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Synthesis of 2-Thio-Substituted Benzothiazoles via a Domino Condensation/*S*-Arylation/Heterocyclization Process

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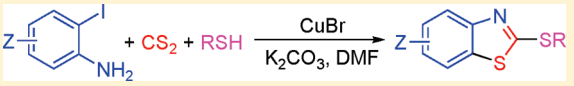
Supporting Information

ABSTRACT: Condensation of carbon disulfide with thiols in the presence of K_2CO_3 generates carbonotrithioate salts *in situ*, which undergo coupling with 2-iodoanilines and subsequent intramolecular condensation and elimination under assistance of CuBr to afford 2-thio-substituted benzothiazoles. Both aliphatic and aromatic thiols are compatible with this process, delivering the corresponding heterocycles with good diversity.



In recent years, an increasing number of 2-thio-substituted benzothiazoles have been designed and synthesized for biological evaluation. The discovered biological activities of these heterocycles include overcoming multidrug resistance in cancer chemotherapy displayed by compound **1** (Figure 1);[1a] inhibiting the enzyme activity of 5-lipoxygenase (5-LO) and cathepsin-D performed by benzothiazoles **2**,[1b] **5**,[1d] and **6**,[1f] respectively; antagonizing the activity of CCR3 receptors shown by compound **3**;[1c] as well as antituberculotic activity exhibited by compound **4**.[1e]

For assembly of 2-thio-substituted benzothiazoles, 2-mercaptobenzothiazoles have been frequently used as the key intermediates. They could react with alkyl halides under basic conditions[2] and alcohols under Mitsunobu conditions[3] to afford 2-alkylthiobenzothiazoles or be coupled with aryl halides and aryl boronic acids under the catalysis of copper and iron to furnish 2-arylthiobenzothiazoles.[4,5] This classical approach requires the prepreparation of 2-mercaptobenzothiazoles via condensation of carbon disulfide with 2-aminothiophenols.[6] Since substituted 2-aminothiophenols are not conveniently available, it is highly desired to explore alternative methods. Recently, Patel and coworkers reported a direct access to 2-arylthiobenzothiazoles by copper-catalyzed intramolecular C−S bond formation of dithocarbamate salts (generated from 2-haloanilines and carbon disulfide) and subsequent coupling with aryl halides.[7] The same group also discovered that 2-thio-substituted benzothiazoles could be elaborated from 2-haloaryl isothiocyanates and thiols via a cascade condensation/coupling process.[8]

In a recent communication, our group described that 2-*N*-substituted benzothiazoles **12** could be prepared via a copper-catalyzed three-component reaction (2-haloanilines, carbon disulfide, and amines as depicted in Scheme 1).[9] The transformation was believed to go through a domino condensation/*S*-arylation/heterocyclization process (Nu = NRR′). We speculated that a similar transformation would occur to provide 2-thio-substituted benzothiazoles **13** if nucleophiles were replaced with thiols. Thus, we undertook an investigation to explore this possibility, and the results are disclosed here.

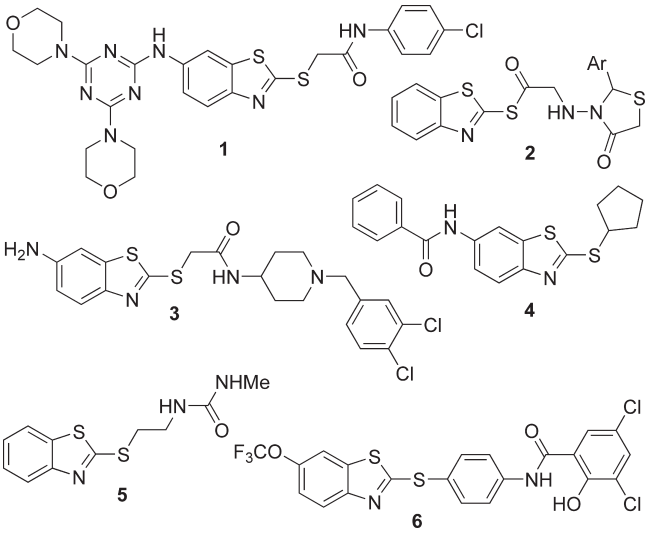


Figure 1. Structures of bioactive 2-thio-substituted benzothiazoles.

Using the reaction of 2-iodoaniline **15a** with carbon disulfide and benzyl mercaptane as a model, we examined the suitable conditions, and the results are summarized in Table 1. Under our previous optimized conditions (1.0 equiv $CuCl_2 \cdot 2H_2O$, 110 °C in DMF),[9] the reaction took place to give the desired product **13a** in 27% yield, together with side product **14a** with 32% yield (entry 1). An improved result was observed by changing copper

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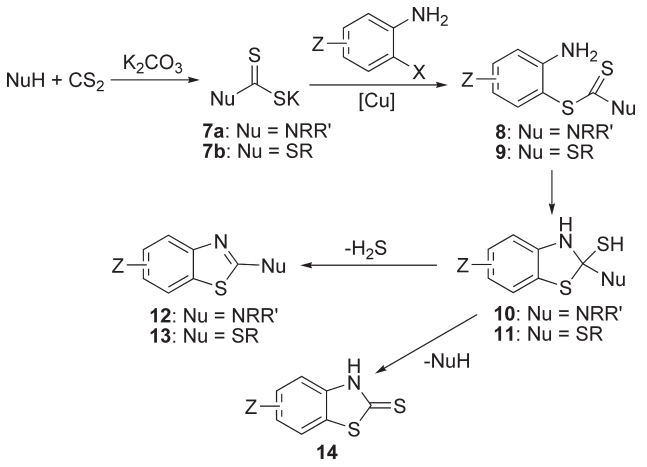
Scheme 1. Possible Reaction Course for Three-Component Syntheses of 2-*N*-Substituted Benzothiazoles 12 and 2-Thio-Substituted Benzothiazoles 13

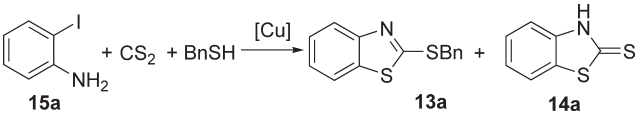


salt to more reactive CuCl and CuBr and increasing their amount to 2 equiv (entries 2 and 3). Further increasing the amount of CuBr to 3 equiv gave a better yield (entry 3). Since the first step of the three-component synthesis is the condensation of thiol with carbon disulfide, we envisioned that changing the operation procedure might be helpful to inhibit the formation of side products. Accordingly, we first reacted BnSH with carbon disulfide at room temperature for 1 h and then added CuBr and 2-iodoaniline before heating. This manipulation was proven useful, providing **13a** with 85% yield (entry 5).

Further studies revealed that changing base to K_3PO_4 and Cs_2CO_3 was possible (entries 6 and 7), although the yields were slightly decreased. However, changing solvent to DMSO, toluene, and 1,4-dioxane all gave considerably low yields (entries 8−10), indicating that using DMF as the reaction media is essential for this transformation. Additionally, it was found that at 90 °C the reaction still worked to give **13a** with 74% yield (entry 11).

Having the optimized reaction conditions in hand, we explored the scope and limitation of the three-component reaction. We first examined the reaction with a series of substituted 2-iodoaniline. It was found that both electron-deficient and electron-rich aryl iodides were applicable for this transformation, affording the corresponding substituted 2-benzylthiobenzothiazols **13b**−**13i** with 58−83% yields (Table 2, entries 1−8). For *S*-nucleophiles, 4-chlorobenzyl mercaptane provided **13j** in 74% yield (entry 9); simple aliphatic thiols including primary, secondary, and tertiary thiols also proceeded well to deliver benzothiazoles **13k**−**13o** with satisfactory yields (entries 10−14); functionalized aliphatic thiols such as *N*-Boc-protected 2-aminoethanethiol, ethyl 3-mercaptopropanoate, and 2-furanylmethanethiol also worked to afford the corresponding products **13p**−**13s** (entries 15−18). In case of ethyl 3-mercaptopropanoate, a relatively low yield was observed (entry 17), presumably because of poor stability of the product **13r**. Additionally, thiophenols were found compatible with this process, although the yields were moderate (entries 19−22). Furthermore, benzothiazolo-[4,5-*b*]pyridine **13x** was obtained from 3-iodo-2-amino-pyridine with 56% yield (entry 23). Noteworthy is that a wide range of functional groups such as nitro, ester, nitrile, ketone, methoxy, and carbamate were tolerated under the present reaction conditions, which would allow preparing more complex 2-thio-substituted benzothiazoles by further operations. Indeed, benzothiazoles **13o** and **13p** could be used for the synthesis of antituberculotic agent **4**[1e] and 5-lipoxylgenase inhibitor **5**,[1d] respectively.

Table 1. Screening of Reaction Conditions for Reaction of 2-Iodoaniline, CS_2, and Benzyl Mercaptane[a]



entry	Cu source	solvent	yield of **13a** (%)[b]
1	$CuCl_2 \cdot 2H_2O$ (1 equiv)	DMF	27[c]
2	CuCl (2 equiv)	DMF	56
3	CuBr (2 equiv)	DMF	59
4	CuBr (3 equiv)	DMF	70
5	CuBr (3 equiv)	DMF	85
6	CuBr (3 equiv)	DMF	78[d]
7	CuBr (3 equiv)	DMF	79[e]
8	CuBr (3 equiv)	DMSO	57
9	CuBr (3 equiv)	toluene	35
10	CuBr (3 equiv)	1,4-dioxane	28
11	CuBr (3 equiv)	DMF	74[f]

[a] Reaction conditions. **A** (for entries 1−4): 2-iodoaniline (1.0 mmol), CS_2 (1.2 mmol), BnSH (1.5 mmol), copper salt (1−3 mmol), K_2CO_3 (3.0 mmol), DMF, 110 °C, 12 h. **B** (for entries 5−11): CS_2 (1.2 mmol), BnSH (1.2 mmol), K_2CO_3 (3.0 mmol), DMF, rt, 1 h; then 2-iodoaniline (1.0 mmol), CuBr (3 mmol), 110 °C, 12 h. [b] Isolated yield. [c] Compound **14a** was isolated in 32% yield. [d] K_3PO_4 was used as the base. [e] Cs_2CO_3 was used as the base. [f] The reaction was carried out at 90 °C.

In conclusion, we have developed a facile and diverse method for assembling 2-thio-substituted benzothiazoles by using conveniently available reagents. This study also demonstrated that the carbonotrithioate salts that generated from thiols and carbon disulfide are suitable coupling partner for copper-catalyzed arylation.[10] Our discovery may prompt further explorations to discover new coupling partners for cross-coupling reactions.

EXPERIMENTAL SECTION

Typical Procedure for Reaction of 2-Iodoanilines with Carbon Disulfide and Aliphatic Thiols. A mixture of K_2CO_3 (3.0 mmol), thiol (1.2 mmol), and CS_2 (1.2 mmol) in DMF (2.0 mL) was stirred at rt for 1 h before CuBr (3.0 mmol) and 2-iodoaniline (1.0 mmol) were added. The resultant mixture was heated at 110 °C for 6 h. The cooled solution was partitioned between ethyl acetate and water. The organic layer was washed with water and brine and dried over Na_2SO_4. After removal of solvent in vacuo, the residue was chromatographed to give the corresponding benzothiazole.

Typical Procedure for Reaction of 2-Iodoanilines with Carbon Disulfide and Thiolphenols. An oven-dried Schlenk tube was charged with K_2CO_3 (1.5 mmol), CuBr (1.75 mmol), evacuated, and backfilled with argon. After DMF (1.0 mL), thiophenol (1.0 mmol), and CS_2 (0.75 mmol) were injected, the reaction mixture was stirred at rt for 1 h before 2-iodoaniline (0.5 mmol) in DMF (1.0 mL) was added. The resultant mixture was heated at 110 °C for 6 h. The cooled solution was partitioned between ethyl acetate and water. Ethyl acetate extract workup followed by chromatography afforded the product.

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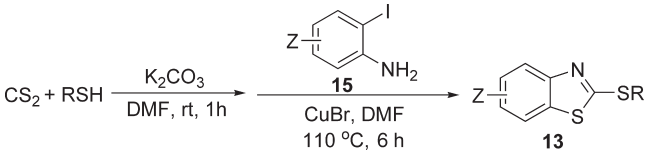
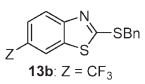
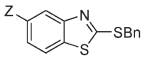
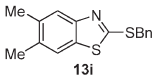
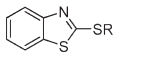
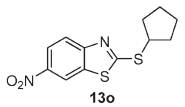
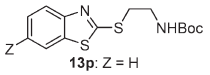
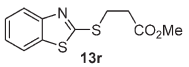
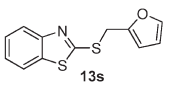
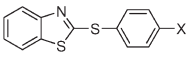
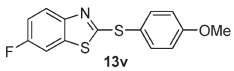
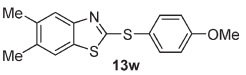
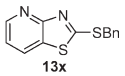
Table 2. Formation of 2-Thio-Substituted Benzothiazoles from 2-Iodoanilines, CS_2, and Thiols[a]



entry	product	yield (%)[b]
1	 **13b**: Z = CF_3	80
2	**13c**: Z = NO_2	66
3	**13d**: Z = CO_2Me	72
4	**13e**: Z = CN	68
5	**13f**: Z = OMe	58
6	 **13g**: Z = CF_3	70
7	**13h**: Z = OMe	78
8	 **13i**	83
9	 **13j**: R = $CH_2C_6H_4Cl$-4	74
10	**13k**: R = *n*-Pr	80
11	**13l**: R = *i*-Pr	82
12	**13m**: R = *t*-Bu	79
13	**13n**: R = cyclopentanyl	83

entry	product	yield (%)[b]
14	 **13o**	61
15	 **13p**: Z = H	71
16	**13q**: Z = COMe	64
17	 **13r**	45[c]
18	 **13s**	66
19	 **13t**: X = H	56
20	**13u**: X = OMe	60
21	 **13v**	52
22	 **13w**	61
23	 **13x**	56

[a] Reaction conditions: CS_2 (1.2 mmol), thiol (1.2 mmol), K_2CO_3 (3.0 mmol), DMF, rt, 1 h; then 2-iodoaniline (1.0 mmol), CuBr (3 mmol), 110 °C, 6 h. [b] Isolated yield. [c] The reaction was carried out at 90 °C.

2-(Benzylthio)benzo[*d*]thiazole (13a). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 8.1 Hz, 1H), 7.74 (d, J = 7.5 Hz, 1H), 7.55−7.20 (m, 7H), 4.60 (s, 2H); ESI-MS m/z 258.1 $(M + H)^+$.

2-(Benzylthio)-6-(trifluoromethyl)benzo[*d*]thiazole (13b). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 7.5 Hz, 2H), 7.38−7.22 (m, 3H), 4.63 (s, 2H); ESI-MS m/z 326.1 $(M + H)^+$.

2-(Benzylthio)-6-nitrobenzo[*d*]thiazole (13c). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.31 (d, J = 9.0 Hz, 1H), 7.93 (d, J = 9.3 Hz, 1H), 7.47 (d, J = 6.9 Hz, 2H), 7.40−7.25 (m, 3H), 4.65 (s, 2H); ESI-MS m/z 303.0 $(M + H)^+$.

Methyl 2-(Benzylthio)benzo[*d*]thiazole-6-carboxylate (13d). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (d, J = 0.9 Hz, 1H), 8.10 (dd, J = 8.7 Hz, J = 1.8 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 6.9 Hz, 2H), 7.39−7.25 (m, 3H), 4.63 (s, 2H), 3.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 166.6, 156.0, 135.8, 135.3, 129.2 (2C), 128.8 (2C), 127.9, 127.5, 126.0, 123.1, 121.1, 52.3, 37.7; ESI-MS m/z 316.1 $(M + H)^+$; HRMS (EI) calcd for $C_{16}H_{13}NO_2S_2$ (M^+) 315.0388, found 315.0385.

2-(Benzylthio)benzo[*d*]thiazole-6-carbonitrile (13e). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 8.8 Hz, 1H), 7.46 (d, J = 6.8 Hz, 2H), 7.38−7.25 (m, 3H), 4.64 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 155.5, 135.8, 135.6, 129.6, 129.2 (2C), 128.9 (2C), 128.1, 125.5, 122.0, 118.8, 107.5, 37.8; ESI-MS m/z 283.0 $(M + H)^+$; HRMS (EI) calcd for $C_{15}H_{10}N_2S_2$ (M^+) 282.0285, found 282.0279.

2-(Benzylthio)-6-methoxybenzo[*d*]thiazole (13f). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 8.7 Hz, 1H), 7.43 (d, J = 6.6 Hz, 2H),

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7.38−7.23 (m, 3H), 7.21 (d, J = 2.4 Hz, 1H), 7.02 (dd, J = 9.0 Hz, J = 2.7 Hz, 1H), 4.56 (s, 2H), 3.84 (s, 3H); ESI-MS m/z 288.1 $(M + H)^+$.

2-(Benzylthio)-5-(trifluoromethyl)benzo[*d*]thiazole (13g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.84 (d, J = 8.7 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.46 (d, J = 6.9 Hz, 2H), 7.38−7.22 (m, 3H), 4.63 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 152.8, 139.1, 136.0, 129.2 (2C), 128.8 (2C), 128.8 (q, J = 32.8 Hz, 1C), 127.9, 124.3 (q, J = 271.3 Hz, 1C), 121.5, 120.7 (q, J = 3.6 Hz, 1C), 118.6 (q, J = 3.6 Hz, 1C), 37.7; ESI-MS m/z 326.1 $(M + H)^+$; HRMS (EI) calcd for $C_{15}H_{10}F_3NS_2$ (M^+) 325.0207, found 325.0211.

2-(Benzylthio)-5-methoxybenzo[*d*]thiazole (13h). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 8.7 Hz, 1H), 7.46 (d, J = 6.3 Hz, 2H), 7.43 (d, J = 2.7 Hz, 1H), 7.38−7.25 (m, 3H), 6.95 (dd, J = 8.7 Hz, J = 2.7 Hz, 1H), 4.59 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 159.1, 154.5, 136.3, 129.2 (2C), 128.8 (2C), 127.9, 127.1, 121.3, 114.0, 104.8, 55.6, 37.8; ESI-MS m/z 288.1 $(M + H)^+$; HRMS (EI) calcd for $C_{15}H_{13}NOS_2$ (M^+) 287.0439, found 287.0440.

2-(Benzylthio)-5,6-dimethylbenzo[*d*]thiazole (13i). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.49 (s, 1H), 7.44 (d, J = 6.9 Hz, 2H), 7.35−7.22 (m, 3H), 4.57 (s, 2H), 2.37 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 152.1, 136.5, 135.2, 133.7, 132.8, 129.2 (2C), 128.8 (2C), 127.8, 122.0, 121.1, 37.9, 20.2, 20.1; ESI-MS m/z 286.1 $(M + H)^+$; HRMS (EI) calcd for $C_{16}H_{15}NS_2$ (M^+) 285.0646, found 285.0643.

2-((4-Chlorobenzyl)thio)benzo[*d*]thiazole (13j). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.47−7.35 (m, 3H), 7.34−7.24 (m, 3H), 4.56 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 153.1, 135.4, 135.0, 133.6, 130.5 (2C), 128.9 (2C), 126.2, 124.5, 121.6, 121.1, 36.9; ESI-MS m/z 292.0 $(M + H)^+$; HRMS (EI) calcd for $C_{14}H_{10}ClNS_2$ (M^+) 290.9943, found 290.9944.

2-(Propylthio)benzo[*d*]thiazole (13k). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.4 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 3.33 (t, J = 7.6 Hz, 2H), 1.90−1.80 (m, 2H), 1.09 (t, J = 7.2 Hz, 3H); ESI-MS m/z 210.0 $(M + H)^+$.

2-(*i*-Propylthio)benzo[*d*]thiazole (13l). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 4.14−4.02 (m, 1H), 1.50 (d, J = 7.2 Hz, 6H); ESI-MS m/z 210.0 $(M + H)^+$.

2-(*tert*-Butylthio)benzo[*d*]thiazole (13m). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 1.60 (s, 9H); ESI-MS m/z 224.1 $(M + H)^+$.

2-(Cyclopentylthio)benzo[*d*]thiazole (13n). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, J = 8.1 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.45−7.36 (m, 1H), 7.33−7.24 (m, 1H), 4.18−4.06 (m, 1H), 2.40−2.20 (m, 2H), 1.90−1.65 (m, 6H); ESI-MS m/z 235.9 $(M + H)^+$.

2-(Cyclopentylthio)-6-nitrobenzo[*d*]thiazole (13o). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 (d, J = 2.1 Hz, 1H), 8.30 (dd, J = 9.0 Hz, J = 2.1 Hz, 1H), 7.90 (d, J = 8.7 Hz, 1H), 4.24−4.12 (m, 1H), 2.45−2.26 (m, 2H), 1.92−1.65 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 157.2, 143.9, 135.5, 121.8, 121.2, 117.3, 46.9, 33.7 (2C), 24.9 (2C); ESI-MS m/z 281.0 $(M + H)^+$; HRMS (EI) calcd for $C_{12}H_{12}N_2O_2S_2$ (M^+) 280.0340, found 280.0335.

***tert*-Butyl (2-(Benzo[*d*]thiazol-2-ylthio)ethyl)carbamate (13p).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 5.30 (s, 1H), 3.63−3.53 (m, 2H), 3.52−3.44 (m, 2H), 1.43 (s, 9H); ESI-MS m/z 311.0 $(M + H)^+$; HRMS (EI) calcd for $C_{14}H_{18}N_2O_2S_2$ (M^+) 310.0810, found 310.0812.

***tert*-Butyl (2-((6-Acetylbenzo[*d*]thiazol-2-yl)thio)ethyl) carbamate (13q).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, J = 1.2 Hz, 1H), 8.02 (dd, J = 8.4 Hz, J = 1.8 Hz, 1H), 7.87 (d, J = 8.7 Hz, 1H), 5.23 (s, 1H), 3.65−3.56 (m, 2H), 3.56−3.47 (m, 2H), 2.67 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9, 171.1, 155.9, 155.8, 135.6, 133.1, 126.5, 121.8, 121.1, 79.2, 39.9, 33.6, 28.4 (3C), 26.7; ESI-MS m/z 353.2 $(M + H)^+$; HRMS (EI) calcd for $C_{16}H_{20}N_2O_3S_2$ (M^+) 352.0915, found 352.0928.

Methyl 3-(Benzo[*d*]thiazol-2-ylthio)propanoate (13r). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.42 (dd, J = 7.2 Hz, J = 7.8 Hz, 1H), 7.30 (dd, J = 7.8 Hz, J = 7.2 Hz, 1H), 3.73 (s, 3H), 3.61 (t, J = 6.9 Hz, 2H), 2.94 (t, J = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 165.9, 153.2, 135.3, 126.1, 124.3, 121.6, 121.0, 51.9, 34.2, 28.2; ESI-MS m/z 254.3 $(M + H)^+$; HRMS (EI) calcd for $C_{11}H_{11}NO_2S_2$ (M^+) 253.0231, found 253.0234.

2-((Furan-2-ylmethyl)thio)benzo[*d*]thiazole (13s). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.37 (s, 1H), 7.30 (t, J = 7.6 Hz, 1H), 6.35 (d, J = 2.8 Hz, 1H), 6.31 (s, 1H), 4.64 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 153.2, 149.6, 142.6, 135.5, 126.1, 124.4, 121.7, 121.1, 110.8, 109.1, 30.1; ESI-MS m/z 248.0 $(M + H)^+$; HRMS (EI) calcd for $C_{12}H_9NOS_2$ (M^+) 247.0126, found 247.0129.

2-(Phenylthio)benzo[*d*]thiazole (13t). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4 Hz, 1H), 7.78−7.70 (m, 2H), 7.65 (d, J = 7.8 Hz, 1H), 7.56−7.44 (m, 3H), 7.41 (td, J = 7.8 Hz, J = 1.2 Hz, 1H), 7.27 (t, J = 7.2 Hz, 1H); ESI-MS m/z 244.1 $(M + H)^+$.

2-((4-Methoxyphenyl)thio)benzo[*d*]thiazole (13u). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 8.1 Hz, 1H), 7.70−7.60 (m, 3H), 7.39 (td, J = 7.5 Hz, J = 1.2 Hz, 1H), 7.25 (td, J = 7.2 Hz, J = 1.2 Hz, 1H), 7.04−6.97 (m, 2H), 3.88 (s, 3H); ESI-MS m/z 274.4 $(M + H)^+$.

6-Fluoro-2-((4-methoxyphenyl)thio)benzo[*d*]thiazole (13v). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82−7.75 (m, 1H), 7.66 (d, J = 8.7 Hz, 2H), 7.32 (dd, J = 7.8 Hz, J = 2.7 Hz, 1H), 7.12 (td, J = 8.7 Hz, J = 2.7 Hz, 1H), 7.01 (d, J = 8.7 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (d, J = 2.9 Hz, 1C), 161.8, 159.8 (d, J = 243.5 Hz, 1C), 150.8 (d, J = 1.4 Hz, 1C), 137.6 (2C), 136.4 (d, J = 10.9 Hz, 1C), 122.6 (d, J = 9.5 Hz, 1C), 119.9, 115.6 (2C), 114.4 (d, J = 24.1 Hz, 1C), 107.2 (d, J = 26.2 Hz, 1C), 55.5; ESI-MS m/z 292.0 $(M + H)^+$; HRMS (EI) calcd for $C_{14}H_{10}FNOS_2$ (M^+) 291.0188, found 291.0191.

2-((4-Methoxyphenyl)thio)-5,6-dimethylbenzo[*d*]thiazole (13w). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 9.0 Hz, 2H), 7.62 (s, 1H), 7.37 (s, 1H), 6.99 (d, J = 9.0 Hz, 2H), 3.87 (s, 3H), 2.34 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 161.6, 152.9, 137.5 (2C), 135.2, 133.5, 132.9, 122.1, 120.8, 120.6, 115.4 (2C), 55.5, 20.1, 20.0; ESI-MS m/z 302.0 $(M + H)^+$; HRMS (EI) calcd for $C_{16}H_{15}NOS_2$ (M^+) 301.0595, found 301.0599.

2-(Benzylthio)thiazolo[4,5-*b*]pyridine (13x). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (dd, J = 4.8 Hz, J = 1.2 Hz, 1H), 8.08 (dd, J = 7.8 Hz, J = 1.8 Hz, 1H), 7.48 (d, J = 7.5 Hz, 2H), 7.38−7.25 (m, 3H), 7.24−7.18 (m, 1H), 4.72 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 163.7, 147.6, 135.9, 129.8, 129.3 (2C), 128.9, 128.8 (2C), 127.9, 119.0, 37.5; ESI-MS m/z 259.3 $(M + H)^+$; HRMS (EI) calcd for $C_{13}H_{10}N_2S_2$ (M^+) 258.0285, found 258.0284.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Copies of ^{1}H NMR and ^{13}C NMR spectra for all heterocycle products. This material is available free of charge via the Internet at http://pubs.acs.org.

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