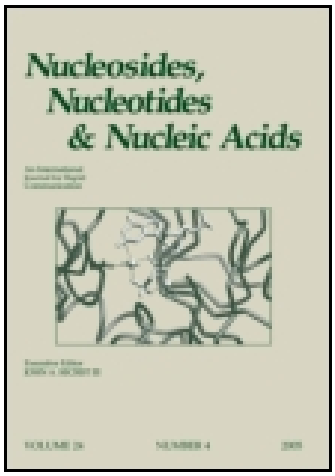

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NEW GLYCOSYL-(CARBOXAMIDE)-1,2,3-TRIAZOLE-N-NUCLEOSIDES: SYNTHESIS AND ANTITUMOR ACTIVITY

Najim A. Al-Masoudi [a] & Yaseen A. Al-Soud [b]
[a] University of Konstanz , P.O. Box 5560, Shinagawa-ku, Konstanz, D-78434, Germany
[b] Department of Chemistry , College of Science , University of Al al-Bayt , Al-Mafraq, Jordan
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NEW GLYCOSYL-(CARBOXAMIDE)-1,2,3-TRIAZOLE-*N*-NUCLEOSIDES: SYNTHESIS AND ANTITUMOR ACTIVITY

Najim A. Al-Masoudi[1],* and Yaseen A. Al-Soud[2]

[1]Faculty of Chemistry, University of Konstanz,
P.O. Box 5560, D-78434 Konstanz, Germany
E-mail: Najim.Al-Masoudi@uni-konstanz.de
[2]Department of Chemistry, College of Science,
University of Al al-Bayt, Al-Mafraq, Jordan

Dedicated to Professor W. Pfleiderer on the occasion of his 75th birthday.

ABSTRACT

A series of potential bioactive compounds, 1-glucopyranosyl-1,2,3-triazole-4,5-dimethylcarboxylate, 1-glucopyranosyl-1,2,3-triazole-4,5-*N*-dicarboxamide,-dialkyl-dicarboxamide-*N*-nucleosides and 6-amino-4*H*-1-(β-D-glucopyranosyl)-8-hydroxy-1,2,3-triazolo[4,5-*e*][1,3]-diazepin-4-one, were synthesized. Primary activity screening of the novel nucleosides showed poor or no anticancer activity against breast, lung and CNS tumors.

Several triazolated compounds and their derivatives are devoid of significant cytotoxic properties and have been extensively studied in connection with cancer chemotherapy. These compounds, such as 1-β-D-glycosyl-(halomethyl)-1,2,3-triazoles **1a,b**[1] (Fig. 1) exhibited anticancer activity, in vitro, ($ED_{50} = 6.0$ and 3.0 μg/mL, respectively) against HeLa [Ehrlich carcinoma ascited (ECA)][2] tumor, with the cytostatic activity dependment on the $-CH_2X$ group attached to the triazole ring and on the N-1 substituent.

*Corresponding author.

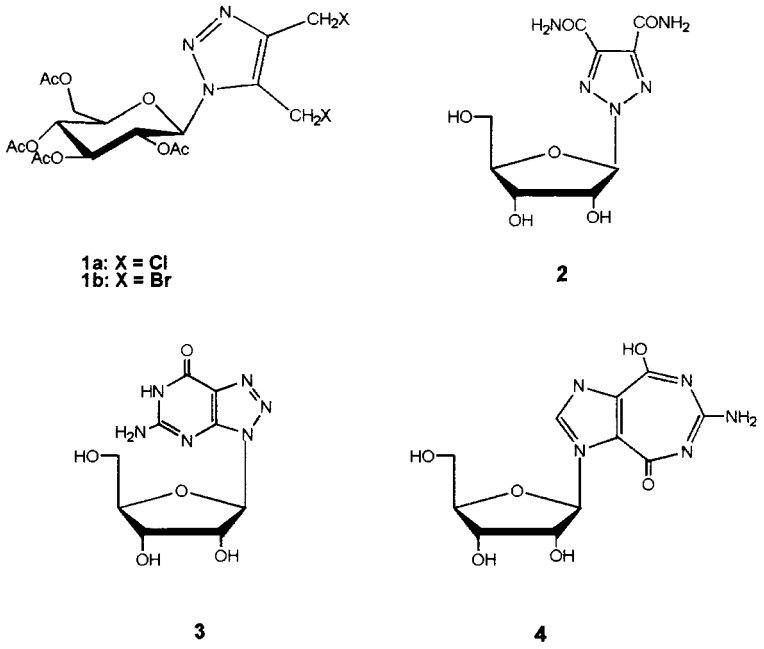


Figure 1.

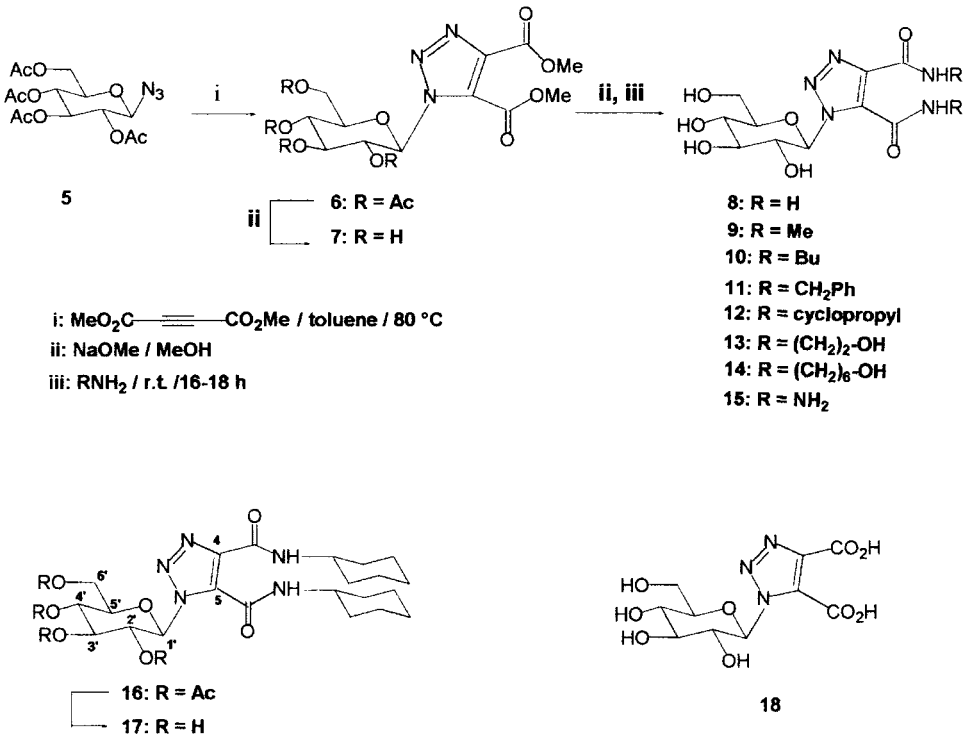
D-β-Glycosyl-1,2,3-trizaol-4,5-dicarboxamide **2**[3] (Fig. 1) is another compound of this class which showed relatively low cytotoxic activity against different tumor cell lines [human B-lymphoblast (WI-L2), $ID_{50} = 41\,\mu M$; human myeloid leukemia (K562), $ID_{50} = 26\,\mu M$; and HL-60, $ID_{50} = 32\,\mu M$] in comparison with therpeutically useful cytotoxic agents, such as cytosine arabinoside and 5-fluorouracil (ID_{50} values of 0.002 and 0.01 μM, respectively), meanwhile **2** was found to be inducer of cellular differentiation of HL-60 in the range 30–60 μM. The analysis study of Revankar et al.[3] on various antiviral ribonucleosides, using computor-aided receptor-modeling procedure,[4] asserted the importance of a hydrogen-bonding carbamoyl group[5] in drug-receptor interactions. In the last decade, Robins et al.[6] have reported the synthesis of 8-azainosine (3-β-D-ribofuranosyl-ν-1,2,3-triazolo[4,5-*d*]pyrimid-7-one) **3** (Fig. 1) with good activity against L-1210 lymphoid leukemia and adenocarcinoma 755 in experimental mice. No activity was observed with some 5′-(1,2,3-triazol-1-yl)-5′-deoxythymidine derivatives[7] against thymidylate kinase, and modification of the anti-AIDS drug AZT to the 3′-(substituted-1,2,3-triazol-1-yl)thymidine[8] did not show activity against HIV-1 in comparison with AZT itself. Townsend et al.[9] have reported two analogues of the nucleoside antibiotic conformycin, one bearing a 1,2,3-triazole residue fused to an expanded ring, namely, 2-aza-conformycin, has been assayed as an inhibitor of the enzyme adenosine deaminase.

Such type of compounds containing imidazo[4,5-*e*]diazepin-4-one moiety **4**[10] (Fig. 1) have been prepared recently and exhibited remarkable activity against hepatitis B virus.

The common method for the synthesis of 1,2,3-triazole compounds involves a 1,3-dipolar cycloaddition from the acetylenic and sugar precursors. Using this method, numerous glycosylated-1,2,3-triazole compounds have been reported in the literature.[11–20] Other approaches to the synthesis of such nucleosides[21–23] have involved coupling of α-cyanoacetamide with a sugar azide in the presence of base. New mimetics of neamine e.g.: 4-(1,2,3-triazol-1-yl)-2-deoxystreptamine were synthesized for RNA recognition via a simple approach[24] involving the reaction of a 4-chloromethyl-2-deoxystreptamine derivative with the sodium salt of 1,2,3-triazole. As part of our program for the search of new anticancer agents, we have studied the synthesis and cytostatic activity of some new glycosylated-4,5-disubstituted carboxamides of 1,2-3-triazole as well as the triazolo-diazepin-4-one derivative.

RESULTS AND DISCUSSION

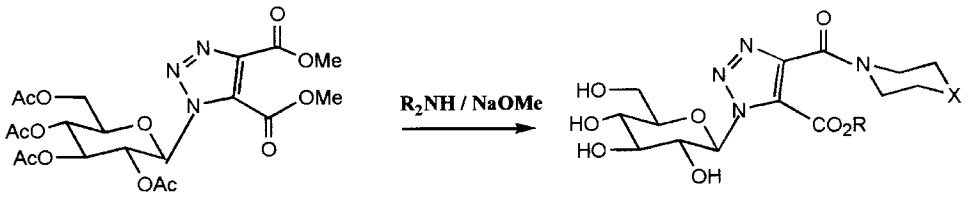
The tetra-*O*-acetate of β-D-glucose azide **5**[25,26] served as the starting material for the synthesis of the triazole *N*-1-nucleosides. Reaction of **5** with dimethylacetylenedicarboxylate (DMAD) in refluxing toluene led to the 1,3-dipolar cycloaddition product **6** in 84% yield, which was deprotected to give the desired triazole **7** in only a modrate yield of 64%. Compound **6** was converted to the 4,5-dicarboxamide derivatives **8–14** in 75–90% yield, (except **12**, obtained in a moderate yield of 65%), by direct treatment at room temperature with 16% NH_3-MeOH, *n*-$MeNH_2$, *n*-butylamine, benzylamine, cyclopropylamine, ethanolamine, and 1-amino-6-hexanol. Treatment with aqueous hydrazine gave the bis-hydrazide **15** in 75% yield. Similar treatment with cyclohexyl amine led to the protected nucleoside **16** in 40% yield, followed by deblocking with NaOMe solution to give the free nucleoside **17** in 64%. Alkaline hydrolysis of **6** with 2.5 N NaOH at 80°C for 4 h resulted in the formation of the sodium carboxylic salt, which on neutralization with 1 N HCl gave the free acid **18** in 60% yield (Sch. 1). Some cyclic *sec*-amines were selected for synthesis as potentially promising nucleosides carrying new carboxamide residues. Thus, reaction of piperazine, *N*-methyl-piperazine, morpholine, and thiomorpholinein the presence of NaOMe with **6** at room temperature led to the 4-monocarboxamide derivatives, associated with hydrolysis of the 5-ester group to the sodium carboxylic salts **19**, **21**, and **22** in 93, 38, and 49% yields, respectively. Altenativelly, neutralization of the salt produced from the *N*-methylpiperazine, with 1N HCl gave the free acid **20** in 41% yield. The formation of monocarboxamide substitutent at C-4 might be explained in term of the steric factor of the cyclic *sec*-amines. However, the substitution at C-4 was confirmed by comparison of the



Scheme 1.

^{13}C-NMR data with those of 1,2,3-triazole derivatives which reported previousley.[1,27,28] (Sch. 2).

Reaction of **6** with guanidine, generated freely in the presence of NaOMe at room temperature followed by neutralization with 1 N HCl gave the crude 6-amino-4*H*-1-(β-D-glucopyranosyl)-8-hydroxy-1,2,3-triazolo[4,5-*e*][1,3]diazepin-4-one **23**. Acetylation of this product led, after chromatographic purification, to the tetraacetate derivative **24** in 49% as a pure faom. Deblocking of **24** with NaOMe at room temperature gave, after purification, the pure nucleoside **23** in 59% (Sch. 3). The structures of the triazoles **8–24** were confirmed by mass spectra, ^{1}H NMR and ^{13}C NMR signals, especially those of the glucopyranose ring, the amido-alkane and alkanol groups, were assigned by ^{1}H-^{1}H and ^{1}H-^{13}C COSY spectra as well as the HMQC spectra.[29] The β-configuration of the glucopyranosyl ring of all the products was confirmed by the large H-1-H-2 coupling constants ($J_{1',2'} = 9.0-9.5$ Hz), meanwhile the $^{4}C_1$ conformation of the sugar moiety was established from the large $J_{4',5'}$ couplings (9.5–9.9 Hz), and these data were measured from compounds **6**, **16** and **24**. H-2′ appeared as triplets,or multiplets with large coupling constants ($J_{2',3'} = 9.0-9.4$ Hz), while the other sugar protons appeared as multiplets. The proton spin system of **13–18**, **21**, **22** and **24** was



6

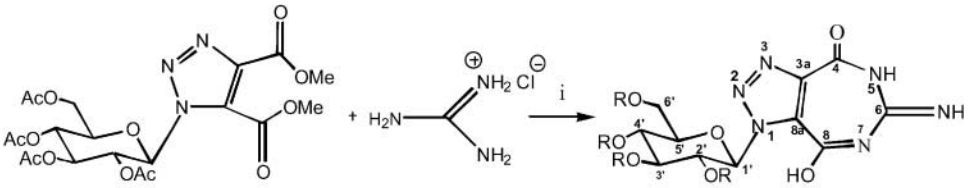
19: X = N; R = Na

20: X = N-Me; R = H

21: X = O; R = Na

22: X = S; R = Na

Scheme 2.



6

i: NaOMe/MeOH

23: R = H

24: R = Ac

Scheme 3.

further identified from the DFQ-COSY[30] spectra, where the sugar protons (H-1′-H-6′a,b) were correlated to the singlets of C-1′-C-6′). Compound **14** has been selected for the structural assignment by the above mentioned NMR study. The multiplets of $2\times CH_2OH$ and $2\times NCH_2$ of the bis(hexan-6-olyl)carboxamide substituents at δ_H 3.37 and δ_H 3.27 were correlated to the singlets at δ_C 60.3 and δ_C 8.6, respectively. The (CH_2-2″)a,b,-(CH_2-5″)a,b were found as multiplets at δ_H 1.29, 1.30, 1.53, and 1.40, respectively and correlated to the singlets at 25.9, 24.9, 28.4 and 32.1 for C-2″a,b; C-3″a,b; C-4″a,b and C-5″a,b, respectively. Nucleosides **23** and **24** were characterized by ^{1}H-, ^{13}C- and HMQC NMR and mass spectral data. It is expected that several tautomeric structures are possible for **23** and **24**, only one of them has been shown in Sch. 3.

Antitumor Activity

The novel compounds were subjected to the National Cancer Institute (NCI) in vitro disease-oriented human cell screening panel assay. They were

assayed in vitro against a panel consisting of 60 human tumor cell lines,[31,32] derived from three cancer types: breast, lung and central nervous system (CNS) cancers. Compounds were tested at five- and 10-fold dilutions from a maximium concentration of 10^{-4} M. In the current protocol, each cell line is inoculated and preincubated on a microtiter plate, test agents are then added at a single concentration and the culture incubated for 48 h. End-point determinations are made with sulforhodamine B, a protein-binding dye (alamar blue).[33] The percentage growth inhibition (GIPRCNT) values are summarized in Table 1. The requirement for cell-line screening set by the NCI is that the GIPRCNT should be 32% or less, in at least one of the cell lines. The results showed that all the novel compounds did not approach this value against the three types of cancers at the mentioned concentration, except **22** which showed a GIPRCNT of 58% against breast cancer. It can be concluded from the results obtained from the new nucleosides that the aliphatic amido substituents on the triazole residue would not effect the anticancer activity, with except of the thiomorpholino-carboxamide group at C-4 of compound **22**, which is associated with weak activity, in comparison with the corresponding analogues, 1-β-D-glycosyl-(halomethyl)-1,2,3-triazoles **1a,b**, and these compounds exhibited good activity aganist HeLa [Ehrlich carcinoma ascited (ECA)] tumor.

Table 1. In Vitro Model Primary Anticancer Data for the New Glycosyl-1,2,3-triazole *N*-1-Nucleosides

	Growth %		
Compd	(Breast) MCF7	(Lung) NCI-H460	(CNS) SF-268
7	89	96	72
8	98	98	97
10	88	94	104
11	91	98	115
12	82	96	108
13	82	94	96
14	100	103	107
15	92	101	110
17	63	91	108
18	95	101	111
19	73	92	103
20	63	94	108
21	75	99	111
22	58	96	109
23	88	98	96

Results for each test agent are reported as the percentage growth of the treated cell compound to the untreated cells.

Experimental

General procedure. Melting points are uncorrected. ^{1}H- and ^{13}C-NMR spectra were recorded on AC 250 and 600 MHz spectrometers, using tetramethylsilane (TMS) as internal standard, with δ: chemical shift in ppm, and coupling constants in Hz. Mass spectra were measured in glycerol as matrix and some molecular ions were measured with sodium ions.

Dimethyl-1-(2,3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl)-1,2,3-triazole-4,5-dicarboxylate (6). To a solution of **5** (3.43 g, 9.19 mmol) in dry toluene (100 mL) was added dimethylacetylenedicarboxylate (7 mL, in excess) and the reaction mixture was stirred at 80°C under nitrogen for 24 h. After cooling, the solution was evaporated to 10 mL and cooled down overnight. The product was filtered and recrystallized from EtOH (4.0 g, 84%), m.p. 146–148°C; R_f (toluene-ethyl acetate 3:2 v/v)) 0.26. δ_H ($CDCl_3$): 6.12 (d, 1H, $J_{1',2'} = 9.4$ Hz, H-1′); 5.94 (t, 1H, $J_{2',3'} = 9.4$ Hz, H-2′); 5.41 (t, 1H, $J_{3',4'} = 9.4$ Hz, H-3′); 5.24 (t, 1H, $J_{4',5'} = 9.5$ Hz, H-4′), 4.29 (dd, 1H, $J_{5',6'a} = 4.8$ Hz, H-6′a); 4.14 (dd, 1H, $J_{6'a,6'b} = 12.6$ Hz, H-6′b); 4.04 (s, 3H, OMe); 4.00 (m, 1H, H-5′); 3.98 (s, 3H, OMe); 2.09, 2.07, 2.05, 1.90 (4s, 12H, 4 × OAc). δ_C ($CDCl_3$): 170.4, 170.2, 169.2, 168.6 (4 × OAc); 159.9, 158.5 (C=O); 140.1 (C-4); 130.8 (C-5); 85.6 (C-1′); 75.2 (C-5′); 73.2 (C-3′); 69.7 (C-2′); 67.4 (C-4′); 61.4 (C-6′); 53.6, 52.8 (2 × OMe); 20.8, 20.6, 20.6, 20.5, 20.2 (4 × OAc). Anal. calc. for $C_{20}H_{25}N_3O_{13}$ (515.4): C, 46.61; H, 4.89; N, 8.15. Found: C, 46.52; H, 4.80; N, 8.01. MS: m/z (EI) 484 $(M\text{-}OMe)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-dimethylcarboxylate (7). A solution of **6** (0.5 g, 0.97 mmol) in MeOH (10 mL) and CH_2Cl_2 (20 mL) containing sodium thiophenolate (0.37 g, 2.61 mmol) was stirred at room temperature for 18 h. The solid was filtered and the residue was chromatographed on SiO_2 column (10 g). Elution, in gradient, with CH_2Cl_2-MeOH (0–10%, 300 mL) afforded the pure nucleoside **3** (0.21 g, 62%); m.p. 191–195°C (from EtOH), R_f (CH_2Cl_2-MeOH 4:1 v/v) 0.38. δ_H (DMSO-d_6): 5.69 (d, 1H, $J_{1',2'} = 9.0$ Hz, H-1′); 5.56 (d, 1H, $J_{2',OH} = 5.8$ Hz, $C_{2'}$-OH); 5.31 (d, 1H, $J_{3',OH} = 5.2$ Hz, $C_{3'}$-OH); 5.19 (d, 1H, $J_{4',OH} = 5.3$ Hz, $C_{4'}$-OH); 4.62 (t, 1H, $J_{6a',6b'} = 5.0$ Hz, $C_{6'}$-OH); 4.10 (m, 1H, H-2′); 3.92, 3.86 (2s, 6H, 2 × OMe); 3.82 (dd, 1H, $J_{5',6'a} = 4.5$ Hz, $J_{6'a,6'b} = 12.5$ Hz, H-6′a); 3.68 (m, 1H, H-6′b); 3.45-2.89 (m, 3H, H-3′, H-4′, H-5′). δ_C (DMSO-d_6): 161.0, 159.8 (C=O); 139.1 (C-4); 132.9 (C-5); 88.9 (C-1′); 81.0 (C-5′); 77.2 (C-3′); 72.9 (C-2′); 70.1 (C-4′); 61.5 (C-6′); 55.0, 53.8 (2 × OMe). Anal. calc. for $C_{12}H_{17}N_3O_9$ (347.3): C, 41.50; 4.93; N, 12.10. Found: C, 41.32; H, 4.85; N, 11.91. MS: m/z (FAB) 348 $(M+H)^+$; 370 $(M+Na)^+$.

General procedure for the synthesis of 1-β-D-glucopyranosyl-1,2,3-triazole-4,5-*N*-dicarboxamide and *N*-dialkyldicarboxamide *N*-nucleosides. A

solution of **6** (0.50 g, 0.97 mmol) in the appropriate amine was stirred at room temperature for 18 h, then the reaction mixture was evaporated to dryness. The residue was partitioned between water (30 mL) and ether (3 × 20 mL) and the aqueous layer was evaporated to dryness. The residue was co-evaporated with EtOH (4 × 10 mL), then recrystallized from EtOH to give the desired nucleoside.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-dicarboxamide (8). From 16% methanolic ammonia (10 mL). Yield: 0.25 g, 83%, m.p. 120–123°C; R_f (CH_2Cl_2-MeOH 7:3 v/v) 0.28. δ_H (DMSO-d_6): 10.21, 8.56 (2s, 2H, NH_2), 8.19 (d, 2H, J = 9.0 Hz, NH_2); 6.45 (d, 1H, $J_{1',2'}$ = 9.2 Hz, H-1′); 5.44 (d, 1H, $J_{2'\text{-OH}}$ = 5.7 Hz, $C_{2'}$-OH); 5.30 (d, 1H, $J_{3'\text{-OH}}$ = 4.9 Hz, $C_{3'}$-OH); 5.16 (d, 1H, $J_{4'\text{-OH}}$ = 5.4 Hz, $C_{4'}$-OH); 4.15 (t, 1H, $J_{6'a,6'b\text{-OH}}$ = 5.7 Hz, $C_{6'}$-OH); 4.03 (m, 1H, H-2′); 3.64 (dd, 1H, $J_{5',6'a}$ = 4.3 Hz, $J_{6'a,6'b}$ = 11.0 Hz, H-6′a); 3.43 (m, 1H, H-6′b); 3.31–3.21 (m, 3H, H-3′, H-4′, H-5′). δ_C (DMSO-d_6): 163.1, 158.0 (C=O); 138.9 (C-4); 132.2 (C-5); 86.2 (C-1′); 80.4 (C-5′); 77.5 (C-3′); 71.8 (C-2′); 69.7 (C-4′); 60.7 (C-6′). Anal. calc. for $C_{10}H_{15}N_5O_7$ (317.3): C, 37.86; H, 4.77; N, 22.07. Found: C, 37.62; H, 4.68; N, 21.82. MS: m/z (FAB) 318 $(M+H)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-*N*-dimethyldicarboxamide (9). From methyl-amine (0.5 mL). Yield: 0.30 g, 90%; m.p. 169–171°C decomp.; R_f (CH_2Cl_2-MeOH 7:3 v/v) 0.55. δ_H (DMSO-d_6): 10.74 (d, 1H, J = 4.7 Hz, NH); 9.18 (d, 1H, J = 4.7 Hz, NH); 6.47 (d, 1H, $J_{1',2'}$ = 9.3 Hz, H-1′); 5.39 (d, 1H, $J_{2',OH}$ = 5.8 Hz, $C_{2'}$-OH); 5.1 (d, 1H, $J_{3',OH}$ = 5.1 Hz, $C_{3'}$-OH); 5.13 (d, 1H, $J_{4',OH}$ = 5.4 Hz, $C_{4'}$-OH); 4.61 (t, 1H, $J_{6'a,6'b,OH}$ = 5.8 Hz, $C_{6'}$-OH); 4.01 (m, 1H, H-2′); 3.67 (dd, 1H, $J_{5',6'a'}$ = 5.4 Hz, $J_{6'a,6'b}$ = 11.7 Hz, H-6′a); 3.44 (m, 1H, H-6′b); 3.34-3.17 (m, 3H, H-3′, H-4′; H-5′); 2.83, 2.81 (2s, 6H, 2 × NMe). δ_C (DMSO-d_6): 161.2, 156.9 (C=O); 138.5 (C-4); 133.0 (C-5); 86.4 (C-1′); 80.4 (C-5′); 77.4 (C-3′); 71.8 (C-2′); 69.6 (C-4′); 61.5 (C-6′); 26.2, 25.8 (2 × NMe). Anal. calc. for $C_{12}H_{19}N_5O_7$ (345.3): C, 41.74; H, 5.55, N, 20.28. Found: C, 41.58; H, 5.48; N, 20.12. MS: m/z (FAB) 346 $(M+H)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-*N*-dibutyldicarboxamide (10). From butyl-amine (7 mL). Yield: 0.36 g, 88%; m.p. 99–103°C decomp.; R_f (CH_2Cl_2-MeOH 7:3 v/v) 0.62 . δ_H (DMSO-d_6): 10.83 (t, 1H, J = 5.2 Hz, NH); 9.23 (t, 1H, J = 5.5 Hz, NH); 6.46 (d, 1H, $J_{1',2'}$ = 9.2 Hz, H-1′); 5.49 (d, 1H, $J_{2',OH}$ = 5.7 Hz, $C_{2'}$-OH); 5.26 (d, 1H, $J_{3',OH}$ = 5.0 Hz, $C_{3'}$-OH); 5.14 (d, 1H, $J_{4',OH}$ = 5.4 Hz, $C_{4'}$-OH); 4.61 (t, 1H, $J_{6'a,6'b,OH}$ = 5.7 Hz, $C_{6'}$-OH); 4.01 (m, 1H, H-2′); 3.66 (dd, 1H, $J_{6'a,6'b}$ = 6.1 Hz, $J_{6'a,6'b}$ = 11.8 Hz, H-6′a); 3.44 (m, 1H, H-6′b); 3.34–3.20 (m, 3H, H-3′, H-4′, H-5′); 1.52–1.22 (m, 12H, 6 × CH_2); 0.88 (t, 6H, 2 × Me). δ_C (DMSO-d_6): 160.7, 156.2 (C=O); 138.7 (C-4); 132.0 (C-5); 86.4 (C-1′); 80.3 (C-5′); 77.3 (C-3′); 71.7 (C-2′); 69.6 (C-4′); 60.6 (C-6′); 38.7/38.6 30.8/30.6; 19.5/194 [(CH_2)a,b-butyl]; 13.6/13.5

[(Me)a,b-butyl]. Anal. calc. for $C_{18}H_{29}N_5O_7$ (427.45): C, 50.58; H, 6.84; N, 16.38. Found: C, 50.41; H, 6.80; N, 16.12. MS: m/z (EI) 410 $[M\text{-}OH]^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-*N*-dibenzyldicarboxamide (11). From benzyl-amine (7 ml). Yield: 0.43 g, 89%; m.p. 120–123°C; R_f ($CHCl_3$-MeOH 7:3 v/v) 0.74. δ_H (DMSO-d_6): 11.09 (t, 1H, J = 5.6 Hz, NH); 9.81 (t, 1H, J = 6.0 Hz, NH); 7.32-7.23 (m, 10H, Ar-H); 6.39 (d, $J_{1',2'} = 9.2$ Hz, H-1′); 5.44 (d, 1H, $J_{2',OH} = 5.6$ Hz, $C_{2'}$-OH); 5.28 (d, 1H, $J_{3',OH} = 5.0$ Hz, $C_{3'}$-OH); 5.15 (d, 1H, $J_{4',OH} = 5.2$ Hz, $C_{4'}$-OH); 4.61 (t, 1H, $J_{6'a,6'b,OH} = 5.7$ Hz, $C_{6'}$-OH); 4.64–4.41 (m, 4H, $2 \times CH_2$); 4.04 (m, 1H, H-2′); 3.66 (dd, 1H, $J_{5',6'a} = 5.7$ Hz, $J_{6'a,6'b} = 11.8$ Hz, H-6′a); 3.45 (m, 1H, H-6′b); 3.36-3.23 (m, 3H, H-3′, H-4′, H-5′). δ_C (DMSO-d_6): 160.7, 156.5 (C=O); 138.7 (C-4, Ph*CH*$_2$); 138.1 (Ph*CH*$_2$); 132.3 (C-5); 86.5 (C-1′); 80.3 (C-5′); 77.3 (C-3′); 71.7 (C-2′); 69.5 (C-4′); 60.8 (C-6′). Anal. calc. for $C_{24}H_{27}N_5O_7$ (497.5): C, 57.94; H, 5.47; N, 14.08. Found: C, 57.71; H, 5.38; N, 13.82. MS: m/z (FAB) 498 $(M+H)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-*N*-dicyclopropyldicarboxamide (12). From cyclopropylamine (0.38 g, 6.65 mmol) in MeOH (10 mL). Yield: 0.25 g, 65%; m.p. 214–218°C decomp.; R_f ($CHCl_3$-MeOH 7:3 v/v) 0.53. δ_H (DMSO-d_6): 10.75 (d, 1H, J = 4.2 Hz, NH); 9.20 (t, 1H, J = 4.6 Hz, NH); 6.36 (d, 1H, $J_{1',2'} = 9.3$ Hz, H-1′); 5.37 (d, 1H, $J_{2',OH} = 5.6$ Hz, $C_{2'}$-OH); 5.24 (d, 1H, $J_{3',OH} = 3.6$ Hz, $C_{3'}$-OH); 5.12 (d, 1H, $J_{4',OH} = 5.4$ Hz, $C_{4'}$-OH); 4.59 (t, 1H, $J_{6'a,6'b,OH} = 5.7$ Hz, $C_{6'}$-OH); 4.00 (m, 1H, H-2′); 3.66 (dd, 1H, $J_{5',6'a} = 5.4$ Hz, $J_{5',6'b} = 12.2$ Hz , H-6′a); 3.44 (m, 1H, H-6′b); 3.33 (m, 1H, H-3′); 3.25 (m, 1H, H-5′); 3.16 (m, 1H, H-4′); 2.91-2.83 [m, 2H, H-1″a, H-1″b (cyclopropyl); 0.77-0.52 [m, 12H, $6 \times CH_2$ (cyclopropyl)]. δ_C (DMSO-d_6): 162.4, 157.9 (C=O); 139.9 (C-4); 132.4 (C-5); 86.8 (C-1′); 80.7 (C-5′); 77.7 (C-3′); 72.1 (C-2′); 70.0 (C-4′); 61.0 (C-6′); 23.4, 23.0 (C-1″a, C-1″b); 6.26, 6.10, 6.00 (C-2″a,b, C-3″-a,b). Anal. calc. for $C_{16}H_{23}N_5O_7$ (397.4): C, 48.36; H, 5.53; N, 17.62. Found: C, 48.17; H, 5.78; N, 17.48. MS: m/z (FAB) 398 $(M+H)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-*N*-di(ethan-2-ol-yl)dicarboxamide (13). From 1-ethanol-2-amine (7 mL) in dry MeOH (20 mL). Yield: 0.30 g, 78%, m.p. 112–115°C; R_f ($CHCl_3$-MeOH 3:2 v/v) 0.3. δ_H (600 MHz, HMQC, DMSO-d_6): 10.80 (bs, 1H, NH); 8.96 (bs, 1H, NH); 6.46 (d, 1H, $J_{1',2'} = 9.2$ Hz, H-1′); 5.35 (d, 1H, $J_{2',OH} = 5.6$ Hz, $C_{2'}$-OH); 5.24 (d, 1H, $J_{3',OH} = 3.6$ Hz, $C_{3'}$-OH); 5.12 (d, 1H, $J_{4',OH} = 5.4$ Hz, $C_{4'}$-OH); 4.59 (t, 1H, $J_{6'a,6'b,OH} = 5.7$ Hz, $C_{6'}$-OH); 4.03 (m, 1H, H-2′); 3.67 (dd, 1H, $J_{5',6'a} = 5.3$ Hz, $J_{5',6'b} = 12.2$ Hz, H-6′a); 3.52 (m, 2H, *CH*$_2$OH); 3.36 (m, 2H, NCH_2); 3.33 (m, 1H, H-5′); 3.33 (m, 1H, H-6′b); 3.32 (m, 1H, H-3′); 3.24 (m, 1H, H-4′). δ_C (DMSO-d_6): 160.8, 156.4 (C=O); 138.7 (C-4); 132.1 (C-5); 86.2 (C-1′); 80.1 (C-5′); 77.1 (C-3′); 72.6 (C-2′); 69.4 (C-4′); 60.4 (C-6′); 59.1

(CH_2OH); 41.7 (NCH_2). Anal. calc. for $C_{14}H_{23}N_5O_9$ (405.36): C, 41.48; H, 5.72; N, 17.28. Found: C, 41.29; H, 5.66; N, 17.09. MS: m/z (FAB) 406 $(M+H)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-*N*-di(hexan-6-ol-yl)dicarboxamide (14). From 1-ethanol-6-amine (0.63 g, 5.36 mmol) in absolute MeOH (20 mL). Yield: 0.37 g, 75%; m.p. 130–134°C; R_f ($CHCl_3$-MeOH 4:1 v/v) 0.2. δ_H (600 MHz, HMQC, DMSO-d_6): 10.80 (t, 1H, J = 5.4 Hz, NH); 9.17 (t, 1H, J = 6.0 Hz, NH); 6.47 (d, 1H, $J_{1',2'} = 9.2$ Hz, H-1′); .5.34 (1H, $J_{2',OH} = 5.5$ Hz, $C_{2'}$-OH); 5.21 (d, 1H, $J_{3',OH} = 4.2$ Hz, $C_{3'}$-OH); 5.09 (d, 1H, $J_{4',OH} = 5.5$ Hz, $C_{4'}$-OH); 4.55 (t, 1H, $J_{6'a,6'b,OH} = 5.5$ Hz, $C_{6'}$-OH); 4.29 (dd, 2H, J = 1.4 Hz, $2 \times CH_2OH$); 4.03 (m, 1H, H-2′); 3.67 (dd, 1H, $J_{5',6'a} = 5.3$ Hz, $J_{6'a,6'b} = 12.0$ Hz H-6′a); 3.46 (m, 1H, H-6′b); 3.37 (m, 4H, $2 \times CH_2OH$); 3.33 (m, 1H, H-5′); 3.32 (m, 1H, H-3′); 3.27 (m, 4H, $2 \times NCH_2$); 3.24 (m, 1H, H-4′), 1.53 (m, 4H, CH_2-4″a,b); 1.40 (m, 4H, CH_2-5″a,b); 1.30 (m, 4H, CH_2-3″a,b); 1.29 (m, 4H, CH_2-2″a,b). δ_C (DMSO-d_6): 160.7, 156.1 (C=O); 138.7 (C-4); 132.0 (C-5); 86.0 (C-1′); 80.0 (C-5′); 77.0 (C-3′); 71.4 (C-2′); 69.2 (C-4′); 60.3 (C-6′, $2 \times CH_2OH$); 38.6 ($2 \times NCH_2$); 32.1 (C-5″a,b); 28.4 (C-4″a,b); 25.9 (C-2″a,b); 24.9 (C-3″a,b). Anal. calc. for $C_{22}H_{39}N_5O_9$ (517.64): C, 51.05; H, 7.59; N, 13.53. Found: C, 50.72; H, 7.48; N, 13.71. MS: m/z (FAB) 518 (MH^+).

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-dihydrazonic acid (15). From hydrated hydrazine (0.50 g, 10 mmol) in a mixture of MeOH (20 mL) and water (2 mL). Yield: 0.27 g, 75%; m.p. 90–95°C decomp. R_f ($CHCl_3$-MeOH 3:2 v/v) 0.2 δ_H (600 MHz, HMQC, DMSO-d_6): 12.91 (bs, 2H, NH_2); 11.94 (bs, 2H, NH_2); 10.60 (bs, 1H, NH); 9.00 (bs, 1H, NH); 6.49 (d, 1H, $J_{1',2'} = 9.5$ Hz, H-1′); .5.31 (d, 1H, $J_{2',OH} = 5.4$ Hz, $C_{2'}$-OH); 5.25 (d, 1H, $J_{3',OH} = 4.1$ Hz, $C_{3'}$-OH); 5.14 (d, 1H, $J_{4',OH} = 4.6$ Hz, $C_{4'}$-OH); 4.83 (m, 1H, $C_{6'}$-OH); 4.04 (m, 1H, H-2′); 3.66 (dd, 1H, $J_{5',6'a} = 5.2$ Hz, $J_{6'a,6'b} = 11.7$ Hz, H-6′a); 3.43 (m, 1H, H-6′b); 3.36 (m, 1H, H-5′); 3.33 (m, 1H, H-3′); 3.24 (m, 1H, H-4′), δ_C (DMSO-d_6): 159.0, 155.1 (C=O); 137.7 (C-4); 130.7 (C-5); 86.3 (C-1′); 80.4 (C-5′); 77.4 (C-3′); 71.7 (C-2′); 69.6 (C-4′); 60.6 (C-6′). Anal. calc. for $C_{10}H_{17}N_7O_7$ (347.3): C, 34.59, H, 4.93; N, 28.23. Found: C, 34.32; H, 4.87; N, 28.01. MS: m/z (FAB) 348 $(M+H)^+$; 370 $(M+Na)^+$.

1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-1,2,3-triazole-4,5-*N*-dicyclohexyl-di-carboxamide (16). A solution of **6** (0.4 g, 0.77 mmol) in MeOH (5 mL) and cyclohexylamine (4 mL) was stirred at room temperature overnight. The solvent was evaporated to dryness and the residue was partitioned the resisue between CH_2Cl_2 (3×15 mL) and water (15 mL). The combined organic extracts were dried (Na_2SO_4), filtered and evaporated to dryness to give a crude product. This was purified on a column of SiO_2 (10 g), using CH_2Cl_2-MeOH (95:5 v/v) as eluent to give **16** (0.20 g, 40%), as crystals,

m.p. 133–135°C (from EtOH). R_f ($CHCl_3$-MeOH 95:5 v/v) 0.72. δ_H ($CDCl_3$): 10.86, 10.54 (m, 2H, NH); 6.45 (d, 1H, $J_{1',2'} = 9.3$ Hz, H-1′); 5.89 (t, 1H, $J_{2',3'} = 9.3$ Hz, H-2′); 5.58 (t, 1H, $J_{3',4'} = 9.3$ Hz, H-3′); 5.11 (t, 1H, $J_{4',5'} = 9.6$ Hz, H-4′); 4.32 (dd, 1H, $J_{5',6'a} = 5.5$ Hz, $J_{6'a,6'b} = 10.5$ Hz, H-6′a); 4.06 (dd, 1H, $J_{5',6'b} = 1.3$ Hz, H-6′b); 3.35 (m, 1H, H-5′); 2.03, 1.98 (2), 1.82 (3s, 12H, 4 × OAc); 1.76-1.10 (m, 20H, cyclohexyl group). Anal. calc. for $C_{30}H_{43}N_5O_{11}$ (649.7): C, 55.46; H, 6.67; N, 10.78. Found: C, 55.21; H, 6.60; N, 10.42. MS: m/z (FAB) 650/651 $(M+H)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-*N*-dicyclohexyldicarboxamide (17). A solution of **16** (120 mg, 0.18 mmol) in NaOMe [from MeOH (4 mL) and Na (5.1 mg)] was stirred at room temperature for 18 h. After neutralization with diluted acetic acid, the solid was filtered and the residue was partitioned between ether (3 × 10 mL) and water (10 mL). The aqueous layer was evaporated to dryness and the residue was co-evaporated with EtOH (4 × 10 mL). The product was recrystallized from EtOH to give **16** (55 mg, 64%), m.p. 147–150°C decomp.; R_f ($CHCl_3$-MeOH 4:1 v/v) 0.47 δ_H (DMSO-d_6): 9.50 (d, 1H, J = 4 .8 Hz, NH); 6.45 (d, 1H, $J_{1',2'} = 9.0$ Hz, H-1′); 3.78-3.16 [m, 10H, H-2′-H-6′b, OH groups); 1.74-131 (m, 20H, cyclohexyl groups). δ_C (DMSO-d_6): 160.1, 156.6 (C=O); 139.1 (C-4); 138.4 (C-5); 86.5 (C-1′); 81.1 (C-5′); 78.3 (C-3′); 72.1 (C-2′); 69.4 (C-4′); 61.2 (C-6′); 48.3 (C-1″a), 47.5 (C-1″b); 33.2 (C-2″a); 33.0 (C-2″b); 32.9 (C-3″a, C-4″a); 32.5 (C-3″b, C-4″b); 25.8 (C-5″a); 25.6 (C-5″b); 25.1 (C-6″a); 24.9 C-6″b). Anal. calc. for $C_{22}H_{35}N_5O_7$ (481.6): C, 54.87; H, 7.33; N, 14.54. Found: C, 54.62; H, 7.26; N, 14.39.MS: m/z (FAB) 482 $(M+H)^+$; 504 $(M+Na)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4,5-dicarboxylic acid (18). A solution of **6** (0.5 g, 0.97 mmol) was heated in 2.5 N NaOH solution (10 mL) at 80°C for 4 h, then neutralized with 1N HCl to give a white precipitate (0.2 g, 60%); m.p. 187–191°C (recrystallized from aceton-water 1:1 v/v); R_f (CH_2Cl_2-MeOH 7:3 v/v) 0.45. δ_H (DMSO-d_6/D_2O): 6.32 (d, 1H, $J_{1',2'} = 9.1$ Hz, H-1′); 4.71 (t, 1H, $J_{2',3'} = 9.1$ Hz, H-2′); 3.66 (dd, 1H, $J_{5',6'a} = 5.3$ Hz, $J_{6'a,6'b} = 11.5$ Hz, H-6′a); 3.47 (m, 1H, H-6′b); 3.26-3.03 (m, 3H, H-3′, H-4′, H-5′). δ_C (DMSO-d_6): 180.0 (CO_2H); 143.1 (C-4); 140.0 (C-5); 87.9 (C-1′); 80.5 (C-5′); 77.6 (C-3′); 73.0 (C-2′); 70.6 (C-4′); 62.1 (C-6′). Anal. calc. for $C_{10}H_{13}N_3O_9 \cdot H_2O$ (337.2): C, 35.62, H, 4.48; N, 12.46. Found: C, 35.47; H, 4.39; N, 12.32. MS: m/z (FAB) 320 $(M+H)^+$; 342 $(M+Na)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4-*N*-piperazinylcarboxamide-5-sodium carboxylate (19). To a stirred solution of **6** (0.53 g, 1.03 mmol) in NaOMe [from Na (31 mg) and dry MeOH (10 mL)] was added anhydrous piperazine (0.27 g, 3.13 mmol) at room temperature. After 48 h, the solution was evaporated to dryness and the residue was recrystallized twice from MeOH to give **19** (0.39 g, 93%); m.p. 256–257°C; R_f (CH_2Cl_2-MeOH-NH_4OH

2:2:1 v/v/v) 0.58. δ_H (DMSO-d_6): 5.72 (bs, 1H, $C_{2'}$-OH); 5.65 (bs, 1H, $C_{3'}$-OH); 5.45 (bs, 1H, $C_{4'}$-OH); 5.10 (d, 1H, $J_{1',2'} = 9.2$ Hz, H-1′); .4.71 (bs, 1H, $C_{6'}$-OH); 4.17 (t, 1H, $J_{2',3'} = 9.2$ Hz, H-2′); 3.90 (m, 1H, H-6′a); 3.65 (m, 1H, H-6′b); 3.52-3.20 (m, 3H, H-3′, H-4′, H-5′); 2.58 (m, 2H, $N(CH_2)$-3″), 2.48 (m, 2H, $N(CH_2)$-5″); 2.15 (m, 4H, $N(CH_2)$-2″, $N(CH_2)$-6″). δ_C (DMSO-d_6): 163.6, 159.6 (C=O); 142.1 (C-4); 133.3 (C-5); 86.2 (C-1′); 80.6 (C-5′); 77.4 (C-3′); 72.3 (C-2′); 69.8 (C-4′); 61.1 (C-6′); 56.4, 49.0 ($N(CH_2)$-2″, $N(CH_2)$-6″); 45.4, 43.0 ($N(CH_2)$-3″, $N(CH_2)$-5″). Anal. calc. for $C_{14}H_{20}N_5O_8{\cdot}Na$ (409.3): C, 41.08; H, 4.92; N, 17.11. Found: C, 41.12; H, 5.02; N, 16.82. MS: m/z (FAB) 410 $(M+H)^+$; 432 $(M+Na)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4-*N*-(*N*-methylpiperazinylcarboxamide)-5-carboxylic acid (20). A solution of **6** (0.6 g, 1.16 mmol) in NaOMe [from Na (45 mg) and dry MeOH (15 mL)] and *N*-methylpiperazine (0.30 g, 3.13 mmol) was stirred at room temperature for 48 h. The solution was neutralized with 1N HCl, and the precipitate was filtered and dried. The product was recrystallized twice from MeOH to give **20** (0.20 g, 41%); m.p. 203–208 decomp.°C.; R_f (CH_2Cl_2-MeOH 3:2 v/v) 0.40. δ_H (600 MHz, HMQC, DMSO-d_6): 5.72 (bs, 1H, $C_{2'}$-OH); 5.65 (bs, 1H, $C_{3'}$-OH); 5.45 (bs, 1H, $C_{4'}$-OH); 5.10 (d, 1H, $J_{1',2'} = 9.2$ Hz, H-1′); 4.71 (bs, 1H, $C_{6'}$-OH); 4.17 (t, 1H, $J_{2',3'} = 9.2$ Hz, H-2′); 3.90 (m, 1H, H-6′a); 3.65 (m, 1H, H-6′b); 3.52-3.20 (m, 3H, H-3′, H-4′, H-5′); 2.58 (m, 2H, $N(CH_2)$-3″), 2.48 (m, 2H, $N(CH_2)$-5″); 2.15 (m, 4H, $N(CH_2)$-2″, $N(CH_2)$-6″). δ_C (DMSO-d_6): 176.7 (CO_2H), 163.6 (C=O); 144.3 (C-4); 135.3 (C-5); 85.2 (C-1′); 80.3 (C-5′); 76.9 (C-3′); 72.2 (C-2′); 69.7 (C-4′); 61.1 (C-6′); 54.5, 53.9 ($N(CH_2)$-2″, $N(CH_2)$-6″); 45.8, 45.7 ($N(CH_2)$-3″, $N(CH_2)$-5″). Anal. calc. for $C_{15}H_{23}N_5O_8{\cdot}H_2O$ (419.4): C, 42.96; H, 6.01; N, 16.70. Found: C, 42.74; H, 5.72; N, 16.72. MS: m/z (FAB) 402 $(M+H)^+$; 424 $(M+Na)^+$. The sodium salt was prepared in the same manner as a semi-solid.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4-*N*-morpholinylcarboxamide-5-sodium carboxylate (21). To a stirred solution of **6** (0.6 g, 1.16 mmol) in NaOMe solution [from Na (32 mg) and dry MeOH (15 mL)] was added morpholine (0.40 g, 4.59 mmol) at room temperature. After stirring for 48 h, the suspension was evaporated to dryness and the residue was recrystallized from MeOH to give **21** (0.20 g, 38%); m.p. 95–98°C decomp.; R_f (CH_2Cl_2-MeOH-(20%) NH_4OH 2:2:0.5 v/v/v) 0.60. δ_H (DMSO-d_6): 5.48 (2bs, 2H, $C_{2'}$-OH, $C_{3'}$-OH); 5.38 (bs, 1H, $C_{4'}$-OH); 5.20 (d, 1H, $J_{1',2'} = 9.3$ Hz, H-1′); 4.69 (bs, 1H, $C_{6'}$-OH); 3.85 (m, 1H, H-2′); 3.71–3.69 (m, 5H, $O(CH_2)$-3″, $O(CH_2)$-5″, H-6′a); 3.60 (m, 1H, Hz, H-6′b); 3.52–3.18 (m, 3, H-3′, H-4′, H-5′); 2.98 (m, 4H, $N(CH_2)$-2″, $N(CH_2)$-6″). δ_C (DMSO-d_6): 160.2, 159.4 (C=O); 142.7 (C-4); 134.7 (C-5); 86.6 (C-1′); 80.5 (C-5′); 77.2 (C-3′); 70.0 (C-2′); 69.9 (C-4′); 65.9 ($O(CH_2)$-3″, $O(CH_2)$-5″); 61.2 (C-6′); 47.1, 43.7 ($N(CH_2)$-2″, $N(CH_2)$-6″). Anal. calc. for

$C_{14}H_{19}N_4O_9 \cdot Na$ (410.3): C, 40.98; H, 4.67; N, 13.65. Found: C, 40.94; H, 4.56; N, 13.43. MS: m/z (FAB) 411 $(M+H)^+$; 424 $(M+Na)^+$.

1-(β-D-Glucopyranosyl)-1,2,3-triazole-4-*N*-thiomorpholinylcarboxamide)-5-sodium carboxylate (22). This compound was prepared according to the previous experiment, using 4-thiomorpholine (0.47 g, 4.59 mmol). Yield: 0.24 g, 49%; m.p. 228–232°C decomp.; R_f (CH_2Cl_2-MeOH-(20%) NH_4OH 2:2:0.5 v/v/v) 0.65. δ_H (600 MHz, HMQC, DMSO-d_6): 5.51 (m, 2H, $C_{2'}$-OH, $C_{3'}$-OH); 5.33 (d, 1H, $J_{4',\text{-OH}} = 5.1$ Hz, $C_{4'}$-OH); 5.13 (d, 1H, $J_{1',2'} = 9.0$ Hz, H-1′); 4.68 (t, 1H, $J_{6'a,6'b,OH} = 4.5$ Hz, $C_{6'}$-OH); 3.85 (m, 1H, H-2′); 3.70 (dd, 1H, $J_{5',6'a} = 5.1$ Hz, $J_{6'a,6'b} = 12.0$ Hz , H-6′a); 3.62 (m, 1H, H-6′b); 3.50–3.18 (m, 7H, H, $N(CH_2)$-2″, $N(CH_2)$-6″, H-3′, H-4′, H-5′); 2.63 (m, 4H, $S(CH_2)$-3″, $S(CH_2)$-5″). δ_C (DMSO-d_6): 163.4, 159.9 (C=O); 144.8 (C-4); 135.5 (C-5); 86.5 (C-1′); 80.5 (C-5′); 77.3 (C-3′); 70.0 (C-2′); 69.9 (C-4′); 61.1 (C-6′); 49.7, 44.1 ($N(CH_2)$-2″, $N(CH_2)$-6″); 26.7, 26.5 ($S(CH_2)$-3″, $S(CH_2)$-6″). Anal. calc. for $C_{14}H_{19}N_4SO_8 \cdot Na$ (426.4): C, 39.44; H, 4.49; N, 13.14. Found: C, 39.14; H, 4.37; N, 12.92. MS: m/z (FAB) 427 $(M+H)^+$; 449 $(M+Na)^+$.

1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-6-amino-8-hydroxy-4*H*-1,2,3-triazolo-[4,5-*e*][1,3]diazepin-4-one (24). Guanidine hydrochloride (0.63 g, 6.63 mmol) was added to NaOMe solution [resulting from Na (0.75 g) dissolved in absolute MeOH (15 mL)]. After stirring in an ice-bath for 30 min, the precipitated NaCl was filtered and the filtrate was added to a solution of the triazole **6** (0.80 g, 1.55 mmol) in absolute MeOH (25 mL). The mixture was stirred at room temperature for 48 h. After neutralization with 1N HCl, the precipitate was filtered and the filtrate was evaporated to dryness. The residue was co-evaporated with absolute EtOH (4 × 20 mL) to give a crude product **23** (0.32 g). This product was treated with dry pyridine (10 mL) and acetic anhydride (5 mL) and the reaction mixture was stirred at room temperature for 48 h. The solution was evaporated to dryness, and the residue was co-evaporated with toluene-EtOH (1:1, 4 × 20 mL v/v) to afford **24** (0.70 g), which was loaded onto SiO_2 column (20 g). Elution with CH_2Cl_2-MeOH (0–2%) affordrd a pure foam (0.36 g, 46%), R_f (CH_2Cl_2-MeOH 10:0.8 v/v) 0.47. δ_H ($CDCl_3$): 9.49 (bs, 1H, NH) 6.27 (d, 1H, $J_{1',2'} = 9.3$ Hz, H-1′); 6.14 (t, 1H, $J_{2',3'} = 9.3$ Hz, H-2′); 5.34 (t, 1H, $J_{3',4'} = 9.4$ Hz, H-3′); 5.27 (t, 1H, $J_{4',5'} = 9.5$ Hz, H-4′); 4.25 (dd, 1H, $J_{5',6'a} = 5.4$ Hz, H-6′a); 4.13 (dd, 1H, $J_{6'a,6'b} = 12.5$ Hz, H-6′b); 4.13 (dd, 1H, $J_{5',6'b} = 2.6$ Hz, H-5′); 2.29, 2.07, 2.04, 1.90 (4s, 12H, 4 × OAc). Anal. calc. for $C_{19}H_{22}N_6O_{11}$ (510.41): C, 44.71; H, 4.34; N, 16.47. Found: C, 44.45; H, 4.69; N, 16.19. MS: m/z (FAB) 511 $(M+H)^+$; 533 $(M+Na)^+$.

6-Amino-4*H*-1-(β-D-glucopyranosyl)-8-hydroxy-1,2,3-triazolo[4,5-*e*][1,3]-diazepin-4-one (23). A solution of **24** (0.30 g, 0.50 mmol) in NaOMe [resulting from Na (20 mg) dissolved in absolute MeOH (5 mL)] was stirred at room

temperature for 24 h. After neutralization of the mixture with diluted acetic acid, the mixture was evaporated to dryness and the residue was partitioned between water (10 mL) and ether (3×10 mL). The aqueous layer was evaporated to dryness and the resulting product was co-evaporated with absolute EtOH (4×15 mL) to give **24** (0.10 g, 59%) as a white powder; m.p. 210–213°C decomp.; R_f (CH_2Cl_2-MeOH-(20%) NH_4OH 2:2:1 v/v/v) 0.70. δ_H (600 MHz, HMQC, DMSO-d_6, D_2O): 8.38 (s, 1H, OH); 6.41 (d, 1H, $J_{1',2'} = 9.3$ Hz, H-1′); 6.25 (bs, 2H, NH_2). 5.75 (m, 4H, $C_{2'}$-OH, $C_{3'}$-OH, $C_{4'}$-OH); 4.75 (bs, 1H, $C_{6'}$-OH); 4.01 (m, 1H, H-2′); 3.67 (dd, 1H, $J_{5',6'a} = 4.2$ Hz, $J_{6'a,6'b} = 12.2$ Hz, H-6′a); 3.45 (dd, 1H, $J_{5',6'b} = 2.0$ Hz, H-6′b); 3.36 (m, 1H, H-5′); 3.34 (dd, 1H, $J_{3',4'} = 9.2$ Hz, H-3′); 3.24 (dd, 1H, $J_{4',5'} = 9.1$ Hz, H-4′), δ_C (DMSO-d_6): 164.6 (C-6 (C=N)); 163.8, 160.6 (C-4, C-8, (C=O)); 143.3 (C-3a, triazole); 13.5 (C-8a, triazole); 85.6 (C-1′); 80.6 (C-5′); 77.9 (C-3′); 72.2 (C-2′); 70.2 (C-4′); 61.2 (C-6′). Anal. calc. for $C_{11}H_{14}N_6O_7$ (342.3): C, 38.60, H, 4.12; N, 24.55. Found: C, 38.40; H, 4.40; N, 24.32. MS: m/z (FAB) 343 $(M+H)^+$; 365 $(M+Na)^+$.

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