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Site-Specific Synthesis of Carbazole Derivatives through Aryl Homocoupling and Amination

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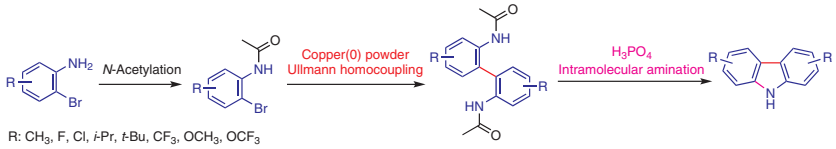

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Abstract We synthesized various carbazoles from anilines through a three-step process with good overall yields (up to 48%). This process comprises *N*-acetylation, copper(0)-mediated Ullmann homocoupling, and acid-mediated intramolecular amination. It permits various functional groups on the substrate. Scale-up of the developed three-step synthetic route to carbazoles was also demonstrated.

Key words *N*-acetylation, aryl homocoupling, Ullmann coupling reaction, Täuber carbazole synthesis, intramolecular amination

Carbazoles are a distinctive class of compounds that have formidable impact due to diverse biological activities[1–3] including anticancer[4–7] and antiparasitic roles.[8,9] There have been numerous studies on carbazoles and their synthetic routes due to their excellent material properties for use as optoelectronic devices,[10] solar cells,[11,12] photo-initiator catalysts,[13,14] chemical and biosensors,[15] luminogens,[16,17] and organic light-emitting diodes[18–21] (Figure 1).

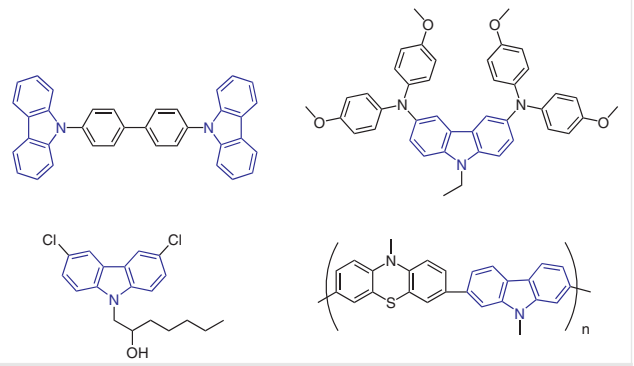

Figure 1 Some carbazoles used for their electronic properties

In view of the paramount significance of carbazoles, numerous methods for the synthesis of carbazole derivatives have been reported.[2,22,23] Recently, transition metals such as rhodium-,[24] palladium-,[25–27] copper-,[28] and cobalt-catalyzed,[29] some other heterogeneous catalysts,[30,31] and even iodine-[32,33] and acid-catalyzed[34–36] reactions have been utilized in the key step in carbazole syntheses. Visible-light-induced synthetic routes[37,38] have also made notable contributions to carbazole synthetic protocols. The aforementioned synthetic routes to carbazoles demonstrate high yields under mild reaction conditions, but are lacking in aspects such as N_2 gas liberation and the use of expensive noble metals, ligands, or additives. In contrast, the current study emphasizes cost-effective and scalable synthetic routes to carbazoles. The Täuber carbazole synthesis[39] appeared to be a reasonable method for a site-specific reaction to synthesize the corresponding carbazole. Therefore, substituted biphenyl-2,2′-diamines are used as key intermediates to afford the corresponding carbazoles through intramolecular amination by Täuber carbazole synthesis. Scheme 1 summarizes overall the reactions of the present work.

Carbazole synthesis was accomplished in three steps starting with *N*-acetylation of various anilines using 4-(dimethylamino)pyridine (DMAP) as a catalyst. Commercially available copper(0) powder was then used to catalyze an Ullmann homocoupling reaction of the synthesized acetanilides to produce 2,2′-bisanilides.[40–42] The final step converted these 2,2′-bisanilides into carbazoles through Täuber carbazole synthesis.

Initially, we envisaged a synthetic route to carbazoles using 2-halonitroaryl precursors instead of 2-haloanilines. However, the result of this sequence was an inseparable mixture of carbazoles, as shown in Scheme 2. Retrosynthetically, the Täuber carbazole synthesis could help to achieve

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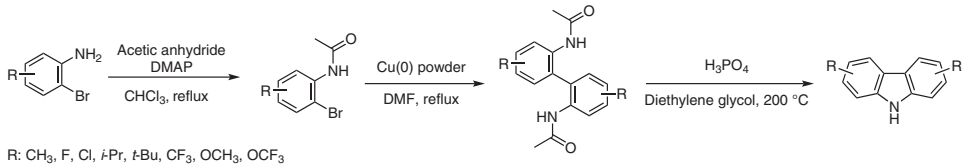
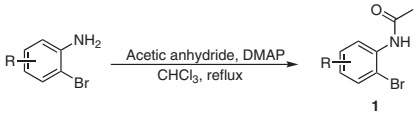
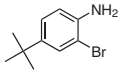
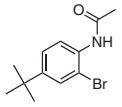
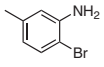
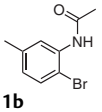
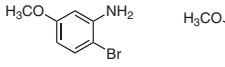
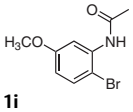
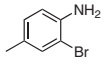
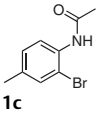
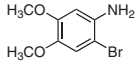
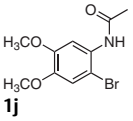
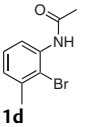
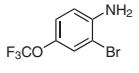
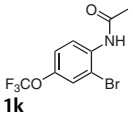
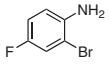
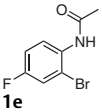
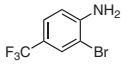
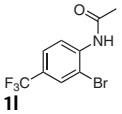
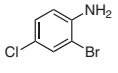
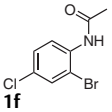
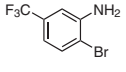
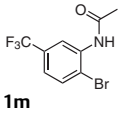
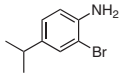
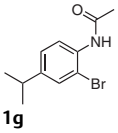
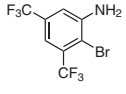
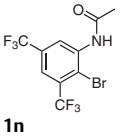


Scheme 1 Three-step reaction sequence for carbazole synthesis

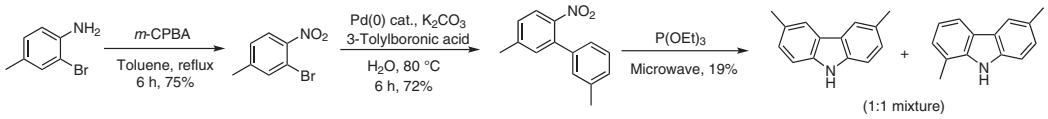
the site-specific synthesis of carbazoles. Therefore, a suitable intermediate, the substituted biphenyl-2,2′-diamine, was synthesized through copper-mediated Ullmann coupling.[43] However, the Ullmann coupling reaction is facilitated by electron-withdrawing groups, with which anilines are unsuitable starting materials as they may lead to a

Table 1 Results of *N*-Acetylation with Various Anilines[a]

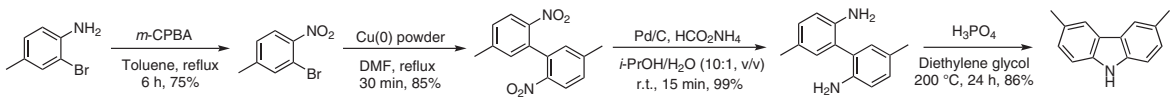


Entry	Aniline	Product	Time (h)	Yield (%)[b]	Entry	Aniline	Product	Time (h)	Yield (%)[b]
1		 **1a**	0.5	quant.	8		 **1h**	3	quant.
2		 **1b**	2	quant.	9		 **1i**	2	quant.
3		 **1c**	2	quant.	10		 **1j**	2	99
4		 **1d**	1	99	11		 **1k**	5	quant.
5		 **1e**	12	97	12		 **1l**	48	98
6		 **1f**	6	99	13		 **1m**	24	93
7		 **1g**	3	quant.	14		 **1n**	60	98

[a] Reaction conditions: aniline (5.0 mmol), Ac_2O (5.0 mmol), DMAP (0.25 mmol), $CHCl_3$ (25 mL).
[b] Isolated yield.



Scheme 2 Carbazole synthesis from a 2-halonitroaryl compound



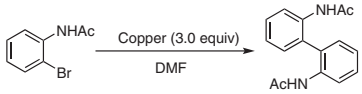
Scheme 3 A synthetic process for carbazoles from anilines

competing C–N coupling reaction catalyzed by copper(0).[44] Moreover, reduction of the nitro group would require an additional step involving use of a metal catalyst (Scheme 3).

In view of these concerns, the synthetic route was amended utilizing the copper(0)-mediated homocoupling reaction of an acetanilide[45–48] to reduce the number of steps by removing the amino-nitro conversion. Acetylation of relatively inexpensive anilines was designed into a carbazole synthesis, providing a benefit from the electron-withdrawing effect. Acetyl groups can be removed under acid catalysis, which also serves to catalyze intramolecular amination to generate the corresponding carbazoles. Scheme 1 summarizes the designed synthetic route to carbazoles. The onset of synthesis was *N*-acetylation of commercially available anilines[49] without using any base, ensuring the cost effectiveness of the process. The reaction was catalyzed by DMAP, and a variety of 2-haloanilines gave quantitative yields of acetanilides, as shown in Table 1. The synthesized acetanilides were subjected to the copper(0)-mediated Ullmann homocoupling reaction. Recent studies have demonstrated Ullmann coupling reactions with diverse ligands under mild reaction conditions such as room temperature and short reaction time.[45–48] However, the use of ligands increases the cost and impairs scale-up reactions. Therefore, we investigated the copper-mediated Ullmann homocoupling reaction without any ligands. A range of copper sources from metallic copper powder to Cu^{+} and Cu^{2+} salts was examined. Of all experiments to optimize the reaction conditions, Cu(0) gave the best results for the Ullmann coupling reaction (Table 2). The optimized conditions are making the most of relatively inexpensive copper powder of all the enlisted cooper sources in the absence ligands. The reaction did not occur below the reflux temperature of DMF (Table 2, entries 1 and 2). However, at reflux temperature, only a short reaction time was required (entry 3). Copper(I) and copper(II) did not facilitate the homocoupling reaction (entries 6–9). In addition, the reaction was found to be insensitive to air as inert conditions had no effect on the yield (entry 4). Ullmann coupling using *N*-(2-iodophenyl)acetamide as reactant gave a similar result to *N*-(2-bromophenyl)acetamide (**1a**), as shown in entry 5.

The aptitude of the optimized reaction conditions was assessed using an assortment of substituted *o*-bromoacetanilides that gave good to moderate yields of substituted 2,2′-bis(acetamido)biphenyls (Table 3). The reaction is facile, with both electron-withdrawing and electron-donating substituents on the aryl skeleton, though the former provided slightly better yields. For all the Ullmann coupling experiments conducted, debrominated starting material was also obtained with the desired product. Especially with trifluoromethyl substitution on the *o*-bromoacetanilide (Table 3, entry 14), debrominated starting material, *N*-(3,5-bis(trifluoromethyl)phenyl)acetamide, only was obtained.[50] Ullmann coupling was followed by Täuber carbazole ring closure that still needed optimization for the present system. To optimize this intramolecular amination, various experiments were performed, as listed in Table 4. Preliminary

Table 2 Optimization of the Copper-Mediated Ullmann Homocoupling Reaction[a]



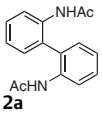
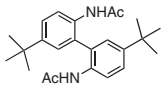
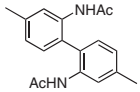
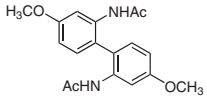
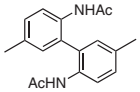
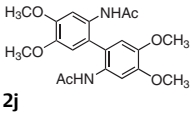
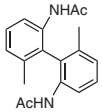
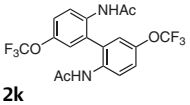
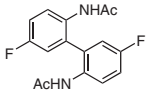
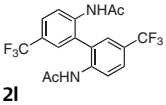
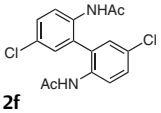
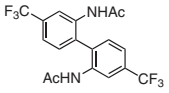
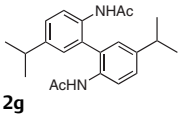
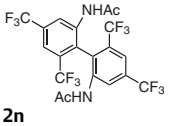
1a **2a**

Entry	Copper	Temp (°C)	Time (h)	Yield (%)[b]
1	Cu(0) powder	100	1	–[c]
2	Cu(0) powder	120	1	–[c]
3	**Cu(0) powder**	**reflux**	**1**	**43**
4	Cu(0) powder	reflux	1	45[d]
5	Cu(0) powder	reflux	1	33[e]
6	CuI	reflux	1	–[c]
7	CuOAc	reflux	1	–[c]
8	$CuSO_4$	reflux	1	–[c]
9	$CuBr_2$	reflux	1	–[c]

[a] Reaction conditions: *N*-(2-bromophenyl)acetamide (**1a**; 1.0 mmol), copper (3.0 mmol), DMF (5.0 mL).
[b] Isolated yield.
[c] No reaction.
[d] Under an inert atmosphere of argon.
[e] Starting material is *N*-(2-iodophenyl)acetamide.

Table 3 Substrate Scope of the Copper(0)-Mediated Ullmann Homocoupling Reaction[a]

1 2

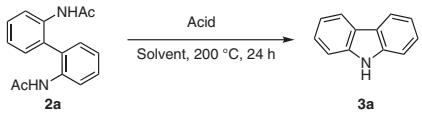
Entry	Acetanilide	Product	Time (h)	Yield (%)[b]	Entry	Acetanilide	Product	Time (h)	Yield (%)[b]
1	**1a**	 **2a**	1	43	8	**1h**	 **2h**	2	35
2	**1b**	 **2b**	1	52	9	**1i**	 **2i**	1	54
3	**1c**	 **2c**	1	52	10	**1j**	 **2j**	1	62
4	**1d**	 **2d**	2	30	11	**1k**	 **2k**	1	77
5	**1e**	 **2e**	1	70	12	**1l**	 **2l**	1	74
6	**1f**	 **2f**	1	66	13	**1m**	 **2m**	1	71
7	**1g**	 **2g**	2	45	14	**1n**	 **2n**	1	–[c]

[a] Reaction conditions: acetanilide (1, 2.0 mmol), Cu(0) powder (6.0 mmol), DMF (10 mL).
[b] Isolated yield of product.
[c] Starting material was completely converted into *N*-[3,5-bis(trifluoromethyl)phenyl]acetamide.

attempts were to identify an appropriate solvent for the reaction in the presence of phosphoric acid. After affirming that diethylene glycol best served this purpose (entry 7), a diverse library of acids was tested for intramolecular amination (entries 8–19). Substrate scope for intramolecular amination showed moderate to good yields of carbazoles (Table 5). For entries 12 and 13, detrifluoromethylated compound **3a** was obtained instead of the desired products (**3i**, **3j**); other research groups have also observed detrifluoromethylation of (trifluoromethyl)arenes under strongly acidic conditions.[51,52]

A scale-up reaction starting with 10 g of 2-bromo-4-fluoroaniline was carried out in which 3,6-difluoro-9*H*-carbazole (**3e**) was collected in 48% overall yield. In this case, recrystallization was used as the prime purification method in contrast to column chromatography for smaller laboratory-scale synthesis. It is noteworthy that both aforementioned purification techniques were facile for the intermediates and products. Moreover, none of the reaction conditions were found alarming at scaled up reactions.

Table 4 Optimization of Intramolecular Amination for Carbazole Synthesis[a]



2a **3a**

Entry	Acid	Solvent	Yield (%)[b]
1	H_3PO_4	–	16
2	H_3PO_4	nitrobenzene	–[c]
3	H_3PO_4	NMP	–[c]
4	H_3PO_4	ethylene glycol	32
5	H_3PO_4	triethylene glycol	25
6	H_3PO_4	4-*tert*-butyl-*o*-toluene	–[c]
7	**H_3PO_4**	**diethylene glycol**	**67**
8	PPA	diethylene glycol	57
9	$HClO_4$	diethylene glycol	–[c]
10	H_2SO_4	diethylene glycol	–[c]
11	dodecylbenezenesulfonic acid	diethylene glycol	–[c]
12	TsOH	diethylene glycol	–[c]
13	Amberlyst 15H$^+$	diethylene glycol	–[c]
14	Nafion H	diethylene glycol	–[c]
15	silica sulfuric acid	diethylene glycol	–[c]
16	phosphotungstic acid	diethylene glycol	–[c]
17	phosphomolybdic acid	diethylene glycol	–[c]
18	silicomolybdic acid	diethylene glycol	–[c]
19	$FeCl_3$	diethylene glycol	11

[a] Reaction conditions: 2,2′-bisacetanilide (**2a**; 1.0 mmol), acid (10.0 mmol), solvent (5 mL).
[b] Isolated yield.
[c] No reaction.

In conclusion, the synthesis of diverse symmetrical carbazoles was carried out with a library of anilines. The synthetic strategy takes advantage of commercially inexpensive reagents. The three-step process, *N*-acetylation, copper(0)-mediated homocoupling reaction, and acid-mediated intramolecular amination, does not require the use of additives. The current method is amenable to scale-up, as demonstrated experimentally at the multigram level. These functionalized carbazoles are expected to allow diverse material applications in the future. The current work is further under investigation for cross Ullmann coupling reaction using functionalized acetanilides precursors.

All chemicals were purchased from commercial sources (Sigma Aldrich, TCI, and Alfa Aesar) and were used without any further purification, unless specifically mentioned. Analytical TLC was conducted on Merck 60 F254 glass-backed silica gel plates (0.2 mm) with a fluorescent indicator. ^{1}H NMR spectroscopy was performed using $CDCl_3$ or DMSO-d_6 containing TMS as an internal standard. Chemical shifts (δ) are reported in ppm and are quoted to the nearest 0.01 ppm relative to the residual protons in $CDCl_3$ or DMSO-d_6. Infrared spectra were recorded on a Bruker Alpha FT-IR spectrometer. Melting points were determined with a Sanyo Gallenkamp melting point apparatus. HRMS data were obtained on a high-resolution mass spectrometer (JMS-700) equipped with double-focusing mass analyzers at the Daegu Center of the Korea Basic Science Institute.

N-Acetylation; General Procedure

In a 50-mL, round-bottom flask, aniline (5.0 mmol, 1.0 equiv) was dissolved in $CHCl_3$ (20 mL), followed by addition of DMAP (0.031 g, 0.25 mmol, 5 mol%). Ac_2O (0.51 g, 5.0 mmol, 1.0 equiv) was added dropwise, and the mixture was stirred at reflux temperature (TLC monitoring) until completion. The mixture was cooled to r.t. and washed with distilled water. The organic layer was dried (anhyd $MgSO_4$), followed by removal of solvent under reduced pressure to obtain the crude product, which was purified by flash chromatography (EtOAc/*n*-hexane).

N-(2-Bromophenyl)acetamide (1a)[53]

White solid; yield: 1.07 g (quant.); mp 96.0–96.5 °C; R_f = 0.25 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 8.0 Hz, 1 H), 7.62 (br s, 1 H), 7.53 (d, *J* = 8.0 Hz, 1 H), 7.31 (t, *J* = 7.2 Hz, 1 H), 6.97 (t, *J* = 7.2 Hz, 1 H), 2.24 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 135.6, 132.1, 128.3, 125.1, 121.9, 113.2, 24.9.

N-(2-Bromo-5-methylphenyl)acetamide (1b)[53]

White solid; yield: 1.17 g (quant.); mp 122.5–123.0 °C; R_f = 0.63 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 7.56 (br s, 1 H), 7.38 (d, *J* = 8.0 Hz, 1 H), 6.79 (d, *J* = 8.0 Hz, 1 H), 2.31 (s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 138.6, 135.2, 131.7, 126.0, 122.5, 109.9, 24.9, 21.3.

N-(2-Bromo-4-methylphenyl)acetamide (1c)[53]

White solid; yield: 1.16 g (quant.); mp 119.0–119.5 °C; R_f = 0.33 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.4 Hz, 1 H), 7.51 (br s, 1 H), 7.35 (s, 1 H), 7.11 (d, *J* = 8.4 Hz, 1 H), 2.29 (s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 135.2, 133.1, 132.4, 129.0, 121.8, 113.1, 24.8, 20.5.

N-(2-Bromo-3-methylphenyl)acetamide (1d)[54]

White solid; yield: 1.14 g (99%); mp 144.5–145.0 °C; R_f = 0.33 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 6.8 Hz, 1 H), 7.72 (br s, 1 H), 7.19 (t, *J* = 7.6 Hz, 1 H), 6.99 (d, *J* = 7.2 Hz, 1 H), 2.41 (s, 3 H), 2.23 (s, 3 H).

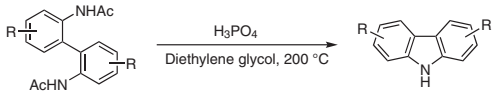
^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 138.3, 135.7, 127.7, 126.1, 119.4, 116.1, 24.8, 23.8.

N-(2-Bromo-4-fluorophenyl)acetamide (1e)[55]

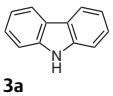
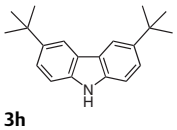
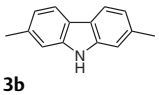
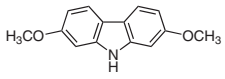
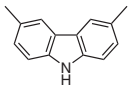
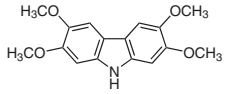
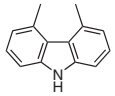
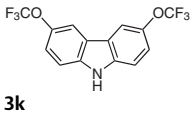
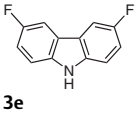
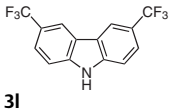
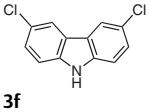
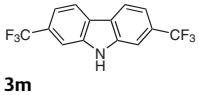
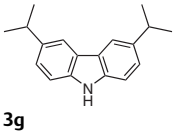
White solid; yield: 1.12 g (97%); mp 118.0–119.0 °C; R_f = 0.20 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (dd, *J* = 8.4, 5.6 Hz, 1 H), 7.53 (br s, 1 H), 7.27 (d, *J* = 5.2 Hz, 1 H), 7.03 (t, *J* = 7.2 Hz, 1 H), 2.22 (s, 3 H).

Table 5 Substrate Scope of Acid-Mediated Intramolecular Amination[a]



2 3

Entry	Bisacetanilide	Product	Time (h)	Yield (%)[b]	Entry	Bisacetanilide	Product	Time (h)	Yield (%)[b]
1	**2a**	 **3a**	24	67	8	**2h**	 **3h**	24	74
2	**2b**	 **3b**	24	78	9	**2i**	 **3i**	24	44
3	**2c**	 **3c**	24	65	10	**2j**	 **3j**	24	52
4	**2d**	 **3d**	24	32	11	**2k**	 **3k**	24	31
5	**2e**	 **3e**	24	71	12	**2l**	 **3l**	48	(83)[c]
6	**2f**	 **3f**	24	57	13	**2m**	 **3m**	30	(75)[c]
7	**2g**	 **3g**	24	61					

[a] Reaction conditions: 2,2′-bisacetanilide **2** (0.5 mmol), H_3PO_4 (5.0 mmol), diethylene glycol (5.0 mL).
[b] Isolated yield.
[c] 9*H*-Carbazole (**3a**) was obtained as the product.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 158.4 (d, *J* = 246.3 Hz), 132.1, 123.3 (d, *J* = 8.0 Hz), 119.2 (d, *J* = 25.5 Hz), 115.1 (d, *J* = 21.5 Hz), 113.6 (d, *J* = 10 Hz), 24.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –116.1.

***N*-(2-Bromo-4-chlorophenyl)acetamide (1f)**[55]

White solid; yield: 1.23 g (99%); mp 138.0–138.5 °C; R_f = 0.25 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 8.8 Hz, 1 H), 7.56 (br s, 1 H), 7.53 (d, *J* = 2.4 Hz, 1 H), 7.28 (dd, *J* = 8.8, 2.4 Hz, 1 H), 2.24 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 134.5, 131.7, 129.4, 128.5, 122.4, 113.2, 24.9.

***N*-(2-Bromo-4-isopropylphenyl)acetamide (1g)**[55]

White solid; yield: 1.28 g (quant.); mp 132.0–132.5 °C; R_f = 0.38 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.0 Hz, 1 H), 7.55 (br s, 1 H), 7.38 (s, 1 H), 7.16 (d, *J* = 8.0 Hz, 1 H), 2.84 (sept, *J* = 6.8 Hz, 1 H), 2.22 (s, 3 H), 1.21 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 146.3, 133.2, 129.9, 126.4, 122.1, 113.4, 33.4, 24.7, 23.8.

***N*-(2-Bromo-4-*tert*-butylphenyl)acetamide (1h)**[56]

White solid; yield: 1.35 g (quant.); mp 160.0–160.5 °C; R_f = 0.38 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 8.4 Hz, 1 H), 7.52 (br s, 1 H), 7.51 (d, *J* = 2.0 Hz, 1 H), 7.32 (dd, *J* = 8.4, 2.0 Hz, 1 H), 2.22 (s, 3 H), 1.28 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 148.7, 133.0, 129.0, 125.4, 121.7, 113.3, 34.4, 31.1, 24.7.

***N*-(2-Bromo-5-methoxyphenyl)acetamide (1i)**[57]

White solid; yield: 1.22 g (quant.); mp 117–118 °C; R_f = 0.20 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 1.6 Hz, 1 H), 7.60 (br s, 1 H), 7.37 (d, *J* = 8.8 Hz, 1 H), 6.55 (dd, *J* = 8.8, 2.8 Hz, 1 H), 3.79 (s, 3 H), 2.23 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 159.4, 136.3, 132.1, 111.6, 106.8, 103.2, 55.5, 24.9.

***N*-(2-Bromo-4,5-dimethoxyphenyl)acetamide (1j)**[58]

White solid; yield: 1.36 g (99%); mp 128–129 °C; R_f = 0.10 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (s, 1 H), 7.43 (br s, 1 H), 6.97 (s, 1 H), 3.88 (s, 3 H), 3.84 (s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 148.4, 145.8, 129.2, 114.3, 105.8, 102.8, 56.2, 56.0, 24.7.

***N*-[2-Bromo-4-(trifluoromethoxy)phenyl]acetamide (1k)**[59]

White solid; yield: 1.49 g (quant.); mp 125.0–125.5 °C; R_f = 0.20 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39 (d, *J* = 8.8 Hz, 1 H), 7.58 (br s, 1 H), 7.43 (d, *J* = 2.0 Hz, 1 H), 7.20 (d, *J* = 8.8, 2.8 Hz, 1 H), 2.25 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 144.6, 134.6, 124.9, 122.2, 121.1, 120.3 (q, *J* = 256.4 Hz), 112.8, 24.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –58.2.

***N*-[2-Bromo-4-(trifluoromethyl)phenyl]acetamide (1l)**[60]

White solid; yield: 1.38 g (98%); mp 146.5–147.0 °C; R_f = 0.33 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.53 (d, *J* = 8.4 Hz, 1 H), 7.79 (s, 1 H), 7.74 (br s, 1 H), 7.56 (d, *J* = 8.4 Hz, 1 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 138.7, 129.2 (q, *J* = 3.9 Hz), 126.7 (q, *J* = 33.3 Hz), 125.6 (q, *J* = 3.6 Hz), 123.1 (q, *J* = 270.4 Hz), 121.1, 112.4, 24.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.3.

***N*-[2-Bromo-5-(trifluoromethyl)phenyl]acetamide (1m)**[54]

White solid; yield: 1.32 g (93%); mp 142.5–143.0 °C; R_f = 0.33 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.71 (s, 1 H), 7.69 (br s, 1 H), 7.66 (d, *J* = 8.4 Hz, 1 H), 7.23 (dd, *J* = 8.4, 1.6 Hz, 1 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 136.2, 132.6, 130.8 (q, *J* = 32.7 Hz), 123.4 (q, *J* = 270.9 Hz), 121.4 (q, *J* = 3.6 Hz), 118.4 (q, *J* = 3.5 Hz), 116.2, 24.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.8.

***N*-[2-Bromo-3,5-bis(trifluoromethyl)phenyl]acetamide (1n)**[61]

White solid; yield: 1.72 g (98%); mp 152.5–153.0 °C; R_f = 0.33 (EtOAc/*n*-hexane 1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.93 (s, 1 H), 7.98 (br s, 1 H), 7.68 (d, *J* = 1.2 Hz, 1 H), 2.31 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 138.2, 131.5 (q, *J* = 32.0 Hz), 130.8 (q, *J* = 33.8 Hz), 122.8 (q, *J* = 271.7 Hz), 122.1 (q, *J* = 272.4 Hz), 121.4 (m), 119.2 (m), 114.1, 24.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –63.0, –63.2.

Copper(0)-Mediated Ullmann Homocoupling Reaction; General Procedure

In a 25-mL, round-bottom flask, *N*-(2-bromophenyl)acetamide **1** (2.0 mmol, 1.0 equiv) was dissolved in DMF (10 mL), followed by the addition of Cu(0) powder (0.38 g, 6.0 mmol, 3.0 equiv). The mixture was stirred at reflux temperature until completion. After completion, the mixture was cooled to r.t. and extracted with CH_2Cl_2, and the combined organic extracts were washed with brine solution. The organic layer was dried (anhyd $MgSO_4$), and the solvents were removed under reduced pressure. The crude product was purified by flash chromatography (EtOAc/CH_2Cl_2).

2,2′-Bis(acetamido)biphenyl (2a)[46]

White solid; yield: 0.12 g (43%); mp 166.0–166.5 °C; R_f = 0.15 (EtOAc/CH_2Cl_2 1:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.0 Hz, 2 H), 7.43 (td, *J* = 7.7, 1.5 Hz, 2 H), 7.27–7.19 (m, 4 H), 7.03 (br s, 2 H), 1.95 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.1, 135.3, 130.4, 129.2, 129.2, 125.2, 123.5, 24.0.

2,2′-Bis(acetamido)-4,4′-dimethylbiphenyl (2b)[62]

Pale yellow solid; yield: 0.15 g (52%); mp 196.0–197.0 °C; R_f = 0.15 (EtOAc/CH_2Cl_2 1:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (s, 2 H), 7.08–7.02 (m, 4 H), 6.90 (br s, 2 H), 2.41 (s, 6 H), 1.96 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 139.3, 135.3, 130.3, 125.9, 125.8, 123.5, 24.2, 21.4.

2,2′-Bis(acetamido)-5,5′-dimethylbiphenyl (2c)

Pale yellow solid; yield: 0.15 g (52%); mp 172.0–172.5 °C; R_f = 0.10 (EtOAc/CH_2Cl_2 1:5).

IR (neat): 3418, 3220, 3003, 1659, 1531, 1368, 1300, 830, 807 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.00 (s, 2 H), 6.97 (br s, 2 H), 2.36 (s, 6 H), 1.95 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.1, 134.9, 132.7, 130.9, 129.7, 129.5, 123.4, 23.9, 20.8.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{20}N_2O_2$: 296.1525; found: 296.1525.

2,2′-Bis(acetamido)-6,6′-dimethylbiphenyl (2d)[63]

Pale brown solid; yield: 0.089 g (30%); mp 55.0–56.0 °C; R_f = 0.45 (EtOAc/CH_2Cl_2 1:5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.52 (br s, 2 H), 7.48 (d, *J* = 8.0 Hz, 2 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 7.11 (d, *J* = 8.0 Hz, 2 H), 2.17 (s, 6 H), 2.04 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 168.4, 138.9, 136.0, 130.4, 130.0, 128.7, 123.4, 22.9, 19.0.

2,2′-Bis(acetamido)-5,5′-difluorobiphenyl (2e)

White solid; yield: 0.21 g (70%); mp 186.0–186.5 °C; R_f = 0.13 (EtOAc/CH_2Cl_2 1:5).

IR (neat): 3180, 3005, 1659, 1535, 1428, 1371, 1294, 1257, 1235, 1193, 1163, 873, 835, 819, 673, 596, 510, 501 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 9.0, 5.2 Hz, 2 H), 7.18–7.13 (m, 2 H), 6.94–6.91 (m, 4 H), 1.98 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.2, 159.4 (d, *J* = 244.6 Hz), 134.2, 132.5, 128.1, 117.6 (d, *J* = 23.2 Hz), 115.4 (d, *J* = 18.0 Hz), 23.4.

^{19}F NMR (376 MHz, DMSO-d_6): δ = –117.7.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{14}F_2N_2O_2$: 304.1023; found: 304.1025.

2,2′-Bis(acetamido)-5,5′-dichlorobiphenyl (2f)[63]

White solid; yield: 0.22 g (66%); mp 252.0–252.5 °C; R_f = 0.20 (EtOAc/CH_2Cl_2 1:5).

^1H NMR (400 MHz, DMSO-d_6): δ = 8.90 (br s, 2 H), 7.62 (d, *J* = 8.8 Hz, 2 H), 7.43 (dd, *J* = 8.8, 2.4 Hz, 2 H), 7.26 (d, *J* = 2.4 Hz, 2 H), 1.80 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.1, 135.2, 133.3, 130.9, 129.2, 128.6, 127.5, 23.5.

2,2′-Bis(acetamido)-5,5′-diisopropylbiphenyl (2g)

Pale yellow solid; yield: 0.16 g (45%); mp 170.0–170.5 °C; R_f = 0.15 (EtOAc/CH_2Cl_2 1:5).

IR (neat): 3393, 3342, 2956, 2922, 2866, 1675, 1588, 1516, 1362, 1303, 1250, 1035, 843, 643, 585, 530, 500, 470 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.4 Hz, 2 H), 7.28 (dd, *J* = 8.4, 1.7 Hz, 2 H), 7.06 (d, *J* = 1.2 Hz, 2 H), 7.00 (br s, 2 H), 2.92 (sept, *J* = 7.2 Hz, 2 H), 1.95 (s, 6 H), 1.26 (d, *J* = 7.2 Hz, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.1, 145.9, 132.9, 129.5, 128.3, 127.1, 123.5, 33.5, 24.0, 23.8.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{22}H_{28}N_2O_2$: 352.2151; found: 352.2153.

2,2′-Bis(acetamido)-5,5′-*tert*-butylbiphenyl (2h)

Pale yellow solid; yield: 0.13 g (35%); mp 172.0–172.5 °C; R_f = 0.22 (EtOAc/CH_2Cl_2 1:5).

IR (neat): 3419, 3337, 2955, 2905, 2869, 1677, 1584, 1513, 1468, 1385, 1361, 1317, 1300, 1254, 831, 569, 516, 502 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.4 Hz, 2 H), 7.46 (dd, *J* = 8.4, 2.0 Hz, 2 H), 7.21 (d, *J* = 2.0 Hz, 2 H), 6.89 (br s, 2 H), 1.95 (s, 6 H), 1.33 (s, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.0, 148.1, 132.7, 129.2, 127.3, 126.0, 123.2, 34.4, 31.2, 23.9.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{24}H_{32}N_2O_2$: 380.2464; found: 380.2467.

2,2′-Bis(acetamido)-4,4′-dimethoxybiphenyl (2i)[64]

White solid; yield: 0.18 g (54%); mp 181.5–182.0 °C; R_f = 0.10 (EtOAc/CH_2Cl_2 1:5).

^1H NMR (400 MHz, DMSO-d_6): δ = 8.58 (br s, 2 H), 7.29 (s, 2 H), 7.04 (d, *J* = 8.4 Hz, 2 H), 6.81 (d, *J* = 8.4 Hz, 2 H), 3.76 (s, 6 H), 1.83 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.2, 159.1, 137.3, 132.2, 124.5, 111.1, 110.7, 55.6, 23.7.

2,2′-Bis(acetamido)-4,4′,5,5′-tetramethoxybiphenyl (2j)[65]

Pale brown solid; yield: 0.24 g (62%); mp 204.0–204.5 °C; R_f = 0.08 (EtOAc/CH_2Cl_2 1:5).

^1H NMR (400 MHz, DMSO-d_6): δ = 8.62 (br s, 2 H), 7.20 (s, 2 H), 6.71 (s, 2 H), 3.75 (s, 6 H), 3.73 (s, 6 H), 1.83 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.3, 148.2, 146.4, 129.3, 125.1, 114.3, 110.2, 56.1, 56.0, 23.5.

2,2′-Bis(acetamido)-5,5′-bis(trifluoromethoxy)biphenyl (2k)

White solid; yield: 0.34 g (77%); mp 200.0–200.5 °C; R_f = 0.25 (EtOAc/CH_2Cl_2 1:5).

IR (neat): 3352, 1677, 1525, 1465, 1438, 1397, 1371, 1258, 1206, 1143, 1039, 1009, 835, 658, 593, 517 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 9.12 (br s, 2 H), 7.70 (d, *J* = 8.8 Hz, 2 H), 7.40 (dd, *J* = 8.8, 2.0 Hz, 2 H), 7.16 (d, *J* = 2.0 Hz, 2 H), 1.85 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.3, 145.4, 135.4, 133.4, 128.1, 123.5, 121.5, 120.5 (q, *J* = 254.7 Hz), 23.3.

^{19}F NMR (376 MHz, DMSO-d_6): δ = –56.8.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{14}F_6N_2O_4$: 436.0858; found: 436.0860.

2,2′-Bis(acetamido)-5,5′-bis(trifluoromethyl)biphenyl (2l)

White solid; yield: 0.30 g (74%); mp 231.0–232.0 °C; R_f = 0.25 (EtOAc/CH_2Cl_2 1:5).

IR (neat): 3362, 1685, 1592, 1523, 1471, 1399, 1375, 1309, 1260, 1229, 1118, 1076, 1031, 1006, 848, 681, 656, 639, 589, 504, 417 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 9.18 (br s, 2 H), 7.90 (d, *J* = 8.0 Hz, 2 H), 7.76 (d, *J* = 8.0 Hz, 2 H), 7.58 (d, *J* = 8.0 Hz, 2 H), 1.86 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.4, 139.9, 131.5, 128.6 (q, *J* = 3.6 Hz), 126.1, 125.8 (q, *J* = 3.7 Hz), 125.6 (q, *J* = 31.7 Hz), 124.7 (q, *J* = 270.2 Hz), 23.5.

^{19}F NMR (376 MHz, DMSO-d_6): δ = –60.4.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{14}F_6N_2O_2$: 404.0959; found: 404.0960.

2,2′-Bis(acetamido)-4,4′-bis(trifluoromethyl)biphenyl (2m)[66]

White solid; yield: 0.29 g (71%); mp 180.0–180.5 °C; R_f = 0.25 (EtOAc/CH_2Cl_2 1:5).

^1H NMR (400 MHz, DMSO-d_6): δ = 9.19 (br s, 2 H), 8.05 (s, 2 H), 7.60 (d, *J* = 7.2 Hz, 2 H), 7.44 (d, *J* = 8.0 Hz, 2 H), 1.86 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.5, 137.0, 135.7, 132.6, 129.3 (q, *J* = 31.6 Hz), 124.5 (q, *J* = 270.6 Hz), 122.1, 121.8, 23.6.

^{19}F NMR (376 MHz, DMSO-d_6): δ = –61.2.

Acid-Mediated Intramolecular Amination; General Procedure

In a 10-mL, round-bottom flask, 2,2′-bis(acetamido)biphenyl **2** (0.5 mmol, 1.0 equiv) was dissolved in diethylene glycol (10 mL), followed by addition of phosphoric acid (0.49 g, 5 mmol, 10 equiv). The mixture was stirred at 200 °C until completion and cooled to r.t. Organic components were extracted into CH_2Cl_2 and the combined organic extracts were washed with brine and dried (anhyd $MgSO_4$). Solvents were removed under reduced pressure to obtain the crude product, which was purified by flash chromatography (EtOAc/*n*-hexane).

9*H*-Carbazole (3a)[67]

Pale yellow solid; yield: 0.056 g (67%); mp 243.5–244.0 °C; R_f = 0.38 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.2 (br s, 1 H), 8.10 (d, *J* = 8.0 Hz, 2 H), 7.48 (d, *J* = 8.0 Hz, 2 H), 7.37 (td, *J* = 7.6, 1.1 Hz, 2 H), 7.15 (td, *J* = 7.6, 1.1 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 140.1, 125.9, 122.8, 120.6, 118.9, 111.3.

2,7-Dimethyl-9*H*-carbazole (3b)[68]

Pale yellow solid; yield: 0.076 g (78%); mp 290.0–291.0 °C; R_f = 0.50 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.0 Hz, 2 H), 7.78 (br s, 1 H), 7.15 (s, 2 H), 7.03 (d, *J* = 8.0 Hz, 2 H), 2.50 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 135.3, 121.0, 120.7, 119.6, 110.6, 21.9.

3,6-Dimethyl-9*H*-carbazole (3c)[69]

Pale yellow solid; yield: 0.063 g (65%); mp 219.0–220.0 °C; R_f = 0.50 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (m, 3 H), 7.27 (d, *J* = 8.0 Hz, 2 H), 7.20 (dd, *J* = 8.0, 0.7 Hz, 2 H), 2.51 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0, 128.4, 126.9, 123.3, 120.1, 110.1, 21.4.

4,5-Dimethyl-9*H*-carbazole (3d)[70]

Pale brown solid; yield: 0.031 g (32%); mp 175.0–176.0 °C; R_f = 0.50 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (br s, 1 H), 7.27 (m, 4 H), 6.99 (d, *J* = 6.4 Hz, 2 H), 3.01 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.0, 132.2, 125.4, 122.8, 122.6, 108.4, 26.0.

3,6-Difluoro-9*H*-carbazole (3e)[71]

Pale yellow solid; yield: 0.072 g (71%); mp 197.0–198.0 °C; R_f = 0.38 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.33 (br s, 1 H), 7.97 (dd, *J* = 9.2, 2.4 Hz, 2 H), 7.48 (dd, *J* = 8.8, 4.4 Hz, 2 H), 7.25 (td, *J* = 9.2, 2.4 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 156.6 (d, *J* = 230.8 Hz), 137.7, 122.9 (dd, *J* = 5.8, 4.2 Hz), 114.4 (d, *J* = 25.3 Hz), 112.6 (d, *J* = 9.1 Hz), 106.5 (d, *J* = 23.5 Hz).

^{19}F NMR (376 MHz, DMSO-d_6): δ = –125.0.

3,6-Dichloro-9*H*-carbazole (3f)[72]

Pale yellow solid; yield: 0.067 g (57%); mp 202.0–202.5 °C; R_f = 0.25 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.57 (br s, 1 H), 8.28 (d, *J* = 2.4 Hz, 2 H), 7.51 (d, *J* = 8.8 Hz, 2 H), 7.41 (dd, *J* = 8.8, 2.0 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 139.1, 126.6, 123.6, 123.3, 120.8, 113.2.

3,6-Diisopropyl-9*H*-carbazole (3g)[73]

Pale brown solid; yield: 0.077 g (61%); mp 153.0–155.0 °C; R_f = 0.58 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 2 H), 7.83 (br s, 1 H), 7.31 (d, *J* = 8.3 Hz, 2 H), 7.26 (dd, *J* = 8.3, 1.6 Hz, 2 H), 3.08 (sept, *J* = 6.9 Hz, 2 H), 1.35 (d, *J* = 6.9 Hz, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 138.3, 124.5, 123.4, 117.2, 110.2, 34.1, 24.7.

3,6-Di-*tert*-butyl-9*H*-carbazole (3h)[74]

Pale brown solid; yield: 0.10 g (74%); mp 228.0–229.0 °C; R_f = 0.58 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 1.2 Hz, 2 H), 7.84 (br s, 1 H), 7.45 (dd, *J* = 8.4, 1.2 Hz, 2 H), 7.32 (d, *J* = 8.4 Hz, 2 H), 1.44 (s, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.1, 137.9, 123.4, 123.2, 116.1, 109.9, 34.6, 32.0.

2,7-Dimethoxy-9*H*-carbazole (3i)[75]

Pale yellow solid; yield: 0.050 g (44%); mp 270.0–271.0 °C; R_f = 0.18 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.95 (br s, 1 H), 7.83 (d, *J* = 8.0 Hz, 2 H), 6.92 (d, *J* = 2.0 Hz, 2 H), 6.72 (dd, *J* = 8.0, 2.0 Hz, 2 H), 3.81 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.0, 141.4, 120.4, 116.9, 107.7, 95.1, 55.7.

2,3,6,7-Tetramethoxy-9*H*-carbazole (3j)[34]

White solid; yield: 0.075 g (52%); mp 224.0–225.0 °C; R_f = 0.03 (EtOAc/*n*-hexane 1:5).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.62 (br s, 1 H), 7.55 (s, 2 H), 6.96 (s, 2 H), 3.82 (s, 6 H), 3.81 (s, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 148.2, 143.8, 134.7, 115.4, 103.2, 95.3, 56.6, 56.1.

3,6-Bis(trifluoromethoxy)-9*H*-carbazole (3k)

Pale brown gummy solid; yield: 0.052 g (31%); R_f = 0.25 (EtOAc/CH_2Cl_2 1:5).

IR (neat): 3486, 3436, 2931, 2855, 1495, 1464, 1207, 1140, 1021, 996, 921, 872, 795, 687, 652, 607, 581, 427 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.73 (br s, 1 H), 8.31 (s, 2 H), 7.61 (d, *J* = 8.8 Hz, 2 H), 7.41 (dd, *J* = 8.0, 1.6 Hz, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 141.7 (q, *J* = 1.5 Hz), 139.6, 122.8, 120.9 (q, *J* = 253.1 Hz), 120.4, 114.3, 112.8.

^{19}F NMR (376 MHz, DMSO-d_6): δ = –57.0.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{14}H_7F_6NO_2$: 335.0381; found: 335.0378.

3,6-Difluoro-9*H*-carbazole (3e); Scale-Up Reaction

In a 250-mL, round-bottom flask, 2-bromo-4-fluoroaniline (**1e**; 10 g, 0.053 mol, 1.0 equiv) was dissolved in $CHCl_3$ (100 mL), followed by addition of DMAP (0.32 g, 2.65 mmol, 5 mol%). Ac_2O (5.41 g, 0.053 mol, 1.0 equiv) was added dropwise, and the mixture was stirred at reflux temperature (TLC monitoring) until completion. The mixture was cooled to r.t. and washed with distilled water. The organic layer was dried (anhyd $MgSO_4$), followed by removal of solvent under reduced pressure to obtain the crude product. The crude product was used for the Cu(0)-mediated Ullmann coupling reaction without further purification. The crude product was dissolved in DMF (50 mL), followed by addition of Cu(0) powder (10.10 g, 0.159 mol, 3.0 equiv). The reaction was stirred at reflux temperature until completion. After completion, the mixture was cooled to r.t. and extracted with CH_2Cl_2 and the

combined organic extracts were washed with brine. The organic layer was dried (anhyd $MgSO_4$), and the solvents were removed under reduced pressure. The crude product was purified by recrystallization (CH_2Cl_2/*n*-hexane 1:5). The obtained solid was dissolved in diethylene glycol (100 mL), followed by addition of phosphoric acid (51.93 g, 0.53 mol, 10 equiv). The mixture was stirred at 200 °C until completion and was then cooled to r.t. The organic components were extracted into CH_2Cl_2 and the combined organic extracts were washed with brine and dried (anhyd $MgSO_4$). Solvents were removed under reduced pressure to obtain the crude product. The final product was purified by recrystallization (EtOH/water 10:1) to deliver the product; yield: 2.57 g (overall 48%).

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Supporting Information

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