Facile Synthesis of the Pentasaccharide Repeating Unit of the Exopolysaccharide from *Cryptococcus neoformans* Serotype D

by **Xiao-Bin Zhuo**[a])[1]), **Yan Zou**[b])[1]), **Sheng-Jun Huang**[b]), **Jun Liao**[b]), **Hong-Gang Hu**[b]), **Qing-Jie Zhao***[a])[b]), and **Qiu-Ye Wu***[a])[b])

[a]) School of Pharmacy, Yantai University, No. 30 Qingquan Road, Yantai 264005, P. R. China
[b]) Department of Organic Chemistry, School of Pharmacy, Second Military Medical University, No. 325 Guohe Road, Shanghai 200433, P. R. China
(phone/fax: +86-21-81871228; e-mail: qjzhao@smmu.edu.cn (*Q.-J. Z.*), wuqysmmu@sohu.com (*Q.-Y. W.*))

β-D-Glc*p*A-(1→2)-[β-D-Xyl*p*-(1→2)-α-D-Man*p*-(1→3)]-α-D-Man*p*-(1→3)-α-D-Man*p*, the repeating unit of the exopolysaccharide from *Cryptococcus neoformans* serotype D, was synthesized as its 4-methoxyphenyl glycoside. The approach presented here also provides a route to the synthesis of more complex repeating units of glucuconoxylomannan (GXM) of *C. neoformans* serotypes A–C.

Introduction. – *Cryptococcus neoformans* is an opportunistic fungal pathogen with worldwide distribution that can cause a life-threatening disease, especially for those who suffer from AIDS, renal transplant recipients, and patients undergoing immunosuppressive therapy. Furthermore, the disease has also been distributed in healthy individuals, resulting in 600,000 deaths annually [1–4]. The virulence factors of *C. neoformans* include the presence of a polysaccharide capsule of which glucuronoxylomannan (GXM) is the major constituent [5–7]. Based on the genetic characteristics and serologic properties of capsular polysaccharides (CPS), four major serotypes have been defined as A–D (*Fig.*), in which serotype D owns the simplest pentaose structure, while type C has the most complex octaose structure. All four serotypes are composed of a linear α-(1→3)-linked mannosyl backbone with β-glucopyranosyluronic acid, β-xylopyranosyl, and 6-*O*-Ac substituents [8][9].

Syntheses of the repeating units of the polysaccharides from *C. neoformans* serotypes A–D have been already reported [10–13]. In these syntheses, multiple steps and orthogonal masking groups were involved, rendering the procedure rather complex and tedious. Herein, we report the synthesis of the repeating unit of the serotype D in an efficient way, and the strategy presented here also provides a route to the synthesis of more complex repeating units of GXM of *C. neoformans* serotypes A–C.

Results and Discussion. – Our strategy for the synthesis of the pentaose repeating unit involves the construction of the acceptors **7** and **8** (*Scheme 1*), and donors **13** and **14** (*cf. Schemes 2* and *3*). To obtain the pentaose, β-D-Xyl*p*-(1→2)-α-D-Man*p* and β-D-Glc*p*A-(1→2)-α-D-Man*p*, the two key middle disaccharide blocks, were first synthesized, then coupling of them (2+2) and extension of the tetrasaccharide chain thus

[1]) These two authors contributed equally to this work.

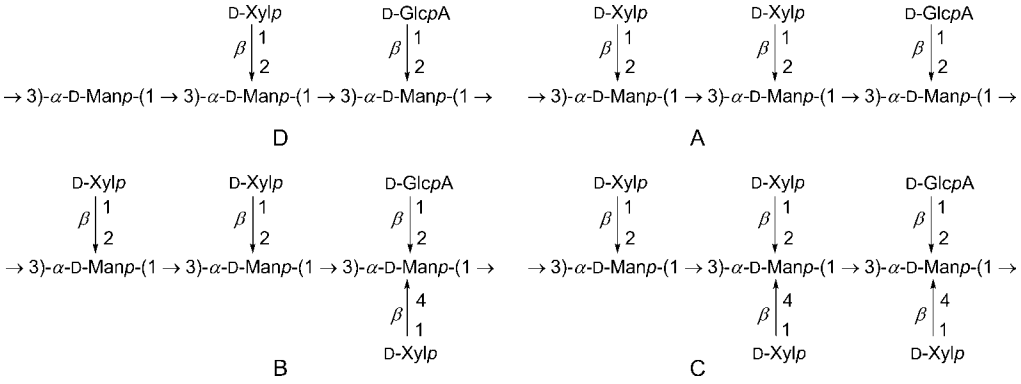
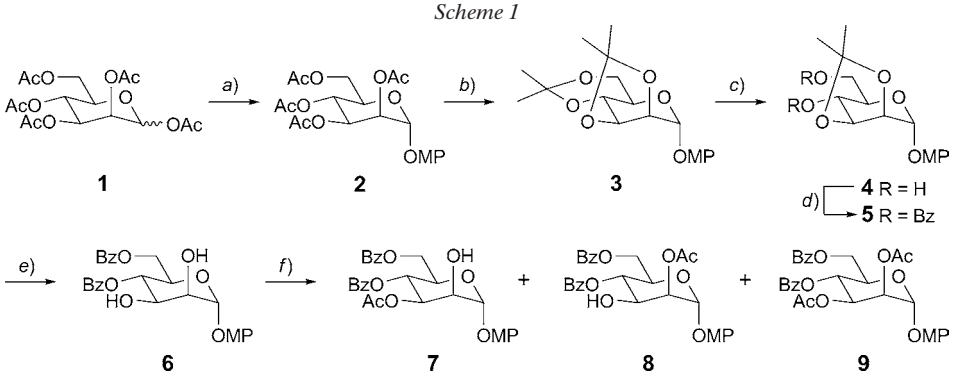


Figure. *Model structures of GXM of* Cryptococcus neoformans *serotypes* A – D

obtained with a monosaccharide acceptor on the reducing end (4 + 1) were carried out at the final stage.

As shown in *Scheme 1*, the 4-methoxyphenyl (MP) group (*Scheme 1*) was introduced to 1,2,3,4,6-penta-*O*-acetyl-D-mannopyranose (**1**) to afford 4-methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**2**) [14][15] in high yield (90%), using TBDMSOTf as promoter. Cleavage of the acetates and then reaction with 2,2-dimethoxypropane under catalysis by TsOH afforded the diacetal **3** as an oil [16]. Treatment with $TsOH \cdot H_2O$ (cat.) in acetone/H_2O 20 : 1 at 50° for 10 min afforded the 2,3-*O*-isopropylidene derivative **4** predominantly [17]. Compound **4** was benzoylated [18] to give 4-methoxyphenyl 4,6-di-*O*-benzoyl-2,3-*O*-isopropylidene-α-D-mannopyranoside (**5**), which exhibited characteristic signals in its ^{1}H-NMR spectrum. Removal of isopropylidene group [19] from **5** was followed by selective 3-*O*-acetylation [20] of the resulting diol **6** with AcCl in the presence of pyridine. In addition to the expected

Scheme 1



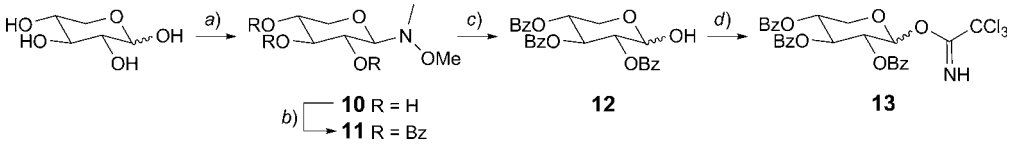
a) 4-MeO–C_6H_4–OH (MP–OH), ^{t}Bu(Me_2)Si OSO_2CF_3 (TBDMSOTf), CH_2Cl_2, r.t. *b*) MeONa, MeOH, then $MeC(MeO)_2Me$, $TsOH \cdot H_2O$ (cat.), acetone, r.t. *c*) $TsOH \cdot H_2O$ (cat.), acetone/H_2O 20 : 1, 50°, 10 min. *d*) BzCl, Pyridine. *e*) 90% CF_3COOH (TFA), r.t. *f*) AcCl, pyridine, CH_2Cl_2, 80% (for **7**), 10% (for **8**), 5% (for **9**).

acceptor 4-methoxyphenyl 3-*O*-acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranoside (**7**; 80%), small portions of 4-methoxyphenyl 2-*O*-acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranoside (**8**; 10%) and 4-methoxyphenyl 2,3-di-*O*-acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranoside (**9**; 5%) were also obtained. This was confirmed by the ^{1}H-NMR spectrum in which compound **7** gave rise to a characteristic *singlet* at δ(H) 2.03 (3-Ac), while the *singlet* at δ(H) 2.21 (2-Ac) was attributed to **8**. When **9** was treated with 1% AcCl/MeOH [10], for the first few hours, compound **9** was only transformed to **8**, but if this reaction was continued for *ca.* 2 d, a total conversion of **9** to **6** was observed. Based on all these findings, it can be concluded that the 3-OH is more reactive than 2-OH. This selective 3-*O*-acetylation was the key step in the synthesis.

The synthesis of the donor 2,3,4-tri-*O*-benzoyl-D-xylopyranosyl trichloroacetimidate (**13**) is shown in *Scheme 2*. Starting from xylose, we applied *N*,*O*-dimethylhydroxylamine as the anomeric protecting group [20], and, in subsequent benzoylation and deprotection of the hydroxylamine, a solution of NCS in THF/H_2O 9 : 1 [21] was used at 50 – 60° to furnish **12**, followed by a reaction with CCl_3CN in the presence of traces of DBU [22] to afford donor **13**. The advantage of this method is that *N*,*O*-dimethylhydroxylamine can be directly introduced in unprotected xylose, reducing the number of synthesis steps when compared with previously reported methods. The trichloroacetimidate donor **14** was easily available from the commercial D-glucofuranurono-6,3-lactone in four steps [23][24].

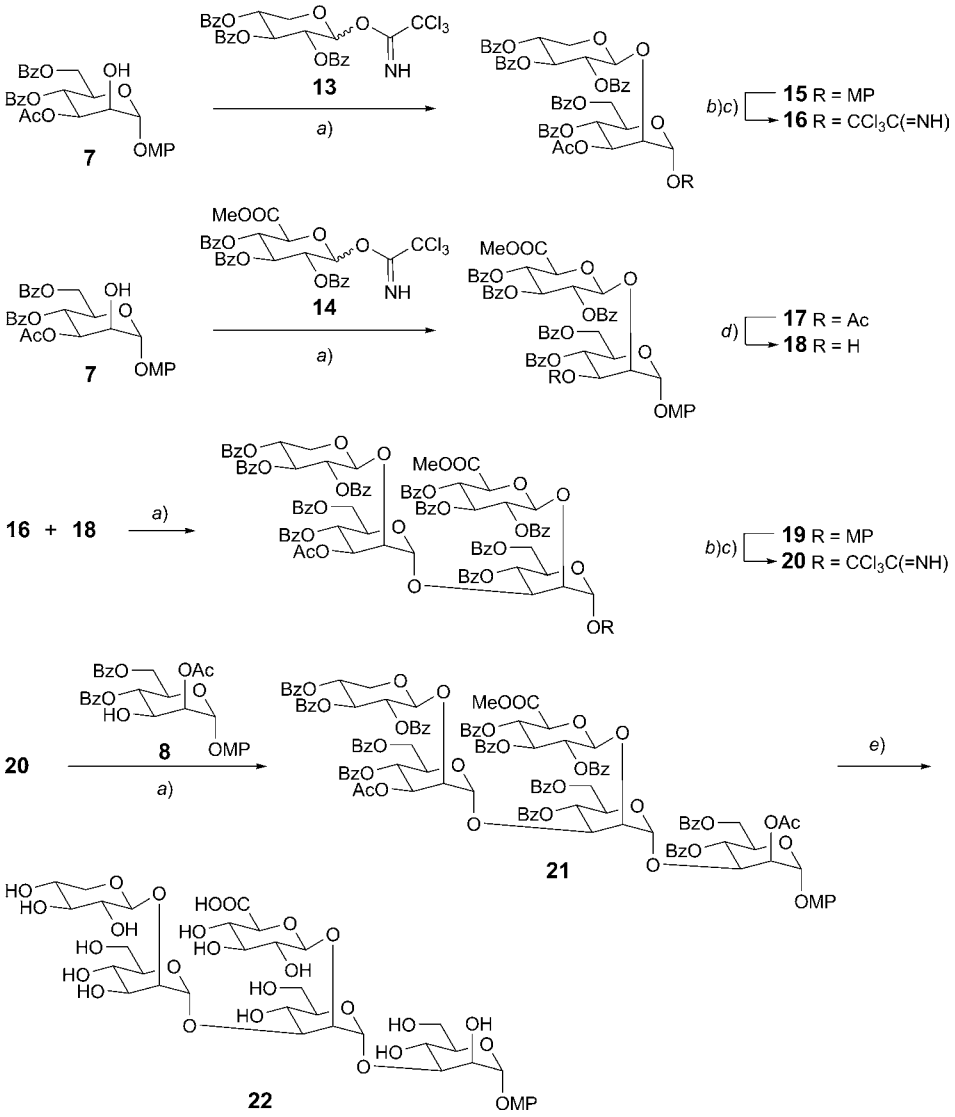
The synthesis of the pentasaccharide β-D-Glc*p*A-(1 → 2)-[β-D-Xyl*p*-(1 → 2)-α-D-Man*p*-(1 → 3)]-α-D-Man*p*-(1 → 3)-α-D-Man*p* was outlined in *Scheme 3*. 4-Methoxyphenyl 3-*O*-acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranoside (**7**) was chosen as the starting material, and glycosylation [25] of **7** with **13** and methyl 2,3,4-tri-*O*-benzoyl-1-*O*-(2,2,2-trichloroethanimidoyl)-D-glucopyranuronate (**14**) furnished the β-(1 → 2)-linked disaccharides **15** and **17**, respectively. Subsequent removal of the MP group by oxidative cleavage [26] of **15** with $(NH_4)_2Ce(NO_3)_6$ (CAN) and trichloroacetimidate formation gave the β-(1 → 2)-linked disaccharide donor **16**. Selective deacetylation of **17** with AcCl, MeOH, and CH_2Cl_2, accompanied with some decomposition, perhaps caused by breaking of xylosyl linkage, furnished the β-(1 → 2)-linked disaccharide acceptor **18**. The condensation of **16** with **18**, promoted by TMSOTf, went smoothly to afford the required tetrasaccharide **19** in a satisfactory yield (60%). Oxidative cleavage of MP group led to the tetrasaccharide donor **20**, along with a trichloroacetimidate formation. Then, the protected pentasaccharide **21** was obtained by coupling **8** with the tetrasaccharide trichloroacetimidate in good yield (71%). Deprotection [27] of **21** was carried out in MeOH with MeONa for 96 h, affording the target pentasaccharide **22** as foamy solid.

Scheme 2



a) HN(Me)OMe · HCl, AcONa, H_2O. *b*) BzCl, Pyridine. *c*) *N*-Chlorosuccinimide (NCS), THF/H_2O 9 : 1. *d*) Cl_3CCN, 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU), CH_2Cl_2.

Scheme 3



a) $Me_3SiOSO_2CF_3$ (TMSOTf), CH_2Cl_2, $-20°$ to r.t. (dry). *b*) $(NH_4)_2Ce(NO_3)_6$ (CAN), MeCN/H_2O 4 : 1, r.t. *c*) Cl_3CCN, DBU, CH_2Cl_2. *d*) 1% AcCl/MeOH, 0° to r.t. *e*) MeONa/MeOH, r.t., 96 h; then H_2O, r.t., 2 h.

In summary, we presented here a facile synthesis of the pentasaccharide repeating unit of GXM of *C. neoformans* serotype D. This strategy offers a route to obtain higher oligosaccharides with similar structures such as the repeating units of GXM of *C. neoformans* serotypes A – C.

We are grateful to the *National Natural Science Foundation of China* (No. 20902109), the *Shanghai Leading Academic Discipline Project* (B906), the *State Project for Essential Drug Research and Development* (2012ZX09502-001-005), and the Instrumental Analysis Center of our university for NMR spectroscopic and mass spectrometric analyses.

Experimental Part

General. Anh. solvents were obtained from a solvent purification system, while commercial anh. reagents were used without further purification. TLC: Silica gel (SiO_2) GF_{254} plates; visualization under UV light or by spraying with a 5% H_2SO_4 soln. in EtOH. Column chromatography (CC): SiO_2 (200–300 mesh, 10–40 mm; *Qingdao Marine Chemical Factory*). ^{1}H- and ^{13}C-NMR spectra: *Bruker Avance*; 300 and 600 (^{1}H), 75, and 150 MHz (^{13}C) spectrometers; δ in ppm rel. to Me_4Si as internal standard, J in Hz. ESI-MS and HR-QTOF-MS: *Finngan LCQ Deca XP Max* instrument and *Agilent 6538 UHD Accurate Mass Q-TOF* LC/MS mass spectrometer, resp.; in m/z.

General Procedure for the Glycosylations. A mixture of the donor and acceptor was dried together under high vacuum for 2 h, then, dissolved in anh. CH_2Cl_2, TMSOTf (0.05 equiv.) was added dropwise at $-30°$ under N_2. The mixture was stirred for 3 h, during which time the temp. was gradually increased to r.t. The mixture was then neutralized with Et_3N. Concentration of the mixture, followed by purification on a silica-gel column, gave the desired products.

4-Methoxyphenyl 2,3,4,6-Tetra-O-*acetyl*-α-D-*mannopyranoside* (**2**). To a cold (0°) soln. of **1** (4.33 g, 11.1 mmol) and 4-methoxyphenol (2.065 g, 16.65 mmol) in dry CH_2Cl_2 (75 ml) was added TBDMSOTf (2.80 ml, 12.21 mmol) under Ar. After 12 h, TLC (petroleum ether (PE)/AcOEt 5:4) indicated that the reaction was complete, and the mixture was diluted with CH_2Cl_2, and washed with H_2O, sat. aq. $NaHCO_3$ soln., and brine. The org. phase was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Purification of the crude product by CC (PE/AcOEt 3:1) gave **2** (4.54 g, 90%). White solid. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.02 (*d*, *J* = 9.1, 2 arom. H); 6.83 (*d*, *J* = 9.1, 2 arom. H); 5.55 (*dd*, *J* = 10.0, 3.4, 1 H); 5.44–5.41 (*m*, 2 H); 5.36 (*t*, *J* = 9.9, 1 H); 4.28 (*dd*, *J* = 11.7, 4.9, 1 H); 4.16–4.06 (*m*, 2 H); 3.77 (*s*, MeO); 2.19, 2.09, 2.06, 2.05 (4*s*, 4 × Ac). ESI-MS: 477.13 ($[M+Na]^+$).

4-Methoxyphenyl 2,3:4,6-Di-O-*isopropylidene*-α-D-*mannopyranoside* (**3**). A soln. of **2** (91 mg, 0.20 mmol) in MeOH (2 ml) was treated with MeONa (2.16 mg, 0.04 mmol) and stirred for 2 h at r.t. The mixture was then neutralized with *Amberlite H*$^+$ resin, filtered, and concentrated. The residue was dried under high vacuum and dissolved in acetone (2 ml), $TsOH \cdot H_2O$ (3.8 mg, 10%) was added, and the resulting soln. was then treated with 2,2-dimethoxypropane (0.15 ml, 1.2 mmol). After the stirring overnight, solid Na_2CO_3 was added, and the mixture was filtered and concentrated. The residue was then separated by CC (PE/AcOEt 5:2) to afford **3** (59 mg, 80%, over two steps). Light-yellow oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.96 (*d*, *J* = 9.0, 2 arom. H); 6.83 (*d*, *J* = 9.0, 2 arom. H); 5.65 (*s*, 1 H); 4.40 (*d*, *J* = 5.6, 1 H); 4.34–4.27 (*m*, 1 H); 3.85–3.71 (*m*, H–C(5), CH_2(6), MeO); 1.59, 1.53, 1.43, 1.40 (4*s*, 2 Me_2C). ESI-MS: 389.17 ($[M+Na]^+$).

4-Methoxyphenyl 2,3-O-*Isopropylidene*-α-D-*mannopyranoside* (**4**). Compound **3** (200 mg, 0.545 mmol) was dissolved in acetone/H_2O 20:1 (2 ml), TsOH (9 mg) was added, and the mixture was stirred at 50° for 10 min; then the reaction was quenched with Et_3N, and the mixture was concentrated. The residue was subjected to CC (PE/AcOEt 1:1) to give **4** (150 mg, 84%). White solid. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.07 (*d*, *J* = 9.0, 2 arom. H); 6.85 (*d*, *J* = 9.0, 2 arom. H); 5.61 (*s*, 1 H); 4.36 (*dd*, *J* = 5.6, 0.7, 1 H); 4.19 (*t*, *J* = 6.1, 1 H); 3.75 (*s*, MeO); 3.71 (*dd*, *J* = 6.9, 3.1, 2 H); 3.67 (*d*, *J* = 2.5, 2 H); 1.52, 1.39 (2*s*, Me_2C). ESI-MS: 349.14 ($[M+Na]^+$).

4-Methoxyphenyl 4,6-Di-O-*benzoyl-2,3*-O-*isopropylidene*-α-D-*mannopyranoside* (**5**). Compound **4** (1.63 g, 5.0 mmol) was dissolved in dry CH_2Cl_2 (20 ml) containing pyridine (3.58 ml, 50 mmol), then, under N_2 protection and stirring, a soln. of BzCl (0.83 ml, 5.0 mmol) in anh. CH_2Cl_2 (10 ml) was added dropwise within 30 min at 0°. The mixture was slowly warmed to r.t. and stirred for 2 h, when TLC indicated the completion of the reaction. The mixture was diluted with CH_2Cl_2, washed with H_2O, 1N HCl, and dried (Na_2SO_4). The soln. was concentrated, and purification by CC (CH_2Cl_2/MeOH 400:1) gave **5** (2.40 g, 90%). White solid. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.08 (*d*, *J* = 8.3, 2 arom. H); 7.91

(*d*, *J* = 8.3, 2 arom. H); 7.70–7.73 (*m*, 6 arom. H); 7.07 (*d*, *J* = 9.0, 2 arom. H); 6.75 (*d*, *J* = 9.0, 2 arom. H); 5.58 (*s*, 1 H); 5.45 (*t*, *J* = 9.5, 1 H); 4.58–4.26 (*m*, 5 H); 3.75 (*s*, MeO). ESI-MS: 535.56 ($[M+H]^+$).

4-Methoxyphenyl 4,6-Di-O-*benzoyl*-α-D-*mannopyranoside* (**6**). Compound **5** (30 mg, 0.056 mmol) was dissolved in CH_2Cl_2 (2 ml) containing 90% aq. CF_3COOH (TFA; 0.5 ml), and the soln. was stirred at r.t. for 2 h, when TLC (CH_2Cl_2/MeOH 100 : 1) indicated that the reaction was complete. Evaporation of the solvent gave **6** (25 mg, 90%) as white solid, which was directly used for next step without further purification. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.07 (*d*, *J* = 8.3, 2 arom. H); 7.90 (*d*, *J* = 8.3, 2 arom. H); 7.69–7.32 (*m*, 6 arom. H); 7.06 (*d*, *J* = 9.0, 2 arom. H); 6.75 (*d*, *J* = 9.0, 2 arom. H); 5.58 (*s*, 1 H); 5.44 (*t*, *J* = 9.5, 1 H); 4.57–4.26 (*m*, 5 H); 3.74 (*s*, MeO). ESI-MS: 517.16 ($[M+Na]^+$).

4-Methoxyphenyl 3-O-*Acetyl-4,6-di*-O-*benzoyl*-α-D-*mannopyranoside* (**7**). Compound **6** (2.18 g, 4.4 mmol) was dissolved in dry CH_2Cl_2 (20 ml) containing pyridine (3.52 ml, 44 mmol), then, under N_2 protection and stirring, a soln. of AcCl (0.8 ml, 4.84 mmol) in anh. CH_2Cl_2 (10 ml) was added dropwise within 30 min at 0°. The mixture was slowly warmed to r.t. and stirred for 2 h, when TLC (CH_2Cl_2/MeOH 100 : 1) indicated that the reaction was complete. The mixture was diluted with CH_2Cl_2, washed with H_2O and 1N HCl, and dried (Na_2SO_4). The soln. was concentrated, and purification by CC (CH_2Cl_2/MeOH 400 : 1) gave **7** (1.90 g, 80%), **8** (236 mg, 10%), and **9** (127mg, 5%) as white solid.

Data of **7**. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.02 (*d*, *J* = 7.9, 2 arom. H); 7.91 (*d*, *J* = 7.9, 2 arom. H); 7.58–7.33 (*m*, 6 arom. H); 7.08 (*d*, *J* = 9.0, 2 arom. H); 6.76 (*d*, *J* = 9.0, 2 arom. H); 5.75 (*s*, 1 H); 5.55 (*t*, *J* = 2.9, 1 H); 4.53–4.35 (*m*, 4 H); 3.74 (*s*, MeO); 2.75 (*s*, 2-OH); 2.03 (*s*, MeCO). ESI-MS: 559.16 ($[M+Na]^+$).

4-Methoxyphenyl 2-O-*Acetyl-4,6-di*-O-*benzoyl*-α-D-*mannopyranoside* (**8**). ^{1}H-NMR (300 MHz, $CDCl_3$): 8.05 (*d*, *J* = 7.9, 2 arom. H); 7.94 (*d*, *J* = 7.9, 2 arom. H); 7.63–7.37 (*m*, 6 arom. H); 7.07 (*t*, *J* = 10.7, 2 arom. H); 6.75 (*t*, *J* = 10.7, 2 arom. H); 5.53 (*s*, 1 H); 5.39–5.29 (*m*, 1 H); 4.64–4.33 (*m*, 4 H); 3.74 (*s*, MeO); 2.21 (*s*, MeCO). ESI-MS: 559.16 ($[M+Na]^+$).

N-*Methoxy*-N-*methyl*-β-D-*xylopyranosylamine* (**10**). Xylose (15.01 g, 0.1 mmol) was dissolved in H_2O (150 ml) in a round-bottomed flask. *N*,*O*-Dimethylhydroxylamine hydrochloride (10.73 g, 0.11 mmol) and AcONa (9.02 g, 0.11 mmol) were dissolved in *ca.* 10 ml of H_2O, and the soln. was added slowly to the xylose soln. at 0°. The reaction was allowed to proceed for 20 h at r.t., when TLC analysis showed conversion of the starting material to a faster-moving product (CH_2Cl_2/MeOH 5 : 1). H_2O was evaporated from the reaction *in vacuo*, and the product was purified by CC (CH_2Cl_2/MeOH 8 : 1) to give **10** (16.4 g, 85%). White solid. ^{1}H-NMR (600 MHz, D_2O): 4.02 (*d*, *J* = 8.5, 1 H); 3.49 (*s*, MeO); 3.38–3.47 (*m*, 3 H); 3.24–3.34 (*m*, 2 H); 2.76 (*s*, MeN). ESI-MS: 216.10 ($[M+Na]^+$).

2,3,4-Tri-O-*benzoyl*-N-*methoxy*-N-*methyl*-β-D-*xylopyranosylamine* (**11**). To the soln. of **10** (2.90 g, 15 mmol) in anh. CH_2Cl_2 (30 ml), containing pyridine (7.24 ml), a soln. of BzCl (7.8 ml) in 20 ml of anh. CH_2Cl_2 was added dropwise at 0° under N_2, and the mixture was stirred overnight at r.t. TLC (PE/AcOEt 5 : 1) indicated that the reaction was complete. Ice-water was added, and the mixture was diluted with CH_2Cl_2, washed with 1N HCl, H_2O, and sat. aq. $NaHCO_3$. The org. layer was combined, dried, and concentrated. Purification of the crude product by CC gave **11** (6.8 g, 90%). White solid. ^{1}H-NMR (600 MHz, $CDCl_3$): 7.98–7.30 (*m*, 15 arom. H); 5.92 (*t*, *J* = 9.6, 1 H); 5.64 (*t*, *J* = 9.4, 1 H); 5.40 (*dt*, *J* = 10.1, 5.5, 1 H); 4.51–4.46 (*m*, 2 H); 3.61–3.55 (*m*, 1 H); 3.46 (*s*, MeO); 2.79 (*s*, MeN). ESI-MS: 528.17 ($[M+Na]^+$).

2,3,4-Tri-O-*benzoyl*-D-*xylopyranose* (**12**). Compound **11** (505.52 mg, 1 mmol) was dissolved in THF/H_2O 9 : 1 (15 ml), and NCS (267.06 mg, 2 mmol) was added. The soln. was warmed to 50° for 2 h when TLC analysis showed complete conversion to a slower-moving product (PE/AcOEt 4 : 1). The solvent was evaporated, and the crude oil was purified by CC (PE/AcOEt 4 : 1) to furnish **12** (416 mg, 90%). White solid. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.02–7.30 (*m*, 15 arom. H); 6.22 (*t*, *J* = 9.5, 1 H); 5.69 (*t*, *J* = 3.5, 1 H); 5.42 (*d*, *J* = 7.1, 1 H); 5.31 (*t*, *J* = 4.9, 1 H); 4.14 (*d*, *J* = 7.8, 2 H); 3.25 (*s*, 1 H). ESI-MS: 485.13 ($[M+Na]^+$).

2,3,4-Tri-O-*benzoyl-1*-O-*(2,2,2-trichloroethanimidoyl)*-D-*xylopyranose* (**13**). Compound **12** (230 mg, 0.5 mmol) was dried under high vacuum for 2 h, then dissolved in CH_2Cl_2 (10 ml), and CCl_3CN (0.5 ml, 5 mmol) and DBU (7 µl, 0.05 mmol) were added in an ice bath. The mixture was stirred for 2 h, when TLC (PE/AcOEt 4 : 1) indicated that the reaction was complete. Concentration of the mixture, followed by purification of the crude product on CC (SiO_2; PE/AcOEt 4 : 1), gave **13** (243 mg, 80%). Foamy solid. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.70 (*s*, C=NH); 8.05–7.31 (*m*, 15 arom. H); 6.83 (*d*, *J* = 3.0, 1 H); 6.13 (*t*,

$J = 9.6$, 2 H); 5.88 (*s*, 1 H); 5.53 (*dd*, $J = 10.0$, 3.5, 1 H); 4.42–4.18 (*m*, 2 H). ESI-MS: 629.84 ($[M + Na]^+$).

4-Methoxyphenyl 2,3,4-Tri-O-*benzoyl-β*-D-*xylopyranosyl-(1 → 2)-3*-O-*acetyl-4,6-di*-O-*benzoyl-α*-D-*mannopyranoside* (**15**). As described in the *General Procedure*, **13** (88 mg, 0.145 mmol) and **7** (65 mg, 0.121 mmol) were coupled, and the product was purified by CC (SiO_2; PE/AcOEt 3 :1) to give **15** (103 mg, 86.8%). White solid. ^{1}H-NMR (600 MHz, $CDCl_3$): 8.12–7.29 (*m*, 25 arom. H); 6.91 (*d*, $J = 9.1$, 2 arom. H); 6.72 (*d*, $J = 9.1$, 2 arom. H); 6.05 (*d*, $J = 4.7$, 1 H); 5.71 (*dd*, $J = 5.0$, 1 H); 5.67 (*dd*, $J = 10.0$, 1 H); 5.50 (*dd*, $J = 10.0$, 3.3, 1 H); 5.37 (*dd*, $J = 5.0$, 3.7, 1 H); 5.28–5.19 (*m*, 1 H); 4.97 (*d*, $J = 3.7$, 1 H); 4.61 (*dd*, $J = 12.5$, 3.2, 1 H); 4.34 (*dd*, $J = 11.8$, 3.0, 1 H); 4.26 (*dd*, $J = 3.3$, 1.4, 1 H); 4.22–4.16 (*m*, 2 H); 4.08–3.97 (*m*, 1 H); 3.65 (*s*, MeO); 1.97 (*s*, MeCO). ^{13}C-NMR (150 MHz, $CDCl_3$): 169.8; 165.3; 165.0; 164.8; 164.7; 164.4; 154.6; 149.2; 133.0; 132.9; 132.8; 132.6; 132.3; 129.5; 129.4; 129.3; 129.1; 129.1; 128.8; 128.7; 128.5; 128.4; 128.3; 128.2; 128.1; 128.0; 127.9; 127.7; 127.7; 127.6; 117.1; 114.0; 99.0; 95.8; 75.4; 69.6; 69.0; 68.6; 68.5; 67.8; 66.7; 63.1; 60.1; 55.0; 20.3. HR-QTOF-MS: 1003.2784 ($[M + Na]^+$, $C_{55}H_{48}NaO_{17}^+$; calc. 1003.2789).

3-O-*Acetyl-4,6-di*-O-*benzoyl-2*-O-*(2,3,4-tri*-O-*benzoyl-β*-D-*xylopyranosyl)-1*-O-*(2,2,2-trichloroethanimidoyl)-α*-D-*mannopyranose* (**16**). To a soln. of **15** (100 mg, 0.1 mmol) in MeCN/H_2O 4 :1 (5 ml) was added $(NH_4)_2Ce(NO_3)_6$ (CAN; 164 mg, 0.3 mmol), and the mixture was stirred at r.t. for 30 min, when TLC (PE/AcOEt 2 :1) indicated that the reaction was complete. The mixture was extracted with CH_2Cl_2 and washed with H_2O. The org. layer was concentrated, and the crude hemiacetal was purified by CC (SiO_2; PE/AcOEt 2 :1) to afford white solid. After drying under high vacuum for 2 h, the solid was dissolved in CH_2Cl_2 (5 ml), and CCl_3CN (0.1 ml, 1 mmol) and DBU (2 µl, 0.01 mmol) were added in an ice bath. The mixture was stirred for 2 h, at the end of which time TLC (PE/AcOEt 2 :1) indicated that the reaction was complete. Concentration of the mixture, followed by purification of the crude product on a SiO_2 column (PE/AcOEt 2 :1), afforded **16** (66 mg, 68%, for two steps). Yellow solid. ^{1}H-NMR (600 MHz, $CDCl_3$): 8.15 (*s*, NH); 8.09–7.23 (*m*, 25 arom. H); 5.69–5.65 (*m*, 2 H); 5.52 (*dd*, $J = 10.1$, 3.2, 1 H); 5.31 (*dd*, $J = 11.0$, 5.9, 2 H); 5.23 (*dd*, $J = 8.4$, 5.0, 1 H); 4.94 (*d*, $J = 3.6$, 1 H); 4.58 (*dd*, $J = 12.5$, 3.2, 1 H); 4.41–4.34 (*m*, 1 H); 4.29 (*dd*, $J = 12.0$, 3.4, 1 H); 4.26–4.23 (*m*, 1 H); 4.10–4.01 (*m*, 2 H); 3.78–3.74 (*m*, 2 H); 3.32 (*s*, 1 H); 1.93 (*s*, MeCO). HR-QTOF-MS: 1040.2839 ($[M + Na]^+$, $C_{50}H_{42}Cl_3NaO_{16}^+$; calc. 1040.1569).

4-Methoxyphenyl 3-O-*Acetyl-4,6-di*-O-*benzoyl-2*-O-*(2,3,4-tri*-O-*benzoyl-6-methyl-β*-D-*glucopyranuronosyl)-α*-D-*mannopyranoside* (**17**). Donor **14** (74 mg, 0.111 mmol) was coupled with **7** (50 mg, 0.09 mmol) as described in the *General Procedure*, and the product was purified by CC (SiO_2; PE/AcOEt 3 :1) to give **17** (80 mg, 85%). Foamy solid. ^{1}H-NMR (600 MHz, $CDCl_3$): 8.00–7.28 (*m*, 25 arom. H); 6.93 (*d*, $J = 9.1$, 2 arom. H); 6.70 (*d*, $J = 9.1$, 2 arom. H); 6.09 (*d*, $J = 4.8$, 1 H); 5.75 (*t*, $J = 9.9$, 1 H); 5.64 (*t*, $J =$ 2.8, 1 H); 5.53 (*dd*, $J = 10.1$, 3.4, 1 H); 5.47 (*dd*, $J = 7.6$, 1.5, 1 H); 5.37 (*d*, $J = 1.7$, 1 H); 4.78–4.75 (*m*, 1 H); 4.45 (*dd*, $J = 11.7$, 2.0, 1 H); 4.25 (*ddt*, $J = 8.2$, 5.8, 2.9, 3 H); 4.14 (*dd*, $J = 3.3$, 2.0, 1 H); 3.68 (*s*, MeO); 3.58 (*s*, COOMe); 1.92 (*s*, MeCO). ^{13}C-NMR (150 MHz, $CDCl_3$): 169.3; 167.8; 165.8; 165.5; 165.1; 165.0; 164.8; 154.7; 149.2; 133.0; 132.9; 132.8; 132.7; 132.4; 129.5; 129.3; 129.3; 129.3; 129.2; 128.5; 128.4; 128.3; 128.2; 128.1; 128.0; 127.9; 127.9; 127.8; 127.7; 117.2; 114.1; 97.6; 90.0; 75.0; 71.0; 70.8; 69.5; 69.0; 68.8; 68.7; 68.6; 68.1; 66.7; 62.8; 55.0; 52.3; 20.2. HR-QTOF-MS: 1061.2839 ($[M + Na]^+$, $C_{57}H_{50}NaO_{19}^+$; calc. 1061.2946).

4-Methoxyphenyl 4,6-Di-O-*benzoyl-2*-O-*(2,3,4-tri*-O-*benzoyl-6-methyl-β*-D-*glucopyranuronosyl)-α*-D-*mannopyranoside* (**18**). To a soln. of **17** (100 mg, 0.1 mmol) in anh. CH_2Cl_2 (2 ml) was added anh. MeOH (0.8 ml). AcCl (20 µl) was then added to the mixture at 0°. The soln. was stirred in a stoppered flask at r.t., until TLC (PE/AcOEt 2 :1) showed that the starting material had disappeared. The soln. was neutralized with Et_3N, then concentrated to dryness. The residue was passed through a short SiO_2 column to give **18** (80.05 mg, 80%). Foamy solid. ^{1}H-NMR (600 MHz, $CDCl_3$): 8.15–7.82 (*m*, 10 arom. H); 7.56–7.26 (*m*, 15 arom. H); 7.09 (*d*, $J = 9.0$, 2 arom. H, $MeOC_6H_4O$); 6.77 (*d*, $J = 9.0$, 2 arom. H, $MeOC_6H_4O$); 6.27 (*t*, $J = 9.6$, 1 H); 5.86 (*t*, $J = 3.6$, 1 H); 5.79–5.63 (*m*, 2 H); 5.58–5.47 (*m*, 1 H); 5.36–5.33 (*m*, 1 H); 4.88 (*d*, $J = 9.9$, 1 H); 4.56–4.40 (*m*, 2 H); 4.26 (*t*, $J = 6.7$, 1 H); 3.73 (*s*, MeO); 3.63 (*s*, COOMe). ^{13}C-NMR (150 MHz, $CDCl_3$): 169.5; 168.0; 165.2; 165.1; 165.1; 164.8; 149.2; 133.1; 133.0; 133.0; 132.9; 132.9; 132.8; 132.7; 132.5; 132.4; 129.4; 129.3; 129.3; 129.2; 129.2; 128.5; 128.3; 128.2; 128.1; 128.0; 127.9;

127.8; 127.8; 127.7; 127.7; 117.4; 117.2; 114.1; 97.7; 90.0; 73.0; 72.4; 71.8; 71.1; 69.5; 68.9; 68.0; 66.7; 62.8; 62.8; 55.0; 52.3. ESI-MS: 997.18 ($[M+H]^+$).

4-Methoxyphenyl 2,3,4-Tri-O-*benzoyl-6-methyl-β*-D-*glucopyranuronosyl-(1 → 2)-[2,3,4-tri*-O-*benzoyl-β*-D-*xylopyranosyl-(1 → 2)-3*-O-*acetyl-4,6-di*-O-*benzoyl-α*-D-*mannopyranosyl-(1 → 3)]-4,6-di*-O-*benzoyl-α*-D-*mannopyranoside* (**19**). Compound **16** (102 mg, 0.10 mmol) and **18** (50 mg, 0.05 mmol) were coupled under the same conditions as those used for the preparation of **17** from **7** and **14**, to give **19** (56 mg, 60%). Foamy solid. ^{1}H-NMR (600 MHz, $CDCl_3$): 8.07 – 7.28 (*m*, 50 arom. H); 6.93 (*d*, *J* = 9.1, 2 arom. H, $MeOC_6H_4O$); 6.76 (*d*, *J* = 9.1, 2 arom. H, $MeOC_6H_4O$); 6.24 (*t*, *J* = 9.9, 1 H); 5.80 – 5.71 (*m*, 4 H); 5.70 – 5.60 (*m*, 2 H); 5.54 (*ddd*, *J* = 13.7, 10.2, 3.5, 3 H); 5.41 (*dd*, *J* = 5.7, 4.1, 1 H); 5.33 (*d*, *J* = 1.8, 1 H); 5.32 – 5.24 (*m*, 2 H); 5.01 (*d*, *J* = 4.1, 1 H); 4.67 (*d*, *J* = 10.0, 1 H); 4.59 (*dd*, *J* = 12.5, 3.4, 1 H); 4.51 (*dd*, *J* = 3.3, 1.8, 1 H); 4.30 (*d*, *J* = 9.7, 1 H); 4.00 (*ddd*, *J* = 11.2, 6.3, 2.9, 1 H); 3.86 – 3.79 (*m*, 2 H); 3.72 (*s*, MeO); 2.03 (*s*, MeCO). ^{13}C-NMR (150 MHz, $CDCl_3$): 171.7; 169.0; 167.4; 167.1; 167.0; 166.8; 166.7; 166.6; 166.5; 166.5; 166.4; 166.2; 156.6; 150.7; 135.0; 134.9; 134.8; 134.7; 134.3; 134.2; 131.4; 131.4; 131.3; 131.2; 131.2; 131.2; 131.1; 131.1; 130.9; 130.8; 130.7; 130.6; 130.5; 130.4; 130.4; 130.3; 130.2; 130.1; 129.9; 129.9; 129.8; 129.7; 129.6; 129.6; 129.5; 119.1; 116.0; 100.5; 100.1; 98.5; 95.1; 93.3; 77.21; 76.6; 76.3; 71.7; 71.7; 71.3; 71.2; 71.2; 71.1; 71.0; 70.9; 70.7; 70.6; 70.3; 69.7; 69.4; 69.3; 69.0; 68.1; 65.3; 64.9; 64.4; 61.9; 61.4; 56.9; 54.4; 31.1. HR-QTOF-MS: 1853.5664 ($[M+H]^+$, $C_{103}H_{89}O_{33}^+$; calc. 1853.5286).

2,3,4-Tri-O-*benzoyl-6-methyl-β*-D-*glucopyranuronosyl-(1 → 2)-[2,3,4-tri*-O-*benzoyl-β*-D-*xylopyranosyl-(1 → 2)-3*-O-*acetyl-4,6-di*-O-*benzoyl-α*-D-*mannopyranosyl-(1 → 3)]-4,6-di*-O-*benzoyl-1*-O-*(2,2,2-trichloroethanimidoyl)-α*-D-*mannopyranose* (**20**). To a soln. of **19** (56 mg, 0.03 mmol) in MeCN/H_2O 4 : 1 (5 ml) was added CAN (50 mg, 0.09 mmol), and the mixture was treated as described for **16** to afford **20** (28 mg, 50%, over two steps). Yellow solid. ^{1}H-NMR (600 MHz, $CDCl_3$): 8.30 (*s*, NH); 8.02 – 7.23 (*m*, 50 arom. H); 6.72 (*d*, *J* = 3.6, 1 H); 6.03 (*d*, *J* = 3.6, 1 H); 5.87 – 5.84 (*m*, 3 H); 5.78 (*dd*, *J* = 10.4, 3.6, 1 H); 5.61 (*dd*, *J* = 10.4, 8.0, 1 H); 5.57 (*dd*, *J* = 10.4, 8.0, 1 H); 5.44 (*dd*, *J* = 5.7, 4.1, 1 H); 5.33 (*d*, *J* = 1.8, 1 H); 5.32 – 5.24 (*m*, 2 H); 5.01 (*d*, *J* = 4.1, 1 H); 4.80 (*d*, *J* = 8.0, 1 H); 4.67 (*d*, *J* = 10.0, 1 H); 4.59 (*dd*, *J* = 12.5, 3.4, 1 H); 4.51 (*dd*, *J* = 3.3, 1.8, 1 H); 4.32 (*d*, *J* = 9.7, 1 H); 4.16 (*dd*, *J* = 11.2, 6.0, 1 H); 4 .14 – 4.03 (*m*, 3 H); 3.79 – 3.70 (*m*, 2 H); 3.68 (*s*, MeO) 2.03 (*s*, MeCO). HR-QTOF-MS: 1912.5709 ($[M+Na]^+$, $C_{98}H_{82}Cl_3NaO_{32}^+$; calc. 1912.3783).

4-Methoxyphenyl 2,3,4-Tri-O-*benzoyl-6-methyl-β*-D-*glucopyranuronosyl-(1 → 2)-[2,3,4-tri*-O-*benzoyl-β*-D-*xylopyranosyl-(1 → 2)-3*-O-*acetyl-4,6-di*-O-*benzoyl-α*-D-*mannopyranosyl-(1 → 3)]-4,6-di*-O-*benzoyl-α*-D-*mannopyranosyl-(1 → 3)-2*-O-*acetyl-4,6-di*-O-*benzoyl-α*-D-*mannopyranoside* (**21**). Donor **20** (28 mg, 0.015 mmol) was coupled with acceptor **8** (80 mg, 0.15 mmol) as described in the *General Procedure*, and the product was purified by CC (PE/AcOEt 3 : 1) to give **21** (24 mg, 71%). Foamy solid. ^{1}H-NMR (600 MHz, $CDCl_3$): 8.10 – 7.25 (*m*, 60 arom. H); 6.83 (*d*, *J* = 9.1, 2 arom. H, $MeOC_6H_4O$); 6.59 (*d*, *J* = 9.1, 2 arom. H, $MeOC_6H_4O$); 5.83 (*dd*, *J* = 9.0, 1 H); 5.73 – 5.69 (*m*, 3 H); 5.65 – 5.57 (*m*, 2 H); 5.53 – 5.48 (*m*, 3 H); 5.41 (*dd*, *J* = 5.7, 4.1, 1 H); 5.33 (*d*, *J* = 1.8, 1 H); 5.32 – 5.24 (*m*, 2 H); 5.01 (*d*, *J* = 4.1, 1 H); 4.91 (*d*, *J* = 7.5, 1 H); 4.67 (*d*, *J* = 10.0, 1 H); 4.59 (*dd*, *J* = 12.5, 3.4, 1 H); 4.52 (*dd*, *J* = 3.3, 1.8, 1 H); 4.44 (*dd*, *J* = 5.9, 12.0, 1 H); 4.27 (*d*, *J* = 9.7, 1 H); 4.21 – 4.17 (*m*, 3 H); 4.04 – 3.93 (*m*, 6 H); 3.86 – 3.79 (*m*, 2 H); 3.67 (*s*, MeO); 2.08 (*s*, MeCO); 1.97 (*s*, MeCO). ^{13}C-NMR (150 MHz, $CDCl_3$): 171.9; 171.7; 169.8; 168.1; 167.9; 167.5; 167.1; 167.0; 166.9; 166.8; 166.8; 166.5; 166.4; 166.3; 156.7; 151.2; 135.0; 134.8; 134.6; 134.5; 134.3; 131.3; 131.3; 131.2; 131.1; 131.0; 130.9; 130.8; 130.6; 130.5; 130.4; 130.3; 130.2; 129.9; 129.8; 129.7; 129.7; 119.3; 116.0; 100.5; 100.3; 100.1; 97.7; 91.9; 76.3; 74.9; 74.5; 74.4; 73.7; 73.0; 71.7; 71.5; 71.3; 71.2; 71.1; 71.0; 70.9; 70.7; 70.4; 70.0; 70.0; 69.7; 69.2; 68.1; 64.7; 61.9; 56.9; 54.2; 31.1; 22.3. HR-QTOF-MS: 2287.2782 ($[M+Na]^+$; $C_{125}H_{108}NaO_{41}^+$; calc. 2287.6264).

4-Methoxyphenyl β-D-*Glucopyranuronosyl-(1 → 2)-[β*-D-*xylopyranosyl-(1 → 2)-α*-D-*mannopyranosyl-(1 → 3)]-α*-D-*mannopyranosyl-(1 → 3)-α*-D-*mannopyranoside* (**22**). Compound **21** (490 mg, 0.2 mmol) was dissolved in a sat. MeONa/MeOH soln. (50 ml). After 36 h at r.t., H_2O (1.0 ml) was added to the mixture to cleave the methyl ester. After stirring at r.t. for 5 h, the mixture was concentrated and separated by CC (SiO_2; MeOH), to affording **22** (126 mg, 63.0%). Foamy solid. ^{1}H-NMR (600 MHz, $CDCl_3$): 6.83 (*d*, *J* = 9.1, 2 H); 6.59 (*d*, *J* = 9.1, 2 H); 5.22 (*d*, *J* = 9.0, 1 H); 5.20 (*d*, *J* = 1.7, 1 H); 4.75 (*d*, *J* = 7.5, 1 H); 4.48 (*d*, *J* = 7.8, 1 H); 4.38 (*d*, *J* = 4.1, 1 H); 4.26 – 3.97 (*m*, 5 H); 3.95 (*m*, 1 H); 3.92 – 3.74, 3.67 – 3.64 (*m*, 12 H); 3.91 (*dd*, *J* = 3.5, 1 H); 3.67 (*d*, *J* = 5.4, 1 H); 3.67 (*s*, MeO); 3.65 (*d*, *J* = 11.1, 1 H); 3.57 (*d*, *J* = 9.2, 1 H); 3.55 (*d*, *J* = 10.0, 1 H); 3.49 (*dd*, *J* = 9.2, 1 H); 3.44 (*t*, *J* = 9.2, 1 H); 3.38 (*d*, *J* = 9.2,

1 H); 3.34 (*d*, *J* = 7.7, 1 H); 3.29 (*d*, *J* = 11.1, 1 H). ^{13}C-NMR (150 MHz, $CDCl_3$): 176.6; 166.8; 166.8; 166.5; 166.4; 166.3; 156.7; 103.6; 102.9; 76.42; 76.3; 74.4; 74.1; 73.6; 73.4; 72.6; 70.5; 70.4; 70.1; 68.5; 67.2; 67.; 66.2; 61.8; 61.5; 61.1; 55.7. HR-QTOF-MS: 941.2830 ($[M+Na]^+$, $C_{36}H_{54}NaO_{27}^+$; calc. 941.2750).

REFERENCES

[1] L. Kozubowski, J. Heitman, *FEMS Microbiol. Rev.* **2012**, *36*, 78.
[2] J. J. C. Sidrim, A. K. F. Costa, R. A. Cordeiro, R. S. N. Brilhante, F. E. A. Moura, D. S. C. M. Castelo-Branco, M. P. de Araújo Neto, M. F. G. Rocha, *Can. J. Microbiol.* **2010**, *56*, 445.
[3] M. R. Botts, C. M. Hull, *Curr. Opin. Microbiol.* **2010**, *13*, 437.
[4] A. Nakouzi, T. Zhang, S. Oscarson, A. Casadevall, *Vaccine* **2009**, *27*, 3513.
[5] Z. Guo, G.-J. Boons, 'Carbohydrate-Based Vaccines and Immunotherapies', Ed. B. Wang, John Wiley & Sons, Inc., Hoboken, New Jersey, 2009.
[6] L. Tissi, M. Puliti, F. Bistoni, P. Mosci, T. R. Kozel, A. Vecchiarelli, *Infect. Immun.* **2004**, *72*, 6367.
[7] S. Oscarson, M. Alpe, P. Svahnberg, A. Nakouzi, A. Casadevall, *Vaccine* **2005**, *23*, 3961.
[8] A. Enache-Angoulvant, J. Chandenier, F. Symoens, P. Lacube, J. Bolognini, C. Douchet, J. L. Poirot1, C. Hennequin, *J. Clin. Microbiol.* **2007**, *45*, 1261.
[9] R. Cherniak, J. B. Sundstrom, *Infect. Immun.* **1994**, *62*, 1507.
[10] J. Zhang, F. Kong, *Carbohydr. Res.* **2003**, *338*, 1719.
[11] P. J. Garegg, L. Olsson, S. Oscarson, *Bioorg. Med. Chem.* **1996**, *4*, 1867.
[12] W. Zhao, F. Kong, *Carbohydr. Res.* **2005**, *340*, 1673.
[13] K. Zegelaar-Jaarsveld, S. A. W. Smits, G. A. van der Marel, J. H. van Boom, *Bioorg. Med. Chem.* **1996**, *4*, 1819.
[14] H. Kuyama, T. Nukadz, Y. Nakahara, T. Ogawa, *Tetrahedron Lett.* **1993**, *34*, 2171.
[15] Z. Zhang, G. Magnusson, *Carbohydr. Res.* **1996**, *925*, 41.
[16] A. M. Gómez, M. Casillas, A. Barrio, A. Gawel, J. C. López, *Eur. J. Org. Chem.* **2008**, 3933.
[17] S. Sarbajna, A. K. Misra, N. Roy, *Synth. Commun.* **1998**, *28*, 2559.
[18] L. Chen, S.-D. Shi, Y.-Q. Liu, Q.-J. Gao, X. Yi, K.-K. Liu, H. Liu, *Carbohydr. Res.* **2011**, *346*, 1250.
[19] N. W. McGill, S. J. Williams, *J. Org. Chem.* **2009**, *74*, 9388.
[20] F. Peri, P. Dumy, M. Mutter, *Tetrahedron* **1998**, *54*, 12269.
[21] S. Dasgupta, M. Nitz, *J. Org. Chem.* **2011**, *76*, 1918.
[22] P. K. Mandal, A. K. Misra, *Tetrahedron* **2008**, *64*, 8685.
[23] C. Coutant, J.-C. Jacquinet, *J. Chem. Soc., Perkin Trans. 1* **1995**, 1573.
[24] J. D. Kenealey, L. Subramanian, P. R. Van Ginkel, S. Darjatmoko, M. J. Lindstrom, V. Somoza, S. K. Ghosh, Z. Song, R. P. Hsung, G. S. Kwon, K. W. Eliceiri, D. M. Albert, A. S. Polans, *J. Agric. Food Chem.* **2011**, *59*, 4979.
[25] Z. Ma, J. Zhang, F. Kong, *Tetrahedron: Asymmetry* **2004**, *15*, 1517.
[26] A. Li, F. Kong, *Carbohydr. Res.* **2005**, *340*, 1949.
[27] J. Zhang, F. Kong, *Bioorg. Med. Chem.* **2003**, *11*, 4027.

Received September 18, 2014