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Nucleophilic disulfurating reagents for unsymmetrical disulfides construction via copper-catalyzed oxidative cross coupling

Zhihong Dai [a, 1], Xiao Xiao [a, 1], Xuefeng Jiang [a, b, *]

[a] Shanghai Key Laboratory of Green Chemistry and Chemical Process, Department of Chemistry, East China Normal University, 3663 North Zhongshan Road, Shanghai 200062, PR China
[b] State Key Laboratory of Elemento-organic Chemistry, Nankai University, Tianjin 300071, PR China

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ABSTRACT

Novel disulfuration was established via cross coupling between nucleophilic disulfurating reagent and arylsilane introducing two sulfur atoms in one step. This methodology was applied to synthesize various unsymmetrical disulfides under mild conditions via copper-catalyzed oxidative Hiyama-type cross coupling, providing a new pathway for disulfide synthesis. In addition, pH value of system displayed a key role in alcoholysis process.

1. Introduction

Disulfide extensively exists in numerous significant molecules with biological and pharmaceutical activity (Scheme 1).[1] Therefore, development of highly efficient synthetic methods to access sulfur-sulfur bond has been intensively pursued by synthetic community.[2,3] Symmetrical disulfide can be facilely synthesized via oxidation of thiol,[2a] while efficient examples have been scarcely reported for the unsymmetrical disulfide synthesis.[2b,3] Continuous with our concept of sulfur atom transfer study,[4] a strategy of constructing unsymmetrical disulfides with two different valent inorganic sulfur source via a comproportionation process had been reported.[5a] On the basis of masked strategy, a new type of nucleophilic disulfurating reagent had been designed and synthesized, which was utilized to construct unsymmetrical disulfide with arylboronic acid under mild copper-catalyzed oxidative cross-coupling conditions through a highly selective C–S bond cleavage and reformation (Scheme 2a).[5b]

In our previous Suzuki-type cross-coupling, prooxidant of molysite/manganese dioxide have to be utilized, and pH value of the system regulated by sodium carbonate plays a key role in the disulfuration. Compared to organoboron reagents and other metal reagents employed in cross coupling processes, silicon-based nucleophiles possess the characteristic of neutrality, easy handling, high chemical stability, low toxicity, and relatively low cost.[6,7] In this manuscript, we report a novel and facile methodology for Hiyama-type cross-coupling of disulfurating reagent with oxygen as sole oxidant under mild conditions.

2. Result and discussion

We commenced our study with trimethoxy(phenyl)silane **1a** and BnSSAc **2a** as the disulfur coupling partner in the presence of copper sulfate pentahydrate (10 mol %) and 2,2'-bipyridine (12 mol %) in MeOH at room temperature. When one equivalent of TBAF as the activator of inert C–Si bond was added, the desired unsymmetrical disulfide **4a** was obtained in 12% yield (Table 1, entry 1). Ligand screening shown that 4,4'-dimethoxy-2,2'-bipyridine was the best ligand in this disulfurtion (Table 1, entries 1–3). Further investigation revealed the yields were improved when phenolic derivatives were utilized as additive (Table 1, entries 4–7).[8] However, decreasing the amount of fluoride source did not affected the yield of desired product **4a** (Table 1, entry 8). A better result was achieved when TsOH·H_2O (0.3 equiv.) as pH value conditioner was

* Corresponding author. Shanghai Key Laboratory of Green Chemistry and Chemical Process, Department of Chemistry, East China Normal University, 3663 North Zhongshan Road, Shanghai 200062, PR China.
E-mail address: xfjiang@chem.ecnu.edu.cn (X. Jiang).
[1] Z. D. and X. X. contributed equally to this work.

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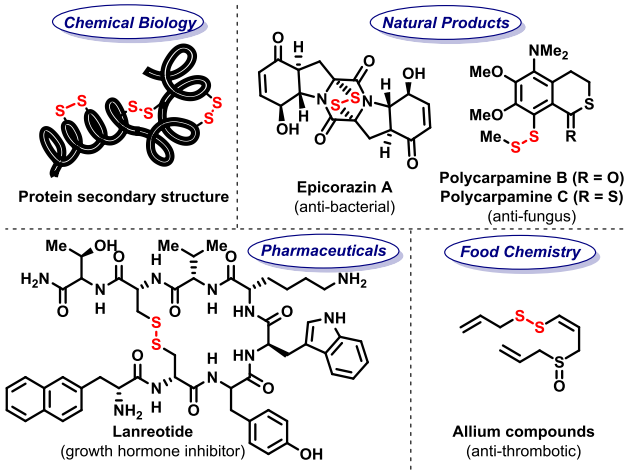
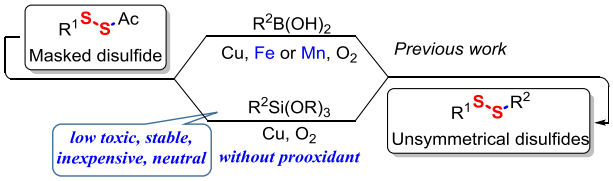


Scheme 1. Representative significant disulfides.

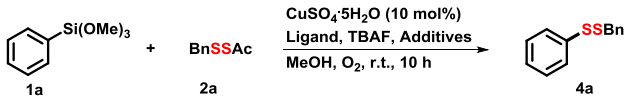


Scheme 2. Strategies for disulfide construction.

donating functional groups are compatible with the cross-coupling conditions (Scheme 3; **3a**-**h**). Arylsilane with amide containing active hydrogen was successfully used to afford the corresponding disulfane (Scheme 3; **3d**). Notably, the halogen-substituted arylsilane, proceed favourably in the transformation, which was arduously compatible in traditional cross-coupling reactions (Scheme 3; **3e**, **f**). Thiophenylsilane leads to formation of the desired product in more modest yield as well (Scheme 3; **3i**). Significantly, vinylsilane performed efficiently in this transformation (Scheme 3; **3j**). The scope with respect to the disulfurating reagents was further studied. For most cases, the reaction of disulfurating reagent was found to tolerate both benzyl and alkyl groups with various substituents in moderate to excellent yields (Scheme 3; **4a**–**i**). For example, reaction of trimethoxy(phenyl) silane **1a** and disulfurating reagents **2b** or **2c** gave rise to the corresponding products **4b** or **4c** in 85% or 89 yields (Scheme 3; **4b**, **c**), respectively. Disulfurating reagents with halide groups were also found to be suitable substrates for coupling with trimethoxy(phenyl)silane **1a** (Scheme 3; **4d**-**h**), and the desired products were generated in moderate to high yields. Propargyl substituted reagent was also tolerant in this transformation (Scheme 3; **4l**). Secondary disulfurating reagents were well compatible in this cross-coupling (Scheme 3; **4m**, **n**). A host of disulfide reagents with heterocycles, indolyl and benzofuranyl, were suitable partners in this process and the desired products were isolated in good yields (Scheme 3; **4o**-**q**). When 6 mmol of **2a** was carried out in the reaction, the unsymmetrical disulfide **4a** was afforded in 61% yield.

A plausible mechanism for the Hiyama-type cross-coupling reaction of disulfurating reagents with arylsilanes is shown in Scheme 4.[6,9] Disulfur anion **5**[10] was tardily released in-situ through alcoholysis of disulfane reagent **2** under the appropriate pH value conditions. Ligand-exchange of Cu(II) **6** with intermediate **5** proceeded to complex **7**. The complex **8** was generated via transmetalation with arylsilane. The resulting aryl Cu(II) **8** specie was furtherly oxidized through single electron transfer process under the assistance of another Cu(II) **6** to afford aryl Cu(III) **10** intermediate and Cu(I) **9**.[9a-c] Product **3** was subsequently formed through reductive elimination, releasing Cu(I) **9** simultaneously.[9d] Rapid

Table 1
Optimization of disulfuration.[a]

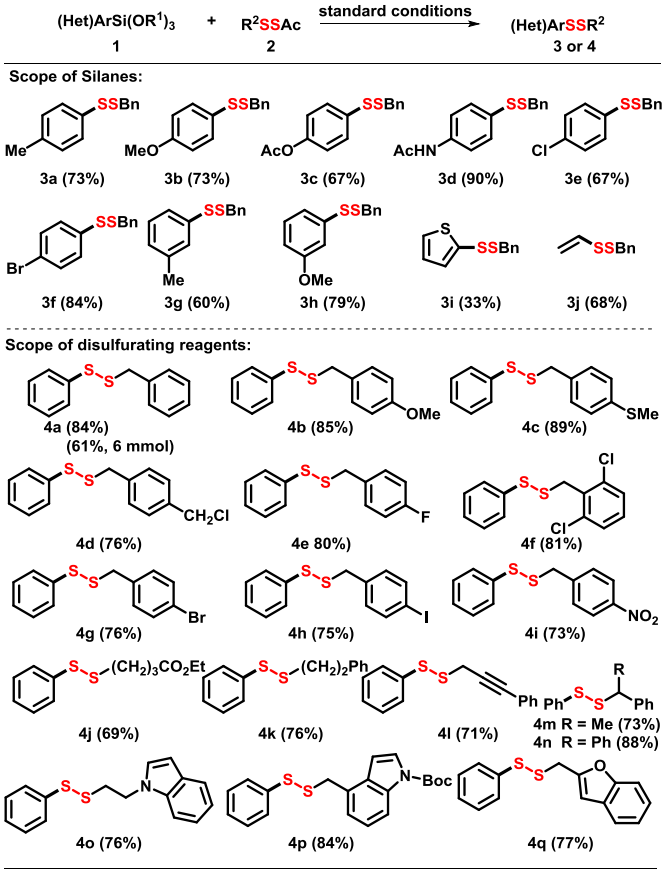


Entry	TBAF (equiv.)	Ligand (mol%)	Additive 1 (equiv.)	Additive 2 (equiv.)	Yield[b] (%)
1	1	Bipy (12)	–	–	12
2	1	4,4'-diMe-Bipy (12)	–	–	14
3	1	4,4'-diMeO-Bipy (12)	–	–	33
4	1	4,4'-diMeO-Bipy (12)	PhOH (1.0)	–	45
5	1	4,4'-diMeO-Bipy (12)	C_6F_6OH (1.0)	–	46
6	1	4,4'-diMeO-Bipy (12)	*p*-$CF_3C_6H_4OH$ (1.0)	–	37
7	1	4,4'-diMeO-Bipy (12)	*p*-FC_6H_4OH (1.0)	–	48
8	0.5	4,4'-diMeO-Bipy (12)	*p*-FC_6H_4OH (1.0)	–	47
9	0.5	4,4'-diMeO-Bipy (12)	*p*-FC_6H_4OH (1.0)	TsOH·H_2O (0.3)	57
10	0.5	4,4'-diMeO-Bipy (20)	*p*-FC_6H_4OH (1.0)	TsOH·H_2O (0.3)	92
11	0.5	4,4'-diMeO-Bipy (20)	PhOH (1.0)	TsOH·H_2O (0.3)	92 (85)[c]
12	***0.5***	***4,4'-diMeO-Bipy (20)***	***PhOH (0.5)***	***TsOH·H_2O (0.3)***	***92 (84)***[c]

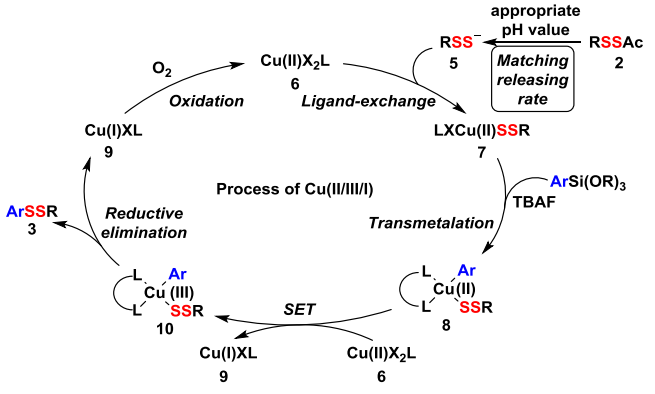
[a] Trimethoxy(phenyl)silane (0.6 mmol, 3 equiv.), **2**a (0.2 mmol, 1 equiv.), $CuSO_4·5H_2O$ (0.02 mmol, 10 mol%), 4,4'-dimethoxy-2,2'-bipyridine (0.04 mmol, 20 mol%), TBAF (0.1 mmol, 0.5 equiv.), PhOH (0.1 mmol, 0.5 equiv.) and TsOH·H_2O (0.06 mmol, 0.3 equiv.) were added to MeOH (2 mL) stirring at r.t. for 10 h under O_2 atmosphere.
[b] Yield was determined by ^1H NMR of the crude reaction mixture using an internal standard.
[c] Isolated yield.

employed in the reaction (Table 1, entry 9). The optimized conditions were obtained by enhancing the loading of ligand to afford 92% yield of benzyl(phenyl)disulfane (Table 1, entry 10). Finally, we were pleased to observe that cross-coupling was also efficient with phenol as additive (Table 1, entries 11 and 12).

With this preliminary result in hand, the scope of these copper-catalyzed Hiyama-type coupling reactions of silane reagents was investigated under the optimized conditions, and the results are shown in Scheme 3. A spectrum of functional groups furnished on silane substrates, bearing electron-withdrawing and electron-



Scheme 3. The scope of disulfuration.



Scheme 4. Plausible mechanistic cycle.

aerobic oxidation from Cu(I) **9** to Cu(II) **6** was realized with the help of oxygen, which regenerated the catalytic cycle.

3. Conclusion

In summary, we have developed the first example of achieving Hiyama-type oxidative cross-coupling reaction for unsymmetrical disulfide catalyzed by copper complex under mild conditions. Both electron-rich and electron-deficient arylsilanes are found to be compatible with this new transformation. The matching pH value of system provided by the additives was shown key role in alcoholysis process. Our current efforts are directed at further expanding new disulfurating reagents to unsymmetrical disulfides.

4. Experimental section

4.1. General experimental

NMR spectra were recorded on BRUKERDRX 400 spectrometers. Chemical shifts were recorded in parts per million (ppm, δ) relative to chloroform (δ = 7.26, singlet). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets), m (multiplets), and etc. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker (100 MHz) spectrometer.

4.2. Preparation of ***3a-3j***

To a tube were added RSSAc **2a-2q** (0.2 mmol, 1 equiv.), $CuSO_4{\cdot}5H_2O$ (0.02 mmol, 10 mol%), 4,4'-diMeObipy (0.04 mmol, 20 mol%), $TsOH{\cdot}H_2O$ (0.06 mmol, 0.3 equiv.), PhOH (0.1 mmol, 0.5 equiv.), aryltriethoxylsilane (0.6 mmol, 3 equiv.), TBAF solution 1.0 M in THF (0.1 mmol, 0.5 equiv.) and MeOH (2 mL), the mixture was stirred at 25 °C for 10 h under O_2 atmosphere before it was concentrated under vacuum. Purification by column chromatography afforded the desired product **3**.

4.2.1. 1-Benzyl-2-(p-tolyl)disulfane (***3a***)

73% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.2 Hz, 2H), 7.35–7.26 (m, 5H), 7.14 (d, J = 8.0 Hz, 2H), 3.97 (s, 2H), 2.37 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.1, 136.7, 133.6, 129.7, 129.4, 128.6, 128.5, 127.4, 43.3, 21.0; **MS** (EI) m/z 246 (M^+).

4.2.2. 1-Benzyl-2-(4-methoxyphenyl)disulfane (***3b***)

73% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 2H), 7.27–7.16 (m, 5H), 6.79–6.74 (m, 2H), 3.88 (s, 2H), 3.74 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.5, 136.8, 131.9, 129.4, 128.5, 127.9, 127.4, 114.6, 55.4, 43.3; **MS** (EI) m/z 262 (M^+).

4.2.3. 4-(benzyldisulfanyl)phenyl acetate (***3c***)

67% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ7.43–7.38 (m, 2H), 7.28–7.21 (m, 5H), 7.02–6.93 (m, 2H), 3.92 (s, 2H), 2.27 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ169.2, 149.7, 136.5, 134.3, 129.4, 129.2, 128.5, 127.6, 122.1, 43.4, 21.1; **HRMS** (EI) Calcd for $C_{15}H_{14}O_2S_2$ 290.0435, Found 290.0434.

4.2.4. N-(4-(benzyldisulfanyl)phenyl)acetamide (***3d***)

90% yield, white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.42 (d, J = 8.5 Hz, 2H), 7.38–7.33 (m, 2H), 7.29–7.20 (m, 5H), 3.91 (s, 2H), 2.14 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 168.5, 137.2, 136.5, 132.2, 129.5, 129.3, 128.5, 127.5, 120.4, 43.3, 24.5; **HRMS** (EI) Calcd for $C_{15}H_{15}NOS_2$ 289.0595, Found 285.0596.

4.2.5. 1-Benzyl-2-(4-chlorophenyl)disulfane (***3e***)

67% yield, white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38–7.33 (m, 2H), 7.32–7.27 (m, 5H), 7.27–7.23 (m, 2H), 3.96 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.4, 135.7, 132.8, 129.4, 129.0, 128.9, 128.5, 127.6, 43.4; **MS** (EI) m/z 266 (M^+).

4.2.6. 1-Benzyl-2-(4-bromophenyl)disulfane (***3f***)

84% yield, white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43–7.37 (m, 2H), 7.34–7.25 (m, 7H), 3.96 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.3(4), 136.3(2), 131.8, 129.3, 129.2, 128.5, 127.6, 120.6, 43.4; **MS** (EI) m/z 310 (M^+).

4.2.7. 1-Benzyl-2-(m-tolyl)disulfane (***3g***)

60% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33–7.24 (m, 6H), 7.23 (s, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 7.4 Hz, 1H),

3.96 (s, 2H), 2.33 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 138.8, 136.7, 129.4, 128.7, 128.5, 128.2, 127.7, 127.5, 124.8, 43.5, 21.3; **MS** (EI) *m*/*z* 246 (M^+).

*4.2.8. 1-Benzyl-2-(3-methoxyphenyl)disulfane (**3h**)*

79% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31–7.22 (m, 5H), 7.22–7.17 (m, 1H), 7.07–7.00 (m, 2H), 6.74 (ddd, *J* = 8.3, 2.4, 1.1 Hz, 1H), 3.94 (s, 2H), 3.78 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.0, 138.3, 136.6, 129.7, 129.3, 128.5, 127.5, 119.6, 112.8, 112.3, 55.3, 43.4; **MS** (EI) *m*/*z* 262 (M^+).

*4.2.9. 2-(benzyldisulfanyl)thiophene (**3i**)*

33% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 5.3, 1.3 Hz, 1H), 7.28–7.19 (m, 5H), 7.06 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.89 (dd, *J* = 5.3, 3.6 Hz, 1H), 3.99 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.5, 133.9, 130.6, 129.5, 128.6, 127.5, 43.5; **HRMS** (EI) Calcd for $C_{11}H_{10}S_3$ 237.9945, Found 237.9947.

*4.2.10. 1-Benzyl-2-vinyldisulfane (**3j**)*

68% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38–7.27 (m, 5H), 6.25 (dd, *J* = 16.3, 9.5 Hz, 1H), 5.50 (d, *J* = 16.3 Hz, 1H), 5.31 (d, *J* = 9.5 Hz, 1H), 3.93 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.8, 133.2, 129.3, 128.5, 127.5, 113.7, 42.5; **HRMS** (EI) Calcd for $C_9H_{10}S_2$ 182.0224, Found 182.0223.

*4.3. Preparation of **4a**-**4q***

To a tube were added RSSAc **2a-2q** (0.2 mmol, 1 equiv.), $CuSO_4{\cdot}5H_2O$ (0.02 mmol, 10 mol%), 4,4'-diMeObipy (0.04 mmol, 20 mol%), $TsOH{\cdot}H_2O$ (0.06 mmol, 0.3 equiv.), PhOH (0.1 mmol, 0.5 equiv.), phenyltrimethoxylsilane (0.6 mmol, 3 equiv.), TBAF solution 1.0 M in THF (0.1 mmol, 0.5 equiv.) and MeOH (2 mL), the mixture was stirred at 25 °C for 10 h under O_2 atmosphere before it was concentrated under vacuum. Purification by column chromatography afforded the desired product **4**.

*4.3.1. 1-Benzyl-2-phenyldisulfane (**4a**)*

84% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46–7.41 (m, 2H), 7.30–7.16 (m, 8H), 3.92 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.9, 136.5129.3, 128.9, 128.5, 127.5(4), 127.5(0), 126.7, 43.2; **MS** (EI) *m*/*z* 232 (M^+).

*4.3.2. 1-(4-methoxybenzyl)-2-phenyldisulfane (**4b**)*

85% yield, white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (dt, *J* = 3.1, 1.9 Hz, 2H), 7.33–7.28 (m, 2H), 7.24–7.18 (m, 3H), 6.85–6.79 (m, 2H), 3.92 (s, 2H), 3.79 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.0, 137.1, 130.5, 128.9, 128.4, 127.5, 126.7, 113.9, 55.2, 42.7; **MS** (EI) *m*/*z* 262 (M^+).

*4.3.3. 1-(4-(methylthio)benzyl)-2-phenyldisulfane (**4c**)*

89% yield, white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49–7.43 (m, 2H), 7.33–7.27 (m, 2H), 7.24–7.14 (m, 5H), 3.91 (s, 2H), 2.47 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.8, 136.9, 133.2, 129.8, 128.8, 127.6, 126.7, 126.5, 42.8, 15.7; **MS** (EI) *m*/*z* 278 (M^+).

*4.3.4. 1-(3-(chloromethyl)benzyl)-2-phenyldisulfane (**4d**)*

76% yield, white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46–7.41 (m, 2H), 7.31–7.18 (m, 7H), 4.52 (s, 2H), 3.95 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.6, 137.2, 136.8, 129.5, 129.4, 128.9, 127.6(7), 127.6(5), 126.8, 45.9, 43.0; **MS** (EI) *m*/*z* 280 (M^+).

*4.3.5. 1-(4-fluorobenzyl)-2-phenyldisulfane (**4e**)*

80% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48–7.42 (m, 2H), 7.33–7.27 (m, 2H), 7.27–7.20 (m, 3H), 7.00–6.93 (m, 2H), 3.92 (s, 2H); **^{19}F NMR** (282 MHz, $CDCl_3$) δ −114.67; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.2 (d, $^1J_{C\text{-}F}$ = 246.1 Hz), 136.75 (s), 132.3 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 131.0 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 128.9, 127.6 (s), 126.8 (s), 115.3 (d, $^2J_{C\text{-}F}$ = 21.3 Hz), 42.32 (s); **HRMS** (EI) Calcd for $C_{13}H_{11}FS_2$ 250.0285, Found 250.0282.

*4.3.6. 1-(2,6-dichlorobenzyl)-2-phenyldisulfane (**4f**)*

81% yield, colorless oil; **^{1}H** NMR (400 MHz, $CDCl_3$) δ 7.54–7.49 (m, 2H), 7.32–7.25 (m, 2H), 7.24 (s, 1H), 7.22–7.17 (m, 1H), 7.13–7.06 (m, 1H), 4.34 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.1, 136.0, 132.9, 129.0, 128.7, 128.2, 127.2, 126.7, 38.6; **MS** (EI) *m*/*z* 300 (M^+).

*4.3.7. 1-(4-bromobenzyl)-2-phenyldisulfane (**4g**)*

76% yield, colorless oil;**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47–7.36 (m, 4H), 7.31–7.26 (m, 2H), 7.23 (ddd, *J* = 7.4, 3.7, 1.3 Hz, 1H), 7.15–7.11 (m, 2H), 3.88 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.7, 135.7, 131.6, 131.0, 128.9, 127.9, 126.9, 121.5, 42.5; **MS** (EI) *m*/*z* 310 (M^+).

*4.3.8. 1-(4-iodobenzyl)-2-phenyldisulfane (**4h**)*

75% yield, white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61–7.55 (m, 2H), 7.45–7.39 (m, 2H), 7.32–7.26 (m, 2H), 7.26–7.20 (m, 1H), 7.00 (d, *J* = 8.3 Hz, 2H), 3.86 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 137.5, 136.6, 136.2, 131.2, 128.9, 127.7, 126.9, 93.1, 42.5; **HRMS** (EI) Calcd for $C_{13}H_{11}IS_2$ 357.9347, Found 357.9349.

*4.3.9. 1-(4-nitrobenzyl)-2-phenyldisulfane (**4i**)*

73% yield, white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12–8.06 (m, 2H), 7.40 (d, *J* = 8.4 Hz, 4H), 7.29–7.24 (m, 2H), 7.23–7.18 (m, 1H), 3.98 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.2, 144.3, 136.2, 130.2, 128.9, 128.0, 127.2, 123.6, 42.2; **HRMS** (EI) Calcd for $C_{13}H_{11}NO_2S_2$ 277.0231, Found 277.0229.

*4.3.10. Ethyl 4-(phenyldisulfanyl)butanoate (**4j**)*

69% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56–7.50 (m, 2H), 7.35–7.**29** (m, 2H), 7.25–7.19 (m, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 2.76 (t, *J* = 7.1 Hz, 2H), 2.40 (t, *J* = 7.3 Hz, 2H), 2.01 (p, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.8, 137.1, 128.9, 127.6, 126.8, 60.4, 37.6, 32.5, 23.8, 14.2; **MS** (EI) *m*/*z* 256 (M^+).

*4.3.11. 1-Phenethyl-2-phenyldisulfane (**4k**)*

76% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 2H), 7.38–7.28 (m, 4H), 7.25 (t, *J* = 6.5 Hz, 2H), 7.18 (d, *J* = 7.3 Hz, 2H), 3.00 (s, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.8, 137.3, 129.0, 128.6, 128.5, 127.5, 126.8, 126.4, 39.9, 35.2; **MS** (EI) *m*/*z* 246 (M^+).

*4.3.12. 1-Phenyl-2-(3-phenylprop-2-yn-1-yl)disulfane (**4l**)*

71% yield, yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64–7.59 (m, 2H), 7.33–7.24 (m, 7H), 7.24–7.19 (m, 1H), 3.74 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.7, 131.7, 129.0, 128.3, 128.1, 127.9, 127.1, 122.6, 84.8, 84.2, 28.4; **HRMS** (EI) Calcd for $C_{15}H_{12}S_2$ 256.0380, Found 256.0383.

*4.3.13. 1-Phenyl-2-(1-phenylethyl)disulfane (**4m**)*

73% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49–7.43 (m, 2H), 7.36–7.25 (m, 7H), 7.23–7.18 (m, 1H), 4.13 (q, *J* = 7.0 Hz, 1H), 1.71 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 141.3, 137.5, 128.8, 128.5, 127.6, 127.3, 126.5, 50.1, 20.5, **MS** (EI) *m*/*z* 246 (M^+).

*4.3.14. 1-Benzhydryl-2-phenyldisulfane (**4n**)*

88% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48–7.42 (m, 6H), 7.38–7.32 (m, 4H), 7.32–7.23 (m, 5H), 5.35 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.6, 136.9, 128.7(9), 128.8(3), 128.5, 128.4, 127.5, 126.9, 60.3; **MS** (EI) *m*/*z* 308 (M^+).

*4.3.15. 1-(2-(phenyldisulfanyl)ethyl)-1H-indole (**4o**)*

76% yield, yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.9 Hz, 1H), 7.61–7.56 (m, 2H), 7.39–7.31 (m, 3H), 7.30–7.25 (m, 1H), 7.25–7.20 (m, 1H), 7.16–7.11 (m, 1H), 7.06 (d, J = 3.1 Hz, 1H), 6.51 (d, J = 3.1 Hz, 1H), 4.44 (t, J = 8.0 Hz, 2H), 3.09 (t, J = 8.0 Hz 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.7, 135.7, 129.2, 128.7, 128.2, 127.8, 127.4, 121.7, 121.1, 119.6, 109.0, 101.7, 45.2, 37.8; **HRMS** (EI) Calcd for $C_{16}H_{15}NS_2$ 285.0646, Found 285.0641.

*4.3.16. Tert-butyl 4-((phenyldisulfanyl)methyl)-1H-indole-1-carboxylate (**4p**)*

84% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.2 Hz, 1H), 7.64 (d, J = 3.6 Hz, 1H), 7.52–7.45 (m, 2H), 7.34–7.20 (m, 4H), 7.15 (d, J = 7.3 Hz, 1H), 6.65 (d, J = 3.8 Hz, 1H), 4.25 (s, 2H), 1.71 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6, 137.0, 135.3, 129.9, 128.8, 128.3, 127.7, 126.7, 125.9, 124.1, 123.9, 114.8, 105.3, 83.7, 41.1, 28.2; **HRMS** (EI) Calcd for $C_{20}H_{21}NO_2S_2$ 371.1014, Found 371.1010.

*4.3.17. 2-((phenyldisulfanyl)methyl)benzofuran (**4q**)*

77% yield, colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49–7.42 (m, 3H), 7.41–7.37 (m, 1H), 7.29–7.23 (m, 1H), 7.22–7.17 (m, 3H), 7.16–7.10 (m, 1H), 6.60 (s, 1H), 4.07 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 155.1, 152.5, 136.5, 128.7, 128.3, 127.8, 126.8, 124.2, 122.7, 120.7, 111.1, 106.1, 36.1; **HRMS** (EI) Calcd for $C_{15}H_{12}OS_2$ 272.0330, Found 272.0331.

4.4. Gram-scale operation

To a tube were added BnSSAc **2a** (6 mmol, 1.19 g, 1 equiv.), $CuSO_4{\cdot}5H_2O$ (0.6 mmol, 150 mg, 10 mol%), 4,4'-diMeObipy (1.2 mmol, 259.5 mg, 20 mol%), $TsOH{\cdot}H_2O$ (1.8 mmol, 342.4 mg, 0.3 equiv.), PhOH (3 mmol, 282.4 mg, 0.5 equiv.), phenyltrimethoxylsilane (18 mmol, 3.57 g, 3 equiv.), TBAF solution 1.0 M in THF (3 mmol, 3 mL, 0.5 equiv.) and MeOH (60 mL), the mixture was stirred at 25 °C for 10 h under O_2 atmosphere before it was concentrated under vacuum. Purification by column chromatography afforded the desired product **4a** (850 mg, 61%).

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Appendix ASupplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2017.05.010.

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