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Synthesis of β-D-Glc*p*NAc-(1→3)-α-L-Rha*p*-(1→2)-[β-L-Xyl*p*-(1→4)]-α-L-Rha*p*-(1→3)-α-L-Rha*p*, the repeating unit of the O-antigen produced by *Pseudomonas solanacearum* **ICMP 7942**

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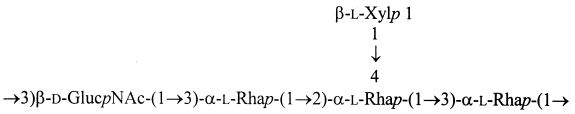
Abstract

An efficient synthesis of β-D-Glc*p*NAc-(1→3)-α-L-Rha*p*-(1→2)-[β-L-Xyl*p*-(1→4)]-α-L-Rha*p*-(1→3)-α-L-Rha*p*, the repeating unit of the O-antigen produced by *Pseudomonas solanacearum* **ICMP 7942** and its isomer β-D-Glc*p*NAc-(1→3)-α-L-Rha*p*-(1→4)-[β-L-Xyl*p*-(1→2)]-α-L-Rha*p*-(1→3)-α-L-Rha*p* was achieved via sequential assembly of the building blocks, allyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**2**), allyl 3,4-*O*-isopropylidene-α-L-rhamnopyranoside (**3**), allyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**6**), 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate (**7**), and 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl trichloroacetimidate (**12**). The process was carried out in a regio- and stereoselective manner using glycosyl trichloroacetimidates as donors and unprotected or partially protected rhamnopyranosides as acceptors in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf).

Keywords: Oligosaccharide; Rhamnose; Glucosamine

1. Introduction

It was reported that the repeating unit of O-antigen produced by *Pseudomonas solanacearum* **ICMP 7942** is a branched pentasaccharide with a backbone consisting of one β-D-Glc*p*NAc and three α-L-Rha*p* residues, and a β-L-Xyl*p* group attached as a side chain to one of the α-L-Rha*p* residues:[1]



Pseudomonas solanacearum is a phytopathogenic, gram-negative microorganism having many heterogeneous biological and biochemical properties.[2–4] Each of the *P. solanacearum* strains is characterized by an O-antigen consisting of more than one type of repeating unit.[5] Synthesis of these compounds and their isomers can help to provide a detailed knowledge of the chemical behavior and the structure–bioactivity relationships among these oligosaccharides.

Rhamnose-containing oligosaccharides are widely distributed in natural products, such as triterpenoid glycosides,[6] K-antigens,[7] and a series of phenolic glycolipids from mycobacteria.[8] Synthesis of these target compounds will need orthogonal masking groups and multiple protection–deprotection steps if traditional stepwise methods[9,10] are used. Our previous work on regio- and stereoselective syntheses of rhamnans revealed that very high 3-selectivity was achieved when unprotected rhamnose residue was used as acceptor, and good 2-selectivity was obtained when a rhamnose residue with 2,3-free OH groups was the acceptor,[11,12] As part of our ongoing research project on the synthesis of rhamnans, we present herein the synthesis of the well-defined Glc*p*NAc-containing rhamnan pentasaccharide and its isomer.

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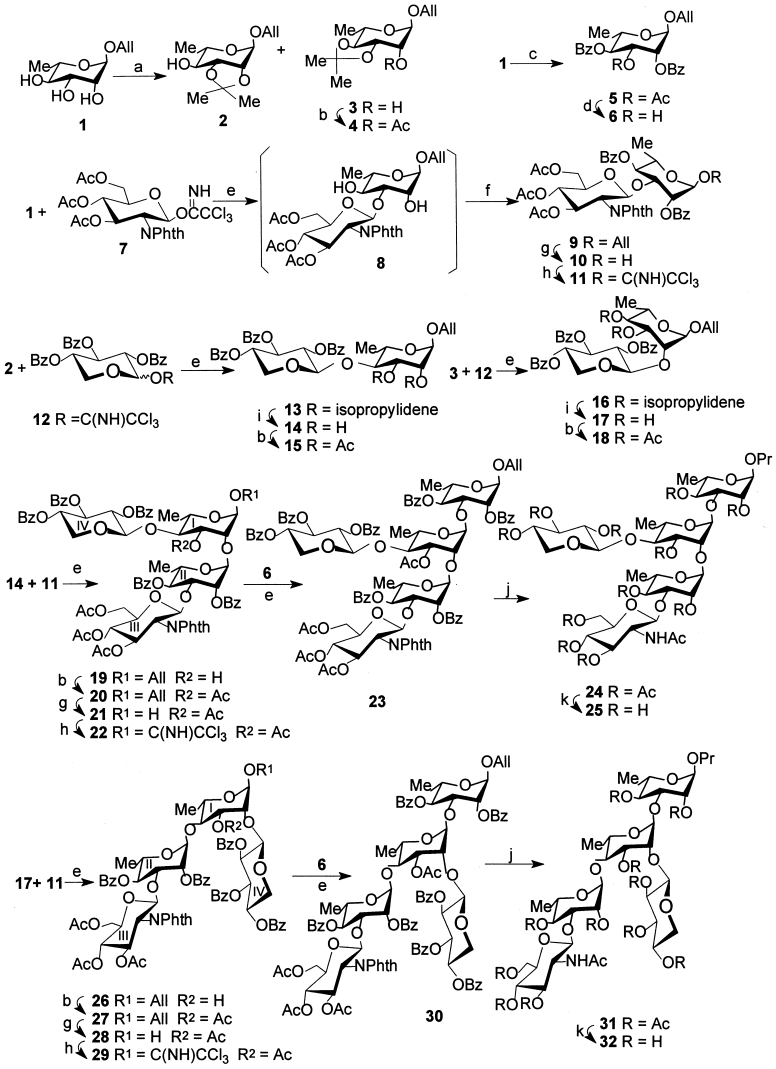
2. Results and discussion

As shown in Scheme 1, condensation of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate (**7**) with unprotected allyl α-L-rhamnopyranoside (**1**) selectively gave allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranoside (**8**) in satisfactory yield (59.5%). Keeping the temperature below −20 °C during the addition of TMSOTf was necessary in order to avoid byproduct formation. The (1→3)-linkage was confirmed by benzoylation of **8** to give **9**, whereby the ^{1}H NMR spectrum of **9** showed characteristic signals at δ 4.31 ppm (dd, $J_{2,3}$ 3.7, $J_{3,4}$ 9.8) for H-3 and δ 5.51 ppm (dd, $J_{1,2}$ 1.8, $J_{2,3}$ 3.7) for H-2, and 5.28 ppm (dd, $J_{3,4} = J_{4,5} = 9.7$) for H-4, respectively. Deallylation with $PdCl_2$, followed by trichloroacetimidation with CCl_3CN in the presence of DBU or K_2CO_3,[13] gave the disaccharide donor **11**. It is known that 4,6-*O*-isopropylidenation of glucose, mannose and their glycosides is efficiently achieved in DMF using 2-methoxypropene in the presence of TsOH.[14] However, reaction of allyl ramnoside under the same conditions surprisingly gave allyl 3,4-*O*-isopropylidene-α-L-rhamnopyranoside (**3**) as the main product, rather than 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**2**). The structure of **3** was confirmed by acetylation to give allyl 2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-rhamnopyranoside (**4**), showing



Scheme 1. Conditions and reagents: (a) 2-methoxypropene, *p*-TsOH, DMF (25 mL), rt, 2 h; 30.3% for **2**; 62.3% for **3**; (b) Ac_2O–Pyridine (dry); 82.4% for **4**; 80.1% for **15**; 83.3% for **18**; (c) i: AcCl–CH_2Cl_2, Pyridine–CH_2Cl_2 0 °C to rt, 2 h; ii: BzCl, rt, 12 h; 79.3% for two steps; (d) 3% CH_3COCl–methanol, rt, 12–14 h; 87.9%; (e) TMSOTf, CH_2Cl_2; 81.9% for **19**; 71.4% for **23**; 88.8% for **26**; 85.2% for **30**; (f) BzCl–Pyridine (dry); 59.5% from **1**; (g) $PdCl_2$, 90% HOAc–NaOAc, rt, 12 h; 94.0% for **10**; 87.7% for **21**; (h) CCl_3CN, DBU, CH_2Cl_2 8 h; 88.9% for **11**; 80.3% for **22**; 66.8% for **29** from **27**; (i) 90% TFA, rt, 2 h; 82.7% for **14**; 83.2% for **17**; (j) i: EtOH–10% hydrazine hydrate, reflux, 48 h; ii: Ac_2O–Pyridine (dry), rt, 12 h; 78.7% for **24** for two steps; 81.8% for **31** for two steps; (k) satd NH_3–MeOH, rt, 72 h; 80.4% for **25**; 82.8% for **32**.

characteristic signals at δ 5.36 ppm (dd, $J_{1,2}$ 0.8, $J_{2,3}$ 2.9 Hz) for H-2 in its ^{1}H NMR spectrum. Coupling of 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl trichloroacetimidate (**12**) with 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**2**) in the presence of a catalytic amount of TMSOTf gave (1→4)-linked disaccharide **13** in high yield, which could be used in the next step without purification. *O*-Deisopropylidenation of **13** in 90% trifluoroacetic acid (TFA) at room temperature furnished the diol **14** in 82.7% overall yield. In the same way, compound **16** could be obtained by condensation of **3** and **12**, its 3,4-*O*-deisopropylidenation gave the (1→2)-linked disaccharide acceptor **17** in satisfactory yield (83.2% for two steps). Both structures of **14** and **17** were confirmed by acetylation to give allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→4)-2,3-*O*-acetyl-α-L-rhamnopyranoside (**15**), showing characteristic signals at δ 3.67 ppm (dd, $J_{3,4} = J_{4,5} = 9.6$ Hz) for H-4, and allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→2)-3,4-*O*-acetyl-α-L-rhamnopyranoside (**18**), showing characteristic signals at δ 4.08 ppm (dd, $J_{1,2}$ 1.6, $J_{2,3}$ 3.4) for H-2, respectively, in their ^{1}H NMR spectra.

As we expected, condensation of the diol acceptor **14** with the disaccharide donor **11** at −20 °C selectively gave 2-*O*-glycosylated tetrasaccharide **19** (81.9%) in dichloromethane in the presence of TMSOTf. Acetylation of compound **19** with acetic anhydride in pyridine, followed by deallylation with $PdCl_2$ and trichloroacetimidation with CCl_3CN in the presence of DBU or K_2CO_3, gave the tetrasaccharide donor **22** (70.4% from **19**). The ^{1}H NMR spectrum of **22** gave H-3^{I} (5.33 ppm, $J_{2,3}$ 3.2, $J_{3,4}$ 9.7 Hz) as a downfield doublet of doublets, and H-3^{II} as an upfield signal, (4.27 ppm, $J_{2,3}$ 3.4, $J_{3,4}$ 9.8 Hz), confirming the structure of **19**. Similarly, coupling of the diol acceptor **17** with **11** selectively gave 4-*O*-glycosylated tetrasaccharide **26** (88.8%). The selectivity was confirmed by acetylation of **26**, then deallylation and trichloroacetimidation, giving the tetrasaccharide donor **29** (66.8% from **26**). ^{1}H NMR spectrum of **29** showed two characteristic rhamnose H-3 signals at δ 5.02 (dd, $J_{2,3}$ 3.1, $J_{3,4}$ 9.8 Hz, H-3^{I}) and 4.35 (dd, $J_{2,3}$ 3.2, $J_{3,4}$ 9.7 Hz, H-3^{II}), respectively. These stereoselective results further revealed that steric factor of the acceptor plays an important role in their glycosylation reactions.

Treatment of allyl α-L-rhamnopyranoside (**1**) with 1.1 equiv of acetyl chloride and 10.0 equiv of pyridine in dry dichloromethane selectively gave allyl 3-*O*-acetyl-α-L-rhamnopyranoside. Without working up, the mixture was benzoylated with benzoyl chloride to give allyl 3-*O*-acetyl-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**5**) in a total yield of 79.3%. Structure of **5** was confirmed by selective deacetylation[15] to give allyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**6**), showing characteristic signals at δ 4.34 ppm (dd, $J_{2,3}$ 3.5, $J_{3,4}$ 10.0) for H-3, δ 5.41 ppm (dd, $J_{1,2}$ 1.7, $J_{2,3}$ 3.5) for H-2, and 5.28 ppm (dd, $J_{3,4} = J_{4,5} = 10.0$) for H-4, respectively, in its ^{1}H NMR spectrum. With the tetrasaccharide donor **22** or **29** and the monosaccharide acceptor **6** in hand, the pentasaccharide **23** or **30** was readily obtained by coupling of the donor and acceptor in dichloromethane in the presence of TMSOTf.

Hydrazinolysis to remove the phthalimido group from **23** or **30** was carried out in 10% hydrazine hydrate–EtOH under reflux, and it was accompanied by reduction of the allyl group and debenzoylation. Subsequent acetylation of the resultant product with acetic anhydride in pyridine readily gave acetylated pentasaccharide **24** or **31**. Their ^{1}H NMR spectra showed a characteristic signal at δ 5.56 ppm (J 6.4 Hz), or 5.55 ppm (J 6.6 Hz) as a broad doublet for AcN*H*. Finally deacylation of **24** or **31** in ammonia-saturated methanol gave the target pentasaccharide **25** or **32**. Their bioassays are in progress and will be reported in due course.

In summary, branched pentasaccharides, containing D-Glc*p*NAc, L-xylose and rhamnose, were synthesized in a highly regioselective way with a simple procedure. Large-scale preparations can be performed with this method.

3. Experimental

3.1. General methods

Melting points were determined with a 'Mel-Temp' apparatus. Optical rotations were determined with a Perkin–Elmer model 241-MC automatic polarimeter for solutions in a 1-dm, jacketed cell. ^{1}H NMR and ^{13}C NMR spectra were recorded with Varian XL-400 and Varian XL-200 spectrometers for solutions in $CDCl_3$ or in D_2O as indicated. Chemical shifts are expressed in ppm downfield from the Me_4Si absorption. Mass spectra were recorded with a VG PLATFORM mass spectrometer using the ESI mode. Thin-layer chromatography (TLC) was performed on silica gel HF with detection by charring with 30% (v/v) sulfuric acid in MeOH or by UV detection. Column chromatography was conducted by elution of a column (8 × 100, 16 × 240, 18 × 300, 35 × 400 mm) of silica gel (100–200 mesh) and EtOAc–petroleum ether (bp 60–90 °C) as the eluent. Analytical LC was performed with a Gilson HPLC consisting of a pump (model 306), stainless steel column packed with silica gel (Spherisorb SiO_2, 10 × 300 mm or 4.6 × 250 mm), differential refractometer (132-RI Detector), UV–Vis detector (model 118). EtOAc–petroleum ether (bp 60–90 °C) was used as the eluent at a flow rate of 1–4 mL/min. Solutions were concentrated at a temperature < 60 °C under diminished pressure.

3.2. Preparation of allyl 3,4-*O*-isopropylidene-α-L-rhamnopyranoside (3)

To a solution of allyl α-L-rhamnoside (**1**) (2.04 g, 10 mmol) in anhyd DMF (25 mL) was added *p*-toluenesulfonic acid monohydrate (19 mg, 0.1 mmol) and 2-methoxypropene (1.5 mL, 15 mmol) under N_2 protection. The mixture was stirred at room temperature (rt) for 2 h, and TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. Sodium bicarbonate (2.52 g, 30 mmol) was added to the reaction mixture, and the mixture was stirred for additional 1 h. After filtration, the mixture was concentrated in vacuo to give a residue, which was subjected to silica gel column chromatography (3:1 petroleum ether–EtOAc) to give **2** (0.74 g, 30.3%) and **3** (1.52 g, 62.3%) as colorless oils. For **2**: $[\alpha]_D$ −33.5° (*c* 1.1, $CHCl_3$); lit.[16] $[\alpha]_D$ −36.6° (*c* 1.0, $CHCl_3$). For **3**: $[\alpha]_D$ −43.3° (*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 5.89 (m, 1 H, OCH_2CH=CH_2), 5.33–5.19 (m, 2 H, OCH_2CH=CH_2), 4.83 (d, 1 H, $J_{1,2}$ 1.4, H-1), 4.19–4.00 (m, 2 H, OCH_2CH=CH_2), 3.96 (dd, 1 H, $J_{1,2}$ 1.4, $J_{2,3}$ 3.4 Hz, H-2), 3.78 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 9.6 Hz, H-3), 3.71 (m, 1 H, H-5), 3.41 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.6$ Hz, H-4), 1.45 (s, 3 H, $C(CH_3)_2$), 1.35 (s, 3 H, $C(CH_3)_2$), 1.31 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6). Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.26. Found: C, 58.89; H, 8.02.

3.3. Allyl 2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-rhamnopyranoside (4)

To a solution of **3** (73 mg, 0.3 mmol) in Py (5 mL) was added Ac_2O (2.0 mL, 2 mmol). The reaction mixture was stirred at rt for 12 h, at the end of which time TLC (4:1 petroleum ether–EtOAc) indicated that the reaction was complete. The reaction mixture was concentrated, and then the residue was purified by flash column chromatography on a silica gel column (4:1 petroleum ether–EtOAc) to give compound **4** (70 mg, 82.4%) as a syrup: $[\alpha]_D$ −30.3° (*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 5.89 (m, 1 H, OCH_2CH=CH_2), 5.36 (dd, 1 H, $J_{1,2}$ 0.8, $J_{2,3}$ 2.9 Hz, H-2), 5.33–5.20 (m, 2 H, OCH_2CH=CH_2), 4.86 (d, 1 H, $J_{1,2}$ 0.8, H-1), 4.21–3.98 (m, 2 H, OCH_2CH=CH_2), 3.93 (m, 1 H, H-5), 3.88 (dd, 1 H, $J_{2,3}$ 2.9, $J_{3,4}$ 9.5 Hz, H-3), 3.52 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 2.12 (s, 3 H, $COCH_3$), 1.44 (s, 3 H, $C(CH_3)_2$), 1.42 (s, 3 H, $C(CH_3)_2$), 1.35 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6). Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.75. Found: C, 58.93; H, 7.50.

3.4. Allyl 3-*O*-acetyl-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (5)

Allyl α-L-rhamnopyranoside (**1**) (2.04 g, 10 mmol) was dissolved in dry CH_2Cl_2 (40 mL) containing Py (8.1 mL, 100 mmol), then under N_2 protection, AcCl (0.8 mL, 11 mmol) in anhyd CH_2Cl_2 (10 mL) was added dropwise to the solution within 30 min at 0 °C. The reaction mixture was slowly raised to rt and stirred for 2 h, at the end of which time TLC (1:2 petroleum ether–EtOAc) indicated that the reaction was complete. Benzoyl chloride (3.0 mL, 25 mmol) was added to the reaction mixture, and stirring was continued until TLC (4:1 petroleum ether–EtOAc) indicated that the reaction was complete. The reaction mixture was diluted with CH_2Cl_2 (100 mL), washed with water, 1 N HCl, and dried (Na_2SO_4). The solution was concentrated, and purification of the residue by flash column chromatography on a silica gel column (4:1 petroleum ether–EtOAc) gave compound **5** (3.60 g, 79.3%) as a syrup. $[\alpha]_D$ +76.3° (*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.13–7.26 (m, 10 H, 2 Bz–H), 5.98 (m, 1 H, OCH_2CH=CH_2), 5.65 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.1 Hz, H-3), 5.54 (dd, 1 H, $J_{1,2}$ 1.7, $J_{2,3}$ 3.4 Hz, H-2), 5.47 (dd, 1 H, $J_{3,4} = J_{4,5} = 10.1$ Hz, H-4), 5.39–5.25 (m, 2 H, OCH_2CH=CH_2), 4.98 (d, 1 H, $J_{1,2}$ 1.7, H-1), 4.21–4.06 (m, 3 H, H-5, OCH_2CH=CH_2), 1.86 (s, 3 H, $COCH_3$), 1.32 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6). Anal. Calcd for $C_{25}H_{26}O_8$: C, 66.07; H, 5.77. Found: C, 66.28; H, 5.50.

3.5. Allyl 2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (6)

To a solution of **5** (2.27 g, 5 mmol) in anhyd MeOH (50 mL) was added AcCl (1.5 mL) at 0 °C. The solution was stoppered in a flask and stirred at rt until TLC (3:1 petroleum ether–EtOAc) showed that the starting material disappeared. The solution was neutralized with Et_3N, then concentrated to dryness. The residue was passed through a short silica gel column to give **6** (1.81 g, 87.9%) as a syrup: $[\alpha]_D$ +46.7° (*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.12–7.45 (m, 10 H, 2 Bz–H), 5.97 (m, 1 H, OCH_2CH=CH_2), 5.41 (dd, 1 H, $J_{1,2}$ 1.7, $J_{2,3}$ 3.5 Hz, H-2), 5.39–5.25 (m, 2 H, OCH_2CH=CH_2), 5.28 (dd, 1 H, $J_{3,4} = J_{4,5} = 10.0$ Hz, H-4), 5.02 (d, 1 H, $J_{1,2}$ 1.7, H-1), 4.34 (dd, 1 H, $J_{2,3}$ 3.5, $J_{3,4}$ 10.0 Hz, H-3), 4.27–4.05 (m, 3 H, H-5, OCH_2CH=CH_2), 1.33 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6). Anal. Calcd for $C_{23}H_{24}O_7$: C, 66.98; H, 5.87. Found: C, 66.73; H, 5.52.

3.6. Allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (9)

3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate (**7**) (5.80 g, 10 mmol) and allyl α-L-rhamnopyranoside (**2**) (2.04 mg, 10 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (40 mL). TMSOTf (60 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 raised

to ambient temperature. Then the mixture was neutralized with Et_3N, and concentrated to dryness under reduced pressure to afford the crude allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranoside (**8**). To a solution of crude **8** in Py (20 mL), benzoyl chloride (3.5 mL, 30 mmol) was added dropwise, and the mixture was stirred overnight at rt. TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. Ice water was added, and the mixture was diluted with CH_2Cl_2, washed with 1 N HCl, water, and satd aq $NaHCO_3$. The organic layer was combined, dried, and concentrated. Purification of the crude product by column chromatography (3:1 petroleum ether–EtOAc) gave **9** (4.93 g, 59.5% for two steps) as a syrup: $[\alpha]_D$ +40.8° (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.10–7.18 (m, 14 H, Ph), 5.97 (m, 1 H, $CH_2CH{=}CH_2$), 5.64–5.55 (m, 2 H, H-3′, H-4′), 5.51 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.7 Hz, H-2), 5.38–5.25 (m, 2 H, $OCH_2CH{=}CH_2$), 5.28 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 5.03 (d, 1 H, $J_{1',2'}$ 9.1 Hz, H-1′), 4.99 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.31 (dd, 1 H, $J_{2,3}$ 3.7, $J_{3,4}$ 9.8, H-3), 4.24–4.17 (m, 2 H, H-2′, $OCH_2CH{=}CH_2$), 4.13–4.11 (m, 2 H), 4.05 (m, 1 H, $OCH_2CH{=}CH_2$), 3.92–3.83 (m, 2 H), 1.95 (s, 3 H, $COCH_3$), 1.91 (s, 3 H, $COCH_3$), 1.71 (s, 3 H, $COCH_3$), 1.22 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 169.5, 168.7, 165.5, 164.4, 98.1, 96.0, 76.0, 72.0, 71.8, 71.1, 70.1, 68.3, 68.2, 65.8, 61.4, 54.1, 20.2, 19.9, 19.7, 17.0. Anal. Calcd for $C_{43}H_{43}NO_{16}$: C, 62.24; H, 5.22. Found: C, 62.28; H, 5.56.

3.7. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate (11)

To a solution of allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**9**) (4.15 g, 5 mmol) in 90% HOAc (50 mL) containing NaOAc (1.46 g, 15 mmol) was added $PdCl_2$ (270 mg, 2.5 mmol), and the mixture was stirred for 12 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was diluted with CH_2Cl_2 (150 mL), washed with water and satd aq $NaHCO_3$. The organic layer was concentrated, and the residue was passed through a short silica gel column with 2:1 petroleum ether–EtOAc as the eluent to give crude 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α,β-L-rhamnopyranose (**10**) (3.71 g, 94.0%). Compound **10** was dissolved in CH_2Cl_2 (30 mL), and CCl_3CN (1.0 mL, 10 mmol) and DBU (135 μL, 0.9 mmol) were added. The reaction mixture was stirred for 2 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. Concentration of the reaction mixture, followed by purification of the crude product on a silica gel column with 2:1 petroleum ether–EtOAc as the eluent, furnished the disaccharide donor **11** (3.90 g, 88.8%) as a syrup: $[\alpha]_D$ +38.4° (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.80 (s, 1 H, $CNHCCl_3$), 8.12–7.22 (m, 14 H, Ph), 6.42 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1), 5.69 (dd, 1 H, $J_{1,2}$ 1.9, $J_{2,3}$ 3.5 Hz, H-2), 6.63 (dd, 1 H, $J_{2',3'}$ 10.7, $J_{3',4'}$ 10.0 Hz, H-3′), 5.58 (d, 1 H, $J_{1',2'}$ 8.3 Hz, H-1′), 5.44 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4), 5.04 (dd, 1 H, $J_{3',4'} = J_{4',5'} = 10.0$ Hz, H-4′), 4.38 (dd, 1 H, $J_{2,3}$ 3.5, $J_{3,4}$ 9.8 Hz, H-3), 4.22 (dd, 1 H, $J_{1',2'}$ 8.3, $J_{2',3'}$ 10.7 Hz, H-2′), 4.11–3.83 (m, 4 H), 1.96 (s, 3 H, $COCH_3$), 1.71 (s, 3 H, $COCH_3$), 1.58 (s, 3 H, $COCH_3$), 1.15 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6). Anal. Calcd for $C_{42}H_{39}Cl_3N_2O_{16}$: C, 54.00; H, 4.21. Found: C, 53.81; H, 4.38.

3.8. Allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→4)-α-L-rhamnopyranoside (14)

2,3,4-Tri-*O*-benzoyl-α-L-xylopyranosyl trichloroacetimidate (**12**) (6.07 g, 10.0 mmol) and allyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**2**) (2.44 g, 10.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (50 mL). TMSOTf (18.0 μL, 0.10 mmol) was added dropwise at −0 °C with N_2 protection. The reaction mixture was stirred for 2 h, during which time the temperature was gradually warmed to ambient temperature. Then the mixture was neutralized with Et_3N and concentrated to dryness under reduced pressure to afford the crude allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**13**). Compound **13** was dissolved in 90% TFA (50 mL) and stirred for 2 h, at the end of which time the reaction mixture was poured into toluene (200 mL), and then the mixture was concentrated. The residue was purified by flash chromatography (1:1 petroleum ether–EtOAc) to give **14** (5.36 g, 82.7% for two steps) as a syrup: $[\alpha]_D$ −9.6° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.97–7.32 (m, 15 H, 3 Ph), 5.89–5.81 (m, 2 H, H-3′, $OCH_2CH{=}CH_2$), 5.53 (dd, 1 H, $J_{1',2'}$ 7.5, $J_{2',3'}$ 9.4 Hz, H-2′), 5.39 (m, 1 H, H-4′), 5.27–5.15 (m, 2 H, $OCH_2CH{=}CH_2$), 4.81 (d, 1 H, $J_{1,2}$ 0.8 Hz, H-1), 4.79 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′), 4.50 (dd, 1 H, *J* 5.3, *J* 11.6 Hz, H-5′$_e$), 4.08–4.02 (m, 2 H, H-2, $OCH_2CH{=}CH_2$), 3.94–3.86 (m, 2 H, H-3, $OCH_2CH{=}CH_2$), 3.70–3.61 (m, 2 H, H-5, H-5′$_a$), 3.46 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 1.06 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6). Anal. Calcd for $C_{35}H_{36}O_{12}$: C, 64.81; H, 5.59. Found: C, 64.72; H, 5.38.

3.9. Allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→4)-2,3-di-*O*-acetyl-α-L-rhamnopyranoside (15)

To a solution of allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→4)-α-L-rhamnopyranoside (**14**) (65 mg, 0.1 mmol) in Py (5 mL) was added Ac_2O (1.0 mL, 1 mmol). The reaction mixture was stirred at rt for 12 h, at the

end of which time TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The reaction mixture was concentrated, and purification of the residue by flash column chromatography on a silica gel column (3:1 petroleum ether–EtOAc) gave compound **15** (586 mg, 80.1%) as a syrup: $[\alpha]_D$ +10.3° (*c* 1.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.05–7.32 (m, 15 H, 3 Ph), 5.83 (m, 1 H, $CH_2CH{=}CH_2$), 5.72 (dd, 1 H, $J_{2',3'} = J_{3',4'} = 6.4$ Hz, H-3′), 5.38 (dd, 1 H, $J_{2,3}$ 3.6, $J_{3,4}$ 9.6 Hz, H-3), 5.32–5.17 (m, 5 H, H-2, H-2′, H-4′, $OCH_2CH{=}CH_2$), 4.95 (d, 1 H, $J_{1',2'}$ 4.6 Hz, H-1′), 4.71 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.44 (dd, 1 H, *J* 3.8, *J* 12.4 Hz, H-5′$_e$), 4.09 (m, 1 H, $OCH_2CH{=}CH_2$), 3.93 (m, 1 H, $OCH_2CH{=}CH_2$), 3.77–3.71 (m, 2 H, H-5, H-5′$_a$), 3.67 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.6$ Hz, H-4), 2.13 (s, 3 H, $COCH_3$), 2.06 (s, 3 H, $COCH_3$), 1.23 (d, 3 H, $J_{5,6}$ 6.0 Hz, H-6). Anal. Calcd for $C_{39}H_{40}O_{14}$: C, 63.93; H, 5.50. Found: C, 63.42; H, 5.38.

3.10. Allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1 → 2)-α-L-rhamnopyranoside (17)

2,3,4-Tri-*O*-benzoyl-α-L-xylopyranosyl trichloroacetimidate (**12**) (6.06 g, 10.0 mmol) and allyl 3,4-*O*-isopropylidene-α-L-rhamnopyranoside (**3**) (2.44 g, 10.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (50 mL). TMSOTf (18 μL, 0.1 mmol) was added dropwise at 0 °C with N_2 protection. The reaction mixture was stirred for 2 h, during which time the temperature was gradually warmed to ambient temperature. Then the mixture was neutralized with Et_3N and concentrated to dryness under reduced pressure to afford the crude allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1 → 2)-3,4-*O*-isopropylidene-α-L-rhamnopyranoside (**16**). Compound **16** was dissolved in 90% TFA (50 mL) and the mixture was stirred for 2 h, at the end of which time the reaction mixture was poured into toluene (200 mL), and then the mixture was concentrated. The residue was purified by flash chromatography (1:1 petroleum ether–EtOAc) to give **17** (5.39 g, 83.2% for two steps) as a syrup. $[\alpha]_D$ +6.0° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.97–7.33 (m, 15 H, 3 Ph), 5.84–5.75 (m, 2 H, H-3′, $OCH_2CH{=}CH_2$), 5.44 (dd, 1 H, $J_{1',2'}$ 6.6, $J_{2',3'}$ 8.4 Hz, H-2′), 5.36 (m, 1 H, H-4′), 5.21–5.10 (m, 2 H, $OCH_2CH{=}CH_2$), 4.84 (d, 1 H, $J_{1',2'}$ 6.6 Hz, H-1′), 4.66 (d, 1 H, $J_{1,2}$ 1.0 Hz, H-1), 4.50 (dd, 1 H, *J* 4.8, *J* 11.8 Hz, H-5′$_e$), 4.05 (m, 1 H, $OCH_2CH{=}CH_2$), 4.00 (dd, 1 H, $J_{1,2}$ 1.0, $J_{2,3}$ 3.1, H-2), 3.82–3.66 (m, 3 H, H-3, H-5′, $OCH_2CH{=}CH_2$), 3.54 (m, 1 H, H-5), 3.34 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 2.62 (bs, 2 H, 2 O*H*), 1.06 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6). Anal. Calcd for $C_{35}H_{36}O_{12}$: C, 64.81; H, 5.59. Found: C, 64.67; H, 5.50.

3.11. Allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1 → 2)-3,4-di-*O*-acetyl-α-L-rhamnopyranoside (18)

To a solution of allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1 → 2)-α-L-rhamnopyranoside (**17**) (65 mg, 0.1 mmol) in Py (5 mL) was added Ac_2O (1.0 mL, 1 mmol). The reaction mixture was stirred at rt for 12 h, at the end of which time TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The reaction mixture was concentrated, and purification of the residue by flash column chromatography on a silica gel column (3:1 petroleum ether–EtOAc) gave compound **18** (61 mg, 83.3%) as a syrup: $[\alpha]_D$ +8.4° (*c* 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.05–7.24 (m, 15 H, 3 Ph), 5.77 (m, 1 H, $CH_2CH{=}CH_2$), 5.58 (dd, 1 H, $J_{2',3'} = J_{3',4'} = 6.7$ Hz, H-3′), 5.28 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 9.9 Hz, H-3), 5.32–5.17 (m, 4 H, H-2′, H-4′, $OCH_2CH{=}CH_2$), 5.07 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4), 4.85 (d, 1 H, $J_{1',2'}$ 4.6 Hz, H-1′), 4.73 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.55 (dd, 1 H, *J* 3.0, *J* 12.6 Hz, H-5′), 4.08 (dd, 1 H, $J_{1,2}$ 1.6, $J_{2,3}$ 3.4, H-2), 4.03 (m, 1 H, $OCH_2CH{=}CH_2$), 3.86 (m, 1 H, $OCH_2CH{=}CH_2$), 3.73–3.67 (m, 2 H, H-5, H-5′), 2.15 (s, 3 H, $COCH_3$), 2.06 (s, 3 H, $COCH_3$), 1.22 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6). Anal. Calcd for $C_{34}H_{40}O_{14}$: C, 63.93; H, 5.50. Found: C, 64.00; H, 5.35.

3.12. Allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosy-(1 → 2)-[2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1 → 4)]-α-L-rhamnopyranoside (19)

3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate (**11**) (4.7 g, 5 mmol) and allyl 2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1 → 4)-α-L-rhamnopyranoside (**14**) (3.3 g, 5 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (40 mL). TMSOTf (36 μL, 0.2 mmol) 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 raised to ambient temperature. Then the mixture was neutralized with Et_3N, and concentrated. Purification of the crude product by column chromatography (2:1 petroleum ether–EtOAc) gave **19** (5.81 g, 81.9%) as a syrup: $[\alpha]_D$ +3.9° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.12–7.22 (m, 29 H, 5 Ph, Phth), 5.86 (m, 1 H, $OCH_2CH{=}CH_2$), 5.84 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4^{II}), 5.76 (dd, 1 H, $J_{1,2}$ 1.0, $J_{2,3}$ 2.7 Hz, H-2^{II}), 5.70 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H-3^{IV}), 5.51–5.47 (m, 2 H, H-1^{III}, H-2^{IV}), 5.38–5.32 (m, 2 H, H-3^{III}, H-4^{IV}), 5.25 (m, 1 H, $OCH_2CH{=}CH_2$), 5.18 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1^{II}), 5.16 (m, 1 H, $OCH_2CH{=}CH_2$), 5.12 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4^{III}), 4.84 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1^{IV}), 4.76 (d, 1 H, $J_{1,2}$ 0.8 Hz, H-1^{I}), 4.32–4.21 (m, 4

H), 5.10–5.06 (m, 2 H), 3.96–3.80 (m, 6 H), 3.63–3.56 (m, 2 H), 2.07 (s, 3 H, COCH_3), 1.99 (s, 3 H, COCH_3), 1.79 (s, 3 H, COCH_3), 1.37 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), 1.03 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 169.9, 169.4, 167.1, 165.7, 165.4, 165.1, 164.9, 164.8, 164.7, 117.3, 102.2, 99.5, 97.8, 97.6, 84.8, 72.4, 72.1, 71.3, 71.1, 70.3, 69.9, 69.4, 69.0, 67.8, 67.6, 66.7, 62.7, 62.0, 54.7, 20.6, 20.5, 20.3, 18.1, 16.8. Anal. Calcd for $C_{75}H_{73}NO_{27}$: C, 63.42; H, 5.18. Found: C, 63.28; H, 5.36.

3.13. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→4)-]3-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate (22)

To a solution of compound **19** (2.84 g, 2 mmol) in Py (25 mL) was added Ac_2O (10 mL, 10 mmol). The reaction mixture was stirred at rt for 12 h and concentrated to give the crude product **20** as a syrup, which was directly used in the next step without separation. To the solution of **20** in 90% HOAc (20 mL) containing NaOAc (60 mg, 6 mmol) was added $PdCl_2$ (180 mg, 1.0 mmol), and the mixture was stirred for 12 h, at the end of which time TLC (1:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was diluted with CH_2Cl_2 (100 mL), washed with water and satd aq $NaHCO_3$. The organic layer was concentrated, and the residue was passed through a short silica gel column with 1:1 petroleum ether–EtOAc as the eluent to give crude 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→4)-]3-*O*-acetyl-α,β-L-rhamnopyranose (**21**) (2.49 g, 87.7% for two steps). Compound **21** was dissolved in CH_2Cl_2 (20 mL), and CCl_3CN (0.5 mL, 5 mmol) and DBU (50 μL, 0.33 mmol) were added. The reaction mixture was stirred for 2 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. Concentration of the reaction mixture, followed by purification of the crude product on a silica gel column with 2:1 petroleum ether–EtOAc as the eluent, furnished the tetrasaccharide donor **22** (2.20 g, 80.3%) as a syrup: $[\alpha]_D$ +25.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (s, 1 H, CN*H*CCl$_3$), 7.97–7.33 (m, 29 H, 5 Ph, Phth), 6.19 (d, 1 H, $J_{1,2}$ 2.1 Hz, H-1^{I}), 5.75–5.56 (m, 2 H, H-3^{IV}, H-4^{II}), 5.55 (dd, 1 H, $J_{1,2}$ 2.0, $J_{2,3}$ 3.4 Hz, H-2^{II}), 5.53 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1^{III}), 5.38–5.34 (m, 2 H, H-2^{IV}, H-3^{III}), 5.33 (dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 9.7 Hz, H-3^{I}), 5.30 (m, 1 H, H-4^{IV}), 5.16 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4^{III}), 4.97 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1^{II}), 4.92 (d, 1 H, $J_{1,2}$ 5.8 Hz, H-1^{IV}), 4.27 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 9.8 Hz, H-3^{II}), 4.26–4.22 (m, 5 H), 4.00–3.92 (m, 4 H), 3.65–3.62 (m, 2 H), 2.09 (s, 3 H, COCH_3), 2.02 (s, 3 H, COCH_3), 2.00 (s, 3 H, COCH_3), 1.78 (s, 3 H, COCH_3), 1.41 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 1.21 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6). Anal. Calcd for $C_{76}H_{71}Cl_3N_2O_{28}$: C, 58.26; H, 4.57. Found: C, 58.40; H, 4.38.

3.14. Allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→4)-]3-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (23)

Compound **22** (1.57 g, 1.0 mmol) and allyl 3,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**6**) (0.42 g, 1.0 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (10 mL). TMSOTf (9.0 μL, 0.05 mmol) was added dropwise at 0 °C with N_2 protection. The reaction mixture was stirred for 3 h, during which time the temperature was gradually raised to ambient temperature. Then the mixture was neutralized with Et_3N, concentrated to dryness. Purification of the residue by column chromatography (1:1 petroleum ether–EtOAc) gave **23** (1.30 g, 71.4%) as a foamy solid: $[\alpha]_D$ +62.0° (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 8.13–7.30 (m, 39 H, 7 Ph, Phth), 5.97 (m, 1 H, $CH_2CH{=}CH_2$), 5.43 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.98 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.92 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.80 (d, 1 H, $J_{1,2}$ 5.8 Hz, H-1), 4.53 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 2.12 (s, 3 H, COCH_3), 2.00 (s, 3 H, COCH_3), 1.79 (s, 6 H, 2 COCH_3), 1.30 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), 1.07 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 1.04 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 169.4, 169.0, 168.8, 166.8, 165.5, 165.1, 165.0, 164.9, 164.5, 164.3, 164.2, 133.5, 133.1, 132.9, 132.8, 132.7, 132.6, 130.6, 130.0, 129.4, 129.3, 129.2, 129.0, 128.9, 128.7, 128.1, 128.0, 127.9, 127.8, 127.6, 117.3, 100.3, 100.0, 98.6, 97.3, 96.2, 20.3, 20.2, 20.1, 19.9, 17.5, 17.2, 16.8. Anal. Calcd for $C_{97}H_{93}NO_{34}$: C, 64.13; H, 5.16. Found: C, 63.91; H, 5.28.

3.15. Propyl 3,4,6-tri-*O*-acetyl-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-acetytyl-β-L-xylopyranosyl-(1→4)-]3-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranoside (24)

Pentasaccharide **23** (910 mg, 0.5 mmol) was dissolved in EtOH (36 mL) to which was added 100% hydrazine hydrate (4 mL), and the solution was refluxed for 48 h. The solution was then concentrated, and the residue was co-evaporated several times with toluene. The residue was taken up in Py (20 mL) to which was added Ac_2O (10 mL). The solution was left to stand for 12 h at rt and then evaporated to dryness. Purification of the residue by column chromatography (EtOAc) gave **24** (510 mg, 78.7% for two steps) as a foamy solid: $[\alpha]_D$

−21.3° (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 5.56 (bd, 1 H, *J* 6.4 Hz, N*H*COCH$_3$), 5.09 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.80 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.72 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.70 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.53 (d, 1 H, $J_{1,2}$ 7.1 Hz, H-1), 2.15, 2.13, 2.10, 2.09, 2.08, 2.07, 2.04, 2.03, 2.02, 2.02, 2.00, 1.91 (12 s, 36 H, 12 COC*H*$_3$), 1.62 (m, 2 H, OCH$_2$C*H*$_2$CH$_3$), 1.26 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 1.24 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 1.18 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 0.94 (t, 3 H, *J* 7.4 Hz, OCH$_2$CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.4, 170.4, 170.3, 170.2, 170.1, 169.8, 169.7, 167.7, 169.6, 169.5, 169.1, 101.4, 100.3, 99.0, 98.9, 97.18. Anal. Calcd for $C_{56}H_{81}NO_{33}$: C, 51.89; H, 6.30. Found: C, 51.81; H, 6.48.

3.16. Propyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-[β-L-xylopyranosyl-(1→4)-]-α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranoside (25)

Pentasaccharide **24** (388 mg, 0.3 mmol) was dissolved in satd NH_3–MeOH (30 mL). After 96 h at rt, the reaction mixture was concentrated, and the residue was purified by chromatography on Sephadex LH-20 (MeOH) to afford **25** as a foamy solid (201 mg, 80.4%): $[\alpha]_D$ −44.0° (*c* 0.5, H_2O); ^{1}H NMR (400 MHz, D_2O): 5.18 (s, 1 H, H-1), 4.96 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.82 (s, 1 H, H-1), 4.76 (d, 1 H, $J_{1,2}$ 6.1 Hz, H-1), 4.47 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 2.00 (s, 3 H, C*H*$_3$CONH), 1.61 (m, 2 H, OCH$_2$C*H*$_2$CH$_3$), 1.38 (d, 3 H, $J_{5,6}$ 6.0 Hz, H-6), 1.32 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 1.28 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), 0.93 (t, 3 H, *J* 7.4 Hz, OCH$_2$CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, D_2O): δ 168.2, 106.5, 104.9,104.6, 103.5, 99.7, 19.1. MS (*m*/*z*) Calcd for $C_{34}H_{59}NO_{22}$: 833.81 $[M]^+$. Found: 856.90 $[M + Na]^+$.

3.17. Allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→4)-[2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→2)]-α-L-rhamnopyranoside (26)

Compound **11**(4.70 g, 5.0 mmol) and **17** (3.30 g, 5.0 mmol) were coupled under the same conditions as that used for the preparation of **19** from **11** and **14**, giving **26** as a foamy solid (6.30 g, 88.8%). $[\alpha]_D$ +39.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12–7.22 (m, 29 H, 5 Ph, Phth), 5.75 (m, 1 H, OCH$_2$C*H*=CH$_2$), 5.71–5.67 (m, 2 H, H-3^{III}, H-3^{IV}), 5.48 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.2 Hz, H-2^{II}), 5.38 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1^{III}), 5.33 (dd, 1 H, $J_{1,2}$ 8.3, $J_{2,3}$ 6.7 Hz, H-2^{IV}), 5.28 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1^{II}), 5.26–5.22 (m, 2 H, H-4^{II}, H-4^{III}), 5.13–5.02 (m, 3 H, H-4^{IV}, OCH$_2$CH=C*H*$_2$), 4.72 (d, 1 H, $J_{1,2}$ 6.4 Hz, H-1^{IV}), 4.53 (s, 1 H, H-1^{I}), 4.37 (dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 9.6 Hz, H-3^{II}), 4.23–4.14 (m, 3 H), 3.96 (m, 1 H, OC*H*$_2$CH=CH$_2$), 3.91 (dd, 1 H, $J_{2,3}$ 2.9, $J_{3,4}$ 9.7 Hz, H-3^{I}), 3.87–3.81 (m, 4 H), 3.70 (m, 1 H, OC*H*$_2$CH=CH$_2$), 3.57–3.47 (m, 2 H), 3.31 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4^{I}), 2.03 (s, 3 H, COC*H*$_3$), 1.92 (s, 3 H, COC*H*$_3$), 1.71 (s, 3 H, COC*H*$_3$), 1.34 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), 1.04 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 169.5, 166.8, 165.1, 165.0, 164.8, 164.6, 164.5, 117.2, 100.2, 98.1, 97.4, 95.9, 80.2, 79.7, 71.5, 70.7, 70.5, 70.4, 70.3, 70.0, 69.9, 68.7, 68.6, 67.3, 66.1, 61.7, 61.6, 54.4, 20.2, 20.1, 19.9, 17.6, 17.5. Anal. Calcd for $C_{75}H_{73}NO_{27}$: C, 63.42; H, 5.18. Found: C, 63.35; H, 5.51.

3.18. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→4)-[2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→2)]-3-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate (29)

A solution of **26** (2.84 g, 2 mmol) was acetylated with Ac_2O (8 mL) in Py (25 mL) to give **27**, which was deallylated and then trichloroacetimidated under the same conditions as those used for the preparation of **22**, giving **29** as a foamy solid (2.09 g, 66.8% for three steps): $[\alpha]_D$ +46.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1 H, CN*H*CCl$_3$), 7.95–7.33 (m, 29 H, 5 Ph, Phth), 6.10 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1^{I}), 5.77–5.70 (m, 2 H, H-3^{III}, H-3^{IV}), 5.46 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1^{III}), 5.41–5.38 (m, 2 H, H-2^{II}, H-2^{IV}), 5.29–5.26 (m, 2 H, H-4^{III}, H-4^{IV}), 5.15 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4^{II}), 5.07 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1^{II}), 5.02 (dd, 1 H, $J_{2,3}$ 3.1, $J_{3,4}$ 9.8 Hz, H-3^{I}), 4.85 (d, 1 H, $J_{1,2}$ 5.8 Hz, H-1^{IV}), 4.43 (dd, 1 H, $J_{1,2}$ 1.8, $J_{2,3}$ 3.1 Hz, H-2^{I}), 4.35 (dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 9.7 Hz, H-3^{II}), 4.29–4.21 (m, 3 H), 3.96–3.89 (m, 4 H), 3.73 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4^{I}), 3.60 (m, 1 H), 2.03 (s, 3 H, COC*H*$_3$), 1.92 (s, 3 H, COC*H*$_3$), 1.71 (s, 3 H, COC*H*$_3$), 1.34 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), 1.04 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6). Anal. Calcd for $C_{76}H_{71}Cl_3N_2O_{28}$: C, 58.26; H, 4.57. Found: C, 58.37; H, 4.40.

3.19. Allyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→4)-[2,3,4-tri-*O*-benzoyl-β-L-xylopyranosyl-(1→2)-]3-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (30)

Compound **29** (1.57 g, 1.0 mmol) and **6** (0.42 g, 1.0 mmol) were coupled under the same conditions as those used for the preparation of **23** from **22** and **6**, giving **30** (1.55 g, 85.2%) as a foamy solid: $[\alpha]_D$ +98.5° (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 8.13–7.35 (m, 39 H, 7 Ph, Phth), 6.00 (m, 1 H, CH$_2$CH=C*H*$_2$), 5.47 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 5.15 (d, 1 H, $J_{1,2}$ 1.4 Hz, H-1), 5.01 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.88 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.71 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 2.09 (s, 3 H, COC*H*$_3$), 1.99 (s, 3 H, COC*H*$_3$), 1.89 (s, 3 H, COC*H*$_3$), 1.78 (s, 3 H, COC*H*$_3$), 1.31 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6),

1.26 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 0.92 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 169.4, 169.3, 169.0, 166.8, 165.6, 165.0, 164.9, 164.5, 164.4, 164.3, 164.2, 133.5, 133.4, 133.2, 133.1, 132.9, 132.8, 132.7, 132.5, 130.6, 129.6, 129.5, 129.4, 129.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.5, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 117.3, 99.3, 99.2, 98.5, 97.4, 96.4, 20.3, 20.2, 20.1, 19.9, 17.4, 17.2, 17.1. Anal. Calcd for $C_{97}H_{93}NO_{34}$: C, 64.13; H, 5.16. Found: C, 64.34; H, 5.20.

3.20. Propyl 3,4,6-tri-*O*-acetyl-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-[2,3,4-tri-*O*-acetyl-β-L-xylopyranosyl-(1→2)]-3-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranoside (31)

Compound **30** (910 mg, 0.5 mmol) was deblocked in 10% hydrazine–EtOH (40 mL) under reflux for 48 h, and then acetylated with Ac_2O (10 mL) in Py (15 mL) to give **31** (530 mg, 81.8% for two steps) as a foamy solid. $[\alpha]_D$ −12.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 5.55 (bd, 1 H, *J* 6.6 Hz, N*H*COCH$_3$), 5.06 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 4.88 (s, 1 H, H-1), 4.74 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.71 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.33 (d, 1 H, $J_{1,2}$ 6.6 Hz, H-1), 2.00, 2.18, 2.16, 2.08, 2.07, 2.05, 2.05, 2.04, 2.04, 2.01, 2.01, 1.90 (9 s, 36 H, 12 COC*H*$_3$), 1.61 (m, 2 H, OCH$_2$C*H*$_2$CH$_3$), 1.26 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 1.23 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), 1.19 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 0.95 (t, 3 H, *J* 7.4 Hz, OCH$_2$CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 170.1, 170.1, 170.0, 169.9, 169.6, 169.6, 169.4, 169.4, 169.4, 169.2, 168.7, 99.7, 98.9, 98.5, 98.0, 96.6. Anal. Calcd for $C_{56}H_{81}NO_{33}$: C, 51.89; H, 6.30. Found: C, 51.70; H, 6.41.

3.21. Propyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→4)-[β-L-xylopyranosyl-(1→2)]-α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranoside (32)

Pentasaccharide **31** (400 mg, 0.31 mmol) was dissolved in satd NH_3–MeOH (50 mL). After 96 h at rt, the reaction mixture was concentrated, and the residue was purified by chromatography on Sephadex LH-20 (MeOH) to afford **32** as a foamy solid (213 mg, 82.8%): $[\alpha]_D$ −52.4° (*c* 0.5, H_2O); ^{1}H NMR (400 MHz, D_2O): 5.03 (s, 1 H, H-1), 5.01 (d, 1 H, $J_{1,2}$ 1.0 Hz, H-1), 4.67 (s, 1 H, H-1), 4.66 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 4.31 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 1.93 (s, 3 H, C*H*$_3$CONH), 1.52 (m, 2 H, OCH$_2$C*H*$_2$CH$_3$), 1.23 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), 1.19 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), 1.10 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 0.81 (t, 3 H, *J* 7.6 Hz, OCH$_2$CH$_2$C*H*$_3$); MS (*m*/*z*) Calcd for $C_{34}H_{59}NO_{22}$: 833.81 $[M]^+$. Found: 856.85 $[M + Na]^+$.

4. Supplementary material

The material is available from the authors on request.

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