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Access to Indole Derivatives from Diaryliodonium Salts and 2-Alkynylanilines

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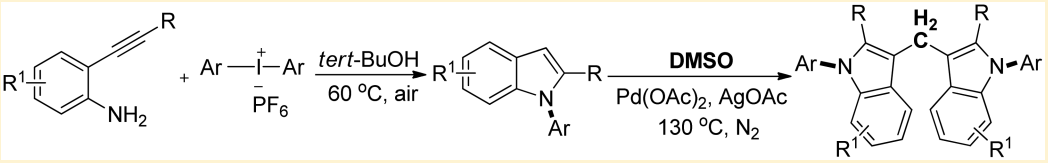
Supporting Information



ABSTRACT: An efficient, environmentally friendly, and operationally simple procedure to 1,2-disubstituted indoles from 2-alkynylanilines and diaryliodonium salts has been developed. This reaction proceeds smoothly under metal-free conditions. The products obtained could be transferred into 3,3′-diindolylmethane with DMSO catalyzed by palladium. The isotopic label experiments indicated that the methylene group in 3,3′-diindolylmethane is derived from DMSO. The diverse indoles were obtained in up to 90% yield for 28 examples.

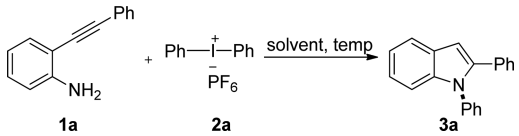
INTRODUCTION

Indole is an important motif and widely exist in natural products, advanced functional materials, and bioactive molecules.[1] Consequently, developing an efficient protocol for the synthesis of indole and its derivatives has received tremendous interest during the past decades.[2] Classical routes include Fischer synthesis,[3] Batcho−Leimgruber synthesis, Gassman synthesis, Madelung cyclization of *N*-acyl-*o*-toluidines, and the reductive cyclization of *o*-nitrobenzyl ketones.[4] Recently, transition-metal-catalyzed transformations and multicomponent reactions have also been widely applied in indole synthesis.[5−7] Although these methods have contributed greatly to this area, there are still some respective limitations, such as harsh reaction conditions and the required transition metal, that may cause the potential contamination of the products, which limits their applications, especially in the pharmaceutical industry. Therefore, development of a green, metal-free, and convenient method is highly desirable. Diaryliodonium salt is an important electrophilic arylating reagent in organic synthesis due to its low toxicity, easy handling, and excellent selectivity.[8] In our continuing interest in hypervalent iodine,[9] we developed a novel protocol to 1,2-disubstituted indoles from 2-alkynylanilines with diaryliodonium salts.

RESULTS AND DISCUSSION

We initially studied the reaction of 2-alkynylanilines **1a** and diphenyliodonium hexafluorophosphate **2a** in 1,2-dichloroethane (DCE) at room temperature. The desired product **3a** was obtained in 25% yield (Table 1, entry 1). Inspired by this result, various solvents were investigated. We found that DMSO, toluene, MeOH, EtOH, and H_2O were ineffective in this reaction (Table 1, entries 2−5 and 7). Interestingly, *t*-BuOH showed optimal influence on this transformation and afforded the desired product **3a** in 48% yield (Table 1, entry 6). Then, the reaction temperature was examined (Table 1, entries 8−10). The best result was obtained at 60 °C (Table 1, entry

Table 1. Optimization of the Reaction Conditions for the Reaction of 2-Alkynylanilines 1a and Diphenyliodonium Hexafluorophosphate 2a[a]



1a **2a** **3a**

entry	solvent	*T* (°C)	yield (%)[b]
1	DCE	rt	25
2	DMSO	rt	27
3	toluene	rt	39
4	MeOH	rt	6
5	EtOH	rt	13
6	*t*-BuOH	rt	48
7	H_2O	rt	<5
8	*t*-BuOH	50	56
9	*t*-BuOH	60	69
10	*t*-BuOH	70	70
11[c]	*t*-BuOH	60	78
12[d]	*t*-BuOH	60	78
13[e]	*t*-BuOH	60	77
14[f]	*t*-BuOH	60	85

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), solvent (1 mL) under air at room temperature. [b]Isolated yields. [c]*t*-BuOH (2 mL). [d]Under N_2. [e]Under O_2. [f]$Cu(OTf)_2$ (0.1 equiv).

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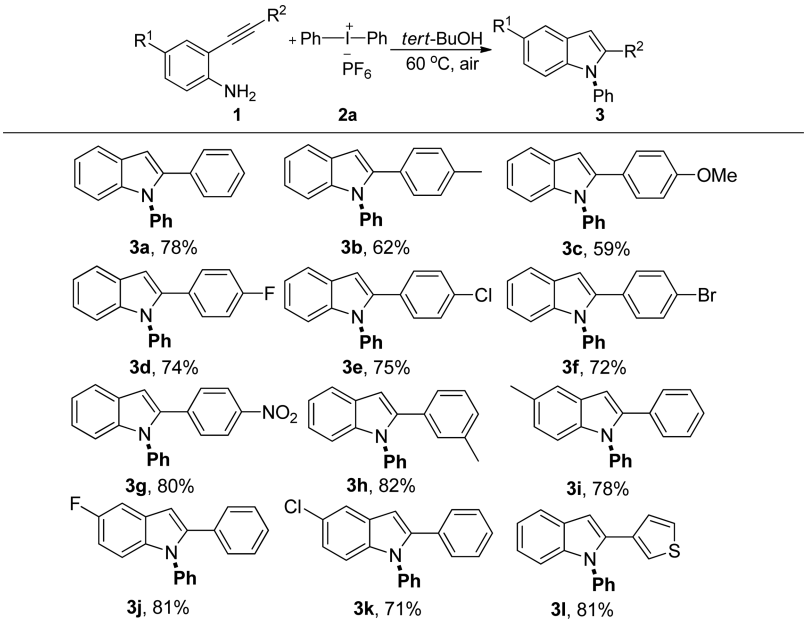
Table 2. Scope of 2-Alkynylanilines 1[a]



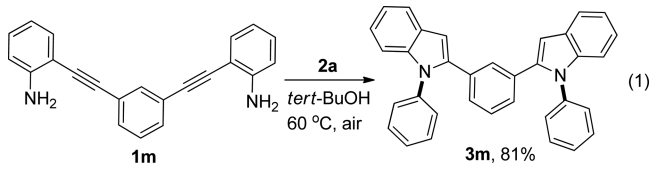
[a]Reaction conditions: **1** (0.2 mmol) and **2a** (0.2 mmol) in *t*-BuOH (2 mL) under air at 60 °C for 18−45 h.

9). When the solvent volume was increased to 2 mL from 1 mL, the yield of **3a** could be further improved to 78% (Table 1, entry 11). The yield of **3a** was not significantly improved under O_2 or N_2 atmosphere (Table 1, entries 12 and 13). The presence of catalyst Cu did not significantly improve this reaction (Table 1, entry 14). Finally, the optimal reaction conditions were identified as follows: **1a** (0.2 mmol) and **2a** (0.2 mmol) in *t*-BuOH (2 mL) under air at 60 °C.

With the optimized reaction conditions in hand, we explored the substrate scope of 2-alkynylanilines **1** first (Table 2). The electron density of the substituent R^2 had no significant influence on this reaction. R^2 can be phenyl. Electron-donating (*p*-Me, *p*-OMe, and *m*-Me) and electron-withdrawing (*p*-F, *p*-Cl, *p*-Br, and *p*-NO_2) groups on the phenyl rings could be well-tolerated. The desired products were obtained in moderate to good yields (Table 2, **3a−h**). The electronic property of the R^1 also had no obvious influence. When R^1 = Me, F, and Cl, the corresponding products were obtained in 78%, 81%, and 71% yields, respectively (Table 2, **3i−k**). A heteroaryl group was tolerated as well. The corresponding product was obtained in 81% yield for thiophene (Table 2, **3l**). Both CO_2R- and alkyl-substituted alkynes were tested under the standard conditions. No reaction occurred for CO_2Et-substituted alkyne, and a trace amount of the desired product (10% yield) was obtained for *n*-pentylalkyne.

Next, the scope of diaryliodonium salts was explored. The electron density of the substituent of the diaryliodonium salts **2** (*p*-Me, *p*-*t*-Bu, *p*-F, *p*-Cl, *p*-Br, *p*-I, *p*-CO_2Et) have no obvious influence on the transformation. The products **3ba−3ha** were obtained in good yields (Table 3, entries 1−7). The steric hindrance of the substituents had slight effect on the yields. 2-Phenyl-1-(*p*-tolyl)-1*H*-indole **3ba** and 2-phenyl-1-(*o*-tolyl)-1*H*-indole **3ia** were obtained in 80% and 71% yield, respectively (Table 3, entry 8 vs entry 1). When unsymmetric diaryliodonium salts **2** were used as substrates, *N*-arylation of indoles is sensitive to the electron density and steric hindrance. *N*-(*p*-I- or-F-phenyl) indole was obtained as a main product because of the electron-withdrawing ability of I or F (Table 3, entries 5 and 6). However, no byproducts were obtained for **2h−2j**, owing to the large steric hindrance (Table 3, entries 7−9).

Indole[1,2-*f*]phenanthridines is widely applied in advanced materials.[10,11] Under the standard conditions, the reaction of **1m** (0.2 mmol) with **2a** (2 equiv) could provide the corresponding product **3m** in 81% yield (eq 1).



To demonstrate the scalability of the method, a gram-scale experiment was conducted with 10 mmol (1.93 g) of **1a**, 10 mmol (4.26 g) of **2a**, and *t*-BuOH (100 mL) (Scheme 1). The product **3a** was obtained in 57% yield (1.53 g) (eq 2).

To further extensive application of our methodology, the synthesis of bis(1,2-diphenyl-1*H*-indol-3-yl)methane from titled products has been explored. The reaction of **3a** with DMSO afforded bis(1,2-diphenyl-1*H*-indol-3-yl)methane (**4a**) in 47% yield in the presence of $Pd(OAc)_2$ (0.1 equiv), AgOAc (2 equiv), and DMSO (2 mL) under N_2 at 100 °C. Inspired by this result, the reaction conditions were optimized. The optimized reaction conditions were identified as follows: **3a** (0.05 mmol), $Pd(OAc)_2$ (0.1 equiv), AgOAc (1 equiv), DMSO (1 mL), 130 °C under N_2 atmosphere (Table 4). The products of **4a−f** could be obtained in good to excellent yields (Table 5).

To gain insight into the mechanism of this process, four control experiments were conducted (Scheme 2). Under the standard reaction conditions, the reaction of **a1**, **1d**, and **2a** gave **3d** in 76% yield in *t*-BuOH (2 mL) at 60 °C (Scheme 2, eq 3). Compound **a1** did not participate in the reaction. Meanwhile, the reaction of 2-phenylindole with diphenyliodonium hexafluorophosphate (**2a**) did not give the desire product under the standard reaction conditions (Scheme 2, eq 4). These results suggested that both **a1** and 2-phenylindole as key intermediates were ruled out in this procedure. When DMSO-

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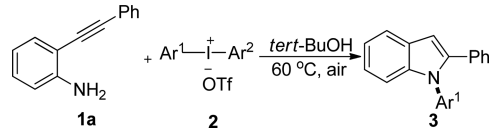
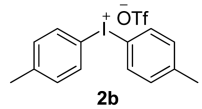
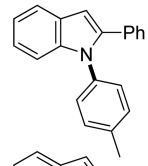
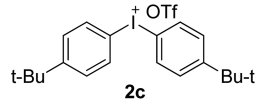
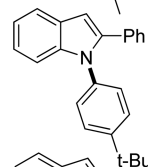
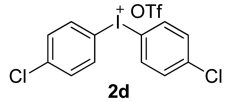
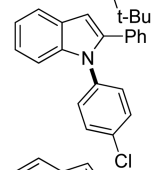
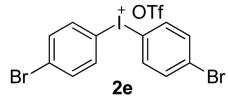
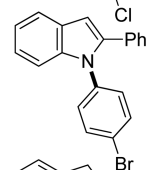
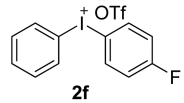
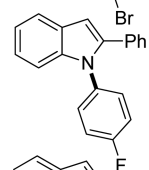
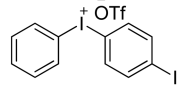
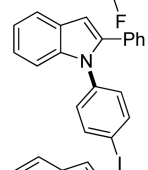
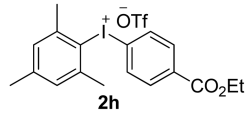
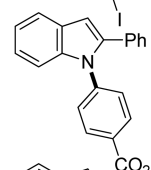
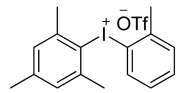
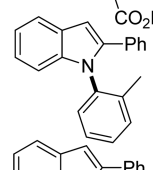
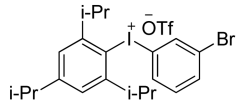
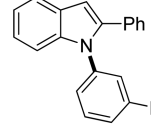
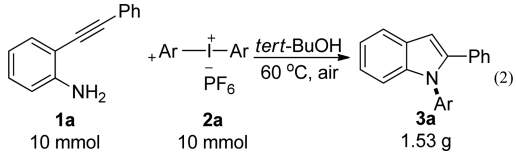
Table 3. Scope of Diaryliodonium Salts 2[a]



entry	substrate **2**	product **3**	yield (%)
1	 **2b**	 **3ba**	80
2	 **2c**	 **3ca**	84
3	 **2d**	 **3da**	75
4	 **2e**	 **3ea**	69
5	 **2f**	 **3fa/3a**	79/12
6	 **2g**	 **3ga/3a**	65/15
7	 **2h**	 **3ha**	77
8	 **2i**	 **3ia**	71
9	 **2j**	 **3ja**	76

[a]Reaction conditions: **1a** (0.2 mmol) and **2** (0.2 mmol) in *t*-BuOH (2 mL) under air at 60 °C.

Scheme 1. Gram-Scale Experiment



d_6 and ^{13}C-labeled DMSO were used as solvent under the standard reaction conditions, **4aa** and **4ab** were provided. The corresponding structures were confirmed by ^{1}H and ^{13}C NMR spectra (Scheme 2, eqs 5 and 6). These results indicated that the methylene carbon atom in the product **4a** was derived from the methyl group of DMSO.

According to results obtained above, a plausible reaction mechanism was proposed and is shown in Scheme 3. In part A,

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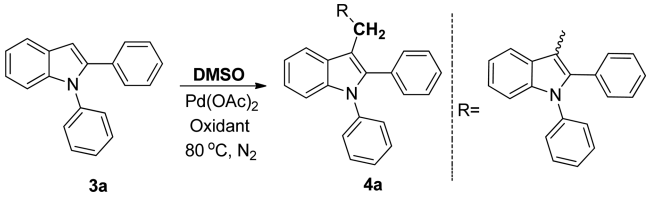
Table 4. Optimization of the Reaction Conditions for the Reaction of 1,2-Diphenyl-1*H*-indole 3 and DMSO[a]



entry	Pd	oxidant	yield (%)[b]
1	$Pd(OAc)_2$	AgO	26
2	$Pd(OAc)_2$	AgOAc	47
3	$Pd(OAc)_2$	$CuSO_4$	15
4	$Pd(OAc)_2$	$Cu(OAc)_2$	20
5[c]	$Pd(OAc)_2$	AgOAc	71
6[d]	$Pd(OAc)_2$	AgOAc	89
7		AgOAc	9
8	$Pd(OAc)_2$		13
9[e]	$Pd(OAc)_2$	AgOAc	35

[a]Reaction conditions: **3a** (0.05 mmol), $Pd(OAc)_2$ (0.1 equiv), oxidant (1 equiv), DMSO (1 mL), N_2, 80 °C. [b]Isolated yields. [c]100 °C. [d]130 °C. [e]Under O_2.

electrophlic attack of diaryliodonium salts **2** at the N atom from 2-(phenylethynyl)aniline (**1**) gave the intermediate **I**, which then transformed into intermediate **II**. The intermediate **II** was detected by NMR (Figure SIA in Supporting Information) and Q-TOF HRMs (Figure SIB in Supporting Information) and finally converted into the 1,2-diphenyl-1*H*-indole **3** as well as PhI. In part B, the C3−H bond of 1,2-diphenyl-1*H*-indole **3** was activated by $Pd(OAc)_2$, affording a palladated intermediate **III**. The palladium atom in intermediate **III** might coordinate with DMSO and gave intermediate **IV**. Reductive elimination of **IV** produced the intermediate **V** (**IV** and **V** were detected by Q-TOF HRMs, as seen in Figures SIC and SID in the Supporting Information). The final product **4** was finally obtained through 1,4-addition of 1,2-diphenyl-1*H*-indole **3** with the intermediate **V**.

CONCLUSION

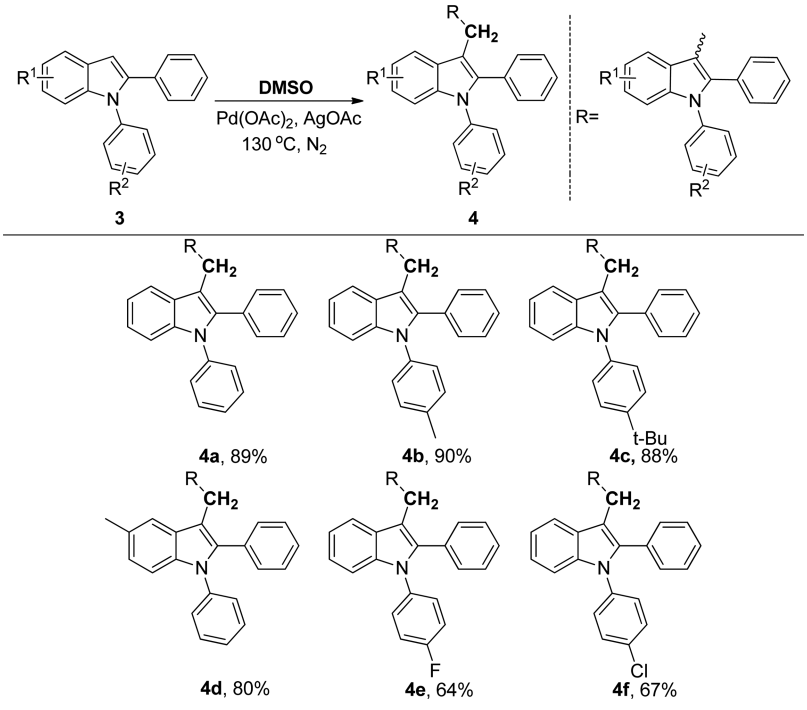
In summary, we have presented an environmentally friendly, efficient, and operationally simple protocol to synthesize 1,2-disubstituted indole derivatives using diaryliodonium salts and 2-alkynylanilines as starting materials. Compared with the previous methods, this method is not sensitive to air and is carried out under metal-free conditions. The products could be transformed into bis(1,2-diphenyl-*1H*-indol-3-yl)methane with DMSO catalyzed by palladium.

EXPERIMENTAL SECTION

General Information. All commercial materials and solvents were used directly without further purification. Melting points were determined in open glass capillaries and were uncorrected. All the compounds were characterized by IR, and only major peaks were reported in cm^{-1}. ^1H NMR spectra were recorded on 400 MHz spectrometers, and ^{13}C NMR spectra were recorded on a 100 MHz spectrometer. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in $CDCl_3$ as an internal standard at room temperature. ^{13}C NMR spectra were obtained by using the same NMR spectrometer and were calibrated with $CDCl_3$ (δ = 77.00 ppm). High-resolution mass spectra (HRMS) were equipped with an ESI source and a TOF detector. Column chromatography was performed on silica gel (70−230 mesh ASTM) using the reported eluents. Thin-layer chromatography (TLC) was carried out on 4 × 15 cm plates with a layer thickness of 0.2 mm (silica gel 60 F254).

Preparation of 2-Alkynylanilines 1. Synthesis of 2-alkynylanilines **1** was accomplished by a modified Sonogashira[12] coupling reaction of the 2-iodoanilines and alkynes as follows: 2-iodoaniline (1 equiv), alkyne (1 equiv), $Pd(PPh_3)_2Cl_2$ (0.02 equiv), CuI (0.02 equiv), and Et_3N (0.2 M) were stirred under N_2 at 60 °C until TLC indicated

Table 5. Scope of 1,2-Diphenyl-1*H*-indole 3[a]



[a]Reaction conditions: **3** (0.05 mmol), $Pd(OAc)_2$ (0.1 equiv), and AgOAc (1 equiv) in DMSO (1 mL) under N_2 at 130 °C for 20 h.

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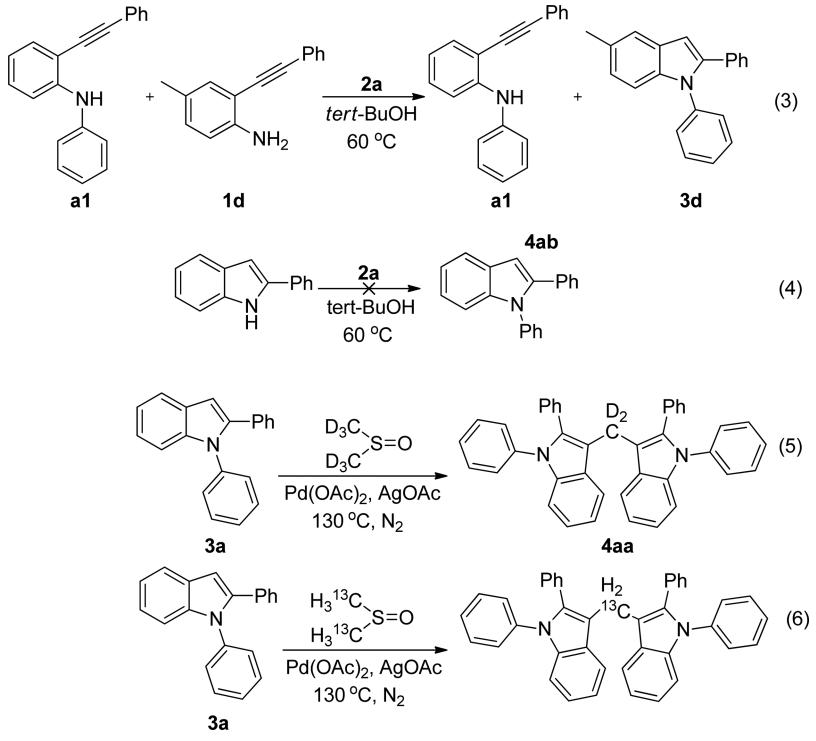
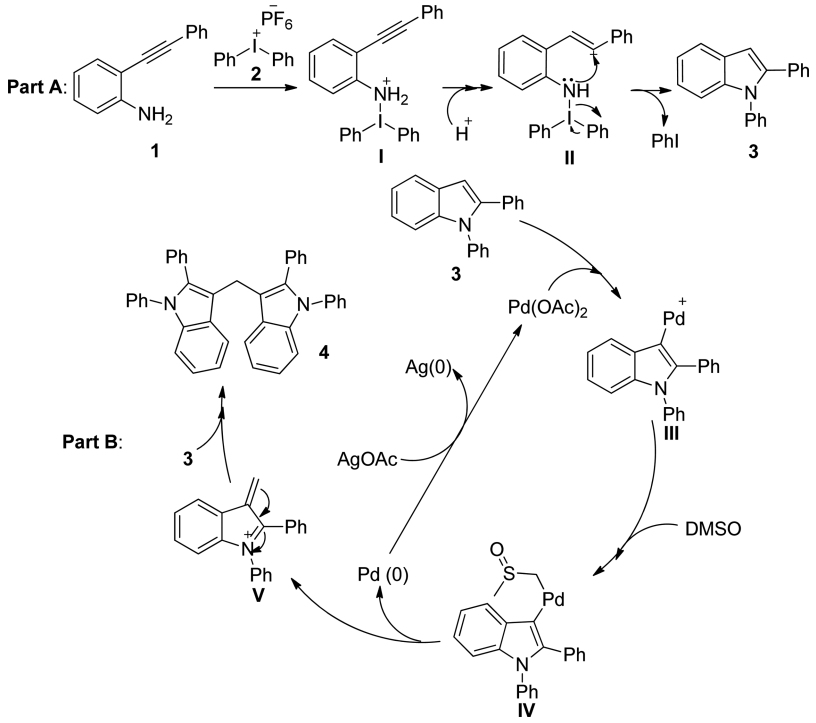
Scheme 2. Control Experiments



Scheme 3. Plausible Reaction Mechanism



complete consumption (for 24−48 h). Then water was added to the solution and the mixture stirred for 0.5 h at room temperature. The organic layer was concentrated under reduced pressure to give a residue, which was purified by flash chromatography (silica gel, eluent EtOAc/PE = 1/50) to give **1**.

Preparation of Diaryliodonium Salts 2. 3-Chloroperoxybenzoic acid (2.6 mmol) and aryl iodide were dissolved in CH_2Cl_2 (10 mL) in a sealed tube. The arene (2.6 mmol) was added. The solution was cooled to 0 °C. Then TfOH was added dropwise. The reaction was stirred at the indicated temperature for 0.2−22 h. The solvent was concentrated under vacuum. Et_2O (10 mL) was added and the mixture was stirred at room temperature for 10 min to precipitate out an off-white solid. To ensure complete precipitation, the flask was stored in the freezer for 30 min before the solid was filtered off, washed with Et_2O, and dried under vacuum to give diaryliodonium salts **2**.[13]

Preparation of 1,2-Diphenyl-1*H*-indoles 3. A mixture of diaryliodonium salts **2** (0.2 mmol, 1 equiv) and 2-alkynylanilines **1** (0.2 mmol, 1 equiv) in *t*-BuOH (2 mL) was stirred at 60 °C in a tube

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under air atmosphere for 18−45 h until TLC indicated complete consumption. Then the solvent was evaporated under reduced pressure and the residue was purified by chromatography (silica gel, eluent EtOAc/PE = 1/40) to give **3**.

Intermediate ***II.*** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 8.24−6.21 (m, 20H), 2.21 (s, 3H).

*1,2-Diphenyl-1H-indole (**3a**).*[14a] Yield 42 mg (78%) of a white solid; mp 79−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.73 (m, 1H), 7.50−7.44 (m, 2H), 7.42−7.28 (m, 9H), 7.27−7.22 (m, 2H), 6.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7 (s), 139.0 (s), 138.5 (s), 132.5 (s), 129.2 (s), 128.9 (s), 128.1 (t, J = 11.2 Hz), 127.2 (d, J = 9.6 Hz), 122.3 (s), 120.6 (d, J = 17.6 Hz), 110.6 (s), 103.7 (s).

*1-Phenyl-2-(p-tolyl)-1H-indole (**3b**).*[14b] Yield 35 mg (62%) of a yellow solid; mp 129−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75−7.71 (m, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.42−7.37 (m, 1H), 7.34−7.28 (m, 3H), 7.24−7.19 (m, 4H), 7.10 (d, J = 8.1 Hz, 2H), 6.83 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ140.9(s), 138.9 (s), 138.6 (s), 137.1 (s), 129.6 (s), 129.2 (s), 128.9 (s), 128.8 (s), 128.3 (s), 128.1 (s), 127.1 (s), 122.1 (s), 120.6 (s), 120.4 (s), 110.5 (s), 103.2 (s), 21.2 (s).

*2-(4-Methoxyphenyl)-1-phenyl-1H-indole (**3c**).*[15a] Yield 35 mg (59%) of a white solid; mp 117−119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74−7.70 (m, 1H), 7.46 (t, J = 7.4 Hz, 2H), 7.40 (d, J = 7.3 Hz, 1H), 7.34−7.28 (m, 3H), 7.23 (ddd, J = 8.4, 5.5, 1.4 Hz, 4H), 6.86−6.77 (m, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9 (s), 140.6 (s), 138.8 (s), 138.6 (s), 130.1 (s), 129.2 (s), 128.3 (s), 128.1 (s),127.1 (s), 125.1 (s), 122.0 (s), 120.6 (s), 120.3 (s), 113.6 (s), 110.5 (s), 102.8 (s), 55.2 (s).

*2-(4-Fluorophenyl)-1-phenyl-1H-indole (**3d**).*[15b] Yield 42 mg (74%) of a yellow solid; mp 125−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J = 6.0, 3.0 Hz, 1H), 7.50−7.45 (m, 2H), 7.43−7.38 (m, 1H), 7.34 (dd, J = 6.0, 3.3 Hz, 1H), 7.31−7.22 (m, 7H), 7.02−6.96 (m, 2H), 6.82 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1 (d, J_{C-F} = 247.5 Hz), 139.6 (s), 138.8 (s), 138.2 (s), 130.5 (d, J_{C-F} = 8.1 Hz), 129.3 (s), 128.6 (d, J_{C-F} = 3.3 Hz), 128.3 (s), 128.2 (s), 127.3 (s), 122.4 (s), 120.8 (s), 120.5 (s), 115.3 (s), 115.2 (d, J_{C-F} = 21.6 Hz), 110.6 (s), 103.5 (s).

*2-(4-Chlorophenyl)-1-phenyl-1H-indole (**3e**).*[15a] Yield 45 mg (75%) of a yellow solid; mp 179−181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76−7.69 (m, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.41 (t, J = 7.3 Hz, 1H), 7.33 (dd, J = 5.5, 3.2 Hz, 1H), 7.30−7.26 (m, 3H), 7.25−7.21 (m, 5H), 6.84 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4 (s), 139.1 (s), 138.3 (s), 133.3 (s), 131.0 (s), 130.0 (s), 129.4 (s), 128.4 (s), 128.1 (s), 128.0 (s), 127.4 (s), 122.6 (s), 120.9 (s), 120.6 (s), 110.6 (s), 104.0 (s).

*2-(4-Bromophenyl)-1-phenyl-1H-indole (**3f**).*[18b] Yield 50 mg (72%) of a yellow solid; mp 175−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75−7.71 (m, 1H), 7.50−7.45 (m, 2H), 7.42 (ddd, J = 6.7, 3.5, 1.6 Hz, 3H), 7.33 (dd, J = 6.1, 3.3 Hz, 1H), 7.30−7.27 (m, 2H), 7.25−7.22 (m, 2H), 7.18−7.15 (m, 2H), 6.85 (d, J = 0.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4 (s), 139.1 (s), 138.2 (s), 131.4 (s), 131.3 (s), 130.3 (s), 129.4 (s), 128.1 (s), 128.0 (s), 127.4 (s), 122.6 (s), 121.5 (s), 120.9 (s), 120.6 (s), 110.6 (s), 104.0 (s).

*2-(4-Nitrophenyl)-1-phenyl-1H-indole (**3g**).* Yield 50 mg (80%) of a yellow solid; mp 138−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15−8.10 (m, 2H), 7.75 (dd, J = 6.6, 1.8 Hz, 1H), 7.53−7.41 (m, 5H), 7.35−7.24 (m, 5H), 7.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4 (s), 139.8 (s), 138.9 (s), 137.9 (s), 129.7 (s), 128.9 (s), 127.9 (s), 127.8 (s), 123.7 (s), 123.5 (s), 121.3 (s), 121.1 (s), 110.9 (s), 106.2 (s); HRMS (ESI) m/z calcd for $C_{20}H_{14}N_2O_2$ $[M + H]^+$ 315.1134, found 315.1133.

*1-Phenyl-2-(m-tolyl)-1H-indole (**3h**).*[15c] Yield 46 mg (82%) of a yellow solid; mp 107−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.73 (m, 1H), 7.48 (t, J = 7.4 Hz, 2H), 7.41 (dd, J = 5.8, 3.8 Hz, 1H), 7.39−7.35 (m, 1H), 7.35−7.31 (m, 2H), 7.25 (dt, J = 7.4, 4.0 Hz, 3H), 7.17 (t, J = 7.6 Hz, 1H), 7.12−7.06 (m, 2H), 6.87 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9 (s), 139.0 (s), 138.6 (s), 137.7 (s), 132.4 (s), 129.6 (s), 129.2 (s), 128.3 (s), 128.0 (s), 127.9 (s), 127.1 (s), 126.0 (s), 122.2 (s), 120.6 (s), 120.5 (s), 110.6 (s), 103.5 (s), 21.4 (s).

*5-Methyl-1,2-diphenyl-1H-indole (**3i**).*[16a] Yield 44 mg (78%) of a yellow solid; mp 91−93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.47−7.41 (m, 2H), 7.38 (dd, J = 4.9, 3.7 Hz, 1H), 7.30−7.21 (m, 8H), 7.04 (dd, J = 8.4, 1.3 Hz, 1H), 6.77 (d, J = 0.5 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7 (s), 138.7 (s), 137.5 (s), 132.7 (s), 130.0 (s), 129.2 (s), 128.8 (s), 128.5 (s), 128.1 (s), 128.0 (s), 127.2 (s), 127.0 (s), 123.9 (s), 120.2 (s), 110.3 (s), 103.3 (s), 21.4 (s).

*5-Fluoro-1,2-diphenyl-1H-indole (**3j**).* Yield 46 mg (81%) of a white solid; 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.43 (m, 2H), 7.42−7.35 (m, 2H), 7.31−7.23 (m, 8H), 6.96 (td, J = 9.1, 2.5 Hz, 1H), 6.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4 (d, J_{C-F} = 235.4 Hz), 142.2 (s), 138.3 (s), 135.6 (s), 132.2 (s), 129.3 (s), 128.9 (s), 128.5 (d, J_{C-F} = 10.3 Hz), 128.2 (s), 127.9 (s), 127.5 (s), 127.4 (s), 111.3 (d, J_{C-F} = 9.6 Hz), 110.5 (d, J_{C-F} = 26.1 Hz), 105.2 (d, J_{C-F} = 23.6 Hz), 103.5 (d, J_{C-F} = 4.5 Hz); HRMS (ESI) m/z calcd for $C_{20}H_{14}FN$ $[M + H]^+$ 288.1189, found 288.1185.

*5-Chloro-1,2-diphenyl-1H-indole (**3k**).*[14b] Yield 43 mg (71%) of a yellow solid; mp 134−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 1.9 Hz, 1H), 7.48−7.39 (m, 3H), 7.29−7.21 (m, 8H), 7.16 (dd, J = 8.7, 2.0 Hz, 1H), 6.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0 (s), 138.1 (s), 137.4 (s), 132.0 (s), 129.4 (s), 129.2 (s), 128.9 (s), 128.2 (s), 127.9 (s), 127.6 (s), 127.5 (s), 126.2 (s), 122.5 (s), 119.8 (s), 111.6 (s), 103.0 (s).

*1-Phenyl-2-(thiophen-3-yl)-1H-indole (**3l**).*[16b] Yield 44 mg (81%) of a white solid; mp 131−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.67 (m, 1H), 7.55−7.44 (m, 3H), 7.39−7.34 (m, 2H), 7.26−7.17 (m, 4H), 7.07 (dd, J = 5.0, 1.2 Hz, 1H), 6.90−6.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0 (s), 138.5 (s), 136.0 (s), 133.0 (s), 129.4 (s), 128.4 (s), 128.0 (s), 127.8 (s), 127.8 (s), 125.0 (s), 122.3 (s), 122.2 (s), 120.6 (s), 120.4 (s), 110.4 (s), 102.6 (s).

*1,3-Bis(1-phenyl-1H-indol-2-yl)benzene (**3m**).* Yield 74 mg (81%) of a yellow solid; mp 141−143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.67 (m, 2H), 7.48 (dd, J = 10.0, 4.7 Hz, 4H), 7.44−7.40 (m, 2H), 7.34−7.31 (m, 3H), 7.29 (s, 1H), 7.27−7.20 (m, 8H), 7.11 (t, J = 1.8 Hz, 2H), 6.60 (d, J = 0.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2 (s), 138.9 (s), 138.4 (s), 132.4 (s), 129.5 (s), 129.3 (s), 127.9 (s), 127.7 (s), 127.3 (s), 122.4 (s), 120.7 (s), 120.5 (s), 110.6 (s), 103.7 (s); HRMS (ESI) m/z calcd for $C_{34}H_{24}N_2$ $[M + H]^+$: 461.2018, found 461.2014.

*2-Phenyl-1-(p-tolyl)-1H-indole (**3ba**).*[16c] Yield 45 mg (80%) of a yellow solid; mp 78−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J = 6.0, 2.9 Hz, 1H), 7.34−7.16 (m, 12H), 6.84 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7 (s), 139.1 (s), 137.0 (s), 135.8 (s), 132.6 (s), 129.9 (s), 128.9 (s), 128.2 (s), 128.1 (s), 127.8 (s), 127.2 (s), 122.2 (s), 120.5 (s), 120.4 (s), 110.7 (s), 103.4 (s), 21.1 (s).

*1-(4-(tert-Butyl)phenyl)-2-phenyl-1H-indole (**3ca**).*[17a] Yield 54 mg (84%) of a white solid; mp 132−134 °C; ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.73 (dd, J = 6.2, 2.9 Hz, 1H), 7.45 (d, J = 8.5 Hz, 2H), 7.37−7.31 (m, 3H), 7.30−7.26 (m, 3H), 7.23−7.19 (m, 4H), 6.84 (s, 1H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2 (s), 140.7 (s), 139.1 (s), 135.7 (s), 132.6 (s), 128.9 (s), 128.1 (s), 128.1 (s), 127.4 (s), 127.2 (s), 126.1 (s), 122.1 (s), 120.5 (s), 120.4 (s), 110.8 (s), 103.4 (s), 34.6 (s), 31.4 (s).

*1-(4-Chlorophenyl)-2-phenyl-1H-indole (**3da**).*[17b] Yield 45 mg (75%) of a yellow solid; mp 105−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.69 (m, 1H), 7.43−7.39 (m, 2H), 7.29 (d, J = 3.0 Hz, 6H), 7.24−7.20 (m, 4H), 6.83 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6 (s), 138.8 (s), 137.1 (s), 132.9 (s), 132.2 (s), 130.9 (s), 129.5 (s), 129.2 (s), 128.9 (s), 128.3 (s), 128.3 (s), 127.5 (s), 122.6 (s), 122.2 (s), 121.5 (s), 120.9 (s), 120.7 (s), 110.4 (s), 104.1 (s).

*1-(4-Bromophenyl)-2-phenyl-1H-indole (**3ea**).* Yield 48 mg (69%) of a yellow solid; mp 111−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74−7.70 (m, 1H), 7.59−7.54 (m, 2H), 7.30 (t, J = 4.8 Hz, 6H), 7.24−7.21 (m, 2H), 7.18−7.14 (m, 2H), 6.83 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6 (s), 138.8 (s), 137.6 (s), 132.5 (s), 132.2 (s), 129.5 (s), 128.9 (s), 128.4 (s), 128.3 (s), 127.5 (s), 122.6 (s), 121.0 (s), 120.8 (s), 120.7 (s), 110.4 (s), 104.2 (s); HRMS (ESI) m/z calcd for $C_{20}H_{14}BrN$ $[M + H]^+$ 348.0388, found 348.0382.

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*1-(4-Fluorophenyl)-2-phenyl-1H-indole (**3fa**).*[14a] Yield 44 mg (79%) of a white solid; mp 99−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.76 (m, 1H), 7.41−7.30 (m, 10H), 7.20 (t, J = 8.5 Hz, 2H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (d, J_{C-F} = 247.2 Hz), 140.7 (s), 139.1 (s), 134.5 (d, J_{C-F} = 3.1 Hz), 132.3 (s), 129.6 (d, J_{C-F} = 8.5 Hz), 129.1 (s), 128.9 (s), 128.2 (s), 127.4 (s), 122.4 (s), 121.5 (s), 120.6 (s), 116.2 (d, J_{C-F} = 22.7 Hz), 110.4 (s), 103.7 (s).

*1-(4-Iodophenyl)-2-phenyl-1H-indole (**3ga**).* Yield 51 mg (65%) of a yellow solid; mp 134−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75−7.69 (m, 1H), 7.48−7.41 (m, 2H), 7.38 (dt, J = 9.6, 4.3 Hz, 1H), 7.31−7.26 (m, 8H), 7.21 (dd, J = 6.1, 3.1 Hz, 2H), 6.83 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7 (s), 139.0 (s), 138.5 (s), 132.5 (s), 129.2 (s), 128.9 (s), 128.2 (s), 128.1 (s), 128.0 (s), 127.3 (s), 127.2 (s), 122.3 (s), 120.7 (s), 120.5 (s), 110.6 (s), 103.7 (s); HRMS (ESI) m/z calcd for $C_{20}H_{14}IN$ $[M + H]^+$ 396.0249, found 396.0238.

*1-(p-Ethoxycarbonylphenyl)-2-phenyl-4-1H-indole (**3ha**).*[18a] Yield 52 mg (77%) of a white solid; mp 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.5 Hz, 2H), 7.74−7.69 (m, 1H), 7.34 (d, J = 8.5 Hz, 2H), 7.28(d, J = 3.5 Hz, 7H), 7.23 (dd, J = 4.4, 2.2 Hz, 1H), 6.85 (s, 1H), 4.42 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0 (s), 142.5 (s), 140.5 (s), 138.5 (s), 132.2 (s), 130.6 (s), 128.9 (s), 128.9 (s), 128.5 (s), 128.3 (s), 127.6 (s), 127.5 (s), 122.7 (s), 121.1 (s), 120.7 (s), 110.4 (s), 104.8 (s), 61.2 (s), 14.3 (s).

*2-Phenyl-1-(o-tolyl)-1H-indole (**3ia**).*[14b] Yield 40 mg (71%) of a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75−7.71(m, 1H), 7.39−7.34 (m, 1H), 7.34−7.27 (m, 6H), 7.25 (qd, J = 4.6, 1.7 Hz, 3H), 7.19 (dd, J = 6.4, 2.7 Hz, 1H), 6.98 (dd, J = 5.9, 2.5 Hz, 1H), 6.89−6.84 (m, 1H), 1.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1 (s), 139.0 (s), 137.6 (s), 136.9 (s), 132.7 (s), 131.2 (s), 129.5 (s), 129.2 (s), 128.4 (s), 128.2 (s), 128.2 (s), 127.5 (s), 127.3 (s), 126.8 (s), 122.2 (s), 120.4 (s), 110.8 (s), 102.6 (s), 17.6 (s).

*1-(3-Bromophenyl)-2-phenyl-1H-indole (**3ja**).*[14b] Yield 53 mg (76%) of a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.68 (m, 1H), 7.54−7.48 (m, 2H), 7.29 (d, J = 3.5 Hz, 8H), 7.23 (dd, J = 6.4, 2.7 Hz, 2H), 7.14 (d, J = 7.7 Hz, 1H), 6.83 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6 (s), 139.9 (s), 138.8 (s), 132.1 (s), 130.9 (s), 130.4 (s), 130.3 (s), 128.9 (s), 128.4 (s), 128.3 (s), 127.6 (s), 126.8 (s), 122.6 (s), 122.5 (s), 121.1 (s), 120.7 (s), 110.4 (s), 104.3 (s).

Preparation of Bis(1,2-diphenyl-1*H*-indol-3-yl)methanes 4. 1,2-Diphenyl-1*H*-indoles **3** (0.05 mmol), $Pd(OAc)_2$ (0.1 equiv), and AgOAc (1 equiv) were added in DMSO (1 mL) in a round-bottomed flask under N_2 and stirred at 130 °C for 20 h until TLC indicated complete consumption. The reaction mixture was diluted with water and extracted with ethyl acetate. Then the combined organic layer was evaporated under reduced pressure and the residue was purified by chromatography (silica gel, eluent EtOAc/PE = 1/100) to give **4**.

*Bis(1,2-diphenyl-1H-indol-3-yl)methane (**4a**).* Yield 12 mg (89%) of a white solid; mp 149−151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, J = 14.7, 7.1 Hz, 6H), 7.29−7.24 (m, 9H), 7.22−7.16 (m, 7H), 7.14−7.10 (m, 2H), 6.98 (dd, J = 11.1, 3.9 Hz, 2H), 4.52 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5 (s), 137.7 (s), 137.2 (s), 132.2 (s), 130.9 (s), 128.9 (s), 128.5 (s), 128.0 (s), 127.8 (s), 127.2 (s), 126.5 (s), 122.1 (s), 119.9 (s), 119.8 (s), 113.9 (s), 110.1 (s), 21.2 (s); HRMS (ESI) m/z calcd for $C_{41}H_{30}N_2$ $[M]^+$ 550.2409, found 550.2404.

*Bis(2-phenyl-1-(p-tolyl)-1H-indol-3-yl)methane (**4b**).* Yield 13 mg (90%) of a yellow solid; mp 153−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 6.1 Hz, 4H), 7.22 (dt, J = 13.3, 2.9 Hz, 10H), 7.14−7.02 (m, 10H), 6.95 (t, J = 7.5 Hz, 2H), 4.48 (s, 2H), 2.36 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8 (s), 137.2 (s), 136.3 (s), 135.9 (s), 132.3 (s), 130.9 (s), 129.5 (s), 128.4 (s), 127.8 (s), 127.7 (s), 127.1 (s), 121.9 (s), 119.8 (s), 119.6 (s), 113.7 (s), 110.2 (s), 21.2 (s), 21.1 (s); HRMS (ESI) m/z calcd for $C_{43}H_{34}N_2$ $[M]^+$ 578.2722, found 578.2719.

*Bis(1-(4-(tert-butyl)phenyl)-2-phenyl-1H-indol-3-yl)methane (**4c**).* Yield 15 mg (88%) of a yellow solid; mp 155−157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 8.5 Hz, 3H), 7.31−7.27 (m, 5H), 7.25−7.20 (m, 10H), 7.09 (dd, J = 13.0, 4.7 Hz, 6H), 6.95 (t, J = 7.2 Hz, 2H), 4.49 (s, 2H), 1.33 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4 (s), 137.8 (s), 137.2 (s), 135.8 (s), 132.3 (s), 130.9 (s), 128.4 (s), 127.7 (s), 127.4 (s), 127.1 (s), 125.7 (s), 121.9 (s), 119.8 (s), 119.6 (s), 113.7 (s), 110.3 (s), 34.5 (s), 31.3 (s), 21.2 (s); HRMS (ESI) m/z calcd for $C_{49}H_{46}N_2$ $[M]^+$ 662.3661, found 662.3657.

*Bis(5-methyl-1,2-diphenyl-1H-indol-3-yl)methane (**4d**).* Yield 12 mg (80%) of a yellow solid; mp 150−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, J = 15.3, 9.6 Hz, 16H), 7.16−7.06 (m, 6H), 6.93−6.82 (m, 4H), 4.50 (s, 2H), 2.24 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8 (s), 137.0 (s), 136.1 (s), 132.6 (s), 131.0 (s), 128.8 (s), 128.6 (s), 128.0 (s), 127.9 (s), 127.2 (s), 126.3 (s), 123.6 (s), 119.7 (s), 113.9 (s), 109.7 (s), 21.2 (s), 20.6 (s); HRMS (ESI) m/z calcd for $C_{43}H_{34}N_2$ $[M]^+$ 578.2722, found 578.2718.

*Bis(1-(4-fluorophenyl)-2-phenyl-1H-indol-3-yl)methane (**4e**).* Yield 9 mg (64%) of a yellow solid; mp 161−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.24 (m, 9H), 7.19−7.09 (m, 11H), 7.05−6.95 (m, 6H), 4.47 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0 (d, J_{C-F} = 246.5 Hz), 137.8 (s), 137.2 (s), 134.5 (d, J_{C-F} = 3.0 Hz), 131.9 (s), 130.9 (s), 129.6 (d, J_{C-F} = 8.5 Hz), 128.4 (s), 127.9 (s), 127.3 (s), 122.2 (s), 119.9 (d, J_{C-F} = 8.8 Hz), 115.8 (d, J_{C-F} = 22.7 Hz), 113.8 (s), 109.9 (s), 21.1 (s); HRMS (ESI) m/z calcd for $C_{41}H_{28}N_2F_2$ $[M]^+$ 586.2221, found 586.2216.

*Bis(1-(4-chlorophenyl)-2-phenyl-1H-indol-3-yl)methane (**4f**).* Yield 10 mg (67%) of a yellow solid; mp 164−167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 10.1 Hz, 9H), 7.26 (d, J = 2.5 Hz, 4H), 7.21 (d, J = 8.2 Hz, 2H), 7.16−7.11 (m, 5H), 7.10−7.05 (m, 4H), 6.98 (dd, J = 11.0, 3.9 Hz, 2H), 4.46 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5 (s), 137.1 (s), 137.0 (s), 132.2 (s), 131.8 (s), 130.8 (s), 129.1 (s), 129.1 (s), 128.6 (s), 128.0 (s), 127.4 (s), 122.3 (s), 120.1 (s), 119.9 (s), 114.2 (s), 109.9 (s), 21.0 (s); HRMS (ESI) m/z calcd for $C_{41}H_{28}N_2Cl_2$ $[M]^+$ 618.1630, found 618.1624.

*Bis(1,2-diphenyl-1H-indol-3-yl)methane (**4aa**).* Yield 12 mg (86%) of a white solid; mp 151−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.31 (m, 5H), 7.30−7.22 (m, 12H), 7.21−7.15 (m, 7H), 7.13−7.08 (m, 2H), 6.98 (dd, J = 11.0, 3.9 Hz, 2H); HRMS (ESI) m/z calcd for $C_{41}H_{28}D_2N_2$ $[M]^+$ 552.2535, found 552.2528.

*Bis(1,2-diphenyl-1H-indol-3-yl)-l2-methane-^{13}C (**4ab**).* Yield 11 mg (83%) of a white solid; mp 150−153 °C; ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5 (s),137.7 (s), 137.7 (s), 132.2 (s), 130.9 (s), 128.9 (s), 128.5 (s), 128.0 (s), 127.8 (s), 127.2 (s), 126.5 (s), 122.1 (s), 119.8 (s), 119.8 (s), 110.1 (s), 21.2 (s); HRMS (ESI) m/z calcd for $C_{40}{}^{13}CH_{30}N_2$ $[M]^+$ 551.2443, found 551.2437.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00106.

^{1}H and ^{13}C NMR spectra for all compounds, ^{1}H NMR spectrum of reaction of **1b** with **2a**, and of ESI-(+)-MS data (PDF)

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Notes

The authors declare no competing financial interest.

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