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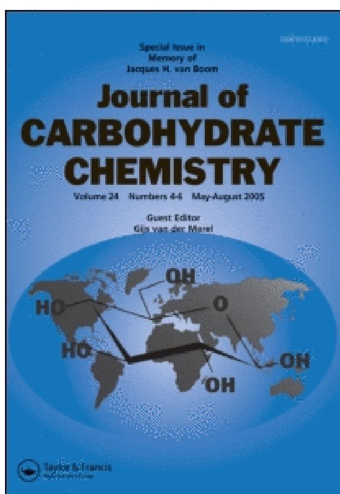

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THE SYNTHESES OF δ-NCS-BUTYL α-L-FUCOSIDES AND FUCOBIOSIDES AND THEIR CLUSTERING TO TRIANTENNARY GLYCOMIMETICS

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ABSTRACT

L-Fucose is an especially important monosaccharide constituent in eukaryotic glycoconjugates. Its recognition by fucose specific lectins might play an important role in embryonic development, cancer development and metastasis. Therefore it is of great interest to develop potent inhibitors of fucose specific lectins, both to investigate as well as to manipulate the respective interactions. A promising approach to high affinity fucoside ligands is the synthesis of oligovalent fucosyl clusters. The synthesis of isothiocyanato-functionalized spacer α-fucosides and fucobiosides is described together with their clustering on tris(2-aminoethyl)amine giving rise to the first thiourea bridged cluster fucosides **14** and **16** in excellent yields.

INTRODUCTION

Carbohydrate-protein interactions are crucial for a great number of events in cell-cell communication.[1] These also include pathological modifications of normal cell behaviour,[2] such as exaggerated leukocyte recruitment during inflammatory diseases[3] or certain aspects in the development of cancer and metastasis.[4] Finally, microbial adhesion to the surface of host cells, which is a prerequisite for infection, often depends on specific interactions between carbohydrate epitopes and microbial proteins.[5]

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Research of glycobiologists is therefore often concentrated on the detailed investigation of carbohydrate-protein interactions, for both the better understanding of the occurring mechanisms and their manipulation, aiming at the design of potent inhibitors, which might eventually lead to the development of carbohydrate-based drugs.

Based on the knowledge that effective carbohydrate-protein interactions possess multivalent character, a variety of multivalent glycomimetics has been designed during the last decade in addition to classical neoglycoconjugates. These comprise glycopolymers and glycotelomers, glycoclusters and glycodendrimers.[6] They have been developed into an important tool for the inhibition of carbohydrate-protein interactions.[7] Among the afore-mentioned classes of multivalent glycomimetics, glycoclusters and glycodendrimers are advantageous for the elucidation of ligand-receptor contacts, because they possess a defined structure with exact molecular weight and a precise number of sugar epitopes. Thus, conclusions can be made about the investigated interactions on a molecular level based on the measured inhibition potencies.

The first glycoclusters were designed for the inhibition of the galactose-specific lectin of liver cells and showed a logarithmic increase of avidity with linear increase of the sugar density in the synthetic cluster.[8] This phenomenon has been termed the cluster or multivalency effect.[9] Other research has further developed this pioneering work, aiming at the inhibition of, for example, neuraminic acid-, mannose- or *N*-acetylglucosamine-specific adhesion systems.[7, 10]

In addition to these monosaccharides, L-fucose is a constituent of glycoconjugates of special importance.[11] It is regularly found at strategic sites of the surface oligosaccharides of eukaroytic cells and might therefore play an especially pronounced role in cell-cell communication. It has been shown that the L-fucose concentration significantly varies depending on different developmental stages of cells and tissues. In carcinoma cells the L-fucose metabolism is typically activated.[12] Furthermore, lung tissue contains L-fucose specific lectins[13] which might assist fucose-presenting cancer cells to colonize the lung in a lectin-ligand-based mechanism of metastasis. It was shown that the L-fucose specific lung lectins can be blocked by the sulfated fucose-polymer fucoidin more efficiently than by L-fucose.[14]

These findings stimulated interest in the development of multivalent fucose derivatives which might serve as high affinity inhibitors of fucose specific adhesion. We

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have recently established a new strategy for carbohydrate clustering using isothiocyanato-functionalized carbohydrate derivatives and branched polyamines to form thiourea-bridged glycoclusters and glycodendrimers in high yields.[15] In this paper we report on the synthesis of suitable isothiocyanato-functionalized L-fucosides and fucobiosides and their clustering according to the thiourea bridging method, giving rise to the first examples of cluster fucosides.

RESULTS AND DISCUSSION

*Synthesis of the isothiocyanato-functionalized α-fucosides **10** and **12***

The L-fucose derivatives for clustering according to the thiourea bridging strategy should meet several requirements: They should be α-L-glycosides because this is the anomeric configuration which is naturally found in eukaryotic cells. Furthermore, a spacer moiety should be introduced as aglycone to increase the flexibilty and availibility of the carbohydrate antennae later in the clusters. Finally, the spacer should be terminated with an isothiocyanato-function which is needed for the thiourea-bridging reaction with branched polyamines.

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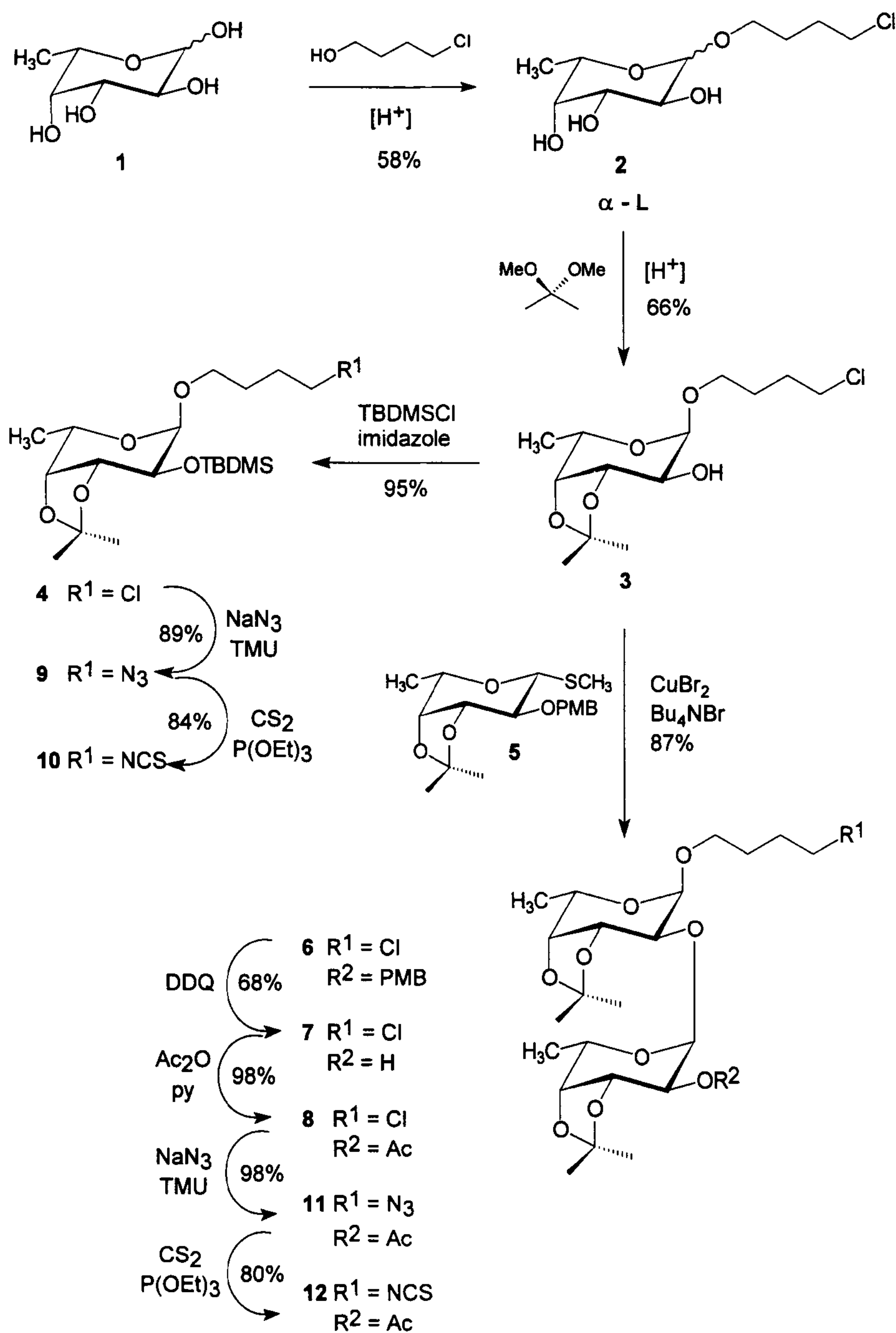
Accordingly, 4-chlorobutanol was chosen as aglycon and was fucosylated in a Fischer-type glycosylation reaction. The fucoside **2** was obtained as an anomeric mixture (α:β=3:1) in good yield (Scheme 1). Subsequent isopropylidenation with 2,2-dimethoxypropane to block the 3- and 4-position led to the anomeric 4-chlorobutyl 3,4-*O*-isopropylidene-L-fucopyranosides. At this stage the anomeric mixture could easily be separated by column chromatography to yield the anomerically pure α-L-fucoside **3**. Then, a silyl ether was formed at the 2-position, and this furnished the fully protected fucoside **4** in high yield. Alternatively, **3** could be glycosylated using methyl 3,4-*O*-isopropylidene-2-*O*-*p*-methoxybenzyl-1-thio-α-L-fucopyranoside (**5**)[16] as donor molecule and a copper bromide-tetrabutylammonium bromide mixture as activator. The desired difucoside **6** was formed in excellent yield, together with traces of the diastereomeric β-L-glycoside, which could be removed after deprotection of the 2'-position with DDQ (**6**→**7**). Standard acetylation of **7** led to the fully protected difucoside **8**.



Scheme 1

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Fucosides **4** and **8** served as starting materials for the preparation of the isothiocyanato functionalized target derivatives **10** and **12**. Analogous reaction sequences for the conversion of the δ-functionality at the spacer gave **9** and **11** by nucleophilic substitution with sodium azide in the presence of tetramethylurea (TMU) and the NCS-functionalized derivatives **10** and **12**, respectively, after conversion of the azide function with triethylphosphite and carbon disulfide[17] in excellent overall yields. Both derivatives, **10** and **12**, are equipped with a protecting group pattern that allows selective derivatization in the 2- or 2'-positions, respectively, prior to clustering or later in the synthesis, and thus opens further prospects for subsequent projects.

Clustering of the isothiocyanato-functionalized α-fucosides 10 and 12 on tris(2-amino-ethyl)amine

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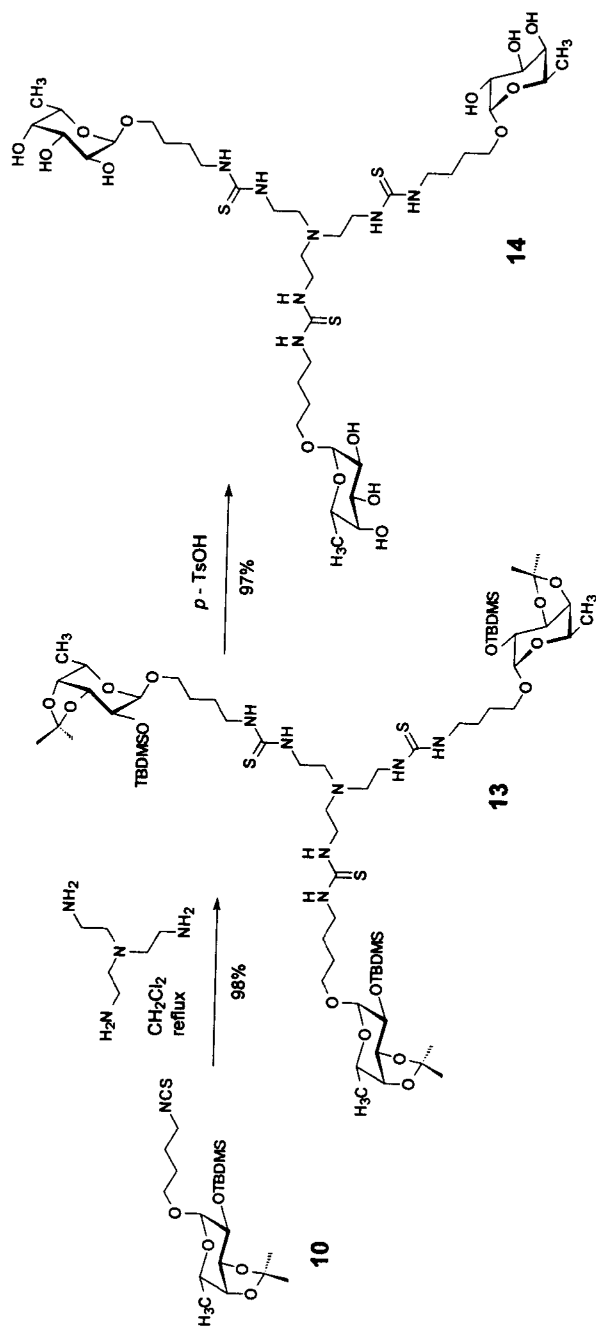
To test fucoside **10** and fucobioside **12** as "donor molecules" in clustering reactions with oligoamines, tris(2-aminoethyl)amine was used as core molecule. The reaction was carried out according to a published procedure.[15a] Only a slight excess (1.1 equivalents per amino group) of the NCS-functionalized fucoside donors had to be used to fully convert the starting materials, within three to five hours, into the triantennary clusters **13** and **15**, which were purified by flash chromatography and isolated in over 95% yield (Schemes 2 and 3).

As the clustering of the monosaccharide derivative **10** and the respective reaction with disaccharide **12** proceeded in complete analogy and in almost equally high yields, it can be concluded that the efficiency of this reaction is predominated by the reactivity of the isothiocyanato function bound to the aglycon moiety and is not notably influenced by the saccharyl part of the molecule. Also, steric hindrance is not of importance for clustering of these spacer equipped glycosides.

The monosaccharide cluster **13** could be deprotected using *p*-toluenesulfonic acid in ethyl acetate to give the unblocked, water soluble cluster fucoside **14** as a colourless syrup after purification on silica gel in excellent yield. The same treatment sufficiently removed the isopropylidene groups in the disaccharide cluster **15**. However, full deprotection of **15** could also be carried out in a one pot procedure, though it is equipped with a base-labile ester group and the acid-sensitive dioxolane rings. Zemplén



Scheme 2

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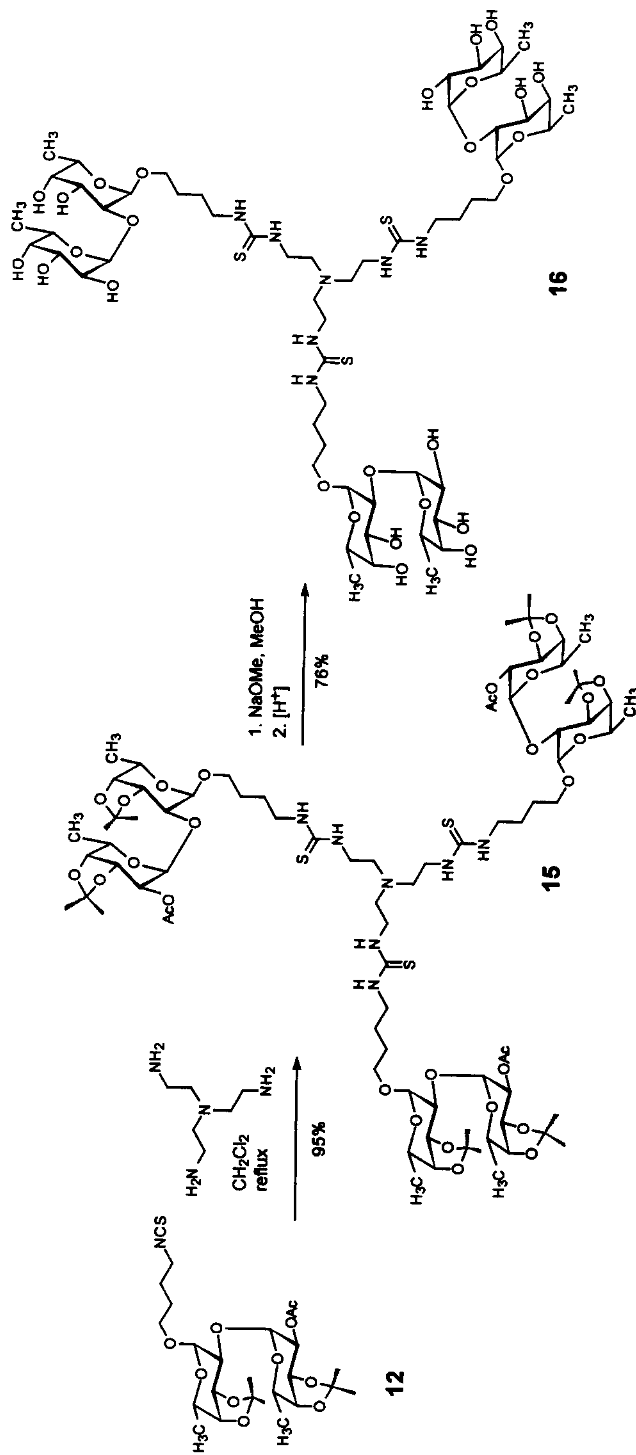

Scheme 3

deacetylation easily removed the 2'-*O*-acetyl group, whereas the isopropylidene groups were cleaved during neutralization with 1N HCl and subsequent filtration over silica gel in the presence of traces of water. Thus, the unprotected **16** could directly be obtained in yields around 75%.

The conformational flexibility of the glycoclusters is reflected by their NMR spectra which typically show broadened peaks for certain protons and carbon atoms. However, all NMR spectra could be unequivocally interpreted, and every peak could be fully assigned, where needed, with the help of two-dimensional NMR methods. In all cases, protected as well as unprotected cluster glycosides, the methylene groups of the glycosidic butyl spacer and those at the tertiary amino core appear as very broad singlets except for the *O*-glycosidically bound CH_2-group, which reflects two distinct multiplets, due to the diastereomeric effect of the carbohydrate ring. The NH-protons give broad peaks around 6.8 and 7.0 ppm in non-protic solvents. The signals for the carbohydrate part of the molecule are completely resolved and coincide for all three antennae. The integration ratio of core and fucoside protons is correct in every case. In the ^{13}C NMR spectra broad peaks are regularly observed for the thiocarbonyl carbon atom around 182 ppm, the methylene groups adjacent to the thiourea bridge (around 44 ppm) and for those at the tertiary nitrogen atom at about 53 ppm. In case of the deprotected disaccharide cluster **16**, the ^{1}H NMR spectrum shows the signals for all protons of the molecule, whereas the typical line broadening effects led to missing peaks in the ^{13}C NMR spectrum: The thiourea-carbon (C=S) and the two sets of thioureylene-attached methylene groups cannot be detected at room temperature.[18] On the other hand, a strong, indicative cross peak between the proton and the carbon signals of the methylene group, adjacent to the tertiary nitrogen of the core, is detected in the HMQC sequence. Furthermore, a HMBC experiment allows the assignment of all carbohydrate carbon atoms of each ring. MALDI-TOF spectrometry (for details see General methods) with **14** as well as **16** gives the correct $[M+H]^+$, $[M+Na]^+$ and $[M+K]^+$ peaks.

In can be concluded that thiourea-bridging of ω-NCS-functionalized alkyl α-fucosides and fucobiosides is a straightforward and high yielding method for the clustering of the expensive sugar. The synthesized clusters **14** and **16** represent new examples of multivalent α-L-fucoside mimetics, with relatively low molecular weight and

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exactly defined structure. Their potency as inhibitors of L-fucose specific lectins should be of great interest.

EXPERIMENTAL

General methods. Reactions were monitored by TLC (on Merck silica gel plates GF_{245}) and the products were purified by flash chromatography (on Merck silica gel 60, 0.040-0.063 mm) and characterized by NMR and mass spectroscopy. NMR spectra were recorded on a Bruker AMX 400 (400.14 MHz for ^{1}H and 100.62 MHz for ^{13}C NMR experiments) or a DRX 500 (500.13 MHz for ^{1}H and 125.76 MHz for ^{13}C NMR experiments). Chemical shifts are given in ppm, relative to $CDCl_3$ (7.24 ppm for ^{1}H and 77.00 for ^{13}C NMR) or methanol-d_4 (3.33 ppm for ^{1}H and 49.00 for ^{13}C NMR) or acetone-d_6 (2.04 ppm for ^{1}H and 29.8 for ^{13}C NMR). Where neccessary, two-dimensional NMR experiments were performed for full assignment. Interchangable assignments are marked with stars. Optical rotation values were measured on a Perkin-Elmer polarimeter 243 or 341. FAB-Mass spectra were recorded on a VG Analytical 70-250S.

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The MALDI mass spectra were measured on a Bruker BIFLEX reflectron time-of-flight mass spectrometer (Bruker-Franzen, Bremen, Germany) equipped with a multiprobe inlet and a gridless delayed extraction ion source. 2,5-Dihydroxybenzoic acid (DHB) was used as a matrix in 40% acetonitrile aqueous solution at a concentration of 10 mg/mL. The samples were deposited on a MALDI target by the back-sandwich method. Ion acceleration voltage was 19 kV and the reflectron (ion mirror) voltage was set to 20 kV. For gridless delayed extraction (GDE), a 5 kV potential difference between the probe and the extraction lens was applied with a time delay in the range of 120-150 ns after each laser pulse. Samples were irradiated at a frequency of 5 Hz by 337 nm photons from a pulsed Laser Science (Cambridge, MA) nitrogen laser. Typically 20-50 shots were summed into a single (conventional) mass spectrum. Spectra were calibrated externally using the monoisotopic $[M+H]^+$ ion of a peptide standard (Bombesin, Aldrich, Germany).

4-Chlorobutyl α- and β-L-fucopyranoside (2). L-Fucose (3.5 g, 21.3 mmol) was dissolved in dry 4-chlorobutanol (50 mL) and stirred together with ion exchange resin

(Amberlite IR 120 (H^+), 3 g wet weight) for four days at rt. Then solids were filtered off and the remaining liquid was evaporated *in vacuo*. The yellow residue, containing unreacted fucose, furanosides, pyranosides and 4-chlorobutanol, was purified by column chromatography (ethyl acetate/methanol, 9:1) to give **2** (3.15 g, 12.4 mmol, 3:1-α:β-mixture, 58%) as colourless syrup: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.86 (d, 1H, $J_{1\alpha,2\alpha}$=3.5 Hz, H-1α), 4.20 (d, 1H, $J_{1\beta,2\beta}$=7.6 Hz, H-1β), 3.93 (dq≈q, 1H, $J_{4\alpha,5\alpha}$<1.0 Hz, $J_{5\alpha,6\alpha}$=6.6 Hz, H-5α), 3.82-3.77 (m, 3H, H-2, H-3, H-4), 3.75 (dt, 1H, J_d=10.2 Hz, J_t=6.6 Hz, OC*H*Hα), 3.62 (dq≈q, 1H, $J_{4\beta,5\beta}$<1.0 Hz, $J_{5\beta,6\beta}$=6.6 Hz, H-5β), 3.58 (t, 2H, J=6.6 Hz, CH_2Clα), 3.50 (dt, 1H, J_d=10.2 Hz, J_t= 6.1Hz, OCH*H*α), 1.86 (m, 2H, CH_2), 1.78 (m, 2H, CH_2), 1.33 (d, 3H, $J_{5\beta,6\beta}$=6.6 Hz, H-6β), 1.29 (d, 3H, $J_{5\alpha,6\alpha}$=6.6 Hz, H-6α); not all peaks could be assigned for the β-anomer.

Anal. Calcd for $C_{10}H_{19}$ O_5Cl (254.71): C 47.16; H 7.52. Found: C 47.20; H 7.49.

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4-Chlorobutyl 3,4-*O*-isopropylidene-α-L-fucopyranoside (3). A solution of **2** (3.0 g, 11.8 mmol) in dry dichloromethane (50 mL) was stirred together with 2,2-dimethoxypropane (10 mL) and a catalytic amount of *p*-toluenesulfonic acid overnight at rt. The reaction mixture was washed twice with saturated sodium hydrogencarbonate solution (50 mL) and sodium chloride solution (50 mL), dried and concentrated under reduced pressure. Column chromatography (petrol ether/ethyl acetate, 5:3) gave **3** (2.31 g, 7.85 mmol, 66%) as a colourless syrup, together with the corresponding β-glycoside (798 mg, 2.73 mmol, 23%).

α-anomer: $[\alpha]_D^{20}$ -113.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.81 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.21 (dd≈t, 1H, $J_{2,3}$≈$J_{3,4}$=6.1 Hz, H-3), 4.12 (dq, 1H, $J_{4,5}$=2.0 Hz, $J_{5,6}$=6.6 Hz, H-5), 4.06 (dd, 1H, $J_{3,4}$=6.1 Hz, $J_{4,5}$=2.0 Hz, H-4), 3.80 (m, 2H, H-2, OCH_2), 3.57 (t, 2H, J=6.6 Hz, CH_2Cl), 3.53 (dt, 1H, J_d=9.6 Hz, J_t=6.1 Hz, OCH_2), 1.85 (m, 2H, CH_2), 1.78 (m, 2H, CH_2), 1.51 (s, 3H, ^{i}pr), 1.36 (s, 3H, ^{i}pr), 1.31 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6).

Anal. Calcd for $C_{13}H_{23}O_5Cl$ (294.78): C 52.97; H 7.86. Found: C 52.80; H 7.89.

β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (d, 1H, $J_{1,2}$=8.1 Hz, H-1), 4.03 (dd≈t, 1H, $J_{2,3}$≈$J_{3,4}$=6.1 Hz, H-3), 4.06 (dd, 1H, $J_{3,4}$=5.6 Hz, $J_{4,5}$=2.0 Hz, H-4), 3.94 (dt, 1H, J_d=9.7 Hz, J_t=6.1 Hz, OC*H*H), 3.87 (dq, 1H, $J_{4,5}$=2.0 Hz, $J_{5,6}$=6.6 Hz, H-5), 3.58 (t, 2H, J=6.3

Hz, CH_2Cl), 3.53 (dt, 2H, J_d=9.1 Hz, J_t=6.6 Hz, OCH*H*, H-2), 1.85 (m, 2H, CH_2), 1.78 (m, 2H, CH_2), 1.51 (s, 3H, ^{i}pr), 1.36 (s, 3H, ^{i}pr), 1.31 (d, 3H, $J_{5,6}$=6.6 Hz, H-6).

4-Chlorobutyl 2-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-α-L-fucopyranoside (4). To a stirred solution of **3** (2.1 g, 7.13 mmol) in dry DMF (12 mL) imidazole (1020 mg, 15 mmol) and *tert*-butyldimethylsilyl chloride (1.5 g, 10 mmol) were added. After 12 h the DMF was evaporated *in vacuo*, the residue was diluted with CH_2Cl_2 (50 mL), washed with saturated sodium hydrogencarbonate solution (2 x 50 mL) and sodium chloride solution (50 mL), dried and concentrated *in vacuo* to give **4** (2.76 g, 6.74 mmol, 95%) as a colourless syrup: $[\alpha]_D^{20}$ -106.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.62 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.13 (dq≈m, 1H, $J_{4,5}$=2.5 Hz, $J_{5,6}$=6.6 Hz, H-5), 4.12 (dd≈m, 1H, $J_{2,3}$=7.6 Hz, $J_{3,4}$=5.6 Hz, H-3), 4.04 (dd, 1H, $J_{3,4}$=5.6 Hz, $J_{4,5}$=2.5 Hz, H-4), 3.75 (dt, 1H, J_d=10.2 Hz, J_t=6.1 Hz, OC*H*H), 3.72 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=7.6 Hz, H-2), 3.58 (t, 2H, J=6.6 Hz, CH_2Cl), 3.43 (dt, 1H, J_d=10.2 Hz, J_t=6.1 Hz, OCH*H*), 1.89 (m, 2H, CH_2), 1.75 (m, 2H, CH_2), 1.50 (s, 3H, ^{i}pr), 1.35 (s, 3H, ^{i}pr), 1.32 (d, 3H, $J_{5,6}$=6.6 Hz, H-6), 0.89 (s, 9H, Si^{t}Bu), 0.11 (s, 3H, SiMe), 0.08 (s, 3H, SiMe).

Anal. Calcd for $C_{19}H_{37}O_5ClSi$ (409.04): C 55.79; H 9.12. Found: C 55.79; H 9.16.

4-Chlorobutyl 3,4-*O*-isopropylidene-2-*O*-*p*-methoxybenzyl-α-L-fucopyranosyl-(1→2)-3,4-*O*-isopropylidene-α-L-fucopyranoside (6). The acceptor fucoside **3** (800 mg, 2.71 mmol) and the fucosyl donor **5** (1085 mg, 3.06 mmol) were co-evaporated three times with toluene and stirred together with freshly activated molecular sieves (3g, 4Å) in a DMF-CH_2Cl_2 mixture (1:1, v/v, 30m L) for 1 h under argon. *tert*-Butylammonium bromide (3.2 g, 10 mmol) was added, and after 1 h the reaction was initiated by the addition of copper(II) bromide (2.2 g, 10 mmol). It was stirred at rt for 4 days. Subsequently, the solution was filtered over celite, diluted with ethyl acetate (50 mL) washed with saturated sodium hydrogencarbonate solution (3 x 50 mL) and saturated sodium chloride solution (50 mL), dried and evaporated. Column chromatography (toluene/ethyl acetate, 6:1) furnished **6** (1.41 g, 2.35 mmol, 87%) as colourless syrup, containing 15% of the β-anomer; $[\alpha]_D^{20}$ -143.1° (*c* 1.0, $CHCl_3$); α-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (m≈d, 2H, aryl-H), 6.84 (m≈d, 2H, aryl-H), 4.85 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.82 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.69 (d, 1H, J_{PMB}=12.2 Hz, benzyl-C*H*H), 4.61 (d, 1H, J_{PMB}=12.2 Hz, benzyl-CH*H*), 4.50 (dq, 1H, $J_{4,5}$=2.5 Hz, $J_{5,6}$=6.6 Hz, H-5), 4.38 (dd,

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1H, $J_{2,3}$=8.1 Hz, $J_{3,4}$=5.6 Hz, H-3), 4.25 (dd, 1H, $J_{2,3}$=8.6 Hz, $J_{3,4}$=5.6 Hz, H-3), 4.11 (dq, 1H, $J_{4,5}$=2.5 Hz, $J_{5,6}$=6.6 Hz, H-5), 4.07 (dd, 1H, $J_{3,4}$=5.6 Hz, $J_{4,5}$=2.5 Hz, H-4), 4.05 (dd, 1H, $J_{3,4}$=5.6 Hz, $J_{4,5}$=2.5 Hz, H-4), 3.79 (s, 3H, OCH_3), 3.75 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=8.6 Hz, H-2), 3.68 (dt, 1H, J_d=10.0 Hz, J_t=6.1 Hz, OC*H*H), 3.50 (m, 2H, J_t=6.6 Hz, H-2, CH_2Cl), 3.40 (dt, 1H, J_d=10.0 Hz, J_t=6.5 Hz, OCH*H*), 1.76 (m, 2H, CH_2), 1.68 (m, 2H, CH_2), 1.52 (s, 3H, ^{i}pr), 1.42 (s, 3H, ^{i}pr), 1.35 (s, 3H, ^{i}pr), 1.34 (s, 3H, ^{i}pr), 1.34 (d≈m, 3H, H-6), 1.29 (d, 3H, $J_{5,6}$=6.6 Hz, H-6); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 159.21, 129.29, 128.23, 113.69 (aryl-C), 108.71 (^{i}pr), 108.55 (^{i}pr), 96.10, 95.32 (C-1, C-1'), 76.32, 75.88 (2x), 75.83, 74.58, 74.10 (C-2, C-2', C-3, C-3', C-4, C-4'), 71.69 (benzyl-CH_2), 68.05 (OCH_2), 63.31, 62.80 (C-5, C-5'), 55.30 (OCH_3), 44.94 (CH_2Cl), 29.50 (CH_2), 28.42 (^{i}pr), 28.30 (^{i}pr), 26.74 (CH_2), 26.49 (2 ^{i}pr), 16.34, 16.16 (C-6, C-6'); β-anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.89 (d, 1H, J_{PMB}=11.2 Hz, benzyl-C*H*H), 4.71 (d, 1H, $J_{1,2}$=8.1 Hz, H-1'), 4.71 (d, 1H, J_{PMB}=11.2 Hz, benzyl-CH*H*), 4.36 (dd≈m, 1H, $J_{3,4}$=5.6 Hz, H-3), 3.94 (dd, 1H, $J_{3,4}$=5.6 Hz, $J_{4,5}$=2.0 Hz, H-4), 3.91 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=8.1 Hz, H-2), 1.25 (d, 3H, $J_{5,6}$=6.6 Hz, H-6).

Anal. Calcd for $C_{30}H_{45}O_{10}Cl$ (601.13): C 59.94; H 7.55. Found: C 60.31; H 7.59.

4-Chlorobutyl 3,4-*O*-isopropylidene-α-L-fucopyranosyl - (1→2) - 3,4- *O* -iso-propylidene-α-L-fucopyranoside (7). The protected fucoside **6** (1.242 g, 2.07 mmol) was dissolved in CH_2Cl_2/H_2O (40 mL, 18:1) and treated with 2,3-dicyano-5,6-dichloro-*p*-benzoquinone (DDQ, 705 mg, 3.11 mmol). After 40 min, solids were filtered off and the solution was washed with aqueous sodium hydrogencarbonate (2 x 40 mL) and aqueous sodium chloride (40 mL). The solution was dried, the solvents evaporated and flash chromatography (petrol ether/ethyl acetate, 1.75:1) led to the anomerically pure fuco-bioside 7 (679 mg, 1.41mmol, 68%); $[\alpha]_D^{20}$ -173.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.88 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.87 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.44 (dq, 1H, $J_{4,5}$=2.5 Hz, $J_{5,6}$=6.6 Hz, H-5), 4.21 (dd, 1H, $J_{2,3}$=7.6 Hz, $J_{3,4}$=5.1 Hz, H-3), 4.13 (dd, 1H, $J_{2,3}$=7.1 Hz, $J_{3,4}$=5.6 Hz, H-3'), 4.06 (m, 3H, H-4, H-4', H-5), 3.85 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=7.6 Hz, H-2), 3.75 (dt, 1H, J_d=10.2 Hz, J_t=6.1 Hz, OC*H*H), 3.66 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=7.1 Hz, H-2'), 3.57 (t, 2H, J=6.6 Hz, CH_2Cl), 3.45 (dt, 1H, J_d=10.2 Hz, J_t=6.1 Hz, OCH*H*), 1.85 (m, 2H, CH_2), 1.76 (m, 2H, CH_2), 1.52 (s, 3H, ^{i}pr), 1.51 (s, 3H, ^{i}pr), 1.38 (s, 3H, ^{i}pr), 1.37 (s, 3H, ^{i}pr), 1.35 (d≈m, 3H, H-6), 1.32 (d, 3H, $J_{5,6}$=6.6 Hz, H-6); ^{13}C-NMR

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(100.62 MHz, $CDCl_3$) δ 109.09 (2 ^{i}pr), 96.49, 95.72 (C-1, C-1'), 76.94, 76.07, 75.85, 74.04, 73.66, 70.17 (C-2, C-2', C-3, C-3', C-4, C-4'), 67.60 (OCH_2), 63.58, 63.43 (C-5, C-5'), 44.72 (CH_2Cl), 29.42 (CH_2), 28.19 (^{i}pr), 28.14 (^{i}pr), 26.83 (CH_2), 26.34 (^{i}pr), 26.27 (^{i}pr), 16.31, 16.19 (C-6, C-6').

Anal. Calcd for $C_{22}H_{37}O_9Cl$ (480.98): C 54.94; H 7.75. Found: C 54.54; H 7.44.

4-Chlorobutyl 2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-fucopyranosyl-(1→2)-3,4-*O*-isopropylidene-α-L-fucopyranoside (8). The fucobioside 7 (592 mg, 1.23 mmol) was dissolved in acetic anhydride and pyridine (1:2, 45 mL) and stirred overnight. Then the solvent was removed, the residue was co-evaporated with toluene (3x) and purified by column chromatography (petrol ether/ethyl acetate, 2:1) to yield **8** (633 mg, 1.21 mmol, 98%) as a syrup: $[\alpha]_D^{20}$ -181.7° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.10 (d, 1H, $J_{1',2'}$=3.5 Hz, H-1'), 4.80 (dd, 1H, $J_{1',2'}$=3.5 Hz, $J_{2',3'}$=8.1 Hz, H-2'), 4.77 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.52 (dq, 1H, $J_{4',5'}$=2.5 Hz, $J_{5',6'}$=6.6 Hz, H-5'), 4.38 (dd, 1H, $J_{2,3}$=8.1 Hz, $J_{3,4}$=5.6 Hz, H-3*), 4.22 (dd, 1H, $J_{2,3}$=8.1 Hz, $J_{3,4}$=5.6 Hz, H-3*), 4.12 (dd, 1H, $J_{3',4'}$=5.1 Hz, $J_{4',5'}$=2.5 Hz, H-4'), 4.09 (dq, 1H, $J_{4,5}$=2.5 Hz, $J_{5,6}$=6.6 Hz, H-5), 4.06 (dd, 1H, $J_{3,4}$=5.6 Hz, $J_{4,5}$=2.5 Hz, H-4), 3.75 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=8.1 Hz, H-2), 3.69 (dt, 1H, J_d=9.7 Hz, J_t=6.6 Hz, OC*H*H), 3.59 (t, 2H, J=6.3 Hz, CH_2Cl), 3.39 (dt, 1H, J_d=9.7 Hz, J_t=6.1 Hz, OCH*H*), 2.12 (OAc), 1.85 (m, 2H, CH_2), 1.76 (m, 2H, CH_2), 1.53 (s, 6H, 2 ^{i}pr), 1.36 (s, 6H, 2 ^{i}pr), 1.35 (d, 3H, $J_{5,6}$=6.6 Hz, H-6), 1.33 (d, 3H, $J_{5,6}$=6.6 Hz, H-6); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ 170.64 (OAc), 109.20 (^{i}pr), 108.81 (^{i}pr), 95.77, 93.54 (C-1, C-1'), 76.15 (2x), 74.42, 73.58, 73.16, 72.56 (C-2, C-2', C-3, C-3', C-4, C-4'), 67.81 (OCH_2), 63.28, 62.65 (C-5, C-5'), 44.70 (CH_2Cl), 29.56 (CH_2), 28.40 (^{i}pr), 28.12 (^{i}pr), 26.98 (CH_2), 26.43 (2 ^{i}pr), 21.08 (OAc), 16.30, 16.11 (C-6, C-6').

Anal. Calcd for $C_{24}H_{39}O_{10}Cl$ (523.02): C 55.12; H 7.52. Found: C 55.56; H 7.86.

4-Azidobutyl 2-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-α-L-fucopyranoside (9). A solution of **4** (1.0 g, 2.36 mmol), sodium azide (455 mg, 7.0 mmol) and tetramethylurea (0.33 mL, 2.95 mmol) in dry DMF (8 mL) was stirred for 1 day at 80 °C. For workup the solvent was removed under reduced pressure, the residue was dissolved in dichloromethane (50 mL), the solution was washed with water (2 x 50 mL), dried, concentrated and purified by column chromatography (petrol ether/ethyl acetate, 10:1) to furnish **9** (872 mg, 2.10 mmol, 89%) as a colourless syrup: $[\alpha]_D^{20}$ -94.3° (*c* 1.0, $CHCl_3$);

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^{1}H NMR (400 MHz, $CDCl_3$) δ 4.62 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.13 (dq, 1H, $J_{4,5}$=2.5 Hz, $J_{5,6}$=6.6 Hz, H-5), 4.12 (dd≈m, 1H, H-3), 4.04 (dd, 1H, $J_{3,4}$=5.6 Hz, $J_{4,5}$= 2.5 Hz, H-4), 3.75 (dt≈m, 1H, J_t=6.1 Hz, OC*H*H), 3.72 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=7.1 Hz, H-2), 3.43 (dt, 1H, J_d=10.2 Hz, J_t=6.1 Hz, OCH*H*), 3.32 (m, 2H, CH_2N_3), 1.69 (m, 4H, 2 CH_2), 1.51 (s, 3H, ^{i}pr), 1.35 (s, 3H, ^{i}pr), 1.32 (d, 3H, $J_{5,6}$=6.6 Hz, H-6), 0.90 (s, 9H, Si^{t}Bu), 0.11 (s, 3H, SiMe), 0.08 (s, 3H, SiMe).

Anal. Calcd for $C_{19}H_{37}O_5N_3Si$ (415.61): C 54.91; H 8.97; N 10.11. Found: C 54.86; H 9.01; N 10.12

4-Isothiocyanatobutyl 2-*O*-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-α-L-fucopyranoside (10). The fucoside **9** (845 mg, 1.97 mmol) was dissolved in toluene (10 mL) and stirred with carbon disulfide (5 mL) and triethyl phosphite (1.2 mL, 6.93 mmol) for 9 h at 70 °C under argon. Subsequently, the solution was allowed to cool to rt. Water (10 mL) and a small amount sodium hydrogencarbonate were added and the mixture was stirred overnight. Then it was diluted with dichloromethane (50 mL), the solution washed with water (50 mL) and aqueous sodium hydrogencarbonate (50 mL), dried and concentrated. Column chromatography (petrol ether/ethyl acetate, 10:1) led to **10** (716 mg, 1.66 mmol, 84%) as a colourless syrup: $[\alpha]_D^{20}$ -89.7° (*c* 1.0, $CHCl_3$); IR ν (NCS) 2102 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.61 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.12 (dq, 1H, $J_{4,5}$=2.5 Hz, $J_{5,6}$=6.6 Hz, H-5), 4.11 (dd≈m, 1H, H-3), 4.04 (dd, 1H, $J_{3,4}$=5.6 Hz, $J_{4,5}$=2.5 Hz, H-4), 3.78 (dt, 1H, J_d=10.2 Hz, J_t=5.6 Hz, OC*H*H), 3.72 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=7.1 Hz, H-2), 3.59 (m, 2H, CH_2NCS), 3.41 (dt, 1H, J_d=10.2 Hz, J_t=6.1 Hz, OCH*H*), 1.81 (m, 2H, CH_2), 1.73 (m, 2H, CH_2), 1.51 (s, 3H, ^{i}pr), 1.36 (s, 3H, ^{i}pr), 1.32 (d, 3H, $J_{5,6}$= 6.6 Hz, H-6), 0.90 (s, 9H, Si^{t}Bu), 0.11 (s, 3H, SiMe), 0.08 (s, 3H, SiMe).

Anal. Calcd for $C_{20}H_{37}O_5NSiS$ (431.66): C 55.65; H 8.64; N 3.24. Found: C 55.76; H 8.66; N 3.20

4-Azidobutyl 2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-fucopyranosyl-(1→2)-3,4-*O*-isopropylidene-α-L-fucopyranoside (11). The chloride **8** (600 mg, 1.147 mmol), sodium azide (260 mg, 4.0 mmol) and tetramethylurea (0.33 mL, 1.52 mmol) were dissolved in dry DMF (6 mL) and stirred for 1 day at 80 °C. Subsequently, the solvent was removed under reduced pressure, the product dissolved in dichloromethane (50 mL), the solution washed with water (2 x 50 mL), dried and concentrated. After repeated co-

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evaporation with toluene **11** (597 mg, 1.13 mmol, 98%) was obtained as a colourless syrup. $[\alpha]_D^{20}$ -180.0° (*c* 1.0, $CHCl_3$); IR ν (N_3) 2097 cm $^{-1}$; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.10 (d, 1H, $J_{1',2'}$=3.5 Hz, H-1'), 4.80 (dd, 1H, $J_{1',2'}$=3.5 Hz, $J_{2',3'}$=8.1 Hz, H-2'), 4.76 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.52 (dq, 1H, $J_{4',5'}$=2.5 Hz, $J_{5',6'}$=6.6 Hz, H-5'), 4.38 (dd, 1H, $J_{2,3}$=8.1 Hz, $J_{3,4}$=5.6 Hz, H-3*), 4.21 (dd, 1H, $J_{2,3}$=8.1 Hz, $J_{3,4}$=.6 Hz, H-3*), 4.13 (dd, 1H, $J_{3',4'}$=5.6 Hz, $J_{4',5'}$=2.5 Hz, H-4'), 4.08 (dq, 1H, $J_{4,5}$=2.5 Hz, $J_{5,6}$=6.6 Hz, H-5), 4.05 (dd, 1H, $J_{3,4}$=5.6 Hz, $J_{4,5}$=2.5 Hz, H-4), 3.76 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=8.1 Hz, H-2), 3.68 (dt, 1H, J_d=9.6 Hz, J_t=6.6 Hz, OC*H*H), 3.39 (dt, 1H, J_d=9.6 Hz, J_t= 6.1 Hz, OCH*H*), 3.32 (m, 2H, CH_2N_3), 2.11 (OAc), 1.67 (m, 4H, 2 CH_2), 1.52 (s, 6H, 2 ^{i}pr), 1.35 (s, 6H, 2 ^{i}pr), 1.34 (d, 3H, $J_{5,6}$=6.6 Hz, H-6), 1.33 (d, 3H, $J_{5,6}$=6.6Hz, H-6); ^{13}C NMR ($CDCl_3$, 100.62 MHz): δ 170.62 (OAc), 109.21 (^{i}pr), 108.82 (^{i}pr), 95.79, 93.52 (C-1, C-1'), 76.15 (2 x), 74.41, 73.56, 73.15, 72.59 (C-2, C-2', C-3, C-3', C-4, C-4'), 67.99 (OCH_2), 63.30, 62.66 (C-5, C-5'), 51.24 (CH_2Cl), 28.40 (^{i}pr), 28.13 (^{i}pr), 26.82 (CH_2), 26.42 (2 ^{i}pr), 25.96 (CH_2), 21.03 (OAc), 16.31, 16.11 (C-6, C-6').

Anal. Calcd for $C_{24}H_{39}O_{10}N_3$ (529.59): C 54.43; H 7.42; N 7.93. Found: C 54.38; H 7.46; N 7.51

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4-Isothiocyanatobutyl 2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-fucopyranosyl-(1→2)-3,4-*O*-isopropylidene-α-L-fucopyranoside (12). The azide **11** (557 mg, 1.05 mmol) was dissolved in toluene (7.5 mL) and treated with carbon disulfide (3.5 mL) and triethyl phosphite (0.6 mL, 3.5 mmol) as described for compound **10**. Column chromatography (petrol ether/ethyl acetate, 2:1) led to **12** (460 mg, 0.84 mmol, 80%) as a colourless syrup: $[\alpha]_D^{20}$ -181.5° (*c* 1.0, $CHCl_3$); IR ν (NCS) 2103 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.09 (d, 1H, $J_{1',2'}$=3.5 Hz, H-1'), 4.80 (dd, 1H, $J_{1',2'}$=3.5 Hz, $J_{2',3'}$=8.1 Hz, H-2'), 4.75 (d, 1H, $J_{1,2}$=3.5 Hz, H-1), 4.52 (dq, 1H, $J_{4',5'}$=2.5 Hz, $J_{5',6'}$=6.6 Hz, H-5'), 4.37 (dd, 1H, $J_{2,3}$=8.1 Hz, $J_{3,4}$=5.6 Hz, H-3*), 4.22 (dd, 1H, $J_{2,3}$=8.1 Hz, $J_{3,4}$=5.6 Hz, H-3*), 4.12 (dd, 1H, $J_{3',4'}$=5.6 Hz, $J_{4',5'}$=2.5 Hz, H-4'), 4.09 (dq≈m, 1H, H-5), 4.08 (dd≈m, 1H, H-4), 3.76 (dd, 1H, $J_{1,2}$=3.5 Hz, $J_{2,3}$=8.1 Hz, H-2), 3.72 (dt, 1H, J_d=10.1 Hz, J_t=6.1 Hz, OC*H*H), 3.60 (m, 2H, CH_2NCS), 3.39 (dt, 1H, J_d=10.1 Hz, J_t=5.7 Hz, OCH*H*), 2.11 (OAc), 1.79 (m, 2H, CH_2), 1.75 (m, 2H, CH_2), 1.53 (s, 6H, 2 ^{i}pr), 1.36 (s, 6H, 2 ^{i}pr), 1.34 (d, 3H, $J_{5,6}$=6.6 Hz, H-6), 1.33 (d, 3H, $J_{5,6}$=6.6 Hz, H-6); ^{13}C NMR ($CDCl_3$, 125.76 MHz): δ 170.52 (OAc), 109.23 (^{i}pr), 108.84 (^{i}pr), 95.92, 93.68 (C-1, C-1'), 76.15, 76.12,

74.37, 73.66, 73.14, 72.57 (C-2, C-2', C-3, C-3', C-4, C-4'), 67.72 (OCH_2), 63.42, 62.72 (C-5, C-5'), 44.88 (CH_2NCS), 28.38 (^{i}pr), 28.12 (^{i}pr), 27.26 (CH_2), 26.57 (2 ^{i}pr), 26.41 (CH_2), 21.11 (OAc), 16.33, 16.11 (C-6, C-6').

Anal. Calcd for $C_{25}H_{39}O_{10}NS$ (545.65): C 55.03; H 7.20; N 2.57. Found: C 54.97; H 7.26; N 2.50

Preparation of clusters. Tris(2-aminoethyl)amine (1 equivalent) was diluted in dichloromethane (approx. 10 mL) and added dropwise to a solution of the sugar isothiocyanate (3.3 equivalents) in dichloromethane (approx. 10-20 mL) at reflux temperature. After the reaction was complete (as monitored by TLC), the mixture was concentrated and purified by flash chromatography.

Tris[2-(thioureylenebutyl 2-*O*-(*tert*- butyldimethylsilyl)-3,4-*O*-isopropylidene-α-L-fucopyranoside)ethyl]amine (13). Tris(2-aminoethyl)amine (15 μL, 14.67 mg, 0.100 mmol) and **10** (144.0 mg, 0.333 mmol) were reacted according to the general procedure and stirred at reflux temperature for 4 h (R_f(**13**) 0.46 in toluene/ethyl acetate, 1:9). Flash chromatography with ethyl acetate as eluent yielded the protected cluster fucoside **13** (141 mg, 0.097 mmol, 98%): $[\alpha]_D^{20}$ -108.7° (*c* 0.13, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87, 6.71 (each bs, each 3H, 6 NH), 4.60 (d, 3H, $J_{1,2}$ = 3.6 Hz, 3 H-1), 4.10 (m_c, 8H, 3 H-3, 3 H-5), 4.03 (dd, 3H, $J_{3,4}$ = 6.6 Hz, $J_{4,5}$ = 2.5 Hz, 3 H-4), 3.70 (dd, $J_{2,3}$ = 7.1 Hz, 3 H-2), 3.63 (bm, 3H, OC*H*H), 3.48 (very bs, 12H, 6 $CH_2NC(S)$), 2.62 (very bs, 6H, 3 CH_2N), 1.64 (very bs, 12H, CCH_2CH_2C), 1.47, 1.31 (each s, each 9H, 2 ^{i}pr), 1.29 (d, 9H, $J_{5,6}$=6.6 Hz, 9 H-6), 0.86 (s, 27H, *t* Bu-CH_3); ^{13}C NMR (100.62 MHz, MeOH-d_4) δ 182.12 (3 C=S), 108.59 (3 ^{i}pr), 98.96 (3 C-1), 76.60, 76.08, 71.56 (3 C-2, 3 C-3, 3 C-4), 63.36 (3 C-5), 68.02 (3 OCH_2), 53.11 (bs, 3 CH_2N), 44.43, 42.55 (each bs, 6 $CH_2NHC(S)$), 28.21, 26.22 (6 ^{i}pr), 26.80, 26.19 (each bs, 3 CCH_2CH_2C), 25.76 (3 Si^{t}Bu), 18.03 (3 Si^{t}Bu), 16.31 (3 C-6), 4.50, 4.75 (6 SiMe).

Tris[2-(thioureylenebutyl α-L-fucopyranoside)ethyl]amine (14). The protected cluster **13** (105 mg, 0.0728 mmol) was dissolved in ethyl acetate (10 mL), treated with *p*-toluenesulfonic acid (20 mg) and stirred at rt. During the reaction methanol (5 mL) was added to dissolve traces of precipitate formed. After 5 h the reaction was complete (R_f(**14**) 0.15 in ethyl acetate/methanol/water, 7:2:1). The mixture was neutralized by the addition of sodium hydrogencarbonate, solids were filtered off and the remaining solution

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was concentrated *in vacuo*. Flash column chromatography (ethyl acetate/methanol/water, 7:2:1) yielded fully deprotected **14** (69 mg, 0.0705 mmol, 97%) as a white foam: $[\alpha]_D^{20}$ -64.4° (*c* 3.09, MeOH); ^{1}H NMR (400 MHz, MeOH-d_4) δ 4.80 (d, 3H, $J_{1,2}$=3.6 Hz, 3 H-1), 4.02 (dq≈q, 3H, $J_{4,5}$<1.0 Hz, 3 H-5), 3.81 (dd, 3H, $J_{2,3}$=10.2, $J_{3,4}$=3.1 Hz, 3 H-3), 3.79 (dd, 3H, $J_{1,2}$=3.6, $J_{2,3}$=10.2 Hz, 3 H-2), 3.75 (m, 3H, 3 OCH*H*), 3.72 (bd, 3H, $J_{3,4}$=3.1 Hz, 3 H-4), 3.42-3.70 (m, 15H, 3 OC*H*H, 6CH$_2$NC(S)), 2.79 (m$_c$, 6H, 3 CH$_2$N), 1.72 (m$_c$, 12H, 3 CCH$_2$CH$_2$C), 1.25 (d, 9H, $J_{5,6}$=6.6 Hz, 9 H-6); ^{13}C NMR (100.62 MHz, MeOH-d_4) δ 182.85 (3 C=S), 100.39 (3 C-1), 73.59, 71.63, 70.00 (3 C-2, 3 C-3, 3 C-4), 67.53 (3 C-5) 68.86 (3 OCH$_2$), 54.41 (b, 3 CH$_2$N), 45.19, 43.10 (each bs, 6 *C*H$_2$NHC(S)), 27.90, 27.21 (each bs, 3 C*C*H$_2$*C*H$_2$C), 16.74 (3 C-6); MALDI-TOF 978.5 $[M+H]^+$ (978.5 calculated for $C_{39}H_{76}N_7O_{15}S_3$); 1000.5 $[M+Na]^+$ (1000.4 calculated for $C_{39}H_{75}N_7O_{15}S_3Na$); 1016.5 $[M+K]^+$ (1016.4 calculated for $C_{39}H_{75}N_7O_{15}S_3K$).

Tris[2-(thioureylenebutyl 2-*O*-acetyl-3,4-*O*-isopropylidene-α-L-fucopyranosyl-(1→2)-3,4-*O*-isopropylidene-α-L-fucopyranoside)ethyl]amine (15). Difucoside **12** (70 mg, 0.128 mmol) was dissolved in dry dichloromethane (10 mL) and treated with tris(2-aminoethyl)amine (5.7 mg, 0.0389 mmol) according to the general procedure. The reaction was complete after 4 h (R_f(**15**) 0.58 in ethyl acetate/methanol, 9:1), the solvent was evaporated and flash chromatography (ethyl acetate/methanol, 10:1) gave **15** (66 mg, 0.037 mmol, 95%) as a colourless glass: $[\alpha]_D^{20}$ -132.2° (*c* 1.47, MeOH); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.03, 6.83 (each very bs, each 3H, 6 NH), 5.08 (d, 3H, $J_{1',2'}$=3.5, 3 H-1'), 4.74 (m$_c$, 6H, $J_{1,2}$=2.5 Hz, $J_{2,3}$=8.20, $J_{2',3'}$=8.2 Hz, 3 H-1, 3 H-2'), 4.46 (dq, 3H, $J_{4',5'}$=2.5 Hz, $J_{5',6'}$=6.6 Hz, 3 H-5'), 4.34 (dd, 3H, $J_{2',3'}$=8.2, $J_{3',4'}$=5.4 Hz, 3 H-3'), 4.19 (dd, 3H, $J_{2,3}$=8.2, $J_{3,4}$=5.6 Hz, 3 H-3), 4.10 (dd, 3H, $J_{4',5'}$=2.5 Hz, 3 H-4'), 4.07 (dq, 3H, $J_{4,5}$=2.5 Hz, $J_{5,6}$=6.6 Hz, 3 H-5), 4.04 (dd, 3H, 3 H-4), 3.73 (dd, 3H, $J_{1,2}$=2.5 Hz, $J_{2,3}$=8.2 Hz, 3 H-2), 3.70-3.40 (m, 15H, 6 C*H*$_2$NHC(S), 3OC*H*H), 3.35 (m, 3H, OCH*H*), 2.78-2.50 (very bs, 6H, 3 NCH$_2$), 2.08 (s, 9H, 3 OAc), 1.61 (bs, 12H, 3 CC*H*$_2$C*H*$_2$C), 1.48(bs, 18H, 6 ^{i}pr), 1.32 (bs, 18H, 6 ^{i}pr), 1.30 (d, 18H, 18 H-6); ^{13}C NMR (125.77 MHz, CDCl$_3$) δ 182.38 (3 C(S)), 170.90 (3 OAc), 109.24, 108.68 (3 ^{i}pr), 95.62 (3 C-1), 93.37 (3 C-1'), 76.14 (3 C-4, 3 C-4'), 74.36 (3 C-3), 73.29 (3 C-2), 73.10 (3 C-3'), 72.57 (3 C-2'), 68.05 (3 OCH$_2$), 63.40 (3 C-5), 62.76 (3 C-5'), 53.44 (3 CH$_2$N), 44.42-44.28 (b, 6 CH$_2$NHC(S)), 28.33,

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28.14 (6 ^{i}pr), 26.89, 26.23 (3 C*C*H$_2$*C*H$_2$C), 26.43, 26.38 (6 ^{i}pr), 21.19 (3 OAc), 16.36, 16.11 (3 C-6, 3 C-6').

Tris [2-(thioureylene butyl α- L- fucopyranosyl-(1→2)- α-L-fucopyranoside) ethyl]amine (16). The protected cluster **15** (48 mg, 0.027 mmol) was dissolved in dry methanol (10 mL) and stirred with sodium methanolate (1M solution in methanol, 100 μL) for 2 h at rt. Then the mixture was neutralized with 1N HCl and concentrated. The residue was passed over silica gel and eluted with ethyl acetate/methanol/water, 7:2:1, followed by methanol. Fractions with R_f 0.08 (in ethyl acetate/methanol/water, 7:2:1) were collected and concentrated *in vacuo*. **16** was obtained as colourless syrup (29 mg, 0.020 mmol, 76%): $[\alpha]_D^{20}$ -90.6° (*c* 0.85, D_2O-acetone-d_6, 8:2); ^{1}H NMR (500 MHz, D_20-acetone-d_6, 10:1) δ 5.05 (d, 3H, $J_{1,2}$=3.8 Hz, 3 H-1), 5.00 (d, 3H, $J_{1',2'}$=4.1 Hz, 3 H-1'), 4.22 (dq≈q, 3H, $J_{5,6}$=6.6 Hz, 3 H-5), 4.05 (dq≈q, 3H, $J_{5',6'}$=6.4 Hz, 3 H-5'), 3.93 (dd, 3H, $J_{2,3}$=11.1 Hz, $J_{3,4}$=3.2 Hz, 3 H-3), 3.90 (dd, 3H, $J_{2',3'}$=10.4 Hz, $J_{3',4'}$=3.5 Hz, 3 H-3'), 3.84-3.71 (m, 12 H, $J_{3,4}$=3.2 Hz, $J_{3',4'}$=3.5 Hz, 3 H-2, 3 H-2', 3 H-4, 3 H-4'), 3.68 (m_c, 3H, 3 OC*H*H), 3.63-3.36 (m, 15H, 6 CH_2NHC(S), 3 OCH*H*), 2.72 (bs, 6H, 3 CH_2N), 1.63 (bs, 12H, 3 C-CH_2CH_2-C), 1.20 (2dd≈t, 18H, $J_{5,6}$=6.6, $J_{5',6'}$=6.3, 9 H-6, 9 H-6'); ^{13}C NMR (125.76 MHz, D_2O-acetone-d_6, 10:1) δ 96.55 (3 C-1'), 96.14 (3 C-1), 72.84 (3 C-4*), 72.35, 72.30 (3 C-2', 3 C-2), 70.15 (3 C-4'*), 69.92 (3 C-3'), 68.50 (3 C-3), 68.37 (3 OCH_2), 67.43 (3 C-5), 67.03 (3 C-5'), 52.92-52.81 (b, 3 CH_2N), 26.62, 26.54 (3 C*C*H$_2$*C*H$_2$C), 15.85, 15.79 (3 C-6, 3 C-6'); MALDI-TOF 1416.7 $[M+H]^+$ (1416.7 calculated for $C_{57}H_{106}N_7O_{27}S_3$); 1438.7 $[M+Na]^+$ (1438.6 calculated for $C_{57}H_{105}N_7O_{27}S_3Na$); 1454.7 $[M+K]^+$ (1454.6 calculated for $C_{57}H_{105}N_7O_{27}S_3K$).

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18. This is a typical NMR behaviour of thiourea bridged glycoclusters, which has often been observed before. When the NMR spectra were recorded at higher temperature, the complete set of signals could be observed.

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