[20] ethyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (**30**, in Scheme 1) with xylopyranosyl imidate **16** to give disaccharide **31** in a low yield (38%). In this respect, it is of interest to note that a similar coupling of donor **16** with the corresponding 1-*O*-methyl acceptor **2** gave disaccharide **32** in a more acceptable yield of 68%. The difference in yield may be explained by the presence of the anomeric ethylthio group, which reduces the reactivity of the axial hydroxyl in acceptor **30**.

Trisaccharide acceptor **37** can be assembled by glycosylation of the earlier prepared disaccharide acceptor **18** with ethyl 6-*O*-allyl-2-*O*-benzoyl-3,4-di-*O*-benzyl-1-thio-β-D-glucopyranoside (**35**), followed by selective deprotection of the resulting trisaccharide **36**. The glucopyranoside donor **35** was accessible (see Scheme 1) by acid hydrolysis of the benzylidene group in **6**, followed by regioselective allylation of the in situ prepared stannylidene derivative of **33** and benzylation of the resulting **34**. Iodonium ion-assisted condensation of acceptor **18** with donor **35** afforded exclusively the β-linked trisaccharide **36**, as gauged by ^{13}C NMR (e.g. $\delta_{C\text{-}Glcp}$ 100.4, $^1J_{C,H} = 155.3$ Hz). Oxidative removal of the



Scheme 3. Reagents and conditions: (i) NIS/TfOH(cat.), 1,2-dichloroethane-Et_2O, 0 °C, 15 min, **17** 84%, **19** 88%, **24** 94%; (ii) KO*t*-Bu, MeOH, 48 h, 85%; (iii) KO*t*-Bu, MeOH, 96 h, 98%; (iv) BnBr, NaH, DMF, 85%; (v) $AlCl_3$, $Et_3N{\cdot}BH_3$, toluene, 30 min, 42%; (vi) DDQ, dichloromethane–water, 3 h, 75%; (vii) 80% HOAc, reflux, 2 h, 83%; (viii) TBDMSCl, DMAP, pyridine, 20 h, 78%; (ix) BOMCl, DIPEA, *n*-Bu_4NI, CH_3CN, 18 h, 76%; (x) KO*t*-Bu, dioxane-MeOH, 55 h, 92%; (xi) TMSOTf, 1,2-dichloroethane, −40 °C→20 °C, 5.5 h, 73%.

p-methoxybenzyl group in **36** with DDQ gave trisaccharide acceptor **37** in an overall yield of 66% based on **18**.

At this stage, we turned our attention to the crucial block-coupling of disaccharide **31** with trisaccharide **37**. Glycosylation of acceptor **37** with donor **31** under the agency of NIS and catalytic TfOH gave, after gel-filtration using Sephadex LH20, pentasaccharide **38** in 67% yield. Conversion of **38** to pentasaccharide **42** containing a HO-6 glucoside residue could be achieved by the following protective group manipulations. Zemplén type deacylation of pentasaccharide **38** afforded, after purification by column chromatography, homogeneous **39**.

Surprisingly, analysis of the ^{13}C NMR spectrum of **39** revealed that the benzoyl group at O-2 in the glucopyranoside residue survived Zemplén deacylation. Fortunately, benzylation of compound **39** with sodium hydride and benzyl bromide was accompanied by replacement of the benzoyl by a benzyl group to afford the pentasaccharide **40**, as evidenced by ^{13}C NMR. Two-step deallylation[24] of compound **40** via iridium-catalysed isomerization of **40** and subsequent acid hydrolysis of the resulting propenyl ether in **41** gave the partially protected pentasaccharide **42**. The key conversion of the glucoside in **42** into the corresponding glucuronide **44** was achieved successfully in two steps. Swern oxidation of **42** yielded the *gluco*-hexodialdo-1,5-pyranosyl derivative **43**, which was further oxidized under buffered conditions with sodium chlorite in the presence of 2-methyl-2-butene,[25] to give the protected glucuronic acid derivative **44**. Finally, removal of the benzyl groups in **44** by hydrogenolysis resulted, after purification by gel filtration, in the isolation of target pentasaccharide **1**, the ^1H, ^{13}C NMR and MS data of which are in complete accordance with the assigned structure: Man*p* $\delta_{H\text{-}1}$ 4.75, 5.20, 5.22 ($J_{1,2}=1.9$, 1.7, and 1.2 Hz, respectively), Glc*p*A $\delta_{H\text{-}1}$ 4.48 ($J_{1,2}=7.8$ Hz), Xyl*p* $\delta_{H\text{-}1}$ 4.38 ($J_{1,2}=7.7$ Hz).

The successful assembly of pentasaccharide **1** clearly demonstrates that the oxidation of a glucoside into a glucuronide presents a convenient approach *en route* to glucuronic acid containing oligosaccharides. Further, the synthetic approach to pentasaccharide **1** described here may be of great value for future development of serodiagnostics and vaccines of *C. neoformans*.

Experimental

General methods and materials

Toluene, 1,2-dichloroethane and dichloromethane were distilled from P_2O_5. Methanol was dried by refluxing with magnesium methoxide, and subsequently distilled. *N*,*N*-Dimethylformamide (DMF) was stirred with calcium hydride for 19 h, then distilled under reduced pressure. Pyridine was refluxed for 18 h in the presence of calcium hydride and then distilled. Diethyl ether was distilled from $LiAlH_4$. Acetonitrile (p.a. Rathburne) was dried over molecular sieves 4 Å (Aldrich). Tetrahydrofuran (THF, p.a. Merck) was dried over molecular sieves 4 Å before use. Toluene and diethyl ether were stored over sodium wire. Methanol was stored over molecular sieves 3 Å. Dichloromethane, 1,2-dichloroethane and DMF were stored over molecular sieves 4 Å. Solvents used for column chromatography were of technical grade and distilled before use.

Reactions were performed under anhydrous conditions at room temperature, unless stated otherwise. Solvents were evaporated under reduced pressure at 40 °C. TLC analyses were conducted on Schleicher & Schüll DC Fertigfolien (F 1500 LS 254). Compounds were visualized by UV light and by charring with H_2SO_4:ethanol (1:4, v/v). Column chromatography was performed on columns of silica gel (Baker, 0.063–0.200 nm). Petroleum ether used for elution of the columns was low-boiling (40–60 °C). Gel filtration was performed on Sephadex LH20 (Pharmacia).

Optical rotations were measured with a Propol polarimeter at 20 °C, for solutions in HPLC-grade chloroform (p.a. Baker). NMR spectra were recorded with a Jeol JNM-FX-200 (^1H and ^{13}C at 200 and 50.1 MHz respectively), a Bruker WM-300 spectrometer equipped with an Aspect 2000 computer (^1H, 300 MHz) and a Bruker 600-DMX spectrometer (^1H and ^{13}C at 600 and 150 MHz, respectively). Chemical shifts are given in ppm (δ) relative to tetramethylsilane as an internal standard. The MS was recorded of compound **1** in a solution in methanol:water (4:1, v/v) with a Finnigan MAT TSQ-70 spectrometer equipped with a custom-made Electrospray Interface (ESI).

Ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (5). The known[14] compound **4** (1.56 g, 5.0 mmol) was dried by evaporation with toluene and subsequently dissolved in methanol (29 mL). The reaction mixture was heated under reflux for 1.5 h in the presence of dibutyltin oxide (1.37 g, 5.5 mmol). The solution was concentrated and the residue was dried by evaporation with toluene. The residue was redissolved in DMF (50 mL) and cesium fluoride (0.99 g, 6.5 mmol) and benzyl bromide (0.89 mL, 7.5 mmol) were added. After stirring for 17 h, the reaction mixture was concentrated and the residue was taken up in diethyl ether (30 mL). The organic layer was washed twice with aq. KF (1 M, 20 mL) and once with water (20 mL), dried ($MgSO_4$), filtered, and concentrated. Compound **5** (1.01 g, 2.5 mmol) was obtained by crystallization with ethyl acetate and petroleum ether. In addition, purification of the filtrate by column chromatography (20→70% ethyl acetate in petroleum ether) yielded compound **5** (0.36 g, 0.9 mmol) and recovered diol **4** (0.39 g, 1.3 mmol). **5**: ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 14.9 (CH_3, SEt), 24.1 (CH_2, SEt), 68.2 (C-6), 74.2 (CH_2, Bn), 70.2, 72.7, 80.7, 81.3 (C-2, C-3, C-4, C-5), 86.2 (C-1), 100.8 (CH, CHPh), 125.7, 127.3, 127.6, 127.8, 128.0, 128.4, 128.6, 128.7 (CH arom), 137.0, 138.1 (qC arom), 165.0 (C=O Bz).

Ethyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (6). To a solution of compound **5** (1.01 g, 2.5 mmol) in pyridine (7 mL) was added benzoyl chloride (0.44 mL, 3.8 mmol). After stirring for 1.5 h, the reaction was quenched with water (2 mL), and the solvents were evaporated. The residue was taken up in ethyl acetate (15 mL), and the resulting solution was washed with water (10 mL) and aq. $NaHCO_3$ (10%, 10 mL), dried ($MgSO_4$), filtered, and concentrated. Crystallization of the crude product from ethyl acetate and light petroleum ether gave compound **6** (1.09 g, 2.2 mmol). $[\alpha]_D$ +25.5° (*c* 1); ^1H NMR (50 MHz, $CDCl_3$): δ 1.22 (t, 3H, CH_3 SEt, $J_{H,H}$ = 7.5 Hz), 2.72 (ABX, 2H, CH_2, SEt), 3.51–3.61 (m, 1H, H-5), 3.78–3.90 (m, 3H, H-3, H-4, H-6), 4.62 (d, 1H, H-1, $J_{1,2}$ 10.0 Hz), 4.76 (AB, 2H, CH_2 Bn), 5.34 (dd, 1H, H-2, $J_{H,H}$ = 8.9 Hz, $J_{H,H}$ = 9.9 Hz), 7.11–7.60 (m, 13H, CH arom), 7.98–8.02 (m, 2H, CH, Bz); ^{13}C ^1H NMR ($CDCl_3$): δ 14.7 (CH_3 SEt), 23.9 (CH_2, SEt), 68.5 (C-6), 74.1 (CH_2, Bn), 70.5, 71.7, 79.1, 81.5 (C-2, C-3, C-4, C-5), 84.2 (C-1), 101.1 (CH CHPh), 125.9, 127.4, 128.0, 128.2, 128.3, 128.9, 129.8 (CH arom), 133.1 (CH Bz), 137.1 (qC arom), 165.0 (C=O Bz). Anal.: calcd for $C_{29}H_{30}O_6S$ (506.62): C, 68.75, H, 5.97; found C, 68.82, H, 6.09%.

Methyl 2-*O*-(2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benylidene-β-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (7). Mannopyranoside acceptor **2** (156 mg, 0.25 mmol) and glucopyranoside donor **6** (152 mg, 0.30 mmol) were dissolved in a mixture of 1,2-dichloroethane:diethyl ether (2:1, v/v, 2 mL). Molecular sieves (4 Å) were added and the mixture was stirred for 20 min and cooled to 0 °C. A suspension of NIS (68 mg, 0.30 mmol) and TfOH (3.3 μL, 37 μmol) in the same solvent mixture was added. After stirring for 15 min, the reaction was quenched with pyridine (0.3 mL) and filtered. The filtrate was diluted with ethyl acetate (15 mL) and washed with aq. $Na_2S_2O_3$ (20%, 10 mL) and aq. $NaHCO_3$ (10%, 10 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated, and the residue was purified by column chromatography (0→20% ethyl acetate in petroleum ether) to give disaccharide **7** (187 mg, 0.21 mmol). ^1H NMR (200 MHz, $CDCl_3$): 3.16 (s, 3H, CH_3 Me), 3.31 (dd, 1H, H-5, $J_{5,4}$ = 6.0 Hz, $J_{5,6}$ = 11.2 Hz), 3.52 (dd, 1H, H-5′, $J_{5,4}$ = 9.7 Hz, $J_{5,6}$ = 4.7 Hz), 3.55–3.66 (m, 2H, H-6), 3.59 (t, 1H, H-4, $J_{4,3} \approx J_{4,5}$ = 10.8 Hz), 3.81 (dd, 1H, H-3, $J_{3,2}$ = 2.7 Hz, $J_{3,4}$ = 7.9 Hz), 3.85 (t, 1H, H-3′, $J_{3,2} \approx J_{3,4}$ = 8.0 Hz), 3.85–3.94 (m, 1H, H-6′), 3.94 (t, 1H, H-4′, $J_{4,3} \approx J_{4,5}$ = 9.1 Hz), 4.02 (dd, 1H, H-2, $J_{2,1}$ = 2.8 Hz, $J_{2,3}$ = 3.4 Hz), 4.22 (AB, 2H, CH_2, Bn), 4.37 (dd, 1H, H-6′, $J_{6,6}$ = 10.3 Hz, $J_{6,5}$ = 4.9 Hz), 4.55 (d, 1H, H-1, $J_{1,2}$ = 2.1 Hz), 4.67 (2× AB, 4H, 2× CH_2, Bn), 4.71 (d, 1H, H-1′, $J_{1,2}$ = 8.3 Hz), 4.77 (AB, 2H, CH_2 Bn), 5.43 (t, 1H, H-2′, $J_{2,1} \approx J_{2,3}$ = 8.4 Hz), 7.05–7.43 (m, 28H, CH arom), 7.95–7.99 (m, 2H, CH Bz); ^{13}C NMR (50 MHz, $CDCl_3$): 54.5 (CH_3 Me), 68.4, 69.8 (C-6, C-6′), 71.6, 72.9, 73.6, 74.7 (4× CH_2, Bn), 66.3, 72.0, 73.0, 74.8, 75.1, 77.6, 78.2, 81.2 (CH sugar rings), 98.0, 100.8, 101.1 (C-1, C-1′, CH CHPh), 125.9, 127.1, 127.3, 127.7, 127.9, 128.0, 128.1, 128.9, 129.6 (CH arom), 130.0, 132.7, 137.1, 137.7, 138.3, 138.5 (qC arom), 164.6 (C=O Bz).

Methyl 4,6-di-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-α-D-mannopyranoside (9). To a solution of mannopyranoside **8** (3.74 g, 10.0 mmol) in methanol (36 mL) was added dibutyltin oxide (2.75 g, 11.0 mmol). The reaction mixture was heated under reflux for 1.5 h. The solvent was evaporated and the residue was dried by repeated evaporation with toluene. The stannylidene derivative was redissolved in DMF (25 mL) and cesium fluoride (1.97 g, 13.0 mmol), *p*-methoxybenzyl chloride (2.05 mL, 15.0 mmol) and sodium iodide (24 mg, 1.0 mmol) were added. After stirring for 19 h, the reaction mixture was concentrated. The residue was taken up in diethyl ether (100 mL) and the organic layer was washed twice with aq. KF (1 M, 70 mL) and once with water (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated. Purification of the crude product by column chromatography (0→30% ethyl acetate in light petroleum ether) yielded **9** (3.93 g, 7.9 mmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.7, 55.1 (2× CH_3 1-*O*-Me, OMe *p*MBn), 69.1 (C-6), 71.4, 73.3, 74.9 (3× CH_2 Bn, *p*MBn), 68.2, 71.1, 74.3, 79.8 (C-2, C-3, C-4, C-5), 100.5 (C-1), 113.8, (CH *p*MBn), 127.5, 127.8, 128.3, 129.5 (CH arom), 130.2 (qC *p*MBn), 138.3, 138.6 (qC Bn), 159.3 (qC *p*MBn).

Methyl 2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (11). Sodium hydride (60%, 0.48 g, 11.9 mmol) and benzyl bromide (1.41 mL, 11.9 mmol) were added at 0 °C to a solution of compound **9** (3.93 g, 7.9 mmol) in DMF (18 mL). After stirring for 1.5 h at room temperature, the solvent was evaporated and the residue was taken up in diethyl ether (100 mL). The solution was washed with water (70 mL) and aq. $NaHCO_3$ (10%, 70 mL), dried ($MgSO_4$), and filtered. The solvents were evaporated and crude product **10** (4.49 g, 7.7 mmol) was dissolved in a mixture of dichloromethane:water (8:1, v/v, 20 mL). DDQ (2.60 g, 11.5 mmol) was added to the solution. After stirring for 1 h, the reaction mixture was filtered. The filtrate was diluted with dichloromethane (15 mL), washed with water (25 mL) and aq. $NaHCO_3$ (10%, 30 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the crude reaction product by silica gel chromatography (0→5% ethyl acetate in petroleum ether) led to **11** (2.84 g, 6.1 mmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.6 (CH_3, 1-*O*-Me), 67.0 (C-6), 72.6, 73.2, 74.5 (3×, CH_2, Bn), 70.6, 71.6, 76.4, 78.1 (C-2, C-3, C-4, C-5), 97.7 (C-1), 127.3, 127.4, 127.5, 127.7, 128.1, 128.3 (CH, Bn), 138.3 (qC Bn). Anal.: calcd for $C_{28}H_{32}O_7$ (464.56): C, 72.39; H, 6.94; found: C, 72.25; H, 7.02%.

Ethyl 4,6-di-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-1-thio-α-D-mannopyranoside (13). The regioselective *p*-methoxybenzylation of mannopyranoside **12** (2.02 g, 5.0 mmol) was executed as described for the preparation of compound **9** to yield, after purification by column chromatography [ethyl acetate in petroleum ether (0→15%)], compound **13** (1.96 g, 3.8 mmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 14.6 (CH_3, SEt), 24.6 (CH_2,

SEt), 54.9 (CH_3, OMe, *p*MBn), 68.7 (C-6), 71.1, 73.1, 74.7 (3× CH_2, Bn, *p*MBn), 69.5, 71.2, 74.3, 79.8 (C-2, C-3, C-4, C-5), 83.3 (C-1), 113.5, 113.6 (CH, *p*MBn), 127.3, 127.5, 128.0, 128.2, 129.4 (CH arom), 129.6 (qC, *p*MBn), 137.9, 138.2 (qC, Bn), 159.1 (qC, *p*MBn).

Ethyl 2-*O*-benzoyl-4,6-di-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-1-thio-α-D-mannopyranoside (14). Treatment of compound **13** (1.96 g, 3.8 mmol) with benzoyl chloride (0.67 mL, 5.7 mmol) was performed as described for the preparation of compound **6**. The crude product was purified by column chromatography. Elution of the column with 0→5% ethyl acetate in petroleum ether gave building block **14** (2.07 g, 3.3 mmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 14.6 (CH_3, SEt), 25.2 (CH_2, SEt), 54.4 (CH_3, OMe, *p*MBn), 68.6 (C-6), 70.8, 72.9, 74.7 (3× CH_2, Bn, *p*MBn), 70.4, 71.7, 74.0, 77.9 (C-2, C-3, C-4, C-5), 82.2 (C-1), 113.5, 113.6 (CH, *p*MBn), 127.0, 127.1, 127.4, 127.5, 127.9, 128.0, 128.2, 129.4, 129.5 (CH, arom), 129.1, 129.5 (qC, *p*MBn, Bz), 132.7 (CH, Bz), 138.0, 138.1 (qC, Bn), 158.8 (qC, *p*MBn), 165.1 (C=O Bz). Anal.: calcd for $C_{36}H_{38}O_8$ (598.70): C, 72.22; H, 6.40; found: C, 72.11; H, 6.53%.

Methyl 3-*O*-[2-*O*-benzoyl-4,6-di-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-α-D-mannopyranosyl]-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (17). Methyl mannopyranoside acceptor **11** (1.07 g, 2.3 mmol) and donor saccharide **14** (2.00 g, 3.2 mmol) were dissolved in a mixture of 1,2-dichloroethane:diethyl ether (1:1, v/v, 6.6 mL). Activated molecular sieves (4 Å) were added and the mixture was stirred for 20 min under argon atmosphere. At 0 °C a suspension of NIS (640 mg, 2.8 mmol) and TfOH (20.4 μL, 230 μmol) in the same solvent mixture (8.5 mL) was added. After stirring for 15 min, the reaction was quenched with pyridine (0.5 mL), filtered, and the filtrate was diluted with ethyl acetate (20 mL). The organic layer was washed with aq. $Na_2S_2O_3$ (20%, 10 mL) and aq. $NaHCO_3$ (10%, 10 mL), dried ($MgSO_4$), filtered, and concentrated. The crude product was applied to a silica gel column, which was eluted with 0→10% ethyl acetate in petroleum ether to give the α-linked disaccharide **17** (1.98 g, 1.9 mmol). $[\alpha]_D$ −3.0° (c 1); ^1H NMR (300 MHz, $CDCl_3$, HH-COSY): δ 3.29, 3.65 (2× s, 6H, 2× CH_3, 1-*O*-Me, OMe *p*MBn), 3.67–3.80 (m, 6H, H-5, H-5′, H-6, H-6′), 3.83 (dd, 1H, H-2, $J_{2,1}=1.9$ Hz, $J_{2,3}=3.1$ Hz), 3.98–4.06 (m, 2H, H-4, H-4′), 4.12 (dd, 1H, H-3′, $J_{3,2}=3.1$ Hz, $J_{3,4}=9.3$ Hz), 4.17 (dd, 1H, H-3, $J_{3,2}=3.1$ Hz, $J_{3,4}=9.4$ Hz), 4.42–4.90 (m, 12H, 6× CH_2 Bn, *p*MBn), 4.75 (d, 1H, H-1, $J_{1,2}=2.2$ Hz), 5.32 (d, 1H, H-1′, $J_{1,2}=1.9$ Hz), 5.73 (dd, 1H, H-2′, $J_{2,1}=1.9$ Hz, $J_{2,3}=3.1$ Hz), 6.69–6.73 (m, 2H, CH *p*MBn), 7.17–7.57 (m, 30H, CH arom), 8.02–8.05 (m, 2H, Bz); ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.8, 55.1 (2× CH_3 1-*O*-Me, *p*MBn), 69.1, 69.5 (C-6, C-6′), 71.3, 72.3, 73.5, 75.0, 75.2 (CH_2, Bn, *p*MBn), 71.9, 72.5, 74.4, 75.3, 77.4, 77.7, 78.4 (CH sugar rings), 98.5, 99.7 (C-1, C-1′, $^1J_{C,H}=168.5$, 168.5 Hz, respectively), 113.7 (CH, *p*MBn), 127.6, 127.8, 128.1, 128.4, 129.8, 130.0, 130.1 (CH, arom), 133.1 (CH, Bz), 138.0, 138.3, 138.4, 138.6, 138.8 (qC Bn), 159.2 (qC, *p*MBn), 165.5 (C=O Bz). Anal.: calcd for $C_{63}H_{66}O_{13}$ (1031.22): C, 73.38; H, 6.45; found: C, 73.21; H, 6.38%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (18). Debenzoylation of compound **17** (1.98 g, 1.9 mmol) was achieved by stirring 48 h in methanol (13 mL) containing potassium *tert*-butoxide (107 mg, 1.0 mmol). The reaction mixture was neutralized by Dowex 50W×4 (H^+-form), filtered, and concentrated. The crude product was purified by silica gel column chromatography. The column was eluted with a gradient of ethyl acetate in petroleum ether (0→30%). Concentration of the appropriate fractions gave compound **18** (1.52 g, 1.6 mmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.6, 54.9 (2× CH_3, 1-*O*-Me, OMe, *p*MBn), 68.9, 69.2 (C-6, C-6′), 71.5, 72.0, 73.2, 74.6, 74.8 (CH_2, Bn, *p*MBn), 68.5, 71.6, 71.8, 74.2, 75.0, 77.3, 78.3, 79.4 (CH sugar rings), 98.3, 101.2 (C-1, C-1′), 113.6 (CH, *p*MBn), 127.3, 127.3, 127.5, 127.5, 127.7, 128.0, 128.1, 128.2, 129.3 (CH, arom), 129.9 (qC, *p*MBn), 138.0, 138.2, 138.5 (qC, Bn), 159.6 (qC, *p*MBn). Anal.: calcd for $C_{56}H_{62}O_{12}$ (927.11): C, 72.55; H, 6.74; found: C, 72.46; H, 6.88%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-(2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (19). The glycosylation of mannobiosyl acceptor **18** (0.99 g, 1.1 mmol) with glucopyranoside donor **6** (0.68 g, 1.3 mmol) was performed in the same fashion as the preparation of disaccharide **17**. The crude product was purified by column chromatography (0→20% ethyl acetate in petroleum ether) to yield trisaccharide **19** (1.29 g, 0.9 mmol). $[\alpha]_D$ +9.2° (*c* 1); ^1H NMR (300 MHz, $CDCl_3$, HH-COSY): δ 2.82 (dt, 1H, H-5 Man*p*, $J_{5,4}\approx J_{5,6}=9.6$ Hz, $J_{5,6}=4.7$ Hz), 3.17 (dd, 1H, H-6, $^2J_{6,6}=-11.1$ Hz, $J_{6,5}=7.3$ Hz), 3.24 (s, 3H, CH_3 1-*O*-Me), 3.42 (t, 1H, H-3 Glc*p*, $J_{3,2}\approx J_{3,4}=9.2$ Hz), 3.50 (m, 1H, H-4 Man*p*, $J_{4,3}\approx J_{4,5}=9.6$ Hz), 3.65 (s, 3H, CH_3, OMe, PMB), 3.65–3.90 (m, 12H, 2× H-2 Man*p*, 2× H-3 Man*p*, H-4 Glc*p*/Man*p*, H-5 Glc*p*/Man*p*, 4× H-6), 3.95 (d, 1H, H-1 Glc*p*, $J_{1,2}=8.0$ Hz), 3.98 (AB, 2H, CH_2, Bn/*p*MBn), 4.25 (dd, 1H, H-6, $^2J_{6,6}=-10.3$ Hz, $J_{6,5}=4.9$ Hz), 4.43–4.91 (m, 12H, CH_2, Bn, *p*MBn), 4.61 (m, 1H, H-1, Man*p*, $J_{1,2}=1.7$ Hz), 4.96 (d, 1H, H-1, Man*p*, $J_{1,2}=1.7$ Hz), 5.28 (dd, 2H, H-2, Glc*p*, $J_{2,1}=7.9$ Hz, $J_{2,3}=9.2$ Hz), 5.52 (s, 1H, CH, CHPh), 6.72–6.75 (m, 2H, CH, *p*MBn), 7.11–7.53 (m, 40H, CH arom), 7.97–7.99 (m, 2H, CH Bz); ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.6, 54.9 (2× CH_3, 1-*O*-Me, OMe *p*MBn), 68.4, 68.9, 70.5 (3× C-6), 71.6, 72.3, 73.1, 73.4, 73.6, 74.8 (CH_2, Bn, *p*MBn), 65.8, 71.8, 72.5, 73.2, 74.6, 75.0, 75.9, 77.1, 77.3, 78.0, 81.0 (CH sugar rings), 98.6, 99.0, 100.7, 101.1 (3× C-1, CH CHPh), 113.4 (CH, *p*MBn), 125.7, 125.9, 126.9, 127.2, 127.4, 127.6, 127.8, 127.9, 128.0, 128.2, 128.5, 128.9, 129.6, 129.8 (CH, arom), 130.1 (qC, arom), 132.6 (CH, Bz), 137.3, 137.9, 138.1, 138.6, 138.7 (qC, Bn, CHPh), 159.1 (qC, *p*MBn), 164.5 (C=O Bz). Anal.: cald for $C_{83}H_{86}O_{18}$ (1371.60): C, 72.68; H, 6.32; found: C, 72.61; H, 6.39%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-(3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (20). To a solution of compound **19** (1.29 g, 0.9 mmol) in methanol (5.0 mL) was added potassium *tert*-butoxide (52 mg, 0.5 mmol). The solution was stirred for 96 h, neutralized with Dowex W50 × 4 (H^+-form), and concentrated. The residue was dried by evaporation with toluene to give compound **20** (1.16 g, 0.9 mmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.5, 54.7 (2 × CH_3, 1-*O*-Me, OMe *p*MBn), 68.2, 68.7 (3 × C-6), 72.0, 73.1, 73.6, 73.8, 74.7 (CH_2 Bn, *p*MBn), 66.1, 71.7, 72.2, 73.5, 74.1, 74.8, 77.2, 77.4, 78.3, 79.0, 80.2 (CH sugar rings), 98.3, 99.4, 100.9, 101.7 (3 × C-1, CH CHPh), 113.4 (CH *p*MBn), 125.8, 127.3, 127.4, 127.5, 127.9, 128.1, 128.2, 129.9 (CH arom), 129.6 (qC, *p*MBn), 137.3, 137.9, 138.0, 138.3, 138.5, 138.7 (qC, Bn, CHPh), 159.1 (qC, *p*MBn).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (21). To a solution of crude trisaccharide **20** (1.16 g, 0.9 mmol) in DMF (5 mL) were added at 0 °C sodium hydride (60%, 55 mg, 1.4 mmol) and benzyl bromide (0.15 mL, 1.3 mmol). After stirring for 1 h, the reaction was quenched with methanol (1 mL) and the solvents were evaporated. The residue was taken up in diethyl ether (10 mL) and the resulting solution was washed with water (7 mL) and aq. $NaHCO_3$ (10%, 7 mL), dried ($MgSO_4$), filtered, and concentrated. Pure product **21** (1.08 g, 0.80 mmol) was isolated after purification by column chromatography (0→20% ethyl acetate in petroleum ether). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.4, 54.6 (2 × CH_3, 1-*O*-Me, OMe, *p*MBn), 68.3, 68.6, 69.5 (3 × C-6, C-6′, C-6″), 71.1, 71.9, 72.9, 73.0, 73.5, 74.3, 74.5, 74.7 (CH_2 Bn, *p*MBn), 65.4, 71.6, 72.1, 74.2, 74.4, 75.4, 77.3, 77.5, 78.7, 79.9, 80.4, 80.8 (CH sugar rings), 98.2, 99.6, 100.7, 103.1 (3 × C-1, CH, CHPh), 113.3 (CH *p*MBn), 125.7, 126.9, 127.0, 127.2, 127.3, 127.6, 127.7, 127.8, 128.0, 128.2, 128.5, 129.6 (CH arom), 129.8 (qC, *p*MBn), 137.2, 137.9, 138.3, 138.6 (qC, Bn, CHPh), 158.9 (qC, *p*MBn). Anal.: calcd for $C_{83}H_{88}O_{17}$ (1357.62): C, 73.43; H, 6.53; found: C, 73.35; H, 6.45%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (22). Aluminium trichloride (53 mg, 0.40 mmol) and the borane-triethylamine complex (29 mg, 0.40 mmol) were added to a mixture of trisaccharide **21** (136 mg, 0.10 mmol) and molecular sieves (4 Å) in toluene (2 mL). After stirring for 30 min, the reaction mixture was filtered, neutralized with Dowex W × 4 (H^+ form), and concentrated. The residue was evaporated with toluene and subsequently applied to a silica gel column. Elution with 0→30% ethyl acetate in petroleum ether to gave compound **22** (57 mg, 42 μmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.7 (CH_3, 1-*O*-Me), 61.7 (C-6″), 69.0, 69.6 (C-6, C-6′), 72.1, 73.2, 73.3, 74.2, 74.3, 74.5, 74.7, 75.4 (CH_2 Bn), 70.7, 71.9, 74.9, 75.2, 76.6, 76.9, 77.4, 79.0, 80.4, 80.9, 83.8 (CH sugar rings), 98.5, 100.3, 103.3 (3 × C-1), 126.6, 127.2, 127.4, 127.5, 127.6, 127.7, 127.9, 128.1, 128.2, 128.3, 128.5 (CH arom), 137.9, 138.1, 138.2, 138.4, 138.7 (qC, Bn).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-2-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (23). Trisaccharide **21** (1.49 g, 1.1 mmol) was dissolved in a mixture of dichloromethane:water (8:1, v/v, 21 mL) and DDQ (0.5 g, 2.2 mmol) was added. After stirring for 3 h, the solids were filtered and the filtrate was diluted with dichloromethane (15 mL). The solution was washed with water (15 mL) and aq. $NaHCO_3$ (10%, 15 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated, and the residual oil was purified by column chromatography. Elution with 0→20% ethyl acetate in petroleum ether afforded compound **23** (1.55 g, 1.3 mmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.5 (CH_3, 1-*O*-Me), 68.1, 68.8, 69.4 (3 × C-6), 71.9, 73.1, 73.7, 74.4, 74.5 (CH_2, Bn), 65.6, 70.5, 71.6, 71.7, 74.7, 76.5, 77.2, 78.9, 79.5, 80.0, 80.6, 80.7 (CH sugar rings), 98.3, 99.9, 100.8, 103.4 (3 × C-1, CH, CHPh), 125.7, 125.9, 127.1, 127.2, 127.4, 127.7, 127.9, 128.0, 128.3, 128.6 (CH arom), 137.1, 137.9, 138.0, 138.2, 138.3, 138.5 (qC, Bn). Anal.: calcd for $C_{75}H_{80}O_{16}$ (1237.46): C, 72.80; H, 6.52; found: C, 72.72; H, 6.63%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-2-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-3-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (24). Mannopyranoside donor **15** (562 mg, 0.9 mmol) and acceptor **23** (772 mg, 0.6 mmol) were condensed as described for the preparation of disaccharide **17**. The crude product was purified by column chromatography (0→10% ethyl acetate in petroleum ether) to give tetrasaccharide **24** (2.10 g, 1.2 mmol). $[\alpha]_S -31.6°$ (*c* 1); ^{13}C NMR (50 MHz, $CDCl_3$): δ 54.6 (CH_3, 1-*O*-Me), 68.5, 68.9, 69.3 (4 × C-6), 71.4, 71.9, 73.2, 73.3, 73.8, 74.6, 74.8, 75.0, 75.3 (CH_2, Bn), 65.6, 69.1, 71.8, 72.0, 72.2, 74.3, 75.1, 76.6, 77.3, 77.7, 78.2, 79.2, 80.3, 80.7, 81.1 (CH sugar rings), 98.2, 99.6, 100.1, 100.4, 102.8 (4 × C-1, CH, CHPh), 125.9, 126.0, 127.2, 127.3, 127.4, 127.6, 127.7, 128.0, 128.1, 128.2, 128.3, 128.5, 129.7 (CH arom), 129.8 (qC, Bz), 132.8 (CH, Bz), 137.6, 137.9, 138.0, 138.1, 138.3, 138.6 (qC, Bn), 165.2 (C=O Bz). Anal.: calcd for $C_{109}H_{112}O_{23}$ (1790.09): C, 73.14; H, 6.31; found: C, 73.05; H, 6.24%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-2-*O*-(2,3-di-*O*-benzyl-β-D-glucopyranosyl)-3^1*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (25). A solution of compound **24** (1.50 g, 0.84 mmol) in acetic acid:water (4:1, v/v, 21 mL) was heated under reflux for 2 h. The solution was concentrated and the remaining solvents were removed by evaporation with toluene. The residue was applied to a silica gel column, which was

eluted with 10→40% ethyl acetate in petroleum ether. Concentration of the appropriate fractions gave diol **25** (1.18 g, 0.70 mmol). $[\alpha]_D$ −21.2° (*c* 1); ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.8 (CH_3, 1-*O*-Me), 60.6 (C-6, Glc*p*), 68.9, 69.1, 69.4 (3× C-6, Man*p*), 72.1, 73.4, 74.1, 74.6, 74.8, 75.2, 75.7 (CH_2, Bn), 69.2, 71.8, 72.2, 74.2, 74.8, 75.4, 75.5, 76.8, 77.5, 78.1, 79.2, 81.3, 83.7 (CH sugar rings), 98.3, 99.6, 99.7, 102.1 (4× C-1), 126.6, 126.8, 127.2, 127.3, 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.5, 128.8, 129.0, 129.4, 129.9 (CH arom), 133.0 (CH, Bz), 137.1, 138.0, 138.1, 138.2, 138.3, 138.4, 138.8 (qC, Bn), 165.3 (C—O, Bz).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-[2,3-di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl]-3-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranosyl}-α-D-mannopyranoside (26). Compound **25** (0.60 g, 0.36 mmol) was dried by evaporation with pyridine and subsequently dissolved in the same solvent (5 mL). *tert*-Butyldimethylsilyl chloride (60 mg, 0.4 mmol) and DMAP (9 mg, 0.07 mmol) were added. After stirring for 20 h, TLC analysis showed complete conversion of the starting material. The reaction was quenched with water (0.5 mL) and the solvents were evaporated. The residue was taken up in ethyl acetate (10 mL), and the solution was washed with water (8 mL) and aq. $NaHCO_3$ (10%, 8 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Purification of the crude product was achieved by column chromatography (0→30% ethyl acetate in petroleum ether) to furnish compound **26** (0.50 g, 0.28 mmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ −6.0 (CH_3, Me, TBDMS), 25.6 (CH_3, *t*-Bu, TBDMS), 54.6 (CH_3, 1-*O*-Me), 69.0, 69.3, 71.5, 71.8, 73.1, 74.0, 74.6, 75.0 (4× C-6, CH_2, Bn), 69.1, 71.6, 72.2, 72.5, 73.6, 74.8, 75.1, 76.9, 77.3, 78.5, 80.6, 83.8 (CH sugar rings), 98.1, 99.3, 101.7 (4× C-1), 126.6, 127.2, 127.3, 127.4, 127.6, 128.0, 128.2, 129.7 (CH arom), 132.8 (CH, Bz), 137.8, 137.9, 138.1, 138.3, 137.8, 138.9 (qC, Bn), 165.1 (C—O, Bz).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-[2,3-di-*O*-benzyl-4-*O*-benzyloxymethyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl]-3-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranosyl}-α-D-mannopyranoside (27). To a solution of tetrasaccharide **26** (0.50 g, 0.28 mmol) in acetonitrile (1 mL) were added benzyloxymethyl chloride (78 μL, 0.56 mmol), DIPEA (0.2 mL, 1.12 mmol) and tetrabutylammonium iodide (3 mg, 8 μmol). After stirring for 18 h at room temperature, the excess of reagent was destroyed by adding anhyd. methanol (0.5 mL). After stirring for 45 min, the reaction mixture was concentrated. The residue was taken up in diethyl ether (10 mL), and the resulting solution was washed with KH_2PO_4 (1 M, 6 mL) and aq. $NaHCO_3$ (10%, 6 mL), dried ($MgSO_4$), and filtered. The filtrate was concentrated and the resulting oil was purified by silica gel column chromatography. The column was eluted with a gradient of ethyl acetate in petroleum ether (0→20%) to yield the fully protected **27** (0.41 g, 0.21 mmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ −5.3, −4.8 (CH_3, Me TBDMS), 25.8 (CH_3, *t*-Bu, TBDMS), 54.6 (CH_3, 1-*O*-Me), 69.0, 69.4, 70.1, 71.5, 71.8, 73.2, 74.5, 75.0 (C-6, CH_2, Bn), 69.1, 71.6, 71.9, 74.2, 74.7, 76.0, 77.3, 78.4, 83.8 (CH sugar rings), 95.9 (CH_2, BOM), 97.1, 98.2, 99.4, 102.0 (4× C-1), 126.6, 127.2, 127.5, 127.5, 127.8, 128.0, 128.1, 128.4, 128.7, 128.9, 129.7 (CH arom), 132.9 (CH, Bz), 137.1, 137.9, 138.2, 138.3, 137.3 (qC, Bn), 165.2 (C—O, Bz).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-[2,3-di-*O*-benzyl-4-*O*-benzyloxymethyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-glucopyranosyl]-3-*O*-(3,4,6-tri-*O*-benzyl-β-D-mannopyranosyl)-α-D-mannopyranosyl}-α-D-mannopyranoside (28). Potassium *tert*-butoxide (7 mg, 6 μmol) was added to a solution of tetrasaccharide **27** (0.41 g, 0.21 mmol) in a mixture of dioxane:methanol (1:1, v/v, 2 mL). After stirring for 55 h, the reaction mixture was neutralised with Dowex W50×4 (H^+ form), filtered, and concentrated. Purification of the crude compound was achieved by column chromatography. The column was eluted with 0→20% ethyl acetate in light petroleum ether to give **28** (0.35 g, 0.20 mmol). $[\alpha]_D$ +33.0° (c 1); ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ −5.5, −4.9 (CH_3, Me, TBDMS), 25.7 (CH_3, *t*-Bu, TBDMS), 54.5 (CH_3, 1-*O*-Me), 69.3, 69.9, 71.6, 72.9, 73.1, 73.9, 74.4, 74.7, 75.0 (4× C-6, CH_2, Bn), 68.5, 71.2, 71.5, 72.3, 74.1, 74.6, 75.0, 75.8, 77.2, 80.1, 83.7 (CH sugar rings), 95.8 (CH_2, BOM), 98.0, 99.4, 102.4 (4× C-1), 126.8, 127.0, 127.1, 127.2, 127.3, 127.5, 127.6, 128.0 (CH, arom), 137.8, 138.0, 138.3, 138.6 (qC, Bn). Anal.: calcd for $C_{109}H_{126}O_{22}Si$ (1816.29): C, 72.08; H, 6.99; found: C, 71.98; H, 6.91%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-2-*O*-(2,3-di-*O*-benzyl-4-*O*-benzyloxymethyl-α-D-glucopyranosyl)-3-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (29). To a cooled (−40 °C) mixture of tetrasaccharide **28** (180 mg, 0.10 mmol), xylopyranoside donor **16** (50 mg, 0.12 mmol) and molecular sieves (4 Å) in dichloromethane (1 mL) was added a solution of TMSOTf (8 μl, 40 μmol) in dichloromethane (0.8 mL). The temperature was allowed to raise after 1.5 h. After stirring for 3.5 h, donor (51 mg, 0.12 mmol) and TMSOTf (3.3 μL, 17 μmol) in dichloromethane (0.8 mL) were added. TMSOTf (3.3 μL, 17 μmol) in dichloromethane (0.8 mL) was added again after stirring for 1 h. One hour later, the reaction was quenched with pyridine. The resulting mixture was filtered and the filtrate was concentrated. The residual oil was evaporated three times with toluene and subsequently purified by column chromatography (0→40% ethyl acetate in petroleum ether) to give compound **29** (121 mg, 72 μmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$); δ 54.8 (CH_3, 1-*O*-Me), 60.3 (C-6, Glc*p*), 69.1, 69.5, 70.2, 72.2, 72.2, 73.4, 74.1, 74.6, 75.0, 75.2, 75.5 (C-6, Man*p*, CH_2, Bn), 68.5, 71.2, 71.5, 72.3, 74.1, 74.6, 75.0, 75.8, 77.2, 80.1, 83.7 (CH sugar rings), 95.8 (CH_2, BOM), 98.0, 99.4, 102.4 (4× C-1), 126.8, 127.0, 127.1, 127.2, 127.3, 127.5, 127.6, 128.0 (CH arom), 137.8, 138.0, 138.3, 138.6 (qC,

Bn). Anal.: calcd for $C_{103}H_{126}O_{22}$ (1701.24): C, 72.72; H, 6.64; found: C, 72.79; H, 6.70%.

Ethyl 2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (31). To a mixture of xylopyranosyl donor **16** (210 mg, 0.50 mmol), mannopyranosyl acceptor **30** (247 mg, 0.50 mmol) and powdered molecular sieves (4 Å) in dichloromethane (5 mL) was added dropwise at −40 °C a solution of TMSOTf (50 μL, 0.25 mmol) in dichloromethane (0.50 mL). After stirring for 1 h, donor (210 mg, 0.50 mmol) was added followed by dropwise addition of TMSOTf (50 μL, 0.25 mmol) in 1,2-dichloroethane (0.50 mL). After the addition was completed, the ice-bath was removed and the solution was stirred for 3 h at room temperature. The reaction was quenched with pyridine (0.5 mL), filtered, and the filtrate was concentrated. The crude product was purified by column chromatography. The column was eluted by a gradient of 0→30% ethyl acetate in petroleum ether. The residue was purified by gel filtration (dichloromethane:methanol, 1:1, v/v) to give compound **31** (143 mg, 0.19 mmol). ^{1}H NMR (300 MHz, $CDCl_3$, HH-COSY): δ 1.28 (t, 3H, CH_3 SEt, JÛE$_{h,hÛ ÛE}$ 7.4 Hz), 2.01, 2.02, 2.06 (3× s, 9H, 3× CH_3 Ac), 2.63 (ABX, 2H, CH_2 SEt), 3.35 (dd, 1H, H-5′-ax, $J_{5,5}$ = 11.9 Hz, $J_{5,4}$ = 8.1 Hz), 3.67–3.68 (m, 2H, H-6, $J_{6,5}$ = 1.5 Hz, $J_{6,5}$ = 4.8 Hz), 3.77 (t, 1H, H-4, $J_{4,3} \approx J_{4,5}$ = 9.4 Hz), 3.83 (dd, 1H, H-3, $J_{3,2}$ = 3.1 Hz, $J_{3,4}$ = 9.2 Hz), 4.08–4.12 (m, 2H, H-2, H-5), 4.27 (dd, 1H, H-5′-eq, $J_{5,5}$ = 12.0 Hz, $J_{5,4}$ = 4.7 Hz), 4.51, 4.59 (2× AB, 2H, CH_2, Bn), 4.60 (d, 1H, H-1′, $J_{1,2}$ = 6.3 Hz), 4.72 (AB, 2H, CH_2, Bn), 4.95 (dt, 1H, H-4′, $J_{4,3} \approx J_{4,5}$ = 7.9 Hz, $J_{4,5}$ = 4.7 Hz), 5.02 (dd, 1H, H-2′, $J_{2,1}$ = 6.1 Hz, $J_{2,3}$ = 8.0 Hz), 5.16 (t, 1H, H-3′, $J_{3,2} \approx J_{3,4}$ = 7.9 Hz), 5.27 (d, 1H, H-1, $J_{1,2}$ = 1.8 Hz), 7.17–7.37 (m, 15H, CH, Bn); ^{13}C ^{1}H NMR (50 MHz, $CDCl_3$): δ 14.8 (CH_3, SEt), 20.6 (3× CH_3 Ac), 25.3 (CH_2, SEt), 61.7 (C-5′), 69.5 (C-6), 71.6, 73.1, 75.0 (3× CH_2, Bn), 68.5, 70.1, 70.5, 71.8, 74.8, 76.2, 78.8, 81.6 (CH sugar rings), 98.9 (C-1′, $^1J_{C,H}$ = 153.9 Hz), 127.5, 127.6, 127.7, 127.8, 128.2 (CH, Bn), 137.9, 138.2, 138.4 (qC, Bn), 169.7, 169.9 (C=O, Ac). Anal.: calcd for $C_{40}H_{48}O_{12}S$ (752.89): C, 63.81; H, 6.43; found: C, 63.74; H, 6.55%.

Methyl 2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (32). Donor **16** (126 mg, 0.30 mmol) and acceptor **2** (116 mg, 0.25 mmol) were dissolved in dichloromethane (1 mL) and molecular sieves (4 Å) were added. The mixture was cooled to −40 °C and a solution of TMSOTf (8 μL, 40 μmol) in dichloromethane (0.8 mL) was added. After stirring at −40 °C for 1 h, the reaction was quenched with pyridine, filtered, and concentrated. The residue was evaporated three times with toluene and subsequently applied to a silica gel column. Elution with 0→25% ethyl acetate in petroleum ether yielded the disaccharide **32** (123 mg, 0.17 mmol). ^{1}H NMR (300 MHz, $CDCl_3$, HH-COSY): 2.03, 2.04, 2.06 (3× s, 9H, 3× CH_3, Ac), 3.34 (dd, 1H, H-5′-ax., $J_{5,5}$ = 12.0 Hz, $J_{5,4}$ = 7.9 Hz), 3.35 (s, 3H, CH_3, Me), 4.03, dd, 1H, H-2, $J_{2,1}$ = 2.0 Hz, $J_{2,3}$ = 3.2 Hz), 4.30 (dd, 1H, H-5′-eq, $J_{5,5}$ = 12.0 Hz, $J_{5,4}$ = 4.6 Hz), 3.68–3.73 (m, 4H, H-4, H-5, H-6), 3.87 (dd, 1H, H-3, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.0 Hz), 4.54 (AB, 2H, CH_2, Bn), 4.59 (d, 1H, H-1′, $J_{1,2}$ = 5.8 Hz), 4.66 (2× AB, 4H, 2× CH_2, Bn), 4.68 (d, 1H, H-1, $J_{1,2}$ = 2.0 Hz), 4.94 (dt, 1H, H-4′, $J_{4,5}$ = 4.7 Hz, $J_{4,3} \approx J_{4,5}$ = 7.8 Hz), 5.01 (dd, 1H, H-2′, $J_{2,1}$ = 6.1 Hz, $J_{2,3}$ = 7.9 Hz), 5.14 (t, 1H, H-3′, $J_{3,2} \approx J_{3,4}$ = 7.8 Hz), 7.15–7.39 (m, 15H, CH, Bn); ^{13}C NMR (50 MHz, $CDCl_3$): 20.4 (CH_3, Ac), 54.5 (CH_3, Me), 61.4 (C-5′), 69.3 (C-6), 71.2, 72.9, 74.8 (3× CH_2, Bn), 68.3, 69.7, 70.2, 71.3, 74.3, 74.4, 78.2 (CH sugar rings), 98.2, 99.2 (C-1, C-1′), 127.3, 127.4, 127.5, 127.7, 127.8, 128.1 (CH, Bn), 138.0, 138.2 (qC, Bn), 169.1, 169.5, 169.7 (C=O Ac).

Ethyl 2-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-glucopyranoside (33). Glucopyranoside **6** (1.70 g, 3.4 mmol) was dissolved in diluted HOAc (80%, 15 mL). After stirring for 2.5 h at room temperature, the reaction mixture was concentrated and the remaining solvents were removed by evaporation with toluene. Purification of the crude product was achieved by column chromatography. The column was eluted with 20→50% ethyl acetate in petroleum ether. The first product was identified as ethyl 6-*O*-acetyl-2-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-glucopyranoside (172 mg, 0.4 mmol). Further elution of the column gave the required product **33** (1.18 g, 2.8 mmol). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.23 (t, 3H, CH_3, SEt, $J_{h,h}$ = 7.5 Hz), 2.73 (ABX, 2H, CH_2, SEt), 3.45–3.52 (m, 1H, H-5), 3.71–3.79 (m, 2H, H-3, H-4), 3.81 (dd, 1H, H-6, $^2J_{6,6}$ = −11.4 Hz, $J_{6,5}$ = 4.9 Hz), 3.94 (dd, 1H, $^2J_{6,6}$ = −12.0 Hz, $J_{6,5}$ = 3.4 Hz), 4.60 (d, 1H, H-1, $J_{1,2}$ = 10.1 Hz), 4.67 (AB, 2H, CH_2, Bn), 5.23–5.32 (m, 1H, H-2), 7.20–7.64 (m, 8H, CH arom), 8.04–8.11 (m, 2H, CH, Bz); ^{13}C ^{1}H NMR (50 MHz, $CDCl_3$): δ 14.3 (CH_3, SEt), 23.4 (CH_2, SEt), 61.6 (C-6), 74.2 (CH_2, Bn), 70.2, 71.7, 79.6, 83.0, 84.1 (C-1, C-2, C-3, C-4, C-5), 127.0, 127.4, 127.6, 127.9, 129.3, 129.5 (CH arom), 132.6 (CH, Bz), 137.6 (qC, Bn), 165.9 (C=O Bz).

Ethyl 6-*O*-allyl-2-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-glucopyranoside (34). To a solution of diol **33** (1.18 g, 2.8 mmol) in methanol (17 mL) was added dibutyl tin oxide (765 mg, 3.1 mmol) and the suspension was heated under reflux for 2 h. The solvent was evaporated and the residue was dried by evaporation of toluene. The residue was dissolved in DMF (30 mL) and allyl bromide (0.36 mL, 4.2 mmol) and cesium fluoride (640 mg, 4.2 mmol) were added. After stirring for 17 h, the reaction mixture was concentrated and the residue was taken up in diethyl ether (20 mL), washed twice with aq. KF (1 M, 20 mL) and once with water (15 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Purification of the crude product was accomplished by column chromatography with ethyl acetate in petroleum ether (10→40%). Concentration of the appropriate fractions yielded compound **34** (1.01 g, 2.2 mmol). ^{13}C ^{1}H NMR (50 MHz, $CDCl_3$): δ 14.9 (CH_3, SEt), 23.9 (CH_2, SEt), 70.0, 72.4, 74.5 (C-6, CH_2, All, Bn), 71.6, 72.1, 78.9, 83.5,

83.6 (C-1, C-2, C-3, C-4, C-5), 117.0 (CH_2, All), 127.5, 127.8, 128.2, 128.3, 129.7 (CH arom), 133.1, 134.4 (CH, All, Bz), 138.0 (qC, Bn), 165.2 (C=O, Bz).

Ethyl 6-*O*-allyl-2-*O*-benzoyl-3,4-di-*O*-benzyl-1-thio-β-D-glucopyranoside (35). To a solution of compound **34** (1.01 g, 2.2 mmol) in DMF (5 mL) were added at 0 °C benzyl bromide (0.34 mL, 0.3 mmol) and sodium hydride (60%, 88 mg, 2.2 mmol). After stirring for 1.5 h at room temperature, sodium hydride (60%, 9 mg, 0.2 mmol) was added and the reaction was stirred for 30 min. The reaction was quenched with methanol (1 mL), subsequently the solvent was removed and the residue was taken up in diethyl ether (15 mL). The resulting solution was washed with water (10 mL) and aq. $NaHCO_3$ (10%, 10 mL), dried ($MgSO_4$), and filtered. The filtrate was concentrated and the residue was purified by column chromatography (0→20% ethyl acetate in petroleum ether) to furnish donor **35** (987 mg, 1.8 mmol). $[\alpha]_D$ +28.1° (*c* 1); ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 14.8 (CH_3, SEt), 23.7 (CH_2, SEt), 68.8, 75.0, 75.1 (C-6, CH_2, All, Bn), 72.4, 77.8, 79.5, 83.4, 84.2 (C-1, C-2, C-3, C-4, C-5), 116.8 (CH_2, All), 127.5, 127.7, 127.8, 128.1, 128.2, 129.7 (CH arom), 133.0, 134.6 (CH, All, Bz), 137.7, 137.9 (qC, Bn), 165.2 (C=O Bz). Anal.: calcd for $C_{32}H_{36}O_6S$ (548.70): C, 70.05; H, 6.61; found: C, 70.18; H, 6.71%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-(6-*O*-allyl-2-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (36). To a solution of donor **35** (384 mg, 0.70 mmol) and disaccharide acceptor **18** (463 mg, 0.50 mmol) in a mixture of 1,2-dichloroethane:diethyl ether (1:1, v/v, 4 mL) were added powdered molecular sieves (4 Å). The mixture was cooled to −30 °C and a suspension of NIS (158 mg, 0.70 mmol) and TfOH (6.6 μL, 74 μmol) in the same solvent mixture (4 mL). After stirring for 15 min, the reaction was quenched with pyridine (0.2 mL), and the resulting mixture was filtered. The filtrate was diluted with ethyl acetate (10 mL), washed with aq. $Na_2S_2O_3$ (20%, 7 mL) and aq. $NaHCO_3$ (10%, 7 mL), dried ($MgSO_4$), filtered, and concentrated. The crude product was applied to a silica column, which was eluted with 0→30% ethyl acetate in light petroleum ether. Concentration of the appropriate fractions gave trisaccharide **36** (573 mg, 0.41 mmol). $[\alpha]_D$ +19.6° (*c* 1); ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.8, 55.0 (CH_3, 1-*O*-Me, CH_3, OMe *p*MBn), 69.1, 69.3, 70.7, 72.3, 73.2, 73.5, 74.1, 74.8 (CH_2 allyl, C-6, CH_2, Bn), 72.0, 73.1, 75.2, 77.4, 77.6, 77.9, 78.2, 79.8, 82.4 (CH, sugar rings), 98.7, 99.3 (C-1, C-1′, $^1J_{C,H}$ = 168.5, 170.0 Hz, respectively), 100.4 (C-1″, $^1J_{C,H}$ = 155.3 Hz), 116.9 (CH_2, All), 113.6 (CH *p*MBn), 126.6, 127.0, 127.2, 127.4, 127.6, 127.7, 127.9, 128.1, 128.2, 128.3, 128.4, 128.7, 129.8, 129.9 (CH arom), 130.4, 130.5 (qC, arom), 132.7 (CH, Bz), 134.7 (CH All), 137.9, 138.3, 138.7, 138.9, 139.0 (qC, Bn), 159.1 (qC, *p*MBn), 164.8 (C=O, Bz).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-[4,6-di-*O*-benzyl-2-*O*-(6-*O*-allyl-2-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (37). Compound **36** (888 mg, 0.6 mmol) was dissolved in a mixture of dichloromethane:water (8:1, v/v, 2.8 mL) and DDQ (214 mg, 0.9 mmol) was added. After stirring for 1 h at room temperature, the reaction mixture was filtered. The filtrate was diluted with dichloromethane (10 mL), washed with water (10 mL) and aq. $NaHCO_3$ (10%, 10 mL), dried ($MgSO_4$), filtered, and concentrated to yield the crude trisaccharide. Purification was achieved by column chromatography (10→40% ethyl acetate in petroleum ether) to give acceptor **37** (82%). $[\alpha]_D$ +18.6 (*c* 1); ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 54.8 (CH_3, 1-*O*-Me), 68.3, 69.2, 70.2, 72.3, 72.4, 73.2, 73.4, 74.2, 74.7, 74.8 (C-6, CH_2, All, Bn), 71.1, 72.1, 73.1, 75.1, 75.2, 76.9, 77.4, 77.6, 78.8, 80.4, 81.8 (CH sugar rings), 98.7, 100.0, 100.9 (3× C-1), 117.3 (CH_2, All), 126.5, 127.1, 127.3, 127.5, 127.6, 127.7, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 129.8, 132.9 (CH arom), 130.0 (qC, Bz), 134.5 (CH, All, Bz), 137.8, 138.1, 138.2, 138.3, 138.9 (qC, Bn), 165.0 (C=O, Bz). Anal.: calcd for $C_{79}H_{84}O_{17}$ (1305.54): C, 72.68; H, 6.49; found: C, 72.56; H, 6.35%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-(6-*O*-allyl-2-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl)-3-*O*-[3,4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-α-D-mannopyranoside (38). Trisaccharide acceptor **37** (130 mg, 0.10 mmol) and disaccharide donor **31** (90 mg, 0.12 mmol) were dissolved in diethyl ether (1 mL). The solution was stirred for 30 min in the presence of activated molecular sieves (4 Å). The solution was cooled in an ice bath and NIS (29 mg, 0.13 mmol) and a solution of TfOH (1.3 μL, 15 μmol) in diethyl ether (0.5 mL) were added. After stirring for 30 min, the reaction mixture was neutralised with pyridine (0.1 mL), filtered, and diluted with ethyl acetate (5 mL). The resulting solution was washed with aq. $Na_2S_2O_3$ (20%, 3 mL) and aq. (10%, 3 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by gel filtration (dichloromethane:methanol, 1:1, v/v) to give pentasaccharide **38** (133 mg, 67 μmol). ^{13}C ^1H NMR (50 MHz, $CDCl_3$): δ 20.6 (CH_3 Ac), 54.7 (CH_3 1-*O*-Me), 63.7 (C-5 Xyl*p*), 68.2, 69.2, 69.9, 70.2, 71.5, 72.0, 73.2, 73.4, 73.7, 73.7, 74.2, 74.5, 74.7 (C-6, CH_2, All, Bn), 68.7, 70.1, 71.1, 71.8, 72.6, 73.1, 74.6, 74.9, 75.2, 75.4, 76.9, 77.5, 78.6, 78.9, 79.2, 82.1 (CH sugar rings), 98.3, 99.6, 99.7, 100.0, 100.9 (5× C-1), 115.9 (CH_2, All), 125.9, 126.7, 127.4, 127.6, 127.9, 128.1, 128.2, 128.3, 128.5 (CH arom), 132.5, 134.8 (CH, All, Bz), 137.9, 138.1, 138.3, 138.7 (qC, Bn), 164.8 (C=O, Bz), 169.2, 169.7, 169.9 (C=O, Ac).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-(6-*O*-allyl-2-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-glucopyranosyl)-3-*O*-[3,4,6-di-*O*-benzyl-2-*O*-(β-D-xylopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-α-D-mannopyranoside (39). Pentamer **38** (133 mg, 67 μmol) was deacylated with potassium *tert*-butoxide (8 mg, 71 μmol) in a mixture of methanol:dioxane (1:1, v/v, 2 mL). The solution was stirred for 24 h, neutralised with Dowex 50W × 4 (H^+ form), filtered, and concentrated.

The residue was purified by column chromatography (10→50% ethyl acetate in petroleum ether) to give homogenous **39** (91 mg, 49 μmol). ^{13}C ^{1}H NMR (50 MHz, $CDCl_3$): δ 54.7 (CH_3, 1-*O*-Me), 64.7 (C-5, Xyl*p*), 68.3, 69.2, 70.2, 71.6, 72.1, 73.1, 73.4, 74.3, 74.5 (C-6, CH_2, All, Bn), 69.3, 71.0, 71.9, 72.2, 72.9, 73.2, 74.8, 75.1, 75.2, 76.8, 77.5, 77.7, 78.1, 78.7, 79.2, 82.1 (CH sugar rings), 98.2, 99.1, 100.1, 100.6, 101.9 (5× C-1), 116.1 (CH_2, All), 126.6, 126.8, 127.0, 127.4, 127.6, 127.8, 127.9, 128.2, 128.5, 128.6 (CH, arom), 132.5, 134.5 (CH, All, Bz), 137.7, 137.8, 138.0, 138.2, 138.4, 138.5, 138.6 (qC, Bn), 164.8 (C=O, Bz).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-(6-*O*-allyl-2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl)-3-*O*-[3,4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-α-D-mannopyranoside (40). Sodium hydride (60%, 10 mg, 0.25 mmol) and benzyl bromide (35 μL, 0.29 mmol) were added at 0° to a solution of compound **39** (91 mg, 49 μmol) in DMF (1.5 mL). After stirring for 4 h at room temperature, the reaction was quenched with methanol (0.3 mL) and the solvents were evaporated. The residue was taken up in diethyl ether (5 mL), washed with water (4 mL) and aq. $NaHCO_3$ (10%, 4 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the crude product was effected by silica gel column chromatography (10→40% ethyl acetate in petroleum ether) to yield pentasaccharide **40** (81 mg, 40 μmol). ^{13}C ^{1}H NMR (50 MHz, $CDCl_3$): δ 54.8 (CH_3, 1-*O*-Me), 69.3, 71.4, 71.5, 73.0, 73.1, 73.3, 74.4, 75.5 (C-6, CH_2, All, Bn), 71.8, 72.4, 74.5, 75.1, 77.3, 77.4, 77.9, 80.6, 83.2, 84.5 (CH sugar rings), 98.1, 100.4, 103.2, 103.3, 103.5 (5× C-1), 115.8 (CH_2, All), 126.3, 127.0, 127.2, 127.3, 127.5, 127.6, 127.7, 127.8, 128.0, 128.1, 128.2, 128.3, 128.5, 128.7 (CH, Bn), 135.0 (CH, All), 138.3, 138.4, 138.6, 138.8 (qC, Bn). Anal.: calcd for $C_{110}H_{120}O_{26}$ (1858.17): C, 71.10; H, 6.51; found: C, 71.19; H, 6.43%.

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-[2,3,4-tri-*O*-benzyl-6-*O*-(prop-1-enyl)-β-D-glucopyranosyl]-3-*O*-[3,4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-α-D-mannopyranoside (41). Compound **40** (84 mg, 40 μmol) was dried by evaporation of toluene and dissolved in 1,2-dichloroethane (1.5 mL). The solution was degassed and placed under argon. 1,5-Cyclooctadiene-bis(methyldiphenylphosphine)iridium hexafluorophosphate (5 mg) was added. The catalyst was activated by passing over a stream of hydrogen for 5 min. The reaction mixture was degassed and stirred under argon atmosphere for 72 h. The reaction mixture was filtered and the filtrate was concentrated to give crude pentasaccharide **41**, which was used without purifications. ^{13}C ^{1}H NMR (50 MHz, $CDCl_3$): δ 12.5 (CH_3 propenyl), 54.8 (CH_3, 1-*O*-Me), 63.6 (C-5, Xyl*p*), 66.9, 69.2, 71.9, 73.0, 73.1, 73.3, 74.3, 74.7, 75.0, 75.5 (C-6, CH_2, Bn), 71.8, 72.4, 74.5, 75.3, 77.1, 77.2, 77.8, 78.7, 80.3, 80.6, 81.7, 83.2, 84.3 (CH sugar rings), 98.2, 100.3, 103.2, 103.5 (5× C-1, CH, propenyl), 126.3, 127.0, 127.4, 127.5, 127.6, 127.8, 128.0, 128.1, 128.2, 128.3, 128.5 (CH, arom), 138.3, 138.6, 138.6, 138.7, 138.9, 139.2 (qC, Bn), 146.3 (CH, propenyl).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl)-3-*O*-[3,4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-α-D-mannopyranoside (42). The propenyl containing pentasaccharide **41** was dissolved in dichloromethane (1 mL) and a solution of HCl in methanol (0.5 M, 1 mL) was added. The solution was stirred until, according to TLC-analysis, all starting material was consumed (22 h). Water was added and the resulting mixture was diluted with dichloromethane (5 mL). The two layers were separated and the organic phase was washed with aq. $NaHCO_3$ (10%, 4 mL), and water (3 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography. The column was eluted with 20→50% ethyl acetate in petroleum ether to furnish compound **42** (65 mg, 31 μmol). ^{13}C NMR (50 MHz, $CDCl_3$): δ 54.8 (CH_3, 1-*O*-Me), 60.0, 63.6 (C-6, Glc*p*, C-5, Xyl*p*), 69.2, 69.5, 72.0, 73.0, 73.1, 73.4, 73.8, 74.2, 74.3, 74.7, 75.6 (C-6, Man*p*, CH_2, Bn), 71.8, 72.1, 74.4, 75.4, 76.5, 77.2, 77.8, 78.1, 79.7, 80.5, 82.0, 83.0, 84.2 (CH sugar rings), 98.2, 99.5, 100.0, 101.8, 103.4 (5× C-1), 126.1, 126.6, 127.2, 127.4, 127.5, 127.6, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 128.6, 128.8, 128.9, 129.0 (CH, arom), 137.5, 138.2, 138.6, 138.6, 138.8 (qC, Bn).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-β-D-*gluco*-hexodialdo-1,5-pyranosyl)-3-*O*-[3,4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-α-D-mannopyranoside (43). To a cooled (−60°) solution of oxalyl chloride (20 μL, 233 μmol) in dichloromethane (0.1 mL) was added dropwise a solution of dimethylsulfoxide in dichloromethane (1.9 N, 200 μL). After stirring for 5 min under argon atmosphere, a solution of compound **42** (65 mg, 31 μmol) in dichloromethane (0.5 mL) was added. Stirring was continued for 30 min at −60°. Triethylamine (100 μL, 717 μmol) was added dropwise and the temperature was slowly raised. After stirring for 1.5 h, the reaction mixture was diluted with dichloromethane (5 mL) and washed twice with water (5 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated to give crude **43**. ^{13}C NMR (50 MHz, $CDCl_3$): δ 54.7 (CH_3, 1-*O*-Me), 64.2 (C-5, Xyl*p*), 69.4, 71.5, 72.0, 73.0, 73.1, 73.3, 74.1, 74.3, 75.1, 75.5, 76.4 (C-6, Man*p*, CH_2, Bn), 71.9, 72.2, 74.6, 74.8, 76.9, 77.3, 77.8, 78.4, 78.6, 80.6, 80.9, 83.2, 83.5 (CH sugar rings), 98.3, 100.1, 102.6, 103.4 (5× C-1), 126.3, 127.4, 127.5, 127.6, 127.9, 128.1, 128.2, 128.4 (CH, arom), 137.9, 138.1, 138.4, 138.5, 138.8, 138.9 (qC, Bn), 197.2 (C-6, CHO).

Methyl 2,4,6-tri-*O*-benzyl-3-*O*-{4,6-di-*O*-benzyl-2-*O*-[2,3,4-tri-*O*-benzyl-β-D-glucopyranosyluronic acid]-3-*O*-[3,4,6-di-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-α-D-mannopyranoside (44). To a suspension of

aldehyde containing pentasaccharide **43** in *t*-butanol (0.75 mL) was added successively water (0.75 mL), Na_2HPO_3 (25 mg, 0.28 mmol), 2-methyl-2-butene (0.18 mL), and sodium chlorite (25 mg, 0.21 mmol). After stirring for 17 h, the reaction mixture was diluted with ethyl acetate (5 mL). The organic solution was washed water (3 × 4 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was evaporated repeatedly with ethanol and dichloromethane to give the acid-containing pentasaccharide **44**. ^{13}C NMR (50 MHz, $CDCl_3$): δ 54.8 (CH_3, 1-*O*-Me), 63.8 (CH, Xyl*p*), 69.2, 72.2, 72.9, 73.1, 73.4, 73.8, 74.5, 75.1, 75.5 (C-6, Man*p*, CH_2, Bn), 71.8, 72.5, 75.0, 77.8, 78.1, 78.3, 79.9, 80.5, 80.7, 83.0 (CH sugar rings), 98.2, 100.2, 100.4, 102.7, 103.4 (5 × C-1), 126.8, 127.3, 127.5, 127.5, 127.7, 127.9, 128.1, 128.2, 128.4, 128.6, 128.7, 128.8, 129.1 (CH, arom), 137.5, 138.2, 138.3, 138.5, 138.9 (qC, Bn), 168.1 (C-6, Glc*p*A).

Methyl 3-*O*-{2-*O*-(β-D-glucopyranosyluronic acid)-3-*O*-[2-*O*-(β-D-xylopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranosyl}-α-D-mannopyranoside (1). To a solution of crude pentasaccharide **44** in *t*-butanol (5 mL) was added water (1 mL) and palladium on charcoal. The solution was degassed and shaken under hydrogen pressure (0.5 MPa) for 40 h. The reaction mixture was filtered and the filtrate was concentrated. Purification of the crude product was achieved by a gel filtration using Fractogel HW-40 (S, Omnilabo). The column was eluted with 10% acetonitrile:water to give, after lyophilization, pentasaccharide **1** (15 mg, 17 μmol) as a white powder. ^1H NMR (600 MHz, D_2O, HH-COSY): δ 3.29 (br t, 1H, H-5-ax Xyl*p*, $^2J_{5,5} \approx J_{5,4} = 11.1$ Hz), 3.34 (dd, 1H, H-2 Xyl*p*, $J_{2,1} = 7.7$ Hz, $J_{2,3} = 9.5$ Hz), 3.38 (dd, 1H, H-2 Glc*p*A, $J_{2,1} = 7.9$ Hz, $J_{2,3} = 9.4$ Hz), 3.42 (s, 3H, CH_3, 1-*O*-Me), 3.44 (t, 1H, H-3 Xyl*p*, $J_{3,2} \approx J_{3,4} = 9.2$ Hz), 3.49 (t, 1H, H-3 Glc*p*A, $J_{3,2} \approx J_{3,4} = 9.2$ Hz), 3.55 (t, 1H, H-4 Man*p*, $J_{4,3} \approx J_{4,5} = 10.1$ Hz), 3.57 (t, 1H, H-4, Glc*p*A, $J_{4,3} \approx J_{4,5} = 9.4$ Hz), 3.65 (ddd, 1H, H-4, Xyl*p*, $J_{4,3} = 9.0$ Hz, $J_{4,5} = 5.4$ Hz, $J_{5,4} = 11.1$ Hz), 3.67 (d, 1H, H-5, Glc*p*A, $J_{5,4} = 9.7$ Hz), 3.91 (dd, 1H, H-3, Man*p*, $J_{3,2} = 3.5$ Hz, $J_{3,4} = 10.1$ Hz), 3.64–3.67, 3.74–3.92 (m, 12H, 2 × H-3, Man*p*, 2 × H-4, Man*p*, 2 × H-5, Man*p*, 3 × H-6, Man*p*), 3.95 (ddd, 1H, H-5, Man*p*, $J_{5,4} = 10.3$ Hz, $J_{5,6} = 2.3$ Hz, $J_{5,6} = 5.9$ Hz), 3.97 (dd, 1H, H-5-eq, Xyl*p*, $^2J_{5,5} = -11.6$ Hz, $J_{5,4} = 5.5$ Hz), 4.07 (dd, 1H, H-2 Man*p*, $J_{2,1} = 1.9$ Hz, $J_{2,3} = 3.4$ Hz), 4.12 (dd, 1H, H-3, Man*p*, $J_{3,2} = 3.5$ Hz, $J_{3,4} = 9.2$ Hz), 4.20 (dd, 1H, H-2, Man*p*, $J_{2,1} = 1.5$ Hz, $J_{2,3} = 3.7$ Hz), 4.26 (dd, 1H, H-2, Man*p*, $J_{2,1} = 1.8$ Hz, $J_{2,3} = 3.5$ Hz), 4.38 (d, 1H, H-1, Xyl*p*, $J_{1,2} = 7.7$ Hz), 4.48 (d, 1H, H-1, Glc*p*A, $J_{1,2} = 7.8$ Hz), 4.75 (d, 1H, H-1, Man*p*, $J_{1,2} = 1.9$ Hz), 5.20 (d, 1H, H-1, Man*p*, $J_{1,2} = 1.7$ Hz), 5.22 (d, 1H, H-1, Man*p*, $J_{1,2} = 1.2$ Hz); ^{13}C NMR (150 MHz, D_2O, CH-COSY): δ 55.7 (CH_3, 1-*O*-Me), 61.1, 61.5, 61.8 (3 × C-6, Man*p*), 66.2 (C-5, Xyl*p*), 67.0 (CH), 67.2 (CH), 68.5 (C-4 Man*p*), 70.1 (CH), 70.4 (CH), 70.5 (C-2, Man*p*), 72.6 (C-4, Glc*p*A), 73.4 (C-2, Glc*p*A, C-2, Xyl*p*), 73.6 (CH), 74.1 (C-5, Man*p*), 74.4 (CH), 76.3 (C-3, Glc*p*A), 76.4 (Xyl*p*), 77.5 (C-3, Man*p*), 78.2, 78.4, 78.4 (2 × C-2, Man*p*, CH), 79.4 (CH), 101.0 (C-1 Man*p*), 101.7 (2 × C-1, Man*p*), 102.9 (C-1, Glc*p*A), 103.4 (C-1, Xyl*p*), 176.6 (C-6, Glc*p*A).

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