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## Iron-Catalyzed Direct C3-Benzylation of Indoles with Benzyl Alcohols through Borrowing Hydrogen

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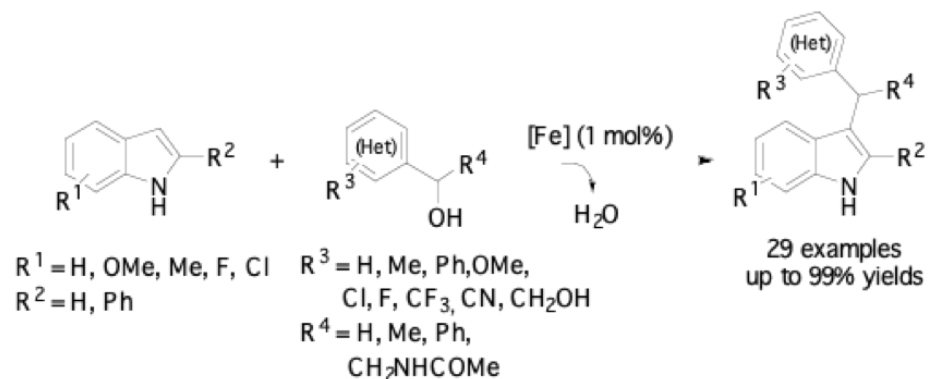
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TABLE OF CONTENTS/ABSTRACTGRAPHIC



### ABSTRACT

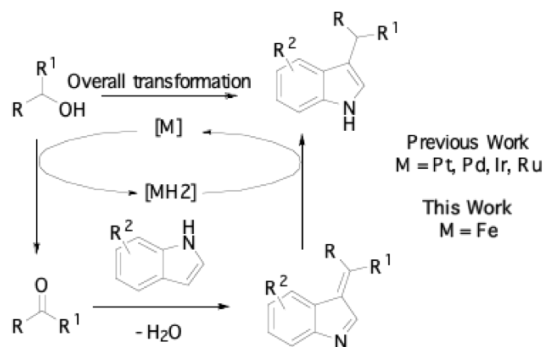
We present the coupling of primary and secondary benzyl alcohols with indoles to form 3-benzylated indoles and  $\text{H}_2\text{O}$  that is catalyzed, for the first time, by a complex of earth-abundant iron. This transformation accommodates a variety of substrates and is distinguished by its operational simplicity, sustainability, high functional-group tol-

erance, and amenability to gram-scale synthesis. On the basis of the preliminary experimental observations, we propose that the reaction proceeds through a borrowing hydrogen process.

The catalytic alkylation of indoles with alcohols represents an environmentally benign and atom-economic pathway for the synthesis of substituted indoles and indolenine, which have important synthetic applications in the synthesis of dyes, fragrances, pharmaceuticals (including controlling bacterial behavior), and agricultural chemicals.<sup>1</sup> In terms of sustainability, the choice of alcohols as substrates is highly desirable as they are readily available by a variety of industrial processes, inexpensive because they can be obtained renewably via fermentation or catalytic conversion of lignocellulosic biomass, relatively nontoxic, and easy to use.<sup>2</sup> The best known method for the alkylation of indoles is the Friedel–Crafts reaction with haloalkanes and related alkyl agents mediated by Lewis acid.<sup>3</sup> However, this method can be problematic due to over alkylation, toxic nature of many alkyl (pseudo)halides and also produce large amounts of inorganic salt. The so-called ‘borrowing hydrogen methodology’<sup>4</sup> has aroused great interest in recent years and is an excellent protocol for the catalytic C-alkylation of ketones and related compounds, using nontoxic alcohols.<sup>5</sup> The catalytic cycle, for the indole alkylation, involves three or four successive steps: (i) acceptorless dehydrogenation of alcohols, (ii) alkylideneindolenine formation (which behaves as an actual vinylogous imine), and (iii) *in situ* hydrogenation of the double bond (borrowing hydrogen methodology) and aromatization generate the alkylated-indole compound. Key features are that the process is hydrogen neutral and that the only stoichiometric byproduct is water (Scheme 1).

Despite the significance of such coupling reactions, homogeneous and heterogeneous catalysts mostly employ precious metals such as Pt,<sup>6</sup> Pd,<sup>7</sup> Ir,<sup>8</sup> and Ru<sup>9</sup>. In comparison, the same reaction with catalysts that utilize nonprecious, less toxic earth-abundant metals<sup>10</sup> is much less developed. However, base metals have been found to readily oxidize alcohols via acceptorless dehydrogenation.<sup>11</sup>

**Scheme 1. Representative Reaction Pathway for the C3-Alkylation of Indoles by Transition Metal-Catalyzed Borrowing Hydrogen Methodology**



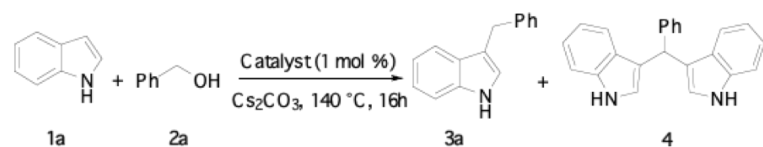
On the other hand, the groups of Feringa and Barta, Wills, and Zhao have reported the alkylation of primary amines with alcohols to give secondary and tertiary amines by utilizing iron catalysts featuring functionalized cyclopentadienone or hydroxy cyclopentadienyl ligands based on Knölker's complex or derivatives thereof.<sup>12</sup> Applications of this methodology based on an iron-catalyzed hydrogen-borrowing strategy process also include the formation of new carbon–carbon bonds.<sup>13</sup>

Inspired by these recent discoveries, we report herein a green, economical and efficient iron-catalyzed C3-selective alkylation of indole. This reaction employs iron(II) phthalocyanine (Fe(II)Pc), an inexpensive commercially available compound that is typically used as an industrial additive for ink as well as photonic and optical material manufacturing. Of note, to date, Fe(II)Pc complexes have not been applied as catalysts for the formation of new carbon–carbon bonds via the borrowing hydrogen process.<sup>14</sup>

The reaction of unsubstituted indole (**1a**) with benzyl alcohol (**2a**) was selected as the model reaction to establish the best reaction conditions. Initially, the effect of various iron-based catalysts was investigated (Table 1). The reaction did not proceed without any catalyst in the presence of Cs<sub>2</sub>CO<sub>3</sub>, which excluded the contribution of the base itself as a catalyst (Table 1, entry 1).<sup>15</sup> The highest activity was observed with Fe(II)Pc and stoichiometric amount of Cs<sub>2</sub>CO<sub>3</sub> (Table 1, entries 5-7). Other iron salts were found to be ineffective and, not surprisingly, led to the formation of bis(indolyl)methane (**4**) in poor yields (Table 1, entries 2–4).<sup>16</sup> Due to its inherent redox properties, the iron(0)tricarbonyl complex such as the Knölker-type catalyst is widely known to activate inert substrates via dehydrogenation/hydrogenation reactions and has been reported previously for C–C bond formation.<sup>17</sup> Neither alone (Table 1, entry 8) nor in the presence of 10 mol% Me<sub>3</sub>NO oxidant (to form active catalyst) and PPh<sub>3</sub> ligand did the alkylated product form (Table 1, entries 9 and 10). This solvent-free reaction with Fe(II)Pc as the catalyst was excellent in terms of both yield and selectivity as compared with the corresponding reaction in

toluene (1.0 M, 54% yield; 0.5 M, 10% yield) or *tert*-amyl alcohol (at reflux under air atmosphere for 16 h afforded the desired alkylated product **3a** in 31% yield). The desired coupling product was also obtained in the absence of light as well as in the presence of radical scavengers such butylated hydroxytoluene (BHT), thus discarding the involvement of radical species in the reaction pathway (Table 1, entries 11 and 12).<sup>18</sup>

**Table 1. Optimization of the Reaction Conditions for C3-Alkylation of Indole with Benzyl Alcohol**



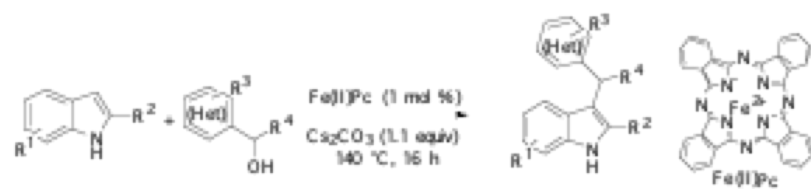
Entry <sup>a</sup>	Catalyst	Yield of <b>3a</b> <sup>b</sup> (%)
1	-	-
2	FeSO <sub>4</sub> <sup>c</sup>	-
3	FeCl <sub>2</sub> <sup>d</sup>	-
4	Fe(acac) <sub>3</sub>	-
5	Fe(II)Pc	99
6	Fe(II)Pc <sup>e</sup>	8
7	Fe(II)Pc <sup>f</sup>	trace
8	Fe-Knölker	-
9	Fe-Knölker with PPh <sub>3</sub>	-
10	Fe-Knölker with Me <sub>3</sub> NO	-
11	Fe(II)Pc in the dark	97
12	Fe(II)Pc with BHT	98

<sup>a</sup> Reaction conditions: indole (0.5 mmol), benzyl alcohol (1 mmol), Cs<sub>2</sub>CO<sub>3</sub> (0.55 mmol), catalyst (1 mol%) at 140 °C for 16 h. <sup>b</sup> Isolated yield. <sup>c</sup> Only **4** was isolated in 13% yield <sup>d</sup> Only **4** was isolated in 21% yield <sup>e</sup> Cs<sub>2</sub>CO<sub>3</sub>

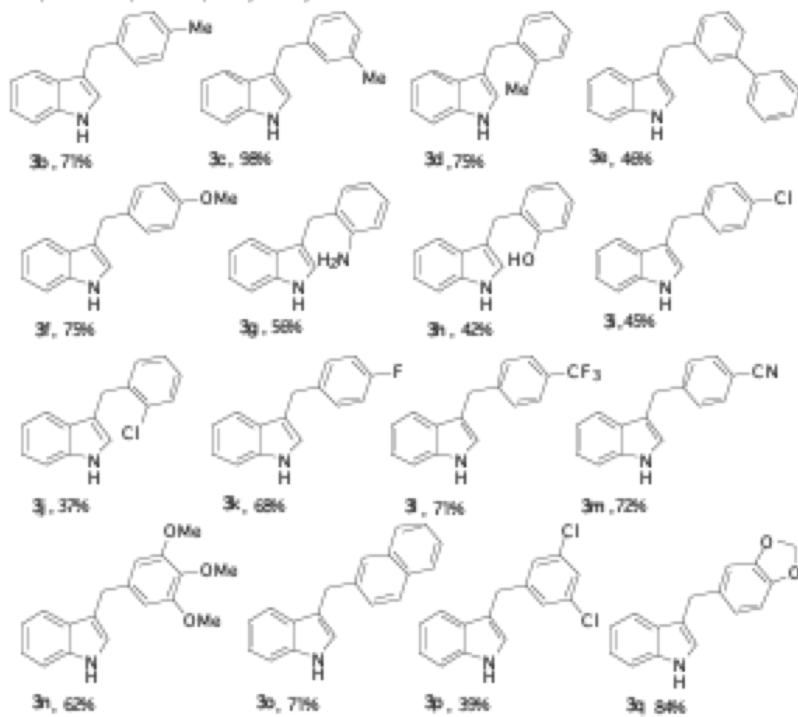
(0.05 mmol). <sup>f</sup> Without base.

Once the optimal reaction conditions were achieved, we examined the scope of the alkylation with respect to alcohols catalyzed by Fe(II)Pc, and these results are outlined in Scheme 2. The C3-alkylation of indole with primary benzylic alcohols bearing an electron-donating substituent such as methyl, phenyl, and methoxy groups afforded the corresponding products **3b–f** in 46–98% yields. Also, (2-aminophenyl)methanol and 2-(hydroxymethyl)phenol provided the products **3g–h** in good yield, 56% and 42%, respectively. Similarly, electronically deactivated benzylic alcohols, which are very poor substrates in Lewis- or Brønsted acid-catalyzed Friedel–Crafts reactions,<sup>19</sup> bearing an electron-withdrawing group such as chloro, fluoro, cyano and trifluoromethyl groups were converted to the desired products **3i–m** in 37–71% yields. A trisubstituted benzyl alcohol, such as 3,4,5-trimethoxybenzyl alcohol, was successfully transformed to 3-(3,4,5-trimethoxybenzyl)-1*H*-indole in 62% yield. A naphthyl alcohol (naphthalen-2-ylmethanol), (3,5-dichlorophenyl)methanol and benzo[1,3]dioxonyl were converted to give the corresponding alkylated indole products **3o–q** in good yields. Heteroaromatic alcohols with furanyl and thienyl groups were also tolerated, and the corresponding indoles **3r–s** were obtained in 95% and 78% yields, respectively.

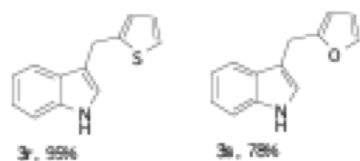
#### **Scheme 2. Scope of C3-Alkylation of Indole with Benzyl Alcohol<sup>a</sup>**



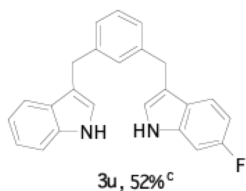
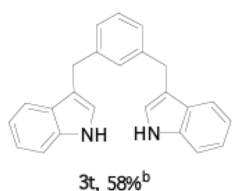
Scope with respect to primary benzyl alcohols



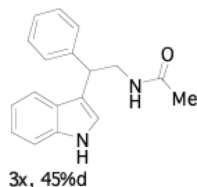
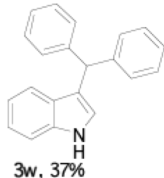
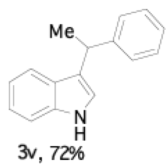
Scope with respect to heteroaromatic alcohols



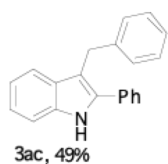
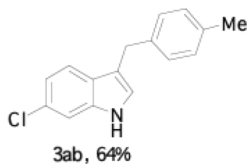
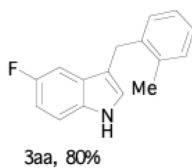
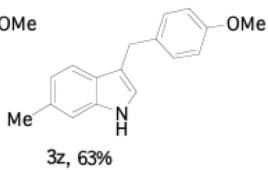
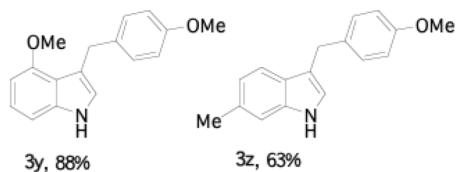
Scope with respect to diol



Scope with respect to secondary benzyl alcohols



Scope with respect to indoles



<sup>a</sup> Reaction conditions: indole (0.5 mmol), alcohol (1 mmol), Cs<sub>2</sub>CO<sub>3</sub> (0.55 mmol), Fe(II)Pc (0.055 mmol) at 140 °C for 16 h. <sup>b</sup>Indole (1 mmol), alcohol (0.5 mmol). <sup>c</sup>1*H*-indole (0.5 mmol), 6-fluoro-1*H*-indole (0.5 mmol), 2-(hydroxymethyl)phenol (0.5 mmol). <sup>d</sup> 140 °C for 36h.

This reaction sequence was demonstrated for the preparation of symmetrical bisindole compound **3t**, whereby indole, used in excess, was double alkylated with 1,3-phenylenedimethanol through a one-pot process in satisfactory yield. Moreover, sequential functionalization of diols is undoubtedly a valuable synthetic tool to obtain compounds with great diversity. We explored a selective iron-catalyzed method that allows for the preparation of non-symmetrical, functionalized bisindoles. This reaction sequence was demonstrated for the preparation of compound **3u**, whereby 1,3-phenylenedimethanol was selectively monoalkylated with indole to form (3-((1*H*-indol-3-yl)methyl)phenyl)methanol and subsequently treated with 6-fluoroindole to provide **3u**.

Next, secondary benzylic alcohols, which are less prone to the condensation and hydrogenation step in comparison to primary ones, were used as the substrate. 1-Phenylethanol, diphenylmethanol and 2-acetamido-1-phenylethanol reacted smoothly with indole, and the corresponding products **3v–x** were obtained in moderate to

good yields.

When cinnamyl alcohol was utilized, the desired product was obtained in poor yield due to large contamination of saturated derivatives; whereas with aliphatic alcohols such as cyclohexanol, cyclopropyl methanol, and 1-octanol, the reaction failed.

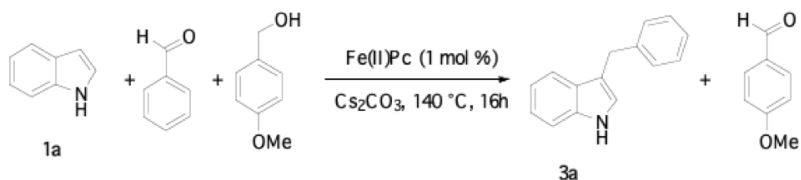
Next, we examined some representative substituted indoles to explore the generality of this novel reaction. For example, the electron-rich and sterically hindered 4-methoxyindole was converted to the desired product **3x** in a very good yield and selectivity. The 6-methyl-, 5-fluoro-, and 6-chloroindole-benzylated derivatives **3z** and **3aa-3ab** were also obtained in decent yields, although the yields were lower than those of the 4-OMe analog. Pleasingly, the presence of a substituent at C2 did not impair the reaction, despite the potential steric crowding around the reaction site. Thus, 2-phenylindole reacted efficiently with benzyl alcohol to give the corresponding product **3ac**. Not surprisingly, *N*-methylindole proved to be inert, suggesting the involvement of the indole N–H in a key interaction with the base during the rate-determining step. However, nearly complete recovery of the starting material was observed when C3-substituted indole, such as 3-methyl or 3-benzylindole, were allowed to react with benzyl alcohol under the reaction conditions reported above. Neither dearomatization of the indole nucleus to 3-benzylindolenine products nor C3- to C2-benzyl migration and rearomatization to afford 2,3-disubstituted indoles were detected, in spite of recent reports.<sup>20</sup> To highlight the synthetic utility of the present protocol, a gram-scale reaction with indole (**1a**) and benzylic alcohol (**2a**) was performed, and the efficiency of the small-scale reaction was retained upon scale-up, delivering **3a** in 92% yield.

To obtain insight into the reaction mechanism of the catalytic process, other experiments were carried out, thus providing significant evidences for a plausible borrowing hydrogen mechanism rather than a general acidic strategy involving the formation of a stabilized benzylic cation. The reaction of indole with benzyl bromide (2 equiv.) under the optimized reaction conditions gave a mixture of 1-benzyl-1*H*-indole (45%) and 1,3-dibenzyl-1*H*-indole (28%). Then, we repeated the reaction using triphenylmethanol, the starting unchanged indole was recovered, which is another indirect proof of that the cationic benzyl intermediate is not involved. When benzylic alcohol was heated in the presence of Fe(II)Pc and cesium carbonate at 140 °C in a sealed tube for 16 h, formation of a small amount of benzaldehyde (11% according to GC-analysis of the crude mixture) was observed. Finally, the competitive reaction of indole with benzaldehyde and (4-methoxyphenyl)methanol (Scheme 3) gave a mixture



6:1 of 3-benzylated compounds (based on  $^1\text{H}$  NMR spectra), in which the main product was that arising from the condensation with benzaldehyde followed by reduction of benzylideneindolenine (obviously, large formation of p-methoxybenzaldehyde was also observed). All these data together with the presence of bisindole side product **4**, obtainable only in presence of aldehyde on the reaction mixture, and the good yields obtained with electron-poor benzylic alcohols (compounds **3l**, **3m**) are confirming our initially borrowing hydrogen mechanistic hypothesis.

### Scheme 3. Competitive experiments between an aldehyde and an alcohol.



In conclusion, we have established, for the first time, a general methodology for the catalytic formation of value-added 3-benzylindoles through the use of indole and primary, secondary, and heteroaromatic benzyl alcohols using an easily handled, air- and moisture-stable earth-abundant iron complex catalyst that operates through a hydrogen borrowing mechanism. Many synthetically challenging routes were systematically explored, starting from readily accessible substrates that do not require prior alcohol activation by stoichiometric methods. This included the one-pot synthesis of symmetrical bisindoles, the sequential functionalization of diols and the use of secondary alcohols coupling partner under the catalytic conditions then enabled the formation of the desired branched alkylated indole cross-coupled products.

## EXPERIMENTAL SECTION

**General Methods.** All reactions were run in air unless otherwise noted. Column chromatography purifications were performed in flash chromatography conditions using 230-400 Mesh silica gel. Analytical thin layer chromatography (TLC) was carried out on silica gel plates (Silica Gel 60 F254), that were visualized by exposure to ultraviolet light and an aqueous solution of KMnO<sub>4</sub>.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on 400 spectrometer, using CDCl<sub>3</sub> and Acetone-*d*<sub>6</sub> as solvent. Chemical shifts ( $\delta$  scale) are reported in parts per million (ppm) relative to the central peak of the solvent. Coupling constants (*J* values) are given in hertz (Hz). ESI-MS spectra was taken on a Waters Micromass ZQ instrument. IR spectra were obtained on FT-IR spectrometer, ab-

sorbance are reported in  $\text{cm}^{-1}$ . Melting points were determined on capillary melting point apparatus and are uncorrected. HRMS analysis was performed using a Q-TOF microTM mass spectrometer.

**Starting Materials.** 1*H*-indole, 6-fluoro-1*H*-indole, 4-methoxy-1*H*-indole, 6-methyl-1*H*-indole, 5-fluoro-1*H*-indole, 6-chloro-1*H*-indole, 2-phenyl-1*H*-indole, benzyl alcohol, p-tolylmethanol, m-tolylmethanol, o-tolylmethanol, biphenyl-3-ylmethanol, (*N*-(2-hydroxy-2-phenylethyl)acetamide, 4-methoxyphenyl)methanol, (2-aminophenyl)methanol, 2-(hydroxymethyl)phenol, (4-chlorophenyl)methanol, (2-chlorophenyl)methanol, (4-fluorophenyl)methanol, (4-(trifluoromethyl)phenyl)methanol, 4-(hydroxymethyl)benzotrile, (3,4,5-trimethoxyphenyl)methanol, naphthalen-2-ylmethanol, (3,5-dichlorophenyl)methanol, furan-2-ylmethanol, thiophen-2-ylmethanol, benzo[d][1,3]dioxol-5-ylmethanol, 1-phenylethanol and diphenylmethanol are commercially available.

**General procedure for C3-Alkylation of Indole with Benzyl Alcohol.** A vials was charged with the appropriate indole (0.5 mmol), the appropriate alcohol (1 mmol), iron(II) phthalocyanine (Fe(II)Pc) (3 mg, 0.005 mmol) and  $\text{Cs}_2\text{CO}_3$  (179 mg, 0.55 mmol). The vials was immersed in a preheated (140 °C) oil bath and stirred at this temperature for 16 h. The reaction mixture was diluted with ethyl acetate and filtered over a plug of Celite. The solvent was evaporated under reduced pressure and the residue obtained was purified by flash chromatography.

**3-Benzyl-1*H*-indole (3a):** The title compound was prepared according to the general procedure using 1*H*-indole and benzyl alcohol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3a** (102 mg, 99%) as white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.92 (br s, 1H), 7.57 (d,  $J$  = 8.0 Hz, 1H), 7.38 (d,  $J$  = 8.0 Hz, 1H), 7.33 – 7.30 (m, 4H), 7.24 – 7.14 (m, 2H), 7.12 (t,  $J$  = 7.0 Hz, 1H), 6.93 (s, 1H), 4.16 (s, 2H); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{13}\text{NNa}$  ( $M + \text{Na}$ )<sup>+</sup> 230.0940; Found 230.0946. The chemical-physical data are in accordance with literature.<sup>21</sup>

**3-(4-Methylbenzyl)-1*H*-indole (3b):** The title compound was prepared according to the general procedure using 1*H*-indole and p-tolylmethanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 9:1) to give **3b** (78 mg, 71%) as pinkish solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.87 (br

s, 1H), 7.59 (d,  $J = 8.0$  Hz, 1H), 7.37 (d,  $J = 8.0$  Hz, 1H), 7.26 – 7.22 (m, 3H), 7.16 – 7.12 (m, 3H), 6.92 – 6.91 (m, 1H), 4.14 (s, 2H), 2.38 (s, 3H); HRMS (ESI)  $m/z$  calcd for  $C_{16}H_{16}N$  ( $M + H$ )<sup>+</sup> 222.1277; Found 222.1286. The chemical-physical data are in accordance with literature.<sup>7a</sup>

**3-(3-Methylbenzyl)-1H-indole (3c):** The title compound was prepared according to the general procedure using 1H-indole and m-tolylmethanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3c** (108 mg, 98%) as brown solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.76 (br s, 1H), 7.70 (d,  $J = 8.0$  Hz, 1H), 7.40 (d,  $J = 8.0$  Hz, 1H), 7.33 (t,  $J = 8.0$  Hz, 2H), 7.27 – 7.23 (m, 3H), 7.17 (d,  $J = 7.0$  Hz, 1H), 6.92 (s, 1H), 4.22 (s, 2H), 2.46 (s, 3H); HRMS (ESI)  $m/z$  calcd for  $C_{16}H_{16}N$  ( $M + H$ )<sup>+</sup> 222.1277; Found 222.1283. The chemical-physical data are in accordance with literature.<sup>7a</sup>

**3-(2-Methylbenzyl)-1H-indole (3d):** The title compound was prepared according to the general procedure using 1H-indole and o-tolylmethanol. The product was purified by flash chromatography (gradient from cyclohexane/ EtOAc 8:2 to cyclohexane/ EtOAc 7:3) to give **3d** (83 mg, 75%) as pinkish solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.85 (br s, 1H), 7.65 (d,  $J = 8.0$  Hz, 1H), 7.39 (d,  $J = 8.0$  Hz, 1H), 7.30 – 7.15 (m, 6H), 6.74 (s, 1H), 4.15 (s, 2H), 2.41 (s, 3H); HRMS (ESI)  $m/z$  calcd for  $C_{16}H_{16}N$  ( $M + H$ )<sup>+</sup> 222.1277; Found 222.1274. The chemical-physical data are in accordance with literature.<sup>7a</sup>

**3-(Biphenyl-3-ylmethyl)-1H-indole (3e):** The title compound was prepared according to the general procedure using 1H-indole and biphenyl-3-ylmethanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 9:1) to give **3e** (65 mg, 46%) as orange solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.99 (br s, 1H), 7.61 – 7.57 (m, 3H), 7.53 (d,  $J = 8.0$  Hz, 3H), 7.44 (t,  $J = 8.0$  Hz, 2H), 7.40 – 7.32 (m, 3H), 7.24 – 7.20 (m, 1H), 7.14 – 7.10 (m, 1H), 6.98 (br s, 1H), 4.18 (s, 2H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  141.1, 140.4, 138.8, 136.4, 129.1, 128.7, 127.5, 127.1, 127.0, 122.4, 122.1, 119.4, 119.2, 115.7, 111.1, 31.2; m.p. 194-196 °C; IR (film): 3412, 3056 cm<sup>-1</sup>; HRMS (ESI)  $m/z$  calcd for  $C_{21}H_{18}N$  ( $M + H$ )<sup>+</sup> 284.1434; Found 284.1439.

**3-(4-Methoxybenzyl)-1H-indole (3f):** The title compound was prepared according to the general procedure using 1H-indole and (4-methoxyphenyl)methanol. The product was purified by flash chroma-

tography (gradient from cyclohexane/ EtOAc 95:5 to cyclohexane/ EtOAc 90:10) to give **3f** (89 mg, 75%) as brown solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96 (br s, 1H), 7.58 (d,  $J = 8.0$  Hz, 1H), 7.39 (d,  $J = 8.0$  Hz, 1H), 7.29 – 7.22 (m, 3H), 7.14 (t,  $J = 8.0$  Hz, 1H), 6.93 (s, 1H), 6.88 (d,  $J = 8.0$  Hz, 2H), 4.11 (s, 2H), 3.83 (s, 3H); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{16}\text{NO}$  ( $\text{M} + \text{H}$ ) $^+$  238.1226; Found 238.1221. The chemical-physical data are in accordance with literature.<sup>8a</sup>

**2-((1*H*-Indol-3-yl)methyl)aniline (3g):** The title compound was prepared according to the general procedure using 1*H*-indole and (2-aminophenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3g** (62 mg, 56%) as off-white solid.  $^1\text{H}$  NMR (400 MHz, Acetone- $d_6$ )  $\delta$  10.05 (br s, 1H), 7.53 – 7.51 (m, 1H), 7.40 (dt,  $J = 8.0, 1.0$  Hz, 1H), 7.13 – 7.05 (m, 3H), 7.01 – 6.95 (m, 2H), 6.72 (dd,  $J = 8.0, 1.5$  Hz, 1H), 6.59 (dt,  $J = 7.5, 1.5$  Hz, 1H), 4.40 (br s, 2H), 3.99 (s, 2H).  $^{13}\text{C}$  NMR (101 MHz, Acetone- $d_6$ )  $\delta$  146.0, 137.1, 129.7, 127.7, 126.8, 125.0, 122.9, 121.3, 118.8, 118.5, 117.1, 115.1, 113.0, 111.3, 27.4; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{15}\text{N}_2$  ( $\text{M} + \text{H}$ ) $^+$  223.1230; Found 223.1241. The chemical-physical data are in accordance with literature.<sup>22</sup>

**2-((1*H*-Indol-3-yl)methyl)phenol (3h):** The title compound was prepared according to the general procedure using 1*H*-indole and 2-(hydroxymethyl)phenol. The product was purified by flash chromatography (cyclohexane/ EtOAc 1:1) to give **3h** (47 mg, 42%) as pale yellow solid.  $^1\text{H}$  NMR (400 MHz, Acetone- $d_6$ )  $\delta$  9.99 (br s, 1H), 8.28 (s, 1H), 7.57 – 7.54 (m, 1H), 7.38 (dt,  $J = 8.0, 1.0$  Hz, 1H), 7.12 – 7.06 (m, 3H), 7.04 – 6.96 (m, 2H), 6.88 (dd,  $J = 8.0, 1.0$  Hz, 1H), 6.71 (dt,  $J = 7.5, 1.0$  Hz, 1H), 4.10 (s, 2H); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{14}\text{NO}$  ( $\text{M} + \text{H}$ ) $^+$  224.1070; Found 224.1079. The chemical-physical data are in accordance with literature.<sup>23</sup>

**3-(4-Chlorobenzyl)-1*H*-indole (3i):** The title compound was prepared according to the general procedure using 1*H*-indole and (4-chlorophenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3i** (54 mg, 45%) as off-white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 (br s, 1H), 7.51 (d,  $J = 8.0$  Hz, 1H), 7.38 (d,  $J = 8.0$  Hz, 1H), 7.33 – 7.22 (m, 5H), 7.12 (t,  $J = 7.0$

Hz, 1H), 6.93 (s, 1H), 4.12 (s, 2H); HRMS (ESI)  $m/z$  calcd for  $C_{15}H_{13}ClN$  ( $M + H$ )<sup>+</sup> 242.0731; Found 242.0726. The chemical-physical data are in accordance with literature.<sup>2</sup>

**3-(2-Chlorobenzyl)-1H-indole (3j):** The title compound was prepared according to the general procedure using 1H-indole and (2-chlorophenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3j** (44 mg, 37%) as white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.98 (br s, 1H), 7.58 (d,  $J = 8.0$  Hz, 1H), 7.43 – 7.38 (m, 2H), 7.25 – 7.11 (m, 5H), 6.96 (s, 1H), 4.25 (s, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 138.7, 136.4, 134.0, 130.6, 129.4, 127.4, 127.3, 126.7, 122.7, 122.1, 119.5, 119.1, 114.0, 111.1, 29.1; HRMS (ESI)  $m/z$  calcd for  $C_{15}H_{13}ClN$  ( $M + H$ )<sup>+</sup> 242.0731; Found 242.0742.

**3-(4-Fluorobenzyl)-1H-indole (3k):** The title compound was prepared according to the general procedure using 1H-indole and (4-fluorophenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3k** (76 mg, 68%) as white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.99 (br s, 1H), 7.58 (d,  $J = 8.0$  Hz, 1H), 7.38 (d,  $J = 8.0$  Hz, 1H), 7.23 – 7.14 (m, 3H), 7.13 – 6.99 (m, 4H), 4.15 (s, 2H); HRMS (ESI)  $m/z$  calcd for  $C_{15}H_{13}FN$  ( $M + H$ )<sup>+</sup> 226.1027; Found 226.1036. The chemical-physical data are in accordance with literature.<sup>7a</sup>

**3-(4-(Trifluoromethyl)benzyl)-1H-indole (3l):** The title compound was prepared according to the general procedure using 1H-indole and (4-(trifluoromethyl)phenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 9:1) to give **3l** (97 mg, 71%) as off-white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.01 (br s, 1H), 7.54 (d,  $J = 8.0$  Hz, 2H), 7.49 (d,  $J = 8.0$  Hz, 1H), 7.41 – 7.39 (m, 3H), 7.23 (t,  $J = 7.5$  Hz, 1H), 7.11 (t,  $J = 7.5$  Hz, 1H), 7.02 – 6.93 (m, 1H), 4.19 (s, 2H); HRMS (ESI)  $m/z$  calcd for  $C_{16}H_{13}F_3N$  ( $M + H$ )<sup>+</sup> 276.0995; Found 275.0988. The chemical-physical data are in accordance with literature.<sup>7a</sup>

**4-((1H-indol-3-yl)methyl)benzotrile (3m):** The title compound was prepared according to the general procedure using 1H-indole and 4-(hydroxymethyl)benzotrile. The product was purified by flash chromatography (from cyclohexane/ EtOAc 1:1 to cyclohexane/ EtOAc 1:9) to give **3m** (83 mg,

72%) as off-white solid. <sup>1</sup>H NMR (400 MHz, Acetone-*d*<sub>6</sub>) δ 10.11 (br s, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.19 – 7.18 (m, 1H), 7.11 – 7.07 (m, 1H), 6.99 – 6.95 (m, 1H), 4.18 (s, 2H); HRMS (ESI) *m/z* calcd for C<sub>16</sub>H<sub>13</sub>N<sub>2</sub> (M + H)<sup>+</sup> 233.1073; Found 233.1068. The chemical-physical data are in accordance with literature.<sup>24</sup>

**3-(3,4,5-Trimethoxybenzyl)-1*H*-indole (3n):** The title compound was prepared according to the general procedure using 1*H*-indole and (3,4,5-trimethoxyphenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3n** (92 mg, 62%) as orange solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.01 (br s, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 6.54 (s, 2H), 4.07 (s, 2H), 3.84 (s, 3H), 3.81 (s, 6H); HRMS (ESI) *m/z* calcd for C<sub>18</sub>H<sub>20</sub>NO<sub>3</sub> (M + H)<sup>+</sup> 298.1438; Found 298.1435. The chemical-physical data are in accordance with literature.<sup>21</sup>

**3-(Naphthalen-2-ylmethyl)-1*H*-indole (3o):** The title compound was prepared according to the general procedure using 1*H*-indole and naphthalen-2-ylmethanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3o** (91 mg, 71%) as off-white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.98 (br s, 1H), 7.83 – 7.74 (m, 4H), 7.56 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.46 – 7.41 (m, 3H), 7.39 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.21 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.09 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 6.96 – 6.95 (m, 1H), 4.30 (s, 2H); HRMS (ESI) *m/z* calcd for C<sub>19</sub>H<sub>16</sub>N (M + H)<sup>+</sup> 258.1277; Found 258.1271. The chemical-physical data are in accordance with literature.<sup>25</sup>

**3-(3,5-Dichlorobenzyl)-1*H*-indole (3p):** The title compound was prepared according to the general procedure using 1*H*-indole and (3,5-dichlorophenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 98:2) to give **3p** (53 mg, 39%) as brown oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.02 (br s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.29 – 7.12 (m, 5H), 6.98 (s, 1H), 4.08 (s, 2H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 144.8, 136.4, 134.7, 127.14, 127.08, 126.2, 122.6, 122.4, 119.7, 118.9, 114.0, 111.2, 31.1; IR (film): 3170, 2949, 2824, 1555 cm<sup>-1</sup>; HRMS (ESI) *m/z* calcd for C<sub>15</sub>H<sub>12</sub>Cl<sub>2</sub>N (M + H)<sup>+</sup> 276.0341; Found 276.0334.

**3-(Benzo[d][1,3]dioxol-5-ylmethyl)-1*H*-indole (3q):** The title compound was prepared according to the general procedure using 1*H*-indole and benzo[d][1,3]dioxol-5-ylmethanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3q** (105 mg, 84%) as brown solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.95 (br s, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 7.13 (t, *J* = 8.0 Hz, 1H), 6.94 (s, 1H), 6.82 – 6.76 (m, 3H), 5.93 (s, 2H), 4.07 (s, 2H); HRMS (ESI) *m/z* calcd for C<sub>16</sub>H<sub>14</sub>NO<sub>2</sub> (M + H)<sup>+</sup> 252.1019; Found 252.1013. The chemical-physical data are in accordance with literature.<sup>8a</sup>

**3-(Thiophen-2-ylmethyl)-1*H*-indole (3r):** The title compound was prepared according to the general procedure using 1*H*-indole and thiophen-2-ylmethanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3r** (101 mg, 95%) as brown solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.96 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.25 – 7.21 (m, 1H), 7.16 – 7.11 (m, 2H), 7.06 – 7.05 (m, 1H), 6.95 (dd, *J* = 5.0, 4.0 Hz, 1H), 6.91 – 6.90 (m, 1H), 4.35 (s, 2H); HRMS (ESI) *m/z* calcd for : C<sub>13</sub>H<sub>12</sub>NS (M + H)<sup>+</sup> 214.0685; Found 214.0677. The chemical-physical data are in accordance with literature.<sup>8a</sup>

**3-(Furan-2-ylmethyl)-1*H*-indole (3s):** The title compound was prepared according to the general procedure using 1*H*-indole and furan-2-ylmethanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 95:5) to give **3s** (76 mg, 78%) as brown solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.80 (br s, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.45 (s, 1H), 7.34 (dt, *J* = 8.0, 7.6 Hz, 2H), 7.27 – 7.21 (m, 1H), 7.02 (s, 1H), 6.41 (dd, *J* = 3.0, 2.0 Hz, 1H), 6.16 (d, *J* = 3.0 Hz, 1H), 4.24 (s, 2H); HRMS (ESI) *m/z* calcd for C<sub>13</sub>H<sub>11</sub>NONa (M + Na)<sup>+</sup> 220.0733; Found 220.0737. The chemical-physical data are in accordance with literature.<sup>8a</sup>

**1,3-Bis((1*H*-indol-3-yl)methyl)benzene (3t):** The title compound was prepared according to the general procedure using 1*H*-indole (234 mg, 2 mmol) and 1,3-phenylenedimethanol (138 mg, 1 mmol). The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3t** (97 mg, 58%) as brown oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.88 (br s, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0

Hz, 2H), 7.28 (br s, 1H), 7.23 – 7.19 (m, 3H), 7.15 – 7.04 (m, 4H), 6.87 (s, 2H), 4.09 (s, 4H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 141.2, 136.4, 129.2, 128.3, 127.5, 126.3, 122.3, 122.0, 119.3, 119.2, 116.0, 111.1, 31.6; IR (film): 3165, 2929, 2820, 1556 cm<sup>-1</sup>; HRMS (ESI) m/z calcd for C<sub>24</sub>H<sub>21</sub>N<sub>2</sub> (M + H)<sup>+</sup> 337.1699; Found 337.1691.

**3-(3-((1*H*-indol-3-yl)methyl)benzyl)-6-fluoro-1*H*-indole (3u):** A vial was charged with 1*H*-indole (59 mg, 0.5 mmol), 1,4-phenylenedimethanol (69 mg, 1 mmol), iron(II) phthalocyanine (2.5 mg, 0.005 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (179 mg, 0.55 mmol). The vial was immersed in a preheated (140 °C) oil bath and stirred at this temperature for 16 h. Then the vials was removed from oil bath and 6-fluoro-1*H*-indole (67 mg, 0.5 mmol) were added to the reaction mixture and stirred again for 16 h at 140°C. The reaction mixture was diluted with ethyl acetate and filtered over a plug of silica gel. The solvent was evaporated under reduced pressure and the residue obtained was purified by flash chromatography (cyclohexane/EtOAc 7:3) to give **3u** (93 mg, 52%) as off-white solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.93 (br s, 1H), 7.94 (br s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.23 – 7.18 (m, 3H), 7.14 – 7.01 (m, 5H), 6.88 – 6.78 (m, 3H), 4.08 (s, 2H), 4.04 (s, 2H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 159.9 (d, *J* = 236 Hz), 141.0 (d, *J* = 39 Hz), 136.43, 136.39, 136.3, 129.1, 128.3, 127.4, 126.4, 126.3, 126.2, 124.1, 122.5 (d, *J* = 3 Hz), 122.2, 122.0, 120.0, 119.9 (d, *J* = 10 Hz), 119.2 (d, *J* = 10 Hz), 116.0 (d, *J* = 12 Hz), 111.0, 108.0 (d, *J* = 25 Hz), 97.3 (d, *J* = 25 Hz), 31.59, 31.57; m.p. 166-168 °C; IR (film): 3161, 2932, 2816, 1549 cm<sup>-1</sup>; HRMS (ESI) m/z calcd for C<sub>24</sub>H<sub>20</sub>FN<sub>2</sub> (M + H)<sup>+</sup> 355.1605; Found 355.1611.

**3-(1-Phenylethyl)-1*H*-indole (3v):** The title compound was prepared according to the general procedure using 1*H*-indole and 1-phenylethanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3v** (79 mg, 72%) as yellowish solid.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.88 (br s, 1H), 7.45 (dd, *J* = 8.0, 2.5 Hz, 1H), 7.38 – 7.35 (m, 4H), 7.26 – 7.21 (m, 2H), 7.11 – 7.07 (m, 1H), 7.02 (s, 1H), 4.45 (q, *J* = 7.0 Hz, 1H), 1.78 (d, *J* = 7.0 Hz, 3H); HRMS (ESI) m/z calcd for C<sub>16</sub>H<sub>16</sub>N (M + H)<sup>+</sup> 222.1277; Found 222.1269. The chemical-physical data are in accordance with literature.<sup>7a</sup>



**3-Benzhydryl-1H-indole (3w):** The title compound was prepared according to the general procedure using 1H-indole and diphenylmethanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 9:1) to give **3w** (52 mg, 37%) as yellowish solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.89 (s, 1H), 7.38 – 7.19 (m, 13H), 7.04 (dt, *J* = 7.5, 1.0 Hz, 1H), 6.57 (t, *J* = 2.0, 1.0 Hz, 1H), 5.73 (s, 1H); HRMS (ESI) *m/z* calcd for C<sub>21</sub>H<sub>18</sub>N (M + H)<sup>+</sup> 284.1434; Found 284.1439. The chemical-physical data are in accordance with literature.<sup>7a</sup>

**N-(2-(1H-indol-3-yl)-2-phenylethyl)acetamide (3x):** The title compound was prepared according to the general procedure using 1H-indole and N-(2-hydroxy-2-phenylethyl)acetamide. The product was purified by flash chromatography (EtOAc) to give **3x** (62 mg, 45%) as yellowish solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.23 (br s, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.32 – 7.31 (m, 4H), 7.24 (dd, *J* = 5.0, 4.0 Hz, 1H), 7.21 – 7.16 (m, 1H), 7.09 (br s, 1H), 7.07 – 7.03 (m, 1H), 5.51 (br s, 1H), 4.44 (t, *J* = 8.0 Hz, 1H), 4.11 – 4.04 (m, 1H), 3.86 – 3.79 (m, 1H), 1.91 (s, 3H); HRMS (ESI) *m/z* calcd for C<sub>18</sub>H<sub>19</sub>N<sub>2</sub>O (M + H)<sup>+</sup> 279.1492; Found 279.1486. The chemical-physical data are in accordance with literature.<sup>8d</sup>

**4-Methoxy-3-(4-methoxybenzyl)-1H-indole (3y):** The title compound was prepared according to the general procedure using 4-methoxy-1H-indole and (3-((1H-indol-3-yl)methyl)phenyl)methanol. The product was purified by flash chromatography (gradient from cyclohexane/ EtOAc 8:2 to cyclohexane/ EtOAc 6:4) to give **3y** (117 mg, 88%) as brown oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.88 (br s, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 8.0, 1H), 6.87 – 6.85 (m, 2H), 6.64 (br s, 1H), 6.51 (d, *J* = 8.0 Hz, 1H), 4.26 (s, 2H), 3.90 (s, 3H), 3.82 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): δ 157.6, 155.1, 138.1, 134.7, 129.8, 122.8, 120.9, 117.4, 117.2, 113.6, 104.4, 99.5, 55.3, 55.1, 32.2; IR (film): 3397, 2848, 1387 cm<sup>-1</sup>; HRMS (ESI) *m/z* calcd for : C<sub>17</sub>H<sub>18</sub>NO<sub>2</sub> (M + H)<sup>+</sup> 268.1332; Found 268.1338.

**3-(4-Methoxybenzyl)-6-methyl-1H-indole (3z):** The title compound was prepared according to the general procedure using 6-methyl-1H-indole and (3-((1H-indol-3-yl)methyl)phenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3z** (79 mg, 63%) as

pinkish solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.78 (br s, 1H), 7.45 (d,  $J = 8.0$  Hz, 1H), 7.29 – 7.23 (m, 2H), 7.16 (s, 1H), 6.98 (d,  $J = 8.0$  Hz, 1H), 6.88 (m, 2H), 6.84 (s, 1H), 4.09 (s, 2H), 3.83 (s, 3H), 2.51 (s, 3H); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{18}\text{NO}$  ( $\text{M} + \text{H}$ ) $^+$  252.1383; Found 252.1379. The chemical-physical data are in accordance with literature.<sup>26</sup>

**5-Fluoro-3-(2-methylbenzyl)-1H-indole (3aa):** The title compound was prepared according to the general procedure using 5-fluoro-1H-indole and (3-((1H-indol-3-yl)methyl)phenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 9:1) to give **3aa** (95 mg, 80%) as orange solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.94 (br s, 1H), 7.30 – 7.26 (m, 2H), 7.23 – 7.14 (m, 4H), 6.95 (td,  $J = 9.0, 2.5$  Hz, 1H), 6.80 (s, 1H), 4.03 (s, 2H), 2.33 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.8 (d,  $J = 234$  Hz), 138.8, 136.5, 133.0, 130.3, 129.4, 128.0 (d,  $J = 10$  Hz), 126.4, 126.1, 124.4, 115.3 (d,  $J = 5$  Hz), 111.8 (d,  $J = 10$  Hz), 110.4 (d,  $J = 26$  Hz), 104.0 (d,  $J = 23$  Hz), 29.3, 19.6; m.p. 65-66 °C; IR (film): 3310, 2901, 1354  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{15}\text{FN}$  ( $\text{M} + \text{H}$ ) $^+$  240.1183; Found 240.1180.

**6-Chloro-3-(4-methylbenzyl)-1H-indole (3ab):** The title compound was prepared according to the general procedure using 6-chloro-1H-indole and (3-((1H-indol-3-yl)methyl)phenyl)methanol. The product was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3ab** (82 mg, 64%) as brown solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.93 (br s, 1H), 7.41 (d,  $J = 8.0$  Hz, 1H), 7.35 (d,  $J = 2.0$  Hz, 1H), 7.16 (d,  $J = 8.0$  Hz, 2H), 7.10 (d,  $J = 8.0$  Hz, 2H), 7.05 (dd,  $J = 8.0, 2.0$  Hz, 1H), 6.92 (d,  $J = 1.0$  Hz, 1H), 4.06 (s, 2H), 2.33 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  137.7, 136.8, 135.5, 129.1, 128.5, 128.0, 126.1, 122.8, 120.1, 116.3, 110.9, 31.0, 21.0; m.p. 98-99 °C; IR (film): 3220, 2965, 2837, 1601  $\text{cm}^{-1}$ ; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{15}\text{ClN}$  ( $\text{M} + \text{H}$ ) $^+$  256.0888; Found 256.0895.

**3-Benzyl-2-phenyl-1H-indole (3ac):** The title compound was prepared according to the general procedure using 2-phenyl-1H-indole and benzyl alcohol. The product was purified by flash chromatography (cyclohexane/ DCM 1:9) to give **3ac** (69 mg, 49%) as off-white solid.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15 (br s, 1H), 7.55 – 7.52 (m, 2H), 7.46 – 7.44 (m, 4H), 7.38 – 7.31 (m, 2H), 7.26 – 7.16 (m, 5H),

7.10 – 7.06 (m, 1H), 4.29 (s, 2H); HRMS (ESI)  $m/z$  calcd for  $C_{21}H_{18}N$  ( $M + H$ )<sup>+</sup> 284.1434; Found 284.1438. The chemical-physical data are in accordance with literature.<sup>27</sup>

**Procedure for large scale synthesis of compound 3a.** A 50 mL Schlenk equipped with a magnetic stir bar was charged with indole (1 g, 8.5 mmol), benzyl alcohol (1.8 g, 17 mmol), iron(II) phthalocyanine (48 mg, 0.085 mmol) and  $Cs_2CO_3$  (3 g, 9.35 mmol). The reaction mixture was immersed in a preheated (140 °C) oil bath and stirred at this temperature for 16 h. The reaction mixture was diluted with ethyl acetate and filtered over a plug of Celite. The solvent was evaporated under reduced pressure and the residue obtained was purified by flash chromatography (cyclohexane/ EtOAc 8:2) to give **3a** (1.6 g, 92%) as white solid. The chemical-physical data are in accordance as reported above.

## ACKNOWLEDGMENT

We are grateful to Professor Rita Mazzoni and Dott. Andrea Cingolani for generous samples of their Fe-Knölker catalyst.

## SUPPORTING INFORMATION

Copies of <sup>1</sup>H NMR, <sup>13</sup>C NMR spectra for all compounds were reported.

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