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Synthesis of *N*-glycosyl amides: conformational analysis and evaluation as inhibitors of β-galactosidase from *E. coli*†

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The synthesis of *N*-glycosyl amides typically involves the use of glycosyl amines as direct precursors, resulting in low yields due to hydrolysis and the loss of stereocontrol through anomerization processes. In this study, a sequential synthesis of *N*-glycosyl amides is proposed, employing glycosyl amines as intermediates obtained from glycosyl azides. Derivatives with *gluco*, *galacto*, or *xylo* configurations were synthesized. Hexose derivatives were obtained under stereocontrol to give only the β anomer, while the *xylo* derivatives provided a mixture of α and β anomers. Conformational analysis revealed that all β anomers adopted the $^4C_1$ conformation, while α anomers were found in the $^1C_4$ chair as the major conformer. After de-*O*-acetylation, the derivatives containing a galactose unit were evaluated as inhibitors of β-galactosidase from *E. coli* and were found to be moderate inhibitors.

Introduction

Glycomimetics are molecules that have structures similar to carbohydrates, but with some chemical modifications. These modifications often involve the glycosidic linkage, for example, replacing the oxygen atom with nitrogen, sulfur, or even carbon to modify the properties of that bond. The modified glycosidic linkage usually shows enhanced stability towards enzyme degradation and, in many cases, the glycomimetics act as enzyme inhibitors, being able to regulate the activity of glycosidases or glycosyltransferases. This has led to a growing interest in obtaining new synthetic sugar analogs for use as tools in glycobiology and medicinal chemistry.[1–5]

N-Glycosyl amides, and more importantly *N*-glycopeptides, are known to be involved in numerous cell recognition processes, such as in inflammation,[6] immune response,[7] tumor proliferation and metastasis.[8,9] In particular, *N*-glycosylation of peptides and proteins is one of the most complex and abundant types of co-translational modifications in nature.[10] Glycosyl amides have been tested as inhibitors of glycogen phosphorylase, enzyme that catalyzes the rate-limiting step in glycogenolysis. Modulating the activity of this enzyme is believed to be essential for developing a treatment for type 2 diabetes.[11–15] Furthermore, it is known that these compounds can also act as inhibitors of glycosidases,[16] lectins[17,18] or glycosyltransferases,[19] displaying a wide range of biological activities.[20]

Since *N*-glycosyl amides **1** are involved in many functions and processes, the synthesis of this type of compounds, which can serve as glycomimetics, is a current objective. Formation of the amide bond can be carried out by coupling a *N*-glycosyl amine **2** with the corresponding acyl derivative **3**. However, glycosyl amines **2** are known to anomerize when long reaction times are required (Scheme 1), thus losing selectivity towards the desired anomer. Furthermore, compounds **2** are susceptible to hydrolysis to give hemiacetals **4** as reaction by-products.[21,22]

For this reason, glycosyl azides **5** (easily accessible from hemiacetals **4**) are used as precursors for glycosyl amides **1**, as they have shown to be chemically and configurationally stable at their anomeric centre.[23] Compounds **5** can be reduced by various methods prior to coupling with the acyl derivatives **3**.[24] For example, the modified Staudinger protocol involves coupling of the iminophosphorane intermediate **6** with an acyl halide **7** to afford the β-chloroimine **8**, which is hydrolyzed to the desired amides **1** (Scheme 1).[22] This methodology has been developed as an alternative to avoid the anomerization of amine **2**. However, examples of anomeric interconversion have been reported, mostly for extended reaction times[25] and when α-glycopyranosyl azides are employed.[26] Additionally, the phosphine oxide obtained as a by-product of Staudinger reactions is difficult to separate, decreasing the yields of the products in the

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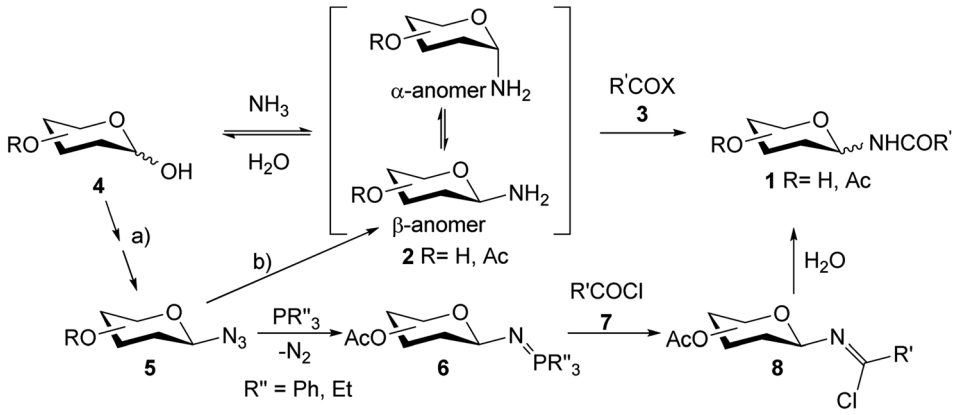


Scheme 1 Some methodologies described for the synthesis of *N*-glycosil amides.

purification steps. Another disadvantage lies in the use of activated carboxylic acids, such as acid halides **7**, which are highly reactive and susceptible to hydrolysis.

Taking into account the interesting biological properties of *N*-glycosyl amides, we describe herein the synthesis of this type of compounds using the hydrogenolysis of glycosyl azides with *gluco*, *galacto*, or *xylo* configuration as the key step. The catalytic hydrogenation of glycosyl azide **5** in the presence of Pd/C constitutes a cleaner alternative to the Staudinger procedure, as this catalyst can be readily removed by filtration to yield the respective glycosyl amine **2**. To avoid hydrolysis and anomerization of glycosylamines **2**, their derivatization with activated carboxylic acids **3** was carried out immediately after obtaining them. Furthermore, to prevent the use of acyl halides, the amidation of carboxylic acids was performed using DCC. The per-*O*-acetyl derivatives of glycosyl amides were de-*O*-acetylated and those containing a galactose residue were tested as inhibitors of the of *E. coli* β-galactosidase.

Results and discussion

The synthesis of the glycosyl azides of *gluco* (**5a**), *galacto* (**5b**), or *xylo* (**5c**) configuration was performed as shown in Scheme 2.

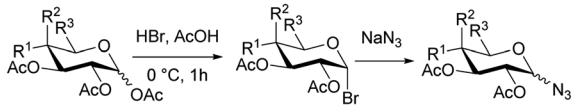
The per-*O*-acetyl monosaccharides **9a–c** were treated with a mixture of hydrogen bromide in acetic acid to yield the α-glycosyl bromides **10a–c**. These compounds **10a–c** were substituted with sodium azide in DMF using protocols similar to those described in the literature,[27–29] to afford diastereoselectively the glycosyl azides **5a** and **5b** of β configuration (Table 1, entry 1 and 2). On the other hand, a mixture of α/β (1 : 1.1) anomers was obtained in the case of *xylo* derivate **5c** (Table 1, entry 3). Ibatulin and coworkers (2000)[30] reported that β-glycosyl azides can be selectively obtained using a water/acetone mixture as a solvent, without significant losses due to hydrolysis of bromide **10**. Thereby, employing these conditions, the *xylo* derivate **5c** was obtained exclusively with the β configuration (Table 1, entry 4).

The β-configuration of the glycosyl azides was stablished according to the large coupling constant values in the ^{1}H NMR spectra ($J_{1,2} \approx$ 9–10 Hz) of **10a–c**, which is indicative of a *trans* diaxial orientation for H-1 and H-2.

With the glycosyl azides in hand, we proceed to select the carboxylic acids **11–13β** to obtain the corresponding amides (Chart 1). The carboxylic acid derivatives **11** and **12** were selected since they are commercially available and are also stable solids that can be easily handled. Furthermore, the aromatic moiety of these compounds could contribute to the interaction with the active site of the enzyme, since an aromatic hydrophobic residue in galactose derivatives is usually relevant in the recognition process by *E. coli* β-galactosidase.[31,32]

In order to obtain bridged disaccharides containing the thio and amide functionalities, the thioglyco acid **13** was synthesized. The thioglycosylation of per-*O*-acetyl galactose **9b** with 3-mercaptopropionic acid (**14**) was conducted in the presence of a Lewis acid. The reaction conditions have been evaluated, as shown in Table 2.

The reaction performed in anhydrous acetonitrile or dichloromethane led to **13** as a mixture of anomers, which could be separated by column chromatography, to afford the β anomer as main product. The compound previously reported



Scheme 2 Synthesis of glycosyl azides of *gluco* (**5a**), *galacto* (**5b**), or *xylo* (**5c**) configuration.

Table 1 Azidation reactions of glycosyl halides **10a–c**

Entry	Substrate	Reaction conditions	Isolated yield of **5**
1	**10a**	NaN_3, DMF 70 °C, 5 h	73% (β only)
2	**10b**	NaN_3, DMF 70 °C, 5 h	71% (β only)
3	**10c**	NaN_3, DMF, 70 °C, 5 h	72% (α/β; 1 : 1.2)
4	**10c**	NaN_3, acetone/H_2O, 40 °C, 3 h	63% (β only)

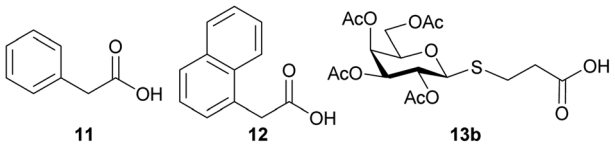
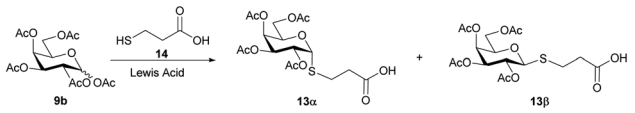


Chart 1 Carboxylic acids selected for amidation reactions with glycosyl amines **2a–c**.

Table 2 Conditions employed for the synthesis of thioglyco acid **13**



			Isolated yield		
Entry[a]	Solvent	Lewis acid	**13α** (%)	**13β** (%)	α/β ratio
1	CH_3CN	$SnCl_4$	21	34	1 : 1.6
2	CH_2Cl_2	$SnCl_4$	20	32	1 : 1.6
3	CH_3CN	$BF_3 \cdot OEt_2$	25	43	1 : 1.7
4	CH_2Cl_2	$BF_3 \cdot OEt_2$	14	31	1 : 2.4
5[b]	CH_2Cl_2	$BF_3 \cdot OEt_2$	17	23	1 : 1.4

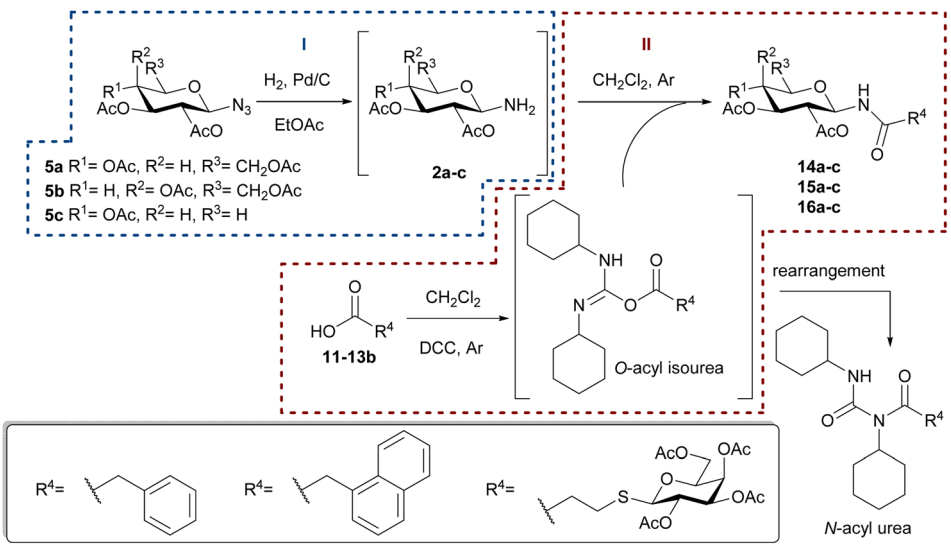
[a] Reaction conditions: **9b** (2.5 mmol), **14** (1.1 equiv.), Lewis acid (1.1 equiv.), solvent (30 mL), reflux, 2 h. [b] Reaction conditions: **9b** (2.5 mmol), **14** (4.4 equiv.), Lewis acid (4.4 equiv.), solvent (30 mL), 0 °C, 9 h.

in the literature[33] as α-anomer had in fact the β-configuration, according to the analysis of the ^{1}H NMR spectrum. The use of $SnCl_4$ in acetonitrile (ESI Table 4.2,† entry 1) or in dichloromethane (ESI Table 4.2,† entry 2) lead to almost identical results in terms of isolated yield and selectivity towards the anomer of interest (≈50–55%; α/β, 1 : 1.6). When using BF_3 OEt_2 as Lewis acid, an improvement in the yield was observed in acetonitrile (ESI Table 4.2,† entry 3, 68%; α/β, 1 : 1.7), while a lower yield was obtained in dichloromethane, compared to that obtained using $SnCl_4$. However, the latter conditions (ESI Table 4.2,† entry 4, 45%; α/β, 1 : 2.4) led to a higher selectivity toward the β anomer. Additionally, in an attempt to enhance the selectivity, the reaction was carried out at 0 °C (ESI Table 4.2,† entry 5), unfortunately, a decrease in overall yield and selectivity (40%; α/β, 1 : 1.4) was observed, and a longer reaction time was required.

Once all the precursors were obtained, the synthesis of glycosyl amides **1** was carried out through a two-step reaction sequence as illustrated in Scheme 3.

The catalytic hydrogenation of glycosyl azides **5a–c** was performed using H_2 in the presence of Pd/C as the catalyst, in anhydrous ethyl acetate (Scheme 3, Reaction I). The temperature control is a key factor, as below 40 °C the substrate conversion is very low. Upon complete consumption of the substrate, the catalyst was filtered, and the solvent evaporated to afford quantitatively the glycosyl amines **2a–c**. Immediately after the hydrogenation, and to prevent the anomerization, the amino group of **2a–c** was acylated with carboxylic acids **11–13β**, with DCC as coupling agent, to yield the desired glycosyl amides **1** (Scheme 3, Reaction II). The products having *gluco* (**14a**, **15a**), *galacto* (**14b**, **15b**) or *xylo* (**14c**, **15c**) configurations were obtained in good yields after the two-step synthetic sequence (Chart 2). Somewhat lower yields were obtained for *N*-glycosyl amides **16a–c**, which were accompanied by significant amounts of the *N*-acyl urea, derived from acid **13β**. The formation of this byproduct was attributed to the rearrangement of the *O*-acyl isourea intermediate[34] that, in this case, derived from **13β** and DCC. Additionally, lower yields have also been reported in similar coupling reactions using bulky acids or amines derivatives.[35,36]

To improve the yields in the production of bridged disaccharide derivatives, alternative conditions were evaluated using as a model the synthesis of **16a** from the glycosyl azide **5a** and the thioglyco acid **13β** (Table 3). The Steglich amidation was



Scheme 3 Synthesis of *N*-glycosylamides **14a–c**, **15a–c**, and **16a–c**.

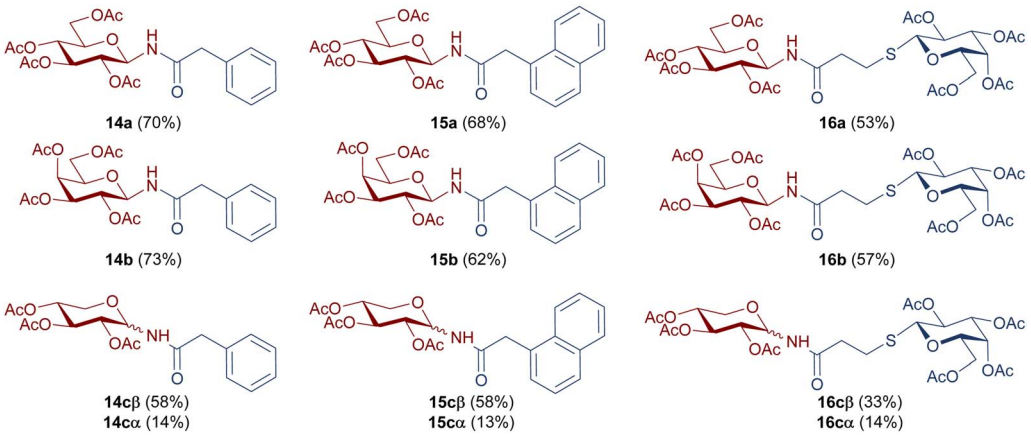


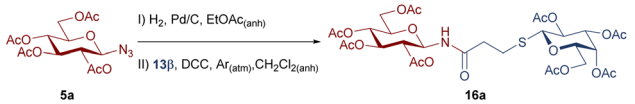
Chart 2 Structure and isolated yields of per-*O*-acetylated *N*-glycosyl amides **14a–c**, **15a–c**, and **16a–c**.

attempted, since the use of *N*,*N*-dimethylaminopyridine (DMAP) and carbodiimides was reported to facilitate the formation of esters[37–39] or amides[40,41] of sterically hindered acids or low-reactivity nucleophiles (alcohols or amines).

The addition of catalytic amounts of DMAP (Table 3, entries 1 and 2) led to a slightly decreased in yield, compared to the conditions initially employed for the production of **16a** (53%). When the quantity of DMAP was increased to 1 equiv., the yield underwent a subtle improvement (Table 3, entry 3), approaching the initial value. Finally, the reaction was also carried out under reflux in the absence or presence of 1 equiv. of DMAP (Table 3, entries 4 and 5). However, even under these conditions, the yields were similar to those obtained initially.

It should be noted that glycosyl amides with *gluco* (**14a–16a**) or *galacto* configuration (**14b–16b**) were diastereoselectivity obtained, with exclusive formation of β anomers. Therefore, no anomerization of the glycosyl amine **2a**, **2b** took place. In contrast, the glycosyl amides with the *xylo* configuration (**14c–16c**) were obtained as a mixture of α and β anomers (Scheme 4), which were separated by column chromatography (the β anomer was the main product). In these cases, an anomerization process occurred in glycosyl amine **2c** prior to amidation.

Table 3 Reaction conditions evaluated for the synthesis of **16a**[a]

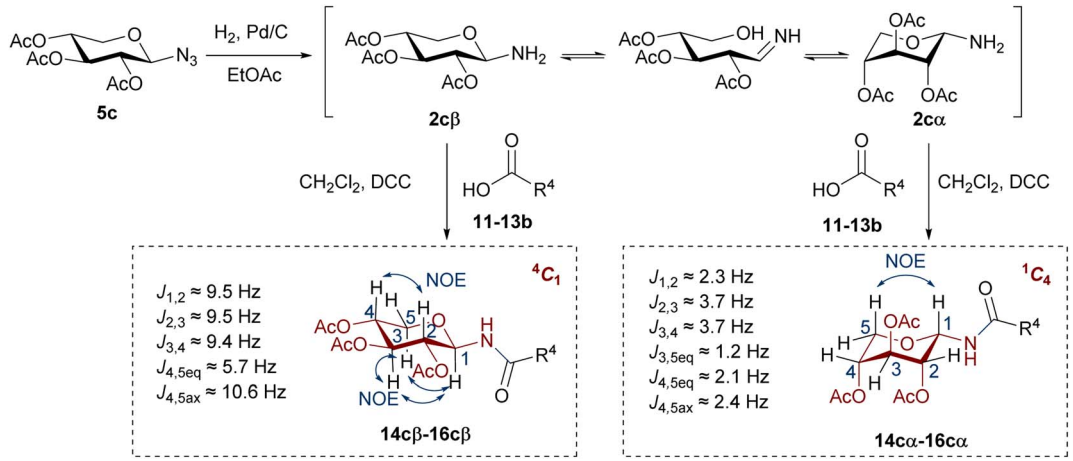


Entry	Additive	Temperature (°C)	Isolated yield of **16a** (%)
1	DMAP (5 mol%)	30	46
2	DMAP (10 mol%)	30	45
3	DMAP (1 equiv.)	30	51
4	—	Reflux	47
5	DMAP (1 equiv.)	Reflux	54

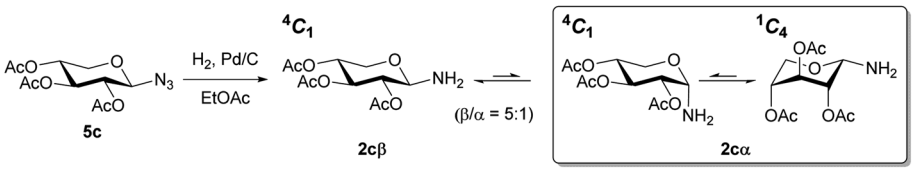
[a] Reaction conditions: (I) **5a** (0.33 mmol), Pd/C 10% (18.6 mg), $EtOAc_{(anh)}$ (3 mL), H_2(atm), 40 °C, 1 h. (II) **13β** (0.36 mmol, 1.1 equiv.), DCC (0.5 mmol, 1.5 equiv.), CH_2Cl_2(anh) (3 mL), $Ar_{(atm)}$, 16 h.

The configuration of the anomeric centre of the amides was established according to the value of the coupling constant $J_{1,2}$, determined from the ^{1}H NMR spectra. The configuration β was assigned for the derivatives with higher values ($J_{1,2} \sim 9$–10 Hz), and α to those with lower values ($J_{1,2} \sim 2$–3 Hz). However, the analysis of the coupling constants of the remaining ring protons in the *xylo* derivatives **14c–16c** ($J_{2,3}$, $J_{3,4}$, $J_{4,5eq}$, $J_{4,5ax}$) showed significant differences in the respective J values determined for the α or β anomers. The amides with β configuration showed high J values (~9–10 Hz) for the protons of the pyranose ring, indicative of a *trans*-diaxial arrangement characteristic of the $^4C_1$ chair conformation (Scheme 4). In contrast, α anomers exhibited smaller J values ($J \sim 2$–4 Hz), consistent with a *trans*-diequatorial arrangement of the coupled protons, and hence a preferential $^1C_4$ chair. Additionally, long-range coupling constants (^4J) between diequatorial protons in a W disposition (H2, H4 or H3, $H5_{eq}$) support the $^1C_4$ conformation for α anomers. Finally, 2D-NOESY spectra of the β glycosyl amides confirmed the assigned conformations. Thus, NOE contacts were observed between the 1,3-diaxial protons (H1, H3, and $H5_{ax}$), as well as between H2 and H4, justifying the $^4C_1$ conformation. These NOE contacts were absent in the α anomers, which instead exhibited a spatial interaction between H1 and $H5_{ax}$, as expected for the $^1C_4$ chair. In this conformation of α anomers the *O*-acetyl substituents are found in an axial arrangement, with those at C-2 and C-4 displaying a repulsive 1,3-diaxial interaction. However, the $^1C_4$ chair is stabilized by the equatorial orientation of the bulky anomeric substituent, which in turn leads to the *exo*-anomeric effect, characteristic of *N*-glycosydic linked derivatives.[42]

To verify the anomerization of glycosyl amine **2cβ**, this compound was synthesized from **5c** (Scheme 5). Thus, the mixture of hydrogenation of **5c** was subjected to the usual work-up and the resulting product was immediately analyzed by NMR spectroscopy. The ^{1}H NMR spectrum (Fig. 1) showed, as expected, a mixture of **2cβ** and **2cα** (β/α = 5 : 1). Similar to hemiacetals the aminoacetals undergo rapid anomerization through the open-chain intermediate, as shown in Scheme 4. In



Scheme 4 Synthesis of glycosyl amides with the *xylo* configuration.



Scheme 5 Hydrogenation of azide **5c** to afford *N*-glycosyl amine **2cβ** and anomerization to **2cα**.

the $^4C_1$ conformation the β anomer is stabilized by the *exo*-anomeric effect, while the α anomer should be stabilized by both, the anomeric and *exo*-anomeric effects. However, in the $^4C_1$ conformation of the α anomer the $n_N \rightarrow {}^*\sigma_{CO}$ orbital interaction, associated with the *exo*-anomeric effect, necessarily points the hydrogen atom on nitrogen under the pyranose ring, resulting in a destabilizing steric effect.[43] Thus, the major anomer **2cβ** adopted the $^4C_1$ conformation, similar to **14cβ–16cβ**, which is stabilized by the *exo*-anomeric effect and the equatorial orientation of the ring substituents. This conformation was evidenced by the large coupling constant values for the ring protons.

In contrast, glycosyl amine **2cα** was found preferentially in the $^1C_4$ conformation, as dictated by the small coupling

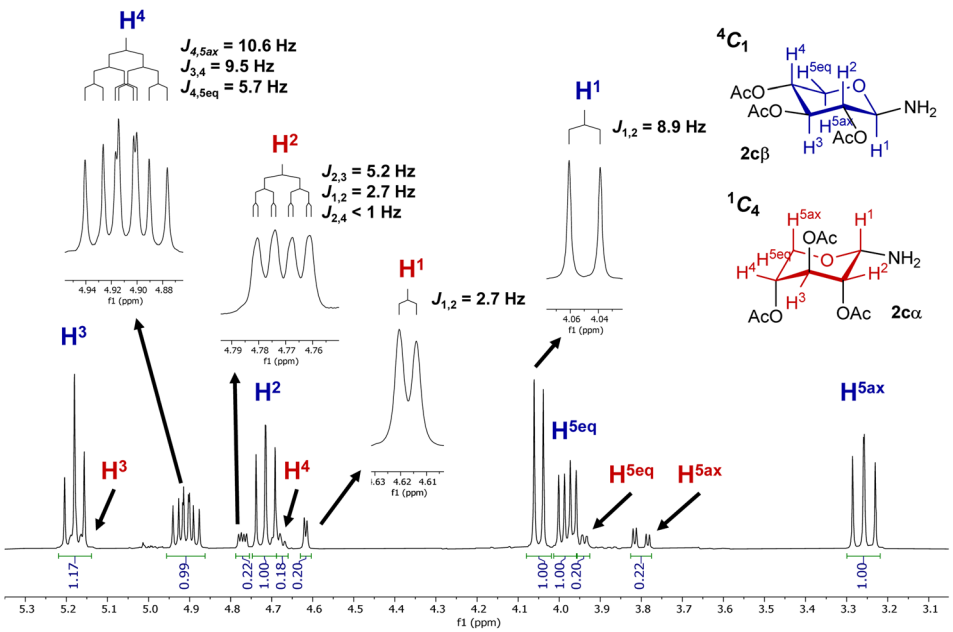


Fig. 1 ^{1}H NMR spectrum of the mixture of *N*-glycosyl amines **2cβ** and **2cα**.

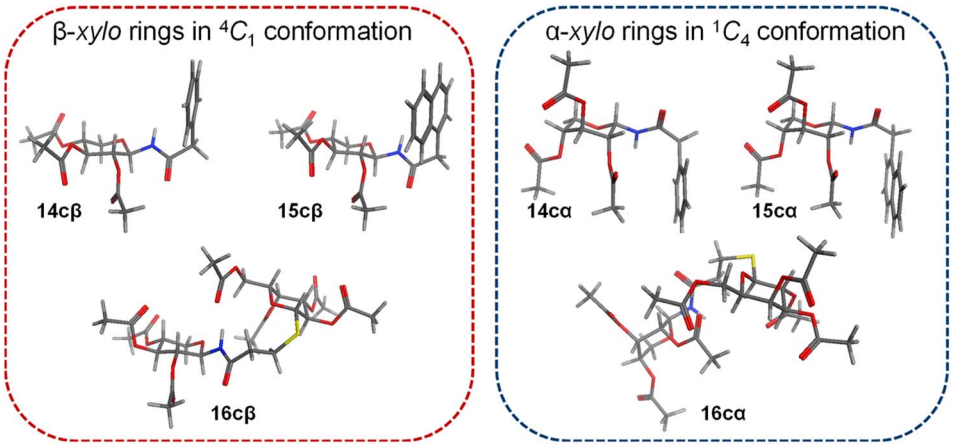


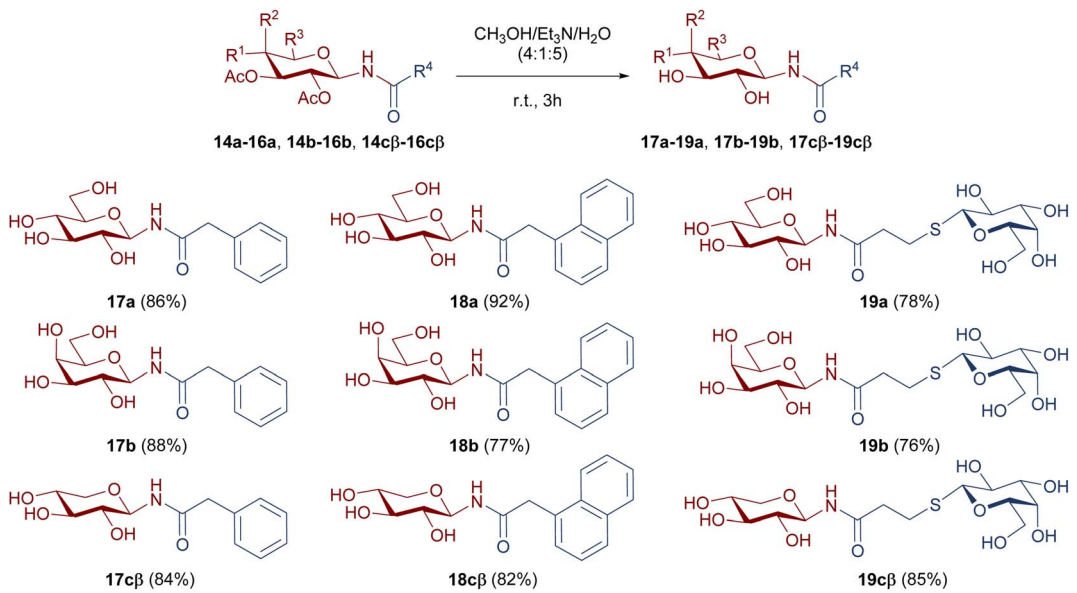
Fig. 2 Stable conformations of xylopyranosyl amides, determined by NMR and MM calculations.

constant values and the presence of W-type coupling (^4J) between H2 and H4 (as was observed for **14cα–16cα**). However, the values of $J_{2,3}$ (5.2 Hz) and $J_{4,5eq}$ (4.4 Hz) are rather large for diequatorially arranged protons (in $^1C_4$) and suggest some contribution of the $^4C_1$ chair to the conformational equilibrium. The fact that the **2cβ** structure is free of the 1,3-diaxial interactions observed for **2cα**, is in agreement with the general observation that for D-glycosyl amines the α configuration is less stable than the β configuration.[23] To support the findings on the conformational behaviour of *N*-glycosyl amides having the *xylo* configuration, a conformational search was performed using Molecular Mechanics and MMFF94 as the force field. All conformations up to 3.00 kcal mol^{-1} above the conformer with the minimum energy were analysed.

As a selection criterion, among the various conformations obtained, only those that showed chair forms ($^1C_4$ and $^4C_1$) were considered.

The conformational search revealed that for all β anomers the $^4C_1$ chair was the lowest energy conformer (Fig. 2), and that was the one exclusively populated within the energy window of 3.00 kcal mol^{-1} (ESI Table 1,† entries 1–3). On the other hand, for α *N*-glycosyl amides the $^4C_1$ and $^1C_4$ chairs were found to have similar energy (except for **16cα**, which was determined to populate only the $^1C_4$ form). However, in all cases, the $^1C_4$ chair was the lowest energy conformation (ESI Table 1,† entries 4–6). These results agree completely with those obtained from the analysis of ^{1}H NMR and 2D NOESY spectra.

For the evaluation of the inhibitory activity, OH free compounds were required. For this reason, the de-*O*-acetylation of **14a-cβ**, **15a-cβ**, and **16a-cβ** was carried out under mild conditions, as shown in Scheme 6. The hydrolysis of acetoxy functionalities was performed with a mixture of $CH_3OH/Et_3N/H_2O$ (4 : 1 : 5), to afford the hydroxyl free derivatives **17a-cβ**, **18a-cβ**, and **19a-cβ** with very good to excellent yields.



Scheme 6 de-*O*-Acetylation of *N*-glycosyl amides **14a-cβ**, **15a-cβ**, and **16a-cβ**.

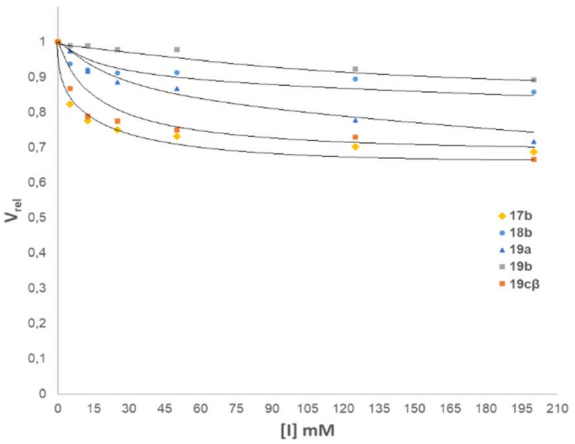


Fig. 3 Effect of the concentration of *N*-glycosyl amides **17b**, **18b**, **19a**, **19b**, and **19cβ** on the enzymatic activity of the β-galactosidase from *E. coli*.

Biological evaluation

The *N*-glycosyl amides **17b**, **18b**, **19a-cβ**, containing a galactopyranose residue, were evaluated as inhibitors of β-galactosidase from *E. coli*. Thus, the enzyme was incubated in a solution of *o*-nitrophenyl β-D-galactopyranoside as a substrate and with increasing concentrations of the glycomimetics. After 10 min at 37 °C, the enzyme was denatured upon addition of a 0.2 M sodium borate buffer and the released *o*-nitrophenol was quantified spectrophotometrically. All compounds were inhibitors of β-galactosidase from *E. coli*, as shown in the inhibition diagram in (Fig. 3).

The inhibition studies showed that the *N*-glycosylamides investigated were moderate inhibitors of *E. coli* β-galactosidase. The compounds that displayed a better inhibition profile were the thio-bridged *N*-glycosyl amide disaccharide **19cβ** and the *N*-glycosyl amide **17b** (Fig. 3). Even in these cases, the concentration of inhibitor needed to decrease the relative velocity by 30% was greater than 2.5 mM, for a substrate concentration of 1 mM. It is clear that these compounds have an effect on the inhibition of the enzyme, but this effect is moderate.

Since these glycomimetics exhibit low structural similarity to the natural enzyme substrate (lactose), it is not surprising that they display moderate inhibition profiles. Nevertheless, this study represents a significant contribution as an initial starting point for the design and development of novel and improved inhibitors, as this work constitutes the first report of *N*-glycosyl amides with inhibitory activity against the β-galactosidase from *E. coli*.

Experimental

Materials and methods

Column chromatography was carried out with silica gel 60 (230–400 mesh). Analytical thin layer chromatography (TLC) was carried out on silica gel 60 F_{254} aluminium-backed plates (layer thickness 0.2 mm). The spots were visualized by charring with a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ 25 g L^{-1}, $(NH_4)_4Ce(SO_4)_4\cdot 2H_2O$ 10 g L^{-1} and 10% H_2SO_4 in H_2O. Nuclear magnetic resonance (NMR) spectra were recorded at 400 MHz (^1H) or 100 MHz (^{13}C). Chemical shifts were calibrated to tetramethylsilane or to a residual solvent peak ($CHCl_3$: ^1H: δ 7.26 ppm, ^{13}C: δ 77.2 ppm or H_2O: δ 4.79 ppm). Assignments of ^1H and ^{13}C NMR spectra were assisted by 2D ^1H-COSY and 2D ^1H–^{13}C HSQC and HMBC experiments. 2D NOESY Spectra were also recorded. To assign the NMR signals of bridged disaccharides, the H and C atoms of the thiogalactopyranose residue have been labeled with primed locators. The coupling constants values are reported in Hz and resonance multiplicities abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sx = sextet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were obtained using the electrospray ionization (ESI) technique and Q-TOF detection.

Synthetic procedures

General procedure for synthesis of per-*O*-acetyl-α-D-pyranosyl-bromides (10a–c).[44–46] Per-*O*-acetyl-D-pyranose **9a–c** (10.8 mmol) (*gluco*, *galacto* or *xylo*) was dissolved in anhydrous CH_2Cl_2 (4.4 mL) at 0 °C. Then, hydrogen bromide solution 33% (wt) in acetic acid (4.2 mL) was added. The reaction was stirred at 0 °C for 1 hour, and then for an additional 1 h at room temperature. The mixture was diluted with ethyl acetate (100 mL) and successively extracted with ice/water (1 × 50 mL), sodium bicarbonate (2 × 50 mL) and brine (1 × 50 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated to obtain the glycosyl bromide **10a–c** as a light-yellow syrup that was used for the next step without further purification.

General procedure for the synthesis of per-*O*-acetyl-β-D-pyranosyl-1-azides[27–29]

Method A. Sodium azide (2.117 g, 32.6 mmol) was added to a solution of per-*O*-acetylated glycosyl bromide (*gluco*, *galacto* or *xylo*) **10a–c** (10.8 mmol) in DMF (20 mL). The reaction was stirred at 70 °C for 5 h and then cooled to room temperature. The mixture was diluted with distilled water (100 mL) and extracted with diethyl ether (4 × 50 mL). The organic layer was dried (Na_2SO_4) and filtered. Evaporation of the solvent gave an oily residue, which was purified by column chromatography employing hexane/EtOAc (4 : 1 → 2 : 1) to afford the per-*O*-acetyl-β-D-pyranosyl-1-azides **5a–c**.

2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-1-azide (5a).[27–29,47–50] Following the general procedure, glycosyl azide **5a** was obtained as a white solid. M.p. 125.2–126.7 °C. Yield: 73% (2.911 g). R_f = 0.49; pentane/EtOAc (2 : 1). $[\alpha_D^{24}] = -31.3$ (c = 0.9, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 5.20 (t, $J_{2,3} = J_{3,4}$ = 9.5 Hz, 1H, 3-H), 5.08 (t, $J_{3,4} = J_{4,5}$ = 9.7 Hz, 1H, 4-H), 4.93 (t, $J_{1,2} = J_{2,3}$ = 9.2 Hz, 1H, 2-H), 4.63 (d, $J_{1,2}$ = 8.9 Hz, 1H, 1-H), 4.25 (dd, $J_{6a,6b}$ = 12.5, $J_{5,6a}$ = 4.8 Hz, 1H, 6a-H), 4.15 (dd, $J_{6a,6b}$ = 12.5, $J_{5,6b}$ = 2.2 Hz, 1H, 6b-H), 3.78 (ddd, $J_{4,5}$ = 10.0, $J_{5,6a}$ = 4.7, $J_{5,6b}$ = 2.3 Hz, 1H, 5-H), 2.08, 2.05, 2.01, 1.99 (4s, 12H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) = 170.7, 170.2, 169.4, 169.3 ($COCH_3$), 88.0 (C-1), 74.2 (C-5), 72.7 (C-3), 70.8 (C-2), 68.0 (C-4), 61.8 (C-6), 20.8, 20.6 (×3) ($COCH_3$) ppm. HRMS (ESI): calcd for $C_{14}H_{19}N_3NaO_9$ 396.1013 $[M + Na]^+$; found 396.1014.

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-1-azide (5b).[27–29,50–53] Following the general procedure, glycosyl azide **5b** was obtained as a white solid. M.p. 94.7–96.3 °C. Yield: 71% (2.837 g). $R_f = 0.49$; pentane/EtOAc (2 : 1). $[\alpha_D^{25}] = -15.9$ ($c = 0.9$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.40$ (br. d, $J_{3,4} = 3.2$, $J_{4,5} < 1$ Hz, 1H, 4-H), 5.14 (dd, $J_{2,3} = 10.2$, $J_{1,2} = 8.9$ Hz, 1H, 2-H), 5.02 (dd, $J_{2,3} = 10.4$, $J_{3,4} = 3.3$ Hz, 1H, 3-H), 4.59 (d, $J_{1,2} = 8.7$ Hz, 1H, 1-H), 4.17 (dd, $J_{6a,6b} = 11.3$, $J_{5,6a} = 6.9$ Hz, 1H, 6a-H), 4.13 (dd, $J_{6a,6b} = 11.3$, $J_{5,6b} = 6.2$ Hz, 1H, 6b-H), 4.00 (br. t, $J_{5,6a} = J_{5,6b} = 6.5$, $J_{4,5} < 1$ Hz, 1H, 5-H), 2.15, 2.07, 2.04, 1.97 (4s, 12H, COC*H*$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.4, 170.2, 170.1, 169.4 (*C*OCH$_3$), 88.4 (C-1), 73.0 (C-5), 70.9 (C-3), 68.2 (C-2), 67.0 (C-4), 61.3 (C-6), 20.7 (×3), 20.6 (CO*C*H$_3$) ppm. HRMS (ESI): calcd for $C_{14}H_{19}N_3NaO_9$ 396.1013 $[M + Na]^+$; found 396.1006.

When the general procedure (method A) was applied to bromide **10c**, both anomers of azide **5c** were isolated as an anomeric mixture (α/β = 1 : 1.2) that could not be separated by column chromatography. Yield: 73%. $R_f = 0.61$, pentane/EtOAc (2 : 1).

2,3,4,-Tri-*O*-acetyl-α-D-xylopyranosyl-1-azide (5cα).[54] This compound was obtained together with compound **5cβ** in a mixture (α/β = 1 : 1.2). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.49$ (d, $J_{1,2} = 4.0$ Hz, 1H, 1-H), 5.34 (t, $J_{2,3} = J_{3,4} = 9.5$ Hz, 1H, 3-H), 4.92 (td, $J_{3,4} = J_{4,5ax} = 9.6$, $J_{4,5eq} = 5.9$ Hz, 1H, 4-H overlapped with 4-H of **5cβ**), 4.86 (dd, $J_{2,3} = 9.2$, $J_{1,2} = 4.0$ Hz, 1H, 2-H overlapped with 2-H of **5cβ**), 3.91 (dd, $J_{5ax,5eq} = 11.3$, $J_{4,5eq} = 5.8$ Hz, 1H, 5eq-H), 3.75 (t, $J_{4,5ax} = J_{5ax,5eq} = 10.8$ Hz, 1H, 5ax-H), 2.07, 2.01 (×2) (3s, 9H, COC*H*$_3$ overlapped with COC*H*$_3$ of **5cβ**) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.0, 169.9, 169.8 (*C*OCH$_3$), 86.5 (C-1), 70.2 (C-2), 69.0 (C-3), 68.7 (C-4), 60.6 (C-5), 20.7 (×2), 20.6 (CO*C*H$_3$ overlapped with CO*C*H$_3$ of **5cβ**) ppm.

The β anomer was obtained diastereoselectively using Method B, as mentioned below.

Method B

2,3,4,-Tri-O-acetyl-β-D-xylopyranosyl-1-azide (5cβ).[30,55,56] To a solution of glycosyl bromide **10c** (4.32 g, 10.5 mmol) in acetone (38 mL), a solution of NaN_3 (0.82 g, 12.6 mmol) in H_2O (9.5 mL) was added, and the mixture was stirred at room temperature for 3 h, when TLC showed complete consumption of the starting bromide. The solvent was evaporated under reduced pressure, and the crude reaction mixture was purified by column chromatography using pentane/EtOAc (4 : 1 → 2 : 1) to afford the glycosyl azide **5c** (β anomer) as a white solid. M.p. 83.9–85.5 °C. Yield: 63% (1.986 g). $R_f = 0.61$; pentane/EtOAc (2 : 1). $[\alpha_D^{24}] = -82.7$ ($c = 0.9$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.18$ (t, $J_{2,3} = J_{3,4} = 8.9$ Hz, 1H, 3-H), 4.97 (td, $J_{3,4} = J_{4,5ax} = 9.3$, $J_{4,5eq} = 5.3$ Hz, 1H, 4-H), 4.86 (t, $J_{1,2} = J_{2,3} = 8.5$ Hz, 1H, 2-H), 4.62 (d, $J_{1,2} = 8.1$ Hz, 1H, 1-H), 4.20 (dd, $J_{5ax,5eq} = 11.7$, $J_{4,5eq} = 5.3$ Hz, 1H, 5eq-H), 3.43 (dd, $J_{5ax,5eq} = 11.7$, $J_{4,5ax} = 9.6$ Hz, 1H, 5ax-H), 2.07, 2.04, 2.03 (3s, 9H, COC*H*$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.1, 169.8, 169.4 (*C*OCH$_3$), 88.4 (C-1), 71.6 (C-3), 70.5 (C-2), 68.5 (C-4), 64.4 (C-5), 20.8, 20.7 (×2) (CO*C*H$_3$)-ppm. HRMS (ESI): calcd for $C_{11}H_{15}N_3NaO_7$ 324.0802 $[M + Na]^+$; found 324.0793.

3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl) thiopropionic acid (13β) and 3-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl) thiopropionic acid (13α). To a solution of penta-*O*-acetyl galactopyranose **9b** (0.976 g, 2.5 mmol) in anhydrous CH_3CN (30 mL), mercaptopropionic acid (265 μL, 2.75 mmol) was added, followed by the slow addition of $BF_3 \cdot OEt_2$ (348 μL, 2.75 mmol). The reaction mixture was refluxed for 2 hours, cooled to room temperature, and stirred overnight. At this time, complete conversion of the starting material was confirmed by TLC. The solvent was removed under reduced pressure and the products were purified by column chromatography using hexane/EtOAc (8 : 1 → 1 : 1) with 1% v/v AcOH.

The major product was isolated as a clear yellow syrup and was identified as thioglyco acid **13β.**[57–59] Yield: 43% (469 mg, β-anomer). $R_f = 0.25$; hexane/EtOAc (1 : 1; 1% v/v AcOH). $[\alpha_D^{24}] = -9.3$ ($c = 1.1$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.41$ (d, $J_{3,4} = 2.9$ Hz, 1H, 4-H), 5.20 (t, $J_{1,2} = J_{2,3} = 10.0$ Hz, 1H, 2-H), 5.03 (dd, $J_{2,3} = 9.9$, $J_{3,4} = 3.3$ Hz, 1H, 3-H), 4.54 (d, $J_{1,2} = 9.9$ Hz, 1H, 1-H), 4.16 (dd, $J_{6a,6b} = 11.3$, $J_{5,6a} = 6.7$ Hz, 1H, 6a-H), 4.07 (dd, $J_{6a,6b} = 11.3$, $J_{5,6b} = 6.5$ Hz, 1H, 6b-H), 3.92 (t, $J_{5,6a} = J_{5,6b} = 6.4$ Hz, 1H, 5-H), 2.97 (dt, $J_{gem} = 13.9$, $J_{CH_2S,CH_2COOH} = 7.1$ Hz, 1H, C*H*$_2$S), 2.89 (dt, $J_{gem} = 13.7$, $J_{CH_2S,CH_2COOH} = 6.8$ Hz, 1H, C*H*$_2$S), 2.73 (t, $J_{CH_2S,CH_2COOH} = 6.9$ Hz, 2H, C*H*$_2$COOH), 2.14, 2.04 (×2), 1.97 (4s, 12H, COC*H*$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.5 (*C*OOH), 170.7, 170.4, 170.2, 169.8 (*C*OCH$_3$), 84.7 (C-1), 74.6 (C-5), 72.0 (C-3), 67.4 (C-4), 67.3 (C-2), 61.7 (C-6), 35.4 (*C*H$_2$COOH), 25.5 (*C*H$_2$S), 20.9, 20.7 (×3) (CO*C*H$_3$) ppm. HRMS (ESI): calcd for $C_{17}H_{24}NaO_{11}S$ 459.0932 $[M + Na]^+$; found 459.0916.

The minor product was isolated as a light-yellow syrup and identified as the thioglyco acid **13α**. The structure of this compound has been misassigned[33] as the signals reported agreed with those of the β-anomer. Yield: 25% (273 mg, α-anomer). $R_f = 0.30$; hexane/EtOAc (1 : 1; 1% v/v AcOH). $[\alpha_D^{18}] = +127.3$ ($c = 1.1$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.77$ (d, $J_{1,2} = 5.5$ Hz, 1H, 1-H), 5.44 (d, $J_{3,4} = 2.4$ Hz, 1H, 4-H), 5.26 (dd, $J_{2,3} = 10.9$, $J_{1,2} = 5.5$ Hz, 1H, 2-H), 5.17 (dd, $J_{2,3} = 10.9$, $J_{3,4} = 3.1$ Hz, 1H, 3-H), 4.57 (t, $J_{5,6} = 6.3$ Hz, 1H, 5-H), 4.12 (d, $J_{5,6} = 6.3$ Hz, 2H, 6a-H and 6b-H), 2.88 (dt, $J_{gem} = 14.0$, $J_{CH_2S,CH_2COOH} = 7.1$ Hz, 1H, CH_2S), 2.82–2.76 (m, 1H, CH_2S), 2.71 (t, $J_{CH_2S,CH_2COOH} = 6.9$ Hz, 2H, C*H*$_2$COOH), 2.14, 2.07, 2.06, 1.99 (4s, 12H, $COCH_3$) ppm. ^{13}C NMR (101 MHz, CDCl3) δ = 175.8 (COOH), 170.7, 170.3 (×2), 170.0 (COCH3), 83.1 (C-1), 68.3 (C-3), 68.1 (×2, C-2, C-4), 67.0 (C-5), 62.1 (C-6), 34.6 (CH_2COOH), 25.2 (CH_2S), 20.9, 20.8, 20.7 (×2) ($COCH_3$) ppm. HRMS (ESI): calcd for $C_{17}H_{24}NaO_{11}S$ 459.0932 [M + Na]+; found 459.0917.

General procedure for the synthesis of glycosyl amides 14a–c, 15a–c, and 16a–c. To a solution of glycosyl azide **5a–c** (0.33 mmol) in anhydrous EtOAc (3 mL), 10% Pd/C (18.6 mg) was added. The mixture was stirred, and H_2 was bubbled into the solution using a needle with a balloon until complete conversion of the starting material to the more polar glycosyl amine **2a–c** was observed. The reaction mixture was filtered through a pad of Celite, the residue was washed with anhydrous EtOAc, the liquors were collected and the solvent was then evaporated under reduced pressure.

Meanwhile, to a solution of carboxylic acid **11–13β** (0.36 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (3 mL) was added

DCC (103 mg, 0.5 mmol, 1.5 equiv.), under Argon atmosphere. To the resulting suspension, the glycosyl amine **2a–c** (obtained in the previous step), was added and stirred overnight under Argon. The mixture was cooled in a freezer for 2 h, filtered (to separate the dicyclohexylurea byproduct) and washed with cold CH_2Cl_2. The resulting solution was evaporated under reduced pressure and the crude was purified by column chromatography using hexane/EtOAc (4 : 1 → 1 : 1) for amides **14a–c** and **15a–c**, and toluene/EtOAc (4 : 1 → 1 : 1) for amides **16a–c**.

Only the glycosyl amines derived from xylose **2c** were characterized by NMR, to perform a conformational analysis of the product obtained (**2cβ** and **2cα**).

2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl amine (2cβ) and 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl amine (2cα). The reduction of **5c** under the general conditions led to the anomeric mixture of **2c** (α/β = 1 : 5). Yield: 90%. R_f = 0.13; hexane/EtOAc (1 : 1).

^{1}H NMR (400 MHz, $CDCl_3$) of **2cβ**[55] δ = 5.17 (t, $J_{2,3}$ = $J_{3,4}$ = 9.6 Hz, 1H, 3-H), 4.91 (ddd, $J_{4,5ax}$ = 10.6, $J_{3,4}$ = 9.5, $J_{4,5eq}$ = 5.7 Hz, 1H, 4-H), 4.71 (dd, $J_{2,3}$ = 9.7, $J_{1,2}$ = 8.9 Hz, 1H, 2-H), 4.05 (d, $J_{1,2}$ = 8.9 Hz, 1H, 1-H), 3.98 (dd, $J_{5ax,5eq}$ = 11.4, $J_{4,5eq}$ = 5.7, 1H, 5eq-H), 3.26 (dd, $J_{5ax,5eq}$ = 11.5, $J_{4,5ax}$ = 10.5 Hz, 1H, 5ax-H), 2.02, 1.98, 1.98 (3s, 9H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) of **2cβ** δ = 170.3, 170.2, 170.0 ($COCH_3$), 85.5 (C-1), 72.7 (C-3), 72.3 (C-2), 69.5 (C-4), 63.8 (C-5), 20.9, 20.7 (×2) ($COCH_3$) ppm.

^{1}H NMR (400 MHz, $CDCl_3$) of **2cα** δ = 5.19–5.16 (m, 1H, 3-H overlapped with 3-H of **2cβ**), 4.77 (ddd, $J_{2,3}$ = 5.2, $J_{1,2}$ = 2.7, $J_{2,4}$ < 1 Hz, 1H, 2-H), 4.70–4.67 (m, 1H, 4-H overlapped with 2-H of **2cβ**), 4.62 (d, $J_{1,2}$ = 2.7 Hz, 1H, 1-H), 3.95 (ddd, $J_{5ax,5eq}$ = 12.7, $J_{4,5eq}$ = 4.4, $J_{3,5eq}$ < 1.0 Hz, 1H, 5eq-H overlapped with 5eq-H of **2cβ**), 3.80 (dd, $J_{5ax,5eq}$ = 12.8, $J_{4,5ax}$ = 3.2 Hz, 1H, 5ax-H), 2.09, 2.05, 2.05 (3s, 9H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) of **2cα** δ = 169.8, 169.7, 169.0 ($COCH_3$), 79.6 (C-1), 69.6 (C-2), 67.8 (C-3), 67.2 (C-4), 62.4 (C-5), 21.0, 20.8 (×2) ($COCH_3$) ppm.

2-(Phenyl)-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) acetamide (14a).[60,61] Following the general procedure, glycosyl amide **14a** was obtained as a white solid. M.p. 159.2–160.8 °C. Yield: 70% (108 mg). R_f = 0.45; pentane/EtOAc (1 : 1). $[\alpha_D^{24}]$ = +1.0 (c = 1.1, $CHCl_3$)·^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37–7.21 (m, 5H, *Ph*CH_2CONH), 6.33 (d, $J_{NH,1}$ = 9.1 Hz, 1H, CON*H*), 5.27 (t, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, 1H, 3-H), 5.20 (t, $J_{NH,1}$ = $J_{1,2}$ = 9.3 Hz, 1H, 1-H), 5.03 (t, $J_{3,4}$ = $J_{4,5}$ = 9.7 Hz, 1H, 4-H), 4.83 (t, $J_{1,2}$ = $J_{2,3}$ = 9.6 Hz, 1H, 2-H), 4.30 (dd, $J_{6a,6b}$ = 12.5, $J_{5,6a}$ = 4.3 Hz, 1H, 6a-H), 4.07 (dd, $J_{6a,6b}$ = 12.4, $J_{5,6b}$ = 1.5 Hz, 1H, 6b-H), 3.80 (ddd, $J_{4,5}$ = 10.0, $J_{5,6a}$ = 3.9, $J_{5,6b}$ = 2.0 Hz, 1H, 5-H), 3.58 (d, J_{gem} = 15.2 Hz, 1H, PhCH_2CONH), 3.50 (d, J_{gem} = 15.2 Hz, 1H, PhCH_2CONH), 2.07, 2.02, 1.98, 1.83 (4s, 12H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.4 ($CONH$), 170.7 (×2), 169.9, 169.6 ($COCH_3$), 133.9, 129.3, 129.1, 127.6 (*Ph*CH_2CONH), 78.4 (C-1), 73.7 (C-5), 72.7 (C-3), 70.3 (C-2), 68.2 (C-4), 61.7 (C-6), 43.9 (PhCH_2-CONH), 20.8, 20.6 (×2), 20.4 ($COCH_3$) ppm. HRMS (ESI): calcd for $C_{22}H_{27}NNaO_{10}$ 488.1527 $[M + Na]^+$; found 488.1483.

2-(Phenyl)-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl) acetamide (14b). Following the general procedure, glycosyl amide **14b** was obtained as a white solid. M.p. 119.5–121.3 °C. Yield: 73% (112 mg). R_f = 0.34; hexane/EtOAc (1 : 1). $[\alpha_D^{26}]$ = +17.2 (c = 1.0, $CHCl_3$)·^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38–7.23 (m, 5H, *Ph*CH_2CO), 6.31 (d, $J_{NH,1}$ = 9.2 Hz, 1H, NH), 5.41 (br. d, $J_{3,4}$ = 2.9 Hz, $J_{4,5}$ < 1 Hz, 1H, 4-H), 5.20 (t, $J_{NH,1}$ = $J_{1,2}$ = 9.2 Hz, 1H, 1-H), 5.09 (dd, $J_{2,3}$ = 10.3, $J_{3,4}$ = 3.3 Hz, 1H, 3-H), 5.01 (t, $J_{1,2}$ = $J_{2,3}$ = 9.8 Hz, 1H, 2-H), 4.14–4.03 (m, 2H, 6b-H and 6a-H), 4.02 (br. t, $J_{5,6a}$ = $J_{5,6b}$ = 6.6, $J_{4,5}$ < 1 Hz, 1H, 5-H), 3.58 (d, J_{gem} = 15.3 Hz, 1H, NHCOCH_2Ph), 3.50 (d, J_{gem} = 15.2 Hz, 1H, NHCOCH_2Ph), 2.12, 2.03, 1.96, 1.85 (4s, 12H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.3 ($CONH$), 170.9, 170.4, 170.1, 169.8 ($COCH_3$), 134.0, 129.3, 129.1, 127.6 (*Ph*CH_2CO), 78.7 (C-1), 72.5 (C-5), 70.9 (C-3), 68.0 (C-2), 67.3 (C-4), 61.2 (C-6), 43.9 (NHCOCH_2Ph), 20.7, 20.6 (×2), 20.5 ($COCH_3$) ppm. HRMS (ESI): calcd for $C_{22}H_{27}NNaO_{10}$ 488.1527 $[M + Na]^+$; found 488.1503.

2-(Phenyl)-*N*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl) acetamide (14cβ). Following the general procedure, amide **14cβ** was isolated as the major product as a white solid. M.p. 155.8–157.0 °C. Yield: 58% (75 mg). R_f = 0.38; hexane/EtOAc (1 : 1). $[\alpha_D^{23}]$ = −3.6 (c = 1.0, $CHCl_3$)·^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35–7.23 (m, 5H, *Ph*CH_2CO), 6.71 (d, $J_{NH,1}$ = 9.2 Hz, 1H, NH), 5.25 (t, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, 1H, 3-H), 5.15 (t, $J_{NH,1}$ = $J_{1,2}$ = 9.3 Hz, 1H, 1-H), 4.95 (ddd, $J_{4,5ax}$ = 10.6, $J_{3,4}$ = 9.4, $J_{4,5eq}$ = 5.7 Hz, 1H, 4-H), 4.83 (t, $J_{1,2}$ = $J_{2,3}$ = 9.5 Hz, 1H, 2-H), 4.05 (dd, $J_{5ax,5eq}$ = 11.6, $J_{4,5eq}$ = 5.7 Hz, 1H, 5eq-H), 3.57 (d, J_{gem} = 15.0 Hz, 1H, NHCOCH_2Ph), 3.51 (d, J_{gem} = 14.9 Hz, 1H, NHCOCH_2Ph), 3.42 (dd, $J_{5ax,5eq}$ = 11.6, $J_{4,5ax}$ = 10.6 Hz, 1H, 5ax-H), 2.01, 2.00, 1.86 (3s, 9H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.7 ($CONH$), 170.6, 169.9, 169.8 ($COCH_3$), 133.2, 129.2, 129.0, 127.4 (*Ph*CH_2CO), 78.7 (C-1), 72.3 (C-3), 70.4 (C-2), 69.0 (C-4), 64.5 (C-5), 43.7 (NHCOCH_2Ph), 20.7, 20.6, 20.4 ($COCH_3$) ppm. HRMS (ESI): calcd for $C_{19}H_{23}NNaO_8$ 416.1316 $[M + Na]^+$; found 416.1298.

2-(Phenyl)-*N*-(2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl) acetamide (14cα). The α anomer **14cα** was isolated as a byproduct, as a colorless syrup. Yield: 14% (18 mg). R_f = 0.28; hexane/EtOAc (1 : 1). $[\alpha_D^{18}]$ = −22.6 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37–7.21 (m, 5H, *Ph*CH_2CO), 6.17 (d, $J_{NH,1}$ = 9.0 Hz, 1H, NH), 5.54 (dd, $J_{NH,1}$ = 9.3, $J_{1,2}$ = 2.3 Hz, 1H, 1-H), 5.05 (td, $J_{2,3}$ = $J_{3,4}$ = 3.8, $J_{3,5eq}$ = 1.5 Hz, 1H, 3-H), 4.69–4.68 (m, 1H, 2-H), 4.66 (br. q, $J_{3,4}$ = $J_{4,5ax}$ = $J_{4,5eq}$ = 2.6, $J_{2,4}$ < 1 Hz, 1H, 4-H), 3.98 (dd, $J_{5ax,5eq}$ = 13.4, $J_{4,5ax}$ = 2.4 Hz, 1H, 5ax-H), 3.91 (dt, $J_{5ax,5eq}$ = 13.5, $J_{4,5eq}$ = $J_{3,5eq}$ = 1.9 Hz, 1H, 5eq-H), 3.64 (d, J_{gem} = 16.5 Hz, 1H, NHCOCH_2Ph), 3.59 (d, J_{gem} = 16.4 Hz, 1H, NHCOCH_2Ph), 2.10, 2.05, 1.90 (3s, 9H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.7 ($CONH$), 169.6, 169.3, 168.7 ($COCH_3$), 134.0, 129.7, 129.3, 127.8 (*Ph*CH_2CO), 74.2 (C-1), 67.9 (C-3), 67.0 (C-2), 66.1 (C-4), 65.0 (C-5), 43.7 (NHCOCH_2Ph), 21.0, 20.8, 20.5 ($COCH_3$) ppm. HRMS (ESI): calcd for $C_{19}H_{23}NNaO_8$ 416.1316 $[M + Na]^+$; found 416.1294.

2-(Naphthalen-1-yl)-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl) acetamide (15a). Following the general procedure, glycosyl amide **15a** was obtained as a white solid. M.p. 174.7 °C (dec.). Yield: 68% (116 mg). R_f = 0.38; pentane/EtOAc (1 : 1). $[\alpha_D^{25}]$ = +6.6 (c = 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.91 (dd, J_{ortho} = 6.4, J_{meta} = 2.7 Hz, 1H, *Npth*CH_2CO), 7.90 (dd, J_{ortho} = 6.3, J_{meta} = 2.6 Hz, 1H, *Npth*CH_2CO), 7.87 (br. d, J_{ortho} = 8.1 Hz, 1H, *Npth*CH_2CO), 7.53 (td, J_{ortho} = J_{ortho} = 7.1, J_{meta} = 2.3 Hz, 1H, *Npth*CH_2CO), 7.53–7.49 (m, 1H, *Npth*CH_2CO), 7.49 (dd, J_{ortho} = 8.1, J_{ortho} = 7.2 Hz, 1H, *Npth*CH_2CO), 7.40 (dd, J_{ortho} = 6.9, J_{meta} = 1.3 Hz, 1H, *Npth*CH_2CO), 6.20 (d, $J_{NH,1}$ = 8.9 Hz,

1H, NH), 5.16 (t, $J_{2,3} = J_{3,4} = 9.5$ Hz, 1H, 3-H), 5.13 (t, $J_{NH,1} = J_{1,2} = 9.3$ Hz, 1H, 1-H), 4.96 (dd, $J_{4,5} = 10.1$, $J_{3,4} = 9.3$ Hz, 1H, 4-H), 4.60 (t, $J_{1,2} = J_{2,3} = 9.6$ Hz, 1H, 2-H), 4.29 (dd, $J_{6a,6b} = 12.5$, $J_{5,6b} = 4.2$ Hz, 1H, 6a-H), 4.12 (d, $J_{gem} = 16.1$ Hz, 1H, NHCOCH_2), 4.06 (dd, $J_{6a,6b} = 12.5$, $J_{5,6b} = 2.2$ Hz, 1H, 6b-H), 3.91 (d, $J_{gem} = 16.1$ Hz, 1H, NHCOCH_2), 3.78 (ddd, $J_{4,5} = 10.1$, $J_{5,6a} = 4.3$, $J_{5,6b} = 2.2$ Hz, 1H, 5-H), 2.07, 1.99, 1.90, 1.27 (4s, 12H, COCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.5 (*C*ONH), 170.7, 170.3, 169.9, 169.6 (*C*OCH$_3$), 134.3, 132.2, 130.1, 129.1, 128.9, 128.7, 127.0, 126.3, 125.9, 123.7 (*Npth*CH$_2$CO), 78.5 (C-1), 73.7 (C-5), 72.7 (C-3), 69.9 (C-2), 68.3 (C-4), 61.7 (C-6), 42.2 (NHCO*C*H$_2$), 20.8, 20.7, 20.6, 19.6 (CO*C*H$_3$) ppm. HRMS (ESI): calcd for $C_{26}H_{29}NNaO_{10}$ 538.1684 [M + Na]$^+$; found 538.1671.

2-(Naphthalen-1-yl)-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl) acetamide (15b). Following the general procedure, glycosyl amide **15b** was obtained as a colorless syrup. Yield: 62% (105 mg). $R_f = 0.38$; pentane/EtOAc (1 : 1). $[\alpha_D^{26}] = +18.7$ ($c = 1.2$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93–7.89 (m, 2H, *Npth*CH$_2$CO), 7.87 (br. d, $J_{ortho} = 8.5$ Hz, 1H, *Npth*CH$_2$CO), 7.55–7.48 (m, 3H, *Npth*CH$_2$CO), 7.41 (br. d, $J_{ortho} = 6.8$ Hz, 1H, *Npth*CH$_2$CO), 6.23 (d, $J_{NH,1} = 8.9$ Hz, 1H, NHCO), 5.36 (br. d, $J_{3,4} = 2.8$, $J_{4,5} < 1$ Hz, 1H, 4-H), 5.12 (t, $J_{NH,1} = J_{1,2} = 9.2$ Hz, 1H, 1-H), 4.99 (dd, $J_{2,3} = 10.3$, $J_{3,4} = 3.3$ Hz, 1H, 3-H), 4.79 (t, $J_{1,2} = J_{2,3} = 9.9$ Hz, 1H, 2-H), 4.11 (d, $J_{gem} = 16.7$ Hz, 1H, NHCOCH_2), 4.08–4.06 (m, 2H, 6b-H and 6a-H), 3.98 (br. t, $J_{5,6a} = J_{5,6b} = 6.6$, $J_{4,5} < 1$ Hz, 1H, 5-H), 3.91 (d, $J_{gem} = 16.0$ Hz, 1H, NHCOCH_2), 2.07, 2.02, 1.89, 1.30 (4s, 12H, COCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.4 (NH*C*O), 170.5 (×2), 170.1, 169.8 (*C*OCH$_3$), 134.3, 132.2, 130.2, 129.0, 128.9, 128.7, 127.0, 126.3, 125.9, 123.7 (*Npth*CH$_2$CO), 78.8 (C-1), 72.4 (C-5), 70.8 (C-3), 67.6 (C-2), 67.2 (C-4), 61.1 (C-6), 42.3 (NHCO*C*H$_2$), 20.8, 20.7, 20.5, 19.7 (CO*C*H$_3$) ppm. HRMS (ESI): calcd for $C_{26}H_{29}NNaO_{10}$ 538.1684 [M + Na]$^+$; found 538.1633.

2-(Naphthalen-1-yl)-*N*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl) acetamide (15cβ). Following the general procedure, glycosyl amide **15cβ** was obtained as the main product as a white solid. M.p. 171.7 °C (dec.). Yield: 58% (85 mg). $R_f = 0.43$; pentane/EtOAc (1 : 1). $[\alpha_D^{22}] = +1.11$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92–7.87 (m, 2H, *Npth*CH$_2$CO), 7.86 (dd, $J_{ortho} = 8.2$, $J_{meta} = 1.2$ Hz, 1H, *Npth*CH$_2$CO), 7.55–7.50 (m, 2H, *Npth*CH$_2$CO), 7.48 (dd, $J_{ortho} = 8.1$, $J_{ortho} = 7.0$ Hz, 1H, *Npth*CH$_2$CO), 7.39 (dd, $J_{ortho} = 7.0$, $J_{meta} = 1.2$ Hz, 1H, *Npth*CH$_2$CO), 6.20 (d, $J_{NH,1} = 8.8$ Hz, 1H, NHCO), 5.15 (t, $J_{2,3} = J_{3,4} = 9.5$ Hz, 1H, 3-H), 5.04 (t, $J_{NH,1} = J_{1,2} = 9.1$ Hz, 1H, 1-H), 4.84 (ddd, $J_{4,5ax} = 10.5$, $J_{3,4} = 9.3$, $J_{4,5eq} = 5.7$ Hz, 1H, 4-H), 4.53 (t, $J_{1,2} = J_{2,3} = 9.5$ Hz, 1H, 2-H), 4.09 (d, $J_{gem} = 16.2$ Hz, 1H, NHCOCH_2), 4.01 (dd, $J_{5ax,5eq} = 11.6$, $J_{4,5eq} = 5.7$ Hz, 1H, 5eq-H), 3.92 (d, $J_{gem} = 16.2$ Hz, 1H, NHCOCH_2), 3.39 (dd, $J_{5ax,5eq} = 11.7$, $J_{4,5ax} = 10.5$ Hz, 1H, 5ax-H), 1.99, 1.91, 1.36 (3s, 9H, COCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.7 (NH*C*O), 170.4, 169.9, 169.8 (*C*OCH$_3$), 134.3, 132.2, 130.1, 129.1, 128.9, 128.7, 127.0, 126.3, 125.9, 123.7 (*Npth*CH$_2$CO), 79.0 (C-1), 72.1 (C-3), 70.1 (C-2), 69.1 (C-4), 64.5 (C-5), 42.1 (NHCO*C*H$_2$), 20.8, 20.6, 19.7 (CO*C*H$_3$) ppm. HRMS (ESI): calcd for $C_{23}H_{25}NNaO_8$ 466.1472 [M + Na]$^+$; found 466.1467.

2-(Naphthalen-1-yl)-*N*-(2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl) acetamide (15cα). The α anomer **15cα** was isolated as a byproduct as a colorless syrup. Yield: 13% (19 mg). $R_f = 0.29$; hexane/EtOAc (1 : 1). $[\alpha_D^{22}] = -43.59$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.89–7.88 (m, 2H, *Npth*CH$_2$CO), 7.85 (dd, $J_{ortho} = 8.1$, $J_{meta} = 1.1$ Hz, 1H, *Npth*CH$_2$CO), 7.57–7.51 (m, 2H, *Npth*CH$_2$CO), 7.46 (dd, $J_{ortho} = 8.1$, $J_{ortho} = 6.9$ Hz, 1H, *Npth*CH$_2$CO), 7.41 (dd, $J_{ortho} = 7.4$, $J_{meta} = 1.1$ Hz, 1H, *Npth*CH$_2$CO), 6.06 (d, $J_{NH,1} = 9.0$ Hz, 1H, NHCO), 5.54 (dd, $J_{NH,1} = 9.2$, $J_{1,2} = 2.3$ Hz, 1H, 1-H), 4.94 (td, $J_{3,4} = J_{2,3} = 3.6$, $J_{3,5eq} = 1.6$ Hz, 1H, 3-H), 4.60 (qd, $J_{4,5eq} = J_{4,5ax} = J_{3,4} = 3.5$, $J_{2,4} < 1$ Hz, 1H, 4-H), 4.49 (ddd, $J_{2,3} = 3.5$, $J_{1,2} = 2.3$, $J_{2,4} < 1$ Hz, 1H, 2-H), 4.14 (d, $J_{gem} = 16.9$ Hz, 1H, NHCOCH_2), 4.01 (d, $J_{gem} = 16.9$ Hz, 1H, NHCOCH_2), 3.94 (dd, $J_{5ax,5eq} = 13.4$, $J_{4,5ax} = 2.4$ Hz, 1H, 5ax-H), 3.85 (dt, $J_{5ax,5eq} = 13.6$, $J_{4,5eq} = J_{3,5eq} = 2.0$ Hz, 1H, 5eq-H), 2.10, 1.99, 1.50 (3s, 9H, COCH$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.5 (NH*C*O), 169.6, 168.9, 168.6 (*C*OCH$_3$), 134.1, 132.0, 130.2, 129.0, 129.0, 128.9, 127.4, 126.6, 125.8, 123.5 (*Npth*CH$_2$CO), 74.3 (C-1), 67.9 (C-2), 66.9 (C-3), 66.0 (C-4), 65.1 (C-5), 41.8 (NHCO*C*H$_2$), 21.0, 20.9, 19.9 (CO*C*H$_3$) ppm. HRMS (ESI): calcd for $C_{23}H_{25}NNaO_8$ 466.1472 [M + Na]$^+$; found 466.1457.

3-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-1-thio)-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)propanamide (16a). Following the general procedure, glycosyl amide **16a** was obtained as a colorless syrup. Yield: 53% (134 mg). $R_f = 0.43$; toluene/EtOAc (1 : 2). $[\alpha_D^{22}] = +5.61$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.56 (d, $J_{NH,1} = 9.3$ Hz, 1H, NHCO), 5.44 (dd, $J_{3',4'} = 3.4$, $J_{4',5'} = 1.2$ Hz, 1H, 4′-H), 5.29 (t, $J_{2,3} = J_{3,4} = 9.4$ Hz, 1H, 3-H), 5.28 (t, $J_{NH,1} = J_{1,2} = 9.4$ Hz, 1H, 1-H), 5.24 (t, $J_{1',2'} = J_{2',3'} = 10.1$ Hz, 1H, 2′-H), 5.06 (t, $J_{3,4} = J_{4,5} = 9.8$ Hz, 1H, 4-H), 5.04 (dd, $J_{2',3'} = 10.0$, $J_{3',4'} = 3.5$ Hz, 1H, 3′-H), 4.95 (t, $J_{1,2} = J_{2,3} = 9.6$ Hz, 1H, 2-H), 4.47 (d, $J_{1',2'} = 9.9$ Hz, 1H, 1′-H), 4.30 (dd, $J_{6a,6b} = 12.5$, $J_{5,6a} = 4.3$ Hz, 1H, 6a-H), 4.20 (dd, $J_{6'a,6'b} = 11.5$, $J_{5',6'a} = 6.5$ Hz, 1H, 6′a-H), 4.13 (dd, $J_{6'a,6'b} = 11.2$, $J_{5',6'b} = 6.1$ Hz, 1H, 6′b-H), 4.08 (dd, $J_{6a,6b} = 12.6$, $J_{5,6b} = 2.0$ Hz, 1H, 6b-H), 3.94 (td, $J_{5',6a'} = J_{5',6b'} = 6.2$, $J_{4',5'} = 1.2$ Hz, 1H, 5′-H), 3.82 (ddd, $J_{4,5} = 10.2$, $J_{5,6a} = 4.3$, $J_{5,6b} = 2.2$ Hz, 1H, 5-H), 3.05 (dt, $J_{gem} = 13.5$, $J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 6.7$ Hz, 1H, CH_2S), 2.86 (dt, $J_{gem} = 13.9$, $J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 7.3$ Hz, 1H, CH_2S), 2.58–2.53 (m, 2H, C*H*$_2$CONH), 2.16, 2.08, 2.07, 2.07, 2.05, 2.03, 2.01, 1.98 (8s, 24H, COCH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.4 (NH*C*O), 171.0, 170.7, 170.7, 170.3, 170.1, 170.0, 169.9, 169.7 (*C*OCH$_3$), 84.1 (C-1′), 78.2 (C-1), 75.1 (C-5′), 73.7 (C-5), 73.0 (C-3), 71.9 (C-3′), 70.6 (C-2), 68.2 (C-4), 67.6 (C-4′), 66.8 (C-2′), 61.8 (C-6), 61.7 (C-6′), 37.4 (*C*H$_2$CONH), 25.2 (*C*H$_2$S), 20.9 (×2), 20.9, 20.9, 20.8, 20.7 (×3) (CO*C*H$_3$) ppm. HRMS (ESI): calcd for $C_{31}H_{43}NNaO_{19}S$ 788.2042 [M + Na]$^+$; found 788.2056.

3-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-1-thio)-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl) propanamide (16b). Following the general procedure, glycosyl amide **16b** was obtained as a white solid. M.p. 64.9–66.7 °C. Yield: 57% (144 mg). $R_f = 0.44$; toluene/EtOAc (1 : 2). $[\alpha_D^{20}] = +12.02$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.52 (d, $J_{NH,1} = 9.2$ Hz, 1H, NHCO), 5.44–5.42 (m, 2H, 4-H, 4′-H), 5.25 (t, $J_{NH,1} = J_{1,2} = 9.2$, 1H, 1-H), 5.24 (t, $J_{1',2'} = J_{2',3'} = 10.0$ Hz, 1H, 2′-H), 5.13 (dd, $J_{2,3} = 9.5$, $J_{3,4} = 3.2$ Hz, 1H, 3-H), 5.11 (t, $J_{1,2} = J_{2,3} = 9.3$ Hz, 1H, 2-H), 5.04 (dd, $J_{2',3'} = 10.0$, $J_{3',4'} = 3.3$ Hz, 1H, 3′-H), 4.48 (d, $J_{1',2'} = 9.9$ Hz, 1H, 1′-H), 4.22 (dd, $J_{6a',6b'} = 11.3$, $J_{5',6a'} = 6.4$ Hz, 1H,

6a′-H), 4.11 (dd, $J_{6a',6b'} = 11.4$, $J_{5',6b'} = 6.4$ Hz, 1H, 6b′-H), 4.14–4.07 (m, 2H, 6b-H, 6a-H), 4.03 (td, $J_{5,6a} = J_{5,6b} = 6.6$, $J_{4,5} = 1.1$ Hz, 1H, 5-H), 3.94 (td, $J_{5',6a'} = J_{5',6b'} = 6.4$, $J_{4',5'} = 1.2$ Hz, 1H, 5′-H), 3.03 (dt, $J_{gem} = 13.7$, $J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 6.8$ Hz, 1H, CH_2S), 2.87 (dt, $J_{gem} = 13.7$, $J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 7.3$ Hz, 1H, CH_2S), 2.59–2.50 (m, 2H, CH_2CONH), 2.16, 2.13, 2.07 (×2), 2.06, 2.03, 1.98, 1.98 (8s, 24H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.3 (NH*C*O), 171.3, 170.6, 170.5, 170.3, 170.1 (×2), 169.9, 169.8 (*C*OCH_3), 84.2 (C-1′), 78.5 (C-1), 74.9 (C-5′), 72.5 (C-5), 71.9 (C-3′), 71.0 (C-3), 68.4 (C-2), 67.5 (C-4′), 67.3 (C-4), 66.9 (C-2′), 61.6 (C-6), 61.2 (C-6′), 37.5 (*C*H_2CONH), 25.2 (*C*H_2S), 21.0, 20.9, 20.8, 20.8 (×2), 20.7 (×2), 20.7 ($COCH_3$) ppm. HRMS (ESI): calcd for $C_{31}H_{43}NNaO_{19}S$ 788.2042 $[M + Na]^+$; found 788.2045.

3-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-1-thio)-*N*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl) propanamide (16cβ). Following the general procedure, glycosyl amide **16cβ** was obtained as the main product as a colorless syrup. Yield: 33% (76 mg). R_f = 0.46; toluene/EtOAc (1 : 2). $[\alpha_D^{20}]$ = −5.02 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.63 (d, $J_{NH,1} = 9.2$ Hz, 1H, NHCO), 5.43 (dd, $J_{3',4'} = 3.4$, $J_{4',5'} = 1.1$ Hz, 1H, 4′-H), 5.28 (*t*, $J_{2,3} = J_{3,4} = 9.6$ Hz, 1H, 3-H), 5.23 (*t*, $J_{1',2'} = J_{2',3'} = 10.0$ Hz, 1H, 2′-H), 5.17 (*t*, $J_{NH,1} = 9.3$, $J_{1,2} = 9.5$ Hz, 1H, 1-H), 5.03 (dd, $J_{2',3'} = 10.0$, $J_{3',4'} = 3.3$ Hz, 1H, 3′-H), 4.96 (ddd, $J_{4,5ax} = 10.5$, $J_{3,4} = 9.5$, $J_{4,5eq} = 5.7$ Hz, 1H, 4-H), 4.88 (*t*, $J_{1,2} = J_{2,3} = 9.5$ Hz, 1H, 2-H), 4.47 (d, $J_{1',2'} = 9.9$ Hz, 1H, 1′-H), 4.19 (dd, $J_{6a',6b'} = 11.5$, $J_{5',6a'} = 6.6$ Hz, 1H, 6a′-H), 4.12 (dd, $J_{6a',6b'} = 11.5$, $J_{5',6b'} = 6.0$ Hz, 1H, 6b′-H), 4.05 (dd, $J_{5ax,5eq} = 11.6$, $J_{4,5eq} = 5.7$ Hz, 1H, 5eq-H), 3.93 (td, $J_{5',6a'} = J_{5',6b'} = 6.2$, $J_{4',5'} = 1.1$ Hz, 1H, 5′-H), 3.43 (dd, $J_{5ax,5eq} = 11.6$, $J_{4,5ax} = 10.5$ Hz, 1H, 5ax-H), 3.04 (dt, $J_{gem} = 13.7$, $J_{CH_2S,CH2CONH} = J_{CH_2S,CH_2CONH} = 6.8$ Hz, 1H, CH_2S), 2.85 (dt, $J_{gem} = 14.0$, $J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 7.2$ Hz, 1H, CH_2S), 2.54 (*t*, $J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 7.0$ Hz, 2H, C*H*$_2$CONH), 2.15, 2.07, 2.05, 2.04, 2.02, 2.02, 1.97 (7s, 21H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.6 (NH*C*O), 171.0, 170.7, 170.3, 170.1, 170.0, 169.9, 169.8 (*C*OCH_3), 84.1 (C-1′), 78.7 (C-1), 75.0 (C-5′), 72.6 (C-3), 71.9 (C-3′), 70.8 (C-2), 69.1 (C-4), 67.6 (C-4′), 66.9 (C-2′), 64.6 (C-5), 61.8 (C-6′), 37.4 (*C*H_2CONH), 25.3 (*C*H_2S), 20.9 (×2), 20.9, 20.8 (×2), 20.7, 20.7 ($COCH_3$) ppm. HRMS (ESI): calcd for $C_{28}H_{39}NNaO_{17}S$ 716.1831 $[M + Na]^+$; found 716.1835.

3-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl-1-thio)-*N*-(2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl) propenamide (16cα). The α anomer **16cα** was isolated as a byproduct and it was obtained as a colorless syrup. Yield: 14% (30 mg). R_f = 0.21; toluene/EtOAc (1 : 2). $[\alpha_D^{21}]$ = +1.89 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.77 (d, $J_{NH,1} = 8.9$ Hz, 1H, NHCO), 5.65 (dd, $J_{NH,1} = 8.8$, $J_{1,2} = 2.9$ Hz, 1H, 1-H), 5.44 (dd, $J_{3',4'} = 3.4$, $J_{4',5'} = 1.1$ Hz, 1H, 4′-H), 5.21 (*t*, $J_{1',2'} = J_{2',3'} = 10.0$, 1H, 2′-H), 5.22–5.19 (m, 1H, 3-H), 5.04 (dd, $J_{2',3'} = 10.1$, $J_{3',4'} = 3.4$ Hz, 1H, 3′-H), 4.84 (dd, $J_{2,3} = 5.1$, $J_{1,2} = 2.9$ Hz, 1H, 2-H), 4.76 (br. *q*, $J_{3,4} = J_{4,5ax} = J_{4,5eq} = 4.1$, $J_{2,4} < 1$ Hz, 1H, 4-H), 4.51 (d, $J_{1',2'} = 10.0$ Hz, 1H, 1′-H), 4.33 (dd, $J_{6a',6b'} = 11.6$, $J_{5',6a'} = 7.0$ Hz, 1H, 6a′-H), 4.07 (dd, $J_{6a',6b'} = 11.6$, $J_{5',6b'} = 5.3$ Hz, 1H, 6b′-H), 3.98 (dd, $J_{5ax,5eq} = 12.9$, $J_{4,5ax} = 3.1$ Hz, 1H, 5ax-H), 3.93 (ddd, $J_{5',6a'} = 6.9$, $J_{5',6b'} = 5.4$ Hz, $J_{4',5'} = 1.2$ Hz, 1H, 5′-H), 3.89 (dd, $J_{5ax,5eq} = 13.0$, $J_{4,5eq} = 4.2$ Hz, 1H, 5eq-H), 3.04 (dt, $J_{gem} = 14.2$, $J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 6.5$ Hz, 1H, CH_2S), 2.91 (dt, $J_{gem} = 14.0$, $J_{CH_2S,CH_2CONH} = 6.6$ Hz, 1H, CH_2S), 2.65–2.55 (m, 2H, C*H*$_2$-CONH), 2.16, 2.15, 2.11, 2.08, 2.07, 2.05, 1.98 (7s, 21H, $COCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.4 (NH*C*O), 170.8, 170.3, 170.1, 169.8, 169.7, 169.7, 169.1 (*C*OCH_3), 85.0 (C-1′), 75.2 (C-5′), 74.4 (C-1), 71.8 (C-3′), 68.4 (C-2), 67.6 (C-4′), 67.6 (C-3), 67.0 (C-2′), 66.9 (C-4), 63.9 (C-5), 62.0 (C-6′), 37.4 (*C*H_2-CONH), 26.4 (*C*H_2S), 21.0, 20.9, 20.9 (×2), 20.9, 20.8, 20.7 ($COCH_3$) ppm. HRMS (ESI): calcd for $C_{28}H_{39}NNaO_{17}S$ 716.1831 $[M + Na]^+$; found 716.1850.

General procedure for the *O*-deacetylation of *N*-glycosyl amides 14a–cβ, 15a–cβ, and 16a–cβ. A suspension of *N*-glycosyl amides **14a-cβ**, **15a-cβ**, or **16a-cβ** (0.1 mmol) in a mixture of MeOH/Et_3N/H_2O (4 : 1 : 5, 1.12 mL) was stirred at room temperature. The solid gradually dissolved, and TLC (hexane/EtOAc, 1 : 1 or 1 : 1.5) indicated the complete consumption of the starting material after 3 h. The solution was concentrated, and the residue was dissolved in water (1 mL) and eluted through a column packed with Dowex MR-3C mixed bed ion-exchange resin. The eluate was concentrated and additionally purified by silica gel column chromatography using CH_2Cl_2/CH_3OH (8 : 1 → 4 : 1) for **17a-cβ** and **18a-cβ**; and CH_3CN/H_2O (9 : 1 → 3 : 1) for **19a-cβ**. Evaporation of the solvent afforded the free *N*-glycosylamides, which showed a single spot by TLC. The respective R_f values are given in each individual case.

2-(Phenyl)-*N*-(β-D-glucopyranosyl)acetamide (17a).[14] Following the general procedure, free glycosyl amide **17a** was obtained as a white solid. M.p. 209.6 °C (dec.). Yield: 86% (256 mg). R_f = 0.47, CH_2Cl_2/CH_3OH (4 : 1). $[\alpha_D^{18}]$ = +7.2 (c = 1.0, CH_3OH). ^{1}H NMR (400 MHz, D_2O) δ = 7.44–7.33 (m, 5H, *Ph*CH_2CO), 4.97 (br. d, $J_{1,2} = 9.2$ Hz, 1H, 1-H), 3.87 (br. dd, $J_{6a,6b} = 12.4$, $J_{5,6a} = 1.5$ Hz, 1H, 6a-H), 3.73–3.69 (m, 3H, NHCOC*H*$_2$ and 6b-H), 3.55 (*t*, $J_{2,3} = J_{3,4} = 9.0$ Hz, 1H, 3-H), 3.53–3.49 (m, 1H, 5-H), 3.42 (dd, $J_{4,5} = 9.7$, $J_{3,4} = 9.1$ Hz, 1H, 4-H), 3.41 (*t*, $J_{1,2} = J_{2,3} = 9.2$ Hz, 1H, 2-H) ppm. ^{13}C NMR (100 MHz, D_2O) δ = 175.9 (*C*ONH), 134.5, 129.3, 128.9, 127.4 (*Ph*CH_2CO), 79.4 (C-1), 77.6 (C-5), 76.5 (C-3), 71.8 (C-2), 69.3 (C-4), 60.6 (C-6), 42.2 (NHCOC*H*$_2$Ph) ppm. HRMS (ESI): calcd for $C_{14}H_{19}NNaO_6$ 320.1105 $[M + Na]^+$; found 320.1083.

2-(Phenyl)-*N*-(β-D-galactopyranosyl)acetamide (17b). Following the general procedure, glycosyl amide **17b** was obtained as a white solid. M.p. 204.4 °C (dec.). Yield: 88% (262 mg). R_f = 0.44, CH_2Cl_2/CH_3OH (4 : 1). $[\alpha_D^{19}]$ = +22.5 (c = 1.0, CH_3OH). ^{1}H NMR (400 MHz, D_2O) δ = 7.43–7.33 (m, 5H, *Ph*CH_2CO), 4.91 (d, $J_{1,2} = 8.7$ Hz, 1H, 1-H), 3.96 (br. d, $J_{3,4} = 3.2$ Hz, 1H, 4-H), 3.77–3.74 (m, 1H, 5-H), 3.73–3.68 (m, 5H, 3-H, NHCOCH_2, 6b-H, 6a-H), 3.66 (*t*, $J_{1,2} = J_{2,3} = 8.7$ Hz, 1H, 2-H) ppm. ^{13}C NMR (100 MHz, D_2O) δ = 176.0 (*C*ONH), 134.5, 129.3, 128.9, 127.4 (*Ph*CH_2CO), 79.9 (C-1), 76.7 (C-5), 73.4 (C-3), 69.3 (C-2), 68.7 (C-4), 60.9 (C-6), 42.2 (NHCOCH_2Ph) ppm. HRMS (ESI): calcd for $C_{14}H_{19}NNaO_6$ 320.1105 $[M + Na]^+$; found 320.1109.

2-(Phenyl)-*N*-(β-D-xylopyranosyl)acetamide (17cβ). Following the general procedure, glycosyl amide **17cβ** was obtained as a white solid. M.p. 187.1 °C (des.). Yield: 84% (225 mg). R_f = 0.67, CH_2Cl_2/CH_3OH (4 : 1). $[\alpha_D^{19}]$ = +22.0 (c = 1.0, CH_3OH). ^{1}H NMR (400 MHz, D_2O) δ = 7.39–7.27 (m, 5H, *Ph*CH_2CO), 4.85 (d, $J_{1,2} = 9.0$ Hz, 1H, 1-H), 3.87 (dd, $J_{5ax,5eq} = 11.5$, $J_{4,5eq} = 5.4$ Hz, 1H, 5eq-H), 3.63 (br. s, 2H, NHCOCH_2), 3.57 (ddd, $J_{4,5b} = 10.3$,

$J_{3,4} = 9.3, J_{4,5a} = 5.4$ Hz, 1H, 4-H), 3.44 ($t, J_{2,3} = J_{3,4} = 9.1$ Hz, 1H, 3-H), 3.36 ($t, J_{1,2} = J_{2,3} = 9.0$ Hz, 1H, 2-H), 3.32 ($t, J_{4,5ax} = J_{5ax,5eq} = 11.0$ Hz, 1H, 5ax-H) ppm. ^{13}C NMR (100 MHz, D_2O) $\delta = 175.9$ (*C*ONH), 134.3, 129.2, 128.9, 127.3 (*Ph*CH_2CO), 80.0 (C-1), 76.5 (C-3), 71.6 (C-2), 68.9 (C-4), 66.7 (C-5), 42.1 (NHCO*C*H_2Ph) ppm. HRMS (ESI): calcd for $C_{13}H_{17}NNaO_5$ 290.0999 $[M + Na]^+$; found 290.0994.

2-(Naphthalen-1-yl)-*N*-(β-D-glucopyranosyl)acetamide (18a). Following the general procedure, glycosyl amide **18a** was obtained as a white solid. M.p. 233.3 °C (dec.). Yield: 92% (320 mg). $R_f = 0.49$, CH_2Cl_2/CH_3OH (4 : 1). $[\alpha_D^{19}] = +8.8$ ($c = 1.0$, CH_3OH). ^{1}H NMR (400 MHz, D_2O) $\delta = 8.00$–7.85 (m, 2H, *Npth*CH_2CO), 7.92 (br. d, $J_{ortho} = 7.9$ Hz, 1H, *Npth*CH_2CO), 7.61 (td, $J_{ortho} = J_{ortho} = 6.8, J_{meta} = 1.7$ Hz, 1H, *Npth*CH_2CO), 7.58 (td, $J_{ortho} = J_{ortho} = 6.8, J_{meta} = 1.6$ Hz, 1H, *Npth*CH_2CO), 7.52 (dd, $J_{ortho} = 7.9, J_{ortho} = 7.1$ Hz, 1H, *Npth*CH_2CO), 7.48 (dd, $J_{ortho} = 6.9, J_{meta} = 1.1$ Hz, 1H, *Npth*CH_2CO), 4.97 (d, $J_{1,2} = 9.2$ Hz, 1H, 1-H), 4.20 (d, $J_{gem} = 16.5$ Hz, 1H, NHCOCH_2), 4.15 (d, $J_{gem} = 16.5$ Hz, 1H, NHCOCH_2), 3.84 (dd, $J_{6a,6b} = 12.3, J_{5,6a} = 2.1$ Hz, 1H, 6a-H), 3.70 (dd, $J_{6a,6b} = 12.4, J_{5,6b} = 5.2$ Hz, 1H, 6b-H), 3.52 ($t, J_{2,3} = J_{3,4} = 9.1$ Hz, 1H, 3-H), 3.48 (ddd, $J_{4,5} = 9.7, J_{5,6b} = 5.1, J_{5,6a} = 2.1$ Hz, 1H, 5-H), 3.40 (dd, $J_{3,4} = 9.6, J_{4,5} = 9.1$ Hz, 1H, 4-H), 3.39 ($t, J_{1,2} = J_{2,3} = 9.2$ Hz, 1H, 2-H) ppm. ^{13}C NMR (100 MHz, D_2O) $\delta = 175.8$ (*C*ONH), 133.5, 131.7, 130.5, 128.7, 128.6, 128.2, 126.7, 126.2, 125.8, 123.6 (*Npth*CH_2CO), 79.4 (C-1), 77.5 (C-5), 76.5 (C-3), 71.8 (C-2), 69.2 (C-4), 60.5 (C-6), 39.8 (NHCO*C*H_2) ppm. HRMS (ESI): calcd for $C_{18}H_{21}NNaO_6$ 370.1261 $[M + Na]^+$; found 370.1245.

2-(Naphthalen-1-yl)-*N*-(β-D-galactopyranosyl)acetamide (18b). Following the general procedure, glycosyl amide **18b** was obtained as a white solid. M.p. 211.5 °C (dec.). Yield: 77% (267 mg). $R_f = 0.54$, CH_2Cl_2/CH_3OH (4 : 1). $[\alpha_D^{19}] = +14.1$ ($c = 0.6$, CH_3OH). ^{1}H NMR (400 MHz, D_2O) $\delta = 8.04$–8.00 (m, 2H, *Npth*CH_2CO), 7.96 (dd, $J_{ortho} = 7.9, J_{meta} = 0.8$ Hz, 1H, *Npth*CH_2CO), 7.65 (td, $J_{ortho} = J_{ortho} = 6.7, J_{meta} = 1.7$ Hz, 1H, *Npth*CH_2CO), 7.62 (td, $J_{ortho} = J_{ortho} = 6.8, J_{meta} = 1.6$ Hz, 1H, *Npth*CH_2CO), 7.57 (dd, $J_{ortho} = 7.9, J_{ortho} = 7.1$ Hz, 1H, *Npth*CH_2CO), 7.53 (dd, $J_{ortho} = 7.0, J_{meta} = 1.5$ Hz, 1H, *Npth*CH_2CO), 4.96 (d, $J_{1,2} = 8.6$ Hz, 1H, 1-H), 4.25 (d, $J_{gem} = 16.5$ Hz, 1H, NHCOCH_2), 4.19 (d, $J_{gem} = 16.5$ Hz, 1H, NHCOCH_2), 3.99 (br. d, $J_{3,4} = 3.1$ Hz, 1H, 4-H), 3.79–3.73 (m, 3H, 6b-H, 6a-H, and 5-H), 3.72 (dd, $J_{2,3} = 10.1, J_{3,4} = 3.0$ Hz, 1H, 3-H), 3.67 (dd, $J_{2,3} = 9.6, J_{1,2} = 8.7$ Hz, 1H, 2-H) ppm. ^{13}C NMR (100 MHz, D_2O) $\delta = 178.4$ (*C*ONH), 136.1, 134.3, 133.1, 131.3, 131.2, 130.7, 129.3, 128.8, 128.4, 126.1 (*Npth*CH_2CO), 82.4 (C-1), 79.3 (C-5), 75.9 (C-3), 71.9 (C-2), 71.2 (C-4), 63.5 (C-6), 42.3 (NHCO*C*H_2) ppm. HRMS (ESI): calcd for $C_{18}H_{21}NNaO_6$ 370.1261 $[M + Na]^+$; found 370.1241.

2-(Naphthalen-1-yl)-*N*-(β-D-xylopyranosyl)acetamide (18cβ). Following the general procedure, glycosyl amide **18cβ** was obtained as a white solid. M.p. 223.3 °C (dec.). Yield: 82% (260 mg). $R_f = 0.72$, CH_2Cl_2/CH_3OH (4 : 1). $[\alpha_D^{25}] = +11.64$ ($c = 1.0$, CH_3OH). ^{1}H NMR (400 MHz, D_2O) $\delta = 7.96$–7.89 (m, 2H, *Npth*CH_2CO), 7.88 (dd, $J_{ortho} = 8.0, J_{meta} = 1.1$ Hz, 1H, *Npth*CH_2CO), 7.58–7.52 (m, 2H, *Npth*CH_2CO), 7.48 (dd, $J_{ortho} = 8.1, J_{ortho} = 7.0$ Hz, 1H, *Npth*CH_2CO), 7.43 (dd, $J_{ortho} = 7.0, J_{meta} = 1.1$ Hz, 1H, *Npth*CH_2CO), 4.86 (d, $J_{1,2} = 8.9$ Hz, 1H, 1-H), 4.15 (d, $J_{gem} = 16.6$ Hz, 1H, NHCOCH_2), 4.10 (d, $J_{gem} = 16.5$ Hz, 1H, NHCOCH_2), 3.85 (dd, $J_{5ax,5eq} = 11.5, J_{4,5eq} = 5.3$ Hz, 1H, 5eq-H), 3.56 (ddd, $J_{4,5ax} = 10.6, J_{3,4} = 8.9, J_{4,5eq} = 5.3$ Hz, 1H, 4-H), 3.42 ($t, J_{2,3} = J_{3,4} = 9.0$ Hz, 1H, 3-H), 3.34 ($t, J_{1,2} = J_{2,3} = 9.0$ Hz, 1H, 2-H), 3.29 (dd, $J_{5ax,5eq} = 11.3, J_{4,5ax} = 10.8$ Hz, 1H, 5ax-H) ppm. ^{13}C NMR (100 MHz, D_2O) $\delta = 175.8$ (*C*ONH), 133.4, 131.6, 130.4, 128.7, 128.6, 128.2, 126.7, 126.2, 125.8, 123.4 (*Npth*CH_2CO), 80.0 (C-1), 76.5 (C-3), 71.5 (C-2), 68.9 (C-4), 66.7 (C-5), 39.7 (NHCO*C*H_2) ppm. HRMS (ESI): calcd for $C_{17}H_{19}NNaO_5$ 340.1155 $[M + Na]^+$; found 340.1143.

3-(β-D-Galactopyranosyl-1-thio)-*N*-(β-D-glucopyranosyl) propanamide (19a). Following the standard procedure, glycosyl amide **19a** was obtained as a colorless syrup. Yield: 78% (335 mg). $R_f = 0.22$, BuOH/EtOH/H_2O (10 : 4:4). $[\alpha_D^{25}] = +6.84$ ($c = 0.6$, CH_3OH). ^{1}H NMR (400 MHz, D_2O) $\delta = 4.95$ (d, $J_{1,2} = 9.1$ Hz, 1H, 1-H), 4.48 (d, $J_{1',2'} = 9.7$ Hz, 1H, 1′-H), 3.94 (dd, $J_{3',4'} = 3.4, J_{4',5'} = 0.8$ Hz, 1H, 4′-H), 3.85 (dd, $J_{6a,6b} = 12.4, J_{5,6a} = 2.2$ Hz, 1H, 6a-H), 3.77–3.66 (m, 4H, 6a′-H, 6b′-H, 5′-H, 6b-H), 3.62 (dd, $J_{2',3'} = 9.5, J_{3',4'} = 3.4$ Hz, 1H, 3′-H), 3.52 ($t, J_{1',2'} = J_{2',3'} = 9.5$ Hz, 1H, 2′-H), 3.51 ($t, J_{2,3} = J_{3,4} = 9.1$ Hz, 1H, 3-H), 3.49 (ddd, $J_{4,5} = 9.7, J_{5,6b} = 5.3, J_{5,6a} = 2.2$ Hz, 1H, 5-H), 3.38 (dd, $J_{4,5} = 9.7, J_{3,4} = 9.1$ Hz, 1H, 4-H), 3.36 (dd, $J_{1,2} = J_{2,3} = 9.2$ Hz, 1H, 2-H), 3.02 (dt, $J_{gem} = 13.8, J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 7.2$ Hz, 1H, CH_2S), 2.96 (dt, $J_{gem} = 13.7, J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 6.8$ Hz, 1H, CH_2S), 2.75–2.65 (m, 2H, CH_2CONH) ppm. ^{13}C NMR (100 MHz, D_2O) $\delta = 175.7$ (*C*ONH), 86.1 (C-1′), 79.2 (C-1), 78.9 (C-5′), 77.5 (C-5), 76.4 (C-3), 73.8 (C-3′), 71.7 (C-2), 69.5 (C-2′), 69.2 (C-4), 68.8 (C-4′), 61.1 (C-6′), 60.5 (C-6), 36.4 (*C*H_2CONH), 25.7 (*C*H_2S) ppm. HRMS (ESI): calcd for $C_{15}H_{27}NNaO_{11}S$ 452.1197 $[M + Na]^+$; found 452.1193.

3-(β-D-Galactopyranosyl-1-thio)-*N*-(β-D-galactopyranosyl) propanamide (19b). Following the general procedure, glycosyl amide **19b** was obtained as a colorless syrup. Yield: 76% (326 mg). $R_f = 0.19$, BuOH/EtOH/H_2O (10 : 4:4). $[\alpha_D^{22}] = +4.87$ ($c = 0.8$, CH_3OH). ^{1}H NMR (400 MHz, D_2O) $\delta = 4.89$ (d, $J_{1,2} = 9.0$ Hz, 1H, 1-H), 4.48 (d, $J_{1',2'} = 9.7$ Hz, 1H, 1′-H), 3.94–3.92 (m, 2H, 4-H, 4′-H), 3.74 (dt, $J_{5,6a} = 5.0, J_{5,6b} = J4,5 = 1.0$ Hz, 1H, 5-H), 3.72–3.67 (m, 5H, 6a-H, 6b-H, 5′-H, 6a′-H, 6b′-H), 3.67 (dd, $J_{2,3} = 9.1, J_{3,4} = 3.3$ Hz, 1H, 3-H), 3.61 (dd, $J_{2',3'} = 9.5, J_{3',4'} = 3.4$ Hz, 1H, 3′-H), 3.59 ($t, J_{1,2} = J_{2,3} = 9.1$ Hz, 1H, 2-H), 3.51 ($t, J_{1',2'} = J_{2',3'} = 9.6$ Hz, 1H, 2′-H), 3.03 (dt, $J_{gem} = 14.2, J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 7.2$ Hz, 1H, CH_2S), 2.95 (dt, $J_{gem} = 13.6, J_{CH_2S,CH_2CONH} = J_{CH_2S,CH2CONH} = 6.8$ Hz, 1H, CH_2S), 2.73–2.65 (m, 2H, CH_2CONH) ppm. ^{13}C NMR (100 MHz, D_2O) $\delta = 175.7$ (*C*ONH), 86.0 (C-1′), 79.7 (C-1), 78.9 (C-5′), 76.7 (C-5), 73.8 (C-3′), 73.3 (C-3), 69.5 (C-2′), 69.3 (C-2), 68.8, 68.6 (C-4 and C-4′), 61.1 (C-6′), 60.9 (C-6), 36.4 (*C*H_2CONH), 25.6 (*C*H_2S) ppm. HRMS (ESI): calcd for $C_{15}H_{27}NNaO_{11}S$ 452.1197 $[M + Na]^+$; found 452.1194.

3-(β-D-Galactopyranosyl-1-thio)-*N*-(β-D-xylopyranosyl) propanamide (19cβ). Following the general procedure, glycosyl amide **19cβ** was obtained as a colorless syrup. Yield: 85% (339 mg). $R_f = 0.25$, BuOH/EtOH/H_2O (10 : 4:4). $[\alpha_D^{22}] = +1.09$ ($c = 1.0$, H_2O). ^{1}H NMR (400 MHz, D_2O) $\delta = 4.90$ (d, $J_{1,2} = 9.1$ Hz, 1H, 1-H), 4.51 (d, $J_{1',2'} = 9.7$ Hz, 1H, 1′-H), 3.97 (dd, $J_{3',4'} = 3.4, J_{4',5'} = 0.8$ Hz, 1H, 4′-H), 3.93 (dd, $J_{5ax,5eq} = 11.6, J_{4,5eq} = 5.7$ Hz, 1H, 5eq-H), 3.77–3.71 (m, 3H, 6a′-H, 6b′-H, 5′-H), 3.65 (dd, $J_{2',3'} = 9.6, J_{3',4'} = 3.4$ Hz, 1H, 3′-H), 3.61 (ddd, $J_{4,5ax} = 10.3, J_{3,4} = 9.2, J_{4,5eq} = 5.3$ Hz, 1H, 4-H), 3.55 ($t, J_{1',2'} = J_{2',3'} = 9.6$ Hz, 1H, 2′-H), 3.49 ($t, J_{2,3} = J_{3,4} = 9.1$ Hz, 1H, 3-H), 3.38 ($t, J_{1,2} = J_{2,3} = 9.1$ Hz, 1H, 2-H), 3.37

(dd, $J_{5ax,5eq}$ = 11.6, $J_{4,5ax}$ = 10.4 Hz, 1H, 5ax-H), 3.05 (dt, J_{gem} = 13.9, J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 7.3 Hz, 1H, CH_2S), 2.99 (dt, J_{gem} = 13.9, J_{CH_2S,CH_2CONH} = J_{CH_2S,CH_2CONH} = 6.6 Hz, 1H, CH_2S), 2.77–2.65 (m, 2H, CH_2CONH) ppm. ^{13}C NMR (100 MHz, D_2O) δ = 175.8 (*C*ONH), 86.2 (C-1′), 80.0 (C-1), 79.0 (C-5′), 76.6 (C-3), 73.9 (C-3′), 71.7 (C-2), 69.6 (C-2′), 69.0 (C-4), 68.9 (C-4′), 66.8 (C-5), 61.2 (C-6′), 36.4 (*C*H_2CONH), 25.9 (*C*H_2S) ppm. HRMS (ESI): calcd for $C_{14}H_{25}NNaO_{10}S$ 422.1091 $[M + Na]^+$; found 422.1063.

Inhibition of β-galactosidase from *E. coli* enzymatic assays

Compounds **17b**, **18b**, **19a-cβ** were evaluated as inhibitors against *E. coli* β-galactosidase (grade VIII, Sigma, EC 3.2.1.23, 1019 U mg^{-1} protein). One unit of the enzyme hydrolyzes 1 μmol of *o*-nitrophenyl β-D-galactopyranoside per minute. Thus, the enzyme (0.08 U) was incubated in a solution of *o*-nitrophenyl β-D-galactopyranoside (concentration range: 0.4–4.5 mM) in sodium phosphate buffer (100 mM, pH 7.3, $MgCl_2$ 1.2 mM, 2-mercaptoethanol 130 mM) in the absence or presence of *N*-glycosyl amides. The final volume was adjusted to 0.5 mL, and after incubation at 37 °C for 10 minutes, the enzyme was denatured upon the addition of 0.2 M sodium borate buffer (4.0 mL, pH 10.0). The concentration of the *o*-nitrophenol released was measured by absorption spectroscopy at 410 nm, in the visible region.

Conclusions

β-*N*-glycosyl amides were obtained through a direct sequence from per-*O*-acetyl pyranoses, *via* the intermediate glycosyl azides. Hydrogenation of these compounds to the corresponding glycosyl amine derivatives and subsequent acylation, with carboxylic acids in the presence of DCC, led to the glycosyl amides. Those having the *gluco* or *galacto* configuration were diastereoselectively obtained as the desired β-anomer, while those with *xylo* configuration gave also α-anomers as minor products.

Spectroscopic analysis of the *xylo* derivatives revealed that the amides having α anomeric configuration exclusively populate the $^1C_4$ conformation; in contrast to the β-anomers, which adopt the $^4C_1$ chair. This result was supported by conformational search calculations. Additionally, a similar behavior was observed for the xylopyranosyl amine, since the α-anomer predominantly adopted the $^1C_4$ chair, while the β-anomer exclusively populated the $^4C_1$ chair. These findings are consistent with literature reports[42] describing that anomeric nitrogen substituents preferentially adopt conformations where they are found in equatorial orientation, even at the expense of positioning axially the rest of the substituents. This phenomenon was primarily attributed to the high stabilization generated by the *exo*-anomeric effect and steric factors.

Deprotection of the per-*O*-acetyl-β-*N*-glycosyl amides with *gluco*, *galacto*, or *xylo* configurations provided the compounds with free OH groups in very good yields. Inhibition studies showed that amides containing a D-galactopyranose residue exhibited a moderate inhibitory effect on *E. coli* β-galactosidase. However, it should be noted that this is the first report of *N*-glycosyl amide derivatives exhibiting this activity. These findings are significant as they serve as a starting point for the design and development of future *N*-glycosyl amides with improved inhibition against this enzyme.

Author contributions

Conceptualization and methodology were executed by J. P. C. Synthesis, NMR analysis, and calculations were performed by M. G. T. and J. P. C. The inhibition/kinetic studies were carried out by V. E. M. Funding acquisition, project administration, resources provision, supervision, and validation were made by O. V. and J. P. C. All authors contributed to the writing and revision of the manuscript.

Conflicts of interest

There are no conflicts to declare.

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