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Note

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Copper-Catalyzed 2,2,2-Trifluoroethylthiolation of Aryl Halides

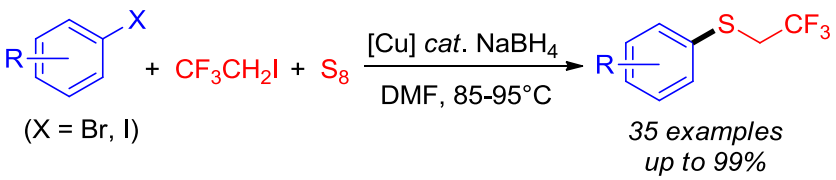
Shouxiong Chen,[†] Mengjia Zhang,[†] Xuebin Liao,[‡,*] and Zhiqiang Weng[†,*]

[†] State Key Laboratory of Photocatalysis on Energy and Environment, College of Chemistry, Fuzhou University, Fujian, China, 350108

[‡] School of Pharmaceutical Sciences, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Tsinghua University, Beijing, China, 100084

Corresponding authors. Tel.: +86 59122866121; fax: +86 59122866121

ABSTRACT:



Herein, a copper-catalyzed 2,2,2-trifluoroethylthiolation reaction of aryl bromides and iodides with elemental sulfur, and 1,1,1-trifluoro-2-iodoethane is described. The reaction showed excellent functional-group tolerance and allowed the synthesis of various substituted aryl 2,2,2-trifluoroethyl thioethers with good to excellent yields. This transformation constitutes a one-pot synthesis of 2,2,2-trifluoroethylthiolated compounds from inexpensive, readily available starting materials. Utility of the protocol was

further demonstrated in the late-stage synthesis of the pirfenidone derivative. The copper thiolate species were prepared and proposed as key intermediates in the catalytic cycle.

The physicochemical properties of organofluorine compounds has aroused the interest of organic chemists, and extensive efforts have been dedicated to the synthesis of fluorine-containing molecules.[1-4] Among them, special interest has been focused on the developing synthetic methods for the preparation of 2,2,2-trifluoroethyl thioethers. The 2,2,2-trifluoroethylthio group (-SCH_2CF_3) is a key functionality in several pharmaceutical and agrochemical compounds (Figure 1), which was used for combating and controlling insects arachnids or nematodes in and on plants, and animal pests, including arthropods.[5-7] The introduction of -SCH_2CF_3 substituents could significantly improve the physicochemical properties, and the metabolic stability of organic molecules.

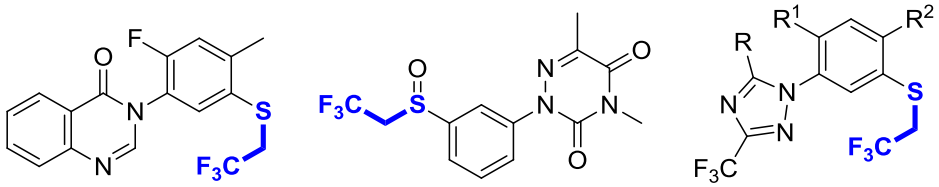
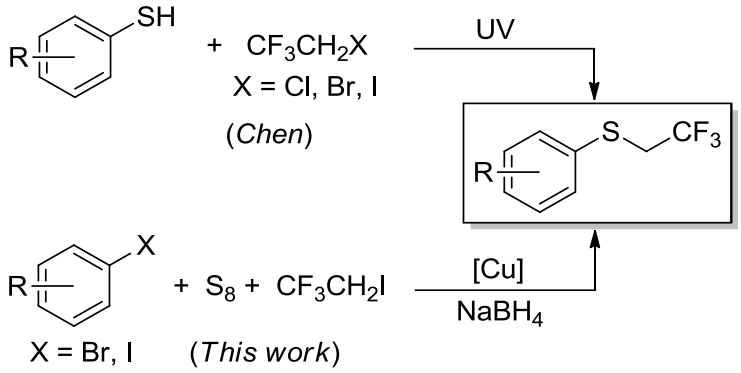


Figure 1. Patented 2,2,2-Trifluoroethylthio-Containg Bioactive Molecules.

To date, the methods for the installation of a 2,2,2-trifluoroethylthio group on an aromatic ring have been only reported in several papers.[8-14] The pioneering work with the polar nucleophilic substitution of 1,1,1-trifluoro-2-iodoethane by sodium thiophenoxide in methanol to 2,2,2-trifluoroethyl thioethers was achieved by Hine and Ghirardell.[15] However, β-fluorine atoms disfavor S_N2 reactivity of CF_3CH_2I.[15,16] In 1998, Chen and co-workers reported the preparation of 2,2,2-trifluoroethylthiol

derivatives in high yields through a $S_{RN}1$ reactions of 2,2,2-trifluoroethyl halides with thiolate ions under UV irradiation (Scheme 1).[17] Unfortunately, these methods usually rely on the use of malodorous thiols. In addition, these methods also often suffer from narrow substrate scopes, which further limit the utility of these procedures in synthetic applications. Thus, the development of an efficient method to access 2,2,2-trifluoroethyl thioethers is highly desirable. In particular, the utilization of aryl halides[18] and elemental sulfur[19] involving the newly developed method is attractive approach, because these starting materials are inexpensive, readily available, and easily handled.



Scheme 1. Methods for the Synthesis of 2,2,2-Trifluoroethyl Thioethers

In 2009, Ma and co-workers elegantly demonstrated a CuI-catalyzed coupling of aryl iodides, sulfur and alkyl halides under reductive conditions to afford aryl alkyl thiol ethers in good to excellent yields.[20] Inspired by their work and our previous work,[19-21] we became interested in whether similar reactions could occur employing

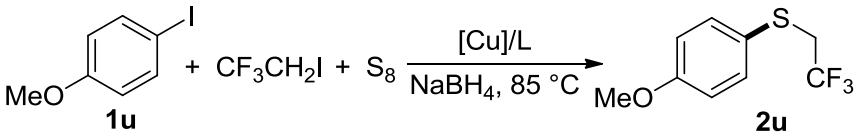
CF_3CH_2I as fluorinated reagent to form 2,2,2-trifluoroethyl thioethers. Herein, we report our findings on the development of copper-catalyzed 2,2,2-trifluoroethylthiolation of aryl halides.

On the basis of our previous work on the synthesis of trifluoromethylthiolated compounds from readily available reagents, such as elemental sulfur,[21-23] we started our investigation with a model reaction using 4-iodoanisole and CF_3CH_2I.

As described in Table 1, in the presence of CuI (0.1 equiv), phen (0.2 equiv), and $NaBH_4$ (3.0 equiv) in DMF at 85 °C, 4-iodoanisole reacted with CF_3CH_2I (2.0 equiv) and elemental sulfur (2.0 equiv) to afford the desired product (4-methoxyphenyl)(2,2,2-trifluoroethyl)sulfane **2u** in 88% NMR yield (Table 1, entry 1). Some factors affecting the 2,2,2-trifluoroethylthiolation reaction were also investigated. Other copper catalysts only show modestly efficient or inefficient under these conditions (Table 1, entries 2-9); no reaction occurred in the absence of copper catalysts (Table 1, entry 10). This observation revealed the crucial role of copper for this reaction. Of note, the use of Ma's conditions[20] for the synthesis of aryl alkyl thiol ethers only led to a very low yield of **2u** (Table 1, entry 11). A range of other diimine and diamine ligands are ineffective (Table 1, entries 12 and 13). Interestingly, the use of 5,5-dimethylcyclohexane-1,3-dione (dimedone) as ligand in DMF at 85 °C gave the product in comparable yield (82%, see Supporting Information) with phen (Table 1, entry 14). After different solvents were screened, DMF proved to be optimal, while other solvents, such as DMSO, CH_3CN, toluene, and THF resulted in the poor yields (Table 1, entries 15-18). Interestingly, in the absence of $NaBH_4$ no product **2u** was

detected (see Supporting Information). The role of $NaBH_4$ was proposed to react with CF_3CH_2I and S_8 to form the $HSCH_2CF_3$ species.

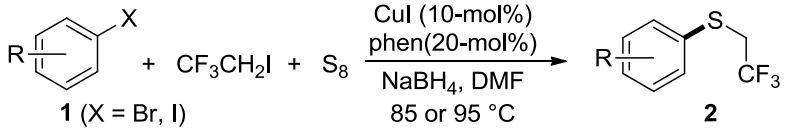
Table 1. Optimization of 2,2,2-Trifluoroethylthiolation of 4-Iodoanisole.[a]



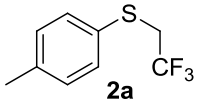
entry	[Cu] (10 mol%)	ligand (20 mol%)	solvent	yield (%) [b]
1	CuI	phen	DMF	88
2	CuBr	phen	DMF	74
3	CuCl	phen	DMF	51
4	CuF_2	phen	DMF	0
5	$Cu(TFA)_2$	phen	DMF	0
6	$Cu(OTf)_2$	phen	DMF	0
7	$Cu(MeCN)_4PF_6$	phen	DMF	0
8	CuCN	phen	DMF	<1
9	CuSCN	phen	DMF	<1
10	-	phen	DMF	0
11	CuI	-	DMF	17
12	CuI	bpy	DMF	64
13	CuI	TMEDA	DMF	20
14	CuI	dimedone	DMF	82
15	CuI	phen	DMSO	37
16	CuI	phen	CH_3CN	0
17	CuI	phen	Toluene	trace
18	CuI	phen	THF	trace

[a] Reaction conditions: [Cu] (0.020 mmol), [ligand] (0.040 mmol), $NaBH_4$ (0.60 mmol), 4-iodoanisole (0.20 mmol), S_8 (0.40 mmol), CF_3CH_2I (0.40 mmol), solvent (2.0 mL), 12 h, N_2. [b] Yields were determined by ^{19}F NMR analysis of the crude reaction mixture with $PhOCF_3$ as internal standard. bpy = 2,2'-bipyridine, TMEDA = tetramethylethylenediamine, dimedone = 5,5-dimethylcyclohexane-1,3-dione, DMF = *N*,*N*-dimethylformamide, DMSO = dimethyl sulfoxide.

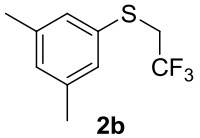
With the optimized conditions in hand, we studied the scope of the 2,2,2-trifluoroethylthiolation reaction with different aryl iodides and bromides. As shown in Scheme 2, aryl iodides bearing either electron-neutral, electron-withdrawing, or electron-donating groups at *ortho*-, *meta*-, and *para*-position on the aromatic ring, afforded the corresponding products in good to excellent yields. Various functional groups, such as nitro, ester, cyano, ketone, trifluoromethyl, trifluoromethoxy, and methoxy were well tolerated. Notably, the 2,2,2-trifluoroethylthiolation reaction proceeded smoothly with 1-chloro-4-iodobenzene and 1-fluoro-3-iodobenzene to give the corresponding products **2v** and **2w** in 82% and 99% yields, respectively. This feature could be quite useful to further introduce various substituents on the aromatic ring to diversify new precursors to biologically active substances through different types of transition metal-catalyzed cross-coupling reactions. Additionally, 1-iodonaphthalene and 3-iodo-9*H*-fluorene could also afford the corresponding 2,2,2-trifluoroethylthiolated products (**2x** and **2y**) under standard conditions in very good yields (91% and 83%, respectively).



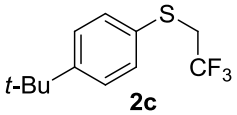
1 (X = Br, I) **2**



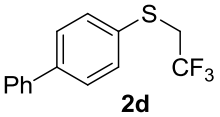
2a
X = I, 81%
X = Br, 71%



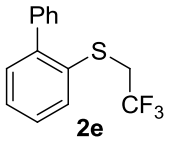
2b
X = I, 93%



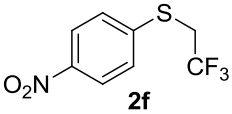
2c
X = I, 71%



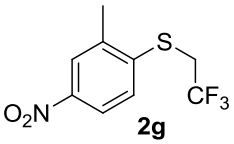
2d
X = I, 75%



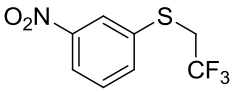
2e
X = I, 97%



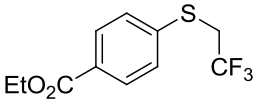
2f
X = I, 99%
X = Br, 96%



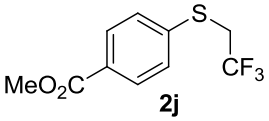
2g
X = I, 99%



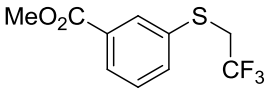
2h
X = I, 85%



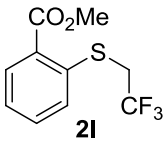
2i
X = I, 99%



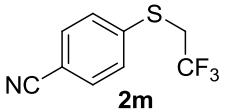
2j
X = Br, 76%



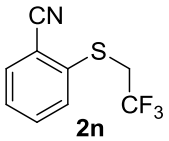
2k
X = I, 95%



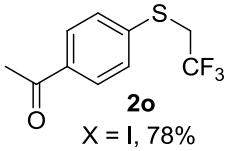
2l
X = I, 88%
X = Br, 83%



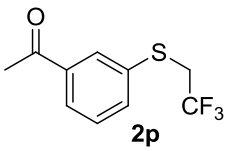
2m
X = I, 90%
X = Br, 85%



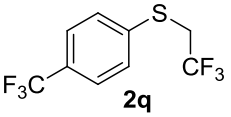
2n
X = Br, 82%



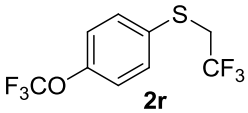
2o
X = I, 78%
X = Br, 83%



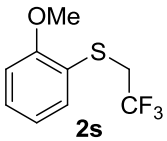
2p
X = I, 97%



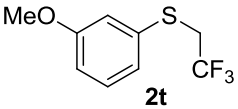
2q
X = I, 84%



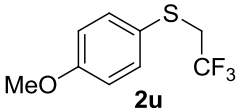
2r
X = I, 81%



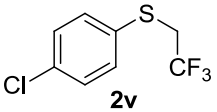
2s
X = I, 62%



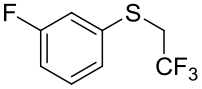
2t
X = I, 93%



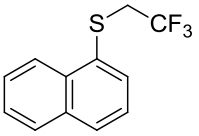
2u
X = I, 84%
X = Br, 60%



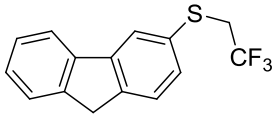
2v
X = I, 82%



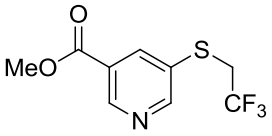
2w
X = I, 99%



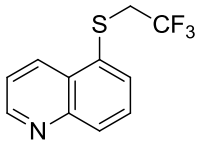
2x
X = I, 91%



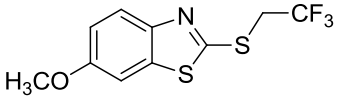
2y
X = I, 83%



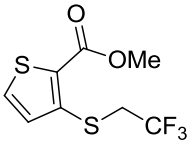
2aa
X = Br, 89%



2ab
X = Br, 61%



2ac
X = Br, 76%

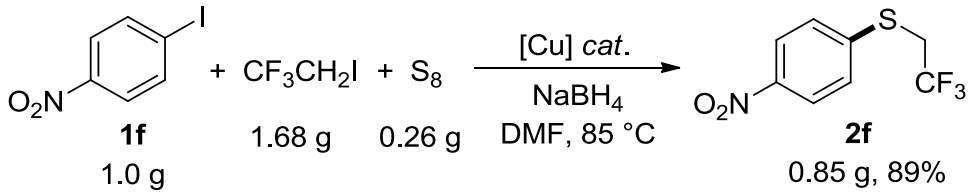


2ad
X = I, 36%

Scheme 2. Copper-Catalyzed Reductive 2,2,2-Trifluoroethylthiolation of Aryl Halides. Reaction conditions: CuI (0.050 mmol), phen (0.10 mmol), $NaBH_4$ (1.5 mmol), **1** (0.50 mmol), S_8 (1.0 mmol), CF_3CH_2I (1.0 mmol), DMF (5.0 mL), 12-16 h, N_2. With aryl iodides at 85 °C; with aryl bromides at 95 °C, and 5,5-dimethylcyclohexane-1,3-dione was used instead of phen.

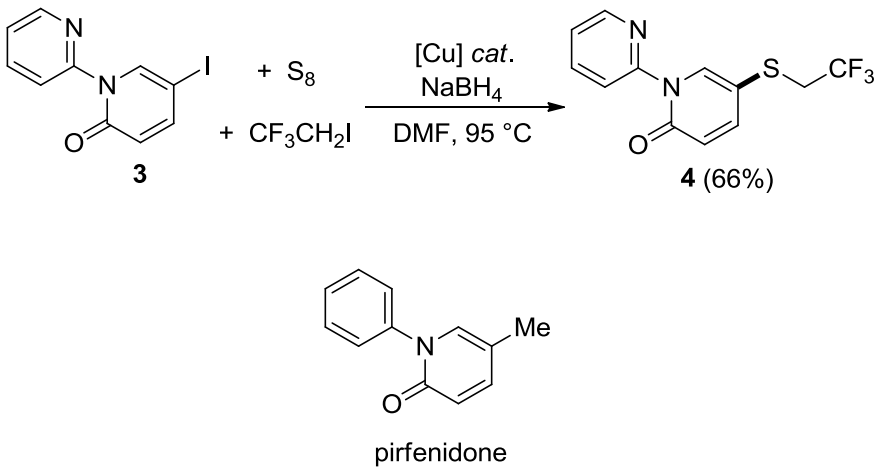
It is important to note that, the reactions occurred with aryl bromides to produce aryl 2,2,2-trifluoroethyl thioethers **2a**, **2f**, **2j**, **2l**–**o** proceeded smoothly with similar yields and **2u** in slightly lower yield compared with those obtained using corresponding aryliodides as substrates, albeit at a slightly higher reaction temperature of 95 °C and the 5,5-dimethylcyclohexane-1,3-dione was chosen as the ligand instead of phen. Interestingly, heteroaryl bromides and iodides, such as methyl 5-bromonicotinate, 5-bromoquinoline, 2-bromo-6-methoxybenzo[*d*]thiazole, and 3-iodothiophene-2-carboxylate could also be successfully used as the substrate, affording the corresponding products **2aa**, **2ab**, **2ac**, and **2ad** in 89%, 61%, 76%, and 36% yields, respectively.

To assess the scalability of the protocol, the 2,2,2-trifluoroethylthiolation reaction of 1-iodo-4-nitrobenzene was performed on a gram scale. The expected 2,2,2-trifluoroethylthiolated **2f** was obtained in 89% yield, only slightly lower than the yield achieved with the submillimolar scale reaction (Scheme 3).



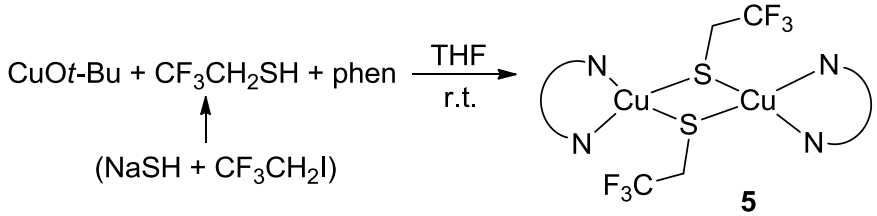
Scheme 3. Scalability of the 2,2,2-Trifluoroethylthiolation of 1-Iodo-4-nitrobenzene

To further demonstrate the synthetic application of this protocol, we have undertaken the late-stage synthesis of the pirfenidone derivative, which has been employed against fibrotic disorder.[24] Under the optimized reaction conditions, the 2,2,2-trifluoroethylthiolation of **3** gave a 66% yield of CF_3CH_2S-containing pirfenidone **4** (Scheme 4). This result indicates that the developed protocol could be readily extended to other biologically active compounds.



Scheme 4. Late-stage 2,2,2-Trifluoroethylthiolation of Pirfenidone Derivative 3

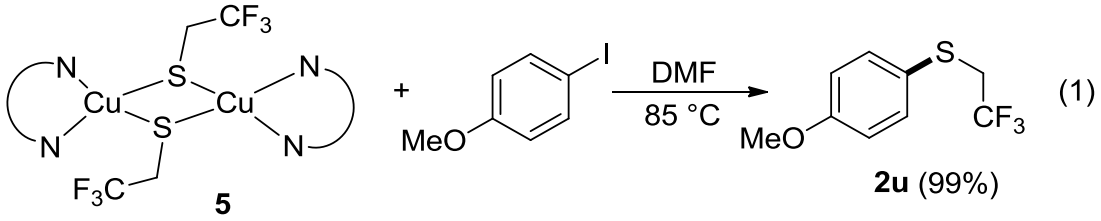
To shed light on mechanism, we initially tried to identify whether copper thiolates species are involved in the reaction mechanism as in the copper mediated Ullmann type of C-S cross-coupling of thiols with aryl halides.[25,26] Thus, we started to isolate the putative copper thiolate intermediates. The reaction of CuO*t*-Bu, phen, and CF_3CH_2SH (prepared in situ from reaction of NaSH with CF_3CH_2I), in THF at r.t. for 20 min led to the isolation of $[(phen)Cu(\mu\text{-}SCH_2CF_3)]_2$ (**5**) in 83% yield (Scheme 5). Alternatively, complex **5** was formed in 74% yield (^{19}F NMR) from the reaction of CuI and phen with CF_3CH_2I, in the presence of $NaBH_4$ at 85 °C for 12 h.

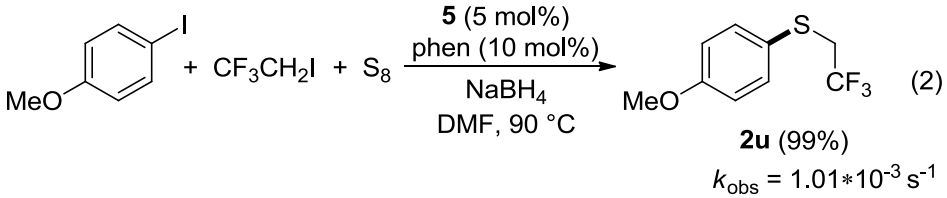


Scheme 5. Synthesis of $[(phen)Cu(\mu\text{-}SCH_2CF_3)]_2$ (5)

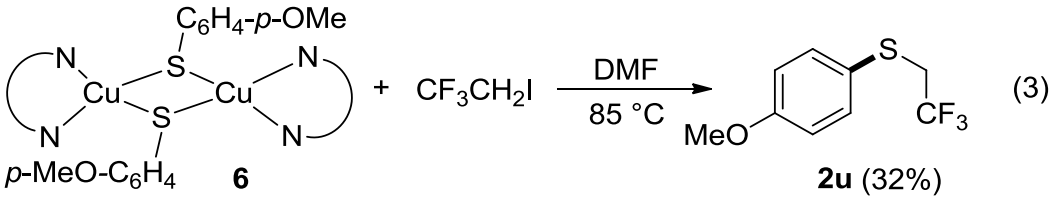
Subsequently, we evaluated the competence of this copper thiolate complex **5** to be intermediates in the copper-catalyzed 2,2,2-trifluoroethylthiolation of aryl halides. The stoichiometric reaction of complex **5** with 4-iodoanisole in DMF at 85 °C for 12 h produced the expected product **2u** in 99% NMR yield (Eqn 1). The catalytic activity of copper thiolate species towards 2,2,2-trifluoroethylthiolation was then investigated by conducting the reaction of 4-iodoanisole with CF_3CH_2I and elemental sulfur in the presence of **5** (5 mol%), phen (10 mol %), and $NaBH_4$ in DMF at 90 °C for 18 h. Complex **5** was found to be an equally active catalyst and the reaction afforded the

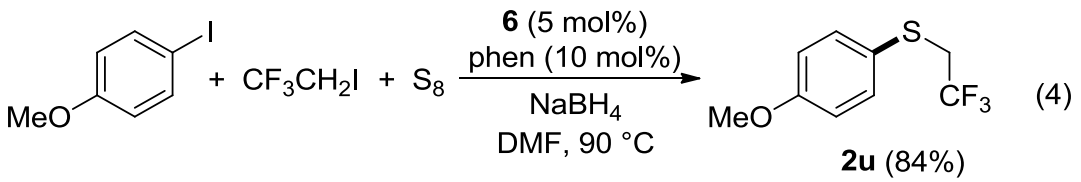
desired product **2u** in 99% yield with a rate constant of 1.01×10^{-3} s^{-1} (Eqn 2). These results provide support for the possible role of **5** as an intermediate in the catalytic cycle of 2,2,2-trifluoroethylthiolation reaction.



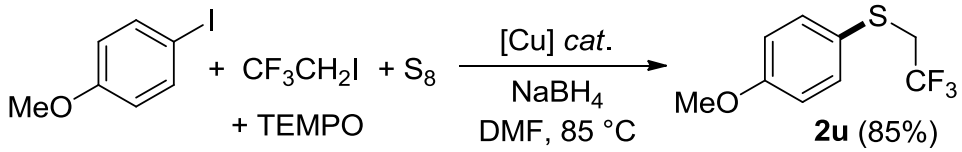


Alternatively, the copper(I) thiophenolato complex could also be involved in the reaction.[20,26] Indeed, the reaction of [(phen)Cu(μ-SC_6H_4-*p*-OMe)]$_2$ (**6**) with 2 equiv of CF_3CH_2I in DMF at 85 °C for 12 h provided the desired product **2u** in only 32% NMR yield (Eqn 3). However, the catalytic 2,2,2-trifluoroethylthiolation of 4-iodoanisole with CF_3CH_2I and elemental sulfur catalyzed by **6** (5 mol%) furnished the desired product **3u** in 84% yield (Eqn 4). These results indicate that **6** may also serve as an intermediate in the catalytic cycle of reaction.





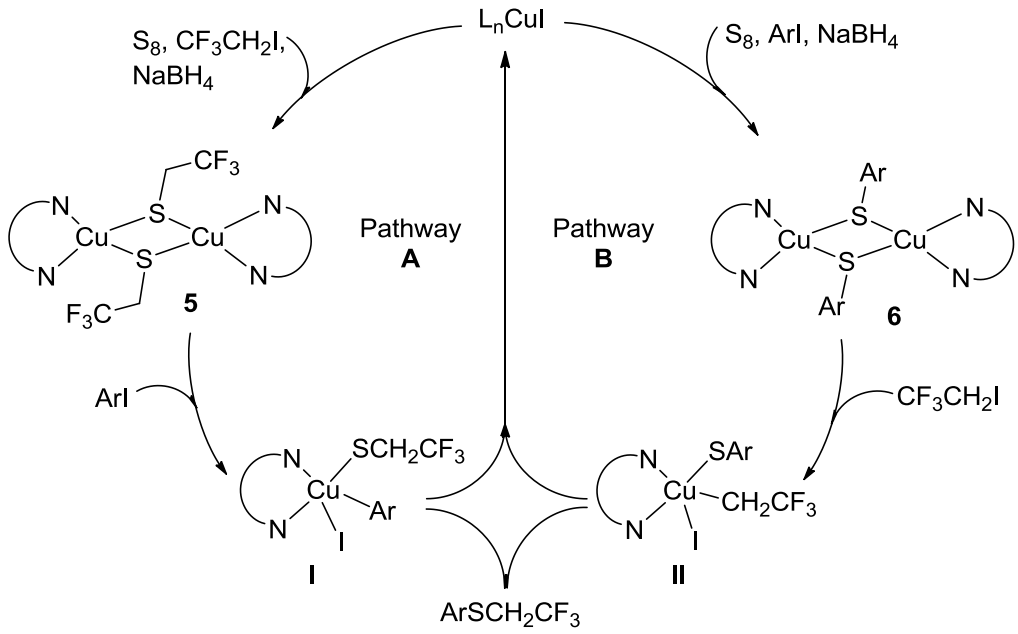
Subsequently, the copper-catalyzed 2,2,2-trifluoroethylthiolation of 4-iodoanisole was performed in the presence of radical scavengers like 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO). Under the optimized reaction conditions, the desired product **2u** was isolated in good yield (Scheme 6). The addition of TEMPO had no apparent effect on the 2,2,2-trifluoroethylthiolation reaction, indicating that radical intermediate may not be involved in this process.



Scheme 6. Inhibition Experiment with TEMPO

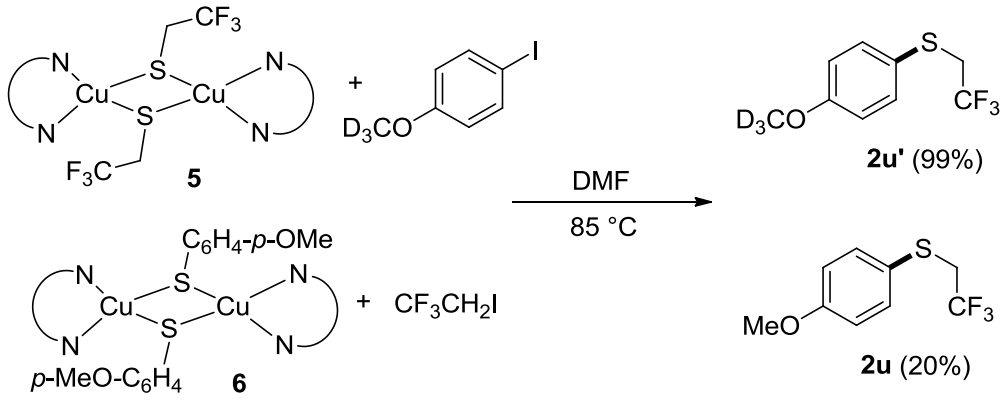
Based on the above studies, a plausible mechanism of the 2,2,2-trifluoroethylthiolation reaction is provided in Scheme 7 based on the experimental observations. The L_nCuI may follow one of two pathways: the reaction with CF_3CH_2I and elemental sulphur in the presence of $NaBH_4$ may form complex **5**, which upon oxidative addition with aryl iodides generates intermediate **I**. Subsequently, intermediate **I** undergoes reductive elimination to afford the desired

2,2,2-trifluoroethylthiolated product and re-generates L_nCuI (Pathway **A**). Another plausible sequence (pathway B) may occur by the reaction of L_nCuI with aryl iodides and elemental sulphur under reductive conditions[20] to form the copper(I) thiophenolato complex **6**,[26] which upon oxidative addition with CF_3CH_2I produces intermediate **II**. The subsequent reductive elimination of **II** gives the desired product $ArSCH_2CF_3$ and generates L_nCuI (Pathway **B**).



Scheme 7. Proposed Reaction Mechanism

To further distinguish which pathway is favoured pathway, a cross-over experiment was carried out. The reaction of **5** with 4-iodoanisole-d_3 reacted faster than that of **6** with CF_3CH_2I (Scheme 8). These results clearly demonstrate that the Pathway **A** involving the formation of **5** probably is favored during the catalytic cycles although we could not rule out Pathway **B**.



Scheme 8. Cross Over Experiments

In summary, the 2,2,2-trifluoroethylthiolation reaction of aryl bromides and iodides with elemental sulfur, and 1,1,1-trifluoro-2-iodoethane was achieved by copper catalysis. This method offers a new strategy to selectively construct aryl 2,2,2-trifluoroethyl thioethers in good to excellent yield from readily available, inexpensive reagents. Moreover, these reactions are operationally simple, scalable and compatible with varied functional groups. These aryl 2,2,2-trifluoroethyl thioethers constitute a group of synthetically demanding and medicinally important compounds. Mechanistic studies indicate that the copper thiolate species **5** may be involved as key intermediates of the catalytic cycle.

EXPERIMENTAL SECTION

General Methods: All manipulations were carried out under an inert atmosphere using a nitrogen-filled glovebox or standard Schlenk techniques. All glassware was oven or flame dried immediately prior to use. Solvents were freshly dried and

degassed according to the procedures in Purification of Laboratory Chemicals prior to use. Deuterated solvents were purchased commercially, and were degassed and stored over activated 4 Å molecular sieves. 5-iodo-2*H*-[1,2'-bipyridin]-2-one (**3**)[27] was prepared according to the published procedures. All other reagents were obtained from commercial sources and used without further purification. The ^{1}H, ^{19}F and $^{13}C\{^{1}H\}$NMR spectra were recorded at 400, 376, and 101 MHz, respectively. ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as outside standard and low field is positive. Mass spectrometry was performed on GC/MS spectrometer under electron impact (EI) ionization technique. HRMS data were recorded on a GC-TOF instrument using EI technique.

General procedure A (for the copper-catalyzed 2,2,2-trifluoroethylthiolation reaction of aryl iodides): In a dry-box, CuI (9.5 mg, 0.050 mmol), phen (18 mg, 0.10 mmol), $NaBH_4$ (57 mg, 1.5 mmol), S_8 (32 mg, 1.0 mmol), CF_3CH_2I (98.5 μL, 1.0 mmol), aryl iodides (0.50 mmol), and 5.0 mL DMF were added to a oven-dried 25 mL test tube with Teflon screw cap. The tube was sealed and the solution was placed into a preheated 85 °C oil bath for 12 h. The tube was removed from the oil bath and cooled to r.t. The reaction mixture was filtered through a layer of Celite, eluted with diethyl ether. Water (5.0 mL) was added to the mixture at 0 ℃. The resulting mixture was extracted by ethyl ether (10 mL × 3), and the combined organic layers was washed with water (10 mL × 3), and then dried over magnesium sulfate. The solvent

was removed by rotary evaporation in ice bath and the resulting product was purified by column chromatography on silica gel with pentane/Et_2O.

General procedure B (for the copper-catalyzed 2,2,2-trifluoroethylthiolation reaction of aryl bromides): In a dry-box, CuI (9.5 mg, 0.050 mmol), 5,5-dimethylcyclohexane-1,3-dione (14 mg, 0.10 mmol), $NaBH_4$ (57 mg, 1.5 mmol), S_8 (32 mg, 1 mmol), ICH_2CF_3 (98.5 μL, 1.0 mmol), aryl bromides 0.50 mmol), and 5.0 mL DMF were added to a oven-dried 25 mL test tube with Teflon screw cap. The tube was sealed and the solution was placed into a preheated 95 °C oil bath for 12 h. The tube was removed from the oil bath and cooled to r.t. The reaction mixture was filtered through a layer of Celite, eluted with diethyl ether. Water (5.0 mL) was added to the mixture at 0 ℃. The resulting mixture was extracted by ethyl ether (10 mL × 3), and the combined organic layers was washed with water (10 mL × 3), and then dried over magnesium sulfate. The solvent was removed by rotary evaporation in ice bath and the resulting product was purified by column chromatography on silica gel with pentane/Et_2O.

***p*-Tolyl(2,2,2-trifluoroethyl)sulfane** (**2a**)**.** According to general procedure A, obtained in 81 % yield (83 mg) as a yellow oil. According to general procedure B, obtained in 71 % yield (73 mg). R_f (*n*-pentane) = 0.73. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 3.42 (q, *J* = 9.8 Hz, 2H), 2.38 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.4 (t, *J* = 9.8 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz,

$CDCl_3$) δ 138.5 (s), 132.6 (s), 131.1 (s), 130.1 (s), 125.5 (q, *J* = 276.3 Hz), 38.7 (q, *J* = 32.4 Hz), 21.1 (s). IR (KBr): ν 2928, 1680, 1607, 1581, 1305, 1242, 1081, 870, 592 cm^{-1}. GC-MS m/z 206 (M^+). HRMS (EI) m/z: calcd. for $C_9H_9SF_3$: 206.0377; found: 206.0383.

(3,5-Dimethylphenyl)(2,2,2-trifluoroethyl)sulfane (**2b**)**.** According to general procedure A, obtained as a yellow oil in 93% yield (102 mg). R_f (*n*-pentane) = 0.59. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.13 (s, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 3.46 (q, *J* = 9.3 Hz, 2H), 2.33 (s, 3H), 2.29 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.4 (t, *J* = 9.3 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 139.0 (s), 133.2 (s), 129.8 (s), 129.2 (s), 125.4 (q, *J* = 277.8 Hz), 38.0 (q, *J* = 32.5 Hz), 21.2 (s). IR (KBr): ν 2934, 1682, 1601, 1581, 1379, 1271, 1125, 848, 546 cm^{-1}. GC-MS m/z 220 (M^+). HRMS (EI) m/z: calcd. for $C_{10}H_{11}SF_3$: 220.0534; found: 220.0537.

(4-(*tert*-Butyl)phenyl)(2,2,2-trifluoroethyl)sulfane (2c). According to general procedure A, obtained as a yellow oil in 71% yield (88 mg). R_f (*n*-pentane) = 0.86. ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.2, Hz, 2H), 7.41 (d, *J* = 8.2 Hz, 2H), 3.46 (q, *J* = 9.7 Hz, 2H), 1.37 (d, *J* = 1.4 Hz, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.3 (t, *J* = 9.7 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 151.6 (s), 132.1 (s), 130.2 (s), 126.3 (s), 125.5 (q, *J* = 276.4 Hz), 38.5 (q, *J* = 32.5 Hz), 34.6 (s), 31.2 (s). IR (KBr): ν 2965, 2870, 1490, 1399, 1364, 1306, 1268, 1119, 1014, 828, 556 cm^{-1}. GC-MS m/z 248 (M^+). HRMS (EI) m/z: calcd. for $C_{12}H_{15}SF_3$: 248.0847; found: 248.0839.

[1,1'-Biphenyl]-4-yl(2,2,2-trifluoroethyl)sulfane (2d). According to general procedure A, obtained as a white solid in 75% yield (101 mg). R_f (*n*-pentane) = 0.41.

M.p: 74-75 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.56 (m, 7H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.44 – 7.36 (m, 1H), 3.51 (q, *J* = 9.5 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.2 (t, *J* = 9.5 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 141.1 (s), 140.1 (s), 132.6 (s), 132.2 (s), 129.5 (s), 128.9 (s), 127.9 (s), 127.7 (s), 127.1 (s), 125.4 (q, *J* = 276.5 Hz), 38.2 (q, *J* = 32.6 Hz). IR (KBr): ν 2927, 1680, 1479, 1398, 1308, 1243, 1127, 1007, 833, 698 cm^{-1}. GC-MS m/z 268 (M^+). HRMS (EI) m/z: calcd. for $C_{14}H_{11}SF_3$: 268.0534; found: 268.0527.

[1,1'-Biphenyl]-2-yl(2,2,2-trifluoroethyl)sulfane (2e). According to general procedure A, obtained as a yellow oil in 97% yield (130 mg). R_f (*n*-pentane) = 0.50. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.57 (m, 1H), 7.51 – 7.42 (m, 5H), 7.37 (m, 3H), 3.18 (q, *J* = 9.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.9 (t, *J* = 9.7 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 144.0 (s), 140.3 (s), 131.9 (s), 131.7 (s), 130.8 (s), 129.4 (s), 128.2 (s), 127.9 (s), 127.7 (s), 125.3 (q, *J* = 277.8 Hz), 36.8 (q, *J* = 32.5 Hz). IR (KBr): ν 2928, 1681, 1586, 1596, 1463, 1307, 1270, 1125, 1039, 840, 650 cm^{-1}. GC-MS m/z 268 (M^+). HRMS (EI) m/z: calcd. for $C_{14}H_{11}SF_3$: 268.0534; found: 268.0531.

(4-Nitrophenyl)(2,2,2-trifluoroethyl)sulfane (2f). According to general procedure A, obtained as a yellow oil in 99% yield (117 mg). According to general procedure B, obtained in 96% yield (114 mg). R_f (*n*-pentane:ether=10:1) = 0.48. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 3.63 (q, *J* = 9.3 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.1 (t, *J* = 9.3 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 146.5 (s), 143.2 (s), 128.8 (s), 124.9 (q, *J* = 276.7

Hz), 124.2 (s), 35.8 (q, *J* = 33.8 Hz). IR (KBr): ν 2925, 2854, 1635, 1582, 1518, 1341, 1242, 1131, 853, 682 cm^{-1}. GC-MS m/z 237 (M^+). HRMS (EI) m/z: calcd. for $C_8H_6SNO_2F_3$: 237.0071; found: 237.0067.

(2-Methyl-4-nitrophenyl)(2,2,2-trifluoroethyl)sulfane (2g). According to general procedure A, obtained as a yellow oil in 99% yield (124 mg). R_f (*n*-pentane:ether=10:1) = 0.61. ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 – 8.02 (m, 2H), 7.46 (d, *J* = 9.2 Hz, 1H), 3.63 (q, *J* = 9.4 Hz, 2H), 2.50 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.2 (t, *J* = 9.4 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 149.5 (s), 136.0 (s), 135.4 (s), 133.6 (s), 132.9 (s), 127.5 (s), 125.1 (q, *J* = 277.8 Hz), 37.8 (q, *J* = 33.3 Hz), 20.2 (s). IR (KBr): ν 2934, 1609, 1525, 1449, 1310, 1243, 1129, 1082, 799, 637 cm^{-1}. GC-MS m/z 251 (M^+). HRMS (EI) m/z: calcd. for $C_9H_8SNO_2F_3$: 251.0228; found: 251.0226.

(3-Nitrophenyl)(2,2,2-trifluoroethyl)sulfane (2h). According to general procedure A, obtained as a yellow oil in 85% yield (101 mg). R_f (*n*-pentane:ether=10:1) = 0.42. ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 3.56 (q, *J* = 9.4 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.2 (t, *J* = 9.4 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 136.8 (s), 136.2 (s), 130.1 (s), 125.5 (s), 125.0 (q, *J* = 277.8 Hz), 122.8 (s), 37.4 (q, *J* = 33.3 Hz). IR (KBr): ν 2940, 1591, 1481, 1427, 1308, 1245, 1268, 1126, 1043, 861, 687 cm^{-1}. GC-MS m/z 237 (M^+). HRMS (EI) m/z: calcd. for $C_8H_6SNO_2F_3$: 237.0071; found: 237.0069.

Ethyl 4-((2,2,2-trifluoroethyl)thio)benzoate (2i). According to general

procedure A, obtained as a yellow oil in 99% yield (131 mg). R_f (*n*-pentane:ether=10:1) = 0.44. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.4 Hz, 2H), 7.47 (d, *J* = 7.4 Hz, 2H), 4.39 (q, *J* = 7.0 Hz, 2H), 3.55 (q, *J* = 9.5 Hz, 2H), 1.40 (t, *J* = 7.0 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.2 (t, *J* = 9.5 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 165.9 (s), 139.9 (s), 130.4 (d, *J* = 3.0 Hz), 130.2 (s), 129.3 (s), 129.2 (s), 125.1 (q, *J* = 277.6 Hz), 61.2 (s), 36.4 (q, *J* = 33.3 Hz), 14.3 (s). IR (KBr): ν 2985, 1711, 1595, 1477, 1368, 1272, 1106, 1017, 843, 637 cm^{-1}. GC-MS m/z 264 (M^+). HRMS (EI) m/z: calcd. for $C_{11}H_{11}SO_2F_3$: 264.0432; found: 264.0430.

Methyl 4-((2,2,2-trifluoroethyl)thio)benzoate (2j). According to general procedure B, obtained as a yellow oil in 76% yield (95 mg). R_f (*n*-pentane:ether=10:1) = 0.41. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.9 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 3.94 (s, 3H), 3.56 (q, *J* = 9.5 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.2 (t, *J* = 9.5 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 166.4 (s), 140.0 (s), 130.3 (s), 129.1 (s), 129.0 (s), 125.1 (q, *J* = 277.6 Hz), 52.3 (s), 36.4 (q, *J* = 33.4 Hz). IR (KBr): ν 2953, 1718, 1596, 1492, 1436, 1308, 1242, 1116, 1015, 842 ,691 cm^{-1}. GC-MS m/z 250 (M^+). HRMS (EI) m/z: calcd. for $C_{10}H_9SO_2F_3$: 250.0275; found: 250.0269.

Methyl 3-((2,2,2-trifluoroethyl)thio)benzoate (2k). According to general procedure A, obtained as a yellow oil in 95% yield (125 mg). R_f (*n*-pentane:ether=10:1) = 0.41. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 3.95 (s, 3H), 3.50 (q, *J* = 9.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.3 (t, *J* = 9.6 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 166.2 (s), 135.9 (s), 134.4 (s), 132.4 (s), 131.3 (s),

129.3 (s), 129.1 (s), 125.2 (q, J = 267.5 Hz), 52.4 (s), 37.8 (q, J = 33.0 Hz). IR (KBr): ν 2953, 1720, 1601, 1523, 1422, 1356, 1245, 1116, 1017, 842 ,637 cm^{-1}. GC-MS m/z 250 (M^+). HRMS (EI) m/z: calcd. for $C_{10}H_9SO_2F_3$: 250.0275; found: 250.0271.

Methyl 2-((2,2,2-trifluoroethyl)thio)benzoate (2l). According to general procedure A, obtained as a yellow oil in 88% yield (110 mg). According to general procedure B, obtained in 83% yield (104 mg). R_f (*n*-pentane:ether=10:1) = 0.31. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.6 Hz, 1H), 7.59 – 7.42 (m, 2H), 7.36 – 7.29 (m, 1H), 3.96 (s, 3H), 3.60 (q, J = 9.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.2 (t, J = 9.7 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 166.9 (s), 137.1 (s), 132.5 (s), 131.2 (s), 130.0 (s), 128.4 (s), 126.1 (s), 125.4 (q, J = 277.7 Hz), 52.4 (s), 35.8 (q, J = 32.5 Hz). IR (KBr): ν 2953, 1713, 1589, 1466, 1435, 1310, 1255, 1126, 1060, 963, 692 cm^{-1}. GC-MS m/z 250 (M^+). HRMS (EI) m/z: calcd. for $C_{10}H_9SO_2F_3$: 250.0275; found: 250.0269.

4-((2,2,2-Trifluoroethyl)thio)benzonitrile (2m). According to general procedure A, obtained as a yellow oil in 90% yield (97 mg). According to general procedure B, obtained in 85% yield (92 mg). R_f (*n*-pentane:ether=10:1) = 0.22. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 7.8 Hz, 2H), 7.50 (d, J = 7.8 Hz, 2H), 3.58 (q, J = 9.4 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.1 (t, J = 9.4 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 140.8 (s), 132.6 (s), 129.3 (s), 125.0 (q, J = 276.7 Hz), 118.3 (s), 110.7 (s), 36.0 (q, J = 33.7 Hz). IR (KBr): ν 2921, 2229, 1594, 1487, 1400, 1315, 1241, 1129, 1016, 823, 637, 545 cm^{-1}. GC-MS m/z 217 (M^+). HRMS (EI) m/z: calcd. for $C_9H_6SNF_3$: 217.0175; found: 217.0173.

2-((2,2,2-Trifluoroethyl)thio)benzonitrile (2n). According to general procedure B, obtained as a yellow oil in 82% yield (89 mg). R_f (*n*-pentane:ether=10:1) = 0.32. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.65 (m, 2H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 3.58 (q, *J* = 9.4 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.1 (t, *J* = 9.4 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 137.2 (s), 134.1 (s), 133.8 (s), 133.3 (s), 128.8 (s), 125.0 (q, *J* = 277.7 Hz), 116.8 (s), 116.6 (s), 37.5 (q, *J* = 33.3 Hz). IR (KBr): ν 2928, 2227, 1675, 1586, 1467, 1312, 1242, 1128, 1084, 840, 637 cm^{-1}. GC-MS m/z 217 (M^+). HRMS (EI) m/z: calcd. for $C_9H_6SNF_3$: 217.0169; found: 217.0173.

1-(4-((2,2,2-Trifluoroethyl)thio)phenyl)ethanone (2o). According to general procedure A, obtained as a yellow oil in 78% yield (91 mg). According to general procedure B, obtained as a yellow oil in 85% yield (100 mg). R_f (*n*-pentane:ether=10:1) = 0.14. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.8 Hz, 2H), 7.50 (d, *J* = 7.8 Hz, 2H), 3.58 (q, *J* = 9.7 Hz, 2H), 2.62 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.2 (t, *J* = 9.5 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 197.1 (s), 140.4 (s), 135.7 (s), 129.1 (s), 129.0 (s), 125.0 (q, *J* = 277.7 Hz), 36.2 (q, *J* = 33.5 Hz), 26.6 (s). IR (KBr): ν 2933, 1682, 1591, 1560, 1359, 1264, 1131, 957, 821, 590 cm^{-1}. GC-MS m/z 234 (M^+). HRMS (EI) m/z: calcd. for $C_{10}H_{11}SOF_3$ (M^++2H): 236.0483; found: 236.0480.

1-(3-((2,2,2-Trifluoroethyl)thio)phenyl)ethanone (2p). According to general procedure A, obtained as a yellow oil in 97% yield (113 mg). R_f (*n*-pentane:ether=10:1) = 0.13. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.40 (d, *J*

= 6.8 Hz, 1H), 7.37 – 7.30 (m, 2H), 3.47 (q, *J* = 9.6 Hz, 2H), 1.49 (d, *J* = 6.3 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.3 (t, *J* = 9.6 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 147.1 (s), 133.9 (s), 130.5 (s), 129.4 (s), 128.6 (s), 125.1 (s), 125.4 (q, *J* = 277.5 Hz), 69.9 (s), 37.9 (q, *J* = 32.7 Hz), 25.3 (s). IR (KBr): ν 2976, 1593, 1473, 1411, 1306, 1242, 1076, 791, 700, 532 cm^{-1}. GC-MS m/z 234 (M^+). HRMS (EI) m/z: calcd. for $C_{10}H_9SOF_3$: 234.0326; found: 234.0317.

(2,2,2-Trifluoroethyl)(4-(trifluoromethyl)phenyl)sulfane (2q). According to general procedure A, obtained as a white oil in 84% yield (110 mg). R_f (*n*-pentane) = 0.75. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 3.54 (q, *J* = 9.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.7 (s, 3F), -66.2 (t, *J* = 9.6 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 138.7 (q, *J* = 1.6 Hz), 130.2 (s), 129.7 (q, *J* = 32.9 Hz), 126.1 (q, *J* = 3.8 Hz), 125.2 (s), 125.1 (q, *J* = 277.6 Hz), 122.5 (s), 36.8 (q, *J* = 33.4 Hz). IR (KBr): ν 2934, 1609, 1506, 1402, 1327, 1240, 1131, 1015, 832, 595 cm^{-1}. GC-MS m/z 260 (M^+). HRMS (EI) m/z: calcd. for $C_9H_6SF_6$: 260.0094; found: 260.0097.

(2,2,2-Trifluoroethyl)(4-(trifluoromethyl)phenyl)sulfane (2r). According to general procedure A, obtained as a yellow oil in 81% yield (112 mg). R_f (*n*-pentane) = 0.64. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.3 Hz, 2H), 3.45 (q, *J* = 9.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (s, 3F), -66.3 (t, *J* = 9.6 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 149.2 (q, *J* = 1.9 Hz), 133.7 (s), 132.2 (s), 125.2 (q, *J* = 276.4 Hz), 121.7 (q, *J* = 1.0 Hz), 120.4 (q, *J* = 258.8 Hz), 38.3 (q, *J* = 32.9 Hz). IR (KBr): ν 2944, 1491, 1445, 1384, 1257, 1208, 1046, 856, 545 cm^{-1}.

GC-MS m/z 276 (M^+). HRMS (EI) m/z: calcd. for $C_9H_6SOF_6$: 276.0044; found: 276.0050.

(2-Methoxyphenyl)(2,2,2-trifluoroethyl)sulfane (2s). According to general procedure A, obtained as a yellow oil in 62% yield (69 mg). R_f (*n*-pentane) = 0.45. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.00 – 6.90 (m, 2H), 3.95 (s, 3H), 3.48 (q, *J* = 9.8 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.0 (t, *J* = 9.8 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 158.7 (s), 134.1 (s), 130.1 (s), 125.6 (q, *J* = 276.5 Hz), 121.1 (s), 120.5 (s), 111.0 (s), 55.8 (s), 35.6 (q, *J* = 32.3 Hz). IR (KBr): ν 2939, 1583, 1478, 1434, 1307, 1240, 1081, 1024, 841, 638 cm^{-1}. GC-MS m/z 222 (M^+). HRMS (EI) m/z: calcd. for $C_9H_9SOF_3$: 222.0326; found: 222.0330.

(3-Methoxyphenyl)(2,2,2-trifluoroethyl)sulfane (2t). According to general procedure A, obtained as a yellow oil in 93% yield (103 mg). R_f (*n*-pentane) = 0.47. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.22 (m, 1H), 7.13 – 7.00 (m, 2H), 6.86 (d, *J* = 8.2 Hz, 1H), 3.84 (s, 3H), 3.48 (q, *J* = 9.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.3 (t, *J* = 9.6 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 159.9 (s), 134.9 (s), 130.1 (s), 125.3 (q, *J* = 276.4 Hz), 123.6 (s), 116.8 (s), 113.7 (s), 55.4 (s), 37.9 (q, *J* = 32.8 Hz). IR (KBr): ν 2940, 1591, 1577, 1481, 1427, 1308, 1245, 1126, 1043, 993, 774 cm^{-1}. GC-MS m/z 222 (M^+). HRMS (EI) m/z: calcd. for $C_9H_9SOF_3$: 222.0326; found: 222.0329.

(4-Methoxyphenyl)(2,2,2-trifluoroethyl)sulfane (2u). According to general procedure A, obtained as a yellow oil in 84% yield (93 mg). According to general

procedure B, obtained in 60% yield (67 mg). R_f (*n*-pentane) = 0.60. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.5 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 2H), 3.83 (s, 3H), 3.34 (q, *J* = 9.8 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.3 (t, *J* = 9.8 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 160.2 (s), 135.4 (s), 132.8 (s), 132.7 (s), 125.5 (q, *J* = 276.5 Hz), 124.0 (s), 114.8 (s), 55.4 (s), 39.6 (q, *J* = 32.0 Hz). IR (KBr): ν 2926, 1598, 1493, 1411, 1307, 1241, 1123, 1018, 841, 502 cm^{-1}. GC-MS m/z 222 (M^+). HRMS (EI) m/z: calcd. for $C_9H_9SOF_3$: 222.0326; found: 222.0323.

(4-Chlorophenyl)(2,2,2-trifluoroethyl)sulfane (2v). According to general procedure A, obtained as a yellow oil in 82% yield (93 mg). R_f (*n*-pentane) = 0.61. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 3.43 (q, *J* = 9.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.3 (t, *J* = 9.6 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 166.4 (s), 140.0 (s), 130.3 (s), 129.1 (s), 128.9 (s), 125.1 (q, *J* = 276.7 Hz), 52.3 (s), 36.4 (q, *J* = 33.4 Hz). IR (KBr): ν 2927, 1574, 1477, 1390, 1309, 1242, 1094, 1013, 820, 500 cm^{-1}. GC-MS m/z 226 (M^+). HRMS (EI) m/z: calcd. for $C_8H_6SClF_3$: 225.9831; found: 225.9837.

(3-Fluorophenyl)(2,2,2-trifluoroethyl)sulfane (2w). According to general procedure A, obtained as a yellow oil in 99% yield (104 mg). R_f (*n*-pentane) = 0.65. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 2H), 7.21 (d, *J* = 9.0 Hz, 1H), 7.02 (t, *J* = 8.4 Hz, 1H), 3.49 (q, *J* = 9.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.3 (t, *J* = 9.6 Hz, 3F), -111.4 - -111.5 (m, 1F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 163.9 (s), 161.4 (s), 135.8 (d, *J* = 7.9 Hz), 130.6 (d, *J* = 8.5 Hz), 126.8 (d, *J* = 3.0 Hz), 125.2 (q, *J* = 276.4 Hz), 118.1 (d, *J* = 22.3 Hz), 37.6 (q, *J* = 33.1 Hz). IR (KBr): ν 2927, 2855,

1598, 1580, 1475, 1310, 1263, 1128, 881, 520 cm^{-1}. GC-MS m/z 210 (M^+). HRMS (EI) m/z: calcd. for $C_8H_6SF_4$: 210.0126; found: 210.0125.

Naphthalen-1-yl(2,2,2-trifluoroethyl)sulfane (2x). According to general procedure A, obtained as a yellow oil in 91% yield (110 mg). R_f (*n*-pentane) = 0.63. ^1H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.5 Hz, 1H), 7.97 – 7.84 (m, 3H), 7.67 (t, *J* = 7.3 Hz, 1H), 7.59 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 3.49 (q, *J* = 9.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.0 (t, *J* = 9.7 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 134.3 (s), 133.6 (s), 133.3 (s), 130.4 (s), 130.0 (s), 128.9 (s), 129.19 – 127.70 (m), 127.3 (s), 126.5 (s), 125.7 (s), 125.4 (q, *J* = 279.8 Hz), 125.2 (s), 38.1 (q, *J* = 32.4 Hz). IR (KBr): ν 3057, 1503, 1411, 1380, 1306, 1242, 1124, 973, 840, 649 cm^{-1}. GC-MS m/z 242 (M^+). HRMS (EI) m/z: calcd. for $C_{12}H_9SF_3$: 242.0377; found: 242.0373.

(9*H*-fluoren-3-yl)(2,2,2-trifluoroethyl)sulfane (2y). According to general procedure A, obtained as a white solid in 83% yield (116 mg). R_f (*n*-pentane) = 0.43. M.p: 69-72 ℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.69 (m, 3H), 7.62 – 7.53 (t, *J* = 8.1 Hz, 2H), 7.47 – 7.32 (m, 2H), 3.92 (s, 2H), 3.51 (q, *J* = 9.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.2 (t, *J* = 9.7 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 144.3 (s), 143.3 (s), 142.1 (s), 140.7 (s), 131.5 (s), 131.1 (s), 129.1 (s), 127.3 (s), 127.0 (s), 125.5 (q, *J* = 276.5 Hz), 125.2 (s), 120.5 (s), 120.2 (s), 38.8 (q, *J* = 32.4 Hz), 36.8 (s). IR (KBr): ν 3065, 2896, 1465, 1450, 1407, 1306, 1241, 1120, 953, 828, 581 cm^{-1}. GC-MS m/z 280 (M^+). HRMS (EI) m/z: calcd. for $C_{15}H_{11}SF_3$: 280.0534; found: 280.0533.

Methyl 5-((2,2,2-trifluoroethyl)thio)nicotinate (2aa). According to general procedure B, obtained as a yellow oil in 89% yield (117 mg). R_f (*n*-pentane:ether=5:1) = 0.40. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.3 Hz, 1H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.47 – 7.35 (m, 1H), 4.14 (q, *J* = 9.9 Hz, 2H), 4.00 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.5 (t, *J* = 9.9 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 165.2 (s), 155.5 (s), 147.7 (s), 137.4 (s), 125.8 (s), 125.3 (q, *J* = 277.0 Hz), 122.1 (s), 52.9 (s), 31.2 (q, *J* = 33.7 Hz). IR (KBr): ν 2999, 2953, 1730, 1580, 1446, 1429, 1308, 1245, 1132, 977, 844 cm^{-1}. GC-MS m/z 251 (M^+). HRMS (EI) m/z: calcd. for $C_9H_8SNO_2F_3$: 251.0228; found: 251.0233.

5-((2,2,2-Trifluoroethyl)thio)quinoline (2ab). According to general procedure B, obtained as a yellow oil in 61% yield (74 mg). R_f (*n*-pentane:ether=5:1) = 0.29. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.36 (s, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.95 – 7.72 (m, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 3.53 (q, *J* = 9.5 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.2 (t, *J* = 9.5 Hz, 3F). ^{13}C{^{1}H}NMR (101 MHz, $CDCl_3$) δ 152.9 (s), 147.3 (s), 139.8 (s), 130.4 (s), 130.0 (s), 129.4 (s), 128.8 – 127.2 (m), 127.6 (d, *J* = 4.8 Hz), 125.2 (q, *J* = 277.8 Hz), 123.8 (s), 38.3 (q, *J* = 32.8 Hz). IR (KBr): ν 2976, 1620, 1567, 1488, 1382, 1272, 1130, 1046, 888, 547 cm^{-1}. GC-MS m/z 242 (M^+-H). HRMS (EI) m/z: calcd. for $C_{11}H_8SNF_3$: 243.0330; found: 243.0331.

6-Methoxy-2-((2,2,2-trifluoroethyl)thio)benzo[*d*]thiazole (2ac). According to general procedure B, obtained as a white solid in 76% yield (106 mg). R_f (*n*-pentane:ether=10:1) = 0.68. M.p: 70-71 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.9 Hz, 1H), 7.25 (d, *J* = 2.5 Hz, 1H), 7.06 (dd, *J* = 8.9, 2.6 Hz, 1H), 4.12 (q, *J* =

9.7 Hz, 2H), 3.87 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.4 (t, *J* = 9.7 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 159.4 (s), 157.5 (s), 147.1 (s), 137.1 (s), 124.8 (q, *J* = 276.4 Hz), 122.4 (s), 115.3 (s), 104.1 (s), 55.8 (s), 34.6 (q, *J* = 34.3 Hz). IR (KBr): ν 2954, 1602, 1560, 1480, 1309, 1224, 1135, 1002, 831, 649 cm^{-1}. GC-MS m/z 280 (M^++H). HRMS (EI) m/z: calcd. for $C_{10}H_8S_2NOF_3$: 278.9999; found: 278.9993.

Methyl 3-((2,2,2-trifluoroethyl)thio)thiophene-2-carboxylate (2ad). According to general procedure A, obtained as a yellow solid in 36% yield (46 mg). R_f (*n*-pentane:ether=10:1) = 0.43. M.p: 73-75 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 5.3 Hz, 1H), 7.08 (d, *J* = 5.3 Hz, 1H), 3.92 (s, 3H), 3.64 (q, *J* = 9.6 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.8 (t, *J* = 9.6 Hz). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 162.1 (s), 139.6 (s), 131.2 (s), 127.7 (q, *J* = 1.6 Hz), 125.3 (s), 125.1 (q, *J* = 276.7 Hz), 52.2 (s), 35.9 (q, *J* = 33.4 Hz). IR (KBr): ν 3096, 2949, 2360, 1686, 1493, 1442, 1401, 1267, 1134, 1075, 896, 767, 636 cm^{-1}. GC-MS m/z 256 (M^+-H). HRMS (EI) m/z: calcd. for $C_8H_7S_2O_2F_3$: 255.9840; found: 255.9842.

5-((2,2,2-Trifluoroethyl)thio)-2*H*-[1,2'-bipyridin]-2-one (4). According to general procedure A, obtained as a yellow oil in 66% yield (94 mg). R_f (*n*-pentane:ether=1:1) = 0.23. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.6 Hz, 1H), 8.25 (s, 1H), 7.97 – 7.82 (m, 2H), 7.52 (d, *J* = 9.6 Hz, 1H), 7.37 (s, 1H), 6.63 (d, *J* = 9.5 Hz, 1H), 3.29 (q, *J* = 9.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.1 (t, *J* = 9.7 Hz, 3F). $^{13}C\{^1H\}$NMR (101 MHz, $CDCl_3$) δ 161.1 (s), 151.0 (s), 149.1 (s), 145.4 (s), 142.3 (s), 138.0 (s), 125.3 (q, *J* = 276.5 Hz), 123.6 (s), 122.5 (s), 121.2 (s), 110.0 (s), 39.3 (q, *J* = 32.1 Hz). IR (KBr): ν 3394, 2973, 1667, 1597, 1525, 1435, 1308, 1269,

1126, 1048, 795, 674, 567 cm^{-1}. GC-MS m/z 285 (M^+-H). HRMS (EI) m/z: calcd. for $C_{12}H_9SON_2F_3$: 286.0388; found: 286.0383.

Gram scale reactions for synthesis of (4-nitrophenyl)(2,2,2-trifluoroethyl)sulfane (2f). CuI (76 mg, 0.40 mmol), phen (144 mg, 0.80 mmol), $NaBH_4$ (454 mg, 12 mmol), S_8 (256 mg, 8.0 mmol), ICH_2CF_3 (788 μL, 8.0 mmol), 1-iodo-4-nitrobenzene (996 mg, 4.0 mmol), and 20 mL DMF were added to a oven-dried 75 mL test tube with Teflon screw cap. The tube was sealed and the solution was placed into a preheated 85 °C oil bath for 12 h. The tube was removed from the oil bath and cooled to r.t. The reaction mixture was filtered through a layer of Celite, eluted with diethyl ether. Water (15.0 mL) was added to the mixture at 0 ℃. The resulting mixture was extracted by ethyl ether (15 mL × 3), and the combined organic layers was washed with water (15 mL × 3), and then dried over magnesium sulfate. The solvent was removed by rotary evaporation in ice bath and the resulting product was purified by column chromatography on silica gel with pentane/Et_2O. Compound **2f** was obtained in 89% yield (0.85 g).

Procedure for the copper-catalyzed 2,2,2-trifluoroethylthiolation reaction of 4-iodoanisole in the presence of 1.0 equiv of TEMPO. CuI (3.8 mg, 0.020 mmol), phen (7.2 mg, 0.040 mmol), $NaBH_4$ (23 mg, 0.60 mmol), S_8 (13 mg, 0.40 mmol), ICH_2CF_3 (40 μL, 0.40 mmol), 4-iodoanisole (47 mg, 0.20 mmol), TEMPO (62.5 mg, 0.40 mmol), and 2 mL DMF were added to a oven-dried 5 mL test tube with Teflon screw cap. The tube was sealed and the solution was placed into a preheated 85 °C oil

bath for 12 h. The tube was removed from the oil bath and cooled to room temperature, and then 10 μL (trifluoromethoxy)benzene was added as an internal standard. The reaction mixture was then filtered through a layer of celite. The filtrate was analyzed by ^{19}F NMR and GC-MS. The yield of (4-methoxyphenyl)(2,2,2-trifluoroethyl)sulfane (**2u**) was calculated to be 85%.

Procedure for the crossover experiment for the copper-catalyzed 2,2,2-trifluoroethylthiolation reaction of aryl bromides): In a dry-box, complex **5** (72 mg, 0.10 mmol), and complex **6** (77 mg, 0.10 mmol), 4-iodoanisole-d_3 (47.5 mg, 0.20 mmol), CF_3CH_2I (42 mg, 0.20 mmol), and 2 mL DMF were added to a oven-dried 5 mL test tube with Teflon screw cap. The tube was sealed and the solution was placed into a preheated 85 °C oil bath for 12 h. The tube was removed from the oil bath and cooled to room temperature, and then 10 μL (trifluoromethoxy)benzene was added as an internal standard. The reaction mixture was then filtered through a layer of celite. The filtrate was analyzed by ^{19}F NMR and GC-MS. The yield of (4-methoxyphenyl)(2,2,2-trifluoroethyl)sulfane (**2u**) and (4-methoxyphenyl)(2,2,2-trifluoroethyl)sulfane-d_3 (**2u′**) was calculated to be 20% and 99%, respectively.

Synthesis of [(phen)Cu(μ-SCH_2CF_3)]$_2$ (5). A solution of NaO*t*-Bu (190 mg, 2.0 mmol) in 10 mL of THF was added to a suspension of CuCl (200 mg, 2 mmol) in 20 mL of THF, and the resulting mixture was stirred at room temperature for 30 min. The resulting light yellow mixture was filtered through a layer of Celite. To this filtrate was added a solution of 1,10-phenanthroline (360 mg, 2.0 mmol) in 10 mL of

THF. The resulting solution turned reddish brown immediately and was stirred at room temperature for an additional 5 min. 2,2,2-trifluoroethanethiol (*ca* 2.0 mmol; prepared in situ from reaction of NaSH with CF_3CH_2I) was added dropwise and the mixture was further stirred at room temperature for 20 min. The solution was filtered, and the filtrate was added 10 ml diethyl ether. The product precipitated from the solution immediately as a red-brown precipitate. The product was separated by filtration through a fine fritted funnel and washed with pentane to afford 610 mg (83% yield) of **5**. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 9.47 (s, 4H), 8.50 (d, J = 8.1 Hz, 4H), 8.01 (s, 4H), 7.92 – 7.82 (m, 4H), 3.21 (s, 4H). ^{19}F NMR (376 MHz, CD_2Cl_2) δ -67.4 (s, 6F). ^{13}C{^{1}H}NMR (101 MHz, CD_2Cl_2) δ 149.7 (s), 143.6 (s), 136.2 (s), 128.8 (s), 126.7 (s), 124.6 (s), 65.7 (s), $\underline{C}F_3$ was not observed. Elemental Analysis (%) calculated for $C_{28}H_{20}Cu_2F_6N_4S_2$: C 46.86, H 2.81, N 7.81. Found: C 46.85, H 2.65, N 7.91.

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■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: liaoxuebin@mail.tsinghua.edu.cn (X.L.).

*E-mail: zweng@fzu.edu.cn (Z.W.).

Supporting Information

Full NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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