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Synthesis of Aza-Heteroaromatic Dithiocarbamates *via* Cross-Coupling Reactions of Aza-Heteroaromatic Bromides with Tetraalkylthiuram Disulfides

Chuance Cheng,[a] Mingqin Zhao,*[a] Miao Lai,[a] Ke Zhai,[a] Bo Shi,[a] Shuai Wang,[a] Rui Luo,[a] Linbao Zhang,[b] and Zhiyong Wu*[a]

Dedication ((optional))

Abstract: The preparation of various aza-heteroaromatic dithiocarbamates from aza-heteroaromatic bromides and tetraalkylthiuram disulfides is reported. The transformation provides a convenient procedure, with good yields and functional group tolerance to various important nitrogen-containing heteroaromatic dithiocarbamates such as benzothiazole, quinoline, pyridine and pyrazine motifs. This protocol allows the facile synthesis of some potential biologically active compounds.

Introduction

Nitrogen-containing heteroaromatics are important heterocyclic compounds and widely present in bio-active natural products, pharmaceuticals, and functional materials.[1] Among them, the aza-heteroaromatic dithiocarbamates, e.g. quinolinyl, pyrazinyl and benzothiazolyl dithiocarbamates, represent one of the typical scaffolds possessing special activities (Figure 1).[2] Although the usefulness of aza-heteroaromatic dithiocarbamates has been extensively studied, the development of methodologies to form such frameworks is extremely rare. Traditionally, the approachs toward aryl dithiocarbamates involves the use of various coupling reagents, for instance, the coupling reactions of organometallic reagents with tetraalkylthiuram disulfides (Scheme 1, **a**),[3] sodium salt of dithiocarbamic acid with diaryliodonium salts[4] or haloarenes.[5] Recently, one-pot three-component reactions of amines, carbon disulfide, and various electrophiles to form the S-aryl dithiocarbamates were extensively reported.[6]

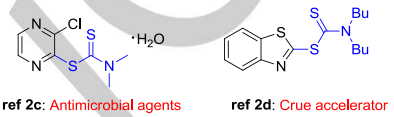
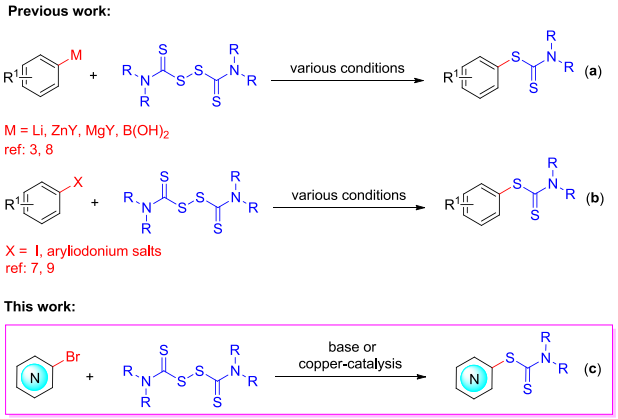


Figure 1. Examples illustrating the importance of aza-heteroaromatic dithiocarbamates.

In addition to these well-established strategies, Bolm and co-workers, in 2017, reported the preparation of aryl dithiocarbamates from aryl iodides and tetraalkylthiuram disulfides.[7a] Subsequently, Dong's group developed some alternative approaches based on the use of aryl iodides,[7b] aryl boronic acid[8] or diaryliodonium salts[9] and tetraalkylthiuram disulfides as the starting materials (Scheme 1, **b**). Despite these methods having had various levels of success, the aryl bromides and chlorides did not undergo the C-S couplings in the aryl iodides participated approach indicating some limitations of those methods.[7] A quick overview of the methodologies commonly applied to the synthesis of S-aryl dithiocarbamates shows that they mainly focus on the benzene series (Scheme 1, **a** and **b**). From the synthetic point of view, a systematic procedure for practical synthesis of aza-heteroaromatic dithiocarbamates, in particular those with benzothiazole and pyrazine skeletons are of great importance. In our continuing effort to the construction of versatile C-C and C-S bonds,[10] we report herein the synthesis of aza-heteroaromatic dithiocarbamates (Scheme 1, **c**).



Scheme 1. Strategies for the synthesis of S-aryl dithiocarbamates.

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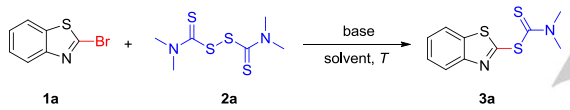
Results and Discussion

The initial screening and optimization of the reaction conditions were conducted with 2-bromo-1,3-benzothiazole (**1a**) and tetramethylthiuram disulfide (TMTD, **2a**) as substrates. The first reaction was carried out in the presence of Cs_2CO_3 (2 equiv.) in DMSO (dimethyl sulfoxide), to our delight, the product **3a** was obtained in 68% yield after 24 h at 80 °C (Table 1, entry 1). Based on these results, a range of other inorganic bases were evaluated in place of Cs_2CO_3 (Table 1, entries 2-8). All these bases proved to be efficient in this transformation. However, none of the new screened bases benefited the outcome (39-60%). No product was obtained in the absence of any bases (Table 1, entry 9). It was found that the solvent always played a crucial role in this kind of transformation. When the DMSO was replaced by DMF, toluene, CH_3CN, DCE and xylene, significantly lower yields were detected (Table 1, entries 10-14). Gratifyingly, increasing the reaction temperature to 100 °C and prolonging the reaction time to 48 h led to a further improvement of the yield (84%, Table 1, entry 17). Disappointedly, the modification of the substrate ratio failed to provide a better result of the reaction (Table 1, entry 18).

Table 1. Optimization of the reaction conditions.[a]



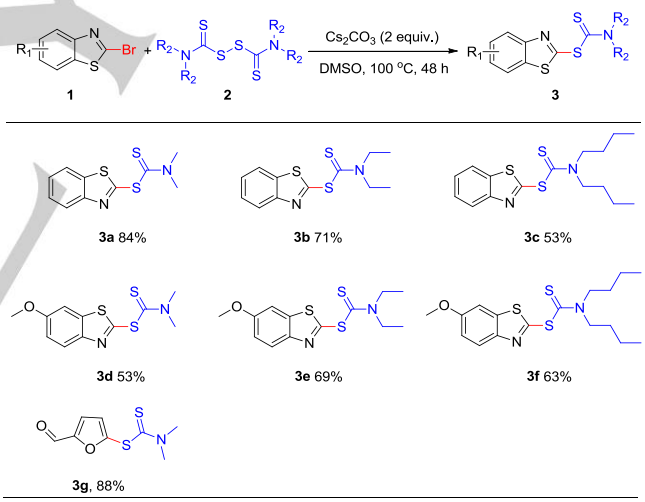
1a 2a 3a

Entry	Base	Solvent	Yield (%)[b]
1	Cs_2CO_3	DMSO	68
2	Na_2CO_3	DMSO	40
3	K_2CO_3	DMSO	60
4	$KHCO_3$	DMSO	53
5	K_3PO_4	DMSO	59
6	KOAc	DMSO	49
7	*t*-BuONa	DMSO	58
8	KOH	DMSO	39
9	none	DMSO	N.R.
10	Cs_2CO_3	DMF	36
11	Cs_2CO_3	Toluene	63
12	Cs_2CO_3	CH_3CN	50
13	Cs_2CO_3	DCE	<5
14	Cs_2CO_3	Xylene	45
15[c]	Cs_2CO_3	DMSO	80
16[d]	Cs_2CO_3	DMSO	73
17[c,e]	**Cs_2CO_3**	**DMSO**	**84**
18[f]	Cs_2CO_3	DMSO	46

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), base (2.0 equiv.), solvent (0.5 mL), 80 °C, 24 h, under air atmosphere. [b] Isolated yields. [c] Run at 100 °C. [d] Run at 120 °C. [e] Run for 48 h. [f] n (**1a**)/n (**2a**) = 0.2/0.1.

With the optimized reaction conditions in hand, 2-bromo-5-methoxy-1,3-benzothiazole **1b**, 5-bromo-2-furaldehyde **1c** were subjected to this reaction and the results were summarized in Table 2. Generally, 2-bromo-1,3-benzothiazole **1a** and 2-bromo-5-methoxy-1,3-benzothiazole **1b** reacted well with thiuram disulfides and gave the desired products in moderate to good yields (**3a-f**, 53-84%), Moreover, 5-bromo-2-furaldehyde **1c** also exhibited good reactivity and furnished the corresponding product **3g** in 88% yield. The yields of these reactions were also modulated by the presence of different alkyl substituent on the thiuram disulfides. Slightly lower yields were obtained when the longer chain substituted thiuram disulfides were used in these reactions (**3a** *vs.* **3b** and **3c**). Probably due to the difficulty of the oxidation addition step, no desired products were observed under the reaction conditions when 2-bromo-thiazole, 2-bromo-oxazole, 2-bromo-benzoxazole, 2-bromo-thiophene, 2-bromo-1H-imidazole, 2-bromo-1H-benzimidazole, 3-bromo-quinoline, bromobenzene, 4-bromotoluene, 4-bromofluorobenzene and 2-chlorobenzothiazole were studied as the substrates. Inspired by the previous published work,[7] 10 mol% of Cu_2O was introduced to the reaction system to further expand the applicability of this reaction. Gratifyingly, when 3-bromo-quinoline was again subjected to this reaction system, 75% yield of quinolin-3-yl dimethylcarbamodithioate was detected under the new conditions. Increasing the temperature to 110 °C led to a further improved yield of quinolin-3-yl dimethylcarbamodithioate (86%).

Table 2. Cross-coupling reactions of benzothiazolyl bromides **1** with thiuram disulfides **2**.[a, b]



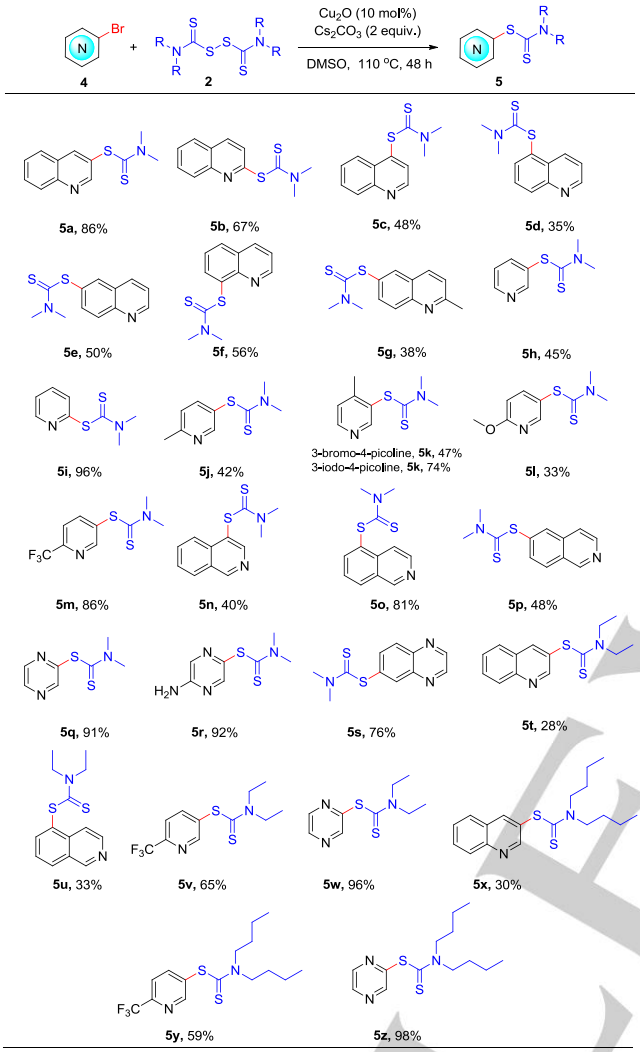
1 2 3

[a] Reaction conditions: **1** (0.2 mmol), **2** (0.2 mmol), Cs_2CO_3 (2.0 equiv.), DMSO (0.5 mL), 100 °C, 48 h. [b] Isolated yields.

With the new reaction conditions in hand, the cross-coupling reactions of other aza-heteroaromatics bromides and thiuram disulfides were investigated, and the results were summarized in Table 3. In general, all of the heterocyclic bromides tested in this new reaction system were tolerated and afforded the aza-heteroaromatic dithiocarbamates in moderate to good yields. Bromo-substituents at the 2-, 3-, 4-, 5-, 6-, and 8-positions of the quinolines were systematically evaluated and the corresponding products **5a-g** were obtained in moderate to good yields (35-86%). Noteworthily, 2, 3-bromo substituted quinolines exhibited higher reactivity compared with other quinolinyl-based

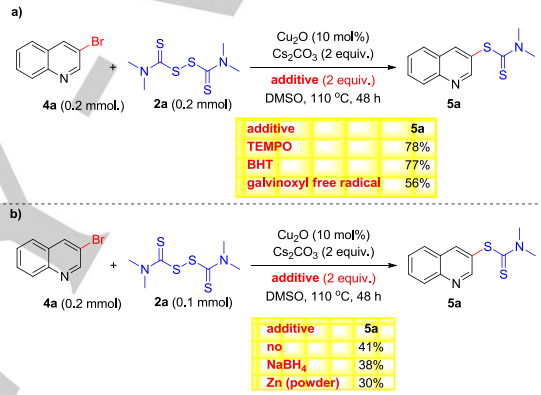
substrates (**5a**-**b** *vs*. **5c**-**f**). 6-Bromo-2-methylquinoline also afforded the desired

Table 3. Cross-coupling reactions of aza-heteroaromatics bromides 4 with thiuram disulfides 2.[a,b]

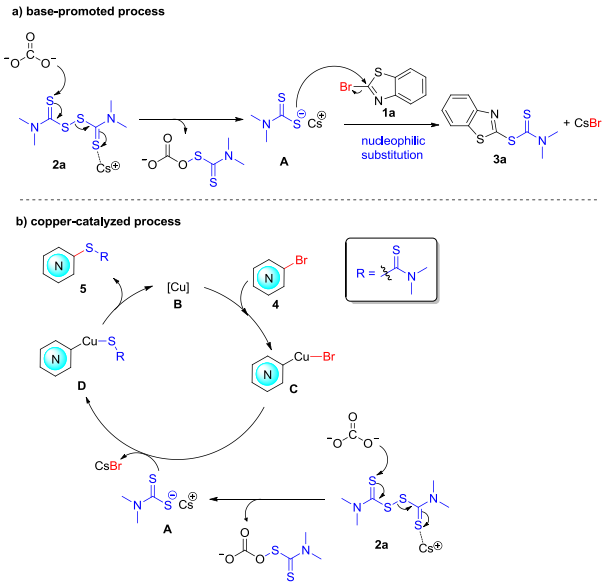


[a] Reaction conditions: **2** (0.2 mmol), **4** (0.2 mmol), Cu_2O (10 mol %), Cs_2CO_3 (2.0 equiv.), DMSO (0.5 mL), 110 °C, 48 h. [b] Isolated yields.

product **5g**, though it exhibited low efficiency in this transformation. A similar trend was observed for bromo-substituted pyridines (**5h**-**m**). In particular, trifluoromethyl pyridine worked well to give the desired product **5m** in 86% yield, which makes this reaction particularly attractive for further applications. Probably because of the unfavorable oxidation addition step, pyridines with electron-withdrawing groups gave higher yields than electron-donating ones (**5m** *vs*. **5j** and **5l**). 3-Iodo-4-picoline has also been studied as the substrate, 74% yield of product (**5k**) was obtained, which indicated a higher reactivity of the corresponding heteroaryl iodide. It was found that isoquinolinyl bromides were also tolerated and afforded the corresponding products (**5n, 5p, 5o** and **5u**) in good to good yields. 2-Bromopyrazine, 2-amino-5-bromopyrazine and 6-bromoquinoxaline also reacted well with tetramethylthiuram disulfide **2a** and the desired pyrazinyl dithiocarbamates (**5q**-**s**) were formed in good to excellent yields (76-92%). To expand the scope of this method, some *N, N, N′, N′*-tetraalkylthiuram disulfides (**2**) were evaluated using selected aza-heteroaromatic bromides as the coupling partners. *N, N, N′, N′*-Tetraalkylthiuram disulfides with ethyl and *n*-butyl (TETD, **2b**, and TBTD, **2c**, respectively) were converted to the corresponding aza-heteroaromatic dithiocarbamates in moderate to excellent yields (**5t**-**z**, 28-98%). In this new reaction system, the yields were also modulated by the presence of different alkyl substituent on the thiuram disulfides. Slightly higher yields were obtained when the longer chain substituted thiuram disulfides were used in these reactions (**5q** *vs*. **5w** and **5z**). Unfortunately, no desired products were obtained under the reaction conditions when bromobenzene, 4-bromotoluene, 4-bromofluorobenzene, 2-chloroquinoline, 4-chloroquinoline and 3-chloropyrazine-2-carbonitrile were selected as the substrates.



Scheme 2. Mechanistic experiments.



Scheme 3. Proposed reaction mechanisms.

In consideration of the versatile nature of the copper-catalyzed cross coupling process, we became interested in elucidating its mode of the reaction and the results were exhibited in Scheme 2. Initially, the reactions were performed in the presence of different radical inhibitors (2.0 equiv. of TEMPO, BHT or galvinoxyl free radical), which still gave the desired product **5a** in 78%, 77% and 56% yields, respectively (Scheme 2, **a**). The results indicated that a radical process might not involve in these transformations. According to the previous report,[7b] a reductant is generally needed to form two thiolate anions by the cleavage of disulphide bond. To determine the effect of the reductants in this reaction, 2 equiv. of sodium borohydride ($NaBH_4$) or zinc powder were added into the reaction system (Scheme 2, **b**). The control experiments indicates that none of the reductants benefited the conversion efficiency of this reaction, as only 30-38% yields of the desired product was observed, which argues against the possibility of a pathway involving the reduction step for the formation of two thiolate anions.

Considering the experimental evidence as well the previous reports,[3d,7a,10h,11] two plausible coupling mechanisms can be proposed. In Scheme 3, **a**, nucleophile **A** can be obtained from tetramethylthiuram disulfide **2a** by the support of carbonate anion and Cs ion from the base,[11a,11d] along with the release of the side product by the interaction of the carbonate anion and sulfur motif. Then, nucleophile **A** undergoes nucleophilic substitution reaction with 2-bromo-1,3-benzothiazole **1a** generating the benzothiazolyl dithiocarbamate **3a** in good yield. For the cross-coupling of heterocyclic bromides **4** and thiuram reagent **2,** a proposed catalytic cycle is depicted in Scheme 3, **b**. Firstly, the oxidative addition of copper salt **B** into heterocyclic bromides **4** may provide the key intermediate **C**. Similarly, the intermediate **A** is generated from thiuram reagent **2a** through the interaction with the base. Subsequently, the nucleophile **A** reacts with intermediate **C** to provide intermediate **D**,[7a] along with the release of CsBr. Finally, intermediate **D** easily provides the desired C–S cross-coupled product **5** by reductive elimination and the catalytic cycle is closed by regeneration of the copper catalyst at its original oxidation state.

Conclusions

In summary, we have developed an efficient and practical method for the synthesis of aza-heteroaromatic dithiocarbamates using inexpensive tetraalkylthiuram disulfides and aza-heteroaromatics bromides as the coupling partners. Several interesting benzothiazole dithiocarbamates could be formed under base promoted reaction conditions. Moreover, in the presence of Cu_2O, other important nitrogen-containing heteroaromatic (quinolyl, pyridyl and pyrazinyl) dithiocarbamates were obtained in good to excellent yields. These reactions have the advantages of efficiency, good atom economy, and broad substrate scope. Further exploration of the synthetic potential and application of these compounds are currently ongoing in our laboratory.

Experimental Section

1. General information

All reactions were carried out under air atmosphere in a dried tube. Chemicals were all purchased without further purification. Silica gel was purchased from Qing Dao Hai Yang Chemical Industry Co. Analytical thin layer chromatography (TLC) was performed on precoated silica gel F_{254} plates. Compounds were visualized by irradiation with UV light (254 nm). ^{1}H NMR and ^{13}C NMR spectra data were recorded by a BRUKER AVANCE III 400 MHz spectrometer (^{1}H 400 MHz, ^{13}C 100 MHz), using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. ^{1}H NMR spectral data are given as chemical shifts in ppm followed by multiplicity (s- singlet; d- doublet; t- triplet; q- quartet; m- multiplet), number of protons and coupling constants. ^{13}C NMR chemical shifts are expressed in ppm. Infrared spectra were recorded with a Thermo Scientific Nicolet 6700 FT-IR Spectrometer. HRMS data were obtained using AB SCIEX Triple TOF 5600+ high resolution mass spectrometer (USA).

1. General procedure for the synthesis of compound 3

Under air atmosphere, benzothiazol-2-yl bromides **1** (0.2 mmol), thiuram disulfides **2** (0.2 mmol) and Cs_2CO_3 (0.4 mmol) were charged into a 10 mL reaction tube, then DMSO (0.5 mL) was added into the tube. The resulting mixture was stirred at 100 °C for 48 h in oil bath, then cooled down to room temperature. The reaction mixture was quenched with a sat. NH_4Cl solution and subsequently extracted with ethyl acetate. The combined organic layers was dried over anhydrous Na_2SO_4, and the solvent was evaporated under *vacuum*. The crude product was purified by flash column chromatography on silica gel (eluent: Petroleum ether-EtOAc) yielding the products **3** in moderate to good yields. In general, the identity and purity of the products were confirmed by ^{1}H and ^{13}C NMR spectroscopy, HRMS (ESI) and IR.

Benzo[d]thiazol-2-yl dimethylcarbamodithioate (3a): Purification by column chromatography on silica gel (R_f = 0.29, petroleum ether/ethyl acetate = 5:1) yielded **3a** (42.7 mg, 84%) as a colorless solid; m. p. 109.3-114.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.12 (d, *J* = 7.9 Hz, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.54-7.50 (m, 1H), 7.48-7.44 (m, 1H), 3.54 (s, 3H), 3.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 191.5, 159.0, 152.8, 138.4, 126.4, 126.1, 124.0, 121.5, 45.4, 42.5; IR(KBr): 3426, 2922, 1511, 1454, 1408, 1380, 1313, 1246, 1156, 1079, 1001, 958, 761, 728 cm^{-1}; HRMS (ESI) calcd. for $C_{10}H_{11}N_2S_3$: $[M+H]^+$: 255.0084, found: 255.0082.

Benzo[d]thiazol-2-yl diethylcarbamodithioate (3b): Purification by column chromatography on silica gel (R_f = 0.30, petroleum ether/ethyl acetate = 5:1) yielded **3a** (40.0 mg, 71%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.12 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.51 (td, *J* = 7.3, 1.2 Hz, 1H), 7.44 (td, *J* = 8.1, 1.2 Hz, 1H), 4.01 (q, *J* = 7.0 Hz, 2H), 3.84 (q, *J* = 7.0 Hz, 2H), 1.42 (t, *J* = 7.0 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 189.8, 159.1, 152.9, 138.5, 126.3, 126.1, 124.0, 121.5, 49.7, 48.0, 13.0, 11.4; IR(KBr): 3443, 2978, 2929, 1697, 1494, 1271, 1202, 1146, 1076, 994, 965, 915, 824, 725 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{15}N_2S_3$: $[M+H]^+$: 283.0397, found: 283.0396.

Benzo[d]thiazol-2-yl dibutylcarbamodithioate (3c): Purification by column chromatography on silica gel (R_f = 0.33, petroleum ether/ethyl acetate = 7:1) yielded **3a** (35.8 mg, 53%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.11 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.50 (td, *J* = 7.4, 1.2 Hz, 1H), 7.44 (td, *J* = 8.1, 1.2 Hz, 1H), 3.93 (t, *J* = 7.7 Hz, 2H), 3.75 (t, *J* = 7.8 Hz, 2H), 1.84-1.78 (m, 2H), 1.76-1.70 (m, 2H), 1.46-1.41 (m, 2H), 1.39-1.31 (m, 2H), 1.01 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 190.0, 159.5, 152.8, 138.3, 126.3, 126.0, 123.9, 121.4, 55.1, 53.8, 29.9, 28.2, 20.1, 13.8, 13.7; IR(KBr): 2958, 2871, 1670, 1412, 1367, 1220, 1092, 976, 939, 759 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{23}N_2S_3$: $[M+H]^+$: 339.1023, found: 339.1021.

6-Methoxybenzo[d]thiazol-2-yl dimethylcarbamodithioate (3d): Purification by column chromatography on silica gel (R_f = 0.35, petroleum ether/ethyl acetate = 5:1) yielded **3a** (30.1 mg, 53%) as a white solid; m. p. 120.5-122.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.00 (d, *J* = 9.0 Hz, 1H), 7.34 (d, *J* = 2.5 Hz, 1H), 7.11 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.89 (s, 3H), 3.54 (s, 3H), 3.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 192.3, 158.5, 155.2, 147.7, 140.3, 124.7, 116.4, 103.4, 55.8, 42.4; IR(KBr): 3442, 2922, 2851, 1601, 1504, 1475, 1378, 1256, 1224, 1023, 965, 838 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{13}N_2OS_3$: $[M+H]^+$: 285.0190, found: 285.0192.

6-Methoxybenzo[d]thiazol-2-yl diethylcarbamodithioate (3e): Purification by column chromatography on silica gel (R_f = 0.34, petroleum ether/ethyl acetate = 5:1) yielded **3a** (43.1 mg, 69%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.01 (d, *J* = 9.0 Hz, 1H), 7.33 (d, *J* = 2.4 Hz, 1H), 7.51 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.00 (q, *J* = 6.9 Hz, 2H), 3.88 (s, 3H), 3.83 (q, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.0 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 190.7, 158.5, 155.3, 147.8, 140.4, 124.7, 116.4, 103.4, 55.9, 49.8, 47.9, 13.0, 11.5; IR(KBr): 3424, 3059, 2928, 1601, 1550, 1487, 1421, 1353, 1277, 1198, 1142, 1024, 910, 672 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{17}N_2OS_3$: $[M+H]^+$: 313.0503, found: 313.0504.

6-Methoxybenzo[d]thiazol-2-yl dibutylcarbamodithioate (3f): Purification by column chromatography on silica gel (R_f = 0.28, petroleum ether/ethyl acetate = 7:1) yielded **3a** (43.4 mg, 63%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.00 (d, *J* = 9.0 Hz, 1H), 7.33 (d, *J* = 2.4 Hz, 1H), 7.10 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.92 (t, *J* = 7.8 Hz, 2H), 3.88 (s, 3H), 3.74 (t, *J* = 7.8 Hz, 2H), 1.84-1.78 (m, 2H), 1.77-1.71 (m, 2H), 1.43 (q, *J* = 7.4 Hz, 2H), 1.35 (q, *J* = 7.5 Hz, 2H), 1.01 (t, *J* = 7.3 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 190.8, 158.4, 155.6, 147.7, 140.4, 124.6, 116.3, 103.4, 55.8, 55.2, 53.7, 29.8, 28.2, 20.1, 13.8, 13.7; IR(KBr): 3423, 2958, 2871, 1602, 1477, 1416, 1367, 1259, 1181, 1027, 819 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{25}N_2OS_3$: $[M+H]^+$: 369.1129, found: 369.1130.

5-Formylfuran-2-yl dimethylcarbamodithioate (3g): Purification by column chromatography on silica gel (R_f = 0.36, petroleum ether/ethyl acetate = 5:1) yielded **3a** (37.8 mg, 88%) as a yellow solid; m. p. 60.5-63.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 9.73 (s, 1H), 7.32 (d, *J* = 3.6 Hz, 1H), 6.95 (d, *J* = 3.6 Hz, 1H), 3.52 (s, 3H), 3.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 192.3, 178.2, 156.0, 147.6, 124.8, 120.5, 45.6, 42.4; IR(KBr): 3135, 2925, 1673, 1518, 1463, 1385, 1248, 1022, 966, 936, 829, 762 cm^{-1}; HRMS (ESI) calcd. for $C_8H_{10}NO_2S_2$: $[M+H]^+$: 216.0153, found: 216.0150.

2. General procedure for the synthesis of compound 5

Under air atmosphere, aza-heteroaromatics bromides **4** (0.2 mmol), thiuram disulfides **2** (0.2 mmol), Cu_2O (10 mol %) and Cs_2CO_3 (0.4 mmol) were charged into a 10 mL sealable tube equipped with a magnetic stirring bar. After the addition of DMSO (0.5 mL), the resulting mixture was stirred at 110 °C for 48 h in oil bath, then cooled down to room temperature. The reaction mixture was quenched with a sat. NH_4Cl solution and subsequently extracted with ethyl acetate. The combined organic layers was dried over anhydrous Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (eluent: petroleum ether-EtOAc) yielding the compounds **5** in moderate to good yields. In general, the identity and purity of the products were confirmed by ^{1}H and ^{13}C NMR spectroscopy, HRMS (ESI) and IR.

Quinolin-3-yl dimethylcarbamodithioate (5a): Purification by column chromatography on silica gel (R_f = 0.31, petroleum ether/ethyl acetate = 7:1) yielded **3a** (42.6 mg, 86%) as a white solid; m. p. 83.3-88.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.85 (s, 1H), 8.26 (s, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.79 (t, *J* = 7.4 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 3.56 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.0, 156.2, 147.7, 143.9, 130.9, 129.4, 128.1, 128.0, 127.1, 125.8, 45.8, 42.1; IR(KBr): 3424, 2923, 1566, 1490, 1380, 1247, 1152, 980, 953, 895, 864, 785, 746, 648 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}N_2S_2$: $[M+H]^+$: 249.0520, found: 249.0521.

Quinolin-2-yl dimethylcarbamodithioate (5b): Purification by column chromatography on silica gel (R_f = 0.35, petroleum ether/ethyl acetate = 10:1) yielded **3a** (33.2 mg, 67%) as a yellow solid; m. p. 126.9-132.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.17 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 7.4 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 3.53 (s, 3H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 194.5, 154.0, 148.4, 136.6, 129.9, 129.7, 129.1, 127.8, 127.6, 127.5, 45.1, 42.5; IR(KBr): 3234, 3059, 2922, 1584, 1495, 1378, 1247, 1101, 942, 782, 767, 746 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}N_2S_2$: $[M+H]^+$: 249.0520, found: 249.0519.

Quinolin-4-yl dimethylcarbamodithioate (5c): Purification by column chromatography on silica gel (R_f = 0.29, petroleum ether/ethyl acetate = 10:1) yielded **3a** (23.8 mg, 48%) as a dark yellow solid; m. p. 109.9-113.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.97 (d, *J* = 4.3 Hz, 1H), 8.22 (d, *J* = 8.2 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.74 (t, *J* = 8.0 Hz, 1H), 7.62-7.57 (m, 2H), 3.59 (s, 3H), 3.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 193.4, 150.0, 149.0, 139.6, 130.2, 129.8, 129.8, 127.6, 125.6, 45.5, 42.5; IR(KBr): 3056, 2923, 1912, 1556, 1494, 1372, 1249, 1151, 1052, 988, 968, 841, 758, 670, 576 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}N_2S_2$: $[M+H]^+$: 249.0520, found: 249.0522.

Quinolin-5-yl dimethylcarbamodithioate (5d): Purification by column chromatography on silica gel (R_f = 0.40, petroleum ether/ethyl acetate = 10:1) yielded **3a** (17.4 mg, 35%) as a white solid; m. p. 120.8-122.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.94 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.53 (d, *J* = 8.1 Hz, 1H), 8.26 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.79 (td, *J* = 7.1, 1.8 Hz, 1H), 7.45 (q, *J* = 4.2 Hz, 1H), 3.61 (s, 3H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 195.8, 150.7, 148.8, 137.3, 134.5, 132.9, 130.8, 129.2, 129.1, 122.0, 45.6, 42.2; IR(KBr): 2922, 1559, 1490, 1372, 1312, 1249, 1149, 987, 961, 795, 662 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}N_2S_2$: $[M+H]^+$: 249.0520, found: 249.0522.

Quinolin-6-yl dimethylcarbamodithioate (5e): Purification by column chromatography on silica gel (R_f = 0.35, petroleum ether/ethyl acetate = 10:1) yielded **3a** (24.8 mg, 50%) as a light yellow solid; m. p. 152.4-153.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.97 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.53 (dd, *J* = 7.5, 5.6 Hz, 2H), 7.98 (d, *J* = 1.8 Hz, 1H), 7.76 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.43 (dd, *J* = 8.8, 1.9 Hz, 1H), 3.57 (s, 3H), 3.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.7, 151.7, 148.5, 137.0, 136.5, 136.3, 130.1, 130.0, 128.4, 121.6, 45.7, 42.1; IR(KBr): 3442, 2921, 1513, 1487, 1387, 1312, 1251, 1165, 981, 943, 865, 833, 798, 526 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}N_2S_2$: $[M+H]^+$: 249.0520, found: 249.0518.

Quinolin-8-yl dimethylcarbamodithioate (5f): Purification by column chromatography on silica gel (R_f = 0.50, petroleum ether/ethyl acetate = 5:1) yielded **3a** (27.8 mg, 56%) as a yellow solid; m. p. 171.3-175.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 9.03 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.21 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.99 (t, *J* = 7.1 Hz, 2H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.44 (dd, *J* = 8.2, 4.2 Hz, 1H), 3.64 (s, 3H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.8, 151.3, 148.5, 140.0, 136.8, 131.6, 131.3, 129.1, 126.6, 121.6, 45.6, 42.4; IR(KBr): 3425, 2924, 1592, 1556, 1488, 1371, 1252, 1150, 992, 973, 827, 789, 558 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}N_2S_2$: $[M+H]^+$: 249.0520, found: 249.0522.

2-Methylquinolin-6-yl dimethylcarbamodithioate (5g): Purification by column chromatography on silica gel (R_f = 0.40, petroleum ether/ethyl acetate = 10:1) yielded **3a** (20 mg, 38%) as a yellow solid; m. p. 153.9-157.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.05 (d, *J* = 2.6 Hz, 1H), 8.03 (d, *J* = 2.1 Hz, 1H), 7.92 (d, *J* = 1.9 Hz, 1H), 7.71 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 3.57 (s, 3H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 197.1, 160.6, 148.2, 137.0, 136.3, 129.4, 128.9, 126.7, 122.5, 45.7, 42.1, 25.5; IR(KBr): 3442, 2922, 1609, 1594, 1485, 1376, 1247, 1147, 979, 887, 829 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{15}N_2S_2$: $[M+H]^+$: 263.0677, found: 263.0675.

Pyridin-3-yl dimethylcarbamodithioate (5h)[7a]**:** Purification by column chromatography on silica gel (R_f = 0.44, petroleum ether/ethyl acetate = 10:1) yielded **3a** (17.8 mg, 45%) as a yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.67 (d, *J* = 3.8 Hz, 1H), 8.61 (s, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 5.0 Hz, 1H), 3.55 (s, 3H), 3.52 (s, 3H),; ^{13}C NMR (100 MHz, $CDCl_3$) 195.8, 156.5, 150.6, 144.5, 129.3, 123.9, 45.8, 42.1; IR(KBr): 3039, 2923, 1566, 1504, 1382, 1253, 1156, 983, 866, 812, 701, 617, 506 cm^{-1}; HRMS (ESI) calcd. for $C_8H_{11}N_2S_2$: $[M+H]^+$: 199.0364, found: 199.0366.

Pyridin-2-yl dimethylcarbamodithioate (5i)[7a]**:** Purification by column chromatography on silica gel (R_f = 0.39, petroleum ether/ethyl acetate = 5:1) yielded **3a** (42.2 mg, 96%) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.67 (dd, *J* = 4.8, 1.1 Hz, 1H), 7.77 (td, *J* = 7.7, 1.9 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.34 (ddd, *J* = 5.8, 4.8, 0.9 Hz, 1H), 3.53 (s, 3H), 3.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 195.1, 153.9, 150.5, 137.3, 133.1, 124.1, 45.3, 42.4; IR(KBr): 3450, 2925, 1572, 1505, 1445, 1422, 1375, 1247, 1152, 980, 767, 738, 511 cm^{-1}; HRMS (ESI) calcd. for $C_8H_{10}N_2NaS_2$: $[M+Na]^+$: 221.0183, found: 221.0182.

6-Methylpyridin-3-yl dimethylcarbamodithioate (5j): Purification by column chromatography on silica gel (R_f = 0.33, petroleum ether/ethyl acetate = 3:1) yielded **3a** (17.8 mg, 42%) as a white solid; m. p. 87.4-91.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.48 (d, *J* = 2.0 Hz, 1H), 7.65 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.26 (t, *J* = 2.8 Hz, 1H), 3.56 (s, 3H), 3.52 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.5, 160.1, 155.8, 144.6, 125.9, 123.7, 45.9, 42.0, 24.5; IR(KBr): 3442, 2921, 1579, 1499, 1376, 1294, 1244, 1136, 1021, 973, 869, 831, 510 cm^{-1}; HRMS (ESI) calcd. for $C_9H_{13}N_2S_2$: $[M+H]^+$: 213.0520, found: 213.0521.

4-Methylpyridin-3-yl dimethylcarbamodithioate (5k): Purification by column chromatography on silica gel (R_f = 0.30, petroleum ether/ethyl acetate = 3:1) yielded **3a** (20 mg, 47%) as a colorless solid; m. p. 86.6-91.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.54 (d, *J* = 5.0 Hz, 1H), 8.51 (s, 1H), 7.27 (d, *J* = 3.6 Hz, 1H), 3.55 (s, 6H), 2.4 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 194.9, 157.1, 153.2, 151.0, 129.1, 125.7, 45.6, 42.1, 20.3; IR(KBr): 3442, 2924, 1582, 1501, 1380, 1246, 1150, 1045, 970, 831, 721 cm^{-1}; HRMS (ESI) calcd. for $C_9H_{13}N_2S_2$: $[M+H]^+$: 213.0520, found: 213.0522.

6-Methoxypyridin-3-yl dimethylcarbamodithioate (5l): Purification by column chromatography on silica gel (R_f = 0.43, petroleum ether/ethyl acetate = 3:1) yielded **3a** (15.0 mg, 33%) as a white solid; m. p. 96.8-101.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.15 (d, *J* = 2.1 Hz, 1H), 7.60 (d, *J* = 8.6, 2.3 Hz, 1H), 6.81 (d, *J* = 8.6 Hz, 1H), 3.98 (s, 3H), 3.56 (s, 3H), 3.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 197.4, 165.1, 154.4, 146.8, 120.7, 111.6, 53.8, 45.9, 41.9; IR(KBr): 3442, 2924, 1588, 1479, 1356, 1303, 1285, 1243, 1146, 1014, 974, 828, 541cm^{-1}; HRMS (ESI) calcd. for $C_9H_{13}N_2OS_2$: $[M+H]^+$: 229.0469, found: 229.0467.

6-(Trifluoromethyl)pyridin-3-yl dimethylcarbamodithioate (5m): Purification by column chromatography on silica gel (R_f = 0.45, petroleum ether/ethyl acetate = 3:1) yielded **3a** (45.8 mg, 86%) as a white solid; m. p. 63.9-64.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.70 (s, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 3.56 (s, 3H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 194.0, 156.5, 148.5 (q, *J* = 34.9 Hz), 145.7, 132.8, 121.4 (q, *J* = 272.6 Hz), 120.5 (d, *J* = 2.4 Hz), 45.8, 42.2; IR(KBr): 3050, 2929, 1501, 1371, 1335, 1256, 1129, 1079, 1019, 981, 842, 721, 633, 573 cm^{-1}; HRMS (ESI) calcd. for $C_9H_{10}F_3N_2S_2$: $[M+H]^+$: 267.0237, found: 267.0235.

Isoquinolin-4-yl dimethylcarbamodithioate (5n): Purification by column chromatography on silica gel (R_f = 0.31, petroleum ether/ethyl acetate = 5:1) yielded **3a** (19.8 mg, 40%) as a light yellow solid; m. p. 133.9-137.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 9.35 (s, 1H), 8.66 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.76 (t, *J* = 7.3 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 3.64 (s, 3H), 3.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 195.3, 155.1, 151.7, 138.0, 131.5, 129.2, 128.3, 127.8, 124.9, 124.5, 45.7, 42.2; IR(KBr): 3443, 2925, 1618, 1499, 1376, 1246, 1150, 972, 776, 756 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}N_2S_2$: $[M+H]^+$: 249.0520, found: 249.0518.

Isoquinolin-5-yl dimethylcarbamodithioate (5o): Purification by column chromatography on silica gel (R_f = 0.32, petroleum ether/ethyl acetate = 1:1) yielded **3a** (40.2 mg, 81%) as a yellow solid; m. p. 169.1-170.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 9.30 (s, 1H), 8.58 (d, *J* = 5.6 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 5.8 Hz, 1H), 7.92 (dd, *J* = 7.2, 0.9 Hz, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 3.62 (s, 3H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 195.5, 153.0, 144.3, 141.1, 138.2, 130.9, 129.4, 128.6, 127.2, 118.4, 45.6, 42.2; IR(KBr): 3441, 2925, 1614, 1560, 1505, 1375, 1245, 1141, 992, 968, 832, 758 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}N_2S_2$: $[M+H]^+$: 249.0520, found: 249.0520.

Isoquinolin-6-yl dimethylcarbamodithioate (5p): Purification by column chromatography on silica gel (R_f = 0.37, petroleum ether/ethyl acetate = 7:1) yielded **3a** (23.8 mg, 48%) as a light yellow solid; m. p. 177.8-179.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 9.32 (s, 1H), 8.59 (s, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.98 (s, 1H), 7.67 (dd, *J* = 8.5, 1.6 Hz, 2H), 3.57 (s, 3H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.0, 152.4, 143.6, 135.9, 134.9, 134.4, 128.5, 128.0, 120.6, 45.6, 42.2; IR(KBr): 3443, 2919, 1620, 1513, 1384, 1247, 1164, 975, 946, 832, 649 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{13}N_2S_2$: $[M+H]^+$: 249.0520, found: 249.0521.

Pyrazin-2-yl dimethylcarbamodithioate (5q): Purification by column chromatography on silica gel (R_f = 0.25, petroleum ether/ethyl acetate = 5:1) yielded **3a** (40.2 mg, 91%) as a white solid; m. p. 96.6-98.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.80 (s, 1H), 8.63 (d, *J* = 1.3 Hz, 1H), 8.58 (d, *J* = 2.4 Hz, 1H), 3.53 (s, 3H), 3.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 193.7, 153.0, 151.4, 144.8, 144.1, 45.3, 42.4; IR(KBr): 3442, 2925, 1503, 1385, 1246, 1141, 1043, 1013, 976, 841, 512 cm^{-1}; HRMS (ESI) calcd. for $C_7H_9N_3NaS_2$: $[M+Na]^+$: 222.0136, found: 222.0136.

5-Aminopyrazin-2-yl dimethylcarbamodithioate (5r): Purification by column chromatography on silica gel (R_f = 0.40, petroleum ether/ethyl acetate = 2:1) yielded **3a** (39.4 mg, 92%) as a white solid; m. p. 167.6-171.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.16 (d, *J* = 0.8 Hz, 1H), 8.04 (d, *J* = 1.0 Hz, 1H), 4.89 (bs, 2H), 3.53 (s, 3H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.6, 154.1, 151.1, 137.3, 132.8, 45.6, 42.1; IR(KBr): 3323, 3157, 1651, 1573, 1529, 1392, 1245, 1147, 1020, 970, 894, 556 cm^{-1}; HRMS (ESI) calcd. for $C_7H_{11}N_4S_2$: $[M+H]^+$: 215.0425, found: 215.0424.

Quinoxalin-6-yl dimethylcarbamodithioate (5s): Purification by column chromatography on silica gel (R_f = 0.30, petroleum ether/ethyl acetate = 3:1) yielded **3a** (37.8 mg, 76%) as a yellow solid; m. p. 127.2-129.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.89 (d, *J* = 4.9 Hz, 2H), 8.26 (s, 1H), 8.14 (d, *J* = 8.7 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 3.57 (s, 3H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 195.7, 145.9, 145.4, 143.4, 143.0, 137.9, 137.5, 134.1, 129.7, 45.6, 42.2; IR(KBr): 3442, 2925, 1508, 1481, 1379, 1342, 1248, 1146, 1026, 978, 951, 900, 867, 826, 550 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{12}N_3S_2$: $[M+H]^+$: 250.0473, found: 250.0471.

Quinolin-3-yl diethylcarbamodithioate (5t): Purification by column chromatography on silica gel (R_f = 0.38, petroleum ether/ethyl acetate = 5:1) yielded **3a** (15.5 mg, 28%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.85 (d, *J* = 2.0 Hz, 1H), 8.27 (d, *J* = 1.8 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.78 (td, *J* = 7.0, 1.3 Hz, 1H), 7.59 (td, *J* = 7.9, 0.8 Hz, 1H), 4.04 (q, *J* = 7.0 Hz, 2H), 3.92 (q, *J* = 7.0 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 194.3, 156.4, 147.6, 144.0, 130.8, 129.4, 128.1, 127.0, 125.6, 50.0, 47.5, 12.9, 11.6; IR(KBr): 3442, 2970, 2919, 1582, 1461, 1383, 1353, 1298, 1122, 981, 875 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}N_2S_2$: $[M+H]^+$: 277.0833, found: 277.0832.

Isoquinolin-5-yl diethylcarbamodithioate (5u): Purification by column chromatography on silica gel (R_f = 0.31, petroleum ether/ethyl acetate = 3:1) yielded **3a** (18.2 mg, 33%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 9.30 (s, 1H), 8.59 (s, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 7.97 (d,

J = 5.4 Hz, 1H), 7.94 (dd, *J* = 7.2, 0.9 Hz, 1H), 7.66 (dd, *J* = 8.1, 7.4 Hz, 1H), 4.05-3.97 (m, 4H), 1.52 (t, *J* = 7.0 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 193.8, 153.0, 144.2, 141.2, 138.4, 130.8, 129.5, 128.5, 127.2, 118.5, 49.9, 47.6, 13.0, 11.6; IR(KBr): 3424, 2973, 2931, 1615, 1490, 1415, 1353, 1272, 1204, 1142, 1088, 975, 820, 754 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}N_2S_2$: $[M+H]^+$: 277.0833, found: 277.0834.

6-(Trifluoromethyl)pyridin-3-yl diethylcarbamodithioate (5v): Purification by column chromatography on silica gel (R_f = 0.30, petroleum ether/ethyl acetate = 5:1) yielded **3a** (38.2 mg, 65%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.70 (s, 1H), 7.97 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 4.02 (q, *J* = 7.0 Hz, 2H), 3.88 (q, *J* = 7.0 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H), 1.30 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 192.4, 156.5, 148.5 (q, *J* = 34.7 Hz), 145.8, 132.7, 121.4 (q, *J* = 272.7 Hz), 120.4 (d, *J* = 2.4 Hz), 50.2, 47.7, 12.9, 11.5; IR(KBr): 3443, 2976, 2934, 1492, 1417, 1332, 1272, 1147, 1077, 976, 917, 826, 636 cm^{-1}; HRMS (ESI) calcd. for $C_{11}H_{14}F_3N_2S_2$: $[M+H]^+$: 295.0550, found: 295.0551.

Pyrazin-2-yl diethylcarbamodithioate (5w): Purification by column chromatography on silica gel (R_f = 0.32, petroleum ether/ethyl acetate = 2:1) yielded **3a** (43.6 mg, 96%) as a light yellow solid; m. p. 77.9-79.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.80 (d, *J* = 1.3 Hz, 1H), 8.63 (dd, *J* = 2.4, 1.5 Hz, 1H), 8.57 (d, *J* = 2.5 Hz, 1H), 4.01 (q, *J* = 7.0 Hz, 2H), 3.85 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 192.1, 153.2, 151.3, 144.7, 144.0, 49.7, 47.9, 12.9, 11.5; IR(KBr): 3425, 2977, 1493, 1425, 1383, 1269, 1203, 1147, 1067, 1013, 974, 914, 826, 563 cm^{-1}; HRMS (ESI) calcd. for $C_9H_{14}N_3S_2$: $[M+H]^+$: 228.0629, found: 228.0630.

Quinolin-3-yl dibutylcarbamodithioate (5x): Purification by column chromatography on silica gel (R_f = 0.35, petroleum ether/ethyl acetate = 7:1) yielded **3a** (20 mg, 30%) as a light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.84 (s, 1H), 8.26 (d, *J* = 1.8 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.78 (td, *J* = 7.0, 1.4 Hz, 1H), 7.58 (td, *J* = 7.9, 0.8 Hz, 1H), 3.95 (t, *J* = 7.8 Hz, 2H), 3.82 (t, *J* = 7.9 Hz, 2H), 1.91-1.83 (m, 2H), 1.78-1.70 (m 2H), 1.51-1.44 (m, 2H), 1.39-1.31 (m 2H), 1.05 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 194.6, 156.4, 147.6, 143.9, 130.7, 129.4, 128.1, 127.0, 125.8, 55.5, 53.3, 29.7, 28.4, 20.2, 20.1, 13.8; IR(KBr): 3234, 2958, 2871, 1488, 1456, 1415, 1368, 1291, 1250, 784, 752 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{25}N_2S_2$: $[M+H]^+$: 333.1459, found: 333.1457.

6-(Trifluoromethyl)pyridin-3-yl dibutylcarbamodithioate (5y): Purification by column chromatography on silica gel (R_f = 0.31, petroleum ether/ethyl acetate = 10:1) yielded **3a** (41.3 mg, 59%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.69 (s, 1H), 7.96 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 3.93 (t, *J* = 7.8 Hz, 2H), 3.79 (t, *J* = 7.8 Hz, 2H), 1.87-1.79 (m, 2H), 1.76-1.68 (m, 2H), 1.49-1.41 (m, 2H), 1.40-1.31 (m 2H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 192.6, 156.5, 148.4 (q, *J* = 34.9 Hz), 145.8, 132.8, 121.4 (q, *J* = 272.3 Hz), 120.4 (d, *J* = 2.2 Hz), 55.6, 53.4, 29.8, 28.3, 20.1, 20.1, 13.8, 13.7; IR(KBr): 3442, 2961, 2874, 1489, 1417, 1369, 1333, 1181, 1145, 1081, 1022, 941, 843, 721 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{22}F_3N_2S_2$: $[M+H]^+$: 351.1176, found: 351.1175.

Pyrazin-2-yl dibutylcarbamodithioate (5z): Purification by column chromatography on silica gel (R_f = 0.35, petroleum ether/ethyl acetate = 7:1) yielded **3a** (55.5 mg, 98%) as a yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.80 (d, *J* = 1.2 Hz, 1H), 8.62 (dd, *J* = 2.4, 1.6 Hz, 1H), 8.56 (d, *J* = 2.5 Hz, 1H), 3.92 (t, *J* = 7.8 Hz, 2H), 3.76 (t, *J* = 7.9 Hz, 2H), 1.87-1.80 (m, 2H), 1.76-1.70 (m 2H), 1.48-1.39 (m, 2H), 1.37-1.30 (m 2H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 192.3, 153.2, 151.5, 144.7, 143.9, 55.1, 53.7, 29.7, 28.3, 20.1, 20.1, 13.8, 13.7; IR(KBr): 3425, 2959, 2872, 1488, 1455, 1417, 1380, 1291, 1249, 1221, 1142, 1013, 744 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{22}N_3S_2$: $[M+H]^+$: 284.1255, found: 284.1256.

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Keywords: Aza-heteroaromatic dithiocarbamates • Aza-heteroaromatics bromides • Tetraalkylthiuram disulfides • Cross coupling reactions • Synthetic methods

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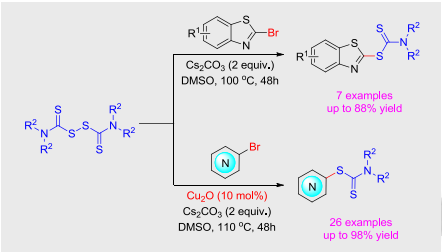
FULL PAPER

The preparation of various aza-heteroaromatic dithiocarbamates from aza-heteroaromatic bromides and tetraalkylthiuram disulfides is reported. This attractive methodology for the synthesis of aza-heteroaromatic dithiocarbamates is of great significance due to the products' potential utilization in pharmaceutical industry.



Key Topic* C-S bond coupling

Chuance Cheng, Mingqin Zhao, Miao Lai, Ke Zhai, Bo Shi, Shuai Wang,Rui Luo, Linbao Zhang and Zhiyong Wu**

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Synthesis of Aza-Heteroaromatic Dithiocarbamates via Cross-Coupling Reactions of Aza-Heteroaromatic Bromides with Tetraalkylthiuram Disulfides