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Graphical Abstract:

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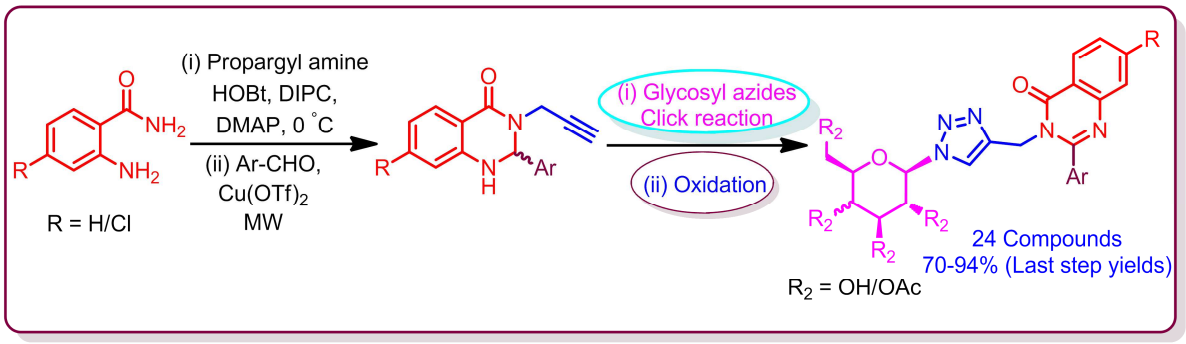

Synthesis of novel glycosyl-1,2,3-1*H*-triazolyl methyl quinazolin-4(3*H*)-ones and their effect on GLUT4 translocation

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Abstract:

$Cu(OTf)_2$ catalyzed synthesis of propargylated 2,3-dihydroquinazolin-4(1*H*)-ones has been accomplished from 2-amino-*N*-propargyl benzamides and aromatic aldehydes under MW irradiation. Next, a series of novel glycosyl triazolyl methyl quinazolin-4(3*H*)-ones have been synthesized by CuAAC reaction of propargylated 2,3-dihydroquinazolin-4(1*H*)-ones with glycosyl azides followed by iodine mediated oxidation. In this series, six compounds showed promising to significant GLUT4 translocation activity comparable to rosiglitazone.

Keywords: Copper(II) triflate, 2,3-Dihydroquinazolin-4(1*H*)-ones, Glycosyl quinazolin-4(3*H*)-ones, GLUT4 translocation activity

1. Introduction

Quinazolinones, a class of nitrogen heterocycle are assigned as privileged structures in drug discovery due to their important roles as key building blocks in the synthesis of a many drugs.[1] This class is associated with diverse range of pharmacological activities such as antihypertensive,[2] antibacterial,[3] anti-inflammatory,[4] anticancer,[5] analgesic,[6] antituberculosis,[7] antidefibrillatory,[8] antihistamine,[9] diuretic,[10] CNS stimulant,[11] tranquilizer,[12] vasodilating agent,[13] antianxietic,[14] and antidepressant[15] activities. The quinazolinone ring is also a ubiquitous pharmacophore in many biologically active natural products like Rutaecarpine (**1**),[16] Bouchardatine (**2**),[17] Luotonine A (**3**),[18] Febrifugine (**4**),[19] Methaqualone (**5**)[19] and 2-(4-Hydroxybutyl)-4(3*H*)-quinazolinone (**6**)[20] as shown in Figure 1. Balaglitazone (**7**),[21] a quinazolinone analogue of thiazolidinedione has excellent antidiabetic and hypolipidemic properties with less adipogenic activity (Figure 1).

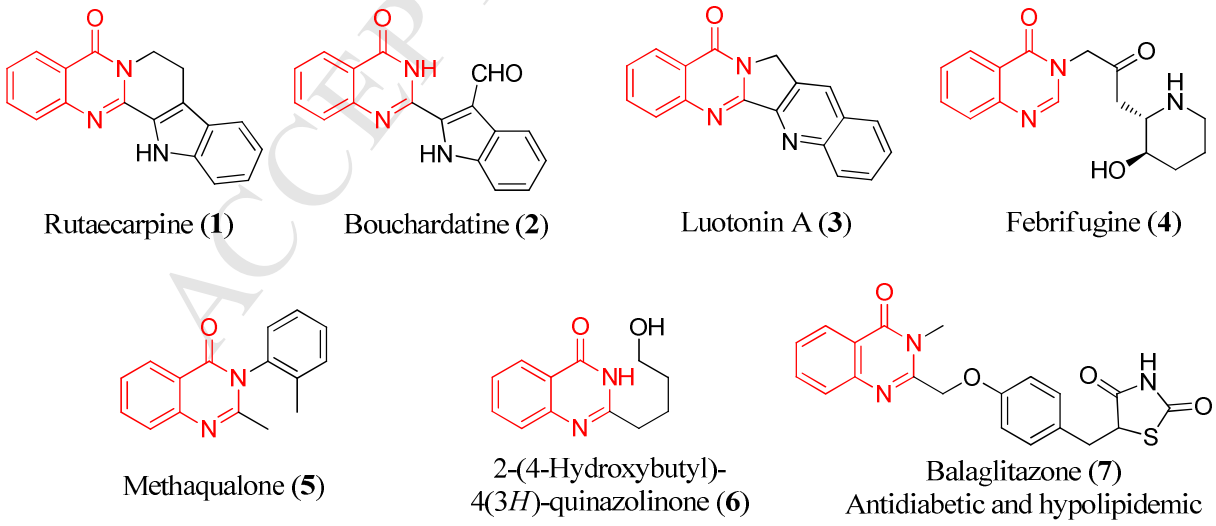


Figure 1. Natural and synthetic examples of bioactive quinazolinones

1,2,3-Triazoles are also important scaffold in drug discovery and development as several molecules with this moiety exhibited important biological activities such as antitubercular,[22] anticancer,[23] anti-HIV,[24] antibacterial,[25] antiviral,[26] antialzheimer,[27] antimycobacterial[28] and glycosidase inhibitors.[29]

Most of the biologically active compounds incorporating glycosyl motifs coupled with heterocycles exhibit potent biological activities.[30] Glycosylation of biomolecules offers better pharmacokinetic parameters to the bioactive molecules, and also helps in creating molecular diversity.[31] Skeletal muscle is the major depot for postprandial glucose utilization and disposal. Insulin stimulates glucose uptake in skeletal muscle is characterized by enhancing translocation and redistribution of insulin sensitive glucose transporter-4 (GLUT-4) from the intracellular compartment to the plasma membrane.[32] Under diabetic condition insulin stimulated translocation of GLUT4 gets impaired, leading to decreased uptake of glucose inside the tissue.[33] Thus interventions with ability to enhance the rate of GLUT4 translocation might be useful for the treatment of diabetes. Quinazolinones have been reported to possess GLUT4 translocation enhancing activity.[34]

Keeping in mind the above facts we were prompted to synthesize a new series of hybrid molecules, consisting of quinazolinones, triazole and sugars and investigate their GLUT4 translocation enhancing activity in a quest for new antidiabetic agents (Figure 2).

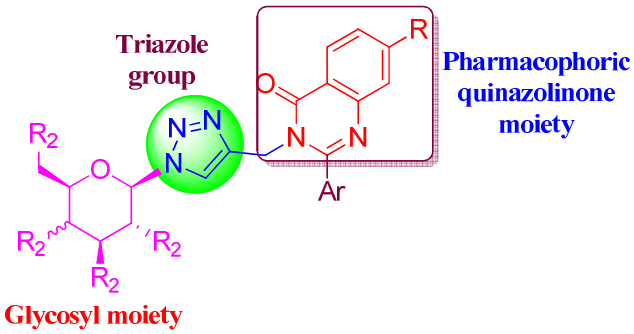


Figure 2. Designing the structure for novel glycosyl quinazolinones

Due to medicinal importance of quinazolinone scaffolds various synthetic methods have been explored.[35] 2,3-Dihydroquinazolin-4(1*H*)-ones have been accessed by reaction of 2-aminobenzamides and aldehydes under the influence of different catalysts such as chiral phosphoric acid,[36] Sc(III)-inda-pybox,[37] $TiCl_4$/Zn,[38] cyanuric chloride,[39] ionic liquid/water,[40] gallium(III) triflate,[41] AcOH,[42] iodine,[43] silica sulfuric acid,[44] montmorillonite K-10,[45] [Zn-$(PFO)_2$],[46] $KAl(SO_4)_2 \cdot 12H_2O$,[47] MCM-41-SO_3H,[48] $Al(H_2PO_4)_3$,[49] [bmim]BF_4,[50] sulfamic acid,[51] β-cyclodextrin,[52] cellulose-SO_3H,[53] ammonium chloride,[54] Cu-CNTs,[55] *p*-TsOH,[56] tartaric acid-SDS,[57] and CuO nanoparticles.[58] Few of the reported methods suffer from drawbacks such as low yields, long reaction time, strongly acidic conditions and use of expensive reagents.

2,3-Dihydroquinazolin-4(1*H*)-ones derivatives have been synthesized from 2-aminobenzamides or 3,1-Benzoxazine-2,4(1*H*)-diones (isatoic anhydrides), in the presence of Cu salt as catalyst. Only one example of a three-component reaction of isatoic anhydrides with amines and ketones in the presence of $Cu(OTf)_2$ is known till date.[59] Herein, we describe a novel and simple method to access a diverse range of 2,3-dihydroquinazolin-4(1*H*)-ones via one-pot two-component

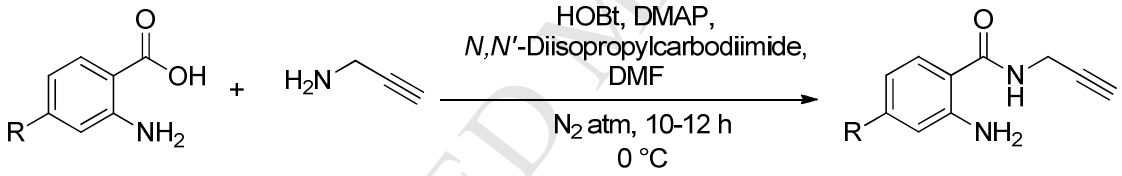
condensation of substituted 2-aminobenzamides with various aldehydes in the presence of $Cu(OTf)_2$ under microwave irradiation.

2. Results and discussion

2.1.Chemistry

2.1.1. Synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones

2-Amino-*N*-propargyl benzamides (**9a** and **9b**) were prepared from commercially available anthranilic acid (**8a**) and 2-amino-4-chloro-benzoic acid (**8b**) following earlier reported protocols[60] as shown in Scheme 1. The structures were established on the basis of their spectroscopic data.[61]



8a, **8b**
8a; R = H
8b; R = Cl

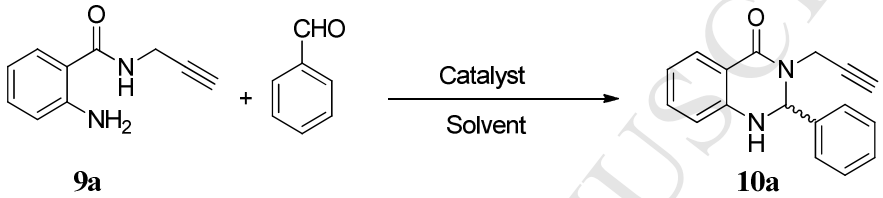
9a, **9b**
9a; R = H, 89%
9b; R = Cl, 88%

Scheme 1. Synthesis of 2-amino-*N*-propargyl benzamide derivatives

To optimize reaction condition for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones initially we carried out the reaction of 2-amino-*N*-propargyl benzamide (**9a**) with benzaldehyde as model substrate to get 2-phenyl-3-propargyl-2,3-dihydroquinazolin-4(1*H*)-one (**10a**) under the influence of various reaction conditions and the results are summarized in Table 1. Using of 20 mol% of $CuCl_2$ in refluxing ethanol and 20 mol% $InCl_3$ in acetonitrile at room temperature offered 62% and 65% yields of 2,3-dihydroquinazolin-4(1*H*)-one **10a** (entries 1 and 2)

respectively. Next, $Cu(OTf)_2$ (20 mol%) in toluene at room temperature gave an increased yield 76% of the compound **10a** (entry 3). However, utilizing the same catalyst $Cu(OTf)_2$ under refluxing and ultrasonic bath in toluene decreased the yield of the compound **10a** (entry 4 and 5).

Table 1. Optimization of the reaction conditions for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one **10a**[a]



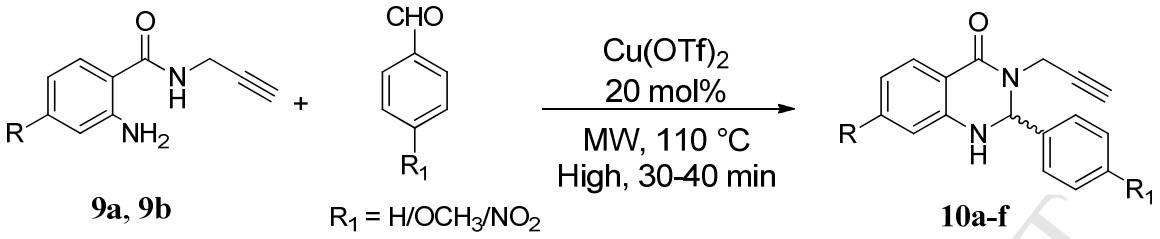
9a **10a**

Entry	Catalyst	Solvent	Conditions	Yield (%)[b]
1	$CuCl_2$ (20 mol%)	EtOH	reflux, 4 h	62
2	$InCl_3$ (20 mol%)	CH_3CN	rt,15 h	65
3	$Cu(OTf)_2$ (20 mol%)	toluene	rt, 36 h	76
4	$Cu(OTf)_2$ (20 mol%)	toluene	reflux, 8 h	60
5	$Cu(OTf)_2$ (20 mol%)	toluene	ultrasonic, 5 h	35
6	**$Cu(OTf)_2$ (20 mol%)**	**toluene**	**MW, 110 °C, High,[c] 30 min**	**93**
7	$Cu(OTf)_2$ (10 mol%)	toluene	MW, 110 °C, High,[c] 30 min	75
8	$Cu(OTf)_2$ (20 mol%)	EtOH	MW, 110 °C, High,[c] 30 min	no reaction
9	*p*-TsOH	toluene	rt, 36 h	no reaction
10	Amberlyst-15	toluene	rt, 48 h	no reaction

[a]*All reactions were performed with* ***9a*** *(1.0 mmol), benzaldehyde (1.1 mmol), catalyst, solvent (5 mL); in microwave vial (5-10 mL) sealed and placed in microwave reactor (400 W);* [b]*Isolated yield as pure product;* [c]*High-absorption condition*

Interestingly, with 20 mol% of $Cu(OTf)_2$ in the microwave (MW, 400W) at 110 °C for 30 min in toluene, the yield of the compound **10a** increased to 93% (entry 6). Apart from increased yield, shorter reaction times and reduction of the byproducts with controlled heating were also observed on employing the microwave irradiation. Further changing the catalyst $Cu(OTf)_2$ loading to 10 mol%, the yield of the desired product **10a** was decreased (entry 7). However, $Cu(OTf)_2$ (20 mol%) in the microwave (MW) at 110 °C for 30 min in EtOH did not give the desired product **10a** (entry 8). Notably, the combination of *p*-TsOH or Amberlyst-15 did not produce the cyclized product **10a** at room temperature (entry 9 and 10). The structural elucidation of known compound **10a** was carried out on the basis of its MS and NMR data. The 2,3-dihydroquinazolin-4(1*H*)-one (**10a**) was identical in all respects to those reported earlier.[62]

In order to assess the scope of this methodology, further reactions of 2-amino-*N*-propargyl benzamide derivatives (**9a** and **9b**) with various aldehydes were examined. These transformations were carried out in the presence of 20 mol% of $Cu(OTf)_2$ and toluene in MW for 30-40 min using the optimized conditions found in the case of compound **10a** (Table 1). The results are summarized in Scheme 2. The direct two-component reactions worked well with a variety of aldehydes. Reactions between 2-amino-*N*-propargyl benzamide (**9a**) with benzaldehyde, 4-methoxybenzaldehyde and 4-nitrobenzaldehyde afforded products **10a-c** in 93, 89 and 86% yield, respectively. Similarly, reactions of 2-amino-4-chloro-*N*-propargyl benzamide (**9b**) with benzaldehyde, 4-methoxybenzaldehyde and 4-nitrobenzaldehyde produced the desired products **10d-f** in 88, 85 and 82% yield, respectively (Scheme 2).



9a, **9b**

R_1 = H/OCH_3/NO_2

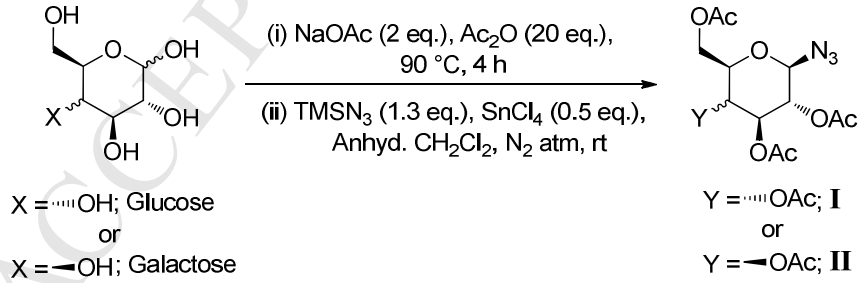
10a-f

Comp.	R	R_1	Yield (%)
10a	H	H	93
10b	H	OCH_3	89
10c	H	NO_2	86
10d	Cl	H	88
10e	Cl	OCH_3	85
10f	Cl	NO_2	82

Scheme 2. Synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones

2.1.2. Synthesis of glycosyl triazolyl quinazolin-4(3*H*)-ones

The glycosyl azides (**I** and **II**) were prepared from commercially available glucose and galactose following the methods already reported[63] in the literature as shown in Scheme 3. The structures were established on the basis of their spectroscopic data. These were identical in all respects to those reported earlier.[64]



X = OH; Glucose
or
X = OH; Galactose

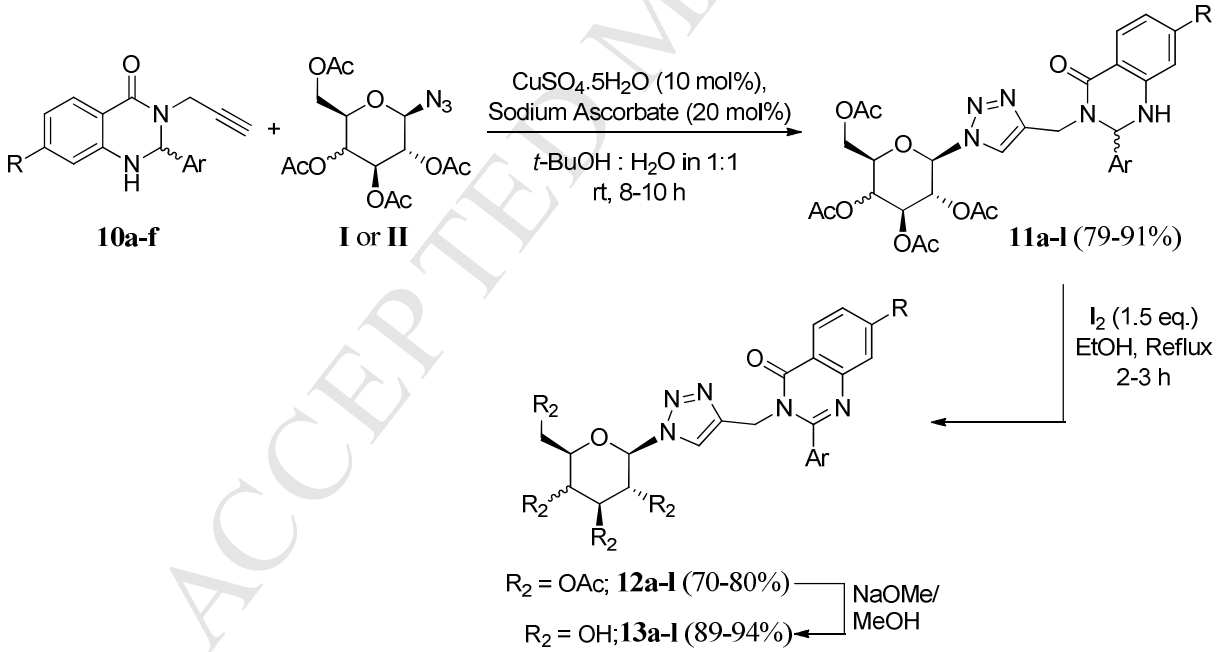
Y = OAc; **I**
or
Y = OAc; **II**

Scheme 3. Synthesis of the glycosyl azides

The strategy for the synthesis of glycosyl triazolyl quinazolin-4(3*H*)-ones is depicted in Scheme 4. Having the 2-phenyl-3-propargyl-2,3-dihydroquinazolin-4(1*H*)-ones (**10a-f**) and glycosyl

azides (**I** and **II**) in our hand the CuAAC reactions were performed in *t*-BuOH/H_2O (1:1) using equimolar quantities of the reagents, $CuSO_4.5H_2O$ (10 mol%) and sodium ascorbate (20 mol%) at ambient temperature to afford epimeric mixtures of peracetyl glycosyl-triazolyl 2,3-dihydroquinazolin-4(1*H*)-ones (**11a-l**) in good yields (Scheme 4, Table 2). Propargyl quinazolinones and glycosyl azides selectively gave only one regioisomer, 1,4-disubstituted triazole via 1,3-dipolar cycloaddition reaction.

The above glycosyl triazolyl 2,3-dihydroquinazolin-4(1*H*)-ones (**11a-l**) were treated with 1.5 eq. of I_2 in ethanol at refluxing conditions[65] which led to the formation of corresponding peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12a-l**) in good yields (Scheme 4, Table 2).



Scheme 4. Synthesis of glycosyl quinazolin-4(3*H*)-ones

The final products were purified by column chromatography and the structures were established on the basis of NMR data. One of the prototype compound **12a** showed all the glycosyl protons

between 5.8 and 3.9 ppm apart from the anomeric proton (H-1") which was shifted to 5.81 ppm in its ^{1}H NMR spectrum. The triazolyl proton (H-5') was observed as a singlet at δ 7.85 ppm. The protons of the methylene group adjacent to triazolyl ring were located as singlet at 5.29 ppm. In ^{13}C NMR spectrum, the position of the anomeric carbon was assigned at 86.0 ppm. The peak at δ 162.5 ppm accounted for the amide group carbon (N-CO), quite distinct from the ester acetyl carbon signals at δ 170.7, 170.1, 169.4 and 168.9 ppm. The 1,4-regioselectivity during cycloaddition reaction was evidenced on the basis of chemical shifts of the triazolyl carbon signals which were visible at δ 143.9 ppm (C-4') and 122.6 ppm (C-5'), a characteristic feature of the ^{1}H and ^{13}C NMR spectra of 1,4-regioisomers as reported earlier in literature.[66] while the methylene carbon was observed at δ 42.1 ppm along with other usual signals.

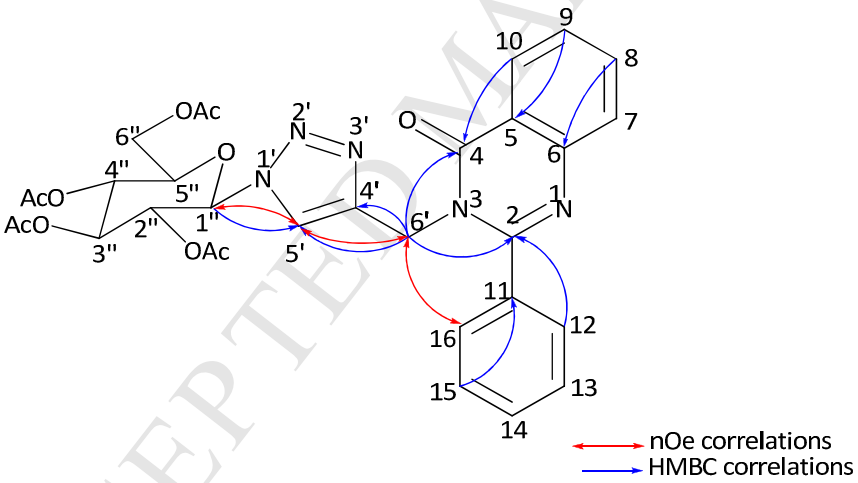
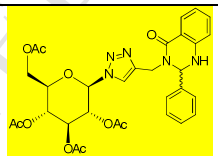
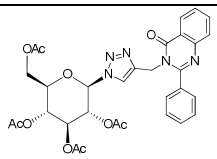
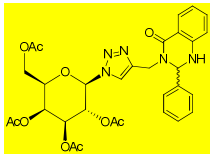
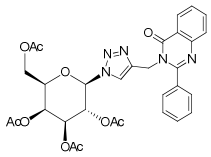
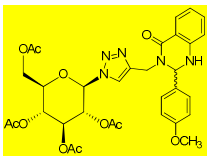
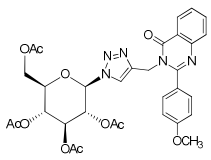


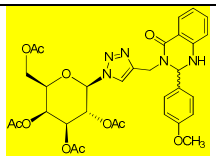
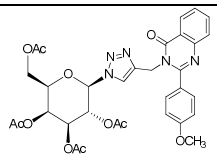
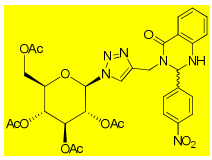
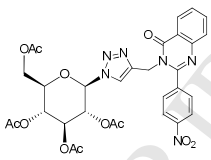
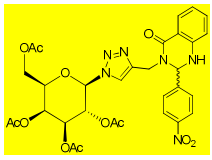
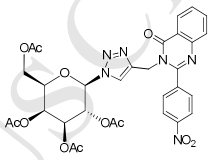
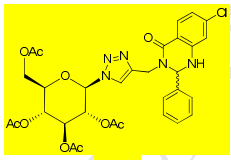
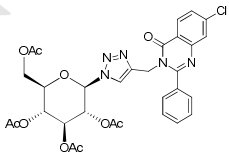
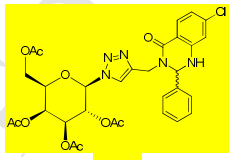
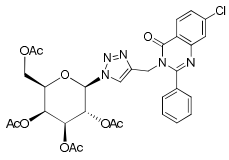
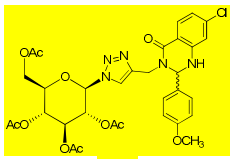
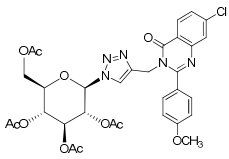
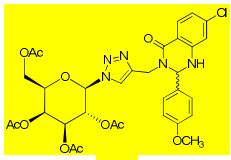
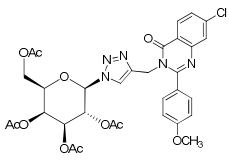
Figure 3. Relevant nOe and HMBC correlations in compound **12a**

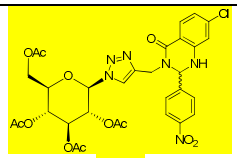
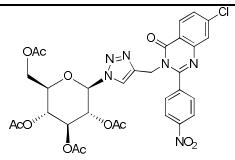
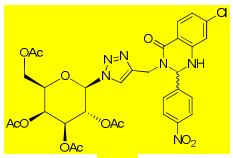
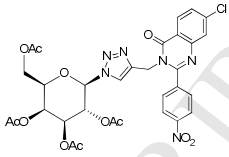
Further the 1,4-regioselectivity of cycloaddition product **12a** was confirmed by 2D NMR experiments. The ^{1}H and ^{13}C NMR signal assignments and connectivity between quinazolin-4-(3*H*)-one ring and glucose to 1,4-disubstituted triazole were determined with the help of various 1D and 2D NMR experiments (Figure 3). COSY and TOCSY correlations established the coupled

systems of glucose sugar, H-7 to H-10 of quinazolin-4-(3*H*)-one ring and a phenyl moiety. HMBC correlation of CH_2-6′ to C-2 and C-4 supported that connectivity of CH_2-6′ to quinazolin-4-(3*H*)-one was through N-3. H-1″ showed HMBC correlation with C5′ of triazole and confirmed the connectivity of glucose sugar with triazole through N-1′. HMBC correlation of CH_2-6′ to C-4′ and C-5′ established the connectivity of CH_2-6′ with triazole through C-4′. These HMBC correlations established the 1,4-disubstituted regioselectivity of the product. Important nOe correlations between CH_2-6′ and H-1″ to H-5′ showed the proximity of protons in the space and supported the formation of 1,4-disubstituted regioisomer (Figure 3).

Table 2. Peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12a-12l**) from glycosyl azides and 2,3-dihydroquinazolin-4(1*H*)-ones

Entry	2,3-Dihydro quinazolin-4(1*H*)-ones	Glycosyl azide	Cyclo adduct	Peracetylated glycosyl quinazolin-4(3*H*)-one	Yield (%)[a]
1	**10a**	**I**	 **11a**	 **12a**	80
2	**10a**	**II**	 **11b**	 **12b**	78
3	**10b**	**I**	 **11c**	 **12c**	77

4	**10b**	**II**	 **11d**	 **12d**	75
5	**10c**	**I**	 **11e**	 **12e**	73
6	**10c**	**II**	 **11f**	 **12f**	71
7	**10d**	**I**	 **11g**	 **12g**	79
8	**10d**	**II**	 **11h**	 **12h**	76
9	**10e**	**I**	 **11i**	 **12i**	74
10	**10e**	**II**	 **11j**	 **12j**	73

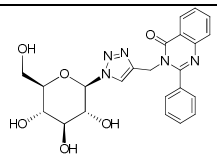
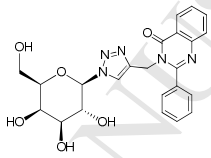
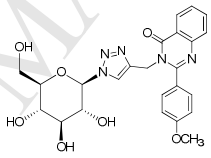
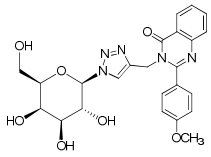
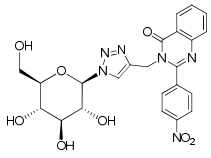
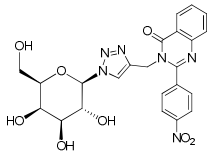
11	**10f**	**I**	 **11k**	 **12k**	72
12	**10f**	**II**	 **11l**	 **12l**	70

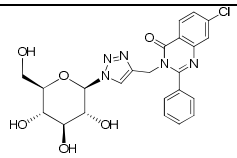
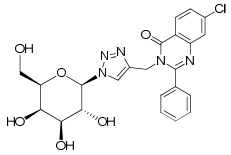
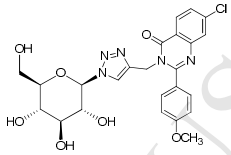
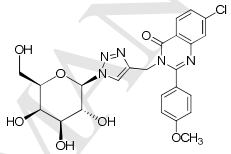
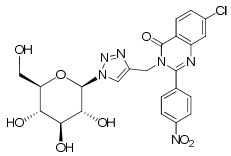
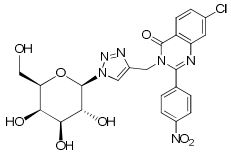
[a] *Isolated yield as pure product*

The unsubstituted phenyl containing peracetylated glycosyl triazolyl 2,3-dihydroquinazolin-4(1*H*)-ones (**11a**, **11b**, **11g** and **11h**) gave the desired oxidation to furnish the peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12a**, **12b**, **12g** and **12h**) respectively in good yields (76-80%). Similarly, *p*-methoxy substituted phenyl containing peracetylated glycosyl triazolyl 2,3-dihydroquinazolin-4(1*H*)-ones (**11c**, **11d** and **11i**) underwent smooth oxidation to furnish the peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12c**, **12d** and **12i**) in 74-77% yield. However, *p*-nitro substituted phenyl containing peracetylated glycosyl triazolyl 2,3-dihydroquinazolin-4(1*H*)-ones (**11e**, **11f**, **11j**, **11k** and **11l**) gave a somewhat lower yield (70-73%) of the corresponding peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12e**, **12f**, **12j**, **12k** and **12l**) compared to the other peracetylated glycosyl triazolyl quinazolin-4(3*H*)-one derivatives.

The Zemplen deacetylation of the above peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12a-l**) with NaOMe/MeOH at room temperature led to the formation of the deacetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**13a-l**) respectively in good yields (Scheme 4, Table 3).

Table 3: Synthesized deacetylated compounds **13a-l** from peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12a-l)**

Entry	Peracetylated substrates	Deacetylated products	Yield (%)[a]
1	**12a**	 **13a**	94
2	**12b**	 **13b**	92
3	**12c**	 **13c**	93
4	**12d**	 **13d**	91
5	**12e**	 **13e**	92
6	**12f**	 **13f**	90

7	**12g**	 **13g**	92
8	**12h**	 **13h**	91
9	**12i**	 **13i**	91
10	**12j**	 **13j**	89
11	**12k**	 **13k**	90
12	**12l**	 **13l**	89

[a] *Isolated yield as pure product*

2.2.Biology

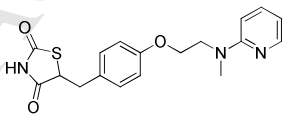
2.2.1. *In vitro* GLUT4 translocation activity

We initially performed bioevalution of 2,3-dihydroquinazolin-4(1*H*)-ones (**10a-f**) for their *in*

vitro GLUT4 translocation activity using L-6 muscle cell lines and the results are shown in Table 4. All the 2,3-dihydroquinazolin-4(1*H*)-ones (**10a-f**) showed promising to significant GLUT4 translocation activity with 1.06-1.27 fold stimulation at 10 µM (Table 4). In this series, the *p*-methoxy phenyl substituted 2,3-dihydroquinazolin-4(1*H*)-ones **10b** and **10e** displayed the most promising GLUT4 translocation activity with 1.27 and 1.24 fold stimulation at 10 µM in L-6 muscle cell lines, respectively. Other phenyl substituted 2,3-dihydroquinazolin-4(1*H*)-ones (**10a**, **10c**, **10d** and **10f**) showed significant GLUT4 translocation activity at 10 µM in L-6 muscle cell lines.

Table 4. *In vitro* GLUT4 translocation activity (10 µM) of glycosyl quinazolin-4(3*H*)-ones

S. No	Compound	GLUT4 translocation (Fold Stimulation)
1	**10a**	1.06
2	**10b**	1.27
3	**10c**	1.22
4	**10d**	1.16
5	**10e**	1.24
6	**10f**	1.21
7	**12a**	0.60
8	**12b**	0.57
9	**12c**	Nil
10	**12d**	**1.18**
11	**12e**	0.51

12	**12f**	**1.08**
13	**12g**	0.40
14	**12h**	0.87
15	**12i**	ND
16	**12j**	ND
17	**12k**	0.84
18	**12l**	**1.09**
19	**13a**	0.55
20	**13b**	0.54
21	**13c**	0.52
22	**13d**	**1.18**
23	**13e**	0.73
24	**13f**	**1.09**
25	**13g**	0.59
26	**13h**	0.57
27	**13i**	0.79
28	**13j**	ND
29	**13k**	ND
30	**13l**	**1.35**
31	 Rosiglitazone (Std)	1.31

Nil – ≤ 0.2 fold response comparison to control, ND – Not determined

The glycosyl 1,2,3-1*H*-triazolyl quinazolin-4(3*H*)-one derivatives (**12a-l** and **13a-l**) were also screened for their *in vitro* GLUT4 translocation activity using rosiglitazone (A thiazolidinedione antidiabetic agent, a key underlying metabolic abnormality in most patients with type 2 diabetes mellitus, improves insulin resistance) as standard (Table 4). As evident in Table 4, most of the galactosyl triazolyl quinazolin-4(3*H*)-ones showed better GLUT4 translocation activity as compared to the glucosyl triazolyl quinazolin-4(3*H*)-ones. Out of all the compounds screened for GLUT4 translocation activity, 6 compounds (**12d**, **12f**, **12l**, **13d**, **13f** and **13l**) exhibited promising to significant GLUT4 translocation activity with 1.08-1.35 fold stimulation at a concentration of 10 µM in L-6 muscle cell lines (Table 4). In this series, the *p*-nitro phenyl substituted hydroxy galactosyl triazolyl chloro quinazolin-4(3*H*)-one **13l (**1.35 fold stimulation) exhibited the most promising GLUT4 translocation activity as compared to its peracetylated analogue **12l (**1.09 fold stimulation) at 10 µM in L-6 muscle cell lines. The *p*-methoxy phenyl substituted hydroxy galactosyl triazolyl quinazolin-4(3*H*)-one **13d (**1.18 fold stimulation) and peracetylated galactosyl triazolyl quinazolin-4(3*H*)-one **12d (**1.18 fold stimulation) showed good GLUT4 translocation activity as compared to **13l**. Another *p*-nitro phenyl substituted hydroxy galactosyl triazolyl quinazolin-4(3*H*)-one **13f (**1.09 fold stimulation) and peracetylated galactosyl triazolyl quinazolin-4(3*H*)-one **12f (**1.08 fold stimulation) showed moderate GLUT4 translocation activity at 10 µM concentration. Other compounds belonging to glycosyl 1,2,3-1*H*-triazolyl quinazolin-4(3*H*)-one showed less GLUT4 translocation activity compared to standard drug rosiglitazone.

3. Conclusion

In conclusion, we have developed an efficient method for the synthesis of 3-propynyl-2,3-dihydroquinazolin-4(1*H*)-ones in high yields. The reaction involves the cyclization of anthranyl derivatives with aromatic aldehydes using $Cu(OTf)_2$ as catalyst under microwave irradiation with short reaction time, simple work-up, and mild reaction conditions. Further subjected to CuAAc reaction of glycosyl azides with these propargylated dihydroquinazolinones through Click reaction afforded the glycosyl triazolyl 2,3-dihydroquinazolin-4(1*H*)-one derivatives in excellent yields. The latter on iodine catalyzed oxidation resulted in a series of novel glycosyl 1,2,3-1*H*-triazolyl quinazolin-4(3*H*)-one derivatives. 24 compounds were screened against *in vitro* GLUT4 translocation activity, six compounds **12d**, **12f**, **12l**, **13d**, **13f** and **13l** showed promising GLUT4 translocation activity (fold stimulation). While the deacetylated galactosyl 1,2,3-1*H*-triazolyl quinazolin-4(3*H*)-one derivative **13l** exhibited the most promising GLUT4 translocation activity with 1.35-fold stimulation at the concentration of 10 µM in L-6 muscle cell lines.

4. Experimental section

4.1. General methods

Commercially available reagent grade chemicals were used as received. All reactions were monitored by TLC on E. Merck Kieselgel 60 F254, with detection in UV light (254 nm), spraying 20% aq $KMnO_4$ solution and/or spraying 4% ethanolic H_2SO_4. Column chromatography was performed on Silica Gel (60-120 mesh, E. Merck). IR spectra were recorded as thin films with a Perkin-Elmer Spectrometer RX-1 (4000–450 cm^{-1}) spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on Bruker AV III HD 400 MHz and 500 MHz instruments, respectively, in $CDCl_3$ and DMSO-d_6. Chemical shift values are reported in ppm relative to TMS (tetramethylsilane) as the internal reference, unless otherwise stated; s

(singlet), d (doublet), t (triplet), dd (doublet of doublets), m (multiplet); Coupling constants (patterns) $^{n}J_{H,H}$ are expressed (given) in Hertz (Hz). HRMS spectra were taken under ESI-Q-TOF conditions. Optical rotations were measured in a 1.0-dm tube with a Rudolf Autopol III polari meter in $CHCl_3$ and MeOH. Microwave mediated reactions were performed in commercial microwave system [maximum output power 400W, built-in magnetic stirrer (300-900 rpm) and an IR temperature sensor (40-250 °C)].

4.2. General procedure for the preparation of *N*-propargyl benzamides (9a and 9b)

Anthranilic or 2-amino-4-chlorobenzoic acid (**8**, 1 mmol) was dissolved in dry DMF (20 mL), resulted solution was degassed with N_2 then cooled at 0 °C and 1-Hydroxybenzotriazole (Bt-OH, 1 mmol), 4-Dimethylaminopyridine (DMAP, 1 mmol) were added to the reaction mixture. *N*,*N'*-Diisopropylcarbodiimide (DIPC, 1 mmol) was added dropwise to the stirring reaction mixture. After 10 mins, propargyl amine (1.1 mmol) was added to the reaction mixture and stirred overnight at ambient temperature. The crude mixture was taken up with water (50 mL) and extracted with ethyl acetate (3 × 40 mL). The combined organic extracts were washed with brine (50 mL), dried over sodium sulfate, filtered, concentrated, and purified by column chromatography (20% EtOAc:Hexane) to afford desired compounds **9a** and **9b**.

4.3. 2-Amino-*N*-(prop-2-yn-1-yl)benzamide (9a)[61a]

A mixture of anthranilic acid **8a** (5.0 g, 36.49 mmol), HOBt (4.92 g, 36.49 mmol), DMAP (4.45 g, 36.49 mmol), DIPC (5.67 mL, 36.49 mmol) and propargyl amine (2.56 mL, 40.14 mmol) in dry DMF (20 mL) was stirred under nitrogen atmosphere at room temperature for 10 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the

crude product, which was purified by column chromatography (20% EtOAc/Hexane) to give the title compound **9a** (5.65 g, 89%) as a white solid; R_f (20% EtOAc/Hexane) 0.50; mp 86-88 °C; IR (ν_{max}): 3372, 3019, 1648, 1586, 1403, 1215, 757 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 7.24 (1H, m, Ar-H), 7.12 (1H, m, Ar-H), 6.57 (2H, m, Ar-H), 6.25 (1H, bs, -NH), 5.43 (2H, bs, $-NH_2$), 4.10 (2H, m, $-CH_2$), 2.16 (1H, m, -CH); δ_C ^{13}C NMR (100 MHz, $CDCl_3$+CCl_4) 168.8 (C=O), 148.9 (Ar-C), 132.6 (Ar-C), 127.2 (Ar-C), 117.3 (Ar-C), 116.5 (Ar-C), 114.9 (Ar-C), 79.7, 71.7 (-CH), 29.4 ($-CH_2$); HRMS: $[M+H]^+$, found 175.0874. $C_{10}H_{11}N_2O$ requires 175.0866.

4.4. 2-Amino-4-chloro-*N*-(prop-2-yn-1-yl)benzamide (9b)[61b]

A mixture of 2-amino-4-chloro-benzoic acid **8b** (5.0 g, 29.23 mmol), HOBt (3.94 g, 29.23 mmol), DMAP (3.56 g, 29.23 mmol), DIPC (4.54 mL, 29.23 mmol) and propargyl amine (2.05 mL, 32.16 mmol) in dry DMF (20 mL) was stirred under nitrogen atmosphere at room temperature for 12 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (20% EtOAc/Hexane) to give the title compound **9b** (5.35 g, 88%) as a light yellow solid; R_f (20% EtOAc/Hexane) 0.51; mp 112-114 °C; IR (ν_{max}): 3391, 3019, 1650, 1385, 1215, 758 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 7.25 (1H, m, Ar-H), 6.65 (1H, m, Ar-H), 6.59 (1H, m, Ar-H), 6.15 (1H, bs, -NH), 5.66 (2H, bs, $-NH_2$), 4.18 (2H, m, $-CH_2$), 2.26 (1H, m, -CH); δ_C (100 MHz, $CDCl_3$+CCl_4): 168.0 (C=O), 150.0 (Ar-C), 138.5 (Ar-C), 128.3 (Ar-C), 116.6 (2 × Ar-C), 113.1 (Ar-C), 79.4, 71.9 (-CH), 29.4 ($-CH_2$); HRMS: $[M+H]^+$, found 209.0477. $C_{10}H_{10}ClN_2O$ requires 209.0476.

4.5. General procedure for the compounds 10a-f

An oven-dried 5 mL microwave reaction vessel containing a stir bar was charged with 2-amino-*N*-(prop-2-yn-1-yl)benzamide derivative **9** (1.0 mmol), aldehyde (1.1 mmol) and $Cu(OTf)_2$ (20 mol%) to this, 5 mL toluene was added and the vessel was sealed with a plastic microwave septum. The vessel was placed into the CEM Discover SP system under the following conditions: pre-stirring 30 s, stirring was set high (absorption). Maximum power and maximum pressure were set 450 Wand 450 psi respectively, with a set temperature of 110 °C for 30-40 min (hold time). After microwave irradiation was complete, the mixture was cooled to room temperature and then diluted with ethyl acetate and water. The organic layer was separated and dried with anhyd. Na_2SO_4 and evaporated under reduced pressure to give the crude mass, which was purified by column chromatography on silica gel (60-120 mesh) using 20% EtOAc/ hexane to give desired products **10a-f**.

4.6. 2-Phenyl-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1*H*)-one (10a)[62]

A mixture of 2-amino-*N*-(prop-2-yn-1-yl)benzamide **9a** (1.0 g, 5.74 mmol), benzaldehyde (0.64 mL, 6.32 mmol) and $Cu(OTf)_2$ (0.41 g, 1.14 mmol) in toluene (5 mL) was stirred under microwave irradiation at 110 °C temperature for 30 min. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (20% EtOAc/Hexane) to give the title compound **10a** (1.40 g, 93%) as a white solid; R_f (20% EtOAc/Hexane) 0.62; mp 141-143 °C; IR (ν_{max}): 3400, 3019, 1647, 1403, 1215, 757 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.97 (1H, d, *J* 8.0 Hz, Ar-H), 7.49 (2H, m, Ar-H), 7.39 (3H, m, Ar-H), 7.29 (1H, m, Ar-H), 6.86 (1H, t, *J* 8.0 Hz, Ar-H), 6.57 (1H, d, *J* 8.0 Hz, Ar-H), 6.04 (1H, s, -CH), 5.00 (1H, dd, J_1 17.5 Hz, J_2 2.3 Hz), 4.55 (1H, bs, -NH), 3.31 (1H, dd, J_1 17.5 Hz, J_2 2.3 Hz), 2.18 (1H, s, -CH); δ_C (125 MHz, $CDCl_3$) 163.2 (C=O), 145.6 (Ar-C),

138.5 (Ar-C), 133.9 (Ar-C), 129.7 (Ar-C), 129.0 (2 × Ar-C), 128.9 (Ar-C), 127.2 (2 × Ar-C), 119.2 (Ar-C), 115.2 (Ar-C), 114.1 (Ar-C), 78.3, 72.0, 71.7, 32.6 (-CH_2); HRMS: $[M+H]^+$, found 263.1185. $C_{17}H_{15}N_2O$ requires 263.1179.

4.7. 2-(4-Methoxyphenyl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1*H*)-one (10b)

A mixture of 2-amino-*N*-(prop-2-yn-1-yl)benzamide **9a** (1.0 g, 5.74 mmol), 4-methoxybenzaldehyde (0.76 mL, 6.32 mmol) and $Cu(OTf)_2$ (0.41 g, 1.14 mmol) in toluene (5 mL) was stirred under microwave irradiation at 110 °C temperature for 30 min. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (20% EtOAc/Hexane) to give the title compound **10b** (1.49 g, 89%) as a white solid; R_f (20% EtOAc/Hexane) 0.63; mp 138-140 °C; IR (ν_{max}): 3399, 3019, 1638, 1403, 1216, 770 cm^{-1}; δ_C (400 MHz, $CDCl_3$) 7.97 (1H, d, *J* 6.8 Hz, Ar-H), 7.44 (2H, m, Ar-H), 7.30 (1H, m, Ar-H), 6.91 (2H, m, Ar-H), 6.88 (1H, m, Ar-H), 6.58 (1H, d, *J* 8.0 Hz, Ar-H), 5.99 (1H, s, -CH), 4.96 (1H, dd, J_1 17.5 Hz, J_2 2.6 Hz), 4.48 (1H, bs, -NH), 3.81 (3H, s, -OCH_3), 3.29 (1H, dd, J_1 17.4 Hz, J_2 2.3 Hz), 2.17 (1H, t, *J* 2.4 Hz, -CH). δ_C (100 MHz, $CDCl_3$) 163.4 (C=O), 160.6 (Ar-C), 145.8 (Ar-C), 133.8 (Ar-C), 130.4 (Ar-C), 128.9 (Ar-C), 128.7 (2 × Ar-C), 119.1 (Ar-C), 115.3 (Ar-C), 114.3 (2 × Ar-C), 114.1 (Ar-C), 78.4, 71.7, 71.5, 55.3 (-OCH_3), 32.4 (-CH_2); HRMS: $[M+H]^+$, found 293.1291. $C_{18}H_{17}N_2O_2$ requires 293.1285.

4.8. 2-(4-Nitrophenyl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1*H*)-one (10c)

A mixture of 2-amino-*N*-(prop-2-yn-1-yl)benzamide **9a** (1.0 g, 5.74 mmol), 4-nitrobenzaldehyde (0.95 g, 6.32 mmol) and $Cu(OTf)_2$ (0.41 g, 1.14 mmol) in toluene (5 mL) was stirred under

microwave irradiation at 110 °C temperature for 40 min. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (20% EtOAc/Hexane) to give the title compound **10c** (1.51 g, 86%) as a yellow solid; R_f (20% EtOAc/Hexane) 0.39; mp 136-138 °C; IR (ν_{max}): 3398, 3019, 1644, 1403, 1215, 757 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 8.21 (2H, m, Ar-H), 7.95 (1H, m, Ar-H), 7.64 (2H, m, Ar-H), 7.33 (1H, m, Ar-H), 6.90 (1H, m, Ar-H), 6.63 (1H, d, *J* 8.0 Hz, Ar-H), 6.16 (1H, s, -CH), 5.01 (1H, dd, J_1 17.7 Hz, J_2 2.6 Hz), 4.82 (1H, bs, -NH), 3.51 (1H, dd, J_1 17.7 Hz, J_2 2.4 Hz), 2.25 (1H, t, *J* 2.5 Hz, -CH); δ_C (100 MHz, $CDCl_3$+CCl_4) 162.6 (C=O), 148.5 (Ar-C), 145.7 (Ar-C), 144.7 (Ar-C), 134.2 (Ar-C), 128.9 (Ar-C), 127.9 (2 × Ar-C), 124.2 (2 × Ar-C), 119.9 (Ar-C), 115.4 (Ar-C), 114.7 (Ar-C), 77.6, 73.2, 70.3, 33.1 (-CH_2); HRMS: $[M+H]^+$, found 308.1015. $C_{17}H_{14}N_3O_3$ requires 308.1030.

4.9. 7-Chloro-2-phenyl-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1*H*)-one (10d)

A mixture of 2-amino-7-chloro-*N*-(prop-2-yn-1-yl)benzamide **9b** (1.0 g, 4.80 mmol), benzaldehyde (0.53 mL, 5.28 mmol) and $Cu(OTf)_2$ (0.34 g, 0.96 mmol) in toluene (5 mL) was stirred under microwave irradiation at 110 °C temperature for 30 min. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (20% EtOAc/Hexane) to give the title compound **10d** (1.25 g, 88%) as a white solid; R_f (20% EtOAc/Hexane) 0.60; mp 160-162 °C; IR (ν_{max}): 3399, 3019, 1638, 1402, 1215, 757 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 7.85 (1H, d, *J* 8.3 Hz, Ar-H), 7.46 (2H, m, Ar-H), 7.39 (3H, m, Ar-H), 6.79 (1H, m, Ar-H), 6.56 (1H, m, Ar-H), 6.02 (1H, s, -CH), 4.97 (1H, dd, J_1 17.5 Hz, J_2 2.5 Hz), 4.74 (1H, bs, -NH), 3.27 (1H, dd, J_1 17.5 Hz, J_2 2.4 Hz), 2.17 (1H, t, *J* 2.4 Hz, -CH); δ_C (100 MHz, $CDCl_3$+CCl_4) 162.2 (C=O), 146.3 (Ar-C), 139.8

(Ar-C), 138.3 (Ar-C), 130.4 (Ar-C), 129.8 (Ar-C), 129.1 (2 × Ar-C), 127.0 (2 × Ar-C), 119.5 (Ar-C), 113.8 (Ar-C), 113.5 (Ar-C), 78.0, 72.2, 71.5, 32.5 (-CH_2); HRMS: $[M+H]^+$, found 297.0799. $C_{17}H_{14}ClN_2O$ requires 297.0789.

4.10. 7-Chloro-2-(4-methoxyphenyl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1*H*)-one (10e)

A mixture of 2-amino-7-chloro-*N*-(prop-2-yn-1-yl)benzamide **9b** (1.0 g, 4.80 mmol), 4-methoxybenzaldehyde (0.64 mL, 5.28 mmol) and $Cu(OTf)_2$ (0.34 g, 0.96 mmol) in toluene (5 mL) was stirred under microwave irradiation at 110 °C temperature for 30 min. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (20% EtOAc/Hexane) to give the title compound **10e** (1.33 g, 85%) as a light yellow solid; R_f (20% EtOAc/Hexane) 0.64; mp 150-152 °C; IR (ν_{max}): 3399, 3019, 1638, 1403, 1215, 769 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 7.86 (1H, d, *J* 8.3 Hz, Ar-H), 7.40 (2H, m, Ar-H), 6.89 (2H, m, Ar-H), 6.79 (1H, m, Ar-H), 6.56 (1H, m, Ar-H), 5.97 (1H, s, -CH), 4.94 (1H, dd, J_1 17.3 Hz, J_2 2.4 Hz), 4.58 (1H, bs, -NH), 3.81 (3H, s, -OCH_3), 3.24 (1H, dd, J_1 17.5 Hz, J_2 2.4 Hz), 2.15 (1H, t, *J* 2.4 Hz, -CH). δ_C (100 MHz, $CDCl_3$+CCl_4) 162.5 (C=O), 160.7 (Ar-C), 146.5 (Ar-C), 139.8 (Ar-C), 130.4 (Ar-C), 130.1 (Ar-C), 128.6 (2 × Ar-C), 119.4 (Ar-C), 114.3 (2 × Ar-C), 113.7 (Ar-C), 113.5 (Ar-C), 78.2, 72.0, 71.3, 55.2 (-OCH_3), 32.4 (-CH_2); HRMS: $[M+H]^+$, found 327.0885. $C_{18}H_{16}ClN_2O_2$ requires 327.0895.

4.11. 7-Chloro-2-(4-nitrophenyl)-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1*H*)-one (10f)

A mixture of 2-amino-7-chloro-*N*-(prop-2-yn-1-yl)benzamide **9b** (1.0 g, 4.80 mmol), 4-nitrobenzaldehyde (0.79 g, 5.28 mmol) and $Cu(OTf)_2$ (0.34 g, 0.96 mmol) in toluene (5 mL) was stirred under microwave irradiation at 110 °C temperature for 40 min. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (20% EtOAc/Hexane) to give the title compound **10f** (1.34 g, 82%) as a light yellow solid; R_f (20% EtOAc/Hexane) 0.38; mp 204-206 °C; IR (ν_{max}): 3398, 3019, 1637, 1403, 1215, 769 cm^{-1}; δ_H (400 MHz, $CDCl_3$+DMSO-d_6) 8.22 (2H, m, Ar-H), 7.72 (1H, m, Ar-H), 7.66 (3H, m, Ar-H, -NH), 6.70 (2H, m, Ar-H), 6.17 (1H, s, -CH), 4.80 (1H, dd, J_1 17.6 Hz, J_2 2.3 Hz), 3.73 (1H, dd, J_1 17.6 Hz, J_2 2.3 Hz), 2.80 (1H, t, J 2.4 Hz, -CH); δ_C (100 MHz, $CDCl_3$+DMSO-d_6) 161.6 (C=O), 148.1 (Ar-C), 147.1 (Ar-C), 146.9 (Ar-C), 139.3 (Ar-C), 129.9 (Ar-C), 127.9 (2 × Ar-C), 124.0 (2 × Ar-C), 118.1 (Ar-C), 114.1 (Ar-C), 112.8 (Ar-C), 78.2, 74.6, 69.7, 33.6 ($-CH_2$); HRMS: $[M+H]^+$, found 342.0760. $C_{17}H_{13}ClN_3O_3$ requires 342.0640.

4.12. General Procedure for the synthesis of 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl azide (I)

To a stirring suspension of sodium acetate (9 g, 111.11 mmol) in acetic anhydride (105 ml, 1111.11 mmol) was added glucose (10 g, 55.55 mmol). The reaction mixture was heated at 90 °C for 4 hours. After completion of the reaction (on TLC), the reaction mixture was immediately transferred into ice-water mixture and stirred vigorously until the white solid precipitates. The white solid is filtered and dried completely on vacuo.

To a solution of glucosyl peracetate (5.0 g, 12.82 mmol) in anhydrous dichloromethane was added trimethylsilyl azide (2.21 mL, 16.66 mmol), followed by 1.0 M solution of Stannic

chloride (0.75 mL, 6.41 mmol). The resulting solution was stirred at room temperature for 12 hours under inert atmosphere. After the completion of the reaction (on TLC), the reaction mixture was diluted with dichloromethane, washed with saturated aqueous solution of sodium bicarbonate, dried over Na_2SO_4, filtered and concentrated in vacuo to give the crude product, which was purified by recrystallization (hexane/dichloromethane) to give the title compound **I** (4.6 g, 96%) as a white solid; R_f (50% EtOAc/Hexane) 0.70; The melting point and the spectral data (IR, ^1H, and ^{13}C NMR) were identical to those previously reported.[64] mp 130-132 °C, lit mp 131-135 ºC.

4.13. General Procedure for the synthesis of 2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl azide (II)

To a stirring suspension of sodium acetate (9 g, 111.11 mmol) in acetic anhydride (105 ml, 1111.11 mmol) was added galactose (10 g, 55.55 mmol). The reaction mixture was heated at 90 °C for 4 hours. After completion of the reaction (on TLC), the reaction mixture was immediately transferred into ice-water mixture and stirred vigorously until the white solid precipitates. The white solid is filtered and dried completely on vacuo.

To a solution of galactosyl peracetate (5.0 g, 12.82 mmol) in anhydrous dichloromethane was added trimethylsilyl azide (2.21 mL, 16.66 mmol), followed by 1.0 M solution of Stannic chloride (0.75 mL, 6.41 mmol). The resulting solution was stirred at room temperature for 12 hours under inert atmosphere. After the completion of the reaction (on TLC), the reaction mixture was diluted with dichloromethane, washed with saturated aqueous solution of sodium bicarbonate, water, dried over Na_2SO_4, filtered and concentrated in vacuo to give the crude

product, which was purified by recrystallization (hexane/dichloromethane) to give the title compound **II** (4.3 g, 89%) as a white solid; R_f (50% EtOAc/Hexane) 0.69; The melting point and the spectral data (IR, ^{1}H, and ^{13}C NMR) were identical to those previously reported.[64] mp 93-95 °C, lit mp 90-92 ºC.

4.14. General procedure for the synthesis of peracetylated compounds 11a-l

2-phenyl-3-(prop-2-yn-1-yl)-2,3-dihydroquinazolin-4(1*H*)-ones **10a-f** (1 mmol) and glycosyl azide (1 mmol) were suspended in a mixture of 1:1 tert-butanol:water (20 mL) and kept for stirring at room temperature. To the stirring reaction mixture freshly prepared solution of sodium ascorbate (20 mol%) in 500 μL and freshly prepared solution of $CuSO_4.5H_2O$ (10 mol%) in 200 μL water were sequentially added. The reaction mixture was stirred at ambient temperature for 8-10 h. The reaction mixture was extracted with ethyl acetate and washed with water. The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to give a white crude product. The latter was purified by silica gel (60-120 mesh) column chromatography to give the cycloaddition product **11a-l**.

4.15. 2-Phenyl-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11a)

A mixture of **10a** (0.49 g, 1.87 mmol), glycosyl azide **I** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 8 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11a** (1.08 g, 91%) as a white

solid; R_f (50% EtOAc/Hexane) 0.25; mp 108-110 °C; IR (ν_{max}): 3405, 3019, 1755, 1643, 1216, 769 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 7.96 (2H, m), 7.87 (2H, m), 7.46 (2H, m), 7.38 (8H, m), 7.24 (2H, m), 6.86 (2H, m), 6.53 (2H, m), 6.01 (1H, s, -CH), 5.81 (2H, m), 5.40 (6H, m), 5.29 (5H, m), 4.33 (2H, m), 4.13 (2H, m), 3.97 (3H, m), 2.08 (6H, m), 2.05 (6H, m), 2.01 (3H, m), 2.00 (3H, m), 1.87 (3H, m), 1.85 (3H, m); δ_C (100 MHz, $CDCl_3$) 170.5, 169.9, 169.2, 168.9, 168.7, 163.2, 163.0, 145.3, 144.9, 139.2, 139.0, 134.6, 133.7, 130.2, 129.4, 129.0, 128.9, 128.7, 128.6, 128.5, 127.1, 126.9, 126.9, 121.7, 119.3, 119.1, 115.7, 114.5, 114.3, 85.8, 75.1, 72.6, 72.5, 71.9, 71.5, 70.6, 70.4, 67.6, 61.5, 38.9, 38.6, 20.6, 20.5, 20.1; HRMS: $[M+H]^+$, found 636.2287. $C_{31}H_{34}N_5O_{10}$ requires 636.2300.

4.16. 2-Phenyl-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11b)

A mixture of **10a** (0.49 g, 1.87 mmol), glycosyl azide **II** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 8 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11b** (1.07 g, 90%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.23; mp 119-121 °C; IR (ν_{max}): 3408, 3019, 1753, 1644, 1215, 758 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 7.98 (4H, m), 7.49 (2H, m), 7.40 (8H, m), 7.24 (2H, m), 6.86 (2H, m), 6.53 (2H, m), 6.03 (1H, s, -CH), 5.81 (3H, m), 5.50 (5H, m), 5.38 (2H, m), 5.24 (2H, m), 4.21 (8H, m), 2.23 (6H, m), 2.03 (6H, m), 2.00 (6H, m), 1.87 (6H, m); δ_C (100 MHz, $CDCl_3$+CCl_4) 169.9, 169.8, 169.5, 169.5, 162.3, 144.4, 139.4, 139.1, 134.8, 133.7, 133.6, 129.4, 129.3, 129.0, 128.9, 128.8, 128.6, 128.5, 126.9, 126.8, 122.6, 121.8, 121.7, 119.1, 115.4,

114.5, 114.2, 86.4, 86.3, 74.1, 74.0, 71.8, 71.4, 70.7, 70.6, 68.2, 68.0, 66.7, 61.0, 38.8, 38.4, 20.6, 20.5, 20.4, 20.2, 20.1; HRMS: $[M+H]^+$, found 636.2271. $C_{31}H_{34}N_5O_{10}$ requires 636.2300.

4.17. 2-(4-Methoxyphenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(*1H*)-one (11c)

A mixture of **10b** (0.54 g, 1.87 mmol), glycosyl azide **I** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 9 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11c** (1.09 g, 88%) as a white solid; R_f (50% EtOAc/Hexane) 0.24; mp 110-112 °C; IR (ν_{max}): 3386, 2922, 1751, 1639, 1229, 757 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.97 (2H, m), 7.83 (2H, m), 7.40 (2H, m), 7.33 (2H, m), 7.29-7.22 (2H, m), 6.89 (6H, m), 6.56 (2H, m), 5.95 (1H, s, -CH), 5.83 (3H, m), 5.41 (4H, m), 5.24 (3H, m), 4.51 (2H, m), 4.32 (2H, m), 4.16 (2H, m), 3.99 (4H, m), 3.80 (6H, m), 2.08 (12H, m), 2.02 (6H, m), 1.86 (6H, m); δ_C (100 MHz, $CDCl_3$) 170.5, 169.9, 169.2, 168.8, 168.7, 163.4, 163.1, 160.5, 145.5, 145.4, 144.9, 144.6, 133.7, 131.2, 130.9, 128.6, 128.5, 128.5, 128.4, 121.7, 119.2, 119.0, 115.6, 115.4, 114.4, 114.3, 114.2, 114.2, 85.8, 75.1, 72.7, 72.5, 71.7, 71.3, 70.6, 70.4, 67.7, 67.6, 61.5, 55.3, 38.7, 38.4, 20.6, 20.5, 20.1; HRMS: $[M+H]^+$, found 666.2383. $C_{32}H_{36}N_5O_{11}$ requires 666.2406.

4.18. 2-(4-Methoxyphenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11d)

A mixture of **10b** (0.54 g, 1.87 mmol), glycosyl azide **II** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 9 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11d** (1.06 g, 86%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.22; mp 120-122 °C; IR (ν_{max}): 3412, 1748, 1637, 1221, 766 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.99 (4H, m), 7.42 (2H, m), 7.33 (2H, m), 7.29 (2H, m), 6.89 (6H, m), 6.56 (2H, m), 5.96 (1H, s, -CH), 5.80 (3H, m), 5.53 (5H, m), 5.35 (5H, m), 4.22 (7H, m), 3.80 (6H, m), 2.23 (6H, m), 2.04 (6H, m), 2.00 (6H, m), 1.87 (6H, m); δ_C (100 MHz, $CDCl_3$) 170.3, 170.1, 169.8, 168.9, 168.9, 160.4, 145,6, 145.4, 133.7, 130.9, 130.2, 128.6, 128.4, 121.8, 119.2, 119.0, 115.3, 114.5, 114.3, 114.2, 86.3, 74.1, 71.6, 71.3, 70.8, 70.6, 68.2, 68.0, 66.8, 61.2, 55.3, 38.7, 38.4, 20.7, 20.6, 20.4, 20.2; HRMS: $[M+H]^+$, found 666.2397. $C_{32}H_{36}N_5O_{11}$ requires 666.2406.

4.19. 2-(4-Nitrophenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11e)

A mixture of **10c** (0.57 g, 1.87 mmol), glycosyl azide **I** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 10 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column

chromatography (50% EtOAc/Hexane) to give the title compound **11e** (1.07 g, 84%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.20; mp 126-128 °C; IR (ν_{max}): 3399, 3019, 1755, 1643, 1215, 758 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.21 (4H, m), 7.98 (2H, m), 7.90 (2H, m), 7.63 (2H, m), 7.55 (2H, m), 7.31 (2H, m), 6.93 (2H, m), 6.61 (2H, m), 6.14 (1H, m), 5.90 (1H, m), 5.84 (2H, m), 5.48 (7H, m), 5.25 (2H, m), 4.81 (2H, m), 4.34 (2H, m), 4.18 (2H, m), 4.01 (3H, m), 2.08 (12H, m), 2.04 (6H, m), 1.89 (6H, m); δ_C (100 MHz, $CDCl_3$) 170.5, 169.9, 169.3, 169.1, 168.8, 162.6, 148.4, 146.2, 144.4, 143.9, 134.1, 128.7, 128.6, 127.8, 127.6, 124.2, 124.1, 121.9, 121.8, 120.2, 119.9, 116.4, 115.7, 115.5, 114.9, 85.9, 75.2, 72.5, 72.3, 70.9, 70.6, 69.9, 67.6, 61.4, 42.2, 31.5, 20.6, 20.5, 20.2, 20.1; HRMS: $[M+H]^+$, found 681.2098. $C_{31}H_{33}N_6O_{12}$ requires 681.2151.

4.20. 2-(4-Nitrophenyl)-3-[{1′-(1″-deoxy-2″,3″,4″,6″-tetra-*O*-acetyl-*β*-D-galactopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11f)

A mixture of **10c** (0.57 g, 1.87 mmol), glycosyl azide **II** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 10 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11f** (1.02 g, 81%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.21; mp 138-140 °C; IR (ν_{max}): 3399, 2925, 1754, 1639, 1403, 1217, 771 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.23 (4H, m), 8.01 (4H, m), 7.67 (2H, m), 7.57 (2H, m), 7.33 (2H, m), 6.95 (2H, m), 6.64 (2H, m), 6.18 (1H, m), 5.92 (1H, m), 5.83 (2H, m), 5.56 (6H, m), 5.31 (2H, m), 4.84 (2H, m), 4.24 (6H, m), 3.88 (2H, m), 2.25 (6H, m), 2.06 (12H, m), 1.91 (6H, m); δ_C (100 MHz, $CDCl_3$) 170.3, 170.0, 162.7, 146.3, 144.4, 134.1, 128.7, 127.8,

127.7, 124.2, 124.1, 122.0, 120.3, 119.9, 115.6, 114.8, 86.4, 70.6, 69.9, 68.5, 68.1, 66.7, 61.2, 42.2, 20.6, 20.4, 20.2; HRMS: $[M+H]^+$, found 681.2128. $C_{31}H_{33}N_6O_{12}$ requires 681.2151.

4.21. 7-Chloro-2-phenyl-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11g)

A mixture of **10d** (0.55 g, 1.87 mmol), glycosyl azide **I** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 8 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11g** (1.08 g, 87%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.24; mp 131-133 °C; IR (ν_{max}): 3398, 3019, 1748, 1642, 1216, 770 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 7.88 (4H, m), 7.44 (2H, m), 7.37 (8H, m), 6.80 (2H, m), 6.53 (2H, m), 6.02 (1H, s), 5.83 (3H, m), 5.41 (11H, m), 4.33 (2H, m), 4.13 (2H, m), 3.99 (2H, m), 2.07 (6H, m), 2.05 (6H, m), 2.01 (6H, m), 1.86 (6H, m); δ_C (100 MHz, $CDCl_3$+CCl_4) 170.4, 170.3, 169.7, 169.1, 168.8, 168.6, 161.5, 157.5, 147.6, 143.3, 141.0, 133.9, 130.6, 130.1, 129.6, 129.5, 129.1, 129.0, 128.8, 128.2, 127.9, 126.9, 126.8, 126. 7, 122.4, 119.5, 119.4, 119.0, 114.2, 113.8, 85.8, 75.2, 72.6, 72.5, 71.2, 70.7, 70.5, 70.4, 67.6, 61.4, 42.0, 20.6, 20.5, 20.4, 20.1, 20.0; HRMS: $[M+H]^+$, found 670.1899. $C_{31}H_{33}ClN_5O_{10}$ requires 670.1910.

4.22. 7-Chloro-2-phenyl-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11h)

A mixture of **10d** (0.55 g, 1.87 mmol), glycosyl azide **II** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40

mL) was stirred at room temperature for 8 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11h** (1.07 g, 86%) as a white solid; R_f (50% EtOAc/Hexane) 0.23; mp 130-132 °C; IR (ν_{max}): 3400, 3019, 1753, 1643 1385, 1215, 758 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 7.89 (4H, m), 7.45 (2H, m), 7.37 (8H, m), 6.80 (2H, m), 6.54 (2H, m), 6.05 (1H, s), 5.82 (3H, m), 5.50 (4H, m), 5.38 (2H, m), 5.25 (2H, m), 4.23 (7H, m), 3.95-3.82 (2H, m), 2.23 (6H, m), 2.03 (6H, m), 2.00 (6H, m), 1.86 (6H, m); δ_C (100 MHz, $CDCl_3$+CCl_4) 169.9, 169.8, 169.4, 168.8, 168.6, 161.9, 146.0, 145.9, 144.1, 139.6, 139.2, 138.9, 130.1, 130.0, 129.5, 129.1, 129.0, 126.8, 126.7, 121.8, 121.7, 119.5, 119.3, 114.2, 113.8, 86.3, 74.0, 73.9, 71.6, 71.2, 70.7, 70.5, 68.3, 68.1, 66.7, 61.0, 38.7, 38.3, 20.7, 20.6, 20.5, 20.4, 20.2, 20.1; HRMS: $[M+H]^+$, found 670.1892. $C_{31}H_{33}ClN_5O_{10}$ requires 670.1910.

4.23. 7-Chloro-2-(4-methoxyphenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11i)

A mixture of **10e** (0.61 g, 1.87 mmol), glycosyl azide **I** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 9 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11i** (1.04 g, 83%) as a white solid; R_f (50% EtOAc/Hexane) 0.25; mp 216-218 °C; IR (ν_{max}): 3400, 3019, 1750, 1639, 1403, 1215, 769 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 7.89 (2H, m), 7.81 (2H, m), 7.38 (2H, m), 7.31 (2H, m), 6.90 (4H, m), 6.81 (2H, m), 6.55 (2H, m), 5.95 (1H, s, -CH), 5.83 (3H, m), 5.43 (4H, m),

5.25 (3H, m), 4.63 (2H, m), 4.32 (2H, m), 4.16 (2H, m), 4.00 (4H, m), 3.80 (6H, m), 2.08 (12H, m), 2.02 (6H, m), 1.86 (6H, m); δ_C (100 MHz, $CDCl_3$+CCl_4) 170.5, 169.9, 169.2, 168.8, 162.3, 160.6, 160.5, 146.2, 139.6, 131.9, 130.9, 130.6, 130.1, 130.0, 128.6, 128.3, 128.3, 121.7, 119.5, 119.3, 114.4, 114.3, 114.0, 113.8, 85.8, 75.1, 72.6, 72.4, 71.5, 71.1, 70.7, 70.5, 67.6, 61.5, 55.3, 38.6, 38.3, 20.6, 20.5, 20.1; HRMS: $[M+H]^+$, found 700.2009. $C_{32}H_{35}ClN_5O_{11}$ requires 700.2016.

4.24. 7-Chloro-2-(4-methoxyphenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11j)

A mixture of **10e** (0.59 g, 1.80 mmol), glycosyl azide **II** (0.68 g, 1.80 mmol), $CuSO_4.5H_2O$ (0.045 g, 0.18 mmol) and sodium ascorbate (0.072 g, 0.36 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 9 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11j** (1.03 g, 81%) as a white solid; R_f (50% EtOAc/Hexane) 0.24; mp 147-149 °C; IR (ν_{max}): 3401, 3019, 1603, 1423, 1215, 757 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.91-7.84 (4H, m), 7.40 (2H, m), 7.31 (2H, m), 6.90-6.86 (4H, m), 6.82-6.77 (2H, m), 6.55-6.51 (2H, m), 5.97 (1H, s, -CH), 5.81-5.75 (3H, m), 5.54-5.46 (4H, m), 5.36-5.30 (2H, m), 5.26-5.21 (3H, m), 4.62 (2H, m), 4.20-4.11 (6H, m), 3.81 (6H, m), 2.23 (6H, m), 2.04 (6H, m), 2.00 (6H, m), 1.88 (6H, m); δ_C (100 MHz, $CDCl_3$) 170.3, 170.1, 169.8, 169.8, 169.0, 168.9, 162.5, 162.3, 160.5, 160.5, 146.3, 146.1, 139.7, 139.6, 131.0, 130.7, 130.3, 130.1, 129.9, 128.3, 121.8, 119.5, 119.3, 114.4, 114.3, 114.1, 114.0, 113.8, 113.6, 86.3,

74.1, 74.0, 71.4, 71.1, 70.7, 70.6, 68.2, 68.0, 66.8, 61.2, 55.3, 38.6, 38.3, 20.7, 20.6, 20.6, 20.4, 20.2, 20.2; HRMS: $[M+H]^+$, found 700.2003. $C_{32}H_{35}ClN_5O_{11}$ requires 700.2016.

4.25. 7-Chloro-2-(4-nitrophenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11k)

A mixture of **10f** (0.63 g, 1.87 mmol), glycosyl azide **I** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 10 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11k** (1.07 g, 80%) as a light yellow solid; R_f (50% EtOAc/Hexane) 0.22; mp 188-190 °C; IR (ν_{max}): 3400, 3019, 1639, 1385, 1215, 758 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.38 (2H, m), 8.24 (4H, m), 7.78 (2H, m), 7.71 (2H, m), 7.59 (4H, m), 6.75 (4H, m), 6.33 (2H, m), 6.09 (2H, m), 5.67 (2H, m), 5.56 (2H, m), 5.21 (4H, m), 4.37 (2H, m), 4.16 (6H, m), 2.02-1.96 (18H, m), 1.80 (6H, m); δ_C (100 MHz, DMSO-d_6) 170.4, 170.0, 169.8, 169.0, 161.6, 148.1, 147.5, 147.3, 143.8, 143.6, 138.7, 130.2, 128.1, 128.0, 124.3, 124.3, 123.5, 118.1, 114.0, 113. 4, 84.3, 84.2, 73.7, 72.5, 70.7, 70.6, 69.7, 69.6, 67.9, 62.2, 20.9, 20.8, 20.7, 20.3; HRMS: $[M+H]^+$, found 715.1735. $C_{31}H_{32}ClN_6O_{12}$ requires 715.1761.

4.26. 7-Chloro-2-(4-nitrophenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]-2,3-dihydroquinazolin-4(1*H*)-one (11l)

A mixture of **10f** (0.63 g, 1.87 mmol), glycosyl azide **II** (0.70 g, 1.87 mmol), $CuSO_4.5H_2O$ (0.046 g, 0.18 mmol) and sodium ascorbate (0.074 g, 0.37 mmol) in 1:1 tert-Butanol:water (40 mL) was stirred at room temperature for 10 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **11l** (1.05 g, 79%) as a light yellow solid; R_f (50% EtOAc/Hexane) 0.20; mp 166-168 °C; IR (ν_{max}): 3399, 3019, 1749, 1639, 1215, 769 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.23 (4H, m), 7.95 (2H, m), 7.90 (2H, m), 7.64 (2H, m), 7.54 (2H, m), 6.88 (2H, m), 6.61 (2H, m), 6.18 (1H, m), 5.91 (1H, m), 5.83 (2H, m), 5.55 (4H, m), 5.50 (4H, m), 5.27 (2H, m), 4.70 (2H, m), 4.23 (6H, m), 2.23 (6H, m), 2.05-2.00 (12H, m), 1.90 (6H, m); δ_C (100 MHz, $CDCl_3$) 170.3, 170.0, 169.8, 169.1, 168.5, 149.8, 145.9, 145.2, 140.1, 138.3, 130.2, 128.7, 127.7, 127.6, 124.3, 124.2, 121.9, 120.6, 120.2, 116.7, 116.5, 115.2, 114.5, 86.4, 86.3, 74.2, 74.1, 70.7, 70.4, 69.7, 68.5, 68.1, 67.9, 66.7, 61.2, 35.0, 20.6, 20.4, 20.2; HRMS: $[M+H]^+$, found 715.1711. $C_{31}H_{32}ClN_6O_{12}$ requires 715.1761.

4.27. General procedure for the synthesis of compounds 12a-l

The solution of **11a-l** (1.0 mmol) and I_2 (1.5 mmol) in ethanol (60 mL) was refluxed for 2-3 h, then cooled to room temperature and concentrated in vacuum. The residue was extracted with ethyl acetate and washed with 10% $Na_2S_2O_4$ solution (50 mL), H_2O (100 mL) and brine (100 mL), then dried with anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by column chromatography on silica gel to afford compounds **12a-l**.

4.28. 2-Phenyl-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12a)

A mixture of **11a** (0.80 g, 1.25 mmol) and I_2 (0.47 g, 1.88 mmol) in EtOH (60 mL) was stirred at reflux condition for 2 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12a** (0.63 g, 80%) as a white solid; R_f (50% EtOAc/Hexane) 0.34; mp 127-129 °C; $[\alpha]_D^{25}$ – 66 (c 0.1, $CHCl_3$); IR (ν_{max}): 3401, 3019, 1755, 1638, 1215, 757 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.33 (1H, d, *J* 8.0 Hz, Ar-H), 7.85 (1H, s, triazol-H), 7.78 (2H, m, Ar-H), 7.60 (2H, m, Ar-H), 7.53 (4H, m, Ar-H), 5.81 (1H, dd, J_1 6.7 Hz, J_2 2.7 Hz, H-1″), 5.40 (2H, m, H-2″, H-3″), 5.29 (3H, m, -CH_2, H-4″), 4.30 (1H, dd, J_1 12.5 Hz, J_2 4.8 Hz, H-6″a), 4.15 (1H, dd, J_1 12.5 Hz, J_2 1.8 Hz, H-6″b), 3.99 (1H, ddd, J_1 10.3 Hz, J_2 5.0 Hz, J_3 1.8 Hz, H-5″), 2.08 (3H, s, -$OCOCH_3$), 2.05 (3H, s, -$OCOCH_3$), 2.01 (3H, s, -$OCOCH_3$), 1.84 (3H, s, -$OCOCH_3$); δ_C (125 MHz, $CDCl_3$) 170.7, 170.1, 169.4, 168.9 (4 × -$COCH_3$), 162.5 (-CO), 156.2, 147.4 (Ar-C), 143.9, 134.9 (Ar-C), 134.8 (Ar-C), 130.4 (Ar-C), 129.0 (Ar-C), 128.7 (Ar-C), 127.8 (Ar-C), 127.3 (Ar-C), 126.9 (Ar-C), 122.6, 120.9 (Ar-C), 86.0 (C-1″), 75.4 (C-5″), 72.8 (C-2″), 70.6 (C-3″), 67.8 (C-4″), 61.7 (C-6″), 42.1 (-CH_2), 20.9, 20.7, 20.7, 20.3 (4 × -$OCOCH_3$); HRMS: $[M+H]^+$, found 634.2167. $C_{31}H_{32}N_5O_{10}$ requires 634.2144.

4.29. 2-Phenyl-3-[{1′-(1″-deoxy-2″,3″,4″,6″-tetra-*O*-acetyl-*β*-D-galactopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12b)

A mixture of **11b** (0.80 g, 1.25 mmol) and I_2 (0.47 g, 1.88 mmol) in EtOH (60 mL) was stirred at reflux condition for 2 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12b** (0.62 g, 78%) as a white solid; R_f (50% EtOAc/Hexane) 0.31; mp 131-133 °C; $[\alpha]_D^{25}$ – 26.8 (c 0.1, $CHCl_3$); IR (ν_{max}): 3405, 3021, 1751,

1659, 1216, 760 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 8.33 (1H, m, Ar-H), 7.92 (1H, s, triazol-H), 7.77 (2H, m, Ar-H), 7.62 (2H, m, Ar-H), 7.51 (4H, m, Ar-H), 5.77 (1H, m, H-1′′), 5.50 (2H, m, H-2′′, H-3′′), 5.23 (3H, m, -CH_2, H-4′′), 4.22 (3H, m, H-5′′, H-6′′), 2.23 (3H, s, -$OCOCH_3$), 2.03 (3H, s, -$OCOCH_3$), 1.98 (3H, s, -$OCOCH_3$), 1.85 (3H, s, -$OCOCH_3$); δ_C (100 MHz, $CDCl_3$+CCl_4) 170.0, 169.9, 169.5, 168.7 (4 × -$COCH_3$), 162.2 (-CO), 156.0, 147.3 (Ar-C), 143.6 (Ar-C), 134.7, 134.5 (Ar-C), 130.2 (Ar-C), 128.7 (Ar-C), 128.6 (Ar-C), 127.7 (Ar-C), 127.0 (Ar-C), 126.7 (Ar-C), 122.6, 120.7 (Ar-C), 86.4 (C-1′′), 74.1 (C-5′′), 70.7 (C-2′′), 68.0 (C-3′′), 66.7 (C-4′′), 61.0 (C-6′′), 42.0 (-CH_2), 20.6, 20.5, 20.4, 20.1 (4 × -$OCOCH_3$); HRMS: $[M+H]^+$, found 634.2147. $C_{31}H_{32}N_5O_{10}$ requires 634.2144.

4.30. 2-(4-Methoxyphenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12c)

A mixture of **11c** (0.80 g, 1.20 mmol) and I_2 (0.45 g, 1.80 mmol) in EtOH (60 mL) was stirred at reflux condition for 2 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12c** (0.61 g, 77%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.32; mp 137-139 °C; $[\alpha]_D^{25}$ – 70.2 (c 0.1, $CHCl_3$); IR (ν_{max}): 3397, 3021, 1753, 1665, 1218, 764 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.32 (1H, m, Ar-H), 7.90 (1H, s, triazol-H), 7.78 (2H, m, Ar-H), 7.58 (2H, m, Ar-H), 7.52 (1H, m, Ar-H), 7.02 (2H, m, Ar-H), 5.82 (1H, m, H-1′′), 5.43 (2H, m, H-2′′, H-3′′), 5.32 (3H, m, -CH_2, H-4′′), 4.31 (1H, m, H-6′′a), 4.16 (1H, m, H-6′′b), 3.99 (1H, m, H-5′′), 3.87 (3H, s, -OCH_3), 2.08 (9H, m, 3 × -$COCH_3$), 1.85 (3H, s, -$OCOCH_3$); δ_C (100 MHz, $CDCl_3$) 170.5, 169.9, 169.2, 168.7 (4 × -$COCH_3$), 162.5 (-CO), 161.0 (Ar-C), 156.0, 147.3 (Ar-C), 143.9 (Ar-C), 134.5, 130.2 (Ar-C), 127.6 (Ar-C), 127.1 (Ar-C),

126.9 (Ar-C), 126.6 (Ar-C), 122.7, 120.5 (Ar-C), 114.1 (Ar-C), 85.8 (C-1′), 75.2 (C-5′), 72.6 (C-2′), 70.4 (C-3′), 67.6 (C-4′), 61.5 (C-6′), 55.4 (-OCH_3), 42.1 (-CH_2), 20.7, 20.5, 20.1 (4 × -$OCOCH_3$); HRMS: $[M+H]^+$, found 664.2230. $C_{32}H_{34}N_5O_{11}$ requires 664.2249.

4.31. 2-(4-Methoxyphenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12d)

A mixture of **11d** (0.80 g, 1.20 mmol) and I_2 (0.45 g, 1.80 mmol) in EtOH (60 mL) was stirred at reflux condition for 2 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12d** (0.59 g, 75%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.30; mp 142-144 °C; $[\alpha]_D^{25}$ – 38.4 (c 0.1, $CHCl_3$); IR (ν_{max}): 3401, 3019, 1752, 1642, 1215, 757 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.33 (1H, m, Ar-H), 7.95 (1H, s, triazol-H), 7.77 (2H, m, Ar-H), 7.59 (2H, m, Ar-H), 7.52 (1H, m, Ar-H), 7.03 (2H, m, Ar-H), 5.79 (1H, m, H-1′′), 5.54 (2H, m, H-2′′, H-3′′), 5.32 (3H, m, -CH_2, H-4′′), 4.22 (3H, m, H-5′′, H-6′′), 3.87 (3H, s, -OCH_3), 2.23 (3H, s, -$OCOCH_3$), 2.03 (3H, s, -$OCOCH_3$), 1.99 (3H, s, -$OCOCH_3$), 1.86 (3H, s, -$OCOCH_3$); δ_C (100 MHz, $CDCl_3$) 170.3, 170.0, 169.8, 168.8 (4 × -$COCH_3$), 162.6 (-CO), 161.0 (Ar-C), 156.1, 147.4 (Ar-C), 143.9 (Ar-C), 134.5, 130.2 (Ar-C), 127.6 (Ar-C), 127.2 (Ar-C), 126.9 (Ar-C), 126.6 (Ar-C), 122.7, 120.5 (Ar-C), 114.1 (Ar-C), 86.4 (C-1′′), 74.1 (C-5′′), 70.7 (C-2′′), 68.0 (C-3′′), 66.8 (C-4′′), 61.2 (C-6′′), 55.4 (-OCH_3), 42.2 (-CH_2), 20.7, 20.6, 20.4, 20.2 (4 × -$OCOCH_3$); HRMS: $[M+H]^+$, found 664.2248. $C_{32}H_{34}N_5O_{11}$ requires 664.2249.

4.32. 2-(4-Nitrophenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-gulcopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12e)

A mixture of **11e** (0.80 g, 1.17 mmol) and I_2 (0.44 g, 1.76 mmol) in EtOH (60 mL) was stirred at reflux condition for 3 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12e** (0.58 g, 73%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.29; mp 173-175 °C; $[\alpha]_D^{25}$ – 21 (c 0.1, CH_3OH); IR (ν_{max}): 3397, 2119, 1751, 1672, 1221, 766 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.35 (1H, s, triazol-H), 8.31 (2H, m, Ar-H), 8.24 (1H, m, Ar-H), 7.93 (1H, m, Ar-H), 7.83 (2H, m, Ar-H), 7.76 (1H, m, Ar-H), 7.66 (1H, m, Ar-H), 6.29 (1H, m, H-1″), 5.59 (2H, m, H-2″, H-3″), 5.22 (3H, m, -CH_2, H-4″), 4.37 (1H, m, H-6″a), 4.10 (2H, m, H-5″, H-6″b), 2.01 (3H, s, -$OCOCH_3$), 1.98 (3H, s, -$OCOCH_3$), 1.95 (3H, s, -$OCOCH_3$), 1.81 (3H, s, -$OCOCH_3$); δ_C (100 MHz, DMSO-d_6) 170.4, 169.9, 169.8, 169.0 (4 × -$COCH_3$), 161.3 (-CO), 154.5, 148.5 (Ar-C),147.2 (Ar-C), 143.7 (Ar-C), 141.2 (Ar-C), 135.3, 130.1 (Ar-C),128.1 (Ar-C), 127.8 (Ar-C), 126.6 (Ar-C), 123.9 (Ar-C), 122.7, 121.0 (Ar-C), 84.3 (C-1″), 73.7 (C-5″), 72.5 (C-2″), 70.7 (C-3″), 67.9 (C-4″), 62.1 (C-6″), 41.7 (-CH_2), 20.9, 20.8, 20.6, 20.3 (4 × -$OCOCH_3$); HRMS: $[M+H]^+$, found 679.1997. $C_{31}H_{31}N_6O_{12}$ requires 679.1994.

4.33. 2-(4-Nitrophenyl)-3-[{1′-(1″-deoxy-2″,3″,4″,6″-tetra-*O*-acetyl-*β*-D-galactopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12f)

A mixture of **11f** (0.80 g, 1.17 mmol) and I_2 (0.44 g, 1.76 mmol) in EtOH (60 mL) was stirred at reflux condition for 3 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12f** (0.56 g, 71%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.30; mp 166-168 °C; $[\alpha]_D^{25}$ – 21.6 (c 0.1, $CHCl_3$); IR (ν_{max}): 3399, 3019, 1753, 1638, 1402, 1216, 770 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.39 (2H, m, Ar-H), 8.36 (1H, m, Ar-H), 7.98

(1H, s, triazol-H), 7.89 (2H, m, Ar-H), 7.84 (1H, m, Ar-H), 7.76 (1H, m, Ar-H), 7.59 (1H, m, Ar-H), 5.78 (1H, d, *J* 9.2 Hz, H-1″), 5.55 (1H, m, H-2″), 5.47 (1H, m, H-3″), 5.25 (1H, m, H-4″), 5.20 (2H, m, $-CH_2$), 4.22 (2H, m, H-6″), 4.16 (1H, m, H-5″), 2.22 (3H, s, $-OCOCH_3$), 2.04 (3H, s, $-OCOCH_3$), 2.00 (3H, s, $-OCOCH_3$), 1.88 (3H, s, $-OCOCH_3$); δ_C (100 MHz, $CDCl_3$) 170.3, 170.0, 169.7, 169.0 (4 × $-COCH_3$), 161.9 (-CO), 153.9, 148.7 (Ar-C), 146.9 (Ar-C), 143.0 (Ar-C), 140.5 (Ar-C), 135.0, 130.1 (Ar-C),127.8 (Ar-C), 126.8 (Ar-C), 124.0 (Ar-C), 123.6 (Ar-C), 122.7, 120.8 (Ar-C), 86.5 (C-1″), 74.2 (C-5″), 70.5 (C-2″), 68.1 (C-3″), 66.7 (C-4″), 61.2 (C-6″), 41.9 ($-CH_2$), 20.7, 20.6, 20.4, 20.2 (4 × $-OCOCH_3$); HRMS: $[M+H]^+$, found 679.1957. $C_{31}H_{31}N_6O_{12}$ requires 679.1994.

4.34. 7-Chloro-2-phenyl-3-[{1′-(1″-deoxy-2″,3″,4″,6″-tetra-*O*-acetyl-*β*-D-glucopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12g)

A mixture of **11g** (0.80 g, 1.19 mmol) and I_2 (0.45 g, 1.79 mmol) in EtOH (60 mL) was stirred at reflux condition for 2 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12g** (0.63 g, 79%) as a white solid; R_f (50% EtOAc/Hexane) 0.33; mp 145-147 °C; $[\alpha]_D^{25}$ – 57.4 (c 0.1, $CHCl_3$); IR (ν_{max}): 3400, 3019, 1756, 1656, 1215, 758 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 8.24 (1H, d, *J* 8.4 Hz, Ar-H), 7.85 (1H, s, triazol-H), 7.72 (1H, m, Ar-H), 7.61 (2H, m, Ar-H), 7.53 (3H, m, Ar-H), 7.45 (1H, m, Ar-H), 5.81 (1H, m, H-1″), 5.39 (2H, m, H-2″, H-3″), 5.26 (3H, m, $-CH_2$, H-4″), 4.32 (1H, m, H-6″a), 4.13 (1H, m, H-6″b), 4.98 (1H, m, H-5″), 2.07 (3H, s, $-OCOCH_3$), 2.05 (3H, s, $-OCOCH_3$), 2.00 (3H, s, $-OCOCH_3$), 1.84 (3H, s, $-OCOCH_3$); δ_C (100 MHz, $CDCl_3$+CCl_4) 170.1, 169.6, 169.0, 168.5 (4 × $-COCH_3$), 161.6 (-CO), 157.2, 148.2 (Ar-C), 143.4 (Ar-C), 140.8 (Ar-C), 134.5, 130.3

(Ar-C), 128.7 (Ar-C), 128.5 (Ar-C), 128.2 (Ar-C), 127.6 (Ar-C), 127.2 (Ar-C), 122.4, 119.1 (Ar-C), 85.8 (C-1″), 75.2 (C-5″), 72.5 (C-2″), 70.4 (C-3″), 67.6 (C-4″), 61.4 (C-6″), 42.0 (-CH_2), 20.6, 20.4, 20.0 (4 × -$OCOCH_3$); HRMS: $[M+H]^+$, found 668.1710. $C_{31}H_{31}ClN_5O_{10}$ requires 668.1754.

4.35. 7-Chloro-2-phenyl-3-[{1′-(1″-deoxy-2″,3″,4″,6″-tetra-*O*-acetyl-*β*-D-galactopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12h)

A mixture of **11h** (0.80 g, 1.19 mmol) and I_2 (0.45 g, 1.79 mmol) in EtOH (60 mL) was stirred at reflux condition for 2 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12h** (0.60 g, 76%) as a white solid; R_f (50% EtOAc/Hexane) 0.31; mp 132-134 °C; $[\alpha]_D^{25}$ – 24.2 (c 0.1, $CHCl_3$); IR (ν_{max}): 3401, 3019, 1753, 1645, 1215, 758 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.29 (1H, m, Ar-H), 7.92 (1H, m, triazol-H), 7.78 (1H, m, Ar-H), 7.62 (2H, m, Ar-H), 7.55 (3H, m, Ar-H), 7.50 (1H, m, Ar-H), 5.80 (1H, m, H-1″), 5.55 (2H, m, H-2″, H-3″), 5.30 (3H, m, -CH_2, H-4″), 4.21 (3H, m, H-5″, H-6″), 2.25 (3H, m, -$OCOCH_3$), 2.06 (3H, m, -$OCOCH_3$), 2.01 (3H, m, -$OCOCH_3$), 1.88 (3H, m, -$OCOCH_3$); δ_C (100 MHz, $CDCl_3$) 170.3, 170.0, 169.7, 168.9 (4 × -$COCH_3$), 161.8 (-CO), 157.4, 148.2 (Ar-C), 143.4 (Ar-C), 140.8 (Ar-C), 134.5, 130.4 (Ar-C), 128.8 (Ar-C), 128.4 (Ar-C), 128.2 (Ar-C), 127.7 (Ar-C), 127.2 (Ar-C), 122.5, 119.1 (Ar-C), 86.4 (C-1″), 74.1 (C-5″), 70.6 (C-2″), 68.0 (C-3″), 66.7 (C-4″), 61.1 (C-6″), 42.0 (-CH_2), 20.7, 20.6, 20.4, 20.2 (4 × -$OCOCH_3$); HRMS: $[M+H]^+$, found 668.1738. $C_{31}H_{31}ClN_5O_{10}$ requires 668.1754.

4.36. 7-Chloro-2-(4-methoxyphenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12i)

A mixture of **11i** (0.80 g, 1.14 mmol) and I_2 (0.43 g, 1.71 mmol) in EtOH (60 mL) was stirred at reflux condition for 2 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12i** (0.58 g, 74%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.34; mp 105-107 °C; $[\alpha]_D^{25}$ – 45.6 (c 0.1, $CHCl_3$); IR (ν_{max}): 3400, 3019, 1754, 1638, 1216, 770 cm^{-1}; δ_H (400 MHz, $CDCl_3$+CCl_4) 8.22 (1H, d, *J* 8.4 Hz, Ar-H), 7.89 (1H, s, triazol-H), 7.71 (1H, s, Ar-H), 7.59 (2H, m, Ar-H), 7.43 (1H, m, Ar-H), 7.02 (2H, d, *J* 8.5 Hz, Ar-H), 5.81 (1H, m, H-1′′), 5.38 (2H, m, H-2′′, H-3′′), 5.29 (3H, m, -CH_2, H-4′′), 4.34 (1H, m, H-6′′a), 4.14 (1H, m, H-6′′b), 3.98 (1H, m, H-5′′), 3.87 (3H, s, -OCH_3), 2.08 (6H, m, -$OCOCH_3$), 2.01 (3H, s, -$OCOCH_3$), 1.84 (3H, s, -$OCOCH_3$); δ_C (100 MHz, $CDCl_3$+CCl_4) 170.1, 169.5, 168.9, 168.4 (4 × -$COCH_3$), 161.8 (-CO), 161.2 (Ar-C), 157.2, 148.3 (Ar-C), 143.6 (Ar-C), 140.6 (Ar-C), 130.3, 128.1 (Ar-C), 127.4 (Ar-C), 127.1 (Ar-C), 126.8 (Ar-C), 122.7, 119.0 (Ar-C), 114.0 (Ar-C), 85.8 (C-1′′), 75.3 (C-5′′), 72.5 (C-2′′), 70.4 (C-3′′), 67.6 (C-4′′), 61.3 (C-6′′), 55.2 (-OCH_3), 42.2 (-CH_2), 20.6, 20.4, 20.0 (4 × -$OCOCH_3$); HRMS: $[M+H]^+$, found 698.1857. $C_{32}H_{33}ClN_5O_{11}$ requires 698.1860.

4.37. 7-Chloro-2-(4-methoxyphenyl)-3-[{1′-(1′′-deoxy-2′′,3′′,4′′,6′′-tetra-*O*-acetyl-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12j)

A mixture of **11j** (0.2 g, 0.29 mmol) and I_2 (0.11 g, 0.44 mmol) in EtOH (30 mL) was stirred at reflux condition for 2 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography

(50% EtOAc/Hexane) to give the title compound **12j** (0.14 g, 73%) as a white solid; R_f (50% EtOAc/Hexane) 0.38; mp 111-113 °C; IR (ν_{max}): 3401, 3020, 1755, 1602, 1215, 757 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.25 (1H, d, *J* 8.6 Hz, Ar-H), 7.93 (1H, s, triazol-H), 7.71 (1H, d, *J* 1.9 Hz, Ar-H), 7.60 (2H, dd, J_1 6.7 Hz, J_2 1.9 Hz, Ar-H), 7.46 (1H, dd, J_1 8.5 Hz, J_2 2.0 Hz, Ar-H), 7.03 (2H, dd, *J* 6.8 Hz, *J* 1.9 Hz, Ar-H), 5.79 (1H, d, *J* 9.1 Hz, H-1″), 5.54 (2H, m, H-2″, H-3″), 5.31-5.21 (3H, m, $-CH_2$, H-4″), 4.22-4.10 (3H, m, H-5″, H-6″), 3.87 (3H, s, $-OCH_3$), 2.23 (3H, m, $-OCOCH_3$), 2.04 (3H, s, $-OCOCH_3$), 1.99 (3H, s, $-OCOCH_3$), 1.86 (3H, s, $-OCOCH_3$); δ_C (100 MHz, $CDCl_3$) 170.3, 170.0, 169.7, 168.9 (4 × $-COCH_3$), 162.0 (-CO), 161.2 (Ar-C), 157.3, 148.3 (Ar-C), 143.6 (Ar-C), 140.7 (Ar-C), 130.3, 128.1 (Ar-C), 127.5 (Ar-C), 127.1 (Ar-C), 126.8 (Ar-C), 122.7, 119.0 (Ar-C), 114.2 (Ar-C), 86.4 (C-1″), 74.1 (C-5″), 70.7 (C-2″), 68.0 (C-3″), 66.7 (C-4″), 61.1 (C-6″), 55.4 ($-OCH_3$), 42.3 ($-CH_2$), 20.7, 20.6, 20.4, 20.2 (4 × $-OCOCH_3$); HRMS: $[M+H]^+$, found 698.1846. $C_{32}H_{33}ClN_5O_{11}$ requires 698.1860.

4.38. 7-Chloro-2-(4-nitrophenyl)-3-[{1′-(1″-deoxy-2″,3″,4″,6″-tetra-*O*-acetyl-*β*-D-glucopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12k)

A mixture of **11k** (0.80 g, 1.12 mmol) and I_2 (0.42 g, 1.68 mmol) in EtOH (60 mL) was stirred at reflux condition for 3 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12k** (0.56 g, 72%) as a yellow solid; R_f (50% EtOAc/Hexane) 0.31; mp 168-170 °C; $[\alpha]_D^{25}$ – 19.2 (c 0.1, CH_3OH); IR (ν_{max}): 3399, 3019, 1754, 1637, 1215, 769 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.40 (1H, s, triazol-H), 8.35 (1H, m, Ar-H), 8.32 (2H, m, Ar-H), 8.23 (1H, m, Ar-H), 7.86 (3H, m, Ar-H), 6.29 (1H, m, H-1″), 5.58 (2H, m, H-2″, H-3″), 5.19 (3H, m, $-CH_2$, H-4″), 4.36 (1H, m, H-6″a), 4.09 (2H, m, H-5″, H-6″b), 2.01

(3H, s, -OCOCH$_3$), 1.98 (3H, s, -OCOCH$_3$), 1.95 (3H, s, -OCOCH$_3$), 1.81 (3H, s, -OCOCH$_3$); δ_C (100 MHz, DMSO-d_6) 170.4, 169.9, 169.8, 169.0 (4 × -COCH$_3$), 160.8 (-CO), 156.0, 148.6 (Ar-C), 148.2 (Ar-C), 143.5 (Ar-C), 140.8 (Ar-C), 140.0, 130.1 (Ar-C), 128.9 (Ar-C), 128.4 (Ar-C), 127.0 (Ar-C), 124.0 (Ar-C), 122.7, 119.8 (Ar-C), 84.3 (C-1″), 73.7 (C-5″), 72.4 (C-2″), 70.7 (C-3″), 67.9 (C-4″), 62.1 (C-6″), 41.8 (-CH$_2$), 21.0, 20.9, 20.8, 20.6 (4 × -OCOCH$_3$); HRMS: $[M+H]^+$, found 713.4277. $C_{31}H_{30}ClN_6O_{12}$ requires 713.1605.

4.39. 7-Chloro-2-(4-nitrophenyl)-3-[{1′-(1″-deoxy-2″,3″,4″,6″-tetra-*O*-acetyl-*β*-D-galactopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (12l)

A mixture of **11l** (0.80 g, 1.12 mmol) and I_2 (0.42 g, 1.68 mmol) in EtOH (60 mL) was stirred at reflux condition for 3 h. The reaction mixture was extracted with ethyl acetate and the solvent evaporated in vacuo to give the crude product, which was purified by column chromatography (50% EtOAc/Hexane) to give the title compound **12l** (0.55 g, 70%) as a light yellow solid; R_f (50% EtOAc/Hexane) 0.30; mp 198-200 °C; $[\alpha]_D^{25}$ – 17 (c 0.1, CH_3OH); IR (ν_{max}): 3399, 3019, 1751, 1638, 1215, 769 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.33 (3H, m, Ar-H, triazol-H), 8.22 (1H, m, Ar-H), 7.85 (3H, m, Ar-H), 7.68 (1H, m, Ar-H), 6.22 (1H, m, H-1″), 5.52 (3H, m, H-2″, H-3″, H-4″), 5.16 (2H, m, -CH$_2$), 4.58 (1H, m, H-6″a), 4.15 (1H, m, H-6″b), 4.04 (1H, m, H-5″), 2.16 (3H, s, -OCOCH$_3$), 1.99 (3H, s, -OCOCH$_3$), 1.93 (3H, s, -OCOCH$_3$), 1.83 (3H, s, -OCOCH$_3$); δ_C (100 MHz, DMSO-d_6) 170.4, 170.3, 169.8, 169.1 (4 × -COCH$_3$), 160.9 (-CO), 156.1, 148.6 (Ar-C), 148.2 (Ar-C), 143.2 (Ar-C), 140.9 (Ar-C), 139.9, 130.1 (Ar-C), 128.9 (Ar-C), 128.3 (Ar-C), 127.0 (Ar-C), 124.0 (Ar-C), 123.0, 119.9 (Ar-C), 84.8 (C-1″), 73.5 (C-5″), 70.7 (C-2″), 68.3 (C-3″), 67.7 (C-4″), 62.0 (C-6″), 41.9 (-CH$_2$), 20.9, 20.8, 20.7, 20.4 (4 × -OCOCH$_3$); HRMS: $[M+H]^+$, found 713.1540. $C_{31}H_{30}ClN_6O_{12}$ requires 713.1605.

4.40. General procedure for the synthesis of the deacetylated compounds 13a-l

The deacetylated glycosyl derivatives were prepared by treating the corresponding peracetylated compounds (**12a-l**) in MeOH with methanolic NaOMe at room temperature. The reaction mixture stirring continued till the reaction was complete (15-30 min, TLC). After that the reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration (the resin is washed several times with methanol) and evaporation of the filtrate to dryness, gives the titled pure compound **13a-l**.

4.41. 2-Phenyl-3-[{1′-(1′′-deoxy-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13a)

A mixture of **12a** (0.40 g, 0.63 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 15 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13a** (0.27 g, 94%) as a yellow solid; R_f (20% MeOH/$CHCl_3$) 0.24; mp 183-185 °C; $[\alpha]_D^{25}$ 0.4 (c 0.1, CH_3OH); IR (ν_{max}): 3411, 3019, 1638, 1215, 758 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.20 (1H, m, Ar-H), 8.16 (1H, s, triazol-H), 7.90 (1H, m, Ar-H), 7.72 (1H, m, Ar-H), 7.63 (3H, m, Ar-H), 7.54 (3H, m, Ar-H), 5.48 (1H, d, *J* 9.2 Hz, H-1′′), 5.20 (2H, m, -CH_2), 3.73 (5H, m, 4 × -OH, H-5′′), 3.46 (4H, m, H-3′, H-4′′, H-6′′), 3.23 (1H, m, H-2′′); δ_C (100 MHz, DMSO-d_6) 161.5 (-CO), 156.5, 147.3 (Ar-C), 142.9 (Ar-C), 135.4, 135.2 (Ar-C), 130.2 (Ar-C), 128.8 (Ar-C), 128.6 (Ar-C), 127.6 (Ar-C), 127.6 (Ar-C), 126.7 (Ar-C), 123.0, 120.8 (Ar-C), 87.9 (C-1′′), 80.4 (C-5′′), 77.4 (C-3′′), 72.4 (C-4′′), 69.9 (C-2′′), 61.1 (C-6′′), 42.0 (-CH_2); HRMS: $[M+H]^+$, found 466.1721. $C_{23}H_{24}N_5O_6$ requires 466.1721.

4.42. 2-Phenyl-3-[{1′-(1′′-deoxy-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13b)

A mixture of **12b** (0.40 g, 0.63 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 20 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13b** (0.26 g, 92%) as a yellow solid; R_f (20% MeOH/$CHCl_3$) 0.22; mp 152-154 °C; $[\alpha]_D^{25}$ 13 (c 0.1, CH_3OH); IR (ν_{max}): 3400, 3019, 1644, 1215, 769 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.20 (1H, d, *J* 7.3 Hz, Ar-H), 8.10 (1H, s, triazol-H), 7.89 (1H, m, Ar-H), 7.72 (1H, m, Ar-H), 7.63 (3H, m, Ar-H), 7.54 (3H, m, Ar-H), 5.44 (1H, d, *J* 9.1 Hz, H-1′′), 5.19 (2H, m, -CH_2), 4.37 (1H, m, H-5′′), 3.98 (2H, m, H-6′′), 3.74 (2H, m, 2 × -OH), 3.68 (3H, m, 2 × -OH, H-3′′), 3.39 (2H, m, H-2′′, H-4′′); δ_C (100 MHz, DMSO-d_6) 161.6 (-CO), 156.5, 147.4 (Ar-C), 142.9 (Ar-C), 135.4, 135.2 (Ar-C), 130.2 (Ar-C), 128.7 (Ar-C), 128.7 (Ar-C), 127.7 (Ar-C), 127.6 (Ar-C), 126.7 (Ar-C), 122.7, 120.8 (Ar-C), 88.5 (C-1′′), 78.0 (C-5′′), 73.7 (C-3′′), 70.6 (C-4′′), 68.5 (C-2′′), 60.8 (C-6′′), 42.0 (-CH_2); HRMS: $[M+H]^+$, found 466.1720. $C_{23}H_{24}N_5O_6$ requires 466.1721.

4.43. 2-(4-Methoxyphenyl)-3-[{1′-(1′′-deoxy-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13c)

A mixture of **12c** (0.40 g, 0.60 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 20 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13c** (0.27 g, 93%) as a yellow solid; R_f (20% MeOH/$CHCl_3$) 0.23; mp 184-186 °C; $[\alpha]_D^{25}$ – 2.4 (c 0.1, CH_3OH); IR (ν_{max}): 3398, 3019, 1638, 1216, 771 cm^{-1}; δ_H (400 MHz, DMSO-

d_6) 8.18 (2H, m, Ar-H, triazol-H), 7.86 (1H, m, Ar-H), 7.71 (1H, m, Ar-H), 7.61 (3H, m, Ar-H), 7.05 (2H, m, Ar-H), 5.49 (1H, d, *J* 9.3 Hz, H-1′′), 5.23 (3H, m, -CH_2, H-5′′), 4.48 (1H, m, -OH), 3.82 (3H, s, -OCH_3), 3.71 (3H, m, H-6′′, -OH), 3.23 (3H, m, 2 × -OH, H-3′′), 3.09 (2H, m, H-2′′, H-4′′); δ_C (100 MHz, DMSO-d_6) 161.7 (-CO), 160.7 (Ar-C), 156.4, 147.5 (Ar-C), 143.0 (Ar-C), 135.1, 130.4 (Ar-C), 127.8 (Ar-C), 127.7 (Ar-C), 127.4 (Ar-C), 126.6 (Ar-C), 123.0, 120.7 (Ar-C), 114.1 (Ar-C), 87.9 (C-1′′), 79.6 (C-5′′), 77.0 (C-3′′), 73.7 (C-4′′), 70.0 (C-2′′), 61.1 (C-6′′), 55.7 (-OCH_3), 42.1 (-CH_2); HRMS: $[M+H]^+$, found 496.1818. $C_{24}H_{26}N_5O_7$ requires 496.1827.

4.44. 2-(4-Methoxyphenyl)-3-[{1′-(1′′-deoxy-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13d)

A mixture of **12d** (0.40 g, 0.60 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 20 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13d** (0.26 g, 91%) as a yellow solid; R_f (20% MeOH/$CHCl_3$) 0.21; mp 191-193 °C; $[\alpha]_D^{25}$ 12.2 (c 0.1, CH_3OH); IR (ν_{max}): 3401, 1643, 1403, 1216, 770 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.18 (2H, m, Ar-H, triazol-H), 7.88 (1H, m, Ar-H), 7.71 (1H, m, Ar-H), 7.61 (3H, m, Ar-H), 7.05 (2H, m, Ar-H), 5.44 (1H, d, *J* 9.1 Hz, H-1′′), 5.23 (2H, m, -CH_2), 3.99 (1H, m, -OH), 3.83 (3H, s, -OCH_3), 3.73 (2H, m, H-6′′), 3.68 (3H, m, 3 × -OH), 3.53 (4H, m, H-2′′, H-3′′, H-4′′, H-5′′); δ_C (100 MHz, DMSO-d_6) 161.8 (-CO), 160.7 (Ar-C), 156.4, 147.3 (Ar-C), 143.1 (Ar-C), 135.1, 130.5 (Ar-C), 127.7 (Ar-C), 127.6 (Ar-C), 127.4 (Ar-C), 126.6 (Ar-C), 122.8, 120.6 (Ar-C), 114.1 (Ar-C), 88.5 (C-1′′), 78.9 (C-5′′), 74.1 (C-3′′), 69.7 (C-4′′), 68.9 (C-2′′), 60.8 (C-6′′), 55.7 (-OCH_3), 42.2 (-CH_2); HRMS: $[M+H]^+$, found 496.1821. $C_{24}H_{26}N_5O_7$ requires 496.1827.

4.45. 2-(4-Nitrophenyl)-3-[{1′-(1″-deoxy-*β*-D-glucopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13e)

A mixture of **12e** (0.40 g, 0.58 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 30 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13e** (0.26 g, 92%) as a yellow solid; R_f (20% MeOH/$CHCl_3$) 0.20; mp 170-172 °C; $[\alpha]_D^{25}$ – 16 (c 0.1, CH_3OH); IR (ν_{max}): 3391, 3019, 1650, 1215, 757 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.34 (2H, m, Ar-H, triazol-H), 8.23 (2H, m, Ar-H), 7.92 (3H, m, Ar-H), 7.75 (1H, m, Ar-H), 7.65 (1H, m, Ar-H), 5.47 (1H, d, *J* 9.2 Hz, H-1″), 5.24 (2H, m, -CH_2), 3.72 (5H, m, 4 × -OH, H-5″), 3.23 (5H, m, H-2″, H-3″, H-4″, H-6″); δ_C (100 MHz, DMSO-d_6) 161.3 (-CO), 155.7, 148.4 (Ar-C), 147.2 (Ar-C), 142.7 (Ar-C), 141.3 (Ar-C), 135.3, 130.3 (Ar-C), 128.0 (Ar-C), 127.8 (Ar-C), 126.8 (Ar-C), 124.0 (Ar-C), 123.1, 121.0 (Ar-C), 87.8 (C-1″), 79.6 (C-5″), 77.3 (C-3″), 72.4 (C-4″), 70.0 (C-2″), 61.1 (C-6″), 41.6 (-CH_2); HRMS: $[M+H]^+$, found 511.1560. $C_{23}H_{23}N_6O_8$ requires 511.1572.

4.46. 2-(4-Nitrophenyl)-3-[{1′-(1″-deoxy-*β*-D-galactopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13f)

A mixture of **12f** (0.40 g, 0.58 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 30 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13f** (0.25 g, 90%) as a yellow solid; R_f (20% MeOH/$CHCl_3$) 0.21; mp 182-184 °C; $[\alpha]_D^{25}$ – 7.0 (c 0.1, CH_3OH); IR (ν_{max}): 3400, 3019, 1638, 1403, 1216, 771 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.34 (2H, m, Ar-H), 8.23 (1H, m, Ar-H), 8.16 (1H, s, triazol-H), 7.92 (3H, m, Ar-H),

7.74 (1H, m, Ar-H), 7.63 (1H, m, Ar-H), 5.43 (1H, d, *J* 9.0 Hz, H-1′′), 5.25 (3H, m, -CH_2, H-5′′), 4.11 (2H, m, 2 × -OH), 4.03 (3H, m, 4 × -OH, H-3′′), 3.74 (2H, m, H-6′′), 3.70 (2H, m, H-2′′, H-4′′); δ_C (100 MHz, DMSO-d_6) 161.7 (-CO), 156.3, 147.6 (Ar-C), 146.8 (Ar-C), 141.9 (Ar-C), 140.7 (Ar-C), 135.1, 131.1 (Ar-C), 128.6 (Ar-C), 127.1 (Ar-C), 125.8 (Ar-C), 124.2 (Ar-C), 123.6, 120.7 (Ar-C), 87.3 (C-1′′), 79.1 (C-5′′), 76.9 (C-3′′), 72.1 (C-4′′), 70.5 (C-2′′), 61.9 (C-6′′), 41.1 (-CH_2); HRMS: $[M+H]^+$, found 511.1527. $C_{23}H_{23}N_6O_8$ requires 511.1572.

4.47. 7-Chloro-2-phenyl-3-[{1′-(1′′-deoxy-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13g)

A mixture of **12g** (0.40 g, 0.59 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 20 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13g** (0.26 g, 92%) as a light yellow solid; R_f (20% MeOH/$CHCl_3$) 0.23; mp 188-190 °C; $[\alpha]_D^{25}$ – 1.2 (c 0.1, CH_3OH); IR (ν_{max}): 3400, 3019, 1644, 1215, 769 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.19 (2H, m, Ar-H, triazol-H), 7.80 (1H, m, Ar-H), 7.63 (3H, m, Ar-H), 7.54 (3H, m, Ar-H), 5.48 (1H, d, *J* 9.2 Hz, H-1′′), 5.19 (2H, m, -CH_2), 3.72 (4H, m, 4 × -OH), 3.46 (4H, m, H-3′′, H-5′′, H-6′′), 3.23 (2H, m, H-2′′, H-4′′); δ_C (100 MHz, DMSO-d_6) 161.0 (-CO), 157.9, 148.5 (Ar-C), 142.7 (Ar-C), 139.7 (Ar-C), 135.2, 130.4 (Ar-C), 128.8 (Ar-C), 128.6 (Ar-C), 127.8 (Ar-C), 126.9 (Ar-C), 123.0, 119.7 (Ar-C), 87.9 (C-1′′), 80.4 (C-5′′), 77.4 (C-3′′), 72.4 (C-4′′), 70.0 (C-2′′), 61.1 (C-6′′), 42.2 (-CH_2); HRMS: $[M+H]^+$, found 500.1330. $C_{23}H_{23}ClN_5O_6$ requires 500.1331.

4.48. 7-Chloro-2-phenyl-3-[{1′-(1′′-deoxy-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13h)

A mixture of **12h** (0.40 g, 0.59 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 20 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13h** (0.25 g, 91%) as a white solid; R_f (20% MeOH/$CHCl_3$) 0.24; mp 180-182 °C; $[\alpha]_D^{25}$ – 5.4 (c 0.1, CH_3OH); IR (ν_{max}): 3409, 3019, 1644, 1215, 757 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.20 (1H, d, *J* 8.5 Hz, Ar-H), 8.12 (1H, s, triazol-H), 7.79 (1H, m, Ar-H), 7.63 (3H, m, Ar-H), 7.55 (3H, m, Ar-H), 5.44 (1H, d, *J* 9.1 Hz, H-1′′), 5.18 (3H, m, -CH_2, H-5′′), 4.68 (2H, m, 2 × -OH), 3.96 (1H, m, -OH), 3.74 (2H, m, -OH, H-3′′), 3.52 (4H, m, H-2′′, H-4′′, H-6′′); δ_C (100 MHz, DMSO-d_6) 161.1 (-CO), 157.9, 148.5 (Ar-C), 142.7 (Ar-C), 139.7 (Ar-C), 135.2, 130.4 (Ar-C), 128.8 (Ar-C), 128.6 (Ar-C), 127.8 (Ar-C), 126.9 (Ar-C), 122.8, 119.7 (Ar-C), 88.5 (C-1′′), 78.9 (C-5′′), 74.1 (C-3′′), 69.7 (C-4′′), 68.9 (C-2′′), 60.8 (C-6′′), 42.2 (-CH_2); HRMS: $[M+H]^+$, found 500.1332. $C_{23}H_{23}ClN_5O_6$ requires 500.1331.

4.49. 7-Chloro-2-(4-methoxyphenyl)-3-[{1′-(1′′-deoxy-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13i)

A mixture of **12i** (0.40 g, 0.57 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 20 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13i** (0.26 g, 91%) as a yellow solid; R_f (20% MeOH/$CHCl_3$) 0.22; mp 169-171 °C; $[\alpha]_D^{25}$ – 10.6 (c 0.1, CH_3OH); IR (ν_{max}): 3399, 3019, 1638, 1216, 770 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.19 (1H, s, triazol-H), 8.16 (1H, d, *J* 8.3 Hz, Ar-H), 7.78 (1H, m, Ar-H), 7.61 (3H,

m, Ar-H), 7.05 (2H, m, Ar-H), 5.49 (1H, d, *J* 9.6 Hz, H-1″), 5.35 (2H, m, 2 × -OH), 5.22 (3H, m, -CH_2, H-5″), 3.82 (3H, s, -OCH_3), 3.70 (2H, m, 2 × -OH), 3.44 (3H, m, H-3″, H-6″), 3.22 (2H, m, H-2″, H-4″); δ_C (100 MHz, DMSO-d_6) 161.2 (-CO), 160.8 (Ar-C), 157.9, 148.5 (Ar-C), 142.9 (Ar-C), 139.7 (Ar-C), 130.4, 128.8 (Ar-C), 127.6 (Ar-C), 127.5 (Ar-C), 126.8 (Ar-C), 123.0, 119.5 (Ar-C), 114.1 (Ar-C), 87.9 (C-1″), 80.4 (C-5″), 77.4 (C-3″), 72.4 (C-4″), 70.0 (C-2″), 61.1 (C-6″), 55.8 (-OCH_3), 42.3 (-CH_2); HRMS: $[M+H]^+$, found 530.1430. $C_{24}H_{25}ClN_5O_7$ requires 530.1437.

4.50. 7-Chloro-2-(4-methoxyphenyl)-3-[{1′-(1″-deoxy-*β*-D-galactopyranos-1″-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13j)

A mixture of **12j** (0.05 g, 0.07 mmol) and NaOMe in methanol (5 mL) was stirred at room temperature for 15 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13j** (0.034 g, 89%) as a white solid; R_f (20% MeOH/$CHCl_3$) 0.22; mp 173-175 °C; IR (ν_{max}): 3401, 3019, 1602, 1215, 757 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.17 (1H, d, *J* 8.5 Hz, Ar-H), 8.10 (1H, s, triazol-H), 7.76 (1H, m, Ar-H), 7.60-7.56 (3H, m, Ar-H), 7.04 (2H, d, *J* 8.7 Hz, Ar-H), 5.43 (1H, d, *J* 9.2 Hz, H-1″), 5.21 (2H, m, -CH_2), 3.98 (2H, m, H-6″), 3.81 (3H, s, -OCH_3), 3.74 (2H, m, H-5″, -OH), 3.69 (6H, m, 3 × -OH, H-2″, H-3″, H-4″); δ_C (100 MHz, DMSO-d_6) 161.8 (-CO), 161.4 (Ar-C), 158.5, 149.2 (Ar-C), 143.5 (Ar-C), 140.3 (Ar-C), 131.0, 129.4 (Ar-C), 128.3 (Ar-C), 128.1 (Ar-C), 127.4 (Ar-C), 123.7, 120.1 (Ar-C), 114.8 (Ar-C), 88.5 (C-1″), 81.0 (C-5″), 78.0 (C-3″), 73.1 (C-4″), 70.6 (C-2″), 61.7 (C-6″), 56.4 (-OCH_3), 42.9 (-CH_2); HRMS: $[M+H]^+$, found 530.1408. $C_{24}H_{25}ClN_5O_7$ requires 530.1437.

4.51. 7-Chloro-2-(4-nitrophenyl)-3-[{1′-(1′′-deoxy-*β*-D-glucopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13k)

A mixture of **12k** (0.40 g, 0.56 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 30 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13k** (0.25 g, 90%) as a red solid; R_f (20% MeOH/$CHCl_3$) 0.20; mp 176-178 °C; $[\alpha]_D^{25}$ – 16.2 (c 0.1, CH_3OH); IR (ν_{max}): 3400, 1638, 1385, 1218, 771 cm^{-1}; δ_H (400 MHz, DMSO-d_6) 8.34 (2H, m, Ar-H, triazol-H), 8.23 (2H, m, Ar-H), 7.88 (2H, m, Ar-H), 7.70 (1H, m, Ar-H), 7.60 (1H, m, Ar-H), 6.74 (1H, m, H-1′′), 5.52 (1H, m, -OH), 5.29 (2H, m, -CH_2), 4.48 (1H, m, -OH), 4.08 (2H, m, 2 × -OH), 3.46 (3H, m, H-5′′, H-6′′), 3.38 (1H, m, H-3′′), 3.22 (2H, m, H-2′′, H-4′′); δ_C (100 MHz, DMSO-d_6) 160.8 (-CO), 140.9, 139.9 (Ar-C), 130.2, 128.9 (Ar-C), 128.5 (Ar-C), 128.0 (Ar-C), 127.0 (Ar-C), 125.9 (Ar-C), 124.4 (Ar-C), 124.0 (Ar-C), 123.1, 118.1 (Ar-C), 114.0 (Ar-C), 87.9 (C-1′′), 79.6 (C-5′′), 77.3 (C-3′′), 72.4 (C-4′′), 70.0 (C-2′′), 61.1 (C-6′′), 41.8 (-CH_2); HRMS: $[M+H]^+$, found 545.1203. $C_{23}H_{22}ClN_6O_8$ requires 545.1182.

4.52. 7-Chloro-2-(4-nitrophenyl)-3-[{1′-(1′′-deoxy-*β*-D-galactopyranos-1′′-yl)-1′*H*-1′,2′,3′-triazol-4′-yl}methyl]quinazolin-4(3*H*)-one (13l)

A mixture of **12l** (0.40 g, 0.56 mmol) and NaOMe in methanol (15 mL) was stirred at room temperature for 30 min. The reaction mixture was neutralized by Amberlite IR-120-H^+ ion-exchange resin, followed by filtration and the solvent evaporated in vacuo to give the title compound **13l** (0.25 g, 89%) as a yellow solid; R_f (20% MeOH/$CHCl_3$) 0.21; mp 158-160 °C; $[\alpha]_D^{25}$ – 8.2 (c 0.1, CH_3OH); IR (ν_{max}): 3400, 1643, 1402, 1215, 758 cm^{-1}; δ_H (500 MHz, DMSO-d_6) 8.34 (2H, m, Ar-H, triazol-H), 8.22 (2H, m, Ar-H), 7.88 (2H, m, Ar-H), 7.70 (1H, m, Ar-H),

7.58 (1H, m, Ar-H), 6.73 (1H, m, H-1″), 5.47 (1H, m, -OH), 5.25 (2H, m, -CH_2), 4.12 (3H, m, 3 × -OH), 3.75 (2H, m, H-6″), 3.70 (4H, m, H-2″, H-3″, H-4″, H-5″); δ_C (125 MHz, DMSO-d_6) 160.9 (-CO), 156.2, 148.6, 142.5, 139.9, 130.3, 128.9, 128.3, 127.9, 127.0, 124.3, 124.0, 122.9, 119.9, 138.9 (Ar-C), 131.3, 129.5 (Ar-C), 128.7 (Ar-C), 127.6 (Ar-C), 126.9 (Ar-C), 125.1 (Ar-C), 124.7 (Ar-C), 123.6 (Ar-C), 122.7, 118.6 (Ar-C), 115.4 (Ar-C), 88.5 (C-1″), 79.5 (C-5″), 78.8 (C-3″), 74.0 (C-4″), 69.7 (C-2″), 60.8 (C-6″), 41.8 (-CH_2); HRMS: $[M+H]^+$, found 545.1183. $C_{23}H_{22}ClN_6O_8$ requires 545.1182.

4.53. Materials & methods

4.54. Cell culture

L6 skeletal muscle cells stably expressing rat GLUT4 with a *myc* epitope inserted in the first exofacial loop (L6-GLUT4*myc*), a kind gift of Dr Amira Klip, Program in Cell Biology, The Hospital for Sick Children, Toronto, Canada, were maintained in α-MEM supplemented with 10% FBS, blasticidin S (2 µg/mL), and 1% antibiotic/antimycotic solution (10,000 U/mL penicillin G, 10 mg/mL streptomycin, 25 µg/mL amphotericin B) in a humidified atmosphere of air and 5% CO_2 at 37 °C. Differentiation was induced by switching confluent cells to medium supplemented with 2% FBS. Experiments were performed in differentiated myotubes 6-7 days after seeding.

4.55. GLUT4 translocation

GLUT4 level at the cell surface of non-permeabilized L6-GLUT4*myc* myotubes was measured by an antibody-coupled colorimetric assay. After the indicated treatments, cells were washed in ice-cold PBS (154 mM NaCl, 5.6 mM Na_2HPO_4, 1.1 mM KH_2PO_4) supplemented with 1 mM

$CaCl_2$ and 1 mM $MgCl_2$ (pH 7.4). Cells were then fixed in 3% paraformaldehyde for 30 min and quenched in 100 mM glycine for 10 min, all at 4 °C. Cells were blocked in 5% skimmed milk for 15 min and then incubated with anti-*myc* antibody solution (1.0 µg/mL in PBS with 3% skimmed milk) for 1 h at 4 °C. After labeling, excess antibodies were removed by extensive washing in ice-cold PBS. Cell surface GLUT4-bound antibodies were probed by HRP-conjugated secondary antibodies followed by detection of bound HRP by O-phenylenediamide assay, as previously described.[67] The fraction of GLUT4 at the cell surface, measured in triplicate, was expressed as fold induction with respect to unstimulated cells.

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Author Contributions

This manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi…

5. References and notes

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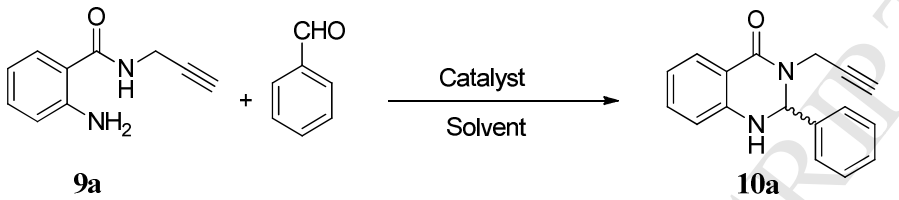
Tables

Table 1. Optimization of the reaction conditions for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one **10a**[a]

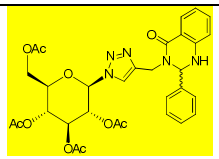
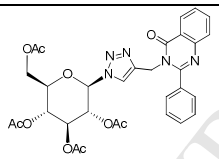
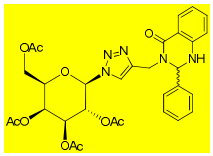
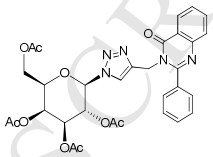
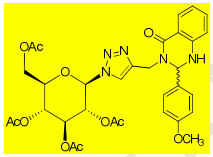
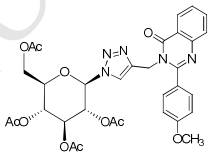
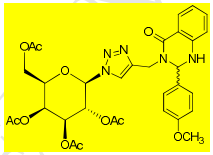
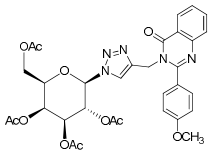
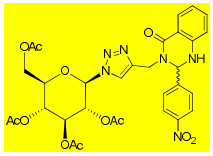
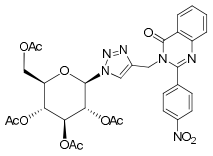
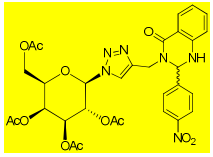
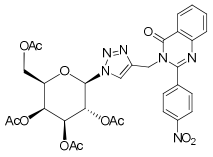
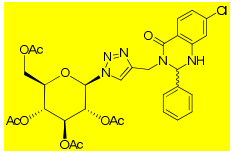
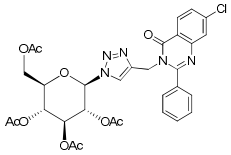


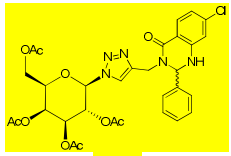
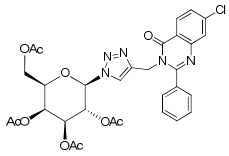
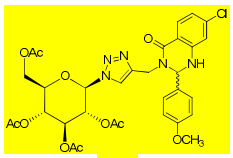
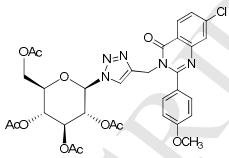
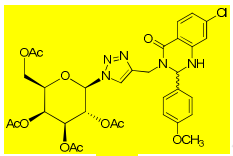
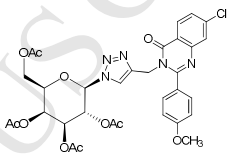
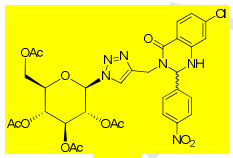
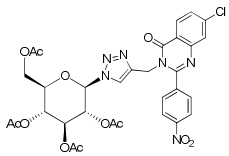
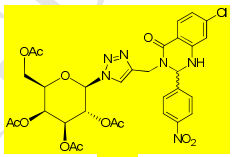
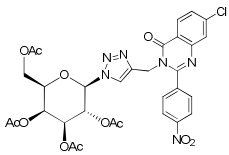
9a **10a**

Entry	Catalyst	Solvent	Conditions	Yield (%)[b]
1	$CuCl_2$ (20 mol%)	EtOH	reflux, 4 h	62
2	$InCl_3$ (20 mol%)	CH_3CN	rt,15 h	65
3	$Cu(OTf)_2$ (20 mol%)	toluene	rt, 36 h	76
4	$Cu(OTf)_2$ (20 mol%)	toluene	reflux, 8 h	60
5	$Cu(OTf)_2$ (20 mol%)	toluene	ultrasonic, 5 h	35
6	**$Cu(OTf)_2$ (20 mol%)**	**toluene**	**MW, 110 °C, High,[c] 30 min**	**93**
7	$Cu(OTf)_2$ (10 mol%)	toluene	MW, 110 °C, High,[c] 30 min	75
8	$Cu(OTf)_2$ (20 mol%)	EtOH	MW, 110 °C, High,[c] 30 min	no reaction
9	*p*-TsOH	toluene	rt, 36 h	no reaction
10	Amberlyst-15	toluene	rt, 48 h	no reaction

[a]*All reactions were performed with* ***9a*** *(1.0 mmol), benzaldehyde (1.1 mmol), catalyst, solvent (5 mL); in microwave vial (5-10 mL) sealed and placed in microwave reactor (400 W);* [b]*Isolated yield as pure product;* [c]*High-absorption condition*

Table 2. Peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12a-12l**) from glycosyl azides and 2,3-dihydroquinazolin-4(1*H*)-ones

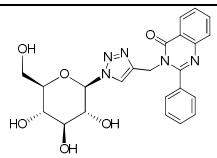
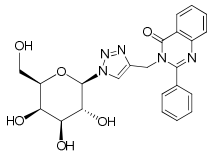
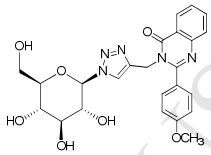
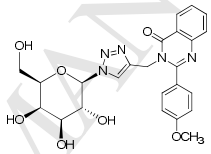
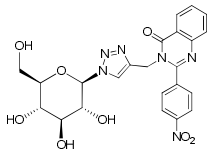
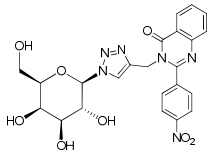
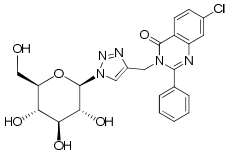
Entry	2,3-Dihydro quinazolin-4(1*H*)-ones	Glycosyl azide	Cyclo adduct	Peracetylated glycosyl quinazolin-4(3*H*)-one	Yield (%)[a]
1	**10a**	**I**	 **11a**	 **12a**	80
2	**10a**	**II**	 **11b**	 **12b**	78
3	**10b**	**I**	 **11c**	 **12c**	77
4	**10b**	**II**	 **11d**	 **12d**	75
5	**10c**	**I**	 **11e**	 **12e**	73
6	**10c**	**II**	 **11f**	 **12f**	71
7	**10d**	**I**			79

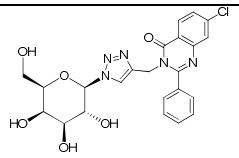
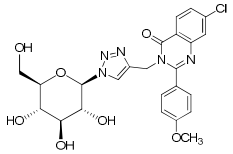
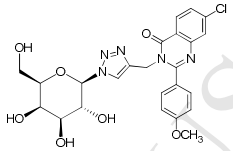
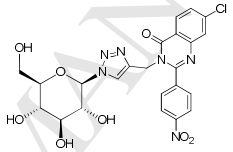
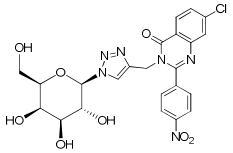
			11g	**12g**	
8	**10d**	**II**	 **11h**	 **12h**	76
9	**10e**	**I**	 **11i**	 **12i**	74
10	**10e**	**II**	 **11j**	 **12j**	73
11	**10f**	**I**	 **11k**	 **12k**	72
12	**10f**	**II**	 **11l**	 **12l**	70

[a] *Isolated yield as pure product*

Table 3: Synthesized deacetylated compounds **13a-l** from peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12a-l)**

Entry	**Peracetylated substrates**	**Deacetylated products**	**Yield (%)[a]**

1	**12a**	 **13a**	94
2	**12b**	 **13b**	92
3	**12c**	 **13c**	93
4	**12d**	 **13d**	91
5	**12e**	 **13e**	92
6	**12f**	 **13f**	90
7	**12g**	 **13g**	92

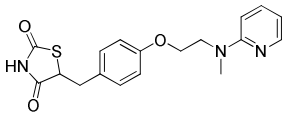
8	**12h**	 **13h**	91
9	**12i**	 **13i**	91
10	**12j**	 **13j**	89
11	**12k**	 **13k**	90
12	**12l**	 **13l**	89

[a] *Isolated yield as pure product*

Table 4. *In vitro* GLUT4 translocation activity (10 µM) of glycosyl quinazolin-4(3*H*)-ones

S. No	Compound	GLUT4 translocation (Fold Stimulation)
1	**10a**	1.06
2	**10b**	1.27
3	**10c**	1.22

4	**10d**	1.16
5	**10e**	1.24
6	**10f**	1.21
7	**12a**	0.60
8	**12b**	0.57
9	**12c**	Nil
10	**12d**	**1.18**
11	**12e**	0.51
12	**12f**	**1.08**
13	**12g**	0.40
14	**12h**	0.87
15	**12i**	ND
16	**12j**	ND
17	**12k**	0.84
18	**12l**	**1.09**
19	**13a**	0.55
20	**13b**	0.54
21	**13c**	0.52
22	**13d**	**1.18**
23	**13e**	0.73
24	**13f**	**1.09**
25	**13g**	0.59
26	**13h**	0.57

27	**13i**	0.79
28	**13j**	ND
29	**13k**	ND
30	**13l**	**1.35**
31	 Rosiglitazone (Std)	1.31

Nil – ≤ 0.2 fold response comparison to control, ND – Not determined

Legends and captions

Figure 1. Natural and synthetic examples of bioactive quinazolinones

Figure 2. Designing the structure for novel glycosyl quinazolinones

Figure 3. Relevant nOe and HMBC correlations in compound **12a**

Scheme 1. Synthesis of 2-amino-*N*-propargyl benzamide derivatives

Scheme 2. Synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones

Scheme 3. Synthesis of the glycosyl azides

Scheme 4. Synthesis of glycosyl quinazolin-4(3*H*)-ones

Table 1. Optimization of the reaction conditions for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one **10a**[a]

Table 2. Peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12a-12l**) from glycosyl azides and 2,3-dihydroquinazolin-4(1*H*)-ones

Table 3: Synthesized deacetylated compounds **13a-l** from peracetylated glycosyl triazolyl quinazolin-4(3*H*)-ones (**12a-l)**

Table 4. *In vitro* GLUT4 translocation activity (10 µM) of glycosyl quinazolin-4(3*H*)-ones

Figures

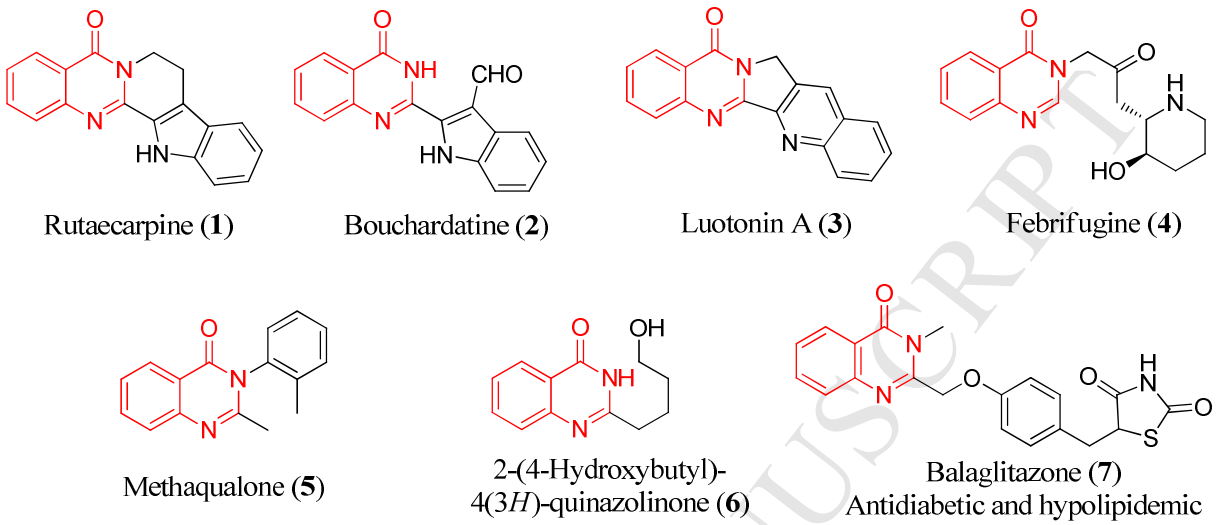


Figure 1. Natural and synthetic examples of bioactive quinazolinones

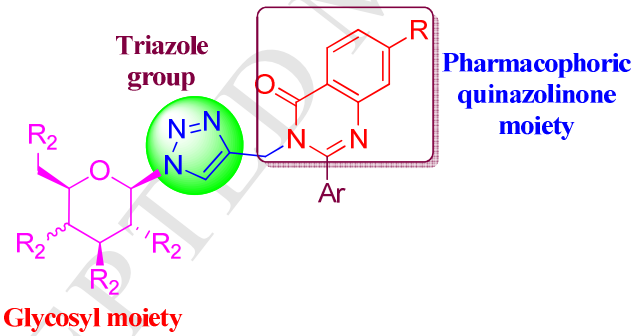


Figure 2. Designing the structure for novel glycosyl quinazolinones

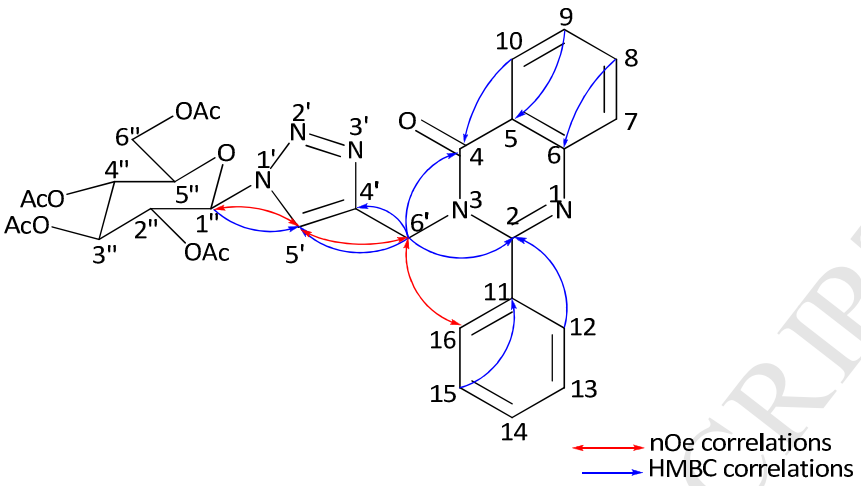
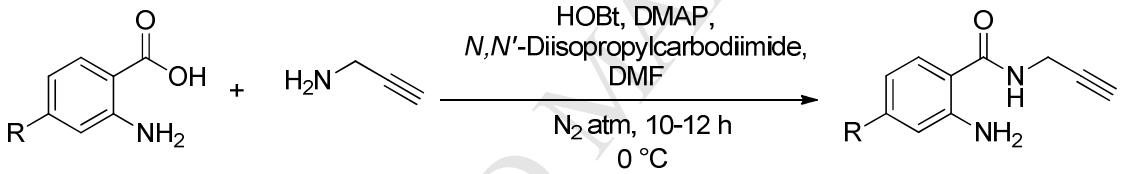


Figure 3. Relevant nOe and HMBC correlations in compound **12a**

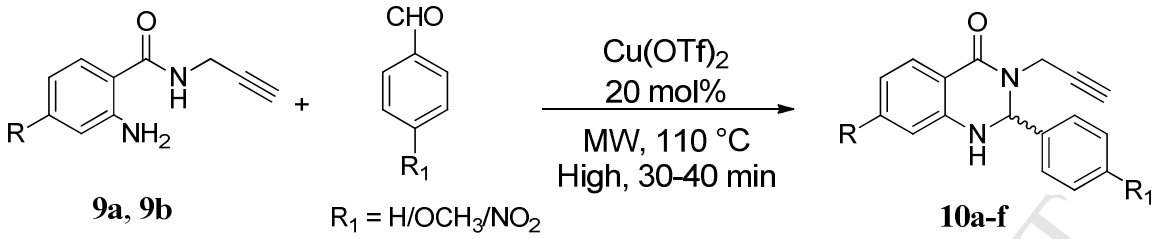
Schemes



8a, **8b**
8a; R = H
8b; R = Cl

9a, **9b**
9a; R = H, 89%
9b; R = Cl, 88%

Scheme 1. Synthesis of 2-amino-*N*-propargyl benzamide derivatives



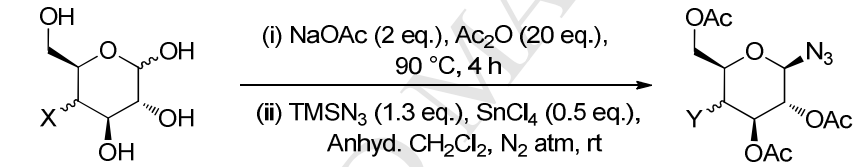
9a, 9b

R_1 = H/OCH_3/NO_2

10a-f

Comp.	R	R_1	Yield (%)
10a	H	H	93
10b	H	OCH_3	89
10c	H	NO_2	86
10d	Cl	H	88
10e	Cl	OCH_3	85
10f	Cl	NO_2	82

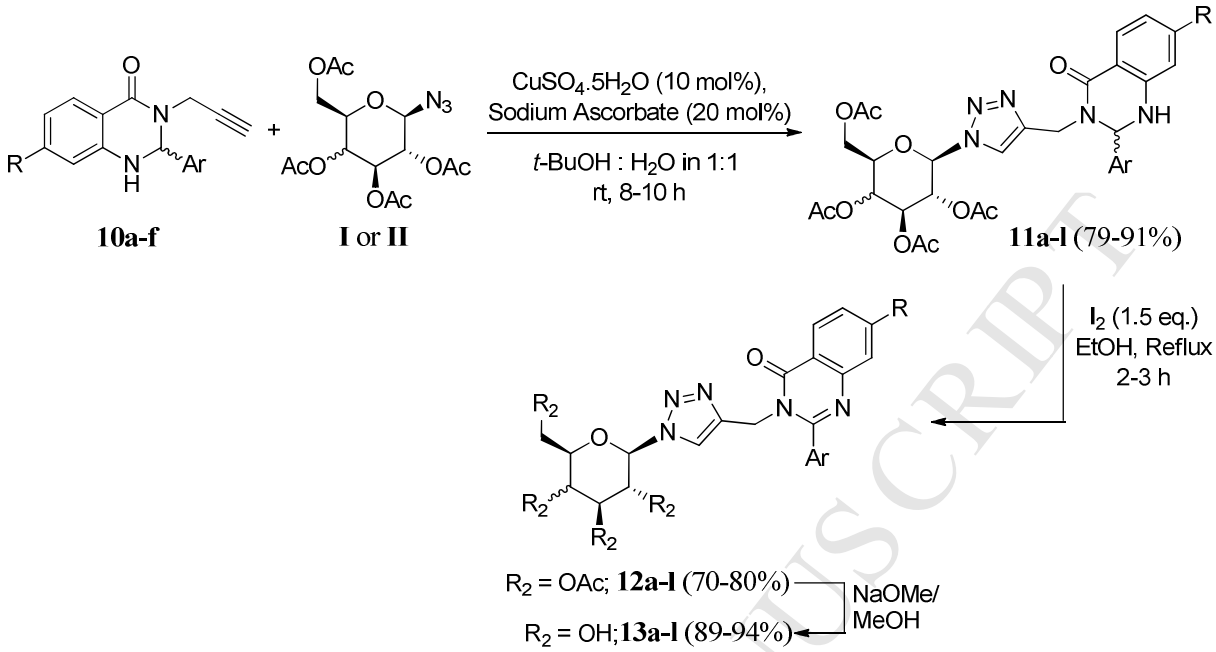
Scheme 2. Synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones



X = OH; Glucose
or
X = OH; Galactose

Y = OAc; **I**
or
Y = OAc; **II**

Scheme 3. Synthesis of the glycosyl azides



Scheme 4. Synthesis of glycosyl quinazolin-4(3*H*)-ones

Highlights

- Synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones using $Cu(OTf)_2$ under MW irradiation
- Short reaction time, simple work-up and mild reaction conditions
- Synthesis of 24 novel glycosyl triazolyl methyl quinazolin-4(3*H*)-ones
- Compound **13l** exhibited the most promising GLUT4 translocation activity