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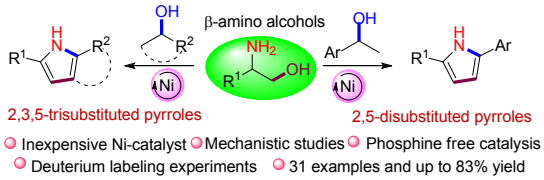
Nickel-Catalyzed Double Dehydrogenative Coupling of Secondary Alcohols and β-Amino Alcohols to Access Substituted Pyrroles

Anitha Alanthadka,‡ Sourajit Bera,‡ Mari Vellakkaran and Debasis Banerjee*

Department of Chemistry, Laboratory of Catalysis and Organic Synthesis, Indian Institute of Technology Roorkee, Roorkee-247667, Uttarakhand, India. Email: dbane.fcy@iitr.ac.in



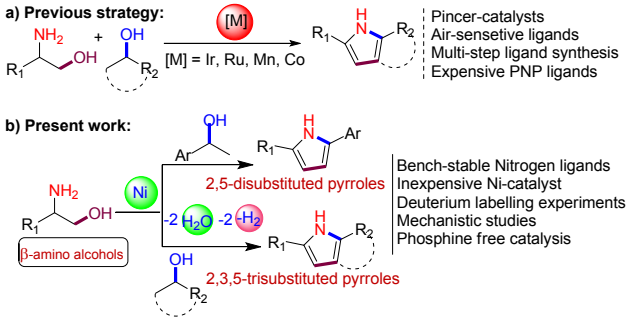
ABSTRACT: Herein, we demonstrated the first nickel-catalyzed double dehydrogenative condensation of secondary alcohols and β-amino alcohols in one-pot operation to the pyrrole derivatives. A series of 2,5 and 2,3,5-substituted pyrroles were obtained in up to 83% yield, releasing water and hydrogen gas as by-products. Initial mechanistic studies including defined Ni-catalysts, deuterium labeling experiments, quantitative determination of hydrogen gas evaluation and detection of water generation in the reaction mixture were performed.

KEYWORDS. β-Amino Alcohols • Nickel • Substituted Pyrrole • Secondary Alcohols • Dehydrogenative Coupling

INTRODUCTION

Nitrogen containing N-heterocycles are highly important and common structural motifs present in various pharmaceuticals, agrochemicals and in functional materials.[1] Among these, pyrroles are significantly utilized in a large no of drug molecules, and play an important role in bio-active compounds, such as, porphyrins, corrins as well as in chlorins. Further, substituted pyrroles derivatives also found in, haemoglobin, vitamin B12 and in chlorophyll including various natural products.[2] Apart from these, a large number of bioactive non-natural pyrroles are widely used for multi-targeted receptor, tyrosine kinase inhibitors and as anti-inflammatory drug zomepirac.[3] Therefore, synthesis of multi-substituted pyrroles remains an attractive target in chemical research. Unfortunately, despite their significant biological importance, straightforward procedures for the synthesis of pyrroles are much less known.

Classical approaches, such as Knorr, Paal–Knorr, and Hantzsch synthesis utilized activated substrates (ketones or esters) and suffer from pre-functionalization of starting materials, harsh reaction conditions, low chemical economy and generation of stoichiometric waste.[4] Therefore, development of an efficient synthetic protocol for substituted pyrroles in an atom and step economic fashion is a challenging goal. In this context, in terms of sustainability, potential and exciting approaches which efficiently utilizes available renewable resources and minimize the waste generation are in high demand.[5] Nevertheless, metal-catalyzed hydrogen-borrowing strategy for alcohols are widely utilised for C-C and C-N bond formations, which releases water and dihydrogen as side products. However, applications of such processes for the tandem one-pot operation involving synthesis of N-heterocycles are much less developed.[6] Notably, such an acceptorless dehydrogenation of alcohol for pyrrole synthesis is often limited with precious metal-catalysts, Ru, and Ir-based complexes.[7-8] In this direction, intermolecular cyclization to pyrroles was independently developed by Kempe and Milstein involving coupling of secondary alcohols with amino alcohols using Ir- and Ru-based catalysts (Scheme 1a). Interesting Ru-catalyzed multi-component transformations to pyrroles involving activated ketones and diols with amines was developed by Beller.[7b-c] Again, catalytic transformations using unsaturated-diols with suitable amines were also reported for pyrroles synthesis using Pd-,[7f] Ru-,[7g] and Pt,[7h] based catalysts.



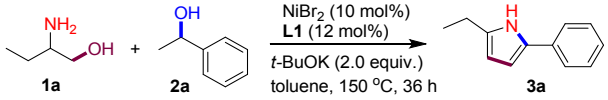
Scheme 1: (a) Metal-catalyzed hydrogen borrowing processes for pyrrole synthesis. (b) Nickel-catalyzed sustainable synthesis of pyrroles.

However, applications of biomass derived alcohols along with earth-abundant base-metals (Fe, Mn, Ni, Co) have attract significant attention for hetero-aryl synthesis.[9] For instance, Mn, Co, and Fe-based pincer complexes have been well studied for the synthesis of N-heterocycles.[10] However, such pincer-complexes required expensive multi-dentate NNS, PNN-, or NNN-ligands as well as sensitive phosphine-based ligands.[7-8,10] Therefore, still there is a need to establish a simple, more

general and inexpensive catalytic protocol for substituted pyrrole derivatives.

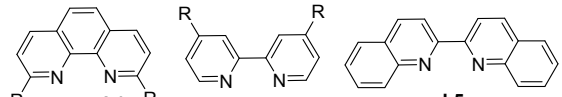
To the best of our knowledge, herein we established the first nickel-catalyzed double de-hydrogenation of secondary alcohols and amino alcohols following one-pot condensation and C-C/C-N bond formations to the pyrrole derivatives. A simple Ni-catalyst enables selective activation of a number of bonds in one-pot operation releasing water and hydrogen gas as by-products. Preliminary mechanistic investigations and deuterium labeling experiments establish the reaction pathways for pyrroles synthesis (Scheme 1b).[10]

Table 1. Optimization of the Reaction Conditions[a,b]



1a 2a 3a

entry	deviations from standard conditions	Conv. **3a** (%)
1	none	53 (48)[b]
2	$NiBr_2$, **L3**, *t*-BuOK (1 equiv.), 130 °C	28
3	$NiCl_2$, **L3**, *t*-BuOK (1 equiv.), 130 °C	17
4	$Ni(acac)_2$, **L3**, *t*-BuOK (1 equiv.), 130 °C	18
5	**L1**, *t*-BuOK (1 equiv.), 130 °C	32
6	**L2**, *t*-BuOK (1 equiv.), 130 °C	22
7	**L4**, *t*-BuOK (1 equiv.), 130 °C	9
8	**L5**, *t*-BuOK (1 equiv.), 130 °C	11
9	*t*-BuONa (1 equiv.), 130 °C	25
10	NaOH (1 equiv.), 130 °C	25
11	130 °C	42
12	*p*-xylene, 130 °C	20
13	toluene, 140 °C	45
14	no base, no catalyst[c]	0



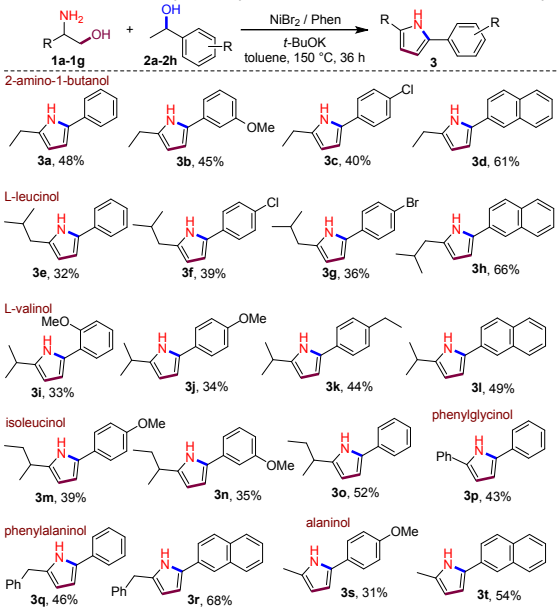
[a]Reaction conditions: 2-aminobutan-1-ol **1a** (0.25 mmol), 1-phenylethanol **2a** (0.5 mmol), $NiBr_2$ (0.025 mmol), **L1** (0.03 mmol), *t*-BuOK (0.5 mmol), toluene (2.0 mL), High pressure reactor under N_2 atmosphere in a heating magnetic stirrer, 150 °C, 36 h reaction time. [b]Conversion was determined by GC-MS (isolated yield in parentheses, average yield of two runs). [c]*t*-BuOK (0.5 mmol) was used.

RESULTS AND DISCUSSION

Recently, we demonstrated Ni-catalyzed a couple of novel protocols involving (de)hydrogenative transformations of renewable alcohols, diols or amino alcohols for the synthesis of indoles, pyrroles, pyridines, quinolines, benzimidazoles and quinoxalines.[11] However, cross-couplings of two different alcohols; secondary alcohols and β-amino alcohols to substituted pyrroles remains challenging involving two key issues; i) self-condensation of secondary alcohols and ii) self-condensation of β-amino alcohol to pyrazine. Notably, couplings of secondary alcohols and β-amino alcohols involves one-pot multi-steps transformations; dehydrogenation of secondary alcohols to carbonyls, condensations to imine followed by β-amino aldehyde, thereby, base-catalyzed condensation to the desired pyrroles (Scheme 4). Initially, we studied the model reaction between 2-aminobutane-1-ol **1a** with 1-phenylethanol **2a** following our recently established intermolecular cyclisation of β-amino alcohols with ketones.[11b] Unfortunately, only 17% conversion to the desired pyrrole **3a** was obtained when using 10 mol% $NiCl_2$, 12 mol% bipyridine **L3**, 1 equiv. of *t*-BuOK at 130 °C in toluene (Table 1, entry 3). At this point we realized that, dehydrogenation of 1-phenylethanol, **2a** to the desired carbonyl is crucial to obtain higher product yield. Therefore, to establish an efficient catalytic protocol, we examined different nickel pre-catalysts having oxidation states of Ni(0) or Ni(II) using bipyridine, **L3** as ligand. However, an increment of product conversion, up to 28%, to pyrrole **3a** was observed (Table 1, entries 2-4 and ESI Table S1). Thereafter, when using different nitrogen ligands **L1-L2** and **L4-L5**; 1,10-phenanthroline **L1** resulted moderate product conversion (Table 1, entries 5-8). At this point, we choose ligand **L1** of our choice and studied the influence and scope of different bases, such as, *t*-BuONa, NaOH, KOH, K_3PO_4, and Cs_2CO_3 did not improve the product yield further (Table 1, entries 9-10 and ESI Table S2), whereas, an increment of base equivalency resulted 42% conversion to product **3a** (Table 1, entry 11). Notably, Ni-catalysts strongly bind with free alcohols to form Ni-alkoxy species and β-hydride elimination resulted the corresponding carbonyl derivatives. Again, base also plays a key role for the cyclisation to pyrrole synthesis following C-C bond formation.

Next, applications of solvents with variable polarities, such as, *t*-amyl alcohol, *p*-xylene, 1,4-dioxane, tetrahydrofuran and 2-methyltetrahydrofuran proof inefficient (Table 1, entry 12 and ESI Table S3). However, when the reaction was performed at 150 °C, 53% conversion to pyrrole **3a** was obtained along with 48% isolated yield (Table 1, entries 1 and 13, and ESI, Table S7). As expected, control experiments in absence of base, ligand as well as catalyst revealed their independent role and we did not observe any desired product (Table 1, entry 14 and ESI Table S4-S6). Further, reactions in presence of hydrogen acceptor (styrene) or molecular sieves, did not improve the yield or selectivity of **3a**. Notably, during optimization studies (Table 1), we observed unreacted alcohols, acetophenone and unidentified mixtures of products in the GC-MS analysis of the crude reactions mixtures.

Table 2. Ni-Catalyzed Synthesis of 2,5-di-Substituted Pyrroles[a]

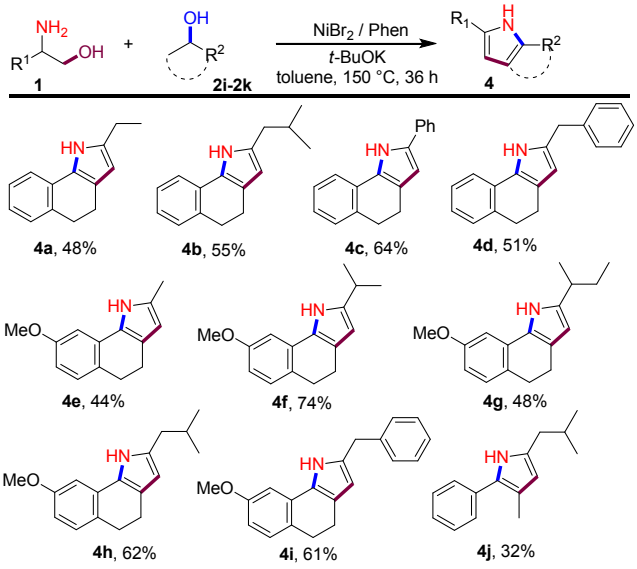


Reaction conditions: [a]**1** (0.25 mmol), **2** (0.5 mmol), $NiBr_2$ (0.025 mol %), **L1** (0.03 mol %), *t*-BuOK (0.5 mmol), toluene (1.0 mL),

high pressure reactor under N_2 atmosphere at 150 °C in a heating magnetic stirrer for 36 h. Isolated yields reported.

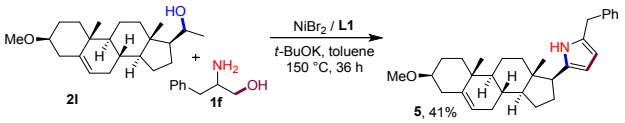
Next we explored the synthesis of 2,5-disubstituted pyrroles using the optimized conditions of Table 1 (entry 1). Initially, we studied the scope of seven different amino alcohols, bearing alkyl, aryl and benzyl groups, with 1-phenylethanol **2a** (Table 2). Interestingly, a series of less reactive amino alcohols having ethyl, iso-butyl, iso-propyl, secondary-butyl as well as methyl groups resulted the desired 2,5-disubstituted pyrroles in up to 61% yields (Table 2, **3a-3o** and **3s-3t**). To our delight, phenylglycinol **1e**, and phenylalaninol **1f**, efficiently transformed into 2,5-diaryl substituted pyrroles **3p-3r** in up to 68% isolated yield (Table 2). The general applicability of the protocol was further demonstrated using a series of electronically different secondary alcohols bearing functional groups such as, *o*-OMe *m*-OMe, *p*-OMe, *p*-Cl, *p*-Br including *p*-ethyl and naphthyl substituents and resulted moderate to good isolated yields of 2,5-disubstituted pyrroles (**3b-3d**, **3f-3h**, **3i-3l**, and **3m-3n**) with different β-amino alcohols (Table 2).

Table 3. Synthesis of 2,3,5-tri-Substituted Pyrroles[a]



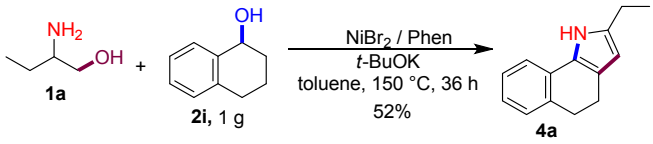
Reaction conditions: [a]**1** (0.25 mmol), **2** (0.5 mmol), $NiBr_2$ (0.025 mol %), **L1** (0.03 mol %), *t*-BuOK (0.5 mmol), toluene (1.0 mL), High pressure reactor under N_2 atmosphere at 150 °C in a heating magnetic stirrer for 36 h. Isolated yields reported.

After having this potential catalytic activity for secondary alcohols, we further explored the synthesis of 2,3,5-trisubstituted bicyclic pyrroles (Table 3). Importantly, when α-tetralol **2i**, was employed with β-amino alcohols, **1a**, **1b**, **1e** and **1f**, tri-substituted bicyclic pyrroles **4a-4d** were obtained in 48-64% isolated yields (Table 3). Further, 7-methoxy-1-tetralol **2j**, with substituted β-amino alcohols also gave the tri-substituted bicyclic pyrroles in up to 74% yield respectively (Table 3, **4e-4i**). Again, intermolecular cyclization of more challenging 1-phenyl-1-propanol **2k**, efficiently transformed into 2,3,5-trisubstituted pyrroles in acceptable yield (Table 3, **4j**). Applications of these challenging alcohols established the potential significance of the present protocol.



Scheme 2. synthetic utility: pyrrole synthesis using steroid derivative.

Again, to establish the synthetic utility, intermolecular cyclization using secondary alcohol derivative of steroid hormone **2l**, with phenylalaninol **1f**, was performed and the desired 2,5-disubstitutedpyrrole **5** was obtained in 41% yield without much affecting the steroid framework (Scheme 2). For a practical utility, a higher scale synthesis of tri-substituted pyrrole **4a** resulted 52% isolated yield (Scheme 3). Importantly, the established protocol is tolerant to amino alcohols including a variety of aryl, alkyl, methoxy, halides (Cl and Br) and unsaturated steroid framework.

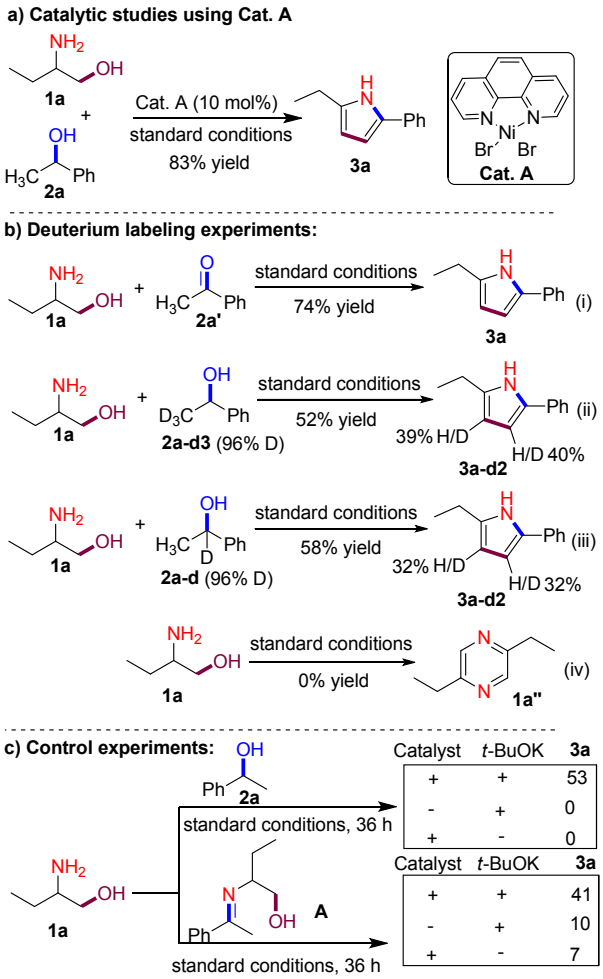


Scheme 3: Higher-Scale Synthesis of **4a**[a]. Reaction conditions: [a]2-aminobutan-1-ol **1a** (3.37 mmol, 300 mg), 1,2,3,4-tetrahydronaphthalen-1-ol **2i** (6.74 mmol, 1 g), $NiBr_2$ (10 mol%, 74 mg), 1,10-phenanthroline **L1** (12 mol%, 121 mg), *t*-BuOK (6.74 mmol, 756 mg), toluene (4.0 mL), High pressure reactor under N_2 atmosphere at 150 °C in a heating magnetic stirrer for 36 h.

Next, to interrogate the reaction mechanism for dehydrogenative couplings of alcohols and to understand the participation of the key Ni-intermediate species, **Cat. A** was independently prepared,[11] and employed using standard conditions of Table 1, **3a** was obtained in 83% yield (Scheme 4a). Nevertheless, reaction of acetophenone **2a'** with 2-aminobutan-1-ol **1a**, resulted 74% yield to pyrrole **3a**, support the dehydrogenation of secondary alcohol to ketone derivative (Scheme 4bi). Again, deuterium labeling experiment using **1a** with **2a-d3** (96% D), resulted **3a-d2** in 52% isolated yield and exhibited almost 40% deuterium incorporation in pyrrole core (Scheme 4b, ii and SI Scheme S3). Further, when **1a** was reacted with **2a-d1** (96% D), **3a-d2** was obtained in 58% yield along with 32% deuterium incorporation in pyrrole ring (Scheme 4b, iii and SI Scheme S4). These deuterium labeling experiments are in agreement for the participation of the alkyl C-H bond of secondary alcohol. Interestingly, under standard conditions, we did not observe any intermolecular cyclization or dimerization of β-amino alcohol **1a** to corresponding 2,5-diethylpyrazine (Scheme 4b, iv).[10]

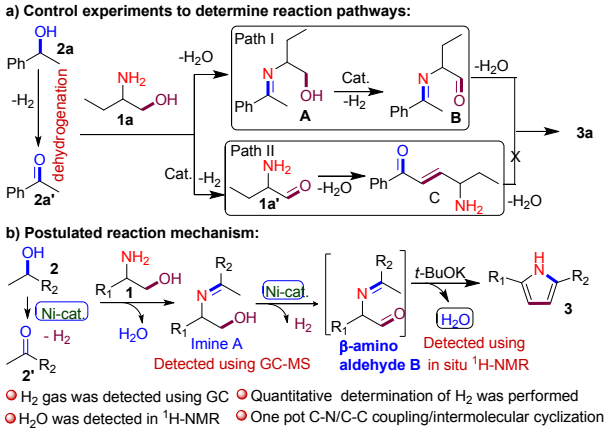
Additionally, we independently performed a series of control experiments in absence of base and catalyst involving β-amino alcohol **1a** with **2a**, which established the potential role of the individual component (Scheme 4c). Next, imine **A** was independently prepared and resulted 41% yield to pyrrole **3a** under standard catalytic conditions, whereas, intramolecular cyclization of imine **A** in absence of base and catalyst resulted albeit with poor product yields (Scheme 4c). Thereafter, to determine the actual reaction pathway a control experiment using *N*,*N*-dimethyl-ethanol with **2a** was performed using standard catalytic conditions, which exclude the possibility of the reaction pathway II (Scheme 5a and SI Scheme S2).

Nevertheless, catalytic reaction of **1a** with **2a** was monitored using GC-MS and intermediate imine **A** was detected, however, we did not observe any β-amino aldehyde **B**. We anticipated that, intra-molecular C-C coupling is reasonably fast to detect in GC-MS analysis, which is in support with the literature observations.[8a] These experiments are in agreement for the involvement of the catalytic pathway I (Scheme 5a and SI Schemes S1-S2)



Scheme 4. preliminary mechanistic studies and control experiments

On the basis of these control experiments, we postulated a probable catalytic pathway for the Ni-catalyzed double dehydrogenative condensation of two different alcohols (Scheme 5b). Initially, acetophenone **2'** was formed from secondary alcohol **2**, following intermolecular condensation with amino alcohol **1** resulted imine **A**. Thereafter, Ni-catalyzed second dehydrogenation of intermediate **A** generates β-amino aldehyde **B**, which subsequently undergoes base catalyzed C-C coupling followed by cyclization to pyrrole **3** (Scheme 5b). Notably, water and di-hydrogen are generated as side products during these processes. Therefore, quantitative evaluation of hydrogen gas was determined, and water generation was confirmed through ^{1}H-NMR studies in the reaction mixture (SI, Schemes S5-S6).



Scheme 5. Plausible mechanism for pyrrole synthesis

CONCLUSIONS

In summary, the first Ni-catalyzed double dehydrogenative couplings of two different alcohols to substituted pyrroles is demonstrated. Inexpensive $NiBr_2$/1,10-phenanthroline enables a series of 2,5-di-substituted and 2,3,5-tri-substituted pyrroles in up to 83% yield. Amino alcohols, alkyl, alkoxy, halides including steroid derivative were efficiently transformed into interesting pyrrole derivatives. Mechanistic studies including defined Ni-catalyst and intermediate species, deuterium labeling and control experiments as well as quantitative determination of hydrogen gas and detection of water generation in the reactions were performed.

Experimental section

General Information:

All solvents and reagents were used, as received from the suppliers. TLC was performed on Merck Kiesel gel 60, F254 plates with the layer thickness of 0.25 mm. Column chromatography was performed on silica gel (100-200 mesh) using a gradient of ethyl acetate and hexane as mobile phase. ^{1}H NMR spectral data were collected at, 400 (JEOL), 500 (Bruker) MHz, while ^{13}C NMR were recorded at 100, 125 MHz. 1H NMR spectral data are given as chemical shifts in ppm followed by multiplicity (s- singlet; d- doublet; t- triplet; q- quartet; m-multiplet), number of protons and coupling constants. 13C{1H} NMR chemical shifts are expressed in ppm. HRMS (ESI) spectral data were collected using Bruker High Resolution Mass Spectrometer. All nickel salts were purchased from Sigma Aldrich. Nickel(II) bromide (Assay- 98%; CAS Number 13462-88-9; EC Number 236-665-0; Pack Size- No 217891-10G). All nitrogen ligands were purchased from Sigma Aldrich or Alfa Aesar. Potassium tert-butoxide was purchased from Avra Synthesis Pvt. Ltd., India. (Purity-98%, CAS No: 865-47-4, Catalog No- ASP2012).

General procedure for synthesis of pyrroles: For the synthesis of 2-ethyl-5-phenyl-1*H*-pyrrole **(3a):** In a 5 mL oven dried high pressure glass vials, 2-aminobutan-1-ol **1a** (0.25 mmol, 23 mg), *t*-BuOK (0.5 mmol, 56 mg), $NiBr_2$ (10 mol%, 10.9 mg), 1,10-phenanthroline **L1** (12 mol%, 10.5 mg), 1-phenylethanol **2a** (0.5 mmol, 61 mg) in a toluene 1.0 mL were taken under an atmosphere of N_2 in a high pressure reactor and heated in heating magnetic stirrer at 150 ˚C for 36 h. The reaction mixture was cooled to room temperature and 3.0 mL

of ethyl acetate was added and concentrated *in vacuo.* The residue was purified by column chromatography using a gradient of hexane and ethyl acetate (eluent system) to afford the pure product **3a**. This procedure was used as general procedure for the synthesis of pyrroles

Preparation of starting material (2l): In a 50 mL oven dried RB flask, 3 methyl ether of 5-Pregnen-3β-ol-20-one [11b] (88 mg, 0.26 mmol) in a MeOH 10 mL were taken and stirred at 0 ˚C. $NaBH_4$ (2.0 equiv.) was added to the reaction mixture in portion wise at 0 ˚C and continued reaction at RT for 15 h. The reaction mixture was quenched with NH_4Cl solution and the reaction mixture was partitioned between ethyl acetate (25.0 mL) and water (25.0 mL) in a separating funnel. The organic layer was washed with water, and brine, dried over anhydrous Na_2SO_4 (s) and concentrated *in vacuo*. The residue was purified by column chromatography using a gradient of hexane and ethyl acetate (eluent system) to afford the pure product as colourless solid (430 mg, 65% yield). **NMR DATA**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (dd, J = 3.4, 1.7 Hz, 1H), 3.73 (d, J = 4.0 Hz, 1H), 3.55-3.47 (m, 1H), 3.34 (s, 3H), 3.09-3.01 (m, 1H), 2.40-2.3 (m, 1H), 2.27 (dd, J = 5.2, 1.9 Hz, 2H), 2.06 (dt, J = 12.5, 3.5 Hz, 2H), 2.01-1.92 (m, 3H), 1.91-1.79 (m, 5H), 1.67-1.61 (m, 3H), 1.50-1.44 (m, 5H), 1.35-1.29 (m, 2H), 1.12 (s, 3H), 1.00 (s, 3H), 0.76 (s, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 141.1, 121.5, 80.4, 71.9, 70.6, 58.6, 56.3, 55.7, 50.3, 42.4, 40.0, 38.8, 37.3, 36.6, 32.0, 31.8, 29.8, 28.1, 25.7, 24.6, 23.7, 21.0, 19.5, 12.5.

Procedure for Gram-Scale Synthesis of 4a: The gram scale reaction was performed using 2-aminobutan-1-ol **1a** (3.37 mmol, 300 mg), *t*-BuOK (6.74 mmol, 756 mg), $NiBr_2$ (10 mol%, 74 mg), 1,10-phenanthroline **L1** (12 mol%, 121 mg), 1,2,3,4-tetrahydronaphthalen-1-ol **2i** (6.74 mmol, 1 g) and toluene (4.0 mL) in a 35 mL ace pressure tube under an atmosphere of N_2 at 150 ˚C in an oil bath for 36 h. The reaction mixture was cooled to room temperature and 8.0 mL of ethyl acetate was added and concentrated *in vacuo.* The residue was purified by column chromatography using a gradient of hexane and ethyl acetate (eluent system) to afford the pure product **4a** (345 mg, 52% yield).

Characterization Data of the Synthesized Compounds:

2-Ethyl-5-phenyl-1*H*-pyrrole (3a):[11b] Following the general procedure, the title product was obtained as a colourless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 20 mg, 48%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.46-7.42 (m, 2H), 7.36-7.31 (m, 2H), 7.16 (t, J = 7.3 Hz, 1H), 6.42 (t, J = 3.0 Hz, 1H), 5.99 (t, J = 3.0 Hz, 1H), 2.69 (q, J = 7.6 Hz, 2H), 1.29 (t, J = 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 135.7, 133.1, 130.7, 128.9, 125.8, 123.5, 106.3, 106.1, 21.1, 13.7.

2-Ethyl-5-(3-methoxyphenyl)-1*H*-pyrrole (3b):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 2% ethyl acetate in hexane. Yield = 22 mg, 45%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.25 (t, J = 8.0 Hz, 1H), 7.02 (d, J = 7.7 Hz, 1H), 6.99-6.95 (m, 1H), 6.72 (dd, J = 8.2, 2.5 Hz, 1H), 6.41 (t, J = 3.0 Hz, 1H), 5.98 (t, J = 2.9 Hz, 1H), 3.83 (s, 3H), 2.68 (q, J = 7.6 Hz, 2H), 1.29 (t, J = 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 160.1, 135.8, 134.5, 130.5, 129.9, 116.1, 111.1, 109.4, 106.4, 106.3, 55.3, 21.1, 13.7.

2-Ethyl-5-(4-chlorophenyl)-1*H*-pyrrole (3c):[10a] Following the general procedure, the title product was obtained as a colourless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 20 mg, 40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.36 (t, J = 2.7 Hz, 1H), 7.34 (d, J = 1.8 Hz, 1H), 7.31-7.29 (m, 1H), 7.25 (s, 1H), 6.39 (t, J = 3.1 Hz, 1H), 6.05-5.94 (m, 1H), 2.67 (q, J = 7.6 Hz, 2H), 1.28 (t, J = 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 136.2, 131.6, 131.2, 129.6, 129.0, 124.6, 106.6, 106.5, 21.1, 13.7.

2-Ethyl-5-(naphthalen-2-yl)-1*H*-pyrrole (3d):[11b] Following the general procedure, the title product was obtained as a colourless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 33 mg, 61%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.83-7.76 (m, 4H), 7.64 (dd, J = 8.6, 1.8 Hz, 1H), 7.48-7.36 (m, 2H), 6.55 (t, J = 3.1 Hz, 1H), 6.04 (t, J = 3.0 Hz, 1H), 2.73 (q, J = 7.6 Hz, 2H), 1.33 (t, J = 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 136.2, 134.0, 132.0, 130.7, 130.5, 128.6, 127.8, 127.6, 126.5, 125.2, 123.2, 120.2, 106.9, 106.6, 21.2, 13.7.

2-Isobutyl-5-phenyl-1*H*-pyrrole (3e):[11b] Following the general procedure, the title product was obtained as a colourless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 15 mg, 32%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.46-7.42 (m, 2H), 7.35 (dd, J = 10.6, 5.0 Hz, 2H), 7.20-7.13 (m, 1H), 6.44 (t, J = 3.0 Hz, 1H), 5.98 (t, J = 3.0 Hz, 1H), 2.51 (d, J = 7.1 Hz, 2H), 1.90 (dp, J = 13.5, 6.7 Hz, 1H), 0.98 (d, J = 6.6 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 133.4, 133.1, 130.5, 128.9, 125.7, 123.4, 108.1, 106.2, 37.5, 29.4, 22.6.

2-(4-Chlorophenyl)-5-isobutyl-1*H*-pyrrole (3f):[11b] Following the general procedure, the title product was obtained as a colourless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 22 mg, 39%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.34 (d, J = 8.7 Hz, 2H), 7.28 (d, J = 8.7 Hz, 2H), 6.39 (t, J = 3.1 Hz, 1H), 5.95 (t, J = 3.0 Hz, 1H), 2.49 (d, J = 7.1 Hz, 2H), 1.94-1.82 (m, 1H), 0.95 (d, J = 6.6 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 133.8, 131.6, 131.1, 129.0, 128.3, 124.5, 108.3, 106.7, 37.4, 29.3, 22.5.

2-(4-Bromophenyl)-5-isobutyl-1*H*-pyrrole (3g):[11b] Following the general procedure A, the title product was obtained as a colourless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 24 mg, 36%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.43 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 6.42-6.38 (m, 1H), 5.95 (t, J = 3.0 Hz, 1H), 2.48 (d, J = 7.1 Hz, 2H), 1.94-1.82 (m, 1H), 0.95 (d, J = 6.6 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 133.9, 131.9, 128.9, 124.8, 123.4, 119.0, 108.4, 106.7, 37.4, 29.3, 22.6.

2-Isobutyl-5-(naphthalen-2-yl)-1*H*-pyrrole (3h):[11b] Following the general procedure, the title product was obtained as a colourless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 41 mg, 66%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.79 (dd, J = 10.7, 6.5 Hz, 4H), 7.67-7.60 (m, 1H), 7.49-7.35 (m, 2H), 6.58-6.53 (m, 1H), 6.05-6.00 (m, 1H), 2.55 (d, J = 7.5 Hz, 2H), 2.00-1.88 (m, 1H), 1.00 (d, J = 6.8 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 134.0, 133.8, 131.9, 130.6, 130.5, 128.6, 127.8, 127.6, 126.5, 125.2, 123.2, 120.1, 108.3, 107.0, 37.5, 29.4, 22.6.

2-Isopropyl-5-(2-methoxyphenyl)-1*H*-pyrrole (3i):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 17 mg, 33%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H), 7.61 (dd, J = 7.7, 1.6 Hz, 1H), 7.14-7.07 (m, 1H), 6.95 (ddd, J = 10.7, 5.9, 2.1 Hz, 2H), 6.52-6.48 (m, 1H), 5.97 (t, J = 3.5 Hz, 1H), 3.95 (s, 3H), 3.03-2.93 (m, 1H), 1.30 (d, J = 6.9 Hz, 6H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 154.4, 139.1, 128.0, 126.2, 126.1, 121.5, 111.8, 106.1, 103.8, 55.8, 27.2, 22.6.

2-Isopropyl-5-(4-methoxyphenyl)-1*H*-pyrrole (3j):[11b] Following the general procedure, the title product was obtained as a white solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 18 mg, 34%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.37 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 6.29 (t, J = 3.0 Hz, 1H), 5.96 (t, J = 2.8 Hz, 1H), 3.81 (s, 3H), 3.01-2.88 (m, 1H), 1.30 (d, J = 6.9 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 158.0, 139.7, 130.6, 126.3, 125.0, 125.0, 114.3, 104.8, 55.4, 27.4, 22.8.

2-(4-Ethylphenyl)-5-isopropyl-1*H*-pyrrole (3k):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 23 mg, 44%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.37 (d, J = 8.3 Hz, 2H), 7.18 (d, J = 8.2 Hz, 2H), 6.39-6.35 (m, 1H), 5.98 (t, J = 3.4 Hz, 1H), 3.03-2.92 (m, 1H), 2.65 (q, J = 7.6 Hz, 2H), 1.31 (d, J = 6.9 Hz, 6H), 1.25 (t, J = 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 141.9, 140.0, 130.8, 130.7, 128.4, 123.7, 105.3, 104.8, 28.6, 27.3, 22.8, 15.7.

2-Isopropyl-5-(naphthalen-2-yl)-1*H*-pyrrole (3l):[11b] Following the general procedure, the title product was obtained as a colourless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 28 mg, 49%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (dt, J = 7.3, 3.3 Hz, 1H), 8.14 (s, 1H), 7.92-7.83 (m, 1H), 7.77 (dd, J = 7.0, 3.2 Hz, 1H), 7.49 (dt, J = 7.2, 4.0 Hz, 4H), 6.43 – 6.39 (m, 1H), 6.12-6.07 (m, 1H), 3.10-2.96 (m, 1H), 1.35 (d, J = 7.1 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 139.9, 134.2, 131.9, 131.4, 129.0, 128.5, 127.6, 126.3, 126.0, 125.9, 125.7, 125.6, 109.4, 104.4, 27.3, 22.8.

2-(*sec*-Butyl)-5-(4-methoxyphenyl)-1*H*-pyrrole (3m):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 22 mg, 39%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.37 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 6.30 (t, J = 3.0 Hz, 1H), 5.95 (t, J = 3.0 Hz, 1H), 3.82 (s, 3H), 2.77-2.66 (m, 1H), 1.72 – 1.57 (m, 2H), 1.28 (d, J = 7.0 Hz, 3H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 157.9, 138.5, 130.3, 126.3, 124.8, 114.3, 105.4, 104.7, 55.3, 34.4, 30.3, 20.1, 11.9.

2-(*sec*-Butyl)-5-(3-methoxyphenyl)-1*H*-pyrrole (3n):[11b] Following the general procedure, the title product was obtained as a light brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 20 mg, 35%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.25 (t, J = 8.0 Hz, 1H), 7.02 (ddd, J = 7.7, 1.5, 0.9 Hz, 1H), 6.98-6.95 (m, 1H), 6.71 (ddd, J = 8.2, 2.5, 0.6 Hz, 1H), 6.43-6.38 (m, 1H), 5.96 (t, J = 2.9 Hz, 1H), 3.83 (s, 3H), 2.75-2.66 (m, 1H), 1.71-1.56 (m, 2H), 1.28 (d, J = 7.0 Hz, 3H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 160.1, 139.3, 134.6, 130.2, 129.9, 116.1, 111.0, 109.4, 106.2, 105.7, 55.4, 34.5, 30.3, 20.1, 11.9.

2-(*sec*-Butyl)-5-phenyl-1*H*-pyrrole (3o):[11b] Following the general procedure, the title product was obtained as a colourless oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 25 mg, 52%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.46 (d, J = 7.7 Hz, 2H), 7.35 (t, J = 7.7 Hz, 2H), 7.17 (t, J = 7.3 Hz, 1H), 6.45 (t, J = 2.9 Hz, 1H), 6.00 (t, J = 2.7 Hz, 1H), 2.79-2.69 (m, 1H), 1.66 (tdd, J = 20.7, 13.7, 7.1 Hz, 2H), 1.31 (d, J = 7.0 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 139.3, 133.1, 130.4, 128.9, 125.7, 123.5, 105.9, 105.8, 34.5, 30.4, 20.2, 12.0.

2,5-Diphenyl-1*H*-pyrrole (3p):[11b] Following the general procedure, the title product was obtained as a colourless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 23 mg, 43%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.56-7.51 (m, 4H), 7.42-7.36 (m, 4H), 7.23 (dd, J = 10.7, 4.3 Hz, 2H), 6.59 (d, J = 2.6 Hz, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 133.2, 132.6, 129.0, 126.5, 123.9, 108.0.

2-Benzyl-5-phenyl-1*H*-pyrrole (3q):[11b] Following the general procedure, the title product was obtained as a colourless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 26 mg, 46%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.41-7.37 (m, 2H), 7.36-7.29 (m, 4H), 7.28-7.23 (m, 3H), 7.16 (t, J = 7.3 Hz, 1H), 6.45 (t, J = 3.0 Hz, 1H), 6.06 (t, J = 3.0 Hz, 1H), 4.03 (s, 2H); ^{13}C{H} NMR (100 MHz, $CDCl_3$) δ 139.4, 132.9, 132.1, 131.6, 128.9, 128.8, 128.8, 126.6, 125.9, 123.6, 108.7, 106.2, 34.4.

2-Benzyl-5-(naphthalen-2-yl)-1*H*-pyrrole (3r):[11b] Following the general procedure, the title product was obtained as a colourless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 48 mg, 68%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.81 (dd, J = 13.1, 5.7 Hz, 3H), 7.76 (s, 1H), 7.64 (dd, J = 8.5, 1.7 Hz, 1H), 7.49 (d, J = 6.8 Hz, 1H), 7.45-7.42 (m, 1H), 7.39 (t, J = 7.4 Hz, 2H), 7.34-7.30 (m, 3H), 6.61 (t, J = 3.0 Hz, 1H), 6.14 (t, J = 2.9 Hz, 1H), 4.10 (s, 2H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 139.3, 133.8, 132.5, 131.9, 131.6, 130.2, 128.8, 128.7, 128.5, 127.7, 127.6, 126.6, 126.4, 125.2, 123.1, 120.4, 109.0, 106.9, 34.3.

2-(4-Methoxyphenyl)-5-methyl-1*H*-pyrrole (3s):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 14 mg, 31%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.35 (d, J = 9.1 Hz, 2H), 6.88 (d, J = 9.0 Hz, 2H), 6.30-6.24 (m, 1H), 5.95-5.88 (m, 1H), 3.81 (s, 3H), 2.32 (s, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 158.0, 130.9, 128.4, 126.3, 124.9, 114.4, 107.7, 105.1, 55.4, 13.3.

2-Methyl-5-(naphthalen-2-yl)-1*H*-pyrrole (3t):[11b] Following the general procedure, the title product was obtained as a colourless solid using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 27 mg, 54%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.81-7.76 (m, 4H), 7.62 (dd, J = 8.6, 1.7 Hz, 1H), 7.46-7.35 (m, 2H), 6.52 (t, J = 3.0 Hz, 1H), 6.00 (t, J = 5.8 Hz, 1H), 2.37 (s, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 133.9, 131.9, 130.8, 130.4, 129.6, 128.5, 127.7, 127.6, 126.4, 125.1, 123.1, 120.1, 108.2, 107.0, 13.3.

8-Methoxy-2-methyl-4,5-dihydro-1*H*-benzo[*g*]indole (4a): Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 23 mg, 48%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.15 (t, J = 7.1 Hz, 2H), 7.09-7.07 (m, 1H), 7.01-6.97 (m, 1H), 5.82 (d, J = 2.3 Hz, 1H), 2.90 (t, J = 7.6 Hz, 2H), 2.71-2.66 (m, 4H), 1.28 (t, J = 7.6 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 135.4, 134.5, 131.2, 129.6, 128.4, 126.4, 124.5, 120.7, 104.7, 104.6, 30.2, 22.0, 21.2, 13.8. HRMS (ESI-TOF) m/z $[M]^+$ Calcd for $C_{14}H_{15}N$ 197.1204, Found 197.1209.

8-Methoxy-2-methyl-4,5-dihydro-1*H*-benzo[*g*]indole (4b): Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 30 mg, 55%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.16 (t, J = 7.3 Hz, 2H), 7.09 (d, J = 7.3 Hz, 1H), 7.02-6.98 (m, 1H), 5.81 (d, J = 2.3 Hz, 1H), 2.91 (t, J = 7.6 Hz, 2H), 2.73-2.68 (m, 2H), 2.49

(d, J = 7.1 Hz, 2H), 1.94-1.84 (m, 1H), 0.98 (s, 3H), 0.97 (s, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 134.4, 133.0, 129.7, 128.3, 126.5, 126.3, 124.4, 120.7, 117.6, 106.4, 37.6, 30.2, 29.4, 22.6, 22.0. HRMS (ESI-TOF) m/z $[M]^+$ Calcd for $C_{16}H_{19}N$ 225.1517, Found 225.1507.

8-Methoxy-2-methyl-4,5-dihydro-1*H*-benzo[*g*]indole (4c): Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 39 mg, 64%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.53 (d, J = 7.6 Hz, 2H), 7.39 (d, J = 7.5 Hz, 2H), 7.24-7.19 (m, 4H), 7.07 (t, J = 6.6 Hz, 1H), 6.43 (d, J = 2.2 Hz, 1H), 2.96 (t, J = 7.1 Hz, 2H), 2.78 (s, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 136.0, 135.1, 132.7, 129.0, 128.6, 128.4, 128.3, 126.7, 126.3, 125.3, 123.8, 122.3, 118.4, 106.1, 30.0, 21.9. HRMS (ESI-TOF) m/z $[M]^+$ Calcd for $C_{18}H_{15}N$: 245.1204, Found 245.1209.

8-Methoxy-2-methyl-4,5-dihydro-1*H*-benzo[*g*]indole (4d): Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 33 mg, 51%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.28-7.23 (m, 2H), 7.19 (t, J = 3.8 Hz, 3H), 7.09-7.03 (m, 2H), 6.95-6.92 (m, 2H), 5.80 (d, J = 2.2 Hz, 1H), 3.94 (s, 2H), 2.83 (t, J = 7.6 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 139.3, 134.4, 131.6, 129.3, 128.6, 128.2, 127.1, 126.4, 126.3, 124.5, 120.5, 117.7, 106.9, 106.8, 34.4, 30.0, 21.8. HRMS (ESI-TOF) m/z $[M]^+$ Calcd for $C_{19}H_{17}N$: 259.1361, Found 282.1390.

8-Methoxy-2-methyl-4,5-dihydro-1*H*-benzo[g]indole (4e):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 28 mg, 44%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.09 (d, J = 8.2 Hz, 1H), 6.67 (d, J = 2.5 Hz, 1H), 6.57 (dd, J = 8.2, 2.5 Hz, 1H), 5.81 (d, J = 1.4 Hz, 1H), 3.81 (s, 3H), 2.84 (t, J = 7.6 Hz, 2H), 2.67 (t, J = 7.6 Hz, 2H), 2.32 (s, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 158.6, 130.5, 129.0, 126.8, 126.5, 121.5, 108.9, 106.5, 106.4, 104.4, 55.4, 29.3, 22.2, 13.4.

2-Isopropyl-8-methoxy-4,5-dihydro-1*H*-benzo[*g*]indole (4f):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 44 mg, 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.06 (d, J = 8.1 Hz, 1H), 6.66 (d, J = 2.5 Hz, 1H), 6.54 (dd, J = 8.2, 2.6 Hz, 1H), 5.83 (d, J = 2.4 Hz, 1H), 3.81 (s, 3H), 2.83 (t, J = 7.6 Hz, 2H), 2.66 (t, J = 7.6 Hz, 2H), 2.17-2.01 (m, 1H), 1.29 (d, J = 6.9 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 158.6, 140.2, 130.5, 128.9, 126.9, 126.2, 121.0, 108.9, 104.4, 103.4, 55.5, 29.3, 27.5, 22.8, 22.2.

2-(*sec*-Butyl)-8-methoxy-4,5-dihydro-1*H*-benzo[*g*]indole (4g):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 30 mg, 48%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.06 (d, J = 8.2 Hz, 1H), 6.64 (d, J = 2.5 Hz, 1H), 6.53 (dd, J = 8.2, 2.5 Hz, 1H), 5.81 (d, J = 2.3 Hz, 1H), 3.80 (s, 3H), 2.83 (t, J = 7.6 Hz, 2H), 2.72-2.62 (m, 3H), 1.70-1.57 (m, 2H), 1.27 (d, J = 7.0 Hz, 3H), 0.92 (t, J = 7.4 Hz, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 158.5, 139.1, 130.5, 128.8, 126.8, 126.0, 121.0, 108.7, 104.3, 104.0, 55.4, 34.6, 30.3, 29.2, 22.2, 20.1, 11.9.

2-(*sec*-Butyl)-8-methoxy-4,5-dihydro-1*H*-benzo[*g*]indole (4h): Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 39 mg, 62%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.07 (d, J = 8.2 Hz, 1H), 6.64 (d, J = 2.5 Hz, 1H), 6.54 (dd, J = 8.2, 2.6 Hz, 1H), 5.79 (d, J = 2.3 Hz, 1H), 3.80 (s, 3H), 2.83 (t, J = 7.6 Hz, 2H), 2.68-2.64 (m, 2H), 2.48 (d, J = 7.1 Hz, 2H), 1.91-1.85 (m, 1H), 0.97 (s, 3H), 0.95 (s, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 158.6, 133.1, 130.6, 128.9, 126.8, 126.2, 121.3, 108.8, 106.4, 104.4, 55.4, 37.6, 29.4, 29.2, 22.6, 22.2. HRMS (ESI-TOF) m/z $[M]^+$ Calcd for $C_{17}H_{21}NO$ 255.1623, Found 255.1625.

2-Benzyl-8-methoxy-4,5-dihydro-1*H*-benzo[*g*]indole (4i):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 44 mg, 61%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.36-7.28 (m, 2H), 7.28-7.23 (m, 3H), 7.06 (d, J = 8.1 Hz, 1H), 6.59-6.52 (m, 2H), 5.87 (d, J = 2.1 Hz, 1H), 4.00 (s, 2H), 3.77 (s, 3H), 2.83 (t, J = 7.6 Hz, 2H), 2.66 (t, J = 7.6 Hz, 2H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 167.2, 139.4, 131.8, 129.0, 128.8, 128.8, 126.9, 126.6, 121.2, 109.8, 109.1, 107.0, 107.0, 104.5, 55.4, 34.5, 29.2, 22.2.

5-Isobutyl-3-methyl-2-phenyl-1*H*-pyrrole (4j):[11b] Following the general procedure, the title product was obtained as a pale brown oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 17 mg, 32%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.41-7.34 (m, 4H), 7.21-7.16 (m, 1H), 5.83 (d, J = 2.8 Hz, 1H), 2.45 (d, J = 7.0 Hz, 2H), 2.24 (s, 3H), 1.92-1.80 (m, 1H), 0.96 (d, J = 6.6 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 134.1, 131.7, 128.7, 126.5, 125.9, 125.4, 116.4, 110.4, 37.4, 29.3, 22.6, 12.7.

2-Benzyl-5-((3*S*,8*S*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-methoxy-10,13-dimethyl-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-1*H*-pyrrole (5):[11b] Following the general procedure, the title product was obtained as a pale yellow oil using silica-gel column chromatography eluting with 1% ethyl acetate in hexane. Yield = 18 mg, 41%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.33 (dd, J = 10.2, 4.6 Hz, 2H), 7.23 (dd, J = 15.3, 7.7 Hz, 3H), 5.90 (t, J = 2.8 Hz, 1H), 5.87 (t, J = 2.9 Hz, 1H), 5.40-5.37 (m, 1H), 3.97 (s, 2H), 3.38 (s, 3H), 3.09 (ddd, J = 11.3, 6.8, 4.6 Hz, 1H), 2.55 (t, J = 9.8 Hz, 1H), 2.44-2.40 (m, 1H), 2.22-2.15 (m, 2H), 2.04-1.94 (m, 3H), 1.92-1.87 (m, 2H), 1.76-1.70 (m, 2H), 1.61-1.56 (m, 2H), 1.47 (ddd, J = 12.4, 9.7, 4.8 Hz, 3H), 1.31-1.27 (m, 1H), 1.26-1.21 (m, 1H), 1.14-1.07 (m, 2H), 1.02 (s, 3H), 0.52 (s, 3H); ^{13}C{1H} NMR (125 MHz, $CDCl_3$) δ 141.0, 139.9, 132.3, 128.8, 128.6, 128.5, 126.3, 121.4, 106.2, 105.4, 80.3, 55.8, 55.6, 50.4, 50.2, 43.6, 38.7, 38.0, 37.2, 37.0, 34.2, 32.3, 31.9, 28.0, 26.3, 24.3, 20.9, 19.4, 13.0.

ASSOCIATED CONTENT

Supporting Information

The supporting Information is available free of charge on the ACS Publications website

Optimization studies, NMR spectra (PDF)

AUTHOR INFORMATION

Corresponding Author

* E-mail: dbane.fcy@iitr.ac.in

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