Supporting Information

Metal-free oxidative cyclization of 2-aminobenzothiazoles and cyclic ketones enabled by the combination of elemental sulfur and oxygen

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General information

All experiments were carried out under an atmosphere of oxygen. Flash column chromatography was performed over silica gel 48-75 μm. $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker-AV (400 and 100 MHz, respectively) instrument internally referenced to SiMe$_4$, chloroform signals. MS analyses were performed on Agilent 5975 GC-MS instrument (EI). The new compounds were characterized by $^1$H NMR, $^{13}$C NMR, and HRMS. All reagents were used as received from commercial sources without further purification.

General procedure for the oxidative cyclization

(3a): A 10 mL oven-dried reaction vessel was charged with sulfur powder (S$_8$, 6.4 mg, 0.025 mmol), 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol). The reaction vessel was purged with oxygen for three times and was added cyclohexanone (2a, 31.2 μL, 0.3 mmol), DMSO (0.1 mL) and cyclohexane (0.5 mL) by syringe. The sealed vessel was stirred at 130 °C for 24 h. After cooling to room temperature, the reaction was diluted with ethyl acetate (5 mL) and washed with saturated sodium bicarbonate solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate for three times. The combined organic layer was dried over sodium sulfate, and evaporated under vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to give 3a.

(5 mmol reaction): A 250 mL oven-dried reaction vessel was charged with elemental sulfur (S$_8$, 160 mg, 0.625 mmol), 2-aminobenzothiazole (5 mmol). The reaction vessel was purged with oxygen for three times and was added ketone (7.5 mmol), DMSO (2.5 mL) and cyclohexane (12.5 mL) by syringe. The sealed vessel was stirred at 130 °C for 48 h. After cooling to room temperature, the reaction was diluted with ethyl acetate (25 mL) and washed with saturated sodium bicarbonate solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate for three times. The combined organic layer was dried over sodium sulfate, and evaporated under vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to give the products.
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7,8,9,10-Tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3a)

White solid; yield: 39.2 mg (86%), mp 140-142 °C. $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.67-7.62 (m, 2H), 7.38 (t, $J$ = 7.76 Hz, 1H), 7.27 (t, $J$ = 7.68 Hz, 1H), 3.07-3.04 (m, 2H), 2.77-2.74 (m, 2H), 2.00-1.95 (m, 2H), 1.92-1.86 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) δ 145.1, 142.4, 132.9, 129.7, 125.5, 123.9, 123.5, 121.8, 111.9, 24.8, 22.8, 22.7, 21.8; MS (EI) m/z (%) 228, 200 (100), 160, 108, 51; HRMS calcd. for: C$_{13}$H$_{13}$N$_2$S$^+$ (M+H)$^+$ 229.07940, found 229.07941.

9-Methyl-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3b)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and 4-methylcyclohexanone (2b, 36.8 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 40.2 mg, 83% yield of 3b as white solid, mp 121-123 °C.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.68-7.64 (m, 2H), 7.41-7.37 (m, 1H), 7.30-7.28 (m, 1H), 3.18 (dd, $J$ = 15.08, 5.4 Hz, 1H), 2.80-2.76 (m, 2H), 2.67-2.60 (m, 1H), 2.13-2.05 (m, 1H), 1.99-1.93 (m, 1H), 1.62-1.52 (m, 1H), 1.19 (d, $J$ = 6.68 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) δ 145.3, 142.2, 132.9, 129.8, 125.6, 124.0, 123.6, 121.7 112.1, 31.2, 29.9, 29.4, 24.3, 21.4; MS (EI) m/z (%) 242, 200 (100), 160, 108, 51; HRMS calcd. for: C$_{14}$H$_{15}$N$_2$S$^+$ (M+H)$^+$ 243.09505, found 243.09482.

9-Ethyl-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3c)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and 4-...
ethylcyclohexanone (2c, 42.3 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 41.9 mg, 82% yield of 3c as white solid, mp 119-120 °C.

\[^1^H\text{NMR (400 MHz, CDCl}_3, \text{ppm)}\ \delta\ 7.68-7.64 (m, 2H), 7.41-7.37 (m, 1H), 7.30-7.28 (m, 1H), 3.18 (dd, J = 15.08, 5.40 Hz, 1H), 2.80-2.76 (m, 2H), 2.67-2.60 (m, 1H), 2.13-2.05 (m, 1H), 1.99-1.93 (m, 1H), 1.62-1.52 (m, 1H), 1.19 (d, J = 6.68 Hz, 3H); \[^{13}\text{C NMR (100 MHz, CDCl}_3, \text{ppm)}\ \delta\ 145.3, 142.2, 132.9, 129.8, 125.6, 124.0, 123.6, 121.7, 112.1, 31.2, 29.9, 29.4, 24.3, 21.4; MS (EI) m/z (%) 256, 225, 200 (100), 160, 77, 51; HRMS calcd. for: C\textsubscript{15}H\textsubscript{17}N\textsubscript{2}S\textsuperscript{+} (M+H\textsuperscript{+}) 257.11070, found 257.11075.

9-Propyl-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3d)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and 4-propylcyclohexanone (2d, 46.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 44.8 mg, 83% yield of 3d as white solid, mp 108-110 °C.

\[^1^H\text{NMR (400 MHz, CDCl}_3, \text{ppm)}\ \delta\ 7.67-7.64 (m, 2H), 7.41-7.36 (m, 1H), 7.30-7.26 (m, 1H), 3.19 (dd, J = 14.92, 5.32 Hz, 1H), 2.79-2.74 (m, 2H), 2.67-2.60 (m, 1H), 2.03-1.93 (m, 2H), 1.60-1.44 (m, 5H), 1.00-0.95 (m, 3H); \[^{13}\text{C NMR (100 MHz, CDCl}_3, \text{ppm)}\ \delta\ 145.4, 142.6, 133.0, 129.8, 125.6, 124.1, 123.6, 121.8, 112.2, 38.2, 34.2, 29.4, 28.1, 24.4, 20.2, 14.2; MS (EI) m/z (%) 270, 200 (100), 160, 77, 51; HRMS calcd. for: C\textsubscript{16}H\textsubscript{19}N\textsubscript{2}S\textsuperscript{+} (M+H\textsuperscript{+}) 271.12635, found 271.12607.

9-(tert-Butyl)-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3e)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and 4-(tert-
butyl)cyclohexanone (2e, 46.3 mg, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 47.7 mg, 84% yield of 3e as white solid, mp 126-128 °C.

^{1}H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.68-7.65 (m, 2H), 7.42-7.38 (m, 1H), 7.30-7.28 (m, 1H), 3.13 (dd, $J$ = 14.60, 5.20 Hz, 1H), 2.86-1.67 (m, 3H), 2.13-2.09 (m, 1H), 1.71-1.64 (m, 1H), 1.53-1.43 (m, 1H), 1.04 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 145.3, 142.6, 132.9, 129.7, 125.5, 124.0, 123.6, 122.4, 45.1, 32.5, 27.3, 25.4, 24.6, 23.2; MS (EI) m/z (%) 284, 200 (100), 160, 149, 57; HRMS calcd. for: C$_{17}$H$_{21}$N$_2$S$^+$ (M+H)$^+$ 285.14200, found 285.14264.

9-Pentyl-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3f)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and 4-pentylcyclohexanone (2f, 56.7 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 49.5 mg, 83% yield of 3f as white solid, mp 61-64 °C.

^{1}H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.69-7.66 (m, 2H), 7.40 (t, $J$ = 7.72 Hz, 1H), 7.31-7.27 (m, 1H), 3.19 (dd, $J$ = 15.08, 5.48 Hz, 1H), 2.83-2.75 (m, 2H), 2.67-2.61 (m, 1H), 2.03-1.91 (m, 2H), 1.61-1.41 (m, 5H), 1.39-1.33 (m, 4H), 0.92 (t, $J$ = 6.78 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 145.5, 142.6, 133.1, 130.0, 125.7, 124.2, 123.8, 121.8, 112.3, 36.0, 34.6, 32.0, 29.5, 28.3, 26.9, 24.4, 22.6, 14.1; MS (EI) m/z (%) 298, 225, 200 (100), 160, 51; HRMS calcd. for: C$_{18}$H$_{23}$N$_2$S$^+$ (M+H)$^+$ 299.15765, found 299.15771.

9-(tert-Pentyl)-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3g)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and 4-(tert-
penty)cyclohexanone (2g, 55.7 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 48.9 mg, 82% yield of 3g as white solid, mp 76-78 °C.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.70-7.66 (m, 2H), 7.41 (t, $J = 7.82$ Hz, 1H), 7.30 (t, $J = 7.72$ Hz, 1H), 3.07 (dd, $J = 15.08$, 5.12 Hz, 1H), 2.87-2.67 (m, 3H), 2.11-2.05 (m, 1H), 1.82-1.75 (m, 1H), 1.54-1.41 (m, 3H), 0.97 (s, 6H), 0.90 (t, $J = 7.48$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 145.5, 142.7, 133.1, 129.9, 125.7, 124.2, 123.7, 122.6, 112.3, 42.6, 34.9, 32.6, 25.6, 24.2, 24.1, 24.05, 22.9, 8.2; MS (EI) $m/z$ (%) 298, 227, 200 (100), 108, 55; HRMS calcd. for: C$_{18}$H$_{23}$N$_2$S$^+$ (M+H)$^+$ 299.15765, found 299.15762.

9-Phenyl-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3h)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and 4-phenylcyclohexanone (2h, 52.3 mg, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 51.7 mg, 85% yield of 3h as white solid, mp 229-231 °C.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.69-7.67 (m, 1H), 7.60 (d, $J = 7.76$ Hz, 1H), 7.40-7.28 (m, 7H), 3.42 (dd, $J = 13.32$, 2.92 Hz, 1H), 3.23-3.11 (m, 2H), 2.92-2.90 (m, 2H), 2.23-2.07 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 145.7, 145.4, 142.2, 132.8, 129.8, 128.5, 126.8, 126.5, 125.6, 124.0, 123.8, 121.6, 112.1, 40.9, 30.2, 29.6, 24.9; MS (EI) $m/z$ (%) 304, 200 (100), 160, 108, 77; HRMS calcd. for: C$_{19}$H$_{17}$N$_2$S$^+$ (M+H)$^+$ 305.11070, found 305.11014.


The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and ethyl 4-oxocyclohexanecarboxylate (2i, 47.8 μL, 0.3 mmol). The crude mixture was purified by flash
column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 51.6 mg, 86% yield of 3i as white solid, mp 48-49 °C.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.69-7.67 (m, 1H), 7.42-7.39 (m, 1H), 7.32-7.28 (m, 1H), 4.27-4.19 (m, 2H), 3.36-3.33 (m, 2H), 2.97-2.90 (m, 1H), 2.85-2.82 (m, 2H), 2.36-2.30 (m, 1H), 2.06-1.96 (m, 1H), 1.32 (t, $J = 7.14$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 174.5, 146.1, 141.8, 132.8, 129.9, 125.8, 124.2, 124.0, 120.3, 112.3, 60.8, 39.9, 26.0, 24.2, 23.9, 14.2; MS (EI) m/z (%) 300, 225, 200 (100), 108, 51; HRMS calcd. for: C$_{16}$H$_{17}$N$_2$O$_2$S$^+$(M+H)$^+$ 301.10052, found 301.10056.

7-Phenyl-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3j)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and 2-phenylcyclohexanone (2j, 52.3 mg, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 27.9 mg, 46% yield of 3j as white solid, mp 201-203 °C.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.69-7.65 (m, 2H), 7.42-7.38 (m, 1H), 7.32-7.27 (m, 3H), 7.21-7.19 (m, 3H), 4.21-4.20 (m, 1H), 3.20-3.10 (m, 2H), 2.28-2.22 (m, 1H), 2.12-2.04 (m, 1H), 1.98-1.88 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 145.9, 144.5, 144.1, 133.1, 130.2, 128.3, 128.1, 126.2, 125.8, 124.2, 123.9, 123.3, 112.3, 42.0, 33.1, 22.1, 20.7; MS (EI) m/z (%) 304 (100), 275, 227, 170, 55; HRMS calcd. for: C$_{19}$H$_{17}$N$_2$S$^+$(M+H)$^+$ 305.11070, found 305.11084.

8-Methyl-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3k)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and 3-methylcyclohexanone (2k, 36.9 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 32.9 mg, 68% yield of 3k as white solid, mp 130-133 °C.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.69-7.64 (m, 2H), 7.40 (t, $J = 7.74$ Hz, 1H), 7.31-7.27 (m,
1H), 3.16-3.00 (m, 2H), 2.85 (dd, J = 15.88, 4.88 Hz, 1H), 2.43-2.37 (m, 1H), 2.07-2.02 (m, 2H),
1.67-1.57 (m, 1H), 1.14 (d, J = 6.56 Hz, 3H); 13C NMR (100 MHz, CDCl₃, ppm) δ 145.6, 142.5,
133.1, 130.0, 125.8, 124.2, 123.8, 121.7, 112.3, 33.1, 30.9, 29.5, 21.4, 21.36; MS (EI) m/z (%)
242, 200 (100), 188, 160, 51; HRMS calcd. for: C₁₄H₁₅N₂S⁺ (M+H)⁺ 243.09505, found 243.09532.

8,9,10,11-Tetrahydro-7H-benzo[d]cyclohepta[4,5]imidazo[2,1-b]thiazole (3l)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and
cycloheptanone (2l, 36 μL, 0.3 mmol). The crude mixture was purified by flash column
chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 37.7 mg, 78% yield of
3l as white solid, mp 135-137 °C.

1H NMR (400 MHz, CDCl₃, ppm) δ 7.80 (d, J = 8.16 Hz, 1H), 7.68-7.66 (m, 1H), 7.41-7.36 (m,
1H), 7.30-7.29 (m, 1H), 3.25-3.21 (m, 2H), 2.92-2.89 (m, 2H), 1.94-1.84 (m, 6H); 13C NMR (100
MHz, CDCl₃, ppm) δ 146.2, 143.8, 133.6, 130.2, 125.6, 125.5, 124.2, 123.6, 112.5, 29.9, 29.5,
27.12, 27.10, 25.4; MS (EI) m/z (%) 242 (100), 213, 200, 188, 51; HRMS calcd. for: C₁₄H₁₅N₂S⁺
(M+H)⁺ 243.09505, found 243.09508.

7,8,9,10,11,12-Hexahydrobenzo[d]cycloocta[4,5]imidazo[2,1-b]thiazole (3m)

The reaction was conducted with 2-aminobenzothiazole (1a, 31 mg, 0.2 mmol) and cyclooctanone
(2m, 39.1 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica
gel, petroleum ether/ethyl acetate = 4:1) to provide 32.8 mg, 64% yield of 3m as white solid, mp
133-135 °C.

1H NMR (400 MHz, CDCl₃, ppm) δ 7.74 (d, J = 8.12 Hz, 1H), 7.69-7.67 (m, 1H), 7.42-7.38 (m,
1H), 7.31-7.27 (m, 1H), 3.21 (t, J = 6.26 Hz, 2H), 2.88 (t, J = 6.38 Hz, 2H), 1.97-1.91 (m, 2H),
1.79-1.73 (m, 2H), 1.56-1.50 (m, 4H); 13C NMR (100 MHz, CDCl₃, ppm) δ 144.4, 144.3, 133.4,
130.3, 125.7, 125.67, 124.3, 123.7, 112.3, 29.6, 28.0, 26.9, 26.3, 24.9, 23.2; MS (EI) m/z (%) 256,
3-Methyl-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3n)

The reaction was conducted with 6-methyl-2-aminobenzothiazole (1b, 32.8 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 41.6 mg, 86% yield of 3n as white solid, mp 151-153 °C.

1H NMR (400 MHz, CDCl3, ppm) δ 7.52 (d, J = 8.28 Hz, 1H), 7.48 (m, 1H), 7.19 (d, J = 7.92 Hz, 1H), 3.05 (t, J = 6.10 Hz, 2H), 2.76 (t, J = 5.98 Hz, 2H), 2.45 (s, 1H), 2.00-1.94 (m, 2H), 1.92-1.86 (m, 2H); 13C NMR (100 MHz, CDCl3, ppm) δ 145.0, 142.2, 133.6, 130.9, 129.2, 126.5, 124.1, 121.7, 111.7, 24.9, 22.9, 22.8, 21.8, 21.1; MS (EI) m/z (%) 242, 214 (100), 173, 77, 51; HRMS calcd. for: C14H15N2S+ (M+H)+ 243.09505, found 243.09518.

3-Methoxy-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3o)

The reaction was conducted with 6-methoxy-2-aminobenzothiazole (1c, 36 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 45.4 mg, 88% yield of 3o as white solid, mp 176-179 °C.

1H NMR (400 MHz, CDCl3, ppm) δ 7.52 (d, J = 8.80 Hz, 1H), 7.18 (d, J = 2.36 Hz, 1H), 6.94 (dd, J = 8.84, 2.36 Hz, 1H), 3.86 (s, 3H), 3.02 (t, J = 5.84 Hz, 2H), 2.75 (t, J = 5.78 Hz, 2H), 1.99-1.86 (m, 4H); 13C NMR (100 MHz, CDCl3, ppm) δ 156.2, 144.6, 142.0, 131.2, 127.3, 121.8, 112.8, 112.6, 108.5, 55.7, 24.9, 22.9, 22.8, 21.8; MS (EI) m/z (%) 258, 230 (100), 215, 187, 51; HRMS calcd. for: C14H15N2OS+ (M+H)+ 259.08996, found 259.08994.

3-Ethoxy-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3p)
The reaction was conducted with 6-ethoxy-2-aminobenzothiazole (1d, 38.8 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 43.5 mg, 80% yield of 3p as white solid, mp 116-118 °C.

1H NMR (400 MHz, CDCl₃, ppm) δ 7.51 (d, J = 8.84 Hz, 1H), 7.17 (m, 1H), 6.93 (dd, J = 8.76, 1.92 Hz, 1H), 4.06 (q, J = 6.90 Hz, 2H), 3.01 (m, 2H), 2.76 (m, 2H), 1.98-1.87 (m, 4H), 1.45 (t, J = 6.94 Hz, 3H); 13C NMR (100 MHz, CDCl₃, ppm) δ 155.6, 144.6, 142.0, 131.2, 127.3, 121.8, 113.4, 112.7, 109.2, 64.1, 24.9, 23.0, 22.8, 21.8, 14.8; MS (EI) m/z (%) 272 (100), 244, 215, 187, 77; HRMS calcd. for: C₁₅H₁₇N₂OŚ + (M+H)⁺ 273.10561, found 273.10583.

3-Fluoro-7,8,9,10-tetrahydrobenzo[4,5]imidazo[2,1-b]thiazole (3q)

The reaction was conducted with 6-fluoro-2-aminobenzothiazole (1e, 33.6 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 35.9 mg, 73% yield of 3q as white solid, mp 130-133 °C.

1H NMR (400 MHz, CDCl₃, ppm) δ 7.58-7.55 (m, 1H), 7.40 (dd, J = 8.08, 2.44 Hz, 1H), 7.14-7.09 (m, 1H), 3.03 (t, J = 5.88 Hz, 2H), 2.75 (t, J = 5.88 Hz, 2H), 2.01-1.86 (m, 4H); 13C NMR (100 MHz, CDCl₃, ppm) δ 159.0 (d, J = 242.71 Hz), 145.0, 142.7, 131.4 (d, J = 9.99 Hz), 129.7, 122.1, 113.3 (d, J = 24.29 Hz), 112.8 (d, J = 8.84 Hz), 111.3 (d, J = 26.94 Hz), 24.9, 22.9, 22.8, 21.8; MS (EI) m/z (%) 246, 218 (100), 205, 178, 51; HRMS calcd. for: C₁₃H₁₃FN₂S⁺ (M+H)⁺ 247.06997, found 247.07042.

3-Chloro-7,8,9,10-tetrahydrobenzo[4,5]imidazo[2,1-b]thiazole (3r)

The reaction was conducted with 6-chloro-2-aminobenzothiazole (1f, 36.8 mg, 0.2 mmol) and
cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 32.5 mg, 62% yield of 3r as white solid, mp 184-187 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta 7.65-7.64 (m, 1H), 7.54-7.52 (m, 1H), 7.34 (dd, J = 8.60, 1.96 Hz, 1H), 3.02 (t, J = 5.30 Hz, 2H), 2.75 (t, J = 5.94 Hz, 2H), 2.00-1.95 (m, 2H), 1.91-1.86 (m, 2H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\), ppm) \(\delta 144.8, 142.8, 131.4, 131.2, 129.0, 125.9, 123.7, 121.9, 112.6, 24.8, 22.8, 22.6, 21.7\); MS (EI) m/z (%) 262, 234 (100), 221, 183, 51; HRMS calcd. for: C\(_{13}\)H\(_{12}\)ClN\(_2\)S\(^+\) (M+H\(^+\)) 263.04042, found 263.04062.

3-Bromo-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3s)

The reaction was conducted with 6-bromo-2-aminobenzothiazole (1g, 45.6 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 33 mg, 54% yield of 3s as white solid, mp 162-163 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta 7.65-7.64 (m, 1H), 7.54-7.52 (m, 1H), 7.34 (dd, J = 8.60, 1.96 Hz, 1H), 3.02 (t, J = 5.30 Hz, 2H), 2.75 (t, J = 5.94 Hz, 2H), 2.00-1.95 (m, 2H), 1.91-1.86 (m, 2H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\), ppm) \(\delta 144.8, 142.8, 131.4, 131.2, 129.0, 125.9, 123.7, 121.9, 112.6, 24.8, 22.8, 22.6, 21.7\); MS (EI) m/z (%) 306, 278 (100), 207, 133, 51; HRMS calcd. for: C\(_{13}\)H\(_{12}\)BrN\(_2\)S\(^+\) (M+H\(^+\)) 306.98991, found 306.98981.

3-(Trifluoromethyl)-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3t)

The reaction was conducted with 6-(trifluoromethyl)-2-aminobenzothiazole (1h, 43.6 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 37.9 mg, 64% yield of 3t as white solid, mp 169-172 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta 7.94 (s, 1H), 7.71-7.69 (m, 1H), 7.65-7.63 (m, 1H), 3.07-3.04 (m, 2H), 2.78-2.75 (m, 2H), 2.02-1.97 (m, 2H), 1.93-1.88 (m, 2H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\), ppm) \(\delta 144.8, 142.8, 131.4, 131.2, 129.0, 125.9, 123.7, 121.9, 112.6, 24.8, 22.8, 22.6, 21.7\); MS (EI) m/z (%) 262, 234 (100), 221, 183, 51; HRMS calcd. for: C\(_{13}\)H\(_{12}\)ClN\(_2\)S\(^+\) (M+H\(^+\)) 263.04042, found 263.04062.
3-(Trifluoromethoxy)-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3u)

The reaction was conducted with 6-(trifluoromethoxy)-2-aminobenzothiazole (1i, 46.8 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 42.4 mg, 68% yield of 3u as white solid, mp 143-146 °C.

1H NMR (400 MHz, CDCl3, ppm) δ 7.64-7.62 (m, 1H), 7.57-7.56 (m, 1H), 7.29-7.28 (m, 1H), 3.05-3.02 (m, 2H), 2.78-2.75 (m, 2H), 2.01-1.87 (m, 4H); 13C NMR (100 MHz, CDCl3, ppm) δ 145.2, 144.9, 131.8, 131.3, 122.1, 120.4 (q, J = 256.07 Hz), 119.2, 117.4, 112.6, 24.9, 22.8, 22.7, 21.8; MS (EI) m/z (%) 312, 284 (100), 271, 215, 51; HRMS calcd. for: C14H12F3N2S+ (M+H)+ 313.06169, found 313.06107.

2-Chloro-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3v)

The reaction was conducted with 5-chloro-2-aminobenzothiazole (1j, 36.8 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 39.8 mg, 76% yield of 3v as white solid, mp 176-178 °C.

1H NMR (400 MHz, CDCl3, ppm) δ 7.57-7.54 (m, 2H), 7.24-7.21 (m, 1H), 3.02-2.99 (m, 2H), 2.76-2.73 (m, 2H), 2.00-1.94 (m, 2H), 1.92-1.86 (m, 2H); 13C NMR (100 MHz, CDCl3, ppm) δ 145.5, 143.0, 133.7, 128.8, 126.6, 125.1, 122.0, 118.9, 115.2, 24.9, 22.8, 22.7, 21.8; MS (EI) m/z (%) 262, 234 (100), 194, 77, 51; HRMS calcd. for: C13H12ClN2S+ (M+H)+ 263.04042, found 263.04041.
2-Bromo-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3w)

The reaction was conducted with 5-bromo-2-aminobenzothiazole (1k, 45.6 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 36.7 mg, 60% yield of 3w as white solid, mp 215-217 °C.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.76 (s, 1H), 7.55-7.52 (m, 1H), 7.42-7.39 (m, 1H), 3.05-3.02 (m, 2H), 2.77-2.74 (m, 2H), 2.01-1.96 (m, 2H), 1.93-1.87 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 145.8, 143.1, 133.6, 131.6, 128.2, 124.8, 123.9, 122.0, 112.5, 24.9, 22.9, 22.7, 21.9; MS (EI) m/z (%) 306, 278 (100), 207, 133, 51; HRMS calcd. for: C$_{13}$H$_{12}$BrN$_2$S$^+$ (M+H)$^+$ 306.98991, found 306.98962.

1-Methyl-7,8,9,10-tetrahydrobenzo[d]benzo[4,5]imidazo[2,1-b]thiazole (3x)

The reaction was conducted with 4-methyl-2-aminobenzothiazole (1l, 32.8 mg, 0.2 mmol) and cyclohexanone (2a, 31.2 μL, 0.3 mmol). The crude mixture was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 4:1) to provide 18.4 mg, 38% yield of 3x as white solid, mp 166-168 °C.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.50-7.48 (m, 1H), 7.18-7.16 (m, 2H), 3.08 (t, $J$ = 5.78 Hz, 2H), 2.78 (t, $J$ = 5.76 Hz, 2H), 2.74 (s, 3H), 1.95-1.83 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$, ppm) $\delta$ 147.1, 143.2, 133.6, 130.5, 129.2, 123.9, 123.3, 122.3, 122.1, 26.7, 25.7, 24.0, 23.3, 22.5; MS (EI) m/z (%) 242, 214 (100), 207, 173, 51; HRMS calcd. for: C$_{14}$H$_{15}$N$_2$S$^+$ (M+H)$^+$ 243.09505, found 243.09525.
Copies of $^1$H and $^{13}$C NMR spectra of products