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Synthesis of variously coupled conjugates of D-glucose, 1,3,4-oxadiazole, and 1,2,3-triazole for inhibition of glycogen phosphorylase

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Dedicated to Professor Dr. András Lipták on the occasion of his 75th birthday

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ABSTRACT

5-(O-Perbenzoylated-β-D-glucopyranosyl)tetrazole was obtained from O-perbenzoylated-β-D-glucopyranosyl cyanide by Bu_3SnN_3 or Me_3SiN_3–Bu_2SnO. This tetrazole was transformed into 5-ethynyl- as well as 5-chloromethyl-2-(O-perbenzoylated-β-D-glucopyranosyl)-1,3,4-oxadiazoles by acylation with propiolic acid–DCC or chloroacetyl chloride, respectively. The chloromethyl oxadiazole gave the corresponding azidomethyl derivative on treatment with NaN_3. These compounds were reacted with several alkynes and azides under Cu(I) catalysed cycloaddition conditions to give, after removal of the protecting groups by the Zemplén protocol, β-D-glucopyranosyl-1,3,4-oxadiazolyl-1,2,3-triazole, β-D-glucopyranosyl-1,2,3-triazolyl-1,3,4-oxadiazole, and β-D-glucopyranosyl-1,3,4-oxadiazolylmethyl-1,2,3-triazole type compounds. 5-Phenyltetrazole was also transformed under the above conditions into a series of aryl-1,3,4-oxadiazolyl-1,2,3-triazoles, aryl-1,2,3-triazolyl-1,3,4-oxadiazoles, and aryl-1,3,4-oxadiazolylmethyl-1,2,3-triazoles. The new compounds were assayed against rabbit muscle glycogen phosphorylase b and the best inhibitors had inhibition constants in the upper micromolar range (2-phenyl-5-[1-(β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole 36: K_i = 854 μM, 2-(β-D-glucopyranosyl)-5-[1-(naphthalen-2-yl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole 47: K_i = 745 μM).

1. Introduction

Glycogen phosphorylase (GP) has been a validated target in combatting type 2 *diabetes mellitus*[1] (for a detailed foundation of inhibiting liver GP as an investigational concept for lowering blood glucose levels, please consult recent review articles[2–6]). GP is a well-known enzyme that has been investigated by various methods as to its structural features and kinetic behaviour.[7,8] By X-ray crystallographic studies on enzyme–inhibitor complexes several binding sites of GP have been discovered and are exploited for the design of new antidiabetic agents: the catalytic centre accommodates mainly glucose derivatives and the inhibitor site binds aromatic compounds of various ring size and annelation type; classification of inhibitors binding to other sites such as the allosteric, the new allosteric, and the storage sites is more complex and can be found in the review literature.[5,9]

Among the glucose-based[10] inhibitors of GP, the first successful series was that of the glucosylamides[11–14] (Chart 1a, **A**). Considering the NHCO moiety as a linker (i) between the sugar and the aromatic part of these compounds several molecules with bioisosteric replacements of the NHCO (see heterocyclic linkers ii–v) were designed and synthesized. Kinetic and crystallographic studies showed a very high resemblance both in strength and structural features of binding between amides **1** and **2** and 1,2,3-triazoles[‡] **3** and **4**, respectively.[16,17] Constitutional isomeric *C*-glucopyranosyl oxadiazoles[18,19] **5**–**10** showed a strong preference for the 3-aryl-5-β-D-glucopyranosyl-1,2,4-oxadiazoles **9** and **10** to exhibit the highest affinity to GP. *N*-Acyl-*N*′-β-D-glucopyranosyl urea derivatives

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E-mail addresses: tpatonay@puma.unideb.hu (T. Patonay), somsak@tigris.unideb.hu (L. Somsák).
† Visiting scientist. Permanent address: Laboratoire des Glucides-UMR 6219, Université de Picardie Jules Verne, Ilot des poulies, 10 rue Baudelocque, 80039 Amiens, France.

‡ A very recent report[15] indicated weak inhibition of GP by 1-β-D-glucopyranosyl-1,2,3-triazole derivatives with coumarinyloxymethyl and other substituents in the 4-position.

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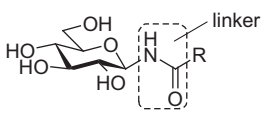
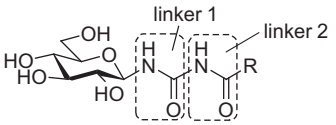
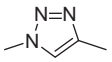
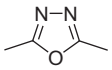
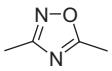
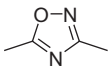
a) Selected glucose analogue inhibitors of glycogen phosphorylase (GP) (K_i [μM] determined against rabbit muscle GPb)



A

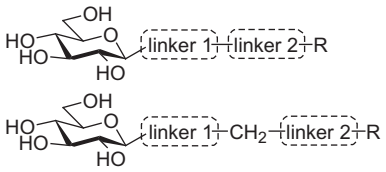


B

	linker		R		R
i	—NHCO—	**1**	81[11] 144[12]	**2**	10[13] 13[16]
ii		**3**	151[16] 162[17]	**4**	16[16] 36[17]
iii		**5**	10% at 625 μM[19]	**6**	10% at 625 μM[19]
iv		**7**	10% at 625 μM[18]	**8**	38[18]
v		**9**	64[19]	**10**	2.4[19]

	linker 1-2		R		R
—	—NHCONHCO—	**11**	4.6[5]	**12**	0.35[5]

b) Target compounds



where linker 1 and linker 2 = 1,2,3-triazole (linker ii) or 1,3,4-oxadiazole (linker iii)

Chart 1.

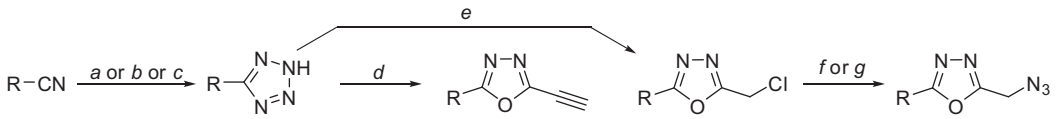
(Chart 1a, **B**) proved significantly better inhibitors than amides **A** with the same aromatic part in the aglycon[5,9] (compare inhibitor constants for **1** and **11** as well as **2** and **12**, respectively). Based on the successful bioisosteric modification of amides **A** we have started a program to synthesize a series of glucosyl heterocyclic compounds (Chart 1b) which can be derived from acyl ureas **B** by substituting each NHCO moiety by a heterocycle (linkers 1 and 2). In addition, compounds with a methylene group between linkers 1 and 2 lending higher flexibility to the molecules were also designed. In this paper we present our results in synthesizing 1,2,3-triazole and 1,2,4-oxadiazole linked derivatives of D-glucose. With the aim of targeting the inhibitor site of GP, compounds with aromatic rings in place of the glucosyl groups were also synthesized.

2. Results and discussion

2.1. Syntheses

Access to suitable precursors to assemble the target oxadiazoles and triazoles is shown in Scheme 1. The O-perbenzoylated 5-β-D-glucopyranosyl tetrazole **17** was first prepared from **13** by the literature protocol[20] using in situ obtained ammonium azide in DMF at reflux (conditions *a*). To avoid chromatographic purification in larger scale preparations, two other methods were investigated, as well. Thus, reaction of **13** with Bu_3SnN_3 in 1,2-dimethoxyethane at reflux (DME, conditions *b*) followed by acidic workup[21] gave **17** in essentially quantitative yield. Another method, applying Me_3SiN_3 and Bu_2SnO (conditions *c*) for in situ generation of dibutyl trimethylsilyloxytin azide[22] was similarly efficient. Conditions *a* afforded tetrazoles **18** and **20** from the corresponding nitriles **14** and **16** in good and excellent yields, respectively; however, reaction of **15** to give the 1-naphthyl derivative **19** failed. The reaction of **15** with Bu_3SnN_3 in boiling DME (conditions *b*) needed three days to give **19**, but using diglyme as a solvent of higher boiling temperature diminished the reaction time to two hours with a concomitant increase of the yield.

5-Substituted tetrazoles can be transformed into 1,3,4-oxadiazoles by acylation.[23,24] Although acid chlorides are generally used in such acylations,[25] the chloride of propiolic acid is rather difficult to prepare and extremely sensitive to air. Therefore, the specific



	R				
13	Bz_4-β-D-Glc_p	**17** (*a*, 3.5 h, 94%) (*b*, DME, 24 h, 99%) (*c*, 19 h, 95%)	**21** (59%)	**25** (96%)	**26** (*f*, 90%)
14	Ph	**18** (*a*, 2 h, 69%)	**22** (47%)	**27** (87%)	**28** (*g*, 94%)
15	1-naphthyl	**19** (*a*, 72 h, traces) (*b*, DME, 72 h, 73%) (*b*, diglyme, 2 h, 86%)	**23** (58%)		
16	2-naphthyl	**20** (*a*, 2 h, 94%)	**24** (51%)		

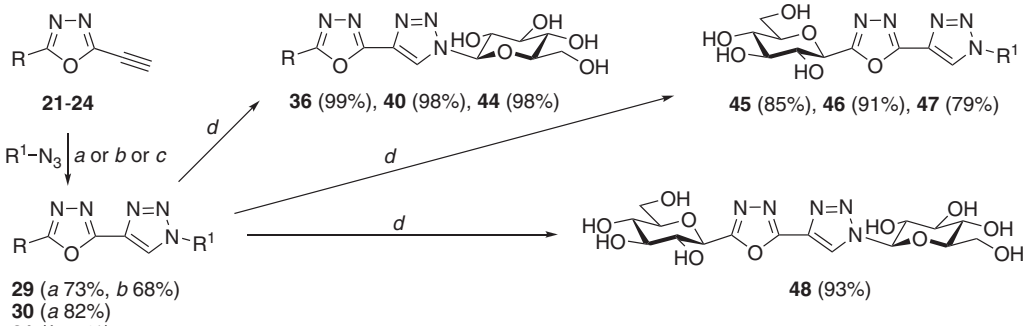
Scheme 1. Reaction conditions: (a) NaN_3 (3 equiv), NH_4Cl (3 equiv), dry DMF, reflux; (b) Bu_3SnN_3 (3 equiv), solvent, reflux; (c) Me_3SiN_3 (2 equiv), Bu_2SnO (0.2 equiv), $PhCH_3$, 80 °C; (d) HC≡C–COOH (2 equiv), DCC (1 equiv), toluene, 80 °C, 2 h (reflux, 4 h in case of **21**); (e) $ClCH_2COCl$ (1.1 equiv), $PhCH_3$, reflux, 24 h; (f) NaN_3 (1 equiv), dry DMF, 50 °C, 24 h; (g) NaN_3 (3 equiv), 18-crown-6 (0.1 equiv), acetone, rt, 2 h.

ethynyl-oxadiazoles **21**–**24** were prepared by DCC mediated reaction[19,26] of propiolic acid with the corresponding tetrazoles **17**–**20** (conditions *d*) to give the target compounds in satisfactory yields. Chloroacetyl chloride under conditions *e*, on the other hand, furnished the chloromethyl-oxadiazoles **25** and **27** in excellent yields. Replacement of the chloride by azide was effected by NaN_3 in DMF (conditions *f*) to give **26** or NaN_3–18-crown-6 in acetone (conditions *g*) to produce **28** in very high yields.

Ethynyl-oxadiazoles **21**–**24** were cyclized with several azides under variants of the copper(I) catalysed azide–alkyne cycloaddition (CuAAC) conditions[27–29] (Scheme 2). The triazole ring formation from **21** was similarly efficient by using phenyl azide (conditions *a*) or by in situ generation of this reagent from the corresponding commercial boronic acid[30] (conditions *b*) to give **29**. The reaction of **21** under conditions *a* gave high yields of **30** and **32** from 1-azidonaphthalene and O-peracetylated β-D-glucopyranosyl azide,[31,32] respectively, and reactions of latter azide with **22**–**24** gave very good yields of the respective **35**, **39**, and **43**, too. In the absence of easily available 2-azidonaphthalene, **31** was obtained from **21** in a one pot, two-step reaction from naphthalene-2-boronic acid under conditions *b*. *O*-Acyl protecting groups were removed by the Zemplén protocol (conditions *d*) to give test compounds **36**, **40**, **44**, and **45**–**48** in very good to excellent yields.

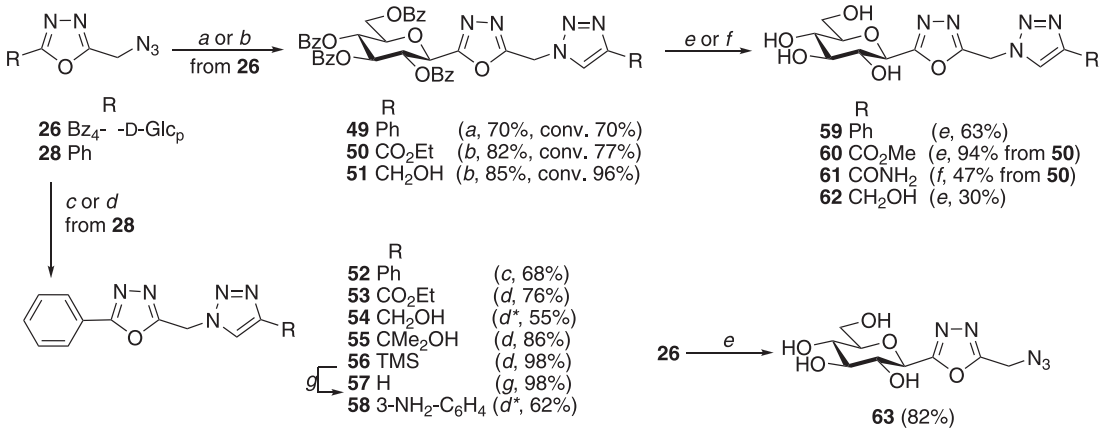
For the transformations of 2-aryl-5-ethynyl-1,3,4-oxadiazoles **22**–**24** to the corresponding triazoles (**33**, **37**, **41** with phenyl azide, **34**, **38**, **42** with 2-azido-ethanol) addition of TMEDA to the reaction mixtures (conditions *c*) proved advantageous and the compounds were isolated in medium to good yields.

CuAAC reaction of **26** with phenylacetylene to give **49** (Scheme 3) was tried with the $Cu(OTf)_2$–Cu system[33] (conditions *a*); however, conversion of the starting material was not complete



R	R1: Ph	CH_2CH_2OH	1-naphthyl	2-naphthyl	Ac_4-β-D-Glc_p	
21 Bz_4-β-D-Glc_p	**29**		**30**	**31**	**32**	
22 Ph	**33**	**34**			**35**	**36**
23 1-naphthyl	**37**	**38**			**39**	**40**
24 2-naphthyl	**41**	**42**			**43**	**44**
	45		**46**	**47**		

Scheme 2. Reaction conditions: (a) R^1N_3 (1 equiv), $CuSO_4{\cdot}5H_2O$ (0.05 equiv), L-ascorbic acid (0.15 equiv), CH_2Cl_2/water 1:1, 50 °C, 2 h; (b) (1) $R^1B(OH)_2$ (3 equiv), NaN_3 (3 equiv), $CuSO_4{\cdot}5H_2O$ (0.3 equiv), MeOH, rt, 16 h; (2) L-ascorbic acid (1.5 equiv), **21** (1 equiv), CH_2Cl_2/water 1:1, 50 °C, 2 h; (c) R^1N_3 (1.2 equiv), $CuSO_4{\cdot}5H_2O$ (0.04 equiv), Na-L-ascorbate (0.16 equiv), TMEDA (0.08 equiv), *t*BuOH–water 1:2; (d) NaOMe (cat.), MeOH, rt.



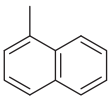
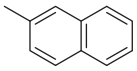
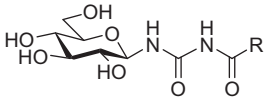
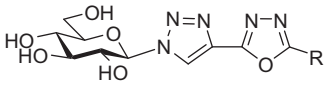
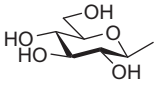
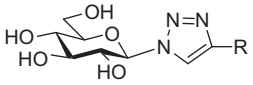
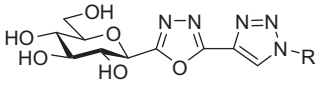
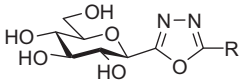
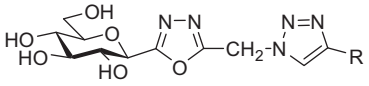
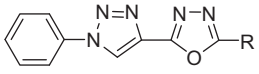
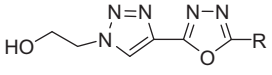
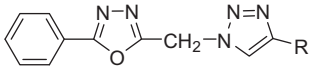
Scheme 3. Reaction conditions: (a) R–C≡CH (1 equiv), $Cu(OTf)_2$ (0.03 equiv), Cu dust (0.03 equiv), CH_2Cl_2/water 1:1, 40 °C, 1 d; (b) R–C≡CH (1 equiv), $CuSO_4{\cdot}5H_2O$ (0.05 equiv), L-ascorbic acid (0.15 equiv), CH_2Cl_2/water 1:1, 50 °C, 1 d; (c) R–C≡CH (1.2 equiv), $CuSO_4{\cdot}5H_2O$ (0.01 equiv), Na-L-ascorbate (0.04 equiv), TMEDA (0.08 equiv), *t*BuOH–water 1:2, rt 2 h; (d) R–C≡CH (1.2 equiv), $CuSO_4{\cdot}5H_2O$ (0.04 equiv), Na-L-ascorbate (0.16 equiv), *t*BuOH–water 1:2, rt 3 h (* with 0.08 equiv TMEDA); (e) NaOMe (cat.), MeOH, rt; (f) NH_3, MeOH, rt; (g) TBAF (0.6 equiv), dry THF, 70 °C, 5 h.

in one day. Incomplete conversion was also observed in reactions of **26** with ethyl propiolate and propargyl alcohol to give **50** and **51**, respectively, when the more conventional $CuSO_4$–L-ascorbic acid reagent was used (conditions *b*). Triazoles **49**–**50** and azidomethyl-oxadiazole **26** were deprotected by the Zemplén method (conditions *e*) to give test compounds **59**, **60**, **62**, and **63**, respectively, while carboxamido triazole **61** was obtained from **50** by NH_3 in MeOH (conditions *f*).

2-Azidomethyl-5-phenyl-1,3,4-oxadiazole **28** was reacted with phenylacetylene to give triazole **52** with as few as 0.01 equiv of Cu(I) in the presence of TMEDA (conditions *c*). Similar reactions of **28** with ethyl propiolate, propargyl alcohol, 1,1-dimethyl-prop-2-ynol, trimethylsilylacetylene, and 3-amino-phenylacetylene leading to the corresponding triazoles **52**–**56** and **58**, respectively, were performed with higher catalyst loading (conditions *d*) in some cases with added TMEDA. Removal of the trimethylsilyl group from **56** was achieved by TBAF (conditions *f*) to give **57** in quantitative yield.

Each azide–alkyne cycloaddition was carried out under Cu(I) catalyzed conditions for which formation of 1,4-disubstituted 1,2,3-triazoles with practically exclusive regioselectivity was reported.[27–29] The 1,4-substitution pattern was confirmed by the carbon NMR spectra of the compounds exhibiting characteristic resonances for C-4 (132–136 ppm in the sugar derivatives, 132–148 ppm for the aromatic compounds) and C-5 (120–128 ppm for each type) in accordance with literature precedents reporting significantly higher chemical shift values for the quaternary C-4 as compared to that of C-5.[34–37]

Table 1
Evaluation of the new compounds as inhibitors of rabbit muscle glycogen phosphorylase b (RMGPb) (K_i [μM] unless otherwise stated) and comparison of inhibition to that of the leads

Entry		R			
					Others
1		**11** 4.6[5]	15[5]	**12** 0.35[5]	
2		**36**[a] 854 ± 17[c]	**40**[b] No inh.[d]	**44**[b] No inh.[d]	**48**[a]  19% at 1 mM
3		**3** 151[16] 162[17]	136[16]	**4** 16[16] 36[17]	–CH_2OH 14[16] 26[17]
4		**45**[a] 31% at 1 mM	**46**[a] 1318 ± 86[c]	**47**[a] 745 ± 36[c]	
5		**5** 10% at 625 μM[19]	10% at 625 μM[19]	**6** 10% at 625 μM[19]	–CH_3 212[20] 145[40] **63**[a] –CH_2N_3 40% at 1 mM
6		**59**[b] No inh.[e]			**60**[b] –COOMe No inh.[e] **61**[b] –$CONH_2$ No inh.[d] **62**[a] –CH_2OH 60% at 1 mM
7		**33**[b] No inh.[d]	**37**[b] No inh.[d]	**41**[b] No inh.[d]	
8		**34**[b] No inh.[d]	**38**[b] No inh.[d]	**42**[b] No inh.[d]	
9		**52**[b] No inh.[d]			**53** –COOEt **54** –CH_2OH **55** –CMe_2OH **56** –$SiMe_3$ **57** –H [b] each: No inh.[d]

[a] Determined by the protocol described in Ref. 38.
[b] Determined by the protocol in described in Ref. 12.
[c] Calculated from the IC_{50} value by the Cheng–Prusoff equation:[41] $K_i = IC_{50}/(1 + [S]/K_m)$.
[d] Tested concentration: 625 μM.
[e] Tested concentration: 312.5 μM.

2.2. Enzyme inhibition studies

The kinetic parameters of the synthesized molecules were determined according to previously described enzymatic protocols[12,38] and the results are summarized in Table 1 showing also the inhibitory efficiency of some reference compounds. Based on the verified bioisosteric replacement of NHCO by 1,2,3-triazole for the glycogen phosphorylase case by enzyme kinetic and X-ray crystallographic investigations[16] (cf. Chart 1a, **1**–**4**), the present study aimed at double replacement of the NHCONHCO moieties in acyl urea derivatives (compounds in entry 1) by two five membered heterocycles. Glucosyl-triazolyl-oxadiazoles (entry 2) proved significantly weaker inhibitors both in comparison to the acyl ureas (entry 1) and the glucosyl-triazoles in entry 3. This might be partially attributed to the increased space required for these molecules to get accommodated in the β-channel, a subsite of the active site: while the phenyl derivative **36** showed weak inhibition, compounds **40** and **44** with the naphthyl moieties were no more active. The polar endgroup of **48** was also not favourable for the binding as it was similarly experienced in a series of glucosyl biuret derivatives.[39] Glucosyl-oxadiazolyl-triazoles (entry 4) with a reversed order of the heterocycles proved similarly weak inhibitors as their counterparts in entry 2 and also glucosyl-oxadiazoles in entry 5. In this latter series[19] (entry 5) only the methyl derivative showed moderate inhibition,[20,40] and any increase in the size of the side chain either by azide substitution in the methyl group as in **63** or appending a cycle to the oxadiazole as in **5** and **6** proved detrimental for the binding. Enhancing the flexibility of the aglycon (entry 6) by insertion of a methylene bridge in between the oxadiazole and the triazole as in compounds **59**–**62** did not strengthen binding to the enzyme. The heterocyclic compounds **33**, **34**, **37**, **38**, **41**, **42**, and **52**–**57** (entries 7–9) targeting the inhibitor site of GP proved also inactive.

3. Conclusion

Synthetic methods using tin azide derivatives adapted for the synthesis of O-perbenzoylated 5-β-D-glucopyranosyl tetrazole (**17**) gave the target compounds in almost quantitative yield. Acylations of tetrazole **17** gave ethynyl- and azidomethyl-1,3,4-oxadiazoles (the latter via the chloromethyl compound) whose further transformations under CuAAC conditions gave several variants of compounds containing a β-D-glucopyranosyl moiety attached to 1,3,4-oxadiazole and 1,2,3-triazole. By using similar chemistry a series of compounds with aromatic rings replacing the β-D-glucopyranosyl part was also prepared. Enzyme kinetic measurements showed the new compounds to have weak or no inhibition towards rabbit muscle glycogen phosphorylase b, with inhibition constants for the best inhibitors in the upper micromolar range (**36**: K_i = 854 μM, **47:** K_i = 745 μM). This might be attributed to the size of the aglycon in these compounds that exceeds the otherwise rather flexible space in the β-channel next to the catalytic site of the enzyme in cases of the sugar derivatives, while the aromatic compounds fit neither in the inhibitor nor in any other binding site.

4. Experimental

4.1. General methods

Melting points were measured in open capillary tubes or on a Kofler hot-stage and are uncorrected. Optical rotations were determined on a Perkin–Elmer 241 polarimeter at room temperature. NMR spectra were recorded with Bruker WP 360 SY (360/90 MHz for $^1H/^{13}C$) and Varian UNITYINOVA 400 WB (400/100 MHz for $^1H/^{13}C$) spectrometers. Chemical shifts are referenced to Me_4Si as the internal reference (^1H) or the residual solvent signal (^{13}C). Thin-layer chromatography (TLC) was carried out on aluminium sheets coated with Silica Gel 60 F_{254} (Merck). TLC plates were inspected by UV light (λ = 254 nm) and after gentle heating for the carbohydrate derivatives. Silica gel column chromatography was performed with silica gel Si 60 (40–63 μm) purchased from Merck (Darmstadt, Germany). Organic solutions were dried over anhydrous $MgSO_4$, and concentrated at diminished pressure at 40–50 °C (water bath). 2-Azidoethanol was prepared according to the literature.[42] 5-Substituted-tetrazoles **17**,[20] **18**,[43] and **20**[43] were prepared by the Finnegan procedure[44] from the corresponding nitriles **13**,[45] **15**,[46] and **16**,[47] respectively. 2-Chloromethyl-5-phenyl-1,3,4-oxadiazole **27** was obtained by the literature protocol.[26]

4.2. General procedure for the Zemplén deacylation

An O-peracylated compound (100 mg) was dissolved in dry MeOH (1 mL) and a solution of NaOMe (1 M in MeOH) was added to the solution in a catalytic amount. The reaction mixture was kept at rt. When the reaction was complete (TLC, 7:3 $CHCl_3$–MeOH) the solution was neutralized with a cation exchange resin Amberlyst 15 (H^+ form). Filtration and removal of the solvent resulted in the corresponding deacylated sugar derivative, which, if necessary, was purified by column chromatography.

4.3. General procedure for the synthesis of 5-substituted-tetrazoles by using Bu_3SnN_3

A nitrile was dissolved in DME or diglyme and 3 equiv of Bu_3SnN_3 were added. The mixture was stirred and heated at reflux for the given time while the reaction was monitored by TLC (4:1 $PhCH_3$–EtOAc) to indicate completion of the transformation. Then it was cooled to rt and toluene and aq HCl (4 M solution) were added and the mixture was stirred for 2 h. The precipitated product was filtered, washed with water, and dried. The two phase filtrate was separated, the organic phase was diluted by hexane to precipitate a further crop of the product which was filtered and dried.

4.3.1. 5-(2′,3′,4′,6′-Tetra-*O*-benzoyl-β-D-glucopyranosyl)tetrazole (17)

(i) Prepared by general procedure 4.3 from **13**[45] (4.0 g, 6.6 mmol) in diglyme (50 mL), reaction time 26 h. After the workup the precipitate was washed with hot hexane to give **17** (4.24 g, 99%) as a white solid.

(ii) A solution of **13**[45] (1.00 g, 1.65 mmol), Me_3SiN_3 (434 μL, 3.3 mmol) and Bu_2SnO (41 mg, 0.16 mmol) in dry toluene (30 mL) was heated for 19 h at 80 °C. Toluene was removed under reduced pressure, the residue was dissolved in MeOH and concentrated again. The residue was dissolved in EtOAc (15 mL), extracted with satd aq $NaHCO_3$ soln (2 × 15 mL). The combined organic phases were dried, and then concentrated to a syrup that was triturated in hexane to give **17** (1.02 g, 95%) as an amorphous white solid.

The material obtained by both methods had spectral characteristics identical with the reported ones.[20]

4.3.2. 5-(Naphthalen-1-yl)-tetrazole (19)

Prepared by general procedure 4.3 from compound **15** (3.68 g, 24 mmol) and Bu_3SnN_3 (19.8 mL, 24 g, 72 mmol) in diglyme (70 mL). Reaction time 2 h. Product **19** (1.30 g, 86%) was obtained as white crystals. Mp: 216–218 °C (lit.[48] mp 165 °C). ^1H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 7.65–7.75 (3H, m, H-3′, H-7′,

H-8′), 8.02 (1H, d, J = 7.1 Hz, H-2′), 8.10 (1H, d, J = 7.7 Hz, H-4′), 8.21 (1H, d, J = 8.2 Hz, H-6′), 8.6 (1H, d, J = 8.1 Hz, H-9′), 17.0 (1H, s, NH-1). ^{13}C NMR (DMSO-d_6, 90 MHz) δ (ppm): 121.9 (C-1′), 125.6 (C-4′), 125.8 (C-6′), 127.2 (C-2′), 128.2 (C-3′), 128.9 (C-7′), 129.1 (C-8′), 130.4 (C-5′), 131.9 (C-9′), 133.8 (C-10′), 165.3 (C-1). Anal. Calcd for $C_{11}H_8N_4$ (196.07): C, 67.34; H, 4.11; N, 28.55. Found: C, 67.16; H, 4.19; N, 28.48.

4.4. General procedure for the synthesis of 2-ethynyl-5-substituted-1,3,4-oxadiazoles

Propiolic acid was dissolved in dry toluene and DCC was added. The precipitated dicyclohexylurea (DCU) was filtered off and washed with dry toluene. The combined filtrate was added to a solution of a tetrazole **17**–**20** in dry toluene. This mixture was stirred at the given temperature. When the reaction was complete (TLC 1:1 EtOAc–hexane for **21**, 10:1 $PhCH_3$–MeOH for **22**–**24**) the solvent was evaporated and the residue was purified by column chromatography (eluent $PhCH_3$ unless stated otherwise).

4.4.1. 2-(2′,3′,4′,6′-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-5-ethynyl-1,3,4-oxadiazole (21)

Prepared by general procedure 4.4 from **17** (1 g, 1.57 mmol), propiolic acid (220 mg, 3.14 mmol) and DCC (320 mg, 1.57 mmol) in 14 mL abs toluene at reflux for 4 h. Column chromatography (3:7 EtOAc–hexane) and crystallization from EtOH gave **21** (615 mg, 59%) as white crystals. R_f = 0.75 (1:1 EtOAc–hexane), mp: 132–135 °C, $[\alpha]_D$ = −151 (c 0.18, $CHCl_3$), ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.05–7.81 (8H, m Ar), 7.57–7.25 (12H, m, Ar), 6.09 (1H, t, J = 9.3, Hz, H-2′ or H-3′ or H-4′), 5.87–5.81 (2H, m, J = 9.3, 10.6 Hz, 2 of H-2′ or H-3′ or H-4′), 5.22 (1H, d, $J_{1',2'}$ = 10.6 Hz, H-1′), 4.67 (1H, dd, $J_{5',6'a}$ = 2.6 Hz, $J_{6'a,6'b}$ = 11.9 Hz, H-6′a), 4.52 (1H, dd, $J_{5',6'b}$ = 5.3, $J_{6'a,6'b}$ = 11.9 Hz, H-6′b), 4.35 (1H, ddd, $J_{5',4'}$ = 9.3 Hz, $J_{5',6'a}$ = 2.6 Hz, $J_{5',6'b}$ = 5.3 Hz, H-5′), 3.57 (1H, s, ethynyl-H). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 165.3, 165.1, 164.6, 164.4 (CO), 162.0, 150.0 (oxadiazole), 133.9–128.0 (Ar), 90.9 (*C*≡CH), 75.1, 73.2, 70.4, 69.6, 68.6 (C-1′–C-5′), 66.7 (C≡*C*H), 62.6 (C-6′). Anal. Calcd for $C_{38}H_{28}N_2O_{10}$ (672.65): C, 67.85; H, 4.20; N, 4.16; O, 23.79. Found: C, 67.78; H, 4.15; N, 4.10.

4.4.2. 2-Ethynyl-5-phenyl-1,3,4-oxadiazole (22)

Prepared by general procedure 4.4 from propiolic acid (3.81 g, 55 mmol), DCC (5.62 g, 27 mmol) in toluene (25 mL, then washing with 25 mL) and **18** (4.00 g, 27 mmol) in toluene (100 mL). Stirring at 80 °C for 1.5 h. Column chromatography gave **22** (2.50 g, 47%) as white crystals. The compound is light sensitive therefore it must be stored in a dark and cold place. Mp: 106–110 °C; ^{1}H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 3.62 (1H, s, C≡C*H*), 7.47–7.57 (3H, m, H-3′, H-4′, H-5′), 8.04 (2H, dd, J = 7.0 Hz, 1.6 Hz, H-2′, H-6′). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 67.6 *C*≡CH), 85.9 (C≡*C*H), 122.9 (C-1′), 127.1 (C-2′, C-6′), 129.1 (C-3′, C-5′), 132.3 (C-4′), 149.4 (C-2), 164.7 (C-5). Anal. Calcd for $C_{10}H_6N_2O$ (170.05): C, 70.58; H, 3.55; N, 16.46; Found: C, 70.46; H, 3.61; N, 16.51.

4.4.3. 2-Ethynyl-5-(naphthalen-1-yl)-1,3,4-oxadiazole (23)

Prepared by general procedure 4.4 from propiolic acid (0.24 g, 3.4 mmol), DCC (0.72 g, 3.4 mmol) in toluene (10 mL, then washing with 10 mL) and **19** (0.68 g, 3.4 mmol) in toluene (50 mL). Stirring at 80 °C for 2 h. Column chromatography gave **23** (445 mg, 58%) as yellow crystals. Mp: 168.5–170.5 °C; ^{1}H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 3.64 (1H, s, C≡C*H*), 7.53–7.61 (2H, m, H-7′, H-8′), 7.69 (1H, t, J = 7.2 Hz, J = 7.9, H-3′), 7.91 (1H, d, J = 8.3 Hz, H-2′), 8.03 (1H, d, J = 8.3 Hz, H-4′), 8.17 (1H, d, J = 7.2 Hz, H-6′), 9.20 (1H, d, J = 8.6 Hz, H-9′). ^{13}C NMR (Me_2SO-d_6 90 MHz) δ (ppm): 67.7 C≡*C*H), 86.1 (*C*≡CH), 119.4 (C-10′), 124.7 (C-2′), 125.7 (C-7′), 126.8 (C-8′), 128.4 (C-3′), 128.7 (C-4′), 128.8 (C-6′), 129.7 (C-5′), 133.2 (C-9′), 133.7 (C-1′), 149.1 (C-2), 165.0 (C-5). Anal. Calcd for $C_{14}H_8N_2O$ (220.06): C, 76.35; H, 3.66; N, 12.72. Found: C, 76.43; H, 3.71; N, 12.79.

4.4.4. 2-Ethynyl-5-(naphthalen-2-yl)-1,3,4-oxadiazole (24)

Prepared by general procedure 4.4 from propiolic acid (3.57 g, 51 mmol), DCC (5.25 g, 25.5 mmol) in toluene (50 mL, then washing with 30 mL) and **20** (0.68 g, 3.4 mmol) in toluene (50 mL). Stirring at 80 °C for 2 h. Column chromatography gave **24** (2.87 g, 51%) as white crystals. Mp: 168.5–170.5 °C; ^{1}H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 5.4 (1H, s, C≡C*H*), 7.67 (2H, m, H-7′, H-8′), 8.02–8.07 (4H, m, H-3′, H-4′, H-6′, H-9′), 8.64 (1H, s, H-1′). ^{13}C NMR (Me_2SO-d_6 90 MHz) δ (ppm): 67.4 C≡*C*H), 90.3 (*C*≡CH), 119.8 (C-2′), 122.7 (C-3′), 127.3 (C-4′), 127.6 (C-6′), 127.8 (C-9′), 128.4 (C-1′), 128.9 (C-7′), 129.1 (C-8′), 133.3 (C-5′), 124.3 (C-10′), 149.2 (C-2), 164.4 (C-5). Anal. Calcd for $C_{14}H_8N_2O$ (220.06): C, 76.35; H, 3.66; N, 12.72; Found: C, 76.45; H, 3.69; N, 12.80.

4.4.5. 2-(2′,3′,4′,6′-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-5-chloromethyl-1,3,4-oxadiazole (25)

Tetrazole **17** (15.00 g, 23.13 mmol) was dissolved in dry toluene (300 mL), and chloroacetyl chloride (7.4 mL, 69.39 mmol) was added. The reaction mixture was heated at reflux. After 2 h TLC (1:1 EtOAc–hexane) indicated completion of the transformation. The solvent was evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2 (50 mL) then washed with cold satd $NaHCO_3$ solution (3 × 15 mL), brine (20 mL), and water (20 mL). The combined organic phase was dried, filtered, and evaporated under reduced pressure to give **25** (15.54 g, 96%) as a yellow syrup. The chromatographically uniform crude product was used for further transformations. R_f = 0.82 (1:1 EtOAc–hexane); ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.08–7.80 (10H, m, Ph), 7.54–7.20 (10H, m, Ph), 6.18 (1H, pt, J = 9.6, 9.5 Hz, H-2′ or H-3′ or H-4′), 5.93 (1H, pt, J = 9.7 Hz, H-2′ or H-3′ or H-4′), 5.90 (1H, pt, J = 9.7 Hz, H-2′ or H-3′ or H-4′), 5.30 (1H, d, $J_{1',2'}$ = 10.0 Hz, H-1′), 4.72–4.65 (3H, m, H-6′a, CH_2), 4.56 (1H, dd, $J_{6'a,\ 6'b}$ = 12.4 Hz, H-6′b), 4.43 (1H, m, $J_{5',6'a}$ = 2.9 Hz, $J_{5',6'b}$ = 5.2 Hz, $J_{4',5'}$ = 10.0 Hz, H-5′). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 165.9, 165.5, 164.9, 164.7 (CO), 163.5, 162.4 (oxadiazole), 133.4–127.9 (Ar), 76.8, 73.2, 71.5, 70.3, 68.7 (C-1′–C-5′), 62.7 (C-6′), 32.4 (CH_2).

4.4.6. 2-(2′,3′,4′,6′-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-5-azidomethyl-1,3,4-oxadiazole (26)

Oxadiazole **25** (15.54 g, 22.29 mmol) was dissolved in dry DMF (40 mL), then NaN_3 (5.80 g, 89.17 mmol) was added. The suspension was heated and stirred at 50 °C. After 2 h, TLC (1:3 EtOAc–hexane) indicated completion of the transformation. The solvent was evaporated under reduced pressure. The residue was diluted with water (400 mL) and extracted with Et_2O (3 × 70 mL), the combined organic phase was washed with water (50 mL), dried, filtered, and concentrated under reduced pressure to give **26** (13.60 g, 90%) as a yellow syrup. The chromatographically uniform crude product was used for further transformations. R_f = 0.81 (1:1 EtOAc–hexane); ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.04–7.81 (10H, m, Ar), 7.58–7.25 (10H, m, Ar), 6.10 (1H, pt, J = 10.7, 9.3 Hz, H-2′ or H-3′ or H-4′), 5.84 (1H, pt, J = 10.5 Hz, H-2′ or H-3′ or H-4′), 5.81 (1H, pt, J = 9.4 Hz, H-2′ or H-3′ or H-4′), 5.20 (1H, d, $J_{1',2'}$ = 10.7 Hz, H-1′), 4.67 (1H, dd, $J_{6'a,6'b}$ = 12.2 Hz, $J_{5',6'b}$ = 2.8 Hz, H-6′b), 4.63–4.50 (3H, m, H-6′a, CH_2), 4.38–4.33 (1H, m, H-5′). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 166.0, 165.6, 165.1, 164.9 (CO), 163.1, 162.3 (oxadiazole), 133.6–128.1 (Ar), 77.1, 73.2, 71.8, 70.5, 68.8 (C-1′–C-5′), 62.8 (C-6′), 44.1 (CH_2).

4.4.7. 2-(Azidomethyl)-5-phenyl-1,3,4-oxadiazole (28)

A mixture of **27**[26] (6.00 g, 31 mmol), NaN_3 (4.00 g, 93 mmol), and 18-crown-6 (0.82 g, 10 mol %) in acetone (50 mL) was stirred

at rt for 2 h. When the reaction was complete (TLC, 4:1 $PhCH_3$–EtOAc) the solids were filtered off. The solvent was evaporated and the residue was purified by flash chromatography on aluminium oxide (CH_2Cl_2) to give **28** (5.72 g, 94%) as white crystals. Mp: 66–68 °C (lit.[49] mp: 72–73 °C); ^{1}H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 3.91 (2H, s, CH_2), 6.58–6.66 (3H, m, H-3′, H-4′, H-5′), 6.99 (2H, dd, J = 8.6 Hz, 2.1 Hz, H-2′, H-6′). ^{13}C NMR (Me_2SO-d_6 90 MHz) δ (ppm): 43.5 CH_2), 122.9 (C-1′), 125.5 (C-2′, C-6′), 129.4 (C-3′, C-5′), 132.1 (C-4′), 162.3 (C-2), 164.6 (C-5). Anal. Calcd for $C_9H_7N_5O$ (201.07): C, 53.73; H, 3.51; N, 34.81. Found: C, 53.78; H, 3.62; N, 34.85.

4.5. General procedures for the synthesis of 1,4-disubstituted-*1H*-1,2,3-triazoles

4.5.1. In CH_2Cl_2–water mixtures with organic azides

Equimolar amounts of an alkyne and an azide were dissolved in CH_2Cl_2 (7 mL/mmol alkyne). Water (the same volume as that of CH_2Cl_2), $CuSO_4{\cdot}5H_2O$ (5 mol %), L-ascorbic-acid (15 mol %) were added and the mixture was stirred at 50 °C and monitored by TLC (1:1 EtOAc–hexane). After disappearance of the starting materials (aromatic azide: 2–3 h, glucosyl azide: overnight) the reaction mixture was diluted with water and CH_2Cl_2, the phases were separated, and the aqueous layer was washed with CH_2Cl_2 (2 × 10 mL/mmol). The combined organic layer was dried, the solvent evaporated, and the residue purified by column chromatography.

4.5.2. In CH_2Cl_2–water mixtures with organic azides prepared in situ from boronic acids

A boronic acid (1 equiv) and NaN_3 (1.2 equiv) were dissolved in MeOH (5 mL/mmol of boronic acid). $CuSO_4{\cdot}5H_2O$ (0.1 equiv) was added and the mixture was stirred overnight at rt. CH_2Cl_2 and water (10 mL of each/mmol of boronic acid), an alkyne (0.3 equiv) and L-ascorbic acid (0.5 equiv) were added and the reaction mixture was heated to 50 °C. After consumption of the alkyne (TLC 1:1 EtOAc–hexane) the reaction mixture was diluted with water and CH_2Cl_2, the phases were separated and the aqueous layer was washed with CH_2Cl_2 (2 × 10 mL/mmol). The combined organic layer was dried, the solvent evaporated, and the residue purified by column chromatography.

4.5.3. In *t*-BuOH–water mixtures

Near equimolar amounts of an alkyne and an azide, catalytic amount (1–4 mol %) of $CuSO_4{\cdot}5H_2O$, Na-L-ascorbate, and TMEDA were placed in a 1:2 mixture of *t*-BuOH and water. The reaction mixture was stirred at the given temperature for the indicated time. When TLC (4:1 $PhCH_3$–EtOAc) indicated complete transformation of the starting materials the precipitate was filtered off and washed with water and then with hexane. Further purification, if necessary, was performed by flash chromatography (4:1 $PhCH_3$–EtOAc).

4.5.4. 2-(2′,3′,4′,6′-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-5-(1-phenyl-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (29)

(i) Prepared by general procedure 4.5.1 from **21** (150 mg, 0.22 mmol) and PhN_3 for 2 h. Column chromatography (3:7 EtOAc–hexane) and crystallization from ethanol gave **29** (128 mg, 73%) as white crystals. R_f = 0.58 (1:1 EtOAc–hexane), mp: 137–140 °C, $[\alpha]_D$ = −194 (*c* 0.16, $CHCl_3$), ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.65 (1H, s, triazole-H), 8.04–7.77 (10H, m, Ar), 7.58–7.28 (15H, m, Ar), 6.14 (1H, t, J = 9.3 Hz, H-2′ or H-3′ or H-4′), 6.02 (1H, pt, J = 9.3, 10.5 Hz, H-2′ or H-3′ or H-4′), 5.89 (1H, pt, J = 9.3, 10.5 Hz, H-2′ or H-3′ or H-4′), 5.33 (1H, d, $J_{1',2'}$ = 9.3 Hz, H-1′), 4.69 (1H, dd, $J_{6'a,6'b}$ = 11.9 Hz, $J_{5',6'a}$ <1 Hz H-6′a), 4.56 (1H, dd, $J_{6'a,6'b}$ = 11.9 Hz, $J_{5',6'b}$ = 5.3 Hz, H-6′b), 4.42 (1H, ddd, J <1 Hz, H-5′). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 166.1, 165.7, 165.1, 164.9 (CO), 161.3, 159.2 (oxadiazole), 136.1–120.8 (Ar, triazole-C, triazole-CH), 77.1, 73.5, 71.8, 70.5, 69.00 (C-1′–C-5′), 63.1 (C-6′). Anal. Calcd for $C_{44}H_{35}N_5O_{10}$ (791.76): C, 66.75; H, 4.20; N, 8.85; O, 20.21. Found: C, 66.82; H, 4.15; N, 8.91.

(ii) Prepared by general procedure 4.5.2 from PhN_3 (prepared in situ from phenylboronic acid (27 mg, 0.22 mmol)) and **21** for 2 h. Column chromatography (3:7 EtOAc–hexane) and crystallization from ethanol gave **29** (40 mg, 68%) as white crystals.

4.5.5. 2-(2′,3′,4′,6′-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-5-(1-phenyl-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (29)

(i) Prepared by general procedure 4.5.1 from **21** (150 mg, 0.22 mmol) and PhN_3 for 2 h. Column chromatography (3:7 EtOAc–hexane) and crystallization from ethanol gave **29** (128 mg, 73%) as white crystals. R_f = 0.58 (1:1 EtOAc–hexane), mp: 137–140 °C, $[\alpha]_D$ = −194 (*c* 0.16, $CHCl_3$), ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.65 (1H, s, triazole-H), 8.04–7.77 (10H, m, Ar), 7.58–7.28 (15H, m, Ar), 6.14 (1H, t, J = 9.3 Hz, H-2′ or H-3′ or H-4′), 6.02 (1H, pt, J = 9.3, 10.5 Hz, H-2′ or H-3′ or H-4′), 5.89 (1H, pt, J = 9.3, 10.5 Hz, H-2′ or H-3′ or H-4′), 5.33 (1H, d, $J_{1',2'}$ = 9.3 Hz, H-1′), 4.69 (1H, dd, $J_{6'a,6'b}$ = 11.9 Hz, $J_{5',6'a}$ <1 Hz H-6′a), 4.56 (1H, dd, $J_{6'a,6'b}$ = 11.9 Hz, $J_{5',6'b}$ = 5.3 Hz, H-6′b), 4.42 (1H, ddd, J <1 Hz, H-5′). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 166.1, 165.7, 165.1, 164.9 (CO), 161.3, 159.2 (oxadiazole), 136.1–120.8 (Ar, triazole-C, triazole-CH), 77.1, 73.5, 71.8, 70.5, 69.00 (C-1′–C-5′), 63.1 (C-6′). Anal. Calcd for $C_{44}H_{35}N_5O_{10}$ (791.76): C, 66.75; H, 4.20; N, 8.85; O, 20.21. Found: C, 66.82; H, 4.15; N, 8.91.

4.5.6. 2-Phenyl-5-(1-phenyl-*1H*-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (33)

Prepared by general procedure 4.5.3 from **22** (171 mg, 1 mmol) and PhN_3 (100 mg, 0.84 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (8 mg, 0.034 mmol), Na-L-ascorbate (27 mg, 0.13 mmol), and TMEDA (10 μL, 0.07 mmol) in 6 mL solvent mixture at rt for 24 h to give **33** (197 mg, 81%) as pale yellow crystals. Mp: 201–202 °C; ^{1}H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 7.56–7.63 (6H, m, H-3″-5″, H-3‴-5‴), 7.84 (2H, d, J = 7.7 Hz, H-2″, H-6″), 8.22 (2H, d, J = 7.9 H-2‴, H-6‴), 8.76 (1H, s, H-5′). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 119.1 (C-3‴, C-5‴), 121.6 (C-1‴), 125.3 C-2‴, C-6‴), 128.0 (C-5′), 128.1 (C-3″, C-5″), 128.6 (C-2″, C-6″, C-4‴), 130.8 (C-4″), 132.2 (C-1″), 134.6 (C-4′), 156.3 (C-5), 162.4 (C-2). Anal. Calcd for $C_{16}H_{11}N_5O$ (289.10): C, 66.43; H, 3.83; N, 24.21. Found: C, 66.51; H, 3.91; N, 24.29.

4.5.7. 2-(4-(5-Phenyl-1,3,4-oxadiazol-2-yl)-*1H*-1,2,3-triazol-1-yl)ethanol (34)

Prepared by general procedure 4.5.3 from **22** (235 mg, 1.38 mmol) and 2-azidoethanol (100 mg, 1.15 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (12 mg, 0.046 mmol), Na-L-ascorbate (36 mg, 0.18 mmol), and TMEDA (14 μL, 0.10 mmol) in 10 mL solvent mixture at rt for 24 h to give **34** (270 mg, 76%) as pale yellow crystals. Mp: 176–178 °C; ^{1}H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 3.88 (2H, d, J = 4.0 Hz, N-CH_2), 4.57 (2H, br s, CH_2–OH), 5.13 (1H, s, OH), 7.66 (3H, br s, H-3″, H-4″, H-5″), 8.11 (2H, d, J = 4.7 Hz, H-2″, H-6″), 9.00 (1H, s, H-5′). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 52.7 N-CH_2), 59.5 (CH_2–OH), 123.0 (C-1″), 126.5 (C-2″, C-6″), 126.8 (C-5′), 129.4 (C-3″, C-5″), 132.1 (C-1″), 132.3 (C-4′), 158.1 (C-5), 163.6 (C-2). Anal. Calcd for $C_{12}H_{11}N_5O_2$ (257.09): C, 56.03; H, 4.31; N, 27.22. Found: C, 56.12; H, 4.35; N, 27.28.

4.5.8. 2-Phenyl-5-[1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (35)

Prepared by general procedure 4.5.1 from 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-azide[31,32] (300 mg, 0.80 mmol) and **22** for 28 h. Column chromatography (1:1 EtOAc–hexane) gave **35** (360 mg, 87%) as a white amorphous solid. R_f = 0.24 (1:1 EtOAc–hexane),

$[\alpha]_D = -139$ (*c* 0.17, $CHCl_3$); ^1H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.68 (1H, s, triazole-H), 8.19 (2H, d, $J = 6.6$ Hz, Ar), 7.58–7.52 (3H, m, Ar), 6.03 (1H, d, $J_{1',2'} = 8.8$ Hz, H-1′), 5.52–5.50 (2H, m, 2 of H-2′ or H-3′ or H-4′), 5.32 (1H, pt, $J = 9.7$, 9.5 Hz, H-2′ or H-3′ or H-4′), 4.35 (1H, dd, $J_{5',6'a} = 4.9$ Hz, $J_{6'a,6'b} = 12.6$ Hz, H-6′a), 4.21 (1H, dd, $J_{5',6'b}$ 1.3 Hz, $J_{6'a,6'b} = 12.6$ Hz, H-6′b) 4.10 (1H, ddd, $J_{5',6'b}$ 1.3 Hz, $J_{5',6'a} = 4.9$ Hz, $J_{5',4'} = 9.7$ Hz, H-5′), 2.11, 2.10, 2.05, 1.92 (12H, 4s, CH_3). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 170.4, 169.8, 169.3, 168.9 (CO), 164.8, 157.6 (oxadiazole), 134.6 (triazole-C), 132.0, 129.1, 127.2, 123.3 (Ar), 123.2 (triazole-CH), 86.0, 75.4, 72.3, 70.5, 67.5 (C-1′–C-5′), 61.4 (C-6′), 20.6, 20.5, 20.4, 20.0 (CH_3). Anal. Calcd for $C_{24}H_{25}N_5O_{10}$ (543.16): C, 53.04; H, 4.64; N, 12.89; O, 29.44. Found: C, 53.00; H, 4.61; N, 12.81.

4.5.9. 2-Phenyl-5-[1-(β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (36)

Prepared by general procedure 4.2 from **35** (146 mg, 0.27 mmol) for 17 h. Filtration of the reaction mixture gave **36** (100 mg, 99%) as a white solid. $R_f = 0.60$ (7:3 $CHCl_3$–MeOH), $[\alpha]_D = -23$ (*c* 0.19, Me_2SO); ^1H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 9.32 (1H, s, triazole-CH), 8.09 (m, 2H, Ar), 7.64 (m, 3H, Ar), 5.69 (1H, d, $J_{1',2'} = 7.9$ Hz, H-1′), 3.87 (1H, pt, $J = 7.9$, 9.3 Hz, H-2′ or H-3′ or H-4′), 3.72 (1H, dd, $J_{6'a,6'b} = 10.6$, $J_{5',6'a}$ <1 Hz, H-6′a), 3.48 (3H, m, H-2′ or H-3′ or H-4′, H-5′, H-6′b), 3.30 (1H, t, $J = 7.9$ Hz, H-2′ or H-3′ or H-4′). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 163.7, 157.9 (oxadiazole), 132.7 (triazole-C), 132.6, 132.1, 129.4, 126.6, 123.1 (Ar, triazole-CH), 88.11, 80.12, 76.83, 72.27, 69.50 (C-1′–C-5′), 60.73 (C-6′). Anal. Calcd for $C_{16}H_{17}N_5O_6$ (375.12): C, 51.20; H, 4.57; N, 18.66; O, 25.58. Found: C, 51.25; H, 4.55; N, 18.68.

4.5.10. 2-(Naphthalen-1-yl)-5-(1-phenyl-*1H*-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (37)

Prepared by general procedure 4.5.3 from **23** (185 mg, 0.84 mmol) and PhN_3 (100 mg, 0.84 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (8 mg, 0.034 mmol), Na-L-ascorbate (27 mg, 0.13 mmol), and TMEDA (10 μL, 0.07 mmol) in 10 mL solvent mixture at 50 °C for 168 h to give **37** (135 mg, 48%) as orange crystals. Mp: 186–188 °C; ^1H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 7.50–7.61 (5H, m, H-2″–H-6″), 7.69 (1H, t, $J = 8.3$ Hz, $J = 7{,}2$ Hz, H-3‴), 7.82 (2H, d, $J = 7.9$ Hz, H-7‴, H-8‴), 7.92 (1H, d, $J = 7.9$ Hz, H-2‴), 8.04 (1H, d, $J = 8.3$ Hz, H-4‴), 8.37 (1H, d, $J = 7.2$ Hz, H-6‴), 8.79 (1H, s, H-5′), 9.32 (1H, d, $J = 8.6$ Hz, H-9‴-H). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 119.8 C-1″), 120.8 (C-3″–C-5″), 122.6 (C-5′), 124.9 – 132.9 (C-2″,C-6″, C-2‴–C-4‴, C-6‴–C-9‴) 132.8 (C-5‴, C-10‴), 133.7(C-1‴), 134.5 (C-1″), 136.2 (C-4′), 157.4 (C-2), 164.7 (C-5). Anal. Calcd for $C_{20}H_{13}N_5O$ (339.11): C, 70.79; H, 3.86; N, 20.64. Found: C, 70.85; H, 3.80; N.

4.5.11. 2-{4-[5-(Naphthalen-1-yl)-1,3,4-oxadiazol-2-yl]-*1H*-1,2,3-triazol-1-yl}ethanol (38)

Prepared by general procedure 4.5.3 from **23** (202 mg, 0.92 mmol) and 2-azidoethanol (80 mg, 0.92 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (9 mg, 0.037 mmol), Na-L-ascorbate (29 mg, 0.15 mmol), and TMEDA (14 μL, 0.10 mmol) in 10 mL solvent mixture at rt for 29 h then then at 50 °C for 16 h to give **34** (243 mg, 76%) as white crystals. Mp: 198–199 °C; ^1H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 3.90 (2H, d, $J = 4{,}7$ Hz, N-CH_2), 4.59 (2H, t, $J = 4{,}7$ Hz, CH_2–OH), 5.17 (1H, t, $J = 5.0$, OH), 7.68–7.81 (3H, m, H-3″, H-7″, H-8″), 8.13 (1H, d, $J = 7.6$ Hz, H-2″), 8.26 (1H, d, $J = 8{,}3$ Hz, H-4″), 8.33 (1H, d, $J = 7.2$ Hz, H-6″), 9.07 (1H, s, H-5′), 9.16 (1H, d, $J = 8.3$ Hz, H-9″). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 52.7 N-CH$_2$), 59.5 (CH$_2$–OH), 119.3 (C-1″), 125.3–132.7 (C-5′, C-2″–C-4″, C-6″–C-8″) 132.7 (C-10″), 133.1 (C-9″), 133.8 (C-4′), 157.6 (C-5), 163.4 (C-2). Anal. Calcd for $C_{16}H_{13}N_5O_2$ (307.11): C, 62.53; H, 4.26; N, 22.79. Found: C, 62.41; H, 4.24; N, 22.72.

4.5.12. 2-(Naphthalen-1-yl)-5-[1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (39)

Prepared by general procedure 4.5.1 from 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-azide[31,32] (300 mg, 0.80 mmol) and **23** for 16 h. Crystallization from EtOH gave **39** (365 mg, 77%) as white crystals. $R_f = 0.38$ (1:1 EtOAc–hexane), mp: 181–182 °C, $[\alpha]_D = -140$ (*c* 0.21, $CHCl_3$); ^1H NMR ($CDCl_3$, 360 MHz) δ (ppm): 9.29 (1H, d, $J = 8.6$ Hz, Ar), 8.76 (1H, s, triazole-CH), 8.31 (1H, d, $J = 7.2$ Hz, Ar), 8.02 (1H, d, $J = 8.2$ Hz, Ar), 7.91 (1H, d, $J = 8.1$ Hz, Ar), 7.70 (1H, pt, $J = 7.8$, 7.5 Hz Ar), 7.58 (2H, m, Ar), 6.10 (1H, d, $J_{1',2'} = 7.9$ Hz, H-1′), 5.59–5.50 (2H, m, 2 of H-2′ or H-3′ or H-4′), 5.35 (1H, pt, $J = 9.6$, 9.4 Hz, H-2′ or H-3′ or H-4′), 4.37 (1H, dd, $J_{5',6'a} = 5.0$ Hz, $J_{6'a,6'b} = 12.7$ Hz, H-6′a), 4.22 (1H, dd, $J_{6'a,6'b} = 12.6$ Hz, $J_{5',6'b} = 1.6$ Hz, H-6′b), 4.14 (1H, ddd, $J_{5',6'b} = 1.6$ Hz, $J_{5',6'a} = 4.9$ Hz, $J_{4',5'} = 9.9$ Hz, H-5′), 2.11, 2.10, 2.06, 1.94 (12H, 4s, CH_3). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 170.4, 169.8, 169.2, 168.8 (CO), 164.6, 157.1 (oxadiazole), 134.6, 133.7, 132.8, 129.9, 128.7, 128.6, 128.2, 126.3, 126.0, 124.8, 123.5, 119.7 (Ar, triazole-C, triazole-CH), 85.9, 75.2, 72.2, 70.5, 67.5 (C-1′–C-5′), 61.3 (C-6′), 20.6, 20.5, 20.4, 20.0 (CH_3). Anal. Calcd for $C_{28}H_{27}N_5O_{10}$ (593.18): C, 56.66; H, 4.59; N, 11.80; O, 26.96. Found: C, 56.58; H, 4.53; N, 11.77.

4.5.13. 2-(Naphthalen-1-yl)-5-[1-(β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (40)

Prepared by general procedure 4.2 from **39** (202 mg, 0.34 mmol) for 4 h. Filtration of the reaction mixture gave **40** (142 mg, 98%) as a white amorphous solid. $R_f = 0.50$ (7:3 $CHCl_3$–MeOH), $[\alpha]_D = -8$ (*c* 0.18, Me_2SO); ^1H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 9.42 (1H, s, triazole-CH), 9.16 (1H, d, $J = 8.6$ Hz, Ar), 8.33 (1H, d, $J = 7.3$ Hz, Ar), 8.24 (1H, d, $J = 8.2$ Hz, Ar), 8.11 (1H, d, $J = 8.1$ Hz, Ar), 7.80–7.67 (3H, m, Ar), 5.75 (1H, d, $J_{1',2'} = 9.2$ Hz, H-1′), 3.91 (1H, pt, $J = 9.0$, 9.1 Hz H-2′ or H-3′ or H-4′), 3.75 (1H, dd, $J_{6'a,6'b} = 10.7$ Hz, $J_{5',6'a}$ <0 Hz, H-6′a), 3.57–3.44 (3H, m, H-2′ or H-3′ or H-4′, H-5′, H-6′b), 3.32 (1H, pt, $J = 9.0$, 8.9 Hz, H-2′ or H-3′ or H-4′). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 163.6, 157.5 (oxadiazole), 133.4, 132.8, 132.7, 129.1, 128.9, 128.8, 128.3, 126.9, 126.0, 125.4, 125.3, 119.4 (Ar, triazole-C, triazole-CH), 87.9, 80.1, 76.6, 72.2, 69.4 (C-1′–C-5′), 60.7 (C-6′). Anal. Calcd for $C_{20}H_{19}N_5O_6$ (425.13): C, 56.47; H, 4.50; N, 16.46; O, 22.57. Found: C, 56.46; H, 4.54; N, 16.52.

4.5.14. 2-(Naphthalen-2-yl)-5-(1-phenyl-*1H*-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (41)

Prepared by general procedure 4.5.3 from **24** (185 mg, 0.84 mmol) and PhN_3 (100 mg, 0.84 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (8 mg, 0.034 mmol), Na-L-ascorbate (27 mg, 0.13 mmol), and TMEDA (10 μL, 0.07 mmol) in 10 mL solvent mixture at 50 °C for 168 h to give **41** (127 mg, 45%) as pale yellow crystals. Mp: 223–225 °C; ^1H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 7.59 (1H, t, $J = 6.5$ Hz, $J = 6{,}8$ Hz, H-4″), 7.60–7.71 (4H, m, H-3″, H-5″, H-6‴, H-7‴), 8.06–8.08 (3H, m, H-2‴, H-2″, H-6″), 8.18–8.21 (3H, m, H-3‴, H-7‴, H-8‴), 8.74 (1H, s, H-9‴), 9.83 (1H, s, H-5′). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 120.5 C-1″), 120.8 (C-2″, C-6″), 123.2 (C-5′), 127.1–130.0 (C-3″–C-5″, C-2‴, C-3‴, C-5‴–C-8‴, C-10‴), 132.8 (C-1‴), 134.6 (C-9‴), 134.8 (C-4‴), 136.2 (C-4′), 157.9 (C-5), 165.0 (C-2). Anal. Calcd for $C_{20}H_{13}N_5O$ (339.11): C, 70.79; H, 3.86; N, 20.64. Found: C, 70.87; H, 3.81; N, 20.65.

4.5.15. 2-{4-[5-(Naphthalen-2-yl)-1,3,4-oxadiazol-2-yl]-1*H*-1,2,3-triazol-1-yl}ethanol (42)

Prepared by general procedure 4.5.3 from **24** (303 mg, 1.38 mmol) and 2-azidoethanol (100 mg, 1.15 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (12 mg, 0.046 mmol), Na-L-ascorbate (36 mg, 0.18 mmol), and TMEDA (14 μL, 0.10 mmol) in 10 mL solvent mixture at rt for 5 d then at 50 °C for 1 d to give **42** (423 mg, 76%) as pale yellow crystals. Mp: 195–198 °C; ^1H NMR (Me_2SO-d_6,

360 MHz) δ (ppm): 3.90 (2H, d, J = 4,0 Hz, N-CH_2), 4.59 (2H, br s, CH_2–OH), 5.16 (1H, s, OH), 7.68 (2H, br s, H-6″, H-7″), 8.06 (1H, d, J = 5.4 Hz, H-2″), 8.17 (3H, br s, H-3″, H-5″, H-8″), 8.72 (1H, s, H-10″), 9.04 (1H, s, H-5′). ^{13}C NMR (Me$_2$SO-d_6, 90 MHz) δ (ppm): 52.7 N-CH_2), 59.5 (CH_2–OH), 120.3 (C-1″), 122.7 (C-5′), 127.0–129.2 (C-2″, C-3″, C-5″–C-8″, C-10″), 132.3 (C-4″), 132.4 (C-9″), 134.2 (C-4′), 158.1 (C-5), 163.7 (C-2). Anal. Calcd for $C_{16}H_{13}N_5O_2$ (307.11): C, 62.53; H, 4.26; N, 22.79. Found: C, 62.45; H, 4.27; N, 22.82.

4.5.16. 2-(Naphthalen-2-yl)-5-[1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (43)

Prepared by general procedure 4.5.1 from 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-azide[31,32] (300 mg, 0.80 mmol) and **24** for 16 h. Column chromatography (1:2 EtOAc–hexane) gave **43** (355 mg, 74%) as white crystals. R_f = 0.38 (6:4 EtOAc–hexane), mp: 210–214 °C, $[\alpha]_D$ = −134 (c 0.22, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.75 (1H, s, Ar), 8.68 (1H, s, Ar), 8.23 (1H, d, J = 1.6, 8.6 Hz, Ar), 7.96 (2H, m, Ar), 7.90 (1H, m, Ar), 7.58 (2H, m, Ar), 6.06 (1H, d, $J_{1',2'}$ = 7.9 Hz, H-1′), 5.53 (2H, m, 2 of H-2′ or H-3′ or H-4′), 5.35 (1H, t, J = 9.3 Hz, H-2′ or H-3′ or H-4′), 4.37 (1H, dd, $J_{5',6'a}$ = 5.3 Hz, $J_{6'a,6'b}$ = 13.2 Hz, H-6′a), 4.22 (1H, dd, $J_{6'a,6'b}$ = 13.2 Hz, $J_{5',6'b}$ = 1.9 Hz, H-6′b), 4.12 (1H, ddd, $J_{4',5'}$ = 9.3 Hz, $J_{5',6'a}$ = 5.3 Hz$_{5'6'b}$ = 1.9 Hz, H-5′), 2.11, 2.10, 2.05, 1.93 (12H, 4s, CH_3). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 170.4, 169.8, 169.3, 168.9 (CO), 164.9, 157.6 (oxadiazole), 137.8, 134.6, 132.7, 129.0, 128.8, 128.0, 127.9, 127.8, 127.1, 123.5, 123.2, 120.5 (Ar, triazole-C, triazole-CH), 86.0, 75.4, 72.3, 70.5, 67.5 (C-1′–C-5′), 61.4 (C-6′), 20.6, 20.5, 20.4, 20.1 (CH_3). Anal. Calcd for: $C_{28}H_{27}N_5O_{10}$ (593.18): C, 56.66; H, 4.59; N, 11.80; O, 26.96. Found: C, 56.61; H, 4.50; N, 11.74.

4.5.17. 2-(Naphthalen-2-yl)-5-[(1-β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (44)

Prepared by general procedure 4.2 from **43** (182 mg, 0.31 mmol) for 2 h. Filtration of the reaction mixture gave **44** (128 mg, 98%) as a white amorphous solid. R_f = 0.60 (7:3 $CHCl_3$–MeOH), $[\alpha]_D$ = −11 (c 0.20, Me$_2$SO); ^{1}H NMR (Me$_2$SO-d_6, 360 MHz) δ (ppm): 9.43 (1H, s, triazole-H), 8.76 (1H, s, Ar), 8.23 (3H, m, Ar), 8.10 (1H, m, Ar), 7.11 (2H, m, Ar), 5.78 (1H, d, $J_{1',2'}$ = 9.3 Hz, H-1′), 3.93 (1H, t, J = 9.3 Hz, H-2′ or H-3′ or H-4′), 3.79 (1H, dd, $J_{6'a,6'b}$ = 11.9, $J_{5',6'a}$ <1 Hz), 3.60–3.47 (3H, m, H-2′ or H-3′ or H-4′, H-5′, H-6′b), 3.35 (1H, t, J = 9.3 Hz, H-2′ or H-3′ or H-4′). ^{13}C NMR (Me$_2$SO-d_6, 90 MHz) δ (ppm): 163.9, 157.9 (oxadiazole), 134.2, 132.7, 132.4, 129.3, 128.9, 128.3, 127.9, 127.4, 127.1, 125.9, 122.8, 120.4 (Ar, triazole-C, triazole-CH), 87.9, 80.1, 76.6, 72.2, 69.4 (C-1′–C-5′), 60.7 (C-6′). Anal. Calcd for $C_{20}H_{19}N_5O_6$ (425.13): C, 56.47; H, 4.50; N, 16.46; O, 22.57. Found: C, 56.50; H, 4.54; N, 16.53.

4.5.18. 2-(β-D-Glucopyranosyl)-5-(1-phenyl-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (45)

Prepared by general procedure 4.2 from **29** (249 mg, 0.31 mmol) for 2 h. Column chromatography (9:1 $CHCl_3$–MeOH) gave **45** (100 mg, 85%) as white crystals. R_f = 0.39 (8:2 $CHCl_3$–MeOH), mp: 219–221 °C, $[\alpha]_D$ = +28 (c 0.22, Me$_2$SO); ^{1}H NMR (Me$_2$SO-d_6, 360 MHz) δ (ppm): 9.78 (1H, s, triazole-H), 8.05 (2H, d, J = 7.9 Hz, Ar), 7.66 (2H, pt, J = 7.9, 6.6 Hz, Ar), 7.57 (1H, pt, J = 6.6, 7.9 Hz, Ar), 5.45 (1H, d, J = 5.3 Hz, OH), 5.22 (1H, d, J = 4.0 Hz, OH), 5.14 (1H, d, J = 4.0 Hz, OH), 4.66 (1H, d, J = 5.3 Hz, OH), 4.61 (1H, d, $J_{1',2'}$ = 10.6 Hz, H-1′), 3.73–3.18 (6H, m, H-2′, H-3′, H-4′, H-5′, H-6′a, H-6′b). ^{13}C NMR (Me$_2$SO-d_6, 90 MHz) δ (ppm): 163.7, 158.1 (oxadiazole), 133.4 (triazole-C), 130.2, 129.9, 124.5 (Ar), 120.5 (triazole-CH), 81.8, 77.2, 72.6, 71.8, 69.8 (C-1′–C-6′), 60.9 (C-6′). Anal. Calcd for $C_{16}H_{17}N_5O_6$ (375.12): C, 51.20; H, 4.57; N, 18.66; O, 25.58. Found: C, 51.15; H, 4.53; N, 18.59.

4.5.19. 2-(β-D-Glucopyranosyl)-5-[1-(naphthalen-1-yl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (46)

Prepared by general procedure 4.2 from **30** (350 mg, 0.42 mmol) for 3 h. Column chromatography (9:1 $CHCl_3$–MeOH) gave **46** (161 mg, 91%) as a pale yellow amorphous solid. R_f = 0.35 (8:2 $CHCl_3$–MeOH), $[\alpha]_D$ = +19 (c 0.17, MeOH); ^{1}H NMR (CD_3OD, 360 MHz) δ (ppm): 9.12 (1H, s, triazole-H), 8.12 (1H, d, J = 8.0 Hz, Ar), 8.02 (1H, d, J = 7.8 Hz, Ar), 7.71–7.55 (5H, m, Ar), 4.72 (1H, d, $J_{1',2'}$ = 10.6 Hz, H-1′), 3.94–3.85 (2H, m, H-6′a, H-2′ or H-3′ or H-4′), 3.66–3.48 (4H, m, 2 of H-2′ or H-3′ or H-4′, H-5′, H-6′b). ^{13}C NMR (CD_3OD, 90 MHz) δ (ppm): 165.6, 160.2 (oxadiazole), 135.6, 134.5, 133.9, 132.3, 129.5, 129.3, 128.5, 126.4, 126.2, 125.2, 123.1, 122.7 (Ar, triazole-C, triazole-CH), 82.5, 79.1, 74.5, 73.4, 71.3 (C1′–C-5′), 62.7 (C-6′). Anal. Calcd for $C_{20}H_{19}N_5O_6$ (425.13): C, 56.47; H, 4.50; N, 16.46; O, 22.57. Found: C, 56.42; H, 4.48; N, 16.42.

4.5.20. 2-(β-D-Glucopyranosyl)-5-[1-(naphthalen-2-yl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (47)

Prepared by general procedure 4.2 from **31** (220 mg, 0.26 mmol) for 3 h. Column chromatography (9:1 $CHCl_3$–MeOH) gave **47** (88 mg, 79%) as a greenish amorphous solid. R_f = 0.32 (8:2 $CHCl_3$–MeOH), $[\alpha]_D$ = +8 (c 0.14, Me$_2$SO); ^{1}H NMR (Me$_2$SO-d_6, 360 MHz) δ (ppm): 9.90 (1H, s, triazole-H), 8.68 (1H, s, Ar), 8.22 (2H, m, Ar) 8.09 (2H, t, J = 7.9 Hz, Ar), 7.66 (2H, m, Ar), 5.51 (1H, d, J = 6.6 Hz, OH), 5.29 (1H, d, J = 4.0 Hz, OH), 5.20 (1H, d, J = 5.3 Hz, OH), 4.70 (1H, t, J = 5.3 Hz, OH), 4.65 (1H, d, $J_{1',2'}$ = 10.6 Hz, H-1′), 3.79–3.66 (2H, m, H-6′a, H-6′b), 3.54–3.26 (4H, m, H-2′, H-3′, H-4′, H-5′). ^{13}C NMR (Me$_2$SO-d_6, 90 MHz) δ (ppm): 163.8, 158.1 (oxadiazole), 133.5, 133.3, 132.7, 132.6, 129.9, 128.3, 127.8, 127.6, 127.3, 124.6, 118.6, 118.5 (Ar, triazole-C, triazole-CH), 81.8, 77.3, 72.6, 71.8, 69.9 (C-1′–C-5′), 60.9 (C-6′). Anal. Calcd for $C_{20}H_{19}N_5O_6$ (425.13): C, 56.47; H, 4.50; N, 16.46; O, 22.57. Found: C, 56.43; H, 4.50; N, 16.47.

4.5.21. 2-(β-D-Glucopyranosyl)-5-[1-(β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (48)

Prepared by general procedure 4.2 from **32** (240 mg, 0.23 mmol) for 16 h. Column chromatography (6:4 $CHCl_3$–MeOH) gave **48** (98 mg, 93%) as a colourless oil. R_f = 0.31 (4:6 $CHCl_3$–MeOH), $[\alpha]_D$ = +24 (c 0.20, MeOH); ^{1}H NMR (CD_3OD, 360 MHz) δ (ppm): 9.04 (1H, s, triazole-H), 5.78 (1H, d, $J_{1',2'}$ = 7.9 Hz, H-1′), 4.70 (1H, d, J = 9.3 Hz, H-1″), 4.01–3.47 (12H, m, H-2′, H-3′, H-4′, H-5′, H-6′a, H-6′b, H-2″, H-3″, H-4″, H-5″, H-6″a, H-6″b). ^{13}C NMR (CD_3OD, 90 MHz) δ (ppm): 165.5, 160.2 (oxadiazole), 134.3 (triazole-C), 126.9 (triazole-CH), 89.8, 81.2, 78.7, 78.2, 74.4, 74.1, 73.4, 71.2, 70.7 (C-1′–C-5′, C-1″-C-5″), 62.7, 62.3 (C-6′, C-6″). Anal. Calcd for $C_{16}H_{23}N_5O_{11}$ (461.14): C, 41.56; H, 5.02; N, 15.18; O, 38.14. Found: C, 41.64; H, 5.01; N, 15.18.

4.5.22. 2-(2″,3″,4″,6″-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-5-(4′-phenyl-1′,2′,3′-triazole-1′-ylmethyl)-1,3,4-oxadiazole (49)

Oxadiazole **26** (100 mg, 0.14 mmol) was dissolved in CH_2Cl_2 (2 mL) and water (2 mL), phenylacetylene (14 μL, 0.14 mmol), copper triflate (2 mg, 5.2×10^{-3} mmol) and copper dust (0.3 mg, 4.7×10^{-3} mmol) was added. The reaction mixture was heated at 40 °C. After 24 h TLC (1:1 EtOAc–hexane) indicated completion of the transformation. The reaction mixture was diluted with CH_2Cl_2 (20 mL), the phases were separated, and the organic phase was washed with cold satd $NaHCO_3$ solution (3×10 mL), water (10 mL), dried, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (1:1 EtOAc–hexane) to give **49** (56 mg, 70%, conversion 70%) as a colourless syrup. R_f = 0.35 (1:1 EtOAc–hexane); $[\alpha]_D$ = −50.4 (c 0.22, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.05 (1H, s, triazole-CH), 8.02–7.72 (10H, m, Ar), 7.56–7.23 (15H, m, Ar), 6.06 (1H, pt,

J = 9.6 Hz, H-2″ or H-3″ or H-4″), 5.89 (2H, bs, CH_2), 5.82 (1H, pt, J = 9.9 Hz, H-2″ or H-3″ or H-4″), 5.74 (1H, pt, J = 10.0, 9.8 Hz, H-2″ or H-3″ or H-4″), 5.71 (1H, d, $J_{1″,2″}$ = 10.1 Hz, H-1″), 4.65 (1H, dd, $J_{6″a,6″b}$ = 12.5 Hz, $J_{5″,6″a}$ = 1.7 Hz, H-6″a), 4.50 (1H, dd, $J_{5″,6″b}$ = 5.3 Hz, H-6″b), 4.36–4.31 (1H, m, H-5″). ^{13}C NMR ($CDCl_3$, 360 MHz) δ (ppm): 166.0, 165.6, 165.1, 165.0 (CO), 162.9, 161.6 (oxadiazole), 148.7 (triazole-C), 133.7–125.8 (Ar), 120.1 (triazole-CH), 77.2, 73.0, 71.8, 70.7, 68.7 (C-2″-C-5″), 62.8 (C-6″), 44.1 (CH_2). Anal. Calcd for $C_{45}H_{35}N_5O_{10}$ (805.79): C, 67.07; H, 4.38; N, 8.69. Found: C, 66.92; H, 4.27; N, 9.36.

4.5.23. 2-(2″,3″,4″,6″-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-5-(4′-ethoxycarbonyl-1′,2′,3′-triazole-1′-ylmethyl)-1,3,4-oxadiazole (50)

Prepared by general procedure 4.5.1 from **26** (150 mg, 0.21 mmol). Column chromatography (1:1 EtOAc–hexane) gave **50** (107 mg, 82%, conversion 77%) as a colourless syrup. R_f = 0.22 (1:1 EtOAc–hexane); $[\alpha]_D$ = +57.1 (c 0.21, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.42 (1H, s, triazole-CH), 8.03–7.78 (8H, m, Ar), 7.58–7.25 (12H, m, Ar), 6.11 (1H, pt, J = 10.0, 9.5 Hz, H-2″ or H-3″ or H-4″), 5.91 (2H, br s, CH_2), 5.82 (1H, pt, J = 9.8, 9.5 Hz, H-2″ or H-3″ or H-4″), 5.68 (1H, pt, J = 10.0, 9.9 Hz, H-2″ or H-3″ or H-4″), 5.20 (1H, d, $J_{1″,2″}$ = 9.9 Hz, H-1″), 4.67 (1H, dd, $J_{5″,6″a}$ = 2.6 Hz, H-6″a), 4.51 (1H, dd, $J_{6″a,6″b}$ = 12.5, $J_{5″,6″b}$ = 5.2 Hz, H-6″b), 4.44–4.33 (3H, m, H-5'', CH_2CH$_3$), 1.40 (3H, t, J = 7.2 Hz, CH$_2$CH_3). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 166.0, 165.6, 165.1, 165.0 (CO), 162.9, 161.0, 160.2 (oxadiazole, *C*OOEt), 141.0 (triazole-C), 133.8–127.7 (Ar, triazole CH), 77.1, 72.9, 71.7, 70.7, 68.7 (C-1″-C-5″), 62.8, 61.3 (CH_2, C-6″), 44.2 (CH_2), 14.2 (CH_3). Anal. Calcd for $C_{42}H_{35}N_5O_{12}$ (801.75): C, 62.92; H, 4.40; N, 8.74. Found: C, 63.05; H, 4.56; N, 8.86.

4.5.24. 2-(2″,3″,4″,6″-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-5-(4′-hydroxymethyl-1′,2′,3′-triazole-1′-ylmethyl)-1,3,4-oxadiazole (51)

Prepared by general procedure 4.5.1 from **26** (224 mg, 0.32 mmol). Column chromatography (1:1 EtOAc–hexane) gave **51** (198 mg, 85%, conversion 96%) as a colourless syrup. R_f = 0.14 (1:1 EtOAc–hexane); $[\alpha]_D$ = −69 (c 0.20, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 8.03–7.79 (9H, m, Ar, triazole CH), 7.77–7.25 (12H, m, Ar), 6.09 (1H, pt, J = 10.4, 9.2 Hz, H-2″ or H-3″ or H-4″), 5.85–5.79 (3H, m, H-2″ or H-3″ or H-4″, CH_2), 5.73 (1H, pt, J = 10.8, 9.1 Hz, H-2″ or H-3″ or H-4″), 5.19 (1H, d, $J_{1″,2″}$ = 10.7 Hz, H-1″), 4.79 (2H, br s, CH_2) 4.66 (1H, dd, $J_{5″,6″a}$ = 1.0 Hz, H-6″a), 4.50 (1H, dd, $J_{5″,6″b}$ = 5.6 Hz, $J_{6″a,6″b}$ = 12.5 Hz, H-6″b), 4.37–4.33 (1H, m, H-5″), 4.06 (1H, s, OH); ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 166.1, 165.6, 165.1, 165.0 (CO), 162.8, 161.5 (oxadiazole), 148.6 (triazole-C), 133.8–127.8 (Ar), 122.6 (triazole-CH), 77.1, 73.1, 71.6, 70.6, 68.7 (C-1″–C-5″), 69.3 (CH_2OH), 62.8 (C-6″), 44.1 (CH_2). Anal. Calcd for $C_{40}H_{33}O_{10}N_5$ (759.72): C, 63.24; H, 4.38; N, 9.22. Found: C, 63.36; H, 4.49; N, 9.15.

4.5.25. 2-Phenyl-5-[(4-phenyl-*1H*-1,2,3-triazol-1-yl)methyl]-1,3,4-oxadiazole (52)

Prepared by general procedure 4.5.3 from **28** (250 mg, 1.24 mmol) and phenylacetylene (152 mg, 1.48 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (3 mg, 0.012 mmol), Na-L-ascorbate (10 mg, 0.05 mmol), and TMEDA (15 μL, 0.11 mmol) in 6 mL solvent mixture at rt for 2 h to give **52** (256 mg, 68%) as white crystals. Mp: 180–181 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 5.93 (2H, s, CH_2), 7.26–7.55 (6H, m, H-3″–H-5″, H-3‴–H-5‴), 7.83 (2H, d, J = 6.9 Hz, H-2‴, H-6‴), 7.99–8.03 (3H, m, H-5′, H-2″, H-6″). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 42.3 (CH_2), 118.0 (C-4‴), 121.0 (C-1‴), 123.9 (C-2‴, C-6‴), 125.2 (C-2″, C-6″), 125.9 (C-5′), 126.6 (C-4″), 127.0 (C-3‴, C-5‴), 127.2 (C-3″, C-5″), 127.9 (C-1″), 134.4 (C-4′), 146.9 (C-2), 158.2 (C-5). Anal. Calcd for $C_{17}H_{13}N_5O$ (303.11): C, 67.32; H, 4.32; N, 23.09. Found: C, 67.39; H, 4.40; N, 23.11.

4.5.26. Ethyl 1-[(5-phenyl-1,3,4-oxadiazol-2-yl)methyl]-*1H*-1,2,3-triazole-4-carboxylate (53)

Prepared by general procedure 4.5.3 from **28** (500 mg, 2.48 mmol) ethyl propiolate (293 mg, 2.96 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (25 mg, 0.01 mmol), Na-L-ascorbate (79 mg, 0.40 mmol) in 12 mL solvent mixture at rt for 75 h to give **52** (567 mg, 76%) as white crystals. Mp: 116–117 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 1.39 (3H, t, J = 6.9 Hz, CH$_2$–CH_3), 4.42 (2H, q, J = 7,0 Hz, CH_2–CH$_3$), 5.13 (2H, s, CH_2), 7.48–7.57 (3H, m, H-3″, H-4″, H-5″), 8.02 (2H, d, J = 8.0 Hz, H-2″, H-6″), 8.40 (1H, s, H-5′). ^{13}C NMR ($CDCl_3$, 360 MHz) δ (ppm): 12.3 (CH$_2$–*C*H$_3$), 42.6 (CH_2), 59.6 (*C*H$_2$–CH$_3$), 120.8 (C-1″), 125.2 (C-2″, C-6″) 126.1 (C-5′), 127.3 (C-3″, C-5″), 130.6 (C-4″), 139.2 (C-4′), 157.6 (C-2), 158.2 (C-5), 164.4 (C=O). Anal. Calcd for $C_{14}H_{13}N_5O_3$ (299.10): C, 56.18; H, 4.38; N, 23.40. Found: C, 56.21; H, 4.39; N, 23.45.

4.5.27. {1-[(5-Phenyl-1,3,4-oxadiazol-2-yl)methyl]-*1H*-1,2,3-triazol-4-yl}methanol (54)

Prepared by general procedure 4.5.3 from **28** (201 mg, 1.00 mmol) prop-2-yn-1-ol (67 mg, 1.2 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (10 mg, 0.04 mmol), Na-L-ascorbate (21 mg, 0.16 mmol), and TMEDA (15 μL, 0.11 mmol) in 9 mL solvent mixture at rt for 3 h to give **54** (41 mg, 55%) as white crystals. Mp: 196–197 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 4.56 (2H, d, J = 5.3 Hz, CH_2–OH), 5.27 (1H, t, J = 5.8 Hz, OH), 6.1 (2H, s, CH_2), 7.60–7.63 (3H, m, H-3″–H-5″), 7.97 (2H, d, J = 6.8 Hz, H-2″, H-6″), 8.22 (1H, s, H-5′). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 42.2 (*C*H$_2$–OH), 53.5 (CH_2), 121.4 (C-1″), 122.3 (C-5′), 125.1 (C-2″, C-6″), 128.0 (C-3″, C-5″), 130.8 (C-4″), 147.1 (C-4′), 160.1 (C-5), 163.3 (C-2). Anal. Calcd for $C_{12}H_{11}N_5O_2$ (257.09): C, 56.03; H, 4.31; N, 27.22. Found: C, 56.011; H, 4.38; N, 27.29.

4.5.28. 2-{1-[(5-Phenyl-1,3,4-oxadiazol-2-yl)methyl]-*1H*-1,2,3-triazol-4-yl}propan-2-ol (55)

Prepared by general procedure 4.5.3 from **28** (250 mg, 1.24 mmol) 2-methylbut-3-yn-2-ol (125 mg, 1.49 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (12 mg, 0.049 mmol), Na-L-ascorbate (40 mg, 0.20 mmol) in 9 mL solvent mixture at rt for 1.5 h to give **55** (306 mg, 86%) as white crystals. Mp: 164–166 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 1.45 (6H, s, 6H, CH_3), 5.18 (1H, s, OH), 6.05 (2H, s, CH_2), 7.57–7.59 (3H, m, H-3″–H-5″), 7.94 (2H, d, J = 6.9 Hz, H-2″, H-6″), 8.08 (1H, s, H-5′). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): 29.1 (–C(CH$_3$)$_2$OH), 42.1 (CH_2), 65.6 (–*C*(CH$_3$)$_2$OH), 120.1 (C-5′), 121.4 (C-1″), 125.1 (C-2″, C-6″), 128.0 (C-3″, C-5″), 130.8 (C-4″), 154.9 (C-4′), 160.1 (C-5), 163.3 (C-2). Anal. Calcd for $C_{14}H_{15}N_5O_2$ (285.12): C, 58.94; H, 5.30; N, 24.55. Found: C, 59.01; H, 5.38; N, 24.59.

4.5.29. 2-Phenyl-5-[(4-trimethylsilyl-*1H*-1,2,3-triazol-1-yl)methyl]-1,3,4-oxadiazole (56)

Prepared by general procedure 4.5.3 from **28** (750 mg, 3.72 mmol) ethynyltrimethylsilane (439 mg, 4.47 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (37 mg, 0.15 mmol), Na-L-ascorbate (120 mg, 0.60 mmol) in 27 mL solvent mixture at rt for 60 h to give **56** (1.090 g, 98%) as white crystals. Mp: 113–117 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ (ppm): 0.32 (9H, s, CH_3), 5.92 (2H, s, CH_2), 7.49–7.55 (3H, m, H-3″, H-4″, H-5″), 7.77 (1H, s, H-5′), 8.02 (2H, d, J = 6.9 Hz, H-2″, H-6″). ^{13}C NMR ($CDCl_3$, 90 MHz) δ (ppm): -3.1 (CH_3), 41.5 (CH_2), 121.0 (C-1″), 125.2 (C-2″,C-6″), 127.2 (C-3″, C-5″), 127.4 (C-5′), 130.4 (C-4″), 146.0 (C-4′), 158.4 (C-5), 164.2 (C-2). Anal. Calcd for $C_{14}H_{17}N_5OSi$ (299.12): C, 56.16; H, 5.72; N, 23.39. Found: C, 56.04; H, 5.61; N, 23.29.

4.5.30. 5-Phenyl-2-[(*1H*-1,2,3-triazol-1-yl)methyl]-1,3,4-oxadiazole (57)

Compound **56** (226 mg, 0.75 mmol) was dissolved in dry THF (7 mL) and a solution of TBAF (80 mg, 0.25 mmol) in THF (0.25 mL) was added. The mixture was stirred at 50 °C (bath temp) for 1 h, and then TBAF (80 mg, 0.25 mmol) in THF (0.25 mL) was added again. After 4 h TLC (2:1 $PhCH_3$–EtOAc) had indicated completion of the transformation, the solvent was evaporated and the residue was purified by flash chromatography (1:1 $PhCH_3$–EtOAc) to give **57** (71 mg, 35%) as white crystals. Mp: 146–147 °C; ^{1}H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 5.92 (2H, s, CH_2), 7.48–7.56 (5H, m, H-2″–H-6″), 7.81 (1H, d, J = 6.5 Hz, H-5′), 8.01 (1H, d, J = 6.7, H-4′). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 43.5 CH_2), 120.0 (C-4′), 122.8 (C-1"), 125.7–129.1 (C-2″–C-6″), 133.8 (C-5′), 161.4 (C-2), 164.7 (C-5). Anal. Calcd for $C_{11}H_9N_5O$ (227.08): C, 58.14; H, 3.99; N, 30.82. Found: C, 58.22; H, 4.05; N, 30.90.

4.5.31. 3-(1-((5-Phenyl-1,3,4-oxadiazol-2-yl)methyl)-*1H*-1,2,3-triazol-4-yl)benzenamine (58)

Prepared by general procedure 4.5.3 from **28** (250 mg, 1.24 mmol) 3-ethynylbenzenamine (174 mg, 1.49 mmol) in the presence of $CuSO_4{\cdot}5H_2O$ (12.4 mg, 0.05 mmol), Na-L-ascorbate (40 mg, 0.20 mmol), and TMEDA (15 μL, 0.11 mmol) in 10 mL solvent mixture at rt for 28 h to give **58** (247 mg, 62%) as brown crystals. Mp: 175–177 °C; ^{1}H NMR (Me_2SO-d_6, 360 MHz) δ (ppm): 5.20 (2H, vbr s, NH_2), 6.17 (2H, s, CH_2), 6.57 (1H, d, J = 4.7 Hz, H-6), 7.00–7.16 (3H, m, H-2, H-4, H-5), 7.61–7.63 (3H, m, H-3‴, H-4‴, H-5‴), 7.99–8.01 (2H, d, J = 5.4 Hz H-2‴, H-6‴), 8.65 (1H, s, H-5′). ^{13}C NMR (Me_2SO-d_6, 90 MHz) δ (ppm): 43.9 (CH_2), 110.5 (C-2), 113.1 (C-4), 113.8 (C-6), 121.9 (C-5), 122.8 (C-1″), 126.6 (C-2″, C-6″), 129.3 (C-5′), 129.4 (C-3″, C-5″), 130.6 (C-1), 132.2 (C-4″), 147.4 (C-4′), 148.9 (C-3), 161.4 (C-5″), 164.8 (C-2″). Anal. Calcd for $C_{17}H_{14}N_6O$ (318.12): C, 64.14; H, 4.43; N, 26.40. Found: C, 64.25; H, 4.51; N, 26.48.

4.5.32. 2-(β-D-Glucopyranosyl)-5-(4′-phenyl-1′,2′,3′-triazole-1′-ylmethyl)-1,3,4-oxadiazole (59)

Prepared by general procedure 4.2 from **49** (131 mg, 0.16 mmol). Column chromatography (2:1 $CHCl_3$–MeOH) gave **59** (40 mg, 63%) as a colourless syrup. R_f = 0.58 (2:1 $CHCl_3$–MeOH); $[\alpha]_D$ = +37 (c 0.19, MeOH); ^{1}H NMR (CD_3OD, 360 MHz) δ (ppm): 8.35 (1H, s, triazole), 7.84–7.82 (5H, m, Ph), 3.83 (1H, d, $J_{1″,2″}$ = 10.4 Hz, H-1″), 3.63 (1H, dd, $J_{6″a,6″b}$ = 11.8 Hz, $J_{5″,6″a}$ = 1.4 Hz, H-6″a), 3.62 (1H, pt, J = 9.7, 8.7 Hz, H-2″ or H-3″ or H-4″), 3.55 (1H, dd, $J_{5″,6″a}$ = 5.4 Hz H-6″b), 3.48 (1H, pt, J = 9.3, 7.9 Hz, H-2″ or H-3″ or H-4″), 3.52–3.38 (2H, m, H-2″ or H-3″ or H-4″ and H-5″), 3.36 (2H, s, CH_2). ^{13}C NMR (CD_3OD, 90 MHz) δ (ppm): 180.0, 175.4 (oxadiazole), 152.6 (triazole-C), 127.9 (triazole-CH) 133.2–127.5 (Ph), 82.3 (C-1″), 80.4, 79.1, 73.4, 71.3 (C-2″-C-5″), 62.7 (C-6″), 52.8 (CH_2). Anal. Calcd for $C_{17}H_{19}N_5O_6$ (389.36): C, 52.44; H, 4.92; N, 17.99. Found: C, 52.37; H, 4.81; N, 17.87.

4.5.33. 2-(β-D-Glucopyranosyl)-5-(4′-methoxycarbonyl-1′,2′,3′-triazole-1′-ylmethyl)-1,3,4 oxadiazole (60)

Prepared by general procedure 4.2 from **50** (150 mg, 0.19 mmol). Column chromatography (9:1 $CHCl_3$–MeOH) gave **60** (68 mg, 96%) as a colourless syrup. R_f = 0.08 (9:1 $CHCl_3$–MeOH); $[\alpha]_D$ = +29 (c 0.21, MeOH); ^{1}H NMR (CD_3OD, 360 MHz) δ (ppm): 8.49 (1H, s, triazole), 3.86 (1H, d, $J_{1″,2″}$ = 10.5 Hz, H-1″), 3.82 (1H, dd, $J_{6a″,6″b}$ = 11.6 Hz, $J_{5″,6″a}$ = 1.3 Hz, H-6″a), 3.52 (1H, pt, J = 9.5, 8.5 Hz, H-2″ or H-3″ or H-4″), 3.38 (s, 2H, CH_2), 3.48 (1H, dd, $J_{5″,6″b}$ = 5.2 Hz, H-6″b), 3.33 (1H, pt, 8.2, 7.9 Hz, H-2″ or H-3″ or H-4″), 3.20–3.03 (2H, m, H-2″ or H-3″ or H-4″ and H-5″), 3.01 (3H, s, CH_3). ^{13}C NMR (CD_3OD, 90 MHz) δ (ppm): 176.9, 173.8 (oxadiazole), 167.9 (CO), 150.6 (triazole-C), 125.4 (triazole-CH), 81.7 (C-1″), 79.6, 75.1, 74.6, 72.3 (C-2″-C-5″), 62.2 (C-6″), 51.2 (CH_2), 42.7 (CH_3). Anal. Calcd for $C_{13}H_{17}$ N_5O_8 (371.30): C, 42.05; H, 4.61; N, 18.86. Found: C, 42.17; H, 4.75; N, 18.92.

4.5.34. 2-(β-D-Glucopyranosyl)-5-(4′-carboxyamido-1′,2′,3′-triazole-1′-ylmethyl)-1,3,4-oxadiazole (61)

Oxadiazole **50** (105 mg, 0.13 mmol) was dissolved in methanolic ammonia solution (5 mL). After 48 h TLC (1:1 $CHCl_3$–MeOH) indicated completion of the transformation. The solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (2:1 $CHCl_3$–MeOH) to give **61** (22 mg, 47%) as a colourless syrup. $[\alpha]_D$ = +30.6 (c 0.20, MeOH); R_f = 0.21 (1:1 $CHCl_3$–MeOH); ^{1}H NMR (CD_3OD, 360 MHz) δ (ppm): 8.51 (1H, s, triazole), 7.85 (2H, s, NH_2), 3.80 (1H, d, $J_{1″,2″}$ = 10.5 Hz, H-1″), 3.85 (1H, dd, $J_{6″a,6″b}$ = 11.9 Hz, $J_{5″,6″a}$ = 1.3 Hz, H-6″a), 3.78 (1H, pt, J = 9.5, 8.7 Hz, H-2″ or H-3″ or H-4″), 3.69 (1H, dd, $J_{5″,6″b}$ = 5.2 Hz, H-6″b), 3.51 (1H, pt, J = 9.2, 7.9 Hz, H-2″ or H-3″ or H-4″), 3.43–3.33 (2H, m, H-2″ or H-3″ or H-4″ and H-5″), 3.25 (2H, s, CH_2). ^{13}C NMR (CD_3OD, 90 MHz) δ (ppm): 177.6, 174.7 (oxadiazole), 172.0 (CO), 151.8 (triazole-C), 128.5 (triazole-CH), 82.0 (C-1″), 79.4, 79.2, 73.5, 70.9 (C-2″–C-5″), 62.2 (C-6″), 43.0 (CH_2). Anal. Calcd for $C_{12}H_{16}N_6O_7$ (356.29): C, 40.45; H, 4.53; N, 23.59. Found: C, 40.39; H, 4.62; N, 23.69.

4.5.35. 2-(β-D-Glucopyranosyl)-5-(4′-hydroxymethyl-1′,2′,3′-triazol-1′-ylmethyl)-1,3,4-oxadiazole (62)

Prepared by general procedure 4.2 from **51** (150 mg, 0.20 mmol). Column chromatography (1:1 $CHCl_3$–MeOH) gave **62** (20 mg, 30%) as a colourless syrup. R_f = 0.58 (2:3 $CHCl_3$–MeOH); $[\alpha]_D$ = +28 (c 0.18, MeOH); ^{1}H NMR (CD_3OD, 360 MHz) δ (ppm): 4.70–4.66 (2H, m, CH_2), 4.53 (1H, d, $J_{1″,2″}$ = 10.6 Hz, H-1″), 3.86 (1H, dd, $J_{6″a,6″b}$ = 11.9 Hz, $J_{5″,6″a}$ = 1.2 Hz, H-6″a), 3.76–3.36 (5H, m, H-2″, H-3″, H-4″, H-5″, H-6″b). ^{13}C NMR (CD_3OD, 90 MHz) δ (ppm): 166.6, 165.4 (oxadiazole), 149.9 (triazole-C), 120.5 (triazole-CH), 82.9, 79.1, 74.5, 73.4, 71.3 (C-1″-C-5″), 62.8 (C-6″), 45.1 (CH_2OH), 33.6 (CH_2). Anal. Calcd for $C_{12}H_{17}N_5O_7$ (343.29): C, 41.98; H, 4.99; N, 20.40. Found: C, 42.08; H, 5.11; N, 20.49.

4.5.36. 2-(β-D-Glucopyranosyl)-5-azidomethyl-1,3,4-oxadiazole (63)

Prepared by general procedure 4.2 from **26** (150 mg, 0.21 mmol) for 2 h. Column chromatography (3:1 $CHCl_3$–MeOH) gave **63** (50 mg, 82%) as a colourless syrup. R_f = 0.48 (7:3 $CHCl_3$–MeOH); $[\alpha]_D$ = +26.6 (c 0.20, MeOH); ^{1}H NMR (CD_3OD, 360 MHz) δ (ppm): 4.70 (2H, s, CH_2), 4.57 (1H, d, $J_{1′,2′}$ = 10.6, Hz, H-1′), 3.87 (1H, dd, $J_{6′a,6′b}$ = 11.9 Hz, $J_{5′,6′a}$ = 1.2 Hz, H-6′a), 3.73 (1H, pst, J = 9.4 Hz, H-2′ or H-3′ or H-4′), 3.67 (1H, dd, $J_{6′a,6′b}$ = 11.9, $J_{5,6′b}$ = 5.4 Hz, H-6′b), 3.51–3.37 (3H, m, H-2′ and/or H-3′ and/or H-4′, H-5′). ^{13}C NMR (CD_3OD, 90 MHz) δ (ppm): 166.8, 163.6 (oxadiazole), 149.8 (triazole C), 125.1 (triazole CH), 82.9, 79.0, 74.5, 73.4, 71.2 (C-1′–C-5′), 73.2 (CH_2–N_3), 62.7 (C-6′), 56.5 (CH_2). Anal. Calcd for $C_9H_{13}O_6N_5$ (287.23): C, 37.63; H, 4.56; N, 24.38. Found: C, 38.11; H, 4.74; N, 24.65.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2011.03.004.

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