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Synthesis of 1,2,3-triazoles from xylosyl and 5-thioxylosyl azides: evaluation of the xylose scaffold for the design of potential glycogen phosphorylase inhibitors

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ABSTRACT

Various acetylenic derivatives and acetylated β-D-xylopyranosyl azide or the 5-thio-β-D-xylopyranosyl analogue were coupled by Cu(I)-catalyzed azide alkyne 1,3-dipolar cycloaddition (CuAAC) to afford a series of 1-xylosyl-4-substituted 1,2,3-triazoles. Controlled oxidation of the endocyclic sulfur atom of the 5-thioxylose moiety led to the corresponding sulfoxides and sulfones. Deacetylation afforded 19 hydroxylated xylose and 5-thioxylose derivatives, found to be only sparingly water-soluble. Compared to glucose-based analogues, they appeared to be much weaker inhibitors of glycogen phosphorylase, as the absence of a hydroxymethyl group weakens their binding at the enzyme active site. However, such new xylose derivatives might be useful glycomimetics.

1. Introduction

As diabetic states result in hyperglycemia, which entails diverse complications if untreated,[1] symptomatic control of type 2 diabetes[2] (*diabetes mellitus*) is managed based on several families of currently marketed molecules,[3–6] that differ in terms of pharmacological target, limitations, and side effects.[7–9] The rising prevalence of type 2 diabetes[2] is another concern, calling for the identification and validation of new therapeutic targets. Among the numerous biological processes addressed by anti-diabetic strategies, glycogen phosphorylase (GP) inhibition appeared as a promising approach for the development of anti-hyperglycemic drugs.[10–13]

Glycogen phosphorylase is a homodimeric enzyme[14] that catalyzes the phosphorolysis (glycogenolysis[15]) of glycogen, the polymeric storage form of glucose. The inhibition of GP with small molecules would therefore provide a useful tool for a better control of glycemia for type 2 diabetic patients.[10–13] Glucose-based molecules represent the main class of GP inhibitors designed to date and display potent inhibition against the enzyme with K_i values in the sub-micromolar range.[16–19] These molecular scaffolds are composed of a glucopyranose ring that binds selectively at the catalytic site of GP and a variety of substituents introduced at the anomeric position of the sugar including heterocyclic moieties (e.g., oxadiazoles[20–25] or triazoles[26,27]) that interact with amino-acid residues present in the so-called β-channel of the enzyme, in the vicinity of the catalytic site.

While a large set of data has been collected from in vitro experiments involving kinetic and structural studies of GP enzyme in the presence of various ligands, additional data from in vivo assessment of potent inhibitors are needed to confirm the potential therapeutic applications of such molecules.[28–30] *N*-Acetyl β-D-glucopyranosylamine (1-GlcNAc, Fig. 1) was among the first molecules evaluated for anti-hyperglycemic properties targeting GP.[31] The study highlighted a potent inhibition in vitro with a K_i value of 32 μM[31] against rabbit muscle glycogen phosphorylase *b* (RMGP*b*) while no effect was observed in vivo.[32] This observation was explained by the metabolization of such glucose derivatives through phosphorylation at the 6-position of the glucopyranose ring leading to the 6-phosphoglucose species (1-GlcNAc-6-P).[32] This phosphate derivative was shown to inhibit glycogen-bound protein phosphatase 1[33] and to exert inhibitory effects through different modes for GP*a* and GS*b* (inactive phosphorylated glycogen synthase). These data account for the fact that 1-GlcNAc prevents the glucose-led activation of GS in whole hepatocytes.

The design of original molecular scaffolds closely related to glucopyranose but non-phosphorylatable at the 6-position should provide GP inhibitors with improved in vivo biological properties.

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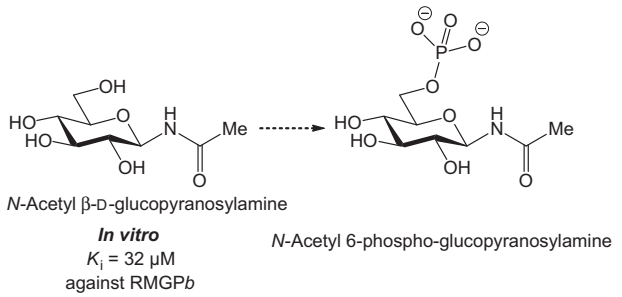


Figure 1. *N*-Acetyl β-D-glucopyranosylamine (1-GlcNAc) as a potent GP inhibitor prone to phosphorylation in hepatocytes.

One of the obvious targets is therefore the xylopyranose motif (Fig. 2) in which the absence of the hydroxymethyl group (located at the 5-position of glucose) prevents the problematic phosphorylation from occurring.[32] Even though xylose does not inhibit GP,[34] 1-xylopyranosylated 1,2,3-triazoles (**A**, X = O) were selected since recent reports have demonstrated the in vitro potent inhibition of GP with their glucose analogues.[26,27] The triazole ring can be obtained from the four chemically accessible protected xylosyl azide derivatives (**B**, X = O, S, SO, and SO_2) and terminal alkynes (**C**) through Cu(I)-catalyzed azide alkyne 1,3-dipolar cycloaddition[35–37] (CuAAC). The four molecular scaffolds based on the xylose structure would provide a family of potential GP inhibitors with different atom patterns at the endocyclic oxygen atom position that could assign interesting different inhibitory properties against the enzyme. Replacement of the ring oxygen atom by a sulfur atom offered additional structural modifications through oxidation (toward sulfoxides and sulfones) or by alkylation to form sulfonium derivatives. The four endocyclic variants of the xylose ring (O, S, SO, and SO_2) were expected to result in related potential GP inhibitors which could display enhanced inhibitory properties, if these unusual features participate in additional stabilizing interactions at the enzyme active site in ligand–enzyme complexes. As this strategy has been essentially unexplored, this investigation offered a possibility for exploring whether modifications introduced in the sugar would lead to stronger inhibitors as previously studied for 5-thio-glucose.[38,39]

It is to be mentioned that the synthetic values of glycosyl azides[40] for preparing various glycosyl-heterocycles[41,42] is well-recognized.[26,27] The CuAAC approach gives access to multivalent glycoconjugates under one-pot conditions,[43,44] to novel glycolipids,[45] or to sugar-based triazole derivatives studied as glycosidic carbonic anhydrase inhibitors.[46] Xylose derivatives are of special interest, as a xylopyranosyl unit occupies a key position in the proteoglycan linkage tetrasaccharide sequence, by joining the protein core to the polysaccharide side chains. Consequently, xylose-based triazoles have been considered for studying the biosynthesis of glycosaminoglycans,[47,48] while a number of 5-thio-D-xylosyl derivatives have been evaluated as oral antithrombotic drugs.[49] Recently, D-arabinofuranosyl-triazoles bearing various alkyl chains were tested as inhibitors of the mycobacterial cell wall biosynthesis.[50] Both 1-glycosyl-4-phenyl triazoles,[51] and thiasugars[52] have been evaluated as glycosidase inhibitors. These valuable informations concerning both xylosyl and 5-thio-xylosyl derivatives provided additional incentives for engaging in the work reported next.

2. Results and discussion

Although the synthetic methodology used in the present study was similar to previously reported procedures, the biological activities targeted were very different and only a few substituents were selected as potential pharmacophores for the catalytic site of GP. Peracetylation of D-xylose afforded the peracetyl protected xylopyranose **1** which was readily converted into the bromo xylose derivative **2** (Scheme 1). Azidation of the anomeric position provided the β-D-xylopyranosyl azide **3**. 1,3-Dipolar cycloaddition of azide **3** with alkynes gave the corresponding acetylated 1,2,3-triazoles **4a–g** which upon deprotection of the ester groups under Zemplén conditions afforded the desired hydroxylated potential GP inhibitors **5a–g**.

Similar synthesis was performed in the 5-thioxylose series (Scheme 2). α-Bromide **6**[53] was converted into the 5-thioxylopyranosyl azide **7**.[54] Oxidation of the sulfur atom was undertaken in order to expand the family of potential GP inhibitors with sulfoxides and sulfones. The mixture of azido-sulfoxides **8** was prepared from **7** by oxidation with *m*-chloroperoxybenzoic acid (*m*-CPBA) in slight excess (1.2 equiv), and under different conditions (Table 1). The diastereoselectivity of the oxidation was always in favor of the equatorial sulfoxide (i.e., *S* stereochemistry at the sulfur atom). The best conditions (THF, room temperature, 15 min) provided a ~4:1 diastereoisomeric mixture of sulfoxides **8**. This constitutes the first clear-cut example of solvent influencing the stereoselectivity of oxidation leading to glycosulfoxides.[55] The parameters that might influence the oxidation of sulfur atoms (attached to either the C-1,[56,57] the C-5,[58,57] or both positions[59]) have been envisaged, but the diastereocontrol issues remain complex. The stereochemical assignment of each isomer of **8** was proposed from comparison with NMR spectroscopy data reported for 5-thioglucose,[55] and 5-thio-xylose[60] derivatives, which were studied by X-ray diffraction analysis.

Sulfoxides **8-*R*** and **8-*S*** could not be readily separated by silica gel chromatography but a small portion of each pure compound could be isolated for NMR studies (Table 2). Their stereochemistry was deduced based on data reported for the oxidation of 5-thioglucose by *m*-CPBA with assignment of the sulfoxides structures by crystal analysis. Comparison of their ^{1}H NMR chemical shifts[55] showed the deshielding effect exerted by lone electron pairs of the sulfoxide oxygen atom on neighboring protons, as schematically represented on the Newman representations of each diastereoisomer **8-*R*** and **8-*S*** (Fig. 3). As seen from the ^{1}H NMR data collected for each sulfoxide **8-*R*** and **8-*S*** (Table 2), the proton signals for H-2 and H-4 of sulfoxide **8-*R*** moved downfield by a $\Delta\delta$ of +0.71 and +0.66 ppm, respectively in comparison to the azide **7**, while they remained almost unchanged for the other diastereoisomer **8-*S***.[55] Moreover, for **8-*R***, the chemical shifts of protons H1 (δ = 4.09) and H-5_{ax} (δ = 2.65) both anti-parallel to the axial sulfoxide bond were shifted upfield, compared to their counterparts in diastereoisomer **8-*S*** (δ = 4.48 and 3.06 ppm, respectively, Fig. 4).

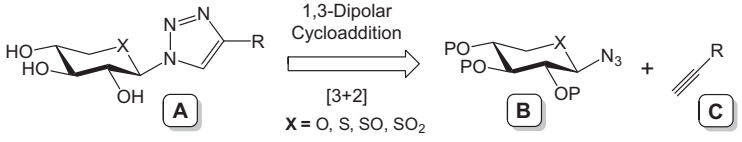
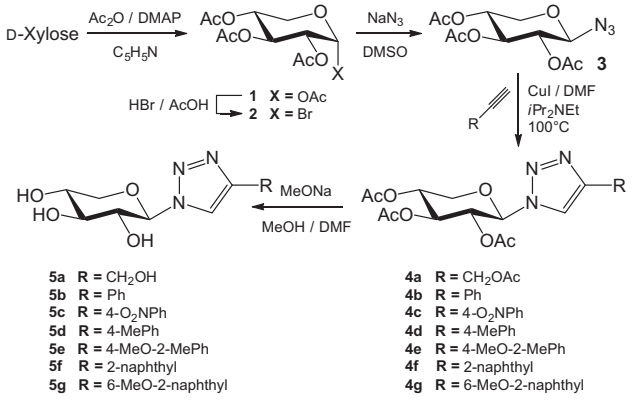


Figure 2. Synthetic strategy for the preparation of xylose-based inhibitors of GP.



Scheme 1. Synthesis of 1-xylopyranosyl-4-substituted 1,2,3-triazoles **5a**–**g**.

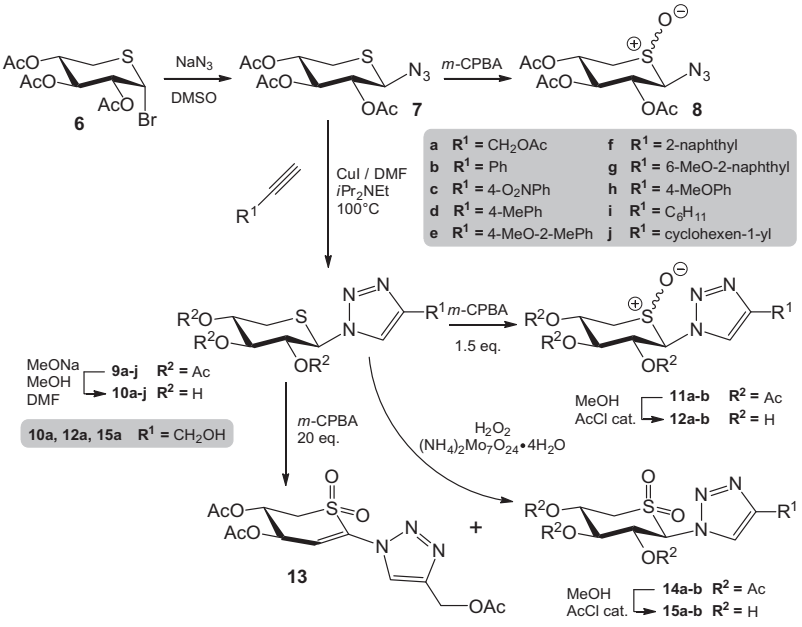
Table 1
Oxidation of azido 2,3,4-tri-*O*-acetyl-5-thioxylopyranose **7**[a]

Solvent	Temperature	Time (min)	Conversion[b] (%)	Selectivity[c]
DME[d]	23 °C	15	75	60:40
DMF	23 °C	15	75	60:40
CH_2Cl_2	23 °C	15	63	70:30
Dioxane	23 °C	15	76	73:27
Et_2O	23 °C	15	75	79:21
THF	−78 °C	60	33	82:18
THF	23 °C	15	85	83:17

[a] Conditions: **7** (100 mg, 0.32 mmol), *m*-CPBA (1.2 equiv) solvent (5 mL). Longer reaction times did not afford higher conversion rates.
[b] A portion of the starting material could be recovered after silica gel column chromatography.
[c] Determined as the ratio of equatorial to axial sulfoxides **8** from their respective integration of ^{1}H NMR signals.
[d] DME = 1,2-dimethoxyethane.

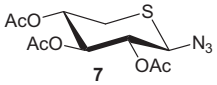
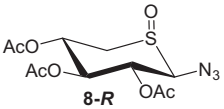
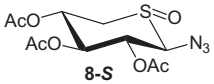
The attempted CuAAC conjugation of the azido-sulfoxides **8** with alkynes did not afford the desired triazoles but instead provided an undefined mixture of products. The sulfoxide zwitterionic moiety was probably chelating the Cu(I) catalyst thus preventing the cycloaddition process. 1,3-Dipolar cycloaddition was therefore performed with the azide **7** to afford the desired triazoles **9a**–**j** in high yields. The subsequent deacetylation using standard Zemplén conditions provided the hydroxylated 1-(5-thioxylopyranosyl)-4-substituted 1,2,3-triazoles **10a**–**j**. The oxidation of the 5-thioxylose sulfur atom was then performed on 1,2,3-triazoles **9a,b** using a slight excess of *m*-CPBA (1.2 equiv) to afford a 83:17 diastereoisomeric mixture of sulfoxides **11a**,**b**. Access to the sulfone functionality was initially attempted from **9a** using a large excess of *m*-CPBA (20 equiv) but the 1,2-glycal derivative **13** was obtained as the sole product, probably through the elimination of acetic acid during the workup under basic conditions. The oxidation of **9a**,**b** was then performed with ammonium molybdate, which did not require a basic workup thus allowing for the isolation of the desired sulfones **14a**,**b** in high yields. Both sulfoxides **11a**,**b** and sulfones **14a**,**b** were deprotected under acidic methanolysis to afford the corresponding hydroxylated GP inhibitor candidates **12a**,**b** and **15a**,**b** respectively while standard Zemplén conditions (MeONa/MeOH) or solvolysis (Et_3N/MeOH/H_2O) afforded complex mixtures of compounds.

A total of 21 potential inhibitors of GP were synthesized in a rapid and efficient synthetic route and afforded seven 1-xylopyranosyl 1,2,3-triazoles **5a**–**g**, 10 1-(5-thioxylopyranosyl) 1,2,3-triazoles **9a**–**h** along with two sulfoxides **12a**,**b** and two sulfones **15a**,**b**. The inhibitory potency against rabbit muscle glycogen phosphorylase *b* (RMGP*b*) was determined for 19 of these inhibitors (Table 3). The xylose-based compounds **5a**–**g** were evaluated at a maximum concentration of 625 μM and did not display any inhibition toward RMGP*b* apart from a very poor inhibition observed for the *p*-tolyl substituted derivative **5d**. The corresponding glucose-based inhibitors recently reported displayed inhibitions in the micromolar range[26,27] with the hydroxymethyl and 2-naphthyl residues as the best pharmacophores for this enzyme (Fig. 5, Table 3). The absence of the hydroxymethyl moiety in the xylose-based inhibitors **5a**–**g** was therefore responsible for a severe loss of interactions with the enzyme's catalytic site resulting in very poor ligands. The 5-thioxylose derivatives **10a**–**h** were also quite poor inhibitors of RMGP*b* since less than 20% inhibition was observed at a concentration of 1 mM and only the hydroxymethyl substituted inhibitor **10a** could provide an IC_{50} value of 1.5 mM. The low inhibitions observed are probably also related to the poor solubility of



Scheme 2. Synthesis of 1-(5-thioxylopyranosyl)-4-substituted 1,2,3-triazoles **10a**–**j** and related sulfoxide and sulfone analogues **8, 12a**,**b**, **15a**,**b**.

Table 2
Chemical shifts (δ in ppm, 300 MHz, $CDCl_3$) for the proton signals of azido 2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranose **7** and the corresponding sulfoxides **8-*R*** and **8-*S***

	 **7**	 **8-*R***	 **8-*S***
H-1	4.48	4.09 $\Delta\delta = -0.39$	4.48 $\Delta\delta = 0.00$
H-2	5.07	5.78 $\Delta\delta = +0.71$	5.01 $\Delta\delta = -0.06$
H-3	5.15	5.35 $\Delta\delta = +0.20$	5.35 $\Delta\delta = +0.20$
H-4	5.04	5.70 $\Delta\delta = +0.66$	5.04 $\Delta\delta = 0.00$
$H\text{-}5_{ax}$	2.70	2.65 $\Delta\delta = -0.05$	3.06 $\Delta\delta = +0.36$
$H\text{-}5_{eq}$	2.94	3.63 $\Delta\delta = +0.69$	3.72 $\Delta\delta = +0.78$

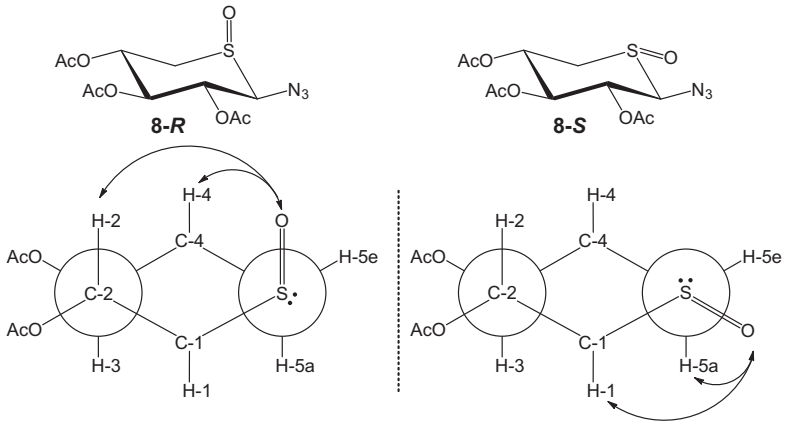


Figure 3. Newman representations of the sulfoxides **8-*R*** and **8-*S***.

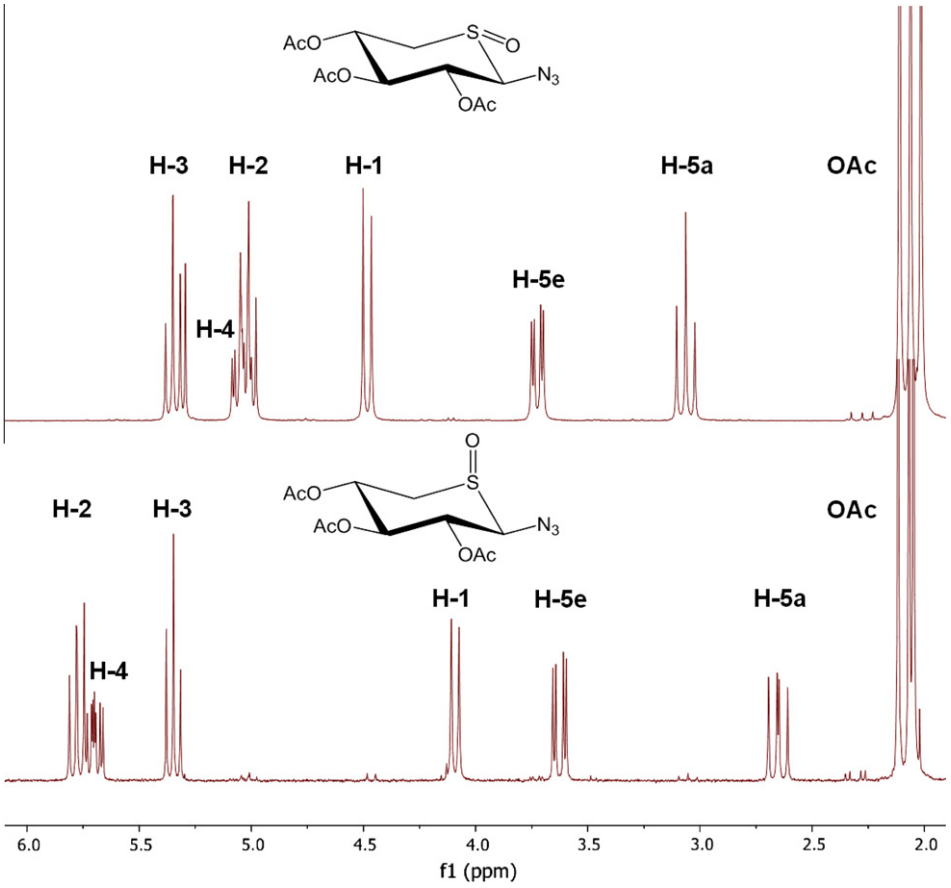
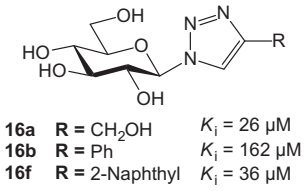


Figure 4. Partial ^1H NMR data (300 MHz, $CDCl_3$) for sulfoxides **8-*R*** (bottom) and **8-*S*** (top).

Table 3
Inhibition of rabbit muscle glycogen phosphorylase *b* (RMGP*b*) by the synthesized (thio)xylosyl triazoles

Scaffold	Compound	Inhibition IC_{50} (μM)
Xylose	**5a**	NI[a]
	5b	NI[a]
	5c	NI[a]
	5d	15%[b]
	5e	NI[a]
	5f	n.d.
	5g	NI[a]
5-Thioxylose[e]	**10a**	1526 ± 156
	10b	15%[c]
	10c	15%[b]
	10d	5%[b]
	10e	2%[b]
	10f	18%[b, c]
	10g	NI @ 500
	10h	Insoluble
5-Thioxylose Sulfoxide[d]	**12a**[e]	NI[f]
	12b	n.d.
5-Thioxylose Sulfone[d]	**15a**	NI[f]
	15b	14%[b]
Glucose	**16a**	26[g]
	16b	162[g]
	16f	36[g]

[a] No inhibition at 625 μM.
[b] Inhibition observed at 625 μM.
[c] Inhibition potency probably underestimated since centrifugation was required to remove insoluble material at a concentration 10 mM in 20% DMSO.
[d] All compounds were initially dissolved in 100% DMSO and suitable dilutions were prepared for kinetic experiments to be performed in the presence of 1–2% DMSO.
[e] 65:35 Mixture of diastereoisomers.
[f] No inhibition at 1000 μM.
[g] K_i values were reported by Bokor et al.[26] (n.d. = not determined).



16a **R** = CH_2OH K_i = 26 μM
16b **R** = Ph K_i = 162 μM
16f **R** = 2-Naphthyl K_i = 36 μM

Figure 5. Glucose-based inhibitors of glycogen phosphorylase and their inhibition toward RMGP*b*.

compounds **10a**–**h** in water. Although the water solubility of the sulfoxides **12a**,**b** and sulfones **15a**,**b** was less critical, the inhibitions measured for these compounds were still disappointing. A comparison of the inhibitory properties of the hydroxymethylated derivatives **5a**, **10a**, **12a** and **15a** revealed neither an influence of the xylose/thioxylose scaffold nor that of the sulfur oxidation state on the inhibition of RMGP*b*. The cyclohexane and cyclohexene-1-yl substituted derivatives **10i** and **10j** were not evaluated as RMGP*b* inhibitors due to the low potencies observed for the other compounds **10a**–**h** and since non-aromatic substituents usually do not perform well in interacting with the β-channel of GP. In our hands, a few attempts aiming at the synthesis of xylose-based sulfonium derivatives failed. Considering the limitations associated to the D-xylose scaffold (weak water-solubility) and the poor inhibition observed with the tested compounds, this route was not investigated further.

3. Conclusion

The synthesis of xylose- and 5-thioxylose-based 1,2,3-triazole inhibitors of GP was achieved through 1,3-dipolar cycloaddition of alkynes to the corresponding D-xylopyranosyl azide. Oxidation of the sulfur atom afforded the sulfoxide and sulfone analogues in good yields. Deacetylation led to twenty one structures found only poorly or even not water-soluble, from which 19 candidates have been evaluated as RMGP*b* inhibitors. The inhibitory potency exhibited was very modest (in the mM range), much weaker compared to D-glucose-based analogues. The D-xylose scaffold should prevent the O-phosphorylation observed in vivo for D-glucopyranosylamines at the 6-position with detrimental consequences. However, the absence of a hydroxymethyl substituent at the 5-position in the xylose-based triazoles was highly detrimental in terms of water-solubility and binding to the catalytic site of GP, resulting in no or poor inhibition of the enzyme. Although a slightly reduced inhibitory potency, compared to that of D-glucopyranose, was anticipated due to the D-xylopyranose motif, the quest for a more favorable heterocyclic moiety to compensate for the modification of the glucose moiety did not meet our expectations. However, the xylose-, and 5-thioxylose-based derivatives reported herein might have potential for other biomedicinal developments which are associated to important health issues.

4. Experimental section

4.1. General methods

All reagents and solvents used for syntheses were commercial and used without further purification. Solvents were distilled over CaH_2 (CH_2Cl_2), Mg/I_2 (MeOH), or purchased dry. Reactions were performed under argon atmosphere. NMR spectra were recorded at 293 K, unless stated otherwise, using a 300 MHz, a 400 MHz or a 500 MHz spectrometer. Shifts are referenced relative to deuterated solvent residual peaks. Low and high resolution mass spectra were recorded in the positive mode using a Bruker MicrOTOF-Q II XL spectrometer. Thin-layer chromatography (TLC) was carried out on aluminium sheets coated with silica gel 60 F_{254} (Merck). TLC plates were inspected by UV light (λ = 254 nm) and developed by treatment with a solution of 10% H_2SO_4 in EtOH/H_2O (1:1 v/v) or $KMnO_4$ in H_2O or ninhydrin in *n*-BuOH/H_2O followed by heating. Silica gel column chromatography was performed with silica gel Si 60 (40–63 μm). Optical rotations were measured using a Perkin Elmer polarimeter and values are given in 10^{-1} deg cm^2 g^{-1}.

4.2. General procedure A for the preparation of 1-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-4-substituted-1,2,3-triazoles (4a–g)

A solution of 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl azide **3** (150 mg, 0.5 mmol) and CuI (47 mg, 0.25 mmol, 0.5 equiv) in dry DMF (10 mL) was stirred under argon. Then a selected alkyne was added (1.0 mmol, 2 equiv) followed by the addition of *i*Pr$_2$NEt (2.49 mmol, 0.435 mL, 5 equiv). The solution was stirred at 100 °C under argon and the reaction was completed within ~1 h as monitored by TLC (EtOAc/PE 1:1). The mixture was cooled to rt then diluted with EtOAc (70 mL). The organic layer was washed with aqueous solutions (HCl 1 N, then saturated Na_2CO_3, finally saturated NaCl—3 × 30 mL in each case), dried, ($MgSO_4$) and concentrated to dryness to afford a solid residue which was washed with MeOH (<5 mL). After solvent removal under vacuum, the solids obtained were found analytically pure by TLC and NMR analyses (^{1}H and ^{13}C).

4.3. General procedure B for the preparation of 1-(β-D-xylopyranosyl)-4-substituted-1,2,3-triazoles (5a–g)

The acetylated xylo-triazole (**4a**–**g**, 0.5 mmol) was dissolved in dry MeOH (15 mL) and dry DMF (5 mL or more according to

solubility). After addition of sodium methoxide (0.3 equiv), the solution was stirred under argon atmosphere. Monitoring by TLC (EtOAc/MeOH 9:1) showed that completion was reached usually within one day. The reaction mixture was treated with IR-120 ion-exchange resin (H^+ form). The resin was filtered off and washed with MeOH (2 × 5 mL). The filtrate was concentrated and co-evaporated several times with toluene to give a solid which was washed with CH_2Cl_2 (2 × 2 mL). After removal of the solvents under high vacuum, the product examined by NMR (^1H and ^{13}C) was found analytically pure.

4.4. General procedure C for the synthesis of 1-[2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl]-4-substituted-1,2,3-triazoles (9a–j)

A suspension of 2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl azide **7** (200 mg, 0.63 mmol, 1 equiv), CuI (11 mg, 0.06 mmol, 0.1 equiv) and alkyne (1.26 mmol, 2 equiv) in dry DMF (5 mL) was sonicated for a few seconds. Then DIPEA (823 μL, 4.73 mmol, 7.5 equiv) was added and the mixture was stirred for 2 h at 110 °C. The mixture was then diluted with EtOAc (100 mL), washed with 1 N HCl (2 × 50 mL), saturated $NaHCO_3$ (2 × 50 mL), water (2 × 50 mL), brine (2 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was suspended in a minimum of CH_2Cl_2 (~5 mL), precipitated with petroleum ether and filtered to afford analytically pure 1-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-substituted-1,2,3-triazoles **9a–j**.

4.5. General procedure D for the synthesis of 5-thio-β-D-xylopyranosyl-4-substituted-1,2,3-triazoles 10a–j

Sodium methoxide (0.4 equiv) was added to a solution of 1-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-(substituted)-1,2,3-triazole **9a–j** (1 equiv) in a DMF/MeOH (9:1) mixture (10 mL). The mixture was stirred at room temperature overnight, neutralized with Amberlite IR 120 resin, and filtered. The filtrate was concentrated under reduced pressure. The crude product was washed with a minimum of methanol and filtered to give an analytically pure product.

4.6. General procedure E for the synthesis of 5-thioxylose-based sulfoxides 8 and 11a–b

To a solution of azido 2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranose **7** or 1-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-substituted-1,2,3-triazoles **9a**,**b** (1 equiv) in dry THF (5 mL/0.3 mmol) was added dropwise a solution of *m*-CPBA (1.2 equiv) in dry THF (5 mL/0.4 mmol). The mixture was stirred at rt for 15 min, diluted with EtOAc (50 mL) and washed successively with saturated solutions of $Na_2S_2O_3$ (50 mL), $NaHCO_3$ (2 × 50 mL) and NaCl (2 × 50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product (white solid) was purified by silica gel chromatography (Et_2O/CH_2Cl_2 9:1) to give a portion of the starting material, a pure fraction of the less polar sulfoxide (e.g., **8-*S***), a mixture of both diastereoisomeric sulfoxides and a pure portion of the more polar sulfoxide (e.g., **8-*R***).

4.7. General procedure F for the synthesis of thioxylose-based sulfones (14a,b)

To a suspension of 1-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-substituted-1,2,3-triazole **9a**,**b** (1 equiv) and 'ammonium molybdate' (0.05 equiv) in dry ethanol (10 mL/0.5 mmol) was added at 0 °C a solution of hydrogen peroxide 35% wt in water (8 equiv). The mixture was stirred at 0 °C for 1 h, allowed to warm up to rt and stirred for an additional 16 h. The mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 × 25 mL). The organic layers were combined, washed with $Na_2S_2O_3$ 10% in water (3 × 50 mL), water (2 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by silica gel chromatography (CH_2Cl_2/EtOAc 9:1) to afford 1-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-substituted-1,2,3-triazole *S*,*S*-dioxide **14a**,**b**.

4.8. General procedure G for the deacetylation of thioxylose-based sulfoxides and sulfones under acidic conditions

To a solution of acetylated derivatives in a mixture of dry THF and dry MeOH (10 mL/100 mg, 1:1) was added acetyl chloride (100 μL/100 mg) at 0 °C. The mixture was stirred at rt overnight and concentrated in vacuo to afford the desired deacetylated product.

4.9. Glycogen phosphorylase inhibition measurements

Kinetic experiments were performed as described previously for the xylose-based analogues **5a–g**[61] and for the other sulfur-containing analogues.[62]

4.10. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-4-acetoxymethyl-1,2,3-triazole (4a)

The title compound was prepared from **3** (291 mg, 0.97 mmol) and propargyl acetate (291 mg, 2.97 mmol) which reacted, following the general procedure A, at rt (because of the volatility of propargyl acetate) and with a slower reaction rate (reaction time: 18 h). It was isolated as yellow solid foam (297 mg, 0.74 mmol, 77%). R_f = 0.75 (EtOAc/PE 1:1). $[\alpha]_D^{20}$ −58.8 (*c* 1.0/CH_2Cl_2). ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.81 (s, 1H, H-5′), 5.77 (d, 1H, *J* = 8.8 Hz,H-1), 5.40 (t, 1H, *J* = 8.8 Hz, H-3), 5.35 (t, 1H, *J* = 8.8 Hz, H-2), 5.18 (s, 2H, C*H*$_2$OAc), 5.09–5.16 (m, 1H, H-4), 4.27 (dd, 1H, *J* = 11.6, 5.6 Hz, H-5 eq), 3.58 (t, 1 H, *J* = 11.6 Hz, H-5ax), 2.05, 2.03, 1.86 (3s, 12H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.0, 170.1, 170.0, 169.2 (4C, C═O), 143.9 (C-4′), 122.4 (C-5′), 86.6 (C-1), 72.3 (C-3), 70.8 (C-2), 68.7 (C-4), 65.9 (C-5), 57.7 (CH_2OAc), 21.1, 20.9, 20.9, 20.5 ($4CH_3$, acetyl). ESI-MS (positive mode) *m/z*: 422.1 $[M+Na]^+$, 920.2 $[2M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{16}H_{21}N_3O_9$ $[M+Na]^+$ 422.1170, found 422.1171.

4.11. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-4-phenyl-1,2,3-triazole (4b)[47]

The title compound was prepared from **3** (147 mg, 0.49 mmol) and phenylacetylene (0.11 mL, 1.0 mmol) according to general procedure A, and isolated as a white solid (158 mg, 0.39 mmol, 80%). R_f = 0.53 (EtOAc/PE 1:1). Mp = 241–246 °C. $[\alpha]_D^{20}$ −127.1 (*c* 1.0/CH_2Cl_2). ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.98 (s, 1H, H-5′), 7.84 (d, 2H, *J* = 7.2 Hz, H-Ar), 7.43 (t, 2H, *J* = 7.5 Hz, H-Ar), 7.37 (t, 1H, *J* = 7.2 Hz, H-Ar), 5.84 (d, 1H, *J* = 4.8 Hz, H-1), 5.45 (m, 2H, H-2, H-3), 5.15–5.23 (m, 1H, H-4), 4.33 (dd, 1H, *J* = 11.2, 5.8 Hz, H-5_{eq}), 3.62 (t, 1H, *J* = 11.2 Hz, H-5_{ax}), 2.08, 2.06, 1.89 (3s, 9H, acetyl); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.2, 170.1, 169.4 (3C═O, acetyl), 148.8 (C-4′), 130.3 (C-Ar), 129.2 (2CH-Ar), 128.9 (CH-Ar), 126.2 (2CH-Ar), 117.9 (C-5′), 86.6 (C-1), 72.5 (C-2) 70.7 (C-3), 68.8 (C-4), 66.0 (C-5), 21.0, 20.9, 20.6 ($3CH_3$, acetyl). ESI-MS (positive mode) *m/z*: 404.1 $[M+H]^+$, 426.1 $[M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{19}H_{21}N_3O_7$ $[M+Na]^+$ 426.1272, found 426.1265.

4.12. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-4-(4-nitrophenyl)-1,2,3-triazole (4c)

The title compound was prepared from **3** (143 mg, 0.47 mmol) and 4-nitrophenyl-ethynyl (147 mg, 1.0 mmol) according to the

general procedure A, and isolated as a pale yellow solid (187 mg, 0.42 mmol, 88%). R_f = 0.52 (EtOAc/PE 1:1). Mp = 204–207 °C. $[\alpha]_D^{20}$ −126.7 (*c* 1.0/CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.30 (d, 2H, *J* = 9.0 Hz, H-Ar), 8.13 (s, 1H, H-5′), 8.01 (d, 2H, *J* = 9.0 Hz, H-Ar), 5.86 (d, 1H, *J* = 9.3 Hz, H-1), 5.47 (t, 1H, *J* = 9.3 Hz, H-2), 5.42 (t, 1H, *J* = 9.3 Hz, H-3), 5.18 (ddd, 1H, *J* = 11.4, 9.3, 5.7 Hz, H-4), 4.35 (dd, 1H, *J* = 11.4, 5.7 Hz, H-5_{eq}), 3.64 (t, 1H, *J* = 11.4 Hz, H-5_{ax}), 2.09, 2.07, 1.91 (3s, 9H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.1, 170.0, 169.4 (3C, C═O), 147.7 (C-Ar), 146.5 (C-Ar), 136.4 (C-4′), 126.6 (2CH-Ar), 124.6 (2CH-Ar), 119.5 (C-5′), 86.8 (C-1), 72.1 (C-3), 70.8 (C-2), 68.6 (C-4), 66.0 (C-5), 20.9, 20.8, 20.5 ($3CH_3$, acetyl). ESI-MS (positive mode) *m/z*: 471.1 $[M+Na]^+$, 919.2 $[2M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{19}H_{20}N_4O_8$ $[M+Na]^+$ 471.1122, found 471.1115.

4.13. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-4-(4-methylphenyl)-1,2,3-triazole (4d)

The title compound was prepared from **3** (138 mg, 0.46 mmol) and 4-tolyl-ethynyl (0.13 mL, 1.00 mmol) according to the general procedure A, and isolated as a white solid (174 mg, 0.42 mmol, 91%). R_f = 0.51 (EtOAc/PE 1:1). Mp = 239–242 °C. $[\alpha]_D^{20}$ −105.0 (*c* 1.0/CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.93 (s, 1H, H-5′), 7.71 (d, 2H, *J* = 8.0 Hz, H-Ar), 7.23 (d, 2H, *J* = 8.0 Hz, H-Ar), 5.83 (d, 1H, *J* = 8.8 Hz, H-1), 5.46 (t, 1H, *J* = 8.8 Hz, H-2), 5.43 (t, 1H, *J* = 8.8 Hz, H-3), 5.18 (ddd, 1H, *J* = 11.6, 8.8, 5.6 Hz H-4), 4.31 (dd, 1H, *J* = 11.6, 5.6 Hz, H-5_{eq}), 3.62 (t, 1H, *J* = 11.6 Hz, H-5_{ax}), 2.38 (s, 3H, PhC*H*$_3$), 2.08, 2.06, 1.88 (3s, 9H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.2, 170.1, 169.4 (3C, C═O), 148.8 (C-4′), 138.8 (C-Ar), 129.9 (2CH-Ar), 127.5 (C-Ar), 126.1 (CH-Ar), 117.6 (C-5′), 86.7 (C-1), 72.5 (C-3), 70.7 (C-2), 68.8 (C-4), 65.9 (C-5), 21.6 (Ph*C*H$_3$), 21.0, 20.9, 20.6 ($3CH_3$, acetyl). ESI-MS (positive mode) *m/z*: 440.1 $[M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{20}H_{23}N_3O_7$ $[M+Na]^+$ 440.1428, found 440.1411.

4.14. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-1,2,3-triazole-4-(4-methoxy-2-methylphenyl) (4e)

The title compound was prepared from **3** (134 mg, 0.45 mmol) and 1-ethynyl-4-methoxy-2-methyl-benzene (159 mg, 1.09 mmol) according to the general procedure A, and isolated as a beige solid (97 mg, 0.22 mmol, 49%). R_f = 0.63 (EtOAc/PE 1:1). Mp = 154–156 °C. $[\alpha]_D^{20}$ −107.6 (*c* 1.0/CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.79 (s, 1H, H-5′), 7.68 (d, 1H, *J* = 8.7 Hz H-Ar), 6.80 (m, 2H, H-Ar), 5.84 (d, 1H, *J* = 9.0 Hz, H-1), 5.45 (m, 2H, H-2, H-3), 5.18 (m, 1H, H-4), 4.31 (dd, 1H, *J* = 11.0, 5.7 Hz, H-5_{eq}), 3.82 (s, 3H, PhOC*H*$_3$), 3.62 (t, 1H, *J* = 11.0 Hz, H-5ax), 2.41 (s, 3H, PhC*H*$_3$), 2.08, 2.05, 1.88 (3s, 9H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.2, 170.1, 169.4 (3C, C═O), 159.9 (C-Ar), 147.8 (C-4′), 137.6 (C-Ar), 130.6 (CH-Ar), 122.4 (C-Ar), 119.5 (C-5′), 116.5 (CH-Ar), 111.8 (CH-Ar), 86.7 (C-1), 72.4 (C-3), 70.7 (C-2), 68.8 (C-4), 65.9 (C-5), 55.6 (PhO*C*H$_3$), 21.8 (Ph*C*H$_3$), 21.0, 20.5, 20.9 ($3CH_3$, acetyl). ESI-MS (positive mode) *m/z*: 448.2 $[M+H]^+$, 470.2 $[M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{21}H_{26}N_3O_8$ $[M+H]^+$ 448.1714, found 448.1708.

4.15. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-4-(2-naphthyl)-1,2,3-triazole (4f)

The title compound was prepared from **3** (146 mg, 0.49 mmol) and 2-ethynyl-naphthalene (138 mg, 0.46 mmol) according to the general procedure A, and isolated as a white solid (202 mg, 0.45 mmol, 98%). R_f = 0.68 (EtOAc/PE 1:1). Mp = 245–249 °C. $[\alpha]_D^{20}$ −130.6 (*c* 1.0/DMSO). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.36 (s, 1H, H-Ar), 8.10 (s, 1H, H-5′), 7.86 (m, 4H, H-Ar), 7.50 (m, 2H, H-Ar), 5.88 (d, 1H, *J* = 8.4 Hz, H-1), 5.50 (t, 1H, *J* = 8.4 Hz, H-2), 5.46 (t, 1H, *J* = 8.4 Hz, H-3), 5.20 (m, 1H, H-4), 4.35 (dd, 1H, *J* = 11.4, 6.0 Hz, H-5 eq), 3.65 (t, 1H, *J* = 11.4 Hz, H-5_{ax}), 2.10, 2.07, 1.91 (3s, 9H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.1, 170.1, 169.5 (3C, C═O), 133.8 (C-4′), 133.7 (C-Ar), 133.4 (C-Ar), 129.0 (CH-Ar), 128.6 (CH-Ar), 128.1 (2CH-Ar), 127.5 (C-Ar), 126.9 (CH-Ar), 126.7 (CH-Ar), 125.2 (CH-Ar), 124.1 (C-5′), 86.9 (C-1), 72.5 (C-3), 70.8 (C-2), 68.8 (C-4), 66.0 (C-5), 21.0, 21.0, 20.6 ($3CH_3$, acetyl). ESI-MS (positive mode) *m/z*: 476.1 $[M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{23}H_{23}N_3O_7$ $[M+Na]^+$ 476.1428, found 476.1422.

4.16. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-4-(6-methoxy-2-naphthyl)-1,2,3-triazole (4g)

The title compound was prepared from **3** (144 mg, 0.48 mmol) and 2-ethynyl-6-methoxynaphthalene (184 mg, 1.01 mmol) according to the general procedure A, and isolated as a white solid (186 mg, 0.38 mmol, 80%). R_f = 0.58 (EtOAc/PE 1:1). Mp = 247–249 °C. $[\alpha]_D^{20}$ −99.6 (*c* 1.0/CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.29 (s, 1H, H-5′), 8.08–8.14 (m, 1H, H-Ar), 7.70–7.90 (m, 3H, H-Ar), 7.14–7.19 (m, 2H, H-Ar), 5.86 (d, 1H, *J* = 8.4 Hz, H-1), 5.50 (m, 1H, H-2), 5.45 (m, 1H, H-3), 5.20 (m, 1H, H-4), 4.34 (dd, 1 H, *J* = 11.2, 5.6 Hz, H-5_{eq}), 3.94 (s, 3H, OCH_3), 3.64 (t, 1H, *J* = 11.2 Hz, H-5_{ax}), 2.09, 2.07, 1.91 (3s, 9H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.2, 170.1, 169.5 (3C, C═O), 158.4 (C-Ar) 134.9 (C-Ar), 134.9 (C-Ar), 130.1 (CH-Ar), 129.3 (C-4′), 127.8 (CH-Ar), 125.0 (C-5′), 124.7 (2CH-Ar), 119.7 (CH-Ar), 106.1 (CH-Ar), 86.9 (C-1), 72.5 (C-3), 70.7 (C-2), 68.8 (C-4), 66.0 (C-5), 55.7 (OCH_3), 21.0, 21.1, 20.6 ($3CH_3$, acetyl). ESI-MS (positive mode) *m/z*: 483.9 $[M+H]^+$, 506.0 $[M+Na]^+$, 966.5 $[2M+H]^+$, 988.8 $[2M+Na]^+$, 1470.8 $[3M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{24}H_{25}N_3O_8$ $[M+Na]^+$ 506.1534, found 506.1526.

4.17. 1-(β-D-Xylopyranosyl)-4-hydroxymethyl-1,2,3-triazole (5a)[47]

The title compound was prepared from **4a** (142 mg, 0.356 mmol) according to the general procedure B, and isolated as a yellow amorphous solid (67 mg, 0.292 mmol, 82%). R_f = 0.20 (EtOAc/MeOH 9:1). $[\alpha]_D^{20}$ −66.0 (*c* 1.00/DMSO). ^{1}H NMR (DMSO-d_6 + ε D2O, 400 MHz): δ = 8.13 (s, 1H, H-5′), 5.47 (d, 1H, *J* = 9.2 Hz, H-1), 4.54 (s, 2H, C*H*$_2$OH), 3.86 (dd, 1H, *J* = 10.8, 5.2 Hz, H-5 eq), 3.78 (t, 1H, *J* = 9.2 Hz, H-2), 3.48–3.54 (m, 1H, H-4), 3.38 (m, 2H, H-3, H-5ax). ^{13}C NMR (DMSO-d_6 + ε D2O, 100 MHz): δ = 148.9 (C-4′), 123.1 (C-5′), 89.1 (C-1), 78.0 (C-3), 73.0 (C-2), 70.1 (C-4), 69.4 (C-5), 55.9 (CH_2OH). ESI-MS (positive mode) *m/z*: 254.1 $[M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_8H_{13}N_3O_5$ $[M+Na]^+$ 254.0747, found 254.0747.

4.18. 1-(β-D-Xylopyranosyl)-4-phenyl-1,2,3-triazole (5b)[47]

The title compound was prepared from **4b** (137 mg, 0.34 mmol) according to the general procedure B, and isolated as a pale yellow solid (95 mg, 0.34 mmol, 99%). R_f = 0.33 (EtOAc/MeOH 9:1). Mp = 163–170 °C. $[\alpha]_D^{20}$ −40.1 (*c* 1.0/DMSO). ^{1}H NMR (DMSO-d_6 + ε D2O, 400 MHz): δ = 8.84 (s, 1H, H-5′), 7.91 (d, 2H, *J* = 7.2 Hz, H-Ar), 7.49 (t, 2H, *J* = 7.6 Hz, H-Ar), 7.38 (t, 1H, *J* = 7.6 Hz, H-Ar), 5.56 (d, 1H, *J* = 9.4 Hz, H-1), 3.90 (dd, 1H, *J* = 10.8, 5.2 Hz, H-5 eq), 3.83 (t, 1H, *J* = 9.4 Hz, H-2), 3.80–3.86 (m, 1H, H-4), 3.39–3.47 (m, 2H, H-3, H-5ax). ^{13}C NMR (DMSO-d_6 + ε D2O, 100 MHz): δ = 147.3 (C-4′), 131.6 (C-Ar), 129.9 (CH-Ar), 129.0 (CH-Ar), 126.2 (CH-Ar), 121.3 (C-5′), 89.3 (C-1), 77.6 (C-3), 73.0 (C-2), 70.0 (C-4), 69.3 (C-5). ESI-MS (positive mode) *m/z*: 300.1 $[M+Na]^+$, 576.9 $[2M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{13}H_{15}N_3O_4$ $[M+Na]^+$ 300.0955, found 300.0957.

4.19. 1-(β-D-Xylopyranosyl)-4-(4-nitrophenyl)-1,2,3-triazole (5c)

The title compound was prepared from **4c** (210 mg, 0.47 mmol) according to the general procedure B, and isolated as a white solid (150 mg, 0.47 mmol, 99%). R_f = 0.33 (EtOAc/MeOH 9:1). Mp = 197–198 °C. $[\alpha]_D^{20}$ – 36.1 (*c* 1.0/DMSO). ^{1}H NMR (DMSO-d_6 + ε D2O, 400 MHz): δ = 9.05 (s, 1H, H-5′), 8.35 (d, 2H, *J* = 8.8 Hz, H-Ar), 8.16 (d, 2H, *J* = 8.8 Hz, H-Ar), 5.60 (d, 1H, *J* = 9.2 Hz, H-1), 3.91 (dd, 1H, *J* = 10.8, 5.2 Hz, H-5$_{eq}$), 3.82 (t, 1H, *J* = 9.2 Hz, H-2), 3.52–3.56 (m, 1H, H-4), 3.39–3.49 (m, 2H, H-3, H-5). ^{13}C NMR (DMSO-d_6 + ε D2O, 100 MHz): δ = 148.1 (C-4′), 145.9 (C-Ar), 138.1 (C-Ar), 127.4 (2CH-Ar), 125.8 (2CH-Ar), 123.8 (C-5′), 89.7 (C-1), 77.9 (C-3), 73.4 (C-2), 70.3 (C-4), 69.6 (C-5). ESI-MS (negative mode) *m/z*: 357.1 $[M+Cl]^-$. HR-LSIMS-MS (negative mode) *m/z*: calculated for $C_{13}H_{14}N_4O_6$ $[M+Cl]^-$ 357.0607, found 357.0607.

4.20. 1-(β-D-Xylopyranosyl)-4-(4-methylphenyl)-1,2,3-triazole (5d)

The title compound was prepared from **4d** (146 mg, 0.35 mmol) according to the general procedure B, and isolated as a pale beige solid (101 mg, 0.35 mmol, 99%). R_f = 0.30 (EtOAc/MeOH 9:1). Mp = 178–181 °C. $[\alpha]_D^{20}$ – 45.3 (*c* 1.0/DMSO). ^{1}H NMR^{1}H NMR (DMSO-d_6 + ε D2O, 400 MHz): 8.77 (s, 1H, H-5′), 7.79 (d, 2H, *J* = 8.0 Hz H-Ar), 7.30 (d, 2H, *J* = 8.0 Hz, H-Ar), 5.54 (d, 1H, *J* = 9.4 Hz, H-1), 3.90 (dd, 1H, *J* = 10.8, 5.2 Hz, H-5 eq), 3.82 (t, 1H, *J* = 9.4 Hz, H-2), 3.51–3.54 (m, 1H, H-4), 3.38–3.50 (m, 2H, H-3, H-5ax), 2.36 (s, 3H, PhCH_3). ^{13}C NMR (DMSO-d_6 + ε D2O, 100 MHz): δ = 147.4 (C-4′), 138.4 (C-Ar), 130.5 (C-5′), 128.8 (C-Ar), 126.1 (2CH-Ar), 120.9 (2CH-Ar), 89.3 (C-1), 77.8 (C-3), 73.0 (C-2), 70.0 (C-4), 69.3 (C-5), 21.9 (PhCH_3). ESI-MS (positive mode) *m/z*: 314.1 $[M+Na]^+$, 604.9 $[2M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{14}H_{17}N_3O_4$ $[M+Na]^+$ 314.1111, found 314.1109.

4.21. 1-(β-D-Xylopyranosyl)-4-(4-methoxy-2-methylphenyl)-1,2,3-triazole (5e)

The title compound was prepared from **4e** (100 mg, 0.223 mmol) according to the general procedure B, and isolated as a beige solid (72 mg, 0.223 mmol, 99%). R_f = 0.37 (EtOAc/MeOH 9:1). Mp = 158–165 °C. $[\alpha]_D^{20}$ – 33.9 (*c* 1.0/DMSO). ^{1}H NMR (DMSO-d_6 + ε D2O, 400 MHz): δ = 8.48 (s, 1H, H-5′), 7.68 (d, 1H, *J* = 8.4 Hz H-Ar), 6.89 (m, 2H, H-Ar), 5.54 (d, 1H, *J* = 9.6 Hz, H-1), 3.87–3.92 (m, 2H, H-2, H-5 eq), 3.81 (s, 3H, PhOCH_3), 3.38–3.53 (m, 3H, H-3, H-4, H-5ax), 2.44 (s, 3H, PhCH_3). ^{13}C NMR (DMSO-d_6 + ε D2O, 100 MHz): δ = 159.9 (C-Ar), 146.5 (C-4′), 137.8 (C-Ar), 130.7 (CH-Ar), 123.5 (C-Ar), 122.5 (C-5′), 117.1 (CH-Ar), 112.6 (CH-Ar), 89.3 (C-1), 77.9 (C-3), 72.8 (C-2), 70.0 (C-4), 69.3 (C-5), 56.1 (PhOCH_3), 22.3 (PhCH_3). ESI-MS (positive mode) *m/z*: 344.1 $[M+Na]^+$, 665.0 $[2M+Na]^+$, 985.8 $[3M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{15}H_{19}N_3O_5$ $[M+Na]^+$ 344.1217, found 344.1213.

4.22. 1-(β-D-Xylopyranosyl)-4-(2-naphthyl)-1,2,3-triazole (5f)

The title compound was prepared from **4f** (178 mg, 0.393 mmol) according to the general procedure B, and isolated as a pale beige solid (123 mg, 0.375 mmol, 95%). R_f = 0.66 (EtOAc/MeOH 9:1). Mp = 207–210 °C. $[\alpha]_D^{20}$ –44.9 (*c* 1.0/DMSO). ^{1}H NMR (DMSO-d_6 + ε D2O, 400 MHz): δ = 8.96 (s, 1 H, H-5′), 8.47 (s, 1H, H-Ar), 7.95–8.05 (m, 4H, H-Ar), 7.57 (m, 2H, H-Ar), 5.59 (d, 1H, *J* = 9.0 Hz, H-1), 3.92 (dd, 1H, *J* = 10.8, 4.8 Hz, H-5 eq), 3.86 (t, 1H, *J* = 9.0 Hz, H-2), 3.52–3.60 (m, 1H, H-4), 3.43–3.49 (m, 2H, H-3, H-5ax). ^{13}C NMR (DMSO-d_6 + ε D2O, 100 MHz): δ = 147.5 (C-4′), 134.3 (C-Ar), 133.7 (C-Ar), 129.7 (CH-Ar), 129.1 (CH-Ar), 129.1 (CH-Ar), 128.8 (CH-Ar), 127.4 (CH-Ar), 124.7 (CH-Ar), 124.7 (CH-Ar), 121.9 (C-5′), 89.4 (C-1), 77.8 (C-3), 73.2 (C-2), 70.1 (C-4), 69.4 (C-5), ppm. ESI-MS (positive mode) *m/z*: 328.1 $[M+H]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{17}H_{17}N_3O_4$ $[M+H]^+$ 328.1292, found 328.1283.

4.23. 1-(β-D-Xylopyranosyl)-4-(6-methoxy-2-naphthyl)-1,2,3-triazole (5g)

The title compound was prepared from **4g** (165 mg, 0.34 mmol) according to the general procedure B, and isolated as a pale beige solid (121 mg, 0.34 mmol, 99%). R_f = 0.33 (EtOAc/MeOH 9:1). Mp = 240–245 °C. $[\alpha]_D^{20}$ –25.6 (*c* 1.00/DMSO). ^{1}H NMR (DMSO-d_6 + ε D2O, 400 MHz): δ = 8.91 (s, 1 H, H-5′), 8.40 (s, 1H, H-Ar), 8.00 (d, 1H, *J* = 8.8 Hz, H-Ar), 7.90–7.93 (m, 2 H, H-Ar), 7.38 (d, 1 H, *J* = 2.4 Hz, H-Ar), 7.23 (dd, 1 H, *J* = 2.4 Hz, *J* = 8.8 Hz, H-Ar), 5.57 (d, 1 H, *J* = 9.0 Hz, H-1), 3.93 (s, 3H, PhOCH_3), 3.88–3.95 (m, 1 H, H-5$_{eq}$), 3.86 (t, 1 H, *J* = 9.0 Hz, H-2), 3.25–3.60 (m, 3 H, H-3, H-4, H-5$_{ax}$). ^{13}C NMR (DMSO-d_6 + ε D2O, 100 MHz): δ = 158.4 (C-Ar), 147.5 (C-4′), 134.9 (C-Ar), 130.5 (CH-Ar), 129.5 (C-Ar), 128.4 (C-Ar), 126.8 (CH-Ar), 125.1 (CH-Ar), 124.4 (CH-Ar), 121.2 (C-5′), 120.1 (CH-Ar), 107.0 (CH-Ar), 89.3 (C-1), 77.8 (C-3), 73.2 (C-2), 70.1 (C-4), 69.3 (C-5), 56.2 (PhOCH_3). ESI-MS (positive mode) *m/z*: 380.1 $[M+Na]^+$, 737.0 $[2\,M+Na]^+$. HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{18}H_{19}N_3O_5$ $[M+Na]^+$ 380.1217, found 380.1217.

4.24. 2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl azide (7)[54]

To a solution of sodium azide (1.83 g, 28.15 mmol, 2 equiv) in DMSO (40 mL) was added 2,3,4-tri-*O*-acetyl-5-thio-α-D-xylopyranosyl bromide **6**[53] (5.00 g, 14.08 mmol, 1 equiv). The reaction was stirred at rt for 2 h, diluted with Et_2O (150 mL), and washed with water (100 mL). The aqueous layer was extracted with Et_2O (3 × 50 mL). The organic layers were combined, washed with water (4 × 150 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was solubilized in a minimum of Et_2O, precipitated with Pet. Ether and filtered to afford azido 2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranose **7** as a white powder (3.84 g, 12.11 mmol, 86%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.03–5.18 (m, 3H, H-2, H-3, H-4), 4.48 (d, 1H, *J* = 9.2 Hz, H-1), 2.95 (dd, 1H, *J* = 13.7, 3.7, H-5e), 2.71 (dd, 1H, *J* = 13.7, 10.5, H-5a), 2.09, 2.03, 2.03 (3s, 9H, acetyl).

4.25. 2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl azide (*S*)-*S*-oxide (8-*S*)

The title compound was prepared from **7** according to the general procedure E, and isolated as a white powder. R_f = 0.27 (PE/EtOAc 1:1). Mp = 135–136 °C (CH_2Cl_2/PE). $[\alpha]_D^{20}$ –62 (*c* 1/CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.34 (pdd, 1H, *J* = 9.8 Hz, H-3), 5.05 (ddd, 1H, *J* = 12.5, 10.0, 3.8 Hz, H-4), 5.00 (dd, 1H, *J* = 10.9, 9.9 Hz, H-2), 4.48 (d, 1H, *J* = 11.1 Hz, H-1), 3.70 (dd, 1H, *J* = 12.2, 3.7 Hz, H-5e), 3.06 (pdd, 1H, *J* = 12.2 Hz, H-5a), 2.09, 2.04, 2.00 (3s, 9H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 169.4, 169.3, 168.9 (3C, acetyl), 83.1 (C-2), 72.3 (C-3), 66.9 (C-4), 64.4 (C-1), 50.9 (C-5), 20.6, 20.5, 20.4 (3CH_3, acetyl). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{11}H_{16}N_3O_7S$ $[M+H]^+$ 334.0709, found 334.0707.

4.26. 2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl azide (*R*)-*S*-oxide (8-*R*)

The title compound was prepared from **7** according to the general procedure E, and isolated as a white powder. R_f = 0.22 (PE/EtOAc 1:1). Mp = 129–130 °C (CH_2Cl_2/PE). $[\alpha]_D^{20}$ –47 (*c* 0.50/CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.78 (dd, 1H, *J* = 10.3, 9.5 Hz, H-2), 5.70 (ddd, 1H, *J* = 11.5, 9.6, 4.0 Hz, H-4), 5.35 (pdd, 1H, *J* = 9.5 Hz,

H-3), 4.09 (d, 1H, J = 10.3 Hz, H-1), 3.63 (dd, 1H, J = 14.1, 4.0 Hz, H-5e), 2.65 (dd, 1H, J = 14.1, 11.5 Hz, H-5a), 2.12, 2.07, 2.05 (3s, 9H, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{11}H_{16}N_3O_7S$ $[M+H]^+$ 334.0709, found 334.0712.

4.27. 1-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-(acetoxymethyl)-1,2,3-triazole (9a)

The title compound was prepared from **7** according to the general procedure C, and isolated as a white powder (243 mg, 0.58 mmol 93%). R_f = 0.11 (PE/EtOAc 6:4). Mp = 158–159 °C (MeOH). $[\alpha]_D^{20}$ +21 (c 1.45/DMSO). ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.79 (br s, 1H, H-5′), 5.77 (d, 1H, J = 10.2 Hz, H-1), 5.52 (pdd, 1H, J = 9.6 Hz, H-2), 5.24 (pdd, 1H, J = 9.4 Hz, H-3), 5.14–5.19 (m, 1H, H-4), 5.17 (s, 2H, CH_2OAc), 3.07 (dd, 1H, J = 13.8, 4.2 Hz, H-5e), 2.91 (dd, 1H, J = 13.8, 10.3 Hz, H-5a), 2.07, 2.06, 2.02, 1.80 (4s, 12H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 170.8, 169.8, 169.5, 169.0 (4C, C=O), 73.9 (C-2), 72.7 (C-3), 72.0 (C-4), 60.9 (C-1), 57.5 (CH_2OAc), 29.6 (C-5), 20.9, 20.8, 20.6, 20.1 ($4CH_3$, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{16}H_{21}NaN_3O_8S$ $[M+Na]^+$ 438.0942, found 438.0946.

4.28. 1-[2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl]-4-phenyl-1,2,3-triazole (9b)

The title compound was prepared from **7** according to the general procedure C, and isolated as a white powder (253 mg, 0.60 mmol, 96%). R_f = 0.61 (PE/EtOAc 1:1). Mp >250 °C (MeOH). $[\alpha]_D^{20}$ +11 (c 0.94/DMSO). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.92 (s, 1H, H-5′), 7.80–7.83 (m, 2H, H-Ar), 7.33–7.46 (m, 3H, H-Ar), 5.85 (d, 1H, J = 10.2 Hz, H-1), 5.63 (dd, 1H, J = 10.2, 9.1 Hz, H-2), 5.17–5.31 (m, 2H, H-3, H-4), 3.10 (dd, 1H, J = 13.6, 4.3 Hz, H-5e), 2.94 (dd, 1H, J = 13.8, 10.5 Hz, H-5a), 2.08, 2.04, 1.82 (3s, 9H, acetyl). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.7, 169.4, 169.0 (3C, C=O), 148.5 (C-4′), 129.8 (C-Ar), 128.9 (2CH-Ar), 128.6 (CH-Ar), 125.9 (2CH-Ar), 118.3 (C-5′), 73.6 (C-2), 72.7 (C-3), 71.9 (C-4), 60.7 (C-1), 29.6 (C-5), 20.8, 20.5, 20.1 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{19}H_{21}N_3NaO_8S$ $[M+Na]^+$ 442.1049, found 442.1048.

4.29. 1-[2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl]-4-(4-nitrophenyl)-1,2,3-triazole (9c)

The title compound was prepared from **7** according to the general procedure C, and isolated as a pale yellow powder (0.59 mmol, 275 mg, 94%). R_f = 0.53 (PE/EtOAc 1:1). Mp = 244–245 °C (MeOH). $[\alpha]_D^{20}$ +15 (c 1/DMSO). ^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.13 (s, 1H, H-5′), 8.33 (d, 2H, J = 8.9 Hz H-Ar), 8.14 (d, 2H, J = 8.9 Hz, H-Ar), 6.45 (d, 1H, J = 10.0 Hz, H-1), 5.59 (pdd, 1H, J = 9.7 Hz, H-2), 5.41 (pdd, 1H, J = 9.6 Hz, H-3), 5.21 (pddd, 1H, J = 10.3, 4.4 Hz, H-4), 3.29 (dd, 1H, J = 13.2, 11.1 Hz, H-5a), 3.07 (dd, 1H, J = 13.3, 4.4 Hz, H-5e), 2.08, 2.04, 1.84 (3s, 9H, acetyl). ^{13}C NMR (DMSO-d_6, 75 MHz): δ = 169.3, 169.1, 168.4 (3C, C=O), 146.8 (C-Ar), 144.9 (C-4′), 136.2 (C-Ar), 126.1 (2CH-Ar), 124.3 (2CH-Ar), 123.2 (C-5′), 73.7 (C-2), 72.0 (C-3), 71.5 (C-4), 58.9 (C-1), 28.1 (C-5), 20.5, 20.1, 19.7 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{19}H_{20}N_4NaO_8S$ $[M+H]^+$ 487.0900, found 487.0900.

4.30. 1-[2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl]-4-(4-methylphenyl)-1,2,3-triazole (9d)

The title compound was prepared from **7** according to the general procedure C, and isolated as a white powder (249 mg, 0.57 mmol, 90%). R_f = 0.80 (PE/EtOAc 1:1). Mp >250 °C (MeOH). $[\alpha]_D^{20}$ +14 (c 1/DMSO). ^{1}H NMR ($(CD_3)_2CO$, 300 MHz): δ = 8.48 (s, 1H, H-5′), 7.78 (d, 2H, J = 8.2 Hz, H-Ar) 7.25 (d, 2H, J = 7.9 Hz, H-Ar), 6.24 (d, 1H, J = 10.2 Hz, H-1), 5.70 (dd, 1H, J = 10.0, 9.5 Hz, H-2), 5.39 (pdd, 1H, J = 9.6 Hz, H-3), 5.20 (ddd, 1H, J = 10.8, 9.9, 4.5 Hz, H-4), 3.28 (dd, 1H, J = 13.5, 10.8 Hz, H-5a), 3.11 (dd, 1H, J = 13.5, 4.5, H-5e), 2.35 (s, 3H, methyl), 2.03, 1.99, 1.76 (3s, 9H, acetyl). ^{13}C NMR (DMSO-d_6, 75 MHz): δ = 169.3, 169.1, 168.4 (3C, C=O), 146.8 (C-4′), 137.5 (C-Ar), 129.4 (2CH-Ar), 127.2 (C-Ar), 125.1 (2CH-Ar), 120.5 (C-5′), 73.7 (C-2), 72.1 (C-3), 71.5 (C-4), 58.8 (C-1), 28.1 (C-5), 20.7 (CH_3, methyl), 20.5, 20.1, 19.7 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{20}H_{23}N_3NaO_6S$ $[M+Na]^+$ 456.1205, found 456.1205.

4.31. 1-[2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl]-4-(2-methyl-4-methoxyphenyl)-1,2,3-triazole (9e)

The title compound was prepared from **7** according to the general procedure C, and isolated as a white powder (280 mg, 0.60 mmol, 96%). R_f = 0.44 (PE/EtOAc 6:4). Mp = 189–190 °C (MeOH). $[\alpha]_D^{20}$ +19 (c 1/DMSO). ^{1}H NMR (DMSO-d_6, 300 MHz MHz): δ 8.45 (s, 1H, H-5′), 7.58 (d, 1H, J = 8.1 Hz, H-Ar), 6.84–6.87 (m, 2H, H-Ar), 6.38 (d, 1H, J = 9.9 Hz, H-1), 5.68 (pdd, 1H, J = 9.8 Hz, H-2), 5.39 (pdd, 1H, J = 9.6 Hz, H-3), 5.13 (pddd, 1H, J = 10.8, 4.3 Hz, H-4), 3.77 (s, 3H, OCH_3), 3.27 (pdd, 1H, J = 13.1, 11.1 Hz, H-5a), 3.03 (dd, 1H, J = 13.2, 4.3 Hz, H-5e), 2.35 (s, 3H, methyl), 2.03, 1.99, 1.76 (3s, 9H, acetyl). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 169.3, 169.1, 168.3 (3C, C=O), 158.9 (C-Ar), 147.1 (C-Ar), 145.9 (C-4′), 136.8 (C-Ar), 129.6 (CH-Ar), 121.9 (C-5′), 115.9 (CH-Ar), 111.5 (CH-Ar), 73.7 (C-2), 72.2, (C-3), 71.5 (C-4), 58.8 (C-1), 55.0 (OCH_3), 28.1 (C-5), 20.9 (CH_3, methyl), 20.5, 20.1, 19.7 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{21}H_{25}N_3NaO_7S$ $[M+Na]^+$ 486.1311, found 486.1311.

4.32. 1-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-(2-naphthyl)-1,2,3-triazole (9f)

The title compound was prepared from **7** according to the general procedure C, and isolated as a white powder (280 mg, 0.59 mmol, 95%). R_f = 0.69 (PE/EtOAc 1:1). Mp >250 °C (MeOH). $[\alpha]_D^{20}$ +22 (c 1.08/DMSO). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.34 (s, 1H, H-5′), 8.04 (s, 1H, H-Ar), 7.83–7.90 (m, 4H, H-Ar), 7.46–7.53 (m, 2H, H-Ar), 5.89 (d, 1H, J = 10.3 Hz, H-1), 5.67 (dd, 1H, J = 10.2, 9.2 Hz, H-2), 5.29 (pdd, 1H, J = 9.4 Hz, H-3), 5.23 (pddd, 1H, J = 10.1, 4.3 Hz, H-4), 3.10 (dd, 1H, J = 13.8, 4.3 Hz, H-5e), 2.96 (dd, 1H, J = 13.8, 10.5 Hz, H-5a), 2.08, 2.05, 1.83 (3s, 9H, acetyl). ^{13}C NMR (100 MHz MHz, $CDCl_3$) δ = 169.6, 169.6, 169.3 (3C, C=O), 148.8 (C-4′), 133.6 (C-Ar), 133.5 (C-Ar), 128.8 (CH-Ar), 128.4 (CH-Ar), 127.9 (CH-Ar), 127.3 (C-Ar), 126.7 (CH-Ar), 126.5 (CH-Ar), 124.9 (C-5′), 123.9 (CH-Ar), 118.7 (CH-Ar), 73.8 (C-2), 72.9 (C-3), 72.1 (C-4), 60.9 (C-1), 29.7 (C-5), 20.9, 20.6, 20.2 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{23}H_{23}N_3NaO_6S$ $[M+Na]^+$ 492.1200, found 492.1200.

4.33. 1-[2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl]-4-(6-methoxy-2-naphthyl)-1,2,3-triazole (9g)

The title compound was prepared from **7** according to the general procedure C, and isolated as a white powder (308 mg, 0.62 mmol, 98%). R_f = 0.61 (PE/EtOAc 1:1). Mp >250 °C (MeOH). $[\alpha]_D^{20}$ +26 (c 0.63/DMSO). ^{1}H NMR (DMSO-d_6, 300 MHz): δ = 8.87 (s, 1H, H-5′), 8.35 (s, 1H, H-Ar), 7.95 (dd, 1H, J = 8.6, 1.3 Hz, H-Ar), 7.88 (d, 2H, J =9.7 Hz, H-Ar), 7.34 (d, 1H, J = 2.2 Hz, H-Ar), 7.20 (dd, 1H, J = 8.9, 2.4 Hz, H-Ar), 6.42 (d, 1H, J = 10.0 Hz, H-1), 5.62 (pdd, 1H, J = 9.7 Hz, H-2), 5.42 (pdd, 1H, J = 9.6 Hz, H-3), 5.12 (pddd, 1H, J = 10.7, 4.3, H-4), 3.89 (s, 3H, OCH_3), 3.30 (dd, 1H, J = 13.1, 11.2, H-5a), 3.06 (dd, 1H, J = 13.2, 4.3 H-5e), 2.04, 1.99, 1.77 (3s, 9H, acetyl). ^{13}C NMR (DMSO-d_6, 75 MHz MHz): δ = 169.3, 169.1, 168.4 (3C, C=O), 157.5 (C-Ar), 147.0 (C-4′), 134.0

(C-Ar), 129.5 (CH-Ar), 128.3 (C-Ar), 127.3 (CH-Ar), 125.1 (C-Ar), 123.9 (CH-Ar), 123.6 (CH-Ar), 120.8 (C-5′), 119.1 (CH-Ar), 105.9 (CH-Ar), 73.7 (C-2), 72.1 (C-3), 71.6 (C-4), 58.8 (C-1), 55.1 (OCH_3), 28.1 (C-5), 20.5, 20.1, 19.7 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{24}H_{25}N_3NaO_7S$ $[M+Na]^+$ 522.1311, found 522.1312.

4.34. 1-[2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl]-4-(4-methoxyphenyl)-1,2,3-triazole (9h)

The title compound was prepared from **7** according to the general procedure C, and isolated as a white powder (229 mg, 0.51 mmol, 81%). R_f = 0.60 (PE/EtOAc 1:1). Mp = 249–250 °C (MeOH). $[\alpha]_D^{20}$ +17 (*c* 1/DMSO). ^{1}H NMR (DMSO-d_6, 300 MHz): δ = 8.69 (s, 1H, H-5′), 7.78 (d, 2H, *J* = 8.8 Hz, H-Ar), 7.00 (d, 2H, *J* = 8.8 Hz, H-Ar), 6.37 (d, 1H, *J* = 10.0 Hz, H-1), 5.63 (pdd, 1H, *J* = 9.7 Hz, H-2), 5.39 (pdd, 1H, *J* = 9.6 Hz, H-3), 5.10 (pddd, 1H, *J* = 10.3, 4.2 Hz, H-4), 3.79 (s, 3H, OCH_3), 3.27 (dd, 1H, *J* = 13.3, 11.4 Hz, H-5a), 2.93 (dd, 1H, *J* = 13.2, 4.5 Hz, H-5e), 2.03, 1.98, 1.95 (3s, 9H, acetyl). ^{13}C NMR (DMSO-d_6, 75 MHz): δ = 169.3, 169.1, 168.3 (3C, C=O), 159.2 (C-Ar), 146.6 (C-4′), 126.6 (2CH-Ar), 122.5 (C-Ar), 119.9 (C-5′), 114.2 (2CH-Ar), 73.6 (C-2), 72.1 (C-3), 71.5 (C-4), 58.8 (C-1), 55.1 (OCH_3), 28.1 (C5), 20.5, 20.1, 19.7 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{20}H_{23}N_3NaO_7S$ $[M+Na]^+$ 472.1154, found 472.1156.

4.35. 1-[2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl]-4-(cyclohexyl)-1,2,3-triazole (9i)

The title compound was prepared from **7** according to the general procedure C, and isolated as a white powder (241 mg, 0.57 mmol, 90%). R_f = 0.77 (PE/EtOAc 1:1). Mp = 209–210 °C (MeOH). $[\alpha]_D^{20}$ +39 (*c* 1/DMSO). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.39 (s, 1H, H-5′), 5.75 (d, 1H, *J* = 10.3 Hz, H-1), 5.53 (pdd, 1H, *J* = 9.7 Hz, H-2), 5.23 (pdd, 1H, *J* = 9.7 Hz, H-3), 5.16 (pddd, 1H, *J* = 9.7, 4.4 Hz, H-4), 3.05 (dd, 1H, *J* = 13.6, 4.2, H-5e), 2.89 (dd, 1H, *J* = 13.7, 10.4, H-5a), 2.69–2.78 (m, 1H, cyclohexyl), 2.06, 2.02, 1.79 (3s, 9H, acetyl), 1.99–2.04 (m, 2H, cyclohexyl), 1.60–1.78 (m, 4H, cyclohexyl), 1.23–1.45 (m, 4H, cyclohexyl). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.7, 169.4, 168.9 (3C, C=O), 154.5 (C-4′), 118.1 (C-5′), 73.7 (C-2), 72.7 (C-3), 72.0 (C-4), 60.5 (C-1), 35.2 (CH, cyclohexyl), 32.7 ($2CH_2$, cyclohexyl), 29.5 (C5), 26.0 ($2CH_2$, cyclohexyl), 25.9 (CH_2, cyclohexyl), 20.7, 20.4, 20.0 (CH_3, acetyl). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{19}H_{27}N_3NaO_6S$ $[M+Na]^+$ 448.1518, found 448.1517.

4.36. 1-[2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl]-4-(cyclohex-1-enyl)-1,2,3-triazole (9j)

The title compound was prepared from **7** according to the general procedure C, and isolated as a white powder (238 mg, 0.56 mmol 89%). Mp = 194–195 °C (MeOH). $[\alpha]_D^{20}$ +31 (*c* 1/DMSO). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.52 (s, 1H, H-5′), 6.54 (m, 1H, CH-sp2), 5.78 (d, 1H, *J* = 10.3 Hz, H-1), 5.56 (pdd, 1H, *J* = 9.6 Hz, H-2), 5.23 (pdd, 1H, *J* = 9.1 Hz, H-3), 5.17 (pddd, 1H, *J* = 9.8, 4.3 Hz, H-4), 3.03 (dd, 1H, *J* = 13.9, 4.2 Hz, H-5e), 2.90 (dd, 1H, *J* = 13.7, 10.3, H-5a), 2.30–2.34 (m, 2H, cyclohexene), 2.17–2.20 (m, 2H, cyclohexene), 2.06, 2.02, 1.81 (3s, 9H, acetyl), 1.71–1.79 (m, 2H, cyclohexene), 1.63–1.69 (m, 2H, cyclohexene). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.7, 169.4, 169.0 (3C, C=O), 126.7 (C-4′), 126.0 (CH, cyclohexene), 116.8 (C-5′), 77.2 (C, cyclohexene), 73.5 (C-2), 72.7 (C-3), 71.9 (C-4), 60.5 (C-1), 29.5 (C-5), 26.2, 25.2, 22.3, 22.1 ($4CH_2$, cyclohexene), 20.7, 20.4, 20.1 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{19}H_{25}N_3NaO_6S$ $[M+Na]^+$ 446.1362, found 446.1362.

4.37. 5-Thio-β-D-xylopyranosyl-4-hydroxymethyl-1,2,3-triazole (10a)

The title compound was prepared from **9a** according to the general procedure D, and isolated as a white powder (99%). R_f = 0.21 (CH_2Cl_2/MeOH 9:1). Mp = 171–172 °C (MeOH/Et_2O). $[\alpha]_D^{20}$ +42 (*c* 0.81/DMSO). ^{1}H NMR (CD_3OD, 400 MHz): δ = 8.01 (s, 1H, H-5′), 5.57 (d, 1H, *J* = 10.0 Hz, H-1), 4.68 (s, 2H, CH_2OH), 4.03 (dd, 1H, *J* = 9.9, 9.0 Hz, H-2), 3.77 (ddd, 1H, *J* = 10.7, 9.1, 4.6, H-4), 3.28–3.32 (m, 1H, H-3), 2.87 (dd, 1H, *J* = 13.6, 107 Hz, H-5a), 2.78 (dd, 1H, *J* = 13.6, 4.6 Hz, H-5e). ^{13}C NMR (CD_3OD, 100 MHz): δ = 149.0 (C-4′), 123.9 (C-5′), 79.5 (C-3), 77.5 (C-2), 74.2 (C-4), 64.1 (C-1), 56.5 (CH_2OH), 33.2 (C-5). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_8H_{13}N_3NaO_4S$ $[M+Na]^+$ 270.0519, found 270.0519.

4.38. 5-Thio-β-D-xylopyranosyl-4-phenyl-1,2,3-triazole (10b)

The title compound was prepared from **9b** according to the general procedure D, and isolated as a white powder (99%). R_f = 0.30 (CH_2Cl_2/MeOH 9:1). Mp = 219–220 °C (MeOH). $[\alpha]_D^{20}$ +14 (*c* 1/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 8.68 (s, 1H, H-5′), 7.87 (m, 2H, H-Ar), 7.42–7.46 (m, 2H, H-Ar), 73.31–7.35 (m, 1H, H-Ar), 5.63 (d, 1H, *J* = 10.0 Hz, H-1), 3.92 (dd, 1H, *J* = 9.9, 8.9 Hz, H-2), 3.58 (ddd, 1H, *J* = 10.8, 9.1, 4.5 Hz, H-4), 3.21 (pdd, 1H, *J* = 8.9 Hz, H-3), 2.82 (dd, 1H, *J* = 13.4, 10.8 Hz, H-5a), 2.71 (dd, 1H, *J* = 13.4, 4.5 Hz, H-5e). ^{13}C NMR (DMSO-d_6 + ε D_2O, 100 MHz): δ = 146.8 (C-Ar), 129.5 (CH-Ar), 129.5 (CH-Ar), 128.7 (CH-Ar), 125.7 (2CH-Ar), 121.5 (C-5′), 77.7 (C-3), 75.8 (C-2), 72.8 (C-4), 62.4 (C-1), 32.0 (C-5). HR-CI-MS (positive mode) *m/z*: calculated for $C_{13}H_{16}N_3O_3S$ $[M+H]^+$ 294.0912, found 294.0913.

4.39. 5-Thio-β-D-xylopyranosyl-4-(4-nitrophenyl)-1,2,3-triazole (10c)

The title compound was prepared from **9c** according to the general procedure D, and isolated as a pale yellow powder (99%). R_f = 0.29 (CH_2Cl_2/MeOH 9:1). Mp = 131–132 °C (MeOH). $[\alpha]_D^{20}$ +16 (*c* 1.25/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz, 45°C): δ = 8.92 (s, 1H, H-5′), 8.30 (d, 2H, *J* = 8.9 Hz, 2H-Ar), 8.13 (d, 2H, *J* = 8.9 Hz, 2H-Ar), 5.66 (d, 1H, *J* = 10.0 Hz, H-1), 3.94 (pdd, 1H, *J* = 9.3 Hz, H-2), 3.61 (ddd, 1H, *J* = 10.4, 9.0, 4.4 Hz, H-4), 3.24 (pdd, 1H, *J* = 8.8 Hz, H-3), 2.83 (dd, 1H, *J* = 13.3, 10.7 Hz, H-5a), 2.74 (dd, 1H, *J* = 13.4, 4.5 Hz, H-5e). ^{13}C NMR (DMSO-d_6 + ε D_2O, 400 MHz, 45°C): δ = 146.7 (C-Ar), 144.3 (C-4′), 136.9 (C-Ar), 126.0 (2CH-Ar), 124.3 (2CH-Ar), 123.1 (C-5′), 77.5 (C-3), 75.6 (C-2), 72.5 (C-4), 62.4 (C-1), 31.8 (C-5). HR-CI-MS (positive mode) *m/z*: calculated for $C_{13}H_{15}N_4O_5S$ $[M+H]^+$ 339.0763, found 339.0762.

4.40. 5-Thio-β-D-xylopyranosyl-4-(4-methylphenyl)-1,2,3-triazole (10d)

The title compound was prepared from **9d** according to the general procedure D, and isolated as a white powder (99%). R_f = 0.31 (CH_2Cl_2/MeOH 9:1). Mp = 235–236 °C (MeOH). $[\alpha]_D^{20}$ +29 (*c* 1.07/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 8.57 (s, 1H, H-5′), 7.72 (d, 2H, *J* = 8.1 Hz, H-Ar), 7.25 (d, 2H, *J* = 8.0 Hz, H-Ar), 5.60 (d, 1H, *J* = 10.0 Hz, H-1), 3.90 (dd, 1H, *J* = 9.9, 8.9 Hz, H-2), 3.58 (ddd, 1H, *J* = 10.6, 9.0, 4.5 Hz, H-4), 3.19 (pdd, 1H, *J* = 8.9 Hz, H-3), 2.80 (dd, 1H, *J* = 13.4, 10.8 Hz, H-5a), 2.71 (dd, 1H, *J* = 13.4, 4.5 Hz, H-5e), 2.30 (s, 3H, methyl). ^{13}C NMR (DMSO-d_6 + ε D_2O, 100 MHz): δ = 146.7 (C-4′), 137.9 (C-Ar), 129.9 (2CH-Ar), 127.8 (C-Ar), 125.5 (2CH-Ar), 120.9 (C-5′), 77.8 (C-3), 75.8 (C-2), 72.8 (C-4), 62.5 (C-1), 32.1 (C-5), 21.1 (C-methyl). HR-CI-MS (positive mode) *m/z*: calculated for $C_{14}H_{18}N_3O_3S$ $[M+H]^+$ 308.1070, found 308.1070.

4.41. 5-Thio-β-D-xylopyranosyl-4-(2-methyl-4-methoxyphenyl)-1,2,3-triazole (10e)

The title compound was prepared from **9e** according to the general procedure D, and isolated as a white powder (99%). R_f = 0.30 (CH_2Cl_2/MeOH 9:1). Mp = 199–200 °C (MeOH). $[\alpha]_D^{20}$ +37 (*c* 1.10/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 8.22 (s, 1H, H-5′), 7.56 (d, 1H, *J* = 8.2 Hz, H-Ar), 6.81–6.84 (m, 2H, H-Ar), 5.56 (d, 1H, 10.0 Hz, H-1), 3.94 (pdd, 1H, *J* = 9.4 Hz, H-2), 3.72 (s, 3H, OCH_3), 3.62 (pddd, 1H, *J* = 9.5, 4.9 Hz, H-4), 3.20 (pdd, 1H, *J* = 8.9 Hz, H-3), 2.68–2.83 (m, 2H, H-5a, H-5e), 2.32 (s, 3H, methyl). ^{13}C NMR (DMSO-d_6 + ε D_2O, 100 MHz): δ = 159.9 (C-Ar), 146.5 (C-4′), 138.0 (C-Ar), 130.8 (CH-Ar), 123.5 (C-5′), 122.8 (C-Ar), 117.0 (CH-Ar), 112.7 (CH-Ar), 78.3 (C-3), 76.4 (C-2), 73.3 (C-4), 63.1 (C-1), 56.0 (CH_3-methoxy), 32.5 (C-5), 21.8 (CH_3-methyl). HR-CI-MS (positive mode) *m/z*: calculated for $C_{15}H_{20}N_3O_4S$ $[M+H]^+$ 338.1175, found 338.1176.

4.42. 5-Thio-β-D-xylopyranosyl-4-(2-naphthyl)-1,2,3-triazole (10f)

The title compound was prepared from **9f** according to the general procedure D, and isolated as a white powder (99%). R_f = 0.29 (CH_2Cl_2/MeOH 9:1). Mp = 239–240 °C (MeOH). $[\alpha]_D^{20}$ +34 (*c* 0.90/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 8.82 (s, 1H, H-5′), 8.42 (s, 1H, H-Ar), 7.91–8.03 (m, 4H, H-Ar), 7.49–7.56 (m, 2H, H-Ar), 5.67 (d, 1H, *J* = 10.0 Hz, H-1), 3.95 (dd, 1H, *J* = 9.9, 8.9 Hz, H-2), 3.60 (ddd, 1H, *J* = 10.7, 9.0, 4.4, H-4), 3.23 (pdd, 1H, *J* = 8.8 Hz, H-3), 2.84 (dd, 1H, *J* = 13.4, 10.8, H-5a), 2.73 (dd, 1H, *J* = 13.4, 4.4 Hz, H-5e). ^{13}C NMR (DMSO-d_6 + ε D_2O, 100 MHz): δ = 146.5 (C-4′), 133.3 (C-Ar), 132.8 (C-Ar), 128.8 (CH-Ar), 128.2 (CH-Ar), 128.1 (C-Ar), 127.9 (CH-Ar), 126.8 (CH-Ar), 126.4 (CH-Ar), 123.8 (CH-Ar), 123.7 (CH-Ar), 121.6 (C-5′), 77.7 (C-3), 75.8 (C-2), 72.8 (C-4), 62.4 (C-1), 32.0 (C-5). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{17}H_{18}N_3O_3S$ $[M+H]^+$ 344.1063, found 344.1064.

4.43. 5-Thio-β-D-xylopyranosyl-4-(6-methoxy-2-naphthyl)-1,2,3-triazole (10g)

The title compound was prepared from **9g** according to the general procedure D, and isolated as a white powder (99%). R_f = 0.30 (CH_2Cl_2/MeOH 9:1). Mp >250 °C (MeOH). $[\alpha]_D^{20}$ +17 (*c* 1.21/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 8.59 (s, 1H, H-5′), 8.22 (s, 1H, H-Ar), 7.81–7.85 (m, 3H, H-Ar), 7.26 (d, 1H, *J* = 2.1 Hz, H-Ar), 7.14 (dd, 1H, *J* = 9.0, 2.3 Hz, H-Ar), 5.59 (d, 1H, *J* = 10.0 Hz, H-1), 3.96 (pdd, 1H, *J* = 9.4 Hz, H-?), 3.81 (s, 3H, H- OCH_3), 3.66 (pddd, 1H, *J* = 9.6, 4.9 Hz, H-4), 3.24 (pdd, 1H, 8.9 Hz), 2.69–2.85 (m, 2H, H-5a, H-5e). ^{13}C NMR (DMSO-d_6 + ε D_2O, 100 MHz): δ = 158.4 (C-Ar), 147.5 (C-4′), 134.8 (C-Ar), 130.4 (CH-Ar), 129.3 (C-Ar), 128.4 (CH-Ar), 125.9 (C-Ar), 124.8 (CH-Ar), 124.6 (CH-Ar), 121.9 (C-5′), 119.8 (CH-Ar), 107.1 (CH-Ar), 78.2 (C-3), 76.3 (C-2), 73.1 (C-4), 63.1 (C-1), 56.1 (CH_3-methoxy), 32.3 (C-5). HR-CI-MS (positive mode) *m/z*: calculated for $C_{18}H_{20}N_3O_4S$ $[M+H]^+$ 374.1175, found 374.1174.

4.44. 5-Thio-β-D-xylopyranosyl-4-(4-methoxyphenyl)-1,2,3-triazole (10h)

The title compound was prepared from **9h** according to the general procedure D, and isolated as a white powder (99%). R_f = 0.31 (CH_2Cl_2/MeOH 9:1). Mp = 236–237 °C (MeOH). $[\alpha]_D^{20}$ +37 (*c* 1.11/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 8.41 (s, 1H, H-5′), 7.71 (d, 2H, *J* = 8.2 Hz, 2H-Ar), 6.97 (d, 2H, *J* = 8.3 Hz, 2H-Ar), 5.55 (d, 1H, *J* = 10.0 Hz, H-1), 3.92 (pdd, 1H, *J* = 9.3 Hz, H-2), 3.72 (s, 3H, OCH_3), 3.60–3.67 (m, 1H, H-4), 3.21 (pdd, 1H, *J* = 8.8 Hz, H-3), 2.70–2.85 (m, 2H, H-5a, H-5e). ^{13}C NMR (DMSO-d_6 + ε D_2O, 100 MHz): δ = 160.2 (C-Ar), 147.5 (C-4′), 127.8 (2CH-Ar), 123.3 (C-Ar), 121.3 (C-5′), 115.5 (2CH-Ar), 78.3 (C-3), 76.4 (C-2), 73.3 (C-4), 63.1 (C-1), 56.1 (CH_3-methoxy), 32.5 (C-5). HR-CI-MS (positive mode) *m/z*: calculated for $C_{14}H_{18}N_3O_4S$ $[M+H]^+$ 324.1018, found 324.1017.

4.45. 5-Thio-β-D-xylopyranosyl-4-cyclohexyl-1,2,3-triazole (10i)

The title compound was prepared from **9i** according to the general procedure D, and isolated as a white powder (99%). R_f = 0.32 (CH_2Cl_2/MeOH 9:1). Mp = 205–206 °C (MeOH). $[\alpha]_D^{20}$ +40 (*c* 1.03/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 7.87 (s, 1H, H-5′), 5.51 (d, 1H, *J* = 10.0 Hz, H-1), 3.85 (dd, 1H, *J* = 9.8, 9.0 Hz, H-2), 3.54 (ddd, 1H, *J* = 10.3, 9.1, 4.5 Hz, H-4), 3.13 (pdd, 1H, *J* = 8.9 Hz, H-3), 2.75 (dd, 1H, *J* = 13.4, 10.8, H-5a), 2.66 (dd, 1H, *J* = 13.4, 4.5 Hz, H-5e), 2.60–2.66 (m, 1H, cyclohexyl), 1.93 (m, 2H, cyclohexyl), 1.73 (m, 2H, cyclohexyl), 1.66 (m, 1H, cyclohexyl), 1.34 (m, 4H, cyclohexyl), 1.19 (m, 1H, cyclohexyl). ^{13}C NMR (DMSO-d_6 + ε D_2O, 100 MHz): δ = 152.0 (C-4′), 120.3 (C-5′), 77.8 (C-3), 75.5 (C-2), 72.7 (C-4), 62.1 (C-1), 34.7 (CH, cyclohexyl), 32.6 (CH_2, cyclohexyl), 32.5 (CH_2, cyclohexyl), 32.0 (C-5), 25.8 (CH_2, cyclohexyl), 25.7 ($2CH_2$, cyclohexyl). HR-LSIMS-MS (positive mode) *m/z*: calculated for $[M+H]^+$ $C_{13}H_{22}N_3O_3S$ 300.1376, found 300.1375.

4.46. 5-Thio-β-D-xylopyranosyl-4-(cyclohex-1-enyl)-1,2,3-triazole (10j)

The title compound was prepared from **9j** according to the general procedure D, and isolated as a white powder (99%). R_f = 0.31 (CH_2Cl_2/MeOH 9:1). Mp = 178–179 °C (MeOH). $[\alpha]_D^{20}$ +28 (*c* 1.10/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 8.10 (s, 1H, H-5′), 6.40 (m, 1H, Csp^2-H cyclohexenyl), 5.52 (d, 1H, *J* = 10.0 Hz, H-1), 3.86 (dd, 1H, *J* = 9.9, 8.9 Hz, H-2), 3.55 (ddd, 1H, *J* = 10.6, 9.0, 4.5 Hz, H-4), 3.15 (pdd, 1H, *J* = 8.9 Hz, H-3), 2.76 (dd, 1H, *J* = 13.4, 10.7 Hz, H-5a), 2.67 (dd, 1H, *J* = 13.4, 4.6 Hz, H-5e), 2.28 (m, 2H, cyclohexenyl), 212 (m, 2H, cyclohexenyl), 1.66 (m, 2H, cyclohexenyl), 1.58 (m, 2H, cyclohexenyl). ^{13}C NMR (DMSO-d_6 + ε D_2O, 100 MHz): δ = 148.3 (C-4′), 127.5 (C, cyclohexenyl), 124.4 (Csp^2-H, cyclohexenyl), 119.8 (C-5′), 77.9 (C-3), 75.8 (C-2), 72.9 (C-4), 62.3 (C-1), 32.1 (C-5), 26.1 (CH_2, cyclohexenyl), 25.0 (CH_2, cyclohexenyl), l22.4 (CH_2, cyclohexenyl), 22.2 (CH_2, cyclohexenyl). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{13}H_{20}N_3O_3S$ $[M+H]^+$ 298.1220, found 298.1213.

4.47. 1-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-acetoxymethyl-1,2,3-triazole (*S*)-*S*-oxide (11a-*S*)

The title compound was prepared from **9a** according to the general procedure E, and isolated as a white powder (<5%). R_f = 0.19 (PE/EtOAc 4:6). Mp = 147–148 °C (CH_2Cl_2/PE). $[\alpha]_D^{20}$ +28 (*c* 1/DMSO). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.87 (s, 1H, H-5′), 5.81 (dd, 1H, *J* = 11.4, 9.5 Hz, H-2), 5.54 (d, 1H, *J* = 11.4 Hz, H-1), 5.54 (pdd, 1H, *J* = 9.6 Hz, H-3), 5.20–5.33 (m, 1H, H-4), 5.22 (s, 2H, CH_2OAc), 3.89 (dd, 1H, *J* = 12.3, 3.7 Hz, H-5e), 3.25 (pdd, 1H, *J* = 12.1 Hz, H-5a), 2.10, 2.07, 2.03, 1.81 (4s, 12H, acetyl). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{16}H_{22}N_3O_9S$ $[M+H]^+$ 432.1077, found 432.1072.

4.48. 1-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-acetoxymethyl-1,2,3-triazole (*R*)-*S*-oxide (11a-*R*)

The title compound was prepared from **9a** according to the general procedure E, and isolated as a white powder (<5%). R_f = 0.13 (PE/EtOAc 4:6). Mp = 142–143 °C (CH_2Cl_2/PE). $[\alpha]_D^{20}$ +15 (*c* 0.49/

DMSO). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (s, 1H, H-5′), 6.15 (dd, (1H, J = 11.3, 9.7 Hz, H-2), 5.81–5.87 (m, 1H, H-4), 5.82 (d, 1H, J = 11.2 Hz, H-1), 5.54 (pdd, 1H, J = 9.8 Hz, H-3), 5.20 (s, 2H, CH_2OAc), 3.75 (dd, 1H, J = 14.3, 4.1 Hz, H-5e), 2.95 (dd, 1H, J = 14.2, 12.0 Hz, H-5a), 2.08, 2.08, 2.06, 1.81 (4s, 12H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.7, 169.6, 169.3, 169.0 (4C, acetyl), 144.2 (C-4′), 123.1 (C-5′), 73.6 (C-1), 72.4 (C-3), 66.9 (C-2), 65.8 (C-4), 57.5 (CH_2OAc), 46.7 (C-5), 20.9, 20.8, 20.6, 20.1 ($4CH_3$, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{16}H_{22}N_3O_9S$ $[M+H]^+$ 432.1077, found 432.1074.

4.49. 1-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-phenyl-1,2,3-triazole (*S*)-*S*-oxide (11b-*S*)

The title compound was prepared from **9b** according to the general procedure E, and isolated as a white powder (<5%). R_f = 0.31 (CH_2Cl_2/EtOAc 8:2). Mp = 248–249 °C (CH_2Cl_2/PE). $[\alpha]_D^{20}$ +14 (c 1/DMSO). ^{1}H NMR ($(CD_3)_2CO$, 400 MHz): δ = 8.62 (s, 1H, H-5′), 7.90–7.92 (m, 2H, H-Ar), 7.44–7.48 (m, 2H, H-Ar), 7.34–7.38 (m, 1H, H-Ar), 6.11 (d, 1H, J = 11.3 Hz, H-1), 5.95 (dd, 1H, J = 11.3, 9.6 Hz, H-2), 5.72 (pdd, 1H, J = 9.8 Hz, H-3), 5.47 (ddd, 1H, J = 12.3, 10.0, 3.6 Hz, H-4), 3.97 (dd, 1H, J = 11.9, 3.6 Hz, H-5e), 3.63 (pdd, 1H, J = 12.1 Hz, H-5a), 2.06, 1.99, 1.78 (3s, 9H, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{19}H_{21}N_3NaO_7S$ $[M+Na]^+$ 458.0998, found 458.0101.

4.50. 1-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-phenyl-1,2,3-triazole (*R*)-*S*-oxide (11b-*R*)

The title compound was prepared from **9b** according to the general procedure E, and isolated as a white powder (<5%). R_f = 0.28 (CH_2Cl_2/EtOAc 8:2). Mp >250 °C (CH_2Cl_2/PE). $[\alpha]_D^{20}$ +8 (c 0.50/DMSO). ^{1}H NMR ($(CD_3)_2CO$, 400 MHz): δ = 8.40 (s, 1H, H-5′), 7.93–7.96 (m, 2H, H-Ar), 7.45–7.48 (m, 2H, H-Ar), 7.35–7.39 (m, 1H, H-Ar), 6.41 (d, 1H, J = 11.4 Hz, H-1), 6.20 (dd, 1H, J = 11.3, 9.6 Hz, H-2), 5.85 (ddd, 1H, J = 11.9, 10.1, 4.0 Hz, H-4), 5.72 (pdd, 1H, J = 9.8 Hz, H-3), 3.86 (dd, 1H, J = 14.2, 4.0 Hz, H-5e), 3.49 (dd, 1H, J = 14.1, 12.1 Hz, H-5a), 2.06, 2.03, 1.78 (3s, 9H, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{19}H_{21}N_3NaO_7S$ $[M+Na]^+$ 458.0998, found 458.0100.

4.51. 1-(5-Thio-β-D-xylopyranosyl)-4-hydroxymethyl-1,2,3-triazole (*S*)- and (*R*)-*S*-oxides (12a)

The title compound was prepared from a 80:20 mixture of **11a-*S*** and **11a-*R*** according to the general procedure G, and isolated as a white powder. Compounds **12a** could not be obtained as pure diastereoisomers and isomerization took place at the sulfur atom under the acidic conditions used for their deacetylation leading to a 65:35 mixture of diastereosiomers. White powder (99%). R_f = 0.12 (CH_2Cl_2/MeOH 8:2); HR-LSIMS-MS (positive mode) m/z calculated for $C_8H_{14}N_3O_6S$ $[M+H]^+$ 280.0603, found 280.0609.

4.52. 1-(5-Thio-β-D-xylopyranosyl)-4-phenyl-1,2,3-triazole (*S*)- and (*R*)-*S*-oxides (12b)

The title compound was prepared from pure **11b-*S*** according to the general procedure G, and isolated as a white powder. Compounds **12b** could not be obtained as pure diastereoisomers and isomerization took place at the sulfur atom under the acidic conditions used for their deacetylation leading to a 85:15 mixture of diastereosiomers. White powder (99%). R_f = 0.14 (CH_2Cl_2/MeOH 9:1); HR-LSIMS-MS (positive mode) m/z calculated for $C_{13}H_{16}N_3O_5S$ $[M+H]^+$ 326.0811, found 326.0806.

4.53. 1-(3,4-Di-*O*-acetyl-β-D-xylal)-4-acetoxymethyl-1,2,3-triazole *S*,*S*-dioxide (13)

To a solution of 1-(2,3,4-tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-acetoxymethyl-1,2,3-triazole **9a** (1 equiv) in dry THF (5 mL/0.3 mmol) was added dropwise a solution of *m*-CPBA (20 equiv) in dry THF (5 mL/0.4 mmol). The mixture was stirred at rt for 60 min, diluted with EtOAc (50 mL), and washed successively with saturated solutions of $Na_2S_2O_3$ (50 mL), $NaHCO_3$ (2 × 50 mL), and NaCl (2 × 50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product (white solid) was purified by silica gel chromatography (Et_2O/CH_2Cl_2 9:1) to afford **13** as a white powder (>99%). R_f = 0.29 (CH_2Cl_2/EtOAc 8:2). Mp >250 °C (CH_2Cl_2/PE). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.23 (s, 1H, H-5′), 6.91 (d, 1H, J = 4.1 Hz, H-2), 5.78 (dd, 1H, J = 6.4, 4.2 Hz, H-3), 5.54 (ddd, 1H, J = 9.1, 6.4, 2.9 Hz, H-4), 5.25 (s, 2H, CH_2OAc), 3.89 (dd, 1H, J = 14.1, 3.0 Hz, H-5e), 3.79 (dd, 1H, J = 14.0, 8.7 Hz, H-5a), 2.16, 2.14, 2.09 (3s, 9H, acetyl). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.8, 169.4, 169.4 (3C, acetyl), 144.0 (C-4′), 137.4 (C-1), 124.2 (C-2), 124.1 (C-5′), 66.9 (C-4), 66.8 (C-3), 57.2 (CH_2OAc), 52.3 (C-5), 20.9, 20.8, 20.7 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{14}H_{18}N_3O_8S$ $[M+H]^+$ 388.0815, found 388.0818.

4.54. 1-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-acetoxymethyl-1,2,3-triazole *S*,*S*-dioxide (14a)

The title compound was prepared from **9a** according to the general procedure F, and isolated as a white powder (>99%). R_f = 0.21 (CH_2Cl_2/EtOAc 9:1). Mp = 206–207 °C (CH_2Cl_2/PE); $[\alpha]_D^{20}$ +24 (c 1/DMSO); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.99 (s, 1H, H-5′), 6.06 (d, 1H, J = 11.3 Hz, H-1), 5.82 (dd, 1H, J = 11.2, 9.6 Hz, H-2), 5.58 (pdd, 1H, J = 9.7 Hz, H-3), 5.39–5.46 (m, 1H, H-4), 5.22 (s, 2H, CH_2OAc), 3.89 (dd, 1H, J = 14.4, 4.6 Hz, H-5e), 3.48 (dd, 1H, J = 14.3, 11.6 Hz, H-5a), 2.10, 2.09, 2.07, 1.83 (4s, 12H, acetyl); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.8, 169.3, 161.2, 168.7 (4C, C=O), 144.2 (C-4′), 123.8 (C-5′), 75.1 (C-1), 71.9 (C-3), 68.3 (C-2), 66.2 (C-4), 57.4 (CH_2OAc), 51.4 (C-5), 20.9, 20.7, 20.5, 20.0 ($4CH_3$, acetyl); HR-LSIMS-MS (positive mode) m/z: calculated for $C_{12}H_{22}N_3O_{10}S$ $[M+H]^+$ 448.1026, found 448.1021.

4.55. 1-(2,3,4-Tri-*O*-acetyl-5-thio-β-D-xylopyranosyl)-4-phenyl-1,2,3-triazole *S*,*S*-dioxide (14b)

The title compound was prepared from **9b** according to the general procedure F, and isolated as a white powder (99%). R_f = 0.13 (PE/EtOAc 7:3). Mp >250 °C (CH_2Cl_2/PE). $[\alpha]_D^{20}$ +13 (c 1, DMSO). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.86 (s, 1H, H-5′), 7.93 (d, 2H, J = 7.4 Hz, H-Ar), 7.48 (t, 2H, J = 7.6 Hz, H-Ar), 7.38 (t, 1H, J = 7.4 Hz, H-Ar), 7.02 (d, 1H, J = 10.7 Hz, H-1), 5.87 (pdd, 1H, J = 9.7 Hz, H-2), 5.78 (pdd, 1H, J = 9.7 Hz, H-3), 5.30 (m, 1H, H-4), 4.28 (dd, 1H, J = 13.9, 4.3 Hz, H-5e), 4.07 (dd, 1H, J = 13.7, 12.0 Hz, H-5a), 2.06, 2.02, 1.80 (3S, 9H, acetyl). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.2, 169.0, 168.4 (3C, acetyl), 147.0 (C-4′), 129.6 (C-Ar), 129.0 (2CH-Ar), 128.6 (CH-Ar), 125.5 (2CH-Ar), 121.8 (C-5′), 73.5 (C-1), 71.4 (C-3), 67.9 (C-2), 65.3 (C-4), 49.8 (C-5), 20.4, 20.1, 19.7 ($3CH_3$, acetyl). HR-LSIMS-MS (positive mode) m/z: calculated for $C_{19}H_{21}N_3NaO_8S$ $[M+Na]^+$ 474.0947, found 474.0944.

4.56. 1-(-5-thio-β-D-xylopyranosyl)-4-hydroxymethyl-1,2,3-triazole *S*,*S*-dioxide (15a)

The title compound was prepared from **14a** according to the general procedure G, and isolated as a white powder (99%). R_f = 0.09 (CH_2Cl_2/MeOH 9:1). Mp = 242–243 °C (MeOH/CH_2Cl_2).

$[\alpha]_D^{20}$ +44 (*c* 1/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 8.01 (s, 1H, H-5′), 6.21 (d, 1H, *J* = 10.9 Hz, H-1), 4.54 (s, 2H, CH_2OH), 3.98 (dd, 1H, *J* = 10.8, 9.0 Hz, H-2), 3.69 (m, 1H, H-4), 3.60 (m, 2H, H-5a, H-5e), 3.54 (pdd, 1H, *J* = 9.0 Hz, H-3). ^{13}C NMR (100 MHz, DMSO-d_6 + ε D_2O) δ = 148.4 (C-4′), 123.4 (C-5′), 76.8 (C-3), 76.4 (C-1), 70.4 (C-2), 67.0 (C-4), 55.1 (CH_2OH), 53.3 (C-5). HR-CI-MS (positive mode) *m/z*: calculated for $C_8H_{14}N_3O_6S$ $[M+H]^+$ 280.0598; found 280.0601.

4.57. 1-(5-Thio-β-D-xylopyranosyl)-4-phenyl-1,2,3-triazole *S,S*-dioxide (15b)

The title compound was prepared from **14b** according to the general procedure G, and isolated as a white powder (99%). R_f = 0.18 (CH_2Cl_2/MeOH 9:1). Mp >250 °C (MeOH/CH_2Cl_2). $[\alpha]_D^{20}$ +17 (*c* 1/DMSO). ^{1}H NMR (DMSO-d_6 + ε D_2O, 400 MHz): δ = 8.74 (s, 1H, H-5′), 7.92 (d, 2H, *J* = 7.4 Hz, H-Ar), 7.47 (pdd, 2H, *J* = 7.6 Hz, H-Ar), 7.36 (pdd, 1H, *J* = 7.3 Hz, H-Ar), 6.33 (d, 1H, *J* = 10.8 Hz, H-1), 4.08 (dd, 1H, *J* = 10.3, 9.3 Hz, H-2), 3.58–3.76 (m, 4H, H-3, H-4, H-5a, H-5e). ^{13}C NMR (DMSO-d_6 + ε D_2O, 100 MHz): δ = 146.6 (C-4′), 130.3 (C-Ar), 129.2 (2CH-Ar), 128.4 (CH-Ar), 125.5 (2CH-Ar), 121.7 (C-5′), 76.4 (C-3), 76.3 (C-1), 70.2 (C-2), 66.8 (C-4), 53.0 (C-5). HR-LSIMS-MS (positive mode) *m/z*: calculated for $C_{13}H_{16}N_3O_5S$ $[M+H]^+$ 326.0805, found 326.0809.

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A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2012.09.020.

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