

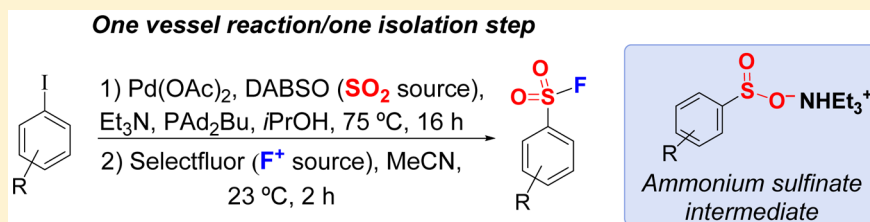
Pd-Catalyzed Conversion of Aryl Iodides to Sulfonyl Fluorides Using SO₂ Surrogate DABSO and Selectfluor

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S Supporting Information



ABSTRACT: A one-pot Pd-catalyzed conversion of aryl iodide to aryl sulfonyl fluorides using DABSO and Selectfluor has been developed generating aryl sulfonyl fluorides in good to excellent yields. The reaction results in the generation of electronically and sterically diverse sulfonyl fluorides. Additionally, sulfonyl fluorides can be converted to aryl sulfonamides and sulfonic esters using Cs₂CO₃ under mild conditions.

Compounds that contain a S–F bond have garnered intense interest in the chemical and biological literature as of late. In particular, sulfonyl fluorides, (RSO₂F), are commonly used as covalent protein inhibitors and biological probes (Figure 1).¹ Considerable efforts have recently focused on new

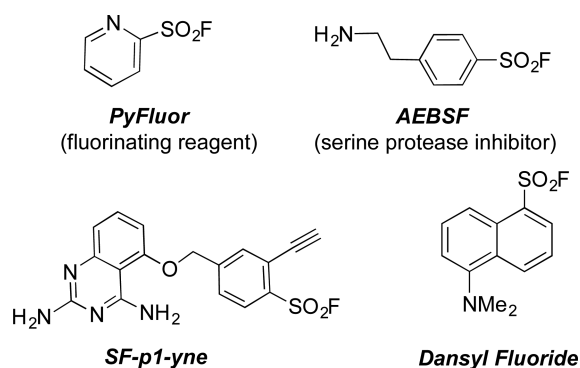


Figure 1. Representative sulfonyl fluorides and their function.

applications in organic chemistry for aromatic sulfonyl fluorides, ranging from fluorinating reagents² and, ¹⁹F radiolabeling,³ to synthons toward sulfonylated compounds using sulfur(VI) exchange (SuFEx) “click chemistry”.⁴ Key to the allure of sulfonyl fluorides are their unique properties compared to other sulfonylated functional groups. Due to their sulfur–fluorine bond, sulfonyl fluorides are hydrolytically stable,⁵ resistant to reduction,⁶ and unlike other sulfonylated groups, resistant to bond cleavage in metal catalysis.⁷

Despite the burgeoning interest in aromatic sulfonyl fluorides, significant challenges remain in their synthesis. The

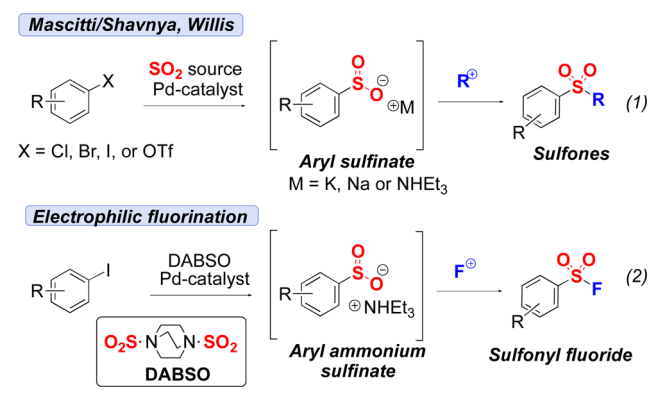
most common approach to synthesize aromatic sulfonyl fluorides requires the corresponding sulfonyl chloride and an F[−] source (e.g., KFHF, HF, etc.).^{4a} However, several challenges exist with this approach, particularly with how it pertains to the synthesis and reactivity of the sulfonyl chloride precursor. First, the synthesis of sulfonyl chlorides requires the use of strong acids, oxidants, or explosive aryl diazonium salts.⁸ These reagents are often incompatible with many functional groups, thus complicating the late-stage functionalization of molecules. Second, the rapid reactivity of some sulfonyl chlorides with water presents operational challenges, creating undesired side products. Thus, there is significant impetus for alternative methods to synthesize aromatic sulfonyl fluorides that circumvent the requirement of sulfonyl chloride intermediates. One strategy involves the development of one-pot methods that begin with more simple, organic starting materials, and permit the incorporation of both SO₂ and fluorine.

Recent efforts have focused on metal-catalyzed generation of sulfones and sulfonamides using bench-stable SO₂ sources [e.g., 1,4-diazabicyclo[2.2.2]octanebis (sulfur dioxide) or DABSO, and potassium metabisulfite].^{9–11} In particular, the generation of organic sulfinate salt intermediates using metal-mediated strategies are of high interest for drug discovery, facilitating rapid derivatization of sulfonylated analogues in structure–activity relationship studies.^{9a} Our approach was to leverage the nucleophilic nature of a sulfinate intermediate and utilize electrophilic fluorinating reagents to generate sulfonyl fluorides (Scheme 1).^{12,13} Herein, we report a one-pot, Pd-catalyzed conversion of aryl iodides to sulfonyl fluorides using DABSO

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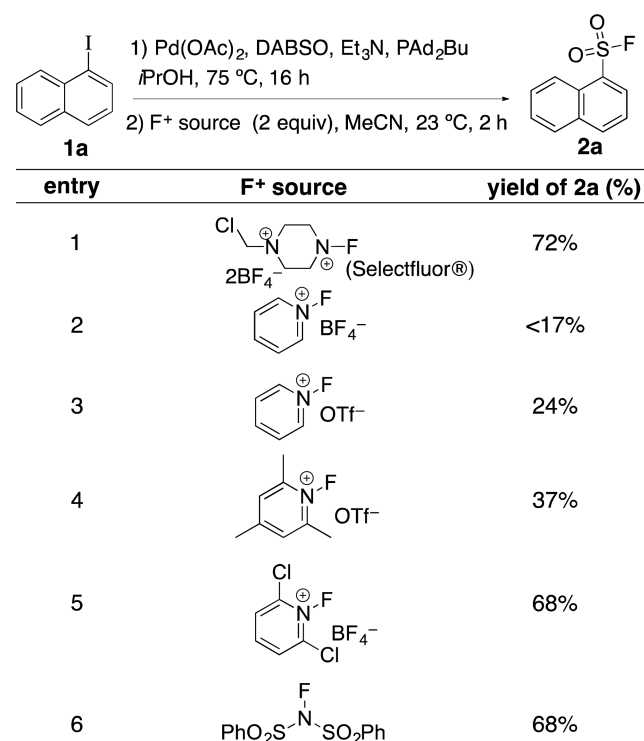
Scheme 1. Strategies Toward Sulfonylation Products Using Aryl Sulfonates



and selectfluor.¹³ This approach incorporates SO₂ and fluorine into aryl iodides in a one-pot reaction and requires only column chromatography for purification. Additionally, new, mild conditions to form sulfonic esters and sulfonamide from sulfonyl fluorides is also described.

We initially endeavored to generate sulfonyl fluorides using existing Pd-catalyzed systems that generate aryl sulfinate intermediates using an aryl halide, a SO₂ source (i.e., DABSO, or K₂S₂O₄), and Selectfluor.⁸ However, these systems proved largely unsuccessful due to the requirement of isolating the crude sulfinate salt and poor yield of the sulfonyl fluoride. As an alternative, we employed a Pd-catalyzed system reported by Willis et al. that has previously been shown to generate an aryl ammonium sulfinate.¹⁴ We surmised that this approach would lead to the in situ generation of a more soluble sulfinate intermediate and allow a more facile fluorination step, obviating the need to isolate the sulfinate salt. This approach revealed that treatment with 1-iodonaphthalene (**1a**), Pd(OAc)₂, DABSO, CataCXium A (PA₂Bu), Et₃N, and *i*PrOH (stirred at 75 °C for 16 h) followed by addition of Selectfluor and MeCN after 2 h generated sulfonyl fluoride **2a** with a 72% yield (Scheme 2, entry 1). Next, we performed optimization studies to identify the best electrophilic fluorinating reagent. To this end, several common fluorinated reagents were tested, generating comparable yields of **2a** to Selectfluor (Scheme 2, entries 1 and 6). Ultimately, Selectfluor was chosen due to its ease of handling, broader commercial availability, and affordability compared to the other reagents.¹⁵

In an effort to demonstrate the broad applicability of this system, we subjected a variety of aryl iodides to the aforementioned reaction conditions. Our studies revealed that both electron-donating and -withdrawing aryl iodides are converted to their corresponding sulfonyl fluoride in good to excellent yield (Scheme 3). Additionally, this method generated sulfonyl fluorides despite increasing steric congestion of the aryl unit (Scheme 3, **2j–2l**). Notably, our experiments revealed the installation of the SO₂F group can be performed even in the presence of a tosylate (**2i**), a functional group that can undergo oxidative addition and functionalization via Pd-catalysts.¹⁶ Since sulfonyl fluorides have been demonstrated to resist C–S bond cleavage in Pd-catalysis,⁷ we next hypothesized that multiple C–I bonds in an organic molecule could be converted to C–SO₂F bonds. This would allow the installation of multiple sulfonyl-based groups in one molecule. Such molecules could have potential as cross-linkers using SuFEx click chemistry.¹⁷ To interrogate this hypothesis, we subjected 1,4-diiodobenzene

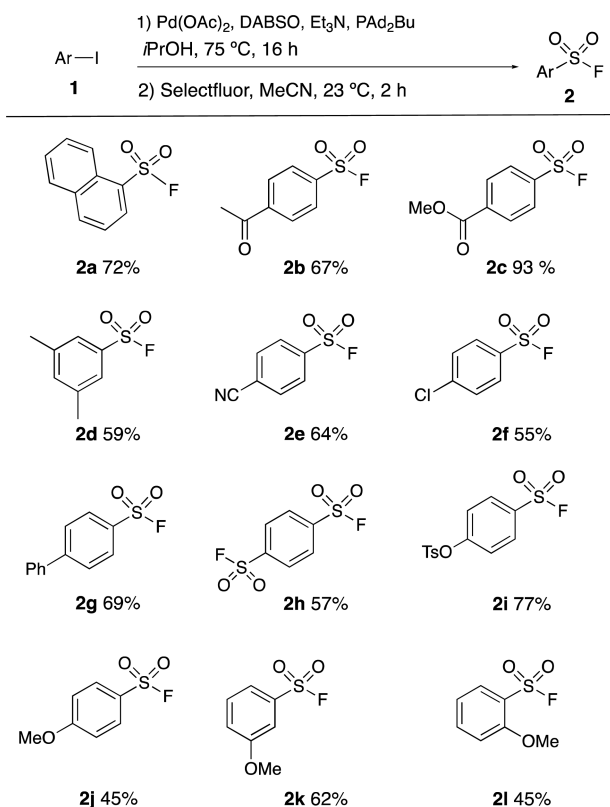
Scheme 2. Optimization Studies^{a,b}

^aReaction conditions: aryl iodide (1 equiv), DABSO (1.2 equiv), Pd(OAc)₂ (0.05 equiv), PA₂Bu (0.08 equiv), Et₃N (3 equiv) in *i*PrOH (0.3 M), 75 °C, 16 h, then Selectfluor and MeCN (0.3 M) at room temperature for 2 h. ^bIsolated yields are an average of two trials.

to our reaction conditions and increased by 2-fold: the catalyst, DABSO, base, Selectfluor, and solvent. Gratifyingly, **2h** was obtained in good (57%) yield (Scheme 3, **2h**), demonstrating the feasibility of installing multiple SO₂F moieties into an organic molecule.

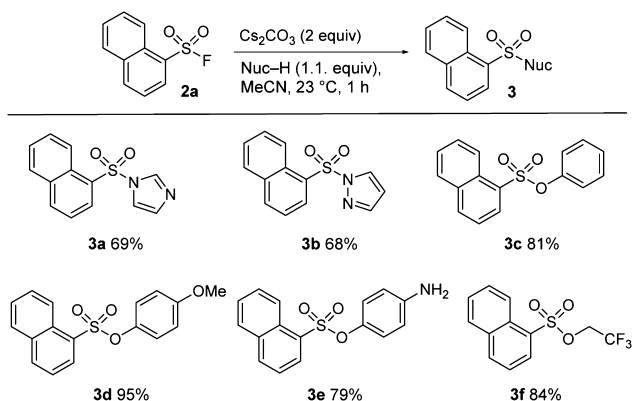
Sulfonic esters and sulfonamides are classes of sulfonylated compounds with a myriad of applications in synthetic chemistry and as drug targets^{18,19} However, compared to sulfonyl chlorides, there are few examples of facile generation of sulfonic esters and sulfonamides from sulfonyl fluorides.^{4a} Additionally, studies investigating the protease activity of sulfonyl fluorides have suggested aromatic sulfonyl fluorides can chemoselectively react with tyrosine residues (phenols) over other nucleophilic amino acid residues.^{1d–f} Therefore, we next investigated the reactivity of sulfonyl fluorides with a variety of nitrogen- and oxygen-based nucleophiles. In contrast to sulfonyl chlorides, we hypothesized that sulfonyl fluoride stability could be leveraged to exhibit chemoselectivity for nucleophiles.²⁰ To test this hypothesis, several nitrogen- and oxygen-based nucleophiles were allowed to react with sulfonyl fluoride **2a** to generate sulfonamides and sulfonate esters.

Our initial studies focused on screening base and phenol combinations to generate a sulfonate ester (Table S1, Supporting Information); Cs₂CO₃ and DBU emerged as the best candidates, providing a high yield of sulfonate ester after just 1 h at room temperature. Notably, in the absence of base, no sulfonate ester formation was detected by TLC or GC/MS, nor was any decomposition of the sulfonyl fluoride detected after 24 h. Ultimately, Cs₂CO₃ was chosen as the base of choice due to ease of purification. Subsequently, a series of electronically diverse phenols were allowed to react with **2a**,

Scheme 3. Pd-Catalyzed Conversion of Aryl Iodides to Sulfonyl Fluorides Using Selectfluor^{a,b}

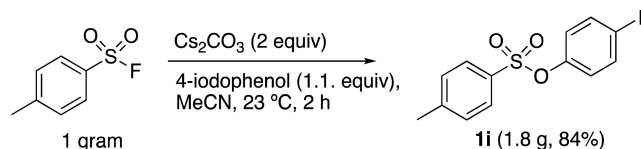
^aReaction conditions: aryl iodide (1 equiv), DABSO (1.2 equiv), Pd(OAc)₂ (0.05 equiv), Pd₂Bu (0.08 equiv), Et₃N (3 equiv) in iPrOH (0.3 M), 75 °C, 16 h, then Selectfluor and MeCN (0.3 M) at room temperature for 2 h. ^bIsolated yields are an average of two trials.

generating sulfonate esters in good to excellent yields (Scheme 4, entries 3c–3f).²¹ Moreover, **2a** in the presence of Cs₂CO₃ and EtOH did not result in any detectable product by GC/MS after 24 h, whereas electron-deficient trifluoroethanol afforded **3h** in excellent yield. In addition to alcohols, aromatic amines (e.g., imidazole and pyrazole) resulted in sulfonamides **3a** and **3b** in great yield. This reaction can be performed on a gram

Scheme 4. Synthesis of Sulfonic Esters and Sulfonamides with **2a**^{a,b}

^aReaction conditions: 1-naphthylsulfonyl fluoride, **2a** (1.0 equiv), Nuc-H (1.1 equiv), Cs₂CO₃ (2.0 equiv), MeCN (0.3 M), at room temperature for 1 h. ^bIsolated yields are an average of two trials.

scale as demonstrated in the synthesis of **1i** using *p*-toluenesulfonyl fluoride and 4-iodophenol (Scheme 5).

Scheme 5. Gram-Scale Synthesis of Sulfonic Ester **1i**

In conclusion, we have developed a new Pd-catalyzed method to convert electronically and sterically diverse aryl iodides to sulfonyl fluorides using DABSO and selectfluor in good to excellent yields, allowing for a versatile generation of sulfonyl fluorides. Additionally, this reaction permits multiple installations of the SO₂F moiety. This reaction utilizes selectfluor, the most economical and readily available source of electrophilic fluorine. Finally, conditions were developed to generate sulfonate esters and sulfonamides from sulfonyl fluorides at room temperature. Ongoing investigations are underway to better understand sulfonyl fluoride reactivity. Further studies will focus on alternative catalytic approaches toward sulfonyl fluorides using cheaper metal-catalysts and fluorinating reagents.

EXPERIMENTAL SECTION

General Considerations. NMR spectra were obtained on a Bruker 400 (400.00 MHz for ¹H; 376.50 MHz for ¹⁹F; 100.61 MHz for ¹³C) spectrometer. ¹H, ¹⁹F, and ¹³C chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual peak used as an internal reference. ¹⁹F NMR are referenced on a unified scale, where the single primary reference is that of the frequency of the residual solvent peak in the ¹H NMR spectrum.²² ¹⁹F NMR is proton coupled. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublet (dd), triplet (t) and multiplet (m). The ¹H, ¹⁹F, and ¹³C were taken at room temperature. Elemental analysis (CHN) was conducted by ALS Environment, Tucson AZ using WO₃ as a combustion catalyst. High-resolution mass spectroscopy was conducted at the California Institute of Technology Mass Spectroscopy Center using a JMS-60H (JEOL) double-focusing magnetic sector mass spectrometer with resolution set to 3000. IR spectra were obtained on a PerkinElmer Spectrum RXI FT-IR spectrometer using a MIRacle ATR attachment. Melting points were obtained on a Mettler Toledo MP50 Melting Point System. Column chromatography was performed on an ISCO Combiflash R² system using a 25 g prepacked standard column.

General Procedure for Aryl Sulfonyl Fluoride Synthesis **2a–**2l**.** In air, a 50 mL Cajon Schlenk tube was loaded with aryl iodide (0.90 mmol, 1.0 equiv), CataCXium A (24 mg, 0.069 mmol, 0.08 equiv), DABSO (0.130 g, 0.54 mmol, 0.6 equiv; 1.2 equiv of SO₂), Pd(OAc)₂ (10 mg, 0.45 mmol, 0.05 equiv), and a magnetic stir bar. The Schlenk tube was sealed with a rubber septum and placed under vacuum for 10 min. The tube was backfilled with argon and evacuated; this was repeated two additional times. Under argon, anhydrous isopropanol (3 mL, 0.3 M) and anhydrous triethylamine (380 μL, 2.7 mmol, 3 equiv) were added via syringe. The tube was sealed with a Teflon screw cap plug and placed in a preheated sand bath at 75 °C (bath temperature) to stir for 14 h. Liquid aryl iodides (**1a**, **1d**, **1e**, and **1g**) were added after the addition of isopropanol and before addition of triethylamine.

1-Naphthylsulfonyl Fluoride **2a.** Isolated as a brown solid (136 mg, 72%). ¹H NMR (CDCl₃): δ 8.56 (d, *J* = 8 Hz, 1H), 8.39 (*J* = 7 Hz, 1H), 8.25 (d, *J* = 8 Hz, 1H), 8.02 (d, *J* = 8 Hz, 1H), 7.79 (t, *J* = 8 Hz, 1H), 7.70 (t, *J* = 8 Hz, 1H), 7.65 (t, *J* = 8 Hz, 1H); ¹⁹F NMR (CDCl₃): δ 62.54 (s, 1F); ¹³C NMR (C CDCl₃): δ 137.0, 134.0, 131.1, 129.5, 129.2, 128.9, 128.3, 127.8, 124.2, 124.1. IR ν (neat, ATR)/cm⁻¹

1508, 1395, 1354, 1195, 1150, 1073, 980, 823, 802, 768, 735, 667, 591. Anal. Calc. for $C_{10}H_7FO_2S$: C, 57.13, H, 3.36; Found: C, 57.14, H, 3.72. mp (EtOAc/hexanes): 50–53 °C

4-Acetylbenzenesulfonyl Fluoride 2b. Isolated as a brown solid (122 mg, 67%). 1H NMR ($CDCl_3$): δ 8.18 (d, J = 8 Hz, 2H), 8.13 (d, J = 9 Hz, 2H), 2.70 (s, 3H); ^{19}F NMR ($CDCl_3$): δ 65.9 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 196.1, 142.2, 136.6 (d, J = 27 Hz, 1C), 129.3, 128.9, 26.96. IR ν (neat, ATR)/ cm^{-1} 1692, 1403, 1359, 1255, 1209, 1097, 836, 789, 750, 636, 578. Anal. Calc. for $C_8H_7FO_3S$: C, 47.52, H, 3.49; Found: C, 47.64, H, 3.62. mp (EtOAc/hexanes): 78–79 °C.

Methyl 4-(Fluorosulfonyl)benzoate 2c. Isolated as an off-white solid (183 mg, 93%). 1H NMR ($CDCl_3$): δ 8.29 (d, J = 8 Hz, 2H), 8.10 (d, J = 8 Hz, 2H), 4.00 (s, 3H); ^{19}F NMR ($CDCl_3$): δ 65.78 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 164.9, 136.6 (d, J = 25 Hz, 1C), 136.5, 130.7, 128.5, 53.0. IR ν (neat, ATR)/ cm^{-1} 3104, 2965, 1724, 1578, 1408, 1277, 1209, 1092, 959, 835, 767, 758, 728, 684, 607. HRMS (FAB-magnetic sector) m/z : $[M+H]^+$ Calcd for $C_8H_8FO_4S$ 219.0125; found 219.0127. mp (EtOAc/hexanes): 84–86 °C.

3,5-Dimethylbenzenesulfonyl Fluoride 2d. Isolated as a brown solid (99 mg, 59%). 1H NMR ($CDCl_3$): δ 7.63 (s, 2H), 7.39 (s, 1H), 2.44 (s, 6H); ^{19}F NMR ($CDCl_3$): δ 65.71 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 139.9, 137.2, 132.7 (d, J = 23 Hz, 1C), 125.9, 21.2. IR ν (neat, ATR)/ cm^{-1} 2908, 1610, 1449, 1273, 1201, 1094, 1040, 865, 756, 668, 609, 537. Anal. Calc. for $C_8H_9FO_2S$: C, 51.05, H, 4.82; Found: C, 51.41, H, 4.76. mp (EtOAc/hexanes): 33–36 °C.

4-Cyanobenzenesulfonyl Fluoride 2e. Isolated as an off-white solid (106 mg, 64%). 1H NMR ($CDCl_3$): δ 8.17 (d, J = 8 Hz, 2H), 7.96 (d, J = 8 Hz, 2H); ^{19}F NMR ($CDCl_3$): δ 66.01 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 136.9 (d, J = 27 Hz, 1C), 133.4, 129.2, 119.4, 116.5. IR ν (neat, ATR)/ cm^{-1} 1410, 1212, 1095, 847, 807, 760, 642, 557. Anal. Calc. for $C_6H_4FNO_2S$: C, 45.40, H, 2.18, N, 7.56; Found: C, 45.74, H, 2.21, N, 7.48. mp (EtOAc/hexanes): 89–92 °C.

4-Chlorobenzenesulfonyl Fluoride 2f. Isolated as a brown solid (97 mg, 55%). 1H NMR ($CDCl_3$): δ 7.97 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H); ^{19}F NMR ($CDCl_3$): δ 66.49 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 142.7, 131.3, 130.1, 129.9. IR ν (neat, ATR)/ cm^{-1} 3099, 2905, 1569, 1461, 1406, 1284, 1209, 1089, 1014, 969, 829, 781, 743, 701, 623, 526. HRMS (FAB-magnetic sector) m/z : $[M-F]^+$ Calcd for $C_6H_4ClO_2S$ 174.9620; found 174.9616. mp (EtOAc/hexanes): 49–53 °C.

[1,1'-Biphenyl]-4-sulfonyl Fluoride 2g. Isolated as a brown solid (147 mg, 69%). 1H NMR ($CDCl_3$): δ 8.09 (d, J = 8 Hz, 2H), 7.83 (d, J = 8 Hz, 2H), 7.64 (d, J = 8 Hz, 2H), 7.51 (m, 3H); ^{19}F NMR ($CDCl_3$): δ 66.50 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 148.7, 138.5, 131.4 (d, J = 24 Hz, 1C), 129.3, 129.2, 129.0, 128.2, 127.5. IR ν (neat, ATR)/ cm^{-1} 2922, 1588, 1480, 1406, 1209, 1099, 1008, 951, 842, 783, 743, 674, 587, 548, 518. HRMS (FAB-magnetic sector) m/z : $[M]^+$ Calcd for $C_{12}H_9FO_2S$ calculated 236.0308; Found 236.0307. mp (EtOAc/hexanes): 78–79 °C.

Benzene-1,3-Disulfonyl Fluoride 2h. Isolated as a brown solid (125 mg, 57%). The general procedure to make aryl sulfonyl fluorides was followed, but with twice the equivalents/volume of $Pd(OAc)_2$, CataXCium A, Et_3N , DABSO, Selectfluor, $iPrOH$, and acetonitrile. (125 mg, 58%, brown solid) 1H NMR ($CDCl_3$): δ 8.30 (s, 4H); ^{19}F NMR ($CDCl_3$): δ 66.08 (check (s, 2F)); ^{13}C NMR ($CDCl_3$): δ 139.5 (d, J = 27 Hz, 1C), 129.8. IR ν (neat, ATR, ATR)/ cm^{-1} 2905, 1407, 1286, 1205, 1093, 1015, 772, 743, 623. HRMS (FAB-magnetic sector) m/z : $[M+H]^+$ Calcd for HRMS Calc. for $C_6H_3F_2O_4S_2$ 242.9609; Found 242.9597. mp (EtOAc/hexanes): 155–156 °C.

4-(Fluorosulfonyl)phenyl 4-Methylbenzenesulfonate 2i. Isolated as a brown solid (229 mg, 77%). 1H NMR ($CDCl_3$): δ 7.98 (d, J = 8 Hz, 2H), 7.75 (d, J = 8 Hz, 2H), 7.37 (d, J = 8 Hz, 2H), 7.29 (d, J = 8 Hz, 2H), 2.48 (s, 3 H); ^{19}F NMR ($CDCl_3$): δ 66.5 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 154.7, 146.4, 131.6 (d, J = 26 Hz, 1C), 131.2, 130.5, 130.2, 128.5, 123.7, 21.8. IR ν (neat, ATR)/ cm^{-1} 1583, 1485, 1411, 1380, 1297, 1212, 1177, 1156, 1091, 1015, 852, 785, 746, 708, 675, 695, 583, 541. HRMS (FAB-magnetic sector) m/z : $[M+H]^+$ Calcd for $C_{13}H_{12}FO_5S_2$ 331.0110; Found 331.0124. mp (EtOAc/hexanes): 76–78 °C.

4-Methoxybenzenesulfonyl Fluoride 2j. Isolated as a brown liquid (77 mg, 45%). 1H NMR ($CDCl_3$): δ 7.95 (d, J = 14 Hz, 2H), 7.07 (d, J

= 9 Hz, 2H), 3.93 (s, 3H); ^{19}F NMR ($CDCl_3$): δ 67.29 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 165.2, 130.8, 124.9 (d, J = 25 Hz, 1C), 114.9, 55.9. IR ν (neat, ATR)/ cm^{-1} 1594, 1578, 1501, 1398, 1319, 1267, 1206, 1172, 1099, 1020, 834, 807, 752, 670, 562, 538. HRMS (FAB-magnetic sector) m/z : $[M+H]^+$ Calcd for $C_7H_8FSO_3$ 191.0178; measured, 191.0178.

3-Methoxybenzenesulfonyl Fluoride 2k. Isolated as a brown liquid (106 mg, 62%). 1H NMR ($CDCl_3$): δ 7.60 (d, 8 Hz, 1 H), 7.53 (dd, 8 Hz, 1 Hz, 1H), 7.48 (m, 1H), 7.29 (dd, 8 Hz, 2 Hz, 1H), 3.90 (s, 3H); ^{19}F NMR ($CDCl_3$): δ 65.57 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 160.2, 133.9 (d, 24 Hz, 2C), 130.7, 122.1, 120.5, 122.7, 55.8. IR ν (neat, ATR)/ cm^{-1} 1601, 1408, 1326, 1247, 1208, 1032, 761, 691, 677, 584. HRMS (FAB-magnetic sector) m/z : $[M]^+$ Calcd for $C_7H_7FO_3S$ 190.0100; Found 190.0126.

2-Methoxybenzenesulfonyl Fluoride 2l.²³ Isolated as a brown liquid (76 mg, 45%, brown liquid). 1H NMR ($CDCl_3$): δ 7.93 (dd, 8 Hz, 2 Hz, 1H), 7.69 (t, 8 Hz, 1H), 7.11 (multiple peaks, 2H); ^{19}F NMR ($CDCl_3$): δ 58.56 (s, 1F); ^{13}C NMR ($CDCl_3$): δ 158.0 (d, J = 2 Hz, 1C), 137.4, 131.1 (d, J = 1 Hz, 1C), 121.2 (d, J = 23 Hz, 1C), 120.4, 112.7, 56.47. IR ν (neat, ATR)/ cm^{-1} 1579, 1483, 1437, 1396, 1285, 1258, 1204, 1166, 1139, 1073, 1014, 807, 751, 698, 590, 569. HRMS (FAB-magnetic sector) m/z : $[M+H]^+$ Calcd for $C_7H_8FSO_3$, 191.0178; Found 191.0187.

General Procedure for Sulfonic Esters and Sulfonamides Synthesis. 2a (0.19 mmol, 1.0 equiv) and the appropriate alcohol or amine (0.21 mmol, 1.1 equiv) were combined in a 20 mL scintillation vial. Acetonitrile was added (0.8 mL, 0.2 M) followed by Cs_2CO_3 (0.00 g, 0.38 mmol, 2 equiv), sealed with PTFE-lined cap, and stirred vigorously for 1 h. After 1 h, the solvent was removed by rotary evaporation. The crude product was isolated using automated flash chromatography (SiO_2) on a 100% hexane to 50%:50% hexane:ethyl acetate gradient over 19 min. Reactions were ran in duplicate and yields are an average of the trials.

1-(Naphthalen-1-ylsulfonyl)-1H-imidazole 3a. Isolated as a white solid (34 mg, 69%). 1H NMR ($CDCl_3$): δ 8.64 (d, J = 8 Hz, 2H), 8.11 (d, J = 9 Hz, 1H), 8.35 (dd, 7 Hz, 1 Hz, 1H), 8.14 (multiple peaks, 2H), 7.92 (dd, 8 Hz, 1 Hz, 1H), 7.68 (m, 1H), 7.58 (multiple peaks, 2H), 7.31 (s, 1H), 7.02 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 136.9, 136.8, 134.2, 132.7, 131.0, 130.5, 129.5, 127.8, 127.6, 124.3, 123.1, 117.8 (one of the signal represents 2Cs; however we were not able to determine which one). IR ν (neat, ATR)/ cm^{-1} 3122, 3101, 2921, 2851, 1513, 1460, 1156, 1055, 801, 762, 680, 592. HRMS (FAB-magnetic sector) m/z : $[M+H]^+$ Calcd for $C_{13}H_{11}N_2O_2S$ 259.0541; Found 259.0560. mp (EtOAc/hexanes): decomposed at 160 °C.

1-(Naphthalen-1-ylsulfonyl)-1H-pyrazole 3b. Isolated as a white solid (33 mg, 68%). 1H NMR (d^6 -DMSO): δ 8.73 (d, J = 3 Hz, 1H), 8.62 (d, J = 8 Hz, 1H), 8.46 (d, J = 8 Hz, 1H), 8.41 (d, J = 8 Hz, 1H), 8.14 (d, J = 8 Hz, 1H), 7.83 (m, 1H), 7.76 (multiple peaks, 3H), 6.59 (dd, J = 3 Hz, 2 Hz, 1H); ^{13}C NMR (d^6 -DMSO): δ 145.4, 136.9, 133.7, 132.5, 131.5, 131.2, 129.5, 129.2, 127.5, 127.2, 124.8, 123.3, 109.3; IR ν (neat, ATR)/ cm^{-1} 3128, 1507, 1400, 1367, 1343, 1281, 1157, 1059, 1025, 930, 834, 804, 763, 682, 628, 616, 603, 588, 586, 579, 576, 567, 563, 542. HRMS (FAB-magnetic sector) m/z : $[M+H]^+$ Calcd for $C_{13}H_{11}N_2O_2S$ 259.0546; Found 259.0541. mp (EtOAc/hexanes): decomposed at 160 °C.

Phenyl Naphthalene-1-sulfonate 3c. Isolated as a white solid (44 mg, 81%) 1H NMR ($CDCl_3$): δ 8.85 (d, J = 8 Hz, 1H), 8.11 (d, J = 8 Hz, 1H), 8.08 (d, J = 7 Hz, 1H), 7.98 (d, J = 8 Hz, 1H), 7.77 (m, 1H), 7.67 (m, 1H), 7.44 (m, 1H), 7.17 (m, 3 H), 6.87 (m, 2 H); ^{13}C NMR ($CDCl_3$): δ 149.5, 135.6, 133.9, 131.2, 130.7, 129.5, 129.0, 128.9, 128.4, 127.3, 127.0, 125.0, 123.9, 121.9; IR ν (neat, ATR)/ cm^{-1} 1590, 1508, 1484, 1369, 1202, 1189, 1167, 1158, 1144, 1137, 1022, 981, 917, 854, 823, 784, 768, 728, 692, 673, 585, 581. HRMS (FAB-magnetic sector) m/z : $[M+H]^+$ Calcd for $C_{16}H_{13}O_3S$ 285.0585; Found 285.0591. mp (EtOAc/hexanes): 71–73 °C.

4-Methoxyphenyl Naphthalene-1-sulfonate 3d. Isolated as a white solid (57 mg, 95%). mp = 108–110 °C 1H NMR ($CDCl_3$): δ 8.83 (d, J = 9 Hz, 1H), 8.11 (d, J = 8 Hz, 1H), 8.06 (d, J = 7 Hz, 1H), 7.98 (d, J = 8 Hz, 1H), 7.78 (m, 1H), 7.67 (m, 1H), 7.47 (m, 1H), 6.75 (d, J = 9 Hz, 2 H), 6.63 (d, J = 9 Hz, 2 H), 3.68 (s, 3H); ^{13}C

NMR (CDCl₃): δ 158.1, 143.0, 135.6, 133.9, 131.2, 130.6, 128.9, 128.9, 128.5, 127.3, 125.02, 123.9, 122.9, 114.3, 55.4; IR ν (neat, ATR)/cm⁻¹ 1591, 1501, 1358, 1299, 1256, 1160 (SO₂), 1132, 1028. Anal. Calc. for C₁₇H₁₄O₄S: C, 64.95, H, 4.49; Found: C, 64.85, H, 4.44. mp (EtOAc/hexanes): 71–73 °C.

4-Aminophenyl Naphthalene-1-sulfonate 3e. Isolated as a light brown solid (45 mg, 79%). ¹H NMR (CDCl₃): δ 8.82 (d, *J* = 9 Hz, 1H), 8.11 (d, *J* = 8 Hz, 1H), 8.06 (d, *J* = 7 Hz, 1H), 7.98 (d, *J* = 8 Hz, 1H), 7.78 (m, 1H), 7.67 (m, 1H), 7.45 (m, 1H), 6.60 (d, *J* = 6 Hz, 2H), 6.40 (d, *J* = 6 Hz, 2H), 3.60 (broad s, 2H); ¹³C NMR (CDCl₃): δ 145.4, 141.6, 135.5, 134.0, 131.4, 130.8, 129.0, 128.90, 128.6, 127.3, 125.2, 124.00, 122.8, 115.3; IR ν (neat, ATR)/cm⁻¹ 2924, 1629, 1505, 1356, 1174, 981, 840, 803, 799, 770, 581. Anal. Calc. for C₁₆H₁₃NO₃S: C, 64.20, H, 4.38; N, 4.68 Found: C, 64.25, H, 4.52, N, 4.47. mp (EtOAc/hexanes): 110–115 °C.

2,2,2-Trifluoroethyl Naphthalene-1-sulfonate 3f. Isolated as a light brown solid (46 mg, 84%). ¹H NMR (CDCl₃): δ 8.59 (d, *J* = 9 Hz, 1H), 8.31 (d, *J* = 8 Hz, 1H), 8.20 (d, *J* = 8 Hz, 1H), 7.99 (d, *J* = 8 Hz, 1H), 7.76 (m, 1H), 7.67 (m, 1H), 7.60 (m, 1H), 4.34 (q, *J* = 8 Hz, 2H); ¹⁹F NMR (CDCl₃): δ -73.71 (s, 3F); ¹³C NMR (CDCl₃): δ 136.3, 134.2, 130.9, 130.0, 129.2, 129.0, 128.3, 127.6, 124.6, 124.0, 121.8 (q, *J* = 278 Hz), 64.8 (q, *J* = 38 Hz); IR ν (neat, ATR)/cm⁻¹ 1372, 1289, 1175, 1035, 982, 864, 800, 788, 681, 594, 565. HRMS (FAB-magnetic sector) *m/z*: [M]⁺ Calcd for C₁₂H₉F₃O₃S 290.0225; Found 290.0222. mp (EtOAc/hexanes): mp =60–61 °C

4-Iodophenyl 4-Methylbenzenesulfonate 1i.²⁴ Isolated as a light brown solid (1.8 g, 84%, light brown solid, mp = 96–99 °C) Procedure to make sulfonate esters was followed on a 1 g scale using *p*-toluene sulfonyl fluoride (1.0 g, 5.74 mmol, 1 equiv), Cs₂CO₃ (3.7 g, 11.48 mmol, 2 equiv), 4-iodophenol (1.4 g, 6.3 mmol, 1.1 equiv), and 19 mL (0.3 M) of acetonitrile. ¹H NMR (CDCl₃): δ 7.69 (d, *J* = 8 Hz, 2H), 7.60 (d, *J* = 8 Hz, 2H), 7.35 (d, *J* = 8 Hz, 2H), 6.74 (d, *J* = 8 Hz, 2H), 2.46 (s, 3H); ¹³C NMR (CDCl₃): δ 149.4, 145.7, 138.7, 132.0, 129.9, 128.5, 124.5, 91.77, 21.78. HRMS (FAB-magnetic sector) *m/z*: [M+H]⁺ Calcd for C₁₃H₁₂IO₃S 374.9552; Found 374.9547.

General Procedure for Electrophilic Fluorinating Reagent Screen. The reaction was setup according to the procedure to generate the sulfonyl fluoride **2a** (229 mg, 0.90 mmol of 1-iodonaphthalene, and 1.8 mmol of the fluorinating reagent). The crude products were isolated using automated flash chromatography (SiO₂) on a 100% hexanes to 60:40 hexanes:ethyl acetate) over 19 min. ¹H NMR spectroscopy was used to compare against the spectra of the isolated and purified **2a** using Selectfluor. Yields are an average of two trials.

General Procedure for the Base Screen Using Phenol and *p*-Toluenesulfonyl Fluoride.²⁴ The reaction was setup according to the previously described procedure to generate the sulfonate esters using commercially available *p*-toluenesulfonyl fluoride (100 mg, 0.57 mmol, 1 equiv), phenol (59 mg, 0.63 mmol, 1.1 equiv), and base (1.15 mmol, 2 equiv). The crude products were isolated using automated flash chromatography (SiO₂) on a 100% hexane to 60:40 hexanes:ethyl acetate). ¹H NMR spectroscopy was used to compare against the spectra of the isolated and purified sulfonate ester **4**. Yields are an average of two trials. ¹H NMR (CDCl₃): δ 7.71 (d, *J* = 8 Hz, 2H), 7.26 (multiple peaks, 5H), 6.99 (d, *J* = 8 Hz, 2H), 2.46 (s, 3H); ¹³C NMR (CDCl₃): δ 149.6, 145.3, 132.4, 129.7, 129.6, 128.5, 127.1, 122.4, 21.73. HRMS (FAB-magnetic sector) *m/z*: [M+H]⁺ Calcd for C₁₃H₁₃O₃S 249.0585; found 249.0593.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00051.

Procedures, methods, characterization data including NMR data (PDF)

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Notes

The authors declare no competing financial interest.

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