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Iodine-Catalyzed Synthesis of 3-Arylthioindoles Employing a 1-Aryltriazene/CS_2 Combination as a New Sulfenylation Source

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ABSTRACT: A practical approach for the regioselective synthesis of 3-arylthioindoles has been accomplished using a combination of 1-aryltriazene/CS_2 as a new sulfenylation source. The methodology employs molecular iodine as a catalyst and is compatible with a variety of structurally diverse reactants.

INTRODUCTION

Sulfenylated organic molecules manifest significant biological activity and are prospective candidates for drug discovery programs (Figure 1).[1] Particularly, the C(sp^2)−S bond has a

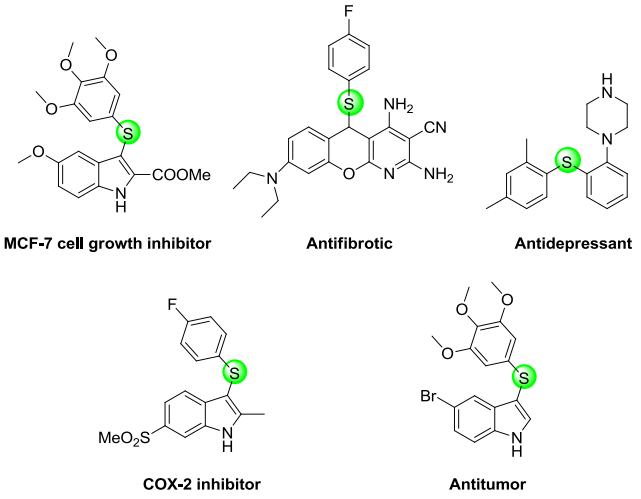

Figure 1. Some biologically active sulfenylated molecules.

definite role in the functional expression of various natural products and biologically active moieties.[2] Indoles constitute a section of most important heterocycles and are amenable to many substitutions so as to comprise the core structure of various bioactive molecules and natural products.[3] The difficulty in synthesizing selected functionalized indoles[4] using pre-eminent traditional methods has, thus, led to the concept of selective substitution.[5]

3-Sulfenylindole derivatives have attained considerable pharmacological significance in the treatment of various diseases, including HIV, heart diseases, cancer, bacterial infection, etc.[6] They have also been explored as potent inhibitors of tubulin polymerization.[7] As a result, the synthesis of 3-sulfenylindoles has garnered a great deal of current interest concerning various protocols.[8] The most eminent strategies for desired functionalization, however, comprise direct sufenylation of the indole core, employing sulfenylating agents, such as thiols,[9] arylsulfonyl hydrazides,[10] sulfinates,[11] disulfides,[12] *N*-thioimides,[13] sulfonium salts,[14] quinone mono-O, *S*-acetals,[15] sulfenyl halides,[16] arylsulfonyl chloride,[17] etc. From this perspective, the use of arylsulfonyl hydrazides by the Tian group[10d] and, more recently, the use of arylsulfonyl chlorides by the Radosevich group[17a] as sulfur electrophiles for the sulfenylation of indoles have drawn special attention (Scheme 1). Nevertheless, a practical and mild synthetic strategy employing a readily available and inexpensive sulfenylating source is still in demand.

1-Aryltriazenes have recently evolved as excellent synthons and are used as masked arenediazonium salts.[18,19] Besides their use as an aryl and diazenyl source, 1-aryltriazenes are also employed as a versatile directing group for selective C−H activation.[20] Easy preparation from commercially available arylamines and the stability of 1-aryltriazenes under air/moisture lend them additional advantages and application expediency over the arenediazonium salts.

In the pursuit of an external sulfur source, highly available carbon disulfide has been newly established as an efficient sulfur source for many organic transformations.[21] Inspired by the recent reports and considering the propensity of 1-aryltriazenes to generate aryl radicals,[22] it was envisioned to design a reaction module for in situ generation of thiyl radicals via the combination of aryl radicals with CS_2 followed by dethiocarbonylation,[21a] which may eventually lead to a new means of sulfenylation of organic molecules.

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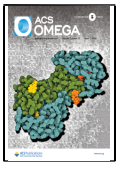
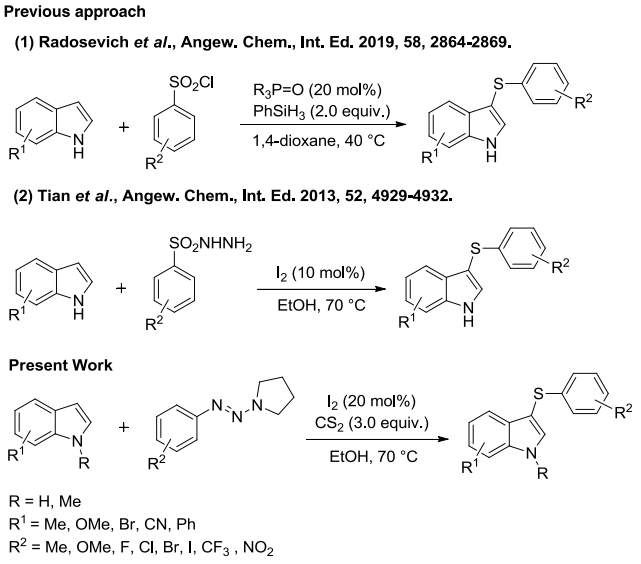


Scheme 1. Synthesis of 3-Arylthioindoles



In view of the above and as a part of our ongoing research on C−S bond formation,[23] we report herein a molecular-iodine-catalyzed facile synthesis of 3-arylthioindoles, employing a blend of 1-aryltriazenes and carbon disulfide as a new sulfenylation source in ethanol at 70 °C (Scheme 1).

RESULTS AND DISCUSSION

To comprehend our idea and to optimize the reaction conditions, a model reaction involving 1*H*-indole (**1a**) and 1-(phenyldiazenyl)pyrrolidine (**2a**) was thoroughly investigated by varying different parameters, such as the catalyst, sulfur source, solvent, and temperature (Table 1).

The studies commenced with a preliminary reaction setup by taking a mixture of **1a** (1.0 mmol), **2a** (1.2 mmol), CS_2 (3.0 mmol), molecular iodine (20 mol %), and DMSO with stirring in a sealed glass vessel at room temperature for 8 h, which led to the formation of the desired product 3-(phenylthio)-1*H*-indole (**3a**) in 46% yield (Table 1, entry 1). An appreciable surge in the product yield was witnessed with an increase in the temperature up to 70 °C, beyond which there was no further increase in the product yield (entries 2−4). A much lower product yield (47%) was obtained on lowering the catalyst loading (10 mol %, entry 5). Notably, no product formation was observed in the absence of the I_2 catalyst (entry 6). Further, a number of other iodine catalysts, *viz.*, KI, NH_4I, NIS, TBAI, and DIB were screened (entries 7−11), out of which only KI, NH_4I, and NIS could cause apparent desired conversion, while TBAI and DIB failed. Among the various solvents tried (entries 12−20), ethanol happened to be the best to afford 86% product yield (entry 14). The attempt to utilize other sulfur sources, namely, Na_2S and S_8, also remained futile (entries 21 and 22).

Under the established reaction conditions (Table 1, entry 14), various secondary amines, *viz.*, piperidine, morpholine, diethylamine, and dipropylamine, employed as the *N*-substituted moiety of 1-phenyltriazenes, were tested for their efficacy on the product yield (Scheme 2). Although all secondary amines afforded good product yields, pyrrolidine remained to be the best option.

Finally, the scope and generality of the reaction was systematically examined using a variety of indoles (**1**) and 1-aryltriazenes (**2**) with different substitution patterns, and the results are given in Table 2.

Gratifyingly, 1-aryltriazenes containing electron-donating (Me, OMe) as well as electron-withdrawing (F, Cl, Br, I, CF_3, NO_2) groups at diverse positions on the aryl ring endured smoothly when reacted with indole (**1a**) under the stipulated conditions to afford the sulfenylation products (**3a**−**3n**) in excellent yields. It was observed that the presence of electron-donating groups on the aromatic ring of 1-aryltriazenes afforded somewhat higher yield in comparison to those bearing electron-withdrawing groups (**3b**−**3f** vs **3g**−**3n**). A hetero-aromatic 1-aryltriazene, namely, 3-(pyrrolidin-1-yldiazenyl)-pyridine, however, failed to afford the desired sulfenylated product (**3o**). Conversely, indole derivatives containing dissimilar electron-donating as well as electron-withdrawing substituents also participated well in the reaction and offered the desired sulfenylated products (**3p**−**3u**) in very high yields. Interestingly, the C2-substituted indoles, such as 2-methyl-indole and 2-phenylindole, also performed well in the reaction to give the corresponding products **3q** and **3r** in very good yields. However, when a C3-substituted indole, *viz.*, 3-

Table 1. Optimization of Reaction Conditions[a]

entry	catalyst	sulfur source	solvent	temp. (°C)	yield (%)[b]
1	I_2	CS_2	DMSO	rt	46
2	I_2	CS_2	DMSO	50	63
3	I_2	CS_2	DMSO	70	73
4	I_2	CS_2	DMSO	80	71
5	I_2	CS_2	DMSO	70	47[c]
6		CS_2	DMSO	70	0
7	KI	CS_2	DMSO	70	43
8	NH_4I	CS_2	DMSO	70	41
9	NIS	CS_2	DMSO	70	28
10	TBAI	CS_2	DMSO	70	trace
11	DIB	CS_2	DMSO	70	trace
12	I_2	CS_2	DMF	70	25
13	I_2	CS_2	CH_3CN	70	46
14[d]	**I_2**	**CS_2**	**EtOH**	**70**	**86**
15	I_2	CS_2	dioxane	70	42
16	I_2	CS_2	toluene	70	37
17	I_2	CS_2	DCE	70	49
18	I_2	CS_2	THF	70	32
19	I_2	CS_2	H_2O	70	0
20	I_2	CS_2	EtOH/H_2O (2:1)	70	46
21	I_2	Na_2S	EtOH	70	trace
22	I_2	S_8	EtOH	70	0

[a]Reaction conditions: **1a** (1.0 mmol), **2a** (1.2 mmol), catalyst (20 mol %), sulfur source (3.0 mmol), solvent (2 mL), 70 °C (in a sealed tube), 8 h. [b]Isolated yield after column chromatography. [c]Using 10 mol % I_2. [d]The bold entries (entry 14) represents the optimized reaction conditions.

Scheme 2. Reaction of 1a with Different 1-Phenyltriazenes

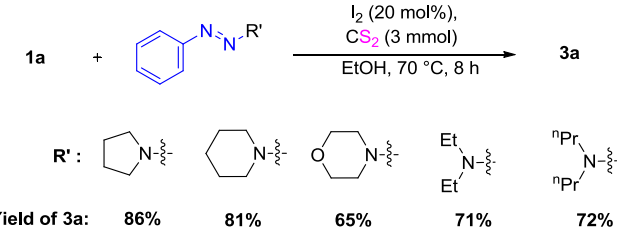


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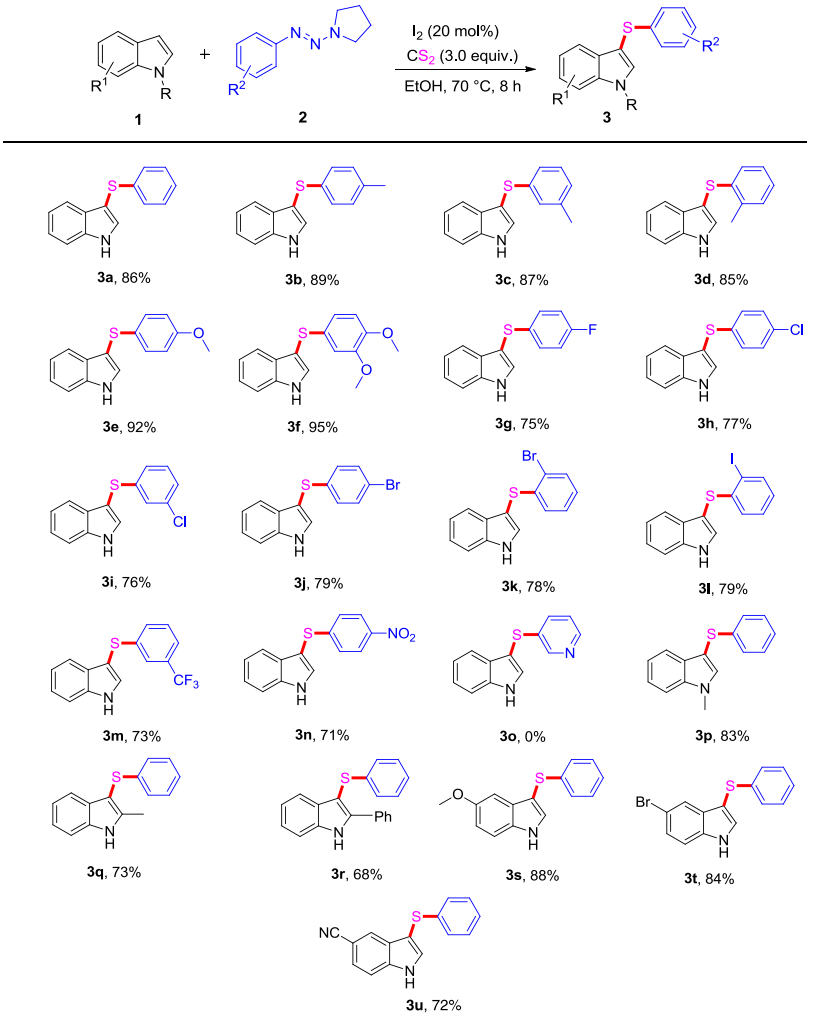
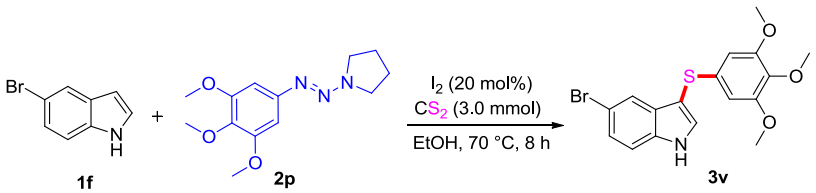
Table 2. Scope of the Reaction[a,b]



[a]Reaction conditions: **1a** (1.0 mmol), **2a** (1.2 mmol), CS_2 (3.0 mmol), I_2 (20 mol %), EtOH (2 mL), 70 °C (in a sealed tube), 8 h. [b]Isolated yield after column chromatography.

Scheme 3. Synthesis of the Antitumor Compound 3v



methylindole, was screened under the stipulated conditions, no conversion was observed.

To demonstrate the viability and usefulness of the realized sulfenylation reaction, a well-known antitumor compound, *viz.*, RS 2518 (5-bromo-3-((3,4,5-trimethoxyphenyl)thio)-1*H*-indole) (**3v**),[24] was also effectively synthesized in 65% yield from 1-((3,4,5-trimethoxyphenyl)pyrrolidine and 5-bromo-1*H*-indole under the established conditions (Scheme 3).

Encouraged by the results obtained with indoles, the sulfenylation strategy was further applied to other electron-rich arenes, such as 1,3,5-trimethoxybenzene (**4a**) and 2-naphthol (**5a**), which also efficiently afforded the likely sulfenylated products (**6** and **7**) in high yields under the standard conditions (Scheme 4). However, the desired sulfenylation of 1-naphthol under the stipulated conditions remained futile and instead gave rise to an azo dye as the major product.

All products were fully characterized on the basis of their physical and spectral data. The structure of a representative product **3c** was conclusively confirmed by single-crystal X-ray diffraction (see the Supporting Information for details).

To gain insight into the reaction mechanism, a number of control experiments were carried out (Scheme 5). The typical reaction involving 1*H*-indole (**1a**) and 1-(phenyldiazenyl)-pyrrolidine (**2a**) under the standard conditions was fully suppressed in the presence of radical inhibitors, such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), 2,6-di-*tert*-butyl-4-methylphenol (BHT), and ascorbic acid, thereby suggesting

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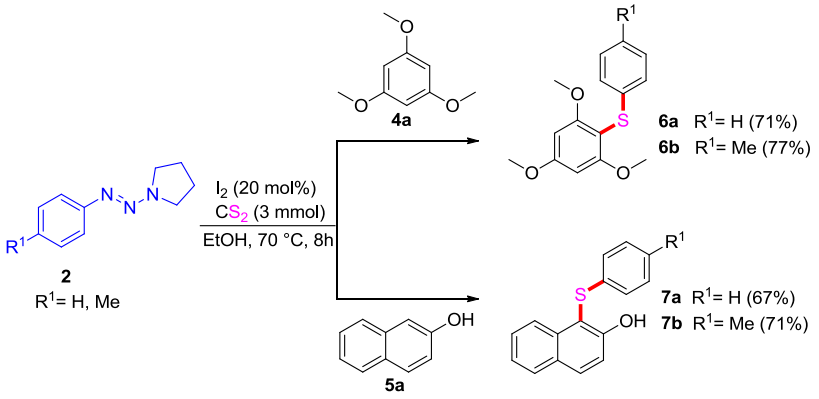
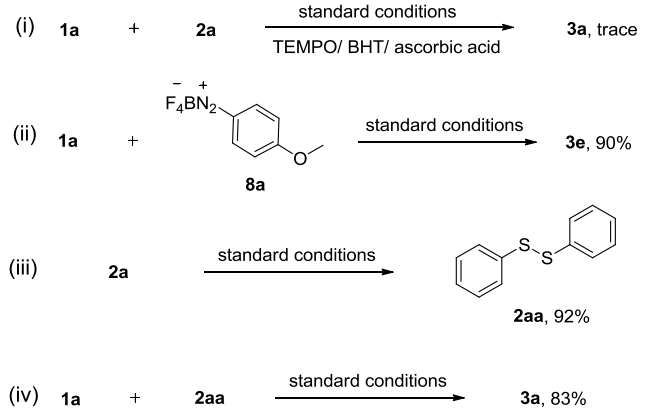
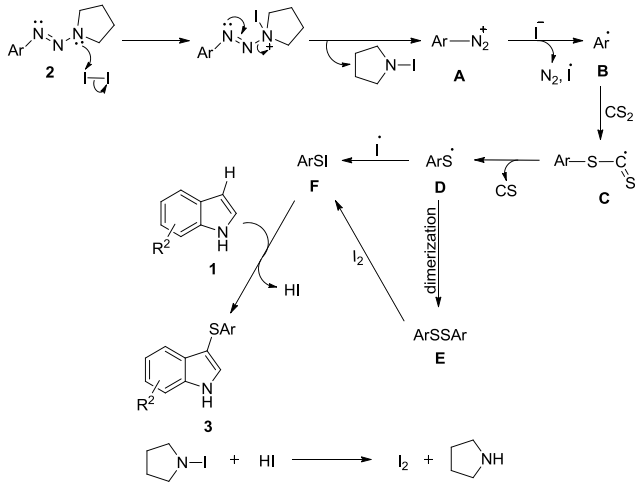
Scheme 4. Sulfenylation of 4a and 5a



Scheme 5. Control Experiments



Scheme 6. Plausible Reaction Mechanism



a radical pathway. Further, the reaction of a representative diazonium salt, *viz.*, *p*-methoxybenzenediazonium tetrafluoroborate (**8a**), with indole (**1a**) under the standard conditions also gave rise to the corresponding product **3e** (90%), suggestive of the intermediacy of the arenediazonium cation during the course of the reaction. Further, the reaction of 1-(phenyldiazenyl)pyrrolidine (**2a**) under the standard conditions gave rise to 1,2-diphenyldisulfane (**2aa**, 92%), which when made to react with indole (**1a**) under the standard conditions also afforded the desired product (**3a**, 83%), implying the involvement of disulfide in the reaction.

Based on control experiments, isolation of products, and existing literature,[21a,22,25] a plausible mechanism is outlined in Scheme 6.

The reaction is assumed to begin with the I_2-assisted formation of arenediazonium ion **A** with the removal of *N*-iodopyrrolidine. The diazonium ion **A** is then reduced by the iodide ion to the aryl radical **B**, which adds on to carbon disulfide to form the radical intermediate **C**, followed by the loss of carbon monosulfide to provide the thiyl radical **D**. An electrophilic species **F** is subsequently formed either via the direct combination of thiyl radical **D** with the iodide radical or via the formation of dimer **E** followed by its reaction with molecular iodine. Finally, the substrate indole **1** undergoes electrophilic substitution involving the species **F** (ArSI) to afford the sulfenylated product **3**.

CONCLUSIONS

In conclusion, a new and efficient sulfenylation strategy has been developed for the regioselective thiolation of indoles to provide 3-arylthiolindoles, employing an inexpensive and readily available 1-aryltriazene/CS_2 combination. The protocol employs mild and easy-to-handle reaction conditions and offers a wide range of substrate scope and functional group tolerance.

EXPERIMENTAL SECTION

General Information. ^{1}H, ^{13}C, and ^{19}F spectra were recorded on a JEOL ECZ 500R FTNMR spectrometer (^{1}H NMR at 500 MHz, ^{13}C NMR at 125 MHz, and ^{19}F NMR at 470 MHz). Chemical shifts are reported in parts per million (ppm) using tetramethylsilane (TMS) as an internal reference. ^{1}H NMR chemical shifts are given in ppm with respect to the residual $CHCl_3$ peak (δ 7.26 ppm), and ^{13}C NMR chemical shifts are given in ppm with respect to $CDCl_3$ (δ 77.16 ppm). NMR data are represented as follows: chemical shift, multiplicity (s = singlet, brs = broad singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (*J*) (Hz), and integration. Mass spectra were recorded on a SCIEX X500R QTOF mass spectrometer. Analytical thin-layer chromatography (TLC) was performed on Merck Kieselgel 60 GF254 plates (thickness 0.25 mm). Visualization was accomplished using a 254 nm UV lamp and by staining in an I_2 chamber. Organic solutions were concentrated under reduced pressure using a Büchi rotary evaporator. Purification of the crude products was done by column chromatography using a silica gel 100−200 mesh. All

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reactions were carried out in an oven-dried glass sealed tube. Yield refers to the isolated analytically pure material.

Materials. 1-Aryltriazene derivatives were prepared adopting an earlier method.[20a] The rest of the reagents were purchased from Sigma-Aldrich and Merck chemical co. and were used without further purification. Solvents were purified by standard methods.

General Experimental Procedure for the Synthesis of Products. A mixture of indole (**1**, 1.0 mmol), 1-aryltriazene (**2**, 1.2 mmol), CS_2 (3.0 mmol), I_2, and EtOH (2 mL), contained in a sealed tube, was stirred at 70 °C for 8 h. After completion of the reaction (monitored through TLC), ethanol was removed under reduced pressure, and the resulting mixture was successively worked-up using aqueous solution of sodium thiosulfate pentahydrate-ethyl acetate. The organic phase was then dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude product was finally purified by silica gel column chromatography using *n*-hexane and ethyl acetate as the eluent to afford the pure product **3**.

3-(Phenylthio)-1H-indole (***3a***).[17a] White solid; mp 151−152 °C, yield = 194 mg (86%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (brs, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 2.5 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.27 (t, J = 7.5 Hz, 1H), 7.17−7.09 (m, 5H), 7.05−7.02 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.4, 136.6, 130.8, 129.2, 128.8, 126.0, 124.9, 123.2, 121.0, 119.8, 111.7, 103.0.

3-(p-Tolylthio)-1H-indole (***3b***).[17a] White solid; mp 124−125 °C, yield = 213 mg (89%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (brs, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 2.5, 1H), 7.39 (d, J = 8.5 Hz, 1H), 7.25 (t, J = 7.5 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 2.23 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.6, 135.6, 134.8, 130.6, 129.6, 129.2, 126.4, 123.1, 121.0, 119.8, 111.7, 103.6, 21.0.

3-(m-Tolylthio)-1H-indole (***3c***).[9b] White solid; mp 126−127 °C, yield = 208 mg (87%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (brs, 1H), 7.62 (d, J = 7.5 Hz, 1H), 7.42 (d, J = 2.0, 1H), 7.40 (d, J = 8.5 Hz, 1H), 7.26 (t, J = 7.5 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.97 (s, 1H), 6.88 (t, J = 6.0 Hz, 2H), 2.21 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.1, 138.6, 136.6, 130.8, 129.3, 128.7, 126.6, 125.9, 123.1, 121.0, 119.8, 111.7, 103.0, 21.5.

3-(o-Tolylthio)-1H-indole (***3d***).[9b] White solid; mp 112−113 °C, yield = 203 mg (85%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (brs, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 9.0 Hz, 2H), 7.28 (t, J = 7.5 Hz, 1H), 7.17−7.12 (m, 2H), 6.98 (t, J = 7.5 Hz, 1H), 6.90 (t, J = 7.5 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4, 136.7, 134.5, 130.9, 130.0, 129.4, 126.4, 125.4, 124.6, 123.2, 121.0, 119.8, 111.7, 102.5, 20.0.

3-((4-Methoxyphenyl)thio)-1H-indole (***3e***).[10d] Orange solid; mp 114−115 °C, yield = 235 mg (92%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (brs, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 2.5 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.27 (t, J = 7.5 Hz, 1H), 7.19−7.14 (m, 3H), 6.77−6.74 (m, 2H), 3.73 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.9, 136.5, 130.2, 129.6, 129.1, 128.7, 123.0, 120.9, 119.7, 114.6, 111.7, 104.6, 55.4.

3-((3,4-Dimethoxyphenyl)thio)-1H-indole (***3f***). White solid; mp 137−138 °C, yield = 271 mg (95%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (brs, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 2.5 Hz, 1H), 7.40 (d, J = 8.5 Hz, 1H), 7.25 (t, J = 7.5 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 6.80 (s, 1H), 6.68 (s, 2H), 3.78 (s, 3H), 3.72 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.3, 147.3, 136.6, 130.2, 129.1, 123.1, 120.9, 119.7, 119.5, 112.0, 111.7, 110.9, 104.3, 56.1, 55.9. High-resolution mass spectrometry (HRMS) (electrospray ionization time-of-flight (ESI-TOF)) calcd for $C_{16}H_{14}NO_2S^-$ $(M - H)^-$ 284.0750; found: 284.0742.

3-((4-Fluorophenyl)thio)-1H-indole (***3g***).[17a] White solid; mp 134−135 °C, yield = 182 mg (75%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37 (brs, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 3.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 7.18 (t, J = 7.5 Hz, 1H), 7.11−7.07 (m, 2H), 6.88−6.84 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.0 (d, J = 242.5 Hz), 136.6, 134.2 (d, J = 2.5 Hz), 130.6, 129.0, 128.1 (d, J = 7.9 Hz), 123.3, 121.1, 119.7, 116.0 (d, J = 21.1 Hz), 111.8, 103.6. ^{19}F NMR (470 MHz, $CDCl_3$): δ −118.1.

3-((4-Chlorophenyl)thio)-1H-indole (***3h***).[10d] White solid; mp 130−131 °C, yield = 199 mg (77%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 (brs, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 2.5 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.13−7.10 (m, 2H), 7.03−7.00 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.0, 136.7, 130.8, 130.7, 129.0, 128.9, 127.3, 123.4, 121.2, 119.7, 111.8, 102.7.

3-((3-Chlorophenyl)thio)-1H-indole (***3i***).[9e] White solid; mp 77−78 °C, yield = 197 mg (76%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (brs, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 2.5 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.07−7.04 (m, 2H), 7.01 (d, J = 8.0 Hz, 1H), 6.96 (d, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.7, 136.6, 134.8, 131.1, 129.8, 129.0, 125.6, 125.1, 124.0, 123.4, 121.3, 119.6, 111.8, 102.0.

3-((4-Bromophenyl)thio)-1H-indole (***3j***).[10d] White solid; mp 141−142 °C, yield = 239 mg (79%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (brs, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 2.5 Hz, 1H), 7.46 (d, J = 8.5 Hz, 1H), 7.29 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.12−7.10 (m, 2H), 7.03−7.00 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.0, 136.7, 130.8, 130.7, 128.9, 128.9, 127.3, 123.4, 121.2, 119.7, 111.8, 102.6.

3-((2-Bromophenyl)thio)-1H-indole (***3k***).[9b] White solid; mp 148−149 °C, yield = 236 mg (78%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 (brs, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.45−7.39 (m, 3H), 7.24 (t, J = 7.5 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 6.92 (t, J = 7.5 Hz, 1H), 6.85 (t, J = 7.5 Hz, 1H), 6.57 (d, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.6, 136.7, 132.7, 131.4, 129.1, 127.6, 126.5, 125.8, 123.4, 121.3, 119.8, 111.8, 102.1.

3-((2-Iodophenyl)thio)-1H-indole (***3l***). Reddish brown solid; mp 151−152 °C, yield = 277 mg (79%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (brs, 1H), 7.69 (d, J = 7.5 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.42−7.37 (m, 2H), 7.23 (t, J = 7.5 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 6.94 (t, J = 7.5 Hz, 1H), 6.68 (t, J = 7.5 Hz, 1H), 6.54 (d, J = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.9, 139.3, 136.7, 131.3, 128.9, 128.4, 126.0, 126.0, 123.4, 121.3, 119.8, 111.8, 103.5, 94.4. HRMS (ESI-TOF) calcd for $C_{14}H_{11}INS^+$ $(M + H)^+$ 351.9652; found: 351.9638.

3-((3-(Trifluoromethyl)phenyl)thio)-1H-indole (***3m***).[12a] Brown viscous liquid; yield = 214 mg (73%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (brs, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 2.5 Hz, 1H), 7.46 (t, J = 8.0 Hz, 2H), 7.31 (t, J = 7.0 Hz, 2H), 7.25−7.19 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.1, 136.6, 131.2 (q, J = 32.3 Hz), 129.2, 128.9, 128.8, 125.1, 123.4 (q, J = 270.5 Hz), 122.4 (d, J = 3.4 Hz), 121.6 (d, J = 3.6

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Hz), 121.3, 119.5, 111.9, 101.5. ^{19}F NMR (470 MHz, $CDCl_3$): δ −62.60.

3-((4-Nitrophenyl)thio)-1H-indole (**3n**).[10d] Yellow solid; mp 174−175 °C, yield = 192 mg (71%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.75 (brs, 1H), 7.96 (d, J = 9.0 Hz, 2H), 7.51 (t, J = 4.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.10 (d, J = 9.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.2, 144.9, 136.7, 131.5, 128.5, 125.2, 123.9, 123.6, 121.4, 119.2, 112.1, 99.9.

1-Methyl-3-(phenylthio)-1H-indole (**3p**).[10d] White solid; mp 83−84 °C, yield = 198 mg (83%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.5 Hz, 1H), 7.35 (s, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.19−7.14 (m, 3H), 7.11−7.10 (m, 2H), 7.07−7.03 (m, 1H), 3.86 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.8, 137.7, 135.2, 130.0, 128.8, 125.8, 124.8, 122.7, 120.6, 119.9, 109.8, 100.6, 33.3.

2-Methyl-3-(phenylthio)-1H-indole (**3q**).[10d] White solid; mp 112−113 °C, yield = 175 mg (73%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (brs, 1H), 7.55 (d, J = 7.5 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.21−7.11 (m, 4H), 7.05 (t, J = 7.0 Hz, 3H), 2.52 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.2, 139.5, 135.6, 130.4, 128.8, 125.6, 124.6, 122.3, 120.8, 119.2, 110.7, 99.6, 12.3.

2-Phenyl-3-(phenylthio)-1H-indole (**3r**).[12f] Light yellow oil; yield = 205 mg (68%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (brs, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 7.5 Hz, 1H), 7.39−7.31 (m, 4H), 7.22 (t, J = 7.0 Hz, 1H), 7.11−7.07 (m, 3H), 7.03 (d, J = 7.0 Hz, 2H), 6.99−6.96 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.2, 139.4, 136.0, 131.6, 131.3, 128.9, 128.8, 128.3, 125.7, 124.8, 123.5, 121.3, 120.1, 111.3, 99.6.

5-Methoxy-3-(phenylthio)-1H-indole (**3s**).[10d] Light yellow liquid; yield = 244 mg (88%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (brs, 1H), 7.37 (d, J = 3.0 Hz, 1H), 7.25 (d, J = 8.5 Hz, 1H), 7.10 (t, J = 8.0 Hz, 2H), 7.03 (d, J = 7.5 Hz, 2H), 6.99−6.96 (m, 2H), 6.85 (dd, J = 2.0, 2.0 Hz, 1H), 3.71 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.3, 139.5, 131.5, 131.4, 130.1, 128.8, 125.9, 124.9, 113.8, 112.5, 102.5, 101.0, 56.0.

5-Bromo-3-(phenylthio)-1H-indole (**3t**).[10d] White solid; mp 121−122 °C, yield = 254 mg (84%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (brs, 1H), 7.75 (s, 1H), 7.48 (d, J = 2.5 Hz, 1H), 7.36−7.30 (m, 2H), 7.19 (t, J = 8.0 Hz, 2H), 7.09 (d, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.8, 135.2, 131.9, 131.1, 128.9, 126.2, 126.0, 125.1, 122.3, 114.6, 113.1, 103.0.

3-(Phenylthio)-1H-indole-5-carbonitrile (**3u**).[9a] White solid; mp 129−130 °C, yield = 180 mg (72%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.77 (brs, 1H), 7.88 (s, 1H), 7.55 (d, J = 2.5 Hz, 1H), 7.45 (q, J = 8.5 Hz, 2H), 7.13 (t, J = 8.0 Hz, 2H), 7.04 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4, 138.0, 132.8, 129.2, 129.1, 126.5, 126.2, 125.6, 125.5, 120.4, 112.8, 105.0, 104.3.

5-Bromo-3-((3,4,5-trimethoxyphenyl)thio)-1H-indole (**3v**).[6a] White solid; mp 153−154 °C, yield = 255 mg (65%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (brs, 1H), 7.78 (s, 1H), 7.49 (d, J = 2.0 Hz, 1H), 7.35−7.26 (m, 2H), 6.36 (s, 2H), 3.79 (s, 3H), 3.68 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): 153.6, 136.0, 135.2, 133.8, 132.0, 131.0, 126.2, 122.3, 114.5, 113.3, 103.7, 103.1, 61.0, 56.2.

Phenyl(2,4,6-trimethoxyphenyl)sulfane (**6a**).[26] White solid; mp 93−94 °C, yield = 196 mg (71%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15 (t, J = 8.0 Hz, 2H), 7.02 (d, J = 7.5 Hz, 3H), 6.20 (s, 2H), 3.85 (s, 3H), 3.79 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0, 162.6, 138.8, 128.6, 125.7, 124.5, 98.8, 91.3, 56.4, 55.5.

p-Tolyl(2,4,6-trimethoxyphenyl)sulfane (**6b**).[26] White solid; mp 112−113 °C, yield = 223 mg (77%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.97−6.93 (m, 4H), 6.20 (s, 2H), 3.85 (s, 3H), 3.80 (s, 6H), 2.24 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9, 162.6, 135.1, 134.2, 129.4, 126.1, 99.5, 91.3, 56.4, 55.5, 21.0.

1-(Phenylthio)naphthalen-2-ol (**7a**).[26] White solid; mp 66−67 °C, yield = 169 mg (67%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.40−7.35 (m, 2H), 7.20−7.16 (m, 3H), 7.12 (d, J = 6.5 Hz, 1H), 7.05 (d, J = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.1, 135.6, 135.5, 133.0, 129.6, 129.3, 128.7, 128.1, 126.5, 126.0, 124.8, 124.0, 117.0, 108.2.

1-(p-Tolylthio)naphthalen-2-ol (**7b**).[26] White solid; mp 78−79 °C, yield = 189 mg (71%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (d, J = 8.5 Hz, 1H), 7.89 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.37−7.31 (m, 2H), 7.20 (s, 1H), 6.98−6.93 (m, 4H), 2.23 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.0, 136.0, 135.6, 132.8, 131.9, 130.1, 129.6, 128.7, 128.0, 126.8, 124.8, 123.9, 117.0, 108.8, 21.0.

1,2-Diphenyldisulfane (**2aa**).[23a] White solid; mp 58−59 °C, yield = 201 mg (92%); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, J = 8.0 Hz, 4H), 7.35−7.26 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.2, 129.2, 127.6, 127.3.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.0c00472.

Copies of ^{1}H, ^{13}C, and ^{19}F NMR spectra for all compounds and ORTEP diagram of compound **3c** (PDF)

The full covariance matrix used to estimate all esds (CIF)

(PDF)
(CIF)

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Notes

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