Syntheses of Guanidinoglycosides with the Inventive use of Mitsunobu Conditions and 1,8-Diazabicyclo[5.4.0]undec-7-ene

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Abstract: A series of novel guanidinoglycosides was successfully synthesized. This was accomplished with the use of Mitsunobu conditions as a strategy to convert the glycopyranose anomeric hydroxy group to give the corresponding substituted masked guanidines in high yields. Subsequent deprotection and coupling with Fmoc protected β-amino acid, afforded a series of *N*,*N*′-substituted-methylisothioureas. Cleavage of Fmoc followed by concomitant cyclization was achieved with a catalytic amount of DBU to give the guanidinoglycosides.

Key words: guanidine, glycosides, Mitsunobu reaction, coupling, cyclization

The significance of the guanidine moiety's role in many biologically active compounds cannot be disputed. Discovered in 1944, Streptomycin contains two essential guanidine groups at C-1 and C-3 and is an important member of the antibiotic family. It is active against gram-negative microbial infections and has beneficial effects in the treatment of infections caused by intracellular pathogens.[2] Over the years, numerous streptomycin analogs have been prepared and analogs without both guanidino groups were found to be inactive.[3] Cotner and Smith performed extensive work on phosphotyrosine binding by ammonium and guanidinium-modified cyclodextrins for the inhibition of inappropriate mitogenic signaling.[4] Meanwhile, Reitz et al. prepared a series of carbohydrate biguanidines as potential hypoglycemic agents and succeeded in achieving activities equivalent to those of Phenformin and Metformin.[5] More recently, Goodman and coworkers synthesized a new class of guanidinylation reagents: *N*,*N*′-diBoc- and *N*,*N*′-diCBz-*N*″-triflylguanidine,[6] which efficiently guanidinylate aryl-, alkyl-amines and amino acids to the corresponding guanidines in quantitative yields. The authors also used the reagents to convert aminoglycosides to their corresponding guanidinoglycosides, and demonstrated that these were able to inhibit replication of the HIV virus with good activities.[7]

Recently, our group reported the synthesis of novel guanidinoglycosides[8] via aza-Wittig type reaction of iminophosphoranes.[9] A series of β-glycosyl isothiocyanates was used as starting materials for the formation of glycosyl carbodiimides, which in turn underwent addition and spontaneous cyclization with β-amino acid methyl esters in the presence of Et_3N to yield the desired products. However, with the former synthetic route, we were restricted to the forming of guanidinoglycosides that were di-substituted at the N-1 position. As such, we embarked on the quest of designing an alternative route to enable the synthesis of guanidinoglycosides that are mono-substituted at the N-3 position (the previously N-1 position). In this paper, we report the successful syntheses of these guanidinoglycosides with the inventive use of the Mitsunobu reaction and DBU in guanidine formation.

Classical Mitsunobu reactions entail the activation of an alcohol entity with triphenylphosphine and diethyl azodicarboxylate so as to allow the 'attack' of a nucleophile that results in an SN_2-like reaction.[10] Applying the theory, we envisaged that, with a powerful guanidinylation reagent, the anomeric hydroxy group of a 2,3,4,6-*O*-acetylated glycopyranose should undergo Mitsunobu reaction to yield the guanidinoglycosides. A search through the literature revealed that diurethane-protected thiopseudourea, diurethane- and triurethane-protected guanidines are excellent guanidinylaton reagents, which react with primary or secondary alcohols under the Mitsunobu conditions to yield the (masked) guanidines.[6b,11]

We have chosen 1,3-bis(*tert*-butoxycarbonyl)-2-methyl-2-thiopseudourea as the guanidinylation reagent for two reasons: it is commercially available and is relatively cheap (US$39.10/5 g). As expected, the Mitsunobu reaction with 2,3,4,6-*O*-acetylated galacto- and gluco-pyranose proceeded with ease to yield 85 and 68% of **1a** and **1b**, respectively (Scheme 1). ^{1}H NMR spectra indicated that both purified glycosyl substituted thiopesudoureas **1a** and **1b** contained five (α_1:α_2:β_1:β_2:β_3 = 1:1:0.5:0.9:0.5) and four products (α_1:α_2:β_1:β_2 = 1:0.5:1:1.5), respectively. The α and β anomers were assigned based on the J_{1-2} coupling constants. We suspected that these products were mixtures of rotomers since HRMS gave only the desired molecular peak. Boc-Deprotection with TFA (80%) gave **2a** (59%, α only) and **2b** (75%, α:β = 19:1). The reaction was completed within 15 min at 0 ºC. Since only the desired deBoc product was obtained from compound **1**, it indicates that the initial mixtures were indeed the rotomers.[12]

Standard coupling conditions were employed during the next step in the syntheses of disubstituted masked guanidines **3a**–**e** (Table 1). It is important to note that the reaction, though it proceeded smoothly, did not reach completion. The progress of the reaction was monitored

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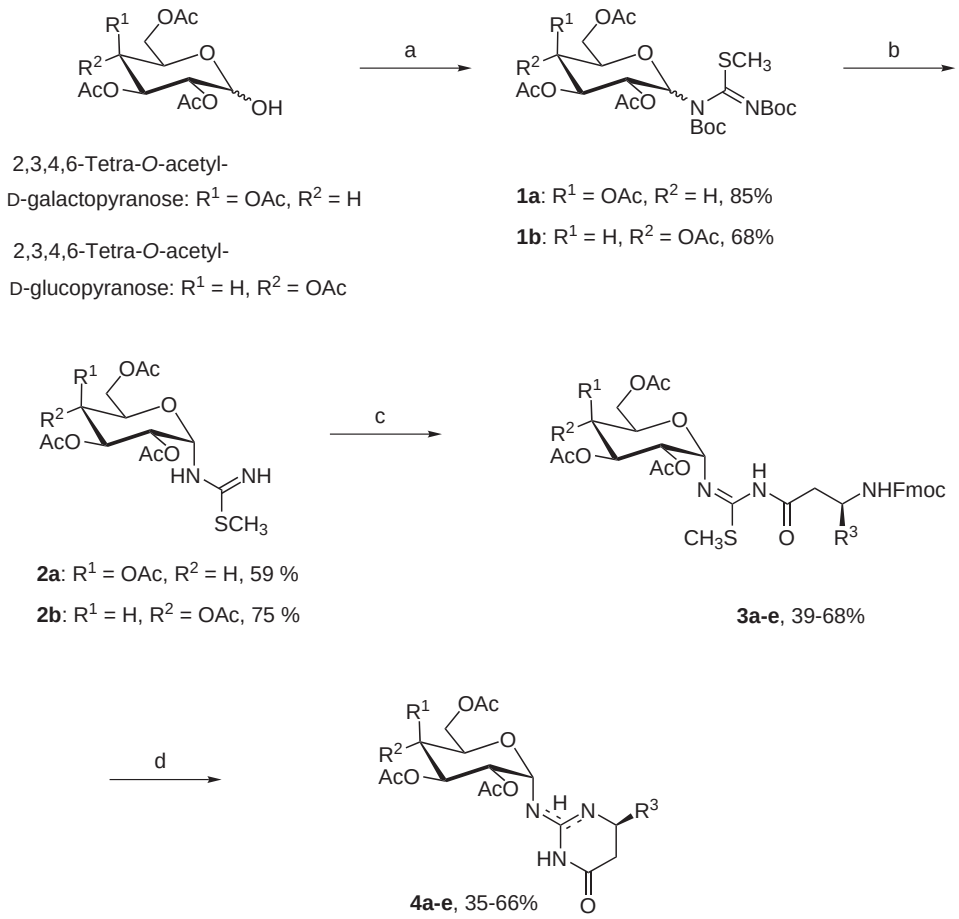


Scheme 1 *Reagents and Conditions*: (a) *N*,*N*′-BocNHC(SMe)NBoc, Ph_3P, DEAD, THF, 0 ºC to r.t., 18 h; (b) TFA, CH_2Cl_2, anisole, 15 min, 0 ºC; (c) Fmoc-protected β-amino acid, HOBt, DIC, DMA, *i*-Pr_2NEt, CH_2Cl_2, 0 ºC to r.t., 24 h; (d) DBU, THF, r.t., 1 h.

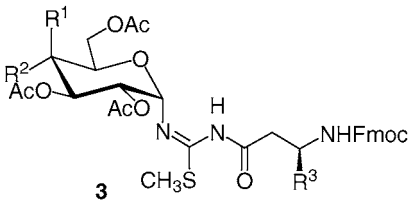
by TLC and MS for 48 hours and observations indicated that the reaction typically reached a plateau after 24 hours. The pure isolated yields of **3a**–**e** were in the range of 39–68% (Table 1). The coupling reactions of α-**2a**,**b** and Fmoc protected β-amino acids gave only the α-disubstituted masked guanidines **3a**–**e**.

The next step was to unmask the guanidine by cleaving the Fmoc protecting group and cyclizing the free amine to yield the guanidinoglycoside. The classical way of cleaving Fmoc employs the use of large excess of secondary amine, such as piperidine in DMF. However, subsequent experiments have been carried out to show the superiority of DBU over other common reagents with Fmoc cleavages.[13] Although DBU is commonly employed as a base for cyclization reactions,[14] none was found using DBU as the reagent for the in situ cleavage of Fmoc and cyclization to form the guanidine moiety. We predicted that the use of DBU should not only cleave the Fmoc protecting group but also cause the in situ intramolecular cyclization to guanidinoglycoside **4**. Using a catalytic amount of DBU (0.7% equiv), **3** was successfully converted to the desired guanidinoglycoside **4** (35–66%) within an hour. In some cases (**4b**–**c**,**e**), hydrolysis of the guanidine moiety at the anomeric position was observed to yield the 2,3,4,6-*O*-acetylated glycopyranoses (17, 15 and 4%, respectively).

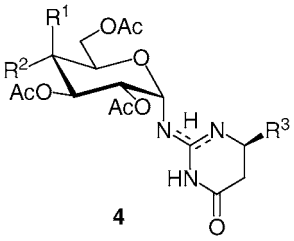
While performing HRMS, compounds **2**–**4** sometimes gave peaks that corresponded to $(M + 45)^+$. For example, with **2a**, on top of the desired molecular peak (HRMS calcd for $C_{16}H_{25}N_2O_9S$: 421.1281; found: 421.1282), an extra peak at 465.1176 (corresponding to $C_{17}H_{25}N_2O_{11}S$) was also observed. The extra peak was suspected to be a result of CO_2 trapped in the basic molecule. It was removed by bubbling argon gas through the sample solution prior to HRMS analysis in neutral conditions. The ^{13}C NMR spectra of compounds **2**–**4** also gave an extra carbon peak at δ = 158–159. The peak disappeared when fresh samples were prepared.

We have also isolated two cyclized products (**4c-I**, **4c-II** and **4d-I**, **4d-II**) from **4c** and **4d**, respectively. The more polar products **4-II** show very broad signals in their ^1H NMR spectra and yet strong $(M + H)^+$ HRMS signals. On the other hand, the less polar compounds **4-I** gave a very strong $(M + H + CO_2)^+$ HRMS signal. We suspected that products **4-I** are actually the trapped CO_2 form of products **4-II**. An experiment was thus carried out by stirring **4c-II** with dry ice in THF. Compound **4c-II** was found to slowly convert to **4c-I** as monitored by TLC and ^1H NMR.

Table 1 Isolated Yields of Methylisothioureas **3** and Guanidinoglycosides **4**



3



4

	R^1	R^2	R^3	Isolated Yields (%)	
				3	**4**
a	OAc	H	$CH_2(4\text{-}CH_3C_6H_4)$	65	45
b	OAc	H	H	56	35
c	H	OAc	$CH_2(4\text{-}CH_3C_6H_4)$	68	65
d	H	OAc	CH_2CH_2Ph	67	56
e	H	OAc	$CH_2(4\text{-}NO_2C_6H_4)$	39	66

The chemical structures of compounds **3** and **4** were carefully studied using ^1H, ^{13}C and 2D NMR spectroscopy. For example, the successful conversion of **3b** to **4b** was confirmed by the disappearance of the SCH_3 group (δ = 14.93 and 174.07) as well as the appearance of the guanidine group (δ = 161.24) from their ^{13}C NMR spectra. Furthermore, a ^1H–^{13}C HMBC experiment on **4b** also showed a correlation between the anomeric proton and the guanidine carbon (C-2) but not the carbonyl carbon (C-4), thus indicating that the amide coupling occurred at the less hindered amine (Figure 1).

Similarly, the ^1H–^{13}C HMBC correlation between the amide proton and carbonyl carbon confirmed the imino position of **3d**. However, unlike our previously reported N-1 disubstituted guanidinoglycosides,[8] we were unable to determine the location of the imino-group on the guanidine moiety of guanidinoglycosides **4** using ^1H–^{15}N 2D NMR experiments.

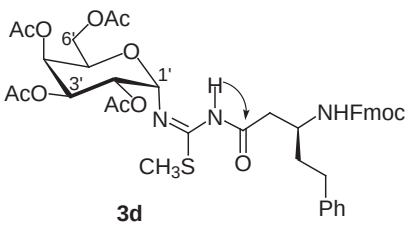
In this report, we have described a synthetic route that not only complements our previous work but also provided another convenient and efficient way to synthesize novel 2-glycosylamino-dihydropyrimidinone for future biological evaluation. More importantly, we have described two novel uses of Mitsunobu conditions and DBU, both of which are efficient and simple in application.

THF was distilled from sodium benzophenone ketyl prior to use. CH_2Cl_2 was distilled from CaH_2. Commercially available chemicals were used without further purification. Analytical TLC was carried out on precoated glass plates (Merck silica gel 60, F_{254}). Column chromatography was performed with silica gel (420–630 mesh) from Merck. All the NMR spectra were recorded with a Bruker Avance DMX 400 MHz instrument in $CDCl_3$ solutions and were calibrated using TMS as an internal standard. HRMS were determined using a Marina Biospectrometry workstation via ESI^+.

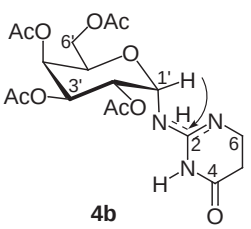
Additional abbreviations: *N*-hydroxybenzotriazole (HOBt), *N*,*N*-dimethylacetamide (DMA), and 1,3-diisopropylcarbodiimide (DIC).

_N_-(2,3,4,6-Tetra-_O_-acetyl-D-galactopyranosyl)-_N_-_N′_-bis(_tert_-butoxycarbonyl)methylisothiourea (1a)

A mixture of Ph_3P (450 mg, 1.72 mmol) and 1,3-bis(*tert*-butoxycarbonyl)-2-methyl-2-thiopseudourea (498 mg, 1.72 mmol) were dissolved in freshly distilled THF under argon. The mixture was cooled to below 0 ºC with an ice/salt-bath, stirred for 10 min before DEAD (271.7 µL, 1.72 mmol) was added dropwise. After another



3d



4b

Figure 1 ^1H–^{13}C HMBC correlations of methylisothiourea **3d** and guanidinoglycoside **4b**.

10 min, a solution of 2,3,4,6-tetra-*O*-acetyl-D-galactopyranose (500 mg, 1.43 mmol) in distilled THF was transferred to it via a delivery needle. The entire mixture was warmed up to r.t., stirred overnight and concentrated. Triphenylphosphine oxide was removed by precipitating the crude mixture in Et_2O. The filtrate was concentrated and purified using flash chromatography (33% EtOAc in hexane) to give pure **1a** (750 mg, 85%, α_1:α_2:β_1:β_2:β_3 = 1:1:0.5:0.9:0.5) as a yellow, viscous syrup. Further separation of **1a** into **1a-I** and **1a-II** was achieved by developing the preparative TLC 3 times (25% EtOAc in hexane).

From 1a-I (α_1, α_2, β_1)

α_1 Anomer

^{1}H NMR: δ = 6.34 (d, 1 H, *J* = 3.5 Hz, H-1), 5.48 (dd, 1 H, *J* = 3.0, 1.0 Hz, H-4), 5.44–5.43 (overlapped with β_1-H-4 and α_2-H-3, 1 H, H-3), 5.28 (dd, 1 H, *J* = 10.9, 3.4 Hz, H-2), 4.38 (t, 1 H, *J* = 6.7 Hz, H-5), 4.11–4.01 (m, 2 H, H-6a, H-6b), 2.40 (s, 3 H, SCH_3), 2.11, 2.00, 1.98, 1.96 (4 s, 12 H, OAc), 1.47, 1.45 (2 s, 18 H, Boc).

^{13}C NMR: δ = 174.79, 170.35, 170.27, 170.17, 170.10 159.07, 150.35, 91.50, 68.50, 67.50, 67.42, 66.79, 61.12, 27.91, 20.72, 14.80.

α_2 Anomer

^{1}H NMR: δ = 6.18 (d, 1 H, *J* = 3.4 Hz, H-1), 5.47 (dd, *J* = 3.0, 1.3 Hz, H-4), 5.44–5.43 (overlapped with α_1-H-3 and β_1-H-4, 1 H, H-3), 5.34 (dd, 1 H, *J* = 11.0, 3.1 Hz, H-2), 4.35 (t, 1 H, *J* = 6.6 Hz, H-5), 4.11–4.01 (m, 2 H, H-6a, H-6b), 2.40 (s, 3 H, SCH_3), 2.11, 2.00, 1.99, 1.95, (4 s, 12 H, OAc), 1.47, 1.45 (2 s, 18 H, Boc).

^{13}C NMR: δ = 170.77, 170.33, 170.09, 169.95, 153.36, 93.10, 68.81, 67.36, 67.18, 66.43, 61.12, 27.91, 20.72, 14.09.

β_1 Anomer

^{1}H NMR: δ = 5.85 (d, 1 H, *J* = 6.2 Hz, H-1), 5.80 (dd, 1 H, *J* = 9.7, 3.5 Hz, H-3), 5.44–5.43 (overlapped with α_1-H-3 and α_2-H-3, 1 H, H-4), 5.42 (dd, 1 H, *J* = 9.6, 6.2 Hz, H-2), 4.55 (dt, 1 H, *J* = 6.4, 1.9 Hz, H-5), 4.11–4.01 (m, 2 H, H-6a, H-6b), 2.38 (s, 3 H, SCH_3), 2.07, 2.02, 1.99, 1.95 (4 s, 12 H, OAc), 1.46 (s, 18 H, Boc).

^{13}C NMR: δ = 170.39, 170.10, 169.96, 169.65, 161.79, 157.34, 151.97, 80.86, 71.20, 67.88, 67.09, 66.41, 61.63, 27.91, 20.72, 15.88.

HRMS: *m*/*z* calcd for $C_{26}H_{41}N_2O_{13}S$ (M + H)$^+$: 621.2328; found: 621.2323.

From 1a-II (β_2, β_3)

β_2 Anomer

^{1}H NMR: δ = 5.66 (d, 1 H, *J* = 8.3 Hz, H-1), 5.42–5.37 (m, 2 H, H-2, H-4), 5.06 (dd, 1 H, *J* = 10.4, 3.4 Hz, H-3), 4.13–4.10 (m, 2 H, H-6a, H-6b), 4.03 (t, 1 H, *J* = 6.5 Hz, H-5), 2.36 (s, 3 H, SCH_3), 2.09, 1.98, 1.97, 1.94 (4 s, 12 H, OAc), 1.44, 1.43 (2 s, 18 H, Boc).

^{13}C NMR: δ = 175.19, 170.30, 170.14, 170.03, 169.19, 158.90, 150.24, 94.06, 71.54, 71.01, 67.07, 66.78, 61.07, 27.94, 20.64, 20.59, 20.53, 15.58.

β_3 Anomer

^{1}H NMR: δ = 5.92 (t, 1 H, *J* = 9.7 Hz, H-2), 5.42–5.37 (overlapped with β_2 protons, 1 H, H-4), 4.99 (dd, 1 H, *J* = 10.0, 3.4 Hz, H-3), 4.94 (br d, 1 H, *J* = 9.5 Hz, H-1), 4.13–4.10 (m, 2 H, H-6a, H-6b), 3.94 (t, 1 H, *J* = 6.6 Hz, H-5), 2.33 (s, 3 H, SCH_3), 2.07, 2.00, 1.97, 1.92 (4 s, 12 H, OAc), 1.47 (s, 18 H, Boc).

^{13}C NMR: δ = 170.35, 170.19, 170.07, 169.48, 160.63, 157.24, 150.45, 85.64, 72.88, 72.35, 67.74, 66.08, 61.16, 27.91, 20.97, 20.71 (carbons overlapped with β_2), 14.71.

HRMS: *m*/*z* calcd for $C_{26}H_{41}N_2O_{13}S$ (M + H)$^+$: 621.2328; found: 621.2327.

***N*-(2,3,4,6-Tetra-*O*-acetyl-D-glucopyranosyl)-*N*-*N*′-bis(*tert*-butoxycarbonyl)methylisothiourea (1b)**

Compound **1b** (602 mg, 68%, α_1:α_2:β_1:β_2 = 1:0.5:1:1.5) was prepared as **1a** from 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (500 mg, 1.43 mmol).

α_1 Anomer

^{1}H NMR: δ = 6.29 (d, 1 H, *J* = 3.7 Hz, H-1), 5.54 (t, 1 H, *J* = 9.9 Hz, H-3), 5.10 (t, 1 H, *J* = 9.9 Hz, H-4), 5.03 (dd, 1 H, *J* = 9.7, 3.8 Hz, H-2), 4.22 (dd, 1 H, *J* = 12.4, 4.5 Hz, H-6a), 4.18–4.12 (m, 1 H, H-5), 4.02 (dd, 1 H, *J* = 12.5, 2.1 Hz, H-6b), 2.39 (s, 3 H, SCH_3), 2.03, 1.97 (9), 1.97 (7), 1.96 (4 s, 12 H, OAc), 1.44, 1.43 (2 s, 18 H, Boc).

^{13}C NMR: δ = 174.87, 170.57, 170.12, 169.92, 169.47, 161.91, 90.81, 69.80, 69.46, 68.18, 67.81, 61.29, 27.85, 20.65, 20.54, 14.76.

α_2 Anomer

^{1}H NMR: δ = 6.11 (d, 1 H, *J* = 3.6 Hz, H-1), 5.45 (t, 1 H, *J* = 10.0 Hz, H-3), 5.09 (dd, 1 H, *J* = 9.5, 4.0 Hz, H-2), 5.05–5.00 (overlapped with other anomers, 1 H, H-4), 4.25–4.00 (overlapped with other anomers, H-5, H-6a, H-6b), 2.34, (s, 3 H, SCH_3), 2.03, 1.98 (3), 1.98 (0), 1.97 (4 s, 12 H, OAc), 1.45, 1.44 (2 s, 18 H, Boc).

^{13}C NMR: δ = 170.46, 169.91, 169.37, 169.32, 160.02, 153.13, 92.39, 69.75, 69.60, 69.14, 67.61, 61.23, 27.82, 20.70, 20.53, 14.03.

β_1 Anomer

^{1}H NMR: δ = 5.75 (t, 1 H, *J* = 7.7 Hz, H-3), 5.70 (d, 1 H, *J* = 6.2 Hz, H-1), 5.24 (dd, 1 H, *J* = 7.8, 6.2 Hz, H-2), 5.00 (dd, 1 H, *J* = 9.5, 7.3 Hz, H-4), 4.41 (ddd, 1 H, *J* = 9.4, 4.0, 2.9 Hz, H-5), 4.20 (dd, 1 H, *J* = 12.2, 4.2 Hz, H-6a), 4.07 (dd, 1 H, *J* = 12.3, 2.6 Hz, H-6b), 2.34 (s, 3 H, SCH_3), 2.01, 2.00, 1.97, 1.96 (4 s, 12 H, OAc), 1.44, 1.43 (2 s, 18 H, Boc).

^{13}C NMR: δ = 170.64, 169.66, 169.54, 169.48, 157.27, 151.86, 80.81, 71.55, 71,13, 68.62, 68.18, 61.95, 27.85, 20.70, 20.65, 15.78.

β_2 Anomer

^{1}H NMR: δ = 5.70 (t, 1 H, *J* = 9.4 Hz, H-3), 5.13 (t, 1 H, *J* = 9.4 Hz, H-2), 5.03 (t, 1 H, *J* = 9.8 Hz, H-4), 5.03 (d, 1 H, *J* = 9.5 Hz, H-1), 4.15 (dd, 1 H, *J* = 12.4, 4.8 Hz, H-6a), 4.09 (dd, 1 H, *J* = 12.3, 2.4 Hz, H-6b), 3.65 (ddd, 1 H, *J* = 9.9, 4.6, 2.5 Hz, H-5), 2.33 (s, 3 H, SCH_3), 2.01, 1.98, 1.96, 1.93 (4 s, 12 H, OAc), 1.45, 1.42 (2 s, 18 H, Boc).

^{13}C NMR: δ = 170.50, 170.14, 169.40, 169.34, 157.09, 150.42, 84.75, 74.08, 73.92, 68.20, 67.81, 61.83, 27.89, 20.66, 20.54, 15.62.

HRMS: *m*/*z* calcd for $C_{26}H_{41}N_2O_{13}S$ (M + H)$^+$: 621.2328; found: 621.2327.

***N*-(2,3,4,6,-Tetra-*O*-acetyl-α-D-galactopyranosyl)methylisothiourea (2a)**

To **1a** (560 mg, 0.90 mmol) in distilled CH_2Cl_2 (1 mL) at 0 ºC was added anisole (70 µL, 0.64 mmol) and TFA (7 mL, 90 mmol). The solution was stirred for 15 min at 0 ºC. The solvent was removed in vacuo, and the residue co-evaporated twice with hexane and then redissolved in MeOH. Powdered $NaHCO_3$ was added portionwise to neutralize the solution. The solution was filtered, concentrated and purified on a column (silica gel; 60% EtOAc in hexane) to afford pure **2a**.

Yield: 223 mg (59%); colorless syrup.

^{1}H NMR: δ = 6.39 (d, 1 H, *J* = 3.7 Hz, H-1), 5.52 (d, 1 H, *J* = 1.3 Hz, H-4), 5.50 (dd, 1 H, *J* = 13.5, 3.2 Hz, H-3), 5.31 (dd, 1 H, *J* = 10.3, 3.7 Hz, H-2), 4.45 (t, 1 H, *J* = 6.7 Hz, H-5), 4.12 (dd, 1 H, *J* = 11.3, 7.2 Hz, H-6a), 4.07 (dd, 1 H, *J* = 11.2, 6.6 Hz, H-6b), 2.49 (s, 3 H, SCH_3), 2.15, 2.04, 2.02, 1.99 (4 s, 12 H, OAc).

^{13}C NMR: δ = 175.60, 170.38, 170.21, 170.05, 91.01, 68.31, 67.63, 67.51, 66.89, 61.20, 20.75, 20.67, 13.68.

HRMS: calcd for $C_{16}H_{25}N_2O_9S$ (M + H)$^+$: 421.1281; found: 421.1282.

_N_-(2,3,4,6-Tetra-_O_-acetyl-D-glucopyranosyl)methylisothiourea (2b)

Compound **2b** was prepared the same way as **2a** from **1b** (560 mg, 0.90 mmol).

Yield: 284 mg (75%); α:β = 19:1; colorless syrup. The α- and β-anomers were separated and characterized individually.

α Anomer

^{1}H NMR: δ = 6.34 (d, 1 H, *J* = 3.7 Hz, H-1), 5.62 (t, 1 H, *J* = 9.9 Hz, H-3), 5.15 (t, 1 H, *J* = 9.8 Hz, H-4), 5.07 (dd, 1 H, *J* = 10.3, 3.8 Hz, H-2), 4.28 (dd, 1 H, *J* = 12.3, 3.7 Hz, H-6a), 4.25–4.21 (m, 1 H, H-5), 4.07 (dd, 1 H, *J* = 12.3, 1.9, H-6b), 2.50 (s, 3 H, SCH_3), 2.08, 2.02, 2.01(9), 2.01 (4 s, 12 H, OAc).

^{13}C NMR: δ = 175.75, 170.73, 170.17, 170.10, 169.58, 90.36, 70.62, 69.61, 69.26, 68.00, 61.44, 20.70, 20.65, 20.62, 13.71.

HRMS: *m*/*z* calcd for $C_{16}H_{25}N_2O_9S$ (M + H)$^+$: 421.1281; found: 421.1282.

β Anomer

^{1}H NMR: δ = 5.29 (t, 1 H, *J* = 9.4 Hz, H-3), 5.08 (t, 1 H, *J* = 9.7 Hz, H-4), 5.02–4.99 (m, 2 H, H-1, H-2), 4.24 (br d, 1 H, *J* = 11.8 Hz, H-6a), 4.13 (br d, 1 H, *J* = 12.4, H-6b), 3.81 (ddd, 1 H, *J* = 10.1, 4.5, 2.5 Hz, H-5), 2.34 (s, 3 H, SCH_3), 2.07, 2.04, 2.03, 2.01 (4 s, 12 H, OAc).

^{13}C NMR: δ = 170.68, 170.19, 169.50, 162.80, 83.20, 73.24, 72.97, 71.34, 68.31, 61.95, 20.74, 20.69, 20.62, 20.59, 13.0

HRMS: *m*/*z* calcd for $C_{16}H_{25}N_2O_9S$ (M + H)$^+$: 421.1281; found: 421.1282.

Compounds 3; General Procedures

To a solution of Fmoc-protected β-amino acid (1.1 equiv) and HOBt (1.1 equiv) in DMA (0.6 mL) and CH_2Cl_2 (5 mL) was added DIC (1.1 equiv). It was stirred for 10 min before being added to an ice-cooled solution of **2** (1 equiv) and *i*-Pr_2NEt (1.1 equiv) in CH_2Cl_2 (5 mL). The resulting solution was allowed to stir at r.t. for 24 h. The mixture was concentrated and by-product urea was removed by precipitation using hexane. Purification of the residue on preparative TLC (50% EtOAc in hexane) afforded pure **3.**

(*S*)-*N*-(2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl)-*N*′-[2-(9-fluorenylmethylcarbonyl)amino-3-(4-methylphenyl)propylcarbonyl]methylisothiourea (3a)

Compound **3a** was prepared from **2a** (64 mg, 0.15 mmol) and Fmoc-(*S*)-3-amino-4-(4-methylphenyl)butyric acid (70 mg, 0.17 mmol).

Yield: 80 mg (65%); white foam.

^{1}H NMR: δ = 12.12 (s, 1 H, NHCO), 7.69 (d, 2 H, *J* = 7.5 Hz, Fmoc), 7.49–7.47 (m, 2 H, Fmoc), 7.33 (t, 2 H, *J* = 7.4 Hz, Fmoc), 7.23 (t, 2 H, *J* = 7.4 Hz, Fmoc), 7.09–6.92 (m, 4 H, C_6H_4), 6.31 (br s, 1 H, H-1), 5.46 (br s, 1 H, H-4), 5.41 (br d, 1 H, *J* = 11.1 Hz, H-3), 5.26 (dd, 1 H, *J* = 10.7, 3.2 Hz, H-2), 5.22 (d, 1 H, *J* = 10.2 Hz, FmocNH), 4.35 (t, 1 H, *J* = 6.4 Hz, H-5), 4.35–4.24 (m, 2 H, OC*H*$_2$CH), 4.20–4.08 (m, 2 H, NC*H*, OCH_2C*H*), 4.08–3.98 (m, 2 H, H-6a. H-6b), 2.94–2.75 (m, 2 H, C*H*$_2$C$_6$H$_4$), 2.65–2.45 (m, 2 H, CH_2CO), 2.39 (s, 3 H, SCH_3), 2.24 (s, 3 H, C*H*$_3$C$_6$H$_4$), 2.09, 1.96, 1.94 (3 s, 12 H, OAc).

^{13}C NMR: δ = 174.04, 170.31, 170.11, 169.65, 155.60, 143.82, 141.27, 136.53, 133.90, 129.43, 129.04, 127.64, 127.00, 125.04, 119.93, 91.64, 68.55, 67.39, 67.33, 66.66, 61.02, 49.39, 47.18, 39.95, 39.44, 21.01, 20.68, 20.63, 14.93.

HRMS: *m*/*z* calcd for $C_{42}H_{48}N_3O_{12}S$ (M + H)$^+$: 818.2959; found: 818.2960.

(*S*)-*N*-(2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl)-*N*′-[2-(9-fluorenylmethylcarbonyl)aminoethylcarbonyl]methylisothiourea (3b)

Compound **3b** was prepared from **2a** (95 mg, 0.23 mmol) and Fmoc-β-alanine (77 mg, 0.25 mmol).

Yield: 90 mg (56%); white foam.

^{1}H NMR: δ = 12.20 (br s, 1 H, NHCO), 7.69 (d, 2 H, *J* = 7.5 Hz, Fmoc), 7.51 (d, 2 H, *J* = 7.3 Hz, Fmoc), 7.33 (t, 2 H, *J* = 7.5 Hz, Fmoc), 7.24 (t, 2 H, *J* = 7.3 Hz, Fmoc), 6.32 (d, 1 H, *J* = 3.1 Hz, H-1), 5.46 (br s, 1 H, H-4), 5.45–5.35 (m, 1 H, H-3), 5.29–5.23 (m, 2 H, NHFmoc, H-2), 4.33 (d, 2 H, *J* = 6.8 Hz, OC*H*$_2$CH), 4.38–4.32 (hidden, 1 H, H-5), 4.18–4.10 (m, 1 H, OCH_2C*H*), 4.08–4.01 (m, 2 H, H-6), 3.48–3.41 (m, 2 H, NCH_2), 2.40 (br s, 2 H, CH_2CO), 2.09 (s, 3 H, SCH_3), 1.97, 1.95, 1.94 (3 s, 12 H, OAc).

^{13}C NMR: δ = 174.07, 170.32, 170.13, 156.29, 143.81, 141.28, 127.68, 127.01, 125.01, 119.96, 91.73, 68.59, 67.38, 67.32, 66.71, 61.01, 47.18, 36.97, 35.89, 20.64, 14.93.

HRMS: *m*/*z* calcd for $C_{34}H_{40}N_3O_{12}S$ (M + H)$^+$: 714.2332; found: 714.2333.

(*S*)-*N*-(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)-*N*′-[2-(*N*-fluorenylmethylcarbonyl)amino-3-(4-methylphenyl)propylcarbonyl]methylisothiourea (3c)

Compound **3c** was prepared from **2b** (100 mg, 0.24 mmol) and Fmoc-(*S*)-3-amino-4-(4-methylphenyl)butyric acid (110 mg, 0.26 mmol).

Yield: 133mg (68%); white foam.

^{1}H NMR: δ = 12.12, (br s, 1 H, NH), 7.69 (d, 2 H, *J* = 7.6 Hz, Fmoc), 7.49–7.47 (m, 2 H, Fmoc), 7.33 (t, 2 H, *J* = 7.4 Hz, Fmoc), 7.24 (t, 2 H, *J* = 7.4 Hz, Fmoc), 7.06–6.98 (m, 4 H, C_6H_4), 6.27 (d, 1 H, *J* = 2.6 Hz, H-1), 5.54 (t, 1 H, *J* = 9.8 Hz, H-3), 5.20 (d, 1 H, *J* = 8.1 Hz, NH), 5.10 (t, 1 H, *J* = 9.9 Hz, H-4), 5.03 (dd, 1 H, *J* = 10.3, 3.5 Hz, H-2), 4.29 (br s, 2 H, OC*H*$_2$CH), 4.22 (dd, 1 H, *J* = 12.6, 3.5 Hz, H-6a), 4.13–4.12 (m, 3 H, H-5, NC*H*, OCH_2C*H*), 4.01 (br d, 1 H, *J* = 13.4 Hz, H-6b), 2.94–2.75 (m, 2 H, C*H*$_2$C$_6$H$_4$), 2.65–2.46 (m, 2 H, CH_2CO), 2.41 (s, 3 H, SCH_3), 2.24 (s, 3 H, $C_6H_4CH_3$), 2.01, 1.98, 1.97, 1.96 (4 s, 12 H, OAc).

^{13}C NMR: δ = 174.26, 170.62, 170.19, 169.95, 169.67, 169.47, 159.00, 155.62, 143.84, 141.29, 136.56, 133.91, 129.45, 129.05, 127.66, 127.02, 125.06, 119.94, 91.00, 69.82, 69.57, 69.41, 67.83, 66.65, 61.29, 49.41, 47.20, 40.00, 39.45, 21.02, 20.68, 20.58, 14.98.

HRMS: *m*/*z* calcd for $C_{42}H_{48}N_3O_{12}S$ (M + H)$^+$: 818.2960; found: 818.2947.

(*S*)-*N*-(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)-*N*′-[2-(9-fluorenylmethylcarbonyl)amino-4-phenylbutylcarbonyl]methylisothiourea (3d)

Compound **3d** was prepared from **2b** (130 mg, 0.31 mmol) and Fmoc-(*S*)-3-amino-5-phenylpentanoic acid (142 mg, 0.34 mmol).

Yield: 169 mg (67%); white foam.

^{1}H NMR: δ = 12.10 (s, 1 H, NHCO), 7.66 (d, 2 H, *J* = 7.4 Hz, Fmoc), 7.50 (d, 2 H, *J* = 7.0 Hz, Fmoc), 7.29 (dd, 2 H, *J* = 10.9, 7.2 Hz, Ph), 7.21 (t, 2 H, *J* = 7.3 Hz, Fmoc), 7.18 (t, 2 H, *J* = 7.0 Hz, Fmoc), 7.10–7.04 (m, 3 H, Ph), 6.26 (d, 1 H, *J* = 3.1 Hz, H-1), 5.53 (t, 1 H, *J* = 9.9 Hz, H-3), 5.28 (d, 1 H, *J* = 9.6 Hz, FmocNH), 5.09 (t, 1 H, *J* = 9.9 Hz, H-4), 5.01 (dd, 1 H, *J* = 10.0, 3.4 Hz, H-2), 4.33 (d, 2 H, *J* = 6.2 Hz, OC*H*$_2$CH), 4.19 (dd, 1 H, *J* = 12.7, 3.5 Hz, H-6a), 4.13–4.11 (m, 2 H, OCH_2C*H*, H-5), 3.98 (br d, 1 H, *J* = 11.1 Hz, H-6b), 3.94–3.91 (m, 1 H, NHC*H*), 2.65–2.50 (m, 4 H, CH_2CO,

CH_2Ph), 2.35 (s, 3 H, SCH_3), 1.98, 1.95, 1.94, 1.93 (4 s, 12 H, OAc), 1.92–1.75 (m, 2 H, CH_2CH_2Ph).

^{13}C NMR: δ = 174.02, 170.48, 170.05, 169.83, 169.41, 169.34, 155.68, 143.74, 143.65, 141.16, 140.76, 128.35, 128.20, 127.54, 126.89, 125.96, 124.89, 124.77, 119.82, 90.84, 69.69, 69.42, 69.27, 67.69, 66.38, 61.16, 47.85, 47.11, 41.57, 35.61, 32.35, 20.54, 20.45, 14.80

HRMS: *m*/*z* calcd for $C_{42}H_{48}N_3O_{12}S$ (M + H)$^+$: 818.2959; found: 818.2951.

(*S*)-*N*-(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)- *N*′-[2-(9-fluorenylmethylcarbonyl)amino-3-(4-nitrophenyl)propylcarbonyl]methylisothiourea (3e)

Compound **3e** was prepared from **2b** (130 mg, 0.31 mmol) and Fmoc-(*S*)-3-amino-4-(4-nitrophenyl)-butyric acid (152 mg, 0.34 mmol).

Yield: 102 mg (39%); white foam.

^{1}H NMR: δ = 12.19 (s, 1 H, NHCO), 8.07 (d, 2 H, *J* = 7.6 Hz, C_6H_4), 7.69 (d, 2 H, *J* = 7.5 Hz, Fmoc), 7.45 (br s, 2 H, Fmoc), 7.33 (t, 2 H, *J* = 7.5 Hz, Fmoc), 7.31–7.23 (m, 4 H, Fmoc, C_6H_4), 6.29 (br s, 1 H, H-1), 5.54 (t, 1 H, *J* = 9.4 Hz, H-3), 5.20 (br s, 1 H, Fmoc-NH), 5.11 (t, 1 H, *J* = 9.9 Hz, H-4), 5.03 (br d, 1 H, *J* = 7.2 Hz, H-2), 4.33 (br s, 2 H, OCH_2CH), 4.23 (dd, 1 H, *J* = 12.5, 3.2 Hz, H-6a), 4.15–4.12 (m, 3 H, H-5, C*H*C_6H_4, OCH_2C*H*), 4.02 (br d, 1 H, *J* = 12.1 Hz, H-6b), 3.07–2.90 (m, 2 H, C$H_2C_6H_4$), 2.72–2.55 (m, 2 H, CH_2CO), 2.42 (s, 3 H, SCH_3), 2.02, 1.98, 1.97 (3 s, 12 H, OAc).

^{13}C NMR: δ = 174.11, 170.62, 170.20, 169.94, 169.45, 169.19, 155.50, 146.95, 145.06, 143.63, 141.33, 130.00, 127.75, 127.02, 124.89, 123.88, 120.01, 91.06, 69.77, 69.60, 69.42, 67.78, 66.49, 61.23, 48.99, 47.14, 40.24, 39.50, 20.67, 20.57, 15.00.

HRMS: *m*/*z* calcd for $C_{41}H_{45}N_4O_{12}S$ (M + H)$^+$: 849.2653; found: 849.2659.

Compounds 4; General Procedures

To **3** (1 equiv) in freshly distilled THF (0.5 mL) was added DBU (0.7% equiv). The mixture was stirred at r.t. for 1 h. The mixture was concentrated and purified on preparative TLC (33% EtOAc in hexane) to afford pure **4**.

(*S*)-2-(2′,3′,4′,6′-Tetra-*O*-acetyl-α-D-galactopyranosyl)amino-6-(4-methylbenzyl)-5,6-dihydro-4-pyrimidinone (4a)

Compound **4a** was prepared from **3a** (20 mg, 0.025 mmol).

Yield: 6 mg (45%); white foam.

^{1}H NMR: δ = 7.10 (d, 2 H, *J* = 7.8 Hz, C_6H_4), 7.00 (d, 2 H, *J* = 8.0 Hz, C_6H_4), 6.23 (d, 1 H, *J* = 3.7 Hz, H-1′), 5.42 (dd, 1 H, *J* = 3.2, 1.1 Hz, H-4′), 5.38 (dd, 1 H, *J* = 10.9, 3.3 Hz, H-3′), 5.24 (dd, 1 H, *J* = 10.8, 3.7 H-2′), 4.37 (t, 1 H, *J* = 6.8 Hz, H-5′), 4.02 (d, 2 H, *J* = 6.6 Hz, H-6a′, H-6b′), 3.92–3.86 (m, 1 H, H-6), 2.86 (dd, 1 H, *J* = 13.8, 6.1 Hz, C$H_2C_6H_4$), 2.78 (dd, 1 H, *J* = 13.8, 7.7 Hz, C$H_2C_6H_4$), 2.70 (dd, 1 H, *J* = 16.8, 5.1 Hz, H-5a), 2.52 (dd, 1 H, *J* = 16.8, 9.6 Hz, H-5b), 2.27 (s, 3 H, $C_6H_4CH_3$), 2.08, 1.98, 1.94, 1.91 (4 s, 12 H, OAc).

^{13}C NMR: δ = 170.36, 170.27, 170.18, 169.79, 167.27, 161.79, 137.49, 131.54, 129.89, 128.99, 90.76, 68.25, 67.63, 67.37, 66.76, 61.13, 50.16, 40.47, 35.78, 21.07, 20.78, 20.68, 20.63.

HRMS: *m*/*z* calcd for $C_{26}H_{34}N_3O_{10}$ (M + H)$^+$: 548.2245; found: 548.2422.

(*S*)-2-(2′,3′,4′,6′-Tetra-*O*-acetyl-α-D-galactopyranosyl)amino-5,6-dihydro-4-pyrimidinone (4b)

Compound **4b** was prepared from **3b** (50 mg, 0.07 mmol).

Yield: 11 mg (35%); colorless foam.

^{1}H NMR: δ = 6.22 (d, 1 H, *J* = 3.5 Hz, H-1′), 5.40 (dd, 1 H, *J* = 3.2, 1.3 Hz, H-4′), 5.36 (dd, 1 H, *J* = 10.9, 3.3 Hz, H-3′), 5.22 (dd, 1 H, *J* = 10.9, 3.5 Hz, H-2′), 4.63 (t, 1 H, *J* = 6.7 Hz, H-5′), 4.05 (d, 2 H, *J* = 6.7 Hz, H-6′a, H-6′b), 3.69 (ddd, 1 H, *J* = 13.2, 10.5, 5.4 Hz, H-6a), 3.58 (dt, 1 H, *J* = 13.1, 6.4 Hz, H-6b), 2.75 (dt, 1 H, *J* = 16.9, 5.4 Hz, H-5a), 2.66 (ddd, *J* = 16.9, 10.4, 6.5 Hz, H-5b), 2.09, 1.98, 1.97, 1.90, (4 s, 12 H, OAc).

^{13}C NMR: δ = 170.49, 170.25, 169.86, 168.62, 161.92, 90.70, 68.19, 68.11, 66.93, 61.36, 37.04, 30.42, 20.82, 20.75, 20.67, 20.63.

HRMS: *m*/*z* calcd for $C_{18}H_{26}N_3O_{10}$ (M + H)$^+$: 444.1618; found: 444.1614.

(*S*)-2-(2′,3′,4′,6′-Tetra-*O*-α-acetyl-α-D-glucopyranosyl)amino-6-(4-methylbenzyl)-5,6-dihydro-4-pyrimidinone (4c)

Compound **4c-I** (8.4 mg, 31%, colorless foam) and **4c-II** (9 mg, 34%, colorless foam) were prepared from **3c** (40 mg, 0.05 mmol).

Compound 4c-I

^{1}H NMR: δ = 7.15 (d, 2 H, *J* = 7.8 Hz, C_6H_4), 7.06 (d, 2 H, *J* = 8.0 Hz, C_6H_4), 6.26 (d, 1 H, *J* = 3.8 Hz, H-1′), 5.56 (t, 1 H, *J* = 9.9 Hz, H-3′), 5.14 (t, 1 H, *J* = 9.9 Hz, H-4′), 5.07 (dd, 1 H, *J* = 10.3, 3.8 Hz, H-2′), 4.26 (dd, 1 H, *J* = 12.5, 3.5 Hz, H-6a′), 4.18 (dt, 1 H, *J* = 10.3, 2.7 Hz, H-5′), 4.05 (dd, 1 H, *J* = 12.5, 2.1 Hz, H-6b′), 3.97–3.91 (m, 1 H, H-6), 2.92 (dd, 1 H, *J* = 13.8, 6.1 Hz, C$H_2C_6H_4$), 2.83 (dd, 1 H, *J* = 13.8, 7.8 Hz, C$H_2C_6H_4$), 2.76 (dd, 1 H, *J* = 16.8, 5.1 Hz, H-5a), 2.57 (dd, 1 H, *J* = 16.8, 9.6 Hz, H-5b), 2.33 (s, 3 H, $C_6H_4CH_3$), 2.07, 2.03, 2.00, 1.99 (4 s, 12 H, OAc).

^{13}C NMR: δ = 170.70, 170.03, 170.00, 169.59, 167.16, 161.59, 137.54, 131.47, 129.90, 128.98, 90.12, 69.96, 69.46, 69.24, 67.87, 61.35, 50.17, 40.46, 35.79, 21.07, 20.71, 20.67, 20.57.

HRMS: *m*/*z* calcd for $C_{26}H_{34}N_3O_{10}$ (M + H)$^+$: 548.2246; found: 548.2243.

Compound 4c-II

^{1}H NMR: δ = 7.09 (d, 2 H, *J* = 7.5 Hz, C_6H_4), 6.97 (d, 2 H, *J* = 7.8 Hz, C_6H_4), 5.61 (br s, 1 H, NH), 5.44 (br s, 1 H, H-3′), 5.23 (br s, 1 H, H-1′), 4.94 (t, 1 H, J = 9.7 Hz, H-4′), 4.87 (br d, 1 H, *J* = 6.5 Hz, H-2′), 4.00 (br d, 1 H, *J* = 10.7 Hz, H-6a′), 3.82–3.72 (br m, 1 H, H-5′), 3.75–3.65 (br m, 1 H, H-6), 3.38 (br d, 1 H, *J* = 11.8 Hz, H-6b′), 2.82 (br d, 1 H, *J* = 11.1 Hz, C$H_2C_6H_4$), 2.65 (br d, 1 H, *J* = 15.6 Hz, H-5a), 2.63–2.57 (m, 1 H, C$H_2C_6H_4$), 2.40 (dd, 1 H, *J* = 16.7, 9.5 Hz, H-5b), 2.25 (s, 3 H, $C_6H_4CH_3$), 2.02, 1.99, 1.95, 1.93 (4 s, 12 H, OAc).

^{13}C NMR: δ = 170.35, 170.13, 169.98, 169.60, 137.29, 132.60, 129.83, 128.88, 79.91, 70.65, 70.09, 68.38, 67.48, 61.86, 50.85, 41.04, 36.85, 20.97, 20.84, 20.68, 20.59.

HRMS: *m*/*z* calcd for $C_{26}H_{34}N_3O_{10}$ (M + H)$^+$: 548.2246; found: 548.2247.

(*S*)-2-(2′,3′,4′,6′-Tetra-*O*-acetyl-α-D-glucopyranosyl)amino-6-ethylphenyl-5,6-dihydro-4-pyrimidinone (4d)

Compound 4d-1 (11.2 mg, 34%, white foam) and **4d-II** (7.2 mg, 22%, white foam) were prepared from **3d** (50 mg, 0.06 mmol).

Compound 4d-I

^{1}H NMR: δ = 7.25 (t, 2 H, *J* = 7.3 Hz, Ph), 7.18 (t, 1 H, *J* = 7.4 Hz, Ph), 7.11 (d, 2 H, *J* = 7.0 Hz, Ph), 6.23 (d, 1 H, *J* = 3.8 Hz, H-1′), 5.52 (t, 1 H, *J* = 9.9 Hz, H-3′), 5.10 (t, 1 H, *J* = 9.8 Hz, H-4′), 5.02 (dd, 1 H, *J* = 10.3, 3.8 Hz, H-2′), 4.23 (dd, 1 H, *J* = 12.3, 3.5 Hz, H-6a′), 4.21–4.17 (m, 1 H, H-5′), 4.02 (dd, 1 H, *J* = 12.2, 1.7 Hz, H-6b′), 3.68–3.61 (m, 1 H, H-6), 2.75 (dd, 1 H, *J* = 16.8, 5.4 Hz, H-5a), 2.70–2.63 (m, 2 H, CH_2Ph), 2.50 (dd, 1 H, *J* = 16.8, 8.4 Hz, H-5b), 2.02, 1.97, 1.95, 1.94 (4 s, 12 H, OAc) 1.97–1.82 (m, 2 H, CH_2CH_2Ph).

^{13}C NMR: δ = 170.71, 170.01, 169.92, 169.56, 167.32, 161.92, 139.19, 128.86, 128.19, 126.71, 90.18, 69.93, 69.47, 69.23, 67.86, 61.37, 47.78, 35.93, 35.83, 31.29, 20.73, 20.66, 20.58.

HRMS: *m*/*z* calcd for $C_{26}H_{34}N_3O_{10}$ (M + H)$^+$: 548.2245; found: 548.2248.

Compound 4d-II

^{1}H NMR: δ = 7.24 (t, 2 H, *J* = 7.3 Hz, Ph), 7.16 (t, 1 H, *J* = 7.3 Hz, Ph), 7.10 (d, 2 H, *J* = 7.3 Hz, Ph), 5.68 (br s, 1 H, NH), 5.48 (t, 1 H, *J* = 9.8 Hz, H-3′), 5.22 (d, 1 H, *J* = 4.3 Hz, H-1′), 4.98 (t, 1 H, *J* = 9.7 Hz, H-4′), 4.89 (dd, 1 H, *J* = 10.3, 4.0 Hz, H-2′), 4.08–4.03 (m, 2 H, H-6a′, H-6b′), 3.94–3.91 (m, 1 H, H-5′), 3.56–3.50 (m, 1 H, H-6), 2.66–2.62 (m, 3 H, C*H*$_2$Ph, H-5a), 2.38 (dd, 1 H, *J* = 16.3, 7.6 Hz, H-5b), 2.11, 1.96, 1.95 (3 s, 12 H, OAc), 1.88–1.79 (m, 2 H, C*H*$_2$CH$_2$Ph).

^{13}C NMR: δ = 170.43, 170.19, 169.99, 169.68, 139.82, 128.78, 128.21, 126.57, 79.46, 70.47, 70.13, 68.72, 67.70, 62.33, 48.46, 36.43, 36.28, 31.55, 20.83, 20.69, 20.64.

HRMS: *m*/*z* calcd for $C_{26}H_{34}N_3O_{10}$ (M + H)$^+$: 548.2246; found: 548.2245.

(*S*)-2-(2′,3′,4′,6′-Tetra-*O*-acetyl-α-D-glucopyranosyl)amino-6-(4-nitrobenzyl)-5,6-dihydro-4-pyrimidinone (4e)

Compound **4e** was prepared from **3e** (20 mg, 0.024 mmol).

Yield: 9 mg (66%); white foam.

^{1}H NMR: δ = 8.18 (d, 2 H, *J* = 8.6 Hz, C_6H_4), 7.23 (d, 2 H, *J* = 8.6 Hz, C_6H_4), 6.19 (d, 1 H, *J* = 3.7 Hz, H-1′), 5.51 (t, 1 H, *J* = 9.9 Hz, H-3′), 5.09 (t, 1 H, *J* = 9.9 Hz, H-4′), 5.01 (dd, 1 H, *J* = 10.3, 3.8 Hz, H-2′), 4.20 (dd, 1 H, *J* = 12.5, 3.4, H-6a′), 4.16–4.11 (m, 1 H, H-5′), 4.00 (dd, 1 H, *J* = 12.6, 2.1 Hz, H-6b′), 4.01–3.95 (m, 1 H, H-6), 3.00 (d, 2 H, *J* = 6.9 Hz, C*H*$_2$C$_6$H$_4$), 2.76 (dd, 1 H, *J* = 16.7, 5.3, H-5a), 2.54 (dd, 1 H, *J* = 16.7, 8.6 Hz, H-5b), 2.01, 1.97, 1.95, 1.94 (4 s, 12 H, OAc).

^{13}C NMR: δ = 170.67, 169.97, 169.92, 169.51, 166.35, 157.65, 147.60, 142.13, 130.13, 124.42, 90.34, 69.87, 69.44, 69.34, 67.82, 61.31, 49.63, 40.59, 35.57, 20.71, 20.65, 20.58.

HRMS: *m*/*z* calcd for $C_{25}H_{31}N_4O_{12}$ (M + H)$^+$: 579.1939; found: 579.1934.

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