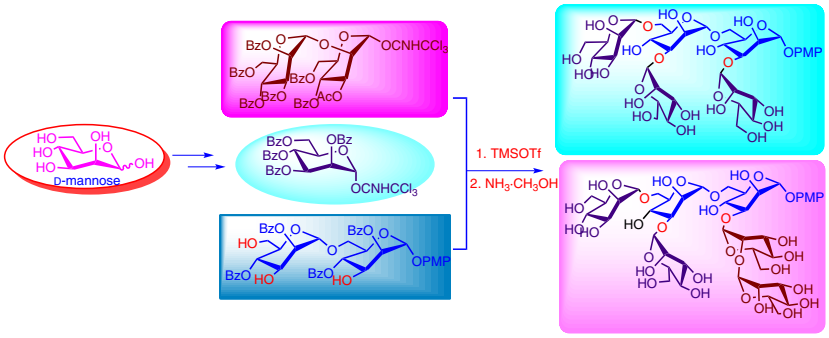
Synthesis R. Jiang et al. Paper

Efficient Synthesis of a High-Mannose-Type Pentasaccharide and Hexasaccharide Related to *N*-Glycans

Rui Jiang
Xiao-mei Liang
Shu-hui Jin*
Hui-zhe Lu
Yan-hong Dong
Dao-quan Wang
Jian-jun Zhang*

Department of Applied Chemistry, China Agricultural University, Beijing 100193, P. R. of China
shuhuij@cau.edu.cn
zhangjianjun@cau.edu.cn



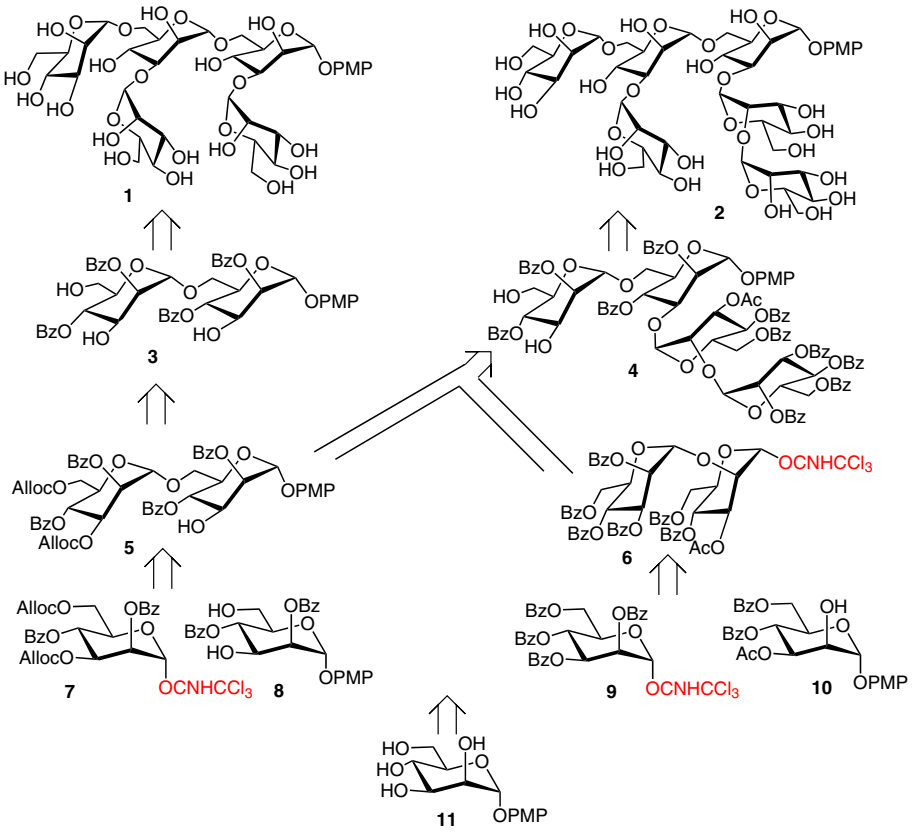
Received: 20.07.2015
Accepted after revision: 31.08.2015
Published online: 28.10.2015
DOI: 10.1055/s-0035-1560323; Art ID: ss-2015-f0446-op

Abstract Two high-mannose-type *N*-glycans, Man5 and Man6 oligosaccharides, were concisely synthesized from 4-methoxyphenyl α-D-mannopyranoside via 9 and 12 steps, and in 23% and 15% overall yields, respectively. The efficiency of the synthesis relies on the large-scale preparation of a key disaccharide intermediate, 4-methoxyphenyl 3,6-di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-2,4-di-*O*-benzoyl-α-D-mannopyranoside, with two hydroxyl groups partially masked by allyloxycarbonyl protection. The disaccharide was obtained in 84% yield by regioselective glycosylation of 4-methoxyphenyl 2,4-di-*O*-benzoyl-α-D-mannopyranoside with 3,6-di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate. The disaccharide could be easily transformed to a tetrasaccharide diol acceptor via condensation of 4-methoxyphenyl 3,6-di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-2,4-di-*O*-benzoyl-α-D-mannopyranoside with a disaccharide donor followed by removal of the two allyloxycarbonyl groups in the resultant tetrasaccharide, or be converted into a triol acceptor by direct deallyloxycarbonylation. Glycosylation of the triol or diol acceptor with 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate provided the desired protected pentasaccharide and hexasaccharide in one step in 64% and 67% yields, respectively. Finally, the target compounds, pentasaccharide and hexasaccharide, were obtained after deprotection. The structures of target compounds and intermediates were characterized by ^{1}H NMR, ^{13}C NMR, and HRMS.

Key words synthesis, oligosaccharides, mannose, *N*-glycan

HIV-1 is reported to have two envelope glycoproteins, the outer and inner envelope glycoproteins, that form trimeric complexes on the viral surface. The outer envelope glycoprotein gp120 has 24 conserved N-glycosylation sites, 13 of which are complex-type *N*-glycans, and the rest are high-mannose-type and/or hybrid-type *N*-glycans. *N*-Glycans play a vital role in many basic biological processes such as viral infection, cell differentiation, protein transportations, and tumor migration.[1] Studies have revealed that the high mannose oligosaccharides in *N*-glycans are essential for human CD2 adhesion function[2] and related to HIV infection.[3] As a highly contagious and deadly disease, HIV/AIDS has become one of the most serious health issues of modern times. The most effective way to prevent disease global HIV epidemic depends on the development of an effective anti-HIV vaccine.[4] Researchers believe that one of the most promising targets for immunogen design is the carbohydrate moieties on HIV-1 envelop protein gp120,[5] which was confirmed by a potent neutralizing human monoclonal antibody 2G12.[6] In order for researchers to study the recognition mechanism in detail, chemically synthesized oligosaccharides are required because such homogeneous oligosaccharide samples can be obtained in only very small amounts from natural sources.

Several papers have reported for the synthesis of high-mannose-type oligosaccharides existing in *N*-glycans.[7] However, the strategies involved in these reports are not suitable for the large-scale preparation of the target pentasaccharide and hexasaccharide due to complex protection–deprotection steps and low overall yields. Therefore, more efficient and practical methods are highly desired for the synthesis of mannose oligosaccharides in *N*-glycans. In this communication, we wish to present a novel approach for the fast and efficient synthesis of the pentasaccharide **1** and hexasaccharide **2** (Scheme 1), using disaccharide triol acceptor **3** and tetrasaccharide diol acceptor **4** as the key intermediates, respectively. We envisioned that mannosylation of the three hydroxyl groups in **3** and two hydroxyl groups in **4** would provide the protected form of pentasaccharide **1** and hexasaccharide **2**, respectively, in a single coupling reaction, and the synthetic procedure would thus be greatly simplified. The disaccharide **3** could be produced from two suitably protected monosaccharide building blocks **7** and **8**, using the allyloxycarbonyl function as an orthogonal protecting group.[8,9] Similarly, the tetrasaccharide

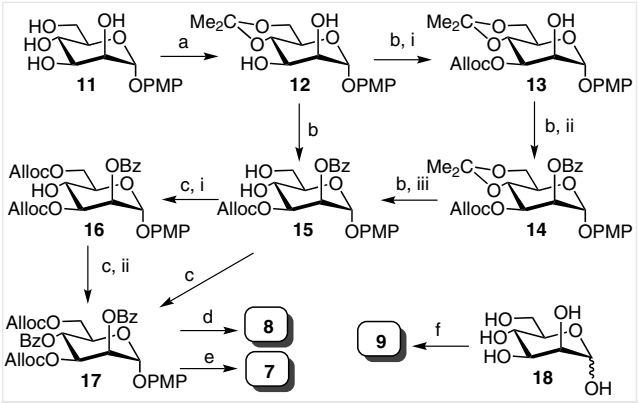


Scheme 1 Structure of the target pentasaccharide **1**, hexasaccharide **2**, and the building blocks **7**–**10** used for its synthesis

4 could be obtained from two suitably protected monosaccharide building blocks **9** and **10** and one protected disaccharide building block **5**, which also use the allyloxycarbonyl group for orthogonal protection.[8,9]

For the synthesis of monosaccharide building blocks, 4-methoxyphenyl α-D-mannopyranoside (**11**)[10] was first transformed into 4,6-*O*-isopropylidene-α-D-mannopyranoside **12** with 2-methoxypropene in *N*,*N*-dimethylformamide in the presence of catalytic amounts of 4-toluenesulfonic acid monohydrate.[11] Regioselective allyloxycarbonylation of **12** in pyridine gave the 3-OH protected derivative **13** exclusively in 90% yield (Scheme 2). The presence of the *O*-allyloxycarbonyl group at C3 was confirmed by the downfield shift of the H3 signal in the ^{1}H NMR spectrum of **13** (δ = 5.22) compared with the data for H3 signal of compound **12** (δ = 4.12). It was found that keeping the reaction temperature below –10 °C was necessary to ensure the desired regioselectivity. Benzoylation of **13** with benzoyl chloride in pyridine provided **14**, which was then transformed to the key intermediate **15** after removal of the isopropylidene protecting group in 70% acetic acid. It should be noted that these three steps can be carried out successively without chromatographic purification for the first two steps, making the preparation of **15** on large scale possible with high yield (88%). Subsequently, regioselective allyloxycarbonylation of the C6-OH of compound **15** with allyloxycarbonyl chloride in pyridine provided **16** (91%), which was transformed to **17** after benzoylation. Significantly, compound **17** could be obtained in a one-pot reaction by adding allyloxycarbonyl chloride and benzoyl chloride to the reaction mixture successively, thus greatly simplifying the preparation. Finally, according to our previously reported method,[9] deallyloxycarbonylation of **17** with palladium catalyst [$Pd(PPh_3)_4$, $NaBH_4$, NH_4OAc, THF–MeOH] gave the monosaccharide acceptor **8** in 88% yields. On the other hand, cleavage of the 4-methoxyphenyl group of **17** with cerium(IV) ammonium nitrate, followed by trichloroacetimidation,[12] provided the monosaccharide donor **7** in good overall yield (87%). Compound **9** was obtained in 82% overall yield for three steps according to the reported method.[13]

Another key intermediate **10** was prepared through the route shown in Scheme 3. 4-Methoxyphenyl α-D-mannopyranoside (**11**)[10] was first transformed into 2,3-*O*-isopropylidene-α-D-mannopyranoside **19** with 2-methoxypropene in *N*,*N*-dimethylformamide in the presence of catalytic amounts of 4-toluenesulfonic acid monohydrate according to our previous reported method.[14] Then benzoylation of **19** with benzoyl chloride in pyridine followed by removal of the isopropylidene protecting group in 70% ace-



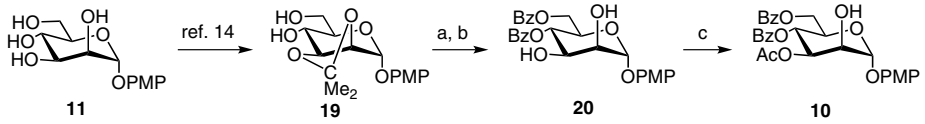
Scheme 2 Synthesis of building blocks **7**–**9**. *Reagents and conditions*: (a) 2-methoxypropene, DMF, TsOH·H_2O, r.t., 2 h, 95%; (b) (i) AllocCl, pyridine, –10 °C to r.t., 2 h, 90%; (ii) BzCl, pyridine, CH_2Cl_2, –10 °C to r.t., 3 h, 92%; (iii) 70% AcOH, 70 °C, 3 h, 94%; overall yield of the one-pot preparation of **15** from **12**: 88%; (c) (i) AllocCl, pyridine, CH_2Cl_2, –10 °C to r.t., 2 h, 91%; (ii) BzCl, pyridine, –10 °C to r.t., 3 h, 96%; overall yield of the one-pot preparation of **17** from **15**: 86%; (d) NH_4OAc, $Pd(PPh_3)_4$, $NaBH_4$, MeOH–THF, –5 °C, 5 min, 88%; (e) (i) CAN, MeCN–H_2O (4:1), 30 °C, 20 min, (ii) Cl_3CCN, DBU, CH_2Cl_2, r.t., 0.5 h, 87% for 2 steps; (f) (i) BzCl, pyridine, –10 °C to 0 °C, 4 h, (ii) MeOH–NH_3, MeOH–THF, 1 h, (iii) Cl_3CCN, DBU, CH_2Cl_2, 0 °C, 2 h, 82% for 3 steps.

tic acid provided the intermediate **20**. Again, we were able to perform these three steps successively without chromatographic purification for the first two steps, allowing **20** to be prepared on a large scale with high yield (84%). Subsequently, regioselective acetylation of the C3-OH of compound **20** with acetyl chloride in pyridine provided **10** in 88% yield.

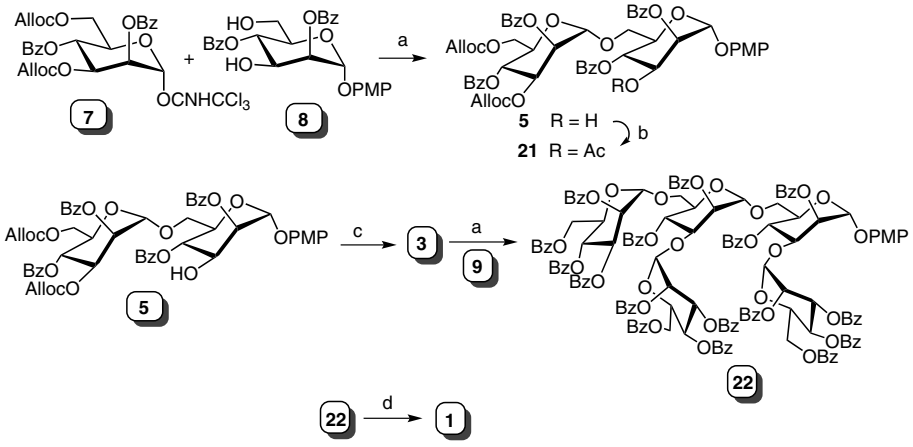
With the monosaccharide synthons **7**, **8**, **9**, and **10** in hand, the pentasaccharide target compound was prepared efficiently as outlined in Scheme 4. The coupling of compounds **7** and **8** in dichloromethane at –20 °C promoted by trimethylsilyl trifluoromethanesulfonate[12] resulted in expected regio- and stereoselective products, giving exclusively α-1→6-linked mannose disaccharide **5** in 84% yield. The configuration of the glycosyl bond in **5** was deduced from the corresponding coupling constants. The regioselectivity of the coupling reaction was confirmed by acetylation of **5** to give **21** (92%), as the ^{1}H NMR spectrum of **21** showed a newly emerged downfield H3 signal. Subsequent removal of the two Alloc groups in compound **5** with tetrakis(triphenylphosphine)palladium(0) provided the key triol acceptor **3** in high yield (84%). Finally, the fully protected pentasaccharide **22** was smoothly obtained in 64% yield by the condensation of triol **3** with 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (**9**).[13] To ensure complete conversion of the triol **3**, excess monosaccharide donor **9** (4–4.5 equiv) was added in the coupling reaction. The ^{1}H NMR spectrum of **22** showed 4-methoxyphenyl signals (δ = 7.04–6.72) and five H1 signals (δ = 5.75, 5.41, 5.36, 5.17, and 4.78), which are characteristic of the structure of the pentasaccharide **22**. Deprotection of **22** in ammonia-saturated methanol gave the title 4-methoxyphenyl α-D-hexamannoside **1**, which precipitated from the solution phase as a white solid when dry acetone was added to the reaction mixture at the end of the deprotection step.

Similarly, the target hexasaccharide was prepared efficiently as outlined in Scheme 5. First of all, the coupling of compounds **9** and **10** in dichloromethane at –20 °C promoted by trimethylsilyl trifluoromethanesulfonate[12] resulted in α-1→2-linked mannose disaccharide **23** in 92% yield. Removal of the 4-methoxyphenyl group of **23** with cerium(IV) ammonium nitrate, and activation with trichloroacetonitrile in the presence of DBU gave the disaccharide donor **6** in good overall yield (87%). Condensation of **6** with the acceptor **5** afforded the (1→3)-linked tetrasaccharide **24** (84%). Subsequent removal of the two Alloc groups in compound **24** with tetrakis(triphenylphosphine)palladium(0) provided the key diol acceptor **4** in high yield (82%). Finally, the fully protected hexasaccharide **25** was smoothly obtained in 67% yield by the condensation of diol **4** with 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (**9**). Again, to ensure complete conversion of the diol **4**, excess **9** (4–4.5 equiv) was used in the coupling reaction. The ^{1}H NMR spectrum of **25** showed one acetyl signal (δ = 1.91), 4-methoxyphenyl signals (δ = 7.04–6.72), and six H1 signals (δ = 5.72, 5.46, 5.33, 5.16, 4.79, and 4.60), which are characteristic of the structure of the hexasaccharide **25**. Deprotection of **25** in ammonia-saturated methanol gave the title 4-methoxyphenyl α-D-hexamannoside **2**, which was precipitated from the reaction mixture as a white solid by adding dry acetone at the end of the deprotection step.

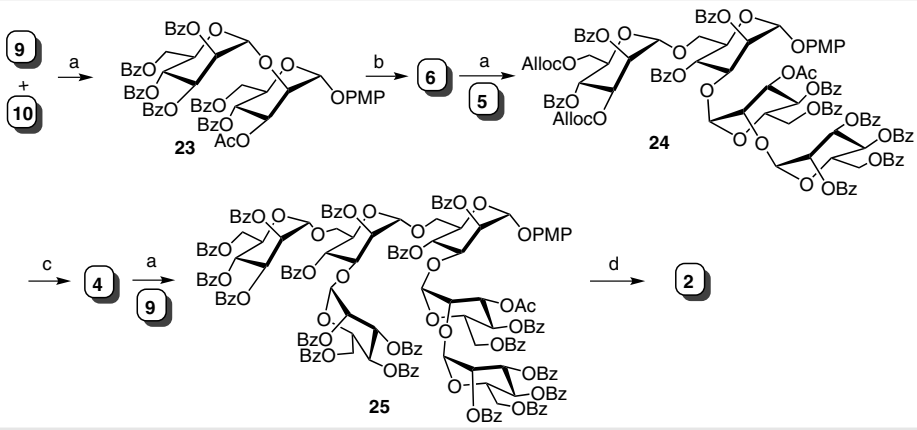
In summary, we have successfully developed a highly efficient strategy for the preparation of high-mannose-type pentasaccharide and hexasaccharide related to *N*-glycans. It is noteworthy that the overall yield of the whole synthesis is 23% and 15% for **1** and **2**, respectively, from 4-methoxyphenyl α-D-mannopyranoside. The reported synthetic procedure is especially suitable for the large-scale preparation of the target saccharides and we are currently working on the application of this method to the synthesis of more



Scheme 3 Synthesis of building block **10**. *Reagents and conditions*: (a) BzCl, pyridine, CH_2Cl_2, –10 °C to r.t., 2 h; (b) 70% AcOH, 70 °C, 3 h, 91% for 2 steps; (c) AcCl, pyridine, CH_2Cl_2, –10 °C to r.t., 2 h, 88%.



Scheme 4 Synthesis of target pentasaccharide **1**. *Reagents and conditions*: (a) TMSOTf, CH_2Cl_2, 4 Å MS, –20 °C to r.t., 0.5 h, 84% for **5**, 64% for **22**; (b) AcCl, pyridine, –10 °C to r.t., 1 h, 92%; (c) NH_4OAc, $Pd(PPh_3)_4$, $NaBH_4$, MeOH–THF, –10 °C, 5 min, 84%; (d) (i) MeOH–NH_3, r.t., 120 h, (ii) warm acetone, 82%.



Scheme 5 Synthesis of target hexasaccharide **2**. *Reagents and conditions*: (a) TMSOTf, CH_2Cl_2, 4 Å MS, –20 °C to r.t., 0.5 h, 92% for **23**, 84% for **24**, 67% for **25**; (b) (i) CAN, MeCN–H_2O (4:1), 30 °C, 20 min, (ii) Cl_3CCN, DBU, CH_2Cl_2, r.t., 0.5 h, 87% for 2 steps; (c) NH_4OAc, $Pd(PPh_3)_4$, $NaBH_4$, MeOH–THF, –10 °C, 5 min, 82%; (d) (i) MeOH–NH_3, r.t., 120 h, (ii) warm acetone, 78%.

complex Man7, Man8, and Man9 oligosaccharides. The bioactivity of **1** and **2** is also being investigated and the results will be reported in due course.

Optical rotations were determined with a Perkin-Elmer model 241-MC automatic polarimeter for solutions in a 1-dm, jacketed cell. ^1H and ^{13}C NMR spectra were recorded with Bruker DPX300 and Bruker Avance600 spectrometers in $CDCl_3$ or D_2O solutions; internal references: TMS (δ = 0.000 for ^1H), $CDCl_3$ (δ = 77.00 for ^{13}C), HOD (δ = 4.700 for ^1H). ^1H NMR signals of some compounds were assigned with the aid of COSY. The following designations are used: H_{mp} = H aryl of the 4-methoxyphenyl group, H_{Bz} = H aryl of the benzoyl group. HRMS was performed by Peking University. TLC was performed on silica gel HF with detection by charring with 30% (v/v) H_2SO_4 in MeOH or by UV detection. Column chromatography was conducted by elution of a column of silica gel (200–300 mesh) with EtOAc–petroleum ether (PE, bp 60–90 °C). Solutions were concentrated at <60 °C under reduced pressure.

4-Methoxyphenyl 4,6-*O*-Isopropylidene-α-D-mannopyranoside (12)

To a solution of 4-methoxyphenyl α-D-mannopyranoside (**11**, 5.72 g, 20 mmol) in anhyd DMF (40 mL) was added $TsOH·H_2O$ (38 mg, 0.2 mmol) and 2-methoxypropene (2.2 mL, 22 mmol) under N_2. The mixture was stirred at r.t. for 2 h; TLC (PE–EtOAc, 2:1) indicated completion. The mixture was poured into crushed ice and the product precipitated from the mixture to give **12** as a white solid; yield: 6.20 g (95%); $[\alpha]_D$ +122 (*c* 1, $CHCl_3$).

^1H NMR (300 MHz, $CDCl_3$): δ = 6.99–6.94 (m, 2 H, H_{mp}), 6.85–6.80 (m, 2 H, H_{mp}), 5.46 (d, $J_{1,2}$ = 1.4 Hz, 1 H, H1), 4.22 (m, 1 H, H2), 4.12 (dd, $J_{2,3}$ = 3.3 Hz, $J_{3,4}$ = 9.4 Hz, 1 H, H3), 4.04–3.98 (m, 1 H), 3.82–3.78 (m, 3 H), 3.77 (s, 3 H, OMe), 2.87, 2.81 (br s, 2 H, OH), 1.53, 1.42 (2 s, 6 H, Me_2C).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.05, 149.84, 117.68, 114.63, 100.11, 99.12, 71.22, 70.99, 68.88, 64.61, 61.96, 55.58, 29.08, 19.22.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{23}O_7$: 327.14383; found: 327.14377.

4-Methoxyphenyl 3-*O*-Allyloxycarbonyl-4,6-*O*-isopropylidene-α-D-mannopyranoside (13)

Compound **12** (3.26 g, 10.0 mmol) was dissolved in pyridine (20 mL), then allyl chloroformate (1.1 mL, 10.5 mmol) in pyridine (10 mL) was added dropwise to the solution over 30 min at –10 °C. The temperature was slowly raised to r.t. and the mixture was stirred for 2 h; TLC (PE–EtOAc, 3:1) indicated completion. The mixture was diluted with CH_2Cl_2 (100 mL), washed with ice-water, 1 M HCl, and water, and dried (Na_2SO_4). The solution was concentrated, and purification of the residue by column chromatography (silica gel, PE–EtOAc, 4:1) gave **13** as a white solid; yield: 3.7 g (90%); $[\alpha]_D$ +88 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): 6.99–6.95 (m, 2 H, H_{mp}), 6.83–6.80 (m, 2 H, H_{mp}), 6.01–5.91 (m, 1 H, CH_2CHCH_2O), 5.45 (d, $J_{1,2}$ = 1.6 Hz, 1 H, H1), 5.43–5.28 (m, 2 H, CH_2CHCH_2O), 5.22 (dd, $J_{2,3}$ = 1.8 Hz, $J_{3,4}$ = 10.0 Hz, 1 H, H3), 4.68 (dt, 2 H, CH_2CHCH_2O), 4.38 (m, 1 H, H2), 4.24 (t, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, 1 H, H4), 3.91–3.78 (m, 3 H, H5, 2 H6), 3.76 (s, 3 H, OCH_3), 2.56 (d, *J* = 3.3 Hz, 1 H, OH), 1.50, 1.39 (2 s, 6 H, CMe_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.99, 153.91, 149.60, 131.12, 119.00, 117.55, 114.54, 100.00, 99.05, 74.84, 69.21, 68.70, 68.35, 65.14, 61.88, 55.46, 28.91, 18.99.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{27}O_9$: 411.16496; found: 411.16425.

4-Methoxyphenyl 3-*O*-Allyloxycarbonyl-2-*O*-benzoyl-4,6-*O*-isopropylidene-α-D-mannopyranoside (14)

Compound **13** (4.10 g, 10.0 mmol) was dissolved in anhyd CH_2Cl_2 (50 mL) containing pyridine (3.2 mL, 40.0 mmol), then under a N_2 atmosphere, BzCl (1.7 mL, 15.0 mmol) in anhyd CH_2Cl_2 (10 mL) was added dropwise to the solution over 30 min at –10 °C. The temperature was slowly raised to r.t. and the mixture was stirred for 3 h; TLC (PE–EtOAc, 3:1) indicated completion. The mixture was diluted with CH_2Cl_2 (100 mL), washed with water, 1 M HCl, and water, and dried (Na_2SO_4). The solution was concentrated, and purification of the residue by column chromatography (silica gel, PE–EtOAc, 5:1) gave **14** as a foamy solid; yield: 4.73 g (92%); $[\alpha]_D$ +102 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09–8.03 (m, 2 H, H_{Bz}), 7.60–7.45 (m, 3 H, H_{Bz}), 7.02–6.99 (m, 2 H, H_{mp}), 6.84–6.81 (m, 2 H, H_{mp}), 5.96–5.85 (m, 1 H, CH_2CHCH_2O), 5.80 (q, 1 H, H2), 5.51 (d, $J_{1,2}$ = 1.6 Hz, 1 H, H1), 5.41–5.29 (m, 2 H, H3, CH_2CHCH_2O), 5.25 (dq, 1 H, CH_2CHCH_2O), 4.67–4.63 (m, 2 H, CH_2CHCH_2O), 4.31 (t, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, 1 H, H4), 4.04–3.98 (m, 1 H, H5), 3.93–3.85 (m, 2 H, 2 H6), 3.75 (s, 3 H, OCH_3), 1.56, 1.42 (2 s, 6 H, CMe_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.44, 155.36, 15.94, 149.69, 133.47, 131.37, 129.86, 128.47, 118.77, 117.88, 114.65, 100.19, 97.59, 72.68, 70.31, 69.09, 68.76, 65.35, 62.04, 55.55, 29.00, 19.11.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{31}O_{10}$: 515.19117; found: 515.19019.

4-Methoxyphenyl 3-*O*-Allyloxycarbonyl-2-*O*-benzoyl-α-D-mannopyranoside (15) from 14

Compound **14** (6.2 g, 12.0 mmol) was dissolved in 70% AcOH (200 mL) and stirred for 3 h at 70 °C; TLC (PE–EtOAc, 2:1) indicated completion. The mixture was concentrated under reduced pressure and then co-evaporated with toluene (2 × 40 mL). The residue was passed through a short silica gel column (PE–EtOAc, 3:1) to give **15** (5.4 g, 94%) as a white solid.

4-Methoxyphenyl 3-*O*-Allyloxycarbonyl-2-*O*-benzoyl-α-D-mannopyranoside (15) from 12

Compound **12** (3.26 g, 10.0 mmol) was dissolved in pyridine (20 mL), then allyl chloroformate (1.11 mL, 10.5 mmol) was added dropwise to the solution over 30 min at –10 °C. The temperature was slowly raised to r.t. and the mixture was stirred for 2 h; TLC (PE–EtOAc, 2:1) indicated completion. The mixture was diluted with anhyd CH_2Cl_2 (50 mL), BzCl (1.7 mL, 15.0 mmol) in anhyd CH_2Cl_2 (10 mL) was added dropwise over 30 min at –10 °C. The temperature was slowly raised to r.t. and the mixture was stirred for 2 h; TLC (PE–EtOAc, 3:1) indicated completion. Then the mixture was diluted with CH_2Cl_2 (100 mL), washed with 1 M HCl, and the organic phase was concentrated to give the crude product, which was dissolved in 70% AcOH (200 mL) and stirred for 3 h at 70 °C. The mixture was concentrated under reduced pressure and then co-evaporated with toluene (2 × 40 mL). The residue was passed through a short silica gel column (PE–EtOAc, 3:1) to give **15** as a white solid; yield: 4.2 g (88%); $[\alpha]_D$ +148 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06–8.00 (m, 2 H, H_{Bz}), 7.55–7.38 (m, 3 H, H_{Bz}), 7.01 (d, *J* = 9.0 Hz, 2 H, H_{mp}), 6.79 (d, *J* = 9.0 Hz, 2 H, H_{mp}), 5.95–5.82 (m, 1 H, CH_2CHCH_2O), 5.72 (m, 1 H, H2), 5.53 (d, $J_{1,2}$ = 1.4 Hz, 1 H, H1), 5.38–5.20 (m, 3 H, H3, CH_2CHCH_2O), 4.64–4.58 (m, 2 H, CH_2CHCH_2O), 4.35 (t, $J_{3,4}$ = $J_{4,5}$ = 9.7 Hz, 1 H, H4, 1 H), 3.98–3.82 (m, 3 H, H5, 2 H6), 3.74 (s, 3 H, OCH_3), 3.7–2.2 (br s, 2 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.42, 154.42, 149.76, 133.39, 131.14, 129.75, 128.39, 118.99, 117.86, 114.61, 96.82, 72.82, 69.90, 68.88, 68.44, 65.41, 61.58, 55.48.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{27}O_{10}$: 475.15987; found: 475.15903.

4-Methoxyphenyl 3,6-Di-*O*-allyloxycarbonyl-2-*O*-benzoyl-α-D-mannopyranoside (16)

Compound **15** (4.74 g, 10.0 mmol) was dissolved in anhyd CH_2Cl_2 (20 mL) containing pyridine (3.2 mL, 40.0 mmol), then under N_2, allyl chloroformate (1.12 mL, 10.5 mmol) in anhyd CH_2Cl_2 (10 mL) was added dropwise to the solution over 30 min at –10 °C. The temperature was slowly raised to r.t. and the mixture stirred for 2 h; TLC (PE–EtOAc, 3:1) indicated completion. The mixture was diluted with CH_2Cl_2 (100 mL), washed with water and 1 M HCl, and dried (Na_2SO_4). The solution was concentrated, and purification of the residue by column chromatography (silica gel, PE–EtOAc, 4:1) gave **16** as a syrup; yield: 5.10 g (91%); $[\alpha]_D$ +66 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06–8.01 (m, 2 H, H_{Bz}), 7.57–7.39 (m, 3 H, H_{Bz}), 7.04 (d, *J* = 9.0 Hz, 2 H, H_{mp}), 6.79 (d, *J* = 9.0 Hz, 2 H, H_{mp}), 5.93–5.83 (m, 2 H, 2 CH_2CHCH_2O), 5.74 (m, 1 H, H2), 5.54 (s, 1 H, H1), 5.39–5.19 (m, 5 H, H3, 2 CH_2CHCH_2O), 4.61–4.43 (m, 6 H, 2 CH_2CHCH_2O, H4, H6), 4.28–4.20 (m, 1 H, H5), 4.10–4.06 (m, 1 H, H6), 3.72 (s, 3 H, OCH_3), 3.36 (br s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.27, 155.25, 155.13, 154.33, 149.80, 133.32, 131.31, 131.09, 129.81, 129.15, 128.34, 118.97, 118.69, 117.79, 114.56, 96.70, 75.45, 71.13, 69.64, 68.87, 68.52, 66.06, 65.26, 55.44.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{31}O_{12}$: 559.17468; found: 559.17433.

4-Methoxyphenyl 3,6-Di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-α-D-mannopyranoside (17) from 16

Compound **16** (4.82 g, 8.64 mmol) was dissolved in pyridine (30 mL), then BzCl (1.5 mL, 14.6 mmol) in pyridine (10 mL) was added dropwise to the solution over 30 min at –10 °C. The temperature was slowly raised to r.t. and the mixture was stirred for 3 h; TLC (PE–

EtOAc, 3:1) indicated completion. The mixture was diluted with CH_2Cl_2 (100 mL), washed with ice-water and 1 M HCl, and dried (Na_2SO_4). The solution was concentrated, and purification of the residue by column chromatography (silica gel, PE–EtOAc, 4:1) gave **17** (5.48 g, 96%) as a foamy solid.

4-Methoxyphenyl 3,6-Di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-α-D-mannopyranoside (17) from 15

Compound **15** (5.7 g, 12.0 mmol) was dissolved in anhyd CH_2Cl_2 (40 mL) containing pyridine (3.9 mL, 48.0 mmol), then under N_2, allyl chloroformate (1.32 mL, 12.6 mmol) in anhyd CH_2Cl_2 (10 mL) was added dropwise to the solution over 30 min at –10 °C. The temperature was slowly raised to r.t. and the mixture was stirred for 2 h; TLC (PE–EtOAc, 3:1) indicated completion. Then BzCl (2.10 mL, 18 mmol) in pyridine (30 mL) was added dropwise to the solution over 30 min at 0 °C. The temperature was slowly raised to r.t. and the mixture was stirred for 4 h; TLC (PE–EtOAc, 4:1) indicated completion. The mixture was diluted with CH_2Cl_2 (100 mL), washed with ice-water, 1 M HCl, and water, and dried (Na_2SO_4). The solution was concentrated, and purification of the residue by column chromatography (silica gel, PE–EtOAc, 4:1) gave **17** as a foamy solid; yield: 6.84 g (86%); $[\alpha]_D$ +42 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14–8.12 (m, 2 H, H_{Bz}), 8.05–8.02 (m, 2 H, H_{Bz}), 7.58–7.56 (m, 2 H, H_{Bz}), 7.48–7.40 (m, 4 H, H_{Bz}), 7.10 (d, *J* = 9.1 Hz, 2 H, H_{mp}), 6.85 (d, *J* = 9.1 Hz, 2 H, H_{mp}), 5.85–5.79 (m, 5 H, 2 CH_2CHCH_2O, H2, H3, H4), 5.62 (d, *J* = 1.7 Hz, 1 H, H1), 5.33–5.26 (m, 1 H, CH_2CHCH_2O), 5.23–5.18 (m, 1 H, CH_2CHCH_2O), 5.17–5.10 (m, 1 H, CH_2CHCH_2O), 5.05–5.00 (m, 1 H, CH_2CHCH_2O), 4.56–4.53 (m, 2 H, CH_2CHCH_2O), 4.50–4.47 (m, 2 H, CH_2CHCH_2O), 4.43–4.35 (m, 3 H, H5, 2 H6), 3.73 (s, 3 H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.54, 165.42, 155.64, 154.72, 154.18, 149.93, 133.66, 133.64, 131.56, 131.08, 130.12, 130.02, 129.13, 128.98, 128.65, 128.54, 128.47, 127.47, 126.92, 118.85, 118.67, 118.07, 114.81, 96.83, 72.86, 70.00, 69.34, 68.90, 68.61, 67.13, 65.99, 65.11, 55.61.

HRMS: *m*/*z* [M + NH_4]$^+$ calcd for $C_{35}H_{38}O_{13}N$: 680.23377; found: 680.23206.

3,6-Di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-α-D-mannopyranosyl Trichloroacetimidate (7)

To a solution of **17** (4.4 g, 6.6 mmol) in MeCN (120 mL) were added water (30 mL) and CAN (14.6 g, 26.4 mmol) successively. The mixture was stirred for 20 min at 30 °C; TLC (PE–EtOAc, 2:1) indicated completion. The solvent was evaporated under reduced pressure at 50 °C to give a residue that was dissolved in CH_2Cl_2 and then washed with water. The organic phase was dried (Na_2SO_4) and concentrated to give a residue that was purified by chromatography (silica gel, PE–EtOAc, 3:1) to afforded 3,6-di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-D-mannopyranose as a slight yellow foamy solid. A mixture of this compound, trichloroacetonitrile (2.0 mL), and DBU (0.2 mL) in anhyd CH_2Cl_2 (100 mL) was stirred at r.t. for 0.5 h and then concentrated. The residue was purified by chromatography (PE–EtOAc, 4:1) to give **7** as a syrup; yield: 4.04 g (87% for 2 steps); $[\alpha]_D$ +54 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.88 (s, 1 H, NH), 8.14 (d, *J* = 7.3 Hz, 2 H, H_{Bz}), 8.02 (d, *J* = 7.3 Hz, 2 H, H_{Bz}), 7.63–7.56 (m, 2 H, H_{Bz}), 7.50–7.42 (m, 4 H, H_{Bz}), 6.51 (d, $J_{1,2}$ = 1.8 Hz, 1 H, H1), 5.90–5.84 (m, 3 H, H2, H4, CH_2CHCH_2O), 5.71–5.58 (m, 2 H, H3, CH_2CHCH_2O), 5.35–5.03 (m, 4 H, 2 CH_2CHCH_2O), 4.60, 4.51 (2 d, *J* = 5.6 Hz, 4 H, 2 CH_2CHCH_2O), 4.51–4.34 (m, 3 H, H5, 2 H6).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.27, 165.22, 159.67, 154.65, 153.99, 133.77, 133.69, 131.48, 130.98, 130.17, 130.02, 128.83, 128.80, 128.65, 128.54, 118.90, 118.85, 94.45, 90.56, 72.64, 71.37, 68.95, 68.68, 68.27, 66.41, 65.74.

4-Methoxyphenyl 2,4-Di-*O*-benzoyl-α-D-mannopyranoside (8)

To a cooled (–5 °C) solution of **17** (4.1 g, 6.2 mmol) in MeOH–THF (1:1, 60 mL) was added NH_4OAc (4.76 g, 62 mmol). The mixture was stirred vigorously and $NaBH_4$ (0.15 g, 4 mmol), $Pd(PPh_3)_4$ (0.28 g, 0.25 mmol), and $NaBH_4$ (0.55 g, 14.5 mmol) were added in 3 portions immediately one after the other; 5 min after the addition of the second portion of $NaBH_4$, TLC (PE–EtOAc, 2:1) indicated that the reaction was complete. The mixture was concentrated under vacuum, the residue was dissolved in CH_2Cl_2 (30 mL) and washed with brine (15 mL), then the organic phase was dried (Na_2SO_4). Concentration of the organic phase and purification of the residue by flash column chromatography (PE–EtOAc, 3:1) afforded **8** as a white solid; yield: 2.7 g (88%); $[\alpha]_D$ +74 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13–8.06 (m, 4 H, H_{Bz}), 7.63–7.59 (m, 2 H, H_{Bz}), 7.51–7.44 (m, 4 H, H_{Bz}), 7.06–7.02 (m, 2 H, H_{mp}), 6.86–6.83 (m, 2 H, H_{mp}), 5.67 (d, $J_{1,2}$ = 1.7 Hz, 1 H, H1), 5.64–5.57 (m, 2 H, H2, H4), 4.66 (d, *J* = 9 Hz, 1 H, H3), 4.13–4.08 (m, 1 H, H5), 3.81–3.74 (m, 5 H, OCH_3, 2 H6), 2.58, 2.38 (2 br, 2 H, 2 OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.29, 166.00, 155.39, 149.94, 133.69, 133.61, 129.92, 129.15, 129.02, 128.60, 128.53, 117.81, 114.75, 96.75, 72.72, 71.23, 70.14, 68.52, 61.25, 55.62.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{27}O_9$: 495.16490; found: 495.16496.

4-Methoxyphenyl 2,3-*O*-Isopropylidene-α-D-mannopyranoside (19)

Compound **19** was prepared according to the literature procedure.[14] White solid; yield: 8.6 g (84%); $[\alpha]_D$ +69.7 (*c* 1.0 $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.00–6.82 (2 m, 4 H, H_{mp}), 5.67 (s, 1 H, H1), 4.38 (d, $J_{2,3}$ = 5.7 Hz, 1 H, H2), 4.32 (m, 1 H, H3), 3.84–3.78 (m, 7 H, H4, H5, H6, OCH_3), 2.82 (d, *J* = 3.9 Hz, 1 H, 4–OH), 2.04 (m, 1 H, 6–OH), 1.56, 1.41 (2 s, 6 H, Me_2C).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.20, 149.81, 117.6, 114.73, 109.87, 96.53, 78.47, 75.63, 70.29, 69.36, 62.09, 55.62, 27.96, 26.21.

HRMS: *m*/*z* [M + NH_4]$^+$ calcd for $C_{16}H_{26}NO_7$: 344.17038; found: 344.17035.

4-Methoxyphenyl 4,6-Di-*O*-benzoyl-α-D-mannopyranoside (20)

Compound **19** (4.6 g, 14.1 mmol) was dissolved in anhyd CH_2Cl_2 (50 mL) containing pyridine (9.1 mL, 113 mmol), then under N_2, BzCl (4.9 mL, 42.3 mmol) was added dropwise to the solution over 15 min at –10 °C. The temperature was slowly raised to r.t. and the mixture was stirred for 2 h; TLC (PE–EtOAc, 3:1) indicated completion. The mixture was diluted with CH_2Cl_2 (100 mL), washed with ice-water, 1 M HCl, and water, and dried (Na_2SO_4). The solution was concentrated, and the residue was dissolved in 70% AcOH (200 mL) and stirred for 3 h at 70 °C; TLC (PE–EtOAc, 2:1) indicated completion. The mixture was concentrated under reduced pressure and then co-evaporated with toluene (2 × 40 mL). The residue was purified by chromatography (PE–EtOAc, 4:1) to give **20** as a syrup; yield: 6.34 g (91% for 2 steps); $[\alpha]_D$ +69 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04–8.01 (m, 2 H, H_{Bz}), 7.88–7.85 (m, 2 H, H_{Bz}), 7.57–7.50 (m, 2 H, H_{Bz}), 7.48–7.32 (m, 2 H, H_{Bz}), 7.05–7.02 (m, 2 H, H_{mp}), 6.73–6.70 (m, 2 H, H_{mp}), 5.55 (d, J = 1.4 Hz, 1 H, H1), 5.46 (t, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, 1 H, H4), 4.51–4.23 (m, 5 H, H2, H3, H5, 2 H6), 3.71 (s, 3 H, OCH_3), 3.59 (br s, 2 H, 2 OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.32, 166.22, 155.19, 149.91, 133.70, 133.01, 130.00, 129.76, 129.72, 129.05, 128.55, 127.96, 117.82, 114.65, 98.27, 71.25, 70.74, 70.45, 68.66, 63.62, 55.58.

HRMS: m/z [M + H]$^+$ calcd for $C_{27}H_{27}O_9$: 495.16490; found: 495.16496.

4-Methoxyphenyl 3-*O*-Acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranoside (10)

To a cooled (–10 °C) solution of **20** (4.94 g, 10.0 mmol) in anhyd CH_2Cl_2 (60 mL) containing pyridine (3.2 mL, 40.0 mmol), then under N_2, AcCl (0.72 mL, 10.5 mmol) in anhyd CH_2Cl_2 (10 mL) was added dropwise to the solution over 30 min. The temperature was slowly raised to r.t. and the mixture was stirred for 2 h; TLC (PE–EtOAc, 3:1) indicated that the reaction was complete. The mixture was diluted with CH_2Cl_2 (100 mL), washed with ice-water, 1 M HCl, and water, and dried (Na_2SO_4). Concentration of the organic phase and purification of the residue by flash column chromatography (PE–EtOAc, 4:1) afforded **10** as a white solid; yield: 4.72 g (88%); $[\alpha]_D$ +102 (c 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01–7.99 (m, 2 H, H_{Bz}), 7.91–7.88 (m, 2 H, H_{Bz}), 7.59–7.33 (m, 6 H, H_{Bz}), 7.09–7.06 (m, 2 H, H_{mp}), 6.78–6.74 (m, 2 H, H_{mp}), 5.75 (m, 2 H, H3, H4), 5.55 (d, $J_{1,2}$ = 1.8 Hz, 1 H, H1), 4.50–4.34 (m, 4 H, H2, H5, 2 H6), 3.73 (s, 3 H, OCH_3), 2.46 (s, 1 H, OH), 2.02 (s, 3 H, CH_3CO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.98, 166.07, 165.60, 155.19, 149.74, 133.49, 132.92, 129.82, 129.68, 129.64, 128.96, 128.49, 128.17, 117.74, 114.60, 98.23, 71.40, 69.46, 69.19, 67.27, 63.38, 55.51, 20.75.

HRMS: m/z [M + H]$^+$ calcd for $C_{29}H_{29}O_{10}$: 537.17552; found: 537.17416.

4-Methoxyphenyl 3,6-Di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-2,4-di-*O*-benzoyl-α-D-mannopyranoside (5)

Compound **8** (2.47 g, 5.00 mmol), **7** (3.85 g, 5.50 mmol), and 4-Å molecular sieves (3 g) were dried together under high vacuum for 2 h, then dissolved in anhyd, redistilled CH_2Cl_2 (50 mL). TMSOTf (36 μL, 0.2 mmol) was added dropwise at –20 °C under N_2. The mixture was stirred for 0.5 h, during the course of which time the mixture was allowed to gradually warm to r.t.; TLC (PE–EtOAc, 3:1) indicated completion. Then the mixture was neutralized with Et_3N and filtered, and the filtrate was concentrated. Purification of the residue by column chromatography (PE–EtOAc, 6:1) gave **5** as a foamy solid; yield: 4.34 g (84%); $[\alpha]_D$ +93 (c 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.20–8.05 (m, 8 H, H_{Bz}), 7.60–7.31 (m, 12 H, H_{Bz}), 7.13 (d, J = 9.1 Hz, 2 H, H_{mp}), 6.88 (d, J = 9.1 Hz, 2 H, H_{mp}), 5.79–5.59 (m, 8 H), 5.30–5.18 (m, 3 H), 5.08–5.04 (m, 2 H), 4.52–4.48 (m, 7 H), 4.07–3.99 (m, 4 H), 3.71 (s, 3 H, OCH_3), 2.58 (d, J = 8.7 Hz, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.71, 166.03, 165.30, 155.48, 154.54, 153.81, 150.08, 13361, 133.49, 133.43, 131.49, 131.14, 130.00, 129.88, 129.18, 129.12, 129.03, 129.01, 128.73, 128.48, 128.44, 118.63, 118.06, 114.81, 97.37, 97.00, 72.88, 72.75, 69.91, 69.63, 69.52, 69.01, 68.64, 68.44, 66.76, 66.52, 65.63, 55.47.

HRMS: m/z [M + NH_4]$^+$ calcd for $C_{55}H_{56}O_{20}N$: 1050.33902; found: 1050.33561.

4-Methoxyphenyl 3,6-Di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-3-*O*-acetyl-2,4-di-*O*-benzoyl-α-D-mannopyranoside (21)

To a cooled (–10 °C) solution of **5** (103 mg, 0.1 mmol) in anhyd pyridine (3.2 mL, 40.0 mmol), then under N_2, AcCl (0.14 mL, 2.1 mmol) in anhyd pyridine (2 mL) was added dropwise to the solution over 30 min. The mixture was slowly raised to r.t. and stirred for 1 h, TLC (PE–EtOAc, 2:1) indicated completion. The mixture was diluted with CH_2Cl_2 (20 mL), washed with ice-water, 1 M HCl, and water, and dried (Na_2SO_4). Concentration of the organic phase and purification of the residue by flash column chromatography (PE–EtOAc, 4:1) afforded **21** as a white solid; yield: 99 mg (92%); $[\alpha]_D$ +67 (c 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.22–8.02 (m, 8 H, H_{Bz}), 7.61–7.37 (m, 12 H, H_{Bz}), 7.15 (d, J = 9.1 Hz, 2 H, H_{mp}), 6.90 (d, J = 9.1 Hz, 2 H, H_{mp}), 5.96–5.68 (m, 7 H), 5.65–5.1 (m, 2 H, H1, H3), 5.30–5.14 (m, 3 H), 5.09–5.05 (m, 2 H), 4.53–4.43 (m, 5 H), 4.16 (m, 3 H), 4.01 (m, 1 H), 3.72 (s, 3 H, OCH_3), 3.67 (m, 1 H), 1.95 (s, 3 H, $COCH_3$).

HRMS: m/z [M + H]$^+$ calcd for $C_{57}H_{55}O_{21}$: 1075.31462; found: 1075.31438.

4-Methoxyphenyl 2,4-Di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-2,4-di-*O*-benzoyl-α-D-mannopyranoside (3)

To a cooled (–10 °C) solution of **5** (1.55 g, 1.5 mmol) in MeOH–THF (1:1, 80 mL) was added NH_4OAc (1.16 g, 15 mmol). The mixture was stirred vigorously and $NaBH_4$ (55 mg, 1.5 mmol), $Pd(PPh_3)_4$ (88 mg, 0.075 mmol), and $NaBH_4$ (27.5 mg, 0.75 mmol) were added in 3 portions immediately one after the other; 5 min after the addition of the second portion of $NaBH_4$; TLC (PE–EtOAc, 1:1) indicated completion. The mixture was concentrated under vacuum at 30 °C, the residue was dissolved in CH_2Cl_2 (10 mL) and washed with brine (10 mL), then the organic phase was dried (Na_2SO_4). Evaporation and purification by flash column chromatography (PE–EtOAc, 3:1) afforded **3** as a foamy solid; yield: 1.09 g (84%); $[\alpha]_D$ +84 (c 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15–8.03 (m, 8 H, H_{Bz}), 7.63– 7.35 (m, 12 H, H_{Bz}), 7.11 (d, J = 9.0 Hz, 2 H, H_{mp}), 6.87 (d, J = 9.0 Hz, 2 H, H_{mp}), 5.78–5.62 (m, 3 H, H4, 2 H2), 5.49–5.40 (m, 2 H, H4, H1), 5.04 (s, 1 H, H1), 4.61 (dd, $J_{2,3}$ = 3.2 Hz, $J_{3,4}$ = 9.8 Hz, 1 H, H3), 4.46 (dd, $J_{2,3}$ = 3.2 Hz, $J_{3,4}$ = 9.7 Hz, 1 H, H3), 4.34 (m, 1 H, H5), 3.97 (m, 1 H, H5), 3.79–3.64 (m, 5 H, OCH_3, 2 H6), 3.45–3.42 (m, 2 H, 2 H6), 2.62 (br s, 3 H, 3 OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.25, 166.79, 165.91, 165.84, 155.38, 149.88, 133.72, 133.67, 133.48, 129.94, 129.85, 129.80, 129.21, 129.17, 129.07, 129.00, 128.67, 128.55, 128.51, 117.87, 114.69, 97.47, 96.59, 72.68, 70.57, 70.09, 69.94, 69.67, 68.98, 68.52, 66.19, 60.95, 55.53.

HRMS: m/z [M + H]$^+$ calcd for $C_{47}H_{45}O_{16}$: 865.27021; found: 865.27048.

4-Methoxyphenyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→2)-3-*O*-acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranoside (23)

Compound **10** (2.68 g, 5.00 mmol), **9** (4.06 g, 5.50 mmol), and 4-Å molecular sieves (2 g) were dried together under high vacuum for 2 h, then dissolved in anhyd, redistilled CH_2Cl_2 (50 mL). TMSOTf (36 μL, 0.2 mmol) was added dropwise at –20 °C under N_2. The mixture was stirred for 0.5 h, during the course of which time the mixture was allowed to gradually warm to r.t.; TLC (PE–EtOAc, 2:1) indicated completion. Then the mixture was neutralized with Et_3N and filtered, and the filtrate was concentrated. Purification of the residue by column chromatography (PE–EtOAc, 5:1) gave **23** as a foamy solid; yield: 5.12 g (92%); $[\alpha]_D$ +47 (c 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05–7.88 (m, 12 H, H_{Bz}), 7.74–7.29 (m, 18 H, H_{Bz}), 7.09–7.06 (m, 2 H, H_{mp}), 6.73–6.70 (m, 2 H, H_{mp}), 6.15 (t, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz, 1 H, H4), 6.05 (dd, $J_{2,3}$ = 3.2 Hz, $J_{3,4}$ = 10.1 Hz, 1 H, H3), 5.85–5.83 (m, 3 H), 5.72 (d, $J_{1,2}$ = 1.8 Hz, 1 H, H1), 5.36 (d, $J_{1,2}$ = 1.7 Hz, 1 H, H1), 4.66–4.42 (m, 7 H), 3.72 (s, 3 H, OCH_3), 2.11 (s, 3 H, CH_3CO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.49, 166.09, 166.05, 165.54, 165.22, 165.19, 165.07, 155.23, 149.36, 133.50, 133.44, 133.13, 132.94, 132.90, 129.87, 129.77, 129.69, 129.62, 129.55, 129.47, 129.13, 129.04, 128.94, 128.72, 128.57, 128.46, 128.39, 128.27, 117.67, 114.60, 99.48, 97.22, 70.44, 7.09, 69.70, 69.46, 69.32, 67.53, 66.86, 63.47, 62.92, 55.48, 20.69.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{63}H_{54}O_{19}Na$: 1137.31515; found: 1137.31225.

2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→2)-3-*O*-acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranosyl Trichloroacetimidate (6)

To a solution of **23** (4.6 g, 4.1 mmol) in MeCN (120 mL) were added water (30 mL) and CAN (9.05 g, 16.4 mmol) successively. The mixture was stirred for 20 min at 30 °C; TLC (PE–EtOAc, 3:1) indicated completion. The solvent was evaporated under reduced pressure at 50 °C to give a residue that was dissolved in CH_2Cl_2 and then washed with water. The organic phase was dried (Na_2SO_4) and concentrated to give a residue that was purified by chromatography (silica gel, PE–EtOAc, 3:1) to afford 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→2)-3-*O*-acetyl-4,6-di-*O*-benzoyl-D-mannopyranose as a slight yellow foamy solid. A mixture of this compound, trichloroacetonitrile (2.0 mL), and DBU (0.2 mL) in anhyd CH_2Cl_2 (40 mL) was stirred at r.t. for 0.5 h and then concentrated. The residue was purified by chromatography (PE–EtOAc, 4:1) to give **6** as a yellow solid; yield: 4.13 g (87% for 2 steps).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.69 (s, 1 H, NH), 8.10–7.89 (m, 12 H, H_{Bz}), 7.59–7.30 (m, 18 H, H_{Bz}), 6.58 (d, $J_{1,2}$ = 1.7 Hz, 1 H, H1), 6.21 (t, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, 1 H, H4), 6.03–5.92 (m, 2 H, H3, H4), 5.85 (m, 1 H, H2), 5.71 (dd, $J_{2,3}$ = 3.2 Hz, $J_{3,4}$ = 9.7 Hz, 1 H, H3), 5.38 (d, $J_{1,2}$ = 1.2 Hz, 1 H, H1), 4.75–4.47 (m, 7 H, H2, 2 H5, 4 H6), 2.09 (s, 3 H, CH_3CO).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{58}H_{48}Cl_3NNaO_{18}$: 1174.1829; found: 1174.1831.

4-Methoxyphenyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→2)-3-*O*-acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-[3,6-di-*O*-allyloxycarbonyl-2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzoyl-α-D-mannopyranoside (24)

Compound **5** (1.03 g, 1.00 mmol), **6** (1.26 g, 1.1 mmol), and 4-Å molecular sieves (1 g) were dried together under high vacuum for 2 h, then dissolved in anhyd, redistilled CH_2Cl_2 (50 mL). TMSOTf (7.2 μL, 0.04 mmol) was added dropwise at –20 °C under N_2. The mixture was stirred for 0.5 h, during the course of which time the mixture was allowed to gradually warm to r.t.; TLC (PE–EtOAc, 3:1) indicated completion. Then the mixture was neutralized with Et_3N and filtered, and the filtrate was concentrated. Purification of the residue by column chromatography (PE–EtOAc, 6:1) gave **24** as a foamy solid; yield: 1.7 g (84%); $[\alpha]_D$ +106 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): 8.14–8.11 (m, 2 H, H_{Bz}), 8.05–7.82 (m, 22 H, H_{Bz}), 7.46–7.34 (m, 26 H, H_{Bz}), 7.08 (m, 2 H, H_{mp}), 6.92 (m, 2 H, H_{mp}), 5.96 (t, $J_{3,4}$ = $J_{4,5}$ = 9.2 Hz, 1 H, H4), 5.90–5.68 (m, 8 H), 5.64–5.55 (m, 4 H, 2 H1, H2, H3), 5.46 (m, 2 H, H1, H2), 5.28–5.15 (m, 3 H), 5.07–5.00 (m, 2 H), 4.76 (dd, $J_{2,3}$ = 3.2 Hz, $J_{3,4}$ = 9.5 Hz, 1 H, H3), 4.55–4.42 (m, 7 H), 4.40–4.28 (m, 4 H), 4.15–4.12 (m, 3 H), 3.93 (m, 2 H), 3.69 (s, 3 H, OCH_3), 3.62 (m, 1 H), 1.96 (s, 3 H, CH_3CO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.53, 166.22, 166.05, 165.89, 165.49, 165.23, 165.20, 165.08, 164.94, 164.82, 164.74, 155.66, 154.48, 153.63, 149.92, 133.41, 133.31, 133.27, 133.09, 133.01, 132.94, 132.81, 132.73, 132.68, 131.39, 131.08, 130.11, 129.89, 129.79, 129.74, 129.68, 129.60, 129.41, 129.20, 129.06, 128.92, 128.74, 128.47, 128.42, 128.37, 128.34, 128.29, 128.23, 128.13, 128.07, 118.74, 118.50, 114.83, 114.71, 100.18, 99.51, 97.61, 97.35, 78.34, 75.18, 72.83, 71.78, 70.07, 69.70, 69.50, 69.42, 69.13, 68.69, 68.53, 68.32, 67.24, 66.72, 66.61, 66.13, 65.66, 63.57, 62.80, 55.33, 29.53, 20.49.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{111}H_{99}O_{37}$: 2023.57824; found: 2023.57802.

4-Methoxyphenyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→2)-3-*O*-acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranosyl-(1→3)-[2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)]-2,4-di-*O*-benzoyl-α-D-mannopyranoside (4)

To a cooled (–10 °C) solution of **24** (1.41 g, 0.7 mmol) in MeOH–THF (1:1, 60 mL) was added NH_4OAc (1.08 g, 14 mmol). The mixture was stirred vigorously and $NaBH_4$ (20 mg, 0.53 mmol), $Pd(PPh_3)_4$ (32 mg, 0.028 mmol), and $NaBH_4$ (20 mg, 0.53 mmol) were added in 3 portions immediately one after the other; 5 min after the addition of the second portion of $NaBH_4$, TLC (PE–EtOAc, 1:1) indicated completion. The mixture was concentrated under vacuum at 30 °C, the residue was dissolved in CH_2Cl_2 (10 mL) and washed with brine (10 mL), then the organic phase was dried (Na_2SO_4) Evaporation and purification by flash column chromatography (PE–EtOAc, 3:1) afforded **4** as a foamy solid; yield: 1.05 g (82%); $[\alpha]_D$ +74 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.12 (m, 2 H, H_{Bz}), 8.09–7.84 (m, 19 H, H_{Bz}), 7.60–7.33 (m, 29 H, H_{Bz}), 7.06 (m, 2 H, H_{mp}), 6.83 (m, 2 H, H_{mp}), 5.96 (t, $J_{3,4}$ = $J_{4,5}$ = 10.2 Hz, 1 H, H4), 5.90–5.82 (m, 3 H, 2 H1, H4), 5.76–5.69 (m, 2 H, H1, H4), 5.59 (m, 1 H, H2), 5.49–5.39 (m, 4 H, H1, H2, 2 H3), 5.02 (s, 1 H, H1), 4.76 (dd, $J_{2,3}$ = 3.3 Hz, $J_{3,4}$ = 9.5 Hz, 1 H, H3), 4.59–4.38 (m, 6 H), 4.36–4.25 (m, 3 H), 3.94–3.79 (m, 3 H), 3.70 (s, 3 H, OCH_3), 3.62–3.52 (m, 3 H), 2.47 (d, *J* = 7.2 Hz, 1 H, OH), 2.29 (m, 1 H, OH), 1.96 (s, 3 H, CH_3CO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.71, 167.34, 166.32, 166.01, 165.99, 165.87, 165.57, 165.38, 165.02, 164.92, 164.87, 155.60, 149.74, 133.75, 133.63, 133.53, 133.49, 133.38, 133.23, 133.10, 133.06, 132.79, 130.10, 129.98, 129.91, 129.88, 129.79, 129.72, 129.69, 129.64, 129.29, 129.27, 129.22, 129.14, 129.11, 128.84, 128.64, 128.58, 128.54, 128.51, 128.39, 128.36, 128.25, 128.13, 118.44, 114.84, 114.66, 100.19, 99.61, 97.60, 97.10, 78.33, 75.28, 72.73, 71.76, 70.64, 70.17, 69.91, 69.61, 69.53, 69.27, 68.77, 68.42, 67.31, 66.62, 66.36, 63.66, 62.80, 61.11, 55.55, 20.64.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{103}H_{91}O_{33}$: 1854.53468; found: 1854.53427.

4-Methoxyphenyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-[2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)]-2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-[2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)]-2,4-di-*O*-benzoyl-α-D-mannopyranoside (22)

Compound **3** (4.32 g, 5 mmol), **9** (14.5 g, 20 mmol), and 4-Å molecular sieves (4 g) were dried together under high vacuum for 2 h, then dissolved in anhyd, redistilled CH_2Cl_2 (80 mL). TMSOTf (72 μL, 0.4 mmol) was added dropwise at –20 °C under N_2. The mixture was stirred for 0.5 h, during the course of which time the mixture was allowed to gradually warm to r.t.; TLC (PE–EtOAc–toluene, 3:1:1) indicated completion. Then the mixture was neutralized with Et_3N and filtered, and

the filtrate was concentrated. Purification of the residue by column chromatography (PE–EtOAc, 6:1) gave **22** as a foamy solid; yield: 8.3 g (64%); $[\alpha]_D$ +132 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.23–7.30 (m, 80 H, H_{Bz}), 7.08 (d, *J* = 9.1 Hz, 2 H, H_{mp}), 6.78 (d, *J* = 9.1 Hz, 2 H, H_{mp}), 6.16 (t, $J_{3,4}$ = $J_{4,5}$ = 10.0 Hz, 1 H, H4), 6.11–6.04 (m, 2 H), 6.02–5.95 (m, 2 H), 5.93–5.88 (m, 2 H), 5.79–5.68 (m, 4 H, H2, H1, 2 H3), 5.58 (m, 1 H, H2), 5.48 (m, 1 H, H2), 5.41 (d, $J_{1,2}$ = 1.4 Hz, 1 H, H1), 5.36 (m, 2 H, H1, H2), 5.17 (s, 1 H, H1), 4.87 (dd, $J_{2,3}$ = 3.3 Hz, $J_{3,4}$ = 9.7 Hz, 1 H, H3), 4.78 (d, $J_{1,2}$ = 1.2 Hz, 1 H, H1), 4.67–4.61 (m, 2 H), 4.57–4.52 (m, 3 H), 4.50–4.32 (m, 4 H), 4.29–4.21 (m, 4 H), 4.01 (m, 1 H), 3.81 (m, 1 H), 3.47 (s, 3 H, OCH_3), 3.44 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.14, 166.11, 166.09, 166.01, 165.90, 165.69, 165.54, 165.47, 165.15, 165.13, 165.06, 164.98, 164.64, 164.63, 164.57, 16.52 (16 COPh), 155.52, 149.84, 133.17, 130.18, 130.03, 129.98, 129.86, 129.84, 129.75, 129.72, 129.70, 129.68, 129.1, 129.59, 129.57, 129.44, 129.19, 129.07, 128.99, 128.94, 128.64, 128.55, 128.47, 128.41, 128.35, 128.33, 128.21, 128.08, 118.39, 114.65, 99.92, 99.67, 97.52, 97.33, 97.09 (5 C1), 72.03, 71.95, 70.17, 70.09, 69.7, 69.63, 69.54, 69.34, 69.21, 68.78, 68.14, 66.55, 66.43, 66.39, 62.65, 62.55, 62.50, 55.31.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{149}H_{123}O_{43}$: 2599.73658; found: 2599.73635.

4-Methoxyphenyl 2,3,4,6-Tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-[2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→3)]-2,4-di-*O*-benzoyl-α-D-mannopyranosyl-(1→6)-[2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl-(1→2)-3-*O*-acetyl-4,6-di-*O*-benzoyl-α-D-mannopyranosyl-(1→3)]-2,4-di-*O*-benzoyl-α-D-mannopyranoside (25)

Compound **4** (1.86 g, 1 mmol), **9** (2.22 g, 3 mmol), and 4-Å molecular sieves (2 g) were dried together under high vacuum for 2 h, then dissolved in anhyd, redistilled CH_2Cl_2 (30 mL). TMSOTf (14.4 μL, 0.08 mmol) was added dropwise at –20 °C under N_2. The mixture was stirred for 0.5 h, during the course of which time the mixture was allowed to gradually warm to r.t.; TLC (PE–EtOAc–toluene, 3:1:2) indicated completion. Then the mixture was neutralized with Et_3N and filtered, and the filtrate was concentrated. Purification of the residue by column chromatography (PE–EtOAc, 6:1) gave **25** as a foamy solid; yield: 2 g (67%); $[\alpha]_D$ +124 (*c* 1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07–7.22 (m, 90 H, H_{Bz}), 7.08 (d, *J* = 9.1 Hz, 2 H, H_{mp}), 6.83 (d, *J* = 9.1 Hz, 2 H, H_{mp}), 6.11–5.89 (m, 7 H), 5.85–5.70 (m, 5 H, H1, 2 H2, 2 H3), 5.60–5.58 (m, 2 H, 2 H2), 5.47–5.43 (m, 3 H, H1, H2, H3), 5.34 (d, $J_{1,2}$ = 1.4 Hz, 1 H, H1), 5.16 (d, $J_{1,2}$ = 1.6 Hz, 1 H, H1), 4.86 (dd, $J_{2,3}$ = 3.4 Hz, $J_{3,4}$ = 9.7 Hz, 1 H, H3), 4.80 (d, $J_{1,2}$ = 1.4 Hz, 1 H, H1), 4.63–4.43 (m, 9 H), 4.37–4.28 (m, 3 H), 4.24–4.15 (m, 5 H), 3.97–3.93 (m, 2 H), 3.77 (m, 1 H), 3.47 (s, 3 H, OCH_3), 3.39 (m, 1 H), 1.91 (s, 3 H, $COCH_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.34, 166.12, 66.08, 165.98, 165.88, 16587, 165.62, 165.53, 165.46, 165.36, 165.12, 165.07, 164.98, 164.94, 164.82, 164.67, 164.54, 133.62, 133.47, 133.37, 133.31, 33.25, 133.20, 133.09, 133.03, 133.00, 132.91, 132.75, 130.14, 129.96, 129.88, 129.84, 129.81, 129.74, 129.67, 129.65, 129.55, 129.45, 129.40, 129.33, 129.3, 2927, 129.23, 129.15, 129.10, 129.06, 129.01, 129.00, 128.91, 128.79, 128.64, 128.57, 128.53, 128.52, 128.49, 128.42, 128.38, 128.34, 128.29, 128.18, 128.06, 118.78, 114.62, 100.12, 99.78, 99.51, 97.56, 97.46, 97.36, 75.22, 71.89, 71.83, 70.1, 70.09, 69.80, 69.69, 69.56, 69.28, 69.14, 68.73, 68.58, 68.02, 67.30, 66.55, 66.40, 66.32, 65.92, 63.65, 62.69, 62.39, 55.27, 20.55.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{171}H_{143}O_{51}$: 3011.85218; found: 3011.85206.

4-Methoxyphenyl α-D-Mannopyranosyl-(1→6)-[α-D-mannopyranosyl-(1→3)]-α-D-mannopyranosyl-(1→6)-[α-D-mannopyranosyl-(1→3)]-α-D-mannopyranoside (1)

Compound **22** (13 g, 5 mmol) was dissolved in sat. NH_3–MeOH (1000 mL). After 120 h at r.t., the mixture was concentrated to a total volume of ca. 50 mL, then warm acetone (500 mL, 50 °C) was added to the mixture under vigorous stirring, and a white solid precipitated from the solution, which was then kept at 0 °C for 24 h; filtration gave **1** as a white solid; yield: 3.8 g (82%); $[\alpha]_D$ +46 (*c* 1, H_2O).

^{1}H NMR (300 MHz, MeOD–D_2O): δ = 7.08 (d, *J* = 9.1 Hz, 2 H, H_{mp}), 6.92 (d, *J* = 9.1 Hz, 2 H, H_{mp}), 5.32 (d, *J* = 1.6 Hz, 1 H, H1), 5.17 (d, *J* = 1.6 Hz, 1 H, H1), 5.08 (d, *J* = 1.3 Hz, 1 H, H1), 4.89 (d, *J* = 1.3 Hz, 1 H, H1), 4.76 (d, *J* = 1.5 Hz, 1 H, H1), 4.27 (m, 1 H), 4.06–4.02 (m, 4 H), 3.91–3.66 (m, 28 H).

^{13}C NMR (75 MHz, MeOD–D_2O): δ = 155.06, 150.40, 117.77, 114.27, 102.40, 102.27, 99.70, 99.55, 99.44, 79.37, 78.79, 73.43, 73.23, 72.79, 72.31, 71.18, 70.93, 70.89, 70.56, 70.52, 70.45, 69.88, 69.70, 67.23, 67.04, 66.03, 65.93, 65.80, 65.64, 61.21, 61.13, 54.78.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{37}H_{59}O_{27}$: 935.32382; found: 935.32395.

4-Methoxyphenyl α-D-Mannopyranosyl-(1→6)-[α-D-mannopyranosyl-(1→3)]-α-D-mannopyranosyl-(1→6)-[α-D-mannopyranosyl-(1→2)-α-D-mannopyranosyl-(1→3)]-α-D-mannopyranoside (2)

Compound **25** (11.2 g, 3.7 mmol) was dissolved in sat. NH_3_MeOH (1200 mL). After 120 h at r.t., the mixture was concentrated to a total volume of ca. 50 mL, then warm acetone (500 mL, 50 °C) was added to the mixture under vigorous stirring, and a white solid precipitated from the solution, which was kept at 0 °C for 24 h and filtered to give **2** as a white solid; yield: 3.2 g (78%); $[\alpha]_D$ +38 (*c* 1, H_2O).

^{1}H NMR (300 MHz, D_2O): δ = 7.01 (d, *J* = 7.0 Hz, 2 H, H_{mp}), 6.87 (d, *J* = 7.0 Hz, 2 H, H_{mp}), 5.39 (d, *J* = 1.6 Hz, 1 H, H1), 5.33 (d, *J* = 1.5 Hz, 1 H, H1), 4.97 (m, 2 H, 2 H1), 4.78 (d, *J* = 1.5 Hz, 1 H, H1), 4.63 (d, *J* = 1.4 Hz, 1 H, H1), 4.20 (m, 1 H), 4.0–3.55 (m, 38 H).

^{13}C NMR (75 MHz, D_2O): δ = 15.51, 149.29, 118.33, 115.07, 102.24, 102.19, 100.76, 99.6, 98.96, 98.62, 7847, 78.43, 73.35, 73.21, 73.19, 72.63, 71.45, 70.70, 70.54, 70.37, 70.31, 70.06, 69.93, 69.43, 66.92, 66.71, 66.68, 65.88, 65.68, 65.37, 65.22, 60.98, 60.92, 55.77, 48.85.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{43}H_{69}O_{32}$: 1097.37664; found: 1097.37691.

Acknowledgment

This work was partially supported by Chinese Universities Scientific Fund (2015QC069), the NSFC (21172257) and the National S&T Pillar Program (2011AA10A206, 2015BAK45B01) of China.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560323.

References

(1) (a) Moremen, K. W.; Molinari, M. *Curr. Opin. Struct. Biol.* **2006**, *16*, 592. (b) Natsuka, S. *Trends Glycosci. Glycotechnol.* **2005**, *17*, 229. (c) Matsuo, I.; Wada, M.; Manabe, S.; Yamaguchi, Y.; Otake, K.; Kato, K.; Ito, Y. *J. Am. Chem. Soc.* **2003**, *125*, 3402.

(2) (a) Recny, M. A.; Luther, M. A.; Knoppers, M. H.; Neidhardt, E. A.; Khandekar, S. S.; Concino, M. F.; Schimke, P. A.; Francis, M. A.; Moebius, U.; Reinhold, B. B.; Reinhold, V. N.; Reinherz, E. L. *J. Biol. Chem.* **1992**, *267*, 22428. (b) Wyss, D. F.; Choi, J. S.; Li, J.; Knoppers, M. H.; Willis, K. J.; Arulanandam, A. R. N.; Smolyar, A.; Reinherz, E. L.; Wagner, G. *Science (Washington, D.C.)* **1995**, *269*, 1273.

(3) (a) Bewley, C. A.; Otero-Quintero, S. *J. Am. Chem. Soc.* **2001**, *123*, 3892. (b) Clausen, H.; Sorensen, T.; White, T.; Wandall, H. H.; Hansen, J.-E. S. *Alfred Benzon Symp.* **1994**, *36*, 297–315.

(4) (a) Girard, M. P.; Osmanov, S. K.; Kieny, M. P. *Vaccine* **2006**, *24*, 4062. (b) McMichael, A. J.; Hanke, T. *Nat. Med. (N. Y., NY, U. S.)* **2003**, *9*, 874. (c) Letvin, N. L.; Walker, B. D. *Nat. Med. (N. Y., NY, U. S.)* **2003**, *9*, 861.

(5) (a) Scanlan, C. N.; Offer, J.; Zitzmann, N.; Dwek, R. A. *Nature (London, U.K.)* **2007**, *446*, 1038. (b) Ni, J.; Song, H.; Wang, Y.; Stamatos, N. M.; Wang, L.-X. *Bioconjugate Chem.* **2006**, *17*, 493. (c) Lee, H.-K.; Scalan, C. N.; Huang, C.-Y.; Chang, A. Y.; Calarese, D. A.; Dwek, R. A.; Rudd, P. M.; Burton, D. R.; Wilson, I. A.; Wong, C.-H. *Angew. Chem. Int. Ed.* **2004**, *43*, 1000.

(6) (a) McReynolds, K. D.; Gervay-Hague, J. *Chem. Rev.* **2007**, *107*, 1533. (b) Calarese, D. A.; Lee, H.-K.; Huang, C.-Y.; Best, M. D.; Astronomo, R. D.; Stanfield, R. L.; Katinger, H.; Burton, D. R.; Wong, C.-H.; Wilson, I. A. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 13372.

(7) (a) Amin, M. N.; Huang, W.; Mizanur, R. M.; Wang, L.-X. *J. Am. Chem. Soc.* **2011**, *133*, 14404. (b) Dan, A.; Lergenmuller, M.; Amano, M.; Nakahara, Y.; Ogawa, T.; Ito, Y. *Chem. Eur. J.* **1998**, *4*, 2182. (c) Depre, D.; Duffels, A.; Green, L. G.; Lenz, R.; Ley, S. V.; Wong, C.-H. *Chem. Eur. J.* **1999**, *5*, 3326. (d) Lam, S. N.; Gervay-Hague, J. *J. Org. Chem.* **2005**, *70*, 8772. (e) Liu, Y.; Chan, Y. M.; Wu, J.; Chen, C.; Benesi, A.; Hu, J.; Wang, Y.; Chen, G. *ChemBioChem* **2011**, *12*, 685. (f) Teumelsan, N.; Huang, X. *J. Org. Chem.* **2007**, *72*, 8976. (g) Wang, W.; Kong, F. *Angew. Chem. Int. Ed.* **1999**, *38*, 1247. (h) Zhang, J. J.; Kong, F. Z. *Tetrahedron: Asymmetry* **2002**, *13*, 243.

(8) (a) Jiang, R.; Liang, X.; Jin, S.; Zhang, J.; Wang, D. *Youji Huaxue* **2014**, *34*, 926. (b) Cai, X.; Zong, G.; Xu, Y.; Zhang, J.; Liang, X.; Wang, D. *Carbohydr. Res.* **2010**, *345*, 1230. (c) Zhao, H.; Jia, H.; Duan, H.; Zhang, J.; Wang, D.; Liang, X. *J. Carbohydr. Chem.* **2010**, *29*, 103. (d) Zong, G.; Cai, X.; Liang, X.; Zhang, J.; Wang, D. *Carbohydr. Res.* **2011**, *346*, 2533. (e) Zong, G.; Feng, Y.; Liang, X.; Chen, L.; Zhang, J.; Wang, D. *Carbohydr. Res.* **2010**, *345*, 2067. (f) Zong, G.; Liang, X.; Zhang, J.; Duan, L.; Tan, W.; Wang, D. *Carbohydr. Res.* **2014**, *388*, 87. (g) Zong, G.; Yu, N.; Xu, Y.; Zhang, J.; Wang, D.; Liang, X. *Synthesis* **2010**, 1666.

(9) Zong, G. H.; Yan, S. Q.; Liang, X. M.; Zhang, J. J.; Wang, D. Q.; Kong, F. Z. *Chin. Chem. Lett.* **2009**, *20*, 127.

(10) Faure, R.; Shiao, T. C.; Damerval, S.; Roy, R. *Tetrahedron Lett.* **2007**, *48*, 2385.

(11) Copeland, C.; Stick, R. V. *Aust. J. Chem.* **1978**, *31*, 1371.

(12) Schmidt, R. R.; Kinzy, W. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21.

(13) Deulofeu, V.; Deferrari, J. O. *J. Org. Chem.* **1952**, *17*, 1097.

(14) Jiang, R.; Zong, G.; Liang, X.; Jin, S.; Zhang, J.; Wang, D. *Molecules* **2014**, *19*, 6683; http://www.mdpi.com/journal/molecules.