Pergamon

Tetrahedron: Asymmetry Vol. 6, No. 5, pp. 1195-1216, 1995

0957-4166/95 $9.50+0.00

0957-4166(95)00146-8

Synthesis of a Nonasaccharide with two Lewis x Trisaccharides Anchored onto a Branched Trimannoside

Yong-Min Zhang†, Annie Brodzky†, Pierre Sinaÿ†*, Guillaume Saint-Marcoux‡ and Bruno Perly‡

†Ecole Normale Supérieure, Département de Chimie, URA 1686, 24 rue Lhomond, 75231 Paris Cedex 05, France

‡CEA, Service de Chimie Moléculaire, CE de Saclay, 91191 Gif sur Yvette Cedex, France

Abstract: Double condensation of phenyl 3,4,6-tri-*O*-benzyl-2-*O*-[6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-1-thio-α-D-mannopyranoside **31** with methyl 2,4-di-*O*-benzyl-β-D-mannopyranoside **35**, in the presence of *N*-iodosuccinimide/trifluoromethanesulfonic acid, gave the protected nonasaccharide **36** in 60% yield. Conventional deprotection gave the nonasaccharide **1**, in which two Lewis x trisaccharides are anchored onto a branched trimannoside.

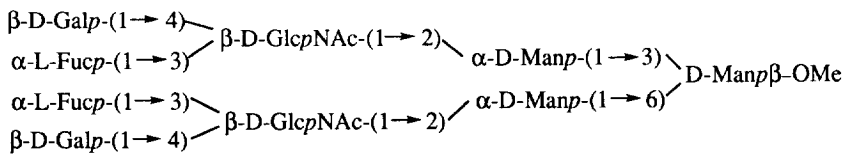
INTRODUCTION

The term glycocalyx is frequently used to describe the carbohydrate-rich noncytoplasmic surface of the cell membrane. It is principally composed of the oligosaccharide moiety of glycolipids and integral membrane glycoproteins and proteoglycans. Specific oligosaccharides of the glycocalyx are probably involved in a variety of important transient cell-cell adhesion processes. Significant examples are the adherence of circulating leukocytes to the activated vascular endothelium and of circulating lymphocytes to the surface of the specialized high endothelial cells in a postcapillary venule (HEV) in a lymph node[1]. This initial adhesion is mediated by membrane proteins called selectins[2]. These proteins, which initiate many critical interactions among blood cells, possess an N-terminal carbohydrate recognition domain analogous to other C-type mammalian lectins[3]. The involvement of sialylated or sulfated Lewis x or Lewis a trisaccharide structures as selectin ligands is now well documented[4-7]. These ligands are expressed at the termini of sugar chains, especially mono or polylactosaminoglycans which are present in *O*-glycans, *N*-glycans and glycosphingolipids, so that all of these molecular species may *a priori* contribute to the *in vivo* expression of high-affinity ligands. Sialylated (or sulfated) Lewis x (or Lewis a) structures are themselves low-affinity ligands for selectins, which means that the *in vivo* carbohydrate molecular or supramolecular structures of high-affinity selectin ligands have yet to be precisely determined.

Several recently identified HEV-associated ligands for L-selectins, such as GlyCAM-1[4] and CD_{34}[5], and a 120 kDa specific ligand for P-selectin on myeloid cells[6], are "mucin like" *O*-linked glycoproteins characterized by the presence of a large number of closely spaced sialylated *O*-linked oligosaccharides. Such systems seem well suited to the formation of clustered saccharide patches which are *in vivo* potential high-affinity supramolecular entities. Glycolipids are also likely candidates for such a molecular scenario. As recently shown[7], it is also possible that unique carbohydrate structures are capable of acting as high-affinity selectin ligands. Another possibility is presented when one questions the functional role of the natural antennae found in N-glycans. It indeed seems reasonable to ask the question as to whether the basic purpose of the forked molecular architecture is indeed to achieve a dramatic increase in the affinity of ligands located at the termini of different branches. A precise evaluation of the respective importance of any "antenna effect" as opposed to the "cluster effect", for the *in vivo* generation of high-affinity patches, largely remains to be undertaken.

Another observation is that the Lewis x determinant is highly expressed during early mammalian development[8]. The appearance of Lewis x on the embryo cell surface at the morula stage correlates in time with compaction. A hypothesis is that specific homotypic interactions between Lewis x and Lewis x determinants provide a basic mechanism for cell recognition during early development. Whether such an attractive idea can be extended to the initial step of blood cell adhesion on the endothelium remains completely uninvestigated. Were this to be the case, then the topological presentation of the Lewis x derivatives at the non-cytoplasmic membrane surface would also be of importance.

As part of a programme involving the synthesis of various natural forked oligosaccharides armed with Lewis x determinants and aimed at evaluating the "antenna effect", we report here the chemical synthesis of the nonasaccharide **1**. This oligosaccharide is a structural element of glycopeptides isolated from urine of patients with fucosidosis[9].

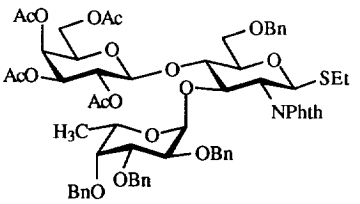


1

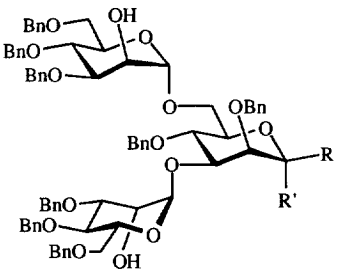
RESULTS AND DISCUSSION

A case of mismatch during a block synthesis of an oligosaccharide

H. Lönn reported[10b] in 1985 a successful methyl trifluoromethanesulfonate promoted condensation of the glycosyl donor **2** with the diol **3** to provide the corresponding nonasaccharide derivative in 61% yield. We thus logically attempted to synthesize **1** via condensation of **2** with the known[11] diol **4**.



2

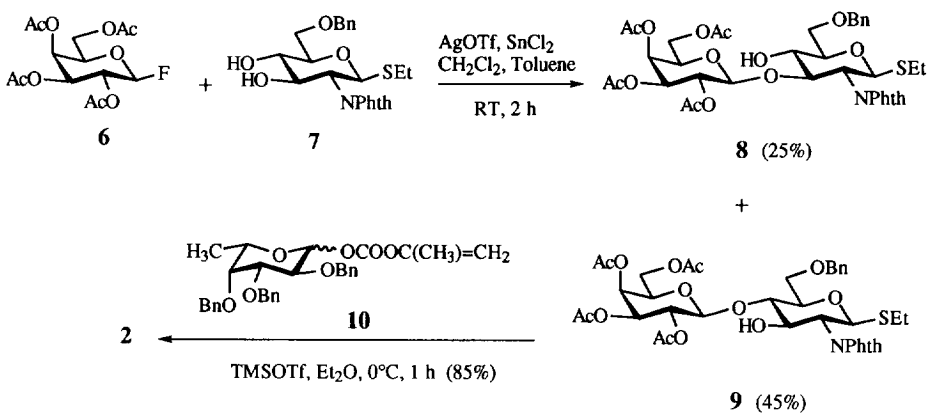


3 R = H, R' = OBn

4 R = OMe, R' = H

5 R = H, R' = OMe

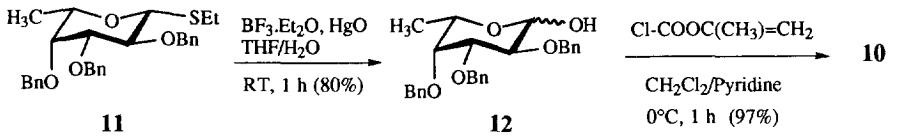
The thioethyl glycoside **2** was prepared by an alternative method, as shown in **Scheme 1**.



6 **7** **8** (25%) + **9** (45%) **10** **2**

Scheme 1

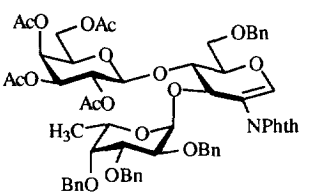
Condensation of the fluoride **6**[12] with the diol **7**, readily obtained from ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[10a], according to Mukaiyama's method[13], selectively gave the β 1→4 linked disaccharide **9** (45%), which was easily separated from the β 1→3 linked isomer **8** (25%). The β configurations of **8** and **9** were assignable from the ^{1}H NMR spectra which showed doublets for H-1' at δ 4.39 ($J_{1',2'}$ 7.8 Hz) and 4.51 ($J_{1',2'}$ 8.0 Hz), respectively. The regiochemistry of the newly introduced glycosidic linkage of **9** was confirmed by the ^{1}H NMR spectrum which showed a signal for H-3 at δ 4.44 (ddd, $J_{3,OH}$ 1.2, $J_{3,4}$ 8.0, $J_{3,2}$ 10.4 Hz). Compound **8** is a potential intermediate for the synthesis of a Lewis a trisaccharidic glycosyl donor, an interesting use of this byproduct, taking into account the biological importance of Lewis a derivatives. The fucosyl donor **10** was easily prepared[14], as shown in **Scheme 2**, from ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside **11**[10a].



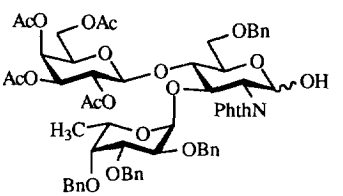
11 12

Scheme 2

Despite a large number of attempts, no trace of condensation product between **2** and **4** was observed in methylene chloride at room temperature using methyl triflate as an activator[15]. The only observable products were the glycal **13** (56%) and the hemiacetal **14** (41%). The use of ether as a solvent proved equally frustrating.

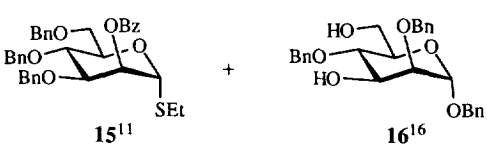


13

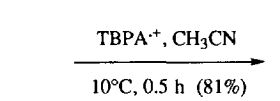


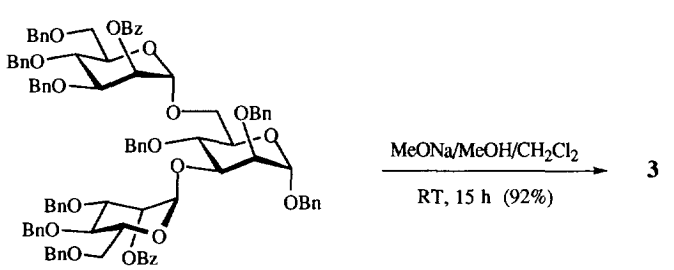
14

In order to give our opinion on the origin of this experimental discrepancy, we had firstly to set aside any improbable influence of the configuration of the anomeric centre at the reducing end of the trimannoside acceptor. The same experimental conditions were thus scrupulously repeated using the donor **2** and the acceptor **3**[16] or **5**[17], **3** being prepared as shown in **Scheme 3** using Sinaÿ's procedure recently developed by us[18].



15[11] **16**[16]

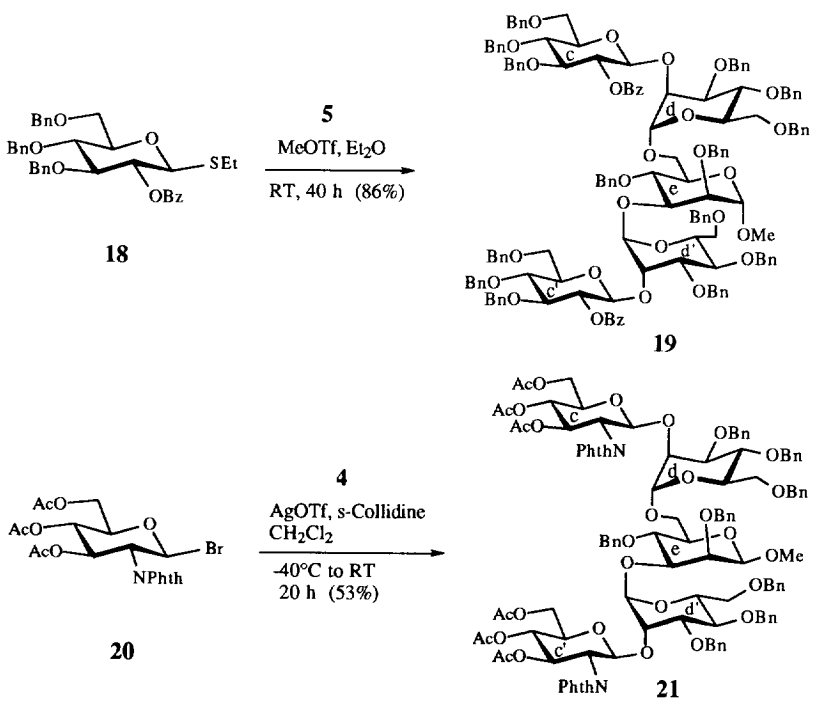




17

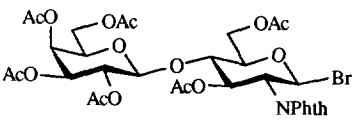
Scheme 3

No condensation was observed in our hands. Neither the use of alternative established promotors such as TBPA·+[18] or *N*-iodosuccinimide/triflic acid[19] at -60°C, nor the use of the trichloroacetimidate procedure[20] improved the situation. The employment of the closely related and known[21] thiophenyl Lewis x donor was equally frustrating. Again glycal and hemiacetal were consistently fished out of the reaction mixture. We are most probably the victims of a miserable, but not uncommon, case of steric mismatch. This constantly jeopardizes the success of thoroughly planned block synthesis of complex oligosaccharides, is made more vicious by the difficulty of prediction, and is now well recognized by experts in the field. In fact, we found that the trimannosyl acceptor **5** reacted well in ether at room temperature with ethyl 3,4,6-tri-*O*-benzyl-2-*O*-benzoyl-1-thio-β-D-glucopyranoside **18**[22] in the presence of methyl triflate (same batch as the one previously used), to give the protected pentasaccharide **19** in 86% yield. Glycosidation of **4** with 3,4,6-tri-*O*-acetyl-2-deoxy-2-phtalimido-β-D-glucopyranosyl bromide **20**[23] in the presence of silver triflate also gave the predicted pentasaccharide **21** in 53% yield (**Scheme 4**). The configurations of the newly introduced anomeric carbons C-1c and C-1c' were expected to be β due to the presence of the benzoyl or phthalimido group in the glycosyl donors, which favor the formation of 1,2-trans stereochemistry. Indeed, the ^{1}H NMR spectra showed the anomeric protons of H-1c and H-1c' as two doublets at δ 4.75 ($J_{1c, 2c}$ 7.9 Hz) and 4.07 ($J_{1c', 2c'}$ 8.1Hz) for **19**, and δ 5.60 ($J_{1c, 2c}$ 8.5 Hz) and 5.08 ($J_{1c', 2c'}$ 8.5 Hz) for **21**.



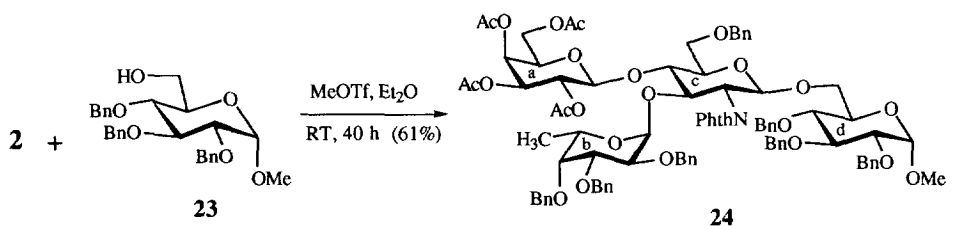
Scheme 4

The bromides **20**[23] and **22**[24] are indeed known[25] to condense with the trimannosyl core. The steric hindrance created by the presence of the benzylated L-fucosyl residue in **2** is thus probably responsible for decreasing the reactivity of the donor **2** with partially benzylated trimannosyl cores, such as **3**, **4** or **5**.



22

We have of course checked that reaction of the glycosyl donor **2** with a reactive alcohol such as **23**[26] under methyl triflate activation gave the protected tetrasaccharide **24** in 61% yield (**Scheme 5**). The β configuration of the newly introduced anomeric carbon was confirmed by the ^{1}H NMR spectrum that showed the anomeric proton of H-1c as a doublet at δ 5.13 ($J_{1c,2c}$ 8.5 Hz).



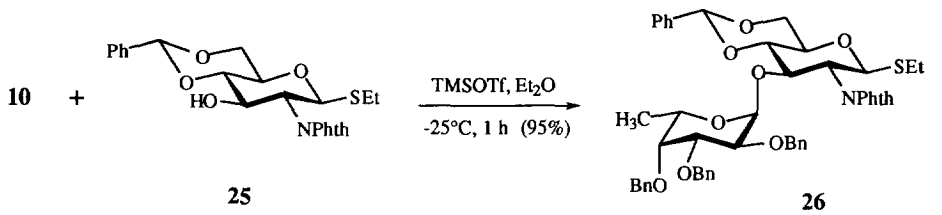
23 **24**

Scheme 5

Thus, in our hands, we were unable to repeat Lönn's experiment[10b] concerning the nonasaccharide. As no elemental analyses nor mass spectroscopic data were provided, it could well be that the reported ^{1}H NMR data corresponds to an unseparated mixture of trisaccharidic species. It is worth noting that Classon *et al.*[27] observed a similar case of mismatch between **2** and galactopyranosides.

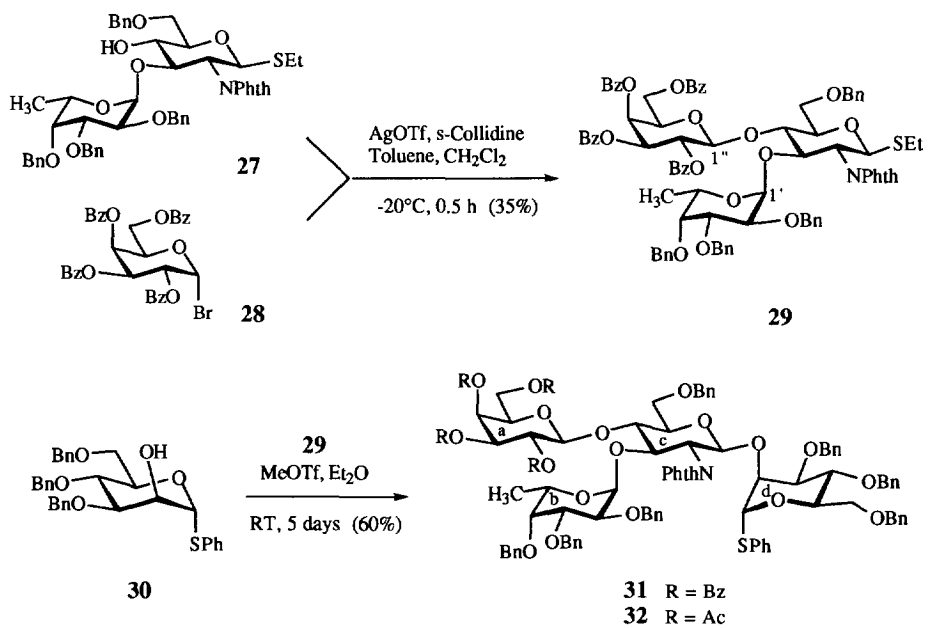
A successful construction of the nonasaccharide

The disaccharide **26** has already been prepared in 81% yield by Lönn[10a] after condensation of ethyl 4,6-*O*-benzylidene-2-deoxy-2-phtalimido-1-thio-β-D-glucopyranoside **25** with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide according to the halide ion catalysed glycosylation procedure[28]. Condensation of **25** with the fucosyl carbonate **10** at -25°C in ether, in the presence of trimethylsilyl triflate, gave the same disaccharide **26** in 95% yield (**Scheme 6**). The successful introduction of the α configuration of the L-fucosyl unit was confirmed by the ^{1}H NMR spectrum for **26** that showed a doublet for H-1' at δ 4.84 ($J_{1',2'}$ 3.1 Hz).



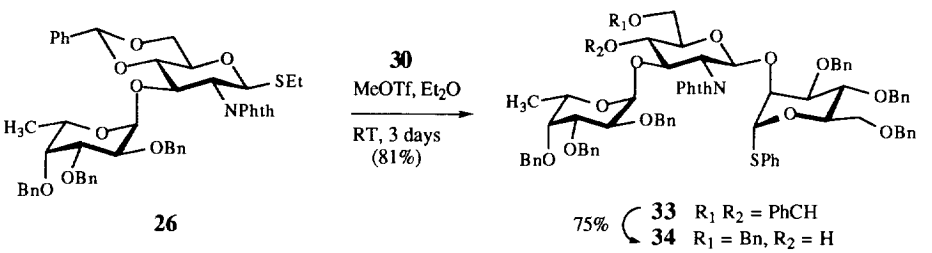
Scheme 6

We then addressed the problem of an efficient synthesis of the thiophenyl glycosyl donor **31**, a key intermediate *en route* to the preparation of the nonasaccharide **1**. When **27**, readily obtained[29] from **26**, was condensed with 2,3,4,6-tetra-*O*-benzoyl-α–D-galactopyranosyl bromide **28**[30], in the presence of silver triflate, the expected trisaccharide **29** was obtained in rather low yield (35%). The β configuration of the newly introduced anomeric carbon was confirmed by the ^{1}H NMR spectrum that showed the anomeric proton of H-1" as a doublet at δ 5.08 ($J_{1",2"}$ 8.3 Hz). Condensation of **29** with phenyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside **30**[31] in ether, in the presence of methyl triflate gave the donor **31** in 60% yield. Using similar conditions, the thioethyl glycoside **2** gave **32** in 50% yield (**Scheme 7**). The β configurations of the newly introduced anomeric carbons were confirmed by the ^{1}H NMR spectra which showed the anomeric proton of H-1c as a doublet at δ 5.24 ($J_{1c,2c}$ 8.6 Hz) for **31** and 5.30 ($J_{1c,2c}$ 8.4 Hz) for **32**, respectively.



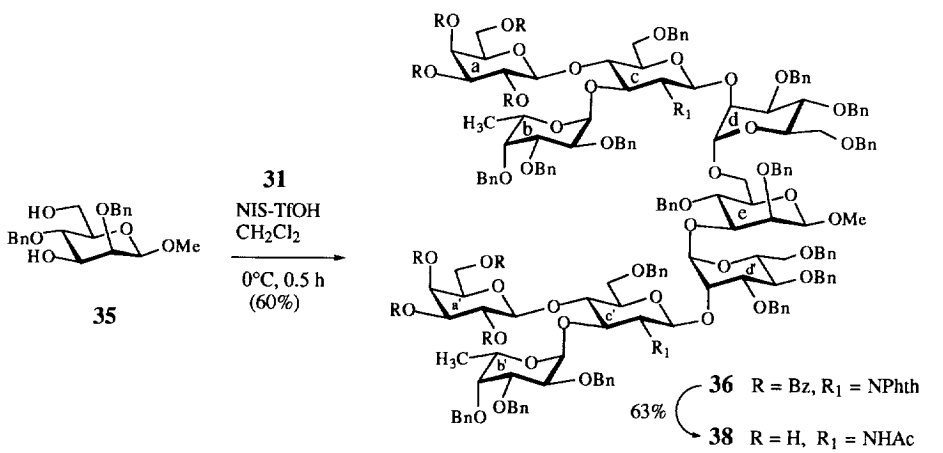
Scheme 7

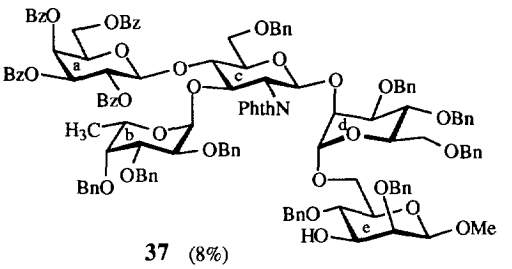
Due to the moderate yield of this process, we adopted a more efficient procedure, which is shown in **Scheme 8**.



Scheme 8

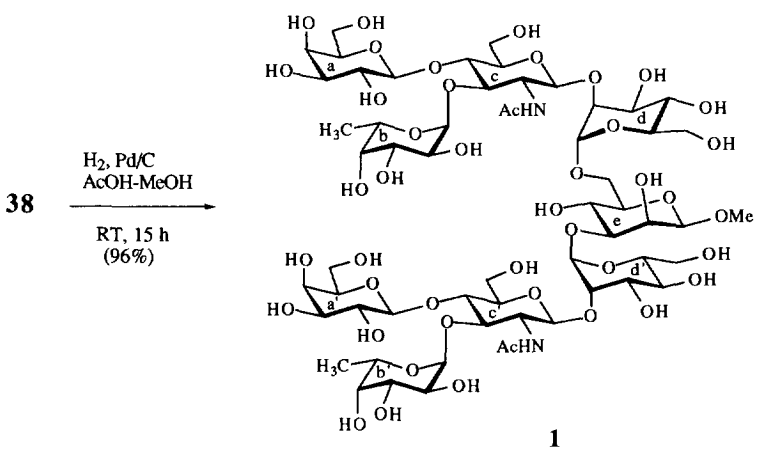
Condensation of **26** with **30** in ether, in the presence of methyl triflate, gave the thiophenyl donor **33** in 81% yield. Again, the stereochemistry of the newly generated anomeric centre was confirmed by its ^{1}H NMR spectrum which showed a doublet at δ 5.49 with $J_{1',2'}$ 8.35 Hz for H-1', clearly indicating that the newly formed glycosidic linkage in trisaccharide **33** was in the β configuration. This represents a good example of the possibilities offered by the appropriate manipulation of thioglycosides for the direct and efficient synthesis of a glycosyl donor. Reductive ring-opening of the benzylidene acetal in **33** with trimethylamine-borane complex and aluminium trichloride in tetrahydrofuran[29] yielded the expected alcohol **34** (75%). Silver triflate promoted glycosylation of **34** with 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide **28** gave the key donor **31** in 78% yield. Double condensation of **31** with methyl 2, 4-di-*O*-benzyl-β-D-mannopyranoside **35**[11] in dichloromethane at 0°C, in the presence of *N*-iodosuccinimide/triflic acid[19], gave the protected nonasaccharide **36** in 60% yield. A small amount (8%) of a product resulting from monocondensation was also isolated and tentatively assigned as **37**. Treatment of **36**, first with hydrazine hydrate in boiling ethanol, then with acetic anhydride/pyridine at room temperature, and finally with sodium methoxide in methanol at room temperature gave the derivative **38** in 63% overall yield from **36** (**Scheme 9**).





Scheme 9

Catalytic hydrogenolysis and purification of the product on Sephadex G-25-150 gave the nonasaccharide **1** in almost quantitative yield (**Scheme 10**).



Scheme 10

The structure of **1** was confirmed by NMR spectroscopy (see Experimental). A complete NMR study will be described elsewhere[32].

EXPERIMENTAL SECTION

General. Melting points (m.p.) were determined with a Büchi model 510 m.p. apparatus and are uncorrected. Optical rotations were measured at 20±2°C with a Perkin Elmer Model 241 digital polarimeter, using a 10 cm, 1 mL cell. C.I.(ammonia)-mass spectra were obtained with a Nermag R10-10 spectrometer. Elemental analyses were performed by Service Central d'Analyse du C.N.R.S., BP 22, 69390 Vernaison, France. ^{1}H-NMR spectra were recorded with a Bruker AC 250 and a Bruker AM 400 spectrometer for solutions in $CDCl_3$

(internal Me_4Si, δ 0) or D_2O (internal acetone, δ 2.225) at ambient temperature. ^{13}C-NMR spectra were recorded at 62.89 MHz with a Bruker AC 250 and at 100.57 MHz with a Bruker AM 400 for solutions in $CDCl_3$ adopting 77.00 ppm for the central line of $CDCl_3$. Assignments were aided by J-mod technique and proton-carbon correlation. Single and double primes refer to the fucosyl and galactosyl residues in Lewis x trisaccharide, or the 3-, 6- attached (or *vice versa*) mannosyl residues in trimannosides; or the glucosyl and fucosyl residues in the Fuc-Glc-Man trisaccharides. The letters a, b, c, d refer to the galactosyl, fucosyl, glucosyl, mannosyl and e to the methyl attached mannosyl residues in tetra- penta- and nonasaccharides, the exact assignments have not been achieved for a, b, c, d and a', b', c', d' in penta- and nonasaccharides except for the end nonasaccharide **1**, for which the determination of branching points and the final sequencing was derived from NOESY and ROESY spectra using a Bruker AMX 500 spectrometer. Reactions were monitored by thin-layer chromatography (TLC) on a precoated plate of silica gel 60 F_{254} (layer thickness, 0.2 mm; E. Merck, Darmstadt, Germany) and detection by charring with sulfuric acid. Flash column chromatography was performed on silica gel 60 (230-400 mesh, Merck).

Ethyl 6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl) -1-thio-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (2). To a cooled (0°C), stirred mixture of **9** (774 mg, 1 mmol), **10** (650 mg, 1.2 mmol), activated 4Å ground molecular sieves (1.5 g), and dry ether (20 mL) was added dropwise TMSOTf (0.23 mL, 1.2 mmol). Stirring was continued for an additional hour at 0°C, then the mixture was neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with cyclohexane-ethyl acetate (1.5:1) to give **2**. Crystallization in ether gave a white solid (1.01 g, 85%): R_f = 0.57 (cyclohexane-ethyl acetate 1:1); m.p. 167-168°C (Lit[10b]: 169°C); $[\alpha]_D$+7.1 (c 1, $CHCl_3$, Lit[10b] +6 , c 0.87, $CHCl_3$); ^1H-NMR (250 MHz) δ 7.82, 7.69 (2 m, 4 H, Pht), 7.46–7.05 (m, 20 H, 4 Ph), 5.24 (dd, 1 H, $J_{4",3"}$ = 3.5 Hz, $J_{4",5"}$ < 1Hz, H-4"), 5.19 (d, 1 H, $J_{1,2}$ = 10.3 Hz, H-1), 5.03 (dd, 1 H, $J_{2",1"}$ = 8.4, $J_{2",3"}$ = 10.4 Hz, H-2"), 4.84 (d, 1 H, $J_{1',2'}$ =3.4 Hz, H-1'), 2.64 (2 dq, 2 H, J_{gem} = 12.1, J_{vic} = 7.4 Hz, SCH_2), 2.04, 2.03, 1.96, 1.83 (4 Ac), 1.23 (d, 3 H, $J_{6',5'}$ = 6.5 Hz, C-6'), 1.19 (t, 3 H, J = 7.4 Hz, CH_3); ^{13}C-NMR (100.57 MHz) δ 169.87, 169.87, 169.69, 168.59 (4 O=C, Ac), 168.30, 167.09 (2 O=C, Pht), 138.69, 138.49, 137.99, 137.73 (4 C, Ph), 134.09 (2 CH, Pht), 131.56 (2 C, Pht), 128.49-126.83 (Ph), 123.62, 123.45 (2 CH, Pht), 99.40 (C-1"), 97.31 (C-1'), 81.18 (C-1), 79.69, 79.43, 76.90, 74.74, 74.33, 73.13, 70.82, 70.16, 68.78, 66.56, 66.29 (ring C), 73.98, 73.37, 72.89, 72.18 (4 $PhCH_2$), 67.66 (C-6), 59.98 (C-6"), 55.21 (C-2), 23.50(SCH_2), 20.61, 20.50, 20.42, 20.40 (4 Ac), 16.59 (C-6'), 14.73 (CH_3); MS (CI) m/z 1207 ($M+NH_4^+$). Anal. Calcd. for $C_{64}H_{71}NO_{19}S$: C, 64.58; H, 6.01. Found: C, 64.41; H, 6.00.

Benzyl 2, 4-di-*O*-benzyl-3, 6-di-*O*-(3, 4, 6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-manno-pyranoside (3). A suspension of benzyl 2,4-di-*O*-benzyl-α-D-mannopyranoside (**16**, 130 mg, 0.29 mmol), tris (4-bromophenyl)ammoniumyl hexachloroantimonate (816 mg, 1 mmol), and 4Å ground molecular sieves (1.5 g) in dry acetonitrile (10 mL) was stirred for 15 min under argon. Then a solution of ethyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (**15**, 470 mg, 0.78 mmol) in acetonitrile (5 mL) was added slowly at 0°C. The reaction mixture was stirred at room temperature for 1 h, filtered through a bed of Celite and

concentrated. The residue was eluted from a column of silica gel with 4:1 cyclohexane-ethyl acetate to give the trisaccharide **17** as a syrup (358 mg, 81%). R_f = 0.39 (cyclohexane-ethyl acetate 4:1). Debenzoylation by MeONa in MeOH gave, after purification on a column of silica gel using cyclohexane-ethyl acetate 3:2 as eluent, **3** (240 mg, 92%) as a syrup: R_f = 0.64 (cyclohexane-ethyl acetate 1:1); $[\alpha]_D$+60 (c 1, $CHCl_3$; Lit.[16] +58 , c 0.2, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 5.31 (d, 1 H, $J_{1',2'}$ = 1.5 Hz, H-1'), 5.15 (d, 1 H, $J_{1'',2''}$ = 1.7 Hz, H-1''); ^{13}C-NMR (62.89 MHz) δ 101.48 (C-1'), 99.72 (C-1''), 96.18 (C-1); MS (CI) m/z 1332 ($M+NH_4^+$). Anal. Calcd. for $C_{81}H_{86}O_{16}$: C, 73.95; H, 6.59. Found: C, 73.80; H, 6.56.

Methyl 2,4-di-*O*-benzyl-3,6-di-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (5). It was prepared from methyl 2,4-di-*O*-benzyl-α-D-mannopyranoside and **15** (78% yield for the double condensation) as described above for the synthesis of **3**. Debenzoylation afforded **5** as a syrup (90%): R_f = 0.33 (cyclohexane-ethyl acetate 1:1); $[\alpha]_D$+51.7 (c 1.3, $CHCl_3$; Lit.[17] +53.8 , c 0.47); ^{1}H-NMR (400 MHz) δ 5.29 (d, 1 H, $J_{1',2'}$ = 1.5 Hz, H-1'), 5.15 (d, 1 H, $J_{1'',2''}$ = 1.5 Hz, H-1''), 4.72 (d, 1 H, $J_{1,2}$ = 1.0 Hz, H-1), 3.31 (s, 3 H, OMe); ^{13}C-NMR (62.89 MHz) δ 101.59 (C-1'), 99.82 (C-1''), 98.22 (C-1), 54.82 (OMe); MS (CI) m/z 1256 ($M+NH_4^+$).

Ethyl 6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (7). To a cold (0°C), stirred mixture of ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (5.9 g, 13.4 mmol), sodium cyanoborohydride (7 g), activated 4Å ground molecular sieves (6 g), and methyl orange (0.2 g), in dry THF (50 mL) was added, dropwise, a saturated solution of HCl in ether until the red color ceases to be discharged (35 mL), and stirring was continued for 30 min. The mixture was diluted with dichloromethane and filtered through Celite. The filtrate was successively washed with cold water, cold saturated $NaHCO_3$ solution, and water, dried, and concentrated. The residue was applied to a column of silica gel and eluted with cyclohexane-ethyl acetate (1:1.5) to give **7** as an amorphous solid (5.7 g, 96%): R_f = 0.36 (cyclohexane-ethyl acetate 1:2); $[\alpha]_D$ -7.1 (c 1, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 7.88 and 7.76 (2 m, 4 H, Pht), 7.38 (m, 5 H, Ph), 5.38 (d, 1 H, $J_{1,2}$ = 10.3 Hz, H-1), 4.67 and 4.62 (2 d, 2 H, J = 12.0 Hz, $PhCH_2$), 4.42 (ddd, 1 H, $J_{3,2}$ = 10.3, $J_{3,4}$ = 7.5, $J_{3,OH}$ = 4.1Hz, H-3), 4.23 (dd, 1 H, H-2), 3.88 (dd, 1 H, $J_{6a,6b}$ = 10.0, $J_{6a,5}$ = 4.0 Hz, H-6a), 3.78 (dd, 1 H, $J_{6b,5}$ = 5.0 Hz, H-6b), 3.68 (m, 2 H, H-4, H-5), 3.47 (d, 1 H, J = 1.5 Hz, OH-4), 3.08 (d, 1 H, J = 4.1 Hz, OH-3), 2.69 (2 dq, 2 H, J_{gem} = 12.0, J_{vic} = 7.5 Hz, SCH_2,), 1.23 (t, 3 H, J = 7.5 Hz, CH_3); ^{13}C-NMR (100.57 MHz) δ 168.28 (2 C=O, Pht), 137.41(Ph), 134.22 (2 C, Pht), 131.40 (2 C, Pht), 128.44, 127.86, 127.75 (3 C, Ph), 123.74, 123.33 (2 C, Pht), 81.02 (C-1), 77.89, 72.89 (C-5, 4), 73.60 ($PhCH_2$), 72.42 (C-3), 70.02 (C-6), 55.53 (C-2), 24.20 (SCH_2), 14.87 (CH_3); MS (CI) m/z 461 ($M+NH_4^+$). Anal. Calcd. for $C_{23}H_{25}NO_6S$: C, 62.29; H, 5.68. Found: C, 62.48; H, 5.91.

Ethyl 6-*O*-benzyl-2-deoxy-2-phthalimido-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-1-thio-β-D-glucopyranoside (8) and **ethyl 6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-1-thio-β-D-glucopyranoside (9).** A solution of **7** (3.3 g, 7.4 mmol) and 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl fluoride **6** (4.4 g, 12.6 mmol) in 50 mL of CH_2Cl_2 and 10 mL of toluene was stirred with 4Å ground molecular sieves (5 g) for 30 min at room temperature under an

argon atmosphere. A mixture of stannous chloride (1.7 g, 9 mmol) and silver triflate (2.3 g, 9 mmol) was added at -15°C, then the reaction mixture was allowed to gradually warm to room temperature, and the stirring was continued for an additional 2 h. The mixture was filtered through Celite and the solids were washed with CH_2Cl_2. The combined filtrate and washings were washed with a saturated $NaHCO_3$ solution, then with water, dried over $MgSO_4$, and concentrated. The residue was applied to a column of silica gel and eluted with cyclohexane-ethyl acetate (1:1). The earlier fractions contained the compound **9**, on concentration, these fractions afforded an amorphous solid (2.6 g, 45%): R_f = 0.33 (cyclohexane-ethyl acetate 1:1); $[\alpha]_D$ +18.3 (c 0.9, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 7.85 and 7.72 (2 m, 4 H, Pht), 7.38 (m, 5 H, Ph), 5.34 (dd, 1 H, $J_{4',3'}$ = 3.5 Hz, $J_{4',5'}$ < 1 Hz, H-4'), 5.33 (d, 1 H, $J_{1,2}$ = 10.4 Hz, H-1), 5.19 (dd, 1 H, $J_{2',3'}$ = 10.3, $J_{2',1'}$ = 8.0 Hz, H-2'), 4.94 (dd, 1 H, H-3'), 4.75 and 4.53 (2 d, 2 H, J = 12.0 Hz, $PhCH_2$), 4.51 (d, 1 H, H-1'), 4.44 (ddd, 1 H, $J_{3,OH}$ = 1.2, $J_{3,4}$ = 8.0, $J_{3,2}$ = 10.4 Hz, H-3), 4.25 (dd, 1 H, H-2), 4.06 and 4.04 (d, 2 H, $J_{6'a,5'} = J_{6'b,5'}$ = 6.6 Hz, H-6'a,6'b), 4.01 (d, 1 H, J = 1.2 Hz, OH), 3.90 (dd, H-5'), 3.71 (m, 4 H, H-4,5,6a,6b), 2.69 (2 dq, 2 H, J_{gem} = 12.4, J_{vic} = 7.4 Hz, SCH_2), 2.12, 2.00, 1.98, 1.93 (4 s, 12 H, 4 Ac), 1.22 (t, 3 H, J = 7.4 Hz, CH_3); ^{13}C-NMR (100.57 MHz) δ 170.25, 169.87, 169.73, 168.96 (4 O=C, Ac), 167.88, 167.48 (2 O=C, Pht), 137.87 (1 C, Ph), 133.93 (2 CH, Pht), 131.58, 131.43 (2 C, Pht), 128.33, 127.69, 127.63 (3 CH, Ph), 123.40, 123.03 (2 CH, Pht), 101.22 (C-1'), 81.54 (C-4), 80.82 (C-1), 77.88 (C-5), 73.42 ($PhCH_2$), 70.93 (C-5'), 70.53 (C-3'), 70.38 (C-3), 68.46 (C-2'), 67.89 (C-6), 66.63 (C-4'), 61.24 (C-6'), 54.93 (C-2), 23.73 (SCH_2), 20.52, 20.36, 20.31, 20.13 (4 Ac), 14.76 (CH_3); MS (CI) m/z 791 ($M+NH_4^+$). Anal. Calcd. for $C_{37}H_{43}NO_{15}S$: C, 57.43; H, 5.60. Found: C, 57.60; H, 5.81.

The later fractions contained the compound **8**, also as an amorphous solid (1.45 g, 25%): R_f = 0.25 (cyclohexane-ethyl acetate 1:1); $[\alpha]_D$ +15.8 (c 1, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 7.88, 7.79 (2 m, 4 H, Pht), 7.37-7.23 (m, 5 H, Ph), 5.28 (dd, 1 H, $J_{4',5'}$ = 1, $J_{4',3'}$ = 3.4 Hz, H-4'), 5.15 (d, 1 H, $J_{1,2}$ = 10.8 Hz, H-1), 5.13 (dd, 1 H, $J_{2',1'}$ = 7.8, $J_{2',3'}$ = 10.5 Hz, H-2'), 4.79 (dd, 1 H, H-3'), 4.64, 4.60 (2 d, J = 12.2 Hz, 2 H, $PhCH_2$), 4.49 (m, 1 H, H-3), 4.39 (d, 1 H, H-1'), 4.32 (dd, 1 H, $J_{2,3}$ = 10 Hz, H-2), 4.11 (m, 2 H, H-6a',6b'), 3.97 (br.s, 1 H, OH), 3.94 (m, 1 H, H-5'), 3.89 (d, 1 H, $J_{6a,6b}$ = 11 Hz, H-6a), 3.73 (m, 1 H, H-6b), 3.65 (m, 2 H, H-4, H-5), 2.65 (2 dq, 2 H, J_{gem} = 12.4, J_{vic} = 7.3 Hz, SCH_2), 2.12, 2.02, 1.87, 1.52 (4 s, 12 H, 4 Ac), 1.17 (t, 3 H, J = 7.3 Hz, CH_3); ^{13}C-NMR (62.89 MHz) δ 170.27, 169.98, 169.80, 168.74 (4 O=C, Ac), 168.39, 167.15 (2 O=C, Pht), 138.31 (1 C, Ph), 134.49 (2 CH, Pht), 131.42, 131.32 (2 C, Pht), 128.22, 127.45, 127.42 (3 CH, Ph), 123.75, 123.57 (2 CH, Pht), 100.89 (C-1'), 82.96 (C-3), 80.95 (C-1), 79.78 (C-5), 73.32 ($PhCH_2$), 71.05 (C-5'), 70.71 (C-3'), 69.64 (C-4), 69.57 (C-6), 68.44 (C-2'), 66.76 (C-4'), 61.46 (C-6'), 53.78 (C-2), 23.91 (SCH_2), 20.48, 20.43, 20.30, 19.77 (4 Ac), 14.85 (CH_3); MS (CI) m/z 791 ($M+NH_4^+$). Anal. Calcd. for $C_{37}H_{43}NO_{15}S$: C, 57.43; H, 5.60. Found: C, 57.58; H, 5.75.

Isopropenyl 2,3,4-tri-*O*-benzyl-α,β-L-fucopyranosyl carbonate (10). To a cooled (0°C), stirred solution of 2,3,4-tri-*O*-benzyl-L-fucopyranose **12** (1.55 g, 3.57 mmol) and isopropenyl chloroformate (0.43 mL, 3.92 mmol) in dry CH_2Cl_2 (15 mL) was added dropwise pyridine (0.47 mL, 5.83 mmol). The mixture was stirred at 0°C for 1 h, then diluted with CH_2Cl_2 (50 mL), washed with saturated solution of $NaHCO_3$, H_2O, dried, and concentrated. The residue was applicated to a column of silica gel and eluted with cyclohexane-ethyl acetate (6:1). The earlier fractions contained the pure α-isomer. On concentration, these fractions afforded

a syrup (1.02 g): R_f = 0.58 (cyclohexane-ethyl acetate 2:1); $[\alpha]_D$ -63.5 (c 1, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 7.42-7.27 (m, 15 H, 3 Ph), 6.24 (d, 1 H $J_{1,2}$ = 3.6 Hz, H-1), 5.01 and 4.67 (2 d, 2 H, J = 11.5 Hz, $PhCH_2$), 4.88 and 4.77 (2 d, 2 H, J = 11.8 Hz, $PhCH_2$), 4.83 (d, 1 H, J_{gem} = 1.5 Hz, Ha of H_2C=C), 4.76 (s, 2 H, $PhCH_2$), 4.72 (d, 1 H, Hb of H_2C=C), 4.19 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, H-2), 4.06 (dq, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{5,4}$ < 1 Hz, H-5), 3.94 (dd, 1 H, $J_{3,4}$ = 2.8 Hz, H-3), 3.72 (dd, 1 H, H-4), 1.98 (s, 3 H, Me), 1.19 (d, 3 H, H-6); ^{13}C-NMR (100.57 MHz) δ 152.84, 151.71 (=C, O=C), 138.54, 138.21, 137.94, 128.31-127.33 (Ph), 101.96 (=CH_2), 95.48 (C-1), 78.74, 77.14, 75.07, 69.45 (C-2,3,4,5), 74.88, 73.30, 73.16 (3 $PhCH_2$), 19.00 (Me), 16.56 (C-6); MS (CI) m/z 536 ($M+NH_4^+$).

The second fractions contained both α- and β-isomers (0.61 g).

The later fractions contained the β-isomer as a syrup (0.15 g, the total yield was 97%): R_f = 0.53 (cyclohexane-ethyl acetate 2:1); ^{1}H-NMR (250 MHz) δ 7.45-7.28 (m, 15 H, 3 Ph), 5.47 (d, 1 H, $J_{1,2}$ = 8.0 Hz, H-1), 5.02, 4.71 (2 d, 2 H, J = 11.7 Hz, $PhCH_2$), 4.85-4.73 (m, 6 H, 2 $PhCH_2$, =CH_2), 4.02 (dq, 1 H, $J_{5,6}$ = 6.4 Hz, $J_{5,4}$ < 1 Hz, H-5), 3.69-3.61 (m, 3 H, H-2,3,4), 1.98 (d, 3 H, J < 1 Hz, Me), 1.24 (d, 3 H, H-6); ^{13}C-NMR (62.89 MHz) δ 152.64, 151.82 (=C, O=C), 138.31, 138.29, 138.23, 128.48-127.60 (Ph), 102.22 (=CH_2), 98.35 (C-1), 82.38, 78.09, 75.97, 75.41, 74.74, 73.12, 71.65 (C-2, 3, 4, 5, 3 $PhCH_2$), 19.06 (Me), 16.88 (C-6); MS (CI) m/z 536 ($M+NH_4^+$). Anal. Calcd. for $C_{31}H_{34}O_7$: C, 71.79; H, 6.61. Found: C, 71.75; H, 6.56.

2,3,4-tri-*O*-benzyl-L-fucopyranose (12)[33]. To a stirred suspension of HgO (1.9 g, 9 mmol), boron trifluoride etherate (2.5 mL) in THF (15 mL) was added dropwise a solution of compound **11** (2.9 g, 6 mmol) in THF (15 mL) and water (3 mL) at room temperature. Stirring was continued for an additional hour, then concentrated, ether (25 mL) was added, and the mixture was washed sequentially with saturated $NaHCO_3$ solution, KI solution (10%) and water, dried over $MgSO_4$, and concentrated. The residue was eluted from a column of silica gel with cyclohexane-ethyl acetate (2:1) to give **12** as a white solid (2.1 g, 80%, α:β = 1.5:1): R_f = 0.3 (cyclohexane-ethyl acetate 2:1); ^{1}H-NMR (250 MHz) δ 7.45–7.26 (m, Ph), 5.25 (dd, 0.6 H, $J_{1,2}$ = 3.3 Hz, $J_{1,OH}$ = 1.7 Hz, H-1α), 3.25 (d, 0.4 H, $J_{OH,1}$ = 7.1 Hz, OH), 3.02 (d, 0.6 H, OH), 1.22 (d, 1.2 H, $J_{6,5}$ = 6.4 Hz, H-6β), 1.16 (d, 1.8 H, $J_{6,5}$ = 6.5 Hz, H-6α); ^{13}C-NMR (62.89 MHz) δ 138.67, 138.00, 137.92, 137.73, 137.69, 137.57, 128.56-127.56 (Ph), 100.77 (C-1β), 96.06 (C-1α), 15.97, 15.68 (C-6α,6β); MS (CI) m/z 452 ($M+NH_4^+$). Anal. Calcd. for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96. Found: C, 74.90; H, 6.77.

(3+3) Glycosylation[18]**: 6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactosyl)-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-glucopyranose (14).** A suspension of phenyl 6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-1-thio-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside[21] (50 mg, 40 μmol), **4**[11] (25 mg, 20 μmol) and 4Å ground molecular sieves (0.4 g) in dry acetonitrile (3 mL) was stirred for 0.5 h under argon at room temperature. Tris (4-bromophenyl)ammoniumyl hexachloroantimonate (150 mg, 183 μmol) was added. The mixture was kept at room temperature for 2 h, TLC showed the disappearance of the donor. The mixture was neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted

from a column of silica gel with cyclohexane-ethyl acetate (1:1) to give a syrup (50 mg): R_f = 0.25 (cyclohexane-ethyl acetate 1:1); ^{1}H- and ^{13}C-NMR revealed a mixture of **4** and **14** (1:2). The mixture was then eluted from a column of silica gel with dichloromethane-ethyl acetate (3:1) to give compound **14** (33 mg) as an amorphous solid (α-isomer predominant, as described by Sato *et al.*[34]): R_f = 0.56 (dichloromethane-ethyl acetate 3:1); ^{13}C-NMR (62.89 MHz) δ 170.02, 169.98, 169.82, 168.72 (4 O=C, Ac), 138.78, 138.57, 138.08, 137.57, 134.18, 131.61, 128.66-126.92, 123.56 (arom. C), 99.51 (C-1"), 97.29 (C-1'), 92.96 (C-1), 79.76, 76.95, 74.99, 74.41, 74.07, 73.59, 72.78, 72.27, 71.95, 70.90, 70.23, 68.85, 67.66, 66.63, 66.36 (ring C, $PhCH_2$, C-6), 60.09 (C-6"), 58.18 (C-2), 20.69, 20.61, 20.52, 20.42 (4 Ac), 16.68 (C-6'); MS (CI) m/z 1163 ($M+NH_4^+$).

Eluted second was **4** (16 mg): R_f = 0.33 (dichloromethane-ethyl acetate 3:1).

(3+3) Glycosylation[10]: 1,5-anhydro-6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-*arabino*-hex-1-enitol (13) and **6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-glucopyranose (14).**

A. Methyl triflate (36 μL, 0.32 mmol) was added to a stirred mixture of **2** (75 mg, 63 μmol), trimannoside **4** (26 mg, 21 μmol), and 4Å ground molecular sieves (0.5 g) in dry ether (5 mL) at room temperature under argon. After 7 days, triethylamine (0.1 mL) was added, the mixture was stirred for 10 min, then filtered through Celite, and concentrated. The residue was purified by flash chromatography (cyclohexane-ethyl acetate 1:1) to yield **13** (36 mg, 51%) as a syrup: R_f = 0.44 (cyclohexane-ethyl acetate 1:1); $[\alpha]_D$ -37 (c 1, $CHCl_3$, Lit.[10b] -39 , c 0.7, CH_2Cl_2); ^{1}H-NMR (250 MHz) δ 7.76-7.70, 7.64-7.59 (2 m, 4 H, Pht), 7.45-7.05 (m, 4 Ph), 6.71 (s, 1 H, H-1), 5.40 (dd, 1 H, $J_{4",3"}$ = 2.9 Hz, $J_{4",5"}$ < 1 Hz, H-4"), 5.29 (dd, 1 H, $J_{2",3"}$ = 10.4, $J_{2",1"}$ = 7.9 Hz, H-2"), 5.02 (dd, 1 H, H-3"), 2.18, 2.09, 2.02, 1.95 (4 s, 12 H, 4 Ac), 0.87 (d, 3 H, $J_{6',5'}$ = 6.4 Hz, H-6'); ^{13}C-NMR (62.89 MHz) δ 170.46, 170.30, 170.12, 169.20 (4 O=C, Ac), 167.94 (O=C, Pht), 145.82 (C-1), 138.82, 138.49, 138.26, 137.77 (4 C, Ph), 133.76, 132.08, 128.43-127.33, 123.20 (arom. C), 107.61 (C-2), 100.49 (C-1"), 98.92 (C-1'), 79.04-66.82 (ring C, $PhCH_2$, C-6), 61.25 (C-6"), 20.70 (2 Ac), 20.58 (Ac), 20.51 (Ac); MS (CI) m/z 1145 ($M+NH_4^+$).

Eluted second was **14** (17 mg, 24%).

B. Methyl triflate (36 μL, 0.32 mmol) was added to a stirred mixture of **2** (75 mg, 63 μmol), trimannoside **4** (29 mg, 23 μmol), and 4 Å ground molecular sieves (0.5 g) in dry dichloromethane (5 mL) at room temperature under argon. After 2 days, TLC revealed the disappearance of **2**. Triethylamine (0.1 mL) was added, the mixture was stirred for 10 min, filtered through Celite, and concentrated. The residue was purified by flash chromatography (toluene-ethyl acetate 2:1) to yield **13** (40 mg, 56%).

Eluted second was a mixture of two compounds (60 mg), which was purified by flash chromatography (dichloromethane-ethyl acetate 3:1) to yield first **14** (30 mg, 41%), eluted second was the unreacted trimannoside **4** (27 mg).

Methyl 2,4-di-*O*-benzyl-3,6-di-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-(2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)-α-D-mannopyranosyl]-α-D-mannopyranoside (19). Methyl triflate (56 μL,

0.5 mmol) was added to a stirred mixture of ethyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside **18** (72 mg, 120 μmol), methyl 2,4-di-*O*-benzyl-3,6-di-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside **5** (50 mg, 40 μmol), and 4Å ground molecular sieves (0.5 g) in dry ether (5 mL) at room temperature under argon. Triethylamine (0.1 mL) was added after 40 h. The mixture was stirred for 10 min, filtered through Celite, and concentrated. The residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 3:1) to yield **19** as a syrup (80 mg, 86%): R_f = 0.47 (cyclohexane-ethyl acetate 2:1); $[\alpha]_D$ +27 (c 0.5, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 8.03-7.99 (m, 4 H, Bz), 7.51-7.07 (m, 76 H, arom.), 5.43 (dd, 1 H, $J_{2,1}$ = 7.9, $J_{2,3}$ = 9.3 Hz, H-2c), 5.29 (dd, 1 H, $J_{2,1}$ = 8.1, $J_{2,3}$ = 9.6 Hz, H-2c'), 5.08 (d, 1 H, $J_{1,2}$ = 1.2 Hz, H-1d), 4.75 (d, 1 H, H-1c), 4.07 (d, 1 H, H-1c'), 3.86 (dd, 1 H, $J_{3,4}$ = 9.3 Hz, H-3c), 3.41 (dd, 1 H, $J_{3,4}$ = 9.1 Hz, H-3c'), 3.17 (s, 3 H, OMe); ^{13}C-NMR (62.89 MHz) δ 164.97, 164.89 (2 O=C, Bz), 138.94, 138.89, 138.67, 138.60, 138.29, 138.06, 138.00, 137.92, 137.87, 130.33, 129.75, 128.62, 128.41-127.03, 126.01 (arom. C), 100.14, 99.90, 99.06, 97.85 (C-1c, 1c', 1d, 1d', 1e), 82.79, 82.19, 77.98-69.23 (ring C, $PhCH_2$), 54.65 (OMe). Anal. Calcd. for $C_{143}H_{146}O_{28}$: C, 74.26; H, 6.36. Found: C, 74.30; H, 6.29.

Methyl 2,4-di-*O*-benzyl-3,6-di-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-(2-deoxy-2-phthalimido-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl)-α-D-mannopyranosyl]-β-D-mannopyranoside (21)[25]. A solution of methyl 2,4-di-*O*-benzyl-3,6-di-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-β-D-mannopyranoside **4** (58 mg, 47 μmol), s-collidine (46 μL), 4Å ground molecular sieves (0.25 g) in dichloromethane (1.5 mL) was stirred at room temperature under argon for 1 h. Silver triflate (90 mg, 0.35 mmol) was introduced and the mixture was cooled to -40°C, then a solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl bromide **20** (89 mg, 0.18 mmol) in dichloromethane (1.5 mL) was added dropwise during 45 min, and the reaction mixture was allowed to gradually warm to room temperature, with stirring continued for an additional 15 h. The mixture was filtered through Celite and the solids were thoroughly washed with dichloromethane. The combined filtrate and washings were washed successively with 3% of aqueous HCl solution, saturated $NaHCO_3$ solution, and water, dried, and concentrated. The residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 1:1 to 1:2) to yield **21** (52 mg, 53%) as an amorphous solid: R_f = 0.39 (toluene-ethyl acetate 2:1); $[\alpha]_D$ -11.5 (c 1, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 7.93-7.59, 7.43-7.07, 6.98-6.95 (m, arom. H), 5.85 (d, 1 H, $J_{3,4}$ = 9.2, $J_{3,2}$ = 10.8 Hz, H-3c), 5.60 (d, 1 H, $J_{1,2}$ = 8.5 Hz, H-1c), 5.56 (dd, 1 H, $J_{3',4'}$ = 9.1, $J_{3',2'}$ = 10.9 Hz, H-3c'), 5.26 (dd, 1 H, $J_{4,5}$ = 10.2 Hz, H-4c), 5.08 (d, 1 H, $J_{1,2}$ = 8.5 Hz, H-1c'), 5.04 (dd, 1 H, $J_{4',5'}$ = 10.2 Hz, H-4c'), 3.51 (s, 3 H, OMe), 2.10, 2.07, 2.04, 1.99, 1.90, 1.88 (6 s, 18 H, 6 Ac); ^{13}C-NMR (100.57 MHz) δ 170.66, 170.58, 170.17, 170.08, 169.42, 169.19 (6 O=C, 6 Ac), 167.60, 167.03 (2 O=C, 2 Pht), 138.55, 138.52, 138.30, 138.25, 138.23, 137.98, 137.78, 134.30, 134.05, 131.58, 128.74, 128.36, 128.15-127.09, 125.86, 123.65, 123.34 (arom. C), 102.73 (C-1e), 98.58, 97.66, 96.51, 95.44 (C-1c, 1c', 1d, 1d'), 80.71, 77.98, 77.75, 76.51, 74.51, 74.14, 74.09, 72.71, 72.52, 71.90, 71.49, 70.81, 68.93, 68.27, 66.89, 65.61 (ring C), 75.15, 74.63, 73.45, 72.63, 72.16, 71.13, 69.94, 69.72, 69.30, 66.22, 62.31, 61.09, 61.03 (8 $PhCH_2$, 5 C-6), 57.35 (OMe), 54.21, 54.14 (C-2c,2c'), 20.75, 20.63, 20.60, 20.59, 20.45, 20.44 (6 Ac). Anal. Calcd. for $C_{115}H_{120}N_2O_{34}$: C, 66.59 ; H, 5.83. Found: C, 66.32 ; H, 5.91.

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-[6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-α-D-glucopyranoside (24). Methyl triflate (37 μL, 0.33 mmol) was added to a stirred mixture of **2** (80 mg, 67 μmol), methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **23** (31 mg, 67 μmol), and 4Å ground molecular sieves (0.5 g) in dry ether (5 mL) at room temperature under argon. After 40 h, triethylamine (0.1 mL) was added, the mixture was stirred for 10 min, filtered through Celite, and concentrated. The residue was purified by flash chromatography (cyclohexane-ethyl acetate 2:1) to yield **24** (65 mg, 61%): R_f = 0.57 (cyclohexane-ethyl acetate 1:1); mp 76-77°C (dichloromethane-cyclohexane-ethyl acetate); $[\alpha]_D$ +10.5 (c 1.5, $CHCl_3$); ^{1}H-NMR (250 MHz) δ 7.59-7.49, 7.41-6.99 (m, aromatic H), 5.24 (dd, 1 H, $J_{4,3}$ = 3.3, $J_{4,5}$ < 1 Hz, H-4a), 5.13 (d, 1 H, $J_{1,2}$ = 8.5 Hz, H-1c), 5.03 (dd, 1 H, $J_{2,3}$ = 10.2, $J_{2,1}$ = 8.2 Hz, H-2a), 3.11 (s, 3 H, OMe), 2.02, 2.01, 1.96, 1.65 (4 s, 12 H, 4 Ac), 1.20 (d, 3 H, $J_{6,5}$ = 6.5 Hz, H-6b); ^{13}C-NMR (62.89 MHz) δ 170.02, 169.94, 169.81, 168.69 (4 O=C, Ac), 168.0, 167.5 (2 O=C, Pht), 138.82, 138.73, 138.62, 138.17, 138.11, 137.91, 137.83 (7 C, arom.), 133.84, 128.54-126.93, 123.31 (arom. C), 99.46 (C-1a), 98.70 (C-1c), 97.59, 97.47 (C-1b,1d), 81.72, 79.77, 77.15, 75.37, 74.58, 74.13, 73.48, 73.20, 72.70, 72.59, 72.28, 70.93, 70.32, 69.27, 69.03 (ring C, $PhCH_2$), 66.74, 66.40 (C-6c,6d), 60.20 (C-6a), 56.09 (C-2c), 54.73 (OMe), 20.66 (Ac), 20.54 (Ac), 20.47 (2 Ac), 16.67 (C-6b); MS (CI) m/z 1610 ($M+NH_4^+$). Anal. Calcd. for $C_{90}H_{97}NO_{25}$: C, 67.87; H, 6.14. Found: C, 67.87; H, 6.15.

Ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (26). To a cooled (-25°C), stirred mixture of **25** (2.8 g, 6.35 mmol), **10** (3.8 g, 7.3 mmol), activated 4Å ground molecular sieves (8 g), and dry ether (100 mL) was added dropwise TMSOTf (1.5 mL, 8 mmol). Stirring was continued for an additional 1 h at -25°C, then the mixture was neutralized with Et_3N, diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was eluted from a column of silica gel with cyclohexane-ethyl acetate (4:1) to give **26** (5.2 g, 95%) as a white amorphous solid: R_f = 0.41 (cyclohexane-ethyl acetate 3:1); $[\alpha]_D$ -37 (c 1, CH_2Cl_2, Lit[10a] -36 , c 1, CH_2Cl_2); ^{1}H-NMR (400 MHz) δ 7.78–7.05 (m, arom. H), 5.57 (s, 1 H, PhCH), 5.49 (d, 1 H, $J_{1,2}$ = 10.7 Hz, H-1), 4.84 (d, 1 H, $J_{1',2'}$ = 3.1 Hz, H-1'), 4.81, 4.51 (2 d, 2 H, J = 11.5 Hz, $PhCH_2$), 4.45 (dd, 1 H, $J_{2,3}$ = 10.7 Hz, H-2), 4.45, 4.41 (2 d, 2 H, J = 12 Hz, $PhCH_2$), 4.29, 3.88 (2 d, 2 H, J = 12.5 Hz, $PhCH_2$), 4.08 (dq, 1 H, $J_{4',5'}$ < 1 Hz, $J_{5',6'}$ = 6.5 Hz, H-5'), 3.71 (dd, 1 H, $J_{2',3'}$ = 9.8 Hz, H-2'), 2.71 (2 dq, 2 H, J_{gem} = 12.0, J_{vic} = 7.5 Hz, SCH_2), 1.23 (t, 3 H, J = 7.5 Hz, CH_3), 0.89 (d, 3 H, H-6'); ^{13}C-NMR (62.89 MHz) δ 168.35, 167.79 (2 O=C, Pht), 138.84–123.29 (arom. C), 101.16 (PhCH), 99.46 (C-1'), 82.04 (C-1), 79.65, 78.00, 76.37, 75.50, 74.75, 73.11, 72.74, 70.61, 68.64, 67.29 (C-3,4,5,6, C-2',3',4',5', 3 $PhCH_2$), 54.66 (C-2), 24.12 (SCH_2), 16.43 (C-6'), 14.93 (CH_3); MS (CI) m/z 875 ($M+NH_4^+$). Anal. Calcd. for $C_{50}H_{51}NO_{10}S$: C, 69.99; H, 5.99. Found: C, 70.16; H, 5.93.

Ethyl 6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2, 3, 4, 6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-1-thio-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (29). A solution of silver triflate (770 mg, 3 mmol) and s-collidine (0.3 mL) in dry dichloromethane (6 mL) and toluene

(4 mL) was added dropwise at -25°C to a stirred solution of **27** (780 mg, 0.9 mmol) and 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide **28** (1.19 g, 1.8 mmol) in toluene (8 mL) containing 4Å ground molecular sieves (2 g) under argon. When TLC indicated complete reaction, 10% aqueous sodium thiosulfate (10 mL) and toluene (30 mL) were added. The mixture was filtered through Celite. The organic layer was separated and washed with water, dried, and concentrated. The residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 2.5:1) to yield **29** (453 mg, 35%) as an amorphous solid: R_f = 0.45 (cyclohexane-ethyl acetate 2:1); $[\alpha]_D$+10.7 (c 1, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 8.17-7.09 (m, 44 H, arom.), 5.85 (dd, 1 H, $J_{4",3"}$ = 3.8, $J_{4",5"}$ = 0.9 Hz, H-4"), 5.76 (dd, 1 H, $J_{2",3"}$ = 10.4, $J_{2",1"}$ = 8.3 Hz, H-2"), 5.41 (dd, 1 H, H-3"), 5.17 (d, 1 H, $J_{1,2}$ = 10.5 Hz, H-1), 5.08 (d, 1 H, H-1"), 5.07 (d, 1 H, $J_{1',2'}$ = 3.6 Hz, H-1'), 4.89, 4.49 (2 d, 2 H, J = 12.1 Hz, $PhCH_2$), 4.78 (dq, 1 H, $J_{5',6'}$ = 6.4 Hz, $J_{5',4'}$ < 1 Hz, H-5'), 4.71, 4.23 (2 d, 2 H, J = 11 Hz, $PhCH_2$), 4.48 (dd, 1 H, $J_{2,3}$ = 9 Hz, H-2), 3.83 (dd, 1 H, $J_{2',3'}$ = 10 Hz, H-2'), 2.64 (2 dq, 2 H, J_{vic} =7.5, J_{gem} = 12.5 Hz, SCH_2), 1.46 (d, 3 H, H-6'), 1.17 (t, 3 H, J = 7.5 Hz, CH_3); ^{13}C-NMR (62.89 MHz) δ 167.36 (2 O=C, Pht), 165.87, 165.84, 165.35, 164.81 (4 O=C, Bz), 139.02, 138.87, 138.30, 137.91, 134.14, 133.58, 133.42, 133.34, 131.78, 129.94-126.73, 123.61 (arom. C), 99.93 (C-1"), 96.87 (C-1'), 81.21 (C-1), 79.38-68.40 (ring C), 75.15, 73.74, 72.86, 72.07 (4 $PhCH_2$), 67.86 (C-6), 66.76 (C-5'), 61.37 (C-6"), 55.38 (C-2), 23.69 (SCH_2), 16.91 (C-6'), 14.87 (CH_3); MS (CI) m/z 1455 ($M+NH_4^+$). Anal. Calcd. for $C_{84}H_{79}NO_{19}S$: C, 70.13; H, 5.53. Found: C, 70.00; H, 5.55.

Phenyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (30). Sodium (20 mg) was added to a solution of 2.8 g (4.8 mmol) of phenyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside in MeOH-CH_2Cl_2(30 mL, 5:1) at room temperature. The reaction mixture was neutralised by Amberlite resin (IR 120, H^+ form) when the reaction was complete (6 h). After filtration and concentration, the residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 3:1) to afford **30** as a syrup (2.53 g, 97%): R_f = 0.44 (cyclohexane-ethyl acetate 2:1); $[\alpha]_D$+182.5 (c 1.26, $CHCl_3$, Lit.[31] +179.4 (c 1.78, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 7.49-7.19 (m, 20 H, 4 Ph), 5.62 (d, 1 H, $J_{1,2}$ = 1.5 Hz, H-1), 4.85, 4.54 (2 d, 2 H, J = 10.8 Hz, $PhCH_2$), 4.73 (s, 2 H, $PhCH_2$), 4.63, 4.47 (2 d, 2 H, J = 11.9 Hz, $PhCH_2$), 4.31 (ddd, 1 H, $J_{5,4}$ = 9.5, $J_{5,6a}$ = 4.5, $J_{5,6b}$ = 1.9 Hz, H-5), 4.27 (ddd, 1 H, $J_{2,3}$ = 3.2, $J_{2,OH}$ = 3.0 Hz, H-2), 3.95 (dd, 1 H, $J_{4,3}$ = 9.0 Hz, H-4), 3.89 (dd, 1 H, H-3), 3.81 (dd, 1 H, $J_{6a,6b}$ = 11.0 Hz, H-6a), 3.69 (dd, 1 H, H-6b), 2.73 (d, 1 H, OH); ^{13}C-NMR (62.89 MHz) δ 138.32, 138.19, 137.73 (3 C, Ph), 133.98 (1 C, PhS), 131.61-127.43 (20 CH, 3 Ph, PhS), 87.47 (C-1), 80.33 (C-3), 75.21 ($PhCH_2$), 74.54 (C-4), 73.39 ($PhCH_2$), 72.31 (C-5), 72.07 ($PhCH_2$), 69.88 (C-2), 68.90 (C-6); MS (CI) m/z 482 ($M+NH_4^+$).

Phenyl 3,4,6-tri-*O*-benzyl-2-*O*-[6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2, 3, 4, 6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-3-*O*-(2, 3, 4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-gluco-pyranosyl]-1-thio-α-D-mannopyranoside (31).

Method 1: Methyl triflate (72 μL, 0.66 mmol) was added to a stirred mixture of **29** (190 mg, 0.132 mmol), **30** (71 mg, 0.132 mmol), and 4Å ground molecular sieves (0.6 g) in dry ether (8 mL) at room temperature under argon. Triethylamine (0.1 mL) was added after 5 days, the mixture was stirred for 10 min, filtered

through Celite, and concentrated. The residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 3:1) to yield **31** as an amorphous solid (152 mg, 60%): R_f = 0.52 (cyclohexane-ethyl acetate 2:1); $[\alpha]_D$ +33.5 (c 0.6, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 8.17, 8.03, 7.96, 7.83, 7.68-7.57, 7.52-7.07 (m, arom. H), 5.84 (dd, 1 H, $J_{4,3}$ = 3.5, $J_{4,5}$ = 0.7 Hz, H-4a), 5.74 (dd, 1 H, $J_{2,3}$ = 10.3, $J_{2,1}$ = 8.2 Hz, H-2a), 5.40 (dd, 1 H, H-3a), 5.24 (d, 1 H, $J_{1,2}$ = 8.6 Hz, H-1c), 5.20 (d, 1 H, $J_{1,2}$ = 2.5 Hz, H-1d), 5.07 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1b), 5.05 (d, 1 H, H-1a), 1.43 (d, 3 H, $J_{6,5}$ = 6.5 Hz, H-6b); ^{13}C-NMR (100.57 MHz) δ 168.98, 167.12 (2 O=C, Pht), 165.87, 165.72, 165.27, 164.66 (4 O=C, Bz), 138.95, 138.87, 138.40, 138.23, 138.23, 138.00, 137.73 (7 C, arom.), 133.35, 130.91, 129.87, 129.65, 129.61, 128.76-126.60, 123.16 (arom. C), 99.94 (C-1a), 96.92 (C-1c), 96.61 (C-1b), 84.55 (C-1d), 79.33, 79.08, 78.04, 75.68, 75.33, 74.96, 74.89, 72.16, 72.10, 71.65, 71.39, 69.76, 68.28, 66.61 (ring C), 75.05 ($PhCH_2$), 73.80 (2 $PhCH_2$), 72.46 (3 $PhCH_2$), 72.03 ($PhCH_2$), 69.93, 68.06 (C-6c,6d), 61.34 (C-6a), 56.10 (C-2c), 16.79 (C-6b); MS (CI) m/z 1935 ($M+NH_4^+$).

Method 2: A solution of silver triflate (385 mg, 1.5 mmol) and s-collidine (0.13 mL) in dichloromethane (4.5 mL) and toluene (3 mL) was added dropwise at -20°C to a stirred solution of **34** (850 mg, 0.63 mmol) and 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide **28** (837 mg, 1.27 mmol) in toluene (7.5 mL) containing 4Å ground molecular sieves (2 g) under argon. 10% aqueous sodium thiosulfate (10 mL) and toluene (30 mL) were added after 0.5 h, and the mixture was filtered through Celite. The organic layer was separated and washed with water, dried, and concentrated. The residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 3:1) to yield **31** as an amorphous solid (943 mg, 78%). Anal. Calcd. for $C_{115}H_{107}NO_{24}S$: C, 71.97; H, 5.62. Found: C, 72.04; H, 5.47.

Phenyl 3, 4 ,6-tri-*O*-benzyl-2-*O*-[6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2, 3, 4, 6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-*O*-(2, 3, 4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-gluco-pyranosyl]-1-thio-α-D-mannopyranoside (32). Methyl triflate (164 μL, 1.5 mmol) was added to a stirred mixture of **2** (357 mg, 0.3 mmol), **30** (162 mg, 0.3 mmol), and 4Å ground molecular sieves (1 g) in dry ether (15 mL) under argon at room temperature. Triethylamine (0.3 mL) was added after 5 days. The mixture was stirred for 15 min, filtered through Celite, and concentrated. The residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 2:1) to yield **32** as an amorphous solid (250 mg, 50%): R_f = 0.32 (cyclohexane-ethyl acetate 2:1); $[\alpha]_D$ +35 (c 0.85, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 7.44-7.06 (m, arom. H), 5.30 (d, 1 H, $J_{1,2}$ = 8.4 Hz, H-1c), 5.28 (d, 1 H, $J_{1,2}$ = 2.5 Hz, H-1d), 5.27 (dd, 1 H, $J_{4,3}$ = 3.6, $J_{4,5}$ = 0.8 Hz, H-4a), 5.04 (dd, 1 H, $J_{2,3}$ = 10.4, $J_{2,1}$ = 8.2 Hz, H-2a), 4.81 (dd, 1 H, H-3a), 4.78 (d, 1 H, $J_{1,2}$ = 3.4 Hz, H-1b), 4.74 (d, 1 H, H-1a), 2.05, 2.04, 1.98, 1.87 (4 s, 12 H, 4 Ac), 1.22 (d, 3 H, $J_{6,5}$ = 6.5 Hz, H-6b); ^{13}C-NMR (62.89 MHz) δ 170.08, 169.98, 169.84, 168.66 (4 O=C, Ac), 169.16, 167.10 (2 O=C, Pht), 138.93, 138.67, 138.48, 138.29, 138.25, 138.15, 137.76, 134.19, 133.82, 130.98 129.05-126.98, 123.25 (arom. C), 99.56 (C-1a), 97.35 (C-1b), 97.02 (C-1c), 84.62 (C-1d), 79.69, 78.19, 75.37, 75.24, 75.05, 74.73, 72.25, 70.98, 70.41, 69.02, 66.81, 66.45 (ring C), 74.57, 74.17, 73.72, 72.71, 72.54, 72.41 (7 $PhCH_2$), 69.99, 68.28 (C-6c,6d), 60.34 (C-6a), 56.23 (C-2c), 20.70 (Ac), 20.61 (Ac), 20.54 (2 Ac), 16.73 (C-6b); MS (CI) m/z 1687 ($M+NH_4^+$). Anal. Calcd. for $C_{95}H_{99}NO_{24}S$: C, 68.29; H, 5.97. Found: C, 68.15; H, 6.05.

Phenyl 3, 4, 6-tri-*O*-benzyl-2-*O*-[4, 6-*O*-benzylidene-2-deoxy-2-phthalimido-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-1-thio-α-D-mannopyranoside (33). Methyl triflate (1.1 mL, 10 mmol) was added to a stirred mixture of **26** (1.98 g, 2.3 mmol), **30** (1.25 g, 2.3 mmol), and 4Å ground molecular sieves (6 g) in dry ether (100 mL) at room temperature under argon. Triethylamine (1 mL) was added after 3 days. The mixture was stirred for 20 min, filtered through Celite, and concentrated. The residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 5:1) to yield **33** as an amorphous solid (2.5 g, 81%): R_f = 0.43 (cyclohexane-ethyl acetate 3:1); $[\alpha]_D$ +37 (c 1.2, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 7.56-7.02 (m, arom. H), 5.58 (s, 1 H, PhCH), 5.49 (d, 1 H, $J_{1',2'}$ = 8.35 Hz, H-1'), 5.28 (1 H, $J_{1,2}$ = 2.1 Hz, H-1), 4.83 (d, 1 H, $J_{1'',2''}$ = 3 Hz, H-1''), 0.89 (d, 3 H, $J_{6'',5''}$ = 6.4 Hz, H-6''); ^{13}C-NMR (100.57 MHz) δ 168.73, 167.57 (2 O=C, Pht), 138.74, 138.41, 138.27, 138.19, 137.75, 136.99, 133.98, 133.40, 130.74, 128.93, 128.28-127.10, 126.92, 125.95, 122.76 (arom. C), 101.08 (PhCH), 99.33 (C-1''), 97.51 (C-1'), 84.60 (C-1), 81.67, 79.42, 78.44, 77.87, 76.29, 75.42, 75.33, 75.00, 72.36, 67.15, 66.38 (ring C), 74.79, 74.58, 72.97, 72.47, 72.43, 71.70 (6 $PhCH_2$), 69.69, 68.41 (C-6,6'), 55.52 (C-2'), 16.30 (C-6''); MS (CI) m/z 1355 ($M+NH_4^+$). Anal. Calcd. for $C_{81}H_{79}NO_{15}S$: C, 72.68; H, 5.95. Found: C, 72.44; H, 5.82.

Phenyl 3,4,6-tri-*O*-benzyl-2-*O*-[6-*O*-benzyl-2-deoxy-2-phthalimido-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-1-thio-α-D-mannopyranoside (34). Aluminium trichloride (1.87 g, 14 mmol) was added at room temperature to a solution of compound **33** (3.5 g, 2.6 mmol) and trimethylamine-borane complex (0.95 g, 13 mmol) in tetrahydrofuran (40 mL). The solution was stirred at 60°C for 18 h. The mixture was cooled to room temperature and partitioned between ice-cold M sulfuric acid and toluene. The organic layer was washed with aqueous sodium hydrogencarbonate, water, dried, and concentrated. The residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 4:1) to yield **34** as an amorphous solid (2.72 g, 78%): R_f = 0.36 (cyclohexane-ethyl acetate 3:1); $[\alpha]_D$ +52 (c 2.8, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 7.57-6.98 (m, arom. H), 5.56 (d, 1 H, $J_{1',2'}$ = 8.6 Hz, H-1'), 5.49 (1 H, $J_{1,2}$ = 2.2 Hz, H-1), 4.91, 4.62 (2 d, 2 H, J = 11.8 Hz, $PhCH_2$), 4.89, 4.57 (2 d, 2 H, J = 11.6 Hz, $PhCH_2$), 4.88 (d, 1 H, $J_{1'',2''}$ = 3.1 Hz, H-1''), 1.09 (d, 3 H, $J_{6'',5''}$ = 6.5 Hz, H-6''); ^{13}C-NMR (100.57 MHz) δ 169.23, 167.73 (2 O=C, Pht), 138.68, 138.46, 138.39, 138.34, 138.04, 137.97, 134.29, 133.34, 130.95, 128.77, 128.37-127.37, 127.15, 126.97, 122.67 (arom. C), 100.71 (C-1''), 96.94 (C-1'), 84.71 (C-1), 83.02, 78.62, 77.93, 77.76, 75.34, 74.83, 73.85, 72.51, 71.33, 68.38 (ring C), 74.65, 73.52, 73.52, 73.23, 72.55, 72.25, 70.81, 70.00, 69.49 (7 $PhCH_2$, C-6, C-6'), 54.39 (C-2'), 16.39 (C-6''); MS (CI) m/z 1357 ($M+NH_4^+$). Anal. Calcd. for $C_{81}H_{81}NO_{15}S$: C, 72.57; H, 6.09. Found: C, 72.62; H, 6.12.

Methyl 2, 4-di-*O*-benzyl-3, 6-di-*O*-{3, 4, 6-tri-*O*-benzyl-2-*O*-[6-*O*-benzyl-2-deoxy-2-phtalimido-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-α-D-mannopyranosyl}-β-D-mannopyranoside (36) and **Methyl *O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-[(3,4,6-tri-*O*-benzyl-α-L-fucopyranosyl)-(1 → 3)]-*O*-(6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-**

(1→2)-*O*-(3, 4, 6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)-2, 4-di-*O*-benzyl-β-D-mannopyranoside (37). A mixture of **31** (690.9 mg, 0.36 mmol), methyl 2,4-di-*O*-benzyl-β-D-mannopyranoside **35** (33.7 mg, 0.09 mmol), and 4Å ground molecular sieves (1 g) in dichloromethane (10 mL) was stirred for 0.5 h at room temperature under argon. *N*-iodosuccinimide (121.5 mg, 0.54 mmol) was introduced at 0°C, and a solution of trifluoromethanesulfonic acid in dichloromethane (0.3 mL, 0.12 M) was added dropwise. The mixture was stirred for 0.5 h at 0°C. The acid was then neutralized with a few drops of triethylamine. The mixture was filtered through Celite, the solids were thoroughly washed with dichloromethane, and the combined filtrate and washings were washed successively with water, sat. sodium hydrogencarbonate solution, and 10% sodium thiosulfate solution, dried, and concentrated. The residue was flash chromatographed on a column of silica gel (cyclohexane-ethyl acetate 2:1) to give a syrup, which was filtered on a column of Sephadex LH-20 (dichloromethane-methanol 1:1) to yield **36** as an amorphous solid (216 mg, 60%): R_f = 0.33 (cyclohexane-ethyl acetate 2:1); $[\alpha]_D$-23 (c 1.4, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 8.22-8.17, 8.09-8.02, 7.97-7.92, 7.87-7.82, 7.71-7.00, 6.91-6.85 (m, arom. H); 5.88 (dd, 1 H, $J_{2,1}$ = 8.5, $J_{2,3}$ = 10.3 Hz, H-2a), 5.86 (dd, 1 H, $J_{4,3}$ = 3.6 Hz, $J_{4,5}$ < 1 Hz, H-4a), 5.85 (dd, 1 H, $J_{4',3'}$ = 3.6 Hz, $J_{4',5'}$ < 1 Hz, H-4a'), 5.81 (dd, 1 H, $J_{2',1'}$ = 8.5, $J_{2',3'}$ = 10.3 Hz, H-2a'); 5.43 (dd, 1 H, H-3a), 5.42 (dd, 1 H, H-3a'), 5.32 (d, 1 H, $J_{1,2}$ = 8.5 Hz, H-1c), 5.21 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1b), 5.14 (d, 1 H, $J_{1',2'}$ = 3.5 Hz, H-1b'), 5.11 (d, 1 H, $J_{1,2}$ = 8.7 Hz, H-1a), 5.10 (d, 1 H, $J_{1',2'}$ = 8.7 Hz, H-1a'), 5.08 (d, 1 H, $J_{1',2'}$ = 8.5 Hz, H-1c'), 4.70 (d, 1 H, $J_{1,2}$ < 1 Hz, H-1d), 4.33 (d, 1 H, $J_{1,2}$ < 1 Hz, H-1e), 4.09 (d, 1 H, $J_{1',2'}$ < 1 Hz, H-1d'), 3.10 (s, 3 H, OMe), 1.62 (d, 3 H, $J_{6,5}$ = 6.5 Hz, H-6b), 1.51 (d, 3 H, $J_{6',5'}$ = 6.5 Hz, H-6b'); ^{13}C-NMR (100.57 MHz) δ 168.89, 167.57 (2 O=C, Pht), 168.76, 167.11 (2 O=C, Pht), 165.94, 165.91, 165.82, 165.72, 165.29, 165.29, 164.83, 164.66 (8 O=C, Bz), 139.12-137.71, 133.57-133.26, 132.33-131.77, 129.92-126.56, 125.48, 123.47, 123.25, 122.89 (arom. C), 101.90 (C-1e), 100.92 (C-1d), 100.08 (C-1a), 99.98 (C-1a'), 99.06 (C-1c), 98.84 (C-1c'), 96.82 (C-1b), 96.06 (C-1d'), 96.02 (C-1b'), 80.78, 79.85, 79.55, 79.49, 79.11, 77.65, 77.53, 76.11-71.43, 70.57-69.66, 68.52, 68.38, 67.78, 66.53 (ring C, $PhCH_2$), 61.45, 61.36 (C-6a,6a'), 56.65 (C-2c), 56.63 (OMe), 55.98 (C-2c'), 16.99 (C-6b), 16.89 (C-6b'). Anal. Calcd. for $C_{239}H_{228}N_2O_{54}$: C, 71.90; H, 5.76. Found: C, 71.95; H, 5.94.

Eluted second was pentasaccharide **37**, obtained as an amorphous solid (16.2 mg, 8%): R_f = 0.32 (cyclohexane-ethyl acetate 2:1); $[\alpha]_D$-33.7 (c 1.6, $CHCl_3$); ^{1}H-NMR (400 MHz) δ 8.17, 8.04, 7.96, 7.83 (4 m, 8 H, Bz), 7.67-7.03 (m, arom. H), 5.84 (dd, 1 H, $J_{4,3}$ = 3.7, $J_{4,5}$ = 0.7 Hz, H-4a), 5.78 (dd, 1 H, $J_{2,3}$ = 10.3, $J_{2,1}$ = 8.2 Hz, H-2a), 5.42 (dd, 1 H, H-3a), 5.38 (d, 1 H, $J_{1,2}$ = 8.6 Hz, H-1c), 5.13 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1b), 5.08 (d, 1 H, H-1a), 4.60 (d, 1 H, $J_{1,2}$ < 1Hz, H-1e), 4.12 (d, 1 H, $J_{1,2}$ = 3.3 Hz, H-1d), 3.32 (s, 3 H, OMe), 2.42 (d, 1 H, $J_{3,OH}$ = 9.6 Hz, OH-3e), 1.50 (d, 3 H, $J_{6,5}$ = 6.5 Hz, H-6b); ^{13}C-NMR (100.57 MHz) δ 168.72, 167.63 (2 O=C, Pht), 165.93, 165.74, 165.28, 164.71 (4 O=C, Bz), 139.06, 139.05, 138.42, 138.38, 138.27, 138.06, 137.77, 133.61, 133.43, 133.36, 133.33, 132.15, 131.85, 129.95-126.61, 123.35, 122.85 (arom. C), 102.33 (C-1e), 100.85 (C-1d), 100.10 (C-1a), 98.75 (C-1c), 96.01 (C-1b), 79.88, 79.55, 79.02, 77.70, 77.60, 76.07, 75.61, 75.37, 74.49, 74.33, 74.33, 73.67, 72.06, 71.64, 71.45, 71.42, 69.87, 68.37, 66.45 (ring C), 75.09, 75.06, 74.97, 74.24, 73.75, 73.10, 73.10, 72.21, 72.02 ($PhCH_2$), 70.49, 69.99, 69.66 (C-6c,6d,6e), 61.38 (C-6a), 56.90 (OMe), 56.59 (C-2c), 16.85 (C-6b). Anal. Calcd. for $C_{130}H_{127}NO_{30}$: C, 71.51; H, 5.86. Found: C, 71.61; H, 5.94.

Methyl 3,6-di-*O*-{2-*O*-[2-acetamido-6-*O*-benzyl-2-deoxy-4-*O*-β-D-galactopyranosyl-3-*O*-(2, 3, 4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-3, 4, 6-tri-*O*-benzyl-α-D-manno-pyranosyl}-2,4-di-*O*-benzyl-β-D-mannopyranoside (38). Hydrazine hydrate[29] (6 mL) was added to a stirred solution of compound **36** (170 mg, 42 μmol) in 90% aqueous ethanol (60 mL) and refluxed for 16 h. The solution was concentrated and the residue was acetylated using acetic anhydride (10 mL) and pyridine (20 mL) at room temperature overnight. The solution was concentrated and the residue was stirred with sodium (6 mg) in methanol-dichloromethane (14 mL, 4:3) overnight at room temperature. The base was neutralized by IR-120 cation exchange resin. The resin was filtered off and thoroughly washed with methanol, and the combined filtrate and washings were concentrated. The residue was flash chromatographed on a column of silica gel (methanol-dichloromethane 1:10) to yield **38** as an amorphous solid (78 mg, 63%): R_f = 0.5 (methanol-dichloromethane 1:9); $[\alpha]_D$-37.6 (c 1.8, $CHCl_3$); ^{1}H-NMR (250 MHz) δ 7.42–7.13 (m, arom. H), 3.39 (s, 3 H, OMe), 1.83, 1.67 (2 s, 6 H, 2 NHAc), 1.16, 1.13 (2 d, 6 H, $J_{6,5}$ = 6.5 Hz, H-6b,6b'); ^{13}C-NMR (100.57 MHz) δ 171.60, 171.37 (2 O=C, Ac), 139.24, 139.10, 138.84, 138.78, 138.63, 138.57, 138.50, 138.35, 138.28, 138.15, 138.06, 138.02, 137.78, 137.56 (arom. C), 128.54-127.17, 127.03, 126.70 (arom. C), 102.78 (C-1e), 101.00, 100.36, 99.98, 99.65, 97.37, 97.08, 96.38 (8 C-1), 79.81-68.94, 67.04, 66.42 (ring C, $PhCH_2$), 62.44, 62.29 (C-6a, 6a'), 58.13, 56.94 (C-2c, 2c'), 57.58 (OMe), 23.73, 23.10 (2 NHAc), 16.65 (C-6b, 6b'). Anal. Calcd. for $C_{171}H_{196}N_2O_{44}$·4 H_2O: C, 67.22; H, 6.73. Found: C, 67.15; H, 6.84.

Methyl 3, 6-di-*O*-[2-*O*-(2-acetamido-2-deoxy-3-*O*-α-L-fucopyranosyl-4-*O*-β-D-galacto-pyranosyl-β-D-glucopyranosyl)-α-D-mannopyranosyl]-β-D-mannopyranoside (1). A solution of **38** (73 mg, 25 μmol) in glacial acetic acid-methanol (5 mL, 1:1) was hydrogenolyzed over Pd/C (10%, 45 mg) at room temperature under 150 kPa for 15 h, filtered, and evaporated. The residue was purified on a Sephadex column (G25-150), using water as eluant. After freeze-drying, compound **1** was obtained as an amorphous solid (39 mg, 96%). R_f = 0.33 (ethyl acetate-isopropanol-water 2:3:3); $[\alpha]_D$+15 (c 0.6, water); ^{1}H-NMR (500 MHz, D_2O) δ 5.304 (d, 1 H, $J_{1,2}$ = 3.9 Hz, H-1b), 5.168 (d, 1 H, $J_{1',2'}$ = 3.9 Hz, H-1b'), 5.163 (d, 1 H, $J_{1',2'}$ < 1 Hz, H-1d'), 4.915 (dq, 1 H, $J_{5,6}$ = 6.5 Hz, $J_{5,4}$ < 1 Hz, H-5b), 4.867 (dq, 1 H, $J_{5',6'}$ = 6.5 Hz, $J_{5',4'}$ < 1Hz, H-5b'), 4.854 (d, 1 H, $J_{1,2}$ = 8.3 Hz, H-1c), 4.720 (d, 1 H, $J_{1,2}$ < 1 Hz, H-1d), 4.688 (d, 1 H, $J_{1,2}$ < 1 Hz, H-1e), 4.645 (d, 1 H, $J_{1',2'}$= 8.1 Hz, H-1c'), 4.485 (d, 1 H, $J_{1',2'}$= 7.7 Hz, H-1a'), 4.455 (d, 1 H, $J_{1,2}$ = 7.9 Hz, H-1a), 3.627 (s, 3 H, OMe), 2.172 (s, 3 H, NHAc), 2.087 (s, 3 H, NHAc), 1.220, 1.213 (2 d, 6 H, $J_{6,5}$ = 6.5 Hz, H-6b,6b'); ^{13}C-NMR (125 MHz) δ 103.21 (C-1a), 103.05 (C-1a'), 102.95 (C-1e), 102.71 (C-1c), 101.49 (C-1d), 100.89 (C-1d'), 100.45 (C-1c'), 99.74 (C-1b'), 99.62 (C-1b), 58.70 (C-2c,2c'), 57.25 (OMe), 24.60 (2 NHAc), 16.7 (C-6b,6b'); FAB-MS ($C_{59}H_{100}N_2O_{44}$, 1540.5): m/z 1539.5 $(M-H)^-$, 1561.5$(M+Na-2H)^-$.

ACKNOWLEDGEMENTS

We thank Miss Véronique Michon for the NMR spectra, Mrs Nicole Morin for the mass spectra, and the CNRS for financial support.

REFERENCES

1. Varki, A. *Proc. Natl. Acad. Sci. USA*, 1994, **91**, 7390.
2. a) Yednock, T. A.; Rosen, S. D. *Adv. Immunol.*, 1989, **44**, 313. b) Stoolman, L. M. *Cell*, 1989, **56**, 907. c) Brandley, B.K.; Swiedler, S. J.; Robbins, P. W. *Cell*, 1990, **63**, 861. d) Bevilacqua, M.; Butcher, E.; Furie, B.; Gallatin, M.; Gimbron, M.; Marlan, J.; Kishimoto, K.; Lasky, L.; McEver, R.; Pauson, J.; Rosen, S.; Seed, B.; Siegelmon, M.; Springer, T.; Stoolman, L.; Tedder, T.; Varki, A.; Wagner, D.; Weissman, I.; Zimmerman, G. *Cell*, 1991, **67**, 233. e) Picker, L.; Butcher, E. C. *Annu. Rev. Immunol.*, 1992, **10**, 561. f) Lasky, L. A. *Science*, 1992, **258**, 964. g) McEver R. P. *Curr. Opin. Immunol.*, 1994, **6**, 75. h) Lefer, A. M.; Weyrich, A. S.; Buecke, M. *Cardiovasc. Res.*, 1994, **28**, 289. i) Springer, T. *Cell*, 1994, **76**, 301.
3. Drickamer, K. *Curr. Opin. Struc. Biol.*, 1993, **3**, 393.
4. a) Hemmerich, S.; Bertozzi, C. R.; Leffler, H.; Rosen, S. D. *Biochemistry*, 1994, **33**, 4820. b) Hemmerich, S.; Rosen, S. D. *Biochemistry*, **1994**, **33**, 4830.
5. Brown, J.; Greeves, M.; Molgoard, H. *Int. Immunol.*, 1991, **3**, 175.
6. Norgard, K. E.; Moore, K. L.; Diaz, S.; Stults, N. L.; Ushiyama, S.; McEver, R. P.; Cummings, R. D.; Varky, A. *J. Biol. Chem.*, 1993, **268**, 12764.
7. Patel, T. P.; Goelz, S. E.; Lobb, R. R.; Parekh, R. B. *Biochemistry*, 1994, **33**, 14815.
8. Fenolerson, B. A.; Holms, E. M.; Fukushi, Y.; Hakomori, S. *Dev. Biol.*, 1986, **122**, 21.
9. Yamashita, K.; Tachibana, Y.; Takada, S.; Matsuda, I.; Araschima, S.; Kobata, A. *J. Biol. Chem.* 1979, **254**, 4820.
10. a) Lönn, H. *Carbohydr. Res.*, 1985, **139**, 105. b) Lönn, H. *ibid*, 1985, **139**, 115.
11. Zhang, Y.-M.; Mallet, J.-M.; Sinaÿ, P. *Carbohydr. Res.*, 1992, **236**, 73.
12. Hall, L. D.; Manville, J. F.; Bhacca, N. S. *Can. J. Chem.*, 1969, **47**, 1.
13. a) Mukaiyama, T.; Murai, Y.; Shoda, S. *Chem. Lett.*, 1981, 431. b) Mukaiyama, T.; Hashimoto, Y.; Shoda, S. *ibid*, 1983, 935.
14. Marra, A.; Esnault, J.; Veyrières, A.; Sinaÿ, P. *J. Am. Chem. Soc.*, 1992, **114**, 6354.
15. Fügedi, P.; Garegg, P. J.; Lönn, H.; Norberg, T. *Glycoconjugate J.*, 1987, **4**, 97.
16. Arnarp, J.; Lönngren, J. *Acta Chem. Scand. B.*, 1978, **32**, 696.
17. Ogawa, T.; Katano, K.; Sasajima, K.; Matsui, M. *Tetrahedron*, 1981, **37**, 2779.
18. Marra, A.; Mallet, J.-M.; Amatore, C.; Sinaÿ, P. *Synlett*, 1990, 572.
19. Veeneman, G. H.; Van Leeuwen, S. H.; Van Boom, J. H. *Tetrahedron Lett.*, 1990, **31**, 1331.
20. a) Schmidt, R. R.; Michel, J. *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 731. b) Schmidt, R. R.; Michel, J. *ibid*, 1982, **21**, 72. c) Schmidt, R. R.; Grundler, G. *ibid*, 1982, **21**, 781; 1983, **22**, 776. d) Schmidt, R. R.; Klager, R. *ibid*, 1985, **24**, 65.
21. Jain, R. K.; Matta, K. L. *Carbohydr. Res.*, 1992, **226**, 91.
22. Mallet, A. *Thesis, University Paris VI, France*, 1994, 166.
23. Lemieux, R. U.; Takeda, T.; Chung, B. Y. *Am. Chem. Soc. Symp. Ser.*, 1976, No. **39**, 90.
24. Arnarp, J.; Lönngren, J. *J. Chem. Soc., Perkin I*, 1981, 2070.
25. Paulsen, H.; Lebuhn, R. *Carbohydr. Res.*, 1984, **125**, 21.
26. a) Eby, R.; Schuerch, C. *Carbohydr. Res.*, 1974, **34**, 79. b) Liptak, A.; Jodal, I.; Nanasi, P. *ibid*, 1975, **44**, 1.
27. Classon, B.; Garegg, P. J.; Helland, A.-C. *J. Carbohydr. Chem.*, 1989, **8**, 543.
28. Lemieux, R. U.; Hendriks, K. B.; Stick, R. V.; James, K. *J. Am. Chem. Soc.*, 1975, **97**, 4056.
29. Ek, M.; Garegg, P. J.; Hultberg, H.; Oscarson, S. *J. Carbohydr. Chem.*, 1983, **2**, 305.
30. Lundt, I.; Pedersen, C. *Acta. Chem. Scand., Ser. B.*, 1976, **30**, 680.
31. Chernyak, A.Y.; Demidov, I. V.; Kochetkov, N. K. *Bioorg. Khim.*, 1989, **15**, 1673; *Chem. Abst.*, 1989, **112**, 233598x.
32. Zhang, Y.-M.; Brodzky, A.; Sinaÿ, P.; Saint-Marcoux, G.; Perly, B. *Carbohydr. Res.*, submitted.
33. a) Dejter-Juszynski, M.; Flowers, H. M. *Carbohydr. Res.*, 1971, **18**, 219. b) Collins, P. M. *Carbohydrates*, Chapman and Hall Ltd, 1987, 227.
34. Sato, S.; Ito, Y.; Nukada, T.; Nakahara, Y.; Ogawa, T. *Carbohydr. Res.*, 1987, **167**, 197.

(*Received in UK* 13 *April* 1995)