Copper-mediated oxidative trifluoromethylthiolation of potassium aryltrifluoroborates with elemental sulfur and Ruppert-Prakash reagent

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Abstract: A facile procedure for the copper-mediated oxidative trifluoromethylthiolation of potassium aryl- and heteroaryltrifluoroborates with Ruppert-Prakash reagent and elemental sulfur is presented. Aryl trifluoromethylthioethers can be prepared in good to moderate yield under mild reaction conditions.

Key Words: Aryl trifluoromethylthioethers, Trifluoromethylthiolation, Potassium aryltrifluoroborates, Copper, Ruppert-Prakash reagent, Elemental sulfur

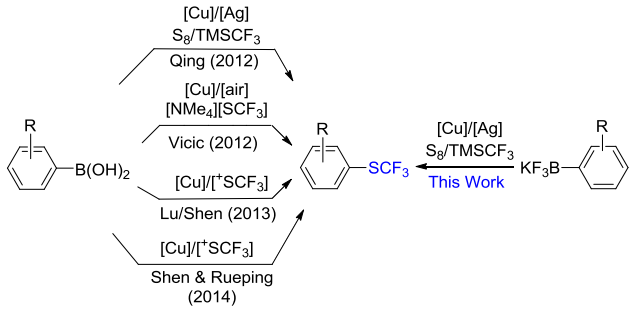
Compounds having fluorinated functional groups are extremely important chemical species because of their widespread biological and therapeutic properties.[1] Approximately 20% of all the pharmaceuticals and 30% of all the agrochemicals on the market do contain fluorine. Among them the trifluoromethylthio (CF_3S) group, especially as aromatic substituent, is a vital structural motif for example in marketed drugs (tiflorex, toltrazuril (Baycox®) and vaniliprole).[2] The CF_3S group plays an important role because of its strong electron-withdrawing effect and high lipophilicity,[3] similar to the related trifluoromethyl (CF_3) and trifluoromethoxy (CF_3O) groups.[4] In addition, aryl trifluoromethylthioethers ($ArSCF_3$) serve as intermediates in the preparation of some trifluoromethylation reagents such as trifluoromethyl sulfoxides and sulfones.[5a] The development of efficient and practical procedures for the construction of the aryl—SCF_3 bond is now a relevant topic for both academic and industrial research.[4,6] Limited procedures are available for the synthesis of aryl trifluoromethylthioethers[4,6] in comparison with trifluoromethylation[7] of arenes in past decades.

Traditionally, an SCF_3 group is introduced to arenes either through halogen–fluorine exchange reactions of trihalogenomethyl thioethers,[8] or through trifluoromethylations of sulfur-containing compounds such as thiols,[9] thiocyanates,[10] sulfenyl chlorides or disulfides.[11] Nucleophilic[11h] or radical reactions have also been reported, *e.g.* reaction of aryl iodides with alumina-supported $CuSCF_3$ at elevated temperature (150 ^oC).[12] However, these methods require multiple steps and expensive reagents. Furthermore, these protocols are limited by way of a combination of high temperatures, and low reactivity of electron-rich aromatic groups. It is highly desirable to develop therefore a general, safe, and efficient method to access aryl trifluoromethylthioethers. In 2011, Buchwald reported a palladium-catalyzed trifluoromethylthiolation of aryl bromides with CF_3SAg[13] reagent. This method is compatible with a variety of functional groups. Similarly, Vicic *et al.* reported nickel-catalyzed coupling of aryl halides with Me_4NSCF_3[14] reagent, and this methodology was further developed by Schoenebeck and co-workers.[15] Weng and Huang *et al.* prepared air stable copper–trifluoromethylthiolate complexes[16], which were reacted with aryl halides[11h] for nucleophilic trifluoromethylthiolation. Billard *et al.* suggested the electrophilic reactions of trifluoromethanesulfonamides with aryl-magnesium or -lithium reagents.[17] Recently, Gooβen *et al.* reported results of a copper-catalyzed trifluoromethylthiolation of arenediazonium salts with sodium thiocyanate and the Ruppert-Prakash reagent ($TMSCF_3$).[18] Additionally, trifluoromethylthiolation can also be accomplished by metal-mediated/catalyzed C–H functionalization of arenes.[19]

Qing *et al.* have reported for the first time the Cu-catalyzed three component oxidative trifluoromethylthiolation of aryl boronic acids with trifluoromethyltrimethylsilane ($TMSCF_3$) and S_8 at ambient temperature (Scheme 1).[20] Their method is essential in the synthesis of $ArSCF_3$ due to its high efficiency and functional group tolerance.[20] Soon after, Zhang and Vicic described a Cu-mediated aerobic two component oxidative trifluoromethylthiolation of arylboronic acids with $[NMe_4][SCF_3]$ (Scheme 1).[21] Latter on, Lu and Shen developed a new electrophilic reagent (initially proposed as electrophilic hypervalent iodine reagent[22a]) and then it was revised by Buchwald *et al*. as trifluoromethanesulfenate[22b], which is effective for the direct transfer of the trifluoromethylthiolate group (CF_3S^-) to aryl boronic acids and other similar species (Scheme 1).[22c] Later on Duan *et al.* reported of a Cu-mediated three component oxidative trifluoromethylthiolation of aryl boronic acids by employing CF_3CO_2Na and S_8 at elevated temperature (130 ^oC) to afford $ArSCF_3$ derivatives in moderate yields.[23] Individually, groups of Shen[24a] and Rueping[24b] utilized shelf-stable N-(trifluoromethylthio)phthalimide reagent for the Cu-catalyzed oxidative trifluoromethylthiolation of aryl and alkenyl boronic acids. Potassium aryltrifluoroborate reagents from the corresponding pinacol ester[25] *via* aryl halides, C-H borylation and others[26] have been employed as starting materials. These potassium aryl and heteroaryltrifluoroborates reagents are used in several transformations,[27] including reports from our group on metal-mediated trifluoromethylation[28] and fluorination.[29]

To the best of our knowledge, there has been no report of the trifluoromethylthiolation of potassium aryltrifluoroborates. In this paper, we report a complementary method for the synthesis of aryl trifluoromethylthioethers in moderate to good yields by the reaction of potassium aryl and heteroaryltrifluoroborates with Ruppert-Prakash reagent ($TMSCF_3$) and elemental sulfur under Cu-mediated reac-

tion conditions (Scheme 1). It is the first report of the use of aryltrifluoroborates in trifluoromethylthiolation reaction.

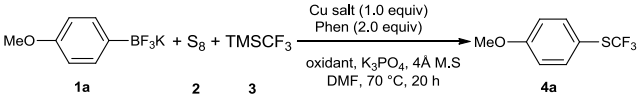


Scheme 1. Trifluoromethylthiolation of organoboron derivatives.

In our initial search for general reaction conditions, we utilized a Cu-catalyzed oxidative trifluoromethylthiolation of potassium aryltrifluoroborates with the following conditions: substrate (1.0 equiv, 0.1 mmol), 4Å molecular sieves, S_8 (3.0 equiv), CuI (0.1 equiv), 1,10-phenanthroline (Phen) (0.2 equiv), K_3PO_4 (2.0 equiv), Ag_2CO_3 (2.0 equiv) and $TMSCF_3$ (5 equiv). Reagents were combined in anhydrous DMF and stirred at room temperature for 24 h. Under these conditions, the trifluoromethylthiolation of potassium (4-methoxyphenyl)trifluoroborate (**1a**) gave 17% of the desired 4-methoxy-[(trifluoromethyl)thio]benzene (**4a**, by ^{19}F NMR) and 5% of 1-methoxy-4-(trifluoromethyl)benzene (**5a**, by ^{19}F NMR). When the stoichiometry of S_8 was increased from 3.0 to 8.0 equiv, we obtained the desired trifluoromethylthiolated product in 25% yield. Furthermore, when we used a stoichiometric amount of CuI (1.0 equiv) the yield increased to 40%, while heating (70 ^oC) raised the yield of **4a** to 50%. After this, we screened the utility of various copper salts and oxidants for trifluoromethylthiolation (Table 1). Even though Cu metal and Cu (II) salts were also screened, none of them gave better results than CuSCN (Table 1, entry 5 *vs* entries 9-14). Therefore CuSCN was chosen as the best mediator (entry 5). Additionally, we investigated oxidant alternatives to Ag_2CO_3 such as AgOTf, benzoylperoxide, dibromoethane, air and oxygen (Table 1, entry 5 *vs* entries 16-20). However, none of them succeeded in improving the yield observed using Ag_2CO_3.

We then explored the use of different bases (Li-OH•H_2O, Na_2CO_3, Cs_2CO_3, $NaHCO_3$, KH_2PO_4, NaOAc, Et_3N, and pyridine) and fluoride sources of various polarizability and size (NaF, KF, and AgF) with trifluoroborate **1a** under the above mentioned conditions. None of them gave better results than K_3PO_4 (Table S1). Lastly, we examined the various polar and non-polar solvents (MeOH, THF/H_2O, THF, CH_3CN, DME, DMSO, DMA, acetone, ^{i}PrOAc, EtOAc, DMF/toluene) with trifluoroborate **1a** using the above procedure. To our delight DMF/toluene (1/1) gave 4-methoxy-[(trifluoromethyl)thio]benzene (**4a**) in 82% yield (Table S2).

Table 1. Identifying optimal Cu salts and oxidants of potassiumaryltrifluoroboroates for trifluoromethylthiolation[a,b]



Entry	Cu salts	Oxidant	%Yield (**4a**)[b]
1	CuI	Ag_2CO_3	50(29)[c]
2	CuBr	Ag_2CO_3	28
3	CuCl	Ag_2CO_3	5
4	CuCN	Ag_2CO_3	69
5	**CuSCN**	**Ag_2CO_3**	**80**
6[d]	CuTC	Ag_2CO_3	48
7	$Cu(MeCN)_4PF_6$	Ag_2CO_3	20
8	$[Cu(OTf)]_2$•C_6H_6	Ag_2CO_3	5
9	Cu	Ag_2CO_3	0
10	CuO	Ag_2CO_3	5
11	$CuCl_2$	Ag_2CO_3	32
12	$CuBr_2$	Ag_2CO_3	28
13	$Cu(OTf)_2$	Ag_2CO_3	0
14	$Cu(TFA)_2$	Ag_2CO_3	0
15	CuSCN	$AgNO_3$	40
16	CuSCN	AgOTf	60
17	CuSCN	$(BzO)_2$	20
18	CuSCN	Dibromoethane	59
19	CuSCN	Air	10
20	CuSCN	Oxygen	8

[a]Reaction conditions: **1a** (1.0 equiv, 0.10 mmol), Cu salt (1.0 equiv), 1,10-phenthroline (Phen, 2.0 equiv), S_8 (8.0 equiv), oxidant (2.0 equiv), K_3PO_4 (2.0 equiv), 4Å M.S. (20 mg), $TMSCF_3$ (5.0 equiv), DMF, 70 °C, 20 h.

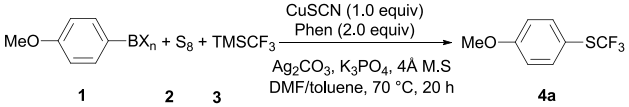
[b]Yield determined by ^{19}F NMR with 4-fluorobenzonitrile as an internal standard added after the reaction.

[c]**1a** (1.0 equiv, 0.10 mmol), Cu salt (0.1 equiv), 1,10-phenthroline (Phen, 0.2 equiv), S_8 (8.0 equiv), oxidant (2.0 equiv), K_3PO_4 (2.0 equiv), 4Å M.S. (20 mg), $TMSCF_3$ (5.0 equiv), DMF, 70 °C, 20 h.

[d]CuTC: Copper(I)-thiophene-2-carboxylate.

Several *p*-$OMeC_6H_4BX_n$ derivatives were tested using optimized reaction conditions (Table 2). The corresponding pinacol ester (entry 2), and MIDA ester (entry 3) gave remarkable yields in comparison with trifluoroborate (entry 1). Under both copper-mediated and -catalyzed oxidative trifluoromethylthiolations, the boronic acid (entry 4 *vs* entry 1) gave better yield (95% and 90%) than the corresponding trifluoroborate (82% and 17%). Optimized reaction conditions for this transformation finally were chosen as follows: trifluoroborate (1.0 equiv, 0.50 mmol), 4Å M. S. (50 mg), CuSCN (1.0 equiv), 1,10-phenthroline (2.0 equiv), S_8 (8.0 equiv), K_3PO_4 (2.5 equiv), Ag_2CO_3 (2.0 equiv), CF_3SiMe_3 (5.0 equiv) in DMF/toluene (5 mL, 1/1) at 70 °C for 20 h.

Table 2. Scope of trifluoromethylthiolation of aryl boronic acid derivatives



Entry	BX_n	%Yield (**4a**)
1		(82)[a](17)[b]
2		5[a]

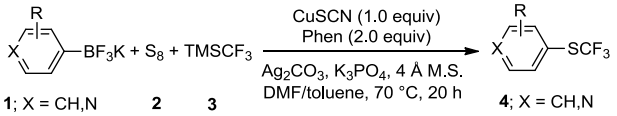
3		Trace [a]
4		(95)[a](90)[b]

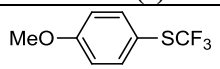
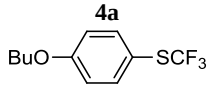
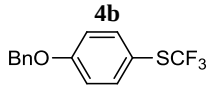
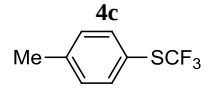
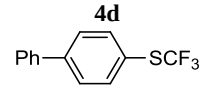
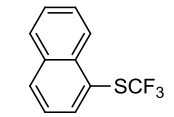
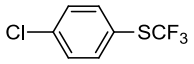
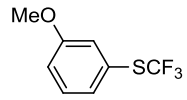
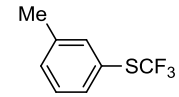
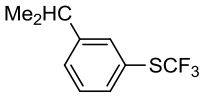
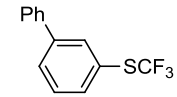
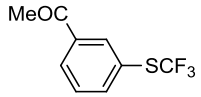
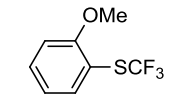
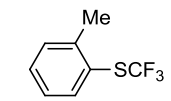
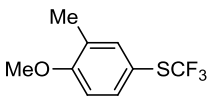
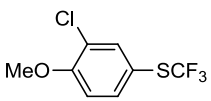
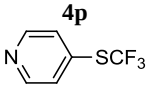
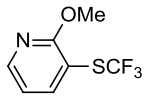
[a]Reaction conditions: *p*-$OMeC_6H_4BX_n$ (1.0 equiv, 0.10 mmol), CuSCN (1.0 equiv), 1,10-phenthroline (2.0 equiv), S_8 (8.0 equiv), Ag_2CO_3 (2.0 equiv), K_3PO_4 (2.0 equiv), $TMSCF_3$ (5.0 equiv), DMF/toluene, 70 °C, 20 h; yield determined by ^{19}F NMR with 4-fluorobenzonitrile as an internal standard added after the reaction.

[b]Reaction conditions: *p*-$OMeC_6H_4BX_n$ (1.0 equiv, 0.10 mmol), CuSCN (0.1 equiv), 1,10-phenthroline (0.2 equiv), S_8 (3.0 equiv), Ag_2CO_3 (2.0 equiv), K_3PO_4 (3.0 equiv), $TMSCF_3$ (5.0 equiv), DMF (3 mL), rt, 20 h; yield determined by ^{19}F NMR with 4-fluorobenzonitrile as an internal standard added after the reaction.

We then set out to explore substrate scope for copper-mediated oxidative trifluoromethylthiolation of potassium aryl-, heteroaryltrifluoroborates. Substrates containing *para*, *meta* or *ortho*-substituents and di-substituents also underwent trifluoromethylthiolation. Aryltrifluoroborates with *para*-substituents (methoxy, butoxy, benzyloxy, methyl, phenyl) underwent trifluoromethylation in good yields (Table 3; **4a-e**). Potassium 1-naphthyltrifluoroborate was converted into the corresponding 1-trifluoromethylthioether (**4f**) in moderate yield. Trifluoromethylthiolation of weak electron-withdrawing substrates (chloro) gave the desired fluorinated product in moderate yield (Table 3; **4g**). This might be due to the unreactivity and/or the formation of the protodeboronation substrate. Aryltrifluoroborates with either electron-donating or withdrawing groups at *meta*-position (methoxy, methyl, iso-propyl, phenyl, acetyl) provided the expected trifluoromethylthiolation products (Table 3; **4h-l**). Our protocol also accommodates *ortho*-substituted trifluoroborates, which do yield corresponding products in moderate yields (Table 2; **4m-n**). Di-substituted aryltrifluoroborates provided the desired trifluoromethylthiolation products in good yields (Table 3; **4o-p**). However, when we employed heteroaryltrifluoroborates, results were mediocre (Table 3; **4q-r**).[30]

Table 3. Substrate scope for trifluoromethylthiolation of potassium aryl and heteroaryl trifluoroborates[a]



Entry	SM (**1**)	Product (**4**)	%Yield
1	**1a**	 **4a**	82(70)
2	**1b**	 **4b**	65(60)
3	**1c**	 **4c**	73(68)
4	**1d**	 **4d**	60(55)
5	**1e**	 **4e**	83(72)
6	**1f**	 **4f**	55(50)
7	**1g**	 **4g**	50(40)
8	**1h**	 **4h**	40
9	**1i**	 **4i**	58(50)
10	**1j**	 **4j**	72(65)
11	**1k**	 **4k**	80(72)
12	**1l**	 **4l**	15
13	**1m**	 **4m**	35
14	**1n**	 **4n**	65(55)
15	**1o**	 **4o**	70(62)
16	**1p**	 **4p**	75(70)
17	**1q**	 **4q**	33
18	**1r**	 **4r**	26

[a] Reaction conditions: **1** (1.0 equiv, 0.20 mmol), CuSCN (1.0 equiv), 1,10-phenthroline (2.0 equiv), S_8 (8.0 equiv), Ag_2CO_3 (2.0 equiv), K_3PO_4 (2.5 equiv), 4Å M.S. (50 mg), $TMSCF_3$ (5.0 equiv), DMF/toluene (5 mL, 1/1), 70 °C, 20 h; Yields were determined by ^{19}F NMR with 4-fluorobenzonitrile as an internal standard (isolated yields); Some of the isolated compound contains 2-5% of by products.

In conclusion, we have developed a convenient three component copper-mediated oxidative trifluoromethylthiolation of potassium aryl- and heteroaryl trifluoroborates with trifluoromethyltrimethylsilane (Ruppert-Prakash rea-

gent) and elemental sulfur. This method uses easily accessible potassium aryltrifluoroborates.

General information: ^{1}H and ^{19}F NMR Spectra were recorded on a Bruker 400 MHz or 300 MHz in the solvents indicated; chemical shifts are reported in units (ppm) by assigning $CDCl_3$ resonance in the ^{1}H spectrum as 7.26 ppm. ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as internal standard and are measured proton decoupled. All coupling constants (*J* values) were reported in Hertz (Hz). GC-MS spectra were measured on Shimadzu GCMS-QP2010S. Column chromatography was performed on silica gel 200-300 mesh on Combiflash®. If not specially mentioned, all the solvents and reagents were used as purchased from Sigma-Aldrich, Combi-Blocks, Matrix and Oakwood and without further purification.

General procedure for the copper-mediated trifluoromethylthiolation of potassium aryl and heteroaryltrifluoroborates with S_8 and $TMSCF_3$ (Table 3).

Trifluoroborate (0.20 mmol, 1.0 equiv), CuSCN (24.3 mg, 0.20 mmol, 1.0 equiv), 1,10-phenthroline (72.0 mg, 0.4 mmol, 2.0 equiv), S_8 (410 mg, 1.6 mmol, 8.0 equiv), Ag_2CO_3 (110 mg, 0.4 mmol, 2.0 equiv) were weighed into a 20 mL tube. 4Å powdered molecular sieves (50 mg) and K_3PO_4 (84.9 mg, 0.5 mmol, 2.5 equiv) were quickly added to the tube under N_2 atmosphere. Anhydrous DMF (2.5 mL), toluene (2.5 mL) and followed by $TMSCF_3$ (150 µL, 1.0 mmol, 5.0 equiv) were added to the reaction mixture under nitrogen atmosphere. The reaction vessel was sealed with a cap and the mixture was stirred at 70 ºC for 20 h. The resulting mixture was cooled to room temperature. For the compounds reported with isolated yields (**4a, 4b**, **4c**, **4d**, **4e, 4f, 4g, 4i, 4j, 4k, 4n, 4o,** and **4p**) the reaction mixture was filtered through Celite and washed with EtOAc (20 mL). The combined solutions were washed with brine. The organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure and the residue was purified Combiflash with hexanes/EtOAc to afford the desired compounds.

The low yielding products (**4h, 4l, 4m, 4q** and **4r**) were not isolated and their yields were determined only by ^{19}F NMR of the reaction mixture. For the compounds reported with ^{19}F NMR yields, 4-fluorobenzonitrile (0.20 mmol) was added as reference to the reaction mixture, which was stirred for 5 min, and then diluted with EtOAc (5 mL) and brine (5 mL). The layers were separated and an organic aliquot was withdrawn for the ^{19}F NMR measurement in $CDCl_3$.

1-Methoxy-4-[(trifluoromethyl)thio]benzene (**4a**).[23] Compound **4a** was isolated in 70% yield (29.1 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.57 (d, *J* = 8.6 Hz, 2H), 6.92 (d, *J* = 8.7 Hz, 2H), 3.83 (s, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –44.40 (s, 3F); GC–MS *m/z* 208 (M^+). The ^{19}F NMR spectral data correspond to previously reported data.

1-Butoxy-4-[(trifluoromethyl)thio]benzene (**4b**).[24a] Compound **4b** was isolated in 60% yield (30.0 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.54 (d, *J* = 6.6 Hz, 2H), 6.91 (d, *J* = 6.8 Hz, 2H), 3.98 (t, *J* = 6.5 Hz, 2H), 1.81–1.74 (m, 2H), 1.52–1.47 (m, 2H), 0.98 (t, *J* = 6.7 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –43.94 (s, 3F); GC–MS *m/z* 250 (M^+). These spectroscopic data correspond to previously reported data.

1-(Benzyloxy)-4-[(trifluoromethyl)thio]benzene (**4c**).[20] Compound **4c** was isolated in 68% yield (38.6 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.57 (d, *J* = 9.0 Hz, 2H), 7.41–7.38 (m, 5H), 7.00 (d, *J* = 8.8 Hz, 2H), 5.09 (s, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –43.83 (s, 3F); GC–MS *m/z* 284 (M^+). These spectroscopic data correspond to previously reported data.

1-Methy-4-[(trifluoromethyl)thio]benzene (**4d**).[23] Compound **4d** was isolated in 55% yield (21.2 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.53 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –43.67 (s, 3F); GC–MS *m/z* 192 (M^+). The ^{19}F NMR spectral data correspond to previously reported data.

4-[(Trifluoromethyl)thio]biphenyl (**4e**).[20] Compound **4e** was isolated in 72% yield (36.6 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.72 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.61−7.57 (m, 2H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –43.45 (s, 3F); GC–MS *m/z* 254 (M^+). These spectroscopic data correspond to previously reported data.

1-[(Trifluoromethyl)thio]naphthalene (**4f**).[20] Compound **4f** was isolated in 50% yield (22.8 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 8.53 (d, *J* = 8.5 Hz, 1H), 7.96 (t, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –42.19 (s, 3F); GC–MS *m/z* 228 (M^+). These spectroscopic data correspond to previously reported data.

1-*Chloro-4-[(trifluoromethyl)thio]benzene* (**4g**).[23] Compound **4g** was isolated in 40% yield (16.9 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.59 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.5 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –43.31 (s, 3F); GC–MS *m/z* 212 (M^+). These spectroscopic data correspond to previously reported data.

1-Methoxy-3-[(trifluoromethyl)thio]benzene (**4h**).[11h] The yield (40%) of **4h** was determined by ^{19}F NMR. ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –43.13 (s, 3F); GC–MS *m/z* 208 (M^+). These spectroscopic data correspond to previously reported data.

1-Methy-3-[(trifluoromethyl)thio]benzene (**4i**).[14,18] Compound **4i** was isolated in 50% yield (19.2 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.48-7.28 (m, 2H), 7.22-7.01 (m, 2H), 2.38 (s, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –42.71 (s, 3F); GC–MS *m/z* 192 (M^+). NMR spectral data correspond to previously reported data.

1-Isopropyl-3-[(trifluoromethyl)thio]benzene (**4j**).[24b] Compound **4j** was isolated in 65% yield (28.6 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.49-7.30 (m, 2H), 7.24-7.07 (m, 2H), 2.91 (sept, *J* = 8.0 Hz, 1H), 1.24 (d, *J* = 8.0 Hz, 6H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –42.71 (s, 3F); GC–MS *m/z* 220 (M^+). NMR spectral data correspond to previously reported data.

3-[(Trifluoromethyl)thio]biphenyl (**4k**).[20] Compound **4k** was isolated in 72% yield (36.6 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.90 (s, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.66−7.58 (m, 3H), 7.53−7.38 (m, 4H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –43.00 (s, 3F); GC–MS *m/z* 254 (M^+). These spectroscopic data correspond to previously reported data.

3-[(Trifluoromethyl)thio]acetophenone (**4l**).[18] The yield (15%) of **4m** was determined by ^{19}F NMR. ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –42.50; GC–MS *m/z* 220 (M^+). The ^{19}F NMR spectral data correspond to previously reported data.

1-Methoxy-2-[(trifluoromethyl)thio]benzene (**4m**).[11h] The yield (35%) of **4m** was determined by ^{19}F NMR. ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –42.40 (s, 3F); GC–MS *m/z* 208 (M^+). The ^{19}F NMR spectral data correspond to previously reported data

1-Methy-2-[(trifluoromethyl)thio]benzene (**4n**).[23] Compound **4n** was isolated in 55% yield (21.2 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.65 (d, *J* = 7.8 Hz, 1H), 7.41-7.30 (m, 2H), 7.24 (d, *J* = 7.4 Hz, 1H), 2.54 (s, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –42.89 (s, 3F); GC–MS *m/z* 192 (M^+). These spectroscopic data correspond to previously reported data.

1-Methoxy-2-methyl-4-[(trifluoromethyl)thio]benzene (**4o**).[31] Compound **4o** was isolated in 62% yield (27.5 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.65 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.40 (brd, *J* = 2.2 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 1H), 3.86 (s, 3H), 2.22 (s, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –43.88 (s, 3F); GC–MS *m/z* 222 (M^+). These spectroscopic data correspond to previously reported data.

1-Methoxy-2-chloro-4-[(trifluoromethyl)thio]benzene (**4p**).[16] Compound **4p** was isolated in 70% yield (33.9 mg). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 7.67 (d, *J* = 2.2 Hz, 1H), 7.53 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 3.94 (s, 3H); ^{19}F NMR ($CDCl_3$, 376 M Hz) δ ppm –43.56 (s, 3F); GC–MS *m/z* 242 (M^+). These spectroscopic data correspond to previously reported data.

4-[(Trifluoromethyl)thio]pyridine (**4q**).[23] The yield (33%) of **4q** was determined by ^{19}F NMR. ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –40.45; GC–MS *m/z* 179 (M^+). The ^{19}F NMR spectral data correspond to previously reported data.

2-Methoxy-3-[(trifluoromethyl)thio]pyridine (**4r**).[24a] The yield (26%) of **4r** was determined by ^{19}F NMR. ^{19}F NMR ($CDCl_3$, 376 MHz) δ ppm –43.88; GC–MS *m/z* 209 (M^+). The ^{19}F NMR spectral data correspond to previously reported data.

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30 Optimization of reaction conditions for heteroaromatic products as well as mechanistic studies are currently undergoing in our group.

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Graphic Abstract: