Note

Diastereoselective synthesis of CF3-containing vicinal diamines

Qiu-Xia Huang, Qu-Tong Zheng, Yaya Duan, Jin-Hong Lin, Ji-Chang Xiao, and Xing Zheng

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b01261 • Publication Date (Web): 07 Jul 2017

Diastereoselective synthesis of CF_3-containing vicinal diamines

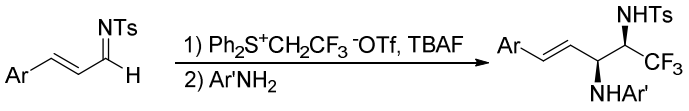
Qiu-xia Huang,[a, b‡] Qu-tong Zheng,[a, b‡] Yaya Duan,[b] Jin-Hong Lin,[b*] Ji-Chang, Xiao[a,b*] and Xing Zheng[a,b*]

[a]*Institute of Pharmacy and Pharmacology, Hunan Province Cooperative Innovation Center for Molecular Target New Drug Study, University of South China, 28 Western Changsheng Road, Hengyang, Hunan, 421001, China.*

[b]*Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, University of Chinese Academy of Sciences, Chinese Academy of Sciences 345 Lingling Road, Shanghai 200032, China.*

[‡]*These two authors contributed equally to this work.*

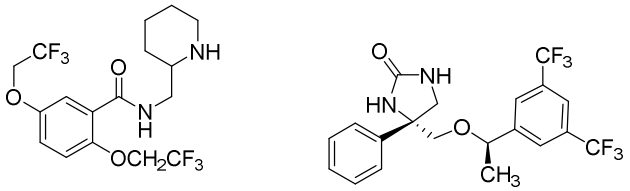
Abstract



The highly diastereoselective synthesis of CF_3-containing vicinal diamines by a convenient two-step procedure without the need to isolate the intermediate products is described.

Vicinal diamines represent highly important scaffolds in natural products, pharmaceuticals, and agrochemicals.[1] As trifluoromethyl group (CF_3) have proved to be a valuable pharmacophore in medicinal chemistry and agrochemistry,[2] its incorporation into vicinal diamines may improve biological properties. Indeed, biologically active CF_3-containing vicinal diamines have appeared. For instance, Flecainide is a commercially available drug which is used to prevent and treat tachyarrhythmias (abnormal fast rhythms of the heart),[3] and Sch 425078 has been shown to be a potent neurokinin antagonist (Scheme 1)[4]. Therefore, it is highly

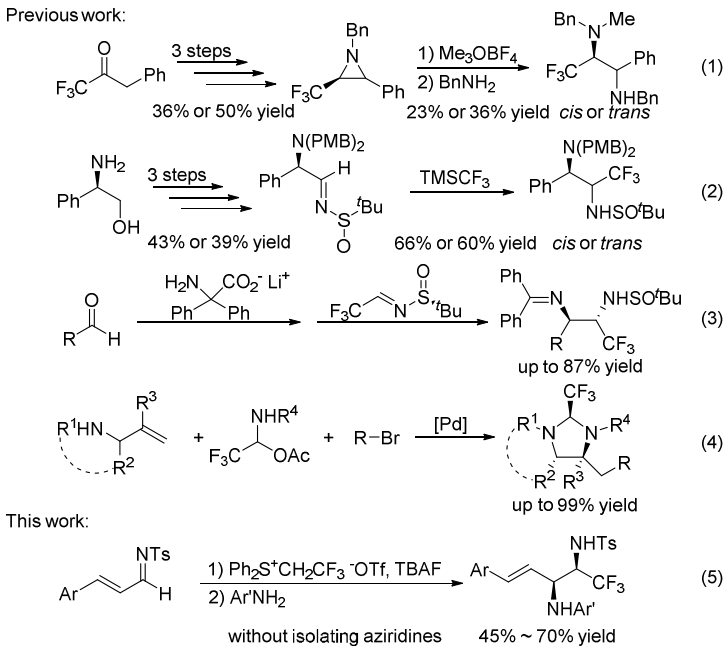
desirable to develop mild protocols to access CF_3-vicinal diamines. Surprisingly, although significant efforts have been directed towards the exploration of efficient methods to prepare vicinal diamines,[1e,5] the diastereoselective synthesis of CF_3-containing vicinal diamines remains largely unexplored.



Flecainide Sch 425078

Scheme 1. Biologically active CF_3-containing vicinal diamines

Although CF_3-containing vicinal diamines could be easily obtained,[6] their diastereoselective synthesis has not been realized until recently. In 2014, D'hooghe, De Kimpe et al. described the Lewis acid-promoted ring-opening of aziridine to give CF_3-vicinal diamines (Scheme 2, eq 1).[7] Almost at the same time, Fustero and co-workers obtained the diamine derivatives by trifluoromethylation of α-amino imines (eq 2).[8] Although these examples represented a breakthrough in the diastereoselective synthesis of CF_3-vicinal diamines, multi-step procedure and low yields limit their synthetic utility. In 2015, Han, Soloshonok et al. reported a two-step procedure to achieve diamines in high yields (eq 3).[9] Recently, the group of Waser disclosed the Pd-catalyzed three-component synthesis of diamines via in situ aminal formation and carboamination (eq 4).[10] In all of these reactions, high diastereoselectivity was obtained (eqs. 1-4). But the convenient and diastereoselective synthesis of CF_3-containing vicinal diamines remains a challenging task.

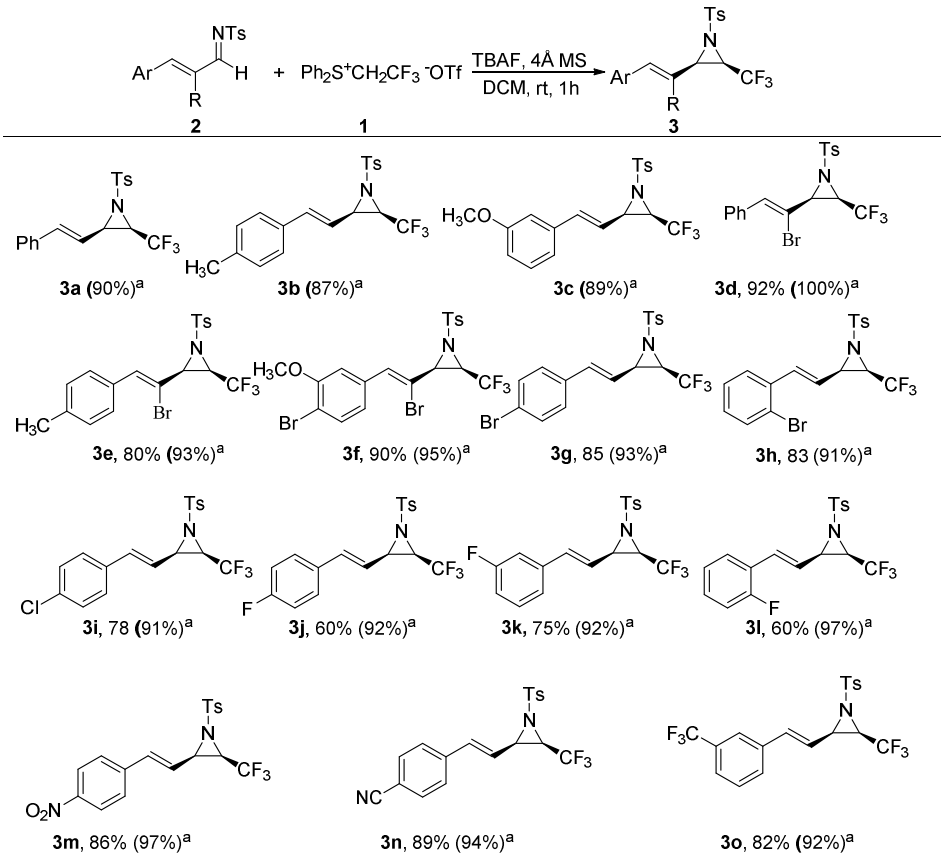


Scheme 2. The synthesis of CF_3-containing vicinal diamines

We have previously found that CF_3-aziridines could be easily prepared in high yields and with high diastereoselectivity by cyclization of imines with sulfonium ylide [$Ph_2S^+CH^-CF_3$] generated in situ from sulfonium salt **1** [$Ph_2S^+CH_2CF_3$ ^-OTf].[11] We speculated that ring-opening of CF_3-azirindes with amines may furnish CF_3-containing vicinal diamines. In continuation of our research interest in the incorporation of CF_3 moiety,[11-12] we have now investigated the convenient synthesis of CF_3-vicinal diamines from imines without the need to isolate the intermediate CF_3-aziridines (Scheme 2, eq 5).

The CF_3-aziridines we have made before were aryl aziridines.[11] In this work, we were interested in vinyl aziridines since the vinyl moiety is also a potential functionality for further transformation. Therefore, we firstly tested if vinyl aziridines could be easily obtained. To our delight, under the same conditions for cyclization of

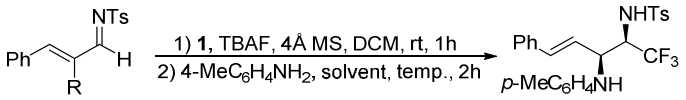
aryl imines,[11] vinyl imines were converted smoothly into vinyl aziridines in high yields (Scheme 3). High diastereoselectivity was observed in all reactions (*cis:trans* > 9:1). Although high yields were obtained for the conversion of electron-neutral and -rich imines, the desired products were unstable and therefore could not be isolated (**3a-3c**). Interestingly, the presence of a bromo-substituent in the vinyl moiety could stabilize the products (**3d-3f**). Electron-deficient imines were well transformed and the expected products were isolated in good yields (**3g-3o**). The structure and relative configuration of product **3m** were confirmed by single crystal X-ray diffraction.[13]



Scheme 3. The synthesis of vinyl imines. Isolated yields. [a]The yields in parentheses were determined by ^{19}F NMR spectrometry.

Since the availability of CF_3-aziridines was not an issue, we then examined the convenient synthesis of CF_3-vicinal diamines without isolating CF_3-aziridines. A two-step procedure was performed, including cyclization of vinyl imine to give aziridines (step 1) and ring-opening of aziridine by aryl amine (step 2) to afford the desired product. To our delight, the one-pot procedure by cyclization of substrate **2a** and the subsequent direct addition of 4-methylphenyl amine (4-$MeC_6H_4NH_2$) could furnish product **4a** in 56% yield (Table 1, entry 1). Elevating the reaction temperature of step 2 increased the yield slightly (entry 2). DCM in step 2 should be replaced by other solvent which has a higher boiling point, otherwise the reaction temperature can't be further elevated. 4 Å MS used in step 1 might have side effects on step 2 since it could act as a Lewis acid. Therefore, 4 Å MS was removed by filtration after step 1. Indeed, the yield was further increased in DMA without 4 Å MS present in step 2 (entry 3). A brief survey of the reaction solvent in step 2 (entries 3-7) revealed that DMA was a suitable solvent (entry 3). Increasing the loading of amine led to the decrease in the yield (entries 8-9). Slightly lower yields were obtained by lowering (entries 10-11) or elevating (entry 12) the reaction temperature in step 2.

Table 1. Screening conditions for the synthesis of CF_3-vicinal diamines[a]



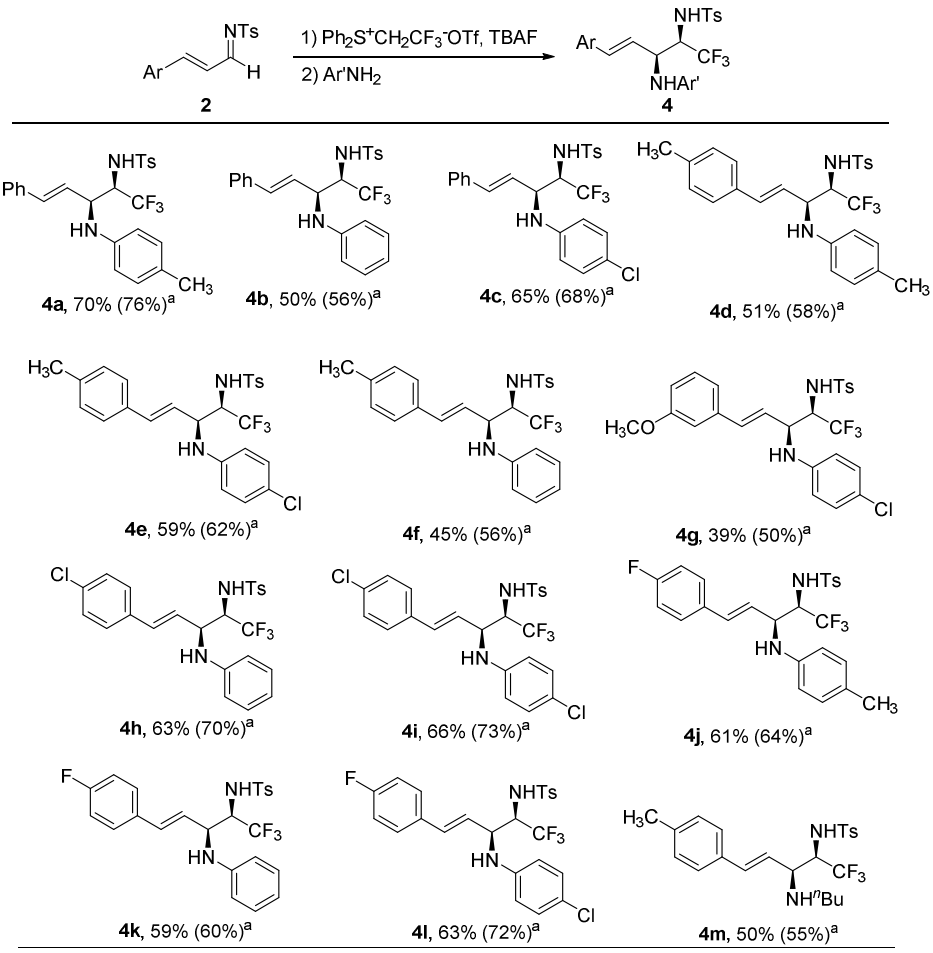
2a **4a**

entry	solvent	temp. (^oC)	ratio[b]	yield (%)[c]
1[d]	DCM	rt	1 : 1 : 1.25:1	56
2[d]	DCM	reflux	1 : 1 : 1.25:1	65
3	DMA	60	1 : 1 : 1.25:1	76
4	NMP	60	1 : 1 : 1.25:1	35
5	CH_3CN	60	1 : 1 : 1.25:1	trace

6	THF	60	1 : 1 : 1.25:1	33
7	1,4-Dioxane	60	1 : 1 : 1.25:1	35
8	DMA	60	1 : 1 : 1.25:1.25	74
9	DMA	60	1 : 1 : 1.25:1.7	65
10	DMA	rt	1 : 1 : 1.25:1	72
11	DMA	40	1 : 1 : 1.25:1	71
12	DMA	80	1 : 1 : 1.25:1	71

[a]Reaction conditions: substrate **2a** (0.2 mmol), salt **1**, TBAF, 4Å MS (80 mg) in DCM (2 mL) at rt under N_2 atmosphere for 1 h (step 1). 4Å MS was removed by filtration. The filtrate was concentrated to give crude aziridine, into which was added 4-$MeC_6H_4NH_2$ and solvent (2 mL) under N_2 atmosphere. The reaction system was further stirred at the indicated temperature for 2 h (step 2); [b]Molar ratio of **2a**:**1**:TBAF:4-$MeC_6H_4NH_2$; [c]The yields were determined by ^{19}F NMR spectrometry; [d]After step 1, 4-$MeC_6H_4NH_2$ was added directly, and the resulting mixture was further stirred to afford product **4a**.

With the optimized reaction conditions in hand (Table 1, entry 3), we then investigated the substrate scope of the convenient two-step reaction for the synthesis of CF_3-vicinal diamines (Scheme 4). It is noteworthy that high diastereoselectivity (*syn:anti* > 94:6) was observed for all reactions. Although electron-neutral and -rich aziridines (**3a-3c** in Scheme 3) were too unstable to be isolated, their corresponding CF_3-vicinal diamines were isolated in moderate to good yields (Scheme 4, **4a-4g**). The structure and relative configuration of product **4b** were confirmed by single crystal X-ray diffraction.[14] Moderate yields were obtained for the conversion of electron-deficient imines (**4h-4l**). Electron-rich (**4a**, **4d** and **4j**), -neutral (**4b**, **4f**, **4h** and **4k**) and -deficient (**4c**, **4e**, **4g**, **4i** and **4l**) aryl amines were all effective to react with aziridines to obtain diamines. Besides aryl amines, alkyl amine could also lead to the ring-opening of aziridines to give CF_3-vicinal diamine (**4m**). In contrast to vinyl imines, although aryl imine such as phenyl imine (PhCH=NHTs) could be converted into aziridine, the resulting azirinde could not undergo further ring-opening with amines to give vicinal diamines.

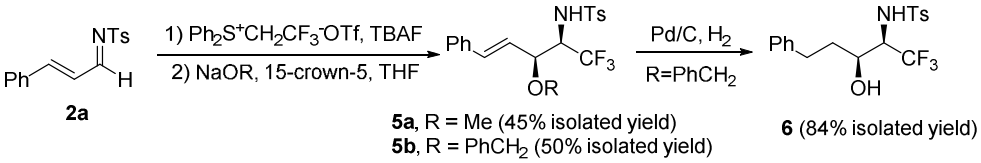


Scheme 4. The synthesis of CF_3-vicinal diamines. Reaction conditions: substrate **2** (0.2 mmol), salt **1** (1 equiv), TBAF (0.25 mL, 1 M), 4Å MS (80 mg) in DCM (2 mL) at rt for 1 h (step 1); 4Å MS was removed by filtration; The filtrate was concentrated to give crude aziridine, into which was added amine (1 equiv) and DMA (2 mL); The reaction system was further stirred at 60 ^{o}C for 2 h (step 2). Isolated yields. [a]The yields in parentheses were determined by ^{19}F NMR spectrometry.

Apparently, the two-step procedure is quite convenient for the preparation of CF_3-containing vicinal diamines. Crude CF_3-aziridines were obtained simply by

filtration and concentration, and the subsequent ring-opening reaction proceeded smoothly to give diamines. Since purification of aziridines is avoided, this protocol is attractive and promising.

The synthesis of vicinal amino alcohols has also received a great deal of attention due to the occurrence of vicinal amino alcohol motif in a vast range of natural products, bioactive compounds, and reagents used for the stereoselective synthesis.[15] The incorporation of CF_3 moiety into vicinal amino alcohols may result in profound modification of their physicochemical properties. Since CF_3-vicinal diamines could be obtained by ring-opening of aziridines with amines, CF_3-containing vicinal amino alcohols may also be prepared by ring-opening of aziridines with alkoxyl anion. Indeed, the use of sodium methoxide and sodium phenylmethanolate as the nucleophiles could give the desired product **5a** and **5b**, respectively, without the need to isolating aziridines (Scheme 5). The structure and relative configuration of product **5a** were confirmed by single crystal X-ray diffraction.[16] The reduction of **5b** successfully gave the expected vicinal amino alcohol **6**.



Scheme 5. The synthesis of CF_3-containing vicinal amino alcohol derivative

In conclusion, we have described the efficient synthesis of CF_3-containing vicinal diamines by a simple two-step procedure without the need to isolate the intermediate products. The convenient procedure could also be applied to the preparation of

CF_3-containing vicinal amino alcohol derivative. This work represents a mild protocol for the incorporation of CF_3 moiety into vicinal diamines with high diastereoselectivity and in good yields. This two-step strategy may also find synthetic utility in the incorporation of fluorinated group into other biologically active compounds.

EXPERIMENTAL SECTION

General Information. ^1H, ^{13}C and ^{19}F NMR spectra were detected on a 500 MHz, 400 MHz or 300 MHz NMR spectrometer. Data for ^1H NMR, ^{13}C NMR and ^{19}F NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, coupling constant (s) in Hz). Mass spectra were obtained on GC-MS or LC-MS (ESI). High resolution mass data were recorded on a high resolution mass spectrometer in the EI, ESI or MALDI mode. The mass analyzer types for HRMS-EI, HRMS-ESI, and HRMS-MALDI are time of flight, Fourier transform mass spectrometer, and Fourier transform mass spectrometer, respectively. Unless otherwise noted, all reagents were obtained commercially and used without further purification. The ^{19}F NMR yields were calculated based on the ^{19}F NMR spectra of the reaction system with being added an internal standard ($PhCF_3$).

Procedure for the Synthesis of sulfonium salt 1[11]: The mixture of 2,2,2-trifluoroethyl triflate (4.64 g, 20 mmol) and diphenyl sulfide (18.6 g, 100 mmol) in a sealed tube was stirred at 150 ^oC for 30 hours. After the reaction mixture was cooled to room temperature, diethyl ether (10 mL) was added to precipitate the crude

product, which was then washed with dry diethyl ether to give the final product **1** (5.9 g, 70% yield; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.36 (d, *J* = 7.6 Hz, 4H), 7.95 - 7.89 (m, 2H), 7.87 - 7.79 (m, 4H), 5.74 (q, *J* = 8.8 Hz, 2H). ^{19}F NMR (376 MHz, acetone-d_6) δ -61.26 (t, *J* = 8.8 Hz, 3F), -78.98 (s, 3F).

General Procedure for the Synthesis of 2: Aldehyde (31.5 mmol), sulfonamide (30 mmol) and tetraethyl orthosilicate (120 mmol) were mixed in a flask equipped with a Dean-Stark apparatus which was used to collect ethanol produced from the reaction. The mixture was stirred at 160°C until no more ethanol was produced. After the reaction system was cooled to room temperature, ethyl acetate/n-hexane (1:3) was added to precipitate the crude product. After filtration, the solid was washed with ethyl acetate/n-hexane(1:3) followed by ethanol to give the pure product **2**.

(E)-4-Methyl-N-((E)-3-phenylallylidene)benzenesulfonamide **(2a)**[17]: 7.78 g, 91% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (d, *J* = 9.4 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 2H), 7.60 - 7.39 (m, 6H), 7.34 (d, *J* = 7.8 Hz, 2H), 6.99 (dd, *J* = 15.7, 9.4 Hz, 1H), 2.44 (s, 3H).

(E)-4-Methyl-N-((E)-3-(p-tolyl)allylidene)benzenesulfonamide **(2b)**[17]: 8.52g, 95% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (d, *J* = 9.4 Hz, 1H), 7.85 (d, *J* = 7.9 Hz, 2H), 7.50 - 7.41 (m, 3H), 7.33 (d, *J* = 7.9 Hz, 2H), 7.22 (d, *J* = 7.7 Hz, 2H), 6.94 (dd, *J* = 15.7, 9.4 Hz, 1H), 2.43 (s, 3H), 2.39 (s, 3H).

(E)-N-((E)-3-(3-Methoxyphenyl)allylidene)-4-methylbenzenesulfonamide **(2c)**[18]: 8.50 g, 90% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 9.4 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 15.8 Hz, 1H), 7.35 - 7.28 (m, 3H), 7.13 (d, *J* = 7.5 Hz, 1H), 7.05 (s, 1H), 7.00 - 6.89 (m, 2H), 3.80 (s, 3H), 2.42 (s, 3H).

(E)-N-((Z)-2-Bromo-3-phenylallylidene)-4-methylbenzenesulfonamide **(2d)**: Yellow

solid, 6.10 g, 56% yield; M.P. 127.3 - 128.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.98 (d, *J* = 5.8 Hz, 2H), 7.92 - 7.83 (m, 3H), 7.55 - 7.39 (m, 3H), 7.33 (d, *J* = 7.4 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5 (s), 151.2 (s), 144.8 (s), 134.9 (s), 133.3 (s), 131.8 (s), 131.2 (s), 129.9 (s), 128.7 (s), 128.1 (s), 118.5 (s), 21.7 (s). IR (neat) ν = 3050, 1611, 1583, 1570, 1449, 1330, 1300, 1289, 1147, 1084, 998, 864, 823, 811, 787, 755, 689, 669, 593, 573, 505 cm^{-1}. HRMS (MALDI/DHB): calcd. for $C_{16}H_{15}BrNO_2S$ $[M+H]^+$: 364.0001. Found: 364.0013.

(Z)-N-((Z)-2-Bromo-3-(p-tolyl)allylidene)-4-methylbenzenesulfonamide **(2e)**: Yellow solid, 7.35 g, 65% yield; M.P. 145.3 - 147.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.91 (d, *J* = 7.5 Hz, 2H), 7.89 (d, *J* = 7.5 Hz, 2H), 7.83 (s, 1H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 2.44 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.4 (s), 151.0 (s), 144.6 (s), 142.9 (s), 135.1 (s), 131.4 (s), 130.6 (s), 129.8 (s), 129.5 (s), 128.0 (s), 117.4 (s), 21.7 (s), 21.6 (s). IR (neat) ν = 3050, 2935, 2835, 1595, 1568, 1468, 1438, 1418, 1319, 1304, 1293, 1242, 1155, 1089, 1058, 1018, 823, 809, 698, 623, 587, 551 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{17}BrNO_2S$ $[M+H]^+$: 378.0158. Found: 378.0153.

(E)-N-((Z)-2-Bromo-3-(4-bromo-3-methoxyphenyl)allylidene)-4-methylbenzenesulf onamide **(2f)**: Yellow solid, 6.63 g, 47% yield; M.P. 145.3 - 147.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.03 (s, 1H), 7.91 (d, *J* = 7.9 Hz, 2H), 7.65 (d, *J* = 2.1 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 2H), 6.90 (dd, *J* = 8.8, 2.2 Hz, 1H), 3.83 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5 (s), 158.4 (s), 149.4 (s), 144.9 (s), 134.7 (s), 133.9 (s), 133.7 (s), 129.9 (s), 128.2 (s), 121.8 (s), 118.5 (s), 116.1 (s), 115.9 (s), 55.7 (s), 21.7 (s). IR (neat) ν = 3050, 2935, 2835, 1595, 1568, 1468, 1438, 1418, 1319, 1304, 1293, 1242, 1155, 1089, 1058, 1018, 823, 809, 698, 623, 587, 551 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{16}Br_2NO_3S$ $[M+H]^+$: 471.9212.

Found: 471.9207.

(E)-N-((E)-3-(4-Bromophenyl)allylidene)-4-methylbenzenesulfonamide **(2g)**: Yellow solid, 9.7 g, 89% yield; M.P. 191.7 - 192.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 9.3 Hz, 1H), 7.87 (d, *J* = 7.9 Hz, 2H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.48 - 7.40 (m, 3H), 7.36 (d, *J* = 7.8 Hz, 2H), 6.97 (dd, *J* = 15.8, 9.4 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5 (s), 152.0 (s), 144.6 (s), 135.2 (s), 133.0 (s), 132.5 (s), 129.8 (s), 129.8 (s), 128.0 (s), 126.1 (s), 125.3 (s), 21.6 (s). IR (neat) ν = 3020, 1621, 1591, 1574, 1486, 1404, 1316, 1304, 1289, 1156, 1085, 1070, 1002, 966, 859, 807, 777, 678, 590, 553 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{14}BrNNaO_2S$ $[M+Na]^+$: 385.9821. Found: 385.9809 .

(E)-N-((E)-3-(2-Bromophenyl)allylidene)-4-methylbenzenesulfonamide **(2h)**: Yellow solid, 5.99 g, 55% yield; M.P. 123.4 - 124.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 9.4 Hz, 1H), 7.95 - 7.85 (m, 3H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.33 - 7.39 (m, 3H), 7.28 (td, *J* = 8.0, 1.6 Hz, 1H), 6.94 (dd, *J* = 15.8, 9.4 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5 (s), 151.4 (s), 144.6 (s), 135.1 (s), 133.9 (s), 133.7 (s), 132.4 (s), 129.8 (s), 128.0 (s), 128.0 (s), 128.0 (s), 126.9 (s), 125.9 (s), 21.6 (s). IR (neat) ν = 3029, 2360, 1915, 1618, 1578, 1440, 1372, 1314, 1303, 1287, 1168, 1153, 1088, 1009, 970, 855, 813, 774, 751, 683, 668, 581, 553 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{15}BrNO_2S$ $[M+H]^+$: 364.0001. Found: 364.0001.

(E)-N-((E)-3-(4-Chlorophenyl)allylidene)-4-methylbenzenesulfonamide **(2i)**[17]: 8.13 g, 85% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (d, *J* = 9.3 Hz, 1H), 7.85 (d, *J* = 7.4 Hz, 2H), 7.60 - 7.27 (m, 7H), 6.94 (dd, *J* = 15.6, 9.3 Hz, 1H), 2.43 (s, 3H).

(E)-N-((E)-3-(4-Fluorophenyl)allylidene)-4-methylbenzenesulfonamide **(2j)**: Yellow solid, 6.45 g, 71% yield; M.P. 108.9 - 109.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 9.4 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.61 - 7.52 (m, 2H), 7.47 (d, *J* = 15.8 Hz,

1H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.09 (t, *J* = 8.3 Hz, 2H), 6.89 (dd, *J* = 15.8, 9.4 Hz, 1H), 2.41 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.58 - -106.86 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8 (s), 164.5 (d, *J* = 254.0 Hz), 152.4 (s), 144.5 (s), 135.3 (s), 130.7 (d, *J* = 8.8 Hz), 130.5 (d, *J* = 3.3 Hz), 129.8 (s), 127.9 (s), 124.3 (s), 116.4 (d, *J* = 22.1 Hz), 21.6 (s). IR (neat) ν = 3052, 1900, 1620, 1591, 1577, 1511, 1363, 1311, 1289, 1256, 1235, 1168, 1085, 1023, 976, 868, 823, 814, 800, 755, 681, 596, 552, 507 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{15}FNO_2S$ $[M+H]^+$: 304.0802. Found: 304.0807.

(E)-N-((E)-3-(3-Fluorophenyl)allylidene)-4-methylbenzenesulfonamide **(2k)**: Yellow solid, 4.54 g, 50% yield; M.P. 107.9 - 109.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 9.3 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 15.8 Hz, 1H), 7.40 - 7.27 (m, 4H), 7.20 (d, *J* = 9.5 Hz, 1H), 7.10 (td, *J* = 8.3, 1.6 Hz, 1H), 6.92 (dd, *J* = 15.8, 9.3 Hz, 1H), 2.41 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.65 - -111.82 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4 (s), 162.9 (d, *J* = 247.7 Hz), 151.9 (d, *J* = 2.8 Hz), 144.6 (s), 136.2 (d, *J* = 7.7 Hz), 135.0 (s), 130.7 (d, *J* = 8.3 Hz), 129.8 (s), 127.9 (s), 125.8 (s), 124.5 (d, *J* = 2.9 Hz), 118.3 (d, *J* = 21.4 Hz), 114.7 (d, *J* = 22.1 Hz), 21.6 (s). IR (neat) ν = 3070, 1624, 1578, 1450, 1318, 1305, 1291, 1265, 1170, 1153, 1090, 963, 821, 803, 793, 786, 747, 680, 583, 550 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{15}FNO_2S$ $[M+H]^+$: 304.0802. Found: 304.0801.

(E)-N-((E)-3-(2-Fluorophenyl)allylidene)-4-methylbenzenesulfonamide **(2l)**: Yellow solid, 8.20 g, 90% yield; M.P. 99.3 - 99.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 9.4 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 2H), 7.62 (d, *J* = 16.0 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.47 - 7.37 (m, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.05 (dd, *J* = 16.0, 9.4 Hz, 1H), 2.43 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.57 - -113.75 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9 (s), 161.3 (d, *J* = 255.7 Hz), 145.8 (d, *J* = 3.2 Hz), 144.6 (s), 135.1 (s), 133.2 (d, *J* = 9.0 Hz), 129.8 (s),

129.0 (s), 128.0 (s), 126.9 (d, *J* = 6.2 Hz), 124.8 (d, *J* = 3.6 Hz), 122.3 (d, *J* = 11.4 Hz), 116.4 (d, *J* = 21.7 Hz), 21.6 (s). IR (neat) ν = 3053, 2980, 1930, 1622, 1587, 1483, 1321, 1291, 1228, 1168, 1153, 1088, 1013, 973, 805, 770, 675, 588 cm^{-1}. HRMS (MALDI/DHB): calcd. for $C_{16}H_{15}FNO_2S$ $[M+H]^+$: 304.0802. Found: 304.0812.

(E)-4-Methyl-N-((E)-3-(4-nitrophenyl)allylidene)benzenesulfonamide **(2m)**[18]: 9.01 g, 91% yield; ^1H NMR (300 MHz, $CDCl_3$) δ 8.80 (d, *J* = 9.1 Hz, 1H), 8.28 (d, *J* = 7.1 Hz, 2H), 7.86 (d, *J* = 6.9 Hz, 2H), 7.70 (d, *J* = 6.9 Hz, 2H), 7.52 (d, *J* = 15.8 Hz, 1H), 7.36 (d, *J* = 7.1 Hz, 2H), 7.08 (dd, *J* = 15.8, 9.1 Hz, 1H), 2.45 (s, 3H).

(E)-N-((E)-3-(4-Cyanophenyl)allylidene)-4-methylbenzenesulfonamide **(2n)**: Yellow solid, 4.74 g, 51% yield; M.P. 188.9 - 190.2 °C. ^1H NMR (400 MHz, CDC_3) δ 8.78 (d, *J* = 9.2 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 15.9 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.04 (dd, *J* = 15.9, 9.2 Hz, 1H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.6 (s), 150.0 (s), 144.8 (s), 138.1 (s), 134.8 (s), 132.8 (s), 129.9 (s), 128.7 (s), 128.1 (s), 127.8 (s), 118.0 (s), 114.4 (s), 21.6 (s). IR (neat) ν = 3051, 2224, 1626, 1607, 1582, 1414, 1314, 1289, 1260, 1180, 1156, 1089, 1017, 997, 964, 875, 820, 805, 782, 683, 597, 558, 545 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{15}N_2O_2S$ $[M+H]^+$: 311.0849. Found: 311.0847.

(E)-4-Methyl-N-((E)-3-(3-(trifluoromethyl) phenyl) allylidene) benzenesulfonamide **(2o)**: Yellow solid, 5.51 g, 52% yield; M.P. 107.4 - 108.7 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 9.3 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.79 (s, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 15.9 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.06 (dd, *J* = 15.9, 9.3 Hz, 1H), 2.47 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -61.40 - -65.31 (m, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0 (s), 151.0 (s), 144.7 (s), 135.0 (s), 134.9 (s), 131.8 (q, *J* = 32.8 Hz), 131.2 (s), 129.8 (s), 129.8 (s), 128.0 (s), 127.7 (q, *J* = 3.6 Hz), 126.5 (s), 125.1 (q, *J* = 3.8 Hz), 123.5

(q, J = 272.6 Hz), 21.6 (s). IR (neat) ν = 3029, 1626, 1595, 1581, 1566, 1334, 1314, 1291, 1250, 1206, 1170, 1131, 1092, 1072, 1011, 969, 803, 790, 755, 694, 679, 665, 589, 553 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{15}F_3NO_2S$ $[M+H]^+$: 354.0770. Found: 354.0768.

Procedure for the Synthesis of 3: Into the mixture of diphenyl(2,2,2-Trifluoroethyl)sulfonium triflate **1** (209.2 mg, 0.5 mmol), imine **2** (1 mmol) and 4Å MS (400 mg) in dichloromethane (10 mL) was added TBAF (0.75 mL, 1 M in THF) dropwise under N_2 atmosphere. The reaction mixture was stirred at room temperature for 1 h. After filtration, the solid was washed with DCM (10 mL). The combined organic phase was washed with water, sat. sodium bisulfite and water in sequence and then dried over Na_2SO_4. The solvent was removed by concentration, and the residue was subjected to flash column chromatography with hexane/ethyl acetate (50:1-20:1) as the eluent to afford the final product **3**.

(2SR,3RS)-2-((Z)-1-Bromo-2-phenylvinyl)-1-tosyl-3-(trifluoromethyl)aziridine **(3d)**: Yellow solid, 204.7 mg, 92% yield; M.P. 118.0 - 118.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.2 Hz, 2H), 7.53 (d, J = 6.9 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.41 - 7.31 (m, 3H), 7.11 (s, 1H), 3.96 (d, J = 6.8 Hz, 1H), 3.52 - 3.42 (m, 1H), 2.50 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.86 (d, J = 5.2 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.0 (s), 134.0 (s), 133.0 (s), 131.4 (q, J = 1.2 Hz), 130.1 (s), 128.9 (s), 128.7 (s), 128.3 (s), 128.2 (s), 122.0 (q, J = 276.0 Hz), 111.5 (s), 46.4 (q, J = 1.2 Hz), 42.7 (q, J = 40.5 Hz), 21.7 (s). IR (neat) ν = 3068, 3022, 2975, 2926, 1595, 1493, 1447, 1428, 1365, 1338, 1283, 1198, 1186, 1163, 1104, 1088, 1021, 935, 923, 862, 813, 771, 756, 692, 675, 548, 525 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{15}BrF_3NNaO_2S$ $[M+Na]^+$: 467.9851. Found: 467.9849.

(2SR,3RS)-2-((Z)-1-Bromo-2-(p-tolyl)vinyl)-1-tosyl-3-(trifluoromethyl)aziridine **(3e)**: Yellow solid, 183.6 mg, 80% yield; M.P. 124.45 - 125.56 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.1 Hz, 2H), 7.46 - 7.44 (m, 4H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.07 (s, 1H), 3.95 (d, *J* = 6.7 Hz, 1H), 3.51 - 3.38 (m, 1H), 2.51 (s, 3H), 2.37 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.90 (d, *J* = 5.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.0 (s), 138.8 (s), 133.1 (s), 131.3 (s), 131.2 (s), 130.1 (s), 128.9 (s), 128.9 (s), 128.3 (s), 122.0 (q, *J* = 276.0 Hz), 110.5 (s), 46.4 (s), 42.7 (q, *J* = 40.4 Hz), 21.7 (s), 21.3 (s). IR (neat) ν = 3030, 2978, 2922, 1609, 1597, 1512, 1438, 1364, 1342, 1284, 1181, 1166, 1150, 1090, 1021, 934, 910, 882, 869, 812, 801, 792, 751, 674, 610, 547, 527 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{17}BrF_3NNaO_2S$ $[M+Na]^+$: 482.0008. Found: 482.0011.

(2SR,3RS)-2-((Z)-1-Bromo-2-(4-bromo-3-methoxyphenyl)vinyl)-1-tosyl-3-(trifluoro methyl)aziridine **(3f)**: Yellow solid, 248.4 mg, 90% yield; M.P. 97.3 - 98.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.44 - 7.37 (m, 3H), 7.10 (d, *J* = 3.0 Hz, 1H), 7.06 (s, 1H), 6.73 (dd, *J* = 8.8, 3.0 Hz, 1H), 3.90 (d, *J* = 6.8 Hz, 1H), 3.77 (s, 3H), 3.56 - 3.48 (m, 1H), 2.47 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.80 (d, *J* = 5.1 Hz, 3F).^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3 (s), 146.0 (s), 135.3 (s), 133.1 (s), 133.0 (s), 131.4 (s), 130.2 (s), 128.3 (s), 121.9 (q, *J* = 272.3 Hz), 115.9 (s), 115.8 (s), 114.6 (s), 114.0 (s), 55.5 (s), 46.5 (s), 42.1 (q, *J* = 40.7 Hz), 21.7 (s). IR (neat) ν = 3022, 2966, 2941, 2835, 1592, 1468, 1444, 1403, 1372, 1338, 1317, 1295, 1238, 1213, 1167, 1145, 1088, 1049, 1022, 905, 931, 865, 818, 793, 745, 678, 609, 558, 532 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{16}Br2F_3NNaO_3S$ $[M+Na]^+$: 575.9062. Found: 575.9034.

(2R,3R)-2-((E)-4-Bromostyryl)-1-tosyl-3-(trifluoromethyl)aziridine **(3g)**: Yellow solid, 189.1 mg, 85% yield; M.P. 72.7 - 73.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86

(d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 16.0 Hz, 1H), 5.98 (ddd, *J* = 16.0, 8.4, 1.2 Hz, 1H), 3.75 (t, *J* = 7.7 Hz, 1H), 3.49 - 3.36 (m, 1H), 2.44 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.01 (d, *J* = 5.7 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.6 (s), 137.3 (s), 134.2 (s), 133.6 (s), 131.8 (s), 130.0 (s), 128.2 (s), 128.0 (s), 122.7 (s), 122.4 (q, *J* = 275.5 Hz), 119.4 (s), 43.8 (q, *J* = 0.7 Hz), 42.3 (q, *J* = 40.1 Hz), 21.7 (s). IR (neat) ν = 3041, 2956, 1742, 1684, 1653, 1596, 1488, 1440, 1407, 1336, 1305, 1291, 1233, 1164, 1110, 1070, 1017, 1008, 938, 857, 828, 840, 755, 670, 600, 553 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{15}BrF_3NNaO_2S$ $[M+Na]^+$: 467.9851. Found: 467.9845.

(2RS,3RS)-2-((E)-2-Bromostyryl)-1-tosyl-3-(trifluoromethyl)aziridine **(3h)**: Yellow solid, 185 mg, 83% yield; M.P. 85.9 - 86.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.25 - 7.17 (m, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 5.92 (dd, *J* = 15.6, 8.3 Hz, 1H), 3.78 (t, *J* = 7.5 Hz, 1H), 3.51 - 3.39 (m, 1H), 2.44 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.98 (d, *J* = 5.9 Hz, 3F).^{13}C NMR (101 MHz, $CDCl_3$) δ 145.6 (s), 137.1 (s), 135.1 (s), 133.5 (s), 133.0 (s), 130.0 (s), 129.9 (s), 128.0 (s), 127.5 (s), 127.1 (s), 123.7 (s), 122.4 (q, *J* = 275.8 Hz), 121.4 (s), 43.9 (s), 42.0 (q, *J* = 40.2 Hz), 21.7 (s). IR (neat) ν = 3062, 3009, 2927, 1598, 1469, 1432, 1389, 1338, 1296, 1277, 1203, 1158, 1089, 1026, 971, 947, 852, 830, 815, 757, 748, 678, 599, 569, 557, 540 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{16}BrF_3NO_2S$ $[M+H]^+$: 446.0032. Found: 446.0028.

(2RS,3RS)-2-((E)-4-Chlorostyryl)-1-tosyl-3-(trifluoromethyl)aziridine **(3i)**: Yellow solid, 156.4 mg, 78% yield; M.P. 77.3 - 78.9 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.33 - 7.26 (m, 4H), 6.84 (d, *J* = 15.9 Hz, 1H), 5.98 (dd, *J* = 15.9, 8.5 Hz, 1H), 3.76 (t, *J* = 7.7 Hz, 1H), 3.49 - 3.37 (m, 1H), 2.47 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.04 (d, *J* = 5.6 Hz, 3F).^{13}C NMR

(126 MHz, $CDCl_3$) δ 145.6 (s), 137.2 (s), 134.5 (s), 133.8 (s), 133.7 (s), 130.0 (s), 128.9 (s), 128.0 (s), 127.9 (s), 122.4 (q, *J* = 275.2 Hz), 119.2 (s), 43.8 (s), 42.3 (q, *J* = 40.1 Hz), 21.7 (s). IR (neat) ν = 3029, 2964, 1652, 1597, 1507, 1491, 1435, 1409, 1336, 1286, 1277, 1229, 1188, 1162,1148, 1088, 1024, 1011, 973, 867, 842, 809, 749, 682, 670, 566, 471 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{15}ClF_3NNaO_2S$ $[M+Na]^+$: 424.0356. Found: 424.0361. Elemental Analysis: calcd. for $C_{18}H_{15}ClF_3NO_2S$ C, 53.80; H, 3.76; N, 3.49. Found: C, 53.67; H, 3.94; N, 3.50.

(2RS,3RS)-2-((E)-4-Fluorostyryl)-1-tosyl-3-(trifluoromethyl)aziridine **(3j)**: Yellow solid, 115.5 mg, 60% yield; M.P. 74.1 - 75.6 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.36 - 7.32 (m, 2H), 7.02 (t, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 15.8 Hz, 1H), 5.92 (dd, *J* = 15.8, 8.5 Hz, 1H), 3.77 (t, *J* = 7.7 Hz, 1H), 3.48 - 3.37 (m, 1H), 2.47 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.03 (d, *J* = 5.7 Hz, 3F), -112.27 - -112.37 (m, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.9 (d, *J* = 248.7 Hz), 145.5 (s), 137.3 (s), 133.7 (s), 131.5 (d, *J* = 3.3 Hz), 129.9 (s), 128.4 (d, *J* = 8.4 Hz), 128.0 (s), 122.5 (q, *J* = 275.4 Hz), 118.3 (s), 115.6 (d, *J* = 21.8 Hz), 43.9 (s), 42.2 (q, *J* = 40.1 Hz), 21.7 (s). IR (neat) ν = 3038, 2926, 1654, 1600, 1508, 1431, 1417, 1342, 1278, 1222, 1187, 1162, 1089, 1028, 970, 947, 857, 816, 747, 675, 599, 572, 545 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{15}F_4NNaO_2S$ $[M+Na]^+$: 408.0652. Found:408.0653.

(2RS,3RS)-2-((E)-3-Fluorostyryl)-1-tosyl-3-(trifluoromethyl)aziridine **(3k)**: Yellow liquid, 145 mg, 75% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.33 - 7.24 (m, 1H), 7.11 (d, *J* = 7.7 Hz, 1H), 7.06 - 7.02 (m, 1H), 6.97 (td, *J* = 8.3, 1.8 Hz, 1H), 6.83 (d, *J* = 15.9 Hz, 1H), 6.00 (ddd, *J* = 15.9, 8.3, 1.4 Hz, 1H), 3.76 (t, *J* = 7.7 Hz, 1H), 3.52 - 3.37 (m, 1H), 2.45 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.04 (d, *J* = 5.9 Hz, 3F), -112.98 (td, *J* = 9.1, 6.1 Hz, 1F). ^{13}C NMR

(126 MHz, $CDCl_3$) δ 162.9 (d, *J* = 246.1 Hz), 145.6 (s), 137.5 (d, *J* = 7.7 Hz), 137.2 (s), 133.6 (s), 130.2 (d, *J* = 8.3 Hz), 130.0 (s), 128.1 (s), 122.6 (d, *J* = 2.8 Hz), 122.4 (q, *J* = 275.3 Hz), 120.1 (s), 115.58 (d, *J* = 21.4 Hz), 113.1 (d, *J* = 22.0 Hz), 43.6 (s), 42.28 (q, *J* = 40.2 Hz), 21.7 (s). IR (neat) ν = 3035, 2924, 1611, 1598, 1585, 1490, 1448, 1340, 1293, 1274, 1214, 1166, 1091, 1025, 972, 928, 872, 849, 818, 758, 746, 678, 585 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{16}F_4NO_2S$ $[M+H]^+$: 386.0832. Found: 386.0830.

(2RS,3RS)-2-((E)-2-Fluorostyryl)-1-tosyl-3-(trifluoromethyl)aziridine **(3l)**: Yellow solid, 129.5 mg, 67% yield; M.P. 76.6 - 78.3 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 2H), 7.41 - 7.33 (m, 3H), 7.30 - 7.20 (m, 1H), 7.10 - 6.97 (m, 3H), 6.09 (ddd, *J* = 16.1, 8.5, 1.5 Hz, 1H), 3.76 (t, *J* = 7.7 Hz, 1H), 3.54 - 3.31 (m, 1H), 2.43 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.00 (d, *J* = 5.7 Hz, 3F), -117.12 (ddd, *J* = 10.9, 7.5, 5.3 Hz, 1F).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3 (d, *J* = 251.0 Hz), 145.6 (s), 133.7 (s), 131.0 (d, *J* = 3.2 Hz), 130.1 (d, *J* = 8.5 Hz), 130.0 (s), 128.1 (s), 127.7 (d, *J* = 3.3 Hz), 124.2 (d, *J* = 3.6 Hz), 123.2 (d, *J* = 11.9 Hz), 122.5 (q, *J* = 274.4 Hz), 121.2 (s), 115.8 (d, *J* = 21.9 Hz), 44.2 (s), 42.2 (q, *J* = 40.2 Hz), 21.6 (s). IR (neat) ν = 3068, 3021, 2926, 1612, 1598, 1581, 1491, 1457, 1436, 1391, 1339, 1306, 1288, 1260, 1235, 1224, 1190, 1152, 1091, 1023, 974, 943, 874, 853, 844, 823, 764, 678, 558, 525 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{16}F_4NO_2S$ $[M+H]^+$: 386.0832. Found: 386.0830.

(2RS,3RS)-2-((E)-4-Nitrostyryl)-1-tosyl-3-(trifluoromethyl)aziridine **(3m)**: Yellow solid, 179.5 mg, 86% yield; M.P. 74.5 - 75.6 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.8 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 2H), 6.97 (d, *J* = 16.0 Hz, 1H), 6.19 (dd, *J* = 16.0, 8.2 Hz, 1H), 3.81 (t, *J* = 7.7 Hz, 1H), 3.55 - 3.39 (m, 1H), 2.49 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.00 (d, *J* = 5.8 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6 (s), 145.8 (s), 141.4 (s), 136.1 (s),

133.5 (s), 130.0 (s), 128.1 (s), 127.3 (s), 124.1 (s), 123.5 (s), 122.3 (q, *J* = 275.3 Hz), 43.0 (s), 42.5 (q, *J* = 38.7 Hz), 21.7 (s). IR (neat) ν = 3039, 2931, 1596, 1517, 1495, 1441, 1417, 1347, 1304, 1283, 1229, 1206, 1187, 1163, 1107, 1091, 1016, 938, 867, 839, 822, 808, 759, 744, 672, 600 cm^{-1}. HRMS (MALDI/DHB): calcd. for $C_{18}H_{16}F_3N_2O_4S$ $[M+H]^+$: 413.0777. Found: 413.0788.

4-((E)-2-((2RS,3RS)-1-Tosyl-3-(trifluoromethyl)aziridin-2-yl)vinyl)benzonitrile **(3n)**: Yellow solid, 174.2 mg, 89% yield; M.P. 71.2 - 72.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.9 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 2H), 7.43 (d, *J* = 7.9 Hz, 2H), 7.38 (d, *J* = 7.7 Hz, 2H), 6.89 (d, *J* = 15.9 Hz, 1H), 6.11 (dd, *J* = 15.9, 8.1 Hz, 1H), 3.77 (t, *J* = 7.7 Hz, 1H), 3.50 - 3.33 (m, 1H), 2.46 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.58 (d, *J* = 5.8 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8 (s), 139.6 (s), 136.5 (s), 133.5 (s), 132.5 (s), 130.0 (s), 128.1 (s), 127.2 (s), 122.7 (s), 122.3 (q, *J* = 276.0 Hz), 118.5 (s), 112.0 (s), 43.2 (s), 42.4 (q, *J* = 39.8 Hz), 21.7 (s). IR (neat) ν = 3024, 2964, 2227, 1607, 1600, 1437, 1412, 1391, 1376, 1330, 1308, 1293, 1281, 1207, 1164, 1140, 1103, 1092, 1032, 967, 948, 856, 829, 818, 750, 676, 601, 571, 556 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{16}F_3N_2O_2S$ $[M+H]^+$: 393.0879. Found: 393.0878.

(2RS,3RS)-1-Tosyl-2-(trifluoromethyl)-3-((E)-3-(trifluoromethyl)styryl)aziridine **(3o)**: Yellow solid, 177.3 mg, 82% yield; M.P. 85.3 - 87.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 2H), 7.57 (s, 1H), 7.55 - 7.50 (m, 2H), 7.48 - 7.41 (m, 1H), 7.38 (d, *J* = 8.3 Hz, 2H), 6.90 (d, *J* = 16.0 Hz, 1H), 6.06 (ddd, *J* = 16.0, 8.2, 1.2 Hz, 1H), 3.77 (t, *J* = 7.6 Hz, 1H), 3.48 - 3.40 (m, 1H), 2.46 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.90 (s, 3F), -66.05 (d, *J* = 5.8 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.7 (s), 136.9 (s), 136.0 (s), 133.6 (s), 131.2 (q, *J* = 32.4 Hz), 130.0 (s), 129.7 (q, *J* = 1.2 Hz), 129.2 (s), 128.1 (s), 125.2 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 274.1 Hz), 123.4 (q, *J* = 3.8 Hz), 122.4 (q, *J* = 275.4 Hz), 120.7 (s), 43.5 (s), 42.3 (q, *J* =

40.2 Hz), 21.7 (s). IR (neat) ν = 3074, 3023, 2930, 1599, 1493, 1451, 1430, 1392, 1332, 1282, 1234, 1201, 1158, 1126, 1090, 1070, 1033, 984, 950, 887, 844, 821, 799, 746, 680, 599, 556 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{15}F_6NNaO_2S$ $[M+Na]^+$: 458.0620. Found: 458.0611.

Procedure for the Synthesis of 4: Into a mixture of diphenyl(2,2,2-trifluoroethyl)sulfonium triflate **1** (0.2 mmol), imine **2** (0.2 mmol) and 4Å MS (80 mg) in dichloromethane (2 mL) was added TBAF (0.25 mL, 1 M in THF) dropwise under N_2 atmosphere. The reaction mixture was stirred at room temperature for 1 h. 4Å MS was removed by filtration. The filtrate was concentrated to give crude aziridine, into which was added aryl amine (0.2 mmol) and DMA (2 mL) under N_2 atmosphere. The reaction mixture was stirred at 60 °C for 2 h. After being cooled to room temperature, the solution was subjected to flash column chromatography (petroleum ether:EA = 20:1) to afford the pure product.

4-Methyl-N-((2S,E)-1,1,1-trifluoro-5-phenyl-3-(p-tolylamino)pent-4-en-2-yl)benzenesulfonamidenamide **(4a)**: Yellow liquid, 66.3 mg, 70% yield ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.35 - 7.17 (m, 7H), 6.98 (d, *J* = 8.1 Hz, 2H), 6.67 - 6.50 (m, 3H), 6.03 (dd, *J* = 15.8, 7.4 Hz, 1H), 5.38 (d, *J* = 9.5 Hz, 1H), 4.41 - 4.28 (m, 1H), 4.22 - 4.04 (m, 1H), 3.68 (br, 1H), 2.38 (s, 3H), 2.22 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.00 (d, *J* = 7.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1 (s), 143.4 (s), 137.1 (s), 135.9 (s), 133.5 (s), 129.9 (s), 129.8 (s), 128.5 (s), 128.3 (s), 128.1 (s), 127.1 (s), 126.7 (s), 125.3 (s), 124.4 (q, *J* = 283.9 Hz), 114.4 (s), 57.6 (q, *J* = 28.1 Hz), 56.3 (s), 21.5 (s), 20.4 (s). IR (neat) ν =549.6, 568.9, 667.6, 694.2, 750.3, 811.5, 966.7, 1092.3, 1160.3, 1265.3, 1329.8, 1448.8, 1520.6, 1598.1, 1616.8, 2921.2,

3027.2, 3282.4 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{25}O_2N_2F_3NaS$ $[M+Na]^+$: 497.1481. Found: 497.1479.

4-Methyl-N-((2S,E)-1,1,1-trifluoro-5-phenyl-3-(phenylamino)pent-4-en-2-yl)benzenesulfonamide **(4b)**: Yellow solid, 45.8 mg, 50% yield; M.P. 151 - 153°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.32 - 7.23 (m, 5H), 7.23 - 7.14 (m, 4H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.67 - 6.56 (m, 3H), 6.05 (dd, *J* = 15.7, 7.0 Hz, 1H), 5.74 (d, *J* = 6.6 Hz, 1H), 4.50 - 4.39 (m, 1H), 4.22 - 4.11 (m, 1H), 3.93 (d, *J* = 8.6 Hz, 1H), 2.36 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.92 (d, *J* = 7.3 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.7 (s), 144.2 (s), 137.0 (s), 135.8 (s), 133.7 (s), 129.8 (s), 129.4 (s), 128.6 (s), 128.2 (s), 127.1 (s), 126.7 (s), 125.0 (s), 124.3 (q, *J* = 281.5 Hz), 119.0 (s), 114.1 (s), 57.5 (q, *J* = 28.2 Hz), 56.0 (s), 21.5 (s). IR (neat) ν = 547.6, 570.6, 688.8, 704.2, 765.1, 812.2, 959.9, 970.8, 1091.8, 1155.5, 1187.5, 1266.7, 1327.3, 1349.1, 1448.1, 1497.6, 1602.2, 2924.6, 324.91, 3363.5, 3413.8 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{22}O_2N_2F_3S$ $[M-H]^-$: 459.1354. Found: 459.1356.

N-((2R,3S,E)-3-((4-Chlorophenyl)amino)-1,1,1-trifluoro-5-phenylpent-4-en-2-yl)-4-methylbenzenesulfonamide **(4c)**: Yellow solid, 64.3 mg, 65% yield; M.P. 120 - 122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.35 - 7.18 (m, 7H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.66 - 6.49 (m, 3H), 6.02 (dd, *J* = 15.9, 7.0 Hz, 1H), 5.53 (d, *J* = 9.8 Hz, 1H), 4.40 - 4.32 (m, 1H), 4.19 - 4.07 (m, 1H), 3.94 (s, 1H), 2.37 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.01 (d, *J* = 7.3 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4 (s), 144.3 (s), 136.9 (s), 135.6 (s), 133.7 (s), 129.8 (s), 129.2 (s), 128.6 (s), 128.2 (s), 127.0 (s), 126.7 (s), 124.8 (s), 124.2 (q, *J* = 283.8 Hz), 123.4 (s), 115.2 (s),

57.6 (q, *J* = 28.9 Hz), 55.9 (s), 21.5 (s). IR (neat) ν = 502.81, 549.39, 568.84, 666.12, 692.63, 732.87, 752.07, 814.30, 909.86, 967.02, 1004.82, 1091.91, 1159.77, 1185.36, 1266.44, 1328.80, 1403.43, 1448.87, 1493.68, 1598.89, 2923.74, 3028.61, 3275.04 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{23}O_2N_2ClF_3S$ $[M+H]^+$: 495.1115. Found: 495.1115.

4-Methyl-N-((2S,E)-1,1,1-trifluoro-5-(p-tolyl)-3-(p-tolylamino)pent-4-en-2-yl)benzenesulfonamide **(4d)**: Yellow liquid, 49.7 mg, 51% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 6.98 (d, *J* = 8.1 Hz, 2H), 6.61 - 6.48 (m, 3H), 5.97 (dd, *J* = 15.6, 7.3 Hz, 1H), 5.52 (d, *J* = 9.7 Hz, 1H), 4.42 - 4.27 (m, 1H), 4.20 - 4.05 (m, 1H), 3.69 (br, 1H), 2.38 (s, 3H), 2.32 (s, 3H), 2.23 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.93 (d, *J* = 7.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0 (s), 143.3 (s), 138.1 (s), 137.1 (s), 133.6 (s), 133.0 (s), 129.9 (s), 129.8 (s), 129.3 (s), 128.4 (s), 127.1 (s), 126.6 (s), 124.4 (q, *J* = 283.7 Hz), 124.0 (s), 114.5 (s), 57.38 (q, *J* = 26.8 Hz), 56.6 (s), 21.5 (s), 21.2 (s), 20.4 (s). IR (neat) ν = 548.9, 667.2, 677.3, 810.5, 919.8, 968.6, 1092.2, 1160.2, 1265.7, 1330.0, 1496.6, 1520.6, 1539.9, 1616.6,2921.6, 3025.2, 3282.6 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{27}O_2N_2F_3NaS$ $[M+Na]^+$: 511.1638. Found: 511.1636.

N-((2S,E)-3-((4-Chlorophenyl)amino)-1,1,1-trifluoro-5-(p-tolyl)pent-4-en-2-yl)-4-methylbenzenesulfonamide **(4e)**: Yellow solid, 60.1 mg, 59% yield; M.P. 120 - 122 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.27 - 7.21 (m, 2H), 7.21 - 7.15 (m, 2H), 7.14 - 7.06 (m, 4H), 6.64 - 6.43 (m, 3H), 5.96 (dd, *J* = 15.7, 7.7 Hz, 1H), 5.40 (d, *J* = 9.9 Hz, 1H), 4.39 - 4.25 (m, 1H), 4.17 - 4.07 (m, 1H), 3.90 (s, 1H), 2.38 (s,

3H), 2.32 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.81 (d, *J* = 6.9 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3 (s), 144.2 (s), 138.3 (s), 136.9 (s), 133.9 (s), 132.8 (s), 129.8 (s), 129.3 (s), 129.2 (s), 127.0 (s), 126.6 (s), 124.3 (q, *J* = 283.7 Hz), 123.6 (s), 123.3 (s), 115.2 (s), 57.4 (q, *J* = 27.7 Hz), 56.4 (s), 21.5 (s), 21.2 (s). IR (neat) ν = 548.41, 566.40, 666.20, 732.15, 813.83, 911.39, 968.56, 1091.55, 1159.08, 1266.10, 1328.43, 1451.36, 1493.31, 1598.54, 2923.38 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{25}O_2N_2ClF_3S$ $[M+H]^+$: 509.1272. Found: 509.1272.

4-Methyl-N-((2S,E)-1,1,1-trifluoro-3-(phenylamino)-5-(p-tolyl)pent-4-en-2-yl)benz enesulfonamide **(4f)**: Yellow liquid, 42.6 mg, 45% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.20 -7.13 (m, 4H), 7.09 (d, *J* = 7.9 Hz, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.63 (d, *J* = 7.9 Hz, 2H), 6.57 (d, *J* = 15.7 Hz, 1H), 5.98 (dd, *J* = 15.9, 7.4 Hz, 1H), 5.38 (d, *J* = 9.9 Hz, 1H), 4.44 - 4.33 (m, 1H), 4.20 - 4.09 (m, 1H), 3.83 (d, *J* = 7.1 Hz, 1H), 2.38 (s, 3H), 2.32 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.79 (d, *J* = 7.4 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.6 (s), 144.1 (s), 138.2 (s), 137.0 (s), 133.9 (s), 132.9 (s), 129.8 (s), 129.4 (s), 129.3 (s), 127.1 (s), 126.6 (s), 124.4 (q, *J* = 283.7 Hz), 123.6 (s), 119.0 (s), 114.1 (s), 57.2 (q, *J* = 28.8 Hz), 56.4 (s), 21.5 (s), 21.2 (s). IR (neat) ν = 549.0, 571.0, 666.1, 690.4, 714.9, 750.2, 812.3, 919.9, 969.0, 1092.7, 1160.2, 1266.2, 1328.3, 1436.5, 1498.5, 1513.3, 1602.2, 2922.1, 3026.8, 3052.0, 3283.1 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{25}O_2N_2F_3NaS$ $[M+Na]^+$: 497.1481. Found: 497.1481.

N-((2S,E)-3-((4-Chlorophenyl)amino)-1,1,1-trifluoro-5-(3-methoxyphenyl)pent-4-e n-2-yl)-4-methylbenzenesulfonamide **(4g)**: Yellow liquid, 40.8 mg, 39% yield; ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.25 - 7.16 (m, 3H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 7.7 Hz, 1H), 6.82 - 6.77 (m, 2H), 6.58 - 6.51 (m, 3H), 6.00 (dd, *J* = 15.8, 7.0 Hz, 1H), 5.79 - 5.65 (m, 1H), 4.42 - 4.31 (m, 1H), 4.17 - 4.06 (m, 1H), 3.99 (br, 1H), 3.77 (s, 3H), 2.36 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.93 (d, *J* = 6.9 Hz, 3F).^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8 (s), 144.3 (s), 144.3 (s), 137.0 (s), 136.8 (s), 133.8 (s), 129.8 (s), 129.6 (s), 129.2 (s), 127.0 (s), 124.9 (s), 124.2 (q, *J* = 283.7 Hz), 123.6 (s), 119.3 (s), 115.2 (s), 113.9 (s), 112.1 (s), 57.5 (q, *J* = 28.3 Hz), 56.1 (s), 55.2 (s), 21.5 (s). IR (neat) ν = 522.4, 549.2, 568.8, 667.1, 703.9, 814.7, 969.8, 1005.1, 1092.1, 1159.1, 1185.0, 1266.5, 1289.8, 1328.0, 1493.0, 1599.2, 2923.6, 3031.4, 3280.6 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{23}O_3N_2F_3ClS$ $[M-H]^-$: 523.1070. Found: 523.1067.

N-((2S,E)-5-(4-Chlorophenyl)-1,1,1-trifluoro-3-(phenylamino)pent-4-en-2-yl)-4-methylbenzenesulfonamide **(4h)**: Yellow liquid, 62.2 mg, 63% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.25 - 7.11 (m, 8H), 6.76 (t, *J* = 7.3, 1H), 6.62 (d, *J* = 8.0 Hz, 2H), 6.54 (d, *J* = 15.8 Hz, 1H), 6.08 - 5.97 (m, 2H), 4.47 (br, 1H), 4.23 - 4.10 (m, 1H), 4.02 (br, 1H), 2.36 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.01 (d, *J* = 7.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.7 (s), 144.2 (s), 136.9 (s), 134.4 (s), 133.8 (s), 132.2 (s), 129.8 (s), 129.4 (s), 128.7 (s), 127.9 (s), 127.0 (s), 125.9 (s), 124.3 (q, *J* = 284.1 Hz), 119.0 (s), 114.0 (s), 57.5 (q, *J* = 28.4 Hz), 55.7 (s), 21.5 (s). IR (neat) ν = 549.0, 570.7, 666.1, 692.6, 750.9, 811.8, 968.4, 994.1, 1092.7, 1159.8, 1265.1, 1328.0, 1436.8, 1492.3, 1559.0, 1602.0, 2924.0, 3054.3, 3281.4 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{21}O_2N_2ClF_3S$ $[M-H]^-$: 493.0964. Found: 493.0965.

N-((2S,E)-5-(4-Chlorophenyl)-3-((4-chlorophenyl)amino)-1,1,1-trifluoropent-4-en-2-yl)-4-methylbenzenesulfonamide **(4i)**: Yellow liquid, 69.8 mg, 66% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.22 - 7.12 (m, 6H), 7.10 - 7.04 (m, 2H), 6.54 - 6.47 (m, 3H), 6.05 (d, *J* = 9.5 Hz, 1H), 5.99 (dd, *J* = 16.3, 6.5 Hz, 1H), 4.43 - 4.36 (m, 1H), 4.18 - 4.09 (m, 1H), 4.07 (d, *J* = 9.1 Hz, 1H), 2.35 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.07 (d, *J* = 7.2 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3 (s), 144.2 (s), 136.8 (s), 134.1 (s), 134.0 (s), 132.6 (s), 129.8 (s), 129.3 (s), 128.8 (s), 127.9 (s), 127.0 (s), 125.4 (s), 124.2 (q, *J* = 284.1 Hz), 123.7 (s), 115.2 (s), 57.5 (q, *J* = 28.4 Hz), 56.1 (s), 21.5 (s). IR (neat) ν = 501.96, 548.73, 664.86, 734.58, 813.27, 910.62, 968.00, 1012.62, 1091.48, 1159.19, 1185.11, 1264.87, 1328.55, 1404.26, 1453.88, 1492.41, 1598.33, 2924.10 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{22}O_2N_2Cl_2F_3S$ $[M+H]^+$: 529.0726. Found: 529.0726.

4-Methyl-N-((2S,E)-1,1,1-trifluoro-5-(4-fluorophenyl)-3-(p-tolylamino)pent-4-en-2-yl)benzenesulfonamide **(4j)**: Yellow liquid, 60.1 mg, 61% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.31 - 7.19 (m, 4H), 7.07 - 6.90 (m, 4H), 6.65 - 6.48 (m, 3H), 5.97 (dd, *J* = 15.6, 7.4 Hz, 1H), 5.42 (d, *J* = 9.6 Hz, 1H), 4.40 (br, 1H), 4.19 - 4.04 (m, 1H), 3.81 (d, *J* = 8.1 Hz, 1H), 2.39 (s, 3H), 2.22 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.05 (d, *J* = 7.3 Hz, 3F), -111.22 - -114.99 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6 (d, *J* = 247.6 Hz), 144.1 (s), 143.3 (s), 137.1 (s), 132.2 (s), 132.1 (d, *J* = 3.3 Hz), 129.9 (s), 129.8 (s), 128.4 (s), 128.3 (d, *J* = 8.1 Hz), 127.0 (s), 125.1 (s), 124.3 (q, *J* = 284.62 Hz), 115.4 (d, *J* = 21.7 Hz), 114.4 (s), 57.5 (q, *J* = 28.1 Hz), 56.2 (s), 21.5 (s), 20.4 (s). IR (neat) ν = 549.1, 586.0, 667.3, 705.3, 811.9, 920.0,

968.1, 1092.6, 1159.3, 1230.4, 1265.7, 1329.9, 1456.1, 1508.5, 1520.3, 1558.5, 1616.7, 1716.7, 2922.4, 3031.8, 3283.2 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{24}O_2N_2F_4NaS$ $[M+Na]^+$: 515.1387. Found: 515.1387.

4-Methyl-N-((2S,E)-1,1,1-trifluoro-5-(4-fluorophenyl)-3-(phenylamino)pent-4-en-2-yl)benzenesulfonamide **(4k)**: Yellow liquid, 56.4 mg, 59% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.30 - 7.22 (m, 4H), 7.18 (t, *J* = 7.8 Hz, 2H), 6.97 (t, *J* = 8.5 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.68 - 6.52 (m, 3H), 5.99 (dd, *J* = 15.6, 7.0 Hz, 1H), 5.38 (d, *J* = 9.9 Hz, 1H), 4.45 - 4.35 (m, 1H), 4.22 - 4.07 (m, 1H), 3.83 (d, *J* = 8.6 Hz, 1H), 2.39 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.97 (d, *J* = 7.3 Hz, 3F), -112.48 - -114.78 (m, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6 (d, *J* = 247.6 Hz), 145.7 (s), 144.2 (s), 137.0 (s), 132.3 (s), 132.0 (d, *J* = 3.3 Hz), 129.8 (s), 129.4 (s), 128.3 (d, *J* = 8.1 Hz), 127.0 (s), 124.9 (s), 124.3 (q, *J* = 283.4 Hz), 119.0 (s), 115.5 (d, *J* = 21.7 Hz), 114.0 (s), 57.6 (q, *J* = 28.1 Hz), 55.8 (s), 21.5 (s). IR (neat) ν = 548.8, 570.8, 665.7, 691.1, 750.9, 813.0, 919.6, 968.2, 1092.9, 1159.0, 1185.1, 1229.1, 1266.0, 1328.0, 1508.2, 1602.2, 2924.5, 3054.1, 3282.6 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{22}O_2N_2F_4NaS$ $[M+Na]^+$: 501.1230. Found: 501.1231

N-((2S,E)-3-((4-Chlorophenyl)amino)-1,1,1-trifluoro-5-(4-fluorophenyl)pent-4-en-2-yl)-4-methylbenzenesulfonamide **(4l)**: Yellow solid, 64.5 mg, 63% yield; M.P. 109 - 111 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.25 - 7.14 (m, 4H), 7.11 - 7.04 (m, 2H), 6.93 (t, *J* = 8.6 Hz, 2H), 6.56 - 6.49 (m, 3H), 6.01 - 5.90 (m, 2H), 4.42 - 4.34 (m, 1H), 4.16 - 4.09 (m, 1H), 4.05 (d, *J* = 9.0 Hz, 1H), 2.36 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.02 (d, *J* = 7.3 Hz, 3F), -113.26 - -113.35 (m, 1F). ^{13}C

NMR (101 MHz, $CDCl_3$) δ 162.6 (d, *J* = 248.0 Hz), 144.3 (s), 136.8 (s), 132.5 (s), 131.9 (d, *J* = 3.2 Hz), 129.8 (s), 129.2 (s), 128.3 (d, *J* = 8.1 Hz), 127.0 (s), 124.5 (s), 124.2 (q, *J* = 283.7 Hz), 123.6 (s), 123.5 (s), 115.5 (d, *J* = 21.7 Hz), 115.1 (s), 57.64 (q, *J* = 29.3 Hz), 55.9 (s), 21.5 (s). IR (neat) ν = 548.89, 566.93, 666.25, 733.40, 814.07, 847.17, 910.10, 968.20, 1092.35, 1158.91, 1184.87, 1231.77, 1265.93, 1291.00, 1328.77, 1403.59, 1452.45, 1493.76, 1508.90, 1600.23, 2924.41, 3277.96 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{22}O_2N_2ClF_4S$ $[M+H]^+$: 513.1021. Found: 513.1021.

(E)-N-(3-(butylamino)-1,1,1-trifluoro-5-(p-tolyl)pent-4-en-2-yl)-4-methylbenzenes ulfonamide **(4m)**: Yellow solid, 45.2 mg, 50% yield; M.P. 71.76 - 72.31 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 7.9 Hz 2H), 7.15 – 7.09 (m, 4H), 6.47 (d, *J* = 15.8 Hz, 1H), 5.69 (dd, *J* = 15.8, 8.8 Hz, 1H), 3.89 (qd, *J* = 7.9, 2.3 Hz, 1H), 3.59 (dd, *J* = 8.8, 2.0 Hz, 1H), 2.65 - 2.40 (m, 2H), 2.36 (s, 3H), 2.33 (s, 3H), 1.41- 1.35 (m, 2H), 1.32- 1.25 (m, 2H), 0.87 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) -72.79 (d, *J* = 7.9 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6 (s), 138.0 (s), 137.8 (s), 133.2 (s), 133.1 (s), 129.6 (s), 129.2 (s), 127.0 (s), 126.6 (s), 125.84 (s), 124.6 (q, *J* = 283.3 Hz), 58.5 (s), 58.1 (q, *J* = 29.1 Hz), 46.9 (s), 32.1 (s), 21.5 (s), 21.2 (s), 20.2 (s), 13.9 (s). IR (neat) ν = 3333.4, 3025.1, 2985.5, 2930.8, 2863.2, 1598.7, 1468.8, 1353.6, 1273.0, 1171.6, 1134.3, 1094.6, 967.4, 815.9, 800.3, 685.7, 576.2, 561.7, 550.9, 464.1cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{28}O_2N_2F_3S$ $[M-H]^-$: 453.1829. Found: 453.1829.

Procedure for the Synthesis of 5: Into the mixture of diphenyl(2,2,2-Trifluoroethyl)sulfonium triflate **1** (209.2 mg, 0.5 mmol), imine **2a**

(285.1 mg, 1 mmol) and 4Å MS (400 mg) in dichloromethane (5 mL) was added TBAF (0.75 mL, 1 M in THF) dropwise under N_2 atmosphere. The reaction mixture was stirred at room temperature for 1 h. 4Å MS was removed by filtration. The filtrate was concentrated to give crude aziridine, into which was added sodium methoxide (135.1 mg, 2.5 mmol), 15-Crown-5 (110.1 mg, 0.5 mmol) and THF (5 mL) under N_2 atmosphere. The reaction mixture was stirred at 80 ^{o}C for 2 h. After being cooled to room temperature, the solution was subjected to flash column chromatography (petroleum ether : EA = 20:1) to afford the pure product.

*4-Methyl-N-((2S,3R,E)-1,1,1-trifluoro-3-methoxy-5-phenylpent-4-en-2-yl)benzenes ulfonamid*e **(5a)**: Yellow solid, 89.8 mg, 45% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.35 - 7.22 (m, 5H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.58 (d, *J* = 15.9 Hz, 1H), 5.82 (dd, *J* = 15.9, 8.0 Hz, 1H), 5.49 (d, *J* = 9.3 Hz, 1H), 4.09 (d, *J* = 8.0 Hz, 1H), 4.04 - 3.92 (m, 1H), 3.29 (s, 3H), 2.33 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -73.34 (d, *J* = 7.4 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6 (s), 137.9 (s), 135.5 (s), 135.1 (s), 129.6 (s), 128.6 (s), 128.4 (s), 126.9 (s), 126.9 (s), 124.0 (q, *J* = 283.5 Hz), 123.9 (s), 78.0 (q, *J* = 1.9 Hz), 58.3 (q, *J* = 30.3 Hz), 56.6 (s), 21.5 (s). IR (neat) ν = 549.0, 570.1, 660.9, 690.0, 757.5, 844.9, 964.3, 1088.3, 1135.2, 1165.2, 1273.9, 1351.8, 1450.8, 1466.3, 1495.9, 1597.1, 2968.1, 3027.9, 3300.2. HRMS (ESI): calcd. for $C_{19}H_{19}O_3NF_3S$ $[M-H]^-$: 398.1038. Found: 398.1038.

(E)-N-(3-(benzyloxy)-1,1,1-trifluoro-5-phenylpent-4-en-2-yl)-4-methylbenzenesulfo namide **(5b)**: Yellow solid, 118.7 mg, 50% yield; M.P. 119.8 - 121.5 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.39 - 7.22 (m, 10H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.58 (d, *J* = 15.9 Hz, 1H), 5.92 (dd, *J* = 15.9, 8.2 Hz, 1H), 5.53 (s, 1H), 4.59

(d, *J* = 11.5 Hz, 1H), 4.38 (d, *J* = 11.5 Hz, 1H), 4.33 (d, *J* = 8.2 Hz, 1H), 4.03 (q, *J* = 6.6 Hz, 1H), 2.34 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.99 (d, *J* = 7.4 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7 (s), 137.8 (s), 136.8 (s), 135.5 (s, *J* = 11.4 Hz), 135.4 (s), 129.6 (s), 128.6 (s), 128.53 (s), 128.50 (s), 128.1 (d, *J* = 1.6 Hz), 128.0 (s), 126.97 (s), 126.96 (s), 124.02 (q, *J* = 283.9 Hz), 123.9 (s), 75.7 (s), 70.6 (s), 58.50 (q, *J* = 30.2 Hz), 21.5 (s). IR (neat) ν = 3289.3, 3065.6, 3027.0, 2922.8, 2876.6, 1597.1, 1495.3, 1429.5, 1340.7, 1272.0, 1242.4, 1174.7, 1125.8, 1049.5, 1011.2, 870.1, 755.7, 695.5, 663.5, 616.9, 550.6, 499.0 cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{23}O_3NF_3S$ $[M-H]^-$: 474.1356 Found: 474.1348.

Procedure for the Synthesis of 6: The mixture of compound **5b** (94.8 mg, 0.2 mmol) and palladium on activated carbon (30mg, 10%) in methanol (15 m) was stirred at room temperature for 24h under a hydrogen atmosphere (30 atm). The solid was removed by filtration. The filtrate was subjected to flash column chromatography (petroleum ether : EA = 10:1) to afford the pure product.

4-methyl-N-((2S,3R)-1,1,1-trifluoro-3-hydroxy-5-phenylpentan-2-yl)benzenesulfonamide (**6**): White solid, 65.8mg, 84% yield; M.P. 115.3 - 116.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.32 - 7.15 (m, 5H), 7.16 - 7.05 (m, 2H), 5.81 (d, *J* = 9.1 Hz, 1H), 4.12 - 3.97 (m, 1H), 3.88 (p, *J* = 8.0 Hz, 1H), 2.75 - 2.57 (m, 2H), 2.42 (d, *J* = 4.5 Hz, 1H), 2.35 (s, 3H), 1.86 - 1.74 (m, 1H), 1.74- 1.60 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.22 (d, *J* = 7.8 Hz, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8 (s), 140.5 (s), 137.8 (s), 129.6 (s), 128.5 (s), 128.3 (s), 126.9 (s), 126.1 (s), 124.5 (q, *J* = 281.9 Hz), 67.5 (s), 57.6 (q, *J* = 29.1 Hz), 35.3 (s), 31.4 (s), 21.5 (s). IR (neat) ν = 3550.8, 3319.8, 3064.8, 2951.9, 2869.6, 1599.6, 1496.4, 1456.7, 1384.1, 1345.3,

1308.4, 1274.5, 1166.2, 1139.5, 1122.7,922.3, 815.3, 724.4, 703.3, 670.3, 578.3, 549.8, 475.0 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{19}O_3NF_3S$ $[M-H]^-$: 386.1043 Found: 386.1039.

ASSOCIATED CONTENT

Supporting Information Available. Copies of $^{1}H/^{19}F/^{13}C$ NMR spectra of compounds and crystal structures of compounds **3m**, **4b** and **5a**. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding author

* Prof. Jin-Hong Lin

Email: jlin@sioc.ac.cn.

* Prof. Ji-Chang Xiao

Email: jchxiao@sioc.ac.cn

* Prof. Xing Zheng

Email: zhengxing5018@yahoo.com

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The authors thank National Basic Research Program of China (2015CB931900, 2012CBA01200), the National Natural Science Foundation (21421002, 21472222, 21502214, 21672242，81273537), the Chinese Academy of Sciences (XDA02020105,

XDA02020106), the Science and Technology Commission of Shanghai Municipality (15DZ1200102), the Key Research Program of Frontier Sciences (CAS) (QYZDJ-SSW-SLH049), the Key Project of Hunan Province Science and Technology Department (2016DK2001), the Key Project of Hunan Provincial Education Department (No. 17A190), and the Zhengxiang Scholar Program of the University of South China for financial support.

REFERENCES

(1) (a) Lucet, D.; Le Gall, T.; Mioskowski, C. *Angew. Chem. Int. Ed.* **1998**, *37*, 2580-2627; (b) Viso, A.; Fernandez de la Pradilla, R.; Garcia, A.; Flores, A. *Chem. Rev.* **2005**, *105*, 3167-3196; (c) Kotti, S. R. S. S.; Timmons, C.; Li, G. *Chem. Biol. Drug Des.* **2006**, *67*, 101-114; (d) Grygorenko, O. O.; Radchenko, D. S.; Volochnyuk, D. M.; Tolmachev, A. A.; Komarov, I. V. *Chem. Rev.* **2011**, *111*, 5506-5568; (e) Zhu, Y.; Cornwall, R. G.; Du, H.; Zhao, B.; Shi, Y. *Acc. Chem. Res.* **2014**, *47*, 3665-3678.

(2) (a) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320-330; (b) Ojima, I. *Fluorine in Medicinal Chemistry and Chemical Biology*; Blackwell Publishing: Chichester, 2009; (c) Qiu, X.-L.; Yue, X.; Qing, F.-L.; *Chiral Drugs: Chemistry and Biological Action*; Lin, G.-Q.; You, Q.-D.; Cheng, J.-F., Eds.; John Wiley & Sons, Inc.: Hoboken, New Jersey, 2011, 195-251; (d) Kirsch, P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*; Second ed.; Wiley-VCH: Weinheim, Germany, 2013.

(3) Apostolakis, S.; Oeff, M.; Tebbe, U.; Fabritz, L.; Breithardt, G.; Kirchhof, P.

Expert Opin. Pharmacother. **2013**, *14*, 347-357.

(4) (a) Shih, N.-Y.; Shue, H.-J.; Reichard, G. A.; Paliwal, S.; Blythin, D. J.; Piwinski, J. J.; Xiao, D.; Chen, X.; WO2001044200A2; (b) Reichard, G. A.; Stengone, C.; Paliwal, S.; Mergelsberg, I.; Majmundar, S.; Wang, C.; Tiberi, R.; McPhail, A. T.; Piwinski, J. J.; Shih, N.-Y. *Org. Lett.* **2003**, *5*, 4249-4251.

(5) (a) Cardona, F.; Goti, A. *Nat Chem* **2009**, *1*, 269-275; (b) de Figueiredo, R. M. *Angew. Chem. Int. Ed.* **2009**, *48*, 1190-1193; (c) Zhao, B.; Peng, X.; Zhu, Y.; Ramirez, T. A.; Cornwall, R. G.; Shi, Y. *J. Am. Chem. Soc.* **2011**, *133*, 20890-20900; (d) Muniz, K.; Martinez, C. *J. Org. Chem.* **2013**, *78*, 2168-2174; (e) Olson, D. E.; Su, J. Y.; Roberts, D. A.; Du Bois, J. *J. Am. Chem. Soc.* **2014**, *136*, 13506-13509; (f) Zhu, X.; Du, H. *Org. Lett.* **2015**, *17*, 3106-3109; (g) Fava, E.; Millet, A.; Nakajima, M.; Loescher, S.; Rueping, M. *Angew. Chem., Int. Ed.* **2016**, *55*, 6776-6779; (h) Muñiz, K.; Barreiro, L.; Romero, R. M.; Martínez, C. *J. Am. Chem. Soc.* **2017**, *139*, 4354-4357.

(6) (a) Katagiri, T.; Katayama, Y.; Taeda, M.; Ohshima, T.; Iguchi, N.; Uneyama, K. *J. Org. Chem.* **2011**, *76*, 9305-9311; (b) Takehiro, Y.; Hirotaki, K.; Takeshita, C.; Furuno, H.; Hanamoto, T. *Tetrahedron* **2013**, *69*, 7448-7454; (c) Waki, M.; Katagiri, T.; Matsuno, K.; Miyachi, H. *Tetrahedron Lett.* **2014**, *55*, 6915-6918.

(7) Moens, M.; De Kimpe, N.; D'hooghe, M. *J. Org. Chem.* **2014**, *79*, 5558-5568.

(8) Sánchez-Roselló, M.; Delgado, O.; Mateu, N.; Trabanco, A. A.; Van Gool, M.; Fustero, S. *J. Org. Chem.* **2014**, *79*, 5887-5894.

(9) Wu, L.; Xie, C.; Mei, H.; Dai, Y.; Han, J.; Soloshonok, V. A.; Pan, Y. *J. Org. Chem.* **2015**, *80*, 3187-3194.

(10) Orcel, U.; Waser, J. *Angew. Chem. Int. Ed.* **2016**, *55*, 12881-12885.

(11) Duan, Y.; Zhou, B.; Lin, J.-H.; Xiao, J.-C. *Chem. Commun.* **2015**, *51*, 13127-13130.

(12) (a) Ji, Y.-L.; Lin, J.-H.; Xiao, J.-C.; Gu, Y.-C. *Org. Chem. Front.* **2014**, *1*, 1280-1284; (b) Zheng, J.; Lin, J.-H.; Deng, X.-Y.; Xiao, J.-C. *Org. Lett.* **2015**, *17*, 532-535; (c) Duan, Y.; Lin, J.-H.; Xiao, J.-C.; Gu, Y. C. *Org Lett* **2016**, *18*, 2471-2474; (d) Ji, Y.-L.; Luo, J.-J.; Lin, J.-H.; Xiao, J.-C.; Gu, Y. C. *Org. Lett.* **2016**, *18*, 1000-1003.

(13) Summary of Data CCDC 1418098.

(14) Summary of Data CCDC 1545327.

(15) (a) Burchak, O. N.; Py, S. *Tetrahedron* **2009**, *65*, 7333-7356; (b) Donohoe, T. J.; Callens, C. K. A.; Flores, A.; Lacy, A. R.; Rathi, A. H. *Chem. Eur. J.* **2011**, *17*, 58-76.

(16) Summary of Data CCDC 1418089.

(17) K.-i. Yamada, H. Umeki, M. Maekawa, Y. Yamamoto, T. Akindele, M. Nakano, K. Tomioka, *Tetrahedron* **2008**, *64*, 7258-7265.

(18) R. Chawla, A. K. Singh, L. D. S. Yadav, T*etrahedron Lett.* **2014**, *55*, 3553-3556.