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Study of carbohydrate–carbohydrate interactions: total synthesis of 6d-deoxy Lewis^x pentaosyl glycosphingolipid

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ABSTRACT

This article describes total synthesis of 6d-deoxy Lewis^x pentaosyl glycosphingolipid, a useful tool for study of the Lewis^x–Lewis^x interaction. A 6-deoxy galactose donor was condensed with a diol of glucosamine to provide regioselectively a β 1→4 linked disaccharide, which was further fucosylated to a protected deoxy Lewis^x trisaccharide. Glycosylation of a lactoside diol with the 6d-deoxy Lewis^x trisaccharide gave regio- and stereoselectively a pentasaccharide in excellent yield. After chemical modification, this pentasaccharide reacted with the 3-*O*-benzoylated azidosphingosine to form a glycosphingolipid, which, after azide reduction followed by condensation with stearic acid and deprotection, afforded the target compound.

1. Introduction

Protein–protein interactions constitute an important mechanism for cell adhesion that controls cellular behaviour.[1] Because most of the cell surface proteins are highly glycosylated, carbohydrate–protein interactions are also involved in cell adhesion and recognition.[2,3] Recent advances in glycobiology revealed the existence of biologically significant carbohydrate–carbohydrate interactions, and this type of interaction could have a general, fundamental character for cell biology.[4] A typical example is the report of Hakomori who proposed that carbohydrate–carbohydrate interaction is responsible for the initial step of cell adhesion.[5] Embryogenesis, metastasis and other proliferation processes are, according to Hakomori, mediated by carbohydrate–carbohydrate interactions.[5] One of the structures involved in this novel mechanism is the Lewis^x (Le^x) trisaccharide determinant (Galβ1→4[Fucα1→3]GlcNAcβ1). Le^x is the terminal trisaccharide moiety of numerous cell surface glycolipids and glycoproteins involved in selectin-mediated cell–cell adhesion and recognition processes.[6] The interaction between Le^x and Le^x was found to be homotypic, and mediated by the presence of divalent cations, such as Ca^{2+}.[7,8]

Recently, the Le^x–Le^x interaction has been extensively studied using a variety of techniques including nuclear magnetic resonance (NMR) spectroscopy,[9] mass spectrometry (MS),[10] vesicle adhesion,[11] atomic force microscopy (AFM)[12] and surface plasmon resonance (SPR) spectroscopy.[13] Rat basophilic leukaemia cells pre-incubated with purified Le^x-containing glycosphingolipids have been used as a model.[14] Another model system termed 'Glycosylated Foldamer' was demonstrated for study of carbohydrate–carbohydrate interaction in terms of individual carbohydrate motifs.[15] By using a vesicle micromanipulation approach with chemically synthesized natural Le^x pentasaccharide glycosphingolipid, we have demonstrated that in contrast to glyconeolipids,[11] which allow strong orientational freedom of the Le^x group, the natural lipid showed a restricted orientation of the Le^x group. The adhesion induced by Le^x–Le^x interaction was thereby considerably enhanced, indicating that relative orientation of the two Le^x groups is a predominant factor in Le^x–Le^x recognition.[16] In another experiment we replaced the Le^x trisaccharide determinant in the headgroup by its isomer Le^a trisaccharide, in which the galactose and fucose are permutated relative to Le^x on one vesicle surface. The adhesion energy observed for Le^x–Le^a pair was very weak, confirming the homotypic characteristic of this type of carbohydrate–carbohydrate interactions.[16]

To date, however, the molecular detail of this type of weak and Ca^{+2}-dependent carbohydrate–carbohydrate interactions has not yet been sufficiently clarified, which necessitates new models to probe the nature of this phenomenon in term of key role played by the different hydroxyl groups on Le^x trisaccharide involved in the Le^x–Le^x interaction. Our objective has been to prepare a series of

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Le^x pentaosyl glycosphingolipids in which one of the eight hydroxyl groups of Le^x trisaccharide is replaced by a hydrogen atom (Fig. 1), and to test the induced adhesion by interaction of these derivatives, in order to gain an insight into the functions of the hydroxyl groups in Le^x trisaccharide molecule.

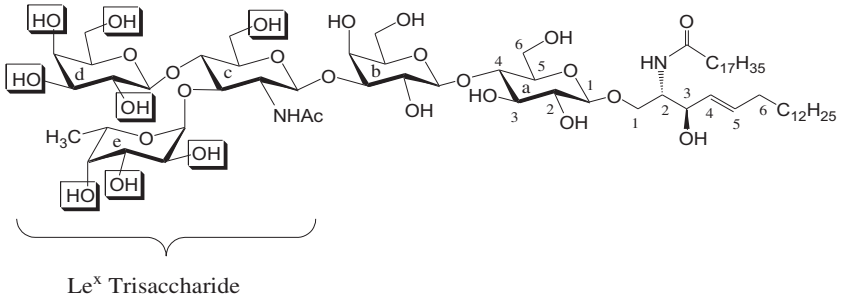


Figure 1. Sites identified as interacting moieties for the Le^x pentaosyl glycosphingolipid.

Taking the cost of different sugar residues of Le^x trisaccharide into account, the synthetic work was started from chemical modification of galactose residue. After successful synthesis of the 3d- and 4d-deoxy Le^x pentaosyl glycosphingolipids,[17] here we report an efficient synthesis of 6d-deoxy Le^x pentaosyl glycosphingolipid **1** (Fig. 2), which would be a useful tool for a mechanistic study of carbohydrate–carbohydrate interactions.

Hydrolysis of the anomeric phenylthio group by $BF_3 \cdot Et_2O$ in the presence of HgO (red) gave the hemiacetal **10**[20] as a mixture of α/β isomers in 56% yield, which were not separated and further characterized. Treatment of **10** with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) gave the desired trichloroacetimidate **2a** in 58% yield. ^{1}H NMR spectrum showed that only α-trichloroacetimidate was formed in the reaction on the basis of the H-1, H-2 coupling constant ($J_{1,2}$=3.5 Hz), as shown in Scheme 1.

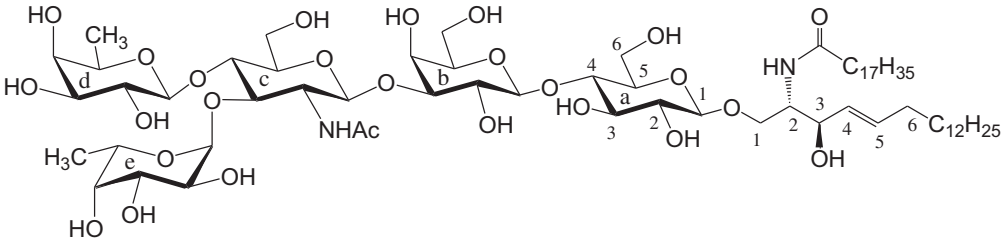


Figure 2. 6d-Deoxy Le^x pentaosyl glycosphingolipid **1**.

2. Results and discussion

For synthesis of the target **1**, compounds **2**–**6** were chosen as building blocks (Fig. 3).

In order to synthesize the 6-deoxy galactosyl donor **2a**, the previously reported phenyl 2,3,4-tri-*O*-acetyl-1-thio-D-galactopyranoside **7**,[18] which was prepared from D-galactose by peracetylation, glycosylation of thiophenol and 6-selective deacetylation, was treated by phenyl chlorothionocarbonate to give compound **8** in 95% yield. Radical reaction of **8**, using tributyltin hydride and AIBN, provided the deoxy derivative **9** in 61% yield. Compound **9** was previously prepared from D-fucose by a shorter route,[19] but the starting material is much more expensive.

As illustrated in Scheme 2, the donor **2a** and acceptor **3** are designed to take advantage of the differences in the reactivity of their leaving groups. Thus, condensation of the trichloroacetimidate **2a** with the previously reported diol **3**,[21] using TMSOTf as promoter, gave regioselectively the β 1→4 linked disaccharide **11** in 79% yield, due to the 'stereo hindrance effect', no β 1→3 linked disaccharide

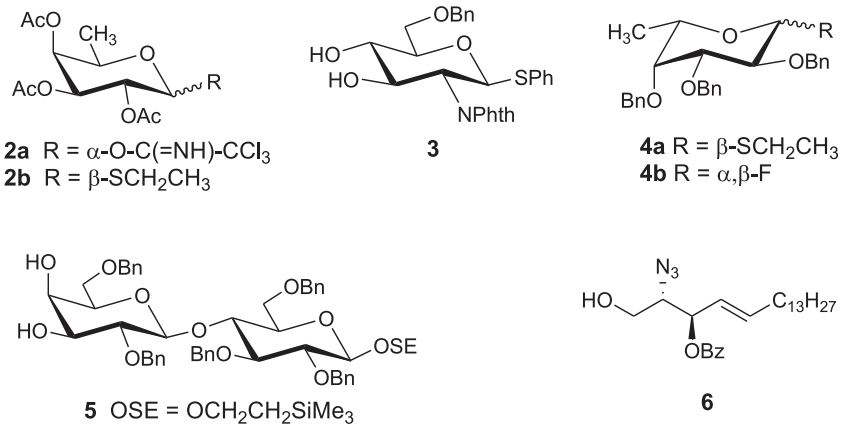
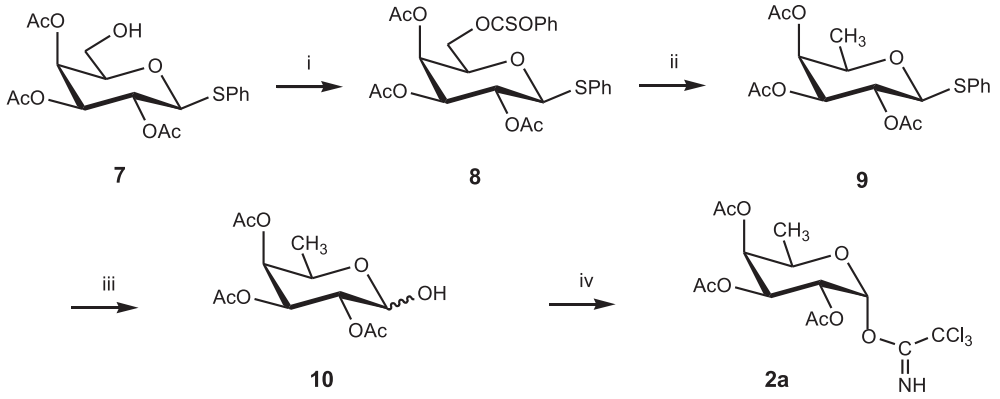
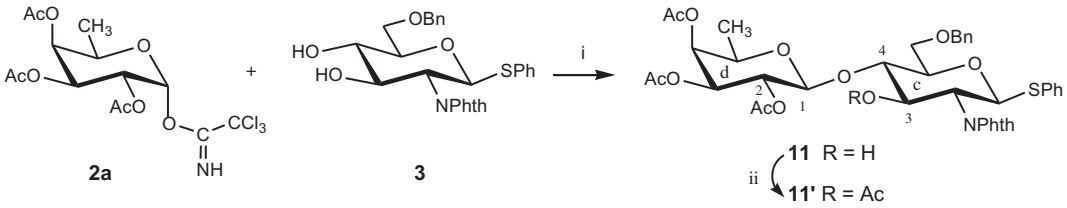


Figure 3. Key building blocks for synthesis of target **1**.



Scheme 1. Reagents and conditions: (i) phenyl chlorothionocarbonate, CH_2Cl_2, pyridine, rt, 3 h, 95%; (ii) tributyltin hydride, AIBN, toluene, 80 °C, 1 h, 61%; (iii) $BF_3{\cdot}Et_2O$, HgO, H_2O, THF, rt, 1 h, 56%; (iv) Cl_3CCN, DBU, CH_2Cl_2, 0 °C, 1 h, 58%.



Scheme 2. Reagents and conditions: (i) TMSOTf, CH_2Cl_2, 4 Å MS, 0 °C, 1 h, 79%; (ii) Ac_2O, pyridine, rt, 14 h, quant.

was isolated. Such a selective behaviour of phenyl 6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **3** has previously been observed by our group[22] during its glycosylation with 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide.

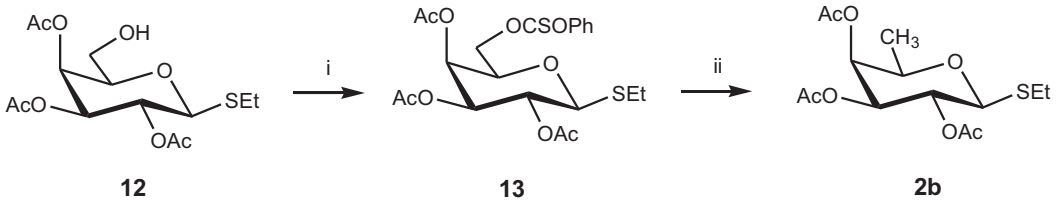
The ^{1}H NMR spectrum of **11** showed the presence of H-3c of the glucosamine residue at δ 4.45 (dd, $J_{2c,3c}$=10.3 Hz, $J_{3c,4c}$=7.9 Hz), indicating the position of the newly formed glycosidic linkage in the disaccharide **11** to be at OH-4 of the acceptor **3**. This regioselectivity was further confirmed from the ^{1}H NMR spectrum of **11′**—obtained from **11** by acetylation—which revealed a deshielded signal for H-3c at 5.72 ppm (dd, $J_{2c,3c}$=10.2 Hz, $J_{3c,4c}$=9.0 Hz), confirming therefore the position of the new glycosidic linkage in **11** as being OH-4 of the diol **3**. Its stereochemistry was determined to be the desired β anomer on the basis of the H-1d, H-2d coupling constant ($J_{1d,2d}$=7.9 Hz).

Another donor **2b** has also been prepared for glycosylation, but with a shorter way. As shown in Scheme 3, ethyl 2,3,4-tri-*O*-acetyl-1-thio-D-galactopyranoside **12**[23] was treated by phenyl chlorothionocarbonate to give compound **13** in 98% yield. Radical reaction of **13**, using tributyltin hydride and AIBN, provided the deoxy derivative **2b** in 82% yield. Glycosyl donor **2b** was previously prepared from expensive D-fucose as a mixture of α/β isomers.[24]

With the disaccharide **11** in hand, we first used ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside **4a**[26] for the fucosylation. The reaction was performed using *N*-iodosuccinimide (NIS)/trifluoromethanesulfonic acid (TfOH) as promoter at low temperature to provide the desired trisaccharide **14**, as shown in Scheme 4.

Surprisingly, the yields of the fucosylation were not satisfactory, varying from 0–45%, despite of changing reaction conditions (temperature, time, solvent, donor equivalence, etc.), we then turned to other donors for fucosylation. The 2,3,4-tri-*O*-benzyl-L-fucosyl fluoride **4b** was therefore prepared from **4a** by treatment with DAST in the presence of NBS, based on the method of Nicolaou et al.[27,28] (Scheme 5). This reaction afforded high yield (98%) of **4b**, NMR revealed that **4b** exist as a mixture of two isomers α and β (1:2). Fucosyl fluoride **4b** was also prepared by Ogawa et al.[29] from methyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside and by Wong et al.[30] from 2,3,4-tri-*O*-benzyl-L-fucose both by reaction with DAST.

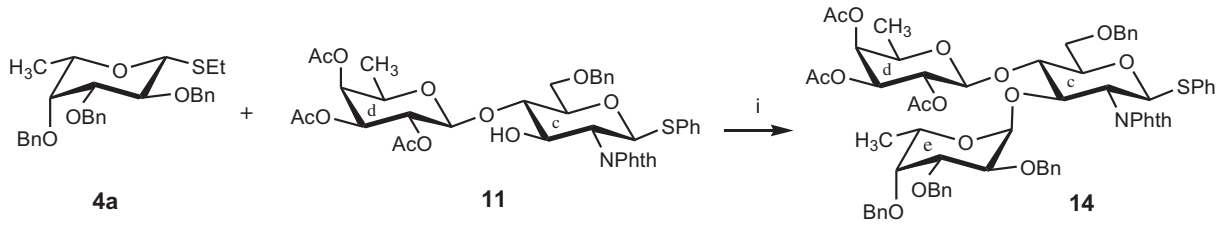
Glycosylation of disaccharide **11** with **4b** was much effective than **4a**. Thus coupling of **4b** and **11** in the presence of silver triflate and stannous chloride provided the trisaccharide **14** in 76% yield and with the newly generated glycosidic linkage of the desired α-configuration on the basis of the low value of the Fuc H-1, H-2 coupling constant ($J_{1e,2e}$=3.8 Hz). No formation of the corresponding β-fucosylated product was detected (Scheme 5). Contrary to **4a**, the glycosylation of **11** with **4b** is easily reproducible.



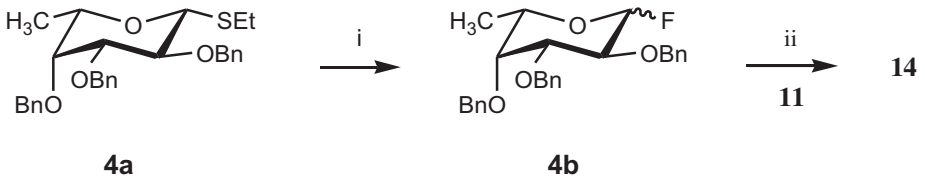
Scheme 3. Reagents and conditions: (i) phenyl chlorothionocarbonate, CH_2Cl_2, pyridine, rt, 3 h, 98%; (ii) tributyltin hydride, AIBN, toluene, 80 °C, 1 h, 82%.

Interestingly, glycosylation of **3** with **2b** gave regio- and stereoselectively the desired disaccharide **11** in 61% yield, using NIS/TfOH as promoter without affecting SPh group of the acceptor **3**. Such a selective reactivity between SEt and SPh groups has been observed in our previous work.[25]

Having the trisaccharide donor **14** at our disposal, we then proceeded towards coupling the latter to the previously reported diol **5**.[31] The reaction was promoted by NIS and triflic acid to afford



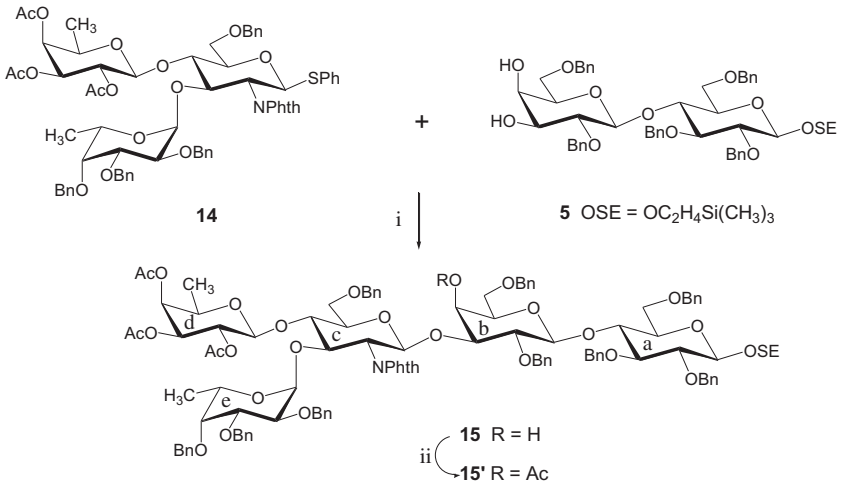
Scheme 4. Reagents and conditions: (i) NIS, TfOH, 4 Å MS, toluene, −30 °C, 1 h, 45%.



Scheme 5. Reagents and conditions: (i) DAST, NBS, −15 °C, 30 min, 98%; (ii) AgOTf, $SnCl_2$, CH_2Cl_2/toluene (5:1), −15 °C, 1 h, 76%.

regio- and stereoselectively the desired pentasaccharide **15** in 82% yield (Scheme 6). The stereochemistry of the newly introduced linkage was determined to be β on the basis of the GlcN H-1, H-2 coupling constant ($J_{1c,2c}$=8.4 Hz). The regioselectivity was confirmed from the ^{1}H NMR spectrum of **15′**—obtained from **15** by acetylation—which revealed a deshielded signal for H-4b at spectrum showed that only the α-trichloroacetimidate was formed on the basis of the H-1, H-2 coupling constant ($J_{1a,2a}$=3.7 Hz) of the glucose residue.

Condensation of trichloroacetimidate **19** with azidosphingosine derivative **6** was performed using $BF_3 \cdot Et_2O$ as promotor to provide the desired glycolipid **20** in 57% yield, as shown in Scheme 9. The



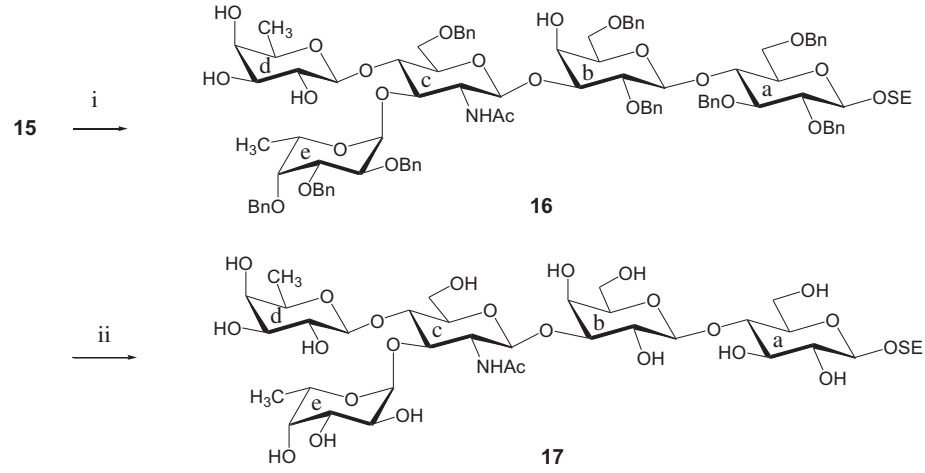
Scheme 6. Reagents and conditions: (i) NIS/TfOH, 4 Å MS, CH_2Cl_2, −15 °C, 1 h, 82%; (ii) Ac_2O, pyridine, rt, 14 h, 95%.

5.43 ppm (d, $J_{3b,4b}$=3.5 Hz), confirming therefore the position of the new glycosidic linkage in **15** as being OH-3b of the diol **5**.

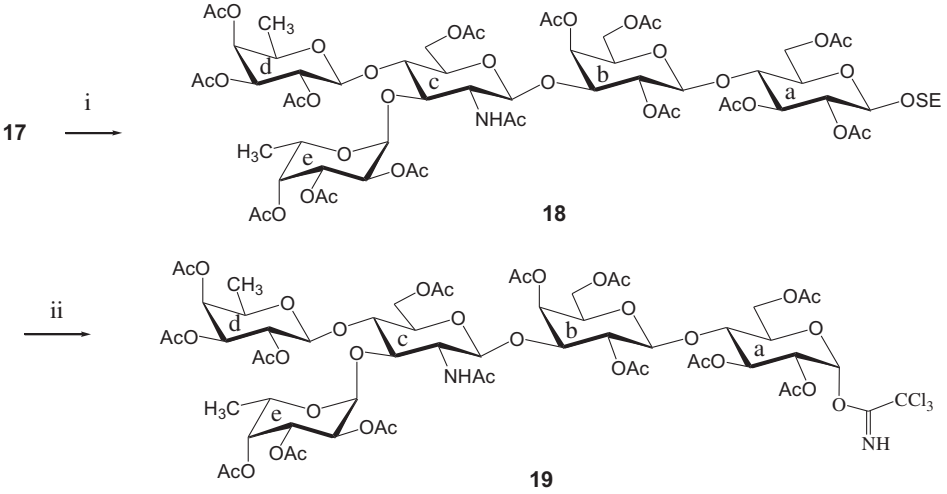
Treatment of pentasaccharide **15** with hydrazine in boiling ethanol, followed by selective *N*-acetylation, afforded the compound **16** in 86% overall yield from **15** (Scheme 7). Catalytic hydrogenolysis of **16** and purification of the product on Sephadex G25 provided quantitatively the pentasaccharide **17** (Scheme 7).

After peracetylation of **17**, pentasaccharide **18** was obtained (97% yield) and converted to a trichloroacetimidate donor in order to couple with azidosphingosine derivative **6**. Acid catalyzed cleavage of the 2-(trimethylsilyl)ethyl glycoside was performed in dichloromethane using trifluoroacetic acid to afford the hemiacetals as a mixture of α/β isomers, which were not separated and further characterized at this stage. The hemiacetals were then treated with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) to give the trichloroacetimidate **19** in 65% yield (Scheme 8). The ^{1}H NMR β configuration of the newly introduced glycosidic linkage was confirmed from the ^{1}H NMR spectrum ($J_{1a,2a}$=7.8 Hz). The azide group of **20** was reduced by triphenyl phosphine in a mixture of toluene and water at 45 °C for 24 h to give an amino derivative. The reaction temperature needs to be carefully controlled (below 50 °C) to avoid formation of byproduct. Due to its unstable property, the amino derivative was not characterized at this stage and condensed directly with stearic acid in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) in dry dichloromethane to give the glycosyl ceramide **21**. ^{1}H NMR spectrum of **21** showed a doublet at δ 5.73 ppm (J=9.2 Hz) corresponding to the proton of NH/CO group of the ceramide. The protecting groups of hydroxyl groups were subsequently removed in basic condition (NaOMe) to afford the target 6d-deoxy Lewis^x pentaosyl glycosphingolipid **1** in 75% yield (Scheme 9).

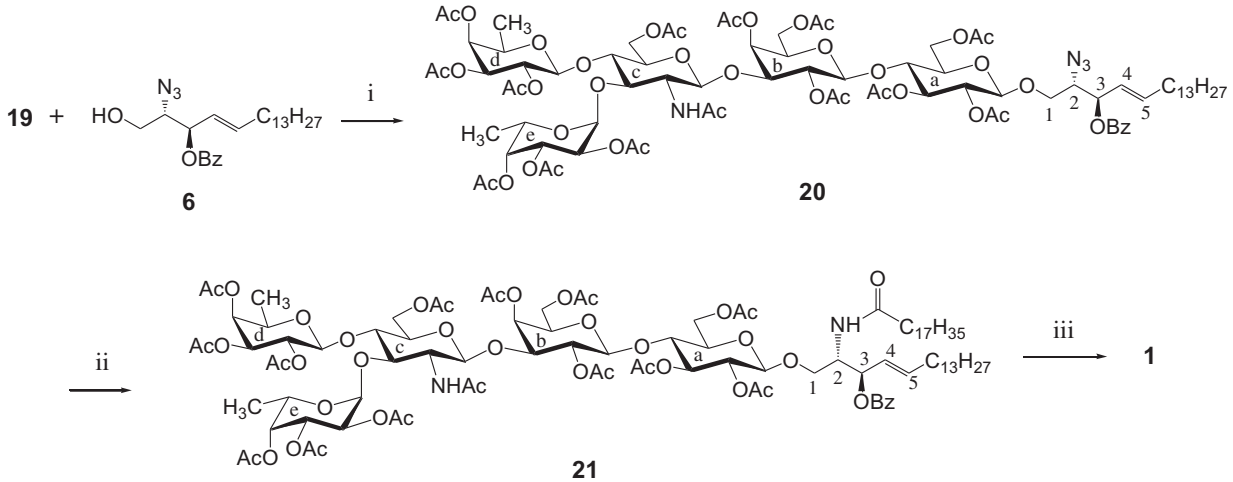
The compound **1** was fully characterized by ^{1}H and ^{13}C NMR, as well as HRMS.



Scheme 7. Reagents and conditions: (i) (a) NH_2NH_2, H_2O, EtOH, 80 °C, 14 h; (b) Ac_2O, MeOH, CH_2Cl_2, rt, 15 h, 86%. (ii) H_2, Pd/C, MeOH, 30 °C, 20 h, quant.



Scheme 8. Reagents and conditions: (i) Ac_2O, pyridine, DMAP, 30 °C, 14 h, 97%; (ii) (a) TFA, CH_2Cl_2, 0 °C for 1 h, then rt for 5 h; (b) Cl_3CCN, DBU, CH_2Cl_2, 0 °C, 4 h, 65% (two steps).



Scheme 9. Reagents and conditions: (i) $BF_3 \cdot Et_2O$, CH_2Cl_2, 4 Å powdered molecular sieves, −10 °C, 3 h, 57%; (ii) (a) Ph_3P, H_2O, toluene, 45 °C, 24 h; (b) stearic acid, EDC, CH_2Cl_2, rt, 24 h, 61%; (iii) NaOMe/MeOH, rt, 14 h, 75%.

3. Conclusion

In conclusion, we have developed a concise synthesis of 6d-deoxy Lewis^x pentaosyl glycosphingolipid in good yield. It has been shown that a two-step deoxygenation of galactose at position 6 could be easily realised by reaction with phenyl chlorothionocarbonate, followed by a radical reaction using Bu_3SnH and catalyzed by AIBN, giving the 6-deoxy derivative in

high yield. Our successful disaccharide synthesis was based on a highly regio- and stereoselective glycosylation, taking advantages of stereo hindrance effect of the acceptor and participating effect of the donor, to provide the β 1→4 linked disaccharide in high yield. Some difficulties were encountered however when preparing the trisaccharide **14** by fucosylation of **11** with the thioglycoside **4a**, which used to be effective for such a glycosylation, this problem was solved by using the fluoride donor **4b**, which was proved to be very powerful for fucosylation of **11**, giving the desired trisaccharide **14** in high yield. Construction of the pentasaccharide **15** was successfully achieved in very good yield by a highly regio- and stereoselective glycosylation of the diol **5** with the donor **14**, taking advantage of the activity difference between OH-3b and OH-4b. With the key pentasaccharide **15** in hand, the classic glycosphingolipid synthesis method was then applied to give smoothly the target compound **1**. After synthesis of the 3d- and 4d-deoxy Le^x pentaosyl glycosphingolipids,[17] this work allowed us to obtain the third member of the deoxy family on galactosyl residue of the Le^x pentaosyl glycosphingolipid. Synthetic work is in progress in our laboratory towards to the last member of this family, the 2d-deoxy Le^x pentaosyl glycosphingolipid. These compounds will be used to perform a mechanistic study of Le^x–Le^x interaction for the effect of hydroxyl groups of galactose on the induced adhesion using the vesicle micromanipulation technique.[16]

4. Experimental

4.1. General

Optical rotations were measured at 589 nm (Na line) at 20±2 °C with a Perkin–Elmer Model 343 digital polarimeter, using a 10 cm, 1 mL cell. High resolution mass spectra (HRMS) were recorded with a Bruker micrOTOF spectrometer in electrospray ionization (ESI) mode. ^{1}H NMR spectra were recorded with a Bruker DRX 400 spectrometer at ambient temperature. Assignments were aided by COSY experiments. ^{13}C NMR spectra were recorded at 100.6 MHz with a Bruker DRX 400 for solutions in $CDCl_3$, CD_3OD or D_2O. Reactions were monitored by thin-layer chromatography (TLC) on a precoated plate of silica gel 60 F_{254} (Merck, 0.2 mm) and detection by charring with sulfuric acid. Flash column chromatography was performed on silica gel 60 (230–400 mesh, Merck).

4.2. Synthesis of phenyl 2,3,4-tri-*O*-acetyl-6-phenoxythiocarbonyl-1-thio-β-D-galactopyranoside (8)

To a solution of **7** (0.63 g, 1.58 mmol, 1 equiv) in anhydrous dichloromethane (6 mL) and pyridine (6 mL) was added dropwise phenyl chlorothionocarbonate (0.33 mL, 2.37 mmol, 1.5 equiv) at room temperature. After stirring for 3 h, the mixture was concentrated and filtered by a short silica gel column using acetone as solvent. The residue was then purified by silica gel column chromatography (cyclohexane/ethyl acetate 4:1) to give product **8** (0.79 g, 95%) as a white amorphous solid: R_f=0.44 (cyclohexane/ethyl acetate 2:1); $[\alpha]_D^{20}$ +17.7 (*c* 1.2, chloroform); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.61–7.43 (m, 4H, arom), 7.37–7.11 (m, 6H, arom), 5.51 (dd, 1H, $J_{3,4}$=3.2 Hz, $J_{4,5}$<1 Hz, H-4), 5.29 (t, 1H, $J_{2,3}$=9.9 Hz, H-2), 5.10 (dd, 1H, $J_{2,3}$=9.9 Hz, $J_{3,4}$=3.3 Hz, H-3), 4.81 (d, 1H, $J_{1,2}$=10.0 Hz, H-1), 4.65 (2dd, 2H, $J_{6b,6a}$=11.4 Hz, H-6a, H-6b), 4.20 (m, 1H, H-5), 2.18, 2.14, 2.03 (3s, 9H, 3×OAc). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 194.65 (C=S), 170.12, 169.92, 169.36 (C=O), 153.3 (O–Ph), 132.45, 132.37 (arom C), 129.55, 128.91, 128.14, 126.67, 121.73 (arom CH), 86.66 (C-1), 74.02, 71.83, 67.35, 67.12(C-2, C-3, C-4, C-5), 70.62 (C-6), 20.78, 20.65, 20.52 (3CH_3, Ac). ESI-HRMS (*m*/*z*) calcd for $C_{25}H_{30}O_9S_2N$ ($M+NH_4^+$): 552.1365. Found: 552.1362.

4.3. Synthesis of *O*-(2,3,4-tri-*O*-acetyl-α-D-fucopyranosyl) trichloroacetimidate (2a)

Compound **9** (320 mg, 0.84 mmol, 1 equiv) was dissolved in THF (2.7 mL) and water (0.5 mL). A mixture of HgO (265 mg, 1.22 mmol, 1.5 equiv) and $BF_3{\cdot}Et_2O$ (0.33 mL, 2.6 mmol, 3 equiv) in THF (2.7 mL) was added dropwise to the preceding solution. The mixture was stirred for 1 h after addition, and then concentrated and poured into ether. The mixture was successively washed with a saturated $NaHCO_3$ solution, a 10% potassium iodide aqueous solution and water, dried over $MgSO_4$ and then concentrated. The crude product **10** obtained in α/β isomers were directly engaged in the following step without further purification. To a solution of **10** (100 mg, 3.44 mmol, 1 equiv) in anhydrous dichloromethane (3.5 mL) were added trichloroacetonitrile (0.39 mL, 3.91 mmol, 11.5 equiv) and DBU (52 μL, 0.34 mmol, 1 equiv) dropwise at 0 °C and stirred for 1 h. After concentration, the residue was purified by silica gel column chromatography (cyclohexane/ethyl acetate/triethylamine 300:100:0.4) to give compound **2a** as a white foam (86.5 mg, 58%). The NMR data were identical to those reported in literature.[32]

4.4. Synthesis of phenyl (2,3,4-tri-*O*-acety-β-D-fucopyranosyl)-(1→4)-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (11)

*4.4.1. Method A (**2a**+**3**).* A solution of **2a** (95 m g, 0.22 mmol, 1 equiv) and **3** (107 mg, 0.22 mmol, 1 equiv) in 2.5 mL of anhydrous dichloromethane was stirred with 4 Å powdered molecular sieves for 40 min at room temperature under nitrogen. Trimethylsilyl triflate (40 μL, 0.22 mmol, 1 equiv) was added at 0 °C, and stirring continued for 1 h. The mixture was filtered through Celite. The filtrate was washed with a saturated aqueous $NaHCO_3$ and then with water, dried over $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography (cyclohexane/ethyl acetate 1.5:1) to give **11** (0.13 g, 79%) as a white amorphous solid.

*4.4.2. Method B (**2b**+**3**).* A mixture of **2b** (0.4 g, 1.20 mmol, 1 equiv), **3** (0.59 g, 1.20 mmol, 1 equiv) and 4 Å powdered molecular sieves (1 g) in dry toluene (12 mL) was stirred at room temperature under nitrogen for 30 min, then cooled to −20 °C. NIS (323 mg, 1.44 mmol, 1.2 equiv) and then TfOH (21.2 μL, 0.24 mmol, 0.2 equiv) were added. The mixture was stirred at −20 °C for 2 h, then neutralized with Et_3N, diluted with dichloromethane, filtered through Celite, washed with aqueous sodium thiosulfate, brine and then dried over $MgSO_4$ and concentrated. After purification by flash column chromatography (cyclohexane/ethyl acetate 1.5:1), compound **11** was obtained (0.56 g, 61%) as a white amorphous solid: R_f=0.42 (cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ +26.1 (*c* 1.0, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89–7.20 (m, 14H, arom), 5.58 (d, 1H, $J_{1,2}$=10.5 Hz, H-1c), 5.17 (dd, 1H, $J_{3,4}$=3.5 Hz, $J_{4,5}$<1 Hz, H-4d), 5.12 (dd, 1H, $J_{1,2}$=7.9 Hz, $J_{2,3}$=10.3 Hz, H-2d), 4.92 (dd, 1H, $J_{2,3}$=10.3 Hz, $J_{3,4}$=3.5 Hz, H-3d), 4.70, 4.51 (2d, 2H, J_{gem}=11.8 Hz, PhCH_2), 4.45 (dd, 1H, $J_{2,3}$=10.3 Hz, $J_{3,4}$=7.9 Hz, H-3c), 4.42 (d, 1H, $J_{1,2}$=7.9 Hz, H-1d), 4.25 (t, 1H, $J_{1,2}$=10.5 Hz, $J_{2,3}$=10.3 Hz, H-2c), 4.11 (s, 1H, exch. D_2O, OH-3c), 3.78–3.66 (m, 5H, H-4c, H-5c, H-5d, H-6c, H-6′c), 2.11, 2.00, 1.96 (s, 9H, 3×OAc), 1.14 (d, 3H, $J_{5,6}$=6.6 Hz, H-6d). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.55, 170.12, 169.25 (3C=O, Ac), 168.23, 167.67 (2C=O, NPhth), 138.20, 132.16, 131.93, 131.85 (arom C), 134.18, 132.78, 128.94, 128.61, 128.00, 127.96, 127.94, 123.86, 123.36 (arom CH), 101.16 (C-1d), 83.54 (C-1c), 81.00 (C-4c), 78.37 (C-5d), 73.72 (PhCH_2), 71.13 (C-3d), 70.81 (C-3c), 69.91 (C-4d), 69.79 (C-2d), 68.93 (C-5c), 68.18 (C-6c), 55.30 (C-2c), 21.14, 20.84, 20.65

(3CH_3, Ac), 15.93 (CH_3). ESI-HRMS (*m*/*z*) calcd for $C_{39}H_{41}NO_{13}SNa$ (M+Na^+): 786.2191. Found: 786.2195.

4.5. Synthesis of phenyl (2,3,4-tri-*O*-acety-β-D-fucopyranosyl)-(1→4)-3-*O*-acetyl-6-*O*- benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (11′)

A solution of **11** (30 mg) in 1 mL of pyridine and 0.5 mL of acetic anhydride was stirred at room temperature for 14 h and then concentrated, co-evaporated with toluene and dried. Compound **11′** was obtained in quantitative yield (32 mg), R_f=0.48 (cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ +20 (*c* 1.0, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85–7.20 (m, 14H, arom), 5.72 (dd, 1H, $J_{3,4}$=9.0 Hz, $J_{2,3}$=10.2 Hz, H-3c), 5.70 (d, 1H, $J_{1,2}$=10.6 Hz, H-1c), 5.11 (d, 1H, $J_{4,5}$=3.4 Hz, H-4d), 5.00 (dd, 1H, $J_{1,2}$=8.0 Hz, $J_{2,3}$=10.4 Hz, H-2d), 4.85 (dd, 1H, $J_{2,3}$=10.4 Hz, $J_{3,4}$=3.5 Hz, H-3d), 4.74 (d, 1H, J_{gem}=12.0 Hz, one of the PhCH_2), 4.53 (d, 1H, J_{gem}=11.9 Hz, one of the PhCH_2), 4.47 (d, 1H, $J_{1,2}$=8.0 Hz, H-1d), 4.28 (t, 1H, $J_{1,2}$=$J_{2,3}$=10.4 Hz, H-2c), 4.00 (t, 1H, $J_{3,4}$=9.3 Hz, $J_{4,5}$=9.6 Hz, H-4c), 3.80 (d, 2H, $J_{5,6}$=2.3 Hz, H-6c, H-6′c), 3.69 (dt, 1H, $J_{4,5}$=10.0 Hz, $J_{5,6}$=2.3 Hz, H-5c), 3.54 (dd, 1H, $J_{5,6}$=6.3 Hz, H-5d), 2.11, 1.96, 1.95, 1.86 (4s, 12H, 4×OAc), 1.11 (d, 3H, $J_{5,6}$=6.4 Hz, H-6d). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.78, 170.31, 170.05, 169.15 (4C=O, Ac), 167.87, 167.43 (2C=O, NPhth), 138.15, 131.89, 131.55, 131.44 (arom C), 134.49, 134.24, 133.26, 129.01, 128.65, 128.31, 128.04, 128.00, 123.88, 123.64 (arom CH), 100.57 (C-1d), 83.15(C-1c), 79.16 (C-5c), 75.48 (C-4c), 73.78 (PhCH_2), 72.40 (C-3c), 71.58 (C-3d), 70.24 (C-4d), 69.42 (C-2d), 69.13 (C-5d), 67.87 (C-6c), 54.08 (C-2c), 20.90, 20.81, 20.79, 20.72 (4CH_3, Ac), 16.17 (C-6d). ESI-HRMS (*m*/*z*) calcd for $C_{41}H_{43}NO_{14}SNa$ (M+Na^+): 828.2296. Found: 828.2334.

4.6. Synthesis of ethyl 2,3,4-tri-*O*-acetyl-6-phenoxythiocarbonyl-1-thio-β-D-galactopyranoside (13)

To a solution of **12** (0.22 g, 0.63 mmol, 1 equiv) in anhydrous dichloromethane (2 mL) and pyridine (2 mL) was added dropwise phenyl chlorothionocarbonate (0.13 mL, 0.94 mmol, 1.5 equiv) at room temperature. After stirring for 3 h, the mixture was concentrated and then filtered by a short silica gel column using acetone as solvent. The residue was then purified by silica gel column chromatography (cyclohexane/ethyl acetate 3.5:1) to give product **13** (0.30 g, 98%) as a white amorphous solid: *Rf*=0.42 (cyclohexane/ethyl acetate 2:1); $[\alpha]_D^{20}$ +45 (*c* 1.0, chloroform); ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.48–7.30 (m, 3H, arom), 7.14–7.10 (m, 2H, arom), 5.56–5.55 (m, 1H, H-4), 5.31 (t, 1H, $J_{2,3}$=9.9 Hz, H-2), 5.13 (dd, 1H, $J_{2,3}$=9.9 Hz, $J_{3,4}$=3.2 Hz, H-3), 4.65–4.56 (m, 3H, H-1, H-6a, H-6b), 4.21–4.15 (m, 1H, H-5), 2.82–2.76 (m, 2H, SCH_2), 2.21, 2.11, 2.03 (3s, 9H, 3×OAc), 1.34 (t, 3H, *J*=7.5 Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 194.47 (C=S), 170.04, 169.80, 169.39 (C=O), 153.25 (O–Ph), 129.47, 126.56, 121.66 (arom CH), 83.92 (C-1), 73.92, 71.67, 67.47, 67.08 (C-2, C-3, C-4, C-5), 70.66 (C-6), 24.23 (CH_2–CH_3), 20.67, 20.60, 20.45 (3CH_3CO), 14.78 (CH_2–CH_3). ESI-HRMS (*m*/*z*) calcd for $C_{21}H_{26}O_9S_2N$ (M+Na^+): 509.0946. Found: 509.0916.

4.7. Synthesis of ethyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-fucopyranoside (2b)

Compound **13** (1.64 g, 3.37 mmol, 1 equiv) was dissolved in anhydrous toluene (65 mL). The tributyltin hydride (1.82 mL, 6.75 mmol, 2 equiv) and AIBN (33.2 mg, 0.20 mmol, 0.06 equiv) were added. The mixture was refluxed at 80 °C for 1 h, then concentrated and purified by silica gel column chromatography (toluene/ethyl acetate 8:1) to give the compound **2b** (0.92 g, 82%) as a white foam, R_f=0.44 (toluene/ethyl acetate 4:1). The NMR data were proved to be identical to those reported in literature.[24]

4.8. Synthesis of 2,3,4-tri-*O*-benzyl-L-fucosyl fluoride (4b)

Ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside **4a** (70 mg, 0.15 mmol, 1 equiv) was dissolved in anhydrous dichloromethane (2 mL) under nitrogen and cooled to −15 °C. The stirred solution was then treated with (diethylamino)sulfur trifluoride and allowed to stir for 3 min before *N*-bromosuccinimide was added. The mixture was stirred for 30 min, then diluted with dichloromethane and poured into an ice-saturated $NaHCO_3$ solution, the organic phase was separated and washed with saturated $NaHCO_3$ solution and brine before drying and evaporation. The residue so obtained was purified by silica gel column chromatography (cyclohexane/ethyl acetate 13:1) to give **4b** as colourless oil (63 mg, 98%, α/β=1:2). Their NMR spectral data were in good agreement with those reported in literature.[28]

4.9. Synthesis of phenyl (2,3,4-tri-*O*-acety-β-D-fucopyranosyl)-(1→4)-[2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (14)

A solution of **11** (0.30 g, 0.39 mmol, 1 equiv) and **4b** (0.29 g, 0.66 mmol, 1.7 equiv) in 10 mL of dry dichloromethane and 2 mL of dry toluene was stirred with 4 Å powdered molecular sieves for 30 min at room temperature under nitrogen. A mixture of stannous chloride and silver triflate was added at −15 °C, and the stirring was continued for 1 h. The mixture was filtered through Celite and washed with dichloromethane. The filtrate was washed with a saturated $NaHCO_3$ solution, then with water, dried over $MgSO_4$ and concentrated. After purification by flash column chromatography (cyclohexane/ethyl acetate 4:1), compound **14** was obtained (0.35 g, 76%) as a white amorphous solid: R_f=0.45 (cyclohexane/ethyl acetate 2:1); $[\alpha]_D^{20}$ +4.7 (*c* 1.0, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73–7.11 (m, 29H, arom), 5.53 (d, 1H, $J_{1,2}$=10.5 Hz, H-1c), 5.10–5.09 (m, 1H, H-4d), 5.04 (dd, 1H, $J_{1,2}$=8.5 Hz, $J_{2,3}$=9.8 Hz, H-2d), 4.88 (d, 1H, $J_{1,2}$=3.8 Hz, H-1e), 4.86 (d, 1H, J_{gem}=11.9 Hz, one of the PhCH_2), 4.85–4.77 (m, 5H, H-3c, H-3d, H-5e, PhCH_2), 4.72 (d, 1H, $J_{1,2}$=8.5 Hz, H-1d), 4.59 (d, 1H, $J_{1,2}$=10.5 Hz, H-2c), 4.68, 4.57 (2d, 2H, J_{gem}=11.6 Hz, PhCH_2), 4.55, 4.48 (2d, 2H, J_{gem}=12.2 Hz, PhCH_2), 4.30–4.21 (m, 2H, one of the PhCH_2, H-4c), 4.03–3.85 (m, 4H, H-2e, H-3e, H-6c, H-6c′), 3.65–3.64 (m, 1H, H-4e), 3.61 (d, 1H, *J*=9.7 Hz, H-5c), 3.43–3.38 (m, 1H, H-5d), 2.06, 1.99, 1.90 (3s, 9H, 3×OAc), 1.26 (d, 3H, $J_{5,6}$=6.5 Hz, H-6e), 1.08 (d, 3H, $J_{5,6}$=6.3 Hz, H-6d). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.26, 170.18, 168.95 (3C=O, Ac), 139.05, 138.85, 138.23, 138.11, 132.53, 131.84, 129.16 (arom C), 134.35, 132.61, 128.94, 128.64, 128.35, 128.23, 128.12, 128.10, 128.01, 127.90, 127.56, 127.40, 127.36, 127.04, 123.83 (arom CH), 99.53 (C-1d), 97.42 (C-1e), 84.43 (C-1c), 79.84 (C-3e), 79.74 (C-5c), 77.94 (C-4e), 75.21 (C-2e), 74.81 (C-4c), 73.37 (C-3c), 74.26, 73.58, 73.12, 72.93 (4×PhCH_2), 71.52 (C-3d), 70.53 (C-4d), 69.16 (C-2d), 68.99 (C-5d), 68.01 (C-6c), 66.59 (C-5e), 55.74 (C-2c), 20.87, 20.69, 20.65 (3×CH_3CO), 16.78 (C-6e), 16.24 (C-6d). ESI-HRMS (*m*/*z*) Calcd for $C_{66}H_{69}NO_{17}SNa$ (M+Na^+): 1202.4178. Found: 1202.4165.

4.10. Synthesis of 2-(trimethylsilyl)ethyl (2,3,4-tri-*O*-acety-β-D-fucopyranosyl)-(1→4)-[2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside-(1→3)-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (15)

A solution of **14** (350 mg, 0.297 mmol, 1 equiv) and **5** (318 mg, 0.356 mmol, 1.2 equiv) in 21 mL of dry dichloromethane was stirred with 4 Å powdered molecular sieves (700 mg) for 30 min at room temperature under nitrogen, then cooled to −15 °C. NIS (146.3 mg,

0.65 mmol, 2.2 equiv), then TfOH (8.61 μL, 0.097 mmol, 0.33 equiv) were added. The mixture was stirred at −15 °C for 1 h, then neutralized with Et_3N, filtered through Celite and concentrated. The residue was washed with aqueous sodium thiosulfate, water, and brine and then dried over $MgSO_4$ and concentrated. After purification by flash column chromatography (cyclohexane/ethyl acetate 2.5:1), compound **15** was obtained (477 mg, 82%) as a white foam: R_f=0.46 (toluene/ethyl acetate 3:1); $[\alpha]_D^{20}$ +5.0 (*c* 1.0, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.02 (m, 49H, arom), 5.31 (d, 1H, $J_{1,2}$=8.4 Hz, H-1c), 5.12–5.11 (m, 1H), 5.07–4.85 (m, 4H), 4.83 (d, 1H, $J_{1,2}$=3.6 Hz, H-1e), 4.82–4.64 (m, 10H, H-1d), 4.58 (d, 1H, J_{gem}=11.9 Hz, one of the PhCH_2), 4.56 (d, 1H, $J_{1,2}$=8.4 Hz, H-2c), 4.53–4.46 (m, 5H), 4.40–4.31 (m, 3H, H-1a), 4.29–4.17 (m, 4H, H-1b), 4.11 (br s, 1H), 3.98–3.96 (m, 2H, 1H of OCH_2), 3.94–3.81 (m, 3H, H-6), 3.77–3.73 (m, 2H, 2×H-6), 3.64–3.62 (m, 2H), 3.58–3.51 (m, 3H, 1H of OCH_2, H-6), 3.49–3.33 (m, 6H, H-5d, PhCH_2, H-6), 3.04–3.02 (m, 1H, one of the PhCH_2), 2.82 (s, 1H, OH), 2.01, 1.96, 1.87 (3s, 9H, OAc), 1.21 (d, 3H, $J_{5,6}$=6.5 Hz, H-6e), 1.05 (d, 3H, $J_{5,6}$=6.4 Hz, H-6d), 1.01–0.96 (m, 2H, OCH_2CH_2Si), 0.002 (s, 9H, $SiMe_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.23, 170.16, 168.89 (3C=O, Ac), 139.10, 138.91, 138.82, 138.71, 138.58, 138.54, 138.38, 138.10, 137.71 (arom C), 133.97–123.38 (49arom CH), 103.07 (C-1b), 102.06 (C-1a), 99.46 (C-1d), 99.00 (C-1c), 97.25 (C-1e), 83.46, 82.90, 81.91, 79.55, 78.06, 77.65, 76.03, 75.24, 75.15, 74.92, 74.69, 72.56, 72.08, 71.40, 70.34, 69.04, 68.94, 67.51 (ring CH), 75.46, 74.96, 74.11, 73.68, 73.39, 72.98, 72.90, 72.83 (PhCH_2), 68.42, 68.00, 67.87 (C-6a, C-6b, C-6c), 67.29 (OCH_2CH_2Si), 66.47 (C-5e), 56.33 (C-2c), 20.82, 20.66, 20.60 (CH_3, Ac), 18.47 (OCH_2CH_2Si), 16.74 (C-6e), 16.15 (C-6d), −1.36 ($SiMe_3$). ESI-HRMS (*m*/*z*) calcd for $C_{112}H_{127}NO_{28}SiNa$ (M+Na^+): 1984.8206. Found: 1984.8190.

4.11. Synthesis of 2-(trimethylsilyl)ethyl (2,3,4-tri-*O*-acety-β-D-fucopyranosyl)-(1→4)-[2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside-(1→3)-(4-*O*-acetyl-2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (15′)

A solution of **15** (46 mg) and 20 mg of DMAP in 1 mL of pyridine and 0.5 mL of acetic anhydride was stirred at room temperature for 14 h and then concentrated, co-evaporated with toluene and dried. Compound **15′** was obtained (45 mg, 95%); R_f=0.48 (toluene/ethyl acetate 3:1); $[\alpha]_D^{20}$ +3.0 (*c* 1.0, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–6.82 (m, 49H, arom), 5.43 (d, 1H, *J*=3.5 Hz, H-4b), 5.21 (d, 1H, $J_{1,2}$=8.2 Hz, H-1c), 5.06–5.05 (m, 1H), 5.00–4.97 (m, 1H, H-2e), 4.90 (d, 1H, J_{gem}=12.2 Hz, one of the PhCH_2), 4.87 (d, 1H, J_{gem}=11.7 Hz, one of the PhCH_2), 4,81–4.76 (m, 2H), 4.74–4.71 (m, 4H, H-1d, H-1e, H-3c, H-5e), 4.67–4.63 (m, 2H, PhCH_2), 4.61–4.50 (m, 4H), 4.42 (d, 1H, J_{gem}=12.2 Hz, one of the PhCH_2), 4.41 (d, 1H, $J_{1,2}$=8.2 Hz, H-2c), 4.40–4.34 (m, 3H, H-2b, H-3e, one of the PhCH_2), 4.26 (d, 1H, *J*=7.6 Hz, H-1a), 4.24–4.21 (m, 3H), 4.19 (d, 1H, *J*=8.0 Hz, H-1b), 4.15–4.11 (m, 2H, H-4e, one of the PhCH_2), 3.95 (d, 1H, J_{gem}=12.0 Hz, one of the PhCH_2), 3.92–3.73 (m, 7H, H-2a, H-4c, H-5c, 2×H-6, OCH_2CH$_2$Si), 3.46–3.41 (m, 3H, H-5d, PhCH_2), 3.37–3.25 (m, 6H, H-6), 3.02–2.99 (m, 1H, one of the PhCH_2), 2.11, 2.06, 1.98, 1.88 (4s, 12H, 4×OAc), 1.24 (d, 3H, *J*=6.5 Hz, H-6e), 1.06 (d, 3H, *J*=6.3 Hz, H-6d), 0.98–0.93 (m, 2H, OCH_2CH_2Si), 0.02 (s, 9H, $SiMe_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.32, 170.23, 170.10, 169.05 (4C=O, Ac), 139.28, 139.14, 138.93, 138.91, 138.62, 138.45, 138.39, 138.29, 131.42 (arom C), 128.57–123.43 (49 arom CH), 103.23 (C-1b), 102.20 (C-2a), 99.48 (C-1d), 99.22 (C-1c), 97.10 (C-1e), 82.76 (C-5d), 75.88 (C-4c), 71.57 (C-4b), 70.11 (C-2e), 66.45 (C-5e), 56.84 (C-2c), 81.88, 79.64, 78.90, 78.84, 77.99, 75.68, 75.22, 74.80, 72.71, 71.80, 71.57, 70.57, 69.16, 68.95, 66.45 (CH), 75.25, 75.02, 74.21, 74.26, 73.60, 73.12, 72.98, 72.80 (PhCH_2), 68.39, 67.82, 67.35 (3C-6, OCH_2), 20.94, 20.86, 20.68, 20.64 (4CH_3, Ac), 18.54 (OCH_2CH_2Si), 16.76 (C-6e), 16.21 (C-6d), −1.32 ($SiMe_3$). ESI-HRMS (*m*/*z*) calcd for $C_{114}H_{129}NO_{29}SiNa$ (M+Na^+): 2026.8312. Found: 2026.8250.

4.12. Synthesis of 2-(trimethylsilyl)ethyl (β-D-fucopyranosyl)-(1→4)-[2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-acetamido-β-D-glucopyranoside-(1→3)-(2,6-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (16)

To a solution of compound **15** (82 mg, 0.042 mmol) in 11 mL of ethanol, were added 0.7 mL of hydrazine monohydrate and 0.7 mL of water. The mixture was refluxed at 80 °C for 14 h. After concentration, the residue was co-evaporated with toluene and dried over P_2O_5, then dissolved in 4 mL of methanol/dichloromethane (1:1), to which 0.4 mL of acetic anhydride was introduced. The mixture was stirred at room temperature overnight. After concentration, the residue was purified by a column of silica gel (dichloromethane/methanol 50:1), and then by a Sephadex column (LH-20) using methanol/dichloromethane (1:1) as eluant. Compound **16** was obtained (62 mg, 86%, two steps) as a white amorphous solid: R_f=0.39 (dichloromethane/methanol 10:1); $[\alpha]_D^{20}$ −15 (*c* 1.0, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.15 (m, 45H, arom), 5.81 (d, 1H, *J*=7.0 Hz, NH), 5.19 (d, 1H, $J_{1,2}$=7.3 Hz, H-1c), 5.02–4.98 (m, 2H, H-1e, one of the PhCH_2), 4.95–4.88 (m, 3H, PhCH_2), 4.74–4.53 (m, 10H), 4.50–4.27 (m, 9H, H-1a, H-1b, H-1d, H-5d), 4.24 (t, 1H, *J*=8.3 Hz, H-3c), 4.07–3.80 (m, 7H, H-2e, H-3e, H-4c, OCHCH$_2$Si), 3.71–3.67 (m, 2H, 2×H-6), 3.62–3.29 (m, 20H, H-2a, H-2b, H-2c, H-2d, H-4e, H-5e, OCHCH$_2$Si, 2×H-6), 1.39 (s, 3H, OAc), 1.25 (d, 3H, $J_{5,6}$=6.4 Hz, H-6e), 1.11 (d, 3H, $J_{5,6}$=6.4 Hz, H-6d), 1.05–1.00 (m, 2H, OCH_2CH_2Si), 0.03 (s, 9H, $SiMe_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.85 (C=O, Ac), 139.27, 139.07, 138.94, 138.72, 138.67, 138.63, 138.54, 138.41, 138.01 (arom C), 128.67–127.29 (arom CH), 103.20 (C-1b), 102.33 (C-1a), 100.73 (C-1d), 99.96 (C-1c), 98.04 (C-1e), 83.05, 82.29, 82.08, 79.53, 79.10, 77.75, 76.61, 76.48, 76.01, 75.19, 74.59, 74.42, 73.92, 73.10, 71.71, 70.96, 70.58, 67.75, 67.19 (ring CH), 75.47, 75.07, 75.03, 74.73, 74.04, 73.47, 73.21, 72.56 (PhCH_2), 69.44, 68.91, 68.46, 67.39 (3C-6, OCH_2CH$_2$), 57.23 (C-2c), 23.03 (CH_3, Ac), 18.58 (OCH_2CH_2Si), 16.85 (C-6e), 16.49 (C-6d), −1.29 ($SiMe_3$). ESI-HRMS (*m*/*z*) calcd for $C_{100}H_{121}NO_{24}SiNa$ (M+Na^+): 1770.7940. Found: 1770.7933.

4.13. Synthesis of 2-(trimethylsilyl)ethyl (β-D-fucopyranosyl)-(1→4)-[α-L-fucopyranosyl-(1→3)]-2-deoxy-2-acetamido-β-D-glucopyranoside-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (17)

A solution of **16** (114 mg) in methanol (11 mL) was treated with Pd/C (10%, 35 mg) under H_2 (160 kPa) for 20 h at 30 °C, then filtered and evaporated. The residue was purified on a Sephadex column (G25) using water as eluant. Compound **17** was obtained in quantitative yield (61 mg) as a white amorphous solid: R_f=0.51 (isopropanol/ethyl acetate/water 3:3:2); $[\alpha]_D^{20}$ −49.6 (*c* 1.0, methanol); ^{1}H NMR (400 MHz, D_2O): δ 5.16 (d, 1H, $J_{1,2}$=4.0 Hz, H-1e), 4.92–4.87 (m, 1H, H-5d), 4.74 (d, 1H, $J_{1,2}$=8.2 Hz, H-1), 4.53 (d, 1H, $J_{1,2}$=8.0 Hz, H-1), 4.47 (d, 1H, $J_{1,2}$=7.8 Hz, H-1), 4.46 (d, 1H, $J_{1,2}$=7.8 Hz, H-1), 4.19 (d, 1H, *J*=3.2 Hz), 4.10–3.59 (m, 25H), 3.49(dd, 1H, $J_{1,2}$=7.8 Hz, $J_{2,3}$=9.8 Hz, H-2), 3.34–3.30 (m, 1H, H-2), 2.06 (s, 3H, Ac), 1.26 (d, 3H, $J_{5,6}$=6.4 Hz, H-6e), 1.21 (d, 3H, $J_{5,6}$=6.6 Hz, H-6d), 1.06 (2dt, 2H, J_{gem}=12.9 Hz, J_{vic}=5.6 Hz, CH_2Si), 0.06 (s, 9H, $SiMe_3$). ^{13}C NMR (100.6 MHz, D_2O): δ 174.67 (C=O, NHAc), 102.84, 102.50, 101.76, 101.28 (C-1a, C-1b, C-1c, C-1d), 98.43 (C-1e), 82.09, 78.32, 75.16, 74.86, 74.75, 74.53, 73.34, 72.61, 71.95, 71.00, 70.33, 69.96, 69.13, 68.29, 67.82, 66.68 (ring, CH), 72.82 (C-2), 70.80 (C-2), 68.43 (OCH_2CH_2Si), 60.94, 60.06, 59.63 (C-6a, C-6b, C-6c), 55.98 (C-2c), 22.25 (CH_3, Ac), 17.56 (CH_2Si), 15.80 (C-6e), 15.29 (C-6d), −2.55

($SiMe_3$). ESI-HRMS (m/z) calcd for $C_{37}H_{67}NO_{24}SiNa$ ($M+Na^+$): 960.3714. Found: 960.3725.

4.14. Synthesis of 2-(trimethylsilyl)ethyl (2,3,4-tri-*O*-acetyl-β-D-fucopyranosyl)-(1→4)-[2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl-(1→3)]-(6-*O*-acetyl-2-deoxy-2-acetamido-β-D-glucopyranosid)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (18)

A solution of **17** (52 mg) and DMAP (20 mg) in 4 mL of pyridine and 2 mL of acetic anhydride was stirred at 30 °C for 14 h and then concentrated, co-evaporated with toluene. The residue was purified by flash column chromatography (dichloromethane/methanol 40:1) to afford **18** (80 mg, 97%) as a white foam: R_f=0.42 (ethyl acetate/dichloromethane 2:1); $[\alpha]_D^{20}$ −33.4 (*c* 1.0, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.38 (d, 1H, *J*=7.7 Hz, NH), 5.33–5.29 (m, 2H), 5.28 (d, 1H, *J*=3.7 Hz, H-1e), 5.26–5.23 (m, 2H, H-4b), 5.14 (t, 1H, $J_{2,3}$=$J_{3,4}$=9.3 Hz, H-3d), 5.08–5.06 (m, 1H, H-5d), 5.04 (d, 1H, $J_{1,2}$=7.7 Hz, H-2a), 5.00–4.93 (m, 4H, H-2b, H-2e, H-6), 4.90 (d, 1H, $J_{1,2}$=7.9 Hz, H-1c), 4.85 (dd, 1H, $J_{1,2}$=7.9 Hz, $J_{2,3}$=9.5 Hz, H-2d), 4.56 (d, 1H, $J_{1,2}$=7.8 Hz, H-1a), 4.44 (d, 1H, $J_{1,2}$=8.0 Hz, H-1d), 4.43–4.40 (m, 1H, H-6), 4.32 (d, 1H, $J_{1,2}$=7.9 Hz, H-1b), 4.24 (t, 1H, $J_{3,4}$=9.5 Hz, H-3c), 4.12–4.00 (m, 3H, 2×H-6), 3.98–3.93 (m, 1H, H-3e), 3.92–3.88 (m, 1H, OC*H*CH$_2$Si), 3.81–3.72 (m, 4H, H-4c, H-4d, H-4e, H-5e), 3.68 (dd, 1H, $J_{2,3}$=10.0 Hz, $J_{3,4}$=3.6 Hz, H-3b), 3.59–3.50 (m, 2H, OC*H*CH$_2$Si), 3.41–3.37 (m, 1H, H-5c), 3.09–3.07 (m, 1H, H-2c), 2.17–1.91 (m, 42H, 14×CH_3CO), 1.38 (d, 3H, $J_{5,6}$=6.4 Hz, H-6e), 1.19 (d, 3H, $J_{5,6}$=6.6 Hz, H-6d), 0.97–0.82 (m, 2H, OCH$_2$C*H*$_2$Si), 0.02 (s, 9H, $SiMe_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 171.34, 171.14, 170.91, 170.80, 170.74, 170.62, 170.44, 170.24, 170.01, 169.79, 169.67, 169.46, 168.97 (14×CH_3*C*O), 100.81 (C-1b), 100.39 (C-1a), 100.10 (C-1d), 99.23 (C-1c), 95.53 (C-1e), 75.92, 75.86, 74.46, 73.24, 72.93, 72.73, 72.54, 71.81, 71.63, 71.31, 71.22, 71.20, 70.30, 70.10, 69.31, 69.24, 69.03, 68.02, 64.14 (19×ring C), 67.58 (O*C*H$_2$CH$_2$Si), 62.35, 61.61, 59.86 (3×C-6), 58.80 (C-2c), 23.54–20.67 (14×*C*H$_3$CO), 17.98 (CH$_2$Si), 16.02 (C-6e), 15.82 (C-6d), −1.33 ($SiMe_3$). ESI-HRMS (m/z) calcd for $C_{63}H_{93}NO_{37}SiNa$ ($M+Na^+$): 1506.5088. Found: 1506.5110.

4.15. Synthesis of (2,3,4-tri-*O*-acetyl-β-D-fucopyranosyl)-(1→4)-[2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl-(1→3)]-(6-*O*-acetyl-2-deoxy-2-acetamido-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (19)

To a solution of compound **18** (124 mg, 0.084 mmol) in 2 mL of dichloromethane was added 4 mL of trifluoroacetic acid dropwise at 0 °C. The mixture was stirred at 0 °C for 1 h and then at room temperature for 5 h. Then the mixture was diluted with dichloromethane and washed with a saturated aqueous $NaHCO_3$ and then with brine, dried over $MgSO_4$. After concentration, the residue was dried in vacuo (R_f=0.3, dichloromethane/methanol 20:1). The residue was then dissolved in 3.6 mL of dry dichloromethane, 0.3 mL of trichloroacetonitrile was added to the solution and then 30 μL of DBU was added dropwise at 0 °C under nitrogen. The mixture was stirred at 0 °C for 4 h. After concentration, the residue was purified by flash column chromatography (ethyl acetate/dichloromethane/triethylamine 10:10:0.01) to afford compound **19** as white foam (83 mg, 65%): R_f=0.36 (ethyl acetate/dichloromethane 2:1); $[\alpha]_D^{20}$ +2.6 (*c* 0.7, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (s, 1H, HN=C), 6.46 (d, 1H, *J*=3.7 Hz, H-1a), 5.51 (t, 1H, $J_{2,3}$=$J_{3,4}$=9.7 Hz, H-3a), 5.44 (d, 1H, *J*=7.7 Hz, NHAc), 5.29–5.26 (m, 2H, H-4e), 5.28 (d, 1H, *J*=3.8 Hz, H-1e), 5.24–5.23 (m, 1H, H-4d), 5.07 (d, 1H, $J_{1,2}$=7.8 Hz, H-2b), 5.03 (d, 1H, $J_{1,2}$=3.3 Hz, H-2a), 5.02–4.91 (m, 6H, H-1c, H-2d, H-3e, H-5d, H-6), 4.57(d, 1H, $J_{1,2}$=7.8 Hz, H-1b), 4.44–4.40 (m, 1H, H-6), 4.35 (d, 1H, *J*=7.9 Hz, H-1d), 4.25 (t, 1H, $J_{2,3}$=$J_{3,4}$=9.2 Hz, H-3c), 4.15–3.92 (m, 5H, 4×H-6), 3.82–3.72 (m, 5H, H-2e, H-4a, H-5c, H-5e), 3.68 (dd, 1H, $J_{2,3}$=9.9 Hz, $J_{3,4}$=3.6 Hz, H-3d), 3.40–3.37 (m, 1H, H-5a), 3.12–3.07 (m, 1H, H-2c), 2.17–1.92 (m, 42H, 14×CH_3CO), 1.39 (d, 3H, $J_{5,6}$=6.4 Hz, H-6e), 1.19 (d, 3H, $J_{5,6}$=6.5 Hz, H-6d). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 171.47, 171.18, 170.95, 170.83, 170.78, 170.53, 170.50, 170.32, 170.22, 169.80, 169.72, 169.58, 169.50, 168.97 (14×CH_3*C*O), 161.09 (C=NH), 100.93 (C-1d), 100.33 (C-1b), 99.22 (C-1c), 95.52 (C-1e), 92.97 (C-1a), 76.00, 75.24, 74.36, 73.19, 72.40, 71.56, 71.25, 71.20, 71.11, 71.07, 70.25, 70.05, 69.98, 69.44, 69.26, 69.17, 69.00, 67.98, 64.09 (19×ring C), 61.67, 61.55, 59.63 (3×C-6), 58.76 (C-2c), 21.19–20.61 (14×*C*H$_3$CO), 16.01 (C-6e), 15.82 (C-6d). ESI-HRMS (m/z) calcd for $C_{60}H_{81}Cl_3N_2O_{37}Na$ ($M+Na^+$): 1549.3476. Found: 1549.3446.

4.16. Synthesis of (2,3,4-tri-*O*-acetyl-β-D-fucopyranosyl)-(1→4)-[2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl-(1→3)]-(6-*O*-acetyl-2-deoxy-2-acetamido-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-l,3-diol (20)

A solution of **19** (83 mg, 0.054 mmol, 1 equiv) and 3-*O*-benzoyl-azido sphingosine **6** (46.6 mg, 0.108 mmol, 2 equiv) in 3.2 mL of dry dichloromethane was stirred with 4 Å powdered molecular sieves (200 mg) for 30 min at room temperature under nitrogen. $BF_3\cdot Et_2O$ (39 μL, 0.308 mmol, 5.7 equiv) was added dropwise at −10 °C. The mixture was stirred for 3 h at −10 °C and then filtered through Celite. The filtrate was washed with a saturated aqueous $NaHCO_3$ and then with water, dried over $MgSO_4$ and concentrated. The residue was applied to a flash chromatography eluted with cyclohexane/ethyl acetate (1:1) to give the product **20** (55 mg, 57%) as an amorphous solid: R_f=0.42 (cyclohexane/ethyl acetate 1:2); $[\alpha]_D^{20}$ −29.5 (*c* 1.0, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04–8.02 (m, 2H, 2×arom H), 7.59–7.54 (m, 1H, arom H), 7.44 (t, 2H, *J*=7.8 Hz, 2×arom H), 5.90 (dt, 1H, $J_{5,6}$=6.8 Hz, $J_{4,5}$=$J_{5,6'}$=14.2 Hz, H-5), 5.60–5.49 (m, 2H, H-3, H-4), 5.40 (d, 1H, *J*=7.6 Hz, *NH*Ac), 5.34–5.33 (m, 1H), 5.28 (d, 1H, *J*=3.8 Hz, H-1e), 5.26–5.24 (m, 3H), 5.15 (t, 1H, *J*=9.3 Hz), 5.08–4.90 (m, 8H, H-1c, H-2a, H-2b, H-2d, H-3e, 2×H-6), 4.58 (d, 1H, *J*=7.8 Hz, H-1a), 4.49 (d, 1H, *J*=7.8 Hz, H-1b), 4.42 (d, 1H, *J*=11.7 Hz, H-6), 4.33 (d, 1H, *J*=7.9 Hz, H-1d), 4.27 (t, 1H, $J_{2,3}$=$J_{3,4}$=9.3 Hz, H-3c), 4.12–3.90 (m, 5H, H-2, 3×H-6), 3.86–3.74 (m, 5H, H-1, H-4c, H-5e), 3.70–3.67 (m, 1H), 3.60–3.54 (m, 2H, H-1′), 3.40 (d, 1H, *J*=9.8 Hz, H-5c), 3.07–3.05 (m, 1H, H-2c), 2.18–1.92 (m, 44H, 14×CH_3CO, CH_2-6), 1.40 (d, 3H, $J_{5,6}$=6.4 Hz, H-6e), 1.24–1.22 (m, 22H, 11×CH_2), 1.20 (d, 3H, $J_{5,6}$=6.6 Hz, H-6d), 0.87 (t, 3H, *J*=7.0 Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 171.38, 171.17, 170.94, 170.82, 170.78, 170.54, 170.47, 170.28, 170.00, 169.81, 169.70, 169.64, 169.50, 169.00 (14×CH_3*C*O), 165.21 (Ph*C*=O), 139.15 (C-5cer), 133.34 (arom CH), 130.07 (arom C), 129.87 (2×arom CH), 128.59 (2×arom CH), 122.77 (C-4), 100.93 (C-1d), 100.52 (C-1a), 100.42 (C-1b), 99.26 (C-1c), 95.55 (C-1e), 77.36, 75.86, 75.66, 74.40, 72.85, 72.72, 71.58, 71.42, 71.27, 71.20, 71.11, 70.27, 70.07, 69.28, 69.18, 69.05, 67.99 (17×ring C), 74.77 (C-3), 73.18 (C-5c), 72.39 (C-3c), 64.12 (C-2a), 63.58 (C-2), 68.47 (C-1), 62.06, 61.58, 59.70 (3×C-6), 58.87 (C-2c), 32.50 (C-6), 32.03, 29.79, 29.76, 29.70, 29.51, 29.47, 29.27, 28.82, 22.80 (11×CH_2), 23.58, 21.18–20.74 (14×*C*H$_3$CO), 16.02 (C-6e), 15.83 (C-6d), 14.26 (CH_3). ESI-HRMS (m/z) calcd for $C_{83}H_{118}N_4O_{39}Na$ ($M+Na^+$): 1817.7265. Found: 1817.7218.

4.17. Synthesis of (2,3,4-tri-*O*-acetyl-β-D-fucopyranosyl)-(1→4)-[2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl-(1→3)]-(6-*O*-acetyl-2-deoxy-2-acetamido-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl) -(1→1)-(2*S*,3*R*,4*E*)-2-octadecanamido-3-*O*-benzoyl-4-octadecene-l,3-diol (21)

To a solution of compound **20** (32 mg, 0.018 mmol) in 4 mL of toluene and 0.16 mL of water was added 18.8 mg of triphenyl

phosphine. The mixture was stirred at 45 °C for 24 h. After concentration, the residue was used directly for the next step. R_f=0.42 (dichloromethane/methanol 15:1). The mixture of the residue, stearic acid (19 mg, 0.066 mmol), EDC (12.6 mg, 0.066 mmoL) in 4 mL of dichloromethane was stirred at room temperature for 24 h. Then the mixture was washed with water, dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography (dichloromethane/methanol 50:1) to give **21** as an amorphous solid (22 mg, 61% for two steps): R_f=0.51 (ehtyl acetate/dichloromethane 3:1); $[\alpha]_D^{20}$ −22.2 (*c* 1.0, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00–7.40 (m, 5H, 5×arom H), 5.85 (dt, 1H, $J_{5,6}$=6.8 Hz, $J_{4,5}$=$J_{5,6'}$=14.8 Hz, H-5cer), 5.73 (d, 1H, *J*=9.2 Hz, NH-cer), 5.52 (t, 1H, $J_{3,4}$=$J_{2,3}$=7.3 Hz, H-3cer), 5.44 (dd, 1H, $J_{3,4}$=7.6 Hz, $J_{4,5}$=15.2 Hz, H-4cer), 5.38 (d, 1H, *J*=7.7 Hz, *NH*Ac), 5.33–5.23 (m, 5H, H-1e), 5.13 (t, 1H, $J_{3,4}$=$J_{2,3}$=9.3 Hz, H-3a), 5.08–5.04 (m, 2H, H-2d), 5.01–4.95 (m, 2H), 4.94–4.85 (m, 4H, H-1c, H-2a, H-3e, H-6c), 4.57 (d, 1H, $J_{1,2}$=7.8 Hz, H-1d), 4.49–4.44 (m, 1H, H-2cer), 4.42 (d, 1H, $J_{1,2}$=7.8 Hz, H-1a), 4.30–4.21(m, 3H, H-1b, H-3c, H-6a), 4.08–3.94 (m, 5H, H-1cer, 4×H-6), 3.82–3.66 (m, 5H, H-2b, H-2e, H-4a, H-4c, H-5e), 3.60 (dd, 1H, $J_{1',2}$=4.5 Hz, J_{gem}=10.0 Hz, H-1′cer), 3.54–3.50 (m, 1H, H-5a), 3.39 (dt, 1H, $J_{4,5}$=$J_{5,6}$=2.2 Hz, $J_{5,6'}$=9.8 Hz, H-5c), 3.10–3.04 (m, 1H, H-2c), 2.17–1.91 (m, 46H, 14×CH_3CO, CH_2-6cer, HNCOCH_2), 1.59–1.56 (m, 2H, HNCOCH$_2$CH_2), 1.39 (d, 3H, $J_{5,6}$=6.5 Hz, H-6e), 1.24–1.21 (m, 53H, 25×CH_2, H-6d), 0.86 (t, 6H, *J*=7.0 Hz, 2×CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 172. 83, 171.37, 171.15, 170.93, 170.81, 170.76, 170.50, 170.47, 170.27, 169.90, 169.78, 169.69, 169.48, 168.98 (14×CH_3CO), 165.31 (PhC=O), 137.72 (C-5cer), 133.16 (arom CH), 130.38 (arom C), 129.72 (2×arom CH), 128.52 (2×arom CH), 124.75 (C-4cer), 100.82 (C-1d), 100.49 (C-1a), 100.40 (C-1b), 99.24 (C-1c), 95.54 (C-1e), 75.85, 75.53, 74.45, 73.25, 72.91, 72.54, 72.47, 71.79, 71.63, 71.32, 71.26, 71.14, 70.31, 70.11, 69.32, 69.25, 69.05, 68.03, 64.16 (19×ring C), 74.18 (C-3cer), 67.57 (C-1cer), 62.09, 61.62, 59.83 (3×C-6), 58.80 (C-2c), 50.76 (C-2cer), 36.97 (NHCOCH_2), 32.45 (CH_2-6cer), 25.85 (HNCOCH$_2$CH_2), 32.03, 29.82–29.06, 22.80 (25×CH_2), 23.56, 21.14–20.68 (14×CH_3CO), 16.03 (C-6e), 15.83 (C-6d), 14.22 (CH_3). ESI-HRMS (*m*/*z*) calcd for $C_{101}H_{154}N_2O_{40}Na$ (M+Na^+): 2057.9970. Found: 2057.9904.

4.18. Synthesis of (β-D-fucopyranosyl)-(1→4)-[α-L-fucopyranosyl-(1→3)]-(2-deoxy-2-acetamido-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-(β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-octadecanamido-4-octadecene-l,3-diol (1)

A solution of compound **21** (50 mg, 0.024 mmol) in 6.2 mL of NaOMe/MeOH (0.04 M) was stirred at room temperature for 14 h. The mixture was neutralized by Amberlite IR 120/H^+ ion exchange resin. After filtration and concentration, the residue was purified on a Sephadex column (LH-20) using dichloromethane/methanol 1:1 as eluant. Compound **1** was obtained as a white amorphous solid (25.5 mg, 75%): R_f=0.48 (ethyl acetate/isopropanol/water 7:7:3); $[\alpha]_D^{20}$ −14.5 (*c* 0.4, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ 5.69 (dt, 1H, $J_{5,6}$=6.7 Hz, $J_{4,5}$=$J_{5,6'}$=15.0 Hz, H-5cer), 5.45 (dd, 1H, $J_{3,4}$=7.7 Hz, $J_{4,5}$=15.3 Hz, H-4cer), 5.04 (d, 1H, *J*=3.9 Hz, H-1e), 4.92 (dd, 1H, $J_{5,6}$=6.6 Hz, H-5d), 4.71 (d, 1H, *J*=7.6 Hz, H-1), 4.41 (d, 1H, *J*=7.1 Hz, H-1), 4.37 (d, 1H, *J*=7.6 Hz, H-1), 4.30 (d, 1H, *J*=7.8 Hz, H-1), 4.18 (dd, 1H, *J*=4.4, 10.1 Hz, H-1cer), 4.09–4.05 (m, 2H, H-1cer, H-3cer), 4.01–3.95 (m, 2H, H-2cer), 3.92–3.84 (m, 7H, H-2c, 2×H-6), 3.83–3.75 (m, 2H), 3.70 (dd, 1H, $J_{5,6}$=4.6 Hz, J_{gem}=11.4 Hz, H-6), 3.64–3.50 (m, 9H, H-5e, 3×H-6), 3.48–3.46 (m, 2H), 3.44–3.40 (m, 2H), 2.17 (t, 2H, *J*=7.5 Hz, HNCOCH_2), 2.05–2.00 (m, 2H, CH_2-6cer), 1.98 (s, 3H, NHCOCH_3), 1.60–1.57 (m, 2H, HNCOCH$_2$CH_2), 1.29 (s, 50H, 25×CH_2), 1.26 (d, 3H, *J*=6.4 Hz, H-6e), 1.18 (d, 3H, *J*=6.6 Hz, H-6d), 0.90 (t, 6H, *J*=6.8 Hz, 2×CH_3). ^{13}C NMR (100.6 MHz, CD_3OD): δ 175. 92, 174.62 (2×C=O), 135.10 (C-5cer), 131.37 (C-4cer), 105.01, 104.48, 103.81, 103.72 (4×C-1), 100.37 (C-1e), 83.85, 80.35, 77.24, 76.68, 76.62, 76.48, 76.25, 75.02, 74.98, 74.82, 73.72, 72.98, 72.66, 72.52, 71.74, 71.48, 71.22, 70.16, 69.78, 67.67 (19×ring C, C-3cer), 69.91 (C-1cer), 62.42, 61.75, 61.19 (3×C-6), 57.70 (C-2c), 54.68 (C-2cer), 37.37 (HNCOCH_2), 33.47 (C-6cer), 27.16 (HNCOCH$_2$CH_2), 30.88–30.43, 23.74 (25×CH_2), 23.18 (NHCOCH_3), 17.14 (C-6e), 16.63 (C-6d), 14.45 (2×CH_3). ESI-HRMS (*m*/*z*) calcd for $C_{68}H_{124}N_2O_{26}Na$ (M+Na^+): 1407.8335. Found: 1407.8319.

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Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.07.025. This data include MOL files and InChIKeys of the most important compounds described in this article.

References and notes

1. Rouslahti, E.; Pierschbacher, M. D. *Science* **1987**, *238*, 491–497.
2. Varki, V. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 7390–7397.
3. Brewer, C. F.; Miceli, M. C.; Baum, L. G. *Curr. Opin. Struct. Biol.* **2002**, *12*, 616–623.
4. For reviews on carbohydrate–carbohydrate interactions, see: (a) Bovin, N. V. In *Glycosciences, Status and Perspectives*; Gabius, H.-J., Gabius, S., Eds.; Chapman & Hall: Weinheim, 1997; p 277; (b) Spillmann, D.; Burger, M. M. In *Carbohydrates in Chemistry and Biology*; Ernst, B., Hart, G. W., Sinaÿ, P., Eds.; Wiley-VCH: Weinheim, 2000; Vol. 2, p 1061; (c) Rojo, J.; Morales, J. C.; Penadés, S. In *Topics in Current Chemistry, Host Guest Chemistry*; Penadés, S., Ed.; Spring: Berlin, Heidelberg, 2002; p 45; (d) Hakomori, S. *Arch. Biochem. Biophys.* **2004**, *426*, 173–181.
5. Hakomori, H. *Pure Appl. Chem.* **1991**, *63*, 473–482.
6. Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683–720.
7. Eggens, I.; Fenderson, B.; Toyokuni, T.; Dean, B.; Stroud, M.; Hakomori, S. *J. Biol. Chem.* **1989**, *264*, 9476–9484.
8. Kojima, N.; Fenderson, B. A.; Stroud, M. R.; Goldberg, R. I.; Habermann, R.; Toyokuni, T.; Hakomori, S. *Glycoconjugate J.* **1994**, *11*, 238–248.
9. (a) Wormald, M. R.; Edge, C. J.; Dwek, R. A. *Biochem. Biophys. Res. Commun.* **1991**, *180*, 1214–1221; (b) Henry, B.; Desvaux, H.; Pristchepa, M.; Berthault, P.; Zhang, Y.; Mallet, J.-M.; Esnault, J.; Sinaÿ, P. *Carbohydr. Res.* **1999**, *315*, 48–62; (c) Geyer, A.; Gege, C.; Schmidt, R. R. *Angew. Chem., Int. Ed.* **1999**, *38*, 1466–1468; (d) Geyer, A.; Gege, C.; Schmidt, R. R. *Angew. Chem., Int. Ed.* **2000**, *39*, 3246–3249; (e) Gege, C.; Geyer, A.; Schmidt, R. R. *Eur. J. Org. Chem.* **2002**, 2475–2485; (f) Nodet, G.; Poggi, L.; Abergel, D.; Gourmala, C.; Dong, D.; Zhang, Y.; Mallet, J.-M.; Bodenhausen, G. *J. Am. Chem. Soc.* **2007**, *129*, 9080–9085.
10. Siuzdak, G.; Ichikawa, Y.; Caulfield, T. J.; Munoz, B.; Wong, C.-H.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1993**, *115*, 2877–2881.
11. (a) Pincet, F.; Le Bouar, T.; Zhang, Y.; Esnault, J.; Mallet, J.-M.; Perez, E.; Sinaÿ, P. *Biophys. J.* **2001**, *80*, 1354–1358; (b) Gourier, C.; Pincet, F.; Perez, E.; Zhang, Y.; Mallet, J.-M.; Sinaÿ, P. *Glycoconjugate J.* **2004**, *21*, 165–174.
12. (a) Tromas, C.; Rojo, J.; de la Fuente, J. M.; Barrientos, A. G.; Garcia, R.; Penadés, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 3052–3055; (b) de la Fuente, J. M.; Eaton, P.; Barrientos, A. G.; Menéndez, M.; Penadés, S. *J. Am. Chem. Soc.* **2005**, *127*, 6192–6197.
13. Hernaiz, M. J.; de la Fuente, J. M.; Barrientos, A. G.; Penadés, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1554–1557.
14. Boubelik, M.; Floryk, D.; Bohata, J.; Drabevora, L.; Macak, J.; Smid, F.; Draber, P. *Glycobiology* **1998**, *8*, 139–146.
15. Simpson, G. L.; Gordon, A. H.; Lindsay, D. M.; Promsawan, N.; Crump, M. P.; Mulholland, K.; Hayter, B. R.; Gallagher, T. *J. Am. Chem. Soc.* **2006**, *128*, 10638–10639.
16. Gourier, C.; Pincet, F.; Perez, E.; Zhang, Y.; Zhu, Z.; Mallet, J.-M.; Sinaÿ, P. *Angew. Chem., Int. Ed.* **2005**, *44*, 1683–1687.
17. Luo, Y.; Gourmala, C.; Dong, D.; Barbault, F.; Fan, B.; Hu, Y.; Zhang, Y. *Glycoconjugate J.* **2008**, *25*, 335–344.
18. Orita, A.; Hamada, Y.; Nakano, T.; Toyoshima, S.; Otera, J. *Chem.—Eur. J.* **2001**, *7*, 3321–3327.
19. Janczuk, A. J.; Zhang, W.; Andreana, P. R.; Warrick, J.; Wang, P. G. *Carbohydr. Res.* **2002**, 1247–1259.
20. Lu, S.-F.; O'yang, Q.; Guo, Z.-W.; Yu, B.; Hui, Y.-Z. *J. Org. Chem.* **1997**, *62*, 8400–8405.
21. Jain, R. K.; Matta, K. L. *Carbohydr. Res.* **1992**, *226*, 91–100.
22. Zhang, Y.; Esnault, J.; Mallet, J.-M.; Sinaÿ, P. *J. Carbohydr. Chem.* **1999**, *18*, 419–427.

23. Mandal, P. K.; Misra, A. K. *Lett. Org. Chem.* **2008**, *5*, 194–201.
24. Sjölin, P.; George, S. K.; Bergquist, K.-E.; Roy, S.; Svensson, A.; Kihlberg, J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1731–1742.
25. Zhang, Y.; Brodzky, A.; Sinaÿ, P.; Saint-Marcoux, G.; Perly, B. *Tetrahedron: Asymmetry* **1995**, *6*, 1195–1216.
26. Lönn, H. *Carbohydr. Res.* **1985**, *139*, 105–113.
27. Nicolaou, K. C.; Dolle, R. E.; Papahatjis, D. P.; Randall, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 4189–4192.
28. Nicolaou, K. C.; Caulfield, T. J.; Kataoka, H.; Stylianides, N. A. *J. Am. Chem. Soc.* **1990**, *112*, 3693–3695.
29. Macindoe, W. M.; Nakahara, Y.; Ogawa, T. *Carbohydr. Res.* **1995**, *271*, 207–216.
30. Huang, H.; Wong, C.-H. *J. Org. Chem.* **1995**, *60*, 3100–3106.
31. Jansson, K.; Ahlfors, S.; Frejd, T.; Kihlberg, J.; Magnusson, G. *J. Org. Chem.* **1988**, *53*, 5629–5647.
32. Shoufu, L.; Qinqin, O'y.; Zhongwu, G.; Biao, Y.; Yongzheng, H. *J. Org. Chem.* **1997**, *62*, 8400–8405.