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Synthesis and Biological Evaluation of *S*-Neofucopeptides as E- and P-Selectin Inhibitors

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The synthesis of α/β-L-fucosylated cysteamine, 3-thiopropionic acid, and 3-thioacetic acid derivatives as building blocks for the preparation of *S*-neofucopeptides is shown. These compounds were used in the synthesis of new thiofucosides derivatives (**8**α, **9**α, **9**β, **10**α, **22**α, **22**β, **24**α, **26**α) that show affinity towards E- and P-selectins. They constitute a new series of hydrolytically stable and low-molecular-weight mimetics of the natural SLe^x tetrasaccharide.

Introduction

The carbohydrate–protein recognition between tetrasaccharide sialyl Lewis X (SLe^x) (Figure 1) and E- or P-selectin mediates the early stage of an inflammatory response, which leads to the migration of leukocytes from the blood stream to inflamed tissue.[1] It has been envisaged that disruption of these selectin–carbohydrate interactions might serve as a novel target for palliative treatment of acute and chronic inflammatory diseases.[2] SLe^x is a leading structure in the design and development of selectin antagonists, and this tetrasaccharide was identified as an antiinflammatory agent, although its binding affinity is relatively low.[3] The complex saccharidic structure of SLe^x and its sensitivity towards acid and enzymatic hydrolysis, which makes it orally inactive and unstable in the blood stream,[4] has promoted the search for compounds that could act as SLe^x but possess a simpler structure, higher binding affinity, and be resistant to enzymatic hydrolysis.[5–8]

The common design element is based on the nature of the known pharmacophores,[9] which are the hydroxy groups of L-fucose and D-galactose, and the carboxyl group of the sialic acid, which are all involved in the recognition between SLe^x and E-selectin. The GlcNAc moiety merely acts as a scaffold to guarantee the effective conformation for binding.[10] Although non-carbohydrate structures have been examined,[6] the majority of these approaches have focused on carbohydrate-type ligands[7] and related structures consisting of hybrid molecules[8,11,12] with varying degrees of similarity to SLe^x. *O*-Fucopeptides incorporating residues of threonine and hydroxyproline amino acids instead of GlcNAc and D-galactose and glutaric acid instead of sialic acid have been described.[11,12] Although these compounds have shown good affinity towards E- and P-selectins, the difficult glycosylation of *N*-acylated β-hydroxy amino acid derivatives, caused by the decreased nucleophilicity of the glycosyl acceptors coming from the hydrogen-bonding interaction between the acceptor OH and NH groups[13] and the lability of the *O*-glycosidic linkage represent drawbacks in the case of their use as drugs. *C*-Glycoside[14] mimetics as non-hydrolizable mimetics of SLe^x as well as *S*-linked analogues of carbohydrate antigens of SLe^x have been prepared and characterized;[15] however, their thioglycopeptide counterparts are relatively unexplored.[16]

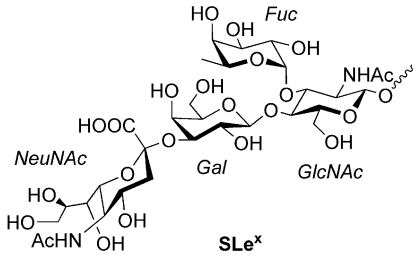

Figure 1. Structure of the natural tetrasaccharide sialyl Lewis X (SLe^x).

We now present the synthesis of new *S*-linked fucosides **I**–**III** (Figure 2) containing the functional groups deemed critical for binding to selectins. The introduction of a sulfur group at the anomeric position provides good acid- and enzyme-mediated hydrolytic stability.[16] In addition, the higher water solubility of sulfur derivatives relative to that of their oxygen counterparts is an important advantage for

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our compounds with regard to tolerance by most biological systems.[17] Compounds of type **I** incorporate glutaric acid instead of neuraminic acid and hydroxyproline derivatives instead of D-galactose as in the *O*-fucopeptides designed by Wong.[11,12] Compounds **II** and **III** bear a trihydroxyalkylfuran aminoester moiety as a novel non-proteinogenic polyhydroxylated amino acid, which could be able to mimic both the galactose and the sialic acid residues of SLe^x. Additionally, the furan ring could favor affinity to selectins by aromatic–aromatic interactions. The overall synthetic procedure of the target compounds is highly advantageous due to the superior nucleophilicity of sulfur, which makes the fucosylation reaction proceed readily, and to the use of simpler spacers[18] derived from cysteamine (compounds **I**) or from 3-thiopropionic/thioacetic acid (compounds **II** and **III**).

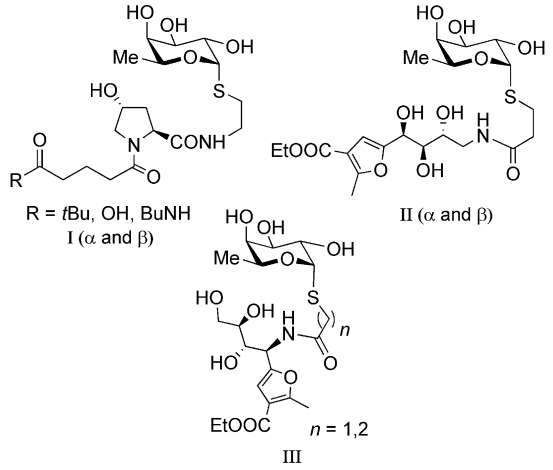


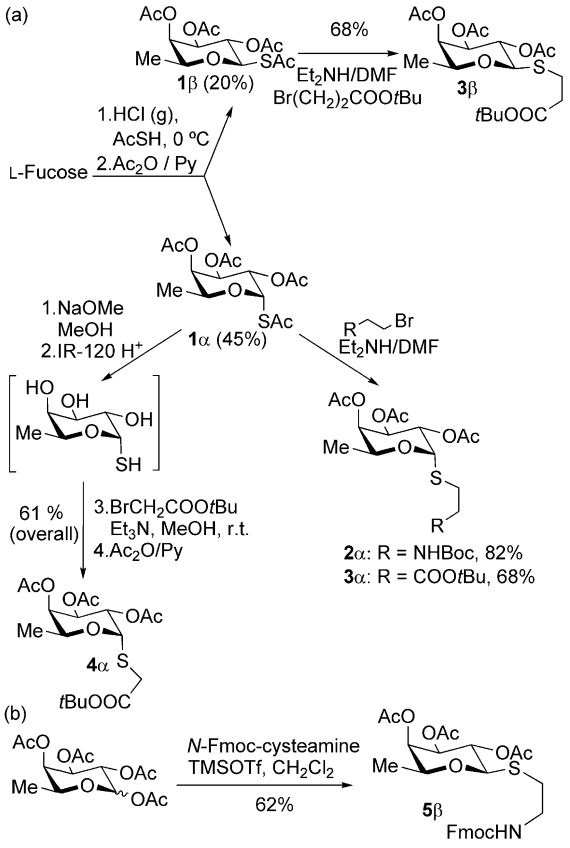
Figure 2. Structure of the new *S*-linked fucosides.

Results and Discussion

Synthesis

Compounds **I**–**III** were prepared from α/β-aminoalkylthiofucopyranosides **2**α and **5**β or from α/β-carboxyalkylthiofucopyranosides **3**α, **3**β, and **4**α. Two main strategies were used for the preparation of compounds **2**–**5** and they include (a) nucleophilic displacement of the appropriate bromo derivative by an anomeric glycosyl thiolate nucleophile and (b) glycosylation of a thiol-containing compound such as cysteamine (Scheme 1).

Condensation of L-fucose with thioacetic acid in the presence of hydrogen chloride followed by acetylation in pyridine gave 1-thio-α- and -β-L-fucose tetraacetate **1**α (45%) and **1**β (20%) according to the procedure of Hashimoto[19] et al. (Scheme 1). One-pot reaction of thioacetate **1**α with *N*-Boc-bromoethylamine or *tert*-butyl 3-bromopropionate with the use of diethylamine in DMF[20] gave the *S*-linked-fucoside building blocks **2**α and **3**α in good yield. Under such reaction conditions, selective deacetylation at the sulfur atom takes place while retaining the anomeric integrity. This procedure failed in the synthesis of building

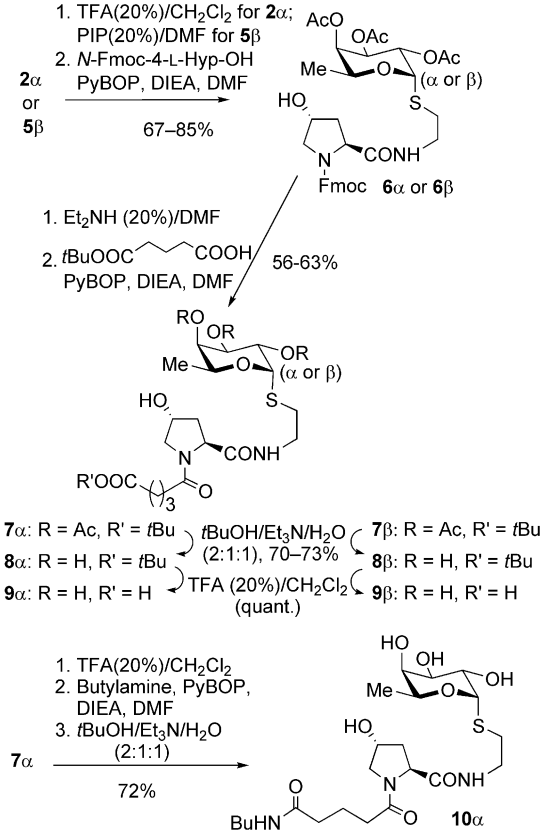


Scheme 1. Synthesis of the *S*-linked fucoside building blocks.

block **4**α from thiofucoside **1**α, probably due to the consumption of the highly reactive alkylating agent *tert*-butyl bromoacetate by the excess amount of diethylamine. So, a simple "two-step, one-pot" reaction was required to carry out *S*-fucosylation of the bromoacetate derivative. Thus, reaction of thiofucoside **1**α with NaOMe in anhydrous methanol followed by acidic resin neutralization gave 1-mercaptofucose, which was subjected to nucleophilic substitution with *tert*-butyl bromoacetate in the presence of Et_3N to furnish the desired *S*-linked fucosyl derivative. This compound was peracetylated to afford **4**α in 61% overall yield. The anomeric configuration was also preserved under these conditions. Compound **3**β was obtained in a similar way in 68% yield starting from compound **1**β. Alternatively, the synthesis of *N*-Fmoc-aminoethyl β-fucoside building block **5**β[21] was carried out in good yield by glycosylation of *N*-Fmoc cysteamine with tetra-*O*-acetyl fucose as a donor in the presence of TMSOTf. Compounds **2**–**5** are attractive and versatile building blocks for the generation of libraries of new *S*-neofucopeptides.[22]

The synthesis of thiofucoside derivatives of 4-hydroxyproline (compounds of type **I**) was carried out in a linear sequence by using standard peptide chemistry (Scheme 2).

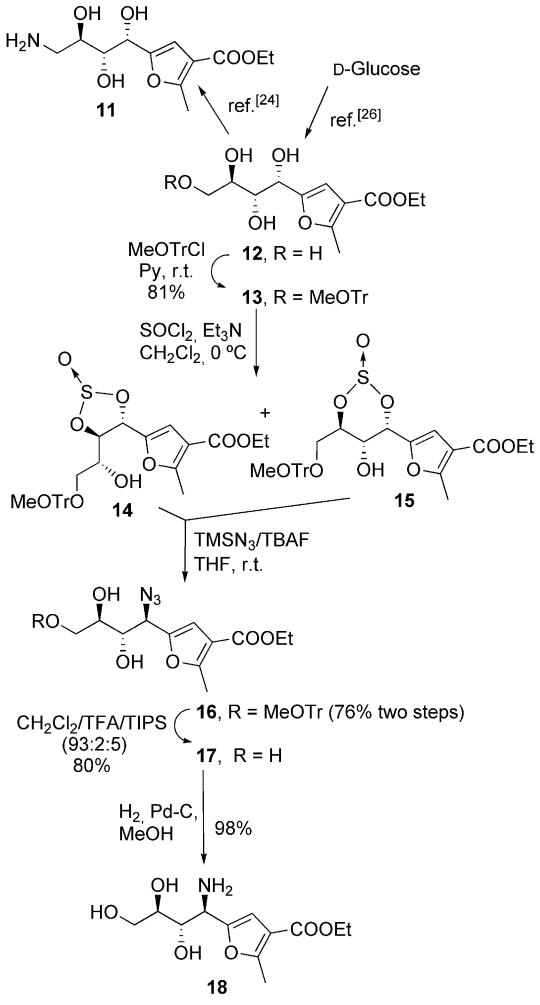
N-Deprotection of compounds **2**α or **5**β followed by coupling with commercial *N*-Fmoc-4-L-hydroxyproline by using (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate/diisopropyl(ethyl)amine (PyBOP/



Scheme 2. Synthesis of *S*-linked fucosides containing 4-hydroxyproline.

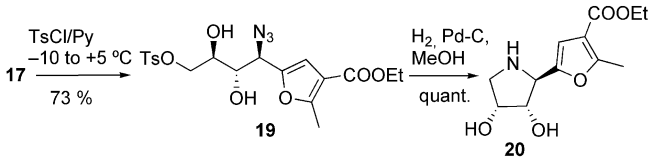
DIEA) as coupling reagents gave **6**α or **6**β in 67–85% overall yield. Fmoc-group removal (20% diethylamine in DMF) and condensation with mono-*tert*-butyl glutaric acid gave adduct **7**α or **7**β in 56–63% yield. Hydrolysis of the acetyl groups with *t*BuOH/Et_3N/H_2O (2:1:1) afforded cleanly the *S*-linked fucoside **8**α or **8**β. These mild deacetylation conditions do not need neutralization with ion-exchange resins as normally happens when Zemplén methodology is employed. The compounds so-obtained are free of polyanions (traces) released from the resins (bleeding), which are difficult to detect by routine analysis and that can also mask selectin binding assays.[23] Finally, deprotection of the *tert*-butyl ester by using TFA (20%)/CH_2Cl_2 afforded acid **9**α or **9**β in quantitative yield. Amide **10**α was prepared from **7**α by acidic deprotection followed by condensation with butylamine and deacetylation.

The synthesis of tetritol-1-yl-furyl derivatives of type **II** and **III** was carried out by starting from carboxyalkylthiofucosides **3**α, **3**β, and **4**α by coupling with synthetic 4′-aminotrihydroxyalkylfuryl ester **11** and 1′-aminotrihydroxyalkylfuryl ester **18**. Compound **11** can be easily obtained from D-glucose in four steps as was described previously by our research group.[24] We also recently reported a methodology for the stereoselective synthesis of α-furfurylamines starting from D-aldopentoses.[25] As an extension of this work, we now describe the preparation of ethyl 5-(1-amino-1-deoxy-D-*arabino*-tetritol-1-yl)-2-methylfuran-3-carboxylate (**18**) starting from D-glucose. Regioselective methoxytritylation of the readily available tetrahydroxyalkyl furan **12**[26] afforded **13** in 81% yield (Scheme 3). Reaction of **13** with thionyl chloride and triethylamine afforded a mixture of cyclic sulfites, which after reaction with trimethylsilyl azide in the presence of TBAF by using THF as solvent gave azidoderivative **16** in 76% yield (two steps) as the unique product. The cyclic sulfite opening occurred through an S_N2 mechanism, which allowed the total stereoselective introduction of the azide functionality. After removal of the 4-methoxytrityl group in **16**, followed by hydrogenation of the azide group under atmospheric pressure, desired aminotrihydroxyalkylfuryl ester **18** was obtained in nearly quantitative yield. In order to confirm the C-1 configuration in **18**, azido derivative **17** was treated sequentially with TsCl/Py and H_2/Pd for chemical correlation with the known α-L-fucosidase inhibitor **20**[27] (Scheme 4). This reaction sequence demonstrates the success of this methodology in the synthesis of imino-C-heterocycles.



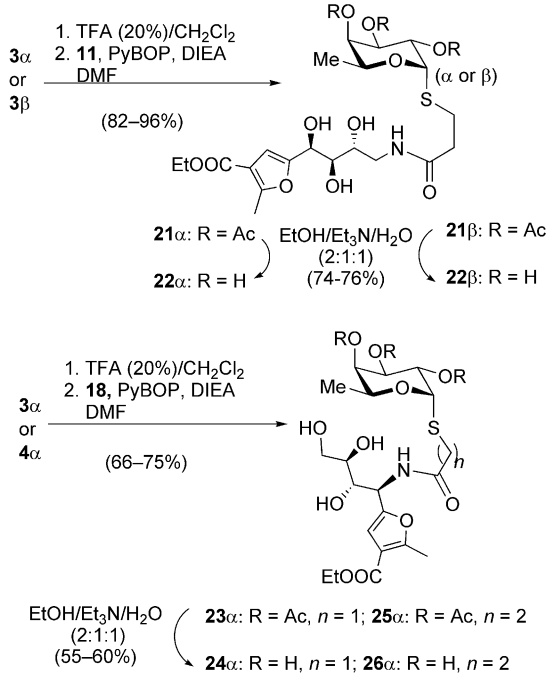
Scheme 3. Stereoselective synthesis of the new 1′-aminotrihydroxyalkylfuryl ester **18**.

Removal of the *tert*-butyl ester group in compounds **3**α, **3**β, and **4**α with TFA (20%)/CH_2Cl_2 followed by coupling with aminopolyol derivatives **11** and **18** by using PyBOP/



Scheme 4. Synthesis of imino-*C*-heterocycle **20**.

DIEA as condensing reagents afforded adducts **21**α, **21**β, **23**α, and **25**α in moderate-to-good yields. Deacetylation with EtOH/Et_3N/H_2O (2:1:1) afforded cleanly the *S*-linked fucosides **22**α, **22**β, **24**α, and **26**α, which could be isolated in 55–76% yield after final purification (Scheme 5).



Scheme 5. Synthesis of *S*-linked fucosides containing aminotrihydroxyalkylfuryl esters.

Biological Evaluation of Thiofucoside Derivatives Towards E- and P-Selectins

The biological activity of ester derivatives **8**α, **22**α, **22**β, **24**α, and **26**α, acid derivatives **9**α and **9**β, amide derivative **10**α, and tetrasaccharide SLe^x itself evaluated in an ELISA-based assay[28] was determined as their IC_{50} values in inhibiting the SLe^x–BSA binding to E-selectin and the PSGL-1 binding to P-selectin (Table 1). All the new SLe^x mimetics presented here are recognized by E- and P-selectins and show inhibitory activities in the low mM range; under our assay conditions, tetrasaccharide SLe^x has an IC_{50} = 0.7 mM against E-selectin and it is inactive against P-selectin (at 8 mM concentration). We must be aware that because of the absence of a universal assay to measure selectin binding interactions[5,7b,14a] and because of the difficulty in reproducing the same assay results, the IC_{50} values so-obtained for the new compounds should not be directly compared to those of other reported SLe^x analogues.

Table 1. IC_{50} [mM] values for the affinity of compounds **8**, **9**, **10**, **22**, **24**, **26**, and SLe^x sodium salt toward E- and P-selectins by an ELISA test.

Head 1[a]	**8**α	**9**α	**9**β	**10**α	**22**α	**22**β	**24**α	**26**α	SLe^x
E-Selectin	2.5	3.5	3.4	3.1	2.4	5.7	3.0	2.8	0.7
P-Selectin	2.3	3.0[a]	3.2	2.4	2.2	5.1	2.6	2.5	n.i.[b]

[a] In the presence of $CaCl_2$ (1 mM), the value obtained is 2.5 mM. [b] No inhibition under these assay conditions at 8 mM.

We have observed that α-thiofucoside derivatives of furylamino polyols (**22**α, **24**α, **26**α) are more active than the β-analogue **22**β, as expected considering that the fucose moiety is α-linked in the natural tetrasaccharide. However, α- and β-thiofucoside derivatives of 4-hydroxyprolines (compounds **9**α and **9**β) present similar inhibition. The best inhibitory values are obtained for compounds **8**α and **22**α, which show IC_{50} = 2.5 and 2.4 mM, respectively, towards E-selectin, that is, 3.5-fold weaker than SLe^x but, remarkably, an IC_{50} = 2.3 and 2.2 mM, respectively, towards P-selectin under conditions where SLe^x shows no inhibition. Non-acidic compounds **8**α and **10**α with *tert*-butyl ester and butylamide moieties, respectively, show slightly better inhibitory values than compound **9**α with a free carboxylic acid group. Simpler neutral analogues **24**α and **26**α having a trihydroxyalkylfuran ester moiety are also active. These results could be in agreement with the 3D structure of the E-selectin/SLe^x complex determined by Somers et al.,[29] and the quantum chemical calculations on the SLe^x molecule reported by Pichierri et al.[30] These compounds may be considered a type of uncharged selectin inhibitors of which there are few examples in the literature.[31,14c]

Conclusions

We showed the synthesis of α/β-L-fucosylated cysteamine derivatives (**2**α, **5**β), α/β-L-fucosylated 3-thiopropionic acid derivatives (**3**α, **3**β), and α-L-fucosylated 3-thioacetic acid derivative (**4**α) as building blocks for the preparation of *S*-neofucopeptides. These compounds were used in the synthesis of new thiofucoside derivatives (**8**α, **9**α, **9b**, **10**α, **22**α, **22b**, **24**α, **26**α) that show affinity towards E- and P-selectins; therefore, they act as non-hydrolyzable mimetics of the natural SLe^x tetrasaccharide. Most of them are neutral compounds that additionally incorporate not only polar functionalities but also lipophilic moieties. This fact together with their good hydrolytic stability and their easy preparation will provide new possibilities for the discovery of low-molecular-weight blockers of E- and P-selectin that are different from the conventional molecules incorporating ionic groups. In view of these interesting results, further modifications of our compounds have to be continued in order to find better candidates that could lead to a new generation of selectin antagonists in the μM or nM range. Progress in this area is currently underway in our laboratory.

Experimental Section

General Methods: Optical rotations were measured in a 1.0-cm or 1.0-dm tube with a Perkin–Elmer 241MC spectropolarimeter. ^{1}H and ^{13}C NMR spectra were obtained for solutions in $CDCl_3$, [D_6]-DMSO, CD_3OD, and D_2O. All the assignments were confirmed by 2D NMR experiments. The FAB mass spectra were obtained by using glycerol or 3-nitrobenzyl alcohol as the matrix. TLC was performed on silica gel HF_{254} (Merck), detection by UV light, and charring with H_2SO_4 or with Pancaldi reagent [$(NH_4)_6MoO_4$, $Ce(SO_4)_2$, H_2SO_4, H_2O]. Silica gel 60 (Merck, 230 mesh) was used for preparative chromatography. All reagents and solvents were purchased from Sigma–Aldrich. Tetrasaccharide sialyl Lewis X (SLe^x) sodium salt was purchased from Calbiochem.

2-(*tert*-Butoxycarbonylamino)ethyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-fucopyranoside (2α): To a solution of thiofucoside **1**α[19] (379 mg, 1.09 mmol) and *N*-Boc-2-bromoethylamine (235 mg, 1.05 mmol) in dry DMF (6 mL) was added Et_2NH (0.7 mL). The mixture was stirred at room temperature for 1 h and then evaporated. Purification of the residue by flash column chromatography (AcOEt/petroleum ether, 1:2) afforded **2**α (400 mg, 82%) as a colorless oil. $[\alpha]_D^{20}$ = –174 (*c* = 0.95, CH_2Cl_2). IR: $\tilde{\nu}$ = 3419, 2983, 2095, 1747, 1643, 1517, 1369, 1226, 1059 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 5.67 (d, $J_{1,2}$ = 5.2 Hz, 1 H, 1-H), 5.28 (br. d, $J_{3,4}$ = 3.3 Hz, 1 H, 4-H), 5.20 (dd, $J_{2,3}$ = 10.9 Hz, $J_{1,2}$ = 5.2 Hz, 1 H, 2-H), 5.18 (dd, $J_{2,3}$ = 10.9 Hz, $J_{3,4}$ = 3.3 Hz, 1 H, 3-H), 4.90 (br. s, 1 H, N*H*Boc), 4.45 (q, $J_{5,CH}$ = 6.5 Hz, 1 H, 5-H), 3.33–3.26 (m, 2 H, 2′a-H, 2′b-H), 2.79–2.60 (m, 2 H, 1′a-H, 1′b-H), 2.16 (s, 3 H, CH_3CO), 2.07 (s, 3 H, CH_3CO), 1.99 (s, 3 H, CH_3CO), 1.44 {s, 9 H, [(CH_3)$_3$C-]}, 1.16 (d, $J_{5,CH}$ = 6.5 Hz, 3 H, CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.5, 170.2, 169.9 (3-*C*OO-), 155.6 (-CO- of Boc), 82.8 (1-C), 79.5 [$(CH_3)C$-], 70.8 (4-C), 68.5 (3-C), 67.9 (2-C), 65.0 (5-C), 40.2 (2′-C), 30.9 (1′-C), 28.4 [(*C*H$_3$)$_3$C-], 20.8, 20.6, 20.5 (3 *C*H$_3$CO-), 15.9 (CH_3 of fucose) ppm. MS (FAB): *m*/*z* = 472 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{19}H_{31}NO_9SNa$ [M + Na]$^+$ 472.1617; found 472.1627.

2-(*tert*-Butoxycarbonyl)ethyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-fucopyranoside (3α): To a solution of thiofucoside **1**α (379 mg, 1.09 mmol) and *tert*-butyl 3-bromopropionate (260 μL, 1.56 mmol) in dry DMF (6 mL) was added Et_2NH (0.9 mL). The mixture was stirred at room temperature for 1 h and then evaporated. Purification of the residue by flash column chromatography (AcOEt/petroleum ether, 1:5) afforded **3**α (460 mg, 68%) as a white solid. $[\alpha]_D^{20}$ = –151 (*c* = 0.76, CH_2Cl_2). IR: $\tilde{\nu}$ = 3434, 1748, 1643, 1369, 1225, 1059 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 5.70 (d, $J_{1,2}$ = 5.2 Hz, 1 H, 1-H), 5.28 (br. d, $J_{3,4}$ = 3.2 Hz, 1 H, 4-H), 5.25 (dd, $J_{2,3}$ = 10.7 Hz, $J_{1,2}$ = 5.2 Hz, 1 H, 2-H), 5.18 (dd, $J_{2,3}$ = 10.7 Hz, $J_{3,4}$ = 3.2 Hz, 1 H, 3-H), 4.46 (q, $J_{5,CH}$ = 7.0 Hz, 1 H, 5-H), 2.68–2.86 (m, 2 H, 1′a-H, 1′b-H), 2.54–2.49 (m, 2 H, 2′a-H, 2′b-H), 2.16 (s, 3 H, CH_3CO-), 2.05 (s, 3 H, CH_3CO-), 2.01 (s, 3 H, CH_3CO-), 1.45 [s, 9 H, (CH_3)$_3$C-], 1.16 (d, $J_{5,CH}$ = 7.0 Hz, 3 H, CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.9, 170.5, 170.2, 169.9 (4 -*C*OO-), 82.6 (1-C), 80.9 [$(CH_3)C$-], 70.9 (4-C), 68.6 (3-C), 68.0 (2-C), 64.8 (5-C), 35.9 (2′-C), 28.1 [(*C*H$_3$)$_3$C-], 25.6 (1′-C), 20.8, 20.7, 20.6 (3 *C*H$_3$CO-), 15.9 (CH_3 of fucose) ppm. MS (FAB): *m*/*z* = 273 [M – $SCH_2CH_2COOtBu$]$^+$. MS (ESI): *m*/*z* = 457 [M + Na]$^+$, 273 [M – $SCH_2CH_2COOtBu$]$^+$. MS (CI): *m*/*z* = 435 [M + H]$^+$. HRMS (CI): calcd. for $C_{19}H_{31}O_9S$ [M + H]$^+$ 435.1689; found 435.1693.

2-(*tert*-Butoxycarbonyl)ethyl 2,3,4-Tri-*O*-acetyl-1-thio-β-L-fucopyranoside (3β): This compound was prepared in the way described for **3**α except that pure **1**β was used as starting material. Compound **3**β was purified by column chromatography on silica gel (AcOEt/petroleum ether, 1:5) and was obtained in 68% yield as a colorless oil. $[\alpha]_D^{25}$ = 7.4 (*c* = 0.95, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 5.21 (d, $J_{3,4}$ = 2.8 Hz, 1 H, 4-H), 5.14 (t, $J_{1,2}$ = $J_{2,3}$ = 9.9 Hz, 1 H, 2-H), 4.97 (dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 2.8 Hz, 1 H, 3-H), 4.43 (d, $J_{1,2}$ = 9.9 Hz, 1 H, 1-H), 3.75 (q, $J_{5,CH}$ = 6.4 Hz, 1 H 5-H), 2.82 (m, 1 H, 1′a-H, 1′b-H), 2.50 (t, $J_{2,1'a}$ = $J_{2,1'b}$ = 7.4 Hz, 2 H, 2′a-H, 2′b-H), 2.11 (s, 3 H, CH_3CO-), 1.98 (s, 3 H, CH_3CO-), 1.91 (s, 3 H, CH_3CO-), 1.38 [s, 9 H, (CH_3)$_3$C-], 1.15 (d, $J_{5,CH}$ = 6.4 Hz, 3 H, CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 171.0, 170.7, 170.1, 169.7 (4 -*C*OO-), 83.7 (1-C), 80.9 [$(CH_3)C$-], 73.2 (4-C), 72.3 (3-C), 70.4 (2-C), 67.3 (5-C), 36.3 (2′-C), 28.1 [(*C*H$_3$)$_3$C-], 25.3 (1′-C), 20.8, 20.7, 20.6 (3 *C*H$_3$CO-), 16.4 (CH_3 of fucose) ppm. MS (FAB): *m*/*z* = 457 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{19}H_{30}O_9SNa$ [M + Na]$^+$ 457.1508; found 457.1522.

(*tert*-Butoxycarbonyl)methyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-fucopyranoside (4α): To a solution of thiofucoside **1**α (1.06 g, 3.05 mmol) in dry MeOH (20 mL) was added MeONa/MeOH (1 M) dropwise until basic pH. After stirring for 3 h at room temperature, the mixture was neutralized with IR-120 H^+ resin, filtered, and concentrated. The resulting crude was redissolved in dry MeOH (20 mL) and cooled to 0 °C. Triethylamine (0.94 mL, 6.71 mmol) and *tert*-butyl bromoacetate (1.26 mL, 8.23 mmol) were added, and the mixture was stirred at room temperature for 2 h. The solvent was then evaporated, and the residue was conventionally acetylated (15 mL of Ac_2O/15 mL of Py) overnight. Evaporation and chromatographic purification (AcOEt/petroleum ether, 1:4) afforded **4**α (781 mg, 61%) as a white solid. $[\alpha]_D^{20}$ = –193 (*c* = 1.04, CH_2Cl_2). IR: $\tilde{\nu}$ = 2980, 1748, 1370, 1221, 1137, 1083, 1061, 967, 916 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 5.79 (d, $J_{1,2}$ = 5.4 Hz, 1 H, 1-H), 5.29 (m, 2 H, 2-H, 4-H), 5.22 (dd, $J_{2,3}$ = 10.9 Hz, $J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 4.47 (br. q, $J_{5,CH}$ = 6.5 Hz, 1 H, 5-H), 3.27 (d, $J_{1'a,1'b}$ = 15.0 Hz, 1 H, 1′a-H), 3.07 (d, $J_{1'a,1'b}$ = 15.0 Hz, 1 H, 1′b-H), 2.16 (s, 3 H, CH_3CO-), 2.07 (s, 3 H, CH_3CO-), 1.99 (s, 3 H, CH_3CO-), 1.46 {s, 9 H, [(CH_3)$_3$C-]}, 1.15 (d, $J_{5,CH}$ = 6.5 Hz, 3 H, CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.6, 170.2, 170.0, 169.0 (4 -*C*OO-), 82.4 (1-C), 82.0 [$(CH_3)C$-], 71.1 (4-C), 68.7 (3-C), 68.0 (2-C), 65.4 (5-C), 32.5 (1′-C), 28.1 [(*C*H$_3$)$_3$C-], 20.9, 20.8, 20.7 (3 *C*H$_3$CO-), 16.1 (CH_3 of fucose) ppm. MS (FAB): *m*/*z* = 273 [M – $SCH_2CH_2COOtBu$]$^+$. MS (CI): *m*/*z* = 273 [M – $SCH_2CH_2COOtBu$]$^+$. HRMS (CI): calcd. for $C_{18}H_{29}O_9S$ [M + H]$^+$ 421.1532; found 421.1521.

2-(Fluoren-9-ylmethoxycarbonylamino)ethyl 2,3,4-Tri-*O*-acetyl-1-thio-β-L-fucopyranoside (5β): To a solution of Fmoc-aminoethanothiol (134 mg, 0.45 mmol) and L-fucose peracetate (106 mg, 0.34 mmol) in dry dichloromethane (4 mL) was added 4-Å MS, and the mixture was stirred for 15 min. Then, trimethylsilyl trifluoromethanesulfonate (62 μL, 0.45 mmol) was added, and the solution was stirred at room temperature. After 2 h, the mixture was washed with saturated aqueous solution of $NaHCO_3$ and water, dried with Na_2SO_4, and concentrated. The resulting residue was purified by column chromatography (AcOEt/petroleum ether, 1:2→1:1) to give **5**β (120 mg, 62%) as a colorless oil. $[\alpha]_D^{20}$ = –7 (*c* = 1.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.83–7.31 (m, 5 H, ar-H), 5.55 (br. t, *J* = 5.4 Hz, 1 H, NHFmoc), 5.20 (m, 2 H, 4-H, 2-H), 5.03 (dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 3.0 Hz, 1 H 3-H), 4.68 (dd, ^2J = 10.5 Hz, ^3J = 6.0 Hz, 1 H, -C*H*H- of Fmoc), 4.47 (dd, ^3J = 5.7 Hz, ^2J = 10.5 Hz, 1 H, -CH*H*- of Fmoc), 4.26 (d, $J_{1,2}$ = 9.6 Hz, 1 H, 1-H), 4.22 (t under 1-H, 1 H, CH of fluorenyl), 3.55 (m, 2 H, 5-H, 1′a-H), 3.34 (m, 1 H, 1′b-H, -CH_2-), 2.93 (m, 1 H, 2′a-H) 2.65 (m, 1 H, 2′b-H), 2.19 (s, 3 H, CH_3CO-), 2.08 (s, 3 H, CH_3CO-), 2.02 (s, 3 H, CH_3CO-), 1.05 (d, $J_{5,CH}$ = 6.3 Hz, 3 H, CH_3CO-) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.5, 170.1, 169.7

(3 -*C*OO-), 156.3 (CO of Fmoc), 143.9, 143.7, 141.3, 127.7, 127.1, 125.0, 124.7, 120.0 (12 ar-C), 84.2, (1-C), 73.3 (4-C), 72.0 (3-C), 70.2 (2-C), 67.1 (-CH_2- of Fmoc), 65.8 (5-C), 47.4 (-CH- of Fmoc), 41.6 (2′-C), 31.8 (1′-C), 20.8, 20.7, 20.6 (3 *C*H_3CO-), 16.2 (CH_3 of fucose) ppm. MS (FAB): *m*/*z* = 594 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{29}H_{33}NO_9S$ [M + Na]$^+$ 594.1803; found 594.1773.

2-[(2*S*,4*R*)-4-Hydroxy-1-(fluoren-9-ylmethoxycarbonyl)pyrrolidine-2-carbonylamino]ethyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-fucopyranoside (6α): To a solution of compound **2**α (352 mg, 0.782 mmol) in CH_2Cl_2 (4 mL) was added TFA (1 mL), and the mixture was stirred at room temperature for 15 min. After evaporation of the solvent, the residue was dissolved in DMF (4 mL) and *N*-Fmoc-4-L-Hyp-OH (306 mg, 0.868 mmol), DIEA (0.67 mL, 3.9 mmol), and PyBOP (442 mg, 0.86 mmol) were sequentially added. After stirring for 5 h at room temperature, the solvent was removed, and the residue was diluted with CH_2Cl_2 and washed with 1 N HCl, saturated aqueous solution of $NaHCO_3$, and brine. The organic phase was then dried (Na_2SO_4), filtered, and concentrated. Chromatographic purification on silica gel (ether/ acetone, 7:1) afforded **6**α (454 mg, 85%) as a colorless oil. $[\alpha]_D^{20}$ = –95 (*c* = 1.1, CH_2Cl_2). IR: $\tilde{\nu}$ = 3433, 2972, 2867, 2095, 1747, 1651, 1424, 1360, 1223, 1084 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO, 75 °C): δ = 7.85 (d, *J* = 7.6 Hz, 2 H, ar-H), 7.64 (d, *J* = 7.3 Hz, 2 H, ar-H), 7.41 (t, *J* = 7.3 Hz, 2 H, ar-H), 7.31 (t, *J* = 7.3 Hz, 2 H, ar-H), 5.58 (d, $J_{1,2}$ = 5.0 Hz, 1 H, 1-H), 5.18 (br. s, 1 H, 4-H), 5.13 (dd, $J_{2,3}$ = 10.8 Hz, $J_{1,2}$ = 5.0 Hz, 1 H, 2-H), 5.09 (br. d, $J_{2,3}$ = 10.8 Hz, 1 H, 3-H), 4.4 (br. s, 1 H, 5-H), 4.35–4.10 (m, 5 H, 2′′-H, 4′′-H, -CH_2- of Fmoc and -CH- of Fmoc), 3.51 (dd, $J_{5'',5''b}$ = 11.0 Hz, $J_{5''a,4''}$ = 4.6 Hz, 1 H, 5′′a-H), 3.40 (br. d, $J_{5'',5''b}$ = 11.0 Hz, 1 H, 5′′b-H), 3.25 (m, 2 H, 2′a-H, 2′b-H), 2.61 (m, 2 H, 1′a-H, 1′b-H), 2.11 (s, 3 H, C*H*$_3$CO-), 1.98 (s, 3 H, C*H*$_3$CO-), 1.95 (m, 2 H, 3′′a-H, 3′′b-H), 1.92 (s, 3 H, C*H*$_3$CO-), 1.04 (br. s, 3 H, CH_3 of fucose) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO, 75 °C): δ = 171.4 (-CONH-), 169.6, 169.1, 168.9 (3 CH_3*C*OO-), 143.5, 140.3, 127.2, 126.6, 124.7, 119.6 (6 ar-C), 81.6 (1-C), 70.2 (4-C), 67.7, 67.6, 67.1, 66.4 (2-C, 3-C, 4′′-C, CH_2 of Fmoc), 64.5 (5-C), 58.7 (2′′-C), 54.3 (5′′-C), 46.5 (CH of Fmoc), 39.5 (3′′-C), 38.4 (2′-C), 28.8 (1′-C), 19.9, 19.8, 19.7 (3 *C*H_3CO-), 15.1 (CH_3 of fucose) ppm. MS (FAB): *m*/*z* = 707 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{34}H_{40}N_2O_{11}SNa$ [M + Na]$^+$ 707.2251; found 707.2269.

2-[(2*S*,4*R*)-4-Hydroxy-1-(fluoren-9-ylmethoxycarbonyl)pyrrolidine-2-carbonylamino]ethyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-fucopyranoside (6β): To a solution of compound **5**β (68 mg, 0.109 mmol) in DMF (2 mL) was added Et_2NH (0.4 mL), and the mixture was stirred at room temperature for 15 min. After evaporation of the solvent, the residue was dissolved in DMF (2 mL) and *N*-Fmoc-4-L-Hyp-OH (42 mg, 0.12 mmol), DIEA (41 μL, 0.24 mmol), and PyBOP (62 mg, 0.12 mmol) were sequentially added. After stirring for 5 h at room temperature, the solvent was removed, and the residue was diluted with CH_2Cl_2 and washed with 1 N HCl, saturated aqueous solution of $NaHCO_3$, and brine. The organic phase was then dried (Na_2SO_4), filtered, and concentrated. Chromatographic purification on silica gel (ether/acetone, 7:1) afforded **6**β (50 mg, 67%) as a colorless oil. $[\alpha]_D^{20}$ = –13 (*c* = 1.2, CH_2Cl_2). ^{1}H NMR (300 MHz, [D$_6$]DMSO, 75 °C): δ = 7.93 (br. s, 1 H, -NH-), 7.90 (d, *J* = 7.6 Hz, 2 H, ar-H), 7.84 (d, *J* = 7.3 Hz, 2 H, ar-H), 7.44 (t, *J* = 7.3 Hz, 2 H, ar-H), 7.34 (t, *J* = 7.3 Hz, 2 H, ar-H), 5.15 (m, 2 H, 4-H, 3-H), 4.97 (t, $J_{2,3}$ = $J_{1,2}$ = 9.6 Hz, 1 H, 2-H), 4.90 (br. s, 1 H, -OH), 4.76 (d, $J_{1,2}$ = 9.6 Hz, 1 H, 1-H), 4.41–4.16 (m, 5 H, 2′′-H, 4′′-H, -CH_2- of Fmoc and -CH- of Fmoc), 4.02 (br. q, $J_{5,CH}$ = 6.5 Hz, 1 H, 5-H), 3.52 (dd, $J_{5'',5''b}$ = 11.0, $J_{5''a,4}$ = 4.5, 5′′a-H), 3.42–3.24 (m, 3 H, 5′′b-H, 2′a-H, 2′b-H), 2.75 (m, 1 H, 1′a-H), 2.63 (m, 1 H, 1′b-H), 2.12 (s, 3 H, C*H*$_3$CO-), 1.99 (s, 3 H, C*H*$_3$CO-), 1.95 (m, 2 H, 3′′a-H, 3′′b-H), 1.92 (s, 3 H, C*H*$_3$CO-), 1.05 (br. d, $J_{5,CH}$ = 6.5 Hz, 3 H, CH_3 of fucose) ppm. ^{13}C NMR (75.4 MHz, [D$_6$]DMSO, 75 °C): δ = 173.9 (-CONH-), 169.7, 168.9, 168.8 (3 CH_3*C*OO-), 154.0 (CO of Fmoc), 143.5, 140.3, 128.5, 127.2, 126.8, 126.7, 120.9, 119.5 (6 ar-C), 82.0 (1-C), 71.7 (4-C), 71.3 (5-C), 71.0 (3-C), 70.2 (2-C), 67.3 (4′′-C, CH_2 of Fmoc), 59.1 (2′′-C), 54.8 (5′′-C), 46.5 (CH of Fmoc), 39.5 (under DMSO, 3′′-C), 38.2 (2′-C), 29.2 (1′-C), 20.0, 19.8 (3 *C*H_3CO-), 15.6 (CH_3 of fucose) ppm. MS (FAB): *m*/*z* = 707 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{34}H_{40}N_2O_{11}SNa$ [M + Na]$^+$ 707.2251; found 707.2258.

***S*-Linked Fucosides 8α and 8β:** To a solution of **6**α or **6**β (345 mg, 0.50 mmol) in DMF (4 mL) was added Et_2NH (1 mL), and the mixture was stirred at room temperature for 20 min. The residue obtained after evaporation was then dissolved in DMF (4 mL) and a solution of mono-*tert*-butyl glutarate (110 mg, 0.6 mmol) in DMF (4 mL) followed by DIEA (206 μL, 1.2 mmol) and PyBOP (310 mg, 0.6 mmol) were added. After stirring for 3 h at room temperature, the mixture was evaporated, and the residue was diluted with CH_2Cl_2 and washed with 1 N HCl, saturated aqueous solution of $NaHCO_3$, and brine. The organic phase was then dried (Na_2SO_4), filtered, and concentrated. Chromatographic purification on silica gel (ether/acetone, 5:1) afforded **7**α (200 mg, 63%) or **7**β (56%). Compound **7**α or **7**β (160 mg, 0.253 mmol) was then dissolved in *t*BuOH/Et_3N/H_2O (2:1:1, 4 mL), and the mixture was stirred at room temperature for 24 h. Evaporation of the solvent and chromatographic purification (CH_2Cl_2/MeOH, 8:1) of the residue afforded **8**α (90 mg, 70%) as a white foam or **8**β (73%). Compound **8**β was used in the following step without characterization. Data for **8**α: $[\alpha]_D^{20}$ = –177 (*c* = 1.2, MeOH). ^{1}H NMR (300 MHz, CD_3OD, mixture of rotamers, 25 °C): Data for major rotamer, δ = 5.36 (d, $J_{1,2}$ = 5.6 Hz, 1 H, 1-H), 4.51–4.43 (m, 2 H, 2′′-H, 4′′-H), 4.29 (q, $J_{5,CH}$ = 6.6 Hz, 1 H, 5-H), 4.06 (dd, $J_{2,3}$ = 10.1 Hz, $J_{1,2}$ = 5.6 Hz, 1 H, 2-H), 3.75 (dd, $J_{5'',5''b}$ = 10.9 Hz, $J_{5''a,4''}$ = 4.4 Hz, 1 H, 5′′a-H), 3.67 (br. d, $J_{3,4}$ = 3.2 Hz, 1 H, 4-H), 3.60 (dd, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 3.2 Hz, 1 H, 3-H), 3.52 (br. d, $J_{5'',5''b}$ = 10.9 Hz, 1 H, 5′′b-H), 3.43 (m, 2 H, 2′a-H, 2′b-H), 2.77–2.65 (m, 2 H, 1′a-H, 1′b-H), 2.42 (t, $J_{2''',3'''}$ = 7.6 Hz, 2 H, 2′′′-H), 2.32 (t, $J_{3''',4'''}$ = 7.4 Hz, 2 H, 4′′′-H), 2.27–1.83 (m, 4 H, 3′′a-H, 3′′b-H, 3′′′-H), 1.46 [s, 9 H, (C*H*$_3$)$_3$C-], 1.24 (d, $J_{5,CH}$ = 6.6 Hz, 3 H, -CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, CD_3OD, 25 °C mixture of rotamers): Data for major rotamer, δ = 175.1, 175.0, 174.7 (3 -CO), 88.4 (1-C), 82.0 [-*C*(CH$_3$)$_3$], 73.9 (4-C), 72.9 (3-C), 71.3 (4′′-C), 70.0 (2-C), 68.7 (5-C), 60.9 (2′′-C), 57.0 (5′′-C), 41.0 (2′-C), 39.8 (3′′-C), 36.0 (4′′′-C), 35.0 (2′′′-C), 31.1 (1′-C), 28.9 [(C*H*$_3$)$_3$C-], 21.8 (3′′′-C), 17.1 (-CH_3 of fucose) ppm. MS (FAB): *m*/*z* = 529 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{22}H_{38}N_2O_9SNa$ [M + Na]$^+$ 529.2195; found 529.2196.

[(2*S*,4*R*)-1-(4-Carboxybutanoyl)-4-hydroxypyrrolidine-2-carbonylamino]ethyl 1-Thio-α and β-L-Fucopyranoside (9α and 9β): A 20% solution of TFA in CH_2Cl_2 (5 mL) was added to compound **8**α (65 mg, 0.128 mmol) or **8**β, and the mixture was stirred at room temperature for 20 min. Evaporation of the solvent afforded **9**α (55 mg, quant.) or **9**β (quant.) as a white solid. Data for **9**α: $[\alpha]_D^{20}$ = –59 (*c* = 0.75, H_2O). ^{1}H NMR (300 MHz, D_2O, 25 °C mixture of rotamers): Data for major rotamer, δ = 5.36 (d, $J_{1,2}$ = 5.6 Hz, 1 H, 1-H), 4.51 (m, 1 H, 4′′-H), 4.39 (t, $J_{2'',3''a}$ = $J_{2'',3''b}$ = 8.6 Hz, 1 H, 2′′-H), 4.28 (q, $J_{5,CH}$ = 6.6 Hz, 1 H, 5-H), 4.00 (dd, $J_{2,3}$ = 10.4 Hz, $J_{1,2}$ = 5.6 Hz, 1 H, 2-H), 3.74 (m, 2 H, 5′′a-H, 4-H), 3.64 (dd, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.3 Hz, 1 H, 3-H), 3.58 (br. d, $J_{5''a,5''b}$ = 11.6 Hz, 1 H, 5′′b-H), 3.44–3.32 (m, 2 H, 2′a-H, 2′b-H), 2.78–2.65 (m, 2 H, 1′a-H, 1′b-H), 2.44–1.79 (m, 8 H, 2′′′-H, 3′′′-H, 4′′′-H, 3′′a-H, 3′′b-H), 2.32 (t, $J_{3''',4'''}$ = 7.4 Hz, 2 H, 4′′′-H), 2.27–1.83 (m, 4 H, 3′′a-H, 3′′b-H, 3′′′-H), 1.16 (d, $J_{5,CH}$ = 6.6 Hz, 3 H,

-CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, D_2O, 25 °C, mixture of rotamers): Data for major rotamer, δ = 180.0 (-COOH), 176.6, 176.0 (2 -CONH-), 88.2 (1-C), 73.6 (4-C), 72.2 (3-C), 71.6 (4′′-C), 69.6, (2-C), 69.3 (5-C), 61.1 (2′′-C), 57.4 (5′′-C), 41.1 (2′-C), 39.4 (3′′-C), 35.0 (4′′′-C), 34.8 (2′′′-C), 31.5 (1′-C), 21.5 (3′′′-C), 17.3 (-CH_3 of fucose) ppm. MS (FAB): *m*/*z* = 473 [M + Na]$^+$. HRMS (FAB) calcd. for $C_{18}H_{30}N_2O_9SNa$ [M + Na]$^+$ 473.1570; found 473.1581. Data for **9**β: $[\alpha]_D^{20}$ = –10 (*c* = 1.4, MeOH). ^{13}C NMR (75 MHz, CD_3OD, 25 °C, mixture of rotamers): Data for major rotamer, δ = 177.0 (-COOH), 174.7, 174.2 (2 -CONH-), 87.5 (1-C), 76.4 (4-C), 76.2 (3-C), 73.3 (4′′-C), 71.2 (2-C), 70.8 (5-C), 60.5 (2′′-C), 56.6 (5′′-C), 40.0 (2′-C), 39.3 (3′′-C), 34.5 (4′′′-C), 33.9 (2′′′-C), 30.5 (1′-C), 21.2 (3′′′-C), 17.1 (-CH_3 of fucose). MS (FAB): *m*/*z* (%) = 473 (100) [M + Na]$^+$. HRMS (FAB) calcd. for $C_{18}H_{30}N_2O_9SNa$ [M + Na]$^+$ 473.1570; found 473.1588.

Ethyl 5-[4-*O*-(*p*-Methoxytrityl)-D-*arabino*-tetritol-1-yl]-2-methylfuran-3-carboxylate (13): To a solution of **12**[26] (1 g, 3.65 mmol) in pyridine (8 mL) cooled to 0 °C was added MeOTrCl (1.4 g, 4.38 mmol). After 3 h at room temperature MeOH (1.5 mL) was added, and the mixture was stirred for 15 min. The residue obtained after evaporation of the solvent was diluted with CH_2Cl_2 and washed with water. The organic phase was then dried (Na_2SO_4), filtered, and concentrated. Chromatographic purification on silica gel (CH_2Cl_2/acetone, 30:1, 1% Et_3N) afforded **13** (1.59 g, 81%) as a yellow oil. $[\alpha]_D^{20}$ = +15 (*c* = 1, CH_2Cl_2). IR: $\tilde{\nu}$ = 3846, 3752, 3472, 2928, 1703, 1508, 1449, 1236, 1080 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.43–6.83 (m, 14 H, ar-H), 6.52 (s, 1 H, 4-H), 4.74 (d, $J_{1',2'}$ = 3.4 Hz, 1 H, 1′-H), 4.27 (q, $^3J_{H,H}$ = 7.1 Hz, 2 H, -C*H*$_2$CH$_3$), 3.93 (dd, $J_{2',3'}$ = 5.9 Hz, $J_{1',2'}$ = 3,4 Hz, 1 H, 2′-H), 3.83 (m, 1 H, 3′-H), 3.80 (s, 3 H, -OCH$_3$), 3.41 (dd, $J_{4'a,4'b}$ = 9.9 Hz, $J_{3',4'a}$ = 4.3 Hz, 1 H, 4′a-H), 3.30 (dd, $J_{4'a,4'b}$ = 9.9 Hz, $J_{3',4'b}$ = 5.8 Hz, 1 H, 4′b-H), 2.72 (br. s, 2 H, -OH), 2.54 (s, 3 H, CH_3- of furan), 1.66 (br. s, 1 H, -OH), 1.33 (t, $^3J_{H,H}$ = 7.1 Hz, 3 H, -CH_2C*H*$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 164.1 (COOEt), 159.1 (ar-C), 158.9 (2-C), 151.8 (5-C), 144.1, 144.0, 135.2, 130.4, 128.4, 128.2, 127.3, 113.5 (17 ar-C), 114.4 (3-C), 108.7 (4-C), 87.2 [(Ar)$_3$*C*-], 73.7 (2′-C), 71.1 (3′-C), 67.3 (1′-C), 64.8 (4′-C), 60.3 (-*C*H$_2$CH$_3$), 55.4 (-O*C*H$_3$), 14.5 (-CH_2*C*H$_3$), 13.9 (*C*H$_3$- of furan) ppm. MS (FAB): *m*/*z* = 569 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{32}H_{34}O_8Na$ [M + Na]$^+$ 569.2151; found 569.2171.

Ethyl 5-[1-Azido-1-deoxy-4-*O*-(*p*-methoxytrityl)-D-*arabino*-tetritol-1-yl]-2-methylfuran-3-carboxylate (16): To a cooled solution of **13** (1.163 g, 1.96 mmol) in dry CH_2Cl_2 (6 mL) was added Et_3N (539 μL, 8.62 mmol) and a solution of $SOCl_2$ (350 μL, 4.9 mmol) in CH_2Cl_2 (1 mL). After 30 min at 0 °C, cold diethyl ether was added, and the mixture was washed with water and brine. The organic phase was then dried (Na_2SO_4), filtered, and concentrated. The mixture of sulfites **14** and **15** thus obtained was dissolved in THF (7 mL) and $TMSN_3$ (885 μL, 6.39 mmol) and TBAF (1 M/THF, 6.39 mL) were sequentially added. After 3 d at room temperature, the solvent was evaporated, and the residue was purified by column chromatography (ether/petroleum ether, 1:1, 1% Et_3N) to afford **16** (850 mg, 76%) as a colorless oil. $[\alpha]_D^{20}$ = +39 (*c* = 0.9, CH_2Cl_2). IR: $\tilde{\nu}$ = 3482, 2933, 2102, 1714, 1609, 1577, 1509, 1446, 1299, 1251, 1229, 1179, 1079, 1033, 902, 831, 796, 777, 707, 632 cm^{-1}. ^1H NMR (300 MHz, CD_3OD, 25 °C): δ = 7.32–6.84 (m, 14 H, ar-H), 6.71 (s, 1 H, 4-H), 4.62 (d, $J_{1',2'}$ = 4.4 Hz, 1 H, 1′-H), 4.28 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, -C*H*$_2$CH$_3$), 3.97 (dd, $J_{2',3'}$ = 7.4 Hz, $J_{1',2'}$ = 4.4 Hz, 1 H, 2′-H), 3.80 (s, 3 H, -OCH$_3$), 3.60 (m, 1 H, 3′-H), 3.35 (dd, $J_{4'a,4'b}$ = 9.8 Hz, $J_{3',4'a}$ = 3.4 Hz, 1 H, 4′a-H), 3.22 (dd, $J_{3',4'b}$ = 6.2 Hz, $J_{4'a,4'b}$ = 9.8 Hz, 1 H, 4′b-H), 2.56 (s, 3 H, CH_3 of furan), 1.35 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, -CH_2C*H*$_3$) ppm. ^{13}C NMR (75 MHz, CD_3OD, 25 °C): δ = 165.4 (COOEt), 160.7 (5-C), 149.2 (2-C), 160.2, 146.1, 136.9, 131.7, 129.7, 128.7, 127.9, 114.0 (18 ar-C), 115.3 (3-C), 111.8 (4-C), 87.8 [(Ar)$_3$*C*-], 74.7 (2′-C), 72.6 (3′-C), 66.5 (4′-C), 61.4 (-*C*H$_2$CH$_3$), 60.9 (1′-C), 55.7 (-O*C*H$_3$), 14.7 (-CH_2*C*H$_3$), 13.8 (*C*H$_3$ of furan) ppm. MS (FAB): *m*/*z* = 594 [M + Na]$^+$. HRMS (FAB) calcd. for $C_{32}H_{33}N_3O_7Na$ [M + Na]$^+$ 594.2216; found 594.2211.

Ethyl 5-(1-Azido-1-deoxy-D-*arabino*-tetritol-1-yl)-2-methylfuran-3-carboxylate (17): Compound **16** (826 mg, 1.45 mmol) was treated with a solution of TFA/CH_2Cl_2/triisopropylsilane (TIPS) (93:2:5) (15 mL) at room temperature for 30 min. After evaporation of the solvent and chromatographic purification (CH_2Cl_2/MeOH, 15:1), compound **17** (345 mg, 80%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = +86 (*c* = 1.5, CH_2Cl_2). IR: $\tilde{\nu}$ = 3412, 2106, 1694, 1230, 1082 cm^{-1}. ^1H NMR (300 MHz, CD_3OD, 25 °C): δ = 6.78 (s, 1 H, 4-H), 4.67 (d, $J_{1',2'}$ = 4.1 Hz, 1 H, 1′-H), 4.28 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, -C*H*$_2$CH$_3$), 3.93 (dd, $J_{2',3'}$ = 8.1 Hz, $J_{1',2'}$ = 4.1 Hz, 1 H, 2′-H), 3.76 (dd, $J_{4'a,4'b}$ = 11.4 Hz, $J_{3',4'a}$ = 3.5 Hz, 1 H, 4′a-H), 3.61 (dd, $J_{4'a,4'b}$ = 11.4 Hz, $J_{3',4'b}$ = 5.8 Hz, 1 H, 4′b-H), 3.46 (ddd, $J_{2',3'}$ = 8.1 Hz, $J_{3,4'b}$ = 5.8 Hz, $J_{3',4'a}$ = 3.5 Hz, 1 H, 3′-H), 2.57 (s, 3 H, CH_3 of furan), 1.35 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, -CH_2C*H*$_3$) ppm. ^{13}C NMR (75 MHz, CD_3OD, 25 °C): δ = 165.4 (COOEt), 160.6 (2-C), 149.2 (5-C), 115.3 (3-C), 111.8 (4-C), 74.6 (2′-C), 73.4 (3′-C), 64.5 (4′-C), 61.4 (-*C*H$_2$CH$_3$), 60.9 (1′-C), 14.6 (-CH_2*C*H$_3$), 13.8 (CH_3 of furan) ppm. MS (CI) *m*/*z* = 257 [M – N_3]$^+$. HRMS (CI): calcd. for $C_{12}H_{18}O_6N_3$ [M + H]$^+$ 300.1196; found 300.1199.

Ethyl 5-(1-Amino-1-deoxy-D-*arabino*-tetritol-1-yl)-2-methylfuran-3-carboxylate (18): A solution of **17** (340 mg, 1.14 mmol) in absolute EtOH (20 mL) was hydrogenated under atmospheric pressure for 1 h by using Pd/C (10%) as a catalyst. Then, the solution was filtered through Celite, and the catalyst was washed with EtOH. The filtered solution was concentrated in vacuo to give pure **18** (307 mg, 1.12 mmol, 98%) as a colorless oil. $[\alpha]_D^{20}$ = –11 (*c* = 0.57, MeOH). ^1H NMR (300 MHz, CD_3OD, 25 °C): δ = 6.58 (s, 1 H, 4-H), 4.26 (q, $^3J_{H,H}$ = 7.1 Hz, 2 H, -C*H*$_2$CH$_3$), 4.23 (d, $J_{1',2'}$ = 4.5 Hz, 1 H, 1′-H), 3.75 (dd, $J_{4'a,4'b}$ = 11.4 Hz, $J_{3',4'a}$ = 3.5 Hz, 1 H, 4′a-H), 3.74 (dd, $J_{2',3'}$ = 8.7 Hz, $J_{1',2'}$ = 4.5 Hz, 1 H, 2′-H), 3.60 (dd, $J_{4'a,4'b}$ = 11.4 Hz, $J_{3',4'b}$ = 5.5 Hz, 1 H, 4′b-H), 3.42 (ddd, $J_{2',3'}$ = 8.7 Hz, $J_{3',4'b}$ = 5.5 Hz, $J_{3',4'a}$ = 3.5 Hz, 1 H, 3′-H), 2.55 (s, 3 H, CH_3 of furan), 1.33 (t, $^3J_{H,H}$ = 7.1 Hz, 3 H, -CH_2C*H*$_3$) ppm. ^{13}C NMR (75 MHz, CD_3OD, 25 °C): δ = 165.7 (COOEt), 159.9 (2-C), 153.6 (5-C), 115.2 (3-C), 109.3 (4-C), 74.5 (2′-C), 74.2 (3′-C), 64.8 (4′-C), 61.3 (-*C*H$_2$CH$_3$), 52.6 (1′-C), 14.7 (-CH_2*C*H$_3$), 13.8 (CH_3 of furan) ppm. MS (CI): *m*/*z* = 274 [M – H]$^+$, 257 [M – NH_3]$^+$. HRMS (CI): calcd. for $C_{12}H_{20}O_6N$ [M – H]$^+$ 274.1291; found 274.1296.

Ethyl 5-(1-Azido-1-deoxy-4-*O*-tosyl-D-*arabino*-tetritol-1-yl)-2-methylfuran-3-carboxylate (19): To a solution of compound **17** (107 mg, 0.357 mmol) in pyridine (1.5 mL) at –15 °C was added TsCl (204 mg, 1.071 mmol) in portions. The mixture was stirred from –15 to 5 °C for 7 h. Then, water was added and the solvent was evaporated. The residue was diluted with CH_2Cl_2 and sequentially washed with 1 N HCl, saturated aqueous solution of $NaHCO_3$, and brine. The organic phase was dried (Na_2SO_4), filtered, and concentrated. Chromatographic purification on silica gel (ether/petroleum ether, 1:2→1:1) afforded **19** (118 mg, 73%). $[\alpha]_D^{20}$ = +74 (*c* = 0.81, CH_2Cl_2). IR: $\tilde{\nu}$ = 3468, 2983, 2925, 2106, 1713, 1360, 1230, 1175, 1094, 980, 810, 775 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.79 (d, *J* = 8.4 Hz, 2 H, ar-H), 7.35 (d, *J* = 8.4 Hz, 2 H, ar-H), 6.74 (s, 1 H, 4-H), 4.75 (d, $J_{1',2'}$ = 4.5 Hz, 1 H, 1′-H), 4.27 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, -C*H*$_2$CH$_3$), 4.23 (m, 2 H, 4′a-H, 4′b-H), 3.96 (dd, $J_{2',3'}$ = 7.8 Hz, $J_{1',2'}$ = 4.5 Hz, 1 H, 2′-H), 3.72 (m, 1 H, 3′-H), 2.64

(br. s, 2 H, O*H*), 2.57 (s, 3 H, CH_3 of furan), 2.45 (s, 3 H, CH_3 of Ts), 1.34 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, -CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 163.6 (*C*OOEt), 160.0 (2-C), 146.3 (5-C), 145.3 (1-C of Ph), 132.3 (4-C of Ph), 130.0 (2 ar-C), 129.0 (2 ar-C), 114.4 (3-C), 111.5 (4-C), 72.3 (2′-C), 71.1 (4′-C), 70.0 (3′-C), 60.4 (-*C*H_2CH_3), 59.6 (1′-C), 21.6 (Me of Ts), 14.3 (-CH_2CH_3), 13.9 (*C*H_3 of furan) ppm. MS (FAB): *m*/*z* = 476 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{19}H_{23}N_3O_8SNa$ [M + Na]$^+$ 476.1104; found 476.1105.

Ethyl 5-[(2*R*,3*S*,4*R*)-3,4-Dihydroxypyrrolidin-2-yl]-2-methylfuran-3-carboxylate (20):[27] A solution of **19** (269 mg, 0.593 mmol) in absolute EtOH (7 mL) was hydrogenated with Pd-C (10%) as catalyst. After 1.5 h, the catalyst was filtered off and the solution was concentrated to afford **20** (250 mg, quant.) as a white solid.

***S*-Linked Fucoside 21α:** Compound **3**α (57 mg, 0.131 mmol) was treated with TFA (25% in CH_2Cl_2, 2.5 mL) at room temperature over 30 min, and the solvent was then evaporated. The residue was dissolved in DMF (3 mL) and DIEA (98 μL, 0.576 mmol), compound **11** (40 mg, 0.144 mmol), and PyBOP (74 mg, 0.144 mmol) were sequentially added. After stirring for 2 h at room temperature, the solvent was removed, and the residue was diluted with AcOEt and washed with 1 N HCl, saturated aqueous solution of $NaHCO_3$, and brine. The organic phase was then dried (Na_2SO_4), filtered, and concentrated. Chromatographic purification on silica gel (CH_2Cl_2/MeOH, 20:1) afforded **21**α (80 mg, 96%), which was used in the following step without characterization.

Compound 21β: This compound was prepared as described for **21**α by using **3**β (70 mg, 0.161 mmol) as the starting material. After purification by column chromatography on silica gel (CH_2Cl_2/MeOH, 30:1), compound **21**β (80 mg, 82%) was obtained as a colorless oil. This compound was used in the following step without characterization.

Compound 22α: Compound **21**α (60 mg, 0.095 mmol) was dissolved in EtOH/Et_3N/H_2O (2:1:1, 4 mL), and the mixture was stirred at room temperature for 24 h. Evaporation of the solvent and chromatographic purification (CH_2Cl_2/MeOH, 6:1) of the residue afforded **22**α (35 mg, 74%) as a white foam. $[\alpha]_D^{20}$ = –89 (*c* = 0.8, MeOH). ^{1}H NMR (300 MHz, CD_3OD, 25 °C): δ = 6.60 (s, 1 H, 4′′′-H), 5.37 (d, $J_{1,2}$ = 5.6 Hz, 1 H, 1-H), 4.87 (d under H_2O, 1 H, 1′′-H), 4.28 (q, $^3J_{H,H}$ = 7.1 Hz, 2 H, -CH_2CH$_3$), 4.25 (m, 1 H, 5-H), 4.05 (dd, $J_{2,3}$ = 10.1 Hz, $J_{1,2}$ = 5.6 Hz, 1 H, 2-H), 3.78 (m, 1 H, 3′′-H), 3.68 (m, 2 H, 2′′-H, 4-H), 3.58 (m, 2 H, 4′′a-H, 3-H), 3.35 (dd under CD_3OD, $J_{4'',3''}$ = 6.6 Hz, 1 H, 4′′b-H), 2.82 (m, 2 H, 2′a-H, 2′b-H), 2.58 (t, $J_{3'a,2'a}$ = $J_{3'a,2'b}$ = $J_{3'b,2'a}$ = $J_{3'b,2'b}$ = 7.1 Hz, 2 H, 3′a-H, 3′b-H), 2.55 (s, 3 H, CH_3 of furan), 1.35 (t, $^3J_{H,H}$ = 7.1 Hz, 3 H, -CH_2CH_3), 1.24 (d, $J_{5,CH}$ = 6.7 Hz, 3 H, CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, CD_3OD, 25 °C): δ = 173.7 (COOEt), 164.3 (1′-C), 158.2, 154.0 (2′′′-C, 5′′′-C), 113.7 (3′′′-C), 107.1 (4′′′-C), 86.2 (1-C), 73.4, 72.0 (2′′-C, 4-C), 71.0 (2-C), 69.8 (3′′-C), 68.1 (2-C), 66.8 (5-C), 66.3 (1′′-C), 59.9 (1′′-C), 42.6 (4′′-C), 35.9 (3′-C), 25.6 (2′-C), 15.2 (CH_3 of fucose), 13.2 (-*C*H_2CH$_3$), 12.4 (CH_3 of furan) ppm. MS (FAB): *m*/*z* = 530 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{21}H_{34}NO_{11}SNa$ [M + H]$^+$ 508.1853; found 508.1840.

Compound 22β: This compound was prepared as described for **22**α by using **21**β (43 mg, 0.068 mmol) as the starting material. After purification by column chromatography on silica gel (CH_2Cl_2/MeOH, 6:1), compound **22**β (26 mg, 74%) was obtained as a white foam. $[\alpha]_D^{20}$ = +15 (*c* = 0.4, MeOH). ^{1}H NMR (300 MHz, CD_3OD, 25 °C): δ = 6.49 (s, 1 H, 4′′′-H), 4.77 (d, $J_{1'',2''}$ = 2.4 Hz, 1 H, 1′′-H), 4.22 (d, $J_{1,2}$ = 9.0 Hz, 1 H, 1-H), 4.16 (q, $^3J_{H,H}$ = 6.9 Hz, 2 H, -CH_2CH$_3$), 3.66 (m, 1 H, 3′′-H), 3.56 (dd, $J_{2'',3''}$ = 6.9 Hz, $J_{1'',2''}$ = 2.4 Hz, 1 H, 2′′-H), 3.54 (m, 2 H, 3-H, 5-H), 3.47 (dd, $J_{4''a,4''b}$ = 14.1 Hz, $J_{4''a,3''}$ = 3.3 Hz, 1 H, 4′′a-H), 3.39 (d, $J_{1,2}$ = 9.0 Hz, 1 H, 2-H), 3.35 (dd, *J* = 8.6 Hz, *J* = 3.4 Hz, 1 H, 4-H), 3.23 (dd under CD_3OD, 1 H, 4′′b-H), 2.84 (m, 2 H, 2′a-H, 2′b-H), 2.49 (t, $J_{3'a,2'a}$ = $J_{3'a,2'b}$ = $J_{3'b,2'a}$ = $J_{3'b,2'b}$ = 7.2 Hz, 2 H, 3′a-H, 3′b-H), 2.44 (s, 3 H, CH_3 of furan), 1.23 (t, $^3J_{H,H}$ = 6.9 Hz, 3 H, -CH_2CH_3), 1.16 (d, $J_{5,CH}$ = 6.6 Hz, 3 H, CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, CD_3OD, 25 °C): δ = 175.7 (COOEt), 166.2 (1′-C), 160.0, 155.9 (2′′′-C, 5′′′-C), 115.6 (3′′′-C), 109.0 (4′′′-C), 87.9 (1-C), 76.9, 76.6 (3-C, 4-C), 75.3 (2′′-C), 73.7 (5-C), 71.6, 71.5 (3′′-C, 2-C), 68.2 (1′′-C), 61.8 (-*C*H_2CH$_3$), 44.5 (4′′-C), 38.5 (3′-C), 27.5 (2′-C), 17.6 (CH_3 of fucose), 15.1 (-*C*H_2CH$_3$), 14.3 (CH_3 of furan) ppm. MS (FAB): *m*/*z* = 530 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{21}H_{34}NO_{11}SNa$ [M + Na]$^+$ 530.1672; found 530.1679.

Compound 23α: This compound was prepared as described for **21**α except that pure thiofucoside **4**α (291 mg, 0.69 mmol) and amino-ester **18** (189 mg, 0.69 mmol) were used as starting materials. After purification by column chromatography on silica gel (CH_2Cl_2/MeOH, 15:1), compound **23**α (284 mg, 66%) was obtained as a colorless oil. This compound was used in the following step without characterization.

Compound 24α: This compound was prepared as described for **22**α except that pure thiofucoside **23**α (256 mg, 0.41 mmol) was used as the starting material. After purification by column chromatography on silica gel (CH_2Cl_2/MeOH, 6:1), compound **24**α (112 mg, 55%) was obtained as a white foam. $[\alpha]_D^{20}$ = –71 (*c* = 0.41, H_2O). ^{1}H NMR (300 MHz, D_2O, 25 °C): δ = 6.68 (s, 1 H, 4′′′-H), 5.44 (d, $J_{1,2}$ = 5.4 Hz, 1 H, 1-H), 5.26 (d, $J_{1'',2''}$ = 4.2 Hz, 1 H, 1′′-H), 4.30 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, -CH_2CH$_3$), 4.13 (q, $J_{5,CH}$ = 6.6 Hz, 1 H, 5-H), 4.07 (dd, $J_{2,3}$ = 9.3 Hz, $J_{1,2}$ = 5.4 Hz, 1 H, 2-H), 3.88 (dd, $J_{2'',3''}$ = 8.4 Hz, $J_{1'',2''}$ = 4.2 Hz, 1 H, 2′′-H), 3.79–3.69 (m, 3 H, 4′′a-H, 3-H, 4-H), 3.62 (dd, $J_{4''a,4''b}$ = 11.9 Hz, $J_{4''b,3''}$ = 6.6 Hz, 1 H, 4′′b-H), 3.50 (m, 1 H, 3′′-H), 3.48 (d, $J_{1'a,1'b}$ = 15.3 Hz, 1 H, 1′a-H), 3.28 (d, $J_{1'a,1'b}$ = 15.3 Hz, 1 H, 1′b-H), 2.55 (s, 3 H, CH_3 of furan), 1.34 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, -CH_2CH_3), 1.07 (d, $J_{5,CH}$ = 6.6 Hz, 3 H, -CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, D_2O): δ = 171.9 (-COOEt), 166.3 (-CONH-), 160.3, 148.6 (2′′′-C, 5′′′-C), 113.5 (3′′′-C), 109.0 (4′′′-C), 86.8 (1-C), 71.9 (2′′-C), 71.6 (4-C), 71.5 (3′′-C), 70.1 (3-C), 67.6 (2-C, 5-C), 61.5 (-*C*H_2CH$_3$), 49.2 (1′′-C), 33.7 (1′-C), 15.1 (CH_3 of fucose), 13.4, 13.2 (-CH_2*C*H_3, CH_3 of furan) ppm. MS (FAB): *m*/*z* = 516 [M + Na]$^+$. HRMS (FAB): calcd. for $C_{20}H_{31}NO_{11}SNa$ [M + Na]$^+$ 516.1516; found 516.1541.

Compound 25α: This compound was prepared as described for **21**α except that pure thiofucoside **3**α (94 mg, 0.216 mmol) and amino-ester **18** (59 mg, 0.216 mmol) were used as starting materials. After purification by column chromatography on silica gel (CH_2Cl_2/MeOH, 20:1), compound **25**α (103 mg, 75%) was obtained as a colorless oil. This compound was used in the following step without characterization.

Compound 26α: This compound was prepared as described for **22**α except that pure thiofucoside **25**α (60 mg, 0.094 mmol) was used as the starting material. Purification by column chromatography on silica gel (CH_2Cl_2/MeOH, 8:1) afforded **26**α (29 mg, 60%) as a white foam. $[\alpha]_D^{20}$ = –64 (*c* = 1.3, MeOH). IR: $\tilde{\nu}$ = 3409, 2936, 1654, 1534, 1428, 1299, 1089, 1028, 780 cm^{-1}. ^{1}H NMR (300 MHz, CD_3OD, 25 °C): δ = 6.61 (s, 1 H, 4′′′-H), 5.36 (d, $J_{1'',2''}$ = 4.2 Hz, 1 H, 1′′-H), 5.34 (d, $J_{1,2}$ = 5.7 Hz, 1 H, 1-H), 4.27 (q, $^3J_{H,H}$ = 7.2 Hz, 2 H, -CH_2CH$_3$), 4.21 (m, 1 H, 5-H), 4.03 (dd, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 5.7 Hz, 1 H, 2-H), 3.80 (dd, $J_{2'',3''}$ = 8.1 Hz, $J_{1'',2''}$ = 4.2 Hz, 1 H, 2′′-H), 3.74 (dd, $J_{4''a,4''b}$ = 11.4 Hz, $J_{4''a,3''}$ = 3.3 Hz, 1 H, 4′′a-H), 3.63–3.54 (m, 3 H, 4′′b-H, 3-H, 4-H), 3.45 (m, 1 H, 3′′-H), 2.82 (m, 2 H, 1′a-H, 1′b-H), 2.57 (m, 2 H, 2′a-H, 2′b-H),

2.54 (s, 3 H, CH_3 of furan), 1.33 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, -CH_2CH_3), 1.21 (d, $J_{5,CH}$ = 6.6 Hz, 3 H, -CH_3 of fucose) ppm. ^{13}C NMR (75 MHz, CD_3OD, 25 °C): δ = 173.4 (-COOEt), 165.7 (-CONH-), 159.8, 151.6 (2‴-C, 5‴-C), 115.1 (3‴-C), 109.9 (4‴-C), 87.7 (1-C), 74.3 (2″-C), 73.4 (4-C), 73.3 (3″-C), 72.4 (3-C), 69.5 (2-C), 68.2 (5-C), 64.6 (4″-C), 61.3 (-CH_2CH_3), 50.4 (1″-C), 37.3 (2′-C), 26.9 (1′-C), 16.6 (CH_3 of fucose), 14.7 (-CH_2CH_3), 13.9 (CH_3 of furan) ppm. MS (FAB): *m*/*z* = 530 [M + Na]$^+$. HRMS (CI): calcd. for $C_{21}H_{34}NO_{11}S$ [M + H]$^+$ 508.1853; found 508.1871.

E- and P-Selectin Inhibition Assays: SLe^x-BSA (2.3 μg/mL) or PSGL1/IgG chimera (5 μg/mL) was coated in 96-well plates O/N at 4 °C, washed with PBS 0.1%BSA 0.05%Tween-20 then blocked with PBS-BSA 2% for 2 h at 37 °C. After washing, plates were incubated for 4 h at room temperature with E-sel/μ (1 μg/mL) pre-complexed with biotinylated goat antihuman IgM (0.5 μg/mL) and streptavidin-HRPO (0.6 μg/mL) in the presence of the investigated carbohydrate inhibitors. After extensive washing, selectin binding was revealed by *O*-phenylenediamine dihydrochloride (0.67 mg/mL, Sigma) in the presence of 0.016% H_2O_2. The reaction was stopped with H_2SO_4 (3 M). OD was read at 490 nm.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra of all new compounds; biological details for the selectin inhibition assays.

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