Copper-Catalyzed Aerobic Oxidation and Cleavage/Formation of C-S Bond: a Novel Synthesis of Aryl Methyl Sulfones from Aryl Halides and DMSO

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A. General Information

All the reagents were analytical grade and used without further purification, unless stated otherwise. \(^{18}\)O\(_2\) gas (\(^{18}\)O, >97%) was purchased from Shanghai Research Institute of Chemical Industry, Shanghai, China). \(H_2^{18}\)O (98%) was purchased from Alfa Aesar. \(^1\)H and \(^{13}\)C NMR spectra were recorded using a Bruker Avance 400 MHz NMR spectrometer. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively, chloroform is solvent with TMS as the internal standard. Mass spectra were recorded on a Shimadzu GCMS-QP5050A spectrometer at an ionization voltage of 70 eV equipped with a DB-WAX capillary column (internal diameter: 0.25 mm, length: 30 m). HRMS analysis was performed in a MAT95XP high resolution mass spectrometer. TLC was performed by using commercially prepared 100–400 mesh silica gel plates (GF254) and visualization was effected at 254 nm.

B. General Procedures for the Synthesis of Aryl Methyl Sulfoxones

In a typical procedure, iodobenzene 1a (0.25 mmol), DMSO 2a (2 mL), acetyl acetone (0.25 mmol), Cu\(_2\)O (0.025 mmol), and \(t\)-BuOK (0.75 mmol) were added into the reactor in turn. The reaction was carried out at 100 °C under air atmosphere with reflux for 20 h. After the reaction finished, the mixture was diluted with the saturated NaCl aqueous solution and extracted with ethyl acetate (3 × 5 mL). The organic layers were combined, and then dried with anhydrous MgSO\(_4\). After the solvent was removed by rotovapor, the product was purified by column chromatograph with a mixture of petroleum ether and ethyl acetate (volume ratio 5:1).

With 2 equiv of \(H_2^{18}\)O as the isotope-labeling agent, the experimental procedure is the same as mentioned above.

C. Effect of Ligands on the Reaction

Table 1. Effect of Ligands on the Reaction

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Base</th>
<th>Ligand</th>
<th>Yield of 3a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cu(_2)O</td>
<td>(t)-BuOK</td>
<td>L1</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>Cu(_2)O</td>
<td>(t)-BuOK</td>
<td>L2</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>Cu(_2)O</td>
<td>(t)-BuOK</td>
<td>L3</td>
<td>53</td>
</tr>
<tr>
<td>4</td>
<td>Cu(_2)O</td>
<td>(t)-BuOK</td>
<td>L4</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>Cu(_2)O</td>
<td>(t)-BuOK</td>
<td>L5</td>
<td>&lt;5</td>
</tr>
<tr>
<td>6</td>
<td>Cu(_2)O</td>
<td>(t)-BuOK</td>
<td>L6</td>
<td>65</td>
</tr>
</tbody>
</table>
a Reaction conditions: PhI (0.25 mmol), DMSO (2.0 mL), ligand (1 equiv), t-BuOK (3 equiv), Cu$_2$O (0.025 mmol) at 100 °C for 20 h. b Isolated yield.

D. $^{18}$O-labeling experiment with $^{18}$O$_2$

Iodobenzene 1a (0.25 mmol), Cu$_2$O (3.6 mg, 0.025 mmol), t-BuOK (84 mg, 0.75 mmol), acetyl acetonate (20 mg, 0.25 mmol), and DMSO (2 mL) were first added into the dried Schlenk tube in turn. Then, the reaction was carried out at 100 °C with magnetic stirring under $^{18}$O$_2$ (balloon) for 20 h. After the reaction finished, the reaction mixture was diluted with the saturated NaCl aqueous solution and extracted with ethyl acetate. The organic layers were combined, and then dried with anhydrous MgSO$_4$. After the solvent was removed by rotovapor, the product was purified by column chromatograph with a mixture of petroleum ether and ethyl acetate (volume ratio 5:1).

The mass spectrum pattern of $^{18}$O-labeled phenyl methyl sulfone (3a):

![Mass Spectrum Pattern](image)
The mass spectrum pattern of $^{18}$O-labeled dimethyl sulfone:

E. Extra mechanistic studies

Table 2 Effect of Catalyst, Ligand and Base on the Oxidation of DMSO to Dimethyl Sulfone

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Base</th>
<th>Ligand</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cu$_2$O</td>
<td>None</td>
<td>acetyl acetone</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>$t$-BuOK</td>
<td>acetyl acetone</td>
<td>NR</td>
</tr>
<tr>
<td>3</td>
<td>Cu$_2$O</td>
<td>$t$-BuOK</td>
<td>None</td>
<td>NR</td>
</tr>
</tbody>
</table>

* Reaction conditions: DMSO (2.0 mL), acetyl acetone (1 equiv), $t$-BuOK (3 equiv), Cu$_2$O (10 mol %)

at 100 °C for 20 h. * Determined by GC.
Table 3 Effect of Catalyst, Ligand and Base on the Coupling Reaction of PhI with Dimethyl Sulfone

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Base</th>
<th>Ligand</th>
<th>Yield of 3a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>t-BuOK</td>
<td>acetyl acetone</td>
<td>NR</td>
</tr>
<tr>
<td>2</td>
<td>Cu₂O</td>
<td>None</td>
<td>acetyl acetone</td>
<td>NR</td>
</tr>
<tr>
<td>3</td>
<td>Cu₂O</td>
<td>t-BuOK</td>
<td>None</td>
<td>Trace</td>
</tr>
<tr>
<td>4</td>
<td>Cu₂O</td>
<td>t-BuOK</td>
<td>acetyl acetone</td>
<td>18</td>
</tr>
</tbody>
</table>

*Reaction conditions: nitroethane (2 mL) as the solvent, Ph-I (0.25 mmol), dimethyl sulfone (3 equiv), acetyl acetone (1 equiv), t-BuOK (3 equiv), Cu₂O (10 mol %) at 100 °C for 20 h.*  

Base on our experimental results, a possible reaction pathway was proposed in Scheme 1.

![Scheme 1 A Plausible Reaction Pathway](image)

F. Analytical Data for 3a-3p

Methylsulfonylbenzene¹ (3a)

¹H NMR (400 MHz, CDCl₃): δ 7.94 (d, J = 8.0 Hz, 2H), 7.65 (t, J = 8.0 Hz, 1H), 7.57 (t, J = 7.6 Hz, 2H), 3.05 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 140.5, 133.7, 129.3, 127.3, 44.4; MS (EI) m/z: 77, 94, 141, 156; HRMS (m/z) calcd for C₇H₈SO₂: 156.0243, found 156.0245.
1-Methoxy-4-(methylsulfonyl)benzene\(^2\) (3b)
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.86\) (d, \(J = 8.8\) Hz, 2H), \(7.02\) (d, \(J = 8.8\) Hz, 2H), \(3.88\) (s, 3H), \(3.02\) (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 163.7, 132.3, 129.6, 114.5, 55.7, 44.9\); MS (EI) \(m/z\): 77, 91, 107, 123, 171, 186.

1-Methyl-4-(methylsulfonyl)benzene\(^3\) (3c)
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.80\) (d, \(J = 8.0\) Hz, 2H), \(7.34\) (d, \(J = 8.0\) Hz, 2H), \(3.01\) (s, 3H), \(2.43\) (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 144.6, 137.6, 129.9, 127.3, 44.5, 21.5\); MS (EI) \(m/z\): 77, 91, 107, 155, 170.

1-Methyl-3-(methylsulfonyl)benzene\(^4\) (3d)
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.30-7.51\) (m, 2H), \(7.45\) (d, \(J = 5.2\) Hz, 2H), \(3.04\) (s, 3H), \(2.45\) (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 140.4, 139.7, 134.4, 129.2, 127.6, 124.4, 44.5, 21.3\); MS (EI) \(m/z\): 65, 91, 107, 155, 170.

1-Methyl-2-(methylsulfonyl)benzene\(^5\) (3e)
\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 8.02\) (d, \(J = 7.2\) Hz, 1H), \(7.51\) (t, \(J = 6.8\) Hz, 1H), \(7.36\) (q, \(J = 7.6\) Hz, 2H), \(3.07\) (s, 3H), \(2.70\) (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta 138.6, 137.5, 133.6, 132.7, 129.2, 126.7, 43.6, 20.2\); MS (EI) \(m/z\): 39, 65, 91, 107, 155, 170.
1-(4-(Methylsulfonyl)phenyl)ethanone (3f)
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.10-8.13 (m, 2H), 8.04-8.06 (m, 2H), 3.08 (s, 3H), 2.66 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 196.6, 144.2, 140.9, 129.1, 127.8, 44.3, 26.9; MS (EI) $m/z$: 43, 77, 91, 121, 152, 183, 198.

1-Fluoro-3-(methylsulfonyl)benzene (3g)
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.47 (d, $J$ = 8.0 Hz, 1H), 7.64-7.47 (m, 1H), 7.55-7.60 (m, 1H), 7.34-7.38 (m, 1H), 3.07 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 163.7, 161.2, 142.6, 142.5, 131.3, 131.3, 123.2, 123.2, 121.1, 120.9, 114.9, 114.7, 44.3; MS (EI) $m/z$: 75, 95, 112, 159, 174.

1-Fluoro-2-(methylsulfonyl)benzene (3h)
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.94-7.98 (m, 2H), 7.23 (d, $J$ = 8.4 Hz, 2H), 3.05 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.0, 164.4, 136.6, 136.0, 130.3, 130.2, 116.7, 116.5, 44.6; MS (EI) $m/z$: 75, 95, 111, 159, 174.

1-Chloro-4-(methylsulfonyl)benzene (3i)
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.88 (d, $J$ = 8.4 Hz, 2H), 7.47 (d, $J$ = 8.4 Hz, 2H), 3.05 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 140.5, 139.0, 129.7, 128.9, 44.5; MS (EI) $m/z$: 50, 76, 111, 127, 175, 190.
1-(Methylsulfonyl)-4-nitrobenzene (3j)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.43 (d, $J= 8.8$ Hz, 2H), 8.16 (d, $J= 8.8$ Hz, 2H), 3.12 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 150.9, 145.9, 129.0, 124.6, 44.3; MS (EI) $m/z$: 50, 63, 76, 92, 109, 122, 139, 186, 201.

1-(Methylsulfonyl)-2-nitrobenzene (3k)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.20 (s, 1H), 7.82 (d, $J= 8.4$ Hz, 3H), 3.43 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 149.1, 134.9, 134.2, 132.8, 131.4, 124.9, 45.1; MS (EI) $m/z$: 50, 63, 79, 109, 139, 155, 186, 201.

1-Ethyl-2-(methylsulfonyl)benzene (3l)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.99 (d, $J= 8.0$ Hz, 1H), 7.54 (t, $J= 7.2$ Hz, 1H), 7.32-7.50 (m, 2H), 3.03-3.08 (m, 5H), 1.31 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 143.9, 138.2, 133.7, 130.9, 129.2, 126.4, 44.5, 25.9, 15.8; MS (EI) $m/z$: 78, 91, 104, 121, 151, 169, 184.

1-Ethyl-4-(methylsulfonyl)benzene (3m)
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.84 (d, $J$= 8.4 Hz, 2H), 7.38 (d, $J$= 8.4 Hz, 2H), 3.03 (s, 3H), 2.74 (q, $J$= 7.6 Hz, 2H), 1.27 (t, $J$= 7.6 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 150.8, 137.9, 128.8, 127.5, 44.6, 28.9, 15.1; MS (EI) m/z: 79, 91, 105, 121, 169, 184.

4-(Methylsulfonyl)-1,1'-biphenyl$^{10}$ (3n)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.01 (d, $J$= 8.4 Hz, 2H), 7.77 (d, $J$= 8.4 Hz, 2H), 7.61 (d, $J$= 8.0 Hz, 2H), 7.43-7.51 (m, 3H), 3.10 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 146.7, 139.1, 129.1, 128.6, 127.9, 127.3, 44.6; MS (EI) m/z: 63, 77, 115, 141, 152, 169, 217, 232.

1,3-Dimethyl-5-(methylsulfonyl)benzene$^{6}$ (3o)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.54 (s, 2H), 7.26 (s, 1H), 3.03 (s, 3H), 2.40 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 140.3, 139.4, 135.2, 124.7, 44.4, 21.1; MS (EI) m/z: 39, 77, 105, 121, 169, 184.

(E)-(2-(Methylsulfonyl)vinyl)benzene$^{11}$ (3p)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.62 (d, $J$=15.6 Hz, 1H), 7.51 (d, $J$= 6.4 Hz, 2H), 7.40-7.43 (m, 3H), 6.92 (d, $J$=15.6 Hz, 1H), 3.03(s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 144.0, 132.0, 131.4, 129.1, 128.5, 126.1, 43.2; MS (EI) m/z: 77, 91, 102, 119, 149, 167, 182.
G. Reference

H. NMR Spectra

Electronic Supplementary Material (ESI) for Chemical Communications
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