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Supporting Information

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 F_{254} 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

Ν

$ \begin{array}{c} N \\ \downarrow \\ N \\ \downarrow \\ O \\ H \end{array} + Ph^{S} S^{Ph} \xrightarrow{base}{solvent} \begin{array}{c} \downarrow \\ N \\ \downarrow \\ O \\ S \\ \downarrow \\ O \\ S \end{array} $					
	1	2a			5a
Entry	2a (equiv.)	Base		Solvent	Yield $(\%)^b$
1	1.5	KOH		Toluene	19
2	0.5	KOH		Toluene	12
3	2.5	KOH		Toluene	25
4	3	KOH		Toluene	25

Table S1. Optimization of reaction conditions^a

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5	2.5	K_2CO_3	Toluene	NR
6	2.5	Cs_2CO_3	Toluene	26
7	2.5	t-BuOLi	Toluene	15
8	2.5	t-BuONa	Toluene	10
9	2.5	KOAc	Toluene	NR
10	2.5	Et ₃ N	Toluene	NR
11	2.5	Cs_2CO_3	CH ₃ CN	10
12	2.5	Cs_2CO_3	DMSO	NR
13	2.5	Cs_2CO_3	DMF	NR
14	2.5	Cs ₂ CO ₃	1,4-Dioxane	36
15	2.5	Cs_2CO_3	DCE	11
16 ^c	2.5	Cs_2CO_3	1,4-Dioxane	35
17^d	2.5	Cs_2CO_3	1,4-Dioxane	32

^{*a*} Reaction conditions: **1a** (0.2 mmol), **2a** (0.5-3 equiv.), base (2 equiv.), solvent (1 mL), 130 °C, under air, 48 h. ^{*b*} Isolated yield. ^{*c*} Run at 150 °C. ^{*d*} Run at 110 °C.

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 solvent (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

Under air atmosphere, aza-heteroaromatic *N*-oxides **1** (0.2 mmol), $R^2 EER^2$ **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



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

Under air atmosphere, methyl-substituted aza-heteroaromatic *N*-oxides **1** (0.2 mmol), $R^2 EER^2$ **2** (0.5 mmol, 2.5 equiv.) and Cs_2CO_3 (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



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



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

silica gel (elute: petroleum ether-EtOAc).

Entry	Radical scavenger (2.0 equiv)	3a Yield (%)
1		80
2	TEMPO	0
3	BHT	0
4	galvinoxyl free radical	0

Table S2. Effect of Radical Scavengers on the Copper-Catalyzed C-H Thiolation^a

^{*a*} 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

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Ma, J. Zhang, C. Xu, F. Chen, Y. M. He, Q. H. Fan, Angew. Chem. Int. Ed. 2016, 55, 12891-12894.

[2] Li M., J. M. Hoover. Chem. Commun. 2016, 52, 8733-8736.

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; ¹H 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); ¹³C 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; ¹H 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); ¹³C 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,

809, 762, 736 cm⁻¹; HRMS (ESI) calcd. for $C_{16}H_{14}NOS$: $[M+H]^+$: 268.0796, found: 268.0802.



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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₅H₁₁FNOS: [M+H]⁺: 272.0545, found: 272.0548.



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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 149.8, 140.8, 137.4, 137.0, 130.9, 130.5, 128.0, 127.6, 127.5, 127.3, 125.7, 118.7, 118.1; IR(KBr): 3445, 3052, 2923, 2850, 1645, 1564, 1471, 1390, 1334, 1216, 1087, 1011, 896, 809, 753, 644 cm⁻¹; HRMS (ESI) calcd. for C₁₅H₁₁ClNOS: [M+H]⁺: 288.0250, found: 288.0249.

¢_ se

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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₅H₁₂NO80Se: [M+H]⁺: 302.0084, found: 302.0083.

2-(Benzylthio)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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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) calcd. for C₁₆H₁₄NOS: [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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₀H₁₀NO80Se: [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; ¹H NMR (400 MHz, CDCl₃) ppm: 8.58 (d, J = 8.9 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); ¹³C NMR (100 MHz, CDCl₃) 149.6, 139.3, 137.5, 136.2, 132.9, 130.3, 130.2, 129.1, 127.4, 127.0, 125.3, 118.5, 118.3, 21.3; IR(KBr): 3050, 2923, 2853, 1566, 1462, 1331, 1210, 896, 809, 748, 689 cm⁻¹; HRMS (ESI) calcd. for C₁₆H₁₄NOS: [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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₅H₁₁FNOS: [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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 158.5, 148.0, 136.6, 136.2, 130.2, 130.1, 129.3, 128.6, 124.7, 122.5, 120.4, 118.9, 106.2, 55.7; 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 C₁₆H₁₄NO₂S: [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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 150.5, 141.2, 136.2, 131.6, 130.8, 130.5, 130.4, 128.3, 128.1, 125.2, 125.0, 119.2, 117.9; IR(KBr): 3443, 3050, 2920, 2850, 1611, 1493, 1326, 1285, 1222, 1157, 1080, 870, 759, 691 cm⁻¹; HRMS (ESI) calcd. for C₁₅H₁₁CINOS: [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 = 1:7) yielded **3l** (21.5 mg, 53%) as a yellow solid; m. p. 111-113 °C (lit.² 110-112 °C); ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 154.3, 138.4, 136.2, 130.4, 130.3, 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 C₁₁H₁₀NOS: [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; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 136.2, 132.4, 130.3, 130.2, 129.9, 129.6, 129.4,

129.1, 128.2, 127.5, 125.4, 121.8, 120.5; IR(KBr): 2923, 2850, 1538, 1451, 1373, 1241, 1062, 843, 762, 700 cm⁻¹; HRMS (ESI) calcd. for $C_{17}H_{14}NOS$: [M+H]⁺: 280.0796, found: 280.0798.



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; ¹H NMR (400 MHz, CDCl₃) 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, CDCl₃) 154.2, 138.6, 138.3, 136.6, 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 C₁₇H₁₄NOS: [M+H]⁺: 280.0796, found: 280.0797.



1-(Phenylthio)isoquinoline 2-oxide (30): Purification by column chromatography on silica gel ($R_f = 0.30$, petroleum ether/ethyl acetate = 1:1) yielded **30** (29.9 mg, 59%) as a yellow solid; m. p. 122-124 °C; ¹H NMR (400 MHz, CDCl₃) 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, CDCl₃) 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 C₁₅H₁₂NOS: [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; ¹H NMR (400 MHz, CDCl₃) 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, CDCl₃) 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 C₁₀H₉N₂OS: [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 ($R_f = 0.46$, 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(*p***-tolylthio)methyl]-5-methylpyrazine** *N*-oxide (5b): Purification by column chromatography on silica gel ($R_f = 0.39$, petroleum ether/ethyl acetate = 1:1) yielded **5b** (30.9 mg, 42%) as a colorless liquid; ¹H NMR (400 MHz, CDCl₃) ppm: 8.32 (s, 1H), 7.96 (s, 1H), 7.27 (d, J = 8.1 Hz, 4H), 7.07 (d, J = 7.9 Hz, 4H), 6.08 (s, 1H), 2.45 (s, 3H), 2.31 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) 155.5, 146.5, 141.7, 139.0, 133.6, 132.1, 129.9, 128.8, 50.1, 21.5 (d, J = 3.2 Hz, CH₃), 21.2, 21.1; IR(KBr): 3105, 2921, 1592, 1487, 1392, 1296, 1238, 961, 806 cm⁻¹; HRMS (ESI) calcd. for C₂₀H₂₀N₂NaOS₂: [M+Na]⁺: 391.0915, found: 391.0912.



2-[Bis(phenylselanyl)methyl]-5-methylpyrazine *N***-oxide** (5c): Purification by column chromatography on silica gel ($R_f = 0.35$, 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 C₁₈H₁₇N₂O80Se₂: [M+H]⁺: 436.9671, found: 436.9672.



2-[Bis(phenylthio)methyl]pyrazine *N*-oxide (5d): Purification by column chromatography on silica gel ($R_f = 0.42$, 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 ($R_f = 0.43$, 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, 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 ($R_f = 0.26$, 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.





¹³C NMR spectrum of compound **3a**



¹H NMR spectrum of compound **3b**













¹H NMR spectrum of compound **3f**





















¹H NMR spectrum of compound **3**l







S25











¹H NMR spectrum of compound **3**q





S30











S33







 13 C NMR spectrum of compound **6**