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Article

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Catalytic Synthesis of 3-Thioindoles Using Bunte Salts as Sulfur Sources under Metal-Free Conditions

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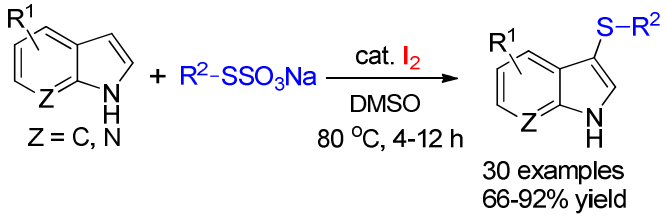
TOC Graphic



Abstract

An efficient catalytic method for the synthesis of 3-thioindoles has been successfully developed, which uses odorless, stable, readily available crystalline Bunte salts as the sulfenylating agents, iodine as nonmetallic catalyst, DMSO as both the oxidant and solvent. This method is practical and environmentally benign in terms of sulfur sources, catalyst and solvent. The catalytic reaction is selective at C3 position of indoles, and compatible with a wide range of substrates giving the desired products in

good to excellent yields.

Introduction

The substituted indoles are prevalent in numerous natural products and are important in medicinal chemistry.[1] Among numerous indole derivatives known, 3-thioindoles have attracted considerable attentions due to their therapeutic values. As for the treatment of HIV,[2] cancer,[3] obesity,[4] heart disease[5] and allergies,[6] 3-thioindole-based medicines have exhibited excellent activities. Besides, they also show potent activities such as inhibitor of tubulin polymerization and cell growth.[7]

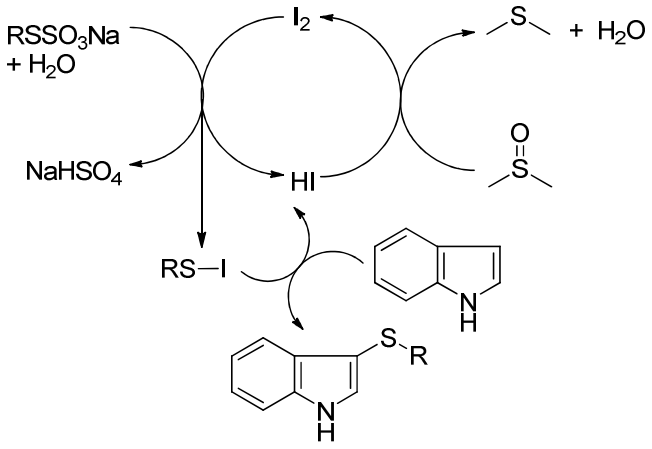
There has been long-standing interest in the development of efficient methods for the synthesis of 3-thioindoles and a number of different strategies have been developed.[8] To date, despite a few electrophilic cyclization methods were reported which employed less commonly available *o*-alkynylanilines or 2-(gem-dibromo(chloro)vinyl)anilines as starting material,[9] the direct sulfenylation of indole core by using electrophilic sulfenylating agents is the major route to 3-thioindoles. The most widely used sulfenylating reagents are thiols,[10] disulfides,[11] and sulfenyl halides.[12] Nevertheless, in the view of green chemistry, disadvantages encountered in those methods should be addressed: (1) thiols are repulsive-smelling and frequently require large amount of strong bases and/or metal catalysts to promote the reaction; (2) disulfides are prepared from smelly thiols; (3) most of the sulfenyl halides (especially sulfenyl iodides) are really unstable compounds, and the formation of sulfenyl halides requires toxic and hard to handle chlorine (or bromine) and thiols. Other sulfenylating agents have also been reported, such as quinone

mono-*O,S*-acetals,[13] *N*-(arylthio)phthalimides,[14] arylsulfonyl chlorides,[15] arylsulfonyl cyanides,[16] sodium sulfinates[17] and sulfonyl hydrazides.[18] However, many of those sulfenylating agents are complicated, expensive or air- and water-sensitive, and some of them need excess of reductants. Thus, developing a green and generally efficient method for the C3 sulfenylation of indole core, which uses odorless, stable and readily available sulfur sources and nonmetallic catalyst, is challenging and highly desirable.

Bunte salts ($RSSO_3Na$) are stable, easy to handle crystalline solid-salts and generally have little or no odor.[19] In addition to traditional synthetic methods starting from thiols,[20] Bunte salts can also be conveniently prepared by the reaction of odorless and inexpensive sodium thiosulfate with various alkyl halides,[21] aryl halides,[22] alkenes,[23] and aromatic thiocyanates.[24] It was reported that Bunte salts reacted with iodine to generate electrophilic sulfenyl iodide (RSI) species[25] which was known to undergo sulfenylation reaction of indoles with concomitant formation of HI.[11b, 11d, 17a] On the other hand, iodide anions are readily oxidized to iodine by dimethyl sulfoxide (DMSO) in the presence of an acid.[26] Thus, we surmised that a catalytic route to 3-thioindoles might be designed by using Bunte salts as environmental benign sulfur sources,[22] iodine as nonmetalic catalyst, and DMSO as both the oxidant and solvent (Scheme 1). Moreover, additional advantage can be found by using DMSO as solvent since it has been claimed as a green solvent suitable for replacing toxic solvents due to its high boiling point, a very low vapor pressure (0.6 mmHg at 25 °C), and ready biodegradability.[27] DMSO has been also classified as a nontoxic solvent with no risk

to human health by the U.S. Environmental Protection Agency (EPA).[28] In the designed catalysis, Bunte salts may react with iodine to form sulfenyl iodide (RSI) species which then undergoes electrophilic substitution with indole core to yield 3-thioindole and HI. HI is then oxidized into iodine by DMSO to complete the catalytic cycle (Scheme 1). Based on this proposed route, herein we report an efficient method for the synthesis of 3-thioindoles in DMSO by using Bunte salts as odorless, stable and readily available sulfur sources and iodine as the nonmetallic catalyst.

Scheme 1. Proposed Iodine-Catalyzed Synthesis of 3-Thioindoles Using Bunte Salts as Sulfur Sources.

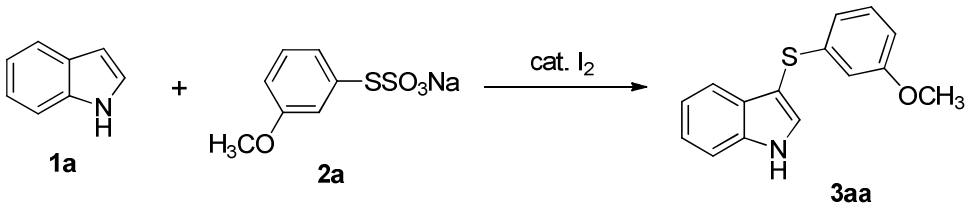


Results and Discussion

Initially, the reaction of 1*H*-indole with sodium *S*-(3-methoxyphenyl)thiosulfate was investigated in the presence of iodine as a model system to identify and optimize the reaction parameters (Table 1). To our delight, when the reaction was carried out with

iodine (10 mol%) in DMSO at ambient temperature, the desired product could be formed in 45% yield (Table 1, entry 1). It was found that the reaction temperature affected the product yield significantly. The product yield was improved to 82% with the increasing of the reaction temperature to 80 °C (Table 1, entry 4). Higher temperature (100 °C) did not improve the reaction yield further (Table 1, entry 5). The influence of the amount of Bunte salt on the reaction was also examined. The results showed that more than 1.5 eq. Bunte salt was not necessary for the best yield (Table 1, entry 6). Then the catalyst loading was evaluated (Table 1, entries 8-10), the best result was obtained in the presence of 20 mol% of iodine (Table 1, entry 10). Water and ethanol were also explored as solvents (Table 10-12), and DMSO was found to be the best. Thus, the optimized reaction conditions for the C3 sulfenylation reaction of indoles involved using Bunte salt (1.5 eq.) as the sulfenylating agent, iodine (20 mol%) as the catalyst, DMSO as both the oxidant and the solvent, and conducting the reaction at 80 °C.

Table 1. Optimization of the Reaction Conditions[a]



Entry	I_2 (mol%)	Solvent	Temp (^oC)	**2a** (eq.)	Yield (%)
1	10	DMSO	25	2	45
2	10	DMSO	40	2	56
3	10	DMSO	60	2	73

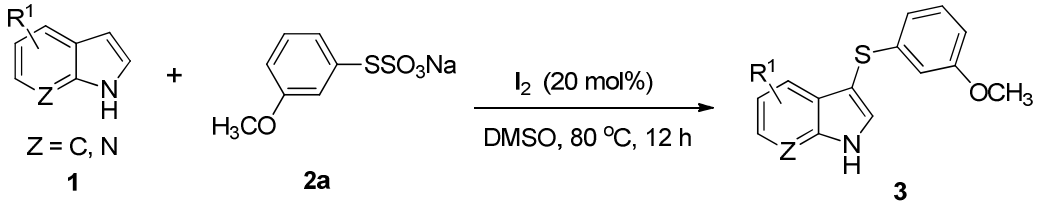
4	10	DMSO	80	2	82
5	10	DMSO	100	2	79
6	10	DMSO	80	1.5	83
7	10	DMSO	80	1.2	76
8	10	DMSO	80	1	57
9	5	DMSO	80	1.5	74
10	20	DMSO	80	1.5	88
11	20	H_2O	80	1.5	n.r.[b]
12	20	Ethanol	80	1.5	n.r.[b]
13	20	DMSO	80	1.5	81[c]

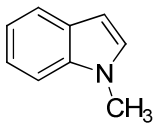
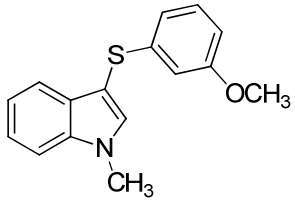
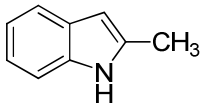
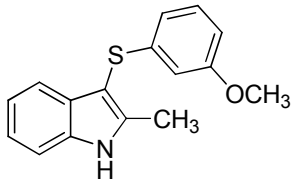
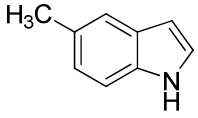
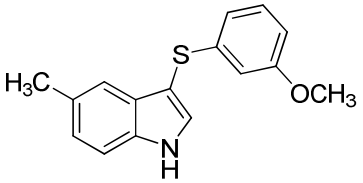
[a] Reaction conditions: 1*H*-indole (0.4 mmol), sodium *S*-3-methoxyphenyl thiosulfate, iodine, solvent (3 mL), Ar, 12 h. [b] 5 eq DMSO was used as the oxidant in the reaction, n.r. = no reaction. [c] The reaction was performed under air.

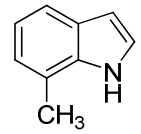
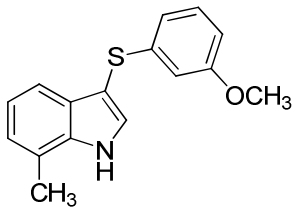
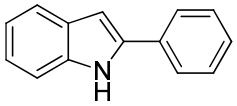
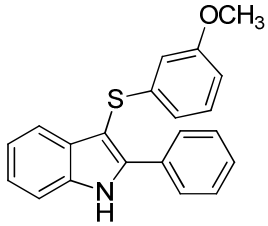
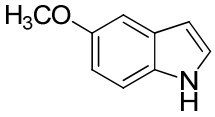
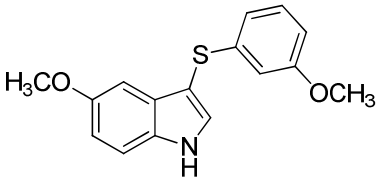
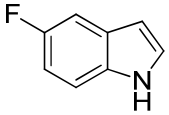
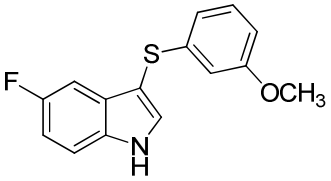
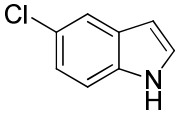
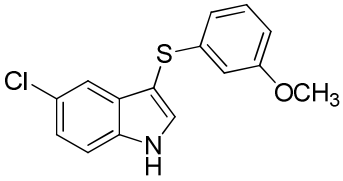
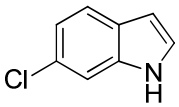
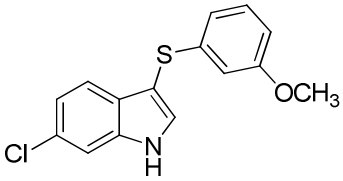
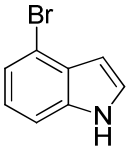
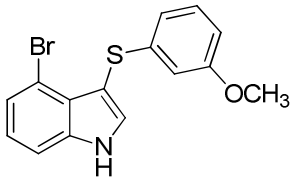
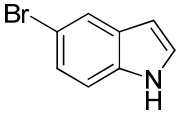
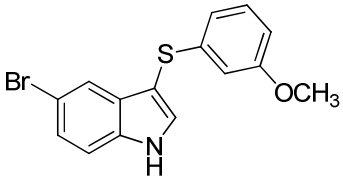
With the optimized reaction conditions in hand, we then evaluated the scope of the reactions of sodium *S*-(3-methoxyphenyl)thiosulfate (**2a**) with various indole derivatives. As shown in Table 2, indoles with electron-donating methyl, phenyl and methoxyl groups (Table 2, entries 1−6) gave higher yields compared to those having electron-withdrawing groups (Table 2, entries 7−16). Methyl group on different positions of indole did not change the product yield significantly (Table 2, entries 1−4). The reaction is tolerant with fluoro, chloro and bromo substituents on the aromatic ring of indole, and the corresponding target products were obtained in good yields (75−82%; Table 2, entries 7−11). Indoles with strong electron-withdrawing nitryl and cyano groups needed longer time to finish the reaction and gave product

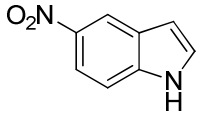
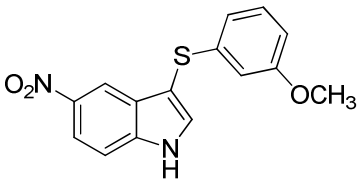
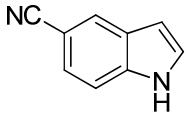
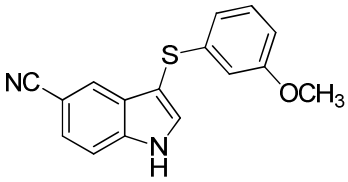
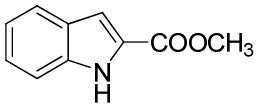
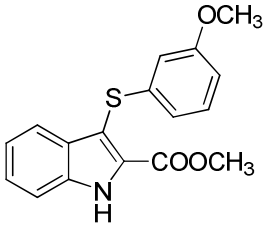
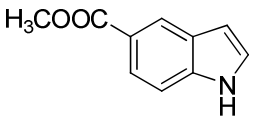
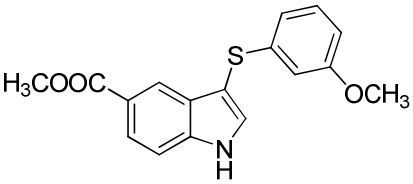
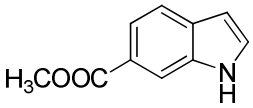
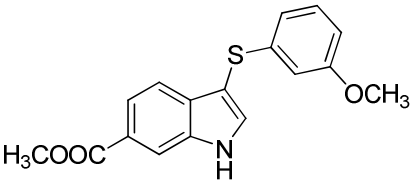
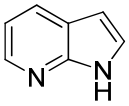
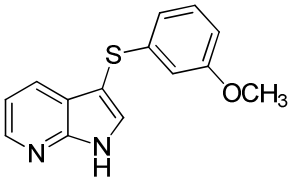
yields of 70% and 71% respectively (Table 2, entries 12 and 13). Meanwhile, probably due to additional steric hindrance, 1*H*-indole-2-carboxylate gave a lower yield of 66% and required longer reaction time (Table 2, entry 14) compared to its 5-carboxylate and 6-carboxylate isomers (Table 2, entries 15 and 16). The protocol was also applied to 1*H*-pyrrolo[2,3-b]pyridine giving the desired product **3ra** in 87% yield (Table 2, entry 17).

Table 2. Reaction of Sodium *S*-(3-Methoxyphenyl)thiosulfate with Various Indole Derivatives [a]



Entry	Indole derivative		Product		Yield (%)
1		**1b**		**3ba**	89
2		**1c**		**3ca**	86
3		**1d**		**3da**	84

4		**1e**		**3ea**	86
5		**1f**		**3fa**	84
6		**1g**		**3ga**	90
7		**1h**		**3ha**	82
8		**1i**		**3ia**	79
9		**1j**		**3ja**	78
10		**1k**		**3ka**	76
11		**1l**		**3la**	75

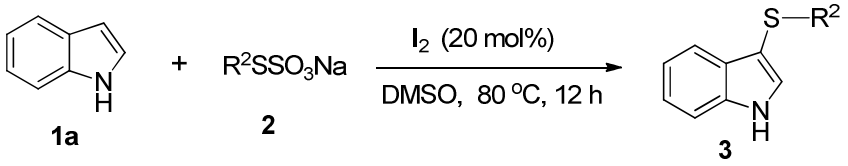
12		**1m**		**3ma**	70[b]
13		**1n**		**3na**	71[b]
14		**1o**		**3oa**	66[b]
15		**1p**		**3pa**	76
16		**1q**		**3qa**	70
17		**1r**		**3ra**	87

[a] Reaction conditions: **1** (0.4 mmol), **2a** (0.6 mmol), iodine (0.08 mmol), DMSO (3 mL), 80 °C, Ar, 12 h. [b] The reaction time was 16 h.

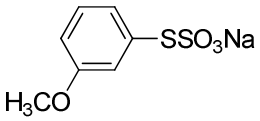
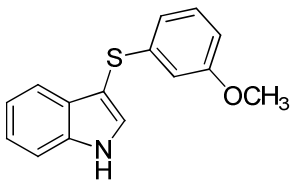
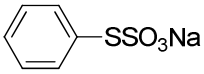
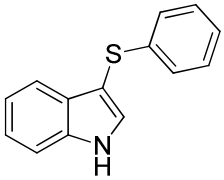
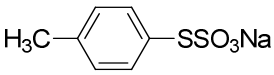
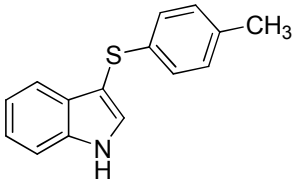
Subsequently, a range of Bunte salts was explored by reacting with 1*H*-indole (**1a**), and the results were listed in Table 3. Aromatic and aliphatic Bunte salts with a

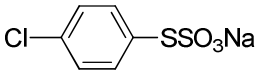
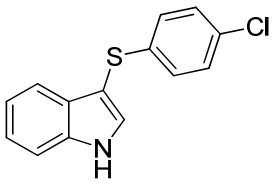
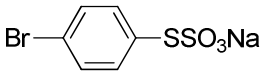
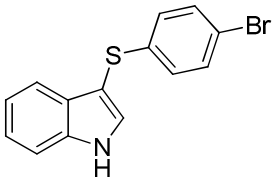
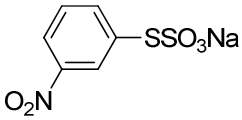
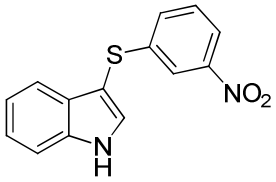
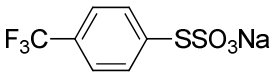
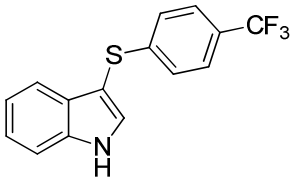
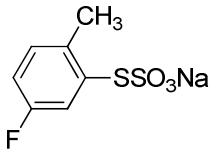
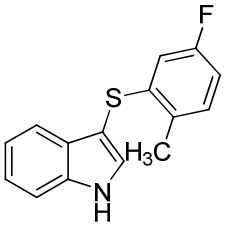
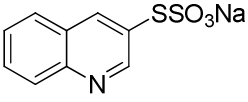
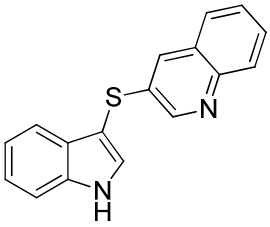
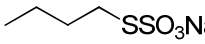
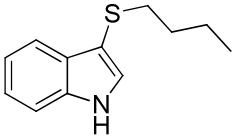
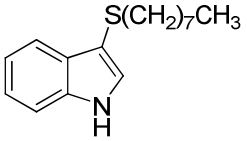
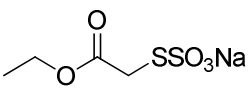
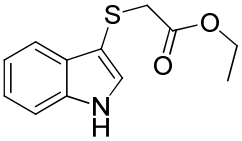
variety of substituents afforded the products in good to excellent yields under the optimum reaction conditions. Aromatic Bunte salts bearing functional groups including methoxyl, methyl, chloro, bromo, fluoro, nitryl, and trifluoromethyl generated the desired products in good to excellent yields (Table 3, entries 1-8). It is noteworthy that the method could apply to quinoline-based Bunte salt, giving a good yield of 70% (Table 3, entry 9). Aliphatic Bunte salts underwent the reaction more quickly than aromatic Bunte salts, giving the desired product **3aj**, **3ak** and **3al** in 85%, 86% and 74% yield respectively (Table 3, entries 10, 11 and 12).

Table 3. Reaction of 1*H*-Indole with Various Bunte Salts[a]



1a + R^2SSO_3Na (**2**) → (**3**)

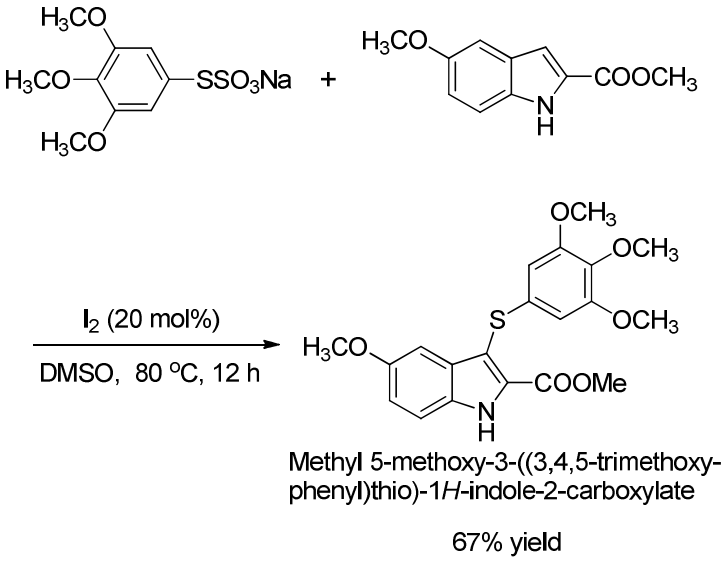
Entry	Bunte salt		Product		Yield (%)
1		**2a**		**3aa**	88
2		**2b**		**3ab**	84
3		**2c**		**3ac**	88

4		**2d**		**3ad**	90
5		**2e**		**3ae**	92
6		**2f**		**3af**	82
7		**2g**		**3ag**	77
8		**2h**		**3ah**	78
9		**2i**		**3ai**	70
10		**2j**		**3aj**	85[b]
11	$CH_3(CH_2)_7SSO_3Na$	**2k**		**3ak**	86[b]
12		**2l**		**3al**	74[c]

[a] Reaction conditions: **1a** (0.4 mmol), **2** (0.6 mmol), iodine (0.08 mmol), DMSO (3 mL), 80 °C, Ar, 12 h. [b] Reaction time: 2 h. [c] Reaction time: 4 h.

Methyl 5-methoxy-3-((3,4,5-trimethoxyphenyl)thio)-1*H*-indole-2-carboxylate, which is known as a potent inhibitor of tublin polymerization[7] and showing excellent antitumor activities,[3a,3b] was synthesized previously in literature in a very low yield of 4% using malodorous thiol as the sulfur source.[29] Notably, using our method as shown in Scheme 2, this compound was successfully prepared in a good yield of 67% on a 2 mmol scale.

Scheme 2. Synthesis of Methyl 5-Methoxy-3-((3,4,5-trimethoxyphenyl)thio)-1*H*-indole-2-carboxylate.



Methyl 5-methoxy-3-((3,4,5-trimethoxy-phenyl)thio)-1*H*-indole-2-carboxylate

67% yield

Conclusions

In summary, we have designed and successfully developed an efficient catalytic method for the synthesis of 3-thioindoles. This protocol displays attractive features including using odorless, stable, readily available and environment-friendly Bunte salts as the sulfenylating agents, using iodine as nonmetallic catalyst, employing DMSO as the oxidant and the solvent. The reaction is compatible with a wide range of functional groups. In particular, it is successfully applied to prepare methyl 5-methoxy-3-((3,4,5-trimethoxyphenyl)thio)-1*H*-indole-2- carboxylate in good yield.

Experimental Section

General. Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Bunte salts were prepared according to the literature.[21,22,24] Column chromatography was performed with silica gel (200 – 300 mesh). Thin layer chromatography was carried out using silica gel GF254 plates. High-resolution mass spectra (HRMS) were obtained with a Q-TOF Premier (ESI). ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz NMR instrument. Spectra were reported relative to Me_4Si (δ 0.0 ppm), $CDCl_3$ (δ 7.26 ppm), and DMSO-d_6 (δ 2.50 ppm). ^{13}C NMR were reported relative to $CDCl_3$ (δ 77.0 ppm) and DMSO-d_6 (δ 39.5 ppm). Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Products were characterized by comparison of ^{1}H and ^{13}C NMR spectroscopic data with those available in the literature. Melting points were determined with a melting point apparatus and uncorrected.

General Procedure for the Synthesis of 3-Thioindoles. A tube with a magnetic stirring bar was charged with indoles (0.4 mmol) and Bunte salts (0.6 mmol) under an argon atmosphere. Then the DMSO (3 mL) solution containing iodine (0.08 mmol) was injected into the tube. The mixture was allowed to react in the sealed tube at 80 °C for the required time. The mixture was then cooled to room temperature, diluted with 30 mL saturated $Na_2S_2O_3$ (aq.), and extracted with CH_2Cl_2 (4 × 20 mL). The organic phase was washed with water (2 × 40 mL), then dried and concentrated in vacuo. The residue was further purified by a short flash chromatography on a silica gel column to afford the pure product.

1-Methyl-3-((3-methoxyphenyl)thio)-1H-indole ***(3ba)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (96 mg, 89%). Mp: 117-118 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 7.62 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.34 (s, 1H), 7.30 (t, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 8.0 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.66-6.70 (m, 2H), 6.58-6.61 (m,1H), 3.85 (s, 3H), 3.69 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 159.9, 141.4, 137.7, 134.8, 130.0, 129.6, 122.7, 120.6, 119.8, 118.2, 110.6, 110.3, 109.8, 100.4, 55.3, 33.3. HRMS (ESI): m/z calcd for $C_{16}H_{16}NOS$ $[M + H]^+$, 270.0953; found, 270.0956.

2-Methyl-3-((3-Methoxyphenyl)thio)-1H-indole[30] ***(3ca)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (93 mg, 86%). Mp: 73-75 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.25 (br s, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 6.8 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.58-6.64 (m, 3H). 3.66 (s, 3H),

2.51 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 159.5, 141.4, 141.1, 135.5, 130.3, 129.7, 122.2, 120.8, 119.0, 118.0, 111.3, 110.8, 110.0, 55.1, 12.0. HRMS (ESI): m/z calcd for $C_{16}H_{16}NOS$ $[M + H]^+$, 270.0953; found, 270.0955.

5-Methyl-3-((3-methoxyphenyl)thio)-1H-indole ***(3da)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (91 mg, 84%). Mp: 106-107 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.34 (br s, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.42 (s, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 2H), 6.67-6.69 (m, 2H), 6.59 (m, 1H), 3.70 (s, 3H), 2.42 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.0, 141.1, 134.8, 131.1, 130.5, 129.7, 129.5, 124.8, 119.2, 117.8, 111.4, 111.4, 110.3, 101.6, 51.2, 21.3. HRMS (ESI): m/z calcd for $C_{16}H_{16}NOS$ $[M + H]^+$, 270.0953.; found, 270.0956.

7-Methyl-3-((3-methoxyphenyl)thio)-1H-indole ***(3ea)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded colorless oil (93 mg, 86%). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.36 (br s, 1H), 7.48 (d, *J* = 2.8 Hz, 2H), 7.06-7.12 (m, 3H), 6.68-6.70 (m, 2H), 6.59-6.62 (m, 1H), 3.69 (s, 3H), 2.53 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.0, 141.0, 136.1, 130.6, 129.6, 128.8, 123.7, 121.2, 120.9, 118.3, 117.4, 111.6, 110.3, 102.9, 55.3, 16.5. HRMS (ESI): m/z calcd for $C_{16}H_{16}NOS$ $[M + H]^+$, 270.0953.; found, 270.0956.

2-Phenyl-3-((3-methoxyphenyl)thio)-1H-indole[30] ***(3fa)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (111 mg, 84%). Mp: 112-114 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.55 (br s, 1H), 7.76 (d, *J* = 7.2 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.37-7.45 (m, 4H),

7.28-7.30 (d, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 8.0 Hz, 1H), 6.68-6.71 (m, 2H), 6.61 (dd, *J* = 2.4 Hz, 8.4 Hz, 1H), 3.68 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.0, 142.2, 140.9, 135.8, 131.5, 131.3, 129.8, 128.9, 128.8, 128.2, 123.5, 121.3, 120.0, 118.1, 111.3, 110.3, 99.2, 55.1. HRMS (ESI): m/z calcd for $C_{21}H_{18}NOS$ $[M + H]^+$, 332.1109; found, 332.1106.

*5-Methoxy-3-((3-methoxyphenyl)thio)-1H-indole (**3ga**).* Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded yellow oil (103 mg, 90%). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.41 (s, 1H), 7.42 (d, *J* = 2.8 Hz, 1H), 7.29 (t, *J* = 8.8 Hz, 1H), 7.07-7.13 (m, 2H), 6.92 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H), 6.68 -6.72 (m, 2H), 6.63 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H). 3.80 (s, 3H), 3.70 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.0, 155.2, 141.1, 131.6, 131.5, 130.1, 129.7, 118.1, 113.7, 111.4, 110.3, 101.9, 1008.8, 55.9, 55.3. HRMS (ESI): m/z calcd for $C_{16}H_{16}NO_2S$ $[M + H]^+$, 286.0902; found, 286.0904.

*5-Fluoro-3-((3-methoxyphenyl)thio)-1H-indole (**3ha**).* Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded colorless oil (90 mg, 82%). ^{1}H NMR ($CDCl_3$, 400MHz, ppm): δ 8.44 (br s, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.32 (dd, *J* = 4.4 Hz, 8.8 Hz, 1H), 7.25-7.28 (m, 1H), 7.08-7.12 (m, 1H), 7.02 (dt, *J* = 2.4 Hz, 8.8 Hz, 1H), 6.66-6.68 (m ,1H), 6.60-6.62 (m, 2H), 3.70 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.0, 158.7 (d, *J* = 235.4 Hz), 140.5, 133.0, 132.6, 130.0 (d, *J* = 10.0 Hz), 129.8, 118.4, 112.6 (d, *J* = 9.5 Hz), 111.8, 111.7 (d, *J* = 26.4 Hz), 110.5, 104.7 (d, *J* = 24.1 Hz), 102.8 (d, *J* = 4.7 Hz), 55.3. HRMS (ESI): m/z calcd for $C_{15}H_{13}FNOS$ $[M + H]^+$, 274.0702; found, 274..0706.

5-Chloro-3-((3-methoxyphenyl)thio)-1H-indole ***(3ia)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (92 mg, 79%). MP: 87-88 ^{0}C. ^{1}H NMR ($CDCl_3$, 400MHz, ppm): δ 8.48 (br s, 1H), 7.60 (d, *J* = 2.0 Hz, 1H), 7.45 (d, *J* = 2.4 Hz, 1H), 7.31 (d, *J* = 8.8 Hz, 1H), 7.20 (dd, *J* = 2.0 Hz, 8.4 Hz, 1H), 7.09-7.14 (m, 1H), 6.69-6.71 (m, 1H), 6.63-6.65 (m, 2H). 3.71 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.0, 140.4, 134.9, 132.3, 130.4, 129.8, 127.0, 123.6, 119.1, 118.4, 112.8, 111.8, 110.4, 102.4, 55.3. HRMS (ESI): m/z calcd for $C_{15}H_{12}ClNOS$ $[M + H]^+$, 290.0406; found, 290.0409.

6-Chloro-3-((3-methoxyphenyl)thio)-1H-indole ***(3ja)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded colorless oil (90 mg, 78%). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.43 (br s, 1H), 7.51 (d, *J* = 8.8 Hz, 1H), 7.43 (d, *J* = 2.4 Hz, 1H), 7.39 (d, *J* = 1.6 Hz, 1H), 7.08-7.14 (m, 2H), 6.62-6.71 (m, 3H), 3.7 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.0, 140.4, 136.9, 131.4, 129.8, 129.1, 127.8, 121.8, 120.7, 118.4, 111.8, 111.7, 110.5, 103.1, 55.3. HRMS (ESI): m/z calcd for $C_{15}H_{13}ClNOS$ $[M + H]^+$, 290.0406; found, 290.0404.

4-Bromo-3-((3-methoxyphenyl)thio)-1H-indole ***(3ka)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (102 mg, 76%). Mp: 144-146 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.52 (br s, 1H), 7.51 (d, *J* = 2.8 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.61-6.69 (m, 3H). 3.70 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 159.9, 142.7, 142.6, 137.8, 133.4, 126.5,

126.3, 126.1, 124.1, 118.4, 114.7, 111.7, 111.2, 110.2, 103.5, 55.3. HRMS (ESI): m/z calcd for $C_{15}H_{13}BrNOS$ $[M + H]^+$, 333.9901; found, 333.9905.

5-Bromo-3-((3-methoxyphenyl)thio)-1H-indole ***(3la)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (100 mg, 75%). Mp: 101-102 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.48 (s, 1H), 7.76 (s, 1H), 7.48 (d, *J* = 2.4 Hz, 1H), 7.29-7.36 (m, 2H), 7.10 (t, *J* = 8.4 Hz, 1H), 6.62-6.68 (m, 3H), 3.70 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.0, 142.0, 135.2, 132.1, 131.0, 129.8, 126.1, 122.2, 118.3, 114.6, 113.2, 111.8, 110.5, 102.4, 55.3. HRMS (ESI): m/z calcd for $C_{15}H_{13}BrNOS$ $[M + H]^+$, 333.9901; found, 333.9904.

5-Nitro-3-((3-methoxyphenyl)thio)-1H-indole ***(3ma)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 2:1, v/v) afforded a yellow solid (84 mg, 70%). Mp: 140-141 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.89 (br s, 1H), 8.57 (d, *J* = 2.0 Hz, 1H), 8.17 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H), 7.65-7.66 (d, *J* = 2.4 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.09-7.14 (m, 1H), 6.69-6.71 (m, 1H), 6.64-6.66 (m, 2H), 3.71 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.1, 142.8, 139.5, 139.3, 134.0, 129.9, 129.0, 118.9, 118.8, 117.0, 112.4, 112.1, 110.9, 106.3, 55.2. HRMS (ESI): m/z calcd for $C_{15}H_{13}N_2O_3S$ $[M + H]^+$, 301.0647; found, 301.0645.

3-((3-Methoxyphenyl)thio)-1H-indole-5-carbonitrile ***(3na)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 2:1, v/v) afforded a white solid (80 mg, 71%). Mp: 137-138 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 9.0 (br s, 1H), 7.96 (s, 1H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.46-7.52 (m, 2H), 7.12 (t, *J* = 8.0

Hz, 1H), 6.61-6.69 (m, 3H), 3.71 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 159.9, 139.5, 138.4, 133.0, 129.9, 129.1, 126.1, 125.4, 120.4, 118.7, 112.7, 112.1, 110.6, 104.5, 55.2. HRMS (ESI): m/z calcd for $C_{16}H_{13}N_2OS$ $[M + H]^+$, 281.0749; found, 281.0746.

Methyl 3-((3-methoxyphenyl)thio)-1H-indole-2-carboxylate[31] ***(3oa)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 2:1, v/v) afforded a white solid (83 mg, 66%). Mp: 154-155 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 9.30 (br s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 8.0 Hz, 1H), 6.73-6.76 (m, 2H), 6.64 (dd, *J* = 2.4 Hz, 8.0 Hz, 1H), 3.94 (s, 3H), 3.69 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 161.9, 159.9, 139.1, 135.9, 130.0, 129.7, 128.7, 126.4, 121.9, 121.7, 119.8, 113.0, 112.2, 111.1, 110.5, 55.3, 52.4. HRMS (ESI): m/z calcd for $C_{17}H_{16}NO_3S$ $[M + H]^+$, 314.0851; found, 314.0855.

Methyl 3-((3-methoxyphenyl)thio)-1H-indole-5-carboxylate ***(3pa)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 2:1, v/v) afforded a yellow solid (95 mg, 76%). Mp: 124-126 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.67 (br s, 1H), 8.39 (s, 1H), 7.98 (dd, *J* = 1.4 Hz, 8.4 Hz, 1H), 7.56 (d, *J* = 2.4 Hz, 1H), 7.45 (d, *J* = 8.8 Hz, 1H), 7.09 (t, *J* = 8.8 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 6.60-6.64 (m, 2H). 3.81 (s, 3H), 3.69 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 168.0, 159.9, 140.4, 139.1, 132.3, 129.6, 128.9, 124.5, 123.1, 122.4, 118.3, 111.7, 111.4, 104.4, 55.2, 52.0. HRMS (ESI): m/z calcd for $C_{17}H_{16}NO_3S$ $[M + H]^+$, 314.0851; found, 314.0854.

Methyl 3-((3-methoxyphenyl)thio)-1H-indole-6-carboxylate ***(3qa)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 2:1, v/v) afforded a white solid (88 mg, 70%). Mp: 130-131 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.74 (br s, 1H), 8.21 (s, 1H), 7.85 (dd, *J* = 1.2 Hz, 8.4 Hz, 1H), 7.63-7.65 (m, 2H), 7.07-7.11 (m, 1H), 6.60-6.68 (m, 3H), 3.94 (s, 3H), 3.68 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 168.0, 160.0, 140.3, 136.0, 134.0, 133.0, 129.8, 125.0, 122.1, 119.5, 118.4, 114.2, 111.8, 110.6, 103.5, 54.8, 52.0. HRMS (ESI): m/z calcd for $C_{17}H_{16}NO_3S$ $[M + H]^+$, 314.0851; found, 314.0850.

3-((3-Methoxyphenyl)thio)-1H-pyrrolo[2,3-b]pyridine ***(3ra)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 10:1, v/v) afforded a white solid (89 mg, 87%). Mp: 165-166 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 11.68 (br s, 1H), 8.41 (d, *J* = 4.4 Hz, 1H), 7.97 (dd, *J* = 1.6 Hz, 7.6 Hz, 1H), 7.71 (d, *J* = 4.4 Hz, 1H), 7.17 (dd, *J* = 4.8 Hz, 8.0 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.68-6.71 (m, 1H), 6.61-6.66 (m, 2H), 3.69 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.1, 149.4, 143.3, 140.5, 132.3, 129.7, 128.7, 122.4, 118.4, 116.9, 111.7, 110.7, 101.1, 55.3. HRMS (ESI): m/z calcd for $C_{14}H_{13}N_2OS$ $[M + H]^+$, 257.0749; found, 257.0746.

3-((3-Methoxyphenyl)thio)-1H-indole [32] ***(3aa)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (90 mg, 88%). Mp: 88-90 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.42 (br s,1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 2.8. Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.27-7.29 (m, 1H), 7.16-7.20 (m, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.68-6.72 (m, 2H),

6.61-6.63 (m, 1H), 3.69 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 159.9, 140.9, 136.5, 129.7, 129.2, 123.2, 121.1, 119.7, 118.3, 110.7, 110.6, 110.4, 102.6, 55.3. HRMS (ESI): m/z calcd for $C_{15}H_{14}NOS$ $[M + H]^+$, 256.0796; found, 256.0798

3-(Phenylthio)-1H-indole[33] ***(3ab)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (76 mg, 84%). Mp: 152-153 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.37 (br s , 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 2.8 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.27-7.31 (m,1H), 7.05-7.20 (m, 6H). ^{13}C NMR($CDCl_3$, 100 MHz, ppm): δ 139.3, 136.6, 130.8, 129.8, 128.8, 126.0, 124.7, 123.2, 121.0, 119.8, 111.7, 102.9. HRMS (ESI): m/z calcd for $C_{14}H_{12}NS$ $[M + H]^+$, 226.0690; found, 226.0693.

3-(p-Tolylthio)-1H-indole[33] ***(3ac)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (95 mg, 88%). Mp: 124-126 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.35 (br s 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.47 (s, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.25-7.29 (m, 1H), 7.17 (t, *J* = 7.6 Hz,1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 2H). 2.26 (s, 3H) ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 136.5, 135.6, 134.8, 130.6, 129.6, 129.2, 126.4, 123.1, 120.9, 119.8, 111.7, 21.0. HRMS (ESI): m/z calcd for $C_{15}H_{14}NS$ $[M + H]^+$, 240.0847; found, 240.0845.

3-((4-Chlorophenyl)thio)-1H-indole[33] ***(3ad)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (103 mg, 90%). Mp: 130-131 ^{0}C.^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.44 (br s, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 2.8 Hz, 1H), 7.45 (d, *J* = 8.0 Hz,

1H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.11-7.14 (m, 2H), 7.01-7.04 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 137.9, 136.6, 130.8, 130.7, 128.9, 127.2, 123.3, 121.2, 119.6, 111.8, 102.6. HRMS (ESI): m/z calcd for $C_{14}H_{11}ClNS$ [M + H]$^+$, 260.0301; found, 260.0304.

3-((4-Bromophenyl)thio)-1H-indole[33] ***(3ae)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (123 mg, 92%). Mp: 142-144 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.36 (br s 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 5.6 Hz, 1H), 7.40 (d, *J* = 8.0 Hz,1H), 7.20-7.24 (m, 3H), 7.14 (t, *J* = 8.0 Hz,1H), 6.90-6.93 (m,2H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 138.7, 136.6, 131.8, 130.9, 129.0, 127.5, 123.4, 121.2, 119.6, 118.4, 111.8, 102.4. HRMS (ESI): m/z calcd for $C_{14}H_{11}BrNS$ [M + H]$^+$, 303.9796; found, 303.9799.

3-((3-Nitrophenyl)thio)-1H-indole[33] ***(3af)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded a white solid (98 mg, 82%). Mp: 136-137 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.5 (br s, 1H), 7.88-7.92 (m, 2H), 7.54-7.57 (m, 2H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.36 (d, *J* = 8.0 Hz,1H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz,ppm): δ 148.7, 142,7, 136.7, 131.5, 131.4, 129.4, 128.6, 123.6, 121.4, 120.3, 119.8, 119.3, 112.0, 100.9. HRMS (ESI): m/z calcd for $C_{14}H_{11}N_2O_2S$ [M + H]$^+$, 271.0541; found, 271.0543.

3-((4-(Trifluoromethyl)phenyl)thio)-1H-indole[34] ***(3ag)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 2:1, v/v) afforded a

white solid (90 mg, 77%). Mp: 130-132 ^{0}C. ^{1}H NMR($CDCl_3$, 400 MHz, ppm): δ 8.51 (br s, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 1.6 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.28-7.33 (m, 1H), 7.18-7.21 (m, 1H), 7.14 (d, *J* = 8.0 Hz, 2H). ^{13}CNMR ($CDCl_3$, 100 MHz,ppm): δ 144.8, 136.7, 131.2, 128.9, 127.0, 126.8 (q, 32.4 Hz), 125.8 (q, *J* = 3.7 Hz), 124.4 (q, *J* = 269.9 Hz), 123.5, 121.4, 119.5, 111.9, 101.3. HRMS (ESI): m/z calcd for $C_{15}H_{11}F_3NS$ $[M + H]^+$, 294.0564; found, 294.0566.

*3-((2-Methyl-4-fluoro-pheny)thio)-1H-indole (**3ah**).* Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 4:1, v/v) afforded yellow oil (80 mg, 78%). ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 8.51（br s, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.46-7.50 (m, 2H), 7.29 (m, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.05-7.08 (m,1H), 6.65 (dt, *J* = 2.8 Hz, 8.4 Hz,1H), 6.37 (dd, *J* = 2.8 Hz, 10.0 Hz, 1H), 2.44 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 161.8 (d, *J* = 242.5 Hz), 140.9 (d, *J* = 7.6 Hz), 136.7, 131.2, 130.9 (d, *J* = 8 Hz), 129.6 (d, *J* = 3 Hz), 129.0, 123.4, 121.3, 119.6, 112.0, 111.8, 111.7, 111.1 (d, *J* = 21.3 Hz), 101.5, 19.2. HRMS (ESI): m/z calcd for $C_{15}H_{13}FNS$ $[M + H]^+$, 258.0753; found, 258.0756.

*3-(3-Quinolinylthio)-1H-indole (**3ai**).* Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 2:1, v/v) afforded a yellow solid (77 mg, 70%). Mp: 196-198 ^{0}C. ^{1}H NMR (DMSO-d_6, 400 MHz, ppm): δ 11.84 (s, 1H), 8.67 (br s, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.85 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.48-7.54 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.06 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz, ppm): δ 148.6, 145.4, 136.8, 133.1, 132.8, 130.9, 128.8, 128.7, 128.3, 127.8, 127.3, 127.1, 122.4, 120.4, 118.1,

112.6, 97.8. HRMS (ESI): m/z calcd for $C_{17}H_{13}N_2S$ $[M + H]^+$, 277.0799; found, 277.0795.

3-(n-Butylthio)-1H-indole[35] ***(3aj)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 10:1, v/v) afforded yellow oil (70 mg, 85%). ^{1}H NMR (DMSO-d_6, 400 MHz, ppm): δ 11.35 (br s, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 2.4 Hz,1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.07-7.15 (m, 2H), 2.63 (t, *J* = 6.8 Hz, 2H), 1.32-1.48 (m, 4H), 0.83 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz, ppm): δ 136.3, 129.6, 129.4, 122.7, 120.5, 119.5, 111.6, 106.2, 36.2, 32.1, 21.8, 13.8. HRMS (ESI): m/z calcd for $C_{12}H_{16}NS$ $[M + H]^+$, 206.1003; found, 206.1007.

3-(n-Octanylthio)-1H-indole[33] ***(3ak)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 10:1, v/v) afforded yellow oil (90 mg, 86%). ^{1}H NMR($CDCl_3$, 400 MHz, ppm): δ 8.22 (br s, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 2.4 Hz, 1H), 7.19-7.25 (m, 2H), 2.70 (t, *J* = 7.2 Hz, 2H), 1.24-1.40 *(m,*12H), 0.87 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 136.4, 129.5, 129.3, 122.7, 120.5, 119.5, 106.3, 36.5, 31.9, 30.0, 29.3, 28.7, 20.6, 14.2. HRMS (ESI): m/z calcd for $C_{16}H_{24}NS$ $[M + H]^+$, 262.1629; found, 262.1627.

Ethyl 2-((1H-indol-3-yl)thio)acetate ***(3al)***. Purification by column chromatography on silica gel (petroleum ether/diethyl ether = 10:1, v/v) afforded yellow oil (70 mg, 74%). ^{1}H NMR($CDCl_3$, 400 MHz, ppm): δ 8.41 (br s, 1H), 7.76 (d, *J* = 7.2 Hz, 1H), 7.37-7.39 (m, 2H), 7.20-7.25 (m, 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.41(s, 2H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 170.7, 136.2, 130.5, 129.1, 123.0, 120.8, 119.2, 111.7, 104.6, 61.38, 39.0, 14.2. HRMS (ESI): m/z calcd for

$C_{12}H_{14}NO_2S$ $[M + H]^+$, 236.0745; found, 236.0743.

Synthesis of Methyl 5-Methoxy-3-((3,4,5-trimethoxyphenyl)thio)-1*H*-indole-2-carboxylate. A tube with a magnetic stirring bar was charged with methyl 5-methoxy-1*H*-indole-2-carboxylate (2 mmol, 410 mg) and sodium *S*-(3,4,5-trimethoxyphenyl)thiosulfate (3 mmol, 907 mg) under an argon atmosphere. Then the DMSO (15 mL) solution containing iodine (0.4 mmol, 101.6 mg) was injected into the tube. The mixture was allowed to react in the sealed tube at 80 °C for 16 h. The mixture was then cooled to room temperature, diluted with 150 mL saturated $Na_2S_2O_3$ (aq.), and extracted with CH_2Cl_2 (4 × 100 mL). The organic phase was washed with water (2 × 100 mL), then dried and concentrated in vacuo. The residue was further purified by column chromatography on silica gel (petroleum ether/ether = 2:1, v/v) to afford methyl 5-methoxy-3-((3,4,5-trimethoxyphenyl)thio)-1*H*-indole-2-carboxylate[29] as a white solid in 67% yield (541 mg). Mp: 150-152 ^{0}C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm): δ 9.46 (br s, 1H), 7.32 (d, J = 8.8 Hz, 1H), 7.00 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 6.92 (d, J = 2.4 Hz, 1H), 6.47 (s, 2H), 3.94 (s, 3H), 3.78 (s, 3H), 3.73 (s, 3H), 3.67 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm): δ 160.8, 154.3, 152.5, 135.4, 131.3, 130.2, 129.4, 127.4, 117.2, 112.4, 109.3, 104.4, 100.3, 60.0, 55.2, 54.7, 51.3. HRMS (ESI): m/z calcd for $C_{20}H_{22}NO_6S$ $[M + H]^+$, 404.1168; found, 404.1164.

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Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org. ^{1}H NMR and ^{13}C NMR spectra of all products.

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