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Iodonium Ion Assisted Synthesis of a Common Inner Core Trisaccharide fragment corresponding to the Cell-Wall Phenolic Glycolipid of *Mycobacterium kansasii*

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Abstract: The spacer containing trimer 4-(aminoethyl)phenyl 2,4-di-*O*-Me-3-*O*-[2-*O*-methyl-3-*O*-(4-*O*-acetyl-2-*O*-methyl-α-L-fucopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranoside (**2**) was prepared by stepwise extension of 4-[2-(benzyloxycarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-α-L-rhamnopyranoside (**19**) with properly protected ethyl thioglycosides of L-rhamnose **8** and L-fucose **12** or **16** using iodonium ions as promotors. The resulting trimers **22** or **23** were deblocked in two steps to give homogeneous **2**. Alternatively, fully protected trimer **22** was assembled by iodonium ion assisted condensation of the phenyl 1-thio-α-L-rhamnopyranoside **29** with **12** followed by extension of dimer **31** with **19**.

Introduction

It is well-established[1] that the mycobacteria *leprea* and *tuberculosis* play a predominant role as the etiologic agents of leprosy and tuberculosis. On the other hand, 'atypical' mycobacteria (*e.g. Mycobacterium kansasii, avium* or *bovis*) may function[2] as important human pathogens. For example, the 'yellow' opportunistic bacillus *Mycobacterium kansasii* (MK) is the cause of pulmonary infections indistinguishable from tuberculosis in humans with chronic pulmonary diseases (*e.g.* bronchitis or silicosis). Furthermore the incidence of MK pulmonary disease is increasing[3] in immunosuppressed patients (*e.g.* AIDS sufferers). Earlier studies showed[4] that the carbohydrate epitope of the major phenolic glycolipid from the cell-wall of *M. leprea* could be used successfully in ELISA for screening lepromatous leprosy. It has been anticipated[5] that the epitope of tubercle bacilli, responsible for a cell-mediated immunological response, resides most likely in the core oligosaccharide components of the major surface glycolipids. It may therefore be expected that synthetic core oligosaccharides corresponding to the major surface oligolipid antigens of MK may be applied for the detection and identification of MK infections in patients and the elaboration of synthetic-vaccines (neoglycoproteins). At present, the oligosaccharide structure of two classes of antigenic oligolipids isolated from the cell-wall of MK have been elucidated: the lipo-oligosaccharides containing the epitope N-acylkansaminyl-(1-3)-Fuc*p*[6] and the phenolic glycolipids **1a-c** presented in Fig 1, which are structurally related to the major triglycosyl phenol-phtiocerol of *M. tuberculosis* (strain Canetti)[7]. It can be seen that the three MK phenolic glycolipids (*i.e.* PheGl K-I[8], K-II[9], K-IV[10]) share a common core assigned to the monoacetylated trisaccharide structure. They differ by the structure of the distal monosaccharide unit S: a 2,6-dideoxy-4-*O*-Me-α-L-*arabino*-Hex*p*, a 2,4-di-*O*-Me-α-D-Man*p* and a 4-*O*-Me-α-D-Man*p* for K-I, K-II and K-IV, respectively.

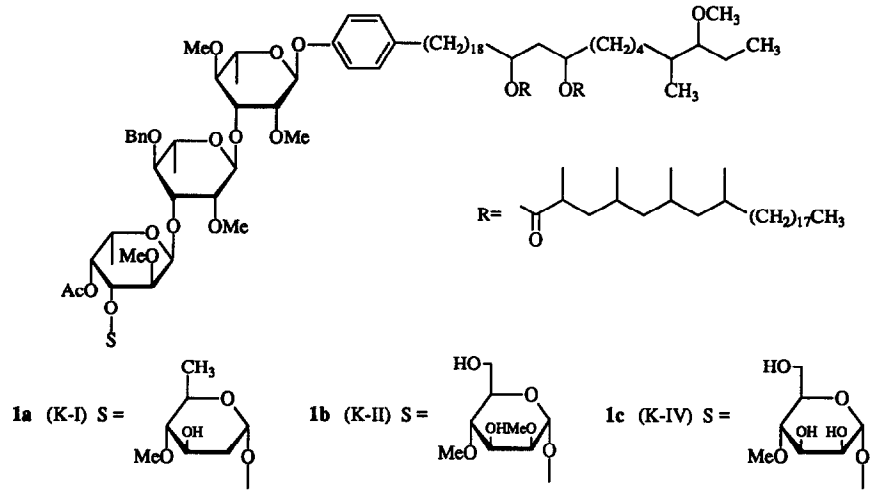
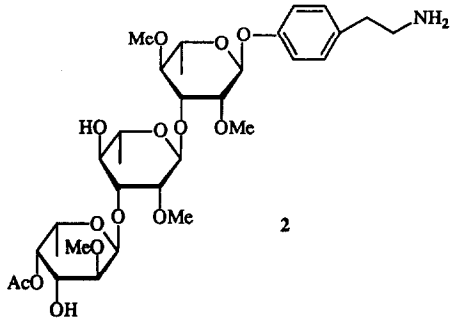


Figure 1. Structure of the phenolic glycolipids PheGl K-I, K-II and K-IV of *Mycobacterium kansasii*.

As part of an ongoing program[11] to develop serodiagnostics and synthetic-vaccines, we here report the synthesis of the anchor bearing MK inner core trisaccharide fragment **2**: 4-*O*-Ac-2-*O*-Me-α-L-Fuc*p*-(1→3)-2-*O*-Me-α-L-Rha*p*-(1→3)-2,4-di-*O*-Me-L-Rha*p*, the terminal rhamnose unit of which is α (*O*)-linked to a tyramine moiety suitable for conjugation with a protein.



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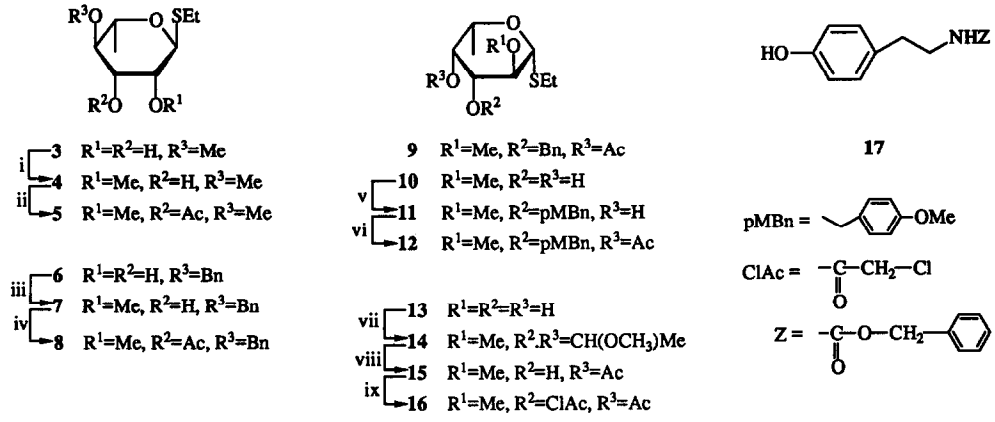
Results and discussion

The route of synthesis we adopted in assembling the target trisaccharide **2** is based on two previously reported observations. Firstly[12], glycosylation of a sugar acceptor with the armed donor ethyl 2,3,4-tri-*O*-benzyl-1-thio-α-L-rhamnopyranoside, in the presence of the weak thiophilic promotor iodonium *sym*-dicollidine perchlorate (IDCP), proceeded stereoselectively giving an α-interglycosidic linkage. Secondly[13], IDCP-assisted condensation of an appropriate protected L-fucopyranoside acceptor with the donor ethyl 4-*O*-acetyl-2,3-di-*O*-benzyl-1-thio-β-L-fucopyranoside resulted also in the exclusive formation of an α-linked disaccharide. On the basis of the above experimental observations it was to be expected that the three α-linkages (*i.e.* one 1,2-*cis* and two 1,2-*trans* orientated bonds) in the target molecule **2** could be introduced stereoselectively starting with suitably protected ethyl 1-thio-α-L-rhamno- and fucopyranoside units.

Accordingly, the requisite L-rhamnopyranosides donors **5** and **8** were prepared by the sequence of

reactions illustrated in Scheme 1. Methylation of known[14] ethyl 4-*O*-methyl-1-thio-α-L-rhamnopyranoside (**3**) with methyl iodide under phase-transfer conditions[15] led to an intractable mixture of the major product **4** and its 3,4-positional isomer. Fortunately, acetylation of the crude mixture followed by silica gel chromatography furnished the homogeneous donor ethyl 3-*O*-acetyl-2,4-di-*O*-methyl-1-thio-rhamnopyranoside (**5**) in 46% yield for the two steps. In a similar fashion, methylation of ethyl 4-*O*-benzyl-1-thio-α-L-rhamnopyranoside[11] (**6**) and subsequent acetylation of **7** and its minor 3-*O*-methyl isomer, gave, after purification, the rhamnopyranoside donor **8** in 58% overall yield.

Scheme 1[a]



[a]Key: (i) MeI, *n*-Bu_4NI, CH_2Cl_2, NaOH/H_2O, 100 h. (ii) Ac_2O, pyridine, 1 h, 46%. (iii) MeI, *n*-Bu_4NI, CH_2Cl_2, NaOH/H_2O, 100 h. (iv) Ac_2O, pyridine, 1 h, 58%. (v) Bu_2SnO, MeOH, reflux, 1.5 h; *p*-methoxybenzyl bromide, CsF, NaI, DMF, 18 h, 80%. (vi) Ac_2O, pyridine, 1.3 h, 88%. (vii) $CH_3C(OCH_3)_3$, DMF, H^+, 50 min; MeI, NaH, 0→20°C, 1.5 h. (viii) HOAc-H_2O 9:1, 15 min, 64%. (ix) $(ClAc)_2O$, DMF, $NaHCO_3$, 1 d, 69%.

It is also evident that the formation of the 1,2-*cis* bond in the target molecule **2** would be feasible using the fucopyranosyl donor **9** as the glycosylating agent. However, it was to be expected that the availability of the fucopyranosyl donors **12** and **16**, the respective HO-3 are protected with a *p*-methoxybenzyl (pMBn) or a chloroacetyl (ClAc) group, would open the way of extending the terminal fucose unit with any of the distal monosaccharides S (see Fig. 1).

The preparation of the fucopyranosyl donor **12** was accomplished by regioselective benzylation of the intermediate stannylidene complex[16] of known[17] ethyl 2-*O*-methyl-1-thio-β-L-fucopyranoside (**10**) with *p*-methoxybenzyl bromide in the presence of cesium fluoride-sodium iodide, then acetylation of **11**, to furnish ethyl 4-*O*-acetyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-methyl-1-thio-β-L-fucopyranoside (**12**) in 70% overall yield. On the other hand, treatment of ethyl 1-thio-β-L-fucopyranoside[11] (**13**) with trimethyl orthoacetate in the presence of catalytic camphorsulfonic acid, followed by methylation of the intermediate orthoester derivative and acid hydrolysis of **14**, resulted in the isolation of **15**. Acylation of **15** with chloroacetic anhydride in the presence of sodium hydrogen carbonate[18] afforded ethyl 4-*O*-acetyl-3-*O*-chloroacetyl-2-*O*-methyl-1-thio-β-L-fucopyranoside (**16**) in 44% yield over the two steps.

The assembly of the target trisaccharide fragment **2** is outlined in Scheme 2, and commences with the condensation of the rhamnopyranosyl donor **5** with the N-protected tyramine aglycon **17**, obtained by the reaction of tyramine with benzyloxycarbonyl chloride[19] (Z-Cl). Unexpectedly, however, coupling of **5** with **17** using the weak thiophilic promoter IDCP[20] was abortive. Fortunately, glycosylation of **17** with **5** in the presence of the promoter NIS/TfOH (cat.) proceeded smoothly yielding exclusively the α-linked rhamno-

Scheme 2[a]

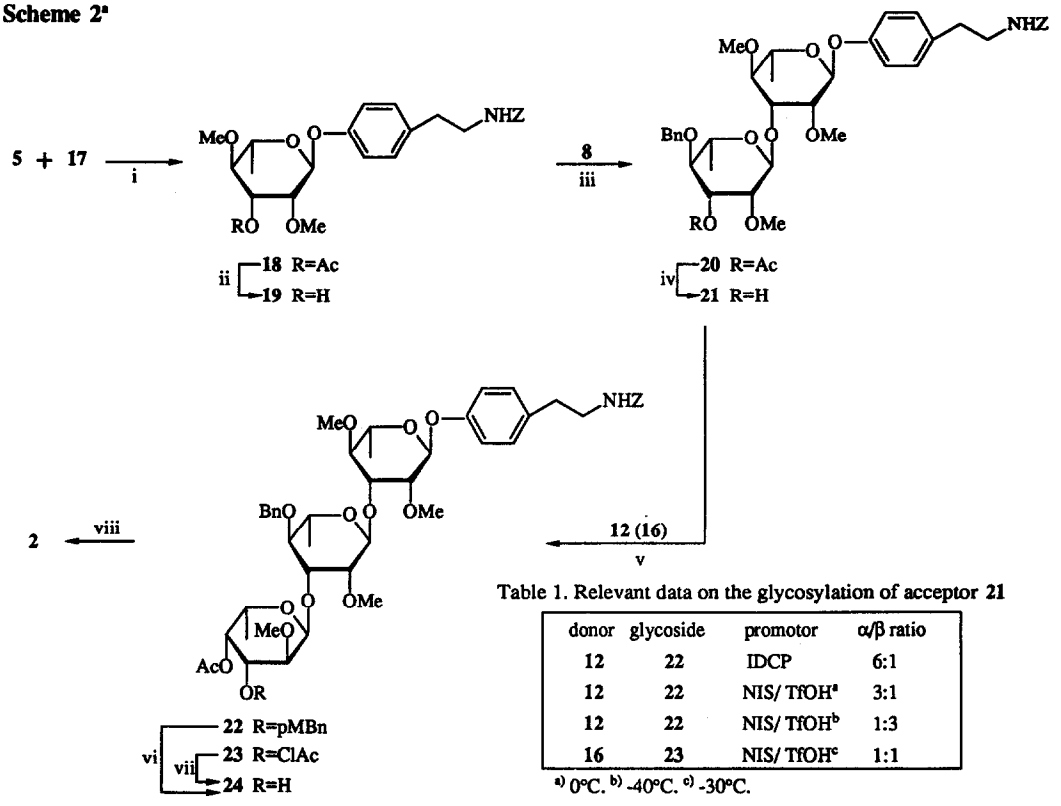


Table 1. Relevant data on the glycosylation of acceptor **21**

donor	glycoside	promotor	α/β ratio
12	22	IDCP	6:1
12	22	NIS/ TfOH[a]	3:1
12	22	NIS/ TfOH[b]	1:3
16	23	NIS/ TfOH[c]	1:1

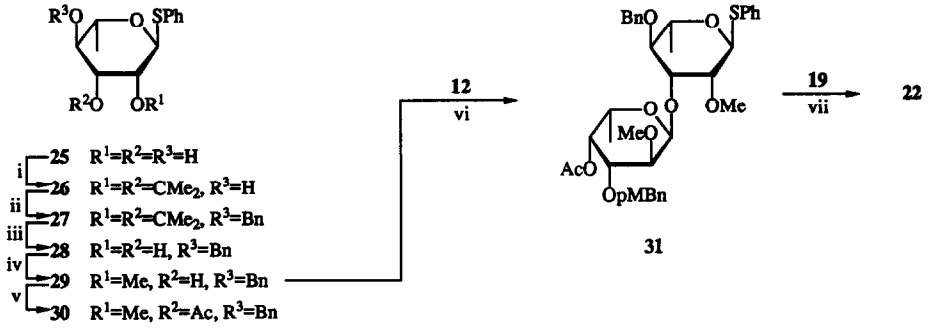
[a] 0°C. [b] -40°C. [c] -30°C.

[a]Key: (i) NIS/TfOH, Et_2O-$(ClCH_2)_2$ 1:1, 0°C, 30 min, 76%. (ii) MeOH, KO*t*-Bu, 1 h, 90%. (iii) NIS/TfOH, Et_2O-$(ClCH_2)_2$ 1:1, -30°C, 15 min, 78%. (iv) MeOH, KO*t*-Bu, 4 h, 93%. (v) a: NIS/TfOH, Et_2O-$(ClCH_2)_2$ 1:1, -30°C, 1.5 h, 76%. b: IDCP, Et_2O-$(ClCH_2)_2$ 5:1, 2 h, 73%. c: NIS/TfOH, Et_2O-$(ClCH_2)_2$ 1:1, 0°C, 1 h, 72%. (vi) HDTC, HOAc, lutidine, 20 h, 82%. (vii) DDQ, CH_2Cl_2-H_2O 8:1, 1 h, 75%. (viii) Pd/C, 2-propanol-H_2O-HOAc 10:5:2, 16 h, 85%.

pyranoside derivative **18** (76%). Zemplén type deacetylation of **18** (→ **19**) and subsequent glycosylation at low temperature with the rhamnopyranosyl donor **8**, using NIS/TfOH (cat.) as promoter, furnished the α-linked and fully protected disaccharide derivative **20** in 70% overall yield (based on **19**). In the next stage, dimer **20** was deacetylated (→ **21**) and condensed with the fucopyranosyl donor **12** in the presence of IDCP. Workup and purification gave trimer **22** as an anomeric mixture (see Table 1) in 73% (based on **21**). It was also established (see Table 1) that the α-stereoselectivity could not be improved by using the strong thiophilic promoter NIS/TfOH (cat.). In addition, the NIS/TfOH (cat.) mediated glycosidation of the rhamnopyranosyl donor **16** with acceptor **21** resulting in trimer **23** does not proceed (see Table 1) with a high degree of stereoselectivity. Removal of the *p*-methoxybenzyl group from **22** (α/β mixture) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[21] (DDQ), and separation of the individual anomers by silica gel chromatography, yielded homogeneous α-linked **24**. Hydrogenolysis of the benzyl and benzyloxycarbonyl groups from **24** gave, after purification, the target molecule **2**, the ^{1}H- and ^{13}C-NMR data of which were in good accord with those reported[10] for the tetrasaccharide part of PhGI K-IV (see Fig. 1). Alternatively, dechloroacetylation of **23** (α/β mixture) with hydrazine dithiocarbonate[22] (HDTC), followed by silica gel purification, and then hydrogenolysis gave homogeneous **2**, which was in every aspect identical with the

same compound isolated earlier after elaboration of **22** (α/β-mixture).

Scheme 3[a]



[a]Key: (i) $(CH_3)_2CO$, $CH_3C(OCH_3)_2CH_3$, TsOH, 18 h, 93%. (ii), BnBr, KH, DMF, 30 min. (iii) HOAc-H_2O 9:1, 50°C, 17 h, 85%. (iv) MeI, *n*-Bu_4NI, CH_2Cl_2, NaOH/H_2O, 100 h. (v) Ac_2O, DMAP, pyridine, 1 h, 56%. (vi) IDCP, Et_2O-$(ClCH_2)_2$ 5:1, 2 h, 58%. (vii) NIS/TfOH, Et_2O-$(ClCH_2)_2$ 1:1, -30°C, 0.75 h, 88%.

The rather disappointing stereochemical outcome of the condensations between the individual donors **12** and **16** with acceptor **21** stimulated us to prepare the partially protected trimer **22** by the alternative pathway depicted in Scheme 3. In this approach, the building unit phenyl 3-*O*-acetyl-4-*O*-benzyl-2-*O*-methyl-1-thio-α-L-rhamnopyranoside (**29**) plays a pivotal role. Thus, it was anticipated[17] that the presence of the anomeric phenylthio function in **29** would not only open the way to increase the chemoselectivity of the iodonium ion assisted condensation of **12** with **29**, but also its *in situ* activation and further extension of the primary condensation product **31** with acceptor **19**.

The synthesis of donor **29** could be realized as follows. Acetonation of phenyl 1-thio-α-L-rhamnopyranoside[17] (**25**), followed by benzylation (**26** → **27**) and then deacetonation furnished **28** in 85% yield (based on **25**). Methylation of **28** under phase-transfer conditions yielded an intractable mixture of major **29** and its 3-*O*-methyl isomer. Acetylation of the crude mixture, followed by separation of the individual isomers and subsequent deacetylation of **30**, gave homogeneous **29**.

Condensation of **12** with **29** in the presence of the promoter IDCP to afford the disaccharide derivative **31** (70%) proceeded with a high degree of α-selectivity (*i.e.* α/β ratio 20:1). Unfortunately, attempts in separating the individual anomers of **31** by silica gel chromatography were abortive. However, glycosidation of **31** (α/β mixture) with **19** using NIS/TfOH (cat.) as promoter afforded the fully protected trisaccharide **22** (88%) having the same α/β ration as donor **31**: indicating that the condensation proceeded in a highly stereospecific manner. Finally, removal of the p-methoxybenzyl group from **22**, under the same conditions as mentioned earlier, furnished, after separation of the individual anomers, the α-linked and partially protected trisaccharide derivative **24**.

In conclusion, the trisaccharide derivative **24**, prepared *via* the route of synthesis presented in Scheme 3, promises to be a valuable starting compound for the future extension of the fucose moiety at HO-3 with the individual sugar units **1a-c** (see Fig. 1). Furthermore, it is also of interest to note that the two approaches presented here towards the assembly of **2** are in several aspects superior over a recently reported synthesis[23] of a similar trisaccharide fragment.

Experimental

General methods and materials - Pyridine was dried by refluxing with CaH_2 (5 gr/L) and then distilled.

Dichloromethane, 1,2-dichloroethane and toluene were distilled from P_2O_5. Diethyl ether was distilled from $LiAlH_4$. *N,N*-dimethylformamide was stirred with CaH_2 at room temperature for 16 h and distilled under reduced pressure. Methanol was dried by refluxing with magnesium methoxide and distilled. Pyridine and methanol were stored over molecular sieves 4Å (Aldrich). Diethyl ether was stored over sodium wire, dichloromethane and 1,2-dichloroethane were stored over alumina. Solvents used for column chromatography were of technical grade and distilled before use.

TLC-analyses were conducted on DC Fertigfolien (Schleicher & Schüll F1500 LS 254), the eluent used are 1:1 ethyl acetate-light petroleum ether for the syntheses of the monosaccharides and 3% methanol in dichloromethane for condensation reactions, unless stated otherwise. Compounds were detected by charring with 20% sulphuric acid in methanol. Column chromatography was performed on silica 60, 70-230 mesh (Merck). Sephadex LH-20 was used for gel-filtration. NMR spectra were recorded with a JEOL JNM-FX-200 (^{13}C-NMR, 50 MHz, internal standard chloroform and methanol and ^{1}H-NMR, 200 MHz, internal standard Me_4Si). Proton spectra were also recorded with a Bruker WM-300 spectrometer equipped with an Aspect-2000 computer (300 MHz, internal standard Me_4Si). Optical rotations were all measured in chloroform.

Ethyl 2,4-di-*O*-methyl-1-thio-α-L-rhamnopyranoside (4). - To a solution of ethyl 4-*O*-methyl-1-thio-α-L-rhamnopyranoside (**3**, 0.40 g, 1.8 mmol) in dichloromethane (11 ml) was added 10% aq. NaOH (4.5 ml), methyl iodide (0.8 ml, 12.8 mmol) and *n*-Bu_4NI (0.13 g, 0.36 mmol). After stirring for 100 h, the two layers were separated and the organic layer was washed with H_2O (5 ml), $NaHCO_3$ (10%, 5 ml), dried ($MgSO_4$) and concentrated. The residual mixture was purified over a silica gel column which was eluted with ethyl acetate in light petroleum ether (0→50%) to give starting material **3** (48 mg, 0.22 mmol), product **4** together with its positional isomer in the ratio 5:1 (268 mg, 1.1 mmol). ^{1}H-NMR ($CDCl_3$) of **4**: δ 1.30 (t, 3H, CH_3 SEt, $J_{H,H}$ 5.9 Hz), 1.30 (d, 3H, H-6, $J_{6,5}$ 7.3 Hz), 2.46 (d, 1H, 3-OH, $J_{HO,3}$ 9.0 Hz), 2.62 (AB, 2H, CH_2 SEt), 3.01 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.4 Hz), 3.48 (s, 3H, CH_3 Me), 3.57 (d, 1H, H-2, $J_{2,3}$ 3.3 Hz), 3.58 (s, 3H, CH_3 Me), 3.80 (dt, 1H, H-3, $J_{3,2}$ 3.8 Hz, $J_{3,4}\approx J_{3,OH}$ 9.2 Hz), 3.95 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 5.37 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$) of **4**: δ 14.5 (CH_3 SEt), 17.3 (C-6), 24.7 (CH_2 SEt), 57.6, 60.2 (2x CH_3 Me), 67.2 (C-5), 73.2, 79.8, 81.8 (C-2, C-3, C-4), 83.4 (C-1).

Ethyl 3-*O*-acetyl-2,4-di-*O*-methyl-1-thio-α-L-rhamnopyranoside (5). - Compound **4** was (268 mg, 1.1 mmol containing 20% of the positional isomer) was dissolved in pyridine (4.5 ml) and acetic anhydride (0.16 ml, 1.6 mmol) and 4-dimethylaminopyridine (DMAP, 12 mg, 0.1 mmol) were added. After stirring for 1 h at 20°C, the mixture was concentrated and the oily residue was purified on silica gel (eluent: ethyl acetate in light petroleum ether (0 → 20%)) to afford **5** (230 mg, 0.82 mmol), $[\alpha]_D$ -145.0° (c 1). ^{1}H-NMR ($CDCl_3$): δ 1.29 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.7 Hz), 1.32 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 2.14 (s, 3H, CH_3 Ac), 2.63 (AB, 2H, CH_2 SEt), 3.27 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.44, 3.48 (2x s, 3H, CH_3 Me), 3.73 (dd, 1H, H-2, $J_{2,1}$ 1.8 Hz, $J_{2,3}$ 3.3 Hz), 4.03 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 5.05 (dd, 1H, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.5 Hz), 5.30 (d, 1H, H-1, $J_{1,2}$ 1.6 Hz); ^{13}C-NMR ($CDCl_3$): δ 14.0 (CH_3 SEt), 16.7 (C-6), 19.9 (CH_3 Ac), 24.1 (CH_2 SEt), 57.2, 59.3 (2x CH_3 Me), 67.0 (C-5), 73.0, 79.0, 79.5 (C-2, C-3, C-4), 79.8 (C-1), 168.63 (qC Ac).

Anal. Calc. for $C_{12}H_{22}O_5S$: C, 51.8; H 7.9. Found: C, 51.7; H, 7.9.

Further elution of the column afforded the positional isomer of **5** (44 mg, 0.16 mmol). ^{1}H-NMR ($CDCl_3$): δ 1.28 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.4 Hz), 1.32 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 2.15 (s, 3H, CH_3 Ac), 2.62 (AB, 2H, CH_2 SEt), 3.09 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.4 Hz), 3.40 (s, 3H, CH_3 Me), 3.48 (dd, 1H, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.5 Hz), 3.55 (s, 3H, CH_3 Me), 3.97 (dq, 1H, H-5, $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.1 Hz), 5.18 (s, 1H, H-1), 5.35 (dd, 1H, H-2, $J_{2,1}$ 1.5 Hz, $J_{2,3}$ 3.3 Hz); ^{13}C-NMR ($CDCl_3$): δ 14.5 (CH_3 SEt), 17.4 (C-6), 20.6 (CH_3 Ac), 25.1 (CH_2

SEt), 57.0, 60.4 (2x CH_3 Me), 67.7 (C-5), 70.0, 79.8, 81.7 (C-2, C-3, C-4), 81.8 (C-1), 169.6 (qC Ac).

Ethyl 4-*O*-benzyl-2-*O*-methyl-1-thio-α-L-rhamnopyranoside (7). - Rhamnopyranoside **6** (714 mg, 2.4 mmol) was dissolved in dichloromethane (15 ml) and 10% aq. NaOH (6 ml), methyl iodide (1.0 ml, 16.0 mmol) and *n*-Bu_4NI (177 mg, 0.48 mmol) were added. After stirring for 100 h, the two layers were separated. The organic layer was washed with H_2O (10 ml) and $NaHCO_3$ (10%, 10 ml), dried ($MgSO_4$) and concentrated. Purification of the residue by column chromatography on silica gel using ethyl acetate in light petroleum ether (0→40%) afforded an intractable mixture of **7** and its positional isomer in the ratio 8:1 (540 mg, 1.73 mmol). ^{1}H-NMR ($CDCl_3$) of **7**: δ 1.29 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.4 Hz), 1.31 (d, 3H, H-6, $J_{6,5}$ 6.4 Hz), 2.62 (AB, CH_2 SEt), 3.30 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.48 (s, 3H, CH_3 Me), 3.58 (d, 1H, H-2, $J_{2,3}$ 3.8 Hz), 3.91 (dt, 1H, H-3, $J_{3,2}$ Hz, $J_{3,4}\approx J_{3,OH}$ 9.1 Hz), 4.42 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.1 Hz), 4.79 (AB, 2H, CH_2 Bn), 5.39 (s, 1H, H-1), 7.26-7.37 (m, 5H, CH arom.); ^{13}C-NMR ($CDCl_3$) of **7**: δ 14.7 (CH_3 SEt), 17.6 (C-6), 24.8 (CH_2 SEt), 58.2 (CH_3 Me), 67.8 (C-5), 73.8, 79.1, 79.9 (C-2, C-3, C-4), 80.7 (C-1), 127.3, 127.4, 128.1 (CH arom.), 138.0, 169.8 (qC Ac).
Further elution of the column gave starting material **6** (106 mg, 0.36 mmol) and the disubstituted adduct (102 mg, 0.31 mmol).

Ethyl 3-*O*-acetyl-4-*O*-benzyl-2-*O*-methyl-1-thio-α-L-rhamnopyranoside (8). - To a solution of **7** (540 mg, 1.73 mmol containing 12% of the positional isomer) in pyridine (6.0 ml) was added acetic anhydride (0.25 ml, 0.23 mmol) and DMAP (21 mg, 0.17 mmol). After stirring for 3 h, the reaction mixture was concentrated and purified on a silica gel column by elution with light petroleum ether in dichloromethane (40→10%) to give **8** (487 mg, 1.38 mmol), $[\alpha]_D$ -128° (c 1). ^{1}H-NMR ($CDCl_3$) of **8**: δ 1.29 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.4 Hz), 1.32 (d, 3H, H-6, $J_{6,5}$ 6.4 Hz), 2.06 (s, 3H, CH_3 Ac), 2.63 (AB, CH_2 SEt), 3.44 (s, 3H, CH_3 Me), 3.57 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.75 (dd, 1H, H-2, $J_{2,1}$ 1.7 Hz, $J_{2,3}$ 3.2 Hz), 4.13 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.4 Hz), 4.67 (AB, 2H, CH_2 Bn), 5.16 (dd, 1H, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.5 Hz), 5.31 (d, 1H, H-1, $J_{1,2}$ 1.5 Hz), 7.28-7.33 (m, 5H, CH arom.); ^{13}C-NMR ($CDCl_3$) of **8**: δ 14.7 (CH_3 SEt), 17.6 (C-6), 20.8 (CH_3 Ac), 24.9 (CH_2 SEt), 58.2 (CH_3 Me), 67.8 (C-5), 73.8, 79.1, 79.9 (C-2, C-3, C-4), 80.6 (C-1), 127.3, 127.4, 128.1 (CH arom.), 138.0 (qC Bn), 169.8 (qC Ac).

Anal. Calc. for $C_{18}H_{26}O_5S$: C, 61.0; H, 7.3. Found: C, 59.9; H 7.2.

Further elution of the column gave the positional isomer of **8** (60 mg, 0.17 mmol, 7%). ^{1}H-NMR ($CDCl_3$): δ 1.27 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.2 Hz), 1.32 (d, 3H, H-6, $J_{6,5}$ 5.9 Hz), 2.16 (s, 3H, CH_3 Ac), 2.61 (AB, 2H CH_2 SEt), 3.39 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.2 Hz), 3.41 (s, 3H, CH_3 Me), 3.60 (dd, 1H, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.2 Hz) 4.09 (dq, 1H, H-5, $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.4 Hz), 4.75 (AB, 2H, CH_2 Bn), 5.18 (d, 1H, H-1, $J_{1,2}$ 1.3 Hz), 5.38 (dd, 1H, H-2, $J_{2,1}$ 1.5 Hz, $J_{2,3}$ 3.1 Hz), 7.30-7.38 (m, 5H, CH-arom.).

Ethyl 3-*O*-(*p*-methoxybenzyl)-2-*O*-methyl-1-thio-ß-L-fucopyranoside (11). - A mixture of dibutyltin oxide (1.37 g, 5.5 mmol) and ethyl 2-*O*-methyl-1-thio-β-L-fucopyranoside (**10**, 1.11 g, 5 mmol) in dry methanol (30 ml) was heated under reflux for 1.5 h. The reaction mixture was concentrated, coevaporated with dry toluene and redissolved in dry *N,N*-dimethylformamide (55 ml). CsF (988 mg, 6.5 mmol), NaI (75 mg, 0.5 mmol) and *p*-methoxybenzyl bromide (1.0 ml, 7.38 mmol) were added and the mixture was stirred for 18 h. The solvent was evaporated and the residue was redissolved in CH_2Cl_2 (50 ml), extracted with 1M KF (50 ml), H_2O (40 ml). The organic layer was dried ($MgSO_4$), concentrated to give, after column chromatography on silica gel (ethyl acetate in light petroleum ether (0→40%)), homogeneous **11** (1.35 g, 4.0 mmol). ^{1}H-NMR ($CDCl_3$): δ 1.29 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.7 Hz), 1.31 (d, 3H, H-6, $J_{6,5}$ 6.4 Hz), 2.68 (br s, 1H, OH), 2.73 (dq, 2H, CH_2 SEt), 3.29 (t, 1H, H-2, $J_{2,1}\approx J_{2,3}$ 9.1 Hz), 3.39-3.52 (m, 2H, H-3, H-5), 3.61 (s, 3H, CH_3 Me), 3.80 (s, 3H, OCH_3 pMBn), 4.28 (d, 1H, H-1, $J_{1,2}$ 9.5 Hz), 6.86-6.90 (m, 2H,

CH arom.), 7.28-7.32 (m, 2H, CH arom.); ^{13}C-NMR ($CDCl_3$): δ 14.4 (CH_3 SEt), 16.1 (C-6), 23,9 (CH_2 SEt), 54,5 (CH_3 Me), 60.4 (CH_3 Me), 68.8 (C-5), 71.0 (CH_2 pMBn), 73.5, 78.8, 81.7 (C-2, C-3, C-4), 83.9 (C-1), 113.2, 128.8 (CH arom.), 129.5 (*i*-qC arom.), 158.7 (*p*-qC arom.).

Ethyl 4-*O*-acetyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-methyl-1-thio-ß-L-fucopyranoside (12). - To a solution of compound **11** (1.35 g, 4.0 mmol) in pyridine (12.5 ml) was added acetic anhydride (0.57 ml, 6 mmol) and DMAP (0.4 mmol). After stirring for 1.5 h, the solvent was evaporated and the residual oil was purified by column chromatography. Elution of the column was effected with ethyl acetate in light petroleum ether (0→30%). Concentration of the appropriate fractions gave **12** (1.35 g, 3.52 mmol), $[\alpha]_D$ -12.2° (c 1). ^{1}H-NMR ($CDCl_3$): δ 1.20 (d, 3H, H-6, $J_{6,5}$ 6.4 Hz), 1.30 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.4 Hz), 2.16 (s, 3H, CH_3 Ac), 2.73 (AB, 2H, CH_2 SEt), 3.26 (t, 1H, H-2, $J_{2,1}\approx J_{2,3}$ 9.4 Hz), 3.50 (dd, 1H, H-3, $J_{3,2}$ 9.1 Hz, $J_{3,4}$ 3.5 Hz), 3.60 (s, 3H, CH_3 Me), 3.59-3.64 (m, 1H, H-5), 3.80 (s, 3H, CH_3 pMBn), 4.34 (d, 1H, H-1, $J_{1,2}$ 9.8 Hz), 4.56 (AB, 2H, CH_2 pMBn), 5.33, (d, 1H, H-4, $J_{4,3}$ 3.6 Hz, $J_{4,5}$ 1.0 Hz); ^{13} C-NMR ($CDCl_3$): δ 14.3 (CH_3 SEt), 16.1 (C-6), 20.3 (CH_3 Ac), 24.1 (CH_2 SEt), 54.5 (CH_3 pMnB), 60.6 (CH_3 Me), 69.2 (C-5), 70.7 (CH_2 pMBn), 72.2, 78.7, 80.0 (C-2, C-3, C-4), 84.1 (C-1), 113.1, 128.9 (CH arom.), 129.5 (*i*-qC arom.), 158.6 (*p*-qC arom.), 170.1 (qC Ac).

Anal. Calc. for $C_{19}H_{28}O_6S$: C, 59.4; H, 7.3. Found: C, 59.3; H, 7.3.

Ethyl 4-*O*-acetyl-2-*O*-methyl-1-thio-β-L-fucopyranoside (15). - Compound **13** (711 mg, 3 mmol) was dissolved in dry *N,N*-dimethylformamide (12 ml) and trimethyl orthoacetate (0.76 ml, 6 mmol) and camphorsulfonic acid monohydrate (75 mg, 0.3 mmol) were added. After 50 min at 20°C, the reaction mixture containing the 3,4-*O*-methoxyethylidene acetal derivative **14** was cooled to 0°C and NaH (116 mg, 4.8 mmol) was added, followed by methyl iodide (0.25 ml, 3.9 mmol). The mixture was allowed to warm to room temperature and stirred for 1.5 h. Excess NaH was quenched with methanol and the reaction mixture was diluted with diethyl ether (10 ml). The solution was washed with H_2O (10 ml), $NaHCO_3$ (10%, 10 ml), dried ($MgSO_4$) and concentrated. The residual oil was redissolved in a mixture of acetic acid-water (9:1, 10 ml) and stirred for 15 min. The reaction mixture was diluted with dichloromethane (15 ml) and subsequently washed with H_2O (10 ml), $NaHCO_3$ (10%, 10 ml), dried ($MgSO_4$) and concentrated. Purification of the residue by column chromatography on silica gel using ethyl acetate in light petroleum ether (0→50%) gave **15** (507 mg, 1.92 mmol). ^{1}H-NMR ($CDCl_3$): δ 1.20 (d, 3H, H-6, $J_{6,5}$ 6.4 Hz), 1.32 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.4 Hz), 2.18 (s, 3H, CH_3 Ac), 2.76 (AB, 2H, CH_2 SEt), 3.21 (t, 1H, H-2, $J_{2,1}\approx J_{2,3}$ 9.4 Hz), 3.34 (s, 3H, CH_3 Me), 3.68-3.80 (m, 2H, H-3, H-5), 4.36 (d, 1H, H-1, $J_{1,2}$ 9.8 Hz), 5.20 (d, 1H, H-4, $J_{4,3}$ 3.6 Hz); ^{13}C-NMR ($CDCl_3$): δ 14.3 (CH_3 SEt), 16.0 (C-6), 20.3 (CH_3 Ac), 24.2 (CH_2 SEt), 60.5 (CH_3 Me), 72.4 (C-5), 72.6 , 72.8, 79.8 (C-2, C-3, C-4), 83.9 (C-1), 170.3 (qC Ac).

Ethyl 4-*O*-acetyl-3-*O*-chloroacetyl-2-*O*-methyl-1-thio-β-L-fucopyranoside (16). - To a stirred solution of **15** (507 mg, 1.92 mmol) in *N,N*-dimethylformamide (8 ml) was added chloroacetic anhydride (658 mg, 3.85 mmol) and sodium hydrogen carbonate (580 mg, 6.9 mmol). After stirring for 28 h, the reaction mixture was concentrated and redissolved in dichloromethane (20 ml), washed with H_2O (15 ml, 2x), $NaHCO_3$ (10% aq., 15 ml), dried ($MgSO_4$), concentrated and purified on a silica gel column which was eluted with ethyl acetate in light petroleum ether (0→10%) to give **16** (450 mg, 1.32 mmol), $[\alpha]_D$ -18.0 (c 1). ^{1}H-NMR ($CDCl_3$): δ 1.21 (d, 3H, H-6, $J_{6,5}$ 6.4 Hz), 1.33 (t, 3H, CH_3 SEt, $J_{H,H}$ 7.5 Hz), 2.17 (s, 3H, CH_3 Ac), 2.78 (AB, 2H, CH_2 SEt), 3.38 (t, 1H, H-2, $J_{2,1}\approx J_{2,3}$ 9.6 Hz), 3.54 (s, 3H, CH_3 Me), 3.78 (q, 1H, H-5, $J_{5,6}$ 6.2), 4.04 (s, 2H, CH_2 CaCl), 4.44 (d, 1H, H-1, $J_{1,2}$ 9.8 Hz), 4.99 (dd, 1H, H-3, $J_{2,3}$ 9.8 Hz, $J_{3,4}$ 3.3 Hz), 5.25 (d, 1H, H-4, $J_{4,3}$ 3.3 Hz); ^{13}C-NMR ($CDCl_3$): δ 14.4 (CH_3 SEt), 15.8 (C-6), 20.1 (CH_3 Ac), 24.4 (CH_2 SEt), 40.2 (CH_2 AcCl), 60.5 (CH_3 Me), 70.0, (C-5), 72.0, 75.8, 76.8 (C-2, C-3, C-4), 84.1 (C-1),

165.9 (qC AcCl), 170.3 (qC Ac).

Anal. Calc. for $C_{19}H_{21}O_6SCl$: C, 45.8; H, 6.2. Found: C, 45.7; H, 6.1.

4-[2-(Benzyloxycarbonylamino)ethyl]phenol (17). - To a solution of tyramine (3.43 gr, 25 mmol) in 2N NaOH/H_2O (15.3 ml) was added at once benzyloxycarbonyl chloride (7.1 ml, 50 mmol) and 2N NaOH (15.3 ml). The mixture was stirred for 18 h, the solid was filtered and redissolved in 98% ethanol (300 ml) and 1N NaOH (100 ml) was added. The reaction mixture was stirred until TLC analysis (5:95 MeOH:CH_2Cl_2) showed complete conversion. The solution was neutralized with aqueous acetic acid, concentrated and redissolved in dichloromethane. The sodium salts were filtered and the filtrate was concentrated to give **17** as a white solid (4.34 g, 16 mmol). ^{13}C-NMR (disubstituted, $CDCl_3$): δ 39.0, 45.0 (2x CH_2), 70.2, 74.1 (2x CH_2 Bn), 124.8, 131.6, 131.8, 132.2, 132.4, 133.6 (CH arom.), 140.8, 153.4, 160.8 (qC arom.). ^{13}C-NMR ($CDCl_3$) of **17**: δ 34.3, 41.8 (2x CH_2), 65.8 (CH_2 Bn), 114.7, 127.1, 127.3, 127.7, 129.0 (CH arom.), 154.6, 156.4 (qC arom.).

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 3-*O*-acetyl-2,4-di-*O*-methyl-α-L-rhamnopyranoside (18). - To a stirred solution of ethyl 3-*O*-acetyl-2,4-di-*O*-methyl-1-thio-α-L-rhamnopyranoside **5** (334 mg, 1.2 mmol), aglycon **17** (271 mg, 1 mmol) and powdered molecular sieves 4Å in a mixture of 1,2-dichloroethane:diethyl ether (1:1, 8 ml) was added a solution of NIS (225 mg, 1 mmol) and TfOH (10 µl, 0.11 mmol), in 1,2-dichloroethane:diethyl ether (1:1, 8 ml). After stirring for 30 min at 20°C, the reaction mixture was filtered, diluted with dichloromethane (20 ml), extracted with NaS_2O_3 (20%, 15 ml) and $NaHCO_3$ (10%, 10 ml), dried ($MgSO_4$) and concentrated. The residual oil was purified by silica gel column chromatography, using a 0 to 40 gradient of ethyl acetate in light petroleum ether, to afford pure **18** (370 mg, 0.76 mmol), $[\alpha]_D$ -45.4° (c 1). ^{1}H-NMR ($CDCl_3$): δ 1.28 (d, 3H, CH_3, $J_{6,5}$ 6.2 Hz), 2.18 (s, 3H, CH_3), 2.74 (q, 2H, CH_2 spacer, $J_{H,H}\approx J_{H,NH}$ 7.5 Hz), 3.32 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.6 Hz), 3.42 (t, 2H, CH_2 spacer, $J_{H,H}$ 5.9 Hz), 3.50 (s, 6H, 2x CH_3 Me), 3.77 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 3.81 (dd, 1H, H-2, $J_{2,1}$ 2.0 Hz, $J_{2,3}$ 3.4 Hz, 4.80 (br s, 1H, NH), 5.09 (s, 2H, CH_2 Z), 5.32 (dd, 1H, H-3, $J_{3,2}$ 3.4 Hz, $J_{3,4}$ 9.6 Hz), 5.45 (d, 1H, H-1, $J_{1,2}$.0 Hz) 6.98-7.12 (m, 4H, CH arom.), 7.34 (s, 5H, CH arom.); ^{13}C-NMR ($CDCl_3$): δ 17.5 (C-6), 20.8 (CH_3 Ac), 34.8, 42.0 (2x CH_2-spacer), 59.0 60.1 (2x CH_3 Me), 66.1 (CH_2 Z), 68.0 (C-5), 73.0, 78.0, 80.0 (C-2, C-3, C-4), 95.0 (C-1), 115.1, 116.1, 127.6, 128.0, 129.4 (CH arom.), 132.2, 154.5, 155.0 (qC arom.), 156.2 (C=O Z), 170.0 (qC Ac).

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-α-L-rhamnopyranoside (19). - Potassium *tert*-butoxide (9 mg, 0.08 mmol) was added to a solution of compound **18** (370 mg, 0.76 mmol) in dry methanol (4 ml). The reaction mixture was stirred for 1 h, neutralized by Dowex (W50, H^+ form), filtered, concentrated and coevaporated by toluene to give crude **19**. Purification was performed by column chromatography on silica gel (ethyl acetate in light petroleum ether (10→50%)) to afford **19** (304 mg, 0.68 mmol), $[\alpha]_D$ -47.2° (c 1). ^{1}H-NMR ($CDCl_3$), δ 1.27 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 2.76 (t, 2H, CH_2 spacer, $J_{H,H}$ 7.0 Hz), 3.05 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.4 Hz), 3.43 (q, 2H, CH_2 spacer, $J_{H,H}\approx J_{H,NH}$ 6.51 Hz), 3.54, 3.59 (2x s, 3H, CH_3 Me), 3.65 (dd, 1H, H-2, $J_{2,1}$ 3.7 Hz, $J_{2,3}$.7 Hz), 3.68 (dq, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.0 Hz) 4.03 (dd, 1H, H-3, $J_{3,2}$ 3.7 Hz, $J_{3,4}$ 9.4 Hz), 4.79 (br s, 1H, NH), 5.09 (s, 2H, CH_2 Z), 5.50 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 6.7-7.34 (m, 9H, CH-aromaten); ^{13}C-NMR ($CDCl_3$): δ 17.6 (C-6), 34.8, 42.0 (2x CH_2 spacer), 58.7, 60.5 (2x CH_3 Me), 66.2 (CH_2 Z), 67.7 (C-5), 70.6, 80.2, 83.1 (C-2, C-3, C-4), 94.4 (C-1, $^1J_{C,H}$ 168.5 Hz), 115.2, 116.1, 127.7, 128.1, 129.4 (CH-arom.), 132.2, 136.2, 154.7 (qC arom.), 156.2 (C=O Z).

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 3-*O*-(3-*O*-acetyl-4-*O*-benzyl-2-*O*-methyl-α-L-rhamnopyranosyl)-2,4-di-*O*-methyl-α-L-rhamnopyranoside (20). - To a cooled (-30°C) solution of thioglycoside **19** (425

mg, 1.2 mmol), aglycon **8** (445 mg, 1.0 mmol) and activated molecular sieves 4Å in 1,2-dichloroethane:diethyl ether (1:1, 8ml), was added a solution of NIS (270 mg, 1.2 mmol) and TfOH (9 µl, 0.11 mmol) in 1,2-dichloroethane:diethyl ether (1:1, 8ml). After stirring for 15 min, the reaction mixture was filtered, diluted with dichloromethane (20 ml), washed with NaS_2O_3 (20%, 15 ml) and $NaHCO_3$ (10% aq, 10 ml), dried ($MgSO_4$) and concentrated. Column chromatography (ethyl acetate in light petroleum ether (0→30%)) of the crude mixture gave the α-linked disaccharide **20** (575 mg, 0.78 mmol). ^{1}H-NMR ($CDCl_3$): δ 1.26 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 1.36 (d, 3H, H-6', $J_{6,5}$ 6.2 Hz), 2.07 (s, 3H, CH_3 Ac), 2.76 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.9 Hz), 3.26 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ 9.6 Hz), 3.42 (q, 2H, CH_2 spacer, $J_{H,H}$≈$J_{H,NH}$ 6.6 Hz), 3.48, 3.52, 3.57 (3x s, 3H, CH_3 Me), 3.59 (t, 1H, H-4', $J_{4,3}$≈$J_{4,5}$ 9.5 Hz), 3.66 (dq, 1H, H-5, $J_{5,4}$ 9.6 Hz, $J_{5,6}$ 6.3 Hz), 3.70 (dd, 1H, H-2, $J_{2,1}$ 2.0 Hz, $J_{2,3}$ 3.2 Hz), 3.77 (dd, 1H, H-2', $J_{2,1}$ 2.0 Hz, $J_{2,3}$ 3.3 Hz), 4.00 (dq, 1H, H-5', $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.2 Hz), 4.09 (dd, 1H, H-3, $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.6 Hz), 4.70 (AB, 2H, CH_2 Bn), 5.09 (s, 2H, CH_2 Z), 5.14 (d, 1H, H-1', $J_{1,2}$ 2.1 Hz), 5.29 (dd, 1H, H-3', $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.5 Hz), 5.45 (d, 1H, H-1, $J_{1,2}$ 1.9 Hz), 7.02 (AB, 4H, CH arom.), 7.32-7.34 (m, 10H, CH arom.); ^{13}C-NMR ($CDCl_3$): δ 17.6, 18.0 (C-6, C-6'), 21.0 (CH_3 Ac), 35.0 , 42.1 (CH_2 spacer), 58.8, 58.9, 60.9 (3x CH_3 Me), 66.3 (CH_2 Z), 68.2, 68.7, 73.5, 78.8, 78.9, 79.1, 79.9, 81.8 (C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5'), 74.8 (CH_2 Bn), 95.0 (C-1, $^1J_{C,H}$ 168.5), 99.0 (C-1', $^1J_{C,H}$ 170.9), 116.3, 127.5, 127.5, 127.9, 128.2, 128.3, 129.6 (CH arom.), 132.2, 138.1, 154.9, 156.1 (qC arom.) 156.1 (C=O Z), 170.2 (qC Ac).

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 3-*O*-(4-*O*-benzyl-2-*O*-methyl-α-L-rhamnopyranosyl)-2,4-di-*O*-methyl-α-L-rhamnopyranoside (21). - Disaccharide **20** (575 mg, 0.78 mmol) was dissolved in dry methanol (5 ml) and potassium *tert*-butoxide (9 mg, 0.08 mmol) was added. After stirring for 4 h, TLC analysis showed complete conversion. The reaction mixture was neutralized by Dowex (W50, H^+ form), concentrated and coevaporated with toluene. The crude product was purified by column chromatography on silica gel with ethyl acetate in light petroleum ether (0→40%), to give **21** in 93% yield (504 mg, 0.70 mmol), $[\alpha]_D$ -90.8° (c 1). ^{1}H-NMR ($CDCl_3$): δ 1.26 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 1.36 (d, 3H, H-6', $J_{6,5}$ 6.2 Hz), 2.46 (d, 1H, OH, $J_{HO,H}$ 9.0 Hz), 2.76 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.8 Hz), 3.25 (t, 1H, H-4, $J_{4,3}$≈$J_{4,5}$ 9.7 Hz), 3.31 (t, 1H, H-4', $J_{4,3}$≈$J_{4,5}$ 9.7 Hz), 3.42 (q, 2H, CH_2 spacer, $J_{H,H}$≈$J_{H,NH}$ 6.7 Hz), 3.51, 3.52, 3.54 (3x s, 3H, CH_3 Me), 3.61 (dd, 1H, H-2', $J_{2,1}$ 1.6 Hz, $J_{2,3}$3.8 Hz), 3.65 (dd, 1H, H-2, $J_{2,1}$ 1.9 Hz, $J_{2,3}$.2 Hz), 3.67 (dd, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$.3 Hz), 3.87 (dq, 1H, H-5', $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 4.01 (dt, 1H, H-3', $J_{3,2}$ 3.7 Hz, $J_{3,4}$ 9.3 Hz $J_{3,HO}$ 9.2 Hz), 4.13 (dd, 1H, H-3, $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.7 Hz), 4.81 (AB, 2H, CH_2 Bn), 4.77 (br s, 1H, NH), 5.09 (s, 2H, CH_2 Z), 5.23 (d, 1H, H-1', $J_{1,2}$ 1.5 Hz), 5.45 (d, 1H, H-1, $J_{1,2}$ 1.9 Hz), 7.07 (AB, 4H, CH arom.), 7.30-7.40 (m, 10H, CH arom.); ^{13}C-NMR ($CDCl_3$): δ 17.5, 17.8 (C-6, C-6'), 34.8, 42.0 (CH_2 spacer), 58.3, 58.8, 60.6 (3x CH_3 Me), 66.1 (CH_2 Z), 67.5, 68.5, 71.0, 77.8, 79.8, 80.9, 81.6, 82.0 (C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5'), 74.63 (CH_2 Bn), 95.0 (C-1), 98.0 (C-1'), 116.1, 127.3, 127.6, 128.0, 128.0, 129.4 (CH arom.), 132.2, 136.3, 138.1, 154.6 (qC arom.), 156.0 (C=O Z).

4-[2-(Benzyloxycarbonylamino)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 (22 α/β).

a) Activation with IDCP: To a stirred mixture of thioglycosyl donor **12** (86 mg, 0.22 mmol), acceptor **21** (130 mg, 0.19 mmol) and activated molecular sieves 4Å in diethyl ether:1,2-dichloroethane (5:1, 4 ml) was added iodonium dicollidine perchlorate (187 mg, 0.40 mmol). After stirring for 2 h, the reaction mixture was filtered, diluted with dichloromethane, washed with $Na_2S_2O_3$ (20%, 10 ml) and $NaHCO_3$ (10%, 7 ml), dried ($MgSO_4$) and concentrated. The oily residue was successively purified by column chromatography on silica gel with ethyl acetate in light petroleum ether (0→30%) and gel filtration over a Sephadex LH-20 column which was eluted with 1:1 dichloromethane:methanol. The product **22** was isolated as an anomeric

mixture α:β = 6:1 (140 mg. 0.14 mmol).

b) Activation with NIS/TfOH: To a cooled (0°C) mixture of donor **12** (92 mg, 0.24 mmol), acceptor **21** (140 mg, 0.20 mmol), powdered molecular sieves 4Å in diethyl ether:1,2-dichloroethane (1:1, 1.5 ml) was added a mixture of NIS (55 mg, 0.24 mmol), TfOH (3 μl, 0.03 mmol) in 1.5 ml of the same solvent mixture. After stirring for 1 h, the reaction mixture was neutralized, filtered and diluted with dichloromethane (15 ml). The filtrate was washed with $Na_2S_2O_3$ (20%, 12 ml) and $NaHCO_3$ (10%, 10 ml), dried ($MgSO_4$) and concentrated. The residual oil was purified on a Sephadex LH-20 column by elution with methanol-dichloromethane (1:1). After concentration of the appropriate fractions, the trisaccharide **22** was obtained as an anomeric mixture (α:β=3:1, 148 mg, 0.14 mmol). ^{13}C-NMR ($CDCl_3$) of **22α**; δ 94.8 (C-1, $^1J_{C,H}$ 170.0 Hz), 98.2, 99.7 (C-1', C-1'', $^1J_{C,H}$ 168.5, 167.05 Hz).

The reaction was also performed at -40°C to give **22** as an anomeric mixture (α:β=1:3). ^{13}C-NMR ($CDCl_3$) of **22β**; δ 94.8 (C-1, $^1J_{C,H}$ 170.0 Hz), 99.2 (C-1', $^1J_{C,H}$ 168.5 Hz), 101.3 (C-1'', $^1J_{C,H}$ 149.5 Hz).

4-[2-(Benzyloxycarbonylamino)ethyl]phenyl 2,4-di-*O*-methyl-3-*O*-[4-*O*-benzyl-2-*O*-methyl-3-*O*-(4-*O*-acetyl-3-*O*-chloroacetyl-2-*O*-methyl-α/β-L-fucopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranoside (23 α/β). - A mixture of donor **16** (104 mg, 0.31 mmol), disaccharide **21** (173 mg, 0.25 mmol) and activated molecular sieves 4Å in 1,2-dichloroethane:diethyl ether (1:1, 2 ml) was stirred at -30°C for 30 min. A solution of NIS (60 mg, 0.27 mmol) and TfOH (3 μl, 0.03 mmol) in the same solvent mixture (2 ml) was added. After stirring for 90 min, the mixture was filtered and diluted with dichloromethane (5 ml). The filtrate was washed with $Na_2S_2O_3$ (20%, 10 ml) and $NaHCO_3$ (10%, 7 ml), dried ($MgSO_4$) and concentrated. The residue was purified using a column of silica gel, which was eluted with ethyl acetate in light petroleum ether (0→50%), to give **23** as an anomeric mixture α:β = 1:1 (185 mg, 0.19 mmol). ^{13}C-NMR ($CDCl_3$): δ 15.8, 17.5, 17.8 (C-6, C-6', C-6''), 20.3 (CH_3 Ac), 29.2, 34.9, 40.3, 40.4 (CH_2 spacer/AcCl), 57.4, 58.3, 58.5, 60.5, 60.8 (CH_3 Me), 64.4, 68.0, 68.3, 70.1, 70.8, 71.8, 75.1, 77.4, 78.0, 78.4, 79.2, 79.8, 80.3, 81.7, 81.9 (C-H), 66.1 CH_2 Z), 74.6 (CH_2 Bn), 94.5 (C-1), 98.8, 99.2, 100.6 (C-1', C-1''), 116.3, 127.0, 127.2, 127.7, 127.8, 128.0, 128.1, 129.5 (CH arom.), 132.3, 138.5, 138.7, 154.7 (qC arom.), 156.0 (C=O Z), 166.3 qC AcCl), 170.4 (qC Ac).

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-α,β-L-fucopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranoside (24α, 24β).

Method A): The anomeric mixture of trisaccharide **22** (140 mg, 0.14 mmol) was dissolved in dichloromethane-water (8:1, 0.63 ml) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (54 mg, 0.24 mmol) was added. After stirring for 1 h, the reaction mixture was filtered over a pad of hyflo and the filtrate was diluted with dichloromethane (10 ml). The filtrate was washed with H_2O (10 ml), $NaHCO_3$ (10% aq, 10 ml), dried ($MgSO_4$) and concentrated. The residue was purified by silica gel column chromatography and elution was effected with ethyl acetate in light petroleum ether (20-60%) to give the two anomers in 75% yield (**24α** 99 mg, 0.09 mmol; **24β**, 14 mg, 0.02 mmol).

Method B): Trisaccharide **23** (α/β=1/1, 185 mg, 0.19 mmol) was dissolved in a mixture of HOAc-lutidine (3:1, 1.6 ml) and a freshly prepared hydrazine dithiocarbonate solution (HDTC, 1.4 ml) was added dropwise. After stirring for 20 h, TLC analysis (3:1 ethyl acetate:light petroleum ether) showed complete conversion of the starting material. The reaction mixture was diluted with dichloromethane (8 ml), washed with H_2O (5 ml, 2x) and $NaHCO_3$ (5 ml), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography with ethyl acetate in light petroleum ether (20→60%) to afford **24α** (69 mg, 0.08 mmol) and **24β** (63 mg, 0.07 mmol).

24α: $[\alpha]_D$ -113.8° (c 1); ^{1}H-NMR ($CDCl_3$) of **24α**: δ 1.15 (d, 3H, H-6'', $J_{6,5}$ 6.6 Hz), 1.27 (d, 3H, H-6/H-6', $J_{6,5}$ 6.6 Hz), 1.32 (d, 3H, H-6/H-6', $J_{6,5}$ 6.2 Hz), 2.18 (s, 3H, CH_3 Ac), 2.76 (br s, 1H, OH), 2.76 (t,

2H, CH_2 spacer, $J_{H,H}$ 6.9 Hz), 3.22 (t, 1H, H-4/H-4', $J_{4,3}\approx J_{4,5}$ 9.6 Hz), 3.31 (s, 3H, CH_3 Me), 3.41 (q, 2H, CH_2 spacer, $J_{H,H}\approx J_{H,NH}$ 6.4 Hz), 3.47 (dd, 1H, H-3'', $J_{3,2}$ 10.3 Hz, $J_{3,4}$ 3.4 Hz), 3.48 (s, 3H, CH_3 Me), 3.51 (t, 1H, H-4/H-4', $J_{4,3}\approx J_{4,5}$ 9.5 Hz), 3.51 (s, 3H, CH_3 Me), 3.52 (dd, 1H, H-2'', $J_{2,1}$ 2.5 Hz, $J_{2,3}$ 9.0 Hz), 3.55 (s, 3H, CH_3 Me), 3.67 (dq, 1H, H-5/H-5', $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.0 Hz), 3.73 (dd, 1H, H-2, $J_{2,1}$ 1.8 Hz, $J_{2,3}$ 3.4 Hz), 3.74 (dd, 1H, H-2, $J_{2,1}$ 1.8 Hz, $J_{2,3}$ 4.0 Hz), 3.95 (dq, 1H, H-5, $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.2 Hz), 4.03 (dd, 1H, H-3/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, $J_{3,4}$ 9.7 Hz), 4.25 (d, 1H, H-3'', $J_{3,2}$ 10.2 Hz, $J_{3,4}$ 3.6 Hz), 4.35 (dq, 1H, H-5'', $J_{5,4}$ 1.3 Hz, $J_{5,6}$ 6.6 Hz), 4.79 (t, 1H, NH, $J_{NH,H}$ 5.5 Hz), 4.86 (AB, 2H, CH_2 Bn), 5.09 (s, 2H, CH_2 Z), 5.12 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 5.25 (d, 1H, H-1'', $J_{1,2}$ 3.6 Hz), 5.29 (dd, 1H, H-4'', $J_{4,3}$ 3.6 Hz, $J_{4,5}$ 1.1 Hz), 5.47 (d, 1H, H-1, $J_{1,2}$ 1.9 Hz), 7.04 (AB, 4H, CH arom.), 7.26-7.34 (m, 10H, CH arom.); ^{13}C-NMR ($CDCl_3$) of **24α**: δ 16.2, 17.6, 18.0 (C-6, C-6', C-6''), 20.6 (CH_3 Ac), 35.0, 42.1 (2x CH_2 spacer), 57.4, 57.9, 58.6, 60.9 (4x CH_3 Me), 66.28 (CH_2 Z), 64.9, 67.6, 68.4, 68.5, 73.0, 78.1, 79.1, 79.5, 79.9, 80.4, 81.0, 81.7, (C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5', C-2'', C-3'', C-4'', C-5''), 74.6 (CH_2 Bn), 94.7 (C-1, $^1J_{C,H}$ 170.0 Hz), 98.1 (C-1'', $^1J_{C,H}$ 168.5 Hz), 99.0 (C-1', $^1J_{C,H}$ 168.5 Hz), 116.2, 127.1, 127.2, 127.8, 127.9, 128.2, 129.5 (CH arom.), 132.3, 136.4, 138.7, 154.8 (qC arom.), 156.1 (C=O Z), 170.8 (qC Ac).

24β: $[\alpha]_D$ -50.0° (c 1); ^{1}H-NMR ($CDCl_3$) of **24β**: δ 1.15 (d, 3H, H-6/H-6'/H-6'', $J_{6,5}$ 6.4 Hz), 1.27 (d, 3H, H-6/H-6'/H-6'', $J_{6,5}$ 6.1 Hz), 1.37 (d, 3H, H-6/H-6'/H-6'', $J_{6,5}$ 6.2 Hz), 2.16 (s, 3H, CH_3 Ac), 2.53 (br s, 1H, OH), 2.76 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.8 Hz), 3.24 (t, 1H, H-4/H-4', $J_{4,3}\approx J_{4,5}$ 9.6 Hz), 3.26 (dd, 1H, H-2'', $J_{2,1}$ 7.6 Hz, $J_{2,3}$ 9.7 Hz), 3.42 (q, 2H, CH_2 spacer, $J_{H,H}\approx J_{H,NH}$ 6.6 Hz), 3.49, 3.53 (2x s, 3H, CH_3 Me), 3.54 (t, 1H, H-4/H-4', $J_{4,3}\approx J_{4,5}$ 9.3 Hz), 3.55 (s, 3H, CH_3 Me), 3.65-3.70 (m, 4H, H-2, H-2', H-5/H-5', H-5''), 3.71 (s, 3H, CH_3 Me), 3.74 (ddd, 1H, H-3'', $J_{3,2}$ 9.7 Hz, $J_{3,4}$ 3.4 Hz, $J_{3,OH}$ 1.4 Hz), 3.89 (dq, 1H, H-5/H-5', $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.2 Hz), 4.14 (dd, 1H, H-3/H-3', $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.7 Hz), 4.28 (dd, 1H, H-3/H-3', $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.1 Hz), 4.46 (d, 1H, H-1'', $J_{1,2}$ 7.6 Hz), 4.78 (br t, 1H, NH, $J_{NH,H}$ 6.2 Hz), 4.82 (AB, 2H, CH_2 Bn), 5.09 (s, 2H, CH_2 Z), 5.18 (dd, 1H, H-4'', $J_{4,3}$ 3.6 Hz, $J_{4,5}$ 1.0 Hz) 5.23 (d, 1H, H-1, $J_{1,2}$ 2.0 Hz), 5.46 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 7.04 (AB, 4H, CH arom.), 7.26-7.34 (m, 10H, CH arom.); ^{13}C-NMR ($CDCl_3$) of **24β**: δ 16.2, 17.7, 18.0 (C-6, C-6', C-6''), 20.6 (CH_3 Ac), 35.0, 42.1 (2x CH_2 spacer), 58.4, 58.8, 60.6, 60.7 (4x CH_3 Me), 66.4 (CH_2 Bn), 68.6, 68.1, 68.6, 69.0, 72.0, 72.3, 76.9, 77.9, 79.0, 80.0, 81.0, 82.2 (C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5', C-2'', C-3'', C-4'', C-5''), 74.6 (CH_2 Bn, Z), 94.9 (C-1, $^1J_{C,H}$ 168.5 Hz) 98.9 (C-1', $^1J_{C,H}$ 174.4 Hz), 100.6 (C-1'', $^1J_{C,H}$ 158.3 Hz), 116.3, 127.1, 127.4, 128.3, 129.6 (CH arom.), 132.3, 138.7, 154.9 (qC arom.), 156.1 (C=O Z), 171.0 (qC Ac).

4-(aminoethyl)phenyl 2,4-di-*O*-Me-3-*O*-[2-*O*-methyl-3-*O*-(4-*O*-acetyl-2-*O*-methyl-α-L-fucopyranosyl)-α-L-rhamnopyranosyl]-α-L-rhamnopyranoside (2). - Trisaccharide **24α** (90 mg, 0.1 mmol) was dissolved in a mixture of 2-propanol-water-acetic acid (10:5:2, 10 ml), and hydrogenated in the presence of palladium on charcoal for 18 h. The reaction mixture was filtered and concentrated to give homogeneous **2** (60 mg, 0.08 mmol). ^{1}H-NMR ($CDCl_3$): δ 1.10 (d, 3H, H-6'', $J_{6,5}$ 6.6 Hz), 1.23 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 1.33 (d, 3H, H-6', $J_{6,5}$ 6.2 Hz), 2.17 (s, 3H, CH_3 Ac), 2.92 (t, 2H, CH_2 spacer, $J_{H,H}$ 7.6 Hz), 3.13 (t, 2H, CH_2 spacer, J_{HH} 7.8 Hz), 3.25 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.6 Hz), 3.36, 3.50 (2x s, 3H, CH_3 Me), 3.51 (dd, 1H, H-2'', $J_{2,1}$ 3.5 Hz, $J_{2,3}$ 10.0 Hz), 3.54 (s, 3H, CH_3 Me), 3.55 (t, 1H, H-4', $J_{4,3}\approx J_{4,5}$ 9.8 Hz), 3.63 (dq, 1H, H-5, $J_{5,4}$ 9.8 Hz, $J_{5,6}$.6 Hz), 3.68 (dd, 1H, H-2', $J_{2,1}$ 1.8 Hz, $J_{2,3}$ 3.2 Hz), 3.77 (dd, 1H, H-2, $J_{2,1}$ 2.2 Hz, $J_{2,3}$ 3.0 Hz), 3.86 (dq, 1H, H-5', $J_{5,4}$ 9.3 Hz, $J_{5,6}$ 6.3 Hz), 3.90 (dd, 1H, H-3', $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.7 Hz), 3.26 (dd, 1H, H-3, $J_{3,2}$ 3.5 Hz, $J_{3,4}$ 9.3 Hz), 4.09 (dd, 1H, H-3'', $J_{3,2}$ 10.4 Hz, $J_{3,4}$ 3.7 Hz), 4.26 (q, 1H, H-5'', $J_{5,6}$ 6.8 Hz), 5.18 (d, 1H, H-1', $J_{1,2}$ 1.6 Hz), 5.21 (d, 1H, H-4'', $J_{4,3}$ 4.3 Hz), 5.33 (dd, 1H, H-1'', $J_{1,2}$ 3.8 Hz), 5.59 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 7.16 (AB, 4H, CH arom.); ^{13}C-NMR ($CDCl_3$): δ 15.4, 16.8, 16.8 (C-6, C-6', C-6''), 19.7 (CH_3 Ac), 32.1, 40.2 (2x CH_2 spacer), 57.2, 57.6, 58.0, 60.2 (4x CH_3 Me), 64.8, 66.8, 68.2, 68.7, 70.8, 73.5, 78.0, 78.4, 79.5, 80.0 (2x), 81.5 (C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5', C-2'', C-3'' C-4'', C-

5''), 94.2 (C-1), 98.1, 98.8 (C-1', C-1''), 116.2, 129.2 (CH arom.), 130.0 (*p*-qC arom.), 154.7 (*i*-qC arom.). 171.3 (qC Ac); FAB(+)MS: [M+H$^+$] for $C_{32}H_{32}NO_{14}$: m/z 674.42.

Phenyl 2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (26). - Phenyl 1-thio-α-L-rhamnopyranoside (**25**, 1.48 g, 5 mmol) was dissolved in a mixture of acetone (5 ml) and 2,2-dimethoxypropane (6 ml) and TsOH (95 mg, 0.5 mmol) was added. The reaction mixture was stirred for 20 h, neutralized, diluted with dichloromethane (25 ml), washed with H_2O (20 ml) and $NaHCO_3$ (10% aq., 20 ml), dried ($MgSO_4$) and concentrated. The resulting oil was chromatographed on silica gel, using the eluent ethyl acetate in light petroleum ether (0→40%), to afford **26** (1.38 g, 4.65 mmol). ^{1}H-NMR ($CDCl_3$): δ 1.25 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 1.38, 1.54 (2x s, 3H, CH_3 isopr.), 3.47 (dq, 1H, H-5, $J_{5,4}$ 10.5 Hz, $J_{5,6}$ 6.7 Hz), 4.08 (dd, 1H, H-3, $J_{3,2}$ 3.5 Hz, $J_{3,4}$ 9.3 Hz), 4.10 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 10.0 Hz), 4.11 (dd, 1H, H-3, $J_{3,2}$ 5.8 Hz, $J_{3,4}$ 7.6 Hz), 4.36 (dd, 1H, H-2, $J_{2,1}$ 0.8 Hz, $J_{2,3}$ 5.4 Hz), 5.75 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$): δ 17.0 (C-6), 26.2, 27.9 (2x CH_3 isopr.), 66.8 (C-5), 74.8, 76.4, 78.3 (C-2, C-3, C-4), 83.5 (C-1), 109.5 (qC isopr), 127.4, 128.8, 131.6 (CH arom.), 133.2 (qC arom.)

Phenyl 4-*O*-benzyl-2,3-*O*-isopropylidene-1-thio-α-L-rhamnopyranoside (27). - Compound **26** (1,38 g, 4.65 mmol) was dissolved in dry *N,N*-dimethylformamide (9 ml) and cooled to 0°C. Potassium hydride (280 mg, 7.0 mmol) and benzyl bromide (0.71 ml, 6.0 mmol) were added. The mixture was allowed to warm to room temperature and stirred for 15 min. Excess KH was destroyed by adding MeOH (1 ml) and the reaction mixture was diluted with diethyl ether (25 ml). The mixture was washed with H_2O (20 ml), $NaHCO_3$ (10% aq., 20 ml), dried ($MgSO_4$) and concentrated to give crude **27**. ^{13}C-NMR ($CDCl_3$): δ 17.3 (C-6), 26.4, 28.0 (2x CH_3 isopr.), 66.1 (C-5), 72.8 (CH_2 Bn), 76.6, 78.3, 81.3 (C-2, C-3, C-4), 83.8 (C-1), 109.3 (qC isopr), 127.5, 127.6, 127.9, 128.2, 129.0, 131.8 (CH arom.), 133.6, 138.3 (qC arom).

Phenyl 4-*O*-benzyl-1-thio-α-L-rhamnopyranoside (28). - Compound **27** was dissolved in a mixture of HOAc-H_2O (9:1, 30 ml) and stirred at 50°C for 17 h. The reaction mixture was concentrated and purified on a silica gel column which was eluted with ethyl acetate in light petroleum ether (0→40%) to afford **28** (1.37 g, 3.95 mmol). ^{13}C-NMR ($CDCl_3$): δ 17.7 (C-6), 68.4 (C-5), 71.8, 72.5, 81.5 (C-2, C-3, C-4), 74.8 (CH_2 Bn), 127.0, 127.7, 128.3, 128.8, 130.9 (CH arom.), 134.1, 138.0 (qC arom.).

Phenyl 3-*O*-acetyl-4-*O*-benzyl-2-*O*-methyl-1-thio-α-L-rhamnopyranoside (30). - Phenyl 4-*O*-benzyl-1-thio-α-L-rhamnopyranoside (**28**, 1.37 g, 3.95 mmol), was dissolved in dichloromethane (25.0 ml), and 10% aq. NaOH (20.0 ml), methyl iodide (1.6 ml, 25 mmol) and *n*-Bu_4NI (0.30 gr, 0.8 mmol) were added. After stirring the reaction mixture for 100 h, the two layers were separated and the organic layer was washed with H_2O (20 ml) and $NaHCO_3$ (10% aq., 20 ml), dried ($MgSO_4$) and concentrated. The residual mixture was purified by column chromatography (ethyl acetate in light petroleum ether (0→50%)) to afford an inseparable mixture of **29** and its positional isomer in a ratio of 9:1 (1.01 g, 2.8 mmol). The product mixture was dissolved in pyridine (10 ml), and acetic anhydride (0.4 ml, 4.2 mmol) and DMAP (34 mg, 0.28 mmol) were added. The reaction was stirred for 1 h, concentrated, purified on a silica gel column, which was eluted with light petroleum ether in dichloromethane (60→0%), to give **30** (903 mg, 2.2 mmol). ^{1}H-NMR ($CDCl_3$): δ 1.34 (d, 3H, H-6, $J_{6,5}$ 6.2 Hz), 2.08 (s, 3H, CH_3 Ac), 3.44 (s, 3H, CH_3 Me), 3.62 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.4 Hz), 3.91 (dd, 1H, H-2, $J_{2,1}$ 1.9 Hz $J_{2,3}$ 3.2 Hz), 4.24 (dd, 1H, H-5, $J_{5,4}$ 9.5 Hz, $J_{5,6}$ 6.2 Hz), 4.70 (AB, 2H, CH_2 Bn), 5.19 (dd, 1H, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.5 Hz), 5.53 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 7.26-7.51 (m, 10H, CH arom.); ^{13}C-NMR ($CDCl_3$): δ 17.5 (C-6), 20.6 (CH_3 Ac), 58.0 (CH_3 Me), 68.5 (C-5), 74.6 (CH_2 Bn), 73.4, 78.5 ,79.60 (C-2, C-3, C-4), 84.1 (C-1), 126.9, 127.2, 127.3, 128.0, 128.6, 130.8 (CH arom.), 134.1, 137.8 (qC arom.), 169.7 (qC Ac).

Further elution of the column gave the positional isomer of **30** (100 mg, 0.25 mmol). ^{1}H-NMR ($CDCl_3$): δ 1.34 (d, 3H, H-6, $J_{5,6}$ 6.2 Hz), 2.15 (s, 3H, CH_3 Ac), 3.44 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.4 Hz), 3.46 (s, 3H, CH_3 Me), 3.64 (dd, 1H, H-3, $J_{3,2}$ 3.3 Hz, $J_{3,4}$ 9.4 Hz) 4.22 (dq, 1H, H-5, $J_{5,4}$ 9.4 Hz, $J_{5,6}$.0 Hz), 4.78 (AB, 2H, CH_2 Bn), 5.42 (d, 1H, H-1, $J_{1,2}$ 1.5 Hz), 5.55 (dd, 1H, H-2, $J_{2,1}$ 1.7 Hz, $J_{2,3}$ 3.2 Hz), 7.25-7.48 (m, 10H, CH arom.); ^{13}C-NMR ($CDCl_3$): δ 17.7 (C-6), 20.9 (CH_3 Ac), 57.4 (CH_3 Me), 68.7 (C-5), 75.2 (CH_2 Bn), 70.0, 80.0, 80.3 (C-2, C-3, C-4), 85.8 (C-1), 127.4, 127.5, 127.7, 128.2, 128.9, 131.5 (CH arom.), 133.8, 138.3 (qC arom.), 170.0 (qC Ac).

Phenyl 4-*O*-benzyl-2-*O*-methyl-1-thio-α-L-rhamnopyranoside (29). - To a solution of **30** in dry methanol (5 ml) was added potassium *tert*-butoxide (25 mg, 0.22 mmol). The reaction mixture was stirred for 1 h, neutralized with Dowex (W50, H^+ form), concentrated and purified by column chromatography. Elution of the column was effected with ethyl acetate in light petroleum ether (0→40%) to afford pure **29** (728 mg, 2.02 mmol), $[\alpha]_D$ -185.0° (c 1). ^{1}H-NMR ($CDCl_3$): δ 1.33 (d, 3H, H-6, $J_{5,6}$ 6.2 Hz), 3.50 (s, 3H, CH_3 Me), 3.35 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.4 Hz), 3.48 (s, 3H, CH_3 Me), 3.76 (dd, 1H, H-2, $J_{2,1}$ 1.4 Hz, $J_{2,3}$ 3.7 Hz), 3.95 (dt, 1H, H-3, $J_{3,2}$ 3.4 Hz, $J_{3,4}\approx J_{3,OH}$ 9.1 Hz), 4.17 (m, 3H, H-5, Bn, $J_{5,4}$ 9.0 Hz, $J_{5,6}$ 5.9 Hz), 5.59 (d, 1H, H-1, $J_{1,2}$ 1.0 Hz), 7.27-7.50 (m, 10H, CH arom.); ^{13}C-NMR ($CDCl_3$): δ 17.7 (C-6), 57.8 CH_3 Me), 68.2 (C-5), 74,9 (CH_2 Bn), 71.8, 82.0 (2x) (C-2, C-3, C-4), 83.8 (C-1), 127.0, 127.5, 127.7, 128.2, 128.8, 131.0 (CH arom.), 134.4, 138.2 (qC arom.).

Anal. Calc. for $C_{22}H_{26}O_5S$: C, 65.7; H, 6.5. Found: C, 65.7; H, 6.4.

Phenyl 3-*O*-(4-*O*-acetyl-3-*O*-(*p*-methoxybenzyl)-2-*O*-methyl-α/β-L-fucopyranosyl)-4-*O*-benzyl-2-*O*-methyl-1-thio-α-L-rhamnopyranoside (31). - IDCP (938 mg, 2 mmol) was added to a stirred solution of ethyl 4-*O*-acetyl-3-*O*-*p*-methoxybenzyl-2-*O*-methyl-1-thio-β-L-fucopyranoside **16** (471 mg, 1.2 mmol), aglycon **29** (370 mg, 1.0 mmol), and activated molecular sieves 4Å in diethyl ether-1,2-dichloroethane (5:1, 15 ml). After stirring for 2.5 h, the mixture was filtered over a pad of hyflo, the filtrate was diluted with dichloromethane, washed with $Na_2S_2O_3$ (20%, 20 ml), $NaHCO_3$ (10%, 15 ml), dried ($MgSO_4$) and concentrated. The residual oil was purified first by column chromatography using ethyl acetate in light petroleum ether (0→30%) and subsequently by Sephadex LH-20 chromatography using the eluent 1:1 methanol-dichloromethane. The disaccharide **31** was obtained as an anomeric mixture α:β=20:1 (398 mg, 0.58 mmol). ^{1}H-NMR ($CDCl_3$): δ 1.17 (d, 3H, H-6', $J_{5,6}$ 6.6 Hz), 1.32 (d, 3H, H-6, $J_{5,6}$ 6.2 Hz), 2.18 (s, 3H, CH_3 Ac), 3.42 (s, 6H, 2x CH_3 Me), 3.52 (t, 1H, H-4, $J_{4,3}\approx J_{4,5}$ 9.3 Hz), 3.60 (dd, 1H, H-2', $J_{2,1}$ 3.6 Hz, $J_{2,3}$ 10.3 Hz), 3.70 (s, 3H, CH_3 pMBn), 3.89 (dd, 1H, H-2, $J_{2,1}$ 1.7 Hz, $J_{2,3}$ 3.2 Hz), 3.93 (dd, 1H, H-3, $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.2 Hz), 3,98 (dd, 1H, H-3', $J_{3,2}$ 10.2 Hz, $J_{4,3}$ 3.4 Hz), 4.18 (dq, 1H, H-5, $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.2 Hz), 4.51 (AB, 2H, CH_2 Bn), 4.90 (AB, 2H, CH_2 pMBn), 5.22 (d, 1H, H-1', $J_{1,2}$ 3.8 Hz), 5.40 (dd, 1H, H-4', $J_{4,3}$.4 Hz, $J_{4,5}$ 1.3 Hz), 5.58 (d, 1H, H-1, $J_{1,2}$ 1.6 Hz), 6.77-6.82 (m, 2H, CH arom.), 7.23-7.49 (m, 12 H, CH arom.); ^{13}C-NMR ($CDCl_3$): δ 16.4, 17.8 (C-6, C-6'), 20.8 (CH_3 Ac), 55.0, 57.1, 59.1 (3x CH_3 Me), 71.0, 75.1 (2x CH_2 pMBn, Bn), 65.3, 69.1, 70.6, 74.9, 77.4, 79.5, 81.5, 81.6 (C-2, C-3, C-4, C-5, C-2', C-3, C-4', C-5'), 83.6 (C-1), 99.8 (C-1'), 113.6, 127.2, 127.4, 127.4, 127.9, 128.1, 128.9, 129.2, 129.4, 131.0 (CH arom.), 130.1, 134.6, 138.7, 159.0 (qC arom.).

4-[2-(Benzyloxycarbonylamino)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 (22 α/β). - To a cooled (-30°C) mixture of 1,2-dichloroethane-diethyl ether (1:1, 4 ml) containing **30** (397 mg, 0.58 ml, α:β=20:1), **19** (214 mg, 0.48 mmol) and powdered molecular sieves 4Å was added dropwise a solution of NIS (216 mg, 0.96 mmol) and TfOH (13 µl, 0.15 mmol) in the same solvent mixture (4 ml). After stirring for 45 min, the reaction mixture was filtered, diluted with

dichloromethane (10 ml), washed with $Na_2S_2O_3$ (20% aq., 12 ml), $NaHCO_3$ (10% aq., 10 ml), dried ($MgSO_4$) and concentrated. The residue was applied onto a Sephadex LH-20 column and elution was effected with dichloromethane-methanol 1:1. The appropriate fractions were collected and concentrated to yield the trisaccharide **22** (428 mg, 0.42 mmol) as an anomeric mixture of α:β=20:1. ^{1}H-NMR ($CDCl_3$) of **22**α: δ 1.15 (d, 3H, H-6'', $J_{6,5}$ 6.6 Hz), 1.26 (d, 3H, H-6/H-6', $J_{6,5}$ 6.2 Hz), 1.33 (d, 3H, H-6/H-6', $J_{6,5}$ 6.2 Hz), 2.17 (s, 3H, CH_3 Ac), 2.76 (t, 2H, CH_2 spacer, $J_{H,H}$ 6.7 Hz), 3.22 (t, 1H, H-4/H-4', $J_{4,3}\approx J_{4,5}$ 9.6 Hz), 3.40 (s, 3H, CH_3 Me), 3.44 (q, 2H, CH_2 spacer, $J_{H,H}\approx J_{H,NH}$ 6.4 Hz), 3.48, 3.50 (2x s, 3H, CH_3 Me), 3.52 (t, 1H, H-4/H-4', $J_{4,3}\approx J_{4,5}$ 9.2 Hz), 3.54 (dd, 1H, H-2'', $J_{2,1}$ 3.0 Hz, $J_{2,3}$ 9.2 Hz), 3.54 (s, 3H, CH_3 Me), 3.66 (dq, 1H, H-5/H-5', $J_{5,4}$ 9.4 Hz, $J_{5,6}$ 6.2 Hz), 3.67-3.72 (m, 2H, H-2, H-2'), 3.71 (s, 3H, CH_3 Me), 3.93 (dq, 1H, H-5/H-5', $J_{5,4}$ 9.3 Hz, $J_{5,6}$ 1.1 Hz), 3.99 (dd, 1H, H-3'', $J_{3,2}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz), 4.05 (dd, 1H, H-3/H-3', $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.4 Hz), 4.08 (dd, 1H, H-3/H-3', $J_{3,2}$ 3.2 Hz, $J_{3,4}$ 9.6 Hz), 4.30 (dq, 1H, H-5'', $J_{5,4}$ 1.4 Hz, $J_{5,6}$ 6.3 Hz), 4.58, 4.83 (AB, 2H, CH_2 Bn/pMBn), 5.09 (s, 2H, CH_2 Z), 5.19 (d, 1H, H-1, $J_{1,2}$ 1.8 Hz), 5.22 (d, 1H, H-1'', $J_{1,2}$ 3.8 Hz), 5.41 (dd, 1H, H-4'', $J_{4,3}$ 3.4 Hz, $J_{4,5}$ 1.0 Hz), 5.46 (d, 1H, H-1, $J_{1,2}$ 1.9 Hz), 6.8-7.1 (m, 6H, CH arom.), 7.2-7.4 (m, 12H, CH-arom.); ^{13}C-NMR ($CDCl_3$) of **22**α: δ 16.3, 17.7, 18.1 (C-6, C-6', C-6''), 20.8 (CH_3 Ac), 35.2, 42.2 (2x CH_2 spacer), 55.0 (CH_3 Me), 57.7, 58.8, 59.1, 61.0 (4x CH_3 Me), 66.5 (CH_2 Z), 71.0, 74.9 (CH_2 Bn/pMBn), 65.0, 68.4, 68.7, 70.7, 77.4 79.4, 80.0, 80.5, 80.7, 81.9 (C-2, C-3, C-4, C-5, C-2', C-3', C-4', C-5', C-2'', C-3'', C-4'', C-5''), 94.9 (C-1, $^1J_{C,H}$ 170.0 Hz), 98.3 (C-1'/C-1'', $^1J_{C,H}$ 171.4 Hz), 99.8 (C-1'/C-1'', $^1J_{C,H}$ 171.4 Hz), 113.6, 116.4, 127.3, 127.8, 127.9, 128.1, 128.3, 129.6 (CH arom.), 130.1, 132.3, 136.5, 138.9, 155.0 (qC arom.), 156.1 (C=O Z), 170.7 (qC Ac).

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