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1*H*-1,2,3-Triazol-1-yl thiodigalactoside derivatives as high affinity galectin-3 inhibitors

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ABSTRACT

Galactose C3-triazole derivatives were synthesized by Cu(I)-catalyzed cycloaddition between acetylenes and galactose C3-azido derivatives. Evaluation against galectin-3, 7, 8N (N-terminal) and 9N (N-terminal) revealed 1,4-disubstituted triazoles to be high-affinity inhibitors of galectin-3 with selectivity over galectin-7, 8N, and 9N. Conformational analysis of 1,4-di- and 1,4,5-tri-substituted galactose C3-triazoles suggested that a triazole C5-substituent interfered sterically with the galectin proteins, which explained their poor affinities compared to the corresponding 1,4-disubstituted triazoles. Introduction of two 1,4-disubstituted triazole moieties onto thiodigalactoside resulted in affinities down to 29 nM for galectin-3.

1. Introduction

The galectins are a family of carbohydrate binding proteins known by their affinity for β-galactosides.[1,2] Fourteen members of galectin family have been discovered so far. They are widely distributed in vertebrates (fish, birds, amphibians, and mammals), and in invertebrates (worms and insects). They have also been found in protists (sponges and fungi). All galectins share a core sequence consisting of about 130 amino acids, many of which are highly conserved. Galectins are soluble proteins and possess properties expected for both extra- and intracellular proteins. Galectin properties, of which a majority involves glycoconjugate binding, have been studied extensively due to the growing evidence of links to immunity, inflammation,[3] and cancer.[4]

In recent years several studies have initiated the emergence of a coherent picture concerning the galectins' biological mechanisms. A central mechanism is the regulation of cell-surface receptors via lattice formations[5–8] and to intracellular glycoprotein trafficking.[9,10] The importance of galectins in regulating activities of cell surface receptors, such as TGF-β or TCR, may be linked to effects of galectin inhibition in animal models. A fragment of galectin-3 containing the CRD inhibited breast cancer in a mouse model by acting as a dominant negative galectin-3 inhibitor[11] and galectin-binding glycoconjugates decrease metastasis in mice through inhibition of galectins.[12,13] More recently, potent efficacy of synthetic galectin inhibitors clinically relevant in vitro and ex vivo cell assays has been demonstrated, including attenuation of tumor cell motility,[14] inhibition of alternative macrophage differentiation and fibrosis,[15] and enhancement of sensitivity to chemo- and radiotherapy by activation of caspase-3-mediated apoptosis.[16] Such observations clearly suggest that efficient and selective inhibitors for galectins can act intracellularly and find potential use in modulating inflammatory processes and cancer growth.[17]

We have reported the rational design of potent inhibitors of galectin-3, by exploiting the X-ray crystal structure of *N*-acetyllactosamine-galectin complex.[18] This complex shows an extending binding groove close to the Lac*N*Ac HO3′ that could be targeted with aromatic amides attached to C3′ of Lac*N*Ac that interact with Arg144.[19,20] Derivatization at C3 of galactose is also expected to result in the added advantage of conferring selectivity over other galactose-recognizing proteins, as these typically recognize terminal galactose residues with free HO3 and HO4. In contrast, galectins can recognize internal galactose with C3 glycosylated and hence tolerate synthetic C3-substituents. Aromatic diamides of thiodigalactoside were subsequently discovered to possess even further enhanced affinity for several members of the galectin family of proteins, which was hypothesized to be a result of both aromatic amides stacking with arginine side-chains.[21,22] The aromatic amides at Lac*N*Ac C3′ or at thiodigalactoside C3 and C3′ were all prepared from a common galactose C3-azido derivative. However, the azido functionality is versatile in the sense that it, in addition

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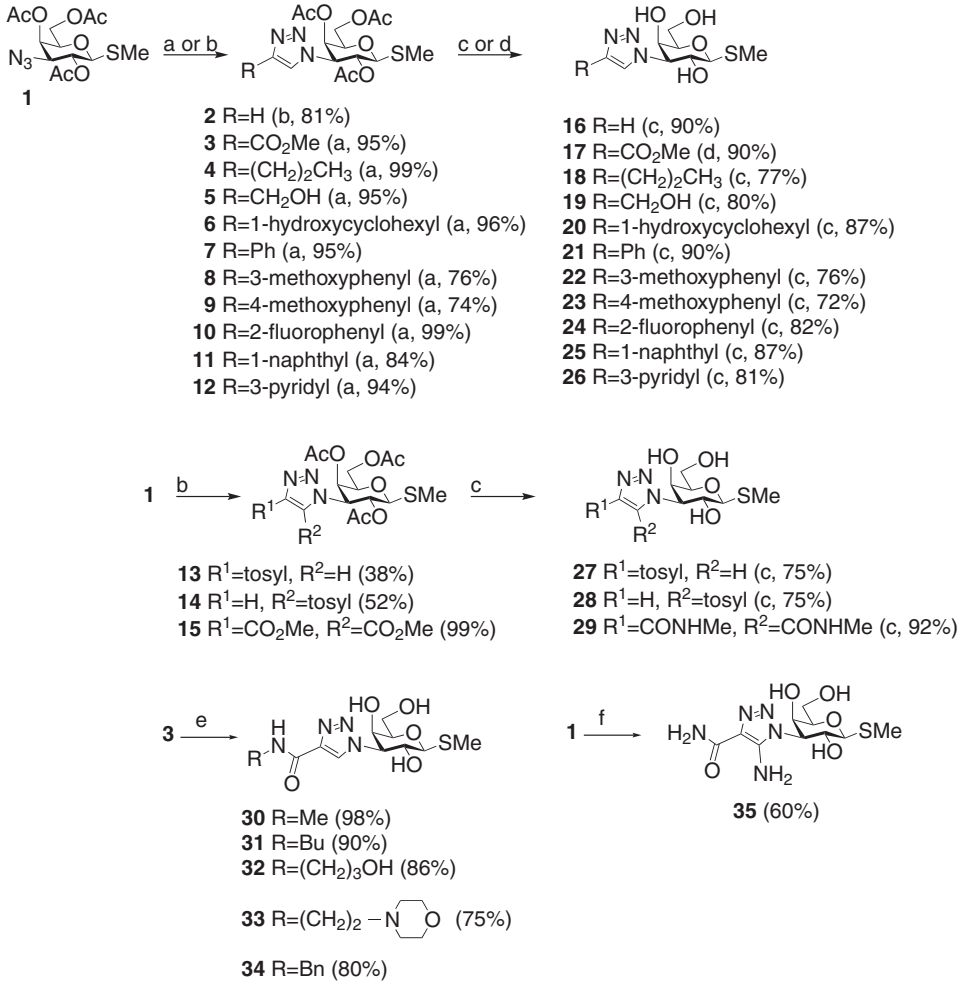
to for example, reduction–acylation, can undergo various mild and selective organic transformations. In particular, the Cu(I)-catalyzed regioselective dipolar cycloaddition between azides and acetylenes to give 1,4-triazoles[23–25] has found widespread use and has become important in drug discovery.[26,27] The stability of the triazole toward oxidation, reduction and hydrolysis,[28] the efficient Cu(I)-catalyzed reaction, as well as the 1,2,3-triazole ring being an bioisostere to the amide-functionality in our earlier inhibitors, attracted our attention for development of novel galectin inhibitors. We have reported preliminary accounts on our efforts on exploiting the azido group of the galactose C3-azido derivative **1** in cycloadditions with monosubstituted acetylene derivatives towards galectin-3 inhibitors[29] and that the acetylene galactose C3-azido cycloaddition can be used in combination with other chemistries to discover galectin inhibitors via a fragment-based strategy.[30] We herein wish to report our continued study on 3-triazol-1-yl-galactosides[29] as galectin inhibitors including synthesis of 1,5-disubstituted and 1,4,5-trisubstituted triazoles, as well as 3′-triazol-1-yl *N*-acetyllactosamine (LacNAc) and 3,3′-di-triazol-1-yl-thiodigalactoside derivatives. Furthermore, the galectins, as many medically relevant protein targets, exist as a class of target proteins with structural similarities, which makes it imperative to address the, in terms of in vivo inhibitor use, important issue of galectin selectivity. Hence, we herein extended our evaluations of the triazol-1-yl galactoside and Lac*N*Ac derivatives against galectin-7, 8N (N-terminal domain), and 9N (N-terminal domain). Finally, conformational analysis of the triazol-1-yl galactoside derivatives provided insight into structure–activity relationships and galectin-selectivities for 1,4-di- and 1,4,5-tri-substituted triazoles, respectively.

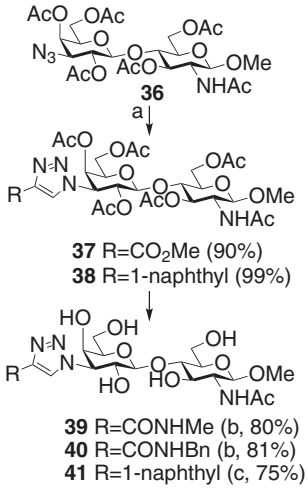
2. Results and discussion

2.1. Synthesis

A collection of triazoles was obtained on the 3-Gal position either by the thermal 1,3-dipolar cycloaddition or by Cu(I)-catalyzed reaction depending on the substituents (Scheme 1). The monosubstituted triazole **2** was obtained by the heating of the azide **1**[19] with propiolic acid under which conditions the initially formed 4-carboxytriazole intermediate decarboxylated in situ.[31] The disubstituted triazoles **3–12** were obtained through the Cu(I) catalyzed reaction of the azide **1** with monosubstituted acetylenes as earlier reported.[29] The reactions were highly regioselective and gave only 1,4-disubstituted triazoles **3–12** in high yields. The conditions, however, varied somewhat depending on the dipolarophilicity of the acetylene. Activated acetylenes, for example, methyl propiolate, needed shorter time and lower temperature, while the electron rich acetylenes required longer times, up to seven days, and temperatures up to 45 °C. In only one case, with 4-methoxyphenylacetylene, traces of 1,5-disubstituted regioisomer could be detected. In the case of tosylacetylene, no reaction was observed



Scheme 1. Reagents and conditions: (a) alkyne, CuI, DIPEA, toluene, rt–40 °C; (b) toluene, 65–80 °C; (c) 40% $MeNH_2$ in H_2O; (d) NaOMe, MeOH; (e) RNH_2, MeOH; (f) [i]cyanoacetamide, K_2CO_3, DMSO, 50 °C, [ii]MeOH.



Scheme 2. Reagents and conditions: (a) alkyne, CuI, DIPEA, toluene; (b) RNH_2, MeOH; (c) 40% $MeNH_2$ in H_2O.

under the Cu(I) catalyzed conditions. Fortunately, both regioisomers of the corresponding triazoles **13** and **14** could be obtained in 90% in a 2:3 ratio by heating **1** with tosylacetylene. The 1,4,5-trisubstituted triazole **15** was obtained in a near quantitative yield by reaction of the azide **1** with dimethyl acetylenedicarboxylate under Huisgen thermal conditions.

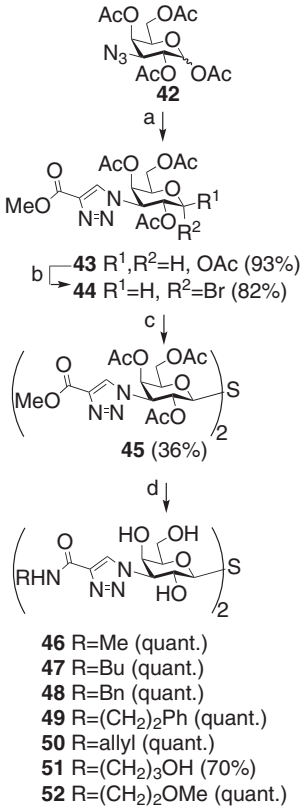
The unprotected triazoles **16** and **18–29** were obtained by treatment of **2** and **4–15** with aqueous methylamine, while the methylester **17** was obtained by the treatment of **3** with methanolic sodium methoxide. Reaction of the triazole methyl ester **3** with different amines gave a panel of amides **30–34**. The amide formation was faster and proceeded at lower temperature for aliphatic amines to give **30–33**, whereas heating at 45 °C was necessary with benzylamine to afford **34**. Finally, an unprotected 1,4,5-trisubstituted triazole **35** was prepared with complete regioselectivity in one step by treatment of **1** with cyanoacetamide.[32]

As Lac*N*Ac and thiodigalactoside are far superior to galactose as natural ligands for galectins, three Lac*N*Ac and eight thiodigalactoside derivatives carrying triazoles at the galactose C3′s were prepared. Again, 4-carbamoyl and 4-aryl triazoles were targeted, because these were earlier demonstrated to enhance affinity for galectin-3 within a galactose series of compounds.[29] The known Lac*N*Ac C3′-azido compound **36**[33] was somewhat less reactive than the corresponding monosaccharide **1**. Nevertheless, the corresponding triazoles **37** and **38** were obtained in good yields (Scheme 2). Treatment of **37** and **38** with methylamine and benzylamine in methanol provided the methyl amide **39** and the benzyl amide **40**, respectively, while the 1-naphthyl triazole **41** was obtained by aminolysis of the acetates with methylamine in water.

The thiodigalactoside triazole ester **45** was obtained starting with cycloaddition between methyl propiolate and the known galacto azide **42**[34] (Scheme 3). The resulting triazole tetraacetate **43** was treated with HBr in AcOH to give the bromide **44**. Dimerisation of the bromide **44** was achieved by treatment with dried sodium sulfide affording the di-triazole-substituted thiodigalactoside **45** in a moderate yield due to purification difficulties arising from low solubility of **45**. Deprotection of the common ester precursor **45** using a panel of primary amines in methanol, with concomitant substitution of the methyl ester to give the respective amides, gave a set of seven compounds **46–52**.

2.2. Affinity evaluation against galectin-3, 7, 8N, and 9N

The triazoles **16–35**, **39–41**, and **46–52** were screened for inhibition potency against the available human galectin-3, 7, 8N, and



Scheme 3. Reagents and conditions: (a) methyl propiolate, CuI, DIPEA, toluene; (b) HBr (33% in AcOH), DCM, Ac_2O; (c) Na_2S (dried), MeCN, 4 Å; (e) RNH_2, MeOH.

9N together with methyl β-D-galactoside **53**, Lac*N*Ac methyl glycoside **54**, and un-derivatized thiodigalactoside **55** (Chart 1) using a competitive fluorescence polarization assay as earlier described in detail[35,36] (Table 1) and shown to correlate well to other protein affinity assays, such as ITC and ELISA,[20,22] and to in vitro and

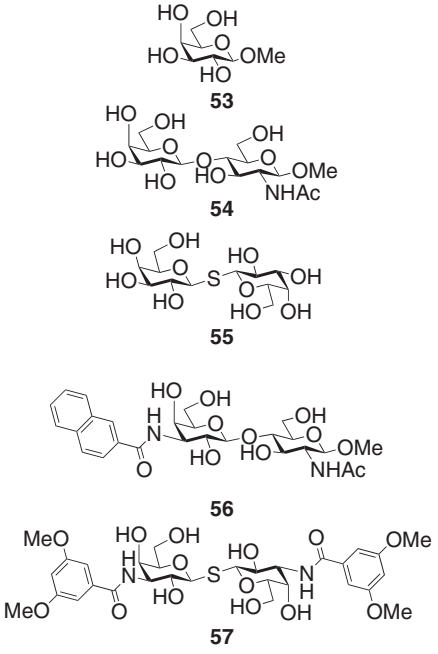


Chart 1.

Table 1
K_d (μM) values[a] for galactose triazoles **16–35**, Lac*NA*c triazoles **39–41**, and thiodigalactoside triazoles **46–52** determined in a competitive fluorescence polarization assay[35,36]

	Triazole substituents		Galectin			
	C4	C5	3	7	8N	9N
Galactose derivatives						
16	–H	–H	>5000[b]	2400 ± 30	>5000	>5000
17	$-CO_2Me$	–H	1300 ± 180	>5000	>5000	430 ± 160
18	$-(CH_2)CH_3$	–H	>5000	2200 ± 1400	>5000	>5000
19	$-CH_2OH$	–H	>5000	2500 ± 170	>5000	>5000
20	1-Hydroxycyclohexyl	–H	1600 ± 260	>5000	>5000	1000 ± 310
21	Ph	–H	150 ± 11	1700 ± 700	>5000	1300 ± 640
22	3-Methoxyphenyl	–H	130 ± 10	≈2800	>5000	2100 ± 1200
23	4-Methoxyphenyl	–H	260 ± 60	≈2000	nd[c]	>5000
24	2-Fluorophenyl	–H	200 ± 38	>2000	>5000	1700 ± 760
25	1-Naphthyl	–H	120 ± 26	810 ± 380	>5000	690 ± 360
26	3-Pyridyl	–H	1900 ± 680	nd	670 ± 290	1600 ± 46
27	Tosyl	–H	130 ± 37	2000 ± 200	nd	330 ± 68
28	–H	–Tosyl	>5000	nd	nd	1600 ± 1200
29	–CONHMe	–CONHMe	>5000	>5000	nd	>5000
30	–CONHMe	–H	230 ± 4	nd	>5000	1100 ± 500
31	–CONHBu	–H	150 ± 38	1100 ± 540	>5000	640 ± 39
32	$-CONH(CH_2)_3OH$	–H	360 ± 41	1500 ± 800	>5000	1900 ± 400
33	$-CONH(CH_2)_2N((CH_2)_2)_2O$	–H	520 ± 95	>5000	>5000	470 ± 360
34	–CONHBn	–H	150 ± 70	2100 ± 500	>5000	540 ± 230
35	$-CONH_2$	$-NH_2$	>2000	2700 ± 1700	>5000	>5000
LacNAc derivatives						
39	–CONHMe	–H	3.8 ± 1.1	130 ± 76	>2000	73 ± 6
40	–CONHBn	–H	1.5 ± 0.3	74 ± 25	>2000	12 ± 4
41	1-Naphthyl	–H	0.66 ± 0.09	83 ± 11	>2000	13 ± 8
Thiodigalactoside derivatives						
46	–CONHMe	–H	0.12 ± 0.08	8.0 ± 1.6	81 ± 27	0.91 ± 0.06
47	–CONHBu	–H	0.029 ± 0.07	5.4 ± 0.9	58 ± 5	1.1 ± 0.3
48	–CONHBn	–H	0.39 ± 0.17	8.3 ± 2.1	47 ± 1	0.53 ± 0.22
49	$-CONHCH_2CH_2Ph$	–H	0.15 ± 0.02	2.0 ± 0.4	20 ± 5	1.1 ± 0.4
50	$-CONHCH_2CHCH_2$	–H	0.065 ± 0.040	3.4 ± 0.2	66 ± 22	0.74 ± 0.17
51	$-CONH(CH_2)_3OH$	–H	0.12 ± 0.02	5.0 ± 0.3	58 ± 9	2.1 ± 0.4
52	$-CONH(CH_2)_2OMe$	–H	0.25 ± 0.15	4.7 ± 1.3	90 ± 19	2.3 ± 1.6
References						
53	Me β-D-galactopyranoside		4400[36,38]	4800[36]	5300[36]	3300[36]
54	Me β-LacNAc		59[39]	5500[39]	1000[39]	490[39]
55	Thiodigalactoside		49[22]	160[22]	61[22]	38[22]
56	Me 3′-naphth-2-amido-LacNAc		0.48[20]	>100	>100	>100
57	Di-(3,5-dimethoxybenzamido)-thiodigalactoside		0.050[22]	2.8[22]	≈100[22]	1.8[22]

Methyl β-D-galactose **53**, methyl β-Lac*NA*c **54**, and thiodigalactoside **55** are included as reference compounds, as are the amido-derivatized high-affinity inhibitors 3′-naphth-2-amido-Lac*NA*c glycosides **56**[20] and thiodigalactoside di-(3,5-dimethoxy)-benzamide **57**.[22]

[a] Average and standard deviation of 4–16 single point measurements. Galectin-3, 8N, and 9N were measured at 20 °C and galectin-7 at 4 °C due to a lower assay sensitivity for the latter.

[b] Inhibitor concentrations were chosen to provide reliable K_d values up to 5 mM for monosaccharides **16-35** and 2 mM for disaccharides **39-41** and **46-52**, as higher K_d values are significantly above those for the corresponding reference compounds ligands and hence judged to be insignificant.

[c] Not determined.

ex vivo evaluations.[14,15,37] Furthermore, two aromatic amides were included as reference to our previous work on galectin-3: the Lac*NA*c 2-naphthamide **56**[20] and the thiodigalactoside di-(3,5-dimethoxy)-benzamide **57**[22] were among the most potent galectin-3 inhibitors with K_d of 480 nM and 50 nM, respectively. The monosubstituted triazole **16** was practically non-inhibitory for galectin-3, 8N, and 9N, while the presence of a triazole ring was tolerated by galectin-7. It is clear that the galactose C3-triazole is unfavorable to recognition by the former three galectins. The inhibition potency, however, was recovered for galectin-3 and to a lesser extent for galectin-7 and 9N, by the presence of triazole 4-substitutents. Thus, although the presence of the triazole ring itself decreases the inhibition activity, it positions the substituent at the 4-position to form favorable interactions with galectin-3, 7, and 9N.

For galectin-3, the aliphatic substituted triazoles **18–20** showed inhibition potency similar to the methyl galactoside **53**, while aromatic (**21–25** and **27**) and carbamoyl (**30–34**) substituents at the triazole 4-position resulted in particularly efficient inhibitors approaching the Lac*NA*c disaccharide **54** in affinity. Interestingly, the substitution pattern of the aromatic rings (**21–25** and **27**) appeared to be less important, while introduction of a heteroatom, that is, the 3-pyridyl substituted compound **26**, decreased the inhibitory power. Substitution at C5 of the triazole ring (**28–29** and **35**) was unfavorable to the interaction with galectin-3.

None of the galactosides **16–35** proved to be good inhibitors of galectin-7 or 8N, with one exception for each of these galectins: the 1-naphthyl-substituted compound **25** was five times better than the reference methyl galactoside **53** against galectin-7 and the 3-pyridyl substituted compound **26** showed seven times higher affinity than **53** for galectin-8N. The relatively good affinity of **26** for galectin-8N is most likely a result of a specific interaction of the pyridine nitrogen with galectin-8N, as the corresponding phenyl substituted compound **21** is inactive against this galectin.

On the contrary, galectin-9N was inhibited well by several compounds, albeit still with modest affinity enhancements relative to **53**.

Attaching selected triazole groups onto the better natural galectin ligand Lac*NA*c to obtain two carbamoyl derivatives **39–40** and one 1-naphthyl derivative **41** resulted in affinity enhancing effects

paralleling those observed for the above discussed triazol-1-yl galactosides **25, 30,** and **34**. The 1-naphthyl compound **41** was particularly potent as inhibitor of galectin-3 with a K_d of 660 nM, which in the range of the reported best LacNAc-based inhibitor 3′-(2-naphthamido)-Lac*N*Ac **56**[20] (K_d 480 nM). Analogously, the amides **39** and **40** were low μM inhibitors of galectin-7 and 9N and are as such among the best LacNAc-derived inhibitors reported of these two galectins.

All the thiodigalactoside-derived amide-triazoles **46–52** showed large increases in binding to galectin-3 compared to underivatised thiodigalactoside **55**. In addition, the methylamide **46** affinity enhancement much greater than the analogous LacNAc-derived compound **39** suggesting that both triazole-methyl amide substituents of **46** interact favorably with galectin-3. The best triazolyl thiodigalactoside, the bis-butylamido compound **47**, binds to galectin-3 with a K_d of 29 nM, which is quite remarkable for a carbohydrate–lectin interaction and similar to that of the corresponding benzamides[22] (e.g., **57**). The variation between the different amides **46–52** was relatively low.

Against galectins-7 and -9N, the amides **46–52** once again showed increases in affinity, but not as big as for galectin-3. In contrast, for galectin-8N very small increase for **46–52** or even loss in affinity was observed. Hence, the di-triazolyl thiodigalactosides **46–55** display significant selectivity for galectin-3 over galectin-7, 8N, and 9N, which points to an important advantage these inhibitors.

Examination of a sequence alignment of the different carbohydrate recognition domains reveals a possible explanation for the high affinity of **46–52** for galectin-3, 7, and 9N. The increases in affinity for these three galectin-3 for the thiodigalactoside di-amides (e.g., **57**) were due to cation–π interactions with two arginine side-chains (Arg-144 and Arg-186).[22] The analogous increases for **46–52** could be due to similar double arginine interactions. In both galectins-7 and -9N, both of these arginine residues are also present in the vicinity of the carbohydrate binding site (Arg-31 and Arg-79 for galectin-7; Arg-44 and Arg-87 for galectin-9N). However, for galectin-8, the arginine residue corresponding to Arg-186 in galectin-3 is missing; instead there is an isoleucine residue.

2.3. Conformational analysis and structure–activity relationships

The three 5-substituted triazoles (**28–29** and **35**) were rather poor inhibitors of the galectins. Conformational analysis (MMFFs force field in water implemented in Macromodel 9.0) of the galactose C3–triazole-N1 bond in compounds **16**, **18**, **27–30**, and **35** all showed two minimum conformations: One minimum with the triazole C5 positioned between galactose H3 and O4 and the triazole N1–N3 placed on the α-side of the galactose ring and a second minimum with the triazole turned approximately 180° and the triazole N2 positioned between galactose H3 and O4 (Fig. 1). The former conformation was favored with around 6 kJ/mol for compounds lacking substituents at the triazole C5 (**16 18**, **21**, **27**, and **30**) and is possibly the bioactive conformation (Fig. 1a). Support that this conformation is significantly populated came from the observation of strong NOE (>10%) enhancements between the galactose H2 and the triazole H5 in compounds **21** and **27**. However, the corresponding conformation was disfavored in the 5-substituted triazoles **28–29** by 20–30 kJ/mol. Thus, compounds **28–29** predominantly populate conformations that project the triazole C5-substituent into a position bound to interfere sterically with the galectin surfaces, that is, to the conserved tryptophan residue that stacks with the β-galactoside α-face of ligands (Fig. 1b). The compound carrying a smaller amino-substituent at triazole C5 (**35**) displayed similar energy for both minima and consequently showed intermediate inhibitory power for galectin-3, 7, and 9N.

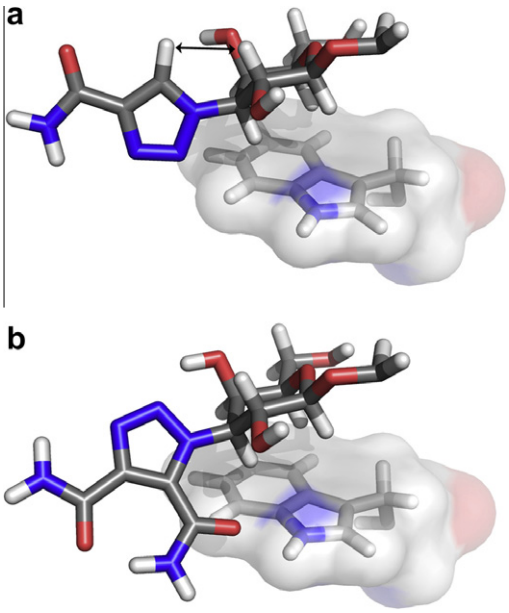


Figure 1. (a) Conformational analysis and NOE experiment of **21** show that it adopts a conformation with the triazole C5 almost antiperiplanar to galactose H3. This conformation is supported by ≈10% NOE from the triazole H5 to galactose H2 (depicted by a black arrow). (b) Conformational analysis and NOE experiment of **29** show it adopts a conformation with the triazole N2 almost antiperiplanar to galactose H3. This conformation positions the triazole C5 substituent in a steric clash with the galectin's conserved tryptophan residue onto which galactose forms a CH–π stacking interaction.

3. Conclusions

In conclusion, we reported the synthesis of a novel class of galectin inhibitors distinguished by their easy preparation, high stability, and high activity that could be applied to monosaccharide and disaccharides. The affinity of Lac*N*Ac C3′-triazoles and thiodigalactoside C3,C3′-di-triazoles reported herein equals that of the corresponding high-affinity aromatic amido compounds, but have an important advantage in that they are easier to synthesize. In particular, the thiodigalactoside derivatives, such as **47**, are promising for development of clinically useful galectin-3 inhibitors due to their low nM affinity, high selectivity over galectin-7, 8N, and 9N, less complex synthesis, and expected improved hydrolytic stability relative to *O*-glycosidic inhibitors.

4. Experimental

4.1. General

Melting points were recorded on a Kofler apparatus (Reichert) and are uncorrected. ^{1}H NMR spectra were recorded with Bruker DRX-400 or ARX-300 instruments. Chemical shifts are reported relative to Me_4Si and were calculated using the residual solvent peak as a reference. Chemical shifts and coupling constants were obtained from ^{1}H NMR spectra and proton resonances were assigned from COSY experiments. Low- and high-resolution (HRMS) fast atom bombardment mass spectra were recorded using a JEOL SX-120 instrument. Matrix-assisted laser desorption/ionization-time of flight mass spectroscopy (MALDI-TOF MS) was carried out with a Bruker Biflex III instrument with gentisic acid as matrix. Optical rotations were measured on a Perkin–Elmer 341 polarimeter with a path length of 1 dm; concentrations are given in g per 100 mL. Thin layer chromatography (TLC) was carried out on Merck Kieselgel sheets, pre-coated with $60F^{254}$ silica. Plates were developed using 10% sulfuric acid. Column Chromatography was performed

on SiO_2 (Matrex, 60 Å, 35 ± 70 μm, Grace Amicon) and thin layer chromatography (TLC) was carried out on $60F^{254}$ silica (Merck). Solutions were concentrated by using rotary evaporation with a bath temperature at or below 40 °C. Dichloromethane was distilled from calcium hydride immediately before use. Acetonitrile was distilled from calcium hydride and stored over 4 Å molecular sieves. All other reagents and solvents were used as supplied. Affinities of compounds for galectins were determined in a competitive fluorescence polarization assay as described previously.[35,36] Molecular modeling was performed with the MMFFs force field with water implemented in MacroModel (version 9.1, Schrödinger, LLC, New York, 2005). Starting conformations were built from the published crystal structure of galectin-3 in complex with a C3′-amido-derivatised LacNAc-based inhibitor,[20] The minimizations converged in all cases and the binding modes and overall structures of the minimized complexes closely resembled that of the crystal structures used for building starting conformations.

4.2. General procedures for the preparation of triazoles 2–15 and 37–38

Method A for compounds **3–12** and **37–38**: A mixture of methyl 2,4,6-tri-*O*-acetyl-3-azido-3-deoxy-1-thio-β-D-galactopyranoside **1**[20] (10 mg, 0.028 mmol) for **3–12** or methyl 2,4,6-tri-*O*-acetyl-3-azido-3-deoxy-β-D-galactopyranosyl-(1–4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranoside **36**[33] (10 mg, 0.0158 mmol) for **37** and **38**, the acetylene derivative (x, 1 equiv), CuI (0.5 mg, 0.1 equiv), diisopropylethylamine (1 equiv) and toluene (1 mL) was stirred together for (*t*) time at (*T*) temperature. The solvent was evaporated and the product was purified by column chromatography using the eluent indicated in each case.

Method B for compounds **2** and **13–15**: A mixture of methyl 2,4,6-tri-*O*-acetyl-3-azido-3-deoxy-1-thio-β-D-galactopyranoside[19] (10 mg, 0.028 mmol), the corresponding acetylene derivative (x, 4 equiv) and toluene (1.5 mL) was heated at (*T*) temperature for 12 h. After evaporation of the solvent, the product was purified by column chromatography using the eluent indicated in each case.

4.2.1. Methyl 2,4,6-tri-i-acetyl-3-(1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 2

Method B, x = propiolic acid, *t* = 17 h, *T* = 80 °C, column eluent heptane–ethyl acetate 3:2. Yield 8.7 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (br d, 1H, $J_{H,H}$ = 0.8, triazole), 7.61 (br d, 1H, triazole), 5.71 (dd, 1H, $J_{2,3}$ = 11.0, H-2), 5.57 (d, 1H, H-4), 5.19 (dd, 1H, $J_{3,4}$ = 3.2, H-3), 4.56 (d, 1H, $J_{1,2}$ = 9.5, H-1), 4.14 (s, 3H, H-5, 2H-6), 2.25, 2.05, 2.04, 1.91 (4s, each 3H, $4CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.5, 168.6 (3C=O), 133.8, 122.0 (C-4′, C-5′), 84.1 (C-1), 75.3 (C-5), 68.7 (C-4), 65.4 (C-2), 62.7 (C-3), 61.3 (C-6), 20.6, 20.4, 20.3 ($3CH_3C$=O), 11.5 (CH_3S). MALDI-TOF MS for $C_{15}H_{22}N_3O_7S$ $[M+H]^+$ 388.

4.2.2. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-methoxycarbonyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 3

Method A, x = methyl propiolate, *t* = 12 h, *T* = rt, column eluent heptane–ethyl acetate 3:2. Yield 11.6 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H, H-5′), 5.70 (dd, 1H, $J_{1,2}$ = 9.5, H-1), 5.57 (d, 1H, $J_{3,4}$ = 3.2, H-4), 5.18 (dd, 1H, H-3), 4.55 (d, 1H, $J_{1,2}$ = 9.5, H-1), 4.14 (m, 3H, H-5, 2H-6), 3.93 (s, 3H, CH_3O), 2.25, 2.08, 2.04, 1.92 (4s, each 3H, $4CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.7, 169.9, 169.2, 161.0 (4C = O), 140.6 (C-4′), 126.8 (C-5′), 84.6 (C-1), 75.8 (C-5), 68.9 (C-4), 65.9 (C-2), 63.8 (C-3), 61.7 (C-6), 52.7 (CH_3O), 21.0, 20.9, 20.8 ($3CH_3C$=O), 11.9 (CH_3S). MALDI-TOF MS for $C_{17}H_{24}N_3O_9S$ $[M+H]^+$ 446.

4.2.3. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-propyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 4

Method A, x = 1-pentyne, *t* = three days, *T* = 50 °C, column eluent heptane–ethyl acetate 5:2. Yield 11.9 mg, 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 1H, H-5′), 5.66 (dd, 1H, $J_{2,3}$ = 11.1, H-2), 5.55 (d, 1H, H-4), 5.12 (dd, 1H, $J_{3,4}$ = 3.2, H-3), 4.53 (d, 1H, $J_{1,2}$ = 9.5, H-1), 2.65 (td, 2H, $J_{H,H}$ = 7.2, $J_{H,H}$ = 1.4, CH_2Ar), 2.24, 2.05, 2.04, 1.91 (4s, each 3H, $4CH_3$), 1.69–1.57 (m, 2H, CH_2), 0.89 (t, 3H, $J_{H,H}$ = 7.3, CH_3CH_2). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.5, 168.5 (3C=O), 148.3 (C-4′), 119.1 (C-5′), 84.2 (C-19,) 75.3 (C-5), 68.8 (C-4), 65,5 (C-2), 62.6 (C-3), 61.3 (C-6), 27.4 (CH_2Ar), 22.6 (CH_2), 20.5, 20.4, 20.3 ($3CH_3C$=O), 13.3 (CH_2), 11.5 (CH_3S). MALDI-TOF MS for $C_{18}H_{28}N_3O_7S$ $[M+H]^+$ 430.

4.2.4. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-hydroxymethyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 5

Method A, x = propargyl alcohol, *t* = 12 h, *T* = rt, column eluent heptane–ethyl acetate 3:1. Yield 11.0 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H, H-5′), 5.70 (dd, 1H, $J_{2,3}$ = 11.0, H-2), 5.54 (d, 1H, $J_{3,4}$ = 3.0, H-4), 5.14 (br d, 1H, H-3), 4.80–4.70 (m, 2H, CH_2OH), 4.55 (d, 1H, $J_{1,2}$ = 9.5, H-1), 4.14 (s, 3H, H-5, 2H-6), 2.25, 2.06, 2.04, 1.93 (4s, each 3H, $4CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.5, 168.8 (3C=O), 147.9 (C-4′), 120.4 (C-5′), 84.1 (C-1), 75.3 (C-5), 68.7 (C-4), 65.4 (C-2), 62.8 (C-3), 61.4 (C-6), 56.4 (CH_2), 20.6, 20.5, 20.3 ($3CH_3C$=O), 11.4 (CH_3S). MALDI-TOF MS $[M+H]^+$ 418, $[M+Na]^+$ 440.

4.2.5. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-(1-hydroxycyclohexyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 6

Method A, x = 1-ethynyl-1-cyclohexanol, *t* = 12 h, *T* = rt, column eluent heptane–ethyl acetate 3:2. Yield 12.0 mg, 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H, H-5′), 5.67 (dd, 1H, $J_{2,3}$ = 11.0, H-2), 5.54 (d, 1H, H-4), 5.13 (dd, 1H, $J_{3,4}$ = 3.2, H-3), 4.55 (d, 1H, $J_{1,2}$ = 9.6, H-1), 4.13 (s, 3H, H-5, 2H-6), 2.24, 2.05, 2.04, 1.91 (4s, each 3H, $4CH_3$), 1.81–1.25 (m, 11H, cyclohexyl). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.4, 168.6 (3C=O), 155.7 (C-4′), 118.4 (C-5′), 84.1 (C-1), 75.3 (C-5), 69.4 (cyclohexyl C-1), 68.8 (C-4), 65.5 (C-2), 62.7 (C-3), 61.3 (C-6), 38.1, 38.0, 25.2, 21.9, 21.8 (cyclohexyl), 20.5, 20.4, 20.3 ($3CH_3C$=O), 11.5 (CH_3S). MALDI-TOF MS for $C_{21}H_{32}N_3O_8S$ $[M+H]^+$ 486.

4.2.6. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-phenyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 7

Method A, x = phenylacetylene, *t* = three days, *T* = rt, column eluent heptane–ethyl acetate 5:2. Yield 12.1 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H, H-5′), 7.80–7.78 (m, 2H, *o*-Ph), 7.44–7.40 (m, 2H, *p*-Ph), 7.34 (tt, 1H, $J_{o,m}$ = 7.3, $J_{o,p}$ = 1.1, *p*-Ph), 5.76 (dd, 1H, $J_{2,3}$ = 11.0, H-2), 5.62 (d, 1H, H-4), 5.19 (dd, 1H, $J_{3,4}$ = 3.2, H-3), 4.57 (d, 1H, $J_{1,2}$ = 9.5, H-1), 4.15 (s, 3H, H-4), 2.27, 2.06, 2.05, 1.93 (4s, each 3H, $3CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.6, 168.6 (3C=O), 147.8 (C-4′), 129.9, 128.8 [2C], 128.3, 128.6 [2C] (Ph), 117.9 (C-5′), 84.1 (C-1), 75.4 (C-5), 68.8 (C-4), 65.4 (C-2), 62.9 (C-3), 61.4 (C-6), 20.6, 20.4, 20.3 ($3CH_3C$=O), 11.5 (CH_3S). MALDI-TOF MS for $C_{21}H_{26}N_3O_7S$ $[M+H]^+$ 464.

4.2.7. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-(3-methoxyphenyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 8

Method A, x = 1-ethynyl-3-methoxybenzene, *t* = seven days, *T* = 40 °C, column eluent heptane–ethyl acetate 5:2. Yield 10.4 mg, 76%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H, H-5′), 7.42–7.30 (m, 3H, Ar), 6.91–6.88 (td, 1H, $J_{H,H}$ = 2.4, 7.0, Ar), 5.75 (dd, 1H, $J_{2,3}$ = 11.0, H-2), 5.62 (d, 1H, $J_{3,4}$ = 3.1, H-4), 5.18 (dd, 1H, H-3), 4.57 (d, 1H, $J_{1,2}$ = 9.5, H-1), 4.15 (s, 3H, H-5, 2H-6), 3.87 (s, 3H, CH_3O), 2.26, 1.93 (2s, each 3H, $2CH_3$), 2.06 (s, 6H, $2CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.6, 168.6 (3C=O), 160.0,

147.7, 131.2 (C-4′, C1-Ph, C3-Ph), 129.8, 118.0, 114.4, 110.8 (Ph), 118.2 (C-5′), 84.2 (C-1), 75.4 (C-5), 68.8 (C-4), 65.4 (C-2), 62.9 (C-3), 61.4 (C-6), 55.3 (CH_3O), 20.6, 20.4, 20.3 ($3CH_3C{=}O$), 11.5 (CH_3S). MALDI-TOF MS $[M+H]^+$ = 494, $[M+Na]^+$ = 516.

4.2.8. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-(4-methoxyphenyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 9

Method A, x = 1-ethynyl-4-methoxybenzene, *t* = seven days, *T* = 40 °C, column eluent heptane–ethyl acetate 5:2. Yield 10.1 mg, 74%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H, H-5′), 7.71 (m, 2H, *m*-Ph), 6.95 (m, 2H, *o*-Ph), 5.75 (dd, 1H, H-2), 5.62 (d, 1H, $J_{1,2}$ = 9.5, H-4), 5.17 (dd, 1H, $J_{2,3}$ = 11.1, H-3), 4.56 (d, 1H, $J_{1,2}$ = 9.5, H-1), 4.15 (s, 3H, H-5, 2H-6), 3.84 (s, 3H, CH_3O), 2.27, 1.96 (2s, each 3H, $2CH_3$), 2.05 (s, 6H, $2CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.6, 168.6 (3C═O), 159.7, 147.7, 122.6 (C-4′, C1-Ph, C4-Ph), 127.0 [2C], 114.2 [2C] (Ph), 117.1 (C-5′), 84.2 (C-1), 75.4 (C-5), 68.8 (C-4), 65.4 (C-2), 62.8 (C-3), 61.4 (C-6), 55.7 (CH_3O), 20.6, 20.5, 20.3 ($3CH_3C{=}O$), 11.5 (CH_3S). MALDI-TOF MS $[M+H]^+$ = 494, $[M+Na]^+$ = 516.

4.2.9. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-(2-fluorophenyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 10

Method A, x = 1-ethynyl-2-fluorobenzene, *t* = 12 h, *T* = 40 °C, column eluent heptane–ethyl acetate 5:2. Yield 13.3 mg, 99%. ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (dt, 1H, *J* = 1.8, 7.8, Ar), 7.98 (d, 1H, $J_{H,F}$ = 3.5, H-5′), 7.31 (m, 1H, Ar), 7.27–7.12 (m, 2H, Ar), 7.13 (ddd, 1H, *J* = 1.1, 8.2, 9.3, Ar), 5.75 (dd, 1H, H-2), 5.61 (d, 1H, $J_{3,4}$ = 3.2, H-4), 5.20 (dd, 1H, $J_{2,3}$ = 11.1, H-3), 4.57 (d, 1H, $J_{1,2}$ = 9.6, H-1), 4.16 (s, 3H, H-5, 2H-6), 2.27, 2.10, 2.05, 1.92 (4s, each 3H, $4CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.4, 168.8 (3C═O), 159.2 (d, J_{C-F} = 248, C2-Ph), 141.3 (d, J_{C-F} = 2.3, C-4′), 129.5 (d, J_{C-F} = 8.5, Ar), 127.8 (d, J_{C-F} = 3.4, Ar), 124.5 (d, J_{C-F} = 3.2, Ar), 121.2 (d, J_{C-F} = 13, C-5′), 118.0 (d, J_{C-F} = 13, C1-Ph,), 115.6 (d, J_{C-F} = 22, Ar), 84.2 (C-1), 75.4 (C-5), 68.6 (C-4), 65.5 (C-2), 62.9 (C-3), 61.4 (C-6), 20.6, 20.4, 20.2 ($3CH_3C{=}O$), 11.5 (CH_3S). MALDI-TOF MS $[M+H]^+$ = 482, $[M+Na]^+$ = 504.

4.2.10. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-(1-naphthyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 11

Method A, x = 1-ethynylnaphthalene, *t* = five days, *T* = 40 °C, column eluent heptane–ethyl acetate 5:2. Yield 11.9 mg, 84%, ^1H NMR (400 MHz, $CDCl_3$) δ 8.20–8.17 (m, 1H, Ar), 7.92–7.89 (m, 2H, Ar), 7.87 (s, 1H, H-5′), 7.65 (dd, 1H, $J_{H,H}$ = 7.2, 1.1, Ar), 7.55–7.50 (m, 3H, Ar), 5.80 (dd, 1H, H-2), 5.71 (d, 1H, H-4), 5.28 (dd, 1H, $J_{2,3}$ = 11.1, $J_{3,4}$ = 3.2, H-3), 4.61 (d, 1H, $J_{1,2}$ = 9.5, H-1), 4.19–4.17 (m, 3H, H-5, 2H-6), 2.23, 2.07, 2.06, 1.99 (4s, each 3H, $4CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.6, 168.7 (3C═O), 146.9, 133.7, 131.1, 129.1, 128.4, 127.4, 127.3, 126.7, 125.9, 125.2, 125.0 (C-4′, naphthalene), 121.1 (C-5′), 84.2 (C-1), 75.4 (C-5), 68.8 (C-4), 65.6 (C-2), 63.0 (C-3), 61.3 (C-6), 20.6, 20.5, 20.4 ($3CH_3C{=}O$), 11.5 (CH_3S). MALDI-TOF MS $[M+H]^+$ = 514.

4.2.11. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-(3-pyridyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 12

Method A, x = 3-ethynyl pyridine, *t* = two days, *T* = 40 °C, column eluent toluene–acetone 3:1. Yield 12.0 mg, 94%, ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (br d, 1H, *J* = *6.8,* Ar), 7.92 (s, 1H, H-5′), 7.80–7.25 (bs, 1H, Ar), 7.27–7.23 (m, 1H, Ar), 7.18–7.14 (m, 1H, Ar), 5.78 (dd, 1H, H-2), 5.62 (d, 1H, $J_{3,4}$ = 3.1, H-4), 5.20 (dd, 1H, $J_{2,3}$ = 11.1, H-3), 4.58 (d, 1H, $J_{1,2}$ = 9.5, H-1), 2.27, 2.08, 2.06, 1.94 (4s, each 3H, $4CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ = 170.3, 169.5, 168.7 (3C═O), 133.0, 128.9, 128.1, 125.2 (C-4′, pyridine), 118.7 (C-5′), 84.1 (C-1), 75.3 (C-5), 68.7 (C-4), 65.5 (C-2), 63.1 (C-3), 61.3 (C-6), 20.6, 20.5, 20.4 ($3CH_3C{=}O$), 11.4 (CH_3S). MALDI-TOF MS $[M+H]^+$ = 465, $[M+Na]^+$ = 487.

4.2.12. Methyl 2,4,6-tri-*O*-acetyl-3-(4-p-tolylsulfonyl-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 13 and methyl 2,4,6-tri-*O*-acetyl-3-(5-p-tolylsulfonyl-1H-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 14

Method B, x = ethynyl-*p*-tolylsulfone, *t* = 20 h, *T* = 65 °C, column eluent heptane–ethyl acetate 5:1–7:2 gradient, gave 13 (5.7 mg, 38%) and 14 (7.8 mg, 52%). ^1H NMR for **13** (400 MHz, $CDCl_3$) δ 8.17 (s, 1H, H-5′), 7.88 (d, 2H, $J_{H,H}$ = 8.4, Ph), 7.33 (d, 2H, Ph), 5.64 (dd, 1H, $J_{2,3}$ = 11.0, H-2), 5.51 (d, 1H, H-4), 5.15 (dd, 1H, $J_{3,4}$ = 3.2, H-3), 4.53 (d, 1H, $J_{1,2}$ = 9.5, H-1), 4.12 (m, 3H, H-5, 2H-6), 2.42, 2.23, 2.03, 2.00, 1.87 (5s, each 3H, $5CH_3$). ^{13}C NMR for **13** (100.6 MHz, $CDCl_3$) δ 170.2, 169.3, 168.6 (3C═O), 149.5, 145.0, 139.9 (C-4′, Ph C-1, Ph C-4), 129.8, 127.9 (each 2C, Ph), 124.9 (C-5′), 83.9 (C-1), 75.2 (C-5), 68.3 (C-4), 65.2 (C-2), 63.5 (C-3), 61.1 (C-6), 21.6, 20.5, 20.3, 20.1 ($3CH_3C{=}O$, CH_3Ph), 11.4 (CH_3S). FAB-HRMS calcd for **13** $C_{22}H_{27}O_9N_3NaS_2$ $[M+Na]^+$ 564.1086; found 564.1103. ^1H NMR for **14** (400 MHz, $CDCl_3$) δ 7.88 (d, 2H, $J_{H,H}$ = 8.3, *o*-Ph), 7.87 (s, 1H, H-4′), 7.43 (d, 2H, *m*-Ph), 6.06 (t, 1H, H-2), 5.43 (dd, 1H, $J_{2,3}$ = 10.7, H-3), 5.25 (d, 1H, $J_{3,4}$ = 2.6, H-4), 4.50 (d, 1H, $J_{1,2}$ = 9.7, H-1), 4.19–4.08 (m, 3H, H-5, 2H-6), 2.47, 2.25, 2.05, 1.99, 1.73 (5s, each 3H, $5CH_3$). ^{13}C NMR for **14** (100.6 MHz, $CDCl_3$) δ 170.3, 169.5, 168.3 (3C═O), 146.5, 138.2, 136.3 (Ph C-1, Ph C-4, C-5′), 136.8 (C-4′), 130.3, 127.9 (each 2C, Ph), 84.1 (C-1), 75.1 (C-5), 67.6 (C-4), 65.3 (C-2), 62.4 (C-3), 61.6 (C-6), 21.7, 20.6, 20.3, 20.2, 11.1 ($5CH_3$). FAB-HRMS calcd for **14** $C_{22}H_{27}O_9N_3NaS_2$ $[M+Na]^+$ 564.1086; found 564.1081.

4.2.13. Methyl 2,4,6-tri-*O*-acetyl-3-(4,5-bis-methoxycarbonyl-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 15

Method B, x = dimethyl acetylenedicarboxylate, *T* = 80 °C, 12 h, column eluent heptane–ethyl acetate 1:1. Yield 13.9 mg, 99%. ^1H NMR (400 MHz, $CDCl_3$) δ 6.12 (dd, 1H, $J_{2,3}$ = 10.6, H-2), 5.59 (d, 1H, H-4), 5.45 (dd, 1H, $J_{3,4}$ = 2.9, H-3), 4.49 (d, 1H, $J_{1,2}$ = 9.7, H-1), 4.24–4.14 (m, 3H, H-5, 2H-6), 4.02 (s, 3H, CH_3O), 2.26, 2.03, 2.01, 1.87 (each s, each 3H, $4CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 169.7, 168.3, 160.2, 158.9 (5C═O), 140.5, 129.5 (C-4′, C-5′), 84.2 (C-1), 75.1 (C-5), 67.7 (C-4), 65.3 (C-2), 62.8 (C-3), 61.5 (C-6), 53.5, 52.7 ($2CH_3O$), 20.6, 20.4, 20.2 ($3CH_3C{=}O$), 11.1 (CH_3S). MALDI-TOF MS $[M+H]^+$ 504, $[M+Na]^+$ 526.

4.2.14. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-methoxycarbonyl-1*H*-[1,2,3]-triazol-1-yl)-β-D-galactopyranosyl-(1–4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranoside 37

Method A, x = methyl propiolate, *t* = 24 h, *T* = 45 °C, column eluent toluene–acetone 2:1. Yield 10.1 mg, 90%. ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H, H-5″), 5.64 (d, 1H, $J_{2,NH}$ = 9.4, NH), 5.55 (dd, 1H, $J'_{2,3'}$ = 11.5, H-2′), 5.49 (d, 1H, $J'_{3,4'}$ = 3.2, H-4′), 5.16 (dd, 1H, H-3′), 5.12 (dd, 1H, $J_{2,3}$ = 9.7, H-3), 4.68 (d, 1H, $J_{1',2'}$ = 7.6, H-1′), 4.49 (dd, 1H, $J_{5,6a}$ = 2.6, $J_{H,H}$ = 11.9, H-6a), 4.40 (d, 1H, $J_{1,2}$ = 7.7, H-1), 4.16 (dd, 1H, $J_{5,6b}$ = 5.4, H-6b), 4.10 (s, 3H, H-5′, 2H-6′), 4.03 (dt, 1H, H-2), 3.93 (s, 3H, CH_3O), 3.83 (t, 1H, *J* = 8.7, H-4), 3.65 (ddd, 1H, H-5), 3.46 (s, 3H, CH_3O), 2.14 (s, 3H, CH_3), 2.08 (s, 6H, $2CH_3$), 2.05, 1.98, 1.89 (each s, each 3H, $3CH_3C{=}O$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.6, 170.3, 170.2, 170.1, 169.0, 168.7, 160.5 (7C═O), 140.1 (C-4″), 126.7 (C-5″), 101.7 (C-1), 101.0 (C-1′), 75.7 (C-4′), 72.5 (C-5), 72.1 (C-3), 71.7 (C-5′), 67.8 [2C] (C-2′, C-4′), 62.1 (C-3′), 62.0 (C-6), 60.7 (C-6′), 56.6 (CH_3O), 53.2 (C-2), 52.2 (CH_3O), 23.2, 20.7 [2C], 20.5, 320.2, 20.1 ($6CH_3$). FAB-HRMS calcd for $C_{29}H_{41}N_4O_{17}$ $[M+H]^+$ 717.2467; found, 717.2457.

4.2.15. Methyl 2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-(1-naphthyl)-1*H*-[1,2,3]-triazol-1-yl)-β-D-galactopyranosyl-(1–4)-2-acetamido-2-deoxy-3,6-di-*O*-acetyl-β-D-glucopyranoside 38

Method A, x = 1-ethynylnaphthalene, *t* = 24 h, *T* = 45 °C, column eluent toluene–acetone 3:1. Yield 12.4 mg, 99%. ^1H NMR (400 MHz,

$CDCl_3$) δ 8.17 (m, 1H, Ar), 7.89 (m, 2H, Ar), 7.84 (s, 1H, H-5″), 7.64 (dd, 1H, $J_{H,H}$ = 1.0, 7.1, Ar), 7.53–7.49 (m, 3H, Ar), 5.68–5.62 (m, 3H, NH, H-4′, H-2′), 5.24 (dd, 1H, $J_{2',3'}$ = 11.5, $J_{3',4'}$ = 3.2, H-3′), 5.14 (dd, 1H, $J_{2,3}$ = 9.8, $J^{3,4}$ = 8.4, H-3), 4.73 (d, 1H, $J_{1',2'}$ = 7.6, H-1′), 4.53 (dd, 1H, $J_{6a,6b}$ = 11.9, $J_{5,6a}$ = 2.6, H-6a), 4.40 (d, 1H, $J_{1,2}$ = 7.7, H-1), 4.18 (dd, 1H, $J_{5,6b}$ = 5.2, H-6b), 4.14 (m, 3H, H-5′, 2H-6′), 4.04 (q, 1H, $J_{H,H}$ = 9.5, H-2), 3.86 (t, 1H, $J_{H,H}$ = 8.7, H-4), 3.68–3.64 (m, 1H, H-5), 3.46 (s, 3H, CH_3O), 2.14, 2.10, 2.07, 2.05, 1.97, 1.95 (6s, each 3H, $6CH_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.6, 170.4, 170.3, 170.1, 169.2, 168.7 (6C=O), 146.9, 133.7, 131.0, 129.1, 128.4, 127.3, 126.7, 126.0, 125.2, 124.9 (C-4″, naphthalene), 121.5 (C-5″), 101.7 (C-1), 101.2 (C-1′), 75.8 (C-4), 72.6 (C-5), 72.2 (C-3), 71.9 (C-5′), 68.2 (C-4′), 68.0 (C-2′), 62.1, 61.9 (C-3′, C-6), 60.8 (C-6′), 56.6 (CH_3O), 53.3 (C-2), 23.2, 20.8 [2C], 20.5, 20.4, 20.3 (CH_3C=O). FAB-HRMS calcd for $C_{37}H_{44}N_4NaO_{15}$ $[M+Na]^+$ 807.2701; found 807.2697.

4.3. General procedure for de-*O*-acetylation of compounds 2 and 4–14 to give 16 and 18–28

The protected sugar (10 mg) was dissolved in methylamine (40% solution in water, 2 mL) and stirred overnight. The mixture was concentrated and the product was purified by column chromatography.

4.3.1. Methyl 3-deoxy-3-(1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 16

Compound **2** gave **16** (column eluent CH_2Cl_2–MeOH 17:1, 6.0 mg, 90%). ^{1}H NMR (400 MHz, CD_3OD) δ 8.08 (d, 1H, $J_{H,H}$ = 1.0, triazole), 7.74 (d, 1H, triazole), 4.83 (dd, 1H, $J_{3,4}$ = 3.0, $J_{2,3}$ = 10.5, H-3), 4.46 (d, 1H, $J_{1,2}$ = 9.4, H-1), 4.20 (dd, 1H, H-2), 4.09 (d, 1H, H-4), 3.80–3.66 (m, 3H, H-5, 2H-6), 2.25 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, CD_3OD) δ 133.8, 125.4 (C-4′, C-5′), 88.7 (C-1), 81.0 (C-5), 69.8 (C-4), 68.8 (C-3), 67.7 (C-2), 62.4 (C-6), 12.6 (CH_3S). FAB-HRMS calcd for $C_9H_{15}N_3NaO_4S$ $[M+Na]^+$ 284.0681; found 284.0677.

4.3.2. Methyl 3-deoxy-3-(4-propyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 18

Compound **4** gave **18** (column eluent CH_2Cl_2–MeOH 20:1, 5.5 mg, 77%). ^{1}H NMR (400 MHz, CD_3OD) δ 7.82 (s, 1H, H-5′), 4.72 (dd, 1H, $J_{3,4}$ = 3.0, H-3), 4.44 (d, 1H, $J_{1,2}$ = 9.4, H-1), 4.17 (dd, 1H, $J_{2,3}$ = 10.4, H-2), 4.07 (d, 1H, H-4), 3.78–3.67 (m, 3H, H-5, 2H-6), 2.67 (t, 2H, $J_{H,H}$ = 7.5, CH_2), 2.25 (s, 3H, CH_3S), 1.69 (m, 2H, CH_2), 0.97 (t, 3H, $J_{H,H}$ = 7.3, CH_3). ^{13}C NMR (100.6 MHz, CD_3OD) δ 148.4 (C-4′), 122.8 (C-5′), 88.8 (C-1), 81.1 (C-5), 69.8 (C-4), 68.8 (C-3), 67.7 (C-2), 62.4 (C-6), 28.5 (CH_2), 23.8 (CH_2), 14.1 (CH_3), 12.1 (CH_3S). FAB-HRMS calcd for $C_{12}H_{22}N_3O_4S$ $[M+H]^+$ 304.1331; found, 304.1346.

4.3.3. Methyl 3-deoxy-3-(4-hydroxymethyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 19

Compound **5** gave **19** (column eluent CH_2Cl_2–MeOH 12:1, 5.6 mg, 80%). ^{1}H NMR (400 MHz, CD_3OD) δ 8.01 (s, 1H, H-5′), 4.76 (dd, 1H, $J_{2,3}$ = 10.6, H-3), 4.69 (s, 2H, CH_2), 4.46 (d, 1H, $J_{1,2}$ = 9.3, H-1), 4.19 (dd, 1H, H-2), 4.09 (d, 1H, $J_{3,4}$ = 2.8, H-4), 3.79–3.65 (m, 3H, H-5, 2H-6), 2.25 (s, 3H, CH_3). ^{13}C NMR (100.6 MHz, CD_3OD) δ 148.4 (C-4′), 123.8 (C-5′), 88.7 (C-1), 81.0 (C-5), 69.8 (C-4), 68.9 (C-3), 67.7 (C-2), 62.4 (C-6), 56.6 (CH_2), 12.1 (CH_3S). FAB-HRMS $C_{10}H_{17}N_3NaO_5S$ $[M+Na]^+$ 314.0787; found, 314.0791.

4.3.4. Methyl 3-deoxy-3-(4-(1-hydroxycyclohexyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 20

Compound **6** gave **20** (column eluent CH_2Cl_2–MeOH 17:1, 6.9 mg, 87%). ^{1}H NMR (300 MHz, CD_3OD) δ 7.93 (s, 1H, H-5′), 4.74 (dd, 1H, $J_{2,3}$ = 10.6, $J_{3,4}$ = 3.0, H-3), 4.45 (d, 1H, $J_{1,2}$ = 9.4, H-1), 4.18 (dd, 1H, H-2), 4.08 (d, 1H, H-4), 3.82–3.53 (m, 3H, H-5, 2H-6), 2.25 (s, 3H, CH_3S), 2.02–1.28 (m, 10H, cyclohexyl). ^{13}C NMR (75 MHz, CD_3OD) δ 156.3 (C-4′), 121.9 (C-5′), 88.7 (C-1), 81.0 (C-5), 70.4 (cyclohexyl), 69.8 (C-4), 68.8 (C-3), 67.7 (C-2), 62.3 (C-6), 38.9 [2C], 26.6, 23.1 [2C] (cyclohexyl), 12.1 (CH_3S). FAB-HRMS calcd for $C_{15}H_{26}N_3O_5S$ $[M+H]^+$ 360.1593; found, 360.1596.

4.3.5. Methyl 3-deoxy-3-(4-phenyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 21

Compound **7** gave **21** (column eluent heptane–ethyl acetate 1:3, 6.5 mg, 90%). ^{1}H NMR (400 MHz, CD_3OD) δ 7.84–7.81 (m, 2H, *o*-Ph), 7.45–7.41 (m, 2H, *m*-Ph), 7.33 (tt, 1H, $J_{m,p}$ = 7.4, $J_{o,p}$ = 1.2, *p*-Ph), 4.83 (dd, 1H, $J_{3,4}$ = 3.0, H-3), 4.49 (d, 1H, $J_{1,2}$ = 9.4, H-1), 4.27 (dd, 1H, $J_{2,3}$ = 10.5, H-2), 4.14 (d, 1H, H-4), 3.82–3.68 (m, 3H, H-5, 2H-6), 2.27 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, CD_3OD) δ 148.3 (C-4′), 131.9, 130.0 [2C], 129.2 [2C], 126.6 (Ph), 121.8 (C-5′), 88.7 (C-1), 81.0 (C-5), 69.8 (C-4), 69.1 (C-3), 67.7 (C-2), 62.4 (C-6), 12.1 (CH_3S). FAB-HRMS calcd for $C_{15}H_{20}N_3O_4S$ $[M+H]^+$ 338.1174; found, 338.1179.

4.3.6. Methyl 3-deoxy-3-(4-(3-methoxyphenyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 22

Compound **8** gave **22** (C18 RP-HPLC eluent H_2O–acetonitrile gradient, 5.6 mg, 75%). ^{1}H NMR (400 MHz, CD_3OD) δ 8.41 (s, 1H, H-5′), 7.42–7.33 (m, 3H, Ar), 6.91–6.88 (m, 1H, Ar), 4.81 (dd, 1H, H-3), 4.49 (d, 1H, $J_{1,2}$ = 9.4, H-1), 4.27 (dd, 1H, $J_{2,3}$ = 10.4, H-2), 4.13 (d, 1H, $J_{3,4}$ = 2.8, H-4), 3.84 (s, 3H, CH_3O), 3.81–3.69 (m, 3H, H-5, 2H-6), 2.27 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, CD_3OD) δ 161.7, 148.2, 133.2 (C-3-Ph, C-1-Ph, C-4′), 131.0, 119.0, 115.0, 111.9 (Ph), 122.0 (C-5′), 88.7 (C-1), 81.0 (C-5), 69.8 (C-4), 69.1 (C-3), 67.7 (C-2), 62.4 (C-6), 55.7 (CH_3O), 12.1 (CH_3S). FAB-HRMS calcd for $C_{16}H_{21}N_3NaO_5S$ $[M+Na]^+$ 390.1100; found 390.1100.

4.3.7. Methyl 3-deoxy-3-(4-(4-methoxyophenyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 23

Compound **9** gave **23** (C18 RP-HPLC eluent H_2O–acetonitrile gradient, 5.4 mg, 72%). ^{1}H NMR (400 MHz, CD_3OD) δ 8.30 (s, 1H, H-5′), 7.76–7.72 (m, 2H, Ph), 7.00–6.97 (m, 2H, Ph), 4.79 (dd, 1H, H-3), 4.48 (d, 1H, $J_{1,2}$ = 9.4, H-1), 4.26 (dd, 1H, $J_{2,3}$ = 10.6, H-2), 4.13 (d, 1H, $J_{3,4}$ = 2.9, H-4), 3.82 (s, 3H, CH_3O), 3.80–3.68 (m, 3H, H-5, 2H-6), 2.27 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, CD_3OD) δ 161.3 (C-4-Ph), 148.3, 124.5 (C-4′, C-1-Ph), 128.0, 115.3 (each 2C, Ph), 121.0 (C-5′), 88.7 (C-1), 81.1 (C-5), 69.8 (C-4), 69.1 (C-3), 67.8 (C-2), 62.4 (C-6), 55.8 (CH_3O), 12.1 (CH_3S). FAB-HRMS calcd for $C_{16}H_{21}N_3NaO_5S$ $[M+Na]^+$ 390.1100; found 390.1103.

4.3.8. Methyl 3-deoxy-3-(4-(2-fluorophenyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 24

Compound **10** gave **24** (C18 RP-HPLC eluent H_2O–acetonitrile gradient, 6.0 mg, 82%). ^{1}H NMR (400 MHz, CD_3OD) δ 8.37 (d, 1H, $J_{H,F}$ = 3.5, H-5′), 8.11 (dd, 1H, *J* = 1.7, 7.7, Ar), 7.38–7.36 (m, 1H, Ar), 7.28 (dt, 1H, *J* = 1.1, 7.7, Ar), 7.22 (ddd, 1H, *J* = 0.9, 8.2, 9.2, Ar), 4.86 (obscured under HDO, H-3), 4.49 (d, 1H, $J_{1,2}$ = 9.3, H-1), 4.86 (t, 1H, $J_{2,3}$ = 10.3, H-2), 4.15 (d, 1H, $J_{3,4}$ = 2.8, H-4), 3.83–3.68 (m, 3H, H-5, 2H-6), 2.27 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, CD_3OD) δ 160.6 (d, $J_{C,F}$ = 248, C-2-Ph), 141.7 (d, $J_{C,F}$ = 2.4, C-4′), 130.8 (d, $J_{C,F}$ = 8.6, Ar), 128.6 (d, $J_{C,F}$ = 3.3, Ar), 125.8 (d, $J_{C,F}$ = 3.6, Ar), 124.3 (d, $J_{C,F}$ = 12.1, C-5′), 119.7 (d, $J_{C,F}$ = 12.1, C-1-Ph), 116.9 (d, $J_{C,F}$ = 21.7, Ar), 88.7 (C-1), 81.0 (C-5), 69.8 (C-4), 69.1 (C-3), 67.7 (C-2), 62.4 (C-6), 12.0 (CH_3S). FAB-HRMS calcd for $C_{15}H_{18}FN_3NaO_4S$ $[M+Na]^+$ 378.0900; found 378.0902.

4.3.9. Methyl 3-deoxy-3-(4-(1-naphthyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 25

Compound **11** gave **25** (C18 RP-HPLC eluent H_2O–acetonitrile gradient, 6.5 mg, 87%). ^{1}H NMR (300 MHz, CD_3OD) δ 8.38 (s, 1H,

H-5′), 8.31–8.27 (m, 1H, Ar), 7.95–7.89 (m, 2H, Ar), 7.70 (dd, 1H, $J_{H,H}$ = 1.1, 7.1, Ar), 7.57–7.49 (m, 3H, Ar), 4.92 (dd, 1H, H-3 partially obscured under HDO peak), 4.53 (d, 1H, $J_{1,2}$ = 9.4, H-1), 4.32 (dd, 1H, $J_{2,3}$ = 10.5, H-2), 4.22 (d, 1H, $J_{3,4}$ = 2.6, H-4), 3.87–3.70 (m, 3H, H-5, 2H-6), 2.28 (s, 3H, CH_3S). ^{13}C NMR (75 MHz, CD_3OD) δ 147.1, 135.4, 132.6, 130.1, 129.5, 129.3, 128.4, 127.7, 127.2, 126.4, 126.3 (C-4′, naphthyl), 124.7 (C-5′), 88.8 (C-1), 81.1 (C-5), 69.9 (C-4), 69.2 (C-3), 67.8 (C-2), 62.4 (C-6), 12.1 (CH_3S). FAB-HRMS $C_{19}H_{21}N_3NaO_4S$ $[M+Na]^+$ 410.1150; found, 410.1150.

4.3.10. Methyl 3-deoxy-3-(4-(3-pyridyl)-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 26

Compound **12** gave **26** (C18 RP-HPLC eluent H_2O–acetonitrile gradient, 5.9 mg, 81%). ^1H NMR (400 MHz, DMSO-*d*6) δ 9.40–8.90 (br s, 2H, Ar), 8.72 (s, 1H, H-5′), 8.24 (d, 1H, $J_{H,H}$ = 7.9, Ar), 7.57 (br s, 1H, Ar), 5.46 (d, 1H, $J_{H,OH}$ = 7.1, OH-2), 5.27 (d, 1H, $J_{H,OH}$ = 6.5, OH-4), 4.81 (dd, 1H, $J_{2,3}$ = 10.6, $J_{3,4}$ = 2.8, H-3), 4.70 (t, 1H, $J_{H,OH}$ = 5.8, OH-6), 4.46 (d, 1H, $J_{1,2}$ = 9.2, H-1), 4.11 (m, 1H, H-2), 3.92 (dd, 1H, H-4), 3.70 (t, 1H, $J_{5,6}$ = 6.4, H-5), 3.56–3.47 (m, 2H, 2H-6), 2.15 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 146.3, 142.9, 132.0, 124.3 (C-4′, Ar), 121.8 (C-5′), 86.3 (C-1), 79.3 (C-5), 67.6 (C-4), 67.2 (C-3), 66.0 (C-2), 60.3 (C-6), 11.3 (CH_3S). FAB-HRMS calcd for $C_{14}H_{18}N_4NaO_4S$ $[M+Na]^+$ 361.0946; found 361.0949.

4.3.11. Methyl 3-deoxy-3-(4-p-tolylsulfonyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 27

Compound **13** gave **27** (column eluent CH_2Cl_2–MeOH 17:1, 5.8 mg, 75%). ^1H NMR (300 MHz, CD_3OD) δ 8.69 (s, 1H, H-5′), 7.91 (d, 2H, $J_{H,H}$ = 8.3, *o*-Ph), 7.41 (d, 2H, $J_{H,H}$ = 8.0, *m*-Ph), 4.88 (dd, 1H, H-3 partially obscured under HDO peak), 4.43 (d, 1H, $J_{1,2}$ = 9.3, H-1), 4.19 (dd, 1H, $J_{2,3}$ = 10.4, H-2), 4.05 (d, 1H, $J_{3,4}$ = 2.9, H-4), 3.78–3.60 (m, 3H, H-5, 2H-6), 2.46, 2.25 (2s, each 3H, $2CH_3$). ^{13}C NMR (75 MHz, CD_3OD) δ 149.6, 146.6, 139.1 (C-4′, C-1-Ph, C-4-Ph), 131.1, 129.0 (each 2C, Ph), 128.0 (C-5′), 88.5 (C-1), 80.8 (C-5), 69.6 (C-3), 69.4 (C-4), 67.5 (C-2), 62.3 (C-6), 21.6 (CH_3Ph), 11.9 (CH_3S). FAB-HRMS calcd for $C_{16}H_{21}N_3NaO_6S_2$ $[M+Na]^+$ 438.0770; found 438.0782.

4.3.12. Methyl 3-deoxy-3-(5-p-tolylsulfonyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 28

Compound **14** gave **28** (C18 RP-HPLC eluent H_2O–acetonitrile gradient, 6.2 mg, 81%). ^1H NMR (300 MHz, CD_3OD) δ 8.24 (s, 1H, H-4′), 7.92 (d, 2H, *o*-Ph), 7.47 (d, 2H, *m*-Ph), 4.97 (dd, 1H, $J_{3,4}$ = 2.8, H-3), 4.66 (t, 1H, $J_{H,H}$ = 9.8, H-2), 4.42 (d, 1H, $J_{1,2}$ = 9.6, H-1), 3.75–3.67 (m, 2H, H-5, 2H-6), 3.57 (dd, 1H, $J_{6a,6b}$ = 13.5, $J_{5,6b}$ = 8.0, H-6b), 2.65, 2.25 (2s, each 3H, $2CH_3$). ^{13}C NMR (75 MHz, CD_3OD) δ 147.9, 139.9, 138.2 (C-5′, C-1-Ph, C-4-Ph), 138.1 (C-5′), 131.7, 129.2 (each 2C, Ph), 88.7 (C-1), 80.9 (C-5), 69.2, 69.1 (C-3, C-4), 66.8 (C-2), 62.2 (C-6), 21.7 (CH_3Ph), 11.8 (CH_3S). FAB-HRMS calcd for $C_{16}H_{21}N_3NaO_6S_2$ $[M+Na]^+$ 438.0770; found 438.0770.

4.3.13. Methyl 3-(4-methoxycarbonyl-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 17

Compound **3** (10 mg, 0.023 mmol) was dissolved in methanol (1.5 mL) and stirred over night at room temperature with sodium methoxide solution 1 M (0.5 mL). The mixture was neutralized with Duolite C 436 (H^+) resin, filtered and concentrated in vacuo. The residue was purified by column chromatography (CH_2Cl_2–MeOH 25:1) to give **17** (5 mg, 70%). ^1H NMR (400 MHz, D_2O) δ 8.73 (s, 1H, H-5′), 5.03 (dd, 1H, $J_{3,4}$ = 3.0, $J_{2,3}$ = 10.7, H-3), 4.65 (d, 1H, $J_{1,2}$ = 9.6, H-1), 4.31 (t, 1H, H-2), 4.22 (d, 1H, H-4), 3.98 (dd, 1H, H-5), 3.95 (s, 3H, CH_3O), 3.80 (dd, 1H, $J_{6a,6b}$ = 11.8, $J_{5,6a}$ = 7.3, H-6a), 3.73 (dd, 1H, $J_{5,6b}$ = 5.0, H-6b), 2.28 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, D_2O) δ 162.8 (C=O), 139.5 (C-4′), 129.0 (C-5′), 87.0 (C-1), 79.6 (C-5), 68.2 (C-4), 67.5 (C-3), 66.4 (C-2), 61.1 (C-6), 53.0 (CH_3O), 11.8 (CH_3S). FAB-HRMS calcd for $C_{11}H_{17}N_3NaO_6S$ $[M+Na]^+$ 342.0734; found, 342.0723.

4.4. General procedure for the preparation of the amides 29–34 and 39–40

The methyl ester **3** (10 mg) for **30–34**, the diester **15** (10 mg) for **29**, or the methyl ester **37** (10 mg) for **38** and **39** were stirred with solution of amine (x) in methanol or water for (*t*) time and at (*T*) temperature. The residue obtained after the evaporation of the solvent was purified by column chromatography using the eluent indicated.

4.4.1. Methyl 3-deoxy-3-(4,5-bis-methylaminocarbonyl-1*H*-[1,2,3]-triazol-1-yl)-1-thio-β-D-galactopyranoside 29

Diester **15**, x = methylamine (40% in H_2O, 2 mL), *t* = 12 h, column eluent CH_2Cl_2–MeOH 10:1 gave **29** (6.8 mg, 92%). ^1H NMR (400 MHz, D_2O) δ 5.38 (dd, 1H, $J_{2,3}$ = 10.2, H-3), 4.72 (t, 1H, H-2), 4.64 (d, 1H, $J_{H,H}$ = 7.6, H-1), 4.28 (d, 1H, H-4), 3.96 (dd, 1H, H-5), 3.80 (dd, 1H, $J_{6a,6b}$ = 11.7, $J_{5,6a}$ = 7.2, H-6a), 3.74 (dd, 1H, $J_{5,6a}$ = 5.0, H-6b), 2.96, 2.95 (2s, each 3H, $2CH_3N$), 2.29 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, D_2O) δ 162.6, 159.5 (2C=O), 139.8, 132.9 (C-4′, C-5′), 87.1 (C-1), 79.7 (C-5), 68.5 (C-4), 67.4 (C-3), 65.8 (C-2), 61.2 (C-6), 26.4, 26.2 ($2CH_3N$), 11.7 (CH_3S). FAB-HRMS calcd for $C_{13}H_{22}N_5O_6S_1$ $[M+H]^+$ 376.1211; found 376.1289.

4.4.2. Methyl 3-(4-methylaminocarbonyl-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 30

Methyl ester **3**, x = methylamine (40% in H_2O, 2 mL), *t* = 12 h, *T* = rt, and column eluent CH_2Cl_2–MeOH 15:1 gave **30** (7.0 mg, 98%). ^1H NMR (400 MHz, CD_3OD) δ 8.43 (s, 1H, H-5′), 4.84 (dd, 1H, $J_{2,3}$ = 10.6, $J_{3,4}$ = 3.0, H-3), 4.46 (d, 1H, $J_{1,2}$ = 9.2, H-1), 4.19 (dd, 1H, H-2), 4.10 (d, 1H, H-4), 3.80–3.67 (m, 3H, H-5, 2H-6), 2.92 (s, 3H, CH_3N), 2.25 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, CD_3OD) δ 163.4 (C=O), 143.5 (C-4′), 126.6 (C-5′), 88.6 (C-1), 81.0 (C-5), 69.6 (C-4), 69.1 (C-3), 67.7 (C-2), 62.4 (C-6), 26.1 (CH_3N), 12.0 (CH3S). FAB-HRMS calcd for $C_{11}H_{18}N_4NaO_5S$ $[M+Na]^+$ 341.0896; found, 341.0892.

4.4.3. Methyl 3-(4-butylaminocarbonyl-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 31

Methyl ester **3**, x = butylamine (20% in MeOH, 1 mL), *t* = 12 h, *T* = rt, and column eluent CH_2Cl_2–MeOH 25:1 gave **31** (7.2 mg, 90%). ^1H NMR (400 MHz, D_2O) δ 8.54 (s, 1H, H-5′), 5.01 (dd, 1H, $J_{2,3}$ = 10.7, H-3), 4.65 (d, 1H, $J_{1,2}$ = 9.6, H-1), 4.32 (t, 1H, H-2), 4.22 (d, 1H, $J_{3,4}$ = 2.8, H-4), 3.98 (dd, 1H, H-5), 3.80 (dd, 1H, $J_{6a,6b}$ = 11.7, $J_{5,6a}$ = 7.3, H-6a), 3.73 (dd, 1H, $J_{5,6b}$ = 5.0, H-6b), 3.40 (t, 2H, $J_{H,H}$ = 7.0, CH_2N), 2.28 (s, 3H, CH_3S), 1.59 (m, 2H, CH_2), 1.37 (m, 2H, CH_2), 0.91 (t, 3H, $J_{H,H}$ = 7.0, CH_3). ^{13}C NMR (100.6 MHz, D_2O) δ 162.3 (C=O), 142.5 (C-4′), 126.4 (C-5′), 87.0 (C-1), 79.7 (C-5), 68.3 (C-4), 67.4 (C-3), 66.4 (C-2), 61.1 (C-6), 39.5 (CH_2N), 30.9 (CH_2), 19.8 (CH_2), 13.3 (CH_3CH_2), 11.8 (CH_3S). FAB-HRMS calcd for $C_{14}H_{25}N_4O_5S$ $[M+H]^+$ 361.1546; found, 361.1542.

4.4.4. Methyl 3-(4-butylaminocarbonyl-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 31

Methyl ester **3**, x = butylamine (20% in MeOH, 1 mL), *t* = 12 h, *T* = rt, and column eluent CH_2Cl_2–MeOH 25:1 gave **31** (7.2 mg, 90%). ^1H NMR (400 MHz, D_2O) δ 8.54 (s, 1H, H-5′), 5.01 (dd, 1H, $J_{2,3}$ = 10.7, H-3), 4.65 (d, 1H, $J_{1,2}$ = 9.6, H-1), 4.32 (t, 1H, H-2), 4.22 (d, 1H, $J_{3,4}$ = 2.8, H-4), 3.98 (dd, 1H, H-5), 3.80 (dd, 1H, $J_{6a,6b}$ = 11.7, $J_{5,6a}$ = 7.3, H-6a), 3.73 (dd, 1H, $J_{5,6b}$ = 5.0, H-6b), 3.40 (t, 2H, $J_{H,H}$ = 7.0, CH_2N), 2.28 (s, 3H, CH_3S), 1.59 (m, 2H, CH_2), 1.37 (m, 2H, CH_2), 0.91 (t, 3H, $J_{H,H}$ = 7.0, CH_3). ^{13}C NMR (100.6 MHz, D_2O) δ 162.3 (C=O), 142.5 (C-4′), 126.4 (C-5′), 87.0 (C-1), 79.7 (C-

5), 68.3 (C-4), 67.4 (C-3), 66.4 (C-2), 61.1 (C-6), 39.5 (CH_2N), 30.9 (CH_2), 19.8 (CH_2), 13.3 (CH_3CH_2), 11.8 (CH_3S). FAB-HRMS calcd for $C_{14}H_{25}N_4O_5S$ $[M+H]^+$ 361.1546; found, 361.1542.

4.4.5. Methyl 3-(4-(3-hydroxyprop-1-yl-aminocarbonyl)-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 32

Methyl ester **3**, x = 3-aminopropanol (20% in MeOH, 1 mL), *t* = two days, *T* = 45 °C, column eluent CH_2Cl_2–MeOH 10:1 gave **32** (7.0 mg, 86%). ^1H NMR (400 MHz, D_2O) δ 8.56 (s, 1H, H-5′), 5.01 (dd, 1H, $J_{3,4}$ = 3.0, $J_{2,3}$ = 10.6, H-3), 4.65 (d, 1H, $J_{1,2}$ = 9.6, H-1), 4.32 (t, 1H, H-2), 4.22 (d, 1H, H-4), 3.98 (dd, 1H, H-5), 3.80 (dd, 1H, $J_{5,6a}$ = 7.4, $J_{6a,6b}$ = 11.8, H-6a), 3.73 (dd, 1H, $J_{5,6b}$ = 5.0, H-6b), 3.69 (t, 2H, $J_{H,H}$ = 6.4, CH_2O), 3.49 (t, 2H, $J_{H,H}$ = 6.9, CH_2N), 2.28 (s, 3H, CH_3S), 1.87 (m, 2H, CH_2). ^{13}C NMR (100.6 MHz, D_2O) δ 162.4 (C=O), 142.5 (C-4′), 126.4 (C-5′), 87.0 (C-1), 79.7 (C-5), 68.3 (C-4), 67.4 (C-3), 66.4 (C-2), 61.1 (C-6), 59.6 (CH_2O), 36.7 (CH_2N), 31.3 (CH_2), 11.8 (CH_3S). FAB-HRMS calcd for $C_{13}H_{22}N_4NaO_6S$ $[M+Na]^+$ 385.1158; found, 385.1180.

4.4.6. Methyl 3-(4-(*N*′-morpholino)ethylaminocarbonyl)-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 33

Methyl ester **3**, x = *N*-morpholinoethylamine (20% in MeOH, 1 mL), *t* = four days, *T* = 45 °C, column eluent CH_2Cl_2–MeOH 17:1 gave **33** (7.0 mg, 75%). ^1H NMR (400 MHz, CD_3OD) δ 8.44 (s, 1H, H-5′), 4.85 (obscured under HDO peak, 1H, H-3), 4.46 (d, 1H, $J_{1,2}$ = 9.2, H-1), 4.19 (dd, 1H, $J_{2,3}$ = 10.4, H-2), 4.09 (d, 1H, $J_{3,4}$ = 2.9, H-4), 3.80–3.66 (m, 7H, H-5, 2H-6, 2 (CH_2O)), 3.55 (t, 2H, $J_{H,H}$ = 6.6, CH_2NC=O), 2.59 (t, 2H, $J_{H,H}$ = 6.6, CH_2N), 2.53 (br t, 4H, 2 (CH_2N), 2.25 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, CD_3OD) δ 162.7 (C=O), 143.5 (C-4′), 126.7 (C-5′), 88.6 (C-1), 80.9 (C-5), 69.6 (C-4), 69.1 (C-3), 67.8 (–CH_2OCH_2–), 67.7 (C-2), 62.3 (C-6), 58.5 (CH_2N), 54.7 ((CH_2)$_2$N), 36.9 (CH_2NC=O), 12.0 (CH_3S). FAB-HRMS calcd for $C_{16}H_{27}N_5NaO_6S$ $[M+Na]^+$ 440.1580; found 440.1579.

4.4.7. Methyl 3-(4-benzylaminocarbonyl-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 34

Methyl ester **3**, x = benzylamine (20% in MeOH, 1 mL), *t* = three days, *T* = 45 °C, column eluent CH_2Cl_2–MeOH 25:1 gave **34** (7.0 mg, 80%). ^1H NMR (400 MHz, D_2O) δ 8.58 (s, 1H, H-5′), 7.41–7.35 (m, 5H, Ph), 5.02 (dd, 1H, $J_{2,3}$ = 10.7, H-3), 4.65 (d, 1H, $J_{1,2}$ = 9.6, H-1), 4.62 (s, 2H, CH_2), 4.32 (t, 1H, H-2), 4.23 (d, 1H, $J_{3,4}$ = 2.8, H-4), 3.98 (dd, 1H, H-5), 3.80 (dd, 1H, $J_{5,6a}$ = 7.4, $J_{6a,6b}$ = 11.7, H-6a), 3.73 (dd, 1H, $J_{5,6b}$ = 5.0, H-6b), 2.28 (s, 3H, CH_3S). ^{13}C NMR (100.6 MHz, D_2O) δ 162.4 (C=O), 142.4 (C-4′), 138.1, 129.2 [2C], 127.9, 127.6 [2C] (Ph), 126.6 (C-5′), 87.0 (C-1), 79.7 (C-5), 68.3 (C-4), 67.4 (C-3), 66.4 (C-2), 61.1 (C-6), 43.2 (CH_2Ph), 11.8 (CH_3S). FAB-HRMS calcd for $C_{17}H_{22}N_4NaO_5S$ $[M+Na]^+$ 417.1209; found, 417.1224.

4.4.8. Methyl 3-(4-methylaminocarbonyl-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-β-D-galactopyranosyl-(1–4)-2-acetamido-2-deoxy-β-D-glucopyranoside 39

Methyl ester **37**, x = methylamine (40% in H_2O, 2 mL), *t* = 12 h, *T* = rt, column eluent CH_2Cl_2–MeOH 5:1 gave **39** (5.6 mg, 80%). ^1H NMR (400 MHz, D_2O) δ 8.55 (s, 1H, H-5″), 5.01 (dd, 1H, $J_{3',4'}$ = 2.9, $J_{2',3'}$ = 11.2, H-3′), 4.74 (d, 1H, $J_{1',2'}$ = 7.6, H-1′), 4.67 (d, 1H, $J_{1,2}$ = 7.8, H-1), 4.24 (dd, 1H, H-2′), 4.17 (d, 1H, H-4′), 4.00 (m, 2H, H-5′, H-6a), 3.87–3.72 (m, 6H, H-2, 2H-6′, H-3, H-4, H-6b), 3.61 (m, 1H, H-5), 3.50 (s, 3H, CH_3O), 2.94 (s, 3H, CH_3N), 2.04 (s, 3H, CH_3C=O). ^{13}C NMR (100.6 MHz, D_2O) δ 175.1, 162.9 (2C=O), 142.4 (C-4″), 126.3 (C-5″), 103.4 (C-1′), 102.2 (C-1), 76.4 (C-5′), 75.1 (C-5), 68.2 (C-2′), 68.0 (C-4′), 66.0 (C-3′), 60.3 (C-6), 57.5 (CH_3O), 55.4 (C-6′), 78.8, 72.9, 61.1 (C-2, C-3, C-4), 26.0 (CH_3N), 22.5 (CH_3C=O). FAB-HRMS calcd for $C_{19}H_{32}N_5O_{11}$ $[M+H]^+$ 506.2099; found, 506.2101.

4.4.9. Methyl 3-(4-benzylaminocarbonyl-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-β-D-galactopyranosyl-(1–4)-2-acetamido-2-deoxy-β-D-glucopyranoside 40

Methyl ester **37**, x = benzylamine (20% in MeOH, 2 mL), *t* = three days, *T* = 40 °C, RP-HPLC (C18, H_2O–acetonitrile gradient) gave **40** (6.6 mg, 81%). ^1H NMR (400 MHz, CD_3OD) δ 8.45 (s, 1H, H-5″), 7.35–7.23 (m, 5H, Ph), 4.87 (dd partially obscured under HDO peak, 1H, H-3′), 4.64 (d, 1H, $J_{1',2'}$ = 7.6, H-1′), 4.58 (s, 2H, CH_2), 4.33 (d, 1H, $J_{1,2}$ = 8.2, H-1), 4.14 (dd, 1H, $J_{2',3'}$ = 11.1, H-2′), 4.02 (d, 1H, $J_{3',4'}$ = 2.8, H-4′), 3.91–3.63 (m, 8H, H-2, H-3, H-4, 2H-6, H-5′, 2H-6′), 3.46 (s, 3H, CH_3O), 3.39 (m, 1H, H-5), 1.97 (s, 3H, CH_3C=O). ^{13}C NMR (100.6 MHz, CD_3OD) δ 173.6, 162.7 (2C=O), 173.5, 140.0 (C-4′, C-1-Ph), 129.5, 128.5, 128.3 (Ph), 126.9 (C-5′), 105.32 (C-1′), 103.6 (C-1), 80.6, 77.8, 76.6, 74.3, 69.4, 69.3, 67.6, 62.6, 61.7, 57.0, 56.6 (C-5, C-5′, C-4, C-4′, C-3, C-3′, C-2, C-2′, C-6, C-6′, CH_3O), 43.7 (CH_2), 22.9 (CH_3S). FAB-HRMS $C_{25}H_{35}N_5NaO_{11}$ $[M+Na]^+$ 604.2231; found, 604.2230.

4.4.10. Methyl 3-(4-aminocarbonyl-5-amino-1*H*-[1,2,3]-triazol-1-yl)-3-deoxy-1-thio-β-D-galactopyranoside 35

Cyanoacetamide (7.0 mg, 3 equiv) and K_2CO_3 (11.5 mg, 3 equiv) in DMSO (0.5 mL) were stirred for 1 h. After this time a solution of the azide **1** (10 mg, 0.028 mmol) in DMSO was added. The resulting mixture was stirred at 50 °C overnight. The solvent was removed and the residue was kept in methanol overnight. After evaporation of the methanol, the residue was purified by column chromatography CH_2Cl_2–MeOH 20:1 to give **35** (5.2 mg, 60%). ^1H NMR (400 MHz, CD_3OD) δ 4.54 (dd, 1H, H-2), 4.46 (dd, 1H, $J_{3,4}$ = 2.7, $J_{2,3}$ = 10.3, H-3), 4.41 (d, 1H, $J_{1,2}$ = 9.2, H-1), 4.19 (d, 1H, H-4), 3.79–3.68 (m, 3H, H-5, 2H-6), 2.24 (s, 3H, CH_3). ^{13}C NMR (100.6 MHz, CD_3OD) δ 167.2 (C = O), 147.5, 123.1 (C-4′, C-5′), 88.9 (C-1), 81.0 (C-5), 69.5 (C-4), 66.4 (C-3), 65.9 (C-2), 62.4 (C-6), 11.9 (CH_3S). FAB-HRMS calcd for $C_{10}H_{17}N_5NaO_5S$ $[M+Na]^+$ 342.0848; found 342.0852.

4.4.11. Methyl 3-deoxy-3-(4-(1-naphthyl)-1*H*-[1,2,3]-triazol-1-yl)-β-D-galactopyranosyl-(1–4)-2-acetamido-2-deoxy-β-D-glucopyranoside 41

Compound **38** (10 mg, 0.013 mmol) was stirred in a solution of methylamine in water 40% (2 mL) for 12 h, concentrated, and purified by RP-HPLC (C18, H_2O–acetonitrile gradient) to give **41** (5.5 mg, 75%). ^1H NMR (400 MHz, CD_3OD) δ 8.34 (s, 1H, H-5″), 8.27 (m, 1H, Ar), 7.93 (m, 2H, Ar), 7.70 (dd, 1H, $J_{H,H}$ = 1.1, 7.1, Ar), 7.53 (m, 3H, Ar), 4.93 (dd, 1H, $J_{2',3'}$ = 11.1, $J_{3',4'}$ = 3.0, H-3′), 4.70 (d, 1H, $J_{1',2'}$ = 7.5, H-1′), 4.34 (d, 1H, $J_{1,2}$ = 8.3, H-1), 4.28 (dd, 1H, H-2′), 4.15 (d, 1H, H-4′), 3.97–3.63 (m, 8H, H-3, H-4, H-5′, 2H-6′, 2H-6, H-2), 3.46 (s, 3H, CH_3O), 3.42 (m, 1H, H-5), 1.97 (s, 3H, CH_3C=O). ^{13}C NMR (100.6 MHz, CD_3OD) δ 173.6 (C=O), 147.1, 135.4, 132.6, 130.1, 129.5, 129.3, 128.4, 127.7, 127.2, 126.4, 126.3 (C-4″, naphthalene), 124.7 (C-5″), 105.4 (C-1′), 103.6 (C-1), 80.8, 77.9, 76.7, 74.4, 69.7, 69.3, 67.7, 62.3, 61.8, 57.0, 56.7 (C-2, C-3, C-4, C-5, C-6, C-2′, C-3′, C-4′, C-5′, C-6′, CH_3O), 22.9 (CH_3C=O). FAB-HRMS $C_{27}H_{34}N_4NaO_{10}S$ $[M+Na]^+$ 597.2173; found, 597.2181.

4.4.12. 1,2,4,6-Tetra-*O*-acetyl-3-deoxy-3-(4-(methoxycarbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranose 43

A mixture of 1,2,4,6-tetra-*O*-acetyl-4-azido-4-deoxy-β-D-galactopyranose **42**[34] (66 mg, 76 μmol), methyl propiolate (16.4 μL, 1 equiv), CuI (3.5 mg, 0.1 equiv), diisopropylethylamine (32 μL, 1 equiv) and toluene (6 mL) was stirred overnight, concentrated and purified by flash chromatography (2:1, heptane–ethyl acetate) to give **43** (75.0 mg, 93%). ^1H NMR (400 MHz, $CDCl_3$) 2.21, 2.15, 2.09, 2.08, 1.88, 1.87 (3H each, s, 8CH_3C=O), 2.04 (6H, s, 2CH_3C=O), 3.95 (6H, s, OCH_3), 4.07–4.21 (4H, m, 2H-6, 2H-6′), 4.24 (1H, at, *J* = 6.5, H-5β), 4.56 (1H, at, *J* = 6.5, H-5α), 5.22 (1H, dd, $J_{2,3}$ = 11.0 Hz, $J_{3,4}$ = 3,3, H-3β), 5.40 (1H, dd, $J_{2,3}$ = 11.8, $J_{3,4}$ = 3,3 Hz,

H-3α), 5.54 (1H, d, H-4β), 5.59 (1H, d, H-4α), 5.83 (2H, m, H-1β and H-2β), 5.92 (1H, dd, $J_{1,2}$ = 3.5, H-2α), 6.50 (1H, d, H-1α), 8.16 and 8.10 (1H, s, triazole-H). ^{13}C NMR (100.6 MHz, $CDCl_3$) 20.0, 20.1, 20.2 (2C), 20.5 (2C), 20.6, 20.7 ($8CH_3C$=O), 52.3 (OCH_3), 58.2, 60.8, 61.0, 62.2. 65.2, 66.5, 67.9, 68.1, 68.9, 72.7, 88.9, 92.4 (C-1, C-2, C-3, C-4, C-5, C-6), 126.6 (triazole-CH), 140.1, 140.2 (triazole-C), 160.5, 160.6, 168.5, 168.6, 168.7, 168.9, 169.0, 169.3, 170.1, 170.2 ($10CH_3C$=O). FAB-HRMS calcd for $C_{18}H_{23}N_3NaO_{11}$ $[M+Na]^+$ 480.1230; Found 480.1234.

4.4.13. 2,4,6-Tri-*O*-acetyl-3-deoxy-3-(4-(methoxycarbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranosyl bromide 44

Compound **43** (28 mg, 61 μmol) was dissolved in dichloromethane (1 ml) that had been dried over 4 Å molecular sieves. Acetic anhydride (12 μl, 0.12 mmol) and HBr (0.2 ml of a 33% solution in AcOH) were added, and the mixture was stirred under N_2 at room temperature. After 2 h 30 min, the reaction mixture was diluted with dichloromethane (30 ml) and washed with $NaHCO_3$ (30 ml of a saturated aqueous solution), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (1:1, heptane–ethyl acetate, 1% Et_3N) to give **44** (24 mg, 82%) as a colourless oil; $[\alpha]_D^{21}$ +177 (*c* 1.0 in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.91 (3H, s, CH_3C=O), 2.02 (6H, s, $2CH_3C$=O), 3.91 (3H, s, OCH_3), 4.09 (1H, dd, $J_{5,6}$ = 6.7, $J_{6,6'}$ = 11.5, H-6), 4.19 (1H, dd, $J_{5,6'}$ = 6.2, H-6′), 4.61 (1H, at, *J* = 6.4, H-5), 5.39 (1H, dd, $J_{2,3}$ = 11.4, $J_{3,4}$ = 1.6, H-3), 5.59 (1H, d, H-4), 5.72 (1H, dd, $J_{1,2}$ = 3.8, H-2), 6.84 (1H, d, H-1), 8.82 (1H, s, triazole-H). ^{13}C NMR (75 MHz, $CDCl_3$) 20.4, 20.5, 20.7 (3q, $3CH_3C$=O), 52.4 (q, OCH_3), 59.1, 60.9, 66.9, 67.7, 71.2, 88.3 (5 × d, t, C-1, C-2, C-3, C-4, C-5, C-6), 128.0 (d, triazole-CH), 140.1 (s, triazole-C), 160.8 (s, CH_3C=O), 169.2, 169.5, 170.3 (3s, $3CH_3C$=O). FAB-HRMS calcd for $C_{16}H_{20}N_3O_9BrNa$ $[M+Na]^+$ 500.0281; Found 500.0291.

4.4.14. Di-(2,4,6-tri-*O*-acetyl-3-deoxy-3-(4-(methoxycarbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranosyl) sulfane 45

Sodium sulfate nonahydrate (170 mg, 0.59 mmol) was dried by dissolving in water and then heating to 50 °C under high vacuum. Molecular sieves 4 Å (ca. 100 mg) were added. Compound **44** (77 mg, 0.16 mmol) was dissolved in distilled acetonitrile (5 ml) and added to the reaction vessel. The mixture was stirred at room temperature for 13 h. After this time, TLC (1:3, heptane–ethyl acetate) indicated the complete consumption of starting material (R_f 0.7) and the presence of a major product (R_f 0.2). The reaction mixture was poured onto a plug of silica and washed through with ethyl acetate–chloroform, 1:1. The eluent was concentrated in vacuo and the residue was purified by flash column chromatography (1:4, heptane–ethyl acetate) to give **45** (24 mg, 36%). White crystals, mp (MeOH) >220 °C; $[\alpha]_D^{21}$ +30.2 (*c* 0.17 in MeOH–$CHCl_3$, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92, 2.07, 2.10 (18H, 3s, $6CH_3C$=O), 3.94 (6H, s, OCH_3), 4.10–4.24 (6H, m, H-5, H-6, H-6′), 5.03 (1H, d, $J_{1,2}$ = 9.7, H-1), 5.25 (1H, dd, $J_{2,3}$ = 11.0, $J_{3,4}$ = 3.2, H3), 5.60 (1H, d, H-4), 5.72 (1H, at, *J* = 10.3, H-2), 8.18 (1H, s, triazole-H). ^{13}C NMR (100.6 MHz, $CDCl_3$) 20.5, 20.6, 20.8 (3q, $3CH_3C$=O), 52.3 (q, OCH_3), 61.4 (t, C-6), 63.4 (d, C-3), 66.5 (d, C-2), 68.5 (d, C-4), 75.8 (d, C-5), 82.4 (d, C-1), 126.8 (d, triazole-CH), 140.4 (s, triazole-C), 160.7 (s, CH_3C=O), 169.0, 169.5, 170.5 (3 s, $3CH_3C$=O). FAB-HRMS calcd for $C_{32}H_{40}N_6NaO_{18}S$ $[M+Na]^+$ 851.2017; Found 851.2017.

4.4.15. Di-(3-deoxy-3-(4-((methylamino)carbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranosyl)sulfane 46

Compound **45** (6.5 mg, 7.8 μmol) was suspended in a methylamine solution (40% in water, 2 ml). The mixture was stirred at room temperature for 48 h. After this time, the mixture was concentrated in vacuo to give **46** (4.5 mg, quant.) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.77 (3H, d, *J* = 4.7, $NHCH_3$), 3.52–3.55 (4H, m, H-6, H-6′), 3.70 (2H, m, H-5), 3.91 (2H, m, H-4), 4.10 (2H, m, H-2), 4.70 (2H, at, $J_{OH,6}$ = 5.7, OH-6), 4.87–4.93 (4H, m, H-1, H-3), 5.26 (2H, d, $J_{OH,4}$ = 7.5, OH-4), 5.49 (2H, d, $J_{OH,2}$ = 6.8, OH-2), 8.36 (2H, s, triazole-H), 8.44 (1H, q, NH). FAB-HRMS calcd for $C_{20}H_{31}N_8O_{10}S$ $[M+H]^+$ 575.1884; Found 575.1887.

4.5. General procedure for deprotection and formation of amides 47–52

The methyl ester **45** (4–8 mg) was stirred with solution of amine (x) 20% in methanol (1 mL) for (*t*) time. The mixture was concentrated in vacuo and the residue was purified by column chromatography to give the deprotected amides **47–52**. In the cases of the less volatile amines, the crude material was left on the high vacuum pump for several days before chromatography.

4.5.1. Di-(3-deoxy-3-(4-((butylamino)carbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranosyl)sulfane 47

x = butylamine, *t* = 26 h, column eluent CH_2Cl_2–MeOH 9:1 gave **47** (quant.) as a white solid. ^{1}H NMR (400 MHz, CD_3OD) 0.96 (6H, t, *J* = 7.4, $NHCH_2CH_2CH_2CH_3$), 1.42 (4H, m, $NHCH_2CH_2CH_2$), 1.60 (4H, m, $NHCH_2CH_2$), 3.39 (4H, t, *J* = 7.1, $NHCH_2$), 3.67 (2H, dd, $J_{5,6}$ = 4.0, $J_{6,6'}$ = 11.1, H-6), 3.77–3.86 (4H, m, H-5, H-6′), 4.10 (2H, d, $J_{3,4}$ = 2.8, H-4), 4.75 (2H, at, *J* = 9.9, H-2), 4.82 (2H, d, $J_{1,2}$ = 9.5, H-1), 4.90 (2H, dd, $J_{2,3}$ = 10.4, H-3), 8.55 (2H, s, triazole-H). ^{13}C NMR (100.6 MHz, CD_3OD) 14.1 (q, $NHCH_2CH_2CH_2CH_3$), 21.1 (t, $NHCH_2CH_2CH_2$), 32.7 (t, $NHCH_2CH_2$), 39.9 (t, $NHCH_2$), 62.8 (t, C-6), 68.3 (d, C-2), 68.7 (d, C-3), 69.5 (d, C-4), 81.4 (d, C-5), 86.7 (d, C-1), 126.8 (d, triazole-CH), 143.6 (s, triazole-C), 162.7 (s, C=O). FAB-HRMS calcd for $C_{26}H_{42}N_8NaO_{10}S$ $[M+Na]^+$ 681.2642; Found 681.2648.

4.5.2. Di-(3-deoxy-3-(4-((benzylamino)carbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranosyl)sulfane 48

x = benzylamine, *t* = 26 h, column eluent CH_2Cl_2–MeOH 9:1 gave **48** (quant.) as a white solid. ^{1}H NMR (400 MHz, CD_3OD) 3.67 (2H, dd, $J_{5,6}$ = 4.0, $J_{6,6'}$ = 11.1, H-6), 3.77–3.85 (4H, m, H-5, H-6′), 4.09 (2H, d, $J_{3,4}$ = 2.8, H-4), 4.58 (4H, ABq, J_{AB} = 12.0, $NHCH_2$), 4.77 (2H, at, *J* = 9.9, H-2), 4.82 (2H, d, $J_{1,2}$ = 9.3, H-1), 4.90 (2H, dd, $J_{2,3}$ = 10.0, H-3), 7.22–7.36 (10H, m, Ar-H), 8.60 (2H, s, triazole-H). ^{13}C NMR (100.6 MHz, CD_3OD) 43.8 (t, $NHCH_2$), 62.8 (t, C-6), 68.3 (d, C-2), 68.7 (d, C-3), 69.5 (d, C-4), 81.4 (d, C-5), 86.8 (d, C-1), 127.1, 128.2, 128.5, 129.5 (4 × d, Ar-CH, triazole-CH), 140.0, 143.5 (2 × s, Ar-C, triazole-C), 162.8 (s, C=O). FAB-HRMS calcd for $C_{32}H_{38}N_8NaO_{10}S$ $[M+Na]^+$ 749.2329; Found 749.2333.

4.5.3. Di-(3-deoxy-3-(4-((2-phenylethylamino)carbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranosyl)sulfane 49

x = phenethylamine, *t* = 28 h, column eluent CH_2Cl_2–MeOH 9:1 gave **49** (quant.)as a white solid. ^{1}H NMR (400 MHz, DMSO-*d*6) 2.84 (4H, at, *J* = 7.5, $NHCH_2$), 3.47–3.56 (8H, m, $NHCH_2CH_2$, H-6, H-6′), 3.71 (2H, at, *J* = 6.2, H-5), 3.92 (2H, m, H-4), 4.14 (2H, m, H-2), 4.71 (2H, at, $J_{OH,6}$ = 5.7, OH-6), 4.87–4.93 (4H, m, H-1, H-3), 5.27 (2H, d, $J_{OH,4}$ = 7.4, OH-4), 5.49 (2H, d, $J_{OH,2}$ = 6.9, OH-2), 7.18–7.31 (10H, m, Ar-H), 8.37 (2H, s, triazole-H) 8.54 (1H, t, *J* = 5.9, NH). FAB-HRMS calcd for $C_{34}H_{42}N_8NaO_{10}S$ $[M+Na]^+$ 777.2642; Found 777.2651.

4.5.4. Di-(3-deoxy-3-(4-((allylamino)carbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranosyl)sulfane 50

x = allylamine, *t* = 28 h, column eluent CH_2Cl_2–MeOH 9:1 gave **50** (quant.) as a white solid. ^{1}H NMR (400 MHz, CD_3OD) 3.67 (2H, dd, $J_{5,6}$ 3.8, $J_{6,6'}$ = 10.8, H-6), 3.76–3.86 (4H, m, H-5, H-6′), 4.01 (4H, d, *J* = 5.3, $NHCH_2$), 4.10 (2H, d, $J_{3,4}$ = 2.6, H-4), 4.75 (2H, at, *J* = 9.8, H-2), 4.81 (2H, d, $J_{1,2}$ = 9.4, H-1), 4.91 (2H, dd (obs), H-3), 5.13 (1H, dd, *J* = 1.4, J_Z = 10.3, CH=CHEHZ), 5.22 (1H, dd, *J* = 1.5, J_E = 17.2, CH=CHEHZ), 5.92 (2H, m, CH=CH_2), 8.57 (2H, s,

triazole-H). ^{13}C NMR (100.6 MHz, CD_3OD) 42.4 (t, $NHCH_2$), 62.8 (t, C-6), 68.3 (d, C-2), 68.7 (d, C-3), 69.5 (d, C-4), 81.4 (d, C-5), 86.7 (d, C-1), 116.3 (t, $CH{=}CH_2$), 127.0 (d, triazole-CH), 135.4 (d, $CH{=}CH_2$), 143.5 (s, triazole-C), 162.7 (s, C=O). FAB-HRMS calcd for $C_{24}H_{34}N_8NaO_{10}S$ $[M+Na]^+$ 649.2016; Found 649.2010.

4.5.5. Di-(3-deoxy-3-(4-((2-hydroxypropylamino)carbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranosyl)sulfane 51

x = 2-hydroxypropylamine, t = 28 h, column eluent CH_2Cl_2–MeOH 9:2 gave **51** (70%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) 1.66 (2H, quint., J = 6.5, $NHCH_2CH_2$), 3.3 (4H, m (obs), $NHCH_2$), 3.45 (4H, m, $NHCH_2CH_2CH_2$), 3.51–3.56 (4H, m, H-6, H-6′), 3.71 (2H, at, J = 6.1, H-5), 3.93 (2H, m, H-4), 4.15 (2H, m, H-2), 4.50 (2H, t, J = 5.2, CH_2CH_2OH), 4.71 (2H, at, $J_{OH,6}$ = 5.7, OH-6), 4.87–4.93 (4H, m, H-1, H-3), 5.27 (2H, d, $J_{OH,4}$ = 7.3, OH-4), 5.48 (2H, d, $J_{OH,2}$ = 6.8, OH-2), 8.37 (2H, s, triazole-H), 8.48 (1H, t, J = 5.8, NH). FAB-HRMS calcd for $C_{24}H_{38}N_8NaO_{12}S$ $[M+Na]^+$ 685.2228; Found 685.2231.

4.5.6. Di-(3-deoxy-3-(4-((2-methoxyethylamino)carbonyl)-1*H*-1,2,3-triazol-1-yl)-β-D-galactopyranosyl)sulfane 52

x = 2-methoxyethylamine, t = 28 h, column eluent CH_2Cl_2–MeOH 9:1 gave **52** (quant.) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) 3.26 (6H, s, OCH_3), 3.41–3.46 (8H, m, $NHCH_2$, H-6, H-6′), 3.50–3.55 (4H, m, $NHCH_2CH_2$), 3.70 (2H, at, J = 6.4, H-5), 3.93 (2H, m, H-4), 4.12 (2H, m, H-2), 4.71 (2H, at, $J_{OH,6}$ = 5.8, OH-6), 4.88–4.93 (4H, m, H-1, H-3), 5.28 (2H, d, $J_{OH,4}$ = 7.4, OH-4), 5.49 (2H, d, $J_{OH,2}$ = 6.9, OH-2), 8.40–8.41 (4H, m, NH, triazole-H). FAB-HRMS calcd for $C_{24}H_{38}N_8NaO_{12}S$ $[M+Na]^+$ 685.2228; Found 685.2214.

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Supplementary data

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