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N-(Heptafluoroisopropylthio)saccharin as a Practical Reagent for Electrophilic –SCF(CF_3)$_2$ Installation

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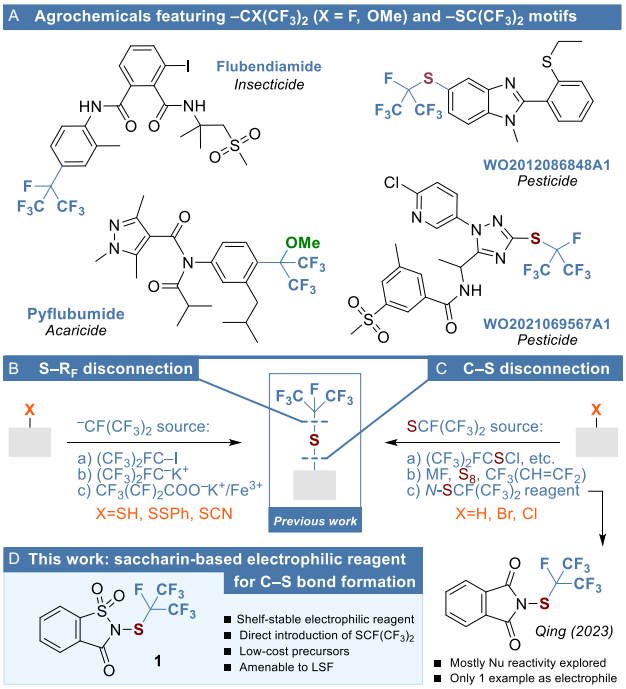
ABSTRACT

We report the multigram-scale synthesis of a shelf-stable, saccharin-based reagent for the direct electrophilic installation of the heptafluoroisopropylthio (–SCF(CF_3)$_2$) group. This bulky, highly fluorinated motif is increasingly valued for tuning lipophilicity, polarity, and metabolic stability in agrochemical design, yet methods for its direct incorporation remain scarce. The reagent enables mild, one-step formation of C—SR_F and N—SR_F bonds with a broad range of nucleophilic substrates, including indoles, pyrroles, phenols, and amines, exhibiting genuine electrophilic reactivity and broad functional-group tolerance. Furthermore, oxidation of the resulting N—SR_F bond provides access to sulfonamide derivatives without the need for conventional sulfonyl chloride precursors. This strategy offers a practical and modular route to complex fluorinated sulfur compounds and expands the synthetic toolbox for late-stage functionalization with valuable polyfluoroalkylthio motifs (–SR_F).

1 | Introduction

Polyfluoroalkylthio groups (–SR_F) are increasingly recognized for their ability to modulate lipophilicity, polarity, and metabolic stability in both pharmaceutical and agrochemical applications [1–9]. While the utility and synthetic toolbox for installing trifluoromethylthio (–SCF_3) [10–17] and difluoromethylthio (–SCF_2H) [18–23] motifs are well established, longer-chain and more sterically demanding thiofluoroalkyl analogs remain comparatively underexplored [24–38], despite their potential to offer a broader diversity of fluorination patterns and enable fine control over molecular physicochemical properties [39–42]. Compact, globular structures such as the heptafluoroisopropylthio group (–SCF(CF_3)$_2$), along with related –CX(CF_3)$_2$ motifs (X = F, OMe), are increasingly incorporated in modern agrochemicals (Scheme 1A) [43–51]. Their high fluorine content (≥6 fluorine atoms), combined with distinct steric and electronic profiles, makes them attractive design elements. Nonetheless, despite their rising relevance and recent synthetic advances enabling access to more exotic variants like –CF(OCF_3)(CF_2H) [52] and –CFCl(CF_2H) [53], general methods for late-stage installation of such motifs—particularly sulfur-based derivatives—remain limited. Although reports featuring the –SCF(CF_3)$_2$ group are emerging, practical methodologies for its direct introduction remain scarce, limiting broader applications in structure–activity relationship (SAR) studies and late-stage functionalization (LSF) strategies.

Access to heptafluoroisopropylthio derivatives has traditionally relied on synthetic routes involving preformed thiols, disulfides, or thiocyanates—typically under harsh radical or nucleophilic conditions via classical S–R_F disconnections (Scheme 1B) [54–58]. These strategies are poorly suited for LSF, as they require a preinstalled sulfur moiety. Alternative direct approaches based on C—S disconnection, such as the in situ generation of thiofluoroalkyl anions followed by nucleophilic substitution with alkyl halides [59] or reaction with quadricyclanes [60], as well as the use of preformed, toxic, and operationally challenging reagents—such as highly reactive (CF_3)$_2$CFSCl, (CF_3)$_2$CFSSCF(CF_3)$_2$, or [(CF_3)$_2$CF]$_2SF_2$—also suffer from limited functional-group tolerance and reduced applicability (Scheme 1C) [61–65]. Consequently, direct fluoroalkylthiolating reagents—enabling

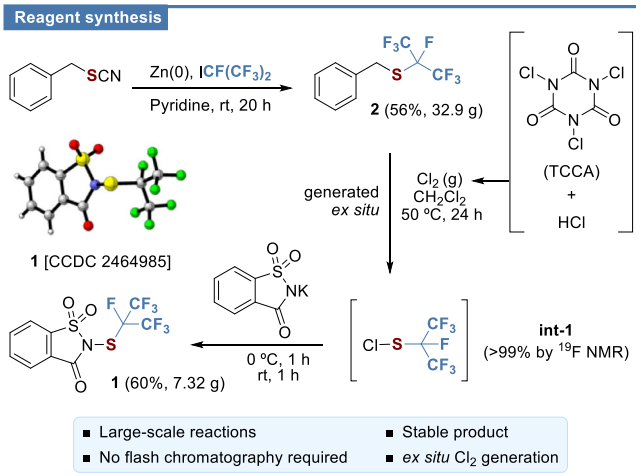


SCHEME 1 | (A) Representative agrochemicals featuring $-CX(CF_3)_2$ (X = F, OMe) and $-SCF(CF_3)_2$ motifs. (B) Prior approaches to heptafluoroisopropylthiolation via S—R_F bond formation. (C) Alternative methods via C—S disconnection. (D) This work. R_F = polyfluoroalkyl (e.g., $-CF(CF_3)_2$); M = Cs^+, K^+; LSF = late-stage functionalization.

C—S bond formation in a single step—have emerged as more attractive alternatives. However, to the best of our knowledge, only one electrophilic reagent bearing a phthalimide leaving group has been reported for direct installation of the heptafluoroisopropylthio group, with reactivity dominated by nucleophilic pathways and only a single example showing genuine electrophilic behavior [66]. These limitations underscore the need for a stable, broadly applicable electrophilic reagent for late-stage incorporation of this valuable motif. Drawing on our group's expertise in organofluorine and chalcogen chemistry [67–73], as well as electrophilic reagent design [24–26, 74]—and leveraging saccharin's established utility as a leaving group in such systems [24–26]—we have developed a novel saccharin-based *N*–$SCF(CF_3)_2$ reagent (**1**) for the direct electrophilic heptafluoroisopropylthiolation of nucleophilic substrates, including indoles, pyrroles, phenols, and amines. This reagent offers operational simplicity, broad substrate scope, and a safer, complementary alternative to existing methodologies for the introduction of this underexplored yet highly valuable motif (Scheme 1D).

2 | Results and Discussion

Our practical and scalable three-step synthesis of reagent **1** begins with benzyl thiocyanate. Reaction with 2-iodoheptafluoropropane in the presence of zinc dust afforded benzyl(perfluoropropan-2-yl)sulfane **2** in 56% yield [75]. Direct substitution with benzyl mercaptan was not pursued, given the well-documented radical reactivity of iodofluoroalkyl species [54–58]. Subsequent chlorination of **2** furnished the corresponding sulfenyl chloride intermediate (**int-1**), which was obtained in >99% conversion as determined by ^{19}F NMR. Without



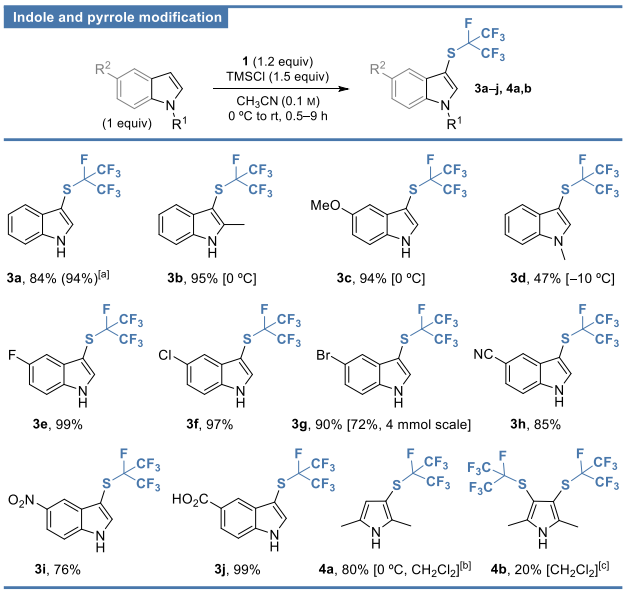
SCHEME 2 | Multigram-scale synthesis of reagent **1** and ORTEP diagram with thermal ellipsoids shown at the 50% probability level. See the Supporting Information for experimental details. TCCA = trichloroisocyanuric acid.

isolation, this intermediate was treated with potassium saccharin to afford the desired electrophilic reagent **1** in 60% overall yield (Scheme 2). The sequence is readily scalable (up to 7.32 g), and compound **1** was efficiently purified by crystallization.

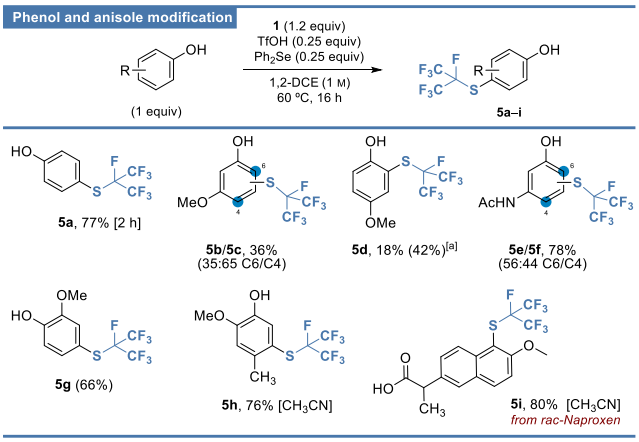
The reagent was characterized by NMR and single-crystal X-ray diffraction (Figures S106, S107, Supporting Information) [76]. Its stability was demonstrated in both solution and solid state by differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) (Figures S1–S3, Supporting Information). Moreover, no decomposition was observed after 1 year of storage at –20°C.

Following an initial reactivity screening to assess the potential substrate scope for electrophilic aromatic substitution (S_EAr) reactions (Figure S4, Supporting Information), 1*H*-indole was selected as a model substrate [77]. Under standard electrophilic substitution conditions (1,2-DCE, TMSCl), the transient, highly reactive sulfenyl chloride intermediate (**int-1**) was generated in situ. Heating to 70°C in a Schlenk flask furnished product **3a** in 97% yield after 3 h (Figure S5, Supporting Information). Subsequent solvent screening revealed that acetonitrile enabled an efficient transformation at milder temperatures (94% at rt vs. 99% at 70°C). Using these conditions (CH_3CN, rt), we evaluated the substrate scope with a series of electron-rich substrates. Indole derivatives **3a**–**3j**, bearing electron-donating or electron-withdrawing substituents (including halogens), as well as pyrrole **4a**, were obtained in good to excellent yields, with compound **3g** successfully prepared on a larger scale (72%, 4 mmol scale) (Scheme 3). Double substitution on pyrrole was feasible (**4b**, 20%), while disubstitution on indole proved unsuccessful, likely due to steric hindrance and lower C2 reactivity. Electron-rich substrates such as *N*-Me-indole **3d** underwent overreaction, affording complex mixtures even at –10°C and limiting the isolated yield to 47%.

Phenols proved unreactive under TMSCl-mediated conditions. However, after a brief screening of reaction conditions (Table S1, Supporting Information), functionalization was achieved using diphenyl selenide and triflic acid (Ph_2Se/TfOH), an adaptation of the conditions reported by Sutherland employing $FeCl_3$ [78]. Under these conditions, products **5a**–**5i** were obtained in moderate to good yields (18%–80%) (Scheme 4).



SCHEME 3 | Scope of indoles and pyrrole. *General conditions:* indole/pyrrole (0.3 mmol), **1** (0.36 mmol), and TMSCl (0.45 mmol) in CH_3CN (0.1 M), unless otherwise noted. Isolated yields are reported. Deviation from standard conditions indicated in square brackets. See the Supporting Information for experimental details. TMS = trimethylsilyl. (a) The yield in parentheses was determined by ^{19}F NMR using 1,4-difluorobenzene (DFB) as an internal standard. (b) **1** (1 equiv.) and TMSCl (1 equiv.) used. (c) **1** (2 equiv.) and TMSCl (3 equiv.) used.



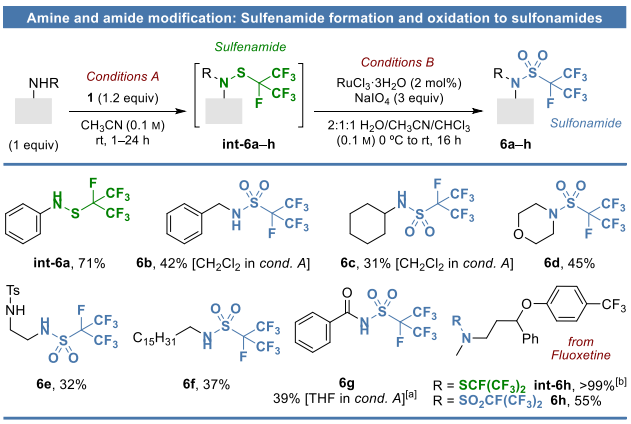
SCHEME 4 | Scope of phenols. *General conditions:* phenol/anisole (0.1 mmol), **1** (0.12 mmol), Ph_2Se (0.025 mmol), and TfOH (0.025 mmol) in 1,2-dichloroethane (1 M), unless otherwise noted. Isolated yields are reported. Deviation from standard conditions indicated in square brackets. See the Supporting Information for experimental details. 1,2-DCE = 1,2-dichloroethane. (a) The low isolated yield of **5d** is attributed to decomposition during purification. Compound **5d** is volatile and decomposes upon standing and during flash column chromatography on SiO_2. The yield in parentheses was determined by ^{19}F NMR using 1,4-difluorobenzene (DFB) as an internal standard.

Ortho-substituted phenols showed superior reactivity, with substitution patterns exerting a pronounced influence on regioselectivity. For example, reactions with 1,3-disubstituted phenols yielded separable mixtures of C6 and C4 regioisomers (e.g., 35:65 **5b**/**5c**, 56:44 **5e**/**5f**). Notably, racemic naproxen, a common nonsteroidal anti-inflammatory drug used to treat pain or inflammation, underwent efficient late-stage derivatization to afford **5i** in good yield (80%) as a single regioisomer.

Next, the reactivity of reagent **1** toward alkenes and alkynes was examined. While all attempts to incorporate the heptafluoroisopropylthio group into alkenes proved unsuccessful, electrophilic quenching of a lithiated alkyne provided the expected alkenylthio product, albeit in a low 13% isolated yield (Schemes S1–S3, Supporting Information).

Additionally, to further demonstrate the synthetic utility of the newly installed C—SR_F motif, we investigated its oxidation to the corresponding sulfone (C—$S(O)_2R_F$) using indole **3g** and phenol **5a** as model substrates. However, despite an extensive screening of oxidation conditions, only complex mixtures of products were obtained (Schemes S4–S7, Supporting Information). Although the –$SCF(CF_3)_2$ group can, in principle, undergo oxidation [79], the outcome is largely dictated by the intrinsic oxidative instability of the indole and phenol scaffolds under the required conditions.

While indole, pyrrole, and phenol derivatives reacted smoothly with reagent **1** under TMSCl- or TfOH-mediated conditions, aniline gave the corresponding sulfenamide **int-6a** (71%) rather than the expected C—S coupled product (Scheme 5, left panel). While *N*-acetylaniline showed no reactivity, the more electron-rich *N*,*N*-dimethylaniline displayed low conversion (<8%), albeit forming multiple unidentified fluorinated species (Figure S4, Supporting Information). Given the preferential formation of the sulfenamide (N—SR_F) with aniline, we next investigated its oxidation to the corresponding sulfonamide (N—$S(O)_2R_F$)—a valuable carboxylic acid bioisostere and a key motif in numerous pharmaceuticals [1–9, 80–83]. Although most sulfonamides are prepared from sulfonyl chlorides (Cl—$S(O)_2R_F$), oxidative routes from sulfenamides remain underexplored and often stop at the sulfinamide (N—$S(O)R_F$) stage [84]. Despite extensive screening



SCHEME 5 | Scope of amines and oxidation of sulfenamide intermediates to sulfonamides. *Conditions A:* amine/amide (0.3 mmol), **1** (0.36 mmol) in CH_3CN (0.1 M), unless otherwise noted. *Conditions B:* sulfenamide (not isolated, except for **int-6a** and **int-6h**) (0.3 mmol), $RuCl_3{\cdot}3H_2O$ (2 mol%), and $NaIO_4$ (0.9 mmol) in 2:1:1 (v/v) H_2O/CH_3CN/$CHCl_3$ (0.1 M), unless otherwise noted. Isolated yields are reported. Deviation from standard conditions indicated in square brackets. See the Supporting Information for experimental details. Ts = *p*-toluenesulfonyl. (a) NaH (1.2 equiv.) used in conditions A. (b) Et_3N (2.2 equiv.) used in conditions A.

of various oxidants, oxidation of **int-6a** was inefficient due to competing side reactions. We therefore turned to a broader evaluation of primary and secondary amines [85, 86]. Owing to the hydrolytic sensitivity of the resulting sulfenamides, in situ oxidation was performed using $RuCl_3{\cdot}3H_2O/NaIO_4$ (Scheme 5, right panel) [39], furnishing sulfonamides **6b–6f** in moderate overall yields (31%–45% over two steps). In some cases, the use of an external base was required (e.g., NaH for benzamide, **6g**, 39%). Finally, LSF of fluoxetine, a widely used antidepressant, was achieved using Et_3N as a base. The resulting sulfenamide **int-6h** was sufficiently stable to be isolated in quantitative yield (>99%), and subsequent oxidation delivered sulfonamide **6h** in 55% yield, highlighting the utility of this protocol in medicinal chemistry applications.

3 | Conclusions

In summary, we have developed a saccharin-based reagent for direct electrophilic installation of the heptafluoroisopropylthio ($-SCF(CF_3)_2$) group through an operationally simple and scalable protocol. The reagent exhibits broad substrate scope and excellent functional-group tolerance, enabling efficient C—SR_F bond formation with electron-rich aromatics such as pyrroles, indoles, and phenols. Additionally, reactions with primary and secondary amines via N—SR_F bond formation afford sulfenamides that can be readily oxidized to fluoroalkyl sulfonamides—valuable motifs in medicinal chemistry. This strategy provides a practical approach for late-stage incorporation of bulky, fluorinated sulfur groups and expands the synthetic toolbox for functional-group diversification.

4 | Experimental Section

4.1 | General Procedure A1 for Heptafluoroisopropylthiolation of Indoles and Pyrroles

A 25 mL round-bottom flask equipped with a magnetic stir bar was charged with indole or pyrrole (1 equiv.) and CH_3CN (or CH_2Cl_2) (0.1 M). The mixture was cooled to 0°C, and reagent **1** (1.2 equiv.) and TMSCl (1.5 equiv.) were added sequentially. The reaction was then allowed to warm to room temperature, and the progress was monitored by TLC. The mixture was concentrated under reduced pressure, and the crude product was purified by flash column chromatography.

4.2 | General Procedure A2 for Heptafluoroisopropylthiolation of Phenols and Anisoles

A 2 mL autosampler vial equipped with a magnetic stir bar was charged with phenol or anisole (1 equiv.), reagent **1** (1.2 equiv.), and 1,2-DCE (or CH_3CN) (1 M). Diphenyl selenide (0.25 equiv.) and TfOH (0.25 equiv.) were then added sequentially. The reaction mixture was heated to 60°C, and the progress was monitored by TLC. After 16 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography.

4.3 | General Procedure B1 for the Synthesis of Sulfonamides

A 10 mL round-bottom flask equipped with a magnetic stir bar was charged with the amine (1 equiv.) and CH_3CN (or CH_2Cl_2) (0.1 M). Reagent **1** (1.2 equiv.) was then added, and the mixture was stirred at room temperature while monitoring the reaction progress by TLC. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography.

4.4 | General Procedure B2 for the Synthesis of Sulfenamides Using Base

A 10 mL round-bottom flask equipped with a magnetic stir bar was dried, evacuated, backfilled with argon, and charged with the amine or amide (1 equiv.), base (1.2–2.2 equiv.), and dry CH_2Cl_2 (or THF) (0.1 M). After stirring at room temperature for 30 min, reagent **1** (1.2 equiv.) was added, and the mixture was stirred at room temperature while monitoring the reaction progress by TLC. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography.

4.5 | General Procedure C for the Oxidation of Sulfenamides to Sulfonamides

A 10 mL round-bottom flask equipped with a magnetic stir bar was charged with the sulfenamide (1 equiv.) and 2:1:1 (v/v) $H_2O/CH_3CN/CHCl_3$ (0.1 M). The mixture was cooled to 0°C, and $RuCl_3{\cdot}3H_2O$ (2 mol%) and $NaIO_4$ (3 equiv.) were added sequentially. The reaction was stirred for 30 min at 0°C, then allowed to warm to room temperature, and the progress monitored by TLC. After 16 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography.

Author Contributions

Javier Jaureguizar, **Jordi Mestre**, and **Miguel Bernús** performed all the experiments. **M. Isabel Matheu** co-supervised the research activities. **Omar Boutureira** supervised the project and was responsible for funding acquisition. All the authors contributed to the preparation of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Supporting Scheme S1:** Reaction of reagent **1** under polar conditions (top). Expanded ^{1}H NMR region in $CDCl_3$ after workup, highlighting the diagnostic signals corresponding to the chlorovinyl products (bottom). **Supporting Scheme S2:** Reaction of reagent **1** under photochemical conditions. **Supporting Scheme S3:** Reactivity of reagent **1** toward alkynes. Cu(I)-catalyzed conditions (top) vs. lithiation followed by electrophilic quenching (bottom). **Supporting Scheme S4:** Oxidation of indole **3g** (top) and phenol **5a** (bottom) using CrO_3. **Supporting Scheme S5:** Oxidation of indole **3g** using CrO_3/H_5IO_6. **Supporting Scheme S6:** Oxidation of indole **3g** using $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O/H_2O_2$. **Supporting Scheme S7:** Oxidation of indole **3g** (top) and phenol **5a** (bottom) using $RuCl_3/NaIO_4$. **Supporting Fig. S1:** Stability of **1** in various solvents at room temperature (left panel) and at 50°C (right panel). **Supporting Fig. S2:** DSC analysis of reagent **1**. Fusion peak = 75.17°C. **Supporting Fig. S3:** TGA analysis of reagents 1.5% weight decomposition = 196.27°C. **Supporting Fig. S4:** Preliminary scope of aromatic compounds for reactivity testing of reagent **1**. **Supporting Fig. S5:** Reaction of electrophilic reagent **1** with 1*H*-Indole in various solvents and different temperatures. TFE = trifluoroethanol. **Supporting Fig. S6:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **2**. **Supporting Fig. S7:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **2**. **Supporting Fig. S8:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **2**. **Supporting Fig. S9:** ^{19}F NMR ($CH2Cl_2$, 375 MHz) of **int-1**. **Supporting Fig. S10:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **1**. **Supporting Fig. S11:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **1**. **Supporting Fig. S12:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **1**. **Supporting Fig. S13:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **3a**. **Supporting Fig. S14:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **3a**. **Supporting Fig. S15:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **3a**. **Supporting Fig. S16:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **3b**. **Supporting Fig. S17:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **3b**. **Supporting Fig. S18:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **3b**. **Supporting Fig. S19:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **3c**. **Supporting Fig. S20:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **3c**. **Supporting Fig. S21:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **3c**. **Supporting Fig. S22:** ^{1}H NMR (CD_3CN, 400 MHz) of **3d**. **Supporting Fig. S23:** ^{13}C NMR (CD_3CN, 100 MHz) of **3d**. **Supporting Fig. S24:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **3d**. **Supporting Fig. S25:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **3e**. **Supporting Fig. S26:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **3e**. **Supporting Fig. S27:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **3e**. **Supporting Fig. S28:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **3f** . **Supporting Fig. S29:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **3f**. **Supporting Fig. S30:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **3f**. **Supporting Fig. S31:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **3g**. **Supporting Fig. S32:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **3g**. **Supporting Fig. S33:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **3g**. **Supporting Fig. S34:** ^{1}H NMR (CD_3CN, 400 MHz) of **3h**. **Supporting Fig. S35:** ^{13}C NMR (CD_3CN, 100 MHz) of **3h**. **Supporting Fig. S36:** ^{19}F NMR (CD_3CN, 375 MHz) of **3h**. **Supporting Fig. S37:** ^{1}H NMR (CD_3CN, 400 MHz) of **3i**. **Supporting Fig. S38:** ^{13}C NMR (CD_3CN, 100 MHz) of **3i**. **Supporting Fig. S39:** ^{19}F NMR (CD_3CN, 375 MHz) of **3i**. **Supporting Fig. S40:** ^{1}H NMR (CD_3CN, 400 MHz) of **3j**. **Supporting Fig. S41:** ^{13}C NMR (CD_3CN, 100 MHz) of **3j**. **Supporting Fig. S42:** ^{19}F NMR (CD_3CN, 375 MHz) of **3j**. **Supporting Fig. S43:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **4a**. **Supporting Fig. S44:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **4a**. **Supporting Fig. S45:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **4b**. **Supporting Fig. S46:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **4b**. **Supporting Fig. S47:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **4b**. **Supporting Fig. S48:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **4b**. **Supporting Fig. S49:** ^{1}H NMR (CD_3CN, 400 MHz) of **5a**. **Supporting Fig. S50:** ^{13}C NMR (CD_3CN, 100 MHz) of **5a**. **Supporting Fig. S51:** ^{19}F NMR (CD_3CN, 375 MHz) of **5a**. **Supporting Fig. S52:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **5b**. **Supporting Fig. S53:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **5b**. **Supporting Fig. S54:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **5b**. **Supporting Fig. S55:** ^{1}H NMR (CD_3CN, 400 MHz) of **5c**. **Supporting Fig. S56:** ^{13}C NMR (CD_3CN, 100 MHz) of **5c**. **Supporting Fig. S57:** ^{19}F NMR (CD_3CN, 375 MHz) of **5c**. **Supporting Fig. S58:** ^{1}H NMR (CD_3CN, 400 MHz) of **5d**. **Supporting Fig. S59:** ^{1}H-decoupled HSQC (CD_3CN, 400 MHz) of **5d**. **Supporting Fig. S60:** ^{1}H NMR (CD_3CN, 400 MHz) of **5d**. **Supporting Fig. S61:** ^{1}H NMR (CD_3CN, 400 MHz) of **5e**. **Supporting Fig. S62:** ^{13}C NMR (CD_3CN, 100 MHz) of **5e**. **Supporting Fig. S63:** ^{19}F NMR (CD_3CN, 375 MHz) of **5e**. **Supporting Fig. S64:** ^{1}H NMR (CD_3CN, 100 MHz) of **5f**. **Supporting Fig. S65:** ^{13}C NMR (CD_3CN, 100 MHz) of **5f**. **Supporting Fig. S66:** ^{19}F NMR (CD_3CN, 375 MHz) of **5f**.

Supporting Fig. S67: ^{1}H NMR (CD_3CN, 400 MHz) of **5g**. **Supporting Fig. S68:** ^{13}C NMR (CD_3CN, 100 MHz) of **5g**. **Supporting Fig. S69:** ^{19}F NMR (CD_3CN, 375 MHz) of **5g**. **Supporting Fig. S70:** ^{1}H NMR (CD_3CN, 400 MHz) of **5h**. **Supporting Fig. S71:** ^{13}C NMR (CD_3CN, 100 MHz) of **5h**. **Supporting Fig. S72:** ^{19}F NMR (CD_3CN, 375 MHz) of **5h**. **Supporting Fig. S73:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **5i**. **Supporting Fig. S74:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **5i**. **Supporting Fig. S75:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **5i**. **Supporting Fig. S76:** ^{1}H NMR (CD_3CN, 400 MHz) of **int-6a**. **Supporting Fig. S77:** ^{13}C NMR (CD3CN, 100 MHz) of **int-6a**. **Supporting Fig. S78:** ^{19}H NMR (CD_3CN, 375 MHz) of **int-6a**. **Supporting Fig. S79:** 1H NMR ($CDCl_3$, 400 MHz) of **6b**. **Supporting Fig. S80:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **6b**. **Supporting Fig. S81:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **6b**. **Supporting Fig. S82:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **6c**. **Supporting Fig. S83:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **6c**. **Supporting Fig. S84:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **6c**. **Supporting Fig. S85:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **6d**. **Supporting Fig. S86:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **6d**. **Supporting Fig. S87:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **6d**. **Supporting Fig. S88:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **6e**. **Supporting Fig. S89:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **6e**. **Supporting Fig. S90:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **6e**. **Supporting Fig. S91:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **6f**. **Supporting Fig. S92:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **6f**. **Supporting Fig. S93:** ^{19}F NMR ($CDCl_3$, 375 MHz) of 6f. **Supporting Fig. S94:** ^{1}H NMR (CD_3CN, 400 MHz) of **6g**. **Supporting Fig. S95:** ^{1}H NMR (CD_3CN, 400 MHz) of **6g**. **Supporting Fig. S96:** ^{19}F NMR (CD_3CN, 375 MHz) of **6g**. **Supporting Fig. S97:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **int-6h**. **Supporting Fig. S98:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **int-6h**. **Supporting Fig. S99:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **int-6h**. **Supporting Fig. S100:** ^{1}H NMR ($CDCl_3$, 400 MHz) of **6h**. **Supporting Fig. S101:** ^{13}C NMR ($CDCl_3$, 100 MHz) of **6h**. **Supporting Fig. S102:** ^{19}F NMR ($CDCl_3$, 375 MHz) of **6h**. **Supporting Fig. S103:** ^{1}H NMR (CD_3CN, 400 MHz) of **S1**. **Supporting Fig. S104:** ^{13}C NMR (CD_3CN, 100 MHz) of **S1**. **Supporting Fig. S105:** ^{19}F NMR (CD_3CN, 375 MHz) of **S1**. **Supporting Fig. S106:** ORTEP diagram of **1** with 50% probability ellipsoid: Black = carbon, Red = oxygen, Blue = hydrogen, Green = fluorine, Yellow = sulfur. **Supporting Fig. S107:** ORTEP diagram of unit cell of 1 with 50% probability ellipsoid: Black = carbon, Red = oxygen, Blue = hydrogen, Green = fluorine, Yellow = sulfur. **Supporting Table S1:** Screening of reaction conditions for the functionalization of phenols. **Supporting Table S2:** Crystal data and structure refinement for **1**.