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Polyvalent *C*-glycomimetics based on L-fucose or D-mannose as potent DC-SIGN antagonists

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The *C*-type lectin DC-SIGN expressed on immature dendritic cells is a promising target for antiviral drug development. Previously, we have demonstrated that mono- and divalent *C*-glycosides based on D-*manno* and L-*fuco* configurations are promising DC-SIGN ligands. Here, we described the convergent synthesis of *C*-glycoside dendrimers decorated with 4, 6, 9, and 12 α-L-fucopyranosyl units and with 9 and 12 α-D-mannopyranosyl units. Their affinity against DC-SIGN was assessed by surface plasmon resonance (SPR) assays. For comparison, parent *O*-glycosidic dendrimers were synthesized and tested, as well. A clear increase of both affinity and multivalency effect was observed for *C*-glycomimetics of both types (mannose and fucose). However, when dodecavalent *C*-glycosidic dendrimers were compared, there was no difference in affinity regarding the sugar unit (L-*fuco*, IC_{50} 17 μM; D-*manno*, IC_{50} 12 μM). For the rest of glycodendrimers with L-fucose or D-mannose attached by *O*- or *C*-glycosidic linkage, *C*-glycosidic dendrimers were significantly more active. These results show that in addition to the expected physiological stability, the biological activity of *C*-glycoside mimetics is higher in comparison to the corresponding *O*-glycosides and therefore these glycomimetic multivalent systems represent potentially promising candidates for targeting DC-SIGN.

Introduction

Interactions between carbohydrates and *C*-type lectin receptors (CLRs) are vital to immune responses initiated by dendritic cells (DCs). Complex molecular information contained in glycan structures is read out by CLRs through highly selective recognition processes. These carbohydrate-CLR complexes must exist at least as long as the reading of the message requires. Paradoxically, a single monosaccharide binding to a single carbohydrate recognition domain (CRD) of a CLR typically is transient with affinity in the mM range. Nature overcomes this problem by introducing the avidity, or multivalency, phenomenon whereby multiple monosaccharide moieties connected into a complex glycan, that covers the pathogen particle, interact with several CRDs of a single CLR, thus enhancing interaction affinity from mM to nM range.[1]

Although most CLR/pathogen interactions result in protective effects from infections, the opposite outcomes have been proven for some particular lectins-pathogen interactions. The most relevant CLR in this context is the dendritic cell-specific intercellular adhesion molecule-3-grabbing nonintegrin (DC-SIGN). This type II tetrameric CLR is overexpressed on the surface of immature DCs that survey mucosal surfaces.[2] DC-SIGN is implicated in promoting some pathogen infections, including HIV-1 or Ebola.[3] Indeed, the discovery[4,5] that DCs act as local facilitators of productive trans-infection of T-cells due to DC-SIGN-mediated capture and protection of HIV-1 virions within DCs has opened a new perspective for DC-SIGN in the rational anti-infective drug development.[6]

In order to compete with multivalent CLR/pathogen interactions successfully, multivalent antagonists have become promising targets to be developed. Numerous glycoclusters have been already designed to achieve high affinity binding to lectins.[7] The design of DC-SIGN high affinity antagonists is primarily inspired by the structure of its natural ligand the branched high-mannose oligosaccharide $(Man)_9(GlcNAc)_2$ that is present in pathogen envelope glycoproteins, such as the gp120 of HIV. DC-SIGN can also recognize Lewis antigens such as the branched trisaccharide $Lewis^x$ (Galβ(1-4)[Fucα(1-3)]GlcNAc).[8]

The first multivalent ligands for DC-SIGN were prepared in 2003.[9] A glycodendrimer structure was based on the hyperbranched commercially available polymer BoltornH30 presenting at the

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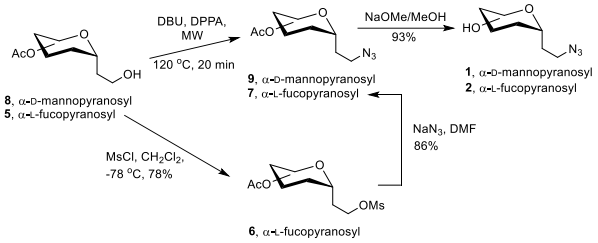
periphery 32 mannose units linked through a succinyl spacer. This polyfunctional glycomimetic exhibited a high antiviral activity (IC_{50} = 0.3 μM) in an artificial Ebola virus infection model. The polydispersity of the Boltorn polymer was a major drawback of this strategy, so a divergent synthesis starting from pentaerythritol as a central core was developed.[10] Glycomimetics with an average of 30 - 32 units of pseudodi- or trimannosides were then tested using pseudotyped viral particles presenting the EboGP envelop glycoprotein and a Jurkat cell line expressing DC-SIGN on the surface. The IC_{50} values were found out in a nanomolar range in both *cis* and *trans* infection assays. A strong difference in the IC_{50} values for the starting pseudodimannosides disappeared when presented on dendrimers. This fact has been clarified later by a clustering effect.[11]

The convergent synthesis of dendrimers offers a convenient approach to well defined polyvalent systems. However, in general terms, dendrimers made in this way are not as large as those made by divergent methods because of the major limitation imposed by the crowding around the core due to steric effects when dendrons have to be conjugated on the core. In addition, the coupling step must be very efficient to enable complete reactions, especially when involving sterically demanding higher generation dendrons avoiding structural defects. In this respect, the click chemistry reaction based on the Cu(I) catalyzed azide–alkyne cycloaddition (CuAAC) introduced by Sharpless and Meldal,[12] met the synthetic requirements to achieve this goal. Several reviews covering the scope of the cycloaddition reaction can be found in the literature.[13]

This strategy was previously employed by some of us for the synthesis of glycodendrons having 3 and 9 α-L-fucopyranosyl or α-D-mannopyranosyl units.[14] The nonavalent glycodendrons present an azido group at the focal point allowing coupling with a BODIPY derivative in order to fluorescently label the systems for internalization and endocytic routing analysis of these dendrons in DCs.[14] Using the convergent approach, tri- and nonavalent *manno* dendrons were incorporated also into virus-like particles bearing up to 1,620 glycans.[15] These glycodendrimer-protein particles were found to be very active from low nanomolar up to high picomolar concentrations inhibiting the infection of Ebola pseudotype virus through competitive blockage of the DC-SIGN receptor.



Scheme 1 Preparation of azides **1** and **2**

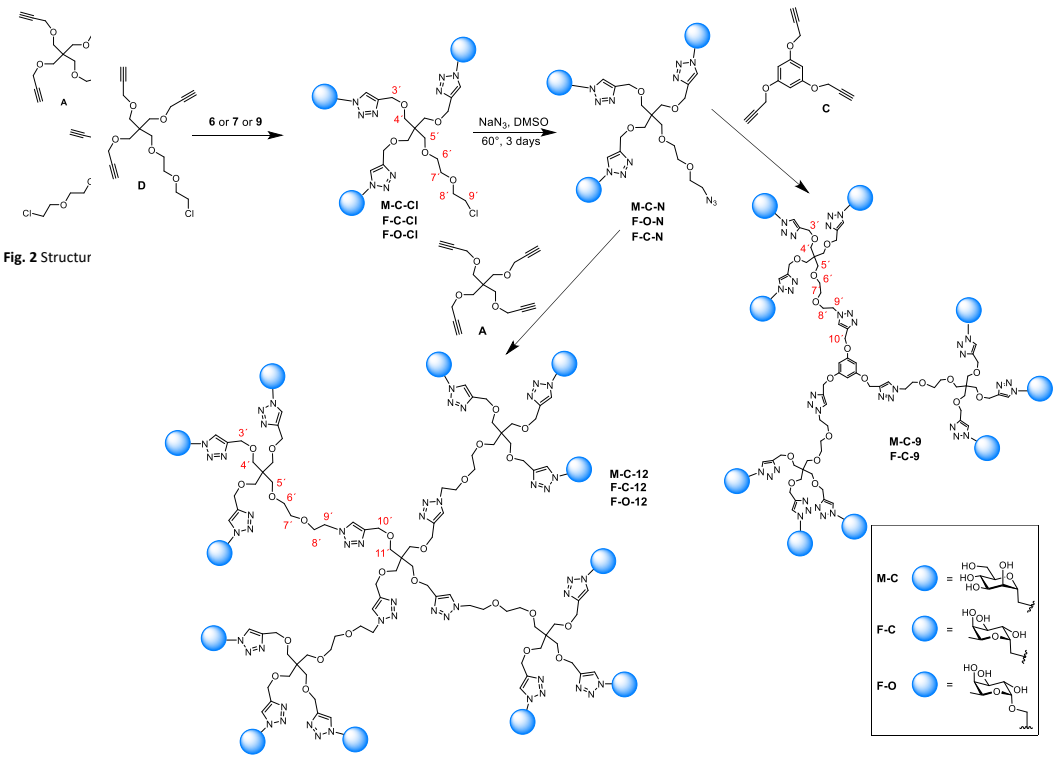
Our ongoing research was focused on the development of a very efficient click chemistry approach to conjugate different carbohydrate and glycomimetic ligands to a variety of multimeric scaffolds with different valence.[16] With this approach, a library of polyvalent constructs was synthesized and the SPR competition assay revealed a gradual increase of activity against DC-SIGN when valence increased.[16] For example, the nonavalent dendrimer **M-O-9** displaying nine copies of α-D-mannopyranose had the IC_{50} = 128 μM while the IC_{50} = 67 μM was assessed for dodecavalent dendrimer **M-O-12** (Fig. 1).

An important issue to be considered when designing ligands for targeting lectins is their stability under physiological conditions. In particular, the stability against glycolytic enzymes arises because the majority of ligand structures have been derived from *O*-glycosides. To overcome this important drawback, one approach lays in the replacement of the exocyclic oxygen with a carbon to provide *C*-glycosidic analogues, which have a high resistance to degradation by glycosidases.[17] Recently we have demonstrated for the first time that divalent *C*-disaccharides based on D-mannose or L-fucose scaffold can be prospective ligands for the DC-SIGN receptor.[18] To verify if *C*-pseudoglycosides are adequate candidates for the construction of multivalent systems, we present here a new class of potentially stable pseudoglycodendrimers with different valences. The affinities of these constructs for DC-SIGN were evaluated by SPR competition assays and compared with their parent *O*-glycosidic dendrimers.

Results and discussion

The general synthetic strategy was based on the Cu(I) catalyzed azide-alkyne cycloaddition (CuAAC) reaction[12] of polypropargyl core compounds **A**, **B** and **C** with 2-(α-D-mannopyranosyl)ethylazide (**1**), 2-(α-L-fucopyranosyl)ethylazide (**2**), 2-azidoethyl α-D-mannopyranoside (**3**) or 2-azidoethyl α-L-fucopyranoside (**4**) (Fig. 2). These cores **A**, **B**, **C** as well as **D** have been prepared according to procedures described previously.[16] The structure of **D** allows subsequent functionalization by CuAAC reaction with three copies of a carbohydrate azide derivative followed by substitution of the chloride attached to the focal position with an azide. Then, it can be clicked again by CuAAC on polyalkyned cores **A**, **B**, or **C** giving more complex structures with higher valency.

Fig. 2 Structur



Scheme 3 Synthesis of nona- and dodecavalent *fuco* and *manno* dendrimers

2-(α-L-Fucopyranosyl)ethylazide (**2**) was synthesized from 2-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)ethanol (**5**) obtained in multi-gram scale from L-fucose by a multistep pathway already described (Scheme 1).[19] For the incorporation of the azido group, two procedures were tested. Traditional two-step process via intermediate mesylate **6** gave fucopyranosylazide **7** in 67 % overall yield while direct azidation of **5** with diphenyl phosphoryl azide and 1,8-diazabicyclo[5.4.0]undec-7-ene under microwave irradiation afforded **7** in excellent yield (90 %).[20] 2-(α-D-Mannopyranosyl)ethylazide (**1**) was synthesized according to the published protocol starting from 2-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)ethanol (**8**).[21] The only modification in regard to the published approach was the first step where the 2-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)prop-1-ene was obtained from methyl α-D-mannopyranoside using silylation-reductive cleavage-deprotection strategy[22] adapted for the *manno* configuration.[18] The alcohol **8** was converted to the azide **9** by a direct azidation as described above in 84% yield. The final Zemplén´s deacetylation of both **7** and **9** produced unprotected azides **2** and **1**, respectively. 2-Azidoethyl glycosides **3**[23] and **4**[24] were synthesized according to known procedures.

The general design of our target dendrimers was based on two important facts. Firstly, it was already published that glycodendrons containing up to nine copies of carbohydrate ligands interact efficiently with the DC-SIGN receptor at the surface of DCs.[14] Therefore we primarily focused on dendrimers having at least nine *C*-glycosidic D-mannose or L-fucose units attached. Secondly, biological tests carried out with our monovalent and divalent *C*-glycosidic ligands were completed indicating L-*fuco* configuration as more active ligand in comparison with D-*manno* configuration.[18] Moreover, very minor affinity improvement of tetra- and hexavalent dendrimers based on the *O*-mannopyranosylated scaffold was found.[16] In this context, a full series of L-*fuco* dendrimers carrying 4, 6, 9, and 12 units were prepared whilst only two constructs with 9 and 12 D-*manno* units attached were made.

The previously developed conditions for these Cu(I) catalyzed azide-alkyne cycloadditions[16] were initially applied to the preparation of tetra- and hexavalent dendrimers (Scheme 2). Constructs having L-fucose units attached either by *O*-glycosidic (**F-O-4**, **F-O-6**) or *C*-glycosidic bonds (**F-C-4**, **F-C-6**) were isolated in 95% yield. Later on, we found that a combination of copper(I)bromide with TBTA under microwave irradiation was more effective for achieving the

preparation of these glycodendrimers with yields in the range of 84 – 95% within reasonable reaction time in the *C*-manno serie (Scheme 3).[14] Trivalent fucosylated chloro dendron **F-O-Cl**, azido dendron **F-O-N**, mannosylated chloro dendron **M-O-Cl** and azido dendron **M-O-N**[14,15] as well as mannosylated nona- (**M-O-9**) and dodecavalent (**M-O-12**) dendrimers[16] have been previously described. The affinity of both dendrimers **M-O-9** and **M-O-12** against DC-SIGN was already assessed and published.[16]

All the pseudoglycodendrimers synthesized and the azido derivatives **6** and **7** were tested by SPR, using previously described procedure.[26] The SPR competition assay was carried out to estimate the potency of the pseudoglycodendrimers to inhibit the binding of tetrameric DC-SIGN extracellular domain (ECD) to mannosylated bovine serum albumin immobilized on the sensor chip surface. The assay allows the determination of the apparent affinity in terms of IC_{50} value and thus, the comparison of test compounds with parent glycodendrimers and natural ligands D-mannose and L-fucose. Furthermore, an affinity improvement factor β was calculated as the relationship $IC_{50,monosaccharide}$/valency$XIC_{50,dendrimer}$ to assess the contribution of valency to the affinity increase.[28]

The reference monosaccharides D-mannose and L-fucose were found to exhibit IC_{50} values of 3.39 and 2.06 mM respectively which are consistent with our previous results.[18, 25, 26] Initially the affinity of azides **1** and **2** was tested in order to check if the affinity of *C*-glycosides could be comparable with those of the parent hexoses. Manno azide **1** (IC_{50} = 3.95 mM) has the same apparent affinity for DC-SIGN ECD as its counterpart D-mannose, so the attachment of the azido ethyl chain at the anomeric position had no effect on D-mannose binding properties in **1**. In contrast, fuco azide **2** (IC_{50} = 1.05 mM) shows two-times stronger affinity to DC-SIGN ECD than its counterpart L-fucose. We can only speculate that the more hydrophobic character of the C-1 substituent may be responsible for the increased affinity in the case of fuco azide **2**.

All *C*-fucosyl dendrimers **F-C-4** - **F-C-12** showed a proportional increase of both affinity and multivalency effect in β term (Fig. 3). In contrast, *O*-fucosylated dendrimers did not show such a trend and the tetra- and hexavalent dendrimers present approximately the same affinity. Surprisingly, the system with 12 fucoses (**F-O-12**) showed an enormous increase in both affinity and multivalency effect. The best improvement of relative inhibitory potency β values[28] was obtained for **F-C-12**. Comparing the activities of the constructs with L-fucose attached by *O*- or *C*-glycosidic bond with the same valency, the higher affinities were found for *C*-glycomimetics. The only exception was the dodecavalent system **F-O-12** displaying 3 times higher affinity than **F-C-12**. It is not clear what the origin for such inversion is.

Respect to the mannosylated series, significantly higher activities of mannose *C*-glycoside-based constructs were observed as compared to the corresponding *O*-mannosides. Gradual improvement effect was discovered in both cases; however, it was more substantial in the *C*-mannose series.

Comparing the same scaffolds with L-fucose or D-mannose attached by *O*- or *C*-glycosidic linkage, it seems that *C*-glycosidic dendrimers present an advantage, which could be attributed to the free rotation around C1-CH_2 bond that caused more flexible conformations on the periphery of the dendrimer. Among dodecavalent *C*-glycosidic dendrimers (**F-C-12** and **M-C-12**), there is no difference in affinity if the configuration of the sugar is L-*fuco* or D-*manno*.

Conclusions

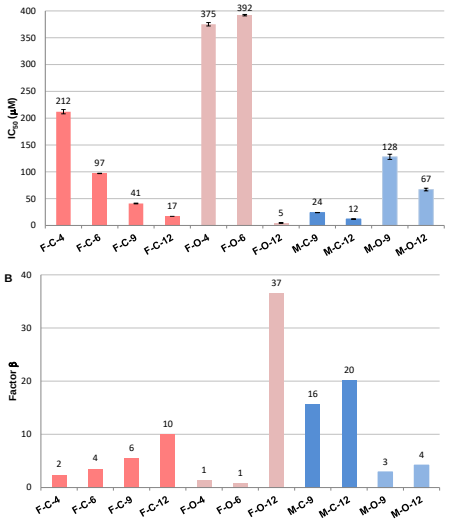


Fig. 3 Inhibition activity of studied dendrimers assessed by SPR (A). Affinity improvement of tested compounds with respect to corresponding natural monosaccharide D-mannose (β = 1) or L-fucose (β = 1) (B).

In conclusion, this work represents a step further in the design of novel multivalent glycomimetics. We introduced fully non-hydrolyzable dendrimeric DC-SIGN antagonists having L-fucose and D-mannose attached by *C*-glycosidic bonds to overcome the potential limitation of low physiological stability of polyvalent glycoside-based constructs. We extended the scope of the Cu(I) catalyzed azide-alkyne cycloaddition to the reaction of novel (L-fuco/D-manno)pyranosylethylazides and their dendrons with polypropargylated scaffolds. The SPR assessment proved that the binding properties of these *C*-glycosidic ligands against DC-SIGN have been improved substantially in comparison with parent *O*-glycosidic constructs. These results could be the starting point for the synthesis of new stable ligands for different lectins in the near future.

Experimental part

General methods

^{1}H, ^{13}C, COSY, HMQC and HMBC spectra were measured on a Bruker DPX-300, DRX-400, DRX-500, or Bruker Advance III 600 (Bruker Corporation, Germany) spectrometer. All spectra were acquired at 298 K. Chemical shifts are given in δ-units (ppm) and are referenced to TMS. Coupling constants (*J*) are reported in Hz. Numbering of atoms is placed in schemes. Optical rotations were measured with an Autopol VI (Rudolph Research Analytical, USA) digital polarimeter in appropriate solvents, at temperature 25 °C and 589 nm sodium line, in 1 dm cuvette and are given at 10^{-1}.deg.cm^2.g^{-1}. Concentrations (*c*) are given in g/100 mL. Low resolution ESI-MS were carried out using an Esquire 6000 ESI-Ion Trap from Bruker Daltonics. ESI high resolution mass spectra were measured with a LTQ Velos Orbitrap XL (Thermo Fisher Scientific, UK) instrument equipped with LockSpray in ES+ and ES- modes with mobile phase of 80% methanol. MALDI high resolution mass analysis was carried out in positive reflectron mode using a MALDI TOF UltrafleXtremeTM MALDI TOF/TOF (Bruker Daltonics, Germany) instrument equipped with 1 kHz smartbeam II laser. 2,5-Dihydroxybenzoic acid was a matrix substance. Nominal and exact *m/z* values are reported in Daltons.

General procedure for the CuAAC reaction

In the optimized procedure, the alkynyl compound (1 eq.), tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amine (TBTA) (1 eq.), a copper salt (CuBr or $CuSO_4.5H_2O$) (0.1 eq.), sodium ascorbate (0.4 eq. if Cu(II) salt was used), and the azide derivative (1.1 eq. per alkyne) were dissolved in THF/H_2O (1:1) or CH_3CN/H_2O (1:1). The reaction mixture was either stirred at room temperature under nitrogen atmosphere and protected from light or heated in a microwave oven (MW) (Tab. 1). A copper scavenger resin, Quadrasil MP, was added to the reaction solution and stirred for 5 min. After that, the mixture was filtered, and the resulting solution was loaded directly on SEPHADEX LH-20 column (MeOH as eluent) to purify the product by size exclusion chromatography.

Table 1
Reaction conditions for the preparation of dendrons and dendrimers

Product	Catalyst	Solvent	Reaction conditions
F-C-Cl, **M-C-Cl**,	Cu^+	CH_3CN/H_2O	r.t., 4 h
F-C-4, **F-C-6**, **F-O-4**, **F-O-6**, **F-O-12**	Cu^{2+}	THF/H_2O	r.t., 4 h
F-C-9, **F-C-12**,	Cu^+	CH_3CN/H_2O	MW, 20 min
M-C-9, **M-C-12**	Cu^{2+}	CH_3CN/H_2O	MW, 20 min

General procedure for deacetylation

A 0.1 M solution of NaOMe in MeOH (1 eq.) was added to a solution of the respective acetate. The reaction mixture was stirred for 1 h at room temperature then the pH was adjusted to 7 by addition of Dowex 50x8 (H^+) resin, which was removed by filtration. The solvent was evaporated and the residue was purified by column flash chromatography on silica.

General procedure for substitution of chloro by an azido group

Sodium azide (large excess) and the corresponding dendron (**F-O-Cl**, **F-C-Cl**, **M-C-Cl**) was dissolved in dimethylformamide (DMF). The mixture was stirred at 60 °C for 3-4 days after the reaction was complete. After evaporation of the solvent, the residue was purified on Sephadex G25 (H_2O/MeOH 9/1).

General procedure for SPR competition assay

DC-SIGN extracellular domain (ECD) was expressed in *E.coli* as inclusion bodies, refolded and purified as described previously.[28] SPR competition experiments were performed using Biacore 3000 instrument, at 25°C as described

previously.[16,25] Briefly, using Biacore amino coupling kit and standard amino coupling procedure, interaction flow cell of sensor chip CM4 was covalently functionalized with BSA-Manα1-3[Manα1-6]Man (Man-BSA), while reference flow cell was EDC/NHS-activated and ethanolamine-deactivated carboxymethyldextran. DC-SIGN ECD alone (20 μM) or in presence of increasing concentrations of test compounds was injected over reference and interaction surfaces at 20 μL/min flow rate. All samples were prepared in running buffer consisting of 25 mM Tris-HCl pH 8, 150 mM NaCl, 4 mM $CaCl_2$ and 0.005% surfactant P20. Binding of DC-SIGN ECD to Man-BSA surface was recorded in sensorgrams. After reference surface correction, DC-SIGN ECD binding responses for each injection were extracted and normalized to DC-SIGN ECD alone binding response. Normalized binding responses were plotted against compound concentration and IC_{50} values were calculated from resulting competition curves using 4-parameter logistic model.[16,25] Each run was repeated twice using two different ManBSA surfaces.

Synthesis and characterization of compounds

2-(2,3,4,6-Tetra-*O*-acetyl-α-L-fucopyranosyl)ethylazide (7)

A solution of **5** (1.30 g, 4.1 mmol), diphenylphosphorylazide (1.3 mL, 5.7 mmol), 1,8-diazabicyclo[5.4.0]undec-7-ene (852 μL, 5.7 mmol) in DMF (12 mL) was treated under microwave irradiation at 120 °C for 20 min. The solvent was evaporated and the residue was purified by column chromatography on silica gel (hexane/EtOAc 4/1 to 2/1) to afford azide **7** (1.0 g, 90%).
$[\alpha]_D^{25}$ - 94.3 (*c* 1.0, $CHCl_3$), IR ($CHCl_3$) ν_{max}/cm^{-1} 2096 (N_3).
δ ^{1}H NMR (600.1 MHz, $CDCl_3$): 5.32 (1 H, dd, $J_{1,2}$ 5.6, $J_{2,3}$ 9.7, H-2), 5.27 (1 H, b dd, H-4), 5.17 (1 H, dd, $J_{3,4}$ 3.6, H-3), 4.30 (1 H, ddd, $J_{1,1'a}$ 11.5, $J_{1,1'b}$ 3.3, H-1), 3.96 (1 H, dq, $J_{5,4}$ 2.6, H-5), 3.45 – 3.35 (2 H, m, H-2'), 2.16, 2.08, 2.02 (9 H, 3 s, CH_3-Ac), 2.03 – 1.95 (1 H, m, H-1$'_a$), 1.72 (1 H, dddd, $J_{1'b,1'a}$ 15.1, H-1$'_b$), 1.18 (3 H, d, $J_{5,6}$ 6.5, H-6).
δ ^{13}C-NMR (125 MHz, $CDCl_3$): 170.4, 170.1, 169.8 (CO), 70.2 (CH-4), 69.6 (CH-1), 68.5 (CH-3), 68.0 (CH-4), 66.1 (CH-5), 48.0 (CH_2-1'), 25.2 (CH_2-2'), 20.8, 20.7, 20.6 (CH_3-Ac), 15.8 (CH_3-6).
HRMS (ESI) for $C_{14}H_{21}N_3O_7Na$: calc. 366.1272; found 366.1276.

2-(α-L-Fucopyranosyl)ethylazide (2)

Deacetylation of **7** (500 mg, 1.45 mmol) followed by purification by column chromatography on silica gel ($CHCl_3$/MeOH 4/1) afforded azide **2** (294 mg, 93%).
$[\alpha]_D^{25}$ - 84.6 (*c* 1.0, MeOH). IR (MeOH) ν_{max}/cm^{-1} 2081 (N_3).
δ ^{1}H NMR (600.1 MHz, D_2O): δ [ppm] 4.05 (1 H, ddd, $J_{1,2}$ 6.1, $J_{1,1'a}$ 11.2, $J_{1,1'b}$ 3., H-1), 3.92 (1 H, dd, $J_{2,3}$ 9.5, H-2), 3.86 – 3.83(1 H, m, H-5), 3.73 – 3.70 (2 H, m, H-3, H-4),), 3.44 – 3.39 (1 H, m, H-2'), 3.36 – 3.31 (1 H, m, H-2'), 1.99 – 1.93 (1 H, m, $J_{1'a,1'b}$ 15.0, H-1$'_a$), 1.80 – 1.76 (1 H, m, H-1$'_b$), 1.14 (3 H, d, H-6).
δ ^{13}C-NMR (125 MHz, D_2O): 73.2 (C-1), 71.7 (C-4), 69.8 (C-3), 67.6 (C-2), 67.3 (C-5), 48.0 (C-2'), 23.0 (C-1'), 15.6 (C-6).
HRMS (ESI) for $C_8H_{15}N_3O_4Na$: calc. 240.0955; found 240.0953.

2-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)ethylazide (9)

A solution of **8** (1.54 g, 4.1 mmol), diphenylphosphorylazide (1.3 ml, 5.7 mmol), 1,8-diazabicyclo[5.4.0]undec-7-ene (852 μL, 5.7 mmol) in DMF (12 mL) was treated under microwave irradiation at 120 °C for 20 min. The solvent was evaporated and the residue was purified by column chromatography on silica gel (hexane/EtOAc 4/1 to 2/1) to afford azide **9** (1.22 g, 74%),
$[\alpha]_D^{25}$ +16.6 (*c* 1.1, $CHCl_3$). IR (MeOH) ν_{max}/cm^{-1} 2102 (N_3).
δ ^{1}H NMR (600.1 MHz, $CDCl_3$): 5.26 (1 H, dd, $J_{3,2}$ 3.4, $J_{3,4}$ 7.7, H-3), 5.17 – 5.13 (2 H, m, H-4, H-2), 4.45 (1 H, dd, $J_{6a,5}$ 7.0, $J_{6a,6b}$ 12.1 H-6a), 4.14 (1 H, dd, $J_{6b,5}$ 3.3, H-6b), 4.13 – 4.08 (1 H, m, H-1), 3.94 – 3.91 (1 H, m, H-5), 3.49 – 3.42 (2 H, m, H-2'), 2.13, 2.12, 2.10, 2.08 (12 H, H-Ac), 2.00 – 1.95 (1H, m, H-1'), 1.85 – 1.80 (1 H, m, H-1').
δ ^{13}C-NMR (125 MHz, $CDCl_3$): 170.6, 170.1, 169.8, 169.6 (C=O), 71.4 (CH-5), 70.6 (CH-1), 70.0 (CH-2), 68.3(CH-3), 67.2 (CH-4), 62.0 (CH_2-6), 47.5 (CH_2-2'), 28.6 (CH_2-1'), 20.9, 20.8, 20.8, 20.7 (CH_3-Ac).
HRMS (ESI) for $C_{16}H_{23}O_9N_3Na$: calc. 424.1332; found 424.1320.

2-(α-D-Mannopyranosyl)ethylazide (1)

Deacetylation of **9** (857 mg, 2.14 mmol) followed by purification by column chromatography on silica gel ($CHCl_3$/MeOH 4/1) afforded azide **1** (465 mg, 93%).
$[\alpha]_D^{25}$-1.2 (*c* 1.0, MeOH). IR (MeOH) ν_{max}/cm^{-1} 2093 (N_3).
δ ^{1}H NMR (600.1 MHz, D_2O): 4.01 – 3.97 (1 H, m, H-1), 3.86 – 3.83 (1 H, m, H-2), 3.80 (1 H, dd, $J_{6a,5}$ 1.9, $J_{6a,6b}$ 12.1 H-6a), 3.76 (1 H, dd, $J_{3,2}$ 3.2, $J_{3,4}$ 9.3, H-3), 3.69 (1H, dd, $J_{6b,5}$ 6.1, H-6b), 3.60 (1 H, dd, $J_{4,5}$ 9.3, H-4), 3.50 – 3.46 (1 H, m, H-5), 3.45 –3.33 (2 H, m, H-2'), 2.10 – 2.02 (1 H, m, H-1'), 1.76 – 1.69 (1 H, m, H-1').
δ ^{13}C-NMR (125 MHz, D_2O): 75.6 (CH-1), 73.9 (CH-5), 71.3 (CH-2), 70.7 (CH-3), 67.3 (CH-4), 61.2 (CH_2-6), 47.7 (CH_2-2'), 26.7 (CH_2-1').
HRMS (ESI) for $C_8H_{15}N_3O_5Na$: calc. 256.0904; found 256.0907.

Dendron F-C-Cl

Cycloaddition of 2-(2-chloroethoxy)ethoxymethyl tris(2-propynyloxymethyl)methane (**D**) (64 mg, 0.18 mmol) with fucopyranosylazide **2** (128 mg, 0.59 mmol) afforded dendron **F-C-Cl** (157 mg, 87%).
$[\alpha]_D^{25}$ - 88.4 (*c* 0.4, MeOH).
δ ^{1}H NMR (600.1 MHz, D_2O): 8.00 (3H, br s, triazolyl-H), 4.35 – 4.59 (12 H, m, 2´-, 3´-CH_2), 3.83 – 3.97 (6 H, m, H-1, H-2), 3.65 – 3.75 (11 H, m, H-3, H-4, H-5, 8´-CH_2), 3.59 – 3.63 (2 H, m, 9´-CH_2), 3.54 – 3.59 (2 H, m, 7´-CH_2), 3.46 – 3.50 (2 H, m, 6´-CH_2), 3.38 – 3.46 (6 H, m, 4´-CH_2), 3.29 – 3.37 (2H, m, 5´-CH_2), 2.26 – 2.37 (3 H, m, 1´a-CH_2), 1.07 – 2.19 (3 H, m, 1´b-CH_2), 1.01 (9 H, d, $J_{5,6}$ 6.5, H-6).
δ ^{13}C NMR (150.9 MHz, D_2O):[30] 73.5 (CH-1), 71.5 (CH-4), 70.8 (CH_2-8´), 70.3 (CH_2-6´), 69.8 (CH-3), 69.5 (CH_2-7´), 69.2 (CH_2-5´), 68.5 (CH_2-4´), 67.4 (CH-2 and CH-5), 63.9 (CH_2-3´), 48.0 (CH_2-2´), 44.7 (C-centre), 43.4 (CH_2-9´), 24.2 (CH_2-1´), 15.6 (6-CH_3).
HRMS (ESI) for $C_{42}H_{70}ClN_9O_{17}Na$: calc. 1030.4470; found 1030.4475

Dendron F-C-N

A reaction of dendron **F-C-Cl** (208 mg, 0.21 mmol) with NaN_3 (137 mg, 2.1 mmol) in DMSO (1.5 mL) gave the dendron **F-C-N** (224 mg, 100%).
$[\alpha]_D^{25}$ - 56.2 (*c* 3.1, MeOH).
δ ^{1}H NMR (600.1 MHz, D_2O): 7.93 (3H, br s, triazolyl-H), 4.49 (6 H, s, 3´-CH_2), 4.45 (6 H, t, *J* 7.0, 2´-CH_2), 3.85 – 3.95 (6 H, m, H-1, H-2), 3.66 – 3.76 (9 H, m, H-3, H-4, H-5), 3.58 – 3.62 (2 H, m, 8´-CH_2), 3.54 – 3.57 (2 H, m, 7´-CH_2), 3.46 – 3.50 (2 H, m, 6´-CH_2), 3.35 – 3.40 (8 H, m, 4´-CH_2, 9´-CH_2), 3.34 (2H, s, 5´-CH_2), 2.26 – 2.37 (3 H, m, 1´a-CH_2), 2.07 – 2.19 (3 H, m, 1´b-CH_2), 1.02 (9 H, d, $J_{5,6}$ 6.4, 6-CH_3).
δ ^{13}C NMR (150.9 MHz, D_2O): 144.1 (C-triazolyl), 125.2 (CH-triazolyl), 73.5 (CH-1), 71.5 (CH-4), 70.5 (CH_2-6´), 69.8 (CH-3), 69.6 (CH_2-7´),

69.3 (CH_2-8´), 69.3 (CH_2-5´), 68.4 (CH_2-4´), 67.4 (CH-2 and CH-5), 63.5 (CH_2-3´), 50.2 (CH_2-9´), 47.8 (CH_2-2´), 44.7 (C-centre), 24.3 (CH_2-1´), 15.6 (6-CH_3).
HRMS (ESI) for $C_{42}H_{70}N_{12}O_{17}Na$: calc: 1037.4874; found 1037.4875.

Dendron M-C-Cl

Cycloaddition of 2-(2-chloroethoxy)ethoxymethyl tris(2-propynyloxymethyl)methane (**D**) (139 mg, 0.39 mmol) with mannopyranosylazide **1** (229 mg, 1.28 mmol) afforded dendron **M-C-Cl** (353 mg, 85%).
$[\alpha]_D^{25}$+ 37.4 (*c* 0.7, MeOH).
δ ^{1}H NMR (600.1 MHz, D_2O): 7.96 (3H, br s, triazolyl-H), 4.42 – 4.54 (12 H, m, 2´-, 3´-CH_2), 3.76 – 3.82 (6 H, m, H-1, H-2), 3.69 – 3.76 (5 H, m, 8´-CH_2, CH_2-6a), 3.63 – 3.69 (6 H, m, CH_2-6b, H-3), 3.57 – 3.63 (5 H, m, H-4, 9´-CH_2), 3.53 – 3.57 (2 H, m, 7´-CH_2), 3.43 – 3.49 (5 H, m, H-5, 6´-CH_2), 3.37 (6 H, br s, 4´-CH_2), 3.33 (2 H, br s, 5´-CH_2), 2.32 – 2.41 (3 H, m, 1´a-CH_2), 1.97 – 2.08 (3 H, m, 1´b-CH_2).
δ ^{13}C NMR (150.9 MHz, D_2O): 144.1 (C-triazolyl), 125.3 (CH-triazolyl), 75.0 (CH-1), 74.1 (CH-5), 71.1 (CH-2), 70.7 (CH_2-8´), 70.7 (CH-3), 70.3 (CH_2-6´), 69.5 (CH_2-7´), 69.2 (CH_2-5´), 68.4 (CH_2-4´), 67.2 (CH-4), 63.5 (CH_2-3´), 61.0 (CH_2-6), 47.0 (CH_2-2´), 44.6 (C-centre), 43.4 (CH_2-9´), 28.0 (CH_2-1´).
HRMS (MALDI) for $C_{42}H_{71}ClN_9O_{20}Na$: calc. 1078.4318; found 1078.4323.

Dendron M-C-N

A reaction of dendron **M-C-Cl** (353 mg, 0.33 mmol) with NaN_3 (214 mg, 3.3 mmol) gave dendron **M-C-N** (361 mg, 100%).
$[\alpha]_D^{25}$ + 29.0 (*c* 4, MeOH).
δ ^{1}H NMR (600.1 MHz, D_2O): 7.96 (3H, br s, triazolyl-H), 4.49 (6 H, s, 3´-CH_2), 4.47 (6 H, t, *J* 6.8, 2´-CH_2), 3.76 – 3.82 (6 H, m, H-1, H-2), 3.70 – 3.76 (5H, m, H-3, CH_2-6b), 3.67 (3H, dd, *J* 12.2, *J* 6.0, CH_2-6a), 3.57 – 3.63 (5 H, m, H-4, 8´-CH_2), 3.53 – 3.57 (2 H, m, 7´-CH_2), 3.43 – 3.50 (5 H, m, 6´-CH_2, H-5), 3.34 – 3.40 (8 H, m, 4´-CH_2, 9´-CH_2), 3.34 (2H, s, 5´-CH_2), 2.33 – 2.42 (3 H, m, 1´a-CH_2), 1.99 – 2.09 (3 H, m, 1´b-CH_2).
δ ^{13}C NMR (150.9 MHz, D_2O): 144.1 (C-triazolyl), 125.3 (CH-triazolyl), 75.0 (CH-1), 74.1 (CH-5), 71.1 (CH-2), 70.7 (CH-3), 70.5 (CH_2-6´), 69.6 (CH_2-7´), 69.3 (CH_2-8´), 69.2 (CH_2-5´), 68.4 (CH_2-4´), 67.2 (CH-4), 63.5 (CH_2-3´), 61.0 (CH_2-6), 50.2 (CH_2-9´), 47.1 (CH_2-2´), 44.6 (C-centre), 28.0 (CH_2-1´).
HRMS (ESI) for $C_{42}H_{70}N_{12}O_{20}Na$: calc 1085.4722; found 1085.4720.

Dendrimer F-O-4

Reaction of 2-azidoethyl α-L-fucopyranoside[14] (20 mg, 0.08 mmol) with tetrakis(2-propinyloxymethyl)methane (**A**) (5.6 mg, 0.019 mmol) gave dendrimer **F-O-4** (19 mg, 95%).
$[\alpha]_D^{25}$ - 71 (*c* 1, MeOH/H_2O 1/1).
δ ^{1}H NMR (500 MHz, D_2O): δ 8.08 (4 H, s, triazolyl-H), 4.85 (4 H, d, $J_{1,2}$ 3.5, H-1), 4.70 – 4.66 (8 H, m, 2´-CH_2), 4.55 (8 H, m, 3´-CH_2), 4.08 – 4.02 (4H, m, 1´-CH_2), 3.97 – 3.92 (4 H, m, 1´-CH_2), 3.72 (4 H, dd, $J_{2,3}$ 10, $J_{2,1}$ 3.5, H-2), 3.65 (4 H, dd, $J_{3,2}$ 10, $J_{3,4}$ 3, H-3) 3.62 – 3.59 (4 H, m, H-4), 3.42 (8 H, s, 4´-CH_2), 3.07 – 3.02 (4 H, m, H-5), 0.99 (12 H, d, $J_{6,5}$ 6.5, H-6).
δ ^{13}C NMR (125 MHz, D_2O): 144.3 (C-triazole), 125.4 (CH-triazole), 97.8 (CH-1), 71.5 (CH-4), 69.42 (CH-3), 68.2 (CH_2-4´), 67.7 (CH-2), 66.4 (CH-5), 65.8 (CH_2-1´), 63.4 (CH_2-3´), 50.1 (CH_2-2´), 44.7 (C-centre), 15.2 (CH_3-6).
MS (ESI) for $C_{49}H_{80}N_{12}O_{24}Na$: calc. 1243.8; found 1244.0.

Dendrimer F-O-6

Reaction of 2-azidoethyl α-L-fucopyranoside[14] (20 mg, 0.08 mmol) with hexapropinyloxymethyl bispentaerythritol (**C**) (6 mg, 0.013 mmol) afforded dendrimer **F-O-6** (15 mg, 75%).
$[\alpha]_D^{25}$ - 62 (*c* 1, MeOH/H_2O 1/1).
δ ^{1}H NMR (500 MHz, D_2O): 8.06 (6 H, s, triazolyl-H), 4.83 (6 H, d, $J_{1,2}$ 4.0, H-1), 4.67 – 4.62 (12 H, m, 2´-CH_2), 4.51 (12 H. m, 3´-CH_2), 4.04 – 3.98 (6 H, m, 1´-CH_2), 3.95 – 3.89 (6 H, m, 1´-CH_2), 3.71 (6 H, dd, $J_{2,3}$ 10.4, $J_{2,1}$ 4.0, H-2), 3.64 (6 H, dd, $J_{3,2}$ 10.4, $J_{3,4}$ 3, H-3) 3.59 – 3.56 (6 H, m, H-4), 3.37 (12 H, s, 4´-CH_2), 3.24 (4 H, s, 4H, 5´-CH_2) 3.05 – 3.00 (6 H, m, H-5), 0.97 (18 H, d, $J_{6,5}$ 6.5, H-6).
δ ^{13}C NMR (125 MHz, D_2O): 144.3 (C-triazole), 125.4 (CH-triazole), 98.0 (CH-1), 71.5 (CH-4), 69.4 (CH-3), 68.9, 68.4 (CH_2-4´, CH_2-5´), 67.8 (CH-2), 66.4 (CH-5), 65.9 (CH_2-1´), 63.6 (CH_2-3´), 50.1 (CH_2-2´), 45.1 (C-centre), 15.3 (CH_3-6).
MS (ESI) for $C_{76}H_{123}N_{18}O_{37}$: calc. 1880.9; found 1880.3.

Dendrimer F-O-12

Reaction of dendron **F-O-N**[14] (30 mg, 0.02 mmol) with tetrakis(2-propinyloxymethyl)methane (**A**) (2.1 mg, 0.007 mmol) gave dendrimer **F-O-12** (15 mg, 75%).
$[\alpha]_D^{25}$ - 47 (*c* 1, MeOH/H_2O 1:1).
δ ^{1}H NMR (500 MHz, D_2O): 8.08 (12 H, s, triazolyl-H), 7.96 (4 H, s, triazolyl-H), 4.85 (12 H, s, H-1), 4.69 – 4.64 (24 H, m, 2´-CH_2), 4.58 – 4.51 (32 H, m, 3´-CH_2, 9´-CH_2), 4.45 (8 H, s, 10´-CH_2), 4.07 – 3.99 (12 H, m, 1´-CH_2), 3.97 – 3.88 (20 H, m, 1´-CH_2, 8´-CH_2), 3.74 (12 H, dd, $J_{2,1}$ 4.5, $J_{2,3}$ 10.3, H-2), 3.66 (12 H, dd, $J_{3,4}$ 3.0, $J_{2,3}$ 10.3, H-3) 3.62 – 3.59 (12 H, m, H-4), 3.57 – 3.52 (8 H, m, 7´-CH_2), 3.49 – 3.45 (8 H, m, 6´-CH_2), 3.42 – 3.35 (32 H, m, 4´-CH_2, 11´-CH_2), 3.33 (8 H, s, 5´-CH_2), 3.10 – 3.05 (12 H, m, H-5), 1.00 (36 H, d, $J_{5,6}$ 6.5, H-6).
δ ^{13}C NMR (D_2O, 125 MHz): 144.3 (C-triazole), 125.4 (CH-triazole), 98.1 (CH-1), 71.5 (CH-4), 70.5 (CH_2-6´), 69.6 (CH_2-7´), 69.5 (CH-3), 68.7 (CH_2-5´), 68.4 (CH_2-8´), 68.1 (CH_2-4´, CH_2-11´), 67.7 (CH-2), 66.4 (CH-5), 65.9 (CH_2-1´), 63.2 (CH_2-3´, CH_2-10´), 50.1 (CH_2-2´, CH_2-9´), 44.8 (2 x C-centre), 15.3 (CH_3-6).
MS (ESI) for $C_{185}H_{300}N_{48}O_{84}$: calc. 4538.0; found 2291.7 $[M+2Na]^{2+}$, 1540.7 $[M+3Na]^{3+}$, 1157.4 $[M+4Na]^{4+}$.

Dendrimer F-C-4

Cycloaddition of 2-(α-L-fucopyranosyl)ethylazide (**2**) (25 mg, 0.115 mmol) with tetrakis(2-propinyloxymethyl)methane (**A**) (7.5 mg, 0.026 mmol) gave dendrimer **F-C-4** (29 mg, 96%).
$[\alpha]_D^{25}$ - 87.2 (*c* 1.0, MeOH).
δ ^{1}H NMR (600.1 MHz, D_2O): 7.98 (4 H, br s, triazolyl-H), 4.43 (16 H, br s, 2´-, 3´-CH_2), 3.85 – 3.95 (8 H, m, H-1, H-2), 3.64 – 3.75 (12 H, m, H-3, H-4, H-5), 3.35 (8 H, br s, 4´-CH_2), 2.25 – 2.35 (4 H, m, 1´a-CH_2), 2.08 – 2.17 (4 H, m, 1´b-CH_2), 1.00 (12 H, d, $J_{5,6}$ 6.4, H-6).
δ ^{13}C NMR (150.9 MHz, D_2O):[29] 73.5 (CH-1), 71.5 (CH-4), 69.8 (CH-3), 68.2 (CH_2-4´), 67.4 and 67.4 (CH-2 and CH-5), 63.9 (CH_2-3´), 48.0 (CH_2-2´), 44.6 (C-centre), 24.2 (CH_2-1´), 15.6 (CH_3-6).
HRMS (ESI) for $C_{49}H_{80}N_{12}O_{20}Na$: calc. 1179.5504; found 1179.5506.

Dendrimer F-C-6

Cycloaddition of 2-(α-L-fucopyranosyl)ethylazide (**2**) (25 mg, 0.115 mmol) with hexapropinyloxymethyl bispentaerythritol (**C**) (12.5 mg, 0.012 mmol) afforded dendrimer **F-C-6** (22 mg, 95%).
$[\alpha]_D^{25}$ - 88.6 (*c* 1.0, MeOH).

δ ^{1}H NMR (600.1 MHz, D_2O): 7.95 (6 H, br s, triazolyl-H), 4.38 – 4.52 (24 H, m, 2´-, 3´-CH_2), 3.84 – 3.96 (12 H, m, H-1, H-2), 3.65 – 3.74 (18 H, m, H-3, H-4, H-5), 3.26 – 3.45 (12 H, m, 4´-CH_2), 3.13 – 3.45 (4 H, br m, 5´-CH_2), 2.23 – 2.36 (6 H, m, 1´a-CH_2), 2.06 – 2.19 (6 H, m, 1´b-CH_2), 1.00 (18 H, d, $J_{5,6}$ 6.3, 6-CH_3).
δ ^{13}C NMR (150.9 MHz, D_2O):[29] 125.2 (CH – triazolyl, from HMQC), 73.5 (CH-1), 71.5 (CH-4), 69.8 (CH-3), 68.8 (CH_2-5´), 68.2 (CH_2-4´), 67.4 and 67.4 (CH-2 and CH-5), 63.7 (CH_2-3´), 47.9 (CH_2-2´), 45.0 (C-centre), 24.3 (CH_2-1´), 15.6 (CH_3-6).
HRMS (MALDI) for $C_{76}H_{124}N_{18}O_{31}Na$: calc. 1807.8572; found 1807.8546.

Dendrimer F-C-9

Reaction of dendron **F-C-N** (25 mg, 0.025 mmol) with 1,3,5-tris(2-propyn-1-yl)oxybenzen (**B**) (1.8 mg, 0.0076 mmol) gave dendrimer **F-C-9** (22 mg, 89%). SEPHADEX G50 (eluent H_2O/MeOH 9/1) was used for the purification.
$[\alpha]_D^{25}$ - 80.7 (*c* 0.4, MeOH).
δ ^{1}H NMR (600.1 MHz, D_2O):[30] 8.03, 7.94 and 7.84 (12 H, br s, triazolyl-H), 6.19 (3 H, br s, Ph), 5.00 (6 H, br s, 10´-CH_2), 4.53 (6 H, br s, 9´-CH_2), 4.51 – 4.31 (36 H, m, 3´-CH_2, 2´-CH_2), 3.95 – 3.72 (24 H, m, H-1, H-2, 8´-CH_2), 3.77 – 3.62 (27 H, m, H-3, H-4, H-5), 3.61 – 3.58 (m), 3.58 – 3.53 (m), 3.50 – 3.43 (m), 3.41 – 3.31 (m), 3.25 (brs) and 3.19 (brs) (36 H, 7´-CH_2, 6´-CH_2, 4´-CH_2, 5´-CH_2), 2.37 – 2.03 (18 H, m, 1´a-CH_2 and 1´b-CH_2), 1.02 and 0.98 (27 H, 2 x d, $J_{6,5}$ 6.3, 6-CH_3).
δ ^{13}C NMR (150.9 MHz, D_2O):[29] 159.7 (C-Ph), 125.2 and 125.1 (2 x CH-triazolyl, from HMQC), 95.3 (CH-Ph), 73.5 (CH-1), 71.5 (CH-4), 70.4 (CH_2-6´), 69.82 and 69.78 (CH-3), 69.6 and 69.3 (CH_2-7´), 69.2 and 69.0 (CH_2-5´), 68.6 (CH_2-8´), 68.43 and 68.36 (CH_2-4´), 67.4 and 67.3 (CH-2 and CH-5), 63.6 and 63.5 (CH_2-3´), 61.2 (CH_2-10´), 50.3 and 50.2 (CH_2-9´), 47.8 (CH_2-2´), 44.8 and 44.7 (C-centre), 24.3 and 24.2 (CH_2-1´), 15.61 and 15.55 (6-CH_3).
HRMS (MALDI) for $C_{141}H_{222}N_{36}O_{54}Na$: calc. 3306.5624; found 3306.5729.

Dendrimer F-C-12

Cycloaddition of dendron **F-C-N** (25 mg, 0.025 mmol) with tetrakis(2-propinyloxymethyl)methane (**A**) (1.6 mg, 0.006 mmol) afforded dendrimer **F-C-12** (26 mg, 100%). The reaction was performed under microwave irradiation (20 min at 60 °C, then 15 min at 80 °C) and SEPHADEX G50 (eluent H_2O/MeOH 9:1) was used for the purification.
$[\alpha]_D^{25}$ - 95.2 (*c* 0.3, MeOH).
δ ^{1}H NMR (600.1 MHz, D_2O): 7.91 (12 H, br s, triazolyl-H), 7.88 (4 H, br s, triazolyl-H), 4.30 – 4.55 (64 H, m, 9´-CH_2, 3´-CH_2, 2´-CH_2, 10´-CH_2,), 3.84 – 3.95 (24 H, m, H-1, H-2), 3.81 (8 H, br t, 8´-CH_2), 3.62 – 3.75 (36 H, m, H-3, H-4, H-5), 3.45 (8 H, br s, 7´-CH_2), 3.37 (8 H, br s, 6´-CH_2), 3.30 (24 H, br s, 4´-CH_2), 3.22 (8 H, br s, 5´-CH_2), 2.21 – 2.33 (12 H, m, 1´a-CH_2), 2.04 – 2.17 (12 H, m, 1´b-CH_2), 1.00 (36 H, d, *J* 6.3, 6-CH_3).
δ ^{13}C NMR (150.9 MHz, D_2O):[29] 125.2 (2 x CH-triazolyl, from HMQC), 73.5 (CH-1), 71.5 (CH-4), 70.4 (CH_2-6´), 69.8 (CH-3), 69.7 (CH_2-7´), 69.1 (CH_2-5´), 68.7 (CH_2-8´), 68.4 (CH_2-4´), 67.4 (CH-2 and CH-5), 63.8 (CH_2-10´), 63.7 (CH_2-3´), 50.1 (CH_2-9´), 47.8 (CH_2-2´), 44.8 (2 x C-centre), 24.3 (CH_2-1´), 15.6 (6-CH_3).
HRMS (MALDI) for $C_{185}H_{301}N_{48}O_{72}$: calc. 4347.1362; found 4347.1236.

Dendrimer M-C-9

Reaction of dendron **M-C-N** (25 mg, 0.023mmol) with 1,3,5-tris(2-propyn-1-yl)oxybenzen (**B**) (1.7 mg, 0.0071 mmol) afforded dendromer **M-C-9** (20 mg, 82%). The reaction was performed under microwave irradiation (20 min at 60 °C) and SEPHADEX G50 (eluent H_2O/MeOH 9/1) was used for the purification.
$[\alpha]_D^{25}$+12.3 (*c* 0.15, MeOH).
δ ^{1}H NMR (600.1 MHz, D_2O): 8.05 (3 H, br s, triazolyl-H), 7.90 (9 H, br s, triazolyl-H), 6.15 (3 H, br s, Ph), 5.00 (6 H, br s, 10´-CH_2), 4.53 (6 H, br s, 9´-CH_2), 4.27 – 4.46 (36 H, m, 3´-CH_2, 2´-CH_2), 3.84 (6 H, br s, 8´-CH_2), 3.62 – 3.81 (45 H, m, H-1, H-2, H-3, 6a-CH_2, 6b-CH_2), 3.60 (9H, dd, *J* 9.0, *J* 9.0, H-4), 3.39 – 3.50 (15 H, m, 7´-CH_2, H-5), 3.35 (6 H, br s, 6´-CH_2), 3.25 (18 H, br s, 4´-CH_2), 3.19 (6H, br s, 5´-CH_2), 2.25 – 2.41 (9 H, m, 1´a-CH_2), 1.88 – 2.01 (9 H, m, 1´b-CH_2).
δ ^{13}C NMR (150.9 MHz, D_2O):[29] 159.6 (C-Ph), 125.7 and 125.4 (2 x CH-triazolyl, from HMQC), 95.3 (CH-Ph), 75.0 (CH-1), 74.1 (CH-5), 71.1 (CH-2), 70.7 (CH-3), 70.4 (CH_2-6´), 69.8 (CH_2-7´), 68.9 (CH_2-5´), 68.6 (CH_2-8´), 68.4 (CH_2-4´), 67.2 (CH-4), 63.7 (CH_2-3´), 61.3 (CH_2-10´), 61.0 (6-CH_2), 50.1 (CH_2-9´), 47.0 (CH_2-2´), 44.8 (C-centre), 28.1 (CH_2-1´).
HRMS (MALDI) for $C_{141}H_{223}N_{36}O_{63}$: calc. 3428.5347; found 3428.5295.

Dendrimer M-C-12

Reaction of dendron **M-C-N** (25 mg, 0.023 mmol) with tetrakis(2-propinyloxymethyl)methane (**A**) (1.5 mg, 0.0053 mmol) gave dendrimer **M-C-12** (21 mg, 85%). The reaction was performed under microwave irradiation (20 min at 60 °C) and SEPHADEX G50 (eluent H_2O/MeOH 9/1) was used for the purification.
$[\alpha]_D^{25}$+10.5 (*c* 0.1, MeOH).
δ ^{1}H NMR (600.1 MHz, D_2O): 7.93 (12 H, br s, triazolyl-H), 7.88 (4 H, br s, triazolyl-H), 4.30 – 4.55 (64 H, m, 9´-CH_2, 3´-CH_2, 2´-CH_2, 10´-CH_2,), 3.77 – 3.82 (20 H, m, 8´-CH_2, H-1), 3.74 – 3.77 (12 H, m, 6a-CH_2), 3.73 – 3.74 (12 H, m, H-2), 3.70 – 3.73 (12 H, m, H-3), 3.68 – 3.71 (8 H, m, 11´-CH_2), 3.65 (12 H, dd, *J* 12.4, *J* 6.3, 6b-CH_2), 3.60 (12 H, dd, *J* 9.0, *J* 9.0, H-4), 3.41 – 3.49 (20 H, m, 7´-CH_2, H-5), 3.36 (8 H, br s, 6´-CH_2), 3.29 (24 H, br s, 4´-CH_2), 3.21 (8 H, br s, 5´-CH_2), 2.29 – 2.39 (12 H, m, 1´a-CH_2), 1.95 – 2.05 (12 H, m, 1´b-CH_2).
δ ^{13}C NMR (150.9 MHz, D_2O): 125.2 (2 x CH-triazolyl, from HMQC), 75.0 (CH-1), 74.1 (CH-5), 71.1 (CH-2), 70.7 (CH-3), 70.4 (CH_2-6´), 69.7 (CH_2-7´), 69.0 (CH_2-5´), 68.7 (CH_2 8´), 68.3 (CH_2-4´), 67.2 (CH-4), 63.7 (CH_2-10´), 63.6 (CH_2-3´), 61.3 (CH_2-11´), 61.0 (6-CH_2), 50.1 (CH_2-9´), 47.0 (CH_2-2´), 44.7 and 44.8 (2 x C-centre), 28.1 (CH_2-1´).
HRMS (MALDI) for $C_{185}H_{301}N_{48}O_{84}$: calc. 4539.0752; found 4539.0891.

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