JOC The Journal of Organic Chemistry

Article

A route to triazole-fused sultams via metal-free base-mediated cyclization of sulfonamide-tethered 5-iodotriazoles

Stepan Spartakovich Tatevosyan, Yury Nikolaevich Kotovshchikov, Gennadij Vladimirovich Latyshev, Dmitry Alexandrovich Erzunov, Darina Vadimovna Sokolova, Irina P. Beletskaya, and Nikolay Vadimovich Lukashev

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c00520 • Publication Date (Web): 21 May 2020

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

A route to triazole-fused sultams via metal-free base-mediated cyclization of sulfonamide-tethered 5-iodotriazoles

Stepan S. Tatevosyan,[a] Yury N. Kotovshchikov,[a] Gennadij V. Latyshev,[a,*] Dmitry A. Erzunov,[a] Darina V. Sokolova,[b,c] Irina P. Beletskaya,[a] and Nikolay V. Lukashev[a]

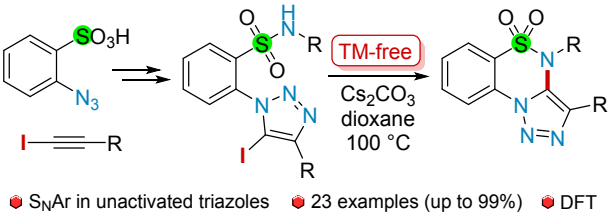
latyshev@org.chem.msu.ru

[a] Chemistry Department, M. V. Lomonosov Moscow State University, 1/3 Leninskiye Gory, Moscow 119991, Russia.

[b] Peoples' Friendship University of Russia, 6 Miklukho-Maklaya str., Moscow 117198, Russia.

[c] N. N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of Russia, 24 Kashirskoe Shosse, Moscow 115478, Russia.

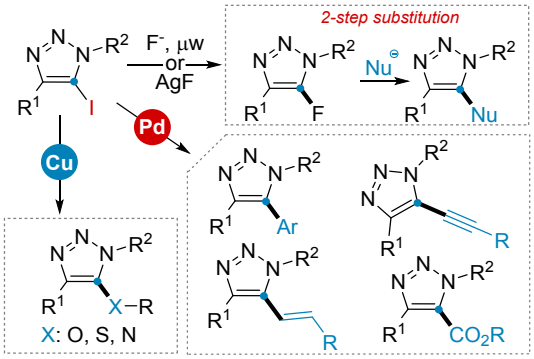
ABSTRACT: An efficient direct approach to triazole-fused sultams has been developed. The key step of the proposed strategy is base-mediated cyclization of sulfonamide-tethered 5-iodo-1,2,3-triazoles which are readily available *via* an improved protocol for Cu-catalyzed 1,3-dipolar cycloaddition. The annulation of the sultam fragment to the triazole ring proceeds smoothly under transition metal-free conditions in the presence of Cs_2CO_3 in dioxane at 100 °C and affords fused heterocycles in high yields up to 99%. A favorability of S_NAr-like mechanism for the cyclization was supported by DFT calculations. An applicability of the developed procedure to modification of natural compounds was demonstrated by a preparation of a deoxycholic acid derivative.



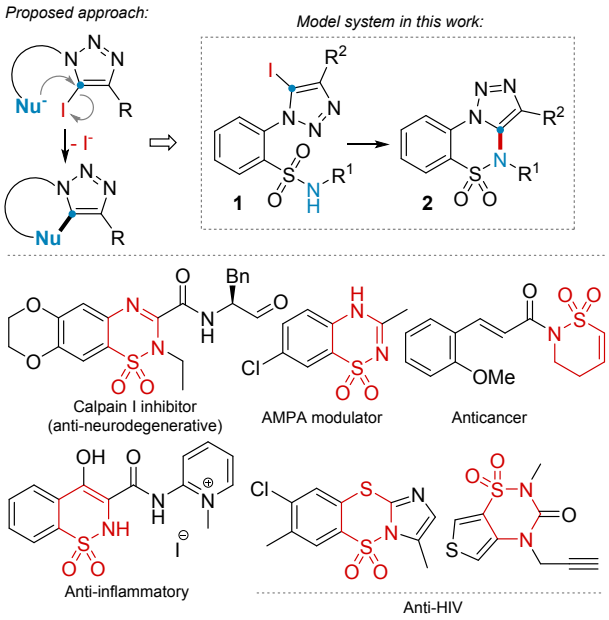
INTRODUCTION

The discovery of Cu-catalyzed azide-alkyne cycloaddition[1] provided the efficient route not only to 1,4-disubstituted 1,2,3-triazoles, but also to some of their 5-elementosubstituted derivatives.[2] Among them, 5-iodotriazoles[3] are of special significance due to the ease of further functionalization *via* metal-catalyzed substitution reactions (Scheme 1). These compounds were extensively used in various Pd-catalyzed processes including Suzuki,[4,5,6,7] Stille,[7,8,9] Heck,[4,10,11] Sonogashira,[4,6,10,12] and carbonylation[13] reactions. Cu-catalyzed post-Ullmann chemistry was used to replace iodine atom by S-,[14,15] O-[14] and N-nucleophiles.[16]

Scheme 1. Functionalization of 5-iodotriazoles



Scheme 2. Proposed approach to triazole-fused sultams



Non-catalyzed substitution of iodine seems to be an attractive approach to the functionalized triazoles. However, this area of triazole reactivity is poorly understood. In general, 5-iodotriazoles were considered as almost inert in nucleophilic substitution. The notable exception is iodine to fluorine exchange under harsh conditions[17] or in the presence of stoichiometric amounts of AgF[18] (Scheme 1). Higher reactivity of 5-fluorotriazoles towards strong nucleophiles allows to implement two-step substitution protocol.

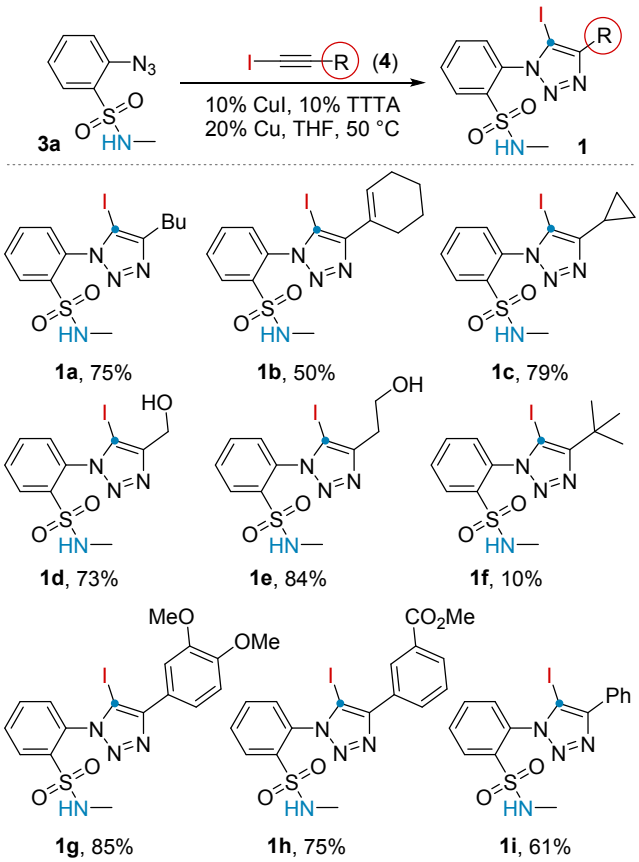
The decreased loss of entropy in intramolecular reaction will significantly facilitate nucleophilic substitution. Recently we have developed the approach to benzoxazoles from 2-(iodotriazolyl)phenols which should include the substitution step.[19] We suppose that this process is general and can be applied to other nucleophiles affording various fused triazoles.

To verify this hypothesis cyclization of triazole-containing sulfonamides **1** was investigated (Scheme 2). This reaction should provide a convenient approach to triazole-fused sultams **2** which can only be obtained by rather sophisticated method.[20] Sultam fragment is present in various compounds possessing a wide range of biological activity,[21] including anti-malarial,[22] anti-inflammatory,[23] anti-HIV,[24] and anticancer[25] effects.

RESULTS AND DISCUSSION

Wide range of 2-azidobenzenesulfonamides **3** was synthesized from commercially available orthanilic acid by high-yielding three-step procedure. The standard conditions[3] for the cycloaddition of azides **3** to iodoalkynes, employing CuI and tris{[1-(*tert*-butyl)-1*H*-1,2,3-triazol-4-yl]methyl}amine (TTTA), turned out to be inefficient leading to recovery of unreacted azide. It was found that addition of catalytic amount of Cu powder afforded **1** in generally good to high yields. Only in some cases the product was contaminated by aminobenzenesulfonamide due to the azide to amine reduction. The beneficial effect of Cu powder is probably associated with reduction of Cu(II) species formed by oxidation of the Cu(I) catalyst by admixtures in iodoalkynes or by traces of oxygen. The addition of stoichiometric amounts of Cu appeared inefficient and afforded a complex mixture of products.

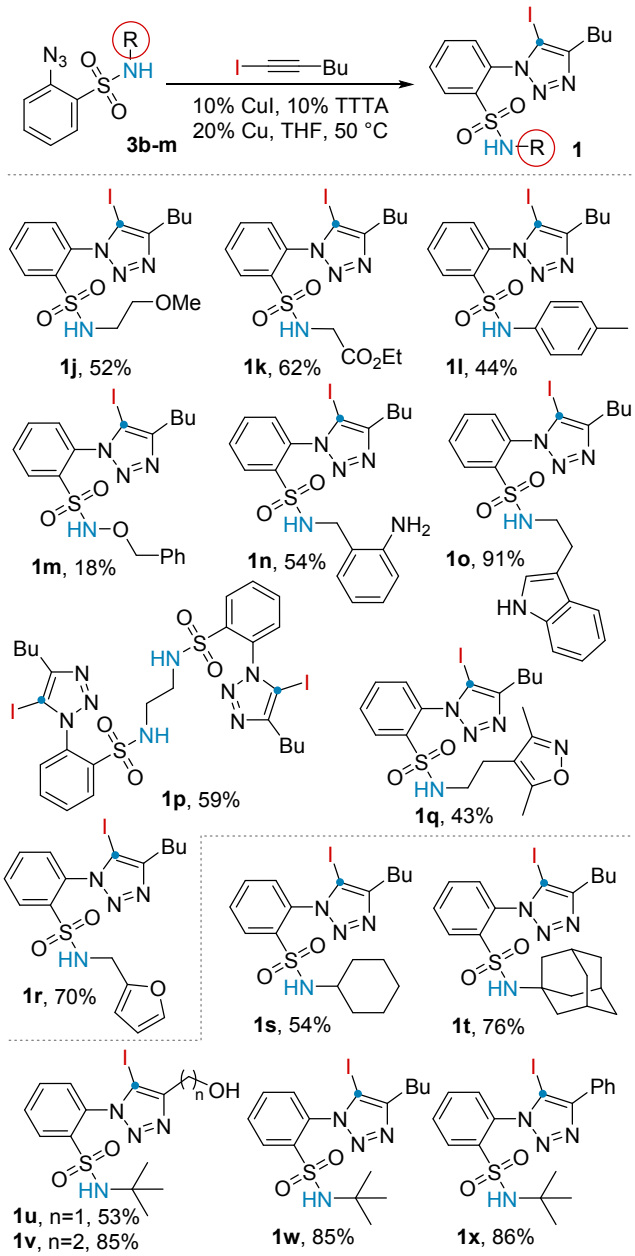
Scheme 3. Scope of various 4-substituted sulfonamide-tethered 5-iodotriazoles



Series of benzenesulfonamides **1** was prepared under the optimized conditions by varying the substituents in the triazole ring and at the sulfonamide nitrogen atom (Schemes 3 and 4).

Iodoalkynes bearing alkyl and vinyl substituents afforded iodotriazoles in good yields (up to 84%). The presence of free hydroxyl groups was tolerated. Even labile cyclopropyl-containing iodoalkyne gave cycloaddition product in rather high yield (**1c**, 79%). Significantly diminished yield was observed only for sterically demanding iodo(*tert*-butyl)acetylene (**1f**, 10%). Good to high yields were achieved for arylalkynes (**1g-i**, 61-85%) with both electron-donating (OMe) and electron-withdrawing (CO_2Me) groups.

Scheme 4. Scope of various *N*-substituted sulfonamide-tethered 5-iodotriazoles



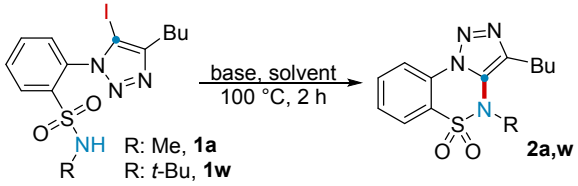
The reaction tolerates various substituents at the sulfonamide nitrogen (Scheme 4). *N*-Alkylsulfonamides afforded iodotriazoles in good to excellent yields (52-91%). The presence of ester (**1k**) as well as unprotected amino group (**1n**) was tolerated. Rather high yields were achieved for compounds bearing various heterocyclic moieties, including electrophile-sensitive indole (**1o**, 91%) and furan (**1r**, 70%). Reaction with *N*-*p*-tolylsulfonamide was accompanied by excessive azide reduction giving the product **1l** only in moderate yield (44%). A sharp decrease in yield occurred for hydroxylamine-containing sulfonamide **1m** due to probable reductive cleavage of N-O bond. In contrast, this side process wasn't observed for isoxazole-containing sulfonamide **1q**.

The steric hindrance at nucleophilic center can significantly influence the subsequent cyclization step. To evaluate this effect we have prepared a number of benzenesulfonamides **1s-x** bearing bulky groups attached to the nitrogen atom. Sulfonamides with

cyclohexyl (**1s**), adamantyl (**1t**), and *tert*-butyl (**1u-x**) moieties were obtained in moderate to rather high yields up to 86%. Unlike the detrimental effect of *tert*-butyl group on the formation of **1f**, sterically demanding substituents at sulfonamide N didn't significantly influence the CuIAAC reaction. In fact, the yield with bulky *N*-substituents was even slightly higher than the average one. Thus, the optimized cycloaddition protocol appeared quite robust. However, the reduction of azide by Cu powder led to the formation of inseparable admixture of 2-aminobenzenesulfonamide in some cases (most notably for **1b,c**,**f**,**j)**.

With a number of benzenesulfonamides **1a-x** in hand, we explored the intramolecular nucleophilic substitution. Compound **1a** was used as a model substrate for base-mediated cyclization. A brief optimization of reaction conditions was carried out at 100 °C using a twofold excess of base (Table 1).

Table 1. Optimization of cyclization conditions[a]

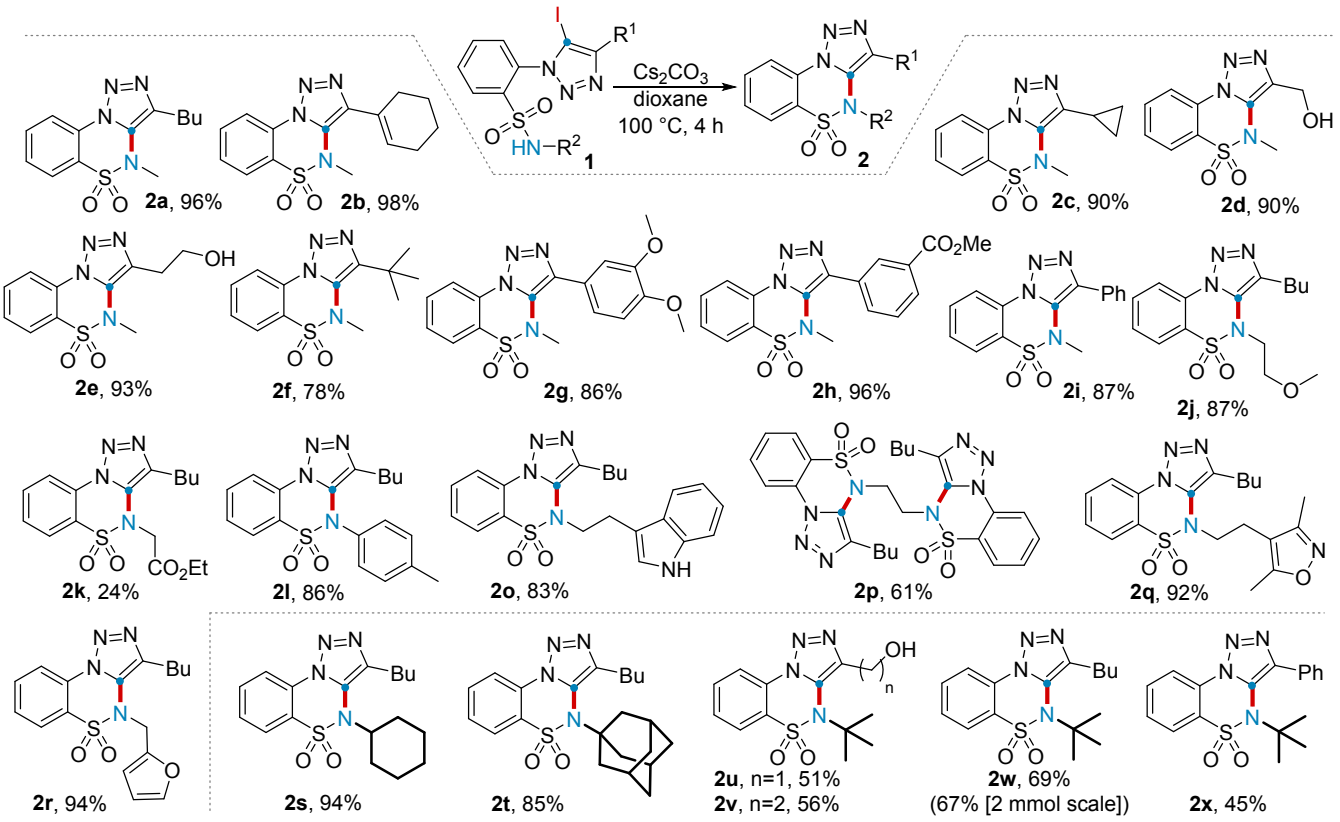


Entry	R	Solvent	Base	Yield, % [b]
1	Me	Dioxane	Li_2CO_3	0
2	Me	Dioxane	K_2CO_3	16
3	Me	Dioxane	Cs_2CO_3	95 (95)
4	Me	DMSO	K_2CO_3	86
5	*t*-Bu	DMSO	K_2CO_3	traces
6	*t*-Bu	Dioxane	Cs_2CO_3	(69)

[a] Reaction run on a 0.1 mmol scale; [b] according to ^{1}H NMR, isolated yield in parentheses.

Intramolecular nucleophilic substitution in sulfonamide **1a** proceeded smoothly with Cs_2CO_3 in dioxane and reached completion in 2 h. The anticipated sultam **2a** was formed in almost quantitative yield (entry 3, Table 1). The reaction with K_2CO_3 in dioxane was much slower (entry 2), whereas only the unchanged starting material was recovered with Li_2CO_3 (entry 1). The complete conversion of **1a** was observed with K_2CO_3 in DMSO, though the product was contaminated by small amounts of unidentified impurities. However, the cyclization of *N*-*tert*-butyl containing sulfonamide **1w** in DMSO (entry 5) afforded complex mixture of products, while 69% isolated yield of **2w** was obtained in dioxane. Thus, the Cs_2CO_3/dioxane system was chosen for the cyclization of sulfonamides **1**.

Scheme 5. Scope of sulfonamide cyclization



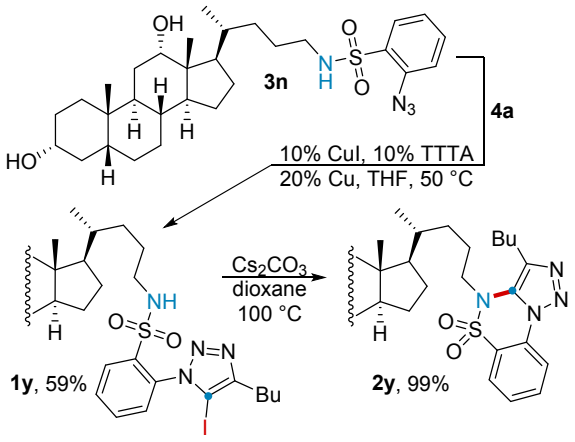
Sultams **2** were obtained in good to high yields regardless of the electronic effects of substituents in the triazole ring and at the sulfonamide N (Scheme 5). Although cyclization benefits from substituents capable to stabilize sulfonamide anion (**2l**, 86%) or negatively charged intermediates (**2h**, 96%), the yields were also high even for aliphatic groups. Additional acidic functionalities, such as OH-groups (**2d,e**) and NH of indole (**2o**), didn't influence the yield substantially. Steric effect of substituents wasn't noticeable for secondary alkyl (**2c,s**) and even adamantyl (**2t**) moieties. However, the presence of *tert*-butyl groups in the triazole ring (**2f**, 78%) and especially attached to the nucleophile led to diminished yields (**2u-x**, down to 45%).

Glycine-derived sulfonamide **1k** was not compatible with basic conditions affording low yield of sultam **2k** (24%) accompanied by numerous condensation byproducts. Surprisingly, a complex mixture of products was obtained in cyclization of **1m** and **1n**. Formation of benzyl alcohol and benzaldehyde in the case of **1m** indicated the cleavage of hydroxylamine moiety. Nevertheless, excellent yields were achieved for sultams bearing various heterocyclic units, namely indole (**2o**, 83%), isoxazole (**2q**, 92%), and furan (**2r**, 94%). Cyclization can even be performed twice giving ethylene-linked bis-sultam **2p** in 61% yield.

Cytotoxic effect of triazole-fused sultams **2c,e,o** was evaluated against ovarian (SKOV-3) and breast (MCF-7) cancer cell lines. While **2c** and **2e** appeared almost inactive (IC_{50} > 50 μM), moderate activity against both SKOV-3 (IC_{50} = 19 μM) and MCF-7 (IC_{50} = 9 μM) was observed for **2o**.

To demonstrate the utility of the developed protocol in derivatization of polyfunctional natural compounds, we have prepared azidobenzenesulfonamide **3n**[26] from deoxycholic acid which is an important member of bile acid group (Scheme 6). Azide **3n** was converted to the corresponding iodotriazole **1y**, which smoothly underwent a cyclization under the standard conditions, furnishing triazole-fused sultam **2y** bearing steroidal moiety in almost quantitative yield (99%).

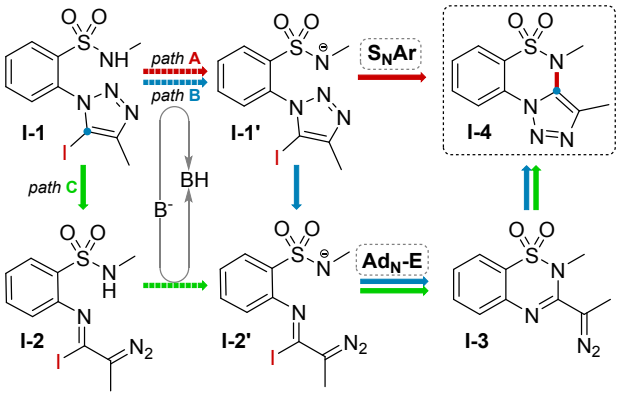
Scheme 6. Synthesis of steroid-containing sultam



Thus, our approach to annulated triazoles, incorporating a sulfonamide fragment, turned out to be quite general and applicable to substrates with various steric and electronic features.

Mechanistic aspects of the reaction were studied by DFT (B3LYP/ma-SVP/dioxane (SMD)) on a model substrate **I-1**. The transformation of **I-1** to sultam **I-4** can proceed through nucleophilic substitution of iodine either in triazole (Scheme 7, path **A**, **I-1** → **I-1'** → **I-4**) or in tautomeric diazo form. The latter path is believed to operate in iodine to fluorine exchange in 5-iodo-1,2,3-triazoles.[17] The key intermediate **I-2'** can be produced in different order of deprotonation and ring-opening events, constituting paths **B** (**I-1** → **I-1'** → **I-2'** → **I-3** → **I4**) and **C** (**I-1** → **I-2** → **I-2'** → **I-3** → **I-4**).

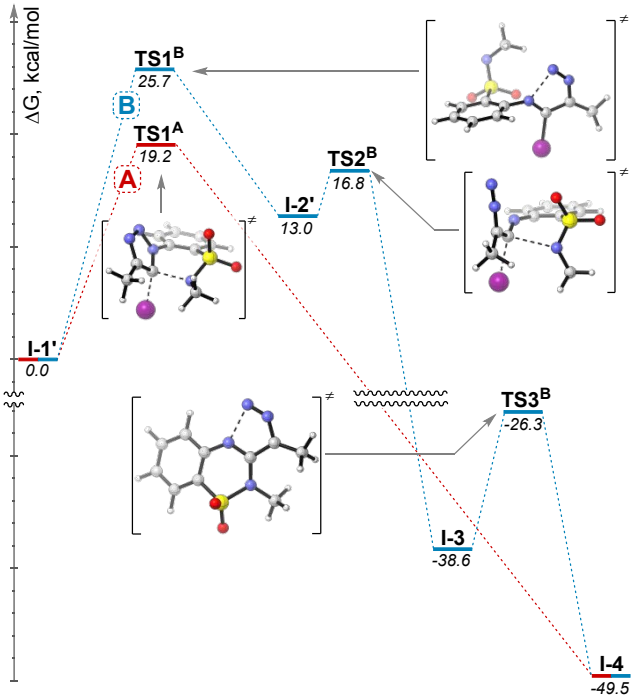
Scheme 7. Possible cyclization mechanisms



The structure of all intermediates and transition states for paths **A** and **B** starting from **I-1'** was located and optimized (Scheme 8). Triazole ring-opening in **I-1'** (path **B**) proceeds with rather high barrier ($\Delta G^{\neq}$ = 25.7 kcal/mol) affording unstable **I-2'**. The C–I

bond in **I-2'** is substantially elongated (2.33 Å), justifying facile ($\Delta G^{\neq}$ = 3.8 kcal/mol) substitution of iodide. Cyclization of diazo tautomer **I-3** to final sultam **I-4** has low activation energy ($\Delta G^{\neq}$ = 12.3 kcal/mol).

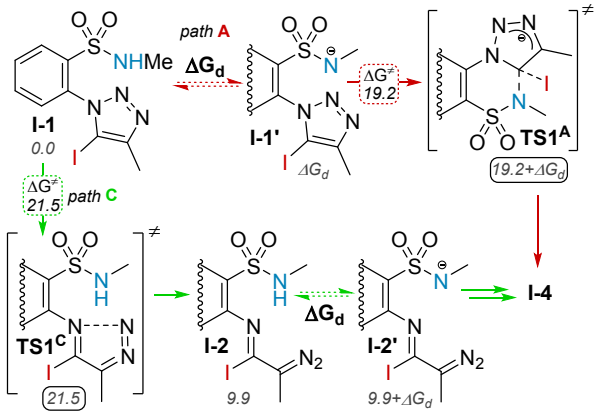
Scheme 8. Free energy profiles for paths A and B



Formation of C–N bond through direct nucleophilic substitution in the triazole ring (S_NAr) (path **A**) takes place simultaneously with C–I bond breaking. We were unable to locate intermediate Meisenheimer complex, typical for classic S_NAr mechanism. Since B3LYP functional is known to predict a synchronous mechanism for reactions of anionic species,[27] we confirmed the absence of the intermediate by the second-order Möller-Plesset perturbation theory (RI-MP2/def2-TZVP/dioxane (SMD)). Since the barrier for aromatic nucleophilic substitution is significantly lower ($\Delta G^{\neq}$ = 19.2 kcal/mol) than the barrier for the triazole ring-opening, path **A** seems to be preferred for sulfonamide anions.

Path **C** is conceptually similar to path **B** but contains a different sequence of deprotonation and ring-opening events. Due to the intrinsic problems with correct description of acidity by QM methods, the direct comparison of paths **A** and **C** was initially attempted for equimolar mixture of **I-1** and **I-1'** (Scheme 9, ΔG_d = 0). The transformation of uncharged **I-1** into diazo form **I-2** is less endergonic (ΔG = 9.9 kcal/mol) and proceeds much easier than the same step for electron-rich anion **I-1'**. However, this barrier ($\Delta G^{\neq}$ = 21.5 kcal/mol) is still higher than the barrier for nucleophilic substitution in **I-1'** (19.2 kcal/mol). Thus, there is a distinct preference for the path **A** (S_NAr mechanism) over paths **B** and **C**.

Scheme 9. Free energies of major intermediates and transition states along paths A and C[a]



[a] Free energies in kcal/mol

The situation may be significantly altered by the basicity of the medium. The stronger base ($\Delta G_d < 0$) will shift the equilibrium towards deprotonated sulfonamide **I-1'**, effectively lowering the energy levels of all anionic intermediates and TSs and favoring path **A**. However, for a weak base ($\Delta G_d > 0$) the contribution of deprotonation step to the apparent activation energy can be decisive. The energy levels of all anionic intermediates will be increased, and **TS1^A** (path **A,** $\Delta G = 19.2+\Delta G_d$) can even become the highest point on the PES (see SI, scheme **S1**).

Thus, in case of weak bases (strongly endergonic deprotonation step) the competition between mechanisms **A** and **C** is possible. If a concentration of anion in the reaction mixture is fairly high, intramolecular nucleophilic substitution proceeds according to the S_NAr mechanism. This path is believed to operate in **1** due to rather high acidity of sulfonamide group.

CONCLUSION

In conclusion, intramolecular cyclization of nucleophile-tethered 5-iodotriazoles was proposed as a convenient route to fused triazoles. To demonstrate the feasibility of this concept we have developed an efficient approach to triazole-fused sultams. It comprises a modified CuIAAC protocol and base-mediated cyclization under catalyst-free conditions. The addition of substoichiometric amounts of Cu powder was found to substantially increase the yields of [3+2]-cycloaddition. The subsequent cyclization proceeded smoothly in the presence of Cs_2CO_3 in dioxane at 100 °C, affording sultams in up to 99% yield. According to DFT analysis of possible reaction pathways, iodine substitution in non-activated triazoles should occur *via* S_NAr-like mechanism. Bearing in mind rather low nucleophilicity of sulfonamides, we believe that the reaction can be expanded on a broad range of other nucleophiles furnishing various types of triazole-fused heterocycles.

EXPERIMENTAL SECTION

General Information

NMR spectra were recorded with Bruker Avance 400, Agilent 400MR (^{1}H 400 MHz, ^{13}C 100.6 MHz), Bruker Avance 600 (^{1}H 600 MHz, ^{13}C 150 MHz), and Bruker AC200 (^{1}H 200 MHz) spectrometers at ambient temperature. Chemical shifts are presented in ppm (δ scale) and referenced to hexamethyldisiloxane (δ = 0.05 ppm) or tetramethylsilane (δ = 0 ppm) in the ^{1}H NMR spectra and to the solvent signal in the ^{13}C{^{1}H} NMR spectra. For compounds with low solubility in $CDCl_3$ a few drops of CD_3OD or DMSO-d^6 were added to NMR samples. MALDI-TOF spectra were recorded with a Bruker Daltonics UltraFlex instrument in a dithranol or a cinnamic acid matrix using PEG 300, PEG 400 or PEG 600 as the internal standard. ESI-TOF spectra were recorded with a Thermo Scientific Orbitrap Elite instrument. Column chromatography was carried out on Macherey–Nagel silica gel 60 (0.040–0.063 mm). Iodoalkynes **4** were prepared according to the reported general procedure.[28]

DFT calculations

The calculations were performed using ORCA 4.2.0 program package.[29] DFT calculations were performed at B3LYP[30,31]/ma-SVP[32,33]/SMD[34] (dioxane) level of theory employing def2-ECP pseudopotential for iodine.[35] RIJCOSX[36] approximation was used to speed up the calculations. Thermodynamic properties were calculated for ideal gas at 298.15 K using QRRHO approach[37] for vibrational entropy correction. The nature of optimized intermediates and transition states was verified by frequency analysis. IRC calculations were performed to verify the connectivity of the PES. CYLView[38] was used to visualize structure of the intermediates.

Experimental procedures

Sodium 2-azidobenzenesulfonate

2-Aminobenzenesulfonic acid (11.57 g, 66 mmol) and 15 mL of 10% H_2SO_4 were mixed in H_2O (45 mL). The reaction mixture was cooled to 0 °C, and $NaNO_2$ (6.0 g, 87 mmol) in H_2O (30 mL) was added. After stirring for 0.5 h, NaN_3 (8.6 g, 133 mmol) in H_2O (30 mL) was added. The reaction mixture was stirred at room temperature for 15 h, evaporated under reduced pressure to half the volume and placed in a refrigerator. The precipitate formed was filtered off and dried in a vacuum desiccator over P_2O_5. Though the compound was described earlier as 2-azidobenzenesulfonic acid,[39] the neutral pH of the aqueous solution is consistent with sodium salt structure. Yield 12.881 g (88%). Beige powder; mp 220 °C (dec.); ^{1}H NMR (400 MHz, DMSO-d^6): δ 7.76 (dd, J = 7.9, 1.6 Hz, 1H), 7.38 (td, J = 8.0, 1.6 Hz, 1H), 7.20 (dd, J = 8.0, 1.1 Hz, 1H), 7.13 (td, J = 7.9, 1.1 Hz, 1H).

2-Azidobenzenesulfonyl chloride (5)

The suspension of sodium 2-azidobenzenesulfonate (1.50 g, 6.8 mmol) in $POCl_3$ (7.5 mL) was stirred under refluxed for 8 h. Then excess of $POCl_3$ was evaporated at 40 °C under reduced pressure. Ice water (100 mL) was added to the residue, and the obtained mixture was stirred for 15 min until complete hydrolysis of $POCl_3$ residue (*Caution:* reaction is highly exothermic). The product was extracted with CH_2Cl_2 (100 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvent was evaporated *in vacuo*. The residue was used in the preparation of sulfonamides **3** without further purification. Yield 1.051 g (71%). Dark powder.

^{1}H NMR (200 MHz, $CDCl_3$): δ 8.05 (dd, J = 8.1, 1.5 Hz, 1H), 7.76 (td, J = 8.1, 1.5 Hz, 1H), 7.42 (dd, J = 8.1, 1.0 Hz, 1H), 7.33 (td, J = 8.1, 1.0 Hz, 1H). Spectral data were consistent with literature.[40]

General procedure for the preparation of 2-azidobenzenesulfonamides

Primary amine (1.8 mmol) was added to a solution of **5** (1.5 mmol) and Et_3N (3.0 mmol) in THF (3.0 mL). The reaction mixture was stirred at room temperature overnight, then diluted with CH_2Cl_2 (50 mL), and washed with water (50 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvents were evaporated *in vacuo*. The residue was purified by column chromatography.

2-Azido-*N*-methylbenzenesulfonamide (3a)

Prepared from **5** (1.04 g. 4.8 mmol) and 40% aq. solution of CH_3NH_2 (1.7 mL, 12.0 mmol) according to the general procedure without addition of Et_3N; eluent: CH_2Cl_2–MeOH = 100:1. Yield 895 mg (88%). Pale yellow powder; mp 150–152 °C (lit.[39] 136–138 °C); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (dd, J = 7.8, 1.3 Hz, 1H), 7.62 (td, J = 7.8, 1.3 Hz, 1H), 7.32-7.27 (m, 2H), 4.99 (br q, J = 5.4 Hz, 1H), 2.62 (d, J = 5.4 Hz, 3H).

2-Azido-*N*-(2-methoxyethyl)benzenesulfonamide (3b)

Prepared from **5** (261.1 mg, 1.2 mmol) and 2-methoxyethanamine (115.5 µL, 1.44 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 100:1. Yield 277 mg (90%). Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, J = 7.8, 1.5 Hz, 1H), 7.61 (td, J = 8.0, 1.5 Hz, 1H), 7.31 (dd, J = 8.0, 1.1 Hz, 1H), 7.27 (td, J = 7.8, 1.1 Hz, 1H), 5.51 (t, J = 5.7 Hz, 1H), 3.38 (t, J = 5.7 Hz, 2H), 3.27 (s, 3H), 3.09 (q, J = 5.7 Hz, 2H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 137.7 (C_{quat}), 134.0, 130.4, 129.8 (C_{quat}), 124.7, 119.3, 70.2, 58.7, 45.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_9H_{13}N_4O_3S$ 257.0703; Found 257.0703. Spectral data were consistent with literature.[41]

Ethyl *N*-[(2-azidophenyl)sulfonyl]glycinate (3c)

Prepared from **5** (261.1 mg, 1.2 mmol) and ethyl glycinate hydrochloride (201.0 mg, 1.44 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 100:1. Yield 200 mg (59%). Dark brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, J = 8.0, 1.4 Hz, 1H), 7.61 (td, J = 7.6, 1.4 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.25 (t, J = 7.6 Hz, 1H), 5.67 (t, J = 5.4 Hz, 1H), 4.08 (q, J = 7.2 Hz, 2H), 3.82 (d, J = 5.4 Hz, 2H), 1.18 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 168.6 (C_{quat}), 138.2 (C_{quat}), 134.1, 130.3, 129.3 (C_{quat}), 124.6, 119.5, 61.8, 44.5, 13.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{13}N_4O_4S$ 285.0652; Found 285.0652.

2-Azido-*N*-(4-methylphenyl)benzenesulfonamide (3d)

Prepared from **5** (261.1 mg, 1.2 mmol) and 4-methylaniline (154 mg, 1.44 mmol) according to the general procedure; eluent: CH_2Cl_2. Yield 278 mg (80%). Pale orange powder; mp 149–151 °C (lit.[39] 138–140 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (dd, J = 7.8, 1.3 Hz, 1H), 7.54 (td, J = 7.8, 1.3 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.09 (s, 1H), 7.00 (s, 4H), 2.23

(s, 3H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 137.6 (C_{quat}), 135.4 (C_{quat}), 134.2, 133.4 (C_{quat}), 131.2, 129.8 (2C), 128.6 (C_{quat}), 124.7, 121.8 (2C), 119.3, 20.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}N_4O_2S$ 289.0754; Found 289.0754.

2-Azido-*N*-(benzyloxy)benzenesulfonamide (3e)

Prepared from **5** (261.1 mg, 1.2 mmol) and *O*-benzylhydroxylamine (174.5 mg, 1.44 mmol) according to the general procedure; eluent: CH_2Cl_2. Yield 320 mg (88%). Pale yellow crystals; mp 133–135 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 7.7 Hz, 1H), 7.83 (s, 1H), 7.64 (t, J = 7.4 Hz, 1H), 7.32-7.28 (m, 7H), 4.98 (s, 2H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 137.8 (C_{quat}), 135.1 (C_{quat}), 135.0, 132.1, 129.4 (2C), 128.7, 128.4 (2C), 126.9 (C_{quat}), 125.0, 119.3, 79.4; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}N_4O_3S$ 305.0703; Found 305.0705.

***N*-(2-Aminobenzyl)-2-azidobenzenesulfonamide (3f)**

Prepared from **5** (261.1 mg, 1.2 mmol) and 2-(aminomethyl)aniline (176 mg, 1.44 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:1. Yield 200 mg (55%). Dark brown powder; mp 147–148 °C; ^1H NMR (400 MHz, $CDCl_3/CD_3OD$): δ 7.96 (dd, J = 7.9, 1.4 Hz, 1H), 7.58 (td, J = 7.8, 1.5 Hz, 1H), 7.25 (td, J = 7.7, 1.0 Hz, 1H), 7.21 (dd, J = 8.0, 0.7 Hz, 1H), 7.05 (td, J = 7.7, 1.5 Hz, 1H), 6.81 (dd, J = 7.5, 1.3 Hz, 1H), 6.67 (dd, J = 8.0, 0.9 Hz, 1H), 6.56 (td, J = 7.4, 1.1 Hz, 1H), 6.17 (m, 1H), 3.99 (br s, 2H), 3.68 (br s, 2H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3/CD_3OD$): δ 145.2 (C_{quat}), 137.7 (C_{quat}), 134.1, 130.6, 130.0, 129.4, 129.2 (C_{quat}), 124.7, 120.6 (C_{quat}), 119.4, 118.3, 116.1, 44.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{14}N_5O_2S$ 304.0863; Found 304.0866.

2-Azido-*N*-[2-(1*H*-indol-3-yl)ethyl]benzenesulfonamide (3g)

Prepared from **5** (261.1 mg, 1.2 mmol) and 2-(1*H*-indol-3-yl)ethanamine (273.9 mg, 1.71 mmol) according to the general procedure; eluent: CH_2Cl_2. Yield 352 mg (86%). Brown oil; ^1H NMR (600 MHz, $CDCl_3$): δ 8.16 (br s, 1H), 7.92 (dd, J = 7.8, 1.4 Hz, 1H), 7.45 (td, J = 7.8, 1.4 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.20-7.15 (m, 2H), 7.04 (d, J = 2.3 Hz, 1H), 6.97 (td, J = 8.1, 0.8 Hz, 1H), 6.84 (dd, J = 8.1, 0.8 Hz, 1H), 4.92 (t, J = 5.7 Hz, 1H), 3.20 (m, 2H), 2.97 (t, J = 6.2 Hz, 2H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 137.2 (C_{quat}), 136.4 (C_{quat}), 133.8, 130.6, 128.5 (C_{quat}), 126.6 (C_{quat}), 124.4, 123.1, 122.3, 119.6, 118.9, 118.2, 111.4, 111.1 (C_{quat}), 43.0, 24.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}N_5O_2S$ 342.1019; Found 342.1019.

***N*,*N*'-Ethane-1,2-diylbis(2-azidobenzenesulfonamide) (3h)**

Prepared from **5** (326.4 mg, 1.5 mmol) and ethylenediamine (50 μL, 0.75 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 50:1. Yield 255 mg (80%). Beige powder; mp 180–182 °C; ^1H NMR (400 MHz, DMSO-$d^6/CD_3OD/CDCl_3/CCl_4$): δ 7.83 (dd, J = 7.9, 1.2 Hz, 2H), 7.65 (td, J = 7.7, 1.3 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.28 (t, J = 7.6 Hz, 2H), 2.89 (s, 4H); $^{13}C\{^1H\}$ NMR (100.6 MHz, DMSO-$d^6/CD_3OD/CDCl_3/CCl_4$): δ 137.3 (2C_{quat}), 133.7 (2C), 129.8 (2C), 126.8

($2C_{quat}$), 124.3 (2C), 119.8 (2C), 42.1 (2C); HRMS (MALDI-TOF, dithranol) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{14}N_8O_4S_2Na$ 445.0472; Found 445.0473.

2-Azido-*N*-[2-(3,5-dimethylisoxazol-4-yl)ethyl]benzenesulfonamide (3i)

Prepared from **5** (261.1 mg, 1.2 mmol) and 2-(3,5-dimethylisoxazol-4-yl)ethanamine (201.6 mg, 1.44 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 50:1. Yield 256 mg (66%). Pale yellow crystals; mp 126–128 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, J = 7.8, 1.4 Hz, 1H), 7.61 (td, J = 7.8, 1.5 Hz, 1H), 7.30-7.25 (m, 2H), 5.21 (t, J = 6.0 Hz, 1H), 2.99 (m, 2H), 2.56 (t, J = 6.9 Hz, 2H), 2.31 (s, 3H), 2.12 (s, 3H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 165.9 (C_{quat}), 159.0 (C_{quat}), 137.1 (C_{quat}), 133.8, 130.2, 129.0 (C_{quat}), 124.4, 119.0, 109.4 (C_{quat}), 42.2, 22.6, 10.6, 9.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{13}H_{16}N_5O_3S$ 322.0968; Found 322.0967.

2-Azido-*N*-(2-furylmethyl)benzenesulfonamide (3j)

Prepared from **5** (326.4 mg, 1.5 mmol) and (2-furylmethyl)amine (166 μL, 1.8 mmol) according to the general procedure; eluent: CH_2Cl_2. Yield 363 mg (87%). Pale yellow powder; mp 92–94 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (dd, J = 7.7, 1.4 Hz, 1H), 7.53 (td, J = 7.7, 1.4 Hz, 1H), 7.22 (td, J = 7.7, 1.4 Hz, 1H), 7.19-7.15 (m, 2H), 6.09 (dd, J = 3.0, 1.3 Hz, 1H), 5.91 (d, J = 3.0 Hz, 1H), 5.50 (t, J = 6.3 Hz, 1H), 4.18 (d, J = 6.3 Hz, 2H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 149.2 (C_{quat}), 142.3, 137.5 (C_{quat}), 133.7, 130.3, 129.9 (C_{quat}), 124.6, 119.1, 110.2, 108.3, 40.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}N_4O_3S$ 279.0546; Found 279.0546.

2-Azido-*N*-cyclohexylbenzenesulfonamide (3k)

Prepared from **5** (326.4 mg, 1.5 mmol) and cyclohexylamine (206 μL, 1.8 mmol) according to the general procedure; eluent: CH_2Cl_2. Yield 350 mg (83%). Light yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 7.6 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.31-7.25 (m, 2H), 4.97 (d, J = 6.9 Hz, 1H), 3.12 (m, 1H), 1.75 (m, 2H), 1.63 (m, 2H), 1.52 (m, 1H), 1.30-1.08 (m, 5H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 137.4 (C_{quat}), 133.7, 131.6 (C_{quat}), 130.1, 124.8, 119.4, 53.0, 33.6 (2C), 25.1, 24.5 (2C); HRMS (MALDI-TOF, dithranol) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{16}N_4O_2SNa$ 303.0886; Found 303.0887.

***N*-1-Adamantyl-2-azidobenzenesulfonamide (3l)**

Prepared from **5** (261.1 mg, 1.2 mmol) and 1-adamantylamine (217.7 mg, 1.44 mmol) according to the general procedure; eluent: CH_2Cl_2. Yield 330 mg (83%). Pale yellow powder; mp > 201 °C (dec.); ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 8.0 Hz, 1H,), 7.58 (t, J = 7.6 Hz, 1H), 7.30-7.24 (m, 2H), 4.96 (s, 1H), 2.00 (m, 3H), 1.77 (m, 6H), 1.58 (m, 6H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 136.9 (C_{quat}), 133.9 (C_{quat}), 133.0, 129.0, 124.6, 119.0, 54.9 (C_{quat}), 42.6 (3C), 35.4 (3C), 29.1 (3C); HRMS (MALDI-TOF, dithranol) m/z: $[M + K]^+$ Calcd for $C_{16}H_{20}N_4O_2SK$ 371.0939; Found 371.0901.

2-Azido-*N*-*tert*-butylbenzenesulfonamide (3m)

Prepared from **5** (99.6 mg. 0.5 mmol) and *tert*-butylamine (158 μL, 1.5 mmol) according to the general procedure without addition of Et_3N; eluent: CH_2Cl_2. Yield 122 mg (96%); mp 162–164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, J = 7.8, 1.4 Hz, 1H), 7.58 (td, J = 7.8, 1.4 Hz, 1H), 7.28-7.24 (m, 2H), 4.98 (br s, 1H), 1.21 (s, 9H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 137.2 (C_{quat}), 133.6 (C_{quat}), 133.4, 129.5, 124.9, 119.3, 54.7 (C_{quat}), 30.0 (3C); HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{10}H_{15}N_4O_2S$ 255.0910; Found 255.0912.

2-Azido-*N*-[(3α,5β,12α)-3,12-dihydroxycholan-24-yl]benzenesulfonamide (3n)

Prepared from **5** (261.1 mg, 1.2 mmol) and (3α,5β,12α)-24-aminocholane-3,12-diol[26] (542.3 mg, 1.44 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 15:1. Yield 592 mg (88%). Beige powder; mp 124–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 7.6 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.32-7.25 (m, 2H), 5.12 (t, J = 6.0 Hz, 1H), 3.95 (m, 1H), 3.60 (tt, J = 11.0, 4.9 Hz, 1H), 2.86 (m, 2H), 2.05-0.93 (m, 28H), 0.90 (m, 6H), 0.64 (s, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 137.1 (C_{quat}), 135.5, 130.3, 129.6 (C_{quat}), 124.5, 118.9, 72.7, 71.3, 47.8, 46.9, 46.0, 43.5, 41.6, 36.0, 35.6, 34.83, 34.78, 33.7, 33.2, 32.2, 30.0, 28.2, 27.2, 26.7, 25.8, 25.7, 23.2, 22.7, 17.1, 12.3; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{30}H_{47}N_4O_4S$ 559.3313; Found 559.3311.

General procedure for the preparation of iodotriazoles

2-Azidobenzenesulfonamide **3** (1.0 mmol), 1-iodoalkyne **4** (1.1 mmol), CuI (19.1 mg, 0.100 mmol, 10 mol%), Cu powder (12.7 mg, 0.200 mmol, 20 mol%), and tris[(1-*tert*-butyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TTTA) (42.8 mg, 0.100 mmol, 10 mol%) were mixed under an Ar atmosphere in THF (1 mL). The reaction mixture was stirred at 50 °C in a dry block overnight or for several days (TLC control), then diluted with CH_2Cl_2 (50 mL), washed with EDTA solution (50 mL) and water (50 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvents were evaporated *in vacuo*. The residue was purified by column chromatography.

2-(4-Butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)-*N*-methylbenzenesulfonamide (1a)

Prepared from **3a** (212.2 mg, 1.0 mmol) and 1-iodohex-1-yne (150 μL, 1.1 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:1. Yield 315 mg (75%). Pale yellow powder; mp 122–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (dd, J = 7.6, 1.6 Hz, 1H), 7.80 (td, J = 7.6, 1.6 Hz, 1H), 7.75 (td, J = 7.6, 1.4 Hz, 1H), 7.43 (dd, J = 7.6, 1.4 Hz, 1H), 5.05 (q, J = 5.3 Hz, 1H), 2.77 (t, J = 7.8 Hz, 2H), 2.68 (d, J = 5.3 Hz, 3H), 1.77 (quint, J = 7.7 Hz, 2H), 1.44 (sext, J = 7.6 Hz, 2H), 1.77 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 152.8 (C_{quat}), 135.6 (C_{quat}), 134.3 (C_{quat}), 133.3, 131.2, 130.8, 130.3, 83.0 (C_{quat}), 30.9, 29.6, 25.8, 22.1, 13.8; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{13}H_{18}IN_4O_2S$ 421.0190; Found 421.0189.

2-[4-(Cyclohex-1-en-1-yl)-5-iodo-1*H*-1,2,3-triazol-1-yl]-*N*-methylbenzenesulfonamide (1b)

Prepared from **3a** (212.2 mg, 1.0 mmol) and 1-(iodoethynyl)cyclohexene (145 μL, 1.1 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 264 mg (50% assuming purity 85%). Light brown crystals; mp 174–176 °C; ^{1}H NMR (400

MHz, $CDCl_3$): δ 8.19 (d, J = 7.7 Hz, 1H), 7.82-7.33 (m, 2H), 7.44 (d, J = 7.7 Hz, 1H), 6.61 (m, 1H), 5.00 (q, J = 5.2 Hz, 1H), 2.67 (d, J = 5.2 Hz, 3H), 2.64-2.60 (m, 2H), 2.26-2.23 (m, 2H), 1.82-1.77 (m, 2H), 1.72-1.66 (m, 2H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$) δ 151.6 (C_{quat}), 135.7 (C_{quat}), 134.1 (C_{quat}), 133.2, 131.2, 130.9, 130.7, 129.5, 127.3 (C_{quat}), 79.6 (C_{quat}), 29.6, 27.1, 25.4, 22.5, 21.8; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}IN_4O_2S$ 445.0190; Found 445.0190.

2-(4-Cyclopropyl-5-iodo-1*H*-1,2,3-triazol-1-yl)-*N*-methylbenzenesulfonamide (1c)

Prepared from **3a** (159.2 mg, 0.75 mmol) and (iodoethynyl)cyclopropane (90 µL, 0.75 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 252 mg (79% assuming purity 95%). Pale yellow powder; ^1H NMR (400 MHz, $CDCl_3/CD_3OD$): δ 8.17 (dd, J = 7.5, 1.6 Hz, 1H), 7.84-7.75 (m, 2H), 7.45 (dd, J = 7.5, 1.3 Hz, 1H), 5.38 (q, J = 5.1 Hz, 1H), 2.66 (br s, 3H), 1.91 (m, 1H), 1.12-1.04 (m, 4H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3/CD_3OD$): δ 153.8 (C_{quat}), 135.5 (C_{quat}), 134.0 (C_{quat}), 133.5, 131.2, 131.1, 130.5, 83.0 (C_{quat}), 29.4, 7.8, 7.4 (2C); HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}IN_4O_2S$ 404.9877; Found 404.9878.

2-[4-(Hydroxymethyl)-5-iodo-1*H*-1,2,3-triazol-1-yl]-*N*-methylbenzenesulfonamide (1d)

Prepared from **3a** (212.2 mg, 1.0 mmol) and 3-iodoprop-2-yn-1-ol (125 mg, 1.1 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:6. Yield 286 mg (73%). White powder; mp 159–161 °C; ^1H NMR (400 MHz, $CDCl_3/CD_3OD$): δ 8.10 (d, J = 7.6 Hz, 1H), 7.77-7.70 (m, 2H), 7.39 (d, J = 7.4 Hz, 1H), 5.45 (m, 1H), 4.69 (s, 2H), 2.57 (br s, 3H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3/CD_3OD$): δ 152.9 (C_{quat}), 135.7 (C_{quat}), 133.9 (C_{quat}), 133.7, 131.4, 131.3, 130.6, 84.8 (C_{quat}), 56.0, 29.3; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{10}H_{12}IN_4O_3S$ 394.9669; Found 394.9669.

2-[4-(Hydroxyethyl)-5-iodo-1*H*-1,2,3-triazol-1-yl]-*N*-methylbenzenesulfonamide (1e)

Prepared from **3a** (212.2 mg, 1.0 mmol) and 3-iodobut-2-yn-1-ol (125 µL, 1.1 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:6. Yield 341 mg (84%). Yellow powder; mp 158–160 °C; ^1H NMR (400 MHz, $CDCl_3/CD_3OD$): δ 8.18 (dd, J = 7.6, 1.6 Hz, 1H), 7.82 (m, 2H), 7.48 (dd, J = 7.6, 1.3 Hz, 1H), 5.64 (m, 1H), 3.97 (t, J = 6.4 Hz, 2H), 3.01 (t, J = 6.4 Hz, 2H), 2.67 (br s, 3H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3/CD_3OD$): δ 150.2 (C_{quat}), 135.7 (C_{quat}), 134.2 (C_{quat}), 133.8, 131.4, 131.4, 130.7, 84.9 (C_{quat}), 60.9, 29.7, 29.4; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}IN_4O_3S$ 408.9826; Found 408.9822.

2-(4-*tert*-Butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)-*N*-methylbenzenesulfonamide (1f)

Prepared from **3a** (212.2 mg, 1.0 mmol) and 1-iodo-3,3-dimethylbut-1-yne (151 µL, 1.1 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 50 mg (10% assuming purity 85%). Orange powder; ^1H NMR (400 MHz, $CDCl_3/CD_3OD$): δ 8.16 (dd, J = 7.6, 1.6 Hz, 1H), 7.84 (m, 2H), 7.50 (dd, J = 7.6, 1.4 Hz, 1H), 4.67 (q, J = 5.3 Hz, 1H), 2.64 (d, J = 5.3 Hz, 3H), 1.55 (s, 9H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3/CD_3OD$): δ 158.0 (C_{quat}), 136.6 (C_{quat}), 135.1 (C_{quat}), 134.2, 132.0, 131.7, 131.6, 81.2 (C_{quat}), 32.5(C_{quat}), 29.9 (3C), 29.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{13}H_{18}IN_4O_2S$ 421.0190; Found 421.0189.

2-[4-(3,4-Dimethoxyphenyl)-5-iodo-1*H*-1,2,3-triazol-1-yl]-*N*-methylbenzenesulfonamide (1g)

Prepared from **3a** (212.2 mg, 1.0 mmol) and 4-(iodoethynyl)-1,2-dimethoxybenzene (316.8 mg, 1.1 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 20:1. Yield 425 mg (85%). White powder; mp 196–197 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (dd, J = 7.6, 1.2 Hz, 1H), 7.85-7.77 (m, 2H), 7.62 (dd, J = 8.3, 1.7 Hz, 1H), 7.58 (m, 1H), 7.51 (d, J = 7.2 Hz, 1H), 7.00 (d, J = 8.3 Hz, 1H), 5.01 (q, J = 5.3 Hz, 1H), 3.99 (s, 3H), 3.96 (s, 3H), 2.71 (d, J = 5.3 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d^6/CCl_4): δ 148.9 (C_{quat}), 148.6 (C_{quat}), 147.7 (C_{quat}), 136.8 (C_{quat}), 134.2 (C_{quat}), 133.4, 131.7, 131.1, 129.7, 122.8 (C_{quat}), 119.2 (C_{quat}), 111.7, 110.3, 84.8 (C_{quat}), 55.5, 55.4, 28.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{17}H_{18}IN_4O_4S$ 501.0088; Found 501.0089.

Methyl 3-{5-iodo-1-[2-(methylsulfamoyl)phenyl]-1*H*-1,2,3-triazol-4-yl}benzoate (1h)

Prepared from **3a** (180.5 mg, 0.85 mmol) and methyl 3-(iodoethynyl)benzoate (267.4 mg, 0.94 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 75:1. Yield 375 mg (75%). White foam; mp 86–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (t, J = 1.7 Hz, 1H), 8.25-8.22 (m, 2H), 8.12 (d, J = 7.8 Hz, 1H), 7.84 (td, J = 7.6, J = 1.6 Hz, 1H), 7.80 (td, J = 7.7, 1.4 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.52 (dd, J = 7.6 Hz, J = 1.4 Hz), 4.96 (q, J = 5.2 Hz, 1H), 3.96 (s, 3H), 2.71 (d, J = 5.2 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 166.7 (C_{quat}), 149.6 (C_{quat}), 135.9 (C_{quat}), 134.0 (C_{quat}), 133.4, 131.9, 131.4, 131.2, 130.7, 130.0, 128.8, 128.7, 81.6 (C_{quat}), 52.3, 29.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}IN_4O_4S$ 498.9931; Found 498.9931.

2-(5-Iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)-*N*-methylbenzenesulfonamide (1i)

Prepared from **3a** (212.2 mg, 1.0 mmol) and (iodoethynyl)benzene (148 μL, 1.1 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 100:1. Yield 267 mg (61%). Yellow powder; mp 181–183 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, J = 7.5 Hz, 1H), 8.04 (d, J = 7.2 Hz, 2H), 7.88-7.77 (m, 2H), 7.53-7.49 (m, 3H), 7.45 (m, 1H), 4.98 (q, J = 5.2 Hz, 1H), 2.71 (d, J = 5.2 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d^6/CCl_4): δ 147.8 (C_{quat}), 140.9 (C_{quat}), 134. 1 (C_{quat}), 133.4 (C_{quat}), 131.7, 131.0, 130.4 (C_{quat}), 129.7, 128.5 (2C), 128.2, 126.7 (2C), 85.7 (C_{quat}), 28.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}IN_4O_2S$ 440.9877; Found 440.9877.

2-(4-Butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)-*N*-(2-methoxyethyl)benzenesulfonamide (1j)

Prepared from **3b** (179.4 mg, 0.7 mmol) and 1-iodohex-1-yne (105 μL, 0.77 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 197 mg (52% assuming purity 86%). Green powder; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.17 (d, J = 7.6 Hz, 1H), 7.77 (t, J = 7.6 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 5.45 (t, J = 5.4 Hz, 1H), 3.43 (m, 2H), 3.26 (s, 3H), 3.16 (br s, 2H), 2.77 (t, J = 7.6 Hz, 2H), 1.77 (m, 2H), 1.44 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 152.7 (C_{quat}), 137.0 (C_{quat}), 134.2 (C_{quat}), 133.1, 130.8, 130.7, 130.3, 82.8 (C_{quat}), 70.6, 58.8, 43.4, 30.9, 25.9, 22.1, 13.8; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{15}H_{22}IN_4O_3S$ 465.0452; Found 465.0450.

Ethyl *N*-{[2-(4-butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)phenyl]sulfonyl}glycinate (1k)

Prepared from **3c** (170.6 mg, 0.6 mmol) and 1-iodohex-1-yne (90 μL, 0.66 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 199 mg (62% assuming purity 93%). Light yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.13 (dd, J = 7.6, 1.4 Hz, 1H), 7.78 (td, J = 7.6, 1.4 Hz, 1H), 7.72 (td, J = 7.7, 1.4 Hz, 1H), 7.45 (d, J = 7.7 Hz, 1H), 5.86 (br t, J = 4.3 Hz, 1H), 4.07 (m, 2H), 3.85 (d, J = 4.3 Hz, 2H), 2.77 (t, J = 7.6 Hz, 2H), 1.77 (m, 2H), 1.44 (m, 2H), 1.17 (t, J = 7.4 Hz, 3H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 168.2 (C_{quat}), 152.7 (C_{quat}), 137.1 (C_{quat}), 134.2 (C_{quat}), 133.3 (C_{quat}), 130.8, 130.3, 130.2, 82.6 (C_{quat}), 61.6, 44.9, 30.9, 25.8, 22.1, 14.0, 13.8; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}IN_4O_4S$ 493.0401; Found 493.0403.

2-(4-Butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)-*N*-(4-methylphenyl)benzenesulfonamide (1l)

Prepared from **3d** (278 mg, 0.9 mmol) and 1-iodohex-1-yne (136 μL, 1.0 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 216 mg (44% assuming purity 92%). Orange crystals; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.77 (d, J = 7.6 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.19 (br s, 1H), 7.11 (m, 2H), 7.01 (m, 2H), 2.80 (t, J = 7.4 Hz, 2H), 2.26 (s, 3H), 1.80 (quint, J = 7.4 Hz, 2H), 1.45 (sext, J = 7.4 Hz, 2H), 0.99 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 152.9 (C_{quat}), 136.1 (C_{quat}), 135.7 (C_{quat}), 134.1 (C_{quat}), 133.4 (C_{quat}), 133.3, 131.3, 130.6, 130.0, 129.7 (2C), 123.6 (2C), 83.0 (C_{quat}), 30.8, 25.8, 22.1, 20.8, 13.8; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}IN_4O_2S$ 497.0503; Found 497.0499.

***N*-(Benzyloxy)-2-(4-butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)benzenesulfonamide (1m)**

Prepared from **3e** (304 mg, 1.0 mmol) and 1-iodohex-1-yne (143 μL, 1.05 mmol) according to the general procedure; eluent: hexanes–EtOAc = 4:1. Yield 94 mg (18%). Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 7.8, 1H), 8.26 (s, 1H), 7.82 (t, J = 7.7, 1H), 7.75 (t, J = 7.6, 1H), 7.45 (d, J = 7.7, 1H), 7.38-7.31 (m, 5H), 5.01 (br s, 2H), 2.75 (t, J = 7.7 Hz, 2H), 1.75 (m, 2H), 1.41 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 153.1 (C_{quat}), 135.1 (C_{quat}), 134.4 (C_{quat}), 134.2, 133.6 (C_{quat}), 133.4, 130.8, 130.0, 129.3 (2C), 128.6, 128.5 (2C), 82.5 (C_{quat}), 79.4, 30.8, 25.8, 22.1, 13.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}IN_4O_3S$ 513.0452; Found 513.0452.

***N*-(2-Aminobenzyl)-2-(4-butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)benzenesulfonamide (1n)**

Prepared from **3f** (303 mg, 1.0 mmol) and 1-iodohex-1-yne (143 μL, 1.05 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 276 mg (54%). Brown foam; mp 68–71 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 7.7 Hz, 1H), 7.78 (td, J = 7.6, 1.2 Hz, 1H), 7.71 (td, J = 7.7, 0.7 Hz, 1H), 7.43 (d, J = 7.7 Hz, 1H), 7.07 (td, J = 7.7, 1.1 Hz, 1H), 6.97 (d, J = 7.3 Hz, 1H), 6.65-6.60 (m, 2H), 5.39 (t, J = 6.3 Hz, 1H), 4.05 (br s, 4H), 2.73 (t, J = 7.6 Hz, 2H), 1.73 (m, 2H), 1.40 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 152.7 (C_{quat}), 145.6 (C_{quat}), 135.9 (C_{quat}), 134.1 (C_{quat}), 133.4, 131.1, 130.9, 130.5, 130.2, 129.5, 119.3 (C_{quat}), 118.2, 116.1, 83.1 (C_{quat}), 45.5, 30.8, 25.7, 22.0, 13.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{23}IN_5O_2S$ 512.0612; Found 512.0611.

_N_-[2-(1_H_-Indol-3-yl)ethyl]-2-(4-butyl-5-iodo-1_H_-1,2,3-triazol-1-yl)benzenesulfonamide (1o)

Prepared from **3g** (307.3 mg, 0.9 mmol) and 1-iodohex-1-yne (136 μL, 1.0 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 450 mg (91%). Light yellow foam; mp 84–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (dd, J = 7.7, 1.6 Hz, 1H), 8.02 (br s, 1H), 7.73-7.63 (m, 2H), 7.46 (d, J = 8.0 Hz, 1H), 7.35 (dd, J = 7.7, 1.3 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 7.16 (t, J = 7.6 Hz, 1H), 7.08-7.04 (m, 2H), 5.23 (t, J = 5.9 Hz, 1H), 3.31 (m, 2H), 2.97 (m, 2H), 2.75 (t, J = 7.6 Hz, 2H), 1.76 (m, 2H), 1.43 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 152.6 (C_{quat}), 136.7 (C_{quat}), 136.3 (C_{quat}), 133.9 (C_{quat}), 133.0, 130.8, 130.5, 130.1, 126.9 (C_{quat}), 122.6, 121.9, 119.3, 118.4, 111.6 (C_{quat}), 111.2, 83.0 (C_{quat}), 44.0, 30.9, 25.8, 25.6, 22.1, 13.8; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{22}H_{25}IN_5O_2S$ 550.0768; Found 550.0764.

***N*,*N*′-Ethane-1,2-diylbis[2-(4-butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)benzenesulfonamide] (1p)**

Prepared from **3h** (169 mg, 0.4 mmol) and 1-iodohex-1-yne (114 μL, 0.84 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:1. Yield 199 mg (59%). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (dd, J = 7.6, 1.3 Hz, 2H), 7.79-7.71 (m, 4H), 7.41 (dd, J = 7.5, 1.2 Hz, 2H), 5.47 (br t, J = 5.8 Hz, 2H), 3.10 (br s, 4H), 2.75 (t, J = 7.6 Hz, 4H), 1.75 (m, 4H), 1.42 (m, 4H), 0.97 (t, J = 7.4 Hz, 6H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 152.7 (C_{quat}), 136.6 (C_{quat}), 134.0 (C_{quat}), 133.4, 131.1, 130.8, 130.4, 83.0 (C_{quat}), 43.2, 30.9, 25.8, 22.2, 13.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{33}I_2N_8O_4S_2$ 839.0150; Found 839.0150.

2-(4-Butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)-*N*-[2-(3,5-dimethylisoxazol-4-yl)ethyl]benzenesulfonamide (1q)

Prepared from **3i** (256.8 mg, 0.8 mmol) and 1-iodohex-1-yne (114 μL, 0.84 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:1. Yield 228 mg (43%). Light yellow foam; mp 184–185 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.13 (dd, J = 7.7, 1.5 Hz, 1H), 7.82-7.72 (m, 2H), 7.44 (dd, J = 7.6, 1.1 Hz, 1H), 5.39 (t, J = 6.1 Hz, 1H), 3.05 (m, 2H), 2.76 (t, J = 7.6 Hz, 2H), 2.53 (t, J = 7.3, 2H), 2.27 (s, 3H), 2.15 (s, 3H), 1.76 (m, 2H), 1.43 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 166.0 (C_{quat}), 159.2 (C_{quat}), 152.7 (C_{quat}), 136.7 (C_{quat}), 134.0 (C_{quat}), 133.3, 130.9, 130.4, 130.3, 109.8 (C_{quat}), 83.1 (C_{quat}), 43.0, 30.8, 25.7, 23.1, 22.0, 13.8, 10.9, 10.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{25}IN_5O_3S$ 530.0717; Found 530.0717.

2-(4-Butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)-*N*-(2-furylmethyl)benzenesulfonamide (1r)

Prepared from **3j** (278 mg, 1.0 mmol) and 1-iodohex-1-yne (150 μL, 1.1 mmol) according to the general procedure; eluent: hexanes–EtOAc = 3:1. Yield 340 mg (70%). Orange crystals; mp 111–113 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.10 (dd, J = 7.8, 1.4 Hz, 1H), 7.73 (td, J = 7.8, 1.4 Hz, 1H), 7.66 (td, J = 7.8, 1.4 Hz, 1H), 7.40 (dd, J = 7.8, 1.4 Hz, 1H), 7.16 (m, 1H), 6.17-6.15 (m, 2H), 5.72 (t, J = 6.1 Hz, 1H), 4.23 (d, J = 6.1 Hz, 2H), 2.76 (t, J = 7.5 Hz, 2H), 1.76 (quint, J = 7.5 Hz, 2H), 1.43 (sext, J = 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 152.8 (C_{quat}), 149.2 (C_{quat}), 142.4, 136.9 (C_{quat}), 134.0 (C_{quat}), 133.0, 130.7, 130.6, 130.0, 110.2, 108.4, 82.8 (C_{quat}), 40.6, 30.8, 25.8, 22.1, 13.8; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{17}H_{20}IN_4O_3S$ 487.0295; Found 487.0279.

2-(4-Butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)-*N*-cyclohexylbenzenesulfonamide (1s)

Prepared from **3k** (280 mg, 1.0 mmol) and 1-iodohex-1-yne (143 μL, 1.05 mmol) according to the general procedure; eluent: hexanes–EtOAc = 4:1. Yield 262 mg (54%). Orange crystals; mp 124–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (dd, J = 7.4, 1.7 Hz, 1H), 7.75 (m, 2H), 7.41 (d, J = 7.6, 1.7 Hz, 1H), 5.09 (d, J = 7.2, 1H), 3.20 (m, 1H), 2.76 (t, J = 7.6, 2H), 1.77 (m, 2H), 1.75-1.54 (m, 3H), 1.50 (m, 2H), 1.43 (m, 2H), 1.35-1.06 (m, 5H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 152.6 (C_{quat}), 138.5 (C_{quat}), 134.0 (C_{quat}), 132.9, 130.9, 130.3, 130.2, 83.0 (C_{quat}), 53.6, 30.9, 25.8, 25.1 (2C), 24.5 (2C), 22.1, 13.8; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{18}H_{26}IN_4O_2S$ 489.0816; Found 489.0816.

***N*-1-Adamantyl-2-(4-butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)benzenesulfonamide (1t)**

Prepared from **3l** (265.6 mg, 0.8 mmol) and 1-iodohex-1-yne (114 μL, 0.84 mmol) according to the general procedure; eluent: hexanes–EtOAc = 4:1. Yield 330 mg (76%). Colorless foam; mp 147–148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (m, 1H), 7.76-7.70 (m, 2H), 7.36 (m, 1H), 4.91 (s, 1H), 2.76 (t, J = 7.6 Hz, 2H), 2.01 (m, 3H), 1.86 (m, 6H), 1.77 (m, 2H), 1.59 (m, 6H), 1.43 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 152.5 (C_{quat}), 141.1 (C_{quat}), 133.9 (C_{quat}), 132.6, 130.9, 130.1, 129.9, 83.4 (C_{quat}), 56.1 (C_{quat}), 42.8 (3C), 35.8 (3C), 30.9, 29.5 (3C), 25.8, 22.1, 13.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{30}IN_4O_2S$ 541.1129; Found 541.1116.

***N-tert*-Butyl-2-[4-(hydroxymethyl)-5-iodo-1*H*-1,2,3-triazol-1-yl]benzenesulfonamide (1u)**

Prepared from **3m** (254.3 mg, 1.0 mmol) and 3-iodoprop-2-yn-1-ol (200 mg, 1.1 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:1. Yield 244 mg (53% assuming purity 94%). White powder; mp 89–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (m, 1H), 7.76-7.73 (m, 2H), 7.35 (m, 1H), 5.68 (s, 1H), 4.74 (s, 2H), 3.34 (br s, 1H), 1.27 (s, 9H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 150.9 (C_{quat}), 140.6 (C_{quat}), 133.6 (C_{quat}), 132.9, 131.2, 130.4, 130.3, 84.4 (C_{quat}), 56.2, 55.4 (C_{quat}), 30.1 (3C); HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{13}H_{18}IN_4O_3S$ 437.0139; Found 437.0137.

***N-tert*-Butyl-2-[4-(2-hydroxyethyl)-5-iodo-1*H*-1,2,3-triazol-1-yl]benzenesulfonamide (1v)**

Prepared from **3m** (254.3 mg, 1.0 mmol) and 3-iodobut-2-yn-1-ol (214.5 mg, 1.1 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:2. Yield 381 mg (85%). White foam; mp 134–136 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.25 (d, J = 7.7 Hz, 1H), 7.77-7.72 (m, 2H), 7.41 (d, J = 7.7 Hz, 1H), 5.02 (s, 1H), 4.04 (t, J = 6.1 Hz, 2H), 3.01 (t, J = 6.1 Hz, 2H), 2.66 (br s, 1H), 1.27 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 150.2 (C_{quat}), 140.5 (C_{quat}), 133.8 (C_{quat}), 132.8, 131.1, 130.2, 130.1, 84.6 (C_{quat}), 61.2, 55.6 (C_{quat}), 30.0 (3C), 29.4; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{14}H_{20}IN_4O_3S$ 451.0295; Found 451.0318.

***N-tert*-Butyl-2-(4-butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)benzenesulfonamide (1w)**

Prepared from **3m** (254.3 mg, 1.0 mmol) and 1-iodohex-1-yne (150 μL, 1.1 mmol) according to the general procedure; eluent: hexanes–EtOAc = 3:1. Yield 394 mg (85%). White crystalline powder; mp 119–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (dd, J = 7.5, 1.9 Hz, 1H), 7.76-7.70 (m, 2H), 7.37 (dd, J = 7.6, 1.4 Hz, 1H), 5.02 (s, 1H), 2.76 (t, J = 7.5 Hz, 2H), 1.77 (quint, J = 7.5 Hz,

2H), 1.43 (sext, J = 7.5 Hz, 2H), 1.27 (s, 9H), 0.98 (t, J = 7.5 Hz, 3H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 152.6 (C_{quat}), 140.6 (C_{quat}), 134.0 (C_{quat}), 132.7, 131.0, 130.2, 130.1, 83.4 (C_{quat}), 55.5 (C_{quat}), 30.9, 30.0 (3C), 25.9, 22.2, 13.8; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{16}H_{24}IN_4O_2S$ 463.0659; Found 463.0659.

***N-tert*-Butyl-2-(5-iodo-4-phenyl-1*H*-1,2,3-triazol-1-yl)benzenesulfonamide (1x)**

Prepared from **3m** (254.3 mg, 1.0 mmol) and (iodoethynyl)benzene (148 μL, 1.1 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 100:1. Yield 414 mg (86%). Light yellow powder; mp 189–191 °C; ^1H NMR (400 MHz, DMSO-d^6/CCl_4): δ 8.21(m, 1H), 8.05 (d, J = 7.5 Hz, 2H), 7.87-7.83 (m, 2H), 7.55-7.49 (m, 3H), 7.42 (t, J = 7.5 Hz, 1H), 7.23 (s, 1H), 1.18 (s, 9H); $^{13}C\{^1H\}$ NMR (100.6 MHz, DMSO-d^6/CCl_4): δ 147.8 (C_{quat}), 141.0 (C_{quat}), 133.5 (C_{quat}), 132.6, 131.1, 130.6, 130.4 (C_{quat}), 129.4, 128.3 (2C), 128.0, 126.7 (2C), 85.0 (C_{quat}), 54.0 (C_{quat}), 29.6 (3C); HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{18}H_{20}IN_4O_2S$ 483.0346; Found 483.0345.

2-(4-Butyl-5-iodo-1*H*-1,2,3-triazol-1-yl)-*N*-[(3α,5β,12α)-3,12-dihydroxycholan-24-yl]benzenesulfonamide (1y)

Prepared from **3n** (558 mg, 1.0 mmol) and 1-iodohex-1-yne (143 μL, 1.05 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:2. Yield 450 mg (59%). Colorless foam; mp 105–107 °C (Ether); ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (dd, J = 7.5, 1.2 Hz, 1H), 7.80-7.71 (m, 2H), 7.43 (d, J = 7.4 Hz, 1H), 5.16 (t, J = 5.9 Hz, 1H), 3.94 (m, 1H), 3.59 (tt, J = 11.0, 4.8 Hz, 1H), 2.93 (m, 2H), 2.76 (t, J = 7.6 Hz, 2H), 1.89-1.68 (m, 6H), 1.77 (m, 2H), 1.68-1.20 (m, 21H), 1.20-1.08 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H), 0.93-0.82 (m, 6H), 0.63 (s, 3H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 152.6 (C_{quat}), 136.9 (C_{quat}), 134.1 (C_{quat}), 133.0, 130.8, 130.7, 130.2, 83.0 (C_{quat}), 73.0, 71.6, 48.1, 47.3, 46.4, 44.2, 42.0, 36.3, 35.9, 35.2, 35.1, 34.0, 33.5, 32.6, 30.8, 30.4, 28.5, 27.4, 27.1, 26.2, 26.1, 25.8, 23.6, 23.1, 22.1, 17.4, 13.8, 12.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{36}H_{56}IN_4O_4S$ 767.3061; Found 767.3060.

General procedure for the preparation of triazole-fused sultams 2

In a vial with a screw cap iodotriazole **1** (0.25 mmol) and Cs_2CO_3 (167 mg, 0.5 mmol, 2 equiv) were mixed under an Ar atmosphere in dioxane (2 mL). The reaction mixture was stirred at 100 °C in a dry block for 4 h, then diluted with CH_2Cl_2 (40 mL), washed with water (20 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvents were evaporated *in vacuo*. The residue was purified by column chromatography.

3-Butyl-4-methyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2a)

Prepared from **1a** (105 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 70 mg (96%). White solid; mp 68–71 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 3.28 (s, 3H), 2.82 (t, J = 7.6 Hz, 2H), 1.80 (quint, J = 7.6 Hz, 2H), 1.46 (sext, J = 7.4 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 138.9 (C_{quat}), 134.4, 133.4 (C_{quat}), 131.7 (C_{quat}), 128.4, 124.4, 124.2 (C_{quat}),

118.5, 37.7, 30.8, 24.3, 22.2, 13.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}N_4O_2S$ 293.1067; Found 293.1063.

3-Cyclohex-1-en-1-yl-4-methyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2b)

Prepared from **1b** (130.7 mg, containing 0.25 mmol of pure **1b**) according to the general procedure; eluent: CH_2Cl_2. Yield 77.5 mg (98%). White crystals; mp 148–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.84 (t, J = 8.3 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 6.53 (m, 1H), 3.16 (s, 3H), 2.61 (m, 2H), 2.28 (m, 2H), 1.82 (m, 2H), 1.72 (m, 2H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 140.0 (C_{quat}), 134.5, 131.7 (C_{quat}), 129.1, 128.6, 127.9 (C_{quat}), 126.8 (C_{quat}), 124.9, 123.9 (C_{quat}), 118.7, 38.0, 26.0, 25.5, 22.4, 21.9; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}N_4O_2S$ 317.1067; Found 317.1067.

3-Cyclopropyl-4-methyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2c)

Prepared from **1c** (106.3 mg, containing 0.25 mmol of pure **1c**) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 62 mg (90%). Light orange oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, J = 8.0 Hz, 1H), 7.96 (dd, J = 7.8, 1.0 Hz, 1H), 7.83 (td, J = 7.8, 1.1 Hz, 1H), 7.62 (td, J = 8.0, 1.1 Hz, 1H), 3.40 (s, 3H), 1.96 (tt, J = 8.3, 5.1 Hz, 1H), 1.15-1.04 (m, 4H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 139.3 (C_{quat}), 134.4, 133.7 (C_{quat}), 131.7 (C_{quat}), 128.4, 124.3 (C_{quat}), 124.2, 118.3, 37.2, 7.19 (2C), 5.5; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{12}H_{13}N_4O_2S$ 277.0754; Found 277.0762.

(4-Methyl-5,5-dioxido-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazin-3-yl)methanol (2d)

Prepared from **1d** (98.5 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:4. Yield 60 mg (90%). White powder; mp 202–204 °C ^{1}H NMR (600 MHz, DMSO-d^6/CCl_4): δ 8.31 (dd, J = 7.9, 1.2 Hz, 1H), 8.05 (dd, J = 7.9, 1.2 Hz, 1H), 8.00 (td, J = 7.8, 1.2 Hz, 1H), 7.78 (td, J = 7.8, 1.2 Hz, 1H), 5.51 (br s, 1H), 4.71 (s, 2H), 3.48 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d^6/CCl_4): δ 136.5 (C_{quat}), 135.1, 134.2 (C_{quat}), 131.0 (C_{quat}), 129.2, 123.8 (C_{quat}), 123.6, 118.2, 53.8, 35.5; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}N_4O_3S$ 267.0547; Found 267.0547.

2-(4-Methyl-5,5-dioxido-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazin-3-yl)ethanol (2e)

Prepared from **1e** (102 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:5. Yield 65 mg (93%). White powder; mp 173–175 °C; ^{1}H NMR (400 MHz, DMSO-d^6/CCl_4): δ 8.30 (d, J = 7.8 Hz, 1H), 8.07 (d, J = 7.8 Hz, 1H), 8.01 (t, J = 7.8 Hz, 1H), 7.78 (t, J = 7.8 Hz, 1H), 4.89 (t, J = 5.8 Hz, 1H), 3.77 (q, J = 5.8 Hz, 2H), 3.22 (s, 3H), 2.93 (t, J = 5.8 Hz, 2H); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d^6/CCl_4): δ 136.2 (C_{quat}), 135.4, 134.3 (C_{quat}), 131.1 (C_{quat}), 129.4, 124.3, 123.6 (C_{quat}), 118.4, 59.8, 37.6, 27.9; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{11}H_{13}N_4O_3S$ 281.0703; Found 281.0705.

3-*tert*-Butyl-4-methyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2f)

Prepared from **1f** (28.2 mg, containing 0.057 mmol of pure **1f**) according to the general procedure; eluent: hexanes–EtOAc = 3:1. Yield 13 mg (78%). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (dd, J = 8.3, 0.6 Hz, 1H), 7.96 (dd, J = 7.8, 1.4 Hz, 1H), 7.84 (td, J = 7.9, 1.4 Hz, 1H), 7.63 (td, J = 7.7, 1.1 Hz, 1H), 3.10 (s, 3H), 1.51 (s, 9H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 138.2

(C_{quat}), 134.7, 133.0 (C_{quat}), 131.8 (C_{quat}), 128.7, 125.7, 123.5 (C_{quat}), 118.8, 41.3, 31.7 (C_{quat}), 29.6 (3C); HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}N_4O_2S$ 293.1067; Found 293.1057.

3-(3,4-Dimethoxyphenyl)-4-methyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2g)

Prepared from **1g** (125 mg, 0.25 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 200:1. Yield 80 mg (86%). White powder; mp 186–187 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.37 (d, J = 8.1 Hz, 1H), 8.00 (dd, J = 8.0, 1.0 Hz, 1H), 7.87 (td, J = 7.9, 1.3 Hz, 1H), 7.66 (td, J = 7.7, 0.9 Hz, 1H), 7.61 (d, J = 1.9 Hz, 1H), 7.55 (dd, J = 8.3, 1.9 Hz, 1H), 7.01 (d, J = 8.3 Hz, 1H), 4.00 (s, 3H), 3.96 (s, 3H), 3.17 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 149.8 (C_{quat}), 149.4 (C_{quat}), 138.1 (C_{quat}), 134.6, 132.1 (C_{quat}), 131.7 (C_{quat}), 128.8, 124.9, 123.9 (C_{quat}), 121.2 (C_{quat}), 119.2, 118.6, 111.4, 109.5, 56.1, 56.0, 37.9; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{17}H_{17}N_4O_4S$ 373.0965; Found 373.0965.

Methyl 3-(4-methyl-5,5-dioxido-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazin-3-yl)benzoate (2h)

Prepared from **1h** (124.5 mg, 0.25 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 200:1. Yield 89 mg (96%). White powder; mp 202–204 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (s, 1H), 8.37 (d, J = 7.7 Hz, 1H), 8.22 (d, J = 7.7 Hz, 1H), 8.11 (d, J = 6.8 Hz, 1H), 8.01 (d, J = 6.8 Hz, 1H), 7.88 (t, J = 7.1 Hz, 1H), 7.68 (t, J = 7.3 Hz, 1H), 7.61 (t, J = 7.3 Hz), 3.97 (s, 3H), 3.19 (s, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 161.5 (C_{quat}), 137.0 (C_{quat}), 134.7, 133.24 (C_{quat}), 131.6 (C_{quat}), 131.1 (C_{quat}), 130.6, 130.1, 129.2, 129.0, 128.9 (C_{quat}), 127.4, 124.8, 124.0 (C_{quat}), 118.7, 52.4, 38.2; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{17}H_{15}N_4O_4S$ 371.0809; Found 371.0792.

4-Methyl-3-phenyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2i)

Prepared from **1i** (110 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 68 mg (87%). Pale yellow powder; mp 193–195 °C (lit.[20] 190 °C); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.37 (d, J = 8.2 Hz, 1H), 8.01 (d, J = 8.0 Hz, 2H), 8.01 (d, J = 7.8 Hz, 1H), 7.87 (t, J = 7.8 Hz, 1H), 7.66 (t, J = 8.2 Hz, 1H), 7.53 (t, J = 8.0 Hz, 2H), 7.44 (t, J = 8.0 Hz, 1H), 3.17 (s, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 138.0 (C_{quat}), 134.6, 132.9 (C_{quat}), 131.7 (C_{quat}), 129.1, 129.1 (2C), 128.9, 128.5 (C_{quat}), 126.5 (2C), 124.8, 124.0 (C_{quat}), 118.7, 38.0; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}N_4O_2S$ 313.0754; Found 313.0751.

3-Butyl-4-(2-methoxyethyl)-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2j)

Prepared from **1j** (135 mg, containing 0.25 mmol of pure **1k**) according to the general procedure; eluent: hexanes–EtOAc = 3:2. Yield 73 mg (87%). Pale yellow crystals; mp 75–77 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.28 (d, J = 7.8 Hz, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.79 (t, J = 7.7 Hz, 1H), 7.59 (t, J = 7.7 Hz, 1H), 3.89 (t, J = 5.1 Hz, 2H), 3.23 (t, J = 5.1 Hz, 2H), 2.78 (t, J = 7.6 Hz, 2H), 2.74 (s, 3H), 1.79 (quint, J = 7.6 Hz, 2H), 1.45 (sext, J = 7.5 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 139.5 (C_{quat}), 133.8, 132.2 (C_{quat}), 132.1 (C_{quat}), 128.2, 126.4 (C_{quat}), 123.5, 118.4, 68.8, 58.2, 51.6, 30.3, 24.3, 22.3, 13.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{15}H_{21}N_4O_3S$ 337.1329; Found 337.1329.

Ethyl (3-butyl-5,5-dioxido-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazin-4-yl)acetate (2k)

Prepared from **1k** (148.3 mg, containing 0.25 mmol of pure **1l**) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 22 mg (24%). Pale yellow crystals; mp 92–94 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.33 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.83 (t, J = 7.8 Hz, 1H), 7.61 (t, J = 8.2 Hz, 1H), 4.55 (s, 2H), 3.94 (q, J = 7.2 Hz, 2H), 2.75 (t, J = 7.6 Hz, 2H), 1.77 (quint, J = 7.6 Hz, 2H), 1.43 (sext, J = 7.6 Hz, 2H), 1.01 (t, J = 7.5 Hz, 3H), 0.97 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 166.9 (C_{quat}), 138.2 (C_{quat}), 134.1, 132.2 (C_{quat}), 131.6 (C_{quat}), 128.2, 126.3 (C_{quat}), 123.0, 118.4, 62.1, 51.0, 30.4, 24.5, 22.3, 13.8, 13.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{16}H_{21}N_4O_4S$ 365.1278; Found 365.1284.

3-Butyl-4-(4-methylphenyl)-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2l)

Prepared from **1l** (134.9 mg, containing 0.25 mmol of pure **1l**) according to the general procedure; eluent: hexanes–EtOAc = 3:1. Yield 90 mg (86% assuming purity 88%). Orange oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.40 (d, J = 7.8 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.85 (t, J = 7.7 Hz, 1H), 7.59 (t, J = 7.7 Hz, 1H), 7.15 (m, 2H), 6.98 (m, 2H), 2.39 (t, J = 7.5 Hz, 2H), 2.34 (s, 3H), 1.48 (quint, J = 7.5 Hz, 2H), 1.21 (sext, J = 7.4 Hz, 2H), 0.79 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 139.3 (C_{quat}), 138.9 (C_{quat}), 134.6, 132.9 (C_{quat}), 132.0 (C_{quat}), 130.2 (2C), 128.9 (C_{quat}), 128.5, 126.3 (2C), 125.1 (C_{quat}), 124.6, 118.7, 30.1, 23.9, 22.0, 21.0, 13.5; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}N_4O_2S$ 369.1380; Found 369.1372.

3-Butyl-4-[2-(1*H*-indol-3-yl)ethyl]-4*H*-[1,2,3]triazolo[5,1-c][1,2,4]benzothiadiazine 5,5-dioxide (2o)

Prepared from **1o** (137.4 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 87 mg (83%). Light yellow foam; mp 125–127 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (d, J = 7.8 Hz, 1H), 7.92 (br s, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.56 (t, J = 7.7 Hz, 1H), 7.40 (t, J = 7.7 Hz, 1H), 7.16 (d, J = 8.0 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.09 (t, J = 7.8 Hz, 1H), 7.01 (t, J = 7.8 Hz, 1H), 6.66 (d, J = 1.9 Hz, 1H), 4.15 (t, J = 7.7 Hz, 2H), 2.85 (t, J = 7.7 Hz, 2H), 2.74 (t, J = 7.6 Hz, 2H), 1.74 (quint, J = 7.6 Hz, 2H), 1.42 (sext, J = 7.5 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 138.8 (C_{quat}), 135.8 (C_{quat}), 133.5, 131.7 (C_{quat}), 131.4 (C_{quat}), 127.9, 126.6 (C_{quat}), 125.6 (C_{quat}), 122.7, 122.3, 122.1, 119.7, 117.9, 111.09, 110.09 (C_{quat}), 51.3, 30.4, 24.5, 23.7, 22.3, 13.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{22}H_{24}N_5O_2S$ 422.1645; Found 422.1644.

4,4'-Ethane-1,2-diylbis(3-butyl-4*H*-[1,2,3]triazolo[5,1-c][1,2,4]benzothiadiazine) 5,5,5',5'-tetraoxide (2p)

Prepared from **1p** (107 mg, 0.128 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:1. Yield 49 mg (61% assuming purity 92%). White crystalline powder; mp > 220 °C (dec., Ether); ^{1}H NMR (400 MHz, $CD_3OD/CDCl_3$): δ 8.16 (d, J = 8.1 Hz, 2H), 7.88 (t, J = 7.8 Hz, 2H), 7.82 (d, J = 7.9 Hz, 2H), 7.64 (t, J = 7.7, 0.7 Hz, 2H), 4.07 (s, 4H), 2.64 (t, J = 7.7 Hz, 4H), 1.69 (m, 4H), 1.40 (m, 4H), 0.96 (t, J = 7.3 Hz, 6H); ^{13}C{^{1}H} NMR (100.6 MHz, $CD_3OD/CDCl_3$): δ 136.8 (2C_{quat}), 134.8 (2C), 131.3 (2C_{quat}), 130.6 (2C_{quat}), 128.7 (2C), 124.6 (2C_{quat}), 123.0 (2C), 118.3 (2C), 48.0 (2C), 30.1 (2C), 24.2 (2C), 21.9 (2C), 13.3 (2C); HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{31}N_8O_4S_2$ 583.1904; Found 583.1907.

3-Butyl-4-[2-(3,5-dimethylisoxazol-4-yl)ethyl]-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2q)

Prepared from **1q** (132.3 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:1. Yield 92 mg (92%). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.83 (t, J = 7.8 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 3.86 (t, J = 7.3 Hz, 2H), 2.75 (t, J = 7.7 Hz, 2H), 2.49 (t, J = 7.3 Hz, 2H), 2.07 (s, 3H), 2.02 (s, 3H), 1.80 (m, 2H), 1.46 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 166.0 (C_{quat}), 158.9 (C_{quat}), 138.5 (C_{quat}), 134.4, 131.6 (C_{quat}), 131.3 (C_{quat}), 128.7, 125.1 (C_{quat}), 123.3, 118.3, 108.4 (C_{quat}), 50.0, 30.5, 24.4, 22.2, 21.4, 13.7, 10.5, 9.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{24}N_5O_3S$ 402.1594; Found 402.1589.

3-Butyl-4-(furan-2-ylmethyl)-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2r)

Prepared from **1r** (122 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 3:1. Yield 84 mg (94%). White powder; mp 115–117 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.09 (d, J = 7.8 Hz, 1H), 7.85 (dd, J = 7.6, 1.3 Hz, 1H), 7.69 (td, J = 7.8, 1.3 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 6.90 (m, 1H), 5.98-5.95 (m, 2H), 4.74 (s, 2H), 2.74 (t, J = 7.6 Hz, 2H), 1.81 (quint, J = 7.6 Hz, 2H), 1.46 (sext, J = 7.4 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 146.4 (C_{quat}), 143.1, 141.1 (C_{quat}), 134.0, 131.8 (C_{quat}), 131.7 (C_{quat}), 128.1, 125.7 (C_{quat}), 124.2, 118.3, 111.0, 110.3, 48.9, 30.3, 24.1, 22.3, 13.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_4O_3S$ 359.1172; Found 359.1173.

3-Butyl-4-cyclohexyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2s)

Prepared from **1s** (122 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 85 mg (94%). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 8.1 Hz, 1H), 7.93 (dd, J = 7.8, 1.0 Hz, 1H), 7.81 (td, J = 7.8, 1.2 Hz, 1H), 7.60 (td, J = 7.8, 0.7 Hz, 1H), 3.94 (m, 1H), 2.81 (t, J = 7.6 Hz, 2H), 1.84 (m, 2H), 1.75-1.64 (m, 4H), 1.59-1.51 (m, 1H), 1.44 (m, 2H), 1.29-1.13 (m, 5H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 142.8 (C_{quat}), 134.2, 132.0 (C_{quat}), 131.0 (C_{quat}), 128.5, 127.6 (C_{quat}), 124.0, 118.7, 64.9, 31.2 (2C), 30.3, 25.5 (2C), 24.8, 24.6, 22.2, 13.7; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{25}N_4O_2S$ 361.1693; Found 361.1697.

4-(1-Adamantyl)-3-butyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2t)

Prepared from **1t** (135 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 4:1. Yield 88 mg (85%). Pale yellow solid; mp 163–165 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 7.8, 1.0 Hz, 1H), 7.80 (t, J = 7.8 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 2.80 (m, Hz, 2H), 2.03 (m, 3H), 1.96-1.82 (m, 6H), 1.87 (m, 2H), 1.56 (m, 6H), 1.43 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 144.5 (C_{quat}), 134.0, 132.3 (C_{quat}), 131.5 (C_{quat}), 129.5 (C_{quat}), 128.5, 124.0, 118.8, 68.2 (C_{quat}), 41.2 (3C), 35.4 (3C), 30.1 (3C), 29.8, 25.4, 22.2, 13.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{22}H_{29}N_4O_2S$ 413.2006; Found 413.2022.

(4-*tert*-Butyl-5,5-dioxido-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazin-3-yl)methanol (2u)

Prepared from **1u** (109.1 mg, containing 0.24 mmol of pure 1**u**) according to the general procedure; eluent: hexanes–EtOAc = 1:2. Yield 37 mg (51%). White powder; mp 250 °C (dec.); ^{1}H NMR (400 MHz, DMSO-d^6/CCl_4): δ 8.24 (d, J = 8.1 Hz, 1H), 8.00-7.94 (m, 2H), 7.75 (t, J = 7.7 Hz, 1H), 5.49 (br s, 1H), 4.62 (s, 2H), 1.28 (s, 9H); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d^6/CCl_4): δ 142.9 (C_{quat}), 134.7, 132.0 (C_{quat}), 131.2 (C_{quat}), 129.3, 128.2 (C_{quat}), 123.8, 118.9, 66.1 (C_{quat}), 53.9, 28.8 (3C); HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}N_4O_3S$ 309.1016; Found 309.1018.

2-(4-*tert*-Butyl-5,5-dioxido-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazin-3-yl)ethanol (2v)

Prepared from **1v** (112.6 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:3. Yield 45 mg (56%). Pale yellow crystals; mp 148–150 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.23 (dd, J = 8.1, 1.3 Hz, 1H), 7.95 (dd, J = 7.8, 1.0 Hz, 1H), 7.84 (m, 1H), 7.63 (td, J = 7.8, 1.0 Hz, 1H), 4.14-3.98 (m, 2H), 3.14-2.98 (m, 2H), 2.88 (br s, 1H), 1.32 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, CD_3OD/$CDCl_3$): δ 142.3 (C_{quat}), 134.3, 132.9 (C_{quat}), 132.1 (C_{quat}), 129.03, 128.97 (C_{quat}), 124.4, 119.0, 67.0 (C_{quat}), 60.7, 29.2 (3C), 29.0; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{14}H_{19}N_4O_3S$ 323.1172; Found 323.1172.

3-Butyl-4-*tert*-butyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2w)

Prepared from **1w** (115.6 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 2:1. Yield 58 mg (69%). The reaction at 2 mmol of **1w** afforded 451 mg (67%) of **2w**. Colorless crystals; mp 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, J = 8.0 Hz, 1H), 7.93 (dd, J = 7.7, 1.1 Hz, 1H), 7.80 (t, J = 8.0 Hz, 1H), 7.59 (t, J = 7.7 Hz, 1H), 2.79 (t, J = 7.5 Hz, 2H), 1.85 (quint, J = 7.5 Hz, 2H), 1.43 (sext, J = 7.5 Hz, 2H), 1.30 (s, 9H), 0.97 (t, J = 7.5 Hz, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 144.3 (C_{quat}), 134.1, 132.2 (C_{quat}), 132.1 (C_{quat}), 128.9 (C_{quat}), 128.6, 124.2, 118.8, 66.7 (C_{quat}), 29.8, 29.2 (3C), 25.4, 22.2, 13.7; HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{16}H_{23}N_4O_2S$ 335.1536; Found 335.1534.

4-*tert*-Butyl-3-phenyl-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide (2x)

Prepared from **1x** (120.6 mg, 0.25 mmol) according to the general procedure; eluent: CH_2Cl_2–MeOH = 100:1. Yield 40 mg (45%). Beige crystals; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 7.3 Hz, 2H), 7.97 (d, J = 7.6 Hz, 1H), 7.84 (t, J = 7.6 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.2 Hz, 2H), 7.43 (m, 1H), 1.23 (s, 9H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 142.6 (C_{quat}), 134.2, 132.0 (C_{quat}), 131.4 (C_{quat}), 129.8 (C_{quat}), 129.1, 128.99, 128.95 (2C), 128.6 (C_{quat}), 127.0 (2C), 124.3, 118.9, 67.9 (C_{quat}), 20.1 (3C); HRMS (MALDI-TOF, dithranol) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}N_4O_2S$ 355.1223; Found 355.1223.

(3*α*,5β,12*α*)-24-(4-Butyl-5,5-dioxido-4*H*-[1,2,3]triazolo[5,1-*c*][1,2,4]benzothiadiazin-3-yl)cholane-3,12-diol (2y)

Prepared from **1y** (191.7 mg, 0.25 mmol) according to the general procedure; eluent: hexanes–EtOAc = 1:2. Yield 159 mg (99%). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 7.3 Hz, 1H), 7.83 (t, J = 7.8 Hz, 1H), 7.62 (t, J = 7.7 Hz, 1H), 3.89 (m, 1H), 3.69 (m, 2H), 3.61 (tt, J = 11.0, 4.7 Hz, 1H), 2.82 (br s, 2H), 2.78 (t, J = 7.6 Hz, 2H), 1.87-0.73 (m, 30H), 0.97 (t, J = 7.3 Hz, 3H), 0.89 (s, 3H), 0.77 (d, J = 6.4 Hz, 3H), 0.58 (s, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ 138.6 (C_{quat}), 134.1, 131.9 (C_{quat}), 131.5 (C_{quat}), 128.3, 125.7 (C_{quat}), 123.5, 118.5, 72.7, 71.3, 51.8, 47.9, 47.0, 46.1, 41.8, 36.1, 35.7, 35.0,

34.9, 33.9, 33.3, 32.2, 30.4, 30.1, 28.5, 27.2, 26.9, 25.9, 24.9, 24.4, 23.4, 22.9, 22.1, 17.0, 13.6, 12.4; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{36}H_{55}N_4O_4S$ 639.3939; Found 639.3926.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the Internet.

^{1}H and ^{13}C{^{1}H} NMR spectra, details of DFT calculations (PDF).

AUTHOR INFORMATION

Corresponding Author

***E-mail: latyshev@org.chem.msu.ru.**

ACKNOWLEDGMENT

This work was supported by the Russian Foundation for Basic Research (Grant No. 18-33-01024-mol_a) and the M. V. Lomonosov Moscow State University Program of Development. I. P. Beletskaya is grateful to the Russian Science Foundation (Grant No. 19-13-00223). The authors would like to acknowledge Thermo Fisher Scientific, Inc., MS Analytica (Moscow, Russia), and Prof. A. Makarov (Thermo Fisher Scientific, Inc.) personally for providing mass spectrometry equipment for this work.

REFERENCES

(1) (a) Tornøe, C. W.; Christensen, C.; Meldal, M. Peptidotriazoles on Solid Phase: [1,2,3]-Triazoles by Regiospecific Copper(I)-Catalyzed 1,3-Dipolar Cycloadditions of Terminal Alkynes to Azides. *J. Org. Chem.* **2002**, *67,* 3057-3064. (b) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. A Stepwise Huisgen Cycloaddition Process: Copper(I)-Catalyzed Regioselective "Ligation" of Azides and Terminal Alkynes. *Angew. Chem. Int. Ed*. **2002**, *41*, 2596-2599.

(2) (a) Yamada, M.; Matsumura, M.; Murata, Y.; Kawahata, M.; Saito, K.; Kakusawa, N.; Yamaguchi, K.; Yasuike, S. Synthesis of 5-organostibano-1*H*-1,2,3-triazoles by Cu-catalyzed azide-alkyne cycloaddition and their application in the acyl-induced deantimonation for the preparation of fully substituted 5-acyl-1,2,3-triazoles. *Tetrahedron* **2017**, *73*, 2614-2622. (b) Li, L.; Hao, G.; Zhu, A.; Fan, X.; Zhang, G.; Zhang, L. A Copper(I)-Catalyzed Three-Component Domino Process: Assembly of Complex 1,2,3-Triazolyl-5-Phosphonates from Azides, Alkynes, and *H*-Phosphates. *Chem. Eur. J.* **2013**, *19*, 14403-14406. (c) Worrell, B. T.; Ellery, S. P.; Fokin, V. V. Copper(I)-Catalyzed Cycloaddition of Bismuth(III) Acetylides

with Organic Azides: Synthesis of Stable Triazole Anion Equivalents. *Angew. Chem. Int. Ed.* **2013**, *52*, 13037-13041. (d) Wang, W.; Peng, X.; Wei, F.; Tung, C-H.; Xu, Z. Copper(I)-Catalyzed Interrupted Click Reaction: Synthesis of Diverse 5-Hetero-Functionalized Triazoles. *Angew. Chem. Int. Ed.* **2016**, *55*, 649-653. (e) Malnuit, V.; Duca, M.; Manout, A.; Bougrin, K.; Benhida, R. Tandem Azide-Alkyne 1,3-Dipolar Cycloaddition/Electrophilic Addition: A Concise Three-Component Route to 4,5-Disubstituted Triazolyl-Nucleosides. *Synlett* **2009**, 2123-2128. (f) Stefani, H. A.; Vasconcelos, S. N. S.; Manarin, F.; Leal, D. M.; Souza, F. B.; Madureira, L. S.; Zukerman-Schpector, J.; Eberlin, M. N.; Godoi, M. N.; De Souza Galaverna, R. Synthesis of 5-organotellanyl-1*H*-1,2,3-triazoles: Functionalization of the 5-position scaffold by the Sonogashira cross-coupling reaction. *Eur. J. Org. Chem.* **2013**, 3780-3785. (g) Stefani, H. A.; Silva, N. C. S.; Vasconcelos, S. N. S.; Manarin, F.; Souza, F. B. Functionalization of 5-telluro-1,2,3-triazoles: Te/Li exchange and Suzuki-Miyaura cross-coupling reaction. *Tetrahedron Lett.* **2013**, *54*, 2809-2812. (h) Yamada, M.; Matsumura, M.; Uchida, Y.; Kawahata, M.; Murata, Y.; Kakusawa, N.; Yamaguchi, K.; Yasuike, S. Copper-catalyzed [3+2] cycloaddition of (phenylethynyl)di-p-tolylstibane with organic azides. *Beilstein J. Org. Chem.* **2016,** *12,* 1309-1313.

(3) Hein, J. E.; Tripp J. C.; Krasnova, L. B.; Sharpless, K. B.; Fokin V. V. Copper(I)-Catalyzed Cycloaddition of Organic Azides and 1-Iodoalkynes. *Angew. Chem. Int. Ed*. **2009**, *48*, 8018-8021.

(4) Deng, J.; Wu, Y-M.; Chen, Q-Y. Cross-coupling Reaction of Iodo-1,2,3-triazoles Catalyzed by Palladium. *Synthesis* **2005**, *16*, 2730-2738.

(5) (a) Diner, P.; Andersson, T.; Kjellen, J.; Elbing, K.; Hohmann, S.; Grotli, M. Short Cut to 1,2,3-Triazole-based P38 MAP Kinase Inhibitors via [3+2]-Cycloaddition Chemistry. *New J. Chem*. **2009**, *33*, 1010-1016. (b) Wang, D.; Chen, S.; Chen, B. "Green" Synthesis of 1,4-Disubstituted 5-Iodo-1,2,3-triazoles under Neat Conditions, and an Efficient Approach of Construction of 1,4,5-Trisubstituted 1,2,3-Triazoles in One Pot. *Tetrahedron Lett*. **2014,** *55*, 7026-7028. (c) Ahmed, N.; Konduru, N. K.; Ahmad, S.; Owais, M. Design, Synthesis and Antiproliferative Activity of Functionalized Flavone-triazole-tetrahydropyran Conjugates Against Human Cancer Cell Lines. *Eur. J. Med. Chem.* **2014**, *82*, 552-564. (d) Yousuf, M.; Mukherjee, D.; Dey, S.; Pal, C.; Adhikari, S. Antileishmanial Ferrocenylquinoline Derivatives: Synthesis and Biological Evaluation Against Eishmania Donovani. *Eur. J. Med. Chem.* **2016**, *124*, 468-479.

(6) (a) Goyard, D.; Chajistamatiou, A. S.; Sotiropoulou, A. I.; Chrysina, E. D.; Praly, J.-P.; Vidal, S. Efficient Atropodiastereoselective Access to 5,5′-Bis-1,2,3-triazoles: Studies on 1-Glucosylated 5-Halogeno 1,2,3-Triazoles and Their 5-Substituted Derivatives as Glycogen Phosphorylase Inhibitors. *Chem. Eur. J.* **2014**, *20*, 5423-5432. (b) Fehr, K.; Gömöry, G.; Skoda-Földes, R. A Modular Synthesis of 1,4,5-Trisubstituted 1,2,3-Triazoles with Ferrocene Moieties. *Monatsh. Chem.* **2015**, *146*, 1455-1463. (c) Govdi, A. I.; Danilkina, N. A.; Ponomarev, A. V.; Balova, I. A. 1-Iodobuta-1,3-diynes in Copper-

Catalyzed Azide-Alkyne Cycloaddition: A One-Step Route to 4-Ethynyl-5-iodo-1,2,3-triazoles. *J. Org. Chem.* **2019**, *84*, 1925-1940.

(7)**.** (a) Thiery, E.; You, V.; Mora, A-S.; Abarbri, M. Synthesis of 5-Substituted 1,2,3-Triazolyl-4-phosphonate through Cross-coupling Reactions of 5-Iodo-1,2,3-triazolyl-4-phosphonate. *Eur. J. Org. Chem.* **2016**, 529-534. (b) Gribanov, P. S.; Chesnokov, G. A.; Dzhevakov, P. B.; Kirilenko, N. Yu.; Rzhevskiy, S. A.; Ageshina, A. A.; Topchiy, M. A.; Bermeshev, M. V.; Asachenko, A. F.; Nechaev, M. S. Solvent-free Suzuki and Stille Cross-coupling Reactions of 4- and 5-Halo-1,2,3-triazoles. *Mendeleev Commun.* **2019**, *29*, 147-149.

(8) (a) Malnuit, V.; Duca, M.; Manout, A.; Bougrin, K.; Benhida, R. Tandem Azide-Alkyne 1,3-dipolar Cycloaddition/Electrophilic Addition: A Concise Three-component Route to 4,5-Disubstituted Triazolyl-nucleosides. *Synlett* **2009**, *13*, 2123-2128. (b) Ostrowski, T.; Januszczyk, P.; Cieslak, M.; Kazmierczak-Baranska, J.; Nawrot, B.; Bartoszak-Adamska, E.; Zeidler, J. 5-Ethynyl-1-β-d-ribofuranosyl-1H-[1,2,3]triazole-4-carboxylic Acid Amide (ETCAR) and Its Analogues: Synthesis and Cytotoxic Properties. *Bioorg. Med. Chem.* **2011**, *19*, 4386-4398. (c) Amdouni, H.; Robert, G.; Driowya, M.; Furstoss, N.; Métier, C.; Dubois, A.; Dufies, M.; Zerhouni, M.; Orange, F.; Lacas-Gervais, S.; Bougrin, K.; Martin, A. R.; Auberger, P.; Benhida, R. In Vitro and in Vivo Evaluation of Fully Substituted (5-(3-Ethoxy-3-oxopropynyl)-4-(ethoxycarbonyl)-1,2,3-triazolyl-glycosides as Original Nucleoside Analogues to Circumvent Resistance in Myeloid Malignancies. *J. Med. Chem.* **2017**, *60*, 1523-1533.

(9) Carcenac, Y.; David-Quillot, F.; Abarbri, M.; Duchêne, A.; Thibonnet, J. Palladium-catalyzed Cross-coupling of 1,4-Disubstituted 5-Iodo-1,2,3-triazoles with Organotin Reagents. *Synthesis* **2013**, *45*, 633-638.

(10) (a) Panteleev, J.; Geyer, K.; Aguilar-Aguilar, A.; Wang, L.; Lautens, M. C-H Bond Functionalization in the Synthesis of Fused 1,2,3-Triazoles. *Org. Lett.* **2010**, *12*, 5092-5095. (b) Schulman, J. M.; Friedman, A. A.; Panteleev, J.; Lautens, M. Synthesis of 1,2,3-Triazole-fused Heterocycles via Pd-Catalyzed Cyclization of 5-Iodotriazoles. *Chem. Commun.* **2012**, *48*, 55-57. (c) Morgen, M.; Jöst, C.; Malz, M.; Janowski, R.; Niessing, D.; Klein, C. D.; Gunkel, N.; Miller, A. K. Spiroepoxytriazoles Are Fumagillin-like Irreversible Inhibitors of MetAP2 with Potent Cellular Activity. *ACS Chem. Biol*. **2016**, *11*, 1001-1011.

(11) Irastorza, A.; Aizpurua, J. M.; Correa, A. Triazole-Directed Pd-Catalyzed C(sp2)-H Oxygenation of Arenes and Alkenes. *Org. Lett.* **2016**, *18*, 1080-1083.

(12) (a) Joubert, Nicolas; Schinazi, Raymond F.; Agrofoglio, Luigi A. Efficient Pd(0)-Catalyzed Synthesis of 1,2,3-Triazolo-3′-deoxycarbanucleosides and Their Analogues. *Tetrahedron* **2005,** *61*, 11744-11750. (b) Wu, Y-M.; Deng, J.; Chen, Q-Y.

Studies on New Strategies for the Synthesis of Oligomeric 1,2,3-Triazoles. *Synlett* **2006**, *4*, 645-647. (c) Morris, J. C.; Chiche, J.; Grellier, C.; Lopez, M.; Bornaghi, L. F.; Maresca, A.; Supuran, C. T.; Pouyssegur, J.; Poulsen, S.-A. Targeting Hypoxic Tumor Cell Viability with Carbohydrate-based Carbonic Anhydrase IX and XII Inhibitors. *J. Med. Chem.* **2011**, *54*, 6905-6918. (d) Ingham, O. J.; Paranal, R. M.; Smith, W. B.; Escobar, R. A.; Yueh, H.; Snyder, T.; Porco, J. A.; Bradner, J. E.; Beeler, A. B. Development of a Potent and Selective HDAC8 Inhibitor. *ACS Med. Chem. Lett.* **2016**, *7*, 929-932. (e) Piras, M.; Andriu, A.; Testa, A.; Wienecke, P.; Fleming, I. N.; Zanda, M. Design and Synthesis of an RGD Peptidomimetic-Paclitaxel Conjugate Targeting $\alpha_v\beta_3$ Integrin for Tumour-Directed Drug Delivery. *Synlett* **2017**, *28*, 2769-2776. (f) Barve, I. J.; Thikekar, T. U.; Sun, C-M. Silver(I)-Catalyzed Regioselective Synthesis of Triazole Fused-1,5-Benzoxazocinones. *Org. Lett.* **2017**, *19*, 2370-2373.

(13) (a) Kotovshchikov, Y. N.; Latyshev, G. V.; Beletskaya, I. P.; Lukashev, N. V. Regioselective Approach to 5-Carboxy-1,2,3-triazoles Based on Palladium-Catalyzed Carbonylation. *Synthesis* **2018**, *50*, 1926-1934. (b) Szuroczki, P.; Sámson, J; Kollár, L. Synthesis of 5-Carboxamidotriazoles via Azide-Alkyne Cycloaddition–Aminocarbonylation Sequence. *ChemistrySelect* **2019**, *4*, 5527-5530. (c) De Albuquerque, D. Y.; de Moraes, J. R.; Schwab, R. S. Palladium-Catalyzed Aminocarbonylation Reaction to Access 1,2,3-Triazole-5-carboxamides Using Dimethyl Carbonate as Sustainable Solvent. *Eur. J. Org. Chem.* **2019**, 6673-6681.

(14) Li, L.; Shang, T.; Ma, X.; Guo, H.; Zhu, A.; Zhang, G. 4-Trimethylsilyl-5-iodo-1,2,3-triazole: A Key Precursor for the Divergent Syntheses of 1,5-Disubstituted 1,2,3-Triazoles. *Synlett* **2015**, *26*, 695-699.

(15) Wen, Y.-N.; Zhang, Z.-F.; Liu, N.-N.; Andrei, G.; Snoeck, R.; Xiang, Y.-H.; Schols, D.; Chen, X.; Zhang, Z.-Y.; Zhang, Q.-S.; Wu, Q.-P. Synthesis and Ativiral Activity of 5-(Benzylthio)-4-carbamyl-1,2,3-triazoles Against Human Cytomegalovirus (CMV) and Varicella-zoster Virus (VZV). *Med. Chem.* **2017**, *13*, 453-464.

(16) Do Nascimento, J. E. R.; Gonçalves, L. C. C.; Hooyberghs, G.; Van der Eycken, E. V.; Alves, D.; Lenardão, E. J.; Perin, G.; Jacob, R. G. Synthesis of Fused 1,2,3-Triazolo-1,3,6-triazonines through Copper-Catalyzed Intramolecular Ullmann Cross-coupling Reaction. *Tetrahedron Lett.* **2016**, *57*, 4885-4889.

(17) Worrell, B. T.; Hein, J. E.; Fokin, V. V. Halogen Exchange (Halex) Reaction of 5-Iodo-1,2,3-triazoles: Synthesis and Applications of 5-Fluorotriazoles. *Angew. Chem. Int. Ed.* **2012**, *51*, 11791-11794.

(18) Wang, D.; Sun, W.; Chu, T. Synthesis of 5-Fluorotriazoles by Silver-Mediated Fluorination of 5-Iodotriazoles. *Eur. J. Org. Chem.* **2015**, 4114-4118.

(19) Kotovshchikov, Y. N; Latyshev, G. V.; Navasardyan, M. A.; Erzunov, D. A.; Beletskaya, I. P.; Lukashev, N. V. Annulation-Induced Cascade Transformation of 5-Iodo-1,2,3-triazoles to 2-(1-Aminoalkyl)benzoxazoles. *Org. Lett.* **2018**, *20*, 4467-4470.

(20) Reddy A. S.; Reddy M. N.; Swamy K. C. K. A Simple Copper-Catalysed Tandem Cyclisation of Ynamides Leading to Triazolo-1,2,4-benzothiadiazine-1,1-dioxides in PEG-400 Medium. *RSC Adv*. **2014**, *4*, 28359-28367.

(21) (a) Mustafa, A. The Chemistry of Sultones and Sultams. *Chem. Rev*. **1954**, *54*, 195-223. (b) Wells, G. J.; Tao, M.; Josef, K. A.; Bihovsky, R. 1,2-Benzothiazine 1,1-Dioxide P_2-P_3 Peptide Mimetic Aldehyde Calpain I Inhibitors. *J. Med. Chem.* **2001**, *44*, 3488-3503. (c) Bihovsky, R.; Tao, M.; Mallamo, J. P.; Wells, G. J. 1,2-Benzothiazine 1,1-dioxide α-ketoamide analogues as potent calpain I inhibitors. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1035-1038. (d) Francotte, P.; Tullio, P.; Goffin, E.; Dintilhac, G.; Graindorge, E.; Fraikin, P.; Lestage, P.; Danober, L.; Thomas, J.-Y.; Caignard, D.-H.; Pirotte, B. Design, Synthesis, and Pharmacology of Novel 7-Substituted 3,4-Dihydro-2H-1,2,4-benzothiadiazine 1,1-Dioxides as Positive Allosteric Modulators of AMPA Receptors. *J. Med. Chem.* **2007**, *50*, 3153-3157. (e) Majumdar, K. C.; Mondal, S. Recent Developments in the Synthesis of Fused Sultams. *Chem. Rev.* **2011**, *111*, 7749-7773.

(22) Valente, C.; Guedes, R. C.; Moreira, R.; Iley, J.; Gut, J.; Rosenthal P. J. Dipeptide Vinyl Sultams: Synthesis via the Wittig–Horner Reaction and Activity against Papain, Falcipain-2 and *Plasmodium Falciparum*. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 4115-4119.

(23) (a) Lombardino, J. G.; Wiseman E. H.; Mclamore W. M. Synthesis and Antiinflammatory Activity of Some 3-Carboxamides of 2-Alkyl-4-hydroxy-2*H*-1,2-benzothiazine 1,l-Dioxide. *J. Med. Chem.* **1971**, *14*, 1171-1175. (b) Lombardino, J. G.; Wiseman, E. H. Sudoxicam and Related N-Heterocyclic Carboxamides of 4-Hydroxy-2*H*-l,2-benzothiazine 1,l -Dioxide. Potent Nonsteroidal Antiinflammatory Agents. *J. Med. Chem.* **1972**, *15*, 848-849. (c) Nicolas, C.; Verny, M.; Giraud, I.; Ollier, M.; Rapp, M.; Maurizis, J. C.; Madelmont, J. C. New Quaternary Ammonium Oxicam Derivatives Targeted toward Cartilage: Synthesis, Pharmacokinetic Studies, and Antiinflammatory Potency. *J. Med. Chem.* **1999**, *42*, 5235-5240. (d) Xu, S.; Rouzer, C. A.; Marnett, L. J. Oxicams, a Class of Nonsteroidal Anti-inflammatory Drugs and Beyond. *IUBMB Life* **2014**, *66*, 803-811.

(24) (a) Buckheit, R. W. Jr.; Fliaka-Boltz, V.; Decker, D. W.; Roberson, L. J.; Pyle, C. A.; White, L. E.; Bowden, B. J.; Barth J. H.; Antonucci T. K. Biological and Biochemical Anti-HIV Activity of the Benzothiadiazine Class of Nonnucleoside Reverse Transcriptase Inhibitors. *Antiviral Res.* **1994**, *25*, 43-54. (b) Arranz, E. M.; Diaz, J. A.; Ingate, S. T.; Witvrouw, M.; Pannecouque C.; Balzarini, J.; Clercq, E. D.; Vega, S. Synthesis and Anti-HIV Activity of 1,1,3-Trioxo-2*H*,4*H*-thieno[3,4-

e][1,2,4]thiadiazines (TTDs): A New Family of HIV-1 Specific Non-Nucleoside Reverse Transcriptase Inhibitors. *Bioorg. Med. Chem.* **1999**, *7*, 2811-2822. (c) Zhuang, L.; Wai, J. S.; Embrey, M. W.; Fisher, T. E.; Egbertson, M. S.; Payne, L. S.; Guare, J. P. Jr.; Vacca, J. P.; Hazuda, D. J.; Felock, P. J.; Wolfe, A. L.; Stillmock, K. A.; Witmer, M. V.; Moyer, G.; Schleif, W. A.; Gabryelski, L. J.; Leonard, Y. M.; Lynch, J. J.; Michelson, S. R.; Young, S. D. Design and Synthesis of 8-Hydroxy-[1,6]Naphthyridines as Novel Inhibitors of HIV-1 Integrase in Vitro and in Infected Cells. *J. Med. Chem.* **2003**, *46*, 453-456.

(25) Lad, N. P.; Kulkarni, S.; Sharma, R.; Mascarenhas, M.; Kulkarni, M. R.; Pandit, S. S. Piperlongumine Derived Cyclic Sulfonamides (Sultams): Synthesis and *in vitro* Exploration for Therapeutic Potential against HeLa Cancer Cell Lines. *Eur. J. Med. Chem.* **2017**, *126*, 870-878.

(26) Lukashev, N. V.; Grabovyi, G. A.; Erzunov, D. A.; Kazantsev, A. V.; Latyshev, G. V.; Averin, A. D.; Beletskaya, I. P. Pd- and Cu-catalyzed approaches in the syntheses of new cholane aminoanthraquinone pincer-like ligands. *Beilstein J. Org. Chem.* **2017**, *13*, 564-570.

(27) Chéron, N.; Jacqueminb, D.; Fleurat-Lessard, P. A qualitative failure of B3LYP for textbook organic reactions. *Phys. Chem. Chem. Phys.* **2012**, *14*, 7170-7175.

(28) Xu, W.; Chen, Q.-Y. 3,3-Difluoro-1-iodocyclopropenes: A Simple Synthesis and Their Reactions. *J. Org. Chem.* **2002**, 67, 9421–9427.

(29) Neese, F. Software update: the ORCA program system, version 4.0. *WIREs Comput. Mol. Sci.* **2018**, *8*, e1327.

(30) Becke, A. D. Density-functional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **1993**, *98*, 5648−5652.

(31) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. Ab Initio Calculation of Vibrational Absorption and Circular Dichroism Spectra Using Density Functional Force Fields. *J. Phys. Chem.* **1994**, *98*, 11623−11627.

(32) Weigend, F.; Ahlrichs, R. Balanced basis sets of split valence, triple zeta valence and quadruple zeta valence quality for H to Rn: Design and assessment of accuracy. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305.

(33) Zheng, J.; Xu, X.; Truhlar, D. G. Minimally augmented Karlsruhe basis sets. *Theor. Chem. Acc.* **2011**, *128*, 295−305.

(34) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal solvation model based on solute electron density and on a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.

(35) Peterson, K. A.; Figgen, D.; Goll, E.; Stoll, H.; Dolg, M. Systematically convergent basis sets with relativistic pseudopotentials. II. Small-core pseudopotentials and correlation consistent basis sets for the post-d group 16–18 elements. *J. Chem. Phys.* **2003**, *119*, 11113–11123.

(36) Neese, F.; Wennmohs, F.; Hansen, A.; Becker, U. Efficient, approximate and parallel Hartree-Fock and hybrid DFT calculations. A 'chain-of-spheres' algorithm for the Hartree-Fock exchange. *Chem. Phys.* **2009**, *356*, 98−109.

(37) Grimme, S. Supramolecular Binding Thermodynamics by Dispersion-Corrected Density Functional Theory. *Chem. Eur. J.* **2012**, *18*, 9955–9964.

(38) CYLview, 1.0b; Legault, C. Y. Université de Sherbrooke, 2009, http://www.cylview.org.

(39) Majumdar, K. C.; Ganai, S. Facile synthesis of benzothiadiazine-1,1-dioxides, a precursor of RSV inhibitors, by tandem amidation/ intramolecular Aza-Wittig reaction. *Beilstein J. Org. Chem.* **2013**, *9*, 503-509.

(40) Májek, M.; Neumeier, M.; von Wangelin, A. J. Aromatic Chlorosulfonylation by Photoredox Catalysis. *ChemSusChem* **2017**, *10*, 151-155.

(41) Blackburn, C.; Achab, A.; Elder, A.; Ghosh, S.; Guo, J.; Harriman, G.; Jones, M. Synthesis of 3-Amino-1,2,4-benzothiadiazine 1,1-Dioxides via a Tandem Aza-Wittig/Heterocumulene Annulation. *J. Org. Chem.* **2005**, *70*, 10206–10209.