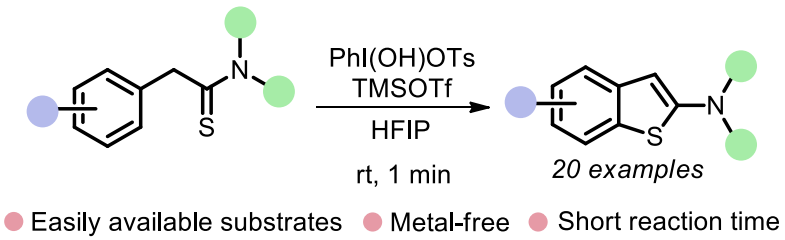
Synthesis of 2-Aminobenzo[*b*]thiophenes *via* an Intramolecular Dehydrogenative C–S Bond Formation Effected by Iodine(III) Reagents

Dmitry I. Bugaenko*
Alexander V. Karchava*

Department of Chemistry, Moscow State University, 1/3 Leninskie Gory, Moscow 119991, Russia

bugaenko@org.chem.msu.ru
karchava@org.chem.msu.ru

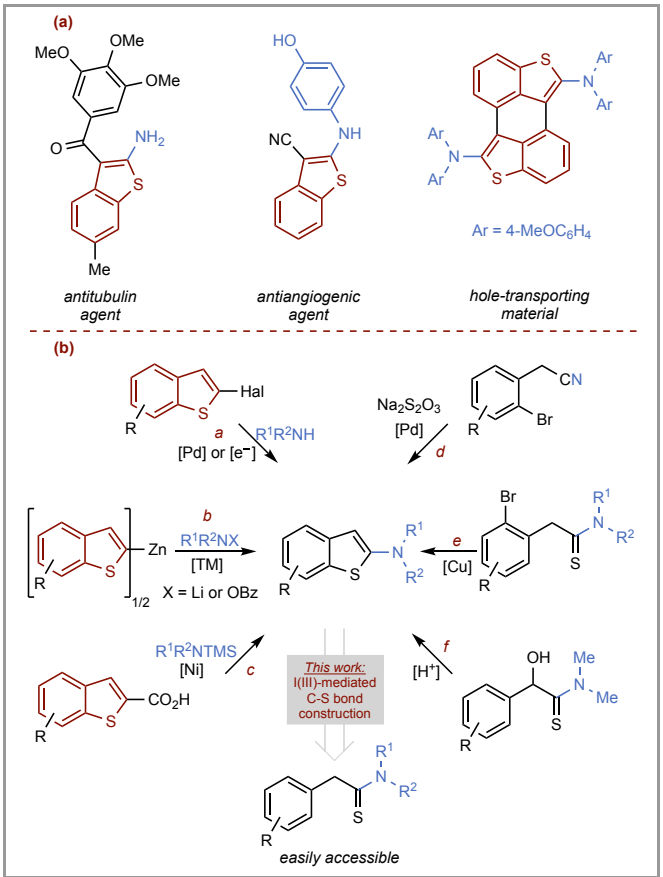


Abstract A direct synthesis of medicinal chemistry-relevant 2-aminobenzo[*b*]thiophenes has been achieved from substituted thioamides of 2-arylacetic acids through a fast intramolecular cross-dehydrogenative cyclization, mediated by hydroxy(tosyloxy)iodobenzene (HTIB, Koser's reagent). This synthetic approach is operationally simple, uses easily accessible substrates, and tolerates a variety of substituents at different sites, providing an opportunity for diversification.

Key words C–S bond formation, hypervalent iodine, benzo[*b*]thiophenes, metal free, oxidative cyclization, thioamides, C–H functionalization

The benzo[*b*]thiophene structural motif has long been recognized as a "privileged" scaffold for the development of biologically active compounds and is currently present in several marketed drugs.[1] Among others, 2-aminobenzo[*b*]thiophenes have also been identified as potent and selective ligands for different biological targets.[1,2] Additionally, substituted 2-aminobenzo[*b*]thiophenes serve as the key intermediate for the synthesis of raloxifene,[3] a clinically used drug, and as hole-transporting materials for perovskite solar cells (Scheme 1a).[4]

To date, 2-aminobenzo[*b*]thiophenes were prepared from 2-halobenzo[*b*]thiophenes by a palladium-catalyzed amination with secondary amines[5] or by an electron-catalyzed amination with magnesium amides (Scheme 1b, route *a*);[6] from benzo[*b*]thiophene-based organozinc reagents through a copper-mediated oxidative amination with lithium amides[7] or a copper-catalyzed electrophilic amination with hydroxylamine derivatives (route *b*);[8] and from benzothiophene-2-carboxylic acid *via* a nickel-catalyzed decarboxylative amination with *N*-trimethylsilyl amines (route *c*).[9] Alternatively, these compounds were prepared from non-benzothiophene precursors using ring-forming reactions. In the context of the latter strategy, a copper-catalyzed intramolecular cyclization of *ortho*-halogenated phenylthioaceamides (route *d*),[10] a palladium-catalyzed reaction of 2-bromophenylacetonitriles with $Na_2S_2O_3$ (route *e*),[11] and the



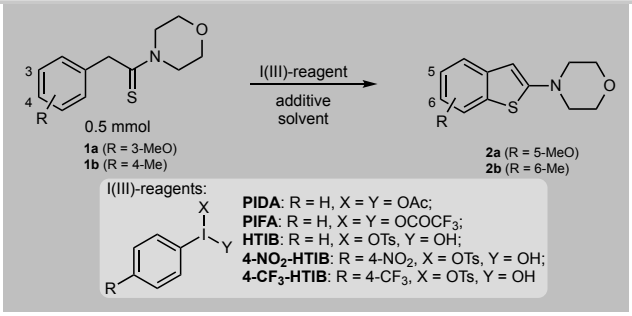
Scheme 1 Benzo[b]thiophenes: (a) examples of useful compounds; (b) synthetic routes

cyclization of thioamides of 2-hydroxy-2-phenylacetic acids in an acid medium[12] were used (route *f*). However, most of these methods have been explored only to a limited extent and/or suffer from the lack of availability of starting materials, low yielding or the use of expensive transition metal-based catalysts, strong acid or base conditions. Apparently, the developing a

novel, more versatile approach to substituted 2-aminobenzothiophenes is of high interest for the synthetic and medicinal chemistry community. Addressing this challenge, we report herein a metal-free protocol that accomplishes the direct conversion of easily accessible thioamides of 2-arylacetic acids into 2-aminobenzothiophenes through a iodine(III)-mediated dehydrogenative C–S coupling reaction. In recent decades, cross-dehydrogenative coupling reactions to form carbon–carbon and carbon–heteroatom bonds mediated by hypervalent iodine reagents have attracted much attention as a superior alternative to the traditional transition metal-catalyzed cross-coupling reactions. Hypervalent iodine reagents are readily accessible, environmentally friendly, mild and highly selective oxidants; their application in organic synthesis allows to avoid the problems associated with transition metal-catalyzed reactions, including toxicity issues and the need for sophisticated ligands.[13] Among recently reported synthetically useful transformations involving hypervalent iodine reagents, there has been a significant number of innovative syntheses of various heterocycles through intramolecular dehydrogenative cyclization. Specifically, as a part of this strategy, 1,3-benzothiazepines,[14] benzothiazoles,[15] and 1,3-benzothiazines[16] have been accessed *via* an intramolecular C–S bond formation.

We started our study by searching for a suitable hypervalent iodine(III)-regent to convert of a 3-methoxy substituted thioamide **1a** as a model substrate into the corresponding benzo[*b*]thiophene **2a** (Table 1). After an extensive survey of the reaction conditions (see the Supporting Information for details), we discovered that when **1a** was reacted with hydroxy(tosyloxy)iodobenzene (**HTIB**, Koser's reagent) in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP, 0.1 M) as a solvent for 1 min, **2a** was produced in an 82% yield as the only regioisomer (entry 1). A slightly lower yield of **2a** was achieved when **1a** and **HTIB** were allowed to react for 1h under the same conditions (entry 2). A higher concentration of the reactants (0.2 M) also resulted in a diminished yield of **2a** (75%, entry 3). Using HFIP as the solvent was found to be important to the success of the reactions as no desired product was obtained when other solvents were employed under otherwise identical reaction conditions (entries 4–6).[17] Notably, other commonly employed hypervalent iodine(III) reagents, (diacetoxyiodo)benzene (**PIDA**) and (bis(trifluoroacetoxy)iodo)benzene (**PIFA**), were completely ineffective compared to **HTIB**, affording little to no desired product **2a** (entries 7, 8, and 9 vs entry 1). After having identified **HTIB** and HFIP as the most effective hypervalent iodine(III)-reagent and solvent respectively to obtain benzo[*b*]thiophene **2a** *via* the oxidative cyclization of **1a**, we applied the same set of conditions to 4-methyl substituted thioamide **2b**. Surprisingly, although the starting thioamide **1b** was totally consumed within 1–2 min, benzothiophene **2b** was not detected in the reaction mixture. This failure can be attributed to a less activated 4-methylphenyl aromatic ring, suggesting that the more electrophilic iodine(III)-reagents should be used. However, using **4-NO_2-HTIB** or **4-CF_3-HTIB** instead of **HTIB** did not result in any improvement. At the same time, the simultaneous addition of 1 equiv. of TMSOTf to the reaction mixture with **HTIB** or **4-CF_3-HTIB** had a beneficial effect on the reaction outcome: the desired product **2b** was generated selectively in yields of 82% and 76% respectively (entries 14 and 15). For our further experiments, the conditions of entry 14 (Table 1) were selected as optimal for conversion of thioamides *1* into benzo[*b*]thiophene **2**.

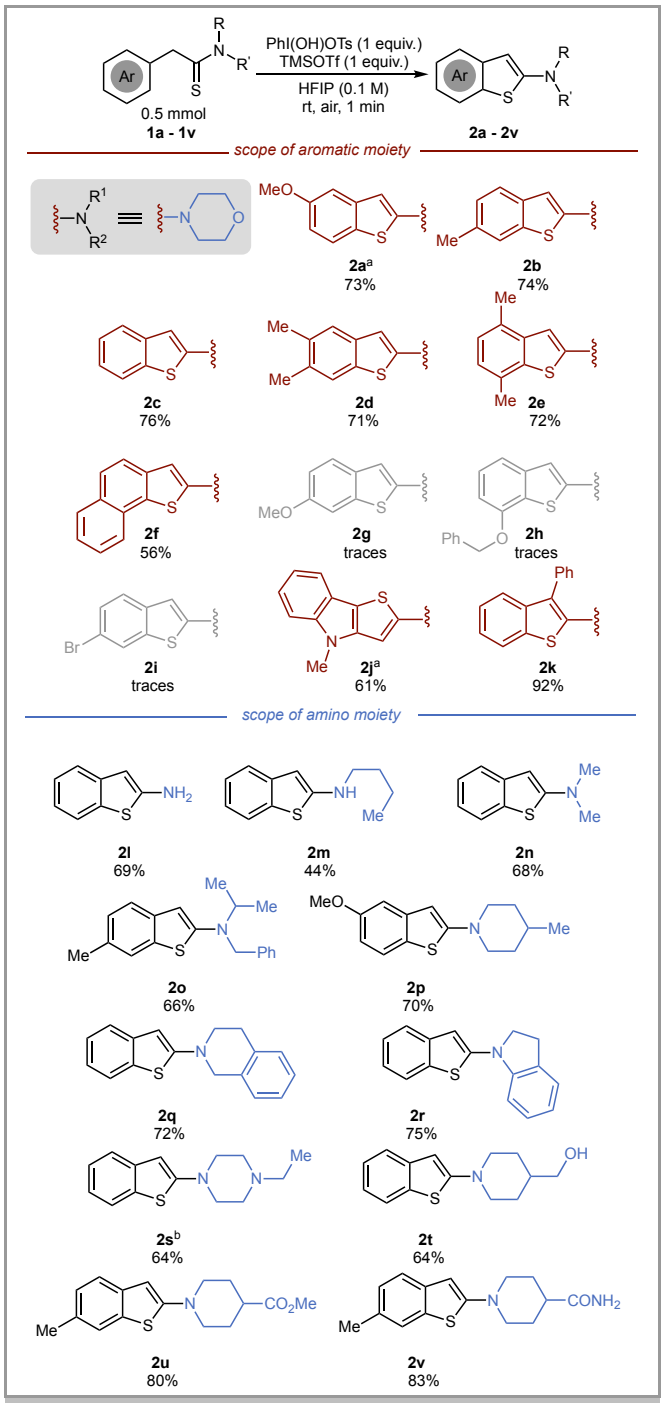
Table 1 Optimization of the reaction conditions[a]



Entry	I(III)-reagent	Solvent (M)/Additive (equiv.)	Yield (%) of **2**[b]
		for **1a** (R = 3-MeO)	
1[c]	**HTIB**	HFIP (0.1)	82
2	**HTIB**	HFIP (0.1)	79
3	**HTIB**	HFIP (0.2)	75
4	**HTIB**	HFIP–MeCN, 1:10 (0.1)	0
5	**HTIB**	TFA–MeCN, 1:10 (0.1)	0
6	**HTIB**	AcOH (0.1)	0
7	**PIDA**	DCM, MeCN or HFIP (0.1)	0
8	**PIFA**	DCM or MeCN (0.1)	0
9	**PIFA**	HFIP (0.1)	17
		for **1b** (R = 4-Me)[c]	
10	**HTIB**	HFIP (0.1)	0
11	**4-NO_2-HTIB**	HFIP (0.1)	0
12	**4-CF_3-HTIB**	HFIP (0.1)	0
13	**PIFA**	HFIP (0.1)	0
14	**HTIB**	HFIP (0.1)/TMSOTf (1)	82
15	**4-CF_3-HTIB**	HFIP (0.1)/TMSOTf (1)	76

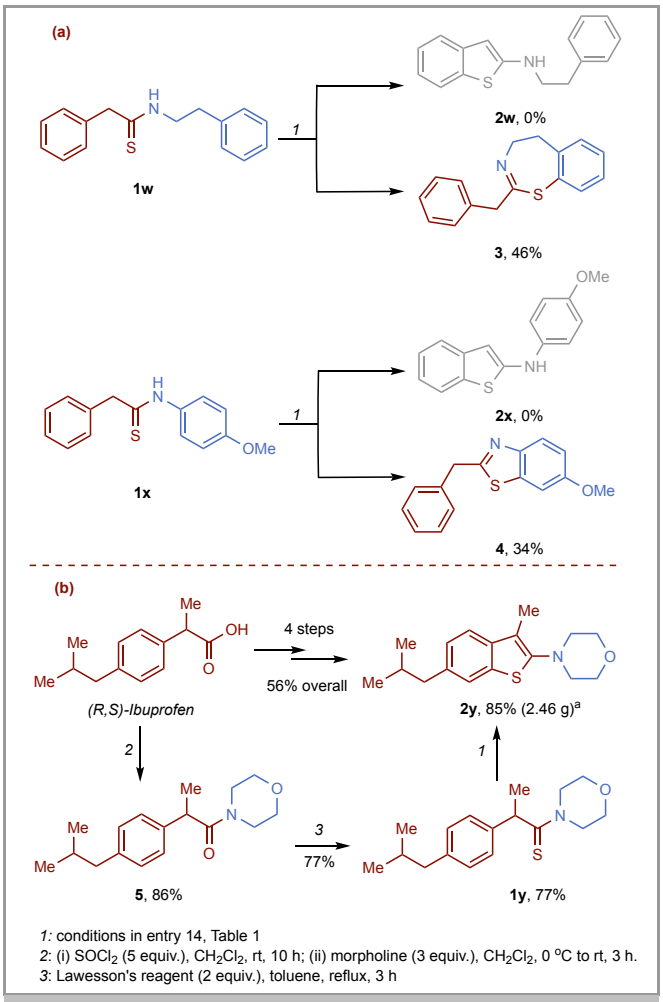
[a] For full optimization results, see the Supporting Information. Reaction conditions: A hypervalent iodine(III) reagent was added portionwise to a mixture of **1a** or **1b** and an additive in a solvent at rt under air atmosphere. The mixture was stirred for 1 h at ambient temperature. Then, the crude reaction mixture was analyzed by ^{1}H NMR after an extractive work-up with 10% $NaHCO_3$–H_2O.
[b] ^{1}H NMR yields using 1,3,5-trimethoxybenzene as the internal standard are reported.
[c] Reaction time of 1 min.

With optimized conditions in hand, we explored the substrate scope of the reaction with respect to substituents in the aryl group and at the nitrogen atom of the starting thioamides **1** (Scheme 2). Benzothiophenes with no substituent in the benzene ring (**2c**) and bearing two methyl groups at different positions (**2d** and **2e**) were smoothly obtained in yields of 71–76%. The reaction was only slightly sensitive to steric hindrance in the aryl group, which allowed us to selectively synthesize a densely substituted product **2e** and a naphthalene derivative **2f** with *ortho* (Me) or pseudo-*ortho* (β-naphthyl) substituents, respectively. However, the reaction was completely unproductive when applied to *ortho* and *para* alkoxy substituted substrates. Here again, while starting thioamides were completely consumed, only complex mixtures of products were obtained in both cases, probably due to an *ipso*-attack on the carbon atoms bearing alkoxy groups and further decomposition. Only trace amount of a bromo substituted benzothiophene **2i** was detected when the corresponding thioamide **1i** was exposed to the optimized conditions. This failure is probably attributed to the decreased nucleophilicity of the bromine substituted aromatic ring. Meanwhile, the reaction was successfully applied to the synthesis of the indole-derived (**2j**) and 3-substituted (**2k**) products in yields of 61% and 92% respectively.



Scheme 2 Scope of the reaction. Isolated yields are reported. [a] Performed without TMSOTf. [b] 2 equiv. of TMSOTf was used.

Variation of substituents at the nitrogen atom in thioamides 1 revealed that the method could be applied to the preparation of benzo[*b*]thiophenes bearing primary (**2l**), secondary (**2m**), and tertiary amino groups (**2c, 2q-2t**) with comparable efficiency. Among others, products with sterically demanded (**2o**) and aromatic amine moieties (**2r**) were obtained in yields of 66% and 75% respectively. Overall, the method is compatible with a range of different substituents and synthetically useful functionalities in the side chain, including tertiary amine (**2s**), hydroxy (**2t**), ester (**2u**), and primary amide groups (**2t**), providing a handle for post-synthetic modification. Unexpectedly, instead of benzothiophenes **2w** and **2x**, 1,3-benzothiazepine **3** and benzothiazole **4** were isolated as the sole products when the corresponding thioamides **1w** and **1x** were submitted to the optimized conditions (Scheme 3a).

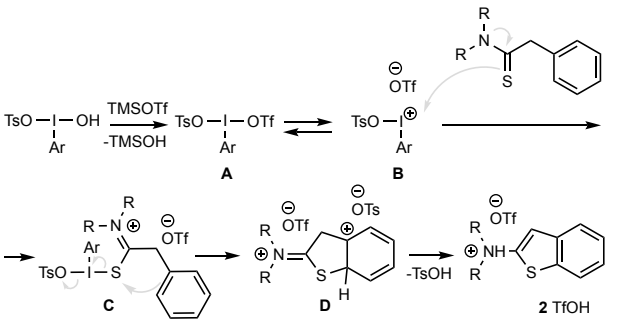


Scheme 3 (a) Unexpected cyclization. (b) Scale-up synthesis. [a] C_6H_5I was also isolated in a 78% yield

To highlight the practicality of this method as well as illustrate its applicability for the synthetic modification of drug molecules, we prepared benzo[*b*]thiophene **2y** on a multi-gram scale starting from ibuprofen (Scheme 3b). Initially, ibuprofen was transformed into the corresponding morpholide **5** in an 86% yield. The latter was in turn converted into thioamide **1y** upon treatment with Lawesson's reagent in toluene. Finally, cyclization of **1y** under the optimized conditions delivered product **2y** in an 85% yield. Altogether, the ibuprofen derived benzo[*b*]thiophene **2y** was obtained in only four-step concise synthesis in an overall yield of 56%. Moreover, iodobenzene was also isolated in an 78% yield in the final step. The latter can be utilized for the re-synthesis of **HTIB**,[18] thus improving the atom economy and cost-efficiency of the method.

Based on previous literature reports,[14–16, 19] the following mechanism for the formation of the benzo[*b*]thiophene ring can be proposed (Scheme 4). The reaction begins with the activation of ArI(OH)OTs with TMSOTf to form ArI(OTf)OTs (**A**). This compound then undergoes isomerization to a species **B** in which the OTf-group is in a *cis*-position to the OTs-group and in a *trans*-position to the Ar-group and is only loosely bound to the iodine atom. The species **B**, which can be regarded as an intimate ion

pair or an iodonium compound, serves as a Lewis acid and forms an adduct **C** with a nucleophilic sulfur atom of the C=S-group, providing its umpolung reactivity. After that, a nucleophilic attack of the aryl group at the electrophilic sulfur atom leads to the formation of an intramolecular C–S bond (intermediate **D**). Finally, the resulting benzothiophene **2** is delivered after deprotonation and isomerization. The role of highly polar and non-nucleophilic HFIP is likely to stabilize cationic intermediates involved in the reaction.[17] Our control experiments with the radical scavengers 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) and butylated hydroxytoluene (BHT) did not show a significant inhibition effect on the reaction, suggesting that an alternative radical mechanism is likely not involved.



Scheme 4 Proposed mechanism for the formation of 2-aminobenzo[*b*]thiophenes **2**

In conclusion, we have developed a novel hypervalent iodine-mediated synthesis of substituted 2-aminobenzo[*b*]thiophenes from easily available thioamides of 2-arylacetic acids. Ring-forming C–H heterofunctionalization of thioamides with the formation of the C–S bond occurs rapidly and selectively under mild metal-free conditions. The operational simplicity, variability of substituents in the aromatic ring (among the electron donating groups) and at the nitrogen atom, compatibility with various functional groups, and possibility of scaling up make this method a promising tool for organic synthesis and medicinal chemistry.

General experimental details are given in the Supporting Information.

2-Aminobenzo[*b*]thiophenes 2, General Procedure

A flame-dried 8-mL vial was charged with a stir bar. Thioamide **1** (0.5 mmol, 1equiv.) and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) (5 mL, 0.1 M) were added to the vial, followed by the dropwise addition of trimethylsilyl trifluoromethanesulfonate (TMSOTf) (91 µL, 111 mg, 0.5 mmol, 1 equiv.). Hydroxy(tosyloxy)iodobenzene, (**HTIB**) (196 mg, 0.5 mmol, 1 equiv) was then added to the stirred solution for 1 min at rt. After another 1 min, the reaction mixture was poured into a saturated aqueous solution of $NaHCO_3$ (20 mL). The product was extracted with CH_2Cl_2 (15 mL × 4). Organic layers were combined, dried with Na_2SO_4, and the solvent was evaporated. The product was purified by column chromatography (a Schott's filter with a height of 5 cm and a diameter of 3 cm was used) with a gradient of EtOAc – *n*-hexane mixture.

Characterization data obtained for compounds **2a**, **2c**, **2l**, **2n**, **4** matched those previously reported in the literature

4-(5-Methoxybenzo[*b*]thiophen-2-yl)morpholine (**2a**)[20] was obtained according to the General Procedure (TMSOTf was not added) from 2-(3-methoxyphenyl)-1-morpholinoethane-1-thione (**1a**) (123 mg, 0.5 mmol).

Yield: 91 mg (73%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 115 – 117 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.6 Hz, 1H), 6.98 (d, *J* = 2.5 Hz, 1H), 6.75 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.16 (s, 1H), 3.80 – 3.92 (m, 4H), 3.83 (s, 3H), 3.19 – 3.28 (m, 4H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 159.1, 157.9, 141.5, 124.8, 122.4, 110.7, 104.6, 99.5, 66.4, 55.6, 50.9.

FT-IR (neat): ν_{max} (cm^{-1}) 2969, 2931, 2891, 2879, 2858, 2850, 2834, 1658, 1591, 1577, 1567, 1551, 1530, 1485, 1457, 1451, 1442, 1433, 1426, 1386, 1375, 1348, 1339, 1333, 1323, 1319, 1313, 1304, 1296, 1279, 1267, 1247, 1233, 1221, 1211, 1199, 1188, 1176, 1156, 1141, 1136, 1129, 1117, 1076, 1066, 1042, 1020, 957, 948, 942, 931, 902, 888, 857, 837, 809, 797, 782, 764, 727, 714, 697, 688, 653, 640, 613, 600, 573, 554, 530.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{16}NO_2S^+$ 250.0896; Found 250.0898 (1 ppm).

R_f (*n*-hexane –EtOAc = 20:1) = 0.19.

4-(6-Methylbenzo[*b*]thiophen-2-yl)morpholine (**2b**) was obtained according to the General Procedure from 1-morpholino-2-(p-tolyl)ethane-1-thione (**1b**) (118 mg, 0.5 mmol).

Yield: 86 mg (74%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 122 – 124 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (s, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.07 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.19 (s, 1H), 3.83 – 3.89 (m, 4H), 3.18 – 3.26 (m, 4H), 2.40 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 156.9, 137.8, 133.1, 131.4, 126.1, 121.7, 120.9, 99.6, 66.4, 51.2, 21.5.

FT-IR (neat): ν_{max} (cm^{-1}) 2960, 2947, 2938, 2928, 2918, 2879, 2863, 2836, 2811, 2749, 2737, 1611, 1560, 1548, 1532, 1482, 1473, 1456, 1443, 1413, 1403, 1384, 1374, 1339, 1334, 1323, 1314, 1307, 1296, 1278, 1267, 1264, 1258, 1232, 1218, 1200, 1187, 1130, 1114, 1077, 1069, 1064, 1060, 1048, 1029, 950, 942, 937, 930, 921, 914, 890, 879, 857, 847, 837, 815, 784, 776, 730, 723, 718, 714, 697, 689, 670, 649, 587, 574, 556, 549, 525.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{16}NOS^+$ 234.0947; Found 234.0951 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.26.

4-(Benzo[*b*]thiophen-2-yl)morpholine (**2c**)[8a] was obtained according to the General Procedure from 1-morpholino-2-phenylethane-1-thione (**1c**) (110 mg, 0.5 mmol).

Yield: 83 mg (76%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 177 – 179 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.22 – 7.28 (m, 1H), 7.06 – 7.15 (m, 1H), 6.23 (s, 1H), 3.83 – 3.90 (m, 4H), 3.21 – 3.28 (m, 4H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 157.8, 140.4, 132.8, 124.6, 121.72, 121.65, 121.1, 99.5, 66.4, 51.0.

FT-IR (neat): ν_{max} (cm^{-1}) 3052, 2992, 2956, 2929, 2885, 2875, 2838, 1592, 1556, 1545, 1526, 1467, 1454, 1449, 1436, 1384, 1375, 1326, 1316, 1309, 1303, 1275, 1263, 1255, 1249, 1229, 1211, 1199, 1186, 1173, 1166, 1132, 1115, 1075, 1064, 1040, 1032, 1027, 1023, 1019, 1012, 949, 932, 913, 901, 881, 868, 830, 822, 798, 780, 761, 743, 730, 723, 705, 701, 664, 652, 601, 592, 580, 568, 544, 536, 525.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{14}NOS^+$ 220.0791; Found 220.0795 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.26.

4-(5,6-Dimethylbenzo[*b*]thiophen-2-yl)morpholine (**2d**) was obtained according to the General Procedure from 2-(3,4-dimethylphenyl)-1-morpholinoethane-1-thione (**1d**) (125 mg, 0.5 mmol).

Yield: 88 mg (71%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 154 – 156 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (s, 1H), 7.26 (s, 1H), 6.15 (s, 1H), 3.83 – 3.88 (m, 4H), 3.18 – 3.25 (m, 4H), 2.31 (s, 6H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 157.1, 138.6, 133.5, 130.8, 130.6, 122.1, 121.9, 99.6, 66.5, 51.3, 20.1, 20.1.

FT-IR (neat): ν_{max} (cm^{-1}) 2966, 2955, 2889, 2871, 2856, 1676, 1645, 1618, 1606, 1586, 1556, 1541, 1531, 1477, 1466, 1459, 1446, 1419, 1408, 1396, 1387, 1382, 1373, 1350, 1340, 1326, 1308, 1304, 1291, 1280, 1261, 1219, 1200, 1170, 1162, 1149, 1115, 1075, 1065, 1049, 1024, 1000, 992, 942, 931, 900, 887, 878, 866, 809, 802, 790, 762, 741, 719, 690, 683, 646, 634, 621, 615, 580, 557, 533, 525.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{18}NOS^+$ 248.1104; Found 248.1105 (0.4 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.31.

4-(4,7-Dimethylbenzo[*b*]thiophen-2-yl)morpholine (**2e**) was obtained according to the General Procedure from 2-(2,5-dimethylphenyl)-1-morpholinoethane-1-thione (**1e**) (125 mg, 0.5 mmol).

Yield: 88 mg (72%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 63 – 65 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.99 (d, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 7.3 Hz, 1H), 6.27 (s, 1H), 3.86. – 3.91 (m, 4H), 3.25 – 3.31 (m, 4H), 2.45 (s, 3H), 2.42 (s, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 157.4, 139.3, 132.5, 128.6, 127.8, 125.6, 122.3, 98.7, 66.5, 51.2, 20.1, 19.5.

FT-IR (neat): ν_{max} (cm^{-1}) 3371, 3151, 2949, 2939, 2925, 2893, 2858, 1637, 1584, 1571, 1532, 1477, 1464, 1458, 1452, 1446, 1440, 1388, 1374, 1350, 1334, 1312, 1302, 1247, 1237, 1168, 1140, 1129, 1122, 1097, 1080, 1025, 1018, 822, 796, 768, 746, 733, 729, 682, 634, 586, 535, 525.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{18}NOS^+$ 248.1104; Found 248.1109 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.31.

4-(**Naphtho[1,2-b]thiophen-2-yl)morpholine** (**2f**) was obtained according to the General Procedure from 1-morpholino-2-(naphthalen-2-yl)ethane-1-thione (**1f**) (136 mg, 0.5 mmol).

Yield: 75 mg (56%).

Physical state: off-white solid.

Mp (EtOAc – *n*-hexane): 119 – 121 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.1 Hz, 1H), 7.85 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.66 (d, *J* = 8.5 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H), 7.39 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 6.39 (s, 1H), 3.87 – 3.94 (m, 4H), 3.27 – 3.34 (m, 4H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 157.9, 138.0, 129.7, 129.0, 128.9, 128.0, 126.6, 125.5, 124.1, 122.6, 121.0, 101.5, 66.4, 51.2.

FT-IR (neat): ν_{max} (cm^{-1}) 3048, 2990, 2967, 2939, 2891, 2879, 2861, 2846, 2831, 1630, 1616, 1577, 1556, 1544, 1522, 1510, 1505, 1463, 1455, 1450, 1443, 1401, 1374, 1351, 1345, 1332, 1326, 1316, 1310, 1304, 1294, 1276, 1267, 1257, 1251, 1234, 1221, 1218, 1213, 1200, 1191, 1171, 1165, 1148, 1144, 1129, 1113, 1075, 1068, 1048, 1040, 1036, 1029, 1026, 1021, 988, 979, 960, 954, 940, 932, 900, 885, 867, 857, 824, 810, 782, 774, 766, 760, 752, 735, 675, 669, 666, 660, 656, 649, 575, 565, 548, 535, 525.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{16}NOS^+$ 270.0947; Found 270.0952 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.28.

4-(4-Methyl-4*H*-thieno[3,2-*b*]indol-2-yl)morpholine (**2j**) was obtained according to the General Procedure (TMSOTf was not added) from 2-(1-methyl-1*H*-indol-2-yl)-1-morpholinoethane-1-thione (**1j**) (137 mg, 0.5 mmol).

Yield: 83 mg (61%).

Physical state: light-yellow solid.

Mp (EtOAc – *n*-hexane): 114 – 116 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.15 – 7.21 (m, 1H), 7.09 – 7.15 (m, 1H), 6.19 (s, 1H), 3.86 – 3.92 (m, 4H), 3.80 (s, 3H), 3.19 – 3.28 (m, 4H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 161.3, 144.3, 139.9, 122.6, 120.4, 119.2, 117.2, 109.2, 103.2, 90.1, 66.5, 51.5, 31.2.

FT-IR (neat): ν_{max} (cm^{-1}) 3048, 2995, 2968, 2947, 2864, 2840, 2821, 1618, 1606, 1583, 1529, 1496, 1486, 1478, 1467, 1463, 1456, 1436, 1423, 1383, 1369, 1350, 1336, 1330, 1324, 1303, 1289, 1283, 1277, 1262, 1253, 1245, 1238, 1219, 1206, 1175, 1157, 1141, 1114, 1076, 1066, 1040, 1029, 1016, 1011, 989, 982, 970, 962, 938, 927, 914, 908, 892, 880, 845, 838, 799, 791, 763, 741, 736, 731, 715, 711, 703, 698, 679, 671, 655, 645, 617, 609, 590, 580, 574, 568, 558, 548, 525.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{17}N_2OS^+$ 273.1056; Found 273.1059 (1 ppm).

Rf (*n*-hexane – EtOAc = 20:1) = 0.13.

4-(3-Phenylbenzo[*b*]thiophen-2-yl)morpholine (**2k**) was obtained according to the General Procedure from 1-morpholino-2,2-diphenylethane-1-thione (**1k**) (149 mg, 0.5 mmol).

Yield: 136 mg (92%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 102 – 104 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 – 7.76 (m, 1H), 7.54 – 7.58 (m, 3H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.20 – 7.30 (m, 2H), 3.64 – 3.71 (m, 4H), 2.95 – 3.02 (m, 4H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 153.5, 139.6, 135.5, 133.9, 129.9, 128.7, 127.1, 124.5, 123.1, 122.3, 121.7, 121.50, 66.8, 52.8.

FT-IR (neat): ν_{max} (cm^{-1}) 2958, 2922, 2850, 1625, 1558, 1549, 1538, 1503, 1493, 1470, 1461, 1449, 1434, 1379, 1357, 1316, 1297, 1282, 1265, 1228, 1211, 1189, 1175, 1153, 1146, 1126, 1111, 1079, 1065, 1041, 1021, 969, 957, 937, 927, 890, 870, 819, 806, 778, 766, 756, 750, 740, 733, 723, 717, 709, 700, 687, 683, 668, 661, 647, 641, 619, 607, 546, 526.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{18}NOS^+$ 296.1104; Found 296.1110 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.44.

Benzo[*b*]thiophen-2-amine (**2l**)[11] was obtained according to the General Procedure from **2-phenylethanethioamide** (**1l**) (76 mg, 0.5 mmol).

Yield: 51 mg (69%).

Physical state: light-yellow solid (the compound darkens in air).

Mp (EtOAc – *n*-hexane): 97 – 99 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.20 – 7.25 (m, 1H), 7.09 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 6.29 (s, 1H), 4.04 (brs, 2H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 150.6, 140.8, 133.3, 124.6, 121.7, 121.6, 120.7, 102.0.

FT-IR (neat): ν_{max} (cm^{-1}) 3422, 3364, 3336, 1655, 1606, 1578, 1558, 1550, 1538, 1462, 1455, 1444, 1436, 1322, 1304, 1289, 1280, 1245, 1237, 1179, 1170, 1135, 1127, 1090, 1062, 1022, 1015, 823, 795, 764, 745, 730, 724, 691, 681, 632, 563, 535, 525.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_8H_8NS^+$ 150.0372; Found 150.0374 (1 ppm).

R_f (*n*-hexane – EtOAc = 4:1) = 0.49.

***N*-Butylbenzo[*b*]thiophen-2-amine** (**2m**) was obtained according to the General Procedure from *N*-butyl-2-phenylethanethioamide (**1m**) (104 mg, 0.5 mmol).

Yield: 45 mg (44%).

Physical state: off-white semisolid (the compound darkens in air).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 7.9 Hz, 1H), 7.24 – 7.30 (m, 1H), 7.01 – 7.07 (m, 1H), 5.04 (s, 1H), 3.21 (q, J = 6.6 Hz, 2H), 1.48 – 1.57 (m, 3H), 1.28 (h, J = 7.4 Hz, 2H), 0.88 (td, J = 7.3, 2.5 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 156.7, 141.5, 130.2, 125.2, 121.9, 120.9, 119.1, 94.5, 47.5, 32.1, 20.0, 13.9.

FT-IR (neat): ν_{max} (cm^{-1}) 3371, 3151, 2949, 2939, 2925, 2893, 2858, 1637, 1584, 1571, 1532, 1477, 1464, 1458, 1452, 1446, 1440, 1388, 1374, 1350, 1334, 1312, 1302, 1247, 1237, 1168, 1140, 1129, 1122, 1097, 1080, 1025, 1018, 822, 796, 768, 746, 733, 729, 682, 634, 586, 535, 525.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{16}NS^+$ 206.0998; Found 206.1003 (2 ppm).

R_f (*n*-hexane – EtOAc = 4:1) = 0.66.

***N*,*N*-Dimethylbenzo[*b*]thiophen-2-amine** (**2n**)[11] was obtained according to the General Procedure from ***N*,*N*-dimethyl-2-phenylethanethioamide** (**1n**) (90 mg, 0.5 mmol).

Yield: 60 mg (68%).

Physical state: yellow semisolid (the compound darkens in air).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (dt, J = 7.7, 0.8 Hz, 1H), 7.42 (dt, J = 7.8, 1.0 Hz, 1H), 7.21 (ddd, J = 8.1, 7.2, 1.1 Hz, 1H), 7.03 (ddd, J = 8.3, 7.3, 1.2 Hz, 1H), 5.98 (s, 1H), 3.01 (s, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 157.8, 141.5, 132.5, 124.5, 121.5, 120.4, 120.2, 96.6, 42.5.

FT-IR (neat): ν_{max} (cm^{-1}) 3053, 3010, 2865, 2815, 2797, 1888, 1627, 1559, 1553, 1543, 1481, 1454, 1434, 1423, 1365, 1352, 1340, 1322, 1312, 1304, 1260, 1234, 1185, 1178, 1165, 1130, 1120, 1111, 1075, 1064, 1027, 1016, 977, 960, 940, 919, 870, 848, 826, 816, 793, 756, 740, 718, 702, 697, 655, 645, 625, 613, 592, 572, 544, 538, 526.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{10}H_{12}NS^+$ 178.0685; Found 178.0687 (1 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.58.

***N*-Benzyl-*N*-isopropyl-6-methylbenzo[*b*]thiophen-2-amine** (**2o**) was obtained according to the General Procedure from ***N*-benzyl-*N*-isopropyl-2-(*p*-tolyl)ethanethioamide** (**1o**) (149 mg, 0.5 mmol).

Yield: 97 mg (66%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 106 – 108 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 – 7.36 (m, 5H), 7.21 – 7.26 (m, 1H), 7.19 (d, J = 8.1 Hz, 1H), 6.97 (d, J = 7.8 Hz, 1H), 5.83 (s, 1H), 4.41 (s, 2H), 4.00 – 4.07 (m, 1H), 2.36 (s, 3H), 1.27 (d, J = 6.6 Hz, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 155.5, 139.3, 138.9, 132.2, 130.0, 128.6, 126.9, 126.7, 125.9, 121.4, 119.9, 97.6, 54.6, 50.4, 21.5, 20.2.

FT-IR (neat): ν_{max} (cm^{-1}) 2970, 1557, 1542, 1529, 1500, 1495, 1483, 1470, 1419, 1404, 1395, 1388, 1378, 1367, 1363, 1358, 1347, 1341, 1299, 1270, 1252, 1244, 1216, 1206, 1198, 1172, 1151, 1138, 1131, 1122, 1090, 1080, 1064, 1046, 1034, 1028, 1012, 1003, 953, 917, 898, 882, 833, 810, 769, 756, 751, 745, 726, 720, 710, 695, 686, 681, 645, 623, 590, 573, 558.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{22}NS^+$ 296.1467; Found 296.1474 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.69.

1-(5-Methoxybenzo[*b*]thiophen-2-yl)-4-methylpiperidine (**2p**) was obtained according to the General Procedure from **2-(3-methoxyphenyl)-1-(4-methylpiperidin-1-yl)ethane-1-thione** (**1p**) (132 mg, 0.5 mmol).

Yield: 91 mg (70%).

Physical state: yellow solid.

Mp (EtOAc – *n*-hexane): 77 – 79 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 (d, J = 8.6 Hz, 1H), 6.94 (d, J = 2.5 Hz, 1H), 6.69 (dd, J = 8.6, 2.5 Hz, 1H), 6.09 (s, 1H), 3.82 (s, 3H), 3.58 – 3.66 (m, 2H), 2.89 (td, J = 12.3, 2.8 Hz, 2H), 1.69 – 1.77 (m, 2H), 1.30 – 1.45 (m, 3H), 0.98 (d, J = 6.5 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 159.6, 157.8, 142.1, 124.8, 122.2, 109.8, 104.2, 98.5, 55.6, 51.4, 33.5, 30.5, 21.9.

FT-IR (neat): ν_{max} (cm^{-1}) 3011, 2982, 2915, 2880, 2865, 2852, 2828, 1631, 1591, 1577, 1567, 1552, 1534, 1483, 1463, 1460, 1455, 1447, 1439, 1430, 1423, 1393, 1383, 1339, 1317, 1302, 1295, 1274, 1257, 1242, 1232, 1223, 1215, 1203, 1192, 1165, 1154, 1142, 1131, 1105, 1090, 1077, 1071, 1050, 1029, 982, 968, 955, 947, 917, 908, 885, 864, 847, 834, 816, 803, 784, 778, 770, 755, 724, 714, 697, 687, 658, 642, 628, 622, 613, 596, 566, 552, 525.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{20}NOS^+$ 262.1260; Found 262.1264 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.46.

2-(Benzo[*b*]thiophen-2-yl)-1,2,3,4-tetrahydroisoquinoline (**2q**) was obtained according to the General Procedure from **1-(3,4-dihydroisoquinolin-2(1*H*)-yl)-2-phenylethane-1-thione** (**1q**) (134 mg, 0.5 mmol).

Yield: 95 mg (72%).

Physical state: light-yellow solid.

Mp (EtOAc – *n*-hexane): 121 – 123 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, J = 7.9 Hz, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.15 – 7.25 (m, 5H), 7.05 – 7.12 (m, 1H), 6.24 (s, 1H), 4.49 (s, 2H), 3.62 (t, J = 5.9 Hz, 2H), 3.04 (t, J = 5.9 Hz, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 157.2, 141.0, 134.1, 133.2, 132.5, 128.8, 126.7, 126.5, 126.4, 124.6, 121.6, 121.1, 120.7, 98.2, 52.2, 48.8, 28.9.

FT-IR (neat): ν_{max} (cm^{-1}) 3025, 2977, 2833, 1595, 1561, 1551, 1538, 1506, 1497, 1467, 1454, 1449, 1442, 1394, 1380, 1361, 1353, 1330, 1317, 1309, 1303, 1281, 1274, 1261, 1253, 1245, 1236, 1226, 1220, 1214, 1205, 1191, 1180, 1135, 1126, 1117, 1108, 1082, 1064, 1058, 1050, 1041, 1036, 1026, 1017, 995, 987, 951, 928, 920, 914, 879, 854, 829, 818, 789, 762, 756, 748, 738, 722, 674, 665, 594, 570, 547, 535, 526.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{16}NS^+$ 266.0998; Found 266.1002 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.56.

1-(Benzo[*b*]thiophen-2-yl)indoline (**2r**) was obtained according to the General Procedure from **1-(indolin-1-yl)-2-phenylethane-1-thione** (**1r**) (127 mg, 0.5 mmol).

Yield: 94 mg (75%).

Physical state: off-white solid.

Mp (EtOAc – *n*-hexane): 78 – 80 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, J = 7.9 Hz, 1H), 7.57 (d, J = 7.9 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.28 – 7.33 (m, 1H), 7.13 – 7.22 (m, 3H), 6.83 – 6.89 (m, 1H), 6.57 (s, 1H), 4.09 (t, J = 8.6 Hz, 2H), 3.25 (t, J = 8.6 Hz, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 147.3, 146.0, 139.6, 132.8, 131.0, 127.6, 125.2, 124.8, 121.9, 121.8, 121.2, 120.2, 109.2, 103.3, 53.5, 28.2.

FT-IR (neat): ν_{max} (cm^{-1}) 3054, 2985, 2926, 2891, 2872, 1619, 1602, 1578, 1562, 1551, 1525, 1492, 1483, 1476, 1472, 1464, 1456, 1448, 1439, 1399, 1385, 1349, 1343, 1334, 1313, 1295, 1281, 1271, 1260, 1241, 1234, 1224, 1216, 1197, 1189, 1176, 1165, 1106, 1095, 1068, 1050, 1033, 1025, 1018, 1013, 942, 925, 909, 903, 880, 839, 783, 761, 750, 735, 717, 711, 628, 618, 594, 579, 569, 559, 530, 525.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{14}NS^+$ 252.0841; Found 252.0846 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.56.

1-(Benzo[*b*]thiophen-2-yl)-4-ethylpiperazine (**2s**) was obtained according to the General Procedure from **1-(4-ethylpiperazin-1-yl)-2-phenylethane-1-thione** (**1s**) (124 mg, 0.5 mmol).

Yield: 79 mg (64%).

Physical state: off-white solid.

Mp (EtOAc – *n*-hexane): 96 – 98 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, J = 7.9 Hz, 1H), 7.45 (d, J = 7.9 Hz, 1H), 7.20 – 7.25 (m, 1H), 7.05 – 7.11 (m, 1H), 6.19 (s, 1H), 3.28 – 3.34 (m, 4H), 2.60 – 2.66 (m, 4H), 2.50 (q, J = 7.2 Hz, 2H), 1.14 (t, J = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 157.8, 140.7, 132.9, 124.6, 121.7, 121.4, 121.0, 99.4, 52.4, 52.2, 50.9, 12.1.

FT-IR (neat): ν_{max} (cm^{-1}) 3054, 2996, 2966, 2951, 2932, 2860, 2814, 1646, 1606, 1562, 1552, 1537, 1477, 1439, 1407, 1401, 1392, 1379, 1357, 1340, 1328, 1319, 1313, 1303, 1292, 1285, 1274, 1252, 1240, 1231, 1218, 1207, 1193, 1186, 1171, 1146, 1135, 1125, 1097, 1090, 1080, 1066, 1027, 1012, 972, 944, 909, 896, 879, 833, 820, 810, 795, 764, 744, 731, 727, 721, 670, 656, 603, 593, 581, 564, 544, 533, 525.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{19}N_2S^+$ 247.1263; Found 247.1266 (1 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.14.

(1-(Benzo[*b*]thiophen-2-yl)piperidin-4-yl)methanol (**2t**) was obtained according to the General Procedure from **1-(4-ethylpiperazin-1-yl)-2-phenylethane-1-thione** (**1t**) (125 mg, 0.5 mmol).

Yield: 79 mg (64%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 118 – 120 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, J = 7.9 Hz, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.19 – 7.24 (m, 1H), 7.02 – 7.10 (m, 1H), 6.18 (s, 1H), 3.66 – 3.73 (m, 2H), 3.56 (d, J = 6.4 Hz, 2H), 2.92 (td, J = 12.3, 2.8 Hz, 2H), 1.82 – 1.90 (m, 2H), 1.63 – 1.76 (m, 1H), 1.40 – 1.52 (m, 2H), 1.35 (brs, 1H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 158.1, 140.9, 132.7, 124.5, 121.6, 121.1, 120.7, 98.9, 67.6, 51.2, 38.3, 28.1.

FT-IR (neat): ν_{max} (cm^{-1}) 3196, 2977, 2914, 2869, 2826, 1604, 1563, 1549, 1536, 1473, 1456, 1448, 1439, 1395, 1381, 1328, 1302, 1289, 1260, 1253, 1246, 1235, 1227, 1195, 1180, 1157, 1146, 1135, 1115, 1103, 1092, 1074, 1067, 1059, 1045, 1037, 1025, 1019, 1014, 998, 991, 972, 955, 937, 928, 903, 893, 862, 841, 817, 776, 749, 733, 728, 722, 662, 655, 601, 593, 580.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{18}NOS^+$ 248.1104; Found 248.1108 (2 ppm).

R_f (*n*-hexane – EtOAc = 4:1) = 0.69.

Methyl 1-(6-methylbenzo[*b*]thiophen-2-yl)piperidine-4-carboxylate (**2u**) was obtained according to the General Procedure from methyl **1-(2-(*p*-tolyl)ethanethioyl)piperidine-4-carboxylate** (**1u**) (146 mg, 0.5 mmol).

Yield: 116 mg (80%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 142 – 144 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.15 (s, 1H), 3.71 (s, 3H), 3.58 – 3.65 (m, 2H), 2.89 – 2.99 (m, 2H), 2.41 – 2.53 (m, 1H), 2.39 (s, 3H), 1.98 – 2.08 (m, 2H), 1.83 – 1.98 (m, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 175.0, 156.9, 138.2, 133.2, 131.1, 126.0, 121.7, 120.7, 99.6, 52.0, 50.8, 40.6, 27.5, 21.5.

FT-IR (neat): ν_{max} (cm^{-1}) 2950, 2864, 2826, 1834, 1726, 1585, 1560, 1548, 1537, 1493, 1474, 1466, 1457, 1442, 1435, 1393, 1385, 1338, 1324, 1314, 1304, 1295, 1289, 1273, 1260, 1254, 1250, 1228, 1179, 1172, 1166, 1154, 1146, 1119, 1104, 1069, 1029, 999, 993, 985, 979, 964, 951, 927, 912, 907, 902, 883, 868, 851, 822, 781, 765, 729, 723, 697, 687, 649, 633, 587.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{20}NO_2S^+$ 290.1209; Found 290.1214 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.31.

1-(6-Methylbenzo[*b*]thiophen-2-yl)piperidine-4-carboxamide (**2v**) was obtained according to the General Procedure from **1-(2-(*p*-tolyl)ethanethioyl)piperidine-4-carboxamide** (**1v**) (138 mg, 0.5 mmol).

Yield: 114 mg (83%).

Physical state: white solid.

Mp (EtOAc–*n*-hexane): ~ 220 °C.

^{1}H NMR (400 MHz, DMSO-*d6*): δ = 7.45 (s, 1H), 7.43 (brs, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.01 (dd, J = 8.0, 1.6 Hz, 1H), 6.83 (brs, 1H), 6.22 (s, 1H), 3.53 -3.61 (m, 2H), 2.85 (td, J = 12.3, 2.9 Hz, 2H), 2.31 (s, 3H), 2.21 – 2.34 (m, 1H), 1.75 – 1.83 (m, 2H), 1.59 – 1.72 (m, 2H).

^{13}C{^{1}H} NMR (100 MHz, DMSO-*d6*): δ = 176.1, 156.5, 138.3, 132.1, 130.1, 125.9, 121.4, 120.3, 98.5, 50.3, 40.9, 27.6, 21.0.

FT-IR (neat): ν_{max} (cm^{-1}) 3370, 3254, 3181, 2993, 2818, 1645, 1578, 1559, 1545, 1531, 1483, 1471, 1464, 1448, 1392, 1383, 1323, 1311, 1302, 1266, 1259, 1252, 1224, 1207, 1193, 1179, 1157, 1146, 1137, 1099, 1066, 1020, 961, 926, 882, 818, 751, 722, 696, 627, 582, 570, 532.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{19}N_2OS^+$ 275.1213; Found 275.1219 (2 ppm).

4-(6-Isobutyl-3-methylbenzo[*b*]thiophen-2-yl)morpholine (**2y**) was obtained according to the General Procedure from 2-**(4-isobutylphenyl)-1-morpholinopropane-1-thione** (**1y**) (2.93 g, 10 mmol) with some modifications: HTIB was added to a cooled to 15 – 20 °C solution for 5 min. After the end of the reaction HFIP was distilled from the reaction mixture (≅ 90 ml). Iodobenzene was also isolated by column chromatography in a 78% (1.61 g) yield.

Yield: 2.46 g (85%).

Physical state: white solid.

Mp (EtOAc – *n*-hexane): 57 – 59 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.53 (m, 2H), 7.14 (dd, J = 8.2, 1.5 Hz, 1H), 3.84 – 3.91 (m, 4H), 2.95 – 3.02 (m, 4H), 2.56 (d, J = 7.2 Hz, 2H), 2.29 (s, 3H), 1.83 – 1.96 (m, 1H), 0.91 (d, J = 6.6 Hz, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 150.9, 137.6, 137.4, 135.4, 125.8, 122.8, 120.9, 120.6, 67.2, 54.2, 45.6, 30.6, 22.5, 11.3.

FT-IR (neat): ν_{max} (cm^{-1}) 2954, 2933, 2915, 2879, 2861, 2835, 2820, 1625, 1582, 1552, 1541, 1501, 1472, 1456, 1439, 1420, 1405, 1393, 1382, 1376, 1366, 1354, 1348, 1332, 1321, 1303, 1293, 1274, 1258, 1229, 1193, 1147, 1138, 1131, 1113, 1095, 1084, 1075, 1069, 1051, 1034, 1004, 985, 936, 923, 897, 879, 845, 836, 814, 799, 784, 777, 746, 741, 715, 707, 693, 682, 653.

HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{24}NOS^+$ 290.1573; Found 290.1578 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.44.

2-Benzyl-4,5-dihydrobenzo[*f*][1,3]thiazepine (**3**) was obtained according to the General Procedure from ***N*-phenethyl-2-phenylethanethioamide** (**1w**) (128 mg, 0.5 mmol).

Yield: 58 mg (46%).

Physical state: light-yellow viscous oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 – 7.39 (m, 4H), 7.24 – 7.28 (m, 1H), 7.00 – 7.21 (m, 4H), 4.06 – 4.13 (m, 2H), 3.73 (s, 2H), 3.14 – 3.21 (m, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 155.7, 143.4, 136.9, 132.8, 129.3, 129.2, 128.6, 128.6, 127.3, 127.0, 126.2, 52.1, 49.2, 35.6.

FT-IR (neat): ν_{max} (cm^{-1}) 3026, 2985, 2912, 1641, 1503, 1494, 1485, 1476, 1460, 1453, 1448, 1442, 1376, 1356, 1314, 1275, 1225, 1189, 1135, 1078, 1055, 1030, 1015, 998, 881, 836, 795, 747, 715, 697, 686, 679, 669, 658, 629, 572, 544, 525.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{16}NS^+$ 254.0998; Found 254.1002 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.22.

2-Benzyl-6-methoxybenzo[*d*]thiazole (**4**)[21] was obtained according to the General Procedure from ***N*-(4-methoxyphenyl)-2-phenylethanethioamide** (**1x**) (128 mg, 0.5 mmol).

Yield: 43 mg (34%).

Physical state: yellow viscous oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, J = 8.9 Hz, 1H), 7.28 – 7.43 (m, 5H), 7.25 (d, J = 2.5 Hz, 1H), 7.05 (dd, J = 8.9, 2.5 Hz, 1H), 4.40 (s, 2H), 3.85 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 168.6, 157.5, 147.8, 137.5, 137.1, 129.2, 129.0, 127.4, 123.3, 115.2, 104.3, 55.9, 40.6.

FT-IR (neat): ν_{max} (cm^{-1}) 3061, 3042, 3027, 2979, 2935, 2862, 2831, 1658, 1602, 1572, 1558, 1541, 1518, 1502, 1494, 1480, 1464, 1456, 1453, 1443, 1433, 1349, 1316, 1290, 1256, 1243, 1226, 1189, 1180, 1143, 1099, 1080, 1052, 1037, 1025, 957, 895, 877, 827, 778, 757, 726, 700, 682, 674, 652, 635, 621, 608, 597, 589, 563, 552, 541, 533, 525.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{14}NOS^+$ 256.0791; Found 256.0796 (2 ppm).

R_f (*n*-hexane – EtOAc = 20:1) = 0.22.

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Supporting Information

Additional optimization results, experimental details, synthesis of starting materials and full characterization data.

Conflict of Interest

The authors declare no conflict of interest.

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