Synthesis W. Xu et al. Feature

# Palladium-Catalyzed Synthesis of 2-Aminobenzothiazoles through Tandem Reaction

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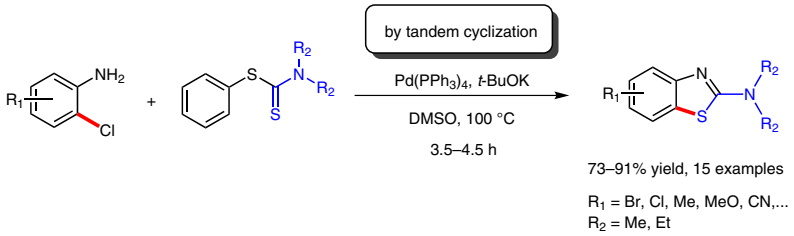


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**Abstract** A variety of 2-aminobenzothiazoles were synthesized by using 2-chloroanilines and dithiocarbamates through a tandem approach in the presence of $Pd(PPh_3)_4$ and *t*-BuOK. The facile and efficient protocol enabled the reaction to proceed at a good rate with excellent yields.

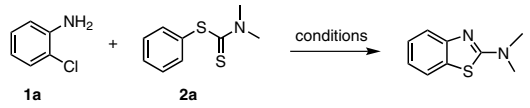
**Key words** potassium *tert*-butoxide, palladium, chloroloaniline, aminobenzothiazole, tandem

Benzothiazoles are an important class of heterocyclic compound that have a wide range of applications as key building blocks in many trade drugs. They can exhibit a wide range of biological activities such as antitumor,[1] antimicrobial,[2] antibubercular,[3] antimalarial,[4] anti-inflammatory,[5] analgesic,[6] and antibacterial[7] action. There are mainly two traditional approaches to prepare the 2-substituted benzothiazole ring system. One of which is a condensation reaction of 2-aminothiophenols with aldehydes or carboxylic acid derivatives under strongly acidic conditions,[8–19] and the second approach is through cyclization of thiobenzanilides.[20–27] Other procedures such as cyclization of *N*-(2-halo)arylthioureas (halogen=Br, I) or direct intramolecular C–S bond formation through C–H functionalization of *N*-arylthioureas catalyzed by transition metals, have enriched the scope of available preparation methods.[28,29] However, few examples have been reported for the synthesis of 2-aminobenzothiazoles that use 2-chloroloanilines as starting materials.[30] Herein, we present a facile and efficient protocol for the synthesis of 2-aminobenzothiazoles by palladium-catalyzed tandem reaction.

Initially, we used 2-chloroaniline (**1a**) and dithiocarbamate (**2a**) as starting materials to optimize the reaction conditions. Various copper and palladium catalysts were examined (Table 1, entries 1–8). We are pleased to find that 2-(dimethylamino)benzothiazole could be afforded in 82% yield in the presence of $Pd(PPh_3)_4$ and *t*-BuOK (entry 4) when the reaction was performed in dimethyl sulfoxide (DMSO). Copper catalysts did not catalyze this reaction and some other palladium catalysts displayed less activity in the transformation, providing the 2-aminobenzothiazole in poor to moderate yields (entries 5–7). Organic and inorganic bases were screened for the model reaction. For example, triethylamine ($NEt_3$), NaH, $CH_3ONa$, $Cs_2CO_3$, NaOH, and $K_2CO_3$ (entries 9–14) were tested and *t*-BuOK was found to be the most suitable base to promote the reaction. Several other solvents were also tested in this reaction, and all proved less efficient (entries 15–19). Among the solvents and reaction temperatures examined (entries 20–23), DMSO proved to be the most suitable solvent and the reaction was optimal at 100 °C. The use of 3 equiv of *t*-BuOK was crucial to achieve complete conversion. When 2 equiv was used, the product yield was much lower (25%) (entry 24) and we could not detect the target product when the base loading was decreased to 1 equiv (entry 25).

With the optimal reaction conditions in hand, we began to establish the scope of the reaction with respect to the substrate 2-chloroanilines and dithiocarbamates. A number of 2-chloroaniline derivatives (Table 2, 1a–h) were investigated in the reaction with dithiocarbamates (Table 2, 2a–b). The results revealed that the optimal conditions had broad substrate compatibility. Substrates **1c**, **1b** and **1d**, having either an electron-donating group or an electron-poor group *para* to the chloro group, reacted with dithiocarbamate (**2a**) smoothly to furnish the desired products in 82, 73, and 79% yield, respectively (entries 3, 2, and 4).

**Table 1** Screening Reaction Conditions with 2-Chloroaniline (**1a**) and Dithiocarbamate (**2a**)[a]



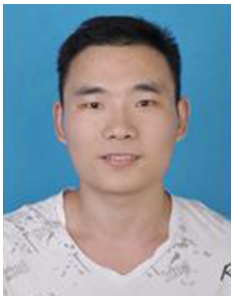

**1a** **2a**

| Entry | Catalyst | Base (equiv) | Solvent | Temp. (°C) | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | CuBr | *t*-BuOK (3.0) | DMSO | 100 | – |
| 2 | CuO | *t*-BuOK (3.0) | DMSO | 100 | – |
| 3 | $Cu(OTf)_2$ | *t*-BuOK (3.0) | DMSO | 100 | – |
| 4 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | DMSO | 100 | 82 |
| 5 | $PdCl_2$ | *t*-BuOK (3.0) | DMSO | 100 | 19 |
| 6 | $PdBr_2$ | *t*-BuOK (3.0) | DMSO | 100 | 24 |
| 7 | $Pd(dba)_2$ | *t*-BuOK (3.0) | DMSO | 100 | 61 |
| 8 | $Pd(OAc)_2$ | *t*-BuOK (3.0) | DMSO | 100 | – |
| 9 | $Pd(PPh_3)_4$ | $NEt_3$ (3.0) | DMSO | 100 | 32 |
| 10 | $Pd(PPh_3)_4$ | NaH (3.0) | DMSO | 100 | 44 |
| 11 | $Pd(PPh_3)_4$ | $CH_3ONa$ (3.0) | DMSO | 100 | 16 |
| 12 | $Pd(PPh_3)_4$ | $Cs_2CO_3$ (3.0) | DMSO | 100 | 45 |
| 13 | $Pd(PPh_3)_4$ | NaOH (3.0) | DMSO | 100 | 39 |
| 14 | $Pd(PPh_3)_4$ | $K_2CO_3$ (3.0) | DMSO | 100 | 34 |
| 15 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | DMAC | 100 | 12 |
| 16 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | DMF | 100 | 8 |
| 17 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | $CH_3CN$ | 100 | 11 |
| 18 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | $CH_2Cl_2$ | 100 | – |
| 19 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | $PhCH_3$ | 100 | 62 |
| 20 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | DMSO | 60 | 24 |
| 21 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | DMSO | 80 | 39 |
| 22 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | DMSO | 90 | 68 |
| 23 | $Pd(PPh_3)_4$ | *t*-BuOK (3.0) | DMSO | 110 | 81 |
| 24 | $Pd(PPh_3)_4$ | *t*-BuOK (2.0) | DMSO | 100 | 25 |
| 25 | $Pd(PPh_3)_4$ | *t*-BuOK (1.0) | DMSO | 100 | – |

[a] Reaction conditions: **1a** (1.0 mmol), **1b** (1.5 mmol), [Cat.] (5 mmol%), solvent (3.0 mL), 4.5 h.
[b] Isolated yield.

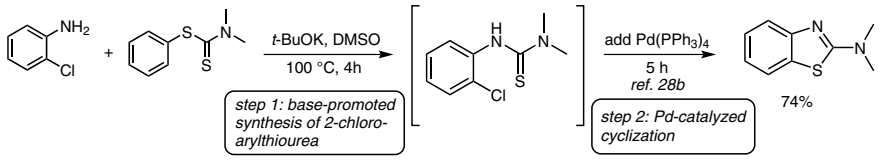
However, substrate **1h**, having an electron-withdrawing group *meta* to the chloro afforded the corresponding product in 76% yield (Table 2, entry 8). Substrates **1e** and **1g**, having an electron-donating (methyl or methoxy group) group *meta* to the chloro furnished the corresponding product in 84% and 91% yield, respectively (entry 5 and 7). Compared with **1d**, substrate **1f**, having a moderate electron-withdrawing group *meta* to the chloro, afforded the desired product in 88% yield (entry 6). Subsequently, the reaction of dithiocarbamate **2b** was examined under the optimal conditions (entries 9–15). We were pleased to find that diethyl dithiocarmamate (**2b**) was a good coupling partner to react with 2-chloroanilines, affording the corresponding products with good to excellent yields. Notably, **1g** reacted well to provide methoxy-substituted benzothiazole **3o** in a remarkable 91% yield (entry 15). The protocol could also be applied to the unreactive 3-amino-2-chloropyridine. Under

## Biographical Sketch



**Wan Xu** was born in 1990 in Hubei, China. He received his Bachelor's degree from Wuhan Institute of Bioengineering in 2013. He is currently a second-year graduate student with Prof. Dong at Wuhan Institute of Technology (WIT).

**Zhi-Bing Dong** is a Chutian Distinguished Professor at Wuhan Institute of Technology (WIT). He spent one year as a visiting PhD student (2007–2008) with Prof. Paul Knochel at Ludwig-Maximilians-University, and then obtained his PhD in 2008. Later he joined Prof. Shu Kobayashi's group at the University of Tokyo (2010–2011), and worked with Prof. Carsten Bolm at RWTH as an Alexander von Humboldt Postdoctoral Fellow (2011–2012). His research interests deal mainly with the transition metal catalyzed C–X (X = S, O, N, C) bond-formation reactions and organic reactions in water.




**Scheme 1** Proposed mechanism

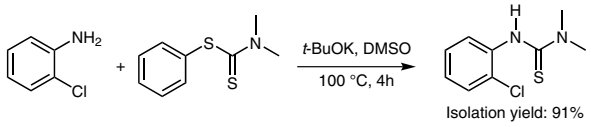
the standard reaction conditions, 3-amino-2-chloropyridine (**1h**) reacted with **2a** to give the desired product **3p** with satisfactory yield (92%; entry 16).

A plausible mechanism for the reaction is proposed (Scheme 1). The first step is the formation of aryl thiourea promoted by base, which is subsequently transformed to aryl-isothiourea. The second step is the palladium-catalyzed intramolecular cross-coupling reaction[28b] which allows the aryl-isothiourea to afford 2-aminobenzothiazole smoothly.

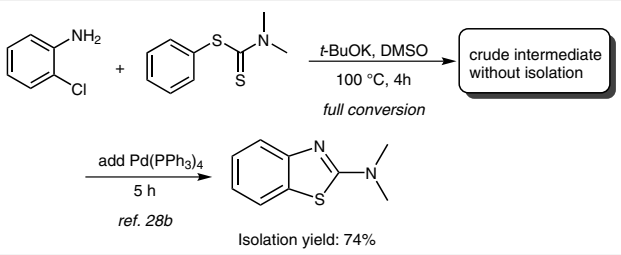
To verify the mechanism, we conducted a control experiment (Scheme 2) with no addition of palladium catalyst. In this case, *N*-(2-chloro)arylthiourea was obtained as the key intermediate (isolated yield: 91%) and the by product (thiophenol) was detected in the aqueous phase by GC-MS.

The control experiment shown in Scheme 3 further illustrates our proposal. Palladium catalyst was added when the generation of (2-chloro)arylthiourea was finished (checked by TLC), and the desired target molecule (2-aminobenzothiazole) could be furnished by Pd-catalyzed cyclization[28b] with 74% isolated yield.

In summary, we have developed a new protocol for the synthesis of 2-aminobenzothiazoles starting from substituted 2-chloroanilines and dithiocarbamates. Various functional groups are tolerated, giving access to a wide range of substituted 2-aminobenzothiazoles. The protocol has practical synthetic value for the preparation of biologically and pharmaceutically active compounds. Further details and the development of related applications for this protocol are under research in our laboratory.

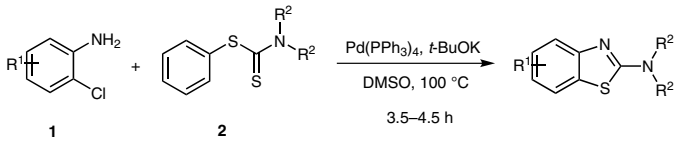



**Scheme 2** A control experiment: isolation of the key intermediate




**Scheme 3** A control experiment: subsequent Pd-catalyzed cyclization

**Table 2** $Pd(PPh_3)_4$-Catalyzed Tandem Reactions of 2-Chloroanilines (**1**) with Dithiocarbamates (**2**)[a]




| Entry | 2-Chloroaniline | Dithiocarbamate | Product | Yield (%)[b] |
|---|---|---|---|---|
| 1 | **1a** | **2a** | **3a** | 82 |
| 2 | **1b** | **2a** | **3b** | 73 |
| 3 | **1c** | **2a** | **3c** | 82 |

Table 2 (continued)

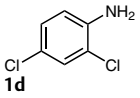
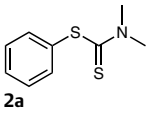
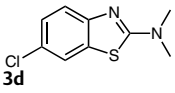
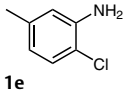
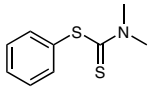
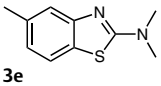
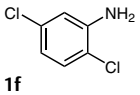
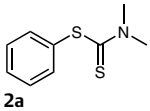
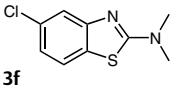
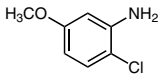
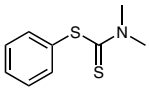
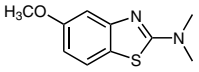
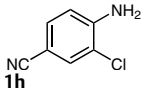
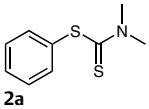
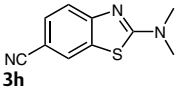
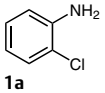
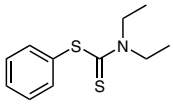
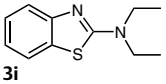
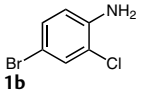
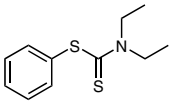
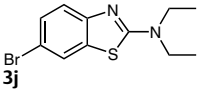
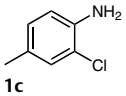
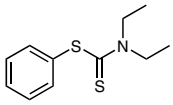
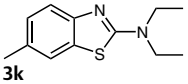
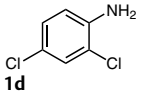
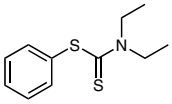
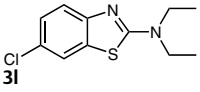
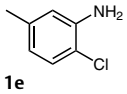
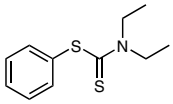
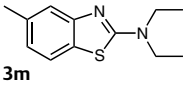
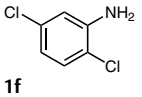
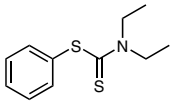
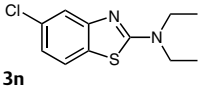
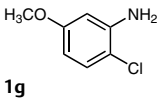
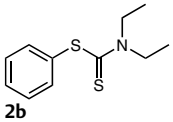
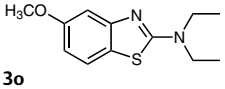
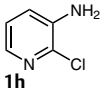
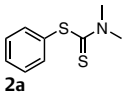
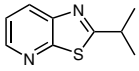
| Entry | 2-Chloroaniline | Dithiocarbamate | Product | Yield (%)[b] |
|---|---|---|---|---|
| 4 |  **1d** |  **2a** |  **3d** | 79 |
| 5 |  **1e** |  **2a** |  **3e** | 84 |
| 6 |  **1f** |  **2a** |  **3f** | 88 |
| 7 |  **1g** |  **2a** |  **3g** | 91 |
| 8 |  **1h** |  **2a** |  **3h** | 76 |
| 9 |  **1a** |  **2b** |  **3i** | 86 |
| 10 |  **1b** |  **2b** |  **3j** | 83 |
| 11 |  **1c** |  **2b** |  **3k** | 89 |
| 12 |  **1d** |  **2b** |  **3l** | 84 |
| 13 |  **1e** |  **2b** |  **3m** | 82 |
| 14 |  **1f** |  **2b** |  **3n** | 87 |

Table 2 (continued)

| Entry | 2-Chloroaniline | Dithiocarbamate | Product | Yield (%)[b] |
|---|---|---|---|---|
| 15 |  **1g** |  **2b** |  **3o** | 91 |
| 16[c] |  **1h** |  **2a** |  **3p** | 92 |

[a] Reaction conditions: **1** (1.0 mmol), **2** (1.5 mmol), $Pd(PPh_3)_4$ (5 mol%), *t*-BuOK (3.0 mmol), DMSO (3 mL), 100 °C.
[b] Isolated yield.
[c] An example of the reaction with a heterocycle.

All reactions were carried out in dried glassware fitted with septum caps. All starting materials were purchased from commercial suppliers and used without further purification, unless otherwise stated. DMSO was dried with molecular sieves. Yields refer to isolated compounds estimated to be >95% pure as determined by $^1$H NMR and capillary GC analysis.

### Preparation of 2-Aminobenzothiazoles with Potassium *tert*-Butoxide and Tetrakis(triphenylphosphine)palladium; Typical Procedure

In a dried tube, equipped with a magnetic stirrer and a septum, 2-chloroaniline (1.0 mmol) was dissolved in DMSO (3 mL), and *t*-BuOK (3.0 mmol) was added. The mixture was stirred for 5 min, then dithiocarbamate (1.5 mmol) and tetrakis(triphenylphosphine) palladium (5 mol %) were added. The reaction mixture was heated at 100 °C and the progress of the reaction was checked by TLC until the starting material was consumed. The mixture was cooled to r.t., and the reaction was quenched with sat. $NH_4Cl$ solution (5 mL). The mixture was extracted with EtOAc, dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. The residue was purified by flash column chromatography to afford the desired product.

### *N*,*N*-Dimethylbenzo[*d*]thiazol-2-amine (3a)

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 3:1) to give the target compound.

Yield: 146 mg (82%); brown solid; mp 83–85 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 7.6 Hz, 2 H), 7.28 (t, *J* = 8.0 Hz, 1 H), 7.09 (t, *J* = 6.8 Hz, 1 H), 3.21 (s, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 168.32, 152.68, 130.44, 125.72, 120.72, 120.40, 118.50, 39.77.

HRMS (ESI): *m*/*z* calcd for $C_9H_{10}N_2S$: 178.0565; found: 178.0572.

### 6-Bromo-*N*,*N*-dimethylbenzo[*d*]thiazol-2-amine (3b)

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 3:1) to give the target compound.

Yield: 187 mg (73%); pale-brown solid; mp 107.0–109 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.66 (s, 1 H), 7.42–7.34 (m, 2 H), 3.19 (s, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 168.80, 151.81, 132.51, 129.22, 123.12, 119.80, 113.26, 40.33.

HRMS (ESI): *m*/*z* calcd for $C_9H_9BrN_2S$: 255.9670; found: 255.9682.

### *N*,*N*-6-Trimethylbenzo[*d*]thiazol-2-amine (3c)

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 3:1) to give the target compound.

Yield: 157 mg (82%); pale-brown solid; mp 82–84 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 4.0 Hz, 1 H), 7.28 (s, 1 H), 7.00 (d, *J* = 3.8 Hz, 1 H), 3.05 (s, 6 H), 2.28 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 168.11, 150.72, 131.06, 130.61, 127.11, 120.72, 118.34, 40.36, 20.86.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{12}N_2S$: 192.0721; found: 192.0713.

### 6-Chloro-*N*,*N*-dimethylbenzo[*d*]thiazol-2-amine (3d)

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 3:1) to give the target compound.

Yield: 168 mg (79%); pale-white solid; mp 100–102 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.51 (s, 1 H), 7.43 (d, *J* = 4.4 Hz, 1 H), 7.20 (d, *J* = 4.4 Hz, 1 H), 3.15 (s, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 168.57, 151.64, 132.14, 126.38, 125.97, 120.29, 119.33, 40.36.

HRMS (ESI): *m*/*z* calcd for $C_9H_9ClN_2S$: 212.0175; found: 212.0166.

### *N*,*N*-5-Trimethylbenzo[*d*]thiazol-2-amine (3e)

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 3:1) to give the target compound.

Yield: 161 mg (84%); pale-white solid; mp 115–116 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.33 (t, *J* = 13.60 Hz, 2 H), 6.78 (d, *J* = 3.8 Hz, 1 H), 3.07 (s, 6 H), 2.30 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 169.06, 153.28, 135.88, 127.60, 122.17, 120.16, 119.27, 39.67, 21.56.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{12}N_2S$: 192.0721; found: 192.0733.

**5-Chloro-*N*,*N*-dimethylbenzo[*d*]thiazol-2-amine (3f)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 3:1) to give the target compound.

Yield: 187 mg (88 %); pale-white solid; mp 108–110 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.46 (s, 1 H), 7.39 (d, *J* = 4.0 Hz, 1 H), 6.93 (s, 1 H), 3.12 (s, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 169.54, 154.18, 131.88, 129.28, 121.20, 120.99, 118.69, 40.12.

HRMS (ESI): *m*/*z* calcd for $C_9H_9ClN_2S$: 212.0175; found: 212.0183.

**5-Methoxy-*N*,*N*-dimethylbenzo[*d*]thiazol-2-amine (3g)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 7:1) to give the target compound.

Yield: 189 mg (91%); light-pink solid; mp 134–136 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.67 (s, 1 H), 7.20 (d, *J* = 8.8 Hz, 1 H), 6.60 (d, *J* = 8.8 Hz, 1 H), 3.73 (s, 3 H), 3.32 (s, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 180.74, 158.19, 137.11, 129.31, 117.99, 112.11, 111.26, 55.68, 41.33.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{12}N_2OS$: 208.0670; found: 208.0679.

**2-(Dimethylamino)benzo[*d*]thiazole-6-carbonitrile (3h)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 3:1) to give the target compound.

Yield: 146 mg (72%); pale-brown solid; mp 160–162 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.73 (s, 1 H), 7.43 (s, 2 H), 3.16 (s, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 170.90, 156.60, 131.68, 129.95, 124.69, 119.70, 118.74, 102.91, 40.30.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_9N_3S$: 203.0517; found: 203.0506.

***N*,*N*-Diethylbenzo[*d*]thiazol-2-amine (3i)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 7:1) to give the target compound.

Yield: 177 mg (86 %); colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.54 (t, *J* = 4.4 Hz, 2 H), 7.25 (t, *J* = 7.6 Hz, 1 H), 7.01 (t, *J* = 6.8 Hz, 1 H). 3.57–3.52 (m, 4 H), 1.26 (t, *J* = 7.2 Hz, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.30, 130.24, 125.93, 120.88, 120.56, 118.45, 45.54, 12.87.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{14}N_2S$: 206.0878; found: 206.0864.

**6-Bromo-*N*,*N*-diethylbenzo[*d*]thiazol-2-amine (3j)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 7:1) to give the target compound.

Yield: 236 mg (83%); very light yellow oil.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.63 (s, 1 H), 7.36–7.31 (m, 2 H), 3.54–3.49 (m, 4 H), 1.24 (t, *J* = 7.2 Hz, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 179.35, 135.89, 131.50, 129.91, 128.47, 128.08, 117.99, 45.77, 12.67.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}BrN_2S$: 283.9983; found: 283.9992.

**6-Methyl-*N*,*N*-diethylbenzo[*d*]thiazol-2-amine (3k)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 7:1) to give the target compound.

Yield: 196 mg (89 %); colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 8.0 Hz, 1 H), 7.36 (s, 1 H), 7.06 (d, *J* = 8.4 Hz, 1 H), 3.56–3.51 (m, 4 H), 2.36 (s, 3 H), 1.27–1.23 (m, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 166.81, 150.91, 130.52, 130.40, 126.97, 120.64, 118.10, 45.34, 21.21, 12.91.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{16}N_2S$: 220.1034; found: 220.1045.

**6-Chloro-*N*,*N*-diethylbenzo[*d*]thiazol-2-amine (3l)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 7:1) to give the target compound.

Yield: 202 mg (84%); light-yellow oil.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.40 (s, 1 H), 7.31 (d, *J* = 8.0 Hz, 1 H), 7.09 (d, *J* = 8.4 Hz, 1 H), 3.46–3.41 (m, 4 H), 1.16 (t, *J* = 7.2 Hz, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.37, 151.78, 131.72, 126.16, 125.63, 120.13, 119.04, 45.48, 12.82.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}ClN_2S$: 240.0488; found: 240.0498.

**5-Methyl-*N*,*N*-diethylbenzo[*d*]thiazol-2-amine (3m)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 7:1) to give the target compound.

Yield: 180 mg (82%); colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 8.0 Hz, 1 H), 7.38 (s, 1 H), 6.85 (d, *J* = 8.0 Hz, 1 H), 3.55–3.50 (m, 4 H), 2.39 (s, 3 H), 1.27–1.23 (m, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.60, 153.43, 135.70, 127.35, 121.99, 120.10, 120.10, 119.05, 45.41, 21.58, 12.92.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{16}N_2S$: 220.1034; found: 220.1022.

**5-Chloro-*N*,*N*-diethylbenzo[*d*]thiazol-2-amine (3n)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 7:1) to give the target compound.

Yield: 209 mg (87%); light-yellow solid; mp 103–104 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 8.21 (s, 1 H), 7.24 (d, *J* = 6.4 Hz, 1 H), 7.02 (d, *J* = 8.4 Hz, 1 H), 3.77–3.72 (m, 4 H), 1.30 (t, *J* = 7.2 Hz, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 179.10, 137.48, 132.30, 129.67, 126.44, 125.62, 124.94, 45.82, 12.64.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}ClN_2S$: 240.0488; found: 240.0475.

**5-Methoxy-*N*,*N*-diethylbenzo[*d*]thiazol-2-amine (3o)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 7:1) to give the target compound.

Yield: 215 mg (91%); light-yellow solid; mp 77–78 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.85 (s, 1 H), 7.18 (d, *J* = 9.2 Hz, 1 H), 6.59 (d, *J* = 9.2 Hz, 1 H), 3.74 (s, 7 H), 1.28 (t, *J* = 7.2 Hz, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 179.13, 158.08, 137.14, 129.14, 117.80, 112.19, 111.29, 55.70, 45.74, 12.66.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{16}N_2OS$: 223.0983; found: 223.0975.

***N*,*N*-Dimethylthiazolo[5,4-*b*]pyridin-2-amine (3p)**

According to the typical procedure, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc, 3:1) to give the target compound.

Yield: 161 mg (92%); yellow solid; mp 90–92 °C.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 4.0 Hz, 1 H), 7.61 (d, *J* = 4.0 Hz, 1 H), 7.11–7.08 (m, 1 H), 3.01 (s, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.46, 155.69, 147.37, 141.67, 124.26, 121.13, 39.74.

HRMS (ESI): *m*/*z* calcd for $C_8H_9N_3S$: 179.0517; found: 179.0525.

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## Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588835.

## References and Notes

(1) Benteau, V.; Besson, T.; Guillar, J.; Pfeiffer, B. *Eur. J. Med. Chem.* **1999**, *34*, 1053.
(2) Yalchin, I.; Oren, I.; Sener, E.; Akin, A.; Ucaryurk, N. *Eur. J. Med. Chem.* **1992**, *27*, 401.
(3) Palmer, P. J.; Trigg, R. B.; Warrington, J. V. *J. Med. Chem.* **1971**, *14*, 248.
(4) Burger, A.; Sawhey, S. N. *J. Med. Chem.* **1968**, *11*, 270.
(5) Kamlesh, N.; Kale, M. *Pharm. Lett.* **2011**, *3*, 276.
(6) Siddiqui, N. A.; Siddiqui, A. A. *Asian J. Chem.* **2004**, *16*, 1005.
(7) Kale, M.; Mene, D. *Int. J. Pharma Bio Sci.* **2013**, *4*, 503.
(8) Chen, Y. X.; Qian, L. F.; Zhang, W.; Han, B. *Angew. Chem. Int. Ed.* **2008**, *47*, 9330.
(9) Bahrami, K.; Khodaei, M. M.; Naali, F. *J. Org. Chem.* **2008**, *73*, 6835.
(10) Chakraborti, A. K.; Rudrawar, S.; Jadhav, K. B.; Kaur, G.; Chankeshwara, S. V. *Green Chem.* **2007**, *9*, 1335.
(11) Li, Y.; Wang, Y. L.; Wang, J. Y. *Chem. Lett.* **2006**, *35*, 460.
(12) Batista, R. M. F.; Costa, S. P. G.; Raposo, M. M. *Tetrahedron Lett.* **2004**, *45*, 2825.
(13) Ranu, B. C.; Jana, R.; Dey, S. *Chem. Lett.* **2004**, *33*, 274.
(14) Kodomari, M.; Tamaru, Y.; Aoyama, T. *Synth. Commun.* **2004**, *34*, 3029.
(15) Mali, J. R.; Jawale, D. V.; Londhe, B. S.; Mane, R. A. *Green Chem. Lett. Rev.* **2010**, *3*, 209.
(16) Moghaddam, F. M.; Ismaili, H.; Bardajee, G. R. *Heteroat. Chem.* **2006**, *17*, 136.
(17) Itoh, T.; Nagata, K.; Ishikawa, H.; Ohsawa, A. *Heterocycles* **2004**, *62*, 197.
(18) Chen, C.; Chen, Y. J. *Tetrahedron Lett.* **2004**, *45*, 113.
(19) Mourtas, S.; Gatos, D.; Barlos, K. *Tetrahedron Lett.* **2001**, *42*, 2201.
(20) Hutchinson, I.; Stevens, M. F. G.; Westwel, A. D. *Tetrahedron Lett.* **2000**, *41*, 425.
(21) Benedi, C.; Bravo, F.; Uriz, P.; Fernandez, E.; Claver, C.; Castillon, S. *Tetrahedron Lett.* **2003**, *44*, 6073.
(22) Joyce, L. L.; Evindar, G.; Batey, R. A. *Chem. Commun.* **2004**, 446.
(23) Mu, X. J.; Zou, J. P.; Zeng, R. S.; Wu, J. C. *Tetrahedron Lett.* **2005**, *46*, 4345.
(24) Moghaddam, F. M.; Boeini, H. Z. *Synlett* **2005**, 1612.
(25) Evindar, G.; Batey, R. A. *J. Org. Chem.* **2006**, *71*, 1802.
(26) Itoh, T.; Mase, T. *Org. Lett.* **2007**, *9*, 3687.
(27) Downer-Riley, N. K.; Jackson, Y. A. *Tetrahedron* **2008**, *64*, 7741.
(28) (a) Muthusamy, S.; Paeamasivam, R.; Ramakrishnan, V. T. *J. Heterocycl. Chem.* **1991**, *28*, 759. (b) Wang, J.; Peng, F.; Jiang, Z. L.; Wang, L.; Bai, J.; Pan, Y. *Tetrahedron Lett.* **2008**, *49*, 467.
(29) (a) Evinder, G.; Batey, R. A. *Org. Lett.* **2003**, *5*, 133. (b) Joyce, L. L.; Batey, R. A. *Org. Lett.* **2009**, *11*, 2792. (c) Sharma, S.; Pathare, R. S.; Maurya, A. K.; Gopal, K.; Roy, T. K.; Sawant, D. M.; Pardasani, R. T. *Org. Lett.* **2016**, *18*, 356. (d) Sahoo, S. K.; Banerjee, A.; Chakraborty, S.; Patel, B. K. *ACS Catal.* **2012**, *2*, 544. (e) Banerjee, A.; Santra, S. K.; Rout, S. K.; Patel, B. K. *Tetrahedron* **2013**, *69*, 9096. (f) Wang, J. K.; Zong, Y. X.; Zhang, X. X.; Gao, Y.; Li, Z. L.; Yue, G. R.; Quan, Z. J.; Wang, C. L. *Synlett* **2014**, *25*, 2143.
(30) (a) Guo, Y. J.; Tang, R. Y.; Zhong, P.; Li, J. H. *Tetrahedron Lett.* **2010**, *51*, 649. (b) Khatun, N.; Jamir, L.; Ganesh, M.; Patel, B. K. *RSC Adv.* **2012**, *2*, 11557. (c) Xu, W.; Zeng, M. T.; Liu, M.; Liu, X.; Chang, C. Z.; Zhu, H.; Li, Y. S.; Dong, Z. B. *Chem. Lett.* **2017**, DOI: 10.1246/cl.170023.