Byproduct Promoted Regioselective Sulfenylation of Indoles with Sulfinic Acids

Congrong Liu,* Lianghui Ding

School of Environment Engineering, Nanjing Institute of Technology, Nanjing, Jiangsu 211167, China

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**General Information**

$^1$H and $^{13}$C NMR spectra were recorded on a Bruker AC-400 FT (400 MHz and 100 MHz, respectively) using tetramethysilane as an internal reference. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, m = multiplet, br = broad signal. Chemical shifts ($\delta$) and coupling constants ($J$) were expressed in ppm and Hz, respectively.

2a-2m were prepared according to the literature procedure. The rest of chemicals were purchased from the Sinopharm Chemical Reagent Co., Meryer, Acros, Alfa Aesar, and TCI, and used as received.

**General Procedure for Byproduct Promoted Regioselective Sulfenylation of Indoles with Sulfinic Acids (Tables 2 and 3)**

To a solution of indole 1 (0.20 mmol) in DCE (1.0 mL) were added sulfinic acid (0.24 mmol), tetrabutylammonium iodide (88.6 mg, 0.24 mmol) and TsOH (6.9 mg, 0.040 mmol). The resulting mixture was stirred at 80 °C for 12 h. The mixture was cooled to room temperature, and purified by flash column chromatography on silica gel, eluting with petroleum ether/ethyl acetate (100:1 to 10:1), to give compound 3.

**Analytical Data for the Products Shown in Tables 2 and 3**

![3a](image)

3a, white solid, m.p. 151–154 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.35 (s, 1H), 7.61 (d, $J$ = 8.0 Hz, 1H), 7.47–7.39 (m, 2H), 7.29–7.22 (m, 1H), 7.19–7.00 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 139.2, 136.5, 130.7, 129.1, 128.7, 125.9, 124.8, 123.1, 120.9, 119.7, 111.6, 102.9.

![3b](image)

3b, white solid, m.p. 81–83 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.60 (d, $J$ = 8.0 Hz, 1H), 7.34 (d, $J$ = 8.0 Hz, 1H), 7.30–7.23 (m, 2H), 7.19–7.05 (m, 5H), 7.05–6.97 (m, 1H), 3.76 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 139.7, 137.5, 135.0, 129.8, 128.6, 125.7, 124.6, 122.5, 120.5, 119.7, 109.7, 100.5, 33.0.
3c, 2 white solid, m.p. 111–112 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.14 (s, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.21–7.07 (m, 4H), 7.06–6.97 (m, 3H), 2.46 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 141.1, 139.3, 135.4, 130.3, 128.7, 125.5, 124.5, 122.2, 120.7, 119.0, 110.6, 99.3, 12.1.

3d, 2 colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 8.52 (s, 1H), 7.75–7.70 (m, 2H), 7.62 (d, J = 7.6 Hz, 1H), 7.43–6.98 (m, 11H); ¹³C NMR (100 MHz, CDCl₃) δ 142.1, 139.3, 135.9, 131.5, 131.2, 128.9, 128.8, 128.7, 128.2, 125.6, 124.7, 123.4, 121.2, 120.0, 111.2.

3e, 2 white solid, m.p. 135–137 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.51 (s, 1H), 7.49 (d, J = 2.8 Hz, 1H), 7.40–7.30 (m, 2H), 7.21–7.14 (m, 2H), 7.12–7.02 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 141.0, 137.7, 133.1, 128.7, 126.3, 125.9, 124.7, 124.0, 114.7, 111.1, 103.8.

3f, 2 white solid, m.p. 118–120 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.66 (s, 1H), 7.74 (d, J = 1.6 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35–7.23 (m, 2H), 7.19–7.12 (m, 2H), 7.10–7.02 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.8, 135.2, 132.0, 131.0, 128.8, 126.0, 125.9, 125.0, 122.1, 114.4, 113.1, 102.5.

3g, 2 white solid, m.p. 77–80 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.36 (s, 1H), 7.35 (d, J = 2.8 Hz, 1H), 7.24 (d, J = 8.8 Hz, 1H), 7.18–7.00 (m, 6H), 6.92–6.85 (m, 1H), 3.74 (s, 3H); ¹³C NMR
(100 MHz, CDCl$_3$) $\delta$ 155.1, 139.3, 131.4, 129.9, 128.7, 125.6, 124.7, 113.5, 112.5, 101.9, 100.8, 55.8.

3h, 2 white solid, m.p. 172–175 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.70 (s, 1H), 8.40–8.36 (m, 1H), 8.02–7.94 (m, 1H), 7.56 (d, $J = 2.8$ Hz, 1H), 7.46 (d, $J = 8.8$ Hz, 1H), 7.20–7.12 (m, 2H), 7.12–7.02 (m, 3H), 3.89 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 167.9, 139.1, 138.8, 132.1, 128.9, 128.8, 126.0, 125.0, 124.5, 123.2, 122.5, 111.4, 104.8, 51.9.

3i, 2 yellow solid, m.p. 151–154 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.93 (s, 1H), 8.57 (d, $J = 2.4$ Hz, 1H), 8.20–8.14 (m, 1H), 7.66 (d, $J = 2.4$ Hz, 1H), 7.53–7.46 (m, 1H), 7.23–7.15 (m, 2H), 7.15–7.05 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.9, 139.5, 137.8, 133.6, 129.0, 128.9, 126.5, 125.6, 118.7, 116.9, 111.9, 106.7.

3j, 2 white solid, m.p. 106–108°C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.39 (s, 1H), 7.52–7.44 (m, 2H), 7.42 (d, $J = 1.6$ Hz, 1H), 7.20–7.02 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 138.7, 136.8, 131.1, 129.1, 128.8, 127.7, 126.0, 125.0, 121.7, 120.6, 111.6, 103.5.

3k, 2 white solid, m.p. 130–133 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.58 (s, 1H), 7.94–7.84 (m, 2H), 7.58–7.52 (m, 2H), 7.50–7.45 (m, 1H), 7.39–7.33 (m, 1H), 7.32–7.25 (m, 2H), 7.22–7.15 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 148.7, 142.6, 136.6, 131.3, 129.3, 128.5, 123.5, 121.3, 120.3, 119.7, 119.2, 111.9, 100.9.
3l, yellow solid, m.p. 180–183 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.71 (s, 1H), 8.01–7.93 (m, 2H), 7.54–7.46 (m, 3H), 7.34–7.27 (m, 1H), 7.22–7.15 (m, 1H), 7.15–7.08 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 149.9, 144.9, 136.6, 131.3, 128.4, 125.1, 123.9, 123.5, 121.4, 119.2, 112.0, 100.1.

3m, white solid, m.p. 130–133 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.36 (s, 1H), 7.59 (d, \(J = 8.8\) Hz, 1H), 7.47–7.39 (m, 2H), 7.29–7.22 (m, 1H), 7.20–7.12 (m, 1H), 7.11–7.04 (m, 2H), 6.90–6.82 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 160.9 (d, \(J = 243\) Hz), 136.5, 134.0 (d, \(J = 2.9\) Hz), 130.5, 128.9, 127.9 (d, \(J = 7.8\) Hz), 123.2, 121.0, 119.6, 115.8 (d, \(J = 22\) Hz), 111.7, 103.4.

3n, white solid, m.p. 130–132 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.39 (s, 1H), 7.57 (d, \(J = 8.0\) Hz, 1H), 7.47–7.39 (m, 2H), 7.30–7.22 (m, 1H), 7.20–7.13 (m, 1H), 7.12–7.07 (m, 2H), 7.04–6.97 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 137.9, 136.5, 130.7, 130.6, 128.8, 127.2, 123.2, 121.1, 119.5, 111.7, 102.5.

3o, white solid, m.p. 144–147 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.40 (s, 1H), 7.59–7.53 (m, 1H), 7.46–7.39 (m, 2H), 7.30–7.21 (m, 3H), 7.20–7.13 (m, 1H), 6.97–6.90 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 138.6, 136.5, 131.7, 130.8, 128.8, 127.5, 123.3, 121.1, 119.5, 118.4, 111.7, 102.3.
3p, 2 white solid, m.p. 129–132 °C; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.43 (s, 1H), 7.58–7.53 (m, 1H), 7.48–7.40 (m, 4H), 7.31–7.22 (m, 1H), 7.20–7.13 (m, 1H), 6.85–6.79 (m, 2H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 139.6, 137.5, 136.5, 130.8, 128.8, 127.7, 123.3, 121.1, 119.5, 111.7, 102.1, 89.0.

\[ \text{S-S-Me} \]

\[ \text{3p} \]

3q, 2 white solid, m.p. 125–127 °C; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.19 (s, 1H), 7.60 (d, \( J = 7.6 \) Hz, 1H), 7.35–7.31 (m, 2H), 7.25–7.18 (m, 1H), 7.16–7.10 (m, 1H), 7.02 (d, \( J = 8.4 \) Hz, 2H), 6.94 (d, \( J = 8.4 \) Hz, 2H), 2.22 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 136.4, 135.4, 134.7, 130.5, 129.5, 129.0, 126.3, 122.9, 120.8, 119.6, 111.6, 103.3, 20.8.

\[ \text{S-S-OMe} \]

\[ \text{3q} \]

3r, 2 yellow solid, m.p. 111–112 °C; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.29 (s, br, 1H), 7.62 (d, \( J = 8.0 \) Hz, 1H), 7.39–7.32 (m, 2H), 7.26–7.18 (m, 1H), 7.17–7.08 (m, 3H), 6.75–6.68 (m, 2H), 3.70 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 157.8, 136.5, 130.1, 129.6, 129.0, 128.6, 123.0, 120.8, 119.6, 114.6, 111.6, 104.5, 55.4.

\[ \text{S-S-O-Me} \]

\[ \text{3r} \]

3s, 2 white solid, m.p. 140–142 °C; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.45 (s, 1H), 7.74–7.69 (m, 1H), 7.66–7.59 (m, 2H), 7.59–7.52 (m, 2H), 7.50–7.48 (m, 1H), 7.47–7.43 (m, 1H), 7.40–7.31 (m, 2H), 7.30–7.24 (m, 2H), 7.18–7.11 (m, 1H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 136.7, 136.6, 133.8, 131.3, 130.7, 129.1, 128.2, 127.7, 126.9, 126.3, 125.0, 124.8, 123.6, 123.1, 121.0, 119.7, 111.6, 102.9.

\[ \text{S-S-Me} \]

\[ \text{3s} \]

3t, 2 colorless oil; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.16 (s, 1H), 7.79–7.74 (m, 1H), 7.39–7.34 (m, 1H), 7.29 (d, \( J = 2.8 \) Hz, 1H), 7.27–7.17 (m, 2H), 2.37 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 136.3, 128.8, 127.8, 122.7, 120.4, 119.3, 111.5, 108.3, 20.2.
$\text{Sulfenylation of Indoles with Sulfinic Acids in the Abscence of Tetrabutylammonium Iodide}$

To a solution of indole $1a$ (23.4 mg, 0.20 mmol) in DCE (1.0 mL) were added benzenesulfinic acid $2a$ (34.1 mg, 0.24 mmol) and TsOH (6.9 mg, 0.040 mmol). The resulting mixture was stirred at 80 °C for 12 h. The mixture was cooled to room temperature, and detect by TLC, found no compound $3a$.

$\text{Reduction of Benzenesulfinic Acid 2a}$

To a solution of benzenesulfinic acid $2a$ (34.1 mg, 0.24 mmol) in DCE (1.0 mL) were added tetrabutylammonium iodide (88.6 mg, 0.24 mmol) and TsOH (6.9 mg, 0.040 mmol). The resulting mixture was stirred at 80 °C for 12 h. The mixture was cooled to room temperature, and purified by flash column chromatography on silica gel, eluting with petroleum ether, to give compound $4a$ (50.2 mg, 96%).

$\text{Reaction of Indole 1a with Diphenyldisulfane 4a in 1.2 eq I}_2$
To a solution of indole 1a (23.4 mg, 0.20 mmol) in DCE (1.0 mL) were added diphenyldisulfane 4a (52.3 mg, 0.24 mmol), iodine (61.0 mg, 0.24 mmol) and TsOH (6.9 mg, 0.040 mmol). The resulting mixture was stirred at 80 °C for 12 h. The mixture was cooled to room temperature, and purified by flash column chromatography on silica gel, eluting with petroleum ether/ethyl acetate (30:1), to give compound 3a (44.6 mg, 99%).

**Reaction of Indole 1a with Diphenyldisulfane 4a under the Optimized Reaction Conditions**

To a solution of indole 1a (23.4 mg, 0.20 mmol) in DCE (1.0 mL) were added diphenyldisulfane 4a (52.3 mg, 0.24 mmol), tetrabutylammonium iodide (88.6 mg, 0.24 mmol) and TsOH (6.9 mg, 0.040 mmol). The resulting mixture was stirred at 80 °C for 12 h. The mixture was cooled to room temperature, and detect by TLC, found no compound 3a.

**References**


$\text{S-10}$

$\text{H N M R (} 400 \text{ MHz, CDCl}_3)$

$3b$

$\text{13C NMR (} 100 \text{ MHz, CDCl}_3)$
$^{1}H$ NMR (400 MHz, CDC$_3$)

$^{13}C$ NMR (100 MHz, CDC$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (100 MHz, CDCl$_3$)
$1^1$H NMR (400 MHz, CDCl$_3$)

$1^3$C NMR (100 MHz, CDCl$_3$)
$\text{MeO} - \text{S-Ph}$

$3g$

$^1H\text{ NMR (400 MHz, CDCl}_3\text{)}$

$\text{MeO} - \text{S-Ph}$

$3g$

$^{13}\text{C NMR (100 MHz, CDCl}_3\text{)}$
$\text{MeOOC} \begin{array}{c} S-\text{Ph} \\ 3h \end{array}$

$\text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3)$

$\begin{array}{c} \text{MeOOC} \\ S-\text{Ph} \\ 3h \end{array}$

$\text{\textsuperscript{13}C NMR (100 MHz, CDCl}_3)$
$^{1}$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
$\text{SH}_3$ $\text{NO}_2$

$\text{HNR} (400 \text{ MHz, CDCl}_3)$

$\text{SH}_3$ $\text{NO}_2$

$\text{HNR} (100 \text{ MHz, CDCl}_3)$
$\text{S-20}$

$\text{N}$

$\text{H}$

$\text{S}$

3

$\text{l}$

$\text{N}$

$\text{O}$2

1

H

M

R

($400$ MHz, CDCl$_3$)

$\text{S-20}$

$\text{N}$

$\text{H}$

$\text{S}$

3

$\text{l}$

$\text{N}$

$\text{O}$2

1

3

C

N

M

R

($100$ MHz, CDCl$_3$)
$30$

$^1H$ NMR (400 MHz, CDCl$_3$)

$^13$C NMR (100 MHz, CDCl$_3$)
$\text{H NMR (400 MHz, CDCl}_3\text{)}$

$\text{C NMR (100 MHz, CDCl}_3\text{)}$
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
$\text{3r}$

$^1\text{H NMR (400 MHz, CDCl}_3)$

$\text{3r}$

$^{13}\text{C NMR (100 MHz, CDCl}_3)$
$^1\text{H NMR (400 MHz, CDCl}_3\text{)}$

$^{13}\text{C NMR (100 MHz, CDCl}_3\text{)}$
S-(CH$_2$)$_7$CH$_3$

$^1$H NMR (400 MHz, CDCl$_3$)

S-(CH$_2$)$_7$CH$_3$

$^1$C NMR (100 MHz, CDCl$_3$)