Suzuki–Miyaura Cross-Coupling Reaction of Naphthyl Triflate with Indole Boronic Acids Catalyzed by a Recyclable Polymer-Supported N-Heterocyclic Carbene–Palladium Complex Catalyst: Synthesis of Naphthalene-Linked Bis-Heterocycles

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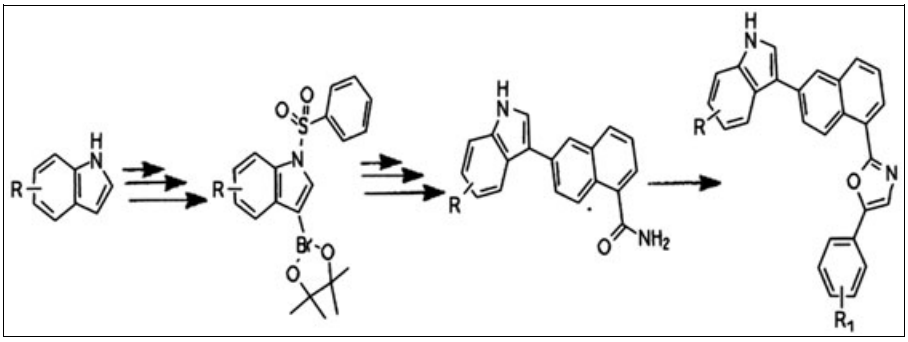

In this study, the Suzuki–Miyaura cross-coupling reaction of naphthyl triflate with indole boronic acids catalyzed by a recyclable polymer-supported Pd–NHC complex catalyst is presented. The polymer-supported catalyst can be reused several times retaining high activity for the transformation. The structures of all the synthesized compounds were established by elemental analysis and from their mass, ^{1}H-NMR, and ^{13}C-NMR spectra.

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INTRODUCTION

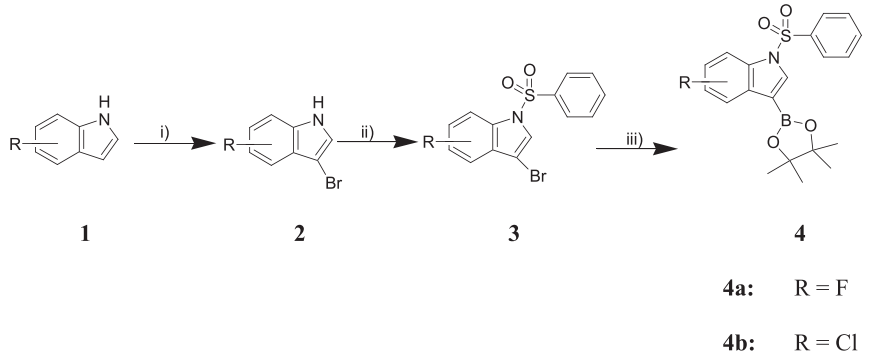
In recent years, attention has been increasingly paid to the synthesis of aromatic bis-heterocyclic compounds that exhibit various biological activities including antibacterial, fungicidal, tuberculostatic, and plant growth–regulative properties [1]. Bis-heterocyclic compounds have numerous applications as electrical materials [2], chelating agents, and metal ligands [3]. Furthermore, it was indicated in several reports [4] that bis-heterocyclic compounds with suitable aryl spacer displayed much better antibacterial activity than heterocyclic compounds.

Among the bis-heterocycles, indole and oxazole have gained importance because of their varied physiological activities. Indole derivatives constitute an important class of therapeutical agents in medicinal chemistry, including anticancer [5], antioxidant [6], antirheumatoidal [7], and anti-HIV [8]. Some of the 2-phenylindolesulfamates are known inhibitors of steroid sulfatase with antiproliferative activity in breast cancer cells [9]. On the other hand, oxazole compounds are useful in pharmaceutical and agricultural chemistry. For example, substituted oxazole derivatives are found to be associated with various biological activities such as antibacterial, antifungal [10], antitubercular [11], and anti-inflammatory activities [12]. Given the biological importance of these individual heterocycles, the authors developed a novel strategy to combine both of these via Suzuki coupling reaction. The palladium-catalyzed Suzuki–Miyaura cross-coupling reaction has evolved as a powerful synthetic tool for the synthesis of unsymmetrical biaryls in both academic laboratories and industries [13–16]. Most of the reported Suzuki–Miyaura reactions are based on the use of aryl halides and aryl boronic acid, and recently, sulfonates and carboxylates as the electrophilic components [17–28]. It is reported in the current investigation that the Suzuki–Miyaura cross-couplings of naphthyl triflate with indole boronic acids can be readily affected with the polystyrene-supported Pd–NHC catalyst, which shows high efficiency and can be easily recovered and reused several times retaining high activity.

RESULTS AND DISCUSSION

The preparation of indole boronic acid **4** was carried out using the procedure shown in Scheme 1. To a solution of substituted indole **1** in dimethyl formamide (DMF), bromine was slowly added, and the resulting compound **2** was treated with phenyl sulfonyl chloride using DMF to

Scheme 1. Synthesis of indole boronic acid. Reagents and conditions: (i) DMF, Br_2, r.t., 0.3 h; (ii) NaOH, $PhSO_2Cl$, DMF, 0°C, 1 h; (iii) CH3COOK, bis (pinacolato)diborane, Pd(dppf)Cl_2, DME 125°C, 0.3 h.



1 **2** **3** **4**

4a: R = F

4b: R = Cl

obtain compound **3**. Compound **3** was irradiated at 125°C in the presence of bis(pinacolato)diborane, potassium acetate, Pd(dppf)Cl_2, and dimethoxy ethane to get compound **4**. The reaction is found to be highly rapid in case of compound **4a** as moderate to high yields of the product can be isolated within 20–30 min of the reaction at ambient temperature.

The synthesis of naphthyl triflate was performed according to the procedure outlined in Scheme 2. 6-Methoxy tetralone **5** was reacted with trimethylsilyl cyanide and zinc iodide in toluene to give compound **6**, which on reduction with Pd on carbon in *p*-cymene results in the formation of compound **7**. Compound **7** treated with boron tribromide in methylene chloride (DCM) yielded compound **8**, which on treatment with pyridine and triflic anhydride yielded naphthyl triflate **9**.

The polystyrene-supported Pd–NHC catalyst **I** was prepared according to the reported procedure [29] Scheme 3. The Pd loading was determined to be 0.1 mmol/g by inductively coupled plasma-atomic emission spectrometry (ICP-AES).

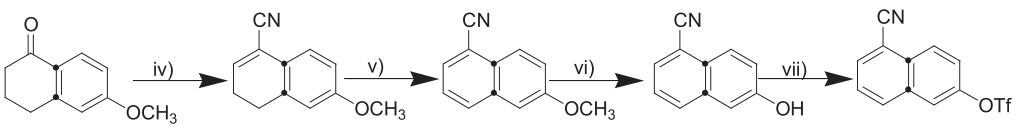
The Suzuki–Miyaura cross-coupling of naphthyl triflate and indole boronic acids catalyzed by the polymer-supported Pd–NHC catalyst was investigated in detail with the coupling of naphthyl triflate and indole boronic acid as a model reaction Scheme 4. As described for the homogeneous catalytic conditions [30], a Lewis acid was essential for the formation of the naphthalene-linked bis-heterocycles. Without tetra butyl ammonium fluoride (TBAF) and tetrahydrofuran (THF), no product was observed. The compounds **4** and **9** are combined by Suzuki coupling reaction to yield intermediate **10**, which on treatment with silica gel G-sulfuric acid yielded amide **11**. Compound **11** was reacted with substituted phenacyl bromide to form title compounds.

The effect of catalyst observed on the cross-coupling reaction based on the amount of the polymer-supported Pd–NHC catalyst used in the reaction is of importance. No product was observed in the absence of catalyst. The yield of the corresponding title compounds increased with the catalyst loading. A high yield of 98% was obtained when 2.0 mol % Pd was used; however, Pd loadings greater than 2.0 mol % Pd did not lead to improved yields. After optimizing the amount of catalyst, solvent, substrate ratio, and temperature, the recyclability of the polymer-supported Pd–NHC catalyst for the Suzuki–Miyaura cross-coupling reactions naphthyl triflate and indole boronic acid was investigated. The catalyst could be reused six times and can still retain high activity after separation, washing, and drying under vacuum, with the same reaction conditions [31].

EXPERIMENTAL

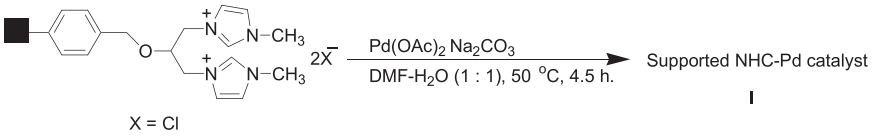
General. All other chemicals were of analytical grade and were used without further purification. ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on a Bruker spectrometer operating at 400 and 100 MHz, respectively. The IR spectra were recorded on a FTIR spectrometer using KBr

Scheme 2. Synthesis of naphthyl triflate. Reagents and conditions: (iv) TMSCN, ZnI, POCl3, pyridine, toluene r.t., 24 h; (v) Pd/C, *p*-cymene, 55–60°C, 24 h; (vi) BBr_3, DCM, 0°C to r.t.; (vii) DCM, pyridine, trifluoromethanesulfonic anhydride, 0°C, 5 h.



5 **6** **7** **8** **9**

Scheme 3. Synthesis of the polymer-supported NHC–Pd catalyst **1**.



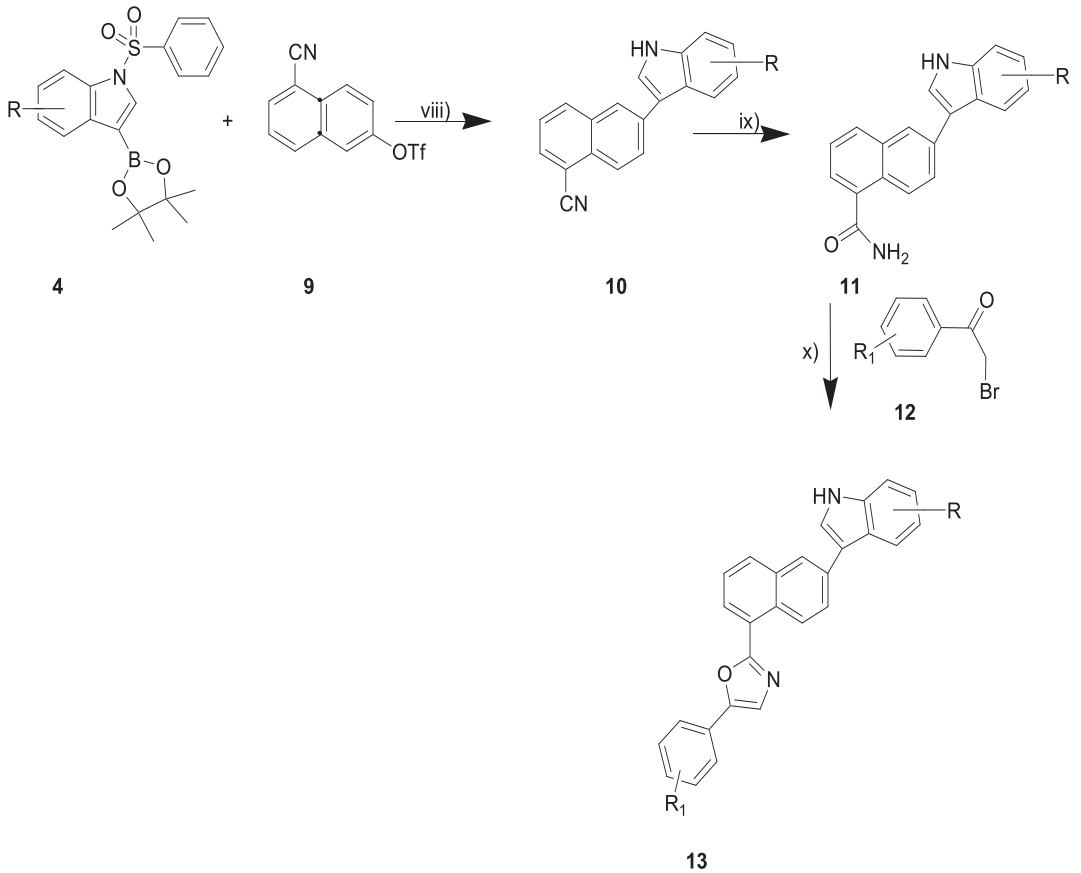
pellets in the 4000–400 cm^{-1} region. Electron spin ionization–mass spectra (ESI-MS) were performed on Waters LCT Premier XE. Palladium content was determined by ICP-AES on IRIS Adv. Pd leaching was determined by inductively coupled plasma mass spectrometry (ICP-MS) on VG PQ Exceu.

Inductively coupled plasma-atomic emission spectrometry. The polystyrene-supported NHC–Pd catalyst **1** (15 mg) in a porcelain crucible was heated at 600°C in a muffle furnace until there was constant weight. The residue in the crucible was treated with a mixture (7 mL) of hydrochloric acid and nitric acid (3:1, v:v) at 100°C for 6 h. The resulting solution was diluted to 50 mL with distilled water and analyzed by ICP-AES. The Pd loading was determined to be 0.1 mmol/g.

Inductively coupled plasma mass spectrometry. When the reaction was completed, the catalyst was filtered and washed with ether (3 × 7 mL). The combined organic phase was evaporated under reduced pressure. The residue was heated in a crucible at 600°C, and ignition continued until there was constant weight. The residue was treated with a mixture (5 mL) of hydrochloric acid and nitric acid (3:1, v:v) at 100°C for 4 h. The resulting solution was diluted to 50 mL with distilled water and analyzed by ICP-MS.

General procedure for preparation of indole boronic acid (4). To a solution of 6-substituted indole **1** (0.014 mol) in DMF, bromine (0.017 mol) in DMF (50 mL) was slowly added, and the reaction mixture was stirred at room temperature for 10 min. After completion of the reaction, it was poured into an ice and aqueous ammonium hydroxide solution. The aqueous layer was extracted with DCM. The combined organic layers were washed with water and dried over sodium sulfate, and then the solvent was removed in vacuum. The crude product **2** was directly taken for next step without purification. To a suspension of sodium hydride (0.042 mol) in DMF at 0°C under nitrogen atmosphere over 15 min, a solution of compound **2** (0.14 mol) in DMF was added dropwise. The reaction mixture was stirred at 0°C for an additional 20 min. Phenyl sulfonyl chloride (0.016 mol) was added at 0°C for 1 h. After completion of the reaction, it was poured into ice. The

Scheme 4. Synthesis of naphthalene-linked bis-heterocycles. Reagents and conditions: (viii) DME, Pd–NHC catalyst, Na_2CO_3, TBAF, THF, 65–85°C, 12 h; (ix) silica gel G-sulfuric acid, toluene, 100°C, 3 h; (x) EtOH, 90°C, 3–5 h.



4 **9** **10** **11** **12** **13**

aqueous layer was extracted with DCM, and the combined organic layers were washed with water and dried over sodium sulfate, and then the solvent was removed in vacuum. The crude solid **3** was purified by flash column chromatography using ethyl acetate in pet ether as eluent. In a 20-mL microwave vial, compound **3** (0.005 mol), bis(pinacolato)diborane (0.008 mol), potassium acetate (0.023 mol), Pd(dppf)$C1_2$ (0.0002 mol), and dimethoxy ethane (18 mL) were added. Then, this reaction mixture was irradiated to 125°C for 30 min. After completion of the reaction, it was filtered through ceilite and diluted with ethyl acetate. The organic layer was washed with water, dried over sodium sulfate, and concentrated under reduced pressure to give crude oil. The crude product **4** was purified by flash column chromatography using ethyl acetate in pet ether as eluent.

General procedure for preparation of naphthyl triflate 9. To a suspension of trimethylsilyl cyanide (19.52 mL, 0.156 mol) and zinc iodide (0.9 g, 0.002 mol) in toluene (2 × 100 mL), a solution of 6-methoxy tetralone (25 g, 0.14 mol) **5** in toluene was slowly added. The reaction mixture was stirred at room temperature overnight. TLC showed disappearance of starting material, and to this resulting mixture, pyridine (66 mL) was added followed by phosphorous oxychloride (22 mL) and refluxed for 3 h under moisture-free condition. The reaction mixture was cooled to room temperature and poured into ice. The compound was extracted with ethyl acetate (thrice), and the combined organic layer was washed with brine, dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography. A suspension of compound **6** (20 g, 0.107 mol) and palladium on carbon in *p*-cymene was refluxed overnight under nitrogen atmosphere. The reaction mixture was filtered through ceilite and concentrated under reduced pressure. The compound was extracted with ethyl acetate, washed with water, dried over magnesium sulfate, and concentrated under reduced pressure. The crude product **7** was purified by flash column chromatography using ethyl acetate and pet ether as eluent. Compound **7** (27 g, 0.148 mol) was dissolved in dichloromethane (500 mL) and cooled to 0°C. Boron tribromide (57 mL, 0.594 mol) was added dropwise to the reaction mixture, and the resulting reaction mixture was stirred under nitrogen atmosphere for 6 h at room temperature. The reaction mixture was cooled to 0°C and quenched with sodium bicarbonate solution. The organic layer was separated, and then the aqueous layer was re-extracted with dichloromethane and the combined organic layer was washed with brine. Finally, it was dried over sodium sulfate, and the solvent was evaporated under reduced pressure affording the desired product (**8**). The crude solid was purified by column chromatography over silica gel using ethyl acetate in pet ether as eluent. To a stirred of compound **8** (0.2 g, 0.001 mol) in dry dichloromethane (30 mL), dry pyridine and triflic anhydride (0.4 g, 0.001 mol) were added dropwise at 0°C. Then, the reaction mixture was stirred for 6 h. After completion of the reaction, it was diluted with DCM, and then the mixture was washed with water and dried over sodium sulfate. The organic layer was concentrated under reduced pressure to give crude solid (**9**). The crude product was purified by flash column chromatography using ethyl acetate in pet ether as eluent.

General procedure for synthesis of naphthalene linked bis-heterocycles 13a-m. To a stirred solution of compound **4** (0.005 mol) in dimethoxy ethane (100 mL), compound **9** (0.004 mol), 2*M* sodium carbonate solution, and polymer-supported N-heterocyclic carbene–palladium complex catalyst (0.002 mol) were added, and then the reaction mixture was heated at 80°C for about 12 h. After completion of the reaction mixture, it was filtered through ceilite and diluted with ethyl acetate. This organic layer was washed with water, dried over sodium sulfate, and concentrated under reduced pressure to give crude oil. The crude product was dissolved in dry tetrahydrofuran (50 mL), TBAF (0.005 mol) was immediately added at room temperature, and then the reaction mixture was heated at 65°C overnight. After completion of the reaction, the mixture was concentrated under reduced pressure and then dissolved in ethyl acetate. Organic layer was washed with (50 mL) ammonium chloride solution. Then the organic layer was dried over sodium sulfate, concentrated under reduced pressure to give crude brown color oil (**10**). A mixture of substituted nitriles **10** (0.1 mol), solid-supported silica gel G-sulfuric acid (1 g, w/w), and toluene (50 mL) was heated at 100°C for 2 h. The reaction medium was cooled to room temperature, filtered to separate silica gel G, and washed to separate substituted amide from a solid support. The filtrate and washings were combined and distilled under reduced pressure to remove toluene, and the crude product left behind was recrystallized from ethanol to obtain substituted amides **11**. A mixture of substituted amides **13a–m** (0.1 mol) and substituted phenacyl bromide 12 (0.1 mol) in absolute ethanol (30 mL) medium was refluxed for 4 h at 80°C under nitrogen atmosphere. The reaction medium was cooled to room temperature and poured into 50 mL of water containing sodium acetate. The precipitate obtained was filtered and recrystallized from ethanol to get pure compounds of naphthalene-linked bis-heterocycles **13a–m**.

3-{7-[5-(4-Chlorophenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13a). Yield: 97%; m.p.: 136–138°C; IR (KBr, cm^{-1}): v = 3240.0, 3026.9, 2928.0, 1727.1, 1626.7, 1528.3, 1492.8, 1443.4, 1222.9, 1203.4, 1183.6, 741.9, 700.4; ^{1}H-NMR ($CDCl_3$): δ = 6.89 (1H, s), 7.08–7.86 (14H, m), 10.47 (1H, brs); ^{13}C-NMR ($CDCl_3$): δ = 99.0, 107.0, 111.8, 121.3, 122.7, 123.9, 125.2, 128.9, 129.2, 130.3, 132.2, 133.8, 135.2, 138.7, 139.4, 141.5, 145.5, 148.9, 150.1, 153.6; MS (EI) *m/z*: (M^++1) 439.39; Anal. Calcd. for $C_{27}H_{16}ClFN_2O$: C, 73.89; H, 3.64; Cl, 8.11; N, 6.38; found: C, 73.85; H, 3.77; Cl, 8.10; N, 6.27.

3-{7-[5-(3-Chlorophenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13b). Yield: 92%; m.p.: 169–170°C; IR (KBr, cm^{-1}): v = 3242.0, 30246.9, 2922.2, 1725.0, 1628.6, 1526.4, 1494.6, 1442.5, 1228.1, 1209.4, 1185.6, 742.9, 712.3; ^{1}H-NMR ($CDCl_3$): δ = 6.95 (1H, s), 7.11–7.88 (14H, m), 10.32 (1H, brs); ^{13}C-NMR ($CDCl_3$): δ = 100.2, 108.5, 112.6, 117.1, 121.4, 122.9, 124.2, 125.8, 128.0, 128.9, 129.2, 130.1, 132.6, 133.7, 134.9, 137.8, 139.2, 142.5, 145.7, 150.2, 153.8; MS (EI) *m/z*: (M^++1) 439.32; Anal. Calcd. for $C_{27}H_{16}ClFN_2O$: C, 73.89; H, 3.64; Cl, 8.11; N, 6.38; found: C, 73.89; H, 3.70; Cl, 8.09; N, 6.29.

3-{7-[5-(2-Chlorophenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13c). Yield: 85%; m.p.: 201–203°C; IR (KBr, cm^{-1}): v = 3236.0, 3025.9, 2928.6, 1726.1, 1623.7, 1525.3, 1497.8, 1445.4, 1226.9, 1213.4, 1184.6, 744.9, 723.4; ^{1}H-NMR ($CDCl_3$): δ = 7.06 (1H, s), 7.12–7.92 (14H, m), 10.32 (1H, brs); ^{13}C-NMR ($CDCl_3$): δ = 99.6, 109.0, 112.8, 121.3, 122.9, 123.2, 125.2, 128.0, 128.9, 129.4, 130.3, 131.2, 133.8, 135.2, 137.5, 139.0, 141.5, 145.5, 148.9, 151.2, 152.9; MS (EI) *m/z*: (M^++1) 439.35; Anal. Calcd. for $C_{27}H_{16}ClFN_2O$: C, 73.89; H, 3.64; Cl, 8.11; N, 6.38; found: C, 73.82; H, 3.72; Cl, 8.13; N, 6.26.

3-{7-[5-(4-Methoxyphenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13d). oil; IR (KBr, cm^{-1}): v = 3297.4, 3059.9, 2916.3, 2851.0, 2229.8, 1678.9, 1664.1, 1619.5, 1593.2, 1563.7, 1534.9, 1481.4, 1444.9, 1316.1, 1286.9, 1190.1, 1014.3, 830.9, 743.1, 702.0, 672.1, 623.5; ^{1}H-NMR ($CDCl_3$): δ = 3.83 (3H, s), 6.99 (1H, s), 7.08–7.86 (14H, m), 10.36 (1H, brs); ^{13}C-NMR (DMSO-d_6): δ = 56.2, 108.1, 114.2, 118.2, 126.1, 126.4, 126.7, 127.9, 128.0, 129.0, 129.1, 132.3, 137.6, 144.0, 146.1, 146.5, 150.8, 163.7; MS (EI) *m/z*: (M^++1) 439.62; Anal. Calcd. for $C_{28}H_{19}FN_2O_2$: C, 77.43; H, 4.40; N, 6.48; found: C, 77.39; H, 4.37; N, 6.52.

3-{7-[5-(3-Methoxyphenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13e). oil; IR (KBr, cm^{-1}): v = 3286.2, 3063.9, 2916.3, 2853.0, 2223.8, 1679.9, 1611.5, 1594.2, 1562.7, 1532.9, 1487.4, 1445.9, 1313.1, 1286.7, 1192.1, 1013.3, 834.9, 745.1, 702.0, 675.1, 629.5; ^{1}H-NMR ($CDCl_3$): δ = 3.89 (3H, s), 6.92 (1H, s), 7.08–7.86 (14H, m), 10.39 (1H, brs); ^{13}C-NMR (DMSO-d_6): δ = 56.8, 109.0, 114.6, 118.3, 125.8, 126.4, 126.7, 127.9, 128.2, 128.9, 129.6, 133.0, 137.5, 144.6, 146.3, 145.5, 150.7, 163.9; MS (EI) *m/z*: (M^++1) 439.34; Anal. Calcd. for $C_{28}H_{19}FN_2O_2$: C, 77.43; H, 4.40; N, 6.48; found: C, 77.43; H, 4.39; N, 6.50.

3-{7-[5-(p-Tolyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13f). Yield: 89%; m.p.: 165–167°C; IR (KBr, cm^{-1}): v = 3246.2, 3083.8, 3047.9, 2960.8, 2926.1, 2226.1, 1647.4, 1622.3, 1593.1, 1563.6, 1484.3, 1444.7, 1308.8, 1274.2, 1188.0, 1065.2, 1008.2, 802.2, 743.0, 700.6, 621.9; ^{1}H-NMR ($CDCl_3$): δ = 2.56 (3H, s), 7.10 (1H, s), 7.15–7.96 (14H, m), 10.42 (1H, brs); ^{13}C-NMR (DMSO-d_6): δ = 19.8, 101.3, 108.6, 110.5, 114.2, 118.3, 126.4, 126.7, 128.0, 129.1, 132.4, 144.1, 146.0, 146.6, 152.7; MS (EI) *m/z*: (M^++1) 419.34; Anal. Calcd. for $C_{28}H_{19}FN_2O$: C, 80.38; H, 4.59; N, 6.69; found: C, 80.41; H, 4.61; N, 6.53.

3-{7-[5-(o-Tolyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13g). Yield: 84%; m.p.: 189–191°C; IR (KBr, cm^{-1}): v = 3245.2, 3084.8, 3046.4, 2961.7, 2923.3, 2226.51, 1647.4, 1622.3, 1594.1, 1567.6, 1489.3, 1442.7, 1304.8, 1277.2, 1189.0, 1063.2, 1021.2, 802.2, 745.0, 704.6, 622.9; ^{1}H-NMR ($CDCl_3$): δ = 2.62 (3H, s), 7.09 (1H, s), 7.08–7.82 (14H, m), 10.39 (1H, brs); ^{13}C-NMR (DMSO-d_6): δ = 19.9, 100.3, 101.6, 108.3, 110.7, 114.9, 118.1, 126.3, 126.7, 128.7, 129.0, 132.4, 144.3, 146.6, 146.7, 152.7; MS (EI) *m/z*: (M^++1) 419.26; Anal. Calcd. for $C_{28}H_{19}FN_2O$: C, 80.38; H, 4.59; N, 6.69; found: C, 80.43; H, 4.62; N, 6.58.

3-{7-[5-(4-Nitrophenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13h). Brown oil, IR (KBr, cm^{-1}): v = 3247.0, 2922.2, 2221.1, 1621.1, 1595.5, 1565.1, 1536.8, 1479.7, 1288.4, 1192.1, 1071.1, 1009.7; ^{1}H-NMR (DMSO-d_6): δ = 6.94 (1H, s), 7.01–7.85 (14H, m), 10.36 (1H, brs); ^{13}C-NMR (DMSO-d_6): δ = 98.0, 115.1, 115.6, 118.7, 120.4, 123.5, 125.7, 132.0, 142.4, 145.3, 147.1, 151.9, 153.3; MS (EI) *m/z*: (M^++1) 450.86; Anal. Calcd. for $C_{27}H_{16}FN_3O_3$: C, 72.18; H, 3.64; N, 9.36; found: C, 72.13; H, 3.62; N, 9.38.

3-{7-[5-(4-Fluorophenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13i). Yield 92%; m.p.: 210–212°C, IR (KBr, cm^{-1}): v = 3248.0, 2954.2, 2232.1, 1624.1, 1674.2, 1585.5, 1572.1, 1538.8, 1454.7, 1265.4, 1192.1, 1071.1, 1009.7; ^{1}H-NMR (DMSO-d_6): δ = 6.94 (1H, s), 7.01–7.85 (14H, m), 10.36 (1H, brs); ^{13}C-NMR (DMSO-d_6): δ = 98.2, 115.4, 115.8, 118.1, 120.7, 123.3, 124.7, 133.0, 142.2, 143.5, 145.1, 150.9, 153.3, 162.4; MS (EI) *m/z*: (M^++1) 423.79; Anal. Calcd. for $C_{27}H_{16}F_2N_2O$: C, 76.77; H, 3.86; N, 6.65; found: C, 77.83; H, 3.92; N, 6.72.

3-{7-[5-(4-Chlorophenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-chloro-1H-indole (13j). Yield: 79%; m.p.: 236–237°C; IR (KBr, cm^{-1}): v = 3248.0, 3027.9, 2931.0, 1729.1, 1625.7, 1529.3, 1494.8, 1444.4, 1225.9, 1213.4, 1182.6, 745.9, 709.4; ^{1}H-NMR ($CDCl_3$): δ = 7.02 (1H, s), 7.11–7.88 (14H, m), 10.41 (1H, brs); ^{13}C-NMR ($CDCl_3$): δ = 100.2, 108.0, 1112.8, 120.6, 121.8, 122.9, 124.9, 125.8, 128.9, 129.2, 130.6, 132.6, 133.9, 134.2, 138.7, 139.4, 141.5, 145.5, 148.9, 150.1, 153.6; MS (EI) *m/z*: (M^++2) 457.52; Anal. Calcd. for $C_{27}H_{16}Cl_2N_2O$: C, 71.22; H, 3.55; Cl, 15.57; N, 6.15; found: C, 71.21; H, 3.50; Cl, 15.59; N, 6.21.

3-{7-[5-(4-Methoxyphenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-chloro-1H-indole (13k). Semi solid; IR (KBr, cm^{-1}): v = 3265.2, 3062.9, 2920.3, 2854.3, 2232.4, 1675.5, 1658.3, 1614.5, 1598.2, 1563.7, 1531.9, 1486.4, 14454.9, 1317.1, 1282.4, 1191.3, 1018.2, 831.0, 745.1, 712.0, 623.5; ^{1}H-NMR ($CDCl_3$): δ = 3.92 (3H, s), 6.97 (1H, s), 7.08–7.86 (14H, m), 10.39 (1H, brs); ^{13}C-NMR (DMSO-d_6): δ = 56.3, 108.0, 114.5, 118.4, 126.6, 126.8, 126.2, 127.4, 128.6, 129.8, 129.1, 132.7, 137.5, 144.2, 146.3, 146.0, 150.7, 163.4; MS (EI) *m/z*: (M^++2) 452.26; Anal. Calcd. for $C_{28}H_{19}ClN_2O_2$: C, 74.58; H, 4.26; Cl, 7.86; N, 6.21; found: C, 74.45; H, 4.30; Cl, 7.86; N, 6.25.

3-{7-[5-(p-Tolyl)-oxazole-2-yl]-naphthalene-2-yl}-6-chloro-1H-indole (13l). Yield: 85%; m.p.: 125–127°C; IR (KBr, cm^{-1}): v = 3245.2, 3084.8, 3048.9, 2962.8, 2927.1, 2223.1, 1645.4, 1623.3, 1594.1, 1567.6, 1485.3, 1445.7, 1306.8, 1271.2, 1187.0, 1063.2, 1018.2, 814.2, 743.0, 700.6; ^{1}H-NMR ($CDCl_3$): δ = 2.43 (3H, s), 7.08 (1H, s), 7.11–7.97 (14H, m), 10.38 (1H, brs); ^{13}C-NMR (DMSO-d_6): δ = 20.8, 101.6, 108.7, 111.4, 114.6, 118.8, 126.5, 127.7, 128.5, 129.3, 132.6, 144.5, 146.4, 146.8, 152.7; MS (EI) *m/z*: (M^++2) 436.34; Anal. Calcd. for $C_{28}H_{19}ClN_2O$: C, 77.35; H, 4.45; Cl, 8.15; N, 6.44; found: C, 77.41; H, 4.41; Cl, 8.12; N, 6.49.

3-{7-[5-(4-Nitrophenyl)-oxazole-2-yl]-naphthalene-2-yl}-6-fluoro-1H-indole (13m). Yield: 85%; m.p.: 163–165°C; IR (KBr, cm^{-1}): v = 3236.0, 2925.2, 2238.1, 1624.1, 1598.5, 1566.1, 1534.2, 1481.3, 1284.3, 1194.6, 1076.1, 1018.7, 712.4, 684; ^{1}H-NMR (DMSO-d_6): δ = 7.01 (1H, s), 7.08–7.79 (14H, m), 10.41 (1H, brs); ^{13}C-NMR (DMSO-d_6): δ = 99.8, 108.6, 114.4, 115.9, 119.7, 121.3, 124.8, 126.2, 132.2, 142.6, 145.6, 148.1, 152.9, 153.4; MS (EI) *m/z*: (M^++2) 467.25; Anal. Calcd. for $C_{27}H_{16}ClN_3O_3$: C, 69.62; H, 3.42; Cl, 7.62; N, 9.02; found: C, 69.62; H, 3.31; Cl, 7.62; N, 9.08.

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