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Simple and efficient synthesis of *O*-unprotected glycosyl thiourea and isourea derivatives from glycosylamines

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Abstract—Practical, facile and high-yielding one-pot syntheses of different *O*-unprotected glycopyranosyl thioureas and thioureido bolaamphiphiles (two-step synthesis) and of 2-amino-4,5-dihydro-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]oxazoles (three-step synthesis) from glycopyranosylamines are reported. The method involves the preparation of *O*-unprotected β-D-gluco (and D-galacto)pyranosyl isothiocyanates which are in equilibrium with the corresponding 1,2-cyclic thiocarbamates, coupling with amines to afford glycosyl thioureas and treatment with yellow mercury (II) oxide to give *trans*-fused bicyclic isoureas. A D-*gluco* trehazolin analogue is prepared in this way. In situ transformation of *N*,*N*-dialkyl, *N*′-glucopyranosyl thioureas into the corresponding ureas is also reported.

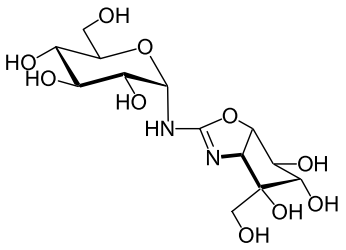
1. Introduction

Isothiocyanates are versatile synthetic intermediates that have been widely used in the synthesis of thiocarbamoyl derivatives. The strong electrophilicity of the NCS group enables these heterocumulenes to take part in addition and cycloaddition reactions, making them extremely useful in the preparation of thioureas and heterocyclic compounds.[1]

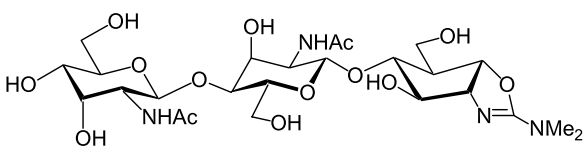
In the last two decades, isothiocyanato derivatives of carbohydrates, mainly *O*-protected glycopyranosyl isothiocyanates have been used to prepare glycoconjugates of biological interest,[2,3] such as thioureidosugars,[4] *N*-nucleosides,[5] *N*-glycopeptides,[6] spiroglycosides,[7] spironucleosides related to (+)-hydantocidin,[8] glycodendrimers and glycoclusters[9] mimetics of natural oligo- and polysaccharides, and bridged thiourea calix-sugars.[10]

Due to the facile reaction between the isothiocyanato and hydroxyl groups, the most readily available isothiocyanato derivatives of sugars are *O*-protected glycosyl isothiocyanates,[2,8] which can be prepared by reaction of *O*-acylated glycosyl halides with silver[11] or potassium thiocyanates,[12] by reaction of per-*O*-acylated aldopyranoses with trimethylsilyl isothiocyanate,[13] by reaction of per-*O*-acylated glycosylamines with thiophosgene,[14] or starting from glycals and potassium thiocyanate in the presence of iodine.[15]

At the same time, 2-amino-2-oxazolines (cyclic isoureas) are biologically active molecules,[16] which are active as imidazoline receptor agonist[17] and as histamine receptor antagonist.[18] They can be used in the treatment of hypertension (e.g. rilmenidine),[19] as appetite suppressant (e.g. aminorex),[20] and to inhibit pheromone synthesis.[21] The isolation of trehazolin[22] **1** and allosamidin[23] **2**, the first natural cyclic isourea derivatives of carbohydrates, with potent activity as threhalase and chitinase inhibitors respectively, has in the last decade encouraged research in the synthesis of trehazolin, allosamidin and related compounds containing modified cyclitol or sugar moieties.[24–26] Syntheses of 2-amino-4,5-dihydro-(1,2-dideoxy-α-D-glucofuranoso)[1,2-*d*]oxazoles from *cis*-fused cyclic sugar thiocarbamates have also been reported.[27]



1 Trehazolin



2 Allosamidin

Recently, we have communicated the preparation of *O*-unprotected glycosyl isothiocyanates and their transformation

Keywords: Isothiocyanates; Thiocarbamates; Thioureas; Isoureas; Thiophosgene; Mercury (II) oxide.
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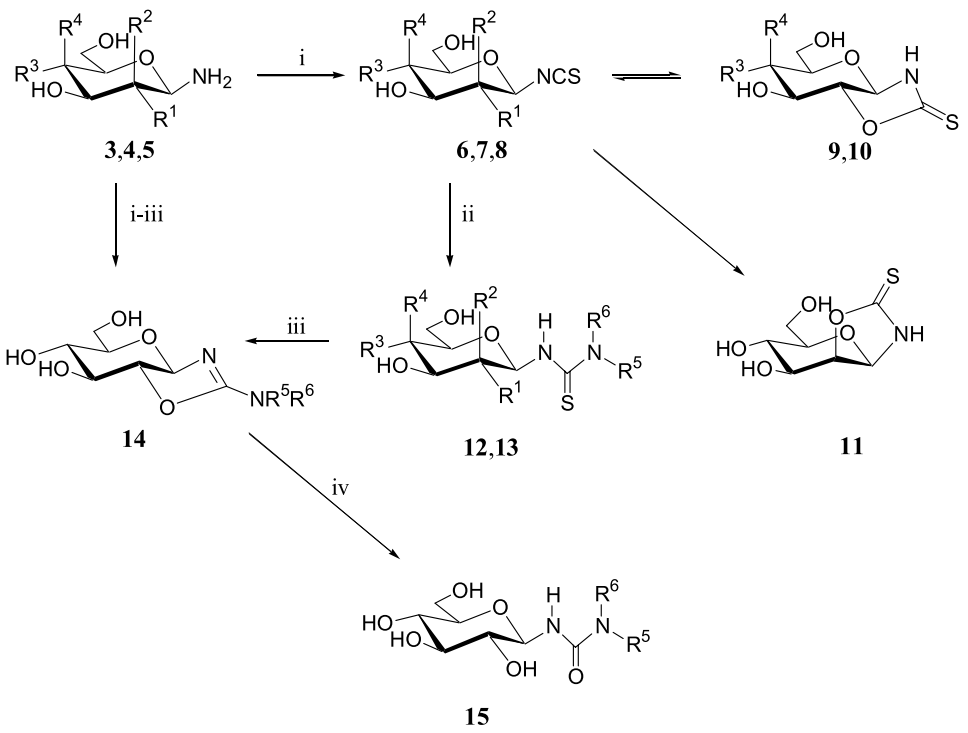


	3,6,12	9	4,7,13	10	5,8
R^1	OH	–	OH	–	H
R^2	H	–	H	–	OH
R^3	OH	OH	H	H	OH
R^4	H	H	OH	OH	H
conf.	D-*gluco*	D-*gluco*	D-*galacto*	D-*galacto*	D-*manno*

Scheme 1. *Reagents and conditions*: (i) $CSCl_2$ (1.2 equiv.), pH 8 ($NaHCO_3/CO_2$), 1:1 water/dioxane, −10 °C, 30 min; (ii) R^5R^6NH (1.2 equiv.), [0.6 equiv. of alkanediamines], pH 9 ($NaHCO_3/CO_2$), rt, 2–5 h; (iii) yellow HgO (3 equiv.), rt, 1–3 h; (iv) yellow HgO (3 equiv.), rt, 2 h.

into glycosyl thioureas[28] and also the preparation of cyclic isourea derivatives.[29] Therein we described the one-pot preparation of the *O*-unprotected glycopyranosyl thioureas **12** and **13** starting from glycopyranosylamines **3** and **4** via intermediate glycopyranosyl isothiocyanates **6** and **7**. The one-pot transformation of the glucosylamine **3** into dihydroglucopyranoso[1,2-*d*]oxazoles **14**, structurally related to trehazolin **1** and allosamidin **2**, was also reported.

2. Results and discussion

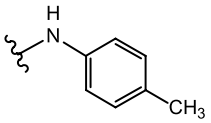
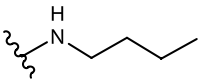
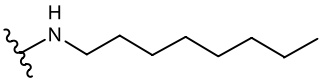
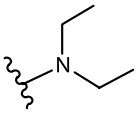
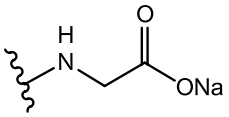
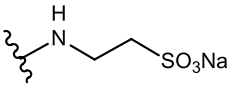
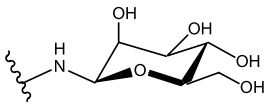
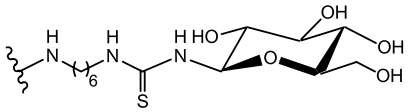
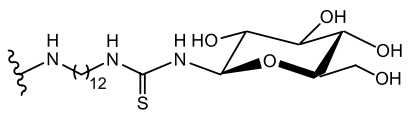
Some data on the reaction of *O*-unprotected glycosyl (glucosyl, maltosyl and lactosyl)amines with thiophosgene to afford the corresponding glycosyl isothiocyanates have been reported.[30] These heterocumulenes were studied as glycosidase inhibitors, and as affinity labels of proteins involved in the transport of carbohydrates through cell membranes, but they were later reported as undergoing ready decomposition under physiological conditions.[31] In the case of β-D-glucopyranosyl isothiocyanate **6**, the synthesis was low-yielding (22%), the characterization was based only on IR spectroscopy, and no further chemistry was reported.[30b]

In our hands, the reaction of β-D-glucopyranosyl amine **3**[32] with thiophosgene leads (Scheme 1) to a mixture of β-D-glucopyranosyl isothiocyanate **6** and 1,2-cyclic thiocarbamate **9** which are in a solvent dependent equilibrium.

The best yield of the mixture of **6** and **9** (64%) was obtained using a buffered ($NaHCO_3/CO_2$, pH 8) suspension in 1:1 water/dioxane, and an excess (20%) of thiophosgene at −10 °C for 40 min. The **6** to **9** ratio, measured by integration of ^1H MNR signals, is 3:2 in D_2O and 1:5 in DMSO-d_6. This behaviour may be explained in terms of the hydrogen bonding of the NH with the solvent, stronger in the case of DMSO than of D_2O.[33]

Similarly, treatment of β-D-galactopyranosyl amine **4**[34] with thiophosgene leads to a mixture of isothiocyanate **7** and thiocarbamate **10** (51%) which were shown to be in a solvent dependent equilibrium that is also shifted towards the thiocarbamate structure in dimethylsulfoxide (1:1 ratio in D_2O and 2:5 in DMSO-d_6). The **6/9** and **7/10** isothiocyanate/thiocarbamate mixtures underwent appreciable decomposition after storage at 0 °C for several days. However, the **6/9** and **7/10** mixtures could be used without further purification in the one-pot synthesis of glucopyranosyl thioureas **12a–k** and galactopyranosyl thioureas **13b** and **13d**, respectively, in good yield (Table 1).

Table 1. Synthesis of thioureas **12**, **13** from β-D-glycopyranosylamines **3**, **4**

Entry	R	**12**, yield (%)	**13**, yield (%)
1		**12a**, 66	—
2		**12b**, 63	**13b**, 53
3		**12c**, 72	—
4		**12d**, 62	**13d**, 69
5		**12e**, 80	—
6		**12f**, 74	—
7		**12g**, 72	—
8		**12h**, 55	—
9		**12i**, 73	—
10		**12j**, 84	—
11		**12k**, 78	—

The reaction of β-D-mannopyranosyl amine[32] **5** with thiophosgene produced the bicyclic thiocarbamate **11**, isolated in a 46% yield. This thiocarbamate is formed through isothiocyanate **8**, but there is no equilibrium between **8** and **11**, as shown by its NMR spectra. Besides that, thiocarbamate **11** did not react with *p*-toluidine as latent isothiocyanate.

The different behaviour of the hydrindane-type systems **9** and **10** on one hand and **11** on the other is due to the differences in the strain of the ring fusion of the tetrahydropyran and the oxazolidine rings. Thiocarbamates **9** and **10** are *trans*-fused bicyclic compounds with unfavourable puckering in the six-member ring due to the decrease of exocyclic equatorial–equatorial angle of the tetrahydropyran unit at the ring junction;[35] the strain of this fusion favours opening with formation of the isothiocyanates **6** and **7**. Compound **11** is a stable *cis*-fused bicyclic system with no tendency to opening, as flattening of the six-membered ring to reduce the exocyclic *cis* torsion angle is relatively facile.

The structures of isothiocyanates **6**, **7** and thiocarbamates

Table 2. Relevant NMR data (δ, ppm; *J*, Hz) for compounds **6**, **7**, **9**–**15**

Compound	Sugar ring					Isothiocyanate, (thio)carbamoyl, isoureido moiety		
	δ H-1	δ H-2	$J_{1,2}$	δ C-1	δ C-2	δ C=X	δ N'–CH_2	δ C-1′[a]
6[b]	4.94	3.43	8.2	86.9	72.5	143.2	—	—
7[b]	4.81	3.63	8.0	87.2	72.9	142.8		
9[b]	5.09	4.08	9.6	88.2	86.8	193.7	—	—
10[b]	4.92	4.35	10.0	89.0	86.1	193.3		
11[b]	5.47	4.98	3.7	82.9	84.7	191.6	—	—
12a[b]	5.42	3.37	8.9	84.6	72.7	183.1	—	—
12b[b]	5.27	3.48	—	84.1	72.7	183.0	45.0	—
12c[c]	5.02	3.14	8.6	83.2	70.1	183.4	43.6	
12d[b]	5.69	3.58	8.8	86.4	73.2	180.0	46.6	
12e[b]	5.62	3.51	8.5	86.6	73.2	180.4	51.4	—
12f[b]	5.33	3.48	8.9	84.2	72.9	183.8	49.2	—
12g[b]	5.29	3.95	9.0	84.0	72.8	183.6	41.1	—
12h[b]	5.49	3.38	9.0	83.9	72.2	—	—	83.9
12i[b]	5.41	3.48	8.9	84.3	72.8	185.0	—	82.4
12j[b]	5.30	3.45	9.0	83.9	72.7	182.0	45.2	83.9
12k[c]	5.02	3.11	8.8	83.3	72.4	183.1	43.6	83.3
13b[b]	5.18	3.75–3.61	—	84.8	70.8	183.1	45.9	—
13d[b]	5.62	3.79	9.0	86.8	70.7	179.9	41.5	—
14a[d]	4.82	3.60	9.6	95.2	85.6	160.0	—	—
14b[b]	4.79	3.54	9.6	94.8	84.6	163.4	41.9	—
14c[d]	4.75	3.49	9.7	96.8	86.7	164.0	43.4	—
14d[d]	4.74	3.48	9.7	97.1	86.8	165.6	43.4	—
14e[d]	4.73	3.49	9.7	96.8	87.2	163.5	47.1	
14h[b]	4.89	3.71	9.8	95.2	86.0	163.0	—	84.3
14j[b]	4.79	3.55	9.5	97.1	86.8	165.6	44.3	97.1
14l[c]	4.59	3.29	9.6	95.9	85.5	161.1	45.4	—
14m[d]	4.69	3.44	9.6	96.9	87.0	164.1	43.9	97.8
15d[b]	4.87	3.42	9.2	81.9	71.9	158.3	41.7	—
15e[b]	4.93	3.48	9.2	83.0	72.9	159.4	46.3	—

[a] C-1′ refers to anomeric carbon of the aglycon part.
[b] In D_2O.
[c] In $(CD_3)_2SO$.
[d] In CD_3OD.

9–**11** were supported on spectroscopic data (Table 2). The most significant difference in the NMR spectra of isothiocyanates **6**, **7** and thiocarbamates **9**–**11** was the ^{13}C chemical shift on the C=S group, which resonated roughly at 143 ppm for **6** and **7**, and about 191–194 ppm for **9**–**11** in agreement with reported data for related isothiocyanato sugars[36] and five-membered thiocarbamate derivatives.[7]

Reaction of the equilibrium mixtures **6/9** and **7/10** in the flask where they were formed, with *p*-tolyl or alkyl primary amines, diethylamine, piperidine, sodium salts of amino-acids glycine and taurine, and *O*-unprotected D-gluco-pyranosyl and D-mannopyranosyl amines afforded the corresponding glycosyl or diglycosylthioureas **12a**–**i**, **13b** and **13d** in moderate to high yields. Similarly, the bola-amphiphiles[37,†] **12j** and **12k** were obtained from **6/9** and 1,6- or 1,12-diamino alkanes, respectively. Thioureas derived from *p*-tolyl, *n*-butyl, *n*-octyl, diethyl amines and piperidine were purified by silica gel column chromatography, whereas the more polar thioureas were isolated by gel filtration chromatography.

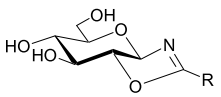
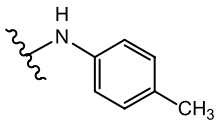
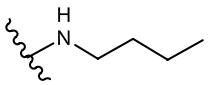
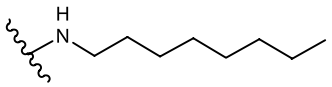
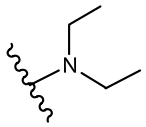
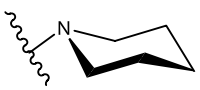
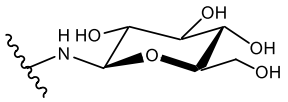
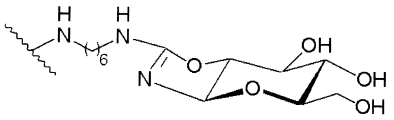
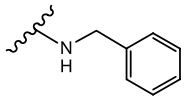
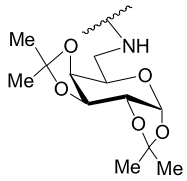
The widely used methodology for the synthesis of glycosyl thioureas involves the coupling of *O*-acylated glycosyl isothiocyanates with amines or aminosugars followed by Zemplen deacetylation.[2,5] However, this reaction has been found to be occasionally unsuccessful or low yielding.[2] In addition, an unexpected base-catalysed anomerization reaction for α and β-D-mannopyranosyl thioureido derivatives has been described upon Zemplen deacetylation.[38] This result contrasts with the preparation of **12i**, which did not show anomerization.

Structures **12** and **13** were supported by analytical and spectroscopic data (Table 2). The chemical shift for the resonance of the C=S group was 180–183 ppm, a value close to that described for *O*-protected acyclic[4] and cyclic[14] glycosylthioureas. The anomeric proton of the D-gluco (**12a**–**k**) and D-galactopyranosyl thioureas **13** resonated in the range 5.0–5.7 ppm, whereas the signal for the corresponding carbon (C-1) was in the range 83–87 ppm in accordance with the presence of a non-strained glycopyranosyl ring in the $^4C_1$ conformation;[39] this conclusion is also supported on the values of the vicinal coupling constants.

The one-pot three-step treatment of β-D-glucopyranosyl-amine **3** successively with thiophosgene (1:1 water/dioxane buffered with $NaHCO_3/CO_2$), then with an amine (*p*-tolyl, *n*-butyl, *n*-octyl, diethylamine, piperidine, 1,6-diamino-hexane, benzylamino, and 6-amino-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose,[40]) and finally with yellow mercury (II) oxide (3 equiv., 1–3 h, rt), yielded the cyclic isourea derivatives **14** (Table 3) in good yields, 50–70% for the three steps (Scheme 1). The trehazolin analogue

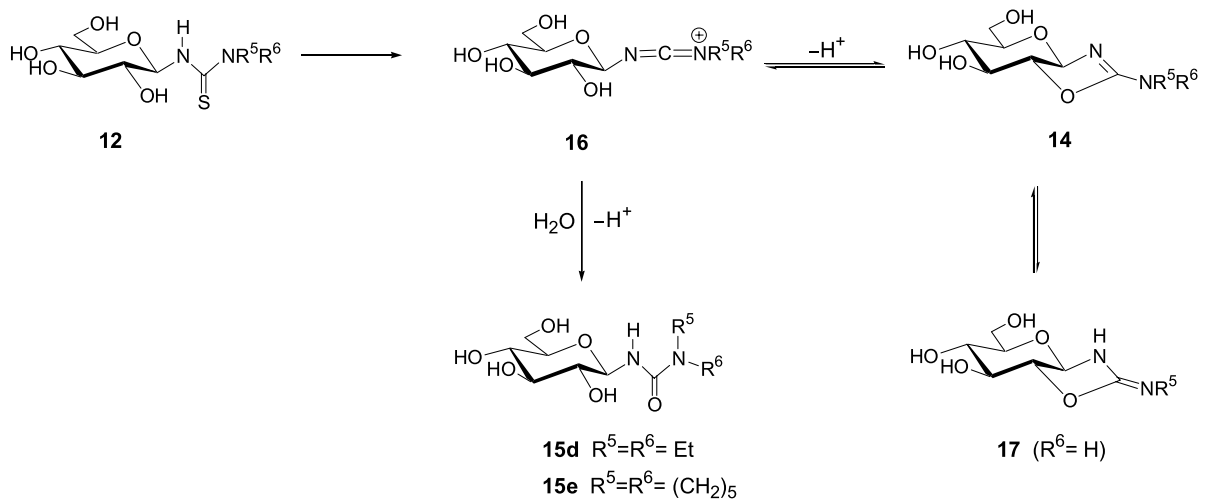
† A bolaamphiphile is defined as a molecule in which two or more hydrophilic groups are connected by one or more hydrophobic chains.

Table 3. Synthesis of cyclic isoureas **14** from β-D-glucopyranosylamine **3** or from β-D-glucopyranosyl thioureas **12**

Entry	R		
		Yield (%)[a]	Yield (%)[b]
1		**14a**, 69	94
2		**14b**, 67	—
3		**14c**, 50	75
4		**14d**, 70	—
5		**14e**, 47	—
6		**14h**, —	89
7		**14j**, 58	—
8		**14l**, 57	—
9		**14m**, 59	—

[a] Isolated yields from **3**.
[b] Isolated yields from **12**.

14h was prepared in a 89% yield starting from the isolated symmetrical *N*,*N*′-bis(β-D-glucopyranosyl) thiourea **12h** by treatment with mercury (II) oxide in 1:1 water/dioxane at rt. Similarly, the *p*-tolyl **14a**, *n*-octyl **14c** derivatives were also obtained from the corresponding isolated thioureas (**12a** and **12c**, respectively) in a 94 and 75% yield using methanol as solvent. Synthesis of **14h** by hydrogenolysis of the derivative of **14h** tetra-*O*-benzylated in the glucopyranose unit has previously been reported by Shiozaki.[41] The reported hydrogenolysis with $Pd(OH)_2$-on-charcoal gave



Scheme 2. Proposed mechanism for the transformation of *N*,*N*-dialkylisoureas into ureas.

an inseparable mixture of **14h** (17%) and *N*,*N*′-bis(β-D-glucopyranosyl)urea (32%).

The isourea derivatives **14** were purified by column chromatography on silica gel, except bolaamphiphile **14j** that was crystallized from ethanol. Attempts to prepare more polar bicyclic isoureas using glycine or taurine as amino compounds were unsuccessful as extensive decomposition took place during the purification by gel filtration chromatography, although the NMR spectra showed the expected isoureas as the major compounds.

Previous results showed that isolated partially *O*-protected sugar thioureas could be cyclodesulfurated to give cyclic isoureas, using freshly prepared dried mercury oxide[42,43] in dried solvents, such as THF,[43] MeCN,[44] Et_2O/Me_2CO,[45] $EtOH/Me_2CO$[42] or using 2-chloro-3-ethylbenzoxazolium tetrafluoroborate in dried MeCN under nitrogen.[41] Our method is experimentally easier as it does not require the isolation of thioureas, and commercial yellow HgO in aqueous dioxane can be used.

The NMR spectra of cyclic isoureas **14** (Table 2) showed significant downfield shifts in the signals of the resonances of C-1 ($\Delta\delta\sim$10 ppm) and C-2 ($\Delta\delta\sim$13 ppm) whereas the resonances for H-1 had a shielding of 0.5–1 ppm, when they were compared with the corresponding signals for the parent thioureas. The $J_{1,2}$ value for **14a**–**m** was 9.5–9.9 Hz, higher than this value for thioureas **12a**–**k** (8.5–9.0 Hz); this might indicate that the pyranoid ring in the *trans*-fused bicyclic compounds is more puckered than that ring in the glycopyranosyl thioureas. Similar behaviour can be observed comparing the *trans*-fused bicyclic thiocarbamates **9** and **10** ($J_{1,2}$=9.6, 10.0 Hz, respectively) with the isothiocyanates **6** and **7** ($J_{1,2}$=8.2, 8.0 Hz, respectively). The chemical shift for the isourea quaternary carbon atom in **14a**–**m** was 160–166 ppm, a value in agreement with that reported for trehazolin and other isourea derivatives.[44]

In situ treatment of crude *N*,*N*-diethyl thiourea **12d** with 3.0 equiv. of yellow HgO for 2 h at rt gave **14d** (70% yield from **3**) together with the glucopyranosyl urea **15d** (18% yield), which was also obtained from **3** using 6.0 equiv of HgO for 4 h (3.0 equiv. each 2 h) in the cyclodesulfurization step (85% yield for the four steps). Under the same conditions piperidine-derived isourea **14e** was not transformed into the corresponding urea. This transformation was achieved in low yield (33%) after 3 months using water as solvent. Attempts at similar transformations involving *N*′-monosubstituted isoureas **14a** and **14b** were unsuccessful, as no evolution from the corresponding isoureas was observed. Relevant NMR data of ureas **15** are included in Table 2. The presence of the urea functional group was confirmed by the characteristic ^{13}C resonance of the carbonyl group (δ 158–159 ppm).[46]

A carbodiimide has been proposed[47] as intermediate in the transformation of thioureas into isourea derivatives; *O*-protected *N*-glycosyl thioureas have been desulfurated with HgO in $CHCl_3$/water to give glycopyranosyl carbodiimides,[48] and desulfuration of sugar derived thioureas with HgO in MeCN/water to give ureas has been reported.[25d] We suggest that the isourea derivatives **14** might be formed via cation **16** (Scheme 2), which undergoes the nucleophilic attack of the *trans* OH-2 to give the isourea derivatives **14**, faster than the attack of H_2O to give ureas **15**. In the case of *N*,*N*-disubstituted thioureas, the positive charge of **16** is stabilized by the two alkyl groups on the nitrogen atom, which provokes the formation of isoureas **14d** and **14e** to be reversible. The attack of H_2O on **16** produces glucosyl ureas **15d**–**e** in an irreversible way. The change from sp^3 hybridized piperidine nitrogen atom to sp^2 for the transformation of **14e** into the intermediate cation **16e** implies a disfavoured strain energy change compared with the acyclic *N*,*N*-diethyl analogues,[35] which might be responsible for the slow formation of urea **15e**.

No presence of the tautomeric tetrahydrooxazole structure **17** was detected by NMR for isoureas **14** in solution, the 2-amino-2-oxazoline **14** being the only possible tautomer for isoureas **14d** and **14e**. As the chemical shifts and coupling constants exhibited by isoureas **14a**–**m** are very close to each other, we can conclude that all of them exist in the 2-amino-2-oxazoline form.

In conclusion, we report expeditious one-pot synthesis in a

buffered aqueous medium of *O*-unprotected glycosyl thioureas (two steps) and dihydroglucopyranoso[1,2-*d*] oxazoles (three steps) starting from easily available β-D-glycopyranosylamines. The *N*/*O* protection–deprotection steps of other described methods to prepare glycosylthioureas, thioureylene oligosaccharides[2] and bolaamphiphiles[49] are avoided. In the case of bicyclic isourea derivatives, not only are the protection–deprotection steps avoided but also we prove that the cyclodesulfuration of the glycosyl thiourea with yellow HgO can be carried out in aqueous media.

3. Experimental

3.1. General procedures

Melting points were recorded on an Electrothermal apparatus and are uncorrected, optical rotations were measured with a Perkin–Elmer 241 polarimeter, and IR spectra (KBr disks) were obtained with an FT-IR Bomem MB-120 spectrophotometer. ^{1}H (300 and 500 MHz) and ^{13}C (75.5 and 125.7 MHz) NMR spectra were recorded on Bruker AMX-300 and AMX-500 spectrometers. The assignments of ^{1}H and ^{13}C signals were confirmed by homonuclear COSY and heteronuclear 2D correlated spectra, respectively. Mass spectra were recorded on Kratos MS 80 RFA and Micromass AutoSpeQ mass spectrometers. TLC was performed on aluminium pre-coated sheets (E. Merck Silica Gel 60 F_{254}); spots were visualized by UV light, by charring with 10% H_2SO_4 in EtOH. Column chromatography was performed using E. Merck Silica Gel 60 (40–63 μm). Microanalysis were performed at the 'Instituto de Investigaciones Químicas', Seville, Spain.

3.1.1. β-D-Glucopyranosyl isothiocyanate (6) and (1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazolidine-2-thione (9). To a suspension of $NaHCO_3$ (281 mg, 3.35 mmol) in 1:1 H_2O/dioxane (5 mL) saturated with CO_2 was added β-D-glucopyranosylamine (250 mg, 1.40 mmol) and thiophosgene (0.13 mL, 1.68 mmol; 1.2 equiv.). The mixture was stirred at −10 °C for 40 min and then it was concentrated to dryness. The residue was dissolved in H_2O (25 mL) and washed with CH_2Cl_2 (3×25 mL). The aqueous layer was concentrated to dryness and the residue was triturated with EtOH and the ethanolic solution was concentrated to dryness and purified by column chromatography (5:1 CH_2Cl_2/MeOH) to give a mixture of **6** and **9** (3:2 ratio in D_2O) together with a small amount of unknown products (198 mg, 64%). R_f=0.39 for both compounds (5:1 CH_2Cl_2/MeOH); IR: ν_{max} 3335, 2027, 1750, 1520, 1364, 1250 cm^{-1}; ^{1}H NMR (500 MHz, D_2O) compound **6**: Table 2 and δ 3.85 (dd, 1H, $J_{5,6a}$=2.3 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.69 (dd, 1H, $J_{5,6b}$=5.6 Hz, H-6b), 3.48 (m, 2H, $J_{2,3}$=8.2 Hz, $J_{3,4}$=8.8 Hz, $J_{4,5}$=8.8 Hz, H-3, H-5), 3.39 (dd, 1H, H-4); compound **9**: Table 2 and δ 4.07–4.09 (m, 2H, H-2, H-3), 3.89 (dd, 1H, $J_{5,6a}$=2.4 Hz, $J_{6a,6b}$=12.5 Hz, H-6a), 3.76 (dd, 1H, $J_{5,6b}$=5.5 Hz, H-6b), 3.66 (ddd, 1H, $J_{4,5}$=8.8 Hz, H-5), 3.50 (dd, 1H, H-4); ^{13}C NMR (127.5 MHz, D_2O) compound **6**: Table 2 and δ 79.2 (C-5), 76.8 (C-3), 70.3 (C-4), 61.6 (C-6); compound **9**: Table 2 and δ 82.2 (C-5), 75.4 (C-4) 74.0 (C-3), 61.6 (C-6); EI-MS *m*/*z* 221 ([M]$^+$, 100%); HREI-MS, *m*/*z* calcd for [M]$^+$ $C_7H_{11}NO_5S$: 221.0358, found: 221.0356.

3.1.2. β-D-Galactopyranosyl isothiocyanate (7) and (1,2-dideoxy-β-D-galactopyranoso)[1,2-*d*]-1,3-oxazolidine-2-thione (10). A suspension of $NaHCO_3$ (281 mg, 3.35 mmol) in 1:1 H_2O/dioxane (5 mL) saturated with CO_2 containing β-D-galactopyranosilamine (250 mg, 1.40 mmol) was treated with thiophosgene (0.13 mL, 1.68 mmol; 1.2 equiv.) as described in Section 3.3.1 to give a mixture of **7** and **10** (1:1 ratio in D_2O) together with a small amount of unknown products (158 mg, 51%). R_f=0.33 for both compounds (5:1 CH_2Cl_2/MeOH); IR: ν_{max} 3368, 2060, 1647, 1364, 1115 cm^{-1}; ^{1}H NMR (500 MHz, D_2O) compound **7**: Table 2 and δ 3.88 (d, 1H, $J_{3,4}$=3.0 Hz, $J_{4,5}$=~0.0 Hz, H-4), 3.70–3.65 (m, 3H, H-5, H-6a, H-6b), 3.59 (dd, 1H, $J_{2,3}$=10.5 Hz, H-3); compound **10**: Table 2 and δ 4.21 (dd, 1H, $J_{2,3}$=11.0 Hz, $J_{3,4}$=3.5 Hz, H-3), 4.05 (dd, 1H, $J_{4,5}$=1.0 Hz, H-4), 3.85 (ddd, 1H, $J_{5,6a}$=7.0 Hz, $J_{5,6b}$=4.5 Hz, H-5), 3.80 (dd, 1H, $J_{6a,6b}$=12.0 Hz, H-6a), 3.76 (dd, 1H, H-6b); ^{13}C NMR (127.5 MHz, D_2O) compound **7**: Table 2 and δ 79.6 (C-4), 78.5 (C-5), 73.6 (C-3), 62.0 (C-6); compound **10**: Table 2 and δ 81.9 (C-5), 71.1 (C-3), 70.7 (C-4), 61.8 (C-6); CI-MS *m*/*z* 222 ([M+H]$^+$, 100%); HRCI-MS *m*/*z* calcd for [M+H]$^+$ $C_7H_{12}NO_5S$: 222.0436, found: 222.0436.

3.2. General methods for the synthesis of β-D-glycopyranosyl thioureas 12 and 13

To a suspension of $NaHCO_3$ (281 mg, 3.35 mmol) in 1:1 H_2O/dioxane (5 mL) saturated with CO_2 was added a β-D-glycopyranosilamine (250 mg, 1.40 mmol) and thiophosgene (0.13 mL, 1.68 mmol; 1.2 equiv.). The mixture was stirred at −10 °C for 40 min, then an amine (1.68 mmol, 1.2 equiv.) was added (in the case of α,ω-alkanediamines 0.84 mmol were used) and the mixture was stirred for 3–6 h at rt until TLC showed disappearance of the isothiocyanate **6**. The mixture was concentrated to dryness and the residue was purified by silica gel column chromatography, preparative TLC or by gel-filtration chromatography, as indicated in each case. The following compounds were prepared by this method.

3.2.1. *N*-(β-D-Glucopyranosyl)-*N'*-(*p*-methylphenyl) thiourea (12a). Purification by column chromatography (CH_2Cl_2→10:1 CH_2Cl_2/MeOH) gave **12a**: 301 mg, 66%. R_f=0.32 (5:1 CH_2Cl_2/MeOH); recrystallization from EtOH/H_2O gave material which shrunk at 98–101 °C and melted at 132–136 °C (dec.); $[\alpha]_D^{25}$ −34° (*c* 1.0, H_2O); IR: ν_{max} 3445, 3327, 1586, 1522, 878, 820, 727 cm^{-1}; ^{1}H NMR (300 MHz, D_2O, 60 °C) Table 2 and δ 7.15–7.26 (m, 4H, Ar-H), 3.83 (dd, 1H, $J_{5,6a}$=2.3 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.67 (dd, 1H, $J_{5,6b}$=5.2 Hz, H-6b), 3.49 (ddd, 1H, $J_{4,5}$=9.7 Hz, H-5), 3.48 (t, 1H, $J_{2,3}$=9.1 Hz, $J_{3,4}$=9.0 Hz, H-3), 3.35 (t, 1H, H-4);^{13}C NMR (75.5 MHz, D_2O, 60 °C) Table 2 and δ 138.8, 134.8, 130.6, 126.9 (Ar), 78.0 (C-5), 77.2 (C-3), 70.0 (C-4), 61.4 (C-6), 20,7 (CH_3); FAB-MS *m*/*z* 351 ([M+Na]$^+$, 100%). Anal. calcd for $C_{14}H_{20}N_2O_5S{\cdot}1/2H_2O$: C, 49.84; H, 6.27; N, 8.30, found: C, 49.63; H, 6.33; N, 8.38.

3.2.2. *N*-Butyl-*N'*-(β-D-glucopyranosyl)thiourea (12b).

Purification by column chromatography (CH_2Cl_2→10:1 CH_2Cl_2/MeOH) gave **12b**: 261 mg, 63%. R_f=0.23 (5:1 CH_2Cl_2/MeOH); crystallization from EtOH gave material which shrunk at 68–72 °C and melted at 102–104 °C (dec.) (from EtOH); $[\alpha]_D^{30}$ −27° (*c* 1.0, H_2O); IR: ν_{max} 3453, 2924, 2872, 1692, 1562, 1352 cm^{-1}; ^1H NMR (300 MHz, D_2O, 60 °C) Table 2 and δ 3.84 (dd, 1H, $J_{5,6a}$=2.2 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.68 (dd, 1H, $J_{5,6b}$=5.2 Hz, H-6b), 3.52 (t, 1H, $J_{2,3}$=8.9 Hz, $J_{3,4}$=8.9 Hz, H-3), 3.48 (ddd, 1H, $J_{4,5}$=9.2 Hz, H-5), 3.52–3.35 (m, 3H, H-2, CH_2), 3.38 (t, 1H, H-4), 1.54 (m, 2H, *J*=7.4 Hz, CH_2), 1.31 (m, 2H, CH_2), 0.86 (t, 3H, CH_3); ^{13}C NMR (75.5 MHz, D_2O, 60 °C) Table 2 and δ 77.9 (C-5) 77.2 (C-3), 70.1 (C-4), 61.4 (C-6), 30.7 ($CH_2\beta$), 19.9 ($CH_2\gamma$), 13.5 (CH_3); FAB-MS *m/z* 317 ($[M+Na]^+$, 100%). Anal. calcd for: $C_{11}H_{22}N_2O_5S\cdot 1/2EtOH$, C, 45.41; H, 7.94; N, 8.82, found: C, 45.55; H, 7.74; N, 8.80.

3.2.3. *N*-(β-D-Glucopyranosyl)-*N′*-octylthiourea (12c). Purification by column chromatography (CH_2Cl_2→10:1 CH_2Cl_2/MeOH) gave **12c**: 353 mg, 72%. R_f=0.20 (5:1 CH_2Cl_2/MeOH); mp 170–172 °C (dec.) from EtOH/H_2O; $[\alpha]_D^{28}$ −17° (*c* 1.0, MeOH); IR: ν_{max} 3298, 2922, 2855, 1564, 1348, 1074 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6, 90 °C) Table 2 and δ 7.49 (d, 1H, $J_{NH,H-1}$=8.2 Hz, NH), 7.42 (t, 1H, J_{NH,CH_2}=5.1 Hz, NH′), 4.64–4.55 (m, 3H, 3OH), 4.02 (m, 1H, OH-6), 3.65 (m, 1H, $J_{6a,6b}$=11.6 Hz, H-6a), 3.56 (m, 1H, H-6b), 3.41 (m, 1H, *J*=6.9 Hz, $CH_2\alpha$), 3.28 (t, 1H, $J_{2,3}$=8.4 Hz, $J_{3,4}$=8.4 Hz, H-3), 3.21–3.11 (m, 1H, H-5), 3.11 (t, 1H, $J_{4,5}$=8.8 Hz, H-4), 1.51 (m, 2H, $CH_2\beta$), 1.28 (m, 10H, $5CH_2$), 0.86 (t, 3H, CH_3); ^{13}C NMR (75.5 MHz, DMSO-d_6, 90 °C) Table 2 and δ 77.5 (C-5), 77.2 (C-3), 72.5 (C-4), 60.9 (C-6), 30.7, 28.2, 28.1, 28.0, 25.9, 21.5, 13.2 (*n*-octyl); FAB-MS *m/z* 373 ($[M+Na]^+$, 100%). Anal. calcd for: $C_{15}H_{32}N_2O_6S\cdot H_2O$: C, 48.89; H, 8.75; N, 7.60, found: C, 49.08; H, 8.61; N, 7.69.

3.2.4. *N,N*-Diethyl-*N′*-(β-D-glucopyranosyl)thiourea (12d). Purification by preparative TLC (5:1 CH_2Cl_2/MeOH, 2 elutions) gave **12d**: 255 mg, 62% as an amorphous solid. R_f=0.23 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{25}$ −8.5° (*c* 1.2, H_2O); IR: ν_{max} 3441, 2932, 1533, 1354, 1279, 1071 cm^{-1}; ^1H NMR (500 MHz, D_2O) Table 2 and δ 3.87 (dd, 1H, $J_{5,6a}$=2.2 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.76–3.63 (m, 4H, *J*=7.0 Hz, $2CH_2$), 3.72 (dd, 1H, $J_{5,6b}$=5.2 Hz, H-6b), 3.55 (t, 1H, $J_{2,3}$=9.0 Hz, $J_{3,4}$=9.0 Hz, H-3), 3.51 (ddd, 1H, $J_{4,5}$=9.6 Hz, H-5), 3.41 (dd, 1H, H-4), 1.18 (t, 6H, $2CH_3$); ^{13}C NMR (125.7 MHz, D_2O) Table 2 and δ 78.6 (C-5), 78.1 (C-3), 70.6 (C-4), 61.9 (C-6), 12.8 ($2CH_3$); CI-MS *m/z* 295 ($[M+H]^+$, 1%); HRCI-MS: *m/z* calcd for $[M+H]^+$ $C_{11}H_{23}N_2O_5S$: 295.1328, found: 295.1329. Anal. calcd for $C_{11}H_{22}N_2O_5S\cdot H_2O$: C, 49.29; H, 7.74; N, 8.97, found: C, 42.40; H, 7.74; N, 9.26.

3.2.5. *N*-[(β-D-Glucopyranosyl)thiocarbamoyl]piperidine (12e). Purification by column chromatography (CH_2Cl_2→5:1 CH_2Cl_2/MeOH) gave **12e**: 344 mg, 80% as a syrup. R_f=0.25 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{26}$ −34° (*c* 1.0, H_2O); IR: ν_{max} 3368, 2930, 2864, 1755, 1564, 1439, 1329, 1252, 1080, 1040, 880 cm^{-1}; ^1H NMR (500 MHz, D_2O) Table 2 and δ 3.84 (dd, 1H, $J_{5,6a}$=2.0 Hz, $J_{6a,6b}$=12.5 Hz, H-6a), 3.81 (m, 4H, $2CH_2$), 3.70 (dd, 1H, $J_{5,6b}$=5.0 Hz, H-6b), 3.51 (m, 1H, $J_{3,4}$=9.0 Hz, H-3), 3.45 (m, 1H, $J_{4,5}$=9.3 Hz, H-5), 3.38 (t, 1H, H-4), 1.64 (m, 2H, CH_2), 1.57 (m, 4H, $2CH_2$); ^{13}C NMR (125.7 MHz, D_2O) Table 2 and δ 78.6 (C-5), 77.9 (C-3), 70.6 (C-4), 61.9 (C-6), 26.5, 24.9 (CH_2). EI-MS *m/z* 306 ($[M]^+$, 3%); HREI-MS *m/z* calcd for $[M]^+$ $C_{12}H_{23}N_2O_5S$: 306.1294, found: 306.1246.

3.2.6. Sodium [3-(β-D-glucopyranosyl)thioureido]acetate (12f). Purification by gel filtration chromatography gave **12f**: 330 mg, 74% as a syrup. R_f=0.23 (3:2:1 EtOAc/EtOH/H_2O; $[\alpha]_D^{24}$ −32° (*c* 0.7, H_2O); IR: ν_{max} 3362, 1649, 1541, 1516, 1366, 1127, 1013, 629 cm^{-1}; ^1H NMR (300 MHz, D_2O, 60 °C) Table 2 and δ 4.06 (m, 2H, CH_2), 3.88 (dd, 1H, $J_{5,6a}$=2.2 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.72 (dd, 1H, $J_{5,6b}$=5.0 Hz, H-6b), 3.57 (t, 1H, $J_{2,3}$=8.9 Hz, $J_{3,4}$=8.9 Hz, H-3), 3.53 (ddd, $J_{4,5}$=9.4 Hz, H-5), 3.43(t, 1H, H-4); ^{13}C NMR (127.5 MHz, D_2O) Table 2 and δ 177.4 (C═O), 78.0 (C-5), 77.3 (C-3), 70.1 (C-4), 61.4 (C-6); FAB-MS *m/z* 341 ($[M+Na]^+$, 23%); HRFABMS *m/z* calcd for $[M+Na]^+$ $C_9H_{15}N_2Na_2O_7S$: 341.0395, found: 341.0399.

3.2.7. Sodium 2-[3-(β-D-glucopyranosyl)thioureido]ethane sulfonate (12g). Purification by gel filtration chromatography gave **12g**: 371 mg, 72% as a syrup. R_f=0.24 (3:2:1 EtOAc/EtOH/H_2O); $[\alpha]_D^{28}$ −23° (*c* 1.4, H_2O); IR: ν_{max} 3298, 3050, 2922, 1655, 1566, 1437, 1362, 1165, 1040, 991 cm^{-1}; ^1H NMR (300 MHz, D_2O, 60 °C) Table 2 and δ 3.95 (m, 2H, *J*=6.5 Hz, CH_2N), 3.91 (dd, 1H, $J_{5,6a}$=2.3 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.75 (dd, 1H, $J_{5,6b}$=5.2 Hz, H-6b), 3.58 (t, 1H, $J_{2,3}$=9.0 Hz, $J_{3,4}$=8.9 Hz, H-3), 3.56 (ddd, 1H, $J_{4,5}$=9.5 Hz, H-5), 3.45 (t, 1H, H-4), 3.21 (t, 2H, CH_2S); ^{13}C NMR (75.5 MHz, D_2O) Table 2 and δ 78.1 (C-5), 77.3 (C-3), 70.1 (C-4), 61.4 (C-6), 50.2 (CH_2S); FAB-MS *m/z* 391 ($[M+Na]^+$, 100%), 759 ($[2M+Na]^+$, 13%); HRFAB-MS *m/z* calcd for $[M+Na]^+$ $C_9H_{17}N_2Na_2O_8S_2$: 391.0222, found: 391.0227.

3.2.8. *N,N′*-Bis(β-D-glucopyranosyl)thiourea (12h). Purification by gel filtration chromatography gave **12h**: 294 mg, 53% as a syrup. R_f=0.38 (3:2:1 EtOAc/EtOH/H_2O); $[\alpha]_D^{24}$ −32° (*c* 0.7, H_2O); IR: ν_{max} 3318, 2899, 1545, 1424, 1364, 1101, 1072 cm^{-1}; ^1H NMR (300 MHz, D_2O) Table 2 and δ 3.84 (dd, 1H, $J_{5,6a}$=2.1 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.69 (dd, 1H, $J_{5,6b}$=5.2 Hz, H-6b), 3.53 (t, 1H, $J_{2,3}$=9.0 Hz, $J_{3,4}$=9.0 Hz, H-3), 3.52 (ddd, 1H, $J_{4,5}$=9.6 Hz, H-5), 3.44 (t, 1H, H-4); ^{13}C NMR (75.5 MHz, D_2O) Table 2 and δ 77.5 (C-5), 76.6 (C-3), 69.4 (C-4), 60.7 (C-6); FAB-MS *m/z* 401 ($[M+H]^+$, 16%), 423 ($[M+Na]^+$, 4%); HRFAB-MS *m/z* calcd for $[M+H]^+$ $C_{13}H_{24}N_2O_{10}S$: 401.1230, found: 401.1232.

3.2.9. *N*-(β-D-Glucopyranosyl)-*N′*-(β-D-mannopyranosyl)thiourea (12i). Purification by gel filtration chromatography gave **12i**: 405 mg, 73% as a syrup; R_f=0.30 (3:2:1 EtOAc/EtOH/H_2O) $[\alpha]_D^{21}$ −24° (*c* 0.5, H_2O); IR: ν_{max} 3380, 2888, 1647, 1541, 1416, 1358, 1099, 1072, 1024, 891 cm^{-1}; ^1H NMR (300 MHz, D_2O, 60 °C) Table 2 and δ 5.66 (bs, 1H, H-1′), 4.04 (dd, 1H, $J_{1',2'}$=1.2 Hz, $J_{2',3'}$=3.3 Hz, H-2′), 3.93 (dd, 1H, $J_{5',6a'}$=2.2 Hz, $J_{6a',6b'}$=12.3 Hz, H-6a′), 3.89 (dd, 1H, $J_{5,6a}$=2.2 Hz, $J_{6a,6b}$=12.3 Hz, H-6a), 3.75 (dd, 1H, $J_{5,6a}$=5.2 Hz, H-6b), 3.75 (dd, 1H, $J_{5',6a'}$=5.2 Hz, H-6b′), 3.75 (dd, 1H, $J_{3',4'}$=9.6 Hz, H-3′), 3.64 (t, 1H, $J_{4',5'}$=9.6 Hz, H-4′), 3.60 (m, 1H, $J_{3,4}$=9.0 Hz, H-3), 3.57–3.47 (m, 2H, H-5, H-5′), 3.48 (t, 1H, $J_{2,3}$=9.0 Hz, H-2), 3.45 (t, 1H,

$J_{3,4}$=9.0 Hz, $J_{4,5}$=9.7 Hz, H-4); ^{13}C NMR (75.5 MHz, D_2O, 60 °C) Table 2 and δ 78.1, 78.0 (C-5, C-5′), 77.1 (C-3), 73.9 (C-3′), 70.7 (C-2′), 70.0 (C-4), 67.2 (C-4′), 61.6, 61.3 (C-6, C-6′); FAB-MS *m/z* 401 ([M+H]$^+$, 43%), 423 ([M+Na]$^+$, 76%); HRFAB-MS *m/z* calcd for [M+Na]$^+$ $C_{13}H_{23}N_2NaO_{10}S$: 423.1049, found: 423.1046.

3.2.10. 1,6-Bis[3-(β-D-glucopyranosyl)thioureido]hexane (12j). Purification by gel filtration chromatography gave **12j**: 325 mg, 84% as a syrup. R_f=0.45 (3:2:1 EtOAc/EtOH/H_2O); $[\alpha]_D^{20}$ −15° (*c* 1.0, H_2O); IR: ν_{max} 3295, 2932, 1691, 1660, 1541, 1364, 1103, 1024, 874 cm^{-1}; ^{1}H NMR (300 MHz, D_2O, 60 °C) Table 2 and δ 3.88 (dd, 1H, $J_{5,6a}$=1.9 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.72 (dd, 1H, $J_{5,6b}$=5.2 Hz, H-6b), 3.56 (t, 1H, $J_{2,3}$=8.9 Hz, $J_{3,4}$=8.9 Hz, H-3), 3.53 (ddd, 1H, $J_{4,5}$=9.2 Hz, H-5), 3.51 (m, 2H, CH_2) 3.45 (t, 1H, H-4), 1.60 (m, 2H, CH_2), 1.36 (m, 2H, CH_2); ^{13}C NMR (75.5 MHz, D_2O, 60 °C) Table 2 and δ 77.8 (C-5), 77.2 (C-3), 70.1 (C-4), 61.4 (C-6), 28.4 (CH_2β), 26.1 (CH_2γ); FAB-MS *m/z* 581 ([M+Na]$^+$, 21%); HRFAB-MS *m/z* calcd for [M+Na]$^+$ $C_{20}H_{38}N_2NaO_{10}S_2$: 581.1927, found: 581.1918.

3.2.11. 1,12-Bis[3-(β-D-glucopyranosyl)thioureido]dodecane (12k). Purification by gel filtration chromatography gave **12k**: 345 mg, 77% as a syrup. R_f=0.69 (3:2:1 EtOAc/EtOH/H_2O); $[\alpha]_D^{27}$ +13° (*c* 0.6, DMSO); IR: ν_{max} 3308, 2915, 1689, 1622, 1520, 1456, 1370, 1105, 1024, 872 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6, 90 °C) Table 2 and δ 7.43 (d, 1H, $J_{NH,H\text{-}1}$=8.2 Hz, NH), 7.37 (t, 1H, J_{NH,CH_2}=5.0 Hz, NH′), 4.62–4.50 (m, 3H, 3OH), 3.99 (m, 1H, OH-6), 3.66 (m, 1H, $J_{5,6a}$=2.5 Hz, $J_{6a,6b}$=11.6 Hz, H-6a), 3.47 (m, 1H, $J_{5,6b}$=4.8 Hz, H-6b), 3.42 (q, 2H, $J_{H,H}$=7.0 Hz, CH_2), 3.25 (t, 1H, $J_{2,3}$=8.5 Hz, $J_{3,4}$=8.5 Hz, H-3), 3.20 (ddd, 1H, $J_{4,5}$=9.2 Hz, H-5), 3.14 (t, 1H, H-4), 1.51 (m, 2H, CH_2), 1.28 (m, 8H, 4CH_2); ^{13}C NMR (75.5 MHz, DMSO-d_6, 90 °C) Table 2 and δ 77.4 (C-5), 77.2 (C-3), 70.1 (C-4), 60.8 (C-6), 28.4, 28.2, 28.1, 25.9 (CH_2, dodecane); FAB-MS *m/z* 665 ([M+Na]$^+$, 100%); HRFAB-MS *m/z* calcd for [M+Na]$^+$ $C_{26}H_{50}N_4NaO_{10}S_2$: 665.2866, found: 665.2869.

3.2.12. *N*-Butyl-*N*′-(β-D-galactopyranosyl)thiourea (13b). Purification by column chromatography (CH_2Cl_2→10:1 CH_2Cl_2/MeOH) gave **13b**: 218 mg, 53% as a syrup. R_f=0.51. (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{24}$ −1° (*c* 1.1, H_2O); IR: ν_{max} 3331, 2932, 1647, 1557, 1360, 1032 cm^{-1}; ^{1}H NMR (500 MHz, D_2O) Table 2 and δ 3.94 (m, 1H, $J_{4,5}$=~0.0 Hz, H-4), 3.75–3.61 (m, 5H, H-2, H-3, H-5, H-6a, H-6b), 3.51 (m, 2H, CH_2), 1.54 (m, 2H, CH_2), 1.31 (m, 2H, CH_2), 0.87 (t, 3H, *J*=7.3 Hz, CH_3); ^{13}C NMR (125.7 MHz, D_2O) Table 2 and δ 77.5 (C-5), 74.6 (C-3), 69.9 (C-4), 62.2 (C-6), 31.4 (CH_2), 20.6 (CH_2), 14.2 (CH_3); FAB-MS *m/z* 295 ([M+H]$^+$, 52%), 317 ([M+Na]$^+$, 100%); HRFAB-MS *m/z* calcd for [M+H]$^+$: 295.1328, found: 295.1326.

3.2.13. *N*,*N*-Diethyl-*N*′-(β-D-galactopyranosyl)thiourea (13d). Purification column chromatography (CH_2Cl_2→10:1 CH_2Cl_2/MeOH) gave **13d**: 282 mg, 69% as an amorphous solid. R_f=0.51 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{28}$ +15° (*c* 0.5, H_2O); IR: ν_{max} 3324, 2974, 1543, 1424, 1354, 1279, 1121 cm^{-1}; ^{1}H NMR (500 MHz, D_2O) Table 2 and δ 3.96 (m, 1H, $J_{4,5}$=~0.0 Hz, H-4), 3.70 (m, 4H, $J_{2,3}$=9.8 Hz, $J_{3,4}$=2.6 Hz, H-3, H-5, H-6a, H-6b), 3.69 (m, 4H, *J*=7.1 Hz, 2CH_2), 1.17 (t, 6H, 2CH_3); ^{13}C NMR (125.7 MHz, D_2O) Table 2 and δ 77.6 (C-5), 74.9 (C-3), 70.0 (C-4), 62.2 (C-6), 12.7 (2CH_3); FAB-MS *m/z* 295 ([M+H]$^+$, 38%), 317 ([M+Na]$^+$, 100%); HRFAB-MS *m/z* calcd for [M+H]$^+$ $C_{11}H_{22}N_2O_5S$: 295.1328, found: 295.1328.

3.3. General methods for the synthesis of cyclic isoureas 14

Method A. To a solution of the crude thiourea **12** prepared as described above starting from β-D-glucopyranosylamine (1.40 mmol) in 1:1 H_2O/dioxane (5 mL) was one-pot added yellow mercury oxide (II) (910 mg, 4.2 mmol, 3.0 equiv.). The mixture was stirred at rt for 1–4 h until TLC showed disappearance of the corresponding thiourea, and then it was filtered through a Celite pad. The filtrate was concentrated to dryness and purified by silica gel column chromatography, except for **14j**, that was crystallized from EtOH.

Method B. To a solution of a purified thiourea **12a**,**c** (0.5 mmol) in MeOH (5 mL) was added yellow mercury oxide (II) (325 mg, 1.5 mmol, 3.0 equiv.). The mixture was stirred at rt for 6 h and then it was filtered through a Celite pad. The filtrate was concentrated to dryness and purified by silica gel column chromatography.

Method C. To a solution of **12h** (0.5 mmol) in 1:1 H_2O/dioxane (5 mL) was added yellow mercury oxide (II) (325 mg, 1.5 mmol, 3.0 equiv.). The mixture was stirred at rt for 3 h and then it was filtered through a Celite pad. The filtrate was concentrated to dryness to give pure **14h**.

3.3.1. 4,5-Dihydro-2-*p*-tolylamino-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazole (14a). *Method A*. Column chromatography (CH_2Cl_2→20:1 CH_2Cl_2/MeOH) gave **14a**: 284 mg, 69% as a yellow solid.

Method B. Filtration through a Celite bed gave **14a**: 138 mg, 94%. R_f=0.80 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{22}$ +84° (*c* 1.0, DMSO); IR: ν_{max} 3289, 3073, 1663, 1549, 1518, 1381, 1138, 1096, 1040, 937, 882, 820, 719 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) Table 2 and δ 7.22, 7.09 (m, 4H, Ar-H), 3.90 (dd, 1H, $J_{2,3}$=10.5 Hz, $J_{3,4}$=7.6 Hz, H-3), 3.89 (dd, 1H, $J_{6a,6b}$=12.2 Hz, H-6a), 3.73 (dd, 1H, $J_{5,6b}$=5.3 Hz, H-6b), 3.53 (m, 1H, H-5), 3.40 (dd, 1H, $J_{4,5}$=9.6 Hz, H-4), 2.27 (s, 3H, CH_3); ^{13}C NMR (75.5 MHz, CD_3OD) Table 2 and δ 133.9, 130.4, 121.1 (Ar), 83.1 (C-5), 75.6 (C-3), 73.6 (C-4), 62.7 (C-6), 20.8 (CH_3); CI-MS *m/z* 295 ([M+H]$^+$, 46%); HRCI-MS *m/z* calcd for [M+H]$^+$ $C_{14}H_{19}N_2O_5$: 295.1294, found: 295.1287.

3.3.2. 2-Butylamino-4,5-dihydro-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazole (14b). *Method A*. Column chromatography (CH_2Cl_2→8:1 CH_2Cl_2/MeOH) gave **14b**: 244 mg, 67% as a white solid. R_f=0.48 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{25}$ +108° (*c* 0.39, DMSO); IR: ν_{max} 3439, 3277, 3090, 2955, 1667, 1592, 1435, 1352, 1289, 1244 cm^{-1}; ^{1}H NMR (300 MHz, D_2O) Table 2 and δ 3.96 (dd, 1H, $J_{2,3}$= 10.6 Hz, $J_{3,4}$=7.9 Hz, H-3), 3.86 (dd, 1H, $J_{5,6a}$=2.2 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.71 (dd, 1H, $J_{5,6b}$=5.6 Hz, H-6b), 3.59 (ddd, 1H, $J_{4,5}$=9.6 Hz, H-5), 3.39 (dd, 1H, H-4), 3.10 (t, 2H, $J_{H,H}$=6.9 Hz, CH_2α), 1.46 (m, 2H, CH_2β),

1.28 (m, 2H, $CH_2\gamma$), 0.84 (t, 3H, CH_3); ^{13}C NMR (75.5 MHz, D_2O) Table 2 and δ 81.1 (C-5), 73.7 (C-3), 71.8 (C-4), 61.0 (C-6), 30.7 ($CH_2\beta$), 19.4 ($CH_2\gamma$), 13.1 (CH_3); CI-MS *m/z* 261 ([M+H]$^+$, 100%), 243 ([M+H−H_2O]$^+$, 16%); HRCI-MS *m/z* calcd for [M+H]$^+$ $C_{11}H_{20}N_2O_5$: 261.1449, found: 261.1450. Anal. calcd for $C_{11}H_{20}N_2O_5$: C, 50.76; H, 7.74; N, 10.76, found: C, 50.61; H, 7.94; N, 11.01.

3.3.3. 4,5-Dihydro-2-octylamino-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazole (14c). *Method A*. Column chromatography (CH_2Cl_2→10:1 CH_2Cl_2/MeOH) gave **4c**: 221 mg, 50% as a white solid.

Method B. Column chromatography (CH_2Cl_2→10:1 CH_2Cl_2/MeOH) gave **14c**: 119 mg, 75%. R_f=0.36 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{25}$+82° (*c* 0.83, DMSO); IR: ν_{max} 3312, 2924, 2855, 1651, 1539, 1456, 1373, 1101, 1038, 876 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) Table 2 and δ 3.86 (dd, 1H, $J_{5,6a}$=2.6 Hz, $J_{6a,6b}$=12.1 Hz, H-6a), 3.85 (t, 1H, $J_{2,3}$= 9.8 Hz, $J_{3,4}$=7.7 Hz, H-3), 3,72 (dd, 1H, $J_{5,6b}$=5.2 Hz, H-6b), 3.48 (ddd, 1H, $J_{4,5}$=9.6 Hz, H-5), 3.37 (dd, 1H, H-4), 3.14 (t, 2H, $J_{H,H}$=7.0 Hz, CH_2), 1.54 (m, 2H, CH_2), 1.31 (m, 10H, 5CH_2), 0.90 (t, 3H, CH_3); ^{13}C NMR (125.7 MHz, CD_3OD) Table 2 and δ 83.1 (C-5), 75.7 (C-3), 73.7 (C-4), 62.7 (C-6), 33.0, 30.5, 30.4, 30.4, 27.8, 23.7 (CH_2), 14.4 (CH_3); CI-MS *m/z* 299 ([M+H−H_2O]$^+$, 35%), 317 ([M+H]$^+$, 100%), 633 ([2M+H]$^+$, 5%); HRCI-MS *m/z* calcd for [M+H]$^+$ $C_{15}H_{29}N_2O_5$: 317.2076, found: 317.2076.

3.3.4. 2-Diethylamino-4,5-dihydro-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazole (14d). *Method A*. Column chromatography (CH_2Cl_2→3:1 CH_2Cl_2/MeOH) gave **14d** (255 mg, 57%) and urea **15d** (70 mg, 18%), which was identical with the product prepared in Section 3.3.10. Data for compound **14d**: R_f=0.69 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{25}$ +114° (*c* 0.56, DMSO); IRν_{max} 3324, 2922, 2855, 1642, 1431, 1358, 1314, 1155, 1065, 876, 735 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) Table 2 and δ 3.85 (dd, 1H, $J_{5,6a}$= 2.0 Hz, $J_{6a,6b}$=12.0 Hz, H-6a), 3.86 (dd, 1H, $J_{2,3}$=10.4 Hz, H-3), 3.71 (dd, 1H, $J_{5,6b}$=5.2 Hz, H-6b), 3.49 (ddd, 1H, H-5), 3.33 (m, 5H, H-4, 2CH_2), 1.15 (1, 3H, $J_{H,H}$=7.1 Hz, CH_3); ^{13}C NMR (75.5 MHz, CD_3OD) Table 2 and δ 83.1 (C-5), 75.8 (C-3), 73.7 (C-4), 62.8 (C-6), 13.7 (2CH_3); CI-MS *m/z* 225 ([M+H−2H_2O]$^+$, 3%), 243 ([M+H−H_2O]$^+$, 14%), 261 ([M+H]$^+$, 100%); HRCI-MS *m/z* calcd for [M+H]$^+$ $C_{11}H_{21}N_2O_5$: 261.1450, found: 261.1454.

3.3.5. 4,5-Dihydro-2-(piperidin-1-yl)-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazole (14e). *Method A*. Column chromatography (CH_2Cl_2→3:1 CH_2Cl_2/MeOH) gave **14e**: 177 mg, 47% as a white solid. R_f=0.48 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{27}$ +107° (*c* 1.0, DMSO); IR: ν_{max} 3376, 3330, 2936, 2855, 1645, 1443, 1356, 1167, 1047, 729 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) Table 2 and δ 3.86 (dd, $J_{2,3}$=10.6 Hz, $J_{3,4}$=7.7 Hz, H-3), 3.85 (dd, 1H, $J_{5,6a}$= 2.3 Hz, $J_{6a,6b}$=12.0 Hz, H-6a), 3.72 (dd, 1H, $J_{5,6b}$=5.2 Hz, H-6b), 3.49 (m, 1H, $J_{4,5}$=9.6 Hz, H-5), 3.36 (dd, 1H, H-4), 1.64 (m, 2H, CH_2), 1.57 (m, 4H, 2CH_2); ^{13}C NMR (125.7 MHz, CD_3OD) Table 2 and δ 83.1 (C-5), 75.8 (C-3), 73.7 (C-4), 62.8 (C-6), 26.4, 25.1 (CH_2); CI-MS *m/z* 273 ([M+H]$^+$, 100%); HRCI-MS *m/z* calcd for [M+H]$^+$ $C_{12}H_{21}N_2O_5$: 273.1450, found: 273.1447.

3.3.6. 2-(β-D-Glucopyranosyl)amino-4,5-dihydro-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazole (14h). *Method C*. Filtration through a Celite bed gave pure **14h**: 82 mg, 89% as a syrup. R_f=0.25 (3:2:1 EtOAc/EtOH/H_2O); [α] +28° (*c* 0.5, H_2O); IR ν_{max} 3306, 2918, 1651, 1559, 1364, 1125, 993 cm^{-1}; ^1H NMR (500 MHz, D_2O) Table 2 and δ 4.72 (d, 1H, $J_{1',2'}$=8.9 Hz, H-1′), 4.04 (dd, 1H, $J_{2,3}$= 10.6 Hz, $J_{3,4}$=7.9 Hz, H-3), 3.89 (dd, 1H, $J_{5',6a'}$=2.0 Hz, $J_{6a',6b'}$=12.4 Hz, H-6a′), 3.85 (dd, 1H, $J_{5,6a}$=2.0 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.74 (dd, 1H, $J_{5,6b}$=5.8 Hz, H-6b), 3.71 (t, 1H, H-2), 3.70 (dd, 1H, $J_{5',6b'}$=5.2 Hz, H-6b′), 3.64 (ddd, 1H, $J_{4,5}$=9.6 Hz, H-5), 3.52 (t, 1H, $J_{2',3'}$=9.4 Hz, $J_{3',4'}$=9.0 Hz, H-3′), 3.47 (ddd, 1H, $J_{4',5'}$=9.4 Hz, H-5′), 3.43 (dd, 1H, H-4), 3.38 (t, 1H, H-2′), 3.35 (t, 1H, H-4′); ^{13}C NMR (125.7 MHz, CD_3OD) Table 2 and δ 86.0 (C-2), 82.3 (C-5), 78.6 (C-5′), 77.6 (C-3′), 74.6 (C-2′), 73.3 (C-3), 72.8 (C-4), 70.4 (C-4′), 62.0, 61.7 (C-6, C-6′); FAB-MS *m/z* 389 ([M+Na]$^+$, 100%); HRFAB-MS *m/z* calcd for [M+Na]$^+$ $C_{13}H_{22}N_2NaO_{10}$: 389.1172, found: 389.1185.

3.3.7. 1,6-Bis{4,5-dihydro-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazol-2-ylamino}hexane (14j). *Method A*. Crystallization from EtOH gave hygroscopic **14j**: 199 mg, 58%. R_f=0.22 (3:2:1 EtOAc/EtOH/H_2O); [α] +43° (*c* 1.0, H_2O); IR: ν_{max} 3347, 2945, 2836, 1651, 1452, 1371, 1026, 712 cm^{-1}; ^1H NMR (300 MHz, D_2O) Table 2 and δ 3.97 (dd, 1H, $J_{2,3}$=10.6 Hz, $J_{3,4}$=7.9 Hz, H-3), 3.87 (dd, 1H, $J_{5,6a}$=2.1 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.72 (dd, 1H, $J_{5,6b}$=5.7 Hz, H-6b), 3.60 (ddd, 1H, $J_{4,5}$=9.6 Hz, H-5), 3.40 (dd, 1H, H-4), 3.11 (t, 4H, $J_{H,H}$=6.8 Hz, 2CH_2), 1.49 (m, 4H, 2CH_2), 1.30 (m, 4H, 2CH_2); ^{13}C NMR (75.5 MHz, D_2O) Table 2 and δ 81.6 (C-5), 74.2 (C-3), 72.3 (C-4), 61.5 (C-6), 29.0 ($CH_2\beta$), 26.2 ($CH_2\gamma$); FAB-MS 513 *m/z* ([M+Na]$^+$, 17%); HRFAB-MS *m/z* calcd for [M+Na]$^+$ $C_{20}H_{34}N_4NaO_{10}$: 513.2173, found: 513.2214.

3.3.8. 2-Bencylamino-4,5-dihydro-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazole (14l). *Method A*. Column chromatography (CH_2Cl_2→3:1 CH_2Cl_2/MeOH) gave **14l**: 235 mg, 57% as a white solid. R_f=0.62 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{25}$ +73° (*c* 1.2, DMSO) IR: ν_{max} 3283, 1633, 1375, 1101, 1040, 874 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) Table 2 and δ 7.34–7.21 (m, 5H, Ar-H), 5.51, 5.29 (bs, 2H, 2OH), 4.65 (bs, 1H, OH-6), 4.22 (s, 2H, CH_2), 3.67 (dd, 1H, $J_{2,3}$=10.2 Hz, $J_{3,4}$=7.6 Hz, H-3), 3.64 (m, 1H, $J_{6a,6b}$= 12.9 Hz, H-6a), 3.46 (m, 1H, H-6b), 3.29 (m, 1H, $J_{4,5}$= 8.9 Hz, H-5), 3.15 (bt, H-4); ^{13}C NMR (300 MHz, DMSO-d_6) Table 2 and δ 139.8, 128.3, 127.2, 126.8 (Ar), 81.9 (C-5), 74.0 (C-3), 72.2 (C-4), 61.0 (C-6); CI-MS *m/z* 277 ([M+H−H_2O]$^+$, 35%), 295 ([M+H]$^+$, 100%); HRCI-MS *m/z* calcd for [M+H]$^+$ $C_{14}H_{19}N_2O_5$: 295.1294, found: 295.1289. Anal. calcd for $C_{14}H_{18}N_2O_5{\cdot}1/2H_2O$: C, 55.44; H, 6.31; N, 9.24, found: C, 55.50; H, 5.98; N, 9.41.

3.3.9. 2-(6-Deoxy-1,2:3,4-di-*O*-isopropilidene-α-D-galactopyranos-6-yl)amino-4,5-dihydro-(1,2-dideoxy-β-D-glucopyranoso)[1,2-*d*]-1,3-oxazole (14m). *Method A*. Column chromatography (CH_2Cl_2→10:1 CH_2Cl_2/MeOH) gave **14m**: 369 mg, 59% as a syrup. R_f=0.66 (5:1 CH_2Cl_2/MeOH); [α] +50° (*c* 0.9, MeOH); IR: ν_{max} 3312, 2928,

1661, 1373, 1101, 1067, 1005, 874 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) Table 2 and δ 5.43 (d, 1H, $J_{1',2'}$=5.0 Hz, H-1′), 4.58 (dd, 1H, $J_{2',3'}$=2.4 Hz, $J_{3',4'}$=7.9 Hz, H-3′), 4.30 (dd, 1H, H-2′), 4.21 (dd, 1H, $J_{4',5'}$=1.6 Hz, H-4′), 3.97 (m, 1H, H-5′), 3.81 (dd, 1H, $J_{5,6a}$=2.2 Hz, $J_{6a,6b}$=12.1 Hz, H-6a), 3.80 (dd, 1H, $J_{2,3}$=10.6 Hz, $J_{3,4}$=7.6 Hz, H-3), 3.66 (dd, 1H, $J_{5,6b}$=5.4 Hz, H-6b), 3.44 (m, 2H, H-2, H-5), 3.33 (dd, 1H, $J_{5',6a'}$=4.0 Hz, $J_{6a',6b'}$=13.8 Hz, H-6a′), 3.26 (dd, 1H, $J_{4,5}$=9.6 Hz, H-4), 3.22 (dd, 1H, $J_{5',6b'}$=8.5 Hz, H-6b′), 1.45, 1.36, 1.29, 1.28 (4s, 3H each, $4CH_3$); ^{13}C NMR (75.5 MHz, CD_3OD) Table 2 and δ 110.5, 110.0 (Me_2C), 83.2 (C-5), 75.7 (C-3), 73.7 (C-4), 72.7 (C-4′), 72.2 (C-3′), 71.9 (C-2′), 67.4 (C-5′), 62.9 (C-6), 43.9 (C-6′), 26.5, 26.3, 25.2, 24.5 (CH_3); CI-MS *m/z* 429 ($[M+H-H_2O]^+$, 4%); FAB-MS *m/z* 469 ($[M+Na]^+$, 100%), 447 ($[M+H]^+$, 40%); HRFAB-MS *m/z* calcd for $[M+H]^+$ $C_{19}H_{31}N_2O_{10}$: 447.1979, found: 447.1969.

3.3.10. *N*,*N*-Diethyl-*N*′-(β-D-glucopyranosyl)urea (15d). To a solution of the crude thiourea **12d** prepared as described above starting from β-D-glucopyranosylamine **3** (250 mg, 1.40 mmol) in 1:1 H_2O/dioxane (5 mL) was one-pot added yellow mercury oxide (II) (910 mg, 4.2 mmol, 3.0 equiv.). The mixture was stirred at rt for 2 h and then an extra amount of yellow mercury oxide (II) (910 mg, 4.2 mmol, 3.0 equiv.) was added and the mixture was stirred for other 2 h. After that it was filtered through a Celite pad, the filtrate was concentrated to dryness and purified by silica gel column chromatography to give **15d** (331 mg, 85% from **3**) as a syrup. R_f=0.19 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{24}$ +5° (*c* 1.0, MeOH); IR: ν_{max} 3266, 2947, 2839, 1663, 1543, 1449, 1103, 1022 cm^{-1}; ^1H NMR (300 MHz, D_2O) Table 2 and δ 3.84 (dd, 1H, $J_{5,6a}$=1.8 Hz, $J_{6a,6b}$=12.4 Hz, H-6a), 3.66 (dd, 1H, $J_{5,6b}$=5.6 Hz, H-6b), 3.50 (t, 1H, $J_{2,3}$=9.2 Hz, $J_{3,4}$=9.2 Hz, H-3), 3.47 (ddd, 1H, $J_{4,5}$=9.7 Hz, H-5), 3.35 (t, 1H, H-4), 3.27 (m, 4H, $2CH_2$), 1.08 (t, 6H, $2CH_3$); ^{13}C NMR (75.5 MHz; D_2O) Table 2 and δ 77.5 (C-5), 77.0 (C-3), 69.8 (C-4), 61.0 (C-6), 12.9 (CH_3); FAB-MS *m/z* 301 ($[M+Na]^+$, 100%); HRFAB-MS *m/z* calcd for $[M+Na]^+$ $C_{11}H_{22}N_2NaO_6$ 301.1376, found: 301.1384.

3.3.11. *N*-[(β-D-Glucopyranosyl)carbamoyl]piperidine (15e). To a solution of the crude thiourea **12e** prepared as described above starting from β-D-glucopyranosylamine (250 mg, 1.40 mmol) in 1:1 H_2O/dioxane (5 mL) was one-pot added yellow mercury oxide (II) (910 mg, 4.2 mmol, 3.0 equiv.). The mixture was stirred at rt for 2 h and TLC showed disappearance of **12e** and formation of isourea **14e**. An extra amount of yellow mercury oxide (II) (910 mg, 4.2 mmol, 3.0 equiv.) was added, the mixture was stirred for 5 days, and TLC showed no appreciable formation of a new compound. The mixture was filtered through a Celite pad, the filtrate was concentrated to dryness and the residue was dissolved in water (5 mL). Mercury oxide (II) (910 mg, 4.2 mmol, 3.0 equiv.) was added and the mixture was kept at rt for 3 months. Conventional work-up and purification by silica gel column chromatography gave isourea **14e** (52 mg, 14%) as the first eluted compound. Eluted second was **15e** (134 mg, 33% from **3**), R_f=0.18 (5:1 CH_2Cl_2/MeOH); $[\alpha]_D^{27}$ −20° (*c* 1.0, H_2O); IR: ν_{max} 3395, 2940, 1647, 1539, 1454, 1364, 1013 cm^{-1}; ^1H NMR (300 MHz, D_2O) Table 2 and δ 3.92 (dd, 1H, $J_{5,6a}$=2.0 Hz, $J_{6a,6b}$=12.3 Hz, H-6a), 3.75 (dd, 1H, $J_{5,6b}$=5.6 Hz, H-6b), 3.58 (t, 1H, $J_{2,3}$=9.2 Hz, $J_{3,4}$=9.2 Hz, H-3), 3.54 (ddd, 1H, $J_{4,5}$=9.9 Hz, H-5), 3.44 (m, 5H, H-4, $2CH_2$), 1.66 (m, 2H, CH_2), 1.58 (m, 4H, $2CH_2$); ^{13}C NMR (75.5 MHz; D_2O) Table 2 and δ 78.4 (C-5), 77.9 (C-3), 70.7 (C-4), 62.0 (C-6), 26.4, 24.9 (CH_2); FAB-MS *m/z* 313 ($[M+Na]^+$, 100%); HRCI-MS *m/z* calcd for $[M+H]^+$ $C_{12}H_{23}N_2O_6$: 291.1556, found: 291.1567.

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