HETEROCYCLES, Vol. 96, No. 7, 2018, pp. 1275 - 1288. © 2018 The Japan Institute of Heterocyclic Chemistry
Received, 14th May, 2018, Accepted, 7th June, 2018, Published online, 13th June, 2018
DOI: 10.3987/COM-18-13923

SYNTHESIS OF (*E*)-*N*-SUBSTITUTED 1,2-BENZOTHIAZOL-3(2*H*)-IMINE 1,1-DIOXIDE DERIVATIVES FROM SECONDARY BENZENESULFONAMIDES AND ISOTHIOCYANATES

Kazuhiro Kobayashi* and Daiki Fujiwara

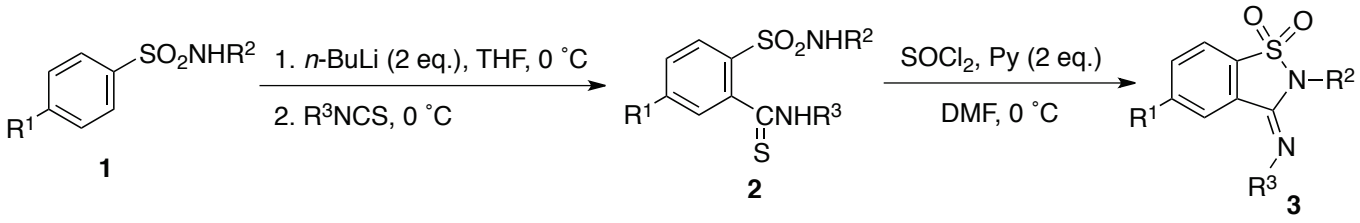
Applied Chemistry Field, Chemistry and Biotechnology Course, Department of Engineering, Graduate School of Sustainability Science, Tottori University, 4-101 Koyama-minami, Tottori 680-8552, Japan. E-mail: kkoba@tottori-u.ac.jp

Abstract – A new and simple method for the preparation of (*E*)-*N*-substituted 1,2-benzothiazol-3(2*H*)-imine 1,1-dioxide derivatives has been developed. 2,*N*-Dilithiobenzenesulfonamides, generated by the treatment of secondary benzenesulfonamides with two equivalents of butyllithium, react with isothiocyanates to afford the corresponding 2-(aminosulfonyl)benzothioamides, which undergo ring closure with a formal elimination of hydrogen sulfide on treatment with thionyl chloride in the presence of two equivalents of pyridine to provide the desired products. Acid hydrolysis of some of these products leads to the formation of *N*-substituted saccharins.

Some 1,2-benzothiazol-3(2*H*)-imine 1,1-dioxide derivatives have been reported to be useful as agrochemicals,[1] such as insecticides[1a] and pesticides,[1b,c] and veterinary drugs, such as animal pest control agents.[1e] These compounds have been traditionally prepared by the reaction of 2-(chlorosulfonyl)benzonitriles with primary amines.[1] Meanwhile, only a few synthetic methods of *N*-substituted derivatives, which may be of medicinal importance, have been developed. The synthesis utilizing Pd-catalyzed annulation of 2*H*-1,2,3,4-benzothiatriazine 1,1-dioxides with 2,6-xylyl isocyanide has been reported by Miura *et al*.,[2] and Liu *et al*. have reported the synthesis by Pd-catalyzed annulation of 2-halobenzenesulfonamides with isocyanides.[3] We envisaged that the reaction of 2,*N*-dilithiobenzenesulfonamides, generated from secondary benzenesulfonamides, with isothiocyanates could give the corresponding 2-(aminosulfonyl)benzothioamides, from which a formal elimination of hydrogen sulfide would provide *N*-substituted 1,2-benzothiazol-3(2*H*)-imine 1,1-dioxide derivatives.[4] We have found that thionyl chloride in the presence of two equivalents of pyridine is effective for this ring closure.

In this paper we wish to describe the results of our study, which offer a facile and general entry to *N*-substituted 1,2-benzothiazol-3(2*H*)-imine 1,1-dioxide derivatives from readily available starting materials.

The preparation of 2,(*E*)-*N*-disubstituted 1,2-benzothiazol-3(2*H*)-imine 1,1-dioxides (**3**) from secondary benzenesulfonamides (**1**) was conducted according to the procedure shown in Scheme 1. In the first step of the method, compounds (**1**) were treated with two equivalents of butyllithium in THF at 0 ˚C to generate 2,*N*-dilithiobenzenesulfonamides following to the procedure reported by Hauser *et al*., whereby this type of dilithio compounds were first generated.[5] Then, these were allowed to react with isothiocyanates at the same temperature to give, after aqueous work-up and subsequent purification, the corresponding 2-(aminosulfonyl)benzothioamides (**2**). The yields of the products were generally fair to good as listed in Table 1. *N*-Arylbenzenesulfonamides (**1e**) and (**1i**) also proved to be satisfactorily used in the reaction to give the desired products (**2e**) and (**2i**), respectively, in relatively good yields (Entries 8 and 13). In the cases using 4-chlorobenzenesulfonamides (**1f**) and (**1g**) (Entries 10-12), yields of the corresponding products were rather lower than those of the others; some structurally undefined by-products were formed. These results may be caused by deprotonation at the ortho position to the chloro substituent and/or nucleophilic substitution with this substituent.



Scheme 1

Cyclization of 2-(aminosulfonyl)benzothioamides (**2**) thus prepared with a formal elimination of hydrogen sulfide to (*E*)-*N*-substituted 1,2-benzothiazol-3(2*H*)-imine 1,1-dioxides (**3**) was then carried out. When compounds (**2**) were treated with thionyl chloride in DMF in the presence of two equivalents of pyridine at 0 ˚C, the desired products (**3**) were obtained, as shown in Scheme 1 as well. Table 1 also shows the yields of **3**, which are generally fair-to-good independent of the substituents R^1, R^2, and R^3 of **2**. The stereochemistry of the products was determined by NOESY analyses. For example, a strong interaction between the signal at δ 3.95 assigned to methylene protons and that at δ 8.07 assigned to 4-H of compound (**3a-ii**) was observed (Figure 1). The high field shifts of the signals due to the 4-protons of *N*-aryl derivatives (**3b-ii**) (δ 6.50) and (**3f-ii**) (δ 6.90) may support the stereochemistry. It is noteworthy that no stereoisomeric products were obtained.

Table 1. Preparation of (*E*)-*N*-substituted 1,2-benzothiazol-3(2*H*)-imines (**3**)

Entry	**1**	R^1	R^2	R^3 in R^3NCS	**2**	Yield/%[a]	**3**	Yield/%[a]
1	**1a**	H	Me	Me	**2a-i**	58	**3a-i**	68
2	**1a**	H	Me	Et	**2a-ii**	76	**3a-ii**	63
3	**1b**	Me	Me	Et	**2b-i**	78	**3b-i**	62
4	**1b**	Me	Me	Ph	**2b-ii**	76	**3b-ii**	60
5	**1c**	Me	Et	Et	**2c**	89	**3c**	65
6	**1d**	Me	*n*-Bu	Me	**2d-i**	60	**3d-i**	66
7	**1d**	Me	*n*-Bu	Et	**2d-ii**	77	**3d-ii**	70
8	**1e**	Me	Ph	Et	**2e**	73	**3e**	72
9	**1f**	Cl	Me	Et	**2f-i**	58	**3f-i**	67
10	**1f**	Cl	Me	4-$MeOC_6H_4$	**2f-ii**	38	**3f-ii**	62
11	**1g**	Cl	Et	Me	**2g**	30	**3g**	66
12	**1h**	OMe	Me	Et	**2h**	70	**3h**	61
13	**1i**	OMe	Ph	Me	**2i**	60	**3i**	71

[a] Yields of isolated products.

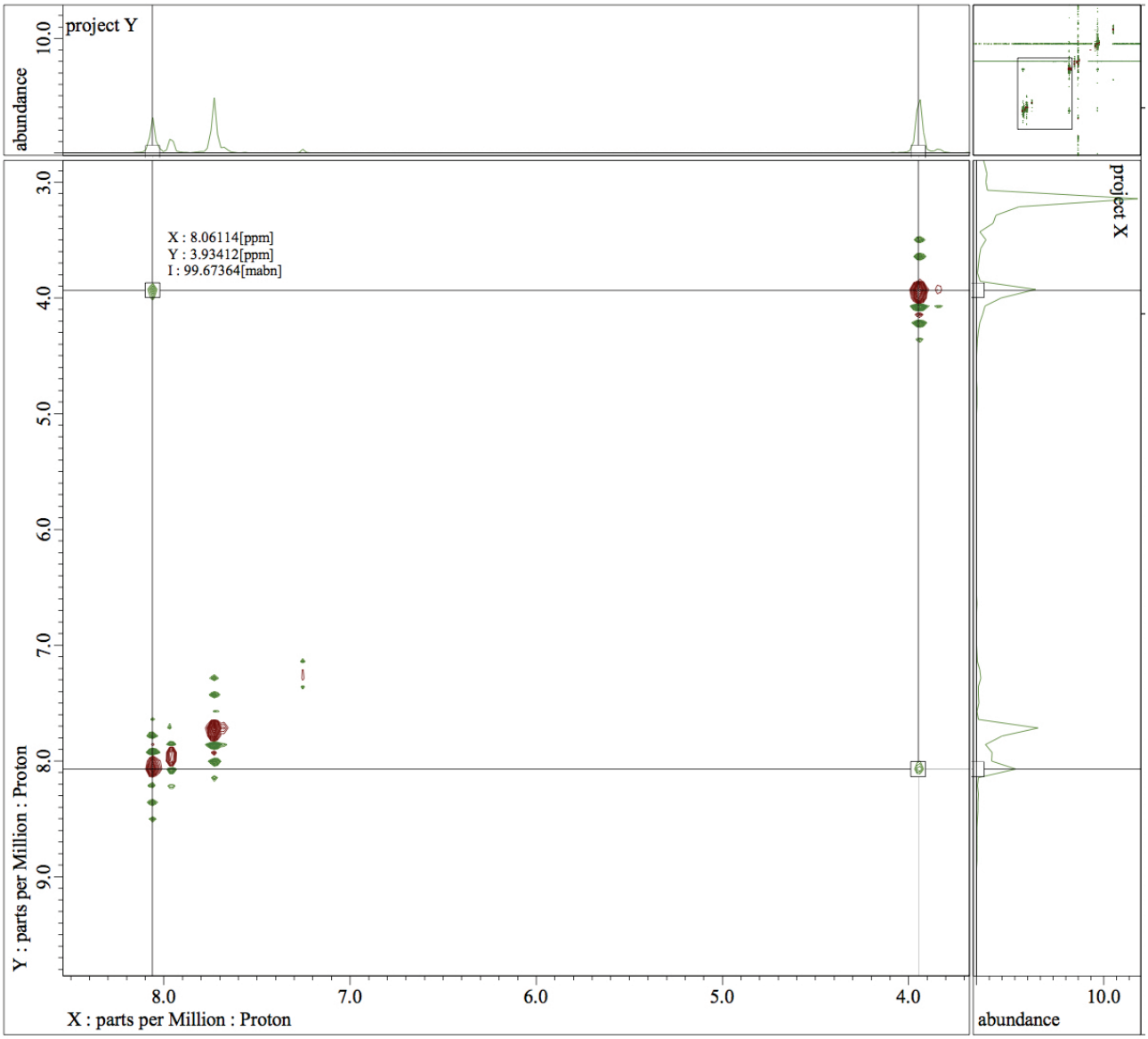
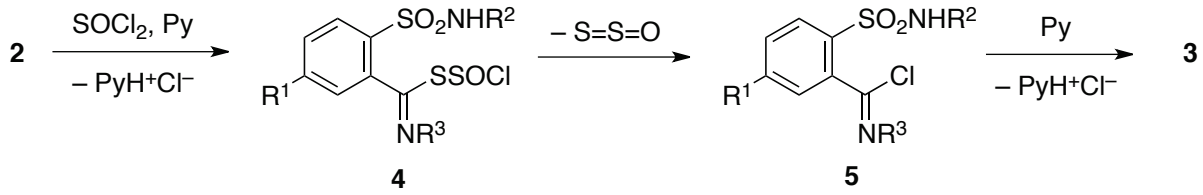
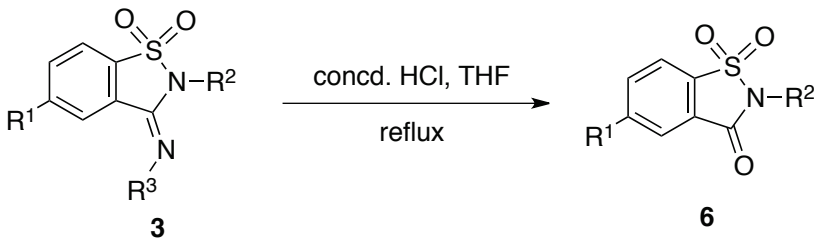


Figure 1. The NOESY spectrum of compound (**3a-ii**)



Scheme 2

The mechanistic rationale, depicted in Scheme 2, commences with the action of thionyl chloride on the thioamide moiety of **2** to give the intermediate (**4**). Rearrangement with elimination of S=S=O gives the imidoyl chloride intermediate (**5**), which undergoes an intramolecular ring closure to give the products (**3**). This mechanism can explain the necessity of two molar amounts of pyridine for the satisfactory production of the desired products.



Scheme 3

Table 2. Preparation of 1,2-benzothiazol-3(2*H*)-one 1,1-dioxides (**4**)

Entry	**3**	R^1	R^2	R^3	**4**	Yield/%[a]
1	**3a-ii**	H	Me	Me	**4a**	74
2	**3d**	Me	*n*-Bu	Et	**4d**	73
3	**3f-i**	Cl	Me	Et	**4f**	72
4	**3g**	Cl	Et	Me	**4g**	87
5	**3i**	OMe	Ph	Me	**4i**	68

[a] Yields of isolated products.

Hydrolysis of *N*-substituted 1,2-benzothiazol-3(2*H*)-imine 1,1-dioxides (**3**) was expected to give *N*-substituted saccharin (1,2-benzothiazol-3(2*H*)-one 1,1-dioxide) derivatives (**4**). Indeed, some of compounds (**3**) were subjected to the treatment with concentrated hydrochloric acid in refluxing THF afforded **4**, as illustrated in Scheme 2. The conversion proceeded quickly and cleanly under the conditions and the desired products were obtained in relatively good yields, as compiled in Table 2. Recently, *N*-substituted saccharins attract considerable attention, because some of them exhibit a variety of biological activities[6] and they have been used as precursors for the construction of other heterocyclic compounds, which are of biological importance as well.[7] Although a number of methods for the

preparation of saccharin derivatives have been recently reported,[8] the present method is unprecedented and features operational simplicity.

In conclusion, we have developed a new and concise procedure for the preparation of 2,(*E*)-*N*-disubstituted 1,2-benzothiazol-3(2*H*)-imine 1,1-dioxides by thionyl chloride-mediated cyclization of the corresponding 2-(aminosulfonyl)benzothioamides, derived from secondary benzenesulfonamides and isothiocyanates. The present method may find some value in organic synthesis because it has some advantages over the previously reported ones[2,3] in terms of the ready availability of the starting materials and the simple synthetic manipulations using ordinary reagents under mild reaction conditions. Current work is centered on utilization of these precursors to the synthesis of related heterocycles.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded as KBr disks with a Perkin–Elmer Spectrum 65 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 and 125 MHz, respectively. High-resolution MS spectra were measured by a Thermo Scientific Exactive spectrometer. Elemental analyses were performed with an Elementar Vario EL II instrument. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. *N*-Butyl-4-methylbenzenesulfonamide (**1d**),[9] 4-chloro-*N*-methylbenzenesulfonamide (**1f**),[10] 4-methoxy-*N*-methylbenzenesulfonamide (**1h**),[11] and 4-methoxy-*N*-phenylbenzenesulfonamide (**1i**)[12] were prepared according to the appropriate reported procedures. *n*-BuLi was supplied by Asia Lithium Corporation. All other chemicals used in this study were commercially available.

4-Chloro-*N*-ethylbenzenesulfonamide (1g).[13] This compound was prepared in 85% yield from 4-chlorobenzenesulfonyl chloride and $EtNH_2$ by a procedure similar to that described for the preparation of **1f**. A white solid; mp 65–67 °C (hexane/CH_2Cl_2) (lit.,[13] 73.5 °C); IR 3278, 1164 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.12 (t, *J* = 7.4 Hz, 3H), 2.99–3.05 (m, 2H), 4.68 (br s, 1H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.82 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 15.0, 38.2, 128.5, 129.4, 128.4, 139.1.

Typical Procedure for the Preparation of 2-(Aminosulfonyl)benzothioamides (2). *N*-Ethyl-2-(methylaminosulfonyl)benzothioamide (2a-ii). To a stirred solution of **1a** (0.17 g, 1.0 mmol) in THF (4 mL) at 0 °C was added dropwise *n*-BuLi (1.6 M in hexane, 2.0 mmol). After 30 min, EtNCS (0.13 g, 1.5 mmol) was added dropwise and stirring was continued at the same temperature for an additional 30 min before addition of aqueous NH_4Cl (20 mL). The mixture was extracted with AcOEt (3 × 10 mL) and the combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation.

The residual solid was recrystallized to give **2a-ii** (0.20 g, 76%); a yellow solid; mp 134–136 ˚C (hexane/CH_2Cl_2); IR 3176, 1546, 1336, 1173 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (t, *J* = 7.4 Hz, 3H), 2.55 (d, *J* = 3.4 Hz, 3H), 3.82–3.87 (m, 2H), 5.61 (br s, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.80 (d, *J* = 7.4 Hz, 1H), 8.08 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.6, 29.5, 41.5, 128.3, 128.7, 129.7, 132.9, 133.5, 141.7, 198.1. HR-MS (DART, negative). Calcd for $C_{10}H_{13}N_2O_2S_2$ (M–H): 257.0419. Found: *m/z* 257.0421.

***N*-Methyl-2-(methylaminosulfonyl)benzothioamide (2a-i):** a pale-yellow solid; mp 134–136 ˚C (hexane/CH_2Cl_2); IR 3273, 3193 1325, 1166 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.54 (d, *J* = 5.2 Hz, 3H), 3.33 (d, *J* = 4.6 Hz, 3H), 5.72 (q, *J* = 5.2 Hz, 1H), 7.31 (d, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 7.4 Hz, 1H), 8.44 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 29.5, 33.3, 128.1, 128.7, 129.7, 133.1 (2 overlapped Cs), 141.4, 199.0. Anal. Calcd for $C_9H_{12}N_2O_2S_2$: C, 44.24; H, 4.95; N, 11.47; S, 26.24. Found: C, 44.07; H, 5.03; N, 11.53; S, 26.32.

***N*-Ethyl-5-methyl-2-(methylaminosulfonyl)benzothioamide (2b-i):** a pale-yellow solid; mp 129–131 ˚C (hexane/CH_2Cl_2); IR 3272, 1548, 1324, 1162 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (t, *J* = 7.4 Hz, 3H), 2.42 (s, 3H), 2.53 (d, *J* = 4.6 Hz, 3H), 3.80–3.86 (m, 2H), 5.61 (q, *J* = 4.6 Hz, 1H), 7.11 (s, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 8.19 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.6, 21.3, 29.5, 41.5, 128.9, 129.2, 129.9, 130.5, 141.5, 144.0, 198.2. HR-MS (DART, negative). Calcd for $C_{11}H_{15}N_2O_2S_2$ (M–H): 271.0575. Found: *m/z* 271.0578.

5-Methyl-2-(methylaminosulfonyl)-*N*-phenylbenzothioamide (2b-ii): a yellow solid; mp 149–151 ˚C (hexane/CH_2Cl_2); IR 3293, 1546, 1329, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.47 (s, 3H), 2.54 (d, *J* = 5.2 Hz, 3H), 5.46 (q, *J* = 5.2 Hz, 1H), 7.25–7.27 (m, 3H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.71 (dd, *J* = 7.4, 1.1 Hz, 2H), 9.87 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.4, 29.5, 123.8, 127.4, 128.86, 128.90, 129.3, 129.9, 130.1, 137.9, 142.0, 144.5, 197.3. HR-MS (DART, positive). Calcd for $C_{15}H_{17}N_2O_2S_2$ (M+H): 321.0731. Found: *m/z* 321.0723.

***N*-Ethyl-2-(ethylaminosulfonyl)-5-methylbenzothioamide (2c):** a white solid; mp 102–104 ˚C (hexane/CH_2Cl_2); IR 3276, 1550, 1325, 1163 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (t, *J* = 7.4 Hz, 3H), 1.37 (t, *J* = 7.4 Hz, 3H), 2.42 (s, 3H), 2.83–2.89 (m, 2H), 3.81–3.86 (m, 2H), 5.60 (t, *J* = 6.3 Hz, 1H), 7.11 (s, 1H), 7.21 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 8.16 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.6, 14.7, 21.3, 38.7, 41.5, 128.9, 129.2, 129.5, 131.5, 141.4, 143.9, 198.2. HR-MS (DART, positive). Calcd for $C_{12}H_{19}N_2O_2S_2$ (M+H): 287.0888. Found: *m/z* 287.0880.

2-(Butylaminosulfonyl)-5,*N*-dimethylbenzothioamide (2d-i): a white solid; mp 61–63 ˚C (hexane/CH_2Cl_2); IR 3271, 1552, 1325, 1164 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (t, *J* = 7.4 Hz, 3H), 1.25–1.33 (m, 2H), 1.33–1.65 (m, 2H), 2.42 (s, 3H), 2.78 (q, *J* = 6.9 Hz, 2H), 3.30 (d, *J* = 5.2 Hz, 3H), 5.79 (t, *J* =

5.2 Hz, 1H), 7.08 (s, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 8.64 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.6, 19.8, 21.3, 31.3, 33.2, 43.3, 128.7, 129.2, 129.4, 131.1, 141.0, 144.2, 199.1. Anal. Calcd for $C_{13}H_{20}N_2O_2S_2$: C, 51.97; H, 6.71; N, 9.32; S, 21.34. Found: C, 51.78; H, 6.89; N, 9.37; S, 21.24.

2-(Butylaminosulfonyl)-*N*-ethyl-5-methylbenzothioamide (2d-ii): a pale-yellow solid; mp 111–113 °C (hexane/CH_2Cl_2); IR 3271, 1556, 1325, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85 (t, *J* = 7.4 Hz, 3H), 1.26–1.33 (m, 2H), 1.37 (t, *J* = 7.4 Hz, 3H), 1.42–1.48 (m, 2H), 2.43 (s, 3H), 2.76–2.80 (m, 2H), 3.80–3.85 (m, 2H), 5.72 (t, *J* = 6.3 Hz, 1H), 7.09 (s, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 8.34 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.6, 13.6, 19.8, 21.3, 32.3, 41.4, 43.3, 128.7, 129.2, 129.5, 131.2, 141.2, 144.0, 198.0. Anal. Calcd for $C_{14}H_{22}N_2O_2S_2$: C, 59.97; H, 7.19; N, 9.99; S, 11.43. Found: C, 59.79; H, 7.31; N, 10.14; S, 11.29.

***N*-Ethyl-5-Methyl-2-(phenylaminosulfonyl)benzothioamide (2e):** a yellow solid; mp 173–175 °C (hexane/CH_2Cl_2); IR 3276, 1551, 1344, 1166 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.41 (t, *J* = 7.4 Hz, 3H), 2.35 (s, 3H), 3.87–3.93 (m, 2H), 6.98 (d, *J* = 8.0 Hz, 1H), 7.07 (s, 1H), 7.11 (td, *J* = 7.4, 1.1 Hz, 1H), 7.18–7.26 (m, 5H), 7.95 (s, 1H), 8.12 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.7, 21.3, 41.5, 123.6, 126.0, 128.4, 128.9, 129.0, 129.6, 131.0, 136.7, 141.2, 144.2, 198.7. Anal. Calcd for $C_{16}H_{18}N_2O_2S_2$: C, 57.46; H, 5.42; N, 8.38. Found: C, 57.25; H, 5.51; N, 8.32.

5-Chloro-*N*-ethyl-2-(methylaminosulfonyl)benzothioamide (2f-i): a white solid; mp 142–144 °C (hexane/CH_2Cl_2); IR 3320, 1543, 1328, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.37 (t, *J* = 7.4 Hz, 3H), 2.56 (d, *J* = 5.7 Hz, 3H), 3.81–3.86 (m, 2H), 5.54 (q, *J* = 5.7 Hz, 1H), 7.31 (d, *J* = 1.7 Hz, 1H), 7.42 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.73 (d, *J* = 8.6 Hz, 1H), 8.09 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.6, 29.5, 41.5, 128.4, 128.7, 131.2, 132.0, 139.3, 142.8, 196.1. Anal. Calcd for $C_{10}H_{13}ClN_2O_2S_2$: C, 41.02; H, 4.48; N, 9.57; S, 21.90. Found: C, 40.95; H, 4.48; N, 9.57; S, 21.82.

5-Chloro-*N*-(4-methoxyphenyl)-2-(methylaminosulfonyl)benzothioamide (2f-ii): a yellow amorphous powder; R_f 0.31 (AcOEt/hexane 1:3); IR 3272, 1510, 1351, 1168 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.57 (d, *J* = 5.7 Hz, 3H), 3.82 (s, 3H), 5.46 (d, *J* = 5.7 Hz, 1H), 6.86 (d, *J* = 9.2 Hz, 2H), 7.44–7.46 (m, 2H), 7.61 (d, *J* = 9.2 Hz, 2H), 7.72 (d, *J* = 9.2 Hz, 1H), 9.70 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 29.5, 55.4, 114.1, 125.3, 128.5, 128.7, 130.6, 131.3, 131.5, 139.6, 143.1, 158.6, 194.6. HR-MS (DART, positive). Calcd for $C_{15}H_{16}ClN_2O_3S_2$ (M+H): 371.0291. Found: *m/z* 371.0277.

5-Chloro-2-(ethylaminosulfonyl)-*N*-methylbenzothioamide (2g): a white solid; mp 109–111 °C (hexane/CH_2Cl_2); IR 3288, 1551, 1334, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.11 (t, *J* = 7.4 Hz, 3H), 2.86–2.91 (m, 2H), 3.32 (d, *J* = 4.6 Hz, 3H), 5.60 (t, *J* = 6.3 Hz, 1H), 7.31 (d, *J* = 2.3 Hz, 1H), 7.41 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.70 (d, *J* = 8.6 Hz, 1H), 8.34 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 14.6, 33.2, 38.7, 128.3, 128.8, 130.7,

132.9, 139.3, 142.5, 197.2. Anal. Calcd for $C_{10}H_{13}ClN_2O_2S_2$: C, 41.02; H, 4.48; N, 9.57. Found: C, 40.99; H, 4.49; N, 9.63.

***N*-Ethyl-5-methoxy-2-(methylaminosulfonyl)benzothioamide (2h):** a white solid; mp 146–148 °C (hexane/CH_2Cl_2); IR 3258, 1570, 1325, 1167 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (t, *J* = 7.4 Hz, 3H), 2.52 (d, *J* = 5.2 Hz, 3H), 3.81–3.85 (m, 2H), 3.89 (s, 3H), 5.56 (q, *J* = 5.2 Hz, 1H), 6.78 (d, *J* = 2.3 Hz, 1H), 6.86 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 8.29 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.6, 29.5, 41.8, 55.8, 113.67, 113.69, 125.0, 132.0, 143.4, 162.7, 197.5. Anal. Calcd for $C_{11}H_{16}N_2O_3S_2$: C, 45.98; H, 5.26; N, 9.75; S, 22.31. Found: C, 45.81; H, 5.58; N, 9.80; S, 22.31.

5-Methoxy-*N*-methyl-2-(phenylaminosulfonyl)benzothioamide (2i): a white solid; mp 154–157 °C (hexane/CH_2Cl_2); IR 3291, 1589, 1344, 1165 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.62 (d, *J* = 4.6 Hz, 3H), 3.78 (s, 3H), 6.72 (d, *J* = 2.3 Hz, 1H), 6.97 (dd, *J* = 9.2, 2.3 Hz, 1H), 7.03 (t, *J* = 6.9 Hz, 1H), 7.15 (d, *J* = 7.4 Hz, 2H), 7.21 (dd, *J* = 7.4, 6.9 Hz, 2H), 7.61 (d, *J* = 9.2 Hz, 1H), 9.50 (br, 1H), 10.55 (br q, *J* = 4.6 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 34.2, 55.9, 112.1, 113.6, 120.7, 124.3, 125.3, 129.0, 131.0, 137.4, 144.6, 162.3, 197.8. Anal. Calcd for $C_{15}H_{16}N_2O_3S_2$: C, 53.55; H, 4.79; N, 8.33. Found: C, 53.43; H, 4.67; N, 8.13.

Typical Procedure for the Preparation of 1,2-Benzothiazol-3(2*H*)-imine 1,1-Dioxides (3). (*E*)-*N*-Ethyl-2-methyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3a-ii). To a stirred solution of **2a-ii** (0.26 g, 1.0 mmol) and pyridine (0.16 g, 2.0 mmol) in DMF (4 mL) at 0 °C was added freshly distilled $SOCl_2$ (0.12 g, 1.0 mmol) dropwise. Stirring was continued at the same temperature for 10 min. Saturated aqueous $NaHCO_3$ and H_2O (20 mL each) were added and the mixture was extracted with AcOEt (3 × 15 mL). The combined extracts were washed with brine (15 mL), dried (Na_2SO_4), and concentrated by evaporation. The residual solid was recrystallized to give **3a-ii** (0.14 g, 63%); a white solid; mp 143–145 °C (hexane/CH_2Cl_2); IR 1662, 1307 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (t, *J* = 7.4 Hz, 3H), 3.16 (s, 3H), 3.95 (q, *J* = 7.4 Hz, 2H), 7.72–7.76 (m, 2H), 7.97 (dd, *J* = 6.9, 2.3 Hz, 1H), 8.07 (dd, *J* = 6.9, 2.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 17.1, 24.4, 44.4, 121.8, 126.0, 127.0, 132.0, 133.4, 137.0, 143.2. HR-MS (ESI, positive). Calcd for $C_{10}H_{13}N_2O_2S$ (M+H): 225.0697. Found: *m/z* 225.0692. Anal. Calcd for $C_{10}H_{12}N_2O_2S$: C, 53.55; H, 5.39; N, 12.49. Found: C, 53.46; H, 5.40; N, 12.36.

2,(*E*)-*N*-Dimethyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3a-i): a pale-yellow solid; mp 186–185 °C (hexane/CH_2Cl_2); IR 1674, 1300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.16 (s, 3H), 3.69 (s, 3H), 7.75–7.80 (m, 2H), 7.99 (dd, *J* = 6.9, 2.3 Hz, 1H), 8.17 (dd, *J* = 6.9, 2.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.4, 37.5, 121.9, 125.8, 127.1, 132.2, 133.4, 136.7, 145.2. HR-MS (DART, positive). Calcd for $C_9H_{11}N_2O_2S$ (M+H): 211.0541. Found: *m/z* 211.0535. Anal. Calcd for $C_9H_{10}N_2O_2S$: C, 51.41; H, 4.79; N, 13.32; S, 15.25. Found: C, 51.11; H, 4.82; N, 13.26; S, 15.26.

(*E*)-*N*-Ethyl-2,5-dimethyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3b-i): a pale-yellow solid; mp 119–121 °C (hexane/CH_2Cl_2); IR 1669, 1302 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (t, *J* = 7.4 Hz, 3H), 2.53 (s, 3H), 3.14 (s, 3H), 3.94 (q, *J* = 7.4 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.85 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 17.2, 22.1, 24.4, 44.4, 121.6, 126.4, 127.4, 132.7, 134.4, 143.3, 144.4. HR-MS (ESI, positive). Calcd for $C_{11}H_{15}N_2O_2S$ (M+H): 239.0854. Found: *m*/*z* 239.0850. Anal. Calcd for $C_{11}H_{14}N_2O_2S$: C, 55.44; H, 5.92; N, 11.76. Found: C, 55.41; H, 5.86; N, 11.62.

2,5-Dimethyl-(*E*)-*N*-phenyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3b-ii): a white solid; mp 89–91 °C (hexane/CH_2Cl_2); IR 1667, 1323 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.16 (s, 3H), 3.31 (s, 3H), 6.50 (s, 1H), 6.91 (d, *J* = 7.4 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.9, 24.7, 119.8, 121.2, 124.0, 125.2, 127.5, 129.6, 133.2, 134.2, 143.8, 144.2, 148.3. HR-MS (DART, positive). Calcd for $C_{15}H_{15}N_2O_2S$ (M+H): 287.0854. Found: *m*/*z* 287.0884. Anal. Calcd for $C_{15}H_{14}N_2O_2S$: C, 62.92; H, 4.93; N, 9.78. Found: C, 62.90; H, 4.86; N, 9.70.

2,(*E*)-*N*-Diethyl-5-methyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3c): a white solid; mp 88–90 °C (hexane/CH_2Cl_2); IR 1667, 1306 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (t, *J* = 7.4 Hz, 3H), 1.40 (t, *J* = 7.4 Hz, 3H), 2.52 (s, 3H), 3.78 (q, *J* = 7.4 Hz, 2H), 3.94 (q, *J* = 7.4 Hz, 2H), 7.51 (d, *J* = 7.4 Hz, 1H), 7,82 (d, *J* = 7.4 Hz, 1H), 7.85 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.5, 17.3, 22.1, 34.4, 44.4, 121.4, 126.3, 127.5, 132.6, 134.7, 142.3, 144.3. HR-MS (DART, positive). Calcd for $C_{12}H_{17}N_2O_2S$ (M+H): 253.1010. Found: *m*/*z* 253.1000. Anal. Calcd for $C_{12}H_{16}N_2O_2S$: C, 57.12; H, 6.39; N, 11.10. Found: C, 57.02; H, 6.43; N, 11.00.

2-Butyl-5,(*E*)-*N*-dimethyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3d-i): a pale-yellow solid; mp 85–87 °C (hexane/CH_2Cl_2); IR 1674, 1301 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, *J* = 7.4 Hz, 3H), 1.34–1.43 (m, 2H), 1.72–1.78 (m, 2H), 2.51 (s, 3H), 3.64 (s, 3H), 3.65 (t, *J* = 7.4 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.91 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.7, 20.2, 22.2, 30.1, 37.6, 39.2, 121.5, 126.1, 127.6, 132.7, 134.1, 144.3, 144.8. HR-MS (DART, positive). Calcd for $C_{13}H_{19}N_2O_2S$ (M+H): 267.1168. Found: *m*/*z* 267.1155. Anal. Calcd for $C_{13}H_{18}N_2O_2S$: C, 58.62; H, 6.81; N, 10.52; S, 12.04. Found: C, 58.46; H, 6.97; N, 10.41; S, 12.01.

2-Butyl-(*E*)-*N*-ethyl-5-methyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3d-ii): a pale-yellow solid; mp 80–82 °C (hexane/CH_2Cl_2); IR 1662, 1305 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (t, *J* = 7.4 Hz, 3H), 1.37–1.45 (m, 5H), 1.75–1.81 (m, 2H), 2.53 (s, 3H), 3.70 (t, *J* = 7.4 Hz, 2H), 3.93 (q, *J* = 7.4 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.85 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.7, 17.3, 20.2, 22.2, 30.0, 39.1, 44.3, 121.4, 126.2, 127.4, 132.6, 134.2, 142.6, 144.3. HR-MS (DART, positive). Calcd for $C_{14}H_{21}N_2O_2S$ (M+H): 281.1323. Found: *m*/*z* 281.1316.

(*E*)-*N*-Ethyl-5-methyl-2-phenyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3e): an orange solid; mp 144–146 °C (hexane/CH_2Cl_2); IR 1669, 1324 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (t, *J* = 7.4 Hz, 3H), 2.52 (s,

3H), 3.00 (q, *J* = 7.4 Hz, 2H), 7.43–7.53 (m, 6H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.93 (s, 1H); ^{13}C NMR δ ($CDCl_3$) 16.6, 21.8, 44.3, 120.6, 124.0, 129.2, 129.4, 129.7, 131.6, 132.0, 133.1, 133.5, 139.1, 145.0. HR-MS (DART, positive). Calcd for $C_{16}H_{17}N_2O_2S$ (M+H): 301.1010. Found: *m/z* 301.1001. Anal. Calcd for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33. Found: C, 63.91; H, 5.41; N, 9.28.

5-Chloro-(*E*)-*N*-ethyl-2-methyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3f-i): a pale-yellow solid; mp 153–155 °C (hexane/CH_2Cl_2); IR 1671, 1311 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.42 (t, *J* = 7.4 Hz, 3H), 3.15 (s, 3H), 3.92 (q, *J* = 7.4 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 8.04 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 17.2, 24.5, 44.4, 123.0, 127.2, 127.4, 132.2, 135.2, 139.9, 141.8. HR-MS (DART, positive). Calcd for $C_{10}H_{12}ClN_2O_2S$ (M+H): 259.0308. Found: *m/z* 259.0302. Anal. Calcd for $C_{10}H_{11}ClN_2O_2S$: C, 46.42; H, 4.29; N, 10.83; S, 12.39. Found: C, 46.36; H, 4.27; N, 10.81; S, 12.43.

5-Chloro-(*E*)-*N*-(4-methoxyphenyl)-2-methyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3f-ii): a yellow solid; mp 139–141 °C (hexane/CH_2Cl_2); IR 1670, 1333 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.31 (s, 3H), 3.86 (s, 3H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.90 (s, 1H), 6.96 (d, *J* = 8.6 Hz, 2H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.84 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.9, 55.6, 115.1, 120.5, 122.6, 126.4, 127.2, 132.6, 132.8, 135.1, 139.6, 140.5, 156.8. HR-MS (DART, positive). Calcd for $C_{15}H_{14}ClN_2O_3S$ (M+H): 337.0413. Found: *m/z* 337.0398. Anal. Calcd for $C_{15}H_{13}ClN_2O_3S$: C, 53.49; H, 3.89; N, 8.32; S, 9.52. Found: C, 53.24; H, 3.89; N, 8.32; S, 9.35.

5-Chloro-(*E*)-2-ethyl-*N*-methyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3g): a white solid; mp 140–142 °C (hexane/CH_2Cl_2); IR 1674, 1308 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.37 (t, *J* = 7.4 Hz, 3H), 3.69 (s, 3H), 3.78 (q, *J* = 7.4 Hz, 2H), 7.72 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.5, 34.6, 37.4, 122.9, 127.2, 127.4, 132.2, 135.2, 139.8, 143.0. HR-MS (DART, positive). Calcd for $C_{10}H_{12}ClN_2O_2S$ (M+H): 259.0308. Found: *m/z* 259.0303. Anal. Calcd for $C_{10}H_{11}ClN_2O_2S$: C, 46.42; H, 4.29; N, 10.83. Found: C, 46.03; H, 4.31; N, 10.64.

(*E*)-*N*-Ethyl-5-methoxy-2-methyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3h): a white solid; mp 174–176 °C (hexane/CH_2Cl_2); IR 1664, 1300 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.43 (t, *J* = 7.4 Hz, 3H), 3.17 (s, 3H), 3.95 (q, *J* = 7.4 Hz, 2H), 3.96 (s, 3H), 7.23 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.54 (d, *J* = 2.3 Hz, 1H), 7.91 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 17.2, 24.4, 44.2, 56.1, 106.1, 113.3, 116.5, 123.3, 128.8, 143.0, 163.4. HR-MS (ESI, positive). Calcd for $C_{11}H_{15}N_2O_3S$ (M+H): 255.0803. Found: *m/z* 255.0791. Anal. Calcd for $C_{11}H_{14}N_2O_3S$: C, 51.95; H, 5.55; N, 11.02; S, 12.61. Found: C, 51.79; H, 5.41; N, 10.99; S, 12.60.

5-Methoxy-(*E*)-*N*-methyl-2-phenyl-1,2-benzothiazol-3(2*H*)-imine 1,1-Dioxide (3i): a pale-yellow solid; mp 163–165 °C (hexane/CH_2Cl_2); IR 1679, 1300 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.87 (s, 3H), 3.95 (s, 3H), 7.23 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.44–7.52 (m, 6H), 7.78 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 37.6,

56.1, 105.9, 120.6, 122.3, 126.5, 129.2, 129.4, 129.7, 133.2, 133.8, 141.0, 164.1. HR-MS (DART, positive). Calcd for $C_{15}H_{15}N_2O_3S$ (M+H): 303.0803. Found: *m/z* 303.0795. Anal. Calcd for $C_{15}H_{14}N_2O_3S$: C, 59.59; H, 4.67; N, 9.27; S, 10.60. Found: C, 59.35; H, 4.74; N, 9.28; S, 10.71.

Typical Procedure for the Preparation of 1,2-Benzothiazol-3(2*H*)-one 1,1-Dioxide (4). 5-Chloro-2-methyl-1,2-benzothiazol-3(2*H*)-one 1,1-Dioxide (4f). A solution of **3f-i** (0.14 g, 0.54 mmol) in THF (12 mL) containing 0.2 mL of concentrated HCl was heated at reflux temperature for 10 min. After cooling to rt, saturated aqueous $NaHCO_3$ (15 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL). The combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residual solid was recrystallized to give **4f** (90 mg, 72%); a white solid; mp 151–153 °C (hexane/CH_2Cl_2); IR 1733, 1342 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.27 (s, 3H), 7.83 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.5, 122.3, 125.4, 129.3, 134.8, 135.6, 141.3, 157.5. HR-MS (DART, positive). Calcd for $C_8H_7ClNO_3S$ (M+H): 231.9835. Found: *m/z* 231.9828. Anal. Calcd for $C_8H_6ClNO_3S$: C, 41.48; H, 2.61; N, 6.05; S, 13.84. Found: C, 41.64; H, 2.58; N, 6.04; S, 13.90.

2-Methyl-1,2-benzothiazol-3(2*H*)-one 1,1-Dioxide (4a):[14] a pale-yellow solid; mp 129–131 °C (hexane/CH_2Cl_2) (lit.,[14] mp 131 °C). The spectral (^1H and ^{13}C NMR) data were identical to those reported previously.[15]

2-Butyl-5-methyl-1,2-benzothiazol-3(2*H*)-one 1,1-Dioxide (4d):[16] a white solid; mp 53–54 °C (hexane/CH_2Cl_2) (lit.,[16] mp 54–55 °C). The spectral (^1H and ^{13}C NMR) data were identical to those reported previously.[17]

5-Chloro-2-ethyl-1,2-benzothiazol-3(2*H*)-one 1,1-Dioxide (4g): a white solid; mp 62–64 °C (hexane/CH_2Cl_2); IR 1735, 1334 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (t, *J* = 7.4 Hz, 3H), 3.85 (q, *J* = 7.4 Hz, 2H), 7.82 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.86 (d, *J* = 8.6 Hz, 1H), 8.02 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9, 34.8, 122.2, 125.3, 129.2, 134.7, 135.7, 141.2, 157.4. HR-MS (DART, positive). Calcd for $C_9H_{12}ClN_2O_3S$ (M+NH_4): 263.0252. Found: *m/z* 263.0239. Anal. Calcd for $C_9H_8ClNO_3S$: C, 44.00; H, 3.28; N, 5.70. Found: C, 43.97; H, 3.34; N, 5.81.

5-Methoxy-2-phenyl-1,2-benzothiazol-3(2*H*)-one 1,1-Dioxide (4i): a white solid; mp 199–201 °C (hexane/CH_2Cl_2); IR 1739, 1312 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.97 (s, 3H), 7.37 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.53–7.57 (m, 6H), 7.88 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 56.3, 108.8, 122.0, 122.8, 128.7, 128.8, 129.0, 129.7, 129.9, 130.1, 158.4, 164.5. HR-MS (DART, positive). Calcd for $C_{14}H_{12}NO_4S$ (M+NH_4): 290.0487. Found: *m/z* 290.0482. Anal. Calcd for $C_{14}H_{11}NO_4S$: C, 58.12; H, 3.83; N, 4.84; S, 11.08. Found: C, 57.91; H, 3.87; N, 4.84; S, 11.22.

ACKNOWLEDGEMENTS

We gratefully acknowledge Mrs. Miyuki Tanmatsu of this university for recording mass spectra and performing combustion analyses.

REFERENCES AND NOTES

1. (a) R. Fischer, B. Alig, C. Arnold, R. Pontzen, and K.-H. Mueller, *PCT Int. Appl.*, 2008, WO 2008145282 (*Chem. Abstr.*, 2008, **150**, 1549); (b) W. Zambach, O. F. Hueter, P. Renold, T. Pitterna, and P. Maienfisch, *PCT Int. Appl.*, 2009, WO 2009141305 (*Chem. Abstr.*, 2009, **152**, 12338); (c) W. Von Deyn, M. Puhl, M. Pohlman, M. Rack, L. P. Rapado, J. Langewald, D. D. Anspaugh, H. Oloumi-Sadeghi, D. L. Culbertson, N. B. Rankl, H. Kamp, and B. Van Ravenzwaay, *PCT Int. Appl.*, 2009, WO 2009153285 (*Chem. Abstr.*, 2009, **152**, 97447); (d) O. F. Hueter, P. Renold, W. Zambach, T. Pitterna, and P. Maienfisch, *PCT Int. Appl.*, 2010, WO 2010054926 (*Chem. Abstr.*, 2010, **152**, 568127); (e) W. Von Deyn, M. Puhl, M. Pohlman, M. Rack, L. P. Rapado, J. Langewald, D. D. Anspaugh, H. Oloumi-Sadeghi, G. F. Matt Hews, D. L. Culbertson, N. B. Rankl, H. Kamp, and B. Van Ravenzwaay, *U.S. Pat. Appl. Publ.*, 2011, US 20110166162 (*Chem. Abstr.*, 2016, **167**, 176052).
2. T. Miura, Y. Nishida, M. Morimoto, M. Yamauchi, and M. Murakami, *Org. Lett.*, 2011, **13**, 1429.
3. B. Liu, Y. Li, H. Jiang, M. Yin, and H. Huang, *Adv. Synth. Catal.*, 2012, **354**, 11.
4. We have recently reported some heterocycle syntheses by the reaction of *o*-functionalized phenyllithiums with isothiocyanates followed by ring closure: (a) K. Kobayashi, Y. Shigemura, and D. Fujiwara, *Heterocycles*, 2017, **94**, 1152; (b) K. Kobayashi and D. Fujiwara, *Heterocycles*, 2017, **94**, 1759; (c) K. Kobayashi, D. Fujiwara, and M. Tanmatsu, *Heterocycles*, 2018, **96**, 902.
5. H. Watanabe, C.-L. Mao, I. T. Bamish, and C. R. Hauser, *J. Org. Chem.*, 1969, **34**, 919.
6. (a) S. Bag, R. Tulsan, A. Sood, H. Cho, H. Redjeb, W. Zhou, H. LeVine III, B. Török, and M. Török, *Bioorg. Med. Chem. Lett.*, 2015, **25**, 626; (b) H. Fu, L. Han, X. Hou, X. Dun, L. Wang, X. Gong, and H. Fang, *Bioorg. Med. Chem.*, 2015, **23**, 5774; (c) S. Carradori, D. Secci, C. De Monte, A. Mollica, M. Ceruso, A. Akdemir, A. P. Sobolev, R. Codispoti, F. De Cosmi, P. Guglielmi, and C. T. Supuran, *Bioorg. Med. Chem.*, 2016, **24**, 1095; (d) D. Panek, A. Wiecowska, T. Wichur, M. Bajda, J. Godyń, J. Jończyk, K. Mika, J. Janockova, O. Soukup, D. Knez, J. Korabecny, S. Gobec, and B. Malawska, *Eur. J. Med. Chem.*, 2017, **125**, 676; (e) H. Chen, B.-B. Xu, T. Sun, Z. Zhou, H.-Y. Ya, and M. Yuan, *Molecules*, 2017, **22**, 1857; (f) J. Ivanova, F. Carta, D. Vullo, J. Leitans, A. Kazaks, K. Tars, R. Žalubovskis, and C. T. Supura, *Bioorg. Med. Chem.*, 2017, **25**, 3583; (g) S. K. Kulkarni, R. N. Laddha, S. A. Patel, D. P. Baradia, and R. R. Patel, *PCT Int. Appl.*, 2018, WO 2018015915 (*Chem. Abstr.*, 2018, **168**, 193228); (h) E. Weinstein, J. Mata-Fink, A. Kahvejian, N. B. Afeyan, L. K. Jeanbart, A. Lantermann, J. B. Hurov, and B. Jonathan, *PCT Int. Appl.*, 2018, WO 2018022668

(*Chem. Abstr.*, 2018, **168**, 230312); (i) E. Weinstein, J. Mata-Fink, A. Kahvejian, N. B. Afeyan, L. K. Jeanbart, A. Lantermann, J. B. Hurov, B. Jonathan, M. A. Fankhauser, C. J. Shu, and E. F. Zhu, *PCT Int. Appl.*, 2018, WO 2018022664 (*Chem. Abstr.*, 2018, **168**, 230313); (j) H. Zhong, Z. Ji, H. Ji, and W. Hua, *PCT Int. Appl.*, 2018, WO 2018040775 (*Chem. Abstr.*, 2018, **168**, 273782).

7. (a) M. Ahmed, S. Aslam, M. H. Bukhari, G. Montero, M. Detorio, M. Parvez, and R. F. Schinazi, *Med. Chem. Res.*, 2014, **23**, 1309; (b) M. R. Gannarapu, S. B. Vasamsetti, N. Punna, N. K. Royya, S. R. Pamulaparthy, J. B. Nanubolu, S. Kotamraju, and N. Banda, *Eur. J. Med. Chem.*, 2014, **75**, 143; (c) S. Aslam, S. Zaib, M. Ahmad, J. M. Gardiner, A. Ahmad, A. Hameed, N. Furtmann, M. Gütschow, J. Bajorath, and J. Iqbal, *Eur. J. Med. Chem.*, 2014, **78**, 106; (d) S. Parveen, S. Hussain, S. Zhu, X. Qin, X. Hao, S. Zhang, J. Lu, and C. Zhu, *RSC Adv.*, 2014, **4**, 21134; (e) G. M. Reddy, P. Nagender, R. N. Kumar, J. H. Ahn, K. P. Kumar, A. K. R. Kanugula, K. V. S. Rama Krishna, S. Kotamraju, and B. Narsaiah, *J. Heterocycl. Chem.*, 2014, **51**, E42; (f) M. R. Gannarapu, S. B. Vasamsetti, N. Punna, S. Kotamraju, and N. Banda, *MedChemComm*, 2015, **6**, 1494; (g) K. Lei, X.-W. Hua, Y.-Y. Tao, Y. Liu, N. Liu, Y. Ma, Y.-H. Li, X.-H. Xu, and C.-H. Kong, *Bioorg. Med. Chem.*, 2016, **24**, 92; (h) I. Elghamry, M. M. Youssef, M. A. Al-Omair, and H. Elsawy, *Eur. J. Med. Chem.*, 2017, **139**, 107.
8. (a) K. Sun, X. Wang, G. Li, Z. Zhu, Y. Jiang, and B. Xiao, *Chem. Commun.*, 2014, **50**, 12880; (b) X. Wang, K. Sun, Y. Lv, F. Ma, G. Li, D. Li, Z. Zhu, Y. Jiang, and F. Zhao, *Chem. Asian J.*, 2014, **9**, 3413; (c) Y. Li, L. Zhang, H. Yuan, F. Liang, and J. Zhang, *Synlett*, 2015, **26**, 116; (d) K. Sun, Y. Lv, Z. Zhu, L. Zhang, H. Wu, L. Liu, Y. Jiang, B. Xiao, and X. Wang, *RSC Adv.*, 2015, **5**, 3094; (e) K. Sun, X. Wang, Y. Jiang, Y. Lv, L. Zhang, B. Xiao, D. Li, Z. Zhu, and L. Liu, *Chem. Asian J.*, 2015, **10**, 536; (f) A. A. Kantak, L. Marchetti, and B. DeBoef, *Chem. Commun.*, 2015, **51**, 3574; (g) F. Teng, S. Sun, Y. Jian, J.-T. Yu, and J. Cheng, *Chem. Commun.*, 2015, **51**, 5902; (h) J. Sun, Y. Wang, and Y. Pin, *J. Org. Chem.*, 2015, **80**, 8945; (i) P. S. Mahajan, S. D. Tanpure, N. A. More, J. M. Gajbhiye, and S. B. Mhaske, *RSC Adv.*, 2015, **5**, 101641; (j) Q. Xiao, Q. He, J. Li, and J. Wang, *Org. Lett.*, 2015, **17**, 6090; (k) Y. Chen, C.-J. Aurell, P. Koresgren, J. Maim, M. Härslätt, M. Fridén-Saxin, and A. Pettersen, *Synthesis*, 2018, **50**, 1471.
9. J. Xuan, B.-J. Li, Z.-J. Feng, G.-D. Sun, H.-H. Ma, Z.-W. Yuan, J.-R. Chen, L.-Q. Lu, and W.-J. Xiao, *Chem. Asian J.*, 2013, **8**, 1090.
10. J. K. Laha, S. Sharma, and N. Dayal, *Eur. J. Org. Chem.*, 2015, 7885.
11. C.-F. Xu, M. Xu, Y.-X. Jia, and C.-Y. Li, *Org. Lett.*, 2011, **13**, 1556.
12. A. Natarajan, Y. Guo, F. Harbinski, Y.-H. Fan, H. Chen, L. Luus, J. Diercks, H. Aktas, M. Chorev, and J. A. Halperin, *J. Med. Chem.*, 2004, **47**, 4979.
13. A. M. Grigorovskii, N. N. Dykhanov, and Z. M. Kimen, *Zh. Obsh. Khim.*, 1957, **27**, 531.

14. E. W. McClelland, L. A. Warren, and J. H. Jackson, *J. Chem. Soc*., 1929, 1582.
15. D. W. Cho, S. W. Oh, D. U. Kim, H. J. Park, J. Y. Xue, U. C. Yoon, and P. S. Mariano, *Bull. Korean Chem. Soc*., 2010, **31**, 2453.
16. R. Ronci, T. Vitall, L. Amoretti, and F. Mossini, *Farmaco, Edi. Sci*., 1967, **22**, 935.
17. P. Mi, P. Liao, T. Tu, and X. Bi, *Chem. Eur. J*., 2015, **21**, 5332.