# Elemental Sulfur as Sulfuration Agent in Copper-Catalyzed C-H Bond Thiolation of Electron-Deficient Arenes

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## **1. General Information**

All manipulations were carried out standard Schlenk techniques. Unless otherwise stated, analytical grade solvents and commercially available reagents were used to conduct the reactions. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (boiling point is between 60-90°C). Gradient flash chromatography was conducted eluting with a continuous gradient from petroleum ether and ethyl acetate. The known compounds were characterized by <sup>1</sup>H NMR and <sup>13</sup>C NMR. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer with tetramethylsilane as an internal standard. The chemical shifts (δ) were given in part per million relative to internal tetramethyl silane (TMS, 0 ppm for <sup>1</sup>H NMR), CDCl<sub>3</sub> (77.3 ppm for <sup>13</sup>C NMR).

## 2. General Procedure

Sulfur powder (0.5 mmol, 16.0 mg), NaO*t*Bu (0.6 mmol, 57.6 mg), CuCl<sub>2</sub> (0.025 mmol, 3.4 mg) and 1,10-phenanthroline (0.050 mmol, 9.0 mg) were added into an oven-dried Schlenk tube equipped with a magnetic stirred bar. And DMF (2 mL), arene (0.5 mmol) were injected in the tube through a syringe in turn under an N<sub>2</sub> atmosphere at room temperature. Then kept stirring for 12h at 25 °C. After completion of the reaction, as indicated by TLC and GC-MS, the mixture was quenched with diluted hydrochloride (4 mL, 2.0 M), and the solution was extracted with ethyl acetate ( $3 \times 15$  mL). The organic layers were combined, and dried over sodium sulfate. The pure product was obtained by flash column chromatography on silica gel.

## 3. Mechanism Study

# **3.1 EPR Experiment**

For the EPR experiment, the spectra was recorded on EPR spectrometer operated at 9.419 GHz, with typical spectrometer parameters shown as follows, scan range: 1000 G; center field set: 3361 G; time constant: 163.84 ms; scan time: 30.72 s; modulation amplitude: 5.0 G; modulation frequency: 100 kHz; receiver gain:  $1.00 \times 10^5$ ; microwave power: 18.53 mW. The reaction was carried out as follows: an oven-dried Schlenk tube was fitted with a magnetic stirring bar, then evacuated under vacuum and flushed with nitrogen for three times. The tube was charged with

solution of reactants. After the appropriate time, the solution sample was taken out into a small tube and analyzed by EPR. EPR spectra was recorded at room temperature.

#### EPR Studies of Interaction between Elemental Sulfur and tBuONa in DMF

The reaction was carried out as follows: Sulfur powder (0.5 mmol, 16.0 mg) and NaOtBu (0.6 mmol, 57.6 mg) was added to an oven-dried Schlenk tube fitted with a magnetic stirring bar. Following evacuation under vacuum and flushing with nitrogen for three times, the tube was charged with 2 mL DMF. The reaction tube was kept at 25 °C. After 30 mins, the solution sample was taken out into a small tube and analyzed by EPR at room temperature.

#### EPR Studies of Interaction between Elemental Sulfur, tBuONa and CuCl in DMF

The reaction was carried out as follows: Sulfur powder (0.5 mmol, 16.0 mg), NaO*t*Bu (0.6 mmol, 57.6 mg) and CuCl (0.025 mmol, 2.5 mg) was added to an oven-dried Schlenk tube fitted with a magnetic stirring bar. Following evacuation under vacuum and flushing with nitrogen for three times, the tube was charged with 2 mL DMF. The reaction tube was kept at 25 °C. After 30 mins, the solution sample was taken out into a small tube and analyzed by EPR at room temperature.

# EPR Studies of Interaction between Elemental Sulfur, *t*BuONa, CuCl and benzothiazole in DMF

The reaction was carried out as follows: Sulfur powder (0.5 mmol, 16.0 mg), NaO*t*Bu (0.6 mmol, 57.6 mg) and CuCl (0.025 mmol, 2.5 mg) was added to an oven-dried Schlenk tube fitted with a magnetic stirring bar. Following evacuation under vacuum and flushing with nitrogen for three times, the tube was charged with 2 mL DMF. And then added benzothiazole (0.5 mmol, 67.5 mg). The reaction tube was kept at 25 °C. After 30 mins, the solution sample was taken out into a small tube and analyzed by EPR at room temperature. Finally, yield of the desired product **2a** was determined by HPLC analysis with naphthalene as the internal standard.

#### **3.2 KIE Experiment**

For the KIE experiment, the reaction spectra were recorded using an IC 15 from Mettler-Toledo AutoChem. Data manipulation was carried out using the iC IR software, version 4.3. The reaction was carried out as follows: Sulfur powder (0.5 mmol, 16.0 mg), NaOtBu (0.6 mmol, 57.6 mg) and CuCl<sub>2</sub> (0.025 mmol, 3.4 mg) was added to a three necked reaction vessel with a magnetic stirred bar. The IR probe was inserted through an adapter into the middle neck; the other two necks were

capped by septa for injections and a nitrogen balloon. The reaction vessel was kept at 25 °C. Following evacuation under vacuum and flushing with nitrogen for three times, the three necked vessel was charged with 2.0 mL DMF and the data collection was started, followed by the addition of benzothiazole (0.5 mmol, 67.5 mg) or deuterated benzothiazole (0.5 mmol, 68.0 mg). The data of 1 min started from benzothiazole's addition were all recorded to measure the initial rate of these two reactions in the same conditions respectively.



The result showed that,  $k_H/k_D =$  Slope-H / Slope-D=10.8\*10<sup>-4</sup> / 8.7\*10<sup>-4</sup> =1.24, which figured out that C-H bond cleavage should not in the rate-limiting step.

# 4. Characterization of Products

benzo[d]thiazole-2-thiol (4a)<sup>1</sup>



Light yellow solid, 82% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 11.56 (br, 1H), 7.48 (d, *J*=8.0 Hz,

1H), 7.40-7.27 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ = 190.9, 140.2, 130.0, 127.3, 124.7, 121.4, 112.3.

#### benzo[d]oxazole-2-thiol (4b)<sup>2</sup>



Light yellow solid, 67% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  11.21 (br, 1H), 7.46 (d, J = 1.8 Hz, 1H), 7.29 (dd, J = 8.4, 1.8 Hz, 2H), 7.15 (d, J = 8.4 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  180.85, 148.81, 130.27, 125.39, 124.50, 110.60, 110.24.

#### 5-chlorobenzo[d]oxazole-2-thiol (4c)<sup>2</sup>



Light yellow solid, 30% yield. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD)  $\delta$  7.45 (d, *J*=1.6 Hz, 1H), 7.28 (d, *J*=6.8 Hz, 1H), 7.15 (d, *J*=8.4 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD)  $\delta$  = 183.08, 150.36, 131.78, 130.40, 126.30, 111.74, 111.59.

#### 5-(tert-butyl)benzo[d]oxazole-2-thiol (4d)<sup>2</sup>



Light yellow solid, 95% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.30 (d, *J*=1.6 Hz, 1H), 7.29 (s, 1H), 7.26 (d, *J*=0.8 Hz, 1H), 1.34 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 180.87, 149.41, 146.86, 130.34, 121.85, 109.79, 107.55, 35.12, 31.62.

#### 5-methylbenzo[d]oxazole-2-thiol (4e)<sup>2</sup>



Light yellow solid, 64% yield. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD)  $\delta$  7.22 (d, J = 8.4 Hz, 1H), 7.05 (d, J = 8.4 Hz, 1H), 7.01 (s, 1H), 2.40 (s, 3H). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD)  $\delta$  182.92, 148.35, 136.63, 132.70, 125.60, 111.38, 110.44, 21.36.

#### 5-phenyl-1,3,4-oxadiazole-2-thiol (4f)<sup>3</sup>



Light yellow solid, 73% yield. <sup>1</sup>H NMR (400 MHz, d<sup>6</sup>-DMSO)  $\delta$  14.76 (br, 1H), 7.95 – 7.82 (m, 2H), 7.69 – 7.54 (m, 3H). <sup>13</sup>C NMR (100 MHz, d<sup>6</sup>-DMSO)  $\delta$  = 177.62, 161.13, 132.60, 129.90, 126.48, 123.11.

#### 5-(4-chlorophenyl)-1,3,4-oxadiazole-2-thiol (4g)<sup>4</sup>



Light yellow solid, 62% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 11.14 (br, 1H), 7.88 (dt, *J*=8.8, 2.0 Hz, 2H), 7.51 (dt, *J*=8.8, 2.0 Hz, 2H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  = 178.05, 160.72, 139.02, 129.71, 127.77, 120.74.

#### 5-(4-bromophenyl)-1,3,4-oxadiazole-2-thiol (4h)<sup>4</sup>



Light yellow solid, 66% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  13.09 (br, 1H), 7.86 – 7.77 (m, 2H), 7.70 – 7.60 (m, 2H). <sup>13</sup>C NMR (100 MHz, d<sup>6</sup>-DMSO)  $\delta$  = 177.86, 160.24, 132.93, 128.37, 126.27, 122.16.

#### 5-(p-tolyl)-1,3,4-oxadiazole-2-thiol (4i)<sup>3</sup>



Light yellow solid, 54% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  10.89 (br, 1H), 7.83 (d, *J*=8.0 Hz, 2H), 7.32 (d, *J*=8.0 Hz, 2H), 2.44 (s, 3H). <sup>13</sup>C NMR (100 MHz, d<sup>6</sup>-DMSO)  $\delta$  = 177.73, 161.06,

142.96, 130.41, 126.45, 120.15, 21.63.

#### 5-(4-methoxyphenyl)-1,3,4-oxadiazole-2-thiol (4j)<sup>4</sup>



Light yellow solid, 79% yield. <sup>1</sup>H NMR (400 MHz, d<sup>6</sup>-DMSO)  $\delta$  7.85 (d, *J*=8.8 Hz, 2H), 7.08 (d, *J*=8.8 Hz, 2H), 3.89 (s, 3H). <sup>13</sup>C NMR (100 MHz, d<sup>6</sup>-DMSO)  $\delta$  = 177.57, 162.66, 161.01, 128.42, 115.34, 115.18, 56.02.

#### 2,3,5,6-tetrachlorobenzenethiol (4k)



Yellow oily liquid, 64% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.64 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 137.94, 137.14, 132.46, 132.30.

#### 2,3,5,6-tetrafluoro-4-methoxybenzenethiol (41)



Yellow oily liquid, 64% yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 4.17 (t, *J*=1.6 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  149.0-148.7, 146.5-146.3, 141.8-141.6, 141.1-140.8, 139.4-139.1, 107.3 (t, 2  $J_{C-F}$ =21.2 Hz), 62.1 (t, 4  $J_{C-F}$ =4.0 Hz).

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# 5. NMR Spectra of Products



<sup>1</sup>H NMR



<sup>13</sup>C NMR



<sup>1</sup>H NMR



9



<sup>13</sup>C NMR



<sup>1</sup>H NMR



<sup>13</sup>C NMR



<sup>13</sup>C NMR



-14.76



<sup>13</sup>C NMR



<sup>1</sup>H NMR



<sup>13</sup>C NMR

# 183 181 181 181 181 181 181 183





<sup>1</sup>H NMR



<sup>13</sup>C NMR



<sup>1</sup>H NMR



<sup>13</sup>C NMR







<sup>13</sup>C NMR



<sup>1</sup>H NMR



<sup>13</sup>C NMR



<sup>1</sup>H NMR



<sup>13</sup>C NMR