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Metal-Free Indole−Phenacyl Bromide Cyclization: A Regioselective Synthesis of 3,5-Diarylcarbazoles

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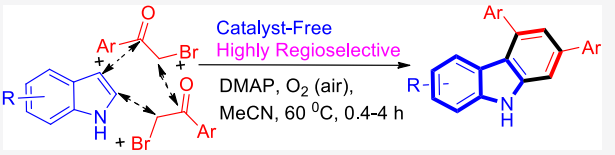
ABSTRACT: A metal-free, simultaneous triple C−C coupling cyclization reaction between phenacyl bromides and indoles is discovered in a highly regioselective fashion to furnish 3,5-diarylcarbazoles. DMAP is utilized as the only reagent for the unusual and rapid cyclization reaction to furnish all new carbazole compounds through installation of a great diversity of substituents. A plausible radical mechanism for the new reaction is predicted by conducting various control experiments, competitive reactions, furoindole formation, and ESI-MS analyses of the ongoing cyclization reaction.



The development of a new reactivity of a common chemical to synthesize a valuable compound, especially without the involvement of any catalyst and special reagent, is highly desirable and challenging. Phenacyl bromide is utilized as a synthon for the alkylation reaction to construct important heterocycles, natural products, innovative compounds, and key building blocks for industry and photochemistry.[1] We envisioned a cyclization reaction of phenacyl bromides and indoles to construct valuable carbazoles, which are well-known as antioxidant, antibacterial, anti-inflammatory, antitumor, antipsychotic, anticonvulsant, antidiabetic, and anticancer agents,[2] and important materials for electronic devices.[3] The 3-, 5-, and 3,5-substituted carbazoles have found important applications such as carprofen as a selective COX-2 inhibitor (**i**), carvedilol as a nonspecific β-adrengic antagonist (**ii**), clausenaline D as a bioactive natural product (**iii**), and hyellazole as a valuable alkaloid (**iv**, Figure 1).[4] A considerable

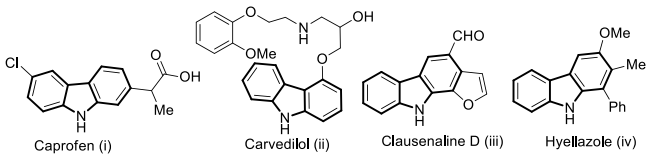


Figure 1. Valuable 3-, 5-, and 3,5-substituted carbazoles.

application of carbazoles in our daily life led to an enormous investigation for their syntheses involving intermolecular amination followed by direct arylation, dehydrogenative cyclization of 2-aminobiphenyls, cyclization of biaryl azides using Rh_2(II)-carboxylate catalyst, Pd(II)-catalyzed C−H bond amination, cyclization using Pd catalyst, tandem iodo-cyclization with migration and aromatization, metal-catalyzed coupling−cyclization reactions, and many others.[5] However, most of the reactions involve metal catalysts, costly and multiple reagents, and/or harsh reaction conditions. Recently, transition-metal-free sustainable reactions have drawn immense attention to the synthetic organic chemists.[6] For instance, Deng and co-workers recently reported a metal-free synthesis of carbazoles utilizing indole, ketones, and nitro alkene promoted by NH_4I.[6d] Kartika and co-workers reported the induction of fused aromatic ring on indole substrates via cascade nucleophilic addition.[6e] Synthesis of functionalized carbazoles may be performed through the addition of olefins or alkynes to indole. In this regard, several investigations were dedicated to C−H activated olefin−indole coupling using Pd^{II}-catalyst to achieve olefin insertion products.[7] Verma and co-workers reported Pd^{II}-assisted triple C−H activated cyclization with formation of a mixture of products including carbazole in moderate yield (eq i, Scheme 1).[7f] On the other hand, Au^{I}/$AgSbF_6$-mediated cyclization of 2-alkynylindole with alkyne was realized by Kundu and co-workers under heating conditions (eq ii, Scheme 1).[8a] In addition, Deng and co-workers developed an efficient indole-to-carbazole strategy under metal-free conditions where NH_4I promotes carbazole formation with high regioselectivity via formal [2 + 2 + 2] annulation of indoles, ketones, and nitroolefins (eq iii, Scheme 1).[8b] Herein, we report a metal-free highly selective and rapid synthesis of valuable 3,5-diarylcarbazoles (**3**, eq (iv) utilizing readily available inexpensive indoles (**1**) and phenacyl bromides (**2**). DMAP is used as the sole reagent for the unusual cyclization.

We have chosen indole (**1a**) and phenacyl bromide (**2a**) as two reacting partners to survey the reaction parameters (Table

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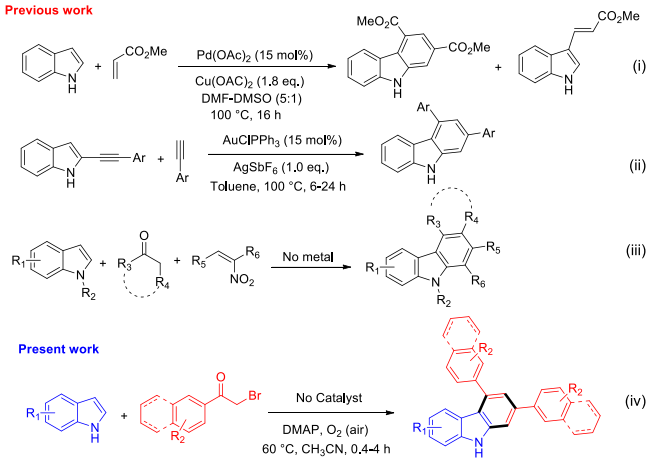
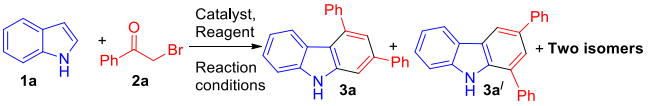
Scheme 1. Attempts to Construct Carbazole from Indole



1). We envisaged a photochemical cross coupling reaction between indole (**1a**) and phenacyl bromide (**2a**) in a 1:2 ratio, where both the molecules of phenacyl bromide (**2a**) may be incorporated into C2 and C3 sites of indole via radical mechanism leading to the construction of the desired carbazole (**3a**). However, **3a** was detected in traces upon use of light and catalysts[9] (entries 1−3, Table 1). We examined the multi C−C cross-coupling reaction using potential metal catalysts under heating and oxidative conditions to produce only traces of **3a** (entries 4−9). Gratifyingly, on the removal of catalysts, the cyclization reaction was rapid (15 min) in acetonitrile, and the yield was significantly improved (62%) under heating and aerobic conditions (entry 10). Herein, indole was consumed within 15 min producing our desired product, but an excess amount of phenacyl bromide remained in the reaction mixture. Indole was probably polymerized during the course of reaction.[10] To our delight, a high yield (79%) of **3a** was obtained upon use of organic base DMAP, which was added in portions (entry 11). Interestingly, the cyclization reaction was highly regioselective as the other three possible regioisomers are not detected. Different solvents were examined instead of CH_3CN. However, no improvement was observed (entries 12−18). As part of our continuous effort to study the reaction inside the nanoreactor built-in aqueous media at ambient temperature, we also studied the annulation reaction in vain.[11] In fact, the yield was not at all encouraging by changing the organic base and its inorganic varieties (entries 20−26) or stoichiometric oxidants (entries 9, 27−29). The lower yield (69%) obtained in the reaction under oxygen balloon may be explained due to the formation of corresponding oxidized and/or polymerized products of **1a** and/or **3a**. The reaction in neat conditions (entry 30) produced only a dark black residue having no desired product. In the absence of air (entry 31), the reaction under developed conditions was very slow and produced only about 20% of the desired product (**3a**) after 12 h.

General applicability of the developed reaction conditions (entry 11, Table 1) was framed using various substituted indoles (**1**) and phenacyl bromides (**2**) to obtain functionalized carbazole moieties (**3**, Scheme 2). Aromatic residue substituted phenacyl bromide and its fused naphthyl analogues rapidly (0.5−2 h) produced respective 3,5-disubstituted new carbazoles (**3b**, **3c**, **3l**, and **3t**) in high yield (70−78%). The phenacyl bromide carrying strongly electron-donating 4-Me, 2-OMe, and 4-OMe groups furnished respective carbazoles such as **3d**, **3e**, **3f**, **3q**, and **3v** in moderate yield (68−72%). On the other hand, slightly better yields (70−76%) and reaction rates (0.8−2 h) were achieved while dealing with electron-deficient substituents like 4-Cl (**3g**, **3o**, **3r**), 4-Br (**3j**, **3n**, **3u**), 4-F (**3h**), and 4-NO_2 (**3i**). The sterically hindered phenacyl bromide also smoothly produced the desired **3f** in 68% yield. The unsubstituted indole delivered the respective carbazoles (**3a**, **3b**, **3d**, **3e**, **3f**, **3g**, **3h**, **3i**, **3j**) with good yields (68−79%) and reaction rates (0.4−2.5 h) depending on the use of various phenacyl bromides. Herein, not only indoles possessing a strong electron-donating group like 5-methoxyindole (**3c**, **3k**, **3l**, **3n**, **3o**) were tolerated, but also indoles like labile acidic 5-hydroxyindole (**3m**).

Table 1. Screening for Optimized Reaction Conditions



entry	catalyst (x mol %)	reaction conditions[a]	**3a**, yield[b] (%)
1	$IrCl_3$ (10)	EY, CH_2Cl_2, rt, 23 W CFL, air, 12 h	trace
2[9b]		RB, CH_2Cl_2, LED (5 W), $PhI(OAc)_2$, 12 h	trace
3[9c]	CuBr (10)	eosin Y, LED (30 W), PhIO, CH_2Cl_2, rt, 9 h	trace
4	AgOTf (10)	CH_2Cl_2, rt, air, 12 h	trace
5	ZnI_2 (10)	CH_2Cl_2, rt, air, 12 h	trace
6	$Pd(OAc)_2$ (10)	CH_2Cl_2, rt, air, 12 h	trace
7	$FeCl_3$ (10)	CH_2Cl_2, rt, air, 12 h	trace
8	$Cu(OTf)_2$ (10)	CH_2Cl_2, rt, air, 3.5 h	trace
9	$RuCl_3$ (10)	CH_2Cl_2, rt, air, 3.5 h	trace
10		CH_3CN, 60 °C, air, 15 min	62
11		**DMAP, CH_3CN, 60 °C, air, 25 min**	**79**
12		DMAP, DMF, 60 °C, air, 12 h	ND[c]
13		DMAP, DMSO, 60 °C, air, 12 h	ND
14		DMAP, THF, rt, 60 °C, 24 h	40
15		DMAP, Dioxane, 60 °C, argon, 3.5 h	45
16		DMAP, EtOAc, 60 °C, air, 25 min	15
17		AcOH, 60 °C, air, 12 h	ND
18		DMAP, CH_3CN:H_2O (10:1), 60 °C, air, 5 h	ND
19		DMAP, H_2O, CTAB, rt, air, 12 h	ND
20		DABCO, CH_3CN, 60 °C, air, 4 h	35
21		Na_2CO_3, CH_3CN, 60 °C, air, 3.5 h	ND
22		pyridine, CH_3CN, 60 °C, air, 3.5 h	15
23[d]		Na_2HPO_4, CH_3CN, 60 °C, air, 5 h	ND
24		K_2CO_3, CH_3CN, 60 °C, air, 5 h	20
25		Cs_2CO_3 (1), CH_3CN, 60 °C, air, 3.5 h	15
26		$NaHCO_3$, CH_3CN, 60 °C, air, 5 h	ND
27		DMAP, O_2 balloon, CH_3CN, 60 °C, 3.5 h	69
28		DDQ, CH_3CN, rt, 4 h	15
29		I_2, CH_3CN, rt, air, 3.5 h	10
30[d]		neat, 60 °C, air, 3.5 h (dark black mass)	ND
31		DMAP, CH_3CN, argon, 60 °C, 12 h	20

[a]Reaction conditions: **1a** (1 mmol), **2a** (2 mmol), and DMAP (0.5 mmol) in acetonitrile (2 mL) heated at 60 °C (in an oil bath). [b]Yield of **3a** after column chromatography. [c]ND: not detected. [d]Reaction mixture immediately turned blackish.

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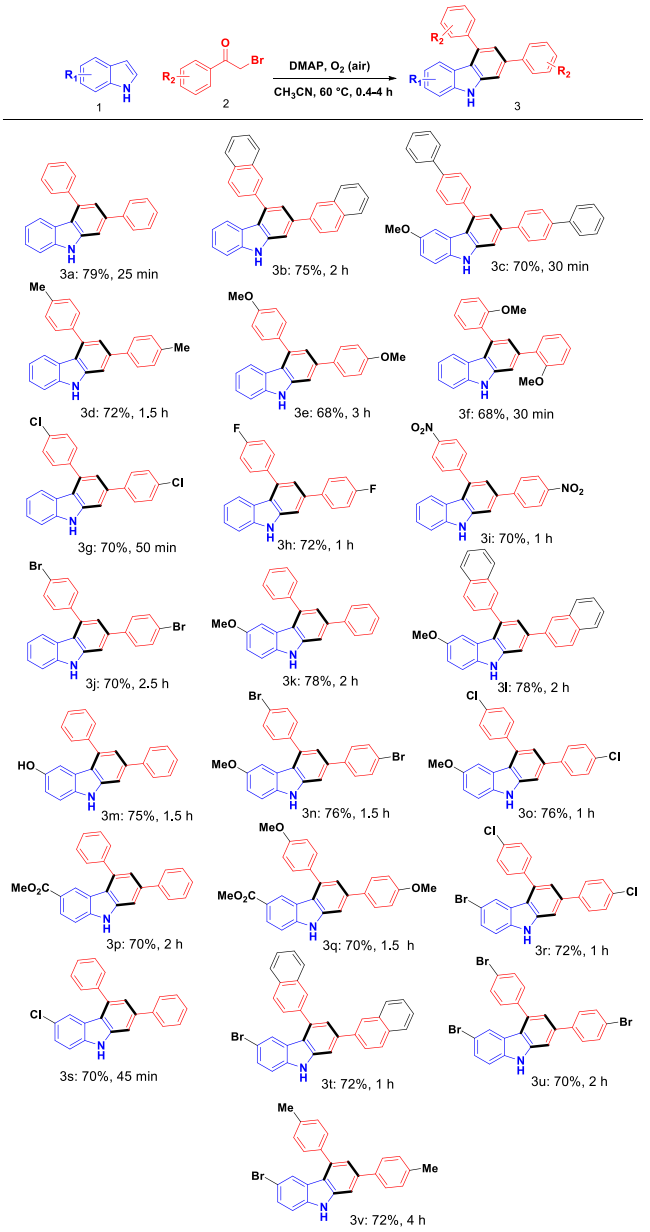
J. Org. Chem. XXXX, XXX, XXX−XXX

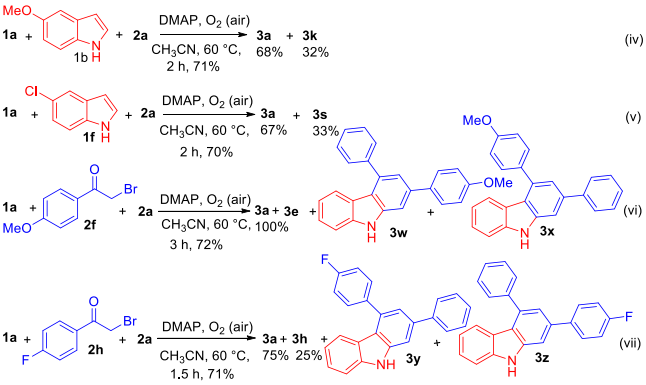
Scheme 2. Synthesis of Diverse 3,5-Diarylcarbazoles (3)



The 5-bromoindole (**3r**, **3t**, **3u**, **3v**), 5-chloroindole (**3s**), and 5-methoxycarbonylindoles (**3p**, **3q**) also responded well in this tandem cyclization reaction. The triple C−C coupled cyclization reaction allowed installations of a great diversity of substituents to achieve all new carbazole compounds. The structure of the new carbazoles was determined by the analyses of spectroscopic data (Supporting Information), and single crystal XRD report of compound **3e** (Supporting Infornmation).[12]

From the competitive experiments (eq iv, v, Scheme 3), it is quite evident that the cascade reaction remains uninfluenced on the electron-donating or electron-withdrawing nature of the substituent in indole residue. The scenario is more prominent when substitution is stationed over the phenyl residue of α-bromo acetophenone derivative (eq vi, vii). No product was detected possessing 4-methoxy substituent (**3e**, **3w**, or **3x**), which might be due to the destabilization of 4-methoxy phenacyl radical intermediate. With 4-fluoro substituent,

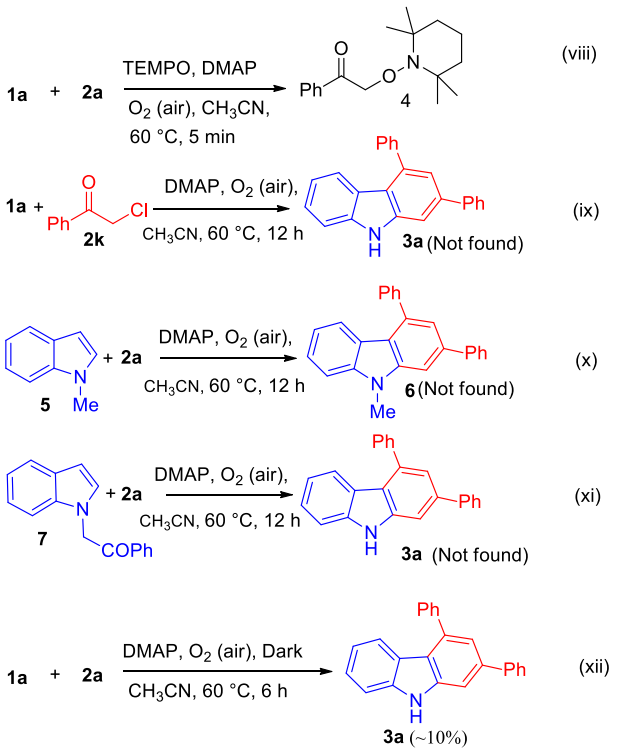
Scheme 3. Competitive Experiments



difluoro derivative (**3h**) was obtained as a minor product (25%), and phenacyl bromide incorporated product appeared as major one (75%), whereas formation of monofluoro derivatives (**3y** or **3z**) was not detected.

We envisioned that phenacyl bromide−indole coupling might occur through a photocatalytic radical mechanism. In order to ascertain whether the reaction is passing through a radical mechanism or not, radical scavenger TEMPO was added to an ongoing reaction. The reaction was completely arrested due to the formation of adduct **4** (eq viii, Scheme 4),

Scheme 4. Control Experiments



which was confirmed by ESI-MS analyses (Supporting Information). Instead of phenacyl bromide (**2a**) when phenacyl chloride (**2k**) was used, the desired carbazole (**3a**, eq ix) was not detected. The treatment of *N*-methylindole (**5**) with $PhCOCH_2Br$ did not produce the desired *N*-methyl carbazole (**6**, eq x). In another control experiment, *N*-acylated indole (**7**) did not generate carbazole, which is also negating the formation of *N*-acylated intermediate (eq xi) during the

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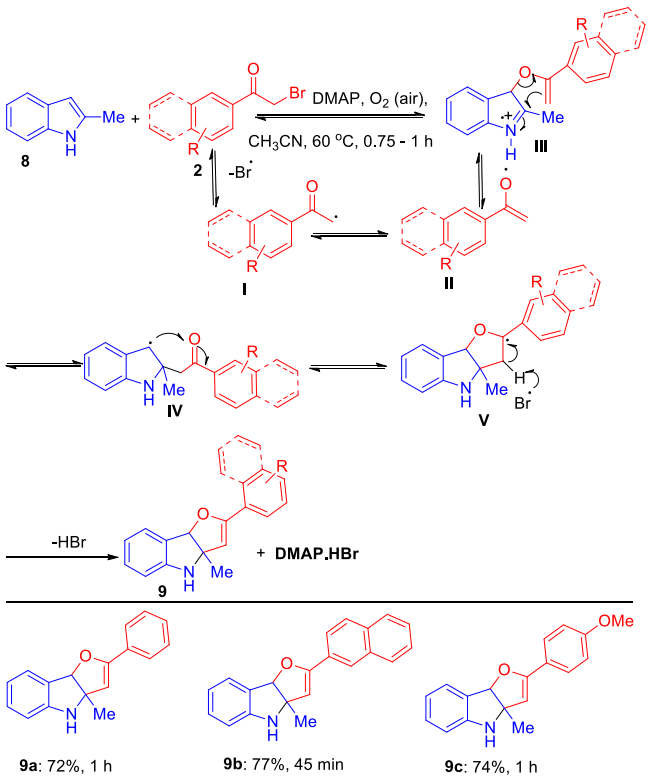
J. Org. Chem. XXXX, XXX, XXX−XXX

course of reaction. Formation of desired product (**3a**) was negligible (~10%, eq xii), when the cyclization reaction was performed in the absence of light.

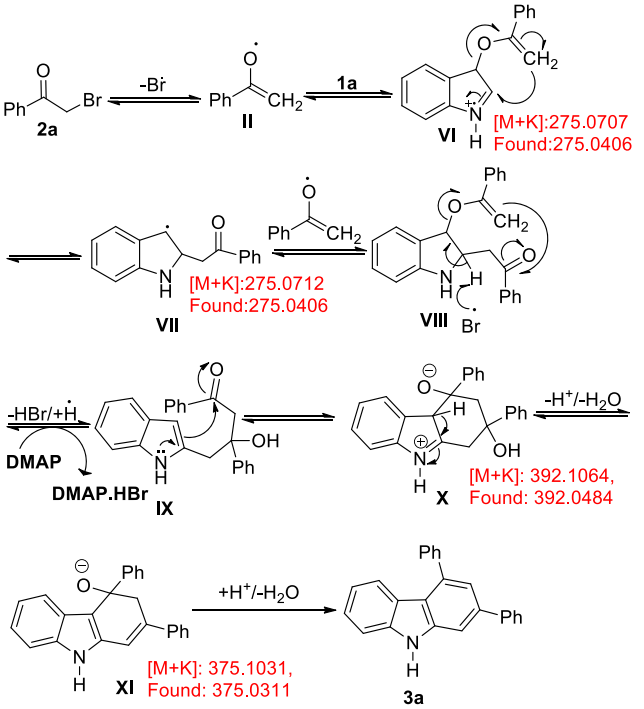
The reactions between 2-methylindole (**8**) and phenacyl bromides were performed to furnish bioactive[13] fused-furoindolo derivatives (**9a–c**, Scheme 5) in good yield (72–77%). The construction of the fluroindoles is expected to pass through a radical mechanism, as displayed in Scheme 5. Herein, an isomerized oxo-radical (**II**) of 1-aryl-2-ethanone may react with 2-methylindole to form the radical intermediate **III**, which transformed to putative intermediate **IV** through C–C coupling. The presence of methyl group at 2-position leads to the formation of radical intermediate **IV** and **V**, followed by the release of hydrogen radical leading to the construction of the final furoindole compound (**9**).

Scheme 5. Furoindoles Synthesized from 2-Methylindole



The exact mechanism of the unusual cyclization process of the new reaction is unknown to us. A plausible radical mechanism is depicted (Scheme 6) depending on the results obtained from the aforementioned competitive, control, furoindole formation experiments, and ESI-MS analyses of an ongoing reaction. An isomerized radical of 1-phenyl-2-ethanone (**II**) possessing oxygen radical may react with indole moiety at 3-position to produce radical cation **VI**, which on 1,2-migration generate radical intermediate **VII**. The putative intermediate couples with another 1-phenyl-2-ethanone oxo-radical to generate intermediate **VIII**, which on successive cyclization with release of HBr, indole-nitrogen-assisted cyclization (**IX**), deprotonation and dehydration (**X**), and aromatization through dehydration (**XI**) furnish the desired carbazole (**3a**). The intermediates **VI**, **VII**, **X**, and **XI** were detected in the ESI-MS spectral analyses (Supporting Information) of an ongoing reaction for synthesis of **3a**. The role of oxygen in this new reaction (entry 31, Table 1) is expected in the last two dehydration steps.

Scheme 6. Plausible Mechanism for the Synthesis of 3,5-Diarylcarbazoles



CONCLUSION

In conclusion, the present study offers an unorthodox catalyst-free method for synthesis of carbazole scaffolds just by treatment of indoles with phenacyl bromide derivatives through simultaneous triple C–C coupling with excellent regioselectivity. Mechanistic studies of the new cyclization reaction provide evidence in favor of radical reaction along with ionic mechanism. The broader sense of this novel strategy is highly advantageous in terms of easily available inexpensive starting materials, simplicity of execution, rapidity, large substrate scope, and excellent functional group tolerance and thus highlights another dimension for building the second carbocycle of carbazole on indole under metal-free conditions.

EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial suppliers and used without further purification. Petroleum ether used in our experiments was in the boiling range of 60–80 °C. Column chromatography was performed on silica gel (230–400 mesh). Reported melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature in $CDCl_3$ or DMSO-d_6 solvent. Chemical shifts are reported in ppm (δ) relative to internal reference tetramethylsilane. Coupling constants are quoted in Hz (J). Proton multiplicities are represented as s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet), and m (multiplet). Splitting patterns that could not be interpreted were designated as multiplet (m). Infrared spectra were recorded on FT-IR spectrometer in thin film. HR-MS data were acquired by electron spray ionization technique on a Q-tof-micro quadriple mass spectrophotometer. X-ray crystallographic data of the single crystal were taken using an X-ray diffractometer instrument.

General Procedure (GP 1) for Synthesis of Compound 3 (3a as an Example). To a solution of indole (1 mmol) in acetonitrile (2 mL) was added phenacyl bromide (2 mmol) and the mixture stirred

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J. Org. Chem. XXXX, XXX, XXX–XXX

at 60 °C in an oil bath under air to complete the reaction. The progress of the reaction was monitored by TLC. DMAP (0.5 mmol) was added in portions to complete the reaction. Acetonitrile was removed from the reaction mixture, and the residue was dissolved in ethyl acetate (20 mL). The organic phase was washed with brine (2 × 10 mL), dried on activated Na_2SO_4, and concentrated in a rotary evaporator under reduced pressure at ambient temperature. The residue was purified by silica gel flash column chromatography using ethyl acetate in petroleum ether as an eluent to afford the desired product.

General Procedure (GP 2) for Synthesis of Compound 9 (9a as an Example). To a solution of 2-methylindole (1 mmol) in acetonitrile (2 mL) was added phenacyl bromide (2 mmol) and the mixture stirred at 60 °C in an oil bath under air. DMAP (0.5 mmol) was added in portions to complete the reaction, which was monitored by TLC. Acetonitrile was removed from the reaction mixture, and residue was dissolved in ethyl acetate (20 mL). The organic phase was washed with brine (2 × 10 mL), dried on activated Na_2SO_4, and concentrated in a rotary evaporator under reduced pressure at ambient temperature. The residue was purified by silica gel flash column chromatography using ethyl acetate in petroleum ether as an eluent to afford the desired product.

Spectral Data. *Characterization Data of Compound **3a**–**v**. 2,4-Diphenyl-9H-carbazole (**3a**):* colorless solid (8% ethyl acetate/petroleum ether); 79% (252 mg, 0.79 mmol); mp 170–172 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.95–7.00 (m, 1H), 7.26–7.36 (m, 4H), 7.41–7.56 (m, 7H), 7.65–7.70 (m, 4H), 8.13 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,75 MHz) δ 108.0, 110.5, 119.3, 120.1, 120.9, 122.4, 122.8, 125.8, 127.2, 127.5, 127.7, 128.5, 128.8, 129.3, 138.0, 139.0, 140.2, 140.5, 141.2, 141.6; FT-IR (KBr, cm^{-1}) 665, 755, 1047, 1324, 1471, 1611, 2928, 3400; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{24}H_{18}N$ 320.1439, found 320.1443.

*2,4-Dinaphthalen-2-yl-9H-carbazole (**3b**):* brown solid (8% ethyl acetate/petroleum ether); 75% (315 mg, 0.75 mmol); mp 180–182 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.96 (s, 1H), 7.38 (d, 1H, J = 6 Hz), 7.44–7.61 (m, 7H), 7.79 (d, 1H, J = 1.5 Hz), 7.86–8.06 (m, 8H), 8.19 (s, 2H), 8.29 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 108.3, 110.5, 119.3, 120.3, 121.3, 122.5, 122.8, 125.6, 125.8, 125.9, 125.9, 126.1, 126.3, 127.5, 127.7, 127.8, 127.8, 127.8, 128.0, 128.0, 128.2, 128.4, 132.6, 132.9, 133.6, 133.8, 137.8, 138.7, 138.9, 138.9, 140.3, 140.6; FT-IR (KBr, cm^{-1}) 669, 750, 1045, 1323, 1456, 1599, 2853, 2924, 3020, 3421; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{32}H_{22}N$ 420.1752, found 420.1749.

*2,4-Bis-biphenyl-4-yl-6-methoxy-9H-carbazole (**3c**):* brown solid (10% ethyl acetate/petroleum ether); 70% (350 mg, 0.70 mmol); mp 186–188 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.66 (s, 3H), 7.03–7.06 (m, 1H), 7.11 (d, 1H, J = 2.1 Hz), 7.34 (d, 1H, J = 8.4 Hz), 7.38 (s, 1H), 7.42 (d, 1H, J = 3.3 Hz), 7.44–7.55 (m, 5H), 7.67–7.74 (m, 7H), 7.82 (d, 6H, J = 10.2 Hz), 8.12 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,75 MHz) δ 55.6, 105.5, 108.0, 111.0, 114.9, 120.2, 123.2, 127.0, 127.1, 127.3, 127.4, 127.5, 127.8, 128.8, 128.9, 129.8, 135.1, 137.4, 138.4, 140.0, 140.4, 140.5, 140.7, 140.9, 141.3, 153.4; FT-IR (KBr, cm^{-1}) 752, 831, 1230, 1323, 1456, 2853, 2924, 2973, 3395, 3416; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{37}H_{28}NO$ 502.2171, found 502.2169.

*2,4-Di-p-tolyl-9H-carbazole (**3d**):* brown solid (6% ethyl acetate/petroleum ether); 72% (250 mg, 0.72 mmol); mp 152–154 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43 (s. 3H), 2.52 (s, 3H), 7.00–7.05 (m, 1H), 7.29 (d, 2H, J = 8.7 Hz), 7.34–7.45 (m, 5H), 7.56–7.66 (m, 6H), 8.19 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,75 MHz) δ 21.0, 21.2, 107.4, 110.2, 119.0, 119.8, 120.6, 122.3, 122.8, 125.4, 127.2, 129.0, 129.0, 129.4, 136.8, 137.1, 137.8, 138.2, 138.6, 138.9, 140.0, 140.4; FT-IR (KBr, cm^{-1}) 736, 1282, 1323, 1455, 1513, 1605, 2852, 2920, 3022, 3050, 3440; HRMS (ESI) (m/z) $[M + Na]^+$ calcd for $C_{26}H_{21}NNa$ 370.1572, found 370.1574.

*2,4-Bis(4-methoxyphenyl)-9H-carbazole (**3e**):* colorless crystalline solid (10% ethyl acetate/petroleum ether); 68% (258 mg, 0.68 mmol); mp 186–188 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.86 (s, 3H), 3.94 (s, 3H), 6.94–7.03 (m, 3H), 7.04–7.11 (m, 2H), 7.32–7.41 (m, 3H), 7.53–7.66 (m, 6H), 8.14 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 55.4, 107.1, 110.3, 113.9, 114.2, 119.1, 119.8, 120.6, 122.3, 123.0, 125.5, 128.5, 130.3, 133.7, 134.2, 137.6, 138.7, 140.1, 140.6, 159.1, 159.2; FT-IR (KBr, cm^{-1}) 829, 1029, 1247, 1513, 1603, 2834, 2930, 2956, 3033, 3408; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{26}H_{22}NO_2$ 380.1651, found 380.1655.

*2,4-Bis(2-methoxyphenyl)-9H-carbazole (**3f**):* yellow solid (10% ethyl acetate/petroleum ether); 68% (259 mg, 0.68 mmol); mp 120–122 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.65 (s, 3H), 3.82 (s, 3H), 6.96–7.17 (m, 7H), 7.24–7.35 (m, 3H), 7.38–7.44 (m, 3H), 7.48–7.52 (m, 1H), 7.89 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 55.3, 55.5, 110.2, 110.6, 110.8, 111.2, 118.8, 120.4, 120.6, 120.7, 121.8, 123.1, 123.2, 125.1, 128.2, 128.9, 130.1, 131.1, 131.3, 132.8, 135.7, 139.4, 139.9, 156.5, 157.1; FT-IR (KBr, cm^{-1}) 1023, 1475, 1458, 1579, 1601, 2853, 2924, 3027, 3050, 3377; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{26}H_{22}NO_2$ 380.1651, found 380.1654.

*2,4-Bis(4-chlorophenyl)-9H-carbazole (**3g**):* yellow solid (8% ethyl acetate/petroleum ether); 70% (272 mg, 0.70 mmol); mp 140–142 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.95–7.01 (m, 1H), 7.20–7.27 (m, 1H), 7.30–7.36 (m, 4H), 7.38–7.48 (m, 3H), 7.51–7.59 (m, 5H), 8.16 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 108.1, 110.6, 119.5, 120.2, 120.4, 122.2, 122.4, 126.1, 128.7, 128.7, 129.0, 130.5, 133.4, 133.7, 136.7, 137.8, 139.4, 139.8, 140.2, 140.5; FT-IR (KBr, cm^{-1}): 821, 1014, 1086, 1322, 1491, 2852, 2924, 2972, 3056, 3412; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{24}H_{16}Cl_2N$ 388.0660, found 388.0657, 390.0636 and 392.0640.

*2,4-Bis(4-fluorophenyl)-9H-carbazole (**3h**):* yellowish color solid (8% ethyl acetate/petroleum ether); 72% (255 mg, 0.72 mmol); mp 164–166 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.02–7.07 (m, 1H), 7.14–7.22 (m, 2H), 7.25–7.29 (m, 3H), 7.36–7.41 (m, 2H), 7.46 (d, 1H, J = 8.7 Hz), 7.50 (s, 1H), 7.55–7.69 (m, 4H), 8.21 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 107.8, 110.4, 115.1, 115.4, 115.7, 119.2, 120.0, 120.5, 122.0, 122.4, 125.8, 128.8, 128.9, 130.2, 130.6, 130.7, 136.7, 136.9, 137.0, 137.4, 137.4, 137.9, 140.0, 140.3; FT-IR (KBr, cm^{-1}) 832, 1156, 1217, 1384, 1456, 2853, 2924, 2991, 3387, 3452; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{24}H_{16}F_2N$ 356.1251, found 356.1246.

*2,4-Bis(4-nitrophenyl)-9H-carbazole (**3i**):* reddish color solid (20% ethyl acetate/petroleum ether); 70% (285 mg, 0.70 mmol); mp 270–272 °C; ^{1}H NMR (DMSO-d_6,300 MHz) δ 6.91–6.99 (m, 1H), 7.33–7.43 (m, 3H), 7.51–7.57 (m, 1H), 7.88–7.94 (m, 3H), 8.02–8.10 (m, 2H), 8.23–8.26 (m, 2H), 8.36–8.40 (m, 2H), 11.73 (brs, 1H); $^{13}C\{^1H\}$ NMR (DMSO-d_6,75 MHz) δ 109.3, 111.0, 118.3, 118.9, 119.1, 120.2, 121.0, 123.2, 123.5, 125.8, 127.6, 129.0, 129.8, 134.5, 134.6, 140.2, 140.4, 145.9, 146.4, 146.6; FT-IR (KBr, cm^{-1}) 819, 1125, 1208, 1345, 1519, 1627, 2856, 2985, 3210, 3434; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{24}H_{16}N_3O_4$410.1141, found 410.1145.

*2,4-Bis(4-bromophenyl)-9H-carbazole (**3j**):* yellow solid (8% ethyl acetate/petroleum ether); 70% (336 mg, 0.70 mmol); mp 144–146 °C; ^{1}H NMR ($CDCl_3$,300 MHz) δ 7.04 (t, 1H, J = 6 Hz), 7.26 (d, 1H, J = 1.2 Hz), 7.40 (d, 2H, J = 6.3 Hz), 7.50–7.60 (m, 8H), 7.68 (d, 2H, J = 8.4 Hz), 8.20 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 107.9, 110.5, 119.4, 120.0, 120.2, 121.4, 121.8, 122.1, 122.3, 126.0, 128.9, 130.8, 131.6, 131.8, 136.6, 137.6, 139.8, 140.1, 140.2, 140.3; FT-IR (KBr, cm^{-1}) 749, 818, 1010, 1072, 1323, 1455, 2852, 2923, 3046, 3413; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{24}H_{16}Br_2N$ 475.9649, found 475.9653, 477.9604 and 479.9590.

*6-Methoxy-2,4-diphenyl-9H-carbazole (**3k**):* brown solid (10% ethyl acetate/petroleum ether); 78% (272 mg, 0.78 mmol); mp 140–142 °C; ^{1}H NMR ($CDCl_3$,300 MHz) δ 3.55 (s, 3H), 6.88–6.94 (m, 2H), 7.18 (d, 1H, J = 0.3 Hz), 7.25 (d, 1H, J = 8.7 Hz), 7.30 (d, 2H, J = 7.2 Hz,), 7.37–7.49 (m, 5H), 7.54 (s, 1H), 7.60–7.66 (m, 3H), 8.03 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,75 MHz) δ 55.5, 105.2, 108.0, 110.9, 114.8, 120.3, 123.1, 127.1, 127.4, 127.6, 128.2, 128.7, 129.2, 130.8, 135.0, 137.7, 138.9, 140.9, 141.2, 141.5, 153.3; FT-IR (KBr, cm^{-1}) 798, 849, 1079, 1513, 1609, 2844, 2951, 2996, 3099, 3422; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{25}H_{20}NO$ 350.1545, found 350.1550.

*6-Methoxy-2,4-dinaphthalen-2-yl-9H-carbazole (**3l**):* brown solid (10% ethyl acetate/petroleum ether); 78% (350 mg, 0.78 mmol); mp 158–160 °C; ^{1}H NMR ($CDCl_3$,300 MHz) δ 3.43 (s, 3H), 6.94 (d,

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J. Org. Chem. XXXX, XXX, XXX–XXX

1H, J = 8.1 Hz), 7.27 (d, 1H, J = 8.1 Hz), 7.25−7.41 (m, 5H), 7.68 (s, 1H), 7.80−7.98 (m, 9H), 8.10−8.13 (m, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 55.6, 105.5, 108.4, 111.0, 115.0, 120.2, 120.9, 123.2, 125.9, 125.9, 126.0, 126.3, 126.3, 127.6, 127.8, 127.8, 127.9, 128.1, 128.2, 128.4, 128.8, 130.9, 132.6, 132.9, 133.5, 133.7, 135.2, 137.8, 138.5, 138.9, 141.4, 153.4; FT-IR (KBr, cm^{-1}) 809, 999, 1241, 1498, 1588, 2831, 2931, 2966, 3013, 3409; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{33}H_{24}NO$ 450.1858, found 450.1855.

5,7-Diphenyl-9H-carbazol-3-ol (**3m**): magenta solid (20% ethyl acetate/petroleum ether); 75% (214 mg, 0.75 mmol); mp 196−198 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 6.91−6.94 (m, 1H), 7.26−7.38 (m, 3H), 7.43−7.55 (m, 7H), 7.58−7.72 (m, 4H), 7.95−8.03 (m, 2H), 8.15 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,75 MHz) δ107.8, 108.1, 111.0, 114.8, 120.5, 123.3, 127.2, 127.5, 127.6, 128.6, 128.8, 129.2, 130.1, 133.2, 135.0, 135.2, 139.1, 141.1, 141.4, 141.6, 148.9; FT-IR (KBr, cm^{-1}) 832, 1165, 1127, 1394, 1466, 2853, 2924, 3322, 3422, 3599; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{24}H_{18}NO$ 336.1388, found 336.1392.

2,4-Bis(4-bromophenyl)-6-methoxy-9H-carbazole (**3n**): yellow solid (10% ethyl acetate/petroleum ether); 76% (384 mg, 0.76 mmol); mp 170−172 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.62 (s, 3H), 6.89 (d, 1H, J = 2.4 Hz), 6.97 (q, 1H, J = 9 Hz), 7.17−7.19 (m, 2H), 7.26 (d, 1H, J = 8.7 Hz), 7.46−7.53 (m, 6H), 7.60 (d, J = 8.4 Hz, 2H), 8.02 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,75 MHz) δ 55.6, 105.4, 108.1, 111.0, 114.9, 119.8, 119.9, 121.4, 121.8, 122.8, 128.9, 130.4, 131.4, 131.8, 135.0, 136.5, 137.6, 139.6, 140.2, 141.1, 153.4; FT-IR (KBr, cm^{-1}) 1010, 1210, 1474, 2925, 2832, 2861, 3002, 3417; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{25}H_{18}Br_2NO$ 505.9755, found 505.9752 (one of the major peaks).

2,4-Bis(4-chlorophenyl)-6-methoxy-9H-carbazole (**3o**): brownish yellow solid (12% ethyl acetate/petroleum ether); 76% (314 mg, 0.76 mmol); mp 158−160 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 3.68 (s, 3H), 6.96 (d, 1H, J = 2.4 Hz), 7.01−7.05 (m, 1H), 7.25 (d, 1H, J = 3.6 Hz,), 7.34 (d, J = 9 Hz, 1H), 7.43 (d, 2H, J = 8.4 Hz), 7.51−7.64 (m, 7H), 8.13 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 55.8, 105.5, 108.2, 111.2, 115.0, 120.1, 122.9, 128.6, 128.7, 128.9, 129.0, 129.4, 133.4, 133.8, 135.2, 136.6, 137.7, 139.3, 139.9, 141.3, 153.5; FT-IR (KBr, cm^{-1}) 1044, 1423, 1323, 1476, 2857, 2927, 2976, 3020, 3433; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{25}H_{18}Cl_2NO$ 418.0765, found 418.0767 (one of the major peaks).

5,7-Diphenyl-9H-carbazole-3-carboxylic acid methyl ester (**3p**): colorless solid (10% ethyl acetate/petroleum ether); 70% (316 mg, 0.70 mmol); mp 206−208 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 3.78 (s, 3H), 7.28−7.56 (m, 9H), 7.61−7.65 (m, 4H), 8.00 (dd, 1H, J_1 = 1.5 Hz, J_2 = 1.5 Hz), 8.23 (s, 1H), 8.41 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 51.7, 108.1, 109.9, 120.0, 121.2, 121.5, 122.5, 124.8, 127.2, 127.3, 127.4, 127.9, 128.5, 128.8, 129.0, 138.2, 139.8, 140.4, 140.9, 141.2, 142.9, 167.6; FT-IR (KBr, cm^{-1}) 763, 1099, 1231, 1299, 1435, 1608, 1688, 2849, 2925, 3318, 3420; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{26}H_{19}NO_2Na$ 400.1313, found 400.1309.

5,7-Bis(4-methoxyphenyl)-9H-carbazole-3-carboxylic acid methyl ester (**3q**): yellow solid (15% ethyl acetate/petroleum ether); 70% (302 mg, 0.70 mmol); mp 220−222 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 3.78 (s, 3H), 3.79 (s, 3H), 3.82 (s, 3H), 6.90 (d, 2H, J = 8.7 Hz), 7.02 (d, 2H, J = 8.7 Hz), 7.28−7.31 (m, 2H), 7.44 (d, 1H, J = 1.2 Hz), 7.51−7.56 (m, 4H), 8.32 (d, 1H, J = 1.2 Hz), 8.50 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,75 MHz) δ 51.8, 55.3, 55.3, 107.3, 109.9, 114.0, 114.2, 119.5, 121.0, 121.2, 122.6, 124.7, 127.0, 128.4, 130.1, 132.9, 133.7, 137.8, 139.3, 141.1, 142.9, 159.1, 159.4, 167.8; FT-IR (KBr, cm^{-1}) 892, 1049, 1274, 1502, 1599, 1689, 2835, 2971, 2965, 3053, 3406; HRMS (ESI) (m/z) $[M + Na]^+$ calcd for $C_{28}H_{23}NO_4Na$ 460.1525, found 460.1530.

6-Bromo-2,4-bis(4-chlorophenyl)-9H-carbazole (**3r**): black solid (7% ethyl acetate/petroleum ether); 72% (337 mg, 0.72 mmol); mp 180−182 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 7.18−7.22 (m, 1H), 7.25 (s, 1H), 7.34−7.40 (m, 3H), 7.44−7.49 (m,6H), 7.53 (d, J = 8.4 Hz, 2H), 8.25 (brs, 1H); $^{13}C\{1H\}$ NMR ($CDCl_3$,75 MHz) δ 108.2, 112.0, 112.3, 119.2, 121.0, 124.2, 124.8, 128.7, 128.8, 128.9, 129.0, 130.4, 133.6, 134.1, 136.9, 138.6, 138.8, 138.9, 139.6, 140.9; FT-IR (KBr, cm^{-1}) 618, 822, 1088, 1290, 1384, 1445, 2853, 2924, 3074, 3419; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{24}H_{15}BrCl_2N$ 465.9765, found 465.9770 (one of the major peaks).

6-Chloro-2,4-diphenyl-9H-carbazole (**3s**): yellow crystalline solid (6% ethyl acetate/petroleum ether); 70% (247 mg, 0.70 mmol); mp 226−228 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 7.27 (s, 1H), 7.30−7.33 (m, 2H), 7.36−7.41 (m, 2H), 7.46−7.53 (m, 3H), 7.54−7.56 (m, 1H), 7.58 (s, 1H), 7.60−7.62 (m, 1H), 7.66−7.69 (m, 2H), 7.72 (d, 2H, J = 7.2 Hz), 8.25 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,75 MHz) δ 108.1, 111.3, 119.3, 121.2, 122.0, 124.0, 124.6, 125.8, 127.4, 127.5, 128.0, 128.6, 128.9, 129.0, 138.2, 138.4, 139.8, 140.6, 141.0, 141.3; FT-IR (KBr, cm^{-1}) 1072, 1269, 1402, 1570, 1612, 2853, 2923, 3024, 3061, 3381; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{24}H_{17}ClN$ 354.1049, found 354.1052 and 356.1007.

6-Bromo-2,4-dinaphthalen-2-yl-9H-carbazole (**3t**): black solid (6% ethyl acetate/petroleum ether); 72% (359 mg, 0.72 mmol); mp 212−214 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.20 (d, 1H, J = 0.9 Hz), 7.26 (d, 1H, J = 8.7 Hz), 7.38−7.56 (m, 7H), 7.63−7.70 (m, 2H), 7.77−8.01 (m, 6H), 8.11 (d, 2H, J = 6.6 Hz), 8.25 (brs, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,75 MHz) δ 108.3, 111.8, 112.0, 119.2, 121.8, 124.5, 125.0, 125.8, 126.0, 126.1, 126.1, 126.3, 126.4, 126.7, 127.3, 127.6, 127.7, 127.9, 128.1, 128.1, 128.4, 128.8, 130.8, 132.6, 133.0, 133.6, 133.7, 138.0, 138.5, 138.8, 139.7, 141.0; FT-IR (KBr, cm^{-1}) 1215, 1046, 1289, 1446, 1599, 2853, 2924, 3020, 3421; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{32}H_{21}BrN$ 498.0857, found 498.0860 (one of the major peaks).

6-Bromo-2,4-bis(4-bromophenyl)-9H-carbazole (**3u**): brown solid (5% ethyl acetate/petroleum ether); 70% (390 mg, 0.70 mmol); mp 210−212 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 7.19 (s, 1H), 7.24 (d, 1H, J = 8.4 Hz), 7.38−7.56 (m, 9H), 7.62 (d, 2H, J = 6.9 Hz), 8.23 (brs, 1H); $^{13}C\{1H\}$ NMR ($CDCl_3$,75 MHz) δ 108.1, 111.9, 112.1, 119.0, 120.7, 121.6, 122.2, 124.1, 124.6, 128.7, 128.9, 130.5, 131.3, 131.7, 131.8, 136.8, 138.4, 138.7, 139.2, 139.9, 140.7; FT-IR (KBr, cm^{-1}) 751, 1215, 1291, 1446, 1457, 2853, 2924, 2956, 3020, 3422; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{24}H_{15}Br_3N$ 553.8755, found 553.8759 (one of the major peaks).

6-Bromo-2,4-di-p-tolyl-9H-carbazole (**3v**): brown solid (5% ethyl acetate/petroleum ether); 72% (304 mg, 0.72 mmol); mp 200−202 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 7.05−7.08 (m, 3H), 7.14−7.24 (m, 4H), 7.32−7.40 (m, 5H), 7.48 (d, J = 1.8 Hz, 1H), 7.99 (brs, 1H); $^{13}C\{1H\}$ NMR ($CDCl_3$,75 MHz) δ 21.0, 21.3, 107.5, 111.6, 111.9, 118.9, 121.1, 124.7, 124.8, 127.2, 128.2, 128.8, 129.2, 129.5, 130.7, 137.1, 137.6, 138.1, 138.4, 138.6, 139.7, 140.8; FT-IR (KBr, cm^{-1}) 699, 814, 1109, 1290, 1384, 2853, 2923, 2969, 3379, 3426; HRMS (ESI) (m/z) $[M + Na]^+$ calcd for $C_{26}H_{20}BrNNa$ 448.0677, found 448.0681 (one of the major peaks).

Characterization Data of Compounds 9a−c. *3a-Methyl-2-phenyl-4,8b-dihydro-3aH-furo[3,2-b]indole* (**9a**):[13] colorless solid (7% ethyl acetate/petroleum ether); 72% (180 mg, 0.72 mmol); mp 110−112 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 2.89 (s, 3H), 5.36 (d, 1H, J = 1.8 Hz), 5.76 (d, 1H, J = 1.8 Hz), 7.02 (t, 1H, J = 7.5 Hz), 7.11−7.17 (m, 2H), 7.23−7.35 (m, 4H), 7.41−7.44 (m, 2H), 7.95 (brs, 1H); $^{13}C\{1H\}$ NMR ($CDCl_3$,75 MHz) δ 12.8, 110.1, 110.3, 114.9, 119.7, 121.2, 127.1, 127.3, 127.5, 128.2, 128.5, 135.1, 141.9; FT-IR (KBr, cm^{-1}) 680, 759, 1025, 1363, 1476, 1589, 2913, 2954, 3050, 3471; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{17}H_{16}NO$ 250.1232, found 250.1228.

3a-Methyl-2-(naphthalen-2-yl)-4,8b-dihydro-3aH-furo[3,2-b]-indole (**9b**): light brown solid (5% ethyl acetate/petroleum ether); 77% (230 mg, 0.77 mmol); mp 130−132 °C; ^1H NMR ($CDCl_3$,300 MHz) δ 2.27 (s, 3H), 5.45 (d, 1H, J = 1.2 Hz), 5.88 (d, 1H, J = 1.2 Hz), 6.96−6.99 (m, 1H), 7.01−7.16 (m, 1H), 7.24−7.33 (m, 2H), 7.43−7.48 (m, 2H), 7.59 (dd, 1H, J_1 = 0.9 Hz, J_2 = 1.2 Hz), 7.40−7.85 (m, 4H), 7.93 (brs, 1H); $^{13}C\{1H\}$ NMR ($CDCl_3$,75 MHz) δ 12.9, 110.2, 114.1, 115.6, 119.7, 119.8, 121.3, 125.7, 125.8, 126.0, 126.2, 127.6, 127.7, 128.3, 128.5, 133.0, 133.2, 133.5, 135.2, 139.4, 142.5; IR (KBr, cm^{-1}) 670, 771, 1055, 1383, 1436, 1601, 2873, 2898, 3048, 3433; HRMS (ESI) (m/z) $[M + H]^+$ calcd for $C_{21}H_{18}NO$ 300.1388, found 300.1393.

2-(4-Methoxyphenyl)-3a-methyl-4,8b-dihydro-3aH-furo[3,2-b]-indole (**9c**): black solid (10% ethyl acetate/petroleum ether); 74%

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J. Org. Chem. XXXX, XXX, XXX−XXX

(206 mg, 0.74 mmol); mp 148−150 °C; ^{1}H NMR ($CDCl_3$,300 MHz) δ 2.30 (s, 3H), 3.81 (s, 3H), 5.23 (d, 1H, J = 1.8 Hz), 5.66 (d, 1H, J = 1.8 Hz), 6.78−6.86 (m, 2H), 6.93−7.02 (m, 1H), 7.08−7.14 (m, 1H), 7.21−7.28 (m, 1H), 7.31−7.94 (m, 3H), 7.97 (brs, 1H); ^{13}C NMR ($CDCl_3$,75 MHz) δ 12.8, 55.2, 110.0, 113.2, 113.5, 113.7, 114.2, 119.6, 119.7, 121.1, 128.4, 130.6, 133.0, 134.4, 135.1, 141.8, 159.2; FT-IR (KBr, cm^{-1}) 1025, 1477, 1596, 1620, 2855, 3057, 3081, 3364; HRMS (ESI) (m/z) [M + H]$^+$ calcd for $C_{18}H_{18}NO_2$ 280.1338, found 280.1342.

■ ASSOCIATED CONTENT

Supporting Information

X-ray crystallography data, CIF file, NMR spectra of synthesized compounds. . The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c01670.

X-ray crystallography data, NMR spectra of synthesized compounds (PDF)

X-ray data (CIF)

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to Prof. Pierre H. Dixneuf.

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