Copper-mediated ortho C-H sulfonylation of benzoic acid derivatives with sodium sulfinates

Jidan Liu, Lin Yu, Shaobo Zhuang, Qingwen Gui, Xiang Chen, Wenduo Wang and Ze Tan*

Supporting Information

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1. General information

$^1$H NMR and $^{13}$C NMR were recorded in CDCl$_3$ or DMSO-$d_6$ at room temperature on the Varian INOVA-400 spectrometer (400 MHz $^1$H) or Bruker spectrometer (400 MHz $^1$H). The chemical-shifts scale is based on internal TMS. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; qui, quintet; sxt, sextet. The coupling constants, $J$ are reported in Hertz (Hz). Mass spectroscopy data were collected on an HRMS-EI instrument.

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Anhydrous Cu(OAc)$_2$ was purchased from Alfa Aesar. All solvents were purified and dried according to standard methods prior to use. Products were purified by flash column chromatography on 200-300 mesh silica gel, SiO$_2$.

2. Typical procedure for the preparation of benzamides

All benzamides 1 were synthesized from the corresponding benzoic acids or benzoyl chlorides and 8-aminoquinoline. The deuterated amides were synthesized according to a literature method, spectral properties are consistent with literature values.$^1$ The following amides were synthesized according to literature procedures.$^2$

![Diagram of benzamides 1a to 1i]
3. Typical procedure for the preparation of sodium sulfinates

Sulfinic acid sodium salts 2a, 2b and 2k were purchased from Alfa-Aesar and were used as received without further purification. 4-Methoxybenzenesulfinic acid sodium salt 2c was prepared by heating 5.0 g of sodium sulfite, 4.12 g of 4-methoxybenzenesulphonyl chloride, and 3.36 g of sodium bicarbonate in 20 mL of water at 80 °C for 8 h. After cooling to room temperature, water was removed under vacuum. Recrystallization of the residue in ethanol afforded the product as a white solid in 67% (2.68 g) yield. Similarly, other sodium arenesulfinates 2d-2j were prepared from their corresponding sulphonyl chlorides.3

4. Cu(II)-mediated sulfonylation of sp² C-H bonds

4.1 Optimization of reaction conditions
Table S1 Screening of temperature\(^a\)

\[
\begin{align*}
\text{HN-} & \text{O} & \text{HN-} & \text{O} \\
1a & + & 2a & \xrightarrow{\text{Cu(OAc)}_2, \text{K}_2\text{CO}_3, \text{DMF, Temp, 4 h, air}} 3a
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temp. (°C)</th>
<th>Yield(^b) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>r.t.</td>
<td>trace</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>70</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>90</td>
<td>74</td>
</tr>
</tbody>
</table>

\(^a\) Reaction condition: amide 1a (0.3 mmol), 2a (0.6 mmol), Cu(OAc)\(_2\) (0.3 mmol), K\(_2\)CO\(_3\) (0.6 mmol), DMF (1 mL) under air for 4 h. \(^b\) Isolated yield.

Table S2 Screening of amount of Cu(OAc)\(_2\)\(^a\)

\[
\begin{align*}
\text{HN-} & \text{O} & \text{HN-} & \text{O} \\
1a & + & 2a & \xrightarrow{\text{Cu(OAc)}_2, \text{K}_2\text{CO}_3, \text{DMF, 80 °C, 4 h, air}} 3a
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cu(OAc)(_2)</th>
<th>Yield(^b) (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0.1 eq</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>0.2 eq</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>0.5 eq</td>
<td>55</td>
</tr>
<tr>
<td>5</td>
<td>1.0 eq</td>
<td>76</td>
</tr>
<tr>
<td>6</td>
<td>1.5 eq</td>
<td>68</td>
</tr>
</tbody>
</table>

\(^a\) Reaction condition: amide 1a (0.3 mmol), 2a (0.6 mmol), K\(_2\)CO\(_3\) (0.6 mmol), DMF (1 mL) under air for 4 h. \(^b\) Isolated yield.
Table S3  Screening of oxidants$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxidant</th>
<th>Yield$^b$ (%)</th>
<th>SM$^b$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ag$_2$CO$_3$</td>
<td>26</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>AgOAc</td>
<td>22</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>Select F</td>
<td>8</td>
<td>67</td>
</tr>
<tr>
<td>4</td>
<td>NFSI</td>
<td>0</td>
<td>52</td>
</tr>
<tr>
<td>5</td>
<td>K$_2$S$_2$O$_8$</td>
<td>trace</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>NMO</td>
<td>34</td>
<td>40</td>
</tr>
</tbody>
</table>

$^a$ Reaction condition: amide 1a (0.3 mmol), 2a (0.6 mmol), Cu(OAc)$_2$ (0.06 mmol), K$_2$CO$_3$ (0.6 mmol), oxidant (0.3 mmol), DMF (1 mL) under air for 4 h. $^b$ Isolated yield.

4.2 General procedure for copper-mediated C-H sulfonylation of benzoic acid derivatives.

Benzamide 1 (0.3 mmol), anhydrous Cu(OAc)$_2$ (55 mg, 0.3 mmol), K$_2$CO$_3$ (83 mg, 0.6 mmol), sulfinic acid sodium salt 2 (0.6 mmol) and anhydrous DMF (1 mL) were added to a 25-mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal. Then the flask was sealed under air and stirred at 80 °C for 4 h. After the completion of the reaction, the solvent was evaporated under reduced pressure and the residue was then quenched with 1 M HCl aqueous solution (10 mL). The mixture was extracted with ethyl acetate, and the combined organic layer was dried over sodium sulfate. Concentration in vacuo followed by silica gel column purification with petroleum ether/ethyl acetate elutent gave the desired product 3.

4.3 Deuterium-labeling experiments.
Intermolecular competition KIE Following general procedure: 1a (74 mg, 0.3 mmol), 1a-d$_5$ (76 mg, 0.3 mmol), Cu(OAc)$_2$ (109 mg, 0.6 mmol), K$_2$CO$_3$ (166 mg, 1.2 mmol), sodium benzenesulfinate (197 mg, 1.2 mmol) and anhydrous DMF (2 mL) were added to a 25-mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal. Then the flask was sealed under air and stirred at 80 °C for 1 h. The product was separated by column chromatography to give the desired product less than 40 % yield. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 10.29 (s, 1H), 8.85 (d, $J = 3.2$ Hz, 1H), 8.72 (d, $J = 7.5$ Hz, 1H), 8.45 (d, $J = 8.0$ Hz, 1H), 8.20 (d, $J = 7.7$ Hz, 0.75H), 8.01 (d, $J = 7.6$ Hz, 2H), 7.87-7.74 (m, 3.26H), 7.71 (d, $J = 7.8$ Hz, 1H), 7.67-7.62 (m, 2H), 7.57 (t, $J = 7.5$ Hz, 2.25H). The KIE value was calculated as $k_H/k_D = 3.0$. 
Intramolecular competition KIE Following general procedure: 1a-d₁ (75 mg, 0.3 mmol), Cu(OAc)₂ (55 mg, 0.3 mmol), K₂CO₃ (83 mg, 0.6 mmol), sodium benzenesulfinylate (98 mg, 0.6 mmol) and anhydrous DMF (1 mL) were added to a 25-mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal. Then the flask was sealed under air and stirred at 80 °C for 1 h. The product was separated by column chromatography to give the desired product less than 40 % yield. ¹H NMR (400 MHz, DMSO-δ) δ 10.29 (s, 1H), 8.95-8.79 (m, 1H), 8.72 (d, J = 7.4 Hz, 1H), 8.46 (dd, J = 8.3, 1.2 Hz, 1H), 8.20 (d, J = 7.8 Hz, 1H), 8.01 (d, J = 7.5 Hz, 2H), 7.88-7.73 (m, 3.34H), 7.71 (d, J = 7.8 Hz, 1H), 7.68-7.61 (m, 2H), 7.57 (t, J = 7.6 Hz, 2H). The KIE value was calculated as kᵦ/kᵦD = 3.5.
4.4 Removal of directing group.

**2-Tosylbenzoic acid:** N-(quinolin-8-yl)-2-tosylbenzamide 3q (402 mg, 1 mmol) was dissolved in anhydrous THF (10 mL) and the resulting solution was cooled to 0°C. To this solution, NaH (80 mg, 2 mmol) was added in portions over 10 min. The resulting solution was allowed to stir for 1 h. Mel (710 mg, 5 mmol) was added dropwise over 5 min, and reaction mixture was stirred for additional 1 hours at 0 °C and stirred overnight at rt. After the reaction was quenched by addition water, the mixture was extracted with Et₂O, and the organic layer was dried by anhydrous Na₂SO₄. After remove the solvent, the residue was purified by column chromatography (eluent: ethyl acetate/petrol ether =1/1) to give intermediate 4 as yellow solid (341 mg, 82%). Intermediate 4 (208 mg, 0.5 mmol) and NaOH (307 mg, 7.5 mmol) were dissolved in EtOH (5 ml). The resulting mixture was stirred at 130 °C for 24 hours. After that, reaction mixture was diluted with EtOAc (100 mL) and 1N HCl (30
mL) was added. Organic layer was washed with 1N HCl (5 x 20 mL), dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated under vacuum affording pure product as a yellow solid (80%).

**1H NMR (400 MHz, DMSO-d₆):** δ 13.62 (br, 1H), 8.13 (d, J = 7.4 Hz, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.78-7.69 (m, 2H), 7.65-7.58 (m, 1H), 7.41 (d, J = 8.1 Hz, 2H), 2.37 (s, 3H). **13C NMR (100 MHz, DMSO-d₆):** δ 168.93, 144.76, 138.72, 138.30, 134.96, 134.38, 131.24, 130.23, 130.21, 129.05, 128.34, 21.56. HRMS (EI, m/z): calcd for C₁₄H₁₂O₄S⁺ [M⁺]: 276.0446; Found: 276.0451.

### 5 Characterization data of products.

#### 2-(Phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3a)

![Chemical structure of 3a]

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 76% yield. **1H NMR (400 MHz, DMSO-d₆):** δ 10.28 (s, 1H), 8.85 (dd, J = 4.1, 1.4 Hz, 1H), 8.72 (d, J = 7.2 Hz, 1H), 8.45 (dd, J = 8.3, 1.4 Hz, 1H), 8.20 (d, J = 7.9 Hz, 1H), 8.01 (d, J = 7.4 Hz, 2H), 7.87-7.74 (m, 4H), 7.71 (d, J = 7.8 Hz, 1H), 7.68-7.62 (m, 2H), 7.57 (t, J = 7.6 Hz, 2H). **13C NMR (100 MHz, DMSO-d₆):** δ 166.04, 149.59, 141.53, 138.63, 138.16, 137.20, 137.14, 134.73, 134.66, 134.17, 131.29, 130.39, 129.82, 129.28, 128.33, 128.29, 127.50, 123.22, 122.77, 117.73. HRMS (EI, m/z): calcd for C₂₂H₁₆N₂O₃S⁺ [M⁺]: 388.0863; Found: 388.0876.

#### 4-Methoxy-2-(phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3b)

![Chemical structure of 3b]

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a yellow solid in 74% yield. **1H NMR (400 MHz, DMSO-d₆):** δ 10.13 (s, 1H), 8.85 (dd, J = 4.1, 1.5 Hz, 1H), 8.68 (d, J = 7.4 Hz, 1H), 8.45 (dd, J = 8.3, 1.5 Hz, 1H), 8.01 (d, J = 7.4 Hz, 2H), 7.79-7.63 (m, 6H), 7.55 (t, J = 7.7 Hz, 2H), 7.38 (dd, J = 8.4, 2.4 Hz, 1H), 3.92 (s, 3H). **13C NMR (100 MHz, DMSO-d₆):** δ 165.71, 160.74, 149.56, 141.34, 139.74, 138.48,
137.15, 134.66, 134.16, 131.10, 129.73, 129.64, 128.39, 128.29, 127.50, 123.03, 122.77, 119.59, 117.34, 115.59, 56.59. HRMS (EI, m/z): calcd for C\textsubscript{23}H\textsubscript{18}N\textsubscript{2}O\textsubscript{4}S\textsuperscript{+} [M\textsuperscript{+}]: 418.0982; Found: 418.0986.

4-Methyl-2-(phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3c)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 71% yield. \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6): \textgreek{d} 10.17 (s, 1H), 8.84 (d, \textit{J} = 2.9 Hz, 1H), 8.71 (d, \textit{J} = 7.4 Hz, 1H), 8.53-8.37 (m, 1H), 8.08-7.98 (m, 3H), 7.77 (d, \textit{J} = 7.8 Hz, 1H), 7.73-7.60 (m, 5H), 7.56 (t, \textit{J} = 7.6 Hz, 2H), 2.46 (s, 3H). \textsuperscript{13}C NMR (100 MHz, DMSO-\textit{d}_6): \textgreek{d} 166.06, 149.57, 141.62, 141.58, 138.50, 138.06, 137.13, 135.10, 134.63, 134.07, 130.45, 129.82, 129.75, 129.17, 128.26, 128.13, 127.50, 123.08, 122.76, 117.45, 21.18. HRMS (EI, m/z): calcd for C\textsubscript{23}H\textsubscript{18}N\textsubscript{2}O\textsubscript{3}S\textsuperscript{+} [M\textsuperscript{+}]: 402.1032; Found: 402.1033.

4-(\textit{tert}-Butyl)-2-(phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3d)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 75% yield. \textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}_6): \textgreek{d} 10.22 (s, 1H), 8.82 (dd, \textit{J} = 4.2, 1.5 Hz, 1H), 8.73 (d, \textit{J} = 7.0 Hz, 1H), 8.42 (dd, \textit{J} = 8.3, 1.5 Hz, 1H), 8.14 (d, \textit{J} = 1.8 Hz, 1H), 8.07-8.01 (m, 2H), 7.84 (dd, \textit{J} = 8.0, 1.8 Hz, 1H), 7.77-7.65 (m, 3H), 7.64-7.59 (m, 2H), 7.55 (t, \textit{J} = 7.5 Hz, 2H), 1.32 (s, 9H). \textsuperscript{13}C NMR (100 MHz, DMSO-\textit{d}_6): \textgreek{d} 165.96, 154.22, 149.48, 141.57, 138.49, 138.07, 137.09, 134.74, 134.63, 134.07, 131.68, 129.76, 129.28, 128.33, 128.27, 127.48, 126.54, 123.07, 122.72, 117.41, 35.37, 31.10. HRMS (EI, m/z): calcd for C\textsubscript{26}H\textsubscript{24}N\textsubscript{2}O\textsubscript{3}S\textsuperscript{+} [M\textsuperscript{+}]: 444.1500; Found: 444.1502.
4-Fluoro-2-(phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3e)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 62% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.40 (s, 1H), 8.86 (dd, $J = 4.0$, 1.2 Hz, 1H), 8.72 (d, $J = 7.3$ Hz, 1H), 8.44 (dd, $J = 8.3$, 1.3 Hz, 1H), 8.13-8.03 (m, 3H), 7.85 (dd, $J = 8.4$, 5.2 Hz, 1H), 7.78 (d, $J = 7.5$ Hz, 1H), 7.71-7.62 (m, 4H), 7.58 (t, $J = 7.6$ Hz, 2H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 165.33, 162.48 (d, $J_{C-F} = 250.1$ Hz), 149.55, 140.91, 140.54 (d, $J_{C-F} = 6.5$ Hz), 138.73, 137.11, 134.71, 134.44, 133.95, 132.50 (d, $J_{C-F} = 8.0$ Hz), 129.84, 128.62, 128.34, 127.46, 123.31, 122.73, 121.70 (d, $J_{C-F} = 21.3$ Hz), 117.97, 117.43 (d, $J_{C-F} = 24.7$ Hz). $^{19}$F NMR (377 MHz, DMSO-$d_6$): $\delta$ -108.03. HRMS (EI, m/z): calcd for C$_{22}$H$_{15}$FN$_2$O$_3$S$^+$ [M$^+$]: 406.0781; Found: 406.0782.

4-Chloro-2-(phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3f)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 68% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.48 (s, 1H), 8.86 (dd, $J = 4.0$, 1.2 Hz, 1H), 8.72 (d, $J = 7.3$ Hz, 1H), 8.44 (dd, $J = 8.3$, 1.3 Hz, 1H), 8.22 (d, $J = 1.9$ Hz, 1H), 8.08 (d, $J = 7.5$ Hz, 2H), 7.87 (dd, $J = 8.2$, 1.9 Hz, 1H), 7.78 (dd, $J = 8.3$, 2.5 Hz, 2H), 7.72-7.62 (m, 3H), 7.58 (t, $J = 7.6$ Hz, 2H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 165.31, 149.54, 140.90, 140.12, 138.79, 137.10, 136.00, 135.51, 134.71, 134.48, 131.33, 129.87, 129.68, 128.65, 128.57, 128.36, 127.45, 123.40, 122.72, 118.17. HRMS (EI, m/z): calcd for C$_{22}$H$_{15}$ClN$_2$O$_3$S$^+$ [M$^+$]: 422.0484; Found: 422.0486.

2-(Phenylsulfonyl)-N-(quinolin-8-yl)-4-(trifluoromethyl)benzamide (3g)
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 59% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.72 (s, 1H), 8.87 (d, $J = 3.0$ Hz, 1H), 8.74 (d, $J = 7.5$ Hz, 1H), 8.51-8.39 (m, 2H), 8.20 (d, $J = 7.9$ Hz, 1H), 8.10 (d, $J = 7.7$ Hz, 2H), 7.98 (d, $J = 7.9$ Hz, 1H), 7.79 (d, $J = 8.0$ Hz, 1H), 7.74-7.63 (m, 3H), 7.59 (t, $J = 7.6$ Hz, 2H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 165.29, 149.59, 140.91, 140.75, 139.52, 139.01, 137.08, 134.81, 134.62, 131.51 (q, $J_{C\text{-}F} = 3.4$ Hz), 131.36, 131.05, 129.96, 128.73, 128.43, 127.45, 126.78 (q, $J_{C\text{-}F} = 3.4$ Hz), 123.58, 123.55 (q, $J_{C\text{-}F} = 271.8$ Hz), 122.74, 118.50. $^{19}$F NMR (377 MHz, DMSO-$d_6$): $\delta$ -61.36. HRMS (EI, m/z): calcd for C$_{23}$H$_{15}$F$_3$N$_2$O$_3$S$^+$ [M$^+$]: 456.0743; Found: 456.0750.

Methyl 3-(phenylsulfonyl)-4-(quinolin-8-ylcarbamoyl)benzoate (3h)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a yellow solid in 57% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.60 (s, 1H), 8.92-8.81 (m, 1H), 8.71 (d, $J = 7.5$ Hz, 1H), 8.59 (d, $J = 1.2$ Hz, 1H), 8.45 (dd, $J = 8.3$, 1.1 Hz, 1H), 8.30 (dd, $J = 7.9$, 1.2 Hz, 1H), 8.03 (d, $J = 7.6$ Hz, 2H), 7.91 (d, $J = 7.9$ Hz, 1H), 7.79 (d, $J = 8.0$ Hz, 1H), 7.73-7.62 (m, 3H), 7.59 (t, $J = 7.6$ Hz, 2H), 3.94 (s, 3H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 165.51, 164.94, 149.63, 140.99, 140.90, 138.93, 138.85, 137.10, 134.94, 134.69, 134.48, 131.98, 130.43, 130.37, 129.98, 128.41, 127.46, 123.56, 122.76, 118.40, 53.43 (one signal was overlapped by other ones). HRMS (EI, m/z): calcd for C$_{23}$H$_{15}$F$_3$N$_2$O$_3$S$^+$ [M$^+$]: 446.0932; Found: 446.0935.

4-Nitro-2-(phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3i)

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Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a yellow solid in 50% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.81 (s, 1H), 8.95-8.85 (m, 1H), 8.74 (d, $J = 7.5$ Hz, 1H), 8.56-8.39 (m, 4H), 8.06 (d, $J = 7.6$ Hz, 2H), 7.81 (d, $J = 8.1$ Hz, 1H), 7.71 (t, $J = 8.0$ Hz, 2H), 7.64 (dt, $J = 15.6$, 5.8 Hz, 3H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 164.49, 150.49, 149.60, 143.32, 140.47, 139.07, 138.64, 137.10, 134.86, 134.81, 132.22, 130.04, 128.71, 128.43, 127.43, 125.68, 124.65, 123.62, 122.73, 118.68. HRMS (EI, m/z): calcd for C$_{22}$H$_{15}$N$_3$O$_5$S$^+$ [M$^+$]: 433.0734; Found: 433.0730.

5-Methyl-2-(phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3j)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 72% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.20 (s, 1H), 8.85 (d, $J = 2.9$ Hz, 1H), 8.72 (d, $J = 7.4$ Hz, 1H), 8.45 (dd, $J = 8.2$, 1.1 Hz, 1H), 8.07 (d, $J = 8.0$ Hz, 1H), 7.98 (d, $J = 7.5$ Hz, 2H), 7.78 (d, $J = 7.8$ Hz, 1H), 7.70 (d, $J = 7.8$ Hz, 1H), 7.68-7.53 (m, 6H), 2.42 (s, 3H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 166.05, 149.58, 145.63, 141.83, 138.52, 137.15, 135.28, 134.63, 133.99, 131.64, 130.42, 129.76, 129.58, 128.30, 128.10, 127.51, 123.14, 122.78, 117.54, 21.32 (one signal was overlapped by other ones). HRMS (EI, m/z): calcd for C$_{23}$H$_{18}$N$_2$O$_3$S$^+$ [M$^+$]: 402.1032; Found: 402.1035.

5-Chloro-2-(phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3k)
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 70% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$

- 10.57 (s, 1H), 8.92-8.84 (m, 1H), 8.72 (d, $J = 7.5$ Hz, 1H), 8.44 (dd, $J = 8.3$, 1.1 Hz, 1H), 8.18 (d, $J = 8.6$ Hz, 1H), 8.02 (d, $J = 7.6$ Hz, 2H), 7.88 (d, $J = 1.9$ Hz, 1H), 7.84-7.76 (m, 2H), 7.67 (ddd, $J = 12.0$, 9.8, 6.1 Hz, 3H), 7.58 (t, $J = 7.6$ Hz, 2H).

$^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$

- 164.79, 149.55, 141.28, 139.38, 138.92, 138.90, 137.06, 136.97, 134.77, 134.30, 132.27, 131.00, 129.85, 129.33, 128.36, 128.34, 127.42, 123.42, 122.70, 118.30.

HRMS (EI, m/z): calcd for C$_{22}$H$_{15}$ClN$_2$O$_3$S$^+$ [M$^+$]: 422.0484; Found: 422.0482.

2-(Phenylsulfonyl)-N-(quinolin-8-yl)-5-(trifluoromethyl)benzamide (3l)

![Chemical Structure](image)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 62% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$

- 10.77 (s, 1H), 8.89 (d, $J = 3.3$ Hz, 1H), 8.78 (d, $J = 7.6$ Hz, 1H), 8.44 (d, $J = 8.1$ Hz, 1H), 8.39 (d, $J = 8.3$ Hz, 1H), 8.15 (s, 1H), 8.11 (d, $J = 8.5$ Hz, 1H), 8.07 (d, $J = 7.8$ Hz, 2H), 7.79 (d, $J = 8.0$ Hz, 1H), 7.73-7.58 (m, 5H).

$^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$

- 165.07, 149.53, 141.90, 140.76, 139.04, 138.26, 137.04, 134.94, 134.58, 133.85 (q, $J_{C,F} = 32.5$ Hz), 131.45, 129.94, 128.61, 128.41, 127.87 (q, $J_{C,F} = 3.4$ Hz), 127.41, 126.74 (q, $J_{C,F} = 3.6$ Hz), 123.51 (q, $J_{C,F} = 271.7$ Hz), 123.48, 122.66, 118.56.

$^{19}$F NMR (377 MHz, DMSO-$d_6$): $\delta$ -61.76. HRMS (EI, m/z): calcd for C$_{23}$H$_{15}$F$_3$N$_2$O$_3$S$^+$ [M$^+$]: 456.0743; Found: 456.0747.

2-Methyl-6-(phenylsulfonyl)-N-(quinolin-8-yl)benzamide (3m)

![Chemical Structure](image)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 65% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$
10.33 (s, 1H), 8.84 (dd, J = 4.2, 1.6 Hz, 1H), 8.78 (dd, J = 7.5, 1.2 Hz, 1H), 8.43 (dd, J = 8.3, 1.6 Hz, 1H), 8.04-7.92 (m, 3H), 7.77 (dd, J = 8.3, 1.2 Hz, 1H), 7.70 (t, J = 7.9 Hz, 1H), 7.66-7.59 (m, 4H), 7.53 (t, J = 7.6 Hz, 2H), 2.38 (s, 3H). 13C NMR (100 MHz, DMSO-d6): δ 165.70, 149.54, 141.81, 138.88, 137.94, 137.24, 137.05, 136.45, 136.65, 136.26, 134.67, 134.07, 130.34, 129.84, 128.39, 128.09, 127.60, 126.51, 123.20, 122.67, 118.12, 19.21. HRMS (EI, m/z): calcd for C23H18N2O3S+ [M+]: 402.1032; Found: 402.1036.

2-(Phenylsulfonyl)-N-(quinolin-8-yl)-1-naphthamide (3n)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 72% yield. 1H NMR (400 MHz, DMSO-d6): δ 10.78 (s, 1H), 8.90 (dd, J = 7.5, 1.2 Hz, 1H), 8.83 (dd, J = 4.2, 1.6 Hz, 1H), 8.46 (dd, J = 8.3, 1.6 Hz, 1H), 8.25 (d, J = 8.9 Hz, 1H), 8.15-8.03 (m, 5H), 7.83 (dd, J = 8.2, 1.2 Hz, 1H), 7.76 (t, J = 7.9 Hz, 2H), 7.72-7.56 (m, 5H). 13C NMR (100 MHz, DMSO-d6): δ 165.51, 149.62, 141.67, 139.18, 137.08, 136.40, 135.19, 134.92, 134.36, 134.31, 131.05, 129.98, 129.24, 128.83, 128.49, 128.20, 127.55, 126.86, 124.31, 123.57, 122.69, 118.82 (two signals were overlapped by other ones). HRMS (EI, m/z): calcd for C26H18N2O3S+[M+]': 438.1036; Found: 438.1039.

3-(Phenylsulfonyl)-N-(quinolin-8-yl)isonicotinamide (3o)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a yellow solid in 47% yield. 1H NMR (400 MHz, DMSO-d6): δ 10.85 (s, 1H), 9.33 (s, 1H), 8.97 (d, J = 4.9 Hz, 1H), 8.89 (dd, J = 4.0, 1.3 Hz, 1H), 8.74 (d, J = 7.4 Hz, 1H), 8.44 (dd, J = 8.2, 1.2 Hz, 1H), 8.10 (d, J = 7.5 Hz, 2H), 7.79 (dd, J = 9.8, 6.6 Hz, 2H), 7.74-7.67 (m, 2H), 7.70-7.59 (m, 3H). 13C NMR (100 MHz, DMSO-d6): δ 164.57, 155.28, 150.53, 149.62, 144.06, 141.12, 139.07, 137.07, 134.74, 134.59, 133.94, 129.97, 128.55, 128.45, 127.42,
123.72, 123.34, 122.74, 118.73. HRMS (EI, m/z): calcd for C_{21}H_{15}N_{3}O_{3}S^{+} [M^{+}]: 389.0831; Found: 389.0833.

3-(Phenylsulfonyl)-N-(quinolin-8-yl)thiophene-2-carboxamide (3p)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 42% yield. ¹H NMR (400 MHz, DMSO-\textit{d}_6): \(\delta\) 10.93 (s, 1H), 8.95 (dd, \(J = 4.1, 1.4\) Hz, 1H), 8.62 (d, \(J = 7.6\) Hz, 1H), 8.47 (dd, \(J = 8.3, 1.3\) Hz, 1H), 8.13-8.04 (m, 2H), 7.97 (d, \(J = 5.3\) Hz, 1H), 7.81 (d, \(J = 8.2\) Hz, 1H), 7.73-7.59 (m, 6H). ¹³C NMR (100 MHz, DMSO-\textit{d}_6): \(\delta\) 158.75, 149.81, 142.70, 141.20, 138.86, 138.84, 137.18, 134.59, 134.18, 130.48, 130.12, 129.02, 128.39, 128.01, 127.42, 123.95, 122.92, 118.37. HRMS (EI, m/z): calcd for C_{20}H_{14}N_{2}O_{3}S_{2}^{+} [M^{+}]: 394.0446; Found: 394.0448.

N-(quinolin-8-yl)-2-tosylbenzamide (3q)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 80% yield. ¹H NMR (400 MHz, DMSO-\textit{d}_6): \(\delta\) 10.18 (s, 1H), 8.84 (d, \(J = 3.0\) Hz, 1H), 8.72 (d, \(J = 7.4\) Hz, 1H), 8.50-8.39 (m, 1H), 8.18 (d, \(J = 7.8\) Hz, 1H), 7.86 (d, \(J = 8.2\) Hz, 2H), 7.83-7.72 (m, 4H), 7.70 (t, \(J = 7.9\) Hz, 1H), 7.64 (dd, \(J = 8.3, 4.2\) Hz, 1H), 7.32 (d, \(J = 8.1\) Hz, 2H), 2.29 (s, 3H). ¹³C NMR (100 MHz, DMSO-\textit{d}_6): \(\delta\) 165.95, 149.53, 144.79, 138.55, 138.51, 138.49, 137.12, 137.03, 134.63, 134.54, 131.22, 130.24, 130.15, 129.22, 128.32, 127.50, 123.14, 122.74, 117.56, 21.47 (one signal was overlapped by other ones). HRMS (EI, m/z): calcd for C_{23}H_{18}N_{2}O_{3}S^{+} [M^{+}]: 402.1032; Found: 402.1034.
2-((4-Methoxyphenyl)sulfonyl)-N-(quinolin-8-yl)benzamide (3r)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/1) as a yellow solid in 75% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.17 (s, 1H), 8.84 (dd, $J = 4.0, 1.2$ Hz, 1H), 8.72 (d, $J = 7.3$ Hz, 1H), 8.45 (dd, $J = 8.3, 1.3$ Hz, 1H), 8.21-8.10 (m, 1H), 7.91 (d, $J = 8.9$ Hz, 2H), 7.84-7.73 (m, 4H), 7.70 (t, $J = 7.9$ Hz, 1H), 7.64 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.03 (d, $J = 8.9$ Hz, 2H), 3.76 (s, 3H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 166.06, 163.65, 149.55, 138.98, 138.52, 137.14, 136.84, 134.65, 134.36, 132.78, 131.22, 130.73, 129.95, 129.18, 128.31, 127.51, 123.15, 122.78, 117.54, 115.01, 56.21. HRMS (EI, m/z): calcd for C$_{23}$H$_{18}$N$_2$O$_4$S$^+$ [M$^+$]: 418.0982; Found: 418.0985.

2-((4-((tert-Butyl)phenyl)sulfonyl)-N-(quinolin-8-yl)benzamide (3s)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 72% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.22 (s, 1H), 8.84 (dd, $J = 4.1, 1.4$ Hz, 1H), 8.74 (d, $J = 7.0$ Hz, 1H), 8.44 (dd, $J = 8.3, 1.4$ Hz, 1H), 8.25-8.17 (m, 1H), 7.93 (d, $J = 8.5$ Hz, 2H), 7.83-7.73 (m, 4H), 7.70 (t, $J = 7.9$ Hz, 1H), 7.63 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.54 (d, $J = 8.6$ Hz, 2H), 1.20 (s, 9H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 166.00, 157.32, 149.52, 138.54, 138.53, 137.13, 137.05, 134.65, 134.55, 131.26, 130.18, 129.32, 127.49, 126.66, 123.15, 122.75, 117.60, 35.36, 31.09 (two signals were overlapped by other ones). HRMS (EI, m/z): calcd for C$_{26}$H$_{24}$N$_2$O$_3$S$^+$ [M$^+$]: 444.1500; Found: 444.1508.

2-((4-Fluorophenyl)sulfonyl)-N-(quinolin-8-yl)benzamide (3t)
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 68% yield. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 10.30 (s, 1H), 8.86 (d, $J$ = 2.8 Hz, 1H), 8.71 (d, $J$ = 7.4 Hz, 1H), 8.45 (d, $J$ = 8.2 Hz, 1H), 8.22 (d, $J$ = 7.7 Hz, 1H), 8.15-8.02 (m, 2H), 7.87-7.75 (m, 4H), 7.69 (t, $J$ = 7.9 Hz, 1H), 7.64 (dd, $J$ = 8.2, 4.2 Hz, 1H), 7.41 (t, $J$ = 8.6 Hz, 2H). $^{13}$C NMR (100 MHz, DMSO-d$_6$): $\delta$ 166.08, 165.38 (d, $J_{C-F}$ = 251.8 Hz), 149.60, 138.66, 138.06, 137.86 (d, $J_{C-F}$ = 2.6 Hz), 137.15 (d, $J_{C-F}$ = 4.1 Hz), 134.83, 134.63, 131.67, 131.57, 131.32, 130.37, 129.29, 128.34, 127.47, 123.29, 122.77, 117.82, 117.06 (d, $J_{C-F}$ = 22.8 Hz). $^{19}$F NMR (377 MHz, DMSO-d$_6$): $\delta$ -104.66. HRMS (EI, m/z): calcd for C$_{22}$H$_{15}$F$_2$N$_2$O$_3$S$^+$ [M$^+$]: 406.0781; Found: 406.0782.

2-((4-Chlorophenyl)sulfonyl)-N-(quinolin-8-yl)benzamide (3u)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 72% yield. $^1$H NMR (400 MHz, DMSO-d$_6$): $\delta$ 10.28 (s, 1H), 8.85 (dd, $J$ = 4.1, 1.4 Hz, 1H), 8.70 (d, $J$ = 7.5 Hz, 1H), 8.45 (dd, $J$ = 8.3, 1.5 Hz, 1H), 8.23 (d, $J$ = 7.7 Hz, 1H), 8.00 (d, $J$ = 8.6 Hz, 2H), 7.87-7.76 (m, 4H), 7.69 (t, $J$ = 7.9 Hz, 1H), 7.66-7.60 (m, 3H). $^{13}$C NMR (100 MHz, DMSO-d$_6$): $\delta$ 165.95, 149.59, 140.37, 139.28, 138.63, 137.71, 137.27, 137.12, 134.97, 134.59, 131.35, 130.45, 130.23, 129.96, 129.33, 128.33, 127.45, 123.30, 122.76, 117.81. HRMS (EI, m/z): calcd for C$_{22}$H$_{15}$ClN$_2$O$_3$S$^+$ [M$^+$]: 422.0484; Found: 422.0490.

2-((4-Bromophenyl)sulfonyl)-N-(quinolin-8-yl)benzamide (3v)
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 65% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.28 (s, 1H), 8.84 (d, $J = 2.3$ Hz, 1H), 8.70 (d, $J = 7.5$ Hz, 1H), 8.44 (d, $J = 8.2$ Hz, 1H), 8.23 (d, $J = 7.6$ Hz, 1H), 7.92 (d, $J = 7.8$ Hz, 2H), 7.86-7.74 (m, 6H), 7.69 (t, $J = 7.9$ Hz, 1H), 7.63 (dd, $J = 7.5$, 4.1 Hz, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 165.93, 149.57, 140.79, 138.61, 137.66, 137.27, 137.10, 134.96, 134.58, 132.89, 131.34, 130.45, 130.24, 129.33, 128.40, 128.32, 127.44, 123.29, 122.75, 117.78. HRMS (EI, m/z): calcd for C$_{22}$H$_{15}$BrN$_2$O$_3$S$^+$ [M$^+$]: 465.9986; Found: 465.9983.

$N$-(Quinolin-8-yl)-2-((4-(trifluoromethyl)phenyl)sulfonyl)benzamide (3w)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 54% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.34 (s, 1H), 8.83 (d, $J = 3.0$ Hz, 1H), 8.69 (d, $J = 7.5$ Hz, 1H), 8.44 (d, $J = 8.2$ Hz, 1H), 8.29 (d, $J = 7.9$ Hz, 1H), 8.20 (d, $J = 8.2$ Hz, 2H), 7.94 (d, $J = 8.3$ Hz, 2H), 7.90-7.77 (m, 4H), 7.69 (t, $J = 7.9$ Hz, 1H), 7.63 (dd, $J = 8.3$, 4.2 Hz, 1H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 165.87, 149.55, 145.46, 138.68, 137.51, 137.08 (d, $J_{C-F} = 5.3$ Hz), 135.27, 134.55, 133.74, 133.42, 131.42, 130.73, 129.41, 129.21, 128.33, 127.41, 126.96 (d, $J_{C-F} = 3.8$ Hz), 123.74 (q, $J_{C-F} = 271.5$ Hz), 123.36, 122.73, 117.92. $^{19}$F NMR (377 MHz, DMSO-$d_6$): $\delta$ -61.78. HRMS (EI, m/z): calcd for C$_{23}$H$_{15}$F$_3$N$_2$O$_3$S$^+$ [M$^+$]: 456.0743; Found: 456.0750.

2-(Naphthalen-2-ylsulfonyl)-$N$-(quinolin-8-yl)benzamide (3x)
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/2) as a yellow solid in 70% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.11 (s, 1H), 8.72 (d, $J = 7.4$ Hz, 1H), 8.62 (d, $J = 3.2$ Hz, 1H), 8.57 (s, 1H), 8.43-8.37 (m, 1H), 8.33-8.27 (m, 1H), 8.06 (d, $J = 8.7$ Hz, 1H), 7.99-7.93 (m, 2H), 7.89-7.74 (m, 5H), 7.71-7.62 (m, 2H), 7.58-7.52 (m, 2H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 165.74, 149.34, 138.39, 138.30, 137.99, 137.25, 136.99, 135.05, 134.78, 134.51, 131.98, 131.29, 130.38, 129.99, 129.81, 129.75, 129.67, 129.40, 128.25, 128.22, 128.11, 127.46, 123.17, 123.07, 122.67, 117.55. HRMS (EI, m/z): calcd for C$_{26}$H$_{18}$N$_2$O$_3$S$^+$ [M$^+$]: 438.1034; Found: 438.1039.

$N$-(quinolin-8-yl)-2-($o$-tolylsulfonyl)benzamide (3y)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/2) as a yellow solid in 52% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.12 (s, 1H), 8.82 (dd, $J = 4.1$, 1.3 Hz, 1H), 8.54 (d, $J = 7.5$ Hz, 1H), 8.43 (dd, $J = 8.3$, 1.3 Hz, 1H), 8.18-8.09 (m, 1H), 7.88-7.73 (m, 5H), 7.67-7.60 (m, 2H), 7.42 (t, $J = 7.5$ Hz, 1H), 7.28 (d, $J = 7.5$ Hz, 1H), 7.18 (t, $J = 7.6$ Hz, 1H), 2.34 (s, 3H). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 164.99, 149.54, 138.87, 138.39, 137.73, 137.45, 137.13, 136.94, 134.72, 134.35, 134.24, 133.04, 131.15, 129.83, 129.75, 129.64, 128.23, 127.43, 126.73, 123.15, 122.78, 117.22, 20.04. HRMS (EI, m/z): calcd for C$_{23}$H$_{18}$N$_2$O$_3$S$^+$ [M$^+$]: 402.1032; Found: 402.1038.

2-(Methylsulfonyl)-$N$-(quinolin-8-yl)benzamide (3z)

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Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/2) as a yellow solid in 46% yield. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.42 (s, 1H), 8.89 (dd, $J = 4.2$, 1.5 Hz, 1H), 8.68 (d, $J = 6.9$ Hz, 1H), 8.45 (dd, $J = 8.3$, 1.5 Hz, 1H), 8.07 (d, $J = 7.8$ Hz, 1H), 7.90 (d, $J = 3.9$ Hz, 2H), 7.85-7.75 (m, 2H), 7.72-7.61 (m, 2H), 3.44 (s, 3H).

$^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 166.56, 149.69, 138.79, 138.48, 137.40, 137.16, 134.67, 134.55, 131.20, 130.00, 129.01, 128.35, 127.42, 123.41, 122.80, 118.01, 45.57. HRMS (EI, m/z): calcd for C$_{17}$H$_{14}$N$_2$O$_3$S$^+$ [M$^+$]: 326.0722; Found: 326.0726.

References


