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Domino C-S/C-N Bond Formation using Well-Defined Copper-Phosphine Complex Catalyst: Divergent Approach to 3-Sulfenylated Indoles

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Abstract: A protocol was developed for the synthesis of 3-thioindoles in good-to-excellent yields involving sulfenylation between 2-nitrocinnamaldehydes and various thiols using a well-defined copper(I)-phosphine complex catalyst. This unconventional divergent approach involves *in situ* generation of indoles via domino C-S/C-N bond formation initiated by sulfa-Michael addition followed by intramolecular *N*-heteroannulation. This protocol shows good chemoselectivity and broad substrate scope. To briefly demonstrate the value of this approach, 2-benzoyl-3-sulfenylated indoles were prepared from commercially available 2-nitrochalcones and thiols.

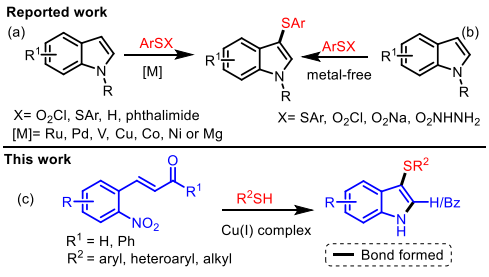
Keywords: Annulation; Copper catalyst; Domino reactions; Nitrogen heterocycles; Sulfa-Michael addition

Introduction

Indoles are widely considered a significant key scaffold in biologically active molecules and pharmaceuticals.[1] Consequently, considerable attention has been paid to the construction of highly functionalized indoles.[2] Among these, 3-sulfenylated indoles exhibit a variety of biological properties, including anti-HIV,[3] anticancer,[4] antiallergy,[5] antiobesity,[6] anti-inflammatory,[7] and cardiovascular activities.[8] They have also been used as building blocks in the syntheses of natural products[9] and potent drugs.[10]

Owing to the fascinating and important biological activities of 3-sulfenylated indoles, a number of methods for their preparation have been reported.[11–14] Typical approaches are based on transition-metal- or metal-catalyzed sulfenylation of indoles in the presence of Ru, Pd, V, Cu, Co, Ni, or Mg using a variety of sulfenylating reagents, such as sulfonyl chlorides,[11a] disulfides,[12a] thiols,[13a] and thiophthalimides[14a] (Scheme 1a). Transition-metal-free synthetic approaches have also been developed, including iodine-[12b,13e,14e] or organophosphorus-catalyzed,[11b] base-promoted,[12d,13f] and electro-catalytic sulfenylation of indoles with sulfenylating reagents.[13g] (Scheme 1b). Although many methods for the construction of 3-sulfenylindoles have been developed, more facile and efficient protocols remain highly desirable. Synthetic approaches for 3-alkylsulfenylindoles in particular are only reported sporadically.[11b,13b,14a] While a number of transition metal complexes, such as Wilkinson's catalyst [$ClRh(PPh_3)_3$], have been utilized for catalytic sulfenylation with arenethiols,[15] it has been reported that most of these complexes are ineffective for sulfenylation with alkanethiols.[16]

In addition, although numerous advances have been made for C-S bond formation using well-defined complexes, limited success has been achieved with Au, Ag, and Cu metals.[17] Recently, we reported on the construction of heterocycles through a base- or CuI/base-promoted cascade reaction of 2-nitrocinnamaldehydes with *β*-ketoesters or benzyl cyanides.[18a-c] While intramolecular *N*-heteroannulation has been employed as a powerful arsenal to construct indoles,[19] one-pot tandem sulfenylation/indolization which exploits readily available 2-nitrocinnamaldehydes has not yet been achieved.[20] As part of our pursuit of effective methodologies to access these privileged scaffolds, herein, we describe the direct construction of aryl-, heteroaryl-, and alkylthioindoles through Cu(I)-phosphine complex-catalyzed heteroannulation of 2-nitrocinnamaldehydes with the corresponding thiols via domino C-N/C-S bond formation (Scheme 1c).



Scheme 1. Synthetic strategies for 3-sulfenylated indoles.

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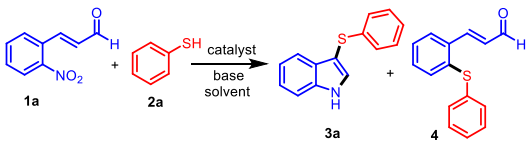
Results and Discussion

To obtain the optimal conditions, reactions between 2-nitrocinnamaldehyde (**1a**) and thiophenol (**2a**) were carried out under N_2 using various bases, catalysts, and solvents (Table 1). Initial attempts using inorganic base Cs_2CO_3 (1 equiv.) in polar dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) at 110 °C for 6 h provided thioether product **4** in 88% and 91% yields, respectively (entries 1 and 2, Table 1). In nonpolar toluene and 1,4-dioxane, **3a** was produced via deformylation in 5% and 7% yields, respectively (entries 3 and 4). Encouraged by these results, other bases were screened. When we used stronger inorganic base *t*-BuOK (1 equiv.), the yield of **3a** increased to 10% (entry 5). However, with organic bases 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 1,4-diazabicyclo[2.2.2]octane (DABCO), no products were isolated (entries 6 and 7). To increase the yield of **3a**, additional reactions using several catalysts were attempted. The reactions featuring 20 mol % I_2 or $FeCl_2$ together with *t*-BuOK did not result in any desired product (entries 8 and 9). Further attempts with 20 mol % copper(II) triflate ($Cu(OTf)_2$) and CuCl afforded **3a** in 43% and 46% yields, respectively (entries 10 and 11). The best yield (87%) was achieved when 20 mol % $CuCl(PPh_3)_3$ (**C1**) was used with *t*-BuOK (1 equiv.) in refluxing 1,4-dioxane for 9 h (entry 12). Carrying out the reaction in open air resulted to a significant decrease in yield of **3a** (entry 13). Moreover, neither decreasing the *t*-BuOK loading to 0.5 equiv. (entry 14) nor increasing it to 2 equiv.

Table 1. Optimization of the reaction conditions.[a]



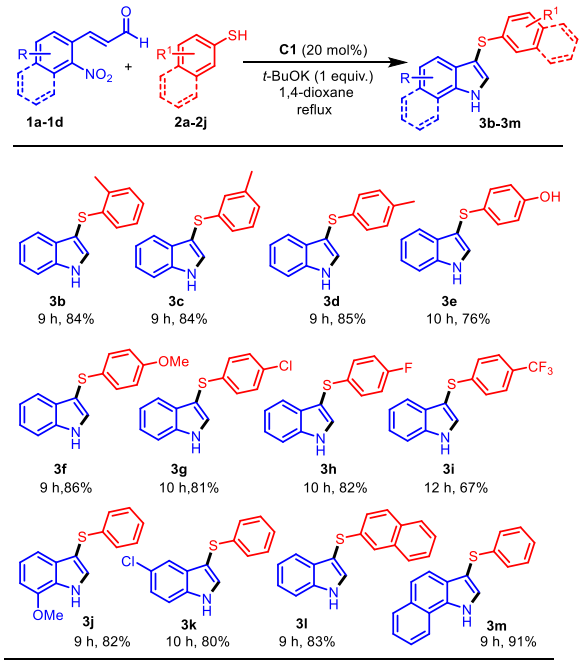
entry	catalyst	base (equiv.)	solvent	temp [°C]	time [h]	yield [%][c] 3a	4
1		Cs_2CO_3 (1)	DMF	110	6	0	88
2		Cs_2CO_3 (1)	DMSO	110	6	0	91
3		Cs_2CO_3 (1)	toluene	110	12	5	0
4		Cs_2CO_3 (1)	1,4-dioxane	100	12	7	0
5		*t*-BuOK (1)	1,4-dioxane	100	12	10	0
6		DBU (1)	1,4-dioxane	100	12	0	0
7		DABCO (1)	1,4-dioxane	100	12	0	0
8	I_2 (20 mol %)	*t*-BuOK (1)	1,4-dioxane	100	12	0	0
9	$FeCl_2$ (20 mol %)	*t*-BuOK (1)	1,4-dioxane	100	12	0	0
10	$Cu(OTf)_2$ (20 mol %)	*t*-BuOK (1)	1,4-dioxane	100	12	43	0
11	CuCl (20 mol %)	*t*-BuOK (1)	1,4-dioxane	100	12	46	0
12	$CuCl(PPh_3)_3$ (20 mol %)	*t*-BuOK (1)	1,4-dioxane	100	9	87	0
13[b]	$CuCl(PPh_3)_3$ (20 mol %)	*t*-BuOK (1)	1,4-dioxane	100	9	53	0
14	$CuCl(PPh_3)_3$ (20 mol %)	*t*-BuOK (0.5)	1,4-dioxane	100	9	61	0
15	$CuCl(PPh_3)_3$ (20 mol %)	*t*-BuOK (2)	1,4-dioxane	100	9	86	0
16	$CuCl(PPh_3)_3$ (10 mol %)	*t*-BuOK (1)	1,4-dioxane	100	9	83	0
17	$Pd(PPh_3)_4$ (20 mol %)	*t*-BuOK (1)	1,4-dioxane	100	9	0	0

[a] Reaction conditions: 1a (0.5 mmol), 2a (0.75 mmol), and solvent (5 mL) under N_2. [b] In open air.
[c] Isolated yields.

(entry 15) improved the yield of **3a**. In addition, decreasing the **C1** catalyst loading to 10 mol % led to **3a** being provided in a somewhat lower yield (83%, entry 16). However, with 20 mol % $Pd(PPh_3)_4$ as the catalyst, **3a** was not produced at all (entry 17). The structure of **3a** was determined through the analysis of its spectral data. The ^{1}H NMR spectrum showed the characteristic signal of the NH proton at δ 8.39 ppm as a broad singlet and the vinyl proton on the indole ring at δ 7.47 ppm as a doublet with a coupling constant of 1.8 Hz.

With the optimized conditions in hand, reactions of 2-nitrocinnamaldehydes with various thiophenols were examined next to explore the generality of this protocol (Table 2). The reactions of **1a** with arylthiols **2b**–**2f** bearing electron-donating groups, namely 2-Me, 3-Me, 4-Me, 4-OH, and 4-OMe, on their benzene ring for 9–10 h provided products **3b**–**3f** in 76–86% yields, while substrates containing electron-withdrawing substituents afforded desired products **3g**–**3i** in slightly lower yields (67–82%). The scope of this reaction was explored further using 2-nitrocinnamaldehydes **1b** and **1c** bearing an electron-donating and -withdrawing group, namely 6-OMe and 4-Cl, on the benzene ring, which afforded the desired products, **3j** and **3k**, in good yields. In addition, the reaction of **1a** with naphthalene-2-thiol (**2j**) afforded 3-(naphthalen-2-ylthio)indole (**3l**) in 83% yield. In addition, we also explored the reaction of (*E*)-3-(1-nitronaphthalen-2-yl)acrylaldehyde (**1d**) with **2a**, which provided **3m** in 91% yield. These results suggest that this reaction protocol tolerates a wide range of functionalities on both 2-nitrocinnamaldehydes and thiols.

Table 2. Results of reactions of **1a**–**1d** with **2a**–**2j** for 3-arylthioindoles **3b**–**3m**.[a,b]



[a] Reaction conditions: **1a-1d** (0.5 mmol), **2a-2j** (0.75 mmol), and solvent (5 mL) under N_2.
[b] Isolated yields.

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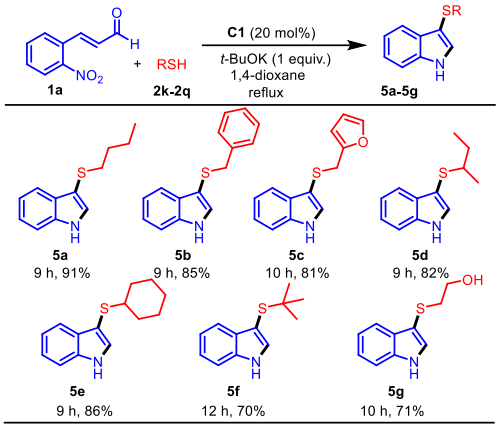
Table 3. Results of reactions of **1a** with **2k–2q** for 3-alkylthioindoles **5a–5g**.[a,b]

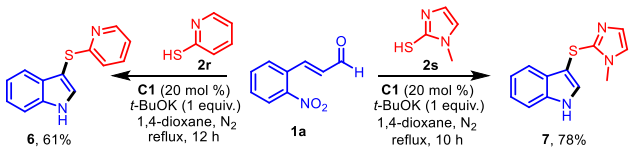


[a] Reaction conditions: **1a** (0.5 mmol), **2k-2q** (0.75 mmol), and solvent (5 mL) under N_2.
[b] Isolated yields.

The scope of this protocol was further demonstrated by using alkyl thiols with various functionalities and degrees of bulkiness (Table 3). The reactions of **1a** with primary alkyl thiols, butane-1-thiol (**2k**), phenylmethanethiol (**2l**), and 2-furfurylthiol (**2m**), successfully furnished desired products **5a**–**5c** in 91%, 85%, and 81% yields, respectively. Moreover, secondary alkyl thiols 2-butanethiol (**2n**) and cyclohexanethiol (**2o**) were also able to afford their corresponding products, **5d** and **5e**, in 82% and 86% yields, respectively. Notably, 2-methyl-2-propanethiol (**2p**) provided the desired product, **5f**, in 70% yield. Thiol **2q** bearing a hydroxyl group was also an efficient substrate in this transformation, giving **5g** chemoselectively in 71% yield.

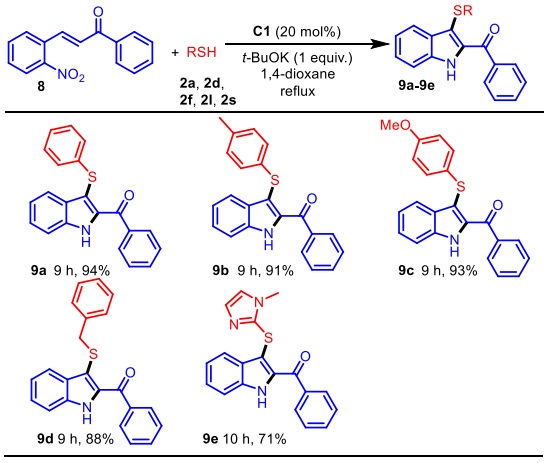
Having seen the generality for the construction of 3-aryl- and 3-alkylthioindoles, we employed heteroaryl thiols as substrates (Scheme 2). When 2-pyridinethiol (**2r**) and 1-methyl-2-imidazolethiol (**2s**) were used, the desired products, **6** and **7**, were isolated in 61% and 78% yields, respectively.

To demonstrate the utility of this protocol, we applied 2-nitrochalcone instead of 2-nitrocinnamaldehydes as the starting material to provide 2-benzoyl-3-sulfenylated indoles (Table 4). The reaction of 2-nitrochalcone (**8**) with **2a** provided product **9a** in 94% yield. In the cases of arylthiols **2d** and **2e**, desired products **9b** and **9c** were obtained in 91% and 93% yields, respectively. Moreover, with phenylmethanethiol (**2l**) and 1-methyl-2-imidazolethiol (**2s**), compounds **9d** and **9e** were produced in 88% and 71% yields. The applicability of this protocol was further demonstrated with the gram-scale synthesis of **9a** (Scheme 3).

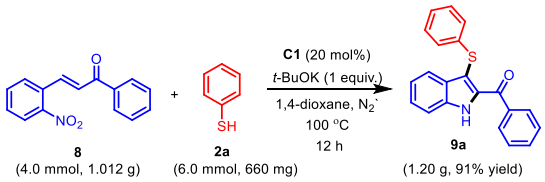


Scheme 2. Reactions of **1a** with **2r** and **2s** for heteroarylthioindoles **6** and **7**.

Table 4. Results of reactions of **8** with **2a**, **2d**, **2f**, **2l**, and **2s** for 2-benzoyl-3-thioindoles **9a–9e**.[a,b]

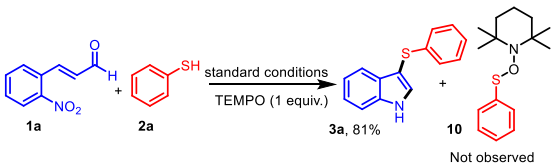


[a] Reaction conditions: **8** (1 mmol), **2a**, **2d**, **2f**, **2l**, or **2s** (1.5 mmol), and solvent (10 mL) under N_2.
[b] Isolated yields.



Scheme 3. Gram-scale synthesis of **9a**.

To elucidate the reaction mechanism, we conducted the control experiment shown in Scheme 4. To eliminate the possibility of a radical sulfenylation pathway, **1a** was reacted with **2a** under the standard reaction conditions in the presence of (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) in one equivalent. Product **3a** was formed in 81% yield, while TEMPO adduct **10** was not observed. Based on this result, this transformation does not directly involve a radical pathway.[15c]



Scheme 4. Control experiment.

Based on literature precedence and our previous studies,[15–25] we propose a plausible reaction pathway, which is shown in Scheme 5. The reaction is initiated by the $CuCl(PPh_3)_3$ complex (**C1**) and *t*-BuOK through salt metathesis to afford Cu-O-^{t}Bu complex **C2**, which is readily attacked by the thiol, affording copper-thiolate species **C3**.[21] Then, **1a** is activated by the coordination of resulting active species **C3** to form transition intermediate **I**, which

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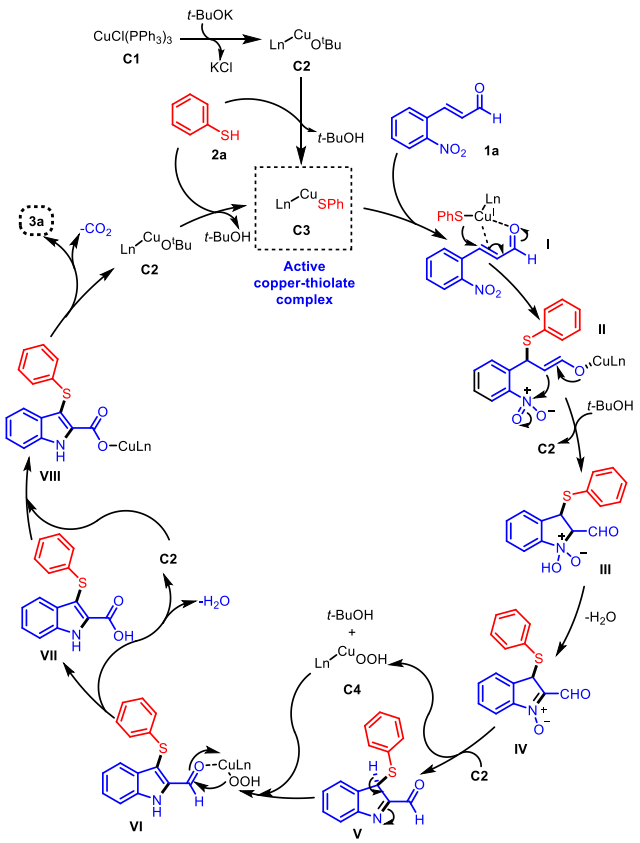
directs the sulfa- Michael addition of a thiolate anion via migratory insertion, resulting in **II**.[22] Next, intramolecular nucleophilic addition occurs to furnish intermediate **III** and copper specie **C2** thru protonation by *t*-BuOH. Intermediate **III** undergoes dehydroxylation leading to nitroso intermediate **IV**. Previously, the intramolecular cyclization of 2-alkenyl nitroarenes via nitroso intermediate was reported by Grignard reagents-, $TiCl_3$- and base-promoted reactions without external reducing agent.[23] Oxidation of **C2** to **C4** enables the conversion of nitroso intermediate **IV** to **V**. The highly reactive hydroperoxide copper intermediate **C4** subsequently coordinates with the aldehyde carbonyl of intermediate **VI** obtained from the isomerization of intermediate **V**. Nucleophilic attack by the hydroperoxide and subsequent dehydration afford carboxylic acid intermediate **VII**,[24] which forms intermediate **VIII** upon direct insertion of **C2** into the aryl carboxylate bond.[25] Finally, decarboxylation of **VIII** gives **3a** and regenerates **C2**, which reacts with **2a**, regenerating **C3** to complete the catalytic cycle. In the case of 2-nitrcochalcone, no further oxidation and decarboxylation for the formation of **9a**-**9e** occur while **C4** and *t*-BuOH possibly recombines to regenerate **C2** by the removal of H_2O_2 to complete the catalytic cycle.



Scheme 5. Plausible reaction pathway.

Conclusion

In summary, we have described a highly divergent protocol to access diverse 3-thioindoles from 2-nitrocinnamaldehydes and various thiols via sulfa-Michael addition followed by intramolecular reductive *N*-heteroannulation using a well-defined complex, chloro-tris(triphenylphosphine)-copper(I) (**C1**), as the catalyst. The reaction shows good tolerance towards various 2-nitrocinnamaldehydes as well as several substituted aryl, alkyl, heteroaryl, bulky secondary, and tertiary thiol systems with good to excellent yields. The present protocol is likely to attract the interest of synthetic chemists because of its efficiency and broad utility. The applicability of this protocol was briefly demonstrated in the synthesis of 3-thiobenzoylindoles using commercially available 2-nitrochalcones. 2-vinyl nitroarenes

Experimental Section

General procedure for the synthesis of 3-thioindoles 3, 5, 6 and 7: A general procedure for the copper-phosphine complex-catalyzed synthesis of 3-thioindoles is as follows: An oven-dried 25 mL two necked round bottom flask was charged with 2-nitrocinnamaldehyde (0.5 mmol), thiol (0.75 mmol, 1.5 equiv.) and 20 mol % of $CuCl(PPh_3)_3$ in 5 mL anhydrous 1,4-dioxane and *t*-BuOK (0.5 mmol, 1 equiv.) was finally added. The reaction was then kept under nitrogen atmosphere with continuous stirring. Then, the reaction mixture was refluxed for about 9-12 h until the completion of the reaction as indicated by TLC. The resulting mixture was then dried in rotary evaporator under reduced pressure to obtain the residue. The residue was purified by column chromatography using silica gel as the stationary phase and Hex/EtOAc (20:1) as the eluent to isolate the pure product.

3-(Phenylthio)-1*H*-indole (3a): Prepared according to the general procedure and obtained as white solid (98 mg, 87% yield). Melting point: 153-155 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.39 (1H, br s), 7.60 (1H, d, J = 8.4 Hz), 7.47 (1H, d, J = 1.8 Hz), 7.42 (1H, d, J = 8.4 Hz), 7.26-7.24 (1H, m), 7.16-7.12 (3H, m), 7.09-7.08 (2H, m), 7.04-7.02 (1H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.2, 136.4, 130.6, 129.1, 128.6, 125.8, 124.7, 123.0, 120.9, 119.6, 111.5, 102.9. IR (neat): 3404.8, 1739.7, 1577.8, 1475.9, 1454.7, 1406.1, 1236.3, 1087.3, 739.3 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{14}H_{11}NS$: 225.0612. Found: 225.0611.

***E*)-3-(2-(Phenylthio)phenyl)acrylaldehyde (4):** Obtained during the screening of reaction conditions – Please see Table 1. Melting point: 86-88 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.61 (1H, d, J = 7.8 Hz), 8.05 (1H, d, J = 15.6 Hz), 7.64-7.62 (1H, m), 7.36-7.35 (1H, m), 7.31-7.30 (2H, m), 7.24 (2H, t, J = 7.8 Hz), 7.20-7.18 (3H, m), 6.60 (1H, dd, J = 15.6, 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.8, 149.7, 136.4, 135.5, 135.4, 133.9, 131.4, 130.2, 130.2, 129.39, 128.3, 127.5, 127.1; IR (neat): 3056.3, 2813.5, 1678.1, 1620.2, 1579.7, 1474.9, 1437.5, 1110.8, 735.1, 688.0 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{15}H_{12}OS$: 240.0609. Found: 240.0609.

3-(*o*-Tolylthio)-1*H*-indole (3b): Prepared according to the general procedure and obtained as dark brown solid (101 mg, 84% yield). Melting point: 114-116 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (1H, br s), 7.62 (1H, d, J = 7.8 Hz), 7.42-7.41 (2H, m), 7.29 (1H, t, J = 7.8 Hz), 7.20-7.16 (2H, m), 7.01 (1H, t, J = 7.8 Hz), 6.92 (1H, t, J = 7.8 Hz), 6.76 (1H, d, J = 7.8 Hz), 2.53 (3H, s); ^{13}C NMR (150 MHz,

$CDCl_3$) δ 138.2, 136.4, 134.3, 130.7, 129.8, 129.1, 126.2, 125.2, 124.4, 122.9, 120.8, 119.5, 111.5, 102.1, 19.8; IR (neat): 3418.8, 1735.1, 1585.0, 1451.8, 1400.7, 1233.1, 1090.2, 824.1, 734.7 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{15}H_{13}NS$: 239.0769. Found: 239.0768.

3-(*m*-Tolylthio)-1*H*-indole (3c): Prepared according to the general procedure and obtained as dark brown solid (101 mg, 84% yield). Melting point: 115-117 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.35 (1H, br s), 7.62 (1H, d, *J* = 8.4 Hz), 7.44 (1H, s), 7.41 (1H, d, *J* = 7.8 Hz), 7.27-7.23 (1H, m), 7.16 (1H, t, *J* = 7.8 Hz), 7.03 (1H, t, *J* = 7.8 Hz), 6.98 (1H, s), 6.87 (2H, t, *J* = 7.8 Hz) 2.22 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.9, 138.4, 136.4, 130.6, 129.1, 128.5, 126.4, 125.7, 122.9, 122.9, 120.8, 119.6, 111.5, 102.9, 21.3; IR (neat): 3411.0, 3107.6, 1588.8, 1453.5, 1404.9, 1336.8, 1236.9, 1093.2, 853.8, 769.7, 745.3 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{15}H_{13}NS$: 239.0769. Found: 239.0770.

3-(*p*-Tolylthio)-1*H*-indole (3d): Prepared according to the general procedure and obtained as black solid (102 mg, 85% yield). Melting point: 91-93 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.34 (1H, br s), 7.60 (1H, d, *J* = 7.8 Hz), 7.44 (1H, s), 7.41 (1H, d, *J* = 7.8 Hz), 7.25-7.23 (1H, m), 7.14 (1H, t, *J* = 7.8 Hz), 7.02 (2H, d, *J* = 8.4 Hz), 6.96 (2H, d, *J* = 7.8 Hz), 2.23 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.4, 135.4, 134.6, 130.3, 129.4, 129.0, 126.2, 122.9, 120.8, 119.6, 111.4, 103.5, 20.8; IR (neat): 3404.4, 2916.4, 1710.7, 1595.5, 1489.7, 1453.4, 1338.2, 1202.8, 1089.4, 1010.1, 802.9, 740.3 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{15}H_{13}NS$: 239.0769. Found: 239.0771.

4-((1*H*-Indol-3-yl)thio)phenol (3e): Prepared according to the general procedure and obtained as dark brown oil (92 mg, 76% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 8.46 (1H, br s), 7.60 (1H, d, *J* = 7.8 Hz), 7.41 (1H, s), 7.38 (1H, d, *J* = 8.4 Hz), 7.21 (1H, t, *J* = 8.4 Hz), 7.12 (1H, t, *J* = 7.8 Hz), 7.05 (2H, d, *J* = 9 Hz), 6.74 (1H, d, *J* = 9 Hz), 6.65 (2H, d, *J* = 9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.1, 136.4, 133.0, 129.9, 128.9, 128.8, 122.8, 120.6, 119.5, 115.9, 111.4, 104.6; IR (neat): 3212.8, 1704.6, 1581.3, 1490.8, 1433.0, 1223.7, 983.9, 822.6, 742. 8 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{14}H_{11}NOS$: 241.0561. Found: 241.0559.

3-((4-Methoxyphenyl)thio)-1*H*-indole (3f): Prepared according to the general procedure and obtained as dark green solid (110 mg, 86% yield). Melting point: 75-77 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.36 (1H, br s), 7.65 (1H, d, *J* = 7.8 Hz), 7.39 (2H, m), 7.26 (1H, t, *J* = 7.8 Hz), 7.18 (1H, t, *J* = 7.8 Hz), 7.09 (1H, t, *J* = 8.4 Hz), 6.73 (1H, d, *J* = 7.8 Hz), 6.70 (1H, s), 6.63 (1H, d, *J* = 8.4 Hz), 3.68 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.7, 140.7, 136.3, 130.7, 129.5, 128.9, 122.9, 120.8, 119.4, 118.2, 111.5, 111.4, 110.26, 102.2, 55.0; IR (neat): 3412.0, 1795.7, 1588.2, 1473.9, 1280.7, 1229.2, 1144.8, 1040.5, 939.2, 837.0, 750.5 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{15}H_{13}NOS$: 255.0718. Found: 255.0716.

3-((4-Chlorophenyl)thio)-1*H*-indole (3g): Prepared according to the general procedure and obtained as white solid (105 mg, 81% yield). Melting point: 123-125 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.41 (1H, br s), 7.55 (1H, d, *J* = 7.8 Hz), 7.47 (1H, d, *J* = 1.8 Hz), 7.43 (1H, d, *J* = 7.8 Hz), 7.26 (1H, t, *J* = 7.8 Hz), 7.15 (1H, t, *J* = 7.8 Hz), 7.1 (2H, d, *J* = 7.8 Hz), 7.00 (2H, d, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.8, 136.5, 130.6, 130.5, 128.7, 128.7, 127.1, 123.2, 121.0, 119.5, 111.6, 102.5; IR (neat): 3401.5, 2972.7, 1738.7, 1471.7, 1385.7, 1232.0, 1088.4, 1006.8, 809.9, 745.5 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{14}H_{10}ClNS$: 259.0222. Found: 259.0225.

3-((4-Fluorophenyl)thio)-1*H*-indole (3h): Prepared according to the general procedure and obtained as white solid (100 mg, 82% yield). Melting point: 136-138 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.35 (1H, br s), 7.59 (1H, d, *J* = 8.4 Hz), 7.46 (1H, d, *J* = 3.0 Hz), 7.42 (1H, d, *J* = 8.4 Hz), 7.26 (1H, t, *J* = 7.8 Hz), 7.18-7.15 (1H, m), 7.10-7.07 (2H, m), 6.87-6.84 (2H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.8 (d, *J* = 242.7), 136.4, 133.9 (d, *J* = 3.4 Hz), 130.4, 128.8, 127.8 (d, *J* = 7.6 Hz), 123.1, 120.9, 119.5, 115.7 (d, *J* = 21.9 Hz), 111.5, 103.4; IR (neat): 3403.2, 1589.7, 1486.1, 1407.8, 1215.8, 1092.9, 1009.8, 819.0, 745.9 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{14}H_{10}FNS$: 243.0518. Found: 243.0520.

3-((4-(Trifluoromethyl)phenyl)thio)-1*H*-indole (3i): Prepared according to the general procedure and obtained as black solid (98 mg, 67% yield). Melting point: 90-92 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.47 (1H, br s), 7.54 (1H, d, *J* = 8.4 Hz), 7.50 (1H, s), 7.45 (1H, d, *J* = 8.4 Hz), 7.36 (2H, d, *J* = 8.4 Hz), 7.28 (1H, t, *J* = 7.8 Hz), 7.17 (1H, t, *J* = 7.8 Hz), 7.11 (2H, d, *J* = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.6, 136.5, 130.9, 128.7, 126.7 (q, *J* = 32.2 Hz), 125.4 (q, *J* = 3.7 Hz), 125.2, 124.4 (q, *J* = 273.7 Hz), 123.3, 121.2, 119.4, 111.7, 101.3; IR (neat): 3413.3, 2920.0, 1604.4, 1452.8, 1402.8, 1322.8, 1116.4, 1010.3, 824.0, 745.1 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{15}H_{10}F_3NS$: 293.0486. Found: 293.0487.

7-Methoxy-3-(phenylthio)-1*H*-indole (3j): Prepared according to the general procedure and obtained as light purple solid (105 mg, 82% yield). Melting point: 103-105 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.62 (1H, br s), 7.42 (1H, d, *J* = 3 Hz), 7.22 (1H, d, *J* = 7.8 Hz), 7.16-7.14 (2H, m), 7.11-7.09 (2H, m), 7.08-7.03 (2H, m), 6.70 (1H, d, *J* = 7.8 Hz), 3.97 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 146.2, 139.3, 130.5, 130.1, 128.6, 127.0, 125.7, 124.6, 121.2, 112.1, 103.0, 102.7, 55.3; IR (neat): 3404.0, 2963.0, 1742.9, 1579.5, 1413.8, 1250.9, 1084.4, 1009.2, 776.1, 730.5 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{15}H_{13}NOS$: 255.0718. Found: 255.0717.

5-Chloro-3-(phenylthio)-1*H*-indole (3k): Prepared according to the general procedure and obtained as dark green solid (104 mg, 80% yield). Melting point: 90-92 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.49 (1H, br s), 7.56 (1H, s), 7.48 (1H, s), 7.33 (1H, d, *J* = 8.4 Hz), 7.19 (3H, m), 7.09-7.04 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.6, 134.7 131.9, 130.3, 128.7, 126.8, 125.87, 124.9, 123.5, 119.1, 112.6, 102.8; IR (neat): 3402.8, 2926.7, 1734.9, 1580.0, 1440.9, 1097.0, 1022.7, 801.0, 736.0 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{14}H_{10}ClNS$: 259.0222. Found: 259.0224.

3-(Naphthalen-2-ylthio)-1*H*-indole (3l): Prepared according to the general procedure and obtained as black solid (114 mg, 83% yield). Melting point: 155-157 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.41 (1H, br s), 7.70 (1H, d, *J* = 7.8 Hz), 7.63-7.60 (2H, m), 7.55-7.53 (2H, m), 7.481 (1H, d, *J* = 1.2 Hz), 7.44 (1H, d, *J* = 7.8 Hz), 7.37-7.31 (2H, m), 7.27-7.25 (2H, m), 7.13 (1H, t, *J* = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.6, 136.5, 133.7, 131.3, 130.6, 129.1, 128.2, 127.6, 126.9, 126.3, 125.0, 124.7, 123.5, 123.0, 120.9, 119.7, 111.5, 102.9; IR (neat): 3410.9, 3052.9, 1801.8, 1586.4, 1499.7, 1337.9, 1088.5, 942.1, 813.0, 740.3 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{18}H_{13}NS$: 275.0769. Found: 275.0765.

3-(Phenylthio)-1*H*-benzo[*g*]indole (3m): Prepared according to the general procedure and obtained as black solid (125 mg, 91% yield). Melting point: 125-127 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 9.11 (1H, br s), 8.00 (1H, d, *J* = 7.8 Hz), 7.93 (1H, d, *J* = 8.4 Hz), 7.66 (1H, d, *J* = 9 Hz), 7.56-7.52 (3H, m), 7.46 (1H, t, *J* = 7.8 Hz), 7.15-7.09 (4H, m), 7.03 (1H, t, *J* = 7.2 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.3, 131.3, 130.8, 129.0, 128.7, 128.5, 125.8, 125.7, 125.5, 124.7, 124.5, 121.8, 121.7, 119.1, 119.1, 104.6; IR: 3305.5, 2920.2, 1711.3, 1573.1, 1469.6, 1181.5, 1120.4, 695.1 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{18}H_{13}NS$: 275.0769. Found: 275.0770.

3-(Butylthio)-1*H*-indole (5a): Prepared according to the general procedure and obtained as dark red oil (93 mg, 91% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 8.21 (1H, br s),

7.77 (1H, d, *J* = 7.8 Hz), 7.34 (1H, d, *J* = 7.8 Hz), 7.26 (1H, d, *J* = 2.4 Hz), 7.23-7.18 (2H, m), 2.69 (2H, t, *J* = 7.2 Hz), 1.54-1.48 (2H, m), 1.42-1.35 (2H, m). 0.87-0.84 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.2, 129.3, 129.1, 122.5, 120.2, 119.3, 111.4, 106.0, 36.0, 31.9, 21.6, 13.6; IR (neat): 3399.6, 2955.5, 2919.8, 2868.9, 1615.8, 1452.3, 1336.4, 1224.9, 1008.0, 740.0 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{12}H_{15}NS$: 205.0925. Found: 205.0923.

3-(Benzylthio)-1*H*-indole (5b): Prepared according to the general procedure and obtained as dark reddish oil (102 mg, 85% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (1H, br s), 7.69 (1H, d, *J* = 7.8 Hz), 7.35 (1H, d, *J* = 7.8 Hz), 7.22-7.15 (5H, m), 7.07 (2H, d, *J* = 6.6 Hz), 6.99 (1H, d, *J* = 2.4 Hz), 3.85 (2H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.0, 136.1, 129.8, 129.2, 128.9, 128.1, 126.7, 122.6, 120.4, 119.2, 111.4, 105.2, 40.9; IR (neat): 3403.8, 3027.4, 1735.4, 1616.4, 1452.0, 1232.8, 1008.2, 741.7, 696.7 cm^{-1}.HRMS *m/z* (M^+) calculated for $C_{15}H_{13}NS$: 239.0769. Found: 239.0770.

3-((Furan-2-ylmethyl)thio)-1*H*-indole (5c): Prepared according to the general procedure and obtained as black solid (93 mg, 81% yield). Melting point: 85-87 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (1H, br s), 7.59 (1H, d, *J* = 10.2 Hz), 7.26-7.24 (2H, m), 7.15-7.08 (2H, m), 7.02 (1H, s), 6.11 (1H, s), 5.76 (1H, s), 3.77 (2H, d, *J* = 3.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 151.8, 141.8, 136.0, 130.19, 129.1, 122.6, 120.4, 119.1, 111.4, 110.3, 107.6, 104.8, 33.4; IR (neat): 3405.8, 3127.0, 1501.0, 1501.0, 1405.2, 1234.3, 1146.1, 1007.4, 933.9, 739.0 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{13}H_{11}NOS$: 229.0561. Found: 229.0564.

3-(*sec*-Butylthio)-1*H*-indole (5d): Prepared according to the general procedure and obtained as dark brown liquid (84 mg, 82% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (1H, br s), 7.84 (1H, d, *J* = 7.2 Hz), 7.37 (1H ,d, *J* = 7.8 Hz), 7.29-7.25 (3H, m), 2.93 (1H, m), 1.70-1.63 (1H, m), 1.54-1.47 (1H, m), 1.25 (3H, d, *J* = 6.6 Hz), 1.06 (3H, t, *J* = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.0, 130.2, 130.1, 122.4, 120.3, 119.5, 111.3, 104.5, 45.7, 29.5, 20.7, 11.6; IR (neat): 3401.8, 2961.6, 2872.0, 1615.7, 1452.1, 1336.8, 1232.5, 1090.8, 1007.9, 740.8 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{12}H_{15}NS$: 205.0925. Found: 205.0923.

3-(Cyclohexylthio)-1*H*-indole (5e): Prepared according to the general procedure and obtained as brown solid (100 mg, 86% yield). Melting point: 82-84 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (1H, br s), 7.81 (1H, d, *J* = 7.8 Hz), 7.35 (1H, d, *J* = 7.8 Hz), 7.27 (1H, d, *J* = 2.4 Hz), 7.25-7.20 (2H, m), 2.83-2.78 (1H, m), 1.97-1.94 (2H, m), 1.75-1.71 (2H, m), 1.57-1.54 (1H, m), 1.36-1.30 (2H, m), 1.25-1.13 (3H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.1, 130.2, 122.4, 120.2, 119.6, 119.5, 111.3, 104.4, 47.4, 33.6, 26.1, 25.6; IR (neat): 3391.9, 2928.2, 2849.6, 1450.7, 1337.0, 1094.8, 996.4, 739.5 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{14}H_{17}NS$: 231.1082. Found: 231.1078.

3-(*tert*-Butylthio)-1*H*-indole (5f): Prepared according to the general procedure and obtained as reddish brown solid (72 mg, 70% yield). Melting point: 66-68 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (1H, br s), 7.72 (1H, d, *J* = 7.2 Hz), 7.26 (1H, d, *J* = 7.2 Hz), 7.19 (1H, d, *J* = 2.4 Hz), 7.14-7.09 (2H, m), 1.20 (9H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.0, 131.5, 130.8, 122.3, 120.4, 120.0, 111.2, 104.4, 45.9, 30.9; IR (neat): 3351.8, 2964.0, 1500.3, 1453.0, 1166.8, 1092.3, 739.8 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{12}H_{15}NS$: 205.0925. Found: 205.0924.

2-((1*H*-Indol-3-yl)thio)ethan-1-ol (5g): Prepared according to the general procedure and obtained as brown liquid (69 mg, 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (1H, br s), 7.75 (1H, d, *J* = 7.8 Hz), 7.37 (1H, d, *J* = 7.8 Hz), 7.31 (1H, s), 7.25-7.19 (2H, m), 3.61 (2H, t, *J* = 6.0 Hz), 2.85 (2H, t, *J* = 6.0 Hz), 2.24 (1H, br s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.2, 129.9, 129.1, 122.8, 120.6, 119.0, 111.5, 103.8, 60.2, 39.1; IR (neat): 3392.9, 3275.1, 2920.7, 2875.0, 1710.5, 1406.0, 1234.9, 1004.6, 741.2 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{10}H_{11}NOS$: 193.0561. Found: 193.0563.

3-(Pyridin-2-ylthio)-1*H*-indole (6): Prepared according to the general procedure and obtained as yellow solid (69 mg, 61% yield). Melting point: 136–137°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.66 (1H, br s), 7.35 (1H, d, *J* = 5.4 Hz), 7.52 (1H, d, *J* = 7.8 Hz), 7.49 (1H, d, *J* = 2.4 Hz), 7.45 (1H, d, *J* = 8.4 Hz), 7.37 (1H, t, *J* = 7.8 Hz), 7.21 (1H, t, *J* = 7.8 Hz), 7.12 (1H, t, *J* = 7.2 Hz), 6.97 (1H, t, *J* = 6.6 Hz), 6.78 (1H, d, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.4, 147.4, 137.9, 136.7, 131.8, 128.5, 123.0, 121.0, 120.6, 119.5, 119.0, 112.1, 99.1; IR (neat): 3092.2, 2503.3, 1721.9, 1603.8, 1448.5, 1234.9, 1128.2, 744.7 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{13}H_{10}N2S$: 226.0565. Found: 226.0563.

3-((1-Methyl-1*H*-imidazol-2-yl)thio)-1*H*-indole (7): Prepared according to the general procedure and obtained as brown solid (90 mg, 78% yield). Melting point: 149-151 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.73 (1H, br s), 7.33 (1H, d, *J* = 7.2 Hz), 7.17 (2H, d, *J* = 10.2 Hz), 7.03-6.99 (2H, m), 6.79 (2H, d, *J* = 16.8 Hz), 3.64 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 134.4, 122.4, 122.3, 121.7, 120.1, 119.7, 118.4, 117.2, 114.0, 112.1, 109.8, 35.5; IR (neat): 3288.3, 1566.5, 1455.4, 1380.7, 1240.7, 1152.5, 925.4, 728.4 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{12}H_{11}N_3S$: 229.0674. Found: 229.0673.

General procedure for the synthesis of 3-thiobenzoylindoles 9: A general procedure for the copper-phosphine complex-catalyzed synthesis of 3-thiobenzoylindoles **9** is as follows: An oven-dried 25 mL two necked round bottom flask was charged with 2-nitrochalcone (1 mmol), thiols (1.5 mmol) and 20 mol % of $CuCl(PPh_3)_3$ in 10 mL anhydrous 1,4-dioxane and *t*-BuOK (1 equiv.) was finally added. The reaction was then kept under nitrogen atmosphere with continuous stirring. Then, the reaction mixture was refluxed for about 9-12 h until the completion of the reaction as indicated by TLC. The resulting mixture was then dried in rotary evaporator under reduced pressure to obtain the residue.The residue was purified by column chromatography using silica gel as the stationary phase and Hex/EtOAc (15:1) as the eluent to isolate the pure product except benzoylindole **9e** which was purified through EtOAc washing of the dried reaction mixture.

Representative gram-scale procedure for the synthesis of 3-thiobenzoylindole 9a: An oven-dried 50 mL two-necked round bottom flask was charged with 2-nitrochalcone **8** (4.0 mmol, 1.012 g.), benzenethiol **2a** (1.5 eq, 6.0 mmol, 660 mg) and $CuCl(PPh_3)_3$ (20 mol %, 708.7 mg) in 20 mL anhydrous 1,4-dioxane and *t*-BuOK (1 equiv.) was finally added. The reaction was then kept under nitrogen atmosphere with continuous stirring. Then, each reaction mixture was refluxed until the completion of the reaction as indicated by TLC for about 12 h. The resulting mixture was then dried in rotary evaporator under reduced pressure to obtain the residue. The residue was purified by column chromatography using silica gel as the stationary phase and Hex/EtOAc (15:1) as the eluent to isolate the pure product.

Phenyl(3-(phenylthio)-1*H*-indol-2-yl)methanone (9a): Prepared using the general procedure and obtained as yellow solid (309 mg, 94% yield). Melting point: 118-120 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.63 (1H, br s), 7.75 (2H, dd, *J* = 8.4, 1.2 Hz), 7.58 (1H, d, *J* = 7.8 Hz), 7.52 (1H, t, *J* = 7.8 Hz), 7.49 (1H, d, *J* = 8.4 Hz), 7.38 (1H, t, *J* = 7.8 Hz), 7.33 (2H, t, *J* = 7.8 Hz), 7.14 (1H, t, *J* = 7.8 Hz), 7.10 (2H, t, *J* = 7.8 Hz), 7.04 (1H, t, *J* = 7.2 Hz), 6.93 (2H, d, *J* = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.9, 138.0, 137.8, 136.4, 136.2, 132.6, 130.2, 129.5, 128.7, 127.9, 126.7, 125.2, 122.0, 121.7, 112.3, 110.5; IR (neat): 3303.2, 1610.4, 1475.6, 1334.9, 1258.3, 951.4,

729.9 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{21}H_{15}NOS$: 329.0874. Found: 329.0875.

Phenyl(3-(*p*-tolylthio)-1*H*-indol-2-yl)methanone (9b): Prepared using the general procedure and obtained as yellow solid (312 mg, 91% yield). Melting point: 155-157 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 9.40 (1H, br s), 7.75 (2H, d, *J* = 7.2 Hz), 7.56 (1H, d, *J* = 7.8 Hz), 7.52 (1H, t, *J* = 7.2 Hz), 7.46 (1H, d, *J* = 8.4 Hz), 7.38-7.33 (3H, m), 7.12 (1H, t, *J* = 7.8 Hz), 6.91 (2H, d, *J* = 7.8 Hz), 6.85 (2H, d, *J* = 8.4 Hz) 2.22 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.8, 138.1, 136.4, 136.0, 135.1, 134.0, 132.5, 130.2, 129.5, 129.5, 127.9, 127.1, 126.6, 122.2, 121.6, 112.2, 111.4, 20.8; IR (neat): 3314.2, 2920.1, 1606.8, 1486.2, 1329.2, 1255.7, 949.8, 728.7 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{22}H_{17}NOS$: 343.1031. Found: 343.1031.

(3-((4-Methoxyphenyl)thio)-1*H*-indol-2-yl)(phenyl) methanone (9c): Prepared using the general procedure and obtained as yellow solid (334 mg, 93% yield). Melting point: 167-169 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 9.42 (1H, br s), 7.77 (2H, d, *J* = 7.8 Hz), 7.57-7.53 (2H, m), 7.44 (1H, d, *J* = 8.4 Hz), 7.40-7.34 (3H, m), 7.11 (1H, t, *J* = 7.8 Hz), 6.92 (2H, d, *J* = 9 Hz), 6.66 (2H, d, *J* = 8.4 Hz), 3.70 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.8, 158.0, 138.1, 136.4, 135.5, 132.5, 130.0, 129.6, 129.5, 128.1, 128.0, 126.6, 122.1, 121.5, 114.4, 112.8, 112.2, 55.2; IR (neat): 3292.4, 2834.8, 1618.8, 1488.6, 1238.7, 1025.0, 951.5, 742.6 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{22}H_{17}NO_2S$: 359.0980. Found: 359.0978.

(3-(Benzylthio)-1*H*-indol-2-yl)(phenyl)methanone (9d): Prepared using the general procedure and obtained as brown oil (343 mg, 88% yield). Melting point: 120-122 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 9.21 (1H, br s), 7.85 (1H, d, *J* = 8.4 Hz), 7.62 (2H, d, *J* = 7.8 Hz), 7.56 (1H, t, *J* = 7.2 Hz), 7.44-7.37 (4H, m), 7.24-7.22 (1H, m), 7.12 (1H, t, *J* = 7.2 Hz), 7.06 (2H, t, *J* = 7.8 Hz), 6.67 (2H, d, *J* = 7.2 Hz), 3.70 (2H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 188.6, 138.0, 137.4, 136.9, 136.1, 132.3, 130.4, 129.8, 128.6, 128.1, 127.8, 126.9, 126.5, 121.6, 121.4, 112.6, 112.2, 41.1; IR (neat): 3286.5, 3059.7, 1624.1, 1491.8, 1330.3, 1259.3, 732.8, 692.0 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{22}H_{17}NOS$: 343.1031. Found: 343.1033.

(3-((1-Methyl-1*H*-imidazol-2-yl)thio)-1*H*-indol-2-yl)(phenyl)methanone (9e): Prepared using the general procedure and obtained as pure yellow solid thru EtOAc washing of dried reaction mixture (236 mg, 71% yield). Melting point: 248-250 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 9.34 (1H, br s), 7.71 (2H, d, *J* = 7.8 Hz), 7.57 (1H, d, *J* = 8.4 Hz), 7.48 (1H, d, *J* = 8.4 Hz), 7.40 (2H, dt, *J* = 12.0, 7.2 Hz), 7.28 (2H, d, *J* = 7.8 Hz), 7.20 (1H, d, *J* = 7.8 Hz), 6.38 (1H, s), 6.34 (1H, s), 3.5 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.0, 137.4, 135.1, 132.1, 132.0, 128.9, 128.8, 127.7, 127.1, 123.9, 121.9, 121.5, 119.2, 118.6, 117.8, 112.6, 35.3; IR (neat): 3290.4, 2916.5, 1724.4, 1618.0, 1469.5, 1336.5, 1258.9, 709.2 cm^{-1}; HRMS *m/z* (M^+) calculated for $C_{19}H_{15}N_3OS$: 333.0936. Found: 333.0938.

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