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SYNTHESIS OF *N*-SUBSTITUTED (*Z*)-3-ARYLBENZO[*c*]THIOPHEN-1(3*H*)-IMINES BY THE REACTION OF 1-[ARYL(METHOXY)METHYL]-2-LITHIOBENZENES WITH ISOTHIOCYANATES FOLLOWED BY ACID-MEDIATED CYCLIZATION

Kazuhiro Kobayashi,* Yuuho Shigemura, and Kosuke Ezaki

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

Abstract – A simple procedure for the preparation of *N*-substituted (*Z*)-3-arylbenzo[*c*]thiophen-1(3*H*)-imines has been developed. Thus, bromine/lithium exchange between 1-[aryl(methoxy)methyl]-2-bromobenzenes and butyllithium, followed by reaction of the resulting 1-[aryl(methoxy)methyl]-2-lithiobenzenes with aliphatic and aromatic isothiocyanates, yields the corresponding *N*-substituted 2-[aryl(methoxy)methyl]benzothioamides. These were treated with concentrated hydrobromic acid to give the desired products.

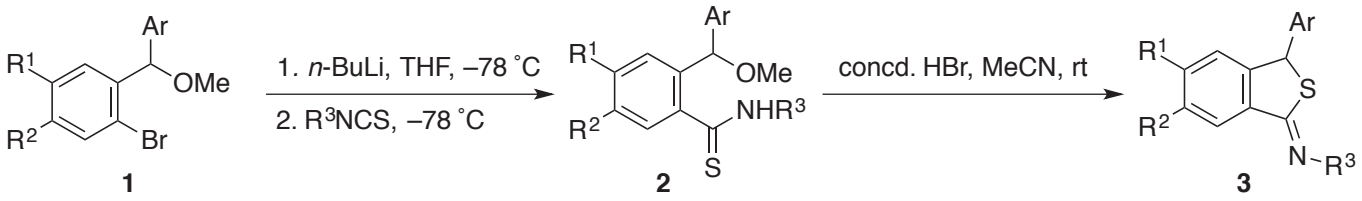
INTRODUCTION

A number of methods for the general preparation of benzo[*c*]thiophen-1(3*H*)-imine derivatives have been reported due to their synthetic importance.[1] Recently, we reported a synthesis of *N*-substituted (*Z*)-3-alkoxybenzo[*c*]thiophen-1(3*H*)-imines by the acid-catalyzed cyclization of *N*-substituted 2-(1,1-dialkoxymethyl)benzamides, derived from the reaction of 1-(1,1-dialkoxymethyl)-2-lithiobenzenes with isothiocyanates.[1e] In this paper, we wish to demonstrated a simple and general preparation of *N*-substituted (*Z*)-3-arylbenzo[*c*]thiophen-1(3*H*)-imines (**3**). We have found that 1-[aryl(methoxy)-methyl]-2-lithiobenzenes, generated from 1-[aryl(methoxy)methyl]-2-bromobenzenes (**1**) by bromine-lithium exchange with butyllithium, reacted with various isothiocyanates to give the corresponding thioamide derivatives (**2**), which in turn were treated with concentrated hydrobromic acid to give the desired products. Acid hydrolysis of these imines to 3-arylbenzo[*c*]thiophen-1(3*H*)-ones (**4**) is also described. So far, only a few methods have been known for the general preparation of

benzo[*c*]thiophen-1(3*H*)-one derivatives,[1e,2] while some of these derivatives have been reported to exhibit biological activities.[3]

RESULTS AND DISCUSSION

The preparation of **3** from **1** was conducted as illustrated in Scheme 1. Thus, the reaction of compounds (**1**) with butyllithium in THF at –78 ˚C generated 1-[aryl(methoxy)methyl]-2-lithiobenzenes by the bromine/lithium exchange, which were allowed to react with isothiocyanates to afford, after aqueous workup, the corresponding *N*-substituted benzothioamide derivatives (**2**). As shown in Table 1, relatively good yields were obtained in general by using aryl isothiocyanate. Although aliphatic isothiocyanates could be used for the reaction, the yields of *N*-alkyl derivatives (**2c**) and (**2h**) were only moderate (Entries 3 and 8, respectively).



Scheme 1

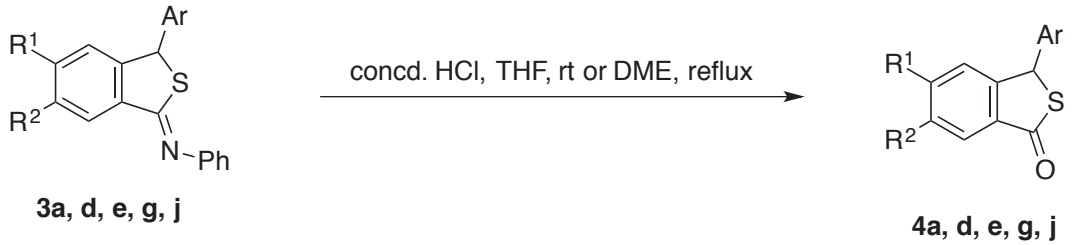
Table 1. Preparation of (*Z*)-*N*-substituted 3-arylbenzo[*c*]thiophen-1(3*H*)-imines (**3**)

Entry	**1**	R^3	**2**	Yield/%[a]	**3**	Yield/%[a]
1	**1a** ($R^1 = R^2 = H$, Ar = Ph)	Ph	**2a**	80	**3a**	86
2	**1a**	2-MeC_6H_4	**2b**	82	**3b**	89
3	**1a**	*n*-Bu	**2c**	54	**3c**	73
4	**1b** ($R^1 = R^2 = H$, Ar = 4-ClC_6H_4)	Ph	**2d**	75	**3d**	59
5	**1c** ($R^1 = R^2 = H$, Ar = 4-$MeOC_6H_4$)	Ph	**2e**	75	**3e**	69
6	**1c**	3-$MeOC_6H_4$	**2f**	76	**3f**	74
7	**1d** ($R^1 = Cl$, $R^2 = H$, Ar = Ph)	Ph	**2g**	72	**3g**	81
8	**1d**	*c*-Hex	**2h**	53	**3h**	79
9	**1d**	4-ClC_6H_4	**2i**	69	**3i**	36
10	**1e** ($R^1 = R^2 = OMe$, Ar = Ph)	Ph	**2j**	75	**3j**	78

[a] Yields of isolated products.

The transformation of **2** into **3** was first attempted with a catalytic amount of *p*-toluenesulfonic acid monohydrate in dichloromethane at room temperature as reported for the preparation of (*Z*)-*N*-substituted 3-arylbenzo[*c*]thiophen-1(3*H*)-imines from *N*-aryl-2-(1,1-dialkoxymethyl)benzamides.[1e] However, the reaction proceeded very reluctantly even under refluxing conditions. Therefore, we felt that treatment with concentrated hydrobromic acid in acetonitrile would be suitable this transformation in view of our

previous success in the preparation of *N,N*-disubstituted 4*H*-3,1-benzothiazin-2-amines from the hydroxy thiourea derivatives, derived by reduction of the adducts of aryl(2-isothiocyanatophenyl)methanones with secondary amines.[4] Initially, compounds (**2**) were treated with a catalytic amount of hydrobromic acid. However, the reactions did not complete and resulted in the formation of the desired products **3** in rather lower yields and recovery of considerable amounts of the starting materials. Further investigation revealed that the reactions proceeded in appropriate extent by treating **2** with an equimolar amount of concentrated hydrobromic acid in acetonitrile at room temperature for a day to give **3** in satisfactory yields,[5] as compiled in Table 1 as well. No stereoisomer was detected in each case. The iminobenzo[*c*]thiophene structure of the products (**3**) was confirmed by the spectral data. For example, the ^{13}C NMR spectra for compound **3a** revealed a signal assignable to the imino carbon at δ 167.78. Any signal was not observed at δ ~180 due to a thiocarbonyl carbon of the thiolactam structure. The preferable formation of **3** may be attributable to the higher nucleophilicity of sulfur atom than that of nitrogen atom.[1b,c,6] The stereochemistry of the products was determined on the basis of their NOESY analyses, in which no interaction was observed between, for example, the signal at δ 8.13 assignable to 8-H and that at δ 7.22 assignable to the *ortho*-protons of *N*-phenyl group of **3a**. The exclusive formation of the less crowded isomer is reasonable. Although cyclization of the *N*-(alkyl)thiobenzamides (**2c**) and (**2h**) was somewhat slower than that of the others, the yields of the corresponding products were comparable to those of the others (Entries 3 and 8, respectively). As can be seen in Entry 9, the yield of the product (**3i**) is rather lower than those of the others. The reaction proceeded rather sluggishly with extensive decomposition after prolonged reaction times. An electron-withdrawing chloro substituent on the *N*-aryl group may decrease the nucleophilicity of the thioamide moiety.



3a, d, e, g, j **4a, d, e, g, j**

Scheme 2

Transformation of **3** into 3-arylbenzo[*c*]thiophen-1(3*H*)-ones (**4**) by acid hydrolysis of the imino group was generally achieved in good yield on treatment with concentrated hydrochloric acid in THF at room temperature, as depicted in Scheme 2. However, hydrolysis of **3j** did not occurred under these conditions at all. Therefore, hydrolysis of this compound was carried out in 1,2-dimethoxyethane (DME) at reflux temperature. Under these modified conditions, hydrolysis of **3j** proceeded cleanly to give the desired

product (**4j**) in high yield. This result may be ascribed to the less reactivity of the imino function of **3j** due to the two-methoxy groups on the benzene ring of the benzo[*c*]thiophene structure. The results of these reactions are summarized in Table 2.

Table 2. Preparation of 3-arylbenzo[*c*]thiophen-1(3*H*)-ones (**4**)

Entry	**3**	Conditions	**4**	Yield/%[a]
1	**3a** ($R^1 = R^2 = H$, Ar = Ph, R^3 = Ph)	THF, rt	**4a**	83
2	**3d** ($R^1 = R^2 = H$, Ar = 4-ClC_6H_4, R^3 = Ph)	THF, rt	**4d**	71
3	**3e** ($R^1 = R^2 = H$, Ar = 4-$MeOC_6H_4$, R^3 = Ph)	THF, rt	**4e**	82
4	**3g** (R^1 = Cl, $R^2 = H$, Ar = Ph, R^3 = Ph)	THF, rt	**4g**	86
5	**3j** ($R^1 = R^2$ = OMe, Ar = Ph, R^3 = Ph)	DME, reflux	**4j**	91

[a] Yields of isolated products.

The forgoing results indicate that a convenient method for the preparation of *N*-substituted (*Z*)-3-arylbenzo[*c*]thiophen-1(3*H*)-imines has been developed using the two-step sequence starting from 1-[aryl(methoxy)methyl]-2-lithiobenzenes; the reaction of 1-[aryl(methoxy)methyl]-2-lithiobenzenes, generated from the starting materials, with isothiocyanates and the subsequent treatment with the resulting *N*-substituted 2-[aryl(methoxy)methyl]benzothioamides with concentrated hydrobromic acid. Hydrolysis of these imines also enables us to obtain 3-arylbenzo[*c*]thiophen-1(3*H*)-ones. The ready availability of the starting materials and the simplicity of the operations make this method attractive.

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 Spectrum65 FTIR spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz. ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. High-resolution MS spectra (DART, positive) 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. (2-Bromophenyl)phenylmethanol,[7] (2-bromophenyl)(4-methoxyphenyl)methanol,[8] (2-bromophenyl)(4-chlorophenyl)methanol,[8] (2-bromo-5-chlorophenyl)phenylmethanol,[9] and (2-bromo-4,5-dimethoxyphenyl)phenylmethanol[10] 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 Compounds (1). 1-Bromo-2-[methoxy(phenyl)methyl]-benzene (1a).[11] To a stirred suspension of NaH (60% in mineral oil; 0.37 g, 9.2 mmol) in THF (7 mL) at 0 ˚C was added a solution of (2-bromophenyl)phenylmethanol (2.4 g, 9.2 mmol) in THF (6 mL) dropwise. After evolution of H_2 gas had ceased, MeI (2.6 g, 18 mmol) was added and the mixture was heated at reflux temperature for 1 h. After cooling to rt, saturated aqueous NH_4Cl (20 mL) was added and the mixture was extracted with AcOEt (3 × 20 mL). The combined extracts were washed with brine, dried (Na_2SO_4), and concentrated by evaporation. The residue was distilled to afford **1a** (2.2 g, 88%); a pale-yellow oil; bp 123–125 ˚C/0.2 mmHg; IR (neat) 1602, 1093 cm^{-1}; ^1H NMR δ 3.40 (s, 3H), 5.67 (s, 1H), 7.13 (td, *J* = 7.6, 1.5 Hz, 1H), 7.25 (tt, *J* = 7.6, 1.5 Hz, 1H), 7.30–7.34 (m, 3H), 7.39 (dd, *J* = 7.6, 1.5 Hz, 2H), 7.52 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.53 (dd, *J* = 7.6, 1.5 Hz, 1H).

1-Bromo-2-[(4-chlorophenyl)(methoxy)methyl]benzene (1b):[11] yield: 82%; a colorless oil; R_f 0.30 (CH_2Cl_2/hexane 1:5); IR (neat) 1488, 1091 cm^{-1}; ^1H NMR δ 3.38 (s, 3H), 5.64 (s, 1H), 7.15 (td, *J* =7.6, 2.3 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.32–7.35 (m, 3H), 7.49 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H).

1-Bromo-2-[(methoxy)(4-methoxyphenyl)methyl]benzene (1c): yield: 84%; a colorless oil; R_f 0.43 (CH_2Cl_2/hexane 1:1); IR (neat) 1610, 1511, 1249, 1090 cm^{-1}; ^1H NMR δ 3.38 (s, 3H), 3.78 (s, 3H), 5.59 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 7.13 (td, *J* = 7.6, 1.5 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.56 (dd, *J* = 7.6, 1.5 Hz, 1H). Anal. Calcd for $C_{15}H_{15}BrO_2$: C, 58.65; H, 4.92. Found: C, 58.38; H, 5.02.

1-Bromo-4-chloro-2-[(methoxy)(phenyl)methyl]benzene (1d): yield: 80%; a colorless oil; R_f 0.30 (CH_2Cl_2/hexane 1:10); IR (neat) 1454, 1095 cm^{-1}; ^1H NMR δ 3.39 (s, 3H), 5.58 (s, 1H), 7.11 (dd, *J* = 8.6, 2.9 Hz, 1H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.38 (d, *J* = 7.4 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 1H), 7.55 (d, *J* = 2.9 Hz, 1H). Anal. Calcd for $C_{14}H_{12}BrClO$: C, 53.96; H, 3.88. Found: C, 53.83; H, 4.01.

1-Bromo-4,5-dimethoxy-2-[(methoxy)(phenyl)methyl]benzene (1e): yield: 91%; a colorless oil; R_f 0.27 (CH_2Cl_2/hexane 1:5); IR (neat) 1602, 1502, 1258 cm^{-1}; ^1H NMR δ 3.39 (s, 3H), 3.84 (s, 3H), 3.86 (s, 3H), 5.62 (s, 1H), 7.00 (s, 1H), 7.25 (t, *J* = 7.4 Hz, 1H), 7.26 (s, 1H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.37 (d, *J* = 7.4 Hz, 2H). Anal. Calcd for $C_{16}H_{17}BrO_3$: C, 56.99; H, 5.08. Found: C, 56.74; H, 5.34.

Typical Procedure for the Preparation of Benzothioamides (2). 2-[Methoxy(phenyl)methyl]-*N*-phenylbenzothioamide (2a). To a stirred solution of **1a** (0.55 g, 2.0 mmol) in THF (5 mL) at –78 ˚C was added dropwise *n*-BuLi (1.6 M in hexane, 2.0 mmol). After 15 min, PhNCS (0.27 g, 2.0 mmol) was added dropwise and stirring was continued for 1 h at the same temperature. Saturated aqueous NH_4Cl (20 mL) was added, and the mixture was warmed to rt and extracted with AcOEt (3 × 20 mL). The combined extracts were washed with brine (20 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on silica gel (AcOEt/hexane 1:5) to give **2a** (0.54 g, 80%); a

yellow solid; mp 123–125 °C (hexane/Et_2O); IR (KBr) 3243, 1086 cm^{-1}; ^1H NMR δ 3.38 (s, 3H), 5.73 (s, 1H), 7.27–7.38 (m, 9H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.60 (dd, *J* = 7.6, 2.3 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 2H), 9.23 (br s, 1H). Anal. Calcd for $C_{21}H_{19}NOS$: C, 75.64; H, 5.74; N, 4.20. Found: C, 75.38; 5.76; N, 4.10.

2-[Methoxy(phenyl)methyl]-*N*-(2-methylphenyl)benzothioamide (2b): a yellow solid; mp 81–83 °C (hexane/Et_2O); IR (KBr) 3216, 1086 cm^{-1}; ^1H NMR δ 2.23 (s, 3H), 3.41 (s, 3H), 5.92 (s, 1H), 7.25–7.38 (m, 11H), 7.54 (d, *J* = 7.6, 2.3 Hz, 1H), 7.64 (dd, *J* = 9.2, 3.0 Hz, 1H), 9.01 (br s, 1H). Anal. Calcd for $C_{22}H_{21}NOS$: C, 76.05; H, 6.09; N, 4.03. Found: C, 76.05; 6.24; N, 3.98.

***N*-Butyl-2-[methoxy(phenyl)methyl]benzothioamide (2c):** a yellow oil; R_f 0.23 (AcOEt/hexane 1:8); IR (neat) 3264, 1086 cm^{-1}; ^1H NMR δ 0.92 (t, *J* = 7.6 Hz, 3H), 1.30–1.37 (m, 2H), 1.49–1.54 (m, 2H), 3.48 (s, 3H), 3.55–3.62 (m, 1H), 3.65–3.72 (m, 1H), 5.68 (s, 1H), 7.28–7.35 (m, 8H), 7.42 (d, *J* = 6.9 Hz, 1H), 7.51 (br, 1H). Anal. Calcd for $C_{19}H_{23}NOS$: C, 72.80; H, 7.40; N, 4.47. Found: C, 72.62; 7.40; N, 4.32.

2-[(4-Chlorophenyl)(methoxy)methyl]-*N*-phenylbenzothioamide (2d): a yellow viscous oil; R_f 0.32 (AcOEt/hexane 1:1); IR (neat) 3235, 1088 cm^{-1}; ^1H NMR δ 3.37 (s, 3H), 5.73 (s, 1H), 7.27–7.30 (m, 6H), 7.35–7.37 (m, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 9.2 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 2H), 9.18 (br s, 1H). Anal. Calcd for $C_{21}H_{18}ClNOS$: C, 68.56; H, 4.93; N, 3.81. Found: C, 68.51; 4.93; N, 3.60.

2-[Methoxy(4-methoxyphenyl)methyl]-*N*-phenylbenzothioamide (2e): a yellow viscous oil; R_f 0.33 (AcOEt/hexane 1:1); IR (neat) 3260, 1610, 1084 cm^{-1}; ^1H NMR δ 3.35 (s, 3H), 3.78 (s, 3H), 5.67 (s, 1H), 6.85 (d, *J* = 9.2 Hz, 2H), 7.27 (t, *J* = 7.6 Hz, 2H), 7.36–7.41 (m, 6H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 9.2 Hz, 2H), 9.19 (br s, 1H). Anal. Calcd for $C_{22}H_{21}NO_2S$: C, 72.70; H, 5.82; N, 3.85. Found: C, 72.61; 5.80; N, 3.59.

2-[Methoxy(4-methoxyphenyl)methyl]-*N*-(3-methoxyphenyl)benzothioamide (2f): a yellow viscous oil; R_f 0.16 (AcOEt/hexane 1:1); IR (neat) 3262, 1609, 1084 cm^{-1}; ^1H NMR δ 3.35 (s, 3H), 3.78 (s, 3H), 3.82 (s, 3H), 5.65 (s, 1H), 6.81 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.24–7.37 (m, 6H), 7.59 (d, *J* = 8.6 Hz, 2H), 9.16 (br s, 1H). Anal. Calcd for $C_{23}H_{23}NO_3S$: C, 70.20; H, 5.89; N, 3.56. Found: C, 70.18; 5.91; N, 3.54.

4-Chloro-2-[methoxy(phenyl)methyl]-*N*-phenylbenzothioamide (2g): a yellow viscous oil; R_f 0.32 (AcOEt/hexane 1:5); IR (neat) 3227, 1075 cm^{-1}; ^1H NMR δ 3.37 (s, 3H), 5.71 (s, 1H), 7.28–7.36 (m, 9H), 7.40 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.49 (d, *J* = 8.6 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 9.15 (br s, 1H). Anal. Calcd for $C_{21}H_{18}ClNOS$: C, 68.56; H, 4.93; N, 3.81. Found: C, 68.43; 4.92; N, 3.70.

4-Chloro-*N*-cyclohexyl-2-[methoxy(phenyl)methyl]benzothioamide (2h): a pale-yellow viscous oil; R_f 0.32 (AcOEt/hexane 1:8); IR (neat) 3262, 1097 cm^{-1}; ^1H NMR δ 0.99–1.06 (m, 1H), 1.12–1.19 (m, 2H), 1.35–1.46 (m, 2H), 1.64–1.73 (m, 3H), 1.92–1.94 (m, 1H), 2.15–2.18 (m, 1H), 3.38 (s, 3H), 4.37–4.42 (m, 1H), 5.76 (s, 1H), 7.25–7.36 (m, 9H). Anal. Calcd for $C_{21}H_{24}ClNOS$: C, 67.45; H, 6.47; N, 3.75. Found: C, 67.50; 6.56; N, 3.70.

4-Chloro-*N*-(4-chlorophenyl)-2-[methoxy(phenyl)methyl]benzothioamide (2i): a yellow solid; mp 137–139 ˚C (hexane); IR (KBr) 3226, 1092 cm^{-1}; ^1H NMR δ 3.38 (s, 3H), 5.64 (s, 1H), 7.28–7.37 (m, 9H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 2H), 9.14 (br s, 1H). Anal. Calcd for $C_{21}H_{17}Cl_2NOS$: C, 62.69; H, 4.26; N, 3.48. Found: C, 62.41; 4.31; N, 3.19.

4,5-Dimethoxy-2-[methoxy(phenyl)methyl]-*N*-phenylbenzothioamide (2j): a yellow solid; mp 133–136 ˚C (hexane/CH_2Cl_2); IR (KBr) 3284, 1601, 1093 cm^{-1}; ^1H NMR δ 3.39 (s, 3H), 3.81 (s, 3H), 3.92 (s, 3H), 5.60 (s, 1H), 6.77 (s, 1H), 7.24–7.40 (m, 10H), 7.66 (d, *J* = 8.0 Hz, 1H), 9.49 (br s, 1H). Anal. Calcd for $C_{23}H_{23}NO_3S$: C, 70.20; H, 5.89; N, 3.56. Found: C, 70.17; 6.04; N, 3.52.

Typical Procedure for the Preparation of Benzo[*c*]thiophen-1(3*H*)-imines (3). (*Z*)-3,*N*-Diphenylbenzo[*c*]thiophen-1(3*H*)-imine (3a). To a stirred solution of **2a** (0.50 g, 1.5 mmol) in MeCN (7 mL) at 0 ˚C was added dropwise concentrated HBr (0.26 g, 1.5 mmol). The mixture was warmed to rt and stirring was continued for a day. To the cooled (0 ˚C) mixture was added aqueous saturated $NaHCO_3$ (20 mL) and the mixture was extracted with AcOEt (3 × 20 mL). The combined extracts were washed with brine (20 mL), dried (Na_2SO_4), and concentrated by evaporation. The residual solid was purified by recrystallization by hexane/Et_2O to give **3a** (0.39 g, 86%); a yellow solid; mp 132–133 ˚C; IR (KBr) 1625, 1591 cm^{-1}; ^1H NMR δ 5.85 (s, 1H), 7.11–7.16 (m, 4H), 7.22 (dd, *J* = 7.6, 1.5 Hz, 2H), 7.25–7.30 (m, 3H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.42–7.47 (m, 2H), 8.13 (dd, *J* = 7.6, 1.5 Hz, 1H); ^{13}C NMR δ 55.97, 120.34, 123.36, 124.67, 125.92, 128.02, 128.05, 128.22, 128.83, 129.11, 131.57, 137.91, 140.31, 148.14, 151.82, 167.78. HR-MS. Calcd for $C_{20}H_{16}NS$ (M+H): 302.1003. Found: *m/z* 302.0988. Anal. Calcd for $C_{20}H_{15}NS$: C, 79.70; H, 5.02; N, 4.65. Found: C, 79.49; H, 4.96; N, 4.59.

(*Z*)-*N*-(2-Methylphenyl)-3-phenylbenzo[*c*]thiophen-1(3*H*)-imine (3b): a yellow solid; mp 134–135 ˚C (hexane/Et_2O); IR (KBr) 1630, 1593 cm^{-1}; ^1H NMR δ 2.25 (s, 3H), 5.84 (s, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 7.04 (ddd, *J* = 8.0, 7.6, 1.5 Hz, 1H),7.16–7.19 (m, 2H), 7.21–7.31 (m, 6H), 7.44–7.49 (m, 2H), 8.16 (dd, *J* = 7.6, 1.5 Hz, 1H) ^{13}C NMR δ 17.70, 55.82, 118.42, 123.36, 124.54, 126.01, 126.52, 128.01, 128.05, 128.20, 128.85, 128.99, 130.56, 131.52, 137.61, 140.48, 148.37, 150.87, 167.46. HR-MS. Calcd for $C_{21}H_{18}NS$ (M+H): 316.1160. Found: *m/z* 316.1141. Anal. Calcd for $C_{21}H_{17}NS$: C, 79.96; H, 5.43; N, 4.44. Found: C, 79.66; H, 5.46; N, 4.43.

(*Z*)-*N*-Butyl-3-phenylbenzo[*c*]thiophen-1(3*H*)-imine (3c): a yellow oil; R_f 0.29 (AcOEt/hexane 1:20); IR (neat) 1634, 1601 cm^{-1}; ^1H NMR δ 0.98 (t, *J* = 7.4 Hz, 3H), 1.44–1.52 (m, 2H), 1.76–1.82 (m, 2H), 3.43–3.53 (m, 2H), 5.85 (s, 1H), 7.10–7.13 (m, 1H), 7.23–7.25 (m, 2H), 7.26–7.33 (m, 3H), 7.36–7.39 (m, 2H), 7.95–7.98 (m, 1H); ^{13}C NMR δ 13.96, 20.75, 32.53, 55.64, 57.51, 122.98, 125.87, 127.84, 127.92, 128.24, 128.83, 130.77, 137.67, 141.12, 147.67, 165.27. HR-MS. Calcd for $C_{18}H_{20}NS$ (M+H): 282.1316. Found: *m/z* 282.1304. Anal. Calcd for $C_{18}H_{19}NS$: C, 76.82; H, 6.81; N, 4.98. Found: C, 76.65; H, 6.81; N, 4.91.

(*Z*)-3-(4-Chlorophenyl)-*N*-phenylbenzo[*c*]thiophen-1(3*H*)-imine (3d): a pale-yellow solid; mp 135–137 °C (hexane/CH_2Cl_2); IR (KBr) 1626, 1590 cm^{-1}; ^1H NMR δ 5.83 (s, 1H), 7.13–7.17 (m. 6H), 7.26 (dd, *J* = 8.6, 6.3 Hz, 2H), 7.37 (t, *J* = 8.0, 7.4 Hz, 2H), 7.46–7.48 (m, 2H), 8.13 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR δ 55.21, 120.30, 123.54, 124.81, 125.84, 128.30, 129.07, 129.17, 129.60, 131.72, 133.90, 137.91, 139.00, 147.68, 151.74, 167.25. HR-MS. Calcd for $C_{20}H_{15}ClNS$ (M+H): 336.0613. Found: *m*/*z* 336.0605. Anal. Calcd for $C_{20}H_{14}ClNS$: C, 71.53; H, 4.20; N, 4.17. Found: C, 71.43; H, 4.38; N, 4.14.

(*Z*)-3-(4-Methoxyphenyl)-*N*-phenylbenzo[*c*]thiophen-1(3*H*)-imine (3e): a yellow solid; mp 94–96 °C (hexane/CH_2Cl_2); IR (KBr) 1627, 1609 cm^{-1}; ^1H NMR δ 3.77 (s, 3H), 5.85 (s, 1H), 6.82 (d, *J* = 8.6 Hz, 2H), 7.12–7.18 (m, 6H), 7.37 (dd, *J* = 8.0, 7.4 Hz, 2H), 7.45–7.47 (m, 2H), 8.12 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR δ 55.27, 55.62, 114.22, 120.36, 123.30, 124.63, 125.88, 128.00, 129.11, 129.39, 131.54, 132.20, 137.89, 148.45, 151.89, 159.33, 167.93. HR-MS. Calcd for $C_{21}H_{18}NOS$ (M+H): 332.1109. Found: *m*/*z* 332.1101. Anal. Calcd for $C_{21}H_{17}NOS$: C, 76.10; H, 5.17; N, 4.23; S, 9.67. Found: C, 75.80; H, 5.15; N, 4.15; S, 9.62.

(*Z*)-*N*-(3-Methoxyphenyl)-3-(4-methoxyphenyl)benzo[*c*]thiophen-1(3*H*)-imine (3f): a yellow solid; mp 112–114 °C (hexane/CH_2Cl_2); IR (KBr) 1631, 1596 cm^{-1}; ^1H NMR δ 3.78 (s, 3H), 3.80 (s, 3H), 5.85 (s, 1H), 6.68–6.92 (m, 2H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 8.6 Hz, 2H), 7.14–7.18 (m, 3H), 7.27 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.44–7.47 (m 2H), 8.11 (dd, *J* = 6.9, 2.3 Hz, 1H); ^{13}C NMR δ 55.25, 55.28, 55.68, 105.97, 110.61, 112.60, 114.23, 123.30, 125.89, 128.00, 129.42, 129.90, 131.56, 132.17, 137.89, 148.50, 153.16, 159.35, 160.32, 168.08. HR-MS. Calcd for $C_{22}H_{20}NO_2S$ (M+H): 362.1214. Found: *m*/*z* 362.1208. Anal. Calcd for $C_{22}H_{19}NO_2S$: C, 73.10; H, 5.30; N, 3.88. Found: C, 72.91; H, 5.27; N, 3.82.

(*Z*)-5-Chloro-*N*,3-diphenylbenzo[*c*]thiophen-1(3*H*)-imine (3g): a white solid; mp 70–78 °C (pentane); IR (KBr) 1620, 1591 cm^{-1}; ^1H NMR δ 5.82 (s, 1H), 7.13–7.16 (m, 4H), 7.23 (dd, *J* = 7.4, 1.7 Hz, 2H), 7.28–7.34 (m, 3H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.44 (dd, *J* = 8.0, 1.7 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR δ 55.54, 120.35, 124.38, 124.92, 126.00, 128.25, 128.36, 128.74, 129.05, 129.18, 136.62, 137.87, 139.55, 149.56, 151.51, 166.09. HR-MS. Calcd for $C_{20}H_{15}ClNS$ (M+H): 336.0613. Found: *m*/*z* 336.0605. Anal. Calcd for $C_{20}H_{14}ClNS$: C, 71.53; H, 4.20; N, 4.17. Found: C, 71.49; H, 4.36; N, 4.08.

(*Z*)-5-Chloro-*N*-cyclohexyl-3-phenylbenzo[*c*]thiophen-1(3*H*)-imine (3h): a white solid; mp 121–124 °C (pentane); IR (KBr) 1634, 1595 cm^{-1}; ^1H NMR δ 1.24–1.41 (m, 3H), 1.49–1.60 (m, 2H), 1.65–1.67 (m, 1H), 1.81–1.92 (m, 4H), 3.14–3.20 (m, 1H), 5.79 (s, 1H), 7.09 (br s, 1H), 7.23–7.25 (m, 2H), 7.28–7.35 (m, 4H), 7.90 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR δ 24.74, 24.79, 25.73, 32.84, 32.95, 55.05, 67.14, 124.21, 125.87, 128.19, 128.22, 128.36, 129.00, 136.49, 136.89, 140.48, 149.04, 161.32. HR-MS. Calcd for $C_{20}H_{21}ClNS$ (M+H): 342.1083. Found: *m*/*z* 342.1074. Anal. Calcd for $C_{20}H_{20}ClNS$: C, 70.26; H, 5.90; N, 4.10. Found: C, 70.16; H, 6.17; N, 3.84.

(*Z*)-5-Chloro-*N*-(4-chlorophenyl)-3-phenylbenzo[*c*]thiophen-1(3*H*)-imine (3i): a white solid; mp 116–119 ˚C (pentane); IR (KBr) 1638, 1591 cm^{-1}; ^1H NMR δ 5.84 (s, 1H), 7.09 (d, *J* = 8.6 Hz, 2H), 7.16 (br s, 1H), 7.23 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.28–7.35 (m, 6H), 7.44 (dd, *J* = 8.0, 1.7 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR δ 55.73, 121.88, 124.37, 126.04, 128.23, 128.47, 128.83, 129.11, 129.28, 130.15, 136.46, 138.11, 139.29, 149.59, 149.88, 166.80. HR-MS. Calcd for $C_{20}H_{14}Cl_2NS$ (M+H): 370.0224. Found: *m/z* 370.0218. Anal. Calcd for $C_{20}H_{13}Cl_2NS$: C, 64.87; H, 3.54; N, 3.78. Found: C, 64.83; H, 3.83; N, 3.80.

(*Z*)-5,6-Dimethoxy-3,*N*-diphenylbenzo[*c*]thiophen-1(3*H*)-imine (3j): a white solid; mp 144–147 ˚C (hexane/CH_2Cl_2); IR (KBr) 1618, 1602, 1587 cm^{-1}; ^1H NMR δ 3.81 (s, 3H), 4.01 (s, 3H), 5.78 (s, 1H), 6.58 (s, 1H), 7.10–7.15 (m, 3H), 7.22 (dd, *J* = 8.0, 1.1 Hz, 2H), 7.26–7.33 (m, 3H), 7.35 (dd, *J* = 8.0, 7.4 Hz, 2H), 7.55 (s, 1H); ^{13}C NMR δ 55.49, 56.16, 56.27, 104.22, 107.16, 120.48, 124.51, 128.03, 128.15, 128.91, 129.11, 130.74, 140.48, 141.66, 149.73, 152.01, 152.67, 167.53. HR-MS. Calcd for $C_{22}H_{20}NO_2S$ (M+H): 362.1214. Found: *m/z* 352.1207. Anal. Calcd for $C_{22}H_{19}NO_2S$: C, 73.10; H, 5.30; N, 3.88. Found: C, 73.07; H, 5.34; N, 3.86.

Typical Procedure for the Preparation of 3-Arylbenzo[*c*]thiophen-1(3*H*)-ones (4). 3-Phenylbenzo[*c*]thiophen-1(3*H*)-one (4a).[12] To a solution of **3a** (0.30 g, 1.0 mmol) in THF (3 mL) at 0 ˚C was added concentrated HCl (0.5 mL). The temperature was raised to rt and stirring was continued for 2 d. Saturated aqueous $NaHCO_3$ (10 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL). The combined extracts were washed with brine, dried (Na_2SO_4), and concentrated by evaporation. The residual solid was purified by recrystallization to give **4a** (0.19 g, 83%); a pale-yellow solid; mp 114–115 ˚C (hexane/Et_2O) (lit.,[12a] mp 114 ˚C). The ^1H NMR data for this product were identical to those reported previously.[12a]

3-(4-Chlorophenyl)benzo[*c*]thiophen-1(3*H*)-one (4d): a white solid; mp 113–115 ˚C (hexane/CH_2Cl_2); IR (KBr) 1680, 1610 cm^{-1}; ^1H NMR δ 5.88 (s, 1H), 7.19 (d, *J* = 8.6 Hz, 2H), 7.24 (d, *J* = 7.4 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.58 (td, *J* = 7.4, 1.1 Hz, 1H), 7.86 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR δ 53.81, 123.71, 126.47, 128.55, 129.27, 129.63, 133.75, 134.27, 135.58, 137.41, 150.65, 196.69. HR-MS. Calcd for $C_{14}H_{10}ClOS$ (M+H): 261.0141. Found: *m/z* 261.0134. Anal. Calcd for $C_{14}H_9ClOS$: C, 64.49; H, 3.48. Found: C, 64.31; H, 3.58.

3-(4-Methoxyphenyl)benzo[*c*]thiophen-1(3*H*)-one (4e): a white solid; mp 92–94 ˚C (hexane/CH_2Cl_2); IR (KBr) 1676, 1611 cm^{-1}; ^1H NMR δ 3.80 (s, 3H), 5.89 (s, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.56 (td, *J* = 7.6, 1.5 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR δ 54.26, 55.30, 114.40, 123.44, 126.49, 128.24, 129.44, 130.50, 133.53, 135.67, 151.48, 159.56, 197.31. HR MS. Calcd for $C_{15}H_{13}O_2S$ (M+H): 256.0636. Found: *m/z* 256.0628. Found: *m/z* 261.0134. Anal. Calcd for $C_{15}H_{12}O_2S$: C, 70.29; H, 4.72. Found: C, 70.29; H, 4.73.

5-Chloro-3-phenylbenzo[*c*]thiophen-1(3*H*)-one (4g): a white solid; mp 171–173 ˚C (hexane/CH_2Cl_2); IR (KBr) 1671 cm^{-1}; ^1H NMR δ 5.86 (s, 1H), 7.24–7.27 (m, 3H), 7.32–7.38 (m, 3H), 7.46 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR δ 54.05, 124.47, 126.69, 128.27, 128.69, 129.11, 129.23, 134.15, 137.89, 140.54, 152.58, 195.57. HR-MS. Calcd for $C_{14}H_{10}ClOS$ (M+H): 261.0141. Found: *m/z* 261.0135. Anal. Calcd for $C_{14}H_9ClOS$: C, 64.49; H, 3.48. Found: C, 64.23; H, 3.43.

5,6-Dimethoxy-3-phenylbenzo[*c*]thiophen-1(3*H*)-one (4j). This compound was obtained by treating **3j** with concentrated HCl in DME at reflux temperature. A pale-yellow solid; mp 114–116 ˚C (pentane); IR (KBr) 1677 cm^{-1}; ^1H NMR δ 3.81 (s, 3H), 3.96 (s, 3H), 5.80 (s, 1H), 6.63 (s, 1H), 7.23–7.26 (m, 3H), 7.31–7.36 (m, 3H); ^{13}C NMR δ 53.89, 56.24, 56.29, 104.01, 107.54, 128.19, 128.32, 128.65, 129.06, 138.98, 145.71, 149.89, 154.35, 196.06. HR-MS. Calcd for $C_{16}H_{15}O_3S$ (M+H): 287.0744. Found: *m/z* 287.0743. Anal. Calcd for $C_{16}H_{14}O_3S$: C, 67.11; H, 4.93. Found: C, 67.04; H, 4.65.

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