1,3-Di-*n*-butylimidazolium Tribromide-Mediated Chemoselective Oxidative Cyclization of Benzothiazoyl Carbaimides: A Novel Approach toward the Synthesis of *N*-bis-benzothiazole Derivatives

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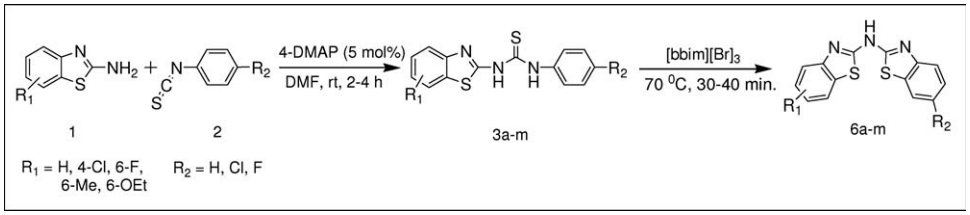

4-(*N*,*N*-Dimethylamino)pyridine is found to be an efficient catalyst for the synthesis of benzothiazoyl carbaimide derivatives using 2-aminobenzothiazoles and phenylisothiocyanates, which on treatment with ionic liquid [bbim][Br_3] at 70°C afforded exclusive formation of *N*-bis-benzothiazole derivatives in good yield.

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INTRODUCTION

2-Aminobenzothiazoles have received much attention due to their unique structures and interesting biological properties that lead to their use as anticonvulsant [1], analgesic [2], anti-tumor [3,4], antibacterial [5,6], and muscle relaxant agents [7]. Especially, interesting are bis-benzothiazole derivatives, which are known to possess remarkable amyloid-imaging [8], antifungal [9], vulcanization accelerators [10], and starting materials for various pharmaceuticals industry [11].

Generally, thioureas are prepared by direct reaction of isothiocyanate with amine. Using this approach, some benzothiazoyl carbaimides [12] have been synthesized. Although these synthetic methods are limited due to harsh reaction conditions, longer reaction time, low yields, and so forth, it is thus evident that there remains a wide scope for the development of clean and efficient methodologies for the preparation of benzothiazoyl carbaimide compounds.

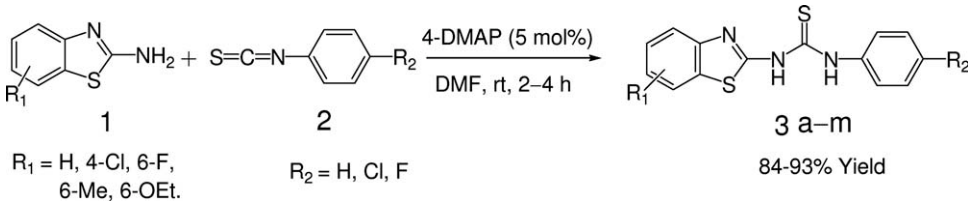
Methods for preparation of *N*-bis-benzothiazole are scarce in literature. Earlier Garin *et al*. [13] synthesized *N*-bis-benzothiazole from Hugershoff's synthesis using NBS and sulphuric acid as an oxidizing agent. But, this method has limitations such as use of stoichiometric or excess amount of toxic reagents like bromine. Although the reported methods provide good isolated yields, these methods suffer from tedious work-up and longer reaction time and not explored for different functionalities. In view of this, there is still a need to develop a general, efficient, and catalyst-free method for the synthesis of more functionalized *N*-bis-benzothiazole derivatives.

4-Dimethylaminopyridine (DMAP) is a nucleophilic catalyst, which catalyzes a variety of reactions examples of which include esterifications with anhydrides [14], Baylis–Hillman reaction [15], hydrosilylation [16], the Steglich rearrangement [17], Staudinger synthesis of β-lactams [18], and phosphorylation of amino and hydroxylgroups [19]. Recently ionic liquid has gained more attention in synthetic organic chemistry [20]. The ionic liquid having low volatility and unique catalytic activity have received considerable attention as ecofriendly solvent as well as catalyst and reagent in the context of green synthesis. Several reactions have been performed successfully showing their great potential as reaction media and some cases enhancing chemical reactivity and selectivity [21].

RESULT AND DISCUSSION

As part of our continuing efforts on the development of new routes for the preparation of biologically active 2-aminobenzothiazole derivatives [22], we report herein a novel method for the synthesis of benzothiazoyl carbaimides from 2-aminobenzothiazoles and phenylisothiocyanates using 4-dimethylaminopyridine (DMAP) as a catalyst, and a new ecofriendly version of Hugershoff's synthesis for chemoselective oxidative cyclization

Scheme 1. 4-DMAP-catalyzed synthesis of benzothiazoyl carbaimide



of benzothiazoyl carbaimides for the synthesis of symmetrical and unsymmetrical *N*-bis-benzothiazole derivatives by using ionic liquid.

Initially, we performed the reaction of 2-aminobenzothiazole **1** with phenyl isothiocyanate **2** in the presence of 4-DMAP (5 mol %) in *N*,*N*-dimethyl formamide. The reaction underwent smoothly at room temperature in 2 h affording benzothiazoyl carbaimide **3a** in 90% yield (Scheme 1).

These results encouraged us to extend this process for various substituted 2-aminobenzothiazoles and substituted phenyl isothiocyanates. Interestingly several 2-aminobenzothiazoles reacted readily with different phenyl isothiocyanates to produce corresponding benzothiazoyl carbaimides. The reaction conditions are compatible with various functionalities such as fluoro, chloro, and ethyl ether (Table 1).

Next, we examined the oxidative cyclization of benzothiazoyl carbaimide using new tribromide-based ionic liquid 1,3-di-*n*-butylimidazolium tribromide [bbim][Br_3] as a reagent of choice. 1,3-Di-*n*-butylimidazolium bromide **4** on drop wise addition of molecular bromine under stirring formed exothermally red liquid 1,3-di-*n*-butylimidazolium tribromide **5** (Scheme 2). Excess of bromine absorbed by **4** was completely removed under a high vacuum. IL **5** can be stored for several months without change of structure and loss of activity.

Subsequently, the reaction of benzothiazoyl carbaimide **3a** was performed in 1,3-di-*n*-butylimidazolium tribromide[bbim][Br_3] (**5**). The reaction was sluggish at room temperature. Surprisingly reaction proceeded well at 70°C giving *N*-bis-benzothiazole **6a** exclusively in 89% yield (Scheme 3).

The structure of product **6a** was determined on the basis of ^{1}H NMR spectrum. It shows only two doublets and two triplets with same coupling constant (J = 7.5 Hz), which are consistent with structure of **6a**. Other benzothiazoyl carbaimides also participated well in this reaction. The scope of above reaction is illustrated with respect to different functionalities, and the results are summarized in Table 2.

It is interesting to mention that the oxidative cyclization of benzothiazoyl carbaimide in ionic liquid **5** is chemoselective. It is known that the C_2 hydrogen atom of the 1,3-dialkylimidazolium cation ionic liquids (ILs) act as hydrogen bond donar [23]. Probably, reaction proceeds via coordination of C_2 proton of ionic liquid **5** with nitrogen of benzothiazole ring in **3** which prevents participation of nitrogen in ring cyclization, leading to product **6** chemoselectively (Scheme 4).

In conclusion, we have developed an efficient protocol for synthesis of benzothiazoyl carbaimides, and symmetrical and unsymmetrical *N*-bis-benzothiazole derivatives. This method can be classified as ''green'' as it uses mild reaction conditions, eliminates toxic bromine vapors, and avoids the use of organic solvents. This work is the first application of synthesis of these compounds using ionic liquid.

EXPERIMENTAL

General procedure for the synthesis of 1-(benzo[d]thiazol-2-yl)-3-phenylthiourea (3a). A mixture of 2-aminobenzothiazole (1.50 g, 1 mmol), phenyl isothiocynate (1.35 g, 1 mmol), and dimethyl amino pyridine (5 mol %) in DMF (8 mL) was stirrer at room temperature for 2.0 h, and the progress of the reaction was followed by TLC. After completion of the reaction, water (10 mL) was added to the reaction mixture and extracted with ethyl acetate (2 × 15 mL). The organic layer was separated and dried over anhydrous Na_2SO_4, and solvent was removed under reduced pressure. The crude product was purified by column chromatography (60–120 mesh) using (ethyl acetate: *n*-hexane, 10:90) to obtain **3a** (2.45 g, 86%) as a white powder.

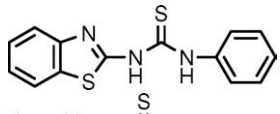
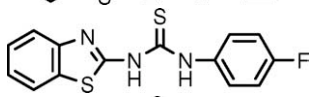
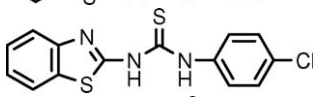
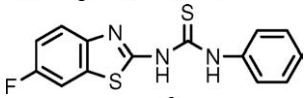
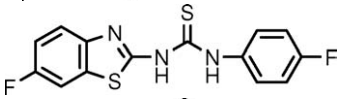
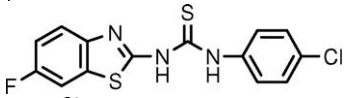
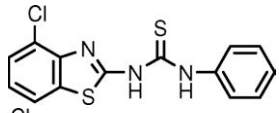
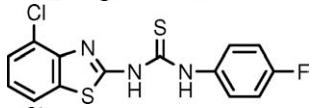
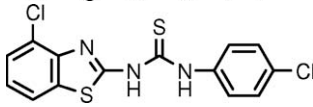
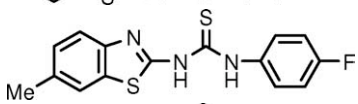
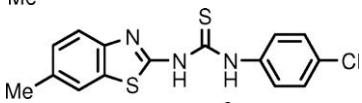
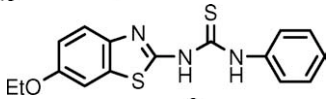
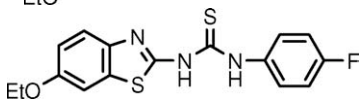
Preparation of 1,3-di-*n*-butylimidazoliumtribromide [bbim][Br_3] (5). In a fume cupboard, molecular bromine (0.97 mL, 0.019 mol) was added drop wise over 10 min to 1,3-di-*n*-butylimidazolium bromide (5.0 g, 0.019 mol) under stirring and cooling in a ice-bath affording a deep red liquid IL (**5**), and stirring was continued for 2 h. Under reduced pressure over 5 h at 60°C, 4.0 g (95.2 %) of the pure IL **5** was obtained as red oil.

^{1}H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 1.00 (t, J = 7.31 Hz, 6H), 1.35–1.43 (m, 4H), 1.86–1.93 (m, 4H), 4.26 (t, J = 7.31 Hz, 4H), 7.68 (s, 2H), 9.25 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 12.34, 18.20, 30.87, 48.49, 121.46, 134.90. ESI-MS (*m*/*z*): 181 (M-X_3); Anal. Calcd. For $C_{11}H_{21}Br_3N_2$: C, 31.16; H, 5.70; N, 6.61. found: C, 31.31; H, 5.25; N, 6.64.

Procedure for the synthesis of *N*-bis-benzothiazole (6). A mixture of benzothiazole carbamide (1 mmol) and 1,3-di-*n*-butylimidazolium bromide (1 mL) was heated at 70°C for 30 min, and the progress of the reaction was monitor by TLC.

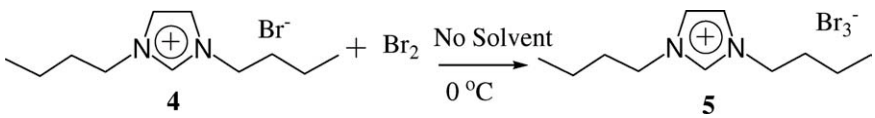
Table 1

DMAP catalysed synthesis of benzothiazoyl carbaimide.[a]

Entry	R^1	R^2	Product[b] (**3**)	Time (h)	Yield[c](%)
a	H	H		3.0	90
b	H	*p*-F		3.5	84
c	H	*p*-Cl		3.5	85
d	6-F	H		3.5	91
e	6-F	*p*-F		5.0	84
f	6-F	*p*-Cl		4.0	86
g	4-Cl	H		3.5	90
h	4-Cl	*p*-F		4.5	88
i	4-Cl	*p*-Cl		5.0	83
j	6-Me	*p*-F		3.0	89
k	6-Me	*p*-Cl		3.0	93
l	6-OEt	H		3.5	91
m	6-OEt	*p*-F		3.5	83

[a] Reaction was performed at 1 mmol scale.
[b] All the products were characterised by ^{1}H NMR, IR, and mass spectroscopy.
[c] Yield refers to pure product after column chromatography.

Scheme 2. Preparation of 1,3-di-*n*-butylimidazolium tribromide [bbim]Br_3.



4 **5**

Scheme 3. Synthesis of *N*-bis-benzothiazole.

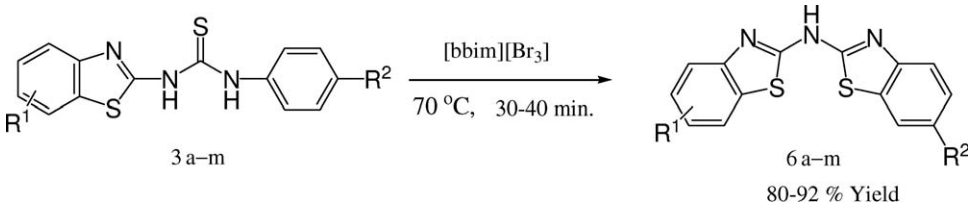
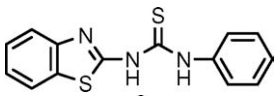
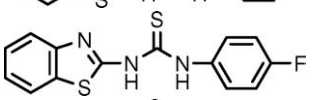
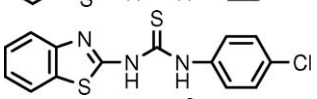
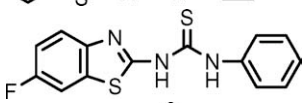
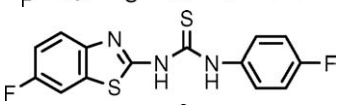
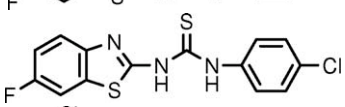
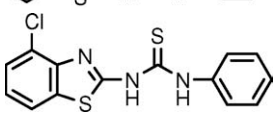
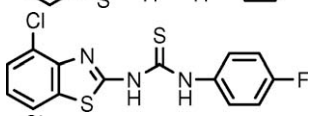
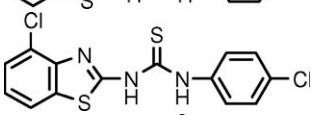
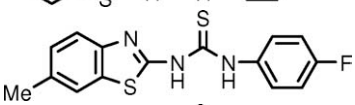
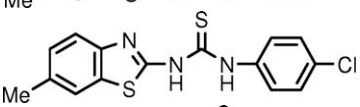
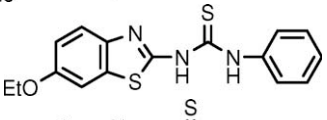
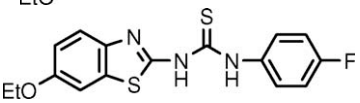


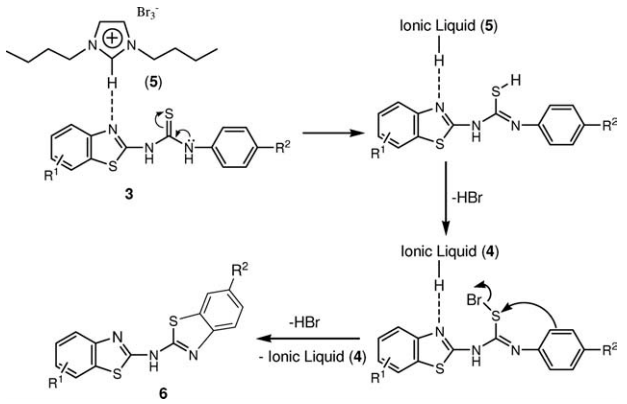
Table 2

Chemoselective oxidative cyclization of thiourea using ionic liquid [bbim][Br3].[a]

Entry	Thiourea (**3**)	Product[b] (**6**)	Time (min)	Yield[c](%)
a	**3a**		30	89
b	**3b**		30	82
c	**3c**		35	86
d	**3d**		40	83
e	**3e**		40	85
f	**3f**		35	80
g	**3g**		35	86
h	**3h**		40	84
i	**3i**		35	80
j	**3j**		35	87
k	**3k**		30	84
l	**3l**		30	90
m	**3m**		30	92

[a] All reaction were run with 1 mmol of thiourea (**3**) in 1 mL ionic liquid [bbim][Br_3] at 70°C.
[b] All compounds showed satisfactory ^{1}H NMR, IR, and mass spectral data.
[c] Isolated yield based on thiourea (**3**).

Scheme 4. Plausible reaction mechanism of chemoselective oxidative cyclization.



After completion of the reaction, chloroform was added in to the reaction mixture and product got separated out. After filtration, the solid product was purified by recrystallization using ethanol as a solvent to give the corresponding *N*-bis-benzothiazole derivatives. The chloroform filtrate was evaporated under reduced pressure to give ionic liquid and recycles repeated for three times.

1-(Benzo[d]thiazol-2-yl)-3-phenylthiourea (3a). White solid, mp 201–203°C. IR (KBr) ν_{max} = 3154, 2986, 1565, 1516, 1441, 1369, 1256, 1183, 685, 641 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO) δ = 7.17 (t, *J* = 6.58 Hz, 1H), 7.24 (t, *J* = 7.40 Hz, 1H), 7.36 (t, *J* = 7.40 Hz, 3H), 7.61 (s, 1H), 7.66–7.76 (m, 4H), 11.97 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ 118.74, 120.17, 122.45, 124.02, 125.04, 127.26, 130.15, 137.57, 145.66, 151.64, 157.82. ESI-MS (*m/z*): 286 (M+H); Anal. Calcd. For $C_{14}H_{11}N_3S_2$: C, 58.92; H, 3.89; N, 14.72. Found: C, 58.93; H, 3.85; N, 14.73.

1-(Benzo[d]thiazol-2-yl)-3-(p-fluorophenyl) thiourea (3b). White solid, mp 194–196°C. IR (KBr) ν_{max} = 3140, 2959, 1576, 1552, 1524, 1446, 1369, 1265, 1190, 828, 750, 696, 606 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.07 (t, *J* = 8.05 Hz, 2H), 7.24 (t, *J* = 7.16 Hz, 1H), 7.36 (t, *J* = 7.16 Hz, 1H), 7.60 (s, 1H), 7.63–7.76 (m, 4H), 12.07 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 113.74, 114.03, 120.22, 122.47, 123.18, 124.67, 125.07, 133.77, 156.89, 160.19, 172.12, 178.45. ESI-MS (*m/z*): 304 (M+H); Anal. Calcd. For $C_{14}H_{10}FN_3S_2$: C, 55.43; H, 3.32; N, 13.85. Found: C, 55.44; H, 3.30; N, 13.86.

1-(Benzo[d]thiazol-2-yl)-3-(p-chlorophenyl) thiourea (3c). White solid, mp 193–194°C. IR (KBr) ν_{max} = 3170, 3027, 1568, 1522, 1488, 1441, 1365, 1262, 1189, 1088, 1014, 755, 653 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.24 (t, *J* = 7.74 Hz, 1H), 7.29–7.41 (m, 3H), 7.59 (d, *J* = 7.55 Hz, 1H), 7.65–7.77 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 118.90, 120.95, 121.15, 124.70, 125.30, 126.96, 127.84, 129.98, 136.10, 152.15, 172.84, 178.30. ESI-MS (*m/z*): 320 (M+H); Anal. Calcd. For $C_{14}H_{10}ClN_3S_2$: C, 52.57; H, 3.15; N, 13.14.found: C, 52.53; H, 3.12; N, 13.16.

1-(6-Fluorobenzo[d]thiazol-2-yl)-3-phenylthiourea (3d). White solid, mp 196–198°C. IR (KBr) ν_{max} = 3155, 3000, 1569, 1527, 1457, 1381, 1251, 1190, 854, 692, 637 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.10 (dt, *J* = 8.87 and 2.45 Hz, 1H), 7.20 (t, *J* = 8.12 Hz, 1H), 7.37 (t, *J* = 7.74 Hz, 2H), 7.43 (dd, *J* = 8.12 and 2.07 Hz, 1H), 7.54–7.61 (m, 2H), 7.67 (d, *J* = 7.93 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 106.50, 111.97, 113.38, 117.58, 123.32, 124.12, 124.69, 127.62, 137.95, 156.52, 161.90, 179.03. ESI-MS (*m/z*): 304 (M+H); Anal. Calcd. For $C_{14}H_{10}FN_3S_2$: C, 55.43; H, 3.32; N, 13.85. Found: C, 55.44; H, 3.30; N, 13.86.

1-(6-Fluorobenzo[d]thiazol-2-yl)-3-(p-fluorophenyl) thiourea (3e). White solid, mp 204–206°C. IR (KBr) ν_{max} = 3167, 3017, 1567, 1532, 1506, 1459, 1250, 1195, 814, 686, 604 cm^{-1}. ^1H NMR (300MHz, $CDCl_3$ + DMSO): δ = 7.01–7.16 (m, 3H), 7.45 (d, *J* = 7.93 Hz, 1H), 7.54–7.75 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 107.04, 113.21, 113.56, 114.30, 114.61, 125.53, 133.67, 148.81, 159.40, 160.80, 168.91, 179.73. ESI-MS (*m/z*): 322 (M+H); Anal. Calcd. For $C_{14}H_9F_2N_3S_2$: C, 52.32; H, 2.82; N, 13.08. Found: C, 52.34; H, 2.80; N, 13.08.

1-(p-Chlorophenyl)-3-(6-fluorobenzo[d] thiazol-2-yl) thiourea (3f). White solid, mp 203–205°C. IR (KBr) ν_{max} = 3171, 3018, 1566, 1533, 1489, 1461, 1313, 1252, 1196, 1089, 1012, 823, 726 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.10 (dt, *J* = 8.68 and 2.45 Hz, 1H), 7.26 (d, *J* = 8.68 Hz, 2H), 7.42 (dd, *J* = 7.93 and 2.26 Hz, 1H), 7.45–7.54 (m, 2H), 7.66 (d, *J* = 8.68 Hz, 1H), 9.40 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 108.10, 114.15, 123.41, 125.96, 126.60, 126.81, 127.96, 129.35, 136.20, 146.15, 161.96, 174.12. ESI-MS (*m/z*): 338 (M+H); Anal. Calcd. For $C_{14}H_9ClFN_3S_2$: C, 49.77; H, 2.69; N, 12.44. Found: C, 49.85; H, 2.67; N, 12.46.

1-(4-Chlorobenzo[d]thiazol-2-yl)-3-phenylthiourea (3g). White solid, mp 198–200°C. IR (KBr) ν_{max} = 3163, 3015, 1566, 1523, 1453, 1412, 1253, 1185, 733, 690, 644 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.20 (dt, *J* = 7.93 and 2.07 Hz, 2H), 7.33–7.43 (m, 3H), 7.68 (t, *J* = 8.30 Hz, 2H), 7.76 (d, *J* = 7.93 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 118.09, 118.74, 120.36, 121.01, 122.28, 123.22, 124.46, 125.09, 127.53, 131.20, 148.28, 166.62. ESI-MS (*m/z*): 320 (M+H); Anal. Calcd. For $C_{14}H_{10}ClN_3S_2$: C, 52.57; H, 3.15; N, 13.14. Found: C, 52.67; H, 3.13; N, 13.17.

1-(4-Chlorobenzo[d]thiazol-2-yl)-3-(p-fluorophenyl) thiourea (3h). White solid, mp 202–204°C. IR (KBr) ν_{max} = 3273, 3048, 1639, 1537, 1452, 1413, 1303, 1270, 1105, 880, 724, 683, 605 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 6.92 (t, *J* = 7.92 Hz, 1H), 7.19 (dd, *J* = 7.93 and 0.94 Hz, 2H), 7.37–7.58 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ 114.15, 114.45, 118.30, 120.65, 121.27, 124.71, 125.69, 125.81, 131.36, 148.41, 167.00. ESI-MS (*m/z*): 338 (M+H); Anal. Calcd. For $C_{14}H_9ClFN_3S_2$: C, 49.77; H, 2.69; N, 12.44. Found: C, 49.85; H, 2.67; N, 12.46.

1-(4-Chlorobenzo[d]thiazol-2-yl)-3-(p-chlorophenyl) thiourea (3i). White solid, mp 207–209°C. IR (KBr) ν_{max} = 3166, 3016, 1565, 1524, 1491, 1455, 1411, 1258, 1188, 1091, 1017, 825, 684 cm^{-1}. ^1H NMR (300MHz, $CDCl_3$ + DMSO): δ = 7.21 (t, *J* = 7.80 Hz, 1H), 7.34 (d, *J* = 8.78 Hz, 2H), 7.40 (dd, *J* = 7.80 and 0.97 Hz, 1H), 7.67 (d, *J* = 7.80 Hz, 2H), 7.77 (dd, *J* = 7.80 and 0.97 Hz, 2H), 12.17 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 118.87, 123.39, 123.69, 125.27, 126.78, 127.63, 136.12, 139.02, 144.94, 146.65, 158.07, 173.10. ESI-MS (*m/z*): 355 (M+H); Anal. Calcd. For $C_{14}H_9Cl_2N_3S_2$: C, 47.46; H, 2.56; N, 11.86. Found: C, 47.60; H, 2.54; N, 11.90.

1-(p-Fluorophenyl)-3-(6-methylbenzo[d] thiazol-2-yl) thiourea (3j). White solid, mp 186–188°C. IR (KBr) ν_{max} = 3172, 3022, 1576, 1524, 1464, 1362, 1264, 1192, 810, 690, 605

cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 2.45 (s, 3H), 7.07 (t, *J* = 8.49 Hz, 2H), 7.17 (d, *J* = 8.68 Hz, 1H), 7.49 (s, 2H), 7.60–7.74 (m, 3H), 11.98 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 19.82, 106.98, 112.09, 114.01, 115.38, 118.89, 119.73, 125.80, 130.68, 155.60, 157.92, 164.72, 170.23; ESI-MS (*m/z*): 318 (M+H); Anal. Calcd. For $C_{15}H_{12}FN_3S_2$: C, 56.76; H, 3.81; N, 13.24. Found: C, 55.77; H, 3.80; N, 13.25.

1-(p-Chlorophenyl)-3-(6-methylbenzo[d] thiazol-2-yl) thiourea (3k). White solid, mp 180–182°C. IR (KBr) ν_{max} = 3168, 3020, 1569, 1525, 1489, 1462, 1365, 1261, 1192, 1088, 1015, 809, 711, 668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 2.45 (s, 3H), 7.17 (d, *J* = 8.30 Hz, 1H), 7.31 (d, *J* = 8.49 Hz, 2H), 7.48 (s, 2H), 7.70 (d, *J* = 8.49 Hz, 3H), 12.07 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 19.80, 105.74, 113.96, 114.92, 118.68, 119.52, 124.97, 130.01, 156.48, 156.79, 163.90, 169.84. ESI-MS (*m/z*): 334 (M+H); Anal. Calcd. For $C_{15}H_{12}ClN_3S_2$: C, 53.96; H, 3.62; N, 12.59. Found: C, 54.05; H, 3.61; N, 12.61.

1-(6-Ethoxybenzo[d]thiazol-2-yl)-3-phenylthiourea (3l). White solid, mp 168–170°C. IR (KBr) ν_{max} = 3191, 3029, 1556, 1527, 1493, 1461, 1384, 1343, 1257, 1194, 1061, 696, 640 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 1.44 (t, *J* = 6.98 Hz, 3H), 4.06 (q, *J* = 6.98 Hz, 2H), 6.93 (dd, *J* = 8.87 and 2.45 Hz, 1H), 7.15 (s, 1H), 7.31 (t, *J* = 7.93 Hz, 2H), 7.38 (d, *J* = 7.74 Hz, 1H), 7.45–7.57 (m, 3H), 7.68 (d, *J* = 7.93 Hz, 1H), 9.08 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 13.70, 62.86, 104.29, 113.98, 123.10, 123.90, 127.46, 137.62, 137.97, 149.48, 154.79, 168.48, 170.67, 178.90. ESI-MS (*m/z*): 330 (M+H); Anal. Calcd. For $C_{16}H_{15}N_3OS_2$: C, 58.33; H, 4.59; N, 12.76. Found: C, 58.35; H, 4.57; N, 12.76.

1-(6-Ethoxybenzo[d]thiazol-2-yl)-3-(p-fluorophenyl) thiourea (3m). White solid, mp 173–175°C. IR (KBr) ν_{max} = 3174, 3023, 2970, 2926, 1566, 1533, 1505, 1459, 1260, 1206, 1060, 815, 680, 607 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 1.40 (t, *J* = 7.16 Hz, 3H), 4.03 (q, *J* = 7.16 Hz, 2H), 6.90 (dd, *J* = 8.95 and 2.68 Hz, 1H), 7.04 (t, *J* = 8.05 Hz, 2H), 7.19 (s, 1H), 7.47 (s, 1H), 7.60–7.66 (m, 2H), 7.80–7.85 (m, 1H), 11.85 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 14.54, 63.85, 105.13, 114.91, 122.45, 125.43, 125.56, 128.47, 128.56, 129.90, 135.28, 155.61, 162.86, 171.73. ESI-MS (*m/z*): 348 (M+H); Anal. Calcd. For $C_{16}H_{14}FN_3OS_2$: C, 55.31; H, 4.06; N, 12.09. Found: C, 55.32; H, 4.05; N, 12.10.

Di(benzo[d]thiazol-2-yl)amine (6a). White solid, mp 246–248°C. IR (KBr) ν_{max} = 3030, 2925, 1601, 1541, 1489, 1438, 1280, 1170, 930, 886, 805, 749, 684 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.18 (t, *J* = 7.55 Hz, 2H), 7.34 (t, *J* = 7.55 Hz, 2H), 7.60 (d, *J* = 7.55 Hz, 2H), 7.70 (d, *J* = 7.55 Hz, 2H), 12.54 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 117.32, 120.42, 121.96, 125.17, 128.16, 146.98, 172.69. ESI-MS (*m/z*): 284 (M+H); Anal. Calcd. For $C_{14}H_9N_3S_2$: C, 59.34; H, 3.20; N, 14.83. Found: C, 59.36; H, 3.18; N, 14.84.

N-(6-Chlorobenzo[d]thiazol-2-yl)benzo[d] thiazol-2-amine (6c), White solid, mp 205–207°C. IR (KBr) ν_{max} = 3162, 2927, 1681, 1590, 1570, 1522, 1488, 1439, 1261, 1189, 1014, 893, 835, 753, 652 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.24 (t, *J* = 7.93 Hz, 1H), 7.29–7.41 (m, 3H), 7.58 (s, 1H), 7.69 (d, *J* = 8.68 Hz, 2H), 12.01 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 118.30, 119.98, 120.92, 121.01, 123.80, 124.10, 125.10, 125.92, 128.74, 130.05, 141.30, 151.30, 173.80. ESI-MS (*m/z*): 318 (M+H); Anal. Calcd. For $C_{14}H_8ClN_3S_2$: C, 52.91; H, 2.54; N, 13.22. Found: C, 52.99; H, 2.52; N, 13.25.

N-(Benzo[d]thiazol-2-yl)-6-fluorobenzo[d] thiazol-2-amine (6d), White solid, mp 269–271°C. IR (KBr) ν_{max} = 3169, 3033, 1605, 1545, 1498, 1454, 1306, 1278, 1251, 1097, 846, 751, 614 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.08 (dt, *J* = 8.87 and 2.45 Hz, 1H), 7.18 (t, *J* = 7.36 Hz, 1H), 7.34 (t, *J* = 7.17 Hz, 1H), 7.43 (dd, *J* = 8.12 and 2.64 Hz, 1H), 7.54–7.71 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 106.15, 112.98, 119.95, 122.84, 123.38, 124.10, 124.53, 125.10, 126.89, 135.10, 146.15, 155.76, 173.80. ESI-MS (*m/z*): 302 (M+H); Anal. Calcd. For $C_{14}H_8FN_3S_2$: C, 55.80; H, 2.68; N, 13.94. Found: C, 55.81; H, 2.67; N, 13.95.

Bis(6-fluorobenzo[d]thiazol-2-yl)amine (6e), White solid, mp 291–293°C. IR (KBr) ν_{max} = 3166, 3067, 2943, 1610, 1549, 1456, 1305, 1252, 1195, 849, 650 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.08 (dt, *J* = 8.95 and 2.68 Hz, 2H), 7.43 (dd, *J* = 8.05 and 1.79 Hz, 2H), 7.58 (dd, *J* = 8.95 and 4.47 Hz, 2H), 12.41 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 108.10, 113.05, 124.68, 130.10, 148.74, 158.93, 172.78. ESI-MS (*m/z*): 320 (M+H); Anal. Calcd. For $C_{14}H_7F_2N_3S_2$: C, 52.65; H, 2.21; N, 13.16. Found: C, 52.66; H, 2.19; N, 13.17.

N-(6-Chlorobenzo[d]thiazol-2-yl)-6-fluorobenzo[d]thiazol-2-amine (6f), White solid, mp 295–297°C. IR (KBr) ν_{max} = 3210, 3072, 2926, 1606, 1541, 1489, 1450, 1309, 1250, 1197, 1097, 854, 807, 730, 618 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.10 (dt, *J* = 9.25 and 1.88 Hz, 1H), 7.31 (dd, *J* = 8.68 and 1.70 Hz, 1H), 7.45 (d, *J* = 7.55 Hz, 1H), 7.56 (dd, *J* = 8.68 and 1.70 Hz, 2H), 7.67–7.81 (m, 1H), 12.53 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 107.73, 112.98, 123.58, 124.96, 125.12, 125.83, 126.43, 128.14, 130.30, 143.10, 144.70, 157.15, 172.25. ESI-MS (*m/z*): 336 (M+H); Anal. Calcd. For $C_{14}H_7ClFN_3S_2$: C, 50.07; H, 2.10; N, 12.51. Found: C, 50.15; H, 2.09; N, 12.54.

N-(Benzo[d]thiazol-2-yl)-4-chlorobenzo[d] thiazol-2-amine (6g), White solid, mp 172–174°C. IR (KBr) ν_{max} = 3159, 2929, 1678, 1610, 1575, 1520, 1491, 1436, 1265, 1191, 896, 840, 748, 654 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 7.08–7.26 (m, 2H), 7.32–7.42 (m, 2H), 7.44–7.55 (m, 1H), 7.63–7.76 (m, 2H), 12.74 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 117.94, 119.10, 120.48, 122.03, 122.26, 123.10, 124.27, 127.43, 128.10, 130.30, 144.80, 147.10, 171.98. ESI-MS (*m/z*): 318 (M+H); Anal. Calcd. For $C_{14}H_8ClN_3S_2$ C, 52.91; H, 2.54; N, 13.22. Found: C, 52.99; H, 2.52; N, 13.25.

4-Chloro-N-(6-fluorobenzo[d]thiazol-2-yl)benzo[d]thiazol-2-amine (6h), White solid, mp 184–186°C. IR (KBr) ν_{max} = 3215, 3084, 2932, 1609, 1545, 1492, 1454, 1402, 1318, 1252, 1201, 1099, 1015, 861, 809, 738, 623 cm^{-1}. ^1H NMR (300MHz, $CDCl_3$ + DMSO): δ = 6.92 (t, *J* = 7.93 Hz, 1H), 7.19 (dd, *J* = 7.93 and 0.75 Hz, 1H), 7.35–7.51 (m, 4H), 7.61 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 109.10, 112.96, 119.53, 121.15, 121.68, 122.29, 123.73, 124.93, 125.30, 130.93, 143.97, 147.81, 174.30. ESI-MS (*m/z*): 336 (M+H); Anal. Calcd. for $C_{14}H_7ClFN_3S_2$: C, 50.07; H, 2.10; N, 12.51. Found: C, 50.15; H, 2.09; N, 12.54.

N-(6-Fluorobenzo[d]thiazol-2-yl)-6-methylbenzo[d]thiazol-2-amine (6j). White solid, mp 209–211°C. IR (KBr) ν_{max} = 3133, 1609, 1562, 1500, 1454, 1401, 1303, 1276, 1251, 1194,

1115, 867, 839, 808, 617 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 2.44 (s, 3H), 7.08 (dt, *J* = 8.87 and 2.45 Hz, 1H), 7.15 (dd, *J* = 8.30 and 1.13 Hz, 1H), 7.39–7.51 (m, 2H), 7.60 (dd, *J* = 8.68 and 4.72 Hz, 1H), 7.75–7.83 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 19.47, 106.2, 106.46, 111.95, 112.18, 113.92, 115.33, 119.76, 125.76, 130.79, 155.56, 157.94, 164.70. ESI-MS (*m/z*): 316 (M+H); Anal. Calcd. for $C_{15}H_{10}FN_3S_2$: C, 57.12; H, 3.20; N, 13.32. Found: C, 57.14; H, 3.17; N, 13.33.

N-(6-Chlorobenzo[d]thiazol-2-yl)-6-methylbenzo[d]thiazol-2-amine (6k). White solid, mp 207–209°C. IR (KBr) ν_{max} = 3164, 2923, 2848, 1687, 1601, 1548, 1497, 1441, 1309, 1274, 1165, 1011, 898, 841, 746, 683 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 2.45 (s, 3H), 7.14 (d, *J* = 9.25 Hz, 1H), 7.29 (dd, *J* = 8.49 and 2.07 Hz, 1H), 7.43–7.51 (m, 2H), 7.57 (d, *J* = 8.49 Hz 1H), 7.67 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 19.46, 106.10, 115.38, 117.93, 120.25, 121.93, 123.63, 124.73, 125.84, 130.15, 143.24, 144.15, 170.94. ESI-MS (*m/z*): 332 (M+H); Anal. Calcd. for $C_{15}H_{10}ClN_3S_2$: C, 54.29; H, 3.04; N, 12.66. Found: C, 54.38; H, 3.02; N, 12.69.

N-(Benzo[d]thiazol-2-yl)-6-ethoxybenzo[d] thiazol-2-amine (6l). White solid, mp 191–193°C. IR (KBr) ν_{max} = 3448, 2967, 2920, 2852, 1601, 1562, 1502, 1457, 1260, 1219, 1060, 924, 742, 620 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 1.44 (t, *J* = 6.98 Hz, 3H), 4.06 (q, *J* = 6.98 Hz, 2H), 6.91 (dd, *J* = 8.87 and 2.45 Hz, 1H), 7.13–7.23 (m, 2H), 7.33 (t, *J* = 7.17 Hz 1H), 7.48–7.60 (m, 2H), 7.67 (d, *J* = 7.55 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 14.03, 63.17, 104.93, 113.79, 116.90, 118.49, 120.47, 121.86, 125.22, 128.76, 131.26, 147.48, 154.44, 170.16, 174.56. ESI-MS (*m/z*): 328 (M+H); Anal. Calcd. for $C_{16}H_{13}N_3OS_2$: C, 58.69; H, 4.00; N, 12.83. Found: C, 58.71; H, 3.98; N, 12.84.

6-Ethoxy-N-(6-fluorobenzo[d]thiazol-2-yl)benzo[d]thiazol-2-amine (6m). White solid, mp 192–194°C. IR (KBr) ν_{max} = 3173, 2926, 1705, 1605, 1550, 1453, 1393, 1260, 1216, 1055, 808, 652 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO): δ = 1.44 (t, *J* = 7.16 Hz, 3H), 4.05 (q, *J* = 7.16 Hz, 2H), 6.90 (dd, *J* = 8.95 and 2.68 Hz, 1H), 7.02–7.10 (m, 2H), 7.16 (s, 1H), 7.39 (dd, *J* = 8.05 and 2.68 Hz, 1H), 7.47–7.52 (m, 1H), 12.05 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ = 14.63, 63.58, 106.34, 108.25, 116.93, 121.95, 122.38, 123.27, 123.83, 124.15, 124.67, 145.30, 146.15, 158.70, 173.63. ESI-MS (*m/z*): 346 (M+H); Anal. Calcd. for $C_{16}H_{12}FN_3OS_2$: C, 55.63; H, 3.50; N, 12.17. Found: C, 55.65; H, 3.48; N, 12.17.

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