A Novel Class of Carbonic Anhydrase Inhibitors: Glycoconjugate Benzene Sulfonamides Prepared by "Click-Tailing"

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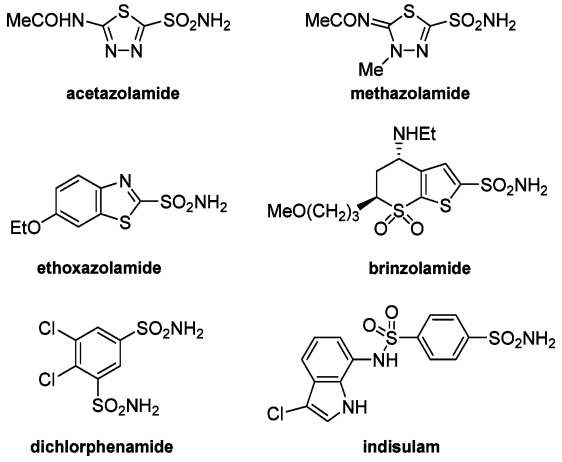
Aryl and heteroaryl sulfonamides ($ArSO_2NH_2$) are therapeutically used to inhibit the catalytic activity of carbonic anhydrases (CAs). Using a "click-tail" approach a novel class of glycoconjugate benzene sulfonamides have been synthesized that contain diverse carbohydrate−triazole tails. These compounds were assessed for their ability to inhibit three human CA isozymes in vitro: cytosolic hCA I and hCA II and transmembrane, tumor-associated hCA IX. This isozyme has a minimal expression in normal tissue but is overexpressed in hypoxic tumors and its inhibition is a current approach toward new cancer therapies. The qualitative structure−activity for all derivatives demonstrated that the stereochemical diversity present within the carbohydrate tails effectively interrogated the CA active site topology, to generate several inhibitors that were potent and selective toward hCA IX, an important outcome in the quest for potential cancer therapy applications based on CA inhibition.

Introduction

The carbonic anhydrase (CA, EC 4.2.1.1)[a] family of Zn(II) metalloenzymes is ubiquitous to all eukaryotic and most prokaryotic cells.[1] This enzyme efficiently catalyses the hydration of carbon dioxide (CO_2) to give bicarbonate anion (HCO_3^-) and a proton (H^+), a regulatory reaction that underpins fundamental physiological processes associated with pH control, ion transport, and fluid secretion.[2−4] For decades, inhibitors of CA have been a mainstay of human clinical intervention for a range of diseases; however, more recently a role for CA inhibition as an anticancer therapy has been identified owing to the overexpression of some CA isoforms (CA IX and CA XII) in cancer cells and a minimal expression in normal tissue. The latter has further increased interest in this enzyme family as a therapeutic target.[5−7] The classical recognition fragment for small molecules to bind the active site of CA is an aromatic sulfonamide moiety, $ArSO_2NH_2$.[1−3,8] The sulfonamide anion ($ArSO_2NH^-$) coordinates to the CA active site Zn(II) and so inhibits the catalytic ability of the enzyme. This aromatic sulfonamide group has served as a very reliable anchor upon which medicinal chemists have appended "tails" to deliver inhibitors with improved potency and desirable selectivity profiles, known in this field as "the tail approach" (there are 16 known human CA isozymes).[1] Clinically used CA inhibitors include acetazolamide, methazolamide, ethoxazolamide, brinzolamide, and dichlorophenamide, while indisulam is in phase II clinical trials as an anticancer agent to treat solid tumors.[6,7]



For drug development the physiochemical properties (for example, aqueous solubility, lipophilicity, stability, bioavailability) that make a compound a good drug must be considered alongside the goal to prepare compounds with desirable potency and selectivity profiles.[9] For poorly soluble chemotherapeutic drugs that are administered by intravenous injection (such as the taxanes) this balance has been achieved indirectly through solubilizing vehicle formulations. Unfortunately the solubilizing additives themselves exhibit adverse effects outside those of the drug, leading to a requirement for cotreatment with other medications, long drug infusion times, and sometimes even preventing the most relevant drug dose to be administered.[10] The development of drug-solubilizing strategies that are free from side effects caused by the formulation vehicle is thus of immense interest, particularly for chemotherapy applications; the recent development of ABRAXANE (human albumin bound paclitaxel) is evidence for the success of this strategy.[11]

An alternative approach to equip drug molecules with improved solubility and tolerability is to attach carbohydrate moieties to generate glycoconjugates.[12−15] This carbohydrate-based strategy has however not often received significant

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[a] Abbreviations: CA, carbonic anhydrase; 1,3-DCR, 1,3-dipolar cycloaddition reaction; HBTU, *O*-benzotriazol-1-yl-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate; AZA, acetazolamide; MZA, methazolamide; EZA, ethoxzolamide; DCP, dichlorophenamide; BRZ, brinzolamide; IND, indisulam

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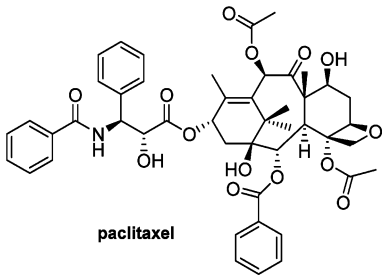


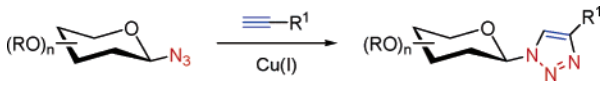
attention by the pharmaceutical industry, with sugars "sidelined" owing to the stigma of both weak binding and a poor ability to cross cell membranes, leaving more traditional small organic molecules to be pursued for drug discovery.[16] The cancer-relevant hCA isozymes, unlike the physiologically dominant cytosolic hCA I and hCA II, are transmembrane proteins with extracellular enzyme active sites. Owing to the success of the tail approach to generate potent CA inhibitors and the extracellular location of the hCA IX active site (circumventing the need for targeting drugs to cross cell membranes) we decided to explore tethering carbohydrate tails to the high-affinity $ArSO_2NH_2$ pharmacophore to synthesize sulfonamide glycoconjugates. We anticipated that the immense stereochemical diversity inherent to carbohydrate scaffolds might facilitate added opportunities to survey regions of biological space removed from the CA active-site core to exploit for improved CA affinity and isozyme selectivity. Despite the synthesis of a vast multitude of CA inhibitors utilizing the tail strategy and the potential benefits of appending carbohydrate moieties to drug molecules, the combination of these two strategies to generate CA inhibitors is essentially unexplored—there is just a single literature example[17] (nine compounds, which were not evaluated against cancer relevant CA isozymes). This relatively untouched medicinal chemistry landscape has served as the primary inspiration for the compounds synthesized and presented in the current study.

We have recently demonstrated the versatility of the 1,3-dipolar cycloaddition reaction (1,3-DCR, "click chemistry") to readily generate 1,4-disubstituted-1,2,3-triazole glycoconjugates from azido sugars and varied alkyne substrates (Scheme 1).[18] This high degree of versatility has encouraged us to now explore 1,3-DCR as a novel "click-tailing" strategy to append carbohydrate tails onto the CA $ArSO_2NH_2$ recognition motif to generate glycoconjugate CA inhibitors. Specifically, we report the synthesis of 28 benzene sulfonamides containing carbohydrate triazole tails. All compounds were investigated for their in vitro inhibition of hCA I, hCA II, and hCA IX. A number of derivatives were found to be selective for the cancer-associated isozyme hCA IX.

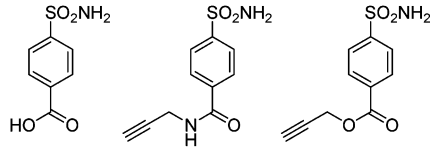
Results and Discussion

Chemistry. To facilitate our synthetic strategy it was necessary to synthesize CA recognition scaffolds that possessed dual functionality, both (i) an anchor for reliable CA affinity (i.e. an aryl sulfonamide), and (ii) either a terminal alkyne or azide moiety to act as the complementary partner for the 1,3-DCR with our panel of sugar building blocks. Many ester and amide derivatives of 4-carboxybenzenesulfonamide (**1**) are potent (low nanomolar) inhibitors of hCA II. The amide derivatives have also shown good in vivo activity and prolonged duration as antiglaucoma agents.[19] The *N*-propynyl amide derivative **2** and *O*-propynyl ester derivative **3** were thus designed as the scaffolds for 1,3-DCR with a panel of azido sugars. Scaffold **2** was synthesized by HBTU-mediated amide coupling of **1** with

Scheme 1. Cu(I) Catalyzed 1,3-Dipolar Cycloaddition Reaction (1,3-DCR) of Azido Sugars and Terminal Alkynes[18]



propargylamine, while scaffold **3** was synthesized by carbodiimide-mediated esterification of **1** with propargyl alcohol.



A panel of seven peracetylated azido sugars **a**−**g** were also prepared, with the carbohydrate derived from (**a**) glucose, (**b**) galactose, (**c**) arabinose, (**d**) *N*-acetylglucosamine, (**e**) glucuronic acid, and (**f**) methyl-α-D-glucopyranoside, respectively (Figure 1). Glycosyl azides **a**−**f** were synthesized by the stereoselective bimolecular displacement of the halide substituent of glycosyl halides precursors with an azide nucleophile,[20] while the methyl 2,3,4-tri-*O*-acetyl-6-azido-6-deoxy-α-D-glucopyranoside **g** was prepared from methyl-α-D-glucopyranoside as previously described.[21] The glycosyl halide precursors were prepared from the corresponding peracetates or purchased from commercial sources.

Scaffolds **2** and **3** were each reacted with the azido sugar panel **a**−**g** to generate the amide and ester series of peracetylated glycoconjugates, **2a**−**2g** and **3a**−**3g**, respectively (Scheme 2, Figure 2). When using catalyst loading as described by Sharpless,[22] the triazole-forming reaction was found to be sluggish, even at elevated temperatures. However, when using 10 mol % of the Cu(I) source and 20 mol % of ascorbate, triazole formation proceeded smoothly in all cases and under very mild conditions. Reactions were generally complete following 30 min of vigorous stirring (as evidenced by TLC). The *O*-acetate groups of the amide series **2a**−**2g** were subsequently removed using methanolic sodium methoxide to liberate the fully deprotected sugar analogues **2a′**−**2g′** in quantitative or near quantitative yields. These basic reaction conditions proved unsuitable for the synthesis of the ester series **3a′**−**3g′**, owing to the methoxide anion participating also in transesterification, whereby cleaving the CA anchor from the sugar triazole tail. More conveniently, the azido sugar panel were first de-*O*-acetylated to give the deprotected azido sugars **a′**−**g′** (R = Ac → R = H) which were then reacted with scaffold **3** to give the deprotected sugar ester series **3a′**−**3g′**. All new compounds were characterized using 1D ^1H and ^{13}C NMR spectroscopy, 2D NMR spectroscopy (gCOSY, gHSQC, gHMBC as required), elemental analysis, and HRMS.

Carbonic Anhydrase Inhibition. hCA I, II, and IX enzyme inhibition data (determined by assaying the CA catalyzed hydration of CO_2)[23] for **2**, **3** and the 28 new glycoconjugate sulfonamides are presented in Table 1. The selectivity ratios for inhibition of isozyme IX versus I and II are also given in Table 1. Data for clinically used CA inhibitors acetazolamide (AZA), methazolamide (MZA), ethoxzolamide (EZA), dichlorophenamide (DCP), brinzolamide (BRZ), and indisulam (IND) are included for comparison.

The parent amide scaffold **2** and ester scaffold **3** exhibited inhibition and isozyme selectivity similar to each other against the three hCA isozymes investigated. Compounds **2** and **3** had greatest efficacy at hCA II (K_is of 47 and 45 nM, respectively),

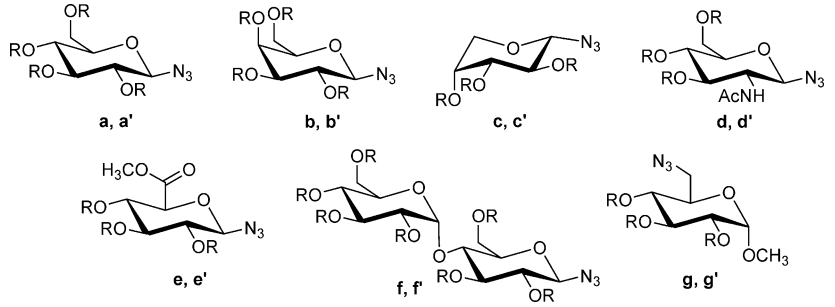
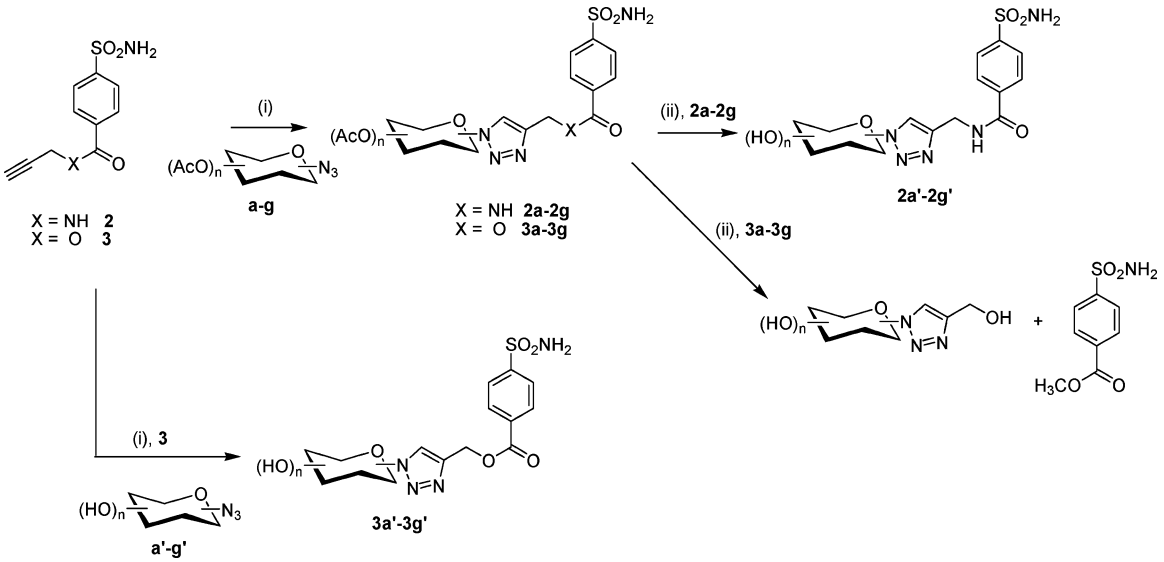


Figure 1. Azido sugar building block panel: **a**−**g** (R = Ac) and **a′**−**g′** (R = H).

Scheme 2[a]



[a] Reagents and conditions: (i) azide (0.2−0.5 M), acetylene (1 equiv), $CuSO_4 \cdot 5H_2O$ (0.1−0.2 equiv), sodium ascorbate (0.2−0.4 equiv), 1:1 t-BuOH/H_2O, 40 °C, 30 min to 1 h, 58−96%; (ii) $NaOCH_3$, CH_3OH, rt, 2 h, quantitative.

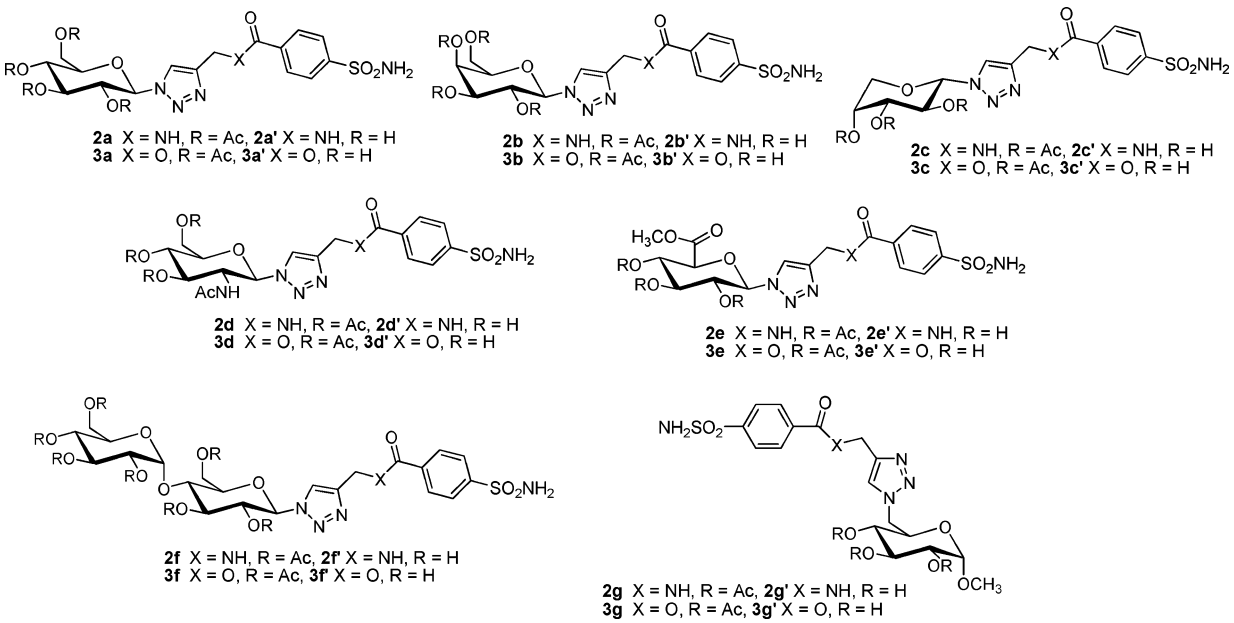


Figure 2. Glycoconjugate benzene sulfonamides.

approximately 2-fold weaker inhibition at hCA IX (113 and 104 nM, respectively) and an order of magnitude again weaker inhibition at hCA I (6100 and 4000 nM, respectively).

Isozyme hCA I. At hCA I the triazole-linked carbohydrate moiety had minimal effect on inhibition, with 26 of the 28 compounds exhibiting affinity similarly (μM range) to the parent compounds **2** and **3**. The two notable exceptions were compounds **3c′** and **3e′**; both contained an ester linkage and a deprotected (free hydroxy) sugar. Compounds **3c′** and **3e′** were 400−500-fold more potent than their parent ester scaffold **3** (K_is of 7.7 and 9.6 nM, respectively) and more potent than any of the standard sulfonamide inhibitors tested. This result was

Table 1. Inhibition and Selectivity Ratio Data for Sulfonamides **2** and **3**, the 28 New Glycoconjugates, and Standard Inhibitors against Human Isozymes hCA I, II, and IX

	K_i (nM)[a]			selectivity ratios[b]	
compd	hCA I[c]	hCA II[c]	hCA IX[d]	K_i(hCA I)/ K_i (hCA IX)	K_i (hCA II)/ K_i (hCA IX)
AZA	900	12	25	36	0.48
MZA	780	14	27	28.9	0.52
EZA	25	8	34	0.74	0.24
BRZ	15	9	42	0.36	0.21
DCP	1200	38	50	24	0.76
IND	31	15	24	1.30	0.63
2	6100	47	113	54.0	0.42
3	4000	45	104	38.5	0.43
2a	5600	384	430	13.0	0.89
2a′	2000	8.2	442	4.5	0.02
3a	2300	119	1238	1.86	0.10
3a′	4400	7.0	183	24.0	0.04
2b	8700	470	76	114.5	6.2
2b′	6600	7.4	360	18.3	0.02
3b	3600	6.8	132	27.3	0.05
3b′	5800	8.1	65	89.2	0.12
2c	2400	279	103	23.3	2.71
2c′	2700	128	420	6.4	0.30
3c	4900	7.3	114	43.0	0.06
3c′	7.7	5.8	96	0.08	0.06
2d	1200	45	124	9.68	0.36
2d′	9100	265	238	38.2	1.11
3d	5100	218	1200	4.25	0.18
3d′	4800	7.3	108	44.4	0.07
2e	5800	7.6	471	12.3	0.02
2e′	2400	378	23	104.3	16.4
3e	5400	7.0	125	43.2	0.06
3e′	9.6	7.2	241	0.04	0.03
2f	9200	7.5	221	41.6	0.03
2f′	9500	267	1100	8.64	0.24
3f	3900	423	130	30.0	3.25
3f′	3500	7.3	39	89.7	0.19
2g	10400	44	135	77.0	0.33
2g′	9300	90	204	45.6	0.44
3g	3400	50	54	63.0	0.93
3g′	3100	8.6	67	46.3	0.13

[a] Errors in the range of ±5−10% of the reported value, from three determinations. [b] The K_i ratios are indicative of isozyme selectivity. [c] Human (cloned) isozymes, by the CO_2 hydration method.[23−28] [d] Catalytic domain of human (cloned) isozyme, by the CO_2 hydration method.[23−28]

extremely encouraging, as it provided confirmation that the subtle structural differences in the sugar tail could indeed discriminate CA isozyme active site topology to substantially influence enzyme inhibition characteristics.

Isozyme hCA II. At hCA II the sugar triazole tail had a variable effect on CA inhibition—with some derivatives improved inhibition was observed while with others weaker inhibition was observed—when compared to the parent compounds **2** and **3**. The ester-linked deprotected sugars (**3a′**−**3g′**) had tightly grouped K_is, ranging from 5.8 to 8.6 nM, that were ∼5−6-fold more potent than the parent **3**. In striking contrast, the amide-linked deprotected sugars (**2a′**−**2g′**) did not exhibit the same tight grouping of K_is and only the glucose and galactose derivatives (**2a′** and **2b′**) paralleled the improved inhibition of their ester counterparts with K_is of 7.0 and 8.1 nM, respectively. The remaining amide-linked deprotected sugars (compounds **2c′**−**2g′**) had weaker inhibition than the parent **2**, with K_i values ranging from 90 to 378 nM. For the ester-linked series with the sugar acetates in place, derivatives **3b**, **3c**, and **3e** had K_is similar to the ester-linked deprotected sugar derivatives, again ∼5−6-fold more potent than the parent **3** (K_is ranging from 6.8 to 7.3 nM), while **3g** had a similar K_i to the parent **3** (50 vs 45 nM), and **3a**, **3d**, and **3f** all exhibited weaker K_is than the parent **3** or deprotected sugar counterparts (K_is ranging from 119 to 423 nM). For the acetylated sugars of the amide series (**2a**−**2g**) the derivative **2g** had 2-fold higher inhibition than the deprotected sugar derivatives **2g′** and similar inhibition to parent amide **2**. Derivatives **2d**, **2e**, and **2f** exhibited 6-, 50-, and 36-fold higher inhibition, respectively, than their deprotected sugar counterparts, while derivatives **2a**, **2b**, and **2c** were each weaker hCA II inhibitors than their deprotected sugar counterparts. In summary, for the seven different glycosyl triazole tails studied, the four groupings of amide, ester, sugar-OAc, or sugar-OH did not behave in a consistent direction with respect to hCA II inhibition. This in vitro data will be important for understanding future in vivo data, as it is clear that the acetates could serves as prodrugs in the in vivo environment.[29] Similarly to the results for hCA I, these results again demonstrate that the sugar tails interrogate the enzyme active site with an intricacy of interactions that permit marked discrimination of enzyme inhibition.

Isozyme hCA IX. At hCA IX the parent compounds **2** and **3** had K_is of 113 and 104 nM, respectively, approximately 2-fold weaker than hCA II inhibition and 40−50-fold more potent than hCA I inhibition. With five of the sugar tails (**b**, **c**, **e**, **f**, **g**) there was at least one compound of the grouping (amide, ester, sugar-OAc, or sugar-OH) that exhibited improved hCA IX inhibition over the parent scaffolds. The exceptions were the glucose tail **a** and the *N*-acetyl glucosamine tail **d**, in which the sugar triazole tail always lead to reduced inhibition when compared to the nonglycoconjugate parent scaffolds. For each sugar tail the amide sugar-OAc derivatives (**2x**) were more potent than sugar-OH derivatives (**2x′**) except for the glucuronic acid derivatives (**2e′** more potent than **2e**), while in the ester series this trend was completely reversed, with sugar-OH derivatives (**3x′**) being more potent than sugar-OAc derivatives (**3x**), again with the exception of the glucuronic acid derivatives (**3e** more potent than **3e′**). Compounds **2b**, **3b′**, **3c′**, **2e′**, **3f′**, **3g**, and **3g′** were all stronger inhibitors of hCA IX than the parents **2** and **3**, with K_is ranging from 23 to 96 nM. The strongest hCA IX inhibitor was the amide linked deprotected glucuronic acid derivative **2e′** (K_i = 23 nM). Importantly, this compound was also 16.4-fold selective for hCA IX over hCA II and 100-fold selective over hCA I. Glucuronate **2e′** has a similar K_i to the sulfonamide indisulam (24 nM) that is in phase II clinical trials as an anticancer agent; however, indisulam is not selective for hCA IX, whereas **2e′** is. There were several other compounds with mild hCA IX selectivity compared to hCA II; of note is the amide-linked acetylated galactose derivative **2b** with 6.2-fold selectivity (76 versus 470 nM). These results demonstrate that by tethering a sugar triazole tail onto the CA anchor pharmacophore it is possible to reverse the CA isozyme selectivity trends observed in the nonglycoconjugate parent compounds **2** and **3** and also all standard inhibitors, none of which are hCA IX selective.

Conclusions

Selective inhibition among isozymes is often a challenging hurdle in the drug discovery process; however, to maximize the benefits of any future therapies involving CA inhibition, it is essential to develop isozyme-specific compounds. Conservation of active site structure and topology within the CA enzyme family has made it difficult to target subtle isozyme differences by rational drug design. Here we have explored click-tailing carbohydrates onto the $ArSO_2NH_2$ CA pharmacophore as a drug-solubilizing and isozyme-differentiating strategy. This work presents a new class of CA inhibitors comprising triazole-tethered carbohydrate tails, the first of which to have been

generated through click chemistry. The qualitative structure−activity demonstrated that the stereochemical diversity within the carbohydrate tails effectively interrogated the CA active site topology, generating in some instances inhibitors with hCA IX selectivity, an important outcome in the quest for potential cancer therapy applications. Sugar tails may therefore prove to be a valuable approach to generate CA isozyme selective compounds. A powerful example is glucose (**2a**, **2a′**, **3a**, **3a′**) and galactose (**2b**, **2b′**, **3b**, **3b′**) epimer derivatives that have drastically different inhibition and selectivity profiles, yet the sole stereochemical difference is over 14 atoms removed from the sulfonamide moiety. The relative ease of synthetic access to azido sugars coupled with the venerability of the cycloaddition reaction has provided an efficient route to the carbohydrate-based CA inhibitors. We intend to more fully explore this click-tailing strategy for the development of CA inhibitors for therapeutic investigation.

Experimental Section

Chemistry. Reagents were purchased from Sigma Aldrich and Fluka chemical companies and were used without further purification. Solvents were dried and distilled where necessary prior to use or purchased as such from Sigma Aldrich. Reactions were monitored by TLC using Merck $F60_{254}$ silica plates with visualization of product bands by UV fluorescence λ_{254} and charring by 10% v/v ethanolic H_2SO_4. Flash chromatography was performed on Merck flash silica gel (0.04−0.06 mm). Melting points were acquired on a Gallenkamp melting point apparatus and are reported as uncorrected. NMR (^{1}H and ^{13}C {^{1}H}) spectra were recorded on a Varian Unity 400 MHz spectrometer at room temperature using DMSO-d_6 solvent unless otherwise stated. Chemical shifts are reported in δ (ppm) from a TMS internal standard (0.0 ppm). Coupling constants (J) are reported in hertz. High-resolution electrospray ionization mass spectra were performed in negative ion mode on an Apex III Bruker Daltonics 4.7T Fourier transform mass spectrometer (FTMS) fitted with an Apollo ESI source.

***N*-(Prop-2-ynyl)-4-sulfamoylbenzamide (2).** To a stirring solution of **1** (2.0 g, 9.9 mmol) and propargylamine (0.64 mL, 9.9 mmol, 1.0 equiv) in dry DMF (40 mL) were successively added *N*-hydroxybenzotriazole monohydrate (0.94 g, 6.6 mmol, 0.6 equiv), diisopropylethylamine (1.7 mL, 9.9 mmol, 1.0 equiv), and HBTU (3.8 g, 9.9 mmol, 1.0 equiv). The deep yellow solution was stirred at room temperature under nitrogen for 1 h when found complete by TLC. The mixture was concentrated under reduced pressure and ethyl acetate (40 mL) was added. The organic extract was washed with water (40 mL) and back-extracted with ethyl acetate (3 × 40 mL). The organic extracts were combined and washed with brine (50 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated to a crude white solid. Recrystallization from hot methanol:water (9:1) afforded the title compound **2** as a white crystalline solid (1.9 g, 8.2 mmol, 82%): R_f 0.58 (100% EtOAc); mp 216−217 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.12 (t, $^4J_{CH-CH}$ = 2.4 Hz, 1H, propynyl CH), 4.05 (dd, $^2J_{CH-NH}$ = 5.6 Hz, $^4J_{CH-CH}$ = 2.8 Hz, 2H, propynyl CH_2), 7.45 (br s, 2H, SO_2NH_2), 7.86−7.98 (m, 4H, Ph), 9.09 (t, $^3J_{NH-CH}$ = 5.6 Hz, 1H, CONH); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 29.03 (propynyl CH_2), 73.81 (propynyl CH), 81.67 (propynyl C), 126.37 (Ph CH), 128.64 (Ph CH), 137.34 (Ph C), 147.14 (Ph C), 165.62 (C═O); HRMS (ESI) calcd for $C_{10}H_9N_2O_3S^-$ 237.033 936, found 237.034 388. Anal. ($C_{10}H_{10}N_2O_3S$) C, H, N, S.

Prop-2-ynyl 4-sulfamoylbenzoate (3). To a stirring solution of **1** (2.0 g, 9.9 mmol) in dry DMF (40 mL) were successively added propargyl alcohol (1.17 mL, 19.8 mmol, 2.0 equiv), Et_3N (2.8 mL, 19.9 mmol, 2.0 equiv), and EDC (1.9 g, 9.9 mmol, 1.0 equiv). The solution was stirred at room temperature under N_2 for an additional 4 h. The mixture was then concentrated under reduced pressure and ethyl acetate (40 mL) was added. The organic extract was washed with saturated aqueous $NaHCO_3$ (40 mL) and back-extracted with ethyl acetate (40 mL). The organic layers were combined and washed with brine (40 mL), dried ($MgSO_4$), filtered, and evaporated. The crude oil was purified by flash silica chromatography (1:1 EtOAc:hexanes) to afford the title compound **3** as a white crystalline solid (0.91 g, 3.8 mmol, 38%): R_f 0.38 (4:6 hexanes:EtOAc); mp 110−111 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.63 (t, $^4J_{CH-CH}$ = 2.4 Hz, 1H, propynyl CH), 4.97 (d, $^4J_{CH-CH}$ = 2.8 Hz, 2H, propynyl CH_2), 7.55 (br s, 2H, SO_2NH_2), 7.93−8.13 (m, 4H, Ph); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 53.00 (propynyl CH_2), 78.12 (propynyl CH), 78.28 (propynyl C), 126.16 (Ph CH), 130.03 (Ph CH), 131.68 (Ph C), 148.32 (Ph C), 164.05 (C═O); HRMS (ESI) calcd for $C_{10}H_8NO_4S^-$ 238.017 952, found 238.017 407. Anal. ($C_{10}H_9NO_4S$) C, H, N, S.

Synthesis of glycosyl triazole aryl sulfonamides (2a−g, 3a−g). General Procedure 1. A mixture of the azide (1.0 equiv) and acetylene (1.0 equiv) was suspended in a *tert*-butyl alcohol and water mixture (1:1, 0.2−0.5 M final concentration). A solution of sodium ascorbate (0.2 equiv) in water, followed by a solution $CuSO_4 \cdot 5H_2O$ (0.1 equiv) in water, was successively added. The bright yellow suspension was stirred vigorously at 40 °C until TLC indicated reaction completion (generally within 2 h). The mixture was evaporated under reduced pressure and the resulting residue was purified by flash chromatography to yield pure material.

Preparation of deprotected glycosyl triazole aryl sulfonamides (2a′−g′ and 3a′−g′). General Procedure 2. Compounds **2a′−g′** were prepared by treating the acetylated precursors **2a−g** (final concentration of ∼0.1−0.2 M) with dry methanolic sodium methoxide (final pH 9−12). Reactions were found to be complete within 30 min by TLC. Neutralization of the solution by Amberlite IR-120 ion-exchange resin, followed by filtration and evaporation of the filtrate to dryness, afforded pure material by NMR. Likewise, the analogous esters **3a′−g′** were prepared by deprotecting the peracetylated glycosyl azides **a−f** or the 6-deoxy-6-azido glucoside **g** in the same way as described above, prior to the cycloaddition reaction with **3** (see Scheme 2).

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-1*H*-1,2,3-triazole (2a). The title compound was prepared according to general procedure 1 and isolated as a white solid (172 mg, 0.28 mmol, 86%): R_f 0.15 (100% EtOAc); mp 198−199 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.75 (s, 3H, OAc CH_3), 1.92 (s, 3H, OAc CH_3), 1.95 (s, 3H, OAc CH_3), 1.99 (s, 3H, OAc CH_3), 4.01−4.10 (m, 2H, $H_{6'}$, $H_{6''}$), 4.27−4.33 (m, 1H, $H_{5'}$), 4.50 (d, $^3J_{CH-NH}$ = 6.0 Hz, 2H, CH_2NH), 5.11−5.16 (m, 1H, $H_{4'}$), 5.47−5.52 (m, 1H, $H_{3'}$), 5.61−5.66 (m, 1H, $H_{2'}$), 6.28 (d, $^3J_{1'-2'}$ = 9.2 Hz, 1H, $H_{1'}$), 7.44 (s, 2H, SO_2NH_2), 7.86−7.99 (m, 4H, Ph H), 8.26 (s, 1H, triazole H), 9.22 (t, $^3J_{NH-CH}$ = 5.2 Hz, 1H, CH_2N*H*); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 20.55 (OAc CH_3), 20.87 (OAc CH_3), 21.00 (OAc CH_3), 21.14 (OAc CH_3), 35.46 (CH_2NH), 62.38 ($C_{6'}$), 68.13 ($C_{4'}$), 70.69 ($C_{3'}$), 72.91 ($C_{2'}$), 73.95 ($C_{5'}$), 84.46 ($C_{1'}$), 122.82 (triazole CH), 126.31 (Ph CH), 128.64 (Ph CH), 137.63 (Ph C), 146.24 (triazole C or Ph C), 146.96 (triazole C or Ph C), 166.05 (C═O), 169.23 (C═O), 170.11 (C═O), 170.34 (C═O), 170.83 (C═O); HRMS (ESI) calcd for $C_{24}H_{28}N_5O_{12}S^-$ 610.146 066, found 610.147 077. Anal. ($C_{24}H_{29}N_5O_{12}S \cdot 0.5H_2O$) C, H, N.

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(*β*-D-glucopyranosyl)-1*H*-1,2,3-triazole (2a′). Title compound was prepared according to general procedure 2 and isolated as a white solid (71 mg, 0.16 mmol, ∼100%); mp 205−210 °C (dec): R_f 0.15 (1:9 H_2O:CH_3CN); ^{1}H NMR (400 MHz, D_2O) δ 3.46−3.51 (m, 1H, $H_{4'}$), 3.55−3.60 (m, 1H, $H_{3'}$), 3.58−3.66 (m, 2H, H_5, $H_{6'}$), 3.74−3.79 (m, 1H, $H_{6''}$), 3.84−3.88 (m, 1H, H_2), 4.59 (s, 2H, CH_2NH), 5.61 (d, $^3J_{1'-2'}$ = 8.8 Hz, 1H, $H_{1'}$), 7.80−7.88 (m, 4H, Ph), 8.07 (s, 1H, triazole CH); ^{13}C {^{1}H} NMR (100 MHz, 2% D_2O in DMSO-d_6) δ 35.19 (CH_2NH), 60.53 ($C_{6'}$), 69.07 ($C_{4'}$), 72.41 ($C_{2'}$), 76.02 ($C_{3'}$), 79.04 ($C_{5'}$), 87.59 ($C_{1'}$), 123.36 (triazole CH), 126.44 (Ph CH), 128.44 (Ph CH), 137.71 (Ph C), 144.35 (triazole C or Ph C), 144.94 (triazole C or Ph C), 169.54 (C═O); HRMS (ESI) calcd for $C_{16}H_{20}N_5O_8S^-$ 442.103 87, found 442.103 042.

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(2′,3′,4′,6′-tetra-*O*-acetyl-*β*-D-galactopyranosyl)-1*H*-1,2,3-triazole (2b). The title compound was prepared according to the general procedure 1

and isolated as a white solid (174 mg, 0.28 mmol, 87%): R_f 0.11 (8:2 EtOAc:hexanes); mp 161−162 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.78 (s, 3H, OAc CH_3), 1.91 (s, 3H, OAc CH_3), 1.95 (s, 3H, OAc CH_3), 2.15 (s, 3H, OAc CH_3), 3.98 (dd, $^2J_{6'-6''}$ = 11.6 Hz, $^3J_{6'-5'}$ = 7.6 Hz, 1H, H$_{6'}$), 4.10 (dd, $^2J_{6''-6'}$ = 11.6 Hz, $^3J_{6''-5'}$ = 5.2 Hz, 1H, H$_{6''}$), 4.51 (d, $^3J_{CH-NH}$ = 5.5 Hz, 2H, CH_2NH), 4.52−4.55 (m, 1H, H$_{5'}$), 5.38−5.43 (m, 2H, H$_{3'}$, H$_{4'}$), 5.55−5.60 (m, 2H, H$_{2'}$), 6.21 (d, $^3J_{1'-2'}$ = 9.2 Hz, 1H, H$_{1'}$), 7.45 (s, 2H, SO_2NH_2), 7.86−7.99 (m, 4H, Ph), 8.16 (s, 1H, triazole H), 9.19 (t, $^3J_{NH-CH}$ = 5.1 Hz, 1H, CH_2NH); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 20.69 (OAc CH_3), 20.98 (OAc CH_3), 21.10 (OAc CH_3), 21.17 (OAc CH_3), 35.46 (CH_2NH), 62.25 (C$_{6'}$), 68.01 (C$_{4'}$), 68.30 (C$_{3'}$), 71.14 (C$_{2'}$), 73.63 (C$_{5'}$), 84.85 (C$_{1'}$), 123.13 (triazole CH), 126.29 (Ph CH), 128.66 (Ph CH), 137.63 (Ph C), 145.97 (triazole C or Ph C), 147.05 (triazole C or Ph C), 165.89 (C═O), 169.18 (C═O), 170.12 (C═O), 170.59 (C═O), 170.66 (C═O); HRMS (ESI) calcd for $C_{24}H_{28}N_5O_{12}S^-$ 610.146 066, found 610.147 458. Anal. ($C_{24}H_{29}N_5O_{12}S\cdot0.5H_2O$) C, H, N.

4-(4-Sulfamoylbenzamido)methyl-1-(β-D-galactopyranosyl)-1*H*-1,2,3-triazole (2b′). The title compound was prepared according to general procedure 2 and isolated as a white foam (72 mg, 0.16 mmol, ∼100%): R_f 0.13 (1:9 H_2O:CH_3CN); ^{1}H NMR (400 MHz, D_2O) δ 3.64−3.65 (m, 2H, H$_{6'}$, H$_{6''}$), 3.74 (dd, $^3J_{3'-2'}$ = 9.6 Hz, $^3J_{3'-4'}$ = 3.2 Hz, 1H, H$_{3'}$), 3.87 (m, 1H, H$_{5'}$), 3.95−3.96 (dd, $^3J_{4'-3'}$ = 3.4 Hz, $^3J_{4'-5'}$ = 0.8 Hz, 1H, H$_{4'}$), 4.05−4.10 (m, 1H, H$_{2'}$), 4.59 (s, 2H, CH_2NH), 5.55 (d, 1H, $^3J_{1'-2'}$ = 8.8 Hz, 1H, H$_{1'}$), 7.80−7.88 (m, 4H, Ph), 8.11 (s, 1H, triazole CH); ^{13}C {^{1}H} NMR (100 MHz, D_2O) δ 35.24 (CH_2NH), 60.99 (C$_{6'}$), 68.71 (C$_{4'}$), 69.91 (C$_{2'}$), 73.06 (C$_{3'}$), 78.45 (C$_{5'}$), 88.20 (C$_{1'}$), 123.05 (triazole CH), 126.44 (Ph H), 128.44 (Ph H), 137.72 (Ph C), 144.32 (Ph C or triazole C), 145.63 (triazole C or Ph C), 169.53 (C═O); HRMS (ESI) calcd for $C_{16}H_{20}N_5O_8S^-$ 442.103 807, found 442.103 051.

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(2′,3′,4′-tri-*O*-acetyl-β-D-arabinopyranosyl)-1*H*-1,2,3-triazole (2c). The title compound was prepared according to the general procedure 1 and isolated as an off-white solid (147 mg, 0.27 mmol, 82%): R_f 0.10 (8:2 EtOAc:hexanes); mp 125−126 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.78 (s, 3H, OAc CH_3), 1.92 (s, 3H, OAc CH_3), 2.12 (s, 3H, OAc CH_3), 3.99 (dd, $^2J_{5'-5''}$ = 13.2 Hz, $^3J_{5'-4'}$ = 2.0 Hz, 1H, H$_{5'}$), 4.13 (dd, 1H, $^2J_{5'-5''}$ = 13.4 Hz, $^3J_{5''-4'}$ = 1.3 Hz, 1H, H$_{5''}$), 4.51 (d, $^3J_{CH-NH}$ = 5.6 Hz, 1H, CH_2NH), 5.27−5.28 (m, 1H, H$_{4'}$), 5.36 (dd, $^3J_{3'-2'}$ = 10.4 Hz, $^3J_{3'-4'}$ = 5.2 Hz, 1H, H$_{3'}$), 5.55−5.59 (m, 1H, H$_{2'}$), 6.07 (d, $^3J_{1'-2'}$ = 9.2 Hz, 1H, H$_{1'}$), 7.45 (br s, 2H, SO_2NH_2), 7.86−7.99 (m, 4H, Ph H), 8.21 (s, 1H, triazole H), 9.18 (t, $^3J_{NH-CH}$ = 5.2 Hz, 1H, CH_2NH); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 20.70 (OAc CH_3), 21.06 (OAc CH_3), 21.40 (OAc CH_3), 67.12 (C$_{5'}$), 68.57 (C$_{4'}$), 68.60 (C$_{3'}$), 71.05 (C$_{2'}$), 85.40 (C$_{1'}$), 123.04 (triazole CH), 126.29 (Ph CH), 128.65 (Ph CH), 137.65 (Ph C), 145.92 (triazole C or Ph C), 147.04 (triazole C or Ph C), 165.89 (C═O), 169.22 (C═O), 170.20 (C═O), 170.55 (C═O); HRMS (ESI) calcd for $C_{21}H_{24}N_5O_{10}S^-$ 538.124 936, found 538.125 762. Anal. ($C_{21}H_{26}N_5O_{10}S\cdot0.5H_2O$) C, N; H: calcd, 4.78; found, 4.17

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(β-D-arabinopyranosyl)-1*H*-1,2,3-triazole (2c′). The title compound was prepared according to general procedure 2 and isolated as a pale yellow solid (77 mg, 0.19 mmol, ∼100%). R_f 0.26 (1:9 CH_3OH:EtOAc); mp 210−212 °C (dec); ^{1}H NMR (400 MHz, 2% D_2O in DMSO-d_6) δ 3.74 (dd, $^3J_{3'-2'}$ = 10.0 Hz, $^3J_{3'-4'}$ = 3.6 Hz, 1H, H$_{3'}$), 3.80−3.83 (m, 1H, H$_{5'}$), 3.93−3.96 (m, 2H, H$_{4'}$, H$_{5''}$), 4.06−4.11 (m, 1H, H$_{2'}$), 4.59 (s, 2H, CH_2NH), 5.48 (d, 1H, $^3J_{1'-2'}$ = 9.2 Hz, 1H, H$_{1'}$), 7.83−7.91 (m, 4H, Ph H), 8.12 (s, 1H, triazole H); ^{13}C {^{1}H} NMR (100 MHz, 2% D_2O in DMSO-d_6) δ 35.20 (CH_2NH), 68.55 (C$_{4'}$), 69.68 (C$_{5'}$), 69.84 (C$_{2'}$), 72.77 (C$_{3'}$), 88.55 (C$_{1'}$), 123.02 (triazole CH), 125.51 (Ph CH), 128.53 (Ph CH), 137.67 (Ph C), 144.64 (triazole C or Ph C), 145.83 (triazole C or Ph C), 169.18 (C═O); HRMS (ESI) calcd for $C_{15}H_{18}N_5O_7S^-$ 412.093 242, found 412.092 448.

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(2′-acetamido-2′-deoxy-3′,4′,6′-tri-*O*-acetyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazole (2d). The title compound was prepared according to general procedure 1 and isolated as a white solid (149 mg, 0.24 mmol, 91%): R_f 0.32 (1:9 CH_3OH:EtOAc); mp 231−232 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.55 (s, 3H, NHAc CH_3), 1.91 (s, 3H, OAc CH_3), 1.95 (s, 3H, OAc, CH_3), 1.97 (s, 3H, OAc CH_3), 4.00 (dd, $^2J_{6'-6''}$ = 12.4 Hz, $^3J_{6'-5'}$ = 2 Hz, 1H, H$_{6'}$), 4.10 (dd, $^2J_{6'-6''}$ = 12 Hz, $^3J_{6''-5'}$ = 4.8 Hz, 1H, H$_{6''}$), 4.18 (ddd, $^3J_{5'-4'}$ = 7.2 Hz, $^3J_{5'-6''}$ = 4.8 Hz, $^3J_{5'-6'}$ = 2 Hz, 1H, H$_{5'}$), 4.50 (d, $^3J_{CH-NH}$ = 6.0 Hz, 2H, CH_2NH), 4.51−4.58 (m, 1H, H$_{2'}$), 5.02−5.08 (m, 1H, H$_{4'}$), 5.29−5.34 (m, 1H, H$_{3'}$), 6.07 (d, $^3J_{1'-2'}$ = 10.0 Hz, 1H, H$_{1'}$), 7.44 (s, 2H, SO_2NH_2), 7.85−8.00 (m, Ph H), 8.03 (d, $^3J_{NH-2'}$ = 9.2 Hz, 1H, NHAc CONH), 8.13 (s, triazole H), 9.20 (t, $^3J_{NH-CH}$ = 6.0 Hz, 1H, CH_2NH); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 20.96 (OAc CH_3), 21.09 (OAc CH_3), 21.20 (OAc CH_3), 23.02 (OAc CH_3), 35.49 (CH_2NH), 52.69 (C$_{2'}$), 62.50 (C$_{6'}$), 68.67 (C$_{3'}$), 73.07 (C$_{4'}$), 74.05 (C$_{5'}$), 85.29 (C$_{1'}$), 122.45 (triazole CH), 126.70 (Ph CH), 128.67 (Ph CH), 137.70 (Ph C), 145.80 (triazole C or Ph C) 147.02 (triazole C or Ph C), 165.87 (C═O), 170.01 (C═O), 170.11 (C═O), 170.27 (C═O), 170.72 (C═O); HRMS (ESI) calcd for $C_{24}H_{29}N_6O_{11}S^-$ 609.162 05, found 609.162 988. Anal. ($C_{24}H_{30}N_6O_{11}S$) C, H; N: calcd, 13.76; found, 12.87.

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(2′-acetamido-2′-deoxy-β-D-glucopyranosyl)-1*H*-1,2,3-triazole (2d′). The title compound was prepared according to general procedure 2 and isolated as a white solid (79 mg, 0.16 mmol, ∼100%): R_f 0.09 (1:9 H_2O:CH_3CN); mp 214−215 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.62 (s, 3H, NHAc CH_3), 3.47−3.52 (m, 1H, H$_{3'}$), 3.64−3.68 (m, 1H, H$_{4'}$), 3.97−4.05 (m, 1H, H$_{2'}$), 4.48 (d, $^3J_{CH-NH}$ = 5.8 Hz, 2H, CH_2NH), 4.58−4.61 (m, 1H, H$_{6'}$), 5.21−5.24 (m, 2H, H$_{3'}$, H$_{4'}$), 5.66 (d, 1H, $^3J_{1'-2'}$ = 9.6 Hz, 1H, H$_{1'}$), 7.44 (br s, 2H, SO_2NH_2), 7.82 (d, $^3J_{NH-2'}$ = 8.8 Hz, 1H, NHAc N*H*), 7.85−8.00 (m, 4H, Ph), 7.97 (s, 1H, triazole 1H), 9.19 (t, $^3J_{NH-CH}$ = 6.0 Hz, 1H, CH_2NH); ^{13}C {^{1}H} NMR (100 MHz, 2% D_2O in DMSO-d_6) δ 23.30 (NHAc CH_3), 35.40 (CH_2NH), 55.00 (C$_{2'}$), 61.81 (C$_{6'}$), 70.44 (C$_{4'}$), 74.46 (C$_{3'}$), 80.63 (C$_{5'}$), 86.59 (C$_{1'}$), 122.22 (triazole CH), 126.32 (Ph CH), 128.66 (Ph CH), 137.68 (Ph C), 145.26 (triazole C or Ph C), 146.87 (triazole C or Ph C), 166.10 (C═O), 169.982 (C═O); HRMS (ESI) calcd for $C_{18}H_{23}N_6O_8S^-$ 483.130 356, found 483.129 389.

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(2′,3′,4′-tri-*O*-acetyl-β-D-glucuronic acid methyl ester)-1*H*-1,2,3-triazole (2e). The title compound was prepared according to general procedure 1 and isolated as a white solid (153 mg, 0.26 mmol, 92%): R_f 0.12 (1:9 hexanes:EtOAc); mp 221−222 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.76 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.98 (s, 3H, OAc), 3.59 (s, 3H, OCH_3), 4.51 (d, $^3J_{CH-NH}$ = 5.2 Hz, 2H, CH_2-NH), 4.76 (d, $^3J_{5'-4'}$ = 10.0 Hz, 1H, H$_{5'}$), 5.19−5.24 (m, 1H, H$_{4'}$), 5.44−5.59 (m, 1H, H$_{3'}$), 5.72−5.76 (m, 1H, H$_{2'}$), 6.34 (d, $^3J_{1'-2'}$ = 9.6 Hz, 1H, H$_{1'}$), 7.45 (br s, 2H, SO_2NH_2), 7.86−8.01 (m, 4H, Ph H), 8.35 (s, 1H, triazole H), 9.23 (t, $^3J_{NH-CH}$ = 5.6 Hz, 1H, N*H*CH_2); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 20.6 (OAc CH_3), 20.9 (OAc CH_3), 21.0 (OAc CH_3), 35.5 (CH_2NH), 53.3 (CO_2CH_3), 69.0 (C$_{4'}$), 70.4 (C$_{2'}$), 72.3 (C$_{3'}$), 73.5 (C$_{5'}$), 84.4 (C$_{1'}$), 122.9 (triazole CH), 126.3 (Ph CH), 128.7 (Ph CH), 137.6 (Ph C), 146.4 (triazole C or Ph C), 147.1 (triazole C or Ph C), 165.9 (C═O), 167.3 (C═O), 169.1 (C═O), 170.0 (C═O), 170.2 (C═O); HRMS (ESI) calcd for $C_{23}H_{26}N_5O_{12}S^-$ 596.130 416, found 596.132 499. Anal. ($C_{23}H_{27}N_5O_{12}S$) C, H, N.

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(β-D-glucuronic acid methyl ester)-1*H*-1,2,3-triazole (2e′). The title compound was prepared according to general procedure 2 and isolated as a clear gum (79 mg, 0.17 mmol, ∼ 100%): R_f 0.13 (1:9 CH_3OH:EtOAc); ^{1}H NMR (400 MHz, 2% D_2O in DMSO-d_6) δ 3.40−3.49 (m, 2H, H$_{3'}$, H$_{4'}$), 3.61 (s, 3H, $COCH_3$), 3.82−3.86 (m, 1H, H$_{2'}$), 4.08 (d, $^3J_{5'-4'}$ = 9.6 Hz, 1H, H$_{5'}$), 4.51 (s, 2H, CH_2NH), 5.66 (d, $^3J_{1'-2'}$ = 9.6 Hz, 1H, H$_{1'}$), 7.85−8.00 (m, 4H, Ph), 8.16 (s, 1H, triazole CH); ^{13}C {^{1}H} NMR (100 MHz, 2% D_2O in DMSO-d_6) δ 35.43 (CH_2NH), 52.74 ($COCH_3$), 71.63 (C$_{3'}$), 71.94 (C$_{4'}$), 76.63 (C$_{2'}$), 78.02 (C$_5$), 87.66 (C$_{1'}$), 123.08 (triazole CH), 126.31 (Ph CH), 128.69 (Ph CH), 137.64 (Ph C), 145.52 (triazole C or Ph C), 146.89 (triazole C or Ph C), 165.85 (C═O), 169.37 (C═O); HRMS (ESI) calcd for $C_{17}H_{20}N_5O_9S^-$ 470.098 722, found 470.097 959.

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(hepta-*O*-acetyl-β-D-maltosyl)-1*H*-1,2,3-triazole (2f). The title compound

was prepared according to general procedure 1 and isolated as a pale yellow foam (424 mg, 0.47 mmol, 78%): R_f 0.23 (2:8 hexanes:EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.72 (s, 3H, OAc CH_3), 1.92 (s, 3H, OAc CH_3), 1.93 (s, 3H, OAc CH_3), 1.96 (s, 3H, OAc CH_3), 1.97 (s, 3H, OAc CH_3), 1.99 (s, 3H, OAc CH_3), 2.00 (s, 3H, OAc CH_3), 3.98−4.01 (m, 2H, Glcα $H_{5'}$, Glcβ $H_{6'}$), 4.05−4.16 (m, 3H, Glcα $H_{6''}$, Glcβ $H_{4'}$, Glcβ $H_{6'}$), 4.29 (ddd, $^3J_{5'-4'} = 9.6$ Hz, $^3J_{5'-6'} = 5.6$ Hz, $^3J_{5'-6''} = 2.4$ Hz, 1H, Glcβ $H_{5'}$), 4.40 (dd, $^2J_{6'-6''} = 12.4$ Hz, $^3J_{6'-5'} = 2.4$ Hz, 1H, Glcβ $H_{6'}$), 4.50 (d, $^3J_{CH-NH} = 5.6$ Hz, 2H, CH_2NH), 4.88 (dd, $^3J_{2'-3'} = 10.8$ Hz, $^3J_{2'-1'} = 4.0$ Hz, 1H, Glcα $H_{2'}$), 4.95−5.00 (m, 1H, Glcα $H_{4'}$), 5.18−5.23 (m, 1H, Glcα $H_{3'}$), 5.32 (d, $^3J_{1'-2'} = 4.0$ Hz, 1H, Glcα $H_{1'}$), 5.47−5.57 (m, 2H, Glcβ $H_{2'}$, Glcβ $H_{3'}$), 6.25 (d, $^3J_{1'-2'} = 9.2$ Hz, 1H, Glcβ $H_{1'}$), 7.45 (br s, 2H, SO_2NH_2), 7.86−7.99 (m, 4H, Ph), 8.16 (s, 1H, triazole CH), 9.21 (t, $^3J_{NH-CH} = 5.6$ Hz, 1H, CH_2NH); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 20.63 (OAc CH_3), 20.94 (OAc CH_3), 21.00 (OAc CH_3), 21.10 (OAc CH_3), 21.20 (OAc CH_3), 21.24 (OAc CH_3), 35.51 (CH_2NH), 62.06 (Glcβ $C_{6'}$), 63.52 (Glcα $C_{6'}$), 68.36 (Glcα $C_{4'}$), 68.83 (Glcα $C_{5'}$), 69.59 (Glcα $C_{3'}$), 70.09 (Glcα $C_{2'}$), 71.30 (Glcβ $C_{3'}$), 73.98 (Glcβ $C_{4'}$), 74.50 (Glcβ $C_{5'}$), 75.13 (Glcβ $C_{2'}$), 84.07 (Glcβ $C_{1'}$), 96.40 (Glcα $C_{1'}$), 122.74 (triazole CH), 126.29 (Ph CH), 128.64 (Ph CH), 137.64 (Ph C), 146.19 (triazole C or Ph C), 147.05 (triazole C or Ph C), 165.87 (C═O); HRMS (ESI) calcd for $C_{36}H_{44}N_5O_{20}S^-$ 898.230 583, found 898.228 045. Anal. ($C_{36}H_{45}N_5O_{20}S\cdot 3H_2O$) C, H, N, S.

4-({[4-(Aminosulfonyl)benzoyl]amino}methyl-1-(β-D-maltosyl)-1*H*-1,2,3-triazole (2f′). The title compound was prepared according to general procedure 2 and isolated as a pale yellow foam (134 mg, 0.22 mmol, ∼100%): R_f 0.10 (1:9 H_2O:CH_3CN); ^{1}H NMR (400 MHz, D_2O) δ 3.27−3.32 (m, 1H, Glcα $H_{4'}$ or Glcβ $H_{4'}$), 3.46 (dd, $^3J_{2'-3'} = 10.0$ Hz, $^3J_{2'-1'} = 4.0$ Hz, Glcα $H_{2'}$), 3.55−3.79 (m, 8 H, Glcα $H_{3'}$, Glcα $H_{5'}$, Glcα H_6/$H_{6''}$, and Glcβ $H_{3'}$, Glcβ $H_{5'}$, Glcβ $H_{6'}$/$H_{6''}$), 3.83−3.87 (m, 1H, Glcβ $H_{3'}$), 3.88−3.92 (m, 1H, Glcβ $H_{2'}$) 4.58 (s, 2H, CH_2NH), 5.33 (d, $^3J_{1'-2'} = 4.0$ Hz, 1H, Glcα $H_{1'}$), 5.62 (d, $^3J_{1'-2'} = 9.2$ Hz 1H, Glcβ $H_{1'}$), 7.77−7.86 (m, 4H, Ph), 8.07 (s, 1H, triazole CH); ^{13}C {^{1}H} NMR (100 MHz, D_2O) δ 35.18 (CH_2NH), 60.58 (Glcα $C_{6'}$ or Glcβ $C_{6'}$), 60.59 (Glcα $C_{6'}$ or Glcβ $C_{6'}$), 69.47, 71.84, 72.27, 72.91, 72.99, 75.97, 76.50, 77.63 (Glcα $C_{2'}$, Glcα $C_{3'}$, Glcα $C_{4'}$, Glcα $C_{5'}$ and Glcβ $C_{2'}$, Glcβ $C_{3'}$, Glcβ $C_{4'}$ Glcβ $C_{5'}$), 87.42 (Glcβ $C_{1'}$), 99.83 (Glcα $C_{1'}$), 123.32 (triazole CH), 126.33 (Ph CH), 128.36 (Ph CH), 137.39 (Ph C), 144.70 (triazole C or Ph C), 144.97 (triazole C or Ph C), 169.32 (C═O); HRMS (ESI) calcd for $C_{22}H_{30}N_5O_{13}S^-$ 604.156 63, found 604.155 698.

Methyl 2′,3′,4′-tri-*O*-acetyl-6-[4-({[aminosulfonyl)benzoyl]-amino}methyl)-1*H*-1,2,3-triazol-1-yl]-6-deoxy-α-D-glucopyranoside (2g). The title compound was prepared according to general procedure 1 and isolated as a white foam (278 mg, 0.48 mmol, 82%). R_f 0.1 (100% EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.92 (s, 3H, OAc CH_3), 1.96 (s, 3H, OAc CH_3), 1.98 (s, 3H, OAc CH_3), 3.03 (s, 3H, OCH_3), 4.08−4.13 (m, 1H, H_5), 4.44−4.49 (m, 2H, H_6, CH_2NH), 4.55 (dd, $^2J_{6'-6''} = 14.4$ Hz, $^3J_{6'-5'} = 2.8$ Hz, 1H, $H_{6'}$), 4.78−4.82 (m, 2H, $H_{1'}$, $H_{2'}$), 4.83−4.88 (m, 1H, $H_{4'}$), 5.21−5.26 (m, 1H, $H_{3'}$), 7.44 (br s, 2H, SO_2NH_2), 7.85−7.98 (m, 4H, Ph), 7.97 (s, 1H, triazole CH), 9.19 (t, $^3J_{NH-CH} = 5.6$ Hz, 1H, CH_2NH); ^{13}C NMR {^{1}H} (100 MHz, DMSO-d_6) δ 20.96 (OAc CH_3), 21.03 (OAc CH_3), 21.13 (OAc CH_3), 35.55 (CH_2NH), 50.40 ($C_{6'}$), 55.28 (OCH_3), 68.00 ($C_{5'}$), 70.12 ($C_{1'}$ or $C_{2'}$), 70.17 ($C_{1'}$ or $C_{2'}$), 70.33 ($C_{3'}$), 96.57 ($C_{1'}$), 124.54 (triazole CH), 126.31 (Ph CH), 128.58 (Ph CH), 137.68 (Ph C), 145.52 (triazole C or Ph C) 146.95 (triazole C or Ph C), 165.89 (C═O), 170.07 (C═O), 170.34 (C═O), 170.41 (C═O); HRMS (ESI) calcd for $C_{23}H_{27}N_4O_{12}S^-$ 582.151 151, found 582.150 947. Anal.($C_{23}H_{29}N_5O_{11}S\cdot H_2O$) C, H, N.

Methyl 6-[4-({[aminosulfonyl)benzoyl]amino}methyl)-1*H*-1,2,3-triazol-1-yl]-6-deoxy-α-D-glucopyranoside (2g′). The title compound was prepared according to general procedure 1 and isolated as a pale yellow foam (76 mg, 0.17 mmol, 97%): R_f 0.21 (1:9 CH_3OH:EtOAc); ^{1}H NMR (400 MHz, 2% D_2O in DMSO-d_6) δ 2.87 (s, 3H, OCH_3), 2.96 (dd, $^3J_{4'-5'} = 10.4$ Hz, $^3J_{4'-3'} = 8.8$ Hz, 1H, $H_{4'}$), 3.14 (dd, $^3J_{2'-3'} = 9.6$ Hz, $^3J_{2'-1'} = 3.6$ Hz, 1H, $H_{2'}$), 3.31−3.36 (m, 1H, $H_{3'}$), 3.59−3.65 (m, 1H, $H_{5'}$), 4.33 (dd, $^2J_{6'-6''} = 14.0$ Hz, $^3J_{6'-5'} = 9.2$ Hz, 1H, $H_{6'}$), 4.42 (d, 1H, $^3J_{1'-2'} = 3.6$ Hz, 1H, $H_{1'}$), 4.47−4.48 (m, 2H, CH_2NH), 4.65 (dd, $^2J_{6''-6'} = 14.0$ Hz, 1H, $H_{6''}$), 7.85 (s, 1H, triazole CH), 7.86−7.97 (m, 4H, Ph), 9.18 (t, $^3J_{NH-CH} = 5.2$ Hz, 1H CH_2NH); ^{13}C NMR {^{1}H} (100 MHz, 2% D_2O in DMSO-d_6) δ 35.45 (CH_2NH), 51.50 ($C_{6'}$), 54.87 (OCH_3), 71.07 ($C_{5'}$), 72.12 ($C_{4'}$ or $C_{2'}$), 72.21 ($C_{4'}$ or $C_{2'}$), 73.53 ($C_{3'}$), 100.31 ($C_{1'}$), 124.50 (triazole CH), 126.33 (Ph CH), 128.57 (Ph CH), 137.67 (Ph C), 145.33 (triazole C or Ph C), 146.87 (triazole C or Ph C), 165.74 (C═O); HRMS (ESI) calcd for $C_{17}H_{21}N_4O_9S^-$ 456.119 457, found 456.118 334.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(2′-3′-4′-6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazole (3a). The title compound was prepared according to general procedure 1 and isolated as a white solid (142 mg, 0.23 mmol, 86%): R_f 0.43 (2:8 hexanes:EtOAc); mp 196−197 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.75 (s, 3H, OAc CH_3), 1.93 (s, 3H, OAc CH_3), 1.97 (s, 3H, OAc CH_3), 2.00 (s, 3H, OAc CH_3), 4.05 (dd, $^2J_{6'-6''} = 12.8$ Hz, $^3J_{6'-5'} = 2.4$ Hz, 1H, $H_{6'}$), 4.10 (dd, $^2J_{6''-6'} = 12.8$ Hz, $^3H_{6''}$-5′ = 5.2 Hz, 1H, $H_{6''}$), 4.35 (ddd, $^3J_{5'-4'} = 10.0$ Hz, $^3J_{5'-6''} = 5.2$ Hz, $^3J_{5'-6'} = 2.4$ Hz, 1H, $H_{5'}$), 5.13−5.18 (m, 1H, $H_{4'}$), 5.40−5.46 (m, 2H, CH_2O), 5.51−5.55 (m, 1H, $H_{3'}$), 5.63−5.67 (m, 1H, $H_{2'}$), 6.35 (d, $^3J_{1'-2'} = 9.2$ Hz, 1H, $H_{1'}$), 7.54 (s, 2H, SO_2NH_2), 7.92−8.11 (m, 4H, Ph H), 8.57 (s, 1H, triazole H); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 20.56 (OAc CH_3), 20.92 (OAc CH_3), 21.06 (OAc CH_3), 21.19 (OAc CH_3), 58.91 (CH_2O), 62.46 ($C_{6'}$), 68.19 ($C_{4'}$), 70.84 ($C_{3'}$), 72.76 ($C_{2'}$), 73.97 ($C_{5'}$), 84.56 ($C_{1'}$), 124.70 (triazole CH), 126.76 (Ph CH), 130.68 (Ph CH), 132.69 (Ph C), 143.16 (triazole C or Ph C), 148.92 (triazole C or Ph C), 165.09 (C═O), 169.16 (C═O), 170.04 (C═O), 170.22 (C═O), 170.70 (C═O); HRMS (ESI) calcd for $C_{24}H_{27}N_4O_{13}S^-$ 611.130 081, found 611.127 932. Anal. ($C_{24}H_{28}N_4O_{13}S$) C, H, N, S.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(β-D-glucopyranosyl)-1*H*-1,2,3-triazole (3a′). The title compound was prepared according to general procedure 1 and isolated as a white foam (82 mg, 0.19 mmol, 72%): R_f 0.10 (3:7 EtOH:$CHCl_3$); ^{1}H NMR (400 MHz, D_2O) δ 3.47−3.53 (m, 2H, $H_{4'}$, $H_{5'}$), 3.56−3.66 (m, 2H, $H_{3'}$, $H_{6'}$), 3.74−3.79 (m, 1H, $H_{6''}$), 3.86−3.90 (m, 1H, $H_{2'}$), 5.65 (d, $^3J_{1'-2'} = 8.0$ Hz, 1H, $H_{1'}$), 7.81−8.00 (Ph H), 8.25 (s, triazole CH); ^{13}C {^{1}H} NMR (100 MHz, D_2O) δ 58.33 (CH_2O), 60.55 ($C_{6'}$), 69.09 ($C_{4'}$), 72.44 ($C_{2'}$), 76.04 ($C_{3'}$), 79.04 ($C_{5'}$), 87.66 ($C_{1'}$), 125.21 (triazole CH), 126.24 (Ph CH), 130.62 (Ph CH), 133.21 (Ph C), 142.80 (triazole C or Ph C), 145.67 (triazole Ph C), 166.64 (C═O); HRMS (ESI) calcd for $C_{16}H_{19}N_4O_9S^-$ 443.087 822, found 443.087 455.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-1*H*-1,2,3-triazole (3b). The title compound was prepared according to general procedure 1 and isolated as a white foam (184 mg, 0.30 mmol, 92%): R_f 0.41 (2:8 hexanes:EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.78 (s, 3H, OAc CH_3), 1.92 (s, 3H, OAc CH_3), 1.96 (s, OAc CH_3), 2.16 (s, OAc CH_3), 4.00 (dd, $^2J_{6'-6''} = 11.6$ Hz, $^3J_{6'-5'} = 1.2$ Hz, 1H, $H_{6'}$), 4.11 (dd, $^2J_{6''-6'} = 11.6$ Hz, $^3J_{6''-5'} = 4.8$ Hz, 1H, $H_{6''}$), 4.55−4.58 (m, 1H, $H_{5'}$), 5.40 (dd, $^3J_{4'-3'} = 3.6$ Hz, $^3J_{4'-5'} = 1.2$ Hz, $H_{4'}$), 5.42 (s, 2H, CH_2O), 5.44−5.45 (m, 1H, $H_{3'}$), 5.56−5.61 (m, 1H, $H_{2'}$), 6.27 (d, $^3J_{1'-2'} = 9.2$ Hz, 1H, $H_{1'}$), 7.53 (s, 2H, SO_2NH_2), 7.91−8.11 (m, 4H, Ph H), 8.50 (s, 1H, triazole H); ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6) δ 20.65 (OAc CH_3), 20.99 (OAc CH_3), 21.09 (OAc CH_3), 21.17 (OAc CH_3), 58.78 (CH_2O), 62.25 ($C_{6'}$), 67.98 ($C_{4'}$), 68.43 ($C_{3'}$), 71.04 ($C_{2'}$), 73.70 ($C_{5'}$), 84.96 ($C_{1'}$), 125.23 (triazole CH), 126.77 (Ph CH), 130.68 (Ph CH), 132.70 (Ph C), 142.92 (Ph C), 148.91 (triazole C), 165.13 (C═O), 169.20 (C═O), 170.13 (C═O), 170.60 (C═O), 170.66 (C═O); HRMS (ESI) calcd for $C_{24}H_{27}N_4O_{13}S^-$ 611.130 081, found 611.129 142. Anal. ($C_{24}H_{28}N_4O_{13}S\cdot 0.5H_2O$) C, H, N, S

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(β-D-galactopyranosyl)-1*H*-1,2,3-triazole (3b′). The title compound was prepared according to general procedure 1 and isolated as a white foam (136 mg, 0.31 mmol, 63%): R_f 0.12 (3:7 EtOH:$CHCl_3$); ^{1}H NMR (400 MHz, 2% D_2O in DMSO-d_6) δ 3.41−3.48 (m, 3H, H_5, $H_{6'}$, $H_{6''}$), 3.51 (dd, $^3J_{3'-2'} = 9.2$ Hz, $^3J_{3'-4'} = 3.2$ Hz, 1H, $H_{3'}$), 3.67−3.73

(m, 1H, $H_{4'}$), 3.98−4.03 (m, 1H, $H_{2'}$), 5.43 (s, 2H, CH_2O), 5.48 (d, $^3J_{1'-2'}$ = 8.8 Hz, 1H, $H_{1'}$), 7.91−8.12 (m, 4H, Ph), 8.37 (s, 1H, triazole CH); ^{13}C {^1H} NMR (100 MHz, 2% D_2O in DMSO-d_6) δ 58.42 (CH_2O), 60.38 ($C_{6'}$), 68.39 ($C_{4'}$), 69.24 ($C_{2'}$), 73.52 ($C_{3'}$), 78.46 ($C_{5'}$), 88.19 ($C_{1'}$), 124.01 (triazole CH), 126.21 (Ph CH), 130.10 (Ph CH), 132.16 (Ph C), 141.69 (Ph C), 148.13 (triazole C), 164.62 (C═O); HRMS (ESI) calcd for $C_{16}H_{19}N_4O_9S^-$ 443.087 822, found 443.087 859.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(2′,3′,4′-tri-*O*-acetyl-*β*-D-arabinopyranosyl)-1*H*-1,2,3-triazole (3c). The title compound was prepared according to general procedure 1 and isolated as a white foam (228 mg, 0.42 mmol, 88%): R_f 0.55 (2:8 hexanes:EtOAc); ^1H NMR (400 MHz, DMSO-d_6) δ 1.78 (s, 3H, OAc CH_3), 1.93 (s, 3H, OAc CH_3), 2.13 (s, 3H, OAc CH_3), 4.02 (dd, $^2J_{5'-5''}$ = 13.2 Hz, $^3J_{5'-4'}$ = 1.6 Hz, 1H, $H_{5'}$), 4.14−4.18 (m, 1H, $H_{5'}$), 5.28−5.30 (m, 1H, $H_{4'}$), 5.38 (dd, $^3J_{3'-2'}$ = 10.0 Hz, $^3J_{3'-4'}$ = 3.6 Hz, 1H, $H_{3'}$), 5.42 (s, 2H, CH_2O), 5.55−5.60 (m, 1H, $H_{2'}$), 6.13 (d, $^3J_{1'-2'}$ = 9.2 Hz, 1H, $H_{1'}$), 7.53 (br s, 2H, SO_2NH_2), 7.91−8.10 (m, 4H, Ph CH), 8.46 (s, 1H, triazole H); ^{13}C {^1H} NMR (100 MHz, DMSO-d_6) δ 20.66 (OAc CH_3), 21.07 (OAc CH_3), 21.40 (OAc CH_3), 58.81 (CH_2O), 67.18 ($C_{5'}$), 68.57 ($C_{4'}$), 68.69 ($C_{2'}$), 70.95 ($C_{3'}$), 85.52 ($C_{1'}$), 125.11 (triazole CH), 126.76 (Ph CH), 130.67 (Ph CH), 132.71 (Ph C), 142.86 (Ph C), 148.91 (triazole C), 165.11 (C═O), 169.24 (C═O), 170.20 (C═O), 170.55 (C═O); HRMS (ESI) calcd for $C_{21}H_{23}N_4O_{11}S^-$ 539.108 952, found 539.107 401. Anal. ($C_{21}H_{24}N_4O_{11}S\cdot1.5H_2O$) C, H, N, S.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(*β*-D-arabinopyranosyl)-1*H*-1,2,3-triazole (3c′). The title compound was prepared according to procedure 1 and isolated as a white solid (105 mg, 0.25 mmol, 84%): R_f 0.26 (3:7 EtOH:$CHCl_3$); mp 184−189 °C; ^1H NMR (400 MHz, 2% D_2O in DMSO-d_6) δ 3.53 (dd, $^3J_{3'-2'}$ = 9.6 Hz, $^3J_{3'-4'}$ = 3.6 Hz, 1H, $H_{3'}$), 3.72−3.74 (m, 2H, $H_{4'}$, $H_{5'}$), 3.78 (dd, $^2J_{5''-5'}$ = 12.4 Hz, $^3J_{5''-4'}$ = 2.0 Hz, 1H, $H_{5''}$), 3.98−4.03 (m, 1H, $H_{2'}$), 5.41 (d, $^3J_{1'-2'}$ = 10.0 Hz, 1H, $H_{1'}$), 5.43 (s, 2H, CH_2O), 8.36 (s, 1H, triazole CH), 7.91−8.12 (m, 4H, Ph); ^{13}C {^1H} NMR (100 MHz, 2% D_2O in DMSO-d_6) δ 59.06 (CH_2O), 69.03 ($C_{4'}$), 69.96 ($C_{5'}$, $C_{2'}$), 73.86 ($C_{3'}$), 89.10 ($C_{1'}$), 124.59 (triazole CH), 126.79 (Ph CH), 130.70 (Ph CH), 132.74 (Ph C), 142.25 (triazole C or Ph C), 148.81 (triazole C or Ph C), 165.21 (C═O); HRMS (ESI) calcd for $C_{15}H_{17}N_4O_8S^-$ 413.077 258, found 413.076 552.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(2′-acetamido-2′-deoxy-3′,4′,6′-tri-*O*-acetyl-*β*-D-glucopyranosyl)-1*H*-1,2,3-triazole (3d). The title compound was prepared according to the general procedure 1 and isolated as a white solid (292 mg, 0.60 mmol, 89%): R_f 0.45 (100% EtOAc); mp 217−218 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 1.55 (s, 3H, NHAc CH_3), 1.92 (s, 3H, OAc CH_3), 1.97 (s, 3H, OAc CH_3), 1.98 (s, OAc CH_3), 4.03 (dd, $^2J_{6'-6''}$ = 12.4 Hz, $^3J_{6'-5'}$ = 2.0 Hz, 1H, $H_{6'}$), 4.12 (dd, $^2J_{6''-5'}$ = 12.8 Hz, $^3J_{6''-5'}$ = 5.6 Hz, 1H, $H_{6'}$), 4.23 (ddd, $^3J_{5'-4'}$ = 10.0 Hz, $^3J_{5'-6''}$ = 5.6 Hz, $^3J_{5'-6'}$ = 2.0 Hz, 1H, $H_{5'}$), 4.56−4.64 (m, 1H, $H_{2'}$), 5.06−5.10 (m, 1H, $H_{4'}$), 5.30−5.35 (m, 1H, $H_{3'}$), 5.38−5.45 (m, 2H, CH_2O), 6.11 (d, $^3J_{1'-2'}$ = 9.6 Hz, 1H, $H_{1'}$), 7.54 (s, 2H, SO_2NH_2), 7.91−8.12 (m, 4H, Ph H), 8.05 (d, $^3J_{NH-2}$ = 9.6 Hz, 1H, NHAc CONH), 8.44 (s, triazole H); ^{13}C {^1H} NMR (100 MHz, DMSO-d_6) δ 20.96 (OAc CH_3), 21.10 (OAc CH_3), 21.20 (OAc CH_3), 22.97 (NHAc CH_3), 52.74 ($C_{2'}$), 58.96 (CH_2O), 62.45 ($C_{6'}$), 68.66 ($C_{3'}$), 72.99 ($C_{4'}$), 74.10 ($C_{5'}$), 85.45 ($C_{1'}$), 124.49 (triazole CH), 126.75 (Ph CH), 130.70 (Ph CH), 132.71 (Ph CH), 142.64 (Ph C), 148.91 (triazole C), 165.10 (C═O), 170.02 (C═O), 170.10 (C═O), 170.27 (C═O), 170.71 (C═O); HRMS (ESI) calcd for $C_{24}H_{28}N_5O_{12}S^-$ 610.146 066, found 610.145 354. Anal. ($C_{24}H_{29}N_5O_{12}S\cdot0.5H_2O$) C, H, N, S.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(2′-acetamido-2′-deoxy-*β*-D-glucopyranosyl)-1*H*-1,2,3-triazole (3d′). The title compound was prepared according to the general procedure 1 and isolated as an off-white solid (180 mg, 0.38 mmol, 68%) R_f 0.09 (3:7 EtOH:$CHCl_3$); mp 205−208 °C (dec); ^1H NMR (400 MHz, 2% D_2O in DMSO-d_6) δ 1.57 (s, 3H, NHAc CH_3), 3.22−3.27 (m, 1H, $H_{4'}$), 3.68−3.46 (m, 2H, $H_{5'}$, $H_{6'}$), 3.49−3.54 (m, 1H, $H_{3'}$), 3.65−3.69 (m, 1H, $H_{6''}$), 4.01−4.08 (m, 1H, $H_{2'}$), 5.39 (s, 2H, CH_2O), 5.71 (d, $^3J_{1'-2'}$ = 9.6 Hz, 1H, $H_{1'}$), 7.85 (d, $^3J_{NH-2}$ = 9.2 Hz, 1H, NHAc CONH), 7.91−8.10 (m, 4H, Ph), 8.27 (s, 1H, triazole CH); ^{13}C {^1H} NMR (100 MHz, DMSO-d_6) δ 23.36 (NHAc CH_3), 55.20 ($C_{2'}$), 58.99 (CH_2O), 61.35 ($C_{6'}$), 70.61 ($C_{4'}$), 74.57 ($C_{3'}$), 80.81 ($C_{5'}$), 86.74 ($C_{1'}$), 124.34 (triazole CH), 126.76 (Ph CH), 130.69 (Ph CH), 132.76 (Ph C), 142.10 (Ph C), 148.87 (triazole C), 165.13 (C═O), 169.82 (C═O); HRMS (ESI) calcd for $C_{18}H_{22}N_5O_9S^-$ 484.114 372, found 484.113 226.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(2′,3′,4′-tri-*O*-acetyl-*β*-D-glucuronic acid methyl ester)-1*H*-1,2,3-triazole (3e). The title compound was prepared according to general procedure 1 and isolated as a white foam (307 mg, 92%): R_f 0.58 (2:8 hexanes: EtOAc); ^1H NMR (400 MHz, DMSO-d_6) δ 1.76 (s, 3H, OAc CH_3), 1.96 (s, 3H, OAc CH_3), 1.99 (s, 3H, OAc CH_3), 3.60 (s, 3H, $COCH_3$), 4.79 (d, $^3J_{5'-4'}$ = 10.0 Hz, 1H, $H_{5'}$), 5.21−5.26 (m, 1H, $H_{4'}$), 5.43 (s, 2H, CH_2O), 5.57−5.62 (m, 1H, $H_{3'}$), 5.73−5.78 (m, 1H, $H_{2'}$), 6.40 (d, $^3J_{1'-2'}$ = 9.2 Hz, 1H, $H_{1'}$), 7.54 (br s, 2H, SO_2NH_2), 7.91−8.12 (m, 4H, Ph H), 8.65 (s, 1H, triazole H); ^{13}C {^1H} NMR (100 MHz, DMSO-d_6) δ 20.56 (OAc CH_3), 20.90 (OAc CH_3), 20.95 (OAc CH_3), 53.30 ($COCH_3$), 58.90 (CH_2O), 69.05 ($C_{4'}$), 70.48 ($C_{3'}$), 72.13 ($C_{2'}$), 73.56 ($C_{5'}$), 84.48 ($C_{1'}$), 124.90 (triazole CH), 126.77 (Ph CH), 130.69 (Ph CH), 132.67 (Ph C), 143.28 (triazole C or Ph C), 148.92 (triazole C or Ph C), 165.09 (C═O), 167.24 (C═O), 169.10 (C═O), 169.98 (C═O), 170.19 (C═O); HRMS (ESI) calcd for $C_{23}H_{25}N_4O_{13}SCl^-$ 633.091 109, found 0.633.094 227. Anal. ($C_{23}H_{26}N_4O_{13}S\cdot1.5H_2O$) C, H, N, S.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(*β*-D-glucuronic acid methyl ester)-1*H*-1,2,3-triazole (3e′). The title compound was prepared according to general procedure 1 and isolated as a hygroscopic white foam (42 mg, 0.08 mmol, 72%): R_f 0.32 (1:9 CH_3OH:EtOAc); ^1H NMR (400 MHz, 2% D_2O in DMSO-d_6) δ 3.27−3.32 (m, 1H, H_3), 3.96−3.01 (m, 1H, $H_{4'}$), 3.65 (s, 3H, $COCH_3$), 3.84−3.88 (m, 1H, $H_{2'}$), 4.63 (d, $^3J_{5'-4'}$ = 9.6 Hz, 1H, $H_{5'}$), 5.42 (s, 2H, CH_2O), 5.72 (d, $^3J_{1'-2'}$ = 9.6 Hz, 1H, $H_{1'}$), 7.91−8.12 (m, 4H, Ph H), 8.46 (s, 1H, triazole CH); ^{13}C {^1H} NMR (100 MHz, 2% D_2O in DMSO-d_6) δ 52.81 ($COCH_3$), 58.92 (CH_2O), 71.56 ($C_{3'}$), 71.89 ($C_{4'}$), 76.68 ($C_{2'}$), 78.00 ($C_{5'}$), 87.79 ($C_{1'}$), 125.09 (triazole CH), 126.80 (Ph CH), 130.73 (Ph CH), 136.85 (Ph C), 142.40 (triazole C or Ph C), 148.49 (triazole C or Ph C), 165.20 (C═O), 169.35 (C═O); HRMS (ESI) calcd for $C_{17}H_{19}N_4O_{10}S^-$ 471.082 737, found 471.082 075.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(hepta-*O*-acetyl-*β*-D-maltosyl)-1*H*-1,2,3-triazole (3f). The title compound was prepared according to general procedure 1 and isolated as a white foam (185 mg, 0.21 mmol, 91%): R_f 0.46 (2:8 hexanes:EtOAc); ^1H NMR (400 MHz, DMSO-d_6) δ 1.71 (s, 3H, OAc CH_3), 1.93 (s, 6H, 2×OAc CH_3), 1.96 (s, 3H, OAc CH_3), 1.97 (s, 3H, OAc CH_3), 1.99 (s, 3H, OAc CH_3), 2.02 (s, 3H, OAc CH_3), 3.97−4.02 (m, 2H, Glcα $H_{5'}$, Glcβ $H_{6'}$), 4.07−4.17 (m, 3H, Glcα $H_{6''}$, Glcβ $H_{4'}$, Glcβ $H_{6'}$), 4.32 (ddd, $^3J_{5'-4'}$ = 10.0 Hz, $^3J_{5'-6'}$ = 5.6 Hz, $^3J_{5'-6''}$ = 2.4 Hz, 1H, Glcβ $H_{5'}$), 4.42 (dd, $^2J_{6''-6'}$ = 12.4 Hz, $^3J_{6''-5'}$ = 2 Hz, 1H, Glcβ $H_{6''}$), 4.89 (dd, 1H, $^3J_{2'-3'}$ = 10.4 Hz, $^3J_{2'-1'}$ = 3.6 Hz, 1H, Glcα $H_{2'}$), 4.96−5.01 (m, 1H, Glcα $H_{4'}$), 5.19−5.24 (m, 1H, Glcα $H_{3'}$), 5.33 (d, $^3J_{1'-2'}$ = 4.0 Hz, 1H, Glcα $H_{1'}$), 5.38−5.45 (m, 2H, CH_2O), 5.49−5.53 (m, 1H, Glcβ $H_{2'}$), 5.55−5.60 (m, 1H, Glcβ $H_{3'}$), 6.31 (d, $^3J_{1'-2'}$ = 8.8 Hz, 1H, Glcβ $H_{1'}$), 7.54 (s, 2H, SO_2NH_2), 7.91−8.10 (m, 4H, Ph CH), 8.47 (s, 1H, triazole H); ^{13}C {^1H} NMR (100 MHz, DMSO-d_6) δ 20.57 (OAc CH_3), 20.95 (OAc CH_3), 21.01 (OAc CH_3), 21.02 (OAc CH_3), 21.12 (OAc CH_3), 21.19 (OAc CH_3), 21.25 (OAc CH_3), 58.91 (CH_2O), 62.06 (Glcα $C_{6'}$), 63.45 (Glcβ $C_{6'}$), 68.37 (Glcα $C_{4'}$), 68.85 (Glcβ $C_{4'}$), 69.58 (Glcα $C_{3'}$), 70.11 (Glcα $C_{2'}$), 71.38 (Glcβ $C_{3'}$), 73.94 (Glcα $C_{5'}$), 74.58 (Glcβ $C_{5'}$), 74.96 (Glcβ $C_{5'}$), 79.85 (Glcβ $C_{2'}$), 84.16 (Glcβ $C_{1'}$), 96.41 (Glcα $C_{1'}$), 124.74 (triazole CH), 126.76 (Ph CH), 130.67 (Ph CH), 132.68 (Ph C), 143.06 (Ph C), 148.91 (triazole C), 165.09 (C═O), 169.36 (C═O), 169.84 (C═O), 170.19 (C═O), 170.35 (C═O), 170.53 (C═O), 170.67 (C═O), 170.78 (C═O); HRMS (ESI) calcd for $C_{36}H_{43}N_4O_{21}S^-$ 899.214 599, found 899.211 425. Anal. ($C_{36}H_{44}N_4O_{21}S\cdot1.5H_2O$) C, H, N, S.

4-({[4-(Aminosulfonyl)benzoyl]oxy}methyl-1-(*β*-D-maltosyl)-1*H*-1,2,3-triazole (3f′). The title compound was prepared according to general procedure 1 and isolated as a white foam (161 mg, 0.26

mmol, 58%): R_f 0.39 (2:8 CH_3OH:EtOAc); ^1H NMR (400 MHz, D_2O) δ 3.27−3.32 (m, 1H, Glcα $H_{4'}$ or Glcβ $H_{4'}$), 3.55−3.79 (m, 8H, Glcα $H_{3'}$, Glcα $H_{5'}$, Glcα $H_{6'}H_{6''}$, and Glcβ $H_{3'}$, Glcβ $H_{5'}$, Glcβ $H_{6'}/H_{6''}$), 3.46 (dd, $^3J_{2'-3'} = 10.0$ Hz, $^3J_{2'-1'} = 3.6$ Hz, 1H, Glcα $H_{2'}$), 3.84−3.94 (m, 2H, Glcβ $H_{2'}$), 3.84−3.94 (Glcβ $H_{2'}$ and Glcβ $H_{3'}$), 5.34 (d, $^3J_{1'-2'} = 3.6$ Hz, 1H, Glcα $H_{1'}$), 5.39 (s, 2H, CH_2O), 5.66 (d, $^3J_{1'-2'} = 8.8$ Hz, 1H, Glcβ $H_{1'}$), 7.78−7.97 (m, 4H, Ph H), 8.25 (s, 1H, triazole CH); ^{13}C {^1H} NMR (100 MHz, D_2O) δ 58.33 (CH_2O), 60.54 (Glcα $C_{6'}$ or Glcβ $C_{6'}$), 69.47, 71.84, 72.31, 72.92, 72.99, 75.93, 76.52, 77.66 (Glcα $C_{2'}$, Glcα $C_{3'}$, Glcα $C_{4'}$, Glcα $C_{5'}$ and Glcβ $C_{2'}$, Glcβ $C_{3'}$, Glcβ $C_{4'}$ Glcβ $C_{5'}$), 87.49 (Glcβ $C_{1'}$), 99.81 (Glcα $C_{2'}$), 125.16 (triazole CH), 126.23 (Ph CH), 130.69 (Ph CH), 133.57 (Ph CH), 142.82 (triazole C or Ph C), 145.68 (triazole C or Ph C), 166.59 (C═O); HRMS (ESI) calcld for $C_{22}H_{29}N_4O_{14}S^-$ 605.140 646, found 605.138 433.

Methyl 2′,3′,4′-tri-*O*-acetyl-6-[4-({[4-(aminosulfonyl)benzoyl]-oxy}methyl)-1*H*-triazol-1-yl]-6-deoxy-α-D-glucopyranoside (3g). The title compound was prepared according to general procedure 1 and isolated as a white foam (123 mg, 0.21 mmol, 89%): R_f 0.42 (2:8 hexanes:EtOAc). ^1H NMR (400 MHz, DMSO-d_6): δ 1.92 (OAc CH_3), 1.96 (OAc CH_3), 1.99 (OAc CH_3), 2.99 (OAc CH_3), 4.13 (ddd, $^3J_{5'-4'} = 10.8$ Hz, $^3J_{5'-6'} = 8.4$ Hz, $^3J_{5'-6''} = 2.8$ Hz, 1H, H_5), 4.52 (dd, $^2J_{6-6'} = 14.4$ Hz, $^3J_{6-5} = 8.4$ Hz, 1H, H_6), 4.62 (dd, $^2J_{6''-6'} = 14.4$ Hz, $^3J_{6''-5} = 3.0$ Hz, 1H, $H_{6''}$), 4.80−4.84 (m, 2H, $H_{1'}$, $H_{2'}$), 4.87−4.91 (m, 1H, $H_{4'}$), 5.22−5.23 (m, 1H, $H_{3'}$), 5.41 (s, 2H, CH_2O), 7.53 (br s, 2H, SO_2NH_2), 7.91−8.08 (m, 4H, Ph CH), 8.27 (s, triazole H); ^{13}C {^1H} NMR (100 MHz, DMSO-d_6) δ 20.99 (OAc CH_3), 21.05 (OAc CH_3), 21.17 (OAc CH_3), 50.59 ($C_{6'}$), 55.17 (OCH_3), 59.06 (CH_2O), 68.03 ($C_{5'}$), 70.08 ($C_{1'}$ or $C_{2'}$), 70.20 ($C_{1'}$ or $C_{2'}$), 70.35 ($C_{3'}$), 96.57 ($C_{1'}$), 126.55 (triazole CH), 126.77 (Ph CH), 130.58 (Ph CH), 132.75 (Ph C), 142.34 (triazole C or Ph C), 148.87 (triazole C or Ph C), 165.11 (C═O), 170.03 (C═O), 170.27 (C═O), 170.34 (C═O); HRMS (ESI) calcd for $C_{23}H_{27}N_4O_{12}S^-$ 583.135 167, found 583.133 906. Anal.($C_{23}H_{28}N_4O_{12}S\cdot0.5H_2O$) C, H; N: calcd, 9.44; found, 8.04; S: calcd, 5.40; found, 4.95.

Methyl 6-deoxy-6-(4-{4-sulfamoylbenzoyloxy}methyl-1*H*-1,2,3-triazol-1-yl)-α-D-glucopyranoside (3g′). The title compound was prepared according to procedure 1 and isolated as a white solid (75 mg, 0.16 mmol, 72%): R_f 0.52 (3:7 EtOH:$CHCl_3$); mp 121−122 °C; ^1H NMR (400 MHz, 2% D_2O in DMSO-d_6) δ 2.85 (s, 3H, OCH_3), 2.98 (dd, $^3J_{4'-5'} = 10.0$ Hz, $^3J_{4'-3'} = 8.8$ Hz, 1H, $H_{4'}$), 3.16 (dd, $^3J_{2'-3'} = 9.6$ Hz, $^3J_{2'-1'} = 3.6$ Hz, 1H, $H_{2'}$), 3.32−3.37 (m, 1H, $H_{3'}$), 3.61−3.66 (m, 1H, $H_{5'}$), 4.38 (dd, $^2J_{6'-6''} = 14.0$, $^3J_{6'-5'} = 9.2$ Hz, 1H, $H_{6'}$), 4.43 (d, $^3J_{1'-2'} = 4.0$ Hz, 1H, $H_{1'}$), 4.70 (dd, $^2J_{6''-6'} = 14.0$ Hz, $^3J_{6''-5'} = 2.4$ Hz, 1H, $H_{6''}$), 5.40 (s, 2H, CH_2O), 7.90−8.07 (m, 4H, Ph), 8.16 (s, 1H, triazole CH); ^{13}C {^1H} NMR (100 MHz, 2% D_2O in DMSO-d_6,) δ 51.01 ($C_{6'}$), 54.04 (OCH_3), 58.39 (CH_2O), 70.41 ($C_{5'}$), 71.66 ($C_{4'}$, $C_{2'}$), 73.06 ($C_{3'}$), 99.67 ($C_{1'}$), 125.89 (triazole CH), 126.08 (Ph CH), 129.89 (Ph CH), 132.08 (Ph C), 141.41 (Ph C), 148.75 (triazole C), 164.43 (C═O); HRMS (ESI) calcd for $C_{17}H_{21}N_4O_9S^-$ 457.103 47, found 457.103 411.

CA Inhibition Assay. An Applied Photophysics stopped-flow instrument has been used for assaying the CA catalyzed CO_2 hydration activity.[23] Phenol red (at a concentration of 0.2 mM) has been used as indicator, working at the absorbance maximum of 557 nm, with 10 mM Hepes (pH 7.5) as buffer, 0.1 M Na_2SO_4 (for maintaining constant the ionic strength), at 25 °C, following the CA-catalyzed CO_2 hydration reaction for a period of 10−100 s (the uncatalyzed reaction needs around 60−100 s under the assay conditions, whereas the catalyzed reactions take around 6−10 s). The CO_2 concentrations ranged from 1.7 to 17 mM for the determination of kinetic parameters. For each inhibitor, tested in the concentration range between 0.01 nM and 100 μM, at least six traces of the initial 5−10% of the reaction have been used for determining the initial velocity. The uncatalyzed rates were determined in the same manner and subtracted from the total observed rates. Stock solutions of inhibitor (1 mM) were prepared in distilled−deionized water with 10−20% (v/v) DMSO (which is not inhibitory at these concentrations), and dilutions up to 0.01 nM were done thereafter with distilled−deionized water. Inhibitor and enzyme solutions were preincubated together for 15 min at room temperature prior to assay, to allow for the formation of the E−I complex. The inhibition constants were obtained by nonlinear least-squares methods using PRISM 3. The curve-fitting algorithm allowed us to obtain the IC_{50} values, working at the lowest concentration of substrate of 1.7 mM), from which K_i values were calculated by using the Cheng−Prusoff equation.[24−28] The catalytic activity (in the absence of inhibitors) of these enzymes was calculated from Lineweaver−Burk plots, as reported earlier, and represent the mean from at least three different determinations.[24−28] Enzyme concentrations in the assay system were 9.2 nM for hCA I, 7.3 nM for hCA II, and 8.5 nM for hCA IX. Enzymes used here were recombinant ones, prepared and purified as described earlier.[24−28,30]

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Supporting Information Available: Elemental analysis data and ^1H NMR spectra for compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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