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Microwave-assisted regioselective sulfenylation of indoles under solvent- and metal-free conditions

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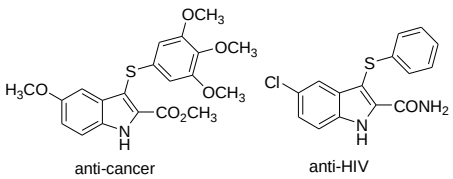
Rajjakfur Rahaman, Namita Devi, Jyoti Rekha Bhagawati and Pranjit Barman*

Herein, we report a solvent- and metal-free methodology for the sulfenylation of Indoles with sulfinic acids in the absence of external catalyst under microwave irradiation. This environmental friendly approach offered the desired products in moderate to excellent yields in only 10 min. Several functional group tolerances were monitored under the optimized conditions.

Introduction

Sulfenylated indole moieties are an important class of organosulfur compounds as they are present in many pharmaceutically and biologically important molecules.[1] Among the sulfenylated indole derivatives, 3-sulfenylindoles have attracted considerable interest due to their greater therapeutic value in the treatment of several diseases (Chart 1), such as, HIV,[2] heart disease,[3] cancer,[4] obesity[5] and allergies.[6] They are also used as potent inhibitor in tubulin polymerization.[7] These fascinating biological profiles are the basic cause of long standing interest in the development of efficient methods for the synthesis of 3-sulfenylindoles. In the last few decades, a number of significant methods have been developed. Variety of sulfenylating reagents have been discovered as reaction partners during the synthetic efforts. For example, sulfenyl halides,[8] disulfides,[9] thiols,[10] quinine mono-O,S-acetals,[11] arylsulfonyl chlorides,[12] N-thioimides,[13] sulfonium salts,[14] and sulfenyl hydrazides[15] are the most effective thiolating reagents for the synthesis of 3-sulfenylindoles.

Although several methodologies have been reported for the reaction of electrophilic sulfur species to indoles, but in most of the cases, they require long reaction times, harsh reaction conditions (such as stoichiometric strong base), toxic reagents, and use of large amount of metals and/or solvents. Thus, development of a new environmentally friendly synthetic method for the sulfenylation of indoles remains an important challenge in organic synthesis.



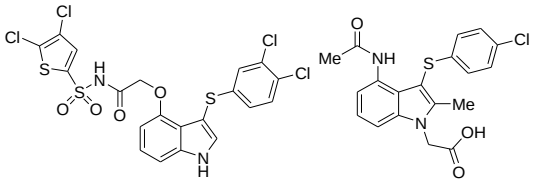


Chart 1 Some biologically active 3-arylthioindoles

In organic transformations, such as, C-S and C-Se bond formations,[16] the use of microwave irradiation can provide excellent yield in a very short reaction time.[17] In addition, with the development of sustainable technologies, solvent-free conditions have emerged as a benign alternative for organic synthesis.[18] In the existing green chemistry scenario, microwave assisted organic synthesis (MAOS) has attained the status of a new and fascinating discipline.[19] Microwave irradiation and solvent-free microwave-assisted techniques have been used for the rapid synthesis of various compounds, which have received special attention in recent years.[20] With the assistance of microwave irradiation, reactions can proceed faster to give higher yields, as compared to conventional methods.

Braga and co-workers[21] reported a highly efficient and solvent-free method for the synthesis of 3-chalcogenyl-indoles. They have used disulfides as sulfenylating agents, DMSO as a stoichiometric oxidant, and molecular iodine (I_2) as catalyst, under microwave irradiation.

Thiols and disulfides were used as sulfenylating agents in many cases, but they have some practical limitations. Thiols are toxic, volatile, and foul smelling, where as disulfides are expensive and moisture sensitive. In addition, disulfide needs to be prepared via oxidative coupling of thiols; an extra operational step which causes low atom economy.[22]

Recently, Liu *et al.* reported the sulfenylation of indoles, employing sulfinic acids as sulfenylating agents.[23] Sulfinic acids are easily accessible, less costly, and are employed to form sulfones, which have versatile applications in medicinal chemistry.[24] Moreover, sulfinic acids can also be reduced to disulfides, which are efficient sulfenylating agents. Taking this idea, herein, we report a

[a] *Department of Chemistry, National Institute of Technology Silchar, Silchar 788010, India. Fax: +91 3842 224797; Tel: +91 9435374128; Email: barmanpranjit@yahoo.co.in.*

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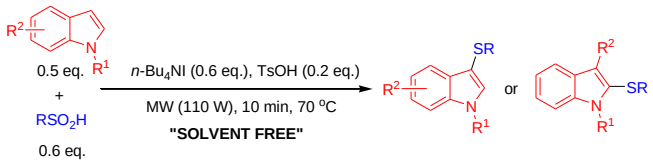
fast and efficient method for the sulfenylation of indoles in the absence of solvent, under microwave irradiation (Scheme 1). The combination of a solvent-free reaction medium with microwave irradiation have been used successfully for the synthesis of 3-sulfenylation of indoles.[25] However, to date, there are no reports of studies in which this attractive strategy has been applied to the synthesis of 3-sulfenylindoles. The protocol we have reported has a broad substrate scope, green reaction conditions, and high yields in a short reaction time.



Scheme 1 3-Sulfenylation of indoles under solvent-free conditions

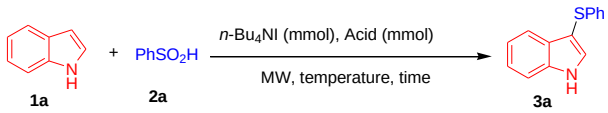
Results and discussion

The reaction conditions were optimized for indole **1a** and benzenesulfinic acid **2a** taken as model substrates in the presence of tetrabutylammonium iodide (*n*-Bu_4NI) and *p*-toluenesulfonic acid (Table 1). The reaction was carried out for reaction times of 3, 5, 7, and 10 mins. The reaction for 10 min offered the desired product in highest yield (Table 1, entry 4).

In the next step, we examined the effect of temperature and influence of microwave irradiation in terms of yield. It was observed that at 70 °C and 110 W, the desired product **3a** gives maximum yield of 97 % (Table 1, entry 4).

Additionally, we examined the reaction under conventional heating in oil bath and at room temperature, which gives the desired product in 80 % and 76 % yield respectively. However, these processes required a very long reaction time (Table 1, entry 9 and 10).

Table 1 Optimization of microwave parameters and reaction conditions[a]



Entry	**1a**/**2a** (mmol)	MW (W)	*T* (°C)	Time (min)	Additive (mmol)	Acid (mmol)	Yield(%)[b]
1	0.5/0.6	110	70	3	*n*-Bu_4NI (0.6)	TsOH (0.2)	40
2	0.5/0.6	110	70	5	*n*-Bu_4NI (0.6)	TsOH (0.2)	65
3	0.5/0.6	110	70	7	*n*-Bu_4NI (0.6)	TsOH (0.2)	75
4	**0.5/0.6**	**110**	**70**	**10**	***n*-Bu_4NI (0.6)**	**TsOH (0.2)**	**95**
5	0.5/0.6	110	70	10	*n*-Bu_4NI (0.6)	TsOH (0.1)	75
6	0.5/0.6	110	70	10	*n*-Bu_4NI (0.6)	TsOH (0.05)	45
7	0.5/0.6	110	80	10	*n*-Bu_4NI (0.6)	TsOH (0.2)	85
8	0.5/0.6	110	60	10	*n*-Bu_4NI (0.6)	TsOH (0.2)	73
9	0.5/0.5	110	70	10	*n*-Bu_4NI (0.6)	TsOH (0.2)	85
10	0.5/0.5	110	70	10	*n*-Bu_4NI (0.5)	TsOH (0.2)	75
11	0.5/0.5	110	70	10	*n*-Bu_4NI (0.25)	TsOH (0.2)	40
12	0.5/0.6	110	70	10	*n*-Bu_4NI (0.6)	HCl (0.2)	70
13	0.5/0.6	110	70	10	*n*-Bu_4NI (0.6)	TfOH (0.2)	85
14	0.5/0.6	110	70	10	*n*-Bu_4NI (0.6)	H_2SO_4 (0.2)	45
15	0.5/0.6	150	70	10	*n*-Bu_4NI (0.6)	TsOH (0.2)	86
16	0.5/0.6	70	70	10	*n*-Bu_4NI (0.6)	TsOH (0.2)	64
17	0.5/0.6	110	70	10	NaI (0.6)	TsOH (0.2)	20
18	0.5/0.6	110	70	10	KI (0.6)	TsOH (0.2)	10
19	0.5/0.6	110	70	10	-	TsOH (0.2)	0
20	0.5/0.6	-	70	18 h	*n*-Bu_4NI (0.6)	TsOH (0.2)	80[c]
21	0.5/0.6	-	r.t.	48 h	*n*-Bu_4NI (0.6)	TsOH (0.2)	76[d]

[a]Reaction conditions: indole **1a** (0.5 mmol), benzenesulfinic acid **2a** (0.6 mmol). [b]Isolated yield. [c]Conventional heating. [d]Reaction performed without microwave irradiation at room temperature.

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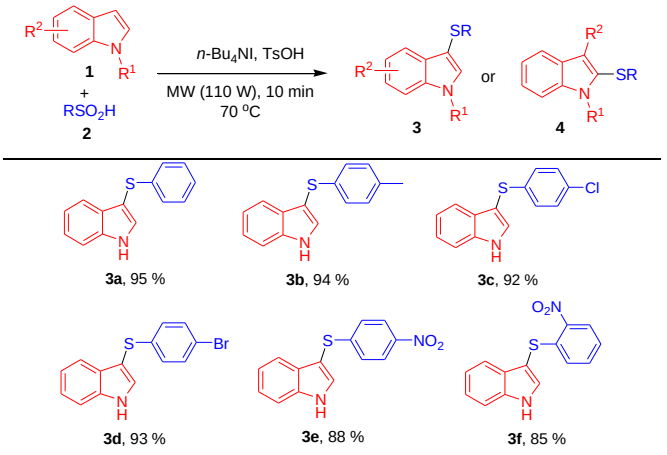
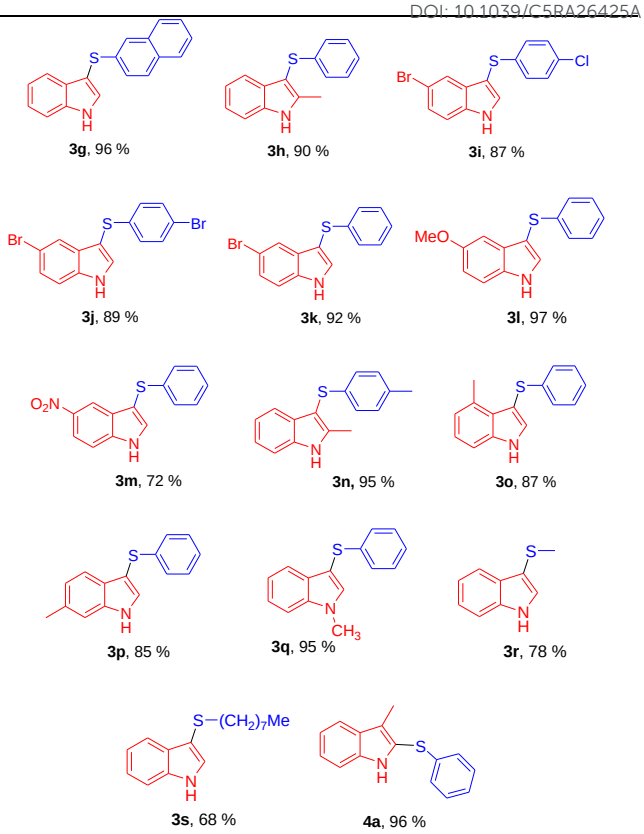
After that, additive loading was screened to improve the yield of the product. On increasing the amount of additive (*n*-Bu_4NI) to 0.6, 0.5, and 0.25 mmol; the desired product was obtained with 85, 75, and 40 % yield (Table 1, entries 9-11). Thus, the additive loading was optimized at 0.6 mmol. However, there was no product formation without using *n*-Bu_4NI (Table 1, entry 19). Other additives, such as NaI and KI were also evaluated, but were not as effective as *n*-Bu_4NI (Table 1, entries 17, 18).

The effect of acids, such as, TsOH, HCl, TfOH, and H_2SO_4 were studied. It was observed that TsOH provided the desired product in highest yield, when used in stoichiometric amount. The best molar ratio of indole/sulfinic acid was found to be 0.5/0.6 (Table 1).

With the optimized reaction conditions in hand (Table 1, entry 4), the scope and limitations of the proposed method were investigated. First, we study the substrate scope of arylsulfinic acids towards indole (**1a**). A variety of arylsulfinic acids with electron donating and electron withdrawing groups were smoothly reacted with indole to form their corresponding 3-arylthioindoles, with moderate to excellent yields (Table 2). The arylsulfinic acids with electron donating groups, such as, –Me and –OMe on the phenyl ring produced the desired products with higher yields than those with electron withdrawing groups (−Cl, −Br, and $-NO_2$). Thereafter, we have investigated the substrate scope of indoles. Similar trends were observed for indoles, where reactions with electron donating groups (−Me and −OMe) gives products with higher yields than those with electron withdrawing groups (−Br and $-NO_2$). N-substituted indoles also offered the corresponding products with higher yields, without any difficulties. In general, sulfenylation occurs at 3-position of the indole ring (Table 2, **3a-3s**). However, 2-position of the indole ring becomes the active reaction site, when 3-position is occupied by alkyl groups, such as, −Me (Table 2, **4a**). No by-product (bis-2,3-arylthioindole) is obtained under the optimized reaction conditions.

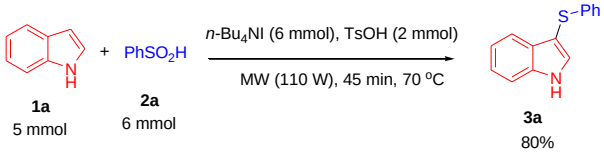
Table 2 Substrates scope for the Reaction of indoles **1** with sulfinic acids **2**[a,b]





[a]Reaction conditions: indole **1** (0.5 mmol), sulfinic acid **2** (0.6 mmol), *n*-Bu_4NI (0.6 mmol), TsOH (0.2 mmol), MW (110 W), 10 min, 70 °C. [b]Isolated yield.

To demonstrate the synthetic utility of the new method, gram scale reaction was carried out under the optimized conditions (Scheme 2). Thereby, the reaction between 1*H*-indole **1a** and benzenesulfinic acid **2a,** *n*-Bu_4NI, and TsOH were taken in a 25 mL sealed glass vial and placed in the Milestone Srl microwave reactor. After, 45 min of reaction time the desired product **3a** obtained in 80 % yield.



Scheme 2 Scale-up reaction between **1a** and **2a**

In order to gain insight of the reaction mechanism, a control experiment was carried out with benzenesulfinic acid **2a,** in the absence of indole **1a**. This led to the formation of corresponding disulfide with excellent yield under optimized conditions (Scheme 3).[23] During the reaction process, a purple colouration of the reaction mixture was observed, which confirmed the formation of iodine. In the presence of 20 mol % of iodine, indole **1a** reacted with diphenyl disulfide **5a** to give corresponding 3-sulfenylindole **3a**

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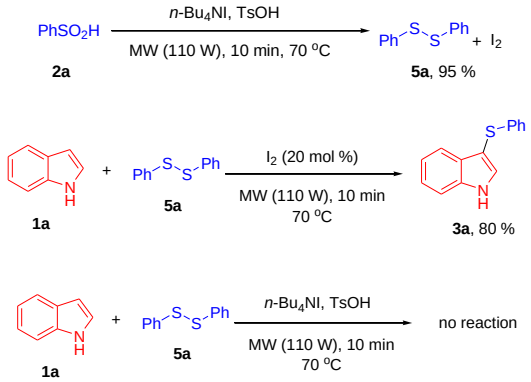
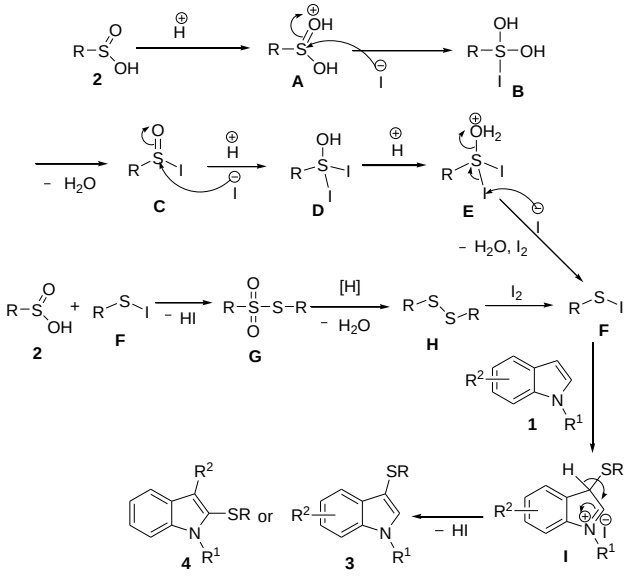
in 95 % yield. However, no product was formed on the treatment of diphenyl disulfide **5a** with indole **1a**, under the optimized reaction conditions.



Scheme 3 Control experiments

On the basis of previous reports,[9d,23,26] above experimental results, and control experiments, we proposed a plausible mechanism for 3-sulfenylation of indoles, as illustrated in Scheme 4. The stepwise removal of hydrogen and oxygen atoms from the SO_2H group in sulfinic acid **2** in the presence of *n*-Bu_4NI and TsOH, led to the formation of RSI. Alternatively, sulfenyl iodide reacts with **2** to give the sulfonothioate **G**. Reduction of **G** by *n*-Bu_4NI/TsOH gives disulfide **H**.[15] Disulfide **H** reacts with I_2, which is produced in the earlier step to form sulfenyl iodide (**F**).[9d,21] In the next step, indole **1** reacts with the sulfenyl iodide to form the intermediate **I**. **I** give the desired product **3**. However, product **4** is formed when a substituent occupy the C-3 positions of indole **1**. HI reacts with sulfinic acid and regenerate I_2.



Scheme 4 Plausible reaction mechanism for the 3-sulfenylation of indoles

Conclusions

We have developed a fast, economic, and highly efficient MW-assisted synthetic method for the regioselective 3-sulfenylation of indoles using sulfinic acids as thiolating agent. The new approach gives the desired products in excellent yields in only 10 min, under metal- and solvent-free conditions. Important advantages associated with this methodology are: no side product is obtained on the completion of the reactions and the by-product I_2 acts as an efficient catalyst. Due to excellent yield, short reaction time, and solvent-free conditions, this methodology promises to be a practical and greener alternative to earlier methods. This study will open a new window to many other useful transformations in organic synthesis. Further studies on the application of sulfinic acids are underway in our laboratory.

Experimental

General methods and materials: All chemicals were purchased from commercially available sources and were used without further purification. Melting points were recorded on an electro thermal digital melting point apparatus and were uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$, DMSO-d_6 and D_2O at 600 MHz, 400 MHz, 150 MHz, 125 MHz, and 100 MHz. Chemical shifts (δ) are reported as parts per million (ppm) and are referenced to tetramethylsilane (TMS) as internal standard. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad signal. Microwave-assisted syntheses were carried out in a monomode Milestone Srl microwave reactor. All reactions were performed in commercially available 10 mL sealed glass tubes. TLC was done on silica gel coated glass slide (Merck silica gel G for TLC). For column chromatography, silica gel 60-120 mesh (SRL, India) was used. Elemental analyses were performed on a Flash 2000 Thermo Scientific instrument. The yields are based on isolated compounds after purification.

Typical procedure for the synthesis of 3-sulfenylindoles: Mixture of indole **1** (0.5 mmol), sulfinic acid **2** (0.6 mmol), tetrabutylammonium iodide (221.5 mg, 0.6 mmol), and TsOH (35.5 mg, 0.2 mmol) were taken in a sealed glass tube (10 mL) and placed in the microwave reactor. A maximum irradiation power of 110 W and 70 °C were applied for 10 min. When the temperature reached 70 °C, the instrument automatically adjust to maintain a constant temperature. After 10 min, the reaction mixture was cooled to room temperature. The reaction mixture was quenched with 10 mL aqueous solution of 10 % sodium thiosulfate and the organic layer was extracted with ethyl acetate (3 x 10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and the solvent was removed under vacuum. The crude was purified by column chromatography on silica gel, with petroleum ether/ethyl acetate (15:1) as the eluent, to get the desired product **3**.

3-(phenylthio)-*1H*-indole (3a).[15] 107 mg, Yield: 95 %; White solid; m.p. 151–152 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.40 (br s, 1 H), 7.66 (d, *J* = 8.0 Hz, 1 H), 7.51 (d, *J* = 2.4 Hz, 1 H), 7.48 (d, *J* = 8.0 Hz, 1 H), 7.32 (t, *J* = 7.2 Hz, 1 H), 7.22–7.18 (m, 3 H), 7.15 (d, *J* = 7.6 Hz, 2

H), 7.11 (t, *J* = 7.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=139.1, 136.3, 130.5, 128.9, 128.5, 125.7, 124.6, 122.9, 120.8, 119.5, 111.4, 102.6; Anal. Calcd. for $C_{14}H_{11}NS$: C, 74.63; H, 4.92; N, 6.22 %. Found: C, 74.61; H, 4.91; N, 6.23 %.

3-(*p*-Tolylthio)-*1H*-indole (3b).[15] 112 mg, Yield: 94 %; White solid; mp 124-125 °C; ^{1}H NMR (300 MHz, $CDCl_3$): *δ* = 8.41 (br s, 1 H), 7.65 (d, 1 H, *J* = 8.0 Hz), 7.50 (d, 1 H, *J* = 2.5 Hz), 7.46 (d, 1 H, *J* = 8.0 Hz), 7.30 (t, 1 H), 7.20 (t, 1 H), 7.06 (d, 2 H, *J* = 8.0 Hz), 7.02 (d, 2 H, *J* = 8.0 Hz), 2.27 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 136.3, 135.3, 134.5, 130.3, 129.3, 128.9, 126.1, 122.8, 120.7, 119.5, 111.4, 20.7; Anal. Calcd. for $C_{15}H_{13}NS$: C, 75.28; H, 5.47; N, 5.85 %; found: C, 75.27; H, 5.48; N, 5.84 %.

3-[(4-Chlorophenyl)thio]-*1H*-indole (3c).[15] 119 mg, Yield: 92 %; White solid; m.p. 126-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.43 (br s, 1 H), 7.62 (d, *J* = 7.6 Hz, 1 H), 7.50-7.46 (m, 2 H), 7.34 (t, *J* = 7.2 Hz, 1 H), 7.23 (t, *J* = 7.2 Hz, 1 H), 7.16 (d, *J* = 7.6 Hz, 2 H), 7.06 (d, *J* = 7.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.7, 136.4, 130.6, 130.4, 128.69, 128.65, 126.9, 123.1, 120.9, 119.4, 111.5, 102.2; Anal. Calcd. for: $C_{14}H_{10}ClNS$: C, 64.73; H, 3.88; N, 5.39 %; found: C, 64.71; H, 3.87; N, 5.40 %.

3-[(4-Bromophenyl)thio]-*1H*-indole (3d).[15] 141 mg, Yield: 93 %; White solid; mp 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.46 (br s, 1 H), 7.61 (d, *J* = 7.6 Hz, 1 H), 7.51 (d, *J* = 2.0 Hz, 1 H), 7.48 (d, *J* = 7.6 Hz, 1 H), 7.33-7.28 (m, 3 H), 7.23 (t, *J* = 7.6 Hz, 1 H), 6.99 (d, *J* = 7.6 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.4, 136.3, 131.5, 130.6, 128.6, 127.2, 123.1, 120.9, 119.4, 118.1, 111.5, 102.1; Anal. Calcd. for $C_{14}H_{10}BrNS$: C, 55.28; H, 3.31; N, 4.60 %; found: C, 55.26; H, 3.33; N, 4.61 %.

3-[(4-Nitrophenyl)thio]-*1H*-indole (3e).[15] 119 mg, Yield: 88 %; Yellow solid; mp 177-178°C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* = 8.65 (br s, 1 H), 8.03 (d, *J* = 8.8 Hz, 2 H), 7.57-7.52 (m, 3 H), 7.36 (t, *J* = 7.6 Hz 1 H), 7.24 (t, *J* = 7.6 Hz 1 H), 7.16 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR (125 MHz, CDCl3): *δ* = 149.6, 143.0, 136.4, 134.0, 131.0, 124.9, 123.7, 123.4, 121.3, 119.1, 111.8, 100.4; Anal. Calcd. for $C_{14}H_{10}N_2O_2S$: C, 62.21; H, 3.73; N, 10.36 %; found: C, 62.23; H, 3.76; N, 10.35 %.

3-[(2-Nitrophenyl)thio]-*1H*-indole (3f). 115 mg, Yield: 85 %; White solid; m.p. 155–157 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.86 (br s, 1 H), 8.33 (d, *J* = 8 Hz, 1 H), 7.50 (t, *J* = 8 Hz, 2 H), 7.30–7.14 (m, 5 H), 6.82 (d, *J* = 8 Hz, 1 H); Anal. Calcd. for $C_{14}H_{10}N_2O_2S$: C, 62.21; H, 3.73; N, 10.36 %; found: C, 62.20; H, 3.71; N, 10.37 %.

3-[(2-naphthyl)thio]-*1H*-indole (3g).[15] 132 mg, Yield: 96 %; White solid; m.p. 141–142 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.47 (br s, 1 H), 7.76 (d, *J* = 7.6 Hz, 1 H), 7.68 (t, *J* = 8.8 Hz, 2 H), 7.60-7.48 (m, 4 H), 7.42–7.35 (m, 2 H), 7.31–7.28 (m, 2 H), 7.19 (t, *J* = 7.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 136.5, 136.4, 133.6, 131.2, 130.6, 128.9, 128.1, 127.5, 126.8, 126.2, 124.9, 124.6, 123.4, 122.9, 120.8, 119.6, 111.4, 102.7; Anal. Calcd. for $C_{18}H_{13}NS$: C, 78.51; H, 4.76; N, 5.09 %; found: C, 78.53; H, 4.75; N, 5.07 %.

2-Methyl-3-(phenylthio)-*1H*-indole (3h).[15] 108 mg, Yield: 90 %; White solid; mp 109-110 °C; ^{1}H NMR (600 MHz, $CDCl_3$): *δ* = 8.28 (br s, 1 H), 7.61 (d, *J* = 7.8 Hz, 1 H), 7.41 (d, *J* = 7.8 Hz, 1 H), 7.27 (t, *J* = 7.2, 1 H), 7.22-7.17 (m, 3 H), 7.11 (d, *J* = 7.2 Hz, 3 H), 2.57 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$); Anal. Calcd. for $C_{15}H_{13}NS$: C, 75.28; H, 5.47; N, 5.85 %. Found: C, 75.25; H, 5.45; N, 5.83 %.

5-Bromo-3-(*p*-chlorophenylthio)-*1H*-indole (3i).[13b] 151 mg, Yield: 89 %; Pale yellow solid; m.p. 142-144 °C; ^{1}H NMR (400 MHz, DMSO-d_6) *δ* = 8.49 (br s, 1 H), 7.71 (s, 1 H), 7.49 (d, 1 H, *J* = 2.4 Hz), 7.36 (d, *J* = 8.4, 1 H), 7.33 (d, *J* = 8.4, 1 H), 7.14 (d, *J* = 8.4, 2 H), 7.0 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 137.4, 135.3, 132, 131, 130.8, 129, 127.2, 126.4, 122.2, 114.8, 113.3, 102.5; Anal. Calcd. for $C_{14}H_9BrClNS$: C, 49.65; H, 2.68; N, 4.14 %; found: C, 49.67; H, 2.69; N, 4.17 %.

5-Bromo-3-(*p*-bromophenylthio)-*1H*-indole (3j).[10h] 167 mg, Yield: 87 %; Pale yellow solid; m.p. 156-158 °C; ^{1}H NMR (400 MHz, DMSO-d_6): *δ* = 11.93 (br s, 1 H), 7.83 (d, *J* = 2.3 Hz, 1 H), 7.45 (d, *J* = 8.7 Hz, 2 H), 7.37 (d, *J* = 8.7 Hz, 2H), 7.29-7.26 (m, 1 H), 6.91 (d, *J* = 8.7 Hz, 2 H); Anal. Calcd. for $C_{14}H_9Br_2NS$: C, 43.89; H, 2.37; N, 3.66 %; found: C, 43.86; H, 2.35; N, 3.68 %.

5-Bromo-3-(phenylthio)-*1H*-indole (3k).[15] 140 mg, Yield: 92 %; White solid; m.p. 120–122 °C; ^{1}H NMR (400 MHz, DMSO-d_6): *δ* = 11.88 (br s, 1 H), 7.81 (d, *J* = 2.8 Hz, 1 H), 7.50-7.42 (m, 2 H), 7.28–7.25 (m, 1 H), 7.17 (t, 2H), 7.06-7.02 (m, 1 H), 6.98-6.96 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 138.9, 136.2, 133.9, 131.3, 129, 128.7, 126.3, 120, 119.4, 115, 111, 99.1; Anal. Calcd. for $C_{14}H_{10}BrNS$: C, 55.28; H, 3.31; N, 4.60 %; found: C, 55.31; H, 3.33; N, 4.63 %.

5-Methoxy-3-(phenylthio)-*1H*-indole (3l).[9d] 124 mg, Yield: 97 %; Colorless crystals; m.p. 77-79°C; ^{1}H NMR (400 MHz, DMSO-d_6) *δ* = 11.94 (br s, 1 H), 7.83 (s, 1H), 7.45-7.43 (m, 2 H), 7.28–7.19 (m, 3 H), 6.97-6.95 (m, 2 H), 3.74 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 155, 139.2, 131.2, 129.8, 129.2, 128.6, 125.6, 124.6, 113.4, 112.3, 101.9, 100.8, 55.6; Anal. Calcd. for $C_{15}H_{13}NOS$: C, 70.56; H, 5.13; N, 5.49 %; found: C, 70.59; H, 5.15; N, 5.47 %.

5-Nitro-3-(phenylthio)-*1H*-indole (3m).[15] 81 mg, Yield: 72 %; Yellow solid; m.p. 151–154 °C; ^{1}H NMR (400 MHz, D_2O): *δ* = 8.76 (br s, 1 H), 8.63 (s, 1 H), 8.14 (d, *J* = 8.8 Hz, 1 H), 7.53 (d, *J* = 8 Hz, 2 H), 7.47 (d. *J* = 9.2 Hz, 1 H), 7.40 (s, 1 H), 7.34 (t, *J* = 7.6 Hz, 2 H), 7.28–7.23 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 143.6, 143.1, 138.4, 134.6, 131.1, 129.2, 128.1, 125.1, 116.1, 114.9, 111.6, 99.7; Anal. Calcd. for $C_{14}H_{10}N_2O_2S$: C, 62.21; H, 3.73; N, 10.36 %; found: C, 62.23; H, 3.70; N, 10.37 %.

2-Methyl-3-(*p*-tolylthio)-*1H*-indole (3n).[9d] 120 mg, Yield: 95 %; White solid; m.p. 97-99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.25 (br s, 1 H), 7.59 (d, *J* = 7.6 Hz, 1 H), 7.37 (d, *J* = 7.6 Hz, 1 H), 7.23 (t, *J* = 7.2 Hz, 1 H), 7.17 (t, *J* = 7.6 Hz, 1 H), 7.01-6.93 (m, 4 H), 2.54 (s, 3 H), 2.27 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* = 136.8, 135.5, 135.2, 134.1, 130.2, 129.3, 125.6, 121.9, 120.4, 118.8, 111.2, 103, 20.7, 12; Anal. Calcd. for $C_{16}H_{15}NS$: C, 75.85; H, 5.97; N, 5.53 %; found: C, 75.82; H, 5.98; N, 5.54 %.

1-Methyl-3-(phenylthio)-*1H*-indole (3q).[9d] 114 mg, Yield: 95 %; White solid; mp 109-110 °C; ^{1}H NMR (400 MHz, DMSO-d_6): *δ* = 7.31

(d, *J* = 8.0 Hz, 2 H), 7.14 (t, *J* = 7.7 Hz, 2 H), 7.09-6.95 (m, 4 H), 6.81 (d, *J* = 7.7 Hz, 2 H), 2.40 (s, 3 H); Anal. Calcd. for $C_{15}H_{13}NS$: C, 75.28; H, 5.47; N, 5.85 %. Found: C, 75.26; H, 5.48; N, 5.84 %.

3-Methyl-2-(phenylthio)-*1H*-indole (4a).[9d] 115 mg, Yield: 96 %; White solid; mp 76-78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 8.24 (br s, 1 H), 7.60 (d, *J* = 8 Hz, 1 H), 7.38 (d, *J* = 8 Hz, 1 H), 7.23-7.17 (m, 4 H), 7.09 (d, *J* = 7.2 Hz, 1 H), 2.44 (s, 3H); Anal. Calcd. for $C_{15}H_{13}NS$: C: 75.28; H: 5.47; N: 5.85 %. Found: C, 75.29; H, 5.46; N, 5.86 %.

Bis(phenyl)disulfide (5a). Yield: 95 %; White solid; mp 59-61 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.0 Hz, 4 H), 7.45 (d, *J* = 8.0 Hz, 4 H), 7.13 (t, *J* = 8.0 Hz, 2 H);^{13}C NMR (100 MHz, $CDCl_3$) δ = 136.6, 130, 129.2, 125; Anal. Calcd. for $C_{12}H_{10}S_2$: C, 66.01; H,4.62. Found: C, 66.04; H, 4.60 %.

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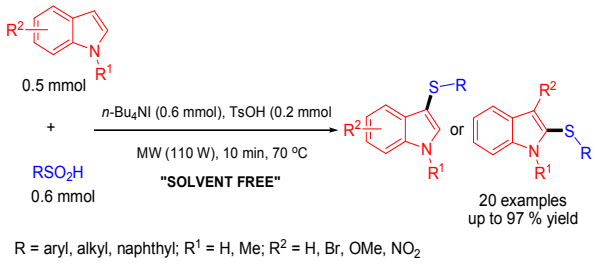
Microwave-assisted regioselective sulfenylation of indoles under solvent- and metal-free conditions

Rajjakfur Rahaman, Namita Devi, Jyoti Rekha Bhagawati and Pranjit Barman*



Formation of 3-sulfenylindoles using sulfinic acid as a sulfenylating agent