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Article

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A protocol for stereoselective construction of highly functionalized dienyl sulfonyl fluoride warheads

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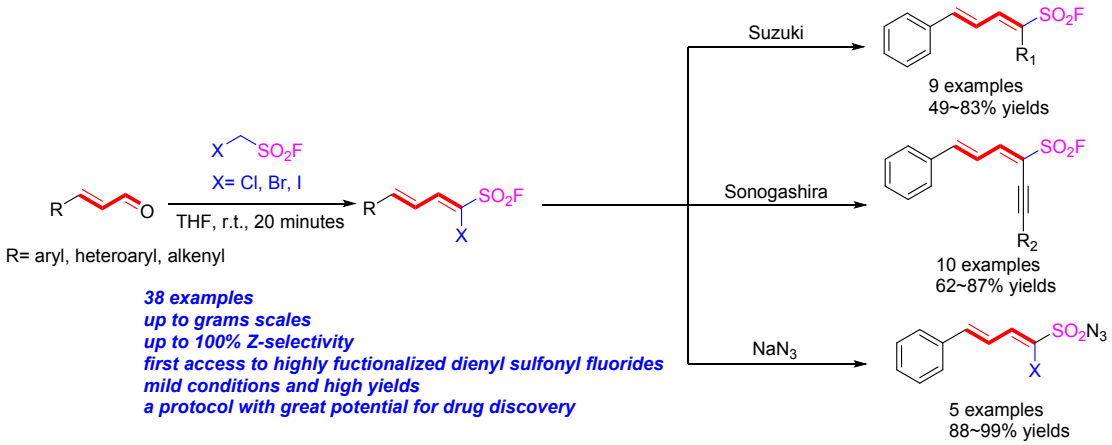


Abstract:

A pyrrolidine-mediated Knoevenagel-type reaction for highly stereoselective construction of novel α-halo-1,3-dienylsulfonyl fluorides was achieved in up to 100% *Z*-selectivity and high yields at room temperature from condensation of the readily available aldehydes and halomethanesulfonyl fluorides. This protocol provided a class of unique α-halo-1,3-dienylsulfonyl fluorides with wide scope and excellent functional group compatibility. The α-bromo-1,3-dienylsulfonyl fluorides

were used as versatile building blocks in SuFEx click chemistry, Suzuki reaction and Sonogashira reaction for assembly of highly functionalized dienyl sulfonyl fluoride derivatives to be applied as covalent warheads for discovery of new drugs.

Introduction

Covalent drugs, exerting pharmacological effects by covalently binding to biological targets, exhibit several advantages in pharmacodynamics and drug resistance comparing to their non-covalent counterparts (Figure 1a).[1] The alkenes conjugated with electron-withdrawing groups have played a significant role for discovery of covalent drugs that undergo irreversible Michael additions with a unique cysteine residue of a specific protein.[2] Meanwhile, sulfonyl fluorides are among the most prominent electrophiles for addressing the ε-amino group of lysine, the hydroxyl groups of tyrosine, serine, or threonine residues and they are somewhat reactive toward cysteine and histidine side chains as well.[3] Vinyl sulfonyl fluoride derivatives, as a representative class of novel scaffolds containing both olefin "Michael" acceptors and sulfonyl fluorides, have been widely applied in searching for covalent inhibitors, fluorogenic probes (Figure 1b), and discovery of new drugs.[4] In addition, with the development of sulfur fluoride exchange (SuFEx) click chemistry, sulfonyl fluorides have also garnered immense interest in organic synthesis, drug discovery, material science and many other fields.[5] The exploration of novel and practical methods for construction of diverse vinyl sulfonyl fluoride scaffolds is highly desirable and of great significance.

On the other hand, the functionalized 1,3-dienes[6] and conjugated polyenes[7] are the core motifs in biologically active molecules and natural products (Figure 1c). As for an efficient *Z*-selective diene synthesis, the convenience of starting materials should also be fully considered along with the aim of gaining a unique stereoselectivity. The Knoevenagel condensation is a well-established C=C double bond-forming reaction in organic synthesis.[8] A broad range of catalytic systems[9] have been exploited for the Knoevenagel condensation reaction. However,

stereoselectivity control is still difficult to achieve for this synthetic strategy. Herein, we report a pyrrolidine-mediated Knoevenagel–type condensation reaction for highly Z-selective C=C double bonds formation, as a novel method for the synthesis of valuable α-halo-1,3-dienylsulfonyl fluorides, using the inexpensive and highly abundant starting materials.

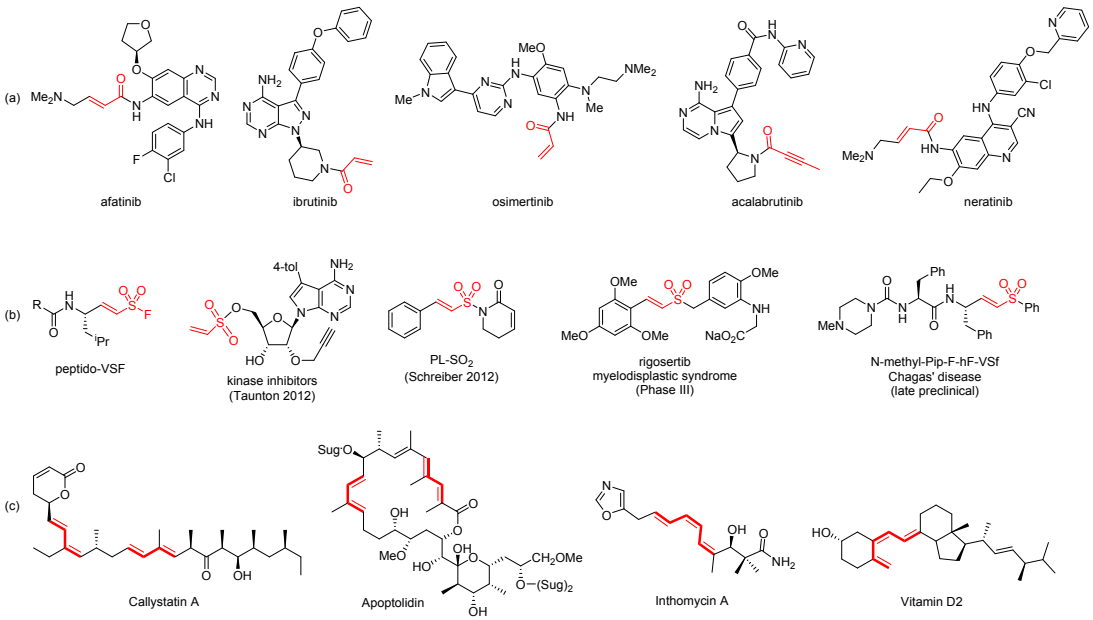


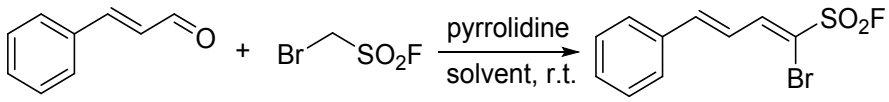
Figure 1. (a) Representative "Michael acceptor" covalent drugs; (b) Fluorogenic probes and drug candidates containing sulfonyl fluoride and vinyl sulfone motifs; (c) Natural products containing dienes and polyenes

There are two major challenges for achieving pyrrolidine-mediated synthesis of vinyl sulfonyl fluorides. The first challenge is that because the vinyl sulfonyl fluorides are very reactive "perfect" Michael acceptors, the secondary amine, pyrrolidine catalyst, may undergo Michael addition to destroy the newly generated olefin with simultaneous devitalizing catalytic activities.[10] The second challenge is that because the sulfonyl fluoride moieties are sensitive to bases, and the reaction of amine with sulfonyl fluoride may occur even under very mild conditions to form sulfonyl amide, which will consume both the amine catalyst and the sulfonyl fluoride products.[11] A cursory index of the literature indicated the Knoevenagel-type condensation of sulfonyl fluoride compounds are still

considerably rare and only one report involving the condensation reaction between methanedisulfonyl fluoride (MDSF) and 4-(dimethylamino)benzaldehyde in the presence of Ac_2O.[12] Accordingly, the relative studies on the Knoevenagel-type condensation of sulfonyl fluoride-containing molecules with aldehydes have been in high demand for the construction of highly functionalized dienyl sulfonyl fluorides.

Results and Discussion

Table 1 Optimization of the reaction conditions[a].



1a **2a** **3aa**

Entry	pyrrolidine (mol%)	**2a** (eq.)	Solvent	Conversion/%[b]	Yield/%[b]
1[c]	30	3	Acetonitrile	81	62
2[c]	30	3	DMF	75	63
3[c]	30	3	DCM	97	69
4[c]	30	3	THF	93	88
5	30	3	THF	93	89
6	**60**	**3**	**THF**	**100**	**95**
7	100	3	THF	100	88
8	60	2.0	THF	100	82
9	60	3.5	THF	100	95

[a]Reaction conditions: cinnamaldehyde (**1a**, 0.5 mmol) and pyrrolidine were dissolved in solvent (0.2 M, 2.5 mL) and the mixture was stirred for 5 minutes before the subsequent addition of **2a**. Then the stirring lasted for 20 minutes at room temperature. [b]The yield was determined by HPLC using **1a**, **3aa** as the external standards respectively ($t_{\mathbf{1a}}$ = 2.4 min, $\lambda_{max,\ \mathbf{1a}}$ = 284.4 nm; $t_{\mathbf{3aa}}$ = 4.1 min, $\lambda_{max,\ \mathbf{3aa}}$ = 322.5 nm; acetonitrile / water = 80 : 20 (v / v)). [c]1.1 equiv. KF was added as additive and the mixture was stirred overnight at room temperature.

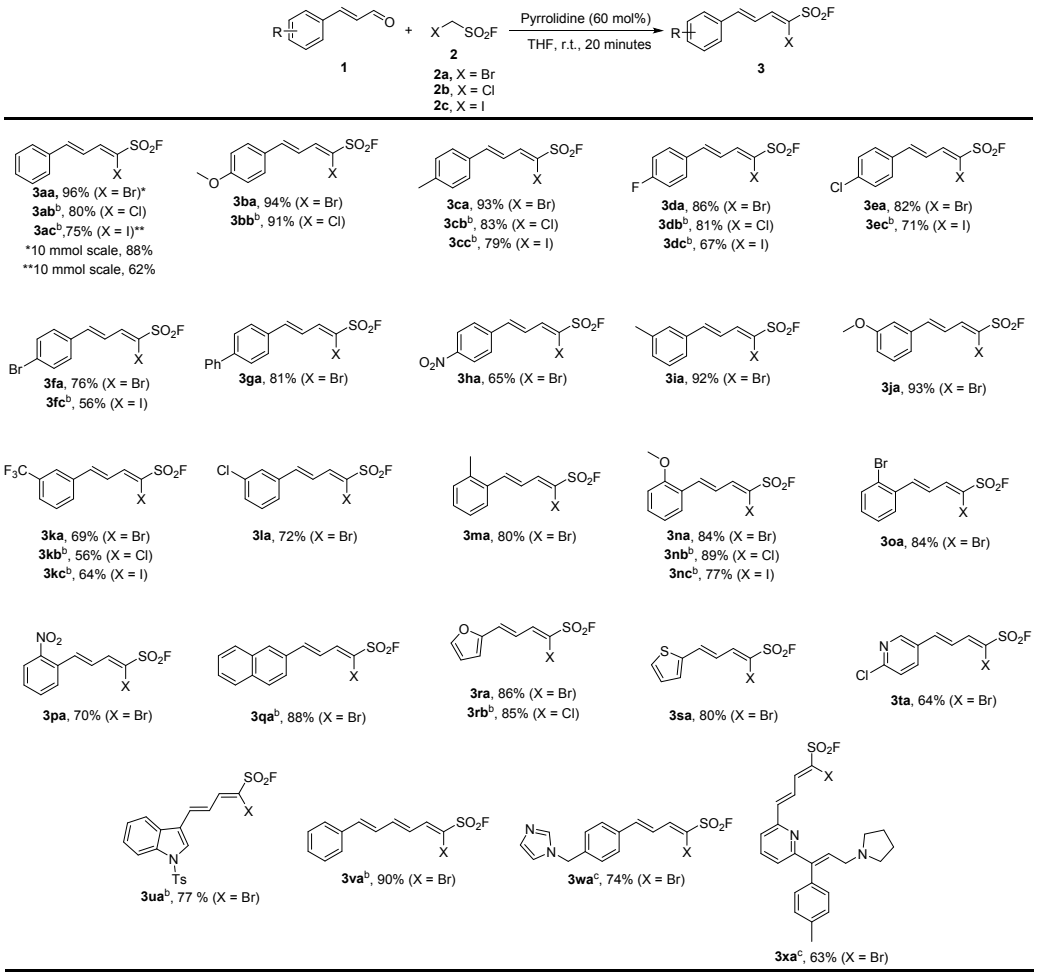
To test the feasibility of the proposed method, we initially examined

cinnamaldehyde (**1a**) and bromomethanesulfonyl fluoride (**2a**) as the model substrates for the construction of α-bromo-1,3-dienylsulfonyl fluoride (**3aa**) (Table 1). Pyrrolidine was found to be the optimal catalyst for this transformation (see Supporting Information for a more detailed account of optimization conditions). The investigation of solvent effect revealed that, despite some good results achieved in MeCN, DMF and DCM, THF was found to be the best choice (Table 1, entries 1-4). The comparable yield of **3aa** was also obtained without the addition of KF (Table 1, entry 4 *vs* entry 5). Elevating the catalyst loading to 60 mol%, the conversion of aldehyde **1a** and yield of product **3aa** was improved obviously (Table 1, entry 6). And further increasing the pyrrolidine amount to 100 mol%, the reaction efficiency was deteriorated slightly, owing to the aforementioned side reactions occurring under strong alkaline conditions (Table 1, entry 7). In addition, the use of an excess amount of bromomethanesulfonyl fluoride (**2a**) (3.0 equivalents) was found to be essential, and a significantly decreased yield was observed when **2a** was reduced to 2.0-fold-excess (Table 1, entries 7-9). Therefore, the entry 6 of Table 1 was eventually selected as the optimized conditions for the following preparative runs.

With the optimized reaction conditions in hand, we next evaluated the generality of this Knoevenagel-type condensation employing various aldehydes **1** to react with bromomethanesulfonyl fluorides (**2a**) for the formation of dienylsulfonyl fluorides (Table 2). A wide range of aryl vinyl aldehydes decorated with both electron-withdrawing and electron-donating groups on aryl rings (**1a-1p**) were efficiently converted to the corresponding α-bromo-1,3-dienylsulfonyl fluorides (**3aa-3pa**) in 70-96% yields. Furthermore, naphthalene aldehyde, heterocyclic aldehydes containing oxygen, sulfur, and nitrogen atoms on aryl rings (**1q-1u**) were smoothly transformed into the corresponding α-bromo-1,3-dienylsulfonyl fluorides (**3qa-3ua**) in 64-88% yields. In addition, dienal (**1v**) substrate was also successfully converted into its corresponding product (**3va**) in 90% yield. Besides, the derivative of drugs Ozagrel (**1w**) and Acrivastine (**1x**) turned out to be suitable substrates,

resulting in the expected transformation with 74% and 63% yields, respectively.

Table 2. Condensation of aldehydes with halomethylsulfonyl fluorides (2)[a].



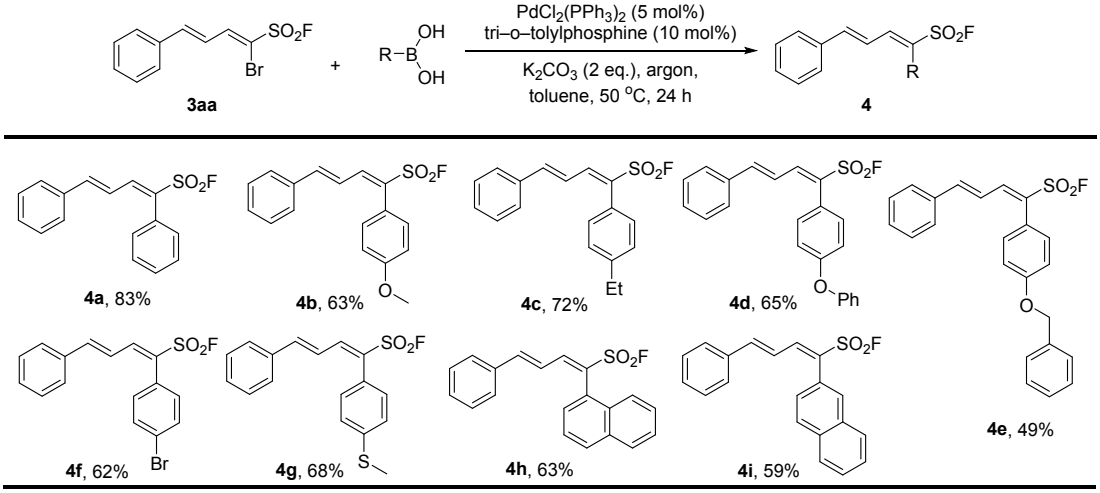
[a] Reaction conditions: aldehyde (**1**, 1.0 mmol), THF (5.0 mL), pyrrolidine (60 mol%, 50.0 μL), and halomethylsulfonyl fluoride (**2**, 3.0 mmol) were added in sequence, r.t., 20 minutes. [b] 0.5 mmol scale. [c] 0.2 mmol scale.

Subsequently, the chloromethanesulfonyl fluoride (**2b**) was also applied to the condensation process with aldehydes for preparing α-chloro-1,3-dienylsulfonyl fluorides. And the experiment results indicated that a series of aldehydes containing different substituents at *ortho*, *meta* or *para* position of aryl ring worked smoothly to generate their corresponding α-chloro-1,3-dienylsulfonyl fluorides (**3ab**-**3db**, **3kb** and **3nb**) in moderate to excellent yields (56% to 91%). O-heterocycle substrate

(**1r**) also underwent the condensation smoothly, furnishing its anticipated product (**3rb**) in 85% yield.

To further examine the scope of this protocol, we also explored the reaction of iodomethanesulfonyl fluoride (**2c**) with enals. Notably, electron-withdrawing and electron-donating groups substituted α-iodo-1,3-dienylsulfonyl fluorides (**3ac, 3cc-3fc, 3kc, 3nc**) were efficiently obtained from the condensation of aldehydes with iodomethanesulfonyl fluoride (**2c)** in moderate to good yields (56% to 79%) under the standard conditions. Nevertheless, the aryl aldehydes were not amenable for the fabrication of corresponding α-halogen arylethenesulfonyl fluorides when reacting with halomethylsulfonyl fluorides (**2**) under the standard conditions resulted in very low conversions together with generating a mixture of *E/Z* configuration of aryl vinyl bromines instead of the desired dienyl sulfonyl fluorides.

Table 3. Suzuki reaction of the *α*-bromo-1,3-dienylsulfonyl fluoride (3aa) with boronic acids

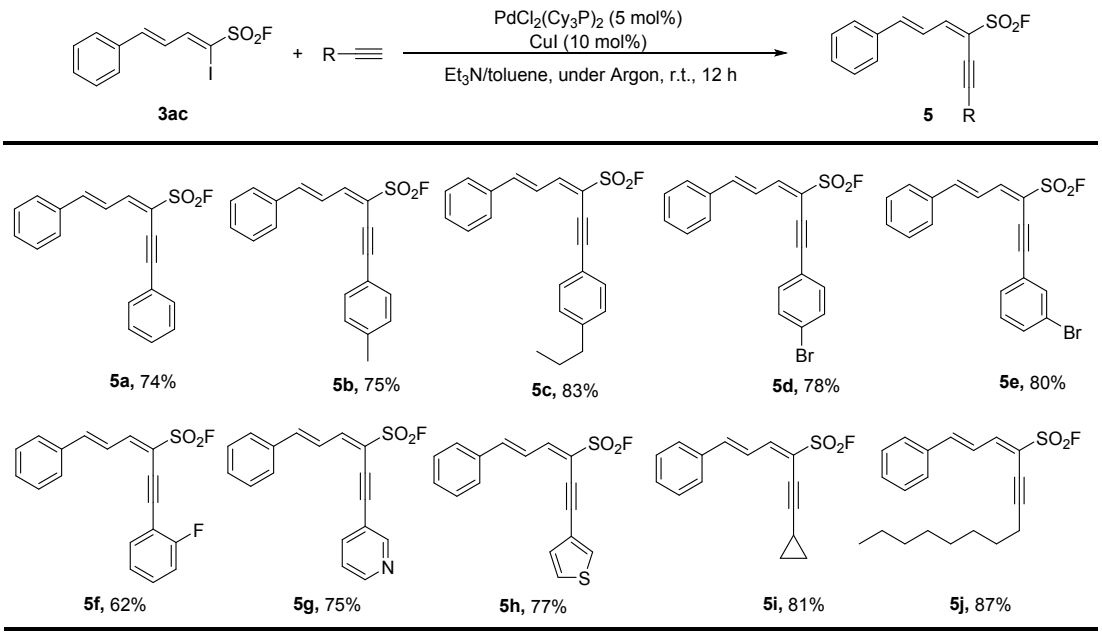


Reaction conditions: (1*Z*,3*E*)-1-bromo-4-phenylbuta-1,3-diene-1-sulfonyl fluoride (**3aa**, 0.5 mmol), phenylboronic acid (1.5 eq.), tri-o-tolylphosphine (10 mol%), $PdCl_2(PPh_3)_2$ (5 mol%), K_2CO_3 (2.0 eq.), toluene (5.0 mL), 50 °C, 24 h, under argon atmosphere.

The previous successful Pd-catalyzed Suzuki coupling of arylboronic acids with 1-bromoethene-1-sulfonyl fluoride (1-Br-ESF)[13] drove us to examine similar

reactions of α-bromo-1,3-dienylsulfonyl fluoride (**3aa**). Satisfyingly, the expected Suzuki coupling reaction proceeded smoothly under the catalysis of $PdCl_2(PPh_3)_2$, affording a series of novel dienylsulfonyl fluorides (Table 3). *Para*-substituted boronic acids were smoothly converted under Suzuki reaction condition to give the desired products (**4a-4g**) in moderate to good yields (49% to 83%). 1-Naphthal and 2-naphthal boronic acids also successfully provided the corresponding products (**4h** and **4i**) in 63% and 59% yields, respectively.

Table 4. Sonogashira reaction of the α- iodo-1,3-dienylsulfonyl fluoride (3ac) with alkynes

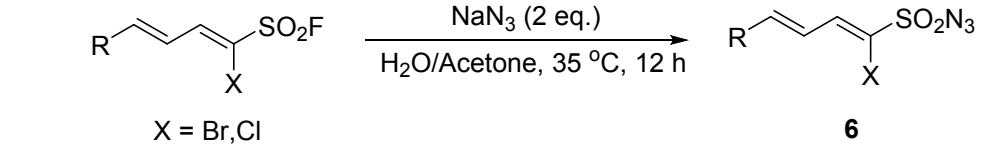


Reaction conditions: (1*Z*, 3*E*)-1-iodo-4-phenylbuta-1,3-diene-1-sulfonyl fluoride (**3ac**, 0.5 mmol), alkyne (1.5 eq.), CuI (10 mol%), $PdCl_2(Cy_3P)_2$ (5 mol%), Et_3N (0.5 mL.), toluene (1.5 mL), 50 ^oC, 12 h, under argon atmosphere.

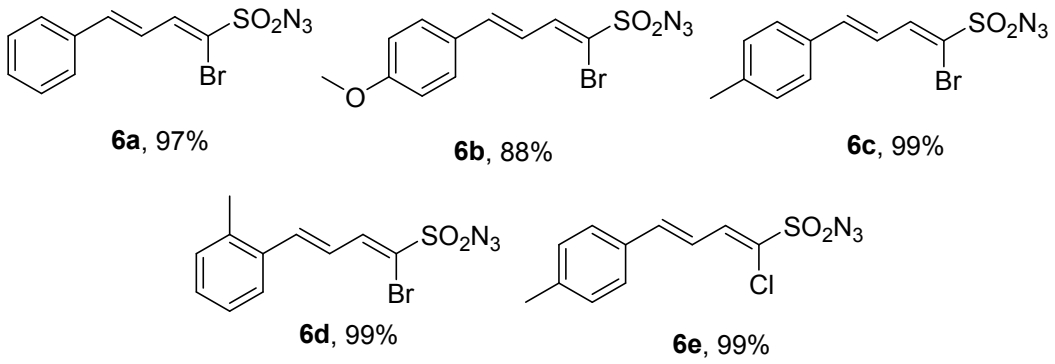
In addition, α-bromo-1,3-dienylsulfonyl fluoride (**3ac**) was further tested for Sonogashira reaction with alkynes to access another class of highly functionalized vinyl sulfonyl fluorides (Table 4). A range of alkynes with both electron-withdrawing and electron-donating groups on aryl ring were efficiently converted to the corresponding products (**5a-5f**) in 62% to 83% yields. Furthermore,

the alkynes contain *N*-, and S-heterocycles were smoothly transformed to their desired products (**5g** and **5h**) in 75% and 77% yields, respectively. Besides, the cyclic and long chain alkynes were also efficiently provided the corresponding products (**5i** and **5j**) in 81% and 87% yields, respectively.

Table 5. Synthesis of *α*-halo-1,3-dienesulfonyl azides from *α*-halo-1,3-dienylsulfonyl fluorides



X = Br,Cl **6**

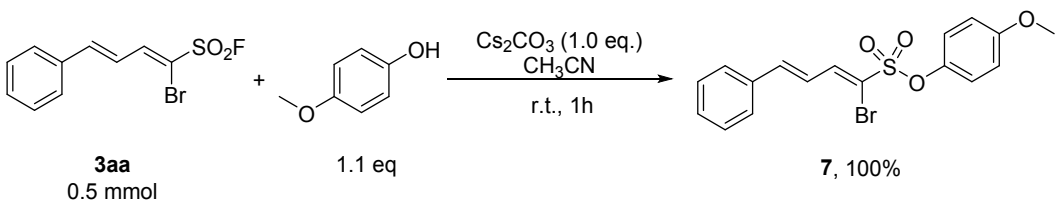


6a, 97% **6b**, 88% **6c**, 99%

6d, 99% **6e**, 99%

Reaction conditions: α-halo-1,3-dienylsulfonyl fluoride (0.25 mmol), Sodium azide (2.0 eq.), acetone (2.0 mL), H_2O (0.5 mL), 35 °C, 12 h.

In our final investigation, *α*-halo-1,3-dienylsulfonyl fluorides efficiently reacted with sodium azide in H_2O/Acetone co-solvent to give the corresponding *α*-halo-1,3-dienesulfonyl azides **6** in good to quantitative yields (Table 5). Under standard reaction conditions, diverse *α*-bromo-1,3-dienesulfonyl azides containing substituents at *ortho* and *para*-position (**6a-6d**) were obtained smoothly in 88-99% yields from the α-bromo-1,3-dienylsulfonyl fluorids. Besides, α-chloro-1,3-dienesulfonyl azide containing methyl substituent at *para*-position (**6e**) was also formed efficiently in quantitative yield.



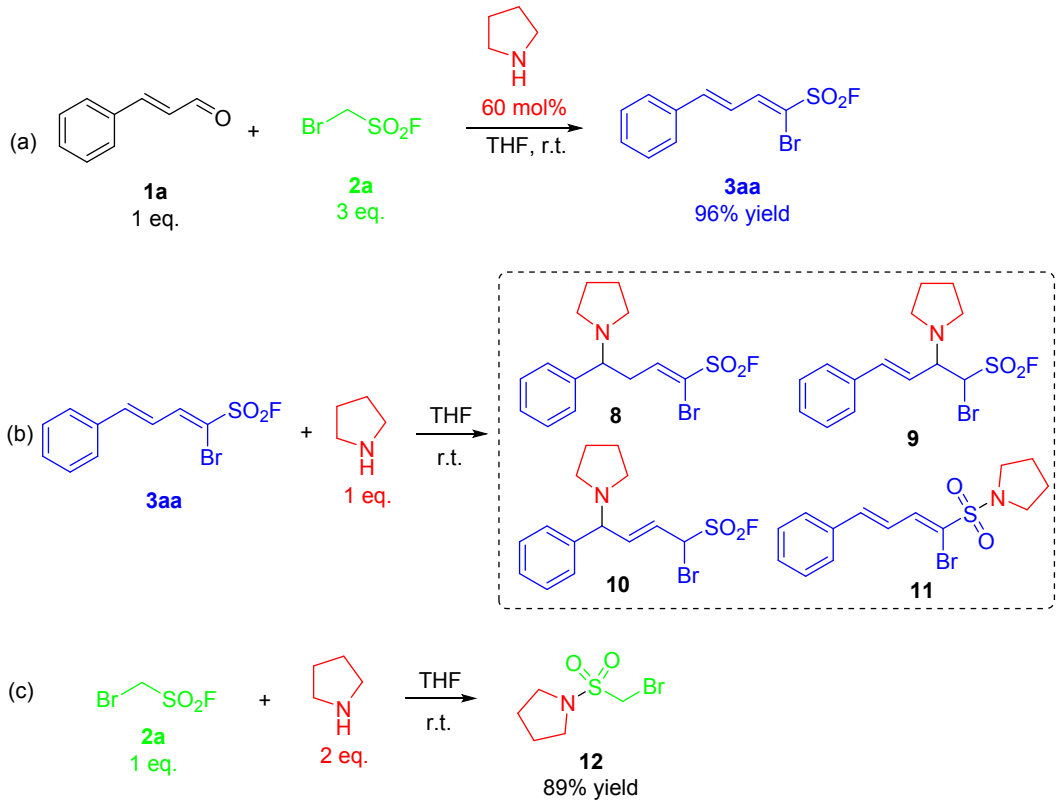
3aa
0.5 mmol

1.1 eq

7, 100%

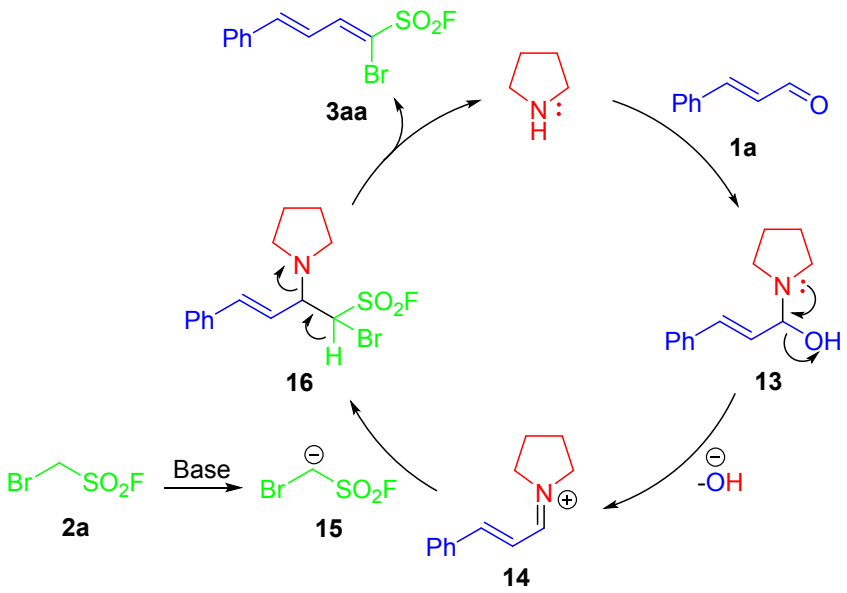
Scheme 1. SuFEx reaction of the new dienylsulfonyl fluoride (3aa)

The sulfonyl fluoride (-SO_2F) group was regarded as a robust connector in SuFEx chemistry. The utilization of the new α-bromo-1,3-dienylsulfonyl fluoride (**3aa**) for further SuFEx click reaction with phenol (Scheme 1) was also accomplished. With the aid of Cs_2CO_3 as a base, SuFEx reaction of **3aa** with the 4-methoxyphenol in acetonitrile at room temperature afforded the desired compound **7** in quantitative yield. It has to be noticed that the SuFEx reactions of **3aa** with amines including pyrrolidine, piperidine, morpholine for the synthesis of corresponding sulfamide were unsuccessful due to the various competitive reactions occurring simultaneously.



Scheme 2. (a) Desired Knoevenagel-type condensation. (b) Various competitive reaction of dienylsulfonyl fluoride 3aa with pyrrolidine. (c) SuFEx reaction of bromomethanesulfonyl fluoride 2a and pyrrolidine

In theory, the aldehyde, halomethylsulfonyl fluoride and dienylsulfonyl fluoride in the reaction system were all reactive to the strong nucleophilie pyrrolidine, resulting in a variety of transformations. Knoevenagel-type condensation distinguished itself from other competitors and become the leading reaction in our system. In order to uncover the process of this developed transformation, some control experiments were carried out in the Scheme 2. The reaction of cinnamaldehyde **1a** with bromomethanesulfonyl fluoride **2a** under the standard condition delivered the dienylsulfonyl fluoride **3aa** in nearly quantitative yield (Scheme 2a). The several reactive sites existing on the dienylsulfonyl fluoride **3aa** led to the reaction with pyrrolidine without regioselectivity and a mixture of Michael addition and nucleophilic substitution products were formed (Scheme 2b), which exactly accounted for the failure of SuFEx reaction of dienylsulfonyl fluorides with amines. Simply stirring the bromomethanesulfonyl fluoride **2a** with pyrrolidine in THF provided the SuFEx product 1-((bromomethyl)sulfonyl)pyrrolidine **12** as a white solid (Scheme 2c). Based on these control experiment results, we postulated that the aldehyde **1** preferentially combined with pyrrolidine to form an active intermediate, which participated in the subsequent condensation with halomethylsulfonyl fluoride **2** to generate the dienylsulfonyl fluoride **3**. After the completion of desired Knoevenagel-type reaction, the catalyst pyrrolidine remaining in the system was captured by excess of halomethylsulfonyl fluoride **2** *via* SuFEx reaction, which obviated aforementioned side reactions occurring with organocatalyst to stabilize the dienylsulfonyl fluoride **3** (Scheme 3).



Scheme 3. Proposed mechanism

Conclusion

In conclusion, a pyrrolidine-mediated Knoevenagel-type stereoselective construction of novel *α*-halo-1,3-dienylsulfonyl fluorides was developed. The transformations of a broad range of abundant, easily accessible, and inexpensive aldehydes into *α*-halo-1,3-dienylsulfonyl fluorides were conducted under mild conditions with up to 100% *Z*-selectivity. The desired *α*-halo-1,3-dienylsulfonyl fluorides were converted to two class of highly functionalized novel dienyl sulfonyl fluorides using Suzuki reaction and Sonogashira reaction. Further examinations of these scaffolds in drug discovery and chemical biology are ongoing in our laboratory.

Experimental section

General Information. All reactions were carried out under air atmosphere, unless otherwise specified. Oil bath was used for heating the reaction flasks. NMR spectra were recorded in $CDCl_3$ on a 500 MHz (for ^{1}H), 471 MHz (for ^{19}F), and 126 MHz (for ^{13}C) spectrometer. All chemical shifts were reported in ppm relative to TMS (^{1}H NMR, 0 ppm) as internal standards. Melting points of the products were

measured on a micro melting point apparatus (SGW X-4) and uncorrected. MS experiments were performed on a TOF-Q ESI or CI/EI instrument. Reagents and solvents used in the reactions were all purchased from commercial sources and used without further purification, unless otherwise noticed. The HPLC experiments were carried out on a Waters e2695 instrument (column: J&K, RP-C18, 5 μm, 4.6 × 150 mm), and the yields of the products were determined by using the corresponding pure compounds as the external standards. The coupling constants were reported in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

Procedure for the synthesis of bromomethanesulfonyl fluoride (2a).

Step 1: A mixture of CH_2Br_2 (343.7 g, 2 mol), Na_2SO_3 (252.1 g, 2 mol), tetrabutylammonium hydrogen sulfate (10.0 g, 0.03 mol), and H_2O (400 mL) / EtOH (200 mL) was refluxed for 36 h with vigorous stirring. The solvent was evaporated under vacuum and the resulting solid residue dissolved in a warm mixture of H_2O (320 mL) and EtOH (1800 mL). After filtration of some insoluble materials, the filtrate was cooled at -20 °C. The crystalline sodium salt was collected by filtration: 301.7 g (77% yield).

Step 2: The sulfonate was placed in a 500-ml, three-necked flask equipped with a stirrer, a glass stopper and a reflux condenser, and cooled with an ice bath. Phosphorus pentachloride (218.6 g, 1.05 mole) was added cautiously to the sulfonate (195.9 g, 1 mol) with vigorous stirring. It liquified immediately and the reddish brown solution was heated at 130 °C for 45 min and then at 70 °C for 30 min. The solution was then poured into 500 mL of ice-water and allowed to stand for 1 h in order to hydrolyze the phosphorus oxychloride. Bromomethanesulfonyl chloride was extracted with three 150-mL portions of methylene chloride. The combined methylene chloride extracts were washed with 200 mL of water, two 200-mL portions of 5% sodium bicarbonate, and finally with 150 mL of water. The solvent was evaporated to give crude bromomethanesulfonyl chloride which was

used directly in the next step.

Step 3: KHF_2 (156.2 g, 2 mol) was added to 400 mL water and a nearly saturated KHF_2 solution formed after 1 h, when the solution approached to room temperature. At this point, the crude bromomethanesulfonyl chloride generated from previous step was all added to KHF_2 solution. With continued stirring, the mixture was stirred for 2 h at room temperature. The stationary mixture separates into two phases. The upper phase is an aqueous solution of salts, and the lower phase is bromomethanesulfonyl fluoride. Bromomethanesulfonyl fluoride was extracted with three 100-mL portions of methylene chloride, the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 and concentrated by rotary evaporator to give crude bromomethanesulfonyl fluoride (slightly yellow liquid). Further distillation at 100 ^oC under reduced pressure with water-pump helped to remove the impurities and gave pure bromomethanesulfonyl fluoride as colorless liquid (105.5 g, 60% yield over two steps).

Bromomethanesulfonyl fluoride. (**2a**). Colorless liquid. ^1H NMR (500 MHz, $CDCl_3$) δ 4.70 (d, J = 4.4 Hz, 2H) $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 49.7 (m, 1F). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) 36.8 (d, J = 29.1 Hz). HRMS (EI) m/z: $[M]^+$ calcd for CH_2BrFO_2S 175.8943; found 175.8932.

Procedure for the synthesis of chloromethanesulfonyl fluoride (2b)

Step 1: A mixture of CH_2Cl_2 (25.4 g, 0.3 mol, 20 mL), Na_2SO_3 (25.2 g, 0.2 mol), tetrabutylammonium hydrogen sulfate (1.0 g, 3 mmol), and H_2O (100 mL) was refluxed for 36 h with vigorous stirring. The solvent was evaporated in vacuo and the resulting solid residue dissolved in a warm mixture of H_2O (32 mL) and EtOH (180 mL). After filtration of some insoluble materials, the filtrate was cooled at -20 °C. The crystalline sodium salt was collected by filtration: 17.0 g (56% yield).

Step 2: The sulfonate was placed in a 250-ml, three-necked flask equipped with a stirrer, a glass stopper and a reflux condenser, and cooled with an ice bath.

Phosphorus pentachloride (1.2 eq., 27.6 g, 133 mmol) was added cautiously to the sulfonate with vigorous stirring. It liquified immediately and the reddish brown solution was heated at 130 °C for 45 min and then at 70 °C for 30 min. The solution was then poured into 100 mL of ice-water and allowed to stand for 1 h in order to hydrolyze the phosphorus oxychloride. Chloromethanesulfonyl chloride was extracted with three 50-mL portions of methylene chloride. The combined methylene chloride extracts were washed with 50 mL of water, two 50-mL portions of 5% sodium bicarbonate, and finally with 50 mL of water. The solvent was evaporated to give crude product chloromethanesulfonyl chloride which was used directly in the next step.

Step3: The crude chloromethanesulfonyl chloride generated from previous step was all added to saturated KHF_2 solution [KHF_2 (15.6 g, 0.2 mol) was added to 40 mL water and a nearly saturated KHF_2 solution formed after 1 h].With continued stirring, the mixture was stirred for 2 h at room temperature. The stationary mixture separates into two phases. The upper phase is an aqueous solution of salts, and the lower phase is chloromethanesulfonyl fluoride. Chloromethanesulfonyl fluoride was extracted with three 50-mL portions of methylene chloride, the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 and concentrated by rotary evaporator to give crude chloromethanesulfonyl fluoride (slightly yellow liquid). Further distillation at 85 ^oC under reduced pressure with water-pump helped to remove the impurities and gave pure chloromethanesulfonyl fluoride as colorless liquid (7.1 g, 48% yield over two steps).

Chloromethanesulfonyl fluoride (**2b**). Colorless liquid. ^1H NMR (500 MHz, $CDCl_3$) δ 4.85 (d, J = 4.9 Hz, 2H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 48.3 (t, J = 5.7 Hz, 1F). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) 53.4 (d, J = 28.2 Hz). HRMS (EI) m/z: $[M]^+$ calcd for CH_2ClFO_2S, 131.9448; found 131.9445.

Procedure for the synthesis of iodomethanesulfonyl fluoride (2c)

Step 1: A mixture of CH_2I_2 (107.1 g, 0.4 mol), Na_2SO_3 (50.4 g, 0.4 mol), tetrabutylammonium hydrogen sulfate (2.0 g, 7.5 mmol), and H_2O (400 mL) / EtOH (200 mL) was refluxed for 36 h with vigorous stirring. The solvent was evaporated under vacuum and the resulting solid residue dissolved in a mixture of acetic acid (400 mL) and ethyl acetate (200 mL), and the mixture was heated to 100 °C for 1 h. The hot mixture was filtered, and another 1,000 mL ethyl acetate was poured into the filtrate. The sodium salt was collected by filtration: 52.7g (54% yield).

Step 2: The sulfonate was placed in a 500-ml, three-necked flask equipped with a stirrer, a glass stopper and a reflux condenser, and cooled with an ice bath. Phosphorus pentachloride (58.5 g, 1.3 eq.) was added cautiously to the sulfonate with vigorous stirring. It liquified after heating and the reddish brown solution was heated at 130 °C for 45 min and then at 70 °C for 30 min. The solution was then poured into 300 mL of ice-water and allowed to stand for 1 h in order to hydrolyze the phosphorus oxychloride. Iodomethanesulfonyl chloride was extracted with three 75-mL portions of methylene chloride. The combined methylene chloride extracts were washed with 200 mL of water, two 200-mL portions of 5% sodium bicarbonate, and finally with 150 mL of water. The solvent was evaporated to give crude product iodomethanesulfonyl chloride which was used directly in the next step.

Step3: The crude iodomethanesulfonyl chloride generated from previous step was all added to saturated KHF_2 solution [KHF_2 (31.2 g, 0.4 mol) was added to 80 mL water and a nearly saturated KHF_2 solution formed after 1 h]. With continued stirring, the mixture was stirred for 2 h at room temperature. The stationary mixture separates into two phases. The upper phase is an aqueous solution of salts, and the lower phase is iodomethanesulfonyl fluoride. Iodomethanesulfonyl fluoride was extracted with three 75-mL portions of methylene chloride. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated by rotary evaporator to give crude iodomethanesulfonyl fluoride (red-brown liquid). Further distillation at 135 ^oC under reduced pressure with oil-pump gave pure

iodomethanesulfonyl fluoride as red-brown liquid (35.3 g, 73% yield).

Iodomethanesulfonyl fluoride (**2c**). Red-brown liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.69 (d, J = 3.7 Hz, 2H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 51.4 (m, 1F). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) 3.5 (d, J = 26.3 Hz). HRMS (EI) m/z: $[M]^+$ calcd for CH_2FIO_2S, 223.8804; found 223.8809.

Preparation of Substrates.

1a-1f, **1k**, **1n**, **1p**, **1r** were purchased from commercial sources. **1g** and **1o** were prepared according to the literature[31]. **1h** and **1l** were prepared according to the literature[32]. **1i**, **1m**, **1q** and **1s** were prepared according to the literature[33]. **1j** was prepared according to the literature[34]. **1v** was prepared according to the literature[35]. **1u** was prepared according to the literature[36].

Preparation of (*E*)-3-(6-chloropyridin-3-yl)acrylaldehyde (1t). An oven-dried reaction flask was charged with 6-chloronicotinaldehyde (6 mmol, 2 eq.), 2-(triphenylphosphoranylidene) acetaldehyde (3 mmol, 1 eq.) and dry toluene (20 mL) under argon atmosphere, and the resulting mixture was stirred at 40 °C overnight. The reaction mixture was cooled to room temperature and the solvent was concentrated to dryness. The residue was purified through silica gel chromatography to afford the desired product (*E*)-3-(6-chloropyridin-3-yl)acrylaldehyde (**1t)** as white solid (266 mg, 53 % yield).

Preparation of (*E*)-3-(4-((1H-imidazol-1-yl)methyl)phenyl)acrylaldehyde (1w).

Step 1: To a solution of Ozagrel (500 mg, 2.19 mmol 1 equiv) dissolved in ethanol (10 mL) was added Me_3SiCl (5.0 eq.) in portion wise at 50 °C under nitrogen atmosphere. The resulting white turbidity slowly disappeared to form a yellow transparent solution. The stirring was lasted until the Ozagrel was completely consumed (monitored by TLC). Then solvent was removed under reduced pressure to get a white solid which was used directly in the next step.

Step 2: An oven-dried round bottom flask was charged with crude ethyl

(*E*)-3-(4-((1H-imidazol-1-yl)methyl)phenyl)acrylate and DCM (10 mL) under nitrogen atmosphere before cooling to -10°C (ice-methanol bath), then DIBAL (2.0 eq., 4.4 mL, 1.0 M solution in hexane) was slowly added via a syringe. Once the reaction was complete (monitored by TLC), the solution was concentrated to dryness and purified through silica gel chromatography using MeOH/DCM (5:95) as eluent to obtain the target alcohol as white solid. (356mg, 76 % yield, over two steps).

Step 3: To a solution of alcohol in DCM (10 mL) at 0 °C was added Dess-Martin periodinane (1.2 eq., 2 mmol) portion wise over 10 min. The reaction mixture was stirred at 0 °C for 30 minutes before warmed to room temperature for another 30 minutes. The mixture was concentrated to dryness and purified through silica gel chromatography using MeOH/DCM (5:95) as eluent to obtain (*E*)-3-(4-((1H-imidazol-1-yl)methyl)phenyl)acrylaldehyde (**1w**) as light yellow solid (226mg, 64 % yield).

Preparation of (*E*)-3-(6-((*E*)-3-(pyrrolidin-1-yl)-1-(*p*-tolyl)prop-1-en-1-yl) pyridine-2-yl)acrylaldehyde (1x).

Step 1: To a solution of Acrivastine (349 mg, 1 mmol 1 equiv) dissolved in ethanol (10 mL) was added Me_3SiCl (5.0 eq.) in portion wise at 50 °C under nitrogen atmosphere. The resulting white turbidity slowly disappeared to form a yellow transparent solution. The stirring was lasted until the Avastin was completely consumed (monitored by TLC). Then solvent was removed under reduced pressure to get a white solid which was used directly in the next step.

Step 2: An oven-dried round bottom flask was charged with crude ethyl (*E*)-3-(6-((*E*)-3-(pyrrolidin-1-yl)-1-(*p*-tolyl)prop-1-en-1-yl)pyridin-2-yl)acrylate and DCM (10 mL) under nitrogen atmosphere before cooling to -10°C (ice-methanol bath), then DIBAL (2 equiv, 2 mL, 1.0 M solution in hexane) was slowly added via a syringe. Once the reaction was complete (monitored by TLC), the solution was concentrated to dryness and purified through silica gel chromatography using

MeOH/DCM (5:95) as eluent to obtain the target alcohol as white solid. (291mg, 87 % yield, over two steps).

Step 3: To a solution of alcohol in DCM (10 mL) at 0 °C was added Dess-Martin periodinane (1.2 eq., 1.0 mmol) portion wise over 10 min. The reaction mixture was stirred at 0 °C for 30 minutes before warmed to room temperature for another 30 minutes. The mixture was concentrated to dryness and purified through silica gel chromatography using MeOH/DCM (5:95) as eluent to obtain (*E*)-3-(6-((*E*)-3-(pyrrolidin-1-yl)-1-(*p*-tolyl)prop-1-en-1-yl)pyridin-2-yl)acrylaldehyde (**1x**) as white solid (170mg, 59 % yield).

General procedures for the synthesis of 3.

To an oven-dried reaction tube was added aldehyde (**1**, 1.0 mmol, 1.0 eq.), pyrrolidine (60 mol%, 50 μL) and THF (0.2 M, 5 mL). And the stirring was lasted for 5 minutes before the subsequent addition of halomethylsulfonyl fluoride (**2**, 3.0 mmol, 3.0 eq.). Then the resulting mixture was allowed to stir at room temperature for about 20 minutes, until the aldehyde was completely consumed monitored by TLC. The mixture was diluted with DCM (10 mL) and concentrated to dryness under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain the desired products (**3aa-3ga**, **3ia-3oa**, **3qa-3sa** and **3va)**, petroleum ether / ethyl acetate = 7:1 (v/v) as eluent to obtain the desired products (**3ha** and **3pa),** MeOH/DCM = 5:95 (v/v) as eluent to obtain the desired product (**3ta**, **3ua**, **3wa** and **3xa**).

(1*Z*,3*E*)-1-bromo-4-phenylbuta-1,3-diene-1-sulfonyl fluoride (**3aa**). White solid, 278 mg, 96% yield. Mp: 76-78 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J = 10.6 Hz, 1H), 7.59-7.57 (m, 2H), 7.44-7.43 (m, 3H), 7.26 (d, J = 15.5 Hz, 1H), 7.01 (dd, J_1 = 15.6 Hz, J_2 = 10.7 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.1. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.1, 145.3, 134.9, 131.1, 129.3, 128.3, 122.0,

109.7 (d, J = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_8BrFO_2S$, 289.9412; found 289.9417.

(1*Z*,3*E*)-1-bromo-4-(4-methoxyphenyl)buta-1,3-diene-1-sulfonyl fluoride (**3ba**). Yellow solid, 301 mg, 94% yield. Mp: 93-95 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 10.7 Hz, 1H), 7.53 (d, J = 8.7 Hz, 2H), 7.20 (d, J = 15.6 Hz, 1H), 6.94 (d, J = 8.7 Hz, 2H), 6.87 (dd, J_1 = 15.5 Hz, J_2 = 10.7 Hz, 1H), 3.87 (s, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.4. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 162.2, 148.0, 145.9, 130.2, 127.8, 119.7, 114.8, 107.7 (d, J = 33.6 Hz), 55.6. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{11}H_{11}BrFO_3S$, 320.9591; found 320.9588.

(1*Z*,3*E*)-1-bromo-4-(p-tolyl)buta-1,3-diene-1-sulfonyl fluoride (**3ca**). Yellow solid, 283 mg, 93% yield. Mp: 109-110 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 10.7 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.24-7.21 (m, 3H), 6.96 (dd, J_1 = 15.6 Hz, J_2 = 10.7 Hz, 1H), 2.40 (s, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.2. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.2, 145.7(d, J = 2.7 Hz), 141.8, 132.3, 130.0, 128.4, 121.0, 108.8 (d, J = 33.6 Hz), 21.7. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{10}BrFO_2S$, 303.9569; found 303.9561.

(1*Z*,3*E*)-1-bromo-4-(4-fluorophenyl)buta-1,3-diene-1-sulfonyl fluoride (**3da**). Yellow solid, 265 mg, 86% yield. Mp: 80-82 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 10.7 Hz, 1H), 7.59-7.55 (m, 2H), 7.22 (d, J = 15.5 Hz 1H), 7.14-7.10 (m, 2H), 6.92 (dd, J_1 = 15.6 Hz, J_2 = 10.5 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.1, -107.9 (m, 1F). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 164.4 (d, J = 253.4 Hz), 146.6, 145.2, 131.2 (d, J = 2.7 Hz) ,130.3 (d, J = 8.2 Hz), 121.7, 116.5 (d, J = 22.7 Hz), 109.7 (d, J = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd. for $C_{10}H_7BrF_2O_2S$, 307.9318; found 307.9299.

(1*Z*,3*E*)-1-bromo-4-(4-chlorophenyl)buta-1,3-diene-1-sulfonyl fluoride (**3ea**). Yellow solid, 266 mg, 82% yield. Mp: 125-127 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 10.6 Hz, 1H), 7.51 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 15.6 Hz, 1H), 6.97 (dd, J_1 = 15.6 Hz, J_2 = 10.6 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.1. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 146.4, 144.9, 137.0, 133.4, 129.6, 129.4, 122.4, 110.3 (d, J = 33.6 Hz). HRMS (EI) m/z: $[M-H]^+$ calcd.

for $C_{10}H_6BrClFO_2S$, 322.8950; found 322.8970.

(1*Z*,3*E*)-1-bromo-4-(4-bromophenyl)buta-1,3-diene-1-sulfonyl fluoride (**3fa**). Yellow solid, 280 mg, 76% yield. Mp: 146–148 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 10.5 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 15.6 Hz, 1H), 6.99 (dd, J_1 = 15.5 Hz, J_2 = 10.5 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.1. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 146.4, 144.9 (d, *J* = 1.8 Hz), 133.8, 132.6, 129.6, 125.4, 122.5, 110.5 (d, *J* = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_7Br_2FO_2S$, 367.8518; found 367.8512.

(1*Z*,3*E*)-4-([1,1'-biphenyl]-4-yl)-1-bromobut a-1,3-diene-1-sulfonyl fluoride (**3ga**). Yellow solid, 296 mg, 81% yield. Mp: 150-152 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 10.5 Hz, 1H), 7.69-7.62 (m, 6H), 7.50-7.47 (m, 2H), 7.42-7.39 (m, 1H), 7.29 (d, J_1 = 15.4 Hz, 1H), 7.04 (dd, J_1 = 15.5 Hz, J_2 = 10.7 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.2. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 147.6, 145.4 (d, *J* = 1.9 Hz), 143.8, 140.0, 133.8, 129.1, 128.9, 128.3, 127.9, 127.2, 121.8, 109.4 (d, *J* = 32.7 Hz). HRMS (EI) m/z: $[M]^+$ calcd. for $C_{16}H_{12}BrFO_2S$, 365.9725; found 365.9707.

(1*Z*,3*E*)-1-bromo-4-(4-nitrophenyl)buta-1,3-diene-1-sulfonyl fluoride (**3ha**). Brown solid, 218 mg, 65% yield. Mp: 158-160 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.8 Hz, 2H), 7.95 (d, *J* = 10.5 Hz, 1H), 7.73 (d, *J* = 8.7 Hz, 2H), 7.31 (d, *J* = 15.5 Hz, 1H), 7.13 (dd, J_1 = 15.7 Hz, J_2 = 10.5 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 52.9. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.8, 144.3, 143.9(d, *J* = 1.8 Hz), 140.8, 128.8, 125.8, 124.5, 113.2 (d, *J* = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_7BrFNO_4S$, 334.9263; found 334.9268.

(1*Z*,3*E*)-1-bromo-4-(m-tolyl)buta-1,3-diene-1-sulfonyl fluoride(**3ia**). Yellow solid, 280 mg, 92% yield. Mp: 69-71 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 10.7 Hz, 1H), 7.37 (m, 2H), 7.34-7.30 (m, 1H), 7.26-7.21 (m, 2H), 6.99 (dd, J_1 = 15.6 Hz, J_2 = 10.7 Hz, 1H), 2.41 (s, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.1. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.4, 145.5 (d, *J* = 1.8 Hz), 139.0, 134.9, 132.0, 129.2, 128.9, 125.6, 121.7, 109.3 (d, *J* = 32.7 Hz), 21.4. HRMS (EI) m/z:

$[M]^+$ calcd. for $C_{11}H_{10}BrFO_2S$, 303.9569; found 303.9551.

(1*Z*,3*E*)-1-bromo-4-(3-methoxyphenyl)buta-1,3-diene-1-sulfonyl fluoride (**3ja**). Yellow solid, 298 mg, 93% yield. Mp: 54-56 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 10.6 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.22 (d, *J* = 15.5 Hz, 1H) , 7.17 (d, *J* = 7.6 Hz, 1H), 7.07 (m, 1H), 7.00-6.95 (m, 2H), 3.86 (s, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.1. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.2, 148.0, 145.3 (d, *J* = 1.8 Hz), 136.3, 130.3, 122.2, 121.0, 116.7, 113.5, 109.8 (d, *J* = 33.6 Hz), 55.5. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{10}BrFO_3S$, 319.9518; found 319.9513.

(1*Z*,3*E*)-1-bromo-4-(3-(trifluoromethyl)phenyl)buta-1,3-diene-1-sulfonyl fluoride (**3ka**). Yellow solid, 247 mg, 69% yield. Mp: 71-73 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 10.5 Hz, 1H), 7.76 (s, 1H), 7.72 (d, *J* = 7.7 Hz, 1H) , 7.65 (d, *J* = 7.7 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.24 (s, 1H), 7.03 (dd, J_1 = 15.5 Hz, J_2 = 10.5 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 52.9, -62.9. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 145.8, 144.5, 135.6, 131.9 (q, *J* = 32.7 Hz), 131.2, 129.9, 127.3 (q, *J* = 3.6 Hz), 124.8 (q, *J* = 3.6 Hz), 123.8 (q, *J* = 273.4 Hz), 123.6, 111.6 (d, *J* = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd. for $C_{11}H_7BrF_4O_2S$, 357.9286; found 357.9267.

(1*Z*,3*E*)-1-bromo-4-(3-chlorophenyl)buta-1,3-diene-1-sulfonyl fluoride (**3la**). Yellow solid, 233 mg, 72% yield. Mp: 65-67 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 10.5 Hz, 1H), 7.55-7.54 (m, 1H), 7.44 (d, *J* = 7.3 Hz, 1H), 7.41-7.35 (m, 2H), 7.18 (d, *J* = 15.7 Hz, 1H), 6.99 (dd, J_1 = 15.6 Hz, J_2 = 10.5 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.0. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 146.0, 144.7 (d, *J* = 1.8 Hz), 136.7, 135.4, 130.8, 130.5, 127.9, 126.5, 123.2, 111.1 (d, *J* = 32.7 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_7BrClFO_2S$, 323.9023; found 323.9029.

(1*Z*,3*E*)-1-bromo-4-(o-tolyl)buta-1,3-diene-1-sulfonyl fluoride (**3ma**). Yellow solid, 243 mg, 80% yield. Mp: 103-105 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 10.6 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 15.4 Hz, 1H) ,7.33 (td, J_1 = 7.4

Hz, J_2 = 1.1 Hz, 1H), 7.29-7.23 (m, 2H), 6.95 (dd, J_1 = 15.4 Hz, J_2 = 10.7 Hz, 1H), 2.44 (s, 3H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.1. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 145.6. 145.6, 137.9, 133.8, 131.2, 130.9, 126.8, 126.5, 122.9, 109.5 (d, J = 32.7 Hz), 19.9. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{10}BrFO_2S$, 303.9569; found 303.9561.

(1*Z*,3*E*)-1-bromo-4-(2-methoxyphenyl)buta-1,3-diene-1-sulfonyl fluoride (**3na**). Yellow solid, 269 mg, 84% yield. Mp: 78-80 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 10.7 Hz, 1H), 7.63-7.58 (m, 2H), 7.40 (t, J = 8.1 Hz, 1H), 7.07 (dd, J_1 = 15.6 Hz, J_2 = 10.7 Hz, 1H), 7.01 (t, J = 7.6 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 3.92 (s, 3H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.3. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 158.5, 146.5, 143.6, 132.5, 128.6, 123.9, 122.3, 121.1, 111.5, 108.3 (d, J = 32.7 Hz), 55.8. HRMS (EI) m/z: $[M]^+$ calcd. for $C_{11}H_{10}BrFO_3S$, 319.9518; found 319.9498.

(1*Z*,3*E*)-1-bromo-4-(2-bromophenyl)buta-1,3-diene-1-sulfonyl fluoride (**3oa**). Yellow solid, 309 mg, 84% yield. Mp: 112-114 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 10.5 Hz, 1H), 7.81-7.70 (m, 3H), 7.60 (t, J = 7.6 Hz 1H), 6.94 (dd, J_1 = 15.4 Hz, J_2 = 10.5 Hz 1H) $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 52.9. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 148.2, 144.2 (d, J = 2.7 Hz), 142.4, 133.9, 130.9, 130.8, 129.1, 126.4, 125.4, 112.9 (d, J = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_7Br_2FO_2S$, 367.8518; found 367.8511.

(1*Z*,3*E*)-1-bromo-4-(2-nitrophenyl)buta-1,3-diene-1-sulfonyl fluoride (**3pa**). Yellow solid, 234 mg, 70% yield. Mp: 109-111 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 8.3 Hz, 1H), 7.98 (d, J = 10.5 Hz, 1H), 7.81-7.70 (m, 3H), 7.59 (t, J = 7.9 Hz, 1H), 6.94 (dd, J_1 = 15.5 Hz, J_2 = 10.6 Hz, 1H) $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 52.9. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 148.2, 144.2 (d, J = 2.7 Hz), 142.4, 133.9, 130.9, 130.8, 129.1, 126.4, 125.4, 112.9 (d, J = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd. for $C_{10}H_7BrFNO_4S$, 334.9263; found 334.9245.

(1*Z*,3*E*)-1-bromo-4-(naphthalen-2-yl)buta-1,3-diene-1-sulfonyl fluoride (**3qa**). Yellow solid, 0.5mmol scale, 150 mg, 88% yield. Mp: 129–131 °C. ^1H NMR (500

MHz, $CDCl_3$) δ 7.97-7.93 (m, 2H), 7.90-7.85 (m, 3H), 7.72 (d, J = 8.5 Hz, 1H), 7.58-7.53 (m, 2H), 7.38 (d, J = 15.4 Hz, 1H), 7.10 (dd, J_1 = 15.5 Hz, J_2 = 10.6 Hz, 1H) $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.3. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 148.1, 145.4, 134.6, 133.4, 132.4, 130.5, 129.1, 128.8, 128.0, 127.9, 127.2, 123.4, 122.0, 109.5 (d, J = 32.7 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{10}BrFO_2S$, 339.9569; found 339.9565.

(1*Z*,3*E*)-1-bromo-4-(furan-2-yl)buta-1,3-diene-1-sulfonyl fluoride (**3ra**). White solid, 241 mg, 86% yield. Mp: 70–72 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 10.8 Hz, 1H), 7.57 (d, J = 1.2 Hz, 1H), 6.99 (d, J = 15.3 Hz, 1H), 6.87 (dd, J_1 = 15.2 Hz, J_2 = 10.8 Hz, 1H), 6.70 (d, J = 3.3 Hz, 1H), 6.53 (dd, J_1 = 3.3 Hz, J_2 = 1.7 Hz, 1H) $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.3. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 151.4, 145.9, 144.9 (d, J = 2.7 Hz), 133.2, 119.9, 116.2, 113.1, 109.1 (d, J = 32.7 Hz). HRMS (EI) m/z: $[M]^+$ calcd. for $C_8H_6BrFO_3S$, 279.9205; found 279.9186.

(1*Z*,3*E*)-1-bromo-4-(thiophen-2-yl)buta-1,3-diene-1-sulfonyl fluoride (**3sa**). Brown solid, 237 mg, 80% yield. Mp: 89–91 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 10.6 Hz, 1H), 7.48 (d, J = 5.0 Hz, 1H), 7.36 (d, J = 15.2 Hz, 1H), 7.31 (d, J = 3.5 Hz, 1H), 7.10 (dd, J_1 = 4.9 Hz, J_2 = 3.7 Hz, 1H), 6.76 (dd, J_1 = 15.3 Hz, J_2 = 10.7 Hz, 1H) $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.4. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 145.0 (d, J = 2.7 Hz), 140.4, 140.0, 131.7, 130.0, 128.7, 121.0, 108.7 (d, J = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_8H_6BrFO_2S_2$, 295.8977; found 295.8981.

(1*Z*,3*E*)-1-bromo-4-(6-chloropyridin-3-yl)buta-1,3-diene-1-sulfonyl fluoride (**3ta**). White solid, 208 mg, 64% yield. Mp: 149–151 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, J = 2.5 Hz, 1H), 7.92 (d, J = 10.5 Hz, 1H), 7.88 (dd, J_1 = 8.3 Hz, J_2 = 2.5 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.22 (d, J = 15.7 Hz, 1H), 7.03 (dd, J_1 = 15.7 Hz, J_2 = 10.5 Hz, 1H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.0. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 153.3, 149.7, 144.0 (d, J = 2.7 Hz), 142.1, 136.5, 129.7, 125.0, 124.3, 112.2 (d, J = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd. for $C_9H_6BrClFNO_2S$,

324.8975; found 324.8951.

(1*Z*,3*E*)-1-bromo-4-(1-tosyl-1H-indol-3-yl)buta-1,3-diene-1-sulfonyl fluoride (**3ua**). Yellow solid, 0.5 mmol scale, 186 mg, 77% yield. Mp: 154–156 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.1 Hz, 1H), 7.92-7.90 (m, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.44-7.27 (m, 5H), 7.04 (dd, J_1 = 15.6 Hz, J_2 = 10.7 Hz, 1H), 2.37 (s, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.5. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 146.0, 145.7 (d, *J* = 1.8 Hz), 138.8, 135.7, 134.7, 130.3, 128.8, 127.8, 127.2, 126.0, 124.6, 122.2, 120.6, 119.0, 114.1, 108.6 (d, *J* = 32.7 Hz), 21.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{15}BrFNO_4S_2$, 482.9610; found 482.9618.

(1*Z*,3*E*,5*E)*-1-bromo-6-phenylhexa-1,3,5-triene-1-sulfonyl fluoride (**3va**). Yellow solid, 0.5 mmol scale, 142 mg, 90% yield. Mp: 78–80 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 10.9 Hz, 1H), 7.50 (d, *J* = 7.0 Hz, 2H), 7.41-7.34 (m, 3H), 7.05 (dd, J_1 = 14.1 Hz, J_2 = 9.6 Hz, 1H), 7.01-6.92 (m, 2H), 6.56 (dd, J_1 = 14.3 Hz, J_2 = 10.9 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.4. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.1, 145.1 (d, *J* = 1.8 Hz), 141.6, 135.9, 129.7, 129.1, 127.6, 127.3, 125.5, 108.9 (d, *J* = 33.6 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{12}H_{10}BrFO_2S$, 315.9569; found 315.9574.

(1*Z*,3*E*)-4-(4-((1H-imidazol-1-yl)methyl)phenyl)-1-bromobuta-1,3-diene-1-sulfonyl fluoride (**3wa**). Gum, 0.2 mmol scale, 55 mg, 74% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 10.7 Hz, 1H), 7.64 (s, 1H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.23 (d, *J* = 15.6 Hz, 1H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.12 (s, 1H), 6.98 (dd, J_1 = 15.6 Hz, J_2 = 10.5 Hz, 1H), 6.91 (s, 1H), 5.17 (s, 2H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.1. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 146.8, 145.0 (d, *J* = 1.8 Hz), 138.9, 137.5, 135.0, 129.5, 128.8, 128.1, 122.5, 119.5, 110.3 (d, *J* = 32.7 Hz), 50.6. HRMS (EI) m/z: $[M]^+$ calcd. for $C_{14}H_{12}BrFN_2O_2S$, 369.9787; found 369.9764.

(1*Z*,3*E*)-1-bromo-4-(6-((*E*)-3-(pyrrolidin-1-yl)-1-(p-tolyl)prop-1-en-1-yl)pyridin-2-yl)buta-1,3-diene-1-sulfonyl fluoride (**3xa**). 0.2 mmol scale, gum, 62 mg, 63% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 10.9 Hz, 1H), 7.63-7.58 (m, 2H), 7.28-7.24 (m, 4H), 7.20 (t, *J* = 7.1 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 2H), 6.98 (d, *J* = 8.0

Hz, 1H), 3.45 (d, J = 7.0 Hz, 2H), 2.83 (m, 4H), 2.41 (s, 3H), 1.91-1.89 (m, 4H). $^{19}F\{^{1}H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 52.8. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 157.8, 152.1, 145.9, 144.4 (d, J = 1.8 Hz), 137.9, 137.4, 134.3, 129.6, 129.6, 126.0, 123.3, 123.2, 112.5 (d, J = 32.7 Hz), 54.2, 53.7, 23.6, 21.4. HRMS (ESI) m/z: $[M]^+$ calcd. for $C_{23}H_{24}BrFN_2O_2S$, 490.0726; found 490.0708.

(1*Z*,3*E*)-1-chloro-4-phenylbuta-1,3-diene-1-sulfonyl fluoride (**3ab**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 98 mg, 80% yield. Mp: 70-72 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 10.7 Hz, 1H), 7.58-7.56 (m, 2H), 7.44-7.42 (m, 3H), 7.20 (d, J = 15.7 Hz, 1H), 7.05 (dd, J_1 = 15.8 Hz, J_2 = 10.9 Hz, 1H). $^{19}F\{^{1}H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 52.6. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 147.4, 141.6 (d, J = 1.8 Hz), 134.9, 131.0, 129.3, 128.3, 121.1 (d, J = 33.6 Hz), 119.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_8ClFO_2S$, 245.9918; found 245.9914.

(1*Z*,3*E*)-1-chloro-4-(4-methoxyphenyl)buta-1,3-diene-1-sulfonyl fluoride (**3bb)**. 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 126 mg, 91% yield. Mp: 62-64 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, J = 10.9 Hz, 1H), 7.52 (d, J = 8.7 Hz, 2H), 7.14 (d, J = 15.6 Hz, 1H), 6.95-6.88 (m, 3H), 3.86 (s, 3H). $^{19}F\{^{1}H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 52.8. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 162.1, 147.3, 142.2 (d, J = 2.7 Hz), 130.1, 127.8, 119.3 (d, J = 32.7 Hz), 117.5, 114.8, 55.6. HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{11}H_9ClFO_3S$, 274.9950; found 274.9962.

(1*Z*,3*E*)-1-chloro-4-phenylbuta-1,3-diene-1-sulfonyl fluoride (**3cb**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 108 mg, 83% yield. Mp: 104-106 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 10.7 Hz, 1H), 7.46 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 15.6 Hz, 1H), 7.00 (dd, J_1 = 15.5 Hz, J_2 = 10.7 Hz, 1H), 2.40 (s, 3H). $^{19}F\{^{1}H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 52.7. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 147.5, 141.9 (d, J = 1.8 Hz), 141.7, 132.2, 130.0, 128.3, 120.3 (d, J = 33.6 Hz), 118.8,

21.7. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{10}ClFO_2S$, 260.0074; found 260.0079.

(1*Z*,3*E*)-1-chloro-4-(4-fluorophenyl)buta-1,3-diene-1-sulfonyl fluoride (**3db**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 107 mg, 81% yield. Mp: 80-82 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 10.7 Hz, 1H), 7.57-7.55 (m, 2H), 7.16 (d, J = 15.7 Hz, 1H), 7.14-7.10 (m, 2H), 6.97 (dd, J_1 = 15.6 Hz, J_2 = 10.8 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 52.5, -108.1 (m, 1F). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 164.3 (d, J = 253.5 Hz), 145.9, 141.4 (d, J = 1.8 Hz), 131.2 (d, J = 2.7 Hz), 130.2 (d, J = 8.2 Hz), 121.2 (d, J = 31.8 Hz), 119.6 (d, J = 2.7 Hz), 116.5 (d, J = 21.8 Hz). HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{10}H_6ClF_2O_2S$, 262.9751; found 262.9760.

(1*Z*,3*E*)-1-chloro-4-(3-(trifluoromethyl)phenyl)buta-1,3-diene-1-sulfonyl fluoride (**3kb**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 88 mg, 56% yield. Mp: 72-75 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.71 (d, J = 10.6 Hz, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7.22 (d, J = 15.7, 1H), 7.11 (dd, J_1 = 15.6 Hz, J_2 = 10.6 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 52.4, -62.9. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 145.1, 140.7 (d, J = 2.7 Hz), 135.7, 131.9 (q, J = 32.7 Hz), 131.1, 129.9, 127.2 (q, J = 3.6 Hz), 124.7 (q, J = 3.6 Hz), 123.8 (q, J = 273.4 Hz), 123.0, 121.5. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_7ClF_4O_2S$, 313.9791; found 313.9798.

(1*Z*,3*E*)-1-chloro-4-(2-methoxyphenyl)buta-1,3-diene-1-sulfonyl fluoride (**3nb**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 123 mg, 89% yield. Mp: 62-64 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 10.9 Hz, 1H), 7.59-7.54 (m, 2H), 7.41-7.38 (m, 1H), 7.11 (dd, J_1 = 15.6 Hz, J_2 = 10.8 Hz, 1H). 7.01 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 8.2 Hz, 1H), 3.91 (s, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 52.7. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 158.5, 142.9, 142.7 (d, J = 2.7 Hz), 132.4, 128.6, 123.9, 121.1, 120.2, 119.9 (d, J = 32.7 Hz), 111.5, 55.7. HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{11}H_9ClFO_3S$, 274.9950; found 274.9961.

(1*Z*,3*E*)-1-chloro-4-(furan-2-yl)buta-1,3-diene-1-sulfonyl fluoride (**3rb**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 100 mg, 85% yield. Mp: 65-67 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66-7.59 (m, 1H), 7.55 (d, J = 1.1 Hz, 1H), 6.95-6.88 (m, 2H), 6.68 (d, J = 3.4 Hz, 1H), 6.52 (dd, J_1 = 3.4 Hz, J_2 = 1.8 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 52.7. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.4, 145.8, 141.2 (d, J = 2.8 Hz), 132.6, 120.6 (d, J = 33.6 Hz), 117.8, 116.0, 113.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_8H_6ClFO_3S$, 235.9710; found 235.9719.

(1*Z*,3*E*)-1-iodo-4-phenylbuta-1,3-diene-1-sulfonyl fluoride (**3ac**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 127 mg, 75% yield. Mp: 103-105 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 10.3 Hz, 1H), 7.59-7.57 (m, 2H), 7.45-7.43 (m, 3H), 7.31 (d, J = 15.4 Hz, 1H), 6.89 (dd, J_1 = 15.5 Hz, J_2 = 10.5 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.8. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.8 (d, J = 1.9 Hz), 148.7, 134.9, 131.2, 129.3, 128.4, 125.9, 82.5 (d, J = 30.9 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_8FIO_2S$, 337.9274; found 337.9279.

(1*Z*,3*E*)-1-iodo-4-(p-tolyl)buta-1,3-diene-1-sulfonyl fluoride (**3cc**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 139 mg, 79% yield. Mp: 107-109 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 10.4 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 15.4 Hz, 1H), 7.24 (d, J = 8.1 Hz, 2H), 6.84 (dd, J_1 = 15.4 Hz, J_2 = 10.4 Hz, 1H), 2.40 (s, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 53.9. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 152.1 (d, J = 2.7 Hz), 148.9, 141.9, 132.2, 130.0, 128.4, 124.9, 81.4 (d, J = 30.9 Hz), 21.7. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{10}FIO_2S$, 351.9430; found 351.9427.

(1*Z*,3*E*)-4-(4-fluorophenyl)-1-iodobuta-1,3-diene-1-sulfonyl fluoride(**3dc**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 119 mg, 67% yield. Mp 84-86 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, J = 10.6 Hz, 1H), 7.59-7.56 (m, 2H), 7.27 (d, J = 15.6 Hz, 1H),

7.14-7.11 (m, 2H), 6.81 (dd, J_1 = 15.4 Hz, J_2 = 10.4 Hz, 1H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.8, -107.8 (m, 1F). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 164.4 (d, J = 253.4 Hz), 151.6 (d, J = 1.8 Hz), 147.2, 131.2 (d, J = 3.6 Hz), 130.3 (d, J = 8.2 Hz), 125.6, 116.5 (d, J = 22.7 Hz), 82.6 (dd, J_1 = 30.9 Hz, J_2 = 1.8 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_7F_2IO_2S$, 355.9179; found 355.9173.

(1*Z*,3*E*)-4-(4-chlorophenyl)-1-iodobuta-1,3-diene-1-sulfonyl fluoride(**3ec**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain white solid, 132 mg, 71% yield. Mp: 130-132 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, J = 10.4 Hz, 1H), 7.51 (d, J = 8.6 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 15.4 Hz, 1H), 6.85 (dd, J_1 = 15.4 Hz, J_2 = 10.4 Hz, 1H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.8. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 151.4 (d, J = 2.7 Hz), 147.0, 137.1, 133.4, 129.6, 129.5, 126.4, 83.3 (d, J = 30.9 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_7ClFIO_2S$, 371.8884; found 371.8887.

(1*Z*,3*E*)-4-(4-bromophenyl)-1-iodobuta-1,3-diene-1-sulfonyl fluoride(**3fc**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 116 mg, 56% yield. Mp: 132-134 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, J = 10.4 Hz, 1H), 7.56 (dt, J_1 = 8.4 Hz, J_2 = 2.5 Hz, 2H), 7.43 (dt, J_1 = 8.4 Hz, J_2 = 2.3 Hz, 2H), 7.23 (d, J = 15.6 Hz, 1H), 6.87 (dd, J_1 = 15.5 Hz, J_2 = 10.5 Hz, 1H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.7. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 151.4 (d, J = 2.7 Hz), 147.1, 133.8, 132.6, 129.6, 126.5, 125.5, 83.4 (d, J = 30.8 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_7BrFIO_2S$, 415.8379; found 415.8376.

(1Z,3E)-1-iodo-4-(3-(trifluoromethyl)phenyl)buta-1,3-diene-1-sulfonyl fluoride (**3kc**).0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain white solid, 130 mg, 64% yield. Mp: 78-80 °C. 1H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 10.4 Hz, 1H), 7.79 (s, 1H), 7.76 (d, J = 7.9 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7.32 (d, J = 15.6 Hz, 1H), 6.94 (dd, J_1 = 15.4 Hz, J_2 = 10.4 Hz, 1H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 53.6, -62.9. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 151.0 (d, J = 1.8 Hz), 146.4, 135.6,

131.9 (q, J = 32.7 Hz), 131.2, 129.9, 127.6, 127.3 (q, J = 3.7 Hz), 124.8 (q, J = 3.6 Hz), 123.8 (q, J = 273.4 Hz), 84.7 (d, J = 31.8 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_7F_4IO_2S$, 405.9148; found 405.9140.

(1*Z*,3*E*)-1-iodo-4-(2-methoxyphenyl)buta-1,3-diene-1-sulfonyl fluoride (**3nc**). 0.5 mmol scale. Using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to obtain yellow solid, 142 mg, 77% yield. Mp: 79-81 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 10.4 Hz, 1H), 7.65 (d, J = 15.5 Hz, 1H), 7.59 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H), 7.40 (td, J_1 = 8.7 Hz, J_2 = 1.6 Hz, 1H), 7.03-6.94 (m, 3H), 3.92 (s, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 54.0. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 158.5, 152.9 (d, J = 1.8 Hz), 144.3, 132.5, 128.8, 126.5, 123.9, 121.1, 111.5, 81.0 (d, J = 30.9 Hz), 55.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{10}FIO_3S$; 367.9379, found 367.9373.

General procedures for the synthesis of 4.

An oven-dried reaction tube was charged with **3aa** (0.5 mmol, 145 mg 1 eq.), phenylboronic acid (1.5 eq.), tri-*o*-tolylphosphine (10 mol%), $PdCl_2(PPh_3)_2$ (5 mol%), K_2CO_3(2.0 eq.) and dry toluene (2.5 mL) under nitrogen atmosphere before reacting at 50 °C for 24 h. Then reaction mixture was concentrated to dryness and the residue was purified through silica gel chromatography using petroleum ether / ethyl acetate = 40:1 (v/v) as eluents to afford the desired product **4**.

(1*E*,3*E*)-1,4-diphenylbuta-1,3-diene-1-sulfonyl fluoride (**4a**). Yellow oil, 120 mg, 83% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 11.3 Hz, 1H), 7.54-7.51 (m, 3H), 7.50-7.47 (m, 2H), 7.40-7.37 (m, 2H), 7.36-7.34 (m, 3H), 7.16 (d, J = 15.6 Hz, 1H), 6.68 (dd, J_1 = 15.5 Hz, J_2 = 11.3 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 56.6. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 145.9, 144.0 (d, J = 1.8 Hz), 135.2, 133.0 (d, J = 22.7 Hz), 130.9, 130.4, 130.2, 129.2, 129.1, 128.0, 121.6. HRMS (EI) m/z: $[M]^+$ calcd for $C_{16}H_{13}FO_2S$, 288.0620; found 288.0624.

(1*E*,3*E*)-1-(4-methoxyphenyl)-4-phenylbuta-1,3-diene-1-sulfonyl fluoride (**4b**).

Yellow solid, mp: 86-88 °C, 100 mg, 63% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 11.3 Hz, 1H), 7.41-7.38 (m, 4H), 7.35-7.34 (m, 3H), 7.13 (d, J = 15.6 Hz, 1H), 7.03 (d, J = 8.7 Hz, 2H), 6.70 (dd, J_1 = 15.6 Hz, J_2 = 11.1 Hz, 1H), 3.89 (s, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 56.0. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 161.0, 145.4, 143.5 (d, J = 1.8 Hz), 135.3, 132.9 (d, J = 21.8 Hz), 132.2, 130.2, 129.0, 127.9, 121.8, 121.0, 114.6, 55.5. HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{17}H_{14}FO_3S$, 317.0653; found 317.0658.

(1*E*,3*E*)-1-(4-ethylphenyl)-4-phenylbuta-1,3-diene-1-sulfonyl fluoride(**4c**). Yellow solid, mp: 96-98 °C, 114 mg, 72% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 11.3 Hz, 1H), 7.41-7.37 (m, 4H), 7.35-7.33 (m, 5H), 7.14 (d, J = 15.5 Hz, 1H), 6.71 (dd, J_1 = 15.5 Hz, J_2 = 11.1 Hz, 1H), 2.75 (q, J = 7.6 Hz, 2H), 1.32 (t, J = 7.6 Hz, 3H) ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 56.5. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 146.6, 145.5, 143.7 (d, J = 1.8 Hz), 135.3, 133.2 (d, J = 22.7 Hz), 130.7, 130.3, 129.0, 128.7, 128.0, 126.3, 121.8, 28.9, 15.3. HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{18}H_{16}FO_2S$, 315.0861; found 315.0870.

(1*E*,3*E*)-1-(4-phenoxyphenyl)-4-phenylbuta-1,3-diene-1-sulfonyl fluoride(**4d**). Yellow solid, mp: 91-93 °C, 124 mg, 65% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 11.1 Hz, 1H), 7.44-7.41 (m, 6H), 7.37-7.36 (m, 3H), 7.21 (t, J = 7.4 Hz, 1H), 7.17-7.13 (m, 3H), 7.10 (d, J = 8.6 Hz, 2H), 6.72 (dd, J_1 = 15.6 Hz, J_2 = 11.3 Hz, 1H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 56.4. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.5, 155.9, 145.8, 143.9 (d, J = 1.8 Hz), 135.2, 132.5(d, J = 22.7 Hz), 132.5, 130.4, 130.2, 129.1, 128.0, 124.5, 123.1, 121.6, 120.2, 118.3. HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{22}H_{16}FO_3S$, 379.0810; found 379.0814.

(1*E*,3*E*)-1-(4-(benzyloxy)phenyl)-4-phenylbuta-1,3-diene-1-sulfonyl fluoride(**4e**). Yellow solid, mp: 113-115 °C, 97 mg, 49% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 11.1 Hz, 1H), 7.49-7.35 (m, 12H), 7.14 (d, J = 15.7 Hz, 1H), 7.12-7.09 (m, 2H), 6.71 (dd, J_1 = 15.5 Hz, J_2 = 11.1 Hz, 1H), 5.14 (s, 2H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 56.2. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.3, 145.4, 143.6 (d, J = 1.8 Hz), 136.5, 135.3, 132.9 (d, J = 22.7 Hz), 132.3, 130.3, 129.1, 128.8,

128.4, 127.9, 127.7, 121.8, 121.3, 115.5, 70.3. HRMS (EI) m/z: $[M]^+$ calcd for $C_{23}H_{19}FO_3S$, 394.1039; found 394.1032.

(1*E*,3*E*)-1-(4-bromophenyl)-4-phenylbuta-1,3-diene-1-sulfonyl fluoride(**4f**). Yellow oil, 113 mg, 62% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 11.3 Hz, 1H),7.67-7.64 (m, 2H), 7.42-7.38 (m, 2H), 7.38-7.34 (m, 5H), 7.18 (d, J = 15.4 Hz, 1H), 6.64 (dd, J_1 = 15.6 Hz, J_2 = 11.3 Hz, 1H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 57.0. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) 146.6, 144.5 (d, J = 1.8 Hz) 135.0, 132.5, 132.4, 131.6 (d, J = 23.6 Hz), 130.6, 129.1, 128.1, 124.9, 121.1. HRMS (EI) m/z: $[M]^+$ calcd for C16H12BrFO2S, 365.9725; found 365.9729.

(1*E*,3*E*)-1-(4-(methylthio)phenyl)-4-phenylbuta-1,3-diene-1-sulfonyl fluoride(**4g**). Yellow solid, mp: 131-133 °C, 114 mg, 68% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 11.3 Hz, 1H), 7.41-7.34 (m, 9H), 7.15 (d, J = 15.5 Hz, 1H), 6.70 (dd, J_1 = 15.5 Hz, J_2 = 11.3 Hz, 1H), 2.55 (s, 3H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 56.7. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 145.9, 143.9 (d, J = 2.7 Hz), 141.9, 135.2, 132.5 (d, J = 22.7 Hz), 131.1, 130.4, 129.1, 128.0, 126.2, 125.2, 121.6, 15.2. HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{17}H_{14}FO_2S_2$, 333.0425; found 333.0429.

(1*E*,3*E*)-1-(naphthalen-1-yl)-4-phenylbuta-1,3-diene-1-sulfonyl fluoride(**4h**). Yellow oil, 106 mg °C, 63% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.8 Hz, 1H), δ 8.00 (d, J = 11.1 Hz, 1H), 7.98-7.96 (m, 1H), 7.84-7.82 (m, 1H), 7.64-7.54 (m, 4H), 7.30-7.21 (m, 5H), 7.17 (d, J = 15.5 Hz, 1H), 6.29 (dd, J_1 = 15.6 Hz, J_2 = 11.3 Hz, 1H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 55.6. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) 146.2, 146.1 (d, J = 1.8 Hz), 135.0, 133.9, 132.1, 131.0, 130.9, 130.4, 130.2, 128.9, 128.8, 128.0, 127.6, 126.7, 126.0, 125.5, 124.9, 121.7. HRMS (EI) m/z: $[M]^+$ calcd for $C_{20}H_{15}FO_2S$, 338.0777; found 338.0770.

(1*E*,3*E*)-1-(naphthalen-2-yl)-4-phenylbuta-1,3-diene-1-sulfonyl fluoride(**4i**). Yellow solid, mp: 92-94 °C, 100 mg, 59% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 8.9 Hz, 2H), δ 7.94 (t, J = 6.2 Hz, 2H), 7.82 (d, J = 11.2 Hz, 1H), 7.64-7.58 (m, 2H), 7.55 (dd, J_1 = 8.4 Hz, J_2 = 1.7 Hz, 1H), 7.37-7.34 (m, 2H), 7.32-7.29 (m, 3H), 7.19 (d, J = 15.5 Hz, 1H), 6.72 (dd, J_1 = 15.4 Hz, J_2 = 11.1 Hz, 1H). $^{19}F\{^1H, ^{13}C\}$ NMR

(471 MHz, $CDCl_3$) δ 56.9. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) 146.0, 144.2 (d, J = 2.7 Hz) 135.2, 133.8, 133.2, 133.0 (d, J = 22.7 Hz) 131.0, 130.4, 129.0, 129.0, 128.6, 128.0, 127.7, 127.4, 127.1, 126.5, 121.6. HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{20}H_{14}FO_2S$, 337.0704; found 337.0707.

General procedures for the synthesis of 5.

An oven-dried reaction tube was charged with **3ac** (0.5 mmol, 169 mg, 1 eq.), $PdCl_2$Bis(tricyclohexylphosphine) (5 mol%), CuI (10 mol%), dry toluene (1.5 mL), Et_3N (0.5 mL) and alkyne (1.5 mmol, 1.5 eq.) under nitrogen atmosphere, and the mixture was stirred at room temperature for 12 h. The mixture was concentrated to dryness and the residue was purified through silica gel chromatography using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to afford the desired product **5**.

(3*E*,5*E*)-1,6-diphenylhexa-3,5-dien-1-yne-3-sulfonyl fluoride (**5a**). Yellow solid, 115 mg, 74% yield. Mp: 104–106 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 10.2 Hz, 1H), 7.62-7.57 (m, 4H), 7.45-7.40 (m, 6H), 7.31-7.21 (m, 2H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 57.2. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 147.7, 147.1, 135.1, 132.1, 130.9, 130.0, 129.2, 128.7, 128.4, 122.6, 121.4, 117.0 (d, J = 27.2 Hz), 102.7, 78.0. HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{13}FO_2S$, 312.0620; found 312.0628.

(3*E*,5*E*)-6-phenyl-1-(p-tolyl)hexa-3,5-dien-1-yne-3-sulfonyl fluoride(**5b**). Yellow solid, 123 mg, 75% yield. Mp: 126–128 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 10.5 Hz, 1H), 7.59-7.57 (m, 2H), 7.50 (d, J = 8.1 Hz, 2H), 7.45-7.41 (m, 3H), 7.30-7.19 (m, 4H), 2.42 (s, 3H). $^{19}F\{^1H, ^{13}C\}$ NMR (471 MHz, $CDCl_3$) δ 57.0. $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 147.3, 146.8, 140.5, 135.2, 132.0, 130.9, 129.5, 129.2, 128.3, 122.7, 118.3, 117.2 (d, J = 27.3 Hz), 103.1, 77.5, 21.8. HRMS (EI) m/z: $[M]^+$ calcd for $C_{19}H_{15}FO_2S$, 326.0777; found 326.0774.

(3*E*,5*E*)-6-phenyl-1-(4-propylphenyl)hexa-3,5-dien-1-yne-3-sulfonyl fluoride(**5c**).

Yellow oil, 147 mg, 83% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, J = 10.7 Hz, 1H), 7.59-7.56 (m, 2H), 7.53 (d, J = 8.3 Hz, 2H), 7.45-7.40 (m, 3H), 7.31-7.19 (m, 4H), 2.65 (t, J = 7.5 Hz, 2H), 1.70-1.64 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 57.0. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 147.3 (d, J = 1.8 Hz), 146.7, 145.3, 135.2, 132.0, 130.8, 129.2, 128.9, 128.3, 122.7, 118.5, 117.3 (d, J = 27.2 Hz), 103.2, 77.5, 38.2, 24.4, 13.8. HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{21}H_{18}FO_2S$, 353.1017; found 353.1021.

(3*E*,5*E*)-1-(4-bromophenyl)-6-phenylhexa-3,5-dien-1-yne-3-sulfonyl fluoride (**5d**). Yellow solid, mp: 97-99 °C, 152 mg, 78% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74-7.68 (m, 1H), 7.59-7.54 (m, 4H), 7.47-7.42 (m, 5H), 7.27-7.20 (m, 2H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 57.5. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.2, 147.5, 135.0, 133.4, 132.1, 131.1, 129.3, 128.4, 124.6, 122.5, 120.3, 116.7 (d, J = 27.2 Hz), 101.5, 79.1. HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{12}BrFO_2S$, 389.9725; found 389.9721.

(3*E*,5*E*)-1-(3-bromophenyl)-6-phenylhexa-3,5-dien-1-yne-3-sulfonyl fluoride (**5e**). Yellow solid, mp: 109-111 °C, 156 mg, 80% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75-7.71 (m, 2H), 7.60-7.57 (m, 3H), 7.53 (d, J = 7.8 Hz, 1H) 7.47-7.41 (m, 3H), 7.31-7.21 (m, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 57.6. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.5 (d, J = 1.9 Hz), 147.8, 135.0, 134.6, 133.2, 131.1, 130.6, 130.2, 129.3, 128.5, 123.3, 122.5, 122.4, 116.5 (d, J = 28.1 Hz), 100.8, 79.1. HRMS (EI) m/z: $[M]^+$ calcd. for $C_{18}H_{12}BrFO_2S$, 389.9725; found 389.9711.

(3*E*,5*E*)-1-(2-fluorophenyl)-6-phenylhexa-3,5-dien-1-yne-3-sulfonyl fluoride (**5f**). Yellow solid, mp: 119-121 °C, 102 mg, 62% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 11.2 Hz, 1H), 7.61-7.56 (m, 3H), 7.46-7.40 (m, 4H), 7.37 (dd, J_1 = 15.4 Hz, J_2 = 11.2 Hz, 1H), 7.26-7.17 (m, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 57.8, -108.6 (m, 1F). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 163.0 (d, J = 253.4 Hz), 148.7, 147.6, 135.1, 133.4, 131.8 (d, J = 8.1 Hz), 131.0, 129.3, 128.5, 124.4 (d, J = 3.6 Hz), 122.7, 116.6 (d, J = 27.2 Hz), 115.9 (d, J = 20.9 Hz), 110.3 (d, J = 15.4 Hz), 96.1, 83.0 (d, J = 2.7 Hz). HRMS (EI) m/z: $[M]^+$ calcd for $C_{18}H_{12}F_2O_2S$,

330.0526; found 330.0520.

(3*E*,5*E*)-6-phenyl-1-(pyridin-3-yl)hexa-3,5-dien-1-yne-3-sulfonyl fluoride (**5g**). Yellow solid, mp: 104-106 °C, 117 mg, 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.65 (d, J = 3.9 Hz, 1H), 7.89 (dt, J_1 = 7.9 Hz, J_2 = 1.7 Hz, 1H), 7.78-7.71 (m, 1H), 7.59-7.57 (m, 2H), 7.46-7.42 (m, 3H), 7.36 (dd, J_1 = 7.8 Hz, J_2 = 4.9 Hz, 1H), 7.29-7.22 (m, 2H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 57.8. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 152.4, 150.1, 148.9, 148.1, 138.9, 134.9, 131.2, 129.3, 128.5, 123.3, 122.3, 118.7, 116.2 (d, J = 28.2 Hz), 98.9, 81.0. HRMS (EI) m/z: $[M-H]^+$ calcd. for $C_{17}H_{11}FNO_2S$, 312.0500; found 312.0501.

(3*E*,5*E*)-6-phenyl-1-(thiophen-3-yl)hexa-3,5-dien-1-yne-3-sulfonyl fluoride(**5h**). Yellow solid, mp: 98-100 °C, 122 mg, 77% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.68 (m, 2H), 7.59-7.56 (m, 2H), 7.45-7.42 (m, 3H), 7.37 (dd, J_1 = 5.0 Hz, J_2 = 3.0 Hz, 1H), 7.28-7.20 (m, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 57.2. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 147.7 (d, J = 1.8 Hz), 147.1, 135.1, 131.3, 130.9, 129.9, 129.2, 128.4, 126.2, 122.6, 120.5, 117.0 (d, J = 26.3 Hz), 97.9, 77.6. HRMS (EI) m/z: $[M]^+$ calcd for $C_{16}H_{11}FO_2S_2$, 318.0184; found 318.0181.

(3*E*,5*E*)-1-cyclopropyl-6-phenylhexa-3,5-dien-1-yne-3-sulfonyl fluoride(**5i**). Yellow solid, mp: 88-90, 112 mg, 81% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (t, J = 5.2 Hz 1H), 7.56-7.53 (m, 2H), 7.44-7.39 (m, 3H), 7.15-7.14 (m, 2H), 1.62-1.56 (m, 1H), 1.04-0.93 (m, 4H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 55.9. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 147.1 (d, J = 1.8 Hz), 146.1, 135.3, 130.6, 129.2, 128.2, 122.7, 117.6 (d, J = 26.3 Hz), 108.6, 64.8, 9.7, 0.9. HRMS (EI) m/z: $[M]^+$ calcd for $C_{15}H_{13}FO_2S$, 276.0620; found 276.0626.

(1*E*,3*E*)-1-phenyltetradeca-1,3-dien-5-yne-4-sulfonyl fluoride(**5j**). Yellow oil, 151 mg, 87% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61-7.59 (m, 1H), 7.56-7.53 (m, 2H), 7.44-7.38 (m, 3H), 7.21-7.13 (m, 2H), 2.55 (t, J = 7.0 Hz, 2H), 1.71-1.65 (m, 2H), 1.53-1.47 (m, 2H), 1.39-1.29 (m, 8H), 0.90-0.88 (m, 3H). ^{19}F{^{1}H, ^{13}C} NMR (471 MHz, $CDCl_3$) δ 55.9. ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 147.0 (d, J = 1.8 Hz), 146.0, 135.3, 130.7, 129.2, 128.2, 122.7, 117.7 (d, J = 26.4 Hz), 105.6, 69.9,

31.9, 29.3, 29.2, 29.0, 28.2, 22.8, 20.1, 14.2. HRMS (EI) m/z: $[M]^+$ calcd for $C_{20}H_{25}FO_2S$, 348.1559; found 348.1554.

General procedures for the synthesis of 6

To a solution of 1-halogen-1,3-diene-1-sulfonyl fluoride (0.25 mmol) in acetone (1.5 mL) was added dropwise a solution of sodium azide (0.5 mmol, 2 eq.) dissolved in water (0.5 mL). Then another portion of acetone (0.5 mL) was introduced subsequently. The reaction mixture was warmed up to 35°C and stirred overnight. The resulting mixture was poured into water (30 mL) and extracted with DCM (20 mL x 3). The combined organic layers were then washed with brine and dried over anhydrous $MgSO_4$. The crude product was purified by silica gel chromatography using a mixture of petroleum ether / ethyl acetate = 40:1 (v/v) as eluent to afford the product **6**.

(1*Z*,3*E*)-1-bromo-4-phenylbuta-1,3-diene-1-sulfonyl azide (**6a**). White solid, 76 mg, 97% yield. Mp: 60–62 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 10.5 Hz, 1H), 7.57-7.55 (m, 2H), 7.43-7.41 (m, 3H), 7.21 (d, J = 15.5 Hz, 1H), 6.97 (dd, J_1 = 15.6 Hz, J_2 = 10.5 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 142.0, 137.3, 130.1, 125.7, 124.2, 123.1, 116.9, 111.7. HRMS (EI) m/z: $[M]^+$ calcd for $C_{10}H_8BrN_3O_2S$, 312.9521; found 312.9527.

(1*Z*,3*E*)-1-bromo-4-(4-methoxyphenyl)buta-1,3-diene-1-sulfonyl azide (**6b**). Yellow solid, 75 mg, 88% yield. Mp: 84–86 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, J_1 = 10.7 Hz, J_2 = 0.5 Hz, 1H), 7.52-7.50 (m, 2H), 7.15 (d, J = 15.6 Hz, 1H), 6.94-6.92 (m, 2H), 6.83 (dd, J_1 = 15.5 Hz, J_2 = 10.6 Hz, 1H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 161.9, 146.9, 142.9, 129.9, 128.0, 119.7, 114.9, 114.7, 55.6. HRMS (EI) m/z: $[M]^+$ calcd. for $C_{11}H_{10}BrN_3O_3S$, 342.9626; found 342.9615.

(1*Z*,3*E*)-1-bromo-4-(p-tolyl)buta-1,3-diene-1-sulfonyl azide (**6c**). white solid, 81 mg, 99% yield. Mp: 64–66 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 10.7 Hz, 1H), 7.46 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 15.6 Hz, 1H),

6.93 (dd, J_1 = 15.5 Hz, J_2 = 10.5 Hz, 1H), 2.40 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 147.2, 142.7, 141.4, 132.5, 130.0, 128.2, 121.1, 116.0, 21.7. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{10}BrN_3O_2S$, 326.9677; found 326.9670.

(1*Z*,3*E*)-1-bromo-4-(o-tolyl)buta-1,3-diene-1-sulfonyl azide (**6d**). Yellow solid, 81 mg, 99% yield. Mp: 81–83 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 10.6 Hz, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.49 (d, J = 15.4 Hz, 1H), 7.31 (td, J_1 = 7.3 Hz, J_2 = 1.2 Hz, 1H), 7.28-7.22 (m, 2H), 6.91 (dd, J_1 = 15.4 Hz, J_2 = 10.6 Hz, 1H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 144.6, 142.6, 137.7, 134.0, 131.2, 130.6, 126.7, 126.4, 123.0, 116.6, 19.9. HRMS (EI) m/z: $[M]^+$ calcd. for $C_{11}H_{10}BrN_3O_2S$, 326.9677; found 326.9666.

(1*Z*,3*E*)-1-chloro-4-(p-tolyl)buta-1,3-diene-1-sulfonyl azide (**6e**). White solid, 70 mg, 99% yield. Mp: 64–66 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 10.6 Hz, 1H), 7.45 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 15.6 Hz, 1H), 6.97 (dd, J_1 = 15.5 Hz, J_2 = 10.7 Hz, 1H), 2.39 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 146.5, 141.3, 139.0, 132.5, 129.9, 128.1, 126.3, 118.9, 21.6. HRMS (EI) m/z: $[M]^+$ calcd for $C_{11}H_{10}ClN_3O_2S$, 283.0182; found 283.0187.

Procedures for the synthesis of 7.

An oven-dried reaction tube was charged with (1*Z*,3*E*)-1-bromo-4-phenylbuta-1,3-diene-1-sulfonyl fluoride (**3aa**, 0.5 mmol, 145 mg), 4-methoxyphenol (0.55 mmol, 69 mg), Cs_2CO_3 (0.5 mmol, 163 mg) and CH_3CN (2 mL), then the mixture was reacted at room temperature for 1 h monitored by TLC. After the reaction reached its completion, the solution was concentrated to dryness and the residue was purified through silica gel chromatography using petroleum ether / ethyl acetate = 10:1 (v/v) as eluent to afford the desired product **7** in 100 % yield (197 mg).

4-methoxyphenyl (1*Z*,3*E*)-1-bromo-4-phenylbuta-1,3-diene-1-sulfonate (**7**). white solid, 197 mg, 100% yield. Mp: 65-67 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J

= 10.2 Hz, 1H), 7.53-7.51 (m, 2H), 7.40-7.38 (m, 3H), 7.22-7.20 (m, 2H), 7.04 (d, J = 15.6 Hz, 1H), 6.96 (dd, J_1 = 15.5 Hz, J_2 = 10.0 Hz, 1H), 6.88-6.86 (m, 2H), 3.78 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 158.6, 146.0, 143.7, 143.1, 135.2, 130.5, 129.2, 128.0, 123.2, 122.4, 114.8, 112.9, 55.7. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{17}H_{16}BrO_qS$, 394.9947; found 394.9941.

Procedures for the synthesis of 12.

An oven-dried reaction tube was charged with bromomethanesulfonyl fluoride (**2a**, 1 mmol, 176 mg), pyrrolidine (2.0 eq., 142 mg) and THF (2.5 mL), and the resulting mixture was stirred at room temperature for 2 h. The mixture was concentrated to dryness and the residue was purified through silica gel chromatography using a mixture of petroleum ether / ethyl acetate = 3:1 (v/v) as eluent to afford the desired product **12**.

1-((bromomethyl)sulfonyl)pyrrolidine (**12**).[14] White solid, 202 mg, 89% yield, Mp: 100-102 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 4.46 (s, 2H), 3.52-3.49 (m, 4H), 2.00-1.98 (m, 4H).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Crystallographic data for **3fa** (CIF)

Optimization studies; copies of ^1H, ^{19}F, ^{13}C NMR, and single-crystal X-ray crystallography data for product **3fa** (CCDC 1976921)

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Notes

The authors declare no competing financial interest.

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