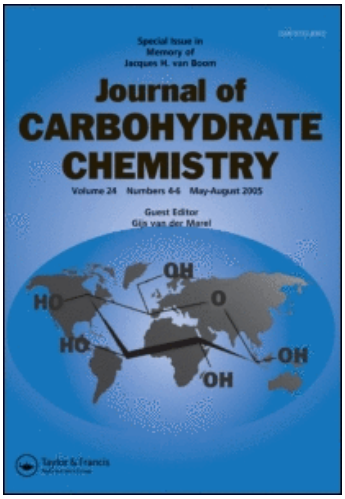


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

AN EFFICIENT AND PRACTICAL SYNTHESIS OF α-(1→3)-LINKED MANNOHEXAOSE AND MANNOOCTAOSE

Langqiu Chen[a]; Fanzuo Kong[a]
[a] Research Center for Eco-Environmental Science, Academia Sinica, Beijing, China

Online publication date: 16 September 2002

To cite this Article Chen, Langqiu and Kong, Fanzuo(2002) 'AN EFFICIENT AND PRACTICAL SYNTHESIS OF α-(1→3)-LINKED MANNOHEXAOSE AND MANNOOCTAOSE', Journal of Carbohydrate Chemistry, 21: 5, 341 — 353
To link to this Article: DOI: 10.1081/CAR-120014899
URL: http://dx.doi.org/10.1081/CAR-120014899

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

JOURNAL OF CARBOHYDRATE CHEMISTRY
Vol. 21, No. 5, pp. 341–353, 2002

AN EFFICIENT AND PRACTICAL SYNTHESIS OF α-(1→3)-LINKED MANNOHEXAOSE AND MANNOOCTAOSE

Langqiu Chen and Fanzuo Kong*

Research Center for Eco-Environmental Science, Academia Sinica,
P.O. Box 2871, Beijing 100085, China

ABSTRACT

α-(1 → 3)-Linked mannohexaose and mannooctaose as their methyl glycosides were synthesized from condensation of the corresponding α-(1 → 3)-linked di- (**9**) and tetrasaccharide donor (**21**) with the tetrasaccharide acceptor (**23**), respectively, followed by deacylation. The donor **21** and acceptor **23** were prepared readily from activation of C-1 of the tetrasaccharide **20** and deallylation of the tetrasaccharide **22**, respectively. The tetrasaccharide **20** was prepared from oxidative cleavage of 1-*O*-*p*-methoxyphenyl of **19**, which was obtained from coupling of **9** with **11**. The tetrasaccharide **22** was obtained from condensation of the donor **13** with the acceptor **18**. These disaccharides **9**, **11**, **13**, and **18** were produced easily by simple chemical transformation using *p*-methoxyphenyl 3-*O*-allyl-α-D-mannopyranoside (**1**) and 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (**6**), and methyl 3-*O*-allyl-α-D-mannopyranoside (**14**) as the synthons.

Key Words: Mannan; Trichloroacetimidate; Synthesis

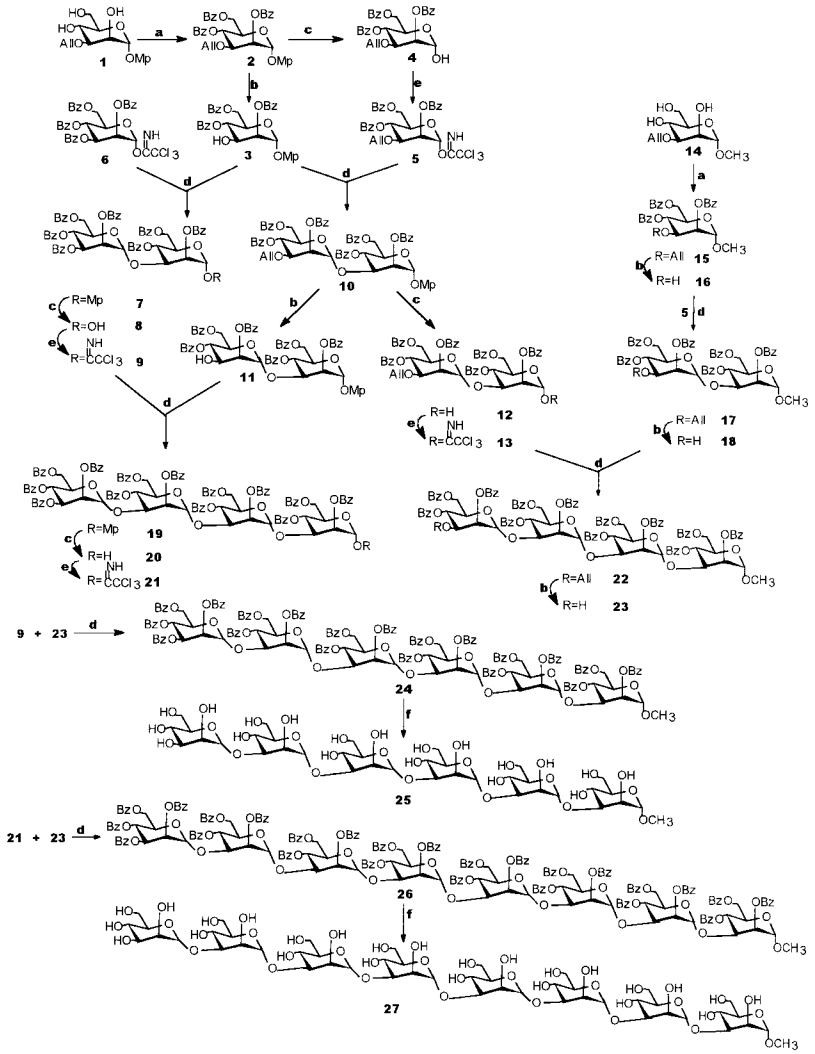
*Corresponding author. Fax: +86-10-62923563; E-mail: fzkong@mail.rcess.ac.cn

DOI: 10.1081/CAR-120014899 0732-8303 (Print); 1532-2327 (Online)

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

INTRODUCTION

α-(1 → 3)-Linked mannans occur in the fruit body polysaccharide of *Tremella fuciformis* and *Dictyophora indusiata* Fisch[1] and are the backbone of glucuronoxylomannan (GXM) antigens.[2] It was also reported that linear α-(1 → 3)-linked mannan reacts with L. ovata agglutinin.[3] Synthesis of α-(1 → 3)-linked mannan is of interest since it can afford a pure sample in enough quantity for structure–bioactivity relationship studies. The synthesis of α-(1 → 3)-linked mannohexaose has been achieved through a



Scheme 1. Reagents and conditions: (a) PhCOCl/Pyr, rt. (b) $PdCl_2$, CH_3OH, 40°C. (c) CAN, CH_3CN—H_2O, rt. (d) TMSOTf, CH_2Cl_2, −25°C to rt. (e) CCl_3CN, CH_2Cl_2, K_2CO_3, rt. (f) NH_3/CH_3OH, rt.

stepwise strategy using 3-*O*-acetyl-2,4,6-tri-*O*-benzyl-α-D-mannopyranosyl chloride as the donor and benzyl 2,4,6-tri-*O*-benzyl-α-D-mannopyranoside as the acceptor. This synthesis involved rather complex procedures for the preparations of both the donor and acceptor.[1] We provide herein a new method for the synthesis of α-(1 → 3)-linked mannohexaose and mannooctaose using an acyl temporary protective group.

RESULTS AND DISCUSSION

As outlined in Scheme 1, *p*-methoxyphenyl 3-*O*-allyl-α-D-mannopyranoside (**1**) was chosen as the starting material, and obtained readily from allylation of *p*-methoxyphenyl α-D-mannopyranoside through a dibutyltin complex under the same conditions used for transformation of allyl α-D-mannopyranoside to allyl 3-*O*-allyl-α-D-mannopyranoside.[4] Benzoylation of **1** with benzoyl chloride in pyridine quantitatively gave 3-*O*-allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (**2**). Deallylation of **2** with $PdCl_2$ was carried out smoothly[5] giving the acceptor *p*-methoxyphenyl 2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (**3**) in high yield (90%). Meanwhile, oxidative cleavage of 1-*O*-*p*-methoxyphenyl of **2** with ammonium ceric nitrate (CAN), followed by trichloroacetimidation[6] afforded the donor 3-*O*-allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (**5**) in satisfactory yield (72% for 2 steps). The acceptor **3** was coupled with 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (**6**)[6] to give the disaccharide **7**. Removal of the *p*-methoxyphenyl group of **7** with CAN, followed by trichloroacetimidation with trichloroacetonitrile in the presence of potassium carbonate afforded the nonreducing end disaccharide donor **9** (72% for 2 steps). Coupling of **3** with **5** afforded the disaccharide **10**, and subsequent deallylation furnished the disaccharide acceptor **11** (72% for 2 steps). Condensation of **9** with **11** gave the tetrasaccharide **19**, and subsequent removal of *p*-methoxyphenyl, and trichloroacetimidation yielded the tetrasaccharide donor **21**. Transformation of **10** to the disaccharide donor **13** was readily carried out by treatment of **10** with CAN, followed by trichloroacetimidation. Coupling of **13** with the disaccharide acceptor **18**, which was obtained from coupling of methyl 2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (**16**) with **5** followed by deallylation, gave the tetrasaccharide **22**, and subsequent deallylation afforded the tetrasaccharide acceptor **23**. Condensation of **9** with **23** gave the protected mannohexaose **24**, while condensation of **21** with **23** gave the acylated mannooctaose **26**. Treatment of **24** and **26** with saturated ammonia–methanol afforded methyl mannohexaoside **25** and mannooctaoside **27** respectively. J_{C1-H1} values (170–172 Hz) were determined for **25** and **27**, confirming the sole α-linkages in the oligosaccharides.[7]

In summary, a facile and practical method was presented for the syntheses of α-(1 → 3)-linked mannose oligosaccharides.

EXPERIMENTAL

General methods. Optical rotations were determined at 25°C with a Perkin–Elmer Model 241-MC automatic polarimeter. Melting points were determined with a ''Mel-Temp'' apparatus. ^{1}H NMR, ^{13}C NMR, and ^{1}H NMR HOMO COSY spectra

were recorded with Bruker ARX 400 spectrometers for solutions in $CDCl_3$ or D_2O as indicated. Chemical shifts are given in parts per million (ppm) downfield from internal Me_4Si. Mass spectra were recorded with a VG PLATFORM mass spectrometer using the electrospray-ionization mode. Thin-layer chromatography (TLC) was performed on Silica Gel HF_{254} with detection by charring with 30% (v/v) H_2SO_4 in MeOH or in some cases by UV detection. Column chromatography was conducted by elution of a column (16×240, 18×300, 35×400 mm) of silica gel (100–200 mesh) with EtOAc–petroleum ether (60–90°C) as the eluent. Solutions were concentrated at <60°C under diminished pressure.

***p*-Methoxyphenyl 3-*O*-Allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (2).** *p*-Methoxyphenyl α-D-mannopyranoside[8] (5.00 g, 17.5 mmol) and Bu_2SnO (4.80 g, 19.3 mmol) were added to CH_3OH (200 mL), the mixture was heated under reflux for 2 h, then concentrated to dryness. The residue was diluted with benzene (200 mL), and allyl bromide (18.0 mL, 211 mmol), and Bu_4NI (6.46 g, 17.5 mmol) were added to the mixture. The reaction was carried out at 60°C for 24 h. TLC (3:1 EtOAc–CH_3OH) indicated that the reaction was complete. Concentration of the reaction mixture and purification by flash chromatography (EtOAc) gave **1** as a syrup (3.70 g, 65%); $[\alpha]_D^{20}$ +95.4° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.98 (d, 2 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 6.82 (d, 2 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 6.00 (m, 1 H, CH_2═C*H*—CH_2—), 5.51 (d, 1 H, $J_{1,2}$ = 1.6 Hz, H-1), 5.40–5.25 (m, 2 H, CH_2═CH—CH_2—), 4.30–4.16 (m, 2 H, CH_2═CH—CH_2—), 4.21 (m, 1 H), 4.11 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4), 3.91–3.87 (dd, 1 H, $J_{5,6}$ = 3.2 Hz, $J_{6,6'}$ = 12.3 Hz, H-6), 3.86–3.83 (dd, 1 H, $J_{2,3}$ = 3.2 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.78–3.73 (m, 2 H), 3.77 (s, 3 H, CH_3), 2.98 (br, 3 H, OH). To a solution of **1** (6.52 g, 20.0 mmol) in pyridine (16 mL) was added benzoyl chloride (8.34 mL, 72.0 mmol). After stirring the mixture overnight at rt, TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. Methanol (6 mL) was added to the reaction mixture, and stirring was continued for 10 min. Water (100 mL) was added, and the mixture was extracted with CH_2Cl_2 (3×100 mL), the extract was washed with M HCl and satd aq $NaHCO_3$, dried (Na_2SO_4) and concentrated. Purification by flash chromatography (3:1 petroleum ether–EtOAc) quantitatively gave **2** as a foamy solid (12.76 g, 100%); $[\alpha]_D$ +19.1° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.12–7.38 (m, 15 H, Ph*H*), 7.08 (d, 2 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 6.76 (d, 2 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 5.86 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.8 Hz, H-4), 5.79–5.69 (m, 2 H, H-2, CH_2═C*H*—CH_2—), 5.61 (d, 1 H, $J_{1,2}$ = 1.8 Hz, H-1), 5.23–5.06 (m, 2 H, CH_2═CH—CH_2—), 4.63–4.61 (m, 1 H), 4.45–4.42 (m, 2 H), 4.38–4.34 (dd, 1 H, $J_{2,3}$ = 3.3 Hz, $J_{3,4}$ = 9.8 Hz, H-3), 4.22–4.04 (m, 2 H, CH_2═CH—CH_2—), 3.73 (s, 3 H, CH_3).

Anal. Calcd for $C_{37}H_{34}O_{10}$: C, 69.59; H, 5.33. Found: C, 69.82; H, 5.31.

***p*-Methoxyphenyl 2,4,6-Tri-*O*-benzoyl-α-D-mannopyranoside (3).** To a solution of **2** (1.28 g, 2.0 mmol) in anhyd CH_3OH (50 mL) was added $PdCl_2$ (0.1 g), and the mixture was stirred at 40°C for 2–4 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was filtered, and the filtrate was concentrated. The residue was passed through a silica-gel column with 2:1 petroleum ether–EtOAc as the eluent to give **3** as a syrup (1.08 g, 90%): $[\alpha]_D$ +10.3° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.17–7.44 (m, 15 H,

PhH), 7.14 (d, 2 H, J = 8.8 Hz, *p*-CH_3O—PhH), 6.85 (d, 2 H, J = 8.8 Hz, *p*-CH_3O—PhH), 5.81 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4), 5.72–5.69 (m, 2 H, H-1, H-2), 4.72–4.69 (m, 2 H, H-3, H-6), 4.56–4.51 (m, 2 H, H-5, H-6), 3.82 (s, 3 H, CH_3O).

Anal. Calcd for $C_{34}H_{30}O_{10}$: C, 68.23; H, 5.02. Found: C, 68.44; H, 5.00.

3-*O*-Allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (5). To a solution of **2** (12.76 g, 20.0 mmol) in 4:1 CH_3CN—H_2O (900 mL) was added CAN [$(NH_4)_2Ce(NO_3)_6$, 43.86 g, 80.0 mmol], and the mixture was stirred at rt for 30 min, at the end of which time TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was extracted with EtOAc, and washed with satd aq $NaHCO_3$. The organic layer was concentrated under reduced pressure, and purified by column chromatography (3:1 petroleum ether–EtOAc) to afford **4** as a syrup (8.52 g, 80%). To a solution of **4** (4.50 g, 8.5 mmol) in CH_2Cl_2 (40 mL) were added trichloroacetonitrile (2.5 mL) and anhyd potassium carbonate (4.50 g). The reaction mixture was stirred overnight at rt and then filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (3:1 petroleum ether–EtOAc) to give **5** (5.15 g, 90%) as a syrup; $[\alpha]_D - 8.9°$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.81 (s, N*H*═), 8.11–7.27 (m, 15 H, PhH), 6.49 (d, 1 H, $J_{1,2} = 1.6$ Hz, H-1), 5.95 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4), 5.79 (dd, 1 H, $J_{1,2} = 1.6$ Hz, $J_{2,3} = 3.3$ Hz, H-2), 5.70 (m, 1 H, CH_2═C*H*—CH_2—), 5.26–5.08 (m, 2 H, CH_2═CH—CH_2—), 4.70–4.67 (dd, 1 H, J = 1.6 Hz, J = 11.7 Hz, H-6), 4.47–4.40 (m, 2 H, H-5, H-6), 4.27–4.24 (dd, 1 H, $J_{2,3} = 3.3$ Hz, $J_{3,4} = 9.8$ Hz, H-3), 4.18–4.01 (m, 2 H, CH_2═CH—CH_2—).

Anal. Calcd for $C_{32}H_{28}Cl_3NO_9$: C, 56.76; H, 4.14. Found: C, 56.60; H, 4.15.

***p*-Methoxyphenyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (7).** 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate[5] (**6**, 1.48 g, 2.0 mmol) and *p*-methoxyphenyl 2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (**3**, 1.20 g, 2.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhydrous CH_2Cl_2 (20 mL). TMSOTf (30 μL, 0.08 equiv) was added dropwise at −25°C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the temperature was gradually warmed to ambient temperature. Then the mixture was neutralized with triethylamine, concentrated and purified by flash chromatography (2:1 petroleum ether–EtOAc) to afford **7** as a foamy solid (2.00 g, 85%); $[\alpha]_D - 42.6°$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.24–7.21 (m, 35 H, Ph*H*), 7.02 (d, 1 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 6.75 (d, 1 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 6.05 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4^{II}), 6.01 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4^{I}), 5.87 (dd, 1 H, $J_{1,2} = 1.8$ Hz, $J_{2,3} = 3.3$ Hz, H-2^{II}), 5.72 (dd, 1 H, H-3^{II}), 5.69 (d, 1 H, H-1^{II}), 5.42 (d, 1 H, H-1^{I}), 5.36 (dd, 1 H, $J_{1,2} = 1.7$ Hz, $J_{2,3} = 3.2$ Hz, H-2^{I}), 4.84 (dd, 1 H, H-3^{I}), 4.65–4.58 (m, 2 H), 4.54–4.45 (m, 3 H), 4.36 (dd, 1 H, $J_{5,6} = 3.9$ Hz, $J_{6,6} = 12.3$ Hz, H-6), 3.74 (s, 1 H, CH_3O).

Anal. Calcd for $C_{68}H_{56}O_{19}$: C, 69.39; H, 4.76. Found: C, 69.30; H, 4.87.

2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (9). To a solution of **7** (5.88 g, 5.0 mmol) in 4:1 CH_3CN—H_2O (450 mL) was added CAN (10.96 g, 20.0 mmol), and the mixture was stirred at rt for 30 min, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was extracted with

EtOAc, and washed with satd aq $NaHCO_3$. The organic layer was concentrated under reduced pressure, and purified by column chromatography (2:1 petroleum ether–EtOAc) to afford **8** as a foamy solid (4.28 g, 80%). A mixture of **8** (4.28 g, 4.0 mmol), trichloroacetonitrile (2.1 mL, 10 mmol), and anhyd potassium carbonate (4.28 g) in dry dichloromethane (30 mL) was stirred overnight and then was filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (2:1 petroleum ether–EtOAc) to give **9** as a foamy solid (4.37 g, 90%); $[\alpha]_D - 48.1°$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.82 (s, 1 H, N*H*), 8.25–7.20 (m, 35 H, Ph*H*), 6.55 (s, 1 H, H-1^I), 6.14 (dd, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4^{II}), 6.06 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4^I), 5.86 (dd, 1 H, H-2^{II}), 5.70 (dd, 1 H, $J_{2,3} = 2.7$ Hz, $J_{3,4} = 10.0$ Hz, H-3^{II}), 5.37–5.36 (m, 2 H, H-1^{II}, H-2^I), 4.74–4.69 (m, 2 H), 4.57–4.45 (m, 4 H), 4.33 (dd, 1 H, $J_{5,6} = 2.6$ Hz, $J_{6,6} = 12.1$ Hz, H-6).

Anal. Calcd for $C_{63}H_{50}Cl_3NO_{18}$: C, 62.25; H, 4.12. Found: C, 62.00; H, 4.14.

***p*-Methoxyphenyl 3-*O*-Allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (10).** 3-*O*-Allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (**5**, 1.35 g, 2.0 mmol) and *p*-methoxyphenyl 2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (**3**, 1.20 g, 2.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (20 mL). TMSOTf (30 μL, 0.08 equiv) was added dropwise at −25°C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the temperature was gradually warmed to ambient temperature. Then the mixture was neutralized with triethylamine, concentrated and purified by flash chromatography (2:1 petroleum ether–EtOAc) to afford **10** (1.89 g, 85%); $[\alpha]_D - 9.0°$ (*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.21–7.26 (m, 30 H, Ph*H*), 7.00 (d, 2 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 6.75 (d, 2 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 5.98 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4^{II}), 5.86 (dd, 1 H, $J_{1,2} = 1.8$ Hz, $J_{2,3} = 3.4$ Hz, H-2^{II}), 5.74 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4^I), 5.66 (d, 1 H, H-1^{II}), 5.43 (m, 1 H, CH_2═C*H*CH_2—), 5.31 (d, 1 H, $J_{1,2} = 1.8$ Hz, H-1^I), 5.20 (dd, 1 H, H-2^I), 4.87–4.74 (m, 2 H, CH_2═CHCH_2—), 4.79 (dd, 1 H, H-3^{II}), 4.60–4.56 (m, 2 H), 4.51–4.44 (m, 2 H), 4.35 (m, 1 H), 4.28(m, 1 H, H-6), 3.91–3.88 (dd, 1 H), 3.76–3.63 (m, 2 H, CH_2═CHCH_2—), 3.75 (s, 3 H, CH_3O).

Anal. Calcd for $C_{64}H_{56}O_{18}$: C, 69.06; H, 5.04. Found: C, 69.24; H, 5.03.

***p*-Methoxyphenyl 2,4,6-Tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (11).** To a solution of **10** (2.22 g, 2.0 mmol) in anhyd CH_3OH (50 mL) was added $PdCl_2$ (0.22 g), and the mixture was stirred at 40°C for 3 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was filtered, and the filtrate was concentrated. The residue was passed through a silica-gel column with 2:1 petroleum ether–EtOAc as the eluent to give **11** as a syrup (1.82 g, 85%): $[\alpha]_D + 4.3°$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.20–7.25 (m, 30 H, Ph*H*), 7.01 (d, 2 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 6.75 (d, 2 H, J = 9.1 Hz, *p*-CH_3O—Ph*H*), 5.99 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4^{II}), 5.84 (dd, 1 H, $J_{1,2} = 1.6$ Hz, $J_{2,3} = 3.0$ Hz, H-2^{II}), 5.67 (d, 1 H, H-1^{II}), 5.60 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4^I), 5.38 (s, 1 H, H-1^I), 5.10 (br, 1 H, H-2^I), 4.79 (dd, 1 H, $J_{2,3} = 3.3$ Hz, $J_{3,4} = 9.7$ Hz H-3^{II}), 4.62–4.58 (m, 2 H), 4.48–4.34 (m, 4 H), 4.21 (dd, 1 H, J = 3.0 Hz, J = 9.8 Hz, H-3^{II}), 3.74 (s, 3 H, CH_3O).

Anal. Calcd for $C_{61}H_{52}O_{18}$: C, 68.28; H, 4.85. Found: C, 68.55; H, 4.94.

3-*O*-Allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (13). To a solution of **10** (5.56 g, 5.0 mmol) in 4:1 CH_3CN—H_2O (450 mL) was added CAN (10.96 g, 20.0 mmol), and the mixture was stirred at rt for 30 min, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was extracted with EtOAc, and washed with satd aq $NaHCO_3$. The organic layer was concentrated under reduced pressure, and purified by column chromatography (2:1 petroleum ether–EtOAc) to afford **12** as a foamy solid (4.02 g, 80%). A mixture of **12** (4.02 g, 4.0 mmol), trichloroacetonitrile (2.1 mL), and anhydrous potassium carbonate (4.02 g) in dry dichloromethane (30 mL) was stirred overnight and then was filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (4:1 petroleum ether–EtOAc) to give **13** (4.14 g, 90%) as a syrup; $[\alpha]_D - 25.5°$ (*c* 1.0, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$): δ 8.85 (s, 1 H, NH), 8.23–7.26 (m, 30 H, Ph*H*), 6.58 (d, 1 H, $J_{1,2} = 1.2$ Hz, H-1^I), 6.10 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4^{II}), 5.87 (br, 1 H, H-2^{II}), 5.81 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4^I), 5.43 (m, 1 H, CH_2═C*H*CH_2—), 5.28 (s, 1 H, H-1^{II}), 5.22 (br, 1 H, H-2^I), 4.89–4.65 (m, 2 H, CH_2═CHCH_2—), 4.77–4.65 (m, 2 H), 4.56–4.50 (m, 3 H), 4.36 (m, 1 H, H-5), 4.26 (dd, 1 H, $J_{5,6} = 2.9$ Hz, $J_{6,6} = 12.3$ Hz, H-6), 3.90 (dd, 1 H, J = 3.0 Hz, J = 9.7 Hz), 3.80–3.63 (m, 2 H, CH_2═CHCH_2—).

Anal. Calcd for $C_{59}H_{50}Cl_3NO_{17}$: C, 61.54; H, 4.35. Found: C, 61.80; H, 4.33.

Methyl 3-*O*-Allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (15). To a solution of methyl 3-*O*-allyl-α-D-mannopyranoside[9] **14** (11.7 g, 50 mmol) in pyridine (40 mL) was added benzoyl chloride (21 mL, 180 mmol). After stirring the mixture at rt overnight, TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. Methanol (15 mL) was added to the reaction mixture, and stirring was continued for 10 min. Water (100 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 100 mL), the extract was washed with M HCl and satd aq $NaHCO_3$, dried (Na_2SO_4) and concentrated. Purification by flash chromatography (3:1 petroleum ether–EtOAc) gave **15** (27.3 g, 100%) as a foamy solid; $[\alpha]_D - 34.4°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10–7.37 (m, 15 H, Ph*H*), 5.82 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4), 5.70 (m, 1 H, CH_2═C*H*CH_2—), 5.58 (dd, 1 H, $J_{1,2} = 1.7$ Hz, $J_{2,3} = 3.3$ Hz, H-2), 5.19–5.02 (m, 2 H, CH_2═CHCH_2—), 4.92 (d, 1 H, H-1), 4.68 (dd, 1 H, $J_{5,6} = 2.6$ Hz, $J_{6,6'} = 12.1$ Hz, H-6^{II}), 4.25 (m, 1 H, H-5), 4.14 (dd, 1 H, $J_{5,6'} = 4.9$ Hz, H-6′), 4.14–3.97 (m, 2 H, CH_2═CHCH_2—), 3.48 (s, 3 H, CH_3O).

Anal. Calcd for $C_{31}H_{30}O_9$: C, 68.13; H, 5.49. Found: C, 68.05; H, 5.51.

Methyl 2,4,6-Tri-*O*-benzoyl-α-D-mannopyranoside (16). To a solution of **15** (5.46 g, 10.0 mmol) in anhyd CH_3OH (80 mL) was added $PdCl_2$ (0.55 g), and the mixture was stirred at 40°C for 2 h, at the end of which time TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was filtered, and the filtrate was concentrated The residue was passed through a silica-gel column with 3:1 petroleum ether–EtOAc as the eluent to give **16** as a syrup (4.55 g, 90%); $[\alpha]_D + 7.1°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07–7.37 (m, 15 H, Ph*H*), 5.71 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4), 5.42 (dd, 1 H, $J_{1,2} = 1.7$ Hz, $J_{2,3} = 3.4$ Hz, H-2), 4.95 (d, 1 H, H-1), 4.68 (dd, 1 H, $J_{5,6} = 2.5$ Hz, $J_{6,6'} = 12.1$ Hz, H-6), 4.47 (dd, 1 H, $J_{5,6'} = 4.7$ Hz, H-6′), 4.41 (dd, 1 H, H-3), 4.28 (m, 1 H, H-5), 3.48 (s, 3 H, CH_3O), 3.47 (br, 1 H, OH).

Anal. Calcd for $C_{28}H_{26}O_9$: C, 66.40; H, 5.14. Found: C, 66.55; H, 5.13.

Methyl 3-*O*-Allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (17). The monosaccharide donor **5** (3.38 g, 5.0 mmol) and the monosaccharide acceptor **16** (2.53 g, 5.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (40 mL). TMSOTf (50 μL, 0.05 equiv) was added dropwise at −25°C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the temperature was gradually warmed to ambient temperature. Then the mixture was neutralized with triethylamine, concentrated and purified by flash chromatography (3:1 petroleum ether–EtOAc) to afford **17** (4.34 g, 85%) as a syrup; $[\alpha]_D$ −32.9° (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11–7.25 (m, 30 H, PhH), 5.97 (dd, 1 H, $J_{3,4}=J_{4,5}=10.0$ Hz, H-4^{II}), 5.72 (dd, 1 H, $J_{3,4}=J_{4,5}=9.9$ Hz, H-4^{I}), 5.67 (dd, 1 H, $J_{1,2}=1.7$ Hz, $J_{2,3}=3.1$ Hz, H-2^{II}), 5.41 (m, 1 H, CH_2═C*H*—CH_2—), 5.21–5.18 (m, 2 H, H-1^{II}, H-2^{I}), 4.95 (d, 1 H, $J_{1,2}=1.4$ Hz, H-1^{I}), 4.87–4.72 (m, 2 H, CH_2═CH—CH_2—), 4.70-4.66 (dd, 1 H, J = 2.6 Hz, J = 12.1 Hz), 4.61–4.57 (m, 2 H), 4.52–4.48 (dd, 1 H), 4.35–4.26 (m, 3 H), 3.89–3.86 (dd, 1 H), 3.76–3.59 (m, 2 H, CH_2═CH—CH_2—), 3.42 (s, 3 H, CH_3O); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.26, 166.26, 165.78, 165.71, 165.22, 165.00 (6 PhCO), 133.85, 133.71, 133.64, 133.23, 133.14, 133.14, 132.92, 129.98, 129.89, 129.81, 129.66, 129.47, 129.02, 128.81, 128.65, 128.51, 128.41, 128.38, 128.34, 117.57 (*C*H_2═CH—CH_2—), 99.67, 98.69 (C-1), 75.47, 73.81, 71.69, 70.54, 69.86, 68.85, 68.85, 68.75, 67.86, 63.12, 62.99 (C-2, 3, 4, 5, 6, CH_2═CH—*C*H_2—), 55.52 (CH_3O).

Anal. Calcd for $C_{58}H_{52}O_{17}$: C, 68.24; H, 5.10. Found: C, 68.30; H, 5.07.

Methyl 2,4,6-Tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (18). To a solution of **17** (4.34 g, 4.3 mmol) in anhyd CH_3OH (80 mL) was added $PdCl_2$ (0.4 g), and the mixture was stirred at 40°C for 3 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was filtered, and the filtrate was concentrated. The residue was purified on a silica-gel column with 2:1 petroleum ether–EtOAc as the eluent to give **18** as a syrup (3.75 g, 90%); $[\alpha]_D$ −27.4° (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18–7.28 (m, 30 H, Ph*H*), 5.97 (dd, 1 H, $J_{3,4}=J_{4,5}=10.0$ Hz, H-4^{II}), 5.65 (dd, 1 H, $J_{1,2}=1.2$ Hz, $J_{2,3}=3.1$ Hz, H-2^{II}), 5.59 (dd, 1 H, $J_{3,4}=J_{4,5}=9.7$ Hz, H-4^{I}), 5.27 (d, 1 H, $J_{1,2}=1.2$ Hz, H-1^{II}), 5.07 (dd, 1 H, $J_{1,2}=1.4$ Hz, $J_{2,3}=3.1$ Hz, H-2^{I}), 4.94 (d, 1 H, $J_{1,2}=1.4$ Hz, H-1^{I}), 4.71–4.67 (dd, 1 H, J = 2.5 Hz, J = 12.1 Hz), 4.61–4.57 (m, 2 H), 4.48–4.44 (dd, 1 H, J = 4.5 Hz, J = 12.2 Hz), 4.40–4.34 (m, 2 H), 4.27–4.24 (m, 1 H), 4.19–4.16 (dd, 1 H, J = 3.2 Hz, J = 9.8 Hz), 3.42 (s, 3 H, CH_3O), 2.40 (br, 1 H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.39, 166.14, 166.06, 165.73, 165.60, 165.07 (6 Ph*C*O), 133.60, 133.41, 133.25, 132.98, 132.87, 129.91, 129.89, 129.83, 129.76, 129.69, 129.62, 129.27, 129.08, 128.97, 128.73, 128.46, 128.37, 128.32, 128.28 (6 Ph), 99.41, 98.52 (C-1), 75.79 (C-3), 72.33, 71.71, 69.78, 69.24, 68.72, 68.55, 68.40, 62.99, 62.75 (C-2,3,4,5,6), 55.39 (CH_3O).

Anal. Calcd for $C_{55}H_{48}O_{17}$: C, 67.35; H, 4.90, Found: C, 67.30; H, 4.98.

***p*-Methoxyphenyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (19).** The disaccharide donor **9** (1.21 g, 1.0 mmol) and the disaccharide acceptor **11** (1.07 g, 1.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (30 mL). TMSOTf (20 μL, 0.1 equiv) was added dropwise at −25°C with N_2 protection. The

reaction mixture was stirred for 3 h, during which time the temperature was gradually warmed to ambient temperature. Then the mixture was neutralized with triethylamine, concentrated and purified by flash chromatography (2:1 petroleum ether–EtOAc) to afford **19** (1.70 g, 80%) as a syrup; $[\alpha]_D - 45.5°$ (*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.23–7.26 (m, 65 H, PhH), 7.03 (d, 2 H, J = 9.2 Hz, *p*-CH_3O—PhH), 6.78 (d, 2 H, J = 9.2 Hz, *p*-CH_3O—PhH), 6.05 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4^{IV}), 5.97–5.90 (m, 4 H, H-4^{III}, H-4^{II}, H-4^{I}, H-2^{IV}), 5.70 (d, 1 H, $J_{1,2} = 1.7$ Hz, H-1^{IV}), 5.57 (dd, 1 H, $J_{2,3} = 3.1$ Hz, $J_{3,4} = 9.8$ Hz, H-3^{IV}), 5.44 (d, 1 H, $J_{1,2} = 1.4$ Hz, H-1^{III}), 5.34 (m, 1 H, H-2^{III}), 5.19 (m, 2 H, H-2^{II}, H-2^{I}), 4.97 (br, 1 H, H-1^{II}), 4.93 (br, 1 H, H-1^{I}), 4.82 (dd, 1 H, $J_{2,3} = 3.3$ Hz, $J_{3,4} = 9.7$ Hz, H-3^{III}), 4.64 (m, 1 H), 4.56 (m, 1 H), 4.51–4.49 (m, 2 H), 4.42–4.38 (m, 2 H), 4.33–4.29 (m, 2 H), 4.11–3.96 (m, 6 H), 3.76 (s, 3 H, CH_3O); ^{13}C NMR (100MHz, $CDCl_3$): δ 166.18, 166.18, 165.94, 165.94, 165.82, 165.82, 165.53, 165.22, 165.17, 165.06, 165.06, 164.74, 164.65 (13 PhCO), 155.54, 149.68 (CH_3O—C_6H_4—O—), 133.93, 133.68, 133.63, 133.59, 133.47, 133.40, 133.20, 133.13, 132.98, 132.92, 130.15, 130.08, 130.02, 129.97, 129.87, 129.84, 129.76, 129.67, 129.28, 129.06, 128.98, 128.93, 128.87, 128.63, 128.57, 128.46, 128.26, 128.18 (Ph), 118.03, 114.76 (CH_3O—C_6H_4—O—), 99.37, 99.31, 99.04, 96.59 (4 C-1), 76.92, 76.78, 76.53 (3 C-3), 71.63, 71.50, 71.50, 70.19, 69.93, 69.56, 69.50, 69.45, 69.26, 68.26, 67.43, 67.13, 66.16, 63.06, 62.56, 62.24, 62.24 (C-2, 3, 4, 5, 6), 55.67 (CH_3O).

Anal. Calcd for $C_{122}H_{100}O_{35}$: C, 68.93; H, 4.71, Found: C, 68.79; H, 4.73.

2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranose (20). To a solution of **19** (2.12 g, 1.0 mmol) in 4:1 CH_3CN—H_2O (100 mL) was added CAN (2.19 g, 4.0 mmol), and the mixture was stirred at rt for 1 h, at the end of which time TLC (1.5:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was extracted with EtOAc, and washed with satd aq $NaHCO_3$. The organic layer was concentrated under reduced pressure, and purified by column chromatography (1.5:1 petroleum ether–EtOAc) to afford **20** as a syrup (1.51 g, 75%); $[\alpha]_D - 51.7°$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.21–7.16 (m, 65 H, PhH), 6.65 (br, 1 H, OH), 6.03 (dd, 1 H, $J_{3,4} = J_{4,5} =$ 10.0 Hz, H-4^{IV}), 5.89 (m, 3 H, H-4^{III}, H-4^{II}, H-4^{I}), 5.71 (br, 1 H, H-2^{IV}), 5.52 (dd,1 H, $J_{2,3} = 3.1$ Hz, H-3^{IV}), 5.48 (s, 1 H, H-1^{IV}), 5.30 (s, 1 H, H-1^{III}), 5.28 (m, 1 H, H-2^{III}), 5.15 (m, 2 H, H-2^{II}, H-2^{I}), 4.92 (s, 1 H, H-1^{II}), 4.87 (s, 1 H, H-1^{I}), 4.74–4.67 (m, 2 H), 4.55–4.53 (m, 2 H), 4.41–4.32 (m, 3 H), 4.27–4.24 (m, 2 H), 4.06–3.91 (m, 6 H).

Anal. Calcd for $C_{115}H_{94}O_{34}$: C, 68.38; H, 4.66, Found: C, 68.45; H, 4.64.

2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (21). A mixture of **20** (1.51 g, 0.75 mmol), trichloroacetonitrile (0.42 mL), and anhyd potassium carbonate (1.51 g) in dry dichloromethane (20 mL) was stirred overnight and then filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (1.5:1 petroleum ether–EtOAc) to give **21** (1.30 g, 80%) as a syrup; $[\alpha]_D - 3.9°$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.80 (br, 1 H, NH), 8.20–7.17 (m, 65 H, PhH), 6.55 (s, 1 H, H-1^{I}), 6.11 (dd, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4^{IV}), 5.98–5.85 (m, 4 H, H-4^{III}, H-4^{II}, H-4^{I}, H-2^{IV}), 5.53 (dd, 1 H, $J_{2,3} = 3.1$ Hz, $J_{3,4} = 10.0$ Hz, H-3^{IV}), 5.35

(d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1^{IV}), 5.31 (m, 1 H, H-2^{III}), 5.15 (m, 2 H, H-2^{II}, H-2^{I}), 4.96 (d, 1 H, $J_{1,2}$ = 1.4 Hz, H-1^{III}), 4.88 (d, 1 H, H-1^{II}), 4.71–4.63 (m, 2 H), 4.52–4.45 (m, 3 H), 4.37–4.33 (m, 2 H), 4.28–4.25 (m, 2 H), 4.06–3.91 (m, 6 H).

Anal. Calcd for $C_{117}H_{94}Cl_3NO_{34}$: C, 64.92; H, 4.35, Found: C, 64.63; H, 4.37.

Methyl 3-*O*-Allyl-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (22). The disaccharide donor **13** (1.15 g, 1.0 mmol) and the disaccharide acceptor **18** (0.98 g, 1.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (40 mL). TMSOTf (20 μL, 0.1 equiv) was added dropwise at −25°C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the temperature was gradually warmed to ambient temperature. Then the mixture was neutralized with triethylamine, concentrated and purified by flash chromatography (2:1 petroleum ether–EtOAc) to afford **22** as a foamy solid (1.57 g, 80%); $[\alpha]_D$ −42.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19–7.17 (m, 60 H, PhH), 5.98 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4^{IV}), 5.89 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4^{III}), 5.82 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4^{II}), 5.68 (m, 1 H, H-2^{IV}), 5.64 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.9 Hz, H-4^{I}), 5.36 (m, 1 H, CH_2 = C*H*—CH_2—), 5.29–5.27 (m, 2 H, H-2^{III}, H-1^{IV}), 5.13 (m, 1 H, H-2^{II}), 5.02 (m, 1 H, H-2^{I}), 4.96 (d, 1 H, $J_{1,2}$ = 1.5 Hz, H-1^{III}), 4.92 (d, 1 H, $J_{1,2}$ = 1.6 Hz, H-1^{II}), 4.80–4.66 (m, 3 H, CH_2=CH—CH_2—, H-1^{I}), 4.69 (m, 1 H), 4.61–4.55 (m, 2 H), 4.49–4.45 (dd, 1 H), 4.39–4.27 (m, 4 H), 4.21 (dd, 1 H), 3.99–3.94 (m, 4 H), 3.88 (m, 1 H, H-5), 3.79–3.72 (m, 2 H), 3.67–3.47 (m, 2 H, CH_2=CH—C*H*$_2$—), 3.44 (s, 3 H, CH_3O); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.27, 166.15, 165.93, 165.93, 165.85, 165.70, 165.56, 165.29, 165.08, 164.95, 164.90, 164.82 (12 PhCO), 133.87, 133.75, 133.57, 133.44, 133.17, 133.12, 133.01, 132.94, 132.90, 132.80, 130.00, 129.82, 129.78, 128.95, 128.79, 128.52, 128.48, 128.41, 128.25 (Ph), 117.29 (*C*H_2=CH—CH_2—), 99.33, 99.19, 99.00, 98.66 (4 C-1), 76.82, 76.44, 76.10, 73.95, 71.61, 71.33, 71.33, 70.36, 69.78, 69.32, 69.32, 68.76, 68.76, 68.47, 67.49, 67.49, 67.48, 63.05, 62.61, 62.47, 62.45 (C-2,3,4,5,6, CH_2=CH—*C*H_2—), 55.55 (CH_3O).

Anal. Calcd for $C_{112}H_{96}O_{33}$: C, 68.29; H, 4.88, Found: C, 68.42; H, 4.96.

Methyl 2,4,6-Tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (23). To a solution of **22** (1.57 g, 0.8 mmol) in anhyd CH_3OH (50 mL) was added $PdCl_2$ (0.16 g), and the mixture was stirred for 4 h at 40°C, at the end of which time TLC (1.5:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was filtered, and the filtrate was concentrated. The residue was purified on a silica-gel column with 1.5:1 petroleum ether–EtOAc as the eluent to give **23** as a syrup (1.23 g, 80%); $[\alpha]_D$ −32.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08–7.17 (m, 60 H, PhH), 5.97 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.9 Hz, H-4^{IV}), 5.87 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.9 Hz, H-4^{III}), 5.81 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.8 Hz, H-4^{II}), 5.66 (m, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 3.3 Hz, H-2^{IV}), 5.47 (dd, 1 H, $J_{3,4} = J_{4,5}$ = 9.9 Hz, H-4^{I}), 5.28 (d, 1 H, H-1^{IV}), 5.25 (dd, 1 H, H-2^{III}), 5.11 (dd, 1 H, H-2^{II}), 4.94 (d, 1 H, $J_{1,2}$ = 1.4 Hz, H-1^{III}), 4.89–4.88 (m, 2 H, H-1^{II}, H-2^{I}), 4.84 (d, 1 H, H-1^{I}), 4.68 (dd, 1 H, $J_{5,6}$ = 2.4 Hz, $J_{6,6'}$ = 12.1 Hz, H-6^{IV}), 4.57 (dd, 1 H, H-3^{IV}), 4.52 (dd, 1 H, $J_{5,6}$ = 2.3 Hz, $J_{6,6'}$ = 12.2 Hz,

H-6^{III}),4.46 (dd, 1 H, $J_{5,6'}$ = 4.6 Hz, $J_{6,6'}$ = 12.1 Hz, H-$6'^{IV}$), 4.36–4.20 (m, 5 H), 4.05–3.88 (m, 7 H), 3.43 (s, 3 H, CH_3O); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.35, 166.27, 166.15, 165.92, 165.85, 165.78, 165.72, 165.48, 165.27, 165.11, 165.08, 164.96 (12 PhCO), 133.74, 133.60, 133.54, 133.39, 133.30, 133.11, 132.94, 132.87, 130.14, 130.07, 129.99, 129.89, 129.85, 129.76, 129.32, 128.94, 128.84, 128.78, 128.55, 128.52, 128.40 (Ph), 99.16, 99.16, 98.95, 98.64 (4 C-1), 76.56, 76.11, 76.01, 72.32, 71.61, 71.47, 71.38, 69.76, 69.57, 69.34, 68.77, 68.76, 68.41, 68.40, 67.46, 67.43, 63.05, 62.28, 62.58, 62.28, 62.28 (C-2,3,4,5,6), 55.55 (CH_3O).

Anal. Calcd for $C_{109}H_{92}O_{33}$: C, 67.84; H, 4.77, Found: C, 67.61; H, 4.79.

Methyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (24). The disaccharide donor **9** (0.30 g, 0.25 mmol) and the tetrasaccharide acceptor **23** (0.48 g, 0.25 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (10 mL). TMSOTf (10 μL, 0.2 equiv) was added dropwise at −25°C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the temperature was gradually warmed to ambient temperature. Then the mixture was neutralized with triethylamine, concentrated and purified by flash chromatography (1.5:1 petroleum ether–EtOAc) to afford **24** (0.56 g, 75%) as a syrup; $[\alpha]_D$ −86.3° (*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.17–7.08 (m, 95 H, PhH), 5.96 (dd, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4^{VI}), 5.89–5.75 (m, 5 H, H-$4^{V, IV, III, II, I}$), 5.65 (dd, 1 H, $J_{1,2}$ = 1.8 Hz, $J_{2,3}$ = 3.2 Hz, H-2^{VI}), 5.50 (dd, 1 H, H-3^{VI}), 5.27 (d, 1 H, H-1^{VI}), 5.25 (m, 1 H, H-2^{V}), 5.12 (m, 2 H, H-$2^{IV, III}$), 5.07 (m, 2 H, H-2^{II}, H-2^{I}), 4.94 (d, 1 H, $J_{1,2}$ = 1.5 Hz, H-1^{V}), 4.88 (d, 1 H, $J_{1,2}$ = 1.7 Hz, H-1^{IV}), 4.82 (m, 3 H, H-$1^{III, II, I}$), 4.69 (dd, 1 H, $J_{5,6}$ = 2.5 Hz, $J_{6,6}$ = 12.1 Hz, H-6^{VI}), 4.59–4.53 (m, 2 H), 4.47–4.43 (dd, 1 H, $J_{5,6'}$ = 4.6 Hz, $J_{6,6'}$ = 12.1 Hz, H-$6'^{VI}$), 4.36–4.17 (m, 8 H), 4.02–3.81 (m, 11 H), 3.43 (s, 3 H, CH_3O); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.28, 166.17, 165.93, 165.87, 165.84, 165.81, 165.74, 165.68, 165.53, 165.34, 165.31, 165.06, 165.06, 164.99, 164.99, 164.94, 164.94, 164.70, 164.59 (19 PhCO), 133.73, 133.56, 133.41, 133.31, 133.25, 133.20, 133.15, 133.10, 133.05, 132.94, 132.84, 130.07, 129.98, 129.89, 129.80, 128.75, 129.72, 129.64, 129.25, 129.21, 129.16, 128.93, 128.80, 128.51, 128.42, 128.39, 128.32, 128.20, 128.12 (Ph), 99.22, 99.22, 98.96, 98.88, 98.85, 98.65 (6 C-1), 76.90, 76.83, 76.66, 76.46, 70.11, 69.76, 69.51, 69.36, 69.29, 69.22, 69.16, 68.75, 68.44, 67.48, 67.07, 66.09, 63.04, 62.60, 62.19 (C-2,3,4,5,6), 55.53 (CH_3O).

Anal. Calcd for $C_{170}H_{140}O_{50}$: C, 68.46; H, 4.70, Found: C, 68.22; H, 4.72.

Methyl α-D-Mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranoside (25). Compound **24** (0.45 g, 0.15 mmol) was dissolved in a satd solution of NH_3 in anhyd CH_3OH (20 mL). After one week at rt, the reaction mixture was concentrated, and the residue was purified by chromatography on Sephadex LH-20 (MeOH) to afford **25** as a syrup (0.14 g, 90%); $[\alpha]_D$ +84.9° (*c* 1.0, CH_3OH); ^1H NMR (400 MHz, D_2O): δ 5.14–5.10 (m, 5 H, H-$1^{VI, V, VI, III, II}$), 4.75 (s, 1 H, H-1^{I}), 4.24 (m, 4 H), 4.08–3.65 (m, 32 H), 3.42 (s, 3 H, CH_3O); ^{13}C NMR (100 MHz, D_2O): δ 104.72,

104.62, 104.62, 104.62, 104.62, 103.13 (C-1), 80.68, 80.58, 80.48, 80.30, 80.21, 75.95, 75.86, 75.80, 75.09, 72.75, 72.42, 72.06, 71.97, 69.27, 68.53, 68.46, 68.38, 63.43, 63.22 (C-2,3,4,5,6), 57.15 (CH_3O); $J_{C1-H1} = 170.0-171.9$ Hz; MALDI-TOF MS Calcd for $C_{37}H_{64}O_{31}$: [M] 1004.3, Found: [M + Na] 1027.8.

Methyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (26). The tetrasaccharide donor **21** (0.54 g, 0.25 mmol) and the tetrasaccharide acceptor **23** (0.48 g, 0.25 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (10 mL). TMSOTf (10 μL, 0.2 equiv) was added dropwise at −25°C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the temperature was gradually warmed to ambient temperature. Then the mixture was neutralized with triethylamine, concentrated and purified by flash chromatography (1.2:1 petroleum ether–EtOAc) to afford **26** (0.74 g, 75%); $[\alpha]_D - 49.4°$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16–7.05 (m, 125 H, PhH), 5.96–5.74 (m, 8 H, H-4$^{VIII, VII, VI, V, IV, III, II, I}$), 5.65 (m, 1 H, H-2^{VIII}), 5.49 (dd, 1 H, H-3^{VIII}), 5.26 (d, 1 H, $J_{1,2} = 1.4$ Hz, H-1^{VIII}), 5.24 (m, 1 H, H-2^{VII}), 5.11–5.04 (m, 5 H, H-2$^{VI, V, IV, III, II}$), 4.94 (d, 1 H, $J_{1,2} = 1.4$ Hz, H-1^{VII}), 4.87 (d, 1 H, $J_{1,2} = 1.6$ Hz, H-1^{VI}), 4.81–4.78 (m, 4 H, H-1$^{V, IV, III, II}$), 4.68 (dd, 1 H), 4.59–4.51 (m, 2 H), 4.45 (dd, 1 H), 4.36–4.16 (m, 11 H), 4.01–3.82 (m, 18 H), 3.43 (s, 3 H, CH_3O); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.28, 166.16, 165.93, 165.87, 165.83, 165.83, 165.79, 165.77, 165.73, 165.68, 165.52, 165.31, 165.31, 165.31, 165.31, 165.05, 165.05, 164.99, 164.97, 164.94, 164.94, 164.91, 164.91, 164.70, 164.57 (25 PhCO), 133.74, 133.58, 133.57, 133.53, 133.47, 133.42, 133.34, 133.30, 133.26, 133.23, 133.16, 133.13, 133.09, 133.03, 132.93, 132.86, 130.14, 130.11, 130.09, 129.98, 129.90, 129.89, 129.80, 129.76, 129.74, 129.25, 129.21, 129.15, 129.03, 128.92, 128.88, 128.79, 128.55, 128.51, 128.41, 128.39, 128.29, 128.20, 128.12 (Ph), 99.21, 99.21, 98.97, 98.89, 99.87, 99.87, 98.81, 98.65 (8 C-1), 76.46, 71.60, 71.44, 71.26, 70.11, 69.76, 69.51, 69.30, 69.22, 68.75, 68.44, 67.48, 67.11, 66.10, 63.02, 62.55, 62.18 (C-2,3,4,5,6), 55.55 (CH_3O).

Anal. Calcd for $C_{224}H_{184}O_{66}$: C, 68.43; H, 4.68, Found: C, 68.64; H, 4.76.

Methyl α-D-Mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranosyl-(1→3)-α-D-mannopyranoside (27). Compound **26** (0.59 g, 0.15 mmol) was dissolved in a satd solution of NH_3 in anhyd CH_3OH (30 mL). After a week at rt, the reaction mixture was concentrated, and the residue was purified by chromatography on Sephadex LH-20 (MeOH) to afford **27** as a syrup (0.18 g, 90%); $[\alpha]_D + 87.7°$ (*c* 1.0, CH_3OH); ^{1}H NMR (400 MHz, D_2O): δ 5.16–5.14 (m, 8 H, H-1$^{VIII, VII, VI, V, VI, III, II, I}$), 4.26 (s, 7 H), 4.10–3.69 (m, 41 H), 3.44 (s, 3 H, CH_3O); ^{13}C NMR (100 MHz, D_2O): δ 104.75, 104.75, 104.63, 104.63, 104.63, 104.63, 104.63, 104.63, 103.19 (8 C-1), 80.72, 80.61, 80.50, 75.97, 75.89, 75.82, 75.12, 72.78, 72.46, 72.09, 71.98, 69.30, 68.62, 68.56, 68.49, 68.41, 63.57, 63.45, 63.25 (C-2,3,4,5,6), 57.18 (CH_3O); MALDI-TOF MS Calcd for $C_{49}H_{84}O_{41}$: [M] 1328.4, Found: [M + Na] 1352.0.

ACKNOWLEDGMENTS

This work was supported by The Chinese Academy of Sciences (RCEES9904), The National Natural Science Foundation of China (Projects 30070185 and 39970864), and The Ministry of Science and Technology.

REFERENCES

1. Ogawa, T.; Yamamoto, H. Synthetic studies on cell surface glycans. Part XXXIII. Synthesis of a model linear mannohexaose for the backbone structure of fruit body polysaccharide of *Tremella fuciformis* and *Dictyophora indusiata* Fisch. Agric. Biol. Chem. **1985**, *49*, 475–482.
2. Cherniak, R.; Reiss, E.; Slodki, M.E.; Plattner, R.D.; Blumer, R.D. Structure and antigenic activity of the capsular polysaccharide from *Cryptococcus neoformans* serotype A. Mol. Immunol. **1980**, *17*, 1025–1031.
3. Saito, K.; Komae, A.; Kakuta, M.; Van Damme, E.J.M.; Peumans, W.J.; Goldstein, I.J.; Misaki, A. The α-mannose-binding lectin from leaves of the orchid twayblade (*Listera ovata*). Application to separation of α-D-mannans from α-D-glucans. Eur. J. Biochem. **1994**, *223*, 1064–1072.
4. Xiong, S.; Kong, F.; Yang, C. Improved synthesis of 1,3-anhydro-2,4-di-*O*-benzyl-β-L-rhamnopyranose and 1,3-anhydro-2,4,6-tri-*O*-benzyl-β-D-mannopyranose. Youji Huaxue **1994**, *14*, 280–285.
5. Ogawa, T.; Yamamoto, Y. Synthesis of a model, linear D-mannopentaose for the nonreducing-end sequence of the cell-surface D-mannan of *Escherichia coli*, *Candida albicans*, and *Saccharomyces cerevisiae*. Carbohydr. Res. **1985**, *137*, 79–87.
6. Schmidt, R.R. Anomeric-oxygen activation for glycoside synthesis: The trichloroacetimidate method. Adv. Carbohydr. Chem. Biochem. **1994**, *50*, 21–125.
7. Podlasek, C.A.; Wu, J.; Stripe, W.A.; Bondo, P.B.; Serianni, A.S. [^{13}C]-Enriched methyl aldopyranosides: Structural interpretations of $^{13}C-^{1}H$ spin coupling constants and ^{1}H chemical shifts. J. Am. Chem. Soc. **1995**, *117*, 8635–8644.
8. Mori, M.; Ito, Y.; Ogawa, T. A highly stereoselective and practical synthesis of cyclomannohexaose, cyclo{→4)-[α-D-Manp-(1→4)-]$_5$α-D-Manp-(1→}, a manno isomer of cyclomaltohexaose. Carbohydr. Res. **1989**, *192*, 131–146.
9. Yang, G.; Kong, F.; Zhou, S. Selective 3-*O*-allylation and benzylation of methyl D-manno-, L-rhamno-, and L-fucopyranoside. Carbohydr. Res. **1991**, *211*, 179–181.

Received January 21, 2002
Accepted May 21, 2002