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Original article

New synthesis of $3-(\beta-D-glucopyranosyl)-5$ -substituted-1,2,4-triazoles, nanomolar inhibitors of glycogen phosphorylase



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1. Introduction

Type 2 diabetes mellitus (T2DM) is a severe disease with large economic consequences, which is significantly under-diagnosed and incompletely treated in the general population [1,2]. Control of blood glucose levels is a key objective in treating diabetic patients, who are most often prescribed modification of diet and exercise, one or more oral hypoglycaemic agents, as well as insulin. In spite of the availability of different classes of hypoglycaemic drugs, current treatments are often unable to achieve an intensive degree of blood glucose control to reduce effectively the incidence and severity of diabetic complications [3].

Hepatic glucose output is elevated in type 2 diabetic patients and current evidence indicates that glycogenolysis (release of monomeric glucose from the glycogen polymer storage form) is an important contributor to the abnormally high production of glucose by the liver. Glycogen phosphorylase (GP) is the enzyme responsible for glycogen breakdown to produce glucose and related metabolites for energy supply [4]. Due to its key role in the modulation of glycogen metabolism, pharmacological inhibition of GP has been regarded as an effective therapeutic approach to treating

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ABSTRACT

O-Perbenzoylated 5-(β-D-glucopyranosyl)tetrazole was reacted with *N*-benzyl carboximidoyl chlorides to give the corresponding 4-benzyl-3-(β-D-glucopyranosyl)-5-substituted-1,2,4-triazoles. Removal of the *O*-benzoyl and *N*-benzyl protecting groups by base catalysed transesterification and catalytic hydrogenation, respectively, furnished a series of 3-(β-D-glucopyranosyl)-5-substituted-1,2,4-triazoles with aliphatic, mono- and bicyclic aromatic, and heterocyclic substituents in the 5-position. Enzyme kinetic studies revealed these compounds to inhibit rabbit muscle glycogen phosphorylase *b*: best inhibitors were the 5-(4-aminophenyl)- (K_i 0.67 µM) and the 5-(2-naphthyl)-substituted (K_i 0.41 µM) derivatives. This study uncovered the *C*-glucopyranosyl-1,2,4-triazoles as a novel skeleton for nanomolar inhibition of glycogen phosphorylase.

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diseases caused by abnormalities in glycogen metabolism, first of all T2DM [5–7], but also myocardial [8,9] and cerebral [10,11] ischaemias and tumours [12–15]. Therefore, the study of glycogen phosphorylase inhibitors [16] (GPIs) is a continuing challenge for synthetic and medicinal chemistry [17,18], computational chemistry [19], protein crystallography [5,20], and physiology [21]. The biochemical and pharmacological background of this research has been thoroughly summarized in several reviews of the past decade, therefore, the reader is kindly referred to those papers [4,22,23].

Several structural classes of GP inhibitors have been reported [5,17,18,24] whose binding sites identified in GP include the catalytic site, the purine inhibitory site, the allosteric site, the glycogen storage site, the new allosteric inhibitor site and the lately discovered benzimidazole-binding site. The most widely studied group of molecules is that of glucose derivatives [7,25–35] which bind primarily to the active site of GP [36]. The best glucose analogue GPIs are glucopyranosylidene-spiro-heterocycles (K_i 0.16–0.63 μ M) and *N*-acyl-*N*'- β -D-glucopyranosyl ureas (*K*_i 0.35–0.7 μ M) exhibiting submicromolar inhibition [26] of rabbit muscle GPb, the prototype of GPs [20]. Glucopyranosylidene-spiro-thiohydantoin (K_i 29.8 µM against rat liver GP) was shown to exert considerable in vivo blood sugar diminishing activity [37], and an N-acyl-N'- β -D-glucopyranosyl urea derivative improved glucose tolerance and had remarkable effects in rearranging hepatic metabolism in diabetic mice [38].

N-Acyl- β -D-glucopyranosylamines (compounds I in Chart 1) were among the first synthetic glucose analogue inhibitors of GP [39] and several derivatives modified in the acyl groups were investigated [40–44]. In this series *N*-(2-naphthoyl)- β -D-glucopyranosylamine (**IC**) was the best inhibitor [41], which also served as a lead structure for bioisosteric replacements [45–48]. X-Ray

crystallographic studies on several RMGP*b*-I complexes showed the presence of a H-bond between the amide NH and the main chain C=O of His377 (outline **X** in Chart 1), and the strong binding was attributed to a large extent to this interaction.

Inserting a 1,2,3-triazole ring in place of the NHCO moiety as in **II** revealed that **I** and **II** were equipotent inhibitors [49] and the



 *A K_i value of 2.4 μ M was measured by N. G. Oikonomakos et al. (unpublished results in ref. [51])

Chart 1. Glycogen phosphorylase inhibitors (GPIs, *K*_i [μM] against rabbit muscle GP*b*, **I–VIII**): synthetic targets of this study (**IX**); outline of binding of glucose analogues at the active site of GP highlighting important H-bonds to His377 and interactions in the so-called β-channel for *N*-acyl-β-D-glucopyranosylamine type inhibitors (**X**) and 2-β-D-glucopyranosyl benzimidazole (**XI**) as observed by X-ray crystallography.



Scheme 1. Retrosynthetic analysis of the target compounds IX based on 1,3-dipolar cycloadditions (Glc = 0-protected β-D-glucopyranosyl residue, PG = protecting group).

structural features of the binding determined by X-ray crystallography were also very similar [42]. Oxadiazoles **III–V**, prepared in each possible variant [50,51,55], showed that the constitution of the heterocycle had a strong bearing on the inhibition: the most efficient inhibitor among these compounds was 5-(β -D-glucopyranosyl)-3-(2-naphthyl)-1,2,4-oxadiazole (**IVC**) which had a similar efficiency to that of **IC**. Other studies with *C*-glucopyranosyl heterocycles showed that benzothiazole **VI** was much less

Table 1

Synthesis of 3-(β-D-glucopyranosyl)-5-substituted-1,2,4-triazoles.



	R	Yield (%)			
		3 (Solvent)	4	5	6
a	CH ₃	_	_	See Ref. [62]	73 (from 5a)
b	$C(CH_3)_3$	_	-	See Ref. [62]	98 (from 5b)
c	CH ₂ OH	_	-	_	93 (from 5t)
d	C ₆ H ₅	69 (toluene)	73	See Ref. [62]	85 (from 4d)
					62 (from 5d)
e	C_6H_4 -4- CH_3	49 (<i>m</i> -xylene)	94	_	90 (from 4e)
f	$C_6H_4-4-C(CH_3)_3$	61 (<i>m</i> -xylene)	98	_	79 (from 4f)
g	C_6H_4 -4- CF_3	88 (toluene)	61	_	77 (from 4g)
h	C ₆ H ₄ -4-OH	_	-	_	67 (from 5u)
i	C_6H_4 -4-OCH ₃	62 (<i>m</i> -xylene)	68	_	95 (from 4i)
j	C_6H_4 -4-NO ₂	38 (toluene)	91	See Ref. [62]	75 (from 5j)
k	C_6H_4 -4- NH_2	_	-	_	94 (from 6j)
1	C ₆ H ₄ -4-COOH	_	_	75 (from 3s)	86 (from 51)
m	$C_6H_3-3,5-(CH_3)_2$	66 (<i>m</i> -xylene)	62	_	98 (from 4m)
n	C ₆ H ₃ -3,5-(NO ₂) ₂	_	-	See Ref. [62]	72 (from 5n)
0	C ₆ H ₃ -3,5-(NH ₂) ₂	_	-	_	72 (from 6n)
р	C ₆ H ₂ -3,4,5-(OCH ₃) ₃	65 (<i>m</i> -xylene)	91	_	92 (from 4p)
q	$C_{10}H_7$ (2-naphthyl)	52 (toluene)	85	See Ref. [62]	90 (from 4q)
-					81 (from 5q)
r	C_5H_4N (2-pyridyl)	_	-	See Ref. [62]	40 (from 5r)
S	C ₆ H ₄ -4-COOBn	69 (<i>m</i> -xylene)	-	_	_
t	CH ₂ OCOCH ₃	_	-	See Ref. [62]	-
u	C ₆ H ₄ -4-OCOCH ₃	-	-	See Ref. [62]	-

Table 2

Inhibition of rabbit muscle glycogen phosphorylase b by 3-(β -D-glucopyranosyl)-5-substituted-1,2,4-triazoles (**6**).





^a Calculated from the IC_{50} value by using a web-based tool [64].

efficient than benzimidazoles **VII** and **VIII** [33,52]. An X-ray crystallographic study of the RMGP*b*–**VII** complex revealed the presence of a specific H-bond between NH of the heterocycle and the main chain C=O of His377 [53] (outline **XI** in Chart 1), and the stronger binding of **VII** was explained by this interaction which cannot exist in the case of **VI**.

Based on these structure–activity relationships it was anticipated that *C*-glucopyranosyl 1,2,4-triazoles of type **IX**, non-classical bioisosteres of compounds **I**–**V**, could be more efficient GPIs. Very recently we have demonstrated in a preliminary communication that **IX** (R = 2-naphthyl, K_i 0.41 µM) indeed fulfils these expectations [54]. In this paper we disclose a new synthesis and structure–activity relationships of **IX** with a wide range of substituents R.

In the literature *C*-glycopyranosyl-1,2,4-triazoles are represented by some 1,3,5-trisubstituted derivatives obtained from glycosyl cyanides with 1-aza-2-azoniaallene salts [56] or with hydrazonoyl chlorides in the presence of Yb(OTf)₃ [57]. 3-Glycopyranosyl-5substituted-1,2,4-triazoles **IX** have been unknown until our very recent preliminary communication describing the synthesis of these compounds by acylation of N^1 -tosyl-*C*-(2,3,4,6-tetra-*O*-benzoyl- β -D-glucopyranosyl)formamidrazone followed by *N*- and/or *O*deprotection [54]. However, this synthetic sequence was rather long (5–6 steps from the corresponding glucosyl cyanide) and complicated by the removal of the *N*-tosyl moiety from the heterocycle. Therefore, a more straightforward synthesis of the target compounds has been sought for and accomplished by the ring transformation of 5-(2,3,4,6-tetra-*O*-benzoyl- β -D-glucopyranosyl) tetrazole.

2. Results and discussion

2.1. Syntheses

To select a suitable synthetic pathway towards compounds IX a retrosynthetic analysis for the construction of the 1,2,4-triazole ring was carried out taking into account 1,3-dipolar cycloadditions (Scheme 1). It was envisaged that synthetic methods [58] for 1,3,5trisubstituted-1,2,4-triazoles [59,60] with a protecting group as the 1-substituent could be applied. Given the tautomeric nature of this heterocycle three N-protected isomers may exist whose disconnections A and B refer to cycloadditions between nitrilimines and nitriles. Following route A the known glucosyl cyanide and 2,5disubstituted-tetrazoles or N-protected hydrazones or their halides would have been the necessary starting compounds, however, this possibility was ruled out due to the costly reagents and catalysts. For the analogous route B precursors of the intermediate Cglucosyl-nitrilimine would have been required which are unknown in the literature. Therefore, our attention turned to disconnection **C**, actually a variant of **B**, which needed the relatively easily available C-glucosyl-tetrazole and imidoyl-halides. The analogous disconnection \mathbf{C}' (not shown in details) was also discarded because of the necessity to prepare a series of tetrazoles and lack of the glucose based precursor of the imidoyl-halide.

Syntheses of the target compounds were started by the preparation of *O*-protected *C*-glucopyranosyl-tetrazole **1** (Table 1) from 2,3,4,6-tetra-*O*-benzoyl- β -D-glucopyranosyl cyanide [61] according to our recent procedure [27]. *N*-Benzyl arenecarboxamides **2**, obtained from the corresponding acid chloride and benzylamine, were converted to imidoyl chlorides by SOCl₂ which were then reacted without purification with tetrazole **1** in a one-pot fashion to give 4-benzyl-1,2,4-triazole derivatives **3**. The *O*-benzoyl protecting groups were removed by the Zemplén method to give **4**. Subsequent catalytic hydrogenation gave fully deprotected *C*-glucopyranosyl-1,2,4-triazoles **6d**–**g**,**i**,**m**,**pq**. Several *O*-perbenzoylated 3-glucopyranosyl-5-substituted derivatives **5** were

obtained in an alternative synthetic pathway published recently [62], and these compounds were also converted to the corresponding unprotected **6a–d,h,j,l,n,q,r** by the Zemplén protocol. Amino compounds **6k** and **6o** were obtained from the corresponding nitro derivatives **6j** and **6n**, respectively, by catalytic hydrogenation.

2.2. Enzyme kinetic studies

The new compounds were assayed against rabbit muscle glycogen phosphorylase b as described in earlier publications [40,63], and the results are collected in Table 2.

Compounds **6a**–**c** with aliphatic substituents proved weak inhibitors and were much less efficient than the corresponding "parent" amides **I** (shown in Chart 1; for R = CH₃: K_i 32 μ M [39]; R = C(CH₃)₃: IC₅₀ 7.5 mM [41]; R = CH₂OH: K_i 18 [42] or 20 [49] μ M), however, the trend in the strength of inhibition remained the same (*t*-butyl derivatives were the less efficient followed by the methyl and hydroxymethyl compounds in both series).

Appending a phenyl substituent to the heterocycle as in 6d resulted in a significantly better inhibitor. A comparison to the corresponding amide I ($R = C_6H_5$: K_i 81 [39] or 144 [40]) indicated more than an order of magnitude stronger inhibition by the triazole, and this strengthening was higher than those observed with the aliphatic amide-triazole pairs. Introduction of substituents in the 4-position of the phenyl ring brought about large changes in the inhibition. The 4-tolvl derivative **6e** was \sim 4 times better than **6d**. and comparing it to the relevant amide I (R = 4-CH₃-C₆H₄: IC₅₀ 4.5 mM [41]) revealed a very large increase of the binding strength in favour of the triazole. The bulky 4-t-butyl substituent in 6f caused a significant weakening of the inhibition. The 4trifluoromethyl derivative 6g proved also a weak inhibitor, and this was surprising especially in the light of the similar size of CH₃ (6e) and CF₃ (6g). The presence of a phenolic hydroxyl group in position 4 (**6h**) made again a good inhibitor, and the 4-methoxy compound 6i proved slightly better and comparable to 6e. Introduction of the 4-nitro substituent weakened the binding in comparison to 6d, however, the 4-amino derivative 6k was inhibiting in the submicromolar range. This may reveal the significance of a basic group in making contacts to the relevant parts of the enzyme. A carboxylic acid function in the 4-position (61) was fully detrimental for the binding and this may be at least in part due to the size of this group (compare with the slightly acidic **6h**).

Multiple substitutions in the phenyl ring (6m-p) resulted in generally weaker inhibitors, although the importance of the basic substituents was corroborated by the diamino derivative **60** showing the highest efficiency within this group of inhibitors.

The 2-naphthyl compound **6q** proved the best inhibitor of the whole series, and its nanomolar inhibition constant rendered this derivative among the most efficient glucose analogue inhibitors of GP. Comparing **6q** to the corresponding amide I(R = 2-naphthyl: K_i 10 [41] or 13 [42]) indicates a ~25–30-fold stronger binding for the triazole.

The 2-pyridyl moiety of **6r** was disadvantageous for the inhibition (a similar tendency was observed in the *N*-acyl-*N*'- β -D-glucopyranosyl urea series [24]).

A comparison of the inhibitory potency of these triazole derivatives clearly shows them to be superior to the corresponding oxadiazoles (III–V in Chart 1), as well. For the directly comparable pairs of 1,2,4-triazoles **6** and the best 1,2,4-oxadiazoles **IV** the increase of the efficiency is in the 9–29-fold range for the phenyl and 2-naphthyl substituted derivatives, respectively.

Further studies to understand the binding peculiarities of this series of GPIs by molecular dockings and X-ray crystallography are in progress and will be disclosed in due course.

3. Conclusion

A new synthetic sequence has been elaborated for the preparation of 3-(β-D-glucopyranosyl)-5-substituted-1,2,4-triazoles by converting 5-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)tetrazole with N-benzyl carboximidoyl chlorides into O-perbenzoylated 4-benzyl-3-(B-D-glucopyranosyl)-5-substituted-1.2.4-triazoles and subsequent O- and N-deprotection. These triazole derivatives with aliphatic, phenyl, substituted phenyl, 2-naphthyl, and 2-pyridyl substituents in the 5-position were evaluated as inhibitors of rabbit muscle glycogen phosphorylase b. Compounds with aliphatic groups exhibited weak inhibition, while several phenyl derivatives were low micromolar inhibitors. Nanomolar inhibition was observed for the 5-(4-aminophenyl)- and the 5-(2-naphthyl)substituted compounds of the series rendering these derivatives to be among the best glucose derived GPIs with similar efficiency as those of glucopyranosylidene-spiro-heterocycles and N-acyl-N'-β-D-glucopyranosyl ureas.

4. Experimental

4.1. General methods

Melting points were measured on a Kofler hot-stage and are uncorrected. Optical rotations were determined with a Perkin– Elmer 241 polarimeter at rt. NMR spectra were recorded with Bruker 360 (360/90 MHz for ¹H/¹³C) spectrometer. Chemical shifts are referenced to Me₄Si (¹H), or to the residual solvent signals (¹³C). Mass spectra were recorded on a Bruker Micro TOF-Q mass spectrometer. Microanalyses were performed on an Elementar Vario Micro Cube. TLC was performed on DC-Alurolle Kieselgel 60 F₂₅₄ (Merck), and the plates were visualised under UV light and by gentle heating. For column chromatography Kieselgel 60 (Merck, particle size 0.063–0.200 mm) was used. 5-(2',3',4',6'-Tetra-Obenzoyl- β -D-glucopyranosyl)tetrazole [27] (1) and 5-substituted-3-(2',3',4',6'-tetra-O-benzoyl- β -D-glucopyranosyl)-1,2,4-triazoles [62] **5a,b,d,j,n,q,r,t,u** were prepared according to published procedures.

4.2. General procedure I for the synthesis of N-benzyl-arenecarboxamides (2)

In a flame dried three necked bottle, equipped with a CaCl₂ tube, benzylamine (1 mL, 9.16 mmol) and TEA (1.53 mL, 11 mmol, 1.2 equiv.) was dissolved in the appropriate anhydrous solvent (5 mL, CH₂Cl₂, THF or toluene, depending on the solubility of acid chloride). To this stirred mixture a solution (in 5 mL anhydrous CH₂Cl₂, THF or toluene) of an acid chloride (9.16 mmol, 1 equiv.) was added dropwise at 0 °C. The mixture was slowly allowed to reach rt, stirred for 2 h, then diluted, and extracted with water. The organic phase was dried over MgSO₄, the solvent was evaporated, and the crude product was crystallised from EtOH.

Yields of the synthesized derivatives: *N*-benzyl-benzamide [65] (2d, 64%), N-benzyl-4-methylbenzamide [66] (2e, 81%), N-benzyl-[67] 4-tert-butylbenzamide (**2f**, 97%), N-benzyl-4trifluoromethylbenzamide [68] (**2g**, 76%), N-benzyl-4methoxybenzamide [66] (2i, 67%), N-benzyl-4-nitrobenzamide [69] (2j, 77%), N-benzyl-3,5-dimethylbenzamide [67] (2m, 81%), *N*-benzyl-3,4,5-trimethoxybenzamide [70] (**2p**, 98%), *N*-benzylnaphthalene-2-carboxamide [71] (2q, 74%), N-benzyl-(4benzyloxycarbonyl)-benzamide (2s, 56%, mp: 127-129 °C). Physical as well as NMR data of the title compounds are in agreement with those reported in the cited literature.

4.3. General procedure II for the synthesis of 4-benzyl-3-(2',3',4',6'-tetra-O-benzoyl- β -D-glucopyranosyl)-5-substituted-1,2,4-triazoles (3)

An *N*-benzyl-arenecarboxamide (**2**, 4.63 mmol, 3 equiv.) was dissolved in thionyl chloride (20 mL), and refluxed for 2 h. After distilling off the excess of thionyl chloride under diminished pressure, 20 mL of anhydrous toluene was evaporated from the residue. $5-(2',3',4',6'-\text{Tetra-}O-\text{benzoyl}-\beta-D-\text{glucopyranosyl})\text{tetra-zole [27,52]}$ (**1**, 1.54 mmol, 1 equiv.) and anhydrous toluene or xylene (20 mL) were added, the mixture was heated to reflux temperature, and the reaction was monitored by TLC (1:1 EtOAchexane). After total consumption of the tetrazole the solvent was removed and the residue was purified by column chromatography.

4.4. General procedure III for removal of O-acyl protecting groups by the Zemplén protocol

An O-acylated compound was dissolved in dry MeOH (5 mL/ 100 mg, a few drops of $CHCl_3$ were added in case of incomplete dissolution) and a catalytic amount of a NaOMe solution (1 M in MeOH) was added. The mixture was kept at rt and monitored by TLC (7:3 $CHCl_3$ –MeOH). When the starting material was consumed the mixture was neutralised with a cation exchange resin Amberlyst 15 (H⁺ form) (or with acetic acid), then the resin was filtered off and the solvent removed. The residue was purified by column chromatography.

4.5. General procedure IV for the removal of benzyl protecting groups

A benzylated compound (0.5 mmol) was dissolved in anhydrous MeOH (25 mL), 10% Pd(C) (20 mg) was added, and H₂ gas was bubbled through the reaction mixture at 50 °C. After disappearance of the starting material (monitored by TLC, 7:3 CHCl₃–MeOH) the reaction mixture was filtered through a pad of celite, the solvent was evaporated, and the residue was purified by column chromatography.

4.6. 4-Benzyl-5-phenyl-3-(2',3',4',6'-tetra-O-benzoyl- β -D-glucopyranosyl)-1,2,4-triazole (**3d**)

From tetrazole **1** (2.00 g, 3.08 mmol) and *N*-benzyl-benzamide (**2d**, 1.95 g, 9.25 mmol) in toluene according to General procedure **II**. Reaction time: 16 h. Purified by column chromatography (1:1 EtOAc-hexane) to yield 1.73 g (69%) colourless syrup. R_f : 0.15 (1:1 EtOAc-hexane); $[\alpha]_D = -25$ (c 0.50, CHCl₃); ¹H NMR (CDCl₃) δ (ppm): 7.95–6.97 (30H, m aromatics), 5.99–5.96 (2 × 1H, m, H-2' and/or H-3' and/or H-4'), 5.67 (1H, pseudo t, *J* = 10.6, 9.3 Hz, H-2' or H-3' or H-4'), 5.63 (1H, d, *J* = 15.9 Hz, PhCH₂), 5.53 (1H, d, *J* = 15.9 Hz, PhCH₂), 5.53 (1H, dd, *J* = 12.2, 2.4 Hz, H-6'a), 4.33 (1H, dd, *J* = 12.2, 5.4 Hz, H-6'b), 4.19 (1H, ddd, *J* = 9.6, 5.4, 2.4 Hz, H-5'); ¹³C NMR (CDCl₃) δ (ppm): 165.9, 165.7, 165.1, 164.8 (CO), 156.7, 149.8 (triazole C-3, C-5), 135.4–126.2 (aromatics), 76.8, 73.8, 73.2, 70.0, 69.1 (C-1' – C-5'), 62.9 (C-6'), 48.1 (PhCH₂). Anal: Calcd for C₄₉H₃₉N₃O₉ (813.85): C, 72.31; H, 4.83; N, 5.16. Found: C, 72.47; H, 4.88; N, 5.03.

4.7. 4-Benzyl-5-(4-methylphenyl)-3-(2',3',4',6'-tetra-O-benzoyl- β -D-glucopyranosyl)-1,2,4-triazole (**3e**)

From tetrazole **1** (0.50 g, 0.77 mmol) and *N*-benzyl-4methylbenzamide (**2e**, 0.52 g, 2.31 mmol) in *m*-xylene according to General procedure **II**. Reaction time: 3 h. Purified by column chromatography (1:1 EtOAc-hexane) to yield 0.32 g (49%) brownish foam. $R_{\rm f}$: 0.20 (1:1 EtOAc-hexane); $[\alpha]_{\rm D} = -4$ (c 0.50, CHCl₃); ¹H NMR (CDCl₃) δ (ppm): 7.97–6.98 (29H, m, aromatics), 6.04, 5.98, 5.68 (3 × 1H, 3 pseudo t, J = 9.5, 9.5 Hz in each, H-2', H-3', H-4'), 5.50 (1H, d, J = 16.5 Hz, PhCH₂), 5.31 (1H, d, J = 16.5 Hz, PhCH₂), 5.13 (1H, d, J = 16.5 Hz, H-1'), 4.48 (1H, dd, J = 12.4, 2.6 Hz, H-6'a), 4.34 (1H, dd, J = 12.4, 5.4 Hz, H-6'b), 4.20 (1H, ddd, J = 9.8, 5.4, 2.6 Hz, H-5'), 2.33 (3H, s, CH₃); ¹³C NMR (CDCl₃) δ (ppm): 165.8, 165.7, 165.0, 164.6 (CO), 156.7, 149.7 (triazole C-3, C-5), 140.2, 135.4, 133.4–123.6 (aromatics), 76.6, 73.8, 73.0, 69.9, 69.0 (C-1' – C-5'), 62.8 (C-6'), 47.9 (PhCH₂), 21.3 (CH₃). Anal: Calcd for C₅₀H₄₁N₃O₉ (827.88): C, 72.54; H, 4.99; N, 5.08. Found: C, 72.65; H, 4.88; N, 5.20.

4.8. 4-Benzyl-5-(4-tert-butylphenyl)-3-(2',3',4',6'-tetra-O-benzoyl- β -D-glucopyranosyl)-1,2,4-triazole (**3f**)

From tetrazole 1 (0.70 g, 1.08 mmol) and N-benzyl-4-tertbutylbenzamide (2f, 0.93 g, 3.23 mmol) in *m*-xylene according to General procedure II. Reaction time: 3 h. Purified by column chromatography (1:1 EtOAc-hexane) to yield 0.57 g (61%) yellow solid. Mp: 231–233 °C; $R_{\rm f}$: 0.28 (1:1 EtOAc-hexane); $[\alpha]_{\rm D} = -43$ (c 0.37, CHCl₃);¹H NMR (CDCl₃) δ (ppm): 7.97–7.00 (29H, m, aromatics), 6.00, 5.97, 5.65 (3 \times 1H, 3 pseudo t, J = 9.6, 9.6 Hz in each, H-2', H-3', H-4'), 5.51 (1H, d, J = 16.5 Hz, PhCH₂), 5.33 (1H, d, J = 16.5 Hz, PhCH₂), 5.11 (1H, d, J = 9.6 Hz, H-1'), 4.49 (1H, dd, J = 12.2, 1.9 Hz, H-6'a), 4.32 (1H, dd, J = 12.2, 5.3 Hz, H-6'b), 4.17 (1H, ddd, J = 9.6, 5.2, 1.9 H-5'), 1.29 (9H, s, C(CH₃)₃); ¹³C NMR (CDCl₃) δ (ppm): 165.9, 165.7, 165.1, 164.7 (CO), 156.7, 153.4 (triazole C-3, C-5), 149.7, 135.5, 133.5–123.7 (aromatics), 76.7, 73.9, 73.1, 69.9, 69.1 (C-1' - C-5'), 62.9 (C-6'), 48.0 (PhCH₂), 34.2 (C(CH₃)₃), 31.1 (C(CH₃)₃). Anal: Calcd for C₅₃H₄₇N₃O₉ (869.95): C, 73.17; H, 5.45; N, 4.83. Found: C, 73.11; H, 5.36; N, 4.91.

4.9. 4-Benzyl-5-(4-trifluoromethylphenyl)-3-(2',3',4',6'-tetra-O-benzoyl- β -D-glucopyranosyl)-1,2,4-triazole (**3g**)

From tetrazole **1** (0.60 g, 0.93 mmol) and N-benzyl-4trifluoromethylbenzamide (2g, 0.78 g, 2.78 mmol) in toluene according to General procedure II. Reaction time: 16 h. Purified by column chromatography (1:4 \rightarrow 1:1 EtOAc-hexane) to yield 0.72 g (88%) white solid. Mp: 213–215 °C; $[\alpha]_D = -26$ (c 0.54, CHCl₃); ¹H NMR (CDCl₃) δ (ppm): 7.94–6.95 (29H, m, aromatics), 6.06–5.98 $(2 \times 1H, m, H-2' \text{ and/or } H-3' \text{ and/or } H-4')$, 5.70 (1H, pseudo t, *J* = 9.2, 9.2 Hz, H-2′ or H-3′ or H-4′), 5.60 (1H, d, *J* = 16.4 Hz, PhCH₂), 5.29 (1H, d, J = 16.4 Hz, PhCH₂), 5.21 (1H, d, J = 8.8 Hz, H-1'), 4.50 (1H, dd, *J* = 12.3, <1 Hz, H-6'a), 4.34 (1H, dd, *J* = 12.3, 4.8 Hz, H-6'b), 4.23 (1H, ddd, J = 9.2, 4.8, <1 Hz, H-5'); ¹³C NMR (CDCl₃) δ (ppm): 165.8, 165.7, 165.1, 164.8 (CO), 155.4, 150.3 (triazole C-3, C-5), 134.9-125.0 (aromatics), 132.0 (q, ${}^{2}J_{(C, F)} = 34.6$ Hz, C–CF₃), 123.5 (q, ${}^{1}J_{(C, F)} = 34.6$ Hz, C–CF₃), 123.5 (q, {}^{1}J_{(C, F)} = 34.6 Hz, 123.5 (q, {}^{1}J_{(C, F)} = 34.6 Hz $F_{\rm F}=271.3$ Hz, CF_3), 76.8, 73.7, 73.2, 69.9, 68.9 (C-1' - C-5'), 62.7 (C-6'), 48.2 (PhCH₂). Anal: Calcd for C₅₀H₃₈F₃N₃O₉ (881.85): C, 68.10; H, 4.34; N, 4.77. Found: C, 68.23; H, 4.41; N, 4.63.

4.10. 4-Benzyl-5-(4-methoxyphenyl)-3-(2',3',4',6'-tetra-O-benzoyl- β -D-glucopyranosyl)-1,2,4-triazole (**3i**)

From tetrazole **1** (1.0 g, 1.54 mmol) and *N*-benzyl-4methoxybenzamide (**2i**, 1.12 g, 4.64 mmol) in *m*-xylene according to General procedure **II**. Purified by column chromatography (1:1 \rightarrow 2:1 EtOAc-hexane) to yield 0.81 g (62%) white amorphous solid. *R*_f: 0.45 (2:1 EtOAc-hexane); $[\alpha]_D = -19$ (c 0.55, CHCl₃); ¹H NMR (CDCl₃) δ (ppm): 7.98–6.98 (27H, m, aromatics); 6.87 (2H, d, *J* = 8.8 Hz, aromatics), 6.06–5.91 (2 × 1H, m, H-2' and/or H-3' and/ or H-4'), 5.65 (1H, pseudo t, *J* = 9.6, 9.6 Hz, H-2' or H-3' or H-4'), 5.50 (1H, d, *J* = 16.6 Hz, PhCH₂), 5.29 (1H, d, *J* = 16.6 Hz, PhCH₂), 5.18 (1H, d, *J* = 9.6, H-1'), 4.48 (1H, dd, *J* = 12.3, 2.6 Hz, H-6'a), 4.32 (1H, dd, J = 12.3 and 5.4 Hz, H-6′b), 4.19 (1H, ddd, J = 9.6, 5.4, 2.6 Hz, H-5′), 3.79 (3H, s, OMe); ¹³C NMR (CDCl₃) δ (ppm): 166.0, 165.8, 165.2, 164.8 (CO), 161.1 (MeOPh C-4), 156.7, 149.7 (triazole C-3, C-5), 135.5–126.1, 118.8, 114.2 (2) (aromatics), 76.7, 73.9, 73.2, 70.0, 69.1 (C-1′ - C-5′), 63.0 (C-6′), 55.3 (OMe), 48.1 (PhCH₂). Anal: Calcd for C₅₀H₄₁N₃O₁₀ (843.87): C, 71.16; H, 4.90; N, 4.98. Found: C, 71.08; H, 5.01; N, 4.91.

4.11. 4-Benzyl-5-(4-nitrophenyl)-3-(2',3',4',6'-tetra-O-benzoyl-β-D-glucopyranosyl)-1,2,4-triazole (**3***j*)

From tetrazole 1 (0.50 g, 0.77 mmol) and N-benzyl-4nitrobenzamide (2j, 0.59 g, 2.31 mmol) in toluene according to General procedure II. Reaction time: 16 h. Purified by column chromatography (1:1 EtOAc-hexane) to yield 0.25 g (38%) yellow syrup. R_{f} : 0.28 (1:1 EtOAc-hexane); $[\alpha]_{D} = -41$ (c 0.50, CHCl₃); ¹H NMR (CDCl₃) δ (ppm): 8.18 (2H, d, J = 8.5 Hz, aromatics), 7.92–7.19 (25H, m, aromatics), 6.95 (2H, d, *J* = 6.9 Hz, aromatics), 6.05, 6.00, 5.72 (3 \times 1H, 3 pseudo t, J = 9.5, 9.5 Hz in each, H-2', H-3', H-4'), 5.66 (1H, d, J = 16.5 Hz, PhCH₂), 5.31 (1H, d, J = 16.5 Hz, PhCH₂), 5.26 (1H, d, J = 9.4 Hz, H-1'), 4.51 (1H, dd, J = 12.1, <1 Hz, H-6'a), 4.35 (1H, dd, J = 12.1, 5.1 Hz, H-6'b), 4.27 (1H, ddd, J = 9.5, 5.1, 2.2 Hz, H-5′); ¹³C NMR (CDCl₃) δ (ppm): 165.8, 165.6, 165.1, 164.9 (CO), 154.6, 150.7 (triazole C-3, C-5), 148.6, 134.6–123.7 (aromatics), 76.8, 73.6, 73.2, 70.1, 68.9 (C-1' - C-5'), 62.7 (C-6'), 48.4 (PhCH₂). Anal: Calcd for C₄₉H₃₈N₄O₁₁ (858.85): C, 68.52; H, 4.46; N, 6.52. Found: C, 68.64; H, 4.52; N, 6.43.

4.12. 4-Benzyl-5-(3,5-dimethylphenyl)-3-(2',3',4',6'-tetra-Obenzoyl-β-D-glucopyranosyl)-1,2,4-triazole (**3m**)

From tetrazole 1 (1.0 g, 1.54 mmol) and N-benzyl-3,5dimethylbenzamide (2m, 1.11 g, 4.64 mmol) in m-xylene according to General procedure II. Reaction time: 3 h. Purified by column chromatography (1:1 \rightarrow 2:1 EtOAc-hexane) to yield 0.85 g (66%) white solid. Mp: 225–227 °C; *R*_f: 0.28 (1:1 EtOAc-hexane); $[\alpha]_{\rm D} = -19$ (c 0.37, CHCl₃); ¹H NMR (CDCl₃) δ (ppm); 7.98–7.00 (28H, m, aromatics), 6.12, 6.05, 5.75 (3 \times 1H, 3 pseudo t, J = 9.5, 9.3 Hz in each, H-2', H-3', H-4'), 5.50 (1H, d, J = 16.4 Hz, PhCH₂), 5.32 (1H, d, J = 16.4 Hz, PhCH₂), 5.22 (1H, d, J = 9.6 Hz, H-1'), 4.52 (1H, dd, J = 12.5, 2.6 Hz, H-6'a), 4.39 (1H, dd, J = 12.6, 5.2 Hz, H-6'b), 4.26 (1H, ddd, J = 9.5, 5.2, 2.6 Hz, H-5'), 2.19 (6H, s, $2 \times CH_3$); ¹³C NMR (CDCl₃) δ (ppm): 165.6, 165.5, 164.9, 164.5 (CO), 156.7, 149.6 (triazole C-3, C-5), 138.0 (2), 135.3-126.0 (aromatics), 76.4, 73.8, 72.6, 69.8, 68.8 (C-1' - C-5'), 62.6 (C-6'), 47.9 (PhCH₂), 20.9 $(2 \times CH_3)$. Anal: Calcd for $C_{51}H_{43}N_3O_9$ (841.90): C, 72.76; H, 5.15; N, 4.99. Found: C, 72.69; H, 5.07; N, 4.86.

4.13. 4-Benzyl-5-(3,4,5-trimethoxyphenyl)-3-(2',3',4',6'-tetra-Obenzoyl- β -D-glucopyranosyl)-1,2,4-triazole (**3p**)

From tetrazole **1** (0.50 g, 0.77 mmol) and *N*-benzyl-3,4,5-trimethoxybenzamide (**2p**, 0.7 g, 2.31 mmol) in *m*-xylene according to General procedure **II**. Reaction time: 8 h. Purified by column chromatography (3:2 EtOAc-hexane) to yield 0.45 g (65%) pale yellow syrup. $R_{\rm f}$: 0.15 (3:2 EtOAc-hexane); $[\alpha]_{\rm D} = -33$ (c 0.60, CHCl₃); ¹H NMR (CDCl₃) δ (ppm): 7.96–7.00 (25H, m, aromatics), 6.62 (2H, s, aromatics), 6.10–5.99 (2 × 1H, m, H-2' and/or H-3' and/or H-4'), 5.70 (1H, pseudo t, J = 9.3, 9.3 Hz, H-2' or H-3' or H-4'), 5.55 (1H, d, J = 16.8 Hz, PhCH₂), 5.31 (1H, d, J = 16.8 Hz, PhCH₂), 5.22 (1H, d, J = 9.3 Hz, H-1'), 4.45 (1H, dd, J = 10.8, <1 Hz, H-6'a), 4.32–4.24 (2 × 1H, m, H-6'b, H-5'), 3.83 (3H, s, OMe), 3.59 (6H, s, 2 × OMe); ¹³C NMR (CDCl₃) δ (ppm): 165.8, 165.7, 165.0, 164.7 (CO), 156.5, 153.2, 150.0 (triazole C-3, C-5, 3,4,5-(MeO)_3Ph C-3, C-5), 135.7–121.5, 106.1 (2) (aromatics), 76.7, 73.8, 73.1, 70.0, 68.9 (C-1' –

C-5'), 62.8 (C-6'), 60.8 (OMe), 55.8 (2 \times OMe), 48.1 (PhCH₂). Anal: Calcd for C₅₂H₄₅N₃O₁₂ (903.93): C, 69.09; H, 5.02; N, 4.65. Found: C, 69.19; H, 4.96; N, 4.51.

4.14. 4-Benzyl-5-(2-naphthyl)-3-(2',3',4',6'-tetra-O-benzoyl- β -D-glucopyranosyl)-1,2,4-triazole (**3q**)

From tetrazole **1** (0.60 g, 0.93 mmol) and *N*-benzyl-naphthalene-2-carboxamide (**2q**, 0.73 g, 2.78 mmol) in toluene according to General procedure **II**. Reaction time: 3 h. Purified by column chromatography (1:1 \rightarrow 3:2 EtOAc-hexane) to yield 0.41 g (52%) pale yellow amorphous solid. *R*_f: 0.25 (1:1 EtOAc-hexane); $[\alpha]_D = -33$ (c 0.50, CHCl₃); ¹H NMR (CDCl₃) δ (ppm): 7.96–7.01 (32H, m, aromatics), 6.08, 6.02, 5.70 (3 × 1H, 3 pseudo t, *J* = 9.3, 9.3 Hz in each, H-2', H-3', H-4'), 5.58 (1H, d, *J* = 15.9 Hz, PhCH₂), 5.38 (1H, d, *J* = 15.9 Hz, PhCH₂), 5.19 (1H, d, *J* = 9.3 Hz, H-1'), 4.49 (1H, dd, *J* = 11.9, 2.6 Hz, H-6'a), 4.35 (1H, dd, *J* = 11.9, 5.3 Hz, H-6'b), 4.23 (1H, ddd, *J* = 9.3, 5.3, 2.6 Hz, H-5'); ¹³C NMR (CDCl₃) δ (ppm): 165.8, 165.7, 165.0, 164.7 (CO), 156.6, 149.9 (triazole C-3, C-5), 135.4–123.9 (aromatics), 76.7, 73.8, 73.0, 69.9, 69.0 (C-1' - C-5'), 62.8 (C-6'), 48.2 (PhCH₂). Anal: Calcd for C₅₃H₄₁N₃O₉ (863.91): C, 73.68; H, 4.78; N, 4.86. Found: C, 73.80; H, 4.69; N, 4.97.

4.15. 4-Benzyl-5-(4-benzyloxycarbonylphenyl)-3-(2',3',4',6'-tetra-O-benzoyl- β -D-glucopyranosyl)-1,2,4-triazole (**3s**)

From tetrazole 1 (0.30 g, 0.46 mmol) and N-benzyl-(4benzvloxvcarbonvl)-benzamide (2s. 0.48 g. 1.39 mmol) in mxylene according to General procedure **II**. Reaction time: 3 h. Purified by column chromatography (1:4 \rightarrow 1:1 EtOAc-hexane) to yield 0.30 g (69%) brownish foam. Rf: 0.23 (1:1 EtOAc-hexane); $[\alpha]_{\rm D} = -26$ (c 0.54, CHCl₃); ¹H NMR (CDCl₃) δ (ppm): 8.07–6.94 $(34H, m, aromatics), 6.01-5.99 (2 \times 1H, m, H-2' and/or H-3' and/or$ H-4′), 5.68 (1H, pseudo t, J = 9.4, 8.6 Hz, H-2′ or H-3′ or H-4′), 5.57 $(1H, d, J = 16.5 Hz, PhCH_2), 5.35 (2H, s, PhCH_2), 5.29 (1H, d, J)$ J = 16.5 Hz, PhCH₂), 5.18 (1H, d, J = 9.2 Hz, H-1'), 4.49 (1H, dd, *J* = 12.3, 2.0 Hz, H-6'a), 4.33 (1H, dd, *J* = 12.3, 5.3 Hz, H-6'b), 4.20 $(1H, ddd, J = 9.5, 5.3, 2.0 Hz, H-5'); {}^{13}C NMR (CDCl_3) \delta (ppm): 165.8,$ 165.7, 165.5, 165.0, 164.8 (CO), 155.8, 150.3 (triazole C-3, C-5), 135.6-126.0 (aromatics), 76.8, 73.7, 73.2, 70.0, 68.9 (C-1' - C-5'), 67.0 (COOCH2Ph), 62.8 (C-6'), 48.2 (PhCH2). Anal: Calcd for C57H45N3O11 (947.98): C, 72.22; H, 4.78; N, 4.43. Found: C, 72.28; H, 4.91; N, 4.34.

4.16. 4-Benzyl-3-(β-D-glucopyranosyl)-5-phenyl-1,2,4-triazole (**4d**)

From triazole **3d** (0.82 g, 1.00 mmol) according to General procedure **III**. Reaction time: 4 days. Purified by column chromatography (9:1 \rightarrow 4:1 CHCl₃–MeOH) to yield 0.29 g (73%) pale yellow syrup. $R_{\rm f}$: 0.55 (7:3 CHCl₃–MeOH); $[\alpha]_{\rm D} = -15$ (c 0.60, MeOH); ¹H NMR (D₂O) δ (ppm): 7.50–6.94 (10H, m, aromatics), 5.31 (2H, s, PhCH₂), 4.48 (1H, d, J = 10.6 Hz, H-1'), 3.98 (1H, pseudo t, J = 9.3, 9.3 Hz, H-2' or H-3' or H-4'), 3.67–3.47 (4 × 1H, m, H-6'a, H-6'b, H-2' and/or H-3' and/or H-4'), 3.34 (1H, m, H-5'); ¹³C NMR (D₂O) δ (ppm): 156.9, 153.2 (triazole C-3, C-5), 135.2, 131.2, 129.3 (2), 129.1 (2), 129.0 (2), 128.3, 126.4 (2), 125.4 (aromatics), 80.3, 77.2, 72.1, 71.8, 69.4 (C-1' – C-5'), 60.8 (C-6'), 47.6 (PhCH₂). Anal: Calcd for C₂₁H₂₃N₃O₅ (397.42): C, 63.46; H, 5.83; N, 10.57. Found: C, 63.32; H, 5.75; N, 10.68.

4.17. 4-Benzyl-3-(β -D-glucopyranosyl)-5-(4-methylphenyl)-1,2,4-triazole (**4e**)

From triazole **3e** (0.52 g, 0.63 mmol) according to General procedure **III**. Reaction time: 2 days. Purified by column

chromatography (9:1 \rightarrow 4:1 CHCl₃–MeOH) to yield 0.25 g (94%) colourless syrup. *R*_f: 0.35 (4:1 CHCl₃–MeOH); $[\alpha]_D = -4$ (c 0.50, MeOH); ¹H NMR (CD₃OD) δ (ppm): 7.34–7.23 (7H, m, aromatics), 7.00 (2H, d, *J* = 6.6 Hz, aromatics), 5.41 (1H, d, *J* = 16.9 Hz, PhCH₂), 5.34 (1H, d, *J* = 16.9 Hz, PhCH₂), 4.34 (1H, d, *J* = 9.7 Hz, H-1'), 3.92 (1H, pseudo t, *J* = 9.1, 8.9 Hz, H-2' or H-3' or H-4'), 3.75 (1H, dd, *J* = 12.0, <1 Hz, H-6'a), 3.63–3.54 (2H, m, H-6'b, H-2' or H-3' or H-4') 3.43–3.72 (2H, m, H-2' or H-3' or H-4', H-5'), 2.34 (3H, s, CH₃); ¹³C NMR (CD₃OD) δ (ppm): 157.4, 155.0 (triazole C-3, C-5), 142.4, 136.9, 130.7 (2), 130.1 (2), 130.0 (2), 129.2, 127.5 (2), 124.7 (aromatics), 82.5, 79.3, 74.2, 73.6, 71.1 (C-1' – C-5'), 62.7 (C-6'), 47.7 (PhCH₂), 21.5 (CH₃). Anal: Calcd for C₂₂H₂₅N₃O₅ (411.45): C, 64.22; H, 6.12; N, 10.21. Found: C, 64.37; H, 6.19; N, 10.10.

4.18. 4-Benzyl-3-(β -D-glucopyranosyl)-5-(4-tert-butylphenyl)-1,2,4-triazole (**4f**)

From triazole 3f (0.49 g, 0.56 mmol) according to General procedure III. Reaction time: 1 day. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.25 g (98%) yellow syrup. R_f: 0.31 (4:1 CHCl₃–MeOH); $[\alpha]_D = -3$ (c 0.31, MeOH); ¹H NMR (CD₃OD) δ (ppm): 7.45 (2H, d, J = 8.3 Hz, aromatics), 7.35 (2H, d, I = 8.3 Hz, aromatics), 7.23 (3H, m, aromatics), 6.99 (2H, d, *J* = 6.4 Hz, aromatics), 5.40 (1H, d, *J* = 16.8 Hz, PhCH₂), 5.33 (1H, d, *J* = 16.8 Hz, PhCH₂), 4.31 (1H, d, *J* = 9.7 Hz, H-1[′]), 3.89 (1H, pseudo t, J = 9.4, 9.0 Hz, H-2' or H-3' or H-4'), 3.74 (1H, dd, J = 12.1, 2.6 Hz, H-6'a), 3.56 (1H, dd, J = 12.1, 5.3 Hz, H-6'b), 3.41-3.34 (2H, m, H-2' and/or H-3' and/or H-4'), 3.25 (1H, ddd, *J* = 9.8, <1 Hz, H-5'), 1.27 (9H, s, C(CH₃)₃), ¹³C NMR (CD₃OD) δ (ppm): 157.3, 155.4, 155.1 (triazole C-3, C-5, 4-tBuPh C-4), 136.9–124.7 (aromatics), 82.5, 79.3, 74.2, 73.6, 71.1 (C-1' - C-5'), 62.7 (C-6'), 48.7 (PhCH₂), 35.8 (C(CH₃)₃), 31.6 (C(CH₃)₃). Anal: Calcd for C₂₅H₃₁N₃O₅ (453.53): C, 66.21; H, 6.89; N, 9.27. Found: C, 66.27; H, 6.78; N, 9.39.

4.19. 4-Benzyl-3-(β -D-glucopyranosyl)-5-(4-trifluoromethyl-phenyl)-1,2,4-triazole (**4g**)

From triazole **3g** (0.50 g, 0.57 mmol) according to General procedure **III**. Reaction time: 4 h. Purified by column chromatography (4:1 CHCl₃—MeOH) to yield 0.16 g (61%) white crystals. Mp: 208–210 °C; $[\alpha]_D = -18$ (c 0.48, MeOH); ¹H NMR (CD₃OD) δ (ppm): 7.77–7.05 (9H, m, aromatics), 5.51 (1H, d, J = 16.9 Hz, PhCH₂), 5.45 (1H, d, J = 16.9 Hz, PhCH₂), 4.48 (1H, d, J = 9.3 Hz, H-1'), 3.99 (1H, m, H-2' or H-3' or H-4'), 3.82 (1H, dd, J = 11.7, <1 Hz, H-6'a), 3.65 (1H, dd, J = 11.7, <1 Hz, H-6'b), 3.47–3.37 (3 × 1H, m, H-2' and/or H-3' and/or H-4', H-5'); ¹³C NMR (CD₃OD) δ (ppm): 156.0, 155.6 (triazole C-3, C-5), 136.6 (aromatics), 133.4 (q, ² $J_{(C, F)} = 31.7$ Hz, C–CF₃), 131.7–127.0 (aromatics), 125.2 (q, ¹ $J_{(C, F)} = 271.3$ Hz, CF₃), 82.5, 79.3, 74.2, 73.6, 71.1 (C-1' – C-5'), 62.7 (C–6'), 48.9 (PhCH₂). Anal: Calcd for C₂₂H₂₂F₃N₃O₅ (465.42): C, 56.77; H, 4.76; N, 9.03. Found: C, 56.69; H, 4.71; N, 9.14.

4.20. 4-Benzyl-3-(β -D-glucopyranosyl)-5-(4-methoxyphenyl)-1,2,4-triazole (**4i**)

From triazole **3i** (0.80 g, 0.95 mmol) according to General procedure **III**. Reaction time: 3 h. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.23 g (68%) yellow syrup. R_f : 0.33 (4:1 CHCl₃–MeOH). [α]_D = -14 (c 0.35, MeOH); ¹H NMR (CD₃OD) δ (ppm): 7.37 (2H, d, J = 8.8 Hz, aromatics), 7.32–7.20 (3H, m, aromatics), 7.05–6.99 (2H, m, aromatics), 6.96 (2H, d, J = 8.8 Hz, aromatics), 5.42 (1H, d, J = 16.8 Hz, PhCH₂), 5.35 (1H, d, J = 16.8 Hz, PhCH₂), 4.35 (1H, d, J = 9.6 Hz, H-1'), 3.84 (1H, pseudo t, J = 10.8 Hz, 9.6 Hz, H-2' or H-3' or H-4'), 3.78 (3H, s, OMe), 3.77 (1H, dd, J = 12.4, 2.3 Hz, H-6'a), 3.61 (1H, dd, J = 12.4, 5.3 Hz, H-6'b), 3.41–3.29 (3H,

m, H-2' and/or H-3' and/or H-4', H-5'); 13 C NMR (CD₃OD) δ (ppm): 163.0 (4-MeOPh C-4), 157.2, 154.9 (triazole C-3, C-5), 136.9, 131.6 (2), 130.1 (2), 129.1, 127.5 (2), 119.5, 115.5 (2) (aromatics), 82.4, 79.3, 74.2, 73.6, 71.1 (C-1' - C-5'), 62.6 (C-6') 55.9 (OMe), 48.6 (PhCH₂). Anal: Calcd for C₂₂H₂₅N₃O₆ (427.45): C, 61.82; H, 5.90; N, 9.83. Found: C, 61.87; H, 6.02; N, 9.75.

4.21. 4-Benzyl-3-(β -D-glucopyranosyl)-5-(4-nitrophenyl)-1,2,4-triazole (**4j**)

From triazole 3j (0.23 g, 0.27 mmol) according to General procedure III. Reaction time: 6 h. The product precipitated from the reaction mixture and was used after filtration without further purification. Yield: 0.11 g (91%), pale yellow needles. Mp: 153–155 °C; $[\alpha]_{\rm D} = -20$ (c 0.50, MeOH); ¹H NMR (CD₃OD) δ (ppm): 8.29 (2H, d, *J* = 8.6 Hz, aromatics), 7.75 (2H, d, *J* = 8.6 Hz, aromatics), 7.28 (3H, m, aromatics), 7.05 (2H, d, J = 6.3 Hz, aromatics), 5.54 (1H, d, J = 16.8 Hz, PhCH₂), 5.48 (1H, d, J = 16.8 Hz, PhCH₂), 4.48 (1H, d, J = 9.7 Hz, H-1'), 3.98 (1H, pseudo t, J = 8.9, 8.9 Hz, H-2' or H-3' or H-4′), 3.82 (1H, dd, *J* = 11.9, <1 Hz, H-6′a), 3.65 (1H, dd, *J* = 12.0, 5.4 Hz, H-6′b), 3.50–3.43 (2 \times 1H, m, H-2′ and/or H-3′ and/or H-4′), 3.72 (1H, m, H-5'); ¹³C NMR (CD₃OD) δ (ppm): 155.9, 155.5 (triazole C-3, C-5), 150.4, 136.5, 133.9, 131.4 (2), 130.2 (2), 129.3, 127.7 (2), 125.0 (2) (aromatics), 82.6, 79.4, 74.2, 73.7, 71.2 (C-1' - C-5'), 62.7 (C-6'), 49.0 (PhCH₂). Anal: Calcd for C₂₁H₂₂N₄O₇ (442.42): C, 57.01; H, 5.01; N, 12.66. Found: C, 56.87; H, 5.11; N, 12.54.

4.22. 4-Benzyl-5-(3,5-dimethylphenyl)-3-(β -D-glucopyranosyl)-1,2,4-triazole (**4m**)

From triazole **3m** (0.64 g, 0.76 mmol) according to General procedure **III**. Reaction time: 3 h. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.20 g (62%) of yellow syrup. $R_{\rm f}$: 0.66 (7:3 CHCl₃–MeOH); $[\alpha]_{\rm D} = -8$ (c 0.69, MeOH); ¹H NMR (CD₃OD) δ (ppm): 7.25–6.95 (8H, m, aromatics), 5.36 (1H, d, J = 16.8 Hz, PhCH₂), 5.29 (1H, d, J = 16.8 Hz, PhCH₂), 4.38 (1H, d, J = 9.7 Hz, H-1'), 3.96 (1H, pseudo t, J = 9.3, 8.9 Hz, H-2' or H-3' or H-4'), 3.76 (1H, dd, J = 12.2, 1.4 Hz, H-6'a), 3.60 (1H, dd, J = 12.2, 5.4 Hz, H-6'b), 3.48–3.40 (2H, m, H-2' and/or H-3' and/or H-4'), 3.33–3.28 (1H, m, H-5'), 2.18 (6H, s, 2 × CH₃); ¹³C NMR (CD₃OD) δ (ppm): 157.7, 155.2 (triazole C-3, C-5), 140.2 (2), 137.2, 133.4, 130.3 (2), 129.4, 128.0 (2), 127.9 (2), 127.6 (aromatics), 82.7, 79.5, 74.4, 73.8, 71.3 (C-1' – C-5'), 62.9 (C-6'), 49.1 (PhCH₂), 21.6 (2 × CH₃). Anal: Calcd for C₂₃H₂₇N₃O₅ (425.48): C, 64.93; H, 6.40; N, 9.88. Found: C, 65.02; H, 6.47; N, 9.74.

4.23. 4-Benzyl-3-(β -D-glucopyranosyl)-5-(3,4,5-trimethoxy-phenyl)-1,2,4-triazole (**4p**)

From triazole **3p** (0.42 g, 0.46 mmol) according to General procedure III. Reaction time: 6 h. Purified by column chromatography (9:1 \rightarrow 4:1 CHCl₃–MeOH) to yield 0.20 g (91%) colourless syrup. R_f : 0.42 (4:1 CHCl₃-MeOH); $[\alpha]_D = -17$ (c 0.53, MeOH); ¹H NMR (CD₃OD) δ (ppm): 7.38–7.28 (3H, m, aromatics), 7.12 (2H, d, J = 7.3 Hz, aromatics), 6.69 (2H, s, aromatics), 5.50 (1H, d, J = 17.1 Hz, PhCH₂), 5.42 (1H, d, J = 17.1 Hz, PhCH₂), 4.45 (1H, d, J = 9.6 Hz, H-1'), 4.00 (1H, pseudo t, J = 8.6, 9.6 Hz, H-2' or H-3' or H-4'), 3.80 (1H, dd, J = 12.0, <1 Hz, H-6'a), 3.77 (4H, m, H-6'b, 1 × OMe), 3.63 (7H, m, H-6'b, 2 × OMe), 3.50–3.43 (2 × 1H, m, H-2' and/or H-3' and/or H-4'), 3.63 (1H, m, H-5'); ¹³C NMR (CD₃OD) δ (ppm): 157.2, 155.2 (triazole C-3, C-5), 154.9 (2), 141.0, 137.4, 130.2 (2), 129.1, 127.4 (2), 122.8, 107.5 (2) (aromatics), 82.5, 79.3, 74.2, 73.6, 71.1 (C-1' - C-5'), 62.8 (C-6'), 61.1 (OMe), 56.6 (2 \times OMe), 48.8 (PhCH₂). Anal: Calcd for C₂₄H₂₉N₃O₈ (487.50): C, 59.13; H, 6.00; N, 8.62. Found: C, 59.22; H, 6.09; N, 8.49.

4.24. 4-Benzyl-3-(β -D-glucopyranosyl)-5-(2-naphthyl)-1,2,4-triazole (**4q**)

From triazole **3q** (0.50 g, 0.58 mmol) according to General procedure **III**. Reaction time: 3 h. Purified by column chromatography (9:1 CHCl₃–MeOH) to yield 0.22 g (85%) white crystals. Mp: 243–245 °C; $[\alpha]_D = -19$ (c 0.51, MeOH); ¹H NMR (DMSO-d₆) δ (ppm): 8.03–7.02 (12H, m, aromatics), 5.48 (1H, d, J = 16.9 Hz, PhCH₂), 5.42 (1H, d, J = 16.9 Hz, PhCH₂), 4.35 (1H, d, J = 9.3 Hz, H-1'), 3.86 (1H, pseudo t, J = 9.3, 9.3 Hz, H-2' or H-3' or H-4'), 3.62 (1H, dd, J = 11.9, <1 Hz, H-6'a), 3.42 (1H, dd, J = 11.9, 5.3 Hz, H-6'b), 3.31–3.17 (3 × 1H, m, H-2' and/or H-3' and/or H-4', H-5'); ¹³C NMR (DMSO-d₆) δ (ppm): 154.3, 153.3 (triazole C-3, C-5), 136.1–124.6 (aromatics), 81.2, 78.0, 72.3, 71.4, 69.8 (C-1' – C-5'), 61.0 (C-6'), 46.8 (PhCH₂). Anal: Calcd for C₂₅H₂₅N₃O₅ (447.48): C, 67.10; H, 5.63; N, 9.39. Found: C, 67.02; H, 5.74; N, 9.27.

4.25. $5-(4-Carboxyphenyl)-3-(\mathbf{2}', \mathbf{3}', \mathbf{4}', \mathbf{6}'-tetra-O-benzoyl-\beta-D-glucopyranosyl)-1, 2, 4-triazole ($ **5***l*)

Triazole 3s (0.56 g, 0.59 mmol) was dissolved in anhydrous EtOAc (35 mL), 10% Pd(C) (55 mg) was added and H₂ was bubbled through the reaction mixture at 50 °C. After disappearance of the starting material (6 h, monitored by TLC, 1:1 EtOAc-hexane) the reaction was filtered through a pad of celite, the solvent was evaporated, and the residue was purified by column chromatography (EtOAc) to yield 0.34 g (75%) colourless syrup. R_f: 0.58 (1:3 AcOH-toluene); $[\alpha]_{D} = -33$ (c 0.48, MeOH); ¹H NMR (CD₃OD) δ (ppm): 8.02–7.12 (24H, m, aromatics), 6.24 (1H, pseudo t, I = 9.5. 9.5 Hz, H-3'), 6.08 (1H, pseudo t, *J* = 9.6, 9.5 Hz, H-2'), 5.95 (1H, pseudo t, J = 9.5, 9.5 Hz, H-4'), 5.38 (1H, d, J = 9.9 Hz, H-1'), 4.66-4.58 (3H, m, H-6'a, H-6'b, H-5'); ¹³C NMR (CD₃OD) δ (ppm): 169.2 (COOH), 167.6, 167.2, 166.7, 166.4 (CO), 134.7-127.4 (aromatics), 77.7 (C-5'), 75.7 (C-3'), 74.8 (C-1'), 73.1 (C-2'), 71.1 (C-4'), 64.6 (C-6'). Anal: Calcd for C₄₃H₃₃N₃O₁₁ (767.74): C, 67.27; H, 4.33; N, 5.47. Found: C, 67.14; H, 4.47; N, 5.39.

4.26. 3-(β-D-Glucopyranosyl)-5-methyl-1,2,4-triazole [54] (**6a**)

From triazole **5a** [62] (0.25 g, 0.38 mmol) according to General procedure **III**. Reaction time: 3 days. Purified by column chromatography (7:3 CHCl₃–MeOH) to yield 0.07 g (73%) colourless syrup. $R_f: 0.55 (1:1 \text{ CHCl}_3-\text{MeOH}); [\alpha]_D = +21 (c 0.36, \text{MeOH}); ^1\text{H NMR} (D_2O) \delta$ (ppm): 4.36 (1H, d, J = 9.2 Hz, H-1'), 3.82 (1H, dd, J = 11.9, <1 Hz, H-6'a), 3.68–3.63 (2H, m, H-2' or H-3' or H-4', H-6'b), 3.56–3.43 (3H, m, H-2' and/or H-3' and/or H-4', H-5'), 2.36 (3H, s, CH₃); ¹³C NMR (D_2O) δ (ppm): 159.6, 156.2 (triazole C-3, C-5), 80.8, 77.7, 75.3, 73.1, 70.1 (C-1' – C-5'), 61.5 (C-6'), 11.4 (CH₃). Anal: Calcd for C₉H₁₅N₃O₅ (245.23): C, 44.08; H, 6.17; N, 17.13. Found: C, 44.19; H, 6.23; N, 17.01.

4.27. 5-(tert-Butyl)-3-(β-D-glucopyranosyl)-1,2,4-triazole (**6b**)

From triazole **5b** [62] (0.25 g, 0.36 mmol) according to General procedure **III**. Reaction time: 2 days. (The mixture was neutralised with acetic acid.) Purified by column chromatography (4:1 CHCl₃—MeOH) to yield 0.10 g (98%) colourless syrup. $R_{\rm f}$: 0.51 (7:3 CHCl₃—MeOH); [α]_D = -6 (c 0.25, MeOH); ¹H NMR (CD₃OD) δ (ppm): 4.33 (1H, d, J = 8.6 Hz, H-1'), 3.82 (1H, dd, J = 11.9, 2.5 Hz, H-6'a), 3.69–3.64 (2H, m, H-2' or H-3' or H-4', H-6'b), 3.50–3.40 (3H, m, H-2' and/or H-3' and/or H-4', H-5'), 1.34 (9H, s, C(CH₃)₃); ¹³C NMR (CD₃OD) δ (ppm): 166.6, 162.1 (triazole C-3, C-5), 82.2, 79.3, 76.9, 74.2, 71.2 (C-1' - C-5'), 62.8 (C-6'), 33.3 (C(CH₃)₃) 29.6 (C(CH₃)₃). Anal: Calcd for C₁₂H₂₁N₃O₅ (287.31): C, 50.16; H, 7.37; N, 14.63. Found: C, 50.09; H, 7.52; N, 14.57.

4.28. 3-(β-D-Glucopyranosyl)-5-hydroxymethyl-1,2,4-triazole [54] (**6c**)

From triazole **5t** [62] (0.18 g, 0.25 mmol) according to General procedure **III**. Reaction time: 5 days. (The mixture was neutralised with acetic acid.) Purified by column chromatography (3:2 CHCl₃– MeOH) to yield 0.06 g (93%) colourless syrup. $R_{\rm f}$: 0.38 (1:1 CHCl₃– MeOH); [α]_D = -3 (c 0.42, MeOH); ¹H NMR (CD₃OD) δ (ppm): 4.67 (2H, s, CH₂), 4.35 (1H, d, J = 9.2 Hz, H-1'), 3.83 (1H, dd, J = 12.3, <1 Hz, H-6'a), 3.68–3.59 (2H, m, H-2' or H-3' or H-4', H-6'b), 3.49– 3.40 (3H, m, H-2' and/or H-3' and/or H-4', H-5'); ¹³C NMR (CD₃OD) δ (ppm): 160.5, 160.4 (triazole C-3, C-5), 82.2, 79.2, 76.3, 74.4, 71.2 (C-1' – C-5'), 62.8 (C-6'), 57.4 (CH₂). Anal: Calcd for C₉H₁₅N₃O₆ (261.23): C, 41.38; H, 5.79; N, 16.09. Found: C, 41.31; H, 5.91; N, 16.23.

4.29. 3-(β-D-Glucopyranosyl)-5-phenyl-1,2,4-triazole [54] (6d)

A) From triazole **4d** (0.20 g, 0.50 mmol) according to General procedure **IV.** Reaction time: 4 h. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.13 g (85%) colourless syrup.

B) From triazole **5d** [62] (0.25 g, 0.35 mmol) according to General procedure **III.** Reaction time: 3 days. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.07 g (62%) colourless syrup. R_f : 0.48 (7:3 CHCl₃–MeOH); $[\alpha]_D = +31$ (c 0.20, H_2O); ¹H NMR (D₂O) δ (ppm): 7.66 (2H, d, J = 7.9 Hz, aromatics), 7.38–7.36 (3H, m, aromatics), 4.45 (1H, d, J = 9.2 Hz, H-1'), 3.87 (1H, dd, J = 11.9, <1 Hz, H-6'a), 3.77–3.69 (2H, m, H-2' or H-3' or H-4', H-6'b), 3.64–3.54 (3H, m, H-2' and/or H-3' and/or H-4', H-5'); ¹³C NMR (D₂O) δ (ppm): 159.1, 157.8 (triazole C-3, C-5), 130.9, 129.3 (2), 126.9, 126.5 (2) (aromatics), 80.2, 77.2, 74.7, 72.8, 69.5 (C-1' – C-5'), 61.0 (C-6'). Anal: Calcd for C₁₄H₁₇N₃O₅ (307.30): C, 54.72; H, 5.58; N, 13.67. Found: C, 54.85; H, 5.45; N, 13.54.

4.30. $3-(\beta-D-Glucopyranosyl)-5-(4-methylphenyl)-1,2,4-triazole$ (**6e**)

From triazole **4e** (0.20 g, 0.49 mmol) according to General procedure **IV**. Reaction time: 3 h. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.14 g (90%) white foam. R_f : 0.51 (7:3 CHCl₃–MeOH); $[\alpha]_D = +6$ (c 0.45, MeOH); ¹H NMR (D₂O) δ (ppm): 7.31 (2H, d, J = 7.9 Hz, aromatics), 6.93 (2H, d, J = 7.9 Hz, aromatics), 4.36 (1H, d, J = 9.5 Hz, H-1'), 3.83 (1H, dd, J = 11.9, <1 Hz, H-6'a), 3.72 (1H, dd, J = 11.9, 3.1 Hz, H-6'b), 3.66 (1H, pseudo t, J = 9.2, 8.9 Hz, H-2' or H-3' or H-4'), 3.59–3.50 (3H, m, H-2' and/or H-3' and/or H-4', H-5'), 2.06 (3H, s, CH₃); ¹³C NMR (D₂O) δ (ppm): 159.5, 157.5 (triazole C-3, C-5), 141.9, 130.0 (2), 126.6 (2), 123.8 (aromatics), 80.5, 77.6, 75.2, 73.3, 69.9 (C-1' – C-5'), 61.4 (C-6'), 21.1 (CH₃). Anal: Calcd for C₁₅H₁₉N₃O₅ (321.33): C, 56.07; H, 5.96; N, 13.08. Found: C, 55.98; H, 5.85; N, 12.96.

4.31. 5-(4-tert-Butylphenyl)-3-(β-D-glucopyranosyl)-1,2,4-triazole [54] (**6f**)

From triazole **4f** (0.20 g, 0.44 mmol) according to General procedure **IV**. Reaction time: 3 h. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.13 g (79%) colourless syrup. R_f : 0.22 (4:1 CHCl₃–MeOH); $[\alpha]_D = +8$ (c 0.55, DMSO); ¹H NMR (CD₃OD) δ (ppm): 7.90 (2H, d, J = 8.0, aromatics), 7.51 (2H, d, J = 8.0, aromatics), 4.48 (1H, d, J = 9.5 Hz, H-1'), 3.90 (1H, dd, J = 11.5, <1 Hz, H-6'a), 3.77–3.73 (2H, m, H-2' or H-3' or H-4', H-6'b), 3.59–3.51 (3H, m, H-2' and/or H-3' and/or H-4', H-5'), 1.33 (9H, s, C(CH₃)₃); ¹³C NMR (CD₃OD) δ (ppm): 161.6, 158.1 (triazole C-3, C-5), 154.7, 127.4 (2), 126.9 (2) (aromatics), 82.0, 79.1, 76.3, 74.3, 71.1 (C-1' – C-5'), 62.6 (C-6'), 35.7 (C(CH₃)₃), 31.6 (C(CH₃)₃). Anal: Calcd for

 $C_{18}H_{25}N_3O_5\,(363.41)$: C, 59.49; H, 6.93; N, 11.56. Found: C, 59.60; H, 6.84; N, 11.47. MS-ESI (*m/z*): 386.169 $[M + Na]^+$

4.32. $3-(\beta-D-Glucopyranosyl)-5-(4-trifluoromethylphenyl)-1,2,4-triazole ($ **6g**)

From triazole **4g** (85 mg, 0.18 mmol) according to General procedure **IV**. Reaction time: 1.5 h. Purified by column chromatography (9:1 CHCl₃–MeOH) to yield 52 mg (77%) white amorphous solid. *R*_f: 0.20 (4:1 CHCl₃–MeOH); $[\alpha]_D = +13$ (c 0.52, MeOH); ¹H NMR (CD₃OD) δ (ppm): 8.09 (2H, br s, aromatics), 7.66 (2H, br s, aromatics), 4.40 (1H, d, *J* = 7.2 Hz, H-1'), 3.80 (1H, dd, *J* = 10.7, <1 Hz, H-6'a), 3.66–3.20 (5H, m, H-2', H-3', H-4', H-5', H-6'b); ¹³C NMR (CD₃OD) δ (ppm): 160.2, 159.1 (triazole C-3, C-5), 134.9, 132.3 (q, ²*J*_{IC}, F) = 34.6 Hz, *C*–CF₃), 127.9 (2), 126.8 (2) (aromatics), 125.6 (q, ¹*J*_I_C, F) = 271.3 Hz, CF₃), 82.3, 79.2, 75.9, 74.6, 71.2 (C-1' – C-5'), 62.7 (C-6'). Anal: Calcd for C₁₅H₁₆F₃N₃O₅ (375.30): C, 48.00; H, 4.30; N, 11.20. Found: C, 48.12; H, 4.35; N, 11.07.

4.33. 3-(β-D-Glucopyranosyl)-5-(4-hydroxyphenyl)-1,2,4-triazole (**6h**)

From triazole **5u** [62] (0.57 g, 0.73 mmol) according to General procedure **III**. Purified by column chromatography (4:1 CHCl₃– MeOH) to yield 0.16 g (67%) white solid. Mp: 172–174 °C; $[\alpha]_D = +14$ (c 0.35, DMSO); ¹H NMR (CD₃OD) δ (ppm): 7.69 (2H, d, J = 8.2 Hz, aromatics), 6.79 (2H, d, J = 8.5 Hz, aromatics), 4.38 (1H, d, J = 9.6 Hz, H-1') 3.82 (1H, d, J = 11.0, <1 Hz, H-6'a), 3.68–3.64 (2H, m, H-2' or H-3' or H-4', H-6'b), 3.53–3.41 (3H, m, H-2' and/or H-3' and/or H-4', H-5'); ¹³C NMR (CD₃OD) δ (ppm): 162.1, 160.6, 157.6 (triazole C-3, C-5, 4-HOPh C-4), 129.2 (2), 126.9, 116.8 (2) (aromatics), 82.0, 79.2, 76.5, 74.4, 71.2 (C-1' – C-5'), 62.7 (C-6'). Anal: Calcd for C₁₄H₁₇N₃O₆ (323.30): C, 52.01; H, 5.30; N, 13.00. Found: C, 51.93; H, 5.41; N, 13.12.

4.34. 3-(β-D-Glucopyranosyl)-5-(4-methoxyphenyl)-1,2,4-triazole (**6i**)

From triazole **4i** (0.24 g, 0.55 mmol) according to General procedure **IV**. Purified by column chromatography (7:3 CHCl₃–MeOH) to yield 0.18 g (95%) colourless syrup. R_f : 0.52 (7:3 CHCl₃–MeOH); $[\alpha]_D = +12$ (c 0.41, MeOH); ¹H NMR (CD₃OD) δ (ppm): 7.82 (2H, d, J = 8.3 Hz, aromatics), 6.92 (2H, d, J = 8.3 Hz, aromatics), 4.46 (1H, d, J = 9.5 Hz, H-1'), 3.86 (1H, dd, J = 12.1, <1 Hz, H-6'), 3.75 (5H, m, H-2' and/or H-3' and/or H-4', H-6'b, OMe), 3.60–3.50 (3H, m, H-2' and/or H-3' and/or H-4', H-5'); ¹³C NMR (CD₃OD) δ (ppm): 162.6 (4-MeOPh C-4), 160.1, 159.1 (triazole C-3, C-5), 129.0 (2), 121.5, 115.3 (2) (aromatics), 82.0, 79.1, 76.3, 74.3, 71.1 (C-1' – C-5'), 62.7 (C-6'), 55.9 (OMe). Anal: Calcd for C₁₅H₁₉N₃O₆ (337.33): C, 53.41; H, 5.68; N, 12.46. Found: C, 53.55; H, 5.63; N, 12.56.

4.35. 3-(β-D-Glucopyranosyl)-5-(4-nitrophenyl)-1,2,4-triazole (**6***j*)

From triazole **5j** [62] (0.65 g, 0.85 mmol) according to General procedure **III**. Reaction time: 1 day. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.22 g (75%) pale yellow solid. Mp: 166–169 °C; $[\alpha]_D = +20$ (c 1.3, DMSO); ¹H NMR (DMSO-d₆) δ (ppm): 8.34 (2H, d, J = 8.2 Hz, aromatics), 8.26 (2H, d, J = 7.8 Hz, aromatics), 5.15, 5.10, 4.57 (4H, 3 br s, OH), 4.34 (1H, d, J = 9.7 Hz, H-1'), 3.71 (1H, dd, J = 11.7, 5.4 Hz, H-6'a), 3.63 (1H, pseudo t, J = 9.2, 9.0 Hz, H-2' or H-3' or H-4'), 3.46–3.28 (3H, m, H-2' and/or H-3' and/or H-4', H-5', H-6'b), 3.18 (1H, pseudo t, J = 9.0, 8.9 Hz, H-2' or H-3' or H-4'); ¹³C NMR (DMSO-d₆) δ (ppm): 158.2, 157.0 (triazole C-3, C-5), 147.5, 136.7, 126.8 (2), 124.2 (2) (aromatics), 81.6, 77.9, 74.0, 72.5, 70.0 (C-1' – C-5'), 61.2 (C-6'). Anal: Calcd for C₁₄H₁₆N₄O₇

(352.30): C, 47.73; H, 4.58; N, 15.90. Found: C, 47.81; H, 4.62; N, 15.78. MS-ESI (*m*/*z*): 375.093 [M + Na]⁺.

4.36. 5-(4-Aminophenyl)-3-(β-D-glucopyranosyl)-1,2,4-triazole (**6k**)

Triazole 6i (0.10 g. 0.28 mmol) was dissolved in dry MeOH (3 mL), and 0.01g Pd-C (10%) was added. The reaction mixture was stirred at rt under hydrogen atmosphere for 1 h. After completion of the transformation monitored by TLC (1:1 CHCl₃-MeOH) Pd-C was filtrated through a pad of celite, the solvent was evaporated in vacuo and the residue was purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.09 g (94%) amorphous yellow product. $R_{\rm f}$: 0.59 (1:1 CHCl₃–MeOH); $[\alpha]_D = +9$ (c 1.46, DMSO); ¹H NMR $(DMSO-d_6) \delta$ (ppm): 7.64 (2H, d, J = 8.0 Hz, aromatics), 6.60 (2H, d, *J* = 8.0 Hz, aromatics), 5.51 (2H, br s, NH₂), 4.98, 4.79, 4.53 (4H, 3 br s, OH), 4.13 (1H, d, J = 9.2 Hz, H-1'), 3.70-3.64 (2H, m, H-2' or H-3' or H-4', H-6'a), 3.42-3.16 (4H, m, H-2' and/or H-3' and/or H-4', H-5′, H-6′b); 13 C NMR (DMSO-d₆) δ (ppm): 161.3, 155.0 (triazole C-3, C-5), 150.3, 127.1 (2), 114.7, 113.6 (2) (aromatics), 81.4, 78.3, 75.7, 72.4, 70.2 (C-1' - C-5'), 61.3 (C-6'). Anal: Calcd for $C_{14}H_{18}N_4O_5$ (322.32): C, 52.17; H, 5.63; N, 17.38. Found: C, 52.21; H, 5.55; N, 17.26. MS-ESI (*m*/*z*): 345.118 [M + Na]⁺.

4.37. 5-(4-Carboxyphenyl)-3-(β -D-glucopyranosyl)-1,2,4-triazole (**6**)

From triazole **5l** (0.24 g, 0.32 mmol) according to General procedure **III**. Reaction time: 5 days. Purified by column chromatography (1:1 CHCl₃–MeOH) to yield 0.10 g (86%) yellowish syrup. $R_{\rm f}$: 0.55 (1:1:1 toluene-AcOH-MeOH); $[\alpha]_{\rm D} = +6$ (c 0.54, MeOH); ¹H NMR (DMSO-d₆) δ (ppm): 8.10–8.04 (4H, m, aromatics), 4.33 (1H, d, J = 9.7 Hz, H-1'), 3.74–3.65 (2H, m, H-2' and/or H-3' and/or H-4', H-6'a), 3.47 (1H, ddd, J = 8.9, 5.3, <1 Hz, H-5'), 3.37–3.25 (2H, m, H-2' and/or H-3' and/or H-4', H-6'b), 3.20 (1H, pseudo t, J = 9.0, 8.9 Hz, H-2' or H-3' or H-4'); ¹³C NMR (DMSO-d₆) δ (ppm): 168.7 (COOH), 158.4, 157.8 (triazole C-3, C-5), 134.1, 133.1, 129.9 (2), 125.7 (2) (aromatics), 81.6, 78.1, 74.5, 72.6, 70.2 (C-1' – C-5'), 61.3 (C-6'). Anal: Calcd for C₁₅H₁₇N₃O₇ (351.31): C, 51.28; H, 4.88; N, 11.96. Found: C, 51.15; H, 4.96; N, 11.89.

4.38. 5-(3,5-Dimethylphenyl)-3-(β-D-glucopyranosyl)-1,2,4triazole (**6m**)

From triazole **4m** (0.14 g, 0.34 mmol) according to General procedure **IV**. Reaction time: 3 h. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.11 g (98%) colourless syrup. $R_{\rm f}$: 0.54 (3:1 CHCl₃–MeOH); $[\alpha]_{\rm D} = +12$ (c 0.57, MeOH); ¹H NMR (CD₃OD) δ (ppm): 7.48 (2H, s, aromatics), 6.99 (1H, s, aromatic), 4.43 (1H, d, J = 9.6 Hz, H-1'), 3.85 (1H, dd, J = 12.0, 1.3 Hz, H-6'a), 3.73–3.68 (2H, m, H-2' or H-3' or H-4', H-6'b), 3.56–3.40 (3H, m, H-2' and/or H-3' and/or H-4', H-5'), 2.25 (6H, s, 2 × CH₃); ¹³C NMR (CD₃OD) δ (ppm): 162.2, 157.6 (triazole C-3, C-5), 139.7 (2), 132.7, 128.0, 125.2 (2) (aromatics), 82.0, 79.1, 76.2, 74.3, 71.1 (C-1' – C-5'), 62.7 (C-6'), 21.3 (2 × CH₃). Anal: Calcd for C₁₆H₂₁N₃O₅ (335.36): C, 57.30; H, 6.31; N, 12.53. Found: C, 57.41; H, 6.24; N, 12.41.

4.39. 5-(3,5-Dinitrophenyl)-3-(β-D-glucopyranosyl)-1,2,4-triazole (**6n**)

From triazole **5n** [62] (0.52 g, 0.63 mmol) according to General procedure **III**. Reaction time: 3 day. Purified by column chromatography (7:3 CHCl₃–MeOH) to yield 0.18 g (72%) white solid. Mp: 203–205 °C; $[\alpha]_D = -21$ (c 0.11, DMSO); ¹H NMR (DMSO-d₆-D₂O) δ (ppm): 9.02 (2H, s, aromatics), 8.83 (1H, s, aromatic), 4.37 (1H, d,

J = 9.8 Hz, H-1'), 3.69 (1H, dd, *J* = 11.9, <1 Hz, H-6'a), 3.58 (1H, pseudo t, *J* = 9.1, 9.1 Hz, H-2' or H-3' or H-4'), 3.47 (1H, dd, *J* = 11.9, 5.6 Hz, H-6'b), 3.35–3.30 (2H, m, H-2' or H-3' or H-4', H-5'), 3.22 (1H, pseudo t, *J* = 9.1, 9.1 Hz, H-2' or H-3' or H-4'); ¹³C NMR (DMSO-d₆) δ (ppm): 162.2, 157.3 (triazole C-3, C-5), 148.5 (2), 137.7, 124.1 (2), 115.5 (aromatics), 80.8, 77.9, 75.8, 73.2, 70.5 (C-1' – C-5'), 61.3 (C-6'). Anal: Calcd for C₁₄H₁₅N₅O₉ (397.30): C, 42.32; H, 3.81; N, 17.63. Found: C, 42.39: H, 3.93: N, 17.56.

4.40. 5-(3,5-Diaminophenyl)-3-(β -D-glucopyranosyl)-1,2,4-triazole (**60**)

Triazole 6n (0.07 g, 0.18 mmol) was dissolved in dry MeOH (10 mL), and 0.015 g Pd–C (10%) was added. The reaction mixture was stirred at rt under hydrogen atmosphere for 1 h. After completion of the transformation monitored by TLC (1:1 CHCl₃-MeOH) Pd-C was filtrated through a pad of celite, the solvent was evaporated in vacuo and the residue was purified by column chromatography (1:1 CHCl₃-MeOH) to yield 0.04 g (72%) amorphous brownish product. R_f: 0.33 (1:1 CHCl₃–MeOH); ¹H NMR $(DMSO-d_6-D_2O) \delta$ (ppm): 6.49 (2H, d, J = 2.0 Hz, aromatics), 5.84 (1H, t, *J* = 2.0, aromatic), 4.16 (1H, d, *J* = 9.9 Hz, H-1'), 3.65 (1H, dd, *I* = 12.6, <1 Hz, H-6'a), 3.57 (1H, pseudo t, *I* = 9.9, 9.2 Hz, H-2' or H-3' or H-4'), 3.42 (1H, dd, J = 12.6, 4.9 Hz, H-6'b), 3.32-3.17 (3H, m, H-2' and/or H-3' and/or H-4', H-5'); ¹³C NMR (DMSO-d₆) δ (ppm): 159.7, 158.8 (triazole C-3, C-5), 149.6 (2), 130.6, 102.3 (2), 102.1 (aromatics), 81.2, 78.2, 75.4, 73.1, 70.3 (C-1' - C-5'), 61.5 (C-6'). Anal: Calcd for C₁₄H₁₉N₅O₅ (337.33): C, 49.85; H, 5.68; N, 20.76. Found: C. 49.99: H. 5.75: N. 20.64.

4.41. $3-(\beta-D-Glucopyranosyl)-5-(3,4,5-trimethoxyphenyl)-1,2,4-triazole ($ **6p**)

From triazole **4p** (0.18 g, 0.37 mmol) according to General procedure **IV**. Reaction time: 3 h. Purified by column chromatography (9:1 CHCl₃–MeOH) to yield 0.14 g (92%) colourless syrup. R_f : 0.37 (4:1 CHCl₃–MeOH); $[\alpha]_D = +5$ (c 0.44, MeOH); ¹H NMR (D₂O) δ (ppm): 6.64 (2H, s, aromatics), 4.57 (1H, d, J = 9.3 Hz, H-1'), 4.05 (1H, dd, J = 11.9, <1 Hz, H-6'a), 3.92 (1H, dd, J = 11.9, <1 Hz, H-6'b), 3.88–3.72 (4H, m, H-2', H-3', H-4', H-5'), 3.65–3.64 (9H, m, 3 × OMe); ¹³C NMR (D₂O) δ (ppm): 159.8, 157.4 (triazole C-3, C-5), 152.6 (2), 138.3, 122.7, 103.2 (2) (aromatics), 80.5, 77.5, 75.0, 73.4, 70.0 (C-1' – C-5'), 61.5 (C-6'), 61.2 (OMe), 56.1 (2 × OMe). Anal: Calcd for C₁₇H₂₃N₃O₈ (397.38): C, 51.38; H, 5.83; N, 10.57. Found: C, 51.25; H, 5.94; N, 10.64.

4.42. 3-(β-D-Glucopyranosyl)-5-(2-naphthyl)-1,2,4-triazole [54] (**6***q*)

A) From triazole **4q** (0.10 g, 0.23 mmol) according to General procedure **IV.** Reaction time: 3 h. Purified by column chromatography (4:1 CHCl₃–MeOH) to yield 0.07 g (90%) colourless syrup.

B) From triazole **5q** [62] (0.27 g, 0.35 mmol) according to General procedure **III.** Reaction time: 3 days. Purified by column chromatography (9:1 CHCl₃–MeOH) to yield 0.10 g (81%) colourless syrup. Compound characterization data were identical with those reported in our preliminary communication [54].

4.43. 3-(β-D-Glucopyranosyl)-5-(2-pyridyl)-1,2,4-triazole (**6r**)

From triazole **5r** [62] (0.31 g, 0.43 mmol) according to General procedure **III**. Reaction time: 3.5 h. Purified by column chromatography (7:3 CHCl₃–MeOH) to yield 0.05 g (40%) colourless syrup. $R_{\rm f}$: 0.36 (1:1 CHCl₃–MeOH); $[\alpha]_{\rm D} = +30$ (c 0.22, H₂O); ¹H NMR (D₂O) δ (ppm): 8.49 (1H, d, J = 4.0 Hz, Py), 7.85–7.78 (2H, m, Py),

7.41–7.38 (1H, m, Py), 4.57 (1H, d, J = 9.2 Hz, H-1'), 3.94 (1H, dd, J = 11.9, <1 Hz, H-6'a), 3.83–3.76 (2H, m, H-2' or H-3' or H-4', H-6'b), 3.70–3.57 (3H, m, H-2' and/or H-3' and/or H-4', H-5'); ¹³C NMR (D₂O) δ (ppm): 158.5, 156.8 (triazole C-3, C-5), 149.4, 145.3, 138.3, 125.5, 122.0 (Py), 80.0, 76.8, 74.3, 72.5, 69.3 (C-1' – C-5'), 60.7 (C-6'). Anal: Calcd for C₁₃H₁₆N₄O₅ (308.29): C, 50.65; H, 5.23; N, 18.17. Found: C, 50.77; H, 5.10; N, 18.29. MS-ESI (*m/z*): 331.100 [M + Na]⁺, 639.217 [2M + Na]⁺, 309.118 [M + H]⁺.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http:// dx.doi.org/10.1016/j.ejmech.2014.02.041.

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