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# Double *N*-Arylation of Primary Amines: Carbazole Synthesis from 2,2′-Biphenyldiols

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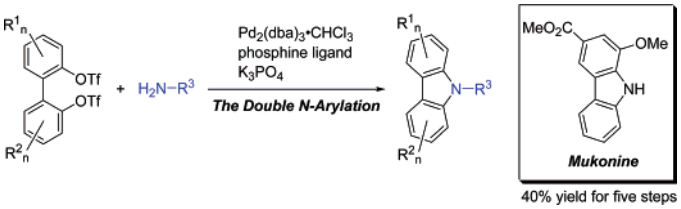


The double *N*-arylation of primary amines with 2,2′-biphenylylene ditriflates was investigated for the synthesis of multisubstituted carbazoles. Palladium complexes supported by 2-dicyclohexylphosphino-2′-methylbiphenyl or Xantphos [4,5-bis(diphenylphosphino)-9,9-dimethylxanthene] were found to be efficient catalysts for the reaction. The catalysts allow the use of anilines with an electron-donating or electron-withdrawing substituent and multisubstituted 2,2′-biphenylylene ditriflates as substrates. Ammonia equivalents, such as *O*-*tert*-butyl carbamate, are also employable as a nitrogen source to give the *N*-protected carbazoles which can easily give the corresponding *N*-unsubstituted carbazoles after deprotection. By using this methodology, a carbazole alkaloid, mukonine, is synthesized in 40% yield for five steps, in comparable efficiency to the recent precedents.

## Introduction

Carbazole derivatives are known as alkaloids from plants, and many of these show antioxidative and biological activities, such as antitumor, psychotropic, antiinflammatory, antihistaminic, and antibiotic activities.[1] Carbazole derivatives are also widely used as organic materials, due to their photorefractive, photoconductive, hole-transporting, and light-emitting properties.[2] To investigate the biological and physical properties of carbazole derivatives, the introduction of substituents onto a carbazole is essential. Because the standard electrophilic substitution takes place mostly at the 3-, 6-, and 9-positions of carbazole, the construction of the carbazole ring itself from readily available synthons is highly desired.

Conventional methodology for carbazole ring construction is briefly summarized below.[3] The classical Fischer−Borsche synthesis starts with appropriate cyclohexanone arylhydrazones.[3a] From indole, cyclization via Diels−Alder reaction or via ketosulfoxide was reported.[4] Alternatively, cyclization of *ortho*-nitrogen-substituted biphenyl via nitrene was developed.[5] Recent development of organometallic chemistry provided successful precedents for metal-catalyzed synthesis of carbazole rings; for example, the electrophilic addition of a cationic metal dienyl complex to a multisubstituted aniline at the *ortho* position of the nitrogen atom, followed by intramolecular metal-catalyzed oxidative cyclization[6] and the *N*-arylation of an aniline by a haloarene followed by oxidative cyclization.[7,8]

In our previous paper, we reported a new synthetic methodology, the double *N*-arylation of primary amines

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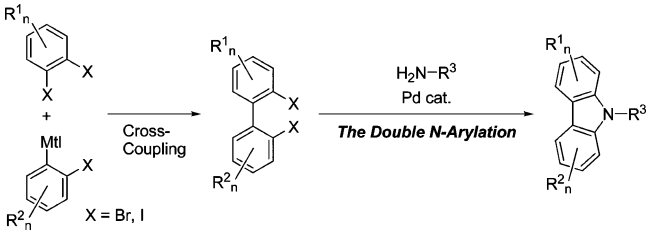
**SCHEME 1. Double *N*-Arylation with 2,2′-Dihalobiphenyl**




with 2,2′-dihalobiphenyls (Scheme 1).[9] In contrast to conventional carbazole-ring construction starting from 2-nitrogen-substituted biphenyls, the nitrogen atom is derived from primary amines which are reacted with biphenyl moieties in the double *N*-arylation strategy. We disclosed that (1) various multisubstituted carbazoles can be synthesized from the corresponding anilines and 2,2′-dihalobiphenyls and that (2) the method is especially effective for the synthesis of sterically crowded carbazoles, 2,2′-dicarbazolyl-1,1′-biaryls, which could not be synthesized by the simple *N*-arylation of carbazole.

To synthesize multisubstituted carbazoles via the double *N*-arylation, it is necessary to prepare the 2,2′-dihalobiphenyls regioselectively.[10] However, the cross-coupling reaction,[11] one of the most general and powerful methods for the synthesis of unsymmetric biphenyls, is not applicable to the regioselective synthesis of 2,2′-dihalobiphenyls because it is difficult to distinguish one of the two halogen atoms of 1,2-dihalobenzene upon its coupling with an organometallic coupling partner (Scheme 1). As a solution for this problem, here we report our successful usage of 2,2′-bis(trifluoromethanesulfonyloxy)-biphenyls (2,2′-biphenylylene ditriflates), in place of 2,2′-dihalobiphenyls, as the double *N*-arylation reagent (Scheme 2).[12] The 2,2′-biphenylylene ditriflates are readily available from 2,2′-biphenyldiols which can be easily prepared by the Suzuki−Miyaura cross-coupling[13] of *o*-halophenols with *o*-hydroxyphenylboronic acids. In addition to primary amines, ammonia equivalents were successfully utilized for the reaction with 2,2′-biphenylylene ditriflates. Furthermore, the synthetic utility of the double *N*-arylation methodology is demonstrated through the total synthesis of mukonine, a carbazole alkaloid.

## Results and Discussion

**The Double *N*-Arylation of Anilines with 2,2′-Biphenylylene Ditriflates.** As substrates, 2,2′-biphenylylene ditriflate and aniline were employed and the reaction conditions were optimized (Table 1). The substrates were mixed in toluene at 80 or 100 °C for 18 h in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$, $K_3PO_4$, and various ligands. The use of P(*t*-Bu)$_3$ as a ligand, which was effective for the reaction of 2,2′-dibromobiphenyl with aniline in our previous study,[9] resulted in no reaction (entry 1). Similarly, Fu reported that the Suzuki−Miyaura coupling of aryl triflate did not proceed by using P(*t*-Bu)$_3$.[14] The use of P(*cyclo*-Hex)$_3$, which was reported to be effective for the Suzuki−Miyaura coupling of aryl triflate,[14] resulted in no reaction either (entry 2). Biphenylphosphines (**2**−**4**)[12a,15] were the ligands of choice (entries 3−7), and finally, the desired product, *N*-phenylcarbazole (**1a**), was obtained in 92% yield using 2-dicyclohexylphosphino-2′-methylbiphenyl (**3**) at 100 °C (entry 6). Carbene ligand **5**[16] and bisphosphine ligand **6**[17] were also effective for the reaction, and especially with **6**, the highest yield of 97% was achieved (entries 8−10). The effect of base was also examined. When $Cs_2CO_3$ or Na(O-*t*-Bu) was employed instead of $K_3PO_4$, otherwise under the same conditions as entry 6, the yield of *N*-phenylcarbazole dropped to 50% or 14%, respectively, and biphenyldiol was obtained as a byproduct in 22% or 50%, respectively. The hydrolysis of triflate was also reported to occur when nucleophilic strong base was employed.[12a]

Thus, using **3** as a ligand and $K_3PO_4$ as a base, the reactions of substituted anilines and biphenyls were examined (Scheme 3). Aniline with an electron-donating or electron-withdrawing substitutent was employable. Although the yield was not satisfactory, multi-substituted carbazole **7** was also produced from 4,4′,5,5′,6,6′-hexamethyl-2,2′-biphenylylene ditriflate. It is noteworthy that the methyl groups are introduced at the 2,4,5,7-positions of carbazole, at which position, a simple electrophilic substitution on carbazole does not take place.

**The Double *N*-Arylation of Ammonia Equivalents.** Because most of the carbazole alkaloids have no substituent on the nitrogen atom, we examined the double *N*-arylation of ammonia and its equivalents.[18] The same reaction conditions as Table 1 were employed unless otherwise stated. No reaction proceeded under continuous ammonia flow at 95 °C for 5 h, and a complex mixture was obtained when triphenylsilylamine was employed.[18a] Further studies were carried out using ammonia equivalents which are advantageous for laboratory handling (Table 2). *N*-Benzyl-protected carbazole

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**SCHEME 2. Double *N*-Arylation with 2,2′-Biphenylylene Ditriflate**

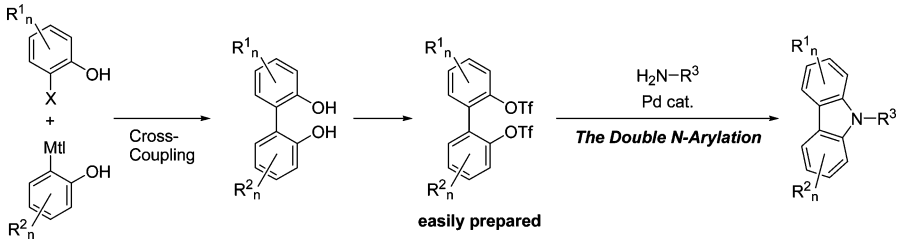
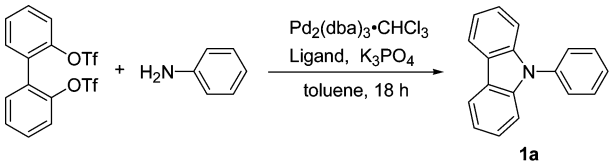
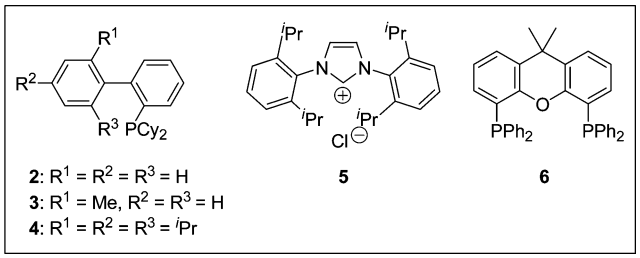



**TABLE 1. Ligand Screening for the Double *N*-Arylation of Aniline with 2,2′-Biphenylylene Ditriflate[a]**



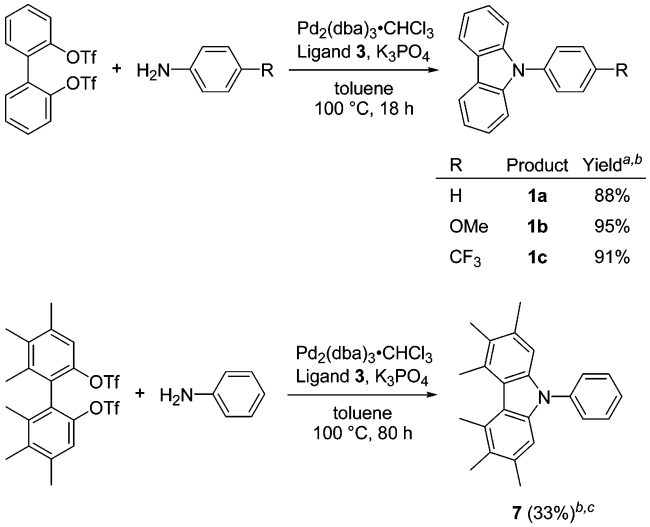

| entry | ligand (mol %) | *T* (°C) | recovered substrate[b] (%) | LC yield[c] (%) |
|---|---|---|---|---|
| 1 | $P^tBu_3$ (10) | 80 | 83 | not detected |
| 2 | $PCy_3$ (20) | 80 | 96 | not detected |
| 3 | **2** (20) | 80 | 39 | 18[d] |
| 4 | **2** (20) | 100 | 8 | 36[d] |
| 5 | **3** (20) | 80 | 7 | 78[d] |
| 6 | **3** (20) | 100 | 0 | 92 |
| 7 | **4** (20) | 80 | 17 | 72[d] |
| 8 | **5** (20) | 80 | 2 | 50[d] |
| 9 | **6** (10) | 80 | 37 | 40[d] |
| 10 | **6** (10) | 100 | 0 | 97 |

[a] Reaction conditions: 2,2′-biphenylylene ditriflate (0.40 mmol), aniline (0.48 mmol), $K_3PO_4$ (2.8 equiv), $Pd_2(dba)3{\cdot}CHCl_3$ (0.020 mmol), ligand (0.040−0.080 mmol), toluene (1.2 mL), 80−100 °C, 18 h. Reaction times have not been minimized. [b] 2′-Hydroxybiphenyl-2-yl triflate and 2,2′-biphenyldiol are also included as a recovered substrate because these two compounds were given by hydrolysis of the substrate not only during the reaction, but also after dilution with methanol for the preparation of LC sample. [c] LC yields were estimated using phenanthrene as internal standard; see the Experimental Section for details. [d] Biphenyl, biphenylphenylamine, and other unidentified biproducts were also detected.

(**8a**) was obtained in 41% from benzylamine (entry 1).[12a] By using Xantphos[19,20] (**6**), *N*-acetylcarbazole (**8b**) was obtained from acetamide[20] in 63% yield accompanied by deprotected carbazole in 15% yield (entry 2). The reaction proceeded with *O*-benzyl carbamate,[20] but the deprotection partially occurred, possibly due to the reductive reaction conditions (entries 3 and 4). If the purpose of the reaction is the direct production of *N*-unsubstituted carbazole, the partial deprotection may not be a problem. Nevertheless, from a synthetic viewpoint, obtaining the product in its perfectly protected form is also significant. Finally, using *O-tert*-butyl carbamate,[21] *N*-protected carbazole **8d** was obtained in 81% yield (entry 6).

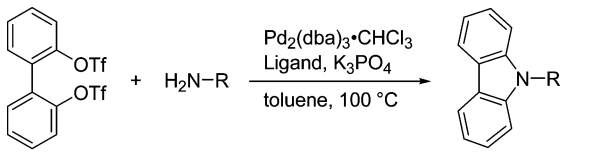
Xantphos (**6**) seems to be a superior ligand to *o*-biphenylphosphine **3** for the double *N*-arylation of carbamate in the following point. The reaction proceeded fast

**SCHEME 3. Double *N*-Arylation of Anilines with 2,2′-Biphenylylene Ditriflate**




[a] 2,2′-Biphenylylene ditriflate (0.50 mmol), aniline (0.60 mmol), $K_3PO_4$ (1.4 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.0125 mmol), ligand **3** (0.050 mmol), toluene (1.5 mL), 100 °C. [b] Isolated yield. [c] 4,4′,5,5′,6,6′-Hexamethyl-2,2′-biphenylylene ditriflate (0.24 mmol), aniline (0.29 mmol), $K_3PO_4$ (0.67 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.012 mmol), ligand **3** (0.048 mmol), toluene (0.75 mL), 100 °C, 80 h.

**TABLE 2. Double *N*-Arylation of Ammonia Equivalents with 2,2′-Biphenylylene Ditriflate[a]**




| entry | R | ligand (mol %) | time (h) | product | yield[b] (%) |
|---|---|---|---|---|---|
| 1 | Bn | **3** (20) | 24 | **8a** | 41[c] |
| 2 | COMe | **6** (10) | 72 | **8b** | 63 (15[d]) |
| 3 | $CO_2Bn$ | **3** (20) | 18 | **8c** | 33 (17[d]) |
| 4 | $CO_2Bn$ | **6** (10) | 64 | **8c** | 27 (25,[d] 10[e]) |
| 5 | $CO_2{}^tBu$ | **3** (20) | 18 | **8d** | 65 (1[d]) |
| 6 | $CO_2{}^tBu$ | **6** (10) | 67 | **8d** | 81 |

[a] Reaction conditions: 2,2′-biphenylylene ditriflate (0.50 mmol), amine (0.60 mmol), $K_3PO_4$ (2.8 equiv), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.025 mmol), ligand (0.05−0.10 mmol), xylene (1.5 mL, entries 1, 2 and 4) or toluene (1.0−1.5 mL, entries 3, 5 and 6), 100 °C. [b] Isolated yield. [c] At 120 °C. [d] *N*−H carbazole. [e] *N*-benzylcarbazole.

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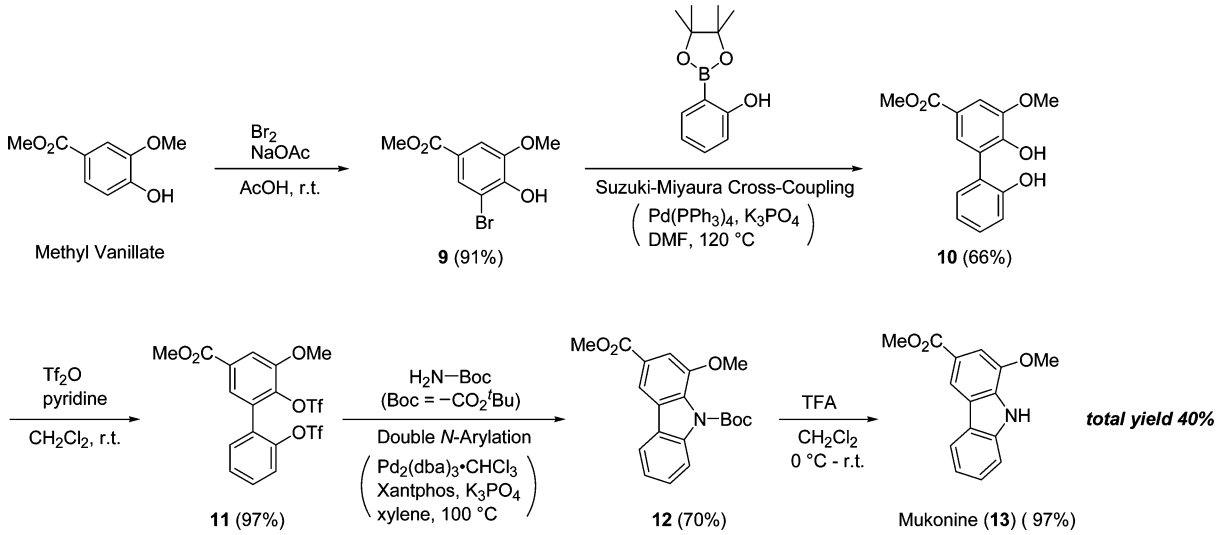
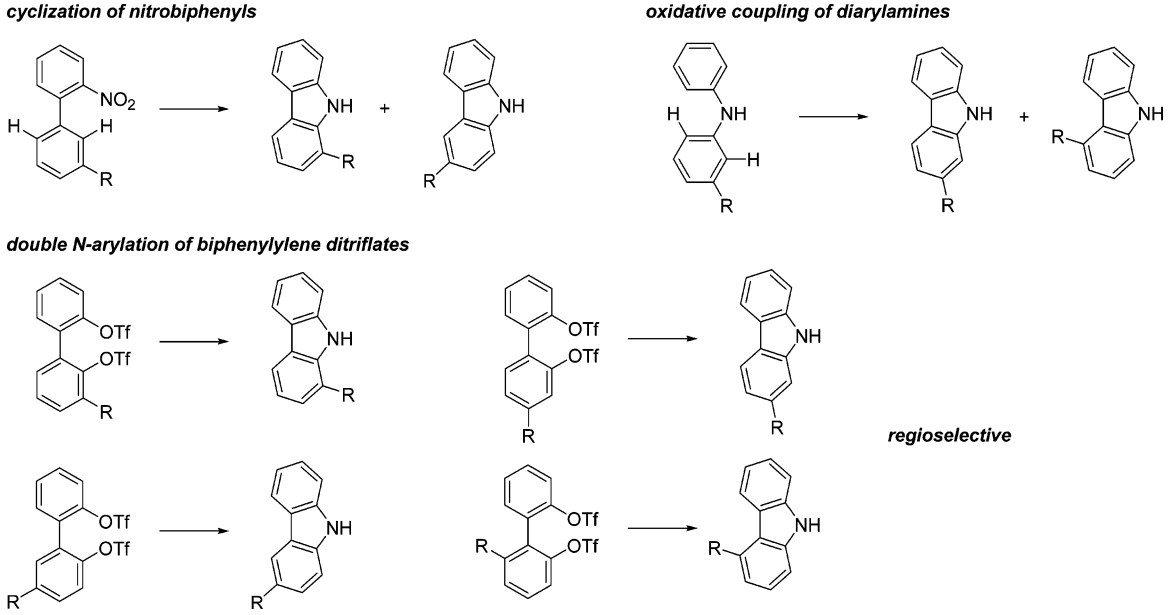
**SCHEME 4. Total Synthesis of Mukonine**




**SCHEME 5. Comparison of the Double *N*-Arylation with Some of Precedents**




with **3**, and the desired product was obtained in 65% yield after 18 h at 100 °C (entry 5). At this stage, the starting material was almost consumed, and byproducts such as biphenyl resulting from reduction were produced. Recently, Bergman and Ellman reported that P(*cyclo*-Hex)$_3$ behaves as a hydride source in their rhodium-catalyzed arylation of an imidazole with a halobenzene.[22] Similarly, the dicyclohexylphosphino group of **3** may have worked as a hydride source in the present reaction. On the other hand, the reaction was slow with **6**, and it took 67 h to consume the starting material. However, the desired product, *N*-Boc-carbazole, was the only isolable major product in this case (entry 6).

**Synthesis of Mukonine by the Double *N*-Arylation Methodology.** Mukonine [1-methoxy-3-(methoxycarbonyl)carbazole], which is an unsymmetrically multisubstituted carbazole, is an alkaloid from the Indian curry-leaf tree (*Murraya koenigii*).[1] Taking advantage of the easy availability of the corresponding biphenyldiol, we synthesized mukonine (**13**) via the double *N*-arylation starting from methyl vanillate and the pinacol ester of 2-hydroxyphenylboronic acid, the total yield being 40% for five steps (Scheme 4). Bromination[23] of methyl vanillate followed by the Suzuki−Miyaura coupling with the pinacol ester of 2-hydroxyphenylboronic acid gave biphenyldiol **10**. The coupling reaction was slow in toluene, a nonpolar solvent, presumably due to the coordination of the hydroxyl group to the catalyst.[13,24] The yield was improved when DMF, a polar solvent, was employed. Biphenyldiol **10** was converted to the corresponding

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ditriflate **11**, which was subjected to the double *N*-arylation with *O-tert*-butyl carbamate. Using Xantphos (**6**) as the ligand, the desired product, *N*-Boc-mukonine (**12**), was obtained in 70% yield. Deprotection of the Boc group by trifluoroacetic acid provided mukonine (**13**) quantitatively. The total yield of 40% for five steps is comparable to the recent precedents with high efficiencies, such as (1) Horner−Emmons reaction of 3-indolecarbaldehyde followed by the intramolecular cyclization, 46% yield for six steps,[25] (2) Stobbe condensation of 3-indolecarbaldehyde with dimethyl succinate followed by the intramolecular cyclization, 32% yield for three steps,[26] and (3) electrophilic substitution of aniline derivative by tricarbonylcyclohexadienylium iron followed by oxidative intramolecular coupling, 33% for two steps.[27]

## Conclusion

Here, we report that 2,2′-biphenylylene ditriflates, easily prepared by the Suzuki−Miyaura coupling of *o*-halophenols with *o*-hydroxyphenylboronic acids, were effectively utilized for the double *N*-arylation of primary amines as well as *O-tert*-butyl carbamate, an ammonia equivalent. The synthesis of mukonine, a carbazole alkaloid, was also demonstrated.

As shown in Scheme 5, the carbazole synthesis via cyclization of nitrobiphenyls or oxidative coupling of diarylamines inherently gives regioisomers. In contrast, the double *N*-arylation strategy can selectively provide each of the isomers. Thus, the double *N*-arylation may be advantageous for the regioselective synthesis of multi-subsutituted carbazole.[28] Considering the recent remarkable advances in the Suzuki−Miyaura cross-coupling and in the Buchwald−Hartwig *N*-arylation, the double *N*-arylation with 2,2′-biphenylylene ditriflates will provide a powerful tool for the synthesis of unsymmetrically multi-substituted carbazoles.

## Experimental Section

**Ligand Screening by HPLC Analysis.** A flame-dried 20-mL Schlenk tube containing a magnetic stirring bar was charged with $Pd_2(dba)_3$·$CHCl_3$ (21 mg, 0.020 mmol), ligand (0.040−0.080 mmol), 2,2′-biphenylylene ditriflate (180 mg, 0.40 mmol), and $K_3PO_4$ (240 mg, 1.12 mmol). The tube was evacuated and backfilled with argon, and then aniline (44 $\mu$L, 0.48 mmol) and toluene (1.2 mL) were added through the septum via syringe. After the mixture was degassed by freeze−pump−thaw cycles, the mixture was stirred at 80 or 100 °C for 18 h under argon. The reaction mixture was cooled to ambient temperature and diluted with methanol, followed by addition of phenanthrene as internal standard. The crude mixture was analyzed by HPLC (methanol/water = 76.5/23.5, 1.2 mL/min). Retention times (min) of major products were as follows: aniline, $t_R$ = 3.0; 2,2′-biphenyldiol, $t_R$ = 3.8; 2-hydroxy-2′-(trifluoromethansulfonyloxy)biphenyl, $t_R$ = 6.0; toluene, $t_R$ = 7.3; 2,2′-biphenylylene ditriflate, $t_R$ = 11.5; biphenyl, $t_R$ = 12.2; phenanthrene $t_R$ = 18; *N*-phenylcarbazole, $t_R$ = 37.

***N*-Phenylcarbazole (1a): General Procedure for the Double *N*-Arylation of Amine with Ditriflate.** A flame-dried 20-mL Schlenk tube containing a magnetic stirring bar was charged with $Pd_2(dba)_3$·$CHCl_3$ (13 mg, 0.0125 mmol), 2-dicyclohexylphosphino-2′-methylbiphenyl (**3**) (18 mg, 0.050 mmol), 2,2′-biphenylylene ditriflate (230 mg, 0.50 mmol), and $K_3PO_4$ (300 mg, 1.4 mmol). The tube was evacuated and backfilled with argon, and then aniline (55 $\mu$L, 0.60 mmol) and toluene (1.5 mL) were added through the septum via syringe. After being degassed by freeze−pump−thaw cycles, the mixture was stirred at 100 °C under argon until the ditriflate was consumed as judged by TLC analysis. The reaction mixture was allowed to cool to ambient temperature, diluted with dichloromethane (40 mL), and transferred to a separatory funnel. The mixture was washed with water (10 mL), and the aqueous phase was extracted with ethyl acetate (20 mL × 3). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography with hexane ($R_f$ 0.33) as an eluent to give **1a** (107 mg, 0.44 mmol, 88%) as a white solid. The structure was identified on the basis of the $^1$H and $^{13}$C NMR spectral data of the commercially available *N*-phenylcarbazole: $^1$H NMR ($CDCl_3$) $\delta$ 8.17−8.13 (m, 2H), 7.63−7.55 (m, 4H), 7.49−7.45 (m, 1H), 7.42−7.39 (m, 4H), 7.31−7.27 (m, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 140.9, 137.7, 129.8, 127.4, 127.1, 125.9, 123.3, 120.3, 119.9, 109.7.

***N*-(*p*-Methoxyphenyl)carbazole (1b).** A crude material was prepared from 2,2′-biphenylylene ditriflate (230 mg, 0.50 mmol) and *p*-methoxyaniline (74 mg, 0.60 mmol) according to the procedure described above. Purification of the crude product by silica gel column chromatography with hexane/ethyl acetate (10/1, $R_f$ 0.39) as an eluent gave **1b** (130 mg, 0.47 mmol, 95%) as a white solid: mp 147−149 °C (hexane/ethyl acetate = 10/1); $^1$H NMR ($CDCl_3$) $\delta$ 8.14 (ddd, $J$ = 7.7, 1.2, 0.8 Hz, 2H), 7.45 (d, $J$ = 9.0 Hz, 2H), 7.40 (ddd, $J$ = 8.2, 7.0, 1.0 Hz, 2H), 7.33 (ddd, $J$ = 8.2, 1.0, 0.8 Hz, 2H), 7.27 (ddd, $J$ = 7.7, 7.0, 1.0 Hz, 2H), 7.11 (d, $J$ = 9.0 Hz, 2H), 3.92 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 158.8, 141.3, 130.3, 128.6, 125.8, 123.1, 120.2, 119.6, 115.0, 109.7, 55.6. Anal. Calcd for $C_{19}H_{15}NO$: C, 83.49; H, 5.53. Found: C, 83.54; H, 5.75.

***N*-[*p*-(Trifluoromethyl)phenyl]carbazole (1c).** Crude material was prepared from 2,2′-biphenylylene ditriflate (230 mg, 0.50 mmol) and *p*-(trifluoromethyl)aniline (78 $\mu$L, 0.60 mmol) according to the procedure described above. Purification of the crude product by silica gel column chromatography with hexane/dichloromethane (10/1, $R_f$ 0.50) as an eluent and recycling preparative GPC gave **1c** (141 mg, 0.45 mmol, 91%) as a white solid: mp 165−167 °C ($CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 8.15 (d, $J$ = 7.8 Hz, 2H), 7.88 (d, $J$ = 8.3 Hz, 2H), 7.73 (d, $J$ = 8.3 Hz, 2H), 7.46−7.41 (m, 4H), 7.32 (ddd, $J$ = 7.8, 5.6, 2.5 Hz, 2H); $^{13}$C NMR ($CDCl_3$) $\delta$ 141.1, 140.3, 129.2 (q, $J_{C-F}$ = 33.4 Hz), 127.09 (q, $J_{C-F}$ = 3.8 Hz), 127.03, 126.2, 123.9 (q, $J_{C-F}$ = 269.9 Hz), 123.7, 120.6, 120.5, 109.5. Anal. Calcd for $C_{19}H_{12}NF_3$: C, 73.31; H, 3.89. Found: C, 73.20; H, 4.17.

***N*-Phenyl-2,3,4,5,6,7-hexamethylcarbazole (7).** According to the procedure described above, a reaction mixture of $Pd_2(dba)_3$·$CHCl_3$ (12 mg, 0.012 mmol), **3** (18 mg, 0.048 mmol), $K_3PO_4$ (140 mg, 0.67 mmol), 4,4′,5,5′,6,6′-hexamethyl-2,2′-biphenylylene ditriflate (130 mg, 0.24 mmol), and aniline (26 $\mu$L, 0.29 mmol) in toluene (0.75 mL) was stirred at 100 °C for 80 h. Purification of the crude product by silica gel column chromatography with hexane/ethyl acetate (30/1, $R_f$ 0.20) as an eluent and recycling preparative GPC gave **7** (26 mg, 0.078 mmol, 33%) as a white solid: mp 192−194 °C ($CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 7.60−7.57 (m, 2H), 7.49−7.44 (m, 3H), 6.93 (s, 2H), 2.77 (s, 6H), 2.34 (s, 6H), 2.34 (s, 6H); $^{13}$C NMR ($CDCl_3$) $\delta$ 140.3, 138.1, 134.2, 130.1, 129.7, 128.1, 127.3, 127.1, 122.0, 107.6, 22.3, 21.7, 15.8. Anal. Calcd for $C_{24}H_{25}N$: C, 88.03; H, 7.70. Found: C, 87.86; H, 7.90.

***N*-Benzylcarbazole (8a).**[29,30] According to the procedure described above, a reaction mixture of $Pd_2(dba)_3$·$CHCl_3$ (26 mg,

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0.025 mmol), **3** (36 mg, 0.10 mmol), $K_3PO_4$ (300 mg, 1.4 mmol), 2,2′-biphenylylene ditriflate (230 mg, 0.50 mmol), and benzylamine (63 μL, 0.60 mmol) in xylene (1.5 mL) was stirred at 120 °C for 24 h. Purification of the crude product by silica gel column chromatography with hexane/dichloromethane (5/1, $R_f$ 0.37) gave **8a** (52 mg, 0.20 mmol, 41%) as a white solid: mp 118−120 °C (hexane/dichloromethane = 5/1, lit.[30] mp 117 °C); $^1$H NMR ($CDCl_3$) δ 8.14 (ddd, $J$ = 7.8, 1.2, 0.7 Hz, 2H), 7.43 (ddd, $J$ = 8.2, 7.0, 1.2 Hz, 2H), 7.37 (br t, $J$ = 8.2 Hz, 2H), 7.28−7.22 (m, 5H), 7.16−7.13 (m, 2H), 5.53 (s, 2H); $^{13}$C NMR ($CDCl_3$) δ 140.6, 137.1, 128.7, 127.4, 126.4, 125.8, 123.0, 120.4, 119.2, 108.9, 46.5. Anal. Calcd for $C_{19}H_{15}N$: C, 88.68; H, 5.88. Found: C, 88.41; H, 6.15.

***N*-Acetylcarbazole (8b).**[29] According to the procedure described above, a reaction mixture of $Pd_2(dba)_3$·$CHCl_3$ (26 mg, 0.025 mmol), **6** (29 mg, 0.050 mmol), $K_3PO_4$ (300 mg, 1.4 mmol), 2,2′-biphenylylene ditriflate (230 mg, 0.50 mmol), and acetamide (36 mg, 0.61 mmol) in xylene (1.5 mL) was stirred at 100 °C for 72 h. Purification of the crude product by silica gel column chromatography with hexane/dichloromethane (2/1, $R_f$ 0.20) gave **8b** (66 mg, 0.31 mmol, 63%) as a white solid: mp 69−71 °C (hexane/dichloromethane = 2/1); IR ($CHCl_3$) 1693 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 8.20 (br d, $J$ = 8.5 Hz, 2H), 7.98 (ddd, $J$ = 7.5, 1.4, 0.6 Hz, 2H), 7.47 (ddd, $J$ = 8.5, 7.5, 1.4 Hz, 2H), 7.38 (dt, $J$ = 7.5, 1.0 Hz, 2H), 2.87 (s, 3H); $^{13}$C NMR ($CDCl_3$) δ 170.1, 138.6, 127.3, 126.4, 123.6, 119.8, 116.2, 27.7. Anal. Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30. Found: C, 80.53; H, 5.50.

***N*-(Benzyloxycarbonyl)carbazole (8c).**[31] According to the procedure described above, a reaction mixture of $Pd_2(dba)_3$·$CHCl_3$ (26 mg, 0.025 mmol), **6** (29 mg, 0.050 mmol), $K_3PO_4$ (300 mg, 1.4 mmol), 2,2′-biphenylylene ditriflate (230 mg, 0.50 mmol), and *O*-benzyl carbamate (91 mg, 0.60 mmol) in xylene (1.5 mL) was stirred at 100 °C for 64 h. Purification of the crude product by silica gel column chromatography with hexane/ethyl acetate (30/1, $R_f$ 0.34) gave **8c** (40 mg, 0.12 mmol, 27%) as a white solid. mp 85−86 °C (hexane/ethyl acetate = 30/1, lit.[31] mp 74 °C); IR ($CHCl_3$) 1724 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 8.31 (d, $J$ = 7.8 Hz, 2H), 7.99 (d, $J$ = 7.8 Hz, 2H), 7.56 (d, $J$ = 6.9 Hz, 2H), 7.48−7.35 (m, 7H), 5.58 (s, 2H); $^{13}$C NMR ($CDCl_3$) δ 152.3, 138.2, 135.2, 128.8, 128.7, 128.6, 127.2, 126.0, 123.4, 119.6, 116.3, 68.7. Anal. Calcd for $C_{20}H_{15}NO_2$: C, 79.72; H, 5.02. Found: C, 79.51; H, 5.20.

***N*-(*tert*-Butoxycarbonyl)carbazole (8d).**[32] According to the procedure described above, a reaction mixture of $Pd_2(dba)_3$·$CHCl_3$ (26 mg, 0.025 mmol), **6** (29 mg, 0.050 mmol), $K_3PO_4$ (300 mg, 1.4 mmol), 2,2′-biphenylylene ditriflate (230 mg, 0.50 mmol), and *O*-*tert*-butyl carbamate (70 mg, 0.60 mmol) in toluene (1.2 mL) was stirred at 100 °C for 67 h. Purification of the crude product by silica gel column chromatography with hexane/ethyl acetate (20/1, $R_f$ 0.40) gave **8d** (108 mg, 0.40 mmol, 81%) as a colorless oil. The structure was identified on the basis of the $^1$H and $^{13}$C NMR spectral data:[32] $^1$H NMR ($CDCl_3$) δ 8.31 (br d, $J$ = 8.4 Hz, 2H), 7.99 (ddd, $J$ = 7.7, 1.4, 0.7 Hz, 2H), 7.47 (ddd, $J$ = 8.4, 7.3, 1.4 Hz, 2H), 7.35 (dt, $J$ = 7.5, 1.0 Hz, 2H), 1.77 (s, 9H); $^{13}$C NMR ($CDCl_3$) δ 151.1, 138.5, 127.0, 125.7, 122.9, 119.5, 116.2, 83.8, 28.4.

**3-Methoxy-5-methoxycarbonyl-2,2′-biphenyldiol (10).** A flame-dried 80-mL Schlenk tube containing a magnetic stirring bar was charged with $Pd(PPh_3)_4$ (190 mg, 0.16 mmol), 2-bromophenol **9** (914 mg, 3.5 mmol), and $K_3PO_4$ (2.7 g, 13 mmol). The tube was evacuated and backfilled with argon, and then the pinacol ester of 2-hydroxyphenylboronic acid (950 μL, 4.2 mmol) in DMF (9.5 mL) was added. After the mixture was degassed by freeze−pump−thaw cycles, the mixture was stirred at 120 °C for 49 h under argon. The reaction mixture was allowed to cool to ambient temperature and then was concentrated under reduced pressure. The resulting residue was dissolved in dichloromethane (50 mL) and saturated aqueous ammonium chloride (20 mL) and transferred into a separatory funnel. After the organic phase was separated, the aqueous phase was extracted with ethyl acetate (40 mL × 4). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography with hexane/2-propanol (10/1, $R_f$ 0.17) to give almost pure **10**. Further purification by silica gel column chromatography with chloroform/methanol (40/1, $R_f$ = 0.25) as an eluent afforded the desired biphenyldiol (640 mg, 2.3 mmol, 66%) as a white solid: mp 144−145 °C (chloroform); IR ($CHCl_3$) 1713 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.74 (d, $J$ = 2.0 Hz, 1H), 7.60 (d, $J$ = 2.0 Hz, 1H), 7.35−7.30 (m, 2H), 7.08−7.04 (m, 2H), 6.66 (bs, 1H), 5.98 (bs, 1H), 4.02 (s, 3H), 3.90 (s, 3H); $^{13}$C NMR ($CDCl_3$) δ 166.6, 153.4, 146.3, 145.8, 131.1, 129.8, 126.4, 124.3, 124.0, 123.0, 121.3, 117.7, 110.8, 56.5, 52.2. Anal. Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15. Found: C, 65.41; H, 5.23.

**2,2′-Bis(trifluoromethansulfonyloxy)-3-methoxy-5-(methoxycarbonyl)biphenyl (11).** Biphenyldiol **10** (160 mg, 0.59 mmol), pyridine (140 μL, 1.8 mmol), and dichloromethane (2.0 mL) were placed in a 20-mL Schlenk tube. To this solution was slowly added trifluoromethanesulfonic acid anhydride (240 μL, 1.4 mmol) at 0 °C. The reaction mixture was allowed to warm slowly to 20 °C and then stirred for 7 h. After the volatile materials were removed under reduced pressure, the resulting residue was dissolved in ethyl acetate (20 mL) and washed with 1 M aqueous HCl (10 mL), water (10 mL), and brine (10 mL). The organic layer was dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography with hexane/2-propanol (10/1, $R_f$ 0.40) to afford **11** (310 mg, 0.57 mmol, 97%) as a white solid: mp 104−105 °C (hexane/2-propanol = 10/1); IR ($CHCl_3$) 1726 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.80 (d, $J$ = 2.0 Hz, 1H), 7.73 (d, $J$ = 2.0 Hz, 1H), 7.57 (ddd, $J$ = 2.4, 6.8, 8.2 Hz, 1H), 7.52−7.47 (m, 2H), 7.43 (d, $J$ = 8.2 Hz, 1H), 4.04 (s, 3H), 3.95 (s, 3H); $^{13}$C NMR ($CDCl_3$) δ 165.3, 151.6, 146.6, 139.4, 132.4, 131.1, 130.5, 130.4, 128.54, 128.48, 124.8, 121.8, 118.3 (q, $J_{C-F}$ = 319 Hz), 118.1 (q, $J_{C-F}$ = 319 Hz), 114.3, 56.8, 52.7; HRMS-FAB$^+$ (*m/z*) $M^+$ calcd for $C_{17}H_{12}F_6O_9S_2$ 537.9827, found 537.9832.

***N*-*tert*-Butoxycarbonyl-1-methoxy-3-(methoxycarbonyl)carbazole (12).** A flame-dried 20-mL Schlenk tube containing a magnetic stirring bar was charged with $Pd_2(dba)_3$·$CHCl_3$ (31 mg, 0.030 mmol), **6** (35 mg, 0.060 mmol), ditriflate **11** (160 mg, 0.30 mmol), *O*-*tert*-butyl carbamate (42 mg, 0.36 mmol), and $K_3PO_4$ (210 mg, 0.96 mmol). The tube was evacuated and backfilled with argon, and then xylene (0.9 mL) was added. After the mixture was degassed by freeze−pump−thaw cycles, the mixture was stirred at 100 °C for 64 h under argon. The reaction mixture was allowed to cool to ambient temperature and then diluted with dichloromethane (40 mL). The resulting mixture was washed with saturated aqueous ammonium chloride (10 mL), and the aqueous phase was extracted with ethyl acetate (20 mL × 4). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography with hexane/ethyl acetate (12/1, $R_f$ 0.12) as an eluent to afford **12** (75 mg, 0.21 mmol, 70%) as a white solid: mp 127−130 °C (hexane/ethyl acetate = 12/1); IR ($CHCl_3$) 1715 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 8.34 (d, $J$ = 0.9 Hz, 1H), 8.08 (d, $J$ = 8.3 Hz, 1H), 8.01 (d, $J$ = 7.8 Hz, 1H), 7.67 (s, 1H), 7.50 (t, $J$ = 7.8 Hz, 1H), 7.37 (t, $J$ = 7.6 Hz, 1H), 4.04 (s, 3H), 3.98 (s, 3H), 1.65 (s, 9H); $^{13}$C NMR ($CDCl_3$) δ 167.3, 150.2, 148.0, 140.4, 131.0, 127.7, 127.6, 125.7, 125.0, 123.0, 120.1, 114.7, 114.2, 109.8, 83.7, 55.8, 52.2, 27.9; HRMS−FAB$^+$ (*m/z*) $M^+$ calcd for $C_{20}H_{21}NO_5$ 355.1420, found 355.1413.

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**Mukonine (13).**[26,27a] To a solution of *N*-Boc-mukonine (**12**, 27 mg, 0.077 mmol) in dichloromethane (2.6 mL) was slowly added 0.1% trifluoroacetic acid anhydride in trifluoroacetic acid (0.23 mL) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C and additionally stirred for 2 h at 20 °C. After the volatile materials were removed under reduced pressure, the resulting residue was purified by silica gel column chromatography with hexane/ethyl acetate (3/1, $R_f$ 0.39) to afford mukonine (19 mg, 0.075 mmol, 97%) as a white solid. The structure was identified based on the $^1$H and $^{13}$C NMR spectral data:[26,27a] $^1$H NMR ($CDCl_3$) $\delta$ 8.48 (dd, $J$ = 1.1, 0.6 Hz, 1H), 8.47 (bs, 1H), 8.10 (m, 1H), 7.60 (d, $J$ = 1.1 Hz, 1H), 7.49 (ddd, $J$ = 8.1, 1.3, 0.8 Hz, 1H), 7.46 (ddd, $J$ = 8.1, 6.8, 1.1, 1H), 7.28 (ddd, $J$ = 8.1, 1.3, 0.8 Hz, 1H), 4.07 (s, 3H), 3.98 (s, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 168.0, 145.0, 139.5, 132.9, 126.3, 123.7, 123.6, 121.9, 120.7, 120.3, 116.2, 111.2, 106.7, 55.7, 52.0.

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**Supporting Information Available:** $^1$H and $^{13}$C NMR spectra for compounds **11** and **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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