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SYNTHESIS OF 2,3-DIHYDROBENZO[*b*]THIOPHEN-3-AMINE 1,1-DIOXIDE DERIVATIVES *VIA* LDA-MEDIATED CYCLIZATION OF *o*-(ALKYLSULFONYL)BENZYL AZIDES WITH DENITROGENATION

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Abstract – A new and efficient method for the synthesis of 2,3-dihydrobenzo[*b*]thiophen-3-amine 1,1-dioxide derivatives has been developed. Thus, treatment of *o*-(alkylsulfonyl)benzyl azides, which are readily obtainable from commercially available starting materials by easily operational sequences, with lithium diisopropylamide (LDA) in THF at –78 ˚C gives, after aqueous workup, 2,3-dihydrobenzo[*b*]thiophen-3-amine 1,1-dioxides. These products can be isolated in moderate to fair yields after *N*-protection with acylating agents.

INTRODUCTION

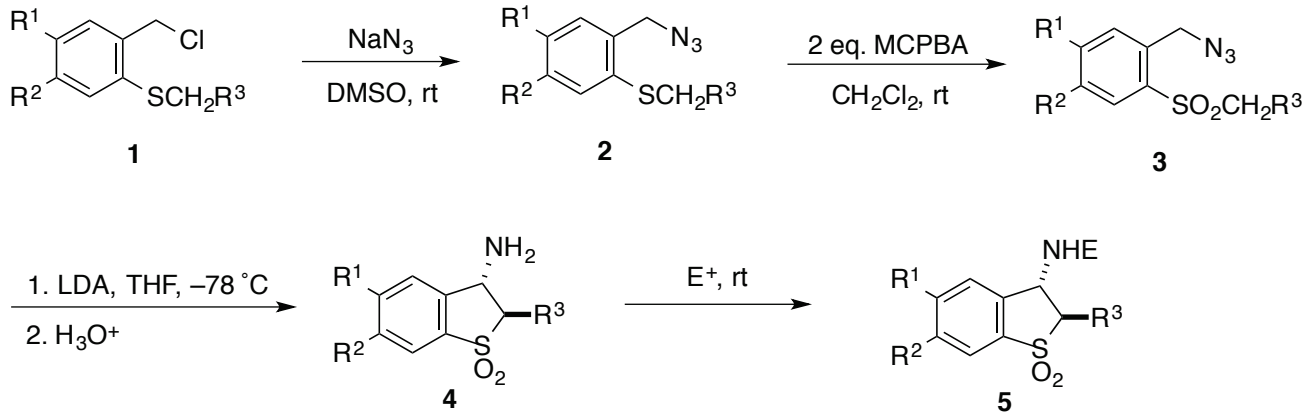
Substituted 2,3-dihydrobenzo[*b*]thiophene 1,1-dioxides are important constituents of biologically active synthetic compounds.[1] The construction of this class of heterocycles has been commonly achieved by oxidation of benzo[*b*]thiophenes followed by hydrogenation of the resulting benzo[*b*]thiophene 1,1-dioxides.[2] However, to the best our knowledge, there is only one example of the synthesis of 2,3-dihydrobenzo[*b*]thiophen-3-amine 1,1-dioxides, which is based on the addition of amines to benzo[*b*]thiophene 1,1-dioxides.[3] Accordingly, the development of new and general routes to these derivatives is meaningful.

We have previously developed new methods for the construction of benzene-fused nitrogen heterocyclic compounds utilizing the cyclization of *o*-functionalized benzylidenaminides, generated by the treatment of *o*-functionalized benzyl azides with appropriate bases accompanying denitrogenation.[4] In order to expand the versatility of these processes, we set out to investigate the possibility of the formation of 2,3-dihydrobenzo[*b*]thiophen-3-amine 1,1-dioxides by the reaction of *o*-(alkylsulfonyl)benzyl azides with an appropriate base. In this paper we wish to report the results of our study, which provide a convenient

process to *N*-protected 2,3-dihydrobenzo[*b*]thiophen-3-amine 1,1-dioxides (**5**) initiated by deprotonation of *o*-(alkylsulfonyl)benzyl azides (**3**) with LDA.

RESULTS AND DISCUSSION

The process we have developed for the synthesis of **5** is illustrated in Scheme 1. *o*-(Alkylsulfanyl)benzyl chlorides (**1**), easily prepared from readily available starting materials using ordinary procedures as described in Experimental section, were first converted into *o*-(alkylsulfanyl)benzyl azides (**2**) in fair to good yields on treatment with sodium azide in DMSO at rt. Subsequent oxidation of these sulfides with two equivalents of *m*-chloroperbenzoic acid (MCPBA) in dichloromethane at rt led to the corresponding sulfonyl azides (**3**) in good yields. The yields of these products (**2**) and (**3**) are compiled in Table 1.



Scheme 1

Table 1. Preparation of sulfonyl azides (**3**)

Entry	**1**	R^1	R^2	R^3	**2**	Yield/%[a,b]	**3**	Yield/%[a]
1	**1a**	H	H	H	**2a**	82[c]	**3a**	78
2	**1b**	H	H	Me	**2b**	91[c]	**3b**	78
3	**1c**	H	H	*n*-Pr	**2c**	89	**3c**	80
4	**1d**	H	H	Ph	**2d**	82[c]	**3d**	72
5	**1e**	Me	H	Me	**2e**	78	**3e**	83
6	**1f**	Cl	H	Me	**2f**	82	**3f**	85
7	**1g**	Cl	H	*n*-Pr	**2g**	78	**3g**	76
8	**1h**	Cl	H	Ph	**2h**	92	**3h**	72
9	**1i**	H	OMe	Ph	**2i**	67	**3i**	82
10	**1j**	OMe	OMe	Ph	**2j**	66	**3j**	71

[a] Yields of isolated products. [b] Overall yields from the respective alcohols unless otherwise indicated.
[c] Yields from **1**.

The sulfonyl azides (**3**), thus obtained, were treated with LDA in THF at –78 °C. Immediate vigorous evolution of nitrogen gas from the reaction solutions was observed. Aqueous workup produced 2,3-dihydrobenzo[*b*]thiophen-3-amine 1,1-dioxides (**4**), which were conveniently isolated as **5** in pure

form by *N*-protection with acylating agents, such as acetic anhydride, ethyl chloroformate and phenyl isothiocyanate, and subsequent purification by column chromatography on silica gel, though **4d** could be isolated in a pure form by recrystallization of the respective crude reaction mixture. Table 2 includes results of these transformations. As can be seen from this table, the yields of compounds (**5a**-**i**) and (**5a**-**ii**) are substantially lower than those of the others. This perhaps is arising from the loss of the corresponding pre-protective compounds (**4a**-**i**) and (**4a**-**ii**) during extraction procedure due to relative high solubility of these two compounds in water. When compounds (**3i**) and (**3j**) were used, some extent of the starting materials remained after treatment with LDA, as judged by TLC analyses of the reaction mixture. However, the use of two equivalents of LDA adversely affected the course of the reaction and decreased the yields of the products; more complex mixtures of products were obtained. Further optimization was not attempted. In the each case of compounds (**4d**) and (**5b**-**5j**), a single stereoisomer was exclusively isolated. The stereochemistry was assumed to be *trans*. Although the ^{1}H NMR spectral analyses of these compounds did not provide firm determination of their stereochemistry, the exclusive formation of sterically favored *trans* isomers is reasonable, taking the basic reaction conditions into account. Attempts for one-pot preparation of **5** from **3** by adding acylating agents after the treatment of **3** with LDA resulted in failure. This is probably due to the presence of diisopropylamine in the reaction mixtures.

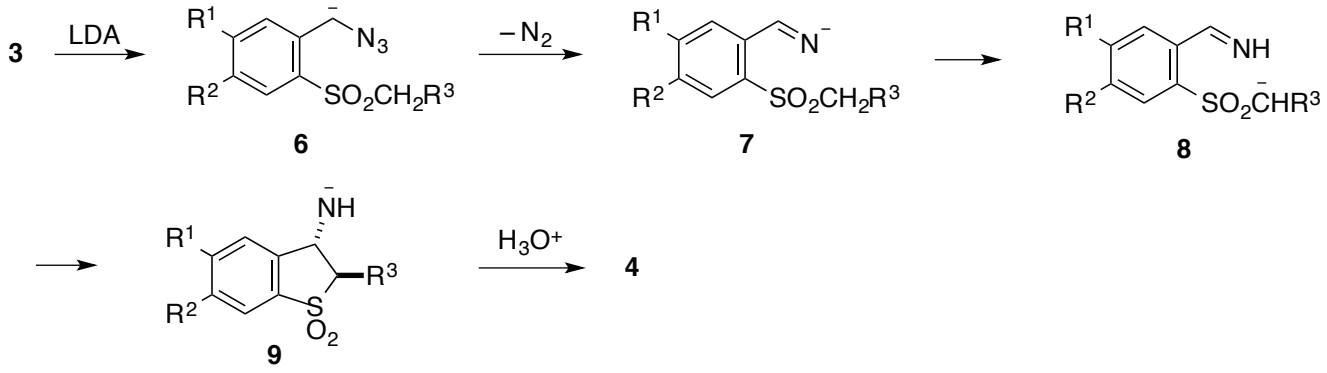
Table 2. Preparation of 2,3-dihydrobenzo[*b*]thiophen-3-amine 1,1-dioxide derivatives (**5**)

Entry	**3**	R^1	R^2	R^3	E^+	E	**5**	Yield/%[a]
1	**3a**	H	H	H	$EtOCOCl/Et_3N$	CO_2Et	**5a-i**	33
2	**3a**	H	H	H	PhNCS	C(S)NHPh	**5a-ii**	35
3	**3b**	H	H	Me	Ac_2O	Ac	**5b-i**	60
4	**3b**	H	H	Me	$EtOCOCl/Et_3N$	CO_2Et	**5b-ii**	55
5	**3c**	H	H	*n*-Pr	Ac_2O	Ac	**5c**	60
6	**3d**	H	H	Ph	$EtOCOCl/Et_3N$	CO_2Et	**5d**	52
7	**3e**	Me	H	Me	Ac_2O	Ac	**5e**	60
8	**3f**	Cl	H	Me	Ac_2O	Ac	**5f-i**	54
9	**3f**	Cl	H	Me	PhNCS	C(S)NHPh	**5f-ii**	63
10	**3g**	Cl	H	*n*-Pr	Ac_2O	Ac	**5g**	67
11	**3h**	Cl	H	Ph	Ac_2O	Ac	**5h-i**	68
12	**3h**	Cl	H	Ph	PhNCS	C(S)NHPh	**5h-ii**	70
13	**3i**	H	OMe	Ph	Ac_2O	Ac	**5i**	62
14	**3j**	OMe	OMe	Ph	$EtOCOCl/Et_3N$	CO_2Et	**5j-i**	60
15	**3j**	OMe	OMe	Ph	Ac_2O	Ac	**5j-ii**	64

[a] Yields of isolated products.

As depicted in Scheme 2, the pathway from **3** to **4** may be rationalized by considering initial deprotonation of the benzylic proton, rather than the α-proton of the sulfonyl function, of **3** with LDA to give the benzyl anion intermediate (**6**), which releases nitrogen gas to afford benzylidenaminide anion intermediate (**7**). This undergoes proton transfer to give the sulfonyl group-stabilized intermediate (**8**), of

which ring closure by the addition of the carbanion α to the sulfonyl group to the imino carbon gives the amide anion intermediate (**9**). Protonation of this by aqueous workup provides **4**.



Scheme 2

In summary, the results reported above demonstrate that the LDA-mediated cyclization of *o*-(alkylsulfonyl)benzyl azide with denitrogenation provides an efficient method for the general synthesis of 2,3-dihydrobenzo[*b*]thiophen-3-amine 1,1-dioxides derivatives. The present method may be of value in organic synthesis because of the ready availability of the starting materials and the simple manipulations, and may provide interesting pharmacophores.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer Spectrum 65 FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded using TMS as an internal reference with a Bruker Biospin AVANCE II 600 spectrometer operating at 600 MHz and 150 MHz, respectively, or 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 (ESI, positive) or a JEOL JMS-T100GCV (EI or FI, TOF; 70eV or 2100V, respectively) 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. 4,5-Dimethoxy-2-[(phenylmethyl)sulfanyl]benzaldehyde,[5] 1-(chloromethyl)-2-(methylsulfanyl)benzene (**1a**),[6] 1-(chloromethyl)-2-(ethylsulfanyl)benzene (**1b**),[7] and 1-(chloromethyl)-2-[(phenylmethyl)sulfanyl]benzene (**1d**)[8] 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.

Typical Procedure for the Preparation of 2-(Alkylsulfanyl)benzaldehydes. 5-Chloro-2-(ethylsulfanyl)benzaldehyde. To a stirred suspension of NaH (60% in mineral oil; 0.44 g, 11 mmol) in DMF (15 mL) at 0 ˚C was added EtSH (0.75 g, 12 mmol) dropwise. After evolution of H_2 gas had ceased, a solution of 2-bromo-5-chlorobenzaldehyde (2.2 g, 10 mmol) in DMF (15 mL) was added dropwise. After 5 min, saturated aqueous NH_4Cl (50 mL) was added and the mixture was extracted with AcOEt (3 × 40 mL). The combined extracts were washed with H_2O (3 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 (CH_2Cl_2/hexane 1:5) to give the desired product (1.4 g, 70%); a yellow solid; mp 32–33 ˚C (pentane); IR (KBr) 2837, 2726, 1692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.36 (t, *J* = 7.4 Hz, 3H), 2.97 (q, *J* = 7.4 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 1H), 7.48 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.82 (d, *J* = 2.3 Hz, 1H), 10.36 (s, 1H). HR-MS (ESI). Calcd for $C_9H_{10}ClOS$ (M+H): 201.0141. Found: *m*/*z* 201.0137.

2-(Butylsulfanyl)benzaldehyde: yield: 99%; a yellow liquid; R_f 0.30 (AcOEt/hexane 1:20). The spectral (IR and ^1H NMR) data for this compound were identical to those reported previously.[9]

2-(Butylsulfanyl)-5-chlorobenzaldehyde: yield: 88%; a yellow solid; mp 26–28 ˚C (hexane/CH_2Cl_2). IR (KBr) 2860, 2723, 1693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.4 Hz, 3H), 1.48 (sext, *J* = 7.4 Hz, 2H), 1.66 (quint, *J* = 7.4 Hz, 2H), 2.94 (t, *J* = 7.4 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.47 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.81 (d, *J* = 2.3 Hz, 1H), 10.36 (s, 1H). HR-MS (EI). Calcd for $C_{11}H_{13}ClOS$ (M): 228.0376. Found: *m*/*z* 228.0382.

5-Chloro-2-[(phenylmethyl)sulfanyl]benzaldehyde: yield: 92%; a yellow solid; mp 68–69 ˚C (hexane/CH_2Cl_2); IR (KBr) 2835, 2726, 1686 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.09 (s, 2H), 7.20–7.40 (m, 5H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.45 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.78 (d, *J* = 2.3 Hz, 1H), 10.31 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.67, 127.68, 128.71, 128.84, 130.32, 132.70, 133.20, 133.83, 135.92, 136.39, 138.71, 190.09. HR-MS (EI). Calcd for $C_{14}H_{11}ClOS$ (M): 262.0219. Found: *m*/*z* 262.0208.

4-Methoxy-2-[(phenylmethyl)sulfanyl]benzaldehyde:[10] yield: 88%; a yellow solid; mp 81–82 ˚C (hexane/CH_2Cl_2); IR (neat) 2814, 2722, 1666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.81 (s, 3H), 4.14 (s, 2H), 6.80 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.86 (d, *J* = 2.3 Hz, 1H), 7.26–7.35 (m, 5H), 7.77 (d, *J* = 8.6 Hz, 1H), 10.11 (s, 1H).

2-(Ethylsulfanyl)-5-methylbenzaldehyde.[10] To a stirred solution of TMEDA (2.3 g, 20 mmol) in cyclohexane (30 mL) at 0 ˚C was added *n*-BuLi (1.6 M in hexane; 20 mmol) and then 4-methylbenzenethiol (1.2 g, 10 mmol) and the mixture was stirred for 24 h at rt as described by Block *et al*.[11] The resulting mixture was treated with *N*-formylpiperidine (1.1 g, 10 mmol) and EtI (1.6 g, 10 mmol) 4 h later, and stirring was continued for an additional 17 h at the same temperature before addition of saturated aqueous NH_4Cl (40 mL). The mixture was extracted with AcOEt (3 × 30 mL). The combined extracts were washed with H_2O (50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated by

evaporation. The residue was purified by column chromatography on SiO_2 (CH_2Cl_2/hexane 1:5) to give the desired product; a yellow oil; R_f 0.24 (AcOEt/hexane 1:20); IR (neat) 2870, 2732, 1683 1666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.33 (t, J = 7.4 Hz, 3H), 2.38 (s, 3H), 2.94 (q, J = 7.4 Hz, 2H), 7.35 (s, 2H), 7.67 (s, 1H), 10.42 (s, 1H).

Typical Procedure for the Reduction of 2-(Alkylsulfanyl)benzaldehydes to the Corresponding [2-(Alkylsulfanyl)phenyl]methanols. [5-Chloro-2-(ethylsulfanyl)phenyl]methanol. To a stirred solution of 5-chloro-2-(ethylsulfanyl)benzaldehyde (1.4 g, 7.0 mmol) in MeOH (20 mL) at 0 °C was added $NaBH_4$ (0.26 g, 7.0 mmol) in several portions. After 5 min, saturated aqueous NH_4Cl (30 mL) was added and most of MeOH was removed by evaporation and the resulting mixture was extracted with AcOEt (3 × 30 mL). The combined extracts were washed with brine (50 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 to give the desired product (1.3 g, 90%); a pale-yellow liquid; R_f 0.24 (CH_2Cl_2/hexane 1:1); IR (neat) 3365 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (t, J = 7.4 Hz, 3H), 2.20 (t, J = 6.3 Hz, 1H), 2.92 (q, J = 7.4 Hz, 2H), 4.75 (d, J = 6.3 Hz, 2H), 7.23 (dd, J = 8.6, 2.3 Hz, 1H), 7.28 (d, J = 8.6 Hz, 1H), 7.43 (d, J = 2.3 Hz, 1H). Anal. Calcd for $C_9H_{11}ClOS$: C, 53.33; H, 5.47. Found: C, 52.96; H, 5.73.

[2-(Butylsulfanyl)phenyl]methanol:[9] yield: 70%; colorless oil; R_f 0.28 (AcOEt/hexane 1:5). The spectral (IR and ^1H NMR) data for this compound were identical to those reported previously.[6]

[2-(Ethylsulfanyl)-5-methylphenyl]methanol: yield: 83%; a colorless liquid; R_f 0.21 (AcOEt/hexane 1:10); IR (neat) 3365 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.28 (t, J = 7.4 Hz, 3H), 2.30 (t, J = 6.3 Hz, 1H), 2.33 (s, 3H), 2.90 (q, J = 7.4 Hz, 2H), 4.76 (d, J = 6.3 Hz, 2H), 7.08 (d, J = 8.0 Hz, 1H), 7.21 (s, 1H), 7.29 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.45, 20.95, 28.76, 63.88, 128.93, 129.27, 130.80, 131.11, 136.82, 141.12. Anal. Calcd for $C_{10}H_{14}OS$: C, 65.89; H, 7.74. Found: C, 65.95; H, 8.08.

[2-(Butylsulfanyl)-5-chlorophenyl]methanol: yield: 99%; a white solid; mp 38–39 °C (hexane/CH_2Cl_2); IR (neat) 3304 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92 (t, J = 7.4 Hz, 3H), 1.44 (sext, J = 7.4 Hz, 2H), 1.61 (quint, J = 7.4 Hz, 2H), 2.22 (t, J = 6.3 Hz, 1H), 2.90 (t, J = 7.4 Hz, 2H), 4.74 (d, J = 6.3 Hz, 2H), 7.22 (dd, J = 8.6, 2.3 Hz, 1H), 7.27 (d, J = 8.6 Hz, 1H), 7.42 (d, J = 2.3 Hz, 1H). Anal. Calcd for $C_{11}H_{15}ClOS$: C, 57.26; H, 6.55. Found: C, 57.08; H, 6.48.

{5-Chloro-2-[(phenylmethyl)sulfanyl]phenyl}methanol: yield: 99%; a white solid; mp 60–61 °C (hexane/CH_2Cl_2); IR (KBr) 3247 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.82 (t, J = 6.3 Hz, 1H), 4.03 (s, 2H), 4.58 (d, J = 6.3 Hz, 2H), 7.16–7.30 (m, 7H), 7.40 (d, J = 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.45, 62.94, 127.42, 128.07, 128.09, 128.57, 128.74, 131.94, 133.40, 133.51, 137.11, 143.81. Anal. Calcd for $C_{14}H_{13}ClOS$: C, 63.51; H, 4.95. Found: C, 63.22; H, 4.95.

{4-Methoxy-2-[(phenylmethyl)sulfanyl]phenyl}methanol: yield: 99%; a colorless oil; R_f 0.33 (AcOEt/hexane 1:3); IR (neat) 3391 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.79 (t, J = 6.3 Hz, 1H), 3.75 (s,

3H), 4.08 (s, 2H), 4.58 (d, *J* = 6.3 Hz, 2H), 6.76 (dd, *J* = 7.6, 2.8 Hz, 1H), 6.91 (d, *J* = 2.8 Hz, 1H), 7.22–7.30 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.72, 55.33, 63.23, 112.59, 116.98, 127.34, 128.55, 128.81, 129.98, 133.84, 135.70, 137.30, 159.32. MR-MS (EI). Calcd for $C_{15}H_{16}O_2S$ (M): 260.0871. Found: *m/z* 260.0872.

{4,5-Dimethoxy-2-[(phenylmethyl)sulfanyl]phenyl}methanol: yield: 92%; a yellow oil; R_f 0.23 (AcOEt/hexane 1:2); IR (neat) 3435 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.68 (t, *J* = 6.3 Hz, 1H), 3.76 (s, 3H), 3.88 (s, 3H), 3.92 (s, 2H), 4.55 (d, *J* = 6.3 Hz, 2H), 6.81 (s, 1H), 6.90 (s, 1H), 7.08 (dd, *J* = 7.4, 1.1 Hz, 2H), 7.21–7.26 (m, 3H). HR-MS (FI). Calcd for $C_{16}H_{18}O_3S$ (M): 290.0977. Found: *m/z* 290.0990.

Typical Procedure for the Conversion of [2-(Alkylsulfanyl)phenyl]methanols into the Corresponding Chlorides (1). 4-Chloro-2-(chloromethyl)-1-(ethylsulfanyl)benzene (1f). To a stirred solution of [5-chloro-2-(ethylsulfanyl)phenyl]methanol (1.3 g, 6.3 mmol) in DMF (15 mL) containing pyridine (0.50 g, 6.3 mmol) at 0 ˚C was added freshly distilled $SOCl_2$ (0.75 g, 6.3 mmol) dropwise. The temperature was then raised to rt and stirring was continued for 1 h. Saturated aqueous $NaHCO_3$ (20 mL) was added and the mixture was extracted with AcOEt (3 × 20 mL). The combined extracts were washed with water (3 × 20 mL) and brine (15 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was used in the next step without purification.

Typical Procedure for the Preparation of Sulfanyl Azides (2). 1-(Azidomethyl)-2-(ethylsulfanyl)benzene (2b).[12] A mixture of **1b** (0.37 g, 2.0 mmol) and NaN_3 (0.14 g, 2.2 mmol) in DMSO (12 mL) was stirred at rt for 2 h. Water (20 mL) was added and the mixture was extracted with AcOEt (3 × 15 mL). The combined extracts were washed with water (3 × 15 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on silica gel to afford **2b** (0.35 g, 91%); a colorless liquid; R_f 0.35 (CH_2Cl_2/hexane 1:10); IR (neat) 2099 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.4 Hz, 3H), 2.96 (q, *J* = 7.4 Hz, 2H), 4.52 (s, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.31 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.34 (d, *J* = 7.4 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H).

1-(Azidomethyl)-2-(methylsulfanyl)benzene (2a): a colorless liquid; R_f 0.33 (CH_2Cl_2/hexane 1:10); IR (neat) 2098 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.50 (s, 3H), 4.48 (s, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.31–7.35 (m, 3H). HR-MS (ESI). Calcd for $C_8H_9N_3NaS$ (M+Na): 202.0415. Found: *m/z* 202.0405.

1-(Azidomethyl)-2-(butylsulfanyl)benzene (2c): a colorless liquid; R_f 0.44 (AcOEt/hexane 1:10); IR (neat) 2099 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.4 Hz, 3H), 1.46 (sext, *J* = 7.4 Hz, 2H), 1.64 (quint, *J* = 7.4 Hz, 2H), 2.93 (t, *J* = 7.4 Hz, 2H), 4.52 (s, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.40 (d, *J* = 7.4 Hz, 1H). Anal. Calcd for $C_{11}H_{15}N_3S$: C, 59.70; H, 6.83; N, 18.99. Found: C, 59.46; H, 7.08; N, 18.73.

1-(Azidomethyl)-2-[(phenylmethyl)sulfanyl]benzene (2d): a colorless oil; R_f 0.19 (CH_2Cl_2/hexane 1:5); IR (neat) 2098, 1602 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.08 (s, 2H), 4.38 (s, 2H), 7.21–7.29 (m, 7H),

7.32 (dd, *J* = 6.9, 1.7 Hz, 1H), 7.41 (dd, *J* = 6.9 Hz, 1.7 Hz, 1H). HR-MS (FI). Calcd for $C_{14}H_{13}N_3S$ (M): 255.0830. Found: *m/z* 255.0822.

2-(Azidomethyl)-1-(ethylsulfanyl)-4-methylbenzene (2e): a colorless liquid; R_f 0.35 (AcOEt/hexane 1:40); IR (neat) 2030, 1603 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.28 (t, *J* = 7.4 Hz, 3H), 2.35 (s, 3H), 2.90 (q, *J* = 7.4 Hz, 2H), 4.51 (s, 2H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.17 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.33, 20.93, 28.90, 52.96, 129.63, 130.24, 131.09, 132.32, 135.85, 136.77. Anal. Calcd for $C_{10}H_{13}N_3S$: C, 57.94; H, 6.32; N, 20.27. Found: C, 58.27; H, 6.35; N, 20.00.

2-(Azidomethyl)-4-chloro-1-(ethylsulfanyl)benzene (2f): a colorless liquid; R_f 0.37 (hexane); IR (neat) 2105 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.31 (t, *J* = 7.4 Hz, 3H), 2.93 (q, *J* = 7.4 Hz, 2H), 4.50 (s, 2H), 7.27 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 2.3 Hz, 1H). Anal. Calcd for $C_9H_{10}ClN_3S$: C, 47.47; H, 4.43; N, 18.45. Found: C, 47.67; H, 4.06; N, 18.57.

2-(Azidomethyl)-1-(butylsulfanyl)-4-chlorobenzene (2g): a colorless oil; R_f 0.41 (AcOEt/hexane 1:20); IR (neat) 2105 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.4 Hz, 3H), 1.45 (sext, *J* = 7.4 Hz, 2H), 1.62 (quint, *J* = 7.4 Hz, 2H), 2.90 (t, *J* = 7.4 Hz, 2H), 4.49 (s, 2H), 7.27 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 1H), 7.35 (d, *J* = 2.3 Hz, 1H). HR-MS (EI). Calcd for $C_{11}H_{14}ClN_3S$ (M): 255.0597. Found: *m/z* 255.0592.

2-(Azidomethyl)-4-chloro-1-[(phenylmethyl)sulfanyl]benzene (2h): a pale-yellow oil; R_f 0.37 (AcOEt/hexane 1:50); IR (neat) 2105, 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.41 (s, 2H), 4.46 (s, 2H), 7.08 (d, *J* = 7.4 Hz, 2H), 7.28–7.38 (m, 4H), 7.50 (s, 1H), 7.68 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.16, 52.40, 127.46, 128.56, 128.76, 128.77, 128.92, 133.38, 133.44, 133.55, 136.82, 138.67. HR-MS (EI). Calcd for $C_{14}H_{12}ClN_3S$ (M): 289.0440. Found: *m/z* 289.0428.

1-(Azidomethyl)-4-methoxy-2-[(phenylmethyl)sulfanyl]benzene (2i): a colorless oil; R_f 0.43 (AcOEt/hexane 1:10); IR (neat) 2099 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.73 (s, 3H), 4.09 (s, 2H), 4.34 (s, 2H), 6.76 (dd, *J* = 8.0, 2.3 Hz, 1H), 6.89 (d, *J* = 2.3 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.24–7.30 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.72, 52.44, 55.31, 112.60, 116.94, 127.32, 128.18, 128.53, 128.89, 130.76, 137.01, 137.08, 159.65. Anal. Calcd for $C_{15}H_{15}N_3OS$: C, 63.13; H, 5.30; N, 14.73. Found: C, 62.98; H, 5.58; N, 14.75.

1-(Azidomethyl)-4,5-dimethoxy-2-[(phenylmethyl)sulfanyl]benzene (2j): a colorless oil; R_f 0.22 (CH_2Cl_2/hexane 1:1); IR (neat) 2099 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.71 (s, 3H), 3.89 (s, 3H), 3.92 (s, 2H), 4.36 (s, 2H), 6.75 (s, 1H), 6.83 (s, 1H), 7.10 (d, *J* = 7.4 Hz, 2H), 7.20–7.26 (m, 3H). HR-MS (ESI). Calcd for $C_{16}H_{17}N_3NaO_2S$ (M+Na): 338.0939. Found: *m/z* 338.0934.

Typical Procedure for the Preparation of Sulfonyl Azides (3). 1-(Azidomethyl)-2-(ethylsulfonyl)benzene (3b). A mixture of **2b** (0.29 g, 1.5 mmol) and MCPBA (70%; 0.75 g, 3.0 mmol)

in CH_2Cl_2 (10 mL) was stirred at 0 ˚C for 3 h. The precipitate was filtered off under reduced pressure and washed with CH_2Cl_2 (10 mL). The filtrate and washing were washed with saturated aqueous $NaHCO_3$ (2 × 10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on silica gel to give **3b** (0.22 g, 65%); a colorless liquid; R_f 0.37 (Et_2O_2/hexane 1:1); IR (neat) 2104, 1310, 1149 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (t, J = 7.4 Hz, 3H), 3.27 (q, J = 7.4 Hz, 2H), 4.91 (s, 2H), 7.55–7.58 (m, 2H), 7.69 (t, J = 7.4 Hz, 1H), 8.06 (d, J = 7.4 Hz, 1H). HR–MS (EI). Calcd for $C_9H_{11}N_3O_2S$ (M): 225.0572. Found: *m/z* 225.0583.

1-(Azidomethyl)-2-(methylsulfonyl)benzene (3a): a pale-yellow oil; R_f 0.40 (CH_2Cl_2/hexane 2:1); IR (neat) 2105, 1307, 1152 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.18 (s, 3H), 4.92 (s, 2H), 7.55–7.59 (m, 2H), 7.69 (td, J = 7.4, 1.1 Hz, 1H), 8.11 (dd, J = 7.4, 1.1 Hz, 1H). HR-MS (ESI). Calcd for $C_8H_9N_3NaO_2S$ (M+Na): 234.0313. Found: *m/z* 234.0308.

1-(Azidomethyl)-2-(butylsulfonyl)benzene (3c): a colorless oil; R_f 0.23 (CH_2Cl_2/hexane 1:2); IR (neat) 2103, 1312, 1148 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, J = 7.4 Hz, 3H), 1.42 (sext, J = 7.4 Hz, 2H), 1.70 (quint, J = 7.4 Hz, 2H), 3.23 (t, J = 7.4 Hz, 2H), 4.91 (s, 2H), 7.55–7.58 (m, 2H), 7.69 (t, J = 7.4 Hz, 1H), 8.06 (d, J = 7.4 Hz, 1H). HR-MS (ESI). Calcd for $C_{11}H_{15}N_3NaO_2S$ (M+Na): 276.0783. Found: *m/z* 276.0781.

1-(Azidomethyl)-2-[(phenylmethyl)sulfonyl]benzene (3d): a white solid; mp 127–129 ˚C (hexane/CH_2Cl_2); IR (neat) 2103, 1314, 1154 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.43 (s, 2H), 4.56 (s, 2H), 7.07 (d, J = 7.4 Hz, 2H), 7.26 (t, J = 7.4 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.4 Hz, 1H), 7.49 (d, J = 7.4 Hz, 1H), 7.62 (t, J = 7.4 Hz, 1H), 7.75 (d, J = 7.4 Hz, 1H). HR-MS (ESI). Calcd for $C_{14}H_{13}N_3NaO_2S$ (M+Na): 310.0626. Found: *m/z* 310.0628.

2-(Azidomethyl)-1-(ethylsulfonyl)-4-methylbenzene (3e): a colorless oil; R_f 0.23 (AcOEt/hexane 1:2); IR (neat) 2104, 1311, 1132 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.28 (t, J = 7.4 Hz, 3H), 2.47 (s, 3H), 3.23 (q, J = 7.4 Hz, 2H), 4.86 (s, 2H), 7.34 (d, J = 8.0 Hz, 1H), 7.35 (s, 1H), 7.92 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.17, 21.46, 51.23, 51.63, 129.54, 131.44, 132.11, 133.69, 135.13, 145.26. HR-MS (ESI). Calcd for $C_{10}H_{13}N_3NaO_2S$ (M+Na): 262.0626. Found: *m/z* 262.0621.

2-(Azidomethyl)-4-chloro-1-(ethylsulfonyl)benzene (3f): a colorless liquid; R_f 0.39 (Et_2O/hexane 1:1); IR (neat) 2109, 1313, 1149 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (t, J = 7.4 Hz, 3H), 3.23 (q, J = 7.4 Hz, 2H), 4.89 (s, 2H), 7.52 (dd, J = 8.6, 2.3 Hz, 1H), 7.59 (d, J = 2.3 Hz, 1H), 7.98 (d, J = 8.6 Hz, 1H). HR-MS (ESI). Calcd for $C_9H_{10}ClN_3NaO_2S$ (M+Na): 282.0080. Found: *m/z* 282.0076.

2-(Azidomethyl)-1-(butylsulfonyl)-4-chlorobenzene (3g): a colorless oil; R_f 0.33 (Et_2O/hexane 1:3); IR (neat) 2109, 1316, 1149 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92 (t, J = 7.4 Hz, 3H), 1.42 (sext, J = 7.4 Hz, 2H), 1.69 (quint, J = 7.4 Hz, 2H), 3.20 (t, J = 7.4 Hz, 2H), 4.89 (s, 2H), 7.52 (dd, J = 8.6, 2.3 Hz, 1H),

7.59 (d, *J* = 2.3 Hz, 1H), 7.98 (d, *J* = 8.6 Hz, 1H). HR-MS (ESI). Calcd for $C_{11}H_{14}ClN_3NaO_2S$ (M+Na): 310.0393. Found: *m/z* 310.0388.

2-(Azidomethyl)-4-chloro-1-[(phenylmethyl)sulfonyl]benzene (3h): a white solid; mp 68–70 ˚C (hexane/CH_2Cl_2); IR (KBr) 2113, 1308, 1143 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.41 (s, 2H), 4.45 (s, 2H), 7.08 (d, *J* = 7.4 Hz, 2H), 7.26–7.38 (m, 4H), 7.50 (s, 1H), 7.68 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.22, 63.55, 127.44, 128.70, 128.83, 129.20, 130.12, 130.87, 132.99, 133.87, 138.44, 140.88. Anal. Calcd for $C_{14}H_{12}ClN_3O_2S$: C, 52.26; H, 3.76; N, 13.06. Found: C, 52.22; H, 3.79; N, 12.85.

1-(Azidomethyl)-4-methoxy-2-[(phenylmethyl)sulfonyl]benzene (3i): a white solid; mp 73–74 ˚C (hexane/CH_2Cl_2); IR (KBr) 2095, 1308, 1156 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.71 (s, 3H), 4.46 (s, 2H), 4.56 (s, 2H), 7.10–7.12 (m, 3H), 7.18 (d, *J* = 2.8 Hz, 1H), 7.28 (t, *J* = 7.4 Hz, 2H), 7.34 (tt, *J* = 7.4, 1.1 Hz, 1H), 7.38 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.20, 55.65, 63.35, 116.05, 120.32, 127.58, 127.77, 128.61, 128.90, 130.90, 132.52, 136.80, 159.38. Anal. Calcd for $C_{15}H_{15}N_3O_3S$: C, 56.77; H, 4.76; N, 13.24. Found: C, 56.77; H, 4.82; N, 13.10.

1-(Azidomethyl)-4,5-dimethoxy-2-[(phenylmethyl)sulfonyl]benzene (3j): a colorless oil; R_f 0.29 (AcOEt/hexane 1:10); IR (neat) 2102, 1305, 1122 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.71 (s, 3H), 3.97 (s, 3H), 4.40 (s, 2H), 4.53 (s, 2H), 6.91 (s, 1H), 7.04 (s, 1H), 7.08 (d, *J* =7.4 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H). HR-MS (ESI). Calcd for $C_{16}H_{17}N_3NaO_4S$ (M+Na): 370.0838. Found: *m/z* 370.0832.

General Procedure for the Preparation of 2,3-Dihydrobenzo[*b*]thiophen-3-amine 1,1-Dioxide Derivatives 5. To a stirred solution of LDA (1.0 mmol), generated from *i*-Pr_2NH and *n*-BuLi by the standard method, in THF (8 mL) at –78 ˚C was added a solution of **3** (1.0 mmol) in THF (6 mL) dropwise. Stirring was continued for 15 min before addition of water (20 mL). The mixture was warmed to rt and extracted with AcOEt (3 × 10 mL). The combined extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was dissolved in THF (4 mL) and treated with acylating agents indicated in Table 2. After appropriate workup, the crude products were purified by column chromatography on silica gel (AcOEt/hexane) to give **5**.

Ethyl (1,1-Dioxo-2,3-dihydrobenzo[*b*]thiophen-3-yl)carbamate (5a-i): a white solid; mp 119–120 ˚C (hexane/CH_2Cl_2); IR (KBr) 3311, 1687, 1305, 1150 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.26 (t, *J* = 6.9 Hz, 3H), 3.39 (dd, *J* = 13.7, 4.6 Hz, 1H), 3.82 (dd, *J* = 13.7, 7.4 Hz, 1H), 4.17 (q, *J* = 6.9 Hz, 2H), 5.42 (br d, *J* = 8.0 Hz, 1H), 5.60 (br s, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.74 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.46, 48.39, 57.19, 61.70, 121.31, 126.69, 130.61, 134.14, 137.69, 139.06, 155.90. HR-MS (EI). Calcd for $C_{11}H_{13}NO_4S$ (M): 255.0565. Found: *m/z* 255.0565. Anal. Calcd for $C_{11}H_{13}NO_4S$: C, 51.75; H, 5.13; N, 5.49. Found: C, 51.72; H, 5.06; N, 5.52.

1-(1,1-Dioxo-2,3-dihydrobenzo[*b*]thiophen-3-yl)-3-phenylthiourea (5a-ii): a colorless viscous oil; R_f 0.32 (CH_2Cl_2/hexane 1:2); IR (neat) 3314, 1529, 1298, 1239, 1122 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.47 (dd, *J* = 13.7, 3.4 Hz, 1H), 3.89 (dd, *J* = 13.7, 7.4 Hz, 1H), 6.50 (ddd, *J* = 8.6, 7.4, 3.4 Hz, 1H), 6.59 (d, *J* = 8.6 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.40 (dd, *J* = 8.0, 7.4 Hz, 2H), 7.55–7.58 (m, 1H), 7.63–7.65 (m, 2H), 7.70 (d, *J* = 7.4 Hz, 1H), 8.25 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.97, 56.93, 121.50, 124.96, 126.91, 127.76, 130.30, 130.86, 134.25, 135.35, 136.81, 139.44, 180.56. HR-MS (ESI). Calcd for $C_{15}H_{15}N_2O_2S_2$ (M+H): 319.0575. Found: *m*/*z* 319.0569.

***N*-[*trans*-(2-Methyl-1,1-dioxo-2,3-dihydrobenzo[*b*]thiophen-3-yl)]acetamide (5b-i):** a white solid; mp 163–165 °C (hexane/CH_2Cl_2); IR (KBr) 3275, 1661, 1538, 1304, 1152 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.52 (d, *J* = 7.4 Hz, 3H), 2.07 (s, 3H), 3.31–3.37 (m, 1H), 5.42–5.45 (dd, *J* = 8.6, 4.6 Hz, 1H), 6.16 (br d, *J* = 8.6 Hz, 1H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.76 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.15, 23.16, 53.37, 62.72, 121.86, 126.69, 130.47, 134.14, 137.13, 137.90, 170.14. HR-MS (ESI). Calcd for $C_{11}H_{14}NO_3S$ (M+H): 240.0694. Found: *m*/*z* 240.0689.

Ethyl *trans*-(2-Methyl-1,1-dioxo-2,3-dihydrobenzo[*b*]thiophen-3-yl)carbamate (5b-ii): a white solid; mp 132–133 °C (hexane/CH_2Cl_2); IR (KBr) 3285, 1688, 1539, 1306, 1160 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.27 (d, *J* = 7.4 Hz, 3H), 1.58 (t, *J* = 7.4 Hz, 3H), 3.36–3.39 (m, 1H), 4.20 (q, *J* = 7.4 Hz, 2H), 5.14–5.21 (m, 2H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.58 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.78 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.12, 14.46, 55.35, 61.75, 62.99, 121.83, 125.99, 126.03, 130.33, 133.98, 137.49, 156.23. HR-MS (ESI). Calcd for $C_{12}H_{15}NNaO_4S$ (M+Na): 292.0620. Found: *m*/*z* 292.0610. Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.52; H, 5.61; N, 5.20. Found: C, 53.48; H, 5.58; N, 5.26.

***N*-[*trans*-1-(1,1-Dioxo-2-propyl-2,3-dihydrobenzo[*b*]thiophen-3-yl)]acetamide (5c):** a white solid; mp 159–160 °C (hexane/CH_2Cl_2); IR (KBr) 3251, 1655, 1305, 1157 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 0.95 (t, *J* = 7.4 Hz, 3H), 1.47–1.53 (m, 1H), 1.57–1.62 (m, 1H), 1.76–1.82 (m, 1H), 1.89–1.96 (m, 1H), 1.97 (s, 3H), 3.45 (dt, *J* = 8.6, 5.1 Hz, 1H), 5.17 (t, *J* = 8.6 Hz, 1H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.72 (t, *J* = 7.4 Hz, 1H), 7.81 (d, *J* = 7.4 Hz, 1H), 8.60 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.71, 19.60, 22.67, 27.72, 51.69, 65.43, 120.90, 125.55, 129.82, 133.93, 138.42, 138.78, 169.97. HR-MS (EI). Calcd for $C_{13}H_{17}NO_3S$ (M): 267.0929. Found: *m*/*z* 267.0927. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.41; H, 6.41; N, 5.24. Found: C, 58.23; H, 6.29; N, 5.30.

Ethyl *trans*-(1,1-Dioxo-2-phenyl-2,3-dihydrobenzo[*b*]thiophen-3-yl)carbamate (5d): a white solid; mp 142–144 °C (hexane/CH_2Cl_2); IR (KBr) 3304, 1690, 1314, 1158 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.20 (t, *J* = 6.9 Hz, 3H), 4.10 (q, *J* = 6.9 Hz, 2H), 4.59 (d, *J* = 8.0 Hz, 1H), 5.30 (d, *J* = 9.2 Hz, 1H), 5.80 (dd, *J* = 9.2, 8.0 Hz, 1H), 7.42–7.44 (m, 5H), 7.57–7.60 (m, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.79 (d, *J* = 7.4 Hz,

1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.35, 53.84, 61.73, 72.85, 122.05, 125.43, 127.80, 128.96, 129.03, 129.69, 129.77, 130.27, 133.95, 138.12, 156.00. HR-MS (FI). Calcd for $C_{17}H_{17}NO_4S$ (M): 331.0878. Found: *m/z* 331.0876. Anal. Calcd for $C_{17}H_{17}NO_4S$: C, 61.62; H, 5.17; N, 4.23. Found: C, 61.50; H, 5.16; N, 4.20.

***N*-[*trans*-1-(2,5-Dimethyl-1,1-dioxo-2,3-dihydrobenzo[*b*]thiophen-3-yl)]acetamide (5e):** a white solid; mp 136–138 °C (hexane/CH_2Cl_2); IR (KBr) 3246, 1655, 1302, 1132 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (d, *J* = 6.9 Hz, 3H), 2.02 (s, 3H), 2.42 (s, 3H), 3.24–3.29 (m, 1H), 5.22 (t, *J* = 8.6 Hz, 1H), 7.09 (d, *J* = 8.6 Hz, 1H), 7.22 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.91, 21.74, 23.10, 53.25, 62.85, 121.49, 126.79, 131.23, 136.18, 137.56, 145.28, 170.24. HR-MS (ESI, positive). Calcd for $C_{12}H_{15}NNaO_3S$ (M+Na): 276.0671. Found: *m/z* 276.0665. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53. Found: C, 56.86; H, 5.87; N, 5.38.

***N*-[*trans*-1-(5-Chloro-2-methyl-1,1-dioxo-2,3-dihydrobenzo[*b*]thiophen-3-yl)]acetamide (5f-i):** a white solid; mp 175–177 °C (hexane/CH_2Cl_2); IR (KBr) 3365, 1665, 1309, 1136 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (d, *J* = 6.9 Hz, 3H), 2.08 (s, 3H), 3.35–3.37 (m, 1H), 5.37 (dd, *J* = 8.6, 5.1 Hz, 1H), 6.36 (d, *J* = 8.6 Hz, 1H), 7.48 (br s, 1H), 7.51 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.65 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.82, 23.10, 53.02, 62.87, 123.13, 126.78, 130.86, 136.46, 139.44, 140.53, 170.21. HR-MS (ESI). Calcd for $C_{11}H_{12}ClNNaO_3S$ (M+Na): 296.0124. Found: *m/z* 296.0119. Anal. Calcd for $C_{11}H_{12}ClNO_3S$: C, 48.27; H, 4.42; N, 5.12. Found: C, 48.04; H, 4.11; N, 4.97.

1-*trans*-(5-Chloro-2-methyl-1,1-dioxo-2,3-dihydrobenzo[*b*]thiophen-3-yl)-3-phenylthiourea (5f-ii): a yellow solid; mp 187–189 °C (hexane/CH_2Cl_2); IR (KBr) 3379, 3165, 1539, 1317, 1120 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.55 (d, *J* = 6.9 Hz, 3H), 3.48–3.52 (m, 1H), 6.15 (dd, *J* = 8.6, 3.4 Hz, 1H), 6.49 (d, *J* = 8.6 Hz, 1H), 7.21 (d, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 1H), 7.64 (s, 1H), 7.65 (d, *J* = 8.6 Hz, 1H), 8.04 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.86, 58.18, 62.97, 123.45, 125.10, 125.15, 127.55, 128.05, 130.42, 130.48, 131.28, 136.51, 138.28, 180.96. HR-MS (ESI). Calcd for $C_{16}H_{15}ClN_2O_2S_2$ (M+H): 367.0341. Found: *m/z* 367.0330.

***N*-[*trans*-1-(5-Chloro-1,1-dioxo-2-propyl-2,3-dihydrobenzo[*b*]thiophen-3-yl)]acetamide (5g):** a white solid; mp 184–186 °C (hexane/CH_2Cl_2); IR (KBr) 3257, 1651, 1305, 1137 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 0.93 (t, *J* = 7.4 Hz, 3H), 1.44–1.50 (m, 1H), 1.52–1.61 (m, 1H), 1.74–1.80 (m, 1H), 1.87–1.95 (m, 1H), 1.97 (s, 3H), 3.48–3.52 (m, 1H), 5.15 (t, *J* = 8.6 Hz, 1H), 7.55 (s, 1H), 7.67 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 1H), 8.64 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.79, 19.63, 22.82, 27.75, 51.43, 65.76, 123.10, 125.60, 130.18, 137.28, 138.86, 141.37, 170.20. HR-MS (ESI). Calcd for $C_{13}H_{16}ClNNaO_3S$ (M+Na): 324.0437. Found: *m/z* 324.0431. Anal. Calcd for $C_{13}H_{16}ClNO_3S$: C, 51.74; H, 5.34; N, 4.64. Found: C, 51.63; H, 5.43; N, 4.56.

***N*-[*trans*-(5-Chloro-1,1-dioxo-2-phenyl-2,3-dihydrobenzo[*b*]thiophen-3-yl)]acetamide (5h-i):** a white solid; mp 172–174 ˚C (hexane/CH_2Cl_2); IR (KBr) 3320, 1657, 1312, 1158 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 1.88 (s, 3H), 4.91 (d, *J* = 9.7 Hz, 1H), 5.86 (dd, *J* = 9.7, 8.6 Hz, 1H), 7.46–7.51 (m, 5H), 7.64 (s, 1H), 7.73 (d, *J* = 8.6 Hz, 1H), 7.96 (d, *J* = 8.6 Hz, 1H), 8.64 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.63, 50.69, 71.13, 123.48, 125.51, 127.46, 128.79, 129.51, 130.01, 130.30, 136.41, 138.94, 141.43, 170.06. HR-MS (FI). Calcd for $C_{16}H_{14}ClNO_3S$ (M): 335.0383. Found: *m/z* 335.0390. Anal. Calcd for $C_{16}H_{14}ClNO_3S$: C, 57.23; H, 4.20; N, 4.17. Found: C, 57.18; H, 4.01; N, 4.08.

1-*trans*-(5-Chloro-1,1-dioxo-2-phenyl-2,3-dihydrobenzo[*b*]thiophen-3-yl)-3-phenylthiourea (5h-ii): a white solid; mp 172–174 ˚C (hexane/CH_2Cl_2); IR (KBr) 3330, 3152, 1541, 1319, 1131 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 5.32 (d, *J* = 6.3 Hz, 1H), 5.75 (s, 1H), 6.89 (br s, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.22 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.51–7.54 (m, 6H), 7.60 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 8.34 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 54.94, 55.44, 70.77, 123.69, 124.16, 125.33, 125.34, 127.29, 128.96, 129.70, 130.10, 130.32, 136.49, 138.01, 138.76, 141.48, 181.48. HR-MS (ESI). Calcd for $C_{21}H_{18}ClN_2O_2S_2$ (M+H): 429.0498. Found: *m/z* 429.0480. Anal. Calcd for $C_{21}H_{17}ClN_2O_2S_2$: C, 58.80; H, 3.99; N, 6.53. Found: C, 58.66; H, 4.19; N, 6.79.

***N*-[*trans*-(6-Methoxy-1,1-dioxo-2-phenyl-2,3-dihydrobenzo[*b*]thiophen-3-yl)]acetamide (5i):** a white solid; mp 195–198 ˚C (hexane/CH_2Cl_2); IR (KBr) 3367, 1664, 1309, 1150 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.00 (s, 3H), 3.88 (s, 3H), 4.54 (d, *J* = 6.3 Hz, 1H), 6.00 (dd, *J* = 8.6, 6.3 Hz, 1H), 6.13 (d, *J* = 8.6 Hz, 1H), 7.21 (dd, *J* = 9.7, 2.9 Hz, 1H), 7.22 (s, 1H), 7.32–7.34 (m, 2H), 7.37–7.40 (m, 3H), 7.45 (d, *J* = 9.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 22.65, 50.43, 56.15, 71.66, 104.51, 121.80, 126.84, 127.99, 128.82, 129.44, 130.00, 130.63, 138.76, 160.52, 169.92. MR-MS (FI). Calcd for $C_{17}H_{17}NO_4S$ (M): 331.0878. Found: *m/z* 331.0887. Anal. Calcd for $C_{17}H_{17}NO_4S$: C, 61.62; H, 5.17; N, 4.23. Found: C, 61.46; H, 5.04; N, 4.21.

Ethyl *trans*-(5,6-Dimethoxy-1,1-dioxo-2-phenyl-2,3-dihydrobenzo[*b*]thiophen-3-yl)carbamate (5j-i): a white solid; mp 241–243 ˚C (hexane/CH_2Cl_2); IR (KBr) 3326, 1695, 1304, 1131 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ 1.13 (t, *J* = 7.7 Hz, 3H), 3.88 (s, 6H), 3.99–4.01 (m, 2H), 4.81 (d, *J* = 8.6 Hz, 1H), 5.54 (t, *J* = 8.6 Hz, 1H), 6.99 (s, 1H), 7.40 (s, 1H), 7.48–7.51 (m, 5H), 7.89 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 14.32, 52.99, 56.11, 56.28, 60.42, 71.49, 103.03, 106.63, 128.13, 128.69, 128.99, 129.31, 130.10, 132.16, 150.46, 153.67, 156.24. Anal. Calcd for $C_{19}H_{21}NO_6S$: C, 58.30; H, 5.41; N, 3.58; S, 8.19. Found: C, 58.09; H, 5.64; N, 3.34; S, 8.09.

***N*-[*trans*-1-(5,6-Dimethoxy-1,1-dioxo-2-phenyl-2,3-dihydrobenzo[*b*]thiophen-3-yl)]acetamide (5j-ii):** a white solid; mp 257–258 ˚C (hexane/CH_2Cl_2); IR (KBr) 3212, 1660, 1310, 1131 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 1.87 (s, 3H), 3.87 (s, 6H), 4.76 (d, *J* = 8.6 Hz, 1H), 5.78 (t, *J* = 8.6 Hz, 1H), 6.98 (s,

1H), 7.38 (s, 1H), 7.46 (s, 5H), 8.58 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 22.67, 50.75, 56.16, 56.27, 71.59, 103.05, 106.96, 128.49, 128.68, 129.13, 129.23, 129.89, 132.02, 150.41, 153.69, 169.88. Anal. Calcd for $C_{18}H_{19}NO_5S$: C, 59.82; H, 5.30; N, 3.88; S, 8.87. Found: C, 59.69; H, 5.24; N, 3.84; S, 8.69.

***trans*-1,1-Dioxo-2-phenyl-2,3-dihydrobenzo[*b*]thiophen-3-amine (4d):** a pale-yellow solid; mp 157–160 °C (hexane/CH_2Cl_2); IR (KBr) 3381, 3315, 1300, 1154 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.25 (d, *J* = 8.9 Hz, 1H), 4.83 (d, *J* = 8.9 Hz, 1H), 7.46–7.48 (m, 4H), 7.50–7.53 (m, 3H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.69 (td, *J* = 7.6, 1.0 Hz, 1H), 7.79–7.81 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 56.10, 77.48, 121.72, 125.15, 127.94, 129.19, 129.74, 129.80, 130.17, 133.77, 138.16, 140.87. HR-MS (EI). Calcd for $C_{14}H_{13}NO_2S$ (M): 259.0667. Found: *m/z* 259.0658.

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