Synthesis of 1,2,3-triazole-linked galactohybrids and their inhibitory activities on galectins

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Dedicated to Professor Pierre Vogel on the occasion of his 70th birthday

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Abstract

Here a synthesis of novel galactose-1,2,3-triazole conjugates is described. The title compounds were obtained from 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranose *via* a copper catalyzed azide-alkyne 1,3-dipolar cycloaddition reaction. It was demonstrated that the title compounds in their isopropylidene-protected form tend to chelate copper. The copper content can be diminished to 10 ppm by successive treatment with EDTA and Na_2S followed by chromatographic purification. Acidic hydrolysis of the acetonide protecting groups provided water soluble galactohybrids that were tested for their affinity towards galectin-1 and galectin-3. The trimeric galactohybrid exhibited a 160-fold preference for galectin-3 binding with K_d 50 μM. One of the obtained disaccharides was characterized by X-ray analysis.

Keywords: Galactose derivatives, 1,2,3-triazoles, extended bis-triazolyl linker, click chemistry, residual copper content, galectins

Introduction

Carbohydrate-protein interactions play many important roles in biochemical processes. These include lectin-carbohydrate recognition[1,2,3] and processes catalyzed by glycosidases,[4,5,6] glycosyltransferases[7] and glycogen phosphorylases.[8] Very often modified carbohydrates are used

to investigate these processes[9,10] and to create suitable inhibitors of the aforementioned enzymes. 1,2,3-Triazole modified carbohydrates became easily available after the discovery of the Cu(I) catalyzed azide-alkyne 1,3-dipolar cycloaddition reaction and quickly became a prominent class of non-natural sugars.[11] The chemistry and biology of triazole modified sugars is dominated by triazolyl glycosides,[12,13] 5-deoxy-5-triazolyl-furanoses[14] and 6-deoxy-6-triazolyl-pyranoses.[15] Nevertheless, few 3-deoxy-3-triazolyl- and 3-deoxy-triazolylmetyl-derivatives of furanoses have been studied as glycosidase inhibitors,[16,17] but 3-deoxy-3-triazolyl-galactopyranose derivatives have proved to be excellent galectin inhibitors[18,19] with enhanced binding affinities if used as dimeric structures.[20]

Here we aimed to develop a user-friendly synthesis of novel C(3)-modified galactohybrids and to determine their affinities towards galectin-1 and galectin-3. The latter are involved in various pathological pathways (e.g.: metastasis, apoptosis, inflammatory response) and their selective inhibition might lead to the development of therapeutics.[21] Since on many occasions multivalent ligands have shown enhanced protein binding affinities,[22] we designed the target structures as depicted in Figure 1. General formula **A** represents disaccharides with extended bis-triazolyl-linkers that can be described as bivalent galectin inhibitors. General formula **B** corresponds to their higher order congeners.

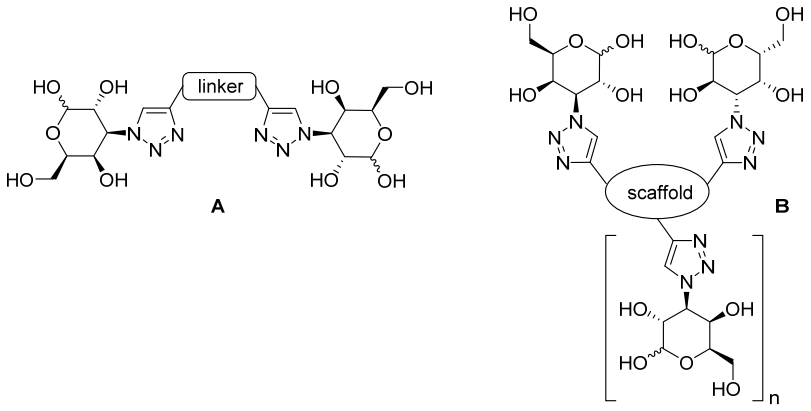
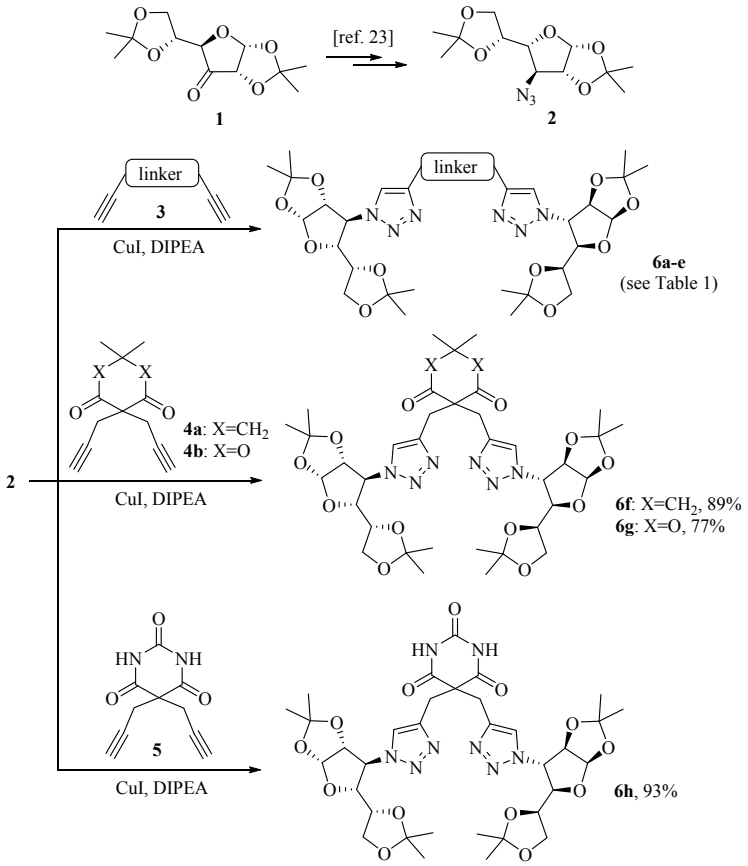


Figure 1. General structures of bivalent galactohybrids (**A**) and their higher order congeners (**B**).

Results and Discussion

The key starting material, 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranose (**2**), was obtained in few straightforward steps[23] from diacetone-D-glucose derived ketone **1**, which is easily available on a hundred gram scale.[24] Copper catalyzed azide-alkyne 1,3-dipolar cycloaddition (CuAAC) between azidogalactose **2** and various diynes provided the expected disaccharides **6a-h** in good to excellent yields (Scheme1, Table 1). The obtained dimeric structures are characterized by an extended bis(1,2,3-triazol-4-yl)linker. The linear alkadiynes

(entries 1-4, Table 1) are commercially available, but other precursors of the linkers (1,2-bis(propargyloxy)ethane,[25] 2,2-dipropargyl dimedone (**4a**),[26] 5,5-dipropargyl Meldrum's acid (**4b**)[27] and 5,5-dipropargyl barbituric acid (**5**)[25]) are readily obtained by previously reported procedures.

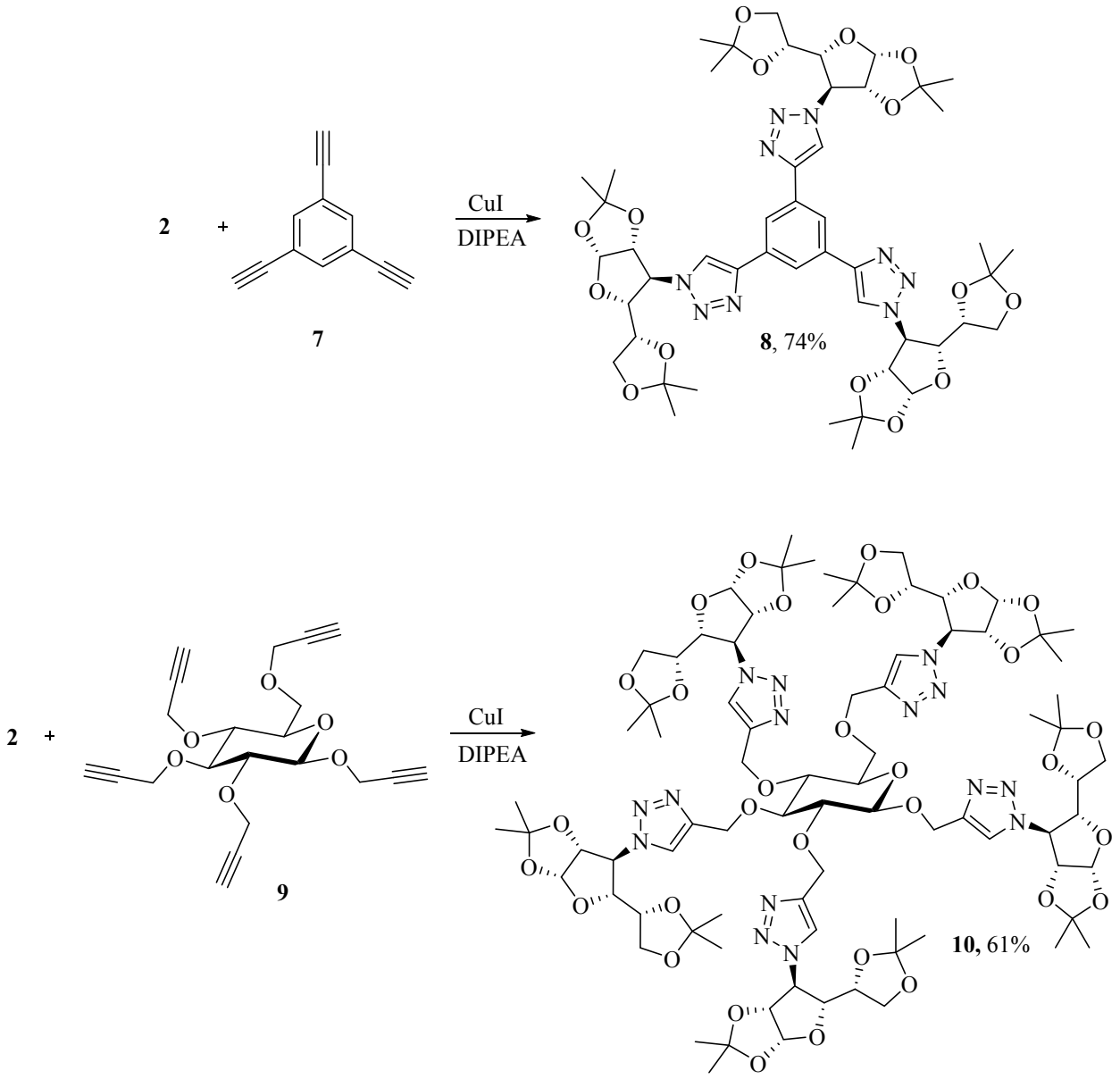


Scheme 1. Synthesis of protected disaccharides **6a-h** with extended bis-triazolyl linkers.

Table 1. Synthesis of disaccharides **6a-e** according to Scheme 1

Entry	Linker	Compound **6**	Yield, %
1	$-(CH_2)_3-$	**6a**	66
2	$-(CH_2)_4-$	**6b**	83
3	$-(CH_2)_5-$	**6c**	69
4	$-(CH_2)_6-$	**6d**	87
5	$-CH_2-O-(CH_2)_2-O-CH_2-$	**6e**	93

Similarly, a combination of 1,3,5-triethynylbenzene (**7**) and penta-*O*-propargyl-β-D-glucose (**9**)[28] with a minimal excess of azidosugar **2** gave trivalent and pentavalent galacto-clusters **8** and **10** in 74 and 61% yields, respectively (Scheme 2).

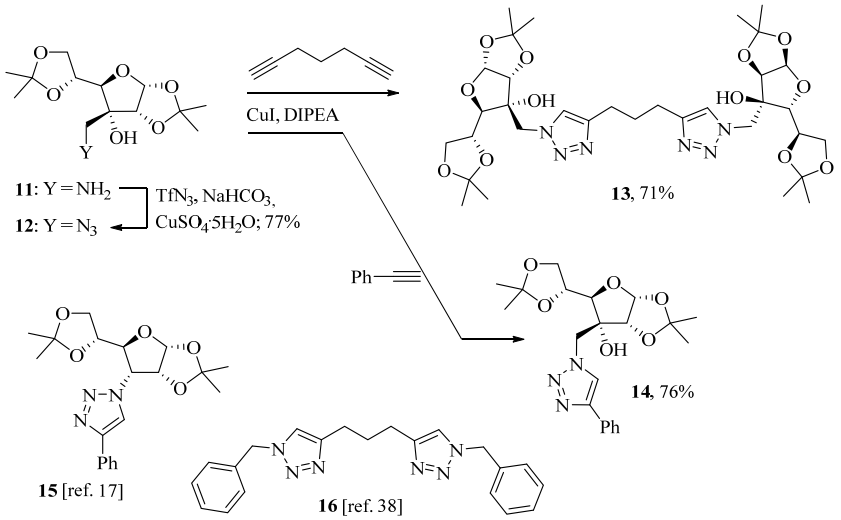


Scheme 2. Synthesis of glycoclusters containing three (**8**) and five (**10**) 3-deoxy-3-triazolyl-galactofuranose residues.

With di-, tri- and pentasaccharides in hand we were intrigued to determine their residual copper content. From a practical point of view it is much easier to analyze and if necessary re-purify sufficiently lipophilic compounds **6a-h**, **8** and **10** than their fully deprotected and water-soluble counterparts. There have been several reports dealing with specific removal of copper from *click* products. These include treatment of peptide-containing dendrimers with Na_2S,[29] multiple extractions with solutions of EDTA,[30] dialysis against EDTA solution[31] and the use of copper chelating resins.[32] Various flow techniques for elimination of copper traces have been developed as well.[30,33] Careful control of copper content is necessitated by aspects such as limits

on heavy metals in pharmaceutically active compounds,[30] product stability[34] and inhibition of enzymes by copper ions.[35,36] Nevertheless, there are not many examples where the residual copper has been analyzed in the carbohydrate-triazole conjugates which were obtained via CuAAC reaction. In a few cases some of the aforementioned methods (e.g. EDTA wash) were used, albeit without any numeric data of the residual copper content in the final products.[37]

Analysis of our *clicked* products **6a-h**, **8** and **10** revealed that after a simple extractive wash with brine the copper content in the solid material ranged from 20000 to 40000 ppm. Consecutive extractive EDTA washes diminished the copper content to levels ≤100 ppm in most cases. Only precipitation with Na_2S followed by filtration through a silica gel pad and crystallization provided substances with copper content ≤5 ppm. In individual cases satisfactory results were achieved solely with the EDTA wash (entry 1, Table 2). In order to identify the main copper chelating structural motif, we prepared model compounds **13** and **14** and known substances **15** and **16** (Scheme 3).[17,38] Compounds **13** (dimer) and **14** (monomer) contain an extra HO-group per monosaccharide unit. They were prepared *via* CuAAC reaction on azide **12**. The latter was obtained in the diazotransfer reaction using amine **11** and trifluoromethanesulfonyl azide in the presence of catalytic amount of copper(II) sulfate.[24,39] The molecular structure of disaccharide **13** was unambiguously established by its single crystal X-ray analysis (Figure 2).



Scheme 3. Synthesis of copper chelating model compounds.

A comparison of residual copper content in two representative title compounds (**6a** and **8**) and model compounds is shown in Table 2. Additional chelating groups (e.g. HO-group) enhance the residual copper content (compound **14** versus **15**). One can also observe that the dimeric structural motif characterized by the bis-triazolyl linker is responsible for enchanced copper chelating properties (compound **13** versus **14**; entries 3 and 4, Table 2). This effect is even more pronounced when the carbohydrate residues are replaced by more lipophilic benzyl groups. It was not possible to diminish the residual copper content in compound **16** below 70 ppm, most probably due to the formation of micelle-like structures.

Table 2. Copper content in the carbohydrate-1,2,3-triazole conjugates depending on the purification procedure

Entry	Compound	Copper content, ppm				
		Purification: subsequent procedures 1→2→3→4→5				
		Extractive wash with brine (1)	Extractive wash with EDTA (2)	Precipitation with Na_2S (3)	Silica gel column chromato-graphy (4)	Crystallization from ethanol (5)
1	**6a**	39500	6	6	4	4
2	**8**	10000	291	22	10	7
3	**13**	47000	215	36	16	14
4	**14**	1000	77	22	7	2
5	**15**	2300	12	11	3	3
6	**16**	49000	2000	930	80	77

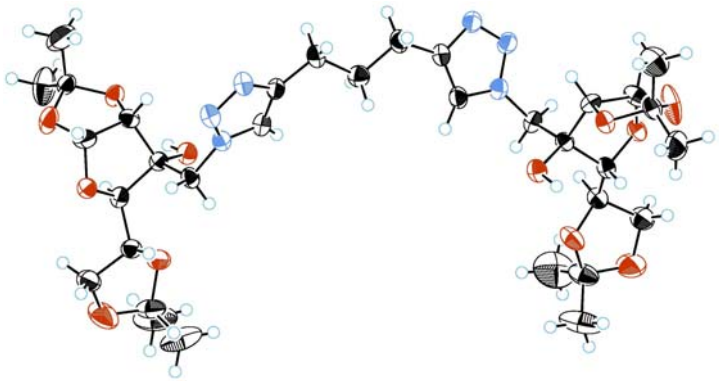
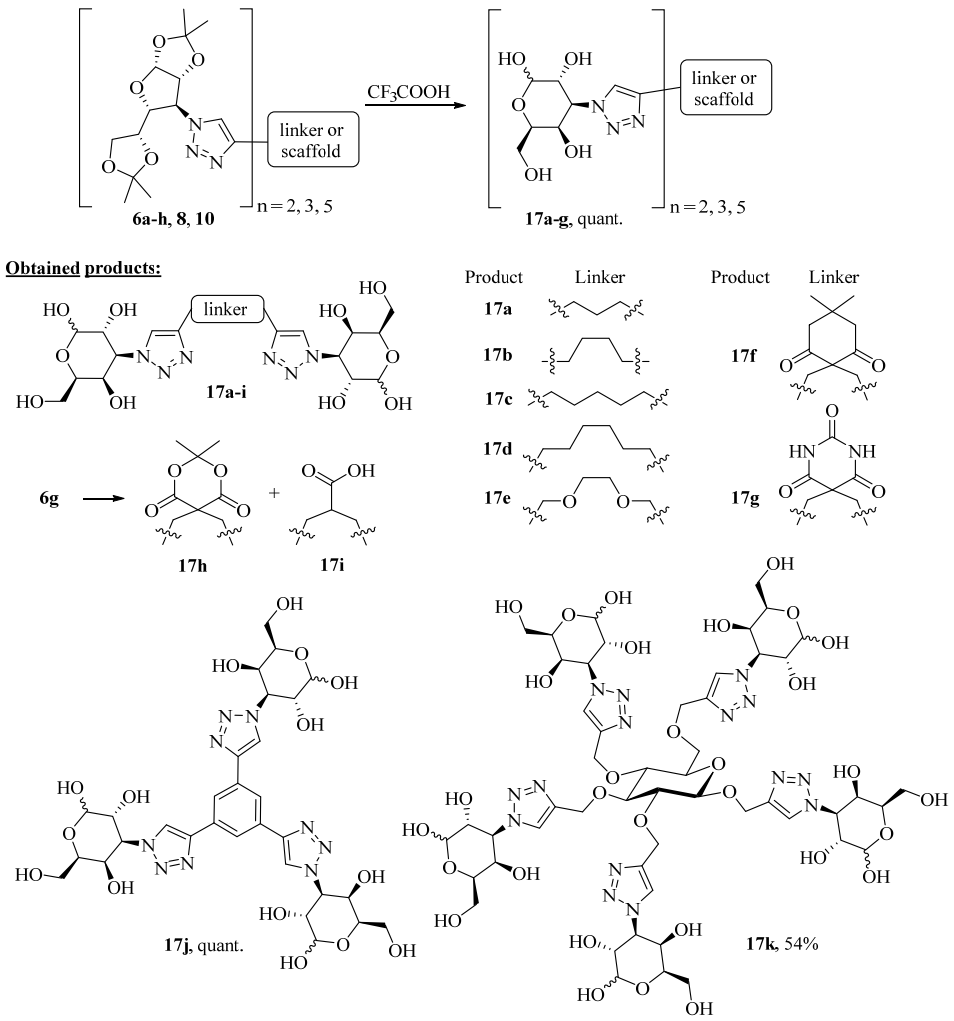


Figure 2. ORTEP representation of compound **13**.

Purified intermediates **6a-h**, **8** and **10** (copper content <10 ppm) were submitted to acidic hydrolysis of their isopropylidene protecting groups. Several hydrolytic methods were tried: HCl/MeOH, H_2O/AcOH/110 ^oC, CF_3COOH/H_2O. The latter, employing an aqueous solution of trifluoroacetic acid at ambient temperature, gave the cleanest transformation and produced water-soluble target compounds in quantitative yields (Scheme 4). Simple evaporation of the acidic solution under reduced pressure followed by lyophilization from water provided products **17a-k** as colorless amorphous powders. Deprotection of **6g** gave a mixture of **17h** and **17i**, with the latter arising from the post-hydrolytic decarboxylation of the Meldrum's acid moiety. To the best of our knowledge, this is the first time where galactopyranose-1,2,3-triazole conjugates have been prepared from the corresponding isopropylidene-protected galactofuranoses.

As expected, deprotection induced furanose-pyranose tautomerism and compounds **17a-k** were obtained as a mixture of their α- and β-pyranose forms. This was demonstrated by 2D HMBC spectra that clearly revealed the correlations H-C(5)↔C(1) and H-C(1)↔C(5). Due to the extended linker each sugar residue gave an "independent" NMR spectrum and it was impossible to establish the ratio between the α,α'-, α,β- and β,β'-forms of disaccharides **17a-i**. Instead, each structural motif (3-deoxy-3-triazolyl-α- or β-D-galactopyranose) was characterized separately and the virtual ratio between all α-pyranose and all β-pyranose forms is given (see Experimental Section). ^{1}H- and ^{13}C-NMR analysis of **17a** is given in Figure 3. It represents the spectral properties of all galactohybrids **17a-k** as the linkers apparently do not significantly influence the conformations of the galactopyranose moieties. The α-anomer is characterized by $^{3}J_{H1\text{-}H2}$ 3.6 Hz, but the β-anomer reveals $^{3}J_{H1\text{-}H2}$ 7.7 Hz. The axial position of H-C(2) and H-C(3) in both anomeric forms is confirmed by $^{3}J_{H2\text{-}H3}$ ~ 11 Hz. Finally, the axial position of HO-C(4) and the equatorial position of H-C(4) in both anomers was proved by $^{3}J_{H4\text{-}H5}$ ~ 0 Hz and $^{3}J_{H3\text{-}H4}$ ~ 2 Hz.



Scheme 4. Synthesis of water-soluble *galacto*-conjugates **17a-k**.

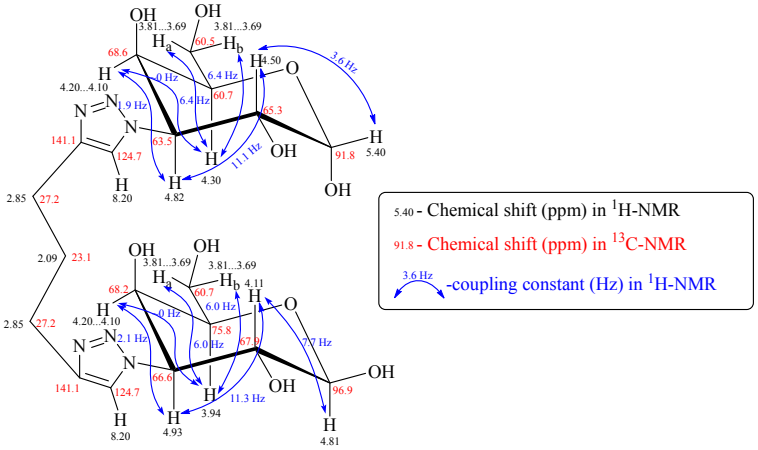


Figure 3. ^{1}H (300 MHz, D_2O) and ^{13}C-NMR (75.5 MHz, D_2O) analysis of disaccharide **17a**.

The binding affinities of galectin-1 and -3 for selected compounds **17** were estimated by a fluorescent anisotropy assay.[40,41,42] Compounds depicted in Table 3 were tested up to 5 mM concentrations and gave K_d values in the range of 1–4 mM, except trisaccharide **17j**. The latter exhibited enhanced galectin-3 binding with K_d 50 μM and 160-fold preference for galectin-3. Galectins bind galactose with affinities of 5–20 mM.[43] The observed K_d value of galectin-3 for **17j** is about 100-fold better than that of free galactose and can be regarded as remarkable for a molecule that does not possess a natural or pseudo-natural disaccharide structural motif.

Table 3. K_d values of galectin-1 and -3 for compounds **17** as measured by a fluorescence anisotropy assay

Compound	Galectin-1 K_d (mM)	Galectin-3 K_d (mM)
17b	1.6	4.2
17f	2.4	1.3
17g	2.4	1.3
17i	2.7	1.9
17j	8.3	**0.05**
17k	3.6	2.6

Conclusions

We have developed a straightforward synthesis of novel divalent and multivalent galactopyranose hybrids. It uses the CuAAC reaction of 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranose to assemble the molecular skeletons of the target compounds. Acidic hydrolysis of the acetonides induces formation of the final products in their

pyranose form. We have also demonstrated that the 1,2,3-triazole-linked sugars chelate copper. In this context careful control of the residual copper content is recommended if one deals with carbohydrate-1,2,3-triazole conjugates. Galectin-1 and galectin-3 exhibited interesting levels of binding affinities for the title compounds. Nearly identical binding affinities were found for bivalent galactohybrids bearing various linkers and pentavalent galactohybrid. It is interesting to note that the relatively simple trivalent molecule **17j** showed 100-fold better binding to galectin-3 than the parent galactopyranose. The fact that it differs from other investigated molecules with the 4-aryl-1*H*-1,2,3-triazol-moiety warrants further study.

Experimental Section

General. Solvents for the reactions were freshly distilled prior to use. Commercially available alkynes and other regents were used as received. CuI used in *click* reactions was purchased from *Acros Organics* and used as received. All reactions were carried out without any special precautions under an atmosphere of air if not noted otherwise. Isolated yields refer to chromatographically homogeneous substances. All reactions were followed by TLC on an *E. Merck Kieselgel 60 F_{254}*, with detection by UV light and thermal visualization. Column chromatography was performed on silica gel (60 Å, 40-63 μm, ROCC). Melting points were recorded with a *Fisher Digital Melting Point Analyzer Model 355* apparatus and are uncorrected. IR spectra were recorded as thin films on KBr plates or in KBr with a *FT-IR Perkin Elmer Spectrum BX* (4000–450 cm^{-1}). Optical rotation was measured at 25 °C on a *Anton Paar MCP 500* polarimeter (1 dm cell) using a sodium lamp as the light source (589 nm). ^{1}H and ^{13}C NMR spectra were recorded on a *Bruker* 300 MHz, *Varian* 600 MHz and *Varian* 400 MHz, in $CDCl_3$, D_2O or DMSO-d_6. Chemical shift (δ) values are reported in ppm. The residual solvent peaks were used as internal reference ($CDCl_3$: 7.26 ppm for ^{1}H nuclei, 77.0 ppm for ^{13}C nuclei; DMSO-d_6: 2.50 ppm for ^{1}H nuclei, 39.5 ppm for ^{13}C nuclei; D_2O: 4.79 ppm for ^{1}H nuclei)), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet); *J* in Hz. HRMS (ESI) spectra were performed using a *Q-TOF Micromass* and elemental analyses were obtained on a *Carlo-Erba Instruments EA1108 Elemental analyser*.

General procedure I for the synthesis of isopropylidene-protected disaccharides 6a-h and 13:

1,3-bis(1-((3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)propane (6a). 1,6-Heptadiyne (173 μl, 1.51 mmol, 1 equiv.) was added to a mixture of azidomonosaccharide **2** (0.90 g, 3.17 mmol, 2.1 equiv.), CuI (57 mg, 0.30 mmol, 0.2 equiv.) and DIPEA (105 μl, 0.60 mmol, 0.4 equiv.) in THF (10 mL). The resulting reaction mixture was stirred in a resealable pressure tube at 70 °C for 1–4 h (TLC control). The solvent was evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2 (DCM) (15 mL). The DCM solution was washed with EDTA solution (5 × 3 mL), brine (2 × 5 mL), dried over

Na_2SO_4 and evaporated under reduced pressure. The solid residue was dissolved in THF (5 mL) and a solution of Na_2S (25 mg) in water (1 mL) was added. The resulting suspension was filtered through a silica gel pad that was suspended in THF. The filtrate was evaporated under reduced pressure and the resulting solid was chromatographically purified by flash chromatography (silica; DCM/MeOH 93/7; R_f 0.49), followed by crystallization from EtOH or BuOH. Disaccharide **6a** (0.66 g, 66%) was obtained as a colorless solid. 0.66 g (66%); mp 212-213 °C (EtOH); $[\alpha]_D^{25}$= 9 (c=3.7, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1})**:** 3130, 2990, 2945, 1460, 1380, 1250, 1215, 1160, 1110, 1070, 1025; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 7.46 (s, 2H, H-C(5')), 6.03 (d, 2H, ^3J 4.0 Hz, H-C(1)), 4.99 (dd, 2H, ^3J 4.0 Hz, ^3J 2.3 Hz, H-C(2)), 4.93 (dd, 2H, ^3J 6.8 Hz, ^3J 2.3 Hz, H-C(3)), 4.39 (dd, 2H, ^3J 6.8 Hz, ^3J 4.3 Hz, H-C(4)), 4.29 (dt, 2H, ^3J 6.8 Hz, ^3J 4.3 Hz, H-C(5)), 4.07 (dd, 2H, ^2J 8.3 Hz, ^3J 6.8 Hz, H_A-C(6)), 3.93 (dd, 2H, ^2J 8.3 Hz, ^3J 6.8 Hz, H_B-C(6)), 2.85...2.73 (m, 4H, H-C(a,c)), 2.14...2.00 (m, 2H, H-C(b)), 1.65, 1.44, 1.39, 1.37 (4s, 24H, $(H_3C)_2$C-O-C(1,2,5,6)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 147.8, 121.4, 114.9, 110.1, 104.9, 86.1, 81.8, 73.8, 65.4, 65.2, 28.8, 27.7, 27.0, 26.2, 25.2, 24.8; Anal. calcd for $C_{31}H_{46}N_6O_{10}$ (662.73): C 56.18, H 7.00, N 12.68; Found C 55.92, H 6.98, N 12.45.

1,4-bis(1-((3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)butane (6b). Compound **6b** was obtained according to the general procedure I: **2** (463 mg, 1.62 mmol, 2.2 equiv.), CuI (29 mg, 0.15 mmol, 0.2 equiv.), DIPEA (52 µl, 0.30 mmol, 0.4 equiv.), 1,7-octadiyne (102 µl, 0.77 mmol, 1 equiv.), THF (10 ml). Yield 414 mg, 83%. Colorless solid, R_f 0.46 (DCM/MeOH 93/7); mp 217-218 °C (*n*-BuOH); $[\alpha]_D^{25}$= 9 (c=1.1, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1})**:** 3110, 3065, 2985, 2945, 2860, 1460, 1375, 1220, 1165, 1070, 1030; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 7.39 (s, 2H, H-C(5')), 6.03 (d, 2H, ^3J 4.0 Hz, H-C(1)), 4.99 (dd, 2H, ^3J 4.0 Hz, ^3J 2.3 Hz, H-C(2)), 4.91 (dd, 2H, ^3J 6.6 Hz, ^3J 2.3 Hz, H-C(3)), 4.39 (dd, 2H, ^3J 6.6 Hz, ^3J 4.3 Hz, H-C(4)), 4.30 (dt, 2H, ^3J 6.8 Hz, ^3J 4.3 Hz, H-C(5)), 4.07 (dd, 2H, ^2J 8.5 Hz, ^3J 6.8 Hz, H_A-C(6)), 3.92 (dd, 2H, ^2J 8.5 Hz, ^3J 6.8 Hz, H_B-C(6)), 2.83...2.68 (m, 4H, H-C(a,d)), 1.80...1.71 (m, 4H, H-C(b,c)), 1.65, 1.44, 1.39, 1.37 (4s, 24H, $(H_3C)_2$C-O-C(1,2,5,6)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 148.3, 121.1, 114.9, 110.1, 104.9, 86.2, 81.9, 73.9, 65.4, 65.2, 28.8, 27.7, 27.1, 26.2, 25.3, 25.2; Anal. calcd for $C_{32}H_{48}N_6O_{10}$ (676.76): C 56.79, H 7.15, N 12.42; Found C 56.94, H 7.23, N 12.22.

1,5-bis(1-((3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)pentane (6c). Compound **6c** was obtained according to the general procedure I: **2** (255 mg, 0.89 mmol, 2.1 equiv.), CuI (16 mg, 0.08 mmol, 0.2 equiv.), DIPEA (30 µl, 0.17 mmol, 0.4 equiv.), 1,8-nonadiyne (64 µl, 0.43 mmol, 1 equiv.), THF (4 ml). Yield 207 mg, 69%. Colorless solid, R_f 0.49 (DCM/MeOH 93/7); mp 199-200 °C (*n*-BuOH); $[\alpha]_D^{25}$= 7 (c=3.1, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 3135, 2990, 2940, 2860, 1460, 1375, 1250, 1220, 1160, 1105, 1070, 1025; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 7.39 (s, 2H, H-C(5')), 6.04 (d, 2H, ^3J 4.0 Hz, H-C(1)), 5.00 (dd, 2H, ^3J 4.0 Hz, ^3J 2.3 Hz, H-C(2)), 4.92 (dd, 2H, ^3J 6.6 Hz, ^3J 2.3 Hz, H-C(3)), 4.40 (dd, 2H, ^3J 6.6 Hz, ^3J 4.3 Hz, H-C(4)), 4.30 (dt, 2H, ^3J 6.6 Hz, ^3J 4.3 Hz, H-C(5)), 4.07 (dd, 2H, ^2J 8.5 Hz, ^3J 6.6 Hz, H_A-C(6)), 3.92 (dd, 2H, ^2J 8.5 Hz, ^3J 6.6 Hz, H_B-C(6)), 2.73 (t, 4H, ^3J

7.7 Hz, H-C(a,e)), 1.73 (qn, 4H, ^3J 7.7 Hz, H-C(b,d)), 1.52...1.43 (m, 2H, H-C(c)), 1.66, 1.45, 1.40, 1.37 (4s, 24H, $(H_3C)_2C$-O-C(1,2,5,6)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_H 148.5, 121.1, 114.9, 110.0, 104.9, 86.1, 81.9, 73.8, 65.4, 65.1, 28.9, 28.6, 27.7, 27.0, 26.2, 25.3, 25.2; Anal. calcd for $C_{33}H_{50}N_6O_{10}\cdot 0.5H_2O$ (699.79): C 56.64, H 7.35, N 12.01; Found C 56.82, H 7.32, N 11.85.

1,6-bis(1-((3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)hexane (6d). Compound **6d** was obtained according to the general procedure I: **2** (300 mg, 1.05 mmol, 2.2 equiv.), CuI (18 mg, 0.09 mmol, 0.2 equiv.), DIPEA (33 µl, 0.19 mmol, 0.4 equiv.), 1,9-decadiyne (80 µl, 0.49 mmol, 1 equiv.), THF (4 ml). Yield 289 mg, 87%. Colorless solid, R_f 0.50 (DCM/MeOH 93/7); mp 158-159 °C (EtOH); $[\alpha]_D^{25}$ = 8 (c=1.5, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 3130, 3070, 2990, 2935, 2860, 1455, 1375, 1250, 1220, 1160, 1105, 1070, 1025; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 7.37 (s, 2H, H-C(5')), 6.03 (d, 2H, ^3J 4.0 Hz, H-C(1)), 4.99 (dd, 2H, ^3J 4.0 Hz, ^3J 2.3 Hz, H-C(2)), 4.91 (dd, 2H, ^3J 6.8 Hz, ^3J 2.3 Hz, H-C(3)), 4.40 (dd, 2H, ^3J 6.8 Hz, ^3J 4.5 Hz, H-C(4)), 4.30 (dt, 2H, ^3J 6.8 Hz, ^3J 4.5 Hz, H-C(5)), 4.07 (dd, 2H, ^2J 8.5 Hz, ^3J 6.8 Hz, H_A-C(6)), 3.92 (dd, 2H, ^2J 8.5 Hz, ^3J 6.8 Hz, H_B-C(6)), 2.71 (t, 4H, ^3J 7.5 Hz, H-C(a,f)), 1.68 (qn, 4H, ^3J 7.5 Hz, H-C(b,e)), 1.44...1.37 (m, 4H, H-C(c,d)), 1.65, 1.44, 1.39, 1.37 (4s, 24H, $(H_3C)_2C$-O-C(1,2,5,6)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 148.7, 121.0, 114.9, 110.1, 104.9, 86.2, 81.9, 73.9, 65.4, 65.1, 29.2, 28.8, 27.7, 27.1, 26.2, 25.5, 25.2; Anal. calcd for $C_{34}H_{52}N_6O_{10}$ (704.81): C 57.94, H 7.44, N 11.92; Found C 57.97, H 7.51, N 11.64.

1,2-bis((1-((3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methoxy)ethane (6e). Compound **6e** was obtained according to the general procedure I: **2** (687 mg, 2.41 mmol, 2.1 equiv.), CuI (45 mg, 0.24 mmol, 0.2 equiv.), DIPEA (80 µl, 0.46 mmol, 0.4 equiv.), bis(propargyloxy)ethane (158 mg, 1.14 mmol, 1 equiv.), THF (5 ml). Yield 750 mg, 93%. Colorless solid, R_f 0.40 (DCM/MeOH 93/7); mp >149 °C (decomp.); $[\alpha]_D^{25}$ = 10 (c=2.1, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 2990, 2940, 1460, 1375, 1220, 1160, 1070; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 7.70 (s, 2H, H-C(5')), 6.04 (d, 2H, ^3J 4.0 Hz, H-C(1)), 4.99 (dd, 2H, ^3J 4.0 Hz, ^3J 2.4 Hz, H-C(2)), 4.96 (dd, 2H, ^3J 6.6 Hz, ^3J 2.4 Hz, H-C(3)), 4.69 (s, 4H, H-C(a,d)), 4.38 (dd, 2H, ^3J 6.6 Hz, ^3J 4.3 Hz, H-C(4)), 4.29 (dt, 2H, ^3J 6.8 Hz, ^3J 4.3 Hz, H-C(5)), 4.07 (dd, 2H, ^2J 8.5 Hz, ^3J 6.8 Hz, H_A-C(6)), 3.92 (dd, 2H, ^2J 8.5 Hz, ^3J 6.8 Hz, H_B-C(6)), 3.73 (s, 4H, H-C(b,c)), 1.65, 1.43, 1.39, 1.36 (4s, 24H, $(H_3C)_2C$-O-C(1,2,5,6)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 145.5, 123.0, 115.0, 110.1, 104.9, 86.1, 81.9, 73.8, 69.9, 65.5, 65.3, 64.6, 27.7, 27.0, 26.2, 25.2; Anal. calcd for $C_{32}H_{48}N_6O_{12}$ (708.76): C 54.23, H 6.83, N 11.86; Found C 53.90, H 6.77, N 11.70.

2,2-bis((1-((3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methyl)-5,5-dimethylcyclohexane-1,3-dione (6f). Compound **6f** was obtained according to the general procedure I: **2** (700 mg, 2.45 mmol, 2.1 equiv.), CuI (46 mg, 0.24 mmol, 0.2 equiv.), DIPEA (80 µl, 0.46 mmol, 0.4 equiv.), 2,2-dipropargyl dimedone (**4a**) (250 mg, 1.16 mmol, 1 equiv.), THF (11 ml). Yield 800 mg, 89%. Colorless solid, R_f 0.49 (DCM/MeOH 93/7); mp 124-125 °C (*n*-BuOH); $[\alpha]_D^{25}$ = 16 (c=3.5, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 3140, 2990, 2940,

1720, 1695, 1375, 1270, 1165, 1070; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 7.80 (s, 2H, H-C(5')), 6.01 (d, 2H, ^3J 4.0 Hz, H-C(1)), 4.97 (dd, 2H, ^3J 4.0 Hz, ^3J 2.3 Hz, H-C(2)), 4.91 (dd, 2H, ^3J 6.6 Hz, ^3J 2.3 Hz, H-C(3)), 4.33 (dd, 2H, ^3J 6.6 Hz, ^3J 4.3 Hz, H-C(4)), 4.27 (dt, 2H, ^3J 6.6 Hz, ^3J 4.3 Hz, H-C(5)), 4.06 (dd, 2H, ^2J 8.5 Hz, ^3J 6.6 Hz, H_A-C(6)), 3.88 (dd, 2H, ^2J 8.5 Hz, ^3J 6.6 Hz, H_B-C(6)), 3.21, 3.15 (2d, AB syst., 4H, ^2J 14.9 Hz, H-C(a,b)), 2.76 (s, 4H, H-C(a,d)), 1.64, 1.45, 1.39, 1.36 (4s, 24H, $(H_3C)_2$C-O-C(1,2,5,6)), 0.95 (s, 6H, $(H_3C)_2$C(e)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 207.2, 142.7, 124.8, 115.0, 110.1, 104.9, 86.1, 81.9, 73.9, 68.9, 65.4, 65.2, 51.7, 30.9, 28.7, 28.6, 27.7, 27.1, 26.2, 25.2; Anal. calcd for $C_{38}H_{54}N_6O_{12}$ (786.87): C 58.00, H 6.92, N 10.68; Found C 58.06, H 7.07, N 10.33.

5,5-bis((1-((3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (6g). Compound **6g** was obtained according to the general procedure I: **2** (1.00 g, 3.50 mmol, 2.1 equiv.), CuI (64 mg, 0.34 mmol, 0.2 equiv.), DIPEA (120 µl, 0.69 mmol, 0.4 equiv.), 5,5-dipropargyl Meldrum's acid (**4b**) (370 mg, 1.68 mmol, 1 equiv.), THF (15 ml). Yield 1.00 g, 77%. Colorless solid, R_f 0.50 (DCM/MeOH 93/7); mp >110 °C (decomp.); $[\alpha]_D^{25}$= 10 (c=4.2, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 3140, 2990, 2940, 1740, 1440, 1375, 1270, 1215, 1160, 1105, 1070; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 7.51 (s, 2H, H-C(5')), 5.99 (d, 2H, ^3J 3.6 Hz, H-C(1)), 4.95...4.88 (m, 4H, H-C(2), H-C(3)), 4.33 (dd, 2H, ^3J 6.8 Hz, ^3J 4.1 Hz, H-C(4)), 4.24 (dt, 2H, ^3J 6.8 Hz, ^3J 4.1 Hz, H-C(5)), 4.05, 3.93 (2dd, AB syst., 4H, ^2J 8.3 Hz, ^3J 6.8 Hz, H_A-C(6), H_B-C(6)), 3.54 (s, 4H, H-C(a,b)), 1.44 (s, 6H, H_3C-C(c)), 1.64, 1.44, 1.38, 1.35 (4 s, 24H, $(H_3C)_2$C-O-C(1,2,5,6)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 167.5, 141.5, 123.3, 115.1, 110.1, 106.9, 104.8, 86.1, 81.6, 73.5, 65.3, 65.2, 54.0, 34.0, 28.9, 27.7, 27.1, 26.2, 25.1; Anal. calcd for $C_{36}H_{50}N_6O_{14}$ (790.81): C 54.68, H 6.37, N 10.63; Found C 54.89, H 6.44, N 10.41.

5,5-bis((1-((3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (6h). Compound **6h** was obtained according to the general procedure I: **2** (775 mg, 2.72 mmol, 2.1 equiv.), CuI (49 mg, 0.26 mmol, 0.2 equiv.), DIPEA (90 µl, 0.84 mmol, 0.4 equiv.), 5,5-dipropargyl barbituric acid (**5**) (264 mg, 1.29 mmol, 1 equiv.), THF (6 ml). Yield 940 mg, 93%. Colorless solid, R_f 0.33 (DCM/MeOH 93/7); mp >160 °C (decomp.); $[\alpha]_D^{25}$= 11 (c=1.1, $CHCl_3$)**;** IR (KBr) (ν_{max}, cm^{-1}): 3545 (br.s.), 3235, 3130, 2990, 2940, 1735, 1420, 1375, 1250, 1220, 1160, 1070, 1030; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 8.75 (s, 2H, H-N(c)), 7.55 (s, 2H, H-C(5')), 5.98 (d, 2H, ^3J 4.0 Hz, H-C(1)), 4.97 (dd, 2H, ^3J 4.0 Hz, ^3J 2.1 Hz, H-C(2)), 4.92 (dd, 2H, ^3J 6.2 Hz, ^3J 2.1 Hz, H-C(3)), 4.33...4.22 (m, 4H, H-C(4), H-C(5)), 4.05 (dd, 2H, ^2J 8.5 Hz, ^3J 6.4 Hz, H_A-C(6)), 3.88 (dd, 2H, ^2J 8.5 Hz, ^3J 6.0 Hz, H_B-C(6)), 3.51 (s, 4H, ^2J 14.9 Hz, H-C(a,d)), 1.62, 1.43, 1.37, 1.36 (4s, 24H, $(H_3C)_2$C-O-C(1,2,5,6)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 171.5, 148.2, 141.6, 122.9, 115.0, 110.2, 104.9, 85.9, 82.1, 73.8, 65.4, 65.2, 55.0, 33.5, 27.7, 27.0, 26.2, 25.2; Anal. calcd for $C_{34}H_{46}N_8O_{13}\cdot 0.5H_2O$ (783.78): C 52.10, H 6.04, N 14.30; Found C 52.16, H 5.88, N 14.12.

1,3,5-tris((1-((3*S*)-3-Deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)benzene (8). Compound **8** was obtained analogically to the general procedure I using 3.3 equivalents of azidomonosaccharide: **2** (942 mg, 3.30 mmol, 3.3 equiv.), CuI (57 mg,

0.30 mmol, 0.3 equiv.), DIPEA (107 µl, 0.61 mmol, 0.6 equiv.), 1,3,5-triethynylbenzene (**7**) (150 mg, 1.00 mmol, 1 equiv.), THF (3 ml). Yield 740 mg, 74%. Colorless solid, R_f 0.56 (DCM/MeOH 93/7); mp >135 °C (decomp.); $[\alpha]_D^{25}$= 16 (c=3.8, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 3135, 2990, 2940, 1620, 1460, 1375, 1220, 1160, 1070, 1040; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 8.29 (s, 3H, H-C(a,b,c)), 8.06 (s, 3H, H-C(5')), 6.10 (d, 3H, ^3J 4.0 Hz, H-C(1)), 5.11 (dd, 3H, ^3J 4.0 Hz, ^3J 2.4 Hz, H-C(2)), 5.06 (dd, 3H, ^3J 6.6 Hz, ^3J 2.4 Hz, H-C(3)), 4.46 (dd, 3H, ^3J 6.6 Hz, ^3J 4.2 Hz, H-C(4)), 4.35 (dt, 3H, ^3J 6.6 Hz, ^3J 4.2 Hz, H-C(5)), 4.13, 3.98 (2dd, AB syst., 6H, ^2J 8.5 Hz, ^3J 6.6 Hz, H_A-C(6), H_B-C(6)), 1.67, 1.47, 1.42, 1.39 (4s, 36H, $(H_3C)_2$C-O-C(1,2,5,6)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 147.3, 131.4, 122.7, 120.6, 115.1, 110.2, 104.9, 86.1, 81.9, 73.7, 65.6, 65.4, 27.7, 27.1, 26.2, 25.2; Anal. calcd for $C_{48}H_{63}N_9O_{15}$ (1006.07): C 57.30, H 6.31, N 12.53; Found C 56.91, H 6.19, N 12.32.

Penta-*O*-((1-((3*S*)-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methyl)-β-D-glucose (10). Compound **10** was obtained analogically to the general procedure I using 5.5 equivalents of azidomonosaccharide: **2** (874 mg, 3.06 mmol, 5.5 equiv.), CuI (53 mg, 0.28 mmol, 0.5 equiv.), DIPEA (97 µl, 0.56 mmol, 1 equiv.), penta-*O*-propargyl-β-D-glucose (**9**) (206 mg, 0.56 mmol, 1 equiv.), THF (7 ml). Yield 606 mg, 61%. Colorless solid, R_f 0.37 (DCM/MeOH 93/7); mp >190 °C (decomp.); $[\alpha]_D^{25}$= 11 (c=2.5, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 3135, 2990, 2940, 1375, 1250, 1220, 1160, 1070; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 8.22 (s, 1H), 8.20 (s, 1H), 8.07 (s, 1H), 8.01 (s, 1H), 7.82 (s, 1H), 6.12 (d, 1H, ^3J 3.8), 6.10 (d, 1H, ^3J 3.2), 6.09 (d, 1H, ^3J 3.2), 6.08 (d, 1H, ^3J 3.9), 6.05 (d, 1H, ^3J 3.6), 5.06...4.90 (m, 15H), 4.90...4.67 (m, 5H), 4.45 (d, 1H, ^3J 7.5), 4.40...4.26 (m, 10H), 4.15...4.02 (m, 5H), 3.94...3.79 (m, 7H), 3.60...3.45 (m, 2H), 3.43...3.31 (m, 2H), 1.65 (s, 15H), 1.42 (s, 12H), 1.45...1.32 (m, 33H); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 145.1, 145.0 (2C), 144.9, 144.8, 124.2, 123.9, 123.4, 123.3 (2C), 115.0 (2C), 114.9 (2C), 114.8, 110.1 (5C), 105.2 (2C), 105.1, 105.0 (2C), 102.4, 86.1 (2C), 86.0 (3C), 83.8, 82.9, 82.8, 82.5 (2C), 82.2, 81.7, 77.2, 74.5, 74.4, 74.3, 74.2 (2C), 74.0, 69.1, 66.2, 65.6, 65.5 (2C), 65.4 (6C), 65.3 (3C), 64.7, 62.8, 27.7 (2C), 27.6 (3C), 27.1, 27.0 (4C), 26.3 (4C), 26.2, 25.2 (5C); Anal. calcd for $C_{81}H_{117}N_{15}O_{31}$ (1796.88): C 54.14, H 6.56, N 11.69; Found C 53.75, H 6.47, N 11.48.

(3*R*)-3-Azidomethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (12). Tf_2O (9 mL, 0.05 mol, 3 equiv.) was added dropwise at 0 °C to a stirred biphasic mixture consisting of NaN_3 (6.7 g, 0.1 mol, 6 equiv.) solution in water (25 mL) and DCM (25 mL). The resulting emulsion was stirred for 2 h at 0 °C and the layers were separated. The aqueous layer was extracted with DCM (2×10 mL). The combined organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (2×5 mL) and used as such. The latter solution was added to a precooled (0 °C) mixture consisting of amine **11** (5.0 g, 0.02 mol, 1 equiv.), MeOH (110 mL), $CuSO_4 \cdot 5H_2O$ (0.22g, 0.88 mmol, 5 mol %), $NaHCO_3$ (1.5 g, 0.015 mol, 0.87 equiv.) and water (40 mL). The resulting reaction mixture was allowed to reach ambient temperature and stirred for 18 h. Then the volatile organic solvents were evaporated under reduced pressure, water (100 mL) was added and the resulting aqueous layer was extracted with EtOAc (4×50 ml). The combined organic layer was consecutively washed with a saturated aqueous solution of $(NH_4)_2SO_4$ (3×15 mL), a 10%

aqueous solution of NaOH (5×15 mL), and brine (15 mL), then dried over Na_2SO_4, filtered and evaporated under reduced pressure. Crystallization of the crude material from hexanes/EtOAc provided pure azide **12** (3.9 g, 77%) as a colorless solid, R_f 0.61 (Tol/EtOAc 2/1); mp 121-122 °C (hexanes/EtOAc); $[\alpha]_D^{25}$ = 216 (c=0.4, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 3465, 2995, 2100, 1080, 1015; ^{1}H-NMR: ($CDCl_3$, 300 MHz)**:** δ_H 5.74 (d, 1H, *J* 3.9 Hz, H-C(1)), 4.57 (d, 1H, *J* 3.9 Hz, H-C(2)), 4.14-4.03 (m, 2H, H-C(6)), 3.95-3.90 (m, 1H, H-C(5)), 3.83 (d, 1H, AB syst., *J*= 13.0 Hz, Ha-C(3')), 3.80 (d, 1H, *J* 8.3 Hz, H-C(4)), 3.07 (d, 1H, AB syst., *J* 13.0 Hz, Hb-C(3')), 2.96 (br.s., 1H, HO-C(3)), 1.60, 1.47, 1.38, 1.37 (4 s, 12H, $(H_3C)_2$C-O-C(1,2,5,6)); ^{13}C-NMR: ($CDCl_3$, 75.5 MHz): δ_C 112.9, 110.0, 103.6, 81.4, 80.3, 80.2, 73.0, 67.9, 51.9, 26.7, 26.5, 26.4, 25.2; HRMS (ESI): calculated for [$C_{13}H_{21}N_3O_6$ + H^+] 316.1503; Found 316.1526.

3,3'-((Propane-1,3-diylbis(1*H*-1,2,3-triazole-4,1-diyl))bis(methylene))bis((3*R*)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose) (13). Compound **13** was obtained according to the general procedure I: **2** (1.00 g, 3.17 mmol, 2.1 equiv.), CuI (57 mg, 0.30 mmol, 0.2 equiv.), DIPEA (105 µl, 0.60 mmol, 0.4 equiv.), 1,6-heptadiyne (173 µl, 1.51 mmol, 1 equiv.), THF (10 ml). Yield 850 mg, 71%. Colorless solid, R_f 0.42 (DCM/MeOH 93/7); mp 207-208 °C (tetrahydrate from MeOH), azeotropic drying with toluene followed by drying at 100 °C for 72 h provided anhydrous form of **13**; $[\alpha]_D^{25}$ = 26 (c=4.9, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 3470 (bs), 2990, 2940, 2900, 1655, 1560, 1460, 1385, 1270, 1220, 1155, 1105, 1070, 1010; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ_H 7.68 (s, 2H, H-C(5'')), 5.87 (d, 2H, ^3J 4.0 Hz, H-C(1)), 4.65, 4.58 (2d, AB syst., 4H, ^2J 14.3 Hz, H-C(1')), 4.22...4.12 (m, 4H, H-C(5), H_A-C(6)), 4.07 (d, 2H, ^3J 4.0 Hz, H-C(2)), 4.02...3.93 (m, 2H, H_B-C(6)), 3.85 (d, 2H, ^3J 8.3 Hz, H-C(4)), 3.08 (bs, 2H, HO-C(3)), 2.81 (t, 4H, ^3J 7.5 Hz, H-C(a,c)), 2.10 (qn, 2H, ^3J 7.5 Hz, H-C(b)), 1.55, 1.50, 1.39, 1.27 (4 s, 24H, $(H_3C)_2$C-O-C(1,2,5,6)); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ_C 147.8, 123.5, 112.9, 110.2, 103.6, 81.5, 79.1, 79.0, 72.9, 68.2, 50.8, 28.6, 26.7, 26.4 (2 signals overlapping), 25.2, 25.0; Anal. calcd for $C_{33}H_{50}N_6O_{12}\cdot 4H_2O$ (794.84): C 49.87, H 7.35, N 10.57; Found C 49.85, H 7.03, N 10.48; Anal. calcd for $C_{33}H_{50}N_6O_{12}$ (722.78): C 54.84, H 6.97, N 11.63; Found C 54.78, H 6.98, N 11.45.

(3*R*)-3-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)methyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (14). Compound **14** was obtained analogically to the general procedure I using 1 equivalent of azidomonosaccharide **12** and phenylacetylene: azide **12** (144 mg, 0.46 mmol, 1 equiv.), CuI (9 mg, 0.05 mmol, 0.1. equiv.), DIPEA (16 µl, 0.09 mmol, 0.2 equiv.), phenylacetylene (61 µl, 0.55 mmol, 1.12 equiv.), THF (4 mL). Yield 145 mg, 76 %, Colorless solid, R_f= 0.55 (T/E =1/2).
mp 193 °C; $[\alpha]_D^{25}$ = 11 (c=0.4, $CHCl_3$); IR (KBr) (ν_{max}, cm^{-1}): 3133, 2974, 2929, 2956, 2887, 1446, 1377, 1244, 1209, 1179, 1111, 1079, 1024; ^{1}H-NMR (DMSO, 300 MHz): δ_H 8.55 (s, 1H, H-C(5')), 7.87 (d, 2H, ^3J 7.2 Hz, 2H-C(Ph)), 7.45(t, 2H, ^3J 7.2 Hz, 2H-C(Ph)), 7.33 (tt, 1H,^3J 7.2 Hz, ^4J 1.1 Hz, H-C(Ph)), 5.88 (d, 1H, ^3J 3.8 Hz, H-C(1)), 5.57 (s, 1H, HO-C(3), 4.53, 4.44 (2d, 2H, AB syst, ^2J 14.3 Hz, H-C(3')), 4.29 (q, 1H, ^3J 6.2 Hz, H-C(5)), 4.16 (d, 1H, ^3J =3.9 Hz, H-C(2)), 4.07 (dd, 1H, ^3J 6.2 Hz, ^2J 8.1 Hz, H_a-C(6)), 4.00 (d, 1H, ^3J =6.0 Hz, H-C(4)), 3.82 (dd, 1H,^3J 6.2 Hz, ^2J 8.1 Hz, H_b-C(6)), 1.46, 1.37, 1.30, 1.21 (4 s, 12H, $(H_3C)_2$C-O-C(1,2,5,6)); ^{13}C-

NMR (DMSO, 75.5 MHz): δ_C 146.2, 130.2, 128.8, 127.8, 125.1, 123.5, 111.7, 108.5, 102.8, 80.3, 79.5, 78.4, 72.5, 65.6, 51.5, 26.5, 26.4, 26.2, 25.1; HRMS (ESI): calculated for $[C_{21}H_{27}N_3O_6 + H^+]$ 418.1982; Found 418.2018.

General procedure II for the synthesis of water soluble modified carbohydrates 17a-k:

1,3-bis(1-((3*S*)-3-Deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)propane, mixture of α- and β-anomers (17a). A suspension of disaccharide **6a** (116 mg, 0.175 mmol) in water (2.5 mL) and CF_3COOH (1.0 mL) was stirred at ambient temperature for 10–18 h (HPLC control). The reaction mixture became clear during the course of the reaction. The solvent was evaporated under reduced pressure. An additional portion of water (2 mL) was added and the resulting solution was again evaporated under reduced pressure in order to remove the traces of CF_3COOH. Then it was dissolved in water (1 mL) and lyophilized at -5 ^oC and 0.01 Torr overnight. The lyophilized product was obtained as a colorless amorphous substance in quantitative yield (88 mg). Its ^{1}H-NMR (D_2O) revealed a β/α ratio of 58/42. NMR signals of the α-galactosyl moiety in α,α'- and α,β-disacharides are identical and NMR signals of the β-galactosyl moiety in β,β' and α,β- disacharides are identical. Therefore, the NMR spectra are described separately for virtual α,α'-dimers ("α-anomer") and virtual β,β'-dimers ("β-anomer"). IR (KBr) (ν_{max}, cm^{-1}): 3370 (br.s.), 2945, 2870, 1630, 1430, 1200, 1140, 1060. Data for β-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.20 (b.s, 2H, H-C(5'')), 4.93 (dd, 2H, ^3J 11.3 Hz, ^3J 2.1 Hz, H-C(3)), 4.81 (d, 2H, ^3J 7.9 Hz, H-C(1)), 4.20...4.10 (m, 2H, H-C(4)), 4.14 (dd, 2H, ^3J 11.3 Hz, ^3J 7.9 Hz, H-C(2)), 3.94 (t, 4H, ^3J 6.0 Hz, H-C(5)), 3.81...3.69 (m, 2H, H-C(6)), 2.85 (b.s, 4H, H-C(a,c)), 2.09 (b.s, 2H, H-C(b)); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 141.1, 124.7, 96.9, 75.8, 68.2, 67.9, 66.6, 60.7, 27.2, 23.1. Data for β-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.20 (b.s, 2H, H-C(5'')), 5.40 (d, 2H, ^3J 3.6 Hz, H-C(1)), 4.82 (dd, 2H, ^3J 11.3 Hz, ^3J 1.9 Hz, H-C(3)), 4.50 (dd, 2H, ^3J 11.3 Hz, ^3J 3.6 Hz, H-C(2)), 4.30 (t, 2H, ^3J 6.4 Hz, H-C(5)), 4.20...4.10 (m, 2H, H-C(4)), 3.81...3.69 (m, 4H, H-C(6)), 2.85 (b.s, 4H, H-C(a,c)), 2.09 (b.s, 2H, H-C(b)); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 141.1, 124.7, 91.8, 70.1, 68.6, 65.3, 63.5, 60.7, 27.2, 23.1. HRMS (ESI) Calcd. for $[C_{19}H_{30}N_6O_{10} + H^+]$ 503.2102; Found 503.2118.

1,4-bis(1-((3*S*)-3-Deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)butane, mixture of α- and β-anomers (17b). Compound **17b** was obtained according to the general procedure II: **6b** (56 mg, 0.08 mmol), TFA (0.5 ml), H_2O (1.3 ml); quantitative yield. Lyophilized product was obtained as a colorless amorphous substance. Its ^{1}H-NMR (D_2O) revealed a β/α ratio of 52/48. IR (KBr) (ν_{max}, cm^{-1}): 3370 (br.s.), 2950, 2870, 1630, 1430, 1200, 1140, 1060. Data for β-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.09 (s, 2H, H-C(5'')), 4.88 (dd, 2H, ^3J 11.1 Hz, ^3J 2.8 Hz, H-C(3)), 4.79...4.71 (m, 2H, H-C(1)), 4.17...4.08 (m, 2H, H-C(4)), 4.07 (dd, 2H, ^3J 11.1 Hz, ^3J 8.1 Hz, H-C(2)), 3.90 (t, 2H, ^3J 6.2 Hz, H-C(5)), 3.78...3.63 (m, 4H, H-C(6)), 2.77 (b.s, 4H, H-C(a,d)), 1.68 (b.s, 4H, H-C(b,c)); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 141.1, 124.7, 96.8, 75.8, 68.2, 67.9, 66.5, 60.7, 27.3, 23.5. Data for α-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.11 (s, 2H, H-C(5'')), 5.35 (d, 2H, ^3J 3.8 Hz, H-C(1)), 5.05 (dd, 2H, ^3J 11.3 Hz, ^3J 2.8 Hz, H-C(3)), 4.45 (dd, 2H, ^3J 11.3 Hz, ^3J 3.8 Hz, H-C(2)), 4.26 (t, 2H, ^3J 6.2 Hz, H-C(5)), 4.17...4.08 (m, 2H, H-C(4)), 3.78...3.63 (m, 4H, H-C(6)), 2.77 (b.s, 4H, H-C(a,d)), 1.68 (b.s, 4H, H-C(b,c)); ^{13}C-NMR (D_2O,

75.5 MHz): δ_C 141.1, 124.7, 91.8, 70.1, 68.6, 65.3, 63.5, 60.8, 27.3, 23.5. HRMS (ESI): Calcd for [$C_{20}H_{32}N_6O_{10}$ + H^+] 517.2258; Found 517.2258.

1,5-bis(1-((3*S*)-3-Deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)pentane, mixture of α- and β-anomers (17c). Compound **17c** was obtained according to the general procedure II: **6c** (46 mg, 0.07 mmol), TFA (0.5 ml), H_2O (1.5 ml); quantitative yield. Lyophilized product was obtained as a colorless amorphous substance. Its ^{1}H-NMR (D_2O) revealed a β/α ratio of 58/42. IR (KBr) (ν_{max}, cm^{-1}): 3370 (br.s.), 2940, 2875, 1630, 1430, 1200, 1140, 1060. Data for β-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.30 (b.s, 2H, H-C(5'')), 4.94 (dd, 2H, ^3J 10.7 Hz, ^3J 1.9 Hz, H-C(3)), 4.82 (d, 2H, ^3J 7.5 Hz, H-C(1)), 4.22...4.12 (m, 2H, H-C(4)), 4.13 (dd, 2H, ^3J 10.7 Hz, ^3J 7.5 Hz, H-C(2)), 3.95 (t, 2H, ^3J 6.2 Hz, H-C(5)), 3.83...3.67 (m, 4H, H-C(6)), 2.79 (b.s, 4H, H-C(a,e)), 1.75 (b.s, 4H, H-C(b,d)), 1.39 (b.s, 2H, H-C(c)); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 141.1, 124.7, 96.9, 75.9, 68.2, 67.8, 66.7, 60.7, 27.5, 27.3, 23.7. Data for α-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.30 (b.s, 2H, H-C(5'')), 5.41 (d, 2H, ^3J 3.5 Hz, H-C(1)), 5.11 (dd, 2H, ^3J 11.3 Hz, ^3J 1.9 Hz, H-C(3)), 4.51 (dd, 2H, ^3J 11.3 Hz, ^3J 3.5 Hz, H-C(2)), 4.31 (t, 2H, ^3J 6.2 Hz, H-C(5)), 4.22...4.12 (m, 2H, H-C(4)), 3.83...3.67 (m, 4H, H-C(6)), 2.79 (b.s, 4H, H-C(a,e)), 1.75 (b.s, 4H, H-C(b,d)), 1.39 (b.s, 2H, H-C(c)); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 141.1, 124.7, 91.9, 70.1, 68.6, 65.3, 63.7, 60.9, 27.5, 27.3, 23.7. HRMS (ESI): Calcd for [$C_{21}H_{34}N_6O_{10}$ + H^+] 531.2415; Found 531.2425.

1,6-bis(1-((3*S*)-3-Deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)hexane, mixture of α- and β-anomers (17d). Compound **17d** was obtained according to the general procedure II: **6d** (122 mg, 0.17 mmol), TFA (1.0 ml), H_2O (3.3 ml); quantitative yield. Lyophilized product was obtained as a colorless amorphous substance. Its ^{1}H-NMR (D_2O) revealed a β/α ratio of 56/44. IR (KBr) (ν_{max}, cm^{-1}): 3370 (br.s.), 2945, 2870, 1630, 1430, 1200, 1140, 1060. Data for β-anomer: ^{1}H-NMR (D_2O, 400 MHz): δ_H 8.26 (s, 2H, H-C(5'')), 4.99 (dd, 2H, ^3J 11.3 Hz, ^3J 2.7 Hz, H-C(3)), 4.84 (d, 2H, ^3J 7.8 Hz, H-C(1)), 4.24...4.17 (m, 2H, H-C(4)), 4.16 (dd, 2H, ^3J 11.3 Hz, ^3J 7.8 Hz, H-C(2)), 3.96 (dd, 2H, ^3J 6.2 Hz, ^3J 5.8 Hz, H-C(5)), 3.83...3.72 (m, 4H, H-C(6)), 2.86...2.78 (m, 4H, H-C(a,f)), 1.70 (qn, 4H, ^3J 6.2 Hz, H-C(b,e)), 1.42...1.35 (m, 4H, H-C(c,d)); ^{13}C-NMR (D_2O, 100.6 MHz): δ_C 146.0, 124.4, 96.7, 75.7, 68.0, 67.7, 66.9, 60.5, 27.5, 27.4, 23.2. Data for α-anomer: ^{1}H-NMR (D_2O, 400 MHz): δ_H 8.23 (s, 2H, H-C(5'')), 5.42 (d, 2H, ^3J 3.5 Hz, H-C(1)), 5.15 (dd, 2H, ^3J 11.3 Hz, ^3J 2.3 Hz, H-C(3)), 4.53 (dd, 2H, ^3J 11.3 Hz, ^3J 3.5 Hz, H-C(2)), 4.32 (t, 2H, ^3J 6.2 Hz, H-C(5)), 4.24...4.17 (m, 2H, H-C(4)), 3.83...3.72 (m, 4H, H-C(6)), 2.86...2.78 (m, 4H, H-C(a,f)), 1.70 (qn, 4H, ^3J 6.2 Hz, H-C(b,e)), 1.42...1.35 (m, 4H, H-C(c,d)); ^{13}C-NMR (D_2O, 100.6 MHz): δ_C 146.0, 124.4, 91.7, 70.0, 68.4, 65.1, 63.9, 60.7, 27.5, 27.4, 23.2. HRMS (ESI): Calcd for [$C_{22}H_{36}N_6O_{10}$ + Na^+] 567.2391; Found 567.2388.

1,2-bis((1-((3*S*)-3-Deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methoxy)ethane (17e). Compound **17e** was obtained according to the general procedure II: **6e** (142 mg, 0.20 mmol), TFA (1.0 ml), H_2O (2.5 ml); quantitative yield. Lyophilized product was obtained as a colorless amorphous substance. Its ^{1}H-NMR (D_2O) revealed a β/α ratio of 60/40. IR (KBr) (ν_{max}, cm^{-1}): 3370 (br.s.), 2930, 2880, 1640, 1450, 1345, 1200, 1140, 1080, 1060. Data for β-anomer: ^{1}H-NMR (D_2O, 400 MHz): δ_H 8.24 (b.s, 2H, H-C(5'')), 4.93 (dd, 2H, ^3J 10.9 Hz, ^3J 2.7 Hz, H-

C(3)), 4.83 (d, 2H, ^3J 7.8 Hz, H-C(1)), 4.70 (s, 4H, H-C(a,d)), 4.20...4.11 (m, 4H, H-C(2), H-C(4)), 3.97 (t, 2H, ^3J 6.2 Hz, H-C(5)), 3.84...3.71 (m, 4H, H-C(6)), 3.75 (s, 4H, H-C(b,c)); ^{13}C-NMR (D_2O, 100.6 MHz): δ_C 143.6, 124.4, 96.8, 75.8, 68.8, 68.2, 67.8, 65.8, 65.4, 60.6. Data for α-anomer: ^{1}H-NMR (D_2O, 400 MHz): δ_H 8.24 (b.s, 2H, H-C(5'')), 5.42 (d, 2H, ^3J 3.5 Hz, H-C(1)), 5.09 (dd, 2H, ^3J 11.3 Hz, ^3J 2.3 Hz, H-C(3)), 4.70 (s, 4H, H-C(a,d)), 4.52 (dd, 2H, ^3J 11.3 Hz, ^3J 3.5 Hz, H-C(2)), 4.33 (t, 2H, ^3J 6.2 Hz, H-C(5)), 4.20...4.11 (m, 2H, H-C(4)), 3.84...3.71 (m, 4H, H-C(6)), 3.75 (s, 4H, H-C(b,c)); ^{13}C-NMR (D_2O, 100.6 MHz): δ_C 143.6, 124.4, 91.8, 70.1, 68.8, 68.7, 65.8, 62.9, 64.4, 60.6. HRMS (ESI): Calcd for [$C_{20}H_{32}N_6O_{10}$ + H^+] 549.2156; Found 549.2131.

2,2-bis((1-((3*S*)-3-Deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methyl)-5,5-dimethylcyclohexane-1,3-dione (17f). Compound **17f** was obtained according to the general procedure II: **6f** (149 mg, 0.19 mmol), TFA (0.9 ml), H_2O (2.3 ml); quantitative yield. Lyophilized product was obtained as a colorless amorphous substance. Its ^{1}H-NMR (D_2O) revealed a β/α ratio of 60/40. IR (KBr) (ν_{max}, cm^{-1}): 3390 (br.s.), 2940, 1730, 1635, 1435, 1400, 1280, 1240, 1200, 1140, 1060. Data for β-anomer: ^{1}H-NMR (D_2O, 400 MHz): δ_H 7.93 (s, 2H, H-C(5'')), 4.86 (dd, 2H, ^3J 11.3 Hz, ^3J 2.7 Hz, H-C(3)), 4.80 (d, 2H, ^3J 7.4 Hz, H-C(1)), 4.16...4.09 (m, 2H, H-C(4)), 4.08 (dd, 2H, ^3J 11.3 Hz, ^3J 7.4 Hz, H-C(2)), 3.94 (t, 2H, ^3J 6.2 Hz, H-C(5)), 3.82...3.69 (m, 4H, H-C(6)), 3.34 (s, 4H, H-C(a,b)), 2.75 (s, 4H, H-C(c,d)), 0.69 (s, 6H, H_3C-C(e)); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 212.1, 141.5, 125.3, 97.0, 75.9, 68.9, 68.3, 68.0, 65.8, 60.7, 51.1, 30.4, 29.8, 27.4. Data for α-anomer: ^{1}H-NMR (D_2O, 400 MHz): δ_H 7.93 (s, 2H, H-C(5'')), 5.39 (d, 2H, ^3J 3.5 Hz, H-C(1)), 5.03 (dd, 2H, ^3J 11.3 Hz, ^3J 2.7 Hz, H-C(3)), 4.45 (dd, 2H, ^3J 11.3 Hz, ^3J 3.5 Hz, H-C(2)), 4.29 (t, 2H, ^3J 6.2 Hz, H-C(5)), 4.16...4.09 (m, 2H, H-C(4)), 3.82...3.69 (m, 4H, H-C(6)), 3.34 (s, 4H, H-C(a,b)), 2.75 (s, 4H, H-C(c,d)), 0.69 (s, 6H, H_3C-C(e)); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 141.1, 141.5, 125.3, 91.9, 70.2, 68.9, 68.6, 65.3, 62.6, 60.9, 51.1, 30.4, 29.8, 27.4. HRMS (ESI): Calcd for [$C_{26}H_{38}N_6O_{12}$ + H^+] 627.2626; Found 627.2645.

5,5-bis((1-((3*S*)-3-Deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (17g). Compound **17g** was obtained according to the general procedure II: **6f** (137 mg, 0.17 mmol), TFA (1.0 ml), H_2O (2.3 ml); quantitative yield. Lyophilized product was obtained as a colorless amorphous substance. Its ^{1}H-NMR (D_2O) revealed a β/α ratio of 50/50. IR (KBr) (ν_{max}, cm^{-1}): 3395 (br.s.), 2860, 1720, 1440, 1380, 1320, 1205, 1140, 1060. Data for β-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 7.97 (s, 2H, H-C(5'')), 4.83 (dd, 2H, ^3J 11.3 Hz, ^3J 3.0 Hz, H-C(3)), 4.77 (d, 2H, ^3J 7.9 Hz, H-C(1)), 4.12...4.06 (m, 2H, H-C(4)), 4.05 (dd, 2H, ^3J 11.3 Hz, ^3J 7.9 Hz, H-C(2)), 3.92 (t, 2H, ^3J 6.4 Hz, H-C(5)), 3.80...3.67 (m, 4H, H-C(6)), 3.55 (s, 4H, H-C(a,b)); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 175.9, 164.1, 147.7, 126.6, 99.5, 78.5, 70.9, 70.5, 68.1, 63.5, 59.0, 35.5. Data for α-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 7.96 (s, 2H, H-C(5'')), 5.37 (d, 2H, ^3J 3.8 Hz, H-C(1)), 5.00 (dd, 2H, ^3J 11.3 Hz, ^3J 3.0 Hz, H-C(3)), 4.42 (dd, 2H, ^3J 11.3 Hz, ^3J 3.8 Hz, H-C(2)), 4.27 (t, 2H, ^3J 6.2 Hz, H-C(5)), 4.12...4.06 (m, 2H, H-C(4)), 3.80...3.67 (m, 4H, H-C(6)), 3.55 (s, 4H, H-C(a,b)); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 175.9,

164.1, 147.7, 126.6, 94.4, 72.8, 71.3, 67.9, 64.8, 63.5, 59.0, 35.5. HRMS (ESI): Calcd for [$C_{22}H_{30}N_8O_{13}$ + H^+] 615.2011; Found 615.2035.

A 1:1 mixture of 5,5-Bis((1-((3*S*)-3-deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (17h) and 3-(1-((3*S*)-3-deoxy-D-galacto-pyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)-2-((1-((3*S*)-3-deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methyl)propanoic acid (17i). Compounds **17h** and **17i** were synthesized according to the general procedure II: **6g** (149 mg, 0.19 mmol), TFA (1.0 ml), H_2O (2.3 ml). Only partial cleavage of acetonide of Meldrum's acid moiety was observed. Lyophilized product (110 mg) was obtained as a colorless amorphous substance. Its ^{1}H-NMR (D_2O) and LC-MS revealed ~1:1 molar ratio of **17h** and **17i**. Compounds **17h** and **17i** were characterized from the NMR spectra of their mixture. Small amount of **17i** was separated by semi-preparative HPLC in order to perform biotests.

Data for **17h** β-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.02 (s, 2H, H-C(5')), 4.86 (dd, 2H, ^3J 9.4 Hz, ^3J 2.5 Hz, H-C(3)), 4.77 (d, 2H, ^3J 7.7 Hz, H-C(1)), 4.14...4.03 (m, 4H, H-C(2,4)), 3.90 (t, 2H, ^3J 7.0 Hz, H-C(5)), 3.76...3.65 (m, 4H, H-C(6)), 3.62 (bs, 4H, H-C(a,c)), 1.01 (s, 6H, CH_3); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 169.4, 141.0, 124.4, 108.2, 97.0, 75.9, 68.3, 67.9, 65.7, 60.9, 56.4, 28.0, 26.2. Data for **17h** α-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.01 (s, 2H, H-C(5')), 5.37 (d, 2H, ^3J 3.7 Hz, H-C(1)), 5.04 (dd, 2H, ^3J 11.4 Hz, ^3J 3.0 Hz, H-C(3)), 4.46 (dd, 2H, ^3J 11.5 Hz, ^3J 3.8 Hz, H-C(2)), 4.26 (t, 2H, ^3J 6.5 Hz, H-C(5)), 4.14...4.03 (m, 2H, H-C(4)), 3.76...3.65 (m, 4H, H-C(6)), 3.62 (bs, 4H, H-C(a,c)), 1.01 (s, 6H, CH_3); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 169.4, 141.1, 124.4, 108.2, 91.9, 70.2, 68.7, 66.0, 62.8, 60.9, 58.2, 28.8, 28.0. HRMS (ESI) for **17h**: Calcd for [$C_{24}H_{34}N_6O_{14}$ + Na^+] 653.2025; Found 653.2031.

Data for **17i** β-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.06 (bs, 2H, H-C(5')), 4.87 (dd, 2H, ^3J 9.4 Hz, ^3J 2.5 Hz, H-C(3)), 4.74 (d, 2H, ^3J 7.7 Hz, H-C(1)), 4.14...4.03 (m, 4H, H-C(2,4)), 3.92 (t, 2H, ^3J 7.0 Hz, H-C(5)), 3.76...3.65 (m, 4H, H-C(6)), 3.32 (bs, 4H, H-C(a,c)), 3.11...3.05 (m, 1H, H-C(b); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 173.6, 141.0, 124.4, 96.9, 75.9, 68.3, 68.0, 65.7, 60.7, 44.8, 33.7. Data for **17i** α-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.07 (bs, 2H, H-C(5')), 5.35 (d, 2H, ^3J 3.7 Hz, H-C(1)), 5.00 (dd, 2H, ^3J 11.4 Hz, ^3J 2.8 Hz, H-C(3)), 4.40 (dd, 2H, ^3J 11.5 Hz, ^3J 3.8 Hz, H-C(2)), 4.27 (t, 2H, ^3J 6.5 Hz, H-C(5)), 4.14...4.03 (m, 2H, H-C(4)), 3.76...3.65 (m, 4H, H-C(6)), 3.32 (bs, 4H, H-C(a,c)), 3.11...3.05 (m, 1H, H-C(b); ^{13}C-NMR (D_2O, 75.5 MHz): δ_C 173.6, 141.1, 124.4, 91.9, 70.2, 68.6, 65.4, 62.3, 60.7, 44.8, 33.7. HRMS (ESI) for **17i**: Calcd for [$C_{20}H_{30}N_6O_{14}$ + H^+] 547.1995; Found 547.2004.

1,3,5-Tris((1-((3*S*)-3-deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)benzene (17j). Compound **17j** was obtained according to the general procedure II: **8** (135 mg, 0.13 mmol), TFA (1.0 ml), H_2O (2.3 ml); quantitative yield. Lyophilized product was obtained as a colorless amorphous substance. Its ^{1}H-NMR (D_2O) revealed a β/α ratio of 58/42. IR (KBr) (ν_{max}, cm^{-1}): 3364 (br.s.), 2940, 2890, 1630, 1380, 1240, 1205, 1140, 1060. Data for β-anomer: ^{1}H-NMR (D_2O, 400 MHz): δ_H 7.98...7.87 (m, 3H, H-C(5')), 7.03...6.88 (m, 3H, H-C(a,b,c)), 4.97 (d, 2H, ^3J 10.5 Hz, H-C(3)), 4.90 (d, ^3J 7.8 Hz, H-C(1)), 4.30...4.13 (m, 3H, H-C(2), H-C(4)), 4.00 (t, 3H, ^3J 5.9 Hz, H-C(5)), 3.91...3.73 (m, 6H, H-C(6)); ^{13}C-NMR (D_2O, 100.6 MHz): δ_C 145.4,

129.5, 121.1, 120.7, 96.9, 75.9, 68.4, 68.0, 65.8, 60.8. Data for α-anomer: ^{1}H-NMR (D_2O, 400 MHz): δ_H 7.98...7.87 (m, 3H, H-C(5')), 7.03...6.88 (m, 3H, H-C(a,b,c)), 5.50 (d, 3H, ^3J 2.3 Hz, H-C(1)), 4.56 (dd, 3H, ^3J 11.7 Hz, ^3J 2.3 Hz, H-C(2)), 4.96...4.72 (m, 3H, H-C(3)), 4.36 (t, 3H, ^3J 5.9 Hz, H-C(5)), 4.30...4.13 (m, 3H, H-C(4)), 3.91...3.73 (m, 6H, H-C(6)); ^{13}C-NMR (D_2O, 100.6 MHz): δ_C 145.4, 129.5, 121.1, 120.7, 91.8, 70.2, 68.6, 65.3, 62.4, 60.8. HRMS (ESI): Calcd for [$C_{30}H_{39}N_9O_{15}$ + H^+] 766.2644; Found 766.2601.

Penta-*O*-((1-((3*S*)-3-deoxy-D-galactopyranos-3-yl)-1*H*-1,2,3-triazol-4-yl)methyl)-β-D-glucose (17k). Compound **17k** was obtained according to the general procedure II: **10** (131 mg, 0.07 mmol), TFA (1.0 ml), H_2O (2.3 ml). The crude product was purified by reverse phase column chromatography (C_{18}-modified silica gel; eluent system: H_2O/MeCN). Yield: 55 mg (54%). Lyophilized product was obtained as a colorless amorphous substance. Its ^{1}H-NMR (D_2O) revealed a β/α ratio of 55/45. IR (KBr) (ν_{max}, cm^{-1}): 3370 (br.s.), 2940, 2870, 1640, 1460, 1360, 1230, 1140, 1060. Data for β-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.27...8.09 (m, 5H, H-C(5'')), 5.11...4.58 (m, 23H, H-C(1)), H-C(3)), H-C(1'), H-C(3'), H-C(5'), H-C(1'')), 4.19...4.07 (m, 10H, H-C(2), H-C(4)), 3.99...3.90 (m, 5H, H-C(5)), 3.84...3.50 (m, 13H, H-C(6), H-C(2'), H-C(6')), 3.38 (t, 1H, ^3J 8.5 Hz, H-C(4')). Data for α-anomer: ^{1}H-NMR (D_2O, 300 MHz): δ_H 8.27...8.09 (m, 5H, H-C(5'')), 5.42...5.37 (m, 5H, H-C(1)), 5.11...4.58 (m, 18H, H-C(3)), H-C(1'), H-C(3'), H-C(5'), H-C(1'')), 4.50 (dd, 5H, ^3J 11.3 Hz, ^3J 3.8 Hz, H-C(2)), 4.31 (dt, 5H, ^3J 6.2 Hz, ^3J 2.4 Hz, H-C(5)), 4.19...4.07 (m, 5H, H-C(4)), 3.84...3.50 (m, 13H, H-C(6), H-C(2'), H-C(6')), 3.38 (t, 1H, ^3J 8.5 Hz, H-C(4')); ^{13}C-NMR (D_2O, 100.6 MHz): δ_C signals of triazole moiety: 143.7 (br. s.), 143.4 (br. s.), 124.9, 124.7 (br. s.); signals of central glucose scaffold, including -O-CH_2-groups: 101.5, 82.7, 80.6, 76.6, 73.4, 64.6 (br. s., CH_2), 63.3 (br. s., CH_2), 62.2 (br. s., CH_2); signals of α-galactosyl moiety: 91.9, 70.3, 68.8, 65.5, 62.4, 60.9 (br. s., CH_2); signals of β-galactosyl moiety: 96.9, 75.9, 68.4, 68.0, 65.7, 60.9 (br. s., CH_2); HRMS (ESI): Calcd for [$C_{51}H_{77}N_{15}O_{31}$ + H^+] 1396.4988; Found 1396.4865.

Determination of the residual copper content: Quantitative determination of Cu was done by electrothermal atomic absorption spectrometry (ETAAS). Measurements were performed on a PerkinElmer Model AAnalyst 800 with longitudinal Zeeman-effect background correction, a stabilized temperature platform furnace and a transversely- heated graphite atomizer. For determination of copper, a linear five point calibration method was used. The analytical conditions of Cu determination by ETAAS were: wavelength 324.8 nm, slit width 0.7 nm, HCL lamp with 30 mA current, Pd-$Mg(NO_3)_3$ as chemical matrix modifier, 1200 ^oC pyrolysis temperature, 2050 ^oC atomization temperature. A 20µL sample volume was used for the analysis. The precision of three replicates on the ETAAS spectrometer was within 2%.

A microwave assisted acid digestion method was used for the sample preparation. A 0.2 – 0.5 g powdered sample aliquot was weighed with a precision of 0.0001 g into a 100 mL pressure resistant (100 bar) PTFE vessel. Then 5 mL of HNO_3 (65%, m/v) and 2 mL of H_2O_2 (30%, m/v) was added. The samples were digested using a three-step program: 5 min at 600 W power with ramp time 10 min, a second step at 360 W power with ramp time 5 min, and finally 30 min at 0 W power. The resulting colorless solutions were diluted to 10 mL with deionized water. Blanks

consisting of deionized water and reagents were subjected to a similar sample preparation. Freshly distilled nitric acid was used for all analysis.

Single crystal X-ray diffraction analysis of disaccharide 13: Diffraction data were collected at –80°C on a Bruker-Nonius KappaCCD diffractometer using graphite monochromated Mo-Kα radiation (λ 0.71073 Å). The crystal structure of **13** was solved by direct methods[44] and refined by the full-matrix least squares technique.[45] All nonhydrogen atoms were refined in anisotropic approximation, all H-atoms were refined by the riding model. The absolute configuration of **13** was determined using known chiral centers. Crystal data for **13**: orthorhombic; a = 5.5052(1), b = 20.8069(3), c = 37.4615(8) Å; V = 4291.1(1) Å^3, Z = 4, μ = 0.099 mm^{-1}, D_{calc} = 1.237 g·cm^{-1}; the space group is $C222_1$. A total of 5591 reflection intensities were collected up to $2\theta_{max}$ = 60°; for structure refinement 1934 independent reflections with $I > 3\sigma(I)$ were used. The final R-factor is 0.071. Crystallographic data of **13** are deposited with the Cambridge Crystallographic Data Centre with a supplementary publication number CCDC 957271. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK.

Galectins and fluorescence anisotropy assay: Inhibition of fluorescence anisotropy by saccharide ligands and calculations of K_d values were performed as previously described.[40] Galectin-3 was produced, purified and tested at about 1 μM with a A-tetrasaccharide fluorescent probe ((A-tetra-probe, 0.1 μM) at ambient temperature.[42] Galectin-1 was produced, purified and tested at about 0.5 μM with a thiodigalactoside amide probe (tdga-probe, 0.1 μM) as previously reported.[41]

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