CJC Chinese Journal of Chemistry 中国化学 An International Journal

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For published articles: https://onlinelibrary.wiley.com/journal/16147065

Concise Report

Cite this paper: *Chin. J. Chem.* **2021**, *39*, 1211—1224. **DOI: 10.1002/cjoc.202000701**

Synthesis of 3-Methylthioindoles *via* Intramolecular Cyclization of 2-Alkynylanilines Mediated by DMSO/DMSO-d_6 and $SOCl_2$

Xuemin Li,[a] Beibei Zhang,[a] Jingran Zhang,[a] Xi Wang,[a] Dongke Zhang,[a] Yunfei Du,*[,a] and Kang Zhao*[,b]

[a] *Tianjin Key Laboratory for Modern Drug Delivery & High-Efficiency, School of Pharmaceutical Science and Technology, Tianjin University, Tianjin 300072, China*
[b] *State Key Laboratory of Microbial Technology, Institute of Microbial Technology, Shandong University, Qingdao, Shandong 266237, China*

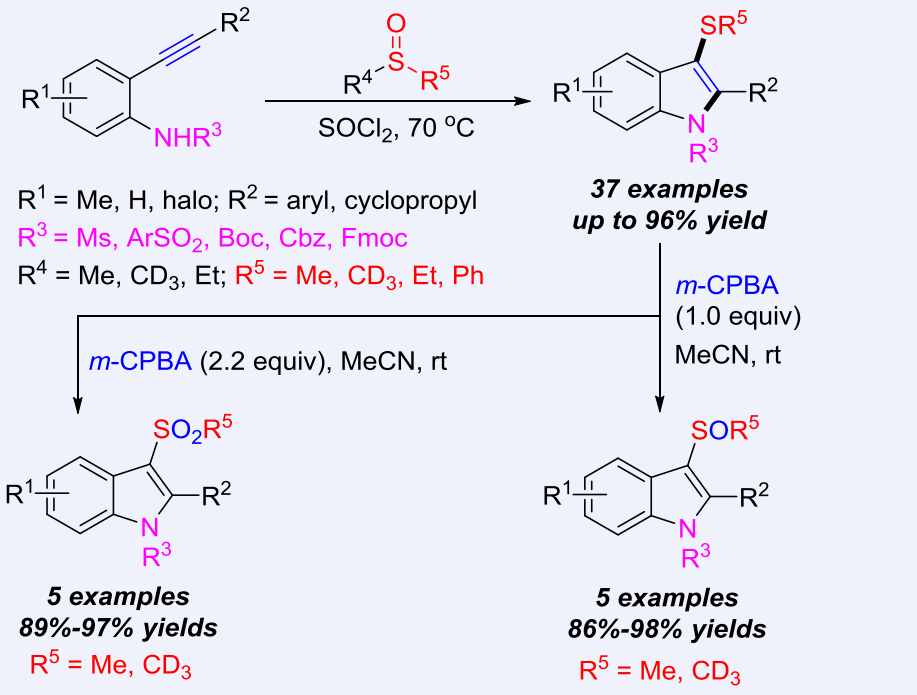
Keywords

DMSO | Electrophilic addition | Cyclization | 3-Methylthioindoles | Synthetic methods

Main observation and conclusion

The intramolecular cyclization of 2-alkynylanilines mediated by DMSO/$SOCl_2$ was found to afford biologically interesting 3-methylthioindoles, which are rarely obtained by the exiting methods. DMSO could also be replaced with its deuterated counterpart, enabling the method applicable to the construction of indole skeleton bearing a SCD_3 moiety at its 3-position.

Comprehensive Graphic Content



✪ *Metal-free reaction* ✪ *Operational simplicity*
✪ *Easily obtainable substrates* ✪ *Functional group tolerance*

*E-mail: duyunfeier@tju.edu.cn; zhaokang@sdu.edu.cn

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Background and Originality Content

Indole compounds represent a class of unique and synthetically useful heterocycles due to their privileged scaffolds,[1] which are omnipresent in a wide range of pharmaceutical agents, biologically active molecules, and naturally-occurring compounds.[2] Especially, the versatile functionalized indoles play a significant role in medicinal chemistry for drug discovery.[3] Specifically, many indoles bearing sulfenyl moieties at the C3-position have been proved to be important pharmaceutical agents.[4-8] For example, AZD1981 (**I**, Figure 1) is currently in development for the treatment of allergic asthma[5] and chronic spontaneous urticarial.[6] MK-886 (**II**, Figure 1) serves as a 5-lipoxygenase-activating protein inhibitor[7] and possesses anti-cancer activity in human colorectal cancer.[4c] The biologically active 3-arythioindole (**III**, Figure 1) can be used as a potent inhibitor tubulin polymerization and shows excellent antitumor activities.[4a,8] As the significance of 3-sulfenylindoles is evident, there has been growing interests in developing efficient synthetic methods for the construction of the privileged heterocyclic skeleton bearing the exclusive substituent.[9]

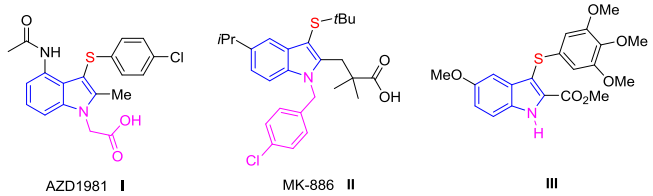
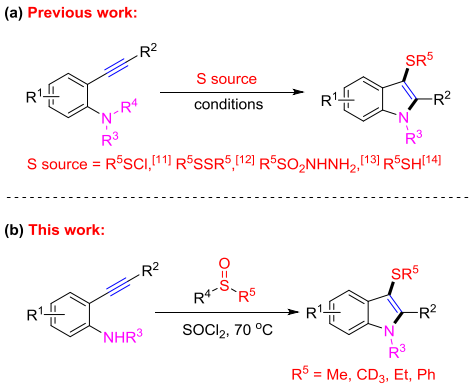


Figure 1 Representative 3-sulfenylindoles with pharmacological activities.

Until now, a variety of efficient methods for the synthesis of 3-sulfenylindoles have been developed.[10-14] Among all these reactions, the most straightforward synthetic strategies involve the direct intramolecular cyclization of 2-alkynylaniline derivatives with aromatic sulfur sources, which include sulfenyl halide,[11] disulfides,[12] sulfonyl hydrazides[13] and thiols[14] (Scheme 1a). For example, Larock and co-workers[11] found a protocol for synthesis of 3-chalcogen-substituted indoles by using the electrophilic ArSCl as sulfur source. In addition, Kuhakarn and co-workers[13a] reported the synthesis of *N*-alkyl-3-sulfenylindoles from the reaction of 2-alkynyl-*N*,*N*-dialkylanilines and sulfonyl hydrazides. All the above methods have been well applied to the synthesis of the corresponding 3-sulfenylindoles. However, the majority of these methods afford 3-arythioindoles and less effort has been devoted to the synthesis of the useful 3-methylthioindoles, which can be converted to the corresponding 3-unsubstitued indoles.[15] It should be noted that the most well-known Gassman indole synthesis realized the synthesis of 3-methylthioindoles from the reaction between anilines and not readily avaliable β-keto sulfide.[16] In these regards, it is still highly desirable to develop facile and efficient approaches to synthesize the biologically interesting 3-methylthioindole compounds.

Scheme 1 Methods for synthesis of 3-sulfenylindoles



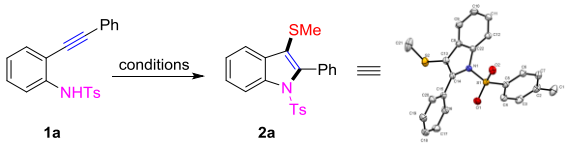
Dimethyl sulfoxide (DMSO), being a commonly used solvent, has also been widely used as an environmentally friendly oxidant in organic synthesis for its advantages such as convenient availability, good solubility and low-toxicity.[17] Furthermore, DMSO has also been proved to be an ideal sulfur source for the introduction of MeS-group into the final products.[18] The most well-known such reaction should be the interrupted Pummerer reaction, in which DMSO reacts with electrophilic reagent to generate the tricoordinate sulfur intermediate, which undergoes further reaction with nucleophile to afford the MeS-containing compounds.[18i] Despite impressive advances have been made on applying DMSO to the synthesis of MeS-containing molecules, to the best of our knowledge, there are few reports utilizing DMSO for assemblage of 3-methylthioindole skeleton.[19]

Herein, we report an efficient and practical protocol for the synthesis of 3-methylthioindoles and deuterated 3-methylthioindoles through intramolecular cyclization of 2-alkynylanilines mediated by DMSO/DMSO-d_6 and $SOCl_2$.

Results and Discussion

Most recently, our group realized the DMSO/$SOCl_2$ mediated synthesis of 3-methylthio-benzo[*b*]furans/benzo[*b*]thiophenes *via* intramolecular cyclization of 2-alkynylanisoles/sulfides.[20] We anticipated that this protocol could also be applicable for the construction of the biologically interesting 3-methylthioindole skeleton. Disappointingly, neither *N*,*N*-dimethyl-2-(phenylethynyl)-aniline nor *N*-methyl-2-(phenylethynyl)aniline afforded the desired 3-methylthioindole product under the standard reaction conditions.[20] In continuation of our work, we were interested to replace the methyl group on the *N*-atom in *N*,*N*'-methyl-2-(phenylenthynyl)aniline or *N*-methyl-2-(phenylethynyl)aniline with some electron-withdrawing substituent. Unfortunately, when *N*,4-dimethyl-*N*-(2-(phenylethynyl)phenyl)benzenesulfonamide was subjected to the standard conditions, no desired 3-methylthioindole product could be obtained. We then initiated our studies by examining the reaction between *N*-Ts-2-(phenylethynyl)-aniline **1a** and DMSO to screen the optimal reaction conditions, with the results being summarized in Table 1. To our delight, the expected 3-methylthioindole **2a** could be isolated in 61% yield after **1a** was treated with DMSO and 1.5 equiv of $SOCl_2$ at room temperature (Table 1, entry 1). The structure of **2a** was undoubtedly confirmed by X-ray crystallographic analysis.[21] Subsequent efforts were devoted to identifying the appropriate activating reagent by switching $SOCl_2$ to TFAA, $(COCl)_2$, AcCl, TsCl and Ac_2O (Table 1, entries 2—6). The results indicated that $SOCl_2$ gave the most satisfactory result (Table 1, entry 1). Specifically, when 3.0 equiv of $SOCl_2$ was used, the yield of product **2a** reached a maximum yield of 66% (Table 1, entry 7). While the dosage of $SOCl_2$ with 3.5 equiv did not lead to a better result, as more byproducts were observed from TLC analysis (Table 1, entry 8). We also investigated the reaction using 3.0 equiv of DMSO as reactant and THF, DCM, DMF, MeCN or toluene as respective solvent. However, the reaction in each case led to a much lower yield of the desired product and it was proved that using DMSO as both solvent and reactant is an optimal choice (Table 1, entries 9—13). Gratifyingly, when the reaction was operated at 70 °C, product **2a** was obtained in a highest yield of 88%, within a much shorter reaction time (Table 1, entries 14—16). Furthermore, it was found that no reaction occurred if the reaction was carried out in the absence of $SOCl_2$ (Table 1, entry 17), which indicated that $SOCl_2$ is indispensable for this reaction. Ultimately, the optimal conditions were concluded to be: 0.5 mmol of substrate with 1.5 mmol of $SOCl_2$

Table 1 Optimization of reaction conditions[a]



1a 2a

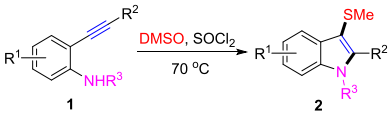
Entry	Additive/equiv	Solvent	Temp./°C	Time/h	Yield[b]/%
1	$SOCl_2$ (1.5)	DMSO	rt	24	61
2	TFAA (1.5)	DMSO	rt	24	0
3	$(COCl)_2$ (1.5)	DMSO	rt	24	56
4	AcCl (1.5)	DMSO	rt	24	33
5	TsCl (1.5)	DMSO	rt	24	20
6	Ac_2O (1.5)	DMSO	rt	24	0
7	$SOCl_2$ (3.0)	DMSO	rt	24	73
8	$SOCl_2$ (3.5)	DMSO	rt	24	63
9[c]	$SOCl_2$ (3.0)	MeCN	rt	6	32
10[c]	$SOCl_2$ (3.0)	THF	rt	12	43
11[c]	$SOCl_2$ (3.0)	DMF	rt	6	37
12[c]	$SOCl_2$ (3.0)	toluene	rt	6	54
13[c]	$SOCl_2$ (3.0)	DCM	rt	6	49
14	$SOCl_2$ (3.0)	DMSO	50	4	80
15	$SOCl_2$(3.0)	DMSO	70	0.08	88
16	$SOCl_2$ (3.0)	DMSO	90	1	85
17	–	DMSO	70	24	0

[a] All the reaction carried out with substrate **1a** (0.5 mmol) in solvent (1 mL). [b] Isolated yield. [c] 3.0 equiv of DMSO was used.

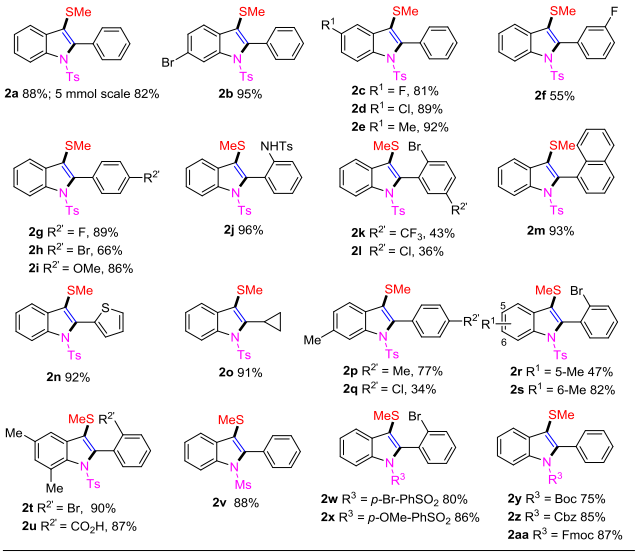
in DMSO (1.0 mL) at 70 °C (Table 1, entry 15).

We next explored the scope and limitation of the method by subjecting a series of 2-alkynylanilines to the optimal conditions, and the results were summarized in Scheme 2. First, we evaluated the effect of different R^1 substituent of the aniline moiety, and the results showed that substrates with F, Cl, Br or Me substituent were all readily converted to the corresponding 3-methylthioindoles in good to excellent yield (Scheme 2, **2b**—**2e**). Next, the alkyne motif R^2 in the substrate was also studied. To our delight, substrates with phenyl ring bearing various substituents (R^2), including electron-withdrawing groups (F, Br), electron-donating groups (OMe, NHTs), all reacted smoothly to afford 3-methylthioindoles derivatives in moderate to excellent yield (Scheme 2, **2f**—**2j**). Furthermore, when substrates with phenyl rings (R^2) bearing two electron-withdrawing groups were applied, the corresponding products **2k** and **2l** were obtained in relatively lower yields due to the formation of some unidentified byproducts (Scheme 2, **2k**—**2l**). Interestingly, when the R^2 substituent of 2-alkynylaniline was 1-naphthyl, 2-thienyl or cyclopropyl group, we were pleased to find that the corresponding 3-methylthioindole was obtained in excellent yield, in each case (Scheme 2, **2m**—**2o**). Meanwhile, substrates bearing both R^1 and R^2 groups also afforded the desired products in 34%—96% yields (Scheme 2, **2p**—**2u**). Gratifyingly, under the standard conditions, the substrates containing other electron-withdrawing R^3 groups including Ms, *p*-OMe-phenylsulfonyl, *p*-Br-phenylsulfonyl, Boc, Cbz, and Fmoc substituent were also converted to the corresponding *N*-substituted indoles in satisfactory yields ranging from 75%—88% (Scheme 2, **2v**—**2aa**). To our disappointment, for the substrates with R^2 being H, TMS, or *n*-butyl group, the reaction delivered no desired product in each case (not shown).[22] Finally, gram scale synthesis of 3-methylthioindoles turned out to be viable. When 5

Scheme 2 Substrate scope studies for synthesis of 3-methylthioindles **2**[a,b]



1 2

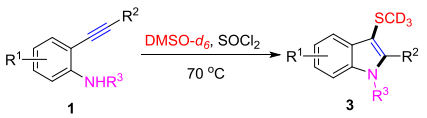


[a] Reaction conditions: **1** (0.5 mmol), $SOCl_2$ (3 equiv), DMSO (1 mL) stirred at 70 °C for 5 min. [b] Isolated yield.

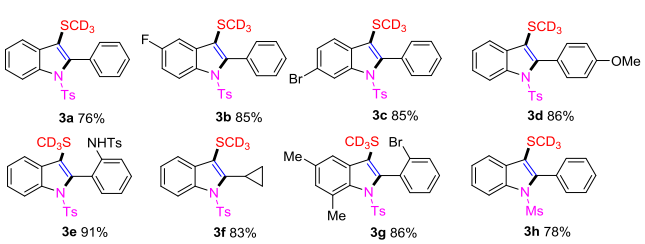
mmol of **1a** was subjected to the standard conditions, the corresponding product **2a** was obtained in a yield of 82% (Scheme 2, **2a**).

DMSO-d_6 is commonly used as a chemical reagent for NMR analysis. Literature survey indicated there are few reports concerning the application of DMSO-d_6 in the installation of the SCD_3 moiety in organic synthesis.[18c,23] Bearing this in mind, we proceeded to investigate whether the method could be applied to the synthesis of deuterated 3-methylthioindoles by replacing DMSO with DMSO-d_6. As shown in Scheme 3, the reaction of 2-alkynylanilines **1** (0.5 mmol) with 3.0 equiv of $SOCl_2$ in 0.5 mL of DMSO-d_6 conveniently afforded the desired deuterated 3-methylthioindoles **3** in good to excellent yield.

Scheme 3 Substrate scope studies for synthesis of deuterated 3-methylthioindles **3**[a,b]



1 3

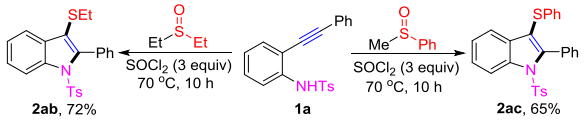


[a] Reaction conditions: **1** (0.5 mmol), $SOCl_2$ (3 equiv), DMSO-d_6 (0.5 mL) stirred at 70 °C for 5 min. [b] Isolated yield.

To further investigate the scope of this transformation, the reaction of substrate **1a** with other sulfoxide reagent was carried out. When diethyl sulfoxide and phenyl methyl sulfoxide were

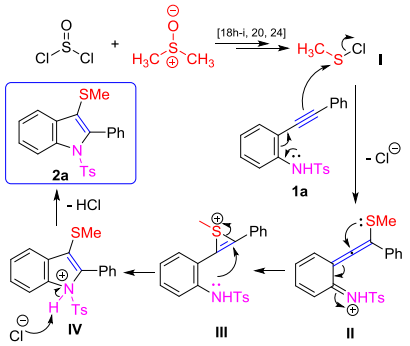
used as sulfur reagent to replace DMSO, gratifyingly, the desired products 3-ethylthioindole **2ab** and 3-phenylthioindole **2ac** was obtained in moderate yield, respectively (Scheme 4).

Scheme 4 Further investigation on different sulfoxides



On the basis of the above experimental results as well as the previous reports,[18h-i,20,24-25] a plausible mechanism is proposed (Scheme 5). Initially, DMSO reacts with $SOCl_2$ to give the reactive electrophilic methionyl chloride **I**, which reacted electrophilically with nucleophilic 2-alkynylaniline **1a** to give the key allene intermediate **II**. Next, intramolecular cyclization occurred in allene **II** to generate a three-membered cyclic sulfonium cation **III**.[25] Subsequently, sulfonium cation **III** undergoes a *5-exo-trig* cyclization to generate the five-membered intermediate **IV**, which is converted to the title product **2a** *via* elimination of a proton.

Scheme 5 Possible reaction mechanism



Sulfoxide and sulfone moieties are interesting functional groups[26] found in many important pharmaceutical agents.[27] For instance, **L-737**, **126** exhibits anti-HIV activity by selectively inhibiting non-nucleoside reverse transcriptase.[27b,c] To further demonstrate the practicality and applicability of this method, some obtained 3-methylthioindoles were further converted to the corresponding sulfoxide and sulfone compounds. Following the literature procedure,[28] the reaction of compounds **2 or 3** with 1.0 equiv of *m*-CPBA delivered sulfoxides **4** in excellent yields (Table 2). Alternatively, when increasing the amount of the oxidant to 2.2 equiv, the reaction gave the corresponding sulfones **5/5'** in good yield (Table 2).

Conclusions

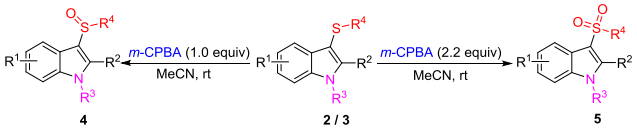
In summary, we have developed a $SOCl_2$/DMSO-mediated synthesis of the biologically interesting 3-methylthioindole compounds *via* intramolecular cyclization of 2-alkynylanilines. Furthermore, this protocol can be applied to the synthesis of the deuterated 3-methylthioindoles by replacing DMSO with DMSO-d_6. Other than the metal-free advantage, the current method also possesses striking desirable features such as the readily availability of the substrates, mild reaction conditions, and remarkably simple workup procedure. Further investigation on the reaction mechanism as well as the application is still in progress in our lab.

Experimental

General information

^{1}H and ^{13}C NMR spectra were recorded on a 400 or 600 MHz spectrometer at 25 °C. Chemical shifts values are relative to the TMS (δ 0.00) internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet). The coupling constants *J* are reported in Hertz (Hz). High resolution mass spectrometry (HRMS) was obtained on a Q-TOF micro spectrometer. Melting points were determined by a Micro melting point apparatus. TLC plates were visualized by exposure to ultraviolet light. Reagents and solvents were purchased as reagent grade and were used without further purification. All reactions were performed in standard glassware, heated at 70 °C for 3 h before use. Flash column chromatography was performed over silica gel (200—300 mesh) using a mixture of ethyl acetate (EtOAc) and petroleum ether (PE).

Table 2 Oxidation of 3-methylthioindoles and deuterated 3-methylthioindles[a]



Entry	Substrate	R^1	R^2	R^3	R^4	**4**/Yield[b] (%)	**5**/Yield[b] (%)
1	**2a**	H	Ph	Ts	Me	**4a**/97	**5a**/96
2	**2d**	5-Cl	Ph	Ts	Me	**4d**/98	**5d**/97
3	**2l**	H	*p*-FC_6H_4	Ts	Me	**4l**/96	**5l**/97
4	**2u**	H	Ph	Ms	Me	**4u**/90	**5u**/94
5	**3f**	H	cyclopropyl	Ts	CD_3	**4f'**/86	**5f'**/89

[a] Reaction conditions: **2/3** (0.5 mmol), *m*-CPBA, MeCN (2.0 mL) stirred at 25 °C for 10 min. [b] Isolated yield.

General procedure A for synthesis of substrates 1 (1a—1e, 1o, 1v, 1y—aa)[29]

To a solution of starting material 2-iodoanilines (10.0 mmol) in Et_3N (50 mL) was added $PdCl_2(PPh_3)_2$ (0.2 mmol) at r.t. The mixture was stirred for 15 min and then CuI (0.6 mmol), terminal alkynes (13.0 mmol) was added. The reaction mixture was stirred at r.t. until TLC indicated the total consumption of the 2-iodoanilines (~2 to 12 h). After completion, inorganic precipitate was filtered through a Celite pad. The filtrate was concentrated *in vacuo*. H_2O (50 mL) was added to the reaction mixture and extracted with EtOAc (30 mL × 3). The combined organic layer was washed with brine, dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography, using a mixture of PE and EtOAc as eluent, to give the desired intermediate.

The obtained intermediate (10 mmol) prepared above was dissolved in dry DCM (30 mL) and the solution was cooled to 0 °C. Pyridine (20 mmol) and R^3Cl (13 mmol) were then added. The reaction mixture was warmed to room temperature and then stirred at this temperature until TLC analysis showed a complete consumption of the starting material (~2 to 12 h). Aq. HCl (3 mol/L, 50 mL) was added and the organic layer was washed with water (50 mL × 3). The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The organic phase was combined, washed with brine, dried with anhydrous Na_2SO_4, concentrated *in vacuo* to give compound **1** as a crude product, which was then purified by flash column chromatography with PE and EtOAc as eluent.

General procedure B for synthesis of substrates 1 (1f—1n, 1p—1u, 1w—1x)[29]

To a solution of starting material 2-iodoanilines (10.0 mmol) in Et_3N (50 mL) was added $PdCl_2(PPh_3)_2$ (0.2 mmol) at r.t. The mix-

ture was stirred for 15 min and then CuI (0.6 mmol) and trimethylsilylacetylene (13.0 mmol) was added, the reaction mixture was stirred at room temperature until TLC indicated the total consumption of 2-iodoanilines. After completion, inorganic precipitate was filtered through a Celite pad. The filtrate was concentrated *in vacuo*. H_2O (50 mL) was added to the reaction mixture, which was then extracted with EtOAc (30 mL × 3). The combined organic layer was washed with brine, dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography, using a mixture of PE and EtOAc as eluent, to give the desired TMS-ethynylaniline.

TMS-ethynylaniline (10 mmol) was dissolved in MeOH (30 mL) followed by addition of anhydrous K_2CO_3 (15 mmol) and the reaction mixture was stirred at r.t. Upon completion of the reaction (monitored by TLC), MeOH was removed *in vacuo*. The residue was admixed with EtOAc (30 mL) and the resultant solution was washed with water (50 mL × 3). The organic layer was concentrated *in vacuo*. The resultant product substituted 2-ethynylaniline obtained in quantitative yield was used in the next step without any further purification.

To a solution of substituted iodobenzene (7.7 mmol) in Et_3N (35 mL) was added $PdCl_2(PPh_3)_2$ (0.154 mmol) at rt. The mixture was stirred for 15 min and then CuI (0.462 mmol) and substituted 2-ethynylanilines (10 mmol) was added, and the reaction mixture was stirred at room temperature until TLC indicated the total consumption of iodobenzene. After completion, inorganic precipitate was filtered through a Celite pad. The filtrate was concentrated *in vacuo*. H_2O (50 mL) was added to the reaction mixture and extracted with EtOAc (30 mL × 3). The combined organic layer was washed with brine, dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography, using a mixture of PE and EtOAc as eluent, to give the desired intermediate.

The obtained intermediate (7.7 mmol) prepared above was dissolved in dry DCM (23 mL) and the solution was cooled to 0 °C. Pyridine (15.4 mmol) and R^3Cl (10.01 mmol) were then added. The reaction mixture was warmed to room temperature and then stirred at this temperature until TLC analysis showed a complete consumption of the starting material (~2 to 12 h). Aq. HCl (3 mol/L, 40 mL) was added and the organic layer was washed with water (40 mL × 3). The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). The organic phase was combined, washed with brine, dried with anhydrous Na_2SO_4, concentrated *in vacuo* to give compound **1** as a crude product, which was then purified by flash column chromatography with EtOAc and PE as eluent.

4-Methyl-*N*-(2-(phenylethynyl)phenyl)benzenesulfonamide (**1a**). Following the general procedure, compound **1a** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 95%, a white solid, m.p. 110—102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, J = 8.3 Hz, 2H), 7.62 (d, J = 8.2 Hz, 1H), 7.47 (dd, J = 6.6, 3.0 Hz, 2H), 7.43—7.34 (m, 4H), 7.33—7.26 (m, 1H), 7.22 (s, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.06 (t, J = 7.3 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 144.1, 137.5, 136.1, 132.0, 131.6, 129.7, 129.1, 128.6, 127.3, 124.7, 122.0, 120.4, 114.7, 96.2, 83.7, 21.6. HRMS (ESI) m/z calcd for $C_{21}H_{17}NNaO_2S^+$ [M + Na^+] 370.0872, found 370.0873.

N-(5-Bromo-2-(phenylethynyl)phenyl)-4-methylbenzenesulfonamide (**1b**). Following the general procedure for preparation of substrates, compound **1b** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 89%, a white solid, m.p. 129—130 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.80 (d, J = 1.8 Hz, 1H), 7.70 (d, J = 8.3 Hz, 2H), 7.50—7.43 (m, 2H), 7.43—7.35 (m, 3H), 7.24—7.15 (m, 5H), 2.35 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 144.4, 138.6, 135.9, 132.9, 131.6, 129.8, 129.3, 128.6, 127.7, 127.3, 123.4, 123.0, 121.7, 113.3, 97.3, 82.9, 21.6. HRMS (ESI) m/z calcd for $C_{21}H_{16}{}^{79}BrNNaO_2S^+$ [M + Na^+] 447.9977, found 447.9978.

N-(4-Fluoro-2-(phenylethynyl)phenyl)-4-methylbenzenesulfonamide (**1c**). Following the general procedure for preparation of substrates, compound **1c** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 87%, a white solid, m.p. 107—108 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.61 (t, J = 7.5 Hz, 3H), 7.43 (dd, J = 5.4, 2.6 Hz, 2H), 7.41—7.33 (m, 3H), 7.13 (d, J = 8.1 Hz, 2H), 7.08 (s, 1H), 7.04 (dd, J = 8.5, 2.9 Hz, 1H), 7.01 (td, J = 8.5, 2.9 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 159.5 (d, $^1J_{C\text{-}F}$ = 245.9 Hz), 144.1, 136.0, 133.7, 131.7, 129.6, 129.4, 128.6, 127.3, 123.7 (d, $^3J_{C\text{-}F}$ = 8.7 Hz), 121.6, 118.3 (d, $^2J_{C\text{-}F}$ = 24.3 Hz), 117.3 (d, $^3J_{C\text{-}F}$ = 9.9 Hz), 116.8 (d, $^2J_{C\text{-}F}$ = 22.7 Hz), 116.8, 96.7, 82.9, 21.5. HRMS (ESI) m/z calcd for $C_{21}H_{16}FNNaO_2S^+$ [M + Na^+] 388.0778, found 388.0780.

N-(4-Chloro-2-(phenylethynyl)phenyl)-4-methylbenzenesulfonamide (**1d**). Following the general procedure for preparation of substrates, compound **1d** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 86%, a white solid, m.p. 128—130 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.65 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 8.8 Hz, 1H), 7.48—7.43 (m, 2H), 7.43—7.36 (m, 3H), 7.34 (d, J = 2.3 Hz, 1H), 7.17 (d, J = 8.5 Hz, 3H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 144.3, 136.2, 135.9, 131.7, 131.5, 130.0, 129.7, 129.7, 129.4, 128.6, 127.3, 121.9, 121.6, 116.4, 97.1, 82.6, 21.5. HRMS (ESI) m/z calcd for $C_{21}H_{16}{}^{35}ClNNaO_2S^+$ [M + Na^+] 404.0482 found 404.0483.

4-Methyl-*N*-(4-methyl-2-(phenylethynyl)phenyl)benzenesulfonamide (**1e**). Following the general procedure for preparation of substrates, compound **1e** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 86%, a white solid, m.p. 126—127 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.64 (d, J = 8.3 Hz, 2H), 7.52 (d, J = 8.3 Hz, 1H), 7.46—7.41 (m, 2H), 7.40—7.35 (m, 3H), 7.17 (d, J = 1.4 Hz, 1H), 7.13 (d, J = 8.4 Hz, 2H), 7.09 (dd, J = 9.5, 2.7 Hz, 2H), 2.31 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 143.9, 136.2, 135.0, 134.6, 132.3, 131.6, 130.5, 129.6, 129.0, 128.5, 127.3, 122.2, 121.1, 115.0, 95.6, 84.0, 21.5, 20.6. HRMS (ESI) m/z calcd for $C_{22}H_{19}NNaO_2S^+$ [M + Na^+] 384.1029 found 384.1027.

N-(2-((3-Fluorophenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (**1f**). Following the general procedure for preparation of substrates, compound **1f** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 86%, a white solid, m.p. 101—102 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.66 (d, J = 8.3 Hz, 2H), 7.62 (d, J = 8.3 Hz, 1H), 7.42—7.28 (m, 3H), 7.24—7.25 (m, 1H), 7.20 (s, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.14—7.03 (m, 3H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 162.4 (d, $^1J_{C\text{-}F}$ = 247.5 Hz), 144.1, 137.7, 136.2, 132.2, 130.2 (d, $^3J_{C\text{-}F}$ = 8.6 Hz), 130.0, 129.7, 127.5 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 127.2, 124.7, 123.9 (d, $^3J_{C\text{-}F}$ = 9.7 Hz), 120.8, 118.4 (d, $^2J_{C\text{-}F}$ = 23.0 Hz), 116.4 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 114.4, 94.6 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 84.7, 21.5. HRMS (ESI) m/z calcd for $C_{21}H_{16}FNNaO_2S^+$ [M + Na^+] 388.0778 found 388.0780.

N-(2-((4-Fluorophenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (**1g**). Following the general procedure for preparation of substrates, compound **1g** was purified by silica gel chromategraphy (10% EtOAc/PE). Yield: 86%, a white solid, m.p. 110—112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.3 Hz, 1H), 7.49—7.41 (m, 2H), 7.36 (d, J = 7.7 Hz, 1H), 7.29 (t, J = 7.9 Hz, 1H), 7.24 (s, 1H), 7.16 (d, J = 7.9 Hz, 2H), 7.04—7.09 (m, 3H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 162.9 (d, $^1J_{C\text{-}F}$ = 252.0 Hz), 144.1, 137.5, 136.1, 133.6 (d, $^3J_{C\text{-}F}$ = 8.5 Hz), 132.1, 129.7, 129.6, 127.3, 124.7, 120.5, 118.2 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 115.9 (d, $^2J_{C\text{-}F}$ = 22.2 Hz), 114.6, 95.0, 83.5, 21.5. HRMS (ESI) m/z calcd for $C_{21}H_{16}FNNaO_2S^+$ [M + Na^+] 388.0778 found 388.0783.

N-(2-((4-Bromophenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (**1h**). Following the general procedure for preparation of substrates, compound **1h** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 88%, a white solid, m.p. 117—118 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.66 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 8.3 Hz, 1H), 7.54—7.47 (m, 2H), 7.36 (d, J = 7.7 Hz, 1H), 7.34—7.27 (m, 3H), 7.17 (dd, J = 9.4, 7.4 Hz, 3H), 7.05—7.08 (m, 1H), 2.33 (d, J = 2.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 144.1, 137.6, 136.2, 133.0, 132.1, 131.9, 129.9, 129.6, 127.2, 124.7,

123.4, 121.0, 120.5, 120.5, 114.4, 94.9, 85.0, 21.5. HRMS (ESI) *m*/*z* calcd for $C_{21}H_{16}{}^{79}BrNNaO_2S^+$ [M + Na^+] 447.9977 found 447.9979.

N-(2-((4-Methoxyphenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (**1i**). Following the general procedure for preparation of substrates, compound **1i** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 80%, a white solid, m.p. 93—95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.67 (d, *J* = 8.3 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.44—7.37 (m, 2H), 7.34 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.29—7.26 (m, 0H), 7.22 (s, 1H), 7.17 (d, *J* = 8.3 Hz, 2H), 7.05 (td, *J* = 7.6, 1.0 Hz, 1H), 6.95—6.87 (m, 2H), 3.85 (d, *J* = 2.0 Hz, 3H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ:* 160.2, 144.0, 137.4, 136.1, 133.1, 131.8, 129.6, 129.3, 127.3, 124.6, 120.2, 115.0, 114.2, 114.1, 96.3, 82.5, 77.4, 77.2, 77.0, 76.7, 55.4, 21.6. HRMS (ESI) *m*/*z* calcd for $C_{22}H_{19}NNaO_3S^+$ [M + Na^+] 400.0978 found 400.0979.

N,N'-(Ethyne-1,2-diylbis(2,1-phenylene))bis(4-methylbenzenesulfonamide) (**1j**). Following the general procedure for preparation of substrates, compound **1j** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 80%, a white solid, m.p. 179—182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.69—7.61 (m, 4H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.37—7.29 (m, 4H), 7.19 (d, *J* = 8.0 Hz, 4H), 7.11 (td, *J* = 7.7, 1.1 Hz, 2H), 7.03 (s, 2H), 2.36 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 144.3, 137.7, 136.1, 132.4, 130.4, 129.8, 127.2, 124.9, 121.0, 114.0, 90.2, 76.7, 21.6. HRMS (ESI) *m*/*z* calcd for $C_{28}H_{24}N_2NaO_4S_2^+$ [M + Na^+] 539.1070 found 539.1079.

N-(2-((2-Bromo-5-(trifluoromethyl)phenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (**1k**). Following the general procedure for preparation of substrates, compound **1k** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 60%, a white solid, m.p. 199—120 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.80 (d, *J* = 8.4 Hz, 1H), 7.73 (dd, *J* = 11.6, 4.9 Hz, 4H), 7.68 (d, *J* = 8.3 Hz, 1H), 7.47 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.42 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.36—7.32 (m, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.07 (td, *J* = 7.6, 0.8 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ:* 144.1, 138.7, 136.2, 133.1, 132.1, 130.7, 130.2 (q, $^2J_{C\text{-}F}$ = 33.4 Hz), 129.6, 129.5 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 129.2, 127.4, 126.3 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 125.5, 124.1, 123.3 (q, $^1J_{C\text{-}F}$ = 273.3 Hz), 119.2, 112.6, 93.5, 90.3, 21.5. HRMS (ESI) calcd for $C_{22}H_{15}{}^{79}BrF_3NaNO_2S^+$ [M + Na^+] 517.9831, found 517.9835.

N-(2-((2-Bromo-5-chlorophenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (**1l**). Following the general procedure for preparation of substrates, compound **1l** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 66%, a white solid, m.p. 123—124 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.79—7.70 (m, 3H), 7.67 (d, *J* = 8.3 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.47 (d, *J* = 1.6 Hz, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.32 (t, *J* = 7.9 Hz, 1H), 7.23—7.19 (m, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.05 (t, *J* = 7.6 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ:* 144.0, 138.6, 136.2, 133.4, 133.4, 132.4, 132.0, 130.5, 130.1, 129.6, 127.4, 126.0, 124.1, 123.4, 119.1, 112.7, 93.7, 89.9, 21.5. HRMS (ESI) calcd for $C_{21}H_{15}{}^{79}Br^{35}ClNaNO_2S^+$ [M + Na^+] 483.9567, found 483.9568.

4-Methyl-*N*-(2-(naphthalen-1-ylethynyl)phenyl)benzenesulfonamide (**1m**). Following the general procedure for preparation of substrates, compound **1m** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 90%, a white solid, m.p. 113—114 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.20 (d, *J* = 8.3 Hz, 1H), 7.90 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.71 (d, *J* = 7.0 Hz, 1H), 7.68 (dd, *J* = 8.3, 1.7 Hz, 3H), 7.65—7.60 (m, 1H), 7.57 (dd, *J* = 11.0, 3.9 Hz, 1H), 7.52—7.46 (m, 2H), 7.33 (dd, *J* = 11.5, 4.2 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 3H), 2.28 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 144.0, 137.6, 136.2, 133.2, 132.9, 132.2, 130.8, 129.8, 129.6, 128.6, 127.3, 127.2, 126.7, 125.8, 125.3, 124.6, 120.4, 119.7, 114.8, 94.4, 88.5, 21.5. HRMS (ESI) calcd for $C_{25}H_{19}NNaO_2S^+$ [M + Na^+] 420.1029, found 420.1026.

4-Methyl-*N*-(2-(thiophen-2-ylethynyl)phenyl)benzenesulfonamide (**1n**). Following the general procedure for preparation of substrates, compound **1n** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 93%, a white solid, m.p. 99—100 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.65 (d, *J* = 8.3 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 1H), 7.33—7.36 (m, 2H), 7.32—7.28 (m, 1H), 7.26 (dd, *J* = 3.6, 0.9 Hz, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.10 (s, 1H), 7.04—7.08 (m, 2H), 2.34 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 144.0, 137.5, 136.1, 132.7, 132.0, 129.8, 129.6, 128.3, 127.32, 127.27, 124.8, 121.9, 121.0, 114.7, 89.1, 87.4, 21.5. HRMS (ESI) calcd for $C_{19}H_{15}NNaO_2S_2^+$ [M + Na^+] 376.0436, found 376.0439.

N-(2-(Cyclopropylethynyl)phenyl)-4-methylbenzenesulfonamide (**1o**). Following the general procedure for preparation of substrates, compound **1o** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 88%, a white solid, m.p. 121—122 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.21 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.63—7.58 (m, 1H), 7.38—7.30 (m, 1H), 7.30—7.26 (m, 1H), 7.19 (d, *J* = 8.1 Hz, 2H), 2.35 (s, 3H), 2.28 (s, 3H), 2.19 (tt, *J* = 8.2, 5.9 Hz, 1H), 1.12—1.01 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 143.7, 137.6, 136.1, 131.8, 129.4, 128.6, 127.1, 124.1, 119.5, 114.9, 100.7, 70.2, 21.4, 8.8. HRMS (ESI) calcd for $C_{18}H_{17}NNaO_2S^+$ [M + Na^+] 334.0872, found 334.0874.

4-Methyl-*N*-(5-methyl-2-(*p*-tolylethynyl)phenyl)benzenesulfonamide (**1p**). Following the general procedure for preparation of substrates, compound **1p** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 70%, a white solid, m.p. 128—130 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.66 (d, *J* = 8.3 Hz, 2H), 7.45 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.17 (dd, *J* = 11.8, 8.0 Hz, 5H), 6.86 (d, *J* = 7.8 Hz, 1H), 2.39 (s, 3H), 2.33 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ:* 143.9, 140.1, 139.2, 137.3, 136.2, 131.6, 131.4, 129.6, 129.3, 127.3, 125.6, 121.1, 119.2, 112.0, 95.7, 83.3, 21.8, 21.6, 21.5. HRMS (ESI) calcd for $C_{23}H_{21}NNaO_2S^+$ [M + Na^+] 398.1185, found 398.1187.

N-(2-((4-Chlorophenyl)ethynyl)-5-methylphenyl)-4-methylbenzenesulfonamide (**1q**). Following the general procedure for preparation of substrates, compound **1q** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 70%, a white solid, m.p. 126—124 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.66 (d, *J* = 8.3 Hz, 2H), 7.44 (s, 1H), 7.39—7.31 (m, 4H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.10 (s, 1H), 6.88 (d, *J* = 7.9 Hz, 1H), 2.34 (d, *J* = 4.7 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 144.0, 140.6, 137.4, 136.1, 135.0, 132.7, 131.8, 129.6, 128.9, 127.2, 125.7, 121.3, 120.7, 111.5, 94.2, 85.0, 21.8, 21.6. HRMS (ESI) calcd for $C_{22}H_{18}{}^{35}ClNNaO_2S^+$ [M + Na^+] 418.0639, found 418.0640.

N-(2-((2-Bromophenyl)ethynyl)-5-methylphenyl)-4-methylbenzenesulfonamide (**1r**). Following the general procedure for preparation of substrates, compound **1r** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 77%, a white solid, m.p. 139—140 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.76 (s, 1H), 7.75—7.70 (m, 2H), 7.65 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.51 (s, 1H), 7.48 (d, *J* = 7.7 Hz, 1H), 7.31 (ddd, *J* = 7.6, 2.2, 1.1 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.24—7.19 (m, 1H), 7.15 (d, *J* = 7.8 Hz, 2H), 6.84 (d, *J* = 7.8 Hz, 1H), 2.34 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 143.8, 140.8, 138.3, 136.3, 132.7, 132.4, 131.6, 129.8, 129.6, 127.4, 127.2, 125.4, 125.0, 124.7, 119.6, 110.3, 94.4, 89.0, 21.9, 21.5. HRMS (ESI) calcd for $C_{22}H_{18}{}^{79}BrNNaO_2S^+$ [M + Na^+] 462.0134, found 462.0137.

N-(2-((2-Bromophenyl)ethynyl)-4-methylphenyl)-4-methylbenzenesulfonamide (**1s**). Following the general procedure for preparation of substrates, compound **1s** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 66%, a white solid, m.p. 130—131 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.71 (d, *J* = 8.3 Hz, 2H), 7.67 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.48 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.31 (td, *J* = 7.6, 0.9 Hz, 1H), 7.22 (td, *J* = 7.9, 1.6 Hz, 1H), 7.20 (d, *J* = 1.2 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.10 (dd, *J* = 8.4, 1.6 Hz, 1H), 2.30 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 143.8, 136.2, 136.0, 133.9, 132.9, 132.4, 132.1, 131.0, 129.9, 129.5, 127.4, 127.3, 125.5, 124.6, 119.5, 113.4, 94.5, 88.9, 77.3, 77.1, 76.8, 21.5, 20.6. HRMS (ESI) calcd for $C_{22}H_{18}{}^{79}BrNNaO_2S^+$ [M + Na^+] 462.0134, found 462.0135.

N-(2-((2-Bromophenyl)ethynyl)-4,6-dimethylphenyl)-4-meth-

ylbenzenesulfonamide (**1t**). Following the general procedure for preparation of substrates, compound **1t** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 69%, a white solid, m.p. 123—125 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.60 (d, J = 8.1 Hz, 1H), 7.49 (d, J = 8.3 Hz, 2H), 7.29—7.26 (m, 2H), 7.25 (d, J = 1.1 Hz, 0H), 7.20 (ddd, J = 14.4, 7.7, 1.7 Hz, 2H), 7.11 (s, 1H), 7.05 (s, 1H), 6.88 (d, J = 8.0 Hz, 2H), 6.62 (s, 1H), 2.55 (s, 3H), 2.29 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 143.3, 138.4, 137.0, 136.7, 133.5, 133.0, 132.8, 132.3, 130.3, 129.6, 129.2, 127.6, 126.9, 125.3, 124.9, 120.8, 92.0, 90.0, 21.4, 20.7, 19.5. HRMS (ESI) calcd for $C_{23}H_{20}{}^{79}BrNNaO_2S^+$ [M + Na^+] 476.0290, found 476.0293.

2-((3,5-Dimethyl-2-((4-methylphenyl)sulfonamido)phenyl)-ethynyl)benzoic acid (**1u**). Following the general procedure for preparation of substrates, compound **1u** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 60%, a white solid, m.p. 170—172 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.13 (dd, J = 7.9, 1.0 Hz, 1H), 7.82 (s, 1H), 7.48 (td, J = 7.6, 1.3 Hz, 1H), 7.40 (dd, J = 12.6, 4.7 Hz, 3H), 7.27 (d, J = 0.9 Hz, 1H), 7.09 (s, 1H), 7.02 (s, 1H), 6.82 (d, J = 8.0 Hz, 2H), 2.55 (s, 3H), 2.28 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 168.4, 143.1, 138.3, 136.8, 136.6, 134.3, 133.5, 133.1, 132.2, 131.5, 130.0, 129.8, 129.0, 128.0, 127.5, 124.3, 120.7, 92.1, 91.5, 77.2, 77.0, 76.8, 21.3, 20.7, 19.7. HRMS (ESI) calcd for $C_{24}H_{21}NNaO_4S^+$ [M + Na^+] 442.1083, found 442.1085.

N-(2-(Phenylethynyl)phenyl)methanesulfonamide (**1v**). Following the general procedure for preparation of substrates, compound **1v** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 83%, a white solid, m.p. 145—147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, J = 8.2 Hz, 1H), 7.59—7.50 (m, 3H), 7.45—7.34 (m, 4H), 7.18 (td, J = 7.6, 1.0 Hz, 1H), 7.05 (s, 1H), 3.05 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.6, 132.4, 131.7, 130.1, 129.3, 128.7, 124.9, 121.8, 119.9, 114.5, 96.7, 83.7, 77.4, 77.1, 76.7, 39.7. HRMS (ESI) calcd for $C_{15}H_{13}NNaO_2S^+$ [M + Na^+] 294.0559, found 294.0560.

4-Bromo-*N*-(2-((2-bromophenyl)ethynyl)phenyl)benzenesulfonamide (**1w**). Following the general procedure for preparation of substrates, compound **1w** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 78%, a white solid, m.p. 140—141 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.81 (s, 1H), 7.71—7.65 (m, 4H), 7.51 (dd, J = 7.7, 1.6 Hz, 1H), 7.49—7.46 (m, 2H), 7.42 (dd, J = 7.7, 1.4 Hz, 1H), 7.36—7.31 (m, 2H), 7.28—7.23 (m, 1H), 7.09 (td, J = 7.6, 0.9 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 138.1, 137.9, 133.0, 132.4, 132.2, 131.9, 130.2, 130.1, 128.9, 128.2, 127.4, 125.4, 124.6, 124.4, 119.7, 113.8, 95.1, 88.5. HRMS (ESI) calcd for $C_{20}H_{13}{}^{79}Br_2NNaO_2S^+$ [M + Na^+] 511.8926, found 511.8928.

N-(2-((2-Bromophenyl)ethynyl)phenyl)-4-methoxybenzenesulfonamide (**1x**). Following the general procedure for preparation of substrates, compound **1x** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 62%, a white solid, m.p. 105—107 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.78 (d, J = 8.9 Hz, 3H), 7.67 (t, J = 7.7 Hz, 2H), 7.52 (d, J = 7.7 Hz, 1H), 7.40 (d, J = 7.7 Hz, 1H), 7.36—7.27 (m, 2H), 7.23 (d, J = 7.6 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 6.82 (d, J = 8.8 Hz, 2H), 3.76 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 163.2, 138.5, 132.9, 132.4, 131.8, 130.7, 130.1, 130.0, 129.6, 127.3, 125.5, 124.5, 124.0, 119.0, 114.2, 113.2, 94.9, 88.8, 55.5. HRMS (ESI) calcd for $C_{21}H_{16}{}^{79}BrNNaO_3S^+$ [M + Na^+] 463.9926, found 463.9928.

tert-Butyl (2-(phenylethynyl)phenyl)carbamate (**1y**). Following the general procedure for preparation of substrates, compound **1y** was purified by silica gel chromatography (1% EtOAc/PE). Yield: 45%, a white solid, m.p. 62—64 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, J = 8.4 Hz, 1H), 7.51—7.43 (m, 2H), 7.38 (dd, J = 7.7, 1.6 Hz, 1H), 7.31 (dd, J = 5.1, 2.0 Hz, 3H), 7.25 (ddd, J = 8.8, 5.7, 1.6 Hz, 2H), 6.91 (td, J = 7.6, 1.2 Hz, 1H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 152.4, 139.5, 131.7, 131.6, 129.7, 128.7, 128.5, 122.7, 122.1, 117.6, 111.2, 96.1, 84.6, 80.9, 28.4. HRMS (ESI) calcd for $C_{19}H_{19}NNaO_2{}^+$ [M + Na^+] 316.1308, found 316.1309.

Benzyl (2-(phenylethynyl)phenyl)carbamate (**1z**). Following the general procedure for preparation of substrates, compound 1z was purified by silica gel chromatography (3% EtOAc/PE). Yield: 60%, a white solid, m.p. 40—42 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21 (d, J = 8.4 Hz, 1H), 7.54 (td, J = 5.4, 4.8, 3.0 Hz, 3H), 7.51—7.42 (m, 3H), 7.37 (td, J = 7.5, 3.7 Hz, 7H), 7.04 (t, J = 7.5 Hz, 1H), 5.26 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 153.1, 138.9, 136.1, 131.9, 131.6, 129.8, 128.8, 128.6, 128.5, 128.4, 128.3, 122.7, 122.5, 117.9, 111.6, 96.3, 84.2, 67.1. HRMS (ESI) calcd for $C_{22}H_{17}NNaO_2{}^+$ [M + Na^+] 350.1151, found 350.1156.

(9*H*-Fluoren-9-yl)methyl 2-(phenylethynyl)phenyl)carbamate (**1aa**). Following the general procedure for preparation of substrates, compound **1aa** was purified by silica gel chromatography (3% EtOAc/PE). Yield: 55%, a white solid, m.p. 110—112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (s, 1H), 7.79 (d, J = 7.6 Hz, 2H), 7.65 (d, J = 7.5 Hz, 2H), 7.57 (td, J = 5.8, 4.8, 2.5 Hz, 3H), 7.51 (dd, J = 7.7, 1.5 Hz, 1H), 7.47—7.40 (m, 5H), 7.39—7.33 (m, 1H), 7.30 (td, J = 7.5, 1.1 Hz, 2H), 7.06 (td, J = 7.6, 1.1 Hz, 1H), 4.55 (d, J = 7.1 Hz, 2H), 4.33 (t, J = 7.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 153.0, 143.7, 141.4, 138.8, 131.6, 131.6, 129.8, 128.9, 128.6, 127.8, 127.1, 125.1, 122.8, 122.5, 120.1, 118.0, 111.7, 96.5, 84.3, 67.2, 47.1. HRMS (ESI) calcd for $C_{29}H_{21}NNaO_2{}^+$ [M + Na^+] 438.1465, found 438.1469.

General procedure for synthesis of 3-methylthioindoles 2 and deuterated 3-methylthioindoles 3

To a solution of substrates **1** (0.5 mmol) in DMSO (1 mL) or other sulfoxides (0.5 mL) was slowly added $SOCl_2$ (1.5 mmol) at 0 °C. The mixture was stirred at 70 °C until TLC indicated the total consumption of substrates **1**. H_2O (25 mL) was added to the reaction mixture and extracted with DCM (30 mL × 3). The combined organic layer was washed with saturated aq. $NaHCO_3$ solution, then washed with brine, dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography, using a mixture of PE and EtOAc as eluent, to give the desired products **2** or **3**.

3-(Methylthio)-2-phenyl-1-tosyl-1*H*-indole (**2a**). Following the general procedure for preparation of products **2**, compound **2a** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 174 mg, 88%, a white solid, m.p. 104—105 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.36 (d, J = 8.3 Hz, 1H), 7.68 (d, J = 7.4 Hz, 1H), 7.53—7.40 (m, 4H), 7.37 (d, J = 7.0 Hz, 3H), 7.29 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.2 Hz, 2H), 2.31 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 144.9, 142.8, 137.1, 135.2, 131.8, 131.2, 130.7, 129.5, 129.1, 127.3, 126.9, 125.6, 124.4, 119.9, 117.5, 116.2, 21.6, 18.4. HRMS (ESI) m/z calcd for $C_{22}H_{19}NNaO_2S_2{}^+$ [M + Na^+] 416.0749, found 416.0750.

6-Bromo-3-(methylthio)-2-phenyl-1-tosyl-1*H*-indole (**2b**). Following the general procedure for preparation of products **2**, compound **2b** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 224 mg, 95%, a white solid, m.p. 138—139 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.55 (d, J = 1.5 Hz, 1H), 7.54 (d, J = 8.3 Hz, 1H), 7.48 (dd, J = 8.2, 1.5 Hz, 2H), 7.43 (t, J = 7.5 Hz, 2H), 7.35—7.30 (m, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 2.33 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 145.2, 143.2, 137.6, 135.0, 131.8, 130.1, 130.0, 129.6, 129.3, 127.6, 127.3, 127.0, 121.0, 119.08, 119.05, 117.0, 21.6, 18.4. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}{}^{79}BrNNaO_2S_2{}^+$ [M + Na^+] 493.9855, found 493.9855.

5-Fluoro-3-(methylthio)-2-phenyl-1-tosyl-1*H*-indole (**2c**). Following the general procedure for preparation of products **2**, compound **2c** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 176 mg, 81%, a white solid, m.p. 120—121 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.30 (dd, J = 9.1, 4.4 Hz, 1H), 7.48—7.50 (m, 1H), 7.46—7.41 (m, 2H), 7.36 (dd, J = 5.1, 3.3 Hz, 2H), 7.32 (dd, J = 8.4, 2.6 Hz, 1H), 7.26 (d, J = 8.4 Hz, 2H), 7.13 (td, J = 9.0, 2.7 Hz, 1H), 7.07 (d, J = 8.1 Hz, 2H), 2.31 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 160.4 (d, $^1J_{C\text{-}F}$ = 241.6 Hz), 145.0, 144.6, 135.0, 133.2, 132.7 (d, $^3J_{C\text{-}F}$ = 9.6 Hz), 131.7, 130.3, 129.4,

129.3, 127.3, 126.9, 117.5 (d, $^{3}J_{C\text{-}F}$ = 9.4 Hz), 117.2, 113.3 (d, $^{2}J_{C\text{-}F}$ = 25.18 Hz), 105.5 (d, $^{2}J_{C\text{-}F}$ = 25.18 Hz), 21.6, 18.2. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}FNNaO_2S_2^+$ [M + Na^+] 434.0655, found 434.0656.

5-Chloro-3-(methylthio)-2-phenyl-1-tosyl-1*H*-indole (**2d**). Following the general procedure for preparation of products **2**, compound **2d** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 190 mg, 89%, a white solid, m.p. 201—203 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.28 (d, *J* = 8.9 Hz, 1H), 7.64 (t, *J* = 8.6 Hz, 1H), 7.53—7.47 (m, 1H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.34—7.37 (m, 3H), 7.26 (d, *J* = 8.5 Hz, 3H), 7.08 (d, *J* = 8.4 Hz, 2H), 2.32 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ:* 145.1, 144.2, 135.3, 135.0, 132.6, 131.7, 130.3, 130.2, 129.5, 129.3, 127.3, 126.9, 125.7, 119.5, 117.3, 116.7, 21.6, 18.3. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}{}^{35}ClNNaO_2S_2^+$ [M + Na^+] 450.0360, found 450.0364.

5-Methyl-3-(methylthio)-2-phenyl-1-tosyl-1*H*-indole (**2e**). Following the general procedure for preparation of products **2**, compound **2e** was purified by silica gel chromatography (3% EtOAc/PE). Yield: 187 mg, 92%, a white solid, m.p. 119—121 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.22 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.50—7.40 (m, 4H), 7.39—7.34 (m, 2H), 7.28 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 2H), 2.47 (s, 3H), 2.30 (s, 3H), 2.05 (d, *J* = 0.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 144.7, 142.9, 135.2, 134.1, 131.8, 131.4, 130.8, 129.3, 129.0, 127.2, 126.9, 119.7, 117.2, 115.9, 21.5, 21.4, 18.3. HRMS (ESI) *m/z* calcd for $C_{23}H_{21}NNaO_2S_2^+$ [M + Na^+] 430.0906 found 430.0909.

2-(3-Fluorophenyl)-3-(methylthio)-1-tosyl-1*H*-indole (**2f**). Following the general procedure for preparation of products **2**, compound **2f** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 113 mg, 55%, a white solid, m.p. 90—91 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.35 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.74—7.66 (m, 1H), 7.48—7.35 (m, 3H), 7.31 (dd, *J* = 8.7, 2.0 Hz, 2H), 7.22—7.15 (m, 2H), 7.11—7.07 (m, 2H), 7.08—7.01 (m, 1H), 2.32 (s, 3H), 2.08 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 161.7 (d, $^{1}J_{C\text{-}F}$ = 246.3 Hz), 145.03, 141.13, 137.10, 135.11, 132.7 (d, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 131.01, 129.45, 128.7 (d, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 127.7 (d, $^{4}J_{C\text{-}F}$ = 2.8 Hz), 126.83, 125.79, 124.41, 120.01, 118.7 (d, $^{2}J_{C\text{-}F}$ = 22.4 Hz), 118.08, 116.21, 116.0 (d, $^{2}J_{C\text{-}F}$ = 21.0 Hz), 21.52, 18.27. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}FNNaO_2S_2^+$ [M + Na^+] 434.0655, found 434.0651.

2-(4-Fluorophenyl)-3-(methylthio)-1-tosyl-1*H*-indole (**2g**). Following the general procedure for preparation of products **2**, compound **2g** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 183 mg, 89%, a white solid, m.p. 123—125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.36 (d, *J* = 8.3 Hz, 1H), 7.68 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.43 (ddd, *J* = 8.4, 7.3, 1.4 Hz, 1H), 7.40—7.31 (m, 3H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.14 (ddd, *J* = 8.7, 5.8, 2.5 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 2.31 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 163.2 (d, $^{1}J_{C\text{-}F}$ = 250.4 Hz), 145.0, 141.6, 137.0, 135.1, 133.6 (d, $^{3}J_{C\text{-}F}$ = 8.5 Hz), 131.0, 129.5, 126.8, 126.5 (d, $^{4}J_{C\text{-}F}$ = 3.5 Hz), 125.7, 124.4, 119.9, 117.7, 116.2, 114.5 (d, $^{2}J_{C\text{-}F}$ = 21.8 Hz), 21.6, 18.3. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}FNNaO_2S_2^+$ [M + Na^+] 434.0655, found 434.0660.

2-(4-Bromophenyl)-3-(methylthio)-1-tosyl-1*H*-indole (**2h**). Following the general procedure for preparation of products **2**, compound **2h** was as purified by silica gel chromatography (5% EtOAc/PE). Yield: 155 mg, 66%, a white solid, m.p. 146—147 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.35 (d, *J* = 8.4 Hz, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.26 (dt, *J* = 11.1, 5.5 Hz, 4H), 7.07 (d, *J* = 8.1 Hz, 2H), 2.30 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 145.1, 141.4, 137.2, 135.0, 133.3, 131.1, 130.6, 129.6, 129.5, 126.8, 125.8, 124.5, 123.6, 120.0, 118.1, 116.3, 21.6, 18.3. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}{}^{79}BrNNaO_2S_2^+$ [M + Na^+] 493.9855, found 493.9855.

2-(4-Methoxyphenyl)-3-(methylthio)-1-tosyl-1*H*-indole (**2i**). Following the general procedure for preparation of products **2**, compound **2i** was as purified by silica gel chromatography (10% EtOAc/PE). Yield: 181 mg, 86%, a white solid, m.p. 147—148 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.35 (d, *J* = 8.3 Hz, 1H), 7.66 (d, *J* = 7.4 Hz, 1H), 7.42—7.38 (m, 1H), 7.37—7.33 (m, 1H), 7.28 (dd, *J* = 11.2, 8.5 Hz, 4H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 3.90 (s, 3H), 2.30 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 160.2, 144.8, 142.8, 137.0, 135.3, 133.1, 131.3, 129.4, 126.9, 125.3, 124.3, 122.7, 119.8, 117.0, 116.3, 112.8, 55.3, 21.6, 18.3. HRMS (ESI) *m/z* calcd for $C_{23}H_{21}NNaO_3S_2^+$ [M + Na^+] 446.0855, found 446.0856.

4-Methyl-*N*-(2-(3-(methylthio)-1-tosyl-1*H*-indol-2-yl)phenyl)-benzenesulfonamide (**2j**). Following the general procedure for preparation of products **2**, compound **2j** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 270 mg, 96%, a white solid, m.p. 174—175 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.40 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 2H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.53—7.47 (m, 2H), 7.41 (dd, *J* = 15.6, 7.9 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.17—7.08 (m, 5H), 6.96 (dd, *J* = 7.6, 1.3 Hz, 1H), 6.75 (d, *J* = 7.3 Hz, 1H), 2.34 (d, *J* = 9.4 Hz, 6H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 145.6, 143.8, 137.2, 137.0, 136.9, 136.7, 134.6, 132.9, 130.9, 130.7, 129.7, 129.6, 127.2, 127.0, 126.3, 124.5, 123.3, 122.0, 120.1, 119.8, 119.7, 116.1, 77.4, 77.1, 76.8, 21.7, 21.6, 18.1. HRMS (ESI) *m/z* calcd for $C_{29}H_{26}N_2NaO_4S_3^+$ [M + Na^+] 585.0947, found 585.0948.

2-(2-Bromo-5-(trifluoromethyl)phenyl)-3-(methylthio)-1-tosyl-1*H*-indole (**2k**). Following the general procedure for preparation of products **2**, compound **2k** was purified by silica gel chromatography (3% EtOAc/PE). Yield: 115 mg, 43%, a white solid, m.p. 110—111 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.37 (dd, *J* = 8.4, 2.9 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.41 (dd, *J* = 17.5, 8.0 Hz, 3H), 7.29 (s, 1H), 7.15 (d, *J* = 8.2 Hz, 2H), 2.34 (s, 3H), 2.17 (d, *J* = 2.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 145.5, 138.8, 136.6, 135.8, 133.8, 133.05, 130.7, 130.3, 130.0 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 129.8, 128.9 (q, $^{2}J_{C\text{-}F}$ = 33.2 Hz), 127.2 (q, $^{3}J_{C\text{-}F}$ = 3.6 Hz), 126.9, 126.1, 124.2, 123.7 (q, $^{1}J_{C\text{-}F}$ = 272.2 Hz), 120.2, 118.0, 115.4, 21.5, 18.1. HRMS (ESI) *m/z* calcd for $C_{23}H_{17}{}^{79}BrF_3NNaO_2S_2^+$ [M + Na^+] 561.9728, found 561.9729.

2-(2-Bromo-5-chlorophenyl)-3-(methylthio)-1-tosyl-1*H*-indole (**2l**). Following the general procedure for preparation of products **2**, compound **2l** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 91 mg, 36%, a white solid, m.p. 144—146 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.34 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.6 Hz, 1H), 7.49—7.45 (m, 3H), 7.41—7.36 (m, 1H), 7.33 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.05 (d, *J* = 2.5 Hz, 1H), 2.35 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 145.3, 139.0, 136.5, 135.8, 134.2, 133.4, 133.1, 132.3, 130.7, 130.2, 129.7, 127.1, 126.0, 124.5, 124.1, 120.1, 117.6, 115.3, 21.6, 18.1. HRMS (ESI) *m/z* calcd for $C_{22}H_{17}{}^{79}BrClNNaO_2S_2^+$ [M + Na^+] 527.9465, found 527.9467.

3-(Methylthio)-2-(naphthalen-1-yl)-1-tosyl-1*H*-indole (**2m**). Following the general procedure for preparation of products **2**, compound **2m** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 205 mg, 93%, a white solid, m.p. 142—143 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.45 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 7.7 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.48 (dd, *J* = 8.3, 7.3 Hz, 1H), 7.42 (q, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 7.0 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.24—7.19 (m, 3H), 6.92 (d, *J* = 8.2 Hz, 2H), 2.24 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 144.8, 140.2, 136.9, 135.4, 133.5, 133.0, 130.6, 130.4, 129.9, 129.3, 128.4, 128.2, 127.0, 126.2, 125.8, 125.7, 125.5, 124.4, 124.0, 119.8, 117.7, 115.6, 21.5, 18.4. HRMS (ESI) m/z calcd for $C_{26}H_{21}NNaO_2S_2^+$ [M + Na^+] 466.0906, found 466.0906.

3-(Methylthio)-2-(thiophen-2-yl)-1-tosyl-1*H*-indole (**2n**). Following the general procedure for preparation of products **2**, compound **2n** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 183 mg, 92%, a white solid, m.p. 80—81 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.35 (d, *J* = 8.4 Hz, 1H), 7.72—7.66 (m,

1H), 7.53 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.42 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H), 7.39—7.32 (m, 3H), 7.16 (ddd, *J* = 8.6, 4.3, 2.4 Hz, 2H), 7.08 (d, *J* = 8.1 Hz, 2H), 2.31 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 144.9, 137.3, 135.3, 135.0, 132.2, 130.8, 130.2, 129.4, 128.6, 126.9, 126.4, 125.9, 124.3, 120.0, 119.7, 116.1, 21.6, 18.6. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}NNaO_2S_3^+$ [M + Na^+] 422.0314, found 422.0314.

2-Cyclopropyl-3-(methylthio)-1-tosyl-1*H*-indole (**2o**). Following the general procedure for preparation of products **2**, compound **2o** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 162 mg, 91%, a white solid, m.p. 66—68 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.24—8.18 (m, 1H), 7.69—7.63 (m, 2H), 7.63—7.57 (m, 1H), 7.35—7.23 (m, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 2.34 (s, 3H), 2.19 (tt, *J* = 7.6, 6.2 Hz, 1H), 1.12—1.02 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 144.7, 143.0, 136.5, 136.5, 131.1, 129.7, 126.6, 125.0, 123.7, 119.3, 115.5, 115.0, 21.6, 9.3, 9.0. HRMS (ESI) *m/z* calcd for $C_{19}H_{19}NNaO_2S_2^+$ [M + Na^+] 380.0749, found 380.0748.

6-Methyl-3-(methylthio)-2-(p-tolyl)-1-tosyl-1*H*-indole (**2p**). Following the general procedure for preparation of products **2**, compound **2p** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 162 mg, 77%, a white solid, m.p. 163—164 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.16 (s, 1H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 7.4 Hz, 3H), 7.18 (d, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 8.2 Hz, 2H), 2.55 (s, 3H), 2.45 (s, 3H), 2.31 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 144.7, 142.2, 138.9, 137.4, 135.6, 135.3, 131.6, 129.4, 129.0, 128.0, 127.9, 126.9, 125.8, 119.4, 117.2, 116.4, 22.1, 21.6, 21.6, 18.3. HRMS (ESI) *m/z* calcd for $C_{24}H_{23}NNaO_2S_2^+$ [M + Na^+] 444.1062, found 444.1064.

2-(4-Chlorophenyl)-6-methyl-3-(methylthio)-1-tosyl-1*H*-indole (**2q**). Following the general procedure for preparation of products **2**, compound **2q** was purified by silica gel chromatography (3% EtOAc/PE). Yield: 75 mg, 34%, a white solid, m.p. 166—168 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.17 (s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.43—7.39 (m, 2H), 7.32—7.24 (m, 4H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 2H), 2.55 (s, 3H), 2.32 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 144.9, 140.7, 137.6, 136.0, 135.1, 135.1, 133.0, 129.4, 129.2, 128.8, 127.5, 126.7, 125.9, 119.5, 118.0, 116.4, 22.1, 21.6, 18.2. HRMS (ESI) *m/z* calcd for $C_{23}H_{20}{}^{35}ClNNaO_2S_2^+$ [M + Na^+] 464.0516, found 464.0518.

2-(2-Bromophenyl)-6-methyl-3-(methylthio)-1-tosyl-1*H*-indole (**2r**). Following the general procedure for preparation of products **2**, compound **2r** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 114 mg, 47%, a white solid, m.p. 162—164 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.14 (s, 1H), 7.65 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.38 (td, *J* = 7.5, 1.1 Hz, 1H), 7.33 (td, *J* = 7.7, 1.7 Hz, 1H), 7.26—7.21 (m, 1H), 7.19 (d, *J* = 7.9 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 2H), 2.54 (s, 3H), 2.31 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 145.0, 139.7, 136.8, 136.0, 135.9, 133.6, 132.8, 132.3, 130.6, 129.6, 128.2, 127.2, 126.6, 126.3, 125.5, 119.6, 117.2, 115.4, 22.2, 21.6, 18.0. HRMS (ESI) *m/z* calcd for $C_{23}H_{20}{}^{79}BrNNaO_2S_2^+$ [M + Na^+] 508.0011, found 508.0012.

2-(2-Bromophenyl)-5-methyl-3-(methylthio)-1-tosyl-1*H*-indole (**2s**). Following the general procedure for preparation of products **2**, compound **2s** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 199 mg, 82%, a white solid, m.p. 141—144 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.19 (d, *J* = 8.5 Hz, 1H), 7.68 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.51 (s, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.40 (td, *J* = 7.4, 1.2 Hz, 1H), 7.36 (td, *J* = 7.7, 1.8 Hz, 1H), 7.29—7.22 (m, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 2.49 (s, 3H), 2.33 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 144.9, 140.5, 135.8, 134.6, 133.7, 133.5, 132.7, 132.4, 130.7, 130.6, 129.6, 127.2, 127.1, 126.4, 126.2, 119.8, 116.9, 115.0, 21.6, 21.4, 18.0. HRMS (ESI) m/z calcd for $C_{23}H_{20}{}^{79}BrNNaO_2S_2^+$ [M + Na^+] 508.0011, found 508.0011.

2-(2-Bromophenyl)-5,7-dimethyl-3-(methylthio)-1-tosyl-1*H*-indole (**2t**). Following the general procedure for preparation of products **2**, compound **2t** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 225 mg, 90%, a white solid, m.p. 118—119 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.66—7.61 (m, 1H), 7.38—7.33 (m, 1H), 7.31 (s, 1H), 7.29 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.24—7.19 (m, 3H), 7.09—7.03 (m, 3H), 2.73 (s, 3H), 2.43 (s, 3H), 2.32 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 144.4, 143.7, 136.6, 135.5, 134.8, 133.7, 133.4, 133.3, 132.7, 131.3, 130.2, 129.2, 128.4, 126.8, 126.2, 125.6, 121.2, 118.1, 22.2, 21.6, 21.2, 17.9. HRMS (ESI) *m/z* calcd for $C_{24}H_{22}{}^{79}BrNNaO_2S_2^+$ [M + Na^+] 522.0168, found 522.0169.

2-(5,7-Dimethyl-3-(methylthio)-1-tosyl-1*H*-indol-2-yl)benzoic acid (**2u**). Following the general procedure for preparation of products **2**, compound **2u** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 203 mg, 87%, a yellow solid, m.p. 214—216 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.23 (dd, *J* = 7.8, 0.8 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.88—7.80 (m, 1H), 7.64—7.54 (m, 1H), 7.31—7.25 (m, 2H), 7.08 (d, *J* = 1.0 Hz, 1H), 6.90 (s, 1H), 6.74 (d, *J* = 8.0 Hz, 2H), 2.56 (s, 3H), 2.34 (s, 3H), 2.17 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 160.8, 155.9, 143.4, 140.4, 137.9, 137.2, 135.0, 134.3, 132.3, 129.4, 129.3, 129.2, 129.0, 128.7, 126.6, 125.1, 120.9, 111.6, 21.5, 21.0, 19.6, 18.6. HRMS (ESI) m/z calcd for $C_{25}H_{23}NNaO_4S_2^+$ [M + Na^+] 488.0961, found 488.0963.

1-(Methylsulfonyl)-3-(methylthio)-2-phenyl-1*H*-indole (**2v**). Following the general procedure for preparation of products **2**, compound **2v** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 139 mg, 88%, a white solid, m.p. 136—137 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.18—8.11 (m, 1H), 7.84—7.78 (m, 1H), 7.52—7.45 (m, 5H), 7.45—7.41 (m, 2H), 2.82 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 142.5, 136.7, 131.3, 131.0, 130.5, 129.3, 127.7, 125.8, 124.6, 120.2, 117.3, 115.5, 40.7, 18.4. HRMS (ESI) *m/z* calcd for $C_{16}H_{15}NNaO_2S_2^+$ [M + Na^+] 340.0436, found 340.0436.

2-(2-Bromophenyl)-1-((4-bromophenyl)sulfonyl)-3-(methylthio)-1*H*-indole (**2w**). Following the general procedure for preparation of products **2**, compound **2w** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 215 mg, 80%, a white solid, m.p. 152—153 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.30 (d, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.68 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.51—7.47 (m, 2H), 7.47—7.43 (m, 3H), 7.42—7.35 (m, 3H), 7.27 (dd, *J* = 7.5, 1.7 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 140.0, 137.4, 136.3, 133.6, 132.4, 132.3, 132.3, 130.9, 130.4, 129.3, 128.6, 126.4, 126.3, 125.9, 124.3, 120.2, 118.0, 115.2, 17.9. HRMS (ESI) *m/z* calcd for $C_{21}H_{15}{}^{79}Br_2NNaO_2S_2^+$ [M + Na^+] 557.8803, found 557.8806.

2-(2-Bromophenyl)-1-((4-methoxyphenyl)sulfonyl)-3-(methylthio)-1*H*-indole (**2x**). Following the general procedure for preparation of products **2**, compound **2x** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 210 mg, 86%, a white solid, m.p. 112—113 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.32 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.56—7.50 (m, 2H), 7.46—7.39 (m, 2H), 7.38—7.34 (m, 2H), 7.27 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.82—6.76 (m, 2H), 3.79 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ:* 163.9, 140.4, 136.3, 133.5, 132.7, 132.4, 130.7, 130.3, 130.2, 129.5, 126.4, 126.3, 125.6, 123.9, 120.0, 117.0, 115.3, 114.1, 55.7, 18.0. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}{}^{79}BrNNaO_3S_2^+$ [M + Na^+] 509.9804, found 509.9807.

tert-Butyl 3-(methylthio)-2-phenyl-1*H*-indole-1-carboxylate (**2y**). Following the general procedure for preparation of products **2**, compound **2y** was purified by silica gel chromatography (3% EtOAc/PE). Yield: 127 mg, 75%, a white solid, m.p.: 48—50 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.25 (d, *J* = 8.2 Hz, 1H), 7.77 (d, *J* = 7.3 Hz, 1H), 7.47—7.42 (m, 3H), 7.41—7.37 (m, 3H), 7.35 (td, *J* = 7.5, 1.1 Hz, 1H), 2.17 (s, 3H), 1.24 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ:* 149.7, 142.1, 136.6, 133.7, 130.3, 130.0, 128.0, 127.7, 125.0, 123.2, 119.5, 115.3, 114.2, 83.6, 27.5, 18.8. HRMS (ESI) calcd for $C_{20}H_{21}NNaO_2S^+$ [M + Na^+] 362.1185, found 362.1189.

Benzyl 3-(methylthio)-2-phenyl-1*H*-indole-1-carboxylate (**2z**).

Following the general procedure for preparation of products **2**, compound **2z** was purified by silica gel chromatography (3% EtOAc/PE). Yield: 159 mg, 85%, a white solid, m.p. 98—100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23 (d, J = 7.4 Hz, 1H), 7.78 (d, J = 7.3 Hz, 1H), 7.45—7.33 (m, 7H), 7.33—7.24 (m, 3H), 7.03 (d, J = 7.5 Hz, 2H), 5.17 (s, 2H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 151.1, 142.0, 136.3, 134.3, 132.9, 130.5, 130.0, 128.5, 128.4, 128.3, 127.7, 125.4, 123.6, 119.7, 115.6, 115.3, 68.8, 18.8. HRMS (ESI) calcd for $C_{23}H_{19}NNaO_2S^+$ [M + Na^+] 396.1029, found 396.1031.

(9*H*-Fluoren-9-yl)methyl-3-(methylthio)-2-phenyl-1*H*-indole-1-carboxylate (**2aa**). Following the general procedure for preparation of products **2**, compound **2aa** was purified by silica gel chromatography (3% EtOAc/PE). Yield: 200 mg, 87%, a white solid, m.p. 120—122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (d, J = 7.6 Hz, 3H), 7.76 (d, J = 8.3 Hz, 1H), 7.51—7.46 (m, 4H), 7.46—7.39 (m, 5H), 7.36 (td, J = 7.5, 1.1 Hz, 1H), 7.33—7.23 (m, 3H), 4.64 (d, J = 6.1 Hz, 2H), 3.98 (t, J = 6.1 Hz, 1H), 2.20 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 151.3, 143.3, 142.1, 141.4, 136.0, 132.8, 130.5, 130.0, 128.5, 128.0, 127.8, 127.3, 125.3, 124.9, 123.6, 120.1, 119.7, 115.7, 115.5, 68.9, 46.6, 18.8. HRMS (ESI) calcd for $C_{30}H_{23}NNaO_2S^+$ [M + Na^+] 484.1342, found 484.1346.

3-(Ethylthio)-2-phenyl-1-tosyl-1*H*-indole (**2ab**). Following the general procedure for preparation of products **2**, compound **2ab** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 154 mg, 72%, a white solid, m.p. 114—116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.37 (dt, J = 8.4, 0.8 Hz, 1H), 7.69 (dt, J = 7.6, 1.0 Hz, 1H), 7.51—7.40 (m, 4H), 7.40—7.33 (m, 3H), 7.33—7.28 (m, 2H), 7.11—7.04 (m, 2H), 2.51 (q, J = 7.3 Hz, 2H), 2.31 (s, 3H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 144.8, 143.8, 137.0, 135.1, 131.9, 131.8, 130.7, 129.4, 129.0, 127.1, 126.9, 125.5, 124.3, 120.0, 116.2, 115.6, 28.8, 21.6, 14.9. HRMS (ESI) calcd for $C_{23}H_{21}NNaO_2S_2^+$ [M + Na^+] 430.0906, found 430.0908.

2-Phenyl-3-(phenylthio)-1-tosyl-1*H*-indole (**2ac**). Following the general procedure for preparation of products **2**, compound **2ac** was purified by silica gel chromatography (3% EtOAc/PE). Yield: 147 mg, 65%, a white solid, m.p. 264—266 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (dd, J = 8.4, 0.9 Hz, 1H), 7.50—7.29 (m, 9H), 7.20—7.17 (m, 2H), 7.15—7.02 (m, 5H), 6.88—6.77 (m, 2H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 145.1, 145.0, 137.5, 136.8, 134.9, 131.5, 131.2, 130.1, 129.4, 129.3, 128.8, 127.3, 127.0, 126.5, 125.8, 125.3, 124.7, 120.3, 116.5, 113.7, 21.7. HRMS (ESI) calcd for $C_{27}H_{21}NNaO_2S_2^+$ [M + Na^+] 478.0906, found 478.0909.

3-((Methyl-d_3)thio)-2-phenyl-1-tosyl-1*H*-indole (**3a**). Following the general procedure for preparation of products **3**, compound **3a** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 152 mg, 76%, a white solid, m.p. 111—112 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.36 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.51—7.39 (m, 4H), 7.39—7.32 (m, 3H), 7.29 (d, J = 8.3 Hz, 2H), 7.04 (d, J = 8.2 Hz, 2H), 2.27 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 144.9, 142.7, 137.0, 135.2, 131.8, 131.2, 130.7, 129.5, 129.1, 127.3, 126.9, 125.6, 124.4, 119.9, 117.4, 116.2, 21.6. HRMS (ESI) m/z calcd for $C_{22}H_{16}D_3NNaO_2S_2^+$ [M + Na^+] 419.0938, found 419.0936.

5-Fluoro-3-((methyl-d_3)thio)-2-phenyl-1-tosyl-1*H*-indole (**3b**). Following the general procedure for preparation of products **3**, compound **3b** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 177 mg, 85%, a white solid, m.p. 112—114 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.30 (dd, J = 9.1, 4.4 Hz, 1H), 7.52—7.47 (m, 1H), 7.47—7.42 (m, 2H), 7.40—7.34 (m, 2H), 7.32 (dd, J = 8.4, 2.5 Hz, 1H), 7.25 (d, J = 1.6 Hz, 2H), 7.13 (td, J = 9.0, 2.7 Hz, 1H), 7.07 (d, J = 8.1 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 160.4 (d, $^1J_{C\text{-}F}$ = 242.1 Hz), 145.0, 144.6, 135.01 133.2, 132.7 (d, $^3J_{C\text{-}F}$ = 9.8 Hz), 131.7, 130.3, 129.4, 129.3, 127.3, 126.9, 117.6 (d, $^3J_{C\text{-}F}$ = 8.6 Hz), 113.4 (d, $^2J_{C\text{-}F}$ = 25.3 Hz), 105.5 (d, $^2J_{C\text{-}F}$ = 24.5 Hz), 21.6. HRMS (ESI) m/z calcd for $C_{22}H_{15}D_3FNNaO_2S_2^+$ [M + Na^+] 437.0843, found 437.0844.

6-Bromo-3-((methyl-d_3)thio)-2-phenyl-1-tosyl-1*H*-indole (**3c**). Following the general procedure for preparation of products **3**, compound **3c** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 201 mg, 85%, a white solid, m.p. 136—137 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.55 (d, J = 1.3 Hz, 1H), 7.54 (d, J = 8.3 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.42 (t, J = 7.5 Hz, 2H), 7.32 (d, J = 7.2 Hz, 2H), 7.27 (d, J = 8.3 Hz, 2H), 7.09 (d, J = 8.2 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 145.2, 143.2, 137.6, 135.1, 131.8, 130.2, 130.1, 129.5, 129.3, 127.6, 127.3, 127.0, 121.0, 119.1, 119.1, 117.0, 21.6. HRMS (ESI) m/z calcd for $C_{22}H_{15}D_3{}^{79}BrNNaO_2S_2^+$ [M + Na^+] 497.0043, found 497.0044.

2-(4-Methoxyphenyl)-3-((methyl-d_3)thio)-1-tosyl-1*H*-indole (**3d**). Following the general procedure for preparation of products **3**, compound **3d** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 184 mg, 86%, a white solid, m.p. 146—147 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.35 (d, J = 8.3 Hz, 1H), 7.66 (dd, J = 7.7, 0.5 Hz, 1H), 7.43—7.37 (m, 1H), 7.37—7.32 (m, 1H), 7.28 (dd, J = 11.6, 8.6 Hz, 4H), 7.05 (d, J = 8.1 Hz, 2H), 6.97 (d, J = 8.7 Hz, 2H), 3.89 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 160.2, 144.7, 142.7, 137.0, 135.3, 133.1, 131.3, 129.3, 126.9, 125.3, 124.2, 122.7, 119.7, 116.9, 116.3, 112.7, 55.3, 21.4. HRMS (ESI) m/z calcd for $C_{23}H_{18}D_3NNaO_3S_2^+$ [M + Na^+] 449.1043, found 449.1044.

4-Methyl-*N*-(2-(3-((methyl-d_3)thio)-1-tosyl-1*H*-indol-2-yl)phenyl)benzenesulfonamide (**3e**). Following the general procedure for preparation of products **3**, compound **3e** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 257 mg, 91%, a white solid, m.p. 161—163 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.39 (d, J = 8.4 Hz, 1H), 7.72—7.68 (m, 2H), 7.67—7.62 (m, 1H), 7.49 (td, J = 7.3, 3.7 Hz, 2H), 7.40 (ddd, J = 15.8, 8.4, 1.2 Hz, 2H), 7.31—7.27 (m, 2H), 7.17—7.05 (m, 5H), 6.95 (dd, J = 7.6, 1.5 Hz, 1H), 6.75 (s, 1H), 2.34 (d, J = 9.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 145.6, 143.7, 137.2, 137.0, 136.8, 136.7, 134.6, 132.9, 130.8, 130.7, 129.7, 129.6, 128.7, 128.2, 127.2, 126.9, 126.2, 124.5, 123.2, 120.1, 119.7, 116.1, 21.6, 21.6. HRMS (ESI) m/z calcd for $C_{29}H_{23}D_3N_2NaO_4S_3^+$ [M + Na^+] 588.1135, found 588.1136.

2-Cyclopropyl-3-((methyl-d_3)thio)-1-tosyl-1*H*-indole (**3f**). Following the general procedure for preparation of products **3**, compound **3f** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 151 mg, 83%, a white solid, m.p. 65—66 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.21 (d, J = 8.3 Hz, 1H), 7.65 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 7.6 Hz, 1H), 7.37—7.30 (m, 1H), 7.30—7.26 (m, 1H), 7.19 (d, J = 8.1 Hz, 2H), 2.35 (s, 3H), 2.19 (dq, J = 8.0, 6.0 Hz, 1H), 1.07 (dd, J = 9.5, 4.9 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 144.7, 143.1, 136.6, 131.2, 129.7, 126.6, 125.0, 123.7, 119.3, 115.5, 115.0, 21.6, 9.3, 9.0. HRMS (ESI) m/z calcd for $C_{19}H_{16}D_3NNaO_2S_2^+$ [M + Na^+] 383.0938, found 383.0939.

2-(2-Bromophenyl)-5,7-dimethyl-3-((methyl-d_3)thio)-1-tosyl-1*H*-indole (**3g**). Following the general procedure for preparation of products **3**, compound **3g** was purified by silica gel chromatography (5% EtOAc/PE). Yield: 217 mg, 86%, a white solid, m.p. 119—120 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.63 (d, J = 8.0 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.31 (s, 1H), 7.27 (t, J = 7.7 Hz, 1H), 7.25—7.18 (m, 3H), 7.09—7.01 (m, 3H), 2.73 (s, 3H), 2.43 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 144.4, 143.7, 136.6, 135.7, 134.8, 133.7, 133.5, 133.4, 132.6, 131.3, 130.2, 129.2, 128.4, 126.8, 126.2, 125.7, 121.1, 118.1, 22.2, 21.6, 21.2. HRMS (ESI) m/z calcd for $C_{24}H_{19}D_3{}^{79}BrNNaO_2S_2^+$ [M + Na^+] 525.0356, found 525.0358.

3-((Methyl-d_3)thio)-1-(methylsulfonyl)-2-phenyl-1*H*-indole (**3h**). Following the general procedure for preparation of products **3**, compound **3h** was purified by silica gel chromatography (10% EtOAc/PE). Yield: 124 mg, 78%, a white solid, m.p. 129—130 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.17—8.11 (m, 1H), 7.83—7.77 (m, 1H), 7.52—7.45 (m, 5H), 7.45—7.39 (m, 2H), 2.82 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ: 142.5, 136.7, 131.3, 131.1, 130.5, 129.3, 127.6, 125.8, 124.5, 120.2, 117.2, 115.5, 40.7. HRMS (ESI) m/z calcd for $C_{16}H_{12}D_3NNaO_2S_2^+$ [M + Na^+] 343.0625, found 343.0628.

General procedure for synthesis of sulfoxides 4[18i,28]

To a solution of compounds 2/3 (0.5 mmol) in MeCN (2.0 mL) was added *meta*-chloroperoxybenzoic acid (*m*-CPBA) (0.5 mmol) at 0 °C, and the mixture was stirred at r.t. The progress of the reaction was monitored by TLC. Upon completion of the reaction, MeCN was removed *in vacuo*. The residue was admixed with DCM (30 mL) and the resultant solution was washed with water (50 mL × 3). The organic layer was further washed with aq. NaOH solution, the washed with brine, dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography, using a mixture of PE and EtOAc as eluent, to afford the corresponding sulfoxides **4**.

3-(Methylsulfinyl)-2-phenyl-1-tosyl-1*H*-indole (**4a**). Following the general procedure for preparation of products **4**, compound **4a** was purified by silica gel chromatography (30% EtOAc/PE). Yield: 199 mg, 97%, a white solid, m.p. 148—150 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.42 (d, *J* = 8.5 Hz, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 7.57—7.48 (m, 2H), 7.43 (ddd, *J* = 7.6, 4.0, 2.0 Hz, 3H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.34—7.29 (m, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 2.77 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 145.9, 143.2, 135.7, 135.4, 131.9, 130.3, 129.8, 127.8, 127.2, 127.1, 126.4, 125.4, 125.1, 121.4, 121.0, 115.3, 44.8, 21.7. HRMS (ESI) *m/z* calcd for $C_{22}H_{19}NNaO_3S_2^+$ [M + Na^+] 432.0699, found 432.0671.

5-Chloro-3-(methylsulfinyl)-2-phenyl-1-tosyl-1*H*-indole (**4d**). Following the general procedure for preparation of products **4**, compound **4d** was purified by silica gel chromatography (30% EtOAc/PE). Yield: 218 mg, 98%, a white solid, m.p. 201—203 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.33 (d, *J* = 9.0 Hz, 1H), 8.25 (d, *J* = 2.0 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.48—7.39 (m, 3H), 7.29 (d, *J* = 8.4 Hz, 3H), 7.13 (d, *J* = 8.2 Hz, 2H), 2.84 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 145.9, 141.6, 135.6, 134.9, 131.7, 130.9, 130.6, 130.3, 129.8, 128.0, 127.8, 127.0, 126.5, 123.3, 120.2, 117.2, 40.4, 21.7. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}{}^{35}ClNNaO_3S_2^+$ [M + Na^+] 466.0309, found 466.0311.

2-(4-Fluorophenyl)-3-(methylsulfinyl)-1-tosyl-1*H*-indole (**4l**). Following the general procedure for preparation of products **4**, compound **4l** was purified by silica gel chromatography (30% EtOAc/PE). Yield: 205 mg, 96%, a white solid, m.p. 175—177 °C. ^{1}H NMR (600 MHz, DMSO) *δ*: 8.23 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.52 (ddd, *J* = 8.5, 7.4, 1.2 Hz, 2H), 7.49—7.45 (m, 3H), 7.44—7.39 (m, 1H), 7.37—7.29 (m, 4H), 2.96 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, DMSO) *δ*: 162.9 (d, $^1J_{C\text{-}F}$ = 247.9 Hz), 145.9, 138.8, 136.1, 134.0, 133.5, 130.2, 126.6, 126.1, 125.0 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 124.9, 124.8, 124.5, 120.7, 115.5, 114.7 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 40.0, 21.1. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}FNNaO_3S_2^+$ [M + Na^+] 450.0604, found 450.0609.

3-(Methylsulfinyl)-1-(methylsulfonyl)-2-phenyl-1*H*-indole (**4u**). Following the general procedure for preparation of products **4**, compound **4u** was purified by silica gel chromatography (30% EtOAc/PE). Yield: 150 mg, 90%, a white solid, m.p. 236—238 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.29—8.23 (m, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.57 (ddd, *J* = 8.7, 6.1, 2.8 Hz, 1H), 7.55—7.44 (m, 6H), 3.07 (s, 3H), 2.86 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 143.0, 135.2, 131.2, 130.5, 127.9, 127.8, 126.6, 125.4, 121.6, 121.3, 114.6, 44.9, 42.7. HRMS (ESI) *m/z* calcd for $C_{16}H_{15}NNaO_3S_2^+$ [M + Na^+] 356.0386, found 356.0389.

2-Cyclopropyl-3-((methyl-d_3)sulfinyl)-1-tosyl-1*H*-indole (**4f'**). Following the general procedure for preparation of products **4**, compound **4f'** was purified by silica gel chromatography (30% EtOAc/PE). Yield: 162 mg, 86%, a white solid, m.p. 101—103 °C. ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 8.27 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 7.9 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 9.9 Hz, 2H), 2.39 (s, 3H), 2.27—1.99 (m, 1H), 1.19—1.11 (m, 1H), 1.09—1.02 (m, 2H), 0.58—0.45 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) *δ:* 145.4, 142.1, 137.2, 136.4, 129.9, 126.6, 125.6, 124.9, 124.1, 120.7, 115.1, 77.2, 77.0, 76.8, 21.6, 10.0, 9.0, 9.0. HRMS (ESI) *m/z* calcd for $C_{19}H_{16}D_3NNaO_3S_2^+$ [M + Na^+] 399.0887, found 399.0889.

General procedure for synthesis of sulfones 5[18i,28]

To a solution of compounds **2**/**3** (0.5 mmol) in MeCN (2.0 mL) was added *m*-CPBA (1.1 mmol) at 0 °C, and the mixture was stirred at rt. The progress of the reaction was monitored by TLC. Upon completion of the reaction, MeCN was removed *in vacuo*. The residue was admixed with DCM (30 mL) and the resultant solution was washed with water (50 mL × 3). The organic layer was further washed with aq. NaOH solution, then washed with brine, dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography, using a mixture of PE and EtOAc as eluent, to afford the corresponding sulfones **5**.

3-(Methylsulfonyl)-2-phenyl-1-tosyl-1*H*-indole (**5a**). Following the general procedure for preparation of products **5**, compound **5a** was purified by silica gel chromatography (20% EtOAc/PE). Yield: 198 mg, 96%, a white solid, m.p. 199—201 °C. ^{1}H NMR (400 MHz, DMSO) *δ*: 8.28 (d, *J* = 8.5 Hz, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.60—7.52 (m, 4H), 7.52—7.41 (m, 5H), 7.38 (d, *J* = 8.2 Hz, 2H), 2.97 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, DMSO) *δ:* 146.7, 143.5, 135.1, 134.7, 131.8, 130.8, 130.3, 128.5, 127.6, 127.4, 126.8, 125.5, 125.4, 121.6, 121.1, 115.3, 45.4, 21.6. HRMS (ESI) *m/z* calcd for $C_{22}H_{19}NNaO_4S_2^+$ [M + Na^+] 448.0648, found 448.0649.

5-Chloro-3-(methylsulfonyl)-2-phenyl-1-tosyl-1*H*-indole (**5d**). Following the general procedure for preparation of products **5**, compound **5d** was purified by silica gel chromatography (20% EtOAc/PE). Yield: 223 mg, 97%, a white solid, m.p. 182—184 °C. ^{1}H NMR (400 MHz, DMSO) *δ*: 8.30 (d, *J* = 9.1 Hz, 1H), 8.05 (d, *J* = 2.1 Hz, 1H), 7.65—7.49 (m, 4H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.43—7.35 (m, 4H), 2.99 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, DMSO) *δ*: 147.0, 144.9, 134.4, 133.6, 131.7, 130.9, 130.5, 130.0, 127.9, 127.6, 127.4, 126.8, 126.7, 120.9, 120.3, 117.1, 45.4, 21.6. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}{}^{35}ClNNaO_4S_2^+$ [M + Na^+] 482.0258, found 482.0259.

2-(4-Fluorophenyl)-3-(methylsulfonyl)-1-tosyl-1*H*-indole (**5l**). Following the general procedure for preparation of products **5**, compound **5l** was purified by silica gel chromatography (20% EtOAc/PE). Yield: 215 mg, 97%, a white solid, m.p. 232—234 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.42 (d, *J* = 8.5 Hz, 1H), 8.23—8.11 (m, 1H), 7.52 (ddd, *J* = 8.6, 7.3, 1.4 Hz, 1H), 7.48—7.40 (m, 1H), 7.39—7.32 (m, 2H), 7.33—7.27 (m, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.11 (ddd, *J* = 10.5, 5.8, 2.5 Hz, 2H), 2.81 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 163.9 (d, $^1J_{C\text{-}F}$ = 252.3 Hz), 146.2, 142.2, 135.8, 135.3, 133.9 (d, $^3J_{C\text{-}F}$ = 8.7 Hz), 129.9, 127.0, 126.6, 125.3, 123.5 (d, $^4J_{C\text{-}F}$ = 3.6 Hz), 121.5, 120.9, 115.4, 114.6 (d, $^2J_{C\text{-}F}$ = 22.1 Hz), 44.9, 21.7. HRMS (ESI) *m/z* calcd for $C_{22}H_{18}FNNaO_4S_2^+$ [M + Na^+] 466.0553, found 466.0558.

1,3-Bis(methylsulfonyl)-2-phenyl-1*H*-indole (**5u**). Following the general procedure for preparation of products **5**, compound **5u** was purified by silica gel chromatography (20% EtOAc/PE). Yield: 164 mg, 94%, a white solid, m.p. 244—246 °C. ^{1}H NMR (600 MHz, DMSO) *δ*: 8.10 (t, *J* = 8.3 Hz, 2H), 7.64—7.58 (m, 2H), 7.57—7.52 (m, 1H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 2H), 3.47 (s, 3H), 3.02 (s, 3H). ^{13}C NMR (151 MHz, DMSO) *δ*: 143.0, 134.5, 130.8, 129.5, 128.6, 127.2, 125.9, 124.8, 124.6, 120.4, 120.1, 114.4, 45.2, 43.1. HRMS (ESI) *m/z* calcd for $C_{16}H_{15}NNaO_4S^+$ [M + Na^+] 372.0335, found 372.0339.

2-Cyclopropyl-3-((methyl-d_3)sulfonyl)-1-tosyl-1*H*-indole (**5f'**). Following the general procedure for preparation of products **5**, compound **5f'** was purified by silica gel chromatography (20% EtOAc/PE). Yield: 175 mg, 89%, a white solid, m.p. 137—139 °C. ^{1}H NMR (600 MHz, DMSO) *δ*: 8.12 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.46—7.41 (m, 3H), 7.40—7.34 (m, 1H), 2.36 (s, 3H), 2.23 (tt, *J* = 8.6, 5.7 Hz, 1H),

1.26—1.06 (m, 2H), 1.02—0.81 (m, 2H). ^{13}C NMR (151 MHz, DMSO) δ: 146.1, 146.0, 134.9, 134.7, 130.3, 126.7, 125.8, 125.3, 124.6, 122.4, 120.4, 114.7, 21.1, 10.4, 8.8. HRMS (ESI) *m/z* calcd for $C_{19}H_{16}D_3NNaO_4S_2^+$ [M + Na^+] 415.0836, found 415.0838.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.202000701.

Acknowledgement

Y. Du acknowledges the National Natural Science Foundation of China (No. 22071175) and K. Zhao acknowledges the National Key R&D Program of China (No. 2019YFA0905104) for financial supports.

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Manuscript received: December 22, 2020
Manuscript revised: January 23, 2021
Manuscript accepted: January 25, 2021
Accepted manuscript online: January 27, 2021

