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A Highly Efficient $CuCl_2$-Catalyzed C–S Coupling of Aryl Iodides with Tetraalkylthiuram Disulfides: Synthesis of Aryl Dithiocarbamates

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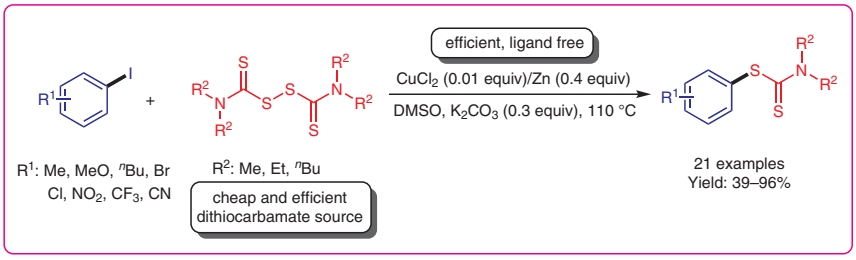

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Abstract A highly efficient copper(II)-catalyzed C–S cross-coupling reaction of aryl iodides with tetraalkylthiuram disulfides was developed. With only 1 mol% of $CuCl_2$ as catalyst, zinc powder as reductant, and K_2CO_3 as base, aryl iodides reacted with tetraalkylthiuram disulfides in DMSO furnishing the corresponding aryl dithiocarbamates in good to excellent yields. This protocol is an improvement of previous work, it features convenient performance, low addition of catalyst, no requirement for any ligand, and provides good yields. The method has a broad substrate scope and uses cheap and readily available starting materials.

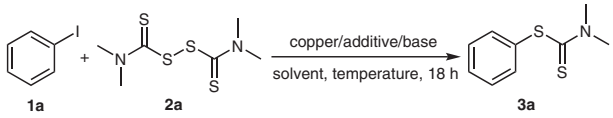
Key words coupling, aryl iodide, disulfide, synthesis, dithiocarbamate

Organic dithiocarbamates (carbamodithioates) are popular in organic chemistry due to their versatile applications. They have attracted wide attention since they serve as important synthetic intermediates.[1] Moreover, they are popular blocks in biologically active compounds, such as monoacylglycerol lipase inhibitors,[2] leukemic cells inhibitors,[3] thymocytes inhibitors,[4] antitumor agents,[5] and antibacterial agents.[6] Compared to methods developed for other carbon–heteroatom bonds, the highly desirably efficient and selective construction of C–S bonds in transition-metal-catalyzed transformations remains relatively rare. In recent decades, several excellent catalytic systems involving transition metals (palladium,[7] nickel,[8] copper,[9] and iron[10]) have been found for C–S bond formation, leading to the development of practical procedures for organic synthesis. Conventionally, protocols for the synthesis of dithiocarbamates involve the use of organometallic reagents with tetramethylthiuram disulfide[11] sodium salt of dithiocarbamic acid with diaryliodonium salts[12] or haloarenes.[13] In recent years, one-pot three-component reactions have been reported using amines and carbon disulfide with electrophiles, including alkyl[14] or aryl halides,[15] arenediazonium fluoroborates,[16] pentafluorobenzonitrile,[17] and arylboronic acids.[18] However, these methods are still limited by the need for multiple reaction steps, air-sensitive organometallic reagents, flammable and explosive substrates or reagents, and high substrate molar ratios. Recently, we described the synthesis of aryl dithiocarbamates catalyzed by Cu_2O in the presence of Cs_2CO_3.[19] To improve this methodology (using less catalyst and cheaper base), and as continuing interests for developing disulfides and relevant applications,[20] we hereby report a more efficient method for the preparation of aryl dithiocarbamates through C–S coupling.

We began the study by examining the cross-coupling reaction of iodobenzene (**1a**) with tetramethylthiuram disulfide (**2a**, TMTD) under open air conditions. A series of reaction parameters, such as catalyst, base, additive, and solvent, as well as their loadings, were surveyed. The reaction did not proceed under 'super base'[21] conditions (Table 1, entry 1). The addition of a catalyst ($CuCl_2$ or CuO, 5 mol%) did not promote the reaction (entries 2–4). To our delight, with the addition of a catalyst (CuO, 5 mol%) and zinc powder (0.6 equiv), the desired aryl dithiocarbamate was obtained in 71% yield (entry 5). Thus, a series of copper sources were examined (entries 5–12) and this revealed that $CuCl_2$ was the best catalyst (entry 8). The base screening (entries 8, 13–17) showed that K_2CO_3 and Na_2CO_3 were helpful for the reaction and K_2CO_3 was slightly better (entry 8). Control experiments listed in entries 17 and 18 showed that copper and K_2CO_3 were crucial for the model reaction. The addition of other additives, such as Mg or Fe (entries 19 and 20) which serve as a reductant, also had a positive effect on the reaction, but they were inferior to Zn. The examination of solvents (entries 8, 21, and 22) and temperatures (entries 8, 23 and 24) showed that DMSO was the best solvent, and 110 °C was the optimal reaction temperature. Surprisingly, the yield dropped very little when the catalyst loading was decreased from 10 mol% to 1 mol% (entries 8,

25, and 26). The screening for base loading (entries 27–30) and zinc loading (entries 31–34) demonstrated that 0.3 equiv of base and 0.4 equiv of Zn was the best loading amount. The optimal reaction conditions are summarized in entry 32.

Table 1 Optimization of the Reaction Conditions[a]



1a 2a 3a

Entry	[Cu] (mol%)	Additive (equiv)	Base (equiv)	Solvent	Temp. (°C)	Yield (%)[b]
1	–	–	KOH (1)	DMSO	110	–[c]
2	$CuCl_2$ (5)	–	KOH (1)	DMSO	110	–[c]
3	$CuCl_2$ (5)	–	K_2CO_3 (1)	DMSO	110	–[c]
4	CuO (5)	–	K_2CO_3 (1)	DMSO	110	–[c]
5	CuO (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	71
6	$CuBr_2$ (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	77
7	$Cu(OAc)_2$ (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	73
8	$CuCl_2$ (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	95
9	CuBr (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	86
10	Cu_2O (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	91
11	CuCl (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	90
12	CuI (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	89
13	$CuCl_2$ (5)	Zn (0.6)	Na_2CO_3 (1)	DMSO	110	92
14	$CuCl_2$ (5)	Zn (0.6)	KOH (1)	DMSO	110	trace
15	$CuCl_2$ (5)	Zn (0.6)	NaOH (1)	DMSO	110	trace
16	$CuCl_2$ (5)	Zn (0.6)	$NaHCO_3$ (1)	DMSO	110	trace
17	$CuCl_2$ (5)	Zn (0.6)	–	DMSO	110	–[c]
18	–	Zn (0.6)	K_2CO_3 (1)	DMSO	110	–[c]
19	$CuCl_2$ (5)	Mg (0.6)	K_2CO_3 (1)	DMSO	110	70
20	$CuCl_2$ (5)	Fe (0.6)	K_2CO_3 (1)	DMSO	110	65
21	$CuCl_2$ (5)	Zn (0.6)	K_2CO_3 (1)	DMF	110	85
22	$CuCl_2$ (5)	Zn (0.6)	K_2CO_3 (1)	DMAc	110	89
23	$CuCl_2$ (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	130	96
24	$CuCl_2$ (5)	Zn (0.6)	K_2CO_3 (1)	DMSO	90	50
25	$CuCl_2$ (10)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	95
26	$CuCl_2$ (1)	Zn (0.6)	K_2CO_3 (1)	DMSO	110	94
27	$CuCl_2$ (1)	Zn (0.6)	K_2CO_3 (0.1)	DMSO	110	43
28	$CuCl_2$ (1)	Zn (0.6)	K_2CO_3 (0.3)	DMSO	110	94
29	$CuCl_2$ (1)	Zn (0.6)	K_2CO_3 (0.5)	DMSO	110	94
30	$CuCl_2$ (1)	Zn (0.6)	K_2CO_3 (0.7)	DMSO	110	95
31	$CuCl_2$ (1)	Zn (0.2)	K_2CO_3 (0.3)	DMSO	110	80
32	**$CuCl_2$ (1)**	**Zn (0.4)**	**K_2CO_3 (0.3)**	**DMSO**	**110**	**93**
33	$CuCl_2$ (1)	Zn (0.8)	K_2CO_3 (0.3)	DMSO	110	94
34	$CuCl_2$ (1)	Zn (1)	K_2CO_3 (0.3)	DMSO	110	95

[a] Reaction conditions: iodobenzene (**1a**, 1.0 mmol), tetramethylthiuram disulfide (**2a**, 0.6 mmol), [Cu] (mol%), additive (equiv), base (equiv), DMSO (2 mL), sealed tube, heat, 18 h.
[b] Isolated yields.
[c] No reaction.

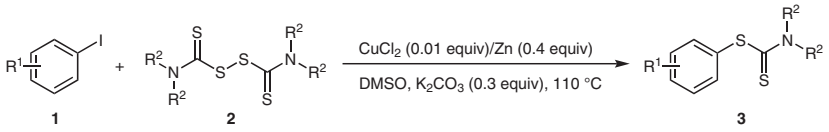
With the optimal reaction conditions in hand, the substrate scope was investigated. As shown in Table 2, a variety of substituted iodobenzenes were coupled with tetramethylthiuram disulfide (**2a**, TMTD), giving the desired products with good to excellent yields (Table 2, entries 1–13). Electron-donating groups (Me, MeO, Bu) attached to the aryl ring promoted the reaction slightly (entries 2–6), and electron-withdrawing groups (Br, NO_2, CN) deactivated the aryl iodides, and provided the products in lower yields (entries 7, 8, 10, 11, and 13). *ortho* Steric hindrance also influenced the reaction and slightly decreased the yields (entries 8, 10, and 11). In addition, tetraethylthiuram disulfide (**2b**, TETD) and tetrabutylthiuram disulfide (**2c**, TBTD) were also suitable for *S*-arylation under standard reaction conditions. The corresponding products were obtained in slightly lower yields due to the possible steric hindrance from the alkyl group of the disulfide (entries 14–19). Subsequently, a fused-ring compound (entry 20) and a heterocyclic substrate (entry 21) underwent the C–S coupling, giving the target molecules in moderate yields. Aryl bromides and chlorides (entries 22 and 23) did not undergo C–S couplings, indicating some limitations of the method.

A possible mechanism is proposed in Scheme 1 according to experiments and previous literature.[18,22] First, oxidative addition of the aryl iodide with the copper catalyst may provide intermediate **a**. Then, the disulfide coordinates to the catalyst to provide intermediate **b**, which undergoes a bond breaking to generate intermediate species **c** and the thiolate **d**. Intermediate **c** easily provides the desired C–S cross-coupled product **e** by reductive elimination. Intermediate **d** together with intermediate **a** regenerate the copper(III) species **c** and then provide the desired product **e**. Zinc plays the role of reductant.

In summary, we developed a highly efficient copper-catalyzed C–S coupling by using tetraalkylthiuram disulfides as starting materials. In the presence of the $CuCl_2$/Zn/K_2CO_3 system, with no additional ligand, aryl iodides reacted with tetraalkylthiuram disulfides in DMSO to give the corresponding aryl dithiocarbamates in good to excellent yields. This method features easy performance, low addition of catalyst, no requirement for any ligand, good yields, broad substrate scope, and the use of cheap and readily available starting materials, illustrating its potential

synthetic value for the convenient preparation of some potentially biologically active compounds.[22] Currently, the protocol could not be applied to the less reactive aryl bromides or chlorides. Further details of this protocol and the related applications are under study in our laboratory.

Table 2 Synthesis of Aryl Dithiocarbamates[a]



1 2 3

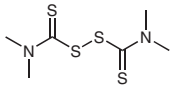
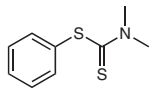
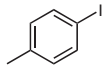
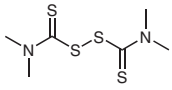
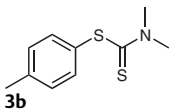
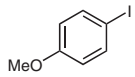
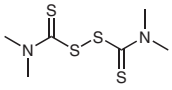
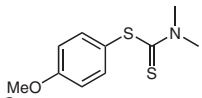
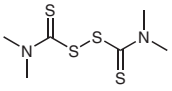
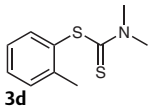
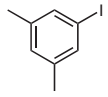
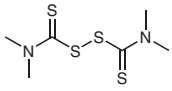
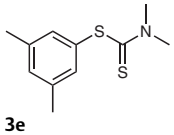
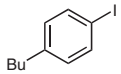
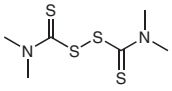
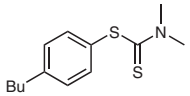
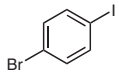
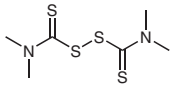
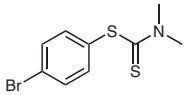
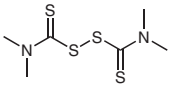
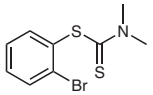
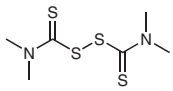
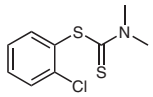
Entry	Substrate **1**	Substrate **2**	Product **3**	Yield (%)[b]
1	 **1a**	 **2a**	 **3a**	94
2	 **1b**	 **2a**	 **3b**	92
3	 **1c**	 **2a**	 **3c**	89
4	 **1d**	 **2a**	 **3d**	90
5	 **1e**	 **2a**	 **3e**	94
6	 **1f**	 **2a**	 **3f**	96
7	 **1g**	 **2a**	 **3g**	89
8	 **1h**	 **2a**	 **3h**	80
9	 **1i**	 **2a**	 **3i**	96

Table 2 (continued)

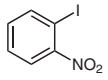
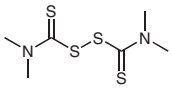
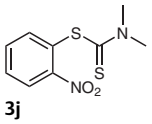
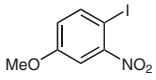
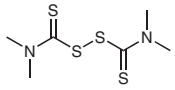
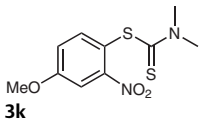
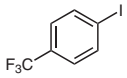
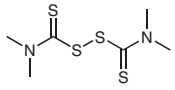
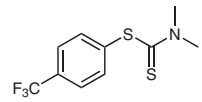
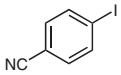
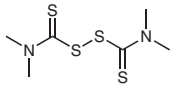
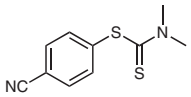
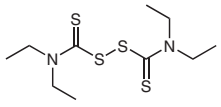
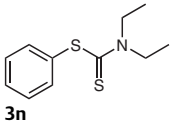
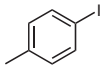
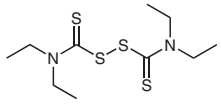
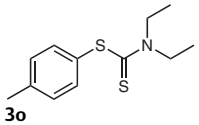
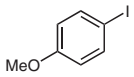
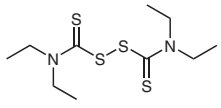
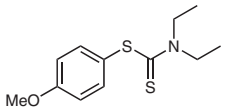
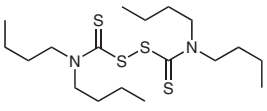
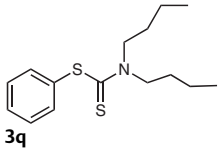
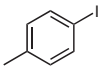
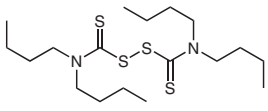
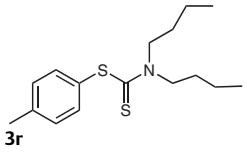
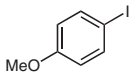
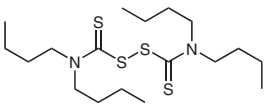
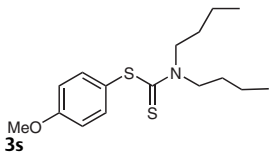
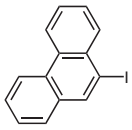
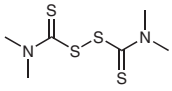
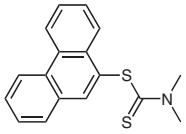
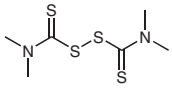
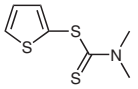
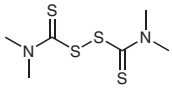
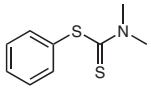
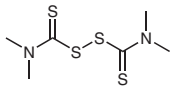
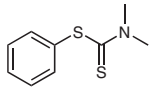
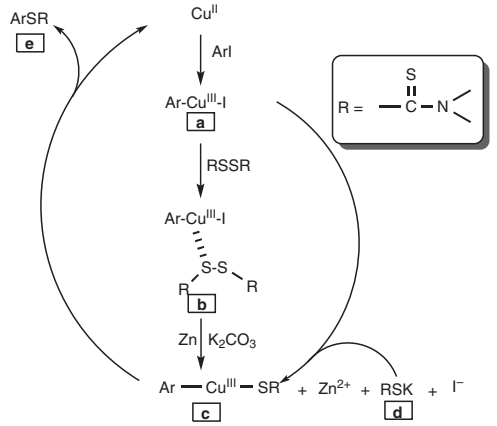
Entry	Substrate **1**	Substrate **2**	Product **3**	Yield (%)[b]
10	 **1j**	 **2a**	 **3j**	84
11	 **1k**	 **2a**	 **3k**	73
12	 **1l**	 **2a**	 **3l**	92
13	 **1m**	 **2a**	 **3m**	74
14	 **1a**	 **2b**	 **3n**	81
15	 **1b**	 **2b**	 **3o**	83
16	 **1c**	 **2b**	 **3p**	80
17	 **1a**	 **2c**	 **3q**	82
18	 **1b**	 **2c**	 **3r**	81
19	 **1c**	 **2c**	 **3s**	82

Table 2 (continued)

Entry	Substrate **1**	Substrate **2**	Product **3**	Yield (%)[b]
20	 **1s**	 **2a**	 **3t**	53
21	 **1t**	 **2a**	 **3u**	39
22[c]	 **1u**	 **2a**	 **3a**	0
23[d]	 **1v**	 **2a**	 **3a**	0

[a] Reaction conditions: iodobenzene **1** (1.0 mmol), tetraalkylthiuram disulfide (0.6 mmol), [Cu] (1 mol%), zinc (0.4 mmol), K_2CO_3 (0.3 mmol), DMSO (2 mL), sealed tube, 110 °C, 18 h.
[b] Isolated yields.
[c] A less reactive aryl bromide was used.
[d] A less reactive aryl chloride was used.



Scheme 1 Possible reaction mechanism for C–S coupling of aryl iodide and disulfide

All starting materials were purchased from commercial suppliers and used without further purification unless otherwise stated. Yields refer to isolated compounds estimated to be >95% pure as determined by ^{1}H NMR and capillary GC analysis. NMR spectra were recorded on a Bruker AM400 or Bruker AM 300 NMR instrument in $CDCl_3$ using TMS as an internal standard. Melting points were determined on a Kofler micro melting point apparatus without correction. HRMS were recorded on a Finnigan MAT 95Q or Finnigan 90 mass instrument (ESI). TLC was performed using aluminum plates coated with silica gel (Merck 60, F-254) and visualized with UV light at 254 nm. Column chromatography was performed on silica gel (200–250 mesh) with petroleum ether (PE)/EtOAc as eluent.

Phenyl Dimethylcarbamodithioate (3a) (Table 2, Entry 1); Typical Procedure

$CuCl_2$ (1.4 mg, 0.01 mmol), zinc (powder) (26 mg, 0.4 mmol), DMSO (2.0 mL), K_2CO_3 (41.4 mg, 0.3 mmol), tetramethylthiuram disulfide (**2a**, 144 mg, 0.6 mmol), and iodobenzene (**1a**, 204 mg, 1 mmol) were added to a sealed tube equipped with a septum and magnetic stirring bar, the mixture was stirred at 110 °C and monitored (TLC) until consumption of the starting material (about 18 h). The mixture was cooled to r.t., quenched with sat. NH_4Cl solution and then extracted with EtOAc. The crude solution was dried (anhyd Na_2SO_4) and evaporated under vacuum. The residue was purified by flash column chromatography (silica gel, PE/EtOAc 5:1) to give **3a** (185 mg, 94%) as a white solid; mp 90–92 °C.

^{1}H NMR(400 MHz, $CDCl_3$): δ = 7.41–7.50 (m, 5 H), 3.55 (s, 3 H), 3.49 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 136.9, 131.7, 130.0, 129.1, 45.7, 41.9.

HRMS (ESI): calcd for $C_9H_{11}NS_2$ (197.0333); found: 197.0339.

p-Tolyl Dimethylcarbamodithioate (3b) (Table 2, Entry 2)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 7:1) to give **3b** (194 mg, 92%) as a white solid; mp 107–111 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (d, *J* = 8.0 Hz, 2 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 3.55 (s, 3 H), 3.49 (s, 3 H), 2.40 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.1, 140.3, 136.7, 130.0, 128.2, 45.7, 41.9, 21.5.

HRMS (ESI): calcd for $C_{10}H_{13}NS_2$ (211.0489); found: 211.0490.

4-Methoxyphenyl Dimethylcarbamodithioate (3c) (Table 2, Entry 3)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 7:1) to give **3c** (202 mg, 89%) as a white solid; mp 97–99 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–6.95 (m, 4 H), 3.83 (s, 3 H), 3.54 (s, 3 H), 3.48 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.7, 161.1, 138.4, 122.6, 114.7, 55.3, 45.8, 41.9.

HRMS (ESI): calcd for $C_{10}H_{13}NOS_2$ (227.0439); found: 227.0445.

***o*-Tolyl Dimethylcarbamodithioate (3d) (Table 2, Entry 4)**

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 7:1) to give **3d** (190 mg, 90%) as a white solid; mp 81–82 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.23 (m, 4 H), 3.53 (s, 3 H), 3.49 (s, 3 H), 2.40 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 143.8, 137.7, 133.7, 131.1, 130.7, 126.72, 45.5, 42.0, 20.9.

HRMS (ESI): calcd for $C_{10}H_{13}NS_2$ (211.0489); found: 211.0469.

3,5-Dimethylphenyl Dimethylcarbamodithioate (3e) (Table 2, Entry 5)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 5:1) to give **3e** (211 mg, 94%) as a white solid; mp 84–85 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10 (s, 3 H), 3.55 (s, 3 H), 3.48 (s, 3 H), 2.34 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0, 138.6, 134.4, 131.9, 131.0, 45.6, 42.0, 21.2.

HRMS (ESI): calcd for $C_{11}H_{15}NS_2$ (225.0646); found: 225.0655.

4-Butylphenyl Dimethylcarbamodithioate (3f) (Table 2, Entry 6)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 7:1) to give **3f** (243 mg, 96%) as a white solid; mp 61–62 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.34 (m, 2 H), 7.25–7.23 (m, 2 H), 3.54 (s, 3 H), 3.48 (s, 3 H), 2.65 (m, 2 H), 1.65–1.58 (m, 2 H), 1.39–1.33 (m, 2 H), 0.92 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.1, 145.2, 136.7, 129.2, 128.4, 45.6, 41.9, 35.5, 33.2, 22.3, 13.9.

HRMS (ESI): calcd for $C_{13}H_{19}NS_2$ (253.0959); found: 253.0962.

4-Bromophenyl Dimethylcarbamodithioate (3g) (Table 2, Entry 7)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 7:1) to give **3g** (246 mg, 89%) as a white solid; mp 120–121 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 3.55 (s, 3 H), 3.49 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 138.4, 132.3, 130.7, 124.9, 45.7, 42.0.

HRMS (ESI): calcd for $C_9H_{10}BrNS_2$ (274.9438); found: 274.9445.

2-Bromophenyl Dimethylcarbamodithioate (3h) (Table 2, Entry 8)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 7:1) to give **3h** (203 mg, 80%) as a white solid; mp 90–92 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.0 Hz, 1 H), 7.55 (d, *J* = 8.0 Hz, 1 H), 7.31–7.22 (m, 2 H), 3.52 (s, 3 H), 3.48 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.9, 139.7, 133.5, 133.1, 131.8, 131.6, 128.1, 45.5, 42.1.

HRMS (ESI): calcd for $C_9H_{10}BrNS_2$ (274.9438); found: 274.9436.

2-Chlorophenyl Dimethylcarbamodithioate (3i) (Table 2, Entry 9)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 7:1) to give **3i** (222 mg, 96%) as a white solid; mp 105–107 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.52 (m, 2 H), 7.45–7.39 (m, 1 H), 7.36–7.30 (m, 1 H), 3.55 (s, 3 H), 3.52 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.9, 140.5, 139.1, 131.7, 131.0, 130.2, 127.4, 45.6, 42.1.

HRMS (ESI): calcd for $C_9H_{10}ClNS_2$ (230.9943); found: 230.9947.

2-Nitrophenyl Dimethylcarbamodithioate (3j) (Table 2, Entry 10)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 4:1) to give **3j** (203 mg, 84%) as a yellow solid; mp 124–126 °C.

^{1}H NMR(400 MHz, $CDCl_3$): δ = 8.00–7.97 (m, 1 H), 7.67–7.60 (m, 3 H), 3.53 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.9, 139.6, 132.6, 131.0, 126.5, 124.9, 45.6, 42.4.

HRMS (ESI): calcd for $C_9H_{10}N_2O_2S_2$ (242.0184); found: 242.0191.

4-Methoxy-2-nitrophenyl Dimethylcarbamodithioate (3k) (Table 2, Entry 11)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 4:1) to give **3k** (199 mg, 73%) as a yellow solid; mp 115–117 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.52 (d, *J* = 9 Hz, 1 H), 7.49 (d, *J* = 3 Hz, 1 H), 7.17–7.13 (m, 1 H), 3.91 (s, 3 H), 3.53 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.4, 161.5, 154.0, 141.0, 118.6, 116.7, 110.4, 56.0, 45.7, 42.2.

HRMS (ESI): calcd for $C_{10}H_{12}N_2O_3S_2$ (272.0289); found: 272.0294.

4-(Trifluoromethyl)phenyl Dimethylcarbamodithioate (3l) (Table 2, Entry 12)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 4:1) to give **3l** (244 mg, 92%) as a white solid; mp 85–86 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.0 Hz, 2 H), 7.59 (d, *J* = 8.0 Hz, 2 H), 3.54 (s, 3 H), 3.49 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 137.1, 136.0, 131.7 (t, *J* = 33 Hz), 125.8 (t, *J* = 4 Hz), 123.8 (d, *J* = 270 Hz), 45.6, 42.0.

HRMS (ESI): calcd for $C_{10}H_{10}F_3NS_2$ (265.0207); found: 265.0211.

4-Cyanophenyl Dimethylcarbamodithioate (3m) (Table 2, Entry 13)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 5:1) to give **3m** (164 mg, 74%) as a white solid; mp 125–126 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.68 (m, 2 H), 7.60–7.57 (m, 2 H), 3.55 (s, 3 H), 3.51 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.9, 137.5, 137.4, 132.4, 118.2, 113.6, 45.6, 42.1.

HRMS (ESI): calcd for $C_{10}H_{10}N_2S_2$ (222.0285); found: 222.0291.

Phenyl Diethylcarbamodithioate (3n) (Table 2, Entry 14)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 10:1) to give **3n** (183 mg, 81%) as pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 12.0 Hz, 5 H), 4.02 (d, *J* = 4.0 Hz, 2 H), 3.84 (d, *J* = 8.0 Hz, 2 H), 1.39 (t, *J* = 4.0 Hz, 3 H), 1.29 (d, *J* = 4.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.9, 137.2, 131.6, 130.0, 129.0, 49.9, 47.3, 12.8, 11.6.

HRMS (ESI): calcd for $C_{11}H_{15}NS_2$ (225.0646); found: 225.0652.

***p*-Tolyl Diethylcarbamodithioate (3o) (Table 2, Entry 15)**

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 15:1) to give **3o** (199 mg, 83%) as a white solid; mp 75–76 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 8.0 Hz, 2 H), 7.16 (d, *J* = 4.0 Hz, 2 H), 3.94 (d, *J* = 8.0 Hz, 2 H), 3.76 (d, *J* = 4.0 Hz, 2 H), 2.32 (s, 3 H), 1.31 (t, *J* = 4.0 Hz, 3 H), 1.20 (t, *J* = 4.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 140.2, 137.0, 129.9, 128.1, 49.9, 47.2, 21.5, 12.7, 11.6.

HRMS (ESI): calcd for $C_{12}H_{17}NS_2$ (239.0802); found: 239.0812.

4-Methoxyphenyl Diethylcarbamodithioate (3p) (Table 2, Entry 16)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 7:1) to give **3p** (204 mg, 80%) as a white solid; mp 73–75 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (d, *J* = 8.0 Hz, 2 H), 6.80 (d, *J* = 8.0 Hz, 2 H), 3.87 (d, *J* = 8.0 Hz, 2 H), 3.68 (s, 5 H), 1.24 (t, *J* = 6.4 Hz, 3 H), 1.13 (t, *J* = 6.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.1, 161.0, 138.6, 122.4, 114.6, 55.3, 50.0, 47.1, 12.7, 11.6.

HRMS (ESI): calcd for $C_{12}H_{17}NOS_2$ (255.0752); found: 255.0759.

Phenyl Dibutylcarbamodithioate (3q) (Table 2, Entry 17)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 20:1) to give **3q** (230 mg, 82%) as a brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.33 (m, 5 H), 3.85 (t, *J* = 4.0 Hz, 2 H), 3.67 (t, *J* = 4.0 Hz, 2 H), 1.72–1.64 (m, 4 H), 1.35–1.25 (m, 4 H), 0.93 (t, *J* = 4.0 Hz, 3 H), 0.85 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 137.1, 131.8, 129.9, 129.0, 55.3, 53.1, 29.6, 28.4, 20.2, 13.9, 13.8.

HRMS (ESI): calcd for $C_{15}H_{23}NS_2$ (281.1272); found: 281.1278.

***p*-Tolyl Dibutylcarbamodithioate (3r) (Table 2, Entry 18)**

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 20:1) to give **3r** (239 mg, 81%) as a brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (d, *J* = 4.0 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 3.89 (t, *J* = 4.0 Hz, 2 H), 3.71 (t, *J* = 8.0 Hz, 2 H), 2.35 (s, 3 H), 1.76–1.68 (m, 4 H), 1.41–1.27 (m, 4 H), 0.96 (t, *J* = 8.0 Hz, 3 H), 0.89 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.8, 140.1, 136.9, 129.9, 128.3, 55.4, 53.0, 29.6, 28.4, 21.5, 20.2, 13.9, 13.8.

HRMS (ESI): calcd for $C_{16}H_{25}NS_2$ (295.1428); found: 295.1433.

4-Methoxyphenyl Dibutylcarbamodithioate (3s) (Table 2, Entry 19)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 20:1) to give **3s** (255 mg, 82%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.0 Hz, 2 H), 6.87 (d, *J* = 12.0 Hz, 2 H), 3.86 (s, 2 H), 3.75 (s, 3 H), 3.69 (t, *J* = 4.0 Hz, 2 H), 1.76–1.72 (m, 4 H), 1.38–1.23 (m, 4 H), 0.93 (t, *J* = 8.0 Hz, 3 H), 0.86 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.4, 161.0, 138.6, 122.6, 114.6, 55.5, 55.3, 52.9, 29.6, 28.4, 20.1, 13.9, 13.8.

HRMS (ESI): calcd for $C_{16}H_{25}NOS_2$ (311.1378); found: 311.1382.

Phenanthren-9-yl Dimethylcarbamodithioate (3t) (Table 2, Entry 20)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 4:1) to give **3t** (157 mg, 53%) as a white solid; mp >175 °C (dec.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.73–8.69 (m, 2 H), 8.32 (m, 1 H), 8.09 (s, 1 H), 7.89 (m, 1 H), 7.73–7.59 (m, 4 H), 3.64 (s, 3 H), 3.57 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.4, 138.8, 132.4, 131.6, 131.5, 131.0, 130.1, 129.1, 128.2, 127.7, 127.1, 126.8, 126.7, 123.0, 122.7, 45.5, 42.1.

HRMS (ESI): calcd for $C_{17}H_{15}NS_2$ (297.0646); found: 297.0652.

Thiophen-2-yl Dimethylcarbamodithioate (3u) (Table 2, Entry 21)

According to the TP, the residue was purified by flash chromatography (silica gel, PE/EtOAc 4:1) give **3u** (79 mg, 39%) as a white solid; mp 94–95.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (m, 1 H), 7.23 (m, 1 H), 7.13 (m, 1 H), 3.54 (s, 3 H), 3.48 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.3, 138.7, 133.4, 129.1, 127.8, 46.0, 41.7.

HRMS (ESI): calcd for $C_7H_9NS_3$ (202.9897); found: 202.9904.

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Supporting Information

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