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Iodonium Ion-Assisted Synthesis of a Tetrameric Fragment Corresponding to the Cell Wall Phenolic Glycolipids of *Mycobacterium kansasii* Serovar I

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Abstract: Two procedures are described towards the assembly of the tyramine spacer-containing tetramer **5**, a derivative of the phenolic glycolipid of *Mycobacterium kansasii* serovar I. First, iodonium ion-mediated glycosylation of trimeric acceptor **2a** with D-rhamnopyranoside donor **10** gave fully protected tetramer **17**. Selective removal of the chloroacetyl group of **17**, subsequent deoxygenation and removal of the protective groups, led to target **5**. The potential occurrence of double stereodifferentiation (DSD) was examined by condensation of L-fucopyranoside model acceptor **14** with both the enantiomeric rhamnopyranoside donors **10** and **13**. The second procedure involves elongation of trimeric acceptor **2b** with 6-deoxy-D-glucopyranoside **28**. Desulfurisation of the resulting tetrameric fragment **36** followed by hydrogenation of **37** gave **38**, the phenylacetyl (PhAc) of which was enzymatically removed to yield target tetramer **5**.

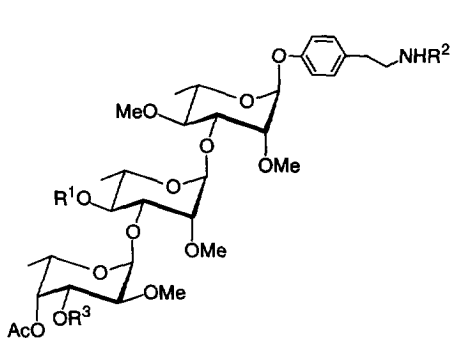
INTRODUCTION

Recent studies[1] from our laboratory showed that the haptenic tetramers **3** and **4**, corresponding to the linear oligosaccharide units of *Mycobacterium kansasii* phenolic glycolipids (PGLs) serovars II[2] and IV[3], were accessible via α-mannosylation of the partially protected trimeric precursor **2a** of the invariable inner core trimer **1** with appropriately protected ethyl 1-thio-α-D-mannopyranosides. The successful synthesis of both tetrameric fragments **3** and **4** was a stimulus in adopting a similar route of synthesis towards the immunodominant tetramer **5** of the PGL from *M. kansasii* serovar I[4].

We here report that the introduction of the α-linked 2,6-dideoxy-4-*O*-methyl-α-D-*arabino*-hexopyranoside moiety in target compound **5** can be achieved in a stereoselective fashion by elongation of the partially protected trimeric fragment **2a** or **2b** with a suitably protected D-rhamno- or 6-deoxy-D-glucopyranoside.

RESULTS AND DISCUSSION

In a first approach to the target tetrameric fragment **5**, the partially protected trimer **2a** was coupled under the agency of *N*-iodosuccinimide (NIS) and catalytic triflic acid (TfOH)[6] with ethyl 3-*O*-benzyl-2-*O*-chloroacetyl-4-*O*-methyl-1-thio-α-D-rhamnopyranoside (*i.e.* compound **10** in Scheme 1). It was expected that the presence of the 2-*O*-chloroacetyl group in thio-glycoside **10** would promote the stereoselective formation of the

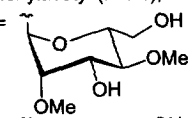


1 $R^1=R^2=R^3=H$

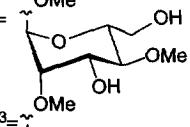
2a R^1=Bn, R^2=benzyloxycarbonyl(Z), $R^3=H$

b R^1=Bn, R^2=phenylacetyl (PhAc), $R^3=H$

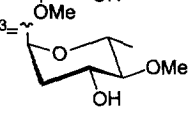
3 $R^1=R^2=H$, R^3=



4 $R^1=R^2=H$, R^3=

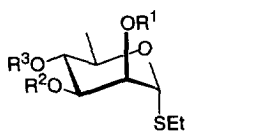


5 $R^1=R^2=H$, R^3=



requisite α-linkage between **10** and **2a**. In addition, it was anticipated[7] that selective removal of the chloroacetyl group in the condensation product **17** (see Scheme 3), which is imperative for the ensuing deoxygenation of the newly generated hydroxyl group, would be compatible with the presence of the acetyl group in the final product **5**.

The preparation of the D-rhamnopyranosyl donor **10** is depicted in Scheme 1, and commences with the methylation of known[8] ethyl 2,3-*O*-isopropylidene-1-thio-α-D-rhamnopyranoside (**6**→**7**). Deacetonation of **7** and regioselective benzylation of the stannylidene complex[9] of **8** affords the 3-*O*-benzyl derivative **9**. Acylation of **9** with chloroacetic anhydride gives donor **10** in 45% yield over the four steps.



i, ii, iii, iv

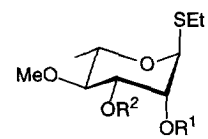
6 R^1,R^2=$C(CH_3)_2$, $R^3=H$

7 R^1,R^2=$C(CH_3)_2$, R^3=Me

8 $R^1=R^2=H$, R^3=Me

9 $R^1=H$, R^2=Bn, R^3=Me

10 R^1=ClAc, R^2=Bn, R^3=Me



iii, iv

11 $R^1=R^2=H$

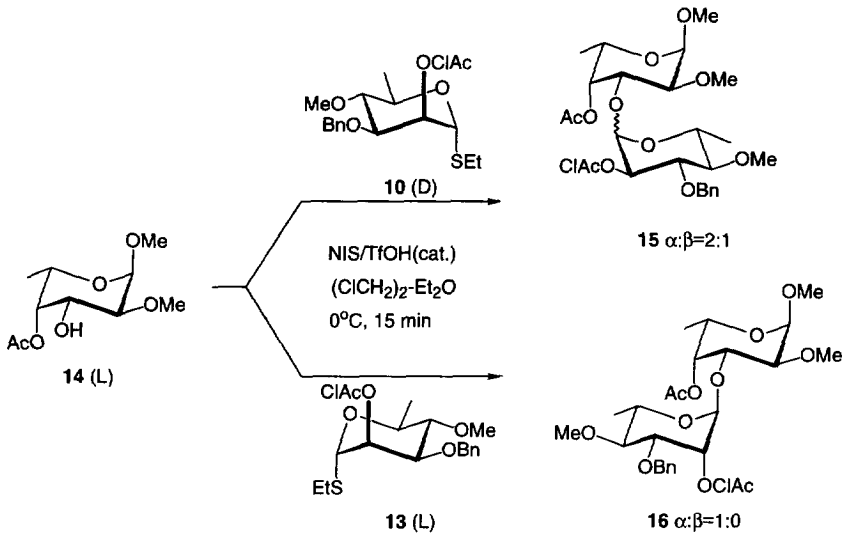
12 $R^1=H$, R^2=Bn

13 R^1=ClAc, R^2=Bn

Reagents and conditions: (i) MeI, NaH, DMF, 1 h, 98%. (ii) HOAc 90%, 50°C, 18 h, 85%. (iii) Bu_2SnO, MeOH, 1.5 h; CsF, BnBr, DMF, 17 h, **9** 78%, **12** 76%. (iv) $(ClAc)_2O$, $NaHCO_3$, DMF, 1.5 h, **10** 95%, **13** 86%.

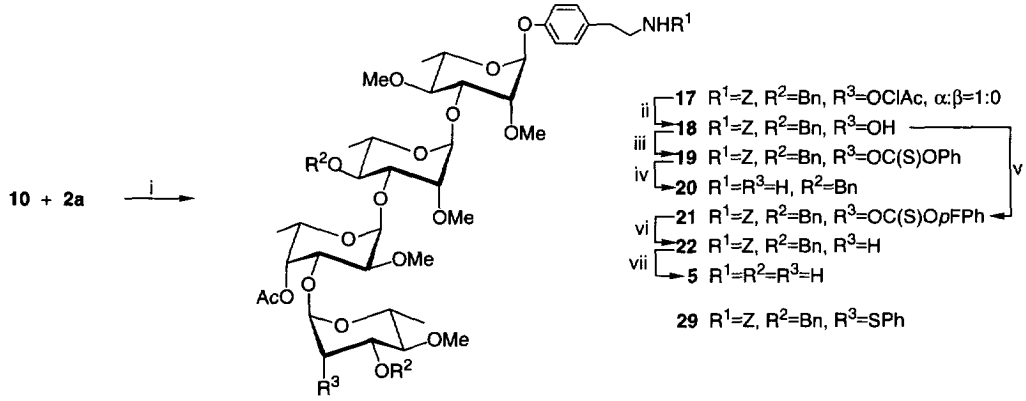
Scheme 1

Prior to the intended NIS/TfOH(cat.)-assisted glycosylation of the trimeric acceptor **2a** with the D-donor **10**, it was of interest to know whether the stereochemical outcome of the glycosylation would be under the influence of double stereodifferentiation[10] (DSD). To this end, known[5] L-fucopyranosyl derivative **14**(L), which mimics the L-trimer acceptor **2a**, was glycosylated (see Scheme 2) with the respective D- and L-rhamnopyranoside donors **10** and **13**. Purification by column chromatography of the reaction mixture resulting from the condensation of **14**(L) with **10**(D) gave dimer **15** as an anomeric mixture (α:β=2:1) in 80% yield. Similarly, glycosylation of **14**(L) with the L-donor **13**, prepared in 65% yield by regioselective benzylation of known ethyl 4-*O*-methyl-1-thio-α-L-rhamnopyranoside[11] (**11**, see Scheme 1) and chloroacetylation of **12**, proceeded in a highly stereoselective manner to give the α-linked dimer **16** in 75% yield (see Scheme 2). The above results indicate that DSD may be a contributing factor in the stereochemical outcome of the glycosylation of the L-trimer acceptor **2a** with the D-donor **10**. However, D-rhamnosylation of trimer acceptor



Scheme 2

2a with D-glycoside **10** led to the exclusive formation of the α-rhamnosylated and fully protected tetramer **17** in 71% yield. Transformation of **17** into fragment **5** entailed (see Scheme 3) the following sequence of reactions. Selective removal of the chloroacetyl group in **17** with hydrazine dithiocarbonate[7] (HDTC), followed by reaction of the free hydroxyl group in **18** with phenyl chlorothionoformate in the presence of 4-(dimethylamino)pyridine (DMAP),[12] led to the isolation of **19** in 69% overall yield. Interestingly, radical-mediated deoxygenation[13] of **19** gave, instead of the expected product **22**, the unprotected amino derivative **20**. The formation of the latter product indicates that the *N*-benzyloxycarbonyl (Z) protective group does not survive the rather severe deoxygenation conditions (see step iv in Scheme 3). The concomitant removal of the Z-group could be circumvented by replacing the phenylthionocarbonyl group by its more reactive *p*-fluorophenyl[14] analogue.



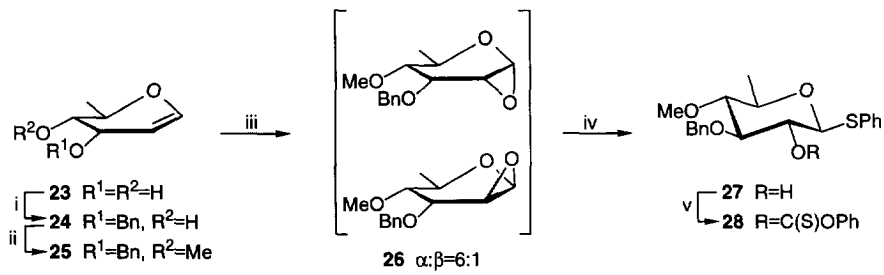
Reagents and conditions: (i) NIS/TfOH(cat.), 1,2-dichloroethane-Et_2O, 0°C, 15 min, 71%. (ii) HDTC, HOAc, lutidine, 92%. (iii) PhOC(S)Cl, DMAP, CH_3CN, 24 h, 75%. (iv) Bu_3SnH, AIBN, toluene, reflux, 3 h, 85%. (v) *p*FPhOC(S)Cl, DMAP, CH_3CN, 48 h, 73%. (vi) see iv, 30 min, 82%. (vii) H_2, Pd(C), isopropanol-H_2O-HOAc-tris(hydroxymethyl)-aminomethane, 30 h, 23%.

Scheme 3

Thus deoxygenation of **21**, obtained in 73% yield by reaction of **18** with *p*-fluorophenyl chlorothionoformate, proceeded smoothly (see step vi in Scheme 3) to give the deoxygenated product **2** as evidenced by NMR spectroscopy. Unfortunately, removal of the benzyl and benzyloxycarbonyl groups in **22** by hydrogenolysis in the presence of catalytic 10% palladium on carbon and acetic acid was accompanied by cleavage of the rather acid-labile interglycosidic bond between the L-fucopyranose and 2,6-dideoxy-*arabino*-D-hexopyranose moiety. A similar result was obtained by subjecting the tetramer **20** to the same hydrogenolysis conditions. Despite many attempts, it was established that the tetramer **5** could be isolated in 23% yield by executing the hydrogenolysis of **22** in the presence of tris(hydroxymethyl)aminomethane.

It occurred to us that the problems encountered in the hydrogenolysis of **20** or **22** could be overcome by protecting the primary amino function of the tyramine unit with the phenylacetyl (PhAc)[15] group. The choice of this particular group is based on the fact that it survives hydrogenolysis conditions. Furthermore, it was anticipated that its enzymatic removal with immobilised penicillin-G acylase would be compatible with the presence of the acetyl group in target compound **5**. The viability of this concept was endorsed by the following pilot experiment (experimental data not given here). Phenylacylation of **20** with phenylacetyl chloride afforded the *N*-PhAc protected tyramine fragment **37** (see Scheme 5). Hydrogenolysis of **37** with palladium on carbon (10%) in the solvent isopropanol-water proceeded smoothly, as evidenced by ^{1}H-NMR spectroscopy. Finally, treatment of **38** with immobilised penicillin-G acylase furnished tetramer **5**, which was in all aspects identical with earlier prepared **5**.

At this stage, it was decided to introduce the requisite α-linked 2-deoxy-mannopyranoside unit by elongation of the *N*-PhAc protected trimeric acceptor **2b** with the phenyl 2-*O*-phenoxythionocarbonyl-1-thio-β-D-glucopyranoside **28** following a two step procedure developed in our laboratory.[16] Thus, condensation of **2b** (see Scheme 5) with **28** under the influence of NIS/TfOH(cat.) will lead, via 1,2-phenylthio migration, to the formation of the fully protected tetramer **36**, the phenylthio of which is then removed by desulfurisation.



Reagents and conditions: (i) Bu_2SnO, MeOH, 2 h; CsF, BnBr, DMF, 17 h, 66%. (ii) MeI, NaH, DMF, 2 h, 79%. (iii) DMD in acetone, dichloromethane, 0°C, 45 min. (iv) PhSK, 18-crown-6, acetone, 30 min, purification, 75%, (v) PhOC(S)Cl, DMAP, CH_3CN, 24 h, 77%.

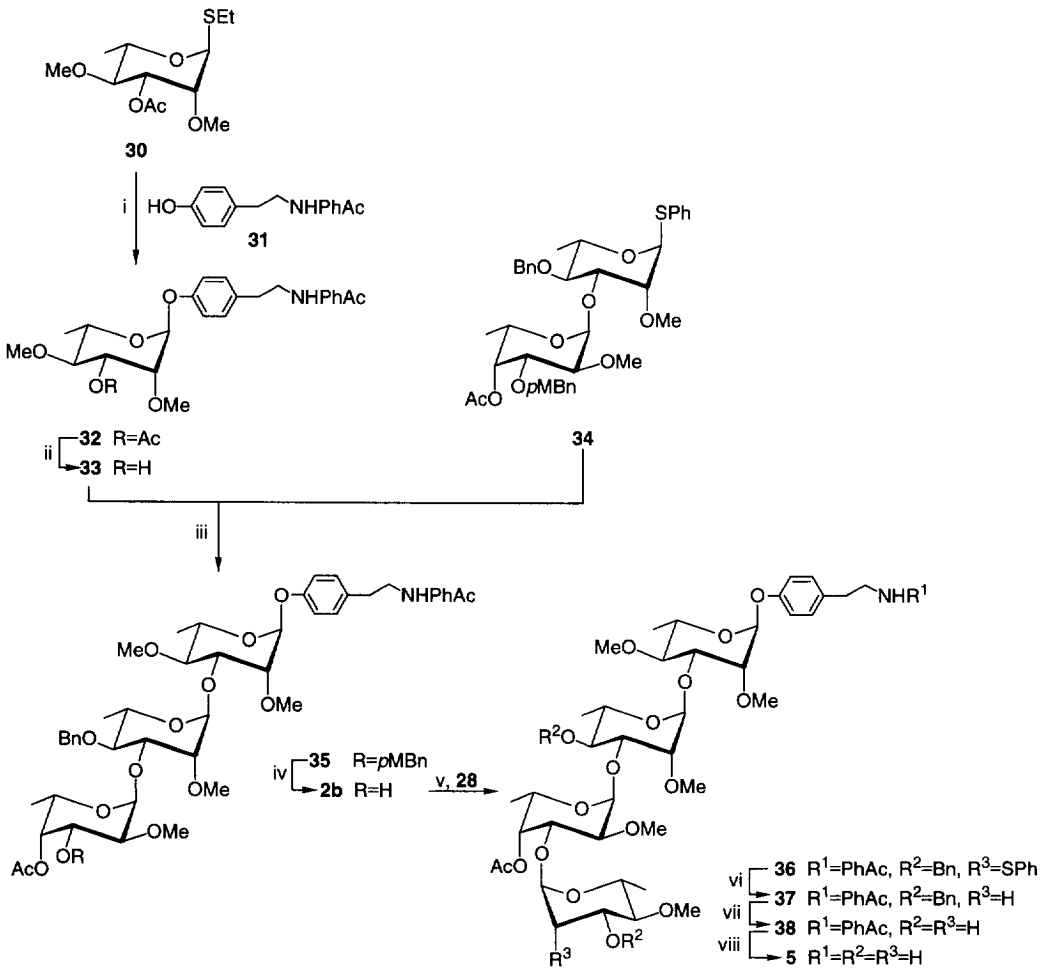
Scheme 4

The suitably protected donor **28** was readily accessible from known[17] 6-deoxy-D-glucal **23** by the sequence of reactions depicted in Scheme 4. In the first step, **23** was converted into the 3-*O*-benzyl derivative **24** *via* regioselective benzylation of its stannylidene complex.[18] Methylation of **24** followed by epoxidation of **25** with 3,3-dimethyldioxirane[19] (DMD) gave the 1,2-epoxide derivative **26** as a mixture of diastereoisomers (α:β=6:1). Nucleophilic ring-opening[20] of the crude diastereoisomeric mixture of **26** with potassium thiophenoxide gave, after purification by silica gel column chromatography, the homogeneous phenyl 1-thio-β-D-glucopyranoside **27**. Treatment of **27** with phenyl chlorothionoformate led to the isolation of donor **28** in 31% yield based on **23**.

The assembly of the partially protected derivative **2b** could be accomplished following a similar route reported[5] for the corresponding *N*-Z protected fragment **2a**. Accordingly, NIS/TfOH(cat.)-mediated glycosidation of the *N*-PhAc protected tyramine aglycon **31**, prepared in 48% yield by reaction of tyramine with phenylacetyl chloride, with L-rhamnopyranoside **30** gave the α-linked spacer-containing rhamnopyranoside **32**

(see Scheme 5). Zemplén type deacetylation of **32** and subsequent glycosylation of **33** with the known[5] dimer **34** (α:β=20:1) in the presence of the promoter NIS/TfOH(cat.) led to trimer **35** (89%) having the same ratio of anomers as dimer **34**. Removal of the *p*-methoxybenzyl group in **35** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[21] (DDQ) and separation of the individual anomers by column chromatography gave α-linked trimeric fragment **2b** in 35% yield based on **30**. Iodonium ion-mediated elongation of acceptor **2b** the with 6-deoxy-β-D-glucopyranoside **28** proceeded, as expected, in a stereoselective fashion to furnish, after purification by Sephadex LH20 gel-filtration, homogeneous **36** in a rather low yield of 48% [*cf.* glycosylation of **2a** with **28** gave **29** (Scheme 3) in 70% yield]. Desulfurisation of **36** (→**37**) followed, as described before, by hydrogenolysis and subsequent enzymatic removal of the PhAc-group, afforded homogeneous **5** in 56% yield based on **36**.

In summary, the results presented in this paper show that the synthesis of the tetramer **5** can be accomplished by elongation of trimeric acceptor **2a** or **2b** with either D-rhamno- **10** or D-glucopyranoside **28**



Reagents and conditions: (i) NIS/TfOH(cat.), 1,2-dichloroethane-Et_2O, 0°C, 15 min, 66%. (ii) KO*t*-Bu, MeOH, 3 h, 89%. (iii) see i, -30°C, 15 min, 89%. (iv) DDQ, 1,2-dichloroethane-H_2O, 1 h, 67%. (v) see i, 20°C, 15 min, 48%. (vi) Raney nickel, THF, 20 h, 78%. (vii) H_2, Pd(C), isopropanol-H_2O, 18 h, 90%. (viii) Immobilised Penicillin-G acylase, MeOH-H_2O, NaOH, 15 min, 80%.

Scheme 5

(Scheme 3 and 5, respectively). The assembly of **5** starting from donor **28** proved to be superior due to the reduced number of reaction steps in the final stage of the synthesis. In addition, protection of the tyramine spacer with the phenylacetyl instead of the benzyloxycarbonyl group had a beneficial effect on the final deblocking.

EXPERIMENTAL

General material and procedures: *N,N*-dimethylformamide (DMF) was stirred with calcium hydride at room temperature for 18 h, then distilled under reduced pressure and stored over molecular sieves 4 Å (Aldrich). Methanol was dried by refluxing with magnesium methoxide, distilled and stored over molecular sieves 3 Å. Toluene, diethyl ether, 1,2-dichloroethane, and dichloromethane were distilled from P_2O_5. Toluene and diethyl ether were stored over sodium wire. 1,2-Dichloroethane and dichloromethane were stored over molecular sieves 4 Å. Acetonitrile was dried by storage over molecular sieves 4 Å. Tetrahydrofuran (p.a. THF, Merck) was pre-dried over molecular sieves 4 Å and freshly distilled from $LiAlH_4$ before use. Solvents used for column chromatography were of technical grade and distilled before use.

Reactions were performed under anhydrous conditions at ambient temperature unless states otherwise. Solvents were evaporated under reduced pressure at 40°C. Schleicher and Schüll DC Fertigfolien were used for TLC-analyses. Detection of the carbohydrates was achieved by UV and charring with sulfuric acid in ethanol (1/4, v/v). Column chromatography was performed on silica 60, 70-230 mesh (Merck). The petroleum ether used for elution of the columns was low-boiling (40-60°C). Gel-filtration was conducted on Sephadex LH20 (Pharmacia).

Optical rotations were measured with a Propol polarimeter for solutions in chloroform (p.a. Baker) at 20°C. ^{1}H- and ^{13}C-NMR spectra were measured at 50.1 and 200 MHz, respectively, using a JEOL JNM-FX-200 spectrometer. NMR spectra were also recorded with a Bruker WM-300 spectrometer (^{1}H-NMR, 300 MHz), a Bruker MSL-400 spectrometer (^{1}H-NMR, 400 MHz), or with a Bruker DMX-600 spectrometer (^{1}H-NMR, 600 MHz). Chemical shifts (δ) are given in ppm relative to tetramethylsilane as an internal standard.

Ethyl 2,3-*O*-isopropylidene-4-*O*-methyl-1-thio-α-D-rhamnopyranoside (7) - Methyl iodide (0.40 ml, 6.5 mmol) was added at 0°C to a suspension of ethyl 2,3-*O*-isopropylidene-1-thio-α-D-rhamnopyranoside (**6**, 1.25 g, 5.0 mmol) and sodium hydride (80%, 225 mg, 7.5 mmol) in DMF (12 ml). After stirring for 1 h at room temperature, the reaction was quenched with methanol (1 ml). DMF was removed and the resulting oil was redissolved in diethyl ether (30 ml). The organic solution was washed with water (20 ml) and aq. $NaHCO_3$ (10%, 20 ml), dried ($MgSO_4$), filtered, and concentrated to give crude **7** (1.28 g, 4.9 mmol).

^{1}H-NMR ($CDCl_3$): δ 1.27 (d, 3H, H-6, $J_{6,5}$ 6.4 Hz), 1.29 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.3 Hz), 1.35, 1.55 (2× s, 6H, 2× CH_3 Isopr), 2.59 (ABX, 2H, CH_2 SEt), 3.03 (dd, 1H, H-4, $J_{4,3}$ 6.7 Hz, $J_{4,5}$ 9.8 Hz), 3.54 (s, 3H, CH_3 Me), 3.94 (dq, 1H, H-5, $J_{5,4}$ 9.9 Hz, $J_{6,5}$ 6.3 Hz), 4.08-4.17 (m, 2H, H-2, H-3, $J_{3,2}$ 5.7 Hz), 5.49 (s, 1H, H-1); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 14.3 (CH_3 SEt), 17.4 (C-6), 24.0 (CH_2 SEt), 26.1, 27.8 (2× CH_3 Isopr), 59.0 (CH_3 Me), 64.8 (C-5), 76.6, 77.8, 79.2 (C-2, C-3, C-4), 83.7 (C-1), 108.7 (qC Isopr).

Ethyl 4-*O*-methyl-1-thio-α-D-rhamnopyranoside (8) - A solution of crude **7** (1.28 g, 4.9 mmol) in a mixture of acetic acid-water (9/1, v/v, 35 ml) was heated at 50°C for 18 h. The solution was concentrated and the remaining solvents were removed by evaporation with toluene. The crude product was purified by column chromatography [ethyl acetate in petroleum ether (20→ 40%)] to give compound **8** (924 mg, 4.2 mmol).

^{1}H-NMR ($CDCl_3$): δ 1.29 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.3 Hz), 1.33 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 2.62 (ABX, 2H, CH_2 SEt), 2.82 (d, 1H, OH, $J_{HO,H}$ 5.1 Hz), 2.89 (d, 1H, OH, $J_{HO,H}$ 3.6 Hz), 3.13 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ 9.3 Hz), 3.57 (s, 3H, CH_3 Me), 3.82 (ddd, 1H, H-3, $J_{3,2}$ 3.7 Hz, $J_{3,OH}$ 5.0 Hz, $J_{3,4}$ 9.0 Hz), 4.01 (dq, 1H, H-5, $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.2 Hz), 4.04 (m, 1H, H-2), 5.24 (d, 1H, H-1, $J_{1,2}$ 1.0 Hz); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 14.8 (CH_3 SEt), 17.7 (C-6), 24.9 (CH_2 SEt), 60.4 (CH_3 Me), 64.7 (C-5), 71.5, 72.4, 83.2 (C-2, C-3, C-4), 83.8 (C-1).

Ethyl 3-*O*-benzyl-4-*O*-methyl-1-thio-α-D-rhamnopyranoside (9) - Dibutyltin oxide (1.20 g, 4.8 mmol) was added to a solution of D-rhamnopyranoside **8** (924 mg, 4.2 mmol) in methanol (25 ml). The mixture was heated under reflux for 1.5 h, and the solvent was evaporated. The residue was dried by evaporation with toluene, and subsequently redissolved in DMF (42 ml). Cesium fluoride (834 mg, 5.5 mmol) and benzyl bromide (0.75 ml, 6.3 mmol) were added to the solution. After stirring for 17 h, the solvent was evaporated and the residue was taken up in diethyl ether (30 ml). The solution was washed twice with aq. KF (1

M, 25 ml), once with water (20 ml), dried ($MgSO_4$), and filtered. The filtrate was concentrated and the oily residue was purified by silica gel column chromatography. The column was eluted with 0→20% ethyl acetate in petroleum ether to give compound **9** (966 mg, 3.2 mmol).

^{1}H-NMR ($CDCl_3$): δ 1.28 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.3 Hz), 1.32 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 2.60 (ABX, 2H, CH_2 SEt), 3.18 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ 9.3 Hz), 3.57 (s, 3H, CH_3 Me), 3.68 (dd, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.0 Hz), 4.05 (dd, 1H, H-2, $J_{2,3}$ 3.3 Hz, $J_{2,OH}$ 3.1 Hz), 3.98 (dq, 1H, H-5, $J_{5,4}$ 9.3 Hz, $J_{5,6}$ 6.2 Hz), 4.67 (s, 2H, CH_2 Bn), 5.27 (s, 1H, H-1), 7.36 (s, 5H, CH Bn); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 14.6 (CH_3 SEt), 17.3 (C-6), 24.6 (CH_2 SEt), 60.6 (CH_3 Me), 71.7 (CH_2 Bn), 67.6, 67.7, 79.6, 81.8 (C-2, C-3, C-4, C-5), 83.0 (C-1), 127.5, 128.1 (CH Bn), 137.6 (qC Bn).

Ethyl 3-*O*-benzyl-2-*O*-chloroacetyl-4-*O*-methyl-1-thio-α-D-rhamnopyranoside (10) - To a solution of compound **9** (966 mg, 3.2 mmol) in DMF (7 ml) were added chloroacetic anhydride (5.47 g, 32.0 mmol) and $NaHCO_3$ (3.93 g, 32.0 mmol). After stirring for 1.5 h, the mixture was poured into ice-water (35 ml) and extracted with dichloromethane (3× 15 ml). The organic layer was washed with water (20 ml), aq. $NaHCO_3$ (10%, 20 ml), dried ($MgSO_4$), filtered, and concentrated to yield crude product. Purification by column chromatography (0→5% ethyl acetate in petroleum ether) gave **10** (1.12 g, 3.0 mmol).

$[\alpha]_D$ +78.8° (c 1); ^{1}H-NMR ($CDCl_3$): δ 1.27 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.5 Hz), 1.31 (d, 3H, H-6, $J_{6,5}$ 6.2), 2.61 (ABX, 2H, CH_2 SEt), 3.12 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ 9.4 Hz), 3.55 (s, 3H, CH_3 Me), 3.76 (dd, 1H, H-3, $J_{3,2}$ 3.1 Hz, $J_{3,4}$ 9.3 Hz), 3.97 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 4.14 (s, 2H, CH_2 ClAc), 4.59 (AB, 2H, CH_2 Bn), 5.18 (s, 1H, H-1), 5.45 (dd, 1H, H-2, $J_{2,1}$ 1.4 Hz, $J_{2,3}$ 3.4 Hz), 7.26-7.33 (m, 5H, CH Bn); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 14.7 (CH_3 SEt), 17.4 (C-6), 25.3 (CH_2 SEt), 40.6 (CH_2 ClAc), 60.8 (CH_3 Me), 71.6 (CH_2 Bn), 68.0, 72.5, 77.7, 81.5 (C-2, C-3, C-4, C-5), 81.7 (C-1), 127.5, 127.7, 128.1, 128.3 (CH Bn), 137.46 (qC Bn), 166.4 (C=O ClAc).

Anal. calcd. for $C_{18}H_{25}O_5SCl$ (388.91): C 55.59, H 6.48; found C 55.49, H 6.57%.

Ethyl 3-*O*-benzyl-4-*O*-methyl-1-thio-α-L-rhamnopyranoside (12) - Compound **11** (665 mg, 3.0 mmol) was regioselectively benzylated as described for its enantiomer **9**. The crude product was purified by silica gel column chromatography. Elution with 0 →10% ethyl acetate in petroleum ether gave compound **12** (667 mg, 2.2 mmol).

^{1}H-NMR ($CDCl_3$): δ 1.25 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.5 Hz), 1.30 (d, 3H, H-6, $J_{6,5}$ 6.4), 2.58 (ABX, 2H, CH_2 SEt), 2.73 (d, 1H, OH, $J_{HO,H}$ 2.1 Hz), 3.18 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ 9.3 Hz), 3.56 (s, 3H, CH_3 Me), 3.67 (dd, 1H, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.0 Hz), 3.97 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 4.04 (dd, 1H, H-2, $J_{2,1}$ 1.7 Hz, $J_{2,3}$ 3.5 Hz), 4.67 (s, 2H, CH_2 Bn), 5.26 (d, 1H, H-1, $J_{1,2}$ 1.3 Hz), 7.27-7.38 (m, 5H, CH Bn); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 14.5 (CH_3 SEt), 17.3 (C-6), 24.5 (CH_2 SEt), 60.5 (CH_3 Me), 71.6 (CH_2 Bn), 67.5, 69.7, 79.6, 81.8 (C-2, C-3, C-4, C-5), 83.1 (C-1), 127.4, 128.0 (CH Bn), 137.6 (qC Bn).

Ethyl 3-*O*-benzyl-2-*O*-chloroacetyl-4-*O*-methyl-1-thio-α-L-rhamnopyranoside (13) - Rhamnopyranoside **12** (667 mg, 2.2 mmol) was treated with chloroacetic anhydride (3.75 g, 22.0 mmol) and $NaHCO_3$ (1.85 g, 22.0 mmol) as described for the preparation of compound **10**. Donor **13** (724 mg, 1.92 mmol) was obtained after purification by column chromatography (0→5% ethyl acetate in petroleum ether).

$[\alpha]_D$ -72.0° (c 1); ^{1}H-NMR ($CDCl_3$): δ 1.27 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.5 Hz), 1.31 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 2.61 (ABX, 2H, CH_2 SEt), 3.12 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ Hz), 3.55 (s, 3H, CH_3 Me), 3.76 (dd, 1H, H-3, $J_{3,2}$ 2.8 Hz, $J_{3,4}$ 9.3 Hz), 3.98 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 4.14 (d, 2H, CH_2 ClAc), 4.59 (AB, 2H, CH_2 Bn), 5.18 (s, 1H, H-1), 5.44 (m, 1H, H-2, $J_{2,1}$ 1.5 Hz, $J_{2,3}$ 3.1 Hz), 7.25-7.37 (m, 5H, CH Bn); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 14.9 (CH_3 SEt), 17.6 (C-6), 25.4 (CH_2 SEt), 40.8 (CH_2 ClAc), 60.9 (CH_3 Me), 71.8 (CH_2 Bn), 68.2, 72.6, 77.9, 81.7 (C-2, C-3, C-4, C-5), 81.9 (C-1), 127.7, 127.9, 128.2 (CH Bn), 137.7 (qC Bn), 166.5 (C=O ClAc).

Anal. calcd. for $C_{18}H_{25}O_5SCl$ (388.91): C 55.59, H 6.48; found C 55.54, H 6.62%.

Methyl 4-*O*-acetyl-3-*O*-(3-*O*-benzyl-2-*O*-chloroacetyl-4-*O*-methyl-α-D-rhamnopyranosyl)-2-*O*-methyl-α-L-fucopyranoside (15-α) and **Methyl 4-*O*-acetyl-3-*O*-(3-*O*-benzyl-2-*O*-chloroacetyl-4-*O*-methyl-β-D-rhamnopyranosyl)-2-*O*-methyl-α-L-fucopyranoside (15-β)** - A solution of donor **10** (93 mg, 0.24 mmol) and glycosyl acceptor **14** (47 mg, 0.20 mmol) in 1,2-dichloroethane-diethyl ether (1/1, v/v, 0.8 ml) was stirred at room temperature for 25 min in the presence of powdered molecular sieves (4 Å). The reaction mixture was cooled to 0°C and a suspension of NIS (54 mg, 0.24 mmol) and TfOH (1.8 µl, 20 µmol) in the same solvent mixture (1.3 ml) was added. After stirring for 15 min, the reaction mixture was neutralised by adding pyridine (0.2 ml). The reaction mixture was filtered, and diluted with ethyl acetate (15 ml). The organic layer was washed

with aq. $Na_2S_2O_3$ (20%, 10 ml), aq. $NaHCO_3$ (10%, 10 ml), dried ($MgSO_4$), and filtered. The solvents were removed and the crude product was purified by column chromatography. The column was eluted with ethyl acetate in petroleum ether (0→20%) to give the α-linked dimer **15-α** (61 mg, 0.11 mmol). Further elution of the column gave the β-linked anomer **15-β** (27 mg, 0.05 mmol).

15-α: $[\alpha]_D$ -42.8° (c 1); ^{1}H-NMR ($CDCl_3$, 300 MHz, HH-COSY): δ 1.12 (d, 3H, H-6, $J_{6,5}$ 6.6 Hz), 1.29 (d, 3H, H-6', $J_{6,5}$ 6.2 Hz), 2.06 (s, 3H, CH_3 Ac), 3.08 (t, 1H, H-4', $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.42, 3.48, 3.53 (3× s, 9H, 3× CH_3 Me), 3.54 (dd, 1H, H-2, $J_{2,1}$ 3.6 Hz, $J_{2,3}$ 10.1 Hz), 3.66 (dd, 1H, H-3', $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.4 Hz), 3.76 (dq, 1H, H-5', $J_{5,4}$ 9.6 Hz, $J_{5,6}$ 6.2 Hz), 4.02 (dq, 1H, H-5, $J_{5,4}$ 1.3 Hz, $J_{5,6}$ 6.5 Hz), 4.06 (dd, 1H, H-3, $J_{3,2}$ 10.1 Hz, $J_{3,4}$ 3.6 Hz), 4.13 (s, 2H, CH_2 ClAc), 4.62 (AB, 2H, CH_2 Bn), 4.87 (d, 1H, H-1, $J_{1,2}$ 3.6 Hz), 5.00 (d, 1H, H-1', $J_{1,2}$ 1.8 Hz), 5.17 (dd, 1H, H-4, $J_{4,3}$ 3.6 Hz, $J_{4,5}$ 1.3 Hz), 5.36 (dd, 1H, H-2', $J_{2,1}$ 1.9 Hz, $J_{2,3}$ 3.4 Hz), 7.28-7.40 (m, 5H, CH Bn); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 15.6, 17.4 (C-6, C-6'), 20.2 (CH_3 Ac), 40.5 (CH_2 ClAc), 55.0 (CH_3 1-*O*-Me), 58.4, 60.3 (2× CH_3 Me), 71.4 (CH_2 Bn), 64.4, 67.9, 70.7, 72.6, 72.8, 76.3, 78.2, 81.5 (CH sugar rings), 97.3, 98.3 (C-1, C-1', $^1J_{C,H}$ 168.5, 174.4 Hz, respectively), 127.3, 127.4, 128.0 (CH Bn), 137.7 (qC Bn), 166.3 (C=O ClAc), 169.8 (C=O Ac).

Anal. calcd. for $C_{26}H_{37}O_{11}Cl$ (545.03): C 57.30, H 6.84; found C 57.43, H 6.71%.

15-β: $[\alpha]_D$ -146.8° (c 1); ^{1}H-NMR ($CDCl_3$, 300 MHz, HH-COSY): δ 1.15 (d, 3H, H-6, $J_{6,5}$ 6.6 Hz), 1.33 (d, 3H, H-6', $J_{6,5}$ 6.1 Hz), 2.21 (s, 3H, CH_3 Ac), 3.04 (t, 1H, H-4', $J_{4,3}\approx J_{4,5}$ 9.3 Hz), 3.23 (dq, 1H, H-5', $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.1 Hz), 3.41 (s, 3H, CH_3 Me), 3.48 (dd, 1H, H-2, $J_{2,1}$ 3.7 Hz, $J_{2,3}$ 9.9 Hz), 3.50 (dd, 1H, H-3', $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.2 Hz), 3.50, 3.54 (2× s, 6H, 2× CH_3 Me), 4.00 (dq, 1H, H-5, $J_{5,4}$ 1.3 Hz, $J_{5,6}$ 6.6 Hz), 4.15 (AB, 2H, CH_2 ClAc), 4.21 (dd, 1H, H-3, $J_{3,2}$ 10.0 Hz, $J_{3,4}$ 3.6 Hz), 4.60 (AB, 2H, CH_2 Bn), 4.63 (d, 1H, H-1', $J_{1,2}$ 1.1 Hz), 4.83 (d, 1H, H-1, $J_{1,2}$ 3.7 Hz), 5.21 (dd, 1H, H-4, $J_{4,3}$ 3.6 Hz, $J_{4,5}$ 1.3 Hz), 5.43 (dd, 1H, H-2', $J_{2,1}$ 0.9 Hz, $J_{2,3}$ 3.4 Hz), 7.30-7.37 (m, 5H, CH Bn); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 15.8, 17.5 (C-6, C-6'), 20.6 (CH_3 Ac), 40.8 (CH_2 ClAc), 55.1 (CH_3 1-*O*-Me), 59.6, 60.8 (2× CH_3 Me), 71.3 (CH_2 Bn), 63.7, 69.8, 70.0, 71.7, 73.5, 76.2, 79.3, 81.3 (CH sugar rings), 95.0 (C-1, $^1J_{C,H}$ 171.4 Hz), 98.4 (C-1', $^1J_{C,H}$ 159.7 Hz), 127.5, 127.8, 128.2 (CH Bn), 137.4 (qC Bn), 166.7 (C=O ClAc), 171.2 (C=O Ac).

Methyl 4-*O*-acetyl-3-*O*-(3-*O*-benzyl-2-*O*-chloroacetyl-4-*O*-methyl-α-L-rhamnopyranosyl)-2-*O*-methyl-α-L-fucopyranoside (16) - L-Fucopyranosyl acceptor **14** (46.8 mg, 0.20 mmol) was glycosylated with L-rhamnopyranosyl donor **13** (93.2 mg, 0.24 mmol) under the same condition as described for the formation of dimer **15**. The crude product was purified by column chromatography (10→40% ethyl acetate in petroleum ether) to give the α-linked dimer **16** (86 mg, 0.15 mmol).

$[\alpha]_D$ -95.4° (c 1); ^{1}H-NMR ($CDCl_3$, 300 MHz, HH-COSY): δ 1.14 (d, 3H, H-6, $J_{6,5}$ 6.5 Hz), 1.29 (d, 3H, H-6', $J_{6,5}$ 6.3 Hz), 2.18 (s, 3H, CH_3 Ac), 3.07 (t, 1H, H-4', $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.41, 3.43 (2× s, 6H, 2× CH_3 Me), 3.45 (dd, 1H, H-2, $J_{2,1}$ 4.0 Hz, $J_{2,3}$ 10.0 Hz), 3.52 (s, 3H, CH_3 Me), 3.74 (dd, 1H, H-3', $J_{3,2}$ 3.4 Hz, $J_{3,4}$ 9.4 Hz), 3.85 (dq, 1H, H-5', $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.1 Hz), 3.98 (dq, 1H, H-5, $J_{5,4}$ 1.0 Hz, $J_{5,6}$ 6.7 Hz), 4.10 (dd, 1H, H-3, $J_{3,2}$ 10.2 Hz, $J_{3,4}$ 3.5 Hz), 4.14 (s, 2H, CH_2 ClAc), 4.61 (AB, 2H, CH_2 Bn), 4.85 (d, 1H, H-1, $J_{1,2}$ 3.8 Hz), 4.90 (d, 1H, H-1', $J_{1,2}$ 1.8 Hz), 5.22 (dd, 1H, H-4, $J_{4,3}$ 3.6 Hz, $J_{4,5}$ 1.7 Hz), 5.22 (dd, 1H, H-2', $J_{2,1}$ 1.9 Hz, $J_{2,3}$ 3.5 Hz), 7.25-7.36 (m, 5H, CH Bn); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 15.9, 17.8 (C-6, C-6'), 20.5 (CH_3 Ac), 40.8 (CH_2 ClAc), 55.2 (CH_3 1-*O*-Me), 59.4, 60.8 (2× CH_3 Me), 71.6 (CH_2 Bn), 63.9, 67.9, 69.4, 70.4, 71.2, 76.6, 77.0, 81.6 (CH sugar rings), 93.8, 97.7 (C-1, C-1', $^1J_{C,H}$ 170.0, 171.4 Hz, respectively), 127.5, 127.9, 128.2 (CH Bn), 137.8 (qC Bn), 166.3 (C=O ClAc), 170.4 (C=O Ac).

Anal. calcd. for $C_{26}H_{37}O_{11}Cl$ (545.03): C 57.30, H 6.84; found C 57.36, H 6.78%.

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(3-*O*-benzyl-2-*O*-chloroacetyl-4-*O*-methyl-α-D-rhamnopyranoside)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (17) - Glycosylation of trimer acceptor **2a** (125 mg, 0.14 mmol) with mannopyranoside donor **10** (65 mg, 0.17 mmol) was performed the same way as the corresponding model condensation (→**15**). The crude tetramer was applied to a silica gel column, which was eluted with 0→30% ethyl acetate in petroleum ether. Concentration of the appropriate fractions gave the α-linked tetramer **17** (117 mg, 0.10 mmol).

$[\alpha]_D$ -61.6° (c 1); ^{1}H-NMR ($CDCl_3$, 400 MHz, HH-COSY); δ 1.12 (d, 3H, CH_3, H-6'', $J_{6,5}$ 6.6 Hz), 1.26 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 1.32 (d, 3H, H-6''', $J_{6,5}$ 6.2 Hz), 1.35 (d, 3H, H-6', $J_{6,5}$ 6.2 Hz), 2.06 (s, 3H, CH_3 Ac), 2.76 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.8 Hz), 3.08 (t, 1H, H-4''', $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.22 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.6 Hz), 3.30 (s, 3H, CH_3 Me), 3.42 (q, 2H, CH_2 spacer, $J_{H,H}\approx J_{H,NH}$ 6.4 Hz), 3.48, 3.50 (2× s, 6H, 2× CH_3 Me), 3.50 (t, 1H, H-4', $J_{4,3}\approx J_{4,5}$ 9.0 Hz), 3.54 (s, 6H, 2× CH_3 Me), 3.54 (dd, 1H,

H_2", $J_{3,2}$ 10.1 Hz, $J_{3,4}$ 3.2 Hz), 3.67 (dq, 1H, H-5, $J_{5,4}$ 9.6 Hz, $J_{5,6}$ 6.4 Hz), 3.67 (dd, 1H, H-3''', $J_{3,2}$ 3.4 Hz, $J_{3,4}$ 9.4 Hz), 3.71 (dd, 1H, H-2, $J_{2,1}$ 2.1 Hz, $J_{2,3}$ 3.0 Hz), 3.73 (dd, 1H, H-2', $J_{2,1}$ 2.0 Hz, $J_{2,3}$ 3.0 Hz), 3.80 (dq, 1H, H-5''', $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 3.94 (dq, 1H, H-5', $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.3 Hz), 4.01 (dd, 1H, H-3', $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.5 Hz), 4.08 (dd, 1H, H-3, $J_{3,2}$ 3.1 Hz, $J_{3,4}$ 9.8 Hz), 4.12 (AB, 2H, CH_2 ClAc), 4.22 (dd, 1H, H-3'', $J_{3,2}$ 10.2, $J_{3,4}$ 3.5 Hz), 4.35 (dq, 1H, H-5'', $J_{5,4}$ 0.8 Hz, $J_{5,6}$ 6.4 Hz), 4.62, 4.83 (2× AB, 4H, 2× CH_2 Bn), 5.04 (d, 1H, H-1''', $J_{1,2}$ 1.8 Hz), 5.09 (s, 2H, CH_2 Z), 5.19 (d, 1H, H-4'', $J_{4,3}$ 3.6 Hz), 5.20 (d, 1H, H-1', $J_{1,2}$ 1.7 Hz), 5.22 (d, 1H, H-1'', $J_{1,2}$ 4.0 Hz), 5.37 (dd, 1H, H-2''', $J_{2,1}$ 1.9 Hz, $J_{2,3}$ 3.3 Hz), 5.46 (d, 1H, H-1, $J_{1,2}$ 1.9 Hz), 6.98-7.09 (m, 4H, CH spacer), 7.26-7.35 (m, 15H, CH arom); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 16.2, 17.8, 18.1 (4× C-6), 20.5 (CH_3 Ac), 35.1, 42.4 (2× CH_2 spacer), 40.9 (CH_2 ClAc), 57.6, 58.5, 58.8, 60.6, 61.0 (5× CH_3 Me), 66.5 (CH_2 Z), 71.7, 75.1 (2× CH_2 Bn), 65.2, 68.1, 68.4, 68.6, 70.9, 72.8, 72.9, 76.4, 78.5, 79.2, 79.4, 80.0, 80.4, 81.4, 81.7, 82.0 (CH sugar rings), 94.9 (C-1, $^1J_{C,H}$ 168.5 Hz), 98.1, 98.6, 99.4 (C-1', C-1'', C-1''', $^1J_{C,H}$ 168.5, 167.1, 171.5 Hz, respectively), 116.4 (CH spacer), 127.3, 127.6, 127.7, 128.0, 128.2, 128.3, 128.4, 129.7 (CH arom), 132.4, 138.8 (qC arom), 155.1, 156.2 (qC spacer, C=O Z), 166.6 (C=O ClAc), 170.2 (C=O Ac).

Anal. calcd. for $C_{63}H_{82}NO_{21}Cl$ (1224.80): C 61.78, H 6.75, N 1.14; found C 61.63, H 6.62, N 1.06%.

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(3-*O*-benzyl-4-*O*-methyl-α-D-rhamnopyranoside)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (18) - Freshly prepared HDTC[6] (1.1 ml) was added dropwise to a solution of tetramer **17** (117 mg, 0.10 mmol) in a mixture of acetic acid (0.24 ml) and lutidine (0.72 ml). After stirring for 1 h, the solvents were evaporated and the residue was taken up in dichloromethane (10 ml). The organic layer was washed with water (5 ml) and aq. $NaHCO_3$ (10%, 5 ml), dried ($MgSO_4$), and filtered. The solution was concentrated, and the crude product was purified by column chromatography. The column was eluted with 0→40% ethyl acetate in petroleum ether to give compound **18** (101 mg, 88 μmol).

13C{1H}-NMR (CDCl3): δ 16.1, 17.6, 18.0 (4× C-6), 20.7 (CH_3 Ac), 35.0, 42.2 (2× CH_2 spacer), 57.4, 58.3, 58.6, 60.4, 60.9 (5× CH_3 Me), 66.3 (CH_2 Z), 71.7, 74.8 (2× CH_2 Bn), 65.2, 67.8, 68.5, 68.6, 68.7, 72.9, 73.1, 78.3, 78.6, 79.1, 79.4, 80.0, 80.4, 81.3, 81.7, 81.8 (CH sugar rings), 94.8 (C-1), 98.1, 99.5, 100.7 (C-1', C-1'', C-1'''), 116.3 (CH spacer), 127.0, 127.3, 127.5, 127.8, 128.0, 128.2, 129.6 (CH arom), 132.4, 138.1, 138.9 (qC arom), 154.9 (qC spacer, C=O Z), 170.1 (C=O Ac).

Anal. calcd. for $C_{61}H_{81}NO_{20}$ (1148.32): C 63.80, H 7.31, N 1.22; found C 63.74, H 7.41, N 1.16%.

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(3-*O*-benzyl-4-*O*-methyl-2-*O*-phenoxythionocarbonyl-α-D-rhamnopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (19) - To a solution of tetramer **18** (101 mg, 88 μmol) in acetonitrile (2 ml) were added phenyl chlorothionoformate (16 μl, 0.11 mmol) and DMAP (21 mg, 0.18 mmol). The reaction mixture was stirred for 24 h, dichloromethane (10 ml) was added and the solution was washed with aq. NaH_2PO_4 (1 M, 8 ml), and water (8 ml). The organic layer was dried ($MgSO_4$), filtered and concentrated. The residue was purified by silica gel chromatography. The column was eluted with 0→40% ethyl acetate in petroleum ether to yield pure tetramer **19** (71 mg, 64 μmol).

$^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 16.2, 17.8, 18.2 (4× C-6), 20.6 (CH_3 Ac), 35.2, 42.2 (2× CH_2 spacer), 57.6, 58.7, 58.8, 60.9, 61.1 (5× CH_3 Me), 66.6 (CH_2 Z), 71.8, 75.3 (2× CH_2 Bn), 65.3, 68.2, 68.6, 68.8, 72.7, 72.9, 76.6, 78.6, 79.0, 79.2, 79.5, 80.1, 80.6, 81.8, 82.0 (CH sugar rings), 94.8 (C-1), 97.8, 98.1, 99.5 (C-1', C-1'', C-1'''), 116.4 (CH spacer), 121.9, 126.4, 127.3, 127.6, 127.7, 128.0, 128.1, 128.2, 128.3, 128.4, 129.3, 129.7 (CH arom), 132.4, 138.1, 138.8 (qC arom), 153.3, 155.1, 156.2 (qC arom, C=O Z), 170.3 (C=O Ac), 194.5 (C=S).

Anal. calcd. for $C_{68}H_{85}NO_{21}S$ (1332.49): C 61.29, H 6.43, N 1.05; found C 61.21, H 6.57, N 1.13%.

4-(Aminoethyl)phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(3-*O*-benzyl-2,6-dideoxy-4-*O*-methyl-α-D-*arabino*-hexopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (20) - Tetramer **19** (71 mg, 64 μmol) was dried by repeated evaporation with toluene, and subsequently dissolved in toluene (2 ml). Tributyltin hydride (26 μl, 0.10 mmol) and a catalytic amount of AIBN (3 mg, 0.02 mmol) were added. The mixture was heated under reflux until TLC-analysis showed conversion of starting saccharide in baseline material. After stirring for 4 h, the reaction mixture was concentrated and the residue was applied to a silica gel column. Elution with 0→25% methanol in ethyl acetate containing 3% Et_3N yielded the amine containing derivative **20** (54 mg, 54 μmol).

$^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 15.9, 17.5, 17.7 (4× C-6), 20.3 (CH_3 Ac), 35.8, 41.5 (2× CH_2 spacer), 57.4, 58.4, 58.5, 59.9, 60.8 (5× CH_3 Me), 71.4, 74.8 (2× CH_2 Bn), 65.2, 67.5, 68.4, 73.0, 73.3, 75.6, 78.1, 79.0, 79.2, 79.8, 80.3, 80.8, 81.8, 86.1 (CH sugar rings), 94.6 (C-1), 98.0, 98.9, 99.4 (C-1', C-1", C-1'"), 116.0, 116.4 (CH spacer), 127.1, 127.3, 127.9, 128.0, 129.5 (CH arom), 138.6 (qC Bn), 170.6 (C=O Ac).

Anal. calcd. for $C_{53}H_{74}NO_{17}$ (997.18): C 63.48, H 7.48, N 1.40; found C 63.41, H 7.36, N 1.49%.

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(3-*O*-benzyl-2-*O*-(*p*-fluorophenylthionocarbonyl)-4-*O*-methyl-α-D-rhamnopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (21) - A mixture of tetramer **18** (112 mg, 0.1 mmol) and DMAP (24 mg, 0.2 mmol) was dried by evaporation with toluene, and subsequently dissolved in acetonitrile (2.5 ml). *p*-Fluorophenyl chlorothionoformate (18 µl) was added and after stirring for 24 h, the same amount of reagent was added. The reaction mixture was stirred for another 24 h and concentrated. The residue was taken up in dichloromethane (5 ml). The solution was washed with aq. NaH_2PO_4 (1 M, 4 ml) and H_2O (4 ml). The organic layer was dried ($MgSO_4$), filtered, and concentrated to dryness. The crude product was purified by column chromatography. The column was eluted with 0→60% ethyl acetate in petroleum ether. Concentration of the appropriate fractions gave compound **21** (94 mg, 73 µmol).

$[\alpha]_D$ -79.2° (c 1); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 16.2, 17.7, 18.1 (4× C-6), 20.6 (CH_3 Ac), 35.1, 42.2 (2× CH_2 spacer), 57.5, 58.6, 58.8, 60.8, 61.0 (5× CH_3 Me), 66.5 (CH_2 Z), 71.8, 75.2 (2× CH_2 Bn), 65.3, 68.2, 68.5, 68.7, 72.8, 76.6, 78.5, 79.2, 79.5, 80.0, 80.5, 81.7, 81.9 (CH sugar rings), 94.8 (C-1), 97.8, 98.1, 99.4 (C-1', C-1", C-1'"), 115.7, 116.2, 116.3, 123.3, 123.4 (CH *p*FPh), 127.2, 127.6, 127.7, 128.0, 128.2, 128.4, 129.7 (CH arom), 132.4, 137.9, 138.9, 149.1, 155.0, 156.2, 158.0, 162.9 (qC arom, C=O Z), 170.2 (C=O Ac), 194.5 (C=S).

Anal. calcd. for $C_{68}H_{84}NO_{21}FS$: C 62.71, H 6.50, N 1.08; found C 62.61, H 6.57, N 0.97%.

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(3-*O*-benzyl-2,6-dideoxy-4-*O*-methyl-α-D-*arabino*-hexopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (22) - Tributyltin hydride (25 µl, 93 µmol) and AIBN (1.60 mg, 0.01 mmol) were added to a solution of tetramer **21** (24 mg, 73 µmol) in toluene (0.7 ml). The reaction mixture was heated under reflux for 25 min and concentrated until dryness. The residue was purified by column chromatography (0→15% EtOAc in petroleum ether containing 3%Et_3N) to yield product **22** (68 mg, 60 µmol).

^1H-NMR ($CDCl_3$, 400 MHz, HH-COSY): δ 1.11 (d, 3H, H-6", $J_{6,5}$ 6.5 Hz), 1.25 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 1.29 (d, 3H, H-6'", $J_{6,5}$ 6.2 Hz), 1.33 (d, 3H, H-6', $J_{6,5}$ 6.3 Hz), 1.62 (ddd, 1H, H-2'"-ax, $J_{2,2}$ 13.0 Hz, $J_{2,1}$ 3.8 Hz, $J_{2,3}$ 11.5 Hz), 2.10 (s, 3H, CH_3 Ac), 2.21 (ddd, 1H, H-2'"-eq, $J_{2,2}$ 13.0 Hz, $J_{2,1}$ 1.4 Hz, $J_{2,3}$ 4.8 Hz), 2.76 (t, 2H, CH_2 spacer, $J_{H,H}$ 7.3 Hz), 2.81 (t, 1H, H-4'", $J_{4,3}\approx J_{4,5}$ 9.1 Hz), 3.22 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.26 (s, 3H, CH_3 Me), 3.42-3.48 (m, 2H, CH_2 spacer), 3.48 (s, 3H, CH_3 Me), 3.50 (t, 1H, H-4'", $J_{4,3}\approx J_{4,5}$ 9.3 Hz), 3.50 (s, 3H, CH_3 Me), 3.51 (dd, 1H, H-2", $J_{2,1}$ 4.0 Hz, $J_{2,3}$ 10.1 Hz), 3.53, 3.57 (2× s, 6H, 2× CH_3 Me), 3.68 (dq, 1H, H-5, $J_{5,4}$ 9.3 Hz, $J_{5,6}$ 6.2 Hz), 3.68 (ddd, 1H, H-3'", $J_{3,2}$ 4.8 Hz, $J_{3,2}$ 11.3 Hz, $J_{3,4}$ 9.0 Hz), 3.71 (dd, 1H, H-2', $J_{2,1}$ 1.8 Hz, $J_{2,3}$ 3.3 Hz), 3.72 (dd, 1H, H-2, $J_{2,1}$ 1.4 Hz, $J_{2,3}$ 3.3 Hz), 3.76 (dq, 1H, H-5'", $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.2 Hz), 3.94 (dq, 1H, H-5', $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 4.02 (dd, 1H, H-3', $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.5 Hz), 4.08 (dd, 1H, H-3', $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.6 Hz), 4.18 (dd, 1H, H-3", $J_{3,2}$ 10.4 Hz, $J_{3,4}$ 3.5 Hz), 4.33 (dq, 1H, H-5", $J_{5,4}$ 1.2 Hz, $J_{5,6}$ 6.6 Hz), 4.65, 5.02 (2× AB, 4H, 2× CH_2 Bn), 5.09 (s, 2H, CH_2 Z), 5.09-5.10 (m, 1H, H-1'"), 5.19 (d, 1H, H-1', $J_{2,1}$ 1.3 Hz), 5.20 (d, 1H, H-1", $J_{1,2}$ 3.9 Hz), 5.22 (dd, 1H, H-4", $J_{4,3}$ 3.5 Hz, $J_{4,5}$ 1.3 Hz), 5.46 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 6.97-7.10 (m, 4H, CH spacer), 7.25-7.47 (m, 15H, CH arom); $^{13}C\{^1H\}$-NMR ($CDCl_3$, 100 MHz, CH-COSY): δ 16.3 (C-6"), 17.8 (C-6), 17.9 (C-6'"), 18.1 (C-6'), 20.7 (CH_3 Ac), 35.2 (CH_2 spacer), 36.0 (C-2'"), 42.3 (CH_2 spacer), 57.6, 58.6, 58.8, 60.4, 61.1 (5× CH_3 Me), 65.4 (C-5"), 66.6 (CH_2 Z), 67.7 (C-5'"), 68.6 (C-5'), 68.8 (C-5), 71.7 (CH_2 Bn), 73.1 (C-3"), 73.2 (C-4"), 75.0 (CH_2 Bn), 76.0 (C-3'"), 78.4, 79.3 (C-2", C-4'), 79.6 (C-3), 80.1, 80.6 (C-2, C-2'), 81.2 (C-3'), 81.9 (C-4), 86.4 (C-4'"), 94.9 (C-1), 98.3 (C-1'/C-1"), 99.1 (C-1'"), 99.7 (C-1'/C-1"), 116.4 (CH spacer), 127.2, 127.4, 127.4, 128.0, 128.1, 128.2, 129.7 (CH arom), 132.4, 138.8, 139.1, 148.0, 155.0 (qC arom, C=O Z), 170.4 (C=O Ac).

Anal. calcd. for $C_{61}H_{81}NO_{19}$ (1170.23): C 62.61, H 6.11, N 1.20; found C 62.72, H 6.19, N 1.08%.

4-(Aminoethyl)phenyl 2,4-di-*O*-methyl-3-*O*-{2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(2,6-dideoxy-4-*O*-methyl-α-D-*arabino*-hexopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (5) - Tetramer **22** (34 mg, 30 µmmol) was dissolved in isopropanol (2 ml) and a solution of tris(hydroxymethyl)aminomethane in water-acetic acid at pH 6.72

(1 ml) was added. The reaction mixture was stirred in the presence of palladium on carbon under a hydrogen atmosphere for 48 h. The reaction mixture was filtered and concentrated. Purification of the residue was accomplished by gel-filtration over Sephadex LH20 (methanol) to give target tetramer **5** (6 mg, 7 μmol).

^{1}H-NMR ($CDCl_3$, 400 MHz, HH-COSY): δ 1.09 (d, 3H, H-6", $J_{6,5}$ 6.6 Hz), 1.24 (d, 6H, 2× H-6 Hex*p*/Rha*p*, $J_{6,5}$ 6.3 Hz), 1.32 (d, 3H, H-6, Rha*p*/Hex*p*, $J_{6,5}$ 6.2 Hz), 1.63 (ddd, 1H, H-2'''-ax, $^2J_{2,2}$ -12.6 Hz, $J_{2,1}$ 3.6 Hz, $J_{2,3}$ 8.7 Hz), 2.08 (br dd, 1H, H-2'''-eq, $^2J_{2,2}$ -12.2 Hz, $J_{2,1}$ 5.1 Hz), 2.15 (s, 3H, CH_3 Ac), 2.90 (t, 2H, CH_2 spacer, $J_{H,H}$ 8.3 Hz), 3.11 (t, 2H, CH_2 spacer, $J_{H,H}$ 7.7 Hz), 3.24 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ 9.6 Hz), 3.50-3.81 (m, 10H, 4× H-2, H-3''', H-4', H-4", H-4''', 2× H-5 Rha*p*/Hex*p*), 3.50, 3.51, 3.54, 3.55, 3.56 (5× s, 15H, 5× CH_3 Me), 3.84 (dq, 1H, H-5 Hex*p*/Rha*p*, $J_{5,4}$ 9.3 Hz, $J_{5,6}$ 6.2 Hz), 3.89 (dd, 1H, H-3', $J_{3,2}$ 3.4 Hz, $J_{3,4}$ 9.7 Hz), 4.06 (dd, 1H, H-3, $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.5 Hz), 4.10 (dd, 1H, H-3", $J_{3,2}$ 10.0 Hz, $J_{3,4}$ 3.6 Hz), 4.25 (q, 1H, H-5", $J_{5,6}$ 6.7 Hz), 5.08 (d, 1H, H-1''', $J_{1,2}$ 3.6 Hz), 5.17 (br s, 1H, H-1'), 5.20 (d, 1H, H-1", $J_{1,2}$ 3.6 Hz), 5.31 (d, 1H, H-4", $J_{4,3}$ 3.7 Hz), 5.58 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 7.07-7.22 (m, 4H, CH spacer); ^{13}C{^{1}H}-NMR (CD_3OD): δ 16.6, 18.1, 18.3 (4× C-6), 20.7 (CH_3 Ac), 39.5, 42.1 (2× CH_2 spacer), 58.8, 59.2, 60.5, 61.6 (5× CH_3 Me), 66.7, 68.8, 68.9, 70.1, 70.8, 72.6, 73.1, 74.1, 74.8, 80.2, 80.4, 81.0, 81.4, 82.0, 83.5 (CH sugar rings), 100.3, 100.5 (4× C-1), 118.1, 130.9 (CH spacer), 156.8 (qC spacer), 172.3 (C=O Ac).

3-*O*-Benzyl-6-deoxy-D-glucal (24) - Regioselective benzylation of glucal **23** (1.30 g, 10.0 mmol) was executed as described for the preparation of compound **9**. Purification of the residue by column chromatography (0→20% ethyl acetate in petroleum ether) gave compound **24** (1.46 g, 6.6 mmol).

^{1}H-NMR ($CDCl_3$): δ 1.38 (d, H-6, $J_{6,5}$ 6.4 Hz), 2.26 (d, 1H, OH, $J_{OH,4}$ 3.6 Hz), 3.61 (ddd, 1H, H-4, $J_{4,OH}$ 3.7 Hz, $J_{4,3}$ 6.9 Hz, $J_{4,5}$ 9.4 Hz), 3.89 (dq, 1H, H-5, $J_{5,4}$ 9.0 Hz, $J_{5,6}$ 6.4 Hz), 4.04 (dt, 1H, H-3, $J_{3,2}$≈$J_{3,1}$ 1.7 Hz, $J_{3,4}$ 6.9 Hz), 4.62 (AB, 2H, CH_2 Bn), 4.84 (dd, 1H, H-2, $J_{2,1}$ 6.2 Hz, $J_{2,3}$ 2.3 Hz), 6.34 (dd, 1H, H-1, $J_{1,2}$ 6.0 Hz, $^4J_{1,3}$ -1.4 Hz), 7.31-7.35 (m, 5H, CH Bn); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 16.9 (C-6), 70.3 (CH_2 Bn), 72.3, 74.4, 76.7 (C-3, C-4, C-5), 99.7 (C-2), 127.5, 127.6, 128.2 (CH Bn), 138.9 (qC Bn), 144.7 (C-1).

3-*O*-Benzyl-6-deoxy-4-*O*-methyl-D-glucal (25) - Methyl iodide (0.53 ml, 8.6 mmol) was added at 0°C to a suspension of glucal **24** (1.46 g, 6.6 mmol) and sodium hydride (80%, 297 mg, 9.9 mmol) in DMF (16 ml). After stirring for 2 h at room temperature, the reaction was quenched with methanol (1 ml), and further processed as described for the synthesis of compound **7**. The crude product was purified by column chromatography (0→5% ethyl acetate in petroleum ether) to give compound **25** (1.22 g, 5.2 mmol).

$[\alpha]_D$ -45.2° (c 1); ^{1}H-NMR ($CDCl_3$): δ 1.38 (d, H-6, $J_{6,5}$ 6.4 Hz), 3.23 (dd, 1H, H-4, $J_{4,3}$ 6.3 Hz, $J_{4,5}$ 8.6 Hz), 3.57 (s, 3H, CH_3 Me), 3.92 (dq, 1H, H-5, $J_{5,4}$ 8.5 Hz, $J_{5,6}$ 6.7 Hz), 4.09 (dt, 1H, H-3, $J_{3,2}$≈$J_{3,1}$ 1.8 Hz, $J_{3,4}$ 5.9 Hz), 4.63 (AB, 2H, CH_2 Bn), 4.83 (dd, 1H, H-2, $J_{2,1}$ 6.2 Hz, $J_{2,3}$ 2.6 Hz), 6.35 (dd, 1H, H-1, $J_{1,2}$ 5.9 Hz, $^4J_{1,3}$ -1.0 Hz), 7.33-7.37 (m, 5H, CH Bn); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 16.9 (C-6), 59.4 (CH_3 Me), 70.1 (CH_2 Bn), 73.4, 75.6, 81.4 (C-3, C-4, C-5), 99.8 (C-2), 127.2, 127.2, 128.0 (CH Bn), 138.3 (qC Bn), 144.3 (C-1).

Anal. calcd. for $C_{14}H_{18}O_3$ (234.30): C 71.77, H 7.74; found C 72.69, H 7.62%.

1,2-Anhydro-3-*O*-benzyl-6-deoxy-4-*O*-methyl-D-*arabino*-hexopyranoside (26) - Glucal **25** (467 mg, 2.0 mmol) was dried by evaporation with toluene and dissolved in dichloromethane (20 ml). The mixture was cooled in an ice-bath and a solution of dimethyldioxirane (DMD) in acetone (30 ml, 0.078 M, 2.3 mmol) was added dropwise. After the addition was completed, the mixture was stirred for 30 min at 0°C. The solvent was evaporated and the epoxide derivative **26** was dried by evaporation with toluene.

^{1}H-NMR ($CDCl_3$): δ 1.25 (d, 3H, $J_{6,5}$ 6.4 Hz), 2.87 (dd, 1H, H-4, $J_{4,3}$ 8.0 Hz, $J_{4,5}$ 9.8 Hz), 3.03 (d, 1H, H-2, $J_{2,1}$ 2.3 Hz), 3.54 (s, 3H, CH_3), 3.64 (dq, 1H, H-5, $J_{5,4}$ 10.2 Hz, $J_{5,6}$ 6.3 Hz), 3.81 (dd, 1H, H-3, $J_{3,2}$ 1.0 Hz, $J_{3,4}$ 7.7 Hz), 4.75 (AB, 2H, CH_2 Bn), 4.86 (d, 1H, H-1, $J_{1,2}$ 2.6 Hz), 7.33-7.40 (m, 5H, CH Bn); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 17.1 (C-6), 52.5 (C-2), 60.2 (CH_3 Me), 65.7 (C-3), 72.0 (CH_2 Bn), 78.2, 81.5 (C-4, C-5), 127.6, 127.7, 128.2, 128.3 (C-1, CH Bn), 137.5 (qC Bn).

Phenyl 3-*O*-benzyl-6-deoxy-4-*O*-methyl-1-thio-β-D-glucopyranoside (27) - Thiophenol (1.03 ml, 10 mmol), potassium carbonate (2.76 g, 20 mmol) and 18-crown-6 (8 mg, 0.03 mmol) were heated under reflux in acetone (40 ml) for 2 h. The mixture was cooled to room temperature and a solution of epoxide **26** in acetone (32 ml) was added. After stirring for 30 min, TLC-analysis showed complete conversion of the epoxide. The mixture was filtered, the solvents were evaporated, and the residue was redissolved in ethyl acetate (100 ml). The solution was washed twice with aq. NaOH (1 M, 50 ml) and once with brine (30 ml),

dried ($MgSO_4$), and concentrated to give crude product. The latter was purified by column chromatography. Elution with 0→5% ethyl acetate in petroleum ether gave homogeneous phenyl 1-thio-β-D-glucopyranoside **27** (545 mg, 1.5 mmol).

$^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 17.7 (C-6), 60.5 (CH_3 Me), 74.7 (CH_2 Bn), 72.5, 75.2, 84.7, 85.3 (C-2, C-3, C-4, C-5), 87.6 (C-1, $^1J_{C,H}$ 153.9 Hz), 127.2, 127.3, 127.5, 128.0, 128.5 (CH arom), 132.1 (CH Bz), 132.2 (qC SPh), 138.3 (qC Bn).

Anal. calcd. for $C_{20}H_{25}O_4S$ (345.48): C 69.53, H 7.29; found C 69.62, H 7.20%.

Phenyl 3-*O*-benzyl-6-deoxy-4-*O*-methyl-1-thio-α-D-mannopyranoside

Characteristic resonances ^{13}C-NMR ($CDCl_3$): δ 74.9 (CH_2 Bn), 72.9, 82.5, 85.7, 87.8 (C-1, C-2, C-3, C-4, C-5).

Phenyl 3-*O*-benzyl-6-deoxy-4-*O*-methyl-2-*O*-phenoxythionocarbonyl-1-thio-β-D-glucopyranoside (28) - Glucopyranoside derivative **27** (545 mg, 1.5 mmol) was treated with phenyl chlorothionoformate (0.27 ml, 1.9 mmol) and DMAP (378 mg, 3.1 mmol) as described for the preparation of **19**. Purification of the crude product by column chromatography (0→5% ethyl acetate in petroleum ether) yielded pure **28** (158 mg, 1.2 mmol).

^1H-NMR ($CDCl_3$): δ 1.39 (d, 3H, H-6, $J_{6,5}$ 5.9 Hz), 3.06 (t, 1H, H-3/H-4, $J_{H,H}$ 9.3 Hz), 3.40 (dq, 1H, H-5, $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.0 Hz), 3.58 (s, 3H, CH_3 Me), 3.73 (t, 1H, H-3/H-4, $J_{H,H}$ 9.0 Hz), 4.81 (d, 1H, H-1, $J_{1,2}$ 10.0 Hz), 4.88 (s, 2H, CH_2 Bn), 5.61 (dd, 1H, H-2, $J_{2,1}$ 10.0 Hz, $J_{2,3}$ 9.3 Hz), 7.14-7.56 (m, 15H, CH arom); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 17.8 (C-6), 60.9 (CH_3 Me), 75.1 (CH_2 Bn), 75.7, 81.4, 83.8, 85.0 (C-2, C-3, C-4, C-5), 86.0 (C-1, $^1J_{C,H}$ 158.3), 121.8, 126.4, 127.7, 127.8, 128.3, 128.8, 129.4, 131.9 (CH arom), 133.4, 137.8, 153.4 (qC arom), 194.2 (C=S).

Anal. calcd. for $C_{27}H_{29}O_5S_2$ (481.66): C 67.33, H 6.07; found C 67.25, H 6.02%.

4-[2-(Benzylcarbonylamino)ethyl]phenol (31) - To a solution of tyramine (700 mg, 5.1 mmol) in aq. NaOH (2 N, 3.1 ml) was added phenylacetyl chloride (1.35 ml, 10.1 mmol) and aq. NaOH (2 N, 3.1 ml). The reaction was stirred for 17 h at room temperature. The solids were filtered and subsequently redissolved in ethanol (98%, 60 ml). The reaction was stirred in the presence of aq. NaOH (1 M, 10 ml) until TLC-analysis showed complete conversion (22 h). The solution was neutralised with diluted acetic acid, concentrated and redissolved in dichloromethane. The sodium salts were filtered and the filtrate was concentrated to yield compound **31** (626 mg, 2.5 mmol) as a white solid.

^1H-NMR ($CDCl_3$): δ 2.64 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.8 Hz), 3.42 (q, 2H, CH_2 spacer, $J_{H,H}$ 6.4 Hz), 3.67 (s, 2H, CH_2 PhAc), 5.30 (br s, 1H, NH), 6.79 (m, 4H, CH spacer), 7.27-7.34 (m, 5H, CH PhAc); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 34.3, 43.5 (2× CH_2 spacer), 41.0 (CH_2 PhAc), 115.5 (CH spacer), 127.1, 127.3, 128.5, 128.6, 128.9, 129.3, 129.4, 129.5, (CH arom), 155.1 (qC spacer), 171.9 (C=O PhAc).

4-[2-(Benzylcarbonylamino)ethyl]phenyl 3-*O*-acetyl-2,4-di-*O*-methyl-α-L-rhamnopyranoside (32) - The condensation of rhamnopyranoside donor **30** (139 mg, 0.50 mmol) and aglycon **31** (140 mg, 0.55 mmol) was carried out as described for the preparation of dimer **15**. The residue was applied to a silica gel column, which was eluted with a gradient of ethyl acetate in petroleum ether (20→50%). Concentration of the appropriate fractions yielded monomer **32** (156 mg, 0.33 mmol).

$[\alpha]_D$ -59.0° (c 1); ^1H-NMR ($CDCl_3$): δ 1.30 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 2.19 (s, 3H, CH_3 Ac), 2.61-2.67 (m, 2H, CH_2 spacer), 3.51, 3.54 (2× s, 6H, 2× CH_3 Me), 3.41-3.58 (m, 6H, H-3, H-5, CH_2 spacer, CH_2 PhAc), 5.32 (dd, 1H, H-4, $J_{4,3}$ 3.3 Hz, $J_{4,5}$ 9.5 Hz), 5.44 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 6.69-6.93 (m, 4H, CH spacer), 7.14-7.37 (m, 5H, CH PhAc); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 17.8 (C-6), 21.2 (CH_3 Ac), 34.5, 43.7 (2× CH_2 spacer), 40.7 (CH_2 PhAc), 59.4, 60.5 (2× CH_3 Me), 68.3, 73.4, 78.4, 80.3 (C-2, C-3, C-4, C-5), 95.4 (C-1, $^1J_{C,H}$ 170.0 Hz), 116.4 (CH spacer), 127.2, 128.9, 129.3, 129.6 (CH arom), 132.4, 134.7 (qC arom), 154.8 (qC spacer), 170.3, 170.8 (C=O Ac, PhAc)

Anal. calcd. for $C_{26}H_{33}NO_7$ (471.56): C 66.23, H 7.05, N 2.97; found C 66.15, H 6.86, N 3.06%.

4-[2-(Benzylcarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-α-L-rhamnopyranoside (33) - Potassium *tert*-butoxide (10 mg, 0.09 mmol) was added to a solution of rhamnopyranoside **32** (156 mg, 0.33 mmol) in methanol (2 ml). The reaction mixture was stirred for 3 h, neutralised with Dowex 50W×4 (H^+-form), filtered, and concentrated. The residue was purified by silica gel chromatography (40→80% ethyl acetate in petroleum ether) to furnish compound **33** (126 mg, 0.30 mmol).

$[\alpha]_D$ -48.0° (c 1); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 17.7 (C-6), 34.4, 43.4 (2× CH_2 spacer), 40.6 (CH_2 PhAc), 58.9, 60.6 (2× CH_3 Me), 67.8, 70.8, 80.3, 83.4 (C-2, C-3, C-4, C-5), 94.6 (C-1), 116.2 (CH spacer), 126.9, 128.6, 129.1, 129.4 (CH arom), 132.2, 134.7 (qC arom), 154.8 (qC spacer), 170.8 (C=O PhAc).

Anal. calcd. for $C_{24}H_{31}NO_6$ (429.52): C 67.11, H 7.27, N 3.26; found C 67.24, H 7.35, N 3.15%.

4-[2-(Benzylcarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-methyl-α,β-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (35) - A solution of dimer donor **34** (205 mg, 0.30 mmol) and rhamnopyranosyl acceptor **33** (107 mg, 0.25 mmol) in 1,2-dichloroethane-diethyl ether (1/1, v/v, 2 ml) was stirred for 20 min in the presence of powdered molecular sieves (4 Å). The mixture was cooled to -30°C and a suspension of NIS (67 mg, 0.30 mmol) and TfOH (5.3 µl, 60 µmol) in the same solvent mixture (2 ml) was added. After stirring for 15 min, pyridine (0.2 ml) was added and the reaction mixture was filtered. The filtrate was diluted with ethyl acetate (10 ml) and the organic solution was washed with aq. $Na_2S_2O_3$ (20%, 8 ml) and aq. $NaHCO_3$ (10%, 8 ml), dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by silica gel chromatography. Elution with ethyl acetate in petroleum ether (0→60%) yielded compound **35** (222 mg, 0.22 mmol).

^{1}H-NMR ($CDCl_3$, 300 MHz, HH-COSY): δ 1.16 (d, 3H, H-6", $J_{6,5}$ 6.6 Hz), 1.28 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 1.34 (d, 3H, H-6', $J_{6,5}$ 6.2 Hz), 2.17 (s, 3H, CH_3 Ac), 2.66 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.8 Hz), 3.22 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ 9.6 Hz), 3.40 (s, 3H, CH_3 Me), 3.42 (q, 2H, CH_2 spacer, $J_{H,H}$≈$J_{H,NH}$ 6.4 Hz), 3.48-3.55 (m, 2H, CH_2 PhAc), 3.48 (s, 3H, CH_3 Me), 3.50 (t, 1H, H-4', $J_{4,3}$≈$J_{4,5}$ 9.4 Hz), 3.51, 3.55 (2× s, 6H, 2× CH_3 Me), 3.58 (dd, 1H, H-2", $J_{2,1}$ 4.2 Hz, $J_{2,3}$ 10.6 Hz), 3.66 (dq, 1H, H-5, $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.12 Hz), 3.69-3.74 (m, 2H, H-2, H-2'), 3.72 (s, 3H, CH_3 Me), 3.94 (dq, 1H, H-5', $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.3 Hz), 4.00 (dd, 1H, H-3", $J_{3,2}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz), 4.05 (dd, 1H, H-3', $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.5 Hz), 4.09 (dd, 1H, H-3, $J_{3,2}$ 3.0 Hz, $J_{3,4}$ 9.5 Hz), 4.31 (dq, 1H, H-5", $J_{5,4}$ 1.2 Hz, $J_{5,6}$ 6.6 Hz), 4.58, 4.83 (2× AB, 4H, 2× CH_2 Bn, *p*MBn), 5.20 (d, 1H, H-1', $J_{1,2}$ 1.8 Hz), 5.23 (d, 1H, H-1", $J_{1,2}$ 3.7 Hz), 5.37 (t, 1H, NH, $J_{NH,H}$ 5.6 Hz), 5.41 (dd, 1H, H-4", $J_{4,3}$ 3.5 Hz, $J_{4,5}$ 1.3 Hz), 5.45 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 6.79-7.04 (m, 4H, CH spacer), 7.18-7.42 (m, 15H, CH arom); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 16.0, 17.4, 17.8 (3× C-6), 20.4 (CH_3 Ac), 34.2, 43.2 (2× CH_2 spacer), 40.4 (CH_2 PhAc), 54.6 (CH_3 OMe *p*MBn), 57.4, 58.4, 58.8, 60.8 (4× CH_3 Me), 70.7, 74.6 (2× CH_2 Bn, *p*MBn), 64.7, 68.2, 68.4, 70.3, 74.7, 77.1, 79.0, 79.7, 80.2, 81.6 (CH sugar rings), 94.5 (C-1, $^1J_{C,H}$ 170.0 Hz), 98.0, 99.5 (C-1', C-1", $^1J_{C,H}$ 172.9, 168.5 Hz, respectively), 113.3 (CH *p*MBn), 116.0 (CH spacer), 126.7, 127.5, 127.8, 128.4, 128.9, 129.3 (CH arom), 129.8, 132.2, 134.7, 138.6 (qC arom), 154.6 (qC spacer), 158.6 (qC *p*MBn), 170.3, 170.5 (C=O Ac, PhAc).

4-[2-(Benzylcarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-[4-*O*-benzyl-2-*O*-methyl-3-*O*-(4-*O*-acetyl-2-*O*-methyl-α-L-fucopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranoside (2b) - DDQ (82 mg, 0.36 mmol) was added to a solution of trimer **35** (222 mg, 0.22 mmol) in dichloromethane-water (8/1, v/v, 10 ml). The reaction was stirred at room temperature for 1 h. The solids were filtered and the filtrate was diluted with dichloromethane (10 ml). The organic layer was washed with water (10 ml) and aq. $NaHCO_3$ (10%, 10 ml), dried ($MgSO_4$), and filtered. The solution was concentrated and the crude reaction mixture was purified by column chromatography using 30→80% ethyl acetate in petroleum ether to give trimer **2b** (130 mg, 0.14 mmol).

$[\alpha]_D$ -111.2° (c 1); ^{1}H-NMR ($CDCl_3$, 300 MHz, HH-COSY): δ 1.16 (d, 3H, H-6", $J_{6,5}$ 6.6 Hz), 1.28 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 1.34 (d, 3H, H-6', $J_{6,5}$ 6.2 Hz), 2.18 (s, 3H, CH_3 Ac), 2.66 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.8 Hz), 3.23 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ 9.6 Hz), 3.31 (s, 3H, CH_3 Me), 3.42 (q, 2H, CH_2 spacer, $J_{H,H}$≈$J_{H,NH}$ 6.4 Hz), 3.48 (dd, 1H, H-2", $J_{2,1}$ 3.3 Hz, $J_{2,3}$ 9.8 Hz), 3.49-3.56 (m, 2H, CH_2 PhAc), 3.49 (s, 3H, CH_3 Me), 3.52 (t, 1H, H-4', $J_{4,3}$≈$J_{4,5}$ 9.2 Hz), 3.53, 3.55 (2× s, 6H, 2× CH_3 Me), 3.67 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.1 Hz), 3.73 (dd, 1H, H-2, $J_{2,1}$ 1.9 Hz, $J_{2,3}$ 3.2 Hz), 3.75 (dd, 1H, H-2, $J_{2,1}$ 1.9 Hz, $J_{2,3}$ 3.3 Hz), 3.94 (dq, 1H, H-5', $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.2 Hz), 4.03 (dd, 1H, H-3', $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.4 Hz), 4.09 (dd, 1H, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.5 Hz), 4.25 (dd, 1H, H-3", $J_{3,2}$ 10.1 Hz, $J_{3,4}$ 3.6 Hz), 4.35 (dq, 1H, H-5", $J_{5,4}$ 1.1 Hz, $J_{5,6}$ 6.6 Hz), 4.86 (AB, 2H, CH_2 Bn), 5.21 (d, 1H, H-1', $J_{1,2}$ 1.7 Hz), 5.25 (d, 1H, H-1", $J_{1,2}$ 3.6 Hz), 5.29 (dd, 1H, H-4", $J_{4,3}$ 3.5 Hz, $J_{4,5}$ 1.3 Hz), 5.38 (t, 1H, NH, $J_{NH,H}$ 5.8 Hz), 5.46 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 6.93 (s, 4H, CH spacer), 7.17-7.39 (m, 10H, CH arom); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 16.1, 17.5, 17.9 (3× C-6), 20.5 (CH_3 Ac), 34.3, 43.3 (2× CH_2 spacer), 40.5 (CH_2 PhAc), 57.3, 57.9, 58.5, 60.8 (4× CH_3 Me), 74.5 (CH_2 Bn), 64.8, 67.5, 68.3, 68.4, 73.0, 78.0, 79.0, 79.4, 79.8, 80.3, 80.8, 81.6 (CH sugar ring), 94.1 (C-1), 98.0, 98.9 (C-1', C-1"), 116.0 (CH spacer), 126.8, 127.0, 127.1, 127.8, 128.5, 129.0, 129.4 (CH arom), 132.2, 134.6, 138.6 (qC arom), 154.6 (qC spacer), 170.3, 170.5 (2× C=O Ac, PhAc).

Anal. calcd. for $C_{47}H_{63}NO_{15}$ (882.02): C 64.00, H 7.20, N 1.59; found C 64.09, H 7.08, N 1.68%.

4-[2-(Benzylcarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(3-*O*-benzyl-2,6-dideoxy-4-*O*-methyl-2-phenylthio-α-D-*arabino*-hexopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (36) - Trimer acceptor **2b** (125 mg, 0.14 mmol) and 6-deoxy-glucopyranosyl donor **28** (85 mg, 0.17 mmol) were dissolved in a mixture of 1,2-dichloroetane-diethyl ether (1/1, v/v, 0.8 ml). After stirring for 30 min in the presence of activated molecular sieves (4 Å), NIS (38 mg, 0.17 mmol) was added, followed by a solution of TfOH (1.6 µl, 18 µ

mol) in the same solvent mixture (0.25 ml). After stirring for 15 min, the reaction was quenched with pyridine (0.1 ml), filtered, and diluted with ethyl acetate (7 ml). The organic layer was washed with aq. $Na_2S_2O_3$ (20%, 5 ml) and aq. $NaHCO_3$ (10%, 5 ml), dried ($MgSO_4$), and filtered. The solution was concentrated and the residue was applied to a silica gel column, which was eluted with 10→60% ethyl acetate in petroleum ether to provide tetramer **36** (100 mg, 82 μmol).

$[\alpha]_D$ -75.4° (c 1); ^{1}H-NMR ($CDCl_3$, 400 MHz, HH-COSY): δ 1.12 (d, 3H, H-6", $J_{6,5}$ 6.5 Hz), 1.27 (d, 3H, H-6, $J_{6,5}$ 6.3 Hz), 1.32 (d, 3H, H-6', $J_{6,5}$ 6.3 Hz), 1.35 (d, 3H, H-6"', $J_{6,5}$ 6.2 Hz), 2.05 (s, 3H, CH_3 Ac), 2.65 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.8 Hz), 3.10 (t, 1H, H-4"', $J_{4,3}\approx J_{4,5}$ 9.2 Hz), 3.22 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.7 Hz), 3.41 (q, 2H, CH_2 spacer, $J_{H,H}\approx J_{H,NH}$ 6.6 Hz), 3.46 (dd, 1H, H-2", $J_{2,1}$ 3.4 Hz, $J_{2,3}$ 9.6 Hz), 3.47 (s, 3H, CH_3 Me), 3.50 (t, 1H, H-4', $J_{4,3}\approx J_{4,5}$ 9.2 Hz), 3.51-3.59 (m, 2H, CH_2 PhAc), 3.51, 3.53, 3.54, 3.58 (4× s, 12H, 4× CH_3 Me), 3.66 (dq, 1H, H-5, $J_{5,4}$ 9.1 Hz, $J_{5,6}$ 6.7 Hz), 3.66-3.70 (m, 1H, H-5"'), 3.70-3.73 (m, 2H, H-2, H-2'), 3.81 (dq, 1H, H-5"', $J_{5,4}$ 9.3 Hz, $J_{5,6}$ 6.3 Hz), 3.94 (dd, 1H, H-3"', $J_{3,2}$ 4.4 Hz, $J_{3,4}$ 9.2 Hz), 3.94 (dq, 1H, H-5', $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.8 Hz), 3.99 (dd, 1H, H-3', $J_{3,2}$ 3.1 Hz, $J_{3,4}$ 9.5 Hz), 4.09 (dd, 1H, H-3, $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.5 Hz), 4.20 (dd, 1H, H-3", $J_{3,2}$ 10.2 Hz, $J_{3,4}$ 3.5 Hz), 4.33 (q, 1H, H-5", $J_{5,6}$ 6.8 Hz), 4.60, 4.81 (2× AB, 4H, 2× CH_2 Bn), 5.17 (d, 1H, H-1", $J_{1,2}$ 3.5 Hz), 5.21 (s, 1H, H-1'), 5.23 (d, 1H, H-4", $J_{4,3}$ 3.2 Hz), 5.24 (s, 1H, H-1"'), 5.43 (t, 1H, NH, $J_{NH,H}$ 5.5 Hz), 5.46 (d, 1H, H-1, $J_{1,2}$ 1.9 Hz), 6.95 (s, 4H, CH spacer), 7.08-7.40 (m, 20H, CH arom); ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz, CH-COSY): δ 16.2 (C-6"), 17.8 (C-6), 18.0 (C-6"'), 18.1 (C-6'), 20.6 (CH_3 Ac), 34.5, 43.8 (2× CH_2 spacer), 40.7 (CH_2 PhAc), 53.3 (C-2"'), 57.5, 57.9, 58.8, 60.6, 61.1 (5× CH_3 Me), 65.2 (C-5"), 68.5 (C-5"'), 68.5 (C-5"), 68.7 (C-5), 71.2 (CH_2 Bn), 72.4 (C-3"), 73.0 (C-4"), 75.0 (CH_2 Bn), 77.3 (C-3"'), 78.5, 79.1 (C-4', C-2"), 79.6 (C-3), 80.1, 80.5 (C-2, C-2'), 81.7 (C-3'), 81.9 (C-4), 82.7 (C-4"'), 94.8 (C-1, $^1J_{C,H}$ 168.5 Hz), 98.1 (C-1', $^1J_{C,H}$ 166.8 Hz), 99.4 (C-1", $^1J_{C,H}$ 167.1 Hz), 101.3 (C-1"', $^1J_{C,H}$ 174.4 Hz), 116.3 (CH spacer), 126.7, 127.1, 127.3, 127.4, 128.0, 128.7, 129.2, 129.5, 131.4 (CH arom), 132.3, 134.7, 138.1, 138.9 (qC arom), 154.8 (qC spacer), 170.1, 170.7 (C=O Ac, PhAc).

Anal. calcd. for $C_{67}H_{85}NO_{18}S$ (1224.48): C 65.72, H 7.00, N 1.14; found C 65.63, H 6.93, N 1.01%.

4-[2-(Benzylcarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(3-*O*-benzyl-2,6-dideoxy-4-*O*-methyl-α-D-*arabino*-hexopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (37) - Compound **36** (98 mg, 80 μmol) was dried by repeated evaporation with toluene and dissolved in freshly distilled THF (2 ml). Raney nickel in THF was added, and after stirring for 18 h, the reaction mixture was filtered. The filtrate was concentrated and the oily residue was purified by column chromatography. Elution with 20→80% ethyl acetate in petroleum ether gave compound **37** (70 mg, 62 μmol).

$[\alpha]_D$ -66.8° (c 1); ^{1}H-NMR ($CDCl_3$, 400 MHz, HH-COSY): δ 1.12 (d, 3H, H-6", $J_{6,5}$ 6.6 Hz), 1.27 (d, 3H, H-6, $J_{6,5}$ 6.4 Hz), 1.29 (d, 3H, H-6"', $J_{6,5}$ 6.4 Hz), 1.34 (d, 3H, H-6', $J_{6,5}$ 6.2 Hz), 1.62 (ddd, 1H, H-2"'-ax, $^2J_{2,2}$ -12.8 Hz, $J_{2,1}$ 3.9 Hz, $J_{2,3}$ 11.7 Hz), 2.04 (s, 3H, CH_3 Ac), 2.22 (br dd, 1H, H-2"'-eq, $^2J_{2,2}$ -13.7 Hz, $J_{2,3}$ 5.0 Hz), 2.66 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.8 Hz), 2.81 (t, 1H, H-4"', $J_{4,3}\approx J_{4,5}$ 9.1 Hz), 3.23 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.27 (s, 3H, CH_3 Me), 3.41 (q, 2H, CH_2 spacer, $J_{H,H}\approx J_{H,NH}$ 6.56 Hz), 3.49-3.57 (m, 2H, H-4', H-2"), 3.49, 3.52, 3.53, 3.54, 3.57 (5× s, 14H, 4× CH_3 Me, CH_2 PhAc), 3.61-3.71 (m, 2H, H-5, H-3"'), 3.72-3.73 (m, 2H, H-2, H-2'), 3.77 (dq, 1H, H-5"', $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 3.95 (dq, 1H, H-5', $J_{5,4}$ 9.3 Hz, $J_{5,6}$ 6.3 Hz), 4.03 (dd, 1H, H-3', $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.4 Hz), 4.09 (dd, 1H, H-3, $J_{3,2}$ 3.0 Hz, $J_{3,4}$ 9.5 Hz), 4.19 (dd, 1H, H-3", $J_{3,2}$ 10.3 Hz, $J_{3,4}$ 3.5 Hz), 4.33 (q, 1H, H-5", $J_{5,6}$ 6.8 Hz), 4.65, 4.87 (2× AB, 4H, 2× CH_2 Bn), 5.10 (s, 1H, H-1"', $J_{1,2}$ 3.4 Hz), 5.20 (d, 1H, H-1", $J_{1,2}$ 3.3 Hz), 5.21 (br s, 1H, H-1'), 5.22 (d, 1H, H-4", $J_{4,3}$ 3.9 Hz), 5.39 (t, 1H, NH, $J_{NH,H}$ 5.8 Hz), 5.45 (d, 1H, H-1, $J_{1,2}$ 1.6 Hz), 6.93 (s, 4H, CH spacer), 7.20-7.40 (m, 15H, CH arom); ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 16.3, 17.8, 17.9, 18.1 (4× C-6), 20.7 (CH_3 Ac), 34.6 (CH_2 spacer), 35.9 (C-2"'), 40.7 (CH_2 PhAc), 43.8 (CH_2 spacer), 57.6, 58.6, 58.8, 60.4, 61.1 (5× CH_3 Me), 71.7, 75.0 (2× CH_2 Bn), 65.4, 67.7, 68.5, 68.7, 73.1, 73.4, 76.0, 78.3, 79.2, 79.4, 79.6, 80.0, 80.6, 81.9, 86.4 (CH sugar rings), 94.8 (C-1), 98.3, 99.1, 99.6 (C-1', C-1", C-1"'), 116.3 (CH spacer), 127.2, 127.4, 127.9, 128.1, 128.2, 128.9, 129.3, 129.6 (CH arom), 132.4, 134.8, 138.9, 139.0 (qC arom), 155.0 (qC spacer), 170.3, 170.7 (C=O Ac, PhAc).

Anal. calcd. for $C_{61}H_{81}NO_{18}$ (1116.32): C 65.63, H 7.31, N 1.50; found C 65.74, H 7.25, N 1.18%.

4-[2-(Benzylcarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(2,6-dideoxy-4-*O*-methyl-α-D-*arabino*-hexopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (38) - Palladium on carbon (10%) was added to a solution of tetramer (70 mg, 62 μmol) in a mixture of isopropanol-water (3/1, v/v, 4 ml). The reaction mixture was stirred for 22 h under a blanket of hydrogen. The reaction mixture was filtered and the filtrate was concentrated. Purification of the crude product was achieved by gel-filtration (methanol) to give compound **38** (52 mg, 56 μmol).

$^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 16.2, 17.8, 18.0 (4× C-6), 20.7 (CH_3 Ac), 34.5 (CH_2 spacer), 37.6 (C-2'''), 40.7 (CH_2 PhAc), 43.7 (2× CH_2 spacer), 58.5, 58.9, 59.7, 60.1, 60.9 (5× CH_3 Me), 65.8, 67.4, 67.6, 68.7, 68.9, 71.4, 73.4, 73.8, 78.7, 79.3, 80.2, 80.4, 82.1, 83.2, 87.2 (CH sugar rings), 94.8 (C-1), 99.2, 100.6 (C-1', C-1'', C-1'''), 116.3 (CH spacer), 127.2, 128.6, 129.3, 129.6 (CH arom), 132.3, 134.7, 139.6 (qC arom), 154.9 (qC spacer), 170.4, 170.8 (C=O Ac, PhAc).

Anal. calcd. for $C_{47}H_{69}NO_{18}$ (936.07): C 60.31, H 7.43, N 1.50; found C 60.39, H 7.55, N 1.43%.

4-(Aminoethyl)phenyl 2,4-di-*O*-methyl-3-*O*-{2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(2,6-dideoxy-4-*O*-methyl-α-D-*arabino*-hexopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (5) - Tetramer **38** (52 mg, 56 μmol) was dissolved in a mixture of methanol-water (1/4, v/v, 5 ml) and immobilised penicillin-G acylase (Gist Brocades) was added. The pH was kept at 7.5 by adding aq. NaOH (0.05 M) employing an automated titration apparatus. When the consumption of aq. NaOH stopped, the immobilised enzyme was removed by filtration and the filtrate was concentrated. The residual oil was purified by gel-filtration over fractogel HW-40 (S, Omnilabo). The column was eluted with a solution of TEAB (0.15 M) in methanol-water (1/9, v/v) to give tetramer **5** (36 mg, 45 μmol).

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-{4-*O*-benzyl-2-*O*-methyl-3-*O*-[4-*O*-acetyl-2-*O*-methyl-3-*O*-(3-*O*-benzyl-2,6-dideoxy-4-*O*-methyl-2-phenylthio-α-D-*arabino*-hexopyranosyl)-α-L-fucopyranosyl]-α-L-rhamnopyranosyl}-α-L-rhamnopyranoside (29) - Glycosylation of trimer acceptor **2a** (224 mg, 0.25 mmol) with 6-deoxy-glucopyranoside donor **28** (161 mg, 0.32 mmol) was executed as described for the preparation of tetramer **36**. The pure α-linked tetramer **29** (228 mg, 0.18 mmol) was obtained after column chromatography (0→50% ethyl acetate in petroleum ether).

^1H-NMR ($CDCl_3$, 400 MHz, HH-COSY): δ 1.11 (d, 3H, H-6'', $J_{6,5}$ 6.5 Hz), 1.31 (d, 3H, H-6, $J_{6,5}$ 6.4 Hz), 1.33 (d, 3H, H-6', $J_{6,5}$ 6.3 Hz), 1.34 (d, 3H, H-6''', $J_{6,5}$ 6.1 Hz), 2.05 (s, 3H, CH_3 Ac), 2.74 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.9 Hz), 3.06 (s, 3H, CH_3 Me), 3.10 (t, 1H, H-4''', $J_{4,3}\approx J_{4,5}$ 9.2 Hz), 3.22 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.42-3.48 (m, 4H, H-4', H-2'', CH_2 spacer), 3.46, 3.50, 3.53, 3.57 (4× s, 12H, 4× CH_3 Me), 3.66 (dd, 1H, H-2''', $J_{2,1}$ 1.7 Hz, $J_{2,3}$ 4.6 Hz), 3.67 (dq, 1H, H-5, $J_{5,4}$ 9.2 Hz, $J_{5,6}$ 6.2 Hz), 3.71-3.72 (m, 2H, H-2, H-2'), 3.81 (dq, 1H, H-5''', $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.3 Hz), 3.92 (dq, 1H, H-5', $J_{5,4}$ 9.2 Hz, $J_{5,6}$ 6.3 Hz), 3.94 (dd, 1H, H-3''', $J_{3,2}$ 4.7 Hz, $J_{3,4}$ 9.1 Hz), 4.00 (dd, 1H, H-3', $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.5 Hz), 4.08 (dd, 1H, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.6 Hz), 4.19 (dd, 1H, H-3'', $J_{3,2}$ 10.2 Hz, $J_{3,4}$ 3.5 Hz), 4.32 (q, 1H, H-5'', $J_{5,6}$ 6.4 Hz), 4.60, 4.80 (2× AB, 4H, 2× CH_2 Bn), 5.09 (s, 2H, CH Z), 5.17 (d, 1H, H-1'', $J_{2,1}$ 3.6 Hz), 5.19 (d, 1H, H-1', $J_{1,2}$ 1.6 Hz), 5.21-5.22 (m, 1H, H-4''), 5.23 (d, 1H, H-1''', $J_{1,2}$ 1.1 Hz), 5.46 (d, 1H, H-1, $J_{1,2}$ 1.7 Hz), 6.97-7.10 (m, 4H, CH spacer), 7.22-7.41 (m, 20H, CH arom); $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 16.1, 17.6, 17.8, 18.0 (4× C-6), 20.5 (CH_3 Ac), 35.0, 42.1 (2× CH_2 spacer), 53.2 (C-2'''), 57.3, 57.8, 58.6, 60.5, 60.9 (5× CH_3 Me), 66.5 (CH_2 Z), 71.1, 74.8 (2× CH_2 Bn), 65.1, 68.1, 68.4, 68.6, 72.3, 72.9, 77.1, 78.3, 79.1, 79.5, 79.9, 80.4, 81.8, 82.5 (CH sugar ring), 94.9 (C-1), 98.0, 99.3, 101.2 (C-1',C-1'', C-1'''), 116.3 (CH spacer), 126.6, 127.0, 127.2, 127.4, 127.9, 128.0, 128.2, 128.3, 128.7, 129.6, 131.3, 131.3 (CH arom), 132.2, 135.7, 138.1, 138.9, 154.9 (qC arom), 170.1 (C=O Ac).

Anal. calcd. for $C_{67}H_{85}NO_{19}S$ (1241.49): C 64.82, H 6.90, N 1.13; found C 64.92, H 7.03, N 1.25%.

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