CSIRO PUBLISHING

Aust. J. Chem. **2012**, *65*, 121–128
http://dx.doi.org/10.1071/CH11330

Full Paper

Divergent Synthesis of Benzo[*d*]thiazoles by PIFA-Mediated Cyclization of β-Oxo Thioamides

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Efficient and divergent synthesis of benzo[*d*]thiazoles is developed from readily available β-oxo thioamides mediated by hypervalent iodine reagent phenyliodine bis(trifluoroaceate) (PIFA) based on reaction conditions selection, which involves the formation of a radical cation and its subsequent intramolecular cyclization process.

Manuscript received: 8 August 2011.
Manuscript accepted: 17 October 2011.
Published online: 28 November 2011.

Introduction

The benzothiazole ring makes up the core structure of numerous natural products and synthetic compounds along with diverse biological properties, such as antitumour,[1] antimicrobial,[2] antiglutamate/antiparkinson,[3] antiparasitic,[4] calcium channel antagonist,[5] and enzyme inhibition including aldose reductase,[6] monoamine oxidase,[7] lipoxygenase,[8] acetylcholinesterase,[9] cyclooxygenase,[10] thrombine,[11] SARS-CoV 3CL protease,[12] and HCV helicase.[13] The therapeutic importance of benzothiazole derivatives and their synthetic utilization as intermediates in organic chemistry have directed great research activity towards the construction of the skeleton of this kind of heterocycle. The most notable method for the synthesis of benzothiazoles involves the condensation of 2-aminothiophenol with substituted nitriles, carboxylic acids, aldehydes, acyl chlorides, or esters.[14] Other methods are reported by means of oxidative cyclization of thioanilides with a large number of oxidizing reagents,[15] and transition metal-catalyzed, particularly palladium or copper, intramolecular nucleophilic aromatic substitution of *o*-halothioanilides.[16] However, some of these methods suffer from drastic reaction conditions, tedious work-up, possibility of side reactions or generation of acidic/metallic wastes. Therefore, to match the increasing scientific and practical demands, it is still of continued interest and great importance to explore simple and efficient synthetic approaches for the construction of benzothiazoles, especially those with wide applicability to achieve more elaborate and flexible substitution patterns.

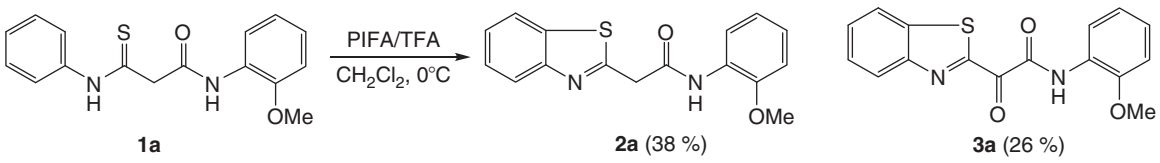
Recently, the synthesis of benzothiazoles by oxidative cyclization of thioanilides with varied hypervalent iodine reagents were reported.[17–19] Hypervalent iodine reagents have been extensively used as oxidation reagents in synthetic organic chemistry because of their ready availability, low toxicity, ease of handling, and reactivity similar to that of heavy metal reagents.[20] Their efficient utilization in metal-free transformations relies on both the extremely mild reaction conditions required and the high chemo-selectivity of the oxidization for a wide range of functionalities such as phenols, amines, sulfides, and carbonyl compounds.[21]

During the course of our studies on the synthesis of carbo- and heterocycles based on β-oxo amides,[22] we successfully achieved efficient syntheses of substituted isothiazol-3(2*H*)-ones, pyrrolin-4-ones, and spiro-fused cycloalkano-(C4)-pyrazolin-5-one *N*-oxides from readily available 1-carbamoyl-ketene-*S,S*-acetals, enaminones, and 1-carbamoyl-1-oximylcycloalkanes, respectively, in the presence of phenyliodine bis(trifluoroaceate) (PIFA). By these reactions, intramolecular N–S, N–C, or N–N bonds are formed.[23]

In connection with these previous studies and following on from our research on the synthesis of highly valuable heterocycles through an oxidative process, we prepared a series of β-oxo thioamides from β-oxo amides and examined their reactivity towards the hypervalent iodine reagent PIFA. As a result of these studies, we have developed a facile and divergent synthesis of benzo[*d*]thiazoles by PIFA-mediated intramolecular C–S bond formation.

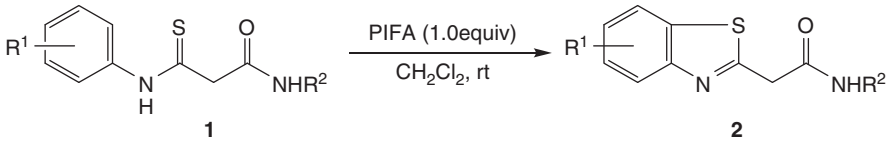
Results and Discussion

The substrates, β-oxo thioamides **1**, were prepared by the reaction of β-oxo amides with isothiocyanates in ethanol in the presence of K_2CO_3 under reflux in excellent yields (up to 96 %) according to the procedure described in our previous work.[24] We then selected *N*-(2-methoxyphenyl)-3-(phenylamino)-3-thioxopropanamide **1a** from a series of substrates **1**, see Table 1, as the model compound to examine its reaction behaviour in the presence of PIFA and trifluoroacetic acid (TFA).[25] Upon treatment of substrate **1a** with PIFA (2.0 equiv) and TFA



Scheme 1. Reaction of **1a** with phenyliodine bis(trifluoroaceate) (PIFA)/trifluoroacetic acid (TFA).

Table 1. Synthesis of benzo[*d*]thiazoles 2 by phenyliodine bis(trifluoroaceate) (PIFA)-mediated oxidative cyclization of β-oxo thioamides 1



Entry[A]	1	R^1	R^2	2	Yield[B] [%]
1	**1a**	H	2-$MeOC_6H_4$	**2a**	73
2	**1b**	H	4-$MeOC_6H_4$	**2b**	66
3	**1c**	H	2-MeC_6H_4	**2c**	68
4	**1d**	H	4-MeC_6H_4	**2d**	62
5	**1e**	H	2,4-$Me_2C_6H_3$	**2e**	75
6	**1f**	H	C_6H_5	**2f**	65
7	**1g**	H	4-ClC_6H_4	**2g**	51
8	**1h**	H	Me	**2h**	60
9	**1i**	4-MeO	C_6H_5	**2i**	64
10	**1j**	2,4-Me_2	C_6H_5	**2j**	71
11	**1k**	4-Cl	2,4-$Me_2C_6H_3$	**2k**	58
12	**1l**	4-CF_3	2,4-$Me_2C_6H_3$	**2l**	46
13	**1m**	3-Me	C_6H_5	**2m–1/2m–2**	61(2/1)[C]
14	**1n**	3-Me	4-$MeOC_6H_4$	**2n–1/2n–2**	67(2/1)[C]

[A]Reagents and conditions: **1** (1.0 mmol), PIFA (1.0 mmol), CH_2Cl_2 (anhydrous, 100 mL), rt, 15–30 min.
[B]Isolated yield.
[C]The data in brackets: ratio of regioisomers **2**.

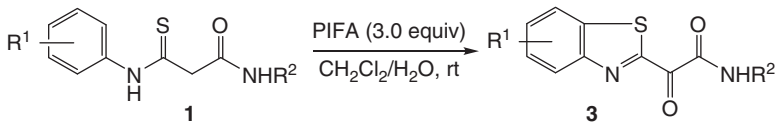
(1.0 equiv) in CH_2Cl_2 at 0°C for 2.0 h, the reaction proceeded smoothly as indicated by TLC, and furnished two products after workup and purification by column chromatography. The products were characterized as 2-(benzo[*d*]thiazol-2-yl)-*N*-(2-methoxyphenyl)-acetamide **2a** and 2-(benzo[*d*]thiazol-2-yl)-*N*-(2-methoxyphenyl)-2-oxoacetamide **3a**, respectively, based on their spectroscopic and analytical data (Scheme 1). Obviously, the formation of **3a**was attributed to further oxidation of **2a** with excess PIFA.

The reaction conditions, including the PIFA/TFA/**1a** ratio, the reaction temperature, and the concentration of PIFA were then investigated to optimize the yield of **2a**. It was observed that when **1a**, PIFA (1.0 equiv), and TFA (3.0 equiv) were subjected to CH_2Cl_2 at 0°C for 20 min, the reaction produced **2a** in 62 % yield. Without addition of TFA, the reaction of **1a** and PIFA (1.0 equiv) could occur to furnish **2a**, which suggested that the additive TFA had no significant influence on the present reaction. Indeed, the reaction of **1a** and PIFA (1.0 equiv) could proceed in other solvents, such as dichloroethane, acetonitrile, and *N,N*-dimethyformamide, but the yield of **2a** was slightly decreased. It was of interest to note that when the reaction of **1a** and PIFA was conducted in anhydrous CH_2Cl_2 even with excess of PIFA (2.0 equiv) and prolonged reaction time (2.0 h), only **2a** could be obtained. After a series of optimization experiments, CH_2Cl_2 was proved to be the best solvent among those tested and the yield of **2a** reached 73 % when the reaction of **1a** with PIFA (1.0 equiv, 0.01 M) was performed in anhydrous CH_2Cl_2 at room temperature for 20 min (Table 1, entry 1).

Having established the optimal conditions for the cyclization process to benzo[*d*]thiazoles **2**, we intended to determine its scope with respect to the amide and thioamide motifs. Thus, a series of β-oxo thioamides **1b**–**n** were subjected to PIFA under the identical conditions as for **2a** in Table 1 (entry 1), and some of the results are listed in Table 1. It was observed that all the reactions of **1b**–**h** with electron-donating and electron-withdrawing aryl amide groups or an alkyl amide group proceeded smoothly to afford the corresponding benzo[*d*]thiazoles **2b**–**h** in moderate to good yields (Table 1, entries 2–8). Under identical conditions, substrates **1i**–**l** bearing electron-donating and electron-withdrawing aryl thioamide groups were also allowed to react with PIFA to give the corresponding benzo[*d*]thiazoles **2i**–**l** in moderate yields (Table 1, entries 9–12). In the cases of substrates **1m** and **1n**, the corresponding benzo[*d*]thiazoles **2m** and **2n** were obtained as a pair of benzannulated regioisomers with a ratio of 2:1 (Table 1, entries 13 and 14, and see Supplementary Material).

In the next studies, we envisaged to optimize the reaction conditions for the synthesis of benzo[*d*]thiazole **3a**. To our delight, **3a** could be exclusively synthesized by subjecting **1a** and 2.5 equivalents of PIFA to CH_2Cl_2 at room temperature for 5.0 h. However, product **3a** was not detectable within the reaction system even when anhydrous CH_2Cl_2 was employed,

Table 2. Synthesis of benzo[*d*]thiazoles 3 by phenyliodine bis(trifluoroaceate) (PIFA)-mediated oxidative cyclization of β-oxo thioamides 1



1 **3**

Entry[A]	**1**	R^1	R^2	**3**	Yield[B] [%]
1	**1a**	H	2-$MeOC_6H_4$	**3a**	62
2	**1b**	H	4-$MeOC_6H_4$	**3b**	57
3	**1c**	H	2-MeC_6H_4	**3c**	55
4	**1d**	H	4-MeC_6H_4	**3d**	52
5	**1e**	H	2,4-$Me_2C_6H_3$	**3e**	61
6	**1f**	H	C_6H_5	**3f**	58
7	**1g**	H	4-ClC_6H_4	**3g**	49
8	**1h**	H	Me	**3h**	54
9	**1i**	4-MeO	C_6H_5	**3i**	57
10	**1j**	2,4-Me_2	C_6H_5	**3j**	60
11	**1k**	4-Cl	2,4-$Me_2C_6H_3$	**3k**	46

[A]Reagents and conditions: **1** (1.0 mmol), PIFA (3.0 mmol), CH_2Cl_2 (100 mL), H_2O (5.0 mmol), rt, 3.0–5.0 h.
[B]Isolated yield.

which indicated that the small amount of water in CH_2Cl_2 might play an important role during the transformation from **1a** to **3a**. In light of this, we added a drop of water to solvent CH_2Cl_2 and performed the reaction of **1a** and PIFA in such solvent. As a result, the reaction proceeded smoothly to afford **3a** and the reaction rate was significantly accelerated. After a series of experiments, optimal conditions for the synthesis of **3a** were obtained when the reaction of **1a** with PIFA (3.0 equiv, 0.03 M) was performed in CH_2Cl_2 (with 5.0 equiv of H_2O) at room temperature for 4.0 h, whereby the yield of **3a** reached 62 % (Table 2, entry 1). Under the same conditions as for **3a**, the synthesis of benzo[*d*]thiazoles **3** was carried out, and some results are summarized in Table 2. It was observed that β-oxo thioamides **1b**–**h** with varied amide groups underwent a cyclization reaction to give the corresponding benzo[*d*]thiazoles **3b**–**h** in moderate yields (Table 2, entries 2–8). The versatility of the protocol proved to be suitable for **1i**–**k** bearing variable thioamide groups affording the corresponding benzo[*d*]thiazoles **3i**–**k** in moderate yields (Table 2, entries 9–11).

The results shown above demonstrate the efficiency and synthetic value of the cyclization reaction with respect to β-oxo thioamides **1** bearing variable amide and thioamide groups.* Therefore, we have provided a novel protocol for the divergent synthesis of benzo[*d*]thiazoles of types **2** and **3**. It should be noted that the richness of the functionality, e.g., thiazole, activated methylene, and amide groups on the benzo[*d*]thiazoles of type **2** may render them extremely versatile as synthons in further synthetic transformations.[26] In particular, benzo[*d*]thiazoles of type **3** can be regarded as both benzothiazol-2-yl ketones[27] and α-ketoamides. α-Ketoamides are frequently encountered as structural subunits in many natural products, and very important synthetic intermediates as well.[28]

On the basis of the obtained results together with some literature results, a plausible mechanism for the synthesis of benzo[*d*]thiazoles **2** and **3** is presented in Scheme 2. β-Oxo thioamide **1** initially reacts with PIFA to generate a radical cation **A** by a single electron transfer (SET) process,[19,29] followed by an intramolecular cyclization reaction to yield benzo[*d*]thiazole **2** through radical **B**. Further oxidization reaction of **2** by PIFA occurs to generate intermediate **C**, which is attacked by water to give intermediates **D** and **E** when aqueous solvent is employed.[30,31] In the presence of PIFA, alcohol **E** is easily oxidized to give rise to final product **3**.[21d,30a,32]

Conclusion

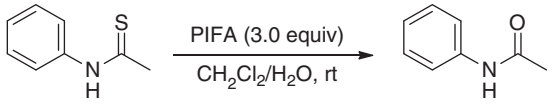
In summary, a facile and divergent synthesis of benzo[*d*]thiazoles of types **2** and **3** has been developed from β-oxo thioamides **1** mediated by PIFA, which involves the formation of a radical cation, and subsequent intramolecular cyclization under rather mild experimental conditions. This protocol is associated with readily available starting materials, mild conditions, good yields, and a broad range of synthetic potential of the products. Further work on the utilization and extension of the scope of the protocol is currently under investigation in our laboratory.

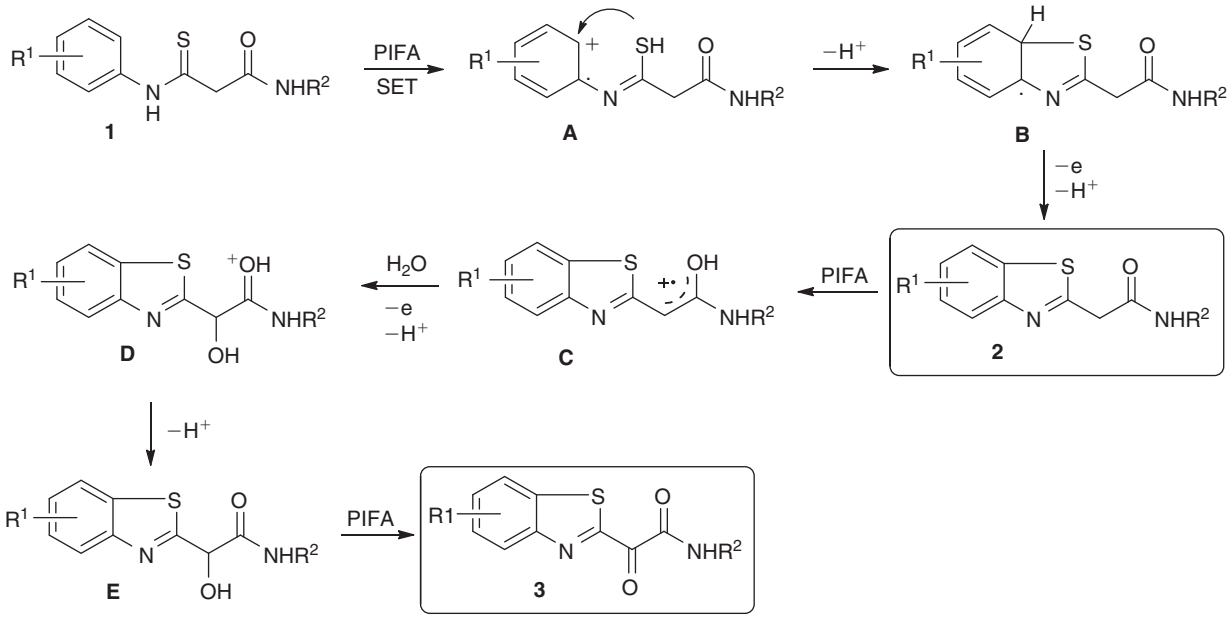
Experimental

Reagents and Instrumentation

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel.

*In an experiment, we examined the reaction of *N*-phenylethanethioamide in the presence of PIFA, but only a desulfurized product *N*-phenylacetamide was obtained in 64 % isolated yield. The result suggested that the amide functionality was essential for the PIFA-mediated oxidative cyclization reaction of arylthioamide 1. For selected work on PIFA-mediated desulfurization of thioamides, see ref. [19].





Scheme 2. Plausible mechanism for the reaction of β-oxo thioamides **1** with phenyliodine bis(trifluoroaceate) (PIFA).

^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Unity spectrometer at 300 and 75 MHz, respectively, with TMS as internal standard. Mass spectra were recorded on an Agilient 1100 LCMsD spectrometer. IR spectra (KBr) were recorded on a Magna-560 FTIR spectrophotometer in the range of 400–4000 cm^{-1}. Melting points were determined on a TECH X-4 micro-melting point apparatus. Elemental analyses were carried out on a Perkin–Elmer PE-2400 analyzer.

*Physical Data of Compounds **1i–n***

1a–h are known compounds, their analytical data are in good agreement with those in the literature.[24]

*Compound **1i***

White solid, mp 129–130°C. δ_H (300 MHz, $CDCl_3$) 3.81 (s, 3H), 4.06 (s, 2H), 6.88–6.93 (m, 2H), 7.14–7.19 (m, 1H), 7.31–7.36 (m, 2H), 7.52 (d, *J* 8.4, 2H), 7.62–7.66 (m, 2H), 8.70 (s, 1H), 11.04 (s, 1H). δ_C (125 MHz, $CDCl_3$) 54.2, 55.4, 113.9, 120.4, 125.1, 129.0, 131.5, 137.0, 158.2, 166.4, 193.2. Anal. Calc. for $C_{16}H_{16}N_2O_2S$: C 63.98, H 5.37, N, 9.33. Found: C 63.82, H 5.48, N 9.41.

*Compound **1j***

White solid, mp 169–170°C. δ_H (300 MHz, $CDCl_3$) 2.23 (s, 3H), 2.33 (s, 3H), 4.07 (s, 2H), 7.04–7.09 (m, 2H), 7.14–7.19 (m, 1H), 7.32–7.40 (m, 3H), 7.52 (d, *J* 7.5, 2H), 8.38 (s, 1H), 10.58 (s, 1H). δ_C (125 MHz, $CDCl_3$) 17.7, 21.1, 53.3, 120.4, 125.1, 126.1, 127.2, 129.0, 131.6, 133.4, 134.4, 137.0, 138.0, 166.3, 195.5. Anal. Calc. for $C_{17}H_{18}N_2OS$: C 68.42, H 6.08, N 9.39. Found: C 68.50, H 6.17, N 9.33.

*Compound **1k***

White solid, mp 157–158°C. δ_H (300 MHz, DMSO) 2.19 (s, 3H), 2.25 (s, 3H), 3.94 (s, 2H), 6.97 (d, *J* 8.1, 1H), 7.02 (s, 1H), 7.27 (d, *J* 8.1, 1H), 7.48 (d, *J* 9.0, 2H), 7.92 (d, *J* 9.0, 2H), 9.49 (s, 1H), 11.90 (s, 1H). δ_C (125 MHz, $CDCl_3$) 18.0, 20.9, 55.1, 123.8, 124.4, 127.1, 128.8, 130.9, 131.4, 131.9, 136.2, 137.1, 166.5, 194.1. Anal. Calc. for $C_{17}H_{17}ClN_2OS$: C 61.34, H 5.15, N 8.42. Found: C 61.48, H 5.09, N 8.26.

*Compound **1l***

White solid, mp 167–169°C. δ_H (400 MHz, DMSO) 2.19 (s, 3H), 2.25 (s, 3H), 3.98 (s, 2H), 6.97 (d, *J* 8.0, 1H), 7.03 (s, 1H), 7.27 (d, *J* 8.0, 1H), 7.80 (d, *J* 8.4, 2H), 8.17 (d, *J* 8.4, 2H), 9.52 (s, 1H), 12.08 (s, 1H). δ_C (100 MHz, DMSO) 17.7, 20.4, 54.6, 122.8, 122.9, 124.9, 125.0, 125.8, 126.4, 130.8, 131.6 (131.7), 133.3 (133.4), 134.4, 142.6 (142.8), 165.3 (165.4), 196.4 (196.5). Anal. Calc. for $C_{18}H_{17}F_3N_2OS$: C 59.00, H 4.68, N 7.65. Found: C 59.17, H 4.65, N 7.61.

*Compound **1m***

White solid,: mp 114–115°C. δ_H (300 MHz, $CDCl_3$) 2.36 (s, 3H), 4.07 (s, 2H), 7.08 (d, *J* 7.8, 1H), 7.14–7.19 (m, 1H), 7.28–7.36 (m, 3H), 7.52 (d, *J* 8.1, 3H), 7.60 (d, *J* 8.1, 1H), 8.68 (s, 1H), 11.12 (s, 1H). δ_C (125 MHz, $CDCl_3$) 21.3, 54.5, 120.4, 120.7, 124.1, 125.2, 127.9, 128.6, 129.0, 137.0, 138.3, 138.9, 166.4, 193.7. Anal. Calc. for $C_{16}H_{16}N_2OS$: C 67.58, H 5.67, N 9.85. Found: C 67.51, H 5.53, N 9.77.

*Compound **1n***

White solid, mp 115–116°C. δ_H (500 MHz, $CDCl_3$) 2.35 (s, 3H), 3.79 (s, 3H), 4.08 (s, 2H), 6.84 (d, *J* 8.5, 2H), 7.08 (d, *J* 7.5, 1H), 7.28 (m, 1H), 7.41 (d, *J* 8.5, 2H), 7.53 (s, 1H), 7.60 (d, *J* 8.0, 1H), 8.77 (s, 1H), 11.35 (s, 1H). δ_C (125 MHz, $CDCl_3$) 21.4, 54.2, 55.4, 114.1, 120.6, 122.3, 124.0, 127.9, 128.6, 129.8, 138.3, 138.9, 157.0, 166.3, 193.5. Anal. Calc. for $C_{17}H_{18}N_2O_2S$: C 64.94, H 5.77, N 8.91. Found: C 65.03, H 5.82, N 8.88.

*Typical Procedure for the Synthesis of Substituted Benzo[d]thiazoles **2***

Preparation of **2a** is described as an example: To a solution of **1a** (0.30 g, 1.0 mmol) in anhydrous CH_2Cl_2 (100 mL) was added PIFA (0.43 g, 1.0 mmol) in one portion at room temperature. After being stirred for 15 min, the reaction mixture was

quenched with saturated aqueous $NaHCO_3$ (50 mL). The organic layer was washed with water (3 × 50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate, 8:1) to give the product **2a** (0.21 g, 73 %) as a pale solid.

Selected Data for Compounds ***2***

Compound ***2a***

Pale solid, mp 149–151°C. δ_H (300 MHz, $CDCl_3$) 3.88 (s, 3H), 4.24 (s, 2H), 6.87 (d, *J* 8.1, 1H), 6.93–6.99 (m, 1H), 7.02–7.08 (m, 1H), 7.40–7.45 (m, 1H), 7.50–7.55 (m, 1H), 7.90 (d, *J* 8.1, 1H), 8.06 (d, *J* 8.1, 1H), 8.38 (dd, J_1 8.1, J_2 1.5, 1H), 9.65 (s, 1H). δ_C (125 MHz, $CDCl_3$) 42.1, 55.7, 110.0, 119.8, 120.9, 121.6, 122.6, 124.0, 125.3, 126.3, 127.5, 135.1, 148.2, 152.9, 164.3, 164.4. MS Calc. *m*/*z* 298.1. Found: 299.1 $[M + 1]^+$. Anal. Calc. for $C_{16}H_{14}N_2O_2S$: C 64.41, H 4.73, N 9.39. Found: C 64.24, H 4.81, N 9.46.

Compound ***2b***

Pale solid, mp 151–153°C. δ_H (300 MHz, $CDCl_3$) 3.79 (s, 3H), 4.21 (s, 2H), 6.86 (d, *J* 8.4, 2H), 7.41–7.55 (m, 4H), 7.90 (d, *J* 7.8, 1H), 8.05 (d, *J* 7.8, 1H), 9.43 (s, 1H). δ_C (125 MHz, $CDCl_3$) 41.3, 55.3, 114.0, 121.6, 121.8, 122.5, 125.3, 126.3, 130.7, 134.8, 152.5, 156.4, 164.4, 164.8. ν_{max} (KBr)/cm^{-1} 3252, 3061, 2936, 2837, 1660, 1608, 1536, 1511, 1455, 1435, 1411, 1402, 1244, 1166, 1114, 1028, 827, 760, 727. Anal. Calc. for $C_{16}H_{14}N_2O_2S$: C 64.41, H 4.73, N 9.39. Found: C 64.46, H 4.69, N 9.28.

Compound ***2c***

Pale solid, mp 151–152°C. δ_H (300 MHz, $CDCl_3$) 2.35 (s, 3H), 4.26 (s, 2H), 7.03–7.08 (m, 1H), 7.17–7.22 (m, 2H), 7.41–7.47 (m, 1H), 7.51–7.56 (m, 1H), 7.91 (d, *J* 7.8, 1H), 8.01 (d, *J* 8.1, 1H), 8.06 (d, *J* 8.1, 1H), 9.88 (s, 1H). δ_C (125 MHz, $CDCl_3$) 18.0, 41.1, 121.6, 121.9, 122.4, 124.7, 125.4, 126.4, 126.6, 128.3, 130.3, 134.6, 135.9, 152.5, 164.3, 165.0. Anal. Calc. for $C_{16}H_{14}N_2OS$: C 68.06, H 5.00, N 9.92. Found: C 68.28, H 4.89, N 9.87.

Compound ***2d***

Pale solid, mp 153–154°C. δ_H (300 MHz, $CDCl_3$) 2.30 (s, 3H), 4.21 (s, 2H), 7.11 (d, *J* 7.8, 2H), 7.42–7.54 (m, 4H), 7.88 (d, *J* 7.8, 1H), 8.04 (d, *J* 7.8, 1H), 9.49 (s, 1H). δ_C (125 MHz, $CDCl_3$) 20.8, 41.5, 120.1, 121.6, 122.6, 125.4, 126.3, 129.3, 134.1, 134.9, 135.0, 152.5, 164.6, 164.9. ν_{max} (KBr)/cm^{-1} 3246, 3031, 2917, 1660, 1594, 1533, 1513, 1455, 1434, 1400, 1245, 1185, 1117, 816, 759, 728. Anal. Calc. for $C_{16}H_{14}N_2OS$: C 68.06, H 5.00, N 9.92. Found: C 68.13, H 5.08, N 9.83.

Compound ***2e***

Pale solid, mp 151–152°C. δ_H (300 MHz, $CDCl_3$) 2.28 (s, 3H), 2.29 (s, 3H), 4.24 (s, 2H), 7.00 (s, 1H), 7.01 (d, *J* 7.5, 1H), 7.41–7.46 (m, 1H), 7.50–7.55 (m, 1H), 7.86 (d, *J* 8.1, 1H), 7.90 (d, *J* 7.5, 1H), 8.00 (d, *J* 8.1, 1H), 9.70 (s, 1H). δ_C (125 MHz, $CDCl_3$) 17.9, 20.8, 41.2, 121.7, 122.2, 122.5, 125.5, 126.5, 127.1, 128.6, 131.0, 133.3, 134.5, 134.7, 152.6, 164.2, 165.2. ν_{max} (KBr)/cm^{-1} 3271, 3008, 2912, 1651, 1615, 1591, 1531, 1454, 1435, 1399, 1340, 1268, 1224, 1195, 1119, 827, 754, 726. Anal. Calc. for $C_{17}H_{16}N_2OS$: C 68.89, H 5.44, N 9.45. Found: C 69.08, H 5.37, N 9.33.

Compound ***2f***

Pale solid, mp 161–162°C. δ_H (300 MHz, $CDCl_3$) 4.22 (s, 2H), 7.09–7.14 (m, 1H), 7.30–7.35 (m, 2H), 7.40–7.45 (m, 1H), 7.50–7.58 (m, 3H), 7.89 (d, *J* 7.8, 1H), 8.05 (d, *J* 7.8, 1H), 9.64 (s, 1H). δ_C (125 MHz, $CDCl_3$) 41.5, 120.0, 121.7, 122.7, 124.5, 125.5, 126.5, 129.0, 134.8, 137.6, 152.6, 164.4, 164.8. Anal. Calc. for $C_{15}H_{12}N_2OS$: C 67.14, H 4.51, N 10.44. Found: C 67.23, H 4.48, N 10.61.

Compound ***2g***

Pale solid, mp 163–164°C. δ_H (300 MHz, $CDCl_3$) 4.22 (s, 2H), 7.29 (d, *J* 8.7, 2H), 7.41–7.47 (m, 1H), 7.51–7.56 (m, 3H), 7.90 (d, *J* 7.8, 1H), 8.05 (d, *J* 7.8, 1H), 9.83 (s, 1H). δ_C (125 MHz, $CDCl_3$) 41.3, 121.2, 121.7, 122.7, 125.7, 126.6, 129.0, 129.5, 134.7, 136.3, 152.6, 164.4, 164.7. Anal. Calc. for $C_{15}H_{11}ClN_2OS$: C 59.50, H 3.66, N 9.25. Found: C 59.57, H 3.54, N 9.36.

Compound ***2h***

Pale solid, mp 101–103°C. δ_H (300 MHz, $CDCl_3$) 2.87 (d, *J* 4.8, 3H), 4.06 (s, 2H), 7.20 (s, 1H), 7.38–7.44 (m, 1H), 7.47–7.53 (m, 1H), 7.88 (d, *J* 8.1, 1H), 8.01 (d, *J* 8.1, 1H). δ_C (125 MHz, $CDCl_3$) 26.4, 40.8, 121.5, 122.5, 125.1, 126.1, 135.1, 152.6, 164.7, 167.3. ν_{max} (KBr)/cm^{-1} 3297, 3093, 3058, 2939, 2903, 1651, 1596, 1560, 1521, 1454, 1436, 1395, 1352, 1249, 1132, 760, 724. Anal. Calc. for $C_{10}H_{10}N_2OS$: C 58.23, H 4.89, N 13.58. Found: C 58.36, H 4.76, N 13.49.

Compound ***2i***

Reddish solid, mp 125–127°C. δ_H (300 MHz, $CDCl_3$) 3.89 (s, 3H), 4.16 (s, 2H), 7.09–7.14 (m, 2H), 7.30–7.36 (m, 3H), 7.57 (d, *J* 7.5, 2H), 7.93 (d, *J* 9.0, 1H), 9.55 (s, 1H). δ_C (125 MHz, $CDCl_3$) 41.4, 55.8, 104.0, 115.8, 120.0, 123.1, 124.5, 128.9, 136.2, 137.7, 147.1, 157.9, 161.9, 164.8. Anal. Calc. for $C_{16}H_{14}N_2O_2S$: C 64.41, H 4.73, N 9.39. Found: C 64.53, H 4.65, N 9.28.

Compound ***2j***

Pale solid, mp 161–162°C. δ_H (300 MHz, $CDCl_3$) 2.46 (s, 3H), 2.78 (s, 3H), 4.18 (s, 2H), 7.09–7.16 (m, 2H), 7.32–7.37 (m, 2H), 7.51 (s, 1H), 7.60 (d, *J* 7.5, 2H), 10.25 (s, 1H). δ_C (125 MHz, $CDCl_3$) 18.4, 21.5, 40.9, 118.8, 119.6, 124.3, 128.7, 129.0, 131.8, 134.5, 135.6, 137.8, 149.9, 162.6, 164.6. ν_{max} (KBr)/cm^{-1} 3262, 3039, 2906, 1660, 1599, 1526, 1498, 1444, 1396, 1250, 1188, 1116, 850, 838, 746, 692. Anal. Calc. for $C_{17}H_{16}N_2OS$: C 68.89, H 5.44, N 9.45. Found: C 69.03, H 5.50, N 9.37.

Compound ***2k***

Pale solid: mp 204–205°C. δ_H (300 MHz, DMSO) 2.18 (s, 3H), 2.25 (s, 3H), 4.13 (s, 2H), 6.98 (d, *J* 7.8, 1H), 7.04 (s, 1H), 7.27 (d, *J* 8.1, 1H), 7.53 (dd, J_1 8.1, J_2 2.1, 1H), 7.97 (d, *J* 8.7, 1H), 8.25 (s, 1H), 9.76 (s, 1H). δ_C (125 MHz, (D_6) DMSO) 18.2, 21.0, 41.5, 122.2, 123.9, 125.5, 126.9, 127.0, 130.0, 131.3, 132.3, 133.7, 135.2, 137.4, 151.5, 166.4, 167.1. Anal. Calc. for $C_{17}H_{15}ClN_2OS$: C 61.72, H 4.57, N 8.47. Found: C 61.94, H 4.60, N 8.43.

Compound ***2l***

Pale solid, mp 168–169°C. δ_H (400 MHz, DMSO) 2.18 (s, 3H), 2.25 (s, 3H), 4.39 (s, 2H), 6.98 (d, *J* 6.8, 1H), 7.04 (s, 1H), 7.28 (d, *J* 6.8, 1H), 7.82 (d, *J* 8.0, 1H), 8.17 (d, *J* 8.0, 1H),

8.63 (s, 1H), 9.79 (s, 1H). δ_C (100 MHz, (D_6)DMSO) 17.7 (17.9), 20.3 (20.4), 41.1, 120.2, 122.7 (122.9), 124.1, 124.9 (125.0), 126.3 (126.5), 128.6, 130.2, 130.7 (130.9), 133.4, 133.8 (134.0), 134.7, 142.2, 157.6, 165.4, 169.7. Anal. Calc. for $C_{18}H_{15}F_3N_2OS$: C 59.33, H 4.15, N 7.69. Found: C 59.15, H 4.13, N 7.71.

*Typical Procedure for the Synthesis of Substituted Benzo[*d*]thiazoles **3***

Preparation of **3a** is described as an example: To a solution of **1a** (0.30 g, 1.0 mmol) in CH_2Cl_2 (100 mL) and water (0.09 g, 5.0 mmol) was added PIFA (1.29 g, 3.0 mmol) in one portion at room temperature under stirring. After being stirred at room temperature for 3.0 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (50 mL). The organic layer was washed with water (3 × 50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate, 8:1) to give the product **3a** (0.19 g, 62 %) as a yellowish solid.

*Selected Data for Compounds **3***

*Compound **3a***

Yellowish solid, mp 184–186°C. δ_H (300 MHz, $CDCl_3$) 4.02 (s, 3H), 6.97–7.08 (m, 2H), 7.16–7.22 (m, 1H), 7.63–7.65 (m, 2H), 8.07 (d, *J* 6.9, 1H), 8.34 (d, *J* 8.1, 1H), 8.56 (d, *J* 8.1, 1H), 10.55 (s, 1H). δ_C (125 MHz, (D_6)DMSO) 56.5, 112.0, 121.1, 121.2, 123.8, 125.9, 126.0, 126.8, 128.4, 129.2, 137.1, 149.7, 152.9, 160.7, 163.5, 180.6. MS Calc. *m/z* 312.06, Found: 335.05 $[M + Na]^+$. Anal. Calc. for $C_{16}H_{12}N_2O_3S$: C 61.53, H 3.87, N 8.97. Found: C 61.58, H 3.77, N 8.85.

*Compound **3b***

Reddish solid, mp 179–180°C. δ_H (300 MHz, $CDCl_3$) 3.84 (s, 3H), 6.96 (d, *J* 9.0, 2H), 7.63–7.67 (m, 2H), 7.72 (dd, $J_1 = 9.0$, $J_2 = 2.1$, 2H), 8.05–8.08 (m, 1H), 8.34–8.37 (m, 1H), 9.92 (s, 1H). δ_C (125 MHz, $CDCl_3$) 55.4, 114.4, 121.7, 122.3, 126.1, 127.7, 128.7, 129.4, 138.4, 152.5, 156.3, 157.4, 158.8, 177.8. ν_{max} (KBr)/cm^{-1} 3328, 3048, 3010, 2950, 2835, 1697, 1670, 1611, 1576, 1542, 1510, 1460, 1250, 1154, 1032, 821, 758, 726. Anal. Calc. for $C_{16}H_{12}N_2O_3S$: C 61.53, H 3.87, N 8.97. Found: C 61.45, H 3.96, N 8.91.

*Compound **3c***

Yellowish solid, mp 138–140°C. δ_H (300 MHz, $CDCl_3$) 2.52 (s, 3H), 7.14–7.19 (m, 1H), 7.30–7.33 (m, 2H), 7.61–7.69 (m, 2H), 8.05–8.08 (m, 1H), 8.26–8.30 (m, 2H), 10.57 (s, 1H). δ_C (125 MHz, $CDCl_3$) 18.0, 121.6, 122.4, 125.6, 125.8, 127.0, 127.8, 128.4, 128.8, 130.6, 134.8, 137.9, 152.3, 156.0, 160.8, 177.4. Anal. Calc. for $C_{16}H_{12}N_2O_2S$: C 64.85, H 4.08, N 9.45. Found: C 64.78, H 4.18, N 9.53.

*Compound **3d***

Yellowish solid, mp 204–205°C. δ_H (300 MHz, (D_6)DMSO) 2.31 (s, 3H), 7.23 (d, *J* 8.1, 2H), 7.64–7.72 (m, 4H), 8.32–8.33 (m, 2H), 11.06 (s, 1H). δ_C (125 MHz, (D_6)DMSO) 21.1, 120.5, 123.8, 126.1, 128.4, 129.2, 130.0, 134.5, 135.5, 137.5, 153.1, 161.5, 161.6, 182.0. ν_{max} (KBr)/cm^{-1} 3332, 3029, 1678, 1591, 1536, 1510, 1457, 1403, 1260, 1149, 818, 759, 727. Anal. Calc. for $C_{16}H_{12}N_2O_2S$: C 64.85, H 4.08, N 9.45. Found: C 64.78, H 4.12, N 9.54.

*Compound **3e***

Yellowish solid, mp 161–162°C. δ_H (500 MHz, $CDCl_3$) 2.33 (s, 3H), 2.47 (s, 3H), 7.09 (d, *J* 8.0, 2H), 7.61–7.67 (m, 2H), 8.05 (d, *J* 7.5, 1H), 8.12 (d, *J* 8.0, 1H), 8.28 (d, *J* 7.5, 1H), 10.46 (s, 1H). δ_C (125 MHz, $CDCl_3$) 18.0, 20.9, 121.7, 122.4, 125.7, 127.5, 127.8, 128.4, 128.8, 131.4, 132.2, 135.8, 138.1, 152.4, 156.1, 160.6, 177.6. ν_{max} (KBr)/cm^{-1} 3252, 3189, 3115, 3056, 2976, 1700, 1681, 1603, 1547, 1478, 1455, 1421, 1322, 1247, 950, 926, 875, 831, 764, 727. Anal. Calc. for $C_{17}H_{14}N_2O_2S$: C 65.79, H 4.55, N 9.03. Found: C 65.85, H 4.46, N 9.10.

*Compound **3f***

Yellowish solid, mp 200–202°C. δ_H (300 MHz, (D_6)DMSO) 7.18–7.23 (m, 1H), 7.40–7.45 (m, 2H), 7.69–7.72 (m, 2H), 7.77 (d, *J* 7.8, 2H), 8.31–8.36 (m, 2H), 11.16 (s, 1H). δ_C (125 MHz, (D_6)DMSO) 120.5, 123.9, 125.4, 126.1, 128.4, 129.3, 129.7, 137.5, 138.0, 153.1, 161.6, 161.7, 182.0. Anal. Calc. for $C_{15}H_{10}N_2O_2S$: C 63.81, H 3.57, N 9.92. Found: C 63.67, H 3.59, N 10.03.

*Compound **3g***

Yellowish solid, mp 231–232°C. δ_H (300 MHz, (D_6)DMSO) 7.49 (d, *J* 8.7, 2H), 7.70–7.72 (m, 2H), 7.82 (d, *J* 8.7, 2H), 8.32–8.34 (m, 2H), 11.30 (s, 1H). δ_C (125 MHz, (D_6)DMSO) 122.3, 123.9, 126.2, 128.4, 129.1, 129.3, 129.6, 137.0, 137.6, 153.1, 161.3, 161.6, 181.5. Anal. Calc. for $C_{15}H_9ClN_2O_2S$: C 56.88, H 2.86, N 8.84. Found: C 56.79, H 2.91, N 8.91.

*Compound **3h***

Yellowish solid, mp 144–145°C. δ_H (300 MHz, $CDCl_3$) 3.09 (d, *J* 5.1, 3H), 7.60–7.64 (m, 2H), 8.03–8.06 (m, 1H), 8.10 (s, 1H), 8.30–8.33 (m, 1H). δ_C (125 MHz, $CDCl_3$) 26.4, 122.2, 125.9, 127.5, 128.5, 138.2, 152.5, 159.2, 159.9, 177.8. ν_{max} (KBr)/cm^{-1} 3365, 3061, 1679, 1538, 1460, 1405, 1320, 1178, 954, 755, 723. Anal. Calc. for $C_{10}H_8N_2O_2S$: C 54.53, H 3.66, N 12.72. Found: C 54.61, H 3.79, N 12.68.

*Compound **3i***

Yellowish solid, mp 187–188°C. δ_H (300 MHz, $CDCl_3$) 3.96 (s, 3H), 7.22–7.24 (m, 2H), 7.41–7.46 (m, 3H), 7.79 (d, *J* 7.8, 2H), 8.21 (d, *J* 9.3, 1H), 9.98 (s, 1H). δ_C (125 MHz, (D_6)DMSO) 56.7, 105.1, 119.4, 120.6, 125.5, 127.2, 129.8, 138.2, 140.0, 148.0, 159.2, 160.8, 162.2, 182.2. Anal. Calc. for $C_{16}H_{12}N_2O_3S$: C 61.53, H 3.87, N 8.97. Found: C 61.39, H 3.95, N 9.04.

*Compound **3j***

Yellowish solid, mp 194–195°C. δ_H (300 MHz, $CDCl_3$) 2.52 (s, 3H), 2.87 (s, 3H), 7,23 (d, *J* 7.2, 1H), 7.28 (s, 1H), 7.42–7.47 (m, 2H), 7.66 (s, 1H), 7.80 (d, *J* 8.4, 2H), 11.07 (s, 1H). δ_C (125 MHz, (D_6)DMSO) 18.3, 21.9, 120.3, 120.6, 125.3, 129.6, 130.2, 135.3, 137.9, 138.0, 139.8, 150.9, 159.3, 161.5, 181.7. ν_{max} (KBr)/cm^{-1} 3339, 3053, 1674, 1598, 1538, 1444, 1387, 1248, 1143, 1016, 893, 753. Anal. Calc. for $C_{17}H_{14}N_2O_2S$: C 65.79, H 4.55, N 9.03. Found: C 65.87, H 4.59, N 8.91.

*Compound **3k***

Yellowish solid, mp 188–189°C. δ_H (300 MHz, $CDCl_3$) 2.34 (s, 3H), 2.43 (s, 3H), 7.10 (d, *J* 8.1, 2H), 7.60 (dd, J_1 8.7, J_2 1.8, 1H), 8.06 (d, *J* 7.5, 2H), 8.22 (d, *J* 8.7, 1H), 9.93 (s, 1H). δ_C (125 MHz, $CDCl_3$) 17.8, 20.9, 121.7, 121.8, 126.7, 127.5,

128.5, 128.9, 131.4, 131.8, 135.2, 136.0, 139.4, 150.9, 156.2, 159.6, 177.5. Anal. Calc. for $C_{17}H_{13}ClN_2O_2S$: C 59.21, H 3.80, N 8.12. Found: C 59.34, H 3.76, N 8.21.

Supplementary Material

NMR spectra of compounds **1i**–**n**, **2a**–**n**, and **3a**–**k** are available on the Journal's website.

Acknowledgement

Financial support of this research by the NNSFC (20872136 and 51073150) is greatly acknowledged.

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