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Copper-catalyzed *S*-arylation of tetraalkylthiuram disulfides by using diaryliodonium salts

Meng-Tian Zeng,[a] Wan Xu,[a] Xing Liu,[a] Cai-Zhu Chang,[a] Hui Zhu,[a] Zhi-Bing Dong*[a], [b]

Abstract: An efficient and convenient procedure for the *S*-arylation of tetraalkylthiuram disulfides by using diaryliodonium salts was explored. In the presence of CuI/KO*t*-Bu, two kinds of *S*-aryl dithiocarbamates could be obtained with good to excellent yields at one time, showing no obvious selectivity. The methodology has advantages of efficiency, good atomic economy and broad substrate scope. The method provides a facile and convenient preparation of some potentially biologically active compounds.

Introduction

Organic dithiocarbamates are popular in organic chemistry due to their versatile applications. They have attracted wide attention since they could be served as important synthetic intermediates,[1] several of which were found to be biologically active, such as monoacylglycerol lipase inhibitors,[2] leukemic cells inhibitors,[3] thymocytes inhibitors,[4] antitumors[5] and antibacterials.[6] Moreover, dithiocarbamates are widely applied in agriculture sphere, serving as fusarium oxysporum agent,[7] crop anti-diseases drugs.[8]

Conventionally, protocols for the synthesis of dithiocarbamates involve the use of organometallic reagents with tetramethylthiuram disulfide,[9] sodium salt of dithiocarbamic acid with diaryliodonium salts[10] or halobenzene.[11] In recent years, one-pot three component reactions of amines, carbon disulfide with electrophiles including alkyl halide[12] or aryl halide,[13] aryl diazonium fluoroborate,[14] pentafluorobenzonitrile,[15] benzene boronic acid[16] were reported. However, these methods are still limited by multiple reaction steps, flammable and explosive substrate or reagents, high substrates molar ratio.[17] As part of our longstanding interests in developing phenylthioureas and the relevant applications,[18] we hereby report a facile method for the synthesis of *S*-aryl dithiocarbamates using CuI as catalyst and KO*t*-Bu as base. In this protocol, symmetric and asymmetric diaryliodonium salts react with tetraalkylthiuram disulfides affording two kinds of *S*-aryl dithiocarbamates in one pot with good yields.

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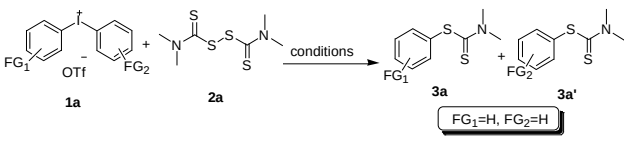
Results and Discussion

In preliminary studies, diphenyliodonium triflate (**1a**) and tetramethylthiuram disulfide (TMTD, **2a**) were selected as substrate for model reaction under various conditions (**Table 1**). For the first trial, we expected the reaction to proceed in green solvents with no addition of metal and base, but phenyl dithiocarbamate was obtained in low yields (25-30%, **Table 1, entries 1–4**). We then added catalyst ($CuCl_2$) and base (K_2CO_3) to the aqueous solution, the yields were still poor (**Table 1, entries 5-6**). To our delight, the target compound could be furnished in a relatively higher yield (65%, **Table 1, entry 7**) in the presence of CuI/K_2CO_3/DMF. Then, a range of bases, such as K_2CO_3, CS_2CO_3, KO*t*-Bu, KOH, Et_3N and CH_3ONa were surveyed and KO*t*-Bu was found to be the most suitable base for this reaction (**Table 1, entries 7-12**). Subsequently, a broad screening of copper, iron, nickel and palladium catalysts was performed (**Table 1, entries 13-20**). It revealed that iron, nickel and palladium salts were not (or less) effective, but copper catalysts could catalyze the model reaction to give reasonable yields (**Table 1, entries 13-17**). Among these copper salts, CuI was the best one (**Table 1, entry 9**). Though a variety of solvents can be used for this reaction (**Table 1, entries 9, 21-24**), the results showed DMF was the best solvent. The effect of the temperature was checked, rising or decreasing the temperature led to significant yield decrease (**Table 1, entries 25-27**). The influence of substrates molar ratio was also surveyed, **1a:2a**=0.5:0.4 was proved to be the optimal (**Table 1, entries 9, 28-29**). Furthermore, the control experiments for the loading of CuI and KO*t*-Bu showed that increasing the loading of CuI or KO*t*-Bu led to almost no yield change (**Table 1, entries 30, 33**), while reducing the loading of CuI or KO*t*-Bu cause sharp yield decrease (**Table 1, entries 31-32, 34**). The best reaction conditions were summarized in **Entry 29**, **Table 1**.

Table 1 Optimization of the reaction conditions[a]



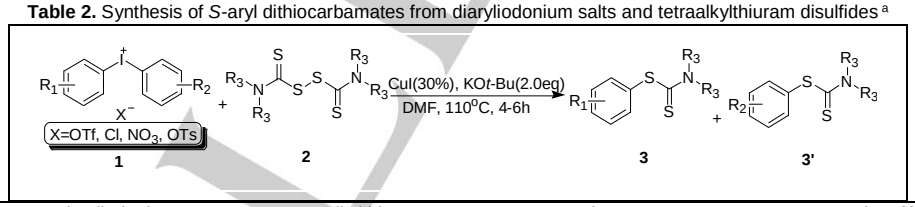
Entry	Catalyst (mmol%)	Base (equiv)	Solvent	Temp.(°C)	Yiled[b](%)
1	---	---	H_2O	110	25
2	---	---	EtOH:H_2O (1:1)	110	29
3	---	---	DMSO:H_2O(1:1)	110	27
4	---	---	DMF:H_2O(1:1)	110	30
5	$CuCl_2$	K_2CO_3	H_2O	110	27
6	CuI	---	DMF	110	26
7	CuI	K_2CO_3	DMF	110	65
8	CuI	Cs_2CO_3	DMF	110	60
9	CuI	KO*t*-Bu	DMF	110	77

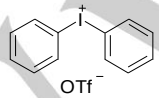
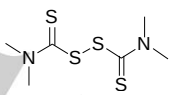
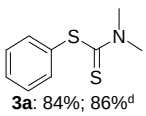
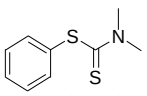
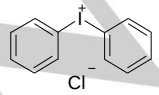
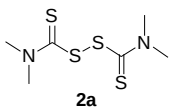
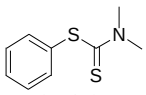
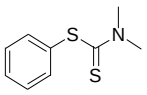
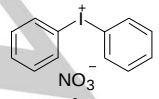
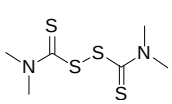
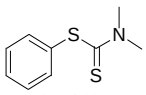
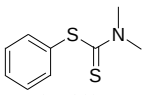
10	CuI	KOH	DMF	110	51
11	CuI	Et_3N	DMF	110	62
12	CuI	CH_3ONa	DMF	110	46
13	CuBr	KO*t*-Bu	DMF	110	57
14	Cu_2O	KO*t*-Bu	DMF	110	67
15	$Cu(OAc)_2$	KO*t*-Bu	DMF	110	50
16	CuCl	KO*t*-Bu	DMF	110	58
17	$CuCl_2$	KO*t*-Bu	DMF	110	48
18	$FeBr_3$	KO*t*-Bu	DMF	110	25
19	$NiBr_2$	KO*t*-Bu	DMF	110	Mess
20	$Pd(OAc)_2$	KO*t*-Bu	DMF	110	Mess
21	CuI	KO*t*-Bu	DMSO	110	48
22	CuI	KO*t*-Bu	DMAC	110	49
23	CuI	KO*t*-Bu	Toluene	110	44
24[c]	CuI	KO*t*-Bu	THF	110	43
25	CuI	KO*t*-Bu	DMF	100	64
26	CuI	KO*t*-Bu	DMF	90	46
27	CuI	KO*t*-Bu	DMF	120	57
28[d]	CuI	KO*t*-Bu	DMF	110	75
29[e]	**CuI**	**KO*t*-Bu**	**DMF**	**110**	**84**
30[f]	CuI	KO*t*-Bu	DMF	110	79
31[g]	CuI	KO*t*-Bu	DMF	110	72
32[h]	CuI	KO*t*-Bu	DMF	110	59
33i	CuI	KO*t*-Bu	DMF	110	82
34[J]	CuI	KO*t*-Bu	DMF	110	43

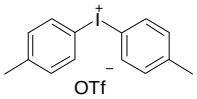
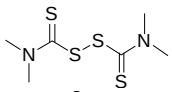
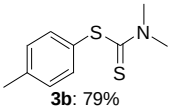
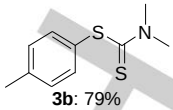
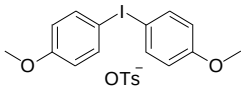
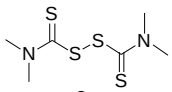
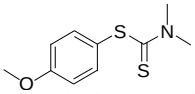
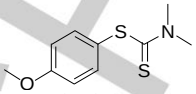
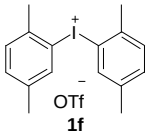
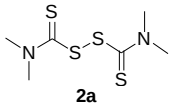
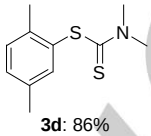
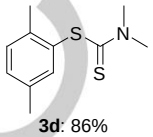
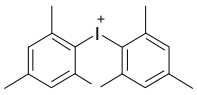
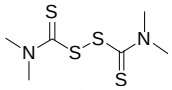
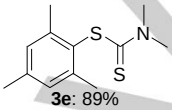
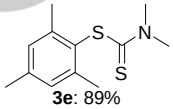
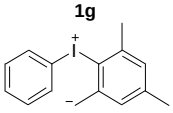
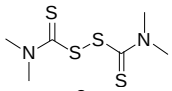
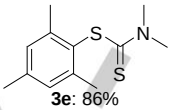
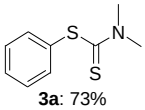
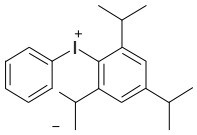
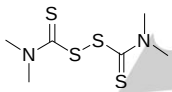
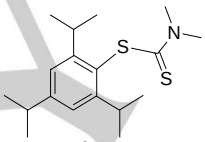
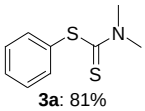
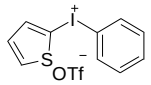
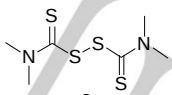
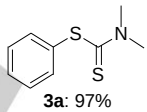
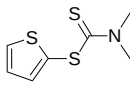
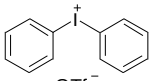
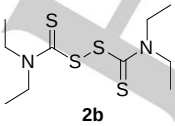
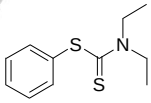
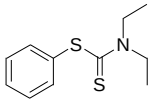
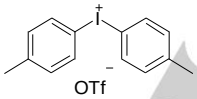
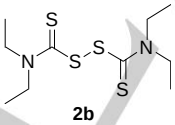
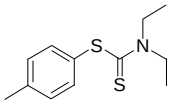
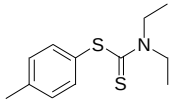
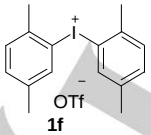
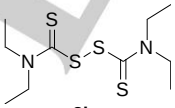
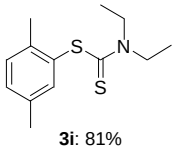
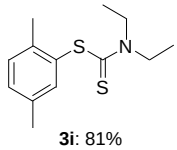
[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.5mmol), catalyst (30% mmol), base (2.0 equiv), DMF (2 mL) for 4–6 h. [b] Isolated yield for **3a** and **3a',** respectively. [c] Reaction at 70 °C. [d] With 0.5 mmol of **1a** and 0.6 mmol of **2a**. [e] With 0.5 mmol of **1a** and 0.4 mmol of **2a**. [f] With CuI (50% mmol). [g] With CuI (20% mmol). [h] With CuI (10% mmol). [i] With KO*t*-Bu (3.0 equiv). [j] With KO*t*-Bu (1.0 equiv).

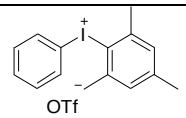
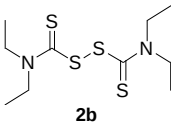
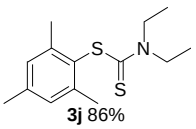
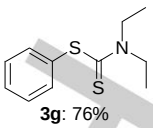
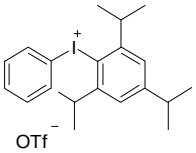
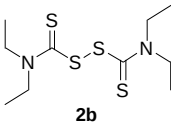
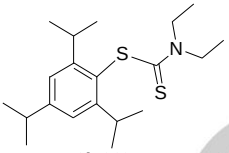
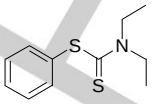
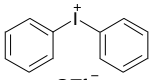
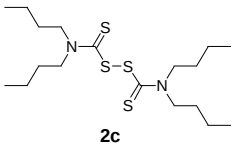
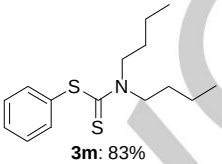
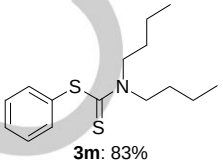
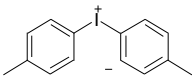
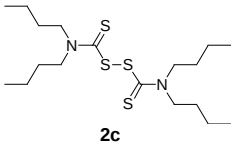
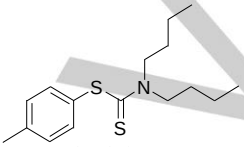
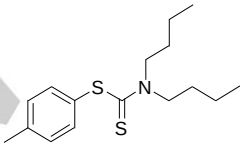
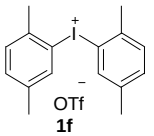
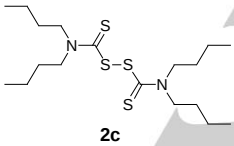
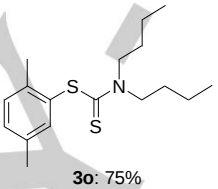
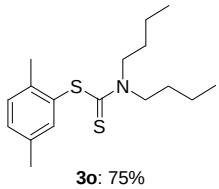
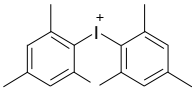
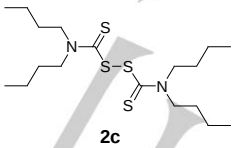
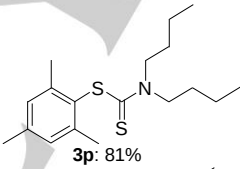
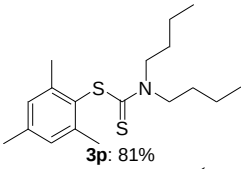
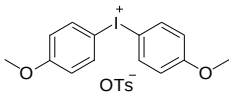
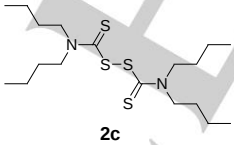
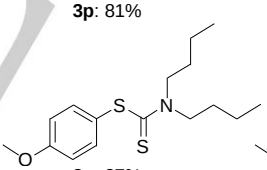
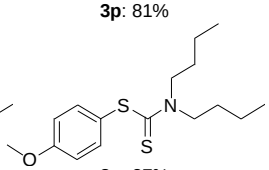
Under the optimized reaction conditions, various substituted *S*-aryl dithiocarbamates were synthesized smoothly in good yields (**Table 2**, **3a-3q**). In the case of reaction with tetramethylthiuram disulfides (TMTD, **2a**), the nature of diphenyliodonium counterion anions showed no effect on the yields of the products (**Table 2**, **entries 1-3**, **5**). A series of symmetrical and unsymmetrical diaryliodonium salts were submitted for reaction survey. Various symmetrical diaryliodonium salts **1X** (**X=d, e, f, g**) reacted with TMTD (**2a**) giving *S*-aryl dithiocarbamates **3** and **3'** in good yields (**Table 2**, **entries 4-7**). Heterocycle dithiocarbamate (**3a'**) were not obtained under standard reaction conditions (**Table 2**, **entry 10**). Tetraethylthiuram disulfide (TETD, **2b**) and tetrabutylthiuram disulfide (TBTD, **2c**) could also be arylated to the corresponding products successfully. Symmetrical diaryliodonium salts (**a**, **d**, **e, f**, **g**,) reacted with TETD and TBTD, respectively giving the desired dithiocarbamates with good yield (**entries 11-15** for TETD, **entries 18-22** for TBTD). Unsymmetrical diaryliodonium salts **1h** and **1i** were slightly selectively transformed to the desired products smoothly, and multi-substituted aryl dithiocarbamates (**3e**, **3f**, **3j**, **3l)** were more favorably obtained (**Table 2**, **entries 8-9**, **16-17**). In general, the reaction was slightly positively affected by electron donating groups on the aromatic ring, the steric hindrance from *N*-substituted amine group put no effect on the reaction, showing its good substrate suitability.

Table 2. Synthesis of *S*-aryl dithiocarbamates from diaryliodonium salts and tetraalkylthiuram disulfides [a]



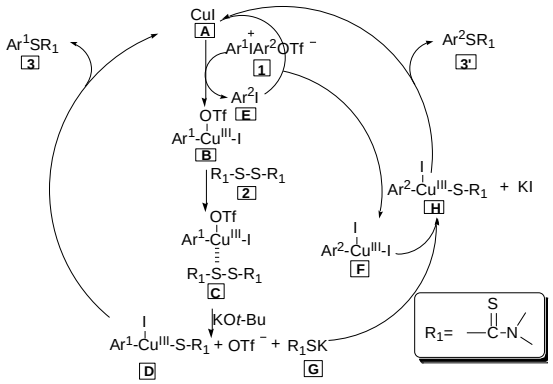
Entry	Diaryliodonium salts	Tetraalkylthiuram disulfides	Product **3** (Yield[b] %)	Product **3'** (Yield[c] %)
1	 **1a**	 **2a**	 **3a**: 84%; 86%[d]	 **3a**: 84%; 86%[d]
2	 **1b**	 **2a**	 **3a**: 85%	 **3a**: 85%
3	 **1c**	 **2a**	 **3a**: 86%	 **3a**: 86%

4	 OTf **1d**	 **2a**	 **3b**: 79%	 **3b**: 79%
5	 OTs **1e**	 **2a**	 **3c**: 84%	 **3c**: 84%
6	 OTf **1f**	 **2a**	 **3d**: 86%	 **3d**: 86%
7	 OTf **1g**	 **2a**	 **3e**: 89%	 **3e**: 89%
8	 OTf **1h**	 **2a**	 **3e**: 86%	 **3a**: 73%
9	 OTf **1i**	 **2a**	 **3f**: 89%	 **3a**: 81%
10	 OTf **1j**	 **2a**	 **3a**: 97%	 **3a'**: 0%
11	 OTf **1a**	 **2b**	 **3g**: 80%	 **3g**: 80%
12	 OTf **1d**	 **2b**	 **3h**: 82%	 **3h**: 82%
13	 OTf **1f**	 **2b**	 **3i**: 81%	 **3i**: 81%
14	OTf **1g**	**2b**	**3j**: 77%	**3j**: 77%
15	OTs **1e**	**2b**	**3k**: 76%	**3k**: 76%

16	 OTf **1h**	 **2b**	 **3j** 86%	 **3g**: 76%
17	 OTf **1i**	 **2b**	 **3l**: 86%	 **3g**: 61%
18	 OTf **1a**	 **2c**	 **3m**: 83%	 **3m**: 83%
19	 OTf **1d**	 **2c**	 **3n**: 81%	 **3n**: 81%
20	 OTf **1f**	 **2c**	 **3o**: 75%	 **3o**: 75%
21	 OTf **1g**	 **2c**	 **3p**: 81%	 **3p**: 81%
22	 OTs **1e**	 **2c**	 **3q**: 87%	 **3q**: 87%

[a] Reaction conditions: **1** (0.5 mmol), **2** (0.4 mmol), CuI (0.15 mmol), KO*t*-Bu (1.0 mmol), DMF (2 mL) at 110 °C for 4-6 h. [b] Isolated yield. [c] Isolated yield. [d] A scaled-up reaction (diaryliodonium salt **1**: 10 mmol) was performed.

The possible reaction mechanism (**Scheme 1**) is proposed according to the related literature.[16, 19] At first, diphenyliodonium triflate (**1**) react with CuI (**A)** generating intermediates **B** (through an oxidative addition manner) and aryl iodobenzene **E**. Tetraalkylthiuram disulfide (**2**) and **B** undergo through transmetallation affording complex **C**. Under the action of base (KO*t*-Bu), complex **C** decomposed to intermediate **D** and potassium salt **G**, a following reductive elimination produced the final product **3** along with copper (I) species **A**. On the other hand, **A** and **E** go the same oxidative addition affording **F**, then transmetallation giving intermediate **H**, and the reductive elimination producing the other main product **3'** along with copper(I) species **A**.



Scheme 1. Plausible mechanism for copper catalyzed *S*-arylation of tetraalkylthiuram disulfides by using diaryliodonium salts.

Conclusions

To summarize, we report an efficient and convenient procedure for the synthesis of *S*-aryl dithiocarbamates from diaryliodonium salts and tetraalkylthiuram disulfides. In the presence of CuI/KO*t*-Bu, two kinds of *S*-aryl dithiocarbamates could be obtained in good yields without obvious selectivity. The reaction has advantages of efficiency, good atomic economy and broad substrate scope. The method might afford an alternative way for the fast preparation of some potentially biologically active compounds.

Experimental Section

Nuclear magnetic resonance (NMR) spectra were obtained on a Bruker AC 400 MHz spectrometer (^{1}H NMR at 400 Hz, ^{13}C NMR at 100 Hz) in $CDCl_3$ using tetramethylsilane as an internal standard. Chemical shifts are given in ppm and coupling constants (*J*) are given in Hz. Electrospray ionization-high-resolution mass spectra (ESI-HRMS) were determined on an Ion Spec (7.0 T) spectrometer. All reactions were performed under dried glassware with septums. All starting materials were purchased from commercial suppliers and used without further purification unless otherwise stated. Yield refers to isolated compounds estimated to be > 95% pure as determined by ^{1}H NMR and capillary GC analysis.

Typical procedure (TP) for the preparation of *S*-aryl dithiocarbamates in the presence of Cu and KO*t*-Bu. Diphenyliodonium triflate (0.5 mmol), TMTD (0.4 mmol), CuI (30% mmol), KO*t*-Bu (2.0 equiv.) were added in dried seal tube equipped with a septum and magnetic stirrer bar, DMF (2 mL) was then added. The mixture was stirred at 110 °C and checked by thin-layer chromatography (TLC) until the starting material was finished (about 4-6 h). The reaction was cooled down to room temperature, quenched with sat. NH_4Cl solution (5 mL), and then extracted with EtOAc (10 mL). The crude solution was dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by flash column chromatography to afford the desired product.

Phenyl dimethylcarbamodithioate (**3a**). According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:7) to give the target compound **3a** (82.7 mg, 84%) as white solid; mp: 91-92 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49-7.45 (m, 5 H), 3.56 (s, 3 H), 3.50 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 137.0, 131.7, 130.1, 129.1, 45.7, 42.0. HRMS (ESI) calcd for $C_9H_{11}NS_2$ (197.0333), found: 197.0337.

4-Methylphenyl dimethylcarbamodithioate **(3b)**. According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:8) to give the target compound **3b** (83.3 mg, 79%) as white solid; mp: 109-110 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 8.0 HZ, 2 H), 7.33 (d, *J* = 4.0 HZ, 2 H), 3.51 (s, 3 H), 3.44 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.1, 140.4, 136.8, 130.0, 128.3, 45.7, 42.0. HRMS (ESI) calcd for $C_{10}H_{11}NS_2$ (211.0498), found: 211.0489.

4-Methoxyphenyl dimethylcarbamodithioate **(3c)**. According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:7) to give the target compound **3c** (95.3 mg, 84%) as white solid; mp: 97-99 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 4.0 HZ, 2 H), 6.96 (d, *J* = 4.0 HZ, 2 H), 3.83 (s, 3 H), 3.54 (s, 3H), 3.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.7, 161.1, 138.4, 122.6, 114.7, 55.3, 45.8, 41.9. HRMS (ESI) calcd for $C_{10}H_{11}NOS_2$ (227.0439), found: 227.0441.

2, 5-Dimethylphenyl dimethylcarbamodithioate **(3d).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:8) to give the target compound **3d** (96.8 mg, 86%) as colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33-7.27 (m, 3 H), 3.58 (s, 3 H), 3.51 (s, 3 H), 2.45 (s, 3 H), 2.41 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.4, 140.7, 138.1, 136.2, 131.6, 130.8, 130.6, 45.6, 42.1, 20.9, 20.5. HRMS (ESI) calcd for $C_{10}H_{16}NOS_2$ (225.0646), found: 225.0652.

2, 4, 6-Trimethylphenyl dimethylcarbamodithioate **(3e)**. According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:7) to give the target compound **3e** (106.4 mg, 89%) as white solid; mp: 77-78 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.00 (s, 2 H), 3.53 (s, 6 H), 2.32 (d, *J* = 16.0 HZ, 9 H), ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.0, 143.8, 140.4, 129.3, 127.5, 45.5, 42.0, 21.6, 21.4. HRMS (ESI) calcd for $C_{12}H_{17}NS_2$ (239.0802), found: 239.0809.

2, 4, 6-triisopropylphenyl dimethylcarbamodithioate **(3f)**. According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:7) to give the target compound **3f** (143.8 mg, 89%) as colorless solid; mp: 122-124 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04 (s, 2 H), 3.47 (s, 6 H), 3.38-3.32 (m, 2 H), 2.90-2.84 (m, 2 H), 1.21 (d, *J* = 8.0 Hz, 6 H), 1.41 (s, 12 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.7, 153.4, 151.3, 125.7, 122.1, 45.5, 42.0, 34.2, 31.9, 23.8. HRMS (ESI) calcd for $C_{18}H_{29}NS_2$ (323.1741), found: 323.1749.

Phenyl diethylcarbamodithioate **(3g)**. According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:10) to give the target compound **3g** (90.0 mg, 80%) 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 $C_{11}H_{15}NS_2$ (225.0604), found: 225.0608.

4-Methylphenyl diethylcarbamodithioate **(3h).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:15) to give the target compound **3h** (98.0 mg, 82%) as 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: 239.0807.

2, 5-Dmethylphenyl diethylcarbamodithioate **(3i).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:15) to give the target compound **3i** (102.5mg, 81%) as pale yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18 (s, 1 H), 7.11 (d, *J* = 8.0 Hz, 2 H), 3.93 (d, *J* = 4.0 Hz, 2 H), 3.77 (d, *J* = 8.0 Hz, 2 H), 2.25 (d, *J* = 8.0 Hz, 6 H), 1.31 (s, 3 H), 1.19 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.0, 140.7, 138.2, 136.2, 131.4, 130.6, 130.5, 49.7, 47.3, 20.8, 20.4, 12.8, 11.7. HRMS (ESI) calcd for $C_{13}H_{18}NS_2$ (253.0959), found: 253.0962.

2, 4, 6-Trimethylphenyl diethylcarbamodithioate **(3j).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:15) to give the target compound **3j** (102.8mg, 77%) as yellow solid; mp: 94-96 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.93 (s, 2 H), 3.96 (d, *J* = 8.0 Hz, 2 H), 3.82 (d, *J* = 4.0 Hz, 2 H), 2.28 (s, 6 H), 2.24 (s, 3 H), 1.34 (s, 3 H), 1.20 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.3, 143.9, 140.3, 129.2, 127.6, 49.7, 47.2, 21.7, 21.3, 12.9, 11.8. HRMS (ESI) calcd for $C_{14}H_{21}NS_2$ (267.1115), found: 267.1114.

4-Methoxy diethylcarbamodithioate **(3k).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:7) to give the target compound **3k** (97.0mg, 76%) as white solid; mp: 73-75 ^{o}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.

2, 4, 6-Triisopropylphenyl diethylcarbamodithioate **(3l).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:20) to give the target compound **3l** (150.9mg, 86%) as yellow solid; mp: 58-59 ^{o}C,^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02 (s, 2 H), 3.94 (d, *J* = 4.0 Hz, 2 H), 3.85 (d, *J* = 8.0 Hz, 2 H), 3.38-3.31 (m, 2 H), 2.89-2.84 (m, 1H), 1.34 (s, 3 H), 1.21 (d, *J* = 4.0 Hz, 9 H), 1.14 (s, 12 H) ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.0, 153.4, 151.1, 125.9, 122.0, 49.6, 47.2, 34.3, 32.0, 23.8, 13.0, 11.8. HRMS (ESI) calcd for $C_{20}H_{33}NS_2$ (351.2054), found: 351.2047.

Phenyl dibutylcarbamodithioate **(3m).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:20) to give the target compound **3m** (116.6mg, 83%) as 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, 4H), 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: 281.1280.

4-Methylphenyl dibutylcarbamodithioate **(3n).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:20) to give the target compound **3n** (119.5mg, 81%) as 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, 3H), 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: 295.1435.

2, 5-Dmethylphenyl dibutylcarbamodithioate **(3o).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:30) to give the target compound **3o** (115.9mg, 75%) as colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (s, 1 H), 7.13-7.08 (m, 2 H), 3.86 (t, *J* = 8.0 Hz, 2 H), 3.69 (t, *J* = 4.0 Hz, 2 H), 2.44 (d, *J* = 4.0 Hz, 6 H), 1.73-1.63 (m, 4 H), 1.37-1.23 (m, 4 H), 0.92 (t, *J* = 4.0 Hz, 3 H), 0.85 (t, *J* = 8.0 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.3, 140.6, 138.2, 136.1, 131.4, 130.8, 130.5, 55.1, 53.0, 29.7, 28.5, 20.8, 20.4, 20.1, 13.9, 13.8. HRMS (ESI) calcd for $C_{17}H_{27}NS_2$ (309.1585), found: 309.1582.

2, 4, 6-Trimethylphenyl dibutylcarbamodithioate **(3p).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:30) to give the target compound **3p** (130.8mg, 81%) as colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.94 (s, 2 H), 3.90 (t, *J* = 8.0 Hz, 2 H), 3.75 (t, *J* = 8.0 Hz, 2 H), 2.30 (s, 6 H), 2.25(s, 3 H), 1.76 (d, *J* = 8.0 Hz, 2 H), 1.65 (d, *J* = 8.0 Hz, 2 H), 1.42-1.36 (m, 2 H), 1.31-1.26 (m, 2 H), 0.96 (t, *J* = 4.0 Hz, 3 H), 0.89 (t, *J* = 8.0 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.7, 140.6, 143.8, 140.2, 129.2, 55.0, 52.9, 29.8, 28.6, 21.7, 21.4, 20.2, 13.9, 13.9. HRMS (ESI) calcd for $C_{18}H_{29}NS_2$ (323.1741), found: 323.1746.

4-Methoxy phenyl dibutylcarbamodithioate **(3q).** According to **TP**, the residue was purified by flash chromatography on silica gel (EtOAc/ PE= 1:20) to give the target compound **3q** (135.3mg, 87%) as 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: 311.1375.

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Keywords: dithiocarbamates • aylation• diaryliodonium salts • tetraalkylthiuram disulfides • copper

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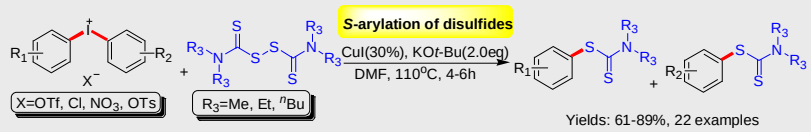

S*-arylation of disulfides

*Meng-Tian Zeng, Wan Xu, Xing Liu, Cai-Zhu Chang, Hui Zhu, Zhi-Bing Dong**

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Copper-catalyzed *S*-arylation of tetraalkylthiuram disulfides by using diaryliodonium salts

An efficient and convenient procedure for the *S*-arylation of tetraalkylthiuram disulfides by using diaryliodonium salts was explored. In the presence of CuI/KO*t*-Bu, two kinds of *S*-aryl dithiocarbamates could be obtained with good to excellent yields at one time, showing no obvious selectivity. The methodology has advantages of efficiency, good atomic economy and broad substrate scope.

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