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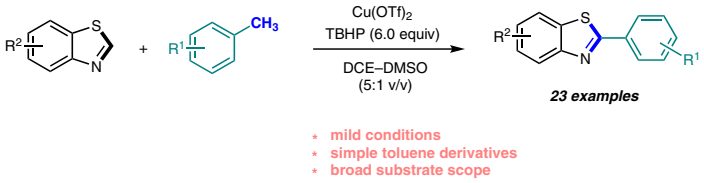
Copper-Catalyzed Arylation of Benzothiazoles with Toluene Derivatives: Synthesis of 2-Arylbenzothiazole

Chengliang Li[a,c]
Hongmei Deng*[b]
Tao Jin[c]
Zhiqiang Liu[c]
Ruolan Jiang[c]
Chunju Li[c]
Xueshun Jia*[c]
Jian Li*[c]

[a] School of Environmental and Chemical Engineering, Shanghai University, Shanghai 200444, P. R. of China
[b] Laboratory for Microstructures, Instrumental Analysis and Research Center of Shanghai University, Shanghai 200444, P. R. of China
hmdeng@staff.shu.edu.cn
[c] Department of Chemistry, Shanghai University, Shanghai 200444, P. R. of China
xsjia@mail.shu.edu.cn
lijian@shu.edu.cn



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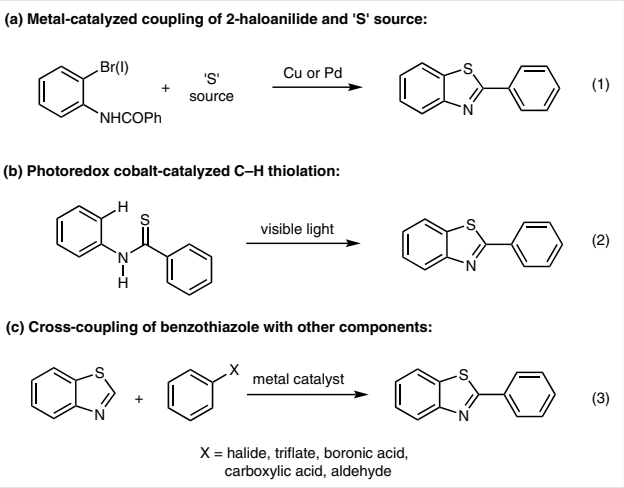
Abstract A copper-catalyzed reaction of benzothiazole and readily available toluene derivatives has been disclosed. This protocol is proposed to proceed through the oxidation of toluene and ring opening of benzothiazole, thus providing a new pathway for the synthesis of 2-arylbenzothiazoles.

Key words toluene, oxidation, copper, benzothiazole, arylation

2-Arylbenzothiazole represents a privileged synthetic motif since many compounds containing this core structure exhibit diverse biological and pharmacological activities, such as antitumor, antiviral, and antimicrobial activity.[1] As a consequence, many efforts have been devoted to the synthesis of such skeletons in an efficient manner.[2] Traditionally, these compounds are prepared from the condensation of 2-aminothiophenol with carboxylic acids or aldehydes.[3] However, these methods often suffer from drawbacks including high reaction temperatures and the difficulties in synthesizing the starting materials. To overcome the drawbacks of traditional methods, there is a continuous demand for the development of efficient and environmentally benign synthetic strategies. In this context, palladium- and copper-catalyzed coupling of a 2-haloanilide and a thiol surrogate via double C–S formation serves as good candidate to achieve this target [Scheme 1 (1)].[2a–d] In 2015, Lei and co-workers disclosed an external oxidant-free C–H functionalization to form 2-arylbenzothiazoles using visible-light photoredox cobalt catalysis [Scheme 1 (2)].[4] This strategy avoided the employment of stoichiometric oxidation reagents and dihydrogen was the only byproduct of the reaction. In addition, palladium-catalyzed double C–H activation involving benzothiazoles was also greatly advanced by You and Ofial.[5] In the past decades, the cross-coupling of benzothiazoles with aryl halides,[6] arylboronic acids,[7] aryl triflates,[8] and many other reaction partners have been well documented [Scheme 1 (3)].[9] Recently, the arylation of benzothiazoles with aromatic aldehydes have also drawn much attention from organic chemists.[10] In 2012, Li and co-workers reported an iron-catalyzed arylation of azoles using aromatic aldehydes as arylation reagents.[10a] The reaction proceeded readily in a solution of water/diglyme with oxygen as the oxidant. Tan and co-workers further demonstrated that $K_2S_2O_8$ could serve as alternative strategy.[10b] It was also worth noting that this reaction allowed the formation of the same products when aldehydes were replaced by phenylglyoxylic acids. Moreover, benzyl alcohol and acetophenone were both proven to be good reaction partners to accomplish the same transformation.[11]

On the other hand, toluene and its derivatives are considered to be the simplest and readily available starting materials in Nature, which has made them highly valuable building blocks in organic synthesis.[12] A careful literature survey revealed that reactions using toluene derivatives as a benzyl precursor were very popular, thus offering a new opportunity for the formation of carbon–carbon and carbon–heteroatom bonds.[13] Additionally, using arylmethanes as an acyl source was another research focus and much progress has been achieved.[14] In this regard, we became interested in exploring novel reactions using toluene derivatives as versatile building blocks. In 2015–2016, we reported the coupling reaction of toluene derivatives with isocyanides and carbonyl compounds, respectively.[15] As a continuation of our previous research,[16] herein we wish to



Scheme 1 Representative examples on the synthesis of 2-arylbenzothiazole

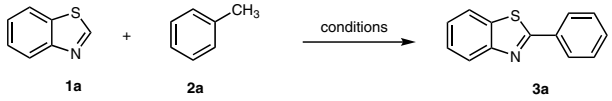
disclose a copper-catalyzed synthesis of 2-arylbenzothiazoles from benzothiazole and toluene derivatives. To the best of our knowledge, no such examples have been previously reported.

In order to optimize the reaction conditions, we commenced our investigation by exploring the coupling reaction of benzothiazole (**1a**) and toluene (**2a**) using TBHP as the oxidant. In the presence of a catalytic amount of $Cu(OAc)_2$, no reaction occurred upon heating the mixture of **1a** and **2a** in toluene under 90 °C (Table 1, entry 1). Pleasingly, a 31% yield of compound **3a** was obtained when copper(II) bromide was used (Table 1, entry 2). Encouraged by this result, we then focused our attention on the variation of different catalysts and representative results are summarized in Table 1. To our delight, the yield of product **3a** increased to 64% with the aid of catalytic amount of copper(II) triflate (Table 1, entry 4). Other catalysts including iodine, TBAI, and $Pd(OAc)_2$ were also examined, yet no formation of compound **3a** was detected (Table 1, entries 5–7). As shown in Table 1, the replacement of TBHP with PIDA, TBPB, and $K_2S_2O_8$ was subsequently conducted, which all led to disappointing results (Table 1, entries 8–10). Additionally, using AcOH and HBF_4 as additives only reduced the efficiency of the reaction (Table 1, entries 12 and 13). The following experimental outcomes also showed that the solvent had a significant impact on the reaction. Using benzene and DCE as solvents only led to decreased yields, whereas no generation of product **3a** was observed when the reaction was performed in chlorobenzene and CH_3CN (Table 1, entries 14–17). Subsequently a mixed solvent DCE/DMSO (5:1) was found to improve the performance significantly (Table 1, entry 19).

With the optimal reaction conditions in hand, we sought to investigate the scope and limitations of the reaction. As shown in Scheme 2, various substituted toluene derivatives **2** were firstly employed to react with benzothiazole (**1a**) under the optimized conditions. The experimental outcome revealed that arylmethanes **2** having electron-deficient and -donating groups on the aromatic ring worked well to afford compounds **3a–m**. In particular, *p*-, *m*-, and *o*-xylenes were found to react readily with benzothiazole (**1a**) to afford the corresponding products **3g–i** while another methyl group remains intact. It was also worth noting that mesitylene (**2n**) also acted as a good reaction partner to produce compound **3n**. No reaction took place when a cyano group was present on the aromatic ring of the arylmethane.

After a broad arylmethane scope was established, the feasibility of substituted benzothiazoles **1** was then examined under the optimized conditions. As shown in Scheme 3, substrates **1** having methoxy, alkyl, and halide groups at positions 6, 5, or 4 of the aromatic ring proceeded smoothly

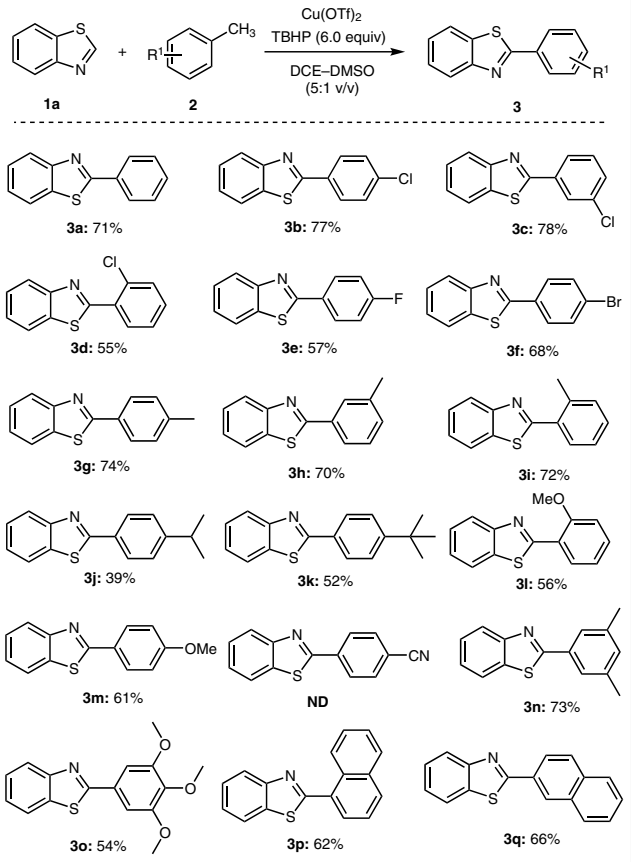
Table 1 Optimization of the Reaction Conditions[a]



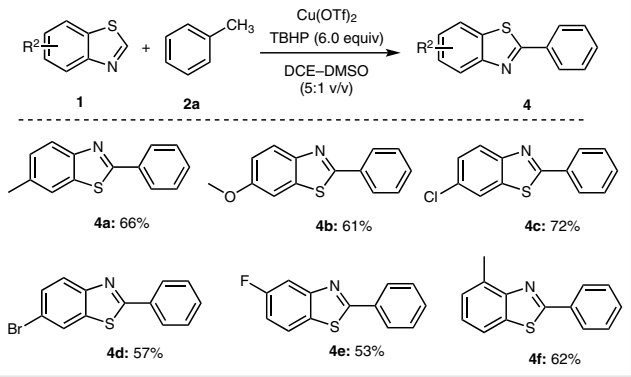
1a 2a 3a

Entry	Catalyst	Oxidant[b]	Solvent	Yield (%)[c]
1	$Cu(OAc)_2$	TBHP	toluene	0
2	$CuBr_2$	TBHP	toluene	31
3	CuCl	TBHP	toluene	47
4	$Cu(OTf)_2$	TBHP	toluene	64
5	I_2	TBHP	toluene	0
6	TBAI	TBHP	toluene	0
7	$Pd(OAc)_2$	TBHP	toluene	0
8	$Cu(OTf)_2$	PIDA	toluene	0
9	$Cu(OTf)_2$	TBPB	toluene	<5
10	$Cu(OTf)_2$	$K_2S_2O_8$	toluene	0
11[d]	$Cu(OTf)_2$	TBHP	toluene	35
12[e]	$Cu(OTf)_2$	TBHP	toluene	22
13[f]	$Cu(OTf)_2$	TBHP	toluene	55
14	$Cu(OTf)_2$	TBHP	benzene	37
15	$Cu(OTf)_2$	TBHP	DCE	60
16	$Cu(OTf)_2$	TBHP	PhCl	0
17	$Cu(OTf)_2$	TBHP	MeCN	0
18	$Cu(OTf)_2$	TBHP	DCE/DMSO (1:1)	0
19	$Cu(OTf)_2$	TBHP	DCE/DMSO (5:1)	71

[a] Reaction conditions: benzothiazole (**1a**, 1 mmol), toluene (**2a**, 3 mmol), catalyst (10 mol%), oxidant (6.0 equiv), solvent (2 mL), 90 °C, sealed tube.
[b] TBHP = *tert*-butyl hydroperoxide (70% w/v in water); PIDA = (diacetoxyiodo)benzene; TBPB = *tert*-butyl peroxybenzoate.
[c] Yields of product after silica gel chromatography.
[d] The reaction temperature was 120 °C.
[e] AcOH (0.5 mmol) was used as additive.
[f] HBF_4 (50% w/v in water, 0.5 mmol) was used as additive.



Scheme 2 Scope of the reaction with respect to the arylmethane substrate **2**. *Reagents and conditions*: benzothiazole (**1a**, 1 mmol), arylmethane **2** (3 mmol), $Cu(OTf)_2$ (10 mol%), TBHP (6.0 equiv), DCE/DMSO (5:1, 2 mL), 90 °C, sealed tube. Isolated yields after silica gel chromatography are given; ND = not detected.

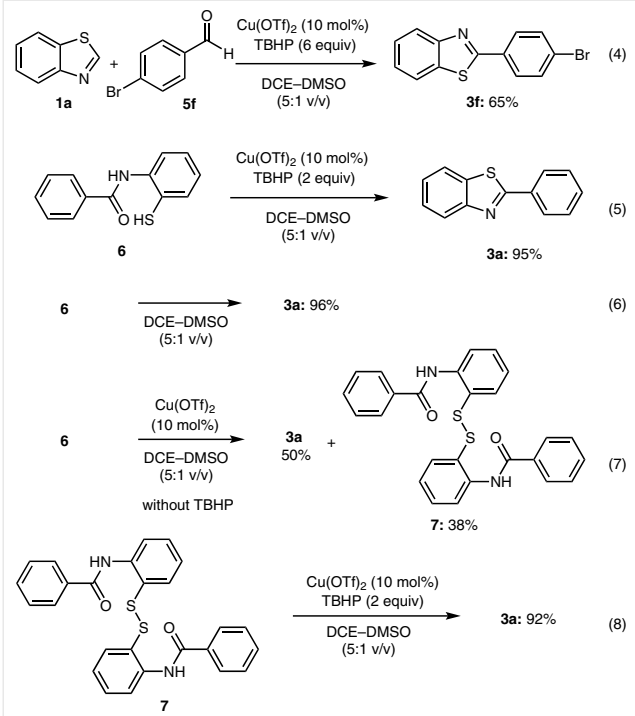


Scheme 3 Scope of the reaction with respect to the benzothiazole substrate **1**. *Reagents and conditions*: benzothiazole **1** (1 mmol), toluene (**2a**, 3 mmol), $Cu(OTf)_2$ (10 mol%), TBHP (6.0 equiv), DCE/DMSO (5:1, 2 mL), 90 °C, sealed tube; isolated yields after silica gel chromatography are given.

to afford the corresponding compounds **4a–f**, thus greatly expanding the substrate scope of this conversion.

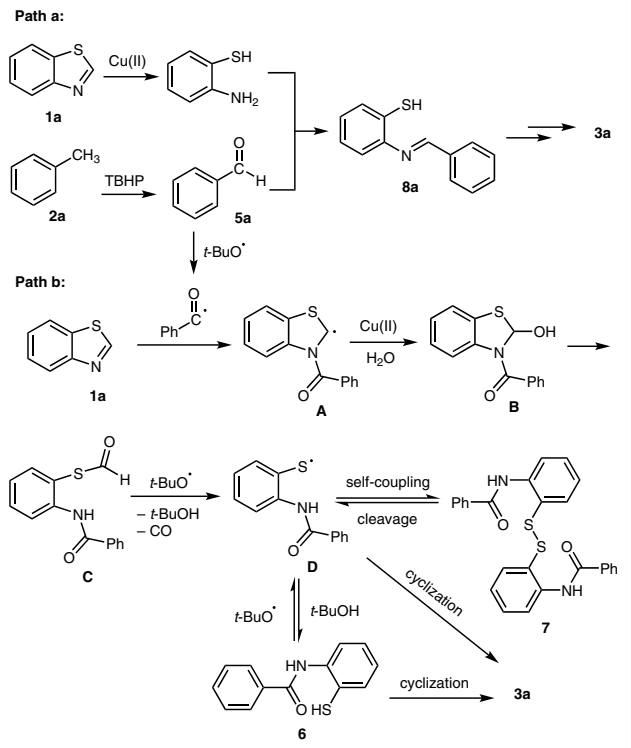
To gain further insight into this reaction, several preliminary mechanistic experiments were conducted. Firstly, reaction of benzothiazole (**1a**) and aldehyde **5f** was conducted. In this case, compound **3f** was isolated in 65% yield under the optimal conditions [Scheme 4 (4)]. To find out the real reaction intermediate, *N*-(2-mercaptophenyl)benzamide (**6**) was prepared and reacted under the optimal conditions. To our delight, 95% **3a** was isolated with two equivalents TBHP, which indicated compound **6** was also a possible reaction intermediate [Scheme 4 (5)]. In fact, heating compound **6** in mixed solvent could directly produce the desired product **3a** without the addition of any catalyst and oxidant [Scheme 4 (6)]. To our surprise, a lower yield (50%) was observed when substrate **6** was subjected to the optimal conditions without the addition of TBHP, whereas a new compound **7** was isolated at the same time [Scheme 4 (7)]. Then the possibility of compound **7** as reaction intermediate was also verified, thereby affording product **3a** in high yield [Scheme 4 (8)].

On the basis of previous reports and our experimental observations, two possible reaction mechanisms are proposed in Scheme 5 to explain the present coupling reaction. The key step in the first pathway is the generation of imine intermediate **8**, which involves the oxidative ring opening of benzothiazole (**1a**) and oxidative generation of benzaldehyde (**5a**) from toluene (**2a**).[14] Once the intermediate **8** is



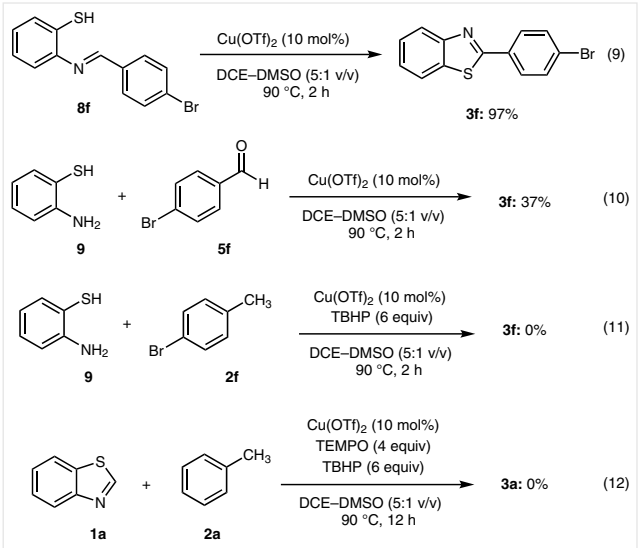
Scheme 4 Preliminary mechanistic studies

formed, it undergoes cyclization and oxidation to yield product **3a**.[10] Another possibility starts from radical addition of a benzoyl radical to benzothiazole (**1a**), which essentially leads to the formation of intermediate **A**. Sequenced hydration of **A** and ring opening produces **C** via intermediate **B**.[10,11] Subsequently, decarbonylation from **C** leads to key radical **D**. On the other hand, intermediate **D** can also abstract a hydride radical to form compound **6**. As shown in Scheme 5, both intermediates **D** and **6** can experience intramolecular cyclization to produce compound **3a** directly.[10,11] It should also be noted that transformations between intermediates **D** and **6** or **7** are reversible. In addition, self-coupling of sulfur radical **D** could also give disulfide **7**. According to our analysis, the presence of $Cu(OTf)_2$ has two important roles: 1) it accelerates the oxidation of toluene to benzaldehyde;[17a] and 2) it facilitates the formation of intermediate **D**.[17b,c]



Scheme 5 Proposed mechanism

To verify the feasibility of the proposed mechanism, we carried out the corresponding control experiments. In the presence of copper catalyst, compound **8f** essentially led to the formation of 97% yield of **3f** without the aid of TBHP [Scheme 6 (9)]. A lower yield of **3f** was obtained when 2-aminothiophenol (**9**) and 4-bromobenzaldehyde (**5f**) were heated under the same conditions [Scheme 6 (10)]. In contrast, no reaction occurred when 2-aminothiophenol (**9**) and 4-bromotoluene (**2f**) were heated under the optimized conditons [Scheme 6 (11)]. This result indicated that the first reaction pathway was unlikely. As a consequence, another proposed reaction mechanism seemed to be more reasonable. The experimental outcome also revealed that the present reaction was completely inhibited when TEMPO as a radical scavenger was added to the solution of **1a** and **2a** under standard conditions [Scheme 6 (12)]. Finally, an isotope experiment with toluene-α-^{13}C was also conducted (see Supporting Information for details).



Scheme 6 Control experiments

In conclusion, we have developed a novel copper-catalyzed synthesis of 2-arylbenzothiazole from readily available toluene derivatives and benzothiazole. Moreover, many mechanistic studies were conducted to explain this coupling reaction. Other features of the present strategy also include the employment of simple starting materials, broad substrate scope, and mild reaction conditions. As a result, this reaction has potential to be further applied in organic synthesis.

The NMR spectra were recorded on Bruker AC 500 spectrometer (500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR) with $CDCl_3$ as the solvent and TMS as internal reference. ^{1}H NMR spectral data were reported as follows: chemical shift (δ, ppm), multiplicity, integration, and coupling constant (Hz). ^{13}C NMR spectral data were reported in terms of the chemical shift. Melting points were obtained on a X-4 digital melting point apparatus without correction. Purification of products was accomplished by column chromatography packed with silica gel. Unless otherwise stated, all reagents were commercially purchased and used without further purification.

2-Arylbenzothiazoles 3a–q, 4a–f; General Procedure

Under an air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with benzothiazole **1** (1.0 mmol), toluene derivative **2** (3.0 mmol), and

$Cu(OTf)_2$ (0.10 mmol) in DCE/DMSO (5:1, 2.0 mL). To this was added 70% aq TBHP (6.0 equiv) at r.t. The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil bath at 90 °C for 24 or 36 h. When the reaction was complete, it was cooled to r.t. and monitored by TLC. To the resulting solution was added 98% hydrazine hydrate (0.5 or 1.0 mL), K_2CO_3 (3.0 mmol), and EtOH (2.0 mL), the mixture was stirred for 5 min and then poured into 10% HCl (15 mL); the mixture was extracted with EtOAc (2 ×). The combined organic layers were dried (anhyd Na_2SO_4) and the solvents were removed in vacuo. The residue was purified by flash chromatography (silica gel, petroleum ether/EtOAc 20:1) to give the product.

2-Phenylbenzothiazole (3a)[17]

White solid; yield: 150 mg (71%); mp 109–110 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.14–8.10 (m, 3 H), 7.85 (d, *J* = 8.0 Hz, 1 H), 7.51–7.46 (m, 4 H), 7.35 (d, *J* = 7.5 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 154.2, 135.2, 133.7, 131.0, 129.1, 127.6, 126.4, 125.2, 123.3, 121.7.

2-(4-Chlorophenyl)benzothiazole (3b)[10b]

White solid; yield: 189 mg (77%); mp 111–112 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.0 Hz, 1 H), 7.95 (d, *J* = 8.5 Hz, 2 H), 7.82 (d, *J* = 8.0 Hz, 1 H), 7.47 (t, *J* = 7.0 Hz, 1 H), 7.39 (d, *J* = 8.5 Hz, 2 H), 7.38 (t, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 154.1, 137.0, 135.1, 132.1, 129.2, 128.7, 126.5, 125.4, 123.3, 121.7.

2-(3-Chlorophenyl)benzothiazole (3c)[10b]

White solid; yield: 191 mg (78%); mp 93–94 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.89–7.84 (m, 2 H), 7.50–7.47 (m, 2 H), 7.43–7.41 (m, 1 H), 7.39–7.37 (m, 1 H), 7.36–7.34 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.2, 153.9, 135.2, 135.1, 135.0, 130.8, 130.2, 127.4, 126.5, 125.7, 125.6, 123.4, 121.7.

2-(2-Chlorophenyl)benzothiazole (3d)[10c]

White solid; yield: 135 mg (55%); mp 83–84 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.23 (dd, *J* = 7.5, 2.0 Hz, 1 H), 8.16 (d, *J* = 8.5 Hz, 1 H), 7.88 (d, *J* = 8.0 Hz, 1 H), 7.51–7.46 (m, 2 H), 7.39–7.35 (m, 1 H), 7.34–7.29 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.1, 152.5, 136.2, 132.7, 132.2, 131.8, 131.1, 130.8, 127.1, 126.3, 125.5, 123.5, 121.4.

2-(4-Fluorophenyl)benzothiazole (3e)[10b]

White solid; yield: 131 mg (57%); mp 87–88 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.0 Hz, 1 H), 8.03–8.00 (m, 2 H), 7.81 (d, *J* = 8.0 Hz, 1 H), 7.48–7.46 (m, 1 H), 7.35–7.32 (m, 1 H), 7.11 (dt, *J* = 8.5, 6.5, 2.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 165.4, 163.4, 154.1, 135.1, 129.9, 129.9, 129.5, 129.4, 126.4, 125.2, 123.2, 121.6, 116.2, 116.0.

2-(4-Bromophenyl)benzothiazole (3f)[18]

White solid; yield: 197 mg (68%); mp 115–117 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.0 Hz, 1 H), 7.86 (d, *J* = 8.5 Hz, 2 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.53 (d, *J* = 7.5 Hz, 2 H), 7.47 (t, *J* = 7.0 Hz, 1 H), 7.35 (t, *J* = 7.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 154.1, 135.1, 132.5, 132.2, 128.8, 126.5, 125.4, 123.3, 121.7.

2-(*p*-Tolyl)benzothiazole (3g)[10b]

White solid; yield: 166 mg (74%); mp 73–74 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.0 Hz, 1 H), 8.01 (d, *J* = 8.0 Hz, 2 H), 7.88 (d, *J* = 8.0 Hz, 1 H), 7.51 (t, *J* = 7.0 Hz, 1 H), 7.38 (t, *J* = 7.0 Hz, 1 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 2.43 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.3, 154.2, 141.4, 135.0, 131.0, 129.8, 127.5, 126.3, 125.1, 123.1, 21.6.

2-(*m*-Tolyl)benzothiazole (3h)[10c]

White solid; yield: 157 mg (70%); mp 86–87 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.5 Hz, 1 H), 7.98 (s, 1 H), 7.91–7.86 (m, 2 H), 7.52 (dt, *J* = 8.0, 1.0 Hz, 1 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 7.29 (d, *J* = 8.0 Hz, 1 H), 2.46 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.3, 154.2, 138.8, 135.1, 133.6, 131.8, 128.9, 128.0, 126.3, 125.2, 124.9, 123.2, 121.7, 21.4.

2-(*o*-Tolyl)benzothiazole (3i)[10b]

Pale yellow oil; yield: 162 mg (72%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.0 Hz, 1 H), 7.94 (d, *J* = 8.0 Hz, 1 H), 7.83 (d, *J* = 8.0 Hz, 1 H), 7.54 (dt, *J* = 8.0, 1.0 Hz, 1 H), 7.45–7.40 (m, 2 H), 7.38–7.33 (m, 1 H), 2.74 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 160.8, 153.9, 137.3, 135.7, 133.2, 131.7, 130.7, 130.1, 126.2, 125.2, 123.5, 121.5, 21.5.

2-(4-Isopropylphenyl)benzothiazole (3j)[19]

White solid; yield: 99 mg (39%); mp 77–78 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.0 Hz, 1 H), 8.06 (d, *J* = 8.5 Hz, 2 H), 7.88 (d, *J* = 7.5 Hz, 1 H), 7.51 (t, *J* = 7.5 Hz, 1 H), 7.39–7.36 (m, 3 H), 3.04–2.95 (m, 1 H), 1.35 (d, *J* = 7.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.2, 154.3, 152.3, 135.0, 131.4, 127.7, 127.2, 126.3, 125.0, 123.1, 121.6, 34.2, 23.9.

2-(4-*tert*-Butylphenyl)benzothiazole (3k)[10c]

White solid; yield: 137 mg (52%); mp 92–93 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.5 Hz, 1 H), 8.07 (d, *J* = 8.5 Hz, 2 H), 7.87 (d, *J* = 8.0 Hz, 1 H), 7.54–7.49 (m, 3 H), 7.37 (t, *J* = 7.5 Hz, 1 H), 1.40 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 154.5, 154.3, 135.1, 131.0, 127.4, 126.3, 126.0, 125.0, 123.2, 121.6, 35.0, 31.3.

2-(2-Methoxyphenyl)benzothiazole (3l)[10b]

White solid; yield: 132 mg (55%); mp 102–103 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.63 (dd, *J* = 7.5, 1.5 Hz, 1 H), 8.18 (d, *J* = 8.0 Hz, 1 H), 7.93 (d, *J* = 8.0 Hz, 1 H), 7.53–7.50 (m, 1 H), 7.42–7.36 (m, 2 H), 7.14 (t, *J* = 7.0 Hz, 1 H), 6.95 (d, *J* = 8.5 Hz, 1 H), 3.94 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.2, 157.3, 152.3, 136.3, 131.9, 129.5, 125.9, 124.7, 122.8, 122.3, 121.3, 121.1, 111.7, 55.6.

2-(4-Methoxyphenyl)benzothiazole (3m)[18]

White solid; yield: 147 mg (61%); mp 125–126 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.0 Hz, 1 H), 7.99 (d, *J* = 8.5 Hz, 2 H), 7.79 (d, *J* = 8.0 Hz, 1 H), 7.45 (t, *J* = 7.0 Hz, 1 H), 7.30 (t, *J* = 7.0 Hz, 1 H), 7.38 (d, *J* = 8.5 Hz, 2 H), 3.76 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8, 161.9, 154.3, 134.9, 129.1, 126.4, 126.2, 124.8, 122.8, 121.5, 114.3, 55.4.

2-(3,5-Dimethylphenyl)benzothiazole (3n)[4]

White solid; yield: 174 mg (73%); mp 70–71 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.0 Hz, 1 H), 7.90 (d, *J* = 8.0 Hz, 1 H), 7.72 (s, 2 H), 7.49 (t, *J* = 7.5 Hz, 1 H), 7.38 (t, *J* = 7.5 Hz, 1 H), 7.13 (s, 1 H), 2.41 (s, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.5, 154.2, 138.7, 135.1, 133.5, 132.8, 126.3, 125.4, 125.1, 123.2, 121.6, 21.3.

2-(3,4,5-Trimethoxyphenyl)benzothiazole (3o)[6d]

White solid; yield: 161 mg (54%); mp 152–153 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.0 Hz, 1 H), 7.83 (d, *J* = 7.5 Hz, 1 H), 7.45 (t, *J* = 7.0 Hz, 1 H), 7.33 (t, *J* = 7.0 Hz, 1 H), 7.28 (s, 2 H), 3.93 (s, 6 H), 3.92 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.7, 154.0, 153.5, 140.6, 135.0, 129.0, 126.3, 125.1, 123.0, 121.5, 104.7, 60.9, 56.3.

2-(Naphthalen-1-yl)benzothiazole (3p)[10b]

White solid; yield: 162 mg (62%); mp 98–99 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.13 (d, *J* = 8.5 Hz, 1 H), 8.34 (d, *J* = 8.1 Hz, 1 H), 8.08–7.93 (m, 4 H), 7.72 (ddd, *J* = 8.5, 7.0, 1.3 Hz, 1 H), 7.66–7.61 (m, 2 H), 7.61–7.56 (m, 1 H), 7.52–7.47 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8, 154.3, 135.6, 134.2, 131.2, 130.9, 130.8, 129.6, 128.6, 127.8, 126.7, 126.4, 126.1, 125.4, 125.1, 123.7, 121.5.

2-(Naphthalen-2-yl)benzothiazole (3q)[10b]

White solid; yield: 172 mg (66%); mp 125–126 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.54 (s, 1 H), 8.19 (dd, *J* = 8.5, 1.5 Hz, 1 H), 8.15 (d, *J* = 8.0 Hz, 1 H), 7.94–7.83 (m, 4 H), 7.54–7.50 (m, 3 H), 7.39–7.36 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 154.3, 135.2, 134.6, 133.2, 130.9, 128.9, 128.8, 127.9, 127.6, 127.5, 126.9, 126.4, 125.3, 124.5, 123.3, 121.7.

6-Methyl-2-phenylbenzothiazole (4a)[10b]

White solid; yield: 149 mg (66%); mp 131–132 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09–8.07 (m, 2 H), 7.98 (d, *J* = 8.5 Hz, 1 H), 7.59 (s, 1 H), 7.47–7.44 (m, 3 H), 7.27 (d, *J* = 7.0 Hz, 1 H), 2.45 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.0, 152.3, 135.3, 135.2, 133.8, 130.8, 129.0, 127.9, 127.5, 122.7, 121.4, 21.6.

6-Methoxy-2-phenylbenzothiazole (4b)[18]

White solid; yield: 147 mg (61%); mp 114–115 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05–8.03 (m, 2 H), 7.98 (d, *J* = 9.0 Hz, 1 H), 7.48–7.44 (m, 3 H), 7.27 (s, 1 H), 7.10 (dd, *J* = 9.0, 2.5 Hz, 1 H), 3.82 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.5, 157.8, 148.7, 136.5, 133.8, 130.53, 128.9, 127.2, 123.7, 115.7, 104.1, 55.7.

6-Chloro-2-phenylbenzothiazole (4c)[10b]

White solid; yield: 176 mg (72%); mp 141–142 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05–8.03 (m, 2 H), 7.95 (d, *J* = 8.5 Hz, 1 H), 7.82 (d, *J* = 2.0 Hz, 1 H), 7.49–7.42 (m, 3 H), 7.43–7.41 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.5, 152.7, 136.2, 133.2, 131.2, 131.1, 129.1, 127.5, 127.1, 123.9, 121.2.

6-Bromo-2-phenylbenzothiazole (4d)[18]

White solid; yield: 165 mg (57%); mp 148–149 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05–8.03 (m, 2 H), 7.98 (d, *J* = 2.0 Hz, 1 H), 7.89 (d, *J* = 8.5 Hz, 1 H), 7.56 (dd, *J* = 9.0, 2.0 Hz, 1 H), 7.49–7.46 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.6, 153.0, 136.7, 133.2, 131.3, 129.8, 129.1, 127.6, 124.3, 124.2, 118.8.

5-Fluoro-2-phenylbenzothiazole (4e)[10b]

White solid; yield: 121 mg (53%); mp 135–136 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.08–8.06 (m, 2 H), 7.80 (m, 1 H), 7.76 (dd, *J* = 9.5, 2.5 Hz, 1 H), 7.50–7.48 (m, 3 H), 7.15 (dt, *J* = 8.5, 2.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 162.9, 160.9, 155.1, 155.0, 133.4, 131.3, 130.5, 129.1, 127.5, 122.3, 122.2, 113.9, 113.8, 109.5, 109.3.

4-Methyl-2-phenylbenzothiazole (4f)[18]

Pale yellow oil; yield: 140 mg (62%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.18–8.16 (m, 2 H), 7.76–7.74 (m, 1 H), 7.53–7.50 (m, 3 H), 7.33–7.29 (m, 2 H), 2.89 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 153.6, 135.1, 134.1, 133.4, 130.8, 129.0, 127.6, 126.8, 125.1, 119.1, 18.5.

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Supporting Information

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