Synthesis of 2-Arylbenzothiazole Derivatives Based on Activated Carbon/Oxygen Oxidation Followed by Suzuki–Miyaura Coupling

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Abstract: A variety of 2-arylbenzothiazole derivatives were synthesized by the reaction of 2-aminobenzenethiol with substituted benzaldehydes in the presence of activated carbon and molecular oxygen system followed by Suzuki–Miyaura coupling using 2-phenylimidazole–$PdCl_2$ complex.

Key words: 2-arylbenzothiazole, activated carbon, molecular oxygen, Suzuki–Miyaura coupling, 2-phenylimidazole

2-Arylbenzothiazoles, -benzimidazoles and -benzothiazoles are a remarkably important class of biologically active compounds. Among these, 2-arylbenzothiazoles and their derivatives have attracted much attention in the field of pharmaceuticals, such as antitumor,[1] antimicrobial,[2] anti-inflammatory,[3] anticonvulsant,[4] anticancer,[5] antifungal,[6] antipsychotic,[7] diuretic,[8] schictosomicidal,[9] anthelmintic,[10] and antidiabetic.[11,12] Furthermore, recently, 2-hetero/aryl-substituted benzothiazoles have been investigated as materials due to their solvatochromic and fluorescence properties,[13] organic light-emitting diodes (OLEDs),[14] nonlinear optical (NLO) properties, and so on.[15,16]

Here, we report on the synthesis of a variety of 2-arylbenzothiazole derivatives by the reaction of 2-aminobenzenethiol with substituted benzaldehydes in the presence of activated carbon and molecular oxygen system[17] followed by Suzuki–Miyaura coupling catalyzed by 2-phenylimidazole–$PdCl_2$ complex.[18]

The reaction of 2-aminobenzenethiol (**1**) with halogenated benzaldehydes **2a**–**e** in the presence of 100 weight% of activated carbon under oxygen atmosphere in xylene at 50 °C for 24 hours was examined first. As shown in Scheme 1, 2-arylbenzothiazoles **3a**–**e** were obtained in 84–97% yield.

On the other hand, we have interest in cross-coupling reactions catalyzed by nitrogen-based ligand metal complexes. For example, we have reported 2-phenylimidazole–$PdCl_2$ and 2-phenylimidazoline–$PdCl_2$ complex catalyzed Mizoroki–Heck and Suzuki–Miyaura coupling reactions. In these reactions, 2-phenylimidazoline–$PdCl_2$ complex was found to exhibit higher reactivity than 2-phenylimidazole–$PdCl_2$ complex.[18] Thus, the reaction of the halogenated 2-arylbenzothiazoles **3a**–**e** with several boronic acids **A**–**I** was examined (Figure 1). The reaction proceeded in the presence of 0.5 mol% of $PdCl_2$ and 1 mol% of 2-phenylimidazole at 120 °C for 20–30 hours to afforded the coupling product in 76–98% yield (Table 1).

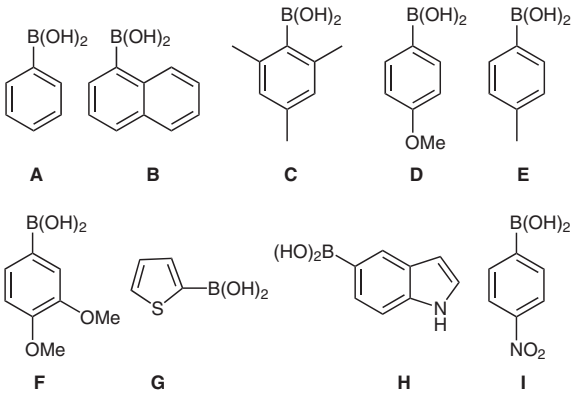
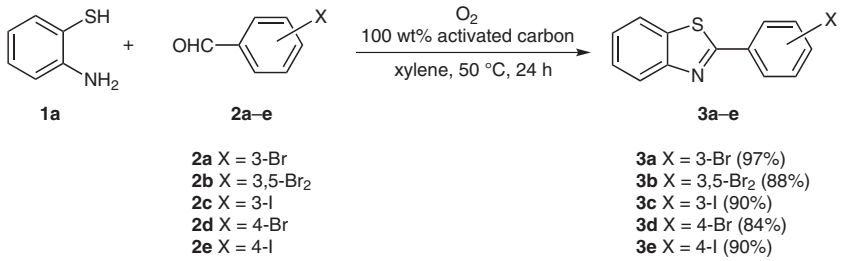


Figure 1 Boronic acids **A**–**I** used for coupling reactions



Scheme 1 Direct synthesis of 2-arylbenzothiazoles

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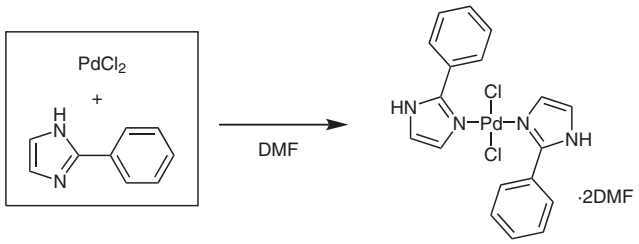
The structure of $PdCl_2$ and 2-phenylimidazole complex was confirmed by single-crystal X-ray diffractometry (XRD) study (Scheme 2).[19]

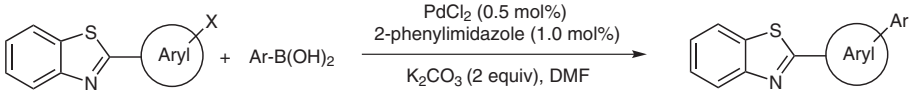


Scheme 2 Synthesis of 2-phenylimidazole–$PdCl_2$ complex

Compared with the previous methods to obtain the 2-arylbenzothiazoles, such as H_2O_2/CAN,[20] methanesufonic acid/SiO_2,[21] or the condensation of 2-aminobenzenthiol with *S*-methylthiamidinium salt in the presence of hexadecacyltrimethylammonium bromide (HTAB),[22,23] the present method is straightforward and gave much higher yield.

In summary, a variety of 2-arylbenzothiazole derivatives were synthesized by the reaction of 2-aminobenzenethiol with substituted benzaldehydes in the presence of activated carbon and molecular oxygen system followed by Suzuki–Miyaura coupling using 2-phenylimidazole–$PdCl_2$ complex. In all steps, operation was simple and chemical yields were high to excellent.

Table 1 Suzuki–Miyaura Cross-Coupling Reaction of 2-(3/4/5-Halophenyl)benzothiazole **3a–e** Using 2-Phenylimidazole–$PdCl_2$ Catalyst[a]



3a–e **A–l** **4aA–dl**, **4eG**

Ar = aryl/heteroaryl

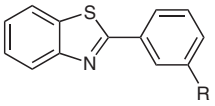
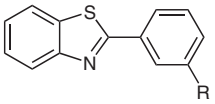
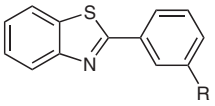
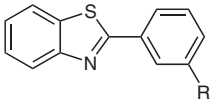
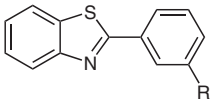
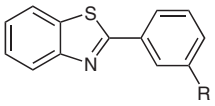
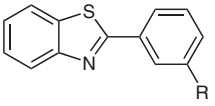
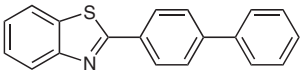
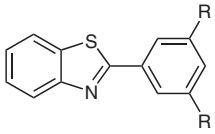
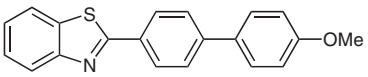
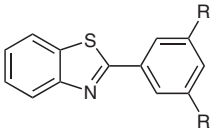
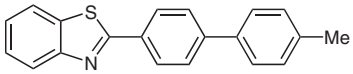
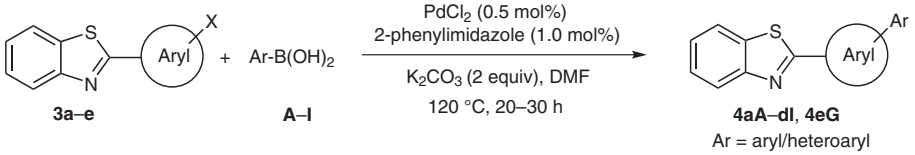
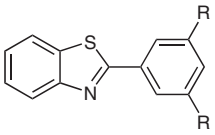
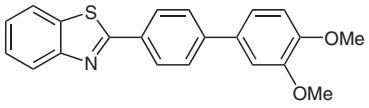
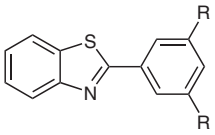
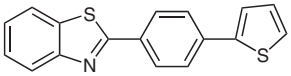
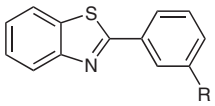
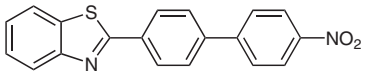
Entry	Product	Yield (%)[b]	Entry	Product	Yield (%)[b]
1	 **4aA**; R = phenyl	94 (from **3a**)[c]	10	 **4cF**; R = 3,4-dimethoxy phenyl	96 (from **3c**)[c]
2	 **4aB**; R = 1-naphthyl	98 (from **3a**)[d]	11	 **4cG**; R = 2-thienyl	98 (from **3c**)[c]
3	 **4aC**; R = 2,4,6-trimethylphenyl	76 (from **3a**)[c]	12	 **4cH**; R = 5-indolyl	98 (from **3c**)[e]
4	 **4aD**; R = 4-anisyl	92 (from **3a**)[c]	13	 **4dA** **4eA**	80 (from **3d**)[f] 95 (from **3e**)[c]
5[g]	 **4bA**; R = phenyl	88 (from **3b**)[h]	14	 **4dD**	96 (from **3d**)[i]
6[g]	 **4bD**; R = 4-anisyl	91 (from **3b**)[h]	15	 **4dE** **4eE**	86 (from **3d**)[c] 84 (from **3e**)[c]

Table 1 Suzuki–Miyaura Cross-Coupling Reaction of 2-(3/4/5-Halophenyl)benzothiazole **3a–e** Using 2-Phenylimidazole–$PdCl_2$ Catalyst[a] (continued)



3a–e **A–I** **4aA–dI, 4eG**
Ar = aryl/heteroaryl

Entry	Product	Yield (%)[b]	Entry	Product	Yield (%)[b]
7[g]	 **4bE**; R = 4-tolyl	97 (from **3b**)[h]	16	 **4dF** **4eF**	95 (from **3d**)[e] 94 (from **3e**)[e]
8	 **4bF**; R = 3,4-dimethoxyphenyl	89 (from **3b**)[h]	17	 **4dG** **4eG**	94 (from **3d**)[c] 95 (from **3e**)[c]
9	 **4cE**; R = 4-tolyl	96 (from **3c**)[c]	18	 **4dI**	90 (from **3d**)[j]

[a] Reaction conditions: Substrate **3** (1 equiv), arylboronic acid (1.5 equiv), $PdCl_2$ (0.5 mol%), ligand (1 mol%), K_2CO_3 (2 equiv), DMF, 120 °C.
[b] Isolated yield after column chromatographic purification.
[c] Reaction time: 24 h.
[d] Reaction time: 30 h.
[e] Reaction time: 23 h.
[f] Reaction time: 20 h.
[g] Using arylboronic acid (3 equiv), $PdCl_2$ (1 mol%), ligand (2 mol%), K_2CO_3 (4 equiv), DMF, 120 °C.
[h] Reaction time: 26 h.
[i] Reaction time: 21 h.
[j] Reaction time: 22 h.

All reactions were carried out in well cleaned and oven-dried glassware with magnetic stirring. Operations were performed under an atmosphere of dry argon using Schlenk and vacuum techniques. All starting materials were obtained from commercial sources and used without further purification, unless otherwise stated. Activated carbon (Charcoal Activated) was obtained from Tokyo Chemical Industry Co., Ltd (TCI). Melting points were measured by Yanaco MP-500D and are not corrected. ^1H and ^{13}C NMR spectra (400 and 100.6 MHz, respectively) were recorded on a Jeol JNM-LA 400 instrument using Me_4Si as an internal standard (0 ppm). Standard abbreviations are used to denote signal multiplicity. Mass spectra were measured using Thermo Quest LCQ DECA plus. Elemental analyses were carried out using Yanako CHN recorder MT-5. Preparative column chromatography was carried out using Fuji Silysia BW-820MH silica gel or YMC-GEL Silica (6 nm I-40–63 um). TLC was carried out on Merck 25 TLC aluminum sheets coated with silica gel 60 F_{254}.

2-(3-Bromophenyl)benzo[*d*]thiazole (3a)
A mixture of 2-aminothiophenol (**1a**; 2 g, 16 mmol), 3-bromobenzaldehyde (**2a**; 2.69 g, 16 mmol), and 100 wt% of activated carbon (370 mg) in xylene (25 mL) was placed in a 200 mL three-necked flask under an O_2 atmosphere and stirred at 50 °C for 29 h. The reaction mixture was then filtered over a Celite pad. After concentration of the filtrate, the product was isolated by silica gel column chromatography (hexane–EtOAc, 96:4) to afford **3a** as colorless needles (4.5 g, 97%); mp 93.4–93.9 °C (hexane–$CHCl_3$, 1:2) (Lit.[24] mp 91–93 °C); R_f = 0.5 (hexane–EtOAc, 9:1).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.28–8.27 (m, 1 H, ArH), 8.08 (d, *J* = 8.4 Hz, 1 H, ArH), 7.98 (d, *J* = 7.6 Hz, 1 H, ArH), 7.90 (d, *J* = 7.6 Hz, 1 H, ArH), 7.60 (d, *J* = 8.8 Hz, 1 H, ArH), 7.50 (t, *J* = 8.0 Hz, 1 H, ArH), 7.42–7.33 (m, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 166.1, 153.9, 135.4, 135.0, 133.7, 130.5, 130.2, 126.5, 126.1, 125.5, 123.4, 123.2, 121.7.

MS (ESI): *m*/*z* = 292 (M + 2 H^+), 290 (M + H^+).

2-(3,5-Dibromophenyl)benzo[*d*]thiazole (3b)
A mixture of 2-aminothiophenol (**1a**; 0.5 g, 4 mmol), 3,5-dibromobenzaldehyde (**2b**; 1.06 g, 4.0 mmol), and 100 wt% of activated carbon (1.06 g) in xylene (10 mL) was placed in a 100 mL three-necked flask under an O_2 atmosphere and stirred at 50 °C for 28 h. The reaction mixture was then filtered over a Celite pad. After concentration of the filtrate, the product was isolated by silica gel column chromatography (hexane–EtOAc, 96:4) to afford **3b** as colorless needles (1.3 g, 88%); mp 153.8–154.4 °C (hexane–$CHCl_3$, 1:2); R_f = 0.5 (hexane–EtOAc, 9:1).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 2 H, ArH), 8.07 (d, *J* = 8.4 Hz, 1 H, ArH), 7.91 (d, *J* = 7.6 Hz, 1 H, ArH), 7.77–7.75 (m, 1 H, ArH), 7.52 (t, *J* = 7.6 Hz, 1 H, ArH), 7.42 (t, *J* = 8.4 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 164.3, 153.8, 136.7, 136.0, 135.1, 129.0, 126.7, 125.9, 123.6, 123.5, 121.7.

MS (ESI): *m*/*z* = 372 (M + 4 H^+), 370 (M + 2 H^+), 368 (M + H^+).

Anal. Calcd for $C_{13}H_7Br_2NS$: C, 42.31; H, 1.91; N, 3.80. Found: C, 42.68; H, 1.41; N, 3.79.

2-(3-Iodophenyl)benzo[*d*]thiazole (3c)
A mixture of 2-aminothiophenol (**1a**; 500 mg, 4 mmol), 3-iodobenzaldehyde (**2c**; 930 mg, 4 mmol), and 100 wt% of activated carbon (930 mg) in xylene (10 mL) was placed in a 100 mL three-necked flask under an O_2 atmosphere and stirred at 50 °C for 24 h. The reaction mixture was then filtered over a Celite pad. After concentration of the filtrate, the product was isolated by silica gel column chromatography (hexane–EtOAc, 97:3) to afford **3c** as colorless needles (1.18 g, 90%); mp 108.1–108.9 °C (hexane–$CHCl_3$, 1:2); R_f = 0.5 (hexane–EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.47–8.46 (m, 1 H, ArH), 8.07 (d, *J* = 8.0 Hz, 1 H, ArH), 8.00 (d, *J* = 8.4 Hz, 1 H, ArH), 7.90 (d, *J* = 7.6 Hz, 1 H, ArH), 7.80 (d, *J* = 8.4 Hz, 1 H, ArH), 7.50 (t, *J* = 8.4 Hz, 1 H, ArH), 7.40 (t, *J* = 8.0 Hz, 1 H, ArH), 7.25–7.19 (m, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 165.9, 153.9, 139.7, 136.0, 135.4, 135.0, 130.5, 126.7, 126.5, 125.5, 123.4, 121.7, 94.7.

MS (ESI): *m*/*z* = 338 (M + H^+).

Anal. Calcd for $C_{13}H_8INS$: C, 46.31; H, 2.39; N, 4.15. Found: C, 46.52; H, 2.41; N, 4.26.

2-(4-Bromophenyl)benzo[*d*]thiazole (3d)
A mixture of 2-aminothiophenol (**1a**; 250 mg, 1.99 mmol), 4-bromobenzaldehyde (**2d**; 370 mg, 1.99 mmol), and 100 wt% of activated carbon (370 mg) in xylene (5 mL) was placed in a 100 mL three-necked flask under an O_2 atmosphere and stirred at 50 °C for 24 h. The reaction mixture was then filtered over a Celite pad. After concentration of the filtrate, the product was isolated by silica gel column chromatography (hexane–EtOAc, 96:4) to afford **3d** as colorless needles (0.49 g, 84%); mp 134.3–134.9 °C (hexane–$CHCl_3$, 1:2) (Lit.[25] mp 133–134 °C); R_f = 0.5 (hexane–EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.0 Hz, 1 H, ArH), 7.97–7.89 (m, 3 H, ArH), 7.64–7.61 (m, 2 H, ArH), 7.50 (t, *J* = 8.0 Hz, 1 H, ArH), 7.40 (t, *J* = 8.4 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 166.6, 154.0, 135.0, 132.5, 132.2, 128.9, 126.5, 125.4 (2 C), 123.3, 121.6.

MS (ESI): *m*/*z* = 292 (M + 2 H^+), 290 (M + H^+).

2-(4-Iodophenyl)benzo[*d*]thiazole (3e)
A mixture of 2-aminothiophenol (**1a**; 250 mg, 2.4 mmol), 4-iodobenzaldehyde (**2e**; 550 mg, 2.4 mmol), and 100 wt% of activated carbon (550 mg) in xylene (6 mL) was placed in a 100 mL three-necked flask under an O_2 atmosphere and stirred at 50 °C for 24 h. The reaction mixture was then filtered using Celite. After concentration of the filtrate, the product was isolated by silica gel column chromatography (hexane–EtOAc, 97:3) to afford **3e** as colorless needles (0.72 g, 90%); mp 156.6–157.2 °C (hexane–$CHCl_3$, 1:2) (Lit.[26] mp 134–135 °C); R_f = 0.5 (hexane–EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.0 Hz, 1 H, ArH), 7.90–7.79 (m, 5 H, ArH), 7.49 (t, *J* = 8.4 Hz, 1 H, ArH), 7.39 (t, *J* = 8.4 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 166.8, 154.0, 138.1, 134.9, 133.0, 128.9, 126.5, 125.4, 123.3, 121.6, 97.5.

MS (ESI): *m*/*z* = 338 (M + H^+).

Suzuki–Miyaura Cross-Coupling Reaction of 3-Bromophenylbenzothiazole 3a with Arylboronic Acids; General Procedure
K_2CO_3 (380 mg, 2.75 mmol) was added to a Schlenk tube equipped with a stirring bar and the tube was dried under vacuum and filled with argon, $PdCl_2$ (1.24 mg, 0.007 mmol), 2-phenylimidazole (2 mg, 0.014 mmol), 2-(3-bromophenyl)benzo[*d*]thiazole (**3a**; 397 mg 1.37 mmol), and arylboronic acid (2.06 mmol) in anhyd DMF (12 mL). Then the mixture was stirred at 120 °C for the indicated reaction time (Table 1) under argon atmosphere. The mixture was cooled and then poured over ice-water (250 mL) containing aq 1 M HCl (2 mL) and extracted with $CHCl_3$ (5 × 40 mL). The combined organic layers were washed with brine (2 × 30 mL) and dried (Na_2SO_4). Removal of solvent followed by column chromatographic purification (silica gel, hexane–$CHCl_3$) afforded the coupling product (Table 1).

2-(Biphenyl-3-yl)benzo[*d*]thiazole (4aA)
Yield: 0.372 g (94%); colorless needles; mp 116.9–117.7 °C (hexane–$CHCl_3$, 1:2); R_f = 0.6 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 1 H, ArH), 8.10–8.05 (m, 2 H, ArH), 7.91 (d, *J* = 7.6 Hz, 1 H, ArH), 7.70 (t, *J* = 8.0 Hz, 3 H, ArH), 7.58–7.37 (m, 6 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.9, 154.2, 142.2, 140.3, 135.1, 134.1, 129.7, 129.4, 128.9, 127.8, 127.3, 126.4, 126.3, 126.2, 125.2, 123.3, 121.6.

MS (ESI): *m*/*z* = 288 (M + H^+).

Anal. Calcd for $C_{19}H_{13}NS$: C, 79.41; H, 4.56; N, 4.87. Found: C, 79.01; H, 4.50; N, 4.90.

2-[3-(Naphthalen-1-yl)phenyl]benzo[*d*]thiazole (4aB)
Yield: 0.455 g (98%); colorless needles; mp 135.9–136.3 °C (hexane–$CHCl_3$, 1:2); R_f = 0.6 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (s, 1 H, ArH), 8.19–8.15 (m, 1 H, ArH), 8.06 (d, *J* = 8.4 Hz, 1 H, ArH), 7.93–7.87 (m, 4 H, ArH), 7.61–7.42 (m, 7 H, ArH), 7.37 (t, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.8, 154.1, 141.7, 139.2, 135.1, 133.8, 132.6, 131.5, 129.1, 128.9, 128.3, 128.1, 127.1, 126.4, 126.3 (2 C), 125.9, 125.7, 125.3, 125.2, 123.3, 121.6.

MS (ESI): *m*/*z* = 338 (M + H^+).

Anal. Calcd for $C_{23}H_{15}NS$: C, 81.87; H, 4.48; N, 4.15. Found: C, 81.41; H, 4.41; N, 4.24.

2-(2′,4′,6′-Trimethylbiphenyl-3-yl)benzo[*d*]thiazole (4aC)
Yield: 0.345 g (76%); colorless needles; mp 101.5–102.9 °C (hexane–$CHCl_3$, 1:2); R_f = 0.7 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (t, *J* = 8.8 Hz, 2 H, ArH), 7.89 (d, *J* = 7.2 Hz, 2 H, ArH), 7.55 (t, *J* = 8.0 Hz, 1 H, ArH), 7.48 (t, *J* = 7.6 Hz, 1 H, ArH), 7.39 (t, *J* = 7.6 Hz, 1 H, ArH), 7.27 (t, *J* = 7.6 Hz, 1 H, ArH), 6.97 (s, 2 H, ArH), 2.35 (s, 3 H, CH_3), 2.05 (s, 6 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 168.1, 154.2, 142.1, 138.0, 137.0, 135.9, 135.1, 133.9, 132.1, 129.2, 128.5, 128.2, 126.3, 125.8, 125.2, 123.2, 121.6, 21.0, 20.8.

MS (ESI): *m*/*z* = 330 (M + H^+).

Anal. Calcd for $C_{22}H_{19}NS$: C, 80.20; H, 5.81; N, 4.25. Found: C, 79.91; H, 5.58; N, 4.25.

2-(4′-Methoxybiphenyl-3-yl)benzo[*d*]thiazole (4aD)
Yield: 0.401 g (92%); pale yellow needles; mp 105.8–106.3 °C (hexane–$CHCl_3$, 1:2); R_f = 0.5 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (s, 1 H, ArH), 8.09 (d, *J* = 8.4 Hz, 1 H, ArH), 7.99 (d, *J* = 8.0 Hz, 1 H, ArH), 7.89 (d, *J* = 7.6 Hz, 1 H, ArH), 7.66–7.59 (m, 3 H, ArH), 7.53–7.47 (m, 2 H, ArH), 7.38 (t, *J* = 8.0 Hz, 1 H, ArH), 7.00 (d, *J* = 8.8 Hz, 2 H, ArH), 3.85 (s, 3 H, OCH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 168.0, 159.5, 154.1, 141.7, 135.1, 134.0, 132.7, 129.4, 129.2, 128.3, 126.3, 125.8, 125.7, 125.2, 123.2, 121.6, 114.3, 55.3.

MS (ESI): *m*/*z* = 318 (M + H^+).

Anal. Calcd for $C_{20}H_{15}NOS$: C, 75.68; H, 4.76; N, 4.41. Found: C, 75.74; H, 4.79; N, 4.58.

Suzuki–Miyaura Cross-Coupling Reaction of 3,5-Dibromophenylbenzothiazole 3b with Arylboronic Acids; General Procedure

K_2CO_3 (450 mg, 3.25 mmol) was added to a Schlenk tube equipped with a stirring bar and the tube was dried under vacuum and filled with argon, $PdCl_2$ (1.4 mg, 0.008 mmol), 2-phenylimidazole (2.3 mg, 0.016 mmol), 2-(3,5-dibromophenyl)benzo[*d*]thiazole (**3b**; 300 mg, 0.81 mmol), and arylboronic acid (2.43 mmol) in anhyd DMF (17 mL). Then the mixture was stirred at 120 °C for the indicated reaction time (Table 1) under argon atmosphere. The mixture was cooled and then poured over ice-water (250 mL) containing aq 1 M HCl (2 mL) and extracted with $CHCl_3$ (5 × 40 mL). The combined organic layers were washed with brine (2 × 30 mL) and dried (Na_2SO_4). Removal of solvent followed by column chromatographic purification (silica gel, hexane–$CHCl_3$) afforded the coupling product (Table 1).

2-[(3,5-Diphenyl)phenyl]benzo[*d*]thiazole (4bA)

Yield: 0.261 (88%); colorless needles; mp 161.8–162.2 °C (hexane–$CHCl_3$, 1:2); R_f = 0.6 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (s, 1 H, ArH), 8.27 (s, 1 H, ArH), 8.10 (d, *J* = 8.0 Hz, 1 H, ArH), 7.91–7.89 (m, 2 H, ArH), 7.72 (d, *J* = 7.2 Hz, 4 H, ArH), 7.49 (t, *J* = 8.4 Hz, 5 H, ArH), 7.43–7.36 (m, 3 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.8, 154.1, 142.7, 140.2, 135.1, 134.6, 128.9, 128.6, 127.9, 127.3, 126.3, 125.3, 125.1, 123.3, 121.6.

MS (ESI): *m*/*z* = 364 ($M + H^+$).

Anal. Calcd for $C_{25}H_{17}NS$: C, 41.61; H, 4.71; N, 3.85. Found: C, 41.58; H, 4.68; N, 3.93.

2-[(3,5-Dianisyl)phenyl]benzo[*d*]thiazole (4bD)

Yield: 0.312 g (91%); colorless needles; mp 160.2–160.8 °C (hexane–EtOAc, 1:3); R_f = 0.4 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (s, 1 H, ArH), 8.18 (s, 1 H, ArH), 8.10 (d, *J* = 8.4 Hz, 1 H, ArH), 7.90 (d, *J* = 7.6 Hz, 1 H, ArH), 7.81 (s, 1 H, ArH), 7.65 (d, *J* = 8.8 Hz, 4 H, ArH), 7.50 (t, *J* = 8.0 Hz, 1 H, ArH), 7.38 (t, *J* = 8.0 Hz, 1 H, ArH), 7.01 (d, *J* = 8.8 Hz, 4 H, ArH), 3.86 (s, 6 H, OCH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 168.1, 159.5, 154.1, 142.2, 135.1, 134.5, 132.8, 128.4, 127.7, 126.3, 125.2, 124.1, 123.2, 121.6, 114.3, 55.3.

MS (ESI): *m*/*z* = 424 ($M + H^+$).

Anal. Calcd for $C_{27}H_{21}NO_2S$: C, 76.57; H, 5.00; N, 3.31. Found: C, 76.37; H, 5.00; N, 3.47.

2-[(3,5-Ditolyl)phenyl]benzo[*d*]thiazole (4bE)

Yield: 0.308 g (97%); colorless needles; mp 184.4–184.8 °C (EtOAc–$CHCl_3$, 1:1); R_f = 0.6 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 8.4 Hz, 2 H, ArH), 8.10 (t, *J* = 8.0 Hz, 1 H, ArH), 7.92–7.86 (m, 2 H, ArH), 7.61 (t, *J* = 8.4 Hz, 4 H, ArH), 7.52–7.45 (m, 1 H, ArH), 7.40–7.34 (m, 1 H, ArH), 7.29 (t, *J* = 8.4 Hz, 4 H, ArH), 2.42 (s, 3 H, CH_3), 2.40 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 168.0, 154.2, 142.5, 137.7, 137.4, 135.1, 134.5, 129.6, 128.2, 127.1, 126.3, 125.2, 124.7, 123.3, 121.6, 21.1.

MS (ESI): *m*/*z* = 392 ($M + H^+$).

Anal. Calcd for $C_{27}H_{21}NS$: C, 41.83; H, 5.41; N, 3.58. Found: C, 41.61; H, 5.37; N, 3.67.

2-[3,5-Di(3,4-dimethoxyphenyl)]benzo[*d*]thiazole (4bF)

Yield: 0.350 g (89%); colorless prisms; mp 189.8–190.2 °C (EtOAc–$CHCl_3$, 1:1); R_f = 0.5 (hexane–EtOAc, 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (s, 1 H, ArH), 8.19 (s, 1 H, ArH), 8.12 (d, *J* = 8.0 Hz, 1 H, ArH), 7.93 (d, *J* = 7.6 Hz, 1 H, ArH), 7.82 (s, 1 H, ArH), 7.52 (t, *J* = 7.2 Hz, 1 H, ArH), 7.40 (t, *J* = 7.6 Hz, 1 H, ArH), 7.27 (d, *J* = 8.4 Hz, 2 H, ArH), 7.22 (s, 2 H, ArH), 7.00 (d, *J* = 8.4 Hz, 2 H, ArH), 4.00 (s, 6 H, OCH_3), 3.95 (s, 6 H, OCH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.9, 154.1, 149.2, 149.0, 142.5, 135.0, 134.4, 133.2, 128.1, 126.3, 125.3, 124.4, 123.2, 121.6, 119.7, 111.4, 110.5, 56.1, 55.9.

MS (ESI): *m*/*z* = 484 ($M + H^+$).

Anal. Calcd for $C_{29}H_{25}NO_4S$: C, 72.03; H, 5.21; N, 2.90. Found: C, 71.75; H, 5.18; N, 2.98.

Suzuki–Miyaura Cross-Coupling Reaction of 3-Iodophenylbenzothiazole 3c with Arylboronic Acids; General Procedure

K_2CO_3 (246 mg, 1.78 mmol) was added to a Schlenk tube equipped with a stirring bar and the tube was dried under vacuum and filled with argon, $PdCl_2$ (0.7 mg, 0.004 mmol), 2-phenylimidazole (1.3 mg, 0.009 mmol), 2-(3-iodophenyl)benzo[*d*]thiazole (**3c**; 300 mg, 0.89 mmol), and arylboronic acid (1.33 mmol) in anhyd DMF (10 mL). Then, the mixture was stirred at 120 °C for the indicated reaction time (Table 1) under argon atmosphere. The mixture was cooled and then poured over ice-water (300 mL) containing aq 1 M HCl (2 mL) and extracted with $CHCl_3$ (5 × 50 mL). The combined organic layers were washed with brine (2 × 30 mL) and dried (Na_2SO_4). Removal of solvent followed by column chromatographic purification (silica gel, hexane–$CHCl_3$) afforded the coupling product (Table 1).

2-(4′-Methylbiphenyl-3-yl)benzo[*d*]thiazole (4cE)

Yield: 0.25 g (96%); colorless prisms; mp 84.1–84.8 °C (hexane–EtOAc, 1:2); R_f = 0.6 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (s, 1 H, ArH), 8.09 (d, *J* = 8.4 Hz, 1 H, ArH), 8.02 (d, *J* = 7.6 Hz, 1 H, ArH), 7.89 (d, *J* = 7.6 Hz, 1 H, ArH), 7.68 (d, *J* = 7.6 Hz, 1 H, ArH), 7.58–7.46 (m, 4 H, ArH), 7.37 (t, *J* = 7.2 Hz, 1 H, ArH), 7.27 (d, *J* = 8.0 Hz, 2 H, ArH), 2.40 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 168.0, 154.2, 142.0, 137.6, 137.3, 135.1, 134.1, 129.6, 129.5, 129.4, 127.1, 126.3, 126.1, 126.0, 125.2, 123.2, 121.6, 21.1.

MS (ESI): *m*/*z* = 302 ($M + H^+$).

Anal. Calcd for $C_{20}H_{15}NS$: C, 79.70; H, 5.02; N, 4.65. Found: C, 79.54; H, 4.95; N, 4.63.

2-(3′,4′-Dimethoxybiphenyl-3-yl)benzo[*d*]thiazole (4cF)

Yield: 0.295 g (96%); colorless powder; mp 127.5–128.1 °C (hexane–EtOAc, 1:2); R_f = 0.3 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (s, 1 H, ArH), 8.10 (d, *J* = 8.4 Hz, 1 H, ArH), 8.01 (d, *J* = 7.6 Hz, 1 H, ArH), 7.91 (d, *J* = 8.0 Hz, 1 H, ArH), 7.67 (d, *J* = 8.0 Hz, 1 H, ArH), 7.55–7.48 (m, 2 H, ArH), 7.39 (t, *J* = 7.6 Hz, 1 H, ArH), 7.25–7.18 (m, 2 H, ArH), 6.97 (d, *J* = 8.4 Hz, 1 H, ArH), 3.98 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 168.0, 154.1, 149.2, 149.0, 142.0, 135.0, 134.0, 133.2, 129.4, 129.3, 126.3, 126.0, 125.8, 125.2, 123.2, 121.6, 119.6, 111.4, 110.4, 56.0, 55.9.

MS (ESI): *m*/*z* = 348 ($M + H^+$).

Anal. Calcd for $C_{21}H_{17}NO_2S$: C, 72.60; H, 4.93; N, 4.03. Found: C, 72.29; H, 4.80; N, 4.00.

2-[3-(Thiophen-2-yl)phenyl]benzo[*d*]thiazole (4cG)

Yield: 0.256 g (98%); pale yellow prisms; mp 109.7–110.1 °C (hexane–EtOAc, 1:2); R_f = 0.5 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 1 H, ArH), 8.09 (d, *J* = 8.4 Hz, 1 H, ArH), 7.96 (d, *J* = 7.6 Hz, 1 H, ArH), 7.90 (d, *J* = 8.0 Hz, 1 H, ArH), 7.70 (d, *J* = 7.6 Hz, 1 H, ArH), 7.51–7.31 (m, 5 H, ArH), 7.10 (t, *J* = 5.6 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.6, 154.1, 143.3, 135.3, 135.1, 134.2, 129.5, 128.3, 128.1, 126.5, 126.4, 125.4, 125.3, 124.7, 123.9, 123.3, 121.6.

MS (ESI): *m*/*z* = 294 (M + H$^+$).

Anal. Calcd for $C_{17}H_{11}NS_2$: C, 69.59; H, 3.78; N, 4.77. Found: C, 69.65; H, 3.77; N, 4.84.

2-[3-(1*H*-Indol-5-yl)phenyl]benzo[*d*]thiazole (4cH)
Yield: 0.283 g (98%); colorless needles; mp 159.1–160.2 °C (hexane–EtOAc, 1:2); R_f = 0.7 (hexane–EtOAc, 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.38 (s, 1 H, ArH), 8.35 (s, 1 H, NH), 8.10 (d, *J* = 8.0 Hz, 1 H, ArH), 8.03 (d, *J* = 7.2 Hz, 1 H, ArH), 7.95 (s, 1 H, ArH), 7.91 (d, *J* = 8.0 Hz, 1 H, ArH), 7.77 (d, *J* = 7.2 Hz, 1 H, ArH), 7.57–7.45 (m, 4 H, ArH), 7.39 (t, *J* = 7.6 Hz, 1 H, ArH), 7.25–7.23 (m, 1 H, ArH), 6.63–6.62 (m, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 168.4, 154.2, 143.5, 135.5, 135.1, 133.9, 132.3, 130.0, 129.3, 128.4, 126.4, 126.3, 125.5, 125.1, 125.0, 123.2, 121.8, 121.6, 119.4, 111.4, 103.1.

MS (ESI): *m*/*z* = 327 (M + H$^+$).

Anal. Calcd for $C_{21}H_{14}N_2S$: C, 77.27; H, 4.32; N, 8.58. Found: C, 77.02; H, 4.31; N, 8.50.

Suzuki–Miyaura Cross-Coupling Reaction of 4-Bromophenylbenzothiazole 3d with Arylboronic Acids; General Procedure
K_2CO_3 (380 mg, 2.75 mmol) was added to a Schlenk tube equipped with a stirring bar and the tube was dried under vacuum and filled with argon, $PdCl_2$ (1.24 mg, 0.007 mmol), 2-phenylimidazole (2 mg, 0.014 mmol), 2-(4-bromophenyl)benzo[*d*]thiazole (**3d**; 397 mg, 1.37 mmol), and arylboronic acid (2.06 mmol) in anhyd DMF (12 mL). Then the mixture was stirred at 120 °C for the indicated reaction time (Table 1) under argon atmosphere. The mixture was cooled and then poured over ice-water (250 mL) containing aq 1 M HCl (2 mL) and extracted with $CHCl_3$ (5 × 40 mL). The combined organic layers were washed with brine (2 × 30 mL) and dried (Na_2SO_4). Removal of solvent followed by column chromatographic purification (silica gel, hexane–$CHCl_3$) afforded the coupling product (Table 1).

2-(Biphenyl-4-yl)benzo[*d*]thiazole (4dA)
Yield: 0.316 g (80%); colorless powder; mp 208.1–209.0 °C (EtOAc–$CHCl_3$, 1:1) (Lit.[20] mp 192–194 °C); R_f = 0.4 (hexane–EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 7.6 Hz, 2 H, ArH), 8.08 (d, *J* = 8.4 Hz, 1 H, ArH), 7.89 (d, *J* = 8.0 Hz, 1 H, ArH), 7.71 (d, *J* = 8.4 Hz, 2 H, ArH), 7.64 (d, *J* = 7.6 Hz, 2 H, ArH), 7.51–7.45 (m, 3 H, ArH), 7.38 (t, *J* = 8.8 Hz, 2 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.7, 154.2, 143.7, 140.0, 135.0, 132.5, 128.9, 128.0, 127.9, 127.6, 127.1, 126.3, 125.2, 123.2, 121.6.

2-(4′-Methoxylbiphenyl-4-yl)benzo[*d*]thiazole (4dD)
Yield: 0.421 g (96%); colorless powder; mp 232.9–233.4 °C ($CHCl_3$); R_f = 0.3 (hexane–EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.4 Hz, 2 H, ArH), 8.07 (d, *J* = 8.4 Hz, 1 H, ArH), 7.89 (d, *J* = 8.4 Hz, 1 H, ArH), 7.66 (d, *J* = 8.4 Hz, 2 H, ArH), 7.58 (d, *J* = 8.8 Hz, 2 H, ArH), 7.47 (t, *J* = 7.6 Hz, 1 H, ArH), 7.36 (t, *J* = 8.4 Hz, 1 H, ArH), 6.99 (d, *J* = 8.8 Hz, 2 H, ArH), 3.85 (s, 3 H, OCH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.8, 160.0, 154.5, 143.5, 135.3, 132.8, 132.2, 128.2, 128.1, 127.1, 126.3, 125.1, 123.3, 121.6, 114.6, 55.4.

MS (ESI): *m*/*z* = 318 (M + H$^+$).

Anal. Calcd for $C_{20}H_{15}NOS$: C, 75.68; H, 4.76; N, 4.41. Found: C, 75.38; H, 4.71; N, 4.54.

2-(4′-Methylbiphenyl-4-yl)benzo[*d*]thiazole (4dE)
Yield: 0.207 g (86%); pale yellow dendrites; mp 215.3–216.1 °C (hexane–$CHCl_3$, 1:2); R_f = 0.6 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 7.6 Hz, 2 H, ArH), 8.08 (d, *J* = 8.4 Hz, 1 H, ArH), 7.89 (d, *J* = 7.6 Hz, 1 H, ArH), 7.69 (d, *J* = 8.4 Hz, 2 H, ArH), 7.54 (d, *J* = 7.6 Hz, 2 H, ArH), 7.49 (t, *J* = 7.2 Hz, 1 H, ArH), 7.37 (t, *J* = 7.2 Hz, 1 H, ArH), 7.27 (d, *J* = 8.4 Hz, 2 H, ArH), 2.40 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.7, 154.2, 143.6, 137.8, 137.1, 135.0, 132.1, 129.6, 127.9, 127.3, 126.9, 126.3, 125.1, 123.1, 121.6, 21.1.

MS (ESI): *m*/*z* = 302 (M + H$^+$).

Anal. Calcd for $C_{20}H_{15}NS$: C, 79.70; H, 5.02; N, 4.65. Found: C, 79.54; H, 4.94; N, 4.97.

2-(3′,4′-Dimethoxylbiphenyl-4-yl)benzo[*d*]thiazole (4dF)
Yield: 0.228 g (95%); colorless needles; mp 193.6–194.3 °C (EtOAc–$CHCl_3$, 1:1); R_f = 0.6 (hexane–EtOAc, 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.4 Hz, 2 H, ArH), 8.07 (d, *J* = 8.0 Hz, 1 H, ArH), 7.88 (d, *J* = 8.0 Hz, 1 H, ArH), 7.66 (d, *J* = 8.0 Hz, 2 H, ArH), 7.47 (t, *J* = 8.4 Hz, 1 H, ArH), 7.36 (t, *J* = 8.4 Hz, 1 H, ArH), 7.24–7.16 (m, 2 H, ArH), 6.95 (d, *J* = 8.4 Hz, 1 H, ArH), 3.95 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.7, 154.2, 149.3, 149.2, 143.5, 135.0, 132.9, 132.0, 127.9, 127.2, 126.3, 125.1, 123.1, 121.6, 119.5, 111.5, 110.2, 56.0.

MS (ESI): *m*/*z* = 348 (M + H$^+$).

Anal. Calcd for $C_{21}H_{17}NO_2S$: C, 72.60; H, 4.93; N, 4.03. Found: C, 72.35; H, 4.95; N, 4.11.

2-[4-(Thiophen-2-yl)phenyl]benzo[*d*]thiazole (4dG)
Yield: 0.190 g (94%); pale yellow prisms; mp 210.6–211.5 °C (EtOAc–$CHCl_3$, 1:1) (Lit.[27] mp 205.5–206.1 °C); R_f = 0.5 (hexane–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.06 (m, 3 H, ArH), 7.89 (d, *J* = 7.6 Hz, 1 H, ArH), 7.71 (d, *J* = 8.0 Hz, 2 H, ArH), 7.49 (t, *J* = 7.6 Hz, 1 H, ArH), 7.41–7.33 (m, 3 H, ArH), 7.11 (t, *J* = 5.6 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 167.4, 154.1, 143.2, 136.8, 135.0, 132.4, 128.3, 128.0, 126.3, 126.1, 125.8, 125.2, 124.0, 123.1, 121.6.

2-(4′-Nitrobiphenyl-4-yl)benzo[*d*]thiazole (4dI)
Yield: 0.41 g (90%); yellow powder; mp 267.5–269.6 °C ($CHCl_3$); R_f = 0.2 (hexane–EtOAc, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 8.8 Hz, 2 H, ArH), 8.21 (d, *J* = 8.0 Hz, 2 H, ArH), 8.09 (d, *J* = 7.6 Hz, 1 H, ArH), 7.92 (d, *J* = 8.8 Hz, 1 H, ArH), 7.80–7.73 (m, 4 H, ArH), 7.50 (t, *J* = 7.2 Hz, 1 H, ArH), 7.40 (t, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 166.9, 154.5, 147.6, 146.5, 141.2, 135.2, 134.4, 128.4, 128.0, 127.9, 126.6, 125.6, 124.3, 123.6, 121.7.

MS (ESI): *m*/*z* = 333 (M + H$^+$).

Anal. Calcd for $C_{19}H_{12}N_2O_2S$: C, 68.66; H, 3.64; N, 8.43. Found: C, 68.85; H, 3.62; N, 8.50.

Suzuki–Miyaura Cross-Coupling Reaction of 4-Iodophenylbenzothiazole 3e with Arylboronic Acids; General procedure
K_2CO_3 (246 mg, 1.78 mmol) was added to a Schlenk tube equipped with a stirring bar and the tube was dried under vacuum and filled with argon, $PdCl_2$ (0.7 mg, 0.004 mmol), 2-phenylimidazole (1.3 mg, 0.009 mmol), 2-(4-iodophenyl)benzo[*d*]thiazole (**3e**; 300 mg,

0.89 mmol), and arylboronic acid (1.33 mmol) in anhyd DMF (10 mL). Then, the mixture was stirred at 120 °C for the indicated reaction time (Table 1) under argon atmosphere. The mixture was cooled and then poured over ice-water (200 mL) containing aq 1 M HCl (2 mL) and extracted with $CHCl_3$ (5 × 50 mL). The combined organic layers were washed with brine (2 × 30 mL) and dried (Na_2SO_4). Removal of solvent followed by column chromatographic purification (silica gel, hexane–$CHCl_3$) afforded the coupling product (Table 1).

2-(Biphenyl-4-yl)benzo[*d*]thiazole (4eA)
Yield: 0.241 g (95%); colorless powder; mp 209.8–210.6 °C (EtOAc–$CHCl_3$, 1:1).

The spectral data are similar to that of compound **4dA**.

2-(4′-Methylbiphenyl-4-yl)benzo[*d*]thiazole (4eE)
Yield: 0.225 g (84%); pale yellow dendrites; mp 212.4–213.7 °C (hexane–$CHCl_3$, 1:2).

The spectral data are similar to that of compound **4dE**.

2-(3′,4′-Dimethoxylbiphenyl-4-yl)benzo[*d*]thiazole (4eF)
Yield: 0.288 g (94%); colorless needles; mp 191.6–192.6 °C (EtOAc–$CHCl_3$, 1:1).

The spectral data are similar to that of compound **4dF**.

2-[4-(Thiophen-2-yl)phenyl]benzo[*d*]thiazole (4eG)
Yield: 0.247 g (95%); pale yellow prisms; mp 208.5–209.8 °C (EtOAc–$CHCl_3$, 1:1).

The spectral data are similar to that of compound **4dG**.

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References

(1) (a) Tan, B. S.; Tiong, K. H.; Muruhadas, A.; Randhawa, N.; Choo, H. L.; Bradshaw, T. D.; Stevens, M. F. G.; Leong, C. O. *Mol. Cancer Ther.* **2011**, *10*, 1982. (b) Racane, L.; Kralj, M.; Suman, L.; Stojkovic, R.; Kulenovic, V. T.; Zamola, G. K. *Bioorg. Med. Chem.* **2010**, *18*, 1038. (c) Caleta, I.; Kralj, M.; Marjanovic, M.; Bertosa, B.; Tomic, S.; Pavlovic, G.; Pavelic, K.; Zamola, G. K. *J. Med. Chem.* **2009**, *52*, 1744.

(2) (a) Rajeeva, B.; Srinivasulu, N.; Shantakumar, S. *E-J. Chem.* **2009**, *6*, 775. (b) Kumbhare, R. M.; Ingle, V. N. *Ind. J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **2009**, *48*, 996. (c) Murthi, Y.; Pathak, D. *J. Pharm. Res.* **2008**, *7*, 153.

(3) (a) Gupta, A.; Rawat, S. *J. Chem. Pharm. Res.* **2010**, *2*, 244. (b) Kaur, H.; Kumar, S.; Singh, I.; Saxena, K. K.; Kumar, A. *Dig. J. Nanomater. Bios.* **2010**, *5*, 67. (c) Venkatesh, P.; Pandeya, S. N. *Int. J. ChemTech. Res.* **2009**, *1*, 1354.

(4) (a) Amnerkar, N.; Bhusari, K. P. *Eur. J. Med. Chem.* **2010**, *45*, 149. (b) Sharma, P.; Pandeya, S. N.; Roy, R. K.; Verma, A. K.; Gupta, S. *Int. J. ChemTech. Res.* **2009**, *1*, 758. (c) Siddiqui, N.; Rana, A.; Khan, S.; Haque, S.; Arshad, M.; Ahmed, S.; Ahsan, W. *Acta Pharm.* **2009**, *59*, 441.

(5) (a) Kok, S. H. L.; Gambari, R.; Chui, C. H.; Yuen, M. C. W.; Lin, E.; Wong, R. S. M.; Lau, F. Y.; Cheng, G. Y. M.; Lam, W. S.; Chan, S. H.; Lam, K. H.; Cheng, C. H.; Lai, P. B. S.; Yu, M. W. Y.; Cheung, F.; Tang, J. C. O.; Chan, A. S. C. *Bioorg. Med. Chem.* **2008**, *16*, 3626. (b) Wang, M.; Gao, M.; Mock, B.; Miller, K.; Sledge, G.; Hutchins, G.; Zheng, Q. *Bioorg. Med. Chem.* **2006**, *14*, 8599. (c) Hutchinson, I.; Chua, M. S.; Browne, H. L.; Trapani, V.; Bradshaw, T. D.; Westwell, A. D. *J. Med. Chem.* **2001**, *44*, 1446.

(6) (a) Sadek, B.; Tabakha, M. M. A.; Fahelelbom, K. M. S. *Molecules* **2011**, *16*, 9386. (b) Pal, N.; Kumar, M.; Seth, G. *E-J. Chem.* **2011**, *8*, 1174.

(7) (a) Arora, P.; Das, S.; Ranawat, M. S.; Arora, N.; Gupta, M. M. *J. Chem. Pharm. Res.* **2010**, *2*, 317. (b) Gawai, A.; Das, S.; Nemade, M.; Wathore, S. *Asian J. Chem.* **2011**, *23*, 3969.

(8) Yar, M. H.; Ansari, Z. H. *Acta Pol. Pharm.* **2009**, *66*, 387; *Chem. Abstr.* **2010**, *153*, 530327.

(9) Maharan, M.; William, S.; Ramzy, F.; Sembel, A. *Molecules* **2007**, *12*, 622.

(10) Sreenivasa, M.; Jaychand, E.; Shivakumar, B.; Jayrajkumar, K.; Vijaykumar, J. *Arch. Pharm. Sci. Res.* **2009**, *1*, 150.

(11) (a) Pattan, S.; Suresh, C.; Pujar, V.; Reddy, V.; Rasal, V.; Koti, B. *Ind. J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **2005**, *44*, 2404. (b) Vazquez, G. N.; Paoli, P.; Rivera, I. L.; Molina, R. V.; Franco, J.; Andrade, R. O.; Soto, S. E.; Camici, G.; Coutino, D.; Ortiz, I.; Mayorga, K.; Diaz, H. *Bioorg. Med. Chem.* **2009**, *17*, 3332. (c) Surya, K. D.; Chen, L. H.; Stebbins, J. L.; Machleidt, T.; Mehan, M.; Dahl, R.; Yuan, H. C.; Barile, E.; Emdadi, A.; Murphy, R.; Pellecchia, M. *Bioorg. Med. Chem.* **2009**, *17*, 2712.

(12) For other bioactivity, see: (a) Mathis, C. A.; Wang, Y.; Holt, D. P.; Huang, G.-F.; Debnath, M. L.; Klunk, W. E. *J. Med. Chem.* **2003**, *46*, 2740. (b) Henriksen, G.; Hauser, A. I.; Westwell, A. D.; Yousefi, B. H.; Schwaiger, M.; Drzezga, A.; Wester, H. J. *J. Med. Chem.* **2007**, *50*, 1087. (c) Cui, M. C.; Li, Z. J.; Tang, R. K.; Liu, B. L. *Bioorg. Med. Chem.* **2010**, *14*, 1777. (d) Yadav, P. S.; Devprakash; Senthilkumar, G. P. *IJPSR* **2011**, *3*, 1. (e) Khokra, S. L.; Arora, K.; Mehta, H.; Aggarwal, A.; Yadav, M. *IJPSR* **2011**, *2*, 1356. (f) Piscitelli, F.; Ballatore, C.; Smith, A. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 644. (g) Sheng, C.; Che, X.; Wang, W.; Wang, S.; Cao, Y.; Yao, J.; Miao, Z.; Zhang, W. *Eur. J. Med. Chem.* **2011**, *46*, 1706.

(13) (a) Costa, S. P. G.; Batista, R. M. F.; Sousa, A. M. R. C. *Mater. Sci. Forum* **2006**, *514*, 147. (b) Padalkar, V. S.; Tathe, A.; Gupta, V. D.; Patil, V. S.; Phatangare, K.; Sekar, N. *J. Fluoresc.* **2012**, *22*, 311.

(14) (a) Yu, G.; Yin, S.; Liu, Y.; Shuai, Z.; Zhu, D. *J. Am. Chem. Soc.* **2003**, *125*, 14816. (b) Kuwabara, J.; Namekawa, T.; Haga, M. A.; Kanbara, T. *Dalton Trans.* **2012**, *41*, 44.

(15) (a) Leng, W.; Zhou, Y.; Xu, Q.; Liu, J. *Macromolecules* **2001**, *34*, 4774. (b) Batista, R. M. F.; Costa, S. P. G.; Malheiro, E. L.; Belsley, M.; Raposo, M. M. M. *Tetrahedron* **2007**, *63*, 4258. (c) Zhao, M.; Samoc, M.; Prasad, P. N. *Chem. Mater.* **1990**, *2*, 670. (d) Costa, S. P. G.; Batista, R. M.; Cardoso, P.; Belsley, M.; Raposo, M. M. M. *Eur. J. Org. Chem.* **2006**, 3938.

(16) For other properties in material field, see: (a) Dikundwar, A. G.; Dutta, G. K.; Row, T. N. G.; Patil, S. *Cryst. Growth. Des.* **2011**, *11*, 1615. (b) Ahmed, E.; Subramaniyan, S.; Kim, F. S.; Xin, H.; Jenekhe, S. A. *Macromolecules* **2011**, *44*, 7207. (c) Wang, H.; Chen, G.; Xu, X.; Chen, H.; Ji, S. *Dyes Pigm.* **2010**, *86*, 238. (d) Raposo, M. M. M.; Castro, M. C. R.; Fonseca, A. M. C.; Schellenberg, P.; Belsley, M. *Tetrahedron* **2011**, *67*, 5189. (e) Sayama, K.; Tsukagoshi, S.; Hara, K.; Ohga, Y.; Shinpou, A.; Abe, Y.; Suga, S.; Arakawa, H. *J. Phys. Chem. B* **2002**, *106*, 1363. (f) Hrobarikova, V.; Hrobarik, P.; Gajdos, P.; Fitilis, I.; Fakis, M.; Persephonis, P.; Zahradnik, P. *J. Org. Chem.* **2010**, *75*, 305. (g) Dalton, M. J.; Kannan, R.; Haley, J. E.; He, G. S.; McLean, D. G.; Cooper, T. M.; Prasad, P. N.; Tan,

L. S. *Macromolecules* **2011**, *44*, 7194. (h) Wang, G.; Pu, K. Y.; Zhang, X.; Li, K.; Wang, L.; Cai, L.; Ding, D.; Lai, Y. H.; Liu, B. *Chem. Mater.* **2011**, *23*, 4428. (i) Morales, A. R.; Belfield, K. D.; Hales, J. M.; Stryland, E. W. V.; Hagan, D. J. *Chem. Mater.* **2006**, *18*, 4972. (j) Belfield, K. D.; Bondar, M. V.; Frazer, A.; Morales, A. R.; Kachkovsky, O. D.; Mikhailov, I.; Masunov, A. E. M.; Przhonska, O. V. *J. Phys. Chem. B* **2010**, *114*, 9313. (k) Nguyen, D. M.; Wang, X.; Ahn, H. Y.; Rodriguez, L.; Mikhailo, V.; Bondar, M. V.; Belfield, K. D. *Appl. Mater. Interfaces* **2010**, *11*, 2978. (l) Qi, J.; Han, M. S.; Tung, C. H. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 1747. (m) Batista, R. M. F.; Costa, S. P. G.; Raposo, M. M. M. *Tetrahedron Lett.* **2004**, *45*, 2825. (n) Barbarella, G.; Favaretto, L.; Sotgiu, G.; Antolini, L.; Gigli, G.; Cingolani, R.; Bongini, A. *Chem. Mater.* **2001**, *13*, 4112. (o) Barbarella, G. *Chem.–Eur. J.* **2002**, *8*, 5073. (p) Nah, M. K.; Rho, S. G.; Kim, H. K.; Kang, J. G. *J. Phys. Chem. A* **2007**, *111*, 11437. (q) Lo, K. K. W.; Li, C. K.; Lau, J. S. Y. *Organometallics* **2005**, *24*, 4594. (r) Zhang, X. H.; Wong, O. Y.; Gao, Z. Q.; Lee, C. S.; Kwong, H. L.; Lee, S. T.; Wu, S. K. *Mater. Sci. Eng. B* **2001**, *85*, 182. (s) Park, M. J.; Kwak, J.; Lee, J.; Jung, I. H.; Kong, H.; Lee, C.; Hwang, D. H.; Shim, H. K. *Macromolecules* **2010**, *43*, 1379.

(17) Hayashi, M. *Chem. Rec.* **2008**, *8*, 252; and references cited therein.

(18) Kawamura, K.; Haneda, S.; Gan, Z. B.; Eda, K.; Hayashi, M. *Organometallics* **2008**, *27*, 3748.

(19) CCDC 660480 contains supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336033; E-mail: deposit@ccdc.cam.ac.uk.

(20) Bahrami, K.; Khodaei, M. M.; Naali, F. *J. Org. Chem.* **2008**, *73*, 6835.

(21) Sharghi, H.; Asemani, O. *Synth. Commun.* **2009**, *39*, 860.

(22) Boeini, H. Z.; Najafabadi, K. H. *Eur. J. Org. Chem.* **2009**, 4926.

(23) For other methods for the synthesis of benzothiazoles, see: (a) Brembilla, A.; Roizard, D.; Lochon, P. *Synth. Commun.* **1990**, *20*, 3379. (b) Moghaddam, F. M.; Bardajee, G. R.; Ismaili, H.; Taimoory, S. M. D. *Synth. Commun.* **2006**, *36*, 2543. (c) Saha, D.; Adak, L.; Ranu, B. C. *Tetrahedron Lett.* **2010**, *51*, 5624. (d) Ranjit, S.; Liu, X. *Chem.–Eur. J.* **2011**, *17*, 1105.

(24) Bahrami, K.; Khodaei, M. M.; Naali, F. *Synlett* **2009**, 569.

(25) Jin, H. L.; Cheng, T. X.; Chen, J. X. *Appl. Organomet. Chem.* **2011**, *25*, 238.

(26) Chen, L.; Yang, C.; Li, S.; Qin, J. *Spectrochim. Acta, Part A* **2007**, *68*, 317.

(27) Costa, S. P. G.; Batista, R. M. F.; Cardoso, P.; Belsley, M.; Raposo, M. M. M. *Eur. J. Org. Chem.* **2006**, 3938.

