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COMMUNICATION

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Indolylbenzimidazole-based ligands catalyze the coupling of arylboronic acids with aryl halides

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A novel class of compounds bearing indole and benzimidazole rings was designed and easily synthesized from 2-indolecarboxylic acid and *o*-phenylenediamine. The catalytic system derived from a 2-indolylbenzimidazole-based ligand and $Pd(OAc)_2$ *in situ* could lead to complete conversion of aryl bromides at 0.5 mol% Pd loading under mild reaction conditions. In the presence of a catalyst, sterically hindered biaryls were selectively generated in excellent yields by adjusting reaction parameters through the coupling of arylboronic acids with aryl halides. The efficiency of this reaction was demonstrated by its compatibility with various functional groups.

KEYWORDS
aryl chloride, benzimidazole, biaryls, indole, Suzuki–Miyaura coupling

1 | INTRODUCTION

The Suzuki–Miyaura coupling reaction is one of the most efficient methods for the construction of C—C bonds.[1] This reaction is typically performed under catalysis using transition metals coordinated to ligands. The development of effective catalytic methods for synthesizing sterically hindered biaryls is attractive because biaryl compounds containing *ortho* substituents are used in pharmaceutical, material and agricultural chemistry.[2] Many phosphorus donor ligands[3] and *N*-heterocyclic carbenes[4] have been synthesized and introduced in the palladium (Pd)-catalyzed Suzuki–Miyaura coupling reaction. In addition, palladacycles have attracted considerable attention in catalytic applications because of their stability in air, high catalytic activity, longevity and recyclability.[5] Compared with phosphorus- and sulfur-based palladacycles, nitrogen-based palladacycles can be generated more easily because starting materials for nitrogen-based palladacycles are more readily available. Moreover, nitrogen substrates are stable in air and can be easily handled compared with phosphorus substrates that require tedious synthetic steps for their preparation. In 1999, Weissman and Milstein first reported the use of NC-palladacycles in Suzuki–Miyaura coupling reactions with excellent yields.[6] Many NC-palladacycles have been developed for cyclopalladation with in the past few decades.[5c,7] These strong σ-donor ligands can strongly coordinate with Pd, facilitating both oxidative addition and reductive elimination steps in the catalytic cycle, and their thermal stability can prevent the necessity of additional ligands.

In 1993, Williams and co-workers reported the structure of a trinuclear complex that was synthesized using a cyclometalation reaction of Pd(II) with benzimidazolylbenzene derivatives.[8] In 2005, Reddy and Krishna described the synthesis of an NC-palladacycle of *N*-methyl-2-phenylbenzimidazole.[9] These complexes showed satisfactory yields when examined in Heck reactions. In 1995, Cenini and co-workers first described the synthesis of 5- and 6-membered indole-fused *ortho*-platinacycles.[10] New cyclometallated Pd(II) or Pt(II) complexes with indole derivatives were synthesized because indole is a π-excessive system with a hydrogen-bond donor atom.[11] Furthermore, in 2005, Tollari and co-workers developed several palladacycle and platinacycle complexes juxtaposed with a pyridine and an indole system.[11a] They found that a new M—C bond could be formed between Pd and C-3 of the indole

ring if *N*-substituted indole was used; otherwise, an N–M–N coordination complex would be formed. To the best of our knowledge, no studies have been reported related to ligands containing an indole and benzimidazole backbone in the Suzuki–Miyaura coupling reaction.

In the present paper, we describe the synthesis of a new class of 2-indolylbenzimidazole derivatives (**1**; Figure 1) and their application in the Suzuki–Miyaura coupling reaction. These compounds as a ligands in the Suzuki–Miyaura coupling reaction exhibit the following characteristics: (1) the nitrogen atom lone pair in the benzimidazole ring can efficiently bind to a metal center; (2) M—C bond formation between Pd and C-3 of the indole ring can be accomplished easily; and (3) substituents in benzimidazole and indole rings induce electronic and steric effects.

2 | RESULTS AND DISCUSSION

The ligand backbone, 2-(1*H*-indol-2-yl)-1*H*-benzo[*d*]imidazole (**2**), could be constructed by a direct assembly of commercially available and inexpensive *o*-phenylenediamine and indole-2-carboxylic acid in the presence of sulfuric acid in ethylene glycol at reflux temperature with a 94% yield (Scheme 1).[12] Subsequently, compounds **1c**–**1e** were obtained through the dialkylation of **2** with corresponding alkyl halides using a strong base, KOH. Because of the difference in acidity between indole and benzimidazole, compound **2** was reacted with one equivalent of bromoethane in dimethylformamide (DMF) using a weak base, K_2CO_3, to obtain monoalkylated compound **1a** in 90% yield. In addition, ligand **1b** was synthesized through the condensation of compound **3** with *o*-phenylenediamine in the presence of sulfuric acid in 60% yield. These new ligand backbones possess tuneable electronic and steric properties, low toxicity and air stability and can be easily prepared.

We applied a general protocol for the coupling of aryl bromides with arylboronic acids using 4-bromoanisole (**7a**) and phenylboronic acid (**8a**) as model substrates (Table 1). The coupling product **9aa** was obtained in the presence of 1 mol% $Pd(OAc)_2$ and 3 mol% ligands **1** at 110 °C. The result indicates that the *N*-substituent of the indole moiety (**1b**) is more important than that of the

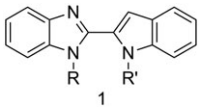

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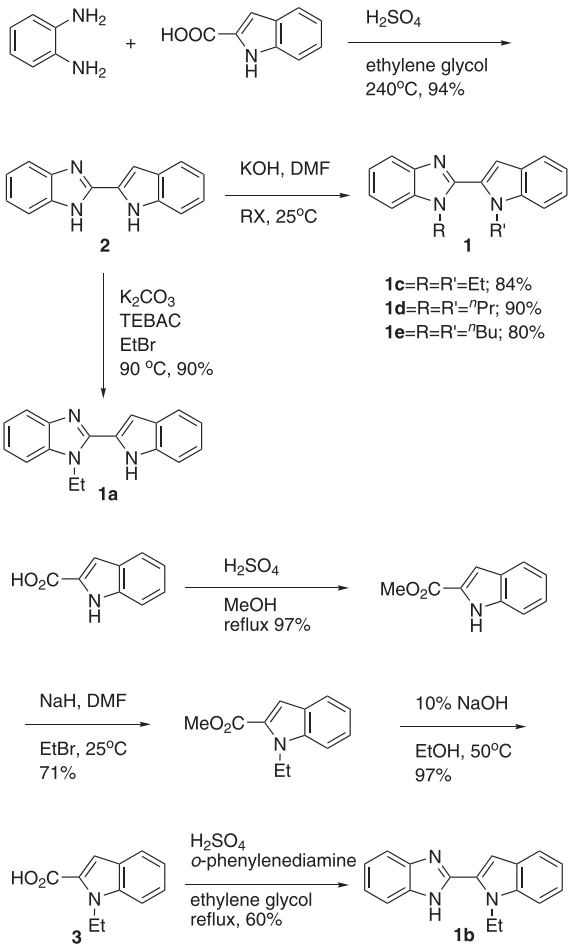
FIGURE 1 Structure of new 2-indolylbenzimidazole ligands

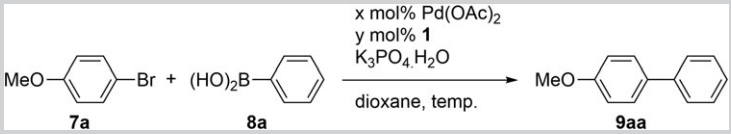


SCHEME 1 Synthesis of 2-indolylbenzimidazole-based ligands (**1**)

benzimidazole moiety (**1a**) (entries 1 and 2). According to the report of Tollari and co-workers,[11a] the speculated N,N-chelate complex **4** between ligand **1a** and a metal ion may be formed *in situ*; by contrast, the proposed ligand **1b** or **1c** may bind to a metal ion as an N,C-chelate ligand through cyclometalation (Figure 2). Regarding the effect of substituents on indole ring and benzimidazole ring (**1c**–**1e**), excellent yields were achieved (entries 3–5). When the reaction temperature was reduced to 60 °C, the catalytic activity of ligands **1c**–**1e** was higher than that of ligand **1b** (entries 6–9). Because of the required preparation and costs, **1c** was selected to optimize the reaction conditions. Upon probing the metal-to-ligand ratio from 1:3 to 1:1, the ratio of 1:3 provided a comparable yield (entries 7, 10 and 11). Moreover, even after the reduction of Pd loading to 0.5 mol%, an excellent yield (99%) was still obtained in 1 h when Pd–**1c** catalytic system was employed (entry 15).

Through the use of the optimized reaction conditions, a wide range of aryl bromide substrates (**7**) were reacted with aylboronic acids (**8**) to investigate the generality of substrates in the Suzuki–Miyaura coupling reaction.

TABLE 1 Initial screening for optimization of the reaction conditions[a]



Entry	Ligand (mol%)	Pd (mol%)	Temp. (°C)	Yield (%)[b]
1	**1a** (3.0)	1.0	110	46
2	**1b** (3.0)	1.0	110	99
3	**1c** (3.0)	1.0	110	99
4	**1d** (3.0)	1.0	110	99
5	**1e** (3.0)	1.0	110	99
6	**1b** (3.0)	1.0	60	57
7	**1c** (3.0)	1.0	60	99
8	**1d** (3.0)	1.0	60	99
9	**1e** (3.0)	1.0	60	99
10	**1c** (2.0)	1.0	60	64
11	**1c** (1.0)	1.0	60	88
12	**1c** (1.5)	0.5	60	99
13	**1c** (0.3)	0.1	60	25
14[c]	**1c** (1.5)	0.5	60	99
15[d]	**1c** (1.5)	0.5	60	99
16[e]	**1c** (1.5)	0.5	60	49
17[f]	**1c** (3.0)	1.0	25	54

[a]Reaction conditions: **7a** (1.0 mmol), $PhB(OH)_2$ **8a** (1.5 mmol), $Pd(OAc)_2$ (*x* mol%), ligand **1** (*y* mol%), $K_3PO_4{\cdot}H_2O$ (3.0 mmol) and dioxane (3.0 ml) were stirred under N_2 at indicated temperature for 24 h.

[b]Isolated yield.

[c]Reaction was stirred for 6 h.

[d]Reaction was stirred for 1 h.

[e]Reaction was stirred for 0.5 h.

[f]Reaction was stirred for 24 h at 25 °C.

Various aryl bromides were successfully coupled with phenylboronic acid **8a** with excellent yield in the presence of 0.5 mol% Pd loading (Table 2, entries 1–11). Even when deactivated aryl chlorides **7′** were used as substrates, excellent yields were obtained when 1.0 mol% Pd loading was employed at 110 °C (Table 2, entries 2, 4, 6 and 10). Mono-*ortho*-aryl bromides (**7h**–**k**) could be coupled with phenylboronic acid **8a** with excellent yield in the presence of 0.5 mol% Pd loading, except for 2-bromoacetophenone **7h** (Table 2, entries 12–15). To further extend the scope of the new catalytic system, sterically hindered aryl bromides were used to couple with sterically congested arylboronic acids (Table 2, entries 17 and 19–21). The di-*ortho*-substituted biaryl synthesis could be accomplished using 1.0 mol% Pd catalyst with good to excellent yields. In addition, a more hindered biaryl (**9co**) was synthesized at 60 °C using 1.0 mol% Pd loading with 25% yield (Table 2, entry 22). These results demonstrate the high catalytic activity of the Pd–**1c** catalytic system for coupling aryl halides with arylboronic acids.

3 | CONCLUSIONS

We developed a new series of ligands bearing a diversified indolylbenzimidazole scaffold. These ligands can be easily prepared and are stable in air. The catalytic system derived from $Pd(OAc)_2$ and a ligand *in situ* exhibits high activity in C—C bond formation, and it was achieved using 0.5 mol% Pd loading under mild reaction conditions. The catalytic system was observed to be compatible with various functional groups

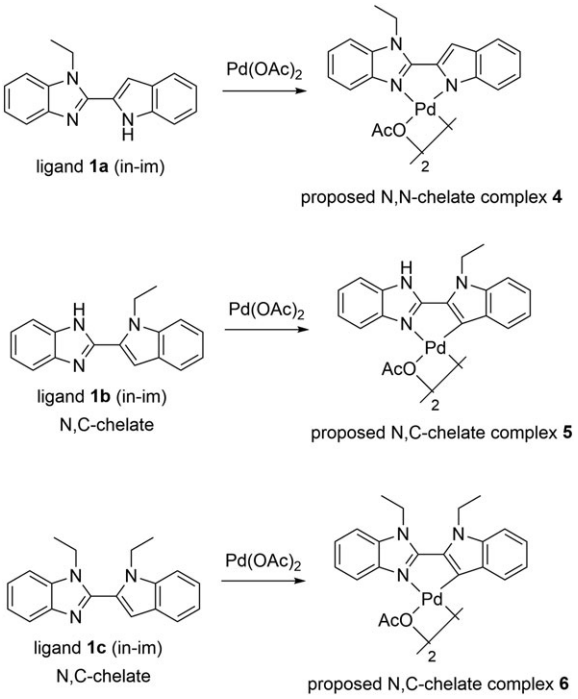


FIGURE 2 Proposed Pd–1 catalytic system

including methoxy, ester, aldehyde and ketone. Notably, we could perform the difficult Pd-catalyzed di- or tri-*ortho*-substituted biaryl synthesis in the presence of the Pd–**1c** catalytic system.

4 | EXPERIMENTAL

4.1 | General Aspects

Anhydrous solvents (tetrahydrofuran, PhMe, *n*-hexane, dioxane) were obtained by distillation over calcium hydride. Reactions were analyzed using pre-coated silica gel 60 (F-254) plates (0.2 mm layer thickness). All products were purified by column chromatography (silica gel, 0.040–0.063 μm) using hexane–ethyl acetate as the eluent. Melting points were determined using a Mel-Temp 1001D (Barnstead/Thermo) digital melting point apparatus and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Varian Mercury 400 spectrometer in $CDCl_3$ solution with chemical shifts given in ppm relative to tetramethylsilane. *J*-values are given in Hz. Chloroform (δ = 7.26 ppm) was used as internal standard in the ^{1}H NMR spectra. The central peak of $CDCl_3$ (δ = 77.0 ppm) was used as internal standard in the ^{13}C NMR spectra. High-resolution mass spectra (HRMS) were recorded using a Finnigan/Thermo Quest MAT 95XL mass spectrometer. Mass spectra were obtained using the electron impact (EI) method.

4.2 | Typical Reaction Procedures

4.2.1 | Procedure for preparation of 2-(1*H*-indol-2-yl)-1*H*-benzo[*d*]imidazole (2)

To a solution of indole-2-carboxylic acid (4.60 g, 28.5 mmol) and *o*-phenylenediamine (3.08 g, 28.5 mmol) in ethylene glycol (28.5 ml) was added slowly sulfuric acid (1.50 ml, 28.5 mmol) at 25 °C. After refluxing for 5 h (monitored by TLC), the resulting mixture was cooled to 25 °C and poured into ice-cold water. The resulting mixture was neutralized with saturated $NaHCO_3$ solution. The brown solid of desired **2** was afforded by filtration (5.79 g, 87%).[12] R_f = 0.4 (EtOAc–*n*-hexane = 1:2); m.p. = 247–250 °C. ^{1}H NMR (DMSO-d_6, 400 MHz, δ, ppm): 12.93 (s, 1H), 11.95 (s, 1H), 7.67–7.62 (m, 2H), 7.53 (d, J = 7.2 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.25–7.14 (m, 4H), 7.03 (t, J = 7.2 Hz, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz, δ, ppm): 146.2, 137.3, 128.7, 128.0, 122.9, 122.2, 119.8, 112.0, 101.7.

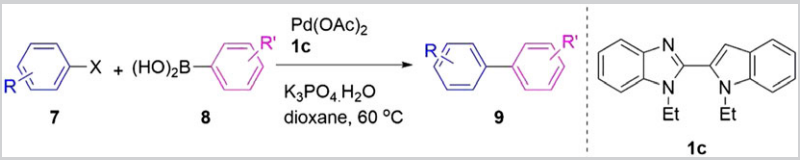
4.2.2 | Procedure for preparation of 1-ethyl-2-(1*H*-indolyl)benzimidazole (1a)

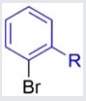
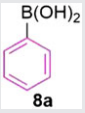
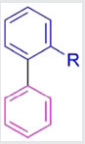
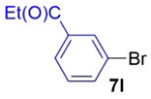
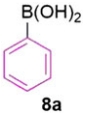
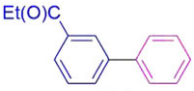
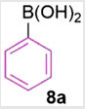
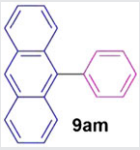
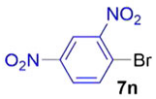
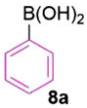
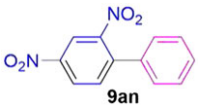
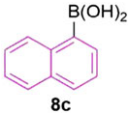
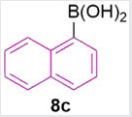
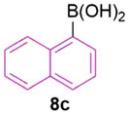
To a solution of **2** (1.01 g, 4.34 mmol), K_2CO_3 (1.80 g, 13.0 mmol) and TEBAC (9.88 mg) in DMF (20 ml) was added slowly bromoethane (0.48 ml, 6.51 mmol) at 25 °C. The resulting mixture was stirred at 90 °C for 4 h (monitored by TLC) and then quenched with water. The aqueous layer was extracted with EtOAc (3 × 20 ml). The combined organic layers were dried over anhydrous $MgSO_4$ and then filtered. The solvent was evaporated *in vacuo* to yield a yellow oil which was purified by chromatography to give brown solid **1a** (0.75 g, 66%). R_f = 0.5 (EtOAc–*n*-hexane = 1:2); m.p. = 168–170 °C. ^{1}H NMR (DMSO-d_6, 400 MHz, δ, ppm): 11.96 (s, 1H), 7.69 (t, J = 8.4 Hz, 3H), 7.51 (d, J = 8.4 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 7.10 (d, J = 1.2 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 4.52 (t, J = 7.2 Hz, 2H), 1.87 (sextet, J = 7.2 Hz, 2H), 0.95 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 146.6, 142.2, 137.0, 136.1, 128.4, 127.0, 123.5, 122.7, 122.6, 121.0, 120.0, 119.1, 112.0, 109.7, 102.7, 46.2, 23.0, 11.3. HRMS-EI (m/z) $[M]^+$ calcd for $C_{17}H_{15}N_3$: 261.1256, found: 261.1261. Anal. Calcd for $C_{17}H_{15}N_3$ (%): C, 78.13; H, 5.79; N, 16.08; found (%): C, 77.91; H, 5.94; N, 15.48.

4.2.3 | Procedure for preparation of methyl indole-2-carboxylate

Indole-2-carboxylic acid (10.0 g, 62.1 mmol) was dissolved in methanol (62 ml). Then H_2SO_4 (5.0 ml, 93.1 mmol) was added dropwise and the mixture was heated to reflux

TABLE 2 Palladium-catalyzed Suzuki–Miyaura coupling of aryl halides[a]



Entry	ArX		$Ar'B(OH)_2$	Product		mol% Pd	Time (h)	%Yield[b]
1		**7a** = R = OMe, X = Br			**9aa**	0.5	1.0	99
2[c]		**7a'** = R = OMe, X = Cl			**9aa**	1.0	24	91
3		**7b** = R = C(O)Me, X = Br			**9ab**	0.5	1.0	99
4[c]		**7b'** = R = C(O)Me, X = Cl			**9ab**	1.0	1.0	97
5		**7c** = R = CHO, X = Br			**9ac**	0.5	1.0	96
6[c]		**7c'** = R = CHO, X = Cl			**9ac**	1.0	24	95
7		**7d** = R = C(O)Et, X = Br			**9ad**	0.5	2.0	99
8		**7e** = R = CO_2Me, X = Br			**9ae**	0.5	2.0	94
9		**7f** = R = NO_2, X = Br			**9af**	0.5	1.0	94
10		**7f'** = R = NO_2, X = Cl			**9af**	0.5	1.0	87
11		**7 g** = R = ^{t}Bu, X = Br			**9ag**	0.5	1.0	99
12		**7 h** = R = C(O)Me			**9ah**	2.0	24	99
13		**7i** = R = CHO			**9ai**	0.5	1.0	94
14		**7j** = R = Me			**9aj**	0.5	24	94
15		**7 k** = R = C(O)N(^{i}Pr)$_2$			**9ak**	0.5	2.0	91
16						1.0	2.0	97
17						0.5	2.0	95
18						0.5	24	98
19						1.0	24	90
20						1.0	24	90
21						1.0	24	70
22						1.0	24	25

[a]Reaction conditions: **7** (1.00 mmol), **8** (1.50 mmol), $K_3PO_4{\cdot}H_2O$ (3.00 mmol), $Pd(OAc)_2$ (mol% as indicated), Pd–**1c** (1:3) and dioxane (3.0 ml) were used.

[b]Isolated yield.

[c]Reaction temperature was 110 °C.

for 24 h. After returning to room temperature, the mixture was washed with saturated $NaHCO_3$ solution (3 × 60 ml) and water (60 ml). The combined organic layer was dried over anhydrous $MgSO_4$ and then filtered. The filtrate was evaporated under reduced pressure to afford methyl indole-2-carboxylate (1.05 g, 97%) as a brown solid. The crude product was used in subsequent reactions without any purification. R_f = 0.4 (EtOAc–*n*-hexane = 1:10); m.p. = 118–120 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 8.95 (s, 1H), 7.79 (dd, J = 8.0, 0.8 Hz, 1H), 7.43 (dd, J = 8.0, 0.8 Hz, 1H), 7.33 (ddd, J = 8.0, 7.2, 0.8 Hz), 7.26–7.23 (m, 1H), 7.16 (ddd, J = 8.0, 7.2, 0.8 Hz), 3.95 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 162.7, 137.0, 127.4, 127.1, 125.4, 122.6, 120.8, 112.0, 108.8, 52.1.

4.2.4 | Procedure for preparation of methyl 1-ethyl-1*H*-indole-2-carboxylate

A solution of sodium hydride (60%, 0.23 g, 9.51 mmol) and methyl indole-2-carboxylate (1.00 g, 5.71 mmol) in DMF (10 ml) was added to a flask, and the flask placed in an ice bath and stirred at 0 °C for 30 min. Bromoethane (0.42 ml, 5.71 mmol) was added, and the reaction was heated to 90 °C for 24 h. The mixture was poured into water, and the product was extracted with EtOAc (3 × 10 ml). The combined organic layers were dried over anhydrous $MgSO_4$ and then filtered. The filtrate was evaporated under reduced pressure to afford methyl 1-ethyl-1*H*-indole-2-carboxylate (0.83 g, 71%) as a clear oil which was purified by silica gel column chromatography. R_f = 0.8 (EtOAc–*n*-hexane = 1:10). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 7.73 (dd, J = 8.0, 0.8 Hz, 1H), 7.45–7.35 (m, 3H), 7.20 (ddd, J = 8.0, 7.2, 0.8 Hz, 1H), 4.66 (q, J = 7.2 Hz, 2H), 3.95 (s, 3H), 1.49 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 161.8, 138.3, 126.3, 125.8, 124.5, 122.3, 120.1, 110.1, 109.8, 50.9, 39.0, 15.1. HRMS-EI (m/z) $[M]^+$ calcd for $C_{12}H_{13}NO_2$: 203.0946, found: 203.0941. Anal. Calcd for $C_{12}H_{13}NO_2$ (%): C, 70.92; H, 6.45; N, 6.89; O, 15.74; found (%): C, 70.88; H, 6.44; N, 6.85; O, 15.69.

4.2.5 | Procedure for preparation of 1-ethylindole-2-carboxylic acid (3)

Methyl 1-ethyl-1*H*-indole-2-carboxylate (0.84 g, 4.15 mmol) was stirred in 10% NaOH (8.30 ml) and ethanol (8 ml) at 50 °C for 5 h. Then ethanol was evaporated under reduced pressure, and the water acidified to pH = 2 with 2 M HCl. The aqueous layer was extracted with EtOAc (3 × 10 ml). The combined organic layers were dried over anhydrous $MgSO_4$ and then filtered. The filtrate was evaporated under reduced pressure to afford **3** (0.76 g, 97%) as a white solid. The crude product was used in subsequent reactions without any purification. M.p. = 152–154 °C. ^{1}H NMR (MeOH-d_4, 400 MHz, δ, ppm): 7.63 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 8.8 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.25 (s, 1H), 7.09 (t, J = 8.0 Hz, 1H), 4.64 (q, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 165.0, 140.2, 128.7, 127.6, 126.0, 123.6, 121.6, 111.8, 111.4, 40.4, 16.1.

4.2.6 | Procedure for preparation of 2-(1-ethyl-1*H*-indol-2-yl)benzo[*d*]imidazole (1b)

To a solution of **3** (0.71 g, 3.75 mmol) and *o*-phenylenediamine (0.41 g, 3.75 mmol) in ethylene glycol (5.0 ml) was added slowly sulfuric acid (0.20 ml, 3.75 mmol) at 25 °C. After refluxing for 5 h (monitored by TLC), the resulting mixture was cooled to 25 °C and poured into ice-cold water. The resulting mixture was neutralized with saturated $NaHCO_3$ solution. The brown solid of desired **1b** was afforded by filtration (0.59 g, 60%). R_f = 0.6 (EtOAc–*n*-hexane = 1:2); m.p. = 148–150 °C. ^{1}H NMR (DMSO-d_6, 400 MHz, δ, ppm): 12.88 (s, 1H), 7.67 (d, J = 8.0 Hz, 2H), 7.59 (d, J = 8.0 Hz, 2H), 7.26–7.23 (m, 4H), 7.10 (t, J = 7.6 Hz, 1H), 4.97 (q, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz, δ, ppm): 145.7, 143.8, 137.6, 134.1, 128.5, 126.9, 123.0, 122.9, 121.7, 121.0, 120.1, 119.0, 111.0, 110.3, 103.8, 15.4. HRMS-EI (m/z) $[M]^+$ calcd for $C_{17}H_{15}N_3$: 261.1266, found: 261.1271. Anal. Calcd for $C_{17}H_{15}N_3$ (%): C, 78.13; H, 5.79; N, 16.08; found (%): C, 76.90; H, 6.51; N, 15.92.

4.3 | General Procedures for Preparation of 2-(1*H*-indolyl)benzimidazole Derivatives 1c–1e

To a solution of **2** (8.79 mmol) and KOH (70.3 mmol) in tetrahydrofuran (20 ml) was added slowly alkyl halide (35.2 mmol) at 25 °C and the resulting mixture stirred at 25 °C for 24 h (monitored by TLC) and then quenched with water. The aqueous layer was extracted with EtOAc (3 × 20 ml). The combined organic layers were dried over anhydrous $MgSO_4$ and then filtered. The solvent was evaporated *in vacuo* to afford a yellow oil which was purified by chromatography on silica gel.

4.3.1 | 1-Ethyl-2-(1-ethylindolyl)benzimidazole (1c)

2-(1*H*-indolyl)benzimidazole (2.05 g, 8.79 mmol), bromoethane (2.61 ml, 35.2 mmol) and potassium hydroxide (3.94 g, 70.3 mmol) were used to afford **1c** (1.63 g, 64%) as a bright yellow solid. R_f = 0.7

(EtOAc–*n*-hexane = 1:2); m.p. = 99–101 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 7.87 (d, J = 7.2 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.39–7.31 (m, 3H), 7.19 (t, J = 7.6 Hz, 1H), 6.83 (s, 1H), 4.55 (q, J = 7.2 Hz, 2H), 4.40 (q, J = 7.2 Hz, 2H), 1.48 (t, J = 7.2 Hz, 3H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 145.5, 143.1, 137.0, 134.5, 127.2, 122.8, 122.8, 121.1, 119.9, 110.0, 109.9, 104.8, 39.2, 38.9, 15.3, 15.1. HRMS-EI (m/z) $[M]^+$ calcd for $C_{19}H_{19}N_3$: 289.1579, found: 289.1578. Anal. Calcd for $C_{19}H_{19}N_3$ (%): C, 78.86; H, 6.62; N, 14.52; found (%): C, 78.95; H, 6.59; N, 14.47.

4.3.2 | 1-Propyl-2-(1-propylindolyl)benzimidazole (1d)

2-(1*H*-indolyl)benzimidazole (1.00 g, 4.29 mmol), 1-bromopropane (1.56 ml, 17.2 mmol) and potassium hydroxide (1.92 g, 34.3 mmol) were used to afford **1d** (0.89 g, 65%) as an orange oil. R_f = 0.7 (EtOAc–*n*-hexane = 1:2). ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 7.89–7.86 (m, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 8.8 Hz, 1H), 7.37–7.31 (m, 4H), 7.19 (t, J = 8.0 Hz, 1H), 6.82 (s, 1H), 4.49 (t, J = 7.2 Hz, 2H), 4.29 (t, J = 7.2 Hz, 2H), 1.90 (sextet, J = 7.6 Hz, 2H), 1.71 (sextet, J = 7.6 Hz, 2H), 0.96 (t, J = 7.6 Hz, 3H), 0.77 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 127.6, 123.2, 122.9, 122.6, 121.6, 120.8, 120.5, 120.4, 120.3, 119.4, 110.6, 110.5, 105.3, 46.6, 46.5, 46.3, 46.1, 24.0, 23.71, 23.65, 23.56, 23.0, 14.5, 11.5. HRMS-EI (m/z) $[M]^+$ calcd for $C_{21}H_{23}N_3$: 3117.1892, found: 317.1897. Anal. Calcd for $C_{21}H_{23}N_3$ (%): C, 79.46; H, 7.30; N, 13.24; found (%): C, 79.33; H, 7.49; N, 12.89.

4.3.3 | 1-Butyl-2-(1-butylindolyl)benzimidazole (1e)

2-(1*H*-indolyl)benzimidazole (1.00 g, 4.29 mmol), 1-bromobutane (1.85 ml, 17.2 mmol) and potassium hydroxide (1.92 g, 34.3 mmol) were used to afford **1e** (0.90 g, 61%) as a brown solid. R_f = 0.6 (EtOAc–*n*-hexane = 1:2); m.p. = 55–57 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, δ, ppm): 7.86–7.84 (m, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.61 (dd, J = 8.0, 0.8 Hz, 2H), 7.37–7.39 (m, 3H), 7.18 (td, J = 8.0, 0.8 Hz, 1H), 6.81 (d, J = 0.4 Hz, 1H), 4.52 (t, J = 7.6 Hz, 2H), 4.33 (t, J = 7.6 Hz, 2H), 1.88–1.80 (m, 2H), 1.69–1.61 (m, 2H), 1.36 (sextet, J = 7.6 Hz, 2H), 1.18 (sextet, J = 7.6 Hz, 2H), 0.92 (t, J = 7.6 Hz, 3H), 0.78 (t, J = 7.2 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz, δ, ppm): 146.0, 143.2, 137.6, 135.0, 127.8, 127.3, 122.9, 122.4, 121.3, 120.2, 120.0, 110.4, 110.2, 105.1, 44.5, 44.0, 32.2, 32.0, 20.1, 20.0, 13.7, 13.6. HRMS-EI (m/z) $[M]^+$ calcd for $C_{23}H_{27}N_3$: 345.2205, found: 345.2195. Anal. Calcd for $C_{23}H_{27}N_3$ (%): C, 79.96; H, 7.88; N, 12.16; found (%): C, 79.96; H, 7.80; N, 12.20.

4.4 | General Procedure for Suzuki–Miyaura Coupling Reaction

All manipulations were carried out under nitrogen using dried solvent. Arylboronic acid **8** (1.50 mmol), aryl halide **7** (1.00 mmol), $K_3PO_4{\cdot}H_2O$ (3.00 mmol), ligands (as indicated) and $Pd(OAc)_2$ (as indicated) were charged into a Schlenk tube. Dry 1,4-dioxane (3.0 ml) was then added. The mixture was stirred at the prescribed temperature for the prescribed time. After completion of the reaction, monitored by TLC, the reaction was quenched by water (3.0 ml). The aqueous layer was extracted with EtOAc (3 × 3.0 ml). The organic layer was dried over anhydrous $MgSO_4$ and then filtered. The solvent was evaporated under reduced pressure and the corresponding crude product of Suzuki–Miyaura coupling reaction was purified by chromatography.

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