Direct Thiolation of Aza-Heteroaromatic N-oxides with Disulfides via Copper-Catalyzed Regioselective C-H Bond Activation

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1. General information

All reactions were carried out under air atmosphere in a dried tube. Chemicals were either purchased or synthesized by standard techniques. All of the compounds of aza-heteroaromatic N-oxide were prepared according to literature1. Silica gel was purchased from Qing Dao Hai Yang Chemical Industry Co. Analytical thin layer chromatography (TLC) was performed on precoated silica gel F254 plates. Compounds were visualized by irradiation with UV light (254 nm).

Analytical information: 1H NMR and 13C NMR spectra data were recorded by a BRUKER AVANCE III 400 MHz spectrometer (1H 400 MHz, 13C 100 MHz), using CDCl3 as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. 1H NMR spectral data are given as chemical shifts in ppm followed by multiplicity (s- singlet; d- doublet; t- triplet; q- quartet; m- multiplet), number of protons and coupling constants. 13C NMR chemical shifts are expressed in ppm. Infrared spectra were recorded with a Thermo Scientific Nicolet 6700 FT-IR Spectrometer. HRMS data were obtained using AB SCIEX Triple TOF 5600+ high resolution mass spectrometer (USA). The products listed below were determined by 1H and 13C NMR spectra. Melting points were measured on a microscopic apparatus and were uncorrected.

2. General method for the screening of reaction conditions (Table 1)

Under air atmosphere, a 10 mL sealable tube equipped with a magnetic stirring bar was charged with all solid reaction components, including quinoline N-oxide 1a (0.2 mmol), PhSSPh 2a (0.3-0.4 mmol), catalyst (10-20 mol %) and base (0.2-0.6 mmol). After the addition of solvent (1 mL), the resulting mixture was stirred at 120-140 °C for 48-72 h in oil bath, then cooled down to room temperature. The crude product was purified by flash column chromatography on silica gel (elute: petroleum ether-EtOAc) to give the compound 3a.

3. Optimization for reaction conditions of 2,5-dimethylpyrazine N-oxide and diphenyl disulfide

Table S1. Optimization of reaction conditionsa

<table>
<thead>
<tr>
<th>Entry</th>
<th>2a (equiv.)</th>
<th>Base</th>
<th>Solvent</th>
<th>Yield (%)b</th>
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<tbody>
<tr>
<td>1</td>
<td>1.5</td>
<td>KOH</td>
<td>Toluene</td>
<td>19</td>
</tr>
<tr>
<td>2</td>
<td>0.5</td>
<td>KOH</td>
<td>Toluene</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>2.5</td>
<td>KOH</td>
<td>Toluene</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>KOH</td>
<td>Toluene</td>
<td>25</td>
</tr>
</tbody>
</table>
### 4. General method for the screening of reaction conditions (Table S1)

To a 10 mL sealable tube equipped with a magnetic stirring bar was charged with 2,5-dimethylpyrazine N-oxide 1 (0.2 mmol), PhSSPh 2a (0.1-0.6 mmol, 0.5-3 equiv.), and base (0.4 mmol, 2.0 equiv.). After the addition of toluene (1 mL), the resulting mixture was stirred at 110-150 °C for 48 h in oil bath, then cooled down to room temperature. The crude product was purified by flash column chromatography on silica gel (elute: petroleum ether -EtOAc) to give the compound 5a.

### 5. General procedures for the preparation of products

#### 5.1 Thiolation reactions producing 3a-3q

![Scheme S1. Thiolation reactions of aza-heteroaromatic N-oxides](image)

Under air atmosphere, aza-heteroaromatic N-oxides 1 (0.2 mmol), R²EER² 2 (0.36 mmol, 1.8 equiv.), Cu(OAc)₂ (20 mol %) and KOH (0.4 mmol, 2.0 equiv.) were charged into a 10 mL sealable tube equipped with a magnetic stirring bar. After the addition of toluene (1 mL), the resulting mixture was stirred at 130 °C for 48 h in oil bath, then cooled down to room temperature. The resulting mixture was purified by flash column chromatography on silica gel (elute: petroleum ether-EtOAc) yielding the compounds 3 in moderate to good yields. In general, the identity and purity of the products were confirmed by ¹H and ¹³C NMR spectroscopy, HRMS (ESI) and IR.
5.2 Thiolation reactions producing 5a-5e

\[
\text{R}^1 \text{N}^+ \text{X} \text{S}^-\text{E}^- \text{R}^2 \xrightarrow{\text{Cs}_2\text{CO}_3 (2.0 \text{ equiv.)}} \text{R}^1 \text{N}^+ \text{X} \text{S}^-\text{ER}^2
\]

\[
\text{1} \quad \text{2} \quad \text{E} = \text{S, Se} \quad \text{X} = \text{CH, N}
\]

Scheme S2. Thiolation reactions of methyl-substituted aza-heteroaromatic N-oxides

Under air atmosphere, methyl-substituted aza-heteroaromatic N-oxides 1 (0.2 mmol), R²EER² 2 (0.5 mmol, 2.5 equiv.) and Cs₂CO₃ (0.4 mmol, 2.0 equiv.) were charged into a 10 mL reaction tube, then 1,4-dioxane (1 mL) was added into the tube. The resulting mixture was stirred at 130 °C for 48 h in oil bath, then cooled down to room temperature. The crude product was purified by flash column chromatography on silica gel (elute: petroleum ether-EtOAc) yielding the products 5 in moderate to good yields. In general, the identity and purity of the products were confirmed by ¹H and ¹³C NMR spectroscopy, HRMS (ESI) and IR.

5.3 Thiolation reaction producing 6

\[
\text{N} \quad \text{O} \quad \text{H} \quad \text{H}
\]

\[
\text{1} \quad \text{2a} \quad \text{3a}
\]

Scheme S3. Thiolation reaction of lepidine N-oxide

Under air atmosphere, lepidine N-oxide 1 (0.2 mmol), PhSSPh 2a (0.5 mmol, 2.5 equiv.) and Cs₂CO₃ (0.4 mmol, 2.0 equiv.) were charged into a 10 mL reaction tube, then 1,4-dioxane (1 mL) was added into the tube. The resulting mixture was stirred at 130 °C for 48 h in oil bath, then cooled down to room temperature. The crude product was purified by flash column chromatography on silica gel (elute: petroleum ether-EtOAc) yielding the product 6 in 38% yield. The identity and purity of the product 6 was confirmed by ¹H and ¹³C NMR spectroscopy, HRMS (ESI) and IR.

6. Mechanistic Studies

Reactions in the Presence of Radical Scavengers

\[
\text{N} \quad \text{O} \quad \text{S} \quad \text{Ph}
\]

\[
\text{1a} \quad \text{2a} \quad \text{3a}
\]

Scheme S4. Control experiments

To an oven-dried 10 mL schlenk tube were added quinoline N-oxide 1a (0.2 mmol), PhSSPh 2a (0.36 mmol), Cu(OAc)₂ (20 mol %), KOH (0.4 mmol) and radical scavenger (0.4 mmol). After the addition of toluene (1 mL), the resulting mixture was stirred under air atmosphere for 48 h at 130 °C in oil bath. After cooling to ambient temperature, the reaction mixture was purified by flash column chromatography on
Table S2. Effect of Radical Scavengers on the Copper-Catalyzed C–H Thiolation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Radical scavenger (2.0 equiv)</th>
<th>3a Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>--</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>TEMPO</td>
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</tr>
<tr>
<td>3</td>
<td>BHT</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>galvinoxyl free radical</td>
<td>0</td>
</tr>
</tbody>
</table>

*Reaction conditions: 1a (0.2 mmol), 2a (0.36 mmol), Cu(OAc)₂ (20 mol %), KOH (2.0 equiv.) radical scavenger (2.0 equiv.), and toluene (1 mL), 130 °C, 48 h, sealed tube; yields of isolated products. TEMPO = (2,2,6,6-Tetramethylpiperidin-1-yl)oxidanyl. BHT = 2,6-Di-tert-butyl-4-methylphenol.

7. References


8. Characterization data of compounds 3a-3q, 5a-5e and 6

**2-(Phenylthio)quinoline N-oxide (3a):** Purification by column chromatography on silica gel (R_f = 0.29, petroleum ether/ethyl acetate = 3:1) yielded 3a (40.8 mg, 80%) as a white solid; m. p. 137-139 °C; ^1^H NMR (400 MHz, CDCl₃) ppm: 8.69 (d, J = 9.0 Hz, 1H), 7.75 (t, J = 7.8 Hz, 2H), 7.68 (t, J = 5.9 Hz, 2H), 7.57-7.50 (m, 4H), 7.48 (d, J = 9.2 Hz, 1H), 6.61 (d, J = 9.0 Hz, 1H); ^13^C NMR (100 MHz, CDCl₃) 150.3, 140.7, 136.1, 130.7, 130.4, 130.2, 128.9, 128.0, 127.3, 127.2, 125.6, 118.5, 118.3; IR(KBr): 3041, 2923, 1561, 1499, 1437, 1334, 1210, 1171, 807, 753, 697 cm⁻¹; HRMS (ESI) calcd. for C₁₅H₁₂NOS: [M+H]^+: 254.0640, found: 254.0638.

**2-((p-Tolylthio)quinoline N-oxide (3b):** Purification by column chromatography on silica gel (R_f = 0.36, petroleum ether/ethyl acetate = 2:1) yielded 3b (40.6 mg, 76%) as a white solid; m. p. 158-160 °C; ^1^H NMR (400 MHz, CDCl₃) ppm: 8.69 (d, J = 8.8 Hz, 1H), 7.74 (t, J = 7.7 Hz, 2H), 7.54 (t, J = 7.6 Hz, 3H), 7.47 (d, J = 9.0 Hz, 1H), 7.32 (d, J = 7.6 Hz, 2H), 6.62 (d, J = 9.0 Hz, 1H), 2.45 (s, 3H); ^13^C NMR (100 MHz, CDCl₃) 150.8, 140.8, 140.7, 136.1, 131.0, 130.7, 128.0, 127.3, 127.2, 125.5, 125.3, 118.6, 118.3, 21.4; IR(KBr): 3050, 2921, 1558, 1491, 1328, 1286, 1210, 1165, 1067,
2-((4-Fluorophenyl)thio)quinoline N-oxide (3c): Purification by column chromatography on silica gel ($R_f = 0.31$, petroleum ether/ethyl acetate = 1:1) yielded 3c (28.2 mg, 52%) as a yellow solid; m. p. 142-144 °C; $^1$H NMR (400 MHz, CDCl$_3$) ppm: 8.69 (d, $J = 9.2$ Hz, 1H), 7.77 (t, $J = 7.8$ Hz, 2H), 7.69-7.65 (m, 2H), 7.56 (td, $J = 7.9, 0.9$ Hz, 1H), 7.51 (d, $J = 9.0$ Hz, 1H), 7.26-7.20 (m, 2H), 6.58 (d, $J = 9.1$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 165.4, 162.9, 150.2, 140.8, 138.4 (d, $J = 8.5$ Hz), 128.0 (t, $J = 285.2$ Hz), 127.5, 127.3, 124.4 (d, $J = 3.6$ Hz), 118.7, 118.0, 117.6, 117.4; IR(KBr): 3450, 3047, 2921, 1589, 1488, 1331, 1210, 1084, 843, 812, 748, 641, 543 cm$^{-1}$; HRMS (ESI) calcd. for C$_{16}$H$_{14}$NOS: [M+H]$^+$: 268.0796, found: 268.0802.

2-((4-Chlorophenyl)thio)quinoline N-oxide (3d): Purification by column chromatography on silica gel ($R_f = 0.48$, petroleum ether/ethyl acetate = 1:1) yielded 3d (22.4 mg, 39%) as a white solid; m. p. 142-145 °C; $^1$H NMR (400 MHz, CDCl$_3$) ppm: 8.69 (d, $J = 9.0$ Hz, 1H), 7.77 (t, $J = 7.8$ Hz, 2H), 7.62 (dd, $J = 6.6, 1.8$ Hz, 2H), 7.57 (t, $J = 7.7$ Hz, 1H), 7.52-7.49 (m, 3H), 6.61 (d, $J = 9.1$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 149.8, 140.8, 137.4, 137.0, 130.9, 130.5, 128.0, 127.6, 127.3, 125.7, 118.7, 118.1; IR(KBr): 3445, 3052, 2923, 2850, 1645, 1564, 1471, 1391, 1334, 1216, 1087, 1011, 896, 809, 753, 644 cm$^{-1}$; HRMS (ESI) calcd. for C$_{15}$H$_{11}$ClNOS: [M+H]$^+$: 288.0250, found: 288.0249.

2-(Phenylselanyl)quinoline N-oxide (3e): Purification by column chromatography on silica gel ($R_f = 0.26$, petroleum ether/ethyl acetate = 3:1) yielded 3e (54.2 mg, 90%) as a yellow solid; m. p. 134-137 °C; $^1$H NMR (400 MHz, CDCl$_3$) ppm: 8.67 (d, $J = 8.5$ Hz, 1H), 7.78-7.71 (m, 4H), 7.54 (q, $J = 7.7$ Hz, 2H), 7.48 (t, $J = 7.4$ Hz, 2H), 7.43 (d, $J = 7.2$ Hz, 1H), 6.72 (d, $J = 9.0$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 149.1, 140.9, 137.4, 130.7, 130.1, 130.0, 128.1, 127.9, 127.4, 126.3, 125.8, 120.3, 118.6; IR(KBr): 3047, 1555, 1493, 1437, 1328, 1283, 1202, 1062, 885, 809, 739, 686 cm$^{-1}$; HRMS (ESI) calcd. for C$_{15}$H$_{12}$NO$_8$OSe: [M+H]$^+$: 302.0084, found: 302.0083.

2-(Benzy1thio)quinoline N-oxide (3f): Purification by column chromatography on silica gel ($R_f = 0.41$, petroleum ether/ethyl acetate = 2:1) yielded 3f (27.2 mg, 51%) as a light yellow solid; m. p. 113-115 °C; $^1$H NMR (400 MHz, CDCl$_3$) ppm: 8.81 (d, $J = 8.8$ Hz, 1H), 7.83 (d, $J = 8.1$ Hz, 1H), 7.78 (t, $J = 8.0$ Hz, 1H), 7.62 (dd, $J = 14.4, 7.6$
Hz, 2H), 7.39-7.28 (m, 5H), 7.08 (d, J = 8.6 Hz, 1H), 4.51 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) 148.3, 141.6, 136.6, 130.5, 129.8, 129.1, 128.9, 128.1, 128.0, 127.0, 125.3, 121.9, 119.8, 37.4; IR(KBr): 2923, 2848, 1564, 1502, 1457, 1415, 1348, 1241, 1084, 815, 767, 708 cm\(^{-1}\); HRMS (ESI) calced. for C\(_{16}\)H\(_{14}\)NOS: [M+H]\(^+\): 268.0796, found: 268.0798.

2-(Methylselanyl)quinoline N-oxide (3g): Purification by column chromatography on silica gel (R\(_f\) = 0.39, petroleum ether/ethyl acetate = 1:3) yielded 3g (28.7 mg, 60%) as a light yellow solid; m. p. 83-85 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) ppm: 8.65 (d, J = 8.7 Hz, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.76 (t, J = 8.2 Hz, 1H), 7.70 (d, J = 8.9 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.27 (d, J = 10.4 Hz, 1H), 2.35 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) 147.5, 141.0, 130.8, 128.1, 127.6, 127.4, 125.8, 119.3, 118.6, 5.3; IR(KBr): 2923, 2848, 1555, 1496, 1421, 1328, 1269, 1207, 1151, 1073, 891, 801, 762, 731 cm\(^{-1}\); HRMS (ESI) calcd. for C\(_{10}\)H\(_{10}\)NOSe: [M+H]\(^+\): 239.9928, found: 239.9924.

6-Methyl-2-(phenylthio)quinoline N-oxide (3h): Purification by column chromatography on silica gel (R\(_f\) = 0.48, petroleum ether/ethyl acetate = 1:1) yielded 3h (26.3 mg, 68%) as a light yellow solid; m. p. 106-109 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) ppm: 8.58 (d, J = 8.7 Hz, 1H), 7.69 (dd, J = 7.2, 1.4 Hz, 2H), 7.58 (d, J = 9.0 Hz, 1H), 7.55-7.49 (m, 4H), 7.41 (d, J = 9.0 Hz, 1H), 6.57 (d, J = 9.0 Hz, 1H), 2.51 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) 149.6, 139.3, 137.5, 136.2, 132.9, 130.3, 130.2, 129.1, 127.4, 125.3, 118.5, 118.3, 21.3; IR(KBr): 3050, 2923, 2853, 1626, 1566, 1462, 1331, 1210, 896, 809, 748, 689 cm\(^{-1}\); HRMS (ESI) calcd. for C\(_{16}\)H\(_{14}\)NOS: [M+H]\(^+\): 268.0796, found: 268.0798.

6-Fluoro-2-(phenylthio)quinoline N-oxide (3i): Purification by column chromatography on silica gel (R\(_f\) = 0.47, petroleum ether/ethyl acetate = 1:1) yielded 3i (43.9 mg, 81%) as a white solid; m. p. 165-168 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) ppm: 8.72 (dd, J = 9.5, 5.1 Hz, 1H), 7.68 (dd, J = 7.3, 1.4 Hz, 2H), 7.56-7.47 (m, 4H), 7.43-7.38 (m, 2H), 6.63 (d, J = 9.1 Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) 162.3, 159.8, 149.8, 137.9, 136.2, 130 (d, J = 22.4 Hz), 128.8, 128.2 (d, J = 9.8 Hz), 124.7 (d, J = 4.9 Hz), 121.6 (d, J = 9.1 Hz), 120.5 (d, J = 25.5 Hz), 119.7, 111.7 (d, J = 22.8 Hz); IR(KBr): 3440, 3051, 2920, 2851, 1626, 1566, 1499, 1336, 1208, 1077, 898, 796, 748, 691cm\(^{-1}\); HRMS (ESI) calcd. for C\(_{15}\)H\(_{11}\)FNOS: [M+H]\(^+\): 272.0545, found: 272.0543.
6-Methoxy-2-(phenylthio)quinoline N-oxide (3j): Purification by column chromatography on silica gel ($R_f = 0.52$, petroleum ether/ethyl acetate = 1:3) yielded 3j (40.8 mg, 72%) as a light yellow solid; m. p. 153-154 °C; $^1$H NMR (400 MHz, CDCl$_3$) ppm: 8.61 (d, $J = 9.5$ Hz, 1H), 7.69-7.67 (m, 2H), 7.55-7.49 (m, 3H), 7.39-7.36 (m, 2H), 7.03 (d, $J = 2.6$ Hz, 1H), 6.57 (d, $J = 9.1$ Hz, 1H), 3.91 (s, 3H); IR(KBr): 3050, 2923, 2848, 1614, 1566, 1468, 1390, 1334, 1238, 1202, 1073, 1022, 899, 857, 804, 748, 694 cm$^{-1}$; HRMS (ESI) calcd. for C$_{16}$H$_{14}$NO$_2$S: [M+H]$^+$: 284.0745, found: 284.0744.

4-Chloro-2-(phenylthio)quinoline N-oxide (3k): Purification by column chromatography on silica gel ($R_f = 0.42$, petroleum ether/ethyl acetate = 1:1) yielded 3k (39.6 mg, 69%) as a yellow solid; m. p. 138-140 °C; $^1$H NMR (400 MHz, CDCl$_3$) ppm: 8.72 (d, $J = 8.7$ Hz, 1H), 8.10 (d, $J = 7.8$ Hz, 1H), 7.85-7.81 (m, 1H), 7.70-7.64 (m, 3H), 7.59-7.53 (m, 3H), 6.66 (s, 1H); IR(KBr): 3443, 3050, 2920, 2850, 1611, 1493, 1326, 1285, 1222, 1157, 1080, 870, 759, 691 cm$^{-1}$; HRMS (ESI) calcd. for C$_{15}$H$_{11}$ClNOS: [M+H]$^+$: 288.0250, found: 288.0249.

2-(Phenylthio)pyridine N-oxide (3l): Purification by column chromatography on silica gel ($R_f = 0.50$, petroleum ether/ethyl acetate = 1:1) yielded 3l (21.5 mg, 53%) as a yellow solid; m. p. 111-113 °C (lit.$^2$ 110-112 °C); $^1$H NMR (400 MHz, CDCl$_3$) ppm: 8.26 (d, $J = 5.7$ Hz, 1H), 7.64 (t, $J = 5.7$ Hz, 2H), 7.53 (dd, $J = 11.5$, 6.6 Hz, 3H), 7.07-7.00 (m, 2H), 6.54 (dd, $J = 8.0$, 2.0 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 154.3, 138.4, 138.2, 136.2, 130.1, 128.6, 125.8, 122.1, 120.7; IR(KBr): 3097, 2921, 2850, 1463, 1409, 1247, 1222, 1137, 1079, 1025, 837, 759, 708, 686 cm$^{-1}$; HRMS (ESI) calcd. for C$_{11}$H$_{10}$NOS: [M+H]$^+$: 204.0483, found: 204.0482.

2-Phenyl-6-(phenylthio)pyridine N-oxide (3m): Purification by column chromatography on silica gel ($R_f = 0.52$, petroleum ether/ethyl acetate = 1:1) yielded 3m (45.8 mg, 82%) as a light yellow solid; m. p. 160-162 °C; $^1$H NMR (400 MHz, CDCl$_3$) ppm: 7.88-7.85 (m, 2H), 7.69-7.66 (m, 2H), 7.54-7.50 (m, 3H), 7.49-7.45 (m, 3H), 7.16 (dd, $J = 7.8, 1.9$ Hz, 1H), 7.07 (t, $J = 8.1$ Hz, 1H), 6.50 (dd, $J = 8.2, 1.8$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 136.2, 132.4, 130.3, 129.9, 129.6, 129.4,
4-Phenyl-2-(phenylthio)pyridine N-oxide (3n): Purification by column chromatography on silica gel (R_f = 0.49, petroleum ether/ethyl acetate = 1:1) yielded 3n (28.0 mg, 50%) as a colorless solid; m. p. 161-163 °C; 'H NMR (400 MHz, CDCl_3) ppm: 8.28 (d, J = 6.8 Hz, 1H), 7.70-7.67 (m, 2H), 7.55-7.50 (m, 3H), 7.40-7.33 (m, 3H), 7.31-7.28 (m, 2H), 7.22 (dd, J = 6.8, 2.5 Hz, 1H), 6.72 (d, J = 2.4 Hz, 1H); ^13C NMR (100 MHz, CDCl_3) 154.2, 138.6, 138.3, 136.6, 136.1, 136.0, 136.1, 130.5, 130.3, 129.2, 129.0, 128.7, 126.4, 119.5, 118.8; IR(KBr): 3450, 3058, 2921, 1642, 1522, 1465, 1395, 1247, 1146, 1076, 753, 697, 591 cm^-1; HRMS (ESI) calcd. for C_{17}H_{14}NOS: [M+H]^+: 280.0796, found: 280.0798.

1-(Phenylthio)isoquinoline 2-oxide (3o): Purification by column chromatography on silica gel (R_f = 0.30, petroleum ether/ethyl acetate = 1:1) yielded 3o (29.9 mg, 59%) as a yellow solid; m. p. 122-124 °C; 'H NMR (400 MHz, CDCl_3) ppm: 8.41 (d, J = 8.4 Hz, 1H), 8.25 (d, J = 7.1 Hz, 1H), 7.79 (d, J = 7.9 Hz, 1H), 7.65 (t, J = 7.2 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.30-7.19 (m, 5H); ^13C NMR (100 MHz, CDCl_3) 145.1, 142.0, 137.5, 132.5, 132.4, 129.9, 129.6, 129.2, 128.7, 128.4, 127.2, 126.2, 124.0; IR(KBr): 3047, 2923, 2853, 1538, 1477, 1407, 1303, 1227, 1137, 958, 815, 753, 692 cm^-1; HRMS (ESI) calcd. for C_{15}H_{12}NOS: [M+H]^+: 254.0640, found: 254.0642.

2-(Phenylthio)pyrazine N-oxide (3p): Purification by column chromatography on silica gel (R_f = 0.31, petroleum ether/ethyl acetate = 1:3) yielded 3p (21.2 mg, 52%) as a colorless liquid; 'H NMR (400 MHz, CDCl_3) ppm: 8.19 (d, J = 3.4 Hz, 1H), 8.13 (d, J = 3.7 Hz, 1H), 7.73 (s, 1H), 7.66 (d, J = 6.8 Hz, 2H), 7.57-7.53 (m, 3H); ^13C NMR (100 MHz, CDCl_3) 149.8, 144.2, 141.7, 135.9, 132.2, 130.9, 130.6, 126.3; IR(KBr): 2921, 2850, 1561, 1446, 1395, 1300, 1174, 1123, 860, 753, 694 cm^-1; HRMS (ESI) calcd. for C_{10}H_{9}N_{2}OS: [M+H]^+: 205.0436, found: 205.0433.

2-(Phenylthio)quinoxaline N-oxide (3q): Purification by column chromatography on silica gel (R_f = 0.47, petroleum ether/ethyl acetate = 3:1) yielded 3q (28.4 mg, 56%)

as a light yellow solid; m. p. 108-109 °C; ¹H NMR (400 MHz, CDCl₃) ppm: 8.58 (d, J = 7.4 Hz, 1H), 8.04 (d, J = 7.2 Hz, 1H), 7.98 (s, 1H), 7.77-7.71 (m, 4H), 7.56 (d, J = 5.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) 144.4, 142.9, 142.1, 136.0, 135.9, 130.9, 130.8, 130.5, 130.1, 129.9, 126.7, 117.9; IR(KBr): 3064, 2923, 2848, 1533, 1477, 1339, 1241, 1159, 1121, 1090, 913, 764, 700 cm⁻¹; HRMS (ESI) calcd. for C₁₄H₁₁N₂OS: [M+H]⁺: 255.0592, found: 255.0592.

2-[(Bis(phenylthio)methyl)-5-methylpyrazine N-oxide (5a): Purification by column chromatography on silica gel (Rᵣ = 0.46, petroleum ether/ethyl acetate = 1:2) yielded 5a (24.5 mg, 36%) as a colorless liquid; ¹H NMR (400 MHz, CDCl₃) ppm: 8.38 (s, 1H), 7.98 (s, 1H), 7.40 (dd, J = 5.9, 2.2 Hz, 4H), 7.29-7.27 (m, 6H), 6.19 (s, 1H), 2.45 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 155.8, 146.4, 141.6, 133.0, 132.6, 132.1, 129.2, 128.6, 49.6, 21.5 (d, J = 4.1 Hz, CH₃); IR(KBr): 3061, 2924, 1590, 1478, 1373, 1240, 1022, 960, 744, 693 cm⁻¹; HRMS (ESI) calcd. for C₁₈H₁₆N₂NaOS₂: [M+Na]⁺: 363.0602, found: 363.0605.

2-[(Bis(phenylselanyl)methyl)-5-methylpyrazine N-oxide (5c): Purification by column chromatography on silica gel (Rᵣ = 0.35, petroleum ether/ethyl acetate = 2:1) yielded 5c (31.4 mg, 36%) as a colorless liquid; ¹H NMR (400 MHz, CDCl₃) ppm: 8.03 (s, 1H), 7.98 (s, 1H), 7.51-7.48 (m, 4H), 7.33-7.29 (m, 2H), 7.27-7.23 (m, 4H), 5.55 (s, 1H), 2.45 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 155.3, 145.0, 142.7, 134.9, 132.2, 131.5, 130.4, 129.3, 128.8, 21.4 (d, J = 4.2 Hz, CH₃); IR(KBr): 2922, 1585, 1476, 1438, 1378, 1019, 961, 740, 692 cm⁻¹; HRMS (ESI) calcd. for C₁₈H₁₇N₂O₈S₂: [M+H]⁺: 436.9671, found: 436.9672.
2-[Bis(phenylthio)methyl]pyrazine N-oxide (5d): Purification by column chromatography on silica gel (RF = 0.42, petroleum ether/ethyl acetate = 1:3) yielded 5d (38.5 mg, 59%) as a colorless liquid; 1H NMR (400 MHz, CDCl3) ppm: 8.46 (s, 1H), 8.27 (d, J = 4.1 Hz, 1H), 8.07 (d, J = 4.0 Hz, 1H), 7.39 (dd, J = 6.5, 1.9 Hz, 4H), 7.29-7.26 (m, 6H), 6.20 (s, 1H); 13C NMR (100 MHz, CDCl3) 147.5, 145.7, 144.6, 133.4, 133.2, 132.3, 129.2, 128.8, 49.7; IR(KBr): 2925, 1583, 1445, 1410, 1315, 1189, 886, 746, 696 cm⁻¹; HRMS (ESI) calcd. for C17H14N2NaOS2: [M+Na]⁺: 349.0445, found: 349.0446.

2-[Bis(phenylselanyl)methyl]quinoline N-oxide (5e): Purification by column chromatography on silica gel (RF = 0.43, petroleum ether/ethyl acetate = 1:2) yielded 5e (43.3 mg, 46%) as a light yellow solid; m. p. 114-116 °C; 1H NMR (400 MHz, CDCl3) ppm: 8.78 (d, J = 8.6 Hz, 1H), 7.79-7.74 (m, 2H), 7.62-7.58 (m, 1H), 7.52 (dd, J = 7.9, 1.0 Hz, 4H), 7.48 (d, J = 8.7 Hz, 1H), 7.28-7.25 (m, 2H), 7.23-7.19 (m, 4H), 7.08 (d, J = 3.2 Hz, 1H), 5.85 (s, 1H); 13C NMR (100 MHz, CDCl3) 146.7, 141.5, 134.6, 131.5, 131.2, 130.5, 129.2, 129.1, 128.3, 128.0, 124.8, 120.6, 119.9; IR(KBr): 3063, 2964, 2922, 1569, 1474, 1375, 1253, 820, 739, 689 cm⁻¹; HRMS (ESI) calcd. for C22H18NO80Se2: [M+H]⁺: 471.9719, found: 471.9715.

4-[Bis(phenylthio)methyl]quinoline (6): Purification by column chromatography on silica gel (RF = 0.26, petroleum ether/ethyl acetate = 1:1) yielded 6 (27.3 mg, 38%) as a colorless liquid; 1H NMR (400 MHz, CDCl3) ppm: 8.78 (d, J = 4.5 Hz, 1H), 8.20 (t, J = 8.4 Hz, 2H), 7.77 (td, J = 6.9, 1.2 Hz, 1H), 7.63 (td, J = 8.2, 1.0 Hz, 1H), 7.49 (s, 1H), 7.35-7.33 (m, 4H), 7.28-7.22 (m, 6H), 6.12 (s, 1H); 13C NMR (100 MHz, CDCl3) 149.8, 148.4, 144.4, 133.7, 132.8, 130.4, 129.5, 129.1, 128.4, 126.9, 125.3, 123.1, 120.3, 56.4; IR(KBr): 2923, 2853, 1583, 1473, 1148, 765, 741, 693 cm⁻¹; HRMS (ESI) calcd. for C22H18NS2: [M+H]⁺: 360.0881, found: 360.0879.
9. $^1$H NMR, $^{13}$C NMR spectra for 3a-3q, 5a-5e and 6

$^1$H NMR spectrum of compound 3a

$^{13}$C NMR spectrum of compound 3a
COSY spectrum of compound 3a

1H NMR spectrum of compound 3b
$^{13}$C NMR spectrum of compound 3b

$^1$H NMR spectrum of compound 3c
$^{13}$C NMR spectrum of compound 3c

$^1$H NMR spectrum of compound 3d
$^1$H NMR spectrum of compound 3e
$^{13}$C NMR spectrum of compound 3e

$^1$H NMR spectrum of compound 3f
$^{13}$C NMR spectrum of compound 3f

$^1$H NMR spectrum of compound 3g
$^{13}$C NMR spectrum of compound 3g

$^1$H NMR spectrum of compound 3h
$^{13}$C NMR spectrum of compound 3h

$^1$H NMR spectrum of compound 3i
$^{13}$C NMR spectrum of compound 3i

$^1$H NMR spectrum of compound 3j
$^{13}$C NMR spectrum of compound 3j

$^1$H NMR spectrum of compound 3k
$^{13}$C NMR spectrum of compound 3k

$^1$H NMR spectrum of compound 3l
\begin{center}
\textbf{13C NMR spectrum of compound 3l}
\end{center}

\begin{center}
\textbf{1H NMR spectrum of compound 3m}
\end{center}
$^{13}$C NMR spectrum of compound 3m

$^1$H NMR spectrum of compound 3n
$^{13}$C NMR spectrum of compound $3n$

$^1$H NMR spectrum of compound $3o$
$^{13}$C NMR spectrum of compound 3o

$^{1}$H NMR spectrum of compound 3p
$^{13}$C NMR spectrum of compound 3p

$^1$H NMR spectrum of compound 3q
$^{13}$C NMR spectrum of compound 3q

$^1$H NMR spectrum of compound 5a
$^{13}$C NMR spectrum of compound 5a

$^1$H NMR spectrum of compound 5b
$^{13}$C NMR spectrum of compound 5b

$^1$H NMR spectrum of compound 5c
$^{13}$C NMR spectrum of compound 5c

$^1$H NMR spectrum of compound 5d
$\text{\textsuperscript{13}C NMR spectrum of compound 5d}$

$\text{\textsuperscript{1}H NMR spectrum of compound 5e}$
$^{13}$C NMR spectrum of compound 5e

$^1$H NMR spectrum of compound 6
$^{13}$C NMR spectrum of compound 6