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Synthesis of Benzothiazoles through Copper-Catalyzed One-Pot Three-Component Reactions with Use of Sodium Hydrosulfide as a Sulfur Surrogate

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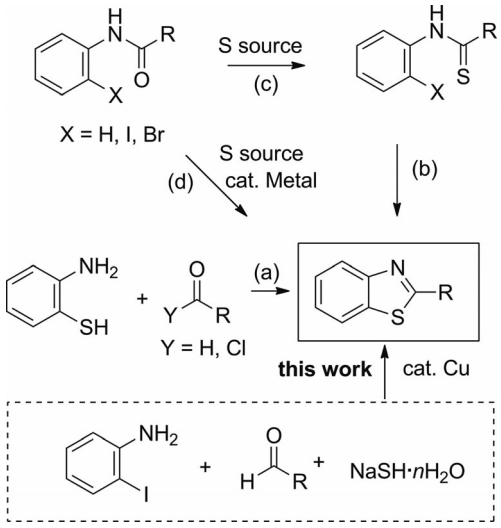
Copper-catalyzed one-pot three-component reactions of 2-iodoanilines, aldehydes, and $NaSH{\cdot}nH_2O$ afford benzothiazoles in good yields. When CuCl was employed as a catalyst in the absence of a ligand, a variety of aromatic aldehydes and substituted 2-iodoanilines reacted with $NaSH{\cdot}nH_2O$ to produce the corresponding 2-arylbenzothiazoles in 70–98 % yields. The copper catalyst plays a key role in C–S bond formation between $NaSH{\cdot}nH_2O$ and the aryl iodide that was formed from the condensation of 2-iodoaniline and aldehyde. It was found that $NaSH{\cdot}nH_2O$ functions as a sulfur surrogate and oxidant in the formation of benzothiazole.

Introduction

The synthesis of 2-substituted azoles such as oxazoles, imidazoles, indazoles, and thiazoles has attracted much attention because of their important roles in bioactive pharmaceutical compounds and new materials.[1] In particular, benzothiazoles have been intensively studied and have found to be employable in biological applications such as antitumor,[2] anti-inflammatory,[3] antimicrobial,[4] antitrypanosomal,[5] anticonvulsant,[6] and antituberculosis[7] agents and also as tracers for β-amyloid plaques in Alzheimer's disease.[8] Benzothiazole moieties are also found in functional molecules such as nonlinear optical materials[9] and ligands for phosphorescent complexes.[10] Much effort has therefore been devoted to the development of new methodologies for the construction of this privileged structure.

The most common methods of synthesizing benzothiazoles involve condensations of 2-aminothiophenol with carboxylic acid derivatives or aldehydes; see Scheme 1 (a).[11] However, they have some drawbacks such as their drastic reaction conditions, tedious workup procedures, and the difficulties involved in the preparation of 2-aminothiophenols, especially substituted ones, which are readily oxidized. In addition, their strong and disagreeable odors can lead to bad environmental problems and a sealing process is needed in scale-up operations. Another alternative strategy is the cyclization of thioformanilides, which has been performed with the aid of transition-metal catalysts,[12] S_NAr conditions,[13] radical conditions,[14] and Jacobson's method (cyclization of an arylthioamide through the use of potassium ferricyanide)[15]; see Scheme 1 (b). These methods suffer from low functional group tolerance in the preparation of thioformanilides, because of the use of P_4S_{10} or Lawesson's reagent in the conversion of the amide to the corresponding thioamide; see Scheme 1 (c).[16] Recently, palladium- or copper-catalyzed coupling reactions of 2-haloanilides and thiol surrogates such as 2-ethylhexyl 3-mercaptopropionate and $Na_2S{\cdot}9H_2O$ have been used in the



Scheme 1. Synthesis of benzothiazoles.

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synthesis of benzothiazoles – see Scheme 1, (d)[17] – but these reactions also need preparation steps for the starting materials.

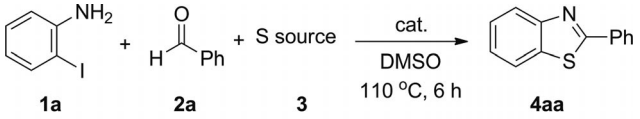
In recent decades, the development of multicomponent methodologies that combine all fragments in one step to produce the desired product with the aid of transition-metal catalysis has received considerable attention.[18] To the best of our knowledge, however, three-component methodology for the construction of benzothiazoles has rarely been exploited, and only the synthesis of 2-*N*-substituted benzothiazoles falls into this category.[19] Very recently, we have reported the synthesis of 2*H*-indazoles[20] and benzimidazoles[21] through three-component coupling reactions in the presence of a copper catalyst. In particular, success in the synthesis of benzimidazoles from 2-haloanilines, aldehydes, and NaN_3 prompted us to develop benzothiazoles, which are analogues of azole compounds. Here we report one-pot, three-component reactions for the construction of benzothiazoles.

Results and Discussion

To determine the optimum conditions, 2-iodoaniline (**1a**), benzaldehyde (**2a**), and NaSH·*n*H_2O (**3a**) were employed as model substrates. The results are summarized in Table 1.

All reactions were carried out in the presence of $MgSO_4$ to accelerate the condensation of 2-iodoaniline with benzaldehyde and to capture the water in the form of sodium hydrosulfide hydrate (NaSH·*n*H_2O). In addition, the reactions were conducted under air. We first investigated a variety of transition metals for the formation of **4aa**. Palladium[22] and nickel[23] catalysts afforded the benzothiazole in low yields, even though they have been reported to function as good catalysts in the formation of C–S bonds (Entries 1–3). When copper catalysts were employed,[24] CuI and CuCl afforded the desired product in 94% and 99% yields, respectively (Entries 4 and 5). The yield of the product from copper(II) was somewhat lower than that from copper(I) (Entry 6). Decreasing the amount of the catalyst to 2 mol-% also produced the benzothiazole with good yield (Entry 7). When the amount of NaSH·*n*H_2O was reduced to 1 equiv., however, the yield of the product decreased to 32%. Use of oxidants,[11f,11g,11j,25] which have been employed in the synthesis of benzothiazoles, or of an additional base did not give satisfactory results (Entries 9–12). When $Na_2S·9H_2O$[17b] was used as a sulfur source instead of NaSH·*n*H_2O, the desired product was obtained in 70% yield (Entry 13). Potassium thioacetate, however, provided only a 44% yield of the product, even though it was a good sulfur surrogate in the synthesis of thioethers from aryl halides (Entry 14).[26] A reduction in the reaction temperature to 60 °C resulted in a 35% yield of the product, but the yield was not significantly improved even when the reaction time was extended to 48 h (Entry 15). The addition of a variety of ligands such as amines, amino acids, and diketones did not improve the yields of the product (Entries 16–18). In view of costs and the yields of the product, we employed the following optimized conditions for the one-pot synthesis of benzothiazoles; 2-haloaniline (1.0 equiv.), aldehydes (1.0 equiv.), NaSH·*n*H_2O (2.0 equiv.), CuCl (2.0 mol-%), and $MgSO_4$ (2.0 equiv.) at 110 °C for 6 h.

Table 1. Optimization for the synthesis of benzothiazole.[a]



1a **2a** **3** **4aa**

3a[b]: NaSH·*n*H_2O
3b: $Na_2S·9H_2O$
3c: KSAc

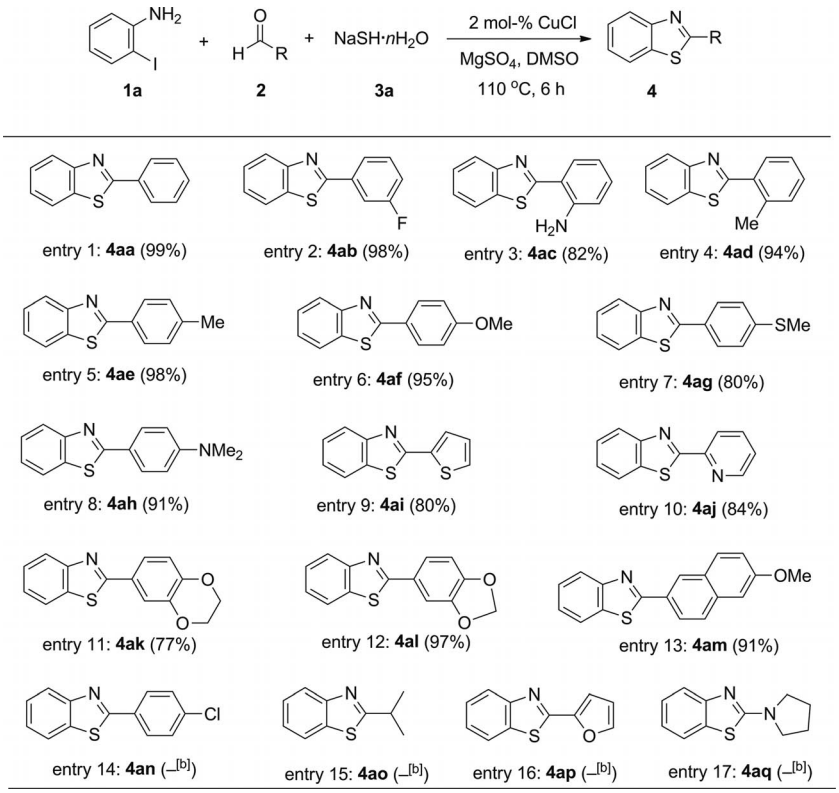
Entry	3	Catalyst [mol-%]	Ligand	Additive	Yield [%][c]
1	**3a**	$Pd(OAc)_2$(5.0)	–	–	36
2	**3a**	$Pd(dba)_2$ (5.0)	–	–	13
3	**3a**	$Ni(OAc)_2$(5.0)	–	–	33
4	**3a**	CuI (5.0)	–	–	94
5	**3a**	CuCl (5.0)	–	–	99
6	**3a**	$CuCl_2$ (5.0)	–	–	88
7	**3a**	CuCl (2.0)	–		98
8[d]	**3a**	CuCl (2.0)	–		32
9	**3a**	CuCl (2.0)	–	$NaHCO_3$[f]	34
10	**3a**	CuCl (2.0)	–	Na_2CO_3[f]	23
11	**3a**	CuCl (2.0)	–	$RuCl_3$[g]	32
12	**3a**	CuCl (2.0)	–	H_2O_2[f]	–
13	**3b**	CuCl (2.0)	–	–	70
14	**3c**	CuCl (2.0)	–	–	44
15[e]	**3a**	CuCl (2.0)	–	–	35 (40[h])
16[e]	**3a**	CuCl (2.0)	TMEDA	–	40
17[e]	**3a**	CuCl (2.0)	L-proline	–	16
18[e]	**3a**	CuCl (2.0)	diketone[i]	–	22

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol), and **3** (0.3 or 0.6 mmol) were treated in the presence of the catalyst and $MgSO_4$ (1.2 mmol) in DMSO at 110 °C for 6 h under air. [b] H_2O content (60 wt.-%) determined by TGA analysis. [c] Determined by GC with internal standard. [d] Compound **3** (0.3 mmol) was used. [e] Reactions were conducted at 60 °C for 6 h. [f] 0.6 mmol were employed. [g] 0.015 mmol were employed. [h] Yield after 48 h. [i] Pentane-2,4-dione.

To evaluate this catalytic system, a variety of aldehydes were employed in the synthesis of benzothiazoles from 2-iodoaniline (**1a**). The results are summarized in Table 2.

As expected, 2-phenylbenzothiazole (**4aa**) was isolated in 99% yield (Entry 1). 3-Fluorobenzaldehyde (**2b**) afforded the desired product in good yield (Entry 2), as did *ortho*-substituted benzaldehydes (Entries 3 and 4). Benzaldehydes bearing electron-donating groups such as methyl, methoxy, methylthio, and dimethylamine at the *para* position gave the corresponding benzothiazoles in 98%, 95%, 80%, and 91% yields, respectively (Entries 5–8). Heteroaromatic aldehydes such as thiophene-2-carbaldehyde (**2i**) and pyridine-2-carbaldehyde (**2j**) showed good yields in the formation of benzothiazoles (Entries 9 and 10). 1,4-Benzodioxan-6-carbaldehyde (**2k**) and piperonal (**2l**) afforded the corresponding benzaldehydes in 77% and 97% yields, respectively (Entries 11 and 12), and 6-methoxy-2-naphthaldehyde (**2m**) also showed a good yield (Entry 13). 4-Chlorobenzaldehyde

Table 2. Synthesis of benzothiazoles from 2-iodoaniline.[a]



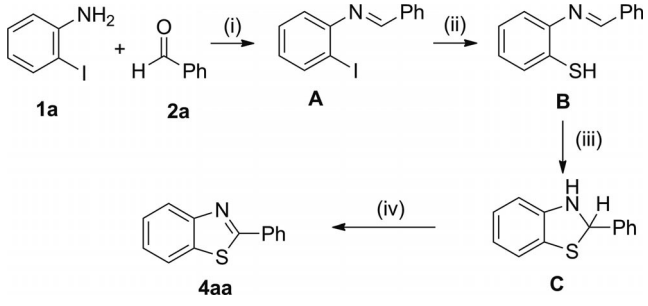
[a] Reaction conditions: **1a** (3.0 mmol), **2** (3.0 mmol), **3a** (6.0 mmol) in the presence of $MgSO_4$ (6.0 mmol) in DMSO at 110 °C for 6 h (% is isolated yield). [b] No product was obtained.

(**2n**), however, did not produce the desired product (Entry 14). Attempts to employ alkyl aldehydes such as isobutyraldehyde (**2o**) and heteroaromatic aldehydes such as furan-2-carbaldehyde (**2p**) did not result in the synthesis of the benzothiazole, even though the corresponding imines were formed (Entries 15 and 16). Formamides such as pyrrolidine-1-carbaldehyde (**2q**) did not produce the desired product, because their condensation reactions with 2-iodoaniline (**1a**) did not take place under these reaction conditions (Entry 17).

We next expanded this method to substituted 2-iodoaniline derivatives for the formation of benzothiazoles as shown in Table 3.

2-Iodoaniline derivatives substituted with a single additional halogen atom, such as 5-chloro-2-iodoaniline (**1b**) and 4-fluoro-2-iodoaniline (**1c**), produced the corresponding benzothiazoles in good yields (Entries 1–14). The yields of the product were similar to those of the products obtained from 2-iodoaniline. 2-Iodoaniline derivatives substituted with two additional halogen atoms, such as 2,4-dichloro-6-iodoaniline (**1d**) and 4-chloro-2-fluoro-6-iodoaniline (**1e**), showed somehow lower yields than those substituted with a single additional halogen atom (Entry 4 vs. Entry 15, and Entries 5 and 12 vs. Entry 16). 2-Iodo-4-(trifluoromethyl)aniline (**1f**) and 2-iodo-4,6-dimethylaniline (**1g**) afforded the desired benzothiazoles in good yields (Entries 17–26).

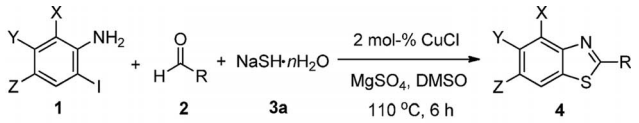
We propose a reaction pathway (Scheme 2) in which the condensation of 2-iodoaniline and benzaldehyde takes place first, the copper-catalyzed coupling reaction between *N*-benzylidene-2-iodoaniline (**A**) and NaSH·*n*H_2O then produces the 2-(benzylidenamino)benzenethiol (**B**) as an intermediate, and the desired product **3** is finally formed through cyclization and oxidation.



Scheme 2. Proposed reaction pathway.

To investigate the proposed reaction pathway in detail, we performed several experiments. When 2-iodoaniline was treated with NaSH·*n*H_2O in the presence of CuCl, no product containing a C–S bond was found in the reaction mixture (Scheme 3). This result supports the hypothesis that the condensation of 2-iodoaniline and benzaldehyde occurs first, rather than NaSH·*n*H_2O-induced C–S bond formation.

Table 3. Synthesis of benzothiazoles from substituted 2-iodoanilines.[a]



1b: X, Z = H, Y = Cl; **1c**: X, Y = H, Z = F ;
1d: Y = H, X, Z = Cl; **1e**: X = F, Y = H, Z = Cl
1f: X, Y = H, Z = CF_3 ; **1g**: Y = H, X, Z = CH_3

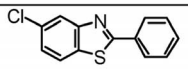
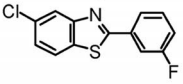
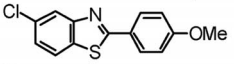
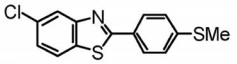
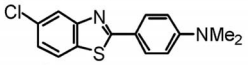
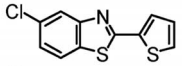
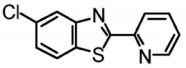
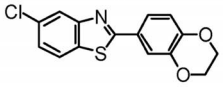
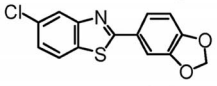
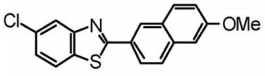
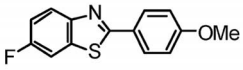
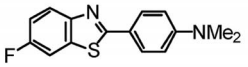
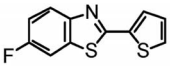
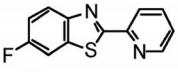
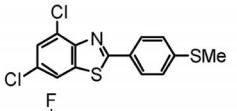
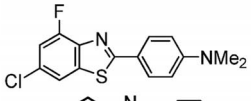
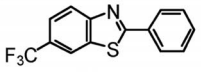
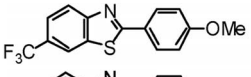
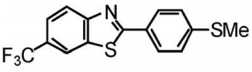
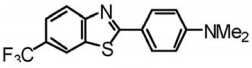
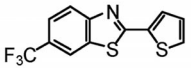
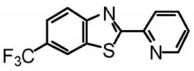
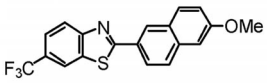
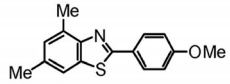
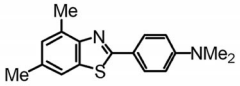
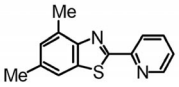
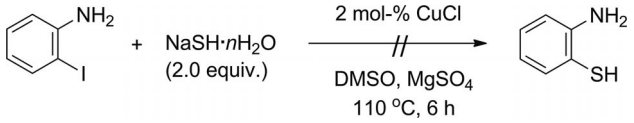
Entry	1	Product		Yield [%][b]
1	**1b**		**4ba**	95
2	**1b**		**4bb**	87
3	**1b**		**4bf**	85
4	**1b**		**4bg**	90
5	**1b**		**4bh**	85
6	**1b**		**4bi**	65
7	**1b**		**4bj**	78
8	**1b**		**4bk**	71
9	**1b**		**4bl**	75
10	**1b**		**4bm**	90
11	**1c**		**4cf**	91
12	**1c**		**4ch**	73
13	**1c**		**4ci**	72
14	**1c**		**4cj**	94
15	**1d**		**4dg**	65
16	**1e**		**4eh**	61
17	**1f**		**4fa**	97
18	**1f**		**4ff**	76
19	**1f**		**4fg**	71
20	**1f**		**4fh**	90

Table 3. (*Continued*)

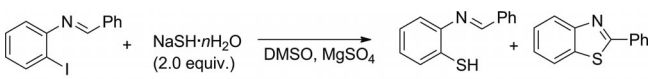
Entry	1	Product		Yield [%][b]
21	**1f**		**4fi**	78
22	**1f**		**4fj**	76
23	**1f**		**4fm**	80
24	**1g**		**4gf**	72
25	**1g**		**4gh**	71
26	**1g**		**4gj**	78

[a] Reaction conditions: **1a** (3.0 mmol), **2** (3.0 mmol), and **3a** (6.0 mmol) in the presence of $MgSO_4$ (6.0 mmol) in DMSO at 110 °C for 6 h. [b] Isolated yields.



Scheme 3. Attempted coupling reaction between 2-iodoaniline and NaSH·*n*H_2O.

To determine the role of CuCl in this reaction, *N*-benzylidene-2-iodoaniline (**A**) was treated with NaSH·*n*H_2O under a variety of reaction conditions, as shown in Scheme 4. In the absence of CuCl, neither 2-(benzylidenamino)benzenethiol (**B**) nor benzothiazole **4** were found in the reaction mixture. When the reaction was conducted at 110 °C in the presence of copper, benzothiazole was formed in 98% yield with a trace amount of **B**. When the reaction temperature was decreased to 60 °C, both 2-(benzylidenamino)benzenethiol (**B**) and benzothiazole **4** were found, in 8% and 35% yields, respectively, in the reaction mixture. This result supports the hypothesis that 2-(benzylidenamino)benzenethiol (**B**) is an intermediate in the reaction pathway.



without CuCl: 110 °C	not found	not found
2 mol-% CuCl: 110 °C, 6 h	< 1%	98%
2 mol-% CuCl: 60 °C, 6 h	8%	35%

Scheme 4. The effect of copper on the synthesis of benzothiazole from *N*-benzylidene-2-iodoaniline.

To study reaction steps (iii) and (iv) in detail, 2-(benzylidenamino)benzenethiol (**B**) was treated under a variety of conditions at 60 °C, as shown in Figure 1.

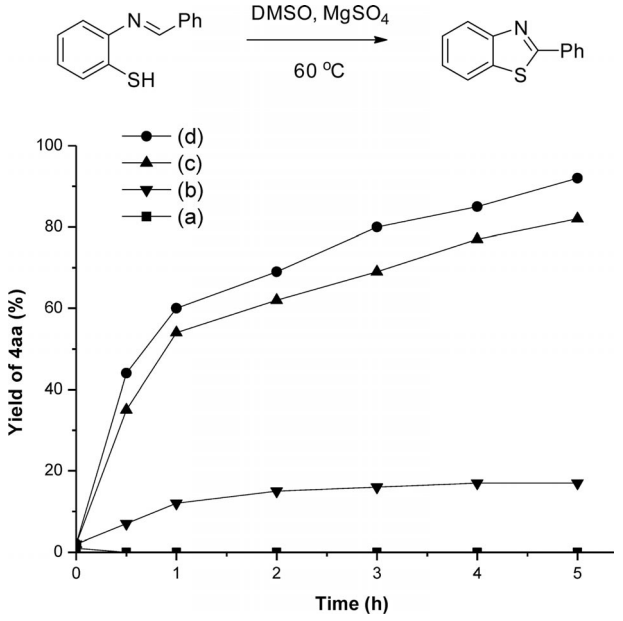


Figure 1. Synthesis of benzothiazole from 2-(benzylidenamino)-benzenethiol. Reaction conditions: **B** (1.0 mmol) was treated in the presence of $MgSO_4$ (2.0 mmol) in DMSO at 60 °C under the following conditions: a) in the absence of CuCl and $NaSH{\cdot}nH_2O$ under N_2, b) CuCl (0.02 mmol) was added in the absence of $NaSH{\cdot}nH_2O$ under N_2, c) $NaSH{\cdot}nH_2O$ (1.0 mmol) was added in the absence of CuCl under N_2, and d) CuCl (0.02 mmol) and $NaSH{\cdot}nH_2O$ (1.0 mmol) were added under air.

No benzothiazole was formed in the absence of the copper catalyst and $NaSH{\cdot}nH_2O$ under nitrogen; see Figure 1 (a). Benzothiazole was formed in good yield when 2-(benzylidenamino)benzenethiol (**B**) was treated with $NaSH{\cdot}nH_2O$ in the absence of the copper catalyst under nitrogen; see Figure 1 (c). However, the yield was very low when the reaction was conducted with only the copper catalyst in the absence of $NaSH{\cdot}nH_2O$ under nitrogen; see Figure 1 (b). When the optimized conditions, with use of the copper catalyst, $NaSH{\cdot}nH_2O$, and air, were employed in this reaction, the yield of the product was the highest; see Figure 1 (d). However, we failed to detect the intermediate **C** in any of the reaction mixtures. From these results we inferred that $NaSH{\cdot}nH_2O$ acts not only as a sulfur source, but also as an oxidant, and that the role of the copper catalyst in the cyclization and oxidation reactions is marginal. Although 2-(benzylidenamino)benzenethiol (**B**) produced the desired benzothiazole in 92% yield at 60 °C, this three-component reaction of 2-iodoaniline, benzaldehyde, and $NaSH{\cdot}nH_2O$ required a temperature of 110 °C to produce a high yield of the product, as shown in Figure 2. Unsatisfactory yields were obtained when the reaction was conducted at 60 °C.

To study the possible existence of another reaction pathway in which $NaSH{\cdot}nH_2O$ attacks at the carbon of the imine in *N*-benzylidene-2-iodoaniline (**A**) and then produces the benzothiazole, we carried out trapping experiments to investigate reaction mixtures in which *N*-benzylidenaniline and $NaSH{\cdot}nH_2O$ were allowed to react in the presence of

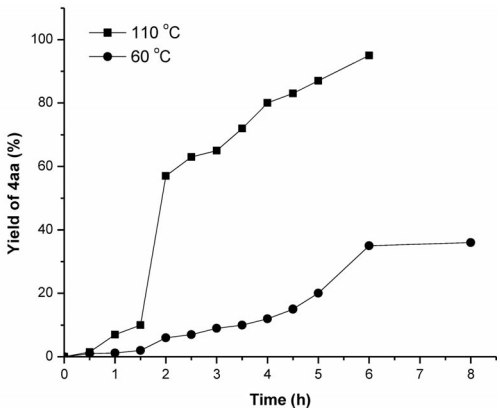


Figure 2. Reaction yields of **4aa** at 110 °C and 60 °C. Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol), **3** (0.6 mmol), and CuCl (0.006 mmol) in the presence of $MgSO_4$ (0.6 mmol) in DMSO.

copper. However, no related structures such as the aminothiol and thioamide were found in the reaction mixture. These results support the proposed reaction pathway shown in Scheme 2. It was found that the rate-determining step is step (ii), because it required a higher temperature than the other steps.

Conclusions

In summary, a copper-based catalytic system has been developed and successfully applied to one-pot syntheses of benzothiazoles from 2-iodoanilines, aldehydes, and $NaSH{\cdot}nH_2O$. This one-pot reaction system represents a significant advantage in not requiring the isolation of the intermediate prior to execution of C–S bond formation and in most instances does not require the preparation of the starting materials. To the best of our knowledge, this is the first example of the employment of $NaSH{\cdot}nH_2O$ as a sulfur source, not only in the synthesis of the benzothiazole, but also in transition-metal-catalyzed C–S bond formation. In addition, the employment of $NaSH{\cdot}nH_2O$ offered economic and environmental advantages, due to its low cost and odor-free nature. From mechanistic studies, we found the following: 1) copper is the crucial factor in the formation of the iminothiol from the reaction between the aryl iodide and $NaSH{\cdot}nH_2O$, 2) reaction step (ii) requires higher temperatures than reaction steps (iii) and (iv), and 3) $NaSH{\cdot}nH_2O$ accelerated the rates of reaction steps (iii) and (iv).

Experimental Section

General Procedure for the Synthesis of Benzothiazoles from 2-Iodoaniline: CuCl (14.9 mg, 0.15 mmol), $NaSH{\cdot}nH_2O$ (60 wt.-%, 560.6 mg, 6.00 mmol), 2-iodoaniline (3.00 mmol), benzaldehyde (3.00 mmol), and $MgSO_4$ (1083.3 mg, 9.00 mmol) were placed in a small round-bottomed flask. DMSO (10.0 mL) was added and the reaction mixture was stirred for 6 h at 110 °C under air and then allowed to cool to room temperature. The reaction mixture was poured into distilled water (10 mL) and extracted with Et_2O

(3 × 15 mL). The combined ether extracts were washed with brine (40 mL), dried with $MgSO_4$, and passed through celite. The solvent was removed under vacuum and the resulting crude product was purified by flash chromatography on silica gel (eluent hexane).

2-Phenylbenzothiazole (4aa):[27] Table 2, Entry 1. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with benzaldehyde (**2a**, 318 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4aa** (627 mg, 2.97 mmol, 99%) as a white solid after chromatography; m.p. 97–99 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.18–8.03 (m, 3 H), 7.90 (dd, J = 4.6, 4.0 Hz, 1 H), 7.58–7.43 (m, 4 H), 7.40 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.2, 154.2, 135.1, 133.7, 131.1, 129.1, 127.6, 126.4, 125.3, 123.3, 121.7 ppm. HRMS (FAB) calcd. for $C_{13}H_{10}NS$ [M + H]$^+$ 212.0528; found 212.0533.

2-(3-Fluorophenyl)benzothiazole (4ab):[28] Table 2, Entry 2. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with 3-fluorobenzaldehyde (**2b**, 372 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ab** (673 mg, 2.94 mmol, 98%) as a yellow solid after chromatography; m.p. 85–87 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09 (ddd, J = 8.2, 1.2, 0.6 Hz, 1 H), 7.90 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.86–7.82 (m, 2 H), 7.55–7.36 (m, 3 H), 7.18 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5 (d, J = 3.1 Hz), 163.1 (d, J = 245.6 Hz), 154.0, 135.7 (d, J = 7.9 Hz), 135.1, 130.7 (d, J = 8.2 Hz), 126.6, 125.6, 123.5, 123.4 (d, J = 2.7 Hz), 121.7, 117.9 (d, J = 21.2 Hz), 114.4 (d, J = 23.4 Hz) ppm. EI-MS: m/z = 229 (100) [M]$^+$, 108 (50), 82 (30), 69 (40).

2-(Benzothiazol-2-yl)aniline (4ac):[29] Table 2, Entry 3. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with 2-nitrobenzaldehyde (**2c**, 453 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ac** (556 mg, 2.46 mmol, 82%) as a yellow solid after chromatography; m.p. 120–122 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99 (ddd, J = 8.1, 1.2, 0.6 Hz, 1 H), 7.88 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.72 (ddd, J = 7.8, 1.5, 0.3 Hz, 1 H), 7.46 (m, 1 H), 7.36 (ddd, J = 7.9, 7.3, 1.2 Hz, 1 H), 7.24 (m, 1 H), 6.83–6.71 (m, 2 H), 6.42 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3, 153.8, 146.8, 133.3, 131.6, 130.4, 126.1, 124.9, 122.5, 121.2, 116.9, 116.8, 115.3 ppm. HRMS (FAB) calcd. for $C_{13}H_{11}N_2S$ [M + H]$^+$ 227.0643; found 227.0642.

2-*o*-Tolylbenzothiazole (4ad):[27] Table 2, Entry 4. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with *o*-tolualdehyde (**2d**, 360 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ad** (635 mg, 2.82 mmol, 94%) as a brown oil after chromatography. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (ddd, J = 8.2, 1.2, 0.6 Hz, 1 H), 7.94 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.76 (d, J = 7.7 Hz, 1 H), 7.41 (m, 1 H), 7.45–7.32 (m, 4 H), 2.67 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.1, 153.9, 137.3, 135.7, 133.2, 131.6, 130.6, 130.1, 126.2 (2 C), 125.2, 123.5, 121.5, 21.48 ppm. EI-MS: m/z = 225 [M]$^+$ (90), 224 (100), 223 (20), 116 (13), 108 (10), 89 (20), 82 (15), 69 (30), 51 (10).

2-*p*-Tolylbenzothiazole (4ae):[27] Table 2, Entry 5. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with *p*-tolualdehyde (**2e**, 360 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ae** (662 mg, 2.94 mmol, 98%) as a brown solid after chromatography; m.p. 86–88 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (ddd, J = 8.2, 1.2, 0.6 Hz, 1 H), 8.01–7.97 (m, 2 H), 7.88 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.49 (m, 1 H), 7.37 (ddd, J = 8.0, 7.2, 1.2 Hz, 1 H), 7.31–7.27 (m, 2 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.2, 154.2, 141.4, 135.0, 131.0, 129.7, 127.5, 126.3, 125.0, 123.1, 121.6, 21.5 ppm. EI-MS: m/z = 225 (100) [M]$^+$, 116 (13), 108 (20), 89 (14), 82 (17), 69 (25).

2-(4-Methoxyphenyl)benzothiazole (4af):[27] Table 2, Entry 6. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with 4-methoxybenzaldehyde (**2f**, 408 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4af** (687 mg, 2.85 mmol, 95%) as an apricot solid after chromatography; m.p. 114–116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09–7.98 (m, 3 H), 7.87 (dd, J = 7.9, 0.6 Hz, 1 H), 7.47 (ddd, J = 8.3, 7.3, 1.3 Hz, 1 H), 7.30 (m, 1 H), 7.04–6.95 (m, 2 H), 3.87 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.9, 162.0, 154.3, 134.9, 129.2, 126.5, 126.3, 124.9, 122.9, 121.6, 114.4, 55.5 ppm. EI-MS: m/z = 241 (100) [M]$^+$, 226 (33), 198 (31), 108 (10), 69 (20).

2-[4-(Methylthio)phenyl]benzothiazole (4ag): Table 2, Entry 7. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with 4-(methylthio)benzaldehyde (**2g**, 457 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ag** (617 mg, 2.40 mmol, 80%) as a light apricot solid after chromatography; m.p. 142–144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05 (ddd, J = 8.2, 1.2, 0.6 Hz, 1 H), 8.02–7.94 (m, 2 H), 7.86 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.47 (m, 1 H), 7.36 (ddd, J = 8.0, 7.2, 1.2 Hz, 1 H), 7.33–7.27 (m, 2 H), 2.52 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.6, 154.2, 142.8, 134.9, 130.1, 127.8, 126.3, 125.9, 125.1, 123.0, 121.6, 15.2 ppm. HRMS (FAB) calcd. for $C_{14}H_{12}NS_2$ [M + H]$^+$ 258.0411; found 258.0411.

4-(Benzothiazol-2-yl)-*N*,*N*-dimethylaniline (4ah):[30] Table 2, Entry 8. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with 4-(dimethylamino)benzaldehyde (**2h**, 537 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ah** (694 mg, 2.73 mmol, 91%) as a yellow solid after chromatography; m.p. 161–163 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01–7.93 (m, 3 H), 7.84 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.44 (m, 1 H), 7.30 (ddd, J = 7.9, 7.3, 1.2 Hz, 1 H), 6.79–6.71 (m, 2 H), 3.08–3.04 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9, 154.5, 152.3, 134.6, 128.9, 126.1, 124.3, 122.3, 121.4, 111.8, 40.3 ppm. EI-MS: m/z = 254 (100) [M]$^+$, 238 (20), 145 (20), 127 (21), 108 (20), 69 (20).

2-(Thiophen-2-yl)benzothiazole (4ai):[31] Table 2, Entry 9. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with thiophene-2-carbaldehyde (**2i**, 336 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ai** (586 mg, 2.70 mmol, 90%) as a dark brown solid after chromatography; m.p. 92–94 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04 (ddd, J = 8.2, 1.2, 0.6 Hz, 1 H), 7.85 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.65 (dd, J = 3.7, 1.1 Hz, 1 H), 7.52–7.45 (m, 2 H), 7.37 (ddd, J = 8.0, 7.3, 1.2 Hz, 1 H), 7.13 (dd, J = 5.1, 3.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.4, 153.7, 137.4, 134.7, 129.4, 128.7, 128.1, 126.5, 125.3, 123.0, 121.5 ppm. EI-MS: m/z = 217 (100) [M]$^+$, 108 (40), 82 (25), 69 (49).

2-(Pyridin-2-yl)benzothiazole (4aj):[27] Table 2, Entry 10. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with pyridine-2-carbaldehyde (**2j**, 321 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4aj** (534 mg, 2.52 mmol, 84%) as a yellow solid after chromatography; m.p. 126–128 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.67 (ddd, J = 4.8, 1.7, 0.9 Hz, 1 H), 8.36 (dt, J = 7.9, 1.1 Hz, 1 H), 8.09 (ddd, J = 8.2, 1.2, 0.6 Hz, 1 H), 7.95 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.82 (td, J = 7.7, 1.7 Hz, 1 H), 7.50 (m, 1 H), 7.43–7.32 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4, 154.3, 151.4, 149.7, 137.0, 136.1, 126.3, 125.7, 125.3, 123.6, 122.1, 120.8 ppm. EI-MS: m/z = 212 (100) [M]$^+$, 108 (21), 78 (22), 69 (30), 51 (25).

2-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)benzothiazole (4ak): Table 2, Entry 11. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with 1,4-benzodioxan-6-carbaldehyde (**2k**, 492 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ak** (622 mg, 2.31 mmol, 77%) as a light brown solid after chromatography; m.p.

121–123 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (ddd, J = 8.2, 1.1, 0.6 Hz, 1 H), 7.86 (ddd, J = 7.9, 1.2, 0.6 Hz, 1 H), 7.65–7.56 (m, 2 H), 7.46 (ddd, J = 8.2, 7.3, 1.3 Hz, 1 H), 7.34 (ddd, J = 8.1, 7.3, 1.2 Hz, 1 H), 6.96 (d, J = 8.4 Hz, 1 H), 4.30 (s, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.6, 154.2, 146.2, 143.9, 135.0, 127.3, 126.2, 124.9, 122.9, 121.5, 121.1, 117.8, 116.6, 64.6, 64.3 ppm. HRMS (FAB) calcd. for $C_{15}H_{12}NO_2S$ [M + H]$^+$ 270.0589; found 270.0590.

2-(Benzo[*d*][1,3]dioxol-5-yl)benzothiazole (4al):[32] Table 2, Entry 12. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with piperonal (**2l**, 450 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4al** (742 mg, 2.91 mmol, 97%) as a light yellow solid after chromatography; m.p. 179–181 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (ddd, J = 8.2, 1.2, 0.6 Hz, 1 H), 7.87 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.62–7.58 (m, 2 H), 7.48 (m, 1 H), 7.36 (m, 1 H), 6.91 (dd, J = 7.8, 0.7 Hz, 1 H), 6.06 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.6, 154.1, 150.2, 148.5, 134.9, 128.1, 126.4, 125.1, 123.0, 122.6, 121.6, 108.8, 107.6, 101.8 ppm. EI-MS: m/z = 255 (100) [M]$^+$, 196 (20), 108 (30), 82 (20), 69 (20).

2-(6-Methoxynaphthalen-2-yl)benzothiazole (4am): Table 2, Entry 13. 2-Iodoaniline (**1a**, 657 mg, 3.00 mmol) was coupled with 6-methoxy-2-naphthaldehyde (**2m**, 559 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4am** (795 mg, 2.73 mmol, 91%) as a yellow solid after chromatography; m.p. 141–143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.49 (d, J = 1.3 Hz, 1 H), 8.17 (dd, J = 8.6, 1.9 Hz, 1 H), 8.09 (ddd, J = 8.2, 1.2, 0.6 Hz, 1 H), 7.92 (ddd, J = 7.9, 1.3, 0.6 Hz, 1 H), 7.85 (t, J = 9.3 Hz, 2 H), 7.50 (ddd, J = 7.9, 7.2, 1.2 Hz, 1 H), 7.39 (ddd, J = 7.9, 7.2, 1.2 Hz, 1 H), 7.24–7.16 (m, 2 H), 3.95 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.4, 159.1, 154.4, 136.2, 135.1, 130.5, 129.0, 128.7, 127.6, 127.5, 126.4, 125.1, 123.1, 121.7 (2 C), 119.9, 106.0, 55.5 ppm. HRMS (FAB) calcd. for $C_{18}H_{14}NOS$ [M + H]$^+$ 292.0796; found 292.0793.

5-Chloro-2-phenylbenzothiazole (4ba):[33] Table 3, Entry 1. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with benzaldehyde (**2a**, 318 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ba** (698 mg, 2.85 mmol, 95%) as a yellow solid after chromatography; m.p. 135–137 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11–8.03 (m, 3 H), 7.81 (dd, J = 8.4, 0.3 Hz, 1 H), 7.54–7.46 (m, 3 H), 7.36 (dd, J = 8.5, 2.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.0, 155.1, 133.4, 133.3, 132.4, 131.4, 129.2, 127.7, 125.7, 123.1, 122.4 ppm. EI-MS: m/z = 247 (35) [M + 2]$^+$, 245 (100) [M]$^+$, 142 (30), 107 (30), 63 (30).

5-Chloro-2-(3-fluorophenyl)benzothiazole (4bb): Table 3, Entry 2. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with 3-fluorobenzaldehyde (**2b**, 372 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4bb** (686 mg, 2.61 mmol, 87%) as a white solid after chromatography; m.p. 143–145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, J = 2.0 Hz, 1 H), 7.82–7.75 (m, 3 H), 7.45 (m, 1 H), 7.36 (dd, J = 8.5, 2.0 Hz, 1 H), 7.19 (tdd, J = 8.3, 2.5, 1.0 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.3 (d, J = 2.9 Hz), 163.1 (d, J = 246.1 Hz), 154.8, 135.3 (d, J = 7.9 Hz), 133.3, 132.6, 130.8 (d, J = 8.2 Hz), 126.0, 123.4 (d, J = 2.8 Hz), 123.3, 122.4, 118.2 (d, J = 21.2 Hz), 114.4 (d, J = 23.4 Hz) ppm. HRMS (FAB) calcd. for $C_{13}H_8ClFNS$ [M + H]$^+$ 264.0050; found 264.0047.

5-Chloro-2-(4-methoxyphenyl)benzothiazole (4bf):[34] Table 3, Entry 3. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with 4-methoxybenzaldehyde (**2f**, 408 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4bf** (701 mg, 2.55 mmol, 85%) as a yellowish solid after chromatography; m.p. 150–152 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04–7.95 (m, 3 H), 7.75 (d, J = 8.5 Hz, 1 H), 7.31 (dd, J = 8.5, 2.0 Hz, 1 H), 7.03–6.93 (m, 2 H), 3.88 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.8, 162.3, 155.2, 133.2, 132.2, 129.3, 126.1, 125.2, 122.7, 122.2, 114.5, 55.5 ppm. EI-MS: m/z = 277 (35) [M + 2]$^+$, 275 (100) [M]$^+$, 260 (30), 232 (30), 196 (16), 107 (20), 63 (35).

5-Chloro-2-[4-(methylthio)phenyl]benzothiazole (4bg): Table 3, Entry 4. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with 4-(methylthio)benzaldehyde (**2g**, 457 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4bg** (786 mg, 2.70 mmol, 90%) as a yellow solid after chromatography; m.p. 159–161 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (dd, J = 2.0, 0.4 Hz, 1 H), 8.00–7.93 (m, 2 H), 7.78 (dd, J = 8.5, 0.5 Hz, 1 H), 7.36–7.31 (m, 2 H), 7.30 (m, 1 H), 2.54 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5, 155.1, 143.5, 133.2, 132.4, 129.8, 127.9, 126.0, 125.6, 122.9, 122.3, 15.2 ppm. HRMS (FAB) calcd. for $C_{14}H_{11}ClNS_2$ [M + H]$^+$ 292.0021; found 292.0020.

4-(5-Chlorobenzothiazol-2-yl)-*N*,*N*-dimethylaniline (4bh): Table 3, Entry 5. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with 4-(dimethylamino)benzaldehyde (**2h**, 537 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4bh** (735 mg, 2.55 mmol, 85%) as a dark yellow solid after chromatography; m.p. 150–152 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.94 (m, 2 H), 7.91 (m, 1 H), 7.73 (d, J = 8.5 Hz, 1 H), 7.27 (dd, J = 8.5, 2.0 Hz, 2 H), 6.74 (d, J = 9.0 Hz, 2 H), 3.06 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7, 155.4, 152.5, 132.9, 132.0, 129.1, 124.6, 122.19, 122.1, 121.0, 111.7, 40.3 ppm. HRMS (FAB) calcd. for $C_{15}H_{14}ClN_2S$ [M + H]$^+$ 289.0566; found 289.0569.

5-Chloro-2-(thiophen-2-yl)benzothiazole (4bi):[35] Table 3, Entry 6. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with thiophene-2-carbaldehyde (**2i**, 336 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4bi** (489 mg, 1.95 mmol, 65%) as a brown solid after chromatography; m.p. 99–101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99 (dd, J = 2.0, 0.5 Hz, 1 H), 7.72 (dd, J = 8.5, 0.5 Hz, 1 H), 7.64 (dd, J = 3.7, 1.2 Hz, 1 H), 7.52 (dd, J = 5.1, 1.2 Hz, 1 H), 7.32 (dd, J = 8.5, 2.0 Hz, 1 H), 7.13 (dd, J = 5.1, 3.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.2, 154.6, 137.0, 133.0, 132.5, 129.9, 129.1, 128.2, 125.7, 122.8, 122.2 ppm. EI-MS: m/z = 253 (35) [M + 2]$^+$, 251 (100) [M]$^+$, 142 (29), 107 (31), 63 (32).

5-Chloro-2-(pyridin-2-yl)benzothiazole (4bj): Table 3, Entry 7. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with pyridine-2-carbaldehyde (**2j**, 321 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4bj** (576 mg, 2.34 mmol, 78%) as a yellow solid after chromatography; m.p. 154–157 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.69 (ddd, J = 4.8, 1.7, 0.9 Hz, 1 H), 8.36 (dt, J = 7.9, 1.1 Hz, 1 H), 8.07 (d, J = 2.0 Hz, 1 H), 7.90–7.84 (m, 2 H), 7.45–7.37 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.4, 155.2, 151.1, 149.8, 137.2, 134.5, 132.4, 126.2, 125.7, 123.4, 122.8, 121.0 ppm. HRMS (FAB) calcd. for $C_{12}H_8ClN_2S$ [M + H]$^+$ 247.0097; found 247.0097.

5-Chloro-2-(pyridin-2-yl)benzothiazole (4bk): Table 3, Entry 8. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with 1,4-benzodioxan-6-carbaldehyde (**2k**, 492 mg, 3.00 mmol) and NaSH·nH$_2$O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4bk** (645 mg, 2.13 mmol, 71%) as a yellow solid after chromatography; m.p. 139–141 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99 (dd, J = 1.8, 0.4 Hz, 1 H), 7.75 (dd, J = 8.5, 0.4 Hz, 1 H), 7.61–7.53 (m, 2 H), 7.31 (dd, J = 8.5, 2.0 Hz, 1 H), 6.95 (d, J = 8.4 Hz, 1 H), 4.33–4.28 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5, 155.1, 146.6, 143.9, 133.3, 132.2, 126.9, 125.3, 122.8, 122.2, 121.2, 117.9, 116.7,

64.7, 64.3 ppm. HRMS (FAB) calcd. for $C_{15}H_{11}ClNO_2S$ [M + H]$^+$ 304.0199; found 304.0197.

2-(Benzo[*d*][1,3]dioxol-5-yl)-5-chlorobenzothiazole (4bl):[36] Table 3, Entry 9. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with piperonal (**2l**, 450 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4bl** (650 mg, 2.25 mmol, 75%) as a yellow solid after chromatography; m.p. 172–174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99 (dd, J = 2.0, 0.4 Hz, 1 H), 7.76 (dd, J = 8.5, 0.4 Hz, 1 H), 7.58–7.55 (m, 2 H), 7.32 (dd, J = 8.5, 2.0 Hz, 1 H), 6.89 (m, 1 H), 6.06 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5, 155.0, 150.5, 148.5, 133.2, 132.3, 127.7, 125.4, 122.8, 122.8, 122.2, 108.8, 107.6, 101.9 ppm. EI-MS: *m*/*z* = 291 (35) [M + 2]$^+$, 289 (100) [M]$^+$, 196 (25), 144 (12), 107 (19), 63 (31).

5-Chloro-2-(6-methoxynaphthalen-2-yl)benzothiazole (4bm): Table 3, Entry 10. 5-Chloro-2-iodoaniline (**1b**, 759 mg, 3.00 mmol) was coupled with 6-methoxy-2-naphthaldehyde (**2m**, 559 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4bm** (878 mg, 2.70 mmol, 90%) as a yellow solid after chromatography; m.p. 205–207 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.46 (d, J = 1.3 Hz, 1 H), 8.13 (dd, J = 8.6, 1.9 Hz, 1 H), 8.06 (dd, J = 2.1, 0.3 Hz, 1 H), 7.89–7.79 (m, 3 H), 7.36 (dd, J = 8.5, 2.0 Hz, 1 H), 7.25–7.15 (m, 2 H), 3.96 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 159.2, 155.2, 136.4, 133.3 (2 C), 132.4 (2 C), 130.5, 128.6, 127.7, 125.6, 125.0, 122.9, 122.4, 120.0, 106.0, 55.5 ppm. HRMS (FAB) calcd. for $C_{18}H_{13}NOSCl$ [M + H]$^+$ 326.0406; found 326.0406.

6-Fluoro-2-(4-methoxyphenyl)benzothiazole (4cf):[32] Table 3, Entry 11. 4-Fluoro-2-iodoaniline (**1c**, 710 mg, 3.00 mmol) was coupled with 4-methoxybenzaldehyde (**2f**, 408 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4cf** (707 mg, 2.73 mmol, 91%) as light yellow solid after chromatography; m.p. 126–128 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99–7.91 (m, 3 H), 7.51 (m, 1 H), 7.18 (td, J = 8.9, 2.6 Hz, 1 H), 6.97 (d, J = 9.0 Hz, 2 H), 3.89 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.6 (d, J = 2.9 Hz), 162.0, 160.3 (d, J = 245.4 Hz), 150.9, 135.8 (d, J = 11.2 Hz), 129.0, 126.2, 123.7 (d, J = 9.3 Hz), 114.7 (d, J = 24.5 Hz), 114.4, 107.8 (d, J = 26.8 Hz), 55.5 ppm. HRMS (FAB) calcd. for $C_{14}H_{11}FNOS$ [M + H]$^+$ 260.0545; found 260.0543.

4-(6-Fluorobenzothiazol-2-yl)-*N*,*N*-dimethylaniline (4ch): Table 3, Entry 12. 4-Fluoro-2-iodoaniline (**1c**, 710 mg, 3.00 mmol) was coupled with 4-(dimethylamino)benzaldehyde (**2h**, 537 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ch** (596 mg, 2.19 mmol, 73%) as a brown solid after chromatography; m.p. 199–201 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.94–7.86 (m, 3 H), 7.50 (m, 1 H), 7.16 (td, J = 9.0, 2.6 Hz, 1 H), 6.73 (d, J = 9.1 Hz, 2 H), 3.05 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.6 (d, J = 2.9 Hz), 160.0 (d, J = 244.0 Hz), 152.2, 151.1, 135.6 (d, J = 11.2 Hz), 128.8, 123.0 (d, J = 9.2 Hz), 121.2, 114.4 (d, J = 24.5 Hz), 111.8, 107.7 (d, J = 26.5 Hz), 40.2 ppm. HRMS (FAB) calcd. for $C_{15}H_{14}FN_2S$ [M + H]$^+$ 27.30862; found 273.0865.

6-Fluoro-2-(thiophen-2-yl)benzothiazole (4ci): Table 3, Entry 13. 4-Fluoro-2-iodoaniline (**1c**, 710 mg, 3.00 mmol) was coupled with thiophene-2-carbaldehyde (**2i**, 336 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ci** (508 mg, 2.16 mmol, 72%) as a light yellow solid after chromatography; m.p. 156–158 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96 (dd, J = 9.0, 4.7 Hz, 1 H), 7.62 (dd, J = 3.7, 1.1 Hz, 1 H), 7.56–7.48 (m, 2 H), 7.20 (td, J = 8.9, 2.6 Hz, 1 H), 7.14 (dd, J = 5.1, 3.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2 (d, J = 0.6 Hz), 160.6 (d, J = 246.1 Hz), 150.4, 137.1, 135.8 (d, J = 11.2 Hz), 129.5, 128.7, 128.2, 123.9 (d, J = 9.4 Hz), 115.1 (d, J = 24.6 Hz), 107.9 (d, J = 26.9 Hz) ppm. HRMS (FAB) calcd. for $C_{11}H_7FNS_2$ [M + H]$^+$ 236.0004; found 236.0004.

6-Fluoro-2-(pyridin-2-yl)benzothiazole (4cj): Table 3, Entry 14. 4-Fluoro-2-iodoaniline (**1c**, 710 mg, 3.00 mmol) was coupled with pyridine-2-carbaldehyde (**2j**, 321 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4cj** (649 mg, 2.82 mmol, 94%) as a light yellow solid after chromatography; m.p. 150–152 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65 (ddd, J = 4.8, 1.7, 1.0 Hz, 1 H), 8.29 (dt, J = 7.9, 1.1 Hz, 1 H), 7.99 (m, 1 H), 7.81 (m, 1 H), 7.59 (m, 1 H), 7.35 (ddd, J = 7.6, 4.8, 1.2 Hz, 1 H), 7.21 (td, J = 8.9, 2.6 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2 (d, J = 3.7 Hz), 160.8 (d, J = 246.6 Hz), 151.1, 151.0, 149.7, 137.3 (d, J = 11.3 Hz), 137.1, 125.3, 124.6 (d, J = 9.5 Hz), 120.6, 115.1 (d, J = 24.9 Hz), 108.2 (d, J = 26.7 Hz) ppm. HRMS (FAB) calcd. for $C_{12}H_8FN_2S$ [M + H]$^+$ 231.0392; found 231.0394.

4,6-Dichloro-2-[4-(methylthio)phenyl]benzothiazole (4dg): Table 3, Entry 15. 2,4-Dichloro-6-iodoaniline (**1d**, 860 mg, 3.00 mmol) was coupled with 4-(methylthio)benzaldehyde (**2g**, 457 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4dg** (634 mg, 1.95 mmol, 65%) as a white solid after chromatography; m.p. 170–172 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.8 Hz, 2 H), 7.75 (d, J = 1.9 Hz, 1 H), 7.50 (d, J = 1.9 Hz, 1 H), 7.31 (d, J = 8.8 Hz, 2 H), 2.55 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.8, 150.0, 143.9, 137.0, 130.8, 129.3, 128.3, 128.1, 127.2, 125.9, 119.9, 15.2 ppm. HRMS (FAB) calcd. for $C_{14}H_{10}Cl_2NS_2$ [M + H]$^+$ 325.9632; found 325.9635.

4-(6-Chloro-4-fluorobenzothiazol-2-yl)-*N*,*N*-dimethylaniline (4eh): Table 3, Entry 16. 4-Chloro-2-fluoro-6-iodoaniline (**1e**, 813 mg, 3.00 mmol) was coupled with 4-(dimethylamino)benzaldehyde (**2h**, 537 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4eh** (595 mg, 1.83 mmol, 61%) as a yellow solid after chromatography; m.p. 193–195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, J = 9.1 Hz, 2 H), 7.59 (dd, J = 1.9, 0.9 Hz, 1 H), 7.16 (dd, J = 10.1, 1.9 Hz, 1 H), 6.73 (d, J = 9.1 Hz, 2 H), 3.07 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.8, 154.6 (d, J = 258.7 Hz), 152.6, 143.6 (d, J = 210.9 Hz), 137.9 (d, J = 4.7 Hz), 129.7 (d, J = 8.9 Hz), 129.3, 120.6, 117.0 (d, J = 4.2 Hz), 113.4 (d, J = 21.8 Hz), 111.7, 40.3 ppm. HRMS (FAB) calcd. for $C_{15}H_{13}ClFN_2S$ [M + H]$^+$ 307.0472; found 307.0472.

2-Phenyl-6-(trifluoromethyl)benzothiazole (4fa):[37] Table 3, Entry 17. 2-Iodo-4-(trifluoromethyl)aniline (**1f**, 861 mg, 3.00 mmol) was coupled with benzaldehyde (**2a**, 318 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4fa** (812 mg, 2.91 mmol, 97%) as a white solid after chromatography; m.p. 152–154 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (m, 1 H), 8.13 (d, J = 8.6 Hz, 1 H), 8.11–8.06 (m, 2 H), 7.72 (m, 1 H), 7.56–7.46 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.2, 156.1, 135.2, 133.1, 131.7, 129.2, 127.8, 127.3 (q, J = 53.9 Hz), 124.3 (q, J = 272.3 Hz), 123.6, 123.4 (q, J = 3.3 Hz), 119.4 (q, J = 4.2 Hz) ppm. EI-MS: *m*/*z* = 279 (100) [M]$^+$, 157 (25), 132 (20), 63 (20), 51 (15).

2-(4-Methoxyphenyl)-6-(trifluoromethyl)benzothiazole (4ff):[37] Table 3, Entry 18. 2-Iodo-4-(trifluoromethyl)aniline (**1f**, 861 mg, 3.00 mmol) was coupled with 4-methoxybenzaldehyde (**2f**, 408 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4ff** (705 mg, 2.28 mmol, 76%) as a white solid after chromatography; m.p. 157–159 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15 (m, 1 H), 8.09 (m, 1 H), 8.04 (d, J = 9.0 Hz, 2 H), 7.70 (ddd, J = 8.6, 1.8, 0.6 Hz, 1 H), 7.01 (d, J = 9.0 Hz, 2 H), 3.89 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.0, 162.6, 156.3, 135.0, 129.5, 126.9 (q, J = 32.5 Hz), 125.9, 124.3 (q, J = 272.0 Hz), 123.3 (q, J = 3.5 Hz), 123.1, 119.2 (q, J = 4.1 Hz), 114.6, 55.6 ppm. EI-MS: *m*/*z* = 309 (100) [M]$^+$, 294 (30), 266 (50), 63 (20).

2-[4-(Methylthio)phenyl]-6-(trifluoromethyl)benzothiazole (4fg): Table 3, Entry 19. 2-Iodo-4-(trifluoromethyl)aniline (**1f**, 861 mg, 3.00 mmol) was coupled with 4-(methylthio)benzaldehyde (**2g**, 457 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4fg** (692 mg, 2.13 mmol, 71%) as a light yellow solid after chromatography; m.p. 172–174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (m, 1 H), 8.11 (m, 1 H), 8.00 (d, J = 8.8 Hz, 2 H), 7.71 (ddd, J = 8.6, 1.8, 0.6 Hz, 1 H), 7.33 (d, J = 8.8 Hz, 2 H), 2.55 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7, 156.2, 144.0, 135.0, 129.5, 128.0, 127.2 (q, J = 32.8 Hz), 126.0, 124.3 (q, J = 272.3 Hz), 123.4 (q, J = 3.4 Hz), 123.3, 119.3 (q, J = 4.2 Hz), 15.1 ppm. HRMS (FAB) calcd. for $C_{15}H_{11}F_3NS_2$ [M + H]$^+$ 326.0285; found 326.0282.

***N*,*N*-Dimethyl-4-[6-(trifluoromethyl)benzothiazol-2-yl]aniline (4fh):** Table 3, Entry 20. 2-Iodo-4-(trifluoromethyl)aniline (**1f**, 861 mg, 3.00 mmol) was coupled with 4-(dimethylamino)benzaldehyde (**2h**, 537 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4fh** (870 mg, 2.70 mmol, 90%) as a yellow solid after chromatography; m.p. 196–198 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (m, 1 H), 8.03 (m, 1 H), 7.96 (d, J = 9.1 Hz, 2 H), 7.66 (ddd, J = 8.6, 1.9, 0.6 Hz, 1 H), 6.74 (d, J = 9.1 Hz, 2 H), 3.07 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.9, 156.6, 152.7, 134.7, 131.0, 129.3, 127.6 (q, J = 199.2 Hz), 126.2 (q, J = 32.0 Hz), 123.1 (q, J = 3.1 Hz), 122.4, 120.7, 119.0 (q, J = 3.5 Hz), 111.7, 40.2 ppm. HRMS (FAB) calcd. for $C_{16}H_{14}F_3N_2S$ [M + H]$^+$ 323.0830; found 323.0833.

2-(Thiophen-2-yl)-6-(trifluoromethyl)benzothiazole (4fi): Table 3, Entry 21. 2-Iodo-4-(trifluoromethyl)aniline (**1f**, 861 mg, 3.00 mmol) was coupled with thiophene-2-carbaldehyde (**2i**, 336 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4fi** (667 mg, 2.34 mmol, 78%) as a white solid after chromatography; m.p. 153–155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14 (m, 1 H), 8.09 (d, J = 8.6 Hz, 1 H), 7.75–7.67 (m, 2 H), 7.57 (dd, J = 5.0, 1.1 Hz, 1 H), 7.17 (dd, J = 5.0, 3.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.4, 155.8, 136.8, 134.9, 130.5, 129.7, 128.4, 127.4 (q, J = 32.3 Hz), 124.2 (q, J = 271.4 Hz), 123.6 (q, J = 3.5 Hz), 123.3, 119.2 (q, J = 4.2 Hz) ppm. HRMS (FAB) calcd. for $C_{12}H_7F_3NS_2$ [M + H]$^+$ 285.9972; found 285.9970.

2-(Pyridin-2-yl)-6-(trifluoromethyl)benzothiazole (4fj): Table 3, Entry 22. 2-Iodo-4-(trifluoromethyl)aniline (**1f**, 861 mg, 3.00 mmol) was coupled with pyridine-2-carbaldehyde (**2j**, 321 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4fj** (638 mg, 2.28 mmol, 76%) as a white solid after chromatography; m.p. 163–165 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.71 (ddd, J = 4.8, 1.7, 0.9 Hz, 1 H), 8.38 (dt, J = 7.9, 1.1 Hz, 1 H), 8.26 (m, 1 H), 8.17 (m, 1 H), 7.88 (td, J = 7.8, 1.8 Hz, 1 H), 7.74 (ddd, J = 8.6, 1.8, 0.5 Hz, 1 H), 7.43 (ddd, J = 7.6, 4.8, 1.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.7, 156.3, 150.9, 149.9, 137.3, 136.3, 127.8 (q, J = 32.5 Hz), 126.0, 124.3 (q, J = 271.8 Hz), 124.0, 123.3 (q, J = 3.2 Hz), 121.1, 119.8 (q, J = 4.2 Hz) ppm. HRMS (FAB) calcd. for $C_{13}H_9F_3N_2S$ [M + H]$^+$ 281.0360; found 281.0363.

2-(6-Methoxynaphthalen-2-yl)-6-(trifluoromethyl)benzothiazole (4fm): Table 3, Entry 23. 2-Iodo-4-(trifluoromethyl)aniline (**1f**, 861 mg, 3.00 mmol) was coupled with 6-methoxy-2-naphthaldehyde (**2m**, 559 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4fm** (862 mg, 2.40 mmol, 80%) as a light yellow solid after chromatography; m.p. 195–197 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.50 (d, J = 1.4 Hz, 1 H), 8.20 (d, J = 0.7 Hz, 1 H), 8.15 (dd, J = 8.5, 1.9 Hz, 2 H), 7.85 (t, J = 9.1 Hz, 2 H), 7.73 (dd, J = 8.6, 1.8 Hz, 1 H), 7.22 (dd, J = 8.9, 2.5 Hz, 1 H), 7.17 (d, J = 2.4 Hz, 1 H), 3.96 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.5, 159.4, 156.3, 136.6, 135.1, 130.6, 128.6, 128.4, 128.0, 127.8, 127.4 (q, J = 119.3 Hz), 127.2 (q, J = 33.4 Hz), 125.0, 123.4 (q, J = 3.2 Hz), 123.3, 120.1, 119.3 (q, J = 4.4 Hz), 106.0, 55.5 ppm. HRMS (FAB) calcd. for $C_{19}H_{13}F_3NOS$ [M + H]$^+$ 360.0670; found 360.0668.

2-(4-Methoxyphenyl)-4,6-dimethylbenzothiazole (4gf): Table 3, Entry 24. 2-Iodo-4,6-dimethylaniline (**1g**, 741 mg, 3.00 mmol) was coupled with 4-methoxybenzaldehyde (**2f**, 408 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4gf** (581 mg, 2.16 mmol, 72%) as a light yellow solid after chromatography; m.p. 141–143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, J = 9.0 Hz, 2 H), 7.48 (m, 1 H), 7.08 (m, 1 H), 6.99 (d, J = 9.0 Hz, 2 H), 3.88 (s, 3 H), 2.76 (s, 3 H), 2.44 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.4, 161.6, 151.8, 135.0, 134.8, 132.4, 129.0, 128.4, 127.1, 118.7, 114.3, 55.5, 21.6, 18.4 ppm. HRMS (FAB) calcd. for $C_{16}H_{16}NOS$ [M + H]$^+$ 270.0953; found 270.0952.

4-(4,6-Dimethylbenzothiazol-2-yl)-*N*,*N*-dimethylaniline (4gh): Table 3, Entry 25. 2-Iodo-4,6-dimethylaniline (**1g**, 741 mg, 3.00 mmol) was coupled with 4-(dimethylamino)benzaldehyde (**2h**, 537 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4gh** (601 mg, 2.13 mmol, 71%) as a brown solid after chromatography; m.p. 130–132 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96 (d, J = 9.0 Hz, 2 H), 7.46 (d, J = 0.6 Hz, 1 H), 7.05 (d, J = 0.6 Hz, 1 H), 6.74 (d, J = 8.9 Hz, 2 H), 3.05 (s, 6 H), 2.74 (s, 3 H), 2.43 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4, 152.0, 151.9, 134.7, 134.1, 131.9, 128.7, 128.2, 122.2, 118.7, 111.8, 40.3, 21.5, 18.4 ppm. HRMS (FAB) calcd. for $C_{17}H_{19}NS_2$ [M + H]$^+$ 283.1269; found 283.1269.

4,6-Dimethyl-2-(pyridin-2-yl)benzothiazole (4gj): Table 3, Entry 26. 2-Iodo-4,6-dimethylaniline (**1g**, 741 mg, 3.00 mmol) was coupled with pyridine-2-carbaldehyde (**2j**, 321 mg, 3.00 mmol) and NaSH·*n*H_2O (60 wt.-%, 560.6 mg, 6.00 mmol) to give **4fj** (562 mg, 2.34 mmol, 78%) as light yellow solid after chromatography; m.p. 120–122 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.67 (ddd, J = 4.9, 1.7, 0.9 Hz, 1 H), 8.40 (dt, J = 8.1, 1.2 Hz, 1 H), 7.81 (m, 1 H), 7.57 (m, 1 H), 7.35 (ddd, J = 7.5, 4.9, 1.2 Hz, 1 H), 7.11 (m, 1 H), 2.77 (s, 3 H), 2.46 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9, 152.0 (2 C), 149.6, 136.9, 136.3, 135.8, 133.1, 128.5, 124.9, 120.8, 119.2, 21.7, 18.2 ppm. HRMS (FAB) calcd. for $C_{14}H_{13}N_2S$ [M + H]$^+$ 241.0799; found 241.0798.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra.

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