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# Ruthenium-Catalyzed Alkylation of Indoles with Tertiary Amines by Oxidation of a $sp^3$ C–H Bond and Lewis Acid Catalysis

**Ming-Zhong Wang,[a] Cong-Ying Zhou,[a] Man-Kin Wong,[a, b] and Chi-Ming Che*[a]**

**Abstract:** Ruthenium porphyrins (particularly [Ru(2,6-$Cl_2$tpp)CO]; tpp = tetraphenylporphinato) and $RuCl_3$ can act as oxidation and/or Lewis acid catalysts for direct C-3 alkylation of indoles, giving the desired products in high yields (up to 82% based on 60–95% substrate conversions). These ruthenium compounds catalyze oxidative coupling reactions of a wide variety of anilines and indoles bearing electron-withdrawing or electron-donating substituents with high regioselectivity when using *t*BuOOH as an oxidant, resulting in the alkylation of *N*-arylindoles to 3-{[(*N*-aryl-*N*-alkyl)amino]methyl}indoles (yield: up to 82%, conversion: up to 95%) and the alkylation of *N*-alkyl or *N*-H indoles to 3-[*p*-(dialkylamino)benzyl]indoles (yield: up to 73%, conversion: up to 92%). A tentative reaction mechanism involving two pathways is proposed: an iminium ion intermediate may be generated by oxidation of an $sp^3$ C–H bond of the alkylated aniline by an oxoruthenium species; this iminium ion could then either be trapped by an *N*-arylindole (pathway A) or converted to formaldehyde, allowing a subsequent three-component coupling reaction of the in situ generated formaldehyde with an *N*-alkylindole and an aniline in the presence of a Lewis acid catalyst (pathway B). The results of deuterium-labeling experiments are consistent with the alkylation of *N*-alkylindoles via pathway B. The relative reaction rates of [Ru(2,6-$Cl_2$tpp)CO]-catalyzed oxidative coupling reactions of 4-X-substituted *N*,*N*-dimethylanilines with *N*-phenylindole (using *t*BuOOH as oxidant), determined through competition experiments, correlate linearly with the substituent constants σ ($R^2 = 0.989$), giving a ρ value of −1.09. This ρ value and the magnitudes of the intra- and intermolecular deuterium isotope effects ($k_H/k_D$) suggest that electron transfer most likely occurs during the initial stage of the oxidation of 4-X-substituted *N*,*N*-dimethylanilines. Ruthenium-catalyzed three-component reaction of *N*-alkyl/*N*-H indoles, paraformaldehyde, and anilines gave 3-[*p*-(dialkylamino)benzyl]-indoles in up to 82% yield (conversion: up to 95%).

**Keywords:** alkylation · indoles · Lewis acids · oxidation · ruthenium

## Introduction

Transition metal-catalyzed cross-coupling reaction through the oxidation of C–H bonds has emerged as a highly efficient and atom-economic organic transformation, which does not require pre-functionalization of the substrates and does not produce undesired byproducts.[1] Oxidation of an $sp^3$ C–H bond adjacent to a nitrogen atom in a tertiary amine, followed by attack of a carbon nucleophile, is a powerful strategy for C–C bond formation. In recent years, Murahashi and co-workers have reported the efficient construction of C–CN bonds[2] by $RuCl_3$-catalyzed oxidation of C–H bonds of tertiary amines followed by attack of the carbon nucleophile $CN^-$, with molecular oxygen or hydrogen peroxide as an oxidant. Li and co-workers reported that copper(I) salts could catalyze the oxidative α-alkylation of tertiary amines with various carbon nucleophiles in the presence of *tert*-butyl hydroperoxide (TBHP).[3] Doyle and co-workers reported an interesting dirhodium(II,II)-catalyzed Mannich reaction of tertiary amines with 2-triisopropoxysilylfuran as carbon nucleophile using TBHP as the oxidant.[4] Vogel and co-workers reported an $FeCl_2$-catalyzed oxidative C–C cross-coupling of tertiary amines with terminal alkynes

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using ($t$BuO)$_2$ as an oxidant.[5] Despite these advances,[6] the search for highly efficient and robust catalysts remains a challenge in the field of metal-catalyzed C–C cross-coupling reactions through oxidation of an sp$^3$ C–H bond.

Alkylated indoles occur widely in bioactive natural products and therapeutic drug molecules,[7] and are usually synthesized by acid- or base-mediated alkylation reactions[8] requiring the use of stoichiometric or excess amounts of strong acid/base and air-/moisture-sensitive organometallic reagents. Thus, there is a need to develop new methods for the efficient synthesis of alkylated indoles under mild conditions.[9] Herein, we describe the ruthenium porphyrin- and $RuCl_3$-catalyzed C-3 alkylation of indoles through oxidation of an sp$^3$ C–H bond of tertiary amines, and a three-component coupling reaction for the synthesis of 3-[*p*-(dialkylamino)benzyl]indoles from indoles, paraformaldehyde, and anilines. In the latter, both ruthenium porphyrins and $RuCl_3$ act as Lewis acid catalysts. Although it is well documented that ruthenium porphyrins[10,11] and $RuCl_3$[2] are efficient oxidative catalysts, there have only been a few reports on the use of ruthenium porphyrins as Lewis acid catalysts.[12,13] We have employed ruthenium porphyrins as catalysts due to their excellent stability and recyclability, features that are often less than satisfactory with commercially available ruthenium salts.

## Results

**Ruthenium-catalyzed oxidative coupling reaction of tertiary amines with indoles**: The ruthenium porphyrin catalysts **1** employed in this work are shown in Figure 1. We examined the catalytic properties of **1** for the reaction of *N*-arylindoles **2** with tertiary amines **3** using TBHP as an oxidant; the results are presented in Table 1, wherein the substrate conversions correspond to the *N*-arylindoles and the product yields are based on the amount of *N*-arylindole consumed in each reaction. Excess tertiary amine and TBHP were used to optimize the conversions of the *N*-arylindoles. Treatment of *N*-phenylindole (**2a**) (0.2 mmol) with *N*,*N*-dimethylaniline **3a** (0.6 mmol) and TBHP (0.6 mmol, 70% in $H_2O$), using 1 mol% (relative to **2a**) of [Ru(2,6-$Cl_2$tpp)CO] (**1a**) as catalyst, in toluene at 110°C for 6 h afforded the cross-coupling product **4a** in 67% yield with 83% conversion (entry 1, Table 1).[14] Lower substrate conversions were obtained on decreasing the reaction temperature to 80°C (67% conversion, 72% yield) and 50°C (35% conversion, 75% yield), or by changing the **2a**/**3a**:TBHP ratio (1:3:3) to 1:2:2 (59% conversion, 75% yield) and 1:1:1 (30% conversion, 62% yield), as shown in Tables S2 and S3 in the Supporting Information. Among the ruthenium porphyrins screened (Figure 1), [Ru(2,6-$Cl_2$tpp)CO] (**1a**) and [Ru($F_{20}$-tpp)CO] (**1b**) were the most effective in terms of substrate conversions and product yields (entry 1, Table 1). Under similar reaction conditions, the use of 1 mol% of $RuCl_3$ led to only 25% substrate conversion, which could be improved to 80% when 5 mol% of $RuCl_3$ catalyst was used. The use of other ruthenium catalysts (5 mol%) such as [Ru($PPh_3$)$_3$$Cl_2$], *cis*-[Ru(acac)$_2$($CH_3CN$)$_2$] (acac = acetylacetone), and [Ru(salen)($OH_2$)$_2$]$PF_6$ (salen = *N*,*N*′-ethylenebis(salicylideneimine)) resulted in substrate conversions of 70–76% and product yields of 60–70% (Table S2 in the Supporting Information).

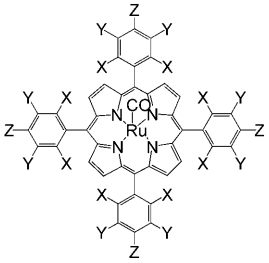


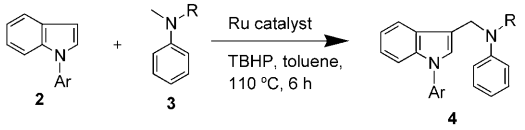

Figure 1. Structures of ruthenium porphyrin catalysts **1a**–**d**.

With 1 mol% [Ru(2,6-$Cl_2$tpp)CO] (**1a**) or 5 mol% $RuCl_3$ as the catalyst, the oxidative coupling reactions of *N*,*N*-dimethylanilines **3a**–**f** with various *N*-aryl-substituted indoles **2a**–**d** afforded the corresponding alkylated indoles **4b**–**i** in up to 82% yield (entries 2–9, Table 1). *N*-(4-Methoxyphenyl)-indole (**2d**) gave slightly higher substrate conversion and product yield than *N*-*p*-tolylindole (**2c**) or *N*-phenylindole (**2a**) (cf. entries 1, 3, and 4, Table 1). Substituted anilines with electron-donating substituents (4-Me, 3-Me, 2-Me, and 4-OMe) displayed higher activities than those with electron-withdrawing substituents (4-Br) (entries 5–9, Table 1). An *ortho* substituent (2-Me) on the aniline, as in **3e**, did not lead to a remarkable change in the product yield and substrate conversion compared with those from an aniline bearing a *meta* or *para* substituent (entries 6–8, Table 1). In the presence of other alkyl group(s), an *N*-methyl group in a tertiary amine was selectively oxidized. For example, the reaction of *N*-methyl-*N*-butyl-aniline (**3g**) gave *N*-butyl-*N*-[(1-phenyl-1*H*-indol-3-yl)methyl]aniline (**4j**) in good yield with no trace of the product derived from oxidation of the *N*-butyl group (entry 10, Table 1). Cyclic amines such as 1,2,3,4-tetrahydroisoquinoline selectively underwent the oxidative coupling reaction to give the α-indolylation product in good yield (entries 11 and 12, Table 1). In no case was any *N*-oxide of the *N*,*N*-dialkylaniline observed.

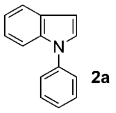
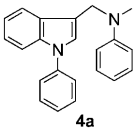
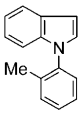
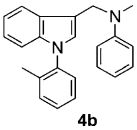
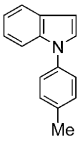
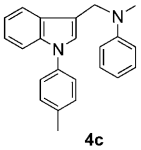
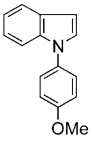
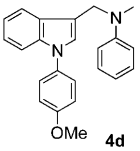
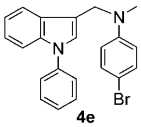
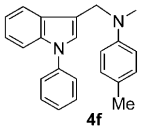
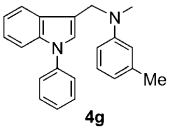
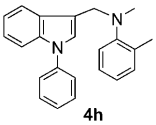
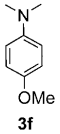
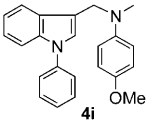
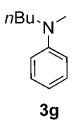
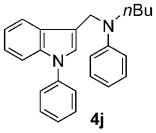
Unexpectedly, reaction of *N*-benzylindole (**2e**) with *N*,*N*-dimethylaniline (**3a**) in the presence of TBHP and **1a** (1 mol%) gave 3-[*p*-(dimethylamino)benzyl]indole (**5a**) in 54% yield, while the oxidative coupling product **4m** was obtained in only 25% yield (entry 1, Table 2). Similarly, the reactions of *N*-ethylindole (**2f**) and *N*-methylindole (**2g**) with *N*,*N*-dimethylaniline (**3a**) afforded 3-[*p*-(dimethylamino)-benzyl]indoles **5b** and **5c**, respectively, both in good yields, and in each case only a trace amount of the oxidative coupling product **4** was detected by analysis of the $^1$H NMR spectrum of the crude reaction mixture (entries 2 and 3, Table 2). Indole **2h**, with a free NH group, could also be converted into the corresponding 3-[*p*-(dimethylamino)ben-

Table 1. Ruthenium-catalyzed oxidative coupling of tertiary amines with indoles.[a]




2 + 3 → 4 (1)

| Entry | Indole | Aniline | Product | Conv. [%][b] | Yield [%][c] |
|---|---|---|---|---|---|
| 1 |  **2a** |  **3a** |  **4a** | 83<br>86[d]<br>65[e]<br>60[f]<br>25[g]<br>80[h] | 67<br>65<br>70<br>63<br>75<br>65 |
| 2 |  **2b** | **3a** |  **4b** | 85<br>82[h] | 73<br>70 |
| 3 |  **2c** | **3a** |  **4c** | 80<br>83[h] | 75<br>72 |
| 4 |  **2d** | **3a** |  **4d** | 91<br>95[h] | 78<br>82 |
| 5 | **2a** |  **3b** |  **4e** | 80<br>86[h] | 70<br>67 |
| 6 | **2a** |  **3c** |  **4f** | 89<br>92[h] | 82<br>75 |
| 7 | **2a** |  **3d** |  **4g** | 85<br>90[h] | 79<br>74 |
| 8 | **2a** |  **3e** |  **4h** | 86<br>88[h] | 76<br>75 |
| 9 | **2a** |  **3f** |  **4i** | 90<br>95[h] | 72<br>65 |
| 10 | **2a** |  **3g** |  **4j** | 60<br>65[h] | 64<br>71 |

zyl]indole (**5d**) in 73% yield (entry 4, Table 2). Both *N*-alkyl- and *N*-H-indoles reacted with unsymmetrical *N*-substituted anilines to give the corresponding 3-[*p*-(dialkylamino)benzyl]indoles **5** in good yields (entries 5–8, Table 2).

We speculate that **5** was formed due to the presence of formaldehyde (Scheme 1), as formaldehyde can be generated through N-demethylation of *N*-methyl-*N*-alkylanilines by metal-catalyzed oxidation processes.[2d] Indeed, a three-component reaction of *N*-methylindole **2g**, paraformaldehyde, and *N*,*N*-dimethylaniline **3a** in toluene in the presence of ruthenium porphyrin catalyst (1 mol%) at 110°C for 6 h gave **5c** as the major product in good yield (Table 3).

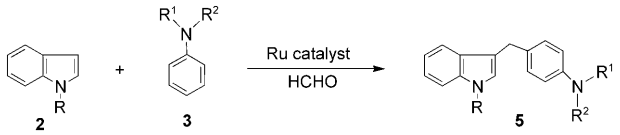
**Ruthenium-catalyzed three-component coupling reaction of indoles, paraformaldehyde, and anilines**: Based on the above observation, we developed a synthesis of 3-[*p*-(dialkylamino)benzyl]indoles by metal-catalyzed three-component coupling reaction of indoles, paraformaldehyde, and anilines. In the literature, 3-[*p*-(dialkylamino)benzyl]indoles have hitherto been obtained through nucleophilic substitution reaction of indoles with benzotriazole-linked anilines,[15a] halogenated anilines,[15b] or hydroxy-substituted anilines,[15c] as well as by acid-catalyzed condensation of 3-hydroxymethyl indoles with anilines.[15d] All of these reported methods require the prior incorporation of leaving group(s) in either the anilines or indoles. After completion of this work and during revision of this manuscript, a three-component coupling reaction of indoles, formaldehyde, and anilines catalyzed by silica-sup-

Table 1. (Continued)

| Entry | Indole | Aniline | Product | Conv. [%][b] | Yield [%][c] |
|---|---|---|---|---|---|
| 11 | **2c** | **3h** | **4k** | 85<br>80[h] | 73<br>75 |
| 12 | **2d** | **3h** | **4l** | 82<br>85[h] | 79<br>80 |

[a] Indole (0.2 mmol), aniline (0.6 mmol), [Ru(2,6-$Cl_2$tpp)CO] **1a** (0.002 mmol), TBHP (0.6 mmol, 70% in water), toluene (0.5 mL). [b] Conversion based on the recovery of indoles. [c] Yield based on conversion. [d] [Ru($F_{20}$-tpp)CO] **1b** (0.002 mmol). [e] [Ru(tpp)CO] (**1c**) (0.002 mmol). [f] [Ru(4-MeOtpp)CO] (**1d**) (0.002 mmol). [g] $RuCl_3$ (0.002 mmol). [h] $RuCl_3$ (0.01 mmol).




Scheme 1. Proposed reaction pathway for the formation of **5**.

ported perchloric acid to give 3-[*p*-(dialkylamino)benzyl]-indoles was reported.[15e]

In initial experiments, a series of Lewis acid catalysts was screened (Table 3). Among these catalysts, **1a** proved to be the best for the three-component coupling reaction of indole **2g** with paraformaldehyde and aniline **3a**, affording **5c** in 72% yield with 90% conversion of **2g** at a catalyst loading of 1 mol% (entry 1, Table 3). In contrast, in the absence of **1a**, <5% conversion of **2g** was observed (entry 2, Table 3). Lower product yield (60%) and substrate conversion (68%) were obtained when 1 mol% of $RuCl_3$ was used as the catalyst (entry 6, Table 3). Using 5 mol% of $RuCl_3$, the substrate conversion (95%) and product yield (75%) were comparable to those obtained with 1 mol% of **1a** as catalyst (cf. entries 1 and 7, Table 3). [$Ru(PPh_3)_3Cl_2$] and [Ru(salen)$(OH_2)_2$]$PF_6$ were also effective in catalyzing the three-component reaction, but *cis*-[$Ru(acac)_2(CH_3CN)_2$] gave <5% conversion (entries 8–10, Table 3). Only 45% and 65% substrate conversions were obtained when Yb-$(OTf)_3$ (10 mol%) and TsOH (10 mol%) were used as the catalyst, respectively (entries 11 and 12, Table 3).

The substrate scope of this ruthenium-catalyzed three-component coupling reaction using **1a** (1 mol%) or $RuCl_3$ (5 mol%) as catalyst has been examined. The results are depicted in Table 4. With *N*-benzylindole (**2e**), good substrate conversions (60–73%) were observed (entry 1, Table 4). Coupling reactions of *N*-alkyl-indoles **2f** and **2g** and *N*-H indoles **2h–k** with substituted anilines in the presence of paraformaldehyde afforded alkylated indoles with good substrate conversions (up to 95%) and product yields (up to 82%) (entries 2–11, Table 4). This three-component coupling reaction tolerates functionalities including phenol, chloro, and methoxy groups. Low substrate conversions were observed for *N*-arylindoles **2a–d** (entries 12–15). Indoles having an *N*-aryl moiety bearing an electron-donating substituent such as 4-Me (**2c**) or 4-OMe (**2d**) displayed higher activities than **2a** with an *N*-phenyl group. Indole dimers **6** (<5%) were detected as byproducts in all of the reactions presented in Tables 3 and 4 by $^1$H NMR spectroscopic analyses of the reaction mixtures.

We have examined the recyclability of **1a** in the three-component coupling reaction of *N*-methylindole (**2g**) with paraformaldehyde and *N*,*N*-dimethylaniline (**3a**). High substrate conversions (85–90%) and good product yields (68–72%) were obtained in five consecutive reactions, with no significant loss of catalytic activity (Table 5).

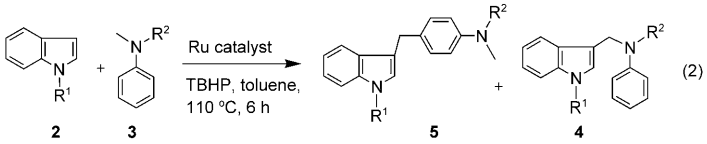
## Discussion

Transition metal-catalyzed oxidative cross-coupling of tertiary amines with carbon nucleophiles has emerged as a powerful strategy for C–C bond formation. In the literature, there have been reports of extensive studies on the oxidative demethylation of tertiary amines catalyzed by cytochrome P450 and its biomimetic model systems.[16] Murahashi and co-workers proposed that $RuCl_3$-catalyzed oxidative coupling reactions of tertiary amines with sodium cyanide, using molecular oxygen or $H_2O_2$ as oxidant, involve an oxoruthenium intermediate, which oxidizes the tertiary amine to give an iminium ion.[2f–h] For the copper-catalyzed cross-dehydrogenation coupling reaction of tertiary amines with terminal alkynes, nitromethane, or malonate in the presence of TBHP, Li and co-workers proposed two types of reaction intermediates: an iminium ion coordinated to copper and a *tert*-butyldioxygenated amine.[3c,e] Doyle and co-workers proposed that a dirhodium(II,II)-catalyzed oxidative Mannich reaction in MeOH proceeds via an intermediate α-methoxylated amine.[4]

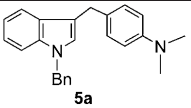
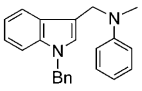
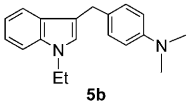
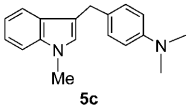
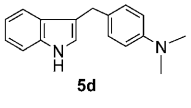
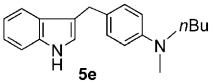
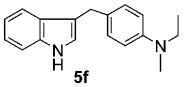
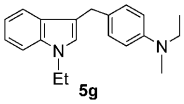
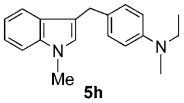
**Mechanism of the ruthenium porphyrin- or $RuCl_3$-catalyzed oxidative coupling reaction of tertiary amines with indoles using TBHP as oxidant**: Based on the results presented in

Table 2. Ruthenium-catalyzed oxidative coupling of anilines with *N*-alkylindoles.[a]




2 3 5 4

| Entry | Indole | Aniline | Product | Conv. [%][b] | Yield [%][c] |
|---|---|---|---|---|---|
| 1 |  **2e** | **3a** |  **5a**  **4m** | 92 | **5a/4m** 54:25 |
| 2 |  **2f** | **3a** |  **5b** | 86 | 67 |
| 3 |  **2g** | **3a** |  **5c** | 90 | 72 |
| 4 |  **2h** | **3a** |  **5d** | 85 | 73 |
| 5 | **2h** |  **3g** |  **5e** | 82 | 67 |
| 6 | **2h** |  **3i** |  **5f** | 88 | 68 |
| 7 | **2f** | **3i** |  **5g** | 85 | 66 |
| 8 | **2g** | **3i** |  **5h** | 90 | 69 |

[a] Indole (0.2 mmol), aniline (0.6 mmol), **1a** (0.002 mmol), TBHP (0.6 mmol, 70% in water), toluene (0.5 mL). [b] Conversion based on the recovery of indoles. [c] Yield based on conversion.

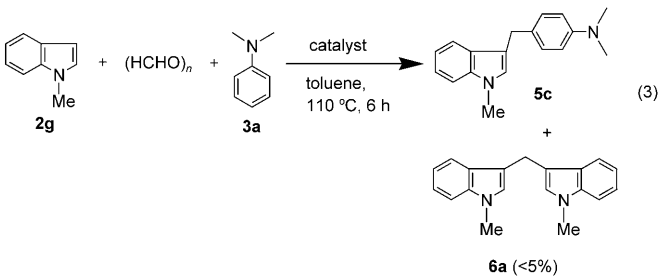
Tables 1 and 2, a tentative reaction mechanism is proposed (Scheme 2), which involves reaction of the ruthenium catalyst with TBHP to form an oxoruthenium intermediate **I**, presumably through pre-generation of an RuOO*t*Bu intermediate with subsequent cleavage of the O–O bond. This is similar to the mechanism proposed by Murahashi and co-workers for a related ruthenium-catalyzed oxidation with TBHP[2a,17c] and the formation of an oxoiron species from FeOOR observed by Groves and Watanabe[17a] (R = C(O)Ar) and proposed by Balch and co-workers[17b] (R = *t*Bu). On the basis of a previous report by Murahashi and co-workers,[2h] intermediate **I** could oxidize the tertiary amine to give an iminium ion intermediate **II**, presumably by electron transfer and subsequent hydrogen-transfer reactions. We propose that nucleophilic attack of intermediate **II** by *N*-arylindoles gives the corresponding alkylated indoles **4** (pathway A, Scheme 2). As *tert*-butyldioxygenated amine **III** was detected during the reaction (see below), the intermediate **II** could also be trapped by *t*BuOOH to give **III**.[2d] In the presence of a Lewis acid, **III** may decompose to regenerate intermediate **II**.[2c] In view of the results in Table 2, we propose that pathway B (Scheme 2) is consistent with the reactions of tertiary amines with *N*-alkyl-indoles, probably owing to the rapid reaction of *N*-alkyl-indoles with formaldehyde. The formation of formaldehyde could be due to trapping of intermediate **II** by coordinated OH (analogous to the oxygen-rebound mechanism proposed by Groves and McClusky for iron-catalyzed aliphatic hydroxylation[18]), or by water,[19] to give α-hydroxylated amine **IV**, which subsequently decomposes to give formaldehyde and the N-demethylation product. This process is reminiscent of the cytochrome P450-catalyzed N-dealkylation of tertiary amines.[16] The proposed mechanism depicted in Scheme 2 is supported by the experiments described in the following three subsections.

**Oxidation of tertiary amines by oxoruthenium complexes**: Ruthenium porphyrin combined with 2,6-dichloropyridine *N*-oxide (2,6-$Cl_2$pyNO) is an oxidation system that is extensively employed for the oxidation of alkenes, hydrocarbons, and alcohols. In this system, a reactive oxoruthenium species is generally believed to be responsible for the oxidation.[20] We found this catalytic oxidation system to also be effective for the oxidative coupling of *N*,*N*-dimethylaniline with *N*-phenylindole, affording **4a** in 75% yield with 95% substrate conversion (Scheme 3), thus providing indirect support for the involvement of a reactive oxoruthenium intermediate in the ruthenium porphyrin-catalyzed oxidative coupling of tertiary amines with indoles.

Previously, we prepared and structurally characterized the *cis*-dioxoruthenium(VI) complex *cis*-[(tet-$Me_6$)$Ru^{VI}O_2$]-

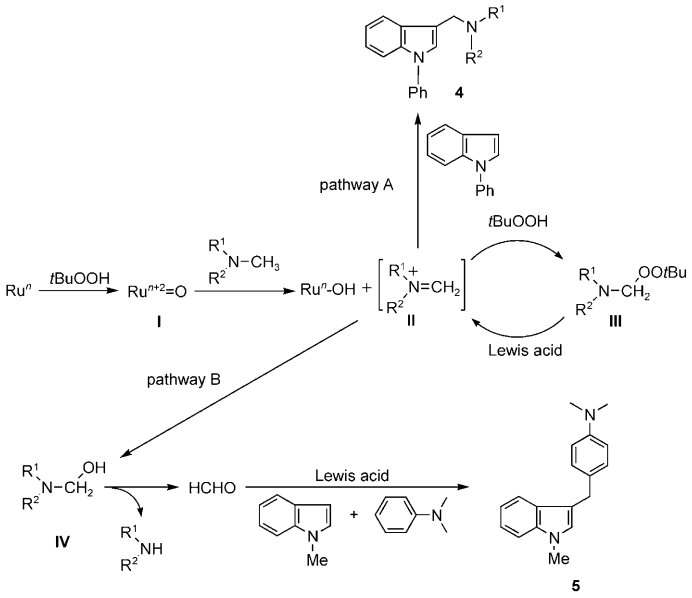
  

Table 3. Lewis acid-catalyzed three-component coupling reaction of **2g**, paraformaldehyde, and aniline **3a**.[a]

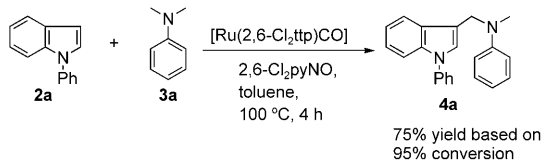



| Entry | Catalyst (mol%) | Conv. [%][b] | Yield [%][c] |
|---|---|---|---|
| 1 | **1a** (1) | 90 | 72 |
| 2 | – | <5 | – |
| 3 | **1b** (1) | 85 | 70 |
| 4 | **1c** (1) | 57 | 61 |
| 5 | **1d** (1) | 65 | 62 |
| 6 | $RuCl_3$ (1) | 68 | 60 |
| 7 | $RuCl_3$ (5) | 95 | 75 |
| 8 | $[Ru(PPh_3)_3Cl_2]$ (5) | 88 | 65 |
| 9 | $[Ru(salen)(OH_2)_2]PF_6$ (1) | 85 | 60 |
| 10 | *cis*-$[Ru(acac)_2(CH_3CN)_2]$ (1) | <5 | – |
| 11 | $Yb(OTf)_3$ (10) | 45 | 71 |
| 12 | TsOH (10) | 65 | 42 |

[a] Indole **2g** (0.2 mmol), paraformaldehyde (0.6 mmol), **3a** (0.6 mmol), catalyst (1–10 mol%), toluene (2 mL). [b] Conversion based on the recovery of indoles. [c] Yield of **5** based on conversion.

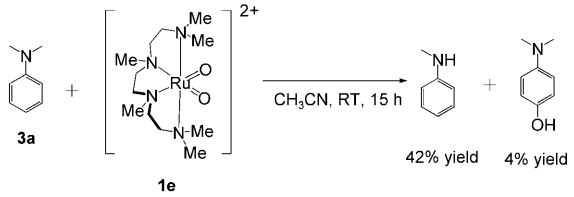



Scheme 2. Proposed reaction pathways for the ruthenium-catalyzed oxidative coupling reaction of tertiary amines with indoles.



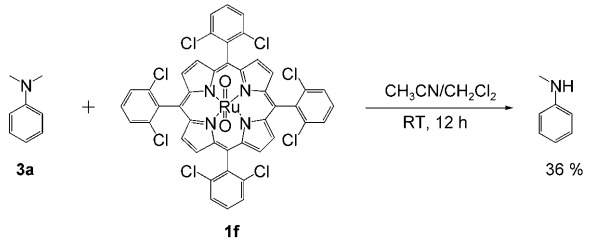

Scheme 3. Ruthenium-catalyzed oxidative coupling of **3a** with **2a** using 2,6-$Cl_2$pyNO as oxidant.

$(ClO_4)_2$ (**1e**, tet-$Me_6$ = *N*,*N*,*N*,*N*-tetramethyl-3,6-dimethyl-3,6-diazaoctane-1,8-diamine),[21] which has an *E* value of 0.8 V ($Ru^{VI/IV}$) vs SCE. Stoichiometric oxidation of *N*,*N*-dimethylaniline **3a** with *cis*-[(tet-$Me_6$)$Ru^{VI}O_2$]$(ClO_4)_2$ (**1e**) was examined (Scheme 4). A mixture of *N*,*N*-dimethylaniline (**3a**)




Scheme 4. Stoichiometric oxidation of *N*,*N*-dimethylaniline by *cis*-[(tet-$Me_6$)$Ru^{VI}O_2$]$(ClO_4)_2$ (**1e**).

and *cis*-[(tet-$Me_6$)$Ru^{VI}O_2$]$(ClO_4)_2$ **1e** in $CH_3CN$ was stirred for 15 h to give the demethylated product *N*-methylaniline in 42% isolated yield and 4-(dimethylamino)phenol in 4% isolated yield. This experiment demonstrated the direct oxidation of *N*,*N*-dimethylaniline **3a** to its demethylated product by a structurally characterized oxoruthenium complex containing a non-porphyrin ligand. We also prepared dioxoruthenium(VI) porphyrin [$Ru^{VI}$(2,6-$Cl_2$tpp)$O_2$] **1f** by the method reported in a previous work[22a] and by reaction of [Ru(2,6-$Cl_2$tpp)CO] **1a** with TBHP,[22b] and used **1f** as a stoichiometric oxidant for the oxidation of *N*,*N*-dimethylaniline **3a** at room temperature for 12 h; the demethylated product *N*-methylaniline was isolated in 36% yield (Scheme 5). All of these experiments support the view that the ruthenium-catalyzed oxidative coupling reactions of tertiary amines with indoles described in this work involve a reactive oxoruthenium intermediate, which may be generated by reaction of the ruthenium porphyrin complex/$RuCl_3$ with TBHP.

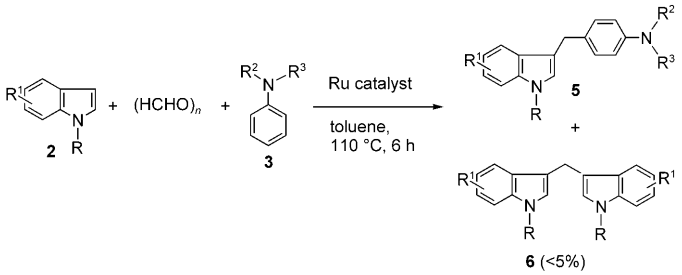


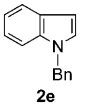
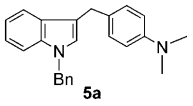
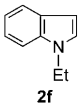
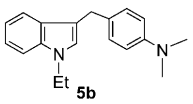
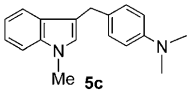
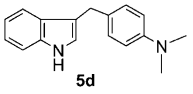
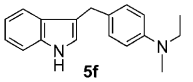
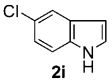
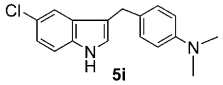
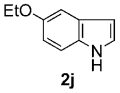
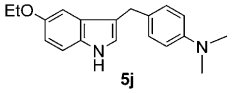
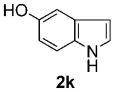
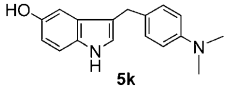
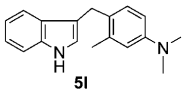
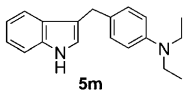
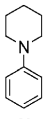
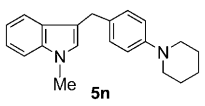
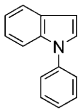

Scheme 5. Stoichiometric oxidation of *N*,*N*-dimethylaniline by [$Ru^{VI}$(2,6-$Cl_2$tpp)$O_2$] (**1f**).

**Hammett correlation and deuterium isotope effect studies**: The relative rates of oxidative coupling reactions of *para*-substituted *N*,*N*-dimethylanilines (*p*-MeO, *p*-Me, H, *p*-Br) with *N*-phenylindole using *t*BuOOH as oxidant and [Ru(2,6-$Cl_2$tpp)CO] as catalyst were examined by $^1$H NMR analysis of the corresponding products (alkylated indoles **4**). A Hammett plot based on these relative rates is depicted in Figure 2, which shows a linear correlation ($R^2$ = 0.989) with a ρ value of −1.09, suggesting the build-up of positive

Table 4. Ruthenium-catalyzed three-component coupling reactions of indoles, paraformaldehyde, and anilines.[a]



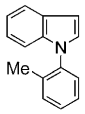
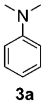
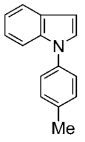
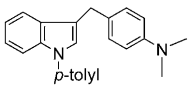
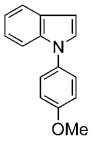
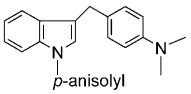

| Entry | Indole | Aniline | Product | Conv. [%][b] | Yield [%][c] |
|---|---|---|---|---|---|
| 1 |  **2e** |  **3a** |  **5a** | 60<br>73[d] | 78<br>75 |
| 2 |  **2f** | **3a** |  **5b** | 86<br>90[d] | 70<br>65 |
| 3 |  **2g** | **3a** |  **5c** | 90<br>95[d] | 72<br>75 |
| 4 |  **2h** | **3a** |  **5d** | 80<br>88[d] | 65<br>75 |
| 5 |  **2h** | **3i** |  **5f** | 85<br>82[d] | 68<br>71 |
| 6 |  **2i** | **3a** |  **5i** | 80<br>82[d] | 69<br>72 |
| 7 |  **2j** | **3a** |  **5j** | 85<br>90[d] | 82<br>78 |
| 8 |  **2k** | **3a** |  **5k** | 82<br>80[d] | 62<br>40 |
| 9 | **2h** |  **3d** |  **5l** | 87<br>92[d] | 65<br>60 |
| 10 | **2h** |  **3j** |  **5m** | 75<br>78[d] | 40<br>70 |
| 11 | **2g** |  **3k** |  **5n** | 72<br>76[d] | 70<br>65 |
| 12 |  **2a** |  **3a** | – | <10<br><10[d] | –<br>– |

charge on the aniline in the transition state. Thus, the reaction is accelerated by an electron-donating substituent but retarded by an electron-withdrawing substituent. The intramolecular and intermolecular deuterium isotope effects for [Ru(2,6-$Cl_2$tpp)CO]-catalyzed oxidative reaction of anilines with *N*-phenylindole have been examined. The $k_H/k_D$ (intra) values for the reactions of 4-X-*N*-methyl-*N*-trideuteriomethylanilines (X = MeO, Me, H, Br) were determined as 3.8, 3.2, 2.2, and 1.2, respectively, which decrease on going from electron-donating to electron-withdrawing substituents, suggesting that electron transfer from the tertiary amine to the oxoruthenium intermediate occurs during the initial stage.[23] The $k_H/k_D$ (inter) values for the reactions of 4-X-substituted *N*,*N*-dimethyl- and *N*,*N*-bis(trideuteriomethyl)anilines (X = MeO, Me, H) were measured as 2.5, 2.1, and 1.7, respectively. The different values of $k_H/k_D$ (inter) and $k_H/k_D$ (intra) are consistent with an electron-transfer mechanism for the ruthenium porphyrin-catalyzed oxidation of tertiary amines to iminium ions.[23]

**Coupling reaction of *tert*-butyldioxygenated amines with indoles**: After the [Ru(2,6-$Cl_2$tpp)CO]-catalyzed oxidative coupling reaction of *N*,*N*-dimethylaniline (**3a**) with *N*-phenylindole (**2a**) (using TBHP as oxidant) had proceeded for 1 h, we detected *tert*-butyldioxygenated amine **III** (Scheme 2) in the crude reaction mixture by $^1$H NMR analysis (see the Supporting Information). In the absence of **2a**, the reaction of **3a** with TBHP catalyzed by [Ru(2,6-$Cl_2$tpp)CO] at 50 °C for 5 h gave **III** in 90 % isolated yield. The following experiments provide further evidence

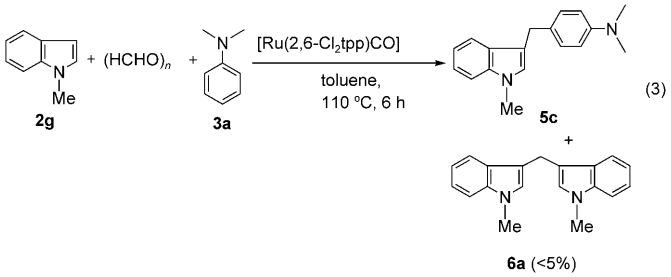
  

Table 4. (Continued)

| Entry | Indole | Aniline | Product | Conv. [%][b] | Yield [%][c] |
|---|---|---|---|---|---|
| 13 |  **2b** |  **3a** | – | <5<br><5[d] | –<br>– |
| 14 |  **2c** |  **3a** |  **5o** | 20<br>25[d] | 90<br>85 |
| 15 |  **2d** |  **3a** |  **5p** | 30<br>32[d] | 87<br>85 |

[a] Indole (0.2 mmol), paraformaldehyde (0.6 mmol), aniline (0.6 mmol), **1a** (0.002 mmol), toluene (2 mL). [b] Conversion based on the recovery of indoles. [c] Yield of **5** based on conversion. [d] $RuCl_3$ (0.01 mmol).

Table 5. Recyclability of the [Ru(2,6-$Cl_2$tpp)CO] catalyst for the three-component reaction of indoles **2g** with paraformaldehyde and **3a**.[a]




(3)

| Entry | Conv. [%][b] | Yield [%] |
|---|---|---|
| 1 | 90 | 72 |
| 2 | 90 | 70 |
| 3 | 88 | 70 |
| 4 | 86 | 71 |
| 5 | 85 | 68 |

[a] A mixture of **2g** (2 mmol), paraformaldehyde (6 mmol), **3a** (6 mmol), and **1a** (0.02 mmol) in toluene (10 mL) was stirred at 110 °C for 6 h. [b] Conversion based on the recovery of indoles. [c] Yield of **5c** based on conversion.

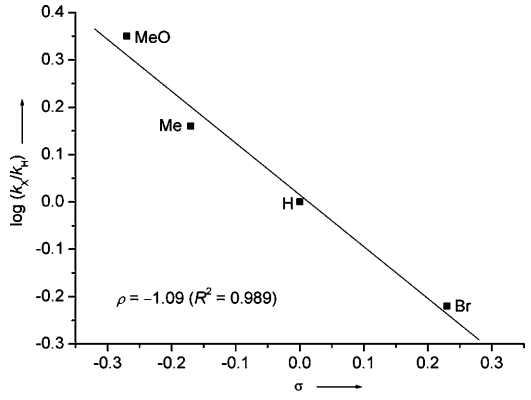
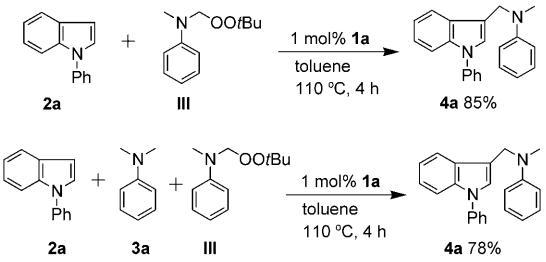


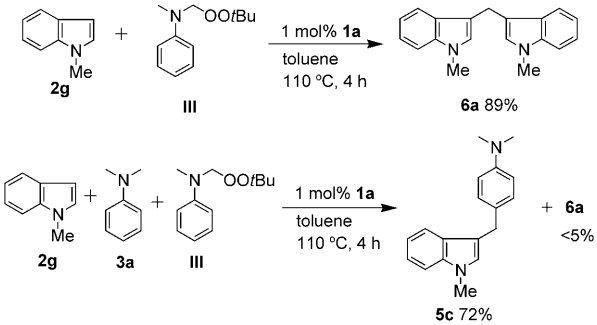

Figure 2. Hammett plot derived for [Ru(2,6-$Cl_2$tpp)CO]-catalyzed oxidative coupling reaction of *p*-X-$C_6H_4N(CH_3)_2$ (X = MeO, Me, H, Br) with **2a**.

for the intermediacy of **III** in the ruthenium-catalyzed oxidative coupling reaction. Using **1a** as catalyst, the reaction of *N*-phenylindole **2a** with **III**[24] in toluene at 110 °C for 4 h afforded **4a** both in the absence and presence of **3a** (Scheme 6); neither the 3-[*p*-(dialkylamino)benzyl]indole nor the indole dimer was detected in the reaction mixtures. These findings support the view that the oxidative coupling reactions of anilines with *N*-arylindoles preferentially afford **4a** (via pathway A). In contrast, the reaction of *N*-methylindole **2g** with **III** catalyzed by **1a** gave indole dimer



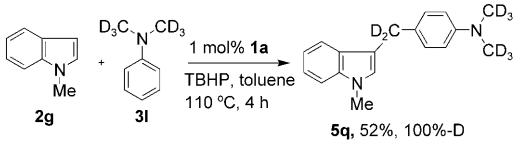

Scheme 6. Reaction of **2a** with **III**.

**6a** in 89% yield (Scheme 7), while the same reaction in the presence of **3a** afforded 3-[*p*-(dimethylamino)benzyl]indole (**5c**) in 72% yield along with a trace amount of **6a** (Scheme 7). The reaction of **2g** with *N*,*N*-di(trideuteromethyl)aniline (**3l**) gave deuterated product **5q** in 52% yield (Scheme 8). These experiments reveal that *N*-alkyl-indoles tend to form 3-[*p*-(dialkylamino)benzyl]indole **5**, and that the $CH_2$ group of **5** comes from the *N*-$CH_3$ group of the ani-

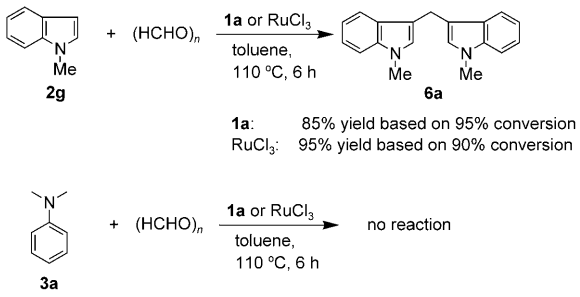



Scheme 7. Reaction of **2g** with *N*-methyl-*N*-(*tert*-butyldioxymethyl)aniline.

line, consistent with the formation of **5** via pathway B depicted in Scheme 2.

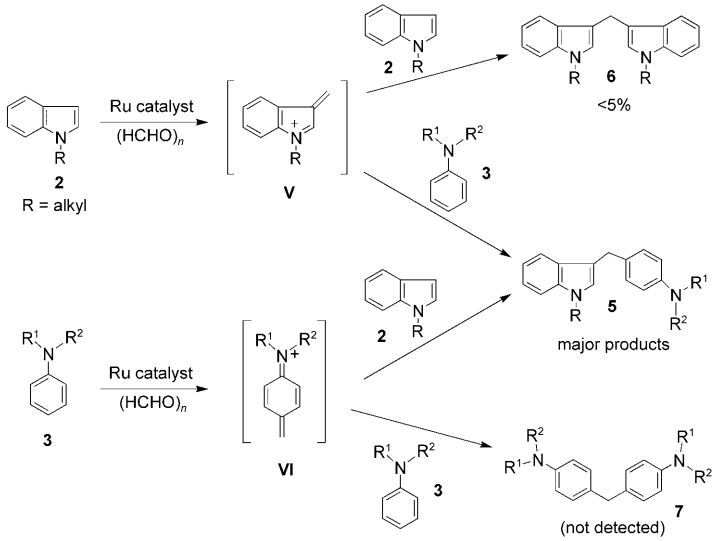



Scheme 8. Reaction of **2g** with *N*,*N*-di(trideuteromethyl)aniline (**3l**).



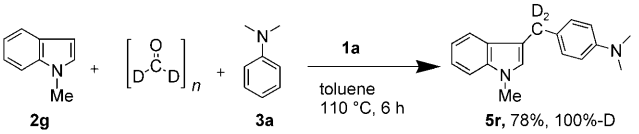

Scheme 10. a) Ruthenium-catalyzed reaction of **2g** with $(HCHO)_n$ and b) ruthenium-catalyzed reaction of **3a** with $(HCHO)_n$.

**Mechanism of the ruthenium-catalyzed three-component coupling reaction of indoles, paraformaldehyde, and anilines**: We propose that the three-component reaction of indoles with formaldehyde and anilines to form 3-[*p*-(dialkylamino)benzyl]indoles **5** involves a 3-alkylidene-3*H*-indolium cation (intermediate **V**, Scheme 9), which may be generated




Scheme 9. Possible pathways for the ruthenium-catalyzed three-component reaction.

by ruthenium-catalyzed condensation of indoles with formaldehyde.[25] The formation of **5** via intermediate **VI** (Scheme 9), as proposed for the three-component coupling reaction of *N*-methyl or *N*-H indoles, formaldehyde, and anilines in methanol catalyzed by silica-supported perchloric acid,[15e] cannot be excluded, but is evidently less favored in the ruthenium-catalyzed reactions in the light of the following observations (Scheme 10): i) in the presence of **1a** (1 mol%) or $RuCl_3$ (5 mol%), *N*-methylindole (**2g**) reacted with paraformaldehyde to give indole dimer **6a** in 85–95% yield; ii) no reaction was observed between aniline **3a** and paraformaldehyde under similar reaction conditions. Moreover, aniline dimers **7**[26] (Scheme 9) were not detected in the reaction mixtures for the ruthenium-catalyzed three-component coupling of indoles, paraformaldehyde, and anilines. Nor were these dimers detected in the reaction mixtures for the ruthenium-catalyzed oxidative coupling of tertiary amines with indoles. The three-component coupling reaction of **2g** with deuterated paraformaldehyde and aniline (**3a**) gave deuterium-substituted product **5r** in 78% yield (Scheme 11), consistent with the mechanism depicted in




Scheme 11. Ruthenium-catalyzed three-component coupling reaction of **2g**, deuterated paraformaldehyde, and **3a**.

Scheme 9. The low substrate conversions (5–32%) in the three-component reactions of *N*-arylindoles, paraformaldehyde, and anilines (Table 4, entries 12–15) might suggest that *N*-arylindoles are reluctant to react with paraformaldehyde to form 3-alkylidene-3*H*-indolium cation **V** under the ruthenium-catalyzed conditions. This could rationalize the finding that ruthenium-catalyzed oxidative coupling reactions of tertiary amines with *N*-arylindoles using TBHP as oxidant did not give 3-[*p*-(dialkylamino)benzyl]indoles **5** (via pathway B, Scheme 2).

## Conclusion

We have developed two types of ruthenium-catalyzed reaction for the C-3 alkylation of indoles in high yields: i) oxidative coupling of tertiary amines with indoles using TBHP as oxidant, and ii) three-component coupling of indoles, paraformaldehyde, and anilines. Through ruthenium-catalyzed reaction i), *N*-arylindoles were alkylated to afford 3-{[(*N*-aryl-*N*-alkyl)amino]methyl}indoles, whereas *N*-alkylindoles were alkylated to give 3-[*p*-(dialkylamino)benzyl]indoles. The same 3-[*p*-(dialkylamino)benzyl]indoles could be obtained from *N*-alkylindoles through ruthenium-catalyzed reaction ii).

## Experimental Section

**General**: Ruthenium porphyrins were prepared according to the literature.[10] Solvents (AR grade) were used as received unless otherwise specified. NMR spectra were recorded on Bruker AMX-300/400 spectrometers from solutions in $CDCl_3$. Chemical shifts are expressed in ppm and coupling constants are given in Hz. $^1$H NMR data are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet), coupling constant (Hz), integration. $^{13}$C NMR data are reported in terms of chemical shift (δ, ppm). Lower resolution mass spectra and high-resolution mass spectra (HRMS) were obtained on Finnigan GC-MS 4021 and Finnigan MAT-8430 instruments, respectively, using the electron-impact ionization technique (70 eV).

**General procedure for ruthenium porphyrin-catalyzed oxidative coupling of tertiary amines with *N*-arylindoles (Table 1)**: *tert*-Butyl hydroperoxide (0.6 mmol, 77 μL, 70% in water) was added to a mixture of tertiary amine (0.6 mmol), [Ru(2,6-$Cl_2$tpp)CO] (**1a**) (2.1 mg, 0.002 mmol), and the requisite indole (0.2 mmol) in toluene (0.5 mL) at room temperature in a flask open to the air. The reaction mixture was heated at 110 °C for 6 h. After cooling, the mixture was diluted with ethyl acetate (30 mL) and washed successively with water (3×10 mL), saturated $NaHCO_3$ solution (5 mL), and brine (5 mL), and then dried over anhydrous sodium sulfate. After filtration of the organic phase through a short pad of Celite, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc, 30:1) to afford the corresponding coupling product.

***N*-Methyl-*N*-[(1-phenyl-1*H*-indol-3-yl)methyl]benzenamine (4a)**: Yellow solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.51; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=3.02 (s, 3H), 4.73 (s, 2H), 6.73 (t, $J$=7.2 Hz, 1H), 6.88 (d, $J$=7.9 Hz, 2H), 7.17–7.31 (m, 6H), 7.41–7.51 (m, 4H), 7.55 (d, $J$=8.2 Hz, 1H), 7.62 ppm (d, $J$=7.9 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=30.19, 49.42, 110.13, 113.74, 117.78, 119.85, 120.68, 123.11, 123.97, 124.59, 124.69, 126.79, 128.68, 129.67, 129.97, 130.05, 136.82, 140.12 ppm; MS (EI): $m/z$: 312 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{22}H_{20}N_2$: 312.1626; found 312.1621.

***N*-Methyl-*N*-[(1-*o*-tolyl-1*H*-indol-3-yl)methyl]benzenamine (4b)**: Yellow solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.50; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=2.08 (s, 3H), 3.08 (s, 3H), 4.89 (s, 2H), 6.69 (t, $J$=7.2 Hz, 1H), 6.90 (d, $J$=8.0 Hz, 2H), 7.00 (s, 1H), 7.09 (d, $J$=6.8 Hz, 1H), 7.18–7.23 (m, 2H), 7.25–7.30 (m, 2H), 7.31–7.35 (m, 2H), 7.36–7.41 (m, 2H), 7.71 ppm (d, $J$=7.1 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=17.59, 37.98, 48.70, 110.61, 113.06, 113.13, 116.61, 118.09, 119.16, 119.61, 122.23, 126.68, 127.09, 128.01, 129.06, 129.22, 131.15, 135.68, 137.69, 145.62, 149.88 ppm; MS (EI): $m/z$: 326 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{23}H_{22}N_2$: 326.1783; found 326.1780.

***N*-Methyl-*N*-[(1-*p*-tolyl-1*H*-indol-3-yl)methyl]benzenamine (4c)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.50; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=2.35 (s, 3H), 3.05 (s, 3H), 4.75 (s, 2H), 6.77 (t, $J$=7.2 Hz, 1H), 6.92 (d, $J$=8.0 Hz, 2H), 7.18–7.21 (m, 2H), 7.23–7.38 (m, 7H), 7.55 (d, $J$=8.2 Hz, 1H), 7.66 ppm (d, $J$=7.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=21.55, 38.53, 49.25, 111.15, 113.55, 114.51, 117.16, 119.89, 120.53, 121.57, 122.72, 124.66, 124.85, 128.58, 129.59, 130.62, 136.67, 137.66, 150.66 ppm; MS (EI): $m/z$: 326 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{23}H_{22}N_2$: 326.1783; found 326.1781.

***N*-{[1-(4-Methoxyphenyl)-1*H*-indol-3-yl]methyl}-*N*-methylbenzenamine (4d)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.38; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=2.99 (s, 3H), 3.83 (s, 3H), 4.70 (s, 2H), 6.71 (t, $J$=7.2 Hz, 1H), 6.89 (d, $J$=8.0 Hz, 2H), 6.97 (d, $J$=6.8 Hz, 2H), 7.09 (s, 1H), 7.15–7.27 (m, 4H), 7.33 (d, $J$=6.7 Hz, 2H), 7.45 (d, $J$=8.0 Hz, 1H), 7.63 ppm (d, $J$=7.3 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=37.95, 48.65, 55.52, 110.43, 112.99, 113.65, 114.64, 115.68, 119.28, 122.36, 125.76, 126.49, 127.80, 129.10, 132.66, 136.78, 150.09, 158.08 ppm; MS (EI): $m/z$: 342 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{23}H_{22}N_2O$: 342.1732; found 342.1731.

**4-Bromo-*N*-methyl-*N*-[(1-phenyl-1*H*-indol-3-yl)methyl]benzenamine (4e)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.52; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=3.00 (s, 3H), 4.69 (s, 2H), 6.97 (d, $J$=8.1 Hz, 2H), 7.12–7.18 (m, 2H), 7.24 (s, 2H), 7.28–7.31 (m, 3H), 7.44–7.51 (m, 4H), 7.54–7.60 ppm (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=38.71, 49.17, 108.95, 111.19, 114.26, 114.42, 114.98, 119.78, 120.76, 123.22, 124.71, 126.56, 126.89, 128.48, 130.09, 132.28, 136.88, 149.40 ppm; MS (EI): $m/z$: 390 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{22}H_{19}N_2Br$: 390.0732; found 390.0735.

***N*,4-Dimethyl-*N*-[(1-phenyl-1*H*-indol-3-yl)methyl]benzenamine (4f)**: Yellow oil, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.52; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=2.28 (s, 3H), 2.97 (s, 3H), 4.67 (s, 2H), 6.81 (d, $J$=8.6 Hz, 2H), 7.04 (d, $J$=8.4 Hz, 2H), 7.15–7.24 (m, 4H), 7.45–7.47 (m, 4H), 7.47 (d, $J$=8.1 Hz, 1H), 7.54 ppm (d, $J$=7.8 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=20.26, 38.23, 49.09, 110.57, 113.48, 114.53, 118.15, 119.47, 120.11, 122.55, 124.17, 126.00, 126.21, 128.28, 129.53, 129.66, 136.31, 139.69, 148.19 ppm; MS (EI): $m/z$: 326 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{23}H_{22}N_2$: 326.1783; found 326.1786.

***N*,3-Dimethyl-*N*-[(1-phenyl-1*H*-indol-3-yl)methyl]benzenamine (4g)**: Yellow oil, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.51; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=2.28 (s, 3H), 2.99 (s, 3H), 4.70 (s, 2H), 6.55 (d, $J$=7.8 Hz, 1H), 6.71 (d, $J$=6.1 Hz, 2H), 7.16–7.36 (m, 5H), 7.45–7.47 (m, 1H), 7.55–7.57 (m, 3H), 7.63 (d, $J$=8.0 Hz, 1H), 7.68 ppm (d, $J$=7.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=22.45, 38.50, 49.25, 110.76, 111.12, 114.23, 117.90, 118.15, 119.32, 119.95, 120.65, 123.09, 124.69, 126.65, 126.75, 128.23, 129.96, 130.06, 131.86, 140.19, 150.75 ppm; MS (EI): $m/z$: 326 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{23}H_{22}N_2$: 326.1783; found 326.1779.

***N*,2-Dimethyl-*N*-[(1-phenyl-1*H*-indol-3-yl)methyl]benzenamine (4h)**: Yellow oil, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.50; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=2.33 (s, 3H), 2.68 (s, 3H), 4.35 (s, 2H), 6.99 (t, $J$=7.2 Hz, 1H), 7.13–7.25 (m, 6H), 7.27–7.31 (m, 1H), 7.49–7.51 (m, 4H), 7.54 (d, $J$=8.0 Hz, 1H), 7.63 ppm (d, $J$=7.9 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=18.45, 41.19, 51.77, 110.44, 114.71, 119.88, 120.00, 120.04, 122.42, 122.94, 124.18, 126.20, 126.39, 126.93, 128.94, 129.57, 131.09, 133.08, 136.22, 139.98, 152.55 ppm; MS (EI): $m/z$: 326 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{23}H_{22}N_2$: 326.1783; found 326.1780.

**4-Methoxy-*N*-methyl-*N*-[(1-phenyl-1*H*-indol-3-yl)methyl]benzenamine (4i)**: Yellow solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.35; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=2.92 (s, 3H), 3.76 (s, 3H), 4.66 (s, 2H), 6.86–6.88 (m, 4H), 7.17–7.46 (m, 4H), 7.48–7.53 (m, 4H), 7.57 (d, $J$=8.0 Hz, 1H), 7.63 ppm (d, $J$=7.7 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=39.10, 50.69, 55.75, 110.62, 114.73, 116.04, 116.97, 119.35, 120.27, 122.60, 124.22, 126.37, 127.01, 128.35, 128.44, 129.57, 136.23, 139.58, 157.82 ppm; MS (EI): $m/z$: 342 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{23}H_{22}N_2O$: 342.1732; found 342.1734.

***N*-Butyl-*N*-[(1-phenyl-1*H*-indol-3-yl)methyl]benzenamine (4j)**: Yellow oil, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.55; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.93 (t, $J$=8.1 Hz, 3H), 1.33–1.39 (m, 2H), 1.65–1.68 (m, 2H), 3.43 (t, $J$=7.2 Hz, 2H), 4.73 (s, 2H), 6.66 (t, $J$=7.2 Hz, 1H), 6.80 (d, $J$=7.8 Hz, 2H), 7.18–7.30 (m, 6H), 7.42–7.48 (m, 4H), 7.50 (d, $J$=8.0 Hz, 1H), 7.72 ppm (d, $J$=7.8 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=13.96, 20.37, 29.32, 46.76, 50.48, 110.64, 112.51, 114.48, 115.83, 119.20, 120.07, 122.57, 124.18, 124.38, 125.97, 126.20, 127.94, 129.13, 129.51, 136.75, 148.83 ppm; MS (EI): $m/z$: 354 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{25}H_{26}N_2$: 354.2096; found 354.2093.

**1,2,3,4-Tetrahydro-2-phenyl-1-(1-*p*-tolyl-1*H*-indol-3-yl)isoquinoline (4k)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.48; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=2.39 (s, 3H), 2.85 (ddd, $J$=15.1, 4.2, 4.2 Hz, 1H), 3.07 (ddd, $J$=15.1, 7.6, 7.6 Hz, 1H), 3.55–3.68 (m, 2H), 6.23 (s, 1H), 6.75 (s, 1H), 6.81 (t, $J$=7.5 Hz, 1H), 7.05–7.10 (m, 3H), 7.15–7.22 (m, 4H), 7.23–7.30 (m, 6H), 7.31–7.38 (m, 1H), 7.40 (d, $J$=8.3 Hz, 1H), 7.63 ppm (d, $J$=7.9 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=21.12, 42.51, 55.81, 57.60, 111.34, 112.58, 113.63, 117.85, 120.16, 121.64, 121.95, 122.38, 123.35, 125.56, 125.86, 126.72, 127.23, 128.07, 128.29, 128.91, 129.81, 132.26, 133.15, 134.65, 137.28, 150.02 ppm; MS (EI): $m/z$: 414 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{30}H_{26}N_2$: 414.2096; found 414.2092.

**1,2,3,4-Tetrahydro-1-[1-(4-methoxyphenyl)-1*H*-indol-3-yl]-2-phenylisoquinoline (4l)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.37; $^1$H NMR (400 MHz, $CDCl_3$); $\delta$=2.85 (ddd, $J$=15.8,

4.3, 4.3 Hz, 1H), 3.07 (ddd, $J$=15.8, 7.5, 7.5 Hz, 1H), 3.66 (d, $J$=3.2 Hz, 1H), 3.67 (d, $J$=12.0 Hz, 1H), 3.84 (s, 3H), 6.24 (s, 1H), 6.72 (s, 1H), 6.80 (t, $J$=7.2 Hz, 1H), 6.95 (d, $J$=8.9 Hz, 2H), 7.05–7.07 (m, 3H), 7.16–7.19 (m, 4H), 7.20–7.26 (m, 4H), 7.26–7.27 (m, 1H), 7.28 (d, $J$=8.8 Hz, 1H), 7.70 ppm (d, $J$=7.5 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$= 26.52, 42.35, 55.57, 56.60, 110.34, 113.55, 114.62, 115.84, 118.16, 119.64, 119.95, 120.37, 122.33, 125.76, 125.91, 126.72, 127.12, 128.08, 128.19, 128.90, 129.24, 132.16, 135.64, 137.26, 149.98, 160.12 ppm; MS (EI): $m/z$: 430 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{30}H_{26}N_2O$: 430.2045; found 430.2042.

**_N_-[(1-Benzyl-1_H_-indol-3-yl)methyl]-_N_-methylbenzenamine (4m)**: Yellow oil, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.45; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=2.94 (s, 3H), 4.65 (s, 2H), 5.20 (s, 2H), 6.68 (t, $J$=7.2 Hz, 1H), 6.87 (d, $J$=8.0 Hz, 2H), 6.94 (s, 1H), 7.04–7.18 (m, 4H), 7.21–7.25 (m, 6H), 7.58 ppm (d, $J$=7.2 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=37.92, 48.72, 49.97, 109.83, 112.41, 113.21, 116.65, 119.34, 121.94, 126.66, 126.82, 127.54, 127.63, 127.84, 129.12, 129.21, 137.62, 138.69, 149.50 ppm; MS (EI): $m/z$: 326 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{23}H_{22}N_2$: 326.1783; found 326.1774.

**General procedure for ruthenium porphyrin-catalyzed oxidative coupling of tertiary amines with _N_-alkylindoles (Table 2)**: *tert*-Butyl hydroperoxide (0.6 mmol, 77 μL, 70% in water) was added to a mixture of the tertiary amine (0.6 mmol), [Ru(2,6-$Cl_2$tpp)CO] **1a** (2.1 mg, 0.002 mmol), and the *N*-alkylindole (0.2 mmol) in toluene (0.5 mL) at room temperature in a flask open to the air. The reaction mixture was heated at 110°C for 6 h. After cooling, the mixture was diluted with ethyl acetate (30 mL) and washed successively with water (3×10 mL), saturated $NaHCO_3$ solution (5 mL), and brine (5 mL), and then dried over anhydrous sodium sulfate. After filtration of the organic phase through a short pad of Celite, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc, 30:1) to afford the corresponding coupling product.

**4-[(1-Benzyl-1_H_-indol-3-yl)methyl]-_N_,_N_-dimethylbenzenamine (5a)**: Yellow oil, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$= 0.41; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=2.86 (s, 6H), 3.96 (s, 2H), 5.18 (s, 2H), 6.62 (d, $J$=8.6 Hz, 2H), 6.77 (s, 1H), 7.07–7.11 (m, 6H), 7.17–7.30 (m, 4H), 7.50 ppm (d, $J$=7.9 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$= 30.46, 40.89, 49.85, 109.53, 112.51, 112.99, 116.10, 118.89, 119.40, 121.62, 126.41, 126.51, 126.67, 127.41, 128.65, 129.23, 129.46, 137.85, 149.68 ppm; MS (EI): $m/z$: 340 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{24}H_{24}N_2$: 340.1939; found 340.1936.

**4-[(1-Ethyl-1_H_-indol-3-yl)methyl]-_N_,_N_-dimethylbenzenamine (5b)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$= 0.55; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.45 (t, $J$=7.3 Hz, 3H), 2.93 (s, 6H), 4.09 (s, 2H), 4.13 (q, $J$=7.3 Hz, 2H), 6.72 (d, $J$=8.5 Hz, 2H), 6.83 (s, 1H), 7.18 (t, $J$=6.8 Hz, 1H), 7.21–7.22 (m, 3H), 7.33 (d, $J$=8.1 Hz, 1H), 7.58 ppm (d, $J$=7.9 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$= 16.01, 31.01, 41.39, 41.45, 109.63, 113.33, 115.78, 119.09, 122.29, 125.71, 128.59, 129.61, 129.75, 136.71, 149.59 ppm; MS (EI): $m/z$: 278 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{19}H_{22}N_2$: 278.1783; found 278.1776.

**4-[(1_H_-Indol-3-yl)methyl]-_N_-butyl-_N_-methylbenzenamine (5e)**: White solid, analytical TLC (silica gel 60) (20% EtOAc in hexane), $R_f$=0.41; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=0.95 (t, $J$=7.6 Hz, 3H), 1.42 (m, 2H), 1.71 (m, 2H), 2.90 (s, 3H), 3.28 (q, $J$=7.6 Hz, 2H), 4.05 (s, 2H), 6.71 (d, $J$=8.7 Hz, 2H), 6.78 (s, 1H), 7.15 (t, $J$=8.1 Hz, 1H), 7.16–7.22 (m, 3H), 7.45 (d, $J$=7.9 Hz, 1H), 7.61 (d, $J$=7.8 Hz, 1H), 7.90 ppm (brs, NH, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=14.52, 20.89, 29.31, 30.96, 38.91, 53.33, 111.46, 112.90, 117.36, 119.69, 128.08, 129.02, 129.83, 136.98, 148.29 ppm; MS (EI): $m/z$: 292 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{20}H_{24}N_2$: 292.1939; found 292.1941.

**4-[(1_H_-Indol-3-yl)methyl]-_N_-ethyl-_N_-methylbenzenamine (5f)**: White solid, analytical TLC (silica gel 60) (20% EtOAc in hexane), $R_f$=0.42; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.12 (t, $J$=7.0 Hz, 3H), 2.89 (s, 3H), 3.37 (q, $J$=7.0 Hz, 2H), 4.05 (s, 2H), 6.68 (d, $J$=8.6 Hz, 2H), 6.89 (s, 1H), 7.12 (t, $J$=8.1 Hz, 1H), 7.13–7.21 (m, 3H), 7.34 (d, $J$=7.5 Hz, 1H), 7.58 (d, $J$=7.9 Hz, 1H), 7.90 ppm (brs, NH, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=11.06, 30.47, 37.59, 47.08, 110.95, 112.64, 116.78, 119.23, 121.85, 122.14, 127.57, 128.06, 129.36, 136.47, 147.52 ppm; MS (EI): $m/z$: 264 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{18}H_{20}N_2$: 264.1626; found 264.1626.

**_N_-Ethyl-4-[(1-ethyl-1_H_-indol-3-yl)methyl]-_N_-methylbenzenamine (5g)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$= 0.52; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.13 (t, $J$=7.1 Hz, 3H), 1.48 (t, $J$= 7.2 Hz, 3H), 2.89 (s, 6H), 3.40 (q, $J$=7.1 Hz, 3H), 4.04 (s, 2H), 4.13 (q, $J$=7.3 Hz, 2H), 6.68 (d, $J$=8.6 Hz, 2H), 6.83 (s, 1H), 7.08 (t, $J$=7.1 Hz, 1H), 7.16–7.24 (m, 3H), 7.31 (d, $J$=8.2 Hz, 1H), 7.57 ppm (d, $J$=7.9 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=11.20, 15.48, 30.46, 37.57, 40.68, 47.05, 109.08, 112.76, 115.32, 119.17, 119.39, 121.76, 125.17, 128.09, 129.03, 136.18, 147.51 ppm; MS (EI): $m/z$ 292 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{20}H_{24}N_2$: 292.1939; found 292.1937.

**_N_-Ethyl-_N_-methyl-4-[(1-methyl-1_H_-indol-3-yl)methyl]benzenamine (5h)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$= 0.51; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.14 (t, $J$=7.1 Hz, 3H), 2.90 (s, 3H), 3.40 (q, $J$=7.1 Hz, 2H), 3.74 (s, 3H), 4.05 (s, 2H), 6.70 (d, $J$= 8.7 Hz, 2H), 6.76 (s, 1H), 7.17 (t, $J$=8.1 Hz, 1H), 7.24 (d, $J$=8.6 Hz, 2H), 7.26–7.32 (m, 2H), 7.59 ppm (d, $J$=7.9 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=11.18, 30.38, 32.50, 37.56, 47.03, 108.99, 112.76, 115.32, 119.05, 119.27, 121.39, 127.07, 127.92, 128.89, 129.35, 137.15, 147.52 ppm; MS (EI): $m/z$: 278 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{19}H_{22}N_2$: 278.1783; found 278.1780.

**General procedure for ruthenium porphyrin-catalyzed three-component coupling reaction of indoles, paraformaldehyde, and anilines (Tables 3 and 4)**: Paraformaldehyde (0.6 mmol) was added to a mixture of tertiary amine (0.6 mmol), [Ru(2,6-$Cl_2$tpp)CO] **1a** (2.1 mg, 0.002 mmol), and indole (0.2 mmol) in toluene (2 mL) at room temperature in a flask open to the air. After heating at 110°C for 6 h, the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate (30 mL) and washed successively with water (3×10 mL), saturated $NaHCO_3$ solution (5 mL), and brine (5 mL), and then dried over anhydrous sodium sulfate. After filtration of the organic phase through a short pad of Celite, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc, 20:1 or hexane/EtOAc, 10:1) to afford the corresponding coupling product.

**4-[(5-Chloro-1_H_-indol-3-yl)methyl]-_N_,_N_-dimethylbenzenamine (5i)**: White solid, analytical TLC (silica gel 60) (20% EtOAc in hexane), $R_f$= 0.42; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=2.92 (s, 6H), 3.97 (s, 2H), 6.70 (d, $J$=6.7 Hz, 2H), 6.91 (s, 1H), 7.11–7.15 (m, 3H), 7.23 (d, $J$=8.6 Hz, 1H), 7.51 (s, 1H), 7.98 ppm (brs, NH, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$= 30.83, 41.40, 112.47, 113.54, 117.09, 119.22, 122.71, 124.05, 125.48, 129.15, 129.36, 129.69, 135.30, 149.68 ppm; MS (EI): $m/z$: 283 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{17}H_{16}ClN_2$: 283.1002; found 283.1000.

**4-[(5-Ethoxy-1_H_-indol-3-yl)methyl]-_N_,_N_-dimethylbenzenamine (5j)**: White solid, analytical TLC (silica gel 60) (20% EtOAc in hexane), $R_f$= 0.38; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.41 (t, $J$=7.0 Hz, 3H), 2.89 (s, 6H), 3.97 (s, 2H), 4.05 (q, $J$=7.0 Hz, 2H), 6.70 (d, $J$=8.6 Hz, 2H), 6.82 (d, $J$=8.0 Hz, 1H), 6.85 (s, 1H), 6.98 (s, 1H), 7.15 (d, $J$=8.7 Hz, 2H), 7.21–7.24 (m, 1H), 7.80 ppm (brs, NH, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=15.23, 30.69, 41.14, 64.38, 102.51, 111.79, 112.76, 113.26, 114.85, 119.18, 123.16, 129.44, 129.50, 129.81, 131.85, 149.82 ppm; MS (EI): $m/z$: 294 [$M^+$], 265 [$M^+-C_2H_5$]; HRMS (EI): $m/z$: calcd for $C_{19}H_{22}N_2O$: 294.1732; found 294.1724.

**3-[4-(Dimethylamino)benzyl]-1_H_-indol-5-ol (5k)**: White solid, analytical TLC (silica gel 60) (50% EtOAc in hexane), $R_f$=0.35; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=2.88 (s, 6H), 3.95 (s, 2H), 6.68 (d, $J$=7.9 Hz, 2H), 6.73 (d, $J$=7.2 Hz, 1H), 6.89 (s, 2H), 7.13–7.18 (m, 3H), 7.80 ppm (brs, NH, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=29.66, 40.91, 103.79, 110.05, 111.56, 111.58, 113.03, 123.34, 128.98, 129.17, 136.78, 145.12, 146.78, 150.12 ppm; MS (EI): $m/z$: 266 [$M^+$]; HRMS (EI): $m/z$: calcd for $C_{17}H_{18}N_2O$: 266.1419; found 266.1415.

**4-[(1_H_-Indol-3-yl)methyl]-_N_,_N_,3-trimethylbenzenamine (5l)**: Pale-yellow solid, analytical TLC (silica gel 60) (20% EtOAc in hexane), $R_f$=0.39; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=2.31 (s, 3H), 2.93 (s, 6H), 4.01 (s, 2H), 6.56 (d, $J$=8.3 Hz, 1H), 6.63 (s, 1H), 6.72 (s, 1H), 7.05–7.13 (m, 2H), 7.20 (d, $J$=7.1 Hz, 1H), 7.34 (d, $J$=8.1 Hz, 1H), 7.61 (d, $J$=7.9 Hz, 1H), 7.90 ppm (brs, NH, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=20.01, 26.38, 28.68, 40.94, 110.67, 110.96, 111.58, 114.99, 116.16, 119.09, 119.16, 121.85,

122.25, 127.61, 130.09, 136.45, 136.95, 149.34 ppm; MS (EI): *m/z*: 264 [$M^+$]; HRMS (EI): *m/z*: calcd for $C_{18}H_{10}N_2$: 264.1626; found 264.1625.

**4-[(1*H*-Indol-3-yl)methyl]-*N*,*N*-diethylbenzenamine (5m)**: White solid, analytical TLC (silica gel 60) (20% EtOAc in hexane), $R_f$=0.45; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$=1.13 (t, $J$=7.0 Hz, 6H), 3.30 (q, $J$=7.0 Hz, 4H), 4.01 (s, 2H), 6.61 (d, $J$=8.4 Hz, 2H), 6.90 (s, 1H), 7.07–7.15 (m, 4H), 7.32 (d, 1H), 7.55 (d, 1H), 7.88 ppm (br s, NH, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=13.08, 30.91, 44.93, 111.43, 112.75, 117.32, 119.68, 119.76, 122.37, 122.62, 127.05, 129.92, 131.12, 137.08, 149.72 ppm; MS (EI): *m/z*: 278 [$M^+$]; HRMS (EI): *m/z*: calcd for $C_{19}H_{22}N_2$: 278.1783; found 278.1785.

**3-[4-(Piperidin-1-yl)benzyl]-1-methyl-1*H*-indole (5n)**: Yellow solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.51; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=1.55–1.58 (m, 2H), 1.72–1.75 (m, 4H), 3.12 (t, $J$=5.7 Hz, 4H), 3.72 (s, 3H), 4.03 (s, 2H), 6.73 (s, 1H), 6.89 (d, $J$=8.5 Hz, 2H), 7.17 (t, $J$=6.7 Hz, 1H), 7.23–7.27 (m, 4H), 7.52 ppm (d, $J$=7.9 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=20.78, 24.18, 30.30, 32.53, 51.28, 109.03, 114.91, 116.89, 118.62, 118.85, 119.24, 121.44, 126.99, 127.85, 129.21, 137.15 ppm; MS (EI): *m/z*: 304 [$M^+$]; HRMS (EI): *m/z*: calcd for $C_{21}H_{24}N_2$: 304.1939; found 304.1941.

***N*,*N*-Dimethyl-4-[(1-*p*-tolyl-1*H*-indol-3-yl)methyl]benzenamine (5o)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.49; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=2.41 (s, 3H), 2.90 (s, 6H), 4.06 (s, 2H), 6.69 (d, $J$=8.2 Hz, 2H), 7.01 (s, 1H), 7.11–7.17 (m, 1H), 7.19 (d, $J$=8.5 Hz, 2H), 7.22–7.28 (m, 3H), 7.33 (d, $J$=8.3 Hz, 2H), 7.52 (d, $J$=8.3 Hz, 1H), 7.58 ppm (d, $J$=7.4 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=29.67, 30.44, 40.89, 110.39, 113.01, 117.46, 119.45, 119.63, 122.18, 123.18, 123.99, 126.06, 127.81, 128.03, 129.33, 129.98, 135.74, 136.28, 138.19 ppm; MS (EI): *m/z*: 340 [$M^+$]; HRMS (EI): *m/z*: calcd for $C_{24}H_{24}N_2$: 340.1939; found 340.1936.

**4-{[1-(4-Methoxyphenyl)-1*H*-indol-3-yl]methyl}-*N*,*N*-dimethylbenzenamine (5p)**: White solid, analytical TLC (silica gel 60) (5% EtOAc in hexane), $R_f$=0.32; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=2.90 (s, 6H), 3.86 (s, 3H), 4.06 (s, 2H), 6.69 (d, $J$=6.9 Hz, 2H), 6.96–6.98 (m, 3H), 7.00–7.18 (m, 2H), 7.19 (d, $J$=8.4 Hz, 2H), 7.34 (d, $J$=8.2 Hz, 2H), 7.37 (d, $J$=8.1 Hz, 1H), 7.65 ppm (d, $J$=7.2 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$=30.44, 40.89, 55.54, 110.23, 113.01, 114.59, 117.68, 119.41, 119.51, 122.11, 125.66, 126.29, 128.35, 128.67, 129.33, 133.15, 137.18, 148.55, 147.82 ppm; MS (EI): *m/z*: 356 [$M^+$]; HRMS (EI): *m/z*: calcd for $C_{24}H_{24}N_2O$: 356.1888; found 356.1878.

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