Synthesis of Carbazoles

The Double *N*-Arylation of Primary Amines: Toward Multisubstituted Carbazoles with Unique Optical Properties**

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Carbazole has been known as an important intermediate for artificial dyes and has recently attracted much attention because of its unique photophysical properties.[1] The introduction of substituents onto carbazole is essential to optimize its absorption, luminescence, and electronic properties.[2] For the synthesis of multisubstituted carbazole derivatives, the construction of the carbazole ring itself is highly desired.[3]

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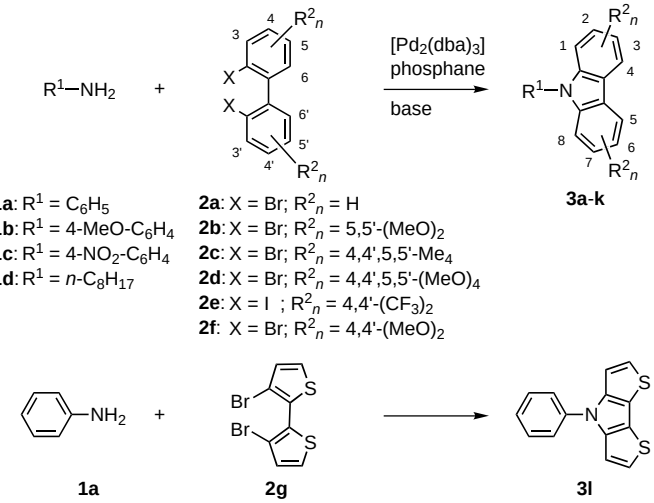
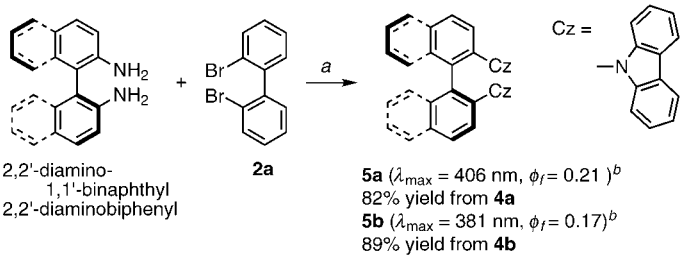
The availability of substituted 2,2′-dihalobiphenyl compounds[4] prompted us to study the double *N*-arylation strategy to synthesize multisubstituted carbazoles as described in Scheme 1. In contrast to conventional carbazole-



Scheme 1. The double *N*-arylation of primary amines in the synthesis of carbazoles (dba = *trans,trans*-dibenzylideneacetone).

ring construction strategies starting from *ortho*-aminobiphenyl compounds,[4b,5,6] the nitrogen atom comes from primary amines in the present double *N*-arylation strategy. Although the double arylation of primary amines was successfully accomplished for the synthesis of triarylamines, the method has not yet been applied to the synthesis of carbazoles.[7] Herein we report that the present method is especially effective for the synthesis of sterically crowded 2,2′-dicarbazolyl-1,1′-biaryl compounds **5a** and **5b**, which could not be synthesized by the simple arylation of carbazole (Scheme 2). The unique optical properties of **5a** and **5b** are also disclosed.

Based on the recent intensive studies on the catalytic *N*-arylation of amines with organic halides,[8] $[Pd_2(dba)_3]$/tBu_3P/NaO*t*Bu (condition A),[9] was first employed for our purpose. Representative results are summarized in Table 1, which also contains the fluorescence data of the resulting carbazoles **3a–l**. The reaction was applicable to various dihalobiphenyl



Scheme 2. Synthesis and optical properties of dicarbazolylbiaryl compounds **5a** and **5b**. a) Reaction conditions: **4** (0.50 mmol), **2a** (1.20 mmol), $[Pd_2(dba)_3]$ (0.050 mmol), tBu_3P (0.20 mmol), NaO*t*Bu (2.40 mmol), toluene (2.0 mL), 80 °C, 24 h. b) Fluorescence spectra were measured in cyclohexane (excited at 295 nm).

Table 1: Synthesis of carbazoles **3a–l** and their fluorescence data.

Entry	1	2	3	Yield [%][a]	λ_{max} [nm^{-1}] (ϕ_f)[b]
1	**a**	**a**	**a**	86^A	342 (0.23)
2	**a**	**b**	**b**	90^A	383 (0.18)
3	**a**	**c**	**c**	53^A	349 (0.42)
4	**a**	**d**	**d**	76^A	373 (0.18)
5	**a**	**e**	**e**	73^A	361 (0.20)
6	**a**	**f**	**f**	67^B	345 (0.19)
7	**b**	**a**	**g**	92^A	347 (0.21)
8	**b**	**b**	**h**	88^A	386 (0.24)
9	**c**	**a**	**i**	84^C	—[c]
10	**c**	**b**	**j**	8^D	—[c]
11	**d**	**a**	**k**	28^A	347 (0.30)
12	**a**	**g**	**l**	35^A	—[c]

[a] Reaction conditions A–D are noted as superscripts. Condition A: **1** (1.00 mmol), **2** (1.20 mmol), $[Pd_2(dba)_3]$ (0.05 mmol), tBu_3P (0.20 mmol), NaO*t*Bu (2.40 mmol), toluene (2 mL), 80 °C. Reaction times are specified in the Supporting Information. Condition B: **1** (1.00 mmol), **2** (2.00 mmol), $[Pd_2(dba)_3]$ (0.05 mmol), tBu_3P (0.20 mmol), NaO*t*Bu (2.40 mmol), toluene (2 mL), 80 °C, 24 h, then 100 °C, 24 h. Condition C: **1** (1.00 mmol), **2** (1.20 mmol), $[Pd_2(dba)_3]$ (0.05 mmol), (*S*)-binap (0.15 mmol), Cs_2CO_3 (2.80 mmol), toluene (2 mL), 100 °C, 72 h. Condition D: **1** (1.00 mmol), **2** (1.20 mmol), $[Pd_2(dba)_3]$ (0.05 mmol), 2-[di(*tert*-butyl)phosphanyl]biphenyl (0.20 mmol), and K_3PO_4 (2.80 mmol), dimethoxyethane (2 mL), 100 °C, 72 h. [b] Fluorescence spectra were measured in cyclohexane. [c] No clear peaks were observed for **3i, 3j, 3l**.

compounds **2a–e** (Table 1, entries 1–5). 4,4′-Dimethoxy-2,2′-dibromobiphenyl (**2f**) showed a lower reactivity and was used in excess at a higher temperature (Table 1, entry 6, condition B). Substituted anilines can be employed. 4-Methoxyaniline (**1b**) was preferable (Table 1, entries 7 and 8), whereas the reaction was retarded with 4-nitroaniline (**1c**). In such a case, a combination of binap[10] and Cs_2CO_3 was effective (Table 1, entry 9, condition C). The reaction of **1c** with **2b** did not proceed under conditions A, B, or C. The coupling product was finally obtained in a small amount by using 2-di(*tert*-butyl)phosphanylbiphenyl[11] and K_3PO_4 in DME (Table 1, entry 10, condition D). A lower reactivity was observed with the aliphatic amine **1d** (Table 1, entry 11). A dithienopyrrole, **3g**, could be synthesized through double *N*-arylation starting from bithiophene **2g** (Table 1, entry 12).

The method is especially effective for sterically hindered aryl amines as shown in Scheme 2. Starting from (*S*)-2,2′-diamino-1,1′-binaphthyl (**4a**) and more than 2 molar amounts of 2,2′-dibromobiphenyl (**2a**), *N*-arylation took place four times per molecule of **4a** to afford the desired chiral dicarbazolylbinaphthyl **5a** in 82% yield. Tri(*tert*-butyl)phosphane was the ligand of choice. Dicarbazolylbiphenyl **5b** was similarly prepared from 2,2′-diaminobiphenyl (**4b**) and **2a**. An alternative approach to **5** in which 2,2′-dibromo-1,1′-binaphthyl (racemic, **6**) or 2,2′-dibromobiphenyl (**2a**) were treated with more than 2 molar amounts of carbazole failed. A Pd/phosphane[12] catalyst gave a monocoupling product, 2-carbazolyl-2′-bromobinaphthyl, in less than 8% yield from **6**. The use of a Ni or Cu catalyst resulted in no reaction.[13]

The fluorescence spectra of **5a** and **5b** both showed broad peaks, suggesting the formation of intramolecular excimers and/or exciplexes.[14,15] Furthermore, the fluorescence wavelengths of **5a** and **5b** significantly depend on the solvent

polarity.[16] When **5a** was excited at 295 nm, the emission peak underwent a red shift as the solvent polarity increased from cyclohexane (dielectric constant 2.0) to chloroform (4.7), and to acetonitrile (37.5) (Figure 1). This observation corresponds to the energetic stabilization of the polar excimer (and/or exciplex) by solvation.

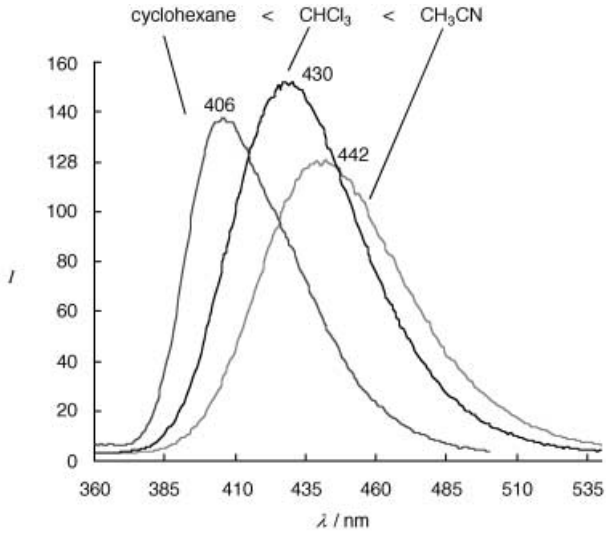


Figure 1. Solvent dependence of fluorescence of **5a**. Each solution (10 mM) was excited at 295 nm. I = intensity (arbitrary units).

In conclusion, we have presented a new strategy toward carbazole synthesis. Dicarbazolylbiaryl compounds **5a** and **5b**, which could not be synthesized by other methods, exhibited solvent-dependent excimer (and/or exciplex) emission. Taking advantage of its chiral nature, further studies on the chiroptical properties of **5a** are currently underway.

Experimental Section

5a: A solution of tri(*tert*-butyl)phosphane (40 mg, 0.20 mmol) in toluene (1.0 mL) was added to a mixture of **2a** (374 mg, 1.20 mmol), **4a** (142 mg, 0.50 mmol), sodium *tert*-butoxide (231 mg, 2.40 mmol), and $[Pd_2(dba)_3]$ (46 mg, 0.050 mmol) in toluene (1.0 mL). After heating under argon at 80 °C for 24 h, the reaction mixture was concentrated, and purification by silica-gel column chromatography afforded **5a** (240 mg, 82 %) as colorless needles. M.p. 277.6–278.1 °C; $R_f = 0.38$ (hexane/EtOAc = 5:1); $[\alpha]_D^{25} = -274.5$ ($c = 0.42$, $CHCl_3$); > 99 % *ee* (HPLC: Chiralcel OD, hexane/*i*PrOH = 99:1, $t_R = 7.9$ min (*R*), 10.4 min (*S*)); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.95$ (d, 2H, $J =$ 8.0 Hz), 7.88–7.78 (m, 6H), 7.68–7.51 (m, 6H), 7.14 (d, 2H, $J =$ 8.8 Hz), 6.96 (dd, 2H, $J = 7.2$, 7.2 Hz), 6.85–6.60 (m, 6H), 6.45 (dd, 2H, $J = 7.7$, 7.7 Hz), 5.57 ppm (d, 2H, $J = 8.2$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 142.1$, 140.8, 135.8, 134.3, 133.0, 131.4, 128.6, 128.1, 127.3, 126.7, 126.3, 125.4, 124.4, 123.7, 119.6, 119.5, 119.2, 118.8, 110.6, 110.2 ppm; MS (FAB$^+$): *m*/*z* (%): 584 (148.7), 585 (122.4), 586 (44.6), 587 (12.4); HRMS (FAB$^+$): calcd for $C_{44}H_{28}N_2$: M^+ 584.2252M, found: *m*/*z* 584.2257; elemental analysis: calcd for **5a**·$CHCl_3$ ($C_{45}H_{29}N_2Cl_3$): C 76.76, H 4.15; found: C 76.82, H 4.14; absorption (λ_{max} nm (log ε)): in cyclohexane: 341 (3.89), 294 (4.51), 229 (5.20); in $CHCl_3$: 343 (3.78), 305 (4.47), 297 (4.45); in CH_3CN: 340 (4.01), 293 (4.48), 228 (5.20); emission: λ_{max} nm in cyclohexane: 407 ($\phi_f = 0.21$); in $CHCl_3$: 430 ($\phi_f = 0.18$); in CH_3CN: 442 ($\phi_f = 0.13$) (quantum yields estimated with reference to *p*-terphenyl ($\phi_f = 0.87$ in cyclohexane when excited at 265 nm)).

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[13] See Supporting Information for experimental details.

[14] Typically, *N*-arylmonocarbazoles exhibit sharp emission peaks, for example, at 342 and 358 nm in cyclohexane for **3a**.

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