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Graphical Abstract

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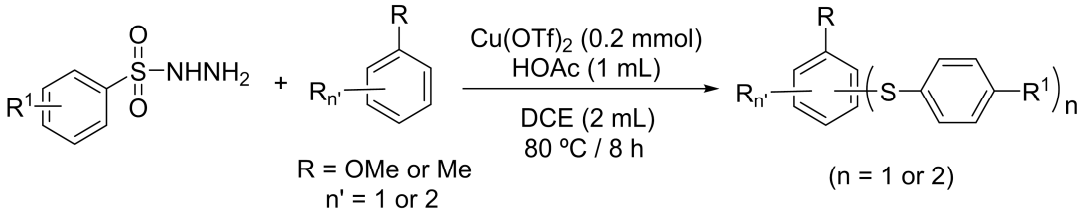

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ABSTRACT

An efficient Cu-catalyzed direct C–H thiolation of electron-rich arenes with arylsulfonyl hydrazides has been developed. Various mono(or bis)-thioether products were obtained in moderate to good yields. Mechanistic studies suggest that the reaction likely proceeds through free-radical formation including arylthio radical and sulfonyl radical, while both disulfanes and sulfonothioates are the major thiolation species in this transformation.

1. Introduction

Construction of C–S bond has become an important reaction in the syntheses of natural products, pharmaceuticals, and organic materials owing to their unique properties.[1,2] Aryl sulfides, as an important member of this family, have attracted considerable attention. Thus, methodologies for the efficient synthesis of this type of skeleton are highly desired. In 2013, Singh et al. reported the synthesis of unsymmetrical sulfides via the reaction of aryl/het-aryl/benzyl halides with sulfonyl hydrazides by means of [DBU][HOAc] and CuI as catalyst under microwave irradiation.[3,4] Tian et al. reported a Cu-catalyzed thiolation of boronic acids with sulfonyl hydrazides.[5] Yoshida et al. also provided results of an efficient thiolation of aryl- and alkenylborons with thiosulfonates under mild conditions using a copper catalyst.[6] However, in contrast, a particularly straightforward approach toward the synthesis of aryl sulfides is direct C-H thiolation of arenes using suitable sulfur sources. In 2014, Anbarasan et al. succeed to carry out palladium-catalyzed thiolation of arenes with electrophilic sulfur reagent derived from succinimide.[7] In addition, metal-catalyzed synthesis of aryl sulfides from disulfides via C-H bond cleavage of arenes was described.[8] In recent years, synthesis of di(hetero)aryl sulfides by metal-free thiolations of electron-rich arenes with arylsulfonyl chlorides or sodium arylsulfinates as sulfur sources was introduced.[9] Meanwhile, the direct thiolation of arenes with thiols as sulfur sources under metal-free conditions was developed.[10]

In the past few years, the sulfonyl hydrazides have been widely used as environmentally friendly sulfur sources since they are stable, readily accessible, odor-free. More importantly, N_2 and water are the only byproducts when the sulfonyl hydrazides are used in organic reaction.[11] Yan et al. and Zhao et al. reported their elegant work on iodine-mediated thiolation of electron-rich arenes with arylsulfonyl hydrazides through the cleavage of S-N/S-O bonds, respectively.[12] However, although the mechanisms for the sulfonyl hydrazide-based metal-free thiolation have been proposed, how the actual thiolation species are generated from sulfonyl hydrazides is not very clear. Herein, we report a Cu-catalyzed direct C-H thiolation of electron-rich arenes with arylsulfonyl hydrazides under acidic conditions and propose a possible reaction mechanism.

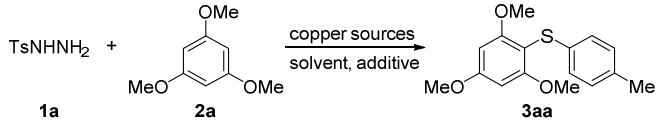
2. Results and Discussion

2.1. Optimization of the reaction conditions

Initially, 1,3,5-trimethoxybenzene and $TsNHNH_2$ were selected as model substrates in the presence of HOAc to optimize the reaction conditions. The results are summarized in Table 1. This reaction is unlikely to take place in the absence of Cu catalyst (Table 1, Entry 1). When CuI was used as the catalyst, only 16% yield of the desired product **3aa** was obtained (Table 1, Entry 2). However, the addition of I_2 could increase the yield to 61% (Table 1, Entry 3). Experiments screening a variety of copper sources showed $Cu(OTf)_2$ was the most suitable catalyst (Table 1, Entries 4-6). Subsequently, we attempt to catalyse the reaction by using CuI_2 generated from KI and $CuSO_4{\cdot}2H_2O$ in situ, but only 28% yield was obtained (Table 1, Entry 7). It is

noteworthy that an excellent yield could be obtained in the absence of I_2 (Table 1, Entry 8). Further investigations were focused on the influence of the solvents on the reaction. We found that DCE was the best solvent, whereas others solvents such as toluene, DMSO, dioxane, and MeOH, gave no good yields (Table 1, Entries 9-12). With respect to the concentration of additives, it was noticed that 1 mL HOAc was the most suitable compared to other concentrations used (Table 1, Entries 13 and 14). When the reaction time was prolonged to 10 h, product **3aa** was obtained in 77% yield (Table 1, Entry 15). Control experiments indicated that the oxidant is essential to this reaction. When the reaction was performed under Ar atmosphere, a yield of only 54% was obtained (Table 1, Entry 16). In addition, with decreasing the amount of $Cu(OTf)_2$ or ratio between of **1a** : **2a**, the yield of the product was accordingly lowered (Table 1, Entries 17 and 18). Then, we examined the reaction at 110 ºC, but low yield of mono-thioether product **3aa** was recorded in comparison to entry 8 (Table 1, entry 19), and accompanied by 68% yield of the bis-thioether product. When acetic acid is replaced by trifluoroacetic acid, the reaction was difficult to carry out (Table 1, Entry 20). Finally, the combination of 1,3,5-trimethoxybenzene (0.3 mmol), $TsNHNH_2$ (0.6 mmol), $Cu(OTf)_2$ (0.2 mmol), HOAc (1 mL) at 80 °C for 8 h in DCE (2 mL) was found to be the optimal reaction conditions.

Table 1. Optimized reaction conditions [a]



1a 2a 3aa

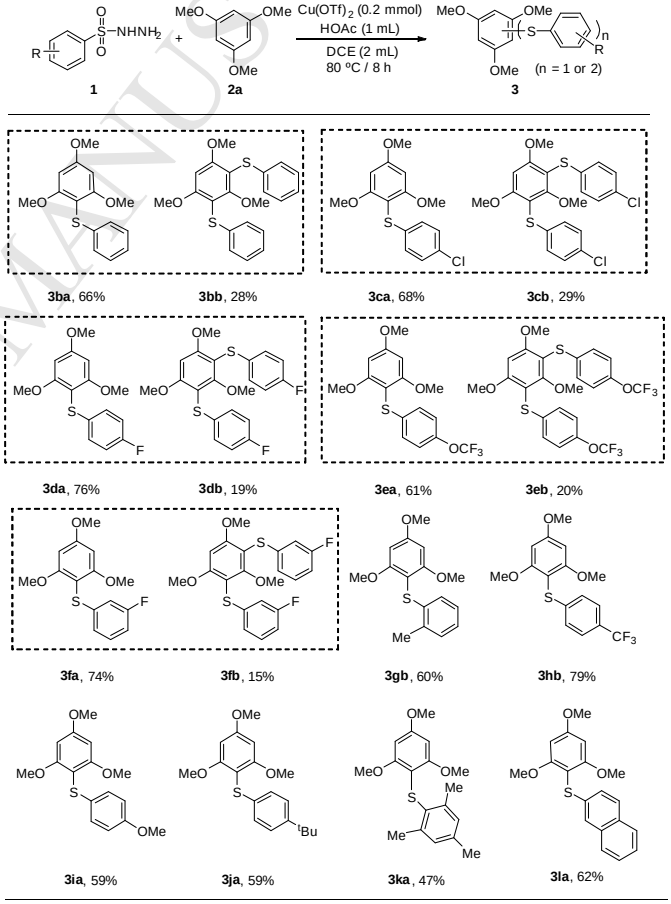
Entry	[Cu](mmol)	Solvent	I_2(mmol)	HOAc(mL)	Yield(%) [b]
1	-	DCE	-	1	0
2	CuI (0.2)	DCE	-	1	16
3	CuI (0.2)	DCE	0.1	1	61
4	CuBr (0.2)	DCE	0.1	1	51
5	$Cu(OTf)_2$ (0.2)	DCE	0.1	1	70
6	$Cu(TFA)_2$ (0.2)	DCE	0.1	1	35
7	$CuSO_4 \cdot 2H_2O$ (0.2) + KI (0.4)	DCE	0.1	1	28
8	$Cu(OTf)_2$ (0.2)	DCE	-	1	93
9	$Cu(OTf)_2$ (0.2)	Toluene	-	1	51
10	$Cu(OTf)_2$ (0.2)	DMSO	-	1	Trace
11	$Cu(OTf)_2$ (0.2)	Dioxane	-	1	38
12	$Cu(OTf)_2$ (0.2)	MeOH	-	1	Trace
13	$Cu(OTf)_2$ (0.2)	DCE	-	0.5	78
14	$Cu(OTf)_2$ (0.2)	DCE	-	2	75
15[c]	$Cu(OTf)_2$ (0.2)	DCE	-	1	77
16[d]	$Cu(OTf)_2$ (0.2)	DCE	-	1	54
17	$Cu(OTf)_2$(0.1)	DCE	-	1	80
18[e]	$Cu(OTf)_2$ (0.2)	DCE	-	1	67
19[f]	$Cu(OTf)_2$ (0.2)	DCE	-	1	19
20[g]	$Cu(OTf)_2$ (0.2)	DCE	-	-	0

[a] Reaction conditions: **1a** (0.6 mmol), **2a** (0.3 mmol), copper source (0.2 mmol), solvent (2 mL), HOAc (1 mL), in air, 80 ºC, 8 h. [b] Isolated yield. [c] Reaction time 10 h. [d] In Argon. [e] **1a** : **2a** = 0.5 : 0.3. [f] 110 ºC. [g] TFA (CF_3CO_2H, 1 mL) was added.

2.2. Scope and limitations of substrates

With the optimized reaction conditions in hand, the thioether reactions of substituted benzenesulfonohydrazides with 1,3,5-trimethoxybenzene were further explored (Table 2). First, benzenesulfonohydrazide underwent the thioether reaction, affording 66% yield of mono-thioether product **3ba** and 28% yield of bis-thioether product **3bb**. The reactions of para-substituted arylsulfonyl hydrazides with electron-withdrawing groups were carried out and gave the corresponding mono-thioether products (**3ca**, **3da**, and **3ea**) and bis-thioether products (**3cb**, **3db**, and **3eb**) in 61-76% and 19-29% yields, respectively. Furthermore, the reaction of 3-fluorobenzenesulfonohydrazide with 1,3,5-trimethoxybenzene generated the desired mono-thioether products **3fa** and bis-thioether product **3fb** in 74% and 15% yields, respectively. Sterically demanding ortho substituents, such as 2-methylbenzenesulfonohydrazide and 2,4,6-trimethylbenzenesulfonohydrazide, gave the bis-thioether product **3gb** and **3ka** in 60% and 47% yields, respectively. 4-(Trifluoromethyl)benzenesulfonohydrazide as thioether reagent also led to the mono-thioether product **3hb** in 79% yield. Moreover, the reactions of substituted aryl sulfonyl hydrazides with electron-donating groups, such as MeO- and ^{t}Bu-, gave the corresponding mono-thioether products (**3ia** and **3ja**) in moderate yields. In addition, naphthalene-2-sulfonohydrazide was also tolerated, affording desired products **3la** in 62% yields.

Table 2. The direct thiolations of 1,3,5-trimethoxybenzene **2a** with arylsulfonyl hydrazides [a]

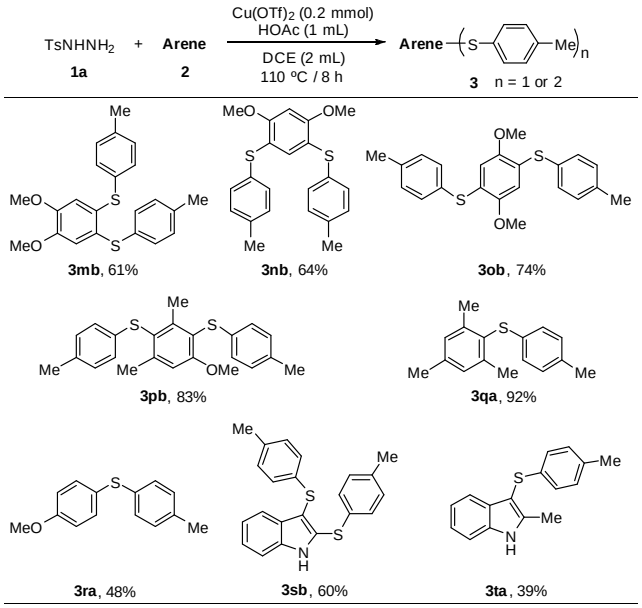


[a] Reaction conditions: **1a** (0.6 mmol), **2a** (0.3 mmol), copper source (0.2 mmol), solvent (2 mL), HOAc (1 mL), in air, 80 ºC, 8 h. The yields of isolated products are given.

Finally, to broaden the substrate scope of this transformation, we tested other electron-rich arenes under the optimized reaction conditions. The results are summarized in Table 3. Substituted toluenes underwent coupling reactions to $TsNHNH_2$ to generate the corresponding mono- and bis-thioether products at 110 ºC. For example, 1,2-dimethoxybenzene, 1,3-dimethoxybenzene, and 1,4-dimethoxybenzene afforded only bis-thioether products **3lb**-

3nb in 61-74% yields. 1-Methoxy-3,5-dimethylbenzene resulted in the formation of bis-thioether product **3ob** in 83% yield, while mesitylene gave only mono-thioether product **3pa** in 92% yield. Moreover, when anisole was used as substrate, the mono-thioether product (4-methoxyphenyl)(p-tolyl)sulfane **3qa** was obtained in 48% yield. In addition, 1-methyl-1*H*-indole is also a suitable substrate to afford the bis-thioether product **3rb** in 70 % yield. When 2-methyl-1*H*-indole was used, the sulfenylation reaction took place at the C3 position of the indole ring to give the desired product **3sa** in 39% yield.

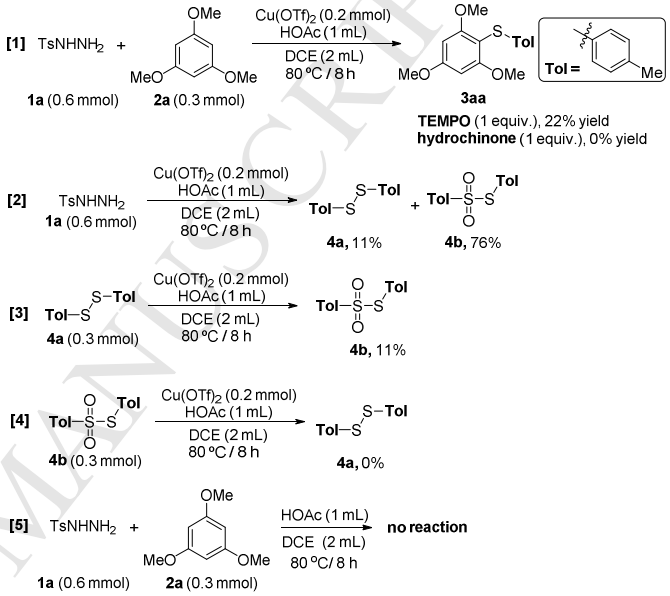
Table 3. The direct thiolation of electron-rich arenes **2** with $TsNHNH_2$ [a]



[a] Reaction conditions: **1a** (0.6 mmol), rich arenes **2** (0.3 mmol), $Cu(OTf)_2$ (0.2 mmol), DCE (2 mL), HOAc (1 mL), under air, 110 °C, 8 h. The yields of isolated products are given.

Subsequently, to gain further insight into the mechanism, a series of control experiments were performed (**Scheme 1**). First, the yield decreased significantly in the presence of TEMPO that indicated the generation of free radical intermediates during the reaction. If hydroquinone is added to the reaction system, the thioether reaction will not take place, which additionally highlights the formation of free radical intermediates that play a key role in the smooth progress of the reaction (**Scheme 1, [1]**). When only $TsNHNH_2$ as substrate is used, S-p-tolyl 4-methylbenzenesulfonothioate (**4a**) and 1,2-di-p-tolyldisulfane (**4b**) can be obtained under optimized reaction conditions(**Scheme 1, [2]**). The product **4a** can partially generate **4b** under standard conditions, but **4b** cannot be converted to **4a** under the same conditions(**Scheme 1, [3]** and **[4]**). In addition, the blank experiments showed that the thioetherification of 1,3,5-trimethoxybenzene (**2a**) with $TsNHNH_2$ is not carried out in the absence of copper catalyst (**Scheme 1, [5]**). Therefore, we can speculate that $Cu(OTf)_2$ plays an important role in the thioetherification.

Next, different sulfur sources were investigated for the reaction with 1,3,5-trimethoxybenzene (**2a**) aiming to find the real thioether species (**Scheme 2**). When **4a** was used as thioether reagent, 47% of the mono-thioether product **3aa** and 46% of the bis-thioether product **3ab** were formed, while **4b** was not detected (**Scheme 2, [1]**). When **4b** was used as thioether reagent, only 36% of the mono-thioether products **3aa** were obtained, whereas **4a** was not identified (**Scheme 2, [2]**). The selection of thiophenol **4c** as sulfur source showed that the reaction of **2a** and **4c** cannot take place (**Scheme 2, [3]**). In contrast, the reaction of **2a** with 4-methylbenzenesulfinic acid **4d** as sulfur source can proceed smoothly and give a 56% yield of mono-thioether product **3aa**, 41% yield of bis-thioether product **3ab**, and 11% yield of product **4b (Scheme 2, [4])**. Moreover, the results for the three-component reactions of **2a**, **4c**, and **4d** show that only *p*-toluenesulfonic acid can react with **2a** and the yields of the mono-thioether product **3aa** and bis-thioether product **3ab** significantly decreased in the presence of thiophenol **4c (Scheme 2, [5])**. Finally, we tested the reaction of (4-methoxyphenyl) 4-methylbenzenesulfonothioate **4e** as sulfur source with **2a** under standard conditions, and the mono-thioether **3ia**, the bis-thioether **3ab**, and **4b** were obtained, and accompanied by 38% yield of the product **3ja**. **(Scheme 2, [6])**.



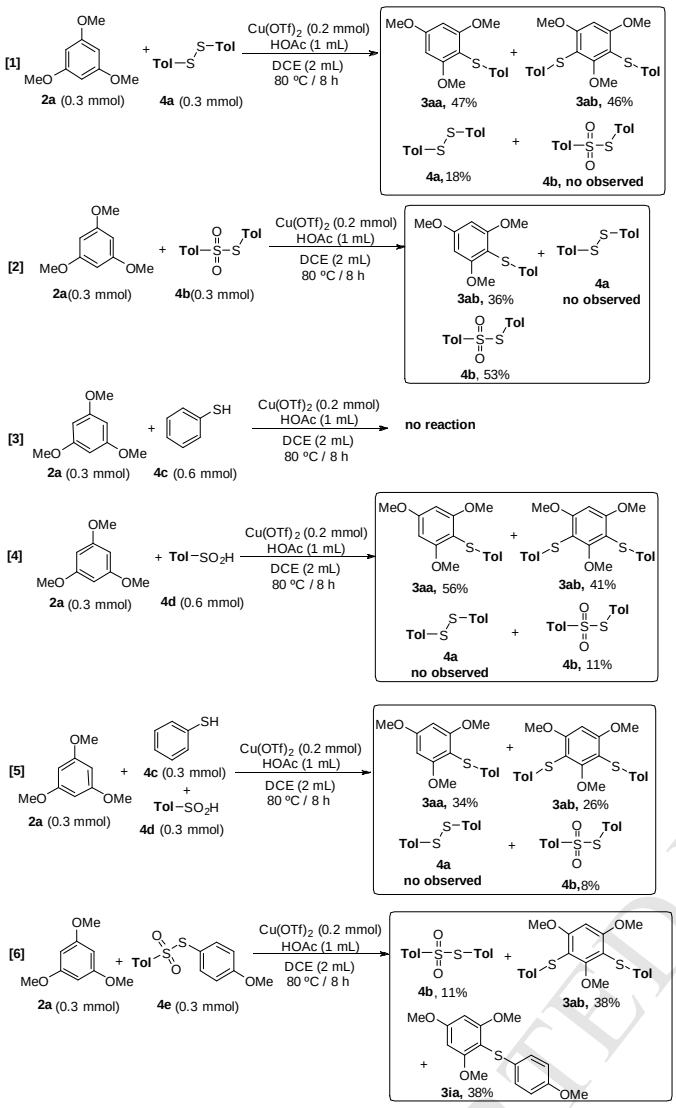
Scheme 1. Control experiments performed to establish the reaction mechanism.

On the basis of the above mentioned experimental details and previous reports,[25] the following reaction mechanism was proposed (**Scheme 3**). First, $TsNHNH_2$ is oxidized to intermediate (**I**) in the presence of $Cu(OTf)_2$ as catalysts, afterward, the intermediate (**I**) is oxidized to generate sulfonyl radicals (**II**). Some of the sulfonyl radicals are subsequently reduced to arylthio radicals (**III**) by monovalent copper ions. Then, the sulfonyl radical interacts with the arylthio radical to yield two important thioether intermediates **4a** and **4b**, respectively. The corresponding catalytic cycle-1 and catalytic cycle-2 are as follows: (1) the arenes react with monovalent copper to produce aryl copper intermediate (**IV**), followed by the oxidative addition of intermediate (**IV**) with **4a** to form the intermediate (**V**), and then, the reductive elimination of intermediate (**V**) to give the thioether product **3**, while Cu(I) catalyst is released and ready for use in the next catalytic cycle. (2) Oxidative addition of intermediate (**IV**) with **4b** forms the intermediate (**V′**), and then, the reductive elimination of intermediate (**V′**) to give the thioether product **3**, arylsulfuric acid (**VI**), and Cu(I) catalyst. Subsequently, aryl sulfuric acid (**VI**) is converted into the intermediate **4b** by Cu(I) catalyst under acidic conditions, and the intermediate **4b** re-enter into a new catalytic cycle.[25c]

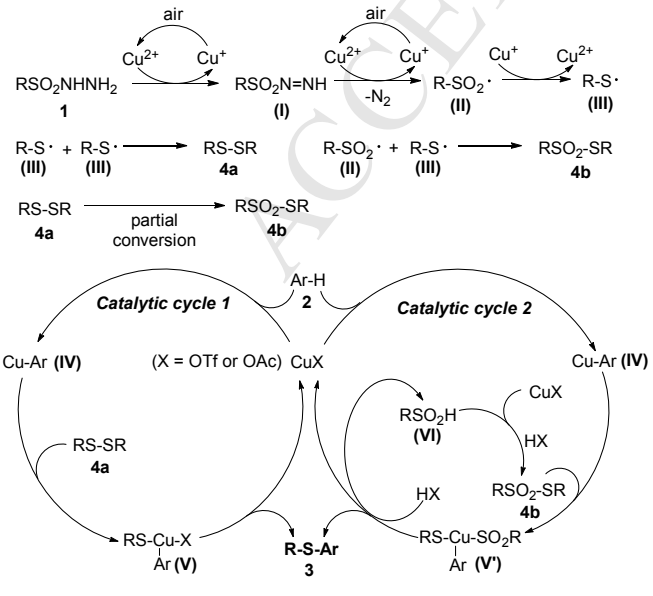
3. Conclusions

In summary, we have proposed an efficient Cu-catalysed direct C-H thiolation of electron-rich arenes with arylsulfonyl

hydrazides. Mechanistic studies suggested that both free-radical formation and Cu-catalysed cycle may be involved in the reaction pathway, and the disulfanes and sulfonothioates are the main thiolation intermediates in this transformation.



Scheme 2. Experimental details for the reaction of **2a** and different sulfur sources.



Scheme 3. Proposed mechanism for Cu-catalyzed direct thiolation of arenes.

4. Experimental Section

4.1. Materials and instruments

Chemicals were obtained commercially and used as received. NMR spectra were recorded on a Bruker DPX–400 spectrometer using TMS as the internal standard. EI–Mass spectrum was measured on a LC/Q–TOF MS (Micromass, England) or GC-MS (Agilent 7890A/5975C) instrument. All products were isolated by short chromatography on a silica gel (200–300 mesh) column using petroleum ether (60–90 °C), unless otherwise noted. Arenes and arylsulfonyl hydrazides were of analytical grade quality, purchased from Adamas-beta Pharmaceuticals, Inc.

4.2. General procedure for the direct thiolation of electron-rich arenes with arylsulfonyl hydrazides

First, a solution of rich arenes (0.3 mmol), arylsulfonyl hydrazides (0.6 mmol), $Cu(OTf)_2$ (0.2 mmol), and HOAc (1 mL) in DCE (2 mL), was stirred at 80 °C (or 110 °C) for 8 h under air. Second, the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (3 × 10 mL). The combined EtOAc extracts were dried over anhydrous $MgSO_4$ and filtered, followed by solvent removal under reduced pressure. The residue was purified by flash column chromatography on silica gel using PE / EtOAc as the eluent.

*4.3. p-Tolyl(2,4,6-trimethoxyphenyl)sulfane [**3aa**] [12b]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.96 (d, J = 3.6 Hz, 4H), 6.21 (s, 2H), 3.86 (s, 3H), 3.80 (s, 6H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.90, 162.64, 134.25, 129.41, 126.14, 91.33, 56.45, 55.56, 21.03.

*4.4. (2,4,6-Trimethoxy-1,3-phenylene)bis(p-tolylsulfane) [**3ab**] [12b]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (s, 8H), 6.41 (s, 1H), 3.86 (s, 6H), 3.76 (s, 3H), 2.25 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.45, 134.80, 129.56, 126.66, 92.55, 62.45, 56.51, 21.06.

*4.5. Phenyl(2,4,6-trimethoxyphenyl)sulfane [**3ba**] [13]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18-7.12 (m, 2H), 7.02 (d, J = 9.2 Hz, 3H), 6.22 (s, 2H), 3.87 (s, 3H), 3.81 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.05, 162.68, 138.81, 128.60, 125.76, 124.48, 91.34, 56.44, 55.57.

*4.6. (2,4,6-Trimethoxy-1,3-phenylene)bis(phenylsulfane) [**3bb**]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21-7.15 (m, 4H), 7.07 (d, J = 6.8 Hz, 6H), 6.44 (s, 1H), 3.87 (s, 6H), 3.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.65, 138.41, 128.78, 126.23, 124.99, 106.91, 92.55, 62.51, 56.51. HRMS (ESI) m/z calcd for $C_{21}H_{21}O_3S_2^+$ $(M+H)^+$ 385.09266, found 385.09265.

*4.7. (4-Chlorophenyl)(2,4,6-trimethoxyphenyl)sulfane [**3ca**] [14]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 6.21 (s, 2H), 3.87 (s, 3H), 3.81 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.25, 162.56, 137.52, 130.20, 128.68, 127.10, 91.36, 56.45, 55.60.

*4.8. (2,4,6-Trimethoxy-1,3-phenylene)bis((4-chlorophenyl)sulfane) [**3cb**]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, J = 8.8 Hz, 4H), 6.99 (d, J = 8.4 Hz, 4H), 6.43 (s, 1H), 3.88 (s, 6H), 3.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.02, 163.64, 136.89, 130.89,

128.89, 127.64, 106.70, 92.57, 62.56, 56.54. HRMS (ESI) m/z calcd for $C_{21}H_{18}Cl_2O_3S_2^+$ $(M+H)^+$ 452.0074, found 452.0056.

*4.9. (4-Fluorophenyl)(2,4,6-trimethoxyphenyl)sulfane [**3da**]* [15]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.02 (dd, J = 9.2Hz, 2H), 6.86 (t, J = 8.8 Hz, 2H), 6.20 (s, 2H), 3.87 (s, 3H), 3.81 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.06, 162.50, 162.10, 159.68, 133.72 (d, J = 3.3 Hz), 128.02, 127.94, 115.74, 115.52, 99.51, 91.36, 91.36, 56.43, 55.58. ^{19}F NMR (376 MHz, $CDCl_3$): δ -118.82.

*4.10. (2,4,6-Trimethoxy-1,3-phenylene)bis((4-fluorophenyl)sulfane) [**3db**]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10 (d, J = 4.8 Hz, 2H), 7.08 (d, J = 5.2 Hz, 2H), 6.92 (s, 2H), 6.89 (d, J = 8.8 Hz, 2H), 6.41 (s, 1H), 3.88 (s, 6H), 3.80 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.42, 128.75, 128.68, 115.97, 115.76, 92.60, 62.55, 56.51. ^{19}F NMR (376 MHz, $CDCl_3$): δ -117.71. HRMS (ESI) m/z calcd for $C_{21}H_{19}F_2O_3S_2^+$ $(M+H)^+$ 421.07382, found 421.07339.

*4.11. (4-(Trifluoromethoxy)phenyl)(2,4,6-trimethoxyphenyl)sulfane [**3ea**]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01 (s, 4H), 6.22 (s, 2H), 3.88 (s, 3H), 3.82 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.33, 162.61, 137.74, 126.89, 121.43, 91.37, 56.45, 55.61. ^{19}F NMR (376 MHz, $CDCl_3$): δ -58.06. HRMS (ESI) m/z calcd for $C_{16}H_{16}F_3O_4S^+$ $(M+H)^+$ 361.07159, found 361.07156.

*4.12. (2,4,6-Trimethoxy-1,3-phenylene)bis((4-(trifluoromethoxy)phenyl) sulfane) [**3eb**]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 (s, 4H), 7.05 (s, 4H), 6.44 (s, 1H), 3.89 (s, 6H), 3.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.76, 146.96, 137.06, 127.54, 121.58, 106.72, 92.61, 62.66, 56.56. ^{19}F NMR (376 MHz, $CDCl_3$): δ -58.06. HRMS (ESI) m/z calcd for $C_{23}H_{19}F_6O_5S_2^+$ $(M+H)^+$ 553.05726, found 553.05682.

*4.13. (3-Fluorophenyl)(2,4,6-trimethoxyphenyl)sulfane [**3fa**]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (s, 1H), 6.86 (s, 1H), 6.71 (s, 1H), 6.63 (d, J = 10.0 Hz, 1H), 6.22 (s, 2H), 3.88 (s, 3H), 3.81 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.44, 163.40, 162.64, 161.99, 141.62 (d, J = 7.7 Hz), 129.77 (d, J = 8.6 Hz), 121.31 (d, J = 2.8 Hz), 112.32 (d, J = 24.2 Hz), 111.34 (d, J = 21.6 Hz), 97.85, 91.38, 56.45, 55.61. ^{19}F NMR (376 MHz, $CDCl_3$): δ -113.38. HRMS (ESI) m/z calcd for $C_{15}H_{16}FO_3S^+$ $(M+H)^+$ 295.07987, found 295.07986.

*4.14. (2,4,6-Trimethoxy-1,3-phenylene)bis((3-fluorophenyl)sulfane) [**3fb**]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, J = 6.0 Hz, 2H), 6.87 (ddd, J = 8.0, 1.8, 1.0 Hz, 2H), 6.80-6.71 (m, 2H), 6.68 (s, 2H), 6.46 (s, 1H), 3.90 (s, 6H), 3.77 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.35 (d, J = 192.0 Hz), 163.92, 161.94, 140.93 (d, J = 7.8 Hz), 130.04 (d, J = 8.7 Hz), 121.65 (d, J = 2.9 Hz), 112.83 (d, J = 24.1 Hz), 111.95 (d, J = 21.6 Hz), 106.14, 92.61, 62.63, 56.58. ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.79. HRMS (ESI) m/z calcd for $C_{21}H_{19}F_2O_3S_2^+$ $(M+H)^+$ 421.07382, found 421.07376.

*4.15. o-Tolyl(2,4,6-trimethoxyphenyl)sulfane [**3ga**]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.117.07 (m, 1H), 6.97- 6.91 (m, 2H), 6.61-6.55 (m, 1H), 6.23 (s, 2H), 3.88 (s, 3H), 3.79 (s, 6H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.76, 129.88, 126.10, 124.60, 124.21, 91.41, 56.45, 55.56, 20.12. HRMS (ESI) m/z calcd for $C_{16}H_{19}O_3S^+$ $(M+H)^+$ 291.10494, found 291.10483.

*4.16. (4-(Trifluoromethyl)phenyl)(2,4,6-trimethoxyphenyl)sulfane [**3ha**]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.23 (s, 2H), 3.89 (s, 3H), 3.81 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.44, 163.40, 162.65, 161.99, 141.62 (d, J = 7.7 Hz), 129.82, 129.73, 121.31 (d, J = 3.1 Hz), 112.44, 112.20, 111.45, 111.23, 97.85, 91.38, 56.45, 55.61. ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.16. HRMS (ESI) m/z calcd for $C_{16}H_{16}F_3O_3S^+$ $(M+H)^+$ 345.07668, found 345.07672.

*4.17. (4-Methoxyphenyl)(2,4,6-trimethoxyphenyl)sulfane [**3ia**]* [16]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (d, J = 8.8 Hz, 2H), 6.73 (d, J = 8.8 Hz, 2H), 6.19 (s, 2H), 3.85 (s, 3H), 3.81 (s, 6H), 3.74 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.70, 162.44, 128.69, 114.37, 91.33, 56.42, 55.54, 55.42.

*4.18. (4-(Tert-butyl)phenyl)(2,4,6-trimethoxyphenyl)sulfane [**3ja**]* [10]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 6.21 (s, 2H), 3.87 (s, 3H), 3.81 (s, 6H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.94, 162.73, 147.52, 135.19, 125.70, 91.31, 56.45, 55.56, 34.40, 31.47.

*4.19. Mesityl(2,4,6-trimethoxyphenyl)sulfane **[3ka]*** [17]

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.81 (s, 2H), 6.08 (s, 2H), 3.77 (s, 3H), 3.69 (s, 6H), 2.37 (s, 6H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.09, 141.85, 128.72, 91.43, 56.11, 55.44, 21.61, 21.03.

*4.20. naphthalen-2-yl(2,4,6-trimethoxyphenyl)sulfane [**3la**]* [18]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.32 (td, *J* = 7.4, 7.2, 1.6 Hz, 1H), 7.21 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.24 (s, 2H), 3.88 (s, 3H), 3.79 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.12, 162.71, 136.45, 133.94, 131.33, 128.05, 127.75, 126.93, 126.23, 124.94, 124.82, 123.06, 98.72, 91.38, 56.43, 55.57.

*4.21. (4,5-Dimethoxy-1,2-phenylene)bis(p-tolylsulfane) [**3mb**]* [12b]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, J = 8.0 Hz, 4H), 7.11 (d, J = 8.0 Hz, 4H), 6.77 (s, 2H), 3.71 (s, 6H), 2.32 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.99, 132.51, 130.72, 130.08, 129.38, 115.59, 56.13, 21.23.

*4.22. (4,6-Dimethoxy-1,3-phenylene)bis(p-tolylsulfane) [**3nb**]* [12b]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (s, 1H), 7.09 (d, J = 8.4 Hz, 4H), 7.02 (d, J = 8.4 Hz, 4H), 6.52 (s, 1H), 3.88 (s, 6H), 2.30 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.53, 138.47, 136.40, 132.26, 130.02, 129.86, 114.98, 96.23, 56.42, 21.19.

*4.23. (2,5-Dimethoxy-1,4-phenylene)bis(p-tolylsulfane) [**3ob**]* [12b]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, J = 8.0 Hz, 4H), 7.14 (d, J = 8.0 Hz, 4H), 6.57 (s, 2H), 3.64 (s, 6H), 2.35 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 151.64, 137.74, 132.27, 130.30, 130.20, 124.41, 113.97, 56.69, 21.31.

*4.24. (4-Methoxy-2,6-dimethyl-1,3-phenylene)bis(p-tolylsulfane) [**3pb**]* [19]

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01-6.97 (m, 4H), 6.89 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 6.0Hz, 2H), 6.79 (s, 1H), 3.83 (s, 3H), 2.62 (s, 3H), 2.49 (s, 3H), 2.26 (s, 6H). ^{13}C NMR (101 MHz,

$CDCl_3$): δ 161.23, 150.81, 147.17, 134.82, 134.65, 134.50, 134.41, 129.81, 129.63, 126.35, 125.58, 123.69, 111.50, 56.25, 23.04, 21.02, 20.98, 20.67.

*4.25. Mesityl(p-tolyl)sulfane [**3qa**] [12b]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, J = 9.2 Hz, 4H), 6.82 (d, J = 8.4 Hz, 2H), 2.38 (s, 6H), 2.31 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.75, 139.20, 134.89, 134.35, 129.77, 129.40, 127.58, 125.81, 21.88, 21.26, 21.00.

*4.26. (4-Methoxyphenyl)(p-tolyl)sulfane [**3ra**] [12b]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 3.80 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.57, 136.23, 134.47, 129.89, 129.50, 125.76, 114.98, 55.47, 21.11.

*4.27. 2,3-bis(p-tolylthio)-1H-indole[**3sb**][20]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.57 (d, *J* = 8.0Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.25-7.19 (m, 3H), 7.15-7.11 (m, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 2.32 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.94, 136.86, 135.02, 134.80, 134.59, 130.94, 130.35, 130.26, 130.18, 129.62, 127.06, 123.60, 121.20, 119.84, 111.05, 108.41, 21.22, 21.05.

*4.28. 2-methyl-3-(p-tolylthio)-1H-indole[**3ta**][21]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (s, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.17 (td, J = 8.0, 7.6, 1.2 Hz, 1H), 7.13-7.08 (m, 1H), 6.95 (s, 4H), 2.49 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.03, 135.79, 135.52, 134.42, 130.45, 129.59, 125.88, 122.23, 120.76, 119.13, 110.71, 100.00, 20.97, 12.28.

*4.29. 1,2-Di-p-tolyldisulfane [**4a**] [22]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, J = 8.0 Hz, 4H), 7.10 (d, J = 8.0 Hz, 4H), 2.32 (s, 6H).

*4.30. S-(p-Tolyl) 4-methylbenzenesulfonothioate [**4b**] [23]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 2.42 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.71, 142.17, 136.62, 130.33, 129.49, 127.73, 124.72, 21.80, 21.62.

*4.31. S-(4-Methoxyphenyl) 4-methylbenzenesulfonothioate [**4e**] [24]*

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 6.84 (d, J = 9.2 Hz, 2H), 3.83 (s, 3H), 2.42 (s, 3H).

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