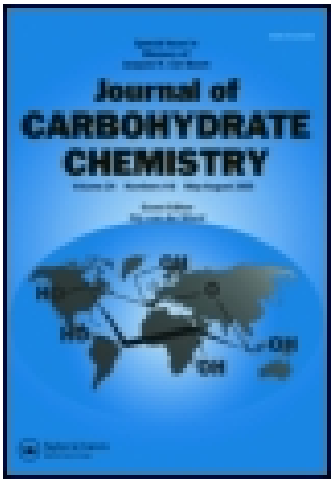


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lcar20

Synthesis of Haptenic Trimers Corresponding to the Cell Wall Glycopeptidolipids of Mycobacterium Avium Serovar 12

Korien Zegelaar-Jaarsveld [a], Simon C. van der Plas [a], Gijs A. van der Marel [a] & Jacques H. van Boom [a]
[a] Leiden Institute of Chemistry, Gorlaeus Laboratoria, Leiden University, P.O. Box 9502, 2300 RA, Leiden, The Netherlands
Published online: 22 Aug 2006.

To cite this article: Korien Zegelaar-Jaarsveld, Simon C. van der Plas, Gijs A. van der Marel & Jacques H. van Boom (1996) Synthesis of Haptenic Trimers Corresponding to the Cell Wall Glycopeptidolipids of Mycobacterium Avium Serovar 12, Journal of Carbohydrate Chemistry, 15:5, 591-610, DOI: 10.1080/07328309608005677

To link to this article: http://dx.doi.org/10.1080/07328309608005677

J. CARBOHYDRATE CHEMISTRY, 15(5), 591-610 (1996)

SYNTHESIS OF HAPTENIC TRIMERS CORRESPONDING TO THE CELL WALL GLYCOPEPTIDOLIPIDS OF *MYCOBACTERIUM AVIUM* SEROVAR 12

Korien Zegelaar-Jaarsveld, Simon C. van der Plas, Gijs A. van der Marel, and Jacques H. van Boom*

Leiden Institute of Chemistry, Gorlaeus Laboratoria, Leiden University, P.O. Box 9502, 2300 RA Leiden, The Netherlands.

Received December 18, 1995 - Final Form April 2, 1996

ABSTRACT

The preparation of the spacer-containing trimers **2**, 3-aminopropyl 3-*O*-[4-*O*-Me-3-*O*-(4-*N*-D,L-lactoyl-3-*O*-Me-β-D-Qui*p*)-α-L-Rha*p*]-α-L-Rha*p*, derivatives of the antigenic determinant of the glycopeptidolipid from *Mycobacterium avium* serotype 12, are described. Thus, iodonium ion-mediated glycosylation of the spacer-containing acceptor **7** with ethyl 1-thio-rhamnopyranoside donor **10**, followed by selective deprotection of the *p*-methoxybenzyl group of thus obtained **19** gave bis-rhamnopyranoside acceptor **20**. Elongation of **20** with ethyl 4-azido-1-thio-β-D-quinovopyranoside **18** and subsequent reduction of the azido function in **21** led to trimer **22**. The amino group in **22** was coupled with both D- and L-lactic acid to give, after removal of the protective groups, trimers **2**.

INTRODUCTION

It is well recognised that mycobacteria are responsible for disseminate infections in people suffering from acquired immune deficiency syndrome (AIDS). For example, more

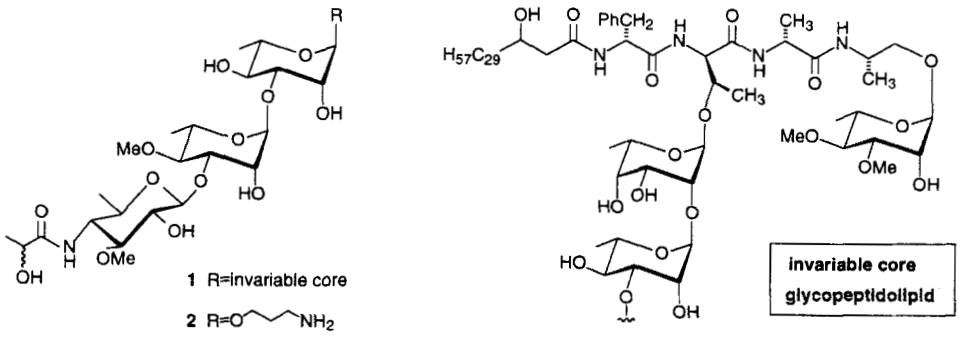


Figure 1

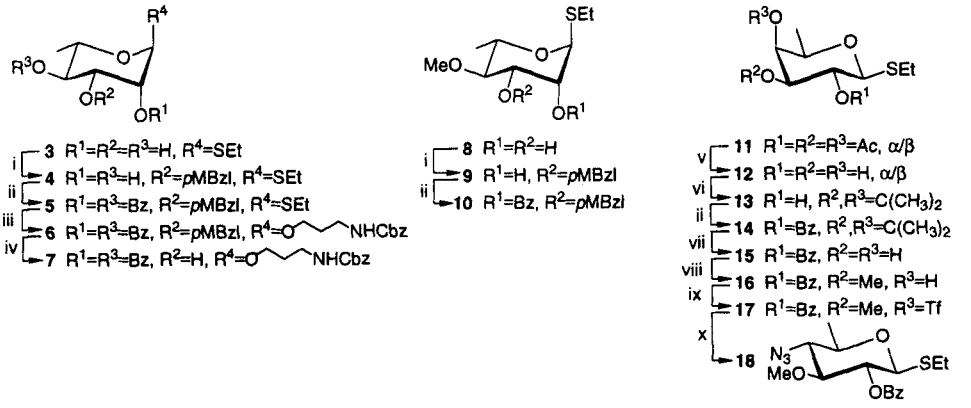
than half of the AIDS patients in the USA are infected[1,2] with *Mycobacterium avium-Mycobacterium intracellulare-Mycobacterium scrofulaceum* (MAIS serogroup). Structural and immunological studies by Brennan et al.[3-10] revealed that the dominant surface antigen of the individual *M. avium* serovars is composed of an invariable core glycopeptidolipid (GPL, see Figure 1) in which HO-3 of the terminal L-rhamnopyranosyl unit is anchored to structurally diverse haptenic oligosaccharides.

In 1988, Brennan et al.[11] also showed that the invariable core of the GPL from *M. avium* serovar 12 of the 31-membered MAIS serogroup is linked, *via* an α-(1→3)-interglycosidic bond, to the haptenic trimer 4-*N*-La-3-*O*-Me-β-Qui*p*-(1→3)-4-*O*-Me-α-L-Rha*p*-(1→3)-α-L-Rha*p* as in compound **1** (see Figure 1). Unfortunately, the absolute configuration (D or L) of the distal quinovose and its 4-*N*-lactoyl substituent could not be assigned. However, it was firmly established that the quinovose unit in the trimer was 1,2-*trans* linked to 4-*O*-methyl-L-Rha*p*.

As part of a programme to determine the relation between the structure and the serological or immunological specificity of the trisaccharide hapten linked to the core of the GPL from *M. avium* serotype 12, we here report the synthesis of the spacer-containing trimers **2**, both of which have a D-quinovose in common but differ from each other by the presence of a D- or L-lactoyl substituent.

RESULTS AND DISCUSSION

Retrosynthetic analysis reveals that the target molecules **2** can be assembled (see Scheme 2) by a stereoselective sequential elongation of ethyl 4-*O*-methyl-1-thio-α-L-rhamnopyranoside **10** with the spacer-containing α-L-rhamnopyranoside **7**, and the

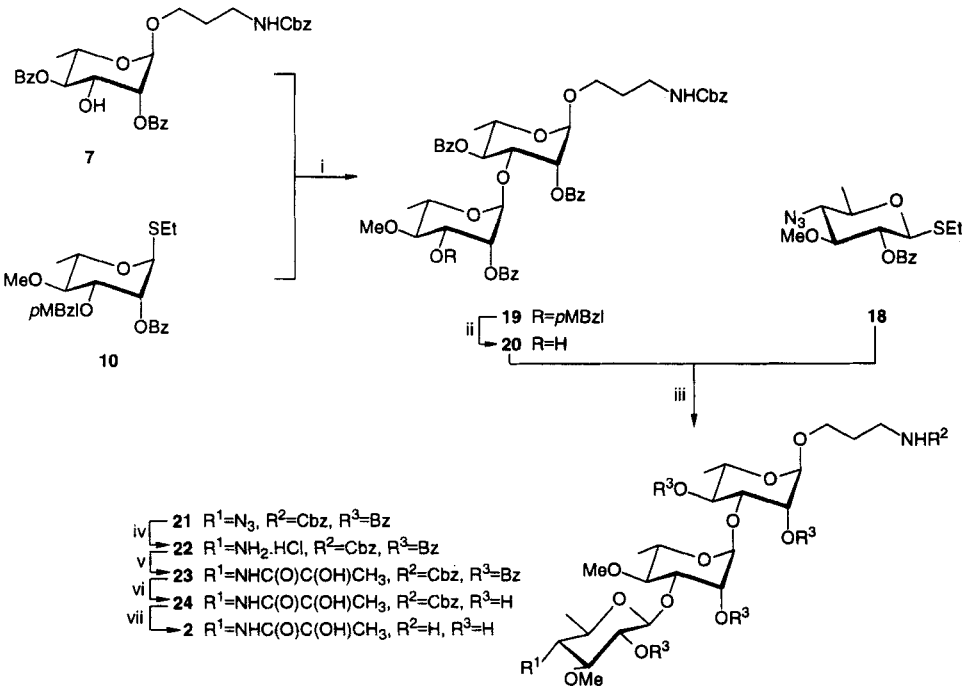


Reagents and conditions: i) Bu_2SnO, MeOH, reflux, 2 h; *p*MBzlCl, CsF, NaI, DMF, 18 h, **4** 70%, **9** 78%. ii) BzCl, pyridine, 1.5 h, **5** 89%, **10** 88%, **14** 98%. iii) $HO(CH_2)_3NHZ$, NIS/TfOH(cat.), 1,2-dichloroethane-Et_2O, 0 °C, 10 min, 97%. iv) DDQ, dichloromethane-water, 1 h, 88%. v) KO*t*-Bu, MeOH, 1.5 h, 98%. vi) $(CH_3)_2C(OCH_3)_2$, acetone, *p*TsOH, 2 h, **13-β** 72% and **13-α** 16%. vii) 80% HOAc, 50 °C, 18 h, 89%. viii) Bu_2SnO, MeOH, reflux, 2 h; MeI, CsF, DMF, 18 h, 57%. ix) Tf_2O, pyridine, dichloromethane, -20 °C, 1 h. x) LiN_3, DMF, 20 °C, 1 h, 76%.

Scheme 1

D-quinovopyranoside derivative **18**. The presence of a 2-*O*-benzoyl participating group in the ethyl 1-thio-glycoside donors **10** and **18** will promote the iodonium ion-mediated formation of the requisite 1,2-*trans* interglycosidic bonds. In addition, selective removal of the temporary *p*-methoxybenzyl (*p*MBzl) protective group enables extension of **10** at HO-3, while reduction of the 4-azido function in **18** opens the way of condensing the newly generated amino group with either D- or L-lactic acid.

The preparation of the three building units **7**, **10**, and **18** is presented in Scheme 1. Ethyl 1-thio-α-L-rhamnopyranoside[12] (**3**) was regioselectively *p*-methoxybenzylated at HO-3 *via* its 2,3-*O*-stannylidene complex[13] to give derivative **4**, benzoylation of which led to the fully protected rhamnopyranoside **5**. The latter compound was allowed to condense with 3-(benzyloxycarbonyl)amino-1-propanol[14] using the promotor *N*-iodosuccinimide (NIS) and catalytic triflic acid (TfOH)[15] to yield the expected α-linked L-rhamnopyranoside **6**. Removal of the *p*-methoxybenzyl group in **6** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[16] (DDQ) led to the isolation of the L-rhamnopyranosyl acceptor **7** (53% yield) in four steps. Regioselective *p*-methoxybenzylation[17] of ethyl 4-*O*-methyl-1-thio-α-L-rhamno-pyranoside[18] (**8**) and subsequent benzoylation of HO-2 in **9**, as described



Reagents and conditions: i) NIS/TfOH(cat.), 1,2-dichloroethane-Et_2O, -30 °C, 15 min, 84%. ii) DDQ, dichloromethane-water, 45 min, 81%. iii) see step i, 0 °C, 15 min, 90%. iv) H_2S-pyridine-water, 3 h, 94%. v) D- or L-lactic acid (lithium or sodium salt), BOP, DIPEA, DMF, 1.5 h, 75%. vi) KO*t*-Bu, MeOH, 79%. vii) Pd(C), H_2, 2-propanol-water, 20 h, 87%.

Scheme 2

previously for the transformation of **3**→**5**, gave the fully protected L-rhamnopyranoside **10** in 68% overall yield.

Zemplén type deacetylation of an anomeric mixture of the 2,3,4-tri-*O*-acetyl-1-thio-D-fucopyranoside **11**, obtained by glycosidation of 1,2,3,4-tetra-*O*-acetyl-α(β)-D-fucopyranoside with ethanethiol and tin tetrachloride followed by acid-catalysed acetonation of an anomeric mixture of **12** gave, after purification by silica gel chromatography, homogeneous **13**. Benzoylation of **13** and subsequent deacetonation of **14** gave, after regioselective methylation of HO-3 in **15**, the partially protected D-fucopyranoside **16**. Triflation of HO-4 in **16** with triflic anhydride and then Walden inversion of the triflate function[18] in crude **17** with lithium azide, gave the fully protected ethyl 4-azido-2-*O*-benzoyl-3-*O*-methyl-1-thio-β-D-quinovopyranosyl donor **18** in 26% yield based on **11**.

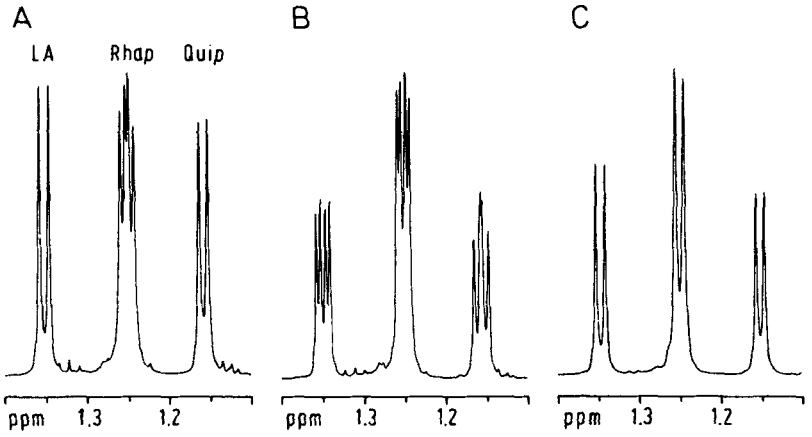


Figure 2: Part of the ^{1}H NMR spectrum (CD_3OD, 600 MHz) of trimers **2**; a: D-lactate **2**, b: equimolar mixture of D- and L-lactate **2**; c: L-lactate **2**.

Having the required building units **7**, **10**, and **18** in hand, trimers **2** bearing either a D- or L-lactoyl moiety were assembled by the sequence of reactions diagrammed in Scheme 2. Iodonium ion-mediated glycosylation of acceptor **7** with the L-rhamno-pyranoside donor **10** proceeded stereoselectively, as gauged by ^{1}H and ^{13}C NMR spectroscopy, to give exclusively the α-linked disaccharide **19**. Removal of the 3'-*O*-*p*-methoxybenzyl group in **19** with DDQ gave the partially protected disaccharide **20** in 70% overall yield. Condensation of the "L-disaccharide" acceptor **20** with the D-quinovo-pyranoside **18** gave, after purification by Sephadex LH20 gel-filtration, the homogeneous trimeric fragment **21** in 90% yield. Transformation of the 4"-azido substituent in derivative **21** into the required amino group was effected using hydrogen sulfide[19] as the reducing agent. Condensation of the 4"-amino group in **22** with D-lactic acid (lithium salt) in the presence of the coupling agent (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate[20] (BOP) led to the D-lactoyl derivative **23**. Zemplén type debenzoylation of **23** followed by hydrogenolysis of the benzyloxycarbonyl (Z) protective group in **24** gave, after purification, homogeneous **2** containing the 4"-*N*-(D)-lactoyl moiety in 48% overall yield based on **21**. The trimer **2** having the 4"-*N*-(L)-lactoyl substituent was obtained in a similar fashion by BOP-assisted condensation of **22** with L-lactic acid (sodium salt) and further processing of the coupling product under the same conditions, as mentioned earlier for the conversion of **23** into **2**.

The chiral purity of the individual diastereomeric forms of **2** was corroborated, as illustrated in Figure 2, by ^{1}H NMR spectroscopy. It can be seen in Figure 2a that the

methyl groups at C-5 in the two L-rhamnose units appear as four distinct resonances (δ_H 1.24-1.25). On the other hand, the latter methyl resonances show up as a doublet (δ_H 1.28, see Figure 2c) in the L-diastereomer of **2**. In addition, a slight but distinctive difference in chemical shifts is observed in the ^1H NMR spectrum (see Figure 5.2b) of a diastereomeric mixture of **2** for the methyl at C-5 of the quinovose (δ_H 1.15) and the methyl in the lactoyl moiety (δ_H 1.35).

EXPERIMENTAL

General methods and materials: Methanol was dried by refluxing with magnesium methoxide, distilled and stored over molecular sieves 3 Å (Aldrich). Toluene, dichloromethane and 1,2-dichloroethane were distilled from P_2O_5. Toluene was stored over sodium wire, dichloromethane and 1,2-dichloroethane over molecular sieves 4 Å. *N,N*-Dimethylformamide (DMF) was stirred with calcium hydride for 19 h, then distilled under reduced pressure and stored over molecular sieves 4 Å. Pyridine was refluxed for 18 h in the presence of calcium hydride, then distilled and stored over molecular sieves 4 Å. Solvents used for column chromatography were of technical grade and distilled before use.

Reactions were performed under anhydrous conditions at room temperature, unless stated otherwise. Solvents were evaporated under reduced pressure at 40 °C. TLC analyses were conducted on Schleicher & Schüll DC Fertigfolien (F 1500 LS 254). Compounds were visualised by UV light and by spraying with H_2SO_4-ethanol (1/4, v/v). Column chromatography was performed on columns of silica gel (Baker, 0.063-0.200 nm). Petroleum ether used for elution of the columns was low-boiling (40-60 °C). Gel-filtration was performed on Sephadex LH20 (Pharmacia).

Optical rotations were measured with a Propol polarimeter at 20 °C, for solutions in chloroform (p.a. Baker) unless stated otherwise. NMR spectra were recorded with a Jeol JNM-FX-200 (^1H and ^{13}C at 200 and 50.1 MHz, respectively), a Bruker WM-300 spectrometer equipped with an Aspect 2000 computer (^1H, 300 MHz) and a Bruker 600-DMX spectrometer (^1H and ^{13}C at 600 and 150 MHz, respectively). Chemical shifts are given in ppm (δ) relative to tetramethylsilane (TMS) as an internal standard. Infrared spectroscopy (IR) was measured with compounds applied between KBr tablets by a Pye Unicam SP3-200 infrared spectrophotometer. Mass spectra were recorded for solutions in methanol-water (4/1, v/v) with a Finnigan MAT TSQ-70 equipped with a custom-made Electrospray Interface (ESI).

Ethyl 3-*O*-(*p*-Methoxybenzyl)-1-thio-α-L-rhamnopyranoside (4). Dibutyltin oxide (0.64 g, 2.6 mmol) was added to a solution of ethyl 1-thio-α-L-rhamnopyranoside

(**3**, 485 mg, 2.3 mmol) in methanol (7 mL), and the mixture was heated under reflux for 2 h. Methanol was evaporated and the residue was dried by evaporation with toluene. The stannylidene derivative was dissolved in DMF (10 mL) and *p*-methoxybenzyl chloride (0.47 mL, 3.5 mmol), cesium fluoride (0.45 g, 3.0 mmol) and sodium iodide (34 mg) were added. After stirring for 18 h, the solvent was removed, and the crude product was dissolved in diethyl ether (25 mL). This solution was washed twice with aq KF (1 M, 15 mL), and once with water (10 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography (20→40% ethyl acetate in petroleum ether) to give compound **4** (518 mg, 1.6 mmol). $[\alpha]_D$ +107.6° (*c* 1); ^1H NMR ($CDCl_3$) δ 1.30 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 2.60 (ABX, 2H, CH_2 SEt), 3.54-3.59 (m, 2H, CH sugar ring), 4.07-4.12 (m, 2H, CH sugar ring), 3.80 (s, 3H, CH_3 OMe), 4.55 (AB, 2H, CH_2 *p*MBzl), 5.30 (d, 1H, $J_{1,2}$ = 0.7 Hz, H-1), 6.90 (d, 2H, $J_{H,H}$ = 6.7 Hz, H_{Ar} *p*MBzl), 7.28 (d, 2H, $J_{H,H}$ = 6.9 Hz, H_{Ar} *p*MBzl); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 14.7 (CH_3 SEt), 17.3 (C-6), 24.8 (CH_2 SEt), 54.9 (CH_3 OMe), 71.1 (CH_2 *p*MBzl), 68.2, 69.2, 71.5, 79.4 (C-2, C-3, C-4, C-5), 83.4 (C-1), 113.7, 129.5 (C_{Ar} *p*MBzl), 129.4, 159.2 (qC_{Ar} *p*MBzl).

Anal. Calcd for $C_{16}H_{24}O_5S$ (328.43): C, 58.51; H, 7.37. Found: C, 58.59; H, 7.51.

Ethyl 2,4-Di-*O*-benzoyl-3-*O*-(*p*-methoxybenzyl)-1-thio-α-L-rhamnopyranoside (5). To a solution of compound **4** (518 mg, 1.6 mmol) in pyridine (6 mL) was added benzoyl chloride (0.21 mL, 2.4 mmol). After stirring for 1.5 h, the reaction was quenched with water (2 mL), and the solution was concentrated. The residue was redissolved in ethyl acetate (10 mL), and the organic solution was washed with water (10 mL) and aq $NaHCO_3$ (10%, 8 mL), dried ($MgSO_4$), and filtered. Ethyl acetate was evaporated and the residue was purified by column chromatography (5→20% ethyl acetate in petroleum ether) to yield rhamnopyranoside **5** (755 mg, 1.4 mmol). $[\alpha]_D$ +32.2° (*c* 1); ^1H NMR ($CDCl_3$) δ 1.32 (t, 3H, $J_{H,H}$ = 7.4 Hz, CH_3 SEt), 1.29 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 2.68 (ABX, 2H, CH_2 SEt), 3.72 (s, 3H, CH_3 OMe *p*MBzl), 3.96 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 4.29 (dq, 1H, $J_{5,4}$ = 9.2 Hz, $J_{5,6}$ = 6.2 Hz, , H-5), 4.46 (AB, 2H, CH_2 *p*MBzl), 5.41 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 5.43 (d, 1H, $J_{4,5}$ = 9.7 Hz, H-4), 5.69 (dd, 1H, $J_{2,1}$ = 1.6 Hz, $J_{2,3}$ = 3.3 Hz, H-2), 6.62 (d, 2H, CH *p*MBzl, $J_{H,H}$ = 8.8 Hz), 7.03 (d, 2H, H_{Ar} *p*MBzl, $J_{H,H}$ = 8.8 Hz), 7.43-7.64 (m, 6H, H_{Ar}), 7.95-8.00 (m, 2H, H_{Ar} Bz), 8.11-8.16 (m, 2H, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 14.7 (CH_3 SEt), 17.4 (C-6), 25.5 (CH_2 SEt), 54.8, (CH_3 OMe *p*MBzl), 70.3 (CH_2 *p*MBzl), 67.1, 70.6, 73.1, 73.9 (C-2, C-3, C-4, C-5), 82.3 (C-1), 113.4 (C_{Ar} *p*MBzl), 128.1, 128.2, 129.4, 129.6, 129.7 (C_{Ar}), 129.1 (qC_{Ar}), 132.9, 133.0 (C_{Ar} Bz), 158.9 (qC_{Ar} *p*MBzl), 165.4, 165.5 (2C=O Bz).

Anal. Calcd for $C_{30}H_{32}O_7S$ (536.65): C, 67.14; H, 6.01. Found: C, 67.22; H, 6.07.

3-(Benzyloxycarbonylamino)propyl 2,4-Di-*O*-benzoyl-3-*O*-(*p*-methoxybenzyl)-α-L-rhamnopyranoside (6). Rhamnopyranoside donor **5** (466 mg, 0.87 mmol) and 3-(benzyloxycarbonyl)amino-1-propanol[14] (218 mg, 1.00 mmol) were dried by repeated evaporation with toluene. The building blocks were subsequently dissolved in a mixture of 1,2-dichloroethane and diethyl ether (1/1, v/v, 6 mL). The resulting solution was stirred for 25 min in the presence of activated molecular sieves (4 Å). The mixture was cooled in an ice-bath and a suspension of NIS (205 mg, 0.91 mmol) and TfOH (12 μL, 135 μmol) in the same solvent mixture (4 mL) was added. After stirring for 5 min, TLC analysis showed total conversion of the two building blocks to one product. The reaction was quenched with pyridine (0.2 mL), filtered, and the filtrate was diluted with ethyl acetate (15 mL). The organic solution was washed with aq $Na_2S_2O_3$ (20%, 10 mL) and aq $NaHCO_3$ (10%, 10 mL), dried ($MgSO_4$), and filtered. The filtrate was concentrated and the crude product was purified by silica gel chromatography. The column was eluted with 10→40% ethyl acetate in petroleum ether to yield the spacer-containing rhamnopyranoside **6** (571 mg, 0.84 mmol). $[\alpha]_D$ +66.2° (*c* 1); ^{1}H NMR ($CDCl_3$) δ 1.28 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.82-1.87 (m, 2H, H-2 spacer), 3.30-3.38 (m, 2H, H-3 spacer), 3.53-3.57 (m, 1H, H-1 spacer), 3.69 (s, 3H, CH_3 OMe *p*MBzl), 3.73-3.84 (m, 1H, H-1 spacer), 3.86 (dq, 1H, $J_{5,4}$ = 9.6 Hz, $J_{5,6}$ = 6.0 Hz, H-5), 4.01 (dd, 1H, $J_{3,2}$ = 3.3 Hz, $J_{3,4}$ = 9.8 Hz, H-3), 4.45 (AB, 2H, CH_2 *p*MBzl), 4.91 (d, 1H, $J_{1,2}$ 1.5 = Hz, H-1), 5.03 (br s, 1H, NH), 5.12 (s, 2H, CH_2 Z), 5.40 (t, 1H, $J_{4,3}$≈$J_{4,5}$ = 9.8 Hz, H-4), 5.55 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.3 Hz, H-2), 6.57-6.61 (m, 2H, CH *p*MBzl), 6.99-7.04 (m, 2H, H_{Ar} *p*MBzl), 7.30-7.59 (m, 8H, H_{Ar}), 7.97-8.02 (m, 2H, H_{Ar} Bz), 8.09-8.14 (m, 2H, H_{Ar} Bz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 17.5 (C-6), 29.4 (C-2 spacer), 38.3 (C-3 spacer), 54.8 (CH_3 OMe *p*MBzl), 65.5, 66.3 (C-1 spacer, CH_2 Z), 70.5 (CH_2 *p*MBzl), 66.6, 69.0, 72.9, 73.7 (C-2, C-3, C-4, C-5), 97.6 (C-1, $^1J_{C,H}$ = 168.5 Hz), 113.3 (C_{Ar} *p*MBzl), 127.8, 128.1, 128.2, 129.2, 129.6, 129.7 (C_{Ar}), 129.4 (qC_{Ar} Bz), 132.9, 133.0 (C_{Ar} Bz), 136.4 (qC_{Ar}), 156.2 (C=O Z), 158.8 (qC_{Ar} *p*MBzl), 165.4, 165.6 (2C=O Bz).

Anal. Calcd for $C_{39}H_{41}NO_{10}$ (683.76): C, 68.51; H, 6.04; N, 2.05. Found: C, 68.42; H, 6.18; N, 1.93.

3-(Benzyloxycarbonylamino)propyl 2,4-Di-*O*-benzoyl-α-L-rhamnopyranoside (7). Compound **6** (571 mg, 0.84 mmol) was dissolved in a mixture of dichloromethane-water (8/1, v/v, 4 mL) and DDQ (288 mg, 1.3 mmol) was added. After stirring for 1 h, the mixture was filtered and diluted with dichloromethane (10 mL). The filtrate was washed with water (5 mL) and aq $NaHCO_3$ (10%, 8 mL), dried ($MgSO_4$), and filtered. Dichloromethane was evaporated and purification of the residue was achieved by silica gel column chromatography. The column was eluted with a gradient of 10→50% ethyl acetate in petroleum ether to furnish compound **26** (418 mg, 0.74 mmol). $[\alpha]_D$ +36.8°

(*c* 1); ^{1}H NMR ($CDCl_3$) δ 1.31 (d, 3H, $J_{6,5}$ = 6.4 Hz, H-6), 1.82-1.90 (m, 2H, H-2 spacer), 3.36 (m, 1H, H-5), 3.32-3.39 (m, 2H, H-3 spacer), 3.49-4.30 (m, 5H, H-2, H-3, H-4, H-1 spacer), 4.95 (d, 1H, $J_{1,2}$ = 1.3 Hz, H-1), 5.12 (s, 2H, CH_2 Z), 5.26 (t, 1H, $J_{4,3} \approx J_{4,5}$ = 9.7 Hz, H-4), 5.36 (dd, 1H, $J_{2,1}$ = 1.3 Hz, $J_{2,3}$ = 3.5 Hz, H-2), 7.31-7.65 (m, 11H, H_{Ar}), 8.06-8.13 (m, 4H, H_{Ar} Bz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 17.4 (C-6), 29.3 (C-2 spacer), 38.1 (C-3 spacer), 65.4 (C-1 spacer), 66.3 (CH_2 Z), 66.2, 68.3, 73.1, 75.1 (C-2, C-3, C-4, C-5), 97.2 (C-1), 127.7, 128.2, 129.6 (C_{Ar}), 129.2 (qC_{Ar} Bz), 133.1 (C_{Ar} Bz), 156.3 (C=O Z), 165.9, 166.5 (C=O Bz).

Anal. Calcd for $C_{31}H_{33}NO_9$ (563.61): C, 66.06; H, 5.90; N, 2.49. Found: C, 65.93; H, 6.04; N, 2.38.

Ethyl 3-*O*-(*p*-Methoxybenzyl)-4-*O*-methyl-1-thio-α-L-rhamnopyranoside (9). Rhamnopyranoside **8** (981 mg, 4.0 mmol) was *p*-methoxybenzylated under the conditions described for the preparation of compound **4**. The crude product was purified by column chromatography (10→40% ethyl acetate in petroleum ether) to give homogeneous **9** (1.17 g, 3.4 mmol). ^{1}H NMR ($CDCl_3$) δ 1.27 (t, 3H, $J_{H,H}$ = 7.6 Hz, CH_3 SEt), 1.30 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 2.61 (ABX, 2H, CH_2 SEt), 3.15 (t, 1H, $J_{4,3} \approx J_{4,5}$ 9.2 = Hz, H-4), 3.55 (s, 3H, CH_3 Me), 3.66 (dd, 1H, $J_{3,2}$ = 3.3 Hz, $J_{3,4}$ = 9.1 Hz, H-3), 3.81 (s, 3H, CH_3 OMe *p*MBzl), 3.97 (dq, 1H, $J_{5,4}$ = 9.4 Hz, $J_{6,5}$ = 6.2 Hz, H-5), 4.02 (br s, 1H, H-2), 4.60 (s, 2H, CH_2 *p*MBzl), 5.26 (s, 1H, H-1), 6.87-6.91 (m, 2H, H_{Ar} *p*MBzl), 7.19-7.31 (m, 2H, H_{Ar} *p*MBzl); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 14.4 (CH_3 SEt), 17.1 (C-6), 24.4 (CH_2 SEt), 54.5 (CH_3 OMe *p*MBzl), 60.2 (CH_3 Me), 71.0 (CH_2 *p*MBzl), 67.4, 69.5, 79.1, 81.6 (C-2, C-3, C-4, C-5), 83.1 (C-1), 113.3, 128.9 (C_{Ar} *p*MBzl), 129.5, 158.8 (qC_{Ar} *p*MBzl).

Ethyl 2-*O*-Benzoyl-3-*O*-(*p*-methoxybenzyl)-4-*O*-methyl-1-thio-α-L-rhamnopyranoside (10). To a solution of compound **9** (1.17 g, 3.4 mmol) in pyridine (12 mL) was added benzoyl chloride (0.60 mL, 5.1 mmol). After stirring for 1.5 h, the reaction was quenched with water (2 mL), and concentrated. The residue was redissolved in ethyl acetate (20 mL) and the solution was washed with water (15 mL) and aq $NaHCO_3$ (10%, 15 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The crude product was applied to a silica gel column, which was eluted with a gradient of ethyl acetate in petroleum ether (0→20%) to yield building block **10** (1.26 g, 2.8 mmol). $[\alpha]_D$ -22.6° (*c* 1); ^{1}H NMR ($CDCl_3$) δ 1.29 (t, 3H, $J_{H,H}$ = 7.4 Hz, CH_3 SEt), 1.36 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 2.63 (ABX, 2H, CH_2 SEt), 3.25 (t, 1H, $J_{4,3} \approx J_{4,5}$ = 9.3 Hz, H-4), 3.56 (s, 3H, CH_3 Me), 3.77 (s, 3H, CH_3 OMe *p*MBzl), 3.83 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.2 Hz, H-3), 4.03 (dq, 1H, $J_{5,4}$ = 9.4 Hz, $J_{5,6}$ = 6.2 Hz, H-5), 4.56 (AB, 2H, CH_2 *p*MBzl), 5.29 (s, 1H, H-1), 5.61 (dd, 1H, $J_{2,1}$ = 1.6 Hz, $J_{2,3}$ = 3.1 Hz, H-2), 6.88-7.30 (m, 2H, H_{Ar} *p*MBzl), 7.21-7.26 (m, 2H, H_{Ar} *p*MBzl), 7.45-7.58 (m, 3H, H_{Ar} Bz), 8.04-8.09 (m, 2H, H_{Ar} Bz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 14.5 (CH_3 SEt), 17.5 (C-6), 25.1 (CH_2 SEt), 54.9

(CH_3 OMe *p*MBzl), 60.4 (CH_3 Me), 70.7 (CH_2 *p*MBzl), 67.9, 70.9, 77.5, 81.9 (C-2, C-3, C-4, C-5), 82.0 (C-1), 113.2 (C_{Ar} *p*MBzl), 127.9, 129.0, 129.3 (C_{Ar}), 132.6 (C_{Ar} Bz), 129.5, 129.6 (qC_{Ar}), 158.8 (qC_{Ar} *p*MBzl), 165.0 (C=O Bz).

Anal. Calcd for $C_{24}H_{30}O_6S$ (446.57): C, 64.55; H, 6.77. Found: C, 64.64; H, 6.86.

Ethyl 3,4-*O*-Isopropylidene-1-thio-β-D-fucopyranoside (13). Ethanethiol (1.70 mL, 23.1 mmol) and tin tetrachloride (0.28 mL, 2.42 mmol) were added at 0 °C to a solution of 1,2,3,4-tetra-*O*-acetyl-D-fucopyranose (α:β=5:1, 7.31 g, 22.0 mmol) in dichloromethane (58 mL). After stirring for 1 h at room temperature, the solution was cooled (0 °C) and tin tetrachloride (0.28 mL, 2.42 mmol) was added. The reaction mixture was stirred for 1 h, diluted with dichloromethane (50 mL), washed twice with aq KF (1 M, 60 mL), and once with water (70 mL). The organic solution was dried ($MgSO_4$), filtered, and dichloromethane was evaporated to give crude compound **11** (7.04 g, 21.1 mmol). Zemplén type deacetylation of compound **11** (7.04 g, 21.1 mmol) with potassium *tert*-butoxide (235 mg, 2.1 mmol) in methanol (55 mL) was executed in 1.5 h. The reaction mixture was neutralised with Dowex 50×4 (H^+ form) and filtered. The filtrate was concentrated to give compound **12** in quantitative yield (5.57 g, 20.7 mmol). To a solution of compound **12** (5.57 g, 20.7 mmol) in acetone (40 mL) were added dimethoxypropane (12 mL) and *p*TsOH (397 mg, 2.1 mmol). After stirring for 2 h, the reaction was quenched with Et_3N (3 mL), and the solvents were evaporated. The residue was taken up in diethyl ether (40 mL). The organic layer was washed with water (30 mL) and aq $NaHCO_3$ (10%, 30 mL), dried ($MgSO_4$), filtered, and concentrated. Separation of the anomeric mixture was accomplished by column chromatography. The column was eluted with ethyl acetate in petroleum ether (0→20%). Concentration of the appropriate fractions gave the α-anomer (808 mg, 3.3 mmol) and the β-anomer **13-β** (3.69 g, 14.9 mmol). **13-α**: $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 14.4 (CH_3 SEt), 15.8 (C-6), 24.0 (CH_2 SEt), 25.3, 27.2 ($2CH_3$ Isopr), 64.0, 68.9, 75.3, 75.8 (C-2, C-3, C-4, C-5), 83.7 (C-1), 108.4 (qC Isopr). **13-β**: ^1H-NMR ($CDCl_3$): δ 1.32 (t, 3H, $J_{H,H}$ = 7.5 Hz, CH_3 SEt), 1.41 (d, 3H, $J_{6,5}$ = 6.6 Hz, H-6), 2.74 (ABX, 2H, CH_2 SEt), 3.54 (br dd, 1H, $J_{2,1}$ = 10.2 Hz, $J_{2,3}$ = 6.4 Hz, H-2), 3.88 (q, 1H, $J_{5,6}$ = 6.4 Hz, H-5), 4.00-4.07 (m, 2H, H-3, H-4), 4.22 (d, 1H, $J_{1,2}$ = 10.1 Hz, H-1); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 15.0 (CH_3 SEt), 16.6 (C-6), 23.9 (CH_2 SEt), 26.1, 28.0 ($2CH_3$ Isopr), 71.7, 72.4, 76.2, 79.1 (C-2, C-3, C-4, C-5), 84.7 (C-1), 109.4 (qC Isopr).

Ethyl 2-*O*-Benzoyl-3,4-*O*-isopropylidene-1-thio-β-D-fucopyranoside (14). Fucopyranoside **13** (1.20 g, 5.0 mmol) was treated with benzoyl chloride (0.84 mL, 7.2 mmol) in pyridine (12 mL) as described for the synthesis of compound **10** to give crude **14** (1.67 g, 4.9 mmol). ^1H NMR ($CDCl_3$) δ 1.23 (t, 3H, $J_{H,H}$ = 7.4 Hz, CH_3 SEt), 1.37 (s, 6H, CH_3 Isopr), 1.46 (d, 3H, $J_{6,5}$ = 6.6 Hz, H-6), 1.63 (s, 6H, CH_3 Isopr), 2.72 (ABX, 2H,

CH_2 SEt), 3.95 (dq, 1H, $J_{5,4}$ = 2.1 Hz, $J_{5,6}$ = 6.6 Hz, H-5), 4.13 (dd, 1H, $J_{4,3}$ = 5.1 Hz, $J_{4,5}$ = 1.8 Hz, H-4), 4.32 (dd, 1H, $J_{3,2}$ = 7.4 Hz, $J_{3,4}$ = 5.2 Hz, H-3), 4.48 (d, 1H, $J_{1,2}$ = 10.3 Hz, H-1), 5.27 (dd, 1H, $J_{2,1}$ = 10.2 Hz, $J_{2,3}$ = 7.4 Hz, H-2), 7.42-7.67 (m, 3H, H_{Ar} Bz), 8.03-8.08 (m, 2H, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 14.6 (CH_3 SEt), 16.6 (C-6), 23.7 (CH_2 SEt), 26.1, 27.7 ($2CH_3$ Isopr), 72.0, 72.4, 76.3, 77.0 (C-2, C-3, C-4, C-5), 82.2 (C-1), 109.6 (qC Isopr), 128.1, 129.5, 132.8 (C_{Ar} Bz), 129.7 (qC_{Ar} Bz), 165.2 (C=O Bz).

Ethyl 2-*O*-Benzoyl-1-thio-β-D-fucopyranoside (15). Compound **14** (1.39 g, 3.92 mmol) was dissolved in acetic acid-water (4/1, v/v, 24 mL) and stirred at 50 °C for 18 h. The solvents were removed and the residue was evaporated three times with toluene. The crude product was applied to a silica gel column, which was eluted with 20→60% ethyl acetate in petroleum ether to give compound **15** (1.16 g, 3.7 mmol). ^1H NMR ($CDCl_3$) δ 1.24 (t, 3H, $J_{H,H}$ = 7.5 Hz, CH_3 SEt), 1.39 (d, 3H, $J_{6,5}$ = 6.4 Hz, H-6), 2.73 (ABX, 2H, CH_2 SEt), 3.72 (q, 1H, $J_{5,6}$ = 6.3 Hz, H-5), 3.77-3.85 (m, 2H, H-3, H-4), 4.54 (d, 1H, $J_{1,2}$ = 9.9 Hz, H-1), 5.24 (t, 1H, $J_{2,1}\approx J_{2,3}$ = 9.4 Hz, H-2), 7.40-7.61 (m, 3H, H_{Ar} Bz), 8.02-8.07 (m, 2H, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 14.4 (CH_3 SEt), 16.2 (C-6), 23.5 (CH_2 SEt), 71.1, 71.4, 73.0, 74.5 (C-2, C-3, C-4, C-5), 82.8 (C-1), 127.8, 129.4, 132.6 (C_{Ar} Bz), 165.9 (C=O Bz).

Anal. Calcd for $C_{15}H_{20}O_5S$ (312.39): C, 57.67; H, 6.45. Found: C, 57.59; H, 6.53.

Ethyl 2-*O*-Benzoyl-3-*O*-methyl-1-thio-β-D-fucopyranoside (16). The stannylidene derivative of fucopyranoside **15** (1.16 g, 3.7 mmol) was synthesised as described for the preparation of compound **4**. The stannylidene derivative was redissolved in DMF (24 mL), cesium fluoride (730 mg, 4.8 mmol) and methyl iodide (0.32 mL, 5.1 mmol) were added. The reaction mixture was processed further as described for **4**. The crude product was purified by column chromatography (20→40% ethyl acetate in petroleum ether) to give compound **16** (686 mg, 2.1 mmol). ^1H NMR ($CDCl_3$) δ 1.22 (t, 3H, $J_{H,H}$ = 7.4 Hz, CH_3 SEt), 1.42 (d, 3H, $J_{6,5}$ = 6.6 Hz, H-6), 2.74 (ABX, 2H, CH_2 SEt), 3.41 (s, 3H, CH_3 Me), 3.48 (dd, 1H, $J_{3,2}$ = 9.3 Hz, $J_{3,4}$ 3.3 Hz, H-3), 3.70 (dq, 1H, $J_{5,4}$ = 0.9 Hz, $J_{5,6}$ = 6.4 Hz, H-5), 3.98 (d, 1H, $J_{4,3}$ = 3.0 Hz, H-4), 4.49 (d, 1H, $J_{1,2}$ = 10.1 Hz, H-1), 5.42 (t, 1H, $J_{2,1}\approx J_{2,3}$ = 9.7 Hz, H-2), 7.41-7.61 (m, 3H, H_{Ar} Bz), 8.04-8.08 (m, 2H, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 14.5 (CH_3 SEt), 16.5 (C-6), 23.4 (CH_2 SEt), 57.5 (CH_3 Me), 68.2, 69.5, 74.3, 82.1, 82.4 (C-1, C-2, C-3, C-4, C-5), 128.1, 129.4, 132.8 (C_{Ar} Bz), 129.7 (qC_{Ar} Bz), 165.1 (C=O Bz).

Anal. Calcd for $C_{16}H_{22}O_5S$ (326.41): C, 58.88; H, 6.79. Found: C, 59.02; H, 6.71.

Ethyl 4-Azido-2-*O*-benzoyl-3-*O*-methyl-1-thio-β-D-quinovopyranoside (18). Triflic anhydride (0.72 mL, 4.3 mmol) was added to a mixture of activated molecular sieves (4 Å) in dichloromethane (8.2 mL). The mixture was cooled to -20 °C, and pyridine (0.43 mL, 5.3 mmol) was added. After stirring for 10 min, a solution of fucopyranoside **16**

(668 mg, 2.1 mmol) in dichloromethane (5.7 mL) was added. After stirring for 1 h, TLC analysis showed the reaction to be complete. The reaction mixture was diluted with ice-cold dichloromethane (10 mL) and filtered. The filtrate was washed with water (10 mL), aq $NaHCO_3$ (10%, 10 mL) and water (10 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The resulting triflate **17** was dried by evaporation with toluene and subsequently dissolved in DMF (4.5 mL). Lithium azide (400 mg, 8.2 mmol) was added and the reaction mixture was stirred for 1 h. The solution was diluted with diethyl ether (10 mL), washed with water (8 mL) and aq $NaHCO_3$ (10%, 8 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The crude reaction mixture was purified by column chromatography. Elution of the column with 0→10% ethyl acetate in petroleum ether yielded glucopyranoside **18** (549 mg, 1.6 mmol). $[\alpha]_D$ +88.6° (*c* 1); IR 2119 cm^{-1} (N_3); ^1H NMR ($CDCl_3$, 300 MHz, HH-COSY) δ 1.22 (t, 3H, $J_{H,H}$ = 7.5 Hz, CH_3 SEt), 1.39 (d, 3H, $J_{6,5}$ = 5.9 Hz, H-6), 2.69 (ABX, 2H, CH_2 SEt), 3.24 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.5 Hz, H-4), 3.33 (dq, 1H, $J_{5,4}$ = 9.9 Hz, $J_{5,6}$ = 5.9 Hz, H-5), 3.48 (t, 1H, $J_{3,2}\approx J_{3,4}$ = 9.1 Hz, H-3), 3.52 (s, 3H, CH_3 Me), 4.49 (d, 1H, $J_{1,2}$ = 10.0 Hz, H-1), 5.21 (dd, 1H, $J_{2,1}$ = 10.0 Hz, $J_{2,3}$ = 9.1 Hz, H-2), 7.44-7.63 (m, 3H, H_{Ar} Bz), 8.06-8.10 (m, 2H, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 14.5 (CH_3 SEt), 18.4 (C-6), 23.7 (CH_2 SEt), 60.2 (CH_3 Me), 66.8 (C-4), 72.3 (C-2), 74.7 (C-5), 83.0 (C-1), 84.6 (C-3), 128.2, 129.5, 133.1 (C_{Ar} Bz), 129.4 (qC_{Ar} Bz), 165.1 (C=O Bz).

Anal. Calcd for $C_{16}H_{21}N_3O_4S$ (351.43): C, 54.68; H, 6.02; N, 11.96. Found: C, 54.75; H, 5.95; N, 11.90.

3-(Benzyloxycarbonylamino)propyl 2,4-Di-*O*-benzoyl-3-*O*-(2-*O*-benzoyl-3-*O*-(*p*-methoxybenzyl)-4-*O*-methyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (19). To a solution of 1,2-dichloroethane-diethyl ether (1/1, v/v, 4 mL) were dissolved donor **10** (268 mg, 0.60 mmol) and acceptor **7** (2.81 g, 0.50 mmol). Activated molecular sieves (4 Å) were added and the reaction was stirred at room temperature for 20 min. It was then cooled to -30 °C and a suspension of NIS (146 mg, 0.65 mmol) and TfOH (7 μL, 79 μmol) in the same solvent mixture (3 mL) was added. After stirring for 15 min, the reaction was neutralised with pyridine (0.2 mL), and filtered. The filtrate was diluted with ethyl acetate (15 mL) and washed with aq $Na_2S_2O_3$ (20%, 10 mL) and aq $NaHCO_3$ (10%, 8 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The crude product was first purified by column chromatography (0→40% ethyl acetate in petroleum ether) and subsequently by gel-filtration (dichloromethane-methanol, 1/1, v/v). Concentration of the appropriate fractions gave disaccharide **19** (401 mg, 0.42 mmol). $[\alpha]_D$ +55.8° (*c* 1); ^1H NMR ($CDCl_3$, 300 MHz, HH-COSY) δ 1.14 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6'), 1.32 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.80-1.87 (m, 2H, H-2 spacer), 3.08 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.5 Hz, H-4'), 3.27-3.36 (m, 2H, H-3 spacer), 3.35 (s, 3H, CH_3 Me), 3.51-3.55 (m,

1H, H-1 spacer), 3.66 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.3 Hz, H-3'), 3.68 (s, 3H, CH_3 OMe *p*MBzl), 3.72 (dq, 1H, $J_{5,4}$ = 9.6 Hz, $J_{5,6}$ = 6.3 Hz, H-5'), 3.74-3.80 (m, 1H, H-1 spacer), 4.02 (dq, 1H, $J_{5,4}$ = 9.5 Hz, $J_{5,6}$ = 6.3 Hz, H-5), 4.09 (AB, 2H, CH_2 *p*MBzl), 4.40 (dd, 1H, $J_{3,2}$ = 3.3 Hz, $J_{3,4}$ = 10.0 Hz, H-3), 4.94 (br s, 1H, H-1), 5.05 (d, 1H, $J_{1,2}$ = 1.7 Hz, H-1'), 5.09 (s, 2H, CH_2 Z), 5.11 (t, 1H, $J_{NH,H}$ = 5.9 Hz, NH), 5.19-5.20 (m, 1H, H-2'), 5.50 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.4 Hz, H-2), 5.54 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.8 Hz, H-4), 6.66-6.69 (m, 2H, H_{Ar} *p*MBzl), 6.98-7.00 (m, 2H, H_{Ar} *p*MBzl), 7.22-7.87 (m, 16H, H_{Ar}), 8.10-8.12 (m, 2H, H_{Ar} Bz), 8.13-8.15 (m, 4H, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 17.6 (C-6, C-6'), 29.6 (C-2 spacer), 38.3 (C-3 spacer), 54.9 (CH_3 OMe *p*MBzl), 60.1 (CH_3 Me), 65.6 (C-1 spacer), 66.4 (CH_2 Z), 70.6 (CH_2 *p*MBzl), 66.7, 68.5, 69.2, 71.9, 73.1, 75.7, 76.7, 81.3 (CH sugar rings), 97.3, 99.3 (C-1, C-1', $^1J_{C,H}$ = 171.4, 168.5 Hz, respectively), 113.3 (C_{Ar} *p*MBzl), 127.8, 128.0, 128.2, 128.4, 129.1, 129.5, 129.6, 129.7 (C_{Ar}), 129.4, 130.0 (qC_{Ar}), 132.7, 133.1, 133.2 (C_{Ar} Bz), 156.2 (C=O Z), 158.8 (qC_{Ar} *p*MBzl), 165.0, 165.6 (C=O Bz).

Anal. Calcd for $C_{53}H_{57}NO_{15}$ (948.04): C, 67.14; H, 6.06; N, 1.48. Found C, 67.23; H, 6.12; N, 1.41.

3-(Benzyloxycarbonylamino)propyl 2,4-Di-*O*-benzoyl-3-*O*-(2-*O*-benzoyl-4-*O*-methyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (20). Oxidative removal of the *p*-methoxybenzyl group in disaccharide **19** (401 mg, 0.42 mmol) was performed as described for the preparation of compound **7**. Column chromatography of the crude product using 10→40% ethyl acetate in petroleum ether gave compound **20** (278 mg, 0.34 mmol). $[\alpha]_D$ +40.2° (*c* 1); ^1H NMR ($CDCl_3$, 300 MHz, HH-COSY) δ 1.21 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6'), 1.29 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6), 1.82-1.90 (m, 2H, H-2 spacer), 3.05 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.5 Hz, H-4'), 3.31-3.41 (m, 2H, H-3 spacer), 3.40 (s, 3H, CH_3 Me), 3.50-3.57 (m, 1H, H-1 spacer), 3.73 (dq, 1H, $J_{5,4}$ = 9.5 Hz, $J_{5,6}$ = 6.3 Hz, H-5'), 3.76-3.84 (m, 1H, H-1 spacer), 3.89 (dd, 1H, $J_{3,2}$ = 3.1 Hz, $J_{3,4}$ = 9.5 Hz, H-3'), 3.98 (dq, 1H, $J_{5,4}$ = 9.7 Hz, $J_{5,6}$ 6.3 Hz, H-5), 4.34 (dd, 1H, $J_{3,2}$ = 3.4 Hz, $J_{3,4}$ = 9.9 Hz, H-3), 4.94 (d, 1H, $J_{1,2}$ = 1.2 Hz, H-1), 4.95 (t, 1H, $J_{NH,H}$ = 4.4 Hz, NH), 5.00 (dd, 1H,, $J_{2,1}$ = 1.7 Hz, $J_{2,3}$ = 3.4 Hz H-2'), 5.03 (d, 1H, $J_{1,2}$ = 1.6 Hz, H-1'), 5.10 (s, 2H, CH_2 Z), 5.45 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.3 Hz, H-2), 5.49 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.8 Hz, H-4), 7.28-7.66 (m, 14H, H_{Ar}), 7.92-7.98 (m, 2H, H_{Ar} Bz), 8.04-8.15 (m, 4H, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 17.6, 17.7 (C-6, C-6'), 29.6 (C-2 spacer), 38.3 (C-3 spacer), 59.6 (CH_3 Me), 65.7 (C-1 spacer), 66.4 (CH_2 Z), 66.8, 68.1, 68.9, 72.2, 73.0, 73.2, 75.5, 82.7 (CH sugar rings), 97.3, 99.4 (C-1, C-1', $^1J_{C,H}$ = 168.5, 170.0 Hz, respectively), 127.9, 128.1, 128.4, 128.5, 129.6, 129.7, 129.8 (C_{Ar}), 129.3, 129.5 (qC_{Ar}), 133.0, 133.2, 133.4 (C_{Ar} Bz), 156.4 (C=O Z), 165.4, 165.8 (C=O Bz).

Anal. Calcd for $C_{45}H_{49}NO_{14}$ (827.89): C, 65.29; H, 5.97; N, 1.69. Found C, 65.18; H, 6.05; N, 1.75.

3-(Benzyloxycarbonylamino)propyl 2,4-Di-*O*-benzoyl-3-*O*-[2-*O*-benzoyl-4-*O*-methyl-3-*O*-(4-azido-2-*O*-benzoyl-3-*O*-methyl-β-D-quinovopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranoside (21). Disaccharide acceptor **20** (339 mg, 0.41 mmol) and quinovopyranoside donor **18** (172 mg, 0.49 mmol) were coupled at 0 °C, according to the procedure described for the preparation of disaccharide **19**. The crude product was purified by column chromatography (10→30% ethyl acetate in petroleum ether) to yield trimer **21** (508 mg, 0.37 mmol). $[\alpha]_D$ +20.8° (*c* 1); ^{1}H NMR ($CDCl_3$, 600 MHz, HH-COSY) δ 0.74 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6"), 0.95 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6'), 1.30 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6), 1.82-1.88 (m, 2H, H-2 spacer), 2.51 (dq, 1H, $J_{5,4}$ = 9.9 Hz, $J_{5,6}$ = 6.0 Hz, H-5"), 2.89 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.7 Hz, H-4"), 2.96 (s, 3H, CH_3 Me), 3.00 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.5 Hz, H-4'), 3.16 (t, 1H, $J_{3,2}\approx J_{3,4}$ = 9.5 Hz, H-3"), 3.29-3.36 (m, 2H, H-3 spacer), 3.41 (s, 3H, CH_3 Me), 3.51-3.56 (m, 1H, H-1 spacer), 3.55 (dq, 1H, $J_{5,4}$ = 9.8 Hz, $J_{5,6}$ = 6.4 Hz, H-5'), 3.76 (dd, 1H, $J_{3,2}$ = 3.3 Hz, $J_{3,4}$ = 9.5 Hz, H-3'), 3.77-3.79 (m, 1H, H-1 spacer), 4.00 (dq, 1H, $J_{5,4}$ = 9.7 Hz, $J_{5,6}$ = 6.2 Hz, H-5), 4.20 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1"), 4.36 (dd, 1H, $J_{3,2}$ = 3.3 Hz, $J_{3,4}$ = 9.9 Hz, H-3), 4.91 (s, 1H, H-1), 4.96 (t, 1H, $J_{NH,H}$ = 5.6 Hz, NH), 4.98-5.00 (m, 1H, H-2'), 4.99-5.02 (m, 1H, H-2"), 5.04 (s, 1H, H-1'), 5.09 (s, 2H, CH_2 Z), 5.45 (m, 1H, H-2), 5.52 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.8 Hz, H-4), 7.26-7.64 (m, 17H, H_{Ar}), 7.86 (d, 2H, $J_{H,H}$ = 7.6 Hz, H_{Ar} Bz), 8.03 (d, 2H, $J_{H,H}$ = 7.5 Hz, H_{Ar} Bz), 8.12 (d, 2H, $J_{H,H}$ = 7.5 Hz, H_{Ar} Bz), 8.18 (d, 2H, $J_{H,H}$ = 7.7 Hz, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 17.3, 17.6 (3C-6), 29.6 (C-2 spacer), 38.2 (C-3 spacer), 59.9, 60.2 ($2CH_3$ Me), 65.7 (C-1 spacer), 66.2 (CH_2 Z), 66.3, 66.7, 68.4, 70.1, 71.9, 72.1, 72.7, 73.2, 76.4, 78.6, 80.8, 83.2 (CH sugar rings), 97.1, 98.8 (C-1, C-1', $^1J_{C,H}$ = 170.0, 171.4 Hz, respectively), 101.5 (C-1", $^1J_{C,H}$ = 153.9 Hz), 127.8, 128.1, 128.3, 128.4, 128.5, 129.7 (C_{Ar}), 129.4 (qC_{Ar}), 132.7, 133.0, 133.2 (C_{Ar} Bz), 164.8, 165.6, 165.7 (C=O Bz).

Anal. Calcd for $C_{59}H_{64}N_4O_{18}$ (1117.18): C, 63.43; H, 5.74; N, 5.01. Found: C, 63.34; H, 5.82; N, 4.93.

3-(Benzyloxycarbonylamino)propyl 2,4-Di-*O*-benzoyl-3-*O*-(2-*O*-benzoyl-4-*O*-methyl-3-*O*-(4-amino-2-benzoyl-3-methyl-β-D-quinovopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (22). Hydrogen sulfide was bubbled through a stirred solution of compound **21** (369 mg, 0.33 mmol) in pyridine-water (3/1, v/v, 2.5 mL) for 3 h. Then TLC analysis showed complete conversion of the azide **21** in a more polar product. The reaction mixture was neutralised with HCl (0.5 N), concentrated, and the remaining solvents were removed by repeated evaporation with toluene. The crude product was purified by gel-filtration (dichloromethane-methanol, 1/1, v/v). Concentration of the appropriate fractions gave the HCl salt of amine trimer **22** (346 mg, 0.31 mmol).

$[\alpha]_D$ -15.6° (*c* 1); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 17.3, 17.5, 17.7 (3C-6), 29.5 (C-2 spacer), 38.2 (C-3 spacer), 56.5 (C-4"), 59.2, 60.1 ($2CH_3$ Me), 65.7 (C-1 spacer), 66.4 (CH_2 Z), 66.7, 68.2, 69.4, 72.0, 72.2, 72.7, 73.4, 76.1, 77.5, 80.6, 81.2 (CH sugar rings), 97.1, 98.9, 100.9 (3C-1), 127.8, 128.0, 128.3, 128.5, 129.5, 129.7 (C_{Ar}), 129.3, 129.4, 129.9 (qC_{Ar} Bz), 132.7, 133.1, 133.3 (C_{Ar} Bz), 136.4 (qC_{Ar} Z), 156.3 (C=O Z), 164.7, 165.3, 165.8 (C=O Bz).

3-(Benzyloxycarbonylamino)propyl 2,4-Di-*O*-benzoyl-3-*O*-(2-*O*-benzoyl-4-*O*-methyl-3-*O*-(2-benzoyl-4-(D-2'-hydroxy)propionamido-3-methyl-β-D-quinovopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside [23(D)] and **3-(Benzyloxycarbonylamino)propyl 2,4-Di-*O*-benzoyl-3-*O*-(2-*O*-benzoyl-4-*O*-methyl-3-*O*-(2-benzoyl-4-(L-2'-hydroxy)propionamido-3-methyl-β-D-quinovopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside [23(L)].** To a solution of trimer **30** (264 mg, 0.23 mmol) in DMF (0.9 mL) were added subsequently lithium D-lactate (Aldrich, 22.1 mg, 0.23 mmol), BOP (102 mg, 0.23 mmol) and DIPEA (120 μL, 0.69 mmol). After stirring for 1 h, water (10 mL) and diethyl ether (15 mL) were added. The layers were separated and the aqueous phase was washed twice with diethyl ether (10 mL). The combined organic layers were washed with aq $NaHCO_3$ (10%, 10 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue was achieved by column chromatography (40→70% ethyl acetate in petroleum ether). Concentration of the appropriate fractions gave compound **23(D)** (204 mg, 0.18 mmol).

The synthesis of the L-lactic isomer was executed in the same fashion. Trimer **22** (321 mg, 0.29 mmol) was dissolved in DMF (1 mL) and sodium L-lactate (Aldrich, 32 mg, 0.29 mmol), BOP (126 mg, 0.29 mmol), and DIPEA (149 μL, 0.86 mmol) were added. After stirring for 1.5 h, water (10 mL) was added and the reaction mixture was filtered. The solids were dissolved in dichloromethane (10 mL) and the solution was washed with water (7 mL) and aq $NaHCO_3$ (10%, 7 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated, and the residue was purified by column chromatography (40→80% ethyl acetate in petroleum ether) to furnish amide containing trimer **23(L)** (249 mg, 0.21 mmol). **23(D)**: $[\alpha]_D$ +5.2° (*c* 1); ^1H NMR ($CDCl_3$, 600 MHz, HH-COSY) δ 0.66 (d, 3H, $J_{6,5}$ = 5.9 Hz, H-6"), 0.95 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6'), 1.29 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6), 1.42 (d, 3H, $J_{H,H}$ = 6.7 Hz, CH_3 La), 1.83-1.90 (m, 2H, H-2 spacer), 2.82 (dq, 1H, $J_{5,4}$ = 9.0 Hz, $J_{5,6}$ = 6.2 Hz, H-5), 2.97 (s, 3H, CH_3 Me), 3.01 (t, 1H, $J_{4,3} \approx J_{4,5}$ = 9.5 Hz, H-4'), 3.23 (s, 3H, CH_3 Me), 3.25-3.37 (m, 2H, H-3 spacer), 3.43 (t, 1H, $J_{3,2} \approx J_{3,4}$ = 9.8 Hz, H-3"), 3.48 (t, 1H, $J_{4,3} \approx J_{4,5}$ = 9.8 Hz, H-4"), 3.52-3.55 (m, 1H, H-1 spacer), 3.55 (dq, 1H, $J_{5,4}$ = 9.4 Hz, $J_{5,6}$ = 6.2 Hz, H-5'), 3.79 (dd, 1H, $J_{3,2}$ = 3.4 Hz, $J_{3,4}$ 9.4 Hz, H-3'), 3.77-3.80 (m, 1H, H-1 spacer), 3.99 (dq, 1H, $J_{5,4}$ = 9.3 Hz, $J_{5,6}$ = 6.1 Hz, H-5), 4.22 (q, 1H, $J_{H,H}$ = 6.7 Hz, CH La), 4.30 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1"), 4.35 (dd, 1H, $J_{3,2}$ = 2.9 Hz, $J_{3,4}$ = 9.7

Hz, H-3), 4.91 (br s, 1H, H-1), 5.01 (dd, 1H, $J_{2,1}\approx J_{2,3}$ = 8.7 Hz, H-2"), 5.03-5.04 (m, 1H, H-2'), 5.05 (s, 1H, H-1), 5.09 (s, 2H, CH_2 Z), 5.45 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 2.7 Hz, H-2), 5.51 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.9 Hz, H-4), 6.31 (d, 1H, $J_{NH,4}$ = 8.7 Hz, NH La), 7.27-7.62 (m, 17H, H_{Ar}), 7.85 (d, 2H, $J_{H,H}$ = 7.7 Hz, CH Bz), 8.01 (d, 2H, $J_{H,H}$ = 7.6 Hz, H_{Ar} Bz), 8.13 (d, 2H, $J_{H,H}$ = 7.7 Hz, H_{Ar} Bz), 8.18 (d, 2H, $J_{H,H}$ = 7.7 Hz, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz, CH-COSY) δ 16.9 (C-6"), 17.3 (C-6'), 17.5 (C-6), 21.0 (CH_3 La), 29.4 (C-2 spacer), 38.2 (C-3 spacer), 53.9 (C-4"), 56.8, 60.2 ($2CH_3$ Me), 65.6 (C-1 spacer), 66.4 (CH_2 Z), 66.6 (C-5), 68.1 (CH La), 68.3 (C-5'), 70.3 (C-5"), 71.9 (C-2), 72.2 (C-2'), 72.7 (C-2"), 72.7 (C-4), 76.3 (C-3), 78.4 (C-3'), 80.0 (C-3"), 80.9 (C-4'), 97.0 (C-1), 98.7 (C-1'), 101.3 (C-1"), 127.8, 128.0, 128.2, 128.3, 128.5, 129.5, 129.7 (C_{Ar}), 129.2, 129.8 (qC_{Ar} Bz), 132.7, 133.3 (C_{Ar} Bz), 136.5 (qC_{Ar} Z), 156.4 (C=O Z), 165.0, 165.5, 165.6, 165.7 (C=O Bz), 174.9 (C=O La).

Anal. Calcd for $C_{62}H_{70}N_2O_{20}$ (1163.25): C, 64.02; H, 6.07; N, 2.41. Found: C, 64.19; H, 5.96; N, 2.47.

23(L): $[\alpha]_D$ -2.2° (*c* 1); ^1H NMR ($CDCl_3$, 600 MHz, HH-COSY) δ 0.67 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6"), 0.95 (d, 3H', $J_{6,5}$ = 6.2 Hz, H-6), 1.29 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6), 1.42 (d, 3H, $J_{H,H}$ = 6.8 Hz, CH_3 La), 1.82-1.88 (m, 2H, H-2 spacer), 2.87 (dq, 1H, $J_{5,4}$ = 9.7 Hz, $J_{5,6}$ = 6.1 Hz, H-5"), 2.97 (s, 3H, CH_3 Me), 3.01 (t, 1H,, $J_{4,3}\approx J_{4,5}$ = 9.5 Hz H-4'), 3.23 (s, 3H, CH_3 Me), 3.30-3.35 (m, 2H, H-3 spacer), 3.41 (q, 1H, $J_{4,3}\approx J_{4,5}\approx J_{4,NH}$ = 9.6 Hz, H-4"), 3.48 (t, 1H, $J_{3,2}\approx J_{3,4}$ = 9.5 Hz, H-3"), 3.50-3.53 (m, 1H, H-1 spacer), 3.56 (dq, 1H, $J_{5,4}$ = 9.5 Hz, $J_{5,6}$ = 6.2 Hz, H-5'), 3.79 (dd, 1H, $J_{3,2}$ = 3.4 Hz, $J_{3,4}$ = 9.4 Hz, H-3'), 3.78-3.80 (m, 1H, H-1 spacer), 3.99 (dq, 1H, $J_{5,4}$ = 9.5 Hz, $J_{5,6}$ = 6.2 Hz, H-5), 4.22 (q, 1H, $J_{H,H}$ = 6.7 Hz, CH La), 4.31 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1"), 4.36 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.9 Hz, H-3), 4.91 (br s, 1H, H-1), 4.93 (br t, 1H, NH), 5.02 (dd, 1H, $J_{2,1}$ = 2.0 Hz, $J_{2,3}$ = 3.3 Hz, H-2'), 5.05 (d, 1H, $J_{1,2}$ = 2.4 Hz, H-1'), 5.05 (dd, 1H, $J_{2,1}$ = 7.8 Hz, $J_{2,3}$ = 9.6 Hz, H-2"), 5.09 (s, 2H, CH_2 Z), 5.45 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.3 Hz, H-2), 5.51 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.8 Hz, H-4), 6.33 (d, 1H, $J_{NH,4}$ = 9.0 Hz, NH), 7.28-7.66 (m, 17H, H_{Ar}), 7.84-8.18 (4m, 8H, H_{Ar} Bz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz, CH-COSY) δ 16.9 (C-6"), 17.2 (C-6'), 17.4 (C-6), 21.0 (CH_3 La), 29.4 (C-2 spacer), 38.1 (C-3 spacer), 54.5 (C-4"), 57.4, 60.0 ($2CH_3$ Me), 65.6 (C-1 spacer), 66.2 (CH_2 Z), 66.5 (C-5), 68.0 (CH La), 68.2 (C-5'), 70.1 (C-5"), 71.9 (C-2), 72.1 (C-2"), 72.6 (C-2'), 72.6 (C-4), 76.2 (C-3), 78.2 (C-3'), 80.2 (C-3"), 81.3 (C-4'), 96.9 (C-1), 98.6 (C-1'), 101.2 (C-1"), 127.7, 127.9, 128.1, 128.4, 129.4, 129.5, 129.6 (C_{Ar}), 129.2, 129.6 (qC_{Ar} Bz), 132.6, 132.8, 133.2 (C_{Ar} Bz), 136.3 (qC_{Ar} Z), 156.3 (C=O Z), 164.8, 165.4, 165.5, 165.6 (C=O Bz), 174.7 (C=O La).

Anal. Calcd for $C_{62}H_{70}N_2O_{20}$ (1163.25): C, 64.02; H, 6.07; N, 2.41. Found: C, 64.14; H, 5.98; N, 2.48.

3-(Benzyloxycarbonylamino)propyl 3-*O*-(4-*O*-Methyl-3-*O*-(4-(D-2'-hydroxyl)-propionamido- 3-*O*- methyl- β- D- quinovopyranosyl)- α- L- rhamnopyranosyl)- α- L-rhamnopyranoside [24(D)] and **3-(Benzyloxycarbonylamino)propyl 3-*O*-(4-*O*-Methyl-3-*O*-(4-(L-2'-hydroxyl)propionamido-3-*O*-methyl-β-D-quinovopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside [24(L)].** Trimer **23(D)** (204 mg, 0.18 mmol) was dissolved in methanol (2 mL) and potassium *tert*-butoxide (20 mg, 0.18 mmol) was added. The solution was stirred until all benzoyl esters were transformed (30 h). The reaction mixture was neutralised with Dowex 50W×4 (H^+ form), filtered, and methanol was removed. The crude product was applied to a silica gel column, which was eluted with 10% methanol in ethyl acetate to give compound **24(D)** (103 mg, 0.14 mmol).

Transesterification of the L-lactic trimer **23(L)** (264 mg, 0.28 mmol) with potassium *tert*-butoxide (31 mg, 0.28 mmol) in methanol (2 mL) yielded after neutralisation, concentration, and purification of the residue by column chromatography (10% methanol in ethyl acetate) compound **24(L)** (165 mg, 0.22 mmol). **24(D)**: $[\alpha]_D$ -49.0° (*c* 1); ^{1}H NMR ($CDCl_3$, 600 MHz, HH-COSY) δ 1.15 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6''), 1.24 (d, 6H, $J_{6,5}$ = 6.0 Hz, H-6, H-6'), 1.35 (d, 3H, $J_{H,H}$ = 6.8 Hz, CH_3 La), 1.76-1.79 (m, 2H, H-2 spacer), 3.19-3.22 (m, 2H, H-3 spacer), 3.22 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.4 Hz, H-4'), 3.33 (t, 1H, $J_{3,2}\approx J_{3,4}$ = 9.5 Hz, H-3''), 3.38 (dd, 1H, $J_{2,1}$ = 7.7 Hz, $J_{2,3}$ = 9.1 Hz, H-2''), 3.42 (AB, 1H, H-1 spacer), 3.48 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.5 Hz, H-4), 3.51 (s, 3H, CH_3 Me), 3.51 (dq, 1H, $J_{5,4}$ = 10.0 Hz, $J_{5,6}$ = 6.1 Hz, H-5''), 3.56 (s, 3H, CH_3 Me), 3.57-3.63 (m, 1H, H-5), 3.61 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.9 Hz, H-4''), 3.72 (dd, 1H, $J_{3,2}$ = 3.4 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 3.68-3.72 (m, 1H, H-1 spacer), 3.82 (dq, 1H, $J_{5,4}$ = 9.5 Hz, $J_{5,6}$ = 6.3 Hz, H-5'), 3.86 (dd, 1H, $J_{2,1}$ = 1.9 Hz, $J_{2,3}$ = 3.2 Hz, H-2), 4.00 (dd, 1H, $J_{3,2}$ = 3.3 Hz, $J_{3,4}$ = 9.4 Hz, H-3'), 4.13 (q, 1H, $J_{H,H}$ = 6.9 Hz, CH La), 4.14 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.3 Hz, H-2'), 4.56 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1''), 4.62 (d, 1H, $J_{1,2}$ 1= 1.3 Hz, H-1), 4.97 (d, 1H, $J_{1,2}$ = 1.6 Hz, H-1'), 5.06 (s, 2H, CH_2 Z), 7.33-7.34 (m, 5H, H_{Ar} Z); $^{13}C\{^1H\}$ NMR ($CDCl_3$) 17.7, 17.8 (3C-6), 21.1 (CH_3 La), 29.9 (C-2 spacer), 38.4 (C-3 spacer), 55.4 (C-4''), 59.3, 60.7 ($2CH_3$ Me), 65.3 (C-1 spacer), 66.9 (CH_2 Z), 68.3, 69.1, 70.7, 71.1, 71.3, 72.3, 74.1, 79.0, 82.7, 82.9 (CH sugar rings, CH_3 La), 100.5, 102.2, 103.6 (3C-1), 128.2, 128.4, 128.8 (C_{Ar} Z), 157.7 (C=O Z), 177.0 (C=O La).

Anal. Calcd for $C_{34}H_{54}N_2O_{16}$ (746.81): C, 54.68; H, 7.23; N, 3.75. Found: C, 54.75; H, 7.16; N, 3.65.

24(L): $[\alpha]_D$ -52.6° (*c* 1); $^{13}C\{^1H\}$ NMR ($CDCl_3$) 16.6, 16.7 (3C-6), 19.9 (CH_3 La), 28.8 (C-2 spacer), 37.4 (C-3 spacer), 54.5 (C-4''), 58.5, 59.5 ($2CH_3$ Me), 64.2 (C-1 spacer), 65.7 (CH_2 Z), 67.2, 67.3, 68.0, 69.7, 70.0, 70.1, 71.2, 73.2, 77.9, 78.1, 81.2, 82.1 (CH sugar rings, CH_3 La), 99.4, 101.2, 102.6 (3C-1), 127.0, 127.2, 127.7 (C_{Ar} Z), 136.1 (qC_{Ar} Z), 156.7 (C=O Z), 175.8 (C=O La).

Anal. Calcd for $C_{34}H_{54}N_2O_{16}$ (746.81): C, 54.68; H, 7.23; N, 3.75. Found: C, 54.82; H, 7.31; N, 3.69.

3-Aminopropyl 3-*O*-(4-*O*-Methyl-3-*O*-(4-(D-2'-hydroxyl)propionamido-3-*O*-methyl-β-D-quinovopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside [2(D)] and **3-Aminopropyl 3-*O*-(4-*O*-Methyl-3-*O*-(4-(D-2'-hydroxyl)propionamido-3-*O*-methyl-β-D-quinovopyranosyl)-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside [2(L)].** To a solution of compound **24(D)** (103 mg, 0.14 mmol) in 2-propanol-water (2:1, 2.5 mL) was added palladium on carbon. The reaction mixture was stirred for 20 h under a blanket of hydrogen. The reaction mixture was filtered, concentrated, and the residue was purified by gel-filtration using HW-40 (Fractogel TSK HW-40, Omnilabo), which was eluted with a solution of triethylammonium bicarbonate (TEAB, 0.15 M) in methanol-water (1/9, v/v). Concentration of the appropriate fractions gave the unprotected trimer **2(D)** (73 mg, 0.12 mmol).

Hydrogenation of compound **24(L)** (141 mg, 0.19 mmol) was performed as described above for the preparation of **2(D)**, to afford trimer **2(L)** (103 mg, 0.17 mmol).

2(D): $[\alpha]_D$ -67.2° (MeOH, *c* 1); ^{1}H NMR (CD_3OD, 600 MHz, HH-COSY) δ 1.15 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6''), 1.25 (d, 3H, $J_{6,5}$ = 6.0 Hz, H-6), 1.25 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6'), 1.35 (d, 3H, $J_{H,H}$ = 6.8 Hz, CH_3 La), 1.88-1.93 (m, 2H, H-2 spacer), 2.93-2.97 (m, 2H, H-3 spacer), 3.22 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.5 Hz, H-4'), 3.33 (t, 1H, $J_{3,2}\approx J_{3,4}$ = 9.4 Hz, H-3''), 3.38 (dd, 1H, $J_{2,1}$ = 7.7 Hz, $J_{2,3}$ = 9.1 Hz, H-2''), 3.47-3.52 (m, 1H, H-1 spacer), 3.50 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.6 H, H-4z), 3.54 (s, 3H, CH_3 Me), 3.55 (dq, 1H, $J_{5,4}$ = 9.5 Hz, $J_{5,6}$ = 6.5 Hz, H-5''), 3.58 (s, 3H, CH_3 Me), 3.56-3.60 (m, 1H, H-5), 3.61 (q, 1H, $J_{4,3}\approx J_{4,5}$ = 9.9 Hz, H-4''), 3.69 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.75-3.79 (m, 1H, H-1 spacer), 3.82 (dq, 1H, $J_{5,4}$ = 9.5 Hz, $J_{5,6}$ = 6.3 Hz, H-5'), 3.85 (dd, 1H, $J_{2,1}$ = 1.9 Hz, $J_{2,3}$ = 2.8 Hz, H-2), 4.00 (dd, 1H, $J_{3,2}$ = 3.2 Hz, $J_{3,4}$ = 9.3 Hz, H-3'), 4.14 (q, 1H, $J_{H,H}$ = 6.8 Hz, CH La), 4.13-4.14 (m, 1H, H-2'), 4.56 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1''), 4.66 (d, 1H, $J_{1,2}$ = 0.9 Hz, H-1), 4.95 (s, 1H, H-1'); $^{13}C\{^1H\}$ NMR (CD_3OD, 150 MHz, CH-COSY) δ 16.6, 16.7, 16.8 (3C-6), 20.1 (CH_3 La), 28.5 (C-2 spacer), 37.6 (C-3 spacer), 55.3 (C-4''), 58.8, 59.8 ($2CH_3$ Me), 64.3 (C-1 spacer), 67.7 (C-5'), 67.7 (CH La), 68.9, 70.5 (C-5, C-5''), 70.5, 70.7 (C-2, C-2'), 71.6 (C-4), 74.0 (C-2''), 78.9 (C-3'), 78.4 (C-3), 82.1 (C-4'), 82.7 (C-3''), 100.2 (C-1), 102.3 (C-1'), 103.7 (C-1''), 176.8 (C=O La); MS: $[M+H]^+$ for $C_{26}H_{48}N_2O_{14}$: *m/z* 613.3.

2(L): $[\alpha]_D$ -54.8° (MeOH, *c* 1); ^{1}H NMR (CD_3OD, 600 MHz, HH-COSY) δ 1.19 (d, 3H, $J_{6,5}$ = 6.1 Hz, H-6''), 1.28 (d, 6H, $J_{6,5}$ = 6.1 Hz, H-6, H-6'), 1.38 (d, 3H, $J_{H,H}$ = 6.8 Hz, CH_3 La), 1.78-1.83 (m, 2H, H-2 spacer), 2.78-2.82 (m, 2H, H-3 spacer), 3.24 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.5 Hz, H-4'), 3.35 (t, 1H, $J_{3,2}\approx J_{3,4}$ = 9.7 Hz), H-3'', 3.40 (dd, 1H, $J_{2,1}$ = 7.7 Hz, $J_{2,3}$ = 9.2 Hz, H-2''), 3.48-3.53 (m, 1H, H-1 spacer), 3.51 (t, 1H, $J_{4,3}\approx J_{4,5}$ = 9.6 Hz, H-4),

3.54 (s, 3H, CH_3 Me), 3.55 (dq, 1H, $J_{5,4}$ = 10.0 Hz, $J_{5,6}$ = 6.0 Hz, H-5"), 3.58 (s, 3H, CH_3 Me), 3.60 (dq, 1H, $J_{5,4}$ = 9.4 Hz, $J_{5,6}$ = 6.1 Hz, H-5), 3.64 (q, 1H, $J_{4,3}\approx J_{4,5}$ = 9.9 Hz, H-4"), 3.73 (dd, 1H, $J_{3,2}$ = 3.3 Hz, $J_{3,4}$ = 9.6 Hz, H-3), 3.75-3.79 (m, 1H, H-1 spacer), 3.84 (dq, 1H, $J_{5,4}$ = 9.6 Hz, $J_{5,6}$ = 6.3 Hz, H-5'), 3.87 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.3 Hz, H-2), 4.02 (dd, 1H, $J_{3,2}$ = 3.3 Hz, $J_{3,4}$ = 9.4 Hz, H-3'), 4.16 (q, 1H, $J_{H,H}$ = 6.8 Hz, CH La), 4.16 (dd, 1H, $J_{2,1}$ = 1.8 Hz, $J_{2,3}$ = 3.3 Hz, H-2'), 4.59 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1"), 4.67 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1), 4.99 (d, 1H, $J_{1,2}$ = 1.8 Hz, H-1'); $^{13}C\{^1H\}$ NMR (CD_3OD, 150 MHz, CH-COSY) δ 18.0, 18.1, 18.2 (3C-6), 21.3 (CH_3 La), 32.9 (C-2 spacer), 39.8 (C-3 spacer), 56.7 (C-4"), 60.3, 61.2 ($2CH_3$ Me), 66.5 (C-1 spacer), 69.1 (C-5'), 69.1 (CH La), 70.2 (C-5), 71.9 (C-5"), 72.0 (C-2), 72.1 (C-2), 73.1 (C-4), 75.4 (C-2"), 79.7 (C-3'), 80.3 (C-3), 83.5 (C-4'), 84.3 (C-3"), 101.6 (C-1), 103.6 (C-1'), 105.1 (C-1"), 177.9 (C=O La); MS: $[M+H]^+$ for $C_{26}H_{48}N_2O_{14}$: *m/z* 613.3.

ACKNOWLEDGMENT

This research was supported by the Netherlands Organisation for Scientific Research (NWO).

REFERENCES

1. D. Armstrong, J.W.M. Gold, J. Dryjanski, E. Whimbey, B. Polsky, C. Hawkins, A.E. Brown, E. Bernard, and T.E. Kiehn, *Ann. Intern. Med.*, **103**, 704 (1985).
2. R.C. Good; *Ann. Rev. Microbiol.*, **39**, 347 (1985).
3. P.J. Brennan, H. Mayer, G.O. Aspinall, and J.E. Nam Shin, *Eur. J. Biochem.*, **115**, 7 (1981).
4. R.T. Camphausen, R.L. Jones, and P.J. Brennan, *J. Bacteriol.*, **168**, 660 (1986).
5. D. Chatterjee, G.O. Aspinall, and P.J. Brennan, *J. Biol. Chem.*, **262**, 3528 (1987).
6. M. McNeill, A.Y. Tsang, and P.J. Brennan, *J. Biol. Chem.*, **262**, 2630 (1987).
7. W.W. Barrow, B.P. Ullom, and P.J. Brennan, *J. Bacteriol.*, **144**, 814 (1980).
8. M. McNeil, H. Gaylord, and P.J. Brennan, *Carbohydr. Res.*, **177**, 185 (1988).
9. P.J. Brennan, G.O. Aspinall, and J.E. Nam Shin, *J. Biol. Chem.*, **256**, 6817 (1981).
10. D. Chatterjee, C. Bozic, G.O. Aspinall, and P.J. Brennan, *J. Biol. Chem.*, **263**, 4092 (1988).
11. C.M. Bozic, M. McNeil, D. Chatterjee, I. Jardines, and P.J. Brennan, *J. Biol. Chem.*, **263**, 14984 (1988).
12. G.H. Veeneman, L.J.F. Gomes, and J.H. van Boom, *Tetrahedron*, **45**, 7433 (1989).
13. a) G. Yang, F. Kong, and S. Zhou, *Carbohydr. Res.*, **211**, 179 (1991). b) P. Kovác, and K.J. Edgar, *J. Org. Chem.*, **57**, 2455 (1992).

14. P. Bernston, A. Brändström, H. Jungren, L. Palme, S.E. Sjöstrand, and G. Sundell, *Acta Pharm. Suec.*, **14**, 229 (1977).
15. G.H. Veeneman, S.H. van Leeuwen, and J.H. van Boom, *Tetrahedron Lett.*, **31**, 1331 (1991).
16. Y. Oikawa, T. Yoshioka, and O. Yonemitsu, *Tetrahedron Lett.*, **24**, 3775 (1983).
17. a) M.A. Nashed, and L. Anderson, *Tetrahedron Lett.*, **17**, 3503 (1976). b) N. Nagashima, and M. Ohno, *Chem. Lett.*, 141 (1987).
18. H.M. Zuurmond, G.H. Veeneman, G.A. van der Marel, and J.H. van Boom, *Carbohydr. Res.*, **241**, 153 (1993).
19. a) C.L. Stevens, P. Blumbergs, D.H. Otterbach, J.L. Strominger, M. Matsuhashi, and D.N. Dietzler, *J. Am. Chem. Soc.*, **86**, 2937 (1964). b) C.L. Stevens, P. Blumbergs, F.A. Daniher, D.H. Otterbach, and K.G. Taylor, *J. Org. Chem.*, **31**, 2822 (1966). c) G.W.J. Fleet; M.J. Gough, and P.W. Smith, *Tetrahedron Lett.*, **25**, 1853 (1984).
20. T. Adachi, Y. Yamada, and I. Inoue, *Synthesis*, 45 (1977).
21. B. Castro, J.-R. Dormay, G. Evin, and C. Selve, *Tetrahedron Lett.*, **16**, 1219 (1975).