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Syntheses of deoxy analogues of methyl 3,6-di-*O*-α-D-mannopyranosyl-α-D-mannopyranoside for studies of the binding site of Concanavalin A

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Abstract

All of the monodeoxy analogues of methyl 3,6-di-*O*-α-D-mannopyranosyl-α-D-mannopyranoside have been synthesized together with two dideoxy (2,3′- and 4,3′-) analogues. The 2′- and 2″-deoxy functions were introduced by NIS-promoted couplings with 2,3,4-tri-*O*-acetyl-D-glucal as donor, followed by reduction of the resulting 2′- and 2″-iodo derivatives, whereas the 3′-, 3″-, 4′-, 4″-, 6′-, and 6″-deoxy functions were introduced by using known deoxyglycosyl chlorides as donors in coupling reactions promoted by silver trifluoromethanesulfonate. The 2- and 4-deoxy functions on the central mannose residue were introduced by displacement, using triiodoimidazole and triphenylphosphine, of a hydroxyl group by iodine on suitably protected derivatives followed by reduction of the resulting iodo analogues.

Keywords: Carbohydrates; Oligosaccharide synthesis; Lectin interactions; Deoxy sugars

1. Introduction

The trisaccharide residue 3,6-di-*O*-α-D-mannopyranosyl-α-D-mannopyranosyl is part of many N-linked glycoproteins and studies of its binding to different proteins are of major biological interest. Several analogues of this trisaccharide have already been synthesized to give more insight into these interactions. Paulsen et al. have synthesized a large number of derivatives, including deoxy analogues of the octyl β-trimannoside

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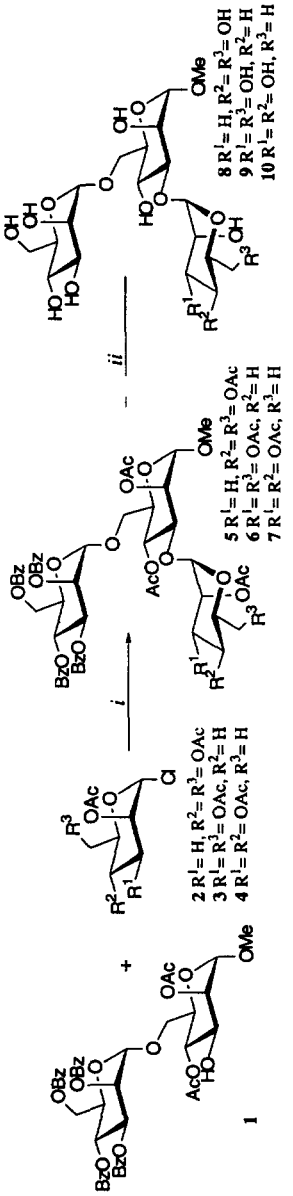
[1,2], to investigate the enzymes (*N*-acetylglucosaminyl-transferases) involved in the biosynthesis of N-linked glycoproteins, and van Boeckel and co-workers [3] have reported the synthesis of 2′- and 2″-amino and -fluoro analogues of the methyl α-trimannoside. Our interest was to explore the binding site(s) of the jack-bean lectin Concanavalin A (Con A). This lectin binds effectively to the trisaccharide methyl 3,6-di-*O*-α-D-mannopyranosyl-α-D-mannopyranoside [4]. This binding has been investigated using different glucose and galactose analogues of the parent trisaccharide, which were synthesized earlier in this laboratory [5]. These studies showed that the binding to the lectin was much less effective with the 3-*O*-α-D-glucose and the 3-*O*-α-D-galactose analogues [6]. To investigate whether this was due to the presence of the equatorial 2′-hydroxyl group or the absence of the axial 2′-hydroxyl group in the *manno* compound, the 2′-deoxy analogue **25** was therefore synthesized. Results [6] with **25** showed that this derivative binds equally well to the lectin as the parent trisaccharide, suggesting that the poorer binding of the glucose analogue was due to the equatorial 2′-hydroxyl group. To study further which of the hydroxyl groups of the 3-*O*-glycosyl moiety of the parent trisaccharide is essential for the binding to the lectin, the 3′-, 4′-, and 6′-deoxy analogues (**8–10**) were prepared. The 2″-, 3″-, 4″-, and 6″-deoxy derivatives (**20**, **15–17**) were also prepared. Binding studies [6] with the derivatives **8–10** showed that only the 3′-hydroxyl group is bound to the lectin, but that **8** still had a better affinity than methyl α-D-mannopyranoside, suggesting a further binding of a hydroxyl group from the central moiety to the lectin. Therefore, the 2,3′-dideoxy and 4,3′-dideoxy analogues (**33** and **41**), as well as a number of deoxy disaccharides (**45**, **46**, **48**, **49**), were prepared. The full results of these binding studies will be presented elsewhere.

2. Results and discussion

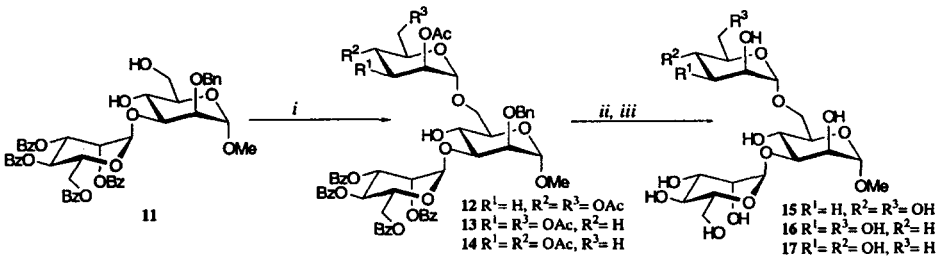
The syntheses were performed using conventional methods. The glycosylations were promoted with silver trifluoromethanesulfonate (silver triflate) [7] using halogen sugars as donors, or by *N*-iodosuccinimide [8] using 3,4,6-tri-*O*-acetyl-D-glucal [9] (**18**) as donor. Iodo functions were introduced using triiodoimidazole or iodine/imidazole and triphenylphosphine [10], and reduced to deoxy functions by catalytic hydrogenolysis.

Thus, the 3′-, 3″-, 4′-, 4″-, 6′-, and 6″-deoxy functions in the mannose substituents were introduced by silver trifluoromethanesulfonate-mediated couplings between known monodeoxyglycosyl chlorides [11] (**2–4**) and two mannose disaccharide acceptors (**1** and **11**), used earlier in the syntheses of the 3- and 6-glucose and -galactose analogues [5] (Schemes 1 and 2). The six resulting monodeoxy trisaccharide derivatives (**5–7** and **12–14**), all obtained in good yields (67–86%), were then deprotected by Zemplén deacylation and, if necessary, catalytic hydrogenolysis to give the first six target compounds **8–10** and **15–17**.

The 2′- and 2″-deoxy functions were introduced by *N*-iodosuccinimide-promoted couplings of **18** with suitable acceptors, followed by reduction of the resulting 2-iodo function as described by Thiem and others [8] (Scheme 3). The regioselective coupling of **18** to the 6-position of acceptor **11** was straightforward and gave the 2″-iodo trisaccharide **19** (83%), which was reduced and debenzylated by hydrogenolysis over



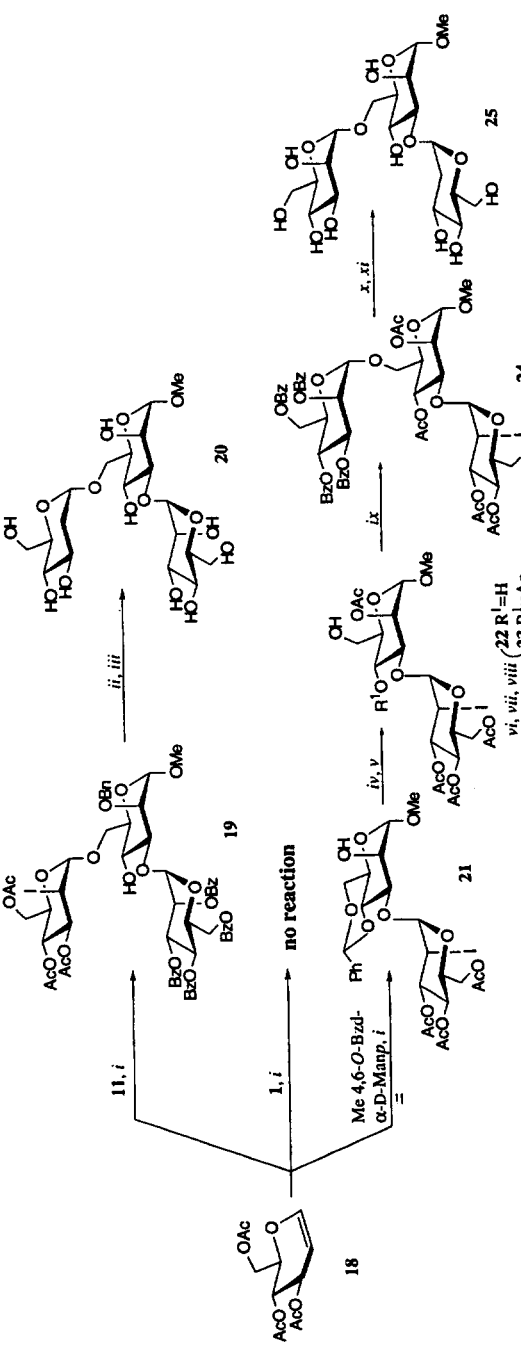
Scheme 1. (*i*) AgOTf; (*ii*) MeO^-.



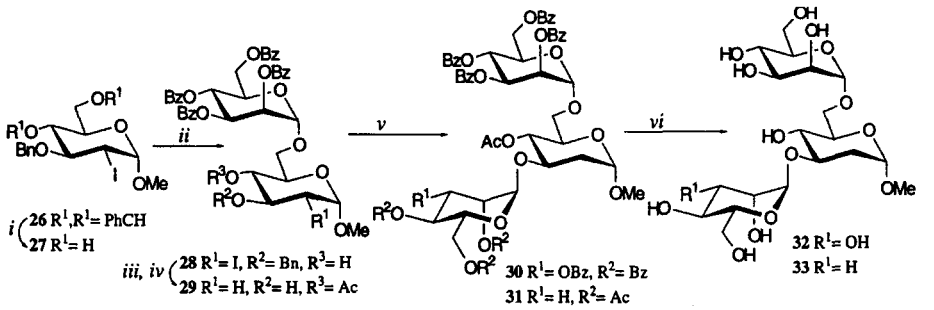
Scheme 2. (*i*) **2**, **3**, or **4**, AgOTf; (*ii*) H_2, Pd–C; (*iii*) MeO^-.

Pd–C and then deacylated to give the 2″-deoxy target product **20** (51%). The synthesis of the 2′-deoxy derivative **25** was more troublesome. Attempts to use the other disaccharide acceptor (i.e., **1**) and **18** in an *N*-iodosuccinimide-promoted reaction failed. Efforts to enhance the reactivity of the aglycon by tin activation [12] were not successful. Iodonium dicollidine perchlorate [13] and triflate [14] were tried as promoters, but without results. The acceptor was therefore changed, first to the monosaccharide derivative methyl 2-*O*-acetyl-4,6-*O*-benzylidene-α-D-mannopyranoside, and when this proved to be too unreactive in an *N*-iodosuccinimide-promoted coupling, to methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside [15], which should be more reactive owing to the benzyl group in the 2-position. However, this coupling also failed. Finally, the diol methyl 4,6-*O*-benzylidene-α-D-mannopyranoside [16], after tin activation, was tested as acceptor in a coupling with **18** as donor and *N*-iodosuccinimide as promoter. This gave a disaccharide product **21** in 59% yield. The ^1H NMR data of the acetylated and debenzylidenated disaccharide **22** showed the glycosylation to have taken place in the 3-position (the H-2 signal is moved downfield to 5.18 ppm due to acetylation of 2-OH) and the configuration to be α-*manno* ($J_{H\text{-}1',H\text{-}2'} < 1.5$ Hz, $J_{H\text{-}2',H\text{-}3'}$ 4 Hz). Coupling reactions without prior tin activation were shown to give the same regioselectivity and the same yield of coupling product. Regioselective dimethoxytritylation at 6-OH of **22** followed by in situ acetylation and detritylation, using aqueous acetic acid, gave the acceptor **23** with a free 6-OH (overall yield 60%). Silver triflate-promoted coupling of **23** with 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl bromide [17] (benzobromomannose) gave the trisaccharide **24** (81%). Reduction of the iodo group followed by deacylation then produced the target compound **25** (64%). After the completion of the above synthesis of **25**, an NIS-promoted coupling between the glucal **18** and the acceptor 6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside [5], with three free hydroxyl groups, was tried. One main product was obtained (36%), and shown to be the 3-*O*-substituted trisaccharide derivative by acetylation to give **24**.

The 2-deoxy function on the central mannose residue was accomplished by iodine displacement (Scheme 4), using triiodoimidazole and triphenylphosphine [10], of the 2-OH of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside [15] to give the 2-iodo derivative **26** (77%). Removal of the benzylidene function (→ **27**, 75%) followed by a regioselective silver triflate-promoted coupling using benzobromomannose as donor gave the (1 → 6)-coupled disaccharide **28** (92%). Acetylation followed by simultaneous reduction of the iodo function and debenzylation by hydrogenolysis yielded **29** (80%),



Scheme 3. (*i*) NIS; (*ii*) H_2, Pd–C; (*iii*) MeO^-; (*iv*) Ac_2O, pyridine; (*v*) HOAc (aq); (*vi*) TrCl, pyridine; (*vii*) Ac_2O; (*viii*) AcOH (aq); (*ix*) benzobromomannose (Bz_4ManBr), AgOTf; (*x*) H_2, Pd–C; (*xi*) MeO^-.



Scheme 4. (*i*) AcOH (aq); (*ii*) Bz_4ManBr, AgOTf; (*iii*) Ac_2O, pyridine; (*iv*) H_2, Pd–C; (*v*) Bz_4ManBr or **2**, AgOTf; (*vi*) MeO^-.

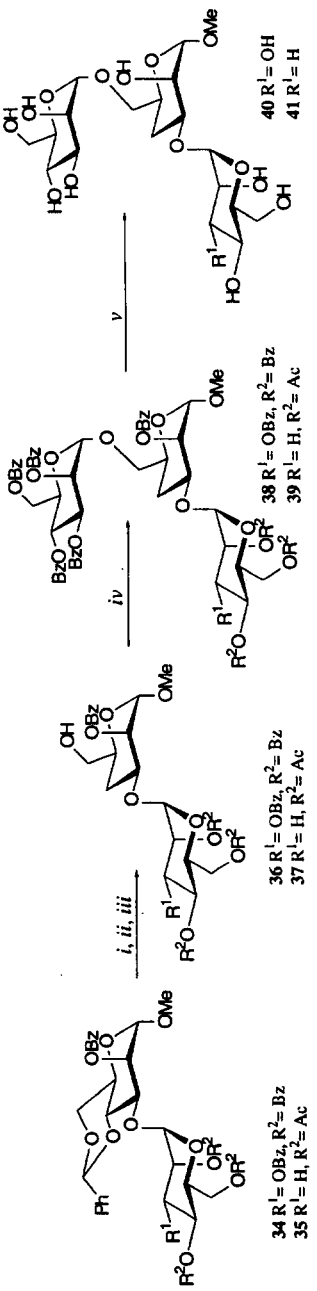
with a 3-hydroxyl group free for glycosylation. Silver triflate-mediated glycosylation of **29** with benzobromomannose or the 3-deoxyglycosyl chloride **2** then gave the 2-deoxy and the 2,3′-dideoxy analogues **30** and **31** in only fair yields (52 and 53%, respectively) due to the instability of the 2-deoxyglycoside. Final deacylation gave the corresponding deprotected derivatives **32** and **33**.

The last deoxy function, in the 4-position on the central mannose residue, was also introduced by triiodoimidazole-promoted iodine displacement followed by reduction, this time on disaccharide derivatives (Scheme 5). Coupling of benzobromomannose or the 3-deoxyglycosyl chloride **2** to methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-mannopyranoside [18] using silver triflate as promoter gave the (1 → 3)-linked disaccharides **34** and **35** (75 and 63%, respectively). The benzylidene acetals were opened reductively with sodium cyanoborohydride/ethereal hydrogen chloride [19], and the resulting 6-*O*-benzyl-4-hydroxyl derivatives were iodinated and then hydrogenolyzed to give the 4-deoxy and the 4,3′-dideoxy disaccharides **36** and **37**, with a free 6-OH group available for the formation of the trisaccharide derivatives. Once more silver triflate-promoted couplings using benzobromomannose as donor produced the required trisaccharides **38** (88%) and **39** (51%), which were deprotected to give the target compounds **40** and **41**.

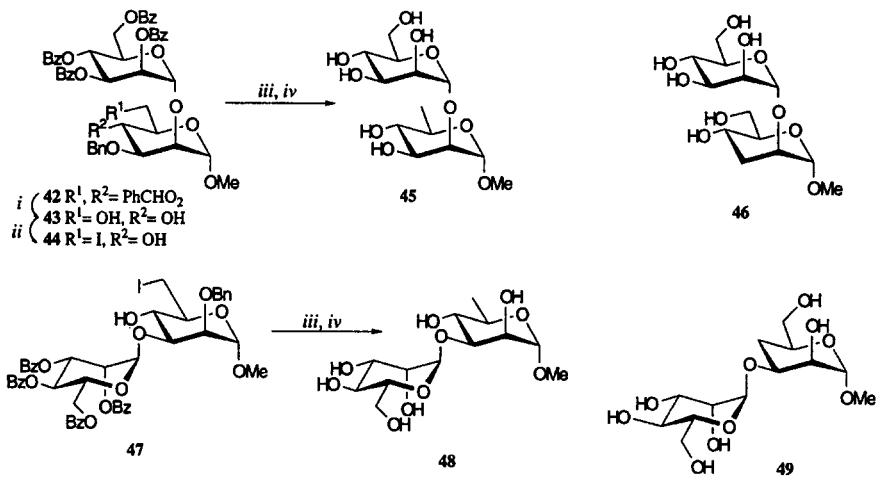
The syntheses of the deoxy disaccharide analogues were also straightforward (Scheme 6). Regioselective iodine displacement using the milder reagent iodine/imidazole and triphenylphosphine in toluene/acetonitrile [10] of **11** and **43** gave the 6-iodo compounds **44** and **47**, whereafter catalytic hydrogenolysis followed by methoxide treatment yielded the 6-deoxy disaccharide targets **45** and **48**. Silver triflate-promoted glycosylation between benzobromomannose and the known methyl 4,6-*O*-benzylidene-3-deoxy-α-D-*arabino*-hexopyranoside [20] followed by deprotection gave the (1 → 2)-linked 3-deoxy disaccharide analogue **46**, whereas deprotection of **36** gave the (1 → 3)-linked 4-deoxy disaccharide **49**.

3. Experimental

General methods.—These were as reported earlier [21]. Purity of the first three target compounds (**8**–**10**) was ensured by combustion analysis. Purity of other compounds was



Scheme 5. (*i*) $NaCNBH_3$–HCl; (*ii*) triiodoimidazole, Ph_3P; (*iii*) H_2, Pd–C; (*iv*) Bz_4ManBr, AgOTf; (*v*) MeO^-.



Scheme 6. (*i*) AcOH (aq); (*ii*) I_2, imidazole, Ph_3P; (*iii*) H_2, Pd–C; (*iv*) MeO^-.

established by ^1H NMR and TLC. The HDO signal was used as reference for ^1H NMR spectra recorded in D_2O: 25°C, δ 4.78; 70°C, δ 4.34.

*Methyl 3-O-(3-deoxy-α-*D*-arabino-hexopyranosyl)-6-O-α-*D*-mannopyranosyl-α-*D*-mannopyranoside* (**8**).—Silver trifluoromethanesulfonate (100 mg) dissolved in toluene (2 mL) was added at 0°C to a stirred solution of methyl 2,4-di-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside [5] (**1**) (200 mg) and 2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*arabino*-hexopyranosyl chloride [11] (**2**) (130 mg) in CH_2Cl_2 (7 mL) containing crushed molecular sieves (4 Å). After 1 h the mixture was chromatographed on silica gel and eluted (3:1 toluene–EtOAc) to give methyl 2,4-di-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3-*O*-(2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*arabino*-hexopyranosyl)-α-D-mannopyranoside (**5**, 190 mg, 72%); $[\alpha]_D$ +7° (*c* 1.1, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.6, 20.8, 21.0, 21.1 (*Me*CO), 29.1 (C-3′), 55.2 (OMe), 62.8, 63.0, 64.4, 66.8, 68.1, 68.9, 69.3, 69.4, 69.6, 70.0, 71.4, 74.3, 77.4 (C-2–6, C-2′, C-4′–6′, C-2″–6″), 97.5, 98.1, 98.5 (C-1,1′,1″), 125.3–133.5 (Ph), 165.4, 165.5, 166.2 (Ph*C*O), 170.0, 170.1, 170.3, 170.5, 170.9 (Me*C*O). Methanolic NaOMe (0.5 mL, 1 M) was added to a solution of **5** (136 mg) in MeOH (5 mL) and left overnight. Dowex 50 (H^+) ion-exchange resin was added and the mixture filtered and concentrated. Purification on a BioGel P-2 column gave, after freeze-drying, **8** (50 mg, 81%); $[\alpha]_D$ +106° (*c* 0.8, water); NMR data (D_2O): ^{13}C, δ 34.0 (C-3′), 55.5 (OMe), 61.6, 61.8, 62.2, 65.8, 66.3, 67.4, 67.9, 70.2, 70.6, 71.3, 71.5, 73.4, 74.9, 79.0 (C-2–6, C-2′, C-4′–6′, C-2″–6″), 100.0, 101.7 (2 C) (C-1,1′,1″); ^1H (70°C), δ 1.92 (1 H, H-3′ax), 2.06 (1 H, H-3′eq), 4.75, 4.92, 4.95 (H-1,1′,1″). Anal. Calcd for $C_{19}H_{34}O_{15} \cdot 0.5\ H_2O$: C, 44.6; H, 6.9. Found: C, 44.6; H, 6.7.

*Methyl 3-O-(4-deoxy-α-*D*-lyxo-hexopyranosyl)-6-O-α-*D*-mannopyranosyl-α-*D*-mannopyranoside* (**9**).—Compound **1** (80 mg) and 2,3,6-tri-*O*-acetyl-4-deoxy-α-D-*lyxo*-hexopyranosyl chloride [11] (**3**) (80 mg) were coupled as described for **1** and **2** above to give methyl 2,4-di-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3-*O*-

(2,3,6-tri-*O*-acetyl-4-deoxy-α-D-*lyxo*-hexopyranosyl)-α-D-mannopyranoside (**6**, 71 mg, 67%); $[\alpha]_D$ +6° (*c* 0.74, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.7, 20.9, 21.4 (*Me*CO), 27.8 (C-4′), 55.1 (OMe), 62.8, 65.9, 66.0, 66.8, 66.9, 67.1, 68.2, 68.3, 68.9, 69.6, 69.9, 70.4, 71.1, 73.8 (C-2–6, C-2′,3′,5′,6′, C-2″–6″), 97.3, 98.5, 99.6 (C-1,1′,1″), 125.3–133.5 (Ph), 165.3, 165.4, 166.1 (Ph*C*O), 169.7, 170.1, 170.2, 170.6, and 170.8 (Me*C*O). Compound **6** (50 mg) was deprotected as described for **5** above to give **9** (16 mg, 73%); $[\alpha]_D$ +83° (*c* 0.8, H_2O); NMR data (D_2O): ^{13}C, δ 29.7 (C-4′), 55.6 (OMe), 61.7, 64.9, 65.7, 65.9, 66.3, 67.5, 68.8, 70.4, 70.5, 70.7, 71.4, 71.6, 73.5, 79.3 (C-2–6, C-2′,3′,5′,6′, C-2″–6″), 100.2, 101.8, 103.9 (C-1,1′,1″); ^1H (70°C), δ 1.65 (1 H, H-4′ax), 1.69 (1 H, H-4′eq), 4.72, 4.90, 5.12 (H-1,1′,1″). Anal. Calcd for $C_{19}H_{34}O_{15} \cdot 1.5\ H_2O$: C, 43.1; H, 7.0. Found: C, 42.9; H, 6.4.

*Methyl 6-*O*-α-*D*-mannopyranosyl-3-*O*-α-*D*-rhamnopyranosyl-α-*D*-mannopyranoside* (**10**).—Compound **1** (138 mg) and 2,3,4-tri-*O*-acetyl-α-D-rhamnopyranosyl chloride [11] (**4**) (90 mg) were coupled as described for **1** and **2** above to give methyl 2,4-di-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3-*O*-(2,3,4-tri-*O*-acetyl-α-D-rhamnopyranosyl)-α-D-mannopyranoside (**7**, 141 mg, 77%); $[\alpha]_D$ +8° (*c* 0.9, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 17.3 (C-6′), 20.7, 20.9 (*Me*CO), 55.3 (OMe), 62.9, 66.8, 67.3, 68.1, 68.5, 68.9, 69.5, 70.0, 70.2, 70.4, 70.8, 71.0, 75.0 (C-2–6, C-2′–5′, C-2″–6″), 97.4, 98.3, 98.9 (C-1,1′,1″), 128.3–133.5 (Ph), 165.4, 165.5, 166.1 (Ph*C*O), 169.6, 170.1, 170.6 (Me*C*O). Compound **7** (100 mg) was deprotected as described for **5** above to give **10** (34 mg, 76%); $[\alpha]_D$ +58° (*c* 0.7, water); NMR data (D_2O): ^{13}C, δ 17.4 (C-6′), 55.5 (OMe), 61.7, 65.9, 67.3, 67.4, 69.8, 70.5, 70.7, 70.9, 71.4, 71.6, 72.8, 73.4, 79.4 (C-2–6, C-2′–5′, C-2″–6″), 100.1, 101.7, 103.2 (C-1,1′,1″); ^1H (25°C), δ 1.28 (3 H, H-6′), 4.87, 4.92, 4.96 (H-1,1′,1″). Anal. Calcd for $C_{19}H_{34}O_{15} \cdot 0.5\ H_2O$: C, 44.6; H, 6.9. Found: C, 44.3; H, 6.6.

*Methyl 6-*O*-(3-deoxy-α-*D*-*arabino*-hexopyranosyl)-3-*O*-α-*D*-mannopyranosyl-α-*D*-mannopyranoside* (**15**).—Methyl 2-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside [5] (**11**, 80 mg) and **2** (40 mg) were coupled as described for **1** and **2** above to give, after silica gel chromatography (6:1 toluene–EtOAc), methyl 2-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-6-*O*-(2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*arabino*-hexopyranosyl)-α-D-mannopyranoside (**12**, 93 mg, 86%); $[\alpha]_D$ +22° (*c* 1.0, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.8, 21.1, 21.4 (*Me*CO), 29.3 (C-3″), 54.9 (OMe), 63.0, 63.3, 64.7, 66.5, 66.8, 66.9, 68.7, 69.4, 70.0, 70.5, 71.3, 71.9, 77.3, 80.3 (C-2–6, C-2′–6′, C-2″, C-4″–6″), 96.4, 98.0, 99.6 (C-1,1′,1″), 125.3–138.0 (Ph), 165.4–166.1 (Ph*C*O), 170.0–171.0 (Me*C*O). Compound **12** (48 mg) dissolved in MeOH was hydrogenolyzed over Pd–C at 400 kPa overnight, whereafter the mixture was filtered and a catalytic amount of NaOMe was added to the filtrate. When TLC showed complete deacylation, Dowex 50 (H^+) resin was added and the mixture filtered and concentrated. The residue was passed through a Biogel P2 column and lyophilized to give **15** (14 mg, 68%); $[\alpha]_D$ +101° (*c* 1.4, water); NMR data (D_2O): ^{13}C, δ 34.3 (C-3″), 55.6 (OMe), 61.7, 61.9, 62.2, 65.8, 66.5, 67.5, 67.9, 70.3, 70.8, 71.1, 71.7, 74.1, 74.4, 79.3 (C-2–6, C-2′–6′, C-2″, C-4″–6″), 98.7, 101.8, 103.2 (C-1,1′,1″); ^1H (70°C), δ 1.88 (1 H, H-3″ax), 2.09 (1 H, H-3″eq), 4.74, 4.75, 5.13 (H-1,1′,1″). FAB-mass spectrum: *m/z* 503.3 [M + 1].

*Methyl 6-*O*-(4-deoxy-α-*D*-lyxo-*hexopyranosyl)-3-*O*-α-*D*-mannopyranosyl-α-*D*-man-*

nopyranoside (**16**).—Compounds **11** (28 mg) and **3** (14 mg) were coupled as described for **1** and **2** to give methyl 2-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-6-*O*-(2,3,6-tri-*O*-acetyl-4-deoxy-α-D-*lyxo*-hexopyranosyl)-α-D-mannopyranoside (**13**, 31 mg, 84%); $[\alpha]_D$ +4° (*c* 0.7, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.8–20.9 (*Me*CO), 28.0 (C-4″), 55.0 (OMe), 63.0, 66.1, 66.4, 66.6, 66.7, 66.8, 67.9, 68.4, 69.3, 70.0, 70.4, 71.3, 71.9, 77.2, 80.5 (C-2–6, C-2′–6′, C-2″,3″,5″,6″), 98.0, 98.0, 99.6 (C-1,1′,1″), 127.4–138.0 (Ph), 165.4–166.1 (Ph*C*O), 169.8–171.1 (Me*C*O). Compound **13** (31 mg) was deprotected as described for **12** above to give **16** (11 mg, 84%); $[\alpha]_D$ +74° (*c* 0.6, H_2O); NMR data (D_2O): ^{13}C, δ 29.6 (C-4″), 55.6 (OMe), 61.7, 64.9, 65.8, 66.5, 67.5, 68.8, 70.0, 70.3, 70.8, 71.1, 71.7, 74.1, 79.3 (C-2–6, C-2′–6′, C-2″,3″,5″,6″), 100.8, 101.8, 103.2 (C-1,1′,1″); ^1H (25°C), δ 1.64 (1 H, H-4″ax), 1.70 (1 H, H-4″eq), 4.72, 4.93, 5.09 (H-1,1′,1″). FAB-mass spectrum: *m*/*z* 503.3 [M + 1].

Methyl 3-O-α-D-mannopyranosyl-6-O-α-D-rhamnopyranosyl-α-D-mannopyranoside (**17**).—Compounds **11** (55 mg) and **4** (100 mg) were coupled as described for **1** and **2** above to give methyl 2-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-6-*O*-(2,3,4-tri-*O*-acetyl-α-D-rhamnopyranosyl)-α-D-mannopyranoside (**14**, 100 mg, 76%); $[\alpha]_D$ +17° (*c* 1.0, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 17.5 (C-6″), 20.7–20.9 (*Me*CO), 54.9 (OMe), 63.0, 66.4, 66.8, 67.0, 67.7, 69.1, 69.4, 69.9, 70.3, 70.4, 71.2, 71.4, 71.9, 72.0, 77.3, 80.5 (C-2–6, C-2′–6′, C-2″–5″), 97.5, 97.9, 99.5 (C-1,1′,1″), 127.3–138.0 (Ph), 165.4–166.1 (Ph*C*O), 169.8–170.1 (Me*C*O). Compound **14** (90 mg) was deprotected as described for **12** above to give **17** (24 mg, 60%); $[\alpha]_D$ +89° (*c* 0.9, water); NMR data (D_2O): ^{13}C, δ 17.4 (C-6″), 55.6 (OMe), 61.7, 65.9, 66.3, 67.5, 69.3, 70.3, 70.8, 71.1, 71.6, 72.8, 74.1, 79.5 (C-2–6, C-2′–6′, C-2″–5″), 100.2, 101.8, 103.2 (C-1,1′,1″); ^1H (25°C), δ 1.29 (3 H, H-6″), 4.73, 4.83, 5.09 (H-1,1′,1″). FAB-mass spectrum: *m*/*z* 503.2 [M + 1].

*Methyl 6-O-(2-deoxy-α-D-*arabino-*hexopyranosyl)-3-O-α-D-mannopyranosyl-α-D-mannopyranoside* (**20**).—*N*-Iodosuccinimide (65 mg) was added to a solution of 3,4,6-tri-*O*-acetyl-D-glucal [9] (**18**, 65 mg) and **11** (164 mg) in MeCN (20 mL), and the mixture was stirred for 3 days at room temperature, whereupon it was diluted with toluene, washed with aq $Na_2S_2O_3$ and water, dried (Na_2SO_4), and concentrated. The residue was purified on a silica gel column (4:1 toluene–EtOAc) to give methyl 2-*O*-benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-6-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl)-α-D-mannopyranoside (**19**, 200 mg, 83%); $[\alpha]_D$ +7° (*c* 0.8, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.7, 20.9, 21.5 (*Me*CO), 29.8 (C-2″), 55.0 (OMe), 62.4, 63.1, 66.7, 67.0, 67.9, 69.0, 69.2, 69.5, 70.1, 70.5, 72.0, 72.2, 77.5, 80.4 (C-2–6, C-2′–6′, C-3″–6″), 98.2, 99.6, 101.4 (C-1,1′,1″), 125.4–138.0 (Ph), 165.4–166.1 (Ph*C*O), 169.6–170.9 (Me*C*O). Compound **19** (42 mg) was treated as described for **12** above, except that $NaHCO_3$ (7 mg) and water (5 drops) were added during the hydrogenolysis, to give **20** (8 mg, 51%); $[\alpha]_D$ +134° (*c* 0.4, water); NMR data (D_2O): ^{13}C, δ 37.4 (C-2″), 55.6 (OMe), 61.4, 61.7, 65.7, 66.5, 67.5, 69.2, 70.3, 70.8, 71.1, 71.6, 73.0, 74.1, 79.3 (C-2–6, C-2′–6′, C-3″–6″), 97.6, 101.8, 103.2 (C-1,1′,1″); ^1H (25°C), δ 1.70 (1 H, H-2″ax), 2.18 (1 H, H-2″eq), 4.72, 5.03, 5.08 (H-1,1′,1″). FAB-mass spectrum: *m*/*z* 503.3 [M + 1].

*Methyl 3-O-(2-deoxy-α-D-*arabino-*hexopyranosyl)-6-O-α-D-mannopyranosyl-α-D-mannopyranoside* (**25**).—*N*-Iodosuccinimide (300 mg) was added to a solution of **18**

(500 mg) and methyl 4,6-*O*-benzylidene-α-D-mannopyranoside [16] (500 mg) in MeCN (20 mL), and the mixture was stirred for 3 days, then diluted with toluene, washed with aq $Na_2S_2O_3$ and water, dried (Na_2SO_4), and concentrated. The residue was purified on a silica gel column (2:1 toluene–EtOAc) to give methyl 4,6-*O*-benzylidene-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl)-α-D-mannopyranoside (**21**, 710 mg, 59%); $[\alpha]_D$ +51° (*c* 1.1, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.6, 21.0 (*Me*CO), 29.0 (C-2′), 54.9 (OMe), 62.5, 63.5 (C-6,6′), 67.9, 68.6, 68.9, 69.4, 70.9, 74.3, 78.3 (C-2–5, C-3′–5′), 101.2, 101.5, 102.1 (C-1,1′, Ph*C*H), 125.9–137.2 (Ph), 169.5, 170.2, 170.9 (Me*C*O). Compound **21** (400 mg) was dissolved in a mixture of Ac_2O and pyridine (1:1, 4 mL). When TLC showed the acetylation to be complete, the mixture was concentrated and toluene was added and evaporated twice. The residue in aq AcOH (70%, 10 mL) was warmed to 70°C and stirred for 2 h. Concentration and silica gel chromatography (2:3 toluene–EtOAc) gave methyl 2-*O*-acetyl-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl)-α-D-mannopyranoside (**22**, 190 mg, 65%); $[\alpha]_D$ +36° (*c* 0.9, $CHCl_3$); NMR data ($CDCl_3$): ^{13}C, δ 20.6, 20.7, 20.9, 21.0 (*Me*CO), 29.1 (C-2′), 55.1 (OMe), 62.1, 62.3 (C-6,6′), 67.4, 69.2, 69.9, 71.3, 72.0, 76.8 (C-2–5, C-3′–5′), 98.7, 103.0 (C-1,1′), 169.6, 170.3, 170.8 (Me*C*O); ^1H, δ 4.52 (dd, H-3′), 4.65 (d, H-2′, $J_{H\text{-}2',H\text{-}3'}$ 4 Hz), 4.68 (s, H-1), 5.18 (bs, H-2), 5.36 (t, H-4′), 5.53 (s, H-1′).

Dimethoxytriphenylmethyl chloride (120 mg, 2 equiv) was added to a solution of **22** (115 mg) in pyridine (3 mL). After 1 h Ac_2O (0.6 mL) was added and stirring was continued for 2 h. Ice was added and after 30 min the mixture was diluted with toluene and more water was added. The phases were separated and the organic phase was washed, dried (Na_2SO_4), and concentrated. The residue was dissolved in aq AcOH (70%, 5 mL), the solution was stirred at room temperature for 4 h, then concentrated, and the residue was chromatographed on a silica gel column (2:3 toluene–EtOAc) to give methyl 2,4-di-*O*-acetyl-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl)-α-D-mannopyranoside (**23**, 74 mg, 60%); $[\alpha]_D$ +46° (*c* 1.0, $CHCl_3$); NMR data ($CDCl_3$): ^{13}C, δ 20.6, 20.7, 20.9 (*Me*CO), 28.6 (C-2′), 55.2 (OMe), 61.2, 62.2 (C-6,6′), 67.2, 68.7, 68.8, 70.0, 70.6, 70.8, 73.5 (C-2–5, C-3′–5′), 98.6, 102.9 (C-1,1′), 169.6, 170.4, 170.7, 170.8 (Me*C*O); ^1H, δ 5.21 (t, H-4).

Silver trifluoromethanesulfonate (180 mg) was added to a solution of **23** (100 mg) and benzobromomannose [17] (200 mg) in CH_2Cl_2 (5 mL) containing molecular sieves (4 Å). After 30 min the mixture was chromatographed on silica gel (4:1 toluene–EtOAc) to give methyl 2,4-di-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl)-α-D-mannopyranoside (**24**, 150 mg, 81%); $[\alpha]_D$ +10° (*c* 1.0, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.6, 20.7, 20.9, 21.5 (*Me*CO), 28.7 (C-2′), 55.2 (OMe), 62.2, 62.8, 66.8, 67.3, 68.7, 68.8, 69.0, 69.4, 69.9, 70.0, 70.3, 70.8, 74.0 (C-2–6, C-3′–6′, C-2″–6″), 97.4, 98.4, 103.0 (C-1,1′,1″), 125.3–133.5 (Ph), 165.4, 166.1 (Ph*C*O), 169.5, 169.7, 170.5, 170.7 (Me*C*O). Compound **24** (78 mg) was reduced and deprotected as described for compound **19** above to give **25** (26 mg, 64%); $[\alpha]_D$ +105° (*c* 0.7, water); NMR data (D_2O): ^{13}C, δ 37.6 (C-2′), 55.6 (OMe), 61.4, 61.7, 66.0, 66.4, 67.5, 68.8, 70.4, 70.7, 71.4, 71.6, 71.8, 73.5, 73.5, 79.1 (C-2–6, C-3′–6′, C-2″–6″), 100.2, 100.8, 101.8 (C-1,1′,1″); ^1H (70°C), δ 1.70 (1 H, H-2′ax), 2.27 (1 H, H-2′eq), 4.71, 4.90, 5.24 (H-1,1′,1″). FAB-mass spectrum: *m/z* 501.2 [M − 1].

Alternative route to **24.** *N*-Iodosuccinimide (97 mg) was added to a solution of **18** (100 mg) and methyl 6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside [5] (258 mg) in MeCN (30 mL). The mixture was stirred for 3 days at room temperature, then diluted with CH_2Cl_2, washed with aq $Na_2S_2O_3$ and water, dried (Na_2SO_4), and concentrated. The residue was purified on a silica gel column (3:2 toluene–EtOAc) to give methyl 6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl)-α-D-mannopyranoside (142 mg, 36%). Acetylation (Ac_2O, pyridine) and purification gave **24** with NMR data identical to those of **24** obtained above.

Methyl 2-deoxy-3,6-di-O-α-D-*mannopyranosyl*-α-D-arabino-*hexopyranoside* (**32**).—Triiodoimidazole (113 mg) and triphenylphosphine (153 mg) were added to a solution of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside [15] (110 mg) in toluene (15 mL), the mixture was refluxed, and after 3 h the same amounts of reagents were added. The mixture was refluxed overnight, then diluted with toluene, washed with aq $Na_2S_2O_3$ and water, dried (Na_2SO_4), and concentrated. The residue was purified on a silica gel column (6:1 toluene–EtOAc) to give methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-iodo-α-D-glucopyranoside (**26**, 113 mg, 77%); $[\alpha]_D$ +75° (*c* 0.8, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 29.3 (C-2), 55.9 (OMe), 62.9, 68.8, 75.4, 78.2, 83.3 (C-3–6, Ph*C*H_2), 101.1, 101.2 (C-1, Ph*C*H), 125.9–137.9 (Ph). Compound **26** (53 mg) was dissolved in aq AcOH (70%, 10 mL) and stirred at room temperature for 2 days, then diluted with CH_2Cl_2, washed with water, aq $NaHCO_3$, and water, dried (Na_2SO_4), and concentrated. The residue was purified on a silica gel column (1:1 toluene–EtOAc) to give methyl 3-*O*-benzyl-2-deoxy-2-iodo-α-D-glucopyranoside (**27**, 32 mg, 75%); $[\alpha]_D$ +111° (*c* 0.64, $CHCl_3$); ^{13}C NMR data (D_2O): δ 29.0 (C-2), 55.8 (OMe), 61.8, 71.6, 71.8, 75.3, 82.2 (C-3–6, Ph*C*H_2), 100.8 (C-1), 128.1–138.0 (Ph).

Silver trifluoromethanesulfonate (53 mg) dissolved in dry toluene (2 mL) was added at −50°C to a solution of **27** (100 mg) and benzobromomannose (163 mg) in CH_2Cl_2 (5 mL) containing crushed molecular sieves (4 Å). The mixture was allowed to reach room temperature and then chromatographed on silica gel (6:1 toluene–EtOAc) to give methyl 3-*O*-benzyl-2-deoxy-2-iodo-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-glucopyranoside (**28**, 220 mg, 92%); $[\alpha]_D$ +8° (*c* 1.2, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 28.7 (C-2), 55.8 (OMe), 63.2, 66.4, 67.3, 68.6, 69.9, 70.4, 70.8, 71.5, 75.2, 82.5 (C-3–6, C-2′–6′, Ph*C*H_2), 97.6, 100.7 (C-1,1′), 128.2–138.0 (Ph), 165.3, 165.6 (Ph*C*O). Compound **28** (107 mg) was dissolved in pyridine (5 mL) and Ac_2O (0.5 mL), and the mixture was warmed at 40°C until TLC showed the acetylation to be complete, whereupon the mixture was concentrated and coevaporated with toluene twice. The residue was dissolved in EtOAc, and $NaHCO_3$ (24 mg), water (15 drops), and Pd–C were added. The solution was hydrogenolyzed at 400 kPa for 2 days, whereupon the mixture was filtered, and some new catalyst was added, and the solution was hydrogenolyzed for one more day, then filtered, and concentrated to give methyl 4-*O*-acetyl-2-deoxy-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-*arabino*-hexopyranoside (**29**, 70 mg, 80%); $[\alpha]_D$ −2° (*c* 0.7, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 21.1 (*Me*CO), 37.9 (C-2), 54.9 (OMe), 62.9, 66.9, 67.2, 67.6, 68.5, 70.1, 70.4, 73.7 (C-3–6, C-2′–6′), 97.4, 98.3 (C-1,1′), 128.3–133.5 (Ph), 165.4–166.2 (Ph*C*O), 171.2 (Me*C*O).

Silver trifluoromethanesulfonate (45 mg) dissolved in dry toluene (1 mL) was added at 0°C to a stirred solution of **29** (70 mg), 2,6-di-*tert*-butyl-4-methylpyridine (10 mg), and benzobromomannose (75 mg) in CH_2Cl_2 (5 mL) containing crushed molecular sieves (4 Å). After 6 h the mixture was chromatographed on silica gel (2:1 toluene–EtOAc) to give methyl 4-*O*-acetyl-2-deoxy-3,6-di-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-*arabino*-hexopyranoside (**30**, 63 mg, 52%); $[\alpha]_D$ +12° (*c* 1.0, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.9 (*Me*CO), 36.8 (C-2), 54.9 (OMe), 63.0, 63.2, 66.9, 67.2, 68.7, 68.9, 69.3, 69.6, 70.1, 70.4, 70.9, 71.2, 76.1 (C-3–6, C-2′–6′, C-2″–6″), 97.2, 97.9, 98.9 (C-1,1′,1″), 128.3–133.5 (Ph), 165.2–166.2 (Ph*C*O), 170.3 (Me*C*O). Compound **30** (63 mg) was deprotected as described for **5** above to give **32** (10 mg, 45%); $[\alpha]_D$ +89° (*c* 0.7 water); NMR data (D_2O): ^{13}C, δ 36.6 (C-2), 55.3 (OMe), 61.7, 65.9, 67.5, 70.4, 70.7, 70.8, 71.1, 71.2, 71.4, 73.4, 73.9, 77.6 (C-3–6, C-2′–6′, C-2″–6″), 99.1, 100.2, 102.6 (C-1,1′,1″); ^1H (25°C), δ 1.81 (1 H, H-2ax), 2.28 (1 H, H-2eq), 4.88 (2 H), 5.07 (H-1,1′,1″). FAB-mass spectrum: *m/z* 503.3 [M + 1].

*Methyl 2-deoxy-3-*O*-(3-deoxy-*α*-*D*-*arabino*-hexopyranosyl)-6-*O*-*α*-*D*-mannopyranosyl-*α*-*D*-arabino-hexopyranoside* (**33**).—Compounds **29** (58 mg) and **2** (36 mg) were coupled as described for compound **29** and benzobromomannose above to give methyl 4-*O*-acetyl-2-deoxy-6-*O*-(2,3,4,6-tetra-O-benzoyl-α-D-mannopyranosyl)-3-*O*-(2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*arabino*-hexopyranosyl)-α-D-*arabino*-hexopyranoside (**31**, 41 mg, 53%); $[\alpha]_D$ +23° (*c* 1.0, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.6, 20.8, 21.0 (*Me*CO), 29.1 (C-3′), 36.8 (C-2), 54.8 (OMe), 62.9, 63.2, 64.7, 66.9, 68.8 × 2, 69.5, 70.0, 70.4, 71.2, 75.1 (C-3–6, C-2′, C-4′–6′, C-2″–6″), 97.4, 97.8, 98.0 (C-1,1′,1″), 128.3–133.5 (Ph), 165.4–166.2 (Ph*C*O), 169.9–170.8 (Me*C*O). Compound **31** (81 mg) was deprotected as described for **5** above to give **33** (25 mg, 70%); $[\alpha]_D$ +120° (*c* 0.8, water); NMR data (D_2O): ^{13}C, δ 34.1 (C-3′), 36.6 (C-2), 55.2 (OMe), 61.6, 61.9, 62.2, 65.9, 67.4, 68.0, 70.4, 70.6, 71.1, 71.3, 73.4, 74.8, 77.3 (C-3–6, C-2′, C-4′–6′, C-2″–6″), 99.1, 100.2, 101.2 (C-1,1′,1″); ^1H (25°C), δ 1.81 (2 H, H-2ax and H-3′ax), 2.07 (1 H, H-3′eq), 2.30 (1 H, H-2eq), 4.88 (2 H), 4.91 (H-1,1′,1″). FAB-mass spectrum: *m/z* 487.3 [M + 1].

*Methyl 4-deoxy-3,6-di-*O*-α-D-mannopyranosyl-α-D-*lyxo*-hexopyranoside* (**40**).—Silver trifluoromethanesulfonate (140 mg) dissolved in dry toluene (3 mL) was added at 0°C to a stirred solution of methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-mannopyranoside [18] (121 mg) and benzobromomannose (310 mg) in CH_2Cl_2 (5 mL) containing crushed molecular sieves (4 Å). After 30 min the mixture was chromatographed on silica gel (12:1 toluene–EtOAc) to give methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**34**, 226 mg, 75%); $[\alpha]_D$ −50° (*c* 0.75, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 55.2 (OMe), 62.9, 63.5, 66.6, 68.7, 69.3, 69.8, 70.0, 72.1, 72.6, 78.9 (C-2–6, C-2′–6′), 98.8, 99.7, 101.4 (C-1,1′, Ph*C*H), 125.9–137.0 (Ph), 165.0–166.2 (Ph*C*O).

Sodium cyanoborohydride (250 mg) was added to a stirred solution of **34** (226 mg) in tetrahydrofuran (50 mL) [19]. After 20 min the solution was treated with ethereal HCl, then concentrated and run through a short column of silica gel (5:2 toluene–EtOAc) to give after concentration a residue which was dissolved in toluene (30 mL) and treated with triiodoimidazole (119 mg) and triphenylphosphine (138 mg) at 110°C overnight [10]. The mixture was diluted with toluene, washed with aq $Na_2S_2O_3$, dried (Na_2SO_4),

and concentrated. The residue was dissolved in EtOAc, and Pd–C, $NaHCO_3$ (35 mg), and water (19 drops) were added. The mixture was hydrogenolyzed at 400 kPa overnight, then filtered, concentrated, redissolved in EtOAc, hydrogenolyzed over palladium-on-charcoal for another night, filtered, concentrated, and then chromatographed on silica gel (6:1 toluene–EtOAc) to give methyl 2-*O*-benzoyl-4-deoxy-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-*lyxo*-hexopyranoside (**36**, 80 mg, 40%); $[\alpha]_D$ −36° (*c* 1.0, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 28.3 (C-4), 55.1 (OMe), 62.6, 65.4, 66.5, 68.8, 69.4, 69.9, 70.1, 70.7, 71.9 (C-2,3,5,6, C-2′–6′), 97.0, 99.0 (C-1,1′), 125.3–133.5 (Ph), 165.2–166.1 (Ph*C*O).

Compound **36** (30 mg) and benzobromomannose (30 mg) were coupled as described for **23** above to give after silica gel chromatography (12:1 toluene–EtOAc) methyl 2-*O*-benzoyl-4-deoxy-3,6-di-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-*lyxo*-hexopyranoside (**38**, 44 mg, 88%); $[\alpha]_D$ −17° (*c* 0.9, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 28.9 (C-4), 55.2 (OMe), 62.6, 66.5, 66.8, 67.1, 68.9, 69.4, 70.0, 70.4, 70.6, 72.0 (C-2,3,5,6, C-2′–6′, C-2″–6″), 97.0, 97.3, 99.1 (C-1,1′,1″), 128.2–133.4 (Ph), 165.2–166.1 (Ph*C*O). Compound **38** (44 mg) was deprotected as described above for compound **5** to give **40** (5.4 mg, 35%); $[\alpha]_D$ +68° (*c* 0.5, water); NMR data (D_2O): ^{13}C, δ 26.9 (C-4), 55.4 (OMe), 61.7 × 2, 67.5 × 2, 67.9, 68.1, 69.5, 70.8, 71.1, 71.2, 71.3, 71.6, 73.6, 73.9 (C-2,3,5,6, C-2′–6′, C-2″–6″), 99.0, 100.1, 102.3 (C-1,1′,1″); ^1H (70°C), δ 1.77 (1 H, H-4ax), 1.84 (1 H, H-4eq), 4.76, 4.89, 5.01 (H-1,1′,1″). FAB-mass spectrum: *m*/*z* 503.3 [M + 1].

*Methyl 4-deoxy-3-*O*-(3-deoxy-α-*D*-arabino-hexopyranosyl)-6-*O*-α-D-mannopyranosyl-α-*D*-lyxo-hexopyranoside* (**41**).—Silver trifluoromethanesulfonate (163 mg) dissolved in dry toluene (5 mL) was added at 0°C to a stirred solution of methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-mannopyranoside (160 mg) [18], **2** (176 mg), and 2,6-di-*tert*-butyl-4-methylpyridine (43 mg) in CH_2Cl_2 (10 mL) containing crushed molecular sieves (4 Å). After 1 h the mixture was chromatographed on silica gel (3:1 toluene–EtOAc) to give methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-(2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*arabino*-hexopyranosyl)-α-D-mannopyranoside (**35**, 173 mg, 63%); $[\alpha]_D$ +4° (*c* 0.6, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.6–21.0 (*Me*CO), 29.0 (C-3′), 55.1 (OMe), 63.0, 63.5, 64.5, 68.7, 69.0, 69.2, 70.7, 72.0, 79.3 (C-2–6, C-2′, C-4′–6′), 97.2, 99.7 (C-1,1′), 101.3 (Ph*C*H), 126.0–137.1 (Ph), 165.7 (Ph*C*O), 169.8–170.9 (Me*C*O). Compound **35** (200 mg) was treated as described for compound **34** above to give methyl 2-*O*-benzoyl-4-deoxy-3-*O*-(2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*arabino*-hexopyranosyl)-α-D-*lyxo*-hexopyranoside (**37**, 138 mg, 82%); $[\alpha]_D$ +18° (*c* 1.4, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.6, 21.0, 21.0 (*Me*CO), 27.8 (C-4), 29.0 (C-3′), 54.9 (OMe), 62.9, 64.3, 65.2, 68.8, 69.2, 69.3, 69.7, 69.9 (C-2,3,5,6, C-2′, C-4′–6′), 94.3, 99.1 (C-1,1′), 128.2–133.3 (Ph), 165.8 (Ph*C*O), 169.8, 170.1, 170.8 (Me*C*O).

Compound **37** (90 mg) and benzobromomannose (140 mg) were coupled as described for compound **23** above to give after silica gel chromatography (4:1 toluene–EtOAc) methyl 2-*O*-benzoyl-4-deoxy-6-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-3-*O*-(2,4,6-tri-*O*-acetyl-3-deoxy-α-D-*arabino*-hexopyranosyl)-α-D-*lyxo*-hexopyranoside (**39**, 94 mg, 51%); $[\alpha]_D$ +1.3° (*c* 1.4, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 20.7, 21.0, 21.1 (*Me*CO), 28.4 (C-4), 29.1 (C-3′), 55.1 (OMe), 62.7, 62.9, 64.3, 66.8, 67.1, 69.0, 69.3, 69.4, 69.7, 70.0, 70.4 (C-2,3,5,6, C-2′, C-4′–6′, C-2″–6″), 94.5, 97.5, 99.3 (C-1,1′,1″),

128.3–133.5 (Ph), 165.3–166.2 (Ph*C*O), 169.9, 170.2, 170.9 (Me*C*O). Compound **39** (94 mg) was deprotected as described above for compound **5** to give **41** (18 mg, 47%); $[\alpha]_D$ +11° (*c* 0.9, water); NMR data (D_2O): ^{13}C, δ 27.1, 34.3 (C-4, C-3′), 55.4 (OMe), 61.8, 61.9, 62.2, 67.5, 67.9, 68.2, 68.3, 69.6, 70.8, 71.3, 71.5, 73.6, 74.8 (C-2,3,5,6, C-2′, C-4′–6′, C-2″–6″), 97.7, 100.1, 102.3 (C-1,1′,1″); ^1H (70°C), δ 1.78 (1 H, H-4ax), 1.89 (2 H, H-4eq and H-3′ax), 2.07 (1 H, H-3′eq), 4.79, 4.86, 4.91 (H-1,1′,1″). FAB-mass spectrum: *m*/*z* 487.3 [M + 1].

*Methyl 2-*O*-α-*D*-mannopyranosyl-α-*D*-rhamnopyranoside* (**45**).—Benzobromomannose (172 mg) and methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside [15] (75 mg) were coupled as described for compounds **1** and **2** above to give after silica gel chromatography (3:1 toluene–EtOAc) methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**42**, 165 mg, 86%); $[\alpha]_D$ −42° (*c* 0.1, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 54.7 (OMe), 63.1, 63.9, 67.2, 68.7, 69.5, 70.0, 71.2, 73.2, 75.6, 79.2 (C-2–6, C-2′–6′), 99.7, 100.8 (C-1,1′), 101.6 (Ph*C*H), 125.2–138.4 (Ph), 164.9–166.0 (Ph*C*O). Compound **42** (50 mg) was dissolved in aq AcOH (70%) and heated at 50°C until TLC showed complete loss of the 4,6-*O*-benzylidene group. The mixture was then diluted with toluene, concentrated, and purified on a silica gel column (3:1 toluene–EtOAc) to give methyl 3-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**43**, 35 mg, 71%); $[\alpha]_D$ −41° (*c* 0.1, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 54.6 (OMe), 62.6, 63.5, 67.0, 67.2, 69.3, 69.9, 70.3, 72.3, 72.3, 75.7, 79.2 (C-2–6, C-2′–6′), 99.1, 99.7 (C-1,1′), 127.8–138.0 (Ph), 165.1–166.4 (Ph*C*O). Compound **43** (70 mg) was dissolved in 2:1 toluene–MeCN, and triphenylphosphine (77 mg), iodine (75 mg), and imidazole were added [10], and the mixture was stirred overnight at 70°C. The mixture was concentrated and purified on a silica gel column (6:1 toluene–EtOAc) to yield methyl 3-*O*-benzyl-6-deoxy-6-iodo-2-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**44**) (55 mg, 70%); $[\alpha]_D$ −31° (*c* 1.1, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 8.2 (C-6), 55.2 (OMe), 62.9, 66.9, 69.4, 69.9, 70.4, 71.1, 72.3, 75.9, 78.8 (C-2–5, C-2′–6′), 99.4, 99.9 (C-1,1′), 127.9–137.9 (Ph), 165.2–166.2 (Ph*C*O). Compound **44** (95 mg) was treated as described for **12** to give **45** (21.1 mg, 64%); $[\alpha]_D$ +78° (*c* 1.0, $CHCl_3$); NMR data (D_2O): ^{13}C, δ 17.3 (C-6), 55.4 (OMe), 61.6, 67.4, 69.3, 70.3, 70.7, 71.1, 72.1, 74.0, 78.6 (C-2–5, C-2′–6′), 101.5, 103.1 (C-1,1′); ^1H (25°C), δ 1.32 (d, 3 H, H-6), 4.92, 5.05 (H-1,1′). FAB-mass spectrum: *m*/*z* 341.2 [M + 1].

*Methyl 3-*O*-α-*D*-mannopyranosyl-α-*D*-rhamnopyranoside* (**48**).—Compound **11** (100 mg) was iodinated as described for compound **43** above to give methyl 2-*O*-benzyl-6-deoxy-6-iodo-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**47**, 95 mg, 84%); $[\alpha]_D$ −10° (*c* 0.9, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 7.0 (C-6), 55.3 (OMe), 63.0, 66.8, 69.4, 70.0, 70.4, 70.7, 71.9, 77.5, 80.1 (C-2–5, C-2′–6′), 98.0, 99.5 (C-1,1′), 127.3–137.8 (Ph), 165.4–166.1 (Ph*C*O). Compound **47** (51 mg) was dissolved in EtOAc (5 mL) containing triethylamine (20 μL), Pd–C was added, and the solution was hydrogenolyzed overnight. The mixture was then filtered, concentrated, and dissolved in MeOH, and a catalytic amount of NaOMe was added. When TLC showed complete deacylation, the mixture was neutralized with Dowex 50 (H^+) resin, then filtered, and evaporated. The residue was passed through a BioGel P2 column and lyophilized to give **48** (8.2 mg, 43%); $[\alpha]_D$ +51° (*c* 0.9, $CHCl_3$); NMR data (D_2O):

^{13}C, δ 17.5 (C-6), 55.6 (OMe), 61.8, 67.5, 69.2, 70.7, 70.8, 71.1, 72.9, 74.1, 79.2 (C-2–5, C-2′–6′), 100.2, 103.1 (C-1,1′); ^{1}H (25°C), δ 1.31 (d, 3 H, H-6), 4.67, 5.11 (H-1,1′). FAB-mass spectrum: m/z 341.2 [M + 1].

*Methyl 3-deoxy-2-*O*-α-*D*-mannopyranosyl-α-*D*-*arabino*-hexopyranoside* (**46**).—Methyl 4,6-*O*-benzylidene-3-deoxy-α-D-*arabino*-hexopyranoside [20] (100 mg) and benzobromomannose (310 mg) were coupled as described for compounds **1** and **2** above (silica gel chromatography, 20:1 toluene–EtOAc) to give methyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl)-α-D-*arabino*-hexopyranoside (160 mg, 51%); $[\alpha]_D$ −38° (*c* 0.8, $CHCl_3$); ^{13}C NMR data ($CDCl_3$): δ 29.5 (C-3), 54.8 (OMe), 63.1, 65.0, 67.0, 69.3, 69.6, 67.0, 70.8, 73.8, 76.2 (C-2, C-4–6, C-2′–6′), 97.6, 98.9 (C-1,1′), 102.0 (Ph*C*H), 126.2–137.8 (Ph), 165.6 (Ph*C*O). This derivative (160 mg) was deprotected as described for compound **47** to give **46** (39.2 mg, 61%); $[\alpha]_D$ +90° (*c* 0.5, water); NMR data (D_2O): ^{13}C, δ 31.3 (C-3), 55.3 (OMe), 61.8, 62.4, 67.6, 71.1, 73.5, 73.9, 74.3 (C-2, C-4–6, C-2′–6′), 99.0 (C-1,1′); ^{1}H (70°C), δ 1.77 (1 H, H-3ax), 2.23 (1 H, H-3eq), 4.77, 5.03 (H-1,1′). FAB-mass spectrum: m/z 341.2 [M + 1].

*Methyl 4-deoxy-3-*O*-α-*D*-mannopyranosyl-α-*D*-lyxo-hexopyranoside* (**49**).—Compound **37** (50 mg) was deprotected as described for compound **5** above to give **49** (4.6 mg, 24%); $[\alpha]_D$ +98° (*c* 0.5, water); NMR data (D_2O): ^{13}C, δ 26.8 (C-4), 55.3 (OMe), 61.6, 64.8, 67.5, 68.2, 69.9, 71.0, 71.2, 71.5, 73.9 (C-2,3,5,6, C-2′–6′), 99.0, 102.1 (C-1,1′); ^{1}H (70°C), δ 1.66 (1 H, H-4ax), 1.85 (1 H, H-4eq), 4.79, 5.03 (H-1,1′). FAB-mass spectrum: m/z 339.2 [M − 1].

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