Copper-Mediated Di- and Monofluoromethanesulfonylation of Arenediazonium Tetrafluoroborates: Probing the Fluorine Effect

Bo Xing, a Chuanfa Ni, a and Jinbo Hu a,*

ABSTRACT A copper-mediated di- and monofluoromethanesulfonylation of arenediazonium tetrafluoroborates using di- and monofluoromethanesulfinate reagents provides aryldifluoromethyl (or monofluoromethyl) sulfoxones in good yields. It was found that the relative reactivity of these sodium difluoromethanesulfimates in the present reactions decreases in the following order: CH3FSO2Na > CF2HHSO2Na > CF2SO2Na. Keywords: difluoromethanesulfonylation, fluoromethanesulfonylation, arenediazonium, sodium sulfinate, fluorine effect

Introduction

Nowadays, fluorinated organic compounds play increasingly important roles in pharmaceutical and agrochemical industries, owing to the fact that fluorine or fluorine-containing groups could effectively improve the metabolic stability, lipophilicity, and biological potency of a target drug molecule. Among various fluorine-containing groups, the gem-difluoromethylene (CF2) is known to be isosteric to the ethereal oxygen atom, and has attracted much attention. Difluoromethyl phenyl sulfoxone, PhSO2CF2H, as an effective nucleophilic reagent to introduce CF2 motif, has been widely used in organic synthesis. The “chemical chameleon” character of the phenylsulfoxyl group enables it a highly useful synthons to difluorinated functionalities such as difluoromethylene (–CF2=), difluoromethyl (–CF2H) and difluoromethyleneidene (–CF2). In addition to their widespread use in organic synthesis, difluoromethyl aryl sulfoxones (such as PT2399) have recently been reported to show biological activity as HIF-2α antagonist in preclinical kidney cancer models (Figure 1). Despite the wide applications of difluoromethyl aryl sulfoxones (ArSO2CF2H) in organic synthesis and life sciences, synthetic methods for their preparation have remained largely unexplored since the first synthesis by Hine and Porter in 1969. Difluoromethyl aryl sulfoxones are often prepared by oxidation of corresponding difluoromethyl aryl sulfides.

Figure 1. PT2399 as HIF-2α antagonist.

Recently, we were interested in two reports on the preparation of trifluoromethyl aryl sulfoxones from sodium trifluoromethanesulfinate (CF3SO2Na): in 2013, Shekhar and co-workers reported a copper-catalyzed coupling of aryl iodides salts with CF3SO2Na (Scheme 1, eq 1) [9]. In 2015, Qing and co-workers reported a copper-promoted coupling of arenediazonium tetrafluoroborates with sodium trifluoromethanesulfinate (Scheme 1, eq 2) [10]. In these reactions, both iodide salts and arenediazonium tetrafluoroborates are not able to oxidize CF3SO2Na to generate trifluoromethyl radical. Indeed, when an external oxidant (such as t-BuOOH) is used, CF3SO2Na can be oxidized to give trifluoromethyl radical and a trifluoromethylation (rather than trifluoromethanesulfinate) reaction takes place. [10] Previously, we reported a practical preparation of sodium fluoroalkanesulfimates (R5SO2Na) via NaH-mediated reduction of corresponding benzothiazol-2-yl sulfoxones (Scheme 1, eq 3), and we also found that the reactivity of these sulfoximates in radical fluoroalkylations decreases in the following order: PhCF2SO2Na > CF2HHSO2Na > CH3FSO2Na. As our continuing effort in probing the unique fluorine effects in organic reactions, we were interested in finding out the reactivity order of R5SO2Na (R5=CF3, CF2H, and CH2F) in the fluoroalkylations. Herein, we report our results on the synthesis of di- and monofluoromethyl aryl sulfoxones via copper-mediated fluoroalkylations of arenediazonium tetrafluoroborates and HCF2SO2Na or FCH2SO2Na (Scheme 1, eqs 3 and 4), and the relative reactivity of R5SO2Na (R5=CF3, CF2H, and CH2F) in these fluoroalkylations.

Scheme 1. Fluoromethanesulfonylations of arenediazonium tetrafluoroborates.

Previous work:

This work:

Results and Discussion

At the outset of our study, we conducted the experiment in DMSO using benzenediazonium tetrafluoroborate 1a as substrate and adding CF3HSO2Na and CuO as reagents. (Table 1, entry 1). However, no desired product 2a was detected. Most of the sub-

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strate 1a was transformed to the reduced product (benzene) and biphenyl (detected by GC-MS), while CF₃HSO₃Na was dominantly recovered (detected by ¹³C NMR). Utilizing other copper species such as CuTc and CuOAc, we were delighted to find that the addition of CuTc successfully gave 8% yield of the sulfonylation product 2a (entry 2). Changing the solvent to MeCN, the yield was increased to 64%, while other copper species displayed low efficiency (entries 4—12). Instead of mixing the substrate 1a with all the reagents together at the beginning, slow dropwise addition of 1a to the acetonitrile solution of CuTc and CF₃HSO₃Na could improve the yield to 79% (entry 13). Furthermore, the amount of CuTc could be reduced to 0.5 equivalent (entry 14). Further reducing the amount of CuTc led to the loss of yield (Table 1, entries 15—17).

Table 1 Optimization of the reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>&quot;Cu&quot;</th>
<th>Solvent</th>
<th>Time</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cu₂O</td>
<td>DMSO</td>
<td>12 h</td>
<td>none</td>
</tr>
<tr>
<td>2</td>
<td>CuTc</td>
<td>DMSO</td>
<td>12 h</td>
<td>8%</td>
</tr>
<tr>
<td>3</td>
<td>CuOAc</td>
<td>DMSO</td>
<td>12 h</td>
<td>none</td>
</tr>
<tr>
<td>4</td>
<td>CuTc</td>
<td>MeCN</td>
<td>12 h</td>
<td>64%</td>
</tr>
<tr>
<td>5</td>
<td>Cu₂O</td>
<td>MeCN</td>
<td>12 h</td>
<td>none</td>
</tr>
<tr>
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<td>CuOAc</td>
<td>MeCN</td>
<td>12 h</td>
<td>none</td>
</tr>
<tr>
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<td>Cu(OAc)₂</td>
<td>MeCN</td>
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<td>48%</td>
</tr>
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<td>CuSO₄</td>
<td>MeCN</td>
<td>12 h</td>
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<tr>
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<td>Cu(acac)₂</td>
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</tr>
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<td>CuCN</td>
<td>MeCN</td>
<td>12 h</td>
<td>19%</td>
</tr>
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<td>CuF₂</td>
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<tr>
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<td>Cu(MeCN)₂(PF₆)₂</td>
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</tr>
<tr>
<td>18</td>
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<td>80%</td>
</tr>
<tr>
<td>19</td>
<td>CuTc</td>
<td>MeCN</td>
<td>0.5 h</td>
<td>80%</td>
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</table>

The reaction was conducted on 0.2 mmol scale: 1a (1.0 equiv), "Cu" (1.0 equiv), and CF₃HSO₃Na (1.5 equiv) were mixed together and 2.0 mL solvent was added. The reaction was stirred for the time indicated in the Table. The yield was determined by ¹³C NMR with trifluoromethylbenzene as internal standard. ¹.0 mL of solution of 1a (1.0 equiv) was added via syringe to 1.0 mL of solution of CuTc (1.0 equiv) and CF₃HSO₃Na (1.5 equiv). ².0.5 equiv of CuTc was used. ³.0.4 equiv of CuTc was used. ⁴.0.3 equiv of CuTc was used. ⁵.0.2 equiv of CuTc was used.

With the optimized conditions in hand (Table 1, entry 18), we examined the scope of this reaction, which is shown in Scheme 2. Although the reaction gave the same results for 1a using either 0.5 or 1.0 equivalent of CuTc (Table 1, entries 18 and 19), for most substrates, reaction with 0.5 equivalent of CuTc delivered 5%—10% lower yields than those utilizing 1.0 equivalent of CuTc. Therefore, the latter conditions were applied in Scheme 2 (for the results using 0.5 equivalent of CuTc, see the yields in parentheses in Scheme 2).

As shown in Table 2, our method has a good compatibility with various functional groups, giving the corresponding products 2 in moderate to good yields. The substrates bearing electron-donating groups give better yields than the electron-deficient ones, which might attribute to the latter’s higher reactivity with CuTc, thus resulting in undesired coupling reaction with thiophene carboxylate (Tc). The reaction conditions are compatible with halogens (2h—2j), ketones (2g, 2a), carboxylate esters (2k, 2t), nitrile (2s) and trimethylsilylacetylene (2u), which makes these compounds ready for further transformations to more complicated structures. To be noted, sulfoxones containing acidic protons, such as carboxylic acid (2v) and amide (2d), which are difficult to prepare using conventional methods, were accessible with high yields. For substrate 1u, the trimethylsilyl group was partially transformed to hydrogen, which delivered the unmasked acetylene compound directly (2u’). Finally, to show the synthetic utility of this method in organic synthesis, the α-Tocopherol derivative was synthesized using this new method in 54% yield (2x).

Scheme 2 Copper-mediated difluoromethanesulfonylation of arenediazonium tetrafluoroborates

This reaction could be expanded to synthesize aromatic sulfoxones containing other fluorooalkyls, such as mono- and trifluoroethyl groups (Schemes 3 and 4). It was found that the monofluoromethanesulfonylation of arenediazonium tetrafluoroborates gave the products 3 in moderate to good yields (Scheme 3). Electron-neutral and electron-rich substrates (1a—1f) displayed better reactivity than those bearing electron-withdrawing groups (1g and 1y), which is consistent with the electronic effect. For trifluoromethanesulfonylation of arenediazonium salts, we chose 1c as the model compound owing to its high reactivity towards sulfonylation as exhibited in Schemes 1 and 2. Although the desired trifluoromethanesulfonylation product 4 was obtained only
in moderate yield (Table 2, entry 11), it is encouraging for us to develop a complementary procedure to synthesize sulfones with electron-rich groups (Scheme 4), which were not easily accessible using known methods.[12]

Scheme 3 Copper-mediated monofluoromethanesulfonylation of arenediazonium tetrafluoroborates

![Scheme 3](image)

The reaction was conducted on 0.5 mmol scale: a solution of substrate 1 (1.0 equiv) was added dropwise to the solution of CuTc (1.0 equiv) and CF3SO2Na (1.5 equiv). Isolated yields are given. More amount of solvent was used to dissolve the substrate.

In 2015, we compared the reactivity of different sodium sulfinites in radical fluoroalkylation reactions.[13] In the oxidative radical fluoroalkylations, the reactivity of sodium sulfinites decreases in the following order: PhCF2SO2Na > CF3HSO2Na > CH2F2SO2Na. Since arenediazonium tetrafluoroborates were not able to oxidize the sulfinites to the fluoroalkyl radicals,[10] it is reasonable to presume that the sodium fluoromethanesulfonates in our reactions react as nucleophiles rather than radical precursors. As our continuing effort in probing the unique fluoride effects in organic reactions,[14] we were interested in probing the reactivity order of R2SO2Na (R2 = CF2, CF3, and CH2) in the current fluoroalkanesulfonylations (Scheme 5). To rule out the influence of solubility of different sulfinites, a mixture of MeCN/H2O was utilized as a co-solvent system (in MeCN, the solubility of these sodium sulfinites decreases as follows: CF3SO2Na > HCF2SO2Na >> FCH2SO2Na). When 1c was subjected to a mixture of CF3SO2Na and CH2F2SO2Na, 3c was formed as the major product with a ratio of 3c/2c = 100/13 (Scheme 5, eq A). When 1c was exposed to a mixture of CH2F2SO2Na and CF3SO2Na, the ratio of 3c to 4c was about 100/0.6 (Scheme 5, eq B). As for the reaction between 1c and CF3HSO2Na/CF3SO2Na, the ratio of compound 2c to 4c was 100/6 (Scheme 5, eq C). Based on the results of these competition experiments, it can be concluded that the relative reactivity of sodium fluoroalkanesulfinites decreases in the following order: CH2F2SO2Na > CF2HSO2Na > CF3SO2Na, which can be explained by their relative nucleophilicity (more electron-rich sulfinites possess higher nucleophilicity). However, this trend is remarkably different from their reactivity in oxidative radical fluoroalkylations.[12] In the radical process, the CF3SO2Na usually displays high tendency to extrude SO2 to generate CF3 radical once oxidized. However, in our present reaction as shown in Table 2 and Scheme 4, trifluoromethylation was not observed when no external oxidant was added. Indeed, most of the CF3SO2Na remained unreacted under our reaction conditions. Furthermore, considering the relatively higher reactivity of CH2F2SO2Na and CF2HSO2Na (compared to CF3SO2Na) in our reactions, it is reasonable to hypothesize that the sodium sulfinites R2SO2Na (R2 = CF2, CF3, and CH2) do not undergo oxidation to generate radicals but probably react as nucleophiles.

Based on the aforementioned information, we propose a plausible reaction mechanism as shown in Scheme 6. In the first step (Scheme 6, eq a), a copper species CuX, either X = Tc or RO2, serves as an initiator to generate aromatic radical through single electron retransfer (SET), and the latter species reacts with fluoralkylsulfinate to a radical anion (Scheme 6, eq b). Then the radical anion can be quenched by either another molecule of substrate (nucleophilic radical chain reaction) or the cuprous compound (redox process).

Conclusions

In summary, we have developed copper-mediated di- and monofluoromethanesulfonylation of arenediazonium salts using CF3HSO2Na and CH2F2SO2Na reagents, which can be readily

![Table 2](image)

Table 2 Optimization of conditions for trifluoromethanesulfonylation of substrate 1c

<table>
<thead>
<tr>
<th>Entry</th>
<th>“Cu”</th>
<th>Solvent</th>
<th>Time</th>
<th>Yield</th>
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<tbody>
<tr>
<td>1</td>
<td>CuTc</td>
<td>DMSO</td>
<td>12 h</td>
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<td>2</td>
<td>CuTc</td>
<td>DMSO</td>
<td>12 h</td>
<td>15%</td>
</tr>
<tr>
<td>3</td>
<td>CuOAc-H2O</td>
<td>DMSO</td>
<td>12 h</td>
<td>19%</td>
</tr>
<tr>
<td>4</td>
<td>CuOTf</td>
<td>DMSO</td>
<td>12 h</td>
<td>21%</td>
</tr>
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<td>5</td>
<td>CuOAc-H2O</td>
<td>MeCN</td>
<td>12 h</td>
<td>7%</td>
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<td>6</td>
<td>CuTc</td>
<td>MeCN</td>
<td>12 h</td>
<td>37%</td>
</tr>
<tr>
<td>7</td>
<td>CuOAc-H2O</td>
<td>MeCN</td>
<td>12 h</td>
<td>16%</td>
</tr>
<tr>
<td>8</td>
<td>CuOTf</td>
<td>MeCN</td>
<td>12 h</td>
<td>9%</td>
</tr>
<tr>
<td>9</td>
<td>CuTc</td>
<td>MeCN</td>
<td>0.5 h</td>
<td>34%</td>
</tr>
<tr>
<td>10</td>
<td>CuTc</td>
<td>MeCN</td>
<td>0.5 h</td>
<td>33%</td>
</tr>
<tr>
<td>11</td>
<td>CuTc</td>
<td>MeCN</td>
<td>0.5 h</td>
<td>40%</td>
</tr>
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</table>

The reaction was conducted on 0.2 mmol scale: a solution of substrate 1 (1.0 equiv), CuTc (1.0 equiv), CF3SO2Na (1.5 equiv) in solvent (2.0 mL). Yield was detected by 19F NMR. The reaction was conducted at 50 °C. The reaction was conducted on 0.5 mmol scale. Isolated yield was given.

Scheme 4 Copper-mediated trifluoromethanesulfonylation of arenediazonium tetrafluoroborates

![Scheme 4](image)

The reaction was conducted on 0.5 mmol scale: a solution of substrate 1 (1.0 equiv) was added dropwise to the solution of CuTc (1.0 equiv) and CF3SO2Na (1.5 equiv). Isolated yields are given. Not isolatable from the by-product. Yield was detected by 19F NMR.

Scheme 5 Competition experiments of sodium fluoromethanesulfinites reacting with compound 1c

![Scheme 5](image)

Optimization of conditions for trifluoromethanesulfonylation of substrate 1c

In summary, we have developed copper-mediated di- and monofluoromethanesulfonylation of arenediazonium salts using CF3HSO2Na and CH2F2SO2Na reagents, which can be readily

prepared from the corresponding benzo[d]thiazol-2-yl sulfones.\textsuperscript{111} Various structurally diverse di- and monofluoromethyl aryl sulfones can be readily synthesized in good yields. This method also offers an alternative protocol for the synthesis of electron-rich trifluoromethyl sulfones. Furthermore, it was found that the relative reactivity of these fluoroalkanesulfonates in the current fluoroalkanesulfonations decreases in the following order: CH$_2$F$_2$SO$_2$Na > CF$_3$HSO$_2$Na > CF$_3$SO$_2$Na. This reactivity order is consistent with their innate nucleophilicity, but different from their relative reactivity in oxidative radical fluoroalkylations.\textsuperscript{111}

**Experimental**

**General Information.** Unless otherwise mentioned, reagents were purchased from commercial sources and used as received. CF$_3$HSO$_2$Na and CF$_3$SO$_2$Na were prepared as per the reported literature,\textsuperscript{111} while CF$_3$SO$_2$Na was purchased from TCI. The aromatic diazonium tetrafluoroborates were synthesized according to reported procedure.\textsuperscript{13}\ The all the reactions were carried out under N$_2$ atmosphere. MeCN and DMSO were distilled over CaH$_2$ and kept over activated 4 Å MS. $^1$H, $^{13}$C and $^{19}$F NMR spectra were recorded on a 400 or 500 MHz NMR spectrometer. $^1$H NMR chemical shifts were determined relative to internal (CH$_3$)$_2$Si(SiMe$_3$)$_2$ at δ 0.0 or to the signal of the residual solvent peak: CHCl$_3$ in CDCl$_3$ at δ 7.26, DMSO in d$_6$-DMSO: δ 2.54. $^{13}$C NMR chemical shifts were determined relative to internal TMS at δ 0.0. $^{19}$F NMR chemical shifts were determined relative to CFCl$_3$ at δ 0.0. Data for $^1$H, $^{13}$C and $^{19}$F NMR were recorded as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Coupling constants are reported in hertz (Hz). High-resolution mass data were recorded on a HR-MS in the El mode or EI mode.

**General procedure for the preparation of diazonium salts 1.** Method A. In a 50 mL round-bottom flask, the aniline (10.0 mmol) was dissolved in a mixture of absolute ethanol (3.0 mL) and an aqueous solution of HBF$_4$ (48%, 2.5 mL), followed by dropwise addition of BuONO (2.7 mL) at 0 °C. After stirring at room temperature for 1 h, diethyl ether (20 mL) was added to precipitate the arenediazonium tetrafluoroborate. After filtration and washing with diethyl ether (3×10 mL), the product was dried in vacuo (10$^{-3}$ mbar) for 10 min and stored in refrigerator under N$_2$ atmosphere.

Method B. In a 50 mL round-bottom flask, aniline (5.0 mmol) was dissolved in a mixture of H$_2$O (1.0 mL) and an aqueous solution of HBF$_4$ (48%, 1.9 mL), followed by dropwise addition of an aqueous solution of NaN$_3$ (680 mg in 1.0 mL H$_2$O). After being stirred at 0 °C for 30 min, the reaction mixture was worked up by filtration, washing successively with a small amount of ice water, alcohol and diethyl ether, and the arenediazonium tetrafluoroborate was dried in vacuo (10$^{-3}$ mbar) for 10 min and stored in refrigerator under N$_2$ atmosphere.

**General procedure for the preparation of compound 2.** To an oven-dried Schlenk tube equipped with a stirring bar and rubber septum stopper was added CuTc (95.0 mg, 0.55 mmol), CF$_3$HSO$_2$Na (103.5 mg, 0.75 mmol) and MeCN (2.5 mL). After stirring for 5 min, a solution of arenediazonium tetrafluoroborate 1 (0.5 mmol) in MeCN (2.5 mL) was added dropwise in 15 min. Then the mixture was sealed and stirred for 30 min, followed by filtration on celite and washing with ethyl acetate. The filtrate was treated with saturated aqueous NaHCO$_3$, and the mixture was extracted by ethyl acetate (3×15 mL). The combined organic layer was washed with brine and dried over anhydrous Na$_2$SO$_4$. After filtration and removal of the solvent under vacuum, the crude product was purified by column chromatography. To be noted: (a) Aqueous NH$_4$Cl was used instead of NaHCO$_3$ for compounds 2a and 2v; (b) 5.0 mL of MeCN was used to dissolve substrates 1e, 1r, 1s and 1v.

![Diagram](image-url)
id (108.6 mg, 68%), mp: 92—93 °C. 1H NMR (400 MHz, CDCl3) δ: 8.04 (d, J = 8.6 Hz, 2H), 7.68 (d, J = 8.5 Hz, 2H), 6.19 (t, J = 5.3 Hz, 1H). 13C NMR (101 MHz, CDCl3) δ: 139.1, 131.7, 131.3, 114.6 (t, J = 286.1 Hz), 104.9. 19F NMR (376 MHz, CDCl3) δ: −121.27 (d, J = 53.4 Hz). HR-MS (EI): m/z calcd for [M] C9H8F2O3S: 284.9794; found: 284.9788.

1-(Difluoromethyl)sulfonyl)benzene (2z). White solid (73.2 mg, 54%), mp: 152—154 °C. 1H NMR (400 MHz, d6-DMsol) δ: 8.28 (d, J = 8.5 Hz, 2H), 8.28 (d, J = 8.5 Hz, 2H). 7.45 (t, J = 5.18 Hz, 1H), 3.39 (s, 3H). 13C NMR (101 MHz, d6-DMsol) δ: 147.8, 136.5, 131.9, 129.2, 115.2 (t, J = 286.2 Hz). 19F NMR (376 MHz, d6-DMsol) δ: −124.04 (d, J = 51.3 Hz). HR-MS (EI): m/z calcd for [M] C7H7F2O2SCl: 234.0162; found: 234.0159.

2-(Difluoromethyl)sulfonyl)benzamide (2a). Yellow solid (84.6 mg, 75%), mp: 66—67 °C. 1H NMR (400 MHz, CDCl3) δ: 7.97—7.91 (m, 2H), 7.70—7.60 (m, 2H), 6.20 (t, J = 3.54 Hz, 1H). 13C NMR (101 MHz, CDCl3) δ: 133.1, 132.1, 130.1, 114.7 (t, J = 285.9 Hz). 19F NMR (376 MHz, CDCl3) δ: −121.25 (d, J = 53.4 Hz). HR-MS (EI): m/z calcd for [M] C9H8F2O3S: 222.0162; found: 229.9175.

1-Chloro-4-(difluoromethyl)sulfonyl)benzene (2y). Yellow solid (84.6 mg, 75%), mp: 66—67 °C. 1H NMR (400 MHz, CDCl3) δ: 7.97—7.91 (m, 2H), 7.70—7.60 (m, 2H), 6.20 (t, J = 3.54 Hz, 1H). 13C NMR (101 MHz, CDCl3) δ: 133.1, 132.1, 130.1, 114.7 (t, J = 285.9 Hz). 19F NMR (376 MHz, CDCl3) δ: −121.25 (d, J = 53.4 Hz). HR-MS (EI): m/z calcd for [M] C9H8F2O3S: 222.0162; found: 229.9175.

Concise Report

Xing, Ni & Hu

The Concise Report is a collection of high-quality research papers in various fields of science. It is a valuable resource for researchers and students seeking to stay updated with the latest developments in their respective fields. The papers are carefully selected and organized to provide a comprehensive overview of the latest research findings.
General procedure for the preparation of compound 3. To an oven-dried Schlenk tube equipped with a stirring bar and rubber septum stopper was added CuTc (95.0 mg, 0.5 mmol), CH$_2$F$_2$SO$_4$Na (90.0 mg, 0.75 mmol) and MeCN (2.5 mL). After stirring for 5 min, a solution of arenediazonium tetrafluoroborates 1 (0.5 mmol) in MeCN (2.5 mL) was added dropwise in 15 min. Then the mixture was sealed and stirred for 30 min, followed by filtration on celite and washing with ethyl acetate. The filtrate was treated with saturated aqueous NaHCO$_3$, and the mixture was extracted by ethyl acetate (3×15 mL). The combined organic layer was washed with brine and dried over anhydrous Na$_2$SO$_4$. After filtration and removal of the solvent under vacuum, the crude product was purified by column chromatography. To be noted: 5.0 mL of MeCN was used to dissolve substrate 1e.

$$[\text{HR}]^+ \text{C}_7\text{H}_5\text{F}_2\text{O}_2\text{S}: 649.3733; \text{found: 649.3727.}$$

General procedure for the preparation of compound 4. To an oven-dried Schlenk tube equipped with a stirring bar and rubber septum stopper was added CuTc (95.0 mg, 0.5 mmol), CF$_3$SO$_3$Na (117.0 mg, 0.75 mmol) and MeCN (2.5 mL). After stirring for 5 min, a solution of arenediazonium tetrafluoroborates 1 (0.5 mmol) in MeCN (2.5 mL) was added dropwise in 15 min. Then the mixture was sealed and stirred for 30 min, followed by filtration on celite and washing with ethyl acetate. The filtrate was treated with saturated aqueous NaHCO$_3$, and the mixture was extracted by ethyl acetate (3×15 mL). The combined organic layer was washed with brine and dried over anhydrous Na$_2$SO$_4$. After filtration and removal of the solvent under vacuum, the crude product was purified by column chromatography.

$$4-([\text{Fluoromethyl}sulfonyl]) \text{benzene (4a).}$$ Yellow liquid (58.4 mg, 41%). $^{1}$H NMR (400 MHz, CDCl$_3$) δ: 7.96 (d, J = 8.9 Hz, 2H), 7.11 (d, J = 9.0 Hz, 2H), 7.11 (d, J = 9.0 Hz, 2H), 7.57–7.46 (m, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ: 149.7, 138.5, 131.4, 129.6, 129.4, 128.5, 127.6, 119.9 (J = 325.8 Hz).

$^{19}$F NMR (376 MHz, CDCl$_3$) δ: –78.44 (s). HR-MS (EI): m/z calcd for [M$^{+}$]C$_7$H$_5$F$_2$O$_2$S: 286.0275; found: 286.0272.

1-Methoxy-4-([Fluoromethyl)sulfonyl]benzene (4n). Yellow liquid (48.1 mg, 40%). $^{1}$H NMR (400 MHz, CDCl$_3$) δ: 7.96 (d, J = 8.9 Hz, 2H), 7.11 (d, J = 9.0 Hz, 2H), 7.71 (d, J = 9.0 Hz, 2H), 6.75 (d, J = 7.2 Hz, 2H), 7.57–7.46 (m, 3H). $^{1}$H NMR (101 MHz, CDCl$_3$) δ: 166.2, 133.3, 122.0, 119.9 (J = 325.8 Hz), 115.3, 56.0.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ: –78.88 (s). HR-MS (EI): m/z calcd for [M$^{+}$]C$_7$H$_5$F$_2$O$_2$S: 240.0668; found: 240.0669.

General procedure for the competition experiments. Experiment A. To an oven-dried Schlenk tube equipped with a stirring bar and rubber septum stopper was added CuTc (95.0 mg, 0.5 mmol), CF$_3$SO$_3$Na (103.5 mg, 0.75 mmol), CH$_2$F$_2$SO$_4$Na (90.0 mg, 0.75 mmol) and MeCN (2.5 mL). After stirring for 5 min, a solution of 4-biphenyl diazonium tetrafluoroborate 1c (134.0 mg, 0.5 mmol) in MeCN (2.5 mL) was added dropwise in 15 min. Then the mixture was sealed and stirred for 30 min, followed by filtration on celite and washing with ethyl acetate. The filtrate was treated with saturated aqueous NaHCO$_3$, and the mixture was extracted by ethyl acetate (3×15 mL). The combined organic layer was washed with brine and dried over anhydrous Na$_2$SO$_4$. After filtration and concentration of the solvent under vacuum, the ratio was detected by $^{19}$F NMR spectroscopy.

Experiment B. To an oven-dried Schlenk tube equipped with a stirring bar and rubber septum stopper was added CuTc (95.0 mg, 0.5 mmol), FCH$_2$SO$_4$Na (90.0 mg, 0.75 mmol), CF$_3$SO$_3$Na (117.0 mg, 0.75 mmol) and MeCN (2.5 mL). After stirring for 5 min, a solution of 4-biphenyl diazonium tetrafluoroborate 1c (134.0 mg, 0.5 mmol) in MeCN (2.5 mL) was added dropwise in 15 min. Then the mixture was sealed and stirred for 30 min, followed by filtration on celite and washing with ethyl acetate. The filtrate was treated with saturated aqueous NaHCO$_3$, and the mixture was extracted by ethyl acetate (3×15 mL). The combined organic layer was washed with brine and dried over anhydrous Na$_2$SO$_4$. After filtration and concentration of the solvent under vacuum, the ratio was detected by $^{19}$F NMR spectroscopy.

Experiment C. To an oven-dried Schlenk tube equipped with a stirring bar and rubber septum stopper was added CuTc (95.0 mg, 0.5 mmol), HCF$_2$SO$_4$Na (103.5 mg, 0.75 mmol), CF$_3$SO$_3$Na (117.0 mg, 0.75 mmol) and MeCN (2.5 mL). After stirring for 5 min, a solution of 4-biphenyl diazonium tetrafluoroborate 1c (134.0 mg,
0.5 mmol) in MeCN (2.5 mL) was added dropwise in 15 min. Then the mixture was sealed and stirred for 30 min, followed by filtration on celite and washing with ethyl acetate. The filtrate was treated with saturated aqueous NaHCO₃ and the mixture was extracted by ethyl acetate (3×15 mL). The combined organic layer was washed with brine and dried over anhydrous Na₂SO₄. After filtration and concentration of the solvent under vacuum, the ratio was detected by ¹³C NMR spectroscopy.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.201700748.

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References


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