Diversification of Indoles via Microwave-assisted Ligand-free Copper-catalyzed N-Arylation

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A simple, efficient Cu_2O catalyst system under microwave irradiation was developed for N-arylation of various indoles without ligands and additives. Diverse *N*-heteroarylated indoles were prepared by coupling indoles with various heteroaryl halides within 1 h. The selective reactivity of bromoindole with aryl iodide provided *N*-aryl bromoindoles, which could be useful intermediates for palladium-catalyzed Heck and Suzuki coupling reactions.

Keywords: Microwave, Ligand-free, Cu_2O, Indole, N-arylation

Introduction

The indole moieties are the most important class of heterocyclic compounds in natural products and pharmaceutical agents. The identification and structural characterization of serotonin and tryptophan in living organisms have inspired chemists to design and synthesize thousands of indole-containing pharmaceuticals, which exhibit activities as 5-HT_3 receptor antagonists, HIV-1 reverse transcriptase inhibitors, HMG-CoA reductase inhibitors, and growth hormone inhibitors, among others.[1] Considerable effort has been expended on the development of versatile, efficient, and economical synthetic routes to synthesize indole derivatives.[2,3] In particular, many synthetic approaches are based on palladium-catalyzed coupling reactions, which have been extensively investigated and can provide highly selective routes to variously substituted indoles.[4]

Mild and efficient N-arylation of indoles has been reported for the development of new, inexpensive, and efficient catalytic systems with palladium and copper. Despite the mild palladium-catalyzed reaction conditions,[5] the palladium-catalyzed N-arylation of indoles has some limitations due to the high cost of the catalyst and the ligand specificity to indole substrates. The traditional method of synthesizing N-arylated indoles consists of copper-mediated Ullmann-type reactions of indoles with aryl halides,[6] but this has a number of limitations, such as the need for high-temperature reaction conditions and stoichiometric amounts of the catalyst. Recently, significant progress has been achieved in the copper-catalyzed N-arylation of indoles with various organic ligands, such as diamine,[7] diimine,[8] benzotriazole,[9] surfactant/copper-based ionic liquid,[10,11] oxazolidin-2-one,[12] 1,10-phenanthroline,[13] and (diphenylphosphine)propanoic acid,[14] among others.[15] The copper-catalyzed N-arylation of indoles has shown that the yield of these indoles depends on the catalyst species and the ligand, with long reaction times (12–48 h) under conventional heating.

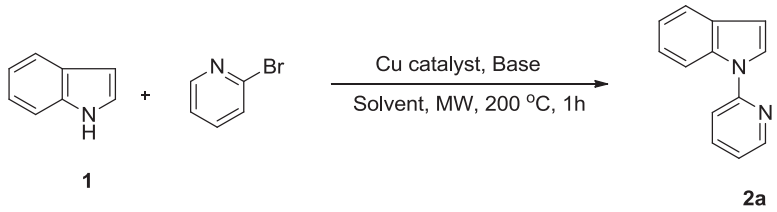
In organic chemistry, microwave-mediated organic reactions have attracted considerable attention because they can accelerate slow thermal reactions with significant energy savings, high chemical yields, and cleaner reactions.[16] Our study also showed that microwave-mediated copper- or palladium-catalyzed diversification of heterocycles[17] has significant advantages over conventional heating in heterocycle diversification. In the course of establishing a chemical compound library of biologically active indoles, we required a convenient and rapid synthetic procedure to obtain diverse N-arylated indoles. In this report, we examined the microwave-assisted ligand-free copper-catalyzed direct N-arylation of indoles as part of our ongoing efforts to develop organometallic approaches for the diversification of indoles.[18]

Results and Discussion

Initially, the reaction of 2-bromopyridine and indole was selected as a preliminary model reaction to overcome the long reaction time with conventional heating. The reaction conditions were optimized by varying the copper source, additive, base, and solvent. The results are summarized in Table 1.

We investigated the effects of different solvents and additives under the same temperature conditions (Table 1, entries 1–5). The reaction using *N,N*-dimethylacetamide (DMA) or *N*-methylpyrrolidone (NMP) as solvent produced 80% yields of the desired product, but DMA was selected as the solvent for the microwave reaction due to its low cost and use as an industrial solvent, in contrast to NMP (entries 1–5). The same reaction had slow and poor yields under a low temperature with a short reaction time. Yields

Table 1. Optimization of conditions for microwave-assisted Cu-catalyzed N-arylation of indoles.



1 **2a**

Entry[a]	Cu source	Additive	Base	Solvent	Yield (%)
1	Cu_2O	–	Cs_2CO_3	DMF	59
2	〃	–	〃	DMA	80
3	〃	LiCl	〃	DMA	50
4	〃	–	〃	NMP	80
5	〃	LiCl	〃	NMP	49
6	CuI	–	〃	DMA	58
7	$Cu(OAc)_2$	–	〃	DMA	40
8	CuO	–	〃	DMA	<10
9	CuBr	–	〃	DMA	51
10	Cu_2O	–	K_3PO_4	DMA	61
11	〃	–	K_2CO_3	DMA	52
12	〃	–	Na_2CO_3	DMA	45
13	〃	–	Rb_2CO_3	DMA	65

[a] All reactions were conducted at a 1.0 mmol scale under 3 mL of solvent in a Biotage 5-mL vial sealed with a crimp cap using an initiator instrument (400 W, 2450 MHz, EXP EU, Biotage). DMF: *N,N*-dimethylformamide , DMA: *N-N*-dimethylacetamide, NMP: *N*-methylpyrrolidone

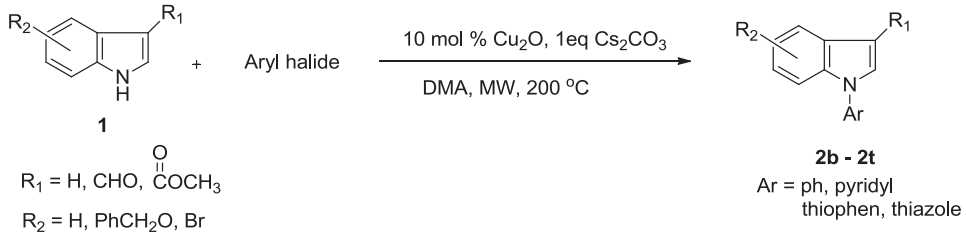
were higher when no chloride source was used than when LiCl was added (Table 1, entries 2–5). We also examined the effects of several commercial copper species that are frequently used for copper-coupling reactions. N-Arylation of indoles using Cu_2O produced higher yields of the desired product than reactions using CuI, $Cu(OAc)_2$, CuBr, and CuO under Cs_2CO_3 (Table 1, 6–9). Reactions using Cs_2CO_3 as a base produced good yields of the desired product. However, reactions using K_2CO_3, K_3PO_4, Na_2CO_3, and Rb_2CO_3 as bases only produced moderate yields of the desired product (Table 1, entries 10–13). The vapor pressure of the reaction mixture in the vial was monitored to keep it at 3–5 bar using an online programmed Biotage microwave reactor at 200°C. The results showed that the optimal conditions for N-arylation of indoles were 1 equiv Cs_2CO_3, 10 mol % Cu_2O in DMA at 200°C. N-arylation was examined using various aryl iodides or bromides under optimal reaction conditions to diversify the N-arylated indole products. The results are summarized in Table 2. The reaction using iodobenzene instead of bromobenzene produced high yields of *N*-phenylindole with short reaction times (Table 2, entries 1 and 2). Additionally, reactions using substituted iodobenzene produced excellent yields of *N*-phenyl indoles (Table 2, entries 3–6). These results indicate that reactions using *ortho, meta, para* substituted phenyl halides produced almost the same yield of the desired product. The reaction using heteroaryl bromides, such as thiophene, and thiazole, produced good yields of N-heteroarylated indoles (Table 2, entries 7 and 8). These results indicate that reactions using nitrogen- or sulfur-containing heteroaryl halides produced the same reactivity as with carboaryl halides. The optimized reaction conditions were applied for 3-acetylindole and 3-formylindole using aryl bromides. N-arylated 3-substituted indoles were obtained with different aryl variations at good to excellent yields (Table 2, entries 9–14). The reactions using 5-benzyloxyindole and 5-bromoindole were examined with various aryl halides. The reactions also provided N-arylated indoles with excellent yields.

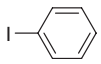
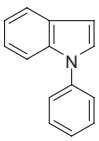
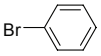
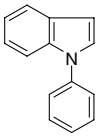
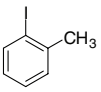
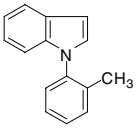
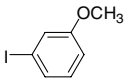
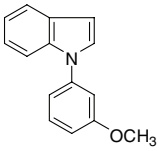
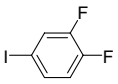
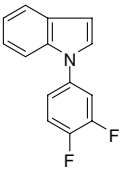
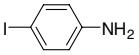
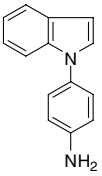
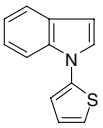
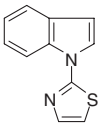
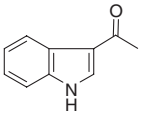
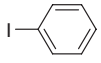
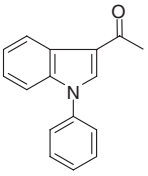
The selective reactivity of aryl iodide with 5-bromoindole provided N-arylated 5-bromoindole, which could be a useful intermediate for diversifying indole compounds with palladium-catalyzed Heck and Suzuki reactions.

Conclusions

The N-arylation of indoles using microwave irradiation could be a valuable synthetic method to prepare various indole compounds in a short reaction time. This catalyst system offered N-arylated haloindoles by the selective reactivity of aryl iodide with bromoindole. The catalyst system also showed the valuable development of green chemistry and simple diversification of the indole chemical library for drug development.

Table 2. Preparation of N-arylated indoles with arylhalides



Entry[a]	Indole	ArX	Product		Time (min)	Yield (%)
1				**2b**	20	97
2				**2b**	60	75
3				**2c**	30	87
4				**2d**	20	94
5				**2e**	20	92
6				**2f**	60	73
7				**2g**	60	85
8				**2h**	60	60
9				**2i**	60	76

(*continued overleaf*)

Table 2 (*continued*)

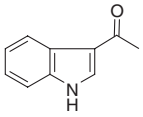
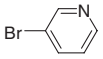
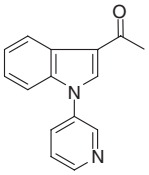
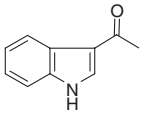
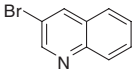
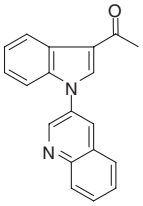
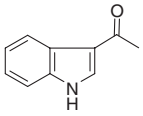
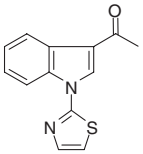
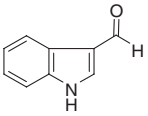
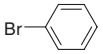
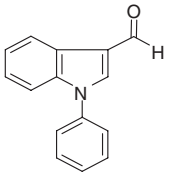
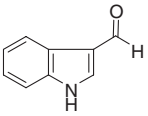
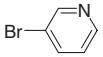
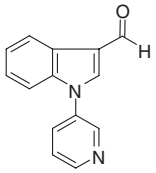
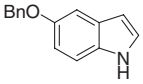
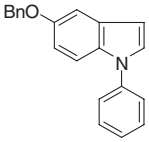
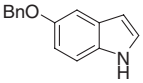
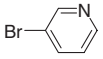
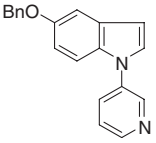
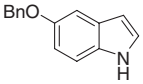
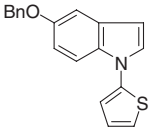
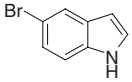
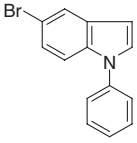
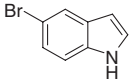
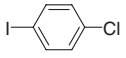
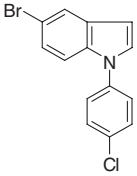
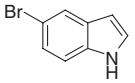
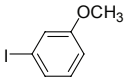
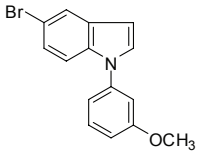
Entry[a]	Indole	ArX	Product		Time (min)	Yield (%)
10				**2j**	40	86
11				**2k**	60	72
12				**2l**	60	83
13				**2m**	60	87
14				**2n**	60	56
15				**2o**	20	87
16				**2p**	60	67
17				**2q**	60	71
18				**2r**	20	90
19				**2s**	20	84

Table 2 (*continued*)

Entry[a]	Indole	ArX	Product		Time (min)	Yield (%)
20				**2t**	20	76

[a] All reactions were conducted at a 1.0 mmol scale under 3 mL of solvent in a Biotage 5-mL vial sealed with a crimp cap using an initiator instrument (400 W, 2450 MHz, EXP EU, Biotage).

Experimental

Instrumentation and Analysis. All ^{1}H and ^{13}C NMR spectra were recorded on a JEOL 400 MHz spectrometer, and chemical shifts were referenced to tetramethylsilane (TMS) as an internal standard. The GC-MS spectra were obtained using a Shimadzu QP 1000 GC-MS (Kyoto, Japan). Microwave-assisted reactions were performed with an initiator instrument (400 W, 2450 MHz, EXP EU, Biotage, Uppsala, Sweden). Each reaction was carried out in a 5-mm-thickness Biotage 5-mL vial sealed with a crimp cap. Reaction temperatures were measured using infrared sensors on the outer surface of the reaction vial. Products were purified by flash chromatography on 230–400-mesh ASTM 60 silica gel. All base and Cu species were purchased from Sigma-Aldrich Chemical Co (St. Louis, MO, USA). Chemicals were used directly as obtained from commercial sources unless otherwise noted.

General Procedure for Microwave-assisted Copper-catalyzed N-Arylation of Indoles. Indole (1.0 mmol), Cs_2CO_3 (1.0 mmol), 2-bromopyridine (1.5 mmol), Cu_2O (0.1 mmol), and DMA (3 mL) were added to a 5-mL vial. The vial was sealed with a crimp cap and placed in a Biotage initiator microwave cavity. After irradiation at 200°C for the appropriate time and subsequent cooling, the reaction mixture was diluted with saturated aqueous ammonium chloride. Products were isolated by extraction into ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated. Products were purified by silica gel column chromatography using a hexane: ethyl acetate solvent. *N*-2-pyridylindole (**2a**)[19] was obtained (80% yield) as yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (m, 1H, Ar–H), 8.22 (d, 1H, Ar–H), 7.74 (m, 1H, Ar–H), 7.71 (d, 1H, J = 3.6 Hz, Ar–H), 7.68 (m, 1H, Ar–H), 7.44 (d, 1H, J = 6.8 Hz, Ar–H), 7.30 (m, 1H, Ar–H), 7.22 (t, 2H, J = 7.6 Hz, Ar–H), 7.14 (m, 1H, Ar–H), 6.71 (d, 1H, J = 3.6 Hz, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.7, 149.2, 138.6, 130.6, 126.2, 123.3, 121.5, 121.3, 120.2, 113.2, 105.7; MS (*m/z*) 195 (M + 1, 15), 193 (57), 167 (12).

The following compounds (**2b–2t**) were prepared with microwave-assisted general experimental procedures.

1-Phenyl-1*H*-indole (2b). Yield (187 mg, 97%), yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (d, 1H, J = 7.8 Hz, Ar–H), 7.54 (d, 1H, J = 7.8 Hz, Ar–H), 7.46–7.48 (m, 4H, Ar–H), 7.30–7.34 (m, 2H, Ar–H), 7.13–7.22 (m, 2H, Ar–H), 6.66 (d, 1H, J = 7.8 Hz, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.59, 135.62, 129.39, 139.11, 127.73, 126.21, 124.15, 122.15, 120.92, 120.15, 110.32, 103.39; MS (*m/z*) 193 (M^+, 100), 192 (21), 165 (33), 124 (51), 116 (20), 89 (20).[20]

1-(2-Methylphenyl)-1*H*-indole (2c). Yield (180 mg, 87%), red oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (d, J = 6.4 Hz, 1H, Ar–H), 7.30–7.45 (m, 4H, Ar–H), 7.15–7.28 (m, 4H, Ar–H), 6.68 (d, J = 3.2 Hz, Ar–H), 2.08 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.23, 136.92, 135.82, 131.85, 128.61, 128.25, 127.59 ,125.40, 122.03, 120.82, 120.52, 110.18, 102.48, 17.6; MS (*m/z*) 207 (M^+, 100).[21]

1-(3-Methoxy-phenyl)-1*H*-indole (2d). Yield (210 mg, 94%), yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (d, 1H, J = 7.2 Hz, Ar–H), 7.41–7.66 (m, 3H, Ar–H), 7.11–7.22 (m, 5H, Ar–H), 6.64 (d, 1H, J = 3.2 Hz, Ar–H) 3.87 (s, 3H, $-OCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.14, 140.26, 136.67, 129.12, 128.28, 127.89, 121.67, 120.65, 119.70, 112.28, 110.81, 102.34, 55.62; MS (*m/z*) 224 (M + 1, 16), 223 (M^+, 100), 208 (50), 180 (21), 152 (12).[20]

1-(3,4-Difluoro-phenyl)-1*H*-indole (2e). Yield (210 mg, 92%), brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (d, 1H, J = 7.6 Hz, Ar–H), 7.48 (d, 1H, J = 7.6 Hz, Ar–H), 7.15–7.34 (m, 6H, Ar–H), 6.67 (d, 1H, J = 3.2 Hz, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.01, 128.82, 128.79, 128.72, 128.68, 128.59, 128.42, 128.71, 122.46, 121.00, 120.45, 111.91, 111.87, 111.69, 111.65, 110.13, 110.11, 105.56, 105.33, 105.31, 105.07, 103.86; MS (*m/z*) 230 (M + 1, 15), 229 (100), 201 (13), 113 (37), 101 (23), 90 (40).

4-(1*H*-indol-1-yl)aniline (2f). Yield (152 mg, 73%), yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66 (d, 1H, J = 7.4 Hz, Ar–H), 7.42 (d, 1H, J = 8.0 Hz, Ar–H), 7.17 (m, 5H, Ar–H), 6.67 (dd, 2H, J = 8.0 Hz, Ar–H), 6.61 (d, 1H, J = 3.2 Hz, Ar–H), 4.02 (brs, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.28, 136.40, 130.81, 128.79, 128.42, 126.00, 121.93, 121.92, 120.90, 120.89, 119.86, 115.56, 110.45, 102.39; MS (*m/z*) 208 (M^+, 100).

1-Thiophen-2-yl-1*H*-indole (2g). Yield (170 mg, 85%), brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66 (d, 1H, J = 8.0 Hz, Ar–H), 7.56 (d, 1H, J = 8.0 Hz, Ar–H), 7.43 (dd, 1H, J = 4.8 Hz, 3.2 Hz, Ar–H), 7.14–7.31 (m, 5H, Ar–H), 6.63 (d, 1H, J = 3.2 Hz, Ar–H); ^{13}C NMR ($CDCl_3$,

100 MHz) δ 136.84, 127.71, 126.58, 126.47, 125.19, 125.07, 124.36, 121.47, 121.02, 110.68, 103.04; MS (*m/z*) 200 (M + 1, 7), 119 (100), 171 (13), 166 (10), 118 (17).[22]

1-Thiazol-2-yl-1*H*-indole (2h). Yield (120 mg, 60%), yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.29 (d, 1H, *J* = 7.6 Hz, Ar–H), 7.57–7.66 (m, 3H, Ar–H), 7.21–7.37 (m, 2H, Ar–H), 7.01(d, 1H, *J* = 3.6 Hz, Ar–H), 6.69 (d, 1H, *J* = 3.6 Hz, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.71, 143.28, 135.59, 127.60, 124.18, 121.74, 120.57, 119.45, 118.72, 111.02, 110.97, 102.28; MS (*m/z*) 201 (M + 1, 18), 200 (40), 174 (6), 143 (5), 128 (5), 116 (5), 101 (5), 89 (8), 57 (100).

1-(1-Phenyl-1*H*-indol-3-yl)ethanone (2i). Yield (202 mg, 86%), brown solid; mp: 143–145°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.45 (d, 1H, *J* = 7.8 Hz, Ar–H), 7.87 (s, 1H, Ar–H), 7.50 (m, 2H, Ar–H), 7.42 (m, 4H, Ar–H), 7.26 (m, 2H, Ar–H), 2.51 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.26, 138.17, 136.83, 134.60, 129.75, 127.85, 126.40, 124.70, 123.77, 122.92, 122.57, 118.40, 110.66, 27.39; MS (*m/z*) 236 (M + 1, 25), 235 (M^+,100).

1-(1-(Pyridin-3-yl)-1*H*-indol-3-yl)ethanone (2j). Yield (180 mg, 76%), white soild; mp = 156–160°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.80 (s, 1H, Ar–H), 8.73 (d, 1H, *J* = 4.4 Hz, Ar–H), 7.93 (s, 1H, Ar–H), 7.89 (m, 1H, Ar–H), 7.54 (m, 1H, Ar–H), 7.43 (d, 1H, *J* = 7.4 Hz, Ar–H), 7.36 (m, 2H, Ar–H), 2.60 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.20, 148.98, 146.01, 136.77, 134.00, 132.14, 126.48, 124.26, 123.32, 122.82, 119.28, 110.12; MS (*m/z*) 236 (M^+, 100).

1-(1-(Quinolin-3-yl)-1*H*-indol-3-yl)ethanone (2k). Yield (207 mg, 72%), yellow solid; mp = 128–130°C; ^{1}H NMR (CDCl3, 400 MHz) δ 9.04 (s, 1H, Ar–H), 8.44 (d, 1H, *J* = 7.8 Hz, Ar–H), 8.18 (m, 2H), 7.96 (s, 1H,Ar–H), 7.85 (d, 1H, *J* = 8.2 Hz, Ar–H), 7.76 (t, 1H, *J* = 7.6 Hz, Ar–H), 7.62 (t, 1H, *J* = 7.6 Hz, Ar–H), 7.38 (d, 1H, *J* = 7.6 Hz, Ar–H), 7.26 (m, 2H, Ar–H), 2.53 (s, 3H, COCH3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.10, 146.97, 146.82, 136.87, 134.20, 131.60, 130.29, 130.08, 129.31, 127.85, 127.65, 127.48, 126.37, 124.17, 123.22, 122.71, 119.21, 110.06, 27.41; MS (*m/z*) 286 (M^+, 100).

1-(1-(Thiazol-2-yl)-1*H*-indol-3-yl)ethanone (2l). Yield (200 mg, 83%), brown solid; mp = 99–104°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.40 (d, 1H, *J* = 7.6 Hz, Ar–H), 8.26 (s, 1H, Ar–H), 8.10 (d, 1H, *J* = 8.2 Hz, Ar–H), 7.60 (d, 1H, *J* = 3.6 Hz, Ar–H), 7.35 (m, 2H, Ar–H), 7.15 (d, 1H, *J* = 3.6 Hz, Ar–H), 2.55 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.42, 158.92, 140.02, 135.10 132.40, 126.95, 125.06, 124.06, 124.24, 120.03, 114.24, 112.38, 27.56; MS (*m/z*) 243 (M + 1, 15), 242 (M^+, 100).

1-Phenyl-1*H*-indole-3-carbaldehyde (2m). Yield (158 mg, 87%) brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.80 (s, 1H, CHO), 8.38 (dd, 1H, *J* = 6.6 Hz, 2.0 Hz, Ar–H), 7.89 (s, 1H, Ar–H), 7.57 (m, 2H, Ar–H), 7.48 (m, 4H, Ar–H), 7.34 (m, 2H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 185.00, 138.18, 138.14, 137.47, 129.97, 128.27, 125.52, 124.82, 124.58, 123.43, 122.21, 119.66, 111.05; MS (*m/z*) 221 (M^+, 100).

1-(Pyridin-3-yl)-1*H*-indole-3-carbaldehyde (2n). Yield (124 mg, 56%), brown solid; mp = 141–146°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.84 (s, 1H, CHO), 8.87 (s, 1H, Ar–H), 8.76 (d, 1H, *J* = 4.4 Hz, Ar–H), 8.40 (m, 1H, Ar–H), 7.92 (s, 1H, Ar–H), 7.89 (m, 1H, Ar–H), 7.57 (m, 1H, Ar–H), 7.45 (m, 1H, Ar–H), 7.38 (m, 2H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 184.91, 149.25, 149.22, 145.91, 137.57, 137.24, 132.07, 125.48, 124.97, 123.73, 122.35, 120.33, 110.43; MS (*m/z*) 221 (M^+, 100).

5-(Benzyloxy)-1-phenyl-1*H*-indole (2o). Yield (260 mg, 87%) yellow solid; mp = 128–130°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41 (m, 7H, Ar–H), 7.33 (t, 2H, *J* = 7.0 Hz, Ar–H), 7.25 (m, 3H, Ar–H), 7.17 (d, 1H, *J* = 2.4 Hz, Ar–H), 5.06 (s, 2H, OCH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.74, 139.85, 137.61, 131.16, 129.82, 129.56, 128.50, 128.33, 127.75, 127.50, 126.18, 123.93, 113.15, 111.29, 104.23, 103.27, 70.66; MS (*m/z*) 300 (M + 1, 24), 299 (M^+, 100), 224 (18), 124 (8).

5-(Benzyloxy)-1-(pyridin-3-yl)-1*H*-indole (2p). Yield (201 mg, 67%), brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.79 (s, 1H, Ar–H), 8.56 (s, 1H, Ar–H), 7.73 (d, 1H, *J* = 8.2 Hz, Ar–H), 7.38 (m, 7H, Ar–H), 7.24 (d, 1H, *J* = 3.2 Hz, Ar–H), 7.20 (d, 1H, *J* = 2.0 Hz, Ar–H), 6.90 (d, 1H, *J* = 2.0 Hz, Ar–H), 6.61(d, 1H, *J* = 3.2 Hz, Ar–H), 5.09 (s, 2H, OCH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.97, 147.19, 145.18, 137.35, 130.87, 130.81, 130.01, 128.47, 128.46, 127.78, 127.76, 127.43, 113.51, 110.75, 104.44, 104.37, 70.52; MS (*m/z*) 303 (M + 1, 10), 302 (M^+, 100), 280 (25).

5-(Benzyloxy)-1-(thiophen-2-yl)-1*H*-indole (2q). Yield (218 mg, 71%), yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43 (t, 3H, *J* = 7.6 Hz, Ar–H), 7.33 (t, 2H, *J* = 7.6 Hz, Ar–H), 7.26 (m, 1H, Ar–H), 7.18 (d, 1H, *J* = 3.2 Hz, Ar–H), 7.14 (d, 1H, *J* = 2.4 Hz, Ar–H), 7.02 (m,1H, Ar–H), 6.94 (m, 3H, Ar–H), 6.51 (d, 1H, *J* = 3.2 Hz, Ar–H), 5.05 (s, 2H, OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.06, 141.83, 137.51, 132.30, 129.66, 129.53, 128.48, 127.74, 127.45, 125.96, 121.10, 119.66, 113.44, 111.38, 104.37, 103.90, 70.65; MS (*m/z*) 306 (M + 1, 20), 305 (M^+, 100.

5-Bromo-1-phenyl-1*H*-indole (2r). Yield (245 mg, 90%), yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, 1H, *J* = 7.6 Hz, Ar–H), 7.45 (t, 2H, *J* = 7.6 Hz, Ar–H), 7.37 (dd, 2H, *J* = 7.8 Hz, 1.2 Hz, Ar–H), 7.31 (m, 2H, Ar–H), 7.24 (m, 2H, Ar–H), 6.56 (d, 1H, *J* = 3.2 Hz, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.26, 134.50, 130.95, 130.57, 129.69, 129.04, 126.79, 125.11, 124.24, 123.53, 113.48, 111.93, 102.96; MS (*m/z*) 274 (M + 2, 89), 272 (M^+,100), 251 (65).[20]

5-Bromo-1-(4-chlorophenyl)-1*H*-indole (2s). Yield (257 mg, 84%), yellow solid; mp = 82–84°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76 (s, 1H, Ar–H), 7.43 (d, 2H, *J* = 8.6 Hz, Ar–H), 7.30 (m, 3H, Ar–H), 7.21 (m, 2H, Ar–H), 6.57 (d, 1H, *J* = 3.2 Hz, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.78, 134.40, 132.34, 130.98, 129.85,

128.80, 128.44, 125.44, 125.38, 123.67, 113.72, 112.18, 111.68, 103.43, 103.16; MS (*m/z*) 308 (M + 2, 100), 306 (M^+, 100).

5-Bromo-1-(3-methoxy-phenyl)-1H-indole (2t). Yield (230 mg, 76%), yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75 (d, 1H, *J* = 2.0 Hz, Ar–H), 7.37 (m, 2H, Ar–H), 7.25 (m, 2H, Ar–H), 6.95 (m, 2H, Ar–H), 6.85 (dd, 1H, *J* = 8.2 Hz, 2.4 Hz, Ar–H), 6.55 (d, 1H, *J* = 3.2 Hz, Ar–H), 3.79 (s, 3H, $-CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.57, 140.36, 134.42, 130.96, 130.44, 129.02, 125.12, 123.51, 116.37, 113.48, 112.12, 112.07, 110.17, 102.95, 55.3; MS (*m/z*) 304 (M + 2, 100), 302 (M^+, 100).[20]

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