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Synthesis of novel *N*-glycoside derivatives via CuSCN-catalyzed reactions and their SGLT2 inhibition activities

Shao-Tao Bai [a,†], De-Cai Xiong [a,†], Youhong Niu [a], Yan-Fen Wu [a,*], Xin-Shan Ye [a,b,*]

[a] State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Xue Yuan Road No. 38, Beijing 100191, China

[b] National Engineering Research Center for Carbohydrate Synthesis, Jiangxi Normal University, Nanchang 330022, Jiangxi, China

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ABSTRACT

A convenient approach to the synthesis of novel triazole-*N*-glycoside derivatives was developed via CuSCN-catalyzed click reaction and Ullmann-type coupling reaction for the first time. The SGLT2 inhibitory activities of these synthetic *N*-glycosides were evaluated, and some compounds showed moderate SGLT2 inhibition activities at 100 nM. The results could benefit the discovery of new SGLT2 inhibitors for the treatment of diabetes.

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1. Introduction

Carbohydrate-based drug discovery has become a subject of an increasing interest. As a result, considerable efforts have been expanded in design and synthesis of carbohydrate-processing enzyme inhibitors or mimics of carbohydrate-protein interactions. Since *O*-glycosides are usually hydrolytically unstable, many carbohydrate analogues such as *C*-glycosides[1] and *S*-glycosides[2] have been synthesized as useful tools or therapeutic agents. In contrast, *N*-glycosides are less described in literature.[3] Actually, a *N*-glycoside known as acarbose carrying nitrogen atom between sugar and pseudosugar is currently used for the oral treatment of diabetes.[4] Some indole-*N*-glycosides (Fig. 1b) have also revealed inhibitory activities[5] against the sodium-glucose co-transporter 2 (SGLT2) at the luminal surface of cells lining the first segment of the proximal tubules responsible for more than 90% renal glucose reabsorption.[6] Moreover, to the best of our knowledge, SGLT2 inhibitors currently used as drugs or drug candidates for clinical trials are *C*-glycosides and *O*-glycosides (Fig. 1a), which generate some drawbacks such as carcinogenesis, while *N*-glycosides, which might solve these problems, have not gained as much attention especially SAR studies as their counterparts.[5,7] Thus, *N*-glycosides represent a new type of carbohydrate analogues with biological importance. On the other hand, heterocyclic components such as triazoles, which can interact with histamine H_4 receptor,[8] are very useful scaffolds in drug discovery and related fields.[8,9] Therefore, we want to prepare a series of new *N*-glycosides combining carbohydrates with triazoles. Due to the structural similarity to indole-*N*-glycosides, we will also test the SGLT2 inhibition activities of the synthetic compounds. For this purpose, we plan to synthesize these novel *N*-glycoside derivatives by using various carbohydrate azides and alkyne compounds via copper-catalyzed click or Ullmann chemistry under mild conditions (Fig. 1c).

Copper-catalyzed coupling reactions have gained rapid development in recent years and have played an important role in the fields of organic synthesis, medicinal chemistry, and material science.[10] Cai and co-workers developed a CuAAC/Ullmann C–C coupling tandem reaction to construct heterocycles,[11] and the similar results were also achieved by using CuI and strong base.[12,13] Shi and co-workers disclosed the synthesis of [1,2,3]triazole[5,1-*a*]isoquinoline derivatives using the copper-catalyzed cascade reaction,[14] whereas Lautens and co-workers synthesized 1,2,3-triazole-fused heterocycles via the Pd-catalyzed cyclization of 5-iodotriazole.[15] In spite of these advances, these copper (or other metal) catalyzed coupling reactions have not yet been applied to carbohydrate substrates for the synthesis of *N*-glycoside derivatives, and the approaches to prepare *N*-glycosides are limited. Based on the previous work, herein we report a convenient strategy

* Corresponding authors. Fax: +86 10 82805736; e-mail addresses: wuyanfen@pku.edu.cn (Y.-F. Wu), xinshan@bjmu.edu.cn (X.-S. Ye).

† These authors contributed equally to this work.

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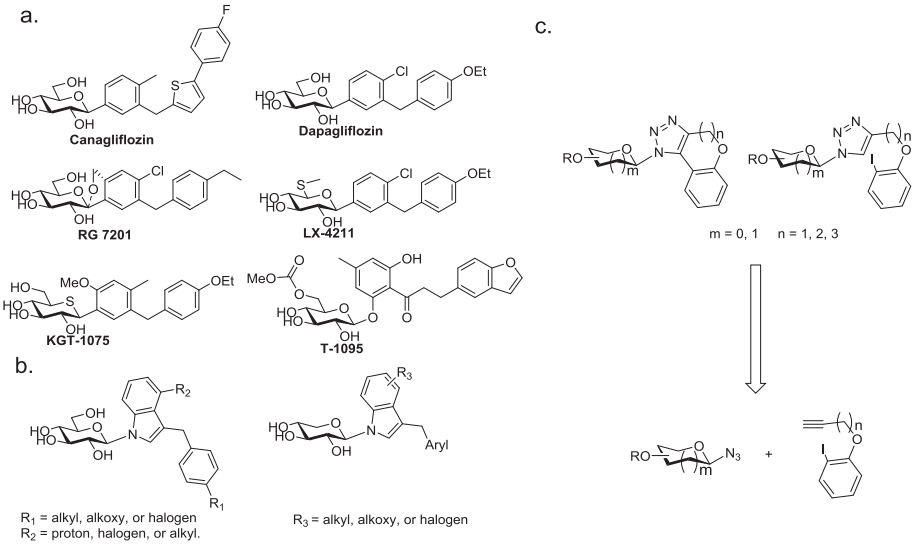


Fig. 1. a. Representative *C*-glycosides and *O*-glycosides as SGLT2 inhibitors in clinical trials or used as drugs; b. *N*-glycosides as SGLT2 inhibitors; c. the design of new triazole-*N*-glycosides.

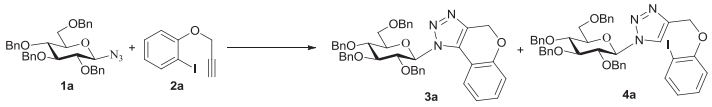
to synthesize triazole-*N*-glycoside derivatives and evaluate their SGLT2 inhibition activities.

2. Results and discussion

Initially, according to our design, using glucose azide **1a**[16] and alkyne compound **2a**[12] as the starting materials, we tried to perform the key copper-catalyzed click reaction followed by Ullmann-type coupling reaction. Under the conditions[11] of CuI as catalyst, DMSO as solvent, and K_2CO_3 as base at 70 °C, the coupling reaction of **1a** and **2a** afforded the target *N*-glycoside **3a** in less than 10% yield accompanied by **4a** as the major product (Table 1, entry 1). In order to improve the yield of **3a**, various reaction parameters such as base, solvent, and catalyst were screened (Table 1).

As shown in Table 1, based on the previous studies,[10b,12,14,15,17] after screening various inorganic bases ranging from mild bases to strong bases, it was found that Cs_2CO_3 is the best base with DMF as the solvent. The yield of **3a** was increased to 47% when Cs_2CO_3 was used (entry 2). To our surprise, silver salts such as Ag_2O had the ability to activate the C–I bond to some extent, but they did not have sound effects for the formation of product **3a** (entry 3). DMF seems to be the best solvent among all kinds of solvents both polar and nonpolar solvents checked (entries 2, 4–7). Interestingly, the use of CuSCN significantly improved the yield of product **3a** (76%) and enhanced the ratio of **3a**/**4a** (4.1/1), while other copper salts such as CuTC,[10b,18] CuOAc, CuCl,[19] CuBr,[13,20] CuCN, and Cu_2O did not give good results (entries 8–12, 14–15). When the amount of catalyst was increased to 150% mmol and the co-solvent (DMF/HMPA) was used, the ratio of **3a**/**4a** was further increased to 7.2/1 (entry

Table 1
Optimization of the reaction conditions for the synthesis of *N*-glycoside **3a**[a]



Entry	Base	T (°C)	Solvent	Catalyst	Ratio of **3a**/**4a**, total yield (%)[e]
1	K_2CO_3	70	DMSO	CuI[b]	1/9, 98
2	Cs_2CO_3	70	DMF	CuI[b]	1.1/1, 89
3	Ag_2O	70	DMF	CuI[b]	1/11.8, 98
4	Cs_2CO_3	70	dioxane	CuI[b]	1/8.6, 99
5	Cs_2CO_3	70	MeCN	CuI[b]	—, 97[f]
6	Cs_2CO_3	70	toluene	CuI[b]	—, 95[f]
7	Cs_2CO_3	70	DMSO	CuI[b]	1/1.3, 83
8	Cs_2CO_3	70	DMF	CuTC[c]	1.1/1, 100
9	Cs_2CO_3	70	DMF	CuOAc[c]	no reaction
10	Cs_2CO_3	70	DMF	CuCl[c]	1.6/1, 99
11	Cs_2CO_3	70	DMF	CuBr[c]	1.0/1, 87
12	Cs_2CO_3	70	DMF	CuSCN[c]	4.1/1, 95
13	Cs_2CO_3	70	DMF/HMPA(3/1)	CuSCN[d]	7.2/1, 92
14	Cs_2CO_3	70	DMF	CuCN[c]	1/1.9, 99
15	Cs_2CO_3	70	DMF	Cu_2O[c]	1/2.7, 89

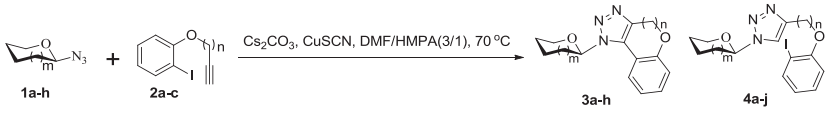
[a] Reaction conditions: **1a** (0.050 mmol), **2a** (0.075 mmol), base (0.150 mmol), solvent (2 mL).
[b] Catalyst used (20%).
[c] Catalyst used (100%).
[d] Catalyst used (150%), reaction for 10 h.
[e] Isolated yield.
[f] Trace amount of **3a**.

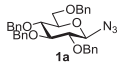
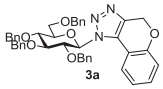
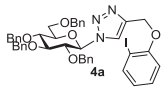
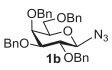
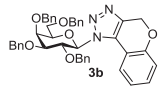
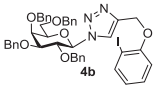
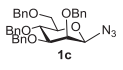
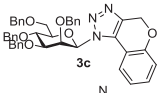
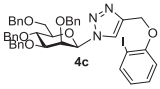
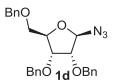
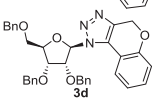
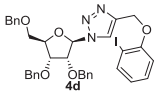
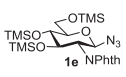
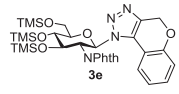
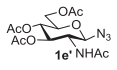
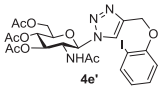
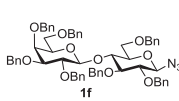
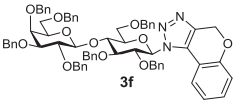
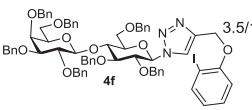
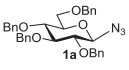
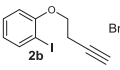
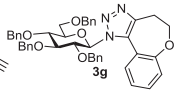
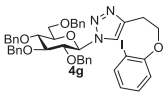
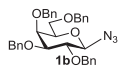
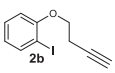
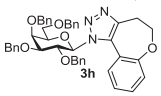
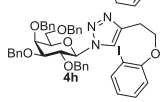
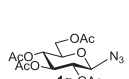
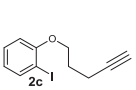
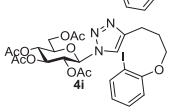
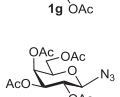
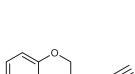
13). In addition, we also tried various additives and other methods such as click reaction followed by Heck reaction[15,17b,17c] to enhance the yield and reduce the amount of catalyst used, but unfortunately, all of these trials failed to achieve better results.

Under the optimized reaction conditions, the substrate scope of this coupling reaction was examined. As displayed in Table 2, for carbohydrate azides, glucosyl azide **1a**, galactosyl azide **1b**,[21] and aminoglucosyl azide **1e** (see Electronic Supplementary data) performed the reaction smoothly to generate the fully fused-triazole-*N*-glycosides with high selectivity (entries 1, 2, 5), while mannosyl azide **1c**[22] and lactosyl azide **1f**[16] just showed moderate selectivity (entries 3 and 7). The fully fused-triazole-*N*-riboside **3d** was also obtained from ribosyl azide **1d**[23] in this way (entry 4). After the successful construction of [6,6]ring-fused triazole-*N*-glycosides, the preparation of [6,7] or [6,8]ring-fused triazole-*N*-glycosides via this protocol was also tried. When using both glucosyl azide **1a** and galactosyl azide **1b** to react with alkyne **2b**,[12] the desired [6,7]ring-fused *N*-glycosides were obtained, but the ratio of **3g (3h)**/**4g (4h)** was not as good as their [6,6]ring-fused counterparts (entries 8 and 9). In addition, when alkyne **2c**[12] was coupled with azides **1g** and **1h**,[16] the [6,8]ring-fused triazole-*N*-glycosides were not afforded, and only uncyclized products **4i** and **4j** were gained instead (entries 10 and 11). Thus, a small library of triazole-*N*-glycoside derivatives was generated.

With these *N*-glycoside derivatives in hand, we next tried to get target compounds by deprotection operations (Table 3). Taking

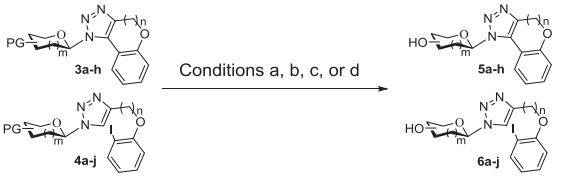
Table 2
Synthesis of triazole-*N*-glycoside derivatives[a].



entry	substrate **1**	substrate **2**	product **3**	product **4**	ratio of **3**/**4**, total yield[b]
1					7.2/1, 92%
2					5.6/1, 91%
3					3.3/1, 88%
4					1.4/1, 91%[c]
5					1/0, 72%[d]
6					0/1, 84%[f]
7					3.5/1, 89%
8					1/2, 86%[e]
9					1/1.9, 80%[e]
10					0/1, 77%[f]
11					0/1, 97%[f]

[a]Reaction conditions: substrate **1** (0.050 mmol), substrate **2** (0.075 mmol), Cs_2CO_3 (0.150 mmol), CuSCN (0.075 mmol), solvent (DMF/HMPA 3/1), reaction time (10 h). [b]Isolated yield. [c]Temperature (65 °C). [d]Temperature (80 °C), reaction time (2 h). [e]Temperature (80 °C). [f]Temperature (90 °C), solvent (DMF), catalyst (1 eq. of CuI), without base.

Table 3
Deprotection of triazole-*N*-glycoside derivatives.



entry	substrate	product	yield (%)[e]	entry	substrate	product	yield (%)[e]
1	3a	5a	100[a]	10	4e'	6e	66[d]
2	4a	6a	95[a]	11	3f	5f	59[a]
3	3b	5b	99[a]	12	4f	6f	55[a]
4	4b	6b	93[a]	13	3g	5g	96[a]
5	3c	5c	96[a]	14	4g	6g	67[a]
6	4c	6c	100[a]	15	3h	5h	88[a]
7	3d	5d	100[b]	16	4h	6h	52[a]
8	4d	6d	77[a]	17	4i	6i	94[d]
9	3e	5e	68[c]	18	4j	6j	53[d]

[a]Deprotection conditions: BCl_3, CH_2Cl_2, -73 °C to 0 °C, 36 h. [b]Conditions: $Pd(OH)_2/C$, H_2, r.t., 18 h. [c]Conditions: 1,2-diaminoethane, 80 °C, overnight; then pyridine, Ac_2O, overnight; then NaOMe/MeOH, r.t.. [d]Conditions: NaOMe/CH_2Cl_2/MeOH, r.t., 1.5 h. [e]Isolated yield.

triazole-*N*-glycoside **3b** as the model reaction, Pd/C- or $Pd(OH)_2/C$-catalyzed hydrogenolysis was tried to remove the benzyl groups, but it failed to complete the reaction. Fortunately, the deprotection was carried out smoothly in the presence of BCl_3 in CH_2Cl_2 at −73 °C to 0 °C for 36 h, affording compound **5b** in excellent yield. Through this protocol, the benzyl-containing *N*-glycosides were deprotected to provide target compounds in high to moderate yields (entries 1–6, 8, 11–16). For the substrates in lower yields such as **3f**, **4f**, **4g** and **4h**, it was found that the partial decomposition occurred during the BCl_3-mediated debenzylation process. Regarding *N*-glycoside **3d**, it totally decomposed in BCl_3 deprotection conditions, but was subjected to hydrogenolysis over $Pd(OH)_2/C$ in THF, successfully providing **5d** in quantitative yield. Compound **3e** was successively treated with 1,2-diaminoethane, acetic anhydride/pyridine, and sodium methoxide, yielding *N*-glycoside **5e**. Finally, the acetyl-containing *N*-glycosides were directly treated with sodium methoxide to obtain the corresponding target compounds.

To test the glucose transportation inhibition activities of these compounds, a cell-based assay was employed.[24] According to the results of cell-based assay (Fig. 2), most triazole-*N*-glycosides show some inhibition activities at the concentration of 100 nM when compared with Dapagliflozin, a SGLT2 inhibitor for the treatment of type 2 diabetes mellitus in clinical. Among these compounds, it was found that both *N*-glucoside derivatives **5a**, **6a**, **5g**, **6g**, **6i** and *N*-galactoside derivatives **5b**, **6b**, **5h**, **6h**, **6j** display inhibition effects with inhibition rates ranging from 10% to 32%. It was also found that compound series **6** have better SGLT2 inhibition activities than

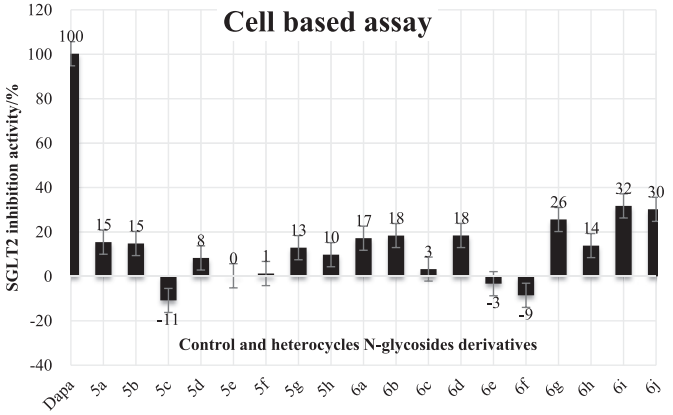


Fig. 2. Inhibitory rates of methyl-α-D-[U−^{14}C]glucopyranoside transportation on NIH3T3-hSGLT2 cell: each compound was tested at concentration of 100 nM. Values are mean values ±SEM.

compound series **5**. More importantly, our results firstly showed that *N*-galactosides and *N*-ribosides have the potential to be used as SGLT2 inhibitors other than the currently used glucoside derivatives and xyloside derivatives.[5a,25]

3. Conclusion

Herein, we firstly disclosed a convenient approach to synthesize various triazole-*N*-glycoside derivatives via the CuSCN-catalyzed coupling reaction. In this way, a small library of triazole-*N*-glycosides was constructed. The SGLT2 inhibitory activities of synthetic compounds were evaluated. The biological assay results showed that triazole-*N*-glycoside derivatives such as *N*-glucosides, *N*-galactosides, and *N*-ribosides might be served as SGLT2 inhibitors for the treatment of diabetes. Moreover, the generated triazole-*N*-glycoside derivatives may have other pharmaceutical applications.

4. Experimental

4.1. General information

All chemicals were purchased as reagent grade and used without further purification, unless otherwise noted. Dichloromethane (CH_2Cl_2), pyridine, and acetonitrile were distilled over calcium hydride (CaH_2). Methanol was distilled from magnesium. DMF and 1,4-dioxane were stirred with calcium hydride (CaH_2) and distilled under reduced pressure. All reactions were carried out under anhydrous conditions with freshly distilled solvents, unless otherwise noted. Reactions were monitored by analytical thin-layer chromatography on silica gel 60-F_{254} precoated on aluminium plates (E. Merck.). Spots were detected under UV (254 nm) and/or by staining with acidic ceric ammonium molybdate. Solvents were evaporated under reduced pressure and below 40 °C (bath). Column chromatography was performed on silica gel (200–300 mesh, TsingDao Ocean or 230–400 mesh, Merck), reversed phase column chromatography was performed on LiChroprep RP-18 (40–63 μm, Merck). ^{1}H NMR spectra were recorded on a Bruker 400M or 600M spectrometers at 25 °C. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ=0 ppm) or $CHCl_3$ (δ=7.26 ppm) in deuterated chloroform. ^{13}C NMR spectra were obtained by using the same NMR spectrometers and were calibrated with $CDCl_3$ (δ=77.00 ppm). Mass spectra were recorded using a Bruker APEX IV FT-MS (7.0 T) spectrometer. Analytical HPLC was performed on an Agilent 1200 series system equipped with an Eclipse XDB-C18 reverse phase column (250*4.6 mm, 5 μm). Optical rotations were recorded on an Autopol III Rudolph research automatic polarimeter.

4.2. Preparation procedures

4.2.1. General procedure of click reaction followed by Ullmann-type reaction catalyzed via CuSCN (A). After drying the glassware with flame under reduced pressure, a round flask was charged with carbohydrate azide (0.050 mmol), alkyne compound (0.075 mmol), Cs_2CO_3 (0.150 mmol) and CuSCN (0.075 mmol), evacuated and backfilled with argon three times. Anhydrous DMF (2.0 mL) and anhydrous HMPA (0.7 mL) were added via syringe under argon. The reaction mixture was heated at 70 °C for 10 h. The reaction was completed (detected by TLC, petroleum ether/EtOAc=2:1). After adding $NH_3\cdot H_2O$ (2 mL) and EtOAc (5 mL) into the reaction mixture, the organic phase was separated and the aqueous phase was extracted with EtOAc (5 mL×3). The combined organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give the desired product.

4.2.2. General procedure of click reaction catalyzed via CuI (B). A round flask was charged with carbohydrate azide (0.050 mmol), alkyne compound (0.075 mmol) and CuI (0.050 mmol), evacuated and backfilled with argon. DMF (2.0 mL) was added via syringe under argon. The reaction mixture was heated at 70 °C for 10 h. The reaction was completed (detected by TLC, petroleum ether/EtOAc=1:1). After adding $NH_3\cdot H_2O$ (2 mL) and EtOAc (5 mL) into the reaction mixture, the organic phase was separated and the aqueous phase was extracted with EtOAc (5 mL×3). The combined organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give the desired product.

4.2.3. General procedure of debenzylation reaction catalyzed via BCl_3 (C). A round flask was charged with triazole-*N*-glycoside (0.040 mmol), evacuated and backfilled with argon. Anhydrous dichloromethane (3.0 mL) was added under argon. The flask was placed in an alcohol-dry ice bath, followed by the addition of boron trichloride (0.30 mmol, 1 M solution in heptane). The reaction mixture was stirred at −78 °C for 2 h, then maintained at 0 °C for 36 h. Methanol was added to the mixture at −78 °C to quench the reaction. The resulting solution was concentrated and the residue was purified by column chromatography on silica gel or C-18 reversed-phase silica gel to give the pure product.

4.2.4. General procedure of debenzylation reaction catalyzed via $Pd(OH)_2/C$ (D). A mixture of triazole-*N*-glycoside (0.035 mmol) and catalytic amount of $Pd(OH)_2$/C in THF (4 mL) was stirred under 4 atm H_2 at ambient temperature for 36 h. The reaction was completed (detected by TLC, CH_2Cl_2/MeOH=9:2). The reaction mixture was filtered and the filtrate was concentrated under reduced pressure, followed by purification through column chromatography on silica gel to give the desired product.

4.2.5. General procedure of dephthaloylation and detrimethylsilylation followed by N-acetylation reaction (E). The reaction mixture of triazole-*N*-gycoside (0.030 mmol) and ethylenediamine (3.0 mL) was stirred under argon at 80 °C overnight. The reaction was completed (detected by TLC, CH_2Cl_2/MeOH=9:2). The reaction mixture was concentrated under reduced pressure, followed by adding Ac_2O (1.5 mL) and pyridine (3.0 mL). The mixture was allowed to stir at ambient temperature overnight and monitored by TLC. After completion, the reaction mixture was concentrated under reduced pressure, followed by adding MeOH (3.0 mL), CH_2Cl_2 (1.0 mL), and NaOMe (20.0 mg). After stirring at ambient temperature for 1.5 h, the reaction mixture was concentrated under reduced pressure and then purified by column chromatography on silica gel to give the desired product.

4.2.6. General procedure of deacetylation reaction (F). A reaction mixture of triazole-*N*-gycoside (0.030 mmol), NaOMe (20.0 mg) in MeOH/CH_2Cl_2 (3/1, 4.0 mL) was stirred under argon at ambient temperature for 1.5 h and monitored by TLC. After completion, the mixture was concentrated under reduced pressure and then purified by column chromatography on silica gel to give the desired product.

4.3. 1-(2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (3a)

The title compound was synthesized from **1a** and **2a** according to procedure A. Yield 80%, yellow oil: $[\alpha]_D^{21}$ −3.0 (*c* 0.70, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J*=7.4 Hz, 1H), 7.35–7.13 (m, 19H),

7.00 (dd, *J*=0.9, 8.2 Hz, 1H), 6.94–6.91 (m, 2H), 6.71 (td, *J*=7.7, 0.7 Hz, 1H), 5.87 (d, *J*=9.2 Hz, 1H), 5.44 (d, *J*=13.2 Hz, 1H), 5.33 (d, *J*=13.2 Hz, 1H), 4.93 (d, *J*=10.8 Hz, 1H), 4.89 (d, *J*=1.1 Hz, 2H), 4.68 (d, *J*=10.8 Hz, 1H), 4.55 (d, *J*=11.6 Hz, 1H), 4.48 (d, *J*=11.6 Hz, 1H), 4.40 (d, *J*=10.5 Hz, 1H), 4.25 (t, *J*=9.1 Hz, 1H), 4.14 (d, *J*=10.5 Hz, 1H), 4.00 (t, *J*=9.2 Hz, 1H), 3.91–3.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.02, 140.45, 138.14, 138.02, 137.96, 137.12, 130.80, 128.95, 128.66, 128.65, 128.54, 128.39, 128.27, 128.10, 128.07, 128.04, 128.02, 128.00, 127.91, 122.76, 117.94, 114.00, 87.88, 85.94, 78.59, 78.08, 77.07, 76.19, 75.43, 74.90, 73.75, 68.44, 64.21, 29.84; HRMS (ESI): Calcd for $C_{43}H_{41}N_3O_6Na$ $[M+Na]^+$, 718.2893; Found, 718.2893.

4.4. 4-[(2-Iodophenoxy)methyl]-1-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazole (4a)

The title compound was synthesized from **1a** and **2a** according to procedure A. Yield 11%, yellow oil: $[\alpha]_D^{21}$ –5.0 (*c* 0.39, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.74 (dd, *J*=7.8, 1.6 Hz, 1H), 7.33–7.16 (m, 19H), 6.97 (dd, *J*=8.3, 1.2 Hz, 1H), 6.95–6.92 (m, 2H), 6.69 (td, *J*=7.6, 1.3 Hz, 1H), 5.60 (d, *J*=9.1 Hz, 1H), 5.29 (s, 2H), 4.94–4.90 (m, 2H), 4.86 (d, *J*=10.8 Hz, 1H), 4.61 (d, *J*=10.7 Hz, 1H), 4.56 (d, *J*=12.1 Hz, 1H), 4.49 (d, *J*=12.1 Hz, 1H), 4.43 (d, *J*=10.5 Hz, 1H), 4.05–3.98 (m, 2H), 3.86–3.79 (m, 2H), 3.77–3.69 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.68, 139.56, 138.14, 137.82, 137.75, 136.91, 129.64, 128.55, 128.49, 128.45, 128.33, 128.06, 128.01, 127.87, 127.83, 127.79, 123.27, 122.44, 112.79, 87.69, 86.73, 85.37, 81.00, 78.17, 77.26, 75.86, 75.27, 75.08, 73.62, 68.41, 63.37, 29.78; HRMS (ESI): Calcd for $C_{43}H_{43}IN_3O_6$ $[M+H]^+$, 824.2197; Found, 824.2195.

4.5. 1-(2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (3b)

The title compound was synthesized from **1b** and **2a** according to procedure A. Yield 77%, yellow oil. $[\alpha]_D^{21}$ –17 (*c* 2.78, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J*=7.7 Hz, 1H), 7.36–7.25 (m, 15H), 7.14–7.08 (m, 3H), 7.02 (dt, *J*=7.8, 1.3 Hz, 1H), 6.90–6.88 (m, 3H), 6.06 (t, *J*=7.2 Hz, 1H), 5.89 (d, *J*=9.4 Hz, 1H), 5.44 (d, *J*=13.2 Hz, 1H), 5.27 (d, *J*=13.2 Hz, 1H), 5.04 (d, *J*=10.6 Hz, 1H), 4.81 (d, *J*=11.7 Hz, 1H), 4.77 (d, *J*=11.7 Hz, 1H), 4.64 (d, *J*=10.6 Hz, 1H), 4.64–4.50 (m, 3H), 4.38 (d, *J*=10.8 Hz, 1H), 4.15 (d, *J*=2.2 Hz, 1H), 4.05 (d, *J*=10.8 Hz, 1H), 3.94 (t, *J*=10.6 Hz, 1H), 3.81–3.76 (m, 2H), 3.68 (dd, *J*=9.2, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.69, 140.14, 138.50, 138.02, 137.67, 137.08, 130.46, 128.70, 128.65, 128.58, 128.48, 128.41, 128.26, 128.13, 128.06, 128.01, 127.95, 127.76, 126.49, 122.37, 117.33, 113.68, 89.04, 83.44, 76.63, 75.60, 75.02, 74.89, 74.00, 73.86, 73.15, 68.10, 64.10, 29.90; HRMS (ESI): Calcd for $C_{43}H_{41}N_3O_6Na$ $[M+Na]^+$, 718.2893; Found, 718.2899.

4.6. 4-[(2-Iodophenoxy)methyl]-1-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-1*H*-1,2,3−triazole (4b)

The title compound was synthesized from **1b** and **2a** according to procedure A. Yield 14%, yellow oil. $[\alpha]_D^{21}$ –13.0 (*c* 1.47, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.73 (d, *J*=7.4 Hz, 1H), 7.35–7.17 (m, 19H), 6.97–6.95 (m, 3H), 6.67 (t, *J*=7.5 Hz, 1H), 5.60 (d, *J*=9.0 Hz, 1H), 5.25 (s, 2H), 5.00 (d, *J*=11.4 Hz, 1H), 4.77 (d, *J*=11.8 Hz, 1H), 4.73 (d, *J*=11.8 Hz, 1H), 4.64 (d, *J*=11.5 Hz, 1H), 4.53 (d, *J*=10.5 Hz, 1H), 4.46 (d, *J*=11.8 Hz, 1H), 4.40 (d, *J*=11.8 Hz, 1H), 4.34 (t, *J*=9.2 Hz, 1H), 4.06–4.04 (m, 2H), 3.80 (t, *J*=6.4 Hz, 1H), 3.74 (dd, *J*=9.5, 2.2 Hz, 1H), 3.63–3.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.89, 144.41, 139.62, 138.57, 138.01, 137.69, 137.27, 129.67, 128.64, 128.59, 128.48, 128.43, 128.09, 128.05, 127.98, 127.92, 127.83, 127.72, 123.26, 122.01, 112.96, 88.11, 86.85, 83.07, 77.96, 76.50, 75.33, 74.84, 73.74, 73.40, 72.95, 68.30, 63.58; HRMS (ESI): Calcd for $C_{43}H_{43}IN_3O_6$ $[M+H]^+$, 824.2197; Found, 824.2195.

4.7. 1-(2,3,4,6-Tetra-*O*-benzyl-β-D-mannopyranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (3c)

The title compound was synthesized from **1c** and **2a** according to procedure A. Yield 68%, yellow oil: $[\alpha]_D^{21}$ –37.0 (*c* 0.95, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, *J*=8.0, 1.1, 1H), 7.33–7.23 (m, 15H), 7.13–7.05 (m, 4H), 6.90 (d, *J*=7.8 Hz, 1H), 6.86–6.84 (m, 2H), 6.57 (t, *J*=7.8 Hz, 1H), 6.04 (s, 1H), 5.33 (d, *J*=1.4, 2H), 4.98 (d, *J*=10.7 Hz, 1H), 4.71 (s, 2H), 4.68 (d, *J*=10.7 Hz, 1H), 4.59 (d, *J*=12.1 Hz, 1H), 4.51 (d, *J*=6.6, 1H), 4.49 (d, *J*=7.4, 1H), 4.35–4.29 (m, 3H), 3.85 (dt, *J*=11.2, 4.0 Hz, 2H), 3.78–3.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.01, 138.23, 138.05, 137.86, 136.99, 130.36, 129.05, 128.69, 128.59, 128.54, 128.15, 128.10, 128.06, 127.99, 127.91, 127.81, 127.77, 127.71, 122.03, 116.87, 114.61, 88.71, 82.83, 78.69, 76.27, 75.63, 74.89, 73.96, 73.68, 72.78, 68.65, 63.97, 29.84; HRMS (ESI): Calcd for $C_{43}H_{41}N_3O_6Na$ $[M+Na]^+$, 718.2893; Found, 718.2889.

4.8. 4-[(2-Iodophenoxy)methyl]-1-(2,3,4,6-tetra-*O*-benzyl-β-D-mannopyranosyl)-1*H*-1,2,3-triazole (4c)

The title compound was synthesized from **1c** and **2a** according to procedure A. Yield 20%, yellow oil: $[\alpha]_D^{21}$ –14.0 (*c* 0.83, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.74 (d, *J*=7.2 Hz, 1H), 7.32–7.21 (m, 19H), 7.12–7.11 (m, 2H), 6.99 (d, *J*=8.1 Hz, 1H), 6.71 (t, *J*=7.4 Hz, 1H), 5.87 (s, 1H), 5.24 (s, 2H), 4.91 (d, *J*=10.7 Hz, 1H), 4.70–4.60 (m, 5H), 4.53 (d, *J*=12.0 Hz, 1H), 4.22–4.19 (m, 2H), 4.11 (t, *J*=9.4 Hz, 1H), 3.85–3.76 (m, 3H), 3.69 (dd, *J*=9.6, 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.09, 139.67, 138.22, 138.09, 137.80, 137.47, 129.64, 128.71, 128.57, 128.52, 128.26, 128.23, 128.11, 127.97, 127.94, 127.82, 127.79, 123.26, 112.94, 86.97, 86.69, 82.67, 78.97, 76.84, 75.99, 75.53, 74.94, 74.03, 73.83, 72.72, 69.00, 63.61, 29.85; HRMS (ESI): Calcd for $C_{43}H_{43}IN_3O_6$ $[M+H]^+$, 824.2197; Found, 824.2196.

4.9. 1-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (3d)

The title compound was synthesized from **1d** and **2a** according to procedure A. Yield 53%, yellow oil: $[\alpha]_D^{21}$ –14.0 (*c* 0.62, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J*=7.6 Hz, 1H), 7.36–7.23 (m, 14H), 7.14–7.13 (m, 2H), 7.04–7.01 (m, 2H), 6.08 (d, *J*=2.0 Hz, 1H), 5.48 (d, *J*=13.2 Hz, 1H), 5.28–5.25 (m, 2H), 4.73–4.60 (m, 4H), 4.52 (s, 2H), 4.38 (s, 2H), 3.58–3.56 (m, 1H), 3.47–3.46 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.81, 139.60, 138.00, 137.68, 137.36, 130.96, 129.13, 128.60, 128.38, 128.31, 128.17, 128.14, 127.63, 127.57, 123.98, 122.58, 117.81, 113.89, 89.61, 83.15, 79.13, 78.09, 73.47, 73.30, 73.05, 69.77, 64.34, 29.87; HRMS (ESI): Calcd for $C_{35}H_{34}N_3O_5$ $[M+H]^+$, 576.2498; Found, 576.2494.

4.10. 4-[(2-Iodophenoxy)methyl]-1-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-1*H*-1,2,3-triazole (4d)

The title compound was synthesized from **1d** and **2a** according to procedure A. Yield 38%, yellow oil: $[\alpha]_D^{21}$ –5.0 (*c* 2.31, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.76 (dd, *J*=7.8, 1.3 Hz, 1H), 7.34–7.20 (m, 16H), 6.96 (d, *J*=7.7 Hz, 1H), 6.73 (dt, *J*=7.7, 0.9 Hz, 1H), 6.20 (d, *J*=2.1 Hz, 1H), 5.12 (d, *J*=12.3 Hz, 1H), 5.07 (d, *J*=12.3 Hz, 1H), 4.68 (d, *J*=12.0 Hz, 1H), 4.63 (d, *J*=12.0 Hz, 1H), 4.59 (d, *J*=11.8 Hz, 1H), 4.51 (d, *J*=11.7 Hz, 1H), 4.47–4.41 (m, 4H), 4.19 (t, *J*=5.8 Hz,1H), 3.77 (dd, *J*=10.9, 2.7 Hz, 1H), 3.57 (dd, *J*=10.9, 3.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.05, 143.82, 139.65, 137.64, 137.48, 137.04, 129.67, 128.68, 128.63, 128.32, 128.30, 128.18, 128.06, 128.01, 127.99, 123.24, 122.24, 113.07, 91.53, 86.88, 82.44, 80.72, 76.20, 73.66, 72.82, 72.71, 68.86, 63.35; HRMS (ESI): Calcd for $C_{35}H_{35}IN_3O_5$ $[M+H]^+$, 704.1621; Found, 704.1621.

4.11. 1-(3,4,6-Tri-*O*-trimethylsilyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (3e)

The title compound was synthesized from **1e** and **2a** according to procedure A. Yield 72%, white solid: $[\alpha]_D^{21}$ −20.0 (*c* 0.62, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J*=7.6 Hz, 1H), 7.76–7.65 (m, 4H), 7.32 (t, *J*=7.4 Hz, 1H), 7.11 (t, *J*=7.5 Hz, 1H), 7.06 (d, *J*=8.2 Hz, 1H), 6.72 (d, *J*=10.0 Hz, 1H), 5.33 (d, *J*=13.1 Hz, 1H), 5.21 (d, *J*=13.2 Hz, 1H), 4.81 (t, *J*=10.0 Hz, 1H), 4.69 (t, *J*=8.0 Hz, 1H), 4.04 (t, *J*=9.1 Hz, 1H), 3.92 (s, 2H), 3.79 (d, *J*=9.5 Hz, 1H), 0.25 (s, 9H), 0.08 (s, 9H), −0.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.66, 166.49, 154.15, 140.22, 134.38, 131.60, 131.26, 130.99, 129.00, 125.73, 123.86, 123.50, 122.64, 117.88, 114.26, 83.95, 79.82, 73.82, 72.03, 64.00, 61.10, 54.99, 0.96, 0.84, −0.32; HRMS (ESI): Calcd for $C_{32}H_{44}N_4O_7Si_3Na$ $[M+Na]^+$, 703.2415; Found, 703.2416.

4.12. 4-[(2-Iodophenoxy)methyl]-1-(2-acetylamino-2-deoxy-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazole (4e′)

The title compound was synthesized from 3,4,6-tri-*O*-acetyl-2-deoxy-2- acetylamino-β-D-glucopyranosyl azide (**1e′**)[26] and **2a** according to procedure B. Yield 84%, white solid: $[\alpha]_D^{21}$ −27.0 (*c* 2.08, pyridine); ^1H NMR (400 MHz, DMSO-d_6) δ 8.39 (s, 1H), 8.09 (d, *J*=9.3 Hz, 1H), 7.77 (dd, *J*=7.8, 1.6 Hz, 1H), 7.36 (dt, *J*=8.4, 1.6 Hz, 1H), 7.19 (dd, *J*=8.3, 1.1 Hz, 1H), 6.77 (dt, *J*=7.5, 1.2 Hz, 1H), 6.15 (d, *J*=10.0 Hz, 1H), 5.35 (t, *J*=9.8 Hz, 1H), 5.22 (s, 2H), 5.11 (t, *J*=9.8 Hz, 1H), 4.66–4.59 (m, 1H), 4.28–4.24 (m, 1H), 4.16 (dd, *J*=12.5, 5.1 Hz, 1H), 4.07 (dd, *J*=12.5, 2.2 Hz, 1H), 2.02 (s, 3H), 2.00 (s, 3H), 1.95 (s, 3H), 1.58 (s, 3H); ^1C NMR (100 MHz, DMSO-d_6) δ 170.04, 169.61, 169.38, 169.35, 156.57, 142.63, 139.09, 129.73, 129.36, 123.52, 123.07, 115.21, 113.27, 86.61, 84.70, 73.41, 72.40, 67.96, 62.09, 61.73, 51.95, 22.34, 20.55, 20.43, 20.29; HRMS (ESI): Calcd for $C_{23}H_{27}IN_4O_9Na$ $[M+Na]^+$, 653.0720; Found, 653.0735.

4.13. 1-(2,3,6-2′,3′,4′,6′-Hepta-*O*-benzyl-β-D-lactosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (3f)

The title compound was synthesized from **1f** and **2a** according to procedure A. Yield 69%, yellow oil: $[\alpha]_D^{21}$ −24.0 (*c* 2.87, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J*=7.5 Hz, 1H), 7.36–7.10 (m, 34H), 6.98 (d, *J*=8.3 Hz, 1H), 6.93–6.92 (m, 2H), 6.67 (t, *J*=7.3 Hz, 1H), 5.81 (d, *J*=9.2 Hz, 1H), 5.42 (d, *J*=13.2 Hz, 1H), 5.31 (d, *J*=13.2 Hz, 1H), 5.14 (d, *J*=10.2 Hz, 1H), 5.00 (d, *J*=11.4 Hz, 1H), 4.90 (d, *J*=11.3 Hz, 1H), 4.80 (d, *J*=11.9 Hz, 1H), 4.73 (t, *J*=7.9 Hz, 3H), 4.56 (t, *J*=11.9 Hz, 2H), 4.47 (t, *J*=6.3 Hz, 2H), 4.37 (t, *J*=10.2 Hz, 2H), 4.28 (d, *J*=11.9 Hz, 2H), 4.23 (d, *J*=8.7 Hz, 1H), 4.17 (d, *J*=11.3 Hz, 1H), 3.97–3.94 (m, 2H), 3.83 (t, *J*=8.3 Hz, 1H), 3.77 (t, *J*=8.9 Hz, 1H), 3.70 (d, *J*=10.8 Hz, 1H), 3.62 (d, *J*=9.8 Hz, 1H), 3.56 (d, *J*=10.5 Hz, 1H), 3.47–3.42 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.88, 140.33, 139.10, 138.85, 138.54, 138.15, 137.36, 130.67, 128.79, 128.55, 128.52, 128.44, 128.42, 128.32, 128.21, 128.09, 127.91, 127.88, 127.85, 127.73, 127.67, 127.57, 127.53, 127.49, 125.18, 122.80, 117.82, 113.94, 102.95, 87.78, 84.18, 82.72, 80.18, 78.24, 77.84, 75.94, 75.74, 75.67, 75.06, 74.89, 73.65, 73.60, 73.36, 73.22, 72.70, 68.22, 67.80, 64.17, 29.88; HRMS (ESI): Calcd for $C_{70}H_{69}N_3O_{11}Na$ $[M+Na]^+$, 1150.4830; Found, 1150.4896.

4.14. 4-[(2-Iodophenoxy)methyl]-1-(2,3,6-2′,3′,4′,6′-hepta-*O*-benzyl-β-D-lactosyl)-1*H*-1,2,3-triazole (4f)

The title compound was synthesized from **1f** and **2a** according to procedure A. Yield 20%, yellow oil: $[\alpha]_D^{21}$ −13.0 (*c* 1.86, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.73 (d, *J*=7.8 Hz, 1H), 7.35–7.12 (m, 34H), 6.96–6.92 (m, 3H), 6.68 (t, *J*=7.5 Hz, 1H), 5.59 (d, *J*=9.1 Hz, 1H), 5.26 (s, 2H), 5.14 (d, *J*=10.5 Hz, 1H), 4.98 (d, *J*=11.4 Hz, 1H), 4.85 (d, *J*=11.2 Hz, 1H), 4.77–4.68 (m, 4H), 4.57 (d, *J*=2.8 Hz, 1H), 4.54 (d, *J*=1.3 Hz, 1H), 4.49–4.45 (m, 2H), 4.37 (d, *J*=12.0 Hz, 1H), 4.33 (d, *J*=12.0 Hz, 1H), 4.26 (d, *J*=11.9 Hz, 1H), 4.14 (t, *J*=9.3 Hz, 1H), 4.03 (d, *J*=10.6 Hz, 1H), 3.93–3.70 (m, 5H), 3.64 (d, *J*=10.9 Hz, 1H), 3.55–3.50 (m, 2H), 3.44–3.38 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.80, 144.47, 139.64, 139.12, 138.80, 138.57, 138.26, 138.11, 137.27, 129.68, 128.54, 128.51, 128.46, 128.44, 128.40, 128.30, 128.19, 128.05, 127.90, 127.83, 127.76, 127.71, 127.56, 127.51, 127.44, 123.29, 121.86, 112.83, 102.82, 87.75, 86.81, 83.78, 82.67, 80.35, 80.08, 78.43, 75.85, 75.69, 75.56, 75.24, 74.85, 73.72, 73.56, 73.37, 72.74, 68.23, 67.76, 63.57, 29.83; HRMS (ESI): Calcd for $C_{70}H_{71}IN_3O_{11}$ $[M+H]^+$, 1256.4133; Found, 1256.4231.

4.15. 1-(2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranosyl)-4,5-dihydrobenzoxepino[4,5-*d*]-1*H*-1,2,3-triazole (3g)

The title compound was synthesized from **1a** and **2b** according to procedure A. Yield 29%, yellow oil: $[\alpha]_D^{21}$=0 (*c* 2.12, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J*=7.7 Hz, 1H), 7.34–7.27 (m, 14H), 7.21–7.15 (m, 6H), 7.06 (t, *J*=7.6 Hz, 1H), 6.89–6.82 (m, 2H), 5.43 (d, *J*=9.0 Hz, 1H), 4.92–4.85 (m, 3H), 4.77 (m, 1H), 4.67–4.49 (m, 6H), 4.10 (dt, *J*=11.6, 3.9 Hz, 1H), 3.87–3.73 (m, 5H), 3.53–3.45 (m, 1H), 3.29 (dt, *J*=17.0, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.93, 143.15, 138.36, 138.11, 137.92, 137.75, 132.40, 130.39, 128.64, 128.62, 128.52, 128.40, 128.13, 128.09, 128.06, 127.88, 127.82, 124.54, 122.43, 119.55, 86.55, 86.05, 79.63, 77.91, 77.69, 75.95, 75.35, 73.76, 72.02, 69.06, 28.47; HRMS (ESI): Calcd for $C_{44}H_{43}N_3O_6Na$ $[M+Na]^+$, 732.3050; Found, 732.3048.

4.16. 4-[2-(2-Iodophenoxy)ethyl]-1-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazole (4g)

The title compound was synthesized from **1a** and **2b** according to procedure A. Yield 57%, yellow oil: $[\alpha]_D^{21}$ −3.0 (*c* 0.97, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.73 (dd, *J*=7.8, 1.4 Hz, 1H), 7.35–7.23 (m, 14H), 7.18–7.09 (m, 5H), 6.88 (d, *J*=6.8 Hz, 2H), 6.76 (d, *J*=7.5 Hz, 1H), 6.69 (dt, *J*=7.7, 1.0 Hz, 1H), 5.60 (d, *J*=9.2 Hz, 1H), 4.93–4.84 (m, 3H), 4.60 (d, *J*=10.8 Hz, 1H), 4.56 (d, *J*=12.2 Hz, 1H), 4.48 (d, *J*=12.2 Hz, 1H), 4.44 (d, *J*=10.7 Hz, 1H), 4.22 (t, *J*=6.0 Hz, 2H), 4.06–4.00 (m, 2H), 3.86–3.79 (m, 2H), 3.76–3.69 (m, 3H) 3.30 (t, *J*=5.80 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.27, 144.81, 139.61, 138.32, 138.00, 137.94, 137.24, 129.68, 128.61, 128.54, 128.38, 128.14, 128.11, 128.05, 127.94, 127.84, 122.88, 122.42, 112.16, 87.75, 86.52, 85.55, 81.36, 78.23, 75.93, 75.34, 75.10, 73.72, 68.60, 68.01, 26.33; HRMS (ESI): Calcd for $C_{44}H_{45}IN_3O_6$ $[M+H]^+$, 838.2353; Found, 838.2328.

4.17. 1-(2,3,4,6-Tetra-*O*-benzyl-β-D-galactopyranosyl)-4,5-dihydro-benzoxepino [4,5-*d*]-1*H*-1,2,3-triazole (3h)

The title compound was synthesized from **1b** and **2b** according to procedure A. Yield 28%, yellow oil: $[\alpha]_D^{21}$ −34.0 (*c* 0.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J*=7.7 Hz, 1H), 7.38–7.21 (m, 16H), 7.18–7.15 (m, 3H), 7.12 (d, *J*=7.2 Hz, 1H), 6.89 (dd, *J*=7.2, 3.6 Hz, 3H), 5.43 (d, *J*=8.0 Hz, 1H), 5.09 (s, 1H), 5.04 (d, *J*=11.5 Hz, 1H), 4.77–4.67 (m, 4H), 4.60 (s, 1H), 4.53 (d, *J*=11.5 Hz, 1H), 4.43 (d, *J*=11.6 Hz, 2H), 4.15–4.13 (m, 1H), 4.02 (d, *J*=2.2 Hz, 1H), 3.86 (t, *J*=5.9 Hz, 1H), 3.76 (dd, *J*=9.6, 6.3 Hz, 1H), 3.68–3.63 (m, 2H), 3.51–3.43 (m, 1H), 3.30 (dt, *J*=17.0, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.75, 143.14, 138.57, 138.09, 137.97, 137.88, 132.15, 130.16, 128.65, 128.58, 128.47, 128.38, 128.33, 128.16, 128.01, 127.98, 127.87, 127.76, 127.75, 124.51, 122.24, 119.62, 84.01, 76.66, 76.42, 75.52, 74.76, 73.82, 73.58, 73.02, 71.98, 69.20, 29.84, 28.50; HRMS (ESI): Calcd for $C_{44}H_{43}N_3O_6Na$ $[M+Na]^+$, 732.3050; Found, 732.3052.

4.18. 4-[2-(2-Iodophenoxy)ethyl]-1-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosy-l)-1*H*-1,2,3-triazole (4h)

The title compound was synthesized from **1b** and **2b** according to procedure A. Yield 52%, yellow oil: $[\alpha]_D^{21}$ −10.0 (*c* 1.28, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.70 (dd, *J*=7.8, 1.4 Hz, 1H), 7.36–7.21 (m, 16H), 7.15–7.09 (m, 3H), 6.88 (dd, *J*=6.0, 1.8 Hz, 2H), 6.73 (d, *J*=8.3 Hz, 1H), 6.67 (dt, *J*=7.7, 1.0 Hz, 1H), 5.61 (d, *J*=9.1 Hz, 1H), 5.00 (d, *J*=11.4 Hz, 1H), 4.77 (d, *J*=12.0 Hz, 1H), 4.74 (d, *J*=12.2 Hz, 1H), 4.63 (d, *J*=11.5 Hz, 1H), 4.52 (d, *J*=10.7 Hz, 1H), 4.46 (d, *J*=11.7 Hz, 1H), 4.40 (d, *J*=11.8 Hz, 1H), 4.36 (t, *J*=9.4 Hz, 1H), 4.20–4.16 (m, 2H), 4.07–4.04 (m, 2H), 3.81 (t, *J*=6.4 Hz, 1H), 3.74 (dd, *J*=9.6, 2.6 Hz, 1H), 3.66–3.56 (m, 2H), 3.26 (t, *J*=6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.26, 144.68, 139.60, 138.70, 138.14, 137.75, 137.52, 129.60, 128.63, 128.60, 128.51, 128.28, 128.13, 128.10, 128.05, 127.94, 127.80, 127.73, 127.70, 122.75, 122.04, 112.07, 88.08, 86.40, 83.10, 78.33, 76.33, 75.33, 74.90, 73.76, 73.60, 72.94, 68.31, 67.93, 26.27; HRMS (ESI): Calcd for $C_{44}H_{45}IN_3O_6$ $[M+H]^+$, 838.2353; Found, 838.2348.

4.19. 4-[3-(2-Iodophenoxy)propyl]-1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazole (4i)

The title compound was synthesized from 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide **1g** and **2c** according to procedure B. Yield 77%, yellow oil: $[\alpha]_D^{21}$ −18 (*c* 1.21, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J*=7.7, 1.2 Hz, 1H), 7.61 (s, 1H), 7.30–7.26 (m, 1H), 6.81 (d, *J*=7.9 Hz, 1H), 6.71 (t, *J*=7.6 Hz, 1H), 5.89–5.84 (m, 1H), 5.45–5.39 (m, 2H), 5.26–5.22 (m, 1H), 4.30 (dd, *J*=12.6, 4.9 Hz, 1H), 4.16–4.08 (m, 1H), 4.06–3.99 (m, 3H), 3.02 (t, *J*=7.3 Hz, 2H), 2.27–2.21 (m, 2H), 2.08 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.55, 169.95, 169.42, 168.92, 157.35, 147.91, 139.43, 129.50, 122.57, 119.49, 112.20, 86.73, 85.71, 75.07, 72.71, 70.31, 67.76, 67.72, 61.61, 60.44, 28.51, 22.21, 20.77, 20.61, 20.59, 20.21; HRMS (ESI): Calcd for $C_{25}H_{31}IN_3O_{10}$ $[M+H]^+$, 660.1054; Found, 660.1064.

4.20. 4-[3-(2-Iodophenoxy)propyl]-1-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-1*H*-1,2,3-triazole (4j)

The title compound was synthesized from 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyra- nosyl azide **1h** and **2c** according to procedure B. Yield 97%, yellow oil: $[\alpha]_D^{21}$ −1.0 (*c* 2.06, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J*=7.7, 1.2 Hz, 1H), 7.66 (s, 1H), 7.30–7.26 (m, 1H), 6.81 (d, *J*=8.1 Hz, 1H), 6.71 (d, *J*=7.6 Hz, 1H), 5.82 (d, *J*=9.3 Hz, 1H), 5.56–5.51 (m, 2H), 5.24 (dd, *J*=10.3, 3.2 Hz, 1H), 4.23–4.11 (m, 3H), 4.09–4.01 (m, 2H), 3.03 (t, *J*=7.1 Hz, 2H), 2.26 (dd, *J*=13.4, 6.9 Hz, 2H), 2.22 (s, 3H), 2.05 (s, 3H), 2.01 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.45, 170.09, 169.93, 169.16, 157.41, 147.93, 139.48, 129.54, 122.60, 119.64, 112.21, 86.75, 86.30, 74.04, 70.91, 67.92, 67.80, 66.97, 61.32, 28.60, 22.30, 20.80, 20.78, 20.63, 20.37; HRMS (ESI): Calcd for $C_{25}H_{31}IN_3O_{10}$ $[M+H]^+$, 660.1054; Found, 660.1054.

4.21. 1-(β-D-Glucopyranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (5a)

The title compound was synthesized from **3a** according to procedure C. Yield 100%, white solid: $[\alpha]_D^{21}$ −48.0 (*c* 1.14, MeOH); ^1H NMR (400 MHz, CD_3OD) δ 7.84 (dd, *J*=7.8, 1.4 Hz, 1H), 7.33 (dt, *J*=8.1, 1.5 Hz, 1H), 7.12 (dt, *J*=7.6, 1.1 Hz, 1H), 7.05 (dd, *J*=8.2, 0.9 Hz, 1H), 5.80 (d, *J*=9.2 Hz, 1H), 5.37 (dd, *J*=15.6, 13.4 Hz, 2H), 4.25 (t, *J*=8.9 Hz, 1H), 3.95 (dd, *J*=12.2, 2.0 Hz, 1H), 3.81 (dd, *J*=12.2, 5.5 Hz, 1H), 3.75–3.71 (m, 1H), 3.66–3.60 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 155.40, 141.12, 132.08, 130.38, 125.97, 123.67, 118.81, 115.12, 89.24, 81.17, 78.61, 72.32, 70.79, 64.77, 62.28; HRMS (ESI): Calcd for $C_{15}H_{17}N_3O_6Na$ $[M+Na]^+$, 358.1015; Found, 358.1025.

4.22. 4-[(2-Iodophenoxy)methyl]-1-(β-D-glucopyranosyl)-1*H*-1,2,3-triazole (6a)

The title compound was synthesized from **4a** according to procedure C. Yield 95%, white solid: $[\alpha]_D^{21}$ −4.0 (*c* 1.56, MeOH); ^1H NMR (400 MHz, CD_3OD) δ 8.30 (s, 1H), 7.77 (dd, *J*=1.6, 7.8 Hz, 1H), 7.35 (dt, *J*=1.6, 7.8 Hz, 1H), 7.13 (dd, *J*=1.1, 8.3 Hz, 1H), 6.75 (dt, *J*=1.3, 7.6 Hz, 1H), 5.64 (d, *J*=9.2 Hz, 1H), 5.25 (s, 2H), 3.93 (t, *J*=9.0 Hz, 1H), 3.89 (dd, *J*=2.0, 12.3 Hz, 1H), 3.72 (dd, *J*=5.5, 12.2 Hz, 1H), 3.61–3.48 (m, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.51, 144.73, 140.75, 130.75, 124.93, 124.21, 114.08, 89.64, 87.02, 81.20, 78.51, 73.98, 70.88, 63.59, 62.38; HRMS (ESI): Calcd for $C_{15}H_{18}IN_3O_6Na$ $[M+Na]^+$, 486.0138; Found, 486.0135.

4.23. 1-(β-D-Galactopyranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (5b)

The title compound was synthesized from **3b** according to procedure C. Yield 99%, white solid: $[\alpha]_D^{21}$ −13.0 (*c* 0.89, MeOH); ^1H NMR (400 MHz, CD_3OD) δ 8.18 (d, *J*=7.8 Hz, 1H), 7.30 (dt, *J*=8.0, 1.5 Hz, 1H), 7.07 (dt, *J*=7.7, 1.1 Hz, 1H), 7.03 (d, *J*=8.2 Hz, 1H), 5.79 (d, *J*=9.3 Hz, 1H), 5.42 (d, *J*=13.3 Hz, 1H), 5.33 (d, *J*=13.3 Hz, 1H), 4.47 (t, *J*=9.4 Hz, 1H), 4.06 (d, *J*=3.0 Hz, 1H), 3.97 (t, *J*=5.8 Hz 1H), 3.90–3.80 (m, 2H), 3.75 (dd, *J*=9.4, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 155.32, 131.90, 130.09, 127.44, 123.59, 118.47, 115.20, 90.66, 80.19, 75.51, 70.33, 69.37, 64.73, 62.65; HRMS (ESI): Calcd for $C_{15}H_{17}N_3O_6Na$ $[M+Na]^+$, 358.1015; Found, 358.1009.

4.24. 4-[(2-Iodophenoxy)methyl]-1-(β-D-galactopyranosyl)-1*H*-1,2,3-triazole (6b)

The title compound was synthesized from **4b** according to procedure C. Yield 93%, white solid: $[\alpha]_D^{21}$ +4.0 (*c* 1.59, MeOH); ^1H NMR (400 MHz, CD_3OD) δ 8.37 (s, 1H), 7.78 (dd, *J*=7.8, 1.3 Hz, 1H), 7.35 (dt, *J*=8.4, 1.3 Hz, 1H), 7.13 (d, *J*=7.9 Hz, 1H), 6.76 (t, *J*=7.4 Hz, 1H), 5.61 (d, *J*=9.2 Hz, 1H), 5.26 (s, 2H), 4.17 (t, *J*=9.4 Hz, 1H), 3.98 (d, *J*=3.0 Hz, 1H), 3.87–3.69 (m, 4H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.47, 140.74, 130.75, 124.20, 114.01, 90.38, 87.00, 80.07, 75.30, 71.42, 70.40, 63.58, 62.45, 28.27; HRMS (ESI): Calcd for $C_{15}H_{18}IN_3O_6Na$ $[M+Na]^+$, 486.0138; Found, 486.0133.

4.25. 1-(β-D-Mannopyranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (5c)

The title compound was synthesized from **3c** according to procedure C. Yield 96%, white solid: $[\alpha]_D^{21}$ −32.0 (*c* 0.84, pyridine); ^1H NMR (400 MHz, DMSO-d_6) δ 8.27 (dd, *J*=8.6, 1.5 Hz, 1H), 7.26 (dt, *J*=7.9, 1.5 Hz, 1H), 6.99 (t, *J*=7.8 Hz, 2H), 6.16 (s, 1H), 5.41 (d, *J*=13.3 Hz, 1H), 5.34 (d, *J*=13.3 Hz, 1H), 5.12 (d, *J*=4.4 Hz, 1H), 5.08–5.01 (m, 1H), 4.66 (t, *J*=4.8 Hz, 1H), 4.10 (s, 1H), 3.80 (dd, *J*=10.8, 4.9 Hz, 1H), 3.67–3.43 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.37, 139.04, 130.18, 129.08, 128.41, 121.67, 116.61, 114.49, 87.58, 80.67, 72.97, 71.26, 66.18, 63.31, 60.87; HRMS (ESI): Calcd for $C_{15}H_{17}N_3O_6Na$ $[M+Na]^+$, 358.1015; Found, 358.1021.

4.26. 4-[(2-Iodophenoxy)methyl]-1-(β-D-mannopyranosyl)-1*H*-1,2,3-triazole (6c)

The title compound was synthesized from **4c** according to procedure C. Yield 100%, white solid: $[\alpha]_D^{21}$ −12.0 (*c* 1.05, MeOH); ^1H NMR (400 MHz, CD_3OD) δ 8.40 (s, 1H), 7.77 (dd, *J*=7.8, 1.5 Hz, 1H), 7.34 (dt, *J*=8.3, 1.6 Hz, 1H), 7.13 (dd, *J*=8.3, 1.2 Hz, 1H), 6.75 (dt, *J*=7.6, 1.2 Hz, 1H), 6.05 (d, *J*=1.1 Hz, 1H), 5.25 (s, 2H), 4.14 (m, 1H), 3.94 (dd,

J=12.1, 2.1 Hz, 1H), 3.80–3.71 (m, 3H), 3.57–3.53 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.55, 144.09, 140.75, 130.74, 125.36, 124.19, 114.14, 88.34, 87.06, 81.62, 75.01, 72.21, 67.83, 63.70, 62.65; HRMS (ESI): Calcd for $C_{15}H_{18}IN_3O_6Na$ $[M+Na]^+$, 486.0138; Found, 486.0127.

4.27. 1-(β-D-Ribofuranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (5d)

The title compound was synthesized from **3d** according to procedure D. Yield 100%, white solid: $[\alpha]_D^{21}$ −72.0 (*c* 0.86, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 7.79 (dd, J=7.8, 1.4 Hz, 1H), 7.32 (dt, J=8.2, 1.5 Hz, 1H), 7.11 (dt, J=7.7, 1.0 Hz, 1H), 7.05 (dd, J=8.2, 0.8 Hz, 1H), 6.15 (d, J=3.4 Hz, 1H), 5.44 (d, J=13.4 Hz, 1H), 5.32 (d, J=13.2 Hz, 1H), 5.15 (dd, J=4.8, 3.4 Hz, 1H), 4.51 (t, J=5.3 Hz, 1H), 4.22 (dt, J=5.3, 3.8 Hz, 1H), 3.74 (dd, J=12.2, 3.6 Hz, 1H), 3.59 (dd, J=12.2, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 155.25, 140.69, 132.14, 130.41, 124.94, 123.60, 118.80, 114.95, 92.57, 87.50, 74.93, 72.35, 64.84, 63.22; HRMS (ESI): Calcd for $C_{14}H_{15}N_3O_5Na$ $[M+Na]^+$, 328.0909; Found, 328.0910.

4.28. 4-[(2-Iodophenoxy)methyl]-1-(β-D-ribofuranosyl)-1*H*-1,2,3-triazole (6d)

The title compound was synthesized from **4d** according to procedure C. Yield 77%, white solid: $[\alpha]_D^{21}$ −31.0 (*c* 1.54, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 8.44 (s, 1H), 7.77 (dd, J=7.8, 1.6 Hz, 1H), 7.35 (dt, J=8.2, 1.5 Hz, 1H), 7.12 (dd, J=8.0, 1.0 Hz, 1H), 6.75 (dt, J=7.7, 1.1 Hz, 1H), 6.08 (d, J=3.8 Hz, 1H), 5.24 (s, 2H), 4.52 (t, J=4.5 Hz, 1H), 4.32 (t, J=5.1 Hz, 1H), 4.15 (dd, J=7.9, 4.2 Hz, 1H), 3.82 (dd, J=12.2, 3.2 Hz, 1H), 3.70 (dd, J=12.2, 4.2 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.52, 140.73, 130.74, 124.29, 114.30, 94.67, 87.24, 77.19, 71.91, 63.73, 62.81; HRMS (ESI): Calcd for $C_{14}H_{17}IN_3O_5$ $[M+H]^+$, 434.0213; Found, 434.0208.

4.29. 1-(2-Acetylamino-2-deoxy-β-D-glucopyranosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (5e)

The title compound was synthesized from compound **3e** according to procedure E. Yield 68%, white solid: $[\alpha]_D^{21}$ −19.0 (*c* 0.58, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 (d, J=7.3 Hz, 1H), 7.86 (d, J=8.6 Hz, 1H), 7.32 (dt, J=8.0, 1.4 Hz, 1H), 7.09 (dt, J=7.7, 1.0 Hz, 1H), 7.05 (dd, J=8.2, 0.8 Hz, 1H), 6.01 (d, J=9.9 Hz, 1H), 5.42 (d, J=13.3 Hz, 1H), 5.35–5.29 (m, 3H), 4.79 (t, J=5.4 Hz, 1H), 4.18–4.09 (m, 1H), 3.77 (dd, J=10.5, 5.8 Hz, 1H), 3.70–3.55 (m, 3H), 3.50–3.44 (m, 1H), 1.56 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.94, 153.40, 139.44, 130.45, 128.03, 125.49, 122.32, 117.40, 114.24, 86.34, 80.16, 73.77, 69.58, 63.34, 60.34, 53.38, 22.58; HRMS (ESI): Calcd for $C_{17}H_{20}N_4O_6Na$ $[M+Na]^+$, 399.1281; Found, 399.1264.

4.30. 4-[(2-Iodophenoxy)methyl]-1-(2-acetylamino-2-deoxy-β-D-glucopyranosyl)-1*H*-1,2,3-triazole (6e)

The title compound was synthesized from **4e′** according to procedure F. Yield 66%, white solid: $[\alpha]_D^{21}$ −6.0 (*c* 0.90, pyridine); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.26 (s, 1H), 7.91 (d, J=9.2 Hz, 1H), 7.77 (dd, J=7.7, 1.5 Hz, 1H), 7.36 (dt, J=8.2, 1.5 Hz, 1H), 7.20 (dd, J=8.3, 1.0 Hz, 1H), 6.77 (dt, J=7.6, 1.2 Hz, 1H), 5.74 (d, J=10.0 Hz, 1H), 5.30 (t, J=5.7 Hz, 2H), 5.20 (s, 2H), 4.70 (t, J=5.6 Hz, 1H), 4.14–4.06 (m, 1H), 3.71 (dd, J=10.7, 5.9 Hz, 1H), 3.59–3.43 (m, 3H), 3.32–3.26 (m, 1H), 1.61 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.13, 156.61, 149.60, 142.12, 139.06, 129.72, 123.24, 122.99, 113.22, 86.60, 86.07, 80.18, 74.00, 69.95, 62.11, 60.60, 54.33, 22.71; HRMS (ESI): Calcd for $C_{17}H_{21}IN_4O_6Na$ $[M+Na]^+$, 527.0403; Found, 527.0399.

4.31. 1-(β-D-lactosyl)-4*H*-benzopyrano[3,4-*d*]-1*H*-1,2,3-triazole (5f)

The title compound was synthesized from **3f** according to procedure C. Yield 59%, white solid: $[\alpha]_D^{21}$ −19.0 (*c* 1.32, pyridine); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.86 (d, J=7.7 Hz, 1H), 7.35 (t, J=7.9 Hz, 1H), 7.13–7.08 (m, 2H), 5.89 (d, J=9.2 Hz, 1H), 5.61 (d, J=5.9 Hz, 1H), 5.45 (d, J=13.4 Hz, 1H), 5.37 (d, J=13.4 Hz, 1H), 5.16 (d, J=4.4 Hz, 1H), 4.94 (s, 1H), 4.86 (d, J=5.2 Hz, 1H), 4.78 (t, J=5.6 Hz, 1H), 4.70 (d, J=5.0 Hz, 1H), 4.58 (d, J=4.5 Hz, 1H), 4.32 (d, J=7.1 Hz, 1H), 4.01–4.00 (m, 1H), 3.89–3.81 (m, 2H), 3.76–3.52 (m, 8H), 3.38 (t, J=9.5 Hz 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.41, 139.62, 130.77, 127.84, 125.05, 122.59, 117.57, 113.85, 103.82, 86.96, 79.73, 77.70, 75.59, 75.21, 73.32, 70.62, 70.29, 68.19, 63.52, 60.48, 59.83; HRMS (ESI): Calcd for $C_{21}H_{27}N_3O_{11}Na$ $[M+Na]^+$, 520.1543; Found, 520.1537.

4.32. 4-[(2-Iodophenoxy)methyl]-1-(β-D-lactosyl)-1*H*-1,2,3-triazole (6f)

The title compound was synthesized from compound **4f** according to procedure C. Yield 55%, white solid: $[\alpha]_D^{21}$ −6.0 (*c* 1.06, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 8.33 (s, 1H), 7.77 (d, J=7.8 Hz, 1H), 7.35 (t, J=7.4 Hz, 1H), 7.14 (d, J=8.2 Hz, 1H), 6.76 (t, J=7.5 Hz, 1H), 5.69 (d, J=9.1 Hz, 1H), 5.25 (s, 2H), 4.42 (d, J=7.6 Hz, 1H), 4.02 (t, J=9.1 Hz, 1H), 3.91 (s, 2H), 3.83–3.70 (m, 6H), 3.62 (dd, J=7.5, 4.5 Hz, 1H), 3.57 (d, J=7.7 Hz, 1H), 3.51 (dd, J=9.6, 3.0 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.51, 144.78, 140.75, 130.76, 124.91, 124.21, 114.04, 105.08, 89.37, 87.00, 79.61, 79.54, 77.15, 76.87, 74.80, 73.62, 72.53, 70.31, 63.56, 62.53, 61.45; HRMS (ESI): Calcd for $C_{21}H_{28}IN_3O_{11}Na$ $[M+Na]^+$, 648.0666; Found, 648.0662.

4.33. 1-(β-D-Glucopyranosyl)-4,5-dihydro-benzoxepino[4,5-*d*]-1*H*-1,2,3-triazole (5g)

The title compound was synthesized from compound **3g** according to procedure C. Yield 96%, white solid: $[\alpha]_D^{21}$ −48.0 (*c* 1.03, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 7.89 (dd, J=7.8, 1.3 Hz, 1H), 7.42 (dt, J=7.8, 1.4 Hz, 1H), 7.32 (dt, J=7.6, 1.1 Hz, 1H), 7.19 (dd, J=8.0, 0.9 Hz, 1H), 5.37 (d, J=9.0 Hz, 1H), 4.70–4.65 (m, 1H), 4.56–4.52 (m, 1H), 4.08–3.99 (m, 2H), 3.76–3.72 (m, 1H), 3.66–3.62 (m, 1H), 3.53–3.39 (m, 3H), 3.25–3.21 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 161.48, 131.72, 129.76, 125.71, 123.27, 120.23, 87.77, 81.17, 78.99, 72.79, 72.59, 71.24, 62.75, 29.12; HRMS (ESI): Calcd for $C_{16}H_{19}N_3O_6Na$ $[M+Na]^+$, 372.1172; Found, 372.1174.

4.34. 4-[2-(2-Iodophenoxy)ethyl]-1-(β-D-glucopyranosyl)-1*H*-1,2,3-triazole (6g)

The title compound was synthesized from compound **4g** according to procedure C. Yield 67%, white solid: $[\alpha]_D^{21}$ +2.0 (*c* 0.80, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 8.23 (s, 1H), 7.75 (dd, J=7.8, 1.5 Hz, 1H), 7.32 (dt, J=8.5, 1.5 Hz, 1H), 6.95 (dd, J=8.3, 0.9 Hz, 1H), 6.72 (dt, J=7.7, 1.1 Hz, 1H), 5.59 (d, J=9.2 Hz, 1H), 4.28–4.25 (m, 2H), 3.92–3.86 (m, 2H), 3.70 (dd, J=12.1, 5.6 Hz, 1H), 3.60–3.54 (m, 2H), 3.48 (t, J=9.4 Hz, 1H), 3.25 (t, J=6.3 Hz, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.74, 140.58, 130.74, 124.11, 123.83, 113.50, 89.55, 86.96, 81.09, 78.47, 74.09, 70.91, 69.00, 62.41, 26.83; HRMS (ESI): Calcd for $C_{16}H_{20}IN_3O_6Na$ $[M+Na]^+$, 500.0294; Found, 500.0288.

4.35. 1-(β-D-Galactopyranosyl)-4,5-dihydro-benzoxepino[4,5-*d*]-1*H*-1,2,3-triazole (5h)

The title compound was synthesized from compound **3h** according to procedure C. Yield 88%, white solid: $[\alpha]_D^{21}$ −37.0 (*c* 0.81, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 7.97 (dd, J=7.8, 1.3 Hz, 1H),

7.41 (dt, J=7.8, 1.4 Hz, 1H), 7.31 (dt, J=7.7, 1.1 Hz, 1H), 7.18 (dd, J=8.0, 1.0 Hz, 1H), 5.32 (d, J=9.1 Hz, 1H), 4.86 (t, J=9.2 Hz, 1H), 4.61–4.69 (m, 1H), 4.06 (dt, J=11.3, 4.1 Hz, 1H), 4.00 (d, J=3.2 Hz, 1H), 3.88–3.94 (m, 2H), 3.78–3.83 (m, 1H), 3.63 (dd, J=9.5, 3.3 Hz, 1H), 3.39–3.47 (m, 1H), 3.23 (td, J=17.0, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 161.44, 131.62, 129.94, 125.73, 123.18, 120.29, 88.41, 80.13, 75.83, 72.78, 70.53, 69.79, 62.80, 29.15; HRMS (ESI): Calcd for $C_{16}H_{19}N_3O_6Na$ $[M+Na]^+$, 372.1172; Found, 372.1166.

4.36. 4-[2-(2-Iodophenoxy)ethyl]-1-(β-D-galactopyranosyl)-1*H*-1,2,3-triazole (6h)

The title compound was synthesized from compound **4h** according to procedure C. Yield 52%, white solid: $[\alpha]_D^{21}$ +4.0 (c 1.94, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 8.26 (s, 1H), 7.75 (dd, J=7.8, 1.5 Hz, 1H), 7.32 (dt, J=8.5, 1.5 Hz, 1H), 6.96 (dd, J=8.2, 0.8 Hz, 1H), 6.72 (dt, J=7.7, 1.1 Hz, 1H), 5.56 (d, J=9.1 Hz, 1H), 4.28 (t, J=6.3 Hz, 2H), 4.17 (t, J=9.4 Hz, 1H), 3.98 (d, J=3.0 Hz, 1H), 3.84–3.68 (m, 4H), 3.26 (t, J=6.3 Hz, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.78, 140.58, 130.72, 123.85, 113.59, 90.30, 87.07, 79.89, 75.34, 71.44, 70.35, 69.01, 62.45, 26.85; HRMS (ESI): Calcd for $C_{16}H_{21}IN_3O_6$ $[M+H]^+$, 478.0475; Found, 478.0474.

4.37. 4-[3-(2-Iodophenoxy)propyl]-1-(β-D-glucopyranosyl)-1*H*-1,2,3-triazole (6i)

The title compound was synthesized from compound **4i** according to procedure F. Yield 94%, white solid: $[\alpha]_D^{21}$ −6.0 (c 1.27, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 8.01 (s, 1H), 7.74 (dd, J=7.8, 1.3 Hz, 1H), 7.30 (dt, J=8.4, 1.2 Hz, 1H), 6.91 (d, J=7.8 Hz, 1H), 6.71 (dt, J=7.4, 0.7 Hz, 1H), 5.58 (d, J=9.2 Hz, 1H), 4.07 (t, J=5.9 Hz, 2H), 3.91–3.86 (m, 2H), 3.71 (dd, J=12.1, 5.1 Hz, 1H), 3.59–3.47 (m, 3H), 3.01 (t, J=7.4 Hz, 2H), 2.22–2.15 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.83, 140.43, 130.70, 123.56, 113.41, 89.48, 87.04, 81.03, 78.44, 73.94, 70.83, 68.98, 62.34, 29.92, 23.05; HRMS (ESI): Calcd for $C_{17}H_{23}IN_3O_6$ $[M+H]^+$, 492.0632; Found, 492.0628.

4.38. 4-[3-(2-Iodophenoxy)propyl]-1-(β-D-galactopyranosyl)-1*H*-1,2,3-triazole (6j)

The title compound was synthesized from compound **4j** according to procedure F. Yield 53%, white solid: $[\alpha]_D^{21}$ +9.0 (c 1.13, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (s, 1H), 7.76 (dd, J=7.8, 1.4 Hz, 1H), 7.31 (dt, J=8.4, 1.5 Hz, 1H), 6.92 (d, J=8.2 Hz, 1H), 6.71 (dt, J=7.6, 1.1 Hz, 1H), 5.56 (d, J=9.2 Hz, 1H), 4.14 (t, J=9.5 Hz, 1H), 4.09 (t, J=6.0 Hz, 2H), 3.98 (d, J=3.1 Hz, 1H), 3.85–3.68 (m, 4H), 3.03 (t, J=7.4 Hz, 2H), 2.24–2.17 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.85, 140.45, 130.72, 123.58, 113.42, 90.34, 87.04, 79.94, 75.24, 71.42, 70.36, 68.95, 62.41, 29.88, 22.99; HRMS (ESI): Calcd for $C_{17}H_{22}IN_3O_6Na$ $[M+Na]^+$, 514.0451; Found, 514.0453.

4.39. Determination of SGLT2 inhibition rates of compounds on cell based assay

SGLT2 expressed NIH3T3 cells (2.5×10^5 cells per well in 100 μL of medium) were seeded on 96-well ScintiPlates (PerkinElmer) in high glucose DMEM containing 10% FBS and incubated at 37 °C under 5% CO_2. After three days, the medium was replaced with 2 mM sodium butyrate. For the uptake assay, cells were washed three times with 100 μL of either sodium buffer (137 mM NaCl, 5.4 mM KCl, 2.8 mM $CaCl_2$, 1.2 mM $MgCl_2$, 10 mM tris(hydroxymethyl)-aminomethane/*N*-2-hydroxyethylpiperazine-*N*′- ethane sulfonic acid [Tris/Hepes], pH 7.2) or sodium-free buffer (137 mM NaCl *N*-methyl-glucamine, 5.4 mM KCl, 2.8 mM $CaCl_2$, 1.2 mM $MgCl_2$, 10 mM Tris/Hepes, pH 7.2), followed by incubating with 100 μL of sodium or sodium-free buffer for 30 min. Tested compounds in 60 μL each of sodium or sodium-free buffer containing 8.3 μCi/mL methyl-α-D-[U−^{14}C]glucopyranoside (Perkinelmer) and 1/6 Mm methyl-α-D- glucopyranoside was added per well of the 96-well plate and incubated at 37 °C for 1 h. Then cells were washed three times with 100 μL of wash buffer (137 mM NaCl, 2.7 mM KCl, 10 mM $Na_2HPO_4\cdot12H_2O$, 2 mM KH_2PO_4), followed by solubilizing with 50 μL of 1‰ Triton-X 100 for 10 min. Their radioactivity was measured with a liquid scintillation counter by adding 150 μL of scintillation solution (Perkin–Elmer 1450-023).

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.05.108.

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