Synthesis of 3-Alkoxybenzo[*c*]thiophen-1(3*H*)-ones by Hydrolysis of *N*-Substituted 3-Alkoxybenzo[*c*]thiophen-1(3*H*)-imines Derived from 1-Bromo-2-(dialkoxymethyl)benzenes and Isothiocyanates

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A convenient procedure for the preparation of a new type of thiophthalides, 3-alkoxybenzo[*c*]thiophen-1(3*H*)-ones **4** and **9** has been developed. Thus, 1-(dialkoxymethyl)-2-lithiobenzenes, generated by Br/Li exchange between 2-bromo-1-(dialkoxymethyl)benzenes **1** and **6**, and BuLi, react with isothiocyanates to afford *N*-substituted 2-(dialkoxymethyl)benzothioamides **2** and **7**, which, on treatment with a catalytic amount of $TsOH \cdot H_2O$, give *N*-substituted 3-alkoxybenzo[*c*]thiophen-1(3*H*)-imines **3** and **8**. The latter are hydrolyzed under acidic conditions to the desired products **4** and **9**, respectively.

Introduction. – The biological activity [1][2] coupled with synthetic utility [3][4] of compounds with the benzo[*c*]thiophen-1(3*H*)-one skeleton has attracted interest in the development of new routes to this class of heterocycles. Although several synthetic methods for benzo[*c*]thiophen-1(3*H*)-one have been reported [5], there are only a few reports on the synthesis of benzo[*c*]thiophen-1(3*H*)-ones with substituents at C(3) [3][6]. 3-Alkylbenzo[*c*]thiophen-1(3*H*)-ones have recently been synthesized as potential anti-ischemic stroke agents by *Wu et al.* The method, however, involves a HI-mediated reaction under harsh conditions [2]. We have found that 3-alkoxybenzo[*c*]thiophen-1(3*H*)-ones can be prepared by hydrolysis of the respective *N*-substituted 3-alkoxybenzo[*c*]thiophen-1(3*H*)-imines, derived from the reaction of 1-(dialkoxymethyl)-2-lithiobenzenes with isothiocyanates, followed by acid-catalyzed cyclization of the resulting *N*-substituted 2-(dialkoxymethyl)benzothioamides. Herein, we describe the results of our investigation, which provide a convenient entry to this new type of benzo[*c*]thiophen-1(3*H*)-ones (thiophthalides). To the best of our knowledge, no procedure exists for their general preparation[1]). Benzo[*c*]thiophen-1(3*H*)-imine derivatives may potentially also be of biological interest[2]).

Results and Discussion. – The synthesis of *N*-substituted (*Z*)-3-alkoxybenzo[*c*]-thiophen-1(3*H*)-imines **3** and conversion of some of them to the corresponding 3-alkoxybenzo[*c*]thiophen-1(3*H*)-ones **4** was accomplished as illustrated in *Scheme 1*.

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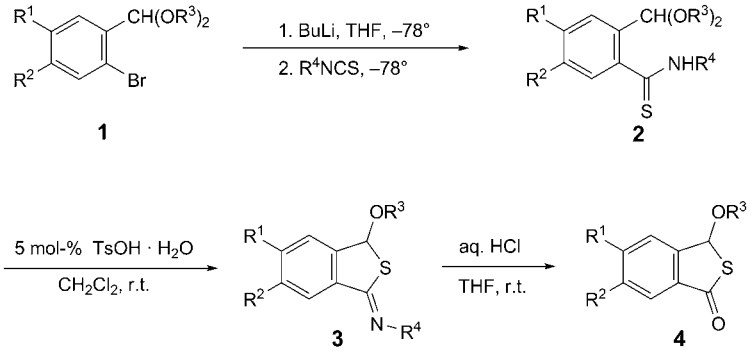
[1]) The formation of 3-ethoxybenzo[*c*]thiophene-1(3*H*)-one has been reported [7].

[2]) For a recent report on the synthesis of benzo[*c*]thiophen-1-imines, see [8].

Scheme 1



First, 1-bromo-2-(dialkoxymethyl)benzenes **1** were treated with BuLi in THF at $-78°$ to furnish 1-(dialkoxymethyl)-2-lithiobenzenes[3]), which were then allowed to react with isothiocyanates. The reaction proceeded immediately and cleanly to afford *N*-substituted 2-(dialkoxymethyl)benzothioamides **2** in fair-to-good yields as compiled in *Table 1*. Not only aromatic isothiocyanates but also an aliphatic isothiocyanate, *i.e.*, BuNCS, could be used in the reaction (*Entry 5*). The transformation of **2** into *N*-substituted 3-alkoxybenzo[*c*]thiophen-1(3*H*)-imines **3** was achieved under operationally convenient and mild conditions, with good yields and complete regioselectivity. Thus, compounds **2** were treated with a catalytic amount (5 mol-%) of $TsOH \cdot H_2O$ in CH_2Cl_2 at room temperature. The reaction proceeded relatively smoothly to give **3** in good yields as listed in *Table 1* as well. The corresponding 2,3-dihydro-1*H*-isoindole-1-thione derivative was not formed at all in each case. This complete chemoselective *S*-substitution *vs. N*-substitution may be ascribable to the higher nucleophilicity of the S- than the N-atom. Although no unambiguous evidences for the configuration of **3** could

Table 1. *Preparation of Benzo[*c*]thiophen-1(3*H*)-imines* **3** *and Benzo[*c*]thiophen-1(3*H*)-ones* **4**

Entry	**1**	R^4	Yield[a]) [%]					
			2		**3**		**4**	
1	**1a** ($R^1 = R^2 = H$, $R^3 = Me$)	Ph	**2a**	83	**3a**	77	**4a**	93
2	**1a**	3-Cl–C_6H_4	**2b**	78	**3b**	72		
3	**1a**	4-Br–C_6H_4	**2c**	72	**3c**	81		
4	**1a**	3-MeO–C_6H_4	**2d**	75	**3d**	87		
5	**1a**	Bu	**2e**	74	**3e**	86		
6	**1b** ($R^1 = Cl$, $R^2 = H$, $R^3 = Et$)	Ph	**2f**	81	**3f**	92	**4b**	92
7	**1b**	3,5-Me_2–C_6H_3	**2g**	73	**3g**	84		
8	**1b**	Naphthalen-2-yl	**2h**	79	**3h**	81		
9	**1c** ($R^1 = R^2 = MeO$, $R^3 = Me$)	Ph	**2i**	80	**3i**	70	**4c**	93

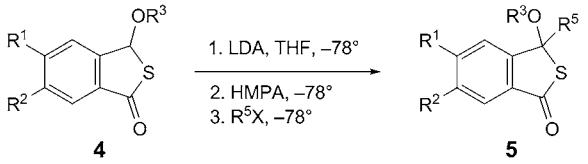
[a]) Yields of isolated products.

[3]) *Hartman et al.* first prepared a 1-(dialkoxymethyl)-2-lithiobenzene, 1-lithio-2-(oxolan-2-yl)benzene, from 1-bromo-2-(oxolan-2-yl)benzene [9].

be obtained, we tentatively determined it to be (*Z*), considering the lower encumbrance of the (*Z*)-form. Subsequently, products **3** proved to be easily hydrolyzed under mild conditions. Thus, hydrolysis of some of **3** with 10% aq. HCl in THF at room temperature proceeded slowly but cleanly, to give the corresponding 3-alkoxybenzo[*c*]thiophen-1(3*H*)-ones **4** in excellent yields (*cf. Table 1*).

Next, the alkylation at C(3) of **4** was examined. As outlined in *Scheme 2*, treatment of **4** with $^{i}Pr_2NLi$ (LDA) in THF at $-78°$ was followed by addition of hexamethylphosphoric triamide (HMPA)[4]) and halides at the same temperature. Starting with 3-methoxybenzo[*c*]thiophen-1(3*H*)-ones **4a** and **4c**, alkylation reactions with active halides, such as MeI, allyl bromide, and $PhCH_2Br$, proceeded slowly but relatively cleanly to give the corresponding 3-alkylated products **5a**–**5c** and **5f** in fair-to-good yields (*Table 2*, *Entries 1–3* and *6*). Elevating the reaction temperature to $-20°$ furnished complex mixtures of products, from which only low yields (20–30%) of the desired products were isolated. It should be mentioned that the use of an ordinary haloalkane, such as EtBr, as an alkylating agent did not afford the corresponding alkylated product. Lithiated 3-ethoxybenzo[*c*]thiophen-1(3*H*)-one (**4b**) underwent very slow alkylation with active halides to give only low yields of products **5d** and **5e** (*Entries 4 and 5*). This may be attributed to the overall increase in the steric bulk at C(3) of **4b** due to the EtO group.

Scheme 2



4 **5**

Table 2. *Preparation of 3-Alkoxy-3-alkylbenzo[c]thiophen-1(3*H*)-ones* **5**

Entry	**4**	R^5X	**5**	Yield[a]) [%]
1	**4a** ($R^1 = R^2 = H$, $R^3 = Me$)	MeI	**5a**	77
2	**4a**	$CH_2{=}CHCH_2Br$	**5b**	65
3	**4a**	$PhCH_2Br$	**5c**	68
4	**4b** ($R^1 = Cl$, $R^2 = H$, $R^3 = Et$)	MeI	**5d**	29
5	**4b**	$NCCH_2Br$	**5e**	34
6	**4c** ($R^1 = R^2 = MeO$, $R^3 = Me$)	MeI	**5f**	76

[a]) Yields of isolated products.

To evaluate the generality of the present procedure, we decided to investigate the usability of 2-(2-bromophenyl)-1,3-dioxolanes **6a** and **6b**, and 2-(2-bromophenyl)-1,3-dioxane (**6c**) as starting materials. The corresponding *N*-substituted benzothioamides **7** were obtained by the same successive treatment of **6** with BuLi and isothiocyanates as described for the preparation of **2** in good yields as shown in *Scheme* 3. Compounds **7**

[4]) In the absence of HMPA, the progress of the alkylation was extremely reluctant.

were subjected to the reaction with $TsOH \cdot H_2O$ under the above-mentioned conditions to afford the corresponding *N*-substituted 3-(*ω*-hydroxyalkyl)benzo[*c*]thiophen-1(3*H*)-imines **8** in excellent yields. Under the same acid hydrolysis conditions as described above, some of compounds **8** were transformed to the corresponding 3-(*ω*-hydroxyalkyl)benzo[*c*]thiophen-1(3*H*)-ones **9** in excellent yields as well. These results are compiled in *Table 3*.

Scheme 3

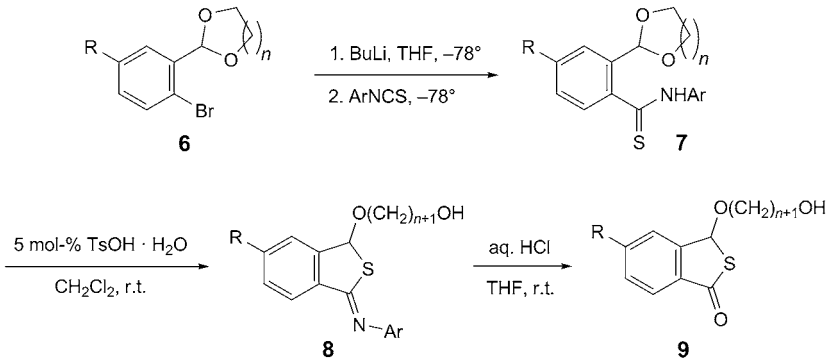


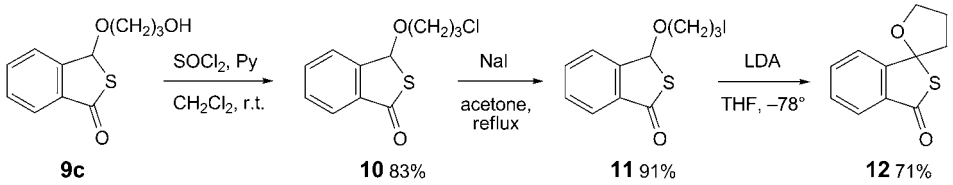
Table 3. *Preparation of 3-(ω-Hydroxyalkoxy)benzo[c]thiophen-1(3H)-imines* **8** *and -ones* **9**

Entry	**6**	Ar	Yield[a]) [%]					
			7		**8**		**9**	
1	**6a** (R = H, *n* = 1)	Ph	**7a**	81	**8a**	97	**9a**	95
2	**6a**	3-MeO–C_6H_4	**7b**	87	**8b**	99		
3	**6b** (R = MeO, *n* = 1)	Ph	**7c**	79	**8c**	94	**9b**	91
4	**6b**	3-Cl–C_6H_4	**7d**	82	**8d**	98		
5	**6c** (R = H, *n* = 2)	Ph	**7e**	88	**8e**	99	**9c**	99

[a]) Yields of isolated products [%].

To demonstrate the synthetic utility of the product **9c**, its transformation to 4′,5′-dihydrospiro[benzo[*c*]thiophen-1(3*H*),2′(3′*H*)-furan]-3-one (**12**) was attempted. This was accomplished by the process outlined in *Scheme 4*. Initially, compound **9c** was converted into 3-(3-chloropropoxy)benzo[*c*]thiophen-1(3*H*)-one (**10**) on treatment with $SOCl_2$/pyridine in CH_2Cl_2 at room temperature in good yield. Then, the reaction of **10** with $^iPr_2NLi$ in THF at $-78°$ in the presence of HMPA was carried out. However, it resulted in the formation of a rather complex mixture of products. ^{1}H-NMR Analyses of the crude product revealed that the desired product was included in only *ca.* 10% yield. Therefore, we decided to examine the cyclization of 3-(3-iodropropoxy)benzo[*c*]thiophen-1(3*H*)-one (**11**). Thus, treatment of **10** with NaI in refluxing acetone furnished **11** in excellent yield. Upon treating with $^iPr_2NLi$ in THF at $-78°$, intramolecular alkylation of this iodide proceeded smoothly, without using HMPA as a cosolvent, and the desired product **12** was obtained in satisfactory yield.

Scheme 4



In summary, we have described the synthesis of *N*-substituted 3-alkoxybenzo[*c*]-thiophen-1(3*H*)-imines from readily available starting materials, *i.e.*, 1-bromo-2-(dialkoxymethyl)benzenes, by simple operations. Hydrolysis of some of these products has proven to provide the first practical general entry to 3-alkoxybenzo[*c*]thiophen-1(3*H*)-ones, which are difficult to prepare by previously reported methods. Therefore, the present method may be of value in organic synthesis.

Experimental Part

General. All of the org. solvents used in this study were dried over appropriate drying agents and distilled prior to use. TLC: *Merck* silica gel *60 PF_{254}*. Column chromatography (CC): *Wako Gel* C-200E. M.p.: *Laboratory Devices MEL-TEMP II* melting-point apparatus; uncorrected. IR Spectra: *Perkin–Elmer Spectrum65* FT-IR spectrophotometer; $\tilde{\nu}$ in cm^{-1}. ^{1}H-NMR Spectra (500 MHz): *JEOL ECP500* FT NMR spectrometer; in $CDCl_3$, δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. ^{13}C-NMR Spectra (125 MHz): *JEOL ECP500* FT NMR spectrometer; in $CDCl_3$, δ in in ppm rel. to Me_4Si as internal standard. LR-EI-MS (70 eV): *JEOL JMS AX505 HA* spectrometer; in *m*/*z* (rel. %). HR-MS (DART, pos. mode): *Thermo Scientific Exactive* spectrometer.

1-Bromo-2-(dimethoxymethyl)benzene (**1a**) [10], *2-(2-bromo-5-methoxyphenyl)-1,3-dioxolane* (**6b**) [11], *2-(2-bromophenyl)-1,3-dioxane* (**6c**) [12], and *2-isothiocyanatonaphthalene* [13] were prepared according to the appropriate reported procedures. BuLi was supplied by *Asia Lithium Corporation*. All other chemicals used in this study were commercially available.

1-Bromo-4-chloro-2-(diethoxymethyl)benzene (**1b**) was prepared from 2-bromo-5-chlorobenzaldehyde as described for **1a** in [10]. Yield: 70%. Colorless liquid. B.p. 81°/0.4 mmHg. IR (neat): 1059. ^{1}H-NMR: 1.25 (*t*, *J* = 6.9, 6 H); 3.55–3.62 (*m*, 2 H); 3.63–3.69 (*m*, 2 H); 5.60 (*s*, 1 H); 7.16 (*dd*, *J* = 8.6, 2.3, 1 H); 7.46 (*d*, *J* = 8.6, 1 H); 7.64 (*d*, *J* = 2.3, 1 H). Anal. calc. for $C_{11}H_{14}BrClO_2$ (293.58): C 45.00, H 4.81; found: C 45.13, H 4.62.

1-Bromo-2-(dimethoxymethyl)-4,5-dimethoxybenzene (**1c**) [14] was prepared from 2-bromo-4,5-dimethoxybenzaldehyde as described for **1a** in [10]. Yield: 77%. Colorless liquid. B.p. 105°/0.4 mmHg. IR (neat): 1602, 1263, 1054. ^{1}H-NMR: 3.39 (*s*, 6 H); 3.87 (*s*, 3 H); 3.89 (*s*, 3 H); 5.49 (*s*, 1 H); 7.01 (*s*, 1 H); 7.12 (*s*, 1 H).

2-(Dimethoxymethyl)-N-*phenylbenzenecarbothioamide* (**2a**). *Representative Procedure for the Preparations of* **2** *and* **7**. To a stirred soln. of **1a** (0.46 g, 2.0 mmol) in THF (6 ml) at −78° was added BuLi (1.6M in hexane; 2.0 mmol). After 15 min, PhNCS (0.27 g, 2.0 mmol) was added, and stirring was continued at the same temp. for 5 min before sat. aq. NH_4Cl (15 ml) was added. The mixture was warmed to r.t. and extracted with AcOEt (3 × 15 ml). The combined extracts were washed with brine (10 ml), dried (Na_2SO_4), and evaporationed. The residue was purified by CC to give **2a** (0.48 g, 83%). Yellow oil. R_f (AcOEt/hexane 1:7) 0.24. IR (neat): 3259, 1372, 1072. ^{1}H-NMR: 3.41 (*s*, 6 H); 5.49 (*s*, 1 H); 7.30 (*t*, *J* = 7.4, 1 H); 7.42–7.47 (*m*, 4 H); 7.57 (*dd*, *J* = 7.4, 1.7, 1 H); 7.83 (*dd*, *J* = 7.4, 1.7, 1 H); 7.91 (*d*, *J* = 7.4, 2 H); 9.92 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{17}NO_2S$ (287.38): C 66.87, H 5.96, N 4.87; found: C 66.64, H 6.04, N 4.81.

N-*(3-Chlorophenyl)-2-(dimethoxymethyl)benzenecarbothioamide* (**2b**). Yellow oil. R_f (AcOEt/hexane 1:7) 0.11. IR (neat): 3260, 1366, 1074. ^{1}H-NMR: 3.42 (*s*, 6 H); 5.44 (*s*, 1 H); 7.27 (*dd*, *J* = 8.0,

1.7, 1 H); 7.37 (*t*, *J* = 8.0, 1 H); 7.41 – 7.46 (*m*, 2 H); 7.55 (*dd*, *J* = 7.4, 2.3, 1 H); 7.74 (*dd*, *J* = 8.0, 1.1, 1 H); 7.84 (*dd*, *J* = 7.4, 2.3, 1 H); 8.07 (*t*, *J* = 2.3, 1 H); 10.02 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{16}ClNO_2S$ (321.82): C 59.71, H 5.01, N 4.35; found: C 59.77, H 5.08, N 4.32.

N-*(4-Bromophenyl)-2-(dimethoxymethyl)benzenecarbothioamide* (**2c**). Yellow oil. R_f (AcOEt/hexane 1:5) 0.28. IR (neat): 3236, 1374, 1071. ^{1}H-NMR: 3.41 (*s*, 6 H); 5.44 (*s*, 1 H); 7.42 – 7.46 (*m*, 2 H); 7.55 (*t*, *J* = 7.4, 1 H); 7.56 (*d*, *J* = 8.6, 2 H); 7.82 – 7.84 (*m*, 3 H); 9.99 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{16}BrNO_2S$ (366.27): C 52.47, H 4.40, N 3.82; found: C 52.31, H 4.68, N 3.61.

2-(Dimethoxymethyl)-N-*(3-methoxyphenyl)benzenecarbothioamide* (**2d**). Yellow oil. R_f (AcOEt/hexane 1:7) 0.11. IR (neat): 3292, 1607, 1374, 1072. ^{1}H-NMR: 3.41 (*s*, 6 H); 3.85 (*s*, 3 H); 5.46 (*s*, 1 H); 6.85 (*dd*, *J* = 7.4, 1.7, 1 H); 7.30 – 7.35 (*m*, 2 H); 7.41 – 7.44 (*m*, 2 H); 7.56 (*dd*, *J* = 6.9, 2.3, 1 H); 7.82 (*dd*, *J* = 6.9, 2.3, 1 H); 7.85 (*s*, 1 H); 9.91 (br. *s*, 1 H). Anal. calc. for $C_{17}H_{19}NO_3S$ (317.40): C 64.33, H 6.03, N 4.41; found: C 64.25, H 6.09, N 4.16.

N-*Butyl-2-(dimethoxymethyl)benzenecarbothioamide* (**2e**). Yellow oil. R_f (AcOEt/hexane 1:4) 0.29. IR (neat): 3284, 1395, 1074. ^{1}H-NMR: 0.99 (*t*, *J* = 7.6, 3 H); 1.43 – 1.55 (*m*, 2 H); 1.69 – 1.75 (*m*, 2 H); 3.37 (*s*, 6 H); 5.38 (*s*, 1 H); 3.78 – 3.82 (*m*, 2 H); 7.35 – 7.40 (*m*, 2 H); 7.54 (*d*, *J* = 6.9, 1 H); 7.72 (*dd*, *J* = 7.6, 1.5, 1 H); 8.31 (br. *s*, 1 H). Anal. calc. for $C_{14}H_{21}NO_2S$ (267.39): C 62.89, H 7.92, N 5.24; found: C 62.77, H 8.03, N 5.27.

4-Chloro-2-(diethoxymethyl)-N-*phenylbenzenecarbothioamide* (**2f**). Yellow solid. M.p. 85 – 86° (hexane). IR (KBr): 3232, 1372, 1057. ^{1}H-NMR: 1.22 (*t*, *J* = 6.9, 6 H); 3.55 (*dq*, *J* = 9.2, 7.6, 2 H); 3.65 (*dq*, *J* = 9.2, 7.6, 2 H); 5.58 (*s*, 1 H); 7.30 (*t*, *J* = 7.4, 1 H); 7.38 (*dd*, *J* = 8.6, 2.3, 1 H); 7.45 (*dd*, *J* = 8.0, 7.4, 2 H); 7.58 (*d*, *J* = 2.3, 1 H); 7.81 (*d*, *J* = 8.6, 1 H); 7.88 (*d*, *J* = 8.0, 2 H); 10.10 (br. *s*, 1 H). Anal. calc. for $C_{18}H_{20}ClNO_2S$ (349.88): C 61.79, H 5.76, N 4.00; found: C 61.74, H 5.76, N 4.14.

4-Chloro-2-(diethoxymethyl)-N-*(3,5-dimethylphenyl)benzenecarbothioamide* (**2g**). Yellow oil. R_f (AcOEt/hexane 1:10) 0.33. IR (neat): 3278, 1372, 1059. ^{1}H-NMR: 1.22 (*t*, *J* = 7.6, 6 H); 2.36 (*s*, 6 H); 3.53 (*dq*, *J* = 9.2, 7.6, 2 H); 3.67 (*dq*, *J* = 9.2, 7.6, 2 H); 5.69 (*s*, 1 H); 6.94 (*s*, 1 H); 7.36 (*dd*, *J* = 8.4, 2.3, 1 H); 7.48 (*s*, 2 H); 7.59 (*d*, *J* = 2.3, 1 H); 7.78 (*d*, *J* = 8.4, 1 H); 9.92 (br. *s*, 1 H). Anal. calc. for $C_{20}H_{24}ClNO_2S$ (377.93): C 63.56, H 6.40, N 3.71; found: C 63.31, H 6.58, N 3.50.

4-Chloro-2-(diethoxymethyl)-N-*(naphthalen-2-yl)benzenecarbothioamide* (**2h**). Yellow viscous oil. R_f (AcOEt/hexane 1:8) 0.27. IR (neat): 3262, 1374, 1058. ^{1}H-NMR: 1.23 (*t*, *J* = 7.6, 6 H); 3.56 (*dq*, *J* = 9.2, 7.6, 2 H); 3.72 (*dq*, *J* = 9.2, 7.6, 2 H); 5.61 (*s*, 1 H); 7.40 (*dd*, *J* = 8.4, 2.3, 1 H); 7.49 – 7.53 (*m*, 2 H); 7.60 (*d*, *J* = 2.3, 1 H); 7.74 (*dd*, *J* = 8.4, 2.3, 1 H); 7.84 – 7.91 (*m*, 4 H); 8.67 (*s*, 1 H); 10.27 (br. *s*, 1 H). Anal. calc. for $C_{22}H_{22}ClNO_2S$ (399.93): C 66.07, H 5.54, N 3.50; found: C 66.01, H 5.62, N 3.49.

2-(Dimethoxymethyl)-4,5-dimethoxy-N-phenylbenzenecarbothioamide (**2i**). Yellow solid. M.p. 131 – 133° (hexane/Et_2O). IR (KBr): 3287, 1369, 1131, 1055. ^{1}H-NMR: 3.40 (*s*, 6 H); 3.95 (*s*, 6 H); 5.44 (*s*, 1 H); 7.07 (*s*, 1 H); 7.30 (*t*, *J* = 7.4, 1 H); 7.45 (*dd*, *J* = 8.0, 7.4, 2 H); 7.47 (*s*, 1 H); 7.92 (*d*, *J* = 8.0, 2 H); 10.09 (*s*, 1 H). Anal. calc. for $C_{18}H_{21}NO_4S$ (347.43): C 62.23, H 6.09, N 4.03; found: C 61.95, H 6.26, N 4.33.

2-(1,3-Dioxolan-2-yl)-N-phenylbenzenecarbothioamide (**7a**). Yellow solid. M.p. 143 – 144° (hexane/THF). IR (KBr): 3206, 1378, 1069. ^{1}H-NMR: 4.03 – 4.09 (*m*, 2 H); 4.16 – 4.23 (*m*, 2 H); 6.01 (*s*, 1 H); 7.30 (*tt*, *J* = 7.4, 1.1, 1 H); 7.43 – 7.46 (*m*, 4 H); 7.66 – 7.67 (*m*, 1 H); 7.78 – 7.80 (*m*, 1 H); 7.94 (*d*, *J* = 8.0, 2 H); 9.68 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{15}NO_2S$ (285.36): C 67.34, H 5.30, N 4.91; found: C 67.07, H 5.38, N 4.86.

2-(1,3-Dioxolan-2-yl)-N-*(3-methoxyphenyl)benzenecarbothioamide* (**7b**). Yellow oil. R_f (AcOEt/hexane 1:3) 0.21. IR (neat): 3286, 1607, 1372, 1077. ^{1}H-NMR: 3.85 (*s*, 3 H); 4.04 – 4.07 (*m*, 2 H); 4.16 – 4.21 (*m*, 2 H); 5.98 (*s*, 1 H); 6.83 – 6.86 (*m*, 1 H); 7.33 – 7.34 (*m*, 2 H); 7.43 – 7.47 (*m*, 2 H); 7.65 – 7.67 (*m*, 1 H); 7.77 – 7.79 (*m*, 1 H); 7.89 (*s*, 1 H); 9.68 (br. *s*, 1 H). Anal. calc. for $C_{17}H_{17}NO_3S$ (315.39): C 64.74, H 5.43, N 4.44; found: C 64.61, H 5.57, N 4.18.

2-(1,3-Dioxolan-2-yl)-4-methoxy-N-*phenylbenzenecarbothioamide* (**7c**). Yellow oil. R_f (AcOEt/hexane 1:3) 0.32. IR (neat): 3314, 1607, 1368, 1072. ^{1}H-NMR: 3.86 (*s*, 3 H); 4.05 – 4.08 (*m*, 2 H); 4.20 – 4.23 (*m*, 2 H); 5.98 (*s*, 1 H); 6.96 (*dd*, *J* = 8.6, 2.3, 1 H); 7.18 (*d*, *J* = 2.3, 1 H); 7.29 (*t*, *J* = 7.4, 1 H); 7.44 (*dd*, *J* = 8.0, 7.4, 2 H); 7.84 (*d*, *J* = 8.6, 1 H); 7.93 (*d*, *J* = 8.0, 2 H); 9.79 (br. *s*, 1 H). Anal. calc. for $C_{17}H_{17}NO_3S$ (315.39): C 64.74, H 5.43, N 4.44; found: C 64.69, H 5.51, N 4.32.

N-*(3-Chlorophenyl)-2-(1,3-dioxolan-2-yl)-4-methoxybenzenecarbothioamide* (**7d**). Yellow oil. R_f (AcOEt/hexane 1:3) 0.34. IR (neat) 3306, 1607, 1361, 1074. ^{1}H-NMR: 3.87 (*s*, 3 H); 4.06 – 4.09 (*m*,

2 H); 4.21–4.23 (*m*, 2 H); 5.96 (*s*, 1 H); 6.96 (*dd*, *J* = 8.8, 2.9, 1 H); 7.17 (*d*, *J* = 2.9, 1 H); 7.26 (*d*, *J* = 8.0, 1 H); 7.36 (*t*, *J* = 8.0, 1 H); 7.79 (*d*, *J* = 8.0, 1 H); 7.83 (*d*, *J* = 8.8, 1 H); 8.08 (*dd*, *J* = 2.3, 1.7, 1 H); 9.80 (br. *s*, 1 H). Anal. calc. for $C_{17}H_{16}ClNO_3S$ (349.83): C 58.37, H 4.61, N 4.00; found: C 58.30, H 4.63, N 3.92.

2-(1,3-Dioxan-2-yl)-N-*phenylbenzenecarbothioamide* (**7e**). Pale-yellow solid. M.p. 113–115° (hexane/THF). IR (KBr): 3221, 1371, 1091. ^{1}H-NMR: 2.11–2.21 (*m*, 2 H), 3.91 (*td*, *J* = 12.0, 2.2, 2 H); 4.24 (*dd*, *J* = 12.0, 5.1, 2 H); 5.68 (*s*, 1 H); 7.30 (*tt*, *J* = 7.4, 1.1, 1 H); 7.40–7.48 (*m*, 4 H); 7.69 (*dd*, *J* = 7.4, 1.7, 1 H); 7.77 (*dd*, *J* = 7.4, 1.1, 1 H); 7.97 (*d*, *J* = 7.4, 2 H); 9.75 (br. *s*, 1 H). Anal. calc. for $C_{17}H_{17}NO_2S$ (299.39): C 68.20, H 5.72, N 4.68; found: C 68.20, H 5.84, N 4.40.

N-*[(Z)-3-Methoxybenzo[c]thiophen-1(3*H*)-ylidene]benzenamine* (**3a**). *Representative Procedure for the Preparations of* **3** *and* **8**. A mixture of **2a** (0.35 g, 1.2 mmol) in CH_2Cl_2 (7 ml) containing TsOH·H_2O (11 mg, 0.060 mmol) was stirred at r.t., until complete consumption of the starting material had been confirmed by TLC (AcOEt/hexane 1:2). The mixture was diluted by adding CH_2Cl_2 (20 ml), washed with sat. aq. $NaHCO_3$ (10 ml), and dried (Na_2SO_4). After evaporation, the residue was purified by CC (AcOEt/hexane 1:8) to afford **3a** (0.24 g, 77%). Pale-yellow solid. M.p. 84–85° (hexane). IR (KBr): 1632, 1591, 1070. ^{1}H-NMR: 3.35 (*s*, 3 H); 6.61 (*s*, 1 H); 7.11 (*d*, *J* = 8.4, 2 H); 7.18 (*dd*, *J* = 7.6, 6.9, 1 H); 7.40 (*dd*, *J* = 8.4, 7.6, 2 H); 7.52–7.58 (*m*, 3 H); 8.08 (*d*, *J* = 6.9, 1 H). ^{13}C-NMR: 55.11; 90.55; 120.25; 123.36; 124.84; 125.63; 129.12; 129.75; 131.68; 137.87; 143.73; 151.71; 165.27. HR-MS: 256.0792 ($[M+H]^+$, $C_{15}H_{14}NOS^+$; calc. 256.0797). Anal. calc. for $C_{15}H_{13}NOS$ (255.34): C 70.56, H 5.13, N 5.49; found: C 70.30, H 5.34, N 5.52.

3-Chloro-N-*[(Z)-3-methoxybenzo[c]thiophen-1(3*H*)-ylidene]benzenamine* (**3b**). Pale-yellow solid, M.p. 91–92° (hexane). IR (KBr): 1627, 1588, 1083. ^{1}H-NMR: 3.36 (*s*, 3 H); 6.62 (*s*, 1 H); 6.99 (*dt*, *J* = 8.0, 1.1, 1 H); 7.11 (*dd*, *J* = 1.7, 1.1, 1 H); 7.15 (*dt*, *J* = 8.0, 1.7, 1 H); 7.32 (*t*, *J* = 8.0, 1 H); 7.53 (*ddd*, *J* = 8.0, 7.4, 1.7, 1 H); 7.56–7.61 (*m*, 2 H); 8.05 (*d*, *J* = 8.0, 1 H). ^{13}C-NMR: 55.29; 90.81; 118.51; 120.59; 123.38; 124.78; 125.67; 129.86; 130.20; 131.96; 134.65; 137.64; 143.87; 152.87; 166.56. HR-MS: 290.0387 ($[M+H]^+$, $C_{15}H_{13}ClNOS^+$; calc. 290.0407). Anal. calc. for $C_{15}H_{12}ClNOS$ (289.78): C 62.17, H 4.17, N 4.83; found: C 62.10, H 4.20, N 4.79.

4-Bromo-N-*[(Z)-3-methoxybenzo[c]thiophen-1(3*H*)-ylidene]benzenamine* (**3c**). Pale-yellow solid. M.p. 132–133° (hexane/CH_2Cl_2). IR (KBr): 1632, 1081. ^{1}H-NMR: 3.36 (*s*, 3 H); 6.62 (*s*, 1 H); 7.00 (*d*, *J* = 8.0, 2 H); 7.50–7.58 (*m*, 5 H); 8.05 (*d*, *J* = 7.4, 1 H). ^{13}C-NMR: 55.27; 90.78; 117.92; 122.15; 123.37; 125.67; 129.84; 131.89; 132.19; 137.72; 143.80; 150.62; 166.05. HR-MS: 333.9897 ($[M+H]^+$, $C_{15}H_{13}BrNOS^+$; calc. 333.9902). Anal. calc. for $C_{15}H_{12}BrNOS$ (334.23): C 53.90, H 3.62, N 4.19; found: C 53.83, H 3.67, N 4.27.

3-Methoxy-N-*[(Z)-3-methoxybenzo[c]thiophen-1(3*H*)-ylidene]benzenamine* (**3d**). Yellow oil. R_f (AcOEt/hexane 1:7) 0.28. IR (KBr): 1633, 1592, 1080. ^{1}H-NMR: 3.35 (*s*, 3 H); 3.83 (*s*, 3 H); 6.60 (*s*, 1 H); 6.67 (br. *s*, 1 H); 6.71–6.74 (*m*, 2 H); 7.30 (*t*, *J* = 8.0, 1 H); 7.51–7.58 (*m*, 3 H); 8.07 (*d*, *J* = 7.4, 1 H). ^{13}C-NMR: 55.17; 55.28; 90.56; 105.84; 110.76; 112.44; 123.35; 125.64; 129.76; 129.93; 131.72; 137.84; 143.78; 152.97; 160.29; 165.47. HR-MS: 286.0892 ($[M+H]^+$, $C_{16}H_{16}NO_2S^+$; calc. 286.0902). Anal. calc. for $C_{16}H_{15}NO_2S$ (285.36): C 67.34, H 5.30, N 4.91; found: C 67.04, H 5.53, N 4.93.

N-*[(Z)-3-Methoxybenzo[c]thiophen-1(3*H*)-ylidene]butan-1-amine* (**3e**). Yellow oil. R_f (AcOEt/hexane 1:15) 0.23. IR (neat): 1638, 1600, 1084. ^{1}H-NMR: 0.98 (*t*, *J* = 7.6, 3 H); 1.44–1.51 (*m*, 2 H); 1.74–1.80 (*m*, 2 H); 3.34 (*s*, 3 H); 3.48–3.59 (*m*, 2 H); 6.62 (*s*, 1 H); 7.44 (*t*, *J* = 7.6, 1 H); 7.49 (*t*, *J* = 7.6, 1 H); 7.52 (*d*, *J* = 7.6, 1 H); 7.92 (*d*, *J* = 7.6, 1 H). ^{13}C-NMR: 13.93; 20.70; 32.46; 54.50; 57.75; 90.07; 122.96; 125.52; 129.53; 130.85; 137.88; 143.18; 162.71. HR-MS: 236.1097 ($[M+H]^+$, $C_{13}H_{18}NOS^+$; calc. 236.1109). Anal. calc. for $C_{13}H_{17}NOS$ (235.35): C 66.34, H 7.28, N 5.95; found: C 66.10, H 7.28, N 5.83.

N-*[(Z)-5-Chloro-3-ethoxybenzo[c]thiophen-1(3*H*)-ylidene]benzenamine* (**3f**). Pale-yellow solid. M.p. 63–64° (hexane). IR (KBr): 1630, 1594, 1086. ^{1}H-NMR: 1.26 (*t*, *J* = 6.9, 3 H); 3.53 (*dq*, *J* = 9.2, 7.4, 1 H); 3.67 (*dq*, *J* = 9.2, 7.4, 1 H); 6.54 (*s*, 1 H); 7.10 (*dd*, *J* = 8.0, 1.1, 2 H); 7.18 (*t*, *J* = 7.4, 1 H); 7.40 (*dd*, *J* = 8.0, 7.4, 2 H); 7.49 (*dd*, *J* = 8.0, 2.3, 1 H); 7.57 (*d*, *J* = 2.3, 1 H); 7.99 (*d*, *J* = 8.0, 1 H). ^{13}C-NMR: 14.91; 64.96; 88.64; 120.20; 124.27; 125.01; 125.87; 129.15; 130.13; 136.21; 137.98; 145.58; 151.44; 163.89. HR-MS: 304.0562 ($[M+H]^+$, $C_{16}H_{15}ClNOS^+$; calc. 304.0564). Anal. calc. for $C_{16}H_{14}ClNOS$ (303.81): C 63.25, H 4.64, N 4.61; found: C 63.08, H 4.68, N 4.55.

N-*[(Z)-5-Chloro-3-ethoxybenzo[c]thiophen-1(3*H*)-ylidene]-3,5-dimethylbenzenamine* (**3g**). Pale-yellow solid. M.p. 78–79° (hexane). IR (KBr): 1630, 1591, 1091. ^{1}H-NMR: 1.25 (*t*, *J* = 7.4, 3 H); 2.33 (*s*, 6 H); 3.53 (*dq*, *J* = 9.2, 7.4, 1 H); 3.67 (*dq*, *J* = 9.2, 7.4, 1 H); 6.53 (*s*, 1 H); 6.72 (*s*, 2 H); 6.82 (*s*, 1 H);

7.47 (*dd*, *J* = 8.6, 2.3, 1 H); 7.56 (*d*, *J* = 2.3, 1 H); 7.97 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR: 14.91; 21.38; 64.90; 88.57; 117.77; 124.24; 125.85; 126.70; 130.07; 136.33; 137.84; 138.80; 145.57; 151.41; 163.19. HR-MS: 332.0874 ([*M* + H]$^+$, $C_{18}H_{19}ClNOS^+$; calc. 332.0877). Anal. calc. for $C_{18}H_{18}ClNOS$ (331.86): C 65.15, H 5.47, N 4.22; found: C 65.28, H 5.54, N 4.09.

N-*[(Z)-5-Chloro-3-ethoxybenzo[c]thiophen-1(3*H*)-ylidene]naphthalen-2-amine* (**3h**). Yellow viscous oil. R_f (AcOEt/hexane 1:20) 0.35. IR (neat): 1618, 1592, 1085. ^{1}H-NMR: 1.25 (*t*, *J* = 6.9, 3 H); 3.53 (*dq*, *J* = 9.2, 6.9, 1 H); 3.66 (*dq*, *J* = 9.2, 6.9, 1 H); 6.55 (*s*, 1 H); 7.30 (*dd*, *J* = 8.6, 2.3, 1 H); 7.42–7.52 (*m*, 4 H); 7.59 (*d*, *J* = 2.3, 1 H); 7.82 (*d*, *J* = 8.6, 1 H); 7.84 (*d*, *J* = 8.6, 1 H); 7.88 (*d*, *J* = 9.2, 1 H); 8.04 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR: 14.91; 65.07; 88.74; 116.59; 120.99; 124.31; 125.16; 125.93; 126.32; 127.78 (two overlapped C-atoms); 129.11; 130.19; 131.27; 133.93; 136.24; 138.05; 145.63; 149.11; 164.30. HR-MS: 354.0706 ([*M* + H]$^+$, $C_{20}H_{17}ClNOS^+$; calc. 354.0720). Anal. calc. for $C_{20}H_{16}ClNOS$ (353.87): C 67.88, H 4.56, N 3.96; found: C 67.72, H 4.62, N 3.72.

N-*[(Z)-3,5,6-Trimethoxybenzo[c]thiophen-1(3*H*)-ylidene]benzenamine* (**3i**). Pale-yellow solid. M.p. 124–125° (hexane/CH_2Cl_2). IR (KBr): 1620, 1604, 1590, 1120, 1069. ^{1}H-NMR: 3.34 (*s*, 3 H); 3.98 (*s*, 3 H); 4.00 (*s*, 3 H); 6.52 (*s*, 1 H); 7.00 (*s*, 1 H); 7.11 (*d*, *J* = 7.4, 2 H); 7.17 (*t*, *J* = 7.4, 1 H); 7.40 (*t*, *J* = 7.4, 2 H); 7.50 (*s*, 1 H). ^{13}C-NMR: 54.83; 56.24; 56.28; 89.96; 104.24; 106.76; 120.33; 124.69; 129.11; 130.62; 137.29; 156.75; 151.84; 152.69; 165.62. HR-MS: 316.0988 ([*M* + H]$^+$, $C_{17}H_{18}NO_3S^+$; calc. 316.1007). Anal. calc. for $C_{17}H_{17}NO_3S$ (315.39): C 64.74, H 5.43, N 4.44; found: C 64.68, H 5.58, N 4.31.

2-{[(Z)-1,3-Dihydro-3-(phenylimino)benzo[c]thiophen-1-yl]oxy}ethanol (**8a**). Pale-yellow solid. M.p. 88–89° (hexane/THF). IR (KBr): 3267, 1613, 1588, 1061. ^{1}H-NMR: 1.93 (br. *s*, 1 H); 3.47–3.50 (*m*, 1 H); 3.71–3.76 (*m*, 3 H); 6.71 (*s*, 1 H); 7.11 (*dd*, *J* = 8.0, 1.1, 2 H); 7.18 (*t*, *J* = 7.4, 1 H); 7.40 (*t*, *J* = 8.0, 2 H); 7.53 (*ddd*, *J* = 8.0, 7.4, 2.3, 1 H); 7.56–7.60 (*m*, 2 H); 8.09 (*d*, *J* = 7.4, 1 H). ^{13}C-NMR: 61.60; 68.90; 89.43; 120.26; 123.47; 124.94; 125.68; 129.15; 129.87; 131.79; 137.83; 143.64; 151.58; 164.96. HR-MS: 286.0901 ([*M* + H]$^+$, $C_{16}H_{16}NO_2S^+$; calc. 286.0902). Anal. calc. for $C_{16}H_{15}NO_2S$ (285.36): C 67.34, H 5.30, N 4.91; found: C 67.21, H 5.46, N 4.80.

2-({(Z)-1,3-Dihydro-3-[(3-methoxyphenyl)imino]benzo[c]thiophen-1-yl}oxy)ethanol (**8b**). Yellow oil. R_f (AcOEt/hexane 1:1) 0.32. IR (neat): 3419, 1632, 1591, 1061. ^{1}H-NMR: 1.91 (br. *s*, 1 H); 3.48–3.50 (*m*, 1 H); 3.72–3.78 (*m*, 3 H); 3.83 (*s*, 3 H); 6.66–6.75 (*m*, 4 H); 7.30 (*t*, *J* = 8.0, 1 H); 7.52–7.60 (*m*, 3 H); 8.08 (*d*, *J* = 7.4, 1 H). ^{13}C-NMR: 53.74; 61.55; 68.94; 89.41; 105.85; 110.80; 112.41; 123.42; 125.68; 129.85; 129.94; 131.80; 137.73; 143.67; 152.41; 160.27; 165.18. HR-MS: 316.0996 ([*M* + H]$^+$, $C_{17}H_{18}NO_3S^+$; calc. 316.1008). Anal. calc. for $C_{17}H_{17}NO_3S$ (315.39): C 64.74, H 5.43, N 4.44; found: C 64.63, H 5.57, N 4.37.

2-{[(Z)-1,3-Dihydro-6-methoxy-3-(phenylimino)benzo[c]thiophen-1-yl]oxy}ethanol (**8c**). White solid. M.p. 122–124° (hexane/THF). IR (KBr): 3401, 1603, 1584, 1065. ^{1}H-NMR: 1.84 (*s*, 1 H); 3.47–3.50 (*m*, 1 H); 3.72–3.77 (*m*, 3 H); 3.91 (*s*, 3 H); 6.64 (*s*, 1 H); 7.05–7.07 (*m*, 2 H); 7.09 (*d*, *J* = 7.4, 2 H); 7.16 (*t*, *J* = 7.4, 2 H); 7.39 (*t*, *J* = 7.4, 1 H); 7.98 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR: 55.79; 61.61; 68.62; 88.77; 109.69; 116.88; 120.38; 124.54; 124.72; 129.10; 130.52; 145.78; 151.77; 163.05; 164.15. MS: 315 (100, M^+). Anal. calc. for $C_{17}H_{17}NO_3S$ (315.39): C 64.74, H 5.43, N 4.44; found: C 64.48, H 5.56, N 4.36.

2-({(3Z)-3-[(3-Chlorophenyl)imino]-1,3-dihydro-6-methoxybenzo[c]thiophen-1-yl}oxy)ethanol (**8d**). Pale-yellow solid. M.p. 98–100° (hexane/THF). IR (KBr): 3400, 1624, 1604, 1583, 1070. ^{1}H-NMR: 1.84 (*s*, 1 H); 3.48–3.52 (*m*, 1 H); 3.72–3.78 (*m*, 3 H); 3.91 (*s*, 3 H); 6.65 (*s*, 1 H), 6.97 (*dd*, *J* = 8.0, 1.1, 1 H); 7.05–7.10 (*m*, 3 H); 7.13 (*dt*, *J* = 8.0, 1.1, 1 H); 7.30 (*t*, *J* = 8.0, 1 H); 7.95 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR: 55.83; 61.58; 68.81; 88.97; 109.34; 116.97; 118.65; 120.72; 124.59; 124.64; 130.16; 130.22; 134.59; 145.97; 152.90; 163.27; 165.38. MS: 349 (100, M^+). Anal. calc. for $C_{17}H_{16}ClNO_3S$ (349.88): C 58.37, H 4.61, N 4.00; found: C 58.09, H 4.69, N 3.95.

3-{[(Z)-1,3-Dihydro-3-(phenylimino)benzo[c]thiophen-1-yl]oxy}propan-1-ol (**8e**). Pale-yellow oil. R_f (AcOEt/hexane 2:3) 0.30. IR (neat): 3378, 1627, 1591, 1072. ^{1}H-NMR: 1.83–1.87 (*m*, 3 H); 3.55 (*dt*, *J* = 9.2, 5.7, 1 H); 3.73–3.79 (*m*, 3 H); 6.63 (*s*, 1 H); 7.11 (*dd*, *J* = 7.4, 1.1, 2 H); 7.18 (*t*, *J* = 7.4, 1 H); 7.40 (*t*, *J* = 7.4, 2 H); 7.50–7.59 (*m*, 3 H); 8.08 (*d*, *J* = 8.0, 1 H). ^{13}C-NMR: 32.01; 60.65; 66.45; 89.47; 120.23; 123.41; 124.89; 125.59; 129.14; 129.79; 131.78; 137.68; 143.84; 151.64; 165.21. MS: 299 (100, M^+). Anal. calc. for $C_{17}H_{17}NO_2S$ (299.39): C 68.20, H 5.72, N 4.68; found: C 68.14, H 5.88, N 4.53.

*3-Methoxybenzo[c]thiophen-1(3*H*)-one* (**4a**). *Representative Procedure for the Preparations of* **4** *and* **9**. To a stirred soln. of **3a** (0.13 g, 0.51 mmol) in THF (3 ml) at r.t. was added 10% aq. HCl (1 ml), and stirring was continued at the same temp. for 1 d, before sat. aq. $NaHCO_3$ (10 ml) was added. The mixture

was extracted with AcOEt (3 × 10 ml), and the combined extracts were washed with brine (10 ml), dried (Na_2SO_4), and evaporated. The residue was purified by CC (AcOEt/hexane 1:8) to give **4a** (0.11 g, 93%). White solid. M.p. 64–65° (hexane). IR (KBr): 1694. ^{1}H-NMR: 3.42 (*s*, 3 H); 6.64 (*s*, 1 H); 7.55 (*t*, *J* = 7.4, 1 H); 7.67 (*t*, *J* = 7.4, 1 H); 7.68 (*d*, *J* = 7.4, 1 H); 7.81 (*d*, *J* = 7.4, 1 H), ^{13}C-NMR: 55.70; 88.84; 123.48; 126.15; 130.04; 133.80; 135.90; 146.68; 194.84. HR-MS: 181.0318 ($[M+H]^+$, $C_9H_9O_2S^+$; calc. 181.0324). Anal. calc. for $C_9H_8O_2S$ (180.22): C 59.98, H 4.47; found: C 60.00, H 4.43.

*5-Chloro-3-ethoxybenzo[*c*]thiophen-1(3*H*)-one* (**4b**). White solid. M.p. 81–83° (hexane). IR (KBr): 1694. ^{1}H-NMR: 1.31 (*t*, *J* = 6.9, 3 H); 3.59–3.65 (*m*, 1 H); 3.74–3.80 (*m*, 1 H); 6.56 (*s*, 1 H); 7.51 (*dd*, *J* = 8.4, 1.5, 1 H); 7.66 (*d*, *J* = 1.5, 1 H); 7.72 (*d*, *J* = 8.4, 1 H). ^{13}C-NMR: 14.92; 65.79; 86.84; 124.36; 126.53; 130.51; 134.10; 140.76; 148.59; 193.49. HR-MS: 229.0090 ($[M+H]^+$, $C_{10}H_{10}ClO_2S^+$; calc. 229.0091). Anal. calc. for $C_{10}H_9ClO_2S$ (228.70): C 52.52, H 3.97; found: C 52.49, H 4.23.

*3,5,6-Trimethoxybenzo[*c*]thiophen-1(3*H*)-one* (**4c**). Yellow solid. M.p. 102–104° (hexane/CH_2Cl_2). IR (KBr): 1695. ^{1}H-NMR: 3.41 (*s*, 3 H); 3.94 (*s*, 3 H); 4.00 (*s*, 3 H); 6.53 (*s*, 1 H); 7.07 (*s*, 1 H); 7.20 (*s*, 1 H). ^{13}C-NMR: 55.47; 56.27; 56.42; 88.00; 104.13; 107.23; 128.76; 141.25; 150.88; 154.40; 193.83. HR-MS: 241.0517 ($[M+H]^+$, $C_{11}H_{13}O_4S^+$; calc. 241.0535). Anal. calc. for $C_{11}H_{12}O_4S$ (240.28): C 54.99, H 5.03; found: C 54.94, H 5.03.

*3-(2-Hydroxyethoxy)benzo[*c*]thiophen-1(3*H*)-one* (**9a**). Yellow solid. M.p. 61–63° (hexane/Et_2O). IR (KBr): 3424, 1693, 1241. ^{1}H-NMR: 2.21 (*s*, 1 H); 3.54–3.58 (*m*, 1 H); 3.78–3.83 (*m*, 3 H); 6.72 (*s*, 1 H); 7.52–7.57 (*m*, 1 H); 7.67–7.69 (*m*, 2 H); 7.80 (*d*, *J* = 7.4, 1 H). ^{13}C-NMR: 61.46; 69.71; 87.71; 123.52; 126.24; 130.11; 133.89; 135.72; 146.59; 194.66. HR-MS: 211.0420 ($[M+H]^+$, $C_{10}H_{11}O_3S^+$; calc. 211.0429). Anal. calc. for $C_{10}H_{10}O_3S$ (210.25): C 57.13, H 4.79; found: C 56.93, H 4.76.

*3-(2-Hydroxyethoxy)-5-methoxybenzo[*c*]thiophen-1(3*H*)-one* (**9b**). Pale-yellow solid. M.p. 86–88° (hexane/THF). IR (KBr): 3436, 1688, 1253. ^{1}H-NMR: 1.96 (br. *s*, 1 H); 3.53–3.58 (*m*, 1 H); 3.77–3.82 (*m*, 3 H); 3.91 (*s*, 3 H); 6.64 (*s*, 1 H); 7.05 (*dd*, *J* = 8.6, 2.3, 1 H); 7.12 (*d*, *J* = 2.3, 1 H); 7.71 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR: 55.98; 61.60; 69.34; 86.84; 110.54; 116.89; 125.04; 128.65; 149.44; 164.85; 193.13. MS: 240 (11, M^+), 178 (100). Anal. calc. for $C_{11}H_{12}O_4S$ (240.28): C 54.99, H 5.03; found: C 54.86, H 5.07.

*3-(3-Hydroxypropoxy)benzo[*c*]thiophen-1(3*H*)-one* (**9c**). Pale-yellow oil. R_f (AcOEt/hexane 1:1) 0.30. IR (neat): 3375, 1693, 1242. ^{1}H-NMR: 1.80 (br. *s*, 1 H); 1.91 (*quint.*, *J* = 6.3, 2 H); 3.64 (*dt*, *J* = 12.0, 6.3, 1 H); 3.78 (*t*, *J* = 5.7, 2 H); 3.87 (*dt*, *J* = 12.0, 6.3, 1 H); 6.56 (*s*, 1 H); 7.55 (*t*, *J* = 7.4, 1 H); 7.66–7.70 (*m*, 2 H); 7.81 (*d*, *J* = 8.0, 1 H). ^{13}C-NMR: 32.05; 60.37; 67.08; 87.80; 123.56; 126.15; 130.08; 133.89; 135.71; 146.81; 194.82. MS: 224 (27, M^+); 154 (100). Anal. calc. for $C_{11}H_{12}O_3S$ (224.28): C 58.91, H 5.39; found: C 58.70, H 5.55.

*3-Methoxy-3-methylbenzo[*c*]thiophen-1(3*H*)-one* (**5a**). *Representative Procedure.* To a stirred soln. of ^{i}Pr$_2$NLi (1.3 mmol), generated *in situ* by the standard method from BuLi and ^{i}Pr$_2$NH, in THF (3 ml) at −78° was added a soln. of **4a** (0.20 g, 1.1 mmol) in THF (2 ml) dropwise. The color of the soln. turned to orange. After 15 min, HMPA (0.24 g, 1.3 mmol) and MeI (0.13 g, 1.3 mmol) were successively added, and stirring was continued at the same temp.; the orange color turned to yellow (*ca.* 3 h). Aq. sat. NH_4Cl (15 ml) was added, and the mixture was warmed to r.t. and extracted with AcOEt (3 × 10 ml). The combined extracts were washed with brine (10 ml), dried (Na_2SO_4), and evaporated. The residue was purified by CC (silica gel; AcOEt/hexane 1:8) to give **5a** (0.17 g, 77%). Pale-yellow solid. M.p. 75–76° (hexane). IR (KBr): 1683. ^{1}H-NMR: 2.12 (*s*, 3 H); 3.11 (*s*, 3 H); 7.53 (*td*, *J* = 7.4, 1.1, 1 H); 7.54 (*d*, *J* = 7.4, 1 H); 7.68 (*td*, *J* = 7.4, 1.1, 1 H), 7.78 (d, *J* = 7.4, 1 H). ^{13}C-NMR: 30.52; 52.48; 98.01; 123.34; 123.45; 129.86; 134.00; 136.12; 150.62; 194.64. HR-MS: 195.0468 ($[M+H]^+$, $C_{10}H_{11}O_2S^+$; calc. 195.0480). Anal. calc. for $C_{10}H_{10}O_2S$ (194.25): C 61.83, H 5.19; found: C 61.53, H 5.34.

*3-Methoxy-3-(prop-2-en-1-yl)benzo[*c*]thiophen-1(3*H*)-one* (**5b**). Pale-yellow oil. R_f (AcOEt/hexane 1:12) 0.32. IR (neat): 1693, 1642. ^{1}H-NMR: 2.89 (*dd*, *J* = 14.4, 7.4, 1 H); 3.13 (*s*, 3 H); 3.16 (*dd*, *J* = 14.4, 6.9, 1 H); 5.11 (*s*, 1 H); 5.13 (*d*, *J* = 6.3, 1 H); 5.78–5.86 (*m*, 1 H); 7.51–7.54 (*m*, 2 H); 7.68 (*t*, *J* = 7.4, 1 H); 7.77 (*d*, *J* = 8.0, 1 H). ^{13}C-NMR: 47.16; 52.25; 101.21; 119.99; 123.36; 123.89; 129.99; 132.10; 133.84; 136.74; 149.21; 194.65. HR-MS: 221.0630 ($[M+H]^+$, $C_{12}H_{13}O_2S^+$; calc. 221.0637). Anal. calc. for $C_{12}H_{12}O_2S$ (220.29): C 65.43, H 5.49, S 14.56; found: C 65.23, H 5.64, S 14.33.

*3-Methoxy-3-(phenylmethyl)benzo[*c*]thiophen-1(3*H*)-one* (**5c**). Pale-yellow solid. M.p. 90–91° (hexane). IR (KBr): 1684. ^{1}H-NMR: 3.12 (*s*, 3 H); 3.39 (*d*, *J* = 13.7, 1 H); 3.65 (*d*, *J* = 13.7, 1 H); 7.20–7.24 (*m*, 5 H); 7.49 (*d*, *J* = 8.0, 1 H); 7.51 (*td*, *J* = 7.4, 1.1, 1 H); 7.66 (*ddd*, *J* = 8.0, 7.4, 1.1, 1 H); 7.73 (*d*,

$J = 7.4$, 1 H). ^{13}C-NMR: 49.06; 52.31; 101.81; 123.36; 124.26; 127.15; 127.79; 130.00; 131.01; 133.62; 135.72; 136.71; 149.47; 194.48. HR-MS: 271.0792 ($[M+H]^+$, $C_{16}H_{15}O_2S^+$; calc. 271.0794). Anal. calc. for $C_{16}H_{14}O_2S$ (270.35): C 71.08, H 5.22; found: C 71.03, H 5.23.

*5-Chloro-3-ethoxy-3-methylbenzo[c]thiophen-1(3*H*)-one* (**5d**). Pale-yellow oil. R_f (AcOEt/hexane 1:20) 0.30. IR (neat): 1697. ^{1}H-NMR: 1.09 (*t*, $J = 6.9$, 3 H); 2.02 (*s*, 3 H); 2.94–3.00 (*m*, 1 H); 3.47–3.88 (*m*, 1 H); 7.42 (*dd*, $J = 7.6$, 2.3, 1 H); 7.46 (*d*, $J = 2.3$, 1 H); 7.62 (*d*, $J = 7.6$, 1 H). ^{13}C-NMR: 14.99; 30.80; 61.09; 96.57; 123.75; 124.29; 130.33; 134.28; 141.03; 152.90; 193.32. HR-MS: 243.0245 ($[M+H]^+$, $C_{11}H_{12}ClO_2S^+$; calc. 243.0247). Anal. calc. for $C_{11}H_{11}ClO_2S$ (242.72): C 54.43, H 4.57; found: C 54.14, H 4.64.

6-Chloro-1-ethoxy-1,3-dihydro-3-oxobenzo[c]thiophene-1-acetonitrile (**5e**). Pale-yellow solid. M.p. 134–135° (hexane). IR (KBr): 2259, 1698. ^{1}H-NMR: 1.22 (*t*, $J = 6.9$, 3 H); 3.14 (*dq*, $J = 9.2$, 6.9, 1 H); 3.35 (*s*, 2 H); 3.64 (*dq*, $J = 9.2$, 6.9, 1 H); 7.59 (*dd*, $J = 8.0$, 1.7, 1 H); 7.68 (*s*, 1 H); 7.76 (*d*, $J = 8.0$, 1 H). ^{13}C-NMR: 14.72; 33.32; 61.86; 94.54; 115.18; 123.99; 125.02; 131.69; 134.54; 141.82; 148.88; 190.71. HR-MS: 268.0193 ($[M+H]^+$, $C_{12}H_{11}ClNO_2S^+$; calc. 268.0200). Anal. calc. for $C_{12}H_{10}ClNO_2S$ (267.73): C 53.83, H 3.76, N 5.23; found: C 53.74, H 3.86, N 5.05.

*3,5,6-Trimethoxy-3-methylbenzo[c]thiophen-1(3*H*)-one* (**5f**). Pale-yellow oil. R_f (AcOEt/hexane 1:3) 0.30. IR (KBr): 1693, 1679. ^{1}H-NMR: 2.09 (*s*, 3 H); 3.13 (*s*, 3 H); 3.95 (*s*, 3 H); 4.00 (*s*, 3 H); 6.93 (*s*, 1 H); 7.18 (*s*, 1 H). ^{13}C-NMR: 30.41; 52.38; 56.25; 56.43; 96.99; 103.89; 104.46; 128.87; 145.06; 150.66; 154.59; 193.64. HR-MS: 255.0681 ($[M+H]^+$, $C_{12}H_{15}O_4S^+$; calc. 255.0692). Anal. calc. for $C_{12}H_{14}O_4S$ (254.30): C 56.68, H 5.55; found: C 56.54, H 5.59.

*3-(3-Chloropropoxy)benzo[c]thiophen-1(3*H*)-one* (**10**). To a stirred soln. of **9c** (0.45 g, 2.0 mmol) in CH_2Cl_2 (8 ml) containing pyridine (0.16 g, 2.0 mmol) at 0° was added $SOCl_2$ (0.24 g, 2.0 mmol) dropwise. The temp. was raised to r.t., and the mixture was stirred for 8 d at the same temp. before adding H_2O and CH_2Cl_2 (20 ml each). The layers were separated, and the aq. layer was extracted with CH_2Cl_2 (2 × 10 ml). The combined org. layers were washed with H_2O and then brine (20 ml each), and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was purified by CC to afford **10** (0.40 g, 83%). Pale-yellow solid. M.p. 63–64° (hexane). IR (KBr): 1694, 1601. ^{1}H-NMR: 2.06–2.11 (*m*, 2 H); 3.59–3.70 (*m*, 3 H); 3.85 (*dt*, $J = 9.2$, 6.3, 1 H); 6.56 (*s*, 1 H); 7.55 (*td*, $J = 7.4$, 1.1, 1 H); 7.66 (*d*, $J = 7.4$, 1 H); 7.69 (*ddd*, $J = 8.0$, 7.4, 1.1, 1 H); 7.81 (*d*, $J = 8.0$, 1 H). Anal. calc. for $C_{11}H_{11}ClO_2S$ (242.72): C 54.43, H 4.57; found: C 54.33, H 4.57.

*3-(3-Iodopropoxy)benzo[c]thiophen-1(3*H*)-one* (**11**). A mixture of **10** (0.37 g, 1.5 mmol) and NaI (0.25 g, 1.7 mmol) in acetone was heated at reflux temp. for 10 h. After cooling to r.t., the precipitate was filtered off, and the filtrate was concentrated by evaporation. The residue was purified by CC to give **11** (0.46 g, 91%). Pale-yellow solid. M.p. 77–78° (hexane). IR (KBr): 1692, 1600. ^{1}H-NMR: 2.07–2.13 (*m*, 2 H); 3.25–3.33 (*m*, 2 H); 3.55 (*dt*, $J = 9.2$, 5.7, 1 H); 3.78 (*dt*, $J = 9.2$, 5.7, 1 H); 6.66 (*s*, 1 H); 7.55 (*ddd*, $J = 8.0$, 7.4, 1.7, 1 H); 7.67–7.71 (*m*, 2 H); 7.81 (*d*, $J = 7.4$, 1 H). Anal. calc. for $C_{11}H_{11}IO_2S$ (334.17): C 39.54, H 3.32; found: C 39.50, H 3.09.

*4′,5′-Dihydrospiro[benzo[c]thiophene-1(3*H*),2′(3′*H*)-furan]-3-one* (**12**). To a stirred soln. of ^{i}Pr$_2$NLi (0.76 mmol), generated from BuLi and ^{i}Pr$_2$NH by the standard method, in THF (2 ml) at −78° was added a soln. of **11** (0.21 g, 0.63 mmol) in THF (2 ml) dropwise. The characteristic orange color gradually turned to yellow (*ca.* 2 h), then sat. aq. NH_4Cl (15 ml) was added at the same temp. The mixture was warmed to r.t. and extracted with AcOEt (3 × 10 ml). The combined org. layers were washed with brine (10 ml), dried (Na_2SO_4), and evaporated. The residue was purified by CC to afford **12** (92 mg, 71%). Pale-yellow oil. R_f (AcOEt/hexane 1:3) 0.31. IR (neat): 1688. ^{1}H-NMR: 2.05–2.40 (*m*, 2 H); 2.59–2.65 (*m*, 1 H); 2.75–2.80 (*m*, 1 H); 4.18–4.23 (*m*, 1 H); 4.32 (*q*, $J = 8.0$, 1 H); 7.52 (*t*, $J = 7.4$, 1 H); 7.57 (*d*, $J = 7.4$, 1 H); 7.66 (*t*, $J = 7.4$, 1 H); 7.78 (*d*, $J = 7.4$, 1 H). ^{13}C-NMR: 26.11; 42.58; 70.45; 102.38; 123.36; 140.04; 129.83; 133.90; 125.72; 150.34; 194.59. MS: 206 (100, M^+). Anal. calc. for $C_{11}H_{10}O_2S$ (206.26): C 64.05, H 4.89; found: C 63.79, H 4.75.

The authors would like to acknowledge Mrs. *Miyuki Tanmatsu* of our university for recording mass spectra and performing combustion analyses.

REFERENCES

[1] M. Romero, P. Renard, D.-H. Caignard, G. Atassi, X. Solans, P. Constans, C. Bailly, M. D. Pujol, *J. Med. Chem.* **2007**, *50*, 294.
[2] J. Wu, J. Ling, X. Wang, T. Li, J. Liu, Y. Lai, H. Ji, S. Peng, J. Tian, Y. Zhang, *J. Med. Chem.* **2012**, *55*, 7173.
[3] G. Majumdar, R. Pal, N. K. V. S. Murty, D. Mal, *J. Chem. Soc., Perkin Trans. 1* **1994**, 309.
[4] P. Mitra, B. Shome, S. Ranjan De, A. Sarkar, D. Mal, *Org. Biomol. Chem.* **2012**, *10*, 2742.
[5] I. Ryu, T. Okuda, K. Nagahara, N. Kambe, M. Komatsu, N. Sonoda, *J. Org. Chem.* **1997**, *62*, 7550; I. Polec, L. Lutsen, D. Vanderzande, J. Gelan, *Eur. J. Org. Chem.* **2002**, 1033; R. B. Boyd, N. D. Sharma, M. A. Kennedy, S. D. Shepherd, J. F. Malone, A. Alves-Areias, R. Holt, S. G. Allenmark, M. A. Lemurell, H. Dalton, H. Luckarift, *Chem. Commun.* **2002**, 1452; R. Pal, K. V. S. N. Murthy, D. Mal, *Synth. Commun.* **1993**, *23*, 1555.
[6] T. Drewnowski, S. Lesniak, G. Mlostoń, R. Siedlecka, J. Skarżewski, *Helv. Chim. Acta* **2006**, *89*, 991.
[7] H. Alper, A. S. K. Chen, *J. Chem. Soc., Chem. Commun.* **1973**, 724.
[8] Q. Ding, X. Liu, H. Wang, M. Chen, Y. Peng, *Synthesis* **2012**, *44*, 920.
[9] G. D. Hartman, B. T. Phillips, W. Halczenko, *J. Org. Chem.* **1985**, *50*, 2423.
[10] S. Ito, A. Hayashi, H. Komai, H. Yamaguchi, Y. Kubota, M. Asami, *Tetrahedron* **2011**, *67*, 2081.
[11] M. Lautens, T. Marquardt, *J. Org. Chem.* **2004**, *69*, 4607.
[12] C. D. Evans, M. F. Mahon, P. C. Andrews, J. Muir, S. D. Bull, *Org. Lett.* **2011**, *13*, 6276.
[13] D. Albanese, M. Penso, *Synthesis* **1991**, 1001.
[14] H. P. Plaumann, R. Rodrigo, *Pol. J. Chem.* **1979**, *53*, 201.

Received March 8, 2013