

# Ligand- and solvent-free synthesis of 2-aminobenzothiazoles by copper-catalyzed tandem reaction of 2-haloanilines with isothiocyanates

Ruiya Yao, Haiyi Liu, Yichao Wu and Mingzhong Cai\*

**We report an environmentally friendly, efficient and practical method for the synthesis of 2-aminobenzothiazoles by a copper (II)-catalyzed tandem reaction of 2-haloanilines with isothiocyanates under ligand- and solvent-free conditions in air. The developed methodology conforms to the principles of 'green chemistry' and addresses the shortage of such methods for the synthesis of 2-aminobenzothiazoles. The reaction is quite general and generates a variety of 2-aminobenzothiazoles in good to excellent yields. Copyright © 2012 John Wiley & Sons, Ltd.**

Supporting information may be found in the online version of this article.

**Keywords:** copper catalysis; tandem reaction; 2-aminobenzothiazole; solvent-free; 2-haloaniline

## Introduction

Development of new organic transformations that are not only efficient, selective and high yielding but that are also environmentally benign is one of the challenges facing chemists in the 21st century.<sup>[1]</sup> During the last decade, the topic of 'green' chemistry has attracted much attention.<sup>[1,2]</sup> 'Green' chemistry aims at the total elimination (or at least the minimization) of waste, and the implementation of sustainable processes.<sup>[1a]</sup> The use of nontoxic chemicals, renewable materials and solvent-free conditions are the key issues in a green synthetic strategy. In the present work, we describe a green approach towards the synthesis of 2-aminobenzothiazoles.

2-Aminobenzothiazoles, an important topical benzothiazole scaffold, are broadly found in biological chemistry and medicinal areas.<sup>[3]</sup> A large number of 2-anilinobenzothiazole derivatives are found to be anticancer active and the 2-aminobenzothiazole moieties are privileged pharmacophores as well as valuable reactive intermediates.<sup>[4]</sup> There are several methods for the synthesis of 2-aminobenzothiazoles, including: (i) cyclization of arylthioureas with liquid bromine and benzyltrimethylammonium tribromide;<sup>[3a,5]</sup> (ii) coupling of arylamines with 2-halobenzothiazole;<sup>[6]</sup> (iii) oxidative cyclization of the intermediates generated by 2-aminothiophenol with isothiocyanates;<sup>[7]</sup> and (iv) intramolecular C—S bond formation catalyzed by palladium.<sup>[4e,8]</sup> Although these methods are efficient for the synthesis of 2-aminobenzothiazoles, they usually suffer from the use of highly toxic and corrosive reagents, expensive palladium catalysts, specific ligands and not readily available substrates. These drawbacks make the methodologies unsuitable for large- or industrial-scale applications. Recently, the copper- or iron-catalyzed one-pot tandem reactions of 2-halobenzenamines with isothiocyanates for the synthesis of 2-aminobenzothiazoles have received much attention because of their efficiency and low costs. For example, Wu

and co-workers described a copper-catalyzed tandem reaction between 2-halobenzenamines and isothiocyanates using the CuI (10 mol%)/1,10-phenanthroline (20 mol%) catalytic system to prepare 2-aminobenzothiazoles;<sup>[4g]</sup> Li and Ding's group reported iron-catalyzed tandem reactions of 2-halobenzenamines and isothiocyanates leading to 2-aminobenzothiazoles.<sup>[9]</sup> Meanwhile, the ligand-free copper-catalyzed one-pot tandem reactions of 2-halobenzenamines and isothiocyanates were also reported.<sup>[10]</sup> However, it should be pointed out that the copper or iron-catalyzed one-pot tandem reactions of 2-halobenzenamines with isothiocyanates generally involve organic solvents such as DMSO, DMF and toluene. Use of organic solvents is environmentally unfriendly, and so it is highly desirable to develop more environmentally friendly and economic methodologies for synthesizing 2-aminobenzothiazoles. To achieve this, we report an environmentally friendly, economic, efficient and simple ligand- and solvent-free system that allows the one-pot tandem reactions of 2-halobenzenamines and isothiocyanates based on a catalytic amount of CuSO<sub>4</sub> using Bu<sub>3</sub>N as a base at 80 °C in air. The results are summarized below.

## Results and Discussion

In order to identify the optimal reaction conditions, the reaction of 2-iodoaniline with phenyl isothiocyanate was chosen as a model reaction. In this preliminary experiment, the reaction of

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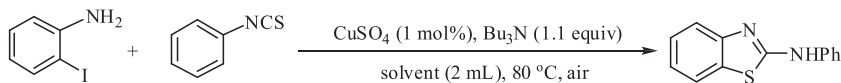
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2-iodoaniline with phenyl isothiocyanate (1.1 equiv.) was carried out in various solvents, with  $\text{CuSO}_4$  (1 mol%) as a catalyst and  $\text{Bu}_3\text{N}$  (1.1 equiv.) as a base without a ligand, at  $80^\circ\text{C}$  in air (Table 1). It was found that the reaction proceeded perfectly in DMSO (Table 1, entry 1), but that the yields decreased when the reaction was carried out in other solvents (Table 1, entries 2–10). However, the reaction surprisingly proceeded very smoothly under solvent-free conditions to afford the desired product in excellent yield within a shorter time (Table 1, entry 11). Considering our goal of an economic and environmentally

friendly reaction, these ligand- and solvent-free conditions are clearly the most favorable.

Our next studies focused on the effect of various copper catalysts on the yields under ligand- and solvent-free conditions. The reaction did not occur in the absence of a catalyst (Table 2, entry 1). Among the copper catalysts examined,  $\text{CuSO}_4$ ,  $\text{CuI}$ ,  $\text{Cu}(\text{OAc})_2$ ,  $\text{CuCl}_2$  and  $\text{CuCl}$  were efficient catalysts and afforded the product in high yields (Table 2, entries 2–4, 6 and 8), and  $\text{CuSO}_4$  was the best choice (entry 2), whereas other copper catalysts such as  $\text{Cu}(\text{OTf})_2$ ,  $\text{CuBr}$ ,  $\text{Cu}_2\text{O}$  and  $\text{CuBr}_2$  were substantially less

**Table 1.** Preliminary survey of solvents for the reaction of 2-iodoaniline with phenyl isothiocyanate catalyzed by  $\text{CuSO}_4$ <sup>a</sup>

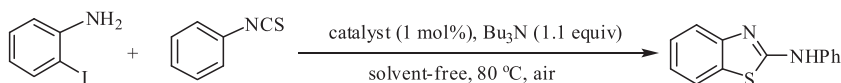


Entry	Solvent	Time (h)	Yield (%) <sup>b</sup>
1	DMSO	12	96
2	DMF	14	81
3	EtOH	24	73
4	Toluene	16	80
5	NMP	15	76
6	Dioxane	24	60
7	$\text{H}_2\text{O}$	24	14
8	Benzene	24	75
9	DCE	24	65
10	MeCN	24	54
11	None	2	95

<sup>a</sup>The reaction was carried out using 2-iodoaniline (1.0 mmol), phenyl isothiocyanate (1.1 mmol),  $\text{CuSO}_4$  (1.0 mol%) and  $\text{Bu}_3\text{N}$  (1.1 mmol) in solvent (2.0 ml) at  $80^\circ\text{C}$  under an air atmosphere.

<sup>b</sup>Isolated yield.

**Table 2.** Screening of copper catalysts for the reaction of 2-iodoaniline with phenyl isothiocyanate<sup>a</sup>



Entry	Catalyst	Time (h)	Yield (%) <sup>b</sup>
1	None	24	0
2	$\text{CuSO}_4$	2	95
3	$\text{Cu}(\text{OAc})_2$	2	90
4	$\text{CuCl}_2$	3	89
5	$\text{Cu}(\text{OTf})_2$	3	82
6	$\text{CuI}$	2	93
7	$\text{CuBr}$	3	84
8	$\text{CuCl}$	3	89
9	$\text{Cu}_2\text{O}$	4	85
10	$\text{CuBr}_2$	4	83
11 <sup>c</sup>	$\text{CuSO}_4$	5	93
12 <sup>d</sup>	$\text{CuSO}_4$	1	94

<sup>a</sup>The reaction was carried out using 2-iodoaniline (1.0 mmol), phenyl isothiocyanate (1.1 mmol) and  $\text{Bu}_3\text{N}$  (1.1 mmol) in the presence of catalyst (0.01 mmol) at  $80^\circ\text{C}$  under an air atmosphere.

<sup>b</sup>Isolated yield.

<sup>c</sup>0.5 mol%  $\text{CuSO}_4$  was used.

<sup>d</sup>2 mol%  $\text{CuSO}_4$  was used.

effective (Table 2, entries 5, 7, 9 and 10). The amount of  $\text{CuSO}_4$  was optimized further. The low copper concentration usually led to a long period of reaction, which was consistent with our experimental result (Table 2, entry 11). Increasing the amount of copper catalyst could shorten the reaction time, but did not increase the yield of *N*-phenylbenzo[d]thiazol-2-amine (Table 2, entry 12).

In order to examine the effect of base on the model reaction, we performed the reaction with various bases under ligand- and solvent-free conditions in air (Table 3). As can be seen, the reaction could not be performed without a base (Table 3, entry 1). Among the bases examined,  $\text{Bu}_3\text{N}$  was found to be the most effective (Table 3, entry 2);  $\text{Et}_3\text{N}$ , 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), *N,N,N',N'*-tetramethylethylenediamine (TMEDA) and 1,4-diazabicyclo[2.2.2]octane (DABCO) also afforded good yields (Table 3, entries 3, 7–9), whereas other bases such as pyridine, *i*- $\text{Pr}_2\text{NH}$ , piperidine,  $\text{Cs}_2\text{CO}_3$  and  $\text{K}_2\text{CO}_3$  were substantially less effective (Table 3, entries 4–6, 10, 11). Therefore, the optimal ligand- and solvent-free system for this reaction involves  $\text{CuSO}_4$  (1 mol%) and  $\text{Bu}_3\text{N}$  (1.1 equiv.) at 80 °C in air.

Encouraged by the efficiency of the reaction protocol described above, we investigated the scope of both 2-halobenzenamines and isothiocyanates under the optimized conditions, and the results are summarized in Table 4. As shown in the table, a variety of isothiocyanates (**2**) were investigated by reacting with 2-iodoaniline in the presence of  $\text{CuSO}_4$  (1 mol%) and  $\text{Bu}_3\text{N}$  (1.1 equiv.) at 80 °C under ligand- and solvent-free conditions in air. The results demonstrated that several functional groups, such as methyl, methoxy, fluoro, chloro and nitro groups, on the aryl moiety were tolerated well, and both electron-rich and electron-poor aryl isothiocyanates underwent the tandem reaction successfully in good to excellent yields (entries 2–6). 4-Methoxyphenyl isothiocyanate, with a strong electron-donating group, for example, was treated with 2-iodoaniline to give the desired product **3c** in 91% yield after 3 h (entry 3), and the reaction of 4-nitrophenyl isothiocyanate, having a strong electron-withdrawing group with 2-iodoaniline, afforded the target product **3f** in 88% yield within 1.5 h (entry 6). To our delight, alkyl isothiocyanates were also suitable substrates for the tandem

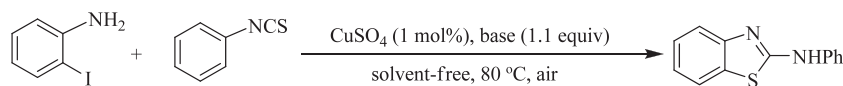
reactions under the standard conditions. Cyclohexyl isothiocyanate, for instance, was treated with 2-iodoaniline to afford the desired product **3g** in 87% yield (entry 7).

Substituted 2-iodoanilines were subsequently investigated to react with a variety of isothiocyanates under the optimized conditions, and the results are also summarized in Table 4. We were pleased to find that the optimized conditions were compatible with various 2-iodoanilines bearing trifluoromethyl, chloro and methyl groups. It was observed that the tandem reactions of electron-withdrawing 2-iodo-4-(trifluoromethyl)aniline with various isothiocyanates were successful in affording the desired products **3h–l** in good to excellent yields under ligand- and solvent-free conditions in air (entries 8–12). The tandem reactions of 4-chloro-2-iodoaniline with phenyl isothiocyanate or substituted phenyl isothiocyanates proceeded very smoothly to give the corresponding 2-aminobenzothiazoles **3m–q** in excellent yields (entries 13–17). The reaction of 2-iodo-4-methylaniline with a variety of isothiocyanates also proceeded efficiently under the same conditions to afford the desired products **3r–u** in good to excellent yields (entries 18–21). Interestingly, a less active substrate, 2-bromoaniline, also displayed high activity for the tandem reaction with various aryl isothiocyanates in excellent yields under ligand- and solvent-free conditions (entries 22–24).

## Conclusions

We have developed an environmentally friendly, efficient and practical method for the synthesis of 2-aminobenzothiazoles by a copper-catalyzed tandem reaction of 2-haloanilines with isothiocyanates using  $\text{CuSO}_4$  (1 mol%) as catalyst and  $\text{Bu}_3\text{N}$  (1.1 equiv.) as a base under ligand- and solvent-free conditions in air. The procedure is suitable for various 2-haloanilines and isothiocyanates, and a variety of 2-aminobenzothiazoles can be produced conveniently with good to excellent yields. The developed methodology has attractive advantages of solvent-free, relatively low catalyst loading and shorter reaction

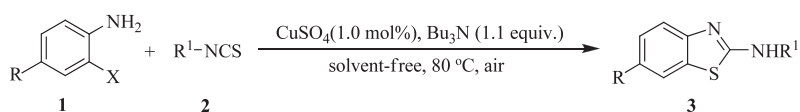
**Table 3.** Screening of bases for the reaction of 2-iodoaniline with phenyl isothiocyanate<sup>a</sup>



Entry	Base	Time (h)	Yield (%) <sup>b</sup>
1	None	24	0
2	$\text{Bu}_3\text{N}$	2	95
3	$\text{Et}_3\text{N}$	5	77
4	<i>i</i> - $\text{Pr}_2\text{NH}$	24	34
5	Piperidine	24	24
6	Pyridine	5	63
7	DABCO	6	76
8	TMEDA	5	78
9	DBU	6	74
10	$\text{Cs}_2\text{CO}_3$	24	14
11	$\text{K}_2\text{CO}_3$	24	11

<sup>a</sup>The reaction was carried out using 2-iodoaniline (1.0 mmol), phenyl isothiocyanate (1.1 mmol) and base (1.1 mmol) in the presence of  $\text{CuSO}_4$  (0.01 mmol) at 80 °C under an air atmosphere.

<sup>b</sup>Isolated yield.

**Table 4.** Ligand- and solvent-free synthesis of a variety of 2-aminobenzothiazoles by CuSO<sub>4</sub>-catalyzed tandem reaction of 2-haloanilines and isothiocyanates<sup>a</sup>

Entry	R/X	R <sup>1</sup>	Time (h)	Product	Yield (%) <sup>b</sup>
1	H/I	C <sub>6</sub> H <sub>5</sub>	2	<b>3a</b> <sup>[10a]</sup>	95
2	H/I	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	2	<b>3b</b> <sup>[10a]</sup>	93
3	H/I	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	3	<b>3c</b> <sup>[9a]</sup>	91
4	H/I	4-FC <sub>6</sub> H <sub>4</sub>	2	<b>3d</b> <sup>[6b]</sup>	93
5	H/I	4-ClC <sub>6</sub> H <sub>4</sub>	2	<b>3e</b> <sup>[9a]</sup>	92
6	H/I	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	1.5	<b>3f</b> <sup>[9a]</sup>	88
7	H/I	Cyclohexyl	4	<b>3g</b> <sup>[11]</sup>	87
8	CF <sub>3</sub> /I	C <sub>6</sub> H <sub>5</sub>	2	<b>3h</b> <sup>[11]</sup>	93
9	CF <sub>3</sub> /I	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	3	<b>3i</b> <sup>[11]</sup>	92
10	CF <sub>3</sub> /I	4-FC <sub>6</sub> H <sub>4</sub>	2	<b>3j</b>	94
11	CF <sub>3</sub> /I	4-ClC <sub>6</sub> H <sub>4</sub>	2	<b>3k</b> <sup>[9a]</sup>	91
12	CF <sub>3</sub> /I	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	1.5	<b>3l</b> <sup>[9b]</sup>	85
13	Cl/I	C <sub>6</sub> H <sub>5</sub>	2	<b>3m</b> <sup>[9a]</sup>	92
14	Cl/I	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	2	<b>3n</b> <sup>[9a]</sup>	93
15	Cl/I	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	3	<b>3o</b>	90
16	Cl/I	4-FC <sub>6</sub> H <sub>4</sub>	2	<b>3p</b>	91
17	Cl/I	4-ClC <sub>6</sub> H <sub>4</sub>	2	<b>3q</b>	92
18	CH <sub>3</sub> /I	C <sub>6</sub> H <sub>5</sub>	2	<b>3r</b> <sup>[11]</sup>	94
19	CH <sub>3</sub> /I	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	3	<b>3s</b> <sup>[11]</sup>	90
20	CH <sub>3</sub> /I	4-ClC <sub>6</sub> H <sub>4</sub>	2	<b>3t</b> <sup>[10a]</sup>	92
21	CH <sub>3</sub> /I	<b>Cyclohexyl</b>	4	<b>3u</b> <sup>[12]</sup>	85
22	H/Br	C <sub>6</sub> H <sub>5</sub>	3	<b>3a</b>	92
23	H/Br	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	3	<b>3b</b>	90
24	H/Br	4-ClC <sub>6</sub> H <sub>4</sub>	3	<b>3e</b>	93

<sup>a</sup>Reaction conditions: **1** (1.0 mmol); **2** (1.1 mmol); CuSO<sub>4</sub> (0.01 mmol); Bu<sub>3</sub>N (1.1 mmol) at 80 °C under an air atmosphere.

<sup>b</sup>Isolated yield.

times as compared with the ligand-free copper-catalyzed tandem reactions reported by other groups.

## Experimental

All chemicals were reagent grade and used as purchased. All solvents were dried and distilled before use. The products were purified by flash chromatography on silica gel and a mixture of EtOAc and petroleum ether was generally used as eluent. IR spectra were determined on a PerkinElmer 683 instrument. UV-visible spectra at room temperature were measured in DMSO solution using a TU-1901 double-beam UV-visible spectrophotometer. <sup>1</sup>H NMR spectra (400 MHz) were recorded on a Bruker Avance 400 MHz spectrometer with tetramethylsilane as an internal standard in DMSO-d<sub>6</sub> as solvent. <sup>13</sup>C NMR spectra (100 MHz) were recorded on a Bruker Avance 400 MHz spectrometer in DMSO-d<sub>6</sub> as solvent. Melting points are uncorrected.

### General Procedure for the Copper-Catalyzed Tandem Reaction of 2-Iodoanilines with Isothiocyanates under Ligand- and Solvent-Free Conditions

A mixture of 2-iodobenzenamine (1.0 mmol), isothiocyanate (1.1 mmol), Bu<sub>3</sub>N (1.1 mmol) and CuSO<sub>4</sub> (0.01 mmol) was stirred

under an air atmosphere at 80 °C for 1.5–4 h. After cooling to room temperature, the mixture was diluted with ethyl acetate (5 ml) and filtered. The filtrate was removed under reduced pressure to give the crude product, which was further purified by silica gel chromatography (petroleum ether–ethyl acetate as eluent) to yield the corresponding 2-aminobenzothiazoles.

Compounds **3a–3i**, **3k–3n** and **3r–3u** are known compounds and were characterized by comparing their melting point, <sup>1</sup>H NMR, <sup>13</sup>C NMR and IR spectra with those found in the literature.

#### *N*-(4-Fluorophenyl)-6-(trifluoromethyl)benzo[*d*]thiazol-2-amine (**3j**)

White solid, m.p. 200–201 °C. IR (KBr)  $\nu$  (cm<sup>-1</sup>) 2957, 1624, 1576, 1468, 1459, 1328, 1307, 1147, 1113. UV (DMSO, nm): 306, 241. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  10.83 (s, 1 H, NH), 8.28 (s, 1 H, 7-CH), 7.90–7.86 (m, 2 H, 2'-CH), 7.75 (d, *J* = 8.0 Hz, 1 H, 4-CH), 7.63 (d, *J* = 8.0 Hz, 1 H, 5-CH), 7.26 (t, *J* = 8.8 Hz, 2 H, 3'-CH). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>)  $\delta$  164.9 (C=N), 158.2 (d, <sup>1</sup>*J*<sub>CF</sub> = 238.0 Hz) (C-F<sub>arom</sub>), 155.4 (C-N<sub>arom</sub>), 137.1 (C-NH<sub>arom</sub>), 131.2 (C-S<sub>arom</sub>), 125.1 (q, <sup>1</sup>*J*<sub>CF</sub> = 270.0 Hz) (CF<sub>3</sub>), 123.2 (q, <sup>3</sup>*J*<sub>CF</sub> = 4.0 Hz) (C<sub>arom</sub>), 122.9 (q, <sup>2</sup>*J*<sub>CF</sub> = 32.0 Hz) (F<sub>3</sub>C-C<sub>arom</sub>), 120.4 (d, <sup>3</sup>*J*<sub>CF</sub> = 8.0 Hz) (2C<sub>arom</sub>), 119.5 (C<sub>arom</sub>), 119.2 (q, <sup>3</sup>*J*<sub>CF</sub> = 4.0 Hz) (C<sub>arom</sub>), 116.0 (d, <sup>2</sup>*J*<sub>CF</sub> = 23.0) (2C<sub>arom</sub>). Anal. calcd for C<sub>14</sub>H<sub>8</sub>N<sub>2</sub>F<sub>4</sub>S: C, 53.84; H, 2.58; found: C, 53.58; H, 2.74.

**N-(4-Methoxyphenyl)-6-chlorobenzothiazol-2-amine (3o)**

White solid, m.p. 185–187 °C. IR (KBr)  $\nu$  (cm<sup>-1</sup>) 3202, 2958, 1628, 1578, 1475, 1452, 1321, 1301, 1141, 1120. UV (DMSO, nm): 300, 216. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  10.28 (s, 1 H, NH), 7.80 (s, 1 H, 7-CH), 7.57 (d, *J* = 8.8 Hz, 2 H, 2'-CH), 7.43 (d, *J* = 8.4 Hz, 1 H, 4-CH), 7.22 (d, *J* = 8.4 Hz, 1 H, 5-CH), 6.87 (d, *J* = 8.8 Hz, 2 H, 3'-CH), 3.66 (s, 3 H, OCH<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>)  $\delta$  162.8 (C=N), 154.9 (CH<sub>3</sub>O—C<sub>arom</sub>), 151.2 (C—N<sub>arom</sub>), 133.7 (C—NH<sub>arom</sub>), 131.6 (C—S<sub>arom</sub>), 125.9 (C—Cl<sub>arom</sub>), 125.7 (C<sub>arom</sub>), 120.6 (C<sub>arom</sub>), 119.9 (C<sub>arom</sub>), 119.7 (2C<sub>arom</sub>), 114.2 (2C<sub>arom</sub>), 55.2 (OCH<sub>3</sub>). Anal. calcd for C<sub>14</sub>H<sub>11</sub>N<sub>2</sub>SOCl: C, 57.82; H, 3.81; found: C, 57.59; H, 3.67.

**N-(4-Fluorophenyl)-6-chlorobenzothiazol-2-amine (3p)**

White solid, m.p. 213–214 °C. IR (KBr)  $\nu$  (cm<sup>-1</sup>) 3164, 2954, 1617, 1579, 1556, 1453, 1321, 1264, 1184, 1145, 1114. UV (DMSO, nm): 297, 223. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  10.63 (s, 1 H, NH), 7.99 (s, 1 H, 7-CH), 7.91–7.83 (m, 2 H, 2'-CH), 7.62 (d, *J* = 8.0 Hz, 1 H, 4-CH), 7.39 (d, *J* = 8.0 Hz, 1 H, 5-CH), 7.27 (t, *J* = 8.8 Hz, 2 H, 3'-CH). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>)  $\delta$  162.3 (C=N), 157.4 (d, <sup>1</sup>*J*<sub>CF</sub> = 237.0 Hz) (C—F<sub>arom</sub>), 150.9 (C—N<sub>arom</sub>), 136.8 (C—NH<sub>arom</sub>), 131.7 (C—S<sub>arom</sub>), 126.1 (C—Cl<sub>arom</sub>), 121.4 (C<sub>arom</sub>), 120.8 (C<sub>arom</sub>), 120.1 (C<sub>arom</sub>), 119.6 (d, <sup>3</sup>*J*<sub>CF</sub> = 7.0 Hz) (2C<sub>arom</sub>), 115.5 (d, <sup>2</sup>*J*<sub>CF</sub> = 22.0 Hz) (2C<sub>arom</sub>). Anal. calcd. for C<sub>13</sub>H<sub>8</sub>N<sub>2</sub>FSCL: C, 56.01; H, 2.89; found: C, 55.79; H, 2.63.

**N-(4-Chlorophenyl)-6-chlorobenzothiazol-2-amine (3q)**

White solid, m.p. 206–207 °C. IR (KBr)  $\nu$  (cm<sup>-1</sup>) 3165, 2944, 1617, 1579, 1522, 1450, 1364, 1263, 1243, 1186, 1143, 1115. UV (DMSO, nm): 304, 234. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  10.68 (s, 1 H, NH), 7.91 (s, 1 H, 7-CH), 7.81 (d, *J* = 7.6 Hz, 2 H, 2'-CH), 7.58 (d, *J* = 8.0 Hz, 1 H, 4-CH), 7.39 (d, *J* = 7.6 Hz, 2 H, 3'-CH), 7.32 (d, *J* = 8.0 Hz, 1 H, 5-CH). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>)  $\delta$  162.4 (C=N), 151.3 (C—N<sub>arom</sub>), 139.7 (C—NH<sub>arom</sub>), 132.2 (C—S<sub>arom</sub>), 129.3 (2C<sub>arom</sub>), 126.8 (C—Cl<sub>arom</sub>), 126.6 (C—Cl<sub>arom</sub>), 126.2 (C<sub>arom</sub>), 121.2 (C<sub>arom</sub>), 120.7 (C<sub>arom</sub>), 119.8 (2C<sub>arom</sub>). Anal. calcd. for C<sub>13</sub>H<sub>8</sub>N<sub>2</sub>SCl<sub>2</sub>: C, 52.88; H, 2.73; found: C, 52.67; H, 2.91.

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