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Pd-catalyzed dehydrogenative C–H activation of iminyl hydrogen with indole C3-H and C2-H bond: An elegant synthesis of indeno[1,2-*b*]indoles and indolo[1,2-*a*]indoles.

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Abstract. $Pd(OAc)_2$-catalyzed two sequential C-H activations (C2-H arylation followed by indole C3-H activation with iminyl hydrogen) were employed for the synthesis of indeno[1,2-*b*]indoles in one pot. This procedure describes a simple way of introducing substituent diversity into this highly important core structure. Indole C2-H activation was also achieved for the synthesis of indolo[1,2-*a*]indoles.

Keywords: Dehydrogentaive C-H activation; Indeno[1,2-*b*]indoles; Indolo[1,2-*a*]indoles; Consecutive C-H activation; One pot cyclization

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Introduction

Polycyclic indoles hold a unique place in organic chemistry due to their immense importance in the bio-related area.[1] Indeno[1,2-*b*]indoles, a class of polycyclic indoles, show a wide range of biological activities.[2] They act as membrane stabilizing agents[3] and potent non-toxic antioxidants.[4] They also protect against chemical mediated hepatotoxicity [5] and effectively regulate aromatic hydrocarbon [Ah] gene battery enzymes and glutathione levels in mouse hepatoma cell lines.[6] Moreover, some recent studies disclose that indeno[1,2-*b*]indolones and its oxime derivatives possess potent apoptotic anticancer activities.[7]

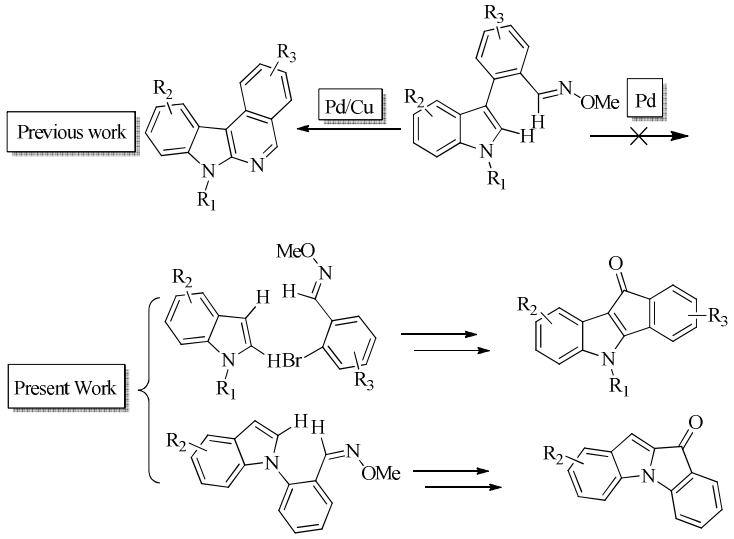


Figure 1. Our works on indole C-H activation and cyclization

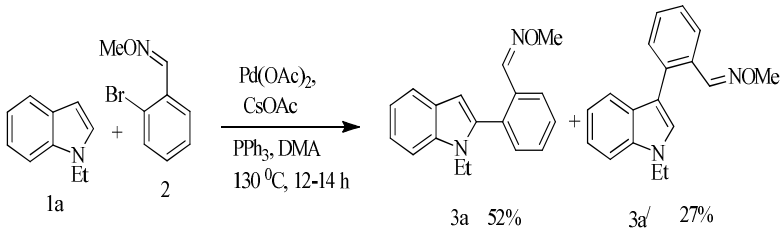
Direct arylation of indole was extensively studied in the last few decades.[8] A number of methods have also been developed to tackle the issue of regioselectivity in regards to C2-H/C3-H bond activations.[9] However, haloarene with bulky substituted group in the *ortho*-position affords mixture of C2 and C3-arylated products.[10] Very recently, while working with the 3-arylated indoles for the synthesis of indoloisoquinolines[11] (Fig 1), we observed that oxime derivatives of 3-arylated indoles tend to remain inactive in the presence of only Pd(II) catalysts but react in the presence of Pd/Cu co-catalyst to give indoloisoquinoline derivatives. According to our hypothesis, copper salt activates the system by forming

N-Cu bond. This observation opens up a window for the investigation of indole C3–H bond activation with iminyl hydrogen of oxime ether.[12]

Previously indeno[1,2-*b*]indolones were prepared using several reaction steps,[2a, b, 13] it limit the generation of substitution-diversity in product, and require harsh reaction conditions. We thought, the success in this experiment, would make it possible to synthesize the indeno[1,2-*b*]indole skeleton in one or two steps *via* two C-H activation reactions. We also envisioned that *N*-arylated aldoximes can similarly be explored for its C2-H bond activation towards the synthesis of indolo[1,2-*a*]indole compounds. Herein, we describe the observations of our experiments.

Results and discussion

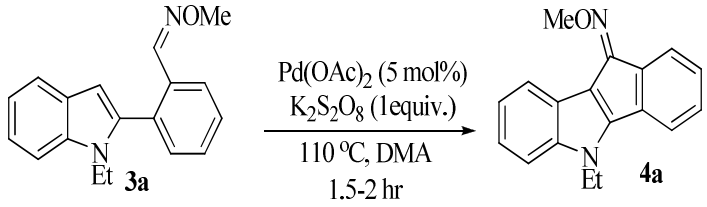
Scheme 1. Synthesis of C-2 arylated indoles



Our initial goal was to prepare 2-arylated indole **3a** as major product in place of 3-arylated indole **3a**$^{/}$, as we found previously.[11] To implement this transformation, rearrangement of 3-palladated indole to 2-palladated indole is necessary. However, the presence of bulky group in the *ortho*-position of haloarene makes the migration of palladium from C3- to C2 slower.[10] After screening several conditions (see SI for details) we were able to obtain the 2-arylated indole **3a** in 52% yield along with 3-arylated indole **3a**$^{/}$.

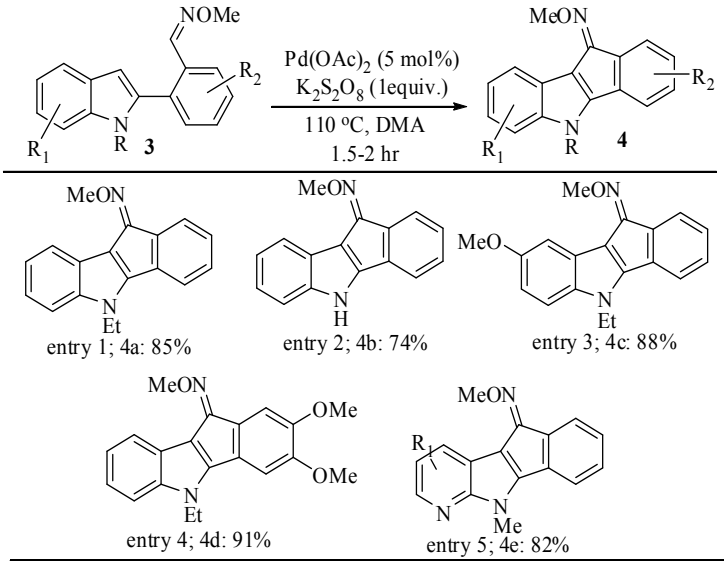
The 2-arylated indole **3a** was then subjected to further explorations for intramolecular dehydrogenative cross coupling reaction between indole C3-H bond and iminyl hydrogen in the presence of $Pd(OAc)_2$ as a catalyst.

Scheme 2. Intramolecular dehydrogenative cross coupling reaction



To our delight, the desired product **4a** was obtained in 85% yield under the optimized conditions using 5 mol% $Pd(OAc)_2$ as a catalyst and 1 equivalent $K_2S_2O_8$ as oxidant in DMA at 110 ^oC (Scheme 2) (see SI for details). Interestingly, though we detected the presence of both geometrical isomers, only the major isomer (**4a**) was successfully purified. The minor isomer (**4a**$^/$; see SI) was obtained as a contaminant with the major isomer. Next, we explored the substrate scope with other oximes (**3b**, **3c**, **3d**, **3e**; Scheme 3) under these optimized condition. All the compounds responded to the reaction excellently. The presence of OMe- groups in the substrate **3c** and **3d** increased the yield (88% and 91%; Scheme 3, entries 3, 4) and rate of the reaction (1.5h). Substrate (**3b**) with free -NH did not hamper the reaction at all though the yield was reduced slightly (74%, Scheme 3, entry 2). Azaindole derivative (**3e**) also gave **4e** with excellent yield. With the substrates **3a**, **3c** and **3e,** we observed the formation of both geometrical isomers. One isomer being the predominant one to a large degree (the minor isomer was obtained as contaminant), interestingly, only a single isomer was formed in case of **3b** and **3d**.

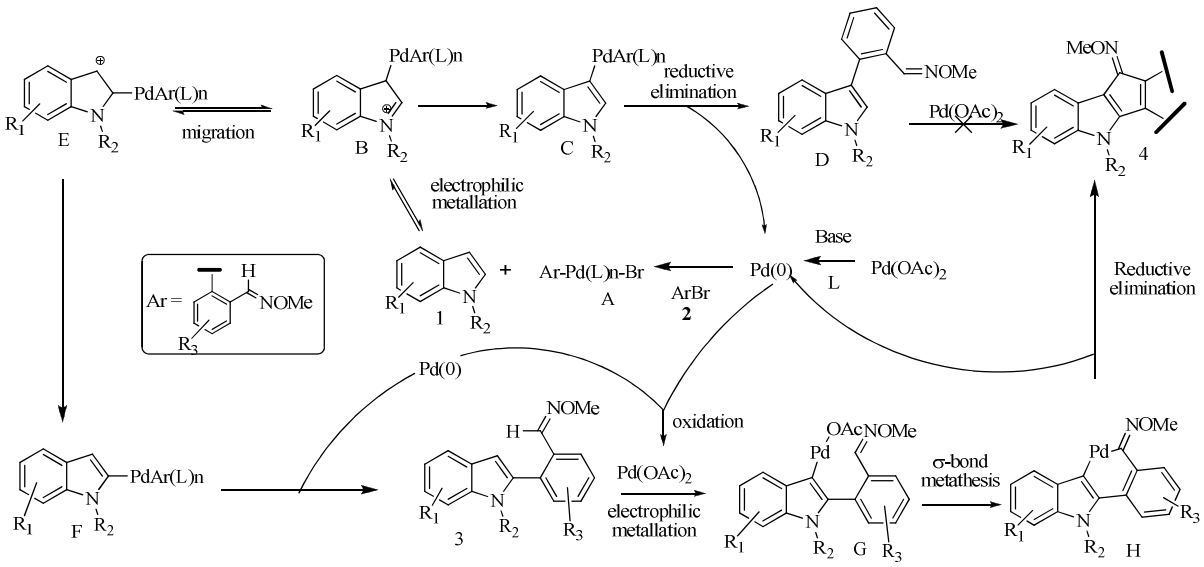
Scheme 3. Intramolecular dehydrogenative cross coupling recation.



Isolated yields of pure compound after flash chromatography

Based on the literature precedent,[8,10] the mechanism for this arylation reaction and the following intramolecular dehydrogenative cross coupling may be depicted in scheme 4. The arylation reaction most probably proceeds *via* Pd(0)/Pd(II) cycle. The active Pd(0) species is generated from $Pd(OAc)_2$ in the presence of PPh_3 and CsOAc, which then undergoes oxidative addition with ArBr to give Pd(II) species **A**. Now, the species **A** reacts with indole to give 3-palladated species **B** which may either rearrange to give 2-palladated species **E**, or afford the 3-arylated product **D** *via* reductive elimination of Pd(0). Our previous study[11] showed that oximes of 3-arylated indoles (**D**) do not give any cross coupling product in the presence of $Pd(OAc)_2$. But the fate of oximes **3**, which may similarly be generated from 2-paladated species F, is very different in the presence of $Pd(OAc)_2$. The product **3** (oximes of 2-arylated indole) easily furnishes the dehydrogenative cross coupling product **4** via electrophilic metalation, σ-bond metathesis, and reductive elimination according to our hypothesis. Nucleophilicity of indole at its C3-position is the main driving force of the reaction and similar type of electrophilic metalation is not possible in C2-position, hence oxime **D** remains inactive for CDC (cross dehydrogenative coupling) reaction.

Scheme 4. Probable mechanistic pathway.



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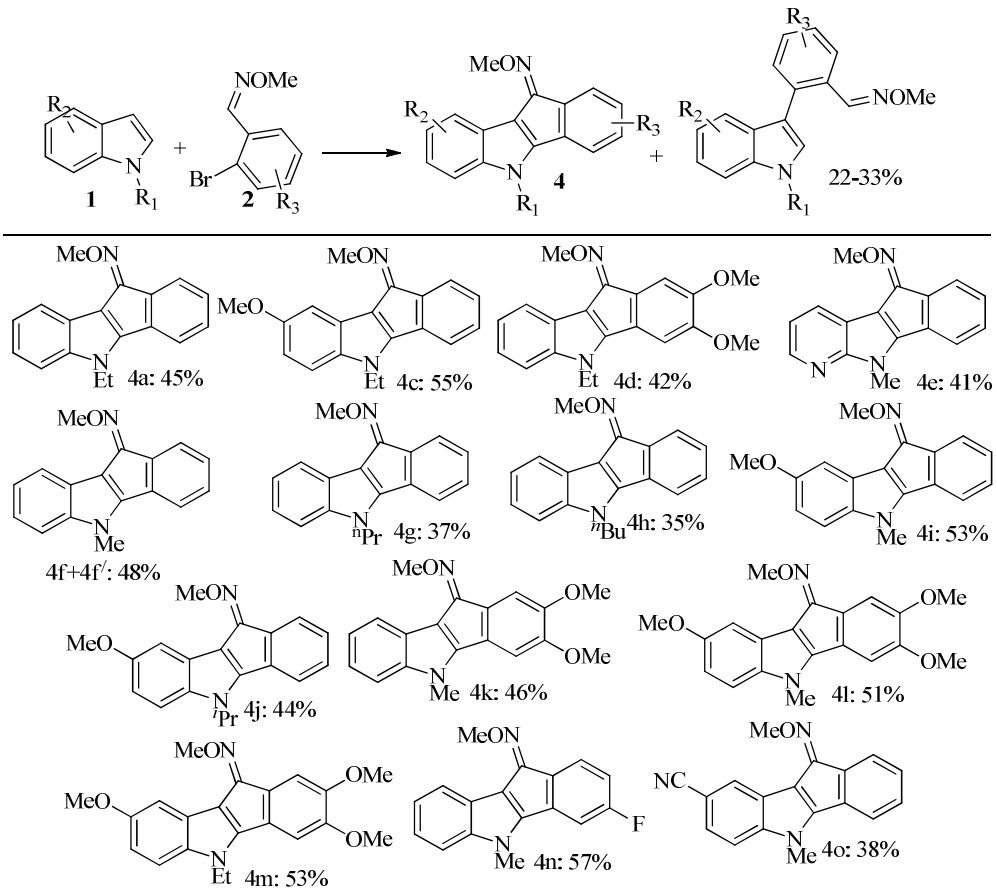
We also noticed the similarity of reaction conditions between the direct arylation and dehydrogenative cross coupling reaction during the optimization study. The reaction conditions and the mechanistic interpretation (Scheme 4) led us to believe that we can carry out the reaction in one pot. But to complete the catalytic cycle for the CDC reaction, Pd(0) has to be reoxidised to Pd(II) and use of oxidizing agent like $K_2S_2O_8$, initially, did not help the cause at all. In literature there are a few reports where air plays such role.[14] Thus we carried out the reaction (with **1a** and **2**) in open air for a longer period of time (30 h). To our delight the CDC reaction product **4**, along with the unreactive 3-arylated indole **D** and 2-arylated indole **3a** were obtained. However, when we changed the base from CsOAc to KOAc and continued the reaction for similar time span (30 h), the oxime of 2-arylated indole vanished completely yielding CDC product along with the 3-arylated indole **3a**/. We then explored this one pot methodology for the construction of indeno[1,2-*b*]indoles skeleton (Scheme 5).

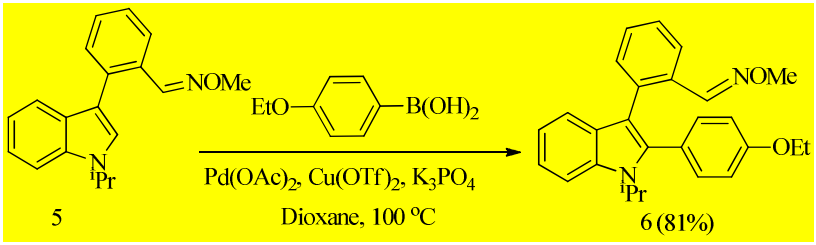
Scheme 5. Synthesis of indeno[1,2-*b*]indoles in one pot *via* two sequential C-H activation reaction.



Yields (pure compound) were calculated after flash chromatography. Both the geomatrical isomer 4f and 4f′ were isolated. Reaction condition: Indole (1 equiv.), 2-arylated indoloxime (1.2 equiv.), $Pd(OAc)_2$ (2 mol %), KOAc (2 equiv.), PPh_3 (5 mol %) open air, stirred at 130 °C in DMA. Reaction time: 30-36 h.

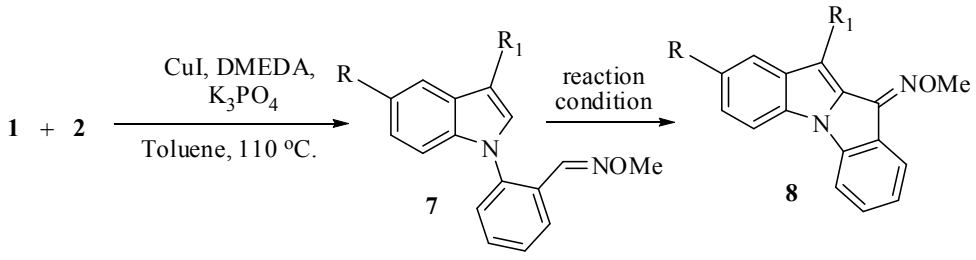
Indole C2-H palladation generally occuars *via* electrophilic metalation (at C3-position) followed by palladium migration from C3 to C2-position. The difficulty of electrophilic metalation for oxime of 3-arylated indoles at C2 position is the main reason for its inactivity towards CDC coupling. However, we found out that the same compound underwent C2-palladation (Scheme 6) when different mechanism like CMD (cross metalation deprotonation) type or sigma bond metathesis operates due to relative acidic nature of indole C2-H bond. Here we think $ArB(OH)_2$ with $Pd(OAc)_2$ generates Ar-Pd-OAc species[15] which undergoes a σ-bond metathesis with indole C2-H bond and then *via* reductive elimination gives the product **6**.

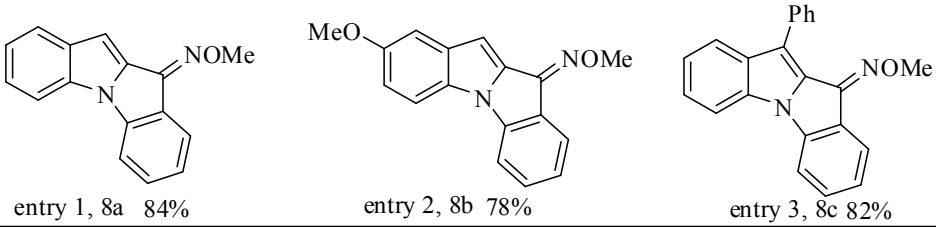
Scheme 6. Indole C2-H bond activation



Next, we wanted to explore the cross dehydrogenative coupling with oximes of *N*-arylated indoles as well. We prepared the oximes **7** by refluxing indole (**1**) with 2-bromo aldoxime (**2**) in toluene, in the presence of CuI (20 mol %), DMEDA (20 mol %), and K_3PO_4 under nitrogen atmosphere. Oximes **7** were then treated under Pd-catalyzed condition for the CDC coupling. The reaction proceeded smoothly but it took longer time for completion (12 h). Toluene was the choice of solvent instead of DMA. Both the substrates **7a** and **7b** gave the CDC product indolo[1,2-*a*]indoles in excellent yields, 84% and 78% respectively (Scheme 7, entry 1, 2). We also carried out the reaction with 3- phenylated oxime **7c** and the reaction proceeded efficiently giving 82% yield (Scheme 7, entry 3). It also suggests that the reaction most probably does not proceed *via* palladium migration from C3 to C2 position. According to literature

Scheme 7. Synthesis of indolo[1,2-*a*]indoles *via* CDC reaction



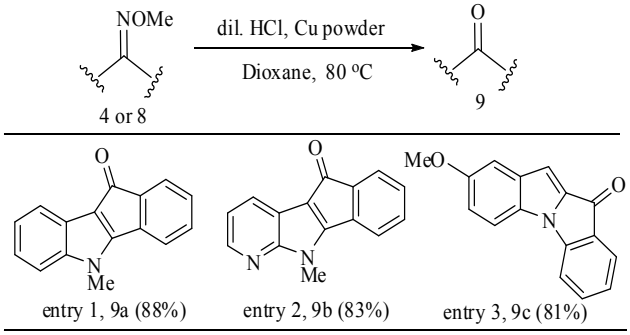


Reaction condition: *N*-arylated indoloxime (1 equiv.), $Pd(OAc)_2$ (5 mol%), $K_2S_2O_8$ (1 equiv.), stirred at 110 °C in toluene. Yields were calculated after flash chromatography

precedent,[16] 5- or 6-membered palladacycles involving indole C2 are more stable compared to benzene series and therefore does not take part in directed C-H activation reaction. Here, we think arylation at indole NH, as well as ligation by N atom of oximes leading to less stable 7-membered palldacycle, induce the indole C2-H activation by a CMD type pathway, which then produces the indoloindoles *via* another C-H activation with iminyl hydrogen.

Next, we easily performed the hydrolysis of both the CDC products **4** (**4e**, **4f**) and **8** (**8b**) to convert the oxime into keto functionality using dil. HCl in dioxane along with 2 equiv. of Cu powder (Scheme 8).

Scheme 8. Hydrolyis of oxime products.



Conclusions

In conclusion, we have developed an elegant method for the synthesis of indeno[1,2-*b*]indoles *via* two sequential C-H activation reactions. Indeno[1,2-*b*]indoles were also synthesized in one pot without adding the external oxidizing agent. The indole C2-H bond activation was also achieved with indole-*N*-aryalted aldoximes resulting in the formation indolo[1,2-*a*]indoles. A successful hydrolysis of these highly important compounds was also achieved to give the keto derivatives.

Experimental Section:

General :

Melting points were determined in open capillaries and are uncorrected. IR spectra (ν_{max} in cm^{-1}) were recorded on a Perkin-Elmer L 120-000A spectrometer on KBr disks. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer in $CDCl_3$ with TMS as internal standard (chemical shift in δ). Chemical shifts of common trace PMR impurities ($CDCl_3$, ppm) in some samples: H_2O, 1.56; solvent impurities: 1.26, 0.86; $CHCl_3$, 7.26. In some low polar samples ^{13}C peak was observed at 29.7 (δ_C) corresponding to solvent greasy impurities. CHN was recorded on 2400 series II CHN analyzer Perkin Elmer instrument. MS were recorded on a Q-TOF micro^{Tm} instrument. Silica gel [(60-120, 230-400 mesh), Rankem, India] was used for chromatographic separation. Silica gel G [CDH, (India)] was used for TLC. Petroleum ether refers to the fraction boiling between 60 °C and 80 °C.

General procedure for the synthesis of indeno[1,2-*b*]indoles in one pot:

N-alkylated indole (1 mmol), $Pd(OAc)_2$ (2 mol%), KOAc (2 mmol), were PPh_3(5 mol%) added in a oven dried reaction vessel. Dry DMA (5 ml) and 2-bromo aryloximes (1.2 mmol) were then added successively via a syringe. The resulting mixture was stirred under open atmosphere for 30-36h at 130^0C. The completion of the reaction and composition of the reaction mixture were observed on the basis of TLC analysis. After completion (monitored by TLC), the reaction mixture was cooled and water (10 ml) was added. This was then extracted with EtOAc (10 ml x 3). The EtOAc extract was washed with water (10 ml x 4) followed by brine (10 ml). The organic layer was dried (Na_2SO_4). Evaporation of EtOAc under reduced pressure furnished a oily substance, which was purified by flash chromatography. Elution of the column with pet. ether afforded the indenoindoles as major product along with the unreacted 3-arylated oximes.

General procedure for the preparation of C2-arylated Indoles:

In a oven dried reaction vessel indoles (1 mmol), $Pd(OAc)_2$ (1 mol%), CsOAc (2 mmol), and PPh_3 (5 mol%) were added. The reaction vessel was fitted with a silicon septum, evacuated, and back-filled with nitrogen. Dry DMA (5 ml) and 2-bromo aryloximes (1.2 mmol) were then added successively under nitrogen atmospehre via a syringe. The resulting mixture was stirred under nitrogen atmosphere for 12-14h at 130 ^{0}C. The completion of the reaction and composition of the reaction mixture were observed on the basis of TLC analysis. After completion (monitored by TLC), the reaction mixture was cooled and water (10 ml) was added. This was then extracted with EtOAc (10 ml x 3). The EtOAc extract was washed with water (10 ml x 4) followed by brine (10 ml). The organic layer was dried (Na_2SO_4). Evaporation of EtOAc under reduced pressure furnished an oily substance, which was purified by column chromatography over silica-gel. Elution of the column with pet. ether afforded the 2-arylated indoles as major product along with some 3-arylated indoles. 3-arylated indoles were previously characterized in our previous work.[11]

Characterization of 2-arylated indoles:

2-(1-ethyl-1*H*-indol-3-yl)benzaldehyde *O*-methyl oxime (3a): Yield 52 %; reddish white solid; m.p. 67-69 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ_H = 1.16 (t, *J* = 7.2Hz, 3H), 3.91 (s, 3H), 3.98 (q, *J* = 6.8Hz, 2H), 6.45 (s, 1H, indole C3-H), 7.15 (t, *J* = 7.2Hz ,1H), 7.25 (t, *J* = 7.2Hz ,1H), 7.37-7.40 (m, 2H), 7.45-7.47 (m, 2H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.94 (s, 1H, oxime C-H), 8.02-8.05 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ_C = 16.2, 41.8, 62.9, 111.3, 118.6, 120.8, 120.9, 121.2, 121.4, 124.1, 124.4, 127.8, 129.7, 134.5, 137.0, 137.3, 142.3, 144.8. **IR (KBr, cm^{-1})**: 1457, 1611, 2931. **HRMS (TOF, ES+)**: *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{18}N_2O$ + H: 279.1497 Found: 279.1477.

2-(1*H*-indol-2-yl)benzaldehyde *O*-methyl oxime (3b): Yield 48%; light yellow solid; m.p. 109-111 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.98 (s, 3H), 6.54 (s, 1H, indole C3-H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 8 Hz, 1H), 7.36 (d, *J* = 8Hz, 2H), 7.38-7.42 (m, 1H), 7.45-7.47 (m, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 8.24 (s, 1H, NH), 8.34 (s, 1H, oxime C-H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 62.1, 104.8, 111.0, 120.4, 120.8, 122.6, 127.1, 128.3, 128.8, 129.4, 129.8, 130.2, 132.8, 135.3, 136.7, 148.0. **IR (KBr, cm^{-1})**: 1438, 1606, 2933, 3247. MS (ES^+): m/z = 251.0$[M+H]^+$, **Anal. Calcd for** $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19; %. Found: C, 76.62; H, 5.53; N, 11.40 %.

2-(1-ethyl-5-methoxy-1*H*-indol-2-yl)benzaldehyde *O*-methyl oxime (3c): Yield 55 %; reddish white solid; m.p. 72-74 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ_H = 1.13 (t, *J* = 7.2Hz, 3H), 3.86 (s, 3H), 3.91 (s, 3H), 3.91-3.96 (m, 2H), 6.38 (s, 1H, indole C3-H), 6.91 (dd, *J* = 2.4Hz, 8.8Hz, 1H), 7.1 (d, *J* = 2.4Hz, 1H), 7.65 (d, *J* = 7.6Hz, 1H), 7.36-7.39 (m, 1H), 7.43-7.45 (m, 2H), 7.96 (s, 1H, oxime C-H) 8.02-8.04 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 15.4, 38.7, 55.9, 62.0, 102.3, 103.7, 110.6, 112.1, 125.6, 128.5, 128.8, 129.3, 131.3, 131.8, 131.9, 132.8, 137.6, 147.2, 154.3. MS (ES^+): m/z = 309.0$[M+H]^+$, **IR (KBr,cm^{-1})**: 1595, 1613, 2934. **Anal. Calcd for** $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08;%. Found: C, 74.09; H, 6.38; N, 9.22 %.

2-(1-ethyl-1*H*-indol-2-yl)-4,5-dimethoxybenzaldehyde *O*-methyl oxime (3d): Yield 51 %; yellow solid; m.p.78-80 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 1.18 (t, *J* = 7.2Hz, 3H), 3.89 (s, 3H), 3.90 (s, 3H), 3.94-4.01 (m, 2H), 4.01 (s, 3H), 6.45 (s, 1H, indole C3-H), 6.84 (s, 1H), 7.14 (t, *J* = 7.6Hz, 1H), 7.23-7.26 (m, 1H), 7.37 (d, *J* = 8.4Hz, 1H), 7.52 (s, 1H), 7.63 (d, *J* = 8.0Hz ,1H), 7.88 (s, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 15.4, 38.6, 56.0, 56.1, 61.9, 103.9, 107.1, 109.8, 113.5, 119.9, 120.6,

121.7, 124.9, 126.1, 128.1, 136.3, 136.9, 147.1, 149.5, 150.0. **IR (neat, cm^{-1}):** 1595, 1613, 2934. MS (ES^+): m/z = 339.0$[M+H]^+$, **Anal. Calcd for** $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.28; %. Found: C, 71.11; H, 6.73; N, 8.13; %.

2-(1-methyl-1*H*-pyrrolo[2,3-*b*]pyridin-2-yl)benzaldehyde *O*-methyl oxime (3e): Yield 45%; white solid; m.p. 94-96 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 4.08 (s, 3H), 4.25 (s, 3H), 6.44 (s, 1H, indole C3-H), 7.11 (dd, *J* = 4.8Hz, 8.0Hz, 1H), 7.39-7.41 (m, 1H), 7.48 (dd, *J* = 3.2Hz ,6.0Hz, 2H), 7.92 (dd, *J* = 1.6Hz ,7.6Hz, 1H), 7.94 (s, 1H, oxime C-H). 8.03-8.05 (m, 1H), 7.48 (dd, *J* = 1.2Hz, 4.4Hz, 1H),. **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 29.3, 62.1, 101.4, 116.2, 120.4, 125.9, 128.4, 129.2, 129.4, 131.2, 131.9, 138.3, 143.0, 146.9, 148.7. **IR (KBr, cm^{-1}):** 1543, 1569, 1594, 1614, 2933. MS (ES^+): m/z = 266.0$[M+H]^+$, **Anal. Calcd for** $C_{16}H_{15}N_3O$: C, 72.43; H, 5.70; N, 15.84%. Found: C, 72.22; H, 5.83; N, 15.91%.

3. **General procedure for the synthesis of indeno[1,2-*b*]indoles from 2-arylated indoles:**

In a oven dried reaction vessel, fitted with a silicon septum, 2-arylated indole oximes (0.5 mmol), $Pd(OAc)_2$ (5 mol%) and $K_2S_2O_8$ (0.5 mmol) were taken. DMA (5 ml) was added subsequently in the vessel and then it was stirred (110^{0}C) under nitrogen atmosphere. After the completetion of the reaction (monitored by TLC) water (5 ml) was added and extracted with EtOAc (10 ml x 3). The organic layer was washed with water (10 ml), brine (10 ml) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to furnish an oily substance which was purified by flash chromatography over silica gel (60–120 mesh) using Pet. Ether as elutant to afford the Indenoindoles products.

Characterization of indeno[1,2-*b*]indoles (4a to 4e):

5-ethylindeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4a): Yield 85%; yellow solid; m.p. 124-126 ^{0}C; **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 1.52 (t, *J* = 7.2 Hz, 3H, NCH$_2$C**H$_3$**), 4.27 (s, 3H, N-OC**H$_3$**), 4.43 (q, *J* = 7.2 Hz, 2H, NC**H$_2$**C**H$_3$**), 7.17-7.23 (m, 3H), 7.30-7.33 (m, 2H), 7.40(d, *J* = 7.2 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.94 (d, *J* = 7.6 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ_C = 15.6, 39.8, 62.6, 109.7, 111.6, 118.2, 121.3, 122.1, 122.3, 122.8, 123.4, 126.9, 129.0, 132.6, 140.5, 141.4, 148.0, 148.2. **IR (KBr, cm^{-1})**: 1457, 1611, 2931 **HRMS (TOF, ES+):** *m/z* [M + H]$^+$ calcd for $C_{18}H_{16}N_2O$ + H: 277.1341 Found: 277.1335.

indeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4b): Yield 74%; yellowish grey solid; m.p. 134-136 ^{0}C; **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 4.27 (s, 3H, N-OC**H$_3$**), 7.16-7.20 (m, 3H), 7.24 (dd, *J* = 2.8, 3.6 Hz, 2H), 7.33-7.35 (m, 1H), 7.73 (d, *J* = 6.8 Hz, 1H), 7.91-7.94 (m, 1H), 8.58 (s, 1H, NH) **^{13}C NMR (100 MHz, CDCl$_3$):** δ_C = 62.7, 112.0, 112.9, 117.9, 121.7, 122.0, 122.6, 122.9, 123.4, 127.1, 129.0, 132.4, 139.9, 140.9, 147.7, 148.5. **IR (KBr, cm^{-1}):** 1708, 2929, 3345. **HRMS (TOF, ES+):** *m/z* [M + H]$^+$ calcd for $C_{16}H_{12}N_2O$ + H: 249.1028 Found: 249.1028.

5-ethyl-8-methoxyindeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4c):Yield 86%; yellow solid; m.p. 111-113 ^{0}C; **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 1.50 (t, *J* = 7.2 Hz, 3H, NCH$_2$C**H$_3$**), 3.90 (s, 3H, OC**H$_3$**), 4.25 (s, 3H, NOC**H$_3$**), 4.37 (q, *J* = 7.6 Hz, 2H, NC**H$_2$**CH$_3$), 6.85 (d, *J* = 8.8 Hz, 1H), 7.19-7.21 (m, 2H), 7.29-7.31(m, 1H), 7.37 (d, *J* = 6.8 Hz ,1H), 7.44 (s, 1H), 7.74 (d, *J*= 7.2 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ_C = 15.6, 39.9, 55.7, 62.6, 105.1, 110.5, 111.9, 118.2, 122.1, 124.1, 126.9, 129.0, 132.6, 132.8, 136.6, 140.5, 148.2, 148.3, 155.1. **IR (KBr, cm^{-1}):** 1617, 2932, 2967. MS (ES$^+$): m/z = 307.0[M+H]$^+$, **Anal. Calcd for** $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14 %. Found: C, 74.57; H, 5.74; N, 9.31 %.

5-ethyl-2,3-dimethoxyindeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4d): Yield 91% ; Yellow solid; m.p. 93-95 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 1.41 (t, *J* = 7.2 Hz, 3H, $NCH_2C\mathbf{H_3}$), 3.87(s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 4.16 (s, 3H, OCH_3), 4.22(q, *J* = 7.2 Hz, 2H, $NC\mathbf{H_2}CH_3$), 6.80 (s, 1H), 7.07-7.09 (m, 2H), 7.16-7.18 (m, 1H), 7.26(s, 1H), 7.77-7.79 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 15.6, 39.6, 56.3, 56.5, 62.5, 103.1, 106.6, 109.7, 121.3, 121.6, 122.2, 123.6, 125.7, 133.6, 140.9, 148.3 (broad signal), 149.6. **IR (neat, cm^{-1}):** 1600, 1618, 2930. MS (ES^+): m/z = 337.0$[M+H]^+$, **Anal. Calcd for** calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.33;%. Found: C, 71.28; H, 5.77; N, 8.49 %.

Compound (4e): Yield 82% ; yellow solid; m.p. 119-121^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 4.08 (s, 3H), 4.25(s, 3H**)**, 7.12 (dd, *J* = 4.8Hz ,8.0Hz, 1H), 7.23(t, *J* = 7.6Hz 1H), 7.31(t, *J* = 7.6Hz 1H), 7.47 (d, *J* = 3.6Hz, 1H), 7.74 (d, *J* = 7.6Hz, 1H), 8.08 (d, *J* = 7.6Hz, 1H), 8.26 (d, *J* = 3.6Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 29.8, 62.8, 108.5, 116.5, 117.5, 118.9, 122.1, 127.5, 129.1, 130.1, 132.5, 139.4, 142.7, 148.2, 148.5, 152.4. **IR (KBr, cm^{-1}):** 1628, 2933. **HRMS (TOF, ES+):** *m*/*z* $[M]^+$ calcd for $C_{16}H_{13}N_3O$: 263.1059 Found: 263.1059.

4. General procedure for the synthesis of indeno[1,2-*b*]indoles in one pot:

N-alkylated indole (1 mmol), $Pd(OAc)_2$ (2 mol%), KOAc (2 mmol), were PPh_3(5 mol%) added in a oven dried reaction vessel. Dry DMA (5 ml) and 2-bromo aryloximes (1.2 mmol) were then added successively via a syringe. The resulting mixture was stirred under open atmosphere for 30-36h at 130^{0}C. The completion of the reaction and composition of the reaction mixture were observed on the basis of TLC analysis. After completion (monitored by TLC), the reaction mixture was cooled and water (10 ml) was added. This was then extracted with EtOAc (10 ml x 3). The EtOAc extract was washed with water (10

ml x 4) followed by brine (10 ml). The organic layer was dried (Na_2SO_4). Evaporation of EtOAc under reduced pressure furnished a oily substance, which was purified by flash chromatography. Elution of the column with pet. ether afforded the indenoindoles as major product along with the unreacted 3-arylatedoximes.

Characterization of indeno[1,2-*b*]indoles (4f to 4o):

5-methylindeno[1,2-*b*]indol-10(5*H*)-one O-methyl oxime (4f):Yield 40%, yellow solid; m.p. 174-176 ^{0}C; **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 3.86 (s, 3H, NOC**H$_3$**), 4.24 (s, 3H, NC**H$_3$)**, 7.14-7.24 (m, 5H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.69 (d, *J* = 7.2 Hz, 1H), 7.87-7.89 (m, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ_C = 31.3, 62.6, 109.8, 111.3, 118.2, 121.3, 122.0, 122.3, 122.6, 123.2, 126.9, 128.9, 132.7, 140.4, 142.4, 148.1, 148.8. **IR (KBr, cm^{-1}):** 1454, 1614, 2934. MS (ES$^+$): m/z = 263.0[M+H]+, **Anal. Calcd for** $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68%. Found : C, 77.91; H, 5.49; N, 10.52%.

5-methylindeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4f$'$): Yield 8%; yellow solid, m.p. 131-132 ^{0}C; **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 3.85 (s, 3H, CH_3), 4.1 (s, 3H, CH_3), 7.06-7.12 (m, 3H), 7.16-7.18 (m, 2H), 7.26 (d, *J* = 7.6Hz, 1H), 7.67-7.70 (m, 1H), 8.10 (d, *J* = 7.2 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ_C = 31.3, 63.1, 110.0, 114.3, 117.9, 120.5, 121.4, 122.2, 127.4, 129.8, 129.8, 134.2, 125.2, 142.3, 147.3, 148.9. **IR (KBr, cm^{-1}):** 1454, 1612, 2932. MS (ES$^+$): m/z = 263.0 [M+H]+, **Anal. Calcd for** $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68 %. Found: C, 77.98; H, 5.21; N, 10.42 %.

5-propylindeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4g): Yield 37% ; deep yellow solid; m.p. 94-96 ^{0}C. **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 0.99 (t, *J* = 7.2 Hz, 3H, $NCH_2CH_2CH_3$), 1.92-1.99

(m, 2H, $NCH_2C\mathbf{H_2}CH_3$), 4.26 (s, 3H, $OC\mathbf{H_3}$), 4.31 (t, *J* = 7.2 Hz, 2H, $NC\mathbf{H_2}CH_2CH_3$), 7.16-7.22 (m, 3H), 7.28-7.31 (m, 2H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.74 (d, *J* = 7.2 Hz, 1H), 7.92-7.94 (m, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 11.5, 23.7, 46.5, 62.7, 110.1, 111.5, 118.4, 121.3, 122.0, 122.3, 122.8, 123.3, 126.9, 128.9, 132.7, 140.5, 141.9, 148.1, 148.5. **IR (KBr, cm^{-1}):** 1458, 1608, 2930. MS (ES^+): m/z = 291.0$[M+H]^+$, **Anal. Calcd for** $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65%. Found: C, 78.71; H, 6.32; N, 9.51%.

5-butylindeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4h):Yield 35% ; yellow gummy; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 0.87 (t, *J* = 7.2 Hz, 3H, $NCH_2CH_2CH_2C\mathbf{H_3}$), 1.30-1.39 (m, 2H, $NCH_2CH_2C\mathbf{H_2}CH_3$), 1.80 (p, *J* = 7.2 Hz, 2H, $NCH_2C\mathbf{H_2}CH_2CH_3$), 4.18 (s, 3H, $OC\mathbf{H_3}$), 4.26 (t, *J* = 7.6 Hz, 2H, $NC\mathbf{H_2}CH_2CH_2CH_3$), 7.08-7.14 (m, 3H), 7.17-7.23 (m, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.67(d, *J* = 7.2 Hz, 1H), 7.84-7.87 (m, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 13.9, 20.3, 32.6, 44.9, 62.7, 110.1, 11.5, 118.4, 121.3, 122.0, 122.3, 122.8, 123.3, 126.9, 128.9, 132.7, 140.5, 141.9, 148.1, 148.4. **IR (neat, cm^{-1}):** 1452, 1608, 2935. MS (ES^+): m/z = 305.0$[M+H]^+$, **Anal. Calcd for** $C_{20}H_{20}N_2O$: C, 78.92; H, 6.62; N, 9.20 %. Found: C, 78.73; H, 6.74; N, 9.06 %.

8-methoxy-5-methylindeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4i): Yield 53%; grey yellow solid; m.p. 130-132 ^{0}C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.73 (s, 3H, $OC\mathbf{H_3}$), 3.75 (s, 3H, $NC\mathbf{H_3}$), 4.14 (s, 3H, $NOC\mathbf{H_3}$), 6.72 (dd, *J* = 2.4, 9.2Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 7.05-7.09(m, 1H), 7.12-7.16 (m, 1H), 7.24 (d, *J*= 7.6 Hz, 1H), 7.28(d, *J*= 2.4 Hz, 1H), 7.60 (d, *J* = 7.2 Hz, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 30.3, 54.6, 61.5, 104.0, 109.4, 110.0, 110.7, 117.1, 120.9, 122.8, 125.8, 127.8, 131.6, 136.6, 139.3, 147.1, 148.0, 154.0. **IR (KBr, cm^{-1}):** 1618, 2927. MS (ES^+): m/z = 293.0$[M+H]^+$, **Anal. Calcd for** $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52; N, 9.58%. Found: C, 74.06; H, 5.64; N, 9.46%.

5-isopropyl-8-methoxyindeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4j): Yield 44% ; yellow solid; m.p. 154-156 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 1.64 (d, *J* = 7.2 Hz, 6H, -CH(C**H$_3$**)$_2$), 3.81 (s, 3H, OC**H$_3$**), 4.17 (s, 3H, NOC**H$_3$**), 4.89-4.96 (m, 1H, -C**H**(CH$_3$)$_2$), 6.74 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.12 (t, *J* = 7.2 Hz, 1H), 7.20 (dd, *J* = 8, 15.2 Hz ,1H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.38-7.42 (m, 2H), 7.68 (d, *J*= 7.2 Hz, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C =21.9, 48.9, 55.6, 62.6, 105.2, 111.7, 112.6, 119.4, 122.0, 124.5, 126.7, 127.1, 128.9, 129.8, 132.8, 135.9, 140.7, 148.0, 154.8 . **IR (KBr, cm^{-1}):** 1612, 2931, 2969. MS (ES$^+$): m/z = 321.0[M+H]$^+$, **Anal. Calcd for** $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74%. Found: C, 74.76; H, 6.39; N, 8.69%.

2,3-dimethoxy-5-methylindeno[1,2-*b*]indol-10(5*H*)-one *O*-methyl oxime (4k):Yield 46%; yellow solid; m.p. 208-210 ^{0}C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.88 (s, 3H, NC**H$_3$**), 3.95 (s, 3H, OC**H$_3$**), 3.95 (s, 3H, OC**H$_3$**), 4.24 (s, 3H, NOC**H$_3$**), 6.91 (s, 1H), 7.16 (dd, *J* = 3.2, 6 Hz, 1H), 7.20-7.22 (m, 1H), 7.26 (s, 1H), 7.31 (s, 1H), 7.83 (dd, *J* = 2.4, 3.6 Hz, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 31.2, 56.2, 56.3, 62.5, 103.0, 106.4, 109.7, 110.1, 121.3, 121.6, 122.0, 123.4, 125.8, 133.4, 142.0, 148.2, 149.1, 149.5 **IR (KBr,cm^{-1}):** 1596, 1616, 2933. MS (ES$^+$): m/z = 323.0[M+H]$^+$, **Anal. Calcd for** $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69 %. Found: C, 70.86; H, 5.84; N, 8.51%.

2,3,8-trimethoxy-5-methylindeno[1,2-*b*]indol-10(5*H*)-one O-methyl oxime (4l):Yield 51% deep yellow solid; m.p.162-164 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.67 (s, 3H, NC**H$_3$**), 3.80 (s, 3H, OC**H$_3$**), 3.84 (s, 3H, OC**H$_3$**), 3.86 (s, 3H, OC**H$_3$**), 4.14 (s, 3H, NOC**H$_3$**), 6.70 (t, *J* = 8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 1H), 7.17 (d, *J* = 8.8 Hz 1H), 7.24 (s, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 31.2, 55.6, 56.2, 56.2, 62.5, 102.8, 104.5, 106.3, 109.8, 110.3, 110.8, 124.1, 125.7, 133.3, 137.2, 148.1, 148.3, 149.4,

149.5, 155.1. **IR (KBr, cm^{-1}):** 1616, 2931. **HRMS (TOF, ES+):** *m/z* $[M + H]^+$ calcd for $C_{20}H_{20}N_2O_4$ + H: 353.1501 Found: 353.1501.

5-ethyl-2,3,8-trimethoxyindeno[1,2-*b*]indol-10(5*H*)-one O-methyl oxime (4m): Yield 53%; brown solid; m.p. 114-116 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 1.39 (t, *J* = 6.8 Hz, 3H, $NCH_2C\mathbf{H_3}$), 3.80 (s, 3H, $OC\mathbf{H_3}$), 3.87 (s, 3H, $OC\mathbf{H_3}$), 3.88 (s, 3H, $OC\mathbf{H_3}$), 4.18-4.10 (m, 5H, $NC\mathbf{H_2}CH_3$ & $NOC\mathbf{H_3}$), 6.71 (d, *J* = 8.4 Hz, 1H), 6.76 (s, 1H), 7.04 (d, *J* = 8.8 Hz, 1H), 7.18-7.28 (m, 2H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 15.6, 39.7, 55.7, 56.3, 56.4, 62.5, 103.0, 104.7, 106.5, 110.2, 110.3, 110.9, 124.3, 125.7, 133.5, 136.1, 148.3, 148.4, 148.5, 149.7, 155.1 . **IR (KBr, cm^{-1}):** 1618, 2926. MS (ES^+): m/z = 367.0[M+H]+, **Anal. Calcd for** $C_{21}H_{22}N_2O_4$: C, 68.84; H, 6.05; N, 7.65%. Found: C, 68.71; H, 6.16; N, 7.71%

3-fluoro-5-methylindeno[1,2-*b*]indol-10(5*H*)-one O-methyl oxime (4n): Yield 57%; yellow solid; m.p. 164-166 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.89 (s, 3H, $NC\mathbf{H_3}$), 4.24 (s, 3H, $NOC\mathbf{H_3}$), 6.91-6.95 (m, 1H), 7.16-7.20 (m, 3H), 7.21-7.24 (m, 1H), 7.29 (dd, *J* = 4.8, 8.4 Hz, 1H), 7.42 (dd, *J* = 2.4, 8 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 30.7, 62.3, 109.3, 109.9 (d, $^2J_{C\text{-}F}$ =25Hz), 114.3 (d, $^2J_{C\text{-}F}$ =22Hz), 118.3 (d, $^3J_{C\text{-}F}$ = 9Hz), 118.3, 120.9, 121.8, 122.0, 122.7, 128.1, 141.7, 142.5, 142.6, 146.6, 147.6, 162.2 (d, $^1J_{C\text{-}F}$=245Hz). **IR (KBr, cm^{-1}):** 1595, 2933. MS (ES^+): m/z = 281.0$[M+H]^+$, **Anal. Calcd for** $C_{17}H_{13}FN_2O$: C, 72.85; H, 4.67; N, 9.99%. Found: C, 72.71; H, 4.59; N, 10.12 %.

10-(methoxyimino)-5-methyl-5,10-dihydroindeno[1,2-*b*]indole-8-carbonitrile (4o): Yield 38%, yellow solid; m.p. >225 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.93 (s, 3H, $NC\mathbf{H_3}$), 4.27 (s, 3H, $NOC\mathbf{H_3}$), 7.24 (t, *J* = 8.8 Hz, 2H) 7.30 (t, *J* = 7.2 Hz, 1H), 7.35-7.40 (m, 2H), 7.71 (d, *J* = 7.2 Hz, 1H), 8.11 (s, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 31.6, 63.0, 104.3, 110.6, 111.3, 118.7, 120.6, 122.3, 122.7, 125.0, 127.6,

127.8, 129.2, 131.6, 139.9, 143.6, 147.1, 150.5. **IR (KBr, cm^{-1}):** 1622, 2220, 2925. MS (ES^+): m/z = 288.0$[M+H]^+$, **Anal. Calcd for** $C_{18}H_{13}N_3O$: C, 75.25; H, 4.56; N, 14.63%. Found: C, 75.15; H, 4.65; N, 14.78%.

5. Reaction with bromo benzene and indole-3-carbaldehyde *O*-methyl oxime:

In a oven dried reaction vessel 1-methyl-1H-indole-3-carbaldehyde O-methyl oxime (1 mmol), $Pd(OAc)_2$ (2 mol%), KOAc (2 mmol), PPh_3(5 mol%) were added. Dry DMA (5 ml) and bromobenzene (1.2 mmol) were then added successively via a syringe. The resulting mixture was stirred under open atmosphere for 36h at 130^{0}C. After completion (monitored by TLC), the reaction mixture was cooled and water (10 ml) was added. This was then extracted with EtOAc (10 ml x 3). The EtOAc extract was washed with water (10 ml x 4) followed by brine (10 ml). The organic layer was dried (Na_2SO_4). Evaporation of EtOAc under reduced pressure furnished a crude mass, which was purified by column chromatography over silica-gel. Elution of the column with pet. ether afforded the 1-methyl-2-phenyl-1H-indole-3-carbaldehyde O-methyl oxime **x** in 74% yield.

Characterization of 2-aryalated product:

1-methyl-2-phenyl-1H-indole-3-carbaldehyde *O*-methyl oxime (x):Yield 74%; whitish solid; m.p. 86-88 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.62 (s, 3H, NC**H$_3$**), 3.96 (s, 3H, NOC**H$_3$**), 7.26-7.31 (m, 1H), 7.33-7.35 (m, 2H), 7.37-7.40 (m, 2H), 7.46-7.51 (m, 3H), 8.07 (s, 1H, oxime-C**H**), 8.31 (d, *J* = 7.6 Hz, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 31.0, 61.7, 107.1, 109.5, 121.5, 122.8, 123.2, 124.8, 128.6, 129.0, 130.0, 130.8, 137.7, 143.4, 145.4. **IR (KBr, cm^{-1}):** 1599, 2955. MS (ES^+): m/z = 265.0$[M+H]^+$, **Anal. Calcd for** $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60%. Found: C, 77.41; H, 6.24; N, 10.51%.

6. Reaction of oxime derivative of C3-arylated indole and aryl boronic acid:

A mixture of 3e (1 mmol), $Pd(OAc)_2$ (0.1 mmol, 10 mol%), arylboronic acids (2.5 mmol) $Cu(OTf)_2$ (1 mmol, 1.0 equiv.), K_3PO_4 (3 mmol, 3.0 equiv.), were kept in oven dried reaction vessel. 1,4-dioxane (3 mL) was added and the reaction mixture was stirred in at 100 °C in open atmosphere for 6h until complete consumption of the substrate (based on TLC monitoring) was observed. After completion, the reaction mixture was cooled and water (10 ml) was added. This was then extracted with EtOAc (10 ml x 3). The EtOAc extract was washed with water (10 ml x 4) followed by brine (10 ml). The organic layer was dried (Na_2SO_4). Evaporation of EtOAc under reduced pressure furnished a oily substance, which was purified by column chromatography over silica-gel. Elution of the column with pet. ether afforded the compound 6 in 81 % yield.

Characterization of the 2-arylated product 6:

2-(2-(4-ethoxyphenyl)-1-isopropyl-1H-indol-3-yl)benzaldehyde *O*-methyl oxime (6): Yield 81%; Off white solid; m.p. 134-136 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 1.31 (t, *J* = 6.8 Hz, 3H, $CH_2C\mathbf{H_3}$), 1.52 (d, *J* = 6.8 Hz, 3H, $CH(C\mathbf{H_3})_2$), 1.58 (d, *J* = 7.2 Hz, 3H, $CH(C\mathbf{H_3})_2$) 3.74 (s, 3H, NOMe), 3.89-3.95 (m, 2H, $C\mathbf{H_2}CH_3$), 4.52-4.59 (m, 1H, $C\mathbf{H}(CH_3)_2$), 6.73 (d, *J* = 8.4 Hz, 2H), 7.00-7.04 (m, 3H), 7.11-7.22 (m, 4H), 7.30 (d, *J* = 8 Hz, 1H), 7.55 (d, *J* = 8 Hz, 1H), 7.75 (d, *J* = 7.2 Hz, 1H), 7.82 (s, 1H, oxime-C**H**). **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 14.8, 21.5, 21.7, 48.0, 61.6, 63.4, 112.2, 112.3, 114.3, 119.8, 121.4, 123.9, 125.6, 126.7, 129.2, 129.3, 131.3, 132.0, 132.3, 134.4, 135.5, 139.0, 148.6, 158.8 **IR (KBr, cm^{-1}):** 1609, 2924. MS (ES^+): m/z = 412.0$[M+H]^+$, **Anal. Calcd for** $C_{27}H_{28}N_2O_2$: C, 78.61; H, 6.84; N, 6.79%. Found: C, 78.43; H, 6.61; N, 6.94%.

7. General procedure for the preparation of N-arylated Indoles

In a oven dried reaction vessel, fitted with a silicon septum, indole (1 mmol), CuI (20 mol%), K_3PO_4 (2 mmol) and dry toluene (5 ml) were added under nitrogen atmosphere. The reaction mixture was degassed for 20 min. 2-bromo aryloximes (1.2 mmol) and DMEDA (20 mol%) were then added successively under nitrogen atmospehre via a syringe. The resulting mixture was stirred under nitrogen atmosphere for 12-14h at 110^0C. The completion of the reaction and composition of the reaction mixture were observed on the basis of TLC analysis. After completion (monitored by TLC), the reaction mixture was cooled and toluene was evaporated under reduced pressure. water (10 ml) and NH_3 solution (1ml) was added subsequently. This was then extracted with EtOAc (10 ml x 3). The EtOAc extract was washed with water (10 ml x 4) followed by brine (10 ml). The organic layer was dried (Na_2SO_4). Evaporation of EtOAc under reduced pressure furnished a oily substance, which was purified by column chromatography over silica-gel. Elution of the column with pet. ether afforded the N-arylated indoles **7**.

Characterization of N-arylated indoles:

2-(1H-indol-1-yl)benzaldehyde O-methyl oxime (7a): Yield 83%; white solid; m.p. 61-63 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.89 (s, 3H, NOMe), 6.69 (d, *J* = 3.2 Hz, 1H), 7.09-7.11 (m, 1H)**,** 7.14-7.24 (m, 3H), 7.35-7.37 (m, 1H), 7.45-7.51 (m, 2H), 7.63 (s, 1H, Oxime-C**H**), 7.67-7.69 (m, 1H), 8.06-8.08 (m, 1H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 62.1, 103.6, 110.4, 120.4, 121.0, 122.5, 126.7, 128.3, 128.3, 128.5, 129.3, 129.6, 130.6, 137.7, 138.2, 144.8. **IR (KBr, cm^{-1}):** 1623, 2927. MS (ES^+): m/z = 251.0 $[M+H]^+$, **Anal. Calcd for** $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19%. Found: C, 76.89; H, 5.52; N, 11.30%.

2-(5-methoxy-1H-indol-1-yl)benzaldehyde *O*-methyl oxime (7b): Yield 78%; white solid; m.p. 104-106 ^{0}C. **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.77 (s, 3H, OMe), 3.81 (s, 3H, NOMe), 6.52 (d, *J* = 2.8 Hz, 1H), 6.75 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 7.13 (d, *J* = 3.2 Hz, 2H), 7.26 (dd, *J* = 1.2,7.6 Hz, 1H), 7.34-7.39 (m, 2H), 7.56 (s, 1H, Oxime-C**H**), 7.97 (dd, *J* = 1.2, 7.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 55.9, 62.1, 102.6, 103.3, 111.2, 112.9, 126.7, 128.1, 128.2, 129.0, 129.5, 129.8, 130.6, 133.1, 138.3, 144.9, 154.7. **IR (KBr, cm^{-1}):** 1609, 2920. MS (ES^+): m/z = 281.0$[M+H]^+$, **Anal. Calcd for** $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99%. Found: 72.87; H, 5.64; N, 9.73%.

2-(3-phenyl-1H-indol-1-yl)benzaldehyde *O*-methyl oxime (7c): Yield 72%; white solid; m.p. 120-122 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.89 (s, 3H, NOMe), 7.10-7.12 (m,1H), 7.21-7.23 (m, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.33 (s, 1H), 7.38 (dd, *J* = 1.6 Hz, 7.2Hz, 1H), 7.43-7.50 (m, 4H), 7.69-7.71 (m, 2H), 7.73 (s, 1H, Oxime-C**H**), 7.97-8.0 (m, 1H), 8.09 (dd, *J* = 1.6 Hz, 7.6Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 62.2, 110.9, 119.2, 120.1, 121.0, 123.0, 126.4, 126.4, 126.7, 126.8, 127.7, 128.4, 128.5, 128.9, 129.7, 130.7, 135.0, 137.9, 138.6, 144.7. **IR (KBr, cm^{-1}):** 1602, 2928. MS (ES^+): m/z = 327.0$[M+H]^+$, **Anal. Calcd for** $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58%. Found: C, 81.14; H, 5.67; N, 8.41%.

8. General procedure for the synthesis of indolo[1,2-*a*]indoles:

In a oven dried reaction vessel, fitted with a silicon septum, oximes of N-arylated indole (0.5 mmol), $Pd(OAc)_2$ (5 mol%) and $K_2S_20_8$ (0.5 mmol) were taken. Dry toluene (5 ml) was added subsequently in the vessel and then it was stirred (110 ^{0}C) under nitrogen atmosphere. . After completion (monitored by TLC), the reaction mixture was cooled and toluene was evaporated under reduced pressure. Subsequently water (5 ml) was added and extracted with EtOAc (10 ml x 3). The organic layer was washed with water (10 ml), brine (10 ml) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to furnish

a oily substance which was purified by flash chromatography over silica gel using Pet. Ether as elutant to afford the Indoloindoles products.

Characterization of indolo[1,2-*a*]indoles:

10*H*-indolo[1,2-*a*]indol-10-one *O*-methyl oxime (8a):Yield 84%; yellow solid; m.p. 60-62 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 4.17 (s, 3H, NOMe), 7.02 (t, *J* = 7.6 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 2H)**,** 7.29 (t, *J* = 7.6 Hz, 1H)**,** 7.34 (t, *J* = 7.6 Hz, 1H)**,**7.40 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 63.5, 107.5, 110.9, 111.0, 121.2, 122.5, 123.0, 123.5, 125.4, 127.6, 130.8, 131.6, 132.1, 133.1, 141.0, 144.2. **IR (KBr, cm^{-1}):** 1614, 2924. MS (ES^+): m/z = 249.0$[M+H]^+$, **Anal. Calcd for** $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.28%. Found: C, 77.53; H, 4.99; N, 11.13 %.

2-methoxy-10*H*-indolo[1,2-*a*]indol-10-one *O*-methyl oxime (8b):Yield 78%; yellow solid; m.p. 70-72 ^{0}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ_H = 3.87 (s, 3H, OMe), 4.24 (s, 3H, NOMe), 7.02-7.11 (m, 4H), 7.41 (d, *J* = 3.6 Hz, 2H), 7.54 (d, *J* = 8.8 Hz, 1H)**,** 7.73 (d, *J* = 7.2 Hz, 1H)**. ^{13}C NMR (100 MHz, $CDCl_3$):** δ_C = 55.7, 63.5, 104.7, 107.1, 110.3, 111.6, 115.6, 122.4, 122.7, 127.5, 130.7, 132.0, 133.7, 141.1, 144.2, 154.9. **IR (KBr, cm^{-1}):** 1625, 2931. **HRMS (TOF, ES+):** *m/z* $[M + H]^+$ calcd for $C_{17}H_{14}N_2O_2$ + H: 279.1134 Found: 279.1140.

11-phenyl-10H-indolo[1,2-a]indol-10-one O-methyl oxime (8c): Yield 82%; yellow solid; m.p. 120-122 ^{0}C; **^{1}H NMR (400 MHz, CDCl$_3$):** **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 4.12 (s, 3H, NOMe), 7.06 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H)**,** 7.32-7.51 (m, 6H)**,** 7.65 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 7.6Hz, 2H), 8.23 (d, *J* = 7.6 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ_C = 63.6, 110.6, 111.0, 117.0, 121.5, 122.0, 123.1, 124.7, 125.3, 127.3, 128.1, 129.4, 130.0, 131.4, 131.6, 131.9, 132.7, 132.7, 140.9, 145.2. **IR (KBr, cm^{-1}):** 1603, 2926. **HRMS (TOF, ES+):** *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{16}N_2O$ + H: 325.1341 Found: 325.1341

9. Hydrolysis of indeno[1,2-*b*]indole and indolo[1,2-*a*]indoles:

oxime **(4f**,**4l**,**8a**, 0.1 mmol**),** dioxane (0.5 ml), 6M HCl (0.5 ml) and copper powder (2 equiv.) was added in a sealed tube. Then the mixture was then heated to 85 ^{0}C for 3-4 h. Reaction was monitored by TLC. After completion the reaction mixture was first cooled then filtered through celite and the filtrate was concentrated under vacuum to afford an oily substance. The crude product was loaded onto a silica gel column for flash column chromatography.

Characterization of keto products:

5-methylindeno[1,2-*b*]indol-10(5*H*)-one (9a): Yield 88%; reddish solid; m.p. 200-202 ^{0}C; **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 3.89 (s, 3H, NC**H$_3$**), 7.15-7.25 (m, 6H), 7.40-7.42 (m, 1H), 7.75-7.77 (m, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ_C = 31.6, 110.5, 115.0, 118.3, 120.7, 122.8, 123.0, 123.2, 123.5, 129.6, 131.9, 134.8, 141.3, 143.0, 158.8, 185.0. **IR (KBr, cm^{-1}):** 1671, 2922. **HRMS (TOF, ES+):** *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{11}NO$ + H: 234.0919 Found: 234.0921

10-methylindeno[2',1':4,5]pyrrolo[2,3-*b*]pyridin-5(10*H*)-one (9b): Yield 83%, red; m.p. 190-192 ^{0}C; **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 4.05 (s, 3H, NC**H$_3$**), 7.15 (dd, *J* = 4.8 Hz, 7.6 Hz, 1H), 7.24-7.31 (m, 3H), 7.46 (d, *J* = 6.8 Hz, 1H). 8.04 (dd, *J* = 1.6 Hz, 8.0 Hz, 1H), 8.24 (dd, *J* = 1.6 Hz, 4.8 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ_C = 30.1, 112.2, 116.2, 119.1, 119.3, 123.4, 128.4, 130.3, 132.3, 134.5, 140.0, 143.4, 153.1, 158.8, 158.2. **IR (KBr, cm^{-1}):** 1698, 2921. MS (ES$^+$): m/z = 235.0[M+H]$^+$, **Anal. Calcd for** $C_{15}H_{10}N_2O$: C, 76.91; H, 4.30; N, 11.96%. Found: C, 76.98; H, 4.41; N, 11.81%.

2-methoxy-10*H*-indolo[1,2-*a*]indol-10-one (9c): Yield 81%; red; m.p. 122-125 ^{0}C; **^{1}H NMR (400 MHz, CDCl$_3$):** δ_H = 3.86 (s, 3H, OC**H$_3$**), 7.05-7.1 (m, 4H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H). 7.63(d, *J* = 7.2 Hz, 1H). **^{13}C NMR (100 MHz, CDCl$_3$):** δ_C = 55.7, 105.5, 107.5, 110.9, 112.1, 119.1, 123.7, 125.1, 129.3, 129.8, 133.2, 135.4, 136.2, 145.6, 155.3, 181.7. **IR (KBr, cm^{-1}):** 1702 2924. MS (ES$^+$): m/z = 250.0[M+H]$^+$, **Anal. Calcd for** $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62%. Found: C, 77.19; H, 4.58; N, 5.47 %.

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Notes and References:

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†Electronic Supplementary Information (ESI) available experimental details, spectroscopic data, copies of the ^{1}H NMR and ^{13}C NMR spectra of all final products.

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Graphical Abstract

Pd-catalyzed dehydrogenative C-H activation of iminyl hydrogen with indole C3-H and C2-H bond: An elegant synthesis of indeno[1,2-*b*]indoles and indolo[1,2-*a*]indoles

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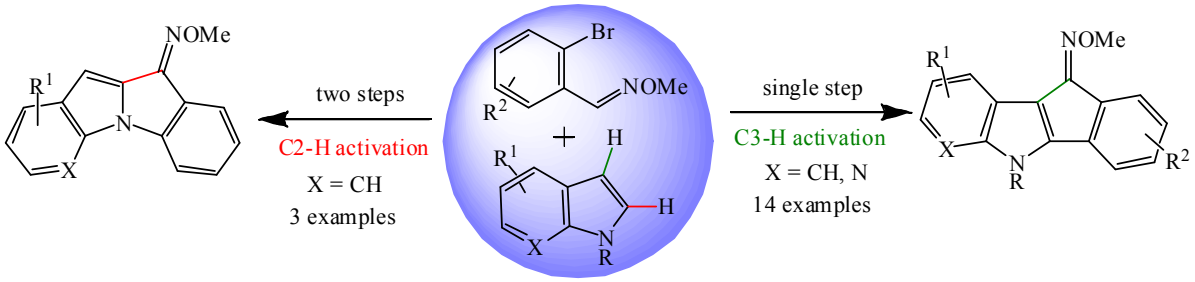

This synthetic protocol describes two sequential C-H activation route towards indeno[1,2-*b*]indoles. indolo[1,2-*a*]indoles were also synthesized by activating Indole C2-H bond.