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Note

Synthesis of an L-rhamnose tetrasaccharide, the common and major structure of the repeating unit of the O-antigenic polysaccharide of a strain of *Klebsiella pneumoniae* and *Pseudomonas holci*

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Abstract

A tetrasaccharide, α-L-Rha*p*-(1→3)-α-L-Rha*p*-(1→2)-α-L-Rha*p*-(1→2)-L-Rha*p*, the common and major structure of the repeating unit of the O-antigenic polysaccharide of a strain of *Klebsiella pneumoniae* and *Pseudomonas holci* was synthesized as its methyl and octyl glycosides. Selective 3-*O*-glycosylation of allyl α-L-rhamnopyranoside with 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate gave allyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranoside (**3**). Benzoylation, deallylation, and trichloroacetimidation afforded 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate (**6**). Self condensation of 3,4-di-*O*-benzoyl-β-L-rhamnopyranose 1,2-methyl orthoester or 1,2-octyl orthoester gave methyl or octyl 2-*O*-acetyl-3,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**16** or **17**), and subsequent selective deacetylation gave the disaccharide acceptor (**18** or **19**). Coupling of **6** with **18** (or **19**), followed by deacylation in ammonia-saturated methanol, produced the target tetrasacharide.

Keywords: Oligosaccharide; Rhamnose; Antigen

The tetrasaccharide, α-L-Rha*p*-(1→3)-α-L-Rha*p*-(1→2)-α-L-Rha*p*-(1→2)-L-Rha*p*, is the common and major structure of the repeating units of the O-antigenic polysaccharide of a strain of *Klebsiella pneumoniae* strain[1] and *Pseudomonas holci*.[2] The former repeating unit contains one more α-(1→2)-linked L-rhamnose residue at the reducing end, while the latter one has a 3-acetylamino-3,6-dideoxy-α-D-galactopyranosyl residue attached to the 3-*O*-position of the rhamnose unit reducing end. For investigation of the oligosaccharide's structure–bioactivity relationships, we present herewith the synthesis of the target tetrasaccharide.

As outlined in Scheme 1, condensation of 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate (**2**) with unprotected allyl α-L-rhamnopyranoside (**1**) selectively gave allyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranoside (**3**) in satis-

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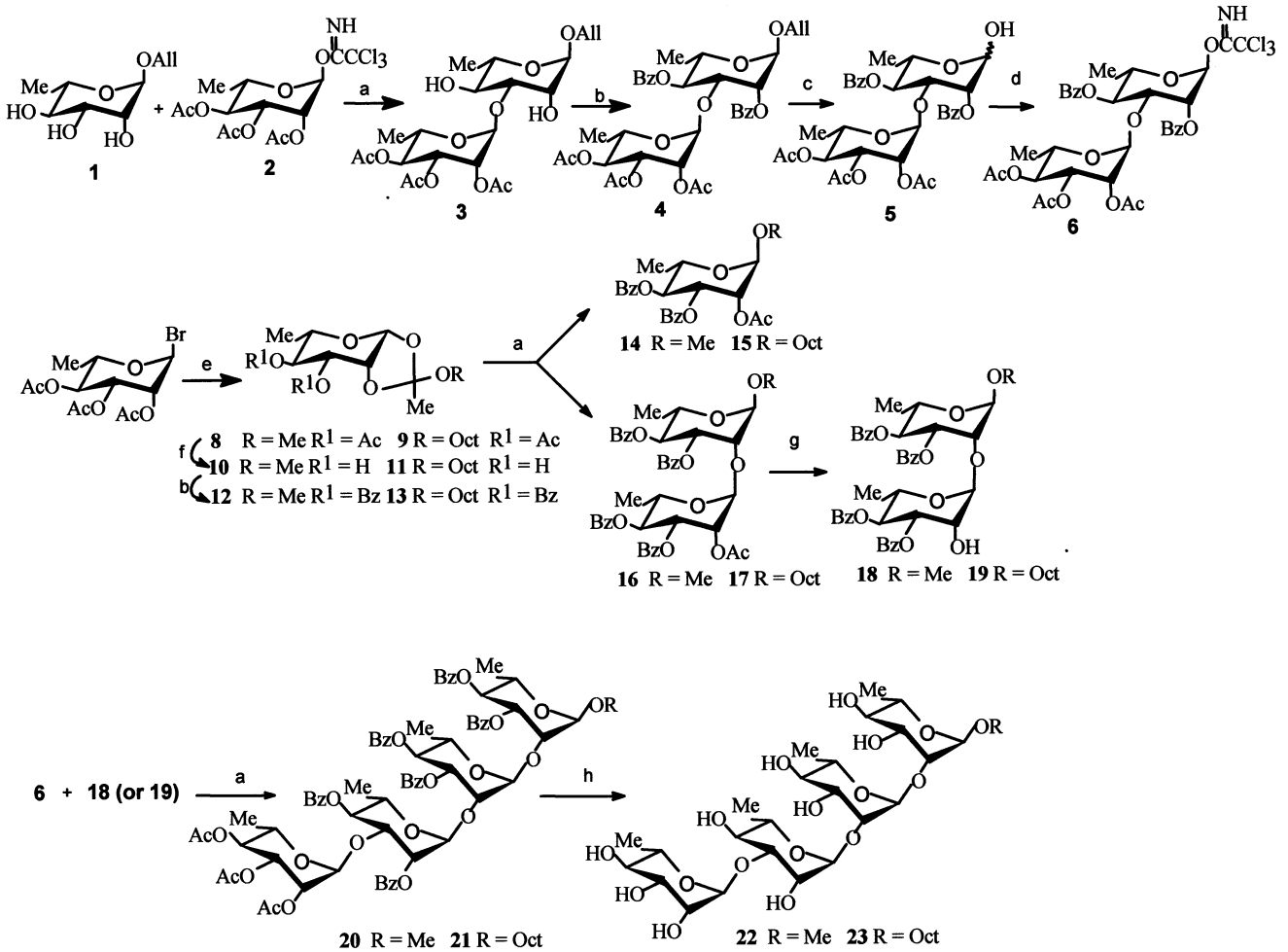
factory yield (64.3%). Keeping the temperature below −10 °C during the addition of TMSOTf was necessary in order to avoid byproduct formation. We rationalized that the good regioselectivity is owing to the formation of 3-*O*-linked orthoester disaccharide, followed by an intramolecular rearrangement.[3] The (1→3) linkage was confirmed by benzoylation of **3**, and the ^{1}H NMR spectrum of the resultant **4** showed a ^{1}H NMR spectrum identical to that reported in the literature.[4] Compared to our previously reported method for preparation of α-(1→3)-linked rhamnose disaccharide with an unprotected rhamnoside as the acceptor via isolated orthoester intermediate,[4] the present technique is simpler. Deallylation with $PdCl_2$, followed by trichloroacetimidation with CCl_3CN in the presence of DBU or K_2CO_3,[5] gave the disaccharide donor **6**. The disaccharide acceptor was readily prepared by the method of self-condensation of the orthoester **12** or **13**.[6] Thus 3,4-di-*O*-benzoyl-β-L-rhamnopyranose 1,2-methyl (**12**) and 1,2-octyl (**13**) orthoesters were prepared by the sequential reaction of tri-*O*-acetyl-α-L-rhamnopyranosyl bromide (**7**) with methanol and octanol, respectively, then Zemplén deacylation, and conventional benzoylation. Self-condensation of the orthoesters **12** or **13** promoted by TMSOTf was carried out readily giving the disaccharides **16** (68.8%) or **17** (70.0%), respectively, as the major product and the monosaccharides **14** (10.7%) or **15** (11.4%) as the minor one. This chemoselectivity means that the self-condensation of the orthoesters is indeed an effective method for the preparation of α-(1→2)-linked rhamnose disaccharides. Selective deacetylation[7] of **16** or



Scheme 1. Reagents and conditions: (a) TMSOTf, CH_2Cl_2, 4 Å MS, N_2, −20 °C to rt, 4 h; (b) BzCl–pyridine (dry); (c) $PdCl_2$, CH_2Cl_2, 2 h; (d) CCl_3CN, DBU or K_2CO_3, CH_2Cl_2 8 h; (e) lutidine, CH_2Cl_2, ROH, 4 Å MS, 4 h; (f) MeONa, MeOH; (g) CH_3OH, CH_3COCl (0.1%, v/v); (h) NH_3, MeOH.

17 with CH_3COCl–methanol afforded the disaccharide acceptor, methyl 3,4-di-*O*-benoyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**18**) or octyl 3,4-di-*O*-benzoyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**19**). We were gratified to find that the self-condensation of the orthoester with a long-chain fatty acid alcohol as the aglycone moiety ran smoothly giving the corresponding disaccharide in good yield. This can be an efficient and concise method for the preparation of α-(1→2)-linked manno- and rhamnopyranose disaccharides with a long-chain fatty acid at the reducing end. With the disaccharide donor **6** and the disaccharide acceptor **18** or **19** at hand, the tetrasaccharide **20** or **21** was readily constructed in dichloromethane in the presence of TMSOTf. Finally deacylation of **20** or **21** in ammonia-saturated methanol gave the target tetrasaccharide **22** or **23**, and their bioassays are in progress and will be reported in due course.

In summary, a very concise and efficient synthesis of methyl or octyl α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranoside was achieved in a regio- and stereoselective way. Because of its simplicity and efficiency, this method could be used for construction of higher rhamnose oligosaccharides with α-(1→3)- and α-(1→2)-linkages.

1. Experimental

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 spectra were recorded with Varian XL-400 and Varian XL-200 spectrometers, for solutions in $CDCl_3$ with tetramethylsilane (Me_4Si) as the internal standard. Chemical shifts are expressed in ppm downfield from the internal 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) H_2SO_4 in MeOH or by UV detection. Column chromatography was conducted by elution of a column (8 × 100 mm, 16 × 240 mm, 18 × 300 mm, 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), a stainless steel column packed with silica gel (Spherisorb SiO_2, 10 × 300 mm or 4.6 × 250 mm), a differential refractometer (132-RI Detector), and a 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.

Allyl 2,3,4-tri-O-*acetyl*-α-L-*rhamnopyranosyl-(1→3)-2,4-di*-O-*benzoyl*-α-L-*rhamnopyranoside* (**4**).—2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranosyl trichloroacetimidate (**1**) (4.350 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 triethylamine and concentrated to dryness under reduced pressure to afford the crude allyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranoside (**3**). To the solution of crude **3** in pyridine (20 mL), BzCl (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 **4** (4.400 g, 64.3% for two steps) as a syrup: $[\alpha]_D$ +62° (*c* 1.0, $CHCl_3$), lit.[4] $[\alpha]_D$ +64° (*c* 1.5, $CHCl_3$). Compound **4** gave ^{1}H NMR data identical to those reported in the literature.[4]

2,3,4-Tri-O-*acetyl*-α-L-*rhamnopyranosyl-(1→3)-2,4-di*-O-*benzoyl*-α-L-*rhamnopyranosyl 2,2,2-trichloroacetimidate* (**6**).—To a solution

of allyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α-L-rhamnopyranoside (**4**) (684 mg, 1 mmol) in 90% AcOH (10 mL) containing AcONa (293 mg, 3 mmol) was added $PdCl_2$ (89 mg, 0.5 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 (30 mL) and 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 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→3)-2,4-di-*O*-benzoyl-α,β-L-rhamnopyranose (**5**) (620 mg, 96%). Compound **5** was dissolved in CH_2Cl_2 (10 mL), and CCl_3CN (0.2 ml, 2 mmol) and DBU (27 μL, 0.18 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 **6** (710 mg, 90%) as a syrup: $[\alpha]_D$ +4.3° (*c* 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.80 (s, 1 H, $CNHCCl_3$), 8.18–7.43 (m, 10 H, 2 Bz-H), 6.44 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1), 5.62 (dd, 1 H, $J_{1,2}$ 1.9, $J_{2,3}$ 3.2 Hz, H-2), 5.59 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4), 5.09 (dd, 1 H, $J_{2',3'}$ 3.2, $J_{3',4'}$ 9.8 Hz, H-3′), 4.94–4.91 (m, 2 H, H-1′, H-2′), 4.89 (dd, 1 H, $J_{3',4'} = J_{4',5'} = 9.8$ Hz, H-4′), 4.49 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 9.8 Hz, H-3), 4.22 (m, 1 H), 3.93 (m, 1 H), 1.94 (s, 3 H, CH_3CO), 1.87 (s, 3 H, CH_3CO), 1.82 (s, 3 H, CH_3CO), 1.35 (d, 3 H, *J* 6.2 Hz), 1.07 (d, 3 H, *J* 6.3 Hz). Anal. Calcd for $C_{34}H_{36}Cl_3NO_{14}$: C, 51.75; H 4.60. Found: C, 51.56; H, 4.58.

3,4-Di-O-*acetyl-1,2*-O-*octoxyethylidene-β-L-rhamnopyranose* (**9**).—A mixture of 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide (**7**) (2.0 g, 5.7 mmol), 2,4-lutidine (0.8 mL, 7.2 mmol), and tetrabutylammonium bromide (0.8 g, 2.4 mmol) in anhyd CH_2Cl_2 (10 mL) was stirred at rt, and $C_8H_{17}OH$ (0.95 mL, 6 mmol) was added. The reaction mixture was stirred for 24 h. TLC (1:1 petroleum ether–EtOAc) indicated that the reaction was complete. The reaction mixture was concentrated and subjected to column chromatography to give **9** (1.8 g, 78.6%) as a syrup: $[\alpha]_D$ +13.5° (*c* 1.2, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 5.37 (d, 1 H, $J_{1,2}$ 2.2 Hz, H-1), 5.09 (dd, 1 H, $J_{2,3}$ 3.9, $J_{3,4}$ 9.9 Hz, H-3), 5.04 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4), 4.55 (dd, 1 H, $J_{1,2}$ 2.2, $J_{2,3}$ 3.9 Hz, H-2), 3.53–3.40 (m, 3 H, H-5, $OCH_2C_7H_{15}$), 2.09 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 1.71 (s, 3 H, CH_3CO_3), 1.53–0.84 (m, 18 H, H-6, $C_7H_{15}CH_2O$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.6, 20.8, 20.8, 22.7, 24.8, 26.1, 29.2, 29.3, 29.5, 31.6, 62.7, 69.2, 70.5, 70.8, 76.6, 97.2, 124.2, 169.8, 169.8, 170.5. Anal. Calcd for $C_{20}H_{34}O_8$: C, 59.68; H, 8.52. found: C, 59.56; H, 8.50.

3,4-Di-O-*benzoyl-1,2*-O-*methoxyethylidene-β-L-rhamnopyranose* (**12**).—A mixture of 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide (**7**) (2.0 g, 5.7 mmol), 2,4-lutidine (0.8 mL, 7.2 mmol), and tetrabutylammonium bromide (0.8 g, 2.4 mmol) in CH_2Cl_2 (1 mL) was stirred at rt, and anhyd MeOH (0.5 mL, 12 mmol) was added. The reaction mixture was stirred for 24 h. TLC (1:1 petroleum ether–EtOAc) indicated that the reaction was complete. The reaction mixture was concentrated and subjected to column chromatography to give crude product **8** (1.6 g, 93%). According to the standard method, compound **8** (1.5 g, 4.9 mmol) was deacetylated with MeONa in MeOH to give **10**, and then **10** was benzoylated with BzCl in pyridine to furnish **12** in quantitative yield. Flash chromatography (3:1 petroleum ether–EtOAc) of the residue gave pure **12** (1.98 g, 93.8%) as a syrup: $[\alpha]_D$ +100.9° (*c* 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.01–7.36 (m, 10 H, 2 Bz-H), 5.54–5.45 (m, 3 H), 4.82 (dd, 1 H, $J_{1,2}$ 2.5, $J_{2,3}$3.6 Hz, H-2), 3.66 (m, 1 H, H-5), 3.26 (s, 3 H, OCH_3), 1.79 (s, 3 H, CCH_3), 0.89 (d, $J_{5,6}$ 6.6 Hz, 3 H, H-6). Anal. Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.29; H, 5.66.

3,4-Di-O-*benzoyl-1,2*-O-*octoxyethylidene-β-L-rhamnopyranose* (**13**).—According to the standard method, compound **9** (2.0 g, 5.0 mmol) was deacetylated with MeONa in MeOH to give **11**, and then **11** was benzoylated with BzCl in pyridine to furnish **13** in quantitative yield. Flash chromatography (4:1 petroleum ether–EtOAc) of the residue gave pure **13** as a syrup (2.5 g, 95%): $[\alpha]_D$ +91.2°

(*c* 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.01–7.36 (m, 10 H, 2 Bz-H), 5.54–5.46 (m, 3 H, H-1, H-3, H-4), 4.80 (dd, 1 H, $J_{1,2}$ 2.5, $J_{2,3}$ 3.6 Hz, H-2), 3.76 (m, 1 H, H-5), 3.46 (m, 2 H, $OCH_2C_7H_{15}$), 1.79 (s, 3 H, CCH_3), 1.52–0.83 (m, 18 H, H-6, $OCH_2C_7H_{15}$). Anal. Calcd for $C_{30}H_{38}O_8$: C, 68.42; H, 7.27. Found C, 68.45; H, 7.32.

Methyl 2-O-*acetyl-3,4-di*-O-*benzoyl-α*-L-*rhamnopyranosyl-(1→2)-3,4-di*-O-*benzoyl-α*-L-*rhamnopyranoside* (**16**).—To a solution of compound **12** (856 mg, 2 mmol) in anhyd CH_2Cl_2 (20mL) was added TMSOTf (18 μL, 0.1 mmol) in the presence of 4 Å molecular sieves under an N_2 atmosphere at −20 °C. The mixture was slowly raised to rt and stirred for 2 h, neutralized with Et_3N and filtered, then the filtrate was concentrated. Purification of the product by column chromatography (3:1 petroleum ether–EtOAc) gave syrupy **16** (538 mg, 68.8%) as the main product and a syrupy **14** (46 mg, 10.7%) as the minor product. For compound **16**: $[\alpha]_D$ +53° (*c* 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.00–7.35 (m, 20 H, 4 Bz-H), 5.80 (dd, 1 H, *J* 3.3, *J* 9.8 Hz), 5.76 (dd, 1 H, *J* 3.1, *J* 10.0 Hz), 5.66 (dd, 1 H, $J_{1',2'}$ 1.8, $J_{2',3'}$ 3.1 Hz, H-2′), 5.63 (dd, 1 H, *J* 9.8 Hz), 5.55 (dd, 1 H, *J* 9.8 Hz), 4.97 (d, 1 H, *J* 1.7 Hz), 4.86 (d, 1 H, *J* 1.8 Hz), 4.30–4.24 (m, 2 H), 4.10 (m, 1 H), 3.49 (s, 3 H, OCH_3), 2.04 (s, 3 H, $COCH_3$), 1.40 (d, 3 H, *J* 6.3 Hz), 1.32 (d, 3 H, *J* 6.4 Hz). Anal. Calcd for $C_{43}H_{42}O_{14}$: C, 65.97; H, 5.41. Found: C, 65.76; H, 5.38. For compound **14**: $[\alpha]_D$ +55.1° (*c* 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.98–7.34 (m, 10 H, 2 Bz-H), 5.69 (dd, 1 H, $J_{2,3}$ 3.5, $J_{3,4}$ 10.1 Hz, H-3), 5.54 (dd, 1 H, $J_{3,4}=J_{4,5}=10.1$ Hz, H-4), 5.46 (dd, 1 H, $J_{1,2}$ 1.6, $J_{2,3}$ 3.5 Hz, H-2), 4.75 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.11 (m, 1 H, H-5), 3.47 (s, 3 H, OCH_3), 2.16 (s, 3 H, CH_3CO), 1.34 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6). Anal. Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.32; H, 5.64.

Octyl 2-O-*acetyl-3,4-di*-O-*benzoyl-α*-L-*rhamnopyranosyl-(1→2)-3,4-di*-O-*benzoyl-α*-L-*rhamnopyranoside* (**17**).—To a solution of compound **13** (1.052 g, 2 mmol) in anhyd CH_2Cl_2 (20 mL) was added TMSOTf (18 μL, 0.1 mmol) in the presence of 4 Å molecular sieves under an N_2 atmosphere at −20 °C. The mixture was slowly raised to rt and stirred for 2 h, neutralized with Et_3N and filtered, then the filtrate was concentrated. Purification of the product by column chromatography (5:1 petroleum ether–EtOAc) gave a syrup **17** (616 mg, 70.0%) as the main product and a syrupy **15** (60 mg, 11.4%) as the minor product. For compound **17**: $[\alpha]_D$ +62° (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.03–7.33 (m, 20 H, 4 Bz-H), 5.85 (dd, 1 H, *J* 3.4, *J* 10.0 Hz), 5.77 (dd, 1 H, *J* 3.2, *J* 10.0 Hz), 5.68 (dd, 1 H, $J_{1',2'}$ 1.8, $J_{2',3'}$ 3.1 Hz, H-2′), 5.63 (dd, 1 H, *J* 9.8 Hz), 5.54 (dd, 1 H, *J* 9.8 Hz), 4.98 (d, 1 H, *J* 1.7 Hz), 4.95 (d, 1 H, *J* 1.8 Hz), 4.28 (m, 2 H), 4.11 (m, 1 H), 3.65 (m, 2 H), 2.05 (s, 3 H, $COCH_3$), 1.70–1.32 (m, 21 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.6, 17.8, 20.8, 22.7, 26.2, 29.3, 29.5, 29.5, 31.9, 66.9, 67.5, 68.3, 69.7, 69.9, 71.3, 71.7, 72.1, 98.7, 99.7, 165.2, 165.4, 165.7, 165.8, 169.8. Anal. Calcd for $C_{50}H_{56}O_{14}$: C, 68.17; H, 6.41. Found: C, 68.33; H, 6.39. For compound **15**: $[\alpha]_D$ +15° (*c* 0.3, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.98–7.34 (m, 10 H, 2 Bz-H), 5.71 (dd, 1 H, $J_{2,3}$ 3.5, $J_{3,4}$ 10.1 Hz, H-3), 5.54 (dd, 1 H, $J_{3,4}=J_{4,5}=$ 10.1 Hz, H-4), 5.46 (dd, 1 H, $J_{1,2}$ 1.7, $J_{2,3}$ 3.4 Hz, H-2), 4.85 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.12 (m,1 H, H-5), 3.64–3.60 (m, 2 H), 2.15 (s, 3 H, CH_3CO), 1.70–0.88 (m, 18 H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.2, 17.7, 21.0, 22.7, 26.2, 29.4, 29.4, 29.5, 29.5, 31.9, 66.6, 68.5, 70.1, 70.4, 71.8, 97.6, 165.5, 165.8, 170.1. Anal. Calcd for $C_{30}H_{38}O_8$: C, 68.42; H, 7.27. Found: C, 68.17; H, 7.25.

Methyl 3,4-di-O-*benzoyl-α*-L-*rhamnopyranosyl-(1→2)-3,4-di*-O-*benzoyl-α*-L-*rhamnopyranoside* (**18**).—To a solution of **16** (782 mg, 1 mmol) in anhyd MeOH (50 mL) was added acetyl chloride (1.5 mL) at 0 °C. The solution was sealed in a flask and stirred at rt until TLC (2:1 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 **18** (688 mg, 93.0%): $[\alpha]_D$ +99° (*c* 1.6, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.98–7.36 (m, 20 H, 4 Bz-H), 5.73–5.69 (m, 2 H), 5.64–5.58 (m, 2 H), 5.05 (d, 1 H, *J* 1.4 Hz), 4.89 (d, 1 H, *J* 1.5 Hz), 4.45 (dd, 1 H, *J* 1.5, *J* 3.4 Hz), 4.33 (dd, 1 H, *J* 1.4, *J* 3.3 Hz), 4.30–4.07 (m, 2 H), 3.48 (s, 3 H, CH_3O), 2.20–1.80 (br, 1 H, OH),

1.40–1.30 (m, 6 H). Anal. Calcd for $C_{41}H_{40}O_{13}$: C, 66.48; H, 5.44. Found: C, 66.59; H, 5.46.

Octyl 3,4-di-O-*benzoyl*-α-L-*rhamnopyranosyl*-(1→2)-*3,4-di*-O-*benzoyl*-α-L-*rhamnopyranoside* (**19**).—To a solution of **17** (880 mg, 1 mmol) in anhyd MeOH (50 mL) was added acetyl chloride (1.5 mL) at 0 °C. The solution was sealed 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 **19** (730 mg, 87.1%): $[\alpha]_D$ +79° (*c* 1.3, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.01–7.36 (m, 20 H, 4 Bz-H), 5.76–5.70 (m, 2 H), 5.62–5.55 (m, 2 H), 5.04 (d, 1 H, *J* 1.5 Hz), 4.96 (d, 1 H, *J* 1.5 Hz), 4.43 (dd, 1 H, *J* 1.5, *J* 3.5 Hz), 4.32 (dd, 1 H, *J* 1.5, *J* 3.3 Hz), 4.12 (m, 1 H), 3.65 (m, 2 H), 1.68–0.88 (m, 21 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.6, 17.7, 22.7, 26.2, 29.3, 29.4, 29.5, 31.9, 66.7, 67.4, 68.2, 69.7, 71.5, 71.7, 72.0, 72.2, 98.8, 101.4, 165.3, 165.6, 165.8, 165.9. Anal. Calcd for $C_{48}H_{54}O_{13}$: C, 68.72; H, 6.49. Found: C, 68.85; H, 6.48.

Methyl 2,3,4-tri-O-*acetyl*-α-L-*rhamnopyranosyl*-(1→3)-*2,4-di*-O-*benzoyl*-α-L-*rhamnopyranosyl*-(1→2)-*3,4-di*-O-*benzoyl*-α-L-*rhamnopyranosyl*-(1→2)-*3,4*-di-O-*benzoyl*-α-L-*rhamnopyranoside* (**20**).—The disaccharide donor **6** (788 mg, 1 mmol) and the disaccharide acceptor **18** (740 mg, 1 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (10 mL). TMSOTf (15 μL, 0.08 equiv) was added dropwise at −20 °C with N_2 protection. The reaction mixture was stirred for 2 h, during which time the reaction temperature was gradually allowed to rise to ambient temperature. Then the mixture was neutralized with triethylamine and concentrated to an oily residue. Purification by column chromatography (2:1 petroleum ether–EtOAc) gave **20** (970 mg, 71.0%): $[\alpha]_D$ +94° (*c* 1.9, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.06–7.33 (m, 30 H, 6 Bz-H), 5.92 (dd, 1 H, *J* 3.2, *J* 10.0 Hz), 5.67–5.48 (m, 4 H), 5.40 (dd, 1 H, *J* 9.9 Hz), 5.18 (d, 1 H, *J* 1.6 Hz, H-1), 5.11 (dd, 1 H, *J* 3.1, *J* 10.1 Hz), 5.02–4.92 (m, 5 H), 4.48–4.41 (m, 3 H), 4.30 (m, 1 H), 4.18 (m, 1 H), 4.01 (m, 1 H), 3.94 (m, 1 H), 3.57 (s, 3 H, OCH_3), 1.98 (s, 3 H, CH_3CO), 1.95 (s, 3 H, CH_3CO), 1.89 (s, 3 H, CH_3CO), 1.49 (d, 3 H, *J* 6.1 Hz), 1.44 (d, 3 H, *J* 6.1 Hz), 1.11 (d, 3 H, *J* 6.1 Hz), 1.01 (d, 3 H, *J* 6.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.1, 17.3, 17.6, 17.7, 20.5, 20.5, 20.7, 55.2, 66.6, 67.2, 67.5, 67.6, 68.5, 69.5, 70.5, 71.1, 71.1, 71.6, 71.8, 71.9, 71.9, 73.1, 74.6, 76.7, 77.7, 99.1, 99.3, 100.0, 100.8, 165.3, 165.4, 165.4, 165.5, 165.7, 165.9, 169.2, 169.3, 170.0. Anal. Calcd for $C_{73}H_{74}O_{26}$: C, 64.12; H, 5.46. Found: C, 64.32; H, 5.45.

Octyl 2,3,4-tri-O-*acetyl*-α-L-*rhamnopyranosyl*-(1→3)-*2,4-di*-O-*benzoyl*-α-L-*rhamnopyranosyl*-(1→2)-*3,4-di*-O-*benzoyl*-α-L-*rhamnopyranosyl*-(1→2)-*3,4-di*-O-*benzoyl*-α-L-*rhamnopyranoside* (**21**).—The disaccharide donor **6** (788 mg, 1 mmol) and the disaccharide acceptor **19** (838 mg, 1 mmol) were dried together under high vacuum for 2 h, then dissolved in anhyd CH_2Cl_2 (10 mL). TMSOTf (15 μL, 0.08 equiv) was added dropwise at −20 °C with N_2 protection. The reaction mixture was stirred for 2 h, during which time the reaction temperature was gradually allowed to rise to ambient temperature. Then the mixture was neutralized with triethylamine and concentrated to an oily residue. Purification by column chromatography (2:1 petroleum ether–EtOAc) gave **21** (1.140 g, 77.9%): $[\alpha]_D$ +74° (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.06–7.33 (m, 30 H, 6 Bz-H), 5.87 (dd, 1 H, *J* 3.2, *J* 10.2 Hz), 5.65–5.58 (m, 3 H), 5.45 (dd, 1 H, *J* 1.4, *J* 3.3 Hz), 5.29 (dd, 1 H, *J* 10.2 Hz), 5.10 (d, 1 H, *J* 1.3 Hz), 5.04 (dd, 1 H, *J* 3.4, *J* 9.8 Hz), 4.94–4.88 (m, 4 H), 4.77 (d, 1 H, *J* 1.4 Hz), 4.39 (dd, 1 H, *J* 3.3, *J* 9.9 Hz), 4.35–4.33 (m, 2 H), 4.24–4.22 (m, 1 H), 4.22–4.20 (m, 1 H), 3.96–3.94 (m, 1 H), 3.89–3.74 (m, 2 H), 3.53–3.51 (m, 1 H), 1.91 (s, 3 H, CH_3CO), 1.87 (s, 3 H, CH_3CO), 1.82 (s, 3 H, CH_3CO), 1.72–1.64 (m, 2 H), 1.43–1.24 (m, 16 H), 1.03 (d, 3 H, *J* 6.1 Hz), 0.93–0.86 (m, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 17.1, 17.3, 17.6, 17.7, 20.5, 20.5, 20.7, 22.7, 26.1, 26.2, 29.3, 29.4, 29.5, 31.8, 67.0, 67.2, 67.5, 67.6, 68.2, 68.5, 69.5, 70.5, 71.1, 71.7, 71.8, 71.9, 72.0, 73.1, 74.6, 77.0, 77.7, 98.9, 99.1, 99.3, 100.8, 165.3, 165.4, 165.5, 165.7, 165.9, 166.5, 169.2, 169.2, 170.0. Anal. Calcd for $C_{80}H_{88}O_{26}$: C, 65.56; H, 6.05. Found: C, 65.79; H, 6.04.

Methyl α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranoside (**22**).—Tetrasaccharide **20** (680 mg, 0.5 mmol) was dissolved in a satd methanolic ammonia (5 mL). After 48 h at rt, the reaction mixture was concentrated, and the residue was purified by chromatography on Sephadex LH-20 (MeOH) to afford **22** as a foamy solid (248 mg, 80.5%): $[\alpha]_D$ +46° (*c* 1.3, CH_3OH). ^1H NMR (CD_3OD): δ 5.08 (d, 1 H, *J* 1.3 Hz,), 5.05 (d, 1 H, *J* 1.4 Hz), 4.94 (d, 1 H, *J* 1.3 Hz), 4.67 (d, 1 H, *J* 1.3 Hz), 4.06 (dd, 1 H, *J* 1.3, *J* 3.2 Hz), 4.03 (dd, 1 H, *J* 1.4, $J_{2,3}$ 3.1 Hz), 3.98 (dd, 1 H, *J* 1.5, *J* 3.2 Hz), 3.79–3.30 (m, 16 H), 1.29–1.23 (m, 12 H); ^{13}C NMR (CD_3OD, 100 MHz): δ 99.7, 100.9, 101.9, 102.1, 78.3, 77.8, 77.5, 53.4, 16.3, 16.3, 16.2, 16.0. MS (*m*/*z*) Calcd for $C_{25}H_{44}O_{17}$: 616 [M]. Found: 639 [M + Na].

Octyl α-L-rhamnopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranosyl-(1→2)-α-L-rhamnopyranoside (**23**).—Tetrasaccharide **21** (732 mg, 0.5 mmol) was dissolved in a satd methanolic ammonia (5 mL). After 48 h at rt, the reaction mixture was concentrated, and the residue was purified by chromatography on Sephadex LH-20 (MeOH) to afford **23** as a foamy solid (284 mg, 79.6%): $[\alpha]_D$ +36° (*c* 1.3, MeOH); ^1H NMR (CD_3OD): δ 5.09 (d, 1 H, *J* 1.3 Hz), 5.05 (d, 1 H, *J* 1.3 Hz), 4.92 (d, 1 H, *J* 1.6 Hz), 4.77 (d, 1 H, *J* 1.5 Hz), 4.06 (dd, 1 H, *J* 1.3, *J* 3.3 Hz,), 4.02 (dd, 1 H, *J* 1.5, *J* 3.3 Hz), 3.98 (dd, 1 H, *J* 1.6, *J* 3.3 Hz), 3.82–3.30 (m, 15 H), 1.62–1.53 (m, 2 H), 1.31–0.86 (m, 25 H); ^{13}C NMR (CD_3OD, 100 MHz): δ 98.4, 100.9, 101.9, 102.1, 78.5, 77.8, 77.5, 31.2, 28.7, 28.6, 28.5, 25.5, 21.9, 16.3, 16.2, 16.1, 16.0, 12.6. MS (*m*/*z*) Calcd for $C_{32}H_{58}O_{17}$: 714.5 [M]. Found: 737.5 [M + Na].

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