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Highly *E*-Selective Synthesis of α-Fluoro-β-arylalkenyl Sulfones from *gem*-Difluoroalkenes with Sodium Sulfinates

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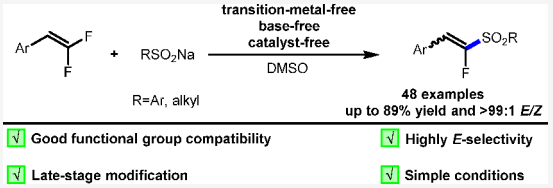
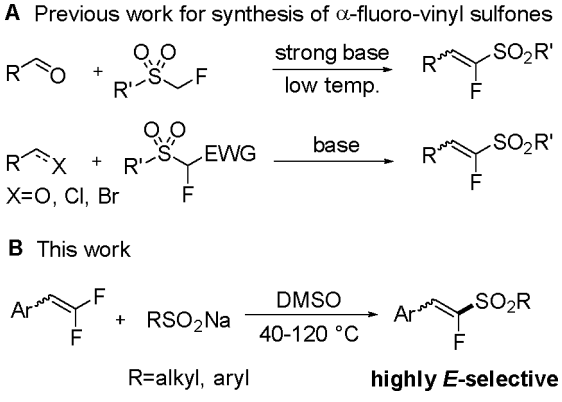
ABSTRACT: The straightforward synthesis of α-fluoro-β-arylalkenyl sulfones under transition-metal- and base-free conditions has been described, which displays broad functional group compatibility and high stereoselectivity. In particular, the strategy is also applied to the late-stage modification of complex natural products and drugs.



Considering the importance of vinyl sulfone compounds in organic chemistry, biology, and the pharmaceutical field, numerous studies have been performed.[1] α-Fluoro-vinyl sulfones make up a valuable class of vinyl sulfones, and the routes to these functional molecules have been studied by many research groups (Scheme 1).[2] Reactions such as

Scheme 1. Strategies for the Synthesis of α-Fluoro-vinyl Sulfones



Horner−Wadsworth−Emmons reaction[2a] and Julia−Kocienski olefination[2b,f−h] involve nucleophilic addition of $RSO_2CHR'F$ to carbonyl compounds with the aid of bases. Olah et al. utilized benzyl halides instead of carbonyl compounds to achieve the Julia−Kocienski olefination.[2d] However, most of them suffer from an excess of strong base, low temperatures, moderate *E*/*Z* selectivity, or low atom economies. Consequently, the development of useful measures to assemble highly stereoselective α-fluoro-vinyl sulfones utilizing bench-stable and easily accessible precursors under mild conditions is still desirable and challenging.

Due to the distinct chemical and biological properties, organofluorinated compounds are gaining prominence in bioorganic and medicinal chemistry.[3] For instance, it was calculated that approximately 30−40% of new drugs approved by the Food and Drug Administration contained fluorine in 2018 and 2019.[4] Therefore, the rapidly growing demand for the introduction of fluorine and fluorine-containing groups into organic functional molecules has also inspired the development of approaches to install and further diversify fluorinated products. In recent years, the functionalization of C−F bonds in polyfluorinated compounds offers an attractive approach for building value-added fluorinated molecules.[5] In particular, selective cleavage and transformation of one C−F bond *gem*-difluoroalkene provides an attractive alternative to functionalized monofluoroalkenes that can be used as peptide bond isosteres in drug discovery.[6] The difluoromethylene carbon of *gem*-difluoroalkenes is susceptible to nucleophilic attack, such as various carbon-,[7] oxygen-,[8] nitrogen-,[9] boron-,[10] silicon-,[11] sulfur-,[12] and phosphine[13]-centered nucleophilic intermediates. Very recently, we disclosed the visible-light-promoted *E*-selective synthesis of α-fluoro-β-arylalkenyl sulfides with *gem*-difluoroalkenes and sodium sulfinates via a deoxygenation/isomerization process.[14] Herein, we report a simple method for installing highly *E*-selective α-fluoro-β-arylalkenyl sulfones under transition-metal- and base-free conditions from *gem*-difluoroalkenes and sodium sulfinates.

Initially, 2-(2,2-difluorovinyl)naphthalene **1a** and sodium benzenesulfinate **2a** were chosen as the starting materials to test this transformation (for more details about the optimization of reaction conditions, see Tables S1−S4). Fortunately, the desired product **3aa** was isolated in 82% yield with excellent stereoselectivity (>99/1 *E*/*Z*)[2] at 100 °C in DMSO.

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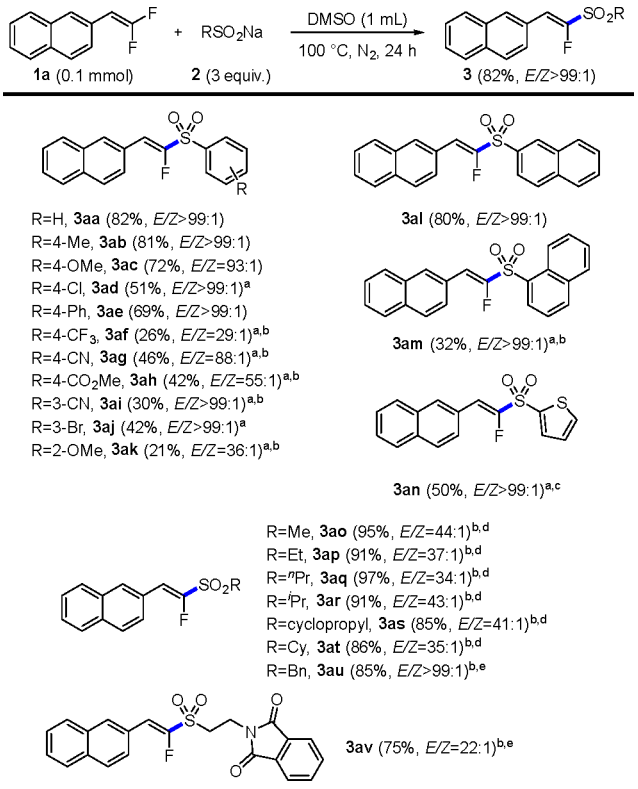
With the optimized conditions in hand, we preliminarily investigated the reaction scope of sodium sulfinates under the optimal conditions. As depicted in Table 1, with *gem*-difluoroalkene **1a** as a representative difluoroalkene partner, we were glad to find that a variety of sodium sulfinates underwent defluorinative cross coupling to furnish the target products in moderate to good yields with excellent stereoselectivities (**3aa**–**av**). Sodium arylsulfinates bearing electron-donating groups (Me and OMe) or electron-withdrawing groups (CF_3, CN, and CO_2Me) at the *para* position of the aryl rings were quite compatible, furnishing the corresponding products in 42–81% yields (**3ab**, **3ac**, and **3af**–**ah**). Generally, electron-rich substrates afforded better product yields than electron-deficient substrates, because the electron-rich substrates were more susceptible to nucleophilic attack. Notably, halogen-functionalized sodium arylsulfinates reacted smoothly to give target products in moderate yields and excellent stereoselectivities (**3ad** and **3aj**), enabling latter availability for additional treatment. Furthermore, an *ortho*-substituted substrate participated in the reaction, albeit in poor yield (**3ak** and **3am**), due to the steric hindrance effect. Gratifyingly, a variety of sodium alkylsulfinates turned out to be efficient substrates, leading to **3ao**–**av** in 75–97% yields with excellent *E*/*Z* selectivities.

Subsequently, we further explored the scope of *gem*-difluoroalkenes, and various substituted *gem*-difluorostyrenes were applied to the reaction with **2b** (Table 2). *gem*-Difluorostyrenes possessing various functional groups on the aryl rings such as 3,4-dimethoxyl, *p*-^{t}Bu, *p*-CO_2Me, *p*-Bnep, *p*-I, etc., converted to the desired products in moderate yields and outstanding *E*/*Z* ratios (**3bb**–**fb**). Moreover, polycyclic aromatic *gem*-difluoroalkenes were amenable to this method, leading to the corresponding products in 73–85% yields (**3ib**–**mb**). Importantly, (hetero)aryl difluoroalkenes were also screened, leading to quinolone (**1n**), benzothiophene (**1o**), carbazole (**1p**), and indole (**1q** and **1r**) heterocycles being transformed into the expected products with satisfactory yields. It is worth mentioning that under the influence of electronic repulsion[7,15] between F and the electron-rich aromatic ring, products **3oo** and **3qb** had poor *E*/*Z* stereoselectivities.

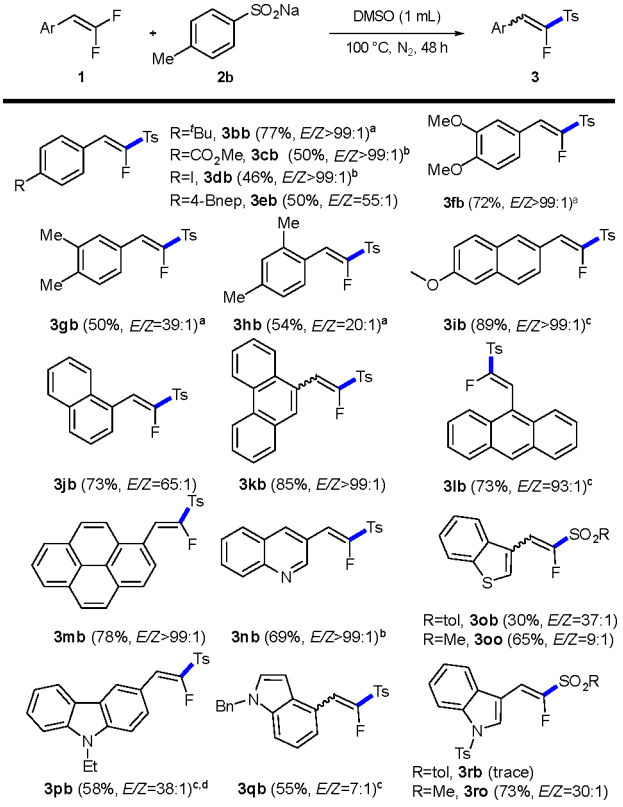
To highlight the robustness and generality of the synthetic utility of our method, we evaluated the protocol in the late-stage modification of complex natural products and drugs (Scheme 2). Small molecule drug mexiletine derivate was coupled with sodium 4-methylbenzenesulfinate **2b** to afford desired product **4a** in high yield (84%). *gem*-Difluoroalkenes bearing cholesterol, menthol, estrone, and tocopherol, four well-known bioactive natural alcohols, were readily adapted to the target α-fluoro-vinyl sulfones **4b**–**e** and **4h** in synthetically useful yields (45–82%) with excellent stereoselectivities. The protocol could also be applied to saccharides, such as ribofuranose and fructose derivatives, providing the corresponding α-fluoro-vinyl sulfone derivatives (**4f** and **4g**, respectively).

Table 1. Substrate Scope of Sodium Sulfinates with *gem*-Difluorostyrene 1a[f]



[a]**2** (4 equiv). [b]For 48 h. [c]For 3 days. [d]At 40 °C. [e]At 70 °C. [f]All reactions were performed with **1a** (0.10 mmol), **2** (3 equiv), and DMSO (1.0 mL) at 100 °C for 24 h under N_2 unless otherwise noted. The *E*/*Z* ratio was determined by ^{19}F NMR.

Table 2. Substrate Scope of *gem*-Difluorostyrenes with Sodium Sulfinate 2b[e]



[a]**2b** (4 equiv), 5 days. [b]At 70 °C. [c]For 3 days. [d]At 120 °C. [e]All reactions were performed with **1** (0.10 mmol), **2b** (3 equiv), and DMSO (1.0 mL) at 100 °C for 48 h under N_2 unless otherwise noted. The *E*/*Z* ratio was determined by ^{19}F NMR.

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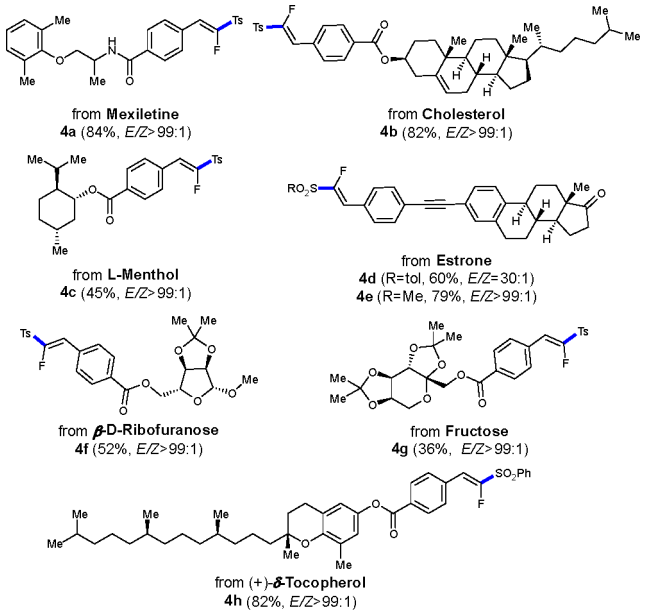
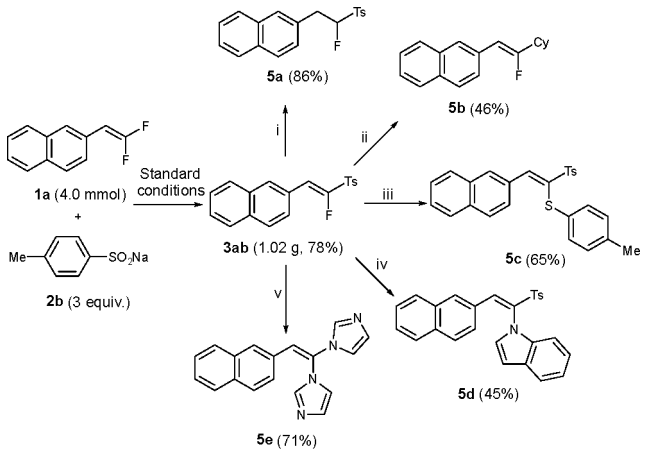
Scheme 2. Late-Stage Modification of Complex Natural Products and Drugs[a]



[a]All reactions were performed with the natural product or drug derivative (0.10 mmol), **2** (3 equiv), and DMSO (1.0 mL) at 70 °C for 48 h under N_2 unless otherwise noted. The *E*/*Z* ratio was determined by ^{19}F NMR.

To our delight, the transformation was scaled up to 4 mmol to provide desired product **3ab** (1.02 g) without sacrificing yield (Scheme 3), which opened up a simple and mild but effective method for the synthesis of biologically active compounds possessing α-fluoro-vinyl sulfone structural scaffolds on a larger scale. Furthermore, synthetic decoration of formed product **3ab** also proceeded well, leading to a series of complex structures (Scheme 3). For example, α-fluorosulfone **5a** could be conveniently prepared in 86% yield through

Scheme 3. Scale-up of the Reaction and Derivatization of Products[a]

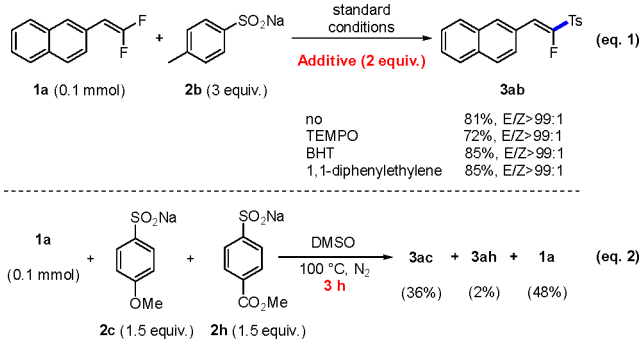


[a]Conditions: (i) Pd/C (10 mol %), $B_2(OH)_4$ (4 equiv), DCM/H_2O, 50 °C; (ii) eosin Y (2 mol %), 1-cyclohexyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (3 equiv), iPr_2NEt (4 equiv), 3/1 MeOH/DCE, geen LED, rt; (iii) sodium 4-methylbenzenethiolate (1.5 equiv), DMSO, rt; (iv) indole (1.2 equiv), K_3PO_4 (2 equiv), DMF, 60 °C; (v) imidazole (2.5 equiv), K_3PO_4 (3 equiv), DMF, 100 °C.

$B_2(OH)_4$-mediated Pd-catalyzed transfer hydrogenation.[16] Treatment of **3ab** with an alkyl radical precursor furnished trisubstituted monofluoroalkene **5b** in 46% yield with retention of configuration.[17] Meanwhile, nucleophilic substitution reaction of **3ab** with sodium 4-methylbenzenethiolate and indole proceeded smoothly to give the corresponding products **5c** and **5d**[9,18] in yields of 65% and 45%, respectively. Impressively, a double-nucleophilic substitution event also transpired in view of the good leaving capacity of F anionic and Ts anionic (**5e**).

To gain further understanding of the cross-coupling mechanism, we carried out a series of control experiments. First, radical trapping experiments were performed. When radical scavengers 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), 2,4-di-*tert*-butyl-4-methylphenol (BHT), and 1,1-diphenylenthyiene were added to the reaction system (Scheme 4, eq 1), the reactions were not obviously inhibited, ruling out

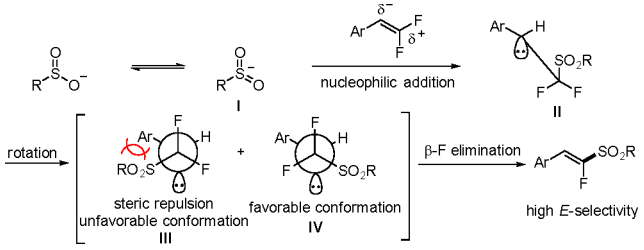
Scheme 4. Control Experiments



the radical process. The result of the competition experiment showed that the electron-rich sodium sulfinates had a large advantage in relative reactivities versus electron-deficient substrates (Scheme 4, eq 2), strongly supporting the nucleophilic substitution process. Alkyl sodium sulfinates with *gem*-difluoroalkenes furnished better desired product yields to reinforce this opinion (Table 1).

On the basis of experimental results and previous reports,[6] a plausible mechanism for the cross-coupling reaction of *gem*-difluoroalkenes and sodium sulfinates to purvey α-fluoro-β-arylalkenyl sulfones is illustrated in Scheme 5. First, the

Scheme 5. A Proposal Mechanism



sulfonate anion resonates with intermediate **I**, following nucleophilic addition to *gem*-difluoroalkene as a consequence of the strong electron-withdrawing capability of fluorine atoms and the repulsion effect from its lone-pair electrons to produce intermediate **II**. On the basis of the observed diastereoselectivity, two conformational models (**III** and **IV**) are proposed by rotation of key intermediate **II**. To weaken steric repulsion

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between the bulky sulfonate group and aryl group, the *anti*-β-F elimination process will proceed via model transition state **IV** preferentially to generate highly *E*-selective product.

In summary, we have presented a novel method for acquiring various α-fluoro-vinyl sulfones in good yields and stereoselectivities under transition-metal- and base-free conditions. The reactions perform well under mild and green conditions and are tolerant of wide varieties of functional groups. Aryl and alkyl sulfinic acid sodium salts are both good coupling partners. The strategy is also applied to the late-stage modification of complex natural products and drugs. Further application to pharmaceuticals is underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All reactions including air- or moisture-sensitive compounds were performed in the argon-filled glovebox or by standard Schlenk techniques in oven-dried reaction vessels under an argon atmosphere in a sealed tube. Unless otherwise noted, all of the solvents and reagents were obtained from commercial suppliers (Strem, Alfa, Aldrich, Adamas-beta, Innochem, Aladdin, Acros, TCI, bidepharm, etc.) and used without further purification. All *gem*-difluoroalkenes[19] and sodium sulfonates[20] were prepared following literature procedures. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Chromatography columns were packed with 200−300 mesh silica gel in petroleum ether (bp 60−90 °C). Gas chromatographic analyses were performed on a Shimadzu GC 2030 gas chromatography instrument with a FID detector, and adamantane was added as an internal standard. ^{1}H, ^{13}C{^{1}H}, and ^{19}F NMR data were recorded with Bruker AVANCE NEO (600 MHz) and Agilent DD2 600 (600 MHz) spectrometers with tetramethylsilane as an internal standard. All chemical shifts (δ) are reported in parts per million and coupling constants (J) in hertz. Singlet (s), doublet (d), doublet of doublets (dd), triplet (t), doublet of triplets (dt), triplet of doublets (td), quartet (q), multiplet (m), and doublet of doublets of doublets (ddd) were used to express the signal. All chemical shifts were reported relative to tetramethylsilane (0 ppm for ^{1}H) and $CDCl_3$ (77.0 ppm for ^{13}C{^{1}H}). High-resolution mass spectra (HRMS) were recorded with a Thermo fisher Q-Exactive instrument, and accurate masses are reported for the molecular ion.

Preparation for the Synthesis of *gem*-Difluoroalkene Substrates.[19] An oven-dried three-neck round-bottom flask equipped with a PTFE-coated stir bar was charged with PPh_3 (6.56 g, 25 mmol, 2.5 equiv), KI (3.32 g, 20 mmol, 2 equiv), and aldehyde (10 mmol, 1 equiv). Under the inert nitrogen atmosphere, acetonitrile (20 mL) was added to the vessel, and the temperature was increased to 70 °C and allowed to stir for 30 min. Then methyl 2,2-difluoro-2-(fluorosulfonyl)acetate (MDFA, 3.36 g, 17.5 mmol, 1.75 equiv) was then added slowly over a period of 0.5 h. The resulting mixture was stirred for 3 h, a nitrogen atmosphere being maintained until the end of the reaction. Then the reaction was quenched with water (50 mL), and the mixture extracted with ethyl acetate (3 × 30 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography to afford *gem*-difluoroalkenes **1**.

Preparation for the Synthesis of Sodium Sulfinate Substrates.[20] A 25 mL round-bottom flask equipped with a PTFE-coated stir bar was charged with Na_2SO_3 (20 mmol, 2.52 g, 2 equiv), $NaHCO_3$ (20 mmol, 1.68 g, 2 equiv), and deionized H_2O (10 mL). After the mixture had been stirred for 5 min, the sulfonyl chloride (10 mmol, 1 equiv) was added portionwise to the flask. The mixture was heated to 80 °C in an oil bath for 12 h. After this time, the reaction mixture was cooled to rt, and the solvent was removed in vacuo by rotary evaporation, affording the crude sulfinate salt. The impurities were triturated with EtOH and removed by filtration. The solvent was removed from the filtrate in vacuo by rotary evaporation, and the residue was washed three times with ethyl acetate to afford pure sodium sulfonates **2**.

General Procedure for the Synthesis of α-Fluoro-β-arylalkenyl Sulfones. A solution of *gem*-difluoroalkene **1** (0.1 mmol, 1 equiv) and sodium benzenesulfinate **2** (0.3 mmol, 3 equiv) in degassed DMSO (1 mL) was stirred under a nitrogen atmosphere at 100 °C for 24 h. After completion of the reaction, 2 mL of water was added to the reaction mixture and the aqueous solution was extracted with ethyl acetate (3 × 4 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The pure product was obtained by flash column chromatography on silica gel (eluent, 20/1−5/1 petroleum ether/ethyl acetate) to afford desired product **3** or **4**.

*(E)-2-[2-Fluoro-2-(phenylsulfonyl)vinyl]naphthalene (**3aa**).*[2b,f,21] Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 25.6 mg, 82% yield. White solid. Mp: 105−106 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.11−8.00 (m, 3H), 7.83 (t, J = 8.2 Hz, 3H), 7.73−7.65 (m, 2H), 7.61 (t, J = 7.8 Hz, 2H), 7.57−7.49 (m, 2H), 7.23 (d, J = 34.6 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.55 (d, J = 304.6 Hz), 137.4, 134.4, 133.8 (d, J = 1.9 Hz), 133.0, 131.1 (d, J = 7.2 Hz), 129.5, 128.7, 128.7, 128.6, 127.7, 127.6, 126.9 (d, J = 4.2 Hz), 126.8, 126.2 (d, J = 7.8 Hz), 115.7. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.65 (d, J = 34.8 Hz). FTMS: (APCI) calcd for $C_{18}H_{12}FO_2S^-$ [M − H$^+$] 311.0548, found 311.0542.

*(E)-2-(2-Fluoro-2-tosylvinyl)naphthalene (**3ab**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 26.4 mg, 81% yield. White solid. Mp: 108−109 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.92 (d, J = 8.3 Hz, 2H), 7.86−7.79 (m, 3H), 7.66 (dd, J = 8.6, 1.5 Hz, 1H), 7.52 (pd, J = 6.8, 1.2 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 34.8 Hz, 1H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.8 (d, J = 304.6 Hz), 145.7, 134.4, 133.7 (d, J = 1.9 Hz), 133.0, 131.0 (d, J = 7.4 Hz), 130.1, 128.7, 128.7, 128.6, 127.7, 127.6, 127.0 (d, J = 4.3 Hz), 126.8, 126.2 (d, J = 7.9 Hz), 115.2, 21.7. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.65 (d, J = 34.9 Hz). FTMS: (APCI) calcd for $C_{19}H_{16}FO_2S^+$ [M + H$^+$] 327.0850, found 327.0843.

*(E)-2-{2-Fluoro-2-[(4-methoxyphenyl)sulfonyl]vinyl}naphthalene (**3ac**).* Purified by silica gel column chromatography (eluent, 10/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 24.6 mg, 72% yield. White solid. Mp: 80−81 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.97 (d, J = 8.9 Hz, 2H), 7.87−7.79 (m, 3H), 7.67 (dd, J = 8.6, 1.2 Hz, 1H), 7.56−7.48 (m, 2H), 7.18 (d, J = 34.9 Hz, 1H), 7.05 (d, J = 9.0 Hz, 2H), 3.89 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 164.4, 154.0 (d, J = 304.1 Hz), 133.7 (d, J = 1.7 Hz), 133.0, 131.0, 130.9 (d, J = 7.3 Hz), 128.6, 128.6, 128.5, 127.6, 127.5, 127.1 (d, J = 4.1 Hz), 126.7, 126.2 (d, J = 7.9 Hz), 114.7, 55.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.61 (d, J = 34.9 Hz). FTMS: (APCI) calcd for $C_{19}H_{16}FO_3S^+$ [M + H$^+$] 343.0799, found 343.0798.

*(E)-2-{2-[(4-Chlorophenyl)sulfonyl]-2-fluorovinyl}naphthalene (**3ad**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 17.6 mg, 51% yield. Yellow solid. Mp: 112−113 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.98 (d, J = 8.6 Hz, 2H), 7.84 (t, J = 8.8 Hz, 3H), 7.67 (dd, J = 8.6, 1.4 Hz, 1H), 7.60−7.49 (m, 4H), 7.22 (d, J = 34.8 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.15 (d, J = 304.3 Hz), 141.3, 135.9, 133.8 (d, J = 1.7 Hz), 131.2 (d, J = 7.3 Hz), 130.1, 129.8, 128.8, 128.6, 127.8, 127.7, 126.8, 126.8 (d, J = 4.3 Hz), 126.2 (d, J = 7.9 Hz), 116.1. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.10 (d, J = 34.8 Hz). FTMS: (APCI) calcd for $C_{18}H_{13}ClFO_2S^+$ [M + H$^+$] 347.0303, found 347.0298.

*(E)-2-[2-([1,1′-Biphenyl]-4-ylsulfonyl)-2-fluorovinyl]naphthalene (**3ae**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 26.6 mg, 69% yield. White solid. Mp: 118−119 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.10 (d, J = 8.4 Hz, 2H), 8.05 (s, 1H), 7.82 (dd, J = 10.8, 7.3 Hz, 3H), 7.78 (d, J = 8.5 Hz, 2H), 7.68 (dd, J = 8.6, 1.5 Hz, 1H), 7.62−7.58 (m, 2H), 7.52 (ddd, J = 9.6, 7.3, 1.2 Hz, 2H), 7.49−7.45 (m, 2H), 7.42 (dd, J = 8.4, 6.2 Hz, 1H), 7.24 (d, J = 34.8 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.8 (d, J = 304.3 Hz), 147.4, 139.0, 135.9, 133.8 (d, J = 1.4 Hz), 133.0, 131.1 (d, J = 7.0 Hz), 129.2, 129.1, 128.8, 128.7, 128.6, 128.1, 127.7, 127.6, 127.4, 127.0 (d, J = 4.2 Hz),

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126.8, 126.2 (d, J = 7.7 Hz), 115.6. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.61. FTMS: (APCI) calcd for $C_{24}H_{16}FO_2S^-$ [M − H$^+$] 387.0860, found 387.0857.

*(E)-2-(2-Fluoro-2-{[4-(trifluoromethyl)phenyl]sulfonyl}vinyl)-naphthalene (**3af**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 9.9 mg, 26% yield. White solid. Mp: 152−153 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (d, J = 8.2 Hz, 2H), 8.06 (s, 1H), 7.91−7.82 (m, 5H), 7.68 (d, J = 8.6 Hz, 1H), 7.54 (dt, J = 15.8, 6.8 Hz, 2H), 7.29 (s, 0.54H), 7.23 (s, 0.48H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.8 (d, J = 304.4 Hz), 141.2, 136.0 (q, J = 33.6 Hz), 134.0, 133.0, 131.5 (d, J = 7.0 Hz), 129.3, 128.9, 128.7, 127.9, 127.8, 126.7 (q, J = 3.7 Hz), 126.6, 126.2 (d, J = 8.0 Hz), 127.0, 123.0 (q, J = 273.3 Hz), 117.0. ^{19}F NMR (564 MHz, $CDCl_3$): δ −63.29, −125.31. FTMS: (APCI) calcd for $C_{19}H_{11}F_4O_2S^-$ [M − H$^+$] 379.0421, found 379.0415.

*(E)-4-{[1-Fluoro-2-(naphthalen-2-yl)vinyl]sulfonyl}benzonitrile (**3ag**).* Purified by silica gel column chromatography (eluent, 10/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 15.7 mg, 46% yield. White solid. Mp: 168−169 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.16 (d, J = 8.4 Hz, 2H), 8.05 (s, 1H), 7.89 (d, J = 8.3 Hz, 2H), 7.84 (t, J = 9.4 Hz, 3H), 7.67 (d, J = 8.6 Hz, 1H), 7.61−7.51 (m, 2H), 7.29 (s, 0.51H), 7.23 (s, 0.48H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.4 (d, J = 304.0 Hz), 141.8, 134.0 (d, J = 1.5 Hz), 133.2, 133.0, 131.6 (d, J = 7.5 Hz), 129.3, 128.9, 128.7, 128.0, 127.7, 127.0, 126.5 (d, J = 4.0 Hz), 126.1 (d, J = 7.7 Hz), 118.1, 117.5, 117.0. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.59. FTMS: (APCI) calcd for $C_{19}H_{13}FNO_2S^+$ [M + H$^+$] 338.0646, found 338.0639.

*Methyl (E)-4-{[1-Fluoro-2-(naphthalen-2-yl)vinyl]sulfonyl}-benzoate (**3ah**).* Purified by silica gel column chromatography (eluent, 10/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 15.6 mg, 42% yield. White solid. Mp: = 134−135 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.27−8.22 (m, 2H), 8.12 (d, J = 8.5 Hz, 2H), 8.05 (s, 1H), 7.83 (t, J = 9.2 Hz, 3H), 7.67 (dd, J = 8.6, 1.6 Hz, 1H), 7.56−7.49 (m, 2H), 7.25 (d, J = 34.7 Hz, 1H), 3.96 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 165.3, 153.0 (d, J = 304.8 Hz), 141.4, 135.4, 133.9 (d, J = 1.5 Hz), 133.0, 131.3 (d, J = 7.4 Hz), 130.6, 128.8, 128.7, 128.6, 127.8, 127.7, 126.9, 126.7 (d, J = 4.3 Hz), 126.2 (d, J = 7.8 Hz), 116.7, 52.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.11. FTMS: (APCI) calcd for $C_{20}H_{14}FO_4S^-$ [M − H$^+$] 369.0602, found 369.0601.

*(E)-3-{[1-Fluoro-2-(naphthalen-2-yl)vinyl]sulfonyl}benzonitrile (**3ai**).* Purified by silica gel column chromatography (eluent, 10/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 10.1 mg, 30% yield. Yellow solid. Mp: 138−139 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.34 (s, 1H), 8.28 (d, J = 8.1 Hz, 1H), 8.07 (s, 1H), 7.98 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 8.5 Hz, 2H), 7.84 (d, J = 7.9 Hz, 1H), 7.77 (t, J = 7.9 Hz, 1H), 7.68 (dd, J = 8.6, 1.2 Hz, 1H), 7.55 (ddd, J = 15.1, 13.8, 6.8 Hz, 2H), 7.30 (s, 0.48H), 7.24 (s, 0.47H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.3 (d, J = 304.5 Hz), 139.4, 137.4, 134.0 (d, J = 1.9 Hz), 132.9, 132.6, 132.3, 131.6 (d, J = 7.3 Hz), 130.6, 128.9, 128.7, 128.0, 127.7, 127.0, 126.4 (d, J = 4.4 Hz), 126.1 (d, J = 7.9 Hz), 117.3, 116.7, 114.3. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.66 (d, J = 34.8 Hz). FTMS: (APCI) calcd for $C_{19}H_{12}FNO_2S^+$ [M$^+$] 337.0567, found 337.0562.

*(E)-2-{2-[(3-Bromophenyl)sulfonyl]-2-fluorovinyl}naphthalene (**3aj**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 16.4 mg, 42% yield. Yellow solid. Mp: 100−101 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.18 (s, 1H), 8.06 (s, 1H), 7.98 (d, J = 7.9 Hz, 1H), 7.87−7.81 (m, 4H), 7.69 (dd, J = 8.6, 1.3 Hz, 1H), 7.58−7.46 (m, 3H), 7.23 (d, J = 34.0 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.9 (d, J = 304.2 Hz), 139.3, 137.5, 133.88 (d, J = 1.8 Hz), 133.0, 131.4, 131.4 (d, J = 7.3 Hz), 131.0, 128.8, 128.6, 127.8, 127.7, 127.3, 126.9, 126.7 (d, J = 4.4 Hz), 126.2 (d, J = 7.9 Hz), 123.4, 116.5. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.04 (d, J = 34.7 Hz). FTMS: (APCI) calcd for $C_{18}H_{12}BrFO_2S^+$ [M$^+$] 389.9720, found 389.9719.

*(E)-2-{2-Fluoro-2-[(2-methoxyphenyl)sulfonyl]vinyl}naphthalene (**3ak**).* Purified by silica gel column chromatography (eluent, 10/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 7.2 mg, 21% yield. White solid. Mp: 119−120 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.11 (dd, J = 7.9, 1.4 Hz, 1H), 8.07 (s, 1H), 7.85 (dd, J = 12.8, 8.1 Hz, 3H), 7.72 (dd, J = 8.6, 1.1 Hz, 1H), 7.67−7.62 (m, 1H), 7.57−7.49 (m, 2H), 7.28 (s, 0.49H), 7.22 (s, 0.5H), 7.16 (t, J = 7.7 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 3.91 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 158.0, 153.7 (d, J = 304.3 Hz), 136.5, 133.7 (d, J = 1.6 Hz), 133.1, 131.7, 130.8 (d, J = 7.4 Hz), 128.7, 128.6, 127.7, 127.5, 126.8, 126.3 (d, J = 7.7 Hz), 124.8, 120.8, 116.5, 112.5, 56.3. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.72. FTMS: (APCI) calcd for $C_{19}H_{16}FO_3S^+$ [M + H$^+$] 343.0799, found 343.0797.

*(E)-2-{[1-Fluoro-2-(naphthalen-2-yl)vinyl]sulfonyl}naphthalene (**3al**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 29.0 mg, 80% yield. White solid. Mp: 102−103 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.66 (s, 1H), 8.08−8.00 (m, 3H), 7.98 (dd, J = 8.7, 1.4 Hz, 1H), 7.94 (d, J = 8.2 Hz, 1H), 7.86−7.79 (m, 3H), 7.74−7.62 (m, 3H), 7.57−7.46 (m, 2H), 7.34−7.23 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.7 (d, J = 304.6 Hz), 135.7, 134.2, 133.8 (d, J = 1.8 Hz), 133.0, 132.2, 131.1 (d, J = 7.3 Hz), 131.0, 129.9, 129.7, 129.6, 128.8, 128.6, 128.0, 127.9, 127.7, 127.7, 127.0 (d, J = 4.1 Hz), 126.8, 126.3 (d, J = 7.9 Hz), 122.9, 115.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.53 (d, J = 34.8 Hz). FTMS: (APCI) calcd for $C_{22}H_{16}FO_2S^+$ [M + H$^+$] 363.0850, found 363.08444.

*(E)-1-{[1-Fluoro-2-(naphthalen-2-yl)vinyl]sulfonyl}naphthalene (**3am**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 11.5 mg, 32% yield. Yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.81 (d, J = 8.7 Hz, 1H), 8.51 (dd, J = 7.4, 1.1 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H), 8.05 (s, 1H), 7.96 (dd, J = 8.2, 0.5 Hz, 1H), 7.83−7.78 (m, 3H), 7.71−7.68 (m, 1H), 7.67−7.64 (m, 2H), 7.62−7.59 (m, 1H), 7.54−7.47 (m, 2H), 7.38 (d, J = 34.6 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 154.3 (d, J = 305.2 Hz), 136.3, 134.3, 133.8 (d, J = 1.7 Hz), 133.0, 132.3, 132.1, 131.1 (d, J = 7.0 Hz), 129.3, 129.0, 128.9, 128.7, 128.6, 127.7, 127.7, 127.2, 127.0 (d, J = 4.1 Hz), 126.8, 126.3 (d, J = 7.9 Hz), 124.6, 124.2, 116.0. ^{19}F NMR (564 MHz, $CDCl_3$): δ −123.74. FTMS: (APCI) calcd for $C_{22}H_{16}FO_2S^+$ [M + H$^+$] 363.0850, found 363.08445.

*(E)-2-{[1-Fluoro-2-(naphthalen-2-yl)vinyl]sulfonyl}thiophene (**3an**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 15.7 mg, 50% yield. Yellow solid. Mp: 108−109 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.87 (dd, J = 3.8, 0.8 Hz, 1H), 7.87−7.82 (m, 3H), 7.81 (dd, J = 4.9, 1.0 Hz, 1H), 7.70 (dd, J = 8.6, 1.2 Hz, 1H), 7.58−7.49 (m, 2H), 7.27−7.18 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.6 (d, J = 303.9 Hz), 138.1, 135.8, 135.7, 133.8 (d, J = 1.8 Hz), 133.0, 131.2 (d, J = 7.4 Hz), 128.8, 128.6, 128.4, 127.7, 127.7, 126.9 (d, J = 4.3 Hz), 126.9, 126.3 (d, J = 7.9 Hz), 115.3. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.74 (d, J = 34.5 Hz). FTMS: (APCI) calcd for $C_{16}H_{12}FO_2S_2^+$ [M + H$^+$] 319.0257, found 319.0254.

*(E)-2-[2-Fluoro-2-(methylsulfonyl)vinyl]naphthalene (**3ao**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 23.8 mg, 95% yield. White solid. Mp: 80−81 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.91−7.81 (m, 3H), 7.72 (dd, J = 8.6, 1.0 Hz, 1H), 7.61−7.48 (m, 2H), 7.09 (d, J = 35.5 Hz, 1H), 3.16 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.2 (d, J = 304.6 Hz), 133.8 (d, J = 2.0 Hz), 133.0, 131.2 (d, J = 7.1 Hz), 128.8, 128.6, 127.8, 127.7, 126.9, 126.5 (d, J = 4.1 Hz), 126.2 (d, J = 7.9 Hz), 116.0, 40.6. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.79 (d, J = 35.5 Hz). FTMS: (APCI) calcd for $C_{13}H_{10}FO_2S^-$ [M − H$^+$] 249.0391, found 249.0390.

*(E)-2-[2-(Ethylsulfonyl)-2-fluorovinyl]naphthalene (**3ap**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 24.2 mg, 91% yield. White solid. Mp: 56−57 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.91−7.83 (m, 3H), 7.73 (dd, J = 8.6, 1.5 Hz, 1H), 7.60−7.52 (m, 2H), 7.08 (d, J = 35.7 Hz, 1H), 3.26 (q, J = 7.5 Hz, 2H), 1.44 (t, J = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 151.7 (d, J = 305.1 Hz), 133.9 (d, J = 1.9 Hz), 133.0, 131.2 (d, J = 7.2 Hz), 128.9, 128.7, 127.8, 127.8, 126.9, 126.7 (d, J = 4.1 Hz), 126.2 (d, J = 7.8 Hz), 117.4, 47.0, 7.0. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.83 (d, J = 35.6

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Hz). FTMS: (APCI) calcd for $C_{14}H_{12}FO_2S^-$ [M − H$^+$] 263.0546, found 263.0544.

*(E)-2-[2-Fluoro-2-(propylsulfonyl)vinyl]naphthalene (**3aq**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 27.2 mg, 97% yield. White solid. Mp: 74−75 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.91−7.83 (m, 3H), 7.73 (dd, J = 8.6, 1.7 Hz, 1H), 7.59−7.52 (m, 2H), 7.07 (d, J = 35.7 Hz, 1H), 3.26−3.17 (m, 2H), 1.98−1.87 (m, 2H), 1.11 (t, J = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.3 (d, J = 305.1 Hz), 133.8 (d, J = 1.7 Hz), 133.0, 131.1 (d, J = 7.2 Hz), 128.8, 128.6, 127.7, 127.7, 126.8, 126.7 (d, J = 4.0 Hz), 126.2 (d, J = 7.7 Hz), 117.0, 54.1, 16.1, 12.9. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.81 (d, J = 35.6 Hz). FTMS: (APCI) calcd for $C_{15}H_{14}FO_2S^-$ [M − H$^+$] 277.0704, found 277.0699.

*(E)-2-[2-Fluoro-2-(isopropylsulfonyl)vinyl]naphthalene (**3ar**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 27.3 mg, 91% yield. White solid. Mp: 76−77 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.91−7.83 (m, 3H), 7.73 (dd, J = 8.6, 1.4 Hz, 1H), 7.59−7.51 (m, 2H), 7.06 (d, J = 35.7 Hz, 1H), 3.41 (hept, J = 6.9 Hz, 1H), 1.47 (d, J = 6.9 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 151.3 (d, J = 306.1 Hz), 133.9 (d, J = 1.8 Hz), 133.0, 131.1 (d, J = 7.3 Hz), 128.8, 128.6, 127.8, 127.7, 126.9, 126.9 (d, J = 3.9 Hz), 126.3 (d, J = 7.9 Hz), 118.1, 53.0, 15.1. ^{19}F NMR (564 MHz, $CDCl_3$): δ −122.44 (d, J = 35.7 Hz). FTMS: (APCI) calcd for $C_{15}H_{14}FO_2S^-$ [M − H$^+$] 277.0704, found 277.0702.

*(E)-2-[2-(Cyclopropylsulfonyl)-2-fluorovinyl]naphthalene (**3as**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 23.5 mg, 85% yield. White solid. Mp: 69−70 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.90−7.84 (m, 3H), 7.73 (dd, J = 8.6, 1.6 Hz, 1H), 7.55 (pd, J = 6.9, 1.3 Hz, 2H), 7.04 (d, J = 35.4 Hz, 1H), 2.65−2.56 (m, 1H), 1.45−1.40 (m, 2H), 1.21−1.15 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.4 (d, J = 304.7 Hz), 133.7 (d, J = 1.8 Hz), 133.0, 131.0 (d, J = 7.4 Hz), 128.7, 128.6, 127.7, 127.6, 126.9 (d, J = 4.1 Hz), 126.8, 126.2 (d, J = 7.8 Hz), 115.7, 29.5, 5.5. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.21 (d, J = 35.4 Hz). FTMS: (APCI) calcd for $C_{15}H_{12}FO_2S^-$ [M − H$^+$] 275.0548, found 275.0543.

*(E)-2-[2-(Cyclohexylsulfonyl)-2-fluorovinyl]naphthalene (**3at**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 27.3 mg, 86% yield. White solid. Mp: 97−98 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.91−7.84 (m, 3H), 7.73 (dd, J = 8.6, 1.4 Hz, 1H), 7.59−7.51 (m, 2H), 7.04 (d, J = 35.7 Hz, 1H), 3.20−3.09 (m, 1H), 2.23 (d, J = 11.8 Hz, 2H), 1.99−1.90 (m, 2H), 1.78−1.70 (m, 1H), 1.64−1.56 (m, 2H), 1.38−1.28 (m, 2H), 1.24 (ddt, J = 16.2, 6.8, 3.1 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 151.5 (d, J = 306.0 Hz), 133.8 (d, J = 1.8 Hz), 133.0, 131.1 (d, J = 7.3 Hz), 128.8, 128.6, 127.7, 127.7, 126.9 (d, J = 4.0 Hz), 126.9, 126.3 (d, J = 7.9 Hz), 118.0, 60.7, 25.0, 24.9. ^{19}F NMR (564 MHz, $CDCl_3$): δ −122.31 (d, J = 35.7 Hz). FTMS: (APCI) calcd for $C_{18}H_{18}FO_2S^-$ [M − H$^+$] 317.1017, found 317.1014.

*(E)-2-[2-(Benzylsulfonyl)-2-fluorovinyl]naphthalene (**3au**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 27.6 mg, 85% yield. White solid. Mp: 141−142 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.85 (dd, J = 9.7, 4.4 Hz, 3H), 7.63 (dd, J = 8.6, 1.5 Hz, 1H), 7.54 (tdd, J = 7.6, 7.0, 1.2 Hz, 2H), 7.42−7.34 (m, 5H), 6.79 (d, J = 35.7 Hz, 1H), 4.47 (s, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 151.1 (d, J = 304.8 Hz), 133.8 (d, J = 1.8 Hz), 132.9, 131.1 (d, J = 7.2 Hz), 130.8, 129.3, 129.0, 128.7, 128.6, 127.7, 127.7, 126.8, 126.7, 126.6 (d, J = 3.9 Hz), 126.1 (d, J = 7.8 Hz), 118.1, 59.0. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.50 (d, J = 32.0 Hz). FTMS: (APCI) calcd for $C_{19}H_{14}FO_2S^-$ [M − H$^+$] 325.0704, found 325.0701.

*(E)-2-(2-{[1-Fluoro-2-(naphthalen-2-yl)vinyl]sulfonyl}ethyl)-isoindoline-1,3-dione (**3av**).* Purified by silica gel column chromatography (eluent, 5/1−2/1 petroleum ether/ethyl acetate). Isolated yield: 30.6 mg, 75% yield. White solid. Mp: 127−128 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.98 (s, 1H), 7.83 (d, J = 8.7 Hz, 2H), 7.80 (d, J = 8.7 Hz, 1H), 7.74−7.69 (m, 2H), 7.61 (dd, J = 8.6, 1.5 Hz, 1H), 7.58−7.51 (m, 4H), 7.07 (d, J = 35.7 Hz, 1H), 4.21 (t, J = 6.3 Hz, 2H), 3.71 (t, J = 6.3 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 167.5, 151.3 (d, J = 304.2 Hz), 134.2, 133.8 (d, J = 1.8 Hz), 132.9, 131.5, 131.4 (d, J = 7.3 Hz), 128.7, 128.7, 127.8, 127.6, 126.8, 126.4 (d, J = 4.2 Hz), 126.1 (d, J = 7.8 Hz), 123.4, 118.3, 49.0, 31.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −126.42 (d, J = 35.6 Hz). FTMS: (APCI) calcd for $C_{22}H_{17}FNO_4S^+$ [M + H$^+$] 410.0857, found 410.0859.

*(E)-1-(tert-Butyl)-4-(2-fluoro-2-tosylvinyl)benzene (**3bb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 20.3 mg, 77% yield. White solid. Mp: 93−94 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, J = 8.2 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 7.03 (d, J = 35.1 Hz, 1H), 2.45 (s, 3H), 1.31 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.9 (d, J = 2.4 Hz), 153.2 (d, J = 302.9 Hz), 145.6, 134.5, 130.1, 130.0, 128.6, 126.8 (d, J = 3.9 Hz), 126.0, 115.1, 34.9, 31.1, 21.7. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.72 (d, J = 35.1 Hz). FTMS: (APCI) calcd for $C_{19}H_{22}FO_2S^+$ [M + H$^+$] 333.1319, found 333.1317.

*Methyl (E)-4-(2-Fluoro-2-tosylvinyl)benzoate (**3cb**).*[2c] Purified by silica gel column chromatography (eluent, 10/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 16.4 mg, 50% yield. White solid. Mp: 137−138 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.05 (d, J = 8.4 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.1 Hz, 2H), 7.07 (d, J = 34.2 Hz, 1H), 3.93 (s, 3H), 2.47 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 166.2, 155.1 (d, J = 308.6 Hz), 146.0, 133.9, 133.8 (d, J = 4.0 Hz), 131.2 (d, J = 2.2 Hz), 130.2, 130.0, 130.0, 128.9, 113.8, 52.4, 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −121.17 (d, J = 34.2 Hz). FTMS: (APCI) calcd for $C_{17}H_{16}FO_4S^+$ [M + H$^+$] 335.0748, found 335.0749.

*(E)-1-{[1-Fluoro-2-(4-iodophenyl)vinyl]sulfonyl}-4-methylbenzene (**3db**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 18.5 mg, 46% yield. White solid. Mp: 166−167 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, J = 8.2 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 34.3 Hz, 1H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 154.5 (d, J = 306.2 Hz), 145.9, 138.2, 134.2, 131.5 (d, J = 7.4 Hz), 130.2, 129.0 (d, J = 3.9 Hz), 128.8, 114.0, 96.8 (d, J = 3.3 Hz), 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −122.77. FTMS: (APCI) calcd for $C_{15}H_{11}FIO_2S^-$ [M − H$^+$] 400.9514, found 400.9506.

*(E)-2-[4-(2-Fluoro-2-tosylvinyl)phenyl]-5,5-dimethyl-1,3,2-dioxaborinane (**3eb**).* Purified by silica gel column chromatography (eluent, 10/1−2/1 petroleum ether/ethyl acetate). Isolated yield: 19.5 mg, 50% yield. White solid. Mp: 129−130 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.89 (d, J = 8.2 Hz, 2H), 7.80 (d, J = 8.1 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 7.04 (d, J = 34.9 Hz, 1H), 3.76 (s, 4H), 2.46 (s, 3H), 1.02 (s, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 154.0 (d, J = 305.3 Hz), 145.6, 134.4, 134.3, 131.4 (d, J = 4.0 Hz), 130.1, 129.2, 129.2, 128.7, 115.2, 72.3, 31.9, 21.9, 21.7. ^{19}F NMR (564 MHz, $CDCl_3$): δ −123.55. FTMS: (APCI) calcd for $C_{20}H_{21}FBO_4S^-$ [M − H$^+$] 387.1243, found 387.1236.

*(E)-4-(2-Fluoro-2-tosylvinyl)-1,2-dimethoxybenzene (**3fb**).* Purified by silica gel column chromatography (eluent, 10/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 24.6 mg, 72% yield. Yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 7.16−7.11 (m, 2H), 6.98 (d, J = 35.0 Hz, 1H), 6.86 (d, J = 8.1 Hz, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.3 (d, J = 300.5 Hz), 150.8 (d, J = 3.2 Hz), 148.9, 145.5, 134.6, 130.1, 128.6, 124.4 (d, J = 6.7 Hz), 122.3 (d, J = 3.9 Hz), 115.3, 112.2 (d, J = 8.9 Hz), 112.0, 55.9, 55.8, 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −128.11 (d, J = 35.0 Hz). FTMS: (APCI) calcd for $C_{17}H_{18}FO_4S^+$ [M + H$^+$] 337.09043, found 337.09030.

*(E)-4-(2-Fluoro-2-tosylvinyl)-1,2-dimethylbenzene (**3gb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 15.3 mg, 50% yield. White solid. Mp: 82−83 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.1 Hz, 2H), 7.33 (s, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.14 (d, J = 7.9 Hz, 1H), 6.98 (d, J = 35.2 Hz, 1H), 2.45 (s, 3H), 2.27

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(s, 3H), 2.25 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 153.1 (d, J = 302.7 Hz), 145.5, 139.6 (d, J = 2.7 Hz), 137.3, 134.7, 131.4 (d, J = 7.4 Hz), 130.2, 130.1, 128.7, 127.8 (d, J = 7.5 Hz), 127.2 (d, J = 3.9 Hz), 115.4, 21.7, 19.8, 19.7. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.97. FTMS: (APCI) calcd for $C_{17}H_{18}FO_2S^+$ [M + H$^+$] 305.1006, found 305.1006.

*(E)-1-(2-Fluoro-2-tosylvinyl)-2,4-dimethylbenzene (**3hb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 16.5 mg, 54% yield. White solid. Mp: 90−91 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.89 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 34.5 Hz, 1H), 7.04 (s, 1H), 7.00 (d, J = 8.0 Hz, 1H), 2.46 (s, 3H), 2.38 (s, 3H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 153.3 (d, J = 303.1 Hz), 145.5, 140.4 (d, J = 1.8 Hz), 137.8 (d, J = 1.4 Hz), 134.6, 131.4, 130.1, 129.6 (d, J = 11.9 Hz), 128.7, 127.1, 125.2 (d, J = 3.6 Hz), 112.2, 21.7, 21.3, 19.9. ^{19}F NMR (564 MHz, $CDCl_3$): δ −126.87. FTMS: (APCI) calcd for $C_{17}H_{18}FO_2S^+$ [M + H$^+$] 305.1006, found 305.1006.

*(E)-2-(2-Fluoro-2-tosylvinyl)-6-methoxynaphthalene (**3ib**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 31.8 mg, 89% yield. White solid. Mp: 147−148 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.92 (d, J = 8.3 Hz, 2H), 7.72 (t, J = 8.7 Hz, 2H), 7.63 (dd, J = 8.6, 1.7 Hz, 1H), 7.39 (d, J = 8.2 Hz, 2H), 7.20−7.12 (m, 2H), 7.11 (d, J = 2.4 Hz, 1H), 3.93 (s, 3H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 159.0, 153.2 (d, J = 302.7 Hz), 145.5, 135.2 (d, J = 2.0 Hz), 134.6, 130.8 (d, J = 7.3 Hz), 130.1, 130.1, 128.6, 128.4, 127.4,126.9 (d, J = 7.9 Hz), 124.8 (d, J = 4.2 Hz), 119.7, 115.5, 105.6, 55.4, 21.7. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.99 (d, J = 35.1 Hz). FTMS: (APCI) calcd for $C_{20}H_{18}FO_3S^+$ [M + H$^+$] 357.0955, found 357.0958.

*(E)-1-(2-Fluoro-2-tosylvinyl)naphthalene (**3jb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 22.6 mg, 73% yield. White solid. Mp: 115−116 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 8.08 (d, J = 8.5 Hz, 1H), 7.96 (d, J = 8.3 Hz, 2H), 7.88 (dd, J = 7.4, 6.0 Hz, 2H), 7.83 (d, J = 7.3 Hz, 1H), 7.82 (d, J = 32.8 Hz, 1H), 7.61 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), 7.57−7.53 (m, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.41 (d, J = 8.2 Hz, 2H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 154.7 (d, J = 305.2 Hz), 145.8, 134.3, 133.6, 131.3, 130.7 (d, J = 1.5 Hz), 130.2, 128.9, 128.8, 128.5 (d, J = 10.7 Hz), 127.2, 126.4, 125.4 (d, J = 3.7 Hz), 125.3, 123.2, 111.5, 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.85 (d, J = 32.8 Hz). FTMS: (APCI) calcd for $C_{19}H_{16}FO_2S^+$ [M + H$^+$] 327.0850, found 327.0851.

*(E)-9-(2-Fluoro-2-tosylvinyl)phenanthrene (**3kb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 31.6 mg, 85% yield. White solid. Mp: 186−187 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 8.76−8.71 (m, 1H), 8.66 (d, J = 8.3 Hz, 1H), 8.13−8.07 (m, 1H), 8.06 (s, 1H), 7.99 (d, J = 8.3 Hz, 2H), 7.82 (t, J = 20.8 Hz, 2H), 7.75−7.66 (m, 3H), 7.60 (t, J = 7.4 Hz, 1H), 7.43 (d, J = 8.1 Hz, 2H), 2.48 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 155.0 (d, J = 305.0 Hz), 145.8, 134.2, 130.8, 130.7, 130.4, 130.3, 130.2, 129.6, 129.3, 128.8, 128.1, 127.2, 127.1, 127.0, 124.0, 123.9 (d, J = 3.2 Hz), 123.2, 122.5, 112.0, 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −123.91 (d, J = 35.6 Hz). FTMS: (APCI) calcd for $C_{23}H_{18}FO_2S^+$ [M + H$^+$] 377.1006, found 377.1007.

*(E)-9-(2-Fluoro-2-tosylvinyl)anthracene (**3lb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 27.5 mg, 73% yield. Yellow solid. Mp: 161−162 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 8.48 (s, 1H), 8.05 (d, J = 8.3 Hz, 2H), 8.02−7.95 (m, 3H), 7.90−7.84 (m, 2H), 7.53−7.47 (m, 4H), 7.46 (d, J = 8.0 Hz, 2H), 2.49 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 154.9 (d, J = 304.5 Hz), 146.0, 134.2, 131.0, 130.3, 129.3 (d, J = 1.0 Hz), 129.2, 128.9, 128.8, 126.8, 125.4, 124.7 (d, J = 1.2 Hz), 121.6, 112.6 (d, J = 5.9 Hz), 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −116.70 (dt, J = 33.9, 2.9 Hz). FTMS: (APCI) calcd for $C_{23}H_{18}FO_2S^+$ [M + H$^+$] 377.1006, found 377.1008.

*(E)-1-(2-Fluoro-2-tosylvinyl)pyrene (**3mb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 31.2 mg, 78% yield. Yellow solid. Mp: 79−80 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 8.29−8.25 (m, 2H), 8.21 (d, J = 7.5 Hz, 2H), 8.15 (d, J = 9.2 Hz, 1H), 8.11−7.96 (m, 7H), 7.43 (d, J = 8.1 Hz, 2H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 154.3 (d, J = 305.4 Hz), 145.7, 134.4, 132.4 (d, J = 1.5 Hz), 131.0, 130.4, 130.2, 129.7 (d, J = 1.4 Hz), 128.9, 128.8, 128.8, 127.2 (d, J = 2.3 Hz), 127.1, 126.3, 126.2, 126.0, 124.7, 124.6, 124.2, 122.4 (d, J = 4.4 Hz), 122.2, 111.7, 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −125.82 (d, J = 33.5 Hz). FTMS: (APCI) calcd for $C_{25}H_{18}FO_2S^+$ [M + H$^+$] 401.1006, found 401.1010.

*(E)-3-(2-Fluoro-2-tosylvinyl)quinoline (**3nb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 toluene/ethyl acetate). Isolated yield: 20.5 mg, 69% yield. White solid. Mp: 160−161 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 9.01 (d, J = 2.1 Hz, 1H), 8.38 (d, J = 1.6 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.94 (d, J = 8.3 Hz, 2H), 7.81 (d, J = 8.2 Hz, 1H), 7.76 (dd, J = 11.3, 4.0 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.41 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 34.7 Hz, 1H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 155.5 (d, J = 307.4 Hz), 150.6 (d, J = 6.5 Hz), 148.1, 146.0, 137.2 (d, J = 9.2 Hz), 134.0, 131.0, 130.2, 129.4, 128.8, 128.4, 127.5, 127.4, 123.0, 123.0, 111.9, 21.7. ^{19}F NMR (564 MHz, $CDCl_3$): δ −120.89. FTMS: (APCI) calcd for $C_{18}H_{15}FNO_2S^+$ [M + H$^+$] 328.0802, found 328.0800.

*(E)-3-(2-Fluoro-2-tosylvinyl)benzo[b]thiophene (**3ob**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 23.8 mg, 30% yield. Yellow solid. Mp: 153−154 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.92 (d, J = 8.2 Hz, 3H), 7.89 (d, J = 8.0 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.46−7.36 (m, 4H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 154.7 (d, J = 303.8 Hz), 145.7, 139.1, 137.5, 134.4, 130.6 (d, J = 14.0 Hz), 130.2, 128.7, 125.2, 125.0, 124.2 (d, J = 3.4 Hz), 122.8, 121.2, 106.6 (d, J = 3.0 Hz), 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −122.44 (d, J = 33.8 Hz). FTMS: (APCI) calcd for $C_{17}H_{14}FO_2S_2^+$ [M + H$^+$] 333.0414, found 333.0411.

*3-[2-Fluoro-2-(methylsulfonyl)vinyl]benzo[b]thiophene (**3oo**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 17.6 mg, 65% yield. The E/Z ratio of 9/1 by ^{19}F NMR. Yellow solid. Mp: 97−98 °C. E isomer ^1H NMR (600 MHz, $CDCl_3$): δ 8.08 (s, 1H), 8.05 (s, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.52−7.47 (m, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.30 (d, J = 34.5 Hz, 1H), 3.17 (s, 3H), 3.05 (d, J = 1.8 Hz, 1H). E isomer $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 154.1 (d, J = 303.8 Hz), 139.2, 137.4, 131.1 (d, J = 13.5 Hz), 125.3, 125.1, 123.8 (d, J = 3.2 Hz), 122.9, 121.1, 107.5 (d, J = 1.9 Hz), 40.8. E isomer ^{19}F NMR (564 MHz, $CDCl_3$): δ −123.55. FTMS: (APCI) calcd for $C_{11}H_8FO_2S_2^-$ [M − H$^+$] 254.9955, found 254.9949.

*(E)-9-Ethyl-3-(2-fluoro-2-tosylvinyl)-9H-carbazole (**3pb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 22.7 mg, 58% yield. Yellow oil. ^1H NMR (600 MHz, $CDCl_3$): δ 8.32 (d, J = 1.1 Hz, 1H), 8.06 (d, J = 7.7 Hz, 1H), 7.93 (d, J = 8.3 Hz, 2H), 7.67 (dd, J = 8.6, 1.5 Hz, 1H), 7.52−7.46 (m, 1H), 7.41 (d, J = 8.2 Hz, 1H), 7.37 (d, J = 7.2 Hz, 3H), 7.27 (d, J = 6.8 Hz, 1H), 7.22 (d, J = 27.2 Hz, 1H), 4.34 (q, J = 7.2 Hz, 2H), 2.44 (s, 3H), 1.42 (t, J = 7.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 151.8 (d, J = 298.8 Hz), 145.3, 140.8 (d, J = 2.0 Hz), 140.4, 135.2, 130.1, 128.6, 128.1 (d, J = 6.9 Hz), 126.4, 123.4, 123.0 (d, J = 8.3 Hz), 122.7, 120.6, 120.3 (d, J = 3.8 Hz), 119.8, 116.7, 108.9, 108.8, 37.8, 21.7, 13.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −129.32. FTMS: (APCI) calcd for $C_{23}H_{21}FNO_2S^+$ [M + H$^+$] 394.1272, found 394.1263.

*1-Benzyl-4-(2-fluoro-2-tosylvinyl)-1H-indole (**3qb**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 22.2 mg, 55% yield. The E/Z ratio is 7/1 by ^{19}F NMR. Green solid. Mp: 107−111 °C. E isomer ^1H NMR (600 MHz, $CDCl_3$): δ 7.92 (d, J = 8.3 Hz, 2H), 7.54 (s, 0.51H), 7.52 (s, 1H), 7.47 (s, 0.48H), 7.37 (d, J = 8.1 Hz, 2H), 7.33−7.25 (m, 4H), 7.24 (d, J = 3.2 Hz, 1H), 7.16 (t, J = 7.9 Hz, 1H), 7.07 (d, J = 7.1 Hz, 2H), 6.73 (d, J = 3.2 Hz, 1H), 5.34 (s, 2H), 2.45 (s, 3H). E isomer $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 153.6 (d, J = 303.9 Hz), 145.5, 137.0, 136.4, 134.8, 130.1, 129.6, 128.9, 128.7,

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127.8, 126.7, 121.9, 121.7, 121.6, 121.3 (d, J = 4.1 Hz), 112.8, 112.0 (d, J = 1.7 Hz), 100.0, 50.3, 21.8. *E* isomer ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.64. FTMS: (APCI) calcd for $C_{24}H_{21}FNO_2S^+$ [M + H^+] 406.1272, found 406.1264.

*(E)-3-[2-Fluoro-2-(methylsulfonyl)vinyl]-1-tosyl-1H-indole (**3ro**).* Purified by silica gel column chromatography (eluent, 10/1−2/1 petroleum ether/ethyl acetate). Isolated yield: 28.7 mg, 73% yield. White solid. Mp: 143−144 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.08 (s, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 7.9 Hz, 1H), 7.43−7.37 (m, 1H), 7.35−7.30 (m, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 35.3 Hz, 1H), 3.16 (s, 3H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 153.4 (d, J = 301.9 Hz), 145.8, 134.6, 134.4, 130.2, 128.6 (d, J = 3.0 Hz), 128.5, 127.1, 125.7, 124.1, 119.2, 113.7, 110.9, 107.0 (d, J = 3.9 Hz), 40.8, 21.6. ^{19}F NMR (564 MHz, $CDCl_3$): δ −120.47. FTMS: (APCI) calcd for $C_{18}H_{15}FNO_4S_2^-$ [M − H^+] 392.0432, found 392.0425.

*(E)-N-[1-(2,6-Dimethylphenoxy)propan-2-yl]-4-(2-fluoro-2-tosylvinyl)benzamide (**4a**).* Purified by silica gel column chromatography (eluent, 10/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 40.4 mg, 84% yield. White solid. Mp: 93−94 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.81 (d, J = 8.3 Hz, 2H), 7.76 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 6.97 (d, J = 34.3 Hz, 1H), 6.91 (d, J = 7.4 Hz, 2H), 6.87−6.82 (m, 1H), 6.72−6.63 (m, 1H), 4.53−4.38 (m, 1H), 3.84 (dd, J = 9.1, 3.9 Hz, 1H), 3.73 (dd, J = 9.2, 3.1 Hz, 1H), 2.38 (s, 3H), 2.17 (s, 6H), 1.44 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 165.9, 154.9 (d, J = 307.7 Hz), 154.8, 146.0, 135.8 (d, J = 1.8 Hz), 134.1, 132.5 (d, J = 4.1 Hz), 130.7, 130.3 (d, J = 7.6 Hz), 130.2, 129.1, 128.8, 127.5, 124.2, 113.9, 73.8, 46.1, 21.8, 17.8, 16.2. ^{19}F NMR (564 MHz, $CDCl_3$): δ −121.91. FTMS: (APCI) calcd for $C_{27}H_{29}FNO_4S^+$ [M + H^+] 482.1796, found 482.1789.

*(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-[(R)-6-methylheptan-2-yl]-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-[(E)-2-Fluoro-2-tosylvinyl]benzoate (**4b**).* Purified by silica gel column chromatography (eluent, 20/20/1−20/20/7 petroleum ether/dichloromethane/ethyl acetate). Isolated yield: 56.3 mg, 82% yield. White solid. Mp: 198−199 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.97 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 6.99 (d, J = 34.3 Hz, 1H), 5.34 (d, J = 3.9 Hz, 1H), 4.92−4.50 (m, 1H), 2.43−2.31 (m, 5H), 1.98−1.87 (m, 3H), 1.84 (dt, J = 13.2, 3.3 Hz, 1H), 1.80−1.72 (m, 1H), 1.70−1.61 (m, 1H), 1.52−1.34 (m, 6H), 1.34−1.22 (m, 3H), 1.21−1.01 (m, 8H), 0.99 (s, 3H), 0.96−0.88 (m, 3H), 0.85 (d, J = 6.5 Hz, 3H), 0.80 (d, J = 2.7 Hz, 3H), 0.79 (d, J = 2.7 Hz, 3H), 0.61 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 165.1, 155.1 (d, J = 308.0 Hz), 146.0, 139.5, 134.1, 133.6 (d, J = 4.0 Hz), 132.0 (d, J = 1.9 Hz), 130.2, 130.0, 130.0 (d, J = 7.5 Hz), 128.9, 122.9, 113.9, 75.0, 56.7, 56.2, 50.0, 42.3, 39.8, 39.5, 38.2, 37.0, 36.7, 36.2, 35.8, 32.0, 31.9, 28.2, 28.0, 27.9, 24.3, 23.9, 22.8, 22.6, 21.8, 21.1, 19.4, 18.7, 11.9. ^{19}F NMR (564 MHz, $CDCl_3$): δ −121.37. FTMS: (APCI) calcd for $C_{43}H_{57}FO_4S^-$ [M^-] 688.3962, found 688.3956.

*(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 4-[(E)-2-Fluoro-2-tosylvinyl]benzoate (**4c**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 20.8 mg, 45% yield. White solid. Mp: 103−104 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H), 7.62 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 34.3 Hz, 1H), 4.93 (td, J = 10.9, 4.4 Hz, 1H), 2.47 (s, 3H), 2.15−2.07 (m, 1H), 1.92 (heptd, J = 6.9, 2.7 Hz, 1H), 1.73 (dt, J = 5.4, 3.0 Hz, 2H), 1.55 (tdd, J = 14.1, 7.3, 3.3 Hz, 2H), 1.18−1.05 (m, 2H), 0.93 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 7.0 Hz, 3H), 0.78 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 165.3, 155.1 (d, J = 308.4 Hz), 146.0, 134.1, 133.6 (d, J = 4.0 Hz), 132.0 (d, J = 1.8 Hz), 130.2, 130.0, 130.0 (d, J = 7.6 Hz), 128.9, 113.9, 75.3, 47.2, 40.9, 34.3, 31.4, 26.6, 23.6, 22.0, 21.8, 20.7, 16.5. ^{19}F NMR (564 MHz, $CDCl_3$): δ −121.43. FTMS: (APCI) calcd for $C_{26}H_{31}FO_4S^-$ [M^-] 458.19326, found 458.19244.

*(8R,9S,13S,14S)-3-({4-[(E)-2-Fluoro-2-tosylvinyl]phenyl}ethynyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (**4d**).* Purified by silica gel column chromatography (eluent, 20/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 33.2 mg, 60% yield. White solid. Mp: 212−213 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.89 (d, J = 8.2 Hz, 2H), 7.52 (q, J = 8.4 Hz, 4H), 7.39 (d, J = 8.1 Hz, 2H), 7.33−7.27 (m, 3H), 7.02 (d, J = 34.6 Hz, 1H), 2.97−2.86 (m, 2H), 2.51 (dd, J = 19.0, 8.8 Hz, 1H), 2.46 (s, 3H), 2.45−2.39 (m, 1H), 2.32 (td, J = 10.9, 3.8 Hz, 1H), 2.20−2.11 (m, 1H), 2.10−2.00 (m, 2H), 2.00−1.95 (m, 1H), 1.65 (dd, J = 12.3, 9.0 Hz, 1H), 1.59−1.40 (m, 5H), 0.92 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 220.7, 154.2 (d, J = 305.9 Hz), 145.8, 140.8, 136.8, 134.4, 132.2, 132.0, 130.2, 130.1, 130.0, 129.1 (d, J = 3.8 Hz), 129.0, 128.8, 125.5, 120.1, 114.4, 92.1, 88.2, 50.5, 47.9, 44.5, 37.9, 35.8, 31.6, 29.1, 26.3, 25.6, 21.8, 21.6, 13.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −123.40. FTMS: (APCI) calcd for $C_{35}H_{34}FO_3S^+$ [M + H^+] 553.2207, found 553.2197.

*(8R,9S,13S,14S)-3-({4-[(E)-2-Fluoro-2-(methylsulfonyl)vinyl]-phenyl}ethynyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (**4e**).* Purified by silica gel column chromatography (eluent, 20/1−3/1 petroleum ether/ethyl acetate). Isolated yield: 37.8 mg, 79% yield. White solid. Mp: 233−234 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.57 (q, J = 8.5 Hz, 4H), 7.33−7.27 (m, 3H), 6.92 (d, J = 35.3 Hz, 1H), 3.13 (s, 3H), 2.96−2.87 (m, 2H), 2.51 (dd, J = 18.9, 8.7 Hz, 1H), 2.46−2.38 (m, 1H), 2.32 (d, J = 3.8 Hz, 1H), 2.20−2.11 (m, 1H), 2.10−2.01 (m, 2H), 2.00−1.94 (m, 1H), 1.68−1.56 (m, 3H), 1.54−1.42 (m, 3H), 0.92 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 220.6, 153.5 (d, J = 305.4 Hz), 140.9, 136.8, 132.2, 132.1, 130.2 (d, J = 7.4 Hz), 129.0, 128.6 (d, J = 3.6 Hz), 125.8 (d, J = 2.4 Hz), 125.5, 120.0, 115.2, 92.3, 88.2, 50.5, 47.9, 44.5, 40.6, 37.9, 35.8, 31.5, 29.1, 26.3, 25.6, 21.6, 13.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −124.55. FTMS: (APCI) calcd for $C_{29}H_{30}FO_3S^+$ [M + H^+] 477.1894, found 477.1882.

*[(3aR,4R,6R,6aR)-6-Methoxy-2,2-dimethyltetrahydrofuro[3,4-d]-[1,3]dioxol-4-yl]methyl 4-[(E)-2-Fluoro-2-tosylvinyl]benzoate (**4f**).* Purified by silica gel column chromatography (eluent, 5/1−2/1 petroleum ether/ethyl acetate). Isolated yield: 26.5 mg, 52% yield. White solid. Mp: 115−116 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.08 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 34.2 Hz, 1H), 5.02 (s, 1H), 4.76 (d, J = 5.9 Hz, 1H), 4.65 (d, J = 5.9 Hz, 1H), 4.52 (t, J = 6.8 Hz, 1H), 4.36 (ddd, J = 24.9, 11.3, 6.8 Hz, 2H), 3.33 (s, 3H), 2.47 (s, 3H), 1.50 (s, 3H), 1.34 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 165.3, 155.3 (d, J = 308.9 Hz), 146.0, 134.1 (d, J = 4.1 Hz), 134.0, 130.9 (d, J = 1.9 Hz), 130.2, 130.2, 130.1 (d, J = 7.4 Hz), 128.9, 113.7, 112.7, 109.5, 85.3, 84.3, 81.9, 65.4, 55.0, 26.5, 25.0, 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −120.94. FTMS: (APCI) calcd for $C_{25}H_{27}FO_8S^-$ [M^-] 506.1416, found 506.1407.

*[(3aS,5aR,8aR,8bS)-2,2,7,7-Tetramethyltetrahydro-3aH-bis([1,3]-dioxolo)[4,5-b:4′,5′-d]pyran-3a-yl]methyl 4-[(E)-2-Fluoro-2-tosylvinyl]benzoate (**4g**).* Purified by silica gel column chromatography (eluent, 5/1−2/1 petroleum ether/ethyl acetate). Isolated yield: 20.2 mg, 36% yield. Colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.08 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 34.2 Hz, 1H), 4.69 (d, J = 11.8 Hz, 1H), 4.64 (dd, J = 7.9, 2.6 Hz, 1H), 4.44 (d, J = 2.6 Hz, 1H), 4.33 (d, J = 11.8 Hz, 1H), 4.26 (dd, J = 7.9, 1.2 Hz, 1H), 3.95 (dd, J = 13.0, 1.9 Hz, 1H), 3.80 (d, J = 13.0 Hz, 1H), 2.47 (s, 3H), 1.54 (s, 3H), 1.45 (s, 3H), 1.34 (s, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 165.1, 155.3 (d, J = 309.2 Hz), 146.1, 134.0 (d, J = 4.4 Hz), 131.1 (d, J = 2.0 Hz), 130.2, 130.0 (d, J = 7.5 Hz), 128.9, 113.7, 109.2, 108.9, 101.6, 70.8, 70.6, 70.1, 65.6, 61.4, 26.5, 25.9, 25.9, 24.0, 21.8. ^{19}F NMR (564 MHz, $CDCl_3$): δ −120.91. FTMS: (APCI) calcd for $C_{28}H_{31}FO_9S^-$ [M^-] 562.1678, found 562.1669.

*(R)-2,8-Dimethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]chroman-6-yl 4-[(E)-2-Fluoro-2-(phenylsulfonyl)vinyl]benzoate (**4h**).* Purified by silica gel column chromatography (eluent, 20/1−5/1 petroleum ether/ethyl acetate). Isolated yield: 56.6 mg, 82% yield. White solid. Mp: 80−81 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.18 (d, J = 8.5 Hz, 2H), 8.07−8.00 (m, 2H), 7.76−7.70 (m, 1H), 7.68 (d, J = 8.5 Hz, 2H), 7.65−7.59 (m, 2H), 7.12 (d, J = 34.1 Hz, 1H), 6.79 (d, J = 2.5 Hz, 1H), 6.74 (d, J = 2.6 Hz, 1H), 2.81−2.69 (m, 2H), 2.17 (s, 3H), 1.82 (dt, J = 13.8, 6.9 Hz, 1H), 1.75 (dt, J = 13.3, 6.4 Hz, 1H), 1.59−

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1.32 (m, 8H), 1.31−1.23 (m, 9H), 1.21−1.16 (m, 1H), 1.16−1.10 (m, 3H), 1.09−1.02 (m, 3H), 0.85 (dd, J = 10.0, 6.6 Hz, 12H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 165.0, 155.1 (d, J = 308.9 Hz), 150.0, 142.5, 137.1, 134.7, 134.1 (d, J = 4.0 Hz), 131.2 (d, J = 1.9 Hz), 130.6, 130.2, 130.1, 129.6, 128.9, 127.5, 121.1, 121.1, 119.0, 114.2, 76.2, 40.2, 39.4, 37.5, 37.4, 37.3, 32.8, 32.7, 31.0, 28.0, 24.8, 24.5, 24.3, 22.7, 22.6, 22.5, 21.0, 19.8, 19.7, 16.2. ^{19}F NMR (564 MHz, $CDCl_3$): δ −120.87. FTMS: (APCI) calcd for $C_{42}H_{55}FO_5S^+$ $[M^+]$ 690.3749, found 690.3746.

Gram-Scale Experiment. A solution of **1a** (4.0 mmol, 760 mg, 1 equiv) and **2b** (12 mmol, 2.14 g, 3 equiv) in degassed DMSO (40 mL) was stirred under a nitrogen atmosphere at 100 °C for 24 h. After completion of the reaction, 100 mL of water was added to the reaction mixture and the aqueous solution was extracted with ethyl acetate (5 × 40 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The pure product was obtained by flash column chromatography on silica gel (eluent, 20/1−5/1 petroleum ether/ethyl acetate) to obtain desired product **3ab** in 78% yield (1.02 g).

*2-(2-Fluoro-2-tosylethyl)naphthalene (**5a**).* The preparation followed literature methods.[18] An oven-dried vial equipped with a PTFE-coated stir bar was charged with tetrahydroxydiboron $[B_2(OH)_4]$ (0.4 mmol, 36 mg, 4 equiv) and Pd/C (5 wt %, 0.01 mmol, 21.2 mg). The vial was capped with a septum, degassed, and backfilled with argon. The vial was charged with 2.0 mL of dichloromethane followed by **3ab** (0.10 mmol, 32.6 mg, 1 equiv) and 50 μL of water. The mixture was heated at 50 °C for 12 h (monitored by TLC). The solution was then filtered through a Celite plug and washed with DCM. The crude product was purified by column chromatography on silica gel, eluting with ethyl 1/5 (v/v) acetate/petroleum ether to afford hydrogenated product **5a** in 86% yield (28.2 mg). White solid. Mp: 102−103 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, J = 8.2 Hz, 2H), 7.83−7.75 (m, 3H), 7.71 (s, 1H), 7.51−7.44 (m, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 8.4 Hz, 1H), 5.32 (ddd, J = 48.5, 10.5, 2.1 Hz, 1H), 3.67 (ddd, J = 40.1, 15.0, 1.8 Hz, 1H), 3.30 (td, J = 15.6, 10.5 Hz, 1H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 146.0, 133.5, 132.6, 132.2, 131.3, 130.1, 129.7, 128.6, 128.4, 127.7, 127.7, 127.1, 126.4, 126.1, 102.8 (d, J = 221.5 Hz), 34.2 (d, J = 19.6 Hz), 21.8. ^{19}F NMR (565 MHz, $CDCl_3$): δ −177.28. FTMS: (APCI) calcd for $C_{19}H_{16}FO_2S^-$ $[M - H^+]$ 327.0860, found 327.0852.

*(Z)-2-(2-Cyclohexyl-2-fluorovinyl)naphthalene (**5b**).*[22] The preparation followed literature methods.[17] An oven-dried vial equipped with a PTFE-coated stir bar was charged with **3ab** (0.10 mmol, 32.6 mg, 1 equiv), eosin Y (2.0 mol %, 1.4 mg), and 1-cyclohexyl-2,4,6-triphenylpyridin-1-ium tetrafluoroborate (0.30 mmol, 143.2 mg, 3 equiv). MeOH (3 mL) and DCE (1 mL) were added, and then the resulting mixture was degassed by three freeze−thaw cycles and backfilled with argon. Subsequently, DIPEA (4 equiv) was added, and the reaction mixture was warmed to room temperature and irradiated with a green LED for 40 h. After this time, the mixture was diluted with DCM (15 mL), transferred to a round-bottom flask, and concentrated in vacuo. A crude product was purified by column chromatography on silica gel, eluting with petroleum ether to afford radical-substituted product **5b** in 46% yield (11.7 mg). Colorless oil. ^1H NMR (600 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.82−7.75 (m, 3H), 7.64 (dd, J = 8.5, 1.3 Hz, 1H), 7.42 (pd, J = 6.8, 1.2 Hz, 2H), 5.59 (d, J = 40.7 Hz, 1H), 2.34−2.23 (m, 1H), 2.04−1.96 (m, 2H), 1.88−1.81 (m, 2H), 1.76−1.69 (m, 1H), 1.43−1.36 (m, 2H), 1.35−1.29 (m, 2H), 1.25−1.20 (m, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 165.5 (d, J = 268.6 Hz), 133.5, 132.2, 131.6 (d, J = 1.7 Hz), 127.9, 127.8, 127.5, 127.0 (d, J = 7.4 Hz), 126.7 (d, J = 7.6 Hz), 126.0, 125.6, 103.7 (d, J = 8.8 Hz), 41.6 (d, J = 24.3 Hz), 30.1 (d, J = 1.7 Hz), 26.0, 25.9. ^{19}F NMR (565 MHz, $CDCl_3$): δ −104.60. FTMS: (APCI) calcd for $C_{18}H_{18}F^-$ $[M - H^+]$ 253.1398, found 253.1393.

*(E)-[2-(Naphthalen-2-yl)-1-tosylvinyl](p-tolyl)sulfane (**5c**).* An oven-dried vial equipped with a PTFE-coated stir bar was charged with **3ab** (0.10 mmol, 32.6 mg, 1 equiv) and sodium 4-methylbenzenethiolate (0.20 mmol, 29.2 mg, 2 equiv). DMSO (1 mL) was added; then the resulting mixture was degassed and backfilled with argon, and the reaction mixture was stirred at rt for 16 h (monitored by TLC). After this amount of time, 4 mL of water was added to the reaction mixture and the aqueous solution was extracted with ethyl acetate (3 × 4 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The pure product was obtained by flash column chromatography on silica gel (eluent, 20/1−5/1 petroleum ether/ethyl acetate) to afford desired product **5c** in 65% yield (28 mg). Yellow solid. Mp: 106−107 °C. ^1H NMR (600 MHz, $CDCl_3$): δ 8.66 (s, 1H), 8.33 (s, 1H), 8.15 (dd, J = 8.7, 1.6 Hz, 1H), 7.85−7.78 (m, 4H), 7.76 (d, J = 8.7 Hz, 1H), 7.54−7.50 (m, 1H), 7.50−7.47 (m, 1H), 7.21 (d, J = 8.3 Hz, 2H), 6.97 (d, J = 8.2 Hz, 2H), 6.87 (d, J = 8.3 Hz, 2H), 2.36 (s, 3H), 2.19 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 147.2, 144.3, 136.6, 135.6, 134.47, 134.0, 133.2, 132.8, 130.0, 130.0, 129.7, 129.4, 129.1, 129.0, 128.3, 128.0, 127.9, 127.6, 126.6, 126.4, 21.6, 20.9. FTMS: (APCI) calcd for $C_{26}H_{21}O_2S_2^-$ $[M - H^+]$ 429.0988, found 429.0980.

*(E)-1-[2-(Naphthalen-2-yl)-1-tosylvinyl]-1H-indole (**5d**).* The preparation followed literature methods.[18] An oven-dried vial equipped with a PTFE-coated stir bar was charged with **3ab** (0.10 mmol, 32.6 mg, 1 equiv), indole (0.12 mmol, 14 mg, 1.2 equiv), K_3PO_4 (0.2 mmol, 42.5 mg, 2 equiv), and DMF (2 mL). Then the reaction mixture was stirred at 60 °C until the reaction was complete (monitored by TLC). After this time, 4 mL of water was added to the reaction mixture and the aqueous solution was extracted with ethyl acetate (3 × 4 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The pure product was obtained by flash column chromatography on silica gel (eluent, 10/1−5/1 petroleum ether/ethyl acetate) to afford desired product **5d** in 45% yield (19 mg). Yellow semisolid. ^1H NMR (600 MHz, $CDCl_3$): δ 8.29 (s, 1H), 7.63 (dd, J = 12.3, 8.1 Hz, 2H), 7.57 (d, J = 7.4 Hz, 2H), 7.47 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 8.5 Hz, 2H), 7.42−7.39 (m, 1H), 7.08 (d, J = 3.3 Hz, 1H), 7.05 (d, J = 8.1 Hz, 2H), 6.99 (dd, J = 11.1, 3.9 Hz, 1H), 6.79 (dd, J = 11.3, 4.0 Hz, 1H), 6.72 (d, J = 2.9 Hz, 1H), 6.59−6.52 (m, 2H), 2.28 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 144.8, 136.4, 135.6, 135.5, 134.6, 134.2, 132.8, 132.6, 129.6, 128.8, 128.7, 128.5, 128.5, 128.1, 127.9, 127.8, 127.5, 126.6, 124.9, 122.7, 120.8, 120.7, 110.3, 105.6, 21.5. FTMS: (APCI) calcd for $C_{27}H_{22}NO_2S^+$ $[M + H^+]$ 424.1366, found 424.1358.

*1,1′-[2-(Naphthalen-2-yl)ethene-1,1-diyl]bis(1H-imidazole) (**5e**).* The preparation followed literature methods.[18] An oven-dried vial equipped with a PTFE-coated stir bar was charged with **3ab** (0.10 mmol, 32.6 mg, 1 equiv), imidazole (0.25 mmol, 17 mg, 2.5 equiv), K_3PO_4 (0.3 mmol, 63.7 mg, 3 equiv), and DMF (2 mL). Then the reaction mixture was stirred at 100 °C until the reaction was complete (monitored by TLC). After this time, 4 mL of water was added to the reaction mixture and the aqueous solution was extracted with ethyl acetate (3 × 4 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The pure product was obtained by flash column chromatography on silica gel (eluent, 10/1−3/1 petroleum ether/ethyl acetate) to afford desired product **5e** in 71% yield (20.3 mg). Yellow oil. ^1H NMR (600 MHz, $CDCl_3$): δ 7.91−7.83 (m, 2H), 7.80 (dd, J = 5.9, 2.5 Hz, 1H), 7.59 (s, 1H), 7.57−7.51 (m, 3H), 7.44 (s, 2H), 7.38 (d, J = 8.6 Hz, 1H), 7.35 (s, 1H), 7.03 (s, 1H), 6.97 (s, 1H), 6.31 (s, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 137.8, 137.5, 133.7, 133.1, 131.8, 131.2, 130.9, 129.2, 128.4, 127.8, 127.4, 127.2, 126.6, 125.6, 122.4, 119.7, 118.5, 117.6. FTMS: (APCI) calcd for $C_{18}H_{15}N_4^+$ $[M + H^+]$ 287.1291, found 287.1287.

Procedure for Control Experiments (Scheme 4, eq 1). A solution of *gem*-difluoroalkene **1a** (0.1 mmol, 19 mg, 1 equiv), sodium benzenesulfinate **2b** (0.3 mmol, 53.5 mg, 3 equiv), and additive (2 equiv) in degassed DMSO (1.0 mL) was stirred under a nitrogen atmosphere at 100 °C for 24 h. After completion of the reaction, 2 mL of water was added to the reaction mixture and the aqueous solution was extracted with ethyl acetate (3 × 4 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The pure product was obtained by flash column chromatography on silica gel (eluent, 20/1−5/1 petroleum ether/ethyl acetate) to afford desired product **3ab**.

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Procedure for the Competition Experiment (Scheme 4, eq 2). A solution of *gem*-difluoroalkene **1a** (0.1 mmol, 19 mg, 1 equiv), sodium benzenesulfinate **2c** (0.15 mmol, 29.1 mg, 1.5 equiv), and **2h** (0.15 mmol, 33.3 mg, 1.5 equiv) in degassed DMSO (1.0 mL) was stirred under a nitrogen atmosphere at 100 °C for 3 h. After completion of the reaction, 2 mL of water was added to the reaction mixture and the aqueous solution was extracted with ethyl acetate (3 × 4 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The pure product was obtained by flash column chromatography on silica gel (eluent, 10/1−3/1 petroleum ether/ethyl acetate) to afford desired products **3ac** and **3ah**.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00490.

Detailed optimization of reaction conditions, some of the mechanistic studies, and copies of ^{1}H, $^{13}C\{^{1}H\}$, and ^{19}F NMR spectra for new compounds (PDF)

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Author Contributions

Y.L. and D.S. conceived the project. Y.L., X.W.L., and X.Q.L. performed the experiments, analyzed the data, and discussed the results. Y.L. and D.S. wrote the paper. Y.L., X.W.L., and X.Q.L. wrote the Supporting Information and contributed other related materials.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Palmer, J. T.; Rasnick, D.; Klaus, J. L.; Bromme, D. Vinyl sulfones as mechanism-based cysteine protease inhibitors. *J. Med. Chem.* **1995**, *38*, 3193−3196. (b) Kondo, T.; Mitsudo, T.-a. Metal-catalyzed carbon-sulfur bond formation. *Chem. Rev.* **2000**, *100*, 3205−3220. (c) Meadows, D. C.; Gervay-Hague, J. Vinyl sulfones: synthetic preparations and medicinal chemistry applications. *Med. Res. Rev.* **2006**, *26*, 793−814. (d) Kisselev, A. F.; van der Linden, W. A.; Overkleeft, H. S. Proteasome inhibitors: an expanding army attacking a unique target. *Chem. Biol.* **2012**, *19*, 99−115. (e) Frankel, B. A.; Bentley, M.; Kruger, R. G.; McCafferty, D. G. Vinyl sulfones: inhibitors of SrtA, a transpeptidase required for cell wall protein anchoring and virulence in Staphylococcus aureus. *J. Am. Chem. Soc.* **2004**, *126*, 3404−3405.

(2) (a) McCarthy, J. R.; Matthews, D. P.; Edwards, M. L.; Stemerick, D. M.; Jarvi, E. T. A new route to vinyl fluorides. *Tetrahedron Lett.* **1990**, *31*, 5449−5452. (b) He, M.; Ghosh, A. K.; Zajc, B. Julia Olefination as a General Route to Phenyl (α-Fluoro)vinyl Sulfones. *Synlett* **2008**, *19*, 999−1004. (c) Shastin, A. V.; Nenajdenko, V. G.; Muzalevskiy, V. M.; Balenkova, E. S.; Fröhlich, R.; Haufe, G. New synthetic approach to α-fluoro-β-arylvinyl sulfones and their application in Diels−Alder reactions. *Tetrahedron* **2008**, *64*, 9725−9732. (d) Prakash, G. K.; Chacko, S.; Vaghoo, H.; Shao, N.; Gurung, L.; Mathew, T.; Olah, G. A. Efficient nucleophilic fluoromethylation and subsequent transformation of alkyl and benzyl halides using fluorobis(phenylsulfonyl)methane. *Org. Lett.* **2009**, *11*, 1127−1130. (e) Yamada, S.; Shimoji, K.; Takahashi, T.; Konno, T.; Ishihara, T. An effective preparation of sulfonyl- or sulfinyl-substituted fluorinated alkenes and their stereoselective addition-elimination reactions with organocuprates. *Chem. - Asian J.* **2010**, *5*, 1846−1853. (f) Zhu, L.; Ni, C.; Zhao, Y.; Hu, J. 1-tert-Butyl-1H-tetrazol-5-yl fluoromethyl sulfone ($TBTSO_2CH_2F$): a versatile fluoromethylidene synthon and its use in the synthesis of monofluorinated alkenes via Julia−Kocienski olefination. *Tetrahedron* **2010**, *66*, 5089−5100. (g) Li, W.; Yin, Y.; Yao, H.; Shuai, W.; Sun, H.; Xu, S.; Liu, J.; Yao, H.; Zhu, Z.; Xu, J. Discovery of novel vinyl sulfone derivatives as anti-tumor agents with microtubule polymerization inhibitory and vascular disrupting activities. *Eur. J. Med. Chem.* **2018**, *157*, 1068−1080. (h) Fang, X.; Zhou, J.; Wang, W.; Yang, X.; Wu, F. Highly stereoselective monofluoroolefination: Facile access to (*E*)-α-fluorinated arylvinyl sulfones from trifluoromethyl α-fluorinated arylsulfonyl *gem*-diols. *Tetrahedron Lett.* **2020**, *61*, 151964.

(3) (a) Muller, K.; Faeh, C.; Diederich, F. Fluorine in Pharmaceuticals: Looking Beyond Intuition. *Science* **2007**, *317*, 1881−1886. (b) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. Fluorine in medicinal chemistry. *Chem. Soc. Rev.* **2008**, *37*, 320−330. (c) Wang, J.; Sanchez-Rosello, M.; Acena, J. L.; del Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. Fluorine in pharmaceutical industry: fluorine-containing drugs introduced to the market in the last decade (2001−2011). *Chem. Rev.* **2014**, *114*, 2432−2506. (d) Preshlock, S.; Tredwell, M.; Gouverneur, V. ^{18}F-Labeling of Arenes and Heteroarenes for Applications in Positron Emission Tomography. *Chem. Rev.* **2016**, *116*, 719−766. (e) Meanwell, N. A. Fluorine and Fluorinated Motifs in the Design and Application of Bioisosteres for Drug Design. *J. Med. Chem.* **2018**, *61*, 5822−5880. (f) Zhu, Y.; Han, J.; Wang, J.; Shibata, N.; Sodeoka, M.; Soloshonok, V. A.; Coelho, J. A. S.; Toste, F. D. Modern Approaches for Asymmetric Construction of Carbon-Fluorine Quaternary Stereogenic Centers: Synthetic Challenges and Pharmaceutical Needs. *Chem. Rev.* **2018**, *118*, 3887−3964. (g) Johnson, B. M.; Shu, Y. Z.; Zhuo, X.; Meanwell, N. A. Metabolic and Pharmaceutical Aspects of Fluorinated Compounds. *J. Med. Chem.* **2020**, *63*, 6315−6386.

(4) (a) Mei, H.; Han, J.; Fustero, S.; Medio-Simon, M.; Sedgwick, D. M.; Santi, C.; Ruzziconi, R.; Soloshonok, V. A. Fluorine-Containing Drugs Approved by the FDA in 2018. *Chem. - Eur. J.* **2019**, *25*, 11797−11819. (b) Mullard, A. 2018 FDA drug approvals. *Nat. Rev. Drug Discovery* **2019**, *18*, 85−89. (c) Mei, H.; Remete, A. M.; Zou, Y.; Moriwaki, H.; Fustero, S.; Kiss, L.; Soloshonok, V. A.; Han, J. Fluorine-containing drugs approved by the FDA in 2019. *Chin. Chem. Lett.* **2020**, *31*, 2401−2413.

(5) (a) Amii, H.; Uneyama, K. C-F bond activation in organic synthesis. *Chem. Rev.* **2009**, *109*, 2119−2183. (b) Clot, E.; Eisenstein, O.; Jasim, N.; Macgregor, S. A.; McGrady, J. E.; Perutz, R. N. C−F and C−H Bond Activation of Fluorobenzenes and Fluoropyridines at Transition Metal Centers: How Fluorine Tips the Scales. *Acc. Chem. Res.* **2011**, *44*, 333−348. (c) Stahl, T.; Klare, H. F. T.; Oestreich, M. Main-Group Lewis Acids for C−F Bond Activation. *ACS Catal.* **2013**, *3*, 1578−1587. (d) Ahrens, T.; Kohlmann, J.; Ahrens, M.; Braun, T. Functionalization of fluorinated molecules by transition-metal-mediated C-F bond activation to access fluorinated building blocks. *Chem. Rev.* **2015**, *115*, 931−972. (e) Eisenstein, O.; Milani, J.; Perutz, R. N. Selectivity of C-H Activation and Competition between C-H and C-F Bond Activation at Fluorocarbons. *Chem. Rev.* **2017**, *117*, 8710−8753. (f) Coates, G.; Rekhroukh, F.; Crimmin, M. R. Breaking Carbon−Fluorine Bonds with Main Group Nucleophiles. *Synlett* **2019**, *30*, 2233−2246.

(6) (a) Landelle, G.; Bergeron, M.; Turcotte-Savard, M. O.; Paquin, J. F. Synthetic approaches to monofluoroalkenes. *Chem. Soc. Rev.* **2011**, *40*, 2867−2908. (b) Chelucci, G. Synthesis and metal-catalyzed reactions of *gem*-dihalovinyl systems. *Chem. Rev.* **2012**, *112*, 1344−1462. (c) Kuehnel, M. F.; Lentz, D.; Braun, T. Synthesis of fluorinated building blocks by transition-metal-mediated hydrodefluorination reactions. *Angew. Chem., Int. Ed.* **2013**, *52*, 3328−3348. (d) Liu, Q.; Ni, C.; Hu, J. China's flourishing synthetic organofluorine chemistry: innovations in the new millennium. *Natl. Sci. Rev.* **2017**, *4*, 303−325. (e) Orsi, D. L.; Altman, R. A. Exploiting the unusual effects of fluorine in methodology. *Chem. Commun.* **2017**, *53*, 7168−7181. (f) Zhang, X.; Cao, S. Recent advances in the synthesis and CF functionalization of *gem*-difluoroalkenes. *Tetrahedron Lett.* **2017**, *58*, 375−392. (g) Fujita, T.; Fuchibe, K.; Ichikawa, J. Transition-Metal-Mediated and -Catalyzed C-F Bond Activation by Fluorine Elimination. *Angew. Chem., Int. Ed.* **2019**, *58*, 390−402.

(7) Jiang, L.-F.; Ren, B.-T.; Li, B.; Zhang, G.-Y.; Peng, Y.; Guan, Z.-Y.; Deng, Q.-H. Nucleophilic Substitution of *gem*-Difluoroalkenes with TMSNu Promoted by Catalytic Amounts of Cs_2CO_3. *J. Org. Chem.* **2019**, *84*, 6557−6564.

(8) Wang, M.; Liang, F.; Xiong, Y.; Cao, S. Synthesis of fluorovinyl aryl ethers by a three-component reaction of *gem*-difluoroalkenes with arylboronic acids and oxygen. *RSC Adv.* **2015**, *5*, 11996−11999.

(9) Xiong, Y.; Zhang, X.; Huang, T.; Cao, S. Synthesis of N-(α-fluorovinyl)azoles by the reaction of difluoroalkenes with azoles. *J. Org. Chem.* **2014**, *79*, 6395−6402.

(10) Sakaguchi, H.; Uetake, Y.; Ohashi, M.; Niwa, T.; Ogoshi, S.; Hosoya, T. Copper-Catalyzed Regioselective Monodefluoroborylation of Polyfluoroalkenes en Route to Diverse Fluoroalkenes. *J. Am. Chem. Soc.* **2017**, *139*, 12855−12862.

(11) Tan, D.-H.; Lin, E.; Ji, W.-W.; Zeng, Y.-F.; Fan, W.-X.; Li, Q.; Gao, H.; Wang, H. Copper-Catalyzed Stereoselective Defluorinative Borylation and Silylation of *gem*-Difluoroalkenes. *Adv. Synth. Catal.* **2018**, *360*, 1032−1037.

(12) Cong, Z. S.; Li, Y. G.; Chen, L.; Xing, F.; Du, G. F.; Gu, C. Z.; He, L. N-Heterocyclic carbene-catalyzed stereoselective construction of olefinic carbon-sulfur bonds via cross-coupling reaction of gem-difluoroalkenes and thiols. *Org. Biomol. Chem.* **2017**, *15*, 3863−3868.

(13) Peng, Y.; Zhang, X.; Qi, X.; He, Q.; Zhang, B.; Hao, J.; Yang, C. Metal-Free Access to (*E*/*Z*)-α-Fluorovinyl Phosphorus Compounds from gem-Difluorostyrenes. *Eur. J. Org. Chem.* **2019**, *2019*, 1170−1177.

(14) Li, Y.; Li, X.; Li, X.; Shi, D. Visible-light-promoted E-selective synthesis of alpha-fluoro-beta-arylalkenyl sulfides via the deoxygenation/isomerization process. *Chem. Commun.* **2021**, *57*, 2152−2155.

(15) (a) Koch, H. F.; Kielbania, A. J. Nucleophilic reactions of fluoroolefins. Evidence for a carbanion intermediate in vinyl and allyl displacement reactions. *J. Am. Chem. Soc.* **1970**, *92*, 729−730. (b) Kim, M. S.; Jeong, I. H. A highly stereoselective preparation of CF_3-substituted 1-aryl-1,2-diphenylethenes: application to the synthesis of panomifene. *Tetrahedron Lett.* **2005**, *46*, 3545−3548. (c) Zhang, J.; Xu, C.; Wu, W.; Cao, S. Mild and Copper-Free Stereoselective Cyanation of *gem*-Difluoroalkenes by Using Benzyl Nitrile as a Cyanating Reagent. *Chem. - Eur. J.* **2016**, *22*, 9902−9908.

(16) Cummings, S. P.; Le, T. N.; Fernandez, G. E.; Quiambao, L. G.; Stokes, B. J. Tetrahydroxydiboron-Mediated Palladium-Catalyzed Transfer Hydrogenation and Deuteriation of Alkenes and Alkynes Using Water as the Stoichiometric H or D Atom Donor. *J. Am. Chem. Soc.* **2016**, *138*, 6107−6110.

(17) Ociepa, M.; Turkowska, J.; Gryko, D. Redox-Activated Amines in $C(sp^3)-C(sp)$ and $C(sp^3)-C(sp^2)$ Bond Formation Enabled by Metal-Free Photoredox Catalysis. *ACS Catal.* **2018**, *8*, 11362−11367.

(18) Ma, T.; Chen, Y.; Li, Y.; Ping, Y.; Kong, W. Nickel-Catalyzed Enantioselective Reductive Aryl Fluoroalkenylation of Alkenes. *ACS Catal.* **2019**, *9*, 9127−9133.

(19) (a) Hu, J.; Han, X.; Yuan, Y.; Shi, Z. Stereoselective Synthesis of *Z* Fluoroalkenes through Copper-Catalyzed Hydrodefluorination of *gem*-Difluoroalkenes with Water. *Angew. Chem., Int. Ed.* **2017**, *56*, 13342−13346. (b) Krishnamoorthy, S.; Kothandaraman, J.; Saldana, J.; Prakash, G. K. S. Direct Difluoromethylenation of Carbonyl Compounds by Using $TMSCF_3$: The Right Conditions. *Eur. J. Org. Chem.* **2016**, *2016*, 4965−4969. (c) Thomoson, C. S.; Martinez, H.; Dolbier, W. R. The use of methyl 2,2-difluoro-2-(fluorosulfonyl)-acetate as the difluorocarbene source to generate an in situ source of difluoromethylene triphenylphosphonium ylide. *J. Fluorine Chem.* **2013**, *150*, 53−59.

(20) Cabrera-Afonso, M. J.; Lu, Z. P.; Kelly, C. B.; Lang, S. B.; Dykstra, R.; Gutierrez, O.; Molander, G. A. Engaging sulfinate salts via Ni/photoredox dual catalysis enables facile Csp^2-SO_2R coupling. *Chem. Sci.* **2018**, *9*, 3186−3191.

(21) Frost, A. B.; Brambilla, M.; Exner, R. M.; Tredwell, M. Synthesis and Derivatization of 1,1-[^{18}F]Difluorinated Alkenes. *Angew. Chem., Int. Ed.* **2019**, *58*, 472−476.

(22) Zhao, Y.; Jiang, F.; Hu, J. Spontaneous resolution of Julia-Kocienski intermediates facilitates phase separation to produce *Z*- and *E*-monofluoroalkenes. *J. Am. Chem. Soc.* **2015**, *137*, 5199−5203.

https://doi.org/10.1021/acs.joc.1c00490
J. Org. Chem. 2021, 86, 6983−6993