ORGANOMETALLICS

Direct Ortho Arylation of 9-(Pyridin-2-yl)-9H-carbazoles Bearing a Removable Directing Group via Palladium(II)-Catalyzed C–H Bond Activation

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Supporting Information

ABSTRACT: A one-pot synthesis of ortho-arylated 9-(pyridin-2-yl)-9*H*-carbazoles via C–H bond activation is presented. Silver nitrate and *tert*-butyl alcohol were found to be the best oxidant and solvent for the process, respectively. The product yields are from modest to excellent, and the reaction showed sufficient functional group tolerance. *p*-Benzoquinone served as an important ligand for the transmetalation and reductive elimination steps in the catalytic process. The key intermediate of the reaction, a 9-(pyridin-2yl)-9*H*-carbazole palladacycle, was isolated, and its structure was unequivocally confirmed by X-ray crystallography. No



kinetic isotope effect ($k_{\rm H}/k_{\rm D} = 1.00 \pm 0.17$) for the C–H bond activation step was observed. In addition, a Hammett experiment gave a negative ρ value, -2.16 ± 0.02 . The directing group, pyridinyl, was demonstrated to be a removable functional group. Finally, a rational catalytic mechanism is presented on the basis of all experimental evidence.

INTRODUCTION

In the past decade, transition-metal-catalyzed direct carbonhydrogen (C–H) bond activation/functionalization has emerged as a powerful protocol for the construction of new carbon-carbon (C–C) bonds and carbon-heteroatom (C–X, X = N, O, S, B, Si) bonds in organic synthesis.¹ To date, many practical syntheses based on these ideas have been widely reported in literature.²

In 2006, a pioneering work on a Suzuki–Miyaura type C–H bond activation/C–C bond cross-coupling reaction was reported by Yu and co-workers.³ In that context, they successfully demonstrated palladium(II)-catalyzed alkylation of sp² and sp³ C–H bonds with methylboroxine and alkylboronic acids. After that, the Shi⁴ and Wu^{2j} groups reported a selective direct arylation of acetyl amides and 3,5diphenylisoxazole with a variety of arylboronic acids via C–H bond activation in time sequence.

The carbazole structure is a crucial motif in natural products,⁵ pharmaceuticals,⁶ and optoelectronic materials.⁷ In general, direct functionalization on simple carbazoles is not easy due to their intrinsic inertness. Therefore, the development of efficient methods to modify simple carbazoles is still an important issue, in which direct and specific ortho arylation is especially challenging. To the best of our knowledge, only a few examples of the ortho phenylation of carbazoles have been reported.⁸

Herein we report the first example of palladium(II)-catalyzed regioselective direct ortho arylation of carbazoles bearing a directing group (pyridinyl). Various syntheses of ortho-arylated 9-(pyridin-2-yl)-9H-carbazoles from carbazoles bearing a

pyridinyl group via C–H bond activation are presented. We not only illustrate the role of the directing group in the reaction but also demonstrate its ease of removal.

RESULTS AND DISCUSSION

Screens of Oxidants and Solvents for Ortho Arylation of 9-(Pyridin-2-yl)-9*H*-carbazole (1) via C–H Bond Activation. The synthesis of ortho-arylated 9-(pyridin-2-yl)-9*H*-carbazoles 3 was initially investigated by the reaction of 9-(pyridin-2-yl)-9*H*-carbazole (1) with potassium phenyltrifluoroborate (2a) via C–H bond activation. We herein utilized palladium(II) acetate as the catalyst and screened a variety of oxidants and solvents for the reaction in the presence of *p*benzoquinone (BQ) at 60–70 °C^{9a} for 24 h. The screening results are summarized in Table 1. Silver nitrate and *tert*-butyl alcohol were found to be the best oxidant and solvent, respectively, for the synthesis of compound 3a (entry 2, Table 1).

Catalytic Reaction of 9-(Pyridin-2-yl)-9*H*-carbazole (1) and Substrates 5 with Borane Reagents 2. With the optimized reaction conditions in hand (2 equiv of Ar-BF₃K, 10 mol % of Pd(OAc)₂, 3 equiv of AgNO₃, 1 equiv of BQ in *tert*butyl alcohol at 60–70 °C for 24 h), we subsequently carried out the direct ortho arylation of 1 with a variety of potassium aryltrifluoroborates 2. The results are summarized in Table 2. These reactions produced the predominant product 3 in

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Table 1. Screens of Oxidants and Solvents for Direct Ortho Arylation of 9-(Pyridin-2-yl)-9H-carbazole (1)

	$H + Ph BF_{3}K$ (2 equiv) 2a	10 mol % Pd(OAc) ₂ oxidant (3 equiv) BQ (1 equiv) solvent 60-70 °C, 24 h 3a	H Ph + 4a (diphenylated adduct)
entry	oxidant	solvent	total yield, % $(3a:4a)^a$
1	absent	tert-butyl alcohol	9 (100:0)
2	AgNO ₃	tert-butyl alcohol	95 (75:25)
3	Ag ₂ O	tert-butyl alcohol	57 (98:2)
4	AgOAc	tert-butyl alcohol	41 (99:1)
5	Ag ₂ CO ₃	tert-butyl alcohol	34 (95:5)
6	Cu(OTf) ₂ ^{9b}	tert-butyl alcohol	12 (100:0)
7	$Cu(OAc)_2^{9b}$	tert-butyl alcohol	5 (100:0)
8	oxone	tert-butyl alcohol	10 (100:0)
9	$K_2S_2O_8$	tert-butyl alcohol	3 (100:0)
10	O ₂	tert-butyl alcohol	10 (100:0)
11	AgNO ₃	dichloromethane	59 (98:2)
12	AgNO ₃	DCE^{b}	55 (99:1)
13	AgNO ₃	benzene	58 (100:0)
14	AgNO ₃	toluene	51 (100:0)
15	AgNO ₃	1,4-dioxane	49 (92:2)
16	AgNO ₃	DMF	30 (100:0)
17	AgNO ₃	THF	25 (100:0)
18	AgNO ₂	acetonitrile	10(100:0)

^{*a*}The total yield was obtained as an average by GC-MS spectroscopy for three runs (using *n*-octadecane as the internal standard). The product ratio **3a:4a** was determined by GC-MS spectroscopy for three runs. ^{*b*}DCE = 1,2-dichloroethane.

modest to good yields (47-95%, entries 1-13, Table 2) with a few concomitant diarylated products 4. In addition, no desired products 3n-p were observed when borane reagents 2n-p were used (entries 14-16, Table 2). Finally, the structures of 3a and 4a were unequivocally characterized by X-ray crystallography (Figure 1).¹⁰

In addition to 9-(pyridin-2-yl)-9*H*-carbazole (1), we also prepared a variety of 9-(pyridin-2-yl)-9*H*-carbazoles $5a-k^{11a}$ with different substituents on the carbazole ring and further investigated the electronic or steric effects on the regioselectivity of the ortho phenylation with potassium phenyltrifluoroborate (2a) under the aforementioned optimal reaction conditions. The experimental results are summarized in Table 3. We herein found that most of 5 can successfully be transformed into the anticipated products 6, 7, and even 8 in modest to excellent yields (45–98%, entries 1–7, Table 3), except for Sh,i (entries 8 and 9, Table 3).

On the basis of experimental results, the direct ortho phenylation was found to preferentially occur at the less sterically hindered side when the substituent is tagged at the meta position, such as in 5a,e,f (entries 1, 5, and 6, Table 3). Nevertheless, a mixture of 6c-8c (product ratio 55:36:9) was obtained by the reaction of 5c with 2a in 57% total yield (entry 3, Table 3). In this case, either steric hindrance or electronic effects appear to be in effect, but the former is slightly predominant over the latter. On the other hand, the formation of products 6b,d and 7b,d were observed by the reaction of 5b,d with 2a, respectively, in which the substituent (NO₂ and OMe) is tagged at the para position (entries 2 and 4, Table 3). In the case of 5b, a 77:23 product ratio of 6b and 7b was observed in 45% total yield, where the direct phenylation

preferentially took place at the more electron rich ring. In addition, a 29:22:49 product ratio of 6d-8d (90% total yield) was observed in the reaction of 5d with 2a. We found that the reactivity of 5d was enhanced by the electron-donating group (i.e., OMe) in the reaction and resulted in diphenylated compound 8d (49% product ratio) as the major product; moreover, no obvious regioselectivity for the formation of 6d (29% product ratio) and 7d (22% product ratio) was observed.

On the basis of the experimental results of the above two cases, we conclude that a strong electron-donating group (e.g., OMe) can induce and promote the phenylation to occur on the more electron rich ring, although steric effects are still dominant here. For the reaction of 5g with 2a, the single product 6g was obtained in 53% yield (entry 7, Table 3). Finally, we found that no desired phenylated products 6h,i were generated in these reactions of 5h,i with 2a (entries 8 and 9, Table 3). Most of the starting materials 5h,i was recovered after the reaction, and some of 5i possibly formed metal complexes with palladium or silver cation that hampered the catalytic reaction.

Investigation of Kinetic Isotope Effects and Hammett Experiments. In order to gain an insight into the catalytic mechanism of the reaction, we carried out a kinetic isotope effect (KIE) experiment by the reaction of monodeuterated 9-(pyridin-2-yl)-9H-carbazole $(1-D)^{11b}$ with potassium 4-formyl-phenyltrifluoroborate $(2d)^{12}$ under the optimized reaction conditions. The value of $k_{\rm H}/k_{\rm D}$ was determined to be 1.00 \pm 0.17 in comparison with the standard spectra of 1 and 3d (Scheme 1). This KIE result¹³ implies that C–H bond cleavage is not the rate-determining step.

On the other hand, we also carried out a Hammett experiment¹⁴ by using the reaction of palladacycle I with a variety of para-substituted phenylborane reagents 2 for the catalytic reaction, and it showed a negative ρ value, $\rho = -2.16 \pm 0.02$, with a reasonable correlation ($R^2 = 0.90$, Figure 2). The Hammett results imply that the reaction builds up positive charge at the reaction center in the transition state.

Characterization of the 9-(Pyridin-2-yl)-9H-carbazole Palladacycle I and Control Experiments in the Presence or Absence of BQ. In addition to dynamic studies (KIE and Hammett experiments), we also independently synthesized the key intermediate, 9-(pyridin-2-yl)-9H-carbazole palladacycle I, by the reaction of 1 with a stoichiometric equivalent of palladium(II) acetate in dichloromethane (Scheme 2). The Xray crystallography results show that I adopts a head-to-tail geometry, as shown in Figure 3.¹⁵ This strongly implies that the direct cross-coupling reaction of 1 with 2 should proceed via intermediate I.

On the other hand, we further investigated the essentiality of BQ in the catalytic reaction. Subsequently, the reaction of intermediate I with 2a in the presence or absence of BQ was carried out (Scheme 3). The experimental results showed that the desired product 3a was only obtained by the addition of BQ, whereas 3a was not detected (by GC-MS spectroscopy) when BQ did not exist in the reaction. This indicated that BQ still serves as a critical promoter in the transmetalation and reductive-elimination process of the catalytic reaction.^{2g,3,16}

Proposed Catalytic Mechanism. According to the above results of mechanistic investigations, a rational catalytic mechanism is proposed for the direct ortho arylation of 1 with arylborane 2, as shown in Figure 4. Initially, Pd(II) is coordinated with the nitrogen atom of pyridine ring of 9-(pyridin-2-yl)-9H-carbazole (1) and, subsequently, the ortho



Table 2. Direct Ortho Arylation of 9-(Pyridin-2-yl)-9H-carbazole (1)

^aThe product ratio 3a:4a was determined by GC-MS spectroscopy for three runs. ^bThe product yield was obtained as an average by GC-MS spectroscopy for three runs (using *n*-octadecane as the internal standard). ^cThree equivalents of borane reagent 2c was used.



Figure 1. ORTEP drawings of (a) 1-phenyl-9-(pyridin-2-yl)-9H-carbazole (3a) and (b) 1,8-diphenyl-9-(pyridin-2-yl)-9H-carbazole (4a).¹⁰ All hydrogen atoms are omitted for clarity. Ellipsoids are shown at the 30% probability level.

C–H bond of the carbazole ring is cleaved by Pd(II) to form I. Then, BQ coordinates with the Pd(II) center of I through a ligand-exchange process to form intermediate II-A.¹⁷ After that, aryldifluoroborane 2-BF₂ (generated from 2)^{2g,h,18} and II-A participate in the transmetalation step to generate intermediate III by the release of F₂BOAc. Finally, intermediate III is converted into the desired product 3, with the release of Pd(0) and BQ, through a reductive-elimination step. Pd(II) is regenerated by the reoxidation of Pd(0) by Ag(I) and/or BQ with the release of Ag(0) and/or hydroquinone, and the regenerated Pd(II) re-enters the catalytic cycle.

Removal of the Directing Group of 1-Aryl-9-(pyridin-2-yl)-9H-carbazoles 3. In many natural products and pharmaceutical compounds, 9H-carbazole is a common structural motif. If we can further remove the directing group (i.e., pyridinyl) of arylated products, it would complete our synthetic approach to modified carbazoles. To demonstrate the pyridinyl group can be not only a directing group but also a removable group, adducts 3a,b,k bearing neutral (H), electronwithdrawing (NO_2) , and electron-donating (OMe) groups, respectively, were chosen as model substrates for the removal of the directing group. Compounds 3a,b,k then underwent depyridination by treatment of methyl trifluoromethanesulfonate (MeOTf) in dichloromethane and sodium hydroxide in methanol.¹⁹ Eventually, 1-aryl-9H-carbazoles 9a,b,k were produced in 80%, 75%, and 70% yields, respectively (Scheme 4).

Synthesis of Hyellazole (15). To further demonstrate the possible application of our newly developed synthetic strategy, we chose to tackle the synthesis of hyellazole (15), the first carbazole alkaloid of marine origin that was isolated from a blue-green algae, *Hyella caespitosa*, and reported by Moore et al. in 1979.²⁰ In order to synthesize it, we first prepared the starting material 10 (see the Supporting Information) and subsequently carried out the direct phenylation of 10 with 2a under the optimized reaction conditions.

The experimental results showed that compound 11 was formed as a major product and 12 as a minor adduct with a trace of diphenylated product 13 (product ratio 11:12:13 =85:10:5) in 81% total product yield due to the steric hindrance of the methyl group (Scheme 5). Unfortunately, the minor product 12 is the desired precursor of the target compound, hyellazole (15). Even so, the successful removal of pyridnyl groups on 11 and 12 was achieved and the new hyellazole analogue 14 and hyellazole (15) were obtained in 87% and 81% yields, respectively (Scheme 5).

CONCLUSION

We have successfully developed a simple and mild one-pot synthesis of 3 through direct ortho arylation of 1 with 2 via C– H bond activation using palladium(II) acetate as the catalyst. The key intermediate I was isolated, and its structure was unequivocally determined by X-ray crystallography. KIE for the C–H bond activation step and a Hammett experiment for the reaction transition state were all investigated. These results provided strong evidence to support the proposed catalytic mechanism. The directing group, pyridinyl, was successfully demonstrated to be a removable functional group. Finally, the reported synthetic methodology provides a fast and convenient path to synthesize ortho-arylated carbazoles, which, in turn, has potential applications in the fields of pharmaceutical chemistry and optoelectronics.

EXPERIMENTAL SECTION

General Considerations. Solvents were purchased from Echo and Mallinckrodt (ACS grade: n-hexane, ethyl acetate, and dichloromethane). Reagents were purchased from Aldrich, Acros, Alfa, TCI, and Seedchem. All solvents and reagents were used without purification. ¹H NMR spectra were measured on 300 MHz Bruker AVIII-300 and 500 MHz Varian Unity plus 500 spectrometers. Natural-abundance ¹³C NMR spectra were measured using pulse Fourier transform Bruker AVIII-300 (300 MHz NMR) and Varian Unity plus 500 (500 MHz NMR) spectrometers operating at 75 and 125 MHz, respectively. Chemical shifts are given in parts per million (ppm) and coupling constant J in hertz (Hz) for both nuclei, with the solvent (usually CDCl₃) peak as an internal standard. The reference peak for ¹H is δ 0.00 of TMS, and for ¹³C it is the central peak at δ 77.0. Low- and high-resolution mass spectrometry was performed on Finnigan/Thermo Quest MAT 95XL and Shimadzu QP2010 spectrometers. Melting points were determined using a Barnstead International-Electrothermal IA1101D melting point meter.

General Procedure for Direct Ortho Arylation of 9-(Pyridin-2-yl)-9H-carbazoles 1 and 5 with Potassium Aryltrifluoroborates 2. (a) A well-stirred solution of 9-(pyridin-2-yl)-9H-carbazole (1; 20.0 mg, 0.082 mmol) with potassium aryltrifluoroborates 2 (2 equiv), 10 mol % Pd(OAc)₂, AgNO₃ (3 equiv), and BQ (1 equiv) in *tert*-butyl alcohol (4 mL) was heated to 60–70 °C and stirred at this temperature for 24 h. After it was cooled to room temperature, the solution was filtered through a pad of Celite and washed with water (5 mL × 2). The aqueous layers were combined and extracted with dichloromethane (5 mL × 2). Finally, the organic layers were combined, dried over MgSO₄, filtered, and evaporated under vacuum.

*tert-*butanol 60-70 °C, 24 ł Total yield Products (6:7:8)^{*a*} Entry Substrate 5 $(\%)^{b}$ 1 64 (100:0:0)45 2 (77:23:0)3 57 (55:36:9)90 4 (29:22:49)5 98 (100:0:0)6 58 (100:0:0)7 53 (100%)8 0 9 0

Table 3. Direct Ortho Phenylation of 9-(Pyridin-2-yl)-9H-carbazoles 5

The residue was purified by silica gel chromatography using *n*-hexane/ ethyl acetate (50/1 to 10/1) as the eluent to give a series of compounds **3** and **4**. All product yields determined by GC-MS spectroscopy using *n*-octadecane as the internal standard are shown as follows: **3a**, 71% (19 mg, 0.058 mmol); **3b**, 73% (22 mg, 0.060 mmol); **3c**, 48% (15 mg, 0.040 mmol); **3d**, 77% (22 mg, 0.063 mmol); **3e**, 78% (22 mg, 0.064 mmol); **3f**, 79% (23 mg, 0.065 mmol); **3g**, 69% (23 mg, 0.056 mmol); **3h**, 47% (17 mg, 0.038 mmol); **3i**, 74% (23 mg, 0.061 mmol); **3j**, 65% (18 mg, 0.053 mmol), **3k**, 64% (18 mg, 0.052 mmol), **3l**, 75% (21 mg, 0.061 mmol), **3m**, 88% (27 mg, 0.072 mmol); **4a**, 24% (7.7 mg, 0.019 mmol); **4j**, 20% (7.1 mg, 0.017 mmol); **4k**, 9% (4 mg, 0.008 mmol); **4l**, 8% (3 mg, 0.007 mmol).

(b) The general procedure for the synthesis of compounds 6-8 was the same with that for compounds 3 and 4. The amounts used of 5 are shown as follows, 5a, 24 mg, 0.083 mmol; 5b, 24 mg, 0.083 mmol; 5c, 24 mg, 0.084 mmol; 5d, 25 mg, 0.083 mmol; 5e, 23 mg, 0.084 mmol; 5f, 23 mg, 0.084 mmol; 5g, 30 mg, 0.075 mmol. All product yields determined by GC-MS spectroscopy using *n*-octadecane as the internal standard are shown as follows: 6a, 64% (20 mg, 0.053 mmol); 6b, 35% (11 mg, 0.029 mmol); 6c, 31% (9 mg, 0.026 mmol); 6d, 26% (8 mg, 0.022 mmol); 6e, 98% (31 mg, 0.082 mmol); 6f, 58% (18 mg, 0.049 mmol); 6g, 53% (19 mg, 0.040 mmol); 7b, 10% (3 mg, 0.009 mmol); 7c, 21% (6.0 mg, 0.017 mmol); 7d, 20% (5.8 mg, 0.017 mmol); 8c, 44% (16 mg, 0.037 mmol).

1-Phenyl-9-(pyridin-2-yl)-9H-carbazole (**3***a*): white solid; mp 147– 148 °C; $R_f = 0.61$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.74 (d, 1 H), 6.95 (dd, *J* = 7.4, 4.8 Hz, 1 H), 7.02– 7.05 (m, 3 H), 7.13–7.17 (m, 2 H), 7.22 (dd, *J* = 7.7, 2.0 Hz, 1 H), 7.32 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.38–7.44 (m, 3 H), 7.64 (d, *J* = 8.1 Hz, 1 H), 8.15–8.18 (m, 2 H), 8.37 (dd, *J* = 5.3, 1.7 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 111.0 (CH), 119.4 (CH), 120.0 (CH), 120.9 (CH), 121.1 (CH), 121.2 (CH), 121.7 (CH), 124.0 (Cq), 125.8 (Cq), 126.2 (CH), 126.4 (CH), 126.9 (Cq), 127.7 (CH × 2), 128.6 (CH × 3), 136.7 (CH), 137.2 (Cq), 139.7 (Cq), 141.6 (Cq), 148.4 (CH), 151.5 (Cq); MS (EI, *m*/*z*) 320 (M⁺, 100); HRMS *m*/*z* calcd for C₂₃H₁₆N₂ 320.1313, found 320.1318.

1-($\overline{4}$ -Nitrophenyl)-9-(pyridin-2-yl)-9H-carbazole (**3b**): yellowgreen solid; mp 212–213 °C; $R_f = 0.58$ (*n*-hexane/ethyl acetate = 4/1); ¹H NMR (300 MHz, CDCl₃) δ 6.92 (d, J = 8.1 Hz, 1 H), 6.99 (ddd, J = 7.4, 4.8, 0.9 Hz, 1 H), 7.31–7.46 (m, 7 H), 7.58 (d, J = 8.1 Hz, 1 H), 7.90 (d, J = 8.7 Hz, 2 H), 8.17 (d, J = 7.8 Hz, 1 H), 8.22 (dd, J = 7.2, 1.7 Hz, 1 H), 8.31 (dd, J = 4.5, 1.5 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 110.8 (CH), 120.3 (CH), 120.8 (CH), 121.1 (CH), 121.4 (CH), 121.6 (CH), 121.8 (CH), 122.8 (CH × 2), 123.8 (Cq), 124.3 (Cq), 126.2 (Cq), 126.9 (CH), 128.3 (CH), 129.2 (CH × 2), 137.1 (Cq), 137.4 (CH), 141.5 (Cq), 146.0 (Cq), 146.9 (Cq), 149.0 (CH), 151.5 (Cq); MS (EI, m/z) 365 (M⁺, 15), 70 (61), 61 (100); HRMS m/z calcd for C₂₃H₁₅N₃O₂ 365.1164, found 365.1166.

1-(3-Nitrophenyl)-9-(pyridin-2-yl)-9H-carbazole (**3c**): yellow viscous liquid; $R_f = 0.45$ (*n*-hexane/ethyl acetate = 4/1); ¹H NMR (300 MHz, CDCl₃) δ 6.96 (ddd, J = 7.2, 5.3, 0.9 Hz, 1 H), 7.01 (d, J = 8.1 Hz, 1 H), 7.23 (dd, J = 7.8, 7.8 Hz, 1 H), 7.31–7.45 (m, 5 H), 7.50–7.55 (m, 2 H), 7.88–7.94 (m, 2 H), 8.16 (d, J = 7.8 Hz, 1 H), 8.20–8.23 (m, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ 110.6 (CH), 120.3 (CH), 120.6 (CH), 121.0 (CH × 2), 121.3 (CH), 121.8 (CH), 123.4 (CH), 123.7 (Cq), 124.1 (Cq), 126.0 (Cq), 126.8 (CH), 128.4 (CH), 128.6 (CH), 134.5 (CH), 137.1 (Cq), 137.4 (CH), 141.5 (Cq × 2), 147.5 (Cq), 149.1 (CH), 151.2 (Cq); MS (EI, *m*/*z*) 365 (M⁺, 76), 129 (45), 88 (52), 70 (64), 61 (100); HRMS *m*/*z* calcd for C₂₃H₁₅N₃O₂ 365.1164, found 365.1158.

1-(4-Formylphenyl)-9-(pyridin-2-yl)-9H-carbazole (**3d**): white solid; mp 177–178 °C; $R_f = 0.37$ (*n*-hexane/ethyl acetate = 4/1); ¹H NMR (300 MHz, CDCl₃) δ 6.85 (d, J = 8.1 Hz, 1 H), 6.93 (dd, J = 7.2, 5.1 Hz, 1 H), 7.28 (dd, J = 7.5, 1.8 Hz, 1 H), 7.32–7.37 (m, 3 H), 7.40–7.46 (m, 3 H), 7.56 (d, J = 8.1 Hz, 2 H), 7.61 (d, J = 8.1 Hz, 1 H), 8.17 (d, J = 7.8 Hz, 1 H), 8.21 (dd, J = 6.0, 3.0 Hz, 1 H), 8.31 (dd, J = 4.5, 1.2 Hz, 1 H), 9.90 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 110.8 (CH), 120.2 (CH), 120.4 (CH), 121.0 (CH), 121.2 (CH), 121.5 (CH × 2), 123.8 (Cq), 125.3 (Cq), 126.0 (Cq), 126.7 (CH), 128.4 (CH), 129.0 (CH), 129.1 (Cq + CH), 134.2 (Cq), 137.1 (CH), 141.5 (Cq), 146.4 (Cq), 148.8 (CH), 151.4 (Cq), 191.8 (CH); MS







Figure 2. Hammett experiment for direct ortho arylation of 9-(pyridin-2-yl)-9H-carbazole (1).

Scheme 2. Synthesis of the 9-(Pyridin-2-yl)-9H-carbazole Palladacycle I



(EI, m/z) 348 (M⁺, 100), 88 (48), 70 (53), 61 (82); HRMS m/z calcd for C₂₄H₁₆N₂O 348.1263, found 348.1272.

1-(4-Fluorophenyl)-9-(pyridin-2-yl)-9H-carbazole (3e): white solid; mp 208–209 °C; $R_f = 0.61$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.70–6.78 (m, 3 H), 7.02 (ddd, J = 7.7, 4.8, 0.9 Hz, 1 H), 7.09–7.14 (m, 2 H), 7.29–7.44 (m, 5 H), 7.60 (d, J = 8.1 Hz, 1 H), 8.14–8.18 (m, 2 H), 8.38 (dd, J = 4.8, 1.4 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 110.9 (CH), 114.6 (d, $J_{C-F} = 21.4$ Hz, CH × 2), 119.6 (CH), 120.1 (CH), 120.9 (CH), 121.1 (CH), 121.4 (CH), 121.8 (CH), 123.9 (Cq), 125.8 (Cq), 125.9 (Cq), 126.5 (CH), 128.5 (CH), 130.1 (d, $J_{C-F} = 8.0$ Hz, CH × 2), 135.8 (d, $J_{C-F} = 2.4$ Hz, Cq), 136.9 (CH), 137.2 (Cq), 141.7 (Cq), 148.6 (CH), 151.5 (Cq), 161.5 (d, $J_{C-F} = 244.3$ Hz, Cq); MS (EI, m/z) 338 (M⁺, 75), 88 (59), 70 (68), 61 (100); HRMS m/z calcd for C₂₃H₁₅N₂F 338.1219, found 338.1214.

1-(4-Chlorophenyl)-9-(pyridin-2-yl)-9H-carbazole (**3f**): white solid; mp 200–201 °C; $R_f = 0.64$ (*n*-hexane/ethyl acetate = 4/1); ¹H NMR (300 MHz, CDCl₃) δ 6.79 (d, J = 8.1 Hz, 1 H), 6.99–7.10 (m, 5 H), 7.30–7.44 (m, 5 H), 7.60 (d, J = 8.1 Hz, 1 H), 8.14–8.18 (m, 2 H),



СНО

Figure 3. ORTEP drawing of the *N*-pyridylcarbazole palladacycle I.¹⁵ Selected bond lengths (Å): Pd1-Pd2 = 2.8861(4); Pd1-N2 = 2.052(3); Pd1-C1 = 1.955(3); Pd1-O1 = 2.045(2); Pd1-O4 = 2.172(2); Pd2-N4 = 2.022(3); Pd2-C18 = 1.964(3); Pd2-O2 = 2.143(2); Pd2-O3 = 2.042(2). All hydrogen atoms are omitted for clarity. Ellipsoids are shown at the 30% probability level.

8.39 (dd, J = 5.4, 1.5 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 110.9 (CH), 119.8 (CH), 120.1 (CH), 120.9 (CH), 121.1 (CH), 121.4 (CH), 121.8 (CH), 123.9 (Cq), 125.5 (Cq), 125.9 (Cq), 126.6 (CH), 127.8 (CH × 2), 128.4 (CH), 129.8 (CH × 2), 132.3 (CH), 137.0 (CH), 137.2 (Cq), 138.3 (Cq), 141.6 (Cq), 148.7 (CH), 151.5 (Cq); MS (EI, m/z) 356 (M⁺ + 2, 5), 354 (M⁺, 16), 88 (48), 70 (63), 61 (100); HRMS m/z calcd for C₂₃H₁₅N₂³⁵Cl 354.0924, found 354.0927.

1-(4-Bromophenyl)-9-(pyridin-2-yl)-9H-carbazole (**3g**): white solid; mp 194–195 °C; $R_f = 0.64$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.79 (d, J = 7.8 Hz, 1 H), 7.00–7.08 (m, 3 H), 7.16 (d, J = 8.4 Hz, 2 H), 7.30–7.44 (m, 5 H), 7.59 (d, J = 8.1 Hz, 1 H), 8.14–8.18 (m, 2 H), 8.38 (dd, J = 4.8, 1.4 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 110.9 (CH), 119.8 (CH), 120.1 (CH), 120.3 (Cq), 120.9 (CH), 121.1 (CH), 121.4 (CH), 121.8 (CH), 123.8 (Cq), 125.5 (Cq), 125.9 (Cq), 126.6 (CH), 128.3 (CH), 130.2 (CH × 2), 130.7 (CH × 2), 137.0 (CH), 137.1 (Cq), 138.7 (Cq), 141.6 (Cq), 148.7 (CH), 151.5 (Cq); MS (EI, *m*/z) 400 (M⁺ + 2, 34), 398 (M⁺, 35), 88 (31), 70 (53), 61 (100); HRMS *m*/z calcd for C₂₃H₁₅N₂⁷⁹Br 398.0419, found 398.0426.

1-(4-lodophenyl)-9-(pyridin-2-yl)-9H-carbazole (**3h**): white solid; mp 192–193 °C; $R_f = 0.66$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.79 (d, J = 8.1 Hz, 1 H), 6.89 (d, J = 8.4 Hz, 2 H), 7.07 (dd, J = 7.7, 4.8 Hz, 1 H), 7.30–7.44 (m, 7 H), 7.59 (d, J = 8.1 Hz, 1 H), 8.14–8.18 (m, 2 H), 8.39 (dd, J = 5.1, 1.2 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 91.6 (Cq), 110.8 (CH), 119.8 (CH), 120.1 (CH), 120.9 (CH), 121.1 (CH), 121.4 (CH), 121.8 (CH), 123.8 (Cq), 125.6 (Cq), 125.8 (Cq), 126.6 (CH), 128.2 (CH), 130.4 (CH × 2), 130.7 (CH × 2), 137.0 (CH), 137.1 (Cq), 139.3 (Cq), 141.5 (Cq), 148.7 (CH), 151.4 (Cq); MS (EI, *m*/z) 446 (M⁺, 26), 88 (35), 70 (65), 61 (100); HRMS *m*/z calcd for C₂₃H₁₅N₂I 446.0280, found 446.0286.

1-(4-tert-Butylphenyl)-9-(pyridin-2-yl)-9H-carbazole (**3i**): white solid; mp 214–215 °C; $R_{\rm f}$ = 0.72 (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 1.26 (s, 9 H), 6.67 (d, J = 7.8 Hz, 1

Scheme 3. Control Experiments in *tert*-Butyl Alcohol at 60–70 °C for 4 h: Reaction of I with 2a in the Presence or Absence of BQ



Figure 4. Proposed catalytic mechanism for synthesis of 1-aryl-9-(pyridin-2-yl)-9H-carbazoles 3 by a palladium(II)-catalyzed cross-coupling reaction of 1 with 2 via C-H bond activation.



H), 6.91 (ddd, *J* = 7.4, 5.0, 0.9 Hz, 1 H), 7.04 (m, 4 H), 7.17 (ddd, *J* = 7.8, 7.8, 1.8 Hz, 1 H), 7.29–7.43 (m, 4 H), 7.62 (d, *J* = 8.1 Hz, 1 H), 8.14–8.17 (m, 2 H), 8.36 (dd, *J* = 4.8, 1.7 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 31.4 (CH₃), 34.3 (Cq), 110.9 (CH), 119.2 (CH), 120.0 (CH), 120.8 (CH), 120.9 (CH), 121.0 (CH), 121.9 (CH), 123.9 (Cq), 124.6 (CH × 2), 125.6 (Cq), 126.4 (CH), 126.8 (Cq), 128.3 (CH × 2), 128.4 (CH), 136.5 (CH × 2), 137.3 (Cq), 141.6 (Cq), 148.2 (CH), 149.2 (Cq), 151.5 (Cq); MS (EI, *m*/*z*) 376 (M⁺, 100), 361 (60); HRMS *m*/*z* calcd for C₂₇H₂₄N₂ 376.1939, found 376.1944.

1-(*p*-Tolyl)-9-(*pyridin*-2-*y*l)-9*H*-carbazole (**3***j*): white solid; mp 147–148 °C; $R_{\rm f} = 0.62$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 2.24 (s, 3 H), 6.71 (d, *J* = 7.8 Hz, 1 H), 6.84 (d, *J* = 8.0 Hz, 2 H), 6.96 (dd, *J* = 7.4, 4.8 Hz, 1 H), 7.03 (d, *J* = 8.0 Hz, 2 H), 7.22 (ddd, *J* = 7.8, 7.8, 2.1 Hz, 1 H), 7.32 (dd, *J* = 7.8, 7.8 Hz, 1 H), 7.38–7.43 (m, 3 H), 7.64 (d, *J* = 8.4 Hz, 1 H), 8.13–8.16 (m, 2 H), 8.38 (dd, *J* = 4.5, 1.5 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 21.0 (CH₃), 111.0 (CH), 119.2 (CH), 120.0 (CH), 120.9 (CH × 2), 121.8 (CH), 124.0 (Cq), 125.8 (Cq), 126.4 (CH), 126.9 (Cq), 128.4 (CH × 5), 128.5 (CH), 135.8 (Cq), 136.6 (CH), 136.8 (Cq), 137.3 (Cq), 141.6 (CH), 148.3 (Cq), 151.6 (Cq); MS (EI, *m*/z) 334 (M⁺, 37), 207 (54), 91 (38), 70 (55), 61 (100); HRMS *m*/z calcd for C₂₄H₁₈N₂ 334.1470, found 334.1481.

1-(4-Methoxyphenyl)-9-(pyridin-2-yl)-9H-carbazole (**3k**): white solid; mp 160–161 °C; $R_f = 0.46$ (*n*-hexane/ethyl acetate = 4/1); ¹H NMR (300 MHz, CDCl₃) δ 3.72 (s, 3 H), 6.58 (d, J = 8.7 Hz, 2 H), 6.71 (d, J = 8.1 Hz, 1 H), 6.98 (ddd, J = 7.3, 5.0, 0.8 Hz, 1 H), 7.06 (d, J = 8.7 Hz, 1 H), 7.23–7.43 (m, 5 H), 7.64 (d, J = 8.1 Hz, 1 H), 8.12–8.16 (m, 2 H), 8.40 (dd, J = 5.1, 1.5 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 55.3 (CH₃), 111.0 (CH), 113.3 (CH × 2), 119.0 (CH), 120.0 (CH), 120.9 (CH × 2), 121.1 (CH), 121.9 (CH), 124.0 (Cq), 125.8 (Cq), 126.4 (CH), 126.6 (Cq), 128.5 (CH), 129.6 (CH × 2))

Article

Scheme 5. Synthesis of the Hyellazole Analogue 14 and Hyellazole (15)



2), 132.2 (Cq), 136.7 (CH), 137.2 (Cq), 141.7 (Cq), 148.3 (CH), 151.6 (Cq), 158.2 (Cq); MS (EI, m/z) 350 (M⁺, 21), 88 (61), 70 (69), 61 (100); HRMS m/z calcd for C₂₄H₁₈N₂O 350.1419, found 350.1412.

1-(3-Methoxyphenyl)-9-(pyridin-2-yl)-9H-carbazole (**3**): pale yellow viscous liquid; $R_f = 0.53$ (*n*-hexane/ethyl acetate = 4/1); ¹H NMR (300 MHz, CDCl₃) δ 3.63 (s, 3 H), 6.59 (dd, J = 8.1, 2.1 Hz, 1 H), 6.65 (s, 1 H), 6.75 (d, J = 8.1 Hz, 1 H), 6.80 (d, J = 7.5 Hz, 1 H), 6.94–7.01 (m, 2 H), 7.22–7.43 (m, 5 H), 7.63 (d, J = 8.1 Hz, 1 H), 8.14–8.17 (m, 2 H), 8.39 (dd, J = 4.8, 1.5 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 55.0 (CH₃), 111.0 (CH), 113.0 (CH), 113.5 (CH), 119.5 (CH), 120.1 (CH), 120.9 (CH), 121.0 (CH), 121.2 (CH), 121.3 (CH), 121.5 (CH), 123.9 (Cq), 125.8 (Cq), 126.5 (CH), 126.7 (Cq), 128.5 (CH), 121.7 (Cq), 156.0 (Cq); MS (EI, *m/z*) 350 (M⁺, 100); HRMS *m/z* calcd for C₂₄H₁₈N₂O 350.1419, found 350.1415.

1-(Naphthalen-2-yl)-9-(pyridin-2-yl)-9H-carbazole (**3m**): white solid; mp 146–147 °C; $R_f = 0.58$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.61 (ddd, J = 7.2, 5.1, 0.6 Hz, 1 H), 6.74 (d, J = 8.1 Hz, 1 H), 6.96 (ddd, J = 7.8, 7.8, 1.8 Hz, 1 H), 7.28–7.53 (m, 8 H), 7.60–7.72 (m, 4 H), 8.17–8.22 (m, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 111.0 (CH), 119.5 (CH), 120.1 (CH), 121.0 (CH × 3 + Cq), 121.6 (CH), 124.0 (Cq), 125.7 (CH), 125.9 (CH), 126.5 (CH), 126.7 (Cq), 126.8 (CH), 127.1 (CH), 127.4 (CH), 127.6 (CH), 127.8 (CH), 128.8 (CH), 131.8 (Cq), 133.0 (Cq), 136.6 (CH), 137.1 (Cq), 137.4 (Cq), 141.6 (Cq), 148.4 (CH), 151.5 (Cq); MS (EI, *m/z*) 370 (M⁺, 100), 291 (20), 70 (32), 61 (66); HRMS *m/z* calcd for C₂₇H₁₈N₂ 370.1470, found 370.1478.

1,8-Diphenyl-9-(pyridin-2-yl)-9H-carbazole (**4a**): white solid; mp 251–252 °C; $R_f = 0.57$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.53–6.60 (m, 2 H), 6.80 (ddd, J = 7.8, 7.8, 1.8 Hz, 1 H), 6.88–6.96 (m, 10 H), 7.24–7.26 (m, 3 H), 7.35 (dd, J = 7.5, 7.5 Hz, 1 H), 7.66 (d, J = 4.5 Hz, 1 H), 8.21 (d, J = 7.5 Hz, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ 119.2 (CH × 2), 120.1 (CH × 2), 121.6

(CH), 124.7 (Cq), 124.8 (CH), 125.7 (CH \times 2), 127.1 (Cq), 127.2 (CH \times 4), 129.0 (CH \times 4), 129.4 (CH \times 2), 135.5 (CH), 138.6 (Cq), 139.9 (Cq), 147.7 (CH), 151.7 (Cq); MS (EI, *m*/*z*) 396 (M⁺, 100); HRMS *m*/*z* calcd for C₂₉H₂₀N₂ 396.1626, found 396.1622.

9-(*Pyridin-2-yl*)-1,8-*di*-*p*-toly*l*-9*H*-*carbazole* (*4j*): white solid; mp 213–214 °C; $R_f = 0.55$ (*n*-hexane/ethyl acetate = 1/5); ¹H NMR (300 MHz, CDCl₃) δ 2.19 (s, 6 H), 6.51 (d, J = 7.8 Hz, 1 H), 6.60 (dd, J = 7.2, 4.8 Hz, 1 H), 6.69 (d, J = 8.1 Hz, 4 H), 6.76 (d, J = 8.1 Hz, 4 H), 6.79 (ddd, J = 7.8, 7.8, 1.8 Hz, 1 H), 7.24 (dd, J = 6.6, 0.6 Hz, 2 H), 7.33 (dd, J = 7.2, 7.2 Hz, 2 H), 7.65 (dd, J = 5.1, 1.2 Hz, 1 H), 8.19 (dd, J = 7.5, 0.9 Hz, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ 21.0 (CH₃ × 2), 119.0 (CH × 2), 120.0 (CH × 2), 120.9 (CH), 124.7 (Cq × 2), 124.8 (CH), 127.1 (Cq × 2), 127.9 (CH × 4), 128.8 (CH × 4), 129.3 (CH × 2), 135.1 (CH), 135.3 (Cq × 2), 137.0 (Cq × 2), 138.6 (Cq × 2), 147.5 (CH), 151.9 (Cq); MS (EI, m/z) 424 (M⁺, 100), 85 (45), 71 (59), 57 (77); HRMS m/z calcd for C₃₁H₂₄N₂ 424.1939, found 424.1938.

1,8-Bis(4-methoxyphenyl)-9-(pyridin-2-yl)-9H-carbazole (4k): white solid; mp 186–187 °C; $R_f = 0.38$ (*n*-hexane/ethyl acetate = 1/3); ¹H NMR (300 MHz, CDCl₃) δ 3.71 (s, 6 H), 6.45 (d, J = 8.7 Hz, 4 H), 6.55 (d, J = 7.8 Hz, 1 H), 6.66 (dd, J = 6.6, 5.1 Hz, 1 H), 6.80 (d, J = 8.7 Hz, 4 H), 6.89 (ddd, J = 7.5, 7.5, 1.8 Hz, 1 H), 7.23 (dd, J = 7.2, 0.9 Hz, 2 H), 7.33 (dd, J = 7.2, 7.2 Hz, 2 H), 7.74 (dd, J = 5.4, 1.5 Hz, 1 H), 8.19 (dd, J = 7.8, 0.9 Hz, 2 H); ¹³C NMR (75 MHz, CDCl₃) δ 55.3 (CH₃ × 2), 112.8 (CH × 4), 119.0 (CH × 2), 120.0 (CH × 2), 121.3 (CH), 124.7 (CH), 124.9 (Cq × 2), 126.7 (Cq), 129.5 (CH × 2), 130.0 (CH × 4), 132.4 (Cq × 2), 135.4 (CH), 138.6 (Cq), 147.6 (CH), 152.0 (Cq), 157.7 (Cq × 2); MS (EI, m/z) 456 (M⁺, 72), 85 (62), 71 (89), 57 (100); HRMS m/z calcd for C₃₁H₂₄O₂N₂ 456.1838, found 456.1838.

1,8-Bis(3-methoxyphenyl)-9-(pyridin-2-yl)-9H-carbazole (4)): white solid; mp 139–140 °C; $R_f = 0.30$ (*n*-hexane/ethyl acetate = 4/1); ¹H NMR (300 MHz, CDCl₃) δ 3.57 (s, 6 H), 6.36 (bs, 2 H), 6.51–6.66 (m, 6 H), 6.84–6.92 (m, 3 H), 7.26–7.37 (m, 5 H), 7.73 (d, J = 4.2 Hz, 1 H), 8.21 (dd, J = 7.8, 1.5 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 54.9 (CH₃ × 2), 112.4 (CH × 2), 114.1 (CH × 2), 119.3 (CH × 2), 120.1 (CH × 2), 121.6 (CH), 121.7 (CH × 2), 124.4 (CH), 124.7 (Cq × 2), 126.8 (Cq × 2), 128.3 (CH × 2), 129.2 (CH × 2), 135.3 (CH), 138.1 (Cq × 2), 141.2 (Cq × 2), 147.8 (CH), 151.9 (Cq), 158.4 (Cq × 2); MS (EI, *m*/*z*) 456 (M⁺, 48), 85 (64), 71 (84), 57 (100); HRMS *m*/*z* calcd for C₃₁H₂₄O₂N₂ 456.1838, found 456.1838.

7-Nitro-1-phenyl-9-(pyridin-2-yl)-9H-carbazole (**6***a*): yellow solid; mp 160–161 °C; $R_{\rm f}$ = 0.44 (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.77 (d, *J* = 7.8 Hz, 1 H), 7.03–7.13 (m, 6 H), 7.29 (ddd, *J* = 7.5, 7.5, 1.8 Hz, 1 H), 7.46–7.54 (m, 2 H), 8.21–8.24 (m, 3 H), 8.43 (dd, *J* = 4.5, 1.5 Hz, 1 H), 8.49 (s, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 107.5 (CH), 116.3 (CH), 120.2 (CH), 120.6 (CH), 121.7 (CH), 121.9 (CH), 122.1 (CH), 124.0 (Cq), 126.6 (CH), 127.5 (Cq), 127.9 (CH × 2), 128.6 (CH × 2), 128.9 (Cq), 130.9 (CH), 137.2 (CH), 138.8 (Cq), 139.3 (Cq), 140.6 (Cq), 146.4 (Cq), 148.9 (CH), 150.4 (Cq); MS (EI, *m*/z) 365 (M⁺, 100), 319 (20); HRMS *m*/ z calcd for C₂₃H₁₅O₂N₃ 365.1164, found 365.1165.

6-Nitro-1-phenyl-9-(pyridin-2-yl)-9H-carbazole (**6b**): yellow solid; mp 151–152 °C; $R_f = 0.50$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.75 (d, J = 8.1 Hz, 1 H), 7.04–7.11 (m, 6 H), 7.28 (ddd, J = 7.8, 7.8, 1.8 Hz, 1 H), 7.50 (s, 1 H), 7.51 (d, J = 2.4 Hz, 1 H), 7.60 (d, J = 9.0 Hz, 1 H), 8.24 (dd, J = 5.4, 3.6 Hz, 1 H), 8.31 (dd, J = 9.3, 2.4 Hz, 1 H), 8.42 (dd, J = 4.5, 1.5 Hz, 1 H), 9.09 (d, J =2.1 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 110.9 (CH), 116.9 (CH), 120.0 (CH), 121.9 (CH), 122.1 (CH), 122.2 (CH), 122.3 (CH), 123.7 (Cq), 124.9 (Cq), 126.6 (CH), 127.6 (Cq), 127.9 (CH × 2), 128.6 (CH × 2), 130.3 (CH), 137.2 (CH), 138.3 (Cq), 138.7 (Cq), 142.2 (Cq), 144.6 (Cq), 148.7 (CH), 150.4 (Cq); MS (EI, m/z) 365 (M⁺, 100), 71 (50), 57 (84); HRMS m/z calcd for C₂₃H₁₅O₂N₃ 365.1164, found 365.1166.

7-Methoxy-1-phenyl-9-(pyridin-2-yl)-9H-carbazole (6*c*): white solid; mp 122–123 °C; $R_f = 0.41$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 3.84 (s, 3 H), 6.69 (d, *J* = 7.8 Hz, 1 H), 6.92–6.96 (m, 2 H), 7.01–7.03 (m, 3 H), 7.13–7.23 (m, 4 H), 7.31–7.40 (m, 2 H), 8.01 (d, *J* = 8.7 Hz, 1 H), 8.05 (dd, *J* = 7.2, 1.5 Hz, 1 H), 8.39 (dd, *J* = 4.5, 1.2 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 55.6 (CH₃), 95.3 (CH), 109.6 (CH), 117.7 (Cq), 120.8 (CH), 121.0 (CH), 121.1 (CH), 121.5 (CH), 126.0 (Cq), 126.1 (CH), 126.7 (Cq), 127.3 (CH), 127.7 (CH × 2), 128.5 (CH × 2), 136.7 (CH), 137.1 (Cq), 139.7 (Cq), 142.9 (Cq), 148.2 (CH), 151.5 (Cq), 159.5 (Cq); MS (EI, *m*/z) 350 (M⁺, 100), 335 (32); HRMS *m*/*z* calcd for C₂₄H₁₈ON₂ 350.1419, found 350.1420.

8-Methoxy-1-phenyl-9-(pyridin-2-yl)-9H-carbazole (**6d**): white solid; mp 236–237 °C; $R_f = 0.46$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 3.95 (s, 3 H), 6.69 (d, J = 7.8 Hz, 1 H), 6.93 (ddd, J = 8.9, 4.8, 0.9 Hz, 1 H), 7.02–7.06 (m, 4 H), 7.15–7.23 (m, 3 H), 7.39 (dd, J = 11.1, 7.5 Hz, 1 H), 7.40 (s, 1 H), 7.59 (d, J = 9.0 Hz, 1 H), 7.62 (d, J = 2.4 Hz, 1 H), 8.11 (dd, J = 6.3, 2.7 Hz, 1 H), 8.36 (dd, J = 5.4, 1.5 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 56.0 (CH₃), 102.8 (CH), 112.0 (CH), 115.3 (CH), 119.3 (CH), 120.6 (CH), 120.9 (CH), 121.3 (CH), 124.5 (Cq), 125.8 (Cq), 126.2 (CH), 127.0 (Cq), 127.7 (CH × 2), 128.5 (CH × 2), 128.6 (CH), 136.5 (Cq), 136.6 (CH), 137.6 (Cq), 139.7 (Cq), 148.2 (CH), 151.6 (Cq), 155.0 (Cq); MS (EI, m/z) 350 (M⁺, 100), 335 (79); HRMS m/z calcd for C₂₄H₁₈ON₂ 350.1419, found 350.1422.

7-tert-Butyl-1-phenyl-9-(pyridin-2-yl)-9H-carbazole (**6e**): white solid; mp 98–99 °C; $R_f = 0.65$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 1.37 (s, 9 H), 6.69 (d, J = 8.1 Hz, 1 H), 6.95 (ddd, J = 6.7, 5.1, 0.6 Hz, 1 H), 7.01–7.04 (m, 3 H), 7.14–7.24 (m, 3 H), 7.37–7.42 (m, 3 H), 7.69 (d, J = 0.9 Hz, 1 H), 8.07 (d, J = 8.4 Hz, 1 H), 8.11 (dd, J = 5.7, 3.3 Hz, 1 H), 8.42 (dd, J = 4.8, 1.2 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 31.7 (CH₃), 35.2 (Cq), 107.4 (CH), 119.1 (CH × 2), 119.5 (CH), 120.8 (CH), 121.0 (CH), 121.6 (Cq + CH), 125.9 (Cq), 126.1 (CH), 126.8 (Cq), 127.7 (CH × 2), 128.1 (CH), 128.6 (CH × 2), 136.7 (CH), 137.4 (Cq), 139.8 (Cq), 141.8 (Cq), 148.2 (CH), 150.3 (Cq), 151.7 (Cq); MS (EI, m/z) 376 (M⁺, 96), 361 (100); HRMS m/z calcd for C₂₇H₂₄N₂ 376.1939, found 376.1939.

1-(8-Phenyl-9-(pyridin-2-yl)-9H-carbazol-2-yl)ethanone (**6f**): orange solid; mp 136–137 °C; $R_f = 0.28$ (*n*-hexane/ethyl acetate = 4/1); ¹H NMR (300 MHz, CDCl₃) δ 2.65(s, 3 H), 6.78 (d, J = 7.8 Hz, 1 H), 6.98–7.05 (m, 4 H), 7.11–7.14 (m, 2 H), 7.28 (ddd, J = 7.8, 7.8, 1.8 Hz, 1 H), 7.41–7.49 (m, 2 H), 7.95 (dd, J = 8.1, 1.2 Hz, 1 H), 8.19– 8.22 (m, 3 H), 8.39 (dd, J = 4.8, 1.2 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 26.9 (CH₃), 111.5 (CH), 119.9 (CH), 120.2 (CH), 121.3 (CH × 2), 121.7 (CH), 121.8 (CH), 124.8 (Cq), 126.4 (CH), 127.2 (Cq), 127.8 (CH × 2), 128.6 (CH × 2), 130.1 (CH), 135.4 (Cq), 137.0 (CH), 138.7 (Cq), 139.3 (Cq), 141.2 (Cq), 148.6 (CH), 150.9 (Cq), 198.2 (Cq); MS (EI, *m*/*z*) 362 (M⁺, 100), 347 (31), 319 (36), 85 (38), 71 (51), 57 (68); HRMS *m*/*z* calcd for C₂₅H₁₈ON₂ 362.1419, found 362.1421.

3,6-Dibromo-1-phenyl-9-(pyridin-2-yl)-9H-carbazole (**6g**): color-less viscous liquid; $R_f = 0.50$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.69 (d, J = 7.8 Hz, 1 H), 6.96–7.10 (m, 6 H), 7.25 (ddd, J = 8.1, 8.1, 2.1 Hz, 1 H), 7.48–7.54 (m, 3 H), 8.21 (s, 2 H), 8.35 (dd, J = 4.2, 1.2 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 112.7 (CH), 113.9 (Cq), 114.1 (Cq), 121.5 (CH), 121.7 (CH), 122.1 (CH), 122.9 (CH), 124.5 (Cq), 126.2 (Cq), 126.8 (CH), 127.8 (CH × 2), 128.4 (CH), 128.6 (Cq), 129.8 (CH), 131.5 (CH), 136.1 (Cq), 137.0 (CH), 137.9 (Cq), 140.5 (Cq), 148.5 (CH), 150.5 (Cq); MS (EI, m/z) 476 (M⁺, 100); HRMS m/z calcd for $C_{23}H_{14}N_2^{-79}Br_2$ 475.9524, found 475.9522.

3-Nitro-1-phenyl-9-(pyridin-2-yl)-9H-carbazole (**7b**): yellow solid; mp 190–191 °C (obtained from the detection of a mixture, **6b** and **7b**); $R_{\rm f} = 0.50$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 6.83 (d, *J* = 8.1 Hz, 1 H), 7.03–7.13 (m, 5 H), 7.35 (ddd, *J* = 7.8, 7.8, 1.8 Hz, 1 H), 7.42 (ddd, *J* = 6.6, 6.6, 1.5 Hz, 1 H), 7.47– 7.54 (m, 3 H), 8.22–8.25 (m, 1 H), 8.29–8.33 (m, 1 H), 8.36 (dd, *J* = 4.8, 1.2 Hz, 1 H), 9.07 (d, *J* = 2.1 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃) δ 111.5 (CH), 115.7 (CH), 120.7 (CH), 121.9–122.4 (CH × 3), 123.4 (Cq), 123.9 (CH), 125.6 (Cq), 126.9 (Cq), 127.1 (CH), 128.0 (CH), 128.6 (CH), 130.3 (CH), 137.2 (CH), 137.6 (Cq), 140.2 (Cq), 141.8 (Cq), 142.7 (Cq), 148.9 (CH), 150.2 (Cq); MS (EI, *m/z*) 365 (M⁺, 100), 318 (40), 158 (20); HRMS *m/z* calcd for C₂₃H₁₅N₃O₂ 365.1164, found 365.1162.

2-Methoxy-1-phenyl-9-(pyridin-2-yl)-9H-carbazole (7c): white solid; mp 176–177 °C; $R_f = 0.46$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 3.83 (s, 3 H), 6.70 (d, J = 8.1 Hz, 1 H), 6.93 (ddd, J = 7.3, 5.3, 0.6 Hz, 1 H), 6.99–7.12 (m, 6 H), 7.20–7.42 (m, 4 H), 8.05 (dd, J = 6.3, 2.1 Hz, 1 H), 8.09 (d, J = 8.4 Hz, 1 H), 8.31 (dd, J = 4.5, 1.2 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 56.7 (CH₃), 105.7 (CH), 110.6 (CH), 114.8 (Cq), 119.2 (CH), 119.7 (Cq), 119.8 (CH), 120.8 (CH), 121.2 (CH), 122.0 (CH), 123.8 (Cq), 125.2 (CH), 126.2 (CH), 127.4 (CH × 2), 130.6 (CH × 2), 134.6 (Cq), 136.8 (CH), 139.0 (Cq), 142.1 (Cq), 148.3 (CH), 151.3 (Cq), 156.0 (Cq); MS (EI, *m*/*z*) 350 (M⁺, 100), 335 (99); HRMS *m*/*z* calcd for C₂₄H₁₈ON₂ 350.1419, found 350.1417.

3-Methoxy-1-phenyl-9-(pyridin-2-yl)-9H-carbazole (**7d**): white solid; mp 107–108 °C; $R_f = 0.43$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 3.99 (s, 3 H), 6.71 (d, J = 8.1 Hz, 1 H), 6.92 (dd, J = 7.0, 5.1 Hz, 1 H), 7.02–7.06 (m, 4 H), 7.16–7.32 (m, 4 H), 7.39 (ddd, J = 7.7, 7.7, 0.9 Hz, 1 H), 7.63–7.67 (m, 2 H), 8.10 (d, J = 7.8 Hz, 1 H), 8.34 (dd, J = 4.5, 1.0 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 56.1 (CH₃), 102.6 (CH), 111.1 (CH), 116.8 (CH), 120.0 (CH), 120.7 (CH), 120.8 (CH), 121.3 (CH), 124.0 (Cq), 126.4 (CH), 125.5 (CH), 126.6 (Cq), 127.7 (CH × 2), 127.8 (Cq), 128.4 (CH × 2), 132.1 (Cq), 136.6 (CH), 139.3 (Cq), 142.2 (Cq), 148.2 (CH), 151.6 (Cq), 154.7 (Cq); MS (EI, m/z) 350 (M⁺, 41), 154 (61), 57 (100); HRMS m/z calcd for C₂₄H₁₈ON₂ 350.1419, found 350.1419.

2-Methoxy-1,8-diphenyl-9-(pyridin-2-yl)-9H-carbazole (8d): white solid; mp 187–188 °C; $R_f = 0.43$ (*n*-hexane/ethyl acetate = 5/1); ¹H NMR (300 MHz, CDCl₃) δ 3.97 (s, 3 H), 6.5 (d, J = 8.1 Hz, 1 H), 6.58 (dd, J = 6.6, 5.1 Hz, 1 H), 6.79 (ddd, J = 7.5, 7.5, 1.8 Hz, 1 H), 6.88–6.97 (m, 11 H), 7.24 (dd, J = 6.9, 0.9 Hz, 1 H), 7.32 (dd, J = 7.2, 7.2 Hz, 1 H), 7.65 (d, J = 6.0 Hz, 1 H), 7.68 (d, J = 2.7 Hz, 1 H), 8.16 (dd, J = 7.8, 0.9 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 56.0 (CH₃), 102.3 (CH), 117.8 (CH), 119.2 (CH), 119.7 (CH), 121.4

(CH), 124.6 (CH), 124.7 (Cq), 125.4 (Cq), 125.7 (CH), 125.9 (CH), 127.1 (Cq), 127.2 (CH \times 4), 128.0 (Cq), 128.8 (CH \times 2), 128.9 (CH \times 2), 129.4 (CH), 133.6 (Cq), 135.4 (CH), 139.0 (Cq), 139.4 (Cq), 139.8 (Cq), 147.6 (CH), 151.7 (Cq), 153.9 (Cq); MS (EI, *m*/*z*) 426 (M⁺, 38), 154 (92), 57 (100); HRMS *m*/*z* calcd for C₃₀H₂₂ON₂ 426.1732, found 426.1733.

ASSOCIATED CONTENT

S Supporting Information

Text, tables, figures, and CIF files giving general procedures for the preparation of all starting substrates, characterization of compounds, X-ray crystallographic data, and ¹H and ¹³C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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(10) Copies of the deposited crystallographic data (CCDC 890263 (3a) and 890264 (4a)) can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/ data request/cif.

(11) (a) For details of the syntheses of 5a-k, please see the Supporting Information. (b) For details of the synthesis of 1-D, please see the Supporting Information.

(12) The reason for the use of potassium 4-formylphenyltrifluoroborate (2d) instead of potassium phenyltrifluoroborate (2a) was mainly due to purification of 3d and 3a. Herein compound 3d is easier to separate than 3a from their crude products.

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