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Metal-Free [2+2+2] Cycloaddition of Ynamide-Nitriles with Ynamides: A Highly Regio- and Chemoselective Synthesis of *δ*-Carboline Derivatives

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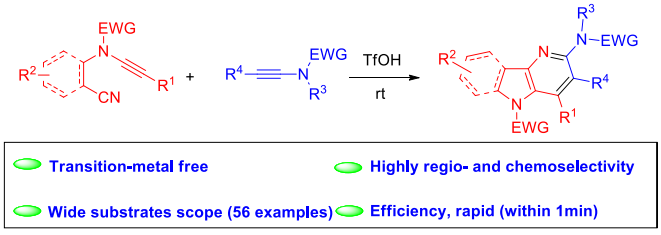
Supporting Information Placeholder

Abstract



A metal-free formal [2+2+2] cycloaddition of functionalized ynamide-nitriles with ynamides is disclosed which offers highly efficient access to polysubstituted *δ*-carboline derivatives under the mediation of TfOH. This strategy is highly regioselective and chemoselective, and

displays mild conditons, high yields and efficiency (within 1 min) in addition to substrates scopes (56 examples).

Introduction

Pyrido[*x,y-b*]indoles, commonly known as carbolines, serve as unique structural units in numerous natural alkaloids, pharmaceutical molecules and functional materials.[1] Among the class of carbolines, *δ*-carbolines have attracted considerable attention, because of which represent a rather broad spectrum of biological activities.[2] For examples, benzo-carbolinium and N^5-*ω*-cyclohexylpentyl-N^1-methyl-*δ*-carbolinium represent antifungal and antibacterial activities,[2a] and SYUIQ-5 is a potential cancer therapeutic.[2b] In addition, *δ*-carboline derivatives (*e.g.*, CzBPDCb) can be commonly used as electron transport unit bipolar host materials for blue phosphorescent organic light-emitting didoes (**Figure 1**).[2c]

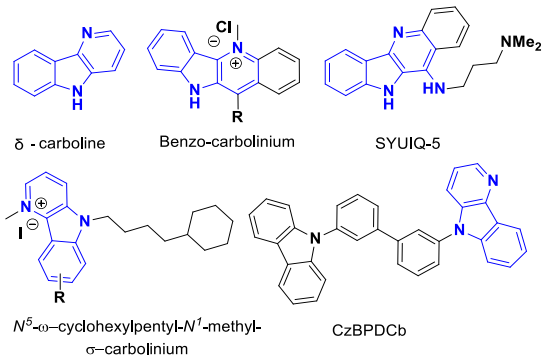
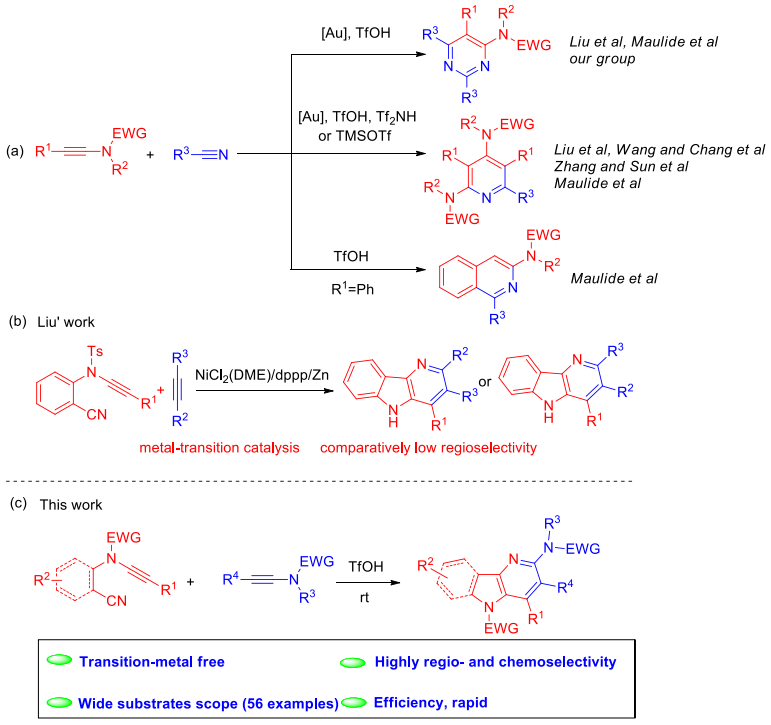


Figure 1. **Biologically Active Molecules and Functional Materials Containing *δ*-Carbolines.**

Due to the potential application of δ-carbolines in both medicinal chemistry and materials chemistry, a multitude of protocols for synthesizing δ-carbolines have been established,[3] which include Fischer reaction,[3b] Graebe-Ullmann reaction,[3c] photochemical cyclization,[3d] Pd-catalyzed amination and intramolecular cross-coupling reactions.[3e] Recently, although some innovative methods have been reported for the construction of δ-carbolines,[4] they still suffer from certain salient drawbacks, *e*. *g*., low step-economy, harsh conditions and indispensability of noble transition metallic catalysts.

Scheme 1. Cycloaddition of Ynamides with Nitriles.



Ynamides bearing an electron-withdrawing group on the nitrogen atom have been well demonstrated as versatile building blocks due to their combined stability and peculiar reactivity.[5]

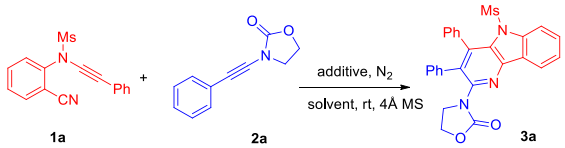
Cycloaddition reactions of ynamides with various precursors provide an efficient method for constructing complex frameworks.[6] In particular, [2+2+2] cycloaddition of ynamides and nitriles represents one of the most convenient and straightforward strategies to construct various nitrogen-containing heterocycles (**Scheme 1**).[7] For examples, Liu and co-workers described an elegant gold-catalyzed [2+2+2] cycloaddition of ynamides and nitriles for the synthesis pyrimidines and pyridines.[7a,7b] In comparison with the important advances in gold catalysis, metal-free catalytic cycloaddition of ynamides were developed, Maulide *et al*,[7c,7d] Wang and Chang *et al*,[7e] Zhang and Sun *et al* [7f] and our group[7g] developed the similar cycloaddition of ynamides and nitriles toward pyrimidines, pyridines and isoquinolines in the presence of acid catalysts. Besides, Liu et al reported an efficient synthesis of *δ*-carbolines *via* $NiCl_2$(DME)/dppp/Zn catalyzed [2+2+2] cycloaddition of alkyne-nitriles with alkynes, which has two innegligible disadvantages, including the employment of transition metallic catalysts and comparatively low regioselectivity when the unsymmetrical alkynes, particularly ynamides, were used as reactants.[4b] Herein, we developed a concise and highly efficient metal-free approach to furnish multi-substituted *δ*-carboline derivatives via TfOH-mediated regio- and chemoselective [2+2+2] cycloaddition of diverse ynamide-nitriles with ynamides under extremely mild reaction conditions.

Results and Discussion

Initially, ynamide-nitrile **1a** and 3-(phenylethynyl)oxazolidin-2-one **2a** were selected as the model substrates to investigate the feasibility of [2+2+2] cycloaddition. To our delight, the desired product δ-carboline **3a** could be obtained in 65% yield in the presence of 1.0 equiv of TfOH with CH_2Cl_2 as a solvent, the reaction completed within 0.5 hour (**Table1**, entry 1). Then, various Brønsted acid catalysts such as $HBF_4{\cdot}OEt_2$, $NHTf_2$ and Lewis acid catalysts including TMSOTf, $BF_3{\cdot}Et_2O$, $Sc(OTf)_3$ and $FeCl_3$ were screened, however, only inferior results could be obtained under the mediation of these acids (entries 2–7). Next, a number of solvents were examined. Notably, the employment of nonpolar solvent afforded the desired product in low to moderate yields (entries 8 and 9), with CH_2Cl_2 shown to be the solvent of choice. In contrast, no conversion was observed with polar solvents, such as THF, DMF and dioxane (entries 10–12), which might be rationalized that the polar solvent can serve as strong proton acceptor to compete for the acidic catalysts. Further investigation showed that there appears to be an obvious stoichiometric effect associated with **2a**: when the proportion of **2a** increased from 1.0 equiv to 1.5 equiv, the yield improved to 71% (entries 13 and 14). Subsequently, the influence of catalyst loading on the reaction was also investigated, and the yield increased to 78% when the catalyst loading of TfOH was increased to 1.2 equiv (entry 15). However, further increase in the catalyst loading decreased the yield (entry 16). In addition, lowering the reaction temperature to 0 °C resulted in a drop in the yield from 78% to 67%, even after prolonging the reaction time (entry 17).

With the optimal conditions in hand, the generality of this protocol was investigated (**Scheme 2**). The scope of ynamides **2** was first examined using ynamide-nitrile **1a** as its reaction partner. When a variety of ynamides with oxazolidin-2-one were subjected to the optimal condition, the desired *δ*-carbolines **3a**–**3h** were furnished in moderate to good yields

Table 1. Condition Optimization of the Cycloaddition[a,b]



entry	additive (equiv)	2a (equiv)	solvent	time(h)	yield (%)
1	TfOH (1.0)	1.0	CH_2Cl_2	0.5	65
2	$HBF_4{\cdot}OEt_2$ (1.0)	1.0	CH_2Cl_2	0.5	26
3	$NHTf_2$ (1.0)	1.0	CH_2Cl_2	0.5	21
4	TMSOTf (1.0)	1.0	CH_2Cl_2	0.5	45
5	$Sc(OTf)_3$ (1.0)	1.0	CH_2Cl_2	0.5	35
6	$BF_3{\cdot}Et_2O$ (1.0)	1.0	CH_2Cl_2	0.5	13
7	$FeCl_3$ (1.0)	1.0	CH_2Cl_2	0.5	9
8	TfOH (1.0)	1.0	DCE	0.5	53
9	TfOH (1.0)	1.0	toluene	0.5	19
10	TfOH (1.0)	1.0	THF	0.5	NR
11	TfOH (1.0)	1.0	DMF	0.5	NR
12	TfOH (1.0)	1.0	dioxane	0.5	trace
13	TfOH (1.0)	1.2	CH_2Cl_2	0.5	67
14	TfOH (1.0)	1.5	CH_2Cl_2	0.5	71
15	TfOH (1.2)	1.5	CH_2Cl_2	0.5	78
16	TfOH (1.5)	1.5	CH_2Cl_2	0.5	76
17[c]	TfOH (1.2)	1.5	CH_2Cl_2	4.0	67

[a]Unless otherwise specified, reactions were conducted with **1a** (0.1 mmol), **2a**, additive and 20 mg 4Å MS in 1.0 ml of solvent at room temperature under N_2 atmosphere. [b]Isolated yield. [c]Temperature was 0 °C.

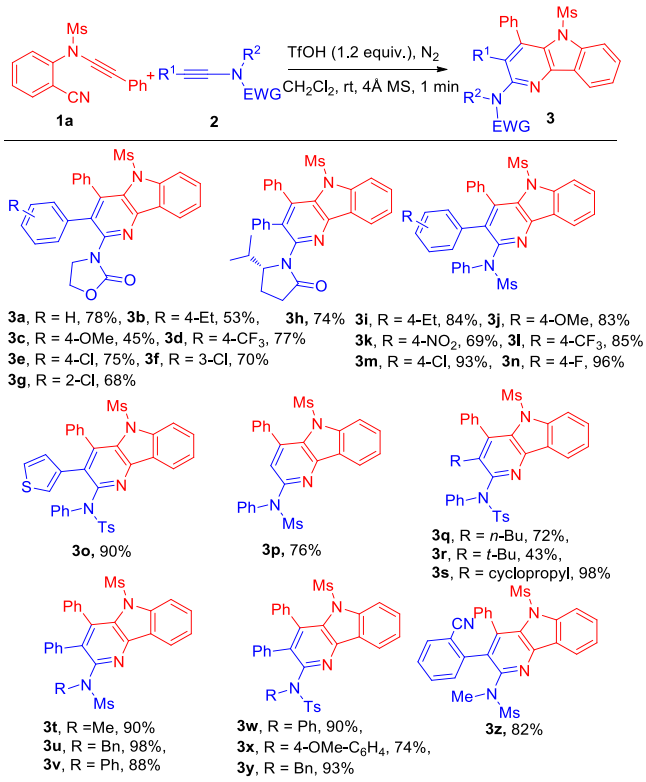
within 0.5 hour. Afterwards, the ynamides incorporating sulfonyl groups were examined. Remarkably, these substrates were better reactants, yielding the corresponding products at higher levels within a shorter reaction time (1 min) compared with those of **2a**–**2h**, which might be ascribed to the higher reactivity of sulfonyl ynamides. When aryl ynamides were employed as reactants, the electronic nature of the substituents (R^1 group) had a trivial

influence on the reaction, and both the electron-withdrawing and electron-donating groups were well-tolerated, affording the corresponding products **3i**–**3n** in moderate to good yields, ranging from 69% to 96%. The 3-thienyl substituted ynamide **2o** was also an ideal substrate, which resulted in the desired product **3o** in 90% yield. Delightedly, this protocol was amenable to terminally unsubstituted ynamide **2p** to deliver the desired product **3p** in 76% yield. Remarkably, the ynamides incorporating alkyl at the alkynyl terminus, such as *n*-Bu and cyclopropyl, were also well tolerated during the smooth formation of the corresponding products in 72% and 98 % yields, respectively (**3q** and **3s**). A considerably lower yield was obtained when the *tert*-butyl-substituted substrate **2r** was subjected to the optimal conditions probably due to the steric hindrance (**3r**). *N*-alkyl and *N*-phenyl substituted ynamides were also tolerable to afford the corresponding *δ*-carbolins **3t**–**3y** in high to excellent yields ranging from 74% to 98%. Notably, the reaction of ynamide bearing an acid-sensitive functional group cyano also proceeded efficiently, producing the desired *δ*-carboline in 82% yield (**3z**).

Next, various ynamide-nitriles **1** were also examined (**Scheme 3**). The ynamide-nitriles terminally substituted with alkyl, and aryl or *N*-aryl-substituted ynamides underwent [2+2+2] cycloaddition smoothly to afford the desired annulation products **4b**–**4j** within 1 min in excellent yields including the bulkier 1-naphthyl-substituted ynamide (**4g**). Heteroaromatic-substituted ynamides, such as **1h** and **1i** also served as ideal reactants, producing **4h** and **4i** in 87% and 52% yields, respectively. Remarkably, when the terminally

unsubstituted ynamide **1k** was employed as the substrate, the reaction also worked well to produce the desired *δ*-carboline in 63% yield. Additionally, ynamides incorporating the electron-donating and electron-withdrawing sulfonyl groups (*e.g.,* Ts and Ns) were compatible with this reaction, resulting in the desired products **4l**–**4m** in excellent yields. Ynamides substituted with a methyl and a bromine atom on *N*-phenyl were also amenable to this transformation, giving the expected *δ*-carboline in 91% and 97% yields (**4n** and **4o**). In particular, with *N*-2-thienyl-substituted ynamide-nitrile **1p** employed as a substrate, a thieno[*3′,2′:4,5*]pyrrolo-[*3,2-b*]-pyridine derivative **4p** was produced.

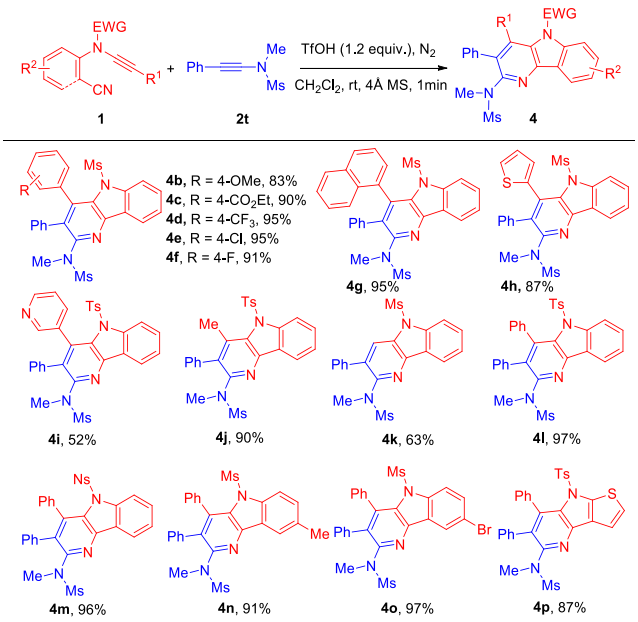
Scheme 2. Scope of the Reaction with Ynamides.[a,b,c]



[a]Unless otherwise specified, reactions were conducted with **1a** (0.1 mmol), **2** (0.15 mmol), TfOH (0.12 mmol) and 20 mg 4Å MS in 1.0 ml of CH_2Cl_2 at room temperature under N_2 atmosphere. [b]Isolated yield. [c]These reactions were completed within 0.5 hour for ynamides (**2a**–**2h**).

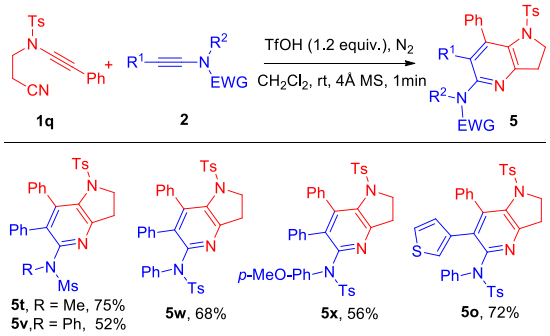
The 4-azaindoline frame is a unique structural core widely existing in biologically important natural alkaloid products and pharmaceutical molecules,[8] such as triazabenzo[*cd*]azulen-9-one PDE4 inhibitors.[9] Despite its biological significance, only sporadic examples were described concerning the synthesis of 4-azaindoline framework[10] and they usually suffered from multistep processes, harsh conditions and low yields. When ynamide-nitrile **1q** was subjected to this reaction with ynamide **2t** as the reaction partner, the desired product 4-azaindoline **5t** was produced in 75% yield (**Scheme 4**). Both *N*-Phenyl- and thienyl-substituted terminally ynamides were compatible with this reaction, affording the corresponding 4-azaindoline derivatives (**5v**, **5w**, **5x** and **5o**) in 52%–75% yields. Hence, this cycloaddition provided a novel and straightforward approach to construct various substituted 4-azaindoline derivatives with a notable degree of versatility.

Scheme 3. Scope of the Reaction with Ynamide-Nitriles.[a,b]



[a]Unless otherwise specified, reactions were conducted with **1** (0.1 mmol), **2t** (0.15 mmol), TfOH (0.12 mmol) and 20 mg 4Å MS in 1.0 ml of CH_2Cl_2 at room temperature under N_2 atmosphere. [b]Isolated yield.

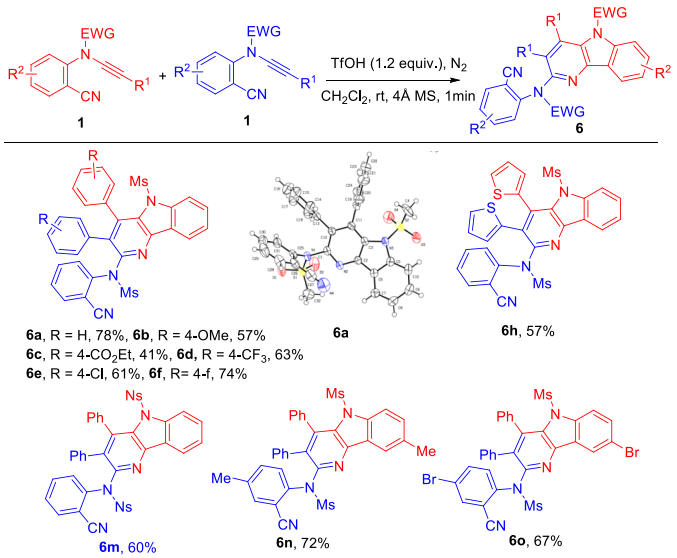
Scheme 4. Scope of the Reaction with Ynamides.[a,b]



[a]Unless otherwise specified, reactions were conducted with **1q** (0.1 mmol), **2** (0.15 mmol), TfOH (0.12 mmol) and 20 mg 4Å MS in 1.0 ml of CH_2Cl_2 at room temperature under N_2 atmosphere. [b]Isolated yield.

Intriguingly, when ynamide-nitrile **1a** was employed as the sole reactant, the self-assembled cycloaddition product **6a** was successfully obtained in 78% yield (**Scheme 5**). Both electron-donating and electron-withdrawing groups on the phenyl substituted at the alkynyl terminal were well tolerated. The desired *δ*-carboline **6b** was furnished in 57% yield by employing the substrate incorporating a methoxyl group, and the substrates carrying electron- withdrawing groups (*e.g.* 4-CO_2Et, 4-CF_3, 4-F, 4-Cl), furnished the corresponding products in yields 41%–75% (**6c**–**6f**). Additionally, the 2-thienyl-substituted ynamide was also compatible with this self-assembled cycloaddition, resulting in the desired compound **6h** in moderate yield. Ynamides substituted with methyl or bromine on *N*-phenyl were also amenable to this transformation, giving the expected products (**6n**–**6o)** in 72% and 67% yields, respectively. Instead, when *N*-Ns protected ynamide was employed, the reaction proceeded smoothly as well (**6m**).

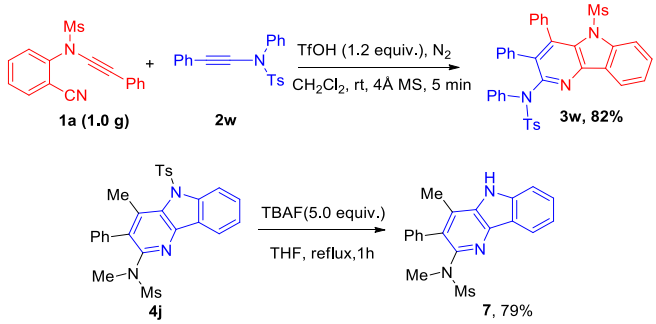
Scheme 5. Scope of the Self-Reaction.[a,b]



[a]Unless otherwise specified, reactions were conducted with **1** (0.1 mmol), TfOH (0.12 mmol) and 20 mg 4Å MS in 1.0 ml of CH_2Cl_2 at room temperature under N_2 atmosphere. [b]Isolated yield.

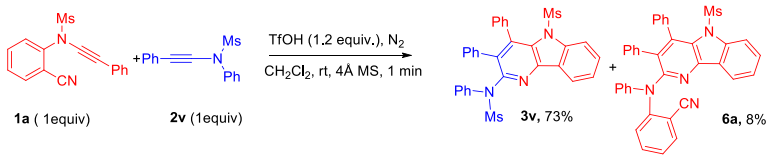
To examine the scalability of this developed protocol, the synthesis of the *δ*-carboline **3w** in a gram-scale was performed under the optimal condition, and the product was furnished in 82% yield. Remarkably, the tosyl-protecting group on these products could be easily removed using over-stoichiometric TBAF, For instance, δ-carboline **4j** was transformed to detosylated product **7** in 79% yield (**Scheme 6**).

Scheme 6. Gram Scale Preparation and Removal of Tosyl-Protecting Group.



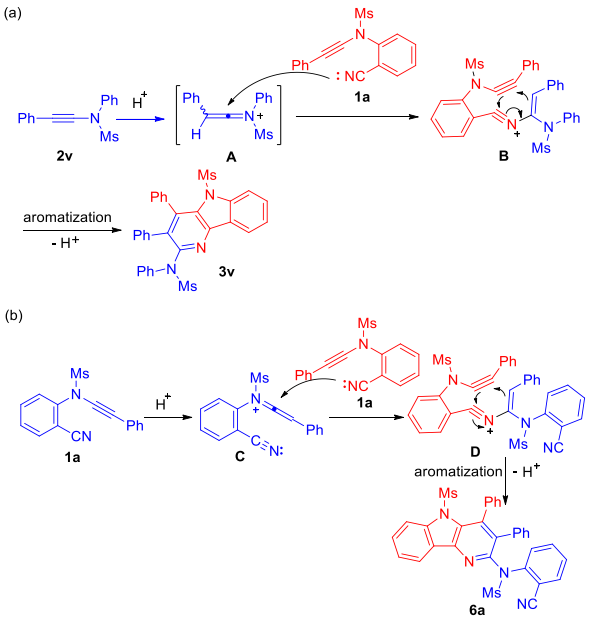
To probe the competitive and mechanistic studies, control experiments were conducted as shown in **scheme 7.** The propotion of **1a** and **2v** was 1.0 equiv, the mixtures of the desired product **3v** and self-assembled product **6a** were observed in 73% and 8% yields. Probably Due to the electron-withdrawing nature of the cyano group, the alkynyl moiety of **2v** is more electron-rich than that of **1a**. Thus **2v** would be more preferentially protonated by TfOH, leading to the major product **3v.**

Scheme 7. Control Experiments



According to the above experimental results, a plausible mechanism leading to *δ*-carboline is depicted in **Scheme 8**.[7c] Because of the electron-withdrawing nature of the cyano group, the alkynyl moiety of **2v** is more electron-rich than that of **1a**. Thus **2v** would be more preferentially protonated by TfOH to furnish the keteniminium intermediate **A** in-situ, which is then attacked by ynamide-nitrile **1a** to afford the intermediate **B**. Subsequently, an intramolecular cyclization of **B** Probably be triggered by the nucleophilicity of enamine, furnishing the final product **3v**. Similarly, ynamide-nitrile **1a** is protonated to furnish the intermediate **C** in the absence of another ynamide **2**, followed by a nucleophilic attack by another molecule of **1a** to produce the intermediate **D**. Finally, an intramolecular cyclization of **D** proceeds to yield the corresponding *δ*-carboline **6a**.

Scheme 8. The Proposed Mechanism for [2+2+2] Cycloaddition



Conclusion

In summary, we have developed a novel and highly efficient TfOH-mediated [2+2+2] cycloaddition of ynamide-nitriles with ynamides, which provides a straightforward access to polysubstituted *δ*-carboline and 4-azaindoline derivatives in excellent yields. This strategy has the features of high regio- and chemoselectivity, metal-free condition, high yields and efficiency (within 1 min) in addition to wide substrate scopes, offering the synthetic chemists more flexibility for construction of the nitrogen-containing heterocycles. Further bioactivity investigation of these *δ*-carboline and 4-azaindoline derivatives are currently ongoing and will be reported in our future work.

EXPERIMENTAL SECTION

General Information. Unless otherwise mentioned, all reactions were performed in flame-dried glassware under air. Solvents were distilled prior to use. Reagents were used as

purchased from commercial available unless otherwise noted. Chromatographic separations were performed using Kangbino 48-75 Å SiO_2. ^1H, ^{19}F and ^{13}C NMR spectra were recorded on Agilent Pro Pulse spectrometers using $CDCl_3$ with TMS or residual solvent as standard unless otherwise noted. Melting points were determined using a melting point apparatus and were uncorrected/calibrated. TLC analysis was performed using Kangbino glass-backed plates (60 Å, 250 μm) and visualized using UV and Iodine stains. Low-resolution mass spectra were obtained using an Agilent 1100 series LS/MSD. High resolution mass spectra for new compounds were recorded on a Thermo Fisher Exactive APCI-orbitrap spectrometer. All spectral data obtained for new compounds are reported here.

General procedure.

General Procedure 1 for the Synthesis of ynamides (2v).[11a] To a solution of phenylacetylene (1020.5 mg, 10.0 mmol, 1.0 equiv) in acetone (100 mL) was added NBS (1780.0 mg, 11.0 mmol, 1.1 equiv) and $AgNO_3$ (169.9 mg, 1.0 mmol, 10 mol %). The resulting solution was stirred under nitrogen at room temperature for 6 hours. After removing excess acetone the reaction was quenched with water, and extracted with EtOAc three times, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was eluted through a short silica column (petroleum ether) to obtain the bromoalkyne (1530.0 mg，85%).

To a dried flask was added *N*-phenylmethanesulfonamide (513.0 mg, 3.0 mmol, 1.0 equiv), $CuSO_4 \cdot 5H_2O$ (375.0 mg, 1.5 mmol, 0.5 equiv), 1,10-phenanthroline (162.0 mg, 0.9 mmol, 30 mol % equiv) and K_2CO_3 (828.0 mg, 6.0 mol, 2.0 equiv), bromoalkyne (648.0 mg, 3.6 mol,

1.2 equiv) and this mixture was subsequently treated with anhydrous toluene (100 mL). The flask was charged with nitrogen, and the solution was heated at 80 ºC overnight. After completion, the crude reaction mixture was cooled to room temperature, filtered through CeliteTM, and concentrated in vacuo. Purification of the crude residue using silica gel flash column chromatography yielded the pure ynamide **2v** (458.6 mg, 52%) as white solid.

General Procedure 2 for the Synthesis of ynamides (2w).[11b] $CuCl_2$ (80.4 mg, 0.6 mmol, 20 mol %), 4-methyl-*N*-phenylbenzenesulfonamide (2964.0 mg, 12.0 mmol, 4.0 equiv) and Na_2CO_3 (636.0 mg, 6.0 mmol, 2.0 equiv) were added to a three-necked round-bottomed flask. The flask was purged with oxygen for 15 min and a solution of pyridine (474.0 mg, 6.0 mmol, 2.0 equiv) in dry toluene (0.2 M) was added. A balloon filled with oxygen was connected to the flask and the stirred mixture was heated at 70 ºC. After 15 min, a solution of phenylacetylene (306.2 mg, 3.0 mmol, 1.0 equiv) in anhydrous toluene (0.2 M) was added by syringe pump over 4 h. The mixture was allowed to stir at 70 ºC for another 4 h and allowed to cool to rt. The reaction mixture was filtered through a plug of silica gel, washed with ethyl acetate and concentrated. The crude residue **2w** (610.5 mg, 55%) was purified by flash chromatography over silica gel.

General Procedure 3 for the Synthesis of ynamide (1k).[11c] To a solution of *N*-(2-cyanophenyl)methanesulfonamide (5.9 g, 30.0 mmol 1.0 equiv) in DMF (70 mL) was added Cs_2CO_3 (12.7 g, 39.0 mmol, 1.3 equiv). The solution was stirred at room temperature for 30 min, then phenyl((trimethylsilyl)ethynyl)iodonium triflate (17.6 g, 39.0 mmol, 1.3

equiv) in dichloromethane (30 mL) was added to the mixture and stirred until the reaction was completed as monitored by TLC. The reaction mixture was quenched by water and stirred for 30 min. The resulting mixture was extracted with CH_2Cl_2, washed with water and brine, and dried over anhydrous $MgSO_4$. The mixture was filtered and the solvent was evaporated under the reduced pressure, then the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1k** (6.63 g，60%) as a white solid.

General Procedure 4 for the Synthesis of ynamide (1a).[11c] The solution of *N*-(2-cyanophenyl)-*N*-ethynyl-4-methylbenzenesulfonamide (2.2 g, 10.0 mmol, 1.0 equiv) in THF (40 mL) was cooled to -40 ºC and $ZnBr_2$ (2.48 g, 11.0 mol, 1.1 equiv) in THF (20 mL) was added dropwise. After stirring at the same temperature for 20 min, LiHMDS (15.0 ml, 15.0 mmol, 1.5 equiv, 1M in THF) was added and stirred for another 20 min at -40 ℃. Then themixture of $Pd_2(dba)_3$ (457.5 mg, 0.5 mmol, 0.05 equiv), PPh_3 (524 mg, 2.0 mmol, 0.2 equiv) and iodobenzene (3.06 g, 15 mmol, 1.5 equiv) in THF (5 mL) was added dropwise. The reaction mixture waswarmed up to room temperature and stirred for 24 h, then quenched by brine and stirred for 30 min. The mixture was filtered over a celite pad, and extracted with ethyl acetate. The combined organic layers were washed with water and brine, and dried over anhydrous $MgSO_4$. The mixture was filtered and the solvent was evaporated under the reduced pressure, and the residue was purified by column chromatography on silica gel to afford the desired product **1a** (2.05 g, 69%).

General Procedure 5 for the Synthesis of ynamide (1r)[11c] To a solution of *N*-(2-cyanophenyl)-4-methylbenzenesulfonamide (816.0 mg, 3.0 mmol 1.0 equiv) in DMF (50 mL) was added Cs_2CO_3 (1271.4 mg, 3.9 mmol, 1.3 equiv). The solution was stirred at room temperature for 30 min, then phenyl((trimethylsilyl)ethynyl)iodoniumtriflate (1755.0 mg, 3.9 mmol, 1.3 equiv) in dichloromethane (30 mL) was added to the mixture and stirred until the reaction was completed as monitored by TLC. The reaction mixture was quenched by water and stirred for 30 min. The resulting mixture was extracted with CH_2Cl_2, washed with water and brine, and dried over anhydrous $MgSO_4$. The mixture was filtered and the solvent was evaporated under the reduced pressure, then the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 topetroleum ether/dichloromethane = 1/1) to afford the desired product **1r** (666.0 mg, 75%).

General Procedure 6 for the Synthesis of ynamide (1l).[11c] The solution of N-(2-cyanophenyl)-N-ethynyl-4-methylbenzenesulfonamide (592.0 mg, 2.0 mmol, 1.0 equiv) in THF (40 mL) was cooled to -40 ℃ and LiHMDS (3.0 ml, 3.0 mmol, 1.5 equiv, 1M in THF) was added dropwise. After stirring at the same temperature for 20 min, $ZnBr_2$ (495.0 mg, 2.2 mol, 1.1 equiv) in THF (20 mL)was added and stirred for another 20 min at -40 ℃. Then themixture of $Pd_2(dba)_3$ (91.5 mg, 0.1 mmol, 0.05 equiv), PPh_3 (104.8 mg, 0.4 mmol, 0.2 equiv) and iodobenzene (612.0 mg, 3.0 mmol, 1.5 equiv) in THF (5 mL) was added dropwise. The reaction mixture waswarmed up to room temperature and stirred for 24 h, then quenched by brine and stirred for 30 min. The mixture was filtered over a celite pad, and extracted with ethyl acetate.

The combined organic layers were washed with water and brine, and dried over anhydrous $MgSO_4$. The mixture was filtered and the solvent was evaporated under the reduced pressure, and the residue was purified by column chromatography on silica gel to afford the desired product **1l** (498.5 mg, 67 %).

General Procedure 7 for the Synthesis of ynamide (1j).[11c] The solution of *N*-(2-cyanophenyl)-*N*-ethynyl-4-methylbenzenesulfonamide (592.0 mg, 2.0 mmol, 1.0 equiv) in THF (10 mL) was cooled to -40 ºC and LiHMDS (3.0 ml, 3.0 mmol, 1.5 equiv 1M in THF) was added dropwise. After stirring at the same temperature for 1 h, iodomethane (0.5 ml, 8 mmol, 4.0 equiv) in THF (2 mL) was added. The temperature was slowly raised to –5 °C and then the reaction mixture was allowed to warm up to room temperature and stirred for 24 h. Thereaction mixture was quenched by brine and stirred for 30 min, then extracted with ethylacetate. The combined organic layers were washed with water and brine, and dried overanhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residuewas purified by column chromatography on silica gel to afford the product **1j** (551.8 mg, 89%).

General Procedure 8 for the Synthesis of ynamide (2z). [11a,11d] Under an atmosphere of argon, a solution of triphenylphosphine (10.5g, 40.0 mmol,4.0 equiv) and tetrabromomethane (6.6 g, 20.0 mmol, 2.0 equiv) in CH_2Cl_2 (0.15 M) was stirred at 0 °C for 30 minutes. The 2-formylbenzonitrile (1.3 g, 10.0 mmol, 1.0 equiv) was added over a period of five minutes, and the mixture as stirred at 0 °C for one hour. After addition of water, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (three times). The

combined organic layerswere dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was dry-loaded on silica and subjected to flash chromatography.

To the vigorously stirred solution of the 1,1-dibromoethene (1.4 g, 5.0 mmol, 1.0 equiv) in CH_2Cl_2 (25 mL) at 0 °C, $BnEt_3Cl$ (1.0 g, 4.4 mmol, 0.88 equiv) was added. Subsequently, a solution of KOH (230 mmol) in H_2O (10 mL) was added to the reaction mixture. After stirring for 5 h at 0 °C, H_2O (20 mL) was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was washed with brine and dried over $MgSO_4$. All volatiles were removed under reduced pressure. The product was purified by silica gel flash column chromatography.

To a dried flask was added *N*-methylmethanesulfonamide (479.6 mg, 4.4 mmol, 1.2 equiv), $CuSO_4 \cdot 5H_2O$ (475.0 mg, 1.9 mmol, 0.5 equiv), 1,10-phenanthroline (198.0 mg, 1.1 mmol, 0.3 equiv) and K_2CO_3 (1021.2 mg, 7.4 mmol, 2.0 equiv), 2-(bromoethynyl)benzonitrile (758.5 mg, 3.7 mmol, 1.0 equiv) and this mixture was subsequently treated with anhydrous toluene (100 mL) and the bromoalkyne. The flask was charged with nitrogen, and the solution was heated at 80 °C overnight. After completion, the crude reaction mixture was cooled to room temperature, filtered through CeliteTM, and concentrated in vacuo. Purification of the crude residue using silica gel flash column chromatography yielded the pure product as white solid **2z** (491.6 mg, 52%).

General Procedure 9 for TfOH-Mediated [2+2+2] Cycloadditions of ynamide-nitrile with ynamide. To a suspension of ynamide-nitrile **1** (0.15 mmol), another ynamide **2** (0.225 mmol) and 4Å MS (20.0 mg) in dry CH_2Cl_2 (1.5 mL) was added TfOH (0.18 mmol) dropwise *via* a syringe pump at room temperature under nitrogen atmosphere. The reaction was monitored by TLC. when progress appeared to be completed within 1 min or 0.5 h at the same temperature, the saturated sodium bicarbonate solution was added to the mixture and the resulting mixture was extracted with CH_2Cl_2. The organic layers were washed with sat aq NaCl and dried over $MgSO_4$. Filtration and concentration of the mixture in vacuo afforded the crude product that was purified by flash silica gel column chromatography [gradient eluent: EtOAc in petroleum ether] to obtain the corresponding products.

General Procedure 10 for the removal of tosyl-protection group.[11c] To a solution of **4j** (52.0 mg, 0.1 mmol) in THF (3 mL) was added tetrabutylammonium fluoride (0.5 mL, 1M in THF, 0.5 mmol). The mixture was refluxed for 1 h, and then quenched by water. Themixture was extracted with dichloromethane and dried over anhydrous $MgSO_4$. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel to afford the desired product **7** (28.9 mg, 79%).

Characterization of products.

***N*-(2-cyanophenyl)-*N*-(phenylethynyl)methanesulfonamide (1a)**

Following the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1a**; white solid; mp: 81 – 83 ºC; yield: 69%; 2.05 g; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.65 (m, 3H), 7.60 – 7.45 (m, 3H), 7.34 – 7.27 (m, 3H), 3.46 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 140.5, 134.2, 134.1, 132.2, 130.0, 129.6, 128.8, 128.4, 121.7, 116.0, 112.1, 80.5, 71.8, 39.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{16}H_{13}N_2O_2S$ $[M+H]^+$ 297.0692, found 297.0689.

***N*-(2-cyanophenyl)-*N*-((4-methoxyphenyl)ethynyl)methanesulfonamide (1b)**

Following the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1b**, pale yellow oil; yield: 82%; 268.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 7.7 Hz, 1H), 7.75 – 7.69 (m, 2H), 7.55 – 7.51 (m, 1H), 7.49 – 7.44 (m, 2H), 6.86 (d, J = 8.9 Hz, 2H), 3.82 (s, 3H), 3.45 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 160.2, 140.7, 134.3, 134.1, 134.0, 130.0, 129.4, 116.1, 114.0, 113.5, 112.1, 79.3, 71.7, 55.3, 39.5; HRMS (APCI–orbitrap) m/z: calcd. for $C_{17}H_{15}N_2O_3S$ $[M+H]^+$ 327.0798, found 327.0792.

ethyl 4-((*N*-(2-cyanophenyl)methylsulfonamido)ethynyl)benzoate (1c)

Following the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1c**; pale yellow solid; mp: 93 – 95 ºC; yield: 73%; 269.4 mg; ^{1}H

NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.3 Hz, 2H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.75 – 7.67 (m, 2H), 7.55 (td, *J* = 6.9 Hz, *J* = 1.5 Hz, 1H), 7.51 (d, *J* = 8.3 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.45 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 165.9, 140.1, 134.3, 134.1, 131.4, 130.1, 130.0, 129.8, 129.5, 126.4, 115.9, 112.1, 83.2, 71.4, 61.2, 39.8, 14.3; HRMS (APCI–orbitrap) m/z: calcd. for $C_{19}H_{17}N_2O_4S$ $[M+H]^+$ 369.0904, found 369.0899.

***N*-(2-cyanophenyl)-*N*-((4-(trifluoromethyl)phenyl)ethynyl)methanesulfonamide (1d)**

Following the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1d**; pale yellow oil; yield: 77%; 281.1 mg; ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.77 – 7.70 (M, 2H), 7.61 – 7.55 (m, 5H), 3.46 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 140.1, 134.3, 134.1, 131.9, 130.21(q, *J* = 32.8), 130.16, 129.8, 125.7(q, *J* = 1.3), 125.3(q, *J* = 3.8 Hz), 123.8(q, *J* = 270.8Hz), 115.9, 112.0, 82.7, 70.8, 39.9; ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.86 (3F, S); HRMS (APCI–orbitrap) m/z: calcd. for $C_{17}H_{12}F_3N_2O_2S$ $[M+H]^+$ 365.0566, found 365.0561.

***N*-((4-chlorophenyl)ethynyl)-*N*-(2-cyanophenyl)methanesulfonamide (1e)**

Following the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1e**; pale yellow oil; yield: 65%; 430.3 mg; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.57 – 7.52 (m, 1H), 7.45 – 7.40 (m, 2H), 7.33 – 7.25 (m, 3H), 3.45 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 140.3, 134.8, 134.2,

134.1, 133.4, 130.1, 129.7, 128.7, 120.2, 116.0, 112.0, 81.3, 70.8, 39.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{16}H_{12}ClN_2O_2S$ $[M+H]^+$ 331.0303, found 331.0298.

***N*-(2-cyanophenyl)-*N*-((4-fluorophenyl)ethynyl)methanesulfonamide (1f)**

Following the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1f**; pale yellow oil; yield: 86%; 541.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.54 (td, *J* = 7.4, 1.7 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.05 – 6.99(m, 2H), 3.44 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 162.9 (d, *J* = 250.4), 140.4, 134.4 (d, *J* = 8.6), 134.2, 134.1, 130.1, 129.6, 117.7 (d, *J* = 3.4), 116.0, 115.7 (d, *J* = 22.3), 112.0, 80.1, 70.8, 39.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -109.9 (ddd, *J* = 13.8, *J* =8.5, *J* =5.2); HRMS (APCI–orbitrap) m/z: calcd. for $C_{16}H_{12}FN_2O_2S$ $[M+H]^+$ 315.0598, found 315.0594.

***N*-(2-cyanophenyl)-*N*-(naphthalen-1-ylethynyl)methanesulfonamide (1g)**

Following the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1g**; pale yellow oil; yield: 51%; 353.9 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.4 Hz, 1H), 7.86 (dd, *J* = 8.1, 4.3 Hz, 2H), 7.82 – 7.78 (m, 2H), 7.77 – 7.72 (m, 2H), 7.64 – 7.59 (m, 1H), 7.57 – 7.52 (m, 2H), 7.46 – 7.42 (m, 1H), 3.53 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 140.5, 134.2, 134.1, 133.5, 133.2, 131.1, 130.1, 129.7, 129.2, 128.3,

127.1, 126.5, 126.1, 125.2, 119.4, 116.2, 112.2, 85.0, 70.2, 39.8; HRMS (APCI–orbitrap) m/z: calcd. for $C_{20}H_{15}N_2O_2S$ $[M+H]^+$ 347.0849, found 347.0844.

***N*-(2-cyanophenyl)-*N*-(thiophen-3-ylethynyl)methanesulfonamide (1h)**

Following the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1h**; pale yellow oil; yield: 81%; 490.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.9 Hz, 1H), 7.73 – 7.67 (m, 2H), 7.57 – 7.50 (m, 2H), 7.28 (dd, *J* = 5.0, 3.1 Hz, 1H), 7.17 (dd, *J* = 5.1, 1.2 Hz, 1H), 3.44 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 140.5, 134.2, 134.1, 130.7, 130.4, 130.0, 129.6, 125.5, 120.5, 116.0, 112.1, 80.1, 66.9, 39.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{14}H_{11}N_2O_2S_2$ $[M+H]^+$ 303.0257, found 303.0253.

N-(2-cyanophenyl)-4-methyl-N-(pyridin-3-ylethynyl)benzenesulfonamide (1i) [11c]

Following the general procedure 6; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 4/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **1i**; pale yellow solid; yield: 68%; 499.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.51(d, *J* = 3.5, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.72 – 7.63 (m, 3H), 7.52 (t, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.23 (dd, *J* = 7.6, 5.0 Hz, 1H), 2.48 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 152.4, 148.7, 146.2, 140.0, 138.8, 134.3, 133.7, 132.6, 130.0, 129.7, 129.6, 128.6, 123.0, 119.4, 115.1, 112.7, 84.4, 68.3, 21.8.

***N*-(2-cyanophenyl)-4-methyl-*N*-(prop-1-yn-1-yl)benzenesulfonamide (1j)**[11c]

Following the general procedure 7; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1j**; white solid; yield: 89%; 551.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.7 Hz, 2H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.40 – 7.32 (m, 3H), 2.47 (s, 3H), 1.91 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 145.5, 140.9, 134.1, 133.5, 132.9, 129.8, 129.4, 129.1, 128.6, 115.3, 112.9, 71.7, 67.0, 21.8, 3.2.

***N*-(2-cyanophenyl)-*N*-ethynylmethanesulfonamide (1k)**

Following the general procedure 3; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1k**; white solid; mp: 99 – 101 ºC; yield: 60%; 6.63 g; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.72 (td, *J* = 7.8, 1.5 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.55 (td, *J* = 7.7, 1.1 Hz, 1H), 3.43 (s, 3H), 3.05 (s, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 139.7, 134.2, 134.0, 129.9, 129.8, 115.9, 112.3, 74.3, 60.8, 39.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{10}H_9N_2O_2S$ $[M+H]^+$ 221.0379, found 221.0377.

***N*-(2-cyanophenyl)-4-methyl-*N*-(phenylethynyl)benzenesulfonamide (1l)**[11c]

Following the general procedure 6; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1l**; white solid; yield: 67%; 498.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.1 Hz, 2H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.54 – 7.47 (m, 2H),

7.44 – 7.40 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.34 – 7.28 (m, 3H), 2.49 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 145.9, 140.5, 134.2, 133.6, 132.7, 132.0, 129.9, 129.7, 129.3, 128.7, 128.5, 128.3, 122.0, 115.2, 112.8, 81.5, 71.3, 21.8.

***N*-(2-cyanophenyl)-4-nitro-*N*-(phenylethynyl)benzenesulfonamide (1m)**

Following the general procedure 6; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 8/1 to petroleum ether/ ethyl acetate = 6/1) to afford the desired product **1m**; pale yellow solid; mp: 93 – 95ºC; yield: 73%; 589.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 – 8.41 (m, 2H), 8.13 – 8.08 (m, 2H), 7.75 – 7.69 (m, 2H), 7.61 – 7.55 (m, 2H), 7.46 – 7.43 (m, 2H), 7.37 – 7.30 (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.2, 141.2, 139.8, 134.4, 134.0, 132.3, 130.1, 130.0, 129.8, 129.1, 128.5, 124.6, 121.2, 114.8, 112.3, 80.1, 72.1; HRMS (APCI–orbitrap) m/z: calcd. for $C_{21}H_{14}N_3O_4S$ $[M+H]^+$ 404.0670, found 404.0696.

***N*-(2-cyano-4-methylphenyl)-*N*-(phenylethynyl)methanesulfonamide (1n)**

ollowing the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **1n**; pale yellow oil; yield: 67%; 416.7 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.54 (m, 2H), 7.52 – 7.46 (m, 3H), 7.34 – 7.30 (d, *J* = 5.2 Hz, 3H), 3.42 (s, 3H), 2.43 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 140.5, 137.9, 134.9, 134.3, 132.1, 129.7, 128.7,

128.4, 121.8, 116.2, 111.8, 80.8, 71.5, 39.5, 20.9; HRMS (APCI–orbitrap) m/z: calcd. for $C_{17}H_{15}N_2O_2S$ $[M+H]^+$ 311.0849, found 311.0845.

_N_-(4-bromo-2-cyanophenyl)-_N_-(phenylethynyl)methanesulfonamide (1o)

Following the general procedure 4; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **1o**; pale yellow oil; yield: 74%; 553.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 2.3 Hz, 1H), 7.83 (dd, J = 8.7, 2.3 Hz, 1H), 7.57 (d, J = 8.6 Hz, 1H), 7.52 – 7.48 (m, 2H), 7.36 – 7.31 (m, 3H), 3.45 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 139.6, 137.4, 136.5, 132.2, 131.3, 128.9, 128.4, 123.2, 121.4, 114.7, 113.7, 80.0, 72.1, 39.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{16}H_{12}BrN_2O_2S$ $[M+H]^+$ 374.9797, found 374.9792.

_N_-(3-cyanothiophen-2-yl)-4-methyl-_N_-(phenylethynyl)benzenesulfonamide (1p)

Following the general procedure 6; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **1p**; pale yellow solid; mp: 274 – 276 ºC; yield: 56%; 449.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 7.2 Hz, 2H), 7.40 (d, J = 7.9 Hz, 2H), 7.35 – 7.29 (m, 4H), 7.10 (d, J = 5.7 Hz, 1H), 2.49 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 148.0, 146.4, 132.1, 131.7, 130.1, 128.74, 128.65, 128.3, 127.5, 125.8, 121.6, 112.1, 108.7, 80.7, 71.5, 21.9; HRMS (APCI–orbitrap) m/z: calcd. for $C_{20}H_{14}N_2O_2S_2Na$ $[M+Na]^+$ 401.0394, found 401.0385.

_N_-(2-cyanoethyl)-4-methyl-_N_-(phenylethynyl)benzenesulfonamide (1q)

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **1q**; white solid; mp: 94 – 96 ºC; yield: 88%; 570.0 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, J = 8.3 Hz, 2H), 7.42 – 7.37 (m, 4H), 7.34 – 7.30 (m, 3H), 3.75 (t, J = 7.2 Hz, 2H), 2.79 (t, J = 7.2 Hz, 2H), 2.48 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 145.5, 133.9, 131.6, 130.1, 128.39, 128.38, 127.8, 122.0, 116.4, 80.6, 71.9, 47.3, 21.7, 17.5; HRMS (APCI–orbitrap) m/z: calcd. for $C_{18}H_{17}N_2O_2S$ $[M+H]^+$ 325,1005, found 325.1004.

_N_-(2-cyanophenyl)-_N_-ethynyl-4-methylbenzenesulfonamide (1r) [11c]

Following the general procedure 5; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **1r**; white solid; yield: 77%; 455.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 2H), 7.69 (d, J = 7.7 Hz, 1H), 7.64 (t, J = 7.9 Hz, 1H), 7.51 (t, J = 7.7 Hz, 1H), 7.43 – 7.35 (m, 3H), 2.90 (s, 1H), 2.48 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 146.0, 139.8, 134.2, 133.7, 132.7, 130.0, 129.6, 129.5, 128.7, 115.1, 113.0, 75.0, 60.0, 21.8.

3-(phenylethynyl)oxazolidin-2-one (2a) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **2a**; white solid; mp: 84 – 85 ºC; yield: 62%; 260.4 mg; ^{1}H NMR

(600 MHz, $CDCl_3$) δ 7.47 – 7.41 (m, 2H), 7.32 – 7.28 (m, 3H), 4.48 (t, *J* = 8.0 Hz, 2H), 3.98 (t, *J* = 8.0 Hz, 2H); ^{13}C {^1H} NMR (150 MHz, $CDCl_3$) δ 155.9, 131.6, 128.3, 128.2, 122.2, 79.0, 71.2, 63.1, 47.1; mass spectrum (ESI): m/e (% relative intensity) 210.1 (100) $[M+Na]^+$.

3-((4-ethylphenyl)ethynyl)oxazolidin-2-one (2b)[11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **2b**; white solid; mp: 90 – 92 ºC; yield: 52%; 371.3 mg; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 2H), 7.17 – 7.12 (m, 2H), 4.50 – 4.45 (m, 2H), 4.03 – 3.97 (m, 2H), 2.65 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.6 Hz, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 155.9, 144.7, 131.7, 127.9, 119.2, 78.3, 71.2, 63.0, 47.1, 28.8, 15.3. mass spectrum (ESI): m/e (% relative intensity) 238.1 (100) $[M+Na]^+$.

3-((4-methoxyphenyl)ethynyl)oxazolidin-2-one (2c) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **2c**; white solid; mp: 99 – 101 ºC; yield: 51%; 367.2 mg; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.5 Hz, 2H), δ 6.84 (d, *J* = 8.5 Hz, 2H), 4.48 (t, *J* = 8.0 Hz, 2H), 4.00 (d, *J* = 8.0 Hz, 2H), 3.82 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 159.7, 156.0, 133.5, 114.0, 113.9, 77.6, 70.9, 63.0, 55.3, 47.1; mass spectrum (ESI): m/e (% relative intensity) 240.1 (100) $[M+Na]^+$.

3-((4-(trifluoromethyl)phenyl)ethynyl)oxazolidin-2-one (2d) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **2d**; white solid; mp: 96 – 97 ºC; yield: 45%; 375.3 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 8.3 Hz, 2H), 4.52 (t, *J* = 8.0 Hz, 2H), 4.05 (t, *J* = 8.0 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 155.6, 131.3, 129.7 (q, *J* = 32.5 Hz), 126.18 (q, *J* = 2.5 Hz), 125.2 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 271.3 Hz), 81.3, 70.5, 63.1, 46.9; ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.82 (s, 3F); mass spectrum (ESI): m/e (% relative intensity) 278.0 (100) $[M+Na]^+$.

3-((4-chlorophenyl)ethynyl)oxazolidin-2-one (2e) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **2e**; white solid; mp: 131 – 132 ºC; yield: 48%; 351.4 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.6 Hz, 2H), 7.28 (d, *J* = 8.6 Hz, 2H), 4.50 (t, *J* = 8.0 Hz, 2H), 4.01 (t, *J* = 8.0 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 155.8, 134.2, 132.7, 128.6, 120.7, 79.8, 70.3, 63.1, 47.0; mass spectrum (ESI): m/e (% relative intensity) 243.9 (100) $[M+Na]^+$.

3-((3-chlorophenyl)ethynyl)oxazolidin-2-one (2f) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **2f**; white solid; mp: 130 – 131 ºC; yield: 68%; 331.8 mg; ^{1}H NMR

(500 MHz, $CDCl_3$) δ 7.44 – 7.42 (m, 1H), 7.34 – 7.21 (m, 3H), 4.51 (t, *J* = 8.0 Hz, 2H), 4.02 (t, *J* = 8.0 Hz, 2H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 155.6, 134.1, 131.2, 129.5, 128.4, 123.9, 80.1, 70.2, 63.1, 46.9; mass spectrum (ESI): m/e (% relative intensity) 244.0 (100) $[M+Na]^+$.

3-((2-chlorophenyl)ethynyl)oxazolidin-2-one (2g) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **2g**; white solid; mp: 119 – 120 ºC; yield: 75%; 366.0 mg; ^1H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.02 – 6.97 (m, 2H), 4.49 (t, *J* = 7.5 Hz, 2H), 4.00 (t, *J* = 7.5 Hz, 2H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ163.3, 161.7, 155.9, 133.7, 133.7, 118.19, 118.17, 115.7, 115.5, 78.6, 70.2, 63.1, 63.1, 47.0; mass spectrum (ESI): m/e (% relative intensity) 244.0 (100) $[M+Na]^+$.

(*S*)-4-isopropyl-3-(phenylethynyl)oxazolidin-2-one (2h) [11f]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2h**; white solid; mp: 83 – 84 ºC; yield: 49%; 370.4 mg;^1H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.42 (m, 2H), 7.31 – 7.29 (m, 3H), 4.43 (t, *J* = 8.5, 1H), 4.42 – 4.19 (m, 1H), 4.07 – 4.03 (m, 1H), 2.33 – 2.26 (m, 1H), 1.04 (d, *J* = 3.5 Hz, 3H), 1.03 (d, *J* = 3.5 Hz, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 156.0, 131.5, 128.3, 128.1, 122.4, 72.3, 64.9, 62.1, 29.3, 17.3, 15.3; mass spectrum (ESI): m/e (% relative intensity) 252.0 (100) $[M + Na]^+$.

***N*-((4-ethylphenyl)ethynyl)-*N*-phenylmethanesulfonamide (2i)** [11e]

Following the general procedure 1; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2i**; white solid; mp: 55 – 56 ºC, yield: 71%; 457.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1Hz, 2H), 7.48 – 7.35 (m, 2H), 7.42 – 7.35 (m, 3H), 7.17 (d, *J* = 7.9, 2H), 3.17 (s, 3H), 2.66 (q, *J* = 7.6 Hz, 2H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 144.8, 138.8, 131.8, 129.5, 128.3, 127.9, 125.5, 119.3, 81.3, 71.1, 36.7, 28.8, 15.4; mass spectrum (ESI): m/e (% relative intensity) 322.1 (100) $[M+Na]^+$.

***N*-((4-methoxyphenyl)ethynyl)-*N*-phenylmethanesulfonamide (2j)** [11e]

Following the general procedure 1; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2j**; white solid; mp: 96 – 97 ºC; yield: 66%; 427.7 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.9 Hz, 2H), 7.48 – 7.33 (m, 5H), 6.86 (d, *J* = 8.7Hz, 2H), 3.82 (s, 3H), 3.16 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.8, 138.9, 133.6, 129.4, 128.2, 125.5, 114.2, 114.0, 80.6, 70.7, 55.3, 42.7, 36.7; mass spectrum (ESI): m/e (% relative intensity) 324.1 (100) $[M+Na]^+$.

***N*-((4-nitrophenyl)ethynyl)-*N*-phenylmethanesulfonamide (2k)**

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2k**; white solid; mp: 114 – 115 ºC; yield: 57%; 460.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.9 Hz, 2H), 7.60 – 7.47 (m, 6H), 7.43 (t, *J* = 7.9 Hz, 1H), 3.19

(s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 146.6, 138.0, 131.3, 129.8, 129.7, 128.9, 125.7, 123.7, 87.5, 70.2, 37.6.; HRMS (APCI–orbitrap) m/z: calcd. for $C_{15}H_{13}N_2O_4S$ $[M+H]^+$ 317.0591, found 317.0586.

***N*-phenyl-*N*-((4-(trifluoromethyl)phenyl)ethynyl)methanesulfonamide (2l)**

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2l**; white solid; mp: 114 – 115 ºC; mp: 98 – 99ºC; yield: 69%; 469.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.56 (m, 4H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 3.18 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 138.3, 131.3, 129.67, 129.66 (q, *J* = 32.8 Hz), 128.7, 126.3 (q, *J* = 1.3 Hz), 125.7, 125.3 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 272.1 Hz), 84.5, 74.1, 37.2; ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.79. HRMS (APCI–orbitrap) m/z: calcd. for $C_{16}H_{13}F_3NO_2S$ $[M+H]^+$ 340.0614, found 340.0609.

***N*-((4-chlorophenyl)ethynyl)-*N*-phenylmethanesulfonamide (2m)** [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2m**; white solid; mp: 112 – 114 ºC; yield: 32%; 314.9 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.8 Hz, 2H), 7.49 – 7.43 (m, 2H), 7.42 – 7.35 (m, 3H), 7.34 – 7.28 (m, 2H), 3.17 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 138.5, 134.2, 132.7, 129.6, 128.7, 128.5, 125.6, 120.8, 82.9, 69.9, 37.0. mass spectrum (ESI): m/e (% relative intensity) 328.0 (100) $[M+Na]^+$.

_N_-((4-fluorophenyl)ethynyl)-_N_-phenylmethanesulfonamide (2n) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2n**; white solid; mp: 82 – 83 ºC; yield: 45%; 288.9 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.56 (m, 2H), 7.49 – 7.42 (m, 4H), 7.41 – 7.36 (m, 1H), 7.05 – 6.99 (m, 2H), 3.17 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 162.5 (d, J = 249.8Hz), 138.6, 133.6 (d, J = 8.4 Hz), 129.5, 128.4, 125.5, 118.3 (d, J = 3.4Hz), 115.6 (d, J = 22.1 Hz), 81.6, 69.9, 36.9; ^{19}F NMR (470 MHz, $CDCl_3$) δ -110.88 (m,1F); mass spectrum (ESI): m/e (% relative intensity) 312.1(100) $[M+Na]^+$.

4-methyl-_N_-phenyl-_N_-(thiophen-3-ylethynyl)benzenesulfonamide (2o) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2o**;white solid; mp: 150 – 151 ºC; yield: 32%; 240.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.60 (m, 2H), 7.41 – 7.38 (m, 1H), 7.36 – 7.23 (m, 8H), 7.07 (d, J = 4.9 Hz, 1H), 2.45 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 144.9, 138.9, 133.0, 130.1, 129.5, 129.1, 128.9, 128.3, 128.2, 126.3, 125.2, 121.4, 82.3, 65.6, 21.7; mass spectrum (ESI): m/e (% relative intensity) 376.1 (100) $(M+Na)^+$.

_N_-ethynyl-_N_-phenylmethanesulfonamide (2p)

Following the general procedure 3; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2p**; white solid; yield: 89%; 388.0 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.38 (t, *J* = 7.2 Hz, 1H), 3.13 (s, 3H), 2.97 (s, 1H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 138.0, 129.5, 128.6, 125.6, 75.8, 59.7, 36.7; HRMS(ESI) calcd. for $C_9H_9NO_2S$ $[M+Na]^+$ 218.0247, found 218.0248.

***N*-(hex-1-yn-1-yl)-4-methyl-*N*-phenylbenzenesulfonamide (2q)** [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2q**; corlourless oil; yield: 51%; 334.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.54 (m, 2H), 7.34 – 7.24 (m, 7H), 2.45 (s, 3H), 2.30 (t, *J* = 7.0 Hz, 2H), 1.53 – 1.46 (m, 2H), 1.44 - 1.35 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 144.6, 139.4, 133.0, 129.3, 128.9, 128.2, 127.8, 126.1, 73.8, 70.4, 30.9, 21.9, 21.7, 18.1, 13.6; mass spectrum (ESI): m/e (% relative intensity) 328.2 (100) $[M+H]^+$.

***N*-(3,3-dimethylbut-1-yn-1-yl)-4-methyl-*N*-phenylbenzenesulfonamide (2r)** [11f]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2r**; white solid; mp: 94 – 95 ºC; yield: 43%; 451.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.33 – 7.24 (m, 7H), 2.44 (s, 3H), 1.24 (s, 9H); ^{13}C

{^{1}H} NMR (125 MHz, $CDCl_3$) δ 144.6, 139.5, 132.7, 129.1, 128.8, 128.4, 127.7, 125.9, 78.5, 73.1, 31.0, 27.5, 21.7; mass spectrum (ESI): m/e (% relative intensity) 350.1 (100) $[M+Na]^+$.

_N_-(cyclopropylethynyl)-4-methyl-_N_-phenylbenzenesulfonamide (2s) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2s**; white solid; mp: 103 – 105 ºC; yield: 41%; 410.8 mg; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 2H), 7.33 – 7.30 (m, 1H), 7.30 – 7.26 (m, 4H), 7.25 – 7.22 (m, 2H), 2.44 (s, 3H), 1.37 – 1.31 (m, 1H), 0.83 – 0.78 (m, 2H), 0.69 – 0.65 (m, 2H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ145.3, 140.1, 133.8, 130.0, 129.6, 128.9, 128.6, 126.8, 75.3, 70.0, 22.4, 9.5; mass spectrum (ESI): m/e (% relative intensity) 334.1 (100) $[M+Na]^+$.

_N_-methyl-_N_-(phenylethynyl)methanesulfonamide (2t) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2t**; white solid; mp: 58 – 60 ºC; yield: 82% (380.65 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.39 (m, 2H), 7.33 – 7.28 (m, 3H), 3.30 (s, 3H), 3.13 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 131.5, 128.3, 128.1, 122.3, 83.0, 69.5, 39.3, 36.8; mass spectrum (ESI): m/e (% relative intensity) 232.0 (100) $[M+Na]^+$.

_N_-benzyl-_N_-(phenylethynyl)methanesulfonamide (2u) [11e]

Following the general procedure 2; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1)

to afford the desired product **2u**; white solid; mp: 55 – 56 ºC; yield: 65%; 415.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 – 7.49 (m, 2H), 7.45 – 7.34 (m, 5H), 7.32 – 7.28 (m, 3H), 4.73 (s, 2H), 2.95 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 134.5, 131.4, 129.0, 128.83, 128.77, 128.3, 128.0, 122.5, 82.0, 71.6, 55.9, 39.0; mass spectrum (ESI): m/e (% relative intensity) 308.1 (100) $[M+Na]^+$.

_N_-phenyl-_N_-(phenylethynyl)methanesulfonamide (2v) [11e]

Following the general procedure 1; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2v**; white solid; mp: 67 – 68 ºC; yield: 52%; 458.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 7.49 – 7.44 (m, 4H), 7.41 – 7.36 (m, 1H), 7.34 – 7.30 (m, 3H), 3.17 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 138.7, 131.6, 129.5, 128.34, 128.32, 128.2, 125.6, 122.3, 82.0, 71.0, 36.9; mass spectrum (ESI): m/e (% relative intensity) 294.0 (100) $[M+Na]^+$.

4-methyl-_N_-phenyl-_N_-(phenylethynyl)benzenesulfonamide (2w) [11e]

Following the general procedure 1; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2w**; white solid; mp: 103 – 105 ºC; yield: 55%; 610.5 mg;^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (d, J = 7.8 Hz, 2H), 7.39 – 7.38 (m, 2H), 7.35 – 7.30 (m, 10H), 2.44 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 145.0, 138.9, 132.9, 131.5, 129.5, 129.1, 128.31,

128.28, 128.0, 126.3, 122.6, 83.0, 70.5, 21.8; mass spectrum (ESI): m/e (% relative intensity) 370.0 (100) $[M+Na]^+$.

_N_-(4-methoxyphenyl)-4-methyl-_N_-(phenylethynyl)benzenesulfonamide (2x) [11g]

Following the general procedure 1; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2x**; white solid; yield: 65%; 490.1 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.2 Hz, 2H), 7.39 – 7.34 (m, 2H), 7.31 – 7.26 (m, 5H), 7.18 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 3.80 (s, 3H), 2.44 (s, 3H).; ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.6, 145.0, 133.0, 131.7, 131.5, 129.6, 128.5, 128.4, 128.1, 128.0, 122.8, 114.4, 83.5, 70.0, 55.6, 21.8.

_N_-benzyl-4-methyl-_N_-(phenylethynyl)benzenesulfonamide (2y) [11e]

Following the general procedure 1; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2y**; white solid; mp: 70 – 72 °C; yield: 43%; 495.4 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.79 (m, 2H), 7.35 – 7.30 (m, 7H), 7.26 – 7.23 (m, 5H), 4.59 (s, 2H), 2.46 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 144.6, 134.7, 134.4, 131.1, 129.7, 128.9, 128.5, 128.3, 128.2, 127.8, 127.6, 122.8, 82.7, 71.4, 55.7, 21.7. mass spectrum (ESI): m/e (% relative intensity) 384.0 (100) $[M + Na]^+$.

_N_-((2-cyanophenyl)ethynyl)-_N_-methylmethanesulfonamide (2z) [11e]

Following the general procedure 8; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **2z**; white solid; mp: 54 – 55 ºC; yield: 52%; 491.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 – 7.61(m, 1H), 7.56 – 7.49 (m, 2H), 7.40 – 7.35 (m, 1H), 3.37 (s, 3H), 3.23 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 132.5, 132.4, 131.4, 127.9, 126.8, 117.8, 114.6, 89.5, 66.9, 39.2, 37.4; mass spectrum (ESI): m/e (% relative intensity) 257.0 (100) $[M+Na]^+$.

3-(5-(methylsulfonyl)-3,4-diphenyl-5*H*-pyrido[3,2-b]indol-2-yl)oxazolidin-2-one (3a)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **3a**; white solid; mp: 251 – 253 ºC; yield: 78%; 37.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 7.7 Hz, 1H), 7.99 (d, J = 8.3 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.24 – 7.19 (m, 6H), 7.18 – 7.13 (m, 2H), 7.12 – 7.06 (m, 2H), 4.24 (t, J = 7.9 Hz, 2H), 3.82 (t, J = 7.9 Hz, 2H), 2.59 (s, 3H); ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.9, 147.0, 146.9, 142.5, 141.8, 136.6, 135.3, 134.3, 132.8, 130.5, 130.1, 129.7, 127.9, 127.7, 127.49, 127.46, 126.6, 125.4, 121.3, 117.6, 62.7, 46.8, 40.3; HRMS (APCI–orbitrap) m/z: calcd. for $C_{27}H_{22}N_3O_4S$ $[M+H]^+$ 484.1326, found 484.1320.

3-(3-(4-ethylphenyl)-5-(methylsulfonyl)-4-phenyl-5*H*-pyrido[3,2-b]indol-2-yl)oxazolidin-2-one (3b)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **3b**; white solid; mp: 248 – 250 ºC; yield: 53%; 27.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (brs, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.56 – 7.49 (m, 1H), 7.25 – 7.12 (m, 5H), 7.08 – 6.95 (m, 4H), 4.24 (t, *J* = 7.0 Hz, 2H), 3.80 (t, *J* = 7.9 Hz, 2H), 2.60 (q, *J* = 7.5 Hz, 2H), 2.57 (s, 3H), 1.19 (t, *J* = 7.6 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 157.0, 147.0, 143.5, 142.5, 141.9, 136.7, 130.5, 130.0, 129.6, 127.8, 127.4, 127.1, 125.5, 121.5, 117.6, 110.0, 62.7, 46.7, 40.2, 28.5, 15.3; HRMS (APCI–orbitrap) m/z: calcd. for $C_{29}H_{26}N_3O_4S$ $[M+H]^+$ 512.1639, found 512.1633.

3-(3-(4-methoxyphenyl)-5-(methylsulfonyl)-4-phenyl-5*H*-pyrido[3,2-b]indol-2-yl)oxazolidin-2-one (3c)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **3c**; white solid; mp: 280 – 282 ºC; yield: 45%; 23.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.26 – 7.22 (m, 3H), 7.18 – 7.13 (m, 2H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.74 (d, *J* = 8.4 Hz, 2H), 4.28 (t, *J* = 7.9 Hz, 2H), 3.82 (t, *J* = 7.9 Hz, 2H), 3.78 (s, 3H), 2.58 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 158.8, 156.9, 147.3, 146.7, 142.5, 142.1, 136.7, 134.1, 132.9, 131.2, 130.5, 129.6, 127.9, 127.5, 127.3, 126.6, 125.4, 121.4, 117.6, 113.2, 62.7, 55.1,

46.7, 40.3; HRMS (APCI–orbitrap) m/z: calcd. for $C_{28}H_{24}N_3O_5S$ $[M+H]^+$ 514.1431, found 514.1426.

3-(5-(methylsulfonyl)-4-phenyl-3-(4-(trifluoromethyl)phenyl)-5*H*-pyrido[3,2-b]indol-2-yl)oxazolidin-2-one (3d)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **3d**; white solid; mp: 263 – 265 ºC; yield: 77%; 42.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.47 – 7.44 (m, 2H), 7.26 – 7.21 (m, 5H), 7.15 – 7.10 (m, 2H), 4.33 (t, *J* = 7.8 Hz, 2H), 4.00 (t, *J* = 7.8 Hz, 2H), 2.61 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 156.6, 147.1, 146.6, 142.6, 141.6, 139.4, 136.2, 132.7, 132.6, 130.7, 130.4, 129.9, 129.5 (q, *J* = 32.7 Hz), 128.3, 127.7, 126.3, 125.4, 124.5 (q, *J* = 3.7 Hz), 124.0 (q, *J* = 271.3 Hz), 121.4, 117.6, 62.7, 46.8, 40.7; ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.60; HRMS (APCI–orbitrap) m/z: calcd. for $C_{28}H_{21}F_3N_3O_4S$ $[M+H]^+$ 552.1199, found 552.1191.

3-(3-(4-chlorophenyl)-5-(methylsulfonyl)-4-phenyl-5*H*-pyrido[3,2-b]indol-2-yl)oxazolidin-2-one (3e)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **3e**; white solid; mp: 279 – 281 ºC; yield: 75%; 38.9 mg; ^{1}H NMR

(500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.7 Hz, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.22 (m, 3H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.15 – 7.11 (m, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 4.32 (t, *J* = 7.8 Hz, 2H), 3.94 (t, *J* = 7.9 Hz, 2H), 2.59 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 156.7, 146.9, 146.8, 142.51, 141.8, 136.4, 133.9, 133.6, 133.0, 132.7, 131.5, 130.5, 129.8, 128.1, 127.9, 127.7, 126.4, 125.4, 121.4, 117.6, 62.7, 46.8, 40.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{27}H_{21}ClN_3O_4S$ $[M+H]^+$ 518.0936, found 518.0930.

3-(3-(3-chlorophenyl)-5-(methylsulfonyl)-4-phenyl-5*H*-pyrido[3,2-b]indol-2-yl)oxazolidin-2-one (3f)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **3f**; white solid; mp: 264 – 266 ºC; yield: 70%; 36.3 mg; ^1H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.24(m, 3H), 7.20 – 7.11 (m, 4H), 7.07 – 7.01(m, 2H), 4.37 (q, *J* = 8.6 Hz, 1H), 4.31 (q, *J* = 8.4 Hz, 1H), 4.06 (q, *J* = 8.4 Hz, 1H), 3.90 (q, *J* = 8.3 Hz, 1H), 2.60 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 156.6, 147.0, 146.7, 142.5, 141.7, 137.2, 136.2, 133.3, 132.7, 132.6, 130.5, 130.0, 129.8, 128.9, 128.7, 128.2, 127.7, 127.6, 126.3, 125.4, 121.3, 117.6, 62.7, 46.9, 40.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{27}H_{21}ClN_3O_4S$ $[M+H]^+$ 518.0936, found 518.0929.

3-(3-(2-chlorophenyl)-5-(methylsulfonyl)-4-phenyl-5*H*-pyrido[3,2-b]indol-2-yl)oxazolidin-2-one (3g)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **3g**; white solid; mp: 247 – 249 ºC; yield: 68%; 35.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.7 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.38 (dd, *J* = 6.4, 2.6 Hz, 1H), 7.25 – 7.18 (m, 6H), 7.17 – 7.12 (m, 2H), 4.55 – 4.42 (m, 2H), 4.22 (q, *J* = 8.5 Hz, 1H), 3.90 (td, *J* = 8.2, 3.3 Hz, 1H), 2.61 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 156.3, 147.2, 146.8, 142.4, 141.9, 136.3, 134.19, 134.16, 133.0, 132.5, 131.4, 129.7, 129.3, 128.3, 128.1, 127.3, 126.3, 126.0, 125.3, 121.3, 117.6, 62.8, 46.6, 40.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{27}H_{21}ClN_3O_4S$ $[M+H]^+$ 518.0936, found 518.0928.

4-isopropyl-3-(5-(methylsulfonyl)-3,4-diphenyl-5*H*-pyrido[3,2-b]indol-2-yl)oxazolidin-2-one (3h)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **3h**; white solid; mp: 233 – 235 ºC; yield: 74%; 38.9 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 7.6 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.00 (m,10H), 4.10 – 4.00 (m, 2H), 3.95 – 3.70 (m, 1H), 2.59 (s, 3H), 1.91 – 1.78 (m, 1H), 0.85 (s, 3H), 0.76 (d, *J* = 7.0 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz,

$CDCl_3$) δ 157.8, 146.8, 142.5, 141.8, 136.7, 135.3, 134.6, 132.6, 130.5, 130.2, 129.7, 127.9, 127.8, 127.50, 127.47, 127.45, 126.8, 125.4, 121.5, 117.6, 64.4, 62.5, 40.1, 29.7, 18.3, 15.3; HRMS (APCI–orbitrap) m/z: calcd. for $C_{30}H_{28}N_3O_4S$ $[M+H]^+$ 526.1795, found 526.1788.

_N_-(3-(4-ethylphenyl)-5-(methylsulfonyl)-4-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-phenylmethanesulfonamide (3i)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3i**; white solid; mp: 230 – 232 ºC; yield: 84%; 50.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.6 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.22 – 7.05 (m, 8H), 6.91 – 6.85 (m, 4H), 6.66 (brs, 2H), 3.54 (s, 3H), 2.59 (s, 3H), 2.56 (q, *J* = 7.6 Hz, 2H), 1.20 (t, *J* = 7.6 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.2, 145.5, 143.1, 142.4, 142.2, 139.5, 136.7, 134.8, 132.5, 132.0, 130.6, 130.5, 129.5, 128.4, 128.2, 127.7, 127.29, 127.25, 126.9, 126.7, 125.3, 120.9, 117.7, 40.5, 28.6, 15.9; HRMS (APCI–orbitrap) m/z: calcd. for $C_{33}H_{30}N_3O_4S_2$ $[M+H]^+$ 596.1672, found 596.1664.

_N_-(3-(4-methoxyphenyl)-5-(methylsulfonyl)-4-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-phenylmethanesulfonamide (3j)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3j**; white solid; mp: 273 – 275 ºC; yield: 83%; 49.6 mg; ^{1}H NMR

(500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.6 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.21 – 7.07 (m, 8H), 6.97 – 6.93 (m, 2H), 6.76 – 6.55 (m, 4H), 3.76 (s, 3H), 3.53 (s, 3H), 2.59 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 158.5, 151.3, 145.5, 142.43, 142.35, 139.5, 136.7, 134.6, 132.5, 131.8, 130.5, 129.5, 128.5, 128.2, 127.8, 127.4, 127.3, 127.1, 126.7, 125.2, 120.9, 117.7, 112.9, 55.2, 40.6, 40.4; HRMS (APCI–orbitrap) m/z: calcd. for $C_{32}H_{28}N_3O_5S_2$ $[M+H]^+$ 598.1465, found 598.1456.

_N_-(5-(methylsulfonyl)-3-(4-nitrophenyl)-4-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-phenylmethanesulfonamide (3k)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3k**; white solid; mp: 262 – 264 ºC; yield: 69%; 42.3 mg; ^1H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 7.6 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.67 (t, *J* = 8.4 Hz,1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.23 – 7.05 (m, 8H), 7.03 – 6.90 (m, 4H), 3.53 (s, 3H), 2.65 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 150.0, 146.7, 146.5, 142.6, 142.4, 141.70, 139.3, 135.8, 132.6, 132.2, 131.8, 130.3, 130.1, 128.9, 128.4, 127.7, 127.63, 127.61, 126.1, 125.4, 122.5, 121.1, 117.6, 41.1, 40.4; HRMS (APCI–orbitrap) m/z: calcd. for $C_{31}H_{25}N_4O_6S_2$ $[M+H]^+$ 613.1210, found 613.1202.

_N_-(5-(methylsulfonyl)-4-phenyl-3-(4-(trifluoromethyl)phenyl)-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-phenylmethanesulfonamide (3l)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3l**; white solid; mp: 246 - 248ºC; yield: 85%; 54.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.5 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.23 – 7.04 (m, 9H), 6.91 – 6.85 (m, 3H), 3.54 (s, 3H), 2.63 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.6, 146.2, 142.5, 141.9, 139.3, 139.0, 136.1, 133.2, 132.3, 131.1, 130.3, 129.2(q, *J* = 32.5 Hz), 128.7, 128.2, 127.8, 127.6, 127.5, 126.3, 125.3, 124.3(q, *J* = 4.0 Hz), 124,0 (q, *J* = 271.3 Hz), 121.1, 117.7, 40.8, 40.5; ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.61; HRMS (APCI–orbitrap) m/z: calcd. for $C_{32}H_{24}F_3N_3O_4S_2$ $[M+H]^+$ 636.1233, found 636.1226.

_N_-(3-(4-chlorophenyl)-5-(methylsulfonyl)-4-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-phenylmethanesulfonamide (3m)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3m**; white solid; mp: 270 – 272 ºC; yield: 93%; 56.0 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 7.7 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.23 – 7.02 (m, 10H), 6.98 – 6.93 (m, 2H), 6.71 (brs, 2H), 3.53 (s, 3H), 2.61 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.7, 145.9, 142.5, 142.0, 139.4, 136.3, 133.5, 133.5, 133.1, 132.4, 132.0, 130.4, 129.8, 128.7, 128.1, 128.0, 127.7, 127.54, 127.46, 126.4, 125.3,

121.0, 117.7, 40.8, 40.4; HRMS (APCI–orbitrap) m/z: calcd. for $C_{31}H_{24}ClN_3O_4S_2$ $[M+H]^+$ 602.0970, found 602.0963.

_N_-(3-(4-fluorophenyl)-5-(methylsulfonyl)-4-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-phenylmethanesulfonamide (3n)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **3n**; white solid; mp: 278 - 280ºC; yield: 96%; 56.3 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 8.3 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.21 – 7.05 (m, 8H), 6.98 – 6.94 (m, 2H), 6.82 – 6.69 (m, 3H), 3.54 (s, 3H), 2.61 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.8(d, J = 246.8Hz), 150.9, 145.8, 142.5, 142.2, 139.5, 136.4, 133.8, 132.41, 132.40 (d, J = 8.8 Hz), 130.9(d, J = 3.5 Hz), 130.4, 129.7, 128.7, 128.0, 127.5, 127.4, 126.5, 125.3, 121.0, 117.7, 114.5(d, J = 21.6 Hz), 40.8, 40.4; ^{19}F NMR (470 MHz, $CDCl_3$) δ -114.82 – -114.88 (m); HRMS (APCI–orbitrap) m/z: calcd. for $C_{31}H_{25}FN_3O_4S_2$ $[M+H]^+$ 586.1265, found 586.1256.

4-methyl-_N_-(5-(methylsulfonyl)-4-phenyl-3-(thiophen-3-yl)-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-phenylbenzenesulfonamide (3o)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3o**; white solid; mp: 240 – 242 ºC; yield: 90%; 58.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 7.5 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.75 (d, J = 8.2 Hz, 2H),

7.60 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.24 – 7.17 (m, 3H), 7.14 – 7.04 (m, 6H), 6.85 (d, *J* = 7.7 Hz, 2H), 6.70 (s, 2H), 2.61 (s, 3H), 2.50 (s, 3H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.2, 145.6, 143.3, 142.4, 142.1, 139.5, 137.1, 136.8, 1346, 132.2, 130.8, 130.2, 130.0, 129.5, 129.4, 128.7, 128.5, 128.3, 127.9, 127.4, 127.3, 126.8, 125.8, 125.2, 124.1, 121.0, 117.7, 40.7, 21.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{35}H_{28}N_3O_4S_3$ $[M+H]^+$ 650.1236, found 650.1230.

_N_-(5-(methylsulfonyl)-4-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-phenylmethanesulfonamide (3p)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **3p**; white solid; mp: 206 – 207 ºC; yield: 76%; 37.4 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.6 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 1H), 7.66 (t, *J* = 8.3 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.55 – 7.50 (m, 4H), 7.47 – 7.38 (m, 6H), 6.88 (s, 1H), 3.68 (s, 3H), 2.52 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 153.5, 147.3, 143.6, 142.5, 139.6, 138.8, 130.1, 129.9, 129.8, 129.3, 128.73, 128.71, 128.5, 128.0, 127.4, 125.9, 121.4, 119.4, 117.7, 41.4, 37.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{25}H_{22}N_3O_4S_2$ $[M+H]^+$ 492.1046, found 492.1039.

4-methyl-_N_-(5-(methylsulfonyl)-4-phenyl-3-propyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-phenylbenzenesulfonamide (3q)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **3q**; white solid; mp: 210 – 212 ºC; yield: 72%; 44.9 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.57 – 7.53 (m, 1H), 7.52 – 7.44 (m, 6H), 7.39 – 7.35 (m, 2H), 7.34 – 7.25 (m, 5H), 2.58 (t, *J* = 8.5 Hz 2H), 2.56(s, 3H), 1.17 (h, *J* = 7.2 Hz, 2H), 0.71 (t, *J* = 7.2 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.9, 143.7, 143.4, 142.0, 141.6, 140.2, 136.7, 136.6, 135.1, 132.9, 130.5, 129.5, 128.83, 128.79, 128.6, 128.4, 128.0, 127.8, 127.3, 126.6, 124.8, 120.6, 117.6, 41.6, 31.9, 28.6, 23.1, 21.7, 13.4; HRMS (APCI–orbitrap) m/z: calcd. for $C_{35}H_{34}N_3O_4S_2$ $[M+H]^+$ 624.1985, found 624.1976.

_N_-(3-(tert-butyl)-5-(methylsulfonyl)-4-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-4-methyl-_N_-phenylbenzenesulfonamide (3r)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 6/1 to petroleum ether/ ethyl acetate = 4/1) to afford the desired product **3r**; white solid; mp: 259 – 261 ºC; yield: 43%; 26.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 1H), 7.72 – 7.68 (m, 3H), 7.54 – 7.48 (m, 2H), 7.46 – 7.38 (m, 4H), 7.32 (d, *J* = 6.8 Hz, 1H), 7.29 – 7.20 (m, 7H), 2.45 (s, 3H), 2.28 (s, 3H), 1.24 (s, 9H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.3, 143.7, 143.44, 143.41, 143.3, 141.8, 139.4, 139.3, 137.3, 135.6, 133.8, 132.2, 129.4, 128.9, 128.6, 128.5, 128.5, 127.4, 127.2, 126.6, 126.5,

126.2, 124.9, 120.8, 118.7, 42.1, 38.0, 33.9, 21.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{35}H_{34}N_3O_4S_2$ $[M+H]^+$ 624.1985, found 624.1976.

_N_-(3-cyclopropyl-5-(methylsulfonyl)-4-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-4-methyl-_N_-phenylbenzenesulfonamide (3s)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3s**; white solid; mp: 232 – 234 ºC; yield: 98%; 59.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 7.4 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.84 (d, J = 8.2 Hz, 2H), 7.59 – 7.53 (m, 1H), 7.51 (t, J = 7.3 Hz, 1H), 7.45 – 7.28 (m, 12H), 2.57 (s, 3H), 2.49 (s, 3H), 1.24 – 1.18 (m, 1H), 0.90 – 0.41 (m, 4H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 154.0, 144.4, 144.17, 143.3, 142.5, 140.2, 137.54, 137.49, 132.3, 131.5, 130.3, 129.4, 129.0, 128.8, 128.7, 128.5, 128.1, 127.8, 127.3, 127.1, 125.2, 121.0, 117.9, 40.4, 21.7, 11.8, 10.4; HRMS (APCI–orbitrap) m/z: calcd. for $C_{34}H_{30}N_3O_4S_2$ $[M+H]^+$ 608.1672, found 608.1666.

_N_-methyl-_N_-(5-(methylsulfonyl)-3,4-diphenyl-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (3t)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3t**; white solid; mp: 264 – 266 ºC; yield: 90%; 45.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 7.7 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H),

7.52 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.18 (m, 6H), 7.17 – 7.10 (m, 4H), 3.29 (s, 3H), 2.98 (s, 3H), 2.60 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.0, 146.2, 142.5, 141.9, 136.8, 135.2, 134.7, 132.7, 130.7, 130.5, 129.6, 127.9, 127.6, 127.5, 127.2, 126.5, 125.3, 120.9, 117.7, 40.6, 38.9, 37.8; HRMS (APCI–orbitrap) m/z:calcd. for $C_{26}H_{24}N_3O_4S_2$ $[M+H]^+$ 506.1203, found 506.1199.

N-benzyl-*N*-(5-(methylsulfonyl)-3,4-diphenyl-5*H*-pyrido[3,2-b]indol-2-yl)methanesulfonamide (3u)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3u**; white solid; mp: 233 – 235 ºC; yield: 98%; 57.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 7.6 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.27 – 7.05 (m, 13H), 6.79 (s, 2H), 4.57 (s, 2H), 3.06 (s, 3H), 2.60 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 149.9, 145.8, 142.5, 141.8, 136.8, 135.6, 135.1, 134.9, 132.5, 131.1, 130.6, 129.63, 129.55, 128.4, 127.9, 127.8, 127.3, 127.2, 126.9, 126.5, 125.2, 120.9, 117.7, 54.9, 40.8, 40.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{32}H_{28}N_3O_4S_2$ $[M+H]^+$ 582.1516, found 582.1508.

***N*-(5-(methylsulfonyl)-3,4-diphenyl-5*H*-pyrido[3,2-b]indol-2-yl)-*N*-phenylmethanesulfonamide (3v)**

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1)

to afford the desired product **3v**; white solid; mp: 244 – 246 ºC; yield: 88%; 50.0 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 7.6 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.20 – 7.05 (m, 6H), 6.93 – 6.89 (m, 2H), 6.77 (brs, 2H), 3.53 (s, 3H), 2.61 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.9, 145.6, 142.4, 142.1, 139.5, 136.6, 134.9, 134.8, 132.5, 130.7, 130.5, 129.6, 128.5, 128.2, 127.8, 127.4, 127.3, 126.9, 126.6, 125.2, 121.0, 117.7, 40.7, 40.4; HRMS (APCI–orbitrap) m/z: calcd. for $C_{31}H_{26}N_3O_4S_2$ $[M+H]^+$ 568.1359, found 568.1351.

4-methyl-*N*-(5-(methylsulfonyl)-3,4-diphenyl-5*H*-pyrido[3,2-b]indol-2-yl)-*N*-phenylbenzenesulfonamide (3w)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3w**; white solid; mp: 244 – 246 ºC; yield: 90%; 58.0 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 – 8.08 (m, 1H), 8.01 – 7.97 (m, 1H), 7.78 – 7.31(m, 2H), 7.64 – 7.59 (m, 1H), 7.56 – 7.51 (m, 1H), 7.33 – 7.30 (m, 2H), 7.19 – 7.07 (m, 9H), 7.04-6.00 (m, 2H), 6.85 (brs, 2H), 6.78 – 6.72 (m, 2H), 2.62 (s, 3H), 2.51 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.6, 145.5, 143.3, 142.4, 141.7, 139.5, 137.1, 136.7, 135.2, 135.1, 132.3, 130.8, 130.5, 129.4, 128.7, 128.6, 128.2, 127.8, 127.4, 127.3, 127.1, 126.9, 126.8, 125.2, 121.0, 117.6, 40.7, 21.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{37}H_{30}N_3O_4S_2$ $[M+H]^+$ 644.1672, found 644.1661.

_N_-(4-methoxyphenyl)-4-methyl-_N_-(5-(methylsulfonyl)-3,4-diphenyl-5_H_-pyrido[3,2-b]indol-2-yl)benzenesulfonamide (3x)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3x**; white solid; mp: 274 – 276 ºC; yield: 74%; 49.9 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, J = 7.6 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 7.75 (d, J = 8.0 Hz, 2H), 7.61 (t, J = 7.8 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.33 (d, J = 8.1 Hz, 2H), 7.21 – 7.07 (m, 8H), 7.00 – 6.81 (m, 2H), 6.63 (d, J = 9.0 Hz, 2H), 6.54 (d, J = 9.0 Hz, 2H), 3.71 (s, 3H), 2.61 (s, 3H), 2.52 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 158.7, 151.2, 145.5, 143.2, 142.3, 141.7, 137.1, 136.7, 135.2, 135.1, 132.2, 132.0, 130.9, 130.5, 130.3, 129.5, 129.3, 128.6, 127.7, 127.4, 127.3, 127.0, 126.9, 125.2, 121.0, 117.6, 113.4, 55.3, 40.7, 21.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{38}H_{32}N_3O_5S_2$ $[M+H]^+$ 674.1778, found 674.1768.

_N_-benzyl-4-methyl-_N_-(5-(methylsulfonyl)-3,4-diphenyl-5_H_-pyrido[3,2-b]indol-2-yl)benzenesulfonamide (3y)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3y**; white solid; mp: 233 – 235 ºC; yield: 93%; 61.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, J = 7.6 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 7.67 (d, J = 8.1 Hz, 2H), 7.62 (t, J = 7.8 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.19 – 7.10 (m, 5H),

7.09 – 6.96 (m, 6H), 6.78 (d, *J* = 7.6 Hz, 2H), 6.58 (brs, 2H), 4.54 (s, 2H), 2.62 (s, 3H), 2.51 (s, 3H); ^{13}C NMR {^{1}H} (125 MHz, $CDCl_3$) δ 148.9, 145.6, 143.5, 142.4, 141.2, 137.2, 137.0, 136.2, 135.1, 134.7, 132.4, 131.3, 130.6, 129.8, 129.33, 129.28, 129.0, 128.1, 127.64, 127.60, 127.2, 126.8, 126.61, 126.55, 125.1, 121.0, 117.6, 54.6, 41.1, 21.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{38}H_{32}N_3O_4S_2$ $[M+H]^+$ 658.1829, found 658.1821.

_N_-(3-(2-cyanophenyl)-5-(methylsulfonyl)-4-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-methylmethanesulfonamide (3z)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **3z**; white solid; mp: 266 – 268 °C; yield: 82%; 43.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, *J* = 7.7 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.68 – 7.63 (m, 1H), 7.58 – 7.51 (m, 3H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.31 (ddd, *J* = 8.0, 6.1, 2.7 Hz, 1H), 7.25 – 7.07 (s, 5H), 3.26 (s, 3H), 3.21 (s, 3H), 2.68 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.4, 147.3, 142.5, 142.0, 140.2, 135.9, 133.6, 132.5, 132.2, 131.9, 131.7, 130.1, 128.3, 128.1, 127.5, 126.0, 125.3, 121.1, 118.1, 117.5, 112.9, 41.1, 38.2, 36.9; HRMS (APCI–orbitrap) m/z: calcd. for $C_{27}H_{23}N_4O_4S_2$ $[M+H]^+$ 531,1155, found 531.1147.

_N_-(4-(4-methoxyphenyl)-5-(methylsulfonyl)-3-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-methylmethanesulfonamide (4b)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4b**; white solid; mp: 259 – 261 ºC; yield: 83%; 44.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.2 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.61 (t, *J* = 8.4 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.14 – 7.10 (m, 2H), 7.08 – 7.04 (m, 2H), 6.77 – 6.72 (m, 2H), 3.77 (s, 3H), 3.29 (s, 3H), 2.97 (s, 3H), 2.62 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.1, 151.1, 146.2, 142.5, 142.0, 135.4, 135.0, 133.1, 131.7, 130.7, 129.6, 129.1, 127.6, 127.2, 126.7, 125.3, 120.9, 117.8, 112.9, 55.1, 40.5, 38.8, 37.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{27}H_{26}N_3O_5S_2$ $[M+H]^+$ 536.1308, found 536.1301.

ethyl4-(2-(*N*-methylmethylsulfonamido)-5-(methylsulfonyl)-3-phenyl-5*H*-pyrido[3,2-b]indol -4-yl)benzoate (4c)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4c**; white solid; mp: 212 – 214 ºC; yield: 90%; 52.0 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.6 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 2H), 7.66 – 7.60 (m, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.24 – 7.17 (m, 5H), 7.09 (dd, *J* = 6.3, 2.7 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.28 (s, 3H), 2.96 (s, 3H), 2.61 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 166.3, 151.5, 146.6, 142.6, 141.6, 141.2, 135.0, 134.5, 132.3, 130.7,

130.4, 130.1, 129.7, 128.8, 127.9, 127.7, 126.7, 125.7, 121.2, 117.7, 61.2, 39.9, 39.0, 37.8, 14.4; HRMS (APCI–orbitrap) m/z: calcd. for $C_{29}H_{28}N_3O_6S_2$ $[M+H]^+$ 578.1414, found 578.1406.

_N_-methyl-_N_-(5-(methylsulfonyl)-3-phenyl-4-(4-(trifluoromethyl)phenyl)-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (4d)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4d**; white solid; mp: 224 – 226 ºC; yield: 95%; 54.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 7.7 Hz, 1H), 8.04 (d, J = 8.3 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.47 (d, J = 8.2 Hz, 2H), 7.28 – 7.21 (m, 5H), 7.09 (dd, J = 6.0, 2.6 Hz, 2H), 3.29 (s, 3H), 2.97 (s, 3H), 2.59 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.5, 146.7, 142.5, 140.7, 140.6(q, J = 1.5 Hz), 134.7, 134.5, 132.1, 130.61, 130.57, 130.1, 129.7(q, J = 32.5 Hz), 127.8, 127.6, 126.6, 125.8, 124.4(q, J = 3.7 Hz), 123.9(q, J = 271.3 Hz), 121.1, 117.6, 39.3, 38.8, 37.7; ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.58; HRMS (APCI–orbitrap) m/z: calcd. for $C_{27}H_{23}F_3N_3O_4S_2$ $[M+H]^+$ 574.1077, found 574.1068.

_N_-(4-(4-chlorophenyl)-5-(methylsulfonyl)-3-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-methylmethanesulfonamide (4e)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4e**; white solid; mp: 256 – 258 ºC; yield: 95%; 51.3 mg; ^{1}H NMR

(500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.6 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.64 (t, *J* = 8.4 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.23 (m, 3H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.11 (dd, *J* = 6.4, 2.7 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 3.29 (s, 3H), 2.97 (s, 3H), 2.62 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 151.4, 146.5, 142.5, 141.0, 135.3, 134.9, 134.6, 133.9, 132.4, 131.6, 130.6, 130.0, 127.8, 127.5, 126.6, 125.6, 121.1, 117.7, 39.7, 38.8, 37.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{26}H_{23}ClN_3O_4S_2$ $[M+H]^+$ 540.0813, found 540.0806.

_N_-(4-(4-fluorophenyl)-5-(methylsulfonyl)-3-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-methylmethanesulfonamide (4f)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4f**; white solid; mp: 288 – 290 ºC; yield: 91%; 47.7 mg; ^1H NMR (500 MHz, $CDCl_3$) δ 8.23 – 8.19 (m, 1H), 8.03 – 8,00 (m, 1H), 7.65 – 7.61 (m, 1H), 7.56 – 7.51 (m, 1H), 7.26 – 7.22 (m, 3H), 7.14 – 7.07 (m, 4H), 6.94 – 6.85 (m, 2H), 3.29 (s, 3H), 2.97 (s, 3H), 2.62 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 162.1(d, *J* = 248.4 Hz), 151.3, 146.5, 142.5, 141.2, 135.1, 134.8, 132.8(d, *J* = 3,4 Hz), 132.6, 132.1(d, *J* = 8.1 Hz), 130.6, 129.9, 127.8, 127.4, 126.6, 125.6, 121.0, 117.7, 114.7(d, *J* = 21.7 Hz), 39.9, 38.8, 37.7; ^{19}F NMR (470 MHz, $CDCl_3$) δ -112.95 (tt, *J* = 9.0, 5.5 Hz). HRMS (APCI–orbitrap) m/z: calcd. for $C_{26}H_{23}FN_3O_4S_2$ $[M+H]^+$ 524.1109, found 524.1101.

_N_-methyl-N-(5-(methylsulfonyl)-4-(naphthalen-1-yl)-3-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (4g)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4g**; white solid; mp: 250 – 252 ºC; yield: 95%; 52.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 7.6 Hz, 1H), 7.92 (d, J = 8.3 Hz, 1H), 7.81 – 7.73 (m, 2H), 7.60 (t, J = 7.7 Hz, 1H), 7.53 (t, J = 7.3 Hz, 1H), 7.43 – 7.32 (m, 3H), 7.29 (t, J = 7.6 Hz, 1H), 7.26 – 7.20 (m, 2H), 7.14 (t, J = 7.5 Hz, 1H), 7.01 (t, J = 7.4 Hz, 1H), 6.85 (t, J = 7.6 Hz, 1H), 6.77 (d, J = 7.7 Hz, 1H), 3.32 (s, 3H), 3.02 (s, 3H), 2.28 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.9, 145.4, 142.1, 139.3, 135.5, 135.4, 133.8, 133.1, 132.7, 131.3, 130.5, 130.0, 129.51, 129.46, 128.6, 128.4, 127.3, 127.1, 126.5, 125.9, 125.8, 125.3, 124.9, 124.5, 120.9, 117.4, 41.2, 39.0, 37.8; HRMS (APCI–orbitrap) m/z: calcd. for $C_{30}H_{26}N_3O_4S_2$ $[M+H]^+$ 556.1359, found 556.1351.

_N_-methyl-_N_-(5-(methylsulfonyl)-3-phenyl-4-(thiophen-2-yl)-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (4h)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4h**; white solid; mp: 229 – 231 ºC; yield: 87%; 44.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 7.6 Hz, 1H), 8.01 (d, J = 8.3 Hz, 1H), 7.62 (ddd, J = 8.5, 7.4, 1.3 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.30 – 7.25 (m, 3H), 7.20 – 7.13 (m, 3H), 7.07 (dd, J = 3.0, 1.3

Hz, 1H), 6.87 (dd, *J* = 5.0, 1.3 Hz, 1H), 3.29 (s, 3H), 2.98 (s, 3H), 2.67 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.0, 146.2, 142.5, 137.7, 136.7, 135.4, 134.9, 133.2, 130.3, 129.9, 129.8, 127.7, 127.5, 126.6, 125.7, 125.4, 124.5, 121.0, 117.7, 40.1, 38.9, 37.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{24}H_{22}N_3O_4S_3$ $[M+H]^+$ 512.0767, found 512.0761.

_N_-methyl-_N_-(3-phenyl-4-(pyridin-3-yl)-5-tosyl-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (4i)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1 to petroleum ether/ ethyl acetate = 1/1) to afford the desired product **4i**; white solid; mp: 234 – 236 ºC; yield: 52%; 27.4 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 5.0, 1.6 Hz, 1H), 8.34 (d, *J* = 2.3 Hz, 1H), 8.21 (d, *J* = 8.3 Hz, 1H), 8.05 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.61 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.43 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.26 – 7.22 (m, 3H), 7.13 – 7.07 (m, 5H), 7.01 (d, *J* = 8.2 Hz, 2H), 3.21 (s, 3H), 2.94 (s, 3H), 2.29 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.4, 149.5, 147.9, 147.5, 145.0, 142.9, 138.7, 137.7, 134.7, 134.6, 133.3, 133.2, 132.6, 130.8, 129.9, 129.4, 128.0, 127.7, 127.0, 126.3, 125.7, 122.4, 120.7, 118.7, 38.7, 37.7, 21.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{31}H_{27}N_4O_4S_2$ $[M+H]^+$ 583.1468, found 583.1460.

_N_-methyl-_N_-(4-methyl-3-phenyl-5-tosyl-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (4j)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4j**; white solid; mp: 194 – 196 ºC; yield: 90%; 46.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.3 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.56 – 7.49 (m, 3H), 7.46 – 7.36 (m, 4H), 7.17 (d, *J* = 8.3 Hz, 2H), 6.98 (d, *J* = 8.3 Hz, 2H), 3.10 (s, 3H), 2.96 (s, 3H), 2.54 (s, 3H), 2.25 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.8, 146.8, 144.9, 143.0, 141.6, 136.1, 135.4, 135.0, 132.3, 130.1, 129.3, 129.1, 128.5, 128.1, 128.0, 126.9, 125.9, 120.6, 119.2, 39.0, 37.4, 21.5, 20.9; HRMS(ESI) calcd. for $C_{27}H_{26}N_3O_4S_2$ $[M+H]^+$ 520.1359, found 520.1353.

_N_-methyl-_N_-(5-(methylsulfonyl)-3-phenyl-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (4k)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4k**; white solid; mp: 238 – 240 ºC; yield: 63%; 27.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.70 – 7.64 (m, 3H), 7.56 – 7.49 (m, 3H), 7.47 – 7.43 (m, 1H), 3.40 (s, 3H), 3.10 (s, 3H), 3.03 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 149.5, 142.5, 139.7, 137.2, 133.9, 131.8, 130.0, 129.3, 128.7, 128.3, 125.5, 124.82, 124.75, 121.1, 114.4, 39.7, 39.3, 37.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{20}H_{20}N_3O_4S_2$ $[M+H]^+$ 430.0890, found 430.0882.

N-(3,4-diphenyl-5-tosyl-5H-pyrido[3,2-b]indol-2-yl)-N-methylmethanesulfonamide (4l)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4l**; white solid; mp: 255 – 257 ºC; yield: 97%; 56.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 7.5 Hz, 1H), 7.58 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.20 (m, 3H), 7.19 – 7.15 (m, 1H), 7.14 – 7.06 (m, 8H), 6.99 (d, *J* = 8.2 Hz, 2H), 3.23 (s, 3H), 2.92 (s, 3H), 2.28 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.3, 147.2, 144.5, 142.9, 142.8, 136.6, 135.4, 134.6, 133.6, 132.9, 130.8, 130.2, 129.6, 129.2, 127.6, 127.5, 127.3, 127.24, 127.19, 126.4, 125.5, 120.6, 118.8, 38.7, 37.6, 21.5; HRMS (APCI–orbitrap) m/z: calcd. for $C_{32}H_{28}N_3O_4S_2$ $[M+H]^+$ 582.1516, found 582.1507.

_N_-methyl-_N_-(5-((4-nitrophenyl)sulfonyl)-3,4-diphenyl-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (4m)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4m**; white solid; mp: 277 – 279 ºC; yield: 96%; 54.5mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.3 Hz, 1H), 8.09 – 8.03 (m, 3H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.25 – 7.19 (m, 3H), 7.16 (t, *J* = 6.9 Hz, 1H), 7.12 – 7.01 (m, 6H), 3.21 (s, 3H), 2.93 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.9, 150.2, 147.2, 142.7, 142.3, 141.9, 136.0, 135.0, 134.9, 132.5, 130.7, 130.3, 129.9, 127.9, 127.7, 127.5, 127.42,

127.38, 126.2, 123.8, 121.0, 118.5, 38.8, 37.5; HRMS (APCI–orbitrap) m/z: calcd. for $C_{31}H_{26}N_3O_4S_2$ $[M+H]^+$ 568.1359, found 568.1352.

_N_-methyl-_N_-(8-methyl-5-(methylsulfonyl)-3,4-diphenyl-5_H_-pyrido[3,2-b]indol-2-yl)methane sulfonamide (4n)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4n**; white solid; mp: 242 – 244 ºC; yield: 91%; 47.3 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.42 (d, J = 8.3 Hz, 1H), 7.24 – 7.18 (m, 5H), 7.16 – 7.09 (m, 4H), 3.31 (s, 3H), 2.97 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.0, 146.4, 142.1, 140.6, 136.8, 135.3, 135.3, 134.5, 133.0, 130.9, 130.7, 130.5, 127.8, 127.6, 127.4, 127.2, 126.7, 120.8, 117.4, 40.1, 38.9, 37.7, 21.28. HRMS (APCI–orbitrap) m/z: calcd. for $C_{27}H_{26}N_3O_4S_2$ $[M+H]^+$ 520.1359, found 520.1353.

_N_-(8-bromo-5-(methylsulfonyl)-3,4-diphenyl-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-methylmethane sulfonamide (4o)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4o**; white solid; mp: 232 – 234 ºC; yield: 97%; 56.7 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, J = 1.9 Hz, 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.69 (dd, J = 8.8, 2.0 Hz, 1H), 7.25 – 7.18 (m, 6H), 7.16 – 7.09 (m, 4H), 3.28 (s, 3H), 2.98 (s, 3H), 2.61 (s, 3H); ^{13}C {^{1}H}

NMR (125 MHz, $CDCl_3$) δ 151.3, 144.6, 142.0, 141.1, 136.4, 135.6, 135.0, 133.1, 132.3, 130.6, 128.2, 128.1, 127.6, 127.5, 127.4, 123.7, 119.2, 118.7, 41.1, 38.9, 37.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{26}H_{23}BrN_3O_4S_2$ $[M+H]^+$ 584.0308, found 584.0299.

_N_-(6,7-diphenyl-8-tosyl-8_H_-thieno[3',2':4,5]pyrrolo[3,2-b]pyridin-5-yl)-_N_-methylmethanesulfonamide (4p)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **4p**; white solid; mp: 250 – 252 ºC; yield: 87%; 51.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, J = 5.5 Hz, 1H), 7.25 – 7.05 (m, 11H), 7.05 – 6.99 (m, 2H), 6.96 (d, J = 7.5 Hz, 2H), 3.21 (s, 3H), 2.89 (s, 3H), 2.34 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 149.9, 148.5, 145.3, 143.6, 140.8, 135.5, 135.3, 133.8, 133.2, 132.2, 130.8, 130.5, 129.6, 129.2, 127.7, 127.4, 127.1, 126.9, 126.6, 124.3, 116.6, 38.9, 37.6, 21.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{30}H_{26}N_3O_4S_3$ $[M+H]^+$ 588.1080, found 588.1071.

4-methyl-_N_-phenyl-_N_-(7-phenyl-6-(thiophen-3-yl)-1-tosyl-2,3-dihydro-1_H_-pyrrolo[3,2-b]pyridin-5-yl)benzenesulfonamide (5o)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **5o**; white solid; mp: 225 – 227ºC; yield: 72%; 48.7 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 7.9 Hz, 2H), 7.32 – 7.26 (m, 5H), 7.20 – 7.05 (m, 11H), 6.84 (d,

J = 8.4 Hz, 2H), 6.77 (s, 1H), 4.13 (t, *J* = 7.4 Hz, 2H), 2.59 (t, *J* = 7.5 Hz, 2H), 2.46 (s, 3H), 2.40 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 158.0, 151.4, 144.8, 144.2, 143.2, 139.4, 136.8, 135.9, 135.3, 134.7, 134.5, 131.6, 130.1, 129.8, 129.7, 129.0, 128.6, 128.4, 128.1, 127.6, 127.5, 127.3, 125.8, 124.2, 51.2, 30.8, 21.6, 21.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{37}H_{32}N_3O_4S_3$ $[M+H]^+$ 678.1550, found 678.1538.

N-(6,7-diphenyl-1-tosyl-2,3-dihydro-1*H*-pyrrolo[3,2-b]pyridin-5-yl)-*N*-methylmethanesulfonamide (5t)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **5t**; white solid; mp: 230 – 232 °C; yield: 75%; 40.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.02 (m, 14H), 4.14 (t, *J* = 7.4 Hz, 2H), 2.97 (s, 3H), 2.92 (s, 3H), 2.78 (t, *J* = 7.5 Hz, 2H), 2.40 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 158.4, 151.3, 144.4, 144.2, 135.8, 135.6, 135.23, 135.15, 135.1, 130.6, 130.1, 129.5, 127.6, 127.5, 127.2, 51.3, 38.4, 37.5, 31.3, 21.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{28}H_{28}N_3O_4S_2$ $[M+H]^+$ 534.1516, found 534.1510.

***N*-(6,7-diphenyl-1-tosyl-2,3-dihydro-1*H*-pyrrolo[3,2-b]pyridin-5-yl)-4-methyl-*N*-phenylbenzenesulfonamide (5v)**

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1)

to afford the desired product **5v**; white solid; mp: 247 – 249 ºC; yield: 52%; 31.0 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.16 (m, 4H), 7.14 – 7.04 (m, 9H), 7.03 – 6.98 (m, 2H), 6.86 (d, *J* = 6.8 Hz, 2H), 6.77 (brs, 2H), 4.15 (t, *J* = 7.5 Hz, 2H), 3.23 (s, 3H), 2.79 (t, *J* = 7.5 Hz, 2H), 2.41 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 157.9, 151.2, 144.6, 144.2, 139.6, 135.62, 135.4, 135.3, 135.1, 134.8, 130.6, 130.0, 129.6, 128.5, 127.9, 127.42, 127.41, 127.33, 127.29, 127.25, 127.0, 51.3, 40.0, 31.4, 21.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{33}H_{30}N_3O_4S_2$ $[M+H]^+$ 596.1672, found 596.1665.

_N_-(6,7-diphenyl-1-tosyl-2,3-dihydro-1_H_-pyrrolo[3,2-b]pyridin-5-yl)-4-methyl-_N_-phenylbenzenesulfonamide (5w)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **5w**; white solid; mp: 237 – 239 ºC; yield: 68%; 45.6 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.2 Hz, 2H), 7.31 – 7.23 (m, 4H), 7.21 – 6.97 (m, 13H), 6.92 (brs, 2H), 6.74 – 6.69 (brs, 2H), 4.12 (t, *J* = 7.5 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.43 (s, 3H), 2.37 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 157.9, 151.2, 144.4, 144.2, 143.1, 139.4, 136.8, 135.9, 135.7, 135.3, 135.0, 134.7, 130.8, 130.1, 129.7, 129.0, 128.6, 128.23, 128.18, 127.43, 127.39, 127.35, 127.1, 51.2, 30.8, 21.61, 21.58; HRMS (APCI–orbitrap) m/z: calcd. for $C_{39}H_{34}N_3O_4S_2$ $[M+H]^+$ 672.1985, found 672.1978.

_N_-(6,7-diphenyl-1-tosyl-2,3-dihydro-1_H_-pyrrolo[3,2-b]pyridin-5-yl)-_N_-(4-methoxyphenyl)-4-methylbenzenesulfonamide (5x)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **5x**; white solid; mp: 199 – 201 ºC; yield: 56%; 39.3 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 7.9 Hz, 2H), 7.31 – 7.26 (m, 4H), 7.24 – 7.16 (m, 3H), 7.14 – 7.05 (m, 7H), 6.99 (brs, 2H), 6.60 (d, J = 8.6 Hz, 2H), 6.53 (d, J = 8.9 Hz, 2H), 4.13 (t, J = 7.6 Hz, 2H), 3.71 (s, 3H), 2.60 (t, J = 7.6 Hz, 2H), 2.45 (s, 3H), 2.40 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 158.7, 157.8, 151.5, 144.4, 144.2, 143.0, 136.8, 135.8, 135.7, 135.14, 135.13, 134.7, 131.9, 130.9, 130.1, 129.7, 129.1, 128.5, 127.5, 127.46, 127.44, 127.3, 127.1, 113.4, 55.3, 51.1, 30.8, 21.6, 21.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{40}H_{36}N_3O_5S_2$ $[M+H]^+$ 702.2066, found 702.2057.

_N_-(2-cyanophenyl)-_N_-(5-(methylsulfonyl)-3,4-diphenyl-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (6a)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6a**; white solid; mp: 290 – 292 ºC; yield: 78%; 46.3 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 7.6 Hz, 1H), 7.99 (d, J = 8.3 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.46 (d, J = 7.5 Hz, 1H), 7.23 – 7.09 (m, 6H), 7.07 – 6.98 (m, 4H), 6.76

(d, *J* = 7.9 Hz, 1H), 6.69 (d, *J* = 7.3 Hz, 2H), 3.79 (s, 3H), 2.59 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 149.7, 145.4, 142.6, 142.2, 140.9, 136.3, 134.6, 134.1, 132.9, 132.6, 132.3, 132.2, 130.5, 130.5, 129.7, 127.9, 127.81, 127.77, 127.23, 127.21, 126.4, 125.3, 121.3, 117.6, 116.1, 112.4, 43.0, 40.7; HRMS (APCI–orbitrap) m/z: calcd. for $C_{32}H_{25}N_4O_4S_2$ $[M+H]^+$ 593.1312, found 593.1305.

_N_-(3,4-bis(4-methoxyphenyl)-5-(methylsulfonyl)-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-(2-cyanophenyl)methanesulfonamide (6b)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6b**; white solid; mp:306 – 308 ºC; yield: 57%; 37.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.47 (dd, *J* = 6.0, 3.4 Hz, 1H), 7.25 – 7.19 (m, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.86 – 6.81 (m, 1H), 6.69 (d, *J* = 8.7 Hz, 2H), 6.63 – 6.56 (m, 4H), 3.77 (s, 6H), 3.74 (s, 3H), 2.61 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $cdcl_3$) δ 159.0, 158.8, 150.3, 145.3, 142.6, 141.0, 134.1, 133.1, 132.7, 132.5, 132.2, 131.7, 131.6, 129.6, 128.8, 127.8, 127.0, 126.7, 125.4, 121.3, 117.69, 116.2, 113.6, 112.7, 112.4, 55.3, 55.1, 42.9, 40.5; HRMS (APCI–orbitrap) m/z: calcd. for $C_{34}H_{29}N_4O_6S_2$ $[M+H]^+$ 653.1523, found 653.1515.

Diethyl4,4'-(2-(N-(2-cyanophenyl)methylsulfonamido)-5-(methylsulfonyl)-5_H_-pyrido[3,2-b]indole-3,4-diyl)dibenzoate (6c)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6c**; white solid; mp: 251 – 253 ºC; yield: 41%; 30.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 7.5 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.67 (ddd, *J* = 8.5, 7.4, 1.4 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.49 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.24 (td, *J* = 7.6, 1.2 Hz, 1H), 7.20 – 7.10 (m, 3H), 6.82 – 6.74 (m, 3H), 4.37 (q, *J* = 7.3 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 2.63 (s, 3H), 1.41 (t, *J* = 7.2 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 166.1, 165.9, 149.5, 146.1, 142.6, 141.1, 140.6, 140.5, 139.2, 134.3, 132.8, 132.2, 131.6, 131.5, 130.6, 130.30, 130.25, 129.8, 129.5, 129.2, 128.7, 128.1, 126.3, 125.7, 121.5, 117.5, 116.0, 112.2, 61.20, 61.15, 42.9, 40.1, 14.3, 14.2; HRMS (APCI–orbitrap) m/z: calcd. for $C_{38}H_{33}N_4O_8S_2$ $[M+H]^+$ 737.1734, found 737.1724.

_N_-(2-cyanophenyl)-_N_-(5-(methylsulfonyl)-3,4-bis(4-(trifluoromethyl)phenyl)-5_H_-pyrido[3,2-b]indol-2-yl)methanesulfonamide (6d)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6d**; white solid; mp: 291 – 293 ºC; yield: 63%; 45.9 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.7 Hz, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 7.69 (t, *J* = 7.2 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 9.1 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.27 – 7.23 (m, 1H), 7.20 – 7.14 (m, 3H), 6.83 (d, *J* = 7.5 Hz, 2H), 6.78 (d, *J* = 8.2 Hz, 1H),

3.79 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.8, 146.5, 142.6, 140.8, 140.6, 140.0, 138.2, 134.3, 132.8, 132.0, 131.5, 130.9, 130.8, 130.6, 130.5, 130.2(q, *J* = 33.8 Hz), 130.0(q, *J* = 33.8 Hz), 128.1, 126.3, 126.0, 125.1, (q, *J* = 3.8 Hz), 124.5(q, *J* = 33.9 Hz), 123.7(q, *J* = 271.3 Hz), 124.7(q, *J* = 270.6 Hz), 121.6, 117.5, 115.9, 111.9, 43.0, 39.5;^{19}F NMR (470 MHz, $CDCl_3$) δ -62.77, -62.82; HRMS (APCI–orbitrap) m/z: calcd. for $C_{34}H_{23}F_6N_4O_4S_2$ $[M+H]^+$ 729.1059, found 729.1050.

_N_-(3,4-bis(4-chlorophenyl)-5-(methylsulfonyl)-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-(2-cyanopheny l)methanesulfonamide (6e)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6e**; white solid; mp: 309 – 311 ºC; yield: 61%; 40.3 mg; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.38 (d, *J* = 7.6 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.74 (ddd, *J* = 8.6, 7.2, 1.4 Hz, 1H), 7.67 – 7.60 (m, 2H), 7.54 (td, *J* = 7.9, 1.7 Hz, 1H), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.24 – 7.21 (m, 2H), 7.13 – 7.07 (m, 4H), 6.63 (d, *J* = 8.1 Hz, 2H), 3.71 (s, 3H), 3.05 (s, 3H); ^{13}C $\{^1$H$\}$ NMR (125 MHz, DMSO-d_6) δ 149.5, 144.7, 142.4, 141.2, 140.9, 135.5, 134.8, 134.0, 133.4, 132.9, 132.5, 132.3, 132.1, 131.7, 130.44, 130.38, 130.1, 129.1, 128.4, 127.7, 125.6, 125.4, 121.3, 118.2, 116.2, 114.0, 42.0, 41.8; HRMS (APCI–orbitrap) m/z: calcd. for $C_{32}H_{23}Cl_2N_4O_4S_2$ $[M+H]^+$ 661.0532, found 661.0524.

_N_-(3,4-bis(4-fluorophenyl)-5-(methylsulfonyl)-5_H_-pyrido[3,2-b]indol-2-yl)-_N_-(2-cyanopheny l)methanesulfonamide(6f)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6f**; white solid; mp: 296 – 298 ºC; yield: 74%; 46.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.7 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.65 (ddd, *J* = 8.5, 7.3, 1.4 Hz, 1H), 7.57 (td, *J* = 7.6, 0.9 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.29 – 7.24 (m, 2H), 7.06 – 6.98 (m, 2H), 6.92 – 6.83 (m, 3H), 6.77 (t, *J* = 8.7 Hz, 2H), 6.71 – 6.63 (m, 2H), 3.77 (s, 3H), 2.63 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 162.11(d, *J* = 247.0 Hz), 162.09(d, *J* = 247.6 Hz), 150.0, 145.9,142.6, 141.6,140.8, 134.3, 132.7, 132.3(d, *J* = 3.5 Hz), 132.2(d, *J* = 8.2 Hz), 132.13, 132.06(d, *J* = 8.0 Hz), 132.0, 130.5(d, *J* = 3.6 Hz), 130.1, 128.0, 126.4, 125.7, 121.4, 117.6, 116.0, 115.3(d, *J* = 21.6 Hz), 114.5(d, *J* = 21.7 Hz), 112.4, 42.8, 40.2;^{19}F NMR (470 MHz, $CDCl_3$) δ -112.64 (ddd, *J* = 14.0, 9.1, 5.3 Hz), -113.67 (ddd, *J* = 13.9, 8.7, 5.3 Hz); HRMS (APCI–orbitrap) m/z: calcd. for $C_{32}H_{23}F_2N_4O_4S_2$ $[M+H]^+$ 629.1123, found 629.1115.

_N_-(2-cyanophenyl)-_N_-(5-(methylsulfonyl)-3,4-di(thiophen-2-yl)-5_H_-pyrido[3,2-b]indol-2-yl) methanesulfonamide (6h)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6h**; white solid; mp: 287 – 289 ºC; yield: 57%; 34.5 mg; ^{1}H NMR

(500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 7.6 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.58 – 7.47 (m, 2H), 7.34 – 7.27 (m, 2H), 7.17 – 7.10 (m, 1H), 7.08 (t, *J* = 4.0 Hz, 1H), 7.03 (s, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 5.0 Hz, 1H), 6.70 (s, 1H), 6.49 (d, *J* = 4.8 Hz, 1H), 3.78 (s, 3H), 2.66 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 150.1, 145.6, 142.6, 140.9, 138.5, 136.4, 134.4, 134.2, 132.8, 132.7, 132.1, 130.0, 129.7, 129.34, 128.4, 128.0, 126.5, 125.7, 125.6, 125.31, 125.25, 124.4, 121.4, 117.6, 116.2, 112.2, 42.9, 40.0; HRMS (APCI–orbitrap) m/z: calcd. for $C_{28}H_{21}N_4O_4S_4$ $[M+H]^+$ 605.0440, found 605.0429.

_N_-(2-cyanophenyl)-4-nitro-_N_-(5-((4-nitrophenyl)sulfonyl)-3,4-diphenyl-5_H_-pyrido[3,2-b]indol-2-yl)benzenesulfonamide (6m)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6m**; white solid; mp: 292 – 294 ºC; yield: 60%; 48.4 mg; ^1H NMR (500 MHz, $CDCl_3$) δ 8.42 (d, *J* = 8.7 Hz, 2H), 8.16 (d, *J* = 8.3 Hz, 1H), 8.09 (dd, *J* = 12.1, 8.8 Hz, 4H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.46 – 7.40 (m, 3H), 7.29 – 7.24 (m, 1H), 7.23 – 7.15 (m, 2H), 7.12 – 7.04 (m, 3H), 6.99 – 6.87 (m, 4H), 6.76 – 7.66 (m, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 150.4, 150.2, 149.7, 146.3, 145.9, 143.0, 142.4, 142.4, 139.8, 135.5, 134.4, 134.1, 133.9, 132.7, 132.3, 132.2, 130.50, 130.46, 130.2, 128.3, 128.1, 127.9, 127.6, 127.3, 127.1, 127.0, 126.5, 124.0, 123.7, 121.2, 118.3, 115.3, 112.5; HRMS (APCI–orbitrap) m/z: calcd. for $C_{42}H_{27}N_6O_8S_2$ $[M+H]^+$ 807.1326, found 807.1314.

N-(2-cyano-4-methylphenyl)-N-(8-methyl-5-(methylsulfonyl)-3,4-diphenyl-5H-pyrido[3,2-b]indol-2-yl)methanesulfonamide (6n)

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6n**; white solid; mp: 277 – 279 ºC; yield: 72%; 44.7 mg; H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.86 (d, *J* = 8.5 Hz, 1H), 7.42 (d, *J* = 8..0 Hz, 1H), 7.26 (s, 1H), 7.17 – 7.09 (m, 4H), 7.08 – 7.00 (m, 4H), 6.96 (d, *J* = 8.5 Hz, 1H), 6.71 (d, *J* = 7.2 Hz, 2H), 6.61 (d, *J* = 8.4 Hz, 1H), 3.77 (s, 3H), 2.58 (s, 3H), 2.55 (s, 3H), 2.27 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 149.8, 145.6, 142.3, 140.7, 138.33, 138.31, 136.4, 135.4, 134.8, 134.3, 133.4, 132.6, 132.4, 132.1, 131.0, 130.6, 130.5, 127.8, 127.7, 127.2, 126.7, 121.1, 117.3, 116.3, 112.1, 42.8, 40.2, 21.3, 20.6; HRMS (APCI–orbitrap) m/z: calcd. for $C_{34}H_{29}N_4O_4S_2$ $[M+H]^+$ 621.1625, found 621.1619.

***N*-(4-bromo-2-cyanophenyl)-*N*-(8-bromo-5-(methylsulfonyl)-3,4-diphenyl-5*H*-pyrido[3,2-b]indol-2-yl)methanesulfonamide (6o)**

Following the general procedure 9; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 3/1 to petroleum ether/ ethyl acetate = 2/1) to afford the desired product **6o**; white solid; mp: 285 – 287 ºC; yield: 67%; 50.2 mg;^1H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, *J* = 2.0 Hz, 1H), 7.86 (d, *J* = 8.9 Hz, 1H), 7.71 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.58 (d, *J* = 2.3 Hz, 1H), 7.25 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.20 – 7.11 (m, 4H), 7.07 – 7.01 (m,

4H), 6.69 (d, *J* = 7.4 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 1H), 3.78 (s, 3H), 2.60 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 149.5, 143.9, 142.3, 141.2, 139.9, 136.2, 135.9, 135.8, 134.4, 133.7, 133.3, 132.6, 132.5, 130.6, 130.4, 128.1, 128.0, 127.9, 127.5, 127.3, 123.8, 121.4, 119.1, 118.8, 114.7, 113.5, 43.3, 41.4; HRMS (APCI–orbitrap) m/z: calcd. for $C_{32}H_{23}Br_2N_4O4S_2$ $[M+H]^+$ 748.9522, found 748.9511.

***N*-methyl-*N*-(4-methyl-3-phenyl-5*H*-pyrido[3,2-b]indol-2-yl)methanesulfonamide (7)**

Following the general procedure 10; the residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 1/1) to afford the desired product **7**; white solid; mp: 307 – 309 ºC; yield: 79%; 28.9 mg; ^{1}H NMR (400 MHz, DMSO-D_6) δ 11.63 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.53 – 7.42 (m, 3H), 7.41 – 7.32 (m, 3H), 7.24 (t, *J* = 7.4 Hz, 1H), 3.20 (s, 3H), 2.86 (s, 3H), 2.30 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-D_6) δ 146.1, 141.7, 138.2, 137.2, 133.1, 132.7, 130.5, 130.3, 128.4, 128.1, 127.7, 121.7, 120.6, 120.2, 112.5, 38.6, 38.3, 15.5; HRMS (APCI–orbitrap) m/z: calcd. for $C_{20}H_{19}N_3O_2S$ $[M+H]^+$ 366.1271, found 366.1266.

Supporting Information: The Supporting Information is available free of charge on the ACS Publications website. NMR spectra of the products, crystal structure determination and X-ray crystallographic data for **6a.**

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