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Synthesis of a 6^V-sulfated mannopentasaccharide analogue related to PI-88

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Abstract—An efficient and convergent synthesis of a regioselectively 6^V-sulfated mannopentasaccharide derivative **1c**, octyl 6-*O*-sulfo-α-D-mannopyranosyl-(1 → 3)-α-D-mannopyranosyl-(1 → 3)-α-D-mannopyranosyl-(1 → 3)-α-D–mannopyranosyl-(1 → 2)-α-D-mannopyranoside, was achieved by a '3 + 2' strategy. The target was designed to mimic the promising anticancer agent PI-88 and was obtained from the building blocks, octyl 3,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (**3**), allyl 2,4,6-tri-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-α-D-mannopyranoside (**6**), and 6-*O*-acetyl-2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (**11**), under TMSOTf-catalyzed glycosylation conditions. Compound **1c** displays a mild anti-angiogenic activity based on a chorio-allantoic membrane (CAM) model study.
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Keywords: Sulfated oligosaccharides; Glycosylation; Mannose; Anti-angiogenic

1. Introduction

The highly branched extracellular phosphomannan (**PS**), yielded by the yeast *pichia (Hansenula) holstii* NRRL Y-2448 when grown in a culture medium containing an excess of orthophosphate,[1] is composed of a high-molecular-weight phosphomannan core (**PC**) and a low-molecular-weight oligosaccharide phosphate fraction.[2] Both of them have become valuable tools and probes for studying mannose-6-phosphate receptors.[3] Recent work has revealed that the low-molecular-weight fraction, which accounts for approximately 90% of the **PS**, is derived from the phosphorylated side-chain oligosaccharides attached to the **PC**.[4] The major oligosaccharide present in this fraction,[2a,4,5] and the main repeating unit found in the phosphorylated side chains, is the mannose-containing pentasaccharide phosphate **1a** (Fig. 1). Its fully sulfated derivative **1b**, known as PI-88, has been identified as a potent inhibitor of tumor growth, metastasis, and angiogenesis, and is currently in

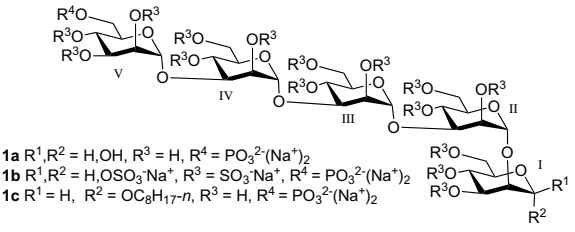

Figure 1. Chemical structures of PI-88 and analogues.

Phase II clinical trials.[6] PI-88 appears to block tumor growth by preventing the interaction of heparan sulfate with fibroblast growth factor and its receptor.[7] PI-88 is believed to block metastasis by inhibiting heparanase, blocking the breakdown of the extracellular matrix, thus preventing the spread of tumor cells.[8] To further understand the structure–activity relationships of this mannose-containing pentasaccharide and its derivatives, we launched a project to prepare PI-88 analogues with different sulfation positions and different numbers of sulfate groups, and investigate the bioactive contribution on each of them. We herein report the first synthesis of a mimic, 6^V-*O*-sulfo pentasaccharide (**1c**), using a '3 + 2' strategy.

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2. Results and discussion

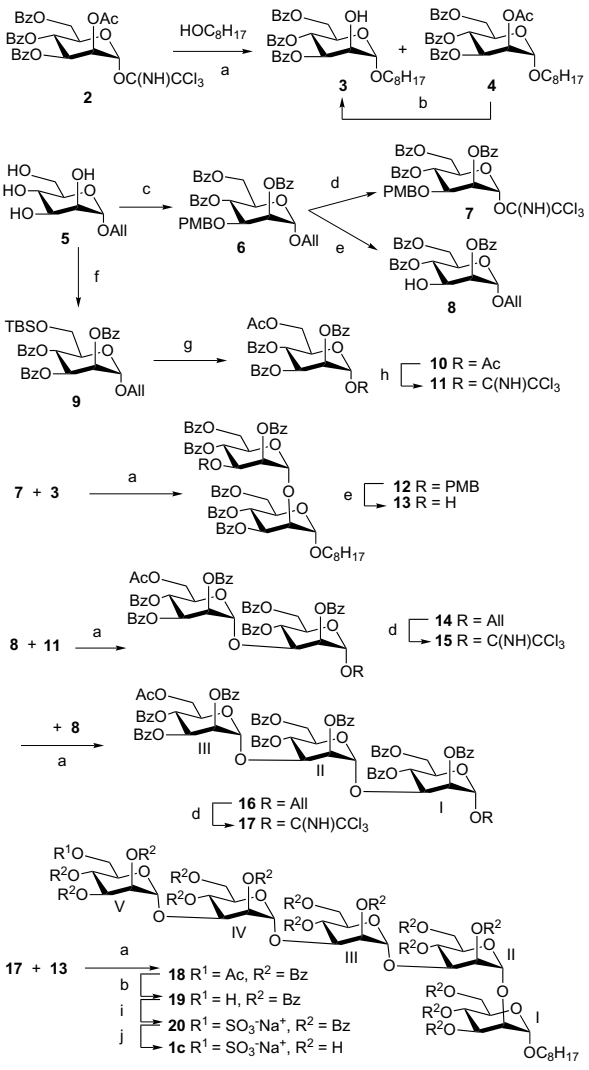
To complete the synthesis of target molecule **1c**, we designed a convergent strategy using disaccharide **13** as acceptor and trisaccharide trichloroacetimidate **17** as donor, which were assembled by the building blocks **3**, **7**, **8**, and **11**, respectively.

We started from the preparation of disaccharide acceptor **13** (Scheme 1). To increase the hydrophobicity of the molecule, an octyl chain was first attached to the mannose residue at the reducing end. To our delight, when coupling of 2-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (**2**)[9] and 1-octanol in anhydrous dichloromethane in the presence of catalytic amount of TMSOTf at 0 °C, deacetylated octyl glycoside **3** was obtained as a major product (61%), while the originally expected compound **4** was obtained in only 37% yield. The similar result was also observed in the preparation of allyl β-D-glucopyranoside.[10] Further deacetylation of **4** with 3% acetyl chloride in MeOH–CH_2Cl_2 (v/v, 1:1) co-solvent smoothly provided 2-OH acceptor **3** in 87% yields.[11] The ^{1}H NMR spectra of **3** gave H-2 (δ: 4.31 ppm) shifted upfield, indicating the correct structure of compound **3**. Treatment of allyl α-D-mannopyranoside (**5**) with dibutyltin oxide and *p*-methoxybenzyl chloride, followed by benzoylation with benzoyl chloride in pyridine, regioselectively furnished *p*-methoxybenzylated derivative **6** in a total yield of 55%. Deallylation of **6** with palladium dichloride (0.5 equiv) in methanol,[12] followed by activation of the anomeric hydroxyl group with trichloroacetonitrile and 1,8-diazabicyclo[4.3.0]non-5-ene (DBU), yielded the mannopyranosyl Schmidt donor **7** (72%, two steps). Treatment of **6** with ceric ammonium nitrate (CAN)[13] in a 1:1:1 CH_3CN–toluene–H_2O solvent system furnished synthon **8** in good yield. Regioselective silylation of **5** with *tert*-butylchlorodimethylsilane (TBSCl) in pyridine and in situ benzoylation with benzoyl chloride gave a high yield of **9**. Building block **11** was prepared in 43% overall yield from **9** via following three steps: acetolysis with 3% concentrated H_2SO_4 in Ac_2O; regioselective deacetylation with NH_3 in 3:1 THF–MeOH[14], and activation of the anomeric carbon with Cl_3CCN and DBU.

Coupling of **7** and **3** in anhyd CH_2Cl_2 at 0 °C in the presence of TMSOTf (10% equiv) afforded the α-(1 → 2)-linked disaccharide **12**. The chemical shifts of H-1 (δ: 5.01 ppm, *J* 1.6 Hz), and H-1′ (δ: 5.18 ppm, *J* 1.7 Hz) on ^{1}H NMR spectra, together with reasonable $^1J_{C\text{-}1,H\text{-}1}$ values (171 and 173 Hz, respectively), confirmed the α bonds in **12**.[9] CAN-promoted cleavage of *p*-methoxybenzyl group from **12** was carried out smoothly to give disaccharide acceptor **13** in 80% yield.

Trisaccharide donor **17** was assembled convergently from building blocks **8** and **11**. Condensation of **8** and **11** in anhyd CH_2Cl_2 with TMSOTf as a promoter furnished high yield of disaccharide **14**, which was then deallylated with palladium chloride (0.5 equiv) in methanol and activated by trichloroacetimidate formation to give disaccharide donor **15** in 67% yield over three steps. Glycosylation of **8** and **15** under standard conditions afforded trisaccharide **16** in a yield of 85%. Trisaccharide donor **17** was thus obtained in 67% yield through two steps (deallylation: $PdCl_2$/MeOH; trichloroacetimidate formation: Cl_3CCN–DBU–CH_2Cl_2).

Coupling of trisaccharide donor **17** and disaccharide acceptor **13** proceeded in anhydrous dichloromethane with the promotion of TMSOTf generated fully protected pentasaccharide **18** (72%). Peaks at δ 4.90, 4.99,



Scheme 1. (a) TMSOTf, CH_2Cl_2, 61% for **3**; 37% for **4**; 91% for **12**; 89% for **14**; 85% for **16**; 72% for **18**. (b) 3% AcCl, 1:1 MeOH–CH_2Cl_2, 87% for **3**; 93% for **19**. (c) Bu_2SnO, MeOH; PMBCl, toluene; BzCl, Pyr, 55%. (d) $PdCl_2$, MeOH; Cl_3CCN, DBU, 72% for **7**; 67% for **15**; 67% for **17**. (e) CAN, MeCN–toluene–H_2O, 88% for **8**; 80% for **13**. (f) TBSCl, BzCl, Pyr, 93%. (g) concd H_2SO_4, Ac_2O, 63%. (h) NH_3, 3:1 THF–MeOH; Cl_3CCN, DBU, 67% for two steps. (i) SO_3·Py, Pyr, 91%. (j) NaOMe, MeOH, 97%.

Table 1. Preliminary study on anti-angiogenic activity of compound **1c**

Sample	Total number of blood vessel	Large blood vessel[a]	Medium blood vessel[b]	Small blood vessel[c]
Control	43.67 ± 9.35	3.87 ± 1.88	5.56 ± 1.81	32.00 ± 6.00
1c (1 mg/mL)	29.75 ± 6.25**	2.50 ± 1.83	2.83 ± 1.64**	23.67 ± 6.71*
1c (2 mg/mL)	27.38 ± 8.17**	1.75 ± 1.03	2.25 ± 1.39**	23.87 ± 6.33*

*$p < 0.01$, **$p < 0.05$.
[a]Blood vessel diameter $\phi \geqslant 0.1$ mm.
[b]$0.1 > \phi \geqslant 0.05$ mm.
[c]$\phi < 0.05$ mm.

5.09, 5.25, 5.36 in the ^{1}H NMR spectrum and δ 98.54, 98.66, 99.17, 99.18, 99.57 in the ^{13}C NMR spectrum showed all H-1s and C-1s in this structure. Regioselective removal of acetyl group of **18** with 3% AcCl in MeOH–CH_2Cl_2 (→**19**), followed by C-6^V sulfation with the SO_3·Py complex in pyridine, after passing through a Dowex-50 ion exchange resin column (Na^+), afforded the sodium salt of mono-sulfated pentasaccharide **20** in 85% yield (over two steps). ^{1}H NMR spectra of compounds **19** and **20** showed that the chemical shifts of H-6a^V and H-6b^V moved apparently from upfield (δ: 3.16, 3.24 ppm, **19**) to downfield (δ: ~3.70 ppm, **20**). Finally, deacylation of **20** with sodium methoxide in methanol completed the desired pentasaccharide **1c** in 97% yield. ^{1}H NMR, ^{13}C NMR, and ESI-mass spectra of **1c** are all fulfilled by the designed structure.

The chorioallantoic membrane (CAM) of the chick embryo has been widely used as a semi-quantitative bioassay of angiogenic activity and a model to screen the angiogenic inhibitor or stimulator. We detected the preliminary anti-angiogenic activity of **1c** with the CAM model following the procedure described in the literature.[15] The result, listed in Table 1, showed that **1c** is a mild angiogenesis inhibitor.

In summary, a practical and convergent synthesis of the 6^V-sulfated mannose-pentasaccharide derivative, a structural analogue of PI-88, was achieved via a '3 + 2' strategy. The strategic principal described here is currently employed in the assembly of clustered derivatives. Preparation and testing of more PI-88 analogues containing specific sulfate groups are under way in our lab and will be reported in due course.

3. Experimental

3.1. General methods

Optical rotations were determined at 25 °C with a Perkin–Elmer Model 241-Mc automatic polarimeter. ^{1}H NMR, ^{13}C NMR spectra were recorded with ARX 400 spectrometers for solutions in $CDCl_3$ and D_2O. Chemical shifts are given in ppm downfield from internal Me_4Si, or DSS in case of D_2O. Mass spectra were measured using the ESI technique to introduce the sample. 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 a UV detector. Column chromatography was conducted by elution of a silica gel column with EtOAc–petroleum ether (bp 60–90 °C) as the eluent. Solutions were concentrated at <60 °C under diminished pressure.

3.2. Octyl 2-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (4) and octyl 3,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (3)

To a solution of 2-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (1.28 g, 1.88 mmol) and 1-octanol (0.36 mL, 2.26 mmol) in anhyd CH_2Cl_2 (8 mL) at 0 °C was added TMSOTf (25 μL, 0.14 mmol) under an N_2 atmosphere. The reaction mixture was stirred under these conditions for 2 h, then neutralized with Et_3N, and concentrated to dryness. Column chromatography (6:1 to 4:1 petroleum ether–EtOAc) of the residue gave syrupy **4** (450 mg, 37%) and **3** (694 mg, 61%), respectively. Acetyl chloride (0.3 mL) was added to a solution of compound **4** (428 mg, 0.66 mmol) in a 1:1 CH_2Cl_2–MeOH (10 mL,) solvent system. The mixture was stirred overnight, and then the resulting mixture was neutralized with pyridine (0.6 mL), concentrated to dryness, and purified on a silica gel column with 4:1 petroleum ether–EtOAc as the eluent to give **3** as an amorphous solid. Physical data for **4**: $[\alpha]_D^{25}$ −7 (*c* 2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 3H, –$(CH_2)_7CH_3$), 1.21–1.39 (m, 10H, –$CH_2CH_2(CH_2)_5CH_3$), 1.61–1.71 (m, 2H, –$CH_2CH_2(CH_2)_5CH_3$), 2.14 (s, 3H, CH_3CO), 3.52, 3.78 (2 dt, 2H, *J* 9.9, 7.0 Hz, OCH_2), 4.37 (ddd, 1H, H-5), 4.48 (dd, 1H, $J_{6a,6b}$ 12.0, $J_{5,6a}$ 5.6 Hz, H-6a), 4.61 (dd, 1H, $J_{5,6b}$ 2.8 Hz, H-6b), 4.93 (d, 1H, $J_{1,2}$ 1.6 Hz, H-1), 5.47 (dd, 1H, $J_{2,3}$ 3.3 Hz, H-2), 5.80 (dd, 1H, $J_{3,4}$ 10.0 Hz, H-3), 5.89 (t, 1H, $J_{4,5}$ 10.0 Hz, H-4), 7.34–8.07 (m, 15H, *Ph*). Anal. Calcd for $C_{37}H_{42}O_{10}$: C, 68.71; H, 6.55. Found: C, 69.02; H, 6.47. Physical data for **3**: $[\alpha]_D^{25}$ +11 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 3H, –$(CH_2)_7CH_3$), 1.22–1.38 (m, 10H, –$CH_2CH_2(CH_2)_5CH_3$), 1.60–1.70 (m, 2H, –$CH_2CH_2(CH_2)_5CH_3$), 3.52, 3.79 (2 dt, 2H, *J* 9.6, 6.8 Hz, OCH_2), 4.31 (br s, 1H, H-2), 4.36 (ddd, 1H, H-5), 4.48 (dd, 1H, $J_{6a,6b}$ 12.0, $J_{5,6a}$ 5.6 Hz, H-6a), 4.58 (dd, 1H, $J_{5,6b}$ 2.8 Hz, H-6b), 4.97 (d, 1H, $J_{1,2}$ 1.6 Hz, H-1), 5.68

(dd, 1H, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0 Hz, H-3), 5.91 (t, 1H, $J_{4,5}$ 10.0 Hz, H-4), 7.34–8.05 (m, 15H, *Ph*). Anal. Calcd for $C_{35}H_{40}O_9$: C, 69.52; H, 6.67. Found: C, 69.87; H, 6.80.

3.3. Allyl 2,4,6-tri-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-α-D-mannopyranoside (6)

The mixtures of allyl α-D-mannopyranoside (4.42 g, 20 mmol) and dibutyltin oxide (5.0 g, 20 mmol) were dissolved into anhyd MeOH (150 mL). The reaction mixture was refluxed for 3 h, concentrated to dryness under reduced pressure. To a solution of the product generated above in anhyd toluene (120 mL) was added Bu_4NI (7.4 g, 20 mmol) and 4-methoxybenzyl chloride (4.1 mL, 30 mmol). The mixture was stirred at 80 °C for 16 h, concentrated to dryness, and purified on a silica gel column (1:3 petroleum ether–EtOAc) to give allyl 3-*O*-(4-methoxybenzyl)-α-D-mannopyranoside. The above product was dissolved in pyridine (20 mL), and benzoyl chloride (7.0 mL) was added dropwise at 0 °C. Then, the reaction mixture was stirred overnight at rt and co-evaporated with toluene under diminished pressure to remove pyridine. Purification of the residue by silica-gel column chromatography (5:1 petroleum ether–EtOAc) afforded **6** (7.18 g, 55%) as a syrup: $[\alpha]_D^{25}$ −35 (*c*2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 3.70 (s, 3H, OCH_3), 4.06–4.11 (m, 1H, one proton of CH_2=CHCH_2O–), 4.16 (dd, 1H, $J_{2,3}$ 3.2, $J_{3,4}$ 9.8 Hz, H-3), 4.20–4.27 (m, 2H, H-5 and one proton of CH_2=CHCH_2O–), 4.37–4.42 (m, 2H, one proton of PhCH_2 and H-6a), 4.58–4.67 (m, 2H, H-6b and one proton of PhCH_2), 5.07 (d, 1H, $J_{1,2}$ 1.2 Hz, H-1), 5.21–5.33 (m, 2H, CH_2=CHCH_2O–), 5.68 (dd, 1H, H-2), 5.84 (t, 1H, $J_{3,4} = J_{4,5}$ 9.8 Hz, H-4), 5.89–5.99 (m, 1H, CH_2=C*H*CH_2O–), 6.60 (d, 2H, $CH_3OC_6H_4CH_2$), 7.04 (d, 2H, $CH_3OC_6H_4CH_2$), 7.07–8.11 (m, 15H, *Ph*). Anal. Calcd for $C_{38}H_{36}O_{10}$: C, 69.93; H, 5.56. Found: C, 70.34; H, 5.50.

3.4. 2,4,6-Tri-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-α-D-mannopyranosyl trichloroacetimidate (7)

To a solution of compound **6** (2.3 g, 3.53 mmol) in anhyd MeOH (20 mL) was added palladium dichloride (312 mg, 1.68 mmol). The mixture was stirred at rt until TLC indicated the completion of the reaction. The resulting mixture was filtered, and the filtrate was concentrated. The residue was subjected to a silica gel column (3:1 petroleum ether–EtOAc) to give a pure intermediate, which was then dissolved in anhyd CH_2Cl_2 (8 mL). To the solution was added trichloroacetonitrile (1.1 mL, 11 mmol) and DBU (0.1 mL, 1.0 mmol) at rt. The reaction mixture was stirred for 2 h, concentrated, and the residue was purified on column chromatography (5:1 petroleum ether–EtOAc) to give syrupy **7** (1.92 g, 72% for two steps): $[\alpha]_D^{25}$ −10 (*c* 2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): 3.74 (s, 3H, OCH_3), 4.19 (dd, 1H, $J_{2,3}$ 3.3, $J_{3,4}$ 9.9 Hz, H-3), 4.34–4.40 (m, 2H, H-5, H-6a), 4.71 (d, 1H, *J* 12.2 Hz, one proton of $CH_3OC_6H_4CH_2$), 4.59–4.68 (m, 2H, H-6b, one proton of $CH_3OC_6H_4CH_2$), 5.79 (dd, 1H, H-2), 5.94 (t, 1H, $J_{4,5}$ 9.9 Hz, H-4), 6.47 (d, 1H, $J_{1,2}$ 2.0 Hz, H-1), 6.64 (d, 2H, $CH_3OC_6H_4CH_2$), 7.06 (d, 2H, $CH_3OC_6H_4CH_2$), 7.37–8.11 (m, 15H, *Ph*), 8.77 (s, 1H, N*H*). Anal. Calcd for $C_{37}H_{32}Cl_3NO_{10}$: C, 58.70; H, 4.26. Found: C, 59.01; H, 4.22.

3.5. Allyl 2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (8)

Ceric ammonium nitrate (CAN; 2.98 g, 5.43 mmol) was added to a solution of **6** (2.36 g, 3.62 mmol) in 3:4:3 toluene–MeCN–H_2O (30 mL), and the mixture was stirred at rt for 2 h, at the end of which time TLC (3:1 petroleum ether–EtOAc) indicated the completion of the reaction. The resulting mixture was diluted with EtOAc, washed successively with water, satd aq $NaHCO_3$, and brine. The organic phase was dried over anhyd Na_2SO_4 and concentrated, then subjected to a silica gel column chromatography (3:1 petroleum ether–EtOAc) to afford syrupy **8** (1.69 g, 88%): $[\alpha]_D^{25}$ −5 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 4.08–4.35 (m, 3H, H-5, CH_2=CHCH_2O), 4.43–4.50 (m, 2H, H-3, H-6a), 4.68 (dd, 1H, $J_{6a,6b}$ 12.1, $J_{5,6b}$ 2.5 Hz, H-6b), 5.11 (d, 1H, $J_{1,2}$ 1.6 Hz, H-1), 5.23–5.37 (m, 2H, CH_2=CHCH_2O), 5.45 (dd, 1H, $J_{2,3}$ 3.4 Hz, H-2), 5.71 (t, 1H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4), 5.89–6.01 (m, 1H, CH_2=C*H*CH_2O), 7.38–8.09 (m, 15H, *Ph*). Anal. Calcd for $C_{30}H_{28}O_9$: C, 67.66; H, 5.30. Found: C, 67.87; H, 5.23.

3.6. Allyl 2,3,4-tri-*O*-benzoyl-6-*O*-(*tert*-butyldimethylsilyl)-α-D-mannopyranoside (9)

To a solution of allyl α-mannopyranoside (2.20 g, 10 mmol) in pyridine (10 mL) was slowly added a solution of TBSCl (1.66 g, 11 mmol) in pyridine (6 mL) over a period of 10 min. The mixture was stirred for 4 h, and then a solution of BzCl (4.70 mL, 40 mmol) in pyridine (8 mL) was added dropwise in 30 min. The reaction mixture was stirred for another 10 h, at which time the reaction was completed. The resulting mixture was co-evaporated with toluene (30 mL) to dryness. The residue was subjected to a silica gel column using 5:1 petroleum ether–EtOAc as eluent to afford **9** (6.04 g, 93%) as a syrup: $[\alpha]_D^{25}$ −111 (*c* 4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.21, 0.32 (s, 6H, 2 CH_3), 0.90 (s, 9H, (CH_3)$_3$CSi), 3.82–3.91 (m, 2H, $J_{6a,6b}$ 11.4, $J_{6a,5}$ 2.8, $J_{6b,5}$ 4.7 Hz, H-6a, H-6b), 4.11–4.20 (m, 2H, H-5, CH_2=CHCH_2O), 4.31–4.36 (m, 1H, CH_2=CHCH_2O), 5.13 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1), 5.27–5.43 (m, 2H, CH_2=CHCH_2O), 5.70 (dd, 1H, $J_{2,3}$ 3.3 Hz, H-2), 5.89 (dd, 1H, $J_{3,4}$ 10.1 Hz, H-3), 5.94–6.06 (m, 2H, H-4, CH_2=CHCH_2O), 7.25–8.13 (m, 15H, *Ph*). Anal. Calcd for $C_{36}H_{42}O_9$: C, 66.85; H, 6.55. Found: C, 66.98; H, 6.42.

3.7. 1,6-Di-*O*-acetyl-2,3,4-tri-*O*-benzoyl-α-D-mannopyranose (10)

To a solution of compound **9** (3.42 g, 5.29 mmol) in Ac_2O (40 mL) was added concentrated H_2SO_4 (2 mL) at rt. The reaction mixture was stirred for 15 h, then poured into water (100 mL), extracted with CH_2Cl_2 (3 × 100 mL). The organic phase was washed successively with satd aq $NaHCO_3$, brine, dried over anhyd Na_2SO_4, concentrated, and purified on a silica gel column with 2:1 petroleum–EtOAc as eluent to afford white solid **10** (1.92 g, 63%): $[\alpha]_D^{25}$ −107 (*c* 2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.08, 2.28 (s, 6H, 2 C*H*$_3$CO), 4.25–4.40 (m, 3H, H-5, H-6a, H-6b), 5.71 (dd, 1H, $J_{2,3}$ 3.2 Hz, H-2), 5.89 (dd, 1H, $J_{3,4}$ 10.0 Hz, H-3), 6.02 (t, 1H, $J_{4,5}$ 10.0 Hz, H-4), 6.37 (d, 1H, $J_{1,2}$ 2.0 Hz, H-1), 7.27–8.12 (m, 15H, *Ph*). Anal. Calcd for $C_{31}H_{28}O_{11}$: C, 64.58; H, 4.90. Found: C, 64.78; H, 4.97.

3.8. 6-*O*-Acetyl-2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (11)

Ammonia was bubbled into a solution of compound **10** (1.86 g, 3.23 mmol) in 7:3 THF–MeOH (20 mL) for 15 min. The resulting mixture was stirred for 30 min and evaporated to dryness under reduced pressure. To the solution of the product generated above in CH_2Cl_2 (8 mL) was added trichloroacetonitrile (1.0 mL, 10 mmol) and DBU (0.1 mL, 1.0 mmol) at rt. The mixture was stirred for 2 h and then concentrated. The residue was subjected to a silica gel column (4:1 petroleum ether–EtOAc) to afford syrupy **11** (1.47 g, 67%): $[\alpha]_D^{25}$ −15 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.08 (s, 3H, C*H*$_3$CO), 4.34 (d, 2H, $J_{5,6}$ 3.9 Hz, H-6a, H-6b), 4.50 (dt, 1H, H-5), 5.90–5.96 (m, 2H, $J_{2,3}$ 3.3 Hz, H-2, H-3), 6.07 (t, 1H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4), 6.56 (d, 1H, $J_{1,2} = 1.9$ Hz, H-1), 7.27–8.13 (m, 15H, *Ph*), 8.88 (s, 1H, N*H*). Anal. Calcd for $C_{31}H_{26}Cl_3NO_{10}$: C, 54.84; H, 3.86. Found: C, 55.12; H, 3.91.

3.9. Octyl 2,4,6-tri-*O*-benzoyl-3-*O*-(4-methoxybenzyl)-α-D-mannopyranosyl-(1 → 2)-3,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (12)

To a solution of compound **3** (660 mg, 1.09 mmol) and **7** (868 mg, 1.15 mmol) in anhyd CH_2Cl_2 (8 mL) at 0 °C was added Me_3SiOTf (20 μL, 0.11 mmol) under an N_2 atmosphere. The mixture was stirred under these conditions for 1 h, neutralized with Et_3N and concentrated under reduced pressure. The residue was purified on a silica gel column with 4:1 petroleum ether–EtOAc as the eluent to give **12** (1.19 g, 91%) as syrup: $[\alpha]_D^{25}$ −51 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (t, 3H, C*H*$_3$), 1.22–1.35 (m, 10H, –C*H*$_2$CH$_2$–), 1.55–1.63 (m, 2H, –CH$_2$C*H*$_2$–), 3.31, 3.67 (2 dt, 2H, *J* 9.4, 7.0 Hz, OC*H*$_2$), 3.70 (s, 3H, OC*H*$_3$), 4.24 (dd, 1H, $J_{2',3'}$ 3.1, $J_{3',4'}$ 9.8 Hz, H-3′), 4.30 (br s, 1H, H-2), 4.31–4.41 (m, 3H, H-5, H-5′, H-6a′), 4.43–4.54 (m, 2H, H-6a, one proton of PhC*H*$_2$), 4.58–4.72 (m, 3H, H-6b, H-6b′, one proton of PhC*H*$_2$), 5.01 (d, 1H, $J_{1,2}$ 1.6 Hz, H-1), 5.18 (d, 1H, $J_{1',2'}$ 1.7 Hz, H-1′), 5.80–5.86 (m, 4H, H-3, H-4, H-2′, H-4′), 6.69, 7.10 (2 d, 4H, *J* 8.6 Hz, $CH_3OC_6H_4CH_2$), 7.30–8.05 (m, 30H, *Ph*). Anal. Calcd for $C_{70}H_{70}O_{18}$: C, 70.10; H, 5.88. Found: C, 70.54; H, 5.67.

3.10. Octyl 2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl-(1 → 2)-3,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (13)

Compound **13** (656 mg, 80%), prepared from **12** (1.06 g, 0.88 mmol) as described in the synthesis of **8**, gave the following physical data: $[\alpha]_D^{25}$ +3 (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.89 (t, 3H, –(CH$_2$)$_7$C*H*$_3$), 1.22–1.33 (m, 10H, –CH$_2$CH$_2$(C*H*$_2$)$_5$CH$_3$), 1.55–1.63 (m, 2H, –CH$_2$C*H*$_2$(CH$_2$)$_5$CH$_3$), 3.32, 3.67 (2 dt, 2H, *J* 9.4, 7.0 Hz, OC*H*$_2$), 4.29–4.34 (m, 2H, H-2, H-5), 4.40–4.51 (m, 4H, H-3′, H-5′, 2H-6′), 4.61–4.67 (dd, 2H, 2H-6), 5.07 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1), 5.22 (d, 1H, $J_{1',2'}$ 1.6 Hz, H-1′), 5.61–5.68 (m, 2H, H-2′, H-4′), 5.86 (dd, 1H, $J_{2,3}$ 3.0, $J_{3,4}$ 10.0 Hz, H-3), 5.98 (t, 1H, $J_{4,5}$ 10.0 Hz, H-4), 7.28–8.09 (m, 30H, *Ph*). Anal. Calcd for $C_{62}H_{62}O_{17}$: C, 69.00; H, 5.79. Found: C, 69.37; H, 5.88.

3.11. Allyl 6-*O*-acetyl-2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl-(1 → 3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (14)

Compound **14** (1.46 g, 89%) was prepared from **11** (1.12 g, 1.64 mmol) and **8** (830 mg, 1.56 mmol) in a similar fashion to that of making **12**: $[\alpha]_D^{25}$ −119 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.08 (s, 3H, C*H*$_3$CO), 4.08–4.18 (m, 2H, H-6a′, CH$_2$=CHC*H*$_2$O–), 4.21–4.43 (m, 4H, H-5, H-5′, H-6b′, CH$_2$=CHC*H*$_2$O–), 4.47 (dd, 1H, $J_{6a,6b}$ 12.2, $J_{5,6a}$ 4.7 Hz, H-6a), 4.65 (dd, 1H, $J_{2,3}$ 3.3, $J_{3,4}$ 9.8 Hz, H-3), 4.70 (dd, 1H, $J_{5,6b}$ 2.5 Hz, H-6b), 5.16 (d, 1H, $J_{1,2}$ 1.6 Hz, H-1), 5.24–5.36 (m, 4H, H-1′, H-2′, C*H*$_2$=CHCH$_2$O–), 5.63–5.68 (m, 2H, H-2, H-3′), 5.76 (t, 1H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4), 5.91–6.05 (m, 2H, H-4′, CH$_2$=C*H*CH$_2$O–), 7.19–8.20 (m, 30H, *Ph*). Anal. Calcd for $C_{59}H_{52}O_{18}$: C, 67.55; H, 5.00. Found: C, 67.31; H, 5.02.

3.12. 6-*O*-Acetyl-2,3,4-tri-*O*-benzoyl-α-D-mannopyranosyl-(1 → 3)-2,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (15)

Syrupy compound **15** (1.05 g, 67%) was prepared from **14** (1.42 g, 1.35 mmol) as described in the preparation of **7** from **6**: $[\alpha]_D^{25}$ −127 (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ

2.06 (s, 3H, CH_3CO), 4.13 (dd, 1H, $J_{6a,6b}$ 12.4, $J_{5,6a}$ 4.8 Hz, H-6a), 4.20 (dd, 1H, $J_{6a,6b}$ 12.4, $J_{5,6b}$ 4.0 Hz, H-6b′), 4.38 (ddd, 1H, H-5′), 4.45–4.53 (m, 2H, H-5, H-6a), 4.66–4.74 (m, 2H, H-3, H-6b), 5.33 (dd, 1H, $J_{1,2}$ 1.7, $J_{2,3}$ 3.1 Hz, H-2′), 5.36 (d, 1H, H-1′), 5.67 (dd, 1H, $J_{2,3}$ 3.2, $J_{3,4}$ 10.0 Hz, H-3′), 5.81–5.87 (m, 2H, H-2, H-4), 6.14 (t, 1H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4′), 6.60 (d, 1H, $J_{1,2}$ 1.9 Hz, H-1), 7.20–8.13 (m, 30H, *Ph*), 8.86 (s, 1H, N*H*). Anal. Calcd for $C_{58}H_{48}Cl_3NO_{18}$: C, 60.40; H, 4.19. Found: C, 60.79; H, 4.23.

3.13. Allyl 6-*O*-acetyl-2,3,4-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 (16)

Syrupy compound **16** (1.03 g, 85%) was prepared from **8** (422 mg, 0.79 mmol) and **15** (960 mg, 0.83 mmol) in a similar fashion to that of making **12**: $[\alpha]_D^{25}$ −97 (*c* 2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.91 (s, 3H, CH_3CO), 3.66 (dd, 1H, $J_{6a,6b}$ 12.3, $J_{5,6a}$ 2.7 Hz, H-6a^{III}), 3.87 (dd, 1H, $J_{5,6b}$ 4.2 Hz, H-6b^{III}), 4.03 (ddd, 1H, $J_{4,5}$ 9.8 Hz, H-5^{III}), 4.06–4.23 (m, 2H, CH_2=CHCH_2O–), 4.26–4.41 (m, 4H, H-3^{I}, H-3^{II}, H-5^{I}, H-5^{II}), 4.46 (dd, 1H, $J_{6a,6b}$ 12.2, $J_{5,6}$ 4.8 Hz, H-6), 4.58–4.69 (m, 3H, 3×H-6), 4.94 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1^{II}), 5.10 (d, 1H, $J_{1,2}$ 1.6 Hz, H-1^{I}), 5.19 (dd, 1H, $J_{2,3}$ 3.0 Hz, H-2^{II}), 5.21–5.33 (m, 3H, H-2^{III}, CH_2=CHCH_2O–), 5.36 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1^{III}), 5.54 (dd, 1H, $J_{2,3}$ 3.2, $J_{3,4}$ 10.1 Hz, H-3^{III}), 5.65–5.71 (m, 2H, H-2^{I}, H-4^{III}), 5.85–5.99 (m, 3H, 2×H-4, CH_2=C*H*CH_2O–), 7.21–8.19 (m, 45H, *Ph*). Anal. Calcd for $C_{86}H_{74}O_{26}$: C, 67.80; H, 4.90. Found: C, 67.99; H, 4.92.

3.14. 6-*O*-Acetyl-2,3,4-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 (17)

Compound **16** (980 mg, 0.64 mmol) was treated as described for **6** to afford syrupy **17** (702 mg, 67% for two steps): $[\alpha]_D^{25}$ −99 (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.90 (s, 3H, CH_3CO), 3.70 (dd, 1H, $J_{6a,6b}$ 12.2, $J_{5,6a}$ 2.5 Hz, H-6a^{III}), 3.90 (dd, 1H, $J_{5,6b}$ 4.3 Hz, H-6b^{III}), 4.01–4.06 (m, 1H, H-5^{III}), 4.30–4.52 (m, 5H, H-6, 2×H-3, H-5^{I}, H-5^{II}), 4.57 (dd, 1H, *J* 12.5, $J_{5,6}$ 2.3 Hz, H-6), 4.67–4.72 (m, 2H, 2×H-6), 4.98 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1^{II}), 5.21 (dd, 1H, $J_{2,3}$ 3.0 Hz, H-2^{II}), 5.28 (dd, 1H, $J_{2,3}$ 2.7 Hz, H-2^{III}), 5.40 (d, 1H, $J_{1,2}$ 1.4 Hz, H-1^{III}), 5.55 (dd, 1H, $J_{2,3}$ 3.1, $J_{3,4}$ 10.0 Hz, H-3^{III}), 5.69 (t, 1H,$J_{3,4} = J_{4,5} = 10.0$ Hz, H-4^{III}), 5.87 (dd, 1H, $J_{2,3}$ 3.0 Hz, H-2^{I}), 6.00–6.10 (m, 2H, 2×H-4), 6.56 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1^{I}), 7.22–8.09 (m, 45H, *Ph*), 8.84 (s, 1H, N*H*). Anal. Calcd for $C_{85}H_{70}Cl_3NO_{26}$: C, 62.72; H, 4.33. Found: C, 62.97; H, 4.25.

3.15. Octyl 6-*O*-acetyl-2,3,4-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 → 2)-3,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (18)

Compound **17** (682 mg, 0.42 mmol) and **13** (432 g, 0.40 mmol) were pre-dried in one flask under vacuum at 60 °C for 3 h. The mixture was then dissolved in CH_2Cl_2 (5 mL). To the solution at 0 °C was slowly added Me_3SiOTf (8 μL, 0.04 mmol) under an N_2 atmosphere. The reaction mixture was stirred for 2 h under these conditions, neutralized with Et_3N and concentrated under reduced pressure, then purified by column chromatography using 2:1 petroleum ether–EtOAc as the eluent gave **18** (732 mg, 72%) as a syrup: $[\alpha]_D^{25}$ −104 (*c* 4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.87 (t, 3H, CH_2CH_3), 1.22–1.31 (m, 10H, $CH_2(CH_2)_5CH_3$), 1.52–1.58 (m, 2H, –OCH_2CH_2), 3.31 (dt, 1H, *J* 9.9, 6.5 Hz, –OCH_2), 3.56–3.67 (m, 2H, H-6a^{V}, –OCH_2), 3.79 (dd, 1H, $J_{6a,6b}$ 12.2, $J_{5,6b}$ 3.9 Hz, H-6b^{V}), 3.80–4.05 (m, 4H, 3×H-6, H-5), 4.25–4.37 (m, 6H, H-2^{I}, H-3^{II}, 3×H-5, H-6), 4.39–4.54 (m, 4H, H-3^{III}, H-5, 2×H-6), 4.57–4.70 (m, 3H, H-3^{IV}, 2×H-6), 4.90 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1^{I}), 4.99 (d, 1H, $J_{1,2}$ 1.8 Hz, H-1^{III}), 5.09 (d, 1H, $J_{1,2}$ 1.7 Hz, H-1^{IV}), 5.12 (dd, 1H, $J_{2,3}$ 3.2 Hz, H-2^{III}), 5.15 (dd, 1H, $J_{2,3}$ 4.6 Hz, H-2^{IV}), 5.25 (d, 1H, $J_{1,2}$ 1.5 Hz, H-1^{II}), 5.32 (dd, 1H, $J_{2,3}$ 4.9 Hz, H-2^{II}), 5.36 (d, 1H, $J_{1,2}$ 1.6 Hz, H-1^{V}), 5.51 (dd, 1H, $J_{2,3}$ 3.1, $J_{3,4}$ 10.0 Hz, H-3^{V}), 5.63 (t, 1H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4^{V}), 5.80–5.98 (m, 6H, H-2^{V}, H-3^{I}, 4×H-4), 7.23–8.06 (m, 75H, *Ph*); ^{13}C NMR: δ 14.05, 22.61, 26.03, 29.19, 29.28, 29.35, 31.75 (7C, –OCH_2 (CH_2)$_6$$CH_3$), 20.41 (1C, C$H_3$CO), 62.03, 62.08, 62.30, 63.05, 63.74, 66.32, 67.01, 67.30, 67.62, 68.11, 68.48, 68.73, 69.02, 69.22, 69.32, 69.72, 69.90, 70.97, 71.18, 71.29, 71.52, 75.91, 76.18, 76.40, 77.20, 77.56 (26 C), 98.54, 98.66, 99.17, 99.18, 99.57 (5C-1), 164.42, 164.53, 164.91, 165.06, 165.14, 165.28, 165.34, 165.62, 165.70, 165.77, 165.83, 166.08, 166.14 (15C, Ph*C*O), 170.27 (1C, CH_3*C*O). Anal. Calcd for $C_{145}H_{130}O_{42}$: C, 68.44; H, 5.15. Found: C, 68.56; H, 5.20.

3.16. Octyl 2,3,4-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 → 2)-3,4,6-tri-*O*-benzoyl-α-D-mannopyranoside (19)

To a solution of compound **18** (526 mg, 0.21 mmol) in 2:1 CH_2Cl_2–MeOH (9 mL) was added acetyl chloride (0.4 mL) dropwise in 10 min. The reaction mixture was stirred overnight until the reaction was complete. The mixture was neutralized with pyridine (0.5 mL), co-evaporated with toluene to dryness under diminished pressure, and purified on a silica gel column with 2:1 petroleum ether–EtOAc as the eluent to give syrupy **19**

(480 mg, 93%): $[\alpha]_D^{25}$ −111 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.87 (t, 3H, $-(CH_2)_7CH_3$), 1.23–1.31 (m, 10H, $-CH_2$ $(CH_2)_5CH_3$), 1.52–1.58 (m, 2H, $-OCH_2CH_2$), 3.16 (dd, 1H, $J_{6a,6b}$ 12.1, $J_{5,6a}$ 3.0 Hz, H-6a^V), 3.24–3.33 (m, 2H, H-6b^V and $-OCH_2$), 3.66 (dt, 1H, *J* 9.4, 7.2 Hz, $-OCH_2$), 3.72–3.77 (ddd, 1H, *J* 9.4, 2.2, 3.5 Hz, H-5), 3.85–4.05 (m, 3H, 2×H-6, H-5), 4.25–4.30 (m, 2H, H-3^{II}, H-6), 4.33–4.39 (m, 4H, H-2^I, 2×H-5, H-6), 4.41–4.53 (m, 4H, H-3^{III}, H-5, 2H-6), 4.60–4.71 (m, 3H, H-3^{IV}, 2×H-6), 4.87 (d, 1H, $J_{1,2}$ 1.6 Hz, H-1^I), 4.92 (d, 1H, $J_{1,2}$ 1.8 Hz, H-1^{III}), 5.07–5.12 (m, 2H, H-1^{IV}, H-2^{III}), 5.14 (dd, 1H, $J_{2,3}$ 4.8 Hz, H-2^{IV}), 5.25 (d, 1H, $J_{1,2}$ 1.4 Hz, H-1^{II}), 5.32 (dd, 1H, $J_{2,3}$ 4.9 Hz, H-2^{II}), 5.37 (d, 1H, $J_{1,2}$ 1.5 Hz, H-1^V), 5.55 (dd, 1H, $J_{2,3}$ 3.1, $J_{3,4}$ 9.8 Hz, H-3^V), 5.62 (t, 1H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4^V), 5.80–6.01 (m, 6H, H-2^V, H-3^I, 4×H-4), 7.23–8.10 (m, 75H, *Ph*). Anal. Calcd for $C_{143}H_{128}O_{41}$: C, 68.63; H, 5.16. Found: C, 68.98; H, 5.25.

3.17. Octyl 6-*O*-(sulfo)-2,3,4-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 → 2)-3,4,6-tri-*O*-benzoyl-α-D-mannopyranoside, sodium salt (20)

To a solution of compound **19** (460 mg, 0.184 mmol) in dry pyridine (5 mL) was added sulfur trioxide–pyridine complex (146 mg, 0.92 mmol). The reaction mixture was heated to 60 °C and stirred for 48 h at this temperature. The reaction was quenched by addition of MeOH (1 mL) and stirred for another 1 h. The solvent was evaporated, and the residue was purified by flash chromatography on a silica gel column (EtOAc), followed by ion exchange on a Dowex-50 (Na^+) column, giving **20** (436 mg, 91%) as a syrup: $[\alpha]_D^{25}$ −102 (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.88 (t, 3H, $-(CH_2)_7CH_3$), 1.22–1.33 (m, 10H, $-CH_2(CH_2)_5CH_3$), 1.53–1.58 (m, 2H, $-OCH_2CH_2$), 3.32, 3.66 (2 dt, 2H, *J* 9.5, 6.9 Hz, OCH_2), 3.70–4.01 (m, 5H, 2×H-5, 3×H-6), 4.21–4.41 (m, 7H, H-2^I, H-3^{II}, 2×H-5, 3×H-6), 4.42–4.70 (m, 7H, H-3^{III}, H-3^{IV}, H-5, 4×H-6), 4.75, 4.93, 5.08 (br s, 3H, 3×H-1), 5.13, 5.19 (br d, 2H, 2×H-2), 5.27–5.33 (m, 2H, H-1, H-2), 5.37 (br s, 1H, H-1), 5.45 (dd, 1H, $J_{2,3}$ 2.8, $J_{3,4}$ 9.7 Hz, H-3), 5.71–6.01 (m, 7H, H-2, H-3, 5×H-4), 7.19–8.06 (m, 75H, *Ph*). Anal. Calcd for $C_{143}H_{127}NaO_{44}S$: C, 65.94; H, 4.91. Found: C, 66.27; H, 5.01.

3.18. Octyl 6-*O*-(sulfo)-α-D-mannopyranosyl-(1 → 3)-α-D-mannopyranosyl-(1 → 3)-α-D-mannopyranosyl-(1 → 3)-α-D-mannopyranosyl-(1 → 2)-α-D-mannopyranoside, sodium salt (1c)

To a solution of compound **20** (380 mg, 0.146 mmol) in anhyd MeOH (15 mL) was added 1 N NaOMe–MeOH until pH 9–10 was reached. The mixture was stirred at rt overnight, then neutralized with Amberlite IR-120 (H^+). The solvents were filtered, and the filtrate was concentrated to dryness under diminished pressure finished **1c** (147 mg, 97%) as a white solid; $[\alpha]_D^{25}$ −3 (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.72 (t, 3H, $-CH_2$ CH_3), 1.12–1.24 (m, 10H, $CH_2(CH_2)_5CH_3$), 1.44–1.52 (m, 2H, $-OCH_2CH_2$), 3.40, 3.49 (2 dt, 2H, *J* 9.2, 7.0 Hz, OCH_2), 3.50–4.17 (m, 29H), 4.25 (br d, 1H, H-3), 4.87 (br s, 1H, H-1), 4.95 (br s, 1H, H-1), 4.97–5.01 (br s, 3H, 3×H-1); ^{13}C NMR: 14.12, 22.76, 26.09, 29.12, 29.18, 31.82 (7C, $-OCH_2(CH_2)_6CH_3$ some overlapped), 61.62, 61.72, 66.74, 66.84, 66.95, 67.25, 67.66, 68.40, 68.76, 70.26, 70.34, 70.47, 70.65, 70.94, 71.07, 72.10, 73.48, 74.11, 74.21, 78.64, 79.09, 79.45, 79.68 (26 C, some overlapped), 98.74, 102.73, 102.98, 103.11, 103.43 (5 C, 5×C-1). ESIMS (negative ion): Calcd for $C_{38}H_{67}NaO_{29}S$: 1042.34 [M]; Found: 1019.1 $[M-Na]^-$.

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