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Practical synthesis of a tetrasaccharide derivative corresponding to ristomycin A and ristocetin A

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Abstract

A practical synthesis of fully benzoylated tetrasaccharide, whose free form is indispensable to the antibiotic ristomycin A for the process of dimerization and binding to the cell wall, was achieved via sequential assembly of the building blocks, allyl 3,4-di-*O*-benzoyl-α-D-glucopyranoside, 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate, 2-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate, and 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl trichloroacetimidate. A one-pot preparation of allyl 3,4-di-*O*-benzoyl-2-*O*-*tert*-butyldimethylsilyl-6-*O*-triphenylmethyl-α-D-glucopyranoside is described, and regioselective glycosylation is carried out using perbenzoylated sugar trichloroacetimidates as glycosyl donors in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf).

Keywords: Ristomycin; Ristocetin; Regioselective reaction; Oligosaccharide

1. Introduction

The antibiotic, ristomycin A, which is a member of the vancomycin group of antibiotics, is a glycopeptide containing a complex peptide aglycone moiety and a branched heterotetrasaccharide side chain. Ristomycin A, together with its chemical and biological analogue ristocetin A, have emerged as promising antibiotics in the treatment of Gram-positive bacterial infections.[1] It has been well established that the biological action of vancomycin-type antibiotics involves reversible binding to nascent bacterial cell-wall peptides terminating in L-Lys-D-Ala-D-Ala through hydrogen bonding.[1,2] This action is also slightly adjusted by the formation of homodimers between two antibiotic monomers.[1] Structural elucidation of ristomycin A and ristocetin A via acetolysis yielded a fully acetylated tetrasaccharide that was determined to have the following sugar sequence: α-D-arabinopyranosyl-(1→2)-α-D-mannopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranose.[3,4] Later, this structure was revised to α-D-arabinofuranosyl-(1→2)-α-D-mannopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranose by more extensive spectroscopic studies, i.e., the α-furanosyl structure for the D-arabinosyl unit was assigned to the oligosaccharide moiety.[5–7]

The tetrasaccharide residue has proved to be indispensable to the biological processing of ristomycin A and ristocetin A, such as in the process of dimerization and binding to the cell wall.[8] Herein, we report the synthesis of a ristomycin-related heterotetrasaccharide by a

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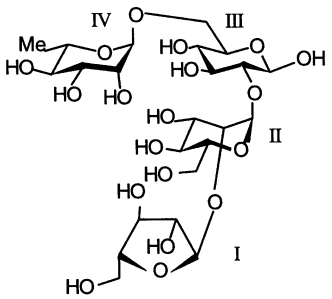
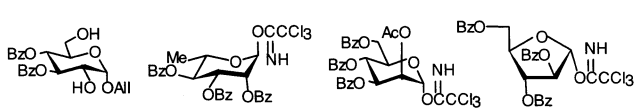
simple method in which a one-pot synthesis of the 2,6-differentiated α-D-glucopyranoside and a regioselective glycosylation were employed.



2. Results and discussion

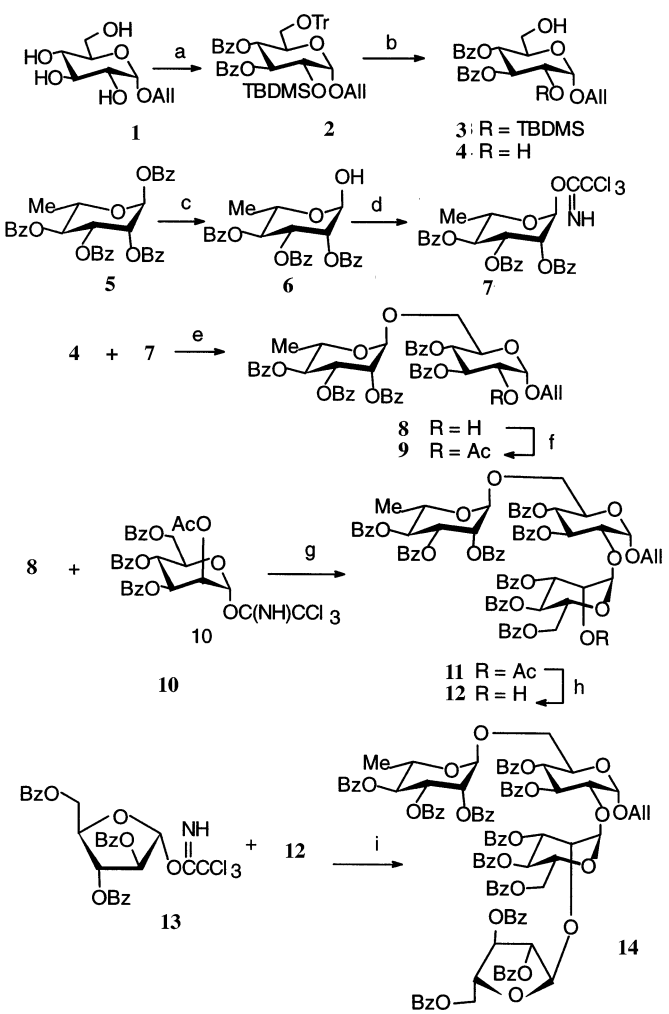
We have previously shown[9] that the use of benzoylated imidates as glycosyl donors gave good yields and regioselectivities in glycosylations. Besides, the common acyl protection group used in the synthesis greatly simplified both the preparation of building blocks and the final deprotection of the product. Accordingly, we designed a practical strategy for the synthesis of the ristomycin A (or ristocetin A) related sugar residue using the building blocks **4**, **7**, **10** and **13**.

Synthon **4** was synthesized via a one-pot, three-step sequential reaction[10] as follows. Allyl α-D-glucopyranoside (**1**) was treated with 1.25 equiv of chlorotriphenylmethane (Tr) and a catalytic amount of 4-dimethylaminopyridine (DMAP) in pyridine at 80 °C. Without working up, the mixture was regioselectively silylated with 1.1 equiv of *tert*-butylchlorodimethylsilane (TBDMSCl) and 2 equiv of imidazole, then benzoylated with benzoyl chloride to give allyl 3,4-di-*O*-benzoyl-2-*O*-*tert*-butyldimethylsilyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**2**) in a total yield of 79%. The ^{1}H NMR spectrum of **2** gave H-2 (4.0 ppm) and H-6 (3.21, 3.25 ppm) as upfield doublets of doublets, while H-3 (5.80 ppm) and H-4 (5.32 ppm) appeared as downfield triplets, which clearly indicates the correct structure of **2** (see Scheme 1).



Treatment of **2** with 90% trifluoroacetic acid (TFA) at room temperature gave diol **4** in 91% yield. Attempted detritylation of **2** with >2 equiv of ferric chloride hexahydrate in CH_2Cl_2[11] was not satisfactory, and monosilylated compounds **3** and diol **4** were obtained in a ratio of 1:1. Elongation of the reaction time generated **4** as a final product, while adding 1.5 equiv of $FeCl_3 \cdot 6H_2O$ gave **3** and **4** in a 4:1 ratio for 1.5 h at 0 °C.

Regioselective debenzoylation of fully benzoylated L-rhamnopyranose (**5**) on C-1 with NH_3 in 3:7 CH_3OH–THF ($\rightarrow$**6**), followed by anomeric activation with CCl_3CN and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave the



Scheme 1. (a) TrCl, Py, DMAP; Im, TBDMSCl in DMF; BzCl, Py; (b) $FeCl_3 \cdot 6H_2O$, DCM; (c) NH_3, 3:7 CH_3OH–THF; (d) DBU, CCl_3CN; (e) TMSOTf, < -15 °C, CH_2Cl_2 (anhyd); (f) Ac_2O, Py; (g) TMSOTf, 0 °C, CH_2Cl_2 (anhyd); (h) 3% CH_3COCl, 1:1 CH_3OH–CH_2Cl_2; (i) TMSOTf, 0 °C, CH_2Cl_2 (anhyd).

2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl-trichloroacetimidate (**7**) in a total yield of 76%. Regioselective coupling of **7** with diol **4** in anhydrous CH_2Cl_2 in the presence of TMSOTf (0.1 equiv) at −15 °C furnished 1→6 linked disaccharide **8** in 72.5% yield after column chromatography. To prove the coupling reaction actually occurred at C-6 of acceptor **4**, disaccharide **8** (20 mg) was treated with Ac_2O in pyridine to give the C-2 acetylated derivative **9**. The ^1H NMR spectrum of **9** clearly showed an downfield shift of H-2 (from 3.90 to 5.17 ppm), indicating the presence of a free C-2 hydroxyl group in **8**. The TMSOTf (0.15 equiv) promoted coupling reaction of 2-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α-D-mannopyranosyl trichloroacetimidate (**10**) with **8** at 0 °C afforded trisacchride **11** in high yield (83%). The structure of **11** was fully assigned from its ^1H–^1H COSY NMR spectroscopy. The stereochemistry with all α glycosidic linkages in **11** was established by measuring the $^1J_{C\text{-}1,H\text{-}1}$ heteronuclear coupling constants ($^1J_{C\text{-}1,H\text{-}1}$ with 173, 172 and 168 Hz at δ 98.4, 94.8 and 93.7 ppm, respectively). No orthoester intermediate was detected in this case. Compound **11** was selectively deacetylated[12] with acetyl chloride (3% in 1:1 CH_3OH–CH_2Cl_2) at room temperature for 20 h to get exclusively the corresponding trisaccharide acceptor **12**. The chemical shift of H-2 on the mannose residue was moved upfield from 5.45 (in **11**) to 4.41 ppm (in **12**), strongly supporting the fact that no acyl migration occurred under these reaction conditions. Similarly, the TMSOTf (0.1 equiv) promoted the coupling reaction of 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl 2,2,2-trichloroacetimidate (**13**)[13] with **12** in anhydrous dichloromethane at 0 °C afforded the target tetrasaccharide **14** in 80% yield. This tetrasaccharide could be useful in the total synthesis of ristomycin A or ristocetin A[14] after transformation into a glycosyl donor via deallylation and activation.[9] Furthermore, we proved here a practical one-pot preparation of 2,6-differentiated α-D-glucopyranoside that may provide an effective strategy for the synthesis of 2,6-branched oligosaccharides.

3. Experimental

General methods.—Optical rotations were determined at 25 °C with a Perkin–Elmer model 241MC automatic polarimeter. ^1H NMR and ^1H–^1H COSY spectra were recorded with a Bruker ARX 400 spectrometer for solutions in $CDCl_3$. Chemical shifts are given in ppm downfield from internal Me_4Si. Mass spectra were recorded with a VG PlARFOEM mass spectrometer using the FAB technique to introduce the sample. Thin-layer chromatography (TLC) was performed on Silica Gel HF_{254} (E. Merck) 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 column of silica gel (100–200 mesh) with EtOAc–petroleum ether (bp 60–90 °C) or in some cases with toluene–EtOAc–petroleum ether as the eluent. Solutions were concentrated at <80 °C under diminished pressure.

*Allyl 3,4-di-*O*-benzoyl-2-*O*-tert-butyldimethylsilyl-6-*O*-triphenylmethyl-α-D-glucopyranoside* (**2**).—Compound **1**[15] (5 g, 22.7 mmol) was dissolved in pyridine (25 mL). A catalytic amount of DMAP was added into the solution. Chlorotriphenylmethane (7.6 g, 27.3 mmol) was then added. The mixture was stirred at 80 °C for 16 h, then cooled down to 0 °C. Imidazole (3.10 g, 45 mmol) was added; then TBDMSCl (3.75 g, 25 mmol) in DMF (5 mL) was added portionwise over 2 h. The mixture was stirred at rt for 6 h, at which time premixed BzCl (7 mL, 55 mmol) and pyridine (5 mL) was added. The reaction mixture was stirred at 50 °C for 24 h, then co-evaporated with toluene to dryness. The residue was dissolved in CH_2Cl_2 (150 mL) and washed with ice-cold water. The washings were re-extracted with CH_2Cl_2. The combined organic phase was dried, concentrated and subjected to column chromatography on silica gel with 15:1 petroleum ether–EtOAc as the eluent to give **2** (14 g, 79%) as a syrup; $[\alpha]_D^{25}$ +1° (*c* 4.1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.05, 0.14 (2 s, 2 × 3 H, Si (CH_3)$_2$), 0.77 (s, 9 H, *t*-Bu), 3.19–3.27 (m, 2 H, H-6a, H-6b), 4.00 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.6 Hz, H-2), 4.14–4.19 (m, 2 H, H-5, CH_2=CH–CH_2–), 4.34 (dd, 1 H, *J* 5.6, 12.8 Hz, CH_2=CH–CH_2–), 4.97 (d, 1 H, $J_{1,2}$ 4.0 Hz,

H-1), 5.26 (dd, 1 H, J 10.4, 1.6 Hz, CH_2=CH–CH_2–), 5.32 (t, 1 H, $J_{3,4}$ 10 Hz, H-4), 5.42 (dd, 1 H, J 1.6, 10.4 Hz, CH_2=CH–CH_2–), 5.80 (t, 1 H, $J_{3,4}$ 9.6 Hz, H-3), 6.01–6.03 (m, 1 H, CH_2=CH–CH_2–), 7.01–7.91 (m, 25 H, 5 Ph). Anal. Calcd for $C_{48}H_{52}O_8Si$: C, 73.47; H, 6.63. Found: C, 73.69; H, 6.56.

Allyl 3,4-di-O-*benzoyl-2*-O-tert-*butyldimethylsilyl-α*-D-*glucopyranoside* (**3**) *and 3,4-di*-O-*benzoyl-α*-D-*glucopyranoside* (**4**).—Method A: $FeCl_3 \cdot 6H_2O$ (2.5 equiv) was added to a mixture of **2** (3 g, 3.8 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred for 2 h at rt, then diluted with more CH_2Cl_2 (50 mL) and washed with ice-cold water twice. The washings were re-extracted with CH_2Cl_2 (30 mL). The organic phases were combined, dried and concentrated, then subjected to column chromatography on silica gel with 4:1–1.5:1 petroleum ether–EtOAc as the eluent to give syrupy **3** (1.06 g, 51%) and syrupy **4** (800 mg, 49%), respectively. Method B: Compound **2** (2.5 g, 3.2 mmol) was dissolved into 90% aq TFA (15 mL). The mixture was stirred at rt for 2 h, then toluene (50 mL) was added, and the solvents were evaporated in vacuo to give a residue, which was purified by a silica gel column chromatography (1:1 petroleum ether–EtOAc) to give **4** (1.26 g, 92%) as a syrup. Compound **3**: $[\alpha]_D^{25}$ −12° (*c* 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.04 (2 s, 2 × 3 H, Si(CH_3)$_2$), 0.77 (s, 9 H, t-Bu), 3.66 (dd, 1 H, $J_{5,6a}$ 2.8, $J_{6a,6b}$ 13.2 Hz, H-6a), 3.76 (dd, 1 H, $J_{5,6b}$ 2.0, $J_{6a,6b}$ 12.8 Hz, H-6b), 3.97–3.99 (m, 1 H, H-5), 4.00 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.6 Hz, H-2), 4.10 (dd, 1 H, J 5.6, 13.0 Hz, CH_2=CH–CH_2–), 4.29 (dd, 1 H, J 5.6, 13.0 Hz, CH_2=CH–CH_2–), 4.96 (d, $J_{1,2}$ 4.0 Hz, H-1), 5.25 (d, J 10.4 Hz, CH_2=CH–CH_2–), 5.34 (t, $J_{3,4}$ 10 Hz, H-4), 5.39 (dd, 1 H, J 1.6, 10.4 Hz, CH_2=CH–CH_2–), 5.96 (t, $J_{3,4}$ 10 Hz, H-3), 5.92–6.02 (m, 1 H, CH_2=CH–CH_2–), 7.26–8.10 (m, 10 H, 2 Ph). Compound **4**: $[\alpha]_D^{25}$ +26° (*c* 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 3.68 (dd, 1 H, $J_{5,6a}$ 3.6, $J_{6a,6b}$ 13 Hz, H-6a), 3.77 (dd, 1 H, $J_{5,6b}$ 2.4, $J_{6a,6b}$ 13 Hz, H-6b), 3,91 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 9.6 Hz, H-2), 3.96–3.98 (m, 1 H, H-5), 4.12 (dd, 1 H, J 5.6, 13.2 Hz, CH_2=CH–CH_2–), 4.31 (dd, 1 H, J 5.6, 12.8 Hz, CH_2=CH–CH_2–), 5.10 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.28 (d, 1 H, J 10.4 Hz, CH_2=CH–CH_2–), 5.38 (t, 1 H, $J_{3,4}$ 10 Hz, H-4), 5.40 (m, 1 H, CH_2=CH–CH_2–), 5.80 (t, 1 H, $J_{3,4} = J_{2,3} = 9.6$ Hz, H-3), 5.92–6.02 (m, 1 H, CH_2=CH–CH_2–), 7.33–7.97 (m, 10 H, 2 Ph). Anal. Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.61. Found: C, 64.21; H, 5.54.

2,3,4-Tri-O-*benzoyl-α*-L-*rhamnopyranosyl trichloroacetimidate* (**7**).—Ammonium was bubbled into a solution of **5**[16] (6 g, 10.3 mmol) in 3:7 MeOH–THF (100 mL) for 15 min. The reaction mixture was stirred at rt for 3 h, then evaporated to dryness. Purification on a flash silica gel column using 1:2 EtOAc–petroleum ether as eluent gave **6**, which was dissolved in anhyd CH_2Cl_2 (100 mL). To this solution was added trichloroacetonitrile (10 mL, 100 mmol) and DBU (1.2 mL). The reaction mixture was stirred at rt for 6 h, then concentrated. The residue was purified by silica gel column chromatography (3:1 petroleum ether–EtOAc) to give **7** (4.87 g, 76%) as a syrup; $[\alpha]_D^{25}$ +110° (*c* 6.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.43 (d, 3 H, J 6.2 Hz, CH_3), 4.40–4.44 (m, 1 H, H-5), 5.78 (t, 1 H, $J_{3,4}$ 10.0 Hz, H-4), 5.90–5.93 (m, 2 H, H-2, H-3), 6.50 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 7.24–8.12 (m, 15 H, 3 Ph), 8.84 (s, 1 H, NH).

Allyl 2,3,4-tri-O-*benzoyl-α*-L-*rhamnopyranosyl-(1→6)-3,4-di*-O-*benzoyl-α*-D-*glucopyranoside* (**8**).—To a mixture of **4** (800 mg, 1.87 mmol) and **7** (1.31 g, 2.1 mmol) in anhyd CH_2Cl_2 (20 mL) was added Me_3SiOTf (10% equiv) dropwise under a N_2 atmosphere at −15 °C. The mixture was stirred under these conditions for 1 h, at the end of which time, TLC (2:1 petroleum ether–EtOAc) indicated that all the starting material had been consumed. The reaction mixture was neutralized with Et_3N, then concentrated. The product was purified by column chromatography twice (3:1 petroleum ether–EtOAc and 0.5:2.5:1 toluene–petroleum ether–EtOAc) to give **8** (1.2 g, 72.5%); $[\alpha]_D^{25}$ +84° (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.26 (d, 3 H, J 6.4 Hz, CH_3^{IV}), 3.77 (dd, 1 H, $J_{5,6a}$ 6.8, $J_{6a,6b}$ 11.6 Hz, H-6a^{III}), 3.89–3.92 (m, 2 H, H-2^{III}, H-6b^{III}), 4.11–4.12 (m, 1 H, H-5^{IV}), 4.25 (q, 1 H, J 6.0, 12.8 Hz, CH_2=CH–CH_2–), 4.29–4.33 (m, 1 H, H-5^{III}), 4.45–4.49 (m, 1 H, CH_2=CH–CH_2–), 5.11–5.13 (m, 2 H, H-1^{III}, H-1^{IV}), 5.33–5.36

(m, 1 H, CH_2=CH–CH_2–), 5.42 (t, 1 H, $J_{3,4}$ 10.0 Hz, H-4^{III}), 5.47–5.52 (m, 1 H, CH_2=CH–CH_2–), 5.63 (t, 1 H, $J_{3,4}$ 10.0 Hz, H-3^{III}), 5.71–5.72 (m, 1 H, H-2^{IV}), 5.76–5.79 (m, 2 H, H-3^{IV}, H-4^{IV}), 6.06 (m, 1 H, CH_2=CH–CH_2–), 7.25–8.10 (m, 25 H, 5 Ph). Anal. Calcd for $C_{50}H_{46}O_{15}$: C, 67.72; H, 5.19. Found: C, 67.95; H, 5.33.

*Allyl 2,3,4-*O*-tri-benzoyl-α-*L*-rhamnopyranosyl-(1→6)-2-*O*-acetyl-3,4-di-*O*-benzoyl-α-*D*-glucopyranoside* (**9**).—Compound **8** (20 mg) was dissolved in pyridine (1 mL). Then Ac_2O (0.5 mL) was added into the solution. The mixture was stirred at rt overnight. The solvents were evaporated under reduced pressure to give **9** for NMR testing; ^{1}H NMR ($CDCl_3$): δ 1.26 (d, 3 H, J 6.2 Hz, CH_3^{IV}), 3.79 (dd, 1 H, $J_{5,6a}$ 7.2, $J_{6a,6b}$ 12 Hz, H-6a^{III}), 3.89 (dd, 1 H, $J_{5,6b}$ 2.0, $J_{6a,6b}$ 12 Hz, H-6b^{III}), 4.11–4.13 (m, 1 H, H-5^{IV}), 4.22 (dd, 1 H, J 6.0, 12.8 Hz, CH_2=CH–CH_2–), 4.36–4.45 (m, 2 H, H-5^{III}, CH_2=CH-CH_2–), 5.11 (d, 1 H, $J_{1',2'}$ 1.4 Hz, H-1^{IV}), 5.17 (dd, 1 H, $J_{1,2}$ 3.6, $J_{2,3}$ 10.4 Hz, H-2^{III}), 5.24-5.25 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1^{III}), 5.30–5.32 (m, 1 H, CH_2=CH–CH_2–), 5.39–5.44 (t, 1 H, $J_{3,4}$ 10.0 Hz, H-4^{III}), 5.46–5.51 (m, 1 H, CH_2=CH–CH_2–), 5.65 (t, 1 H, $J_{3',4'}$ 10.0 Hz, H-4^{IV}), 5.69–5.70 (m, 1 H, H-2^{IV}), 5.77 (dd, 1 H, $J_{2',3'}$ 3.6, $J_{3',4''}$ 10.0 Hz, H-3^{IV}), 6.01–6.06 (m, 2 H, H-3, CH_2=CH–CH_2–), 7.24–8.09 (m, 25 H, 5 Ph). Anal. Calcd for $C_{52}H_{48}O_{16}$: C, 67.24; H, 5.17. Found: C, 67.45; H, 5.30.

*Allyl 2-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α-*D*-mannopyranosyl-(1→2)-[2,3,4-tri-*O*-benzoyl-α-*L*-rhamnopyranosyl-(1→6)]-3,4-di-*O*-benzoyl-α-*D*-glucopyranoside* (**11**).—To a mixture of **8** (920 mg, 1.04 mmol) and **10**[17] (815 mg, 1.2 mmol) in anhyd CH_2Cl_2 (10 mL) was dropped Me_3SiOTf (10% equiv) under a N_2 atmosphere at 0 °C. The mixture was stirred under these conditions for 2 h, at the end of which time, TLC (2:1 petroleum ether–EtOAc) indicated that all the donor was consumed. The reaction mixture was neutralized with Et_3N, then concentrated. The residue was purified by column chromatography (0.5:2:1 toluene–petroleum ether–EtOAc) to give trisaccharide **11** (1.21 g, 83%) as a syrup; $[\alpha]_D^{25}$ +90° (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.27 (d, 3 H, J 6.4 Hz, CH_3), 2.11 (s, 3 H, CH_3CO), 3.75 (dd, 1 H, $J_{5,6a}$ 7.2, $J_{6a,6b}$ 12.0 Hz, H-6a^{III}), 3.91 (dd, 1 H, $J_{5,6b}$ 2.0, $J_{6a,6b}$ 12.0 Hz, H-6b^{III}), 4.13–4.33 (m, 6 H, H-2^{III}, H-5^{IV}, H-5^{II}, H-6a^{II}, H-6b^{II}, CH_2=CH–CH_2–), 4.38–4.42 (m, 1 H, H-5^{III}), 4.50 (dd, 1 H, J 5.2 Hz, CH_2=CH–CH_2–), 5.09 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1^{II}), 5.10 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1^{IV}), 5.25 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1^{III}), 5.37–5.40 (m, 2 H, H-4, CH_2=CH–CH_2–), 5.47–5.48 (m, 1 H, H-2^{II}), 5.56–5.58 (m, 2 H, H-3^{II}, CH_2=CH–CH_2–), 5.64 (t, 1 H, $J_{3,4}$ 10 Hz, H-4^{II}), 5.72–5.73 (dd, 1 H, H-2^{IV}), 5.76–5.78 (m, 2 H, H-3^{IV}, H-4^{IV}), 6.11–6.15 (m, 2 H, $J_{3,4}$ 10 Hz, H-3^{III}, CH_2=CH–CH_2–), 7.23–8.10 (m, 40 H, 8 Ph). Anal. Calcd for $C_{79}H_{70}O_{24}$: C, 67.62; H, 4.99. Found: C, 67.47; H, 5.08.

*Allyl 3,4,6-tri-*O*-benzoyl-α-*D*-mannopyranosyl-(1→2)-[2,3,4-tri-*O*-benzoyl-α-*L*-rhamnopyranosyl-(1→6)]-3,4-di-*O*-benzoyl-α-*D*-glucopyranoside* (**12**).—Compound **11** (196 mg, 0.14 mmol) was dissolved in 1:1 CH_2Cl_2-CH_3OH (14 mL), and 3% (volume ratio) of acetyl chloride was added. The reaction mixture was stirred at rt for 20 h, at the end of which time, TLC (1:2 EtOAc–petroleum ether) indicated the reaction was complete. The solvent was neutralized with Et_3N, concentrated and subjected to the column chromatography (2.5:1 petroleum ether–EtOAc) to give compound **12** (152 mg, 80%) as a syrup; $[\alpha]_D^{25}$ +66° (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.28 (d, 3 H, J 6.2 Hz, CH_3), 3.76 (dd, 1 H, $J_{5,6a}$ 7.2, $J_{6a,6b}$ 12.0 Hz, H-6a^{III}), 3.92 (dd, $J_{5,6b}$ 4.0, $J_{6a,6b}$ 12.0 Hz, H-6b^{III}), 4.11–4.30 (m, 5 H, H-2^{III}, H-5^{IV}, H-5^{II}, H-6a^{II}, CH_2=CH–CH_2–), 4.35–4.40 (m, 2 H, H-5^{III}, H-2^{II}), 4.46–4.51 (m, 2 H, CH_2=CH–CH_2–, H-6b^{II}), 5.12 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1^{II}), 5.14 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1^{IV}), 5.29 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1^{III}), 5.34–5.44 (t, 3 H, H-4^{III}, H-3^{II}, CH_2=CH–CH_2–), 5.52–5.55 (m, 1 H, CH_2=CH–CH_2–), 5.66 (t, 1 H, $J_{3,4}$ 10 Hz, H-4^{II}), 5.72 (dd, 1 H, H-2^{IV}), 5.76–5.79 (m, 2 H, H-3^{IV}, H-4^{IV}), 6.00–6.09 (m, 1 H, CH_2=CH–CH_2–), 6.12 (t, 1 H, $J_{3,4}$ 10 Hz, H-3^{III}), 7.25–8.09 (m, 40 H, 8 Ph). Anal. Calcd for $C_{77}H_{68}O_{23}$: C, 67.94; H, 5.00. Found: C, 67.68; H, 5.16.

*Allyl 2,3,5-tri-*O*-benzoyl-α-*D*-arabinofuranosyl-(1→2)-3,4,6-tri-*O*-benzoyl-α-*D*-mannopyranosyl-(1→2)-[2,3,4-tri-*O*-benzoyl-α-*L*-*

rhamnopyranosyl-(1→6)]-3,4-di-O-*benzoyl-α*-D-*glucopyranoside* (**14**).—To a mixture of compound **12** (100 mg, 0.07 mmol) and **13**[18] (48 mg, 0.08 mmol) in anhyd CH_2Cl_2 (5 mL) was added Me_3SiOTf (15% equiv) under a N_2 atmosphere at 0 °C. The mixture was stirred under these conditions for 3 h, then neutralized with Et_3N and concentrated. The residue was purified by column chromatography (2:1 petroleum ether–EtOAc) to give **14** (106 mg, 80%) as a syrup; $[\alpha]_D^{25}$ +65° (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.28 (d, 3 H, *J* 6.4 Hz, CH_3), 3.72 (dd, 1 H, *J* 7.0, 12.0 Hz, H-6a^{III}), 3.90 (dd, 1 H, *J* 2.3, 12.0 Hz, H-6b^{III}), 4.11–4.26 (m, 6 H, H-2^{III}, H-5^{IV}, H-5^{II}, H-6a^{II}, H-6b^{II}, CH_2=CH–CH_2–), 4.35–4.42 (m, 2 H, H-5^{III}, H-2^{II}), 4.44–4.46 (m, 1 H, CH_2=CH–CH_2–), 4.61–4.63 (m, 2 H, H-4^{I}, H-5a^{I}), 4.69 (dd, 1 H, *J* 5.0, 11.4 Hz, H-5b^{I}), 5.10 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1^{II}), 5.21 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1^{III}), 5.24 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1^{IV}), 5.29 (d, 1 H, *J* 10.4 Hz, H-3^{II}), 5.37 (t, 1 H, H-4^{III}), 5.45–5.49 (dd, 1 H, *J* 1.2 Hz, CH_2=CH–CH_2–), 5.47 (s, 1 H, H-3^{I}/2^{I}), 5.60–5.67 (m, 4 H, H-1^{I}, H-4^{II}, CH_2=CH–CH_2–, H-2^{I}/3^{I}), 5.71 (dd, 1 H, H-2^{IV}), 5.78 (dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 12 Hz, H-3^{IV}), 5.84 (t, 1 H, $J_{3,4}$ 12 Hz, H-4^{IV}), 5.96–6.04 (m, 1 H, CH_2=C*H*–CH_2–), 6.12 (t, 1 H, $J_{3,4}$ 10 Hz, H-3^{III}), 7.23–8.10 (m, 55 H, 11 Ph), MALDI-TOF-MS Calcd for $C_{103}H_{88}O_{30}Na^+$ 1827.5; Found *m*/*z* 1827.3 ($M+Na^+$). Anal. Calcd for $C_{103}H_{88}O_{30}$: C, 68.51; H, 4.88. Found: C, 68.77; H, 4.74.

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