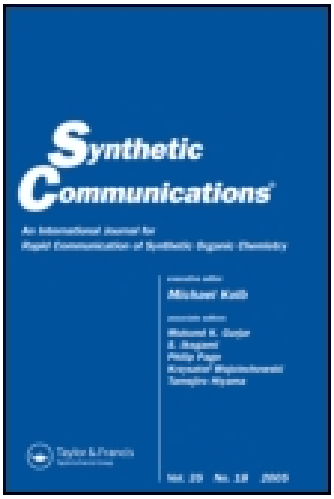

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ONE-POT SYNTHESIS OF 1-PHENYLSULFONYL-2-AROYLINDOLES

Vasudevan Dhayalan, Ganapathy Panchapakesan, and Arasambattu K. Mohanakrishnan

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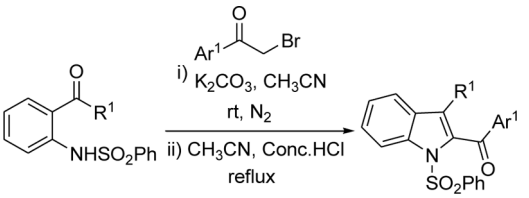
GRAPHICAL ABSTRACT



Abstract *Interaction of phenylsulfonyl-2-aminobenzaldehyde with 2-bromo-1-phenylethanones in the presence of K_2CO_3 followed by acid-catalyzed dehydration led to the formation of 1-phenylsulfonyl-2-aroylindoles.*

Keywords Alkylation; 2-aroylindoles; intramolecular aldol condensation; phenylsulfonyl-2-aminobenzaldehyde

INTRODUCTION

Indole and its myriad derivatives are important fragments of a large number of natural products of both marine and terrestrial origin and continue to capture the attention of synthetic organic chemists. Recently, Gribble has extensively reviewed[1] the various developments involved in the synthesis of indoles. The indole nucleus is one of the most ubiquitous scaffolds found in natural products, pharmaceuticals, functional materials, and agrochemicals.[2] The structural diversity and biological importance of indoles have made them attractive targets.[3] The 3-substituted indoles can be easily prepared via electrophilic substitution reactions. However, the corresponding 2-substituted counterparts can be obtained only through lithiation protocols.[4] The most versatile and widely applied reaction is the Fischer indole synthesis starting from phenylhydrazine with ketones or aldehydes.[5] Arumugam and Srinivasan have reported the synthesis of 1-phenylsulfonyl-2-aroylindoles[6] involving oxidation of corresponding 2-benzylindoles using Sarett reagent. An

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efficient base-mediated intramolecular condensation of 2-(di-substituted amino)-benzonitriles led to the formation of 3-aminoindoles.[7] During the past 20 years, a variety of indole derivatives have been explored as potential antitubulin agents.[8] In particular, 1-aroyl, 2-aroyl, and 3-aroylindoles have been proved as novel and potent tubulin inhibitory, antimitotic agents.[9]

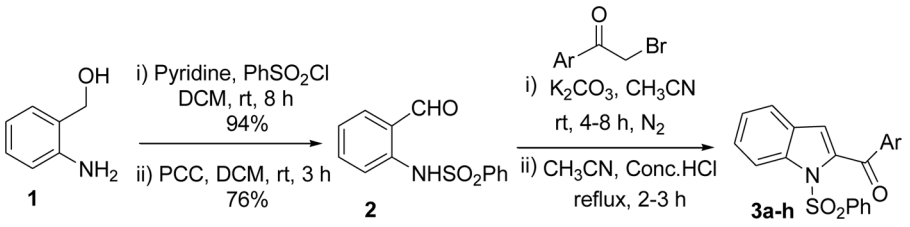
RESULTS AND DISCUSSION

The promising antitubulin activity of 2/3-aroylindoles prompted us to explore a viable procedure for the synthesis of various types of 2-aroylindole analogs. The phenylsulfonylation of 2-aminobenzylalcohol **1** using pyridine/$PhSO_2Cl$ followed by the oxidation of the resulting *N*-phenylsulfonyl-2-aminobenzylalcohol using pyridinium chlorochromate (PCC) afforded aldehyde **2** in 76% yield. Interaction of phenylsulfonyl-2-aminobenzaldehyde **2** with α-bromomethylketones in the presence of 2 eq. of K_2CO_3 in dry acetonitrile at room temperature led to the formation of the alkylation product, which underwent simultaneous intramolecular aldol condensation to afford 3-hydroxy-2-aroylindolines. The intermediate indolines upon dehydration using concentrated HCl at reflux led to the formation of 1-phenylsulfonyl-2-aroylindoles **3a–h** (Scheme 1).

Full details regarding the nature of α-bromomethylketones and the conditions employed along with the yields of respective 2-aroylindoles isolated are presented in Table 1. The formation of 2-aroylindoles via alkylation followed by aldol condensation and subsequent dehydration was found to be successful with a wide variety of *p*-substituted phenacylbromides (entry 1). As a representative case, intermediate aldol product 3-hydroxy-2-aroylindoline was isolated for **3c** (entry 1) and thoroughly characterized by ^1H and ^{13}C NMR spectra (see the Experimental section). The one-pot synthesis of 2-aroylindole could be realized with 2-bromo-1-(thiophen-2-yl)ethanone as well to afford the respective 2-heteroaroylindole **3f** (entry 2).

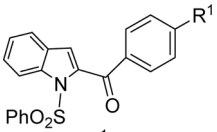
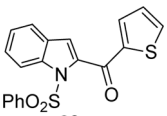
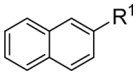
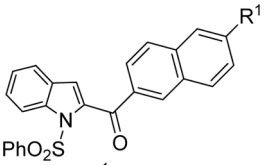
Under identical conditions, interaction of compound **2** with 2-bromo-1-(naphthalen-2-yl)ethanone/2-bromo-1-(2-methoxynaphthalen-6-yl)ethanone in the presence of K_2CO_3 at room temperature followed by acid-catalyzed dehydration afforded the corresponding 2-aroylindoles **3g** and **3h** in 62% and 58% of yields, respectively (entry 3).

Finally, *N*-phenylsulfonylaminobenzaldehyde **2** underwent smooth alkylation with chloroacetone/ethyl bromoacetate followed by aldol condensation and subsequent acid-catalyzed dehydration to afford the respective 2-acetylindole **3i**/2-carbethoxyindole **3j** in 56 and 60% yields, respectively (Scheme 2).



Scheme 1. Preparation of 2-aroylindoles.

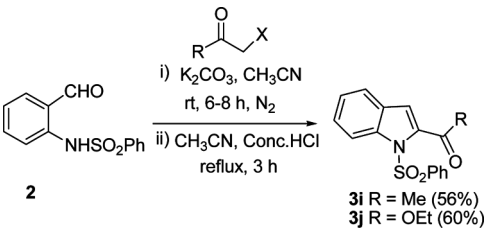
Table 1. Preparation of 1-phenylsulfonyl-2-aroylindoles **3a–h**

Entry	Ar	Condition	Product	Yield (%)[a]
1		rt, 7 h, ref. 3 h rt, 6 h, ref. 3 h rt, 4 h, ref. 2 h rt, 5 h, ref. 2 h rt, 6 h, ref. 2 h	 **3a** R^1 = H **3b** R^1 = F **3c** R^1 = Cl **3d** R^1 = Br **3e** R^1 = OMe	67 68 70 74 60
2		rt, 17 h, ref. 2 h	 **3f**	64
3		rt, 8 h, ref. 3 h rt, 8 h, ref. 3 h	 **3g** R^1 = H **3h** R^1 = OMe	62 58

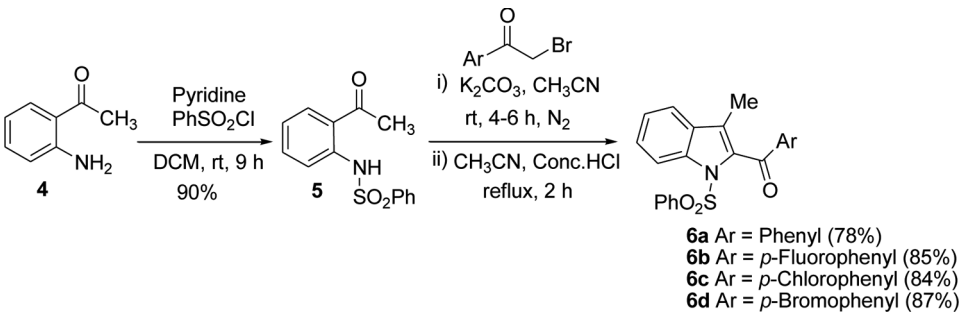
[a]Isolated yield.

As expected, the phenylsulfonylation of 2-aminoacetophenone **4** using pyridine/$PhSO_2Cl$ afforded *N*-phenylsulfonyl-2-aminoacetophenone **5** in 90% yield. Interaction of *N*-phenylsulfonyl-2-aminoacetophenone **5** with α-bromomethylketones using 2 eq. of K_2CO_3 in dry acetonitrile at room temperature followed by acid-catalyzed dehydration led to the formation of 3-methyl-1-phenylsulfonyl-2-aroylindoles **6a–d** (Scheme 3).

Similar to the case of aldehyde **2**, the alkylation, aldol condensation, and subsequent dehydration sequence could be successfully performed with *p*-substituted phenacyl bromides to afford the respective 3-methyl-2-aroylindoles **6a–d** in 78–87% yields. Comparatively, the 2-aroylindoles are obtained in relatively better yields using *N*-phenylsulfonyl-2-aminoacetophenone **5** than the *N*-phenylsulfonyl-2-aminobenzaldehyde **2**.



Scheme 2. Preparation of indole analogs **3i** and **3j**.



Scheme 3. Preparation of 3-methyl-2-aroylindoles.

In conclusion, we have achieved the one-pot synthesis of 1-phenylsulfonyl 3-free and 3-methyl-2-aroylindoles via base-mediated alkylation followed by intramolecular aldol condensation and subsequent acid-catalyzed dehydration. The procedure developed herein is simple, clean, and economically viable for the synthesis of various types of 2-aroylindoles.

EXPERIMENTAL

All melting points were uncorrected. Reagents were purchased from commercial sources and used as received without purification. Solvents were dried by standard procedures. Column chromatography was carried on silica gel (grade 60, mesh size 230–400, Merck). Infrared (IR) spectra were recorded on a Shimadzu Fourier transform (FT)–IR 8300 instrument. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard on a Bruker 300 spectrometer. Chemical shift values were quoted in parts per million (ppm), and coupling constants were quoted in hertz (Hz). Chemical shift multiplicities were reported as s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Mass spectra were recorded on a Jeol DX 303 HF spectrometer. Elemental analyses were carried out on Perkin-Elmer series II 2400 (IIT Madras) equipment.

N-[2-(Hydroxymethyl)phenyl]benzenesulfonamide

Pyridine (9.7 mL, 97.47 mmol) was slowly added to a stirred solution of 2-aminobenzylalcohol **1** (12 g, 98 mmol) in dry DCM (80 mL) at room temperature. After 10 min, $PhSO_2Cl$ (15.0 mL, 117.06 mmol) was added and stirred at room temperature for 8 h. Then the reaction mixture was poured over crushed ice containing concentrated HCl (10 mL), extracted with chloroform (3×20 mL), and dried (Na_2SO_4). Removal of solvent followed by crystallization from MeOH gave the *N*-[2-(hydroxymethyl)phenyl] benzenesulfonamide (24 g, 94%). Mp: 127 °C. IR (KBr): 3448 (OH), 3066 (NH), 1391 & 1157 (SO_2Ph) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08 (s, 1H, N-H), 7.74 (d, $J = 7.8$ Hz, 2H, Ar-H), 7.53 (t, $J = 7.2$ Hz, 1H, Ar-H), 7.43–7.37 (m, 3H, Ar-H), 7.26–7.20 (m, 1H, Ar-H), 7.07 (d, $J = 7.2$ Hz, 2H, Ar-H), 4.35 (s, 2H, CH_2).

N-(2-Formylphenyl)benzenesulfonamide (2)

N-[2-(hydroxymethyl)phenyl]benzenesulfonamide (2.0 g, 7.60 mmol) was added to a stirred solution of PCC (3.27 g, 15.20 mmol) in dry DCM (30 mL) at room temperature and stirred at room temperature for 3 h. Then the reaction mixture was passed through Celite, and the filtrate was concentrated in vacuo to afford an aldehyde **2** (1.5 g, 76%). Mp: 118 °C. IR (KBr): 3140 (NH), 1674 (CHO), 1388 & 1176 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 10.82 (s, 1H, CHO), 9.83 (s, 1H, NH), 7.90–7.15 (m, 9H, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 195.3, 139.9, 139.4, 136.4, 136.1, 133.5, 129.4, 127.4, 123.4, 122.1, 117.9.

2-Aroylindoles (3a–h)

K_2CO_3 (3.82 mmol) and α-bromomethylketone (2.18 mmol) were added to a solution of substrate **2** (1.91 mmol) in dry CH_3CN (20 mL). The reaction mixture was stirred at room temperature for the specified time (Table 1) under an N_2 atmosphere. The solvent was removed, and the residue was quenched with ice water (50 mL), extracted with chloroform (3 × 10 mL), and dried (Na_2SO_4). Removal of solvent followed by the residue was dissolved in CH_3CN (20 mL). Concentrated HCl (3 mL) was added. The reaction mixture was then refluxed for 2–3 h. It was then poured over ice water (50 mL), extracted with $CHCl_3$ (3 × 10 mL), and dried (Na_2SO_4). Removal of solvent followed by crystallization from methanol afforded the 2-aroylindoles **3a–h**.

1-Phenylsulfonyl-(1*H*-indol-2-yl)(phenyl)methanone (3a). Yield: 0.46 g (67%). Mp: 142 °C. IR (KBr): 1659 (CO), 1351 & 1176 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.14 (d, $J = 8.4$ Hz, 1H, Ar-H), 8.06 (d, $J = 7.5$ Hz, 2H, Ar-H), 7.97 (d, $J = 7.5$ Hz, 2H, Ar-H), 7.61–7.43 (m, 8H, Ar-H), 7.27 (t, $J = 7.5$ Hz, 1H, Ar-H), 6.92 (s, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 186.1, 136.8, 136.6, 136.4, 136.1, 132.6, 132.2, 128.7, 127.6, 127.3, 127.2, 126.1, 125.7, 122.9, 121.2, 115.5, 113.7. Mass (*m*/*z*) %: 361 (M^+, 52%). Anal. calcd. for $C_{21}H_{15}NO_3S$: C, 69.79; H, 4.18; N, 3.88; S, 8.87%. Found: C, 69.97; H, 4.03; N, 3.67; S, 8.65%.

1-Phenylsulfonyl-(4-fluorophenyl)(1*H*-indol-2-yl)methanone (3b). Yield: 0.50 g (68%). Mp: 130 °C. IR (KBr): 1658 (CO), 1372 & 1179 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.14–7.98 (m, 5H, Ar-H), 7.57–7.44 (m, 5H, Ar-H), 7.31–7.24 (m, 1H, Ar-H), 7.18–7.10 (m, 2H, Ar-H), 6.93 (s, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 186.1, 138.0, 137.7, 137.6, 134.0, 132.7, 132.6, 129.0, 128.7, 127.5, 127.1, 124.4, 122.6, 116.7, 115.9, 115.6, 115.1. Mass (*m*/*z*) %: 379 (M^+, 65%). Anal. calcd. for $C_{21}H_{14}FNO_3S$: C, 66.48; H, 3.72; N, 3.69; S, 8.45%. Found: C, 66.35; H, 3.53; N, 3.80; S, 8.68%.

1-Phenylsulfonyl-*p*-chlorophenyl-3-(hydroxyindolin-2-yl)methanone

K_2CO_3 (3.82 mmol) and *p*-chlorophenacylbromides (2.18 mmol) were added to a solution of substrate **2** (1.91 mmol) in dry CH_3CN (20 mL). The reaction mixture was stirred at room temperature for 4 h under an N_2 atmosphere. The solvent was

removed, and the residue was quenched with ice water (50 mL), extracted with chloroform (3×10 mL), and dried (Na_2SO_4). Removal of solvent followed by crystallization from methanol afforded the 1-phenylsulfonyl-*p*-chlorophenyl-3-(hydroxyindolin-2-yl)methanone (0.60 g, 76%). Mp: 208–210 °C. IR (KBr): 3440 (OH), 1659 (CO), 1372 & 1179 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.97 (d, $J = 7.8$ Hz, 2H, Ar-H), 7.87 (d, $J = 8.1$ Hz, 2H, Ar-H), 7.60 (d, $J = 6.9$ Hz, 1H, Ar-H), 7.52–7.49 (m, 5H, Ar-H), 7.28 (t, $J = 7.8$ Hz, 2H, Ar-H), 7.04 (t, $J = 7.2$ Hz, 1H, Ar-H), 5.92 (s, 1H, OH), 5.70-5.58 (m, 2H, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.6, 140.8, 138.4, 137.1, 134.9, 133.3, 132.4, 129.8, 129.4, 128.9, 128.8, 128.3, 127.0, 126.8, 125.7, 123.6, 113.5, 71.1, 69.6. Mass (m/z) %: 415 ($M^+ + 2$, 30%), 413 (M^+, 90%). Anal. calcd. for $C_{21}H_{16}ClNO_4S$: C, 60.94; H, 3.90; N, 3.38; S, 7.75%. Found: C, 60.76; H, 3.68; N, 3.20; S, 7.63%.

1-Phenylsulfonyl-(4-chlorophenyl)(1*H*-indol-2-yl)methanone (3c). Yield: 0.53 g (70%). Mp: 120–122 °C. IR (KBr): 1659 (CO), 1370 & 1174 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.13 (d, $J = 8.4$ Hz, 1H, Ar-H), 8.03–8.01 (m, 2H, Ar-H), 7.91 (d, $J = 8.7$ Hz, 2H, Ar-H), 7.58–7.55 (m, 2H, Ar-H), 7.50–7.44 (m, 5H, Ar-H), 7.30 (t, $J = 6.9$ Hz, 1H, Ar-H), 6.94 (s, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 186.4, 140.1, 137.9, 137.7, 137.6, 135.9, 134.0, 131.3, 129.0, 128.9, 128.6, 127.5, 127.2, 124.4, 122.6, 116.9, 115.2. Mass (m/z) %: 397 ($M^+ + 2$, 30%), 395 (M^+, 88%). Anal. calcd. for $C_{21}H_{14}ClNO_3S$: C, 63.72; H, 3.56; N, 3.54; S, 8.10%. Found: C, 63.50; H, 3.40; N, 3.80; S, 8.28%.

1-Phenylsulfonyl-(4-bromophenyl)(1*H*-indol-2-yl)methanone (3d). Yield: 0.62 g (74%). Mp: 146 °C. IR (KBr): 1659 (CO), 1364 & 1170 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.13 (d, $J = 8.1$ Hz, 1H, Ar-H), 8.01 (d, $J = 7.5$ Hz, 2H, Ar-H), 7.82 (d, $J = 8.1$ Hz, 2H, Ar-H), 7.62–7.43 (m, 7H, Ar-H), 7.28 (t, $J = 7.2$ Hz, 1H, Ar-H), 6.94 (s, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 186.5, 137.9, 137.7, 137.5, 136.3, 134.1, 131.9, 131.4, 129.1, 128.8, 128.6, 127.5, 127.3, 124.5, 122.7, 117.1, 115.2. Mass (m/z) %: 441 ($M^+ + 2$, 33%), 439 (M^+, 34%). Anal. calcd. for $C_{21}H_{14}BrNO_3S$: C, 57.28; H, 3.20; N, 3.18; S, 7.28%. Found: C, 57.50; H, 3.40; N, 3.01; S, 7.46%.

1-Phenylsulfonyl-(1*H*-indol-2-yl)(4-methoxyphenyl)methanone (3e). Yield: 0.45 g (60%). IR (KBr): 1655 (CO), 1372 & 1173 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.13–8.04 (m, 3H, Ar-H), 7.95 (d, $J = 9.0$ Hz, 2H, Ar-H), 7.53–7.37 (m, 5H, Ar-H), 7.24 (t, $J = 7.5$ Hz, 1H, Ar-H), 6.92 (d, $J = 9.0$ Hz, 2H, Ar-H), 6.86 (s, 1H, Ar-H), 3.80 (s, 3H, -OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 186.3, 164.1, 138.1, 138.0, 137.4, 134.0, 132.5, 130.4, 129.0, 128.8, 127.5, 126.8, 124.3, 122.5, 115.8, 115.0, 113.9, 55.6. Mass (m/z) %: 391 (M^+, 78%). Anal. calcd. for $C_{22}H_{17}NO_4S$: C, 67.50; H, 4.38; N, 3.58; S, 8.19%. Found: C, 67.80; H, 4.49; N, 3.35; S, 8.40%.

1-Phenylsulfonyl-(1*H*-indol-2-yl)(thiophen-2-yl)methanone (3f). Yield: 0.45 g (64%). Mp: 136–138 °C. IR (KBr): 1642 (CO), 1359 & 1175 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.13 (d, $J = 7.5$ Hz, 3H, Ar-H), 7.76 (d, $J = 5.7$ Hz, 2H, Ar-H), 7.57 (t, $J = 7.2$ Hz, 2H, Ar-H), 7.48 (t, $J = 7.2$ Hz, 3H, Ar-H), 7.32–7.25 (m, 1H, Ar-H), 7.17 (t, $J = 7.2$ Hz, 1H, Ar-H), 7.07 (s, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.0, 144.1, 138.2, 137.8, 137.3, 135.4, 135.2, 134.0, 129.0, 128.4, 128.3, 127.7, 127,1, 124.3, 122.6, 116.6, 115.1. Mass (m/z) %: 367 (M^+,

85%). Anal. calcd. for $C_{19}H_{13}NO_3S_2$: C, 62.11; H, 3.57; N, 3.81; S, 17.45%. Found: C, 62.31; H, 3.43; N, 3.60; S, 17.67%.

1-Phenylsulfonyl-(1*H*-indol-2-yl)(naphthalen-2-yl)methanone (3g). Yield: 0.49 g (62%). IR (KBr): 1659 (CO), 1352 & 1171 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.41 (s, 1H, Ar-H), 8.17 (d, $J = 8.4$ Hz, 1H, Ar-H), 8.08 (d, $J = 7.8$ Hz, 3H, Ar-H), 7.90–7.83 (m, 3H, Ar-H), 7.56–7.39 (m, 7H, Ar-H), 7.27 (t, $J = 7.5$ Hz, 1H, Ar-H), 6.95 (s, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 187.5, 138.3, 138.0, 137.8, 135.9, 134.9, 134.0, 132.7, 132.4, 129.8, 129.1, 128.9, 128.7, 128.6, 127.9, 127.6, 127.1, 126.9, 124.9, 124.4, 122.7, 116.8, 115.2. Mass (m/z) %: 411 (M^+, 65%). Anal. calcd. for $C_{25}H_{17}NO_3S$: C, 72.97; H, 4.16; N, 3.40; S, 7.79%. Found: C, 72.80; H, 4.03; N, 3.60; S, 7.67%.

1-Phenylsulfonyl-(1*H*-indol-2-yl)(2-methoxynaphthalen-6-yl)methanone (3h). Yield: 0.49 g (58%). IR (KBr): 1655 (CO), 1372 & 1174 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.35 (s, 1H, Ar-H), 8.17–8.05 (m, 4H, Ar-H), 7.78 (t, $J = 8.1$ Hz, 2H, Ar-H), 7.58–7.45 (m, 5H, Ar-H), 7.32–7.15 (m, 3H, Ar-H), 6.95 (s, 1H, Ar-H), 3.91 (s, 3H, -OCH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 187.4, 160.1, 138.3, 138,0, 137.7, 137.6, 134.0, 132.8, 132.7, 131.4, 129.0, 128.7, 127.7, 127.6, 127.3, 126.9, 125.7, 124.3, 122.6, 119.8, 116.3, 115.1, 105.9 55.5. Mass (m/z) %: 441 (M^+, 45%). Anal. calcd. for $C_{26}H_{19}NO_4S$: C, 70.73; H, 4.34; N, 3.17; S, 7.26%. Found: C, 70.50; H, 4.09; N, 3.42; S, 7.37%.

Indole Analogs (3i and 3j)

K_2CO_3 (3.82 mmol) and α-halomethylketone (2.18 mmol) were added to a solution of substrate **2** (1.91 mmol) in dry CH_3CN (20 mL). The reaction mixture was stirred at room temperature for 6–8 h under an N_2 atmosphere. The solvent was removed, and the residue was quenched with ice water (50 mL), extracted with chloroform (3 × 10 mL), and dried (Na_2SO_4). Removal of solvent followed by the residue was dissolved in CH_3CN (20 mL), and concentrated HCl (3 mL) was added. The reaction mixture was then refluxed for 3 h. It was poured over ice water (50 mL), extracted with $CHCl_3$ (3 × 10 mL) and dried (Na_2SO_4). Removal of solvent followed by crystallization from methanol afforded the indole analogs **3i** and **3j**.

1-Phenylsulfonyl-(1*H*-indol-2-yl)ethanone (3i). Yield: 0.32 g (56%). IR (KBr): 1689 (CO), 1362 & 1178 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.16 (d, $J = 8.7$ Hz, 1H, Ar-H), 7.96–7.93 (m, 2H, Ar-H), 7.58–7.42 (m, 5H, Ar-H), 7.28 (t, $J = 7.8$ Hz, 1H, Ar-H), 7.13 (s, 1H, Ar-H), 2.64 (s, 3H, -CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.5, 138.9, 138.3, 133.7, 129.7, 128.8, 128.3, 127.7, 127.3, 124.4, 122.8, 117.5, 115.8, 29.6. Mass (m/z) %: 299 (M^+, 67%). Anal. calcd. for $C_{16}H_{13}NO_3S$: C, 64.20; H, 4.38; N, 4.68; S, 10.71%. Found: C, 64.35; H, 4.21; N, 4.88; S, 10.60%.

Ethyl-1-phenylsulfonyl-1*H*-indole-2-carboxylate (3j). Yield: 0.38 g (60%). Mp: 86 °C. IR (KBr): 1732 (CO_2Et), 1367 & 1185 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.06–7.99 (m, 3H, Ar-H), 7.75–7.60 (m, 4H, Ar-H), 7.51 (t, $J = 7.2$ Hz, 1H, Ar-H), 7.42 (s, 1H, Ar-H), 7.35 (t, $J = 7.8$ Hz, 1H, Ar-H), 4.36 (q, $J = 7.2$ Hz, 2H, -OCH_2), 1.32 (t, $J = 7.2$ Hz, 3H, -CH_3). ^{13}C NMR (75 MHz,

$CDCl_3$): δ 160.7, 137.2, 137.1, 134.6, 131.4, 129.5, 128.0, 127.2, 126.8, 124.5, 122.9, 116.7, 114.9, 61.7, 13.8. Mass (*m/z*) %: 329 (M^+, 54%). Anal. calcd. for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59; N, 4.25; S, 9.74%. Found: C, 61.78; H, 4.41; N, 4.45; S, 9.51%.

N-Phenylsulfonyl-(aminophenyl)ethanone (5)

Pyridine (2.2 mL, 22.12 mmol) was slowly added to a stirred solution of 2-aminoacetophenone **4** (3.0 g, 22.19 mmol) in dry DCM (50 mL) at room temperature. After 10 min, $PhSO_2Cl$ (3.40 mL, 26.61 mmol) was added and stirred at room temperature for 9 h. Then the reaction mixture was poured over crushed ice containing concentrated HCl (3 mL), extracted with chloroform (3 × 10 mL), and dried (Na_2SO_4). Removal of solvent followed by crystallization from MeOH gave the compound **5** (5.5 g, 90%) as a colorless solid. Mp: 180 °C. IR (KBr): 3015 (NH), 1651 (CO), 1370 & 1167 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 11.50 (s, 1H, Ar-H) 7.88–7.79 (m, 3H, Ar-H), 7.61–7.45 (m, 5H, Ar-H), 7.12 (t, $J = 7.8$ Hz, 1H, Ar-H), 2.57 (s, 3H, $-CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.4, 138.9, 138.6, 134.5, 132.8, 131.8, 128.7, 126.5, 122.7, 122.2, 118.5, 27.8. Mass (*m/z*) %: 275 (M^+, 66%). Anal. calcd. for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09; S, 11.65%. Found: C, 61.30; H, 4.53; N, 5.21; S, 11.78%.

3-Methyl-2-aroylindoles (6a–d)

K_2CO_3 (2.18 mmol) and α-bromomethylketone (1.30 mmol) were added to a solution of substrate **5** (1.09 mmol) in dry CH_3CN (20 mL). The reaction mixture was stirred at room temperature for 4–6 h under an N_2 atmosphere. The solvent was removed and the residue was quenched with ice water (50 mL), extracted with chloroform (3 × 10 mL), and dried (Na_2SO_4). Removal of solvent followed by the residue was dissolved in CH_3CN (20 mL), conc HCl (2 mL) was added. The reaction mixture was then refluxed for 2 h. It was then poured over ice-water (50 mL), extracted with $CHCl_3$ (3 × 10 mL), and dried (Na_2SO_4). Removal of solvent followed by crystallization from methanol afforded 3-methyl-2-aroylindoles **6a–d**.

1-Phenylsulfonyl-(3-methyl-1*H*-indol-2-yl)(Phenyl)methanone (6a). Yield: 0.53 g (78%). Mp: 138 °C. IR (KBr): 1659 (CO), 1357 & 1174 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.09 (d, $J = 8.4$ Hz, 1H, Ar-H), 7.91 (d, $J = 7.5$ Hz, 2H, Ar-H), 7.82 (d, $J = 7.5$ Hz, 2H, Ar-H), 7.57 (t, $J = 7.2$ Hz, 1H, Ar-H), 7.46 (t, $J = 7.8$ Hz, 5H, Ar-H), 7.40–7.30 (m, 3H, Ar-H), 2.18 (s, 3H, $-CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.5, 138.4, 136.7, 136.4, 133.9, 133.6, 133.4, 131.2, 129.6, 128.9, 128.6, 127.3, 126.8, 124.8, 124.4, 120.5, 115.3, 9.4. Mass (*m/z*) %: 375 (M^+, 66%). Anal. calcd. for $C_{22}H_{17}NO_3S$: C, 70.38; H, 4.56; N, 3.73; S, 8.54%. Found: C, 70.50; H, 4.41; N, 3.90; S, 8.38%.

1-Phenylsulfonyl-(4-fluorophenyl)(3-methyl-1*H*-indol-2-yl)methanone (6b). Yield: 0.60 g (85%). Mp: 142 °C. IR (KBr): 1658 (CO), 1361 & 1165 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.09 (d, $J = 8.4$ Hz, 1H, Ar-H), 7.94 (t, $J = 7.8$ Hz, 2H, Ar-H), 7.80 (d, $J = 7.5$ Hz, 2H, Ar-H), 7.49–7.30 (m, 6H, Ar-H), 7.14 (t, $J = 8.4$ Hz, 2H, Ar-H), 2.18 (s, 3H, $-CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ

187.9, 136.4, 134.9, 133.9, 133.3, 132.3, 132.1, 131.2, 128.9, 127.2, 127.0, 125.2, 124.5, 120.5, 116.0, 115.7, 115.4, 9.4. Mass (m/z) %: 393 (M^+, 43%). Anal. calcd. for $C_{22}H_{16}FNO_3S$: C, 67.16; H, 4.10; N, 3.56; S, 8.15%. Found: C, 67.32; H, 4.35; N, 3.70; S, 8.38%.

1-Phenylsulfonyl-(4-chlorophenyl)(3-methyl-1*H*-indol-2-yl)methanone (6c). Yield: 0.62 g (84%). Mp: 134 °C. IR (KBr): 1659 (CO), 1356 & 1179 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.09 (d, $J = 8.1$ Hz, 1H, Ar-H), 7.87–7.77 (m, 4H, Ar-H), 7.49–7.28 (m, 8H, Ar-H), 2.18 (s, 3H, -CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 188.1, 139.8, 136.9, 136.5, 136.3, 134.0, 133.2, 131.2, 130.9, 129.0, 128.9, 127.2, 127.1, 125.7, 124.6, 120.6, 115.4, 9.4. Mass (m/z) %: 411 ($M^+ + 2$, 33%), 409 (M^+, 98%). Anal. calcd. for $C_{22}H_{16}ClNO_3S$: C, 64.47; H, 3.93; N, 3.42; S, 7.82%. Found: C, 64.61; H, 4.15; N, 3.60; S, 7.54%.

1-Phenylsulfonyl-(4-bromophenyl)(3-methyl-1*H*-indol-2-yl)methanone (6d). Yield: 0.71 g (87%). Mp: 124 °C. IR (KBr): 1659 (CO), 1359 & 1178 (SO_2Ph) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, $J = 8.1$ Hz, 1H, Ar-H), 7.77 (d, $J = 8.1$ Hz, 4H, Ar-H), 7.60 (d, $J = 8.1$ Hz, 2H, Ar-H), 7.49–7.42 (m, 3H, Ar-H), 7.38–7.28 (m, 3H, Ar-H), 2.18 (s, 3H, -CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 188.3, 137.3, 136.5, 136.3, 133.9, 133.2, 132.0, 131.2, 131.0, 128.9, 128.6, 127.2, 127.1, 125.7, 124.6, 120.6, 115.4, 9.4. Mass (m/z) %: 455 ($M^+ + 2$, 67%), 453 (M^+, 66%). Anal. calcd. for $C_{22}H_{16}BrNO_3S$: C, 58.16; H, 3.55; N, 3.08; S, 7.06%. Found: C, 58.34; H, 3.65; N, 3.34; S, 7.32%.

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