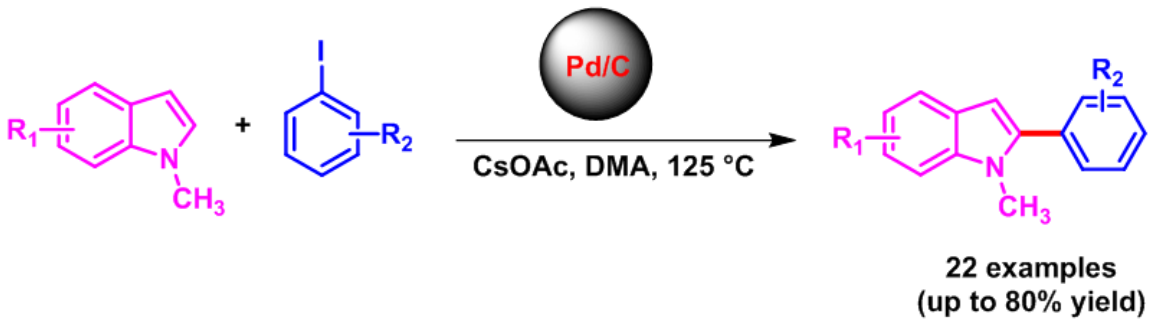
Chapter 3

Pd/C catalyzed C-2 Selective Direct Functionalization of Indoles with Aryl Iodides



- ❖ C-2 selective direct functionalization
- ❖ Directing group, ligand, and additive-free
- ❖ Reusable catalyst
- ❖ Broad substrate scope

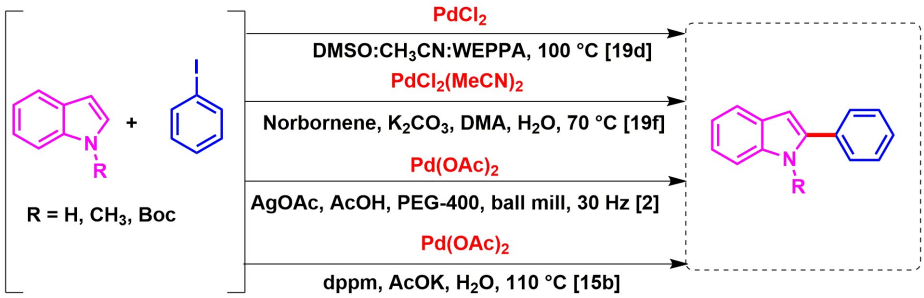
Abstract: The chapter discusses the C-2 selective direct functionalization of *N*-methylindole derivatives with aryl iodides catalyzed by heterogeneous Pd supported on carbon. The developed methodology exclusively results in C-2 arylated indoles in the absence of any ligand or directing group. The catalyst is easily recoverable from the reaction mixture and can be reused for up to four cycles without any significant loss of its catalytic efficiency. Without using any additive, the current protocol is applicable to a wide range of substrates.

3.1 Introduction

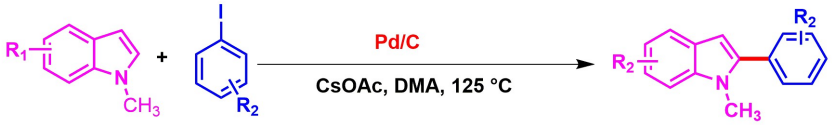
The formation of the aryl-heteroaryl bond is a fascinating class of organic reactions. Such linkages are widely present in biological and pharmaceutical compounds [1]. Arylation of indole at the C-2 position offers important synthetic intermediates of different bioactive compounds [2-7]. The traditional methods for the C-2 arylation of indole derivatives with aryl halides require the prefunctionalization of both coupling partners [8-10]. On the contrary, the development of transition metal-based catalyst systems in recent years leads to the direct arylation of indole through C-H bond functionalization [10-14]. Several reported protocols involve the coupling between electron-rich indole derivatives and aryl halides in presence of phosphine-based ligands [15]. However, phosphine-free C-2 arylation reactions are also available in the literature which are performed in presence of carboxylic acid and silver salt derivatives [9,16]. In recent reports, it was observed that the addition of carboxylic acids can have a significant impact on metal-catalyzed C-H bond functionalization reactions [8,9,17]. Guimond and co-workers have designed some biaryl carboxylic acids, analogous to Buchwald's phosphine ligand, for C-2/C-3 arylation of indoles [18]. The carboxylic acids can facilitate the aryl deprotonation by binding to the transition metal *via* the concerted-metalation-deprotonation process [18]. On the other hand, silver salts are typically employed for the elimination of halide ions from transition metal-complex to provide a more electrophilic metal center [9]. Islam *et al.* have reported the direct C-2 arylation of *N*-protected indoles with aryl iodides in presence of $Pd(OAc)_2$ and silver cyclohexanoate base [16a]. Similarly, Larrosa and co-workers carried out the direct functionalization of indoles at the C-2 position by using $Pd(OAc)_2$ with Ag_2O base and *o*-nitrobenzoic acid additive [9]. Most of these reported methodologies involve the use of phosphine ligands, acid additives, and silver salts [19]. The use of the stoichiometric amount of silver salts essential for catalyst regeneration suffers from high costs and raises environmental concerns [20]. Moreover, the use of transition metal catalysts in homogeneous form creates difficulties in the separation as well as recovery of the metal catalysts [3,10a,21]. On the contrary, heterogeneous catalysis provides an easy separation along with the possibility of catalyst reusability. Djakovitch and co-workers employed palladium supported on zeolite as a heterogeneous catalyst for C-3 arylation of indoles with bromoarenes [22]. In recent times, palladium-on-carbon (Pd/C) has gained significant interest as a heterogeneous catalyst because of its attractive properties that include easy

availability, handling, recovery, and recyclability [10,23]. Considering these suitable properties of the Pd/C catalyst, we have carried out the regioselective C-2 arylation of indole derivatives with aryl iodides under ligand, acid, and metallic silver-free conditions (Scheme **3.1**).

Previous work:



Our work:



Scheme **3.1**. Direct C-2 functionalization of indoles

3.2 Experimental section

3.2.1 General procedure for the synthesis of C-2 arylated indole

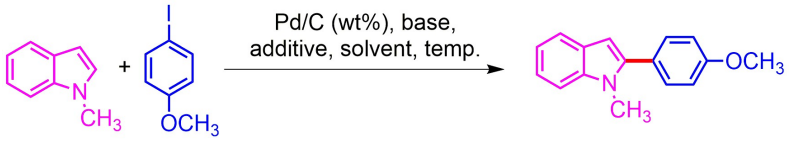
A tube capped with a Teflon screw cap was charged with indole (0.5 mmol), aryl iodide (0.6 mmol), Pd/C (20 wt%), CsOAc (1 mmol), and DMA (2 ml). The reaction mixture was then stirred at 125 °C for 24 hours. After completion of the reaction (monitoring by TLC), the reaction mixture was extracted with ethyl acetate, washed with brine solution, and dried over by anhydrous sodium sulfate. The extract was evaporated under reduced pressure in a rotary evaporator to obtain the crude. Then the crude was purified by column chromatography to get the desired product.

3.3 Results and Discussion

3.3.1 Optimization of reaction conditions

The studies of the reaction under various conditions were carried out by taking *N*-methylindole and 4-Iodoanisole as model substrates to find out the optimized reaction conditions and the results obtained are summarized in Table **3.1**.

Table **3.1**. Optimization of C-2 arylation of *N*-methylindole with 4-Iodoanisole[a]



1a **2a** **3a**

Entry	Pd/C (wt%)	Base (equiv.)	Additive (equiv.)	Solvent (mL)	Temp. (°C)	Yield (%)[b]
1	20	CsOAc (2)	PivCOOH (1)	DMA	120	51
2	20	CsOAc (2)	PivCOOH (2)	DMA	120	51
3	20	CsOAc (2)	PivCOOH (3)	DMA	120	48
4	20	CsOAc (2)	PivCOOH (0.5)	DMA	120	64
5	20	NaOAc (2)	PivCOOH (1)	DMA	120	46
6	20	Cs_2CO_3 (2)	PivCOOH (1)	DMA	120	32
7	20	K_2CO_3 (1.5)	PivCOOH (1)	DMA	110	58
8	20	K_2CO_3 (1.5)	PivCOOH (0.5)	DMA	110	52
9	20	K_3PO_4 (1.5)	PivCOOH (0.5)	DMA	110	45
10	20	K_2CO_3 (1.5)	PivCOOH (1)	DMA	120	53
11	20	K_2CO_3 (2)	PivCOOH (1)	DMA	120	51
12	20	Ag_2O (1)	PivCOOH (1)	DMA	120	Trace
13	20	AgOAc (1)	PivCOOH (1)	DMA	120	Trace
14	20	CsOAc (2)	-	DMA	120	66
15	20	CsOAc (1) K_2CO_3 (1)	-	DMA	120	60
16	**20**	**CsOAc (2)**	**-**	**DMA**	**125**	**75**
17	20	CsOAc (2)	-	DMF	125	65
18	20	CsOAc (2)	-	1,4 dioxane	125	-
19	20	CsOAc (2)	-	NMP	125	35
20	10	CsOAc (2)	-	DMA	125	64
21	20	-	-	DMA	125	-
22	20	CsOAc (2)	-	CH_3CN	125	-
23	20	CsOAc (2)	-	DMSO	125	61

[a]Reaction conditions: **1a** (1 equiv.), **2a** (1.2 equiv.), Solvent (2 mL), 24 hours, [b]Isolated yields

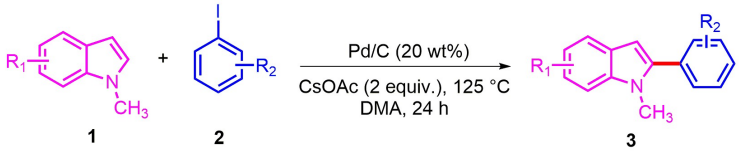
In the case of Pd-catalyzed C-H functionalization reactions, pivalic acid (PivCOOH) is most commonly used as an acid additive although it is not the only potent additive explored till now for this purpose [12]. In our work, we initially added pivalic acid as an additive to facilitate palladation and enhance the electrophilicity of the palladium species. However, a better yield of product was obtained with the addition of a lower amount of pivalic acid (entry **4**, Table **3.1**) in presence of CsOAc base. Encouraged by this result, we have utilized other inorganic bases (NaOAc, Cs_2CO_3, K_2CO_3, K_3PO_4, Ag_2O, AgOAc) to increase the product yield. But in comparison to CsOAc, other bases provided a low to a moderate yield of our desired product (entries **5**-**13**, Table **3.1**). It might be due to the easy removal of halide ion by Cs-salt from the Pd-metal complex. Then we carried out the reaction in absence of pivalic acid and to our surprise, the reaction proceeded smoothly giving up to 66% yield (entry **14**, Table **3.1**) at 120 °C. The acetate ion from CsOAc base might facilitate the formation of the Pd-metal complex to such an extent that the reaction proceeded in absence of pivalic acid. To study the effect of temperature, the reactions were performed at 120 °C and 125 °C, and the best result was obtained at 125 °C (entry **16**, Table **3.1**). Varying the amount of catalyst (entry **20**, Table **3.1**) as well as solvents (entries **17**-**19**, **22**, **23**, Table **3.1**) provided no significant improvement in the yield of the reaction. Moreover, we have observed that in absence of CsOAc base, there is no product formation (entry **21**, Table **3.1**). All these results indicated that 20 wt% of Pd/C at 125 °C along with CsOAc in DMA is the most effective condition for the current protocol.

3.3.2 Substrate scope study

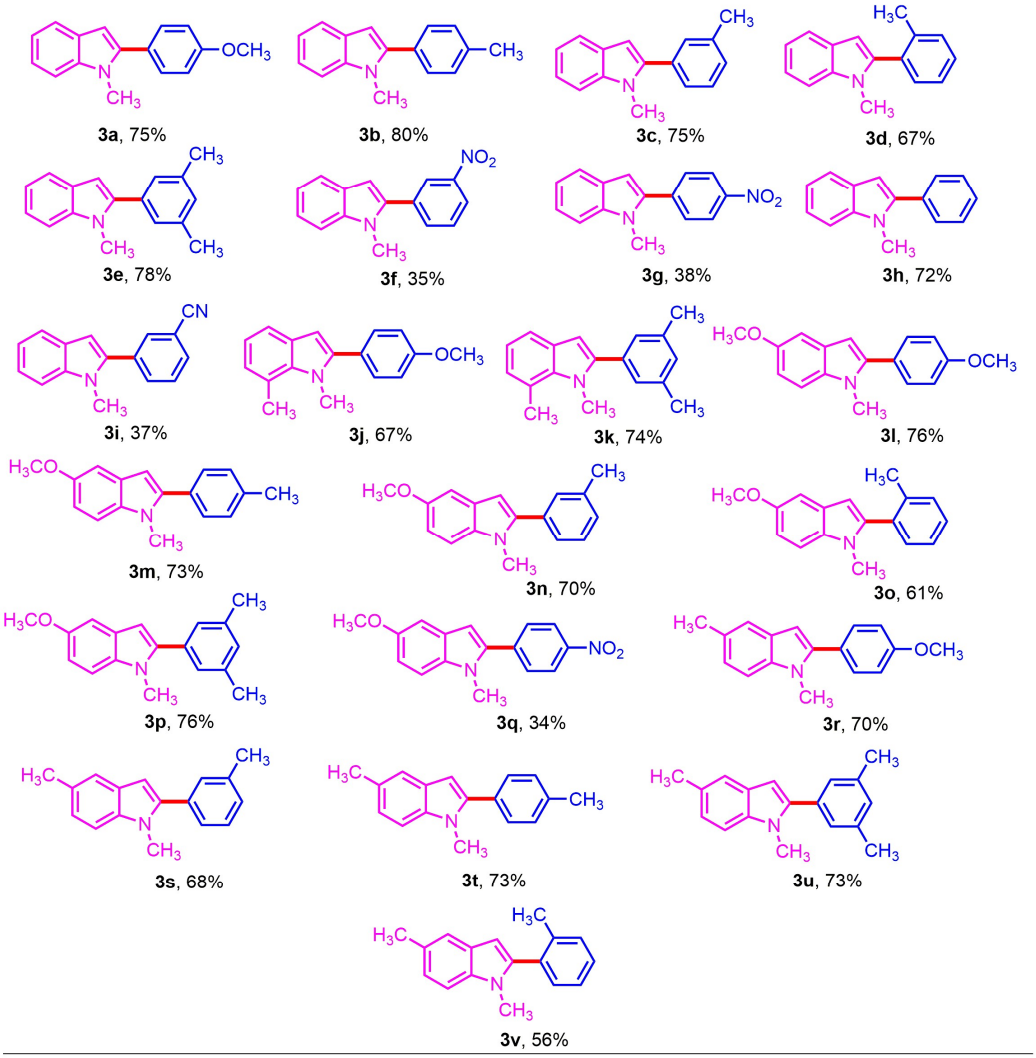
With the optimized reaction condition (entry **16**, Table **3.1**), we have studied the scope and limitations of Pd/C catalyzed C-2 arylation for some electronically and sterically diverse indoles and aryl iodide derivatives (Table **3.2**). The electronic, as well as the steric nature of the aryl iodide derivatives, influenced the yields of the C-2 arylated product. Aryl iodides having electron-donating groups (-CH_3, -OCH_3) at *para*- and *meta*-position afforded C-2 arylated products in good yield (70-80%). Conversely, in presence of electron-withdrawing groups (-NO_2, -CN) in aryl iodides resulted in low yields of arylated products (**3f**, **3g**, **3i**, **3q**, Table **3.2**). Again *ortho*-substituted aryl iodides afforded moderate yields of the C-2 arylated product which might be due to the steric effect of the substituents (**3d**, **3o**, **3v**, Table **3.2**). In the case of *N*-H indole, only the

formation of homocoupling product of aryl iodide was observed. It is worth mentioning that *N*-methylindoles in presence of palladium often generate homocoupling products [24]. However, our protocol successfully furnished C-2 arylated products without any homocoupling products. The substrate studies indicated that the electronic nature of the *N*-methylindole derivatives played an important role in the reaction. Under the developed reaction conditions, *N*-methylindoles having electron-donating groups efficiently furnished the C-2 arylated product with a good yield.

Table **3.2**. Scope exploration of Pd/C catalyzed C-2 selective arylation of indoles with aryl iodide derivatives[a]



1 **2** **3**



3a, 75% **3b**, 80% **3c**, 75% **3d**, 67%

3e, 78% **3f**, 35% **3g**, 38% **3h**, 72%

3i, 37% **3j**, 67% **3k**, 74% **3l**, 76%

3m, 73% **3n**, 70% **3o**, 61%

3p, 76% **3q**, 34% **3r**, 70%

3s, 68% **3t**, 73% **3u**, 73%

3v, 56%

[a]Reaction conditions: **1** (1 equiv.), **2** (1.2 equiv.), Pd/C (20 wt%), CsOAc (2 equiv.), DMA (2 mL)

3.3.3 Heterogeneity test

To confirm the heterogeneous nature of the catalyst, a hot filtration test was performed. In this test, initially, a reaction tube was charged with Pd/C (10 wt%), and CsOAc (2 equiv.) in DMA (2 mL) and stirred at 125 °C for 12 hours. After that, the reaction mixture was filtered and to that filtrate, *N*-methylindole (1 equiv.) and 4-Iodoanisole (1.2 equiv.) were added. After 24 hours of stirring at 125 °C, a trace amount of product formation was observed. Additionally, the inductively coupled plasma optical emission spectrometry (ICP-OES) analysis of the liquid phase revealed that the level of residual Pd is less than 1 ppm. This indicates the heterogeneous nature of the used catalyst.

3.3.4 Reusability test

In the case of heterogeneous catalysis, the reusability of the catalyst is an important factor. In our methodology, we have reused the catalyst up to four cycles (Figure **3.1**). There was a little change in reactivity of the catalyst over the repeated cycles which might be due to the physical loss of the catalyst. In this test, the reaction mixture was centrifuged and then washed with ethyl acetate, and the residue obtained was dried in a vacuum desiccator. The dried catalyst was again used for the next cycle.

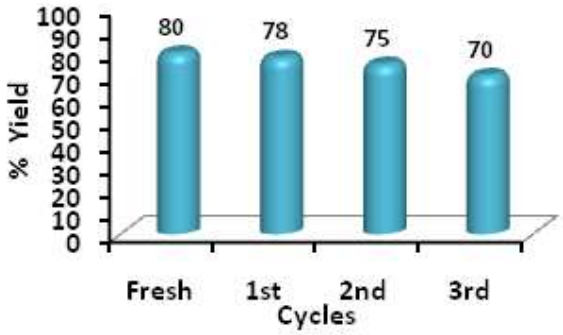
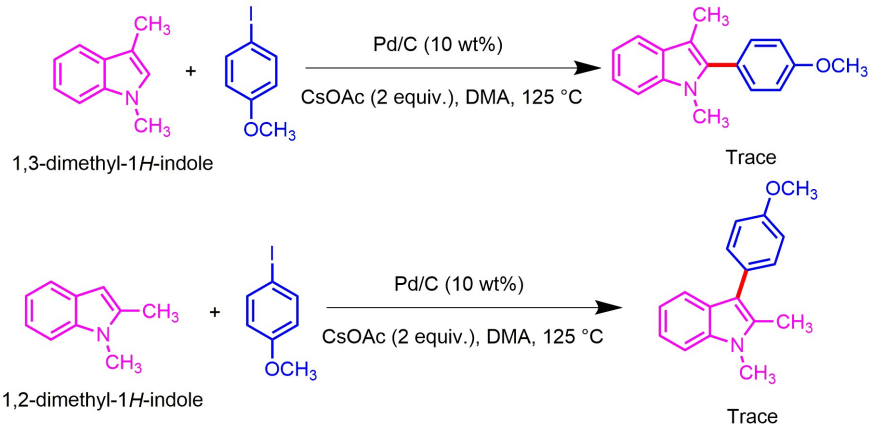


Figure **3.1**. Reusability of the catalyst over four cycles

3.3.5 Control experiment

For a better understanding of the mechanistic pathway, we have carried out two control experiments (Scheme **3.2**). In the first experiment, 1,3-dimethyl-1*H*-indole in reaction

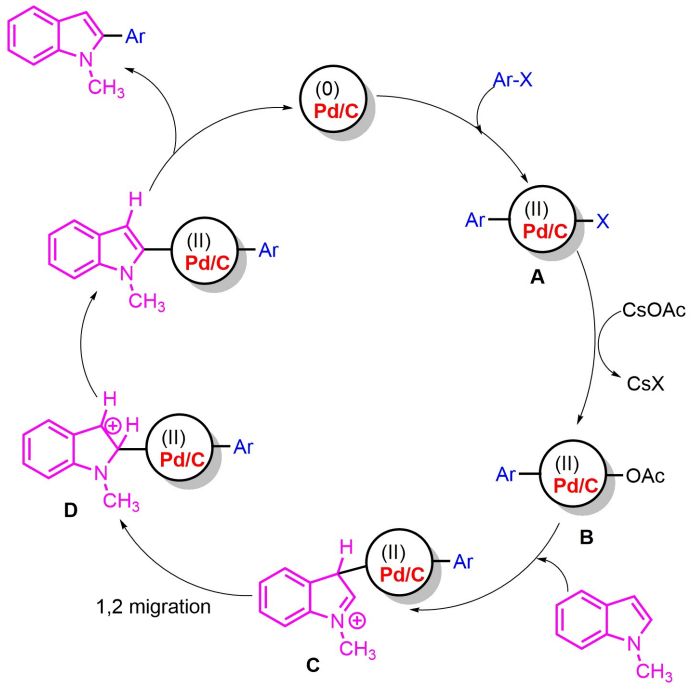
with 4-Iodoanisole furnished a trace amount of C-2 arylated product. Similarly, in the second reaction, 1,2-dimethyl-1*H*-indole with 4-Iodoanisole also afforded a trace amount of the C-3 arylated product. This indicates that initially electrophilic palladation takes place at the highly nucleophilic C-3 position of *N*-methylindole which then undergoes 1,2 migration to form the desired product.



Scheme **3.2**. Control experiments

3.3.6 Plausible mechanism

From the experimental observation and literature reports [7,13], we have proposed the possible mechanism which is shown in Scheme **3.3**. Initially, Pd(II) species (**A**) is generated by the reaction of Pd/C with aryl iodide, which on further reaction with CsOAc base releases the CsI by forming aryl Pd(II) acetate species **B**. The species **B** on reaction with *N*-methylindole undergoes electrophilic palladation at C-3 to form intermediate **C** which then forms another intermediate **D** *via* 1,2 migration. The intermediate **D** finally furnishes the C-2 arylated product after reductive elimination and regenerates the catalyst. The acetate ion from CsOAc base favors the 1,2 migration to stabilize the N-atom of indole.

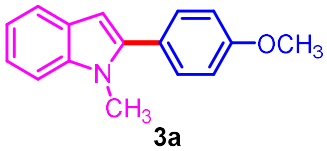


Scheme **3.3**. Possible mechanism for C-2 selective arylation

3.4 Conclusion

In summary, we have developed a new catalytic methodology for C-2 arylation of *N*-methylindole derivatives with aryl iodides using heterogeneous, reusable, and easily available Pd/C catalyst. This methodology furnishes C-2 selective direct functionalization of *N*-methylindoles without using ligand and directing group. Furthermore, under additive (acid and metallic silver) free conditions, this protocol is well-tolerable to the electron-rich substrates and results in good yields of the C-2 arylated product. The catalyst can be reused up to four catalytic cycles with the retention of its catalytic activity.

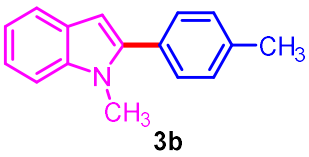
3.5 ^{1}H and ^{13}C NMR analytical data



3a

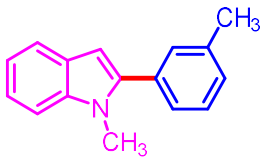
2-(4-methoxyphenyl)-1-methyl-1*H*-indole (3a): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.54 (d, J = 7.8 Hz, 1H), 7.40–7.33 (m, 2H), 7.26 (d, J = 8.2 Hz, 1H), 7.15 (m, 1H), 7.05 (t, J = 7.4 Hz, 1H), 6.95–6.85 (m, 2H), 6.42 (s, 1H), 3.78 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.5, 141.5,

138.2, 130.7, 128.0, 125.3, 121.4, 120.3, 119.8, 114.0, 109.6, 101.1, 55.4, 31.1.



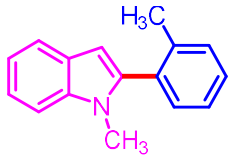
3b

1-methyl-2-(*p*-tolyl)-1*H*-indole (3b): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.69–7.62 (m, 1H), 7.45–7.40 (m, 2H), 7.38 (m, 1H), 7.33–7.24 (m, 3H), 7.16 (m, 1H), 6.56 (d, J = 0.7 Hz, 1H), 3.76 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 142.1, 138.4, 137.9, 129.4, 129.3, 128.1, 121.7, 120.5, 119.8, 109.8, 101.4, 31.7, 21.7.



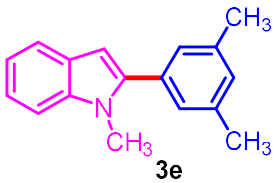
3c

1-methyl-2-(*m*-tolyl)-1*H*-indole (3c): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66–7.62 (m, 1H), 7.39–7.29 (m, 4H), 7.27–7.21 (m, 2H), 7.18–7.12 (m, 1H), 6.61–6.53 (m, 1H), 3.75 (s, 3H), 2.44 (t, J = 3.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 141.8, 138.4, 138.3, 132.9, 130.3, 130.2, 128.5, 128.0, 126.5, 121.7, 120.5, 119.9, 109.7, 101.6, 31.2, 22.1.



3d

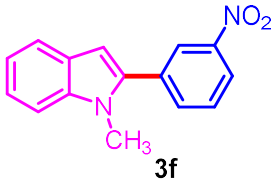
1-methyl-2-(*o*-tolyl)-1*H*-indole (3d): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.64 (d, J = 7.8 Hz, 1H), 7.37–7.21 (m, 6H), 7.15 (t, J = 7.4 Hz, 1H), 6.44 (s, 1H), 3.51 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 140.6, 138.1, 137.3, 132.6, 131.2, 130.1, 128.7, 128.1, 125.6, 121.3, 120.4, 119.7, 109.5, 101.6, 30.4, 20.1.



3e

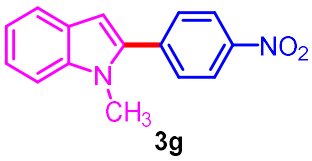
2-(3,5-dimethylphenyl)-1-methyl-1*H*-indole (3e): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 (d, J = 7.8 Hz, 1H), 7.31 (m, 1H), 7.24–7.20 (m, 1H), 7.15–7.10 (m, 3H), 7.01 (d, J = 8.7 Hz, 1H), 6.54–6.46 (m, 1H), 3.71 (d, J = 10.4 Hz, 3H), 2.41–2.33 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 142.0,

138.4, 138.1, 132.8, 129.7, 128.1, 127.3, 121.6, 120.5, 119.9, 109.7, 101.5, 31.3, 21.5.



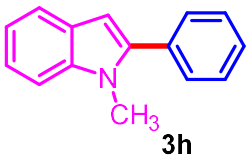
3f

1-methyl-2-(3-nitrophenyl)-1*H*-indole (3f): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.38 (t, J = 1.9 Hz, 1H), 8.29–8.21 (m, 1H), 7.88–7.81 (m, 1H), 7.70–7.62 (m, 2H), 7.38 (m, 1H), 7.34–7.28 (m, 1H), 7.22–7.13 (m, 1H), 6.67 (m, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 148.5, 138.9, 138.8, 135.1, 134.6, 129.6, 127.8, 123.8, 122.8, 122.6, 121.1, 120.5, 109.9, 103.4, 31.7.



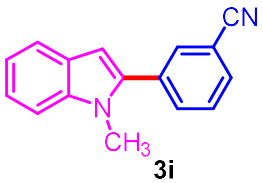
3g

1-methyl-2-(4-nitrophenyl)-1*H*-indole (3g): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.32 (d, J = 8.9 Hz, 2H), 7.68 (d, J = 8.9 Hz, 3H), 7.39 (d, J = 8.3 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.18 (m, 1H), 6.71 (s, 1H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.5, 139.2, 130.1, 128.4, 124.3, 123.4, 121.7, 120.5, 110.5, 104.7, 100.1, 31.7.



3h

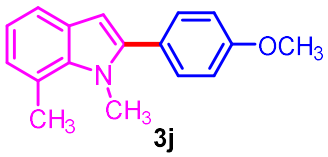
1-methyl-2-phenyl-1*H*-indole (3h): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.63 (m, 1H), 7.53–7.34 (m, 6H), 7.25 (s, 1H), 7.14 (m, 1H), 6.56 (s, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 141.6, 138.4, 132.9, 129.4, 128.5, 128.0, 127.9, 121.7, 120.5, 119.9, 109.6, 101.7, 31.2.



3i

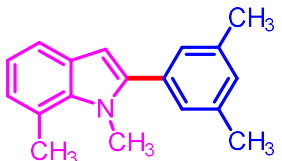
3-(1-methyl-1*H*-indol-2-yl)benzonitrile (3i): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.73–7.63 (m, 2H), 7.61–7.55 (m, 2H), 7.50 (t, J = 7.8 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.24–7.18 (m, 1H), 7.11–7.06 (m, 1H), 6.53 (s, 1H), 3.66 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 138.8, 138.7, 134.2,

133.4, 132.5, 131.2, 129.5, 127.7, 122.6, 120.9, 120.3, 118.6, 112.9, 109.8, 103.1, 31.3.



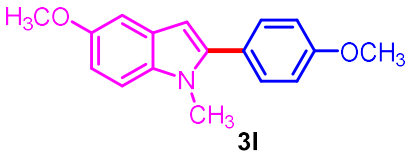
3j

2-(4-methoxyphenyl)-1,7-dimethyl-1*H*-indole (3j): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.47–7.38 (m, 5H), 6.99–6.91 (m, 2H), 6.44 (s, 1H), 3.89–3.83 (d, 6H), 2.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.9, 133.7, 131.1, 129.0, 128.0, 124.7, 121.6, 120.2, 118.7, 114.4, 114.1, 102.1, 55.6, 34.6, 20.4.



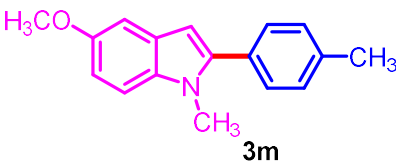
3k

2-(3,5-dimethylphenyl)-1,7-dimethyl-1*H*-indole (3k): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 (m, 1H), 7.09 (s, 2H), 7.05–6.89 (m, 3H), 6.48 (s, 1H), 3.91 (s, 3H), 2.78 (d, J = 7.2 Hz, 3H), 2.38 (d, J = 5.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 143.1, 138.0, 137.7, 133.0, 129.6, 129.0, 127.5, 124.6, 121.5, 120.0, 118.7, 102.3, 34.6, 21.4, 20.3.



3l

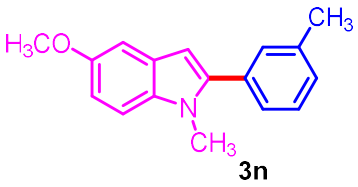
5-methoxy-2-(4-methoxyphenyl)-1-methyl-1*H*-indole (3l): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.43–7.38 (m, 2H), 7.24–7.20 (m, 1H), 7.08 (d, J = 2.4 Hz, 1H), 7.01–6.96 (m, 2H), 6.91–6.86 (m, 1H), 6.42 (s, 1H), 3.86 (t, J = 3.6 Hz, 6H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.4, 154.4, 142.0, 133.6, 130.6, 128.3, 125.4, 114.0, 111.6, 110.3, 102.1, 100.7, 56.0, 55.4, 31.2.



3m

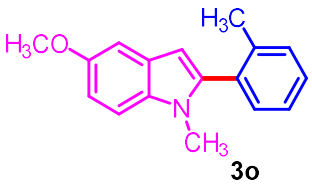
5-methoxy-1-methyl-2-(*p*-tolyl)-1*H*-indole (3m): ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.43 (d, J = 7.4 Hz, 1H), 7.33–7.22 (m, 3H), 7.14 (s, 1H), 7.06–6.92 (m, 2H), 6.52–6.43 (m, 1H), 3.91 (d, J = 1.0 Hz, 2H), 3.75 (d, J = 1.0 Hz, 2H), 2.45 (d, J = 17.5

Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 154.2, 142.1, 137.6, 133.6, 129.9, 129.2, 129.1, 128.2, 111.8, 109.9, 102.3, 100.8, 55.9, 31.1, 21.2.



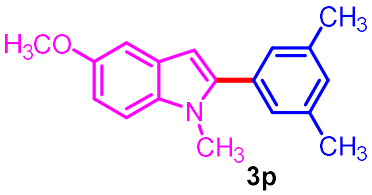
3n

5-methoxy-1-methyl-2-(*m*-tolyl)-1*H*-indole (3n): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.35–7.17 (m, 4H), 7.11–7.07 (m, 1H), 6.94–6.84 (m, 1H), 6.47–6.36 (m, 1H), 3.85 (d, J = 8.0 Hz, 3H), 3.71 (d, J = 20.5 Hz, 3H), 2.37 (d, J = 37.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 154.6, 138.4, 133.1, 130.2, 129.5, 128.8, 128.6, 126.6, 112.0, 110.5, 110.1, 102.5, 101.4, 100.6, 56.2, 31.5, 21.7.



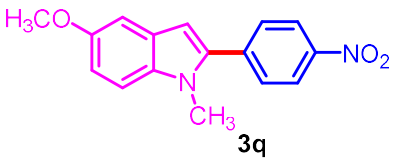
3o

5-methoxy-1-methyl-2-(*o*-tolyl)-1*H*-indole (3o): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39–7.22 (m, 5H), 7.12 (t, J = 3.0 Hz, 1H), 6.92 (m, 1H), 6.41–6.32 (m, 1H), 3.86 (d, J = 10.7 Hz, 3H), 3.49 (d, J = 13.7 Hz, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 154.3, 141.1, 138.0, 132.7, 132.6, 131.1, 130.1, 128.6, 128.3, 125.6, 111.5, 110.2, 102.2, 101.2, 56.0, 30.5, 20.1.



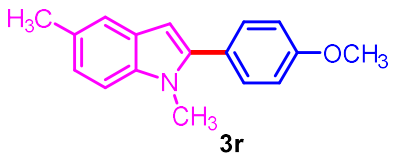
3p

2-(3,5-dimethylphenyl)-5-methoxy-1-methyl-1*H*-indole (3p): ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.18–7.11 (m, 1H), 7.05–6.93 (m, 4H), 6.81 (m, 1H), 6.38 (s, 1H), 3.78 (d, J = 6.7 Hz, 3H), 3.62 (d, J = 8.4 Hz, 3H), 2.31 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 154.3, 142.5, 138.0, 133.8, 132.8, 129.5, 129.3, 128.3, 127.1, 111.7, 110.3, 102.2, 101.1, 56.0, 31.3, 21.4.



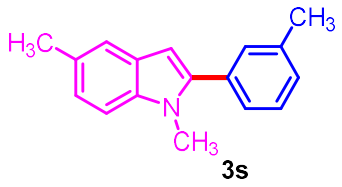
3q

5-methoxy-1-methyl-2-(4-nitrophenyl)-1*H*-indole (3q): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.34 (m, 2H), 7.71 (m, 4H), 6.97 (m, 2H), 3.86 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.3, 145.4, 139.4, 135.0, 129.6, 128.6, 124.6, 124.1, 113.8, 110.9, 103.9, 102.5, 56.1, 31.9.



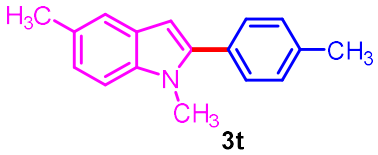
3r

2-(4-methoxyphenyl)-1,5-dimethyl-1*H*-indole (3r): ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.42–7.31 (m, 4H), 7.19–7.15 (m, 1H), 7.01–6.87 (m, 4H), 6.34 (s, 1H), 3.78 (d, J = 11.1 Hz, 3H), 3.62 (s, 3H), 2.41 (d, J = 22.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 159.4, 141.5, 136.6, 130.6, 129.0, 127.8, 125.5, 123.0, 119.9, 113.9, 109.2, 100.5, 55.4, 31.1, 21.5.



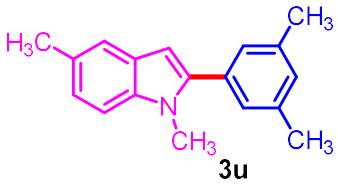
3s

1,5-dimethyl-2-(*m*-tolyl)-1*H*-indole (3s): ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.40 (s, 1H), 7.31 (m, 3H), 7.21 (m, 2H), 7.05 (t, J = 7.0 Hz, 1H), 6.45 (s, 1H), 3.70 (s, 3H), 2.45 (d, J = 6.2 Hz, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 141.8, 138.2, 136.9, 133.0, 130.1, 129.0, 128.6, 128.4, 128.3, 126.4, 123.2, 120.1, 109.3, 101.1, 31.3, 21.6, 21.5.



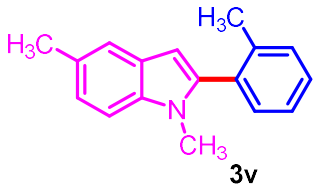
3t

1,5-dimethyl-2-(*p*-tolyl)-1*H*-indole (3t): ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.45 (d, J = 8.3 Hz, 3H), 7.34–7.26 (m, 3H), 7.11 (d, J = 8.3 Hz, 1H), 6.50 (s, 1H), 3.76 (s, 3H), 2.51 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 141.6, 137.5, 136.7, 130.0, 129.1, 129.0, 128.9, 128.1, 123.0, 119.9, 109.1, 100.7, 31.1, 21.3, 21.2.



3u

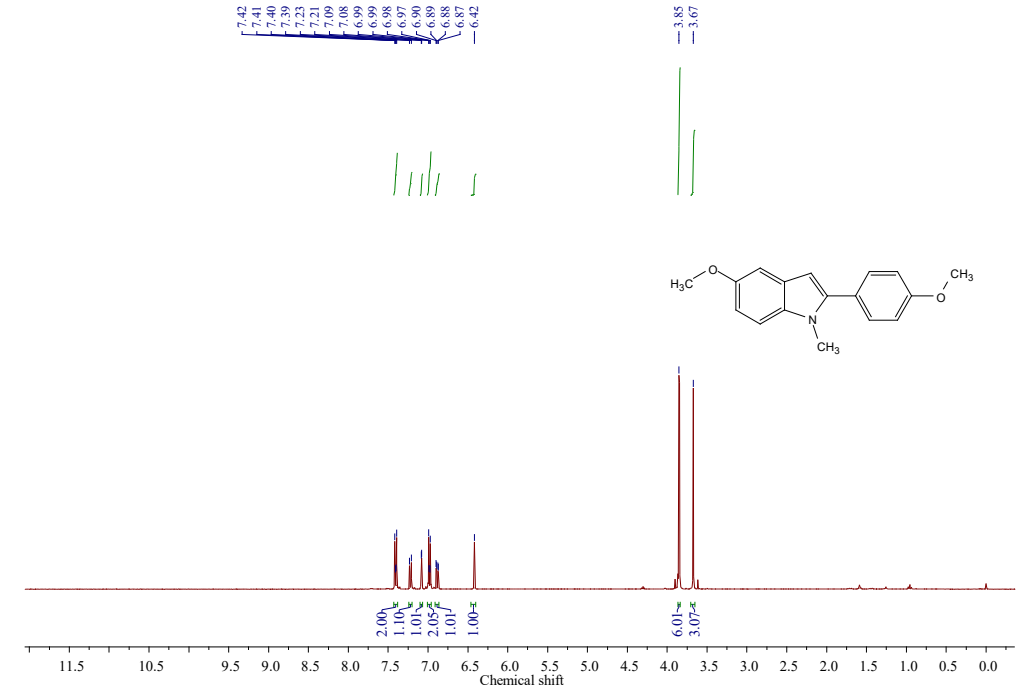
2-(3,5-dimethylphenyl)-1,5-dimethyl-1*H*-indole (3u): ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.50 (d, J = 7.4 Hz, 1H), 7.36–7.28 (m, 1H), 7.24–7.18 (m, 2H), 7.17–7.10 (m, 2H), 6.54 (d, J = 8.0 Hz, 1H), 3.87–3.72 (m, 3H), 2.58–2.53 (m, 3H), 2.53–2.37 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 141.9, 137.9, 136.8, 132.8, 129.4, 128.9, 128.2, 127.1, 123.0, 120.0, 109.2, 100.9, 31.1, 21.4, 21.3.

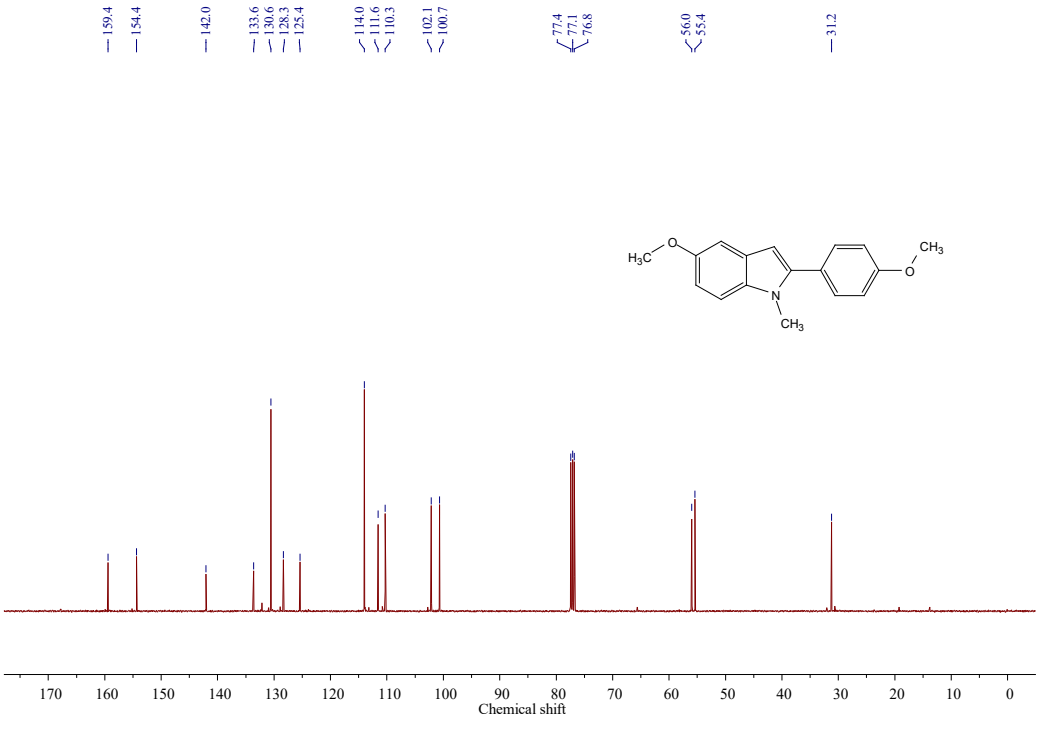


3v

1,5-dimethyl-2-(*o*-tolyl)-1*H*-indole (3v): ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.50 (s, 1H), 7.44–7.26 (m, 5H), 7.14 (d, J = 8.3 Hz, 1H), 6.42 (d, J = 2.7 Hz, 1H), 3.52 (m, 3H), 2.62–2.46 (m, 3H), 2.31–2.19 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 140.5, 138.0, 135.7, 132.6, 131.0, 130.0, 128.8, 128.5, 128.2, 125.4, 122.8, 120.0, 109.0, 100.9, 30.3, 21.4, 19.9.

^{1}H and ^{13}C NMR spectra of 5-methoxy-2-(4-methoxyphenyl)-1-methyl-1*H*-indole





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