Journal Pre-proof

NH_4I/1,10-phenanthroline catalyzed direct sulfenylation of *N*-heteroarenes with ethyl arylsulfinates

Lingjuan Chen, Jun Zhang, Yueting Wei, Zhen Yang, Ping Liu, Jie Zhang, Bin Dai

PII: S0040-4020(19)31033-6

DOI: https://doi.org/10.1016/j.tet.2019.130664

Reference: TET 130664

To appear in: *Tetrahedron*

Received Date: 28 July 2019

Revised Date: 14 September 2019

Accepted Date: 29 September 2019

Please cite this article as: Chen L, Zhang J, Wei Y, Yang Z, Liu P, Zhang J, Dai B, NH_4I/1,10-phenanthroline catalyzed direct sulfenylation of *N*-heteroarenes with ethyl arylsulfinates, *Tetrahedron* (2019), doi: https://doi.org/10.1016/j.tet.2019.130664.

Graphical Abstract

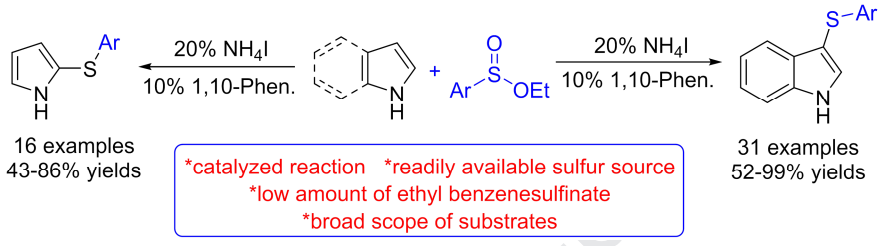
To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

NH_4I/1,10-Phenanthroline catalyzed direct sulfenylation of *N*-heteroarenes with ethyl arylsulfinates

Leave this area blank for abstract info.

Lingjuan Chen, Yueting Wei, Zhen Yang, Ping Liu*, Jie Zhang*, Bin Dai

[a]*School of Chemistry and Chemical Engineering/Key Laboratory for Green Processing of Chemical Engineering of Xinjiang Bingtuan， Shihezi University, Shihezi 832003, China*



Tetrahedron
journal homepage: www.elsevier.com

NH_4I/1,10-Phenanthroline catalyzed direct sulfenylation of *N*-heteroarenes with ethyl arylsulfinates

Lingjuan Chen, Jun Zhang, Yueting Wei, Zhen Yang, Ping Liu*, Jie Zhang*, Bin Dai

[a]*School of Chemistry and Chemical Engineering/Key Laboratory for Green Processing of Chemical Engineering of Xinjiang Bingtuan，Shihezi University, Shihezi 832003, China*

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
sulfenylation
ethyl arylsulfinates
indole
pyrrole
metal-free

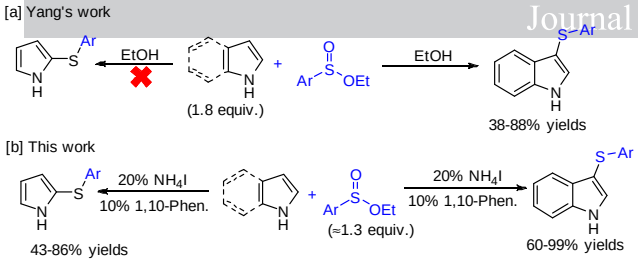
ABSTRACT

An efficient synthesis of *N*-heterocyclic aryl sulfides via NH_4I/1,10-phenanthroline-catalyzed direct sulfenylation reactions was reported. In this reaction, heteroarenes such as indoles, and pyrroles serve as nucleophiles by installing a arylthio group at the C3 and C2 position of heterocycles, respectively. With readily accessible and free of unpleasant odor ethyl arylsulfinates as sulfur reagents, the metal-free-catalyzed direct sulfenylation of *N*-heteroarenes has been developed. 3-Arylthio-indoles and 2-arylthio-pyrroles derivatives were obtained in moderate to excellent yields, even on gram scale. The reaction was general for a broad scope of substrates and demonstrated good tolerance to a variety of functional groups.

1. Introduction

Sulfur-containing compounds are important structural motifs that are widely present in various drugs, pesticides, food ingredients, and material molecules.[1,2] Therefore, effective methods for formation of sulfur-carbon bonds have been attracting attention.[3-20] Indoles and pyrroles, as vital heterocyclic structural skeletons, have been widely found in natural compounds and valuable pharmacological drugs.[21-26] Numerous studies have shown that the introduction of sulfur-containing groups into indole molecules increases both chemical structure diversity and biological activity of the compounds.[27-35] Therefore, the selective formation of carbon-sulfur (C-S) bonds of indoles has become an important field of organic chemistry.[36-41] In recent years, direct sulfenylation of indoles to the synthesis of 3-arylsulfinylindoles have been paid much attention. Various sulfur reagents such as arylsulfonyl chlorides,[42-47] sodium sulfinates,[48-54] sulfenyl halides,[55-59] *N*-thioimides,[60-68] thiols,[69-75] disulfides,[76-81] quinone mono-O,S-acetals,[82-84] sulfonyl hydrazides,[85-89] *N*-hydroxy sulfonamides,[90] sulfinic acids,[91,92] and sulfonium salts[93] have been employed for sulfenylation reactions. Despite the significant advances of direct sulfenylation, most of the established protocols are suffered from some disadvantages, including some sulfur agents which are unstable to air and moisture, not readily available or have an unpleasant odour, the use of metal catalysts, some of these reactions require excess additives as well as high temperatures or yield byproducts unfriendly to the environment. To address such issues, it is highly desirable to develop new sulfenylating agents and efficient reaction conditions for the sulfenylation of *N*-heteroarenes.

In 2018, Yang co-workers reported an excellent catalyst-free directed 3-sulfenylation to prepare 3-arylsulfinylindoles, in which the sulfinic esters were employed as readily accessible and free of unpleasant odor sulfur reagents in their strategy (**Scheme 1a**).[94] However, this method still has certain deficiencies, for example: (i) this system only limits to the 3-sulfenylation of indoles and is not suitable for the 2-sulfenylation of pyrroles; (ii) the amount of indoles must be excessive, and the results show the sulfenylation of indoles is difficult to occur in the presence of excessive aryl sulfinic esters; (iii) the 3-sulfenylation of indoles afford the only 38-88% yields for 12 h. As a consequence, the development of efficient protocols for the sulfenylation of *N*-heteroarenes with good yields, broad scope of substrates, and shorter reaction times is highly desirable and remains a synthetic challenge. Recently, we developed an efficient method for the synthesis of sulfinic esters via the copper-catalyzed reaction of sulfonyl hydrazides with alcohols in air, and various arylsulfinic esters were obtained in good yields.[95] Based on our previous work,[96, 97] we herein describe a new strategy to access 3-arylthio-indoles and 2-arylthio-pyrroles by NH_4I/1,10-phenanthroline catalyzed direct sulfenylation of *N*-heteroarenes with ethyl arylsulfinates (**Scheme 1b**). The remarkable achievements of this catalytic system are: (i) this method is not only suitable for the 3-sulfenylation of indoles, but also for the 2-sulfenylation of pyrroles; (ii) the direct sulfenylation of *N*-heteroarenes including indoles and pyrroles proceeds smoothly in the presence of slightly excessive aryl sulfinic esters to give the desired products in 43-99% yields; (iii) the reaction time was shortened to 6 h in the presence of NH_4I/1,10-phenanthroline as catalyst.

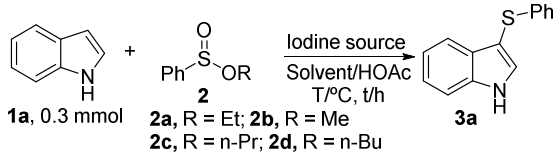


Scheme 1. Sulfenylation of *N*-heteroarenes.

2. Results and Discussion

2.1. Optimization of the reaction conditions

Table 1. Optimized reaction conditions [a]



Entry	2	[I](mol%)	T	Time	Solvent	Yield(%)[b]
1	**2a**	KI(20)	80	10	DCE	45
2	**2a**	NH_4I(20)	80	10	DCE	59
3	**2a**	NH_4I(20)	80	10	DCE	66
4[c]	**2a**	NH_4I(20)	80	10	DCE	82
5[d]	**2a**	NH_4I(20)	80	10	DCE	68
6[e]	**2a**	NH_4I(20)	80	10	DCE	82
7[c]	**2a**	NH_4I(20)	80	6	DCE	82
8[c]	**2a**	NH_4I(20)	80	6	DCE	82
9[c]	**2a**	NH_4I(20)	100	6	DCE	92
10[c]	**2a**	NH_4I(20)	100	6	DMSO	trace
11[c]	**2a**	NH_4I(20)	100	6	DMF	trace
12[c]	**2a**	NH_4I(20)	100	6	EtOH	34
13[c]	**2a**	NH_4I(20)	100	6	toluene	62
14[c]	**2a**	NH_4I(20)	100	6	1,4-dioxane	98
15[c]	**2a**	–	100	6	1,4-dioxane	trace
16[c]	**2b**	NH_4I(20)	100	6	1,4-dioxane	68
17[c]	**2c**	NH_4I(20)	100	6	1,4-dioxane	83
18[c]	**2d**	NH_4I(20)	100	6	1,4-dioxane	95

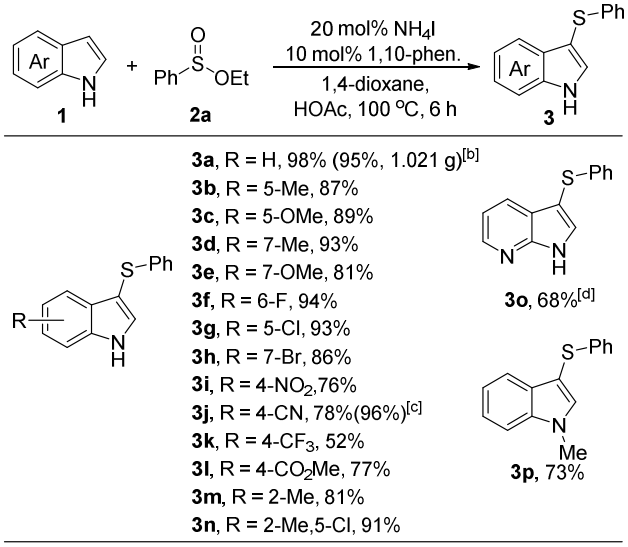
[a] Reaction conditions: **1a** (0.3 mmol), **2** (entries 1-7, 0.6 mmol; entries 8-18, 0.4 mmol), solvent (2 mL), HOAc (entries 3-17, 0.5 mL). [b]Isolated yield. [c]1,10-phenanthroline (10 mol%). [d] PPh_3 (10 mol%).[e]1,10-phenanthroline (20 mol%).

Optimization of the conditions utilized 3-sulfenylation of 1*H*-indole **1a** (0.3 mmol) and ethyl benzenesulfinate **2a** (0.6 mmol) as the model reaction, with 20 mol% KI as catalyst at 80 °C in dichloroethane (DCE) as solvent (**Table 1**). The preliminary reaction gave desired product 3-(phenylthio)-1*H*-indole **3a** in 45% yield after 10 h (entry 1). When NH_4I was used as the catalyst, the product **3a** was obtained in 59% yield (entry 2). By employing the 0.5 mL of HOAc, a 66% yield was observed (entry 3). Additives such as 1,10-phenanthroline and PPh_3 were examined, respectively, 10 mol% of 1,10-phenanthroline was found to be the optimum choice (entries 4-6). A decrease in both the amount of **2a** (0.4 mmol) and reaction time (6 h) had no influence on the reaction yield (entries 7-8). By increasing the temperature to 100 ºC, the yield of **3a** was improved to 92% (entry 9). Further screening of solvents revealed that 1,4-dioxane was the best choice (98% yield, entry14 *vs* entries 10-13). A control experiment confirmed the essential action of the iodine catalyst (entry 15). Subsequently, the R group substituent on the benzenesulfinate such as either methyl or *n*-propyl group (**2b** or **2c**) was examined, a decrease in yield was observed (entries 16 and 17). However, by employing *n*-butyl group comparable results were obtained (95%, entry18). Finally, the combination of 1*H*-indole (0.3 mmol), ethyl benzenesulfinate (0.4 mmol), NH_4I (20 mol%), 1,10-phenanthroline (10 mol%), HOAc (0.5 mL) at 100 °C for 6 h in 1,4-dioxane (2 mL) was found to be the optimal reaction conditions.

2.2. Scope and limitations of substrates

With the optimized conditions in hand, the reaction scope with respect to substituted indoles was examined (**Table 2**). The obtained results indicated that substituted indoles bearing methyl and methoxy groups on the aromatic rings reacted with ethyl benzenesulfinate **2a** affording products **3b-3e** in good yields. The introduction of halogens on the aromatic rings provided products **3f-3h** in good yields, which are potential substrates for further transition-metal-catalyzed functionalization. No obvious steric influence was observed when using 2- or 4-substituted indoles as substrates, giving desired products **3i-3n** in 52-91% yields. Notably, with 1*H*-indole-4-carbonitrile as the substrate, the product **3j** was obtained in 96% yield after 12 h. Furthermore, in the case of 1*H*-pyrrolo[2,3-*b*]pyridine the product **3o** was provided in 64% yield at 120 ºC. When 1-methyl-1*H*-indole was reacted with **2a**, the desired product **3p** was provided in 73% yield. To demonstrate the robustness and practicality of this method, a gram-scale reaction of **1a** (5 mmol) and **2a** (6 mmol) was conducted affording the product **3a** (1.021 g) in 95% yield.

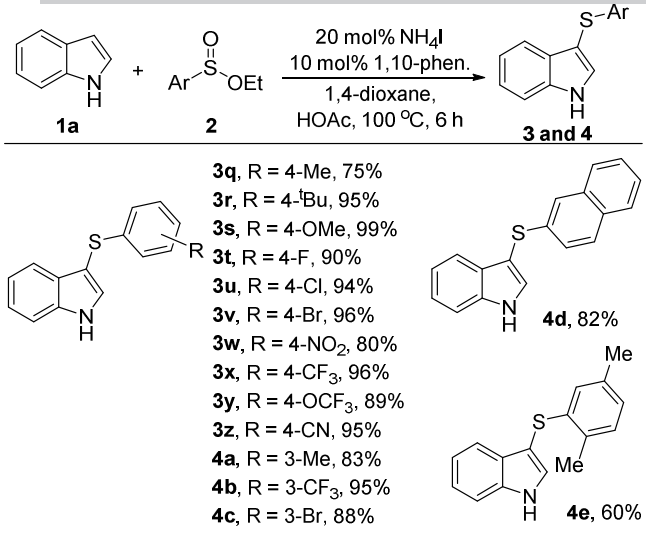
Table 2. Substrate scope of substituted indoles [a]



[a] Reaction conditions: **1** (0.3 mmol), **2a** (0.4 mmol), NH_4I (20 mol%), 1,10-phenanthroline (10 mol%), 100 ºC, 6 h, 1,4-dioxane (2 mL), HOAc (0.5 mL). The yields of isolated products are given. [b]**1a** (5 mmol) and **2a** (6 mmol) were used.[c]t = 12 h. [d]T = 120 ºC.

We next investigated the scope of substituted ethyl arylsulfinates. As indicated in **Table 3**, this protocol was amenable to ethyl arylsulfinates bearing either electron-donating or electron-withdrawing substituents on the phenyl ring, leading to the desired products **3q-4c** in 75-99% yields. It should be noted that the substituent position had no significant effect on the substrate activity. Ethyl naphthalene-2-sulfinate was also suitable for this transformation and gave the product **4d** in 82% yield. Notably, the introduction of a methyl group at 2-position on ethyl arylsulfinate, afforded the desired product **4e** in 60% yield.

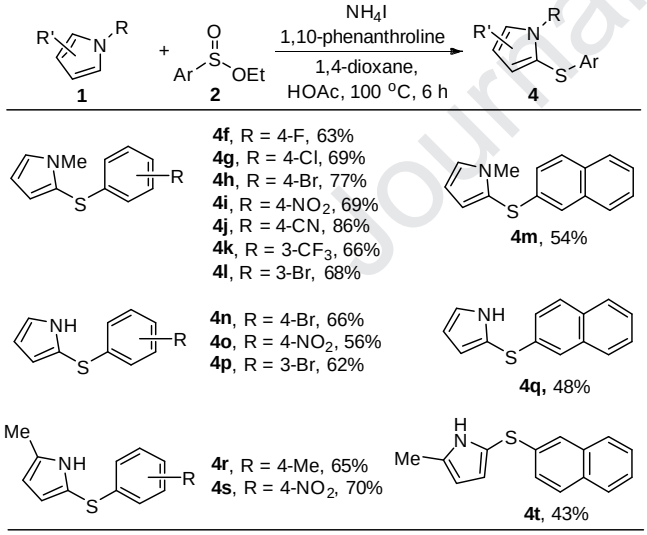
Table 3. Substrate scope of ethyl arysulfinates [a]



[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.4 mmol), NH_4I (20 mol%), 1,10-phenanthroline (10 mol%), 100 ºC, 6 h, 1,4-dioxane (2 mL), HOAc (0.5 mL). The yields of isolated products are given.

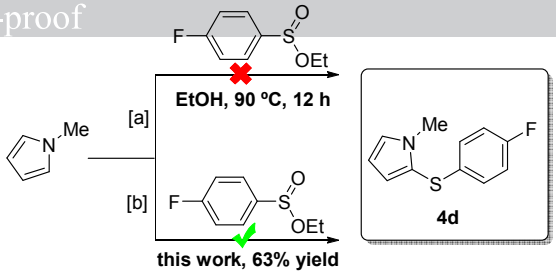
To further expand the scope of this reaction, pyrroles were explored under the optimized conditions. As shown in Table 4, 1-methyl-1*H*-pyrrole underwent reactions with various ethyl arylsulfinates to generate the corresponding 1-methyl-2-(arylthio)-1*H*-pyrroles products **4f-4m** in 54-86% yields. Moreover, 1*H*-pyrrole also underwent this transformation smoothly, affording the desired products **4n-4q** with 48-66% yields. In addition, 2-methyl-1*H*-pyrrole was also suitable for this transformation and gave the products **4r-4u** in 43-70% yields.

Table 4. Substrate scope of pyrroles [a]



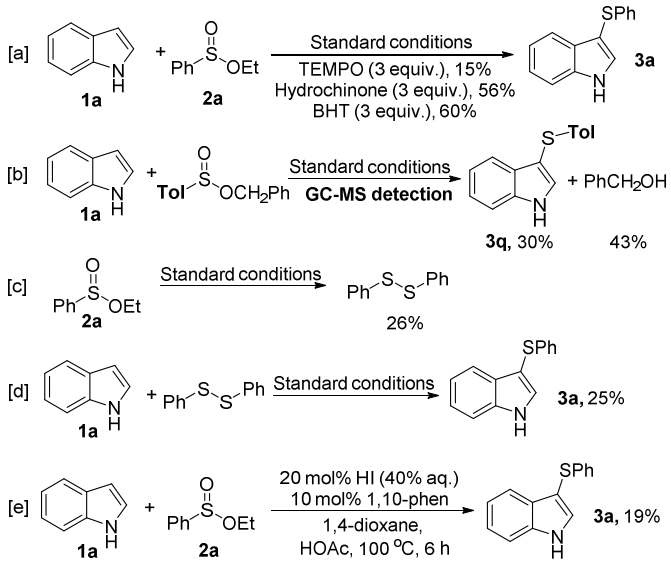
[a]Reaction conditions: **1** (0.3 mmol), **2** (0.4 mmol), NH_4I (20 mol%), 1,10-phenanthroline (10 mol%), 100 ºC, 6 h, 1,4-dioxane (2 mL), HOAc (0.5 mL). The yields of isolated products are given.

Next, we compared our approach to Zhou and Yang et.al reported 3-sulfenylation of indoles using ethyl benzenesulfinate as the sulfur source,[94] and these results were summarized in **Scheme 2**. When 1-methyl-1*H*-pyrrole as substrate reacted with ethyl benzenesulfinate in EtOH at 90 ºC, the desired product **4d** was not observed (**Scheme 2a**). Instead, this reaction proceeds smoothly under our standard conditions to give the desired product in 63% yield (**Scheme 2b**). Therefore, the developed catalytic system has a much wider substrate scope compared to above reported method.



Scheme 2. Comparison of reaction systems.

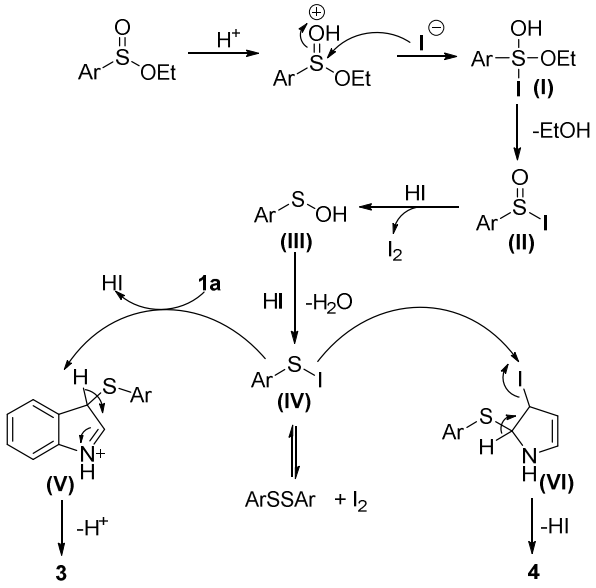
Subsequently, to gain insight into the mechanism, a series of control experiments were performed (**Scheme 3**). With the addition of radical scavenger TEMPO (3 equiv.) under standard reaction conditions, the 3-sulfenylation was not completely inhibited and still gave the desired product **3a** in 15% yield. Moreover, when hydroquinone and 2,6-di-tert-butyl-4-methylphenol (BHT) as radical scavengers were used, the reactions proceeded smoothly and gave yields of 60% and 56%, respectively. So we speculated that this may not be a radical mechanistic pathway (**Scheme 3a**). When benzyl 4-methyl benzenesulfinate as sulfur reagent was subjected to the standard conditions, the desired product **3q** was formed in 30% yield, while 40% yield of benzyl alcohol was also detected by GC-MS (**Scheme 3b**). When only ethyl benzenesulfinate as substrate is used, 1,2-di-*p*-tolyldisulfane can be obtained in 26% yield under normal reaction conditions (**Scheme 3c**). Subsequently, the 1,2-di-p-tolyldisulfane was employed instead of benzyl 4-methylbenzenesulfinate, the desired product **3a** was obtained in 25% yield, thus suggesting that this reaction may involve a mechanistic pathway of 1,2-di-p-tolyldisulfane formation (**Scheme 3d**). In addition, in the presence of HI (40% aqueous solution), the target product was also obtained in 19% yield, indicating that iodine anion isessential during the 3-sulfenylation of indole (**Scheme 3e**).



Scheme 3. Control experiments

On the basis of the above investigations, a possible mechanistic pathway is depicted in **Scheme 4**. The reaction is initiated by the protonation of ethyl arylsulfinate under acidic conditions and addition of iodine anion resulting in intermediate (**I**), which subsequently goes through the loss of an ethanol to form arylsulfinic iodide (**II**). The intermediate (**II**) is successively reduced into the intermediates (**III**) and (**IV**) in the presence of hydroiodic acid.[109] Moreover, the aryl hypoiodothioite (**IV**) produces diaryl disulfide and elemental

iodine by reversible reaction. Next, the intermediate (**IV**) directly reacts with 1*H*-indole by electrophilic substitution to afford the desired product **3**. In addition, 1*H*-pyrrol reacts with the intermediate (**IV**) by electrophilic addition to produce the desired product **4**.



Scheme 4. Proposed mechanism.

3. Conclusions

In summary, we realized a NH_4I/1,10-phenanthroline direct sulfenylation reaction of *N*-heteroarenes including indoles, and pyrroles. In contrast to classical reactions, the reaction features remarkably metal-free conditions, readily available ethyl arylsulfinates as sulfur reagents, and facile synthesis of 3-arylthio-indoles and 2-arylthio-pyrroles. The good reactivity, broad substrate scope, and scalability of this method suggest that this protocol can be a powerful alternative to the existing methodologies for the synthesis of structurally diverse *N*-heterocyclic aryl sulfides. Importantly, the grams scale synthesis was also accomplished.

4. Experimental Section

4.1. Materials and instruments

Unless otherwise noted, all synthetic steps were performed under air atmosphere using Schlenk tubes. The materials obtained from commercial sources were used without further purification. 1,4-Dioxane was distilled from Na/benzophenone. Melting points were determined with a fusiometer and are not corrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Advance III HD 400 MHz spectrometer in $CDCl_3$ solution. All chemical shifts were reported in ppm (δ) relative to the internal standard TMS (0 ppm).

4.2. General Procedure for the NH_4I/1,10-Phenanthroline Catalyzed direct sulfenylation of N-heteroarenes with ethyl arylsulfinates

A Schlenk tube (25 mL) was charged with indole (0.3 mmol), ethyl arylsulfinate (0.4 mmol), NH_4I (20 mol%), and 1,10-phenanthroline (10 mol%). 1,4-Dioxane (2 mL) and HOAc (0.5 mL) were added under air atmosphere, the tube was sealed and heated in an oil bath at 100 ^{o}C for 6 h. The crude mixture was allowed to cool to room temperature. Then, ethyl acetate and saturated aq. solution of NaCl (5 mL) were added and the layers separated. The aqueous phase was washed three times with ethyl acetate (5 mL × 3). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude was purified by flash column chromatography with Al_2O_3 (petroleum ether/EtOAc) giving desired products **3a-z** and **4a-r**.

*4.3. 3-(Phenylthio)-1H-indole [**3a**]*[98]

White solid, mp 121.3-122.6 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.46-7.38 (m, 2H), 7.29-7.22 (m, 1H), 7.15 (td, *J* = 7.8, 3.2 Hz, 3H), 7.10 (d, *J* = 6.8 Hz, 2H), 7.04 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.34, 136.61, 130.81, 129.22, 128.82, 125.97, 124.90, 123.18, 121.04, 119.80, 111.71, 102.95.

*4.4. 5-Methyl-3-(phenylthio)-1H-indole [**3b**]* [99]

White solid, mp 160.9-161.3 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.32 (s, 1H), 7.27 (d, *J* = 2.8 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.08-7.03 (m, 2H), 7.02-6.92 (m, 4H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.61, 134.87, 131.08, 130.47, 129.48, 129.20, 128.82, 125.72, 124.77, 119.20, 111.41, 101.84, 21.55;

*4.5. 5-Methoxy-3-(phenylthio)-1H-indole [**3c**]* [100]

Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.40 (d, *J* = 2.8 Hz, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.18-7.13 (m, 2H), 7.11-7.02 (m, 4H), 6.90 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.24, 139.46, 131.47, 130.08, 128.83, 125.77, 124.83, 113.71, 112.57, 102.24, 100.90, 55.91.

*4.6. 7-Methyl-3-(phenylthio)-1H-indole [**3d**]* [99]

Blue oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.45 (d, *J* = 7.2 Hz, 1H), 7.38 (s, 1H), 7.14-7.01 (m, 7H), 2.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.36, 136.16, 130.57, 128.80, 128.77, 125.93, 124.87, 123.67, 121.16, 120.92, 117.43, 103.11, 16.54.

*4.7. 7-Methoxy-3-(phenylthio)-1H-indole [**3e**]* [101]

Blue solid, mp 115.2-116.3 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.40 (d, *J* = 2.8 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.17-6.99 (m, 6H), 6.68 (d, *J* = 7.6 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.41, 139.48, 130.66, 130.31, 128.78, 127.16, 125.92, 124.82, 121.43, 112.31, 103.14, 102.88, 55.54.

*4.8. 6-Fluoro-3-(phenylthio)-1H-indole [**3f**]* [102]

White solid, mp 161.7-162.5 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.50 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.46 (d, *J* = 2.8 Hz, 1H), 7.19-7.14 (m, 2H), 7.13-7.04 (m, 4H), 6.91 (ddd, *J* = 9.6, 8.8, 2.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.80, 138.97, 136.59, 136.46, 131.02, 130.98, 128.89, 126.06, 125.08, 120.80, 120.70, 110.03, 109.79, 103.42, 98.28, 98.01.

*4.9. 5-Chloro-3-(phenylthio)-1H-indole [**3g**]* [103]

White solid, mp 167.2-168.1 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.59 (d, *J* = 1.6 Hz, 1H), 7.51 (d, *J* = 2.8 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.21 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.20-7.15 (m, 2H), 7.11-7.04 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.79, 132.15, 128.94, 126.00, 125.16, 123.70, 123.64, 120.68, 119.20, 112.82, 112.50, 102.85.

*4.10. 6-Bromo-3-(phenylthio)-1H-indole [**3h**]* [100]

White solid, mp 160.9-161.3 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.56 (d, *J* = 1.2 Hz, 1H), 7.47-7.40 (m, 2H), 7.27-7.22 (m, 1H), 7.19-7.12 (m, 2H), 7.07 (d, *J* = 8.0 Hz, 3H); ^{13}C

NMR (101 MHz, $CDCl_3$) δ 138.81, 137.35, 131.26, 128.90, 128.12, 126.06, 125.14, 124.40, 121.11, 116.79, 114.69, 103.57.

*4.11. 4-Nitro-3-(phenylthio)-1H-indole [**3i**]*

Yellow solid, mp 148.7-149.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 2.4 Hz, 1H), 7.34-7.26 (m, 1H), 7.20-7.13 (m, 2H), 7.13-7.02 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.47, 139.15, 138.98, 135.07, 128.90, 127.01, 125.51, 122.09, 120.29, 117.97, 117.07, 103.63.

*4.12. 3-(Phenylthio)-1H-indole-4-carbonitrile [**3j**]* [104]

White solid, mp 156.3-158.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.33 (s, 1H), 8.05 (d, *J* = 2.8 Hz, 1H), 7.86 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.58 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.39-7.31 (m, 1H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.13-7.01 (m, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) *δ* 139.52, 137.13, 136.51, 128.90, 127.70, 127.47, 125.55, 125.01, 122.16, 117.76, 117.74, 101.08, 99.36.

*4.13. 3-(Phenylthio)-4-(trifluoromethyl)-1H-indole [**3k**]*

White solid, mp 190.2-190.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (S, 1H), 7.58 (d, *J* = 8.0, 1H), 7.54 (d, *J* = 8.0, 2H), 7.27 (t, *J* = 8.0, 1H), 7.14 (t, *J* = 8.0, 2H), 7.03 (d, *J* = 8.0, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.51, 137.85, 135.11, 128.55, 125.64, 124.64, 121.91, 119.74, 119.67, 119.61, 119.55, 115.93, 102.06. ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.58.

*4.14. Methyl 3-(phenylthio)-1H-indole-4-carboxylate [**3l**]*

White solid, mp 188.2-188.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (S, 1H), 7.47 (d, *J* = 8.0, 2H), 7.39 (s, 1H), 7.22 (t, *J* = 8.0, 1H), 7.12 (t, *J* = 8.0, 2H), 7.02 (t, *J* = 8.0, 3H), 3.58 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.63, 140.18, 137.57, 133.91, 128.61, 125.60, 125.38, 125.24, 124.64, 122.20, 122.10, 115.21, 101.98, 51.97.

*4.15. 2-Methyl-3-(phenylthio)-1H-indole [**3m**]* [100]

White solid, mp 118.3-120.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.21-7.14 (m, 2H), 7.14-7.08 (m, 3H), 7.05-6.99 (m, 3H), 2.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.29, 139.45, 135.54, 130.38, 128.80, 125.58, 124.62, 122.27, 120.79, 119.06, 110.79, 99.35, 12.24.

*4.16. 5-Chloro-2-methyl-3-(phenylthio)-1H-indole [**3n**]* [77]

White solid, mp 135.9-136.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.51 (d, *J* = 2.0 Hz, 1H), 7.23 (t, 1H), 7.19-7.09 (m, 3H), 7.08-6.98 (m, 3H), 2.48 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.84, 138.94, 133.88, 131.73, 128.92, 126.72, 125.61, 124.87, 122.61, 118.59, 111.81, 99.47, 12.33.

*4.17. 3-(Phenylthio)-1H-pyrrolo (2,3-b) pyridine [**3o**]* [103]

Pale yellow solid, mp 147.6-147.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.67 (s, 1H), 8.41 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.95 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.70 (s, 1H), 7.22-7.12 (m, 3H), 7.14-7.03 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.27, 143.45, 138.89, 132.02, 128.93, 128.67, 126.15, 125.21, 122.31, 116.97, 101.58.

*4.18. 1-Methyl-3-(phenylthio)-1H-indole [**3p**]* [100]

White solid, mp 116.7-118.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.0 Hz, 1H), 7.41-7.31 (m, 2H), 7.21-7.14 (m, 3H), 7.13-7.10 (m, 4H), 3.80 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.63, 135.96, 129.32, 128.79, 127.53, 126.72, 126.32, 124.12, 121.20, 120.52, 110.32, 31.25.

*4.19. 3-(P-tolylthio)-1H-indole [**3q**]* [94]

White solid, mp 137.6-138.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.28-7.23 (m, 2H), 7.18-7.13 (m, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.59, 135.60, 134.77, 130.53, 129.61, 129.25, 126.39, 120.96, 119.84, 111.65, 103.68, 21.00.

*4.20. 3-((4-(Tert-butyl)phenyl)thio)-1H-indole [**3r**]* [94]

Pale yellow solid, mp 153.4-153.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.46-7.39 (m, 2H), 7.28-7.23 (m, 1H), 7.20-7.15 (m, 3H), 7.07-7.03 (m, 2H), 1.24 (s, 9H);^{13}C NMR (101 MHz, $CDCl_3$) δ 147.95, 136.45, 135.73, 130.59, 130.35, 129.28, 125.79, 122.99, 120.84, 119.74, 111.55, 34.32, 31.32.

*4.21. 3-((4-Methoxyphenyl)thio)-1H-indole [**3s**]* [94]

White solid, mp 138.0-138.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.45-7.36 (m, 2H), 7.27-7.20 (m, 1H), 7.16-7.09 (m, 3H), 6.75-6.71 (m, 2H), 3.71 (s, 3H);^{13}C NMR (101 MHz, $CDCl_3$) δ 157.88, 136.56, 133.79, 130.14, 128.67, 123.05, 120.89, 119.76, 115.28, 114.60, 111.64, 104.71, 55.46.

*4.22. 3-((4-Fluorophenyl)thio)-1H-indole [**3t**]* [94]

White solid, mp 148.5-149.0 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.48-7.41 (m, 2H), 7.29-7.24 (m, 1H), 7.19-7.14 (m, 1H), 7.11-7.06 (m, 2H), 6.89-6.83 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.24, 159.81, 136.62, 134.15, 134.12, 130.62, 128.98, 128.05, 127.97, 123.26, 121.10, 119.65, 115.98, 115.76, 111.76, 103.52.

*4.23. 3-((4-Chlorophenyl)thio)-1H-indole [**3u**]* [94]

White solid, mp 137.6-138.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 2.8 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.30-7.25 (m, 1H), 7.20-7.14 (m, 1H), 7.11 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.8Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.92, 136.63, 130.84, 130.68, 128.92, 128.88, 127.23, 123.35, 121.20, 119.64, 111.80, 102.56.

*4.24. 3-((4-Bromophenyl)thio)-1H-indole [**3v**]* [98]

White solid, mp 149.5-151.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.61-7.54 (m, 1H), 7.50-7.42 (m, 2H), 7.31-7.23 (m, 3H), 7.22-7.13 (m, 2H), 6.95 (dd, *J* = 8.8, 2.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.65, 136.61, 131.76, 130.86, 128.88, 127.51, 123.35, 121.21, 119.62, 118.43, 111.81, 102.36.

*4.25. 3-((4-Nitrophenyl)thio)-1H-indole [**3w**]* [103]

Yellow solid, mp 121.2-121.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.02-7.96 (m, 2H), 7.58-7.45 (m, 3H), 7.36-7.26 (m, 1H), 7.23-7.15 (m, 1H), 7.15-7.08 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.00, 144.98, 136.72, 131.38, 128.54, 125.20, 123.98, 123.64, 121.51, 119.30, 112.10, 100.19.

*4.26. 3-((4-(Trifluoromethyl)phenyl)thio)-1H-indole [**3x**]* [105]

White solid, mp 134.0-134.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.49-7.43 (m, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.34-7.22 (m, 1H), 7.21-7.16 (m, 1H), 7.13 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.67, 131.16, 128.86, 125.67, 125.63, 125.59, 125.55, 125.39, 123.49, 121.35, 119.55, 111.91, 101.34. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.75.

*4.27. 3-((4-(Trifluoromethoxy)phenyl)thio)-1H-indole [**3y**]* [85]

Pale yellow solid, mp 122.3-125.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.50-7.41 (m, 2H), 7.31-7.25 (m, 1H), 7.21-7.15 (m, 1H), 7.08 (d, *J* = 9.2 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.75, 146.73, 138.25, 136.66, 131.01, 128.95, 127.01, 123.36, 121.60, 121.59, 121.22, 119.58, 111.85, 102.35. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.17.

*4.28. 4-((1H-indol-3-yl)thio)benzonitrile [**3z**]* [103]

White solid, mp 165.9-166.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.56-7.45 (m, 3H), 7.38 (d, *J* = 8.6 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.31, 136.70, 132.24, 131.36, 128.63, 125.54, 123.55, 121.42, 119.34, 119.27, 112.04, 107.64, 100.27.

*4.29. 3-(m-Tolylthio)-1H-indole [**4a**]* [106]

White solid, mp 125.1-125.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.49-7.40 (m, 2H), 7.25 (s, 1H), 7.19-7.14 (m, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.98 (s, 1H), 6.91-6.83 (m, 2H), 2.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.07, 138.59, 136.59, 130.77, 129.30, 128.71, 126.60, 125.90, 123.14, 123.12, 120.98, 119.83, 111.67, 103.07, 21.50.

*4.30. 3-((3-(Trifluoromethyl)phenyl)thio)-1H-indole [**4b**]* [94]

White solid, mp 107.5-108.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.49 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 2.6 Hz, 1H), 7.37-7.29 (m, 2H), 7.22-7.16 (m, 2H), 7.13-7.05 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.11, 136.66, 131.18, 129.16, 128.90, 128.84, 123.39, 122.43, 122.38, 121.62, 121.58, 121.26, 119.46, 111.91, 101.51.

*4.31. 3-((3-Bromophenyl)thio)-1H-indole [**4c**]* [94]

White solid, mp 117.8-118.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 2.8 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.27-7.21 (m, 2H), 7.20-7.11 (m, 2H), 7.03-6.92 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.96, 136.56, 131.11, 130.12, 128.89, 128.31, 127.94, 124.42, 123.33, 123.29, 122.94, 121.22, 119.52, 111.84, 101.77.

*4.32. 3-(Naphthalen-2-ylthio)-1H-indole [**4d**]* [94]

White solid, mp 188.2-188.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.71 (d, *J* = 7.2 Hz, 1H), 7.63 (t, *J* = 8.4 Hz, 2H), 7.55 (dd, *J* = 7.6, 5.0 Hz, 2H), 7.50-7.44 (m, 2H), 7.39-7.32 (m, 2H), 7.30-7.25 (m, 2H), 7.14 (t, *J* = 7.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.84, 136.68, 133.89, 131.47, 130.83, 129.25, 128.38, 127.81, 127.05, 126.46, 125.18, 124.91, 123.67, 123.23, 121.10, 119.85, 111.73, 102.99.

*4.33. 3-((2,5-Dimethylphenyl)thio)-1H-indole [**4e**]* [45]

Pale yellow solid, mp 135.8-136.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.49-7.41 (m, 2H), 7.30-7.24 (m, 2H), 7.19-7.13 (m, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.57 (s, 1H), 2.45 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.87, 136.66, 135.95, 131.64, 130.80, 129.88, 129.46, 126.10, 125.60, 123.09, 120.94, 119.88, 111.66, 102.73, 21.20, 19.62.

*4.34. 2-((4-Fluorophenyl)thio)-1-methyl-1H-pyrrole[**4f**]*

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99–6.89 (m, 4H), 6.88–6.84 (m, 1H), 6.56 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.21 (t, *J* = 7.6 Hz, 1H), 3.55 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.40, 159.97, 133.99, 133.95, 127.70, 127.62, 126.20, 119.63, 117.72, 116.26, 116.04, 108.57, 34.12. HRMS (ESI-TOF) *m/z* calculated for $C_{11}H_{11}FNS^+$ $(M + H)^+$ 208.0591, found 208.0587.

*4.35. 2-((4-Chlorophenyl)thio)-1-methyl-1H-pyrrole[**4g**]*[107]

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 (d, *J* = 8.8 Hz, 2H), 6.92–6.82 (m, 3H), 6.56 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.22 (dd, *J* = 3.6, 2.8 Hz, 1H), 3.54 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.82, 131.14, 129.15, 126.91, 126.39, 119.91, 116.81, 108.69, 77.16, 34.12.

*4.36. 2-((4-Bromophenyl)thio)-1-methyl-1H-pyrrole[**4h**]*

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.8 Hz, 2H), 6.89 (t, *J* = 2.2 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 2H), 6.56 (dd, *J* = 4.0, 2.0 Hz, 1H), 6.23 (t, *J* = 3.2 Hz, 1H), 3.55 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.56, 132.04, 127.20, 126.43, 119.95, 118.91, 116.64, 108.71, 77.16, 34.12. HRMS (ESI-TOF) *m/z* calculated for $C_{11}H_{10}BrNNaS^+$ $(M + Na)^+$ 289.9610, found 289.9616.

*4.37. 2-((3-Bromophenyl)thio)-1-methyl-1H-pyrrole[**4i**]*

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22–7.16 (m, 1H), 7.09–7.02 (m, 2H), 6.92–6.82 (m, 2H), 6.57 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.23 (dd, *J* = 3.6, 2.8 Hz, 1H), 3.55 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.82, 130.36, 128.36, 128.08, 126.59, 124.07, 123.23, 120.17, 116.13, 108.80, 77.16, 34.15. HRMS (ESI-TOF) *m/z* calculated for $C_{11}H_{10}BrNNaS^+$ $(M + Na)^+$ 289.9610, found 289.9615.

*4.38. 1-Methyl-2-((3-(trifluoromethyl)phenyl)thio)-1H-pyrrole[**4j**]*

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.27 (m, 2H), 7.22 (s, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.92 (dd, *J* = 2.4, 1.6 Hz, 1H), 6.59 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.25 (dd, *J* = 3.6, 2.8 Hz, 1H), 3.56 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.14, 129.46, 128.58, 128.57, 126.72, 122.11, 122.07, 122.06, 122.03, 122.02, 121.98, 120.31, 115.84, 108.94, 77.16, 34.11. HRMS (ESI-TOF) *m/z* calculated for $C_{12}H_{10}F_3NNaS^+$ $(M + Na)^+$ 280.0378, found 280.0379.

*4.39. 1-Methyl-2-(naphthalen-2-ylthio)-1H-pyrrole[**4k**]*[107]

Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.45–7.35 (m, 2H), 7.33 (d, *J* = 1.6 Hz, 1H), 7.13 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.92 (t, *J* = 2.2 Hz, 1H), 6.63 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.27 (dd, *J* = 3.6, 2.8 Hz, 1H), 3.57 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.66, 133.95, 131.60, 128.72, 127.86, 127.12, 126.66, 126.26, 125.45, 124.34, 123.52, 119.83, 117.31, 108.61, 77.16, 34.21.

*4.40. 1-Methyl-2-((4-nitrophenyl)thio)-1H-pyrrole[**4l**]*

Pale yellow solid, mp 82.6-83.4 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* =8.8 Hz, 2H), 7.00 (d, *J* =8.8 Hz, 2H), 6.98 (dd, *J* = 2.8, 2.0 Hz, 1H), 6.61 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.29 (dd, *J* = 3.6, 2.8 Hz, 1H), 3.58 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.62, 145.40, 127.17, 124.99, 124.19, 120.57, 114.54, 109.22, 77.16, 34.11. HRMS (ESI-TOF) *m/z* calculated for $C_{11}H_{11}N_2O_2S^+$ $(M + H)^+$ 235.0536, found 235.0541.

*4.41. 4-((1-Methyl-1H-pyrrol-2-yl)thio)benzonitrile[**4m**]*

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.4 Hz, 2H), 7.01–6.91 (m, 3H), 6.58 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.27 (dd, *J* = 3.6, 2.8 Hz, 1H), 3.56 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.02, 132.48, 127.01, 125.28, 120.49, 118.92, 114.66, 109.10, 108.40, 34.07. HRMS (ESI-TOF) *m/z* calculated for $C_{12}H_{11}N_2S^+$ $(M + H)^+$ 215.0637, found 215.0639.

*4.42. 2-((4-Nitrophenyl)thio)-1H-pyrrole [**4n**]*[108]

Yellow solid, mp 85.7-86.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (s, 1H), 7.99 (d, *J* = 9.2 Hz, 2H), 7.07–7.03 (m, 1H), 7.01 (d, *J* = 9.2 Hz, 2H), 6.66–6.58 (m, 1H), 6.38 (q, *J* = 3.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.93, 145.23, 124.99, 124.06, 123.16, 119.85, 112.51, 111.16.

*4.43. 2-(Naphthalen-2-ylthio)-1H-pyrrole[**4o**]*

Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.45–7.34 (m, 3H), 7.16 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.99–6.92 (m, 1H), 6.67–6.59 (m, 1H), 6.35 (q, *J* = 3.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.64, 133.85, 131.64, 128.69, 127.84, 127.16, 126.69, 125.56, 124.56, 123.92, 122.06, 118.87, 110.63. HRMS (ESI-TOF) *m/z* calculated for $C_{14}H_{12}NS^+$ $(M + H)^+$ 226.0685, found 226.0686.

*4.44. 2-((4-Bromophenyl)thio)-1H-pyrrole[**4p**]*

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (s, 1H), 7.30 (d, *J* = 8.8 Hz, 2H), 6.96–6.92 (m, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.59–6.53 (m, 1H), 6.32 (q, *J* = 3.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.59, 131.98, 127.44, 122.26, 119.11, 119.09, 114.94, 110.75. HRMS (ESI-TOF) *m/z* calculated for $C_{10}H_{18}BrNNaS^+$ $(M + Na)^+$ 275.9453, found 275.9453.

*4.45. 2-((3-Bromophenyl)thio)-1H-pyrrole[**4q**]*

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (s, 1H), 7.23–7.17 (m, 1H), 7.11 (t, *J* = 1.8 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 6.99–6.86 (m, 2H), 6.62–6.51 (m, 1H), 6.33 (q, *J* = 3.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.85, 130.30, 128.50, 128.31, 124.29, 123.17, 122.45, 119.34, 114.40, 110.85. HRMS (ESI-TOF) *m/z* calculated for $C_{10}H_{18}BrNNaS^+$ $(M + Na)^+$ 275.9453, found 275.9448.

*4.46. 2-Methyl-5-(p-tolylthio)-1H-pyrrole[**4r**]*

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.43 (t, *J* = 3.0 Hz, 1H), 5.99–5.90 (m, 1H), 2.26 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 135.98, 135.27, 132.03, 129.75, 126.23, 119.21, 114.01, 108.36, 77.16, 20.98, 13.39. HRMS (ESI-TOF) *m/z* calculated for $C_{12}H_{14}NS^+$ $(M + H)^+$ 204.0841, found 204.0839.

*4.47. 2-Methyl-5-((4-nitrophenyl)thio)-1H-pyrrole[**4s**]*

Yellow solid, mp 76.5-76.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.98 (d, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 6.49 (t, *J* = 3.0 Hz, 1H), 6.05 (t, *J* = 2.6 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.57, 145.12, 133.57, 124.87, 123.99, 120.60, 110.08, 109.18, 13.42. HRMS (ESI-TOF) *m/z* calculated for $C_{11}H_{11}N_2O_2S^+$ $(M + H)^+$ 235.0536, found 235.0539.

*4.48. 2-Methyl-5-(naphthalen-2-ylthio)-1H-pyrrole[**4t**]*

Pale yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.46–7.42 (m, 1H), 7.42–7.32 (m, 2H), 7.17 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.51 (t, *J* = 2.8 Hz, 1H), 6.00 (t, *J* = 2.6 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.17, 133.84, 132.36, 131.59, 128.60, 127.82, 127.12, 126.62, 125.43, 124.48, 123.65, 119.65, 113.27, 108.59, 13.44. HRMS (ESI-TOF) *m/z* calculated for $C_{15}H_{13}NNaS^+$ $(M + Na)^+$ 262.0661, found 262.0665.

Acknowledgments

We gratefully acknowledge financial support of this work by the National Natural Science Foundation of China (No. 21563025) and the Shihezi University (No. CXRC201602).

References and notes

1. A. Mishra, C.Q. Ma, P. Bauerle, *Chem. Rev*., **2009**, *1091*, 141−1276.
2. K. Takimiya, I. Osaka, T. Mori, M. Nakano, *Acc. Chem. Res*., **2014**, *47*, 1493−1502.
3. G. Qiu, K. Zhou, J. Wu, *Chem. Commun*., **2018**, *54*, 12561-12569.
4. C. Shen, P. Zhang, Q. Sun, S. Bai, T.A. Hor, X. Liu, *Chem. Soc. Rev*. **2015**, *44*, 291−314.
5. C. F. Lee, Y. C. Liu, S. S. Badsara, *Chem. -Asian J*., **2014**, *9*, 706-722.
6. F. Hu, W. Gao, H. Chang, X. Li, W. Wei, *Chin. J. Org. Chem*. **2015**, *35*, 1848−1860.
7. Z. Qiao, X. Jiang, *Org. Biomol. Chem*., **2017**, *15*, 1942−1946.
8. C. Liu, D. Liu, A. Lei, *Acc. Chem. Res*., **2014**, *47*, 3459−3470.
9. F. Sun, X. Liu, X. Chen, C. Qian, X. Ge, *Chin. J. Org. Chem*., **2017**, *37*, 2211−2220.
10. D.Q. Dong, S. H. Hao, D.S. Yang, L. X. Li, Z. L. Wang, *Eur. J. Org. Chem*. **2017**, *45*, 6576-6592.
11. Y. Liu, J. Xiong, L. Wei, *Chin. J. Org. Chem.* **2017**, *37*, 1667−1680.
12. Y. Fu, X. Zhao, B. Hou, *Chin. J. Org. Chem*. **2016**, *36*, 1184−1196.
13. P. Bao, L. Wang, Q. Liu, D. Yang, H. Wang, X. Zhao, H. Yue, W. Wei, *Tetrahedron Lett*., **2019**, *60*, 214−218.
14. G. Xiao, H. Min, Z. Zheng, G. Deng, Y. Liang, *Chin.Chem. Lett*., **2018**, *29*, 1363−1366.
15. W.H. Bao, M. He, J. T. Wang, X. Peng, M. Sung, Z. Tang, S. Jiang, Z. Cao, W. M. He, *J. Org. Chem*., **2019**, *84*, 6065−6071.
16. C. Wu, L. Hong, H. Shu, Q.H. Zhou, Y. Wang, M. Sun, S. Jiang, Z. Cao, W.M. He, *ACS Sustain Chem. Eng*., **2019**, *7*, 8798-8803.
17. L. H. Lu, S. J. Zhou, M. Sun, J. L. Chen, W. Xia, X. Yu, X. Xu, W. M. He, *ACS Sustain. Chem. Eng*., **2019**, *7*, 1574−1579.
18. P. Bao, L. Wang, H. Yue, Y. Shao, J. Wen, D. Yang, X. Zhao, H. Wang, W. Wei, *J. Org. Chem*., **2019**, *84*, 2976−2983.
19. L. Wang, H. Yue, D. Yang, H. Cui, M. Zhu, J. Wang, W. Wei, H. Wang, *J. Org. Chem*., **2017**, *82*, 6857−6864.
20. H. Cui, X. Liu, W. Wei, D. Yang, C. He, T. Zhang, H. Wang, *J. Org. Chem*., **2016**, *81*, 2252−2260.
21. G. R. Humphrey, J. T. Tsutumi, *Chem. Rev*., **2006**, *106*, 2875−2911.
22. A. J. Kochanowska Karamyan, M. T. Hamann, *Chem. Rev*., **2010**, *110*, 4489−4497.
23. J. A. Campbell, V. Bordunov, C. A. Borka, M. F. Browner, J. M. Kress, T. Mirzadegan, C. Ramesha, B. F. Sanpablo, R. Stabler, P. Takahara, A. Villasenor, K. A. M. Walker, J. H. Wang, M. Welch, P. Weller, Bioorg. *Med. Chem. Lett*., **2014**, *14*, 4741−4745.
24. J. Holenz, P. J. Pauwels, J. L. Diaz, R. Mercè, X. Codony, H. Buschmann, *Drug Discovery Today*. **2006**, *11*, 283−299.
25. L. Tong, B. B. Shankar, L. Chen, R. Rizvi, J. Kelly, E. Gilbert, C. Huang, D. Y. Yang, J. A. Kozlowski, N. Y. Shih, W. Gonsiorek, R. W. Hipkin, A. Malikzay, C. A. Lunn, D. J. Lundell, *Bioorg. Med. Chem. Lett*., **2010**, *20*, 6785−6789.
26. T. M. Williams, T. M. Ciccarone, S. C. MacTough, C. S. Rooney, S. K. Balani, J. H. Condra, E. A. Emini, M. E. Goldman, W. J. Greenlee, L. R. Kauffman, J. A. O'Brien, V. V. Sardana, W. A. Schleif, A. D. Theoharides, P. S. Anderson, *J. Med. Chem*., **1993**, *36*, 1291−1294.
27. N. S. Simpkins, In Sulfones in Organic Synthesis; Baldwin, J. E. Ed.; Pergamon Press: Oxford, UK, **1993**.
28. B. M. Trost, In Comprehensive Organic Chemistry; Pergamon Press: Oxford, UK, **1991**.
29. T. Asai, T. Takeuchi, J. Diffenderfer, D. L. Sibley, *Antimicrob. Agents Ch*., **2002**, *46*, 2393−2399.
30. S. Caddick, K. Aboutayab, R. West, *Synlett*. **1993**, *3*, 231−232.
31. R. Ragno, A. Coluccia, G. La Regina, G. De Martino, F. Piscitelli, A. Lavecchia, E. Novellino, A. Bergamini, C. Ciaprini, A. Sinistro, G. Maga, E. Crespan, M. Artico, R. Silvestri, *J. Med. Chem*., **2006**, 49, 3172−3184.
32. R. Silvestri, G. De Martino, G. La Regina, M. Artico, S. Massa, L. Vargiu, M. Mura, A. G. Loi, T. Marceddu, P. La Colla, *J. Med. Chem*., **2003**, *46*, 2482−2493.

33. I. Avis, A. Martínez, J. Tauler, E. Zudaire, A. Mayburd, R. Abu-Ghazaleh, F. Ondrey, J. L. Mulshine, *Cancer Res*., **2005**, *65*, 4181.
34. G. De Martino, G. La Regina, A. Coluccia, M. C. Edler, M. C. Barbera, A. Brancale, E. Wilcox, E. Hamel, M. Artico, R. Silvestri, *J. Med. Chem*., **2004**,*47*, 6120−6123.
35. C. D. Funk, Nat. Rev. *Drug Disc*., **2005**, *4*, 664−672.
36. K. Kaneda, T. Mitsudome, *Chem. Rec*., **2017**, *17*, 1−21.
37. C. Shen, P. Zhang, Q. Sun, S. Bai, T. A. Hor, X. Liu, *Chem. Soc. Rev*., **2015**, *44*, 291−314.
38. G. Qiu, K. Zhou, J. Wu. *Chem. Commun*., **2018**, *54*, 12561−12569.
39. D. Q. Dong, S. H. Hao, D. S. Yang, L. X. Li, Z. L. Wang. *Eur. J. Org. Chem*., **2017**, *45*, 6576−6592.
40. Y. Liu, J. Xiong, L. Wei, *Chin. J. Org. Chem*., **2017**, *37*, 1667−1680.
41. F. Hu, W. Gao, H. Chang, X. Li, W. Wei. *Chin. J. Org. Chem*., **2015**, *35*, 1848−1860.
42. Y. He, J. Jiang, W. Bao, W. Deng, J. Xiang, *Tetrahedron Lett*., 2017, 58, 4583−4586.
43. D. Wang, S. Guo, R. Zhang, S. Lin, Z. Yan, *RSC Adv*., **2016**, *6*, 54377−54381.
44. Z. Wu, Y. C. Li, W. Z. Ding, T. Zhu, S. Z. Liu, X. Ren, L. H. Zou, *Asian J. Org. Chem*., **2016**, *5*, 625−628.
45. G. Kumaraswamy, R. Raju, V. Narayanarao, *RSC Adv*., **2015**, *5*, 22718−22723.
46. M. Chen, Z. T. Huang, Q. Y. Zheng, *Chem. Commun*., **2012**, *48*, 11686−11688.
47. Q. Wu, D. Zhao, X. Qin, J. Lan, J. You, *Chem. Commun*., **2011**, *47*, 9188−9190.
48. X. Ge, F. Sun, X. Liu, X. Chen, C. Qian, S. Zhou, *New J. Chem*., **2017**, *41*, 13175−13180.
49. (a) M. J. Bu, G. P. Lu, C. Cai, *Org. Chem. Front*., **2017**, *4*, 266−270; (b) Z. B. Xu, G. P. Lu, C. Cai, *Org. Biomol. Chem*., **2017**, *15*, 2804−2808.
50. Y. Ding, W. Wu, W. Zhao, Y. Li, P. Xie, Y. Huang, Y. Liu, A. Zhou, *Org. Biomol. Chem*., **2016**, *14*, 1428−1431.
51. L. Jiang, J. Qian, W. Yi, G. Lu, C. Cai, W. Zhang, *Angew. Chem. Int. Ed*., **2015**, *54*, 14965−14969.
52. F. Xiao, H. Xie, S. Liu, G. J. Deng, *Adv. Synth. Catal*., **2014**, *356*, 364−368;
53. H. Rao, P. Wang, J. Wang, Z. Li, X. Sun, S. Cao. *RSC Adv*., **2014**, *4*, 49165−49169.
54. P. Katrun, S. Hongthong, S. Hlekhlai, M. Pohmakotr, V. Reutrakul, D. Soorukram, T. Jaipetch, C. Kuhakarn, *RSC Adv*., **2014**, *4*, 18933−18938.
55. D. Huang, J. Chen, W. Dan, J. Ding, M. Liu, H. Wu, *Adv. Synth. Catal*., **2012**, *354*, 2123−2128.
56. P. Hamel, *J. Org. Chem*., **2002**, *67*, 2854−2858.
57. P. Hamel, *Tetrahedron Lett*., **1997**, *38*, 8473−8474.
58. P. Hamel, P. Préville, *J. Org. Chem*., **1996**, *61*, 1573−1577.
59. M. Raban, L. J. Chern, *J. Org. Chem*., **1980**, *45*, 1688−1691.
60. C. J. Nalbandian, E. M. Miller, S. T. Toenjes, J. L. Gustafson, *Chem. Commun*., **2017**, *53*, 1494−1497.
61. J. B. Ernst, A. Rühling, B. Wibbeling, F. Glorius, *Chem. Eur. J*., **2016**, *22*, 4400-4404.
62. D. Zhu, Y. Gu, L. Lu, Q. Shen, *J. Am. Chem. Soc*. **2015**, *137*, 10547−10553.
63. T. Hostier, V. Ferey, G. Ricci, D. G. Pardo, J. Cossy, *Chem. Commun*., **2015**, *51*, 13898−13901.
64. C. Viglianisi, E. Marcantoni, V. Carapacchi, S. Menichetti, L. Marsili, *Eur. J. Org. Chem*. **2014**, *29*, 6405−6410.
65. P. P. Kumar, Y. D. Reddy, Ch. V. R. Reddy, B. R. Devi, P. K. Dubey, *J. Sulfur. Chem*., **2014**, *35*, 356−361.
66. E. Marcantoni, R. Cipolletti, L. Marsili, S. Menichetti, R. Properzi, C. Viglianisi, *Eur. J. Org. Chem*., **2013**, *1*, 132−140.
67. C. C. Silveira, S. R. Mendes, L. Wolf, G. M. Martins, *Tetrahedron Lett*., **2010**, *51*, 2014−2016.
68. M. Tudge, M. Tamiya, C. Savarin, G. R. Humphrey, *Org. Lett*., **2006**, *8*, 565−568.
69. R. Rahaman, S. Das, P. Barman, *Green Chem*., **2018**, *20*, 141−147.
70. R. Ohkado, T. Ishikawa, H. Iida, *Green Chem*. **2018**, *20*, 984−988.
71. S. Song, Y. Zhang, A. Yeerlan, B. Zhu, J. Liu, N. Jiao, *Angew. Chem. Int. Ed*., **2017**, *56*, 2487−2491.
72. P. Wang, S. Tang, P. Huang, A. Lei, *Angew. Chem. Int. Ed*., **2017**, 56, 3009−3013.
73. W. Guo, W. Tan, M. Zhao, K. Tao, L. Y. Zheng, Y. Wu, D. Chen, X. L. Fan, *RSC Adv*., **2017**, *7*, 37739−37742.
74. P. Choudhury, B. Roy, B. Basu, *Asian J. Org. Chem*., **2017**, *6*, 1569−1574.
75. F. Bai, S. Zhang, L. Wei, Y. Liu. *Asian J. Org. Chem*., **2018**, *7*, 371−373.
76. W. J. Wang, X. C. Wang, *Heterocycles*, **2017**, *94*, 449−464.
77. L. M. Ye, J. Chen, P. Mao, X. J. Zhang, M. Yan, *Tetrahedron Lett*., **2017**, *58*, 2743−2746.
78. S. Vásquez-Céspedes, A. Ferry, L. Candish, F. Glorius, *Angew. Chem. Int. Ed*. **2015**, *54*, 5772−5776.
79. J. B. Azeredo, M. Godoi, G. M. Martins, C. C. Silveira, A. L. Braga, *J. Org. Chem*., **2014**, *79*, 4125−4130.
80. X. Zhou, X. Li, *RSC Adv*., **2014**, *4*, 1241−1245.
81. Z. Gao, X. Zhu, R. Zhang, *RSC Adv*., **2014**, *4*, 19891−19895.
82. M. Matsugi, K. Murata, H. Nambu, Y. Kita, *Tetrahedron Lett*., **2001**, *42*, 1077−1080.
83. M. Matsugi, K. Murata, K. Gotanda, H. Nambu, G. Anilkumar, K. Matsumoto, Y. Kita, *J. Org. Chem*., **2001**, *66*, 2434−2441.
84. M. Matsugi, K. Gotanda, K. Murata, Y. Kita, *Chem. Commun*., **1997**, *15*, 1387−1388.
85. Y. Yang, S. Zhang, L. Tang, Y. Hu, Z. Zha, Z. Wang, *Green Chem*. **2016**, *18*, 2609−2613.
86. R. Rahaman, N. Devi, K. Sarma, P. Barman, *RSC Adv*. **2016**, *6*, 10873−10879.
87. U. Nookaraju, E. Begari, R. R. Yetra, P. Kumar, *ChemistrySelect*, **2016**, *1*, 81−85.
88. X. Li, Y. Xu, W. Wu, C. Jiang, C. Qi, H. Jiang, *Chem. Eur. J*., **2014**, *20*, 7911−7915.
89. F. L. Yang, S. K. Tian, *Angew. Chem. Int. Ed*. 2013, 52, 4929−4932.
90. F. X. Wang, S. D. Zhou, C. Wang, S. K. Tian, *Org. Biomol. Chem*., **2017**, *15*, 5284−5288.
91. R. Rahaman, N. Devi, J. R. Bhagawati, P. Barman, *RSC Adv*., **2016**, *6*, 18929−18935.
92. C. R. Liu, L. H. Ding, *Org. Biomol. Chem*., **2015**, *13*, 2251−2254.
93. S. Jain, K. Shukla, A. Mukhopadhyay, S. N. Suryawanshi, D. S. Bhakuni, *Synth. Commun*., **1990**, *20*, 1315−1320.
94. X. Yang, Y. Bao, Z. Dai, Q. Zhou, F. Yang. *Green Chem*., **2018**, *20*, 3727−3731.
95. L. Chen, J. Pu, P. Liu, B. Dai, *J. Saudi Chem. Soc*., **2019**, DOI: 10.1016/j.jscs.2018.10.007.
96. L. Chen, P. Liu, J. Wu, B. Dai, *Tetrahedron* **2018**, *74*, 1513−1519.
97. L. Chen, J. Pu, P. Liu, B. Dai, *J. Chem. Res*., **2018**, *42*, 456−462.
98. G. S. Sorabad, M. R. Maddani, *Asian J. Org. Chem*., **2019**, *8*, 1336−1343.
99. M. Chen, Y. Luo, C. Zhang, L. Guo, Q. Wang, Y. Wu, *Org. Chem. Front*. **2019**, *6*, 116−120.
100. S. Hazarika, P. Barman, ChemistrySelect **2019**, *4*, 7082−7089.
101. Yu, Y.; Y. Zhou, Z. Song, G. Liang, *Org. Biomol. Chem*., **2018**, *16*, 4958−4962.
102. N. Golzar, N. Nowrouzi, M. Abbasi, A. M. Mehranpour, *New J. Chem*., **2017**, *41*, 11921−11925.
103. D. Equbal, R. Singh, Saima, A. G. Lavekar, A. K. Sinha, *J. Org. Chem*., **2019**, *84*, 2660−2675.
104. J. Rafique, S. Saba, M. S. Franco, L. Bettanin, A. R. Schneider, Silva, L. T.; A. L. Braga, *Chem. -Eur. J*., **2018**, *24*, 4173−4180.
105. A. Ghosh, M. Lecomte, S.-H. Kim-Lee, A. T. Radosevich, *Angew. Chem., Int. Ed*. **2019**, *58*, 2864−2869.
106. X. Luo, Q. Liu, H. Zhu, H. R. Chen, *Soc. Open Sci*., **2018**, *5*, 180170−180176.
107. D. Alves, R. G. Lara, M. E. Contreira, C. S. Radatz, L. F. Duarte, G. Perin, *Tetrahedron Lett*., **2012**, *53*, 3364−3368.
108. R. L. Antipin, A. N. Chernysheva, E. K Beloglazkina, N. V. Zyk, *Chem. Heterocycl. Comp*., **2010**, *46*, 1071−1075.
109. S. Oae, H. Togo, *Bull. Chem. Soc. Japan*, **1983**, *56*, 3813−3817.

Supplementary Material

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.

Highlights

• With readily accessible and free of unpleasant odor ethyl arylsulfinates as sulfur reagents, the metal-free-catalyzed direct sulfenylation of *N*-heteroarenes has been developed.

• 3-Arylthio-indoles and 2-arylthio-pyrroles derivatives were obtained in moderate to excellent yields, even on gram scale.

• The reaction was general for a broad scope of substrates and demonstrated good tolerance to a variety of functional groups.