JOC The Journal of Organic Chemistry

Article

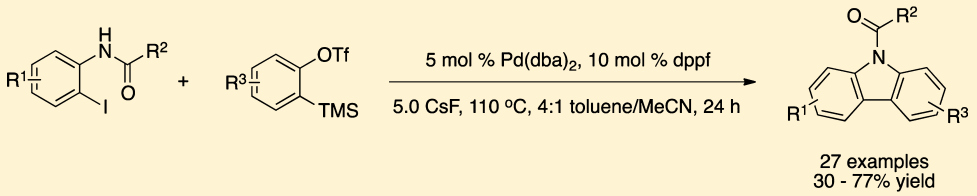
pubs.acs.org/joc

Synthesis of *N*-Acylcarbazoles through Palladium-Catalyzed Aryne Annulation of 2-Haloacetanilides

Chun Lu, Nataliya A. Markina, and Richard C. Larock*

Department of Chemistry, Iowa State University, Ames, Iowa 50011, United States

Supporting Information



ABSTRACT: *N*-Acylcarbazoles have been synthesized in moderate to good yields by the annulation of in situ generated arynes with 2-haloacetanilides in the presence of a palladium catalyst and CsF. Both C−C and C−N bonds are formed simultaneously, and a variety of functional groups are tolerated in this reaction.

INTRODUCTION

Carbazoles have been found to possess a variety of biological activities, including antibacterial, antifungal, antiviral, anti-inflammatory, and antitumor properties.[1] In addition to their use in the pharmaceutical field, some carbazole derivatives also find applications in material science, for example, as photorefractive materials.[2] A number of synthetic routes has been developed for construction of the carbazole core.[3] The majority of these methods require multiple synthetic steps or highly prefunctionalized starting materials, whereas efficient one-step methodologies for the formation of carbazoles from readily available starting materials are still very limited. Synthetic applications of aryne chemistry have attracted considerable attention[4] since a convenient approach to aryne generation by the fluoride-induced 1,2-elimination of *o*-(trimethylsilyl)aryl triflates was first reported in 1983.[5] The high electrophilicity of arynes has been used extensively in our group in the construction of heteroaromatic structures via either simple nucleophilic reactions[6] or annulation reactions.[7] Palladium-mediated reactions are, by far, the most powerful metal-catalyzed processes for constructing carbocycles and heterocycles,[8] due to the high efficiency with which they construct C−C and C−X (X = O, N) bonds and their high compatibility with functional groups. To take advantage of the high reactivity and tremendous synthetic utility of arynes and the tremendous versatility of organopalladium chemistry, we[9] and several other groups[10] have been exploring the palladium-catalyzed annulation reactions of arynes.

Herein, we wish to report the palladium-catalyzed annulation of arynes by substituted 2-haloacetanilides to produce *N*-acylcarbazoles in moderate to good yields. In this reaction, C−C and C−N bonds are formed simultaneously to generate this important heterocyclic ring system.

RESULTS AND DISCUSSION

Optimization Studies. We have optimized the reaction of 2-iodoacetanilide (**1a**) and the benzyne precursor *o*-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2a**) in 4:1 toluene/acetonitrile with CsF as the fluoride source (Table 1). In all cases, side product **4a** was always generated by the cyclotrimerization of benzyne[10g,11] as was the desired benzyne annulation product **3a** (eq 1). Optimization work was conducted with respect to different palladium catalysts, ligands, and solvents, and the results are shown in Table 1.

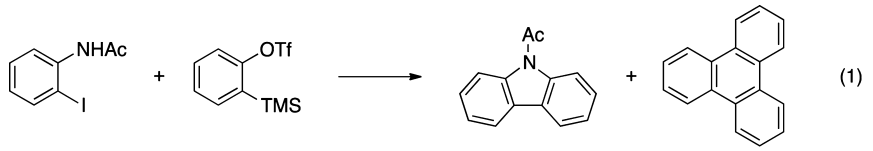
Utilizing $Pd(dba)_2$ as the catalyst, several ligands were examined (entries 1−9) in a 4:1 toluene/acetonitrile mixed solvent. When employing tri(*o*-tolyl)phosphine as the ligand (entry 1), the desired product was obtained in a low yield (23%), alongside large amounts of unreacted aryl halide **1a**. Bidentate ligands were also tested. Both dppm and dppb gave low yields, 42% (entry 2) and 27% (entry 3), respectively. However, the use of dppf improved the yield of the desired product dramatically to 69% (entry 4). Several different biarylphosphine ligands (**L1**−**L5**, Scheme 1) have also been examined in this process (entries 5−9), but yields no more than 50% have been obtained. Besides various ligands, several commonly used Pd catalysts, including $Pd(OAc)_2$ and $Pd(PPh_3)_4$, were also tested in this reaction (entries 10 and 11). $Pd(dba)_2$ still proved to be the most efficient catalyst. An effort to lower the ligand loading (entry 12) was made, but 10% dppf seemed necessary to maintain a higher yield. On the basis of our previous experience, the solvent can often prove critical for palladium-catalyzed benzyne reactions, mostly because the benzyne is generated at vastly different rates in different solvents.[9] For toluene/acetonitrile mixtures and CsF as the fluoride source, benzyne is generated more slowly in mixtures

Received: October 17, 2012
Published: December 5, 2012

ACS Publications © 2012 American Chemical Society

dx.doi.org/10.1021/jo3021727 | J. Org. Chem. 2012, 77, 11153−11160

Table 1. Optimization of the Pd-Catalyzed Annulation of Benzyne (eq 1)[a]

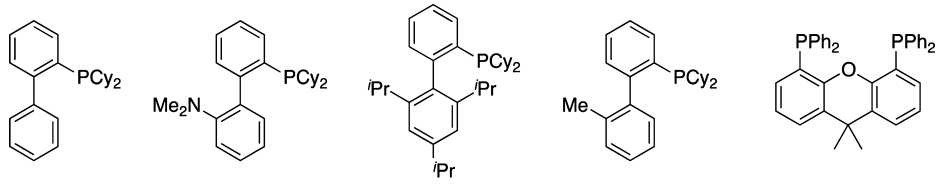


1a 2a 3a 4a

entry	catalyst (5 mol %)	ligand (mol %)	solvent ratio (toluene/MeCN)	% yield[b] of **3a**
1	$Pd(dba)_2$	P(*o*-tol)$_3$ (10)	4:1	23
2	$Pd(dba)_2$	dppm (10)	4:1	42
3	$Pd(dba)_2$	dppb (10)	4:1	27
4	$Pd(dba)_2$	dppf (10)	4:1	69
5	$Pd(dba)_2$	**L1** (10)[c]	4:1	45
6	$Pd(dba)_2$	**L2** (10)[c]	4:1	54
7	$Pd(dba)_2$	**L3** (10)[c]	4:1	56
8	$Pd(dba)_2$	**L4** (10)[c]	4:1	51
9	$Pd(dba)_2$	**L5** (10)[c]	4:1	17
10	$Pd(OAc)_2$	dppf (10)	4:1	54
11	$Pd(PPh_3)_4$	dppf (10)	4:1	60
12	$Pd(dba)_2$	dppf (5)	4:1	60
13	$Pd(dba)_2$	dppf (10)	3:1	54
14	$Pd(dba)_2$	dppf (10)	5:1	35
15	$Pd(dba)_2$	dppf (10)	C_3H_7CN	61
16	$Pd(dba)_2$	dppf (10)	DME[d]	45

[a]All reactions were run using substrate **1a** (0.25 mmol), 2.0 equiv of **2a**, 5.0 equiv of CsF, and 10 mL of solvent at 110 °C for 24 h, unless otherwise specified. [b]Isolated yield. [c]See L in Scheme 1. [d]Reaction was conducted at 90 °C for 36 h.

Scheme 1. Phosphine Ligands Examined



L1 L2 L3 L4 L5

with less acetonitrile, because CsF has a lower solubility in toluene. Therefore, the solvent ratio was tested, and 4:1 toluene/acetonitrile afforded the best result (entries 13 and 14). In case of a 3:1 ratio, more side product, trimer **4a**, was formed. With a 5:1 ratio, the benzyne was generated too slowly, leading to a lower yield. Other solvents, including butyronitrile[12] (entry 15) and DME (entry 16), afforded only moderate yields. In the end, we have chosen the reaction conditions reported in entry 4 of Table 1 as our optimal conditions.

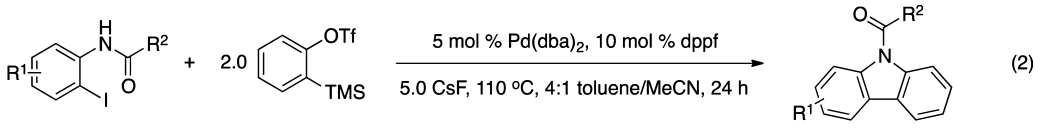
Synthesis of *N*-Acylcarbazoles. To explore the scope and limitations of this process, a number of 2-haloacetanilides were synthesized and allowed to react with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2a**) under our optimized conditions. The results are summarized in Table 2.

Different substituents in the acyl groups of the starting amides, including alkyl (entries 1–4), benzyl (entry 5), and phenyl (entries 6–8) groups, have been examined, and moderate to good yields have been produced, except for the reaction of amide **1d**, which generated only trace amounts of the desired product **3d**, along with a large amount of dehalogenated product and unidentified polymeric material. It is worth noting that the electronic nature of the phenyl group in the acyl substituent has a significant impact on the reaction yield (compare entries 6, 7, and 8). Thus, a substrate with a more electron-rich substituent on a phenyl ring (**1g**) (entry 7) afforded a much higher yield than a similar substrate with a more electron-deficient trifluoromethyl group on a phenyl ring (**1h**) (entry 8). This phenomenon can be explained as follows. An electron-donating OMe group can increase the nucleophilicity of the nitrogen, which promotes nucleophilic attack of the nitrogen on Pd(II) in the cyclization step in going from complex **III** to complex **V** (see Scheme 2). On the other hand, an electron-withdrawing CF_3 group decreases the nucleophilicity, inhibiting the cyclization step. These experimental results suggest that the nucleophilicity of nitrogen, which is involved in the cyclization of complex **III** to complex **V** (see Scheme 2), is critical for this reaction. A lower yield of product **3g** (60%) was produced when using the corresponding bromo-aryl equivalent of **1g**. This is not surprising, since for most palladium-catalyzed reactions of aryl halides, iodine-containing substrates provide better results than bromine-containing substrates, because their oxidative addition to Pd(0) is easier and faster. An acetanilide with a thiophenyl substituent (**1i**, entry 9) has also been tested, and the reaction was observed to provide a larger number of side products than the analogous reaction of an alkyl-substituted substrate, and thus produced a lower yield of 50%.

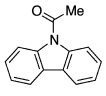
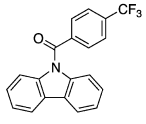
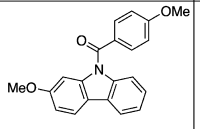
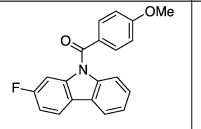
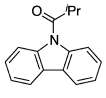
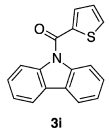
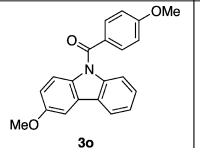
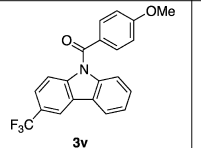
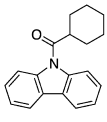
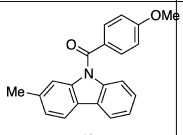
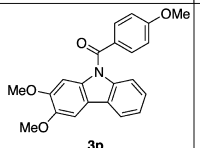
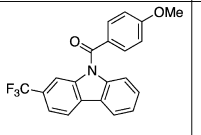
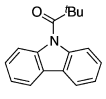
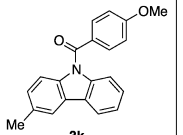
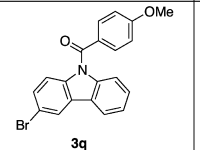
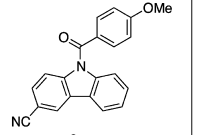
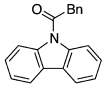
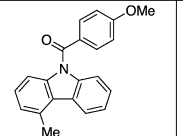
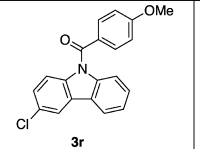
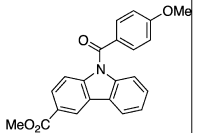
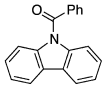
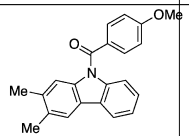
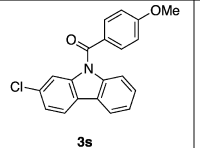
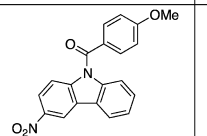
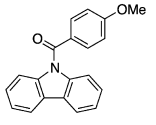
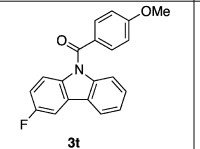
To further test the scope and the limitations of the reaction, we examined a variety of *N*-(2-iodophenyl)benzamides with various functional groups, including halogens (entries 17–21), electron-donating groups (entries 10–16), and electron-

dx.doi.org/10.1021/jo3021727 | J. Org. Chem. 2012, 77, 11153–11160

Table 2. Pd-Catalyzed Annulation of Benzyne 2a[a,b,c,d]



1 2a 3

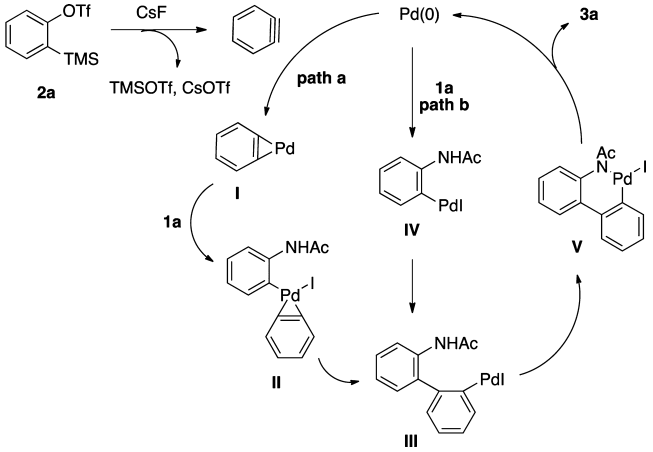
entry	structure of 3	% yield[b] of 3	entry	structure of 3	% yield[b] of 3	entry	structure of 3	% yield[b] of 3	entry	structure of 3	% yield[b] of 3
1	 3a	69	8	 3h	33	14	 3n	55	21	 3u	53
2	 3b	72	9	 3i	50	15	 3o	59	22	 3v	40
3	 3c	73	10	 3j	65	16	 3p	40	23	 3w	54
4	 3d	trace	11	 3k	74	17	 3q	60	24	 3x	43
5	 3e	61	12	 3l	44	18	 3r	55	25	 3y	30
6	 3f	60	13	 3m	77	19	 3s	63	26	 3z	27 (50)[d]
7	 3g	76 (60)[c]				20	 3t	65			

[a]Representative procedure: **1** (0.25 mmol), 2.0 equiv of **2**, 5.0 equiv of CsF, 5 mol % $Pd(dba)_2$, 10 mol % dppf in 10 mL of 4:1 toluene/MeCN at 110 °C for 24 h, unless otherwise specified. [b]Isolated yield. [c]Yield in parentheses starting from 2-bromobenzamide. [d]Yield in parentheses for the reaction conducted in 10 mL of 1:1 toluene/MeCN.

withdrawing groups (entries 22–26). Halogen atoms, including Br (entry 17), Cl (entries 18 and 19), and F (entries 20 and 21), are tolerated in this chemistry, and moderate to good yields are obtained for the corresponding carbazoles **3q**–**3u**. These products provide a valuable extension of the developed methodology, since further elaboration of these products via versatile metal-catalyzed reactions is possible, leading to a variety of polysubstituted carbazoles. Amides with a slightly electron-donating methyl group in positions 4 (entry 11) and 5 (entry 10) and amides substituted with two methyl groups (entry 13) afford products **3k**, **3j**, and **3m** in 74, 65, and 77% yields, respectively. An amide with a methyl group *ortho* to the iodine generates a much lower yield of product **3l** (44%) (entry 12), presumably because the steric hindrance caused by the methyl group disfavors the oxidative addition step (see the later mechanistic discussion). Amides with strong electron-donating methoxy groups (entries 14–16) provide lower yields of products **3n**–**3p** (34–59%). Again, this is presumably because

dx.doi.org/10.1021/jo3021727 | J. Org. Chem. 2012, 77, 11153–11160

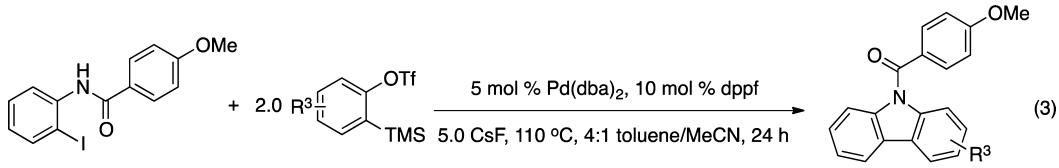
Scheme 2. Tentative Mechanisms



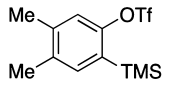
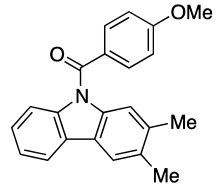
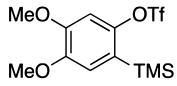
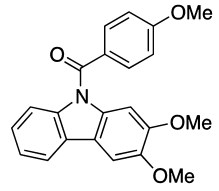
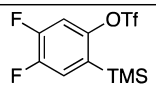
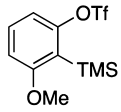
electron-rich aryl halides undergo more sluggish oxidative addition to Pd(0). Strong electron-withdrawing CF_3, CN, ester, and NO_2 groups (entries 22−26) lower the yield as well, providing products **3v**−**3z** in 30−54% yields. Although these electron-withdrawing groups electronically benefit oxidative addition of the aryl halide to Pd(0), they strongly disfavor nucleophilic attack of the nitrogen on Pd(II) in complex **III** in the cyclization step to form complex **V** (see Scheme 2).

In addition to the above reactions, which examined only the use of the benzyne precursor triflate **2a** as an annulation partner, other aryne precursors have been examined in our methodology (Table 3). When 4,5-dimethylbenzyne precursor **2b** was allowed to react with amide **1g** under our optimized conditions, it provided the corresponding annulation product **3m** in a 62% yield. The dimethoxybenzyne precursor **2c** was also examined, and a longer reaction time was necessary to get a 40% yield of the annulation product **3p** (Table 3, entry 2). The low yield for **2c** may be attributed to the slower rate of

Table 3. Investigation of Different Arynes in the Pd-Catalyzed Annulation of 2-Haloacetanilide 1g[a,b,c,d]



1g **2** **3**

entry	aryne precursor **2**	product **3**	% yield[b]
1	 **2b**	 **3m**	62
2	 **2c**	 **3p**	40[c]
3	 **2d**	-	0
4	 **2e**	-	-[d]

[a]Representative procedure: **1g** (0.25 mmol), 2.0 equiv of the aryne precursor, 5.0 equiv of CsF, 5 mol % $Pd(dba)_2$, 10 mol % dppf in 10 mL of 4:1 toluene/MeCN at 110 °C for 24 h. [b]Isolated yield. [c]Reaction was conducted for 48 h. [d]Complex reaction mixture with large amounts of leftover **1g** was obtained.

dx.doi.org/10.1021/jo3021727 | J. Org. Chem. 2012, 77, 11153−11160

generation of the 4,5-dimethoxybenzyne compared with the generation of benzyne from **2a**, as has been suggested by earlier work in our group.[9a,b] The difluorobenzyne precursor **2d** was also allowed to react with **1g** under the optimal conditions (Table 3, entry 3), but none of the desired product was observed and a large amount of **1g** was left unreacted. This might be due to the lack of stability of the difluorobenzyne in the reaction system. The unsymmetrical aryne precursor **2e** afforded a complex mixture of unknown products, and a significant amount of the starting material **1g** was left unreacted.

On the basis of our experimental results and previous experience with related processes,[9b] we propose that this *N*-acylcarbazole synthesis proceeds through one of two possible pathways shown in Scheme 2. One possible pathway proceeds by the oxidative cyclization of Pd(0) with the aryne generated from the silyl triflate to form palladacycle **I** (path a).[13] Oxidative addition of **1a** to this palladacycle forms Pd(IV) intermediate **II**. However, we cannot rule out the possibility that Pd(0) inserts directly into the C−I bond of **1a** to form intermediate **IV**, which then undergoes carbopalladation of the aryne to give rise to intermediate **III**[10d] (path b); then, under the basic conditions, intermediate **V** may be formed. Finally, through reductive elimination, the desired product can be generated alongside Pd(0), which can reenter the catalytic cycle. There does not appear to be any particular evidence favoring either of these pathways over the other.

CONCLUSIONS

In summary, we have developed a novel method for the synthesis of *N*-acylcarbazoles, which involves the palladium-catalyzed annulation of arynes by 2-haloacetanilides. This method provides an efficient synthesis of carbazoles from readily available starting materials. Our process has been shown to be tolerant of various functional groups, which makes further elaboration of these substrates possible.

EXPERIMENTAL SECTION

General Remarks. The ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz, respectively. All melting points are uncorrected. All coupling constants (J) are reported in hertz (Hz). All commercially obtained chemicals were used as received without further purification. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates, and visualization was effected with short wavelength UV light (254 nm). All melting points are uncorrected. High-resolution mass spectra (HRMS) were obtained using a QTOF mass spectrometer (ESI at a voltage of 70 eV). All reagents were used directly as obtained commercially unless otherwise noted. 4,5-Dimethyl-substituted silylaryl triflate **2b**, 4,5-dimethoxy-substituted silylaryl triflate **2c**, and 4,5-difluoro-substituted silylaryl triflate **2d** were prepared according to a literature procedure.[9a,11b,14]

Experimental Details. Noncommercially available starting materials were prepared according to literature procedures.[15]

*N-(2-Iodophenyl)-4-(trifluoromethyl)benzamide (**1h**):* White solid, mp 173−175 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, J = 9.0 Hz, 1H), δ 7.82 (d, J = 9.0 Hz, 1H), 7.71−7.63 (m, 5H), 7.42 (t, J = 6.0 Hz, 1H), 6.92 (t, J = 9.0 Hz, 1H); ^{13}C NMR (300 MHz, d_6- DMSO) δ 165.8, 139.0, 135.8, 132.5, 130.2, 128.9, 128.5, 128.4, 128.1, 126.5, 126.4; HRMS (EI) calcd for $C_{14}H_{10}F_3INO$: 391.9754, found 391.9762.

*N-(2-Iodo-5-methylphenyl)-4-methoxybenzamide (**1j**):* White solid, mp 95−98 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, J = 1.8 Hz, 1H), 8.18 (s, 1H), 7.94 (d, J = 9.0 Hz, 2H), 7.66 (d, J = 8.1 Hz, 1H), 7.02 (d, J = 9.0 Hz, 2H), 6.71 (dd, J = 8.1, 2.1 Hz, 1H), 3.89 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.0, 162.9, 139.9, 138.5, 138.3, 129.3, 127.1, 127.0, 122.6, 114.3, 86.3, 55.7, 21.5; HRMS (EI) calcd for $C_{15}H_{15}INO_2$: 368.0142, found 368.0150.

*N-(2-Iodo-4-methylphenyl)-4-methoxybenzamide (**1k**):* White solid, mp 146−148 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, J = 8.4 Hz, 1H), 8.13 (br s, 1H), 7.92 (dd, J = 8.1, 2.7 Hz, 2H), 7.63 (s, 1H), 7.20 (d, J = 8.4 Hz, 1H), 7.00 (dd, J = 8.7, 3.0 Hz, 2H), 3.88 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.0, 162.9, 139.2, 136.2, 136.0, 130.3, 129.3, 127.1, 121.7, 114.3, 90.5, 55.7, 20.6; HRMS (ESI) calcd for $C_{15}H_{15}INO_2$: 368.0142, found 368.0148.

*N-(2-Iodo-3-methylphenyl)-4-methoxybenzamide (**1l**):* White solid, mp 148−150 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.24 (d, J = 6.0 Hz, 1H), 7.96 (d, J = 6.0 Hz, 2H), 7.27 (t, J = 9.0 Hz, 1H), 7.05−6.99 (d, J = 6.0 Hz, 3H), 3.88 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.0, 162.9, 142.4, 138.8, 129.3, 128.9, 127.1, 125.8, 119.2, 114.3, 98.0, 55.7, 29.9; HRMS (EI) calcd for $C_{15}H_{15}INO_2$: 368.0142, found 368.0142.

*N-(4,5-Dimethyl-2-iodophenyl)-4-methoxybenzamide (**1m**):* White solid, mp 125−127 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.08 (s, 1H), 7.93 (d, J = 9.0 Hz, 2H), 7.55 (s, 1H), 7.00 (d, J = 6.0 Hz, 2H), 3.88 (s, 3H), 2.26 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 164.9, 162.8, 139.1, 138.3, 136.3, 135.0, 129.2, 127.1, 123.1, 114.3, 86.8, 55.7, 20.0, 19.1; HRMS (EI) calcd for $C_{16}H_{17}NO_2I$: 382.0298, found 382.0300.

*N-(2-Iodo-5-methoxyphenyl)-4-methoxybenzamide (**1n**):* White solid, mp 107−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23−8.22 (m, 2H), 7.93 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.7 Hz, 1H), 7.00 (d, J = 8.7 Hz, 2H), 6.49 (dd, J = 8.7, 3.0 Hz, 1H), 3.87 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.0, 163.0, 160.9, 139.4, 138.7, 129.2, 126.9, 114.4, 113.2, 106.7, 78.2, 55.7, 55.7; HRMS (EI) calcd for $C_{15}H_{15}INO_3$: 383.0091, found 383.0091.

*N-(2-Iodo-4-methoxyphenyl)-4-methoxybenzamide (**1o**):* Cream solid, mp 179−181 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.77 (s, 1H), 7.97 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 2.8 Hz, 1H), 7.29 (d, J = 8.7 Hz, 1H), 7.06 (d, J = 8.3 Hz, 2H), 7.01 (dd, J = 8.8, 2.9 Hz, 1H), 3.83 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.9, 161.9, 157.9, 133.0, 129.5, 129.2, 126.4, 123.2, 114.6, 113.6, 99.9, 55.7, 55.4; HRMS (EI) calcd for $C_{15}H_{15}INO_3$: 384.0091, found 384.0086.

*N-(4,5-Dimethoxy-2-iodophenyl)-4-methoxybenzamide (**1p**):* White solid, mp 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.06 (s, 1H), 7.93 (d, J = 8.0 Hz, 2H), 7.20 (s, 1H), 7.01 (d, J = 12.0 Hz, 2H), 3.94 (s, 3H), 3.89 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 164.9, 162.8, 149.7, 146.4, 132.7, 129.1, 126.8, 120.4, 114.3, 105.9, 77.65, 56.5, 56.2, 55.6; HRMS (EI) calcd for $C_{16}H_{17}INO_4$: 414.0197, found 414.0194.

*N-(4-Bromo-2-iodophenyl)-4-methoxybenzamide (**1q**):* White solid, mp 151−152 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, J = 8.7 Hz, 1H), 8.19 (s, 1H), 7.93−7.90 (m, 3H), 7.50 (dd, J = 9.0, 2.1 Hz, 1H), 7.01 (d, J = 8.7 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 166.6, 163.1, 140.6, 137.9, 132.5, 129.7, 126.6, 122.5, 117.3, 114.4, 90.4, 55.7; HRMS (EI) calcd for $C_{14}H_{12}IBrNO_2$: 431.9091, found 431.9102.

*N-(4-Chloro-2-iodophenyl)-4-methoxybenzamide (**1r**):* White solid, mp 148−150 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (d, J = 9.0 Hz, 1H), 8.19 (s, 1H), 7.93 (d, J = 9.0 Hz, 2H), 7.79 (d, J = 2.4 Hz, 1H), 7.37 (dd, J = 9.0, 2.4 Hz, 1H), 7.01 (d, J = 9.0 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.0, 163.1, 138.0, 137.5, 129.8, 129.6, 129.3, 126.6, 122.2, 114.4, 90.0, 55.7; HRMS (EI) calcd for $C_{14}H_{12}ClINO_2$: 387.9596, found 387.9597.

*N-(5-Chloro-2-iodophenyl)-4-methoxybenzamide (**1s**):* White solid, mp 123−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.22 (s, 1H), 7.93 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 12.0 Hz, 1H), 7.02 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 8.0 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 164.9, 163.2, 139.6, 139.3, 135.8, 129.3, 126.5, 125.9, 121.5, 114.5, 86.9, 55.8; HRMS (EI) calcd for $C_{14}H_{12}NO_2ICl$: 387.9596, found 387.9597.

*N-(4-Fluoro-2-iodophenyl)-4-methoxybenzamide (**1t**):* White solid, mp 158−160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, J = 12.0, 8.0 Hz, 1H), 8.09 (s, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.54 (dd, J = 8.0, 4.0 Hz, 1H), 7.26 (s, 1H), 7.14 (td, J = 12.0, 4.0 Hz, 1H), 7.01 (d, J = 8.0 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ

165.0, 163.0, 160.4, 157.1, 135.2, 129.3, 126.7, 125.7, 125.4, 122.8, 122.7, 116.5, 116.2, 114.4, 89.9, 89.8, 55.7 (extra peaks due to $^{13}C-^{19}F$ coupling); HRMS (EI) calcd for $C_{14}H_{12}FINO_2$: 371.9891, found 371.9896.

*N-(5-Fluoro-2-iodophenyl)-4-methoxybenzamide (**1u**):* White solid, mp 133−135 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.39 (dd, J = 11.0, 2.7 Hz, 1H), 8.29 (s, 1H), 7.94 (d, J = 8.7 Hz, 2H), 7.74 (dd, J = 8.7, 6.0 Hz, 1H), 7.03 (d, J = 8.7 Hz, 2H), 6.70−6.63 (m, 1H), 3.90 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.1, 164.9, 163.1, 161.8, 140.0, 139.8, 139.3, 139.2, 129.3, 129.2, 126.4, 114.4, 113.1, 112.8, 109.3, 108.9, 82.5, 55.7 (extra peaks due to $^{13}C-^{19}F$ coupling); HRMS (EI) calcd for $C_{14}H_{12}FINO_2$: 371.9891, found 371.9897.

*N-[2-Iodo-4-(trifluoromethyl)phenyl]-4-methoxybenzamide (**1v**):* White solid, mp 148−150 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.63 (d, J = 9.0 Hz, 1H), 8.38 (s, 1H), 8.04 (s, 1H), 7.94 (d, J = 9.0 Hz, 2H), 7.64 (d, J = 6.0 Hz, 1H), 7.02 (d, J = 9.0 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.1, 163.3, 141.7, 135.9, 129.4, 126.8, 126.3, 120.8, 114.4, 88.9, 82.3, 55.7; HRMS (EI) calcd for $C_{15}H_{12}F_3INO_2$: 421.9859, found 421.9855.

*N-[2-Iodo-5-(trifluoromethyl)phenyl]-4-methoxybenzamide (**1w**):* White solid, mp 146−148 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.83 (d, J = 2.1 Hz, 1H), 8.34 (s, 1H), 7.97−7.92 (m, 3H), 7.11 (dd, J = 8.1, 2.1 Hz, 1H), 7.03 (d, J = 8.7 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.1, 163.3, 139.4, 139.4, 129.4, 126.3, 122.1, 122.0, 118.2, 118.1, 114.5, 93.7, 55.8; HRMS (EI) calcd for $C_{15}H_{12}F_3INO_2$: 421.9859, found 421.9867.

*N-(4-Cyano-2-iodophenyl)-4-methoxybenzamide (**1x**):* White solid, mp 83−85 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, J = 6.0 Hz, 1H), 8.60 (s, 1H), 7.92−7.87 (d, J = 6.0 Hz, 2H; s, 1H), 7.66 (d, J = 9.0 Hz, 1H), 7.03 (d, J = 9.0 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 166.6, 163.5, 140.4, 132.9, 129.4, 126.0, 121.1, 117.7, 114.6, 113.1, 108.0, 82.3, 55.8; HRMS (EI) calcd for $C_{15}H_{12}IN_2O_2$: 378.9938, found 378.9933.

*N-(4-Carbomethoxy-2-iodophenyl)-4-methoxybenzamide (**1y**):* White solid, mp 165−167 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, J = 8.7 Hz, 1H), 8.47 (d, J = 2.1 Hz, 1H), 8.43 (s, 1H), 8.04 (dd, J = 8.7, 2.1 Hz, 1H), 7.93 (d, J = 9.0 Hz, 2H), 7.01 (d, J = 9.0 Hz, 2H), 3.91 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.4, 165.0, 163.2, 142.5, 140.3, 131.1, 129.4, 126.9, 126.4, 120.0, 114.5, 88.9, 55.7, 52.5; HRMS (EI) calcd for $C_{16}H_{15}INO_4$: 412.0040, found 412.0047.

*N-(2-Iodo-4-nitrophenyl)-4-methoxybenzamide (**1z**):* White solid, mp 158−160 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.76 (d, J = 9.0 Hz, 1H), 8.69 (d, J = 3.0 Hz, 1H), 8.55 (s, 1H), 8.28 (dd, J = 9.0, 3.0 Hz, 1H), 7.95 (d, J = 9.0 Hz, 2H), 7.04 (d, J = 9.0 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 165.0, 163.6, 144.3, 134.4, 129.5, 126.2, 125.3, 119.7, 114.6, 87.9, 55.8; HRMS (EI) calcd for $C_{14}H_{11}IN_2O_4$: 398.9833, found 398.9836.

General Procedure for the Palladium-Catalyzed Synthesis of *N*-Acylcarbazoles. The 2-iodoacetanilide (**1**) (0.25 mmol), the 2-(trimethylsilyl)aryl triflate **2** (2.0 equiv), CsF (5.0 equiv), $Pd(dba)_2$ (5 mol %), dppf (10 mol %), 8 mL of toluene, and 2 mL of MeCN were placed in a 4 dram vial, and the vial was sealed. The reaction mixture was stirred, first, at room temperature for 1 min and then heated to 110 °C for 24 h. The mixture was allowed to cool to room temperature, diluted with ethyl acetate, washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The product was isolated by flash chromatography on silica gel using hexanes/EtOAc as the eluent.

*9-Acetylcarbazole (**3a**):* 35.8 mg (69%), white solid, mp 69−71 °C; ^1H NMR (300 MHz, $CDCl_3$) 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 (300 MHz, $CDCl_3$) δ 170.1, 138.6, 127.3, 126.4, 123.6, 119.8, 116.2, 27.7. The ^1H and ^{13}C NMR spectral data are in good agreement with that previously reported.[16]

*9-(Isopropylcarbonyl)carbazole (**3b**):* 43.3 mg (72%), yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.4 Hz, 2H), 8.01 (ddd, J = 7.5, 1.2, 0.6 Hz, 2H), 7.49 (ddd, J = 8.5, 7.3, 1.4 Hz, 2H), 7.39 (td, J = 7.5, 1.0 Hz, 2H), 3.70 (m, 1H), 1.45 (d, J = 6.7 Hz, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 178.2, 138.7, 127.5, 126.6, 123.7, 120.0, 116.5, 35.4, 19.8. The ^1H NMR spectral data are in good agreement with that previously reported.[17]

*9-(Cyclohexylcarbonyl)carbazole (**3c**):* 50.9 mg (73%), light brown oil; ^1H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, J = 9.0 Hz, 2H), 8.02 (d, J = 9.0 Hz, 2H), 7.51 (dd, J = 9.0, 6.0 Hz, 2H), 7.40 (dd, J = 9.0, 6.0 Hz, 2H), 3.38 (tt, J = 12.0, 3.0 Hz, 1H), 2.14 (d, J = 12.0 Hz, 2H), 1.96 (d, J = 12.0 Hz, 2H), 1.86−1.74 (m, 3H), 1.60−1.44 (m, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 177.1, 138.8, 127.5, 126.6, 123.6, 120.0, 116.4, 45.5, 29.7, 26.0, 25.9; HRMS (EI) calcd for $C_{19}H_{20}NO$: 278.1539, found 278.1539.

*9-(Benzylcarbonyl)carbazole (**3e**):* 43.4 mg (61%), white solid, mp 123−124 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.0 Hz, 2H), 8.04 (d, J = 8.0 Hz, 2H), 7.51−7.47 (t, J = 8.0 Hz, 2H), 7.43−7.40 (m, 4H), 7.38−7.34 (m, 3H), 4.53 (s, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 166.6, 138.7, 133.7, 129.7, 129.0, 127.7, 126.8, 126.1, 124.0, 120.1, 116.7, 45.6; HRMS (EI) calcd for $C_{20}H_{16}NO$: 286.1226, found 286.1226.

*9-(Phenylacetyl)carbazole (**3f**):* 40.9 mg (60%), yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.1 Hz, 2H), 7.74 (d, J = 7.7 Hz, 2H), 7.67 (d, J = 7.7 Hz, 1H), 7.54 (t, J = 7.5 Hz, 4H), 7.35 (m, 4H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 169.8, 139.3, 135.9, 132.6, 129.3, 129.1, 126.2, 123.6, 120.0, 116.0; HRMS (ESI) calcd for $C_{19}H_{14}NO$: 272.1070, found 272.1072.

*9-(4-Methoxybenzoyl)carbazole (**3g**):* 57.4 mg (76%), white solid, mp 162−164 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.02−7.99 (m, 2H), 7.72 (d, J = 8.7 Hz, 2H), 7.57−7.52 (m, 2H), 7.36−7.30 (m, 4H), 6.99 (d, J = 9.0 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.3, 163.4, 139.5, 132.0, 127.7, 126.8, 126.0, 123.2, 120.0, 115.7, 114.3, 55.7; HRMS (EI) calcd for $C_{20}H_{16}NO_2$: 302.1176, found 302.1177.

*9-[4-(Trifluoromethyl)benzoyl]carbazole (**3h**):* 28.2 mg (33%), white solid, mp 101−103 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, J = 9.0 Hz, 2H), 7.93 (d, J = 9.0 Hz, 1H), 7.79−7.70 (m, 2H), 7.53 (d, J = 6.0 Hz, 1H), 7.44−7.27 (m, 6H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 166.6, 138.9, 132.9, 131.0, 129.2, 128.6, 127.5, 126.8, 124.4, 120.1, 116.3; HRMS (EI) calcd for $C_{20}H_{13}F_3NO$: 340.0944, found 340.0949.

*9-(Thiophen-2-ylcarbonyl)carbazole (**3i**):* 34.9 mg (50%), light yellow solid, mp 95−98 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.04−8.01 (m, 2H), 7.76−7.70 (m, 3H), 7.60 (d, J = 3.0 Hz, 1H), 7.39−7.36 (m, 4H), 7.16 (dd, J = 6.0, 3.0 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 163.0, 139.4, 138.0, 134.0, 133.4, 127.9, 126.8, 125.6, 123.5, 120.1, 115.5; HRMS (EI) calcd for $C_{17}H_{12}NOS$: 278.0634, found 278.0636.

*9-(4-Methoxybenzoyl)-2-methylcarbazole (**3j**):* 51.3 mg (65%), white solid, mp 129−131 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, J = 6.0 Hz, 1H), 7.90 (d, J = 9.0 Hz, 1H), 7.74 (d, J = 9.0 Hz, 2H), 7.54 (s, 1H), 7.40−7.24 (m, 3H), 7.19 (d, J = 9.0 Hz, 1H), 7.01 (d, J = 9.0 Hz, 2H), 3.93 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.3, 163.4, 140.0, 139.5, 137.5, 132.0, 127.8, 126.1, 124.6, 123.6, 123.1, 119.8, 119.6, 116.1, 115.6, 114.2, 55.7, 22.4; HRMS (EI) calcd for $C_{21}H_{18}NO_2$: 316.1332, found 316.1339.

*9-(4-Methoxybenzoyl)-3-methylcarbazole (**3k**):* 58.1 mg (74%), light brown oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.99 (dd, J = 6.0, 3.0 Hz, 1H), 7.82 (s, 1H), 7.73 (d, J = 9.0 Hz, 2H), 7.60 (dd, J = 6.0, 3.0 Hz, 1H), 7.42(d, J = 9.0 Hz, 1H), 7.37−7.33 (m, 2H), 7.16 (d, J = 9.0 Hz, 1H), 7.00 (d, J = 9.0 Hz, 2H), 3.92 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.2, 163.3, 139.8, 137.7, 132.9, 131.9, 129.2, 128.6, 128.0, 126.7, 126.0, 123.2, 120.1, 119.9, 115.8, 114.2, 55.7, 21.5; HRMS (EI) calcd for $C_{21}H_{18}NO_2$: 316.1332, found 316.1333.

*9-(4-Methoxybenzoyl)-4-methylcarbazole (**3l**):* 34.8 mg (44%), light brown oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (m, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 8.8 Hz, 2H), 7.65 (m, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.34−7.23 (m, 2H), 7.18−7.13 (m, 1H), 7.00 (d, J = 8.8 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.3, 163.4, 140.5, 139.6, 133.1, 132.1, 129.8, 126.5, 126.3, 126.0, 124.9, 123.0, 122.6, 122.4, 115.3, 114.2, 113.1, 55.8, 21.2; HRMS (EI) m/z calcd for $C_{21}H_{18}NO_2$: 316.1332, found 316.1335.

*2,3-Dimethyl-9-(4-methoxybenzoyl)carbazole (**3m**):* 63.8 mg (77%), white solid, mp 156−157 °C; ^1H NMR (300 MHz, $CDCl_3$)

δ 7.95 (d, J = 9.0 Hz, 1H), 7.76 (s, 1H), 7.72 (d, J = 9.0 Hz, 2H), 7.47 (s, 1H), 7.38 (d, J = 9.0 Hz, 1H), 7.32−7.23 (m, 2H), 6.99 (d, J = 9.0 Hz, 2H), 3.92 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1, 163.3, 139.4, 138.3, 136.0, 132.1, 131.9, 128.0, 126.2, 126.0, 124.0, 123.1, 120.4, 119.7, 116.5, 115.7, 114.2, 55.7, 21.1, 20.2; HRMS (EI) m/z calcd for $C_{22}H_{20}NO_2$: 330.14886, found 330.14919.

*2-Methoxy-9-(4-methoxybenzoyl)carbazole (**3n**):* 45.6 mg (55%), white solid, mp 109−111 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92−7.86 (d, J = 9.0 Hz, 2H), 7.73 (d, J = 9.0 Hz, 2H), 7.37−7.22 (m, 4H), 7.01−6.94 (m, 3H), 3.91 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.4, 163.4, 159.4, 140.9, 139.4, 132.0, 127.7, 126.1, 125.3, 123.2, 120.6, 119.4, 119.2, 115.5, 114.3, 111.8, 100.3, 55.7; HRMS (EI) calcd for $C_{21}H_{18}NO_3$: 332.1281, found 332.1289.

*3-Methoxy-9-(4-methoxybenzoyl)carbazole (**3o**):* 48.5 mg (59%), light brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 6.0, 3.1 Hz, 1H), 7.71 (d, J = 8.5 Hz, 2H), 7.53 (dd, J = 6.1, 3.3 Hz, 1H), 7.49 (d, J = 9.1 Hz, 1H), 7.47 (d, J = 2.6 Hz, 1H), 7.35 − 7.29 (m, 2H), 6.99 (d, J = 8.6 Hz, 2H), 6.94 (dd, J = 9.0, 2.6 Hz, 1H), 3.92 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 163.2, 156.3, 140.0, 133.9, 131.8, 127.9, 126.9, 126.8, 126.0, 123.1, 119.9, 116.7, 115.9, 114.8, 114.2, 103.1, 56.0, 55.7; HRMS (EI) calcd for $C_{21}H_{18}NO_3$: 332.1281, found 332.1278.

*2,3-Dimethoxy-9-(4-methoxybenzoyl)carbazole (**3p**):* 37.9 mg (40%), white solid, mp 114−116 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 9.0 Hz, 1H), 7.73 (d, J = 9.0 Hz, 2H), 7.43 (s, 1H), 7.42 (s, 1H), 7.32−7.17 (m, 4H), 7.01 (d, J = 9.0 Hz, 2H), 4.03 (s, 3H), 3.92 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.2, 163.3, 149.3, 146.8, 139.1, 134.0, 131.9, 127.9, 126.4, 125.1, 123.2, 119.0, 118.3, 115.7, 114.3, 101.7, 99.8, 56.5, 56.2, 55.8; HRMS (EI) calcd for $C_{22}H_{20}NO_4$: 362.1387, found 362.1391.

*3-Bromo-9-(4-methoxybenzoyl)carbazole (**3q**):* 56.4 mg (60%), white solid, mp 110−112 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.99−7.96 (m, 1H), 7.72 (d, J = 9.0 Hz, 2H), 7.52−7.42 (m, 3H), 7.38−7.35 (m, 2H), 7.01 (d, J = 6.0 Hz, 2H), 3.93 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 166.6, 163.6, 139.8, 138.3, 132.1, 129.6, 127.8, 127.5, 127.3, 124.8, 123.5, 122.9, 120.3, 117.2, 116.4, 115.8, 114.4, 55.8; HRMS (EI) calcd for $C_{20}H_{15}BrNO_2$: 380.0281, found 380.0279.

*3-Chloro-9-(4-methoxybenzoyl)carbazole (**3r**):* 46.2 mg (55%), light brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98−7.96 (m, 2H), 7.72 (d, J = 9.0 Hz, 2H), 7.56−7.49 (m, 1H), 7.37−7.29 (m, 3H), 7.01 (d, J = 9.0 Hz, 2H), 3.93 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.0, 163.6, 140.0, 137.9, 132.0, 129.2, 128.9, 127.5, 126.8, 124.9, 123.5, 120.7, 120.3, 119.9, 116.8, 115.8, 114.4, 55.8; HRMS (EI) calcd for $C_{20}H_{15}ClNO_2$: 336.0786, found 336.0788.

*2-Chloro-9-(4-methoxybenzoyl)carbazole (**3s**):* 52.7 mg (63%), white solid, mp 93−95 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (m, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.77−7.72 (dd, J = 8.4, 1.8 Hz, 3H), 7.42 (d, J = 3.0 Hz, 1H), 7.35−7.32 (m, 3H), 7.02 (d, J = 9.0 Hz, 2H), 3.93 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.0, 163.7, 143.5, 139.1, 132.1, 130.7, 129.2, 128.6, 126.9, 124.4, 123.8, 123.4, 120.7, 120.1, 116.0, 115.7, 114.4, 55.8; HRMS (EI) m/z calcd for $C_{20}H_{15}ClNO_2$: 336.0786, found 336.0790.

*3-Fluoro-9-(4-methoxybenzoyl)carbazole (**3t**):* 52.0 mg (65%), white solid, mp 90−93 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98−7.95 (m, 1H), 7.72 (d, J = 9.0 Hz, 2H), 7.69−7.60 (m, 2H), 7.48−7.45 (m, 1H), 7.36−7.33 (d, J = 6.0 Hz, 2H), 7.09 (td, J = 9.0, 2.7 Hz, 1H), 7.02 (d, J = 6.9 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1, 163.5, 161.1, 157.9, 140.2, 135.8, 132.0, 130.5, 127.6, 127.4, 123.3, 120.7, 120.3, 117.0, 116.8, 115.9, 114.5, 114.4, 114.2, 106.2, 105.9, 55.8 (extra peaks due to ^{13}C−^{19}F coupling); HRMS (EI) m/z calcd for $C_{20}H_{15}FNO_2$: 320.10813, found 320.10895.

*2-Fluoro-9-(4-methoxybenzoyl)carbazole (**3u**):* 42.1 mg (53%), white solid, mp 115−117 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98−7.92 (m, 2H), 7.73 (d, J = 9.0 Hz, 2H), 7.44−7.41 (m, 2H), 7.32 (td, J = 9.0, 3.0 Hz, 2H), 7.11 (d, J = 6.0 Hz, 1H), 7.02 (d, J = 9.0 Hz, 2H), 3.93 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1, 165.1, 163.6, 160.5, 143.5, 140.2, 132.0, 129.2, 128.6, 126.3, 125.6, 123.5, 120.92, 120.7, 119.8, 115.6, 114.4, 111.4, 111.2, 103.5, 103.2, 55.8 (extra peaks due to ^{13}C−^{19}F coupling); HRMS (EI) calcd for $C_{20}H_{15}FNO_2$: 320.1081, found 320.1083.

*9-(4-Methoxybenzoyl)-3-(trifluoromethyl)carbazole (**3v**):* 36.9 mg (40%), light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 (s, 3H), 6.99−7.03 (m, 2H), 7.39−7.43 (m, 2H), 7.50−7.54 (m, 1H), 7.60 (dd, J = 8.8, 1.8 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.74 (d, J = 8.8 Hz, 2H), 8.04−8.10 (m, 1H), 8.29 (d, J = 1.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 163.8, 143.4, 140.1, 132.2, 130.7, 129.2, 128.6, 127.7, 127.0, 125.8, 125.0, 123.7, 123.6, 123.6, 120.4, 117.5, 117.5, 115.8, 115.7, 114.5, 55.8 (extra peaks due to ^{19}F−^{13}C coupling); HRMS (EI) calcd for $C_{21}H_{15}F_3NO_2$: 370.1049, found 370.1047.

*9-(4-Methoxybenzoyl)-2-(trifluoromethyl)carbazole (**3w**):* 49.4 mg (54%), white solid, mp 107−109 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14−8.06 (m, 3H), 7.74 (d, J = 9.0 Hz, 2H), 7.63 (d, J = 9.0 Hz, 1H), 7.44−7.38 (m, 3H), 7.03 (d, J = 9.0 Hz, 2H), 3.94 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.0, 163.8, 139.0, 138.4, 132.1, 130.5, 129.2, 128.6, 127.9, 127.0, 125.6, 123.5, 120.7, 120.7, 120.3, 115.7, 114.5, 55.8; HRMS (EI) calcd for $C_{21}H_{15}F_3NO_2$: 370.1049, found 370.1051.

*3-Cyano-9-(4-methoxybenzoyl)carbazole (**3x**):* 35.2 mg (43%), white solid, mp 175−177 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.08−8.05 (m, 1H), 7.76−7.70 (m, 3H), 7.63 (dd, J = 9.0, 3.0 Hz, 1H), 7.50−7.40 (m, 3H), 7.03 (d, J = 9.0 Hz, 2H), 3.94 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 168.9, 164.1, 141.6, 140.1, 132.4, 130.1, 128.1, 126.6, 126.2, 124.7, 124.2, 123.9, 120.5, 119.7, 116.3, 115.7, 114.6, 106.4, 55.9; HRMS (EI) calcd for $C_{21}H_{15}N_2O_2$: 327.1128, found 327.1134.

*3-Carbomethoxy-9-(4-methoxybenzoyl)carbazole (**3y**):* 26.8 mg (30%), white solid, mp 134−135 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.11−8.04 (m, 2H), 7.75 (d, J = 9.0 Hz, 2H), 7.60 (d, J = 9.0 Hz, 1H), 7.54 (t, J = 3.6 Hz, 1H), 7.41−7.38 (m, 2H), 7.01 (d, J = 9.0 Hz, 2H), 3.99 (s, 3H), 3.94 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.1, 167.4, 163.8, 141.7, 140.1, 132.3, 129.0, 128.2, 127.4, 125.9, 125.4, 125.0, 123.7, 122.2, 120.4, 115.7, 115.2, 114.4, 55.8, 52.4; HRMS (EI) calcd m/z for $C_{22}H_{18}NO_4$: 360.1230, found 360.1238.

*9-(4-Methoxybenzoyl)-3-nitrocarbazole (**3z**):* 23.3 mg (27%), yellow solid, mp 170−172 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (d, J = 2.1 Hz, 1H), 8.28 (dd, J = 9.0, 2.4 Hz, 1H), 8.14−8.11 (m, 1H), 7.78−7.71 (d, J = 9.0 Hz, 3H), 7.48−7.42 (m, 3H), 7.03 (d, J = 9.0 Hz, 2H), 3.95 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 168.8, 166.6, 164.2, 142.9, 140.6, 132.4, 128.3, 126.4, 126.1, 124.7, 124.0, 122.2, 120.8, 116.4, 115.8, 115.5, 114.6, 55.9; HRMS (EI) m/z calcd for $C_{20}H_{15}N_2O_4$: 347.1026, found 347.1033.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all novel compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: larock@iastate.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Institute of General Medical Sciences (GM070620), the National Institutes of Health Kansas University Center of Excellence for Chemical Methodologies and Library Development (P50 GM069663), and the National Science Foundation for their generous support of this research.

■ REFERENCES

(1) (a) Guthrie, R. W.; Brossi, A.; Mennona, F. A.; Mullin, J. G.; Kierstead, R. W.; Grunverg, E. J. *J. Med. Chem.* **1975**, *18*, 755. (b) Sakano, K. I.; Ishinaru, K.; Nakamura, S. *J. Antibiot.* **1980**, *33*, 683.

(c) Crich, D.; Runthao, S. *Tetrahedron* **2004**, *60*, 1513. (d) Knoelker, H.-J. *Top. Curr. Chem.* **2005**, *244*, 115. (e) Maneerat, W.; Ritthiwigrom, T.; Cheenpracha, S.; Promgool, T.; Yossathera, K.; Deachathai, S.; Phakhodee, W.; Laphookhieo, S. *J. Nat. Prod.* **2012**, *75*, 741. (f) Schmidt, A. W.; Reddy, K. R.; Knoelker, H.-J. *Chem. Rev.* **2012**, *112*, 3193.

(2) Ostroverkhova, O.; Moerner, W. E. *Chem. Rev.* **2004**, *104*, 3267.

(3) For a recent comprehensive review on the synthesis of carbazoles, see: Roy, J.; Jana, A. K.; Mal, D. *Tetrahedron* **2012**, *68*, 6099.

(4) For recent comprehensive reviews on aryne chemistry, see: (a) Chen, Y.; Larock, R. C. *Modern Arylation Methods*; Wiley/VCH: New York, 2009; pp 401−473. (b) Sanz, R. *Org. Prep. Proced. Int.* **2008**, *40*, 215. (c) Yoshida, H.; Takaki, K. *Synlett* **2012**, *23*, 1725. (d) Bhunia, A.; Yetra, S. R.; Biju, A. T. *Chem. Soc. Rev.* **2012**, *41*, 3140. (e) Peña, D.; Pérez, D.; Guitián, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 3579. (f) Tadross, P. M.; Stoltz, B. M. *Chem. Rev.* **2012**, *112*, 3550. (g) Gampe, C. M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766.

(5) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, *12*, 1211.

(6) Liu, Z.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3198.

(7) (a) Rogness, D.; Larock, R. C. *Tetrahedron Lett.* **2009**, *50*, 4003. (b) Zhao, J.; Larock, R. C. *J. Org. Chem.* **2007**, *72*, 583. (c) Liu, Z.; Shi, F.; Martinez, P. D. G.; Raminelli, C.; Larock, R. C. *J. Org. Chem.* **2008**, *73*, 219. (d) Rogness, D. C.; Markina, N. A.; Waldo, J. P.; Larock, R. C. *J. Org. Chem.* **2012**, *77*, 2743.

(8) (a) Majumdar, K. C.; Chattopadhyay, B.; Maji, P. K.; Chattopadhyay, S. K.; Samanta, S. *Heterocycles* **2010**, *81*, 795. (b) Larock, R. C. *Topics in Organometallic Chemistry*; Springer: Berlin, 2005; Vol. *14*, p 147. (c) Tsuji, J., Ed. *Perspectives in Organopalladium Chemistry for the XXI Century*; Elsevier: New York, 1999. (d) Larock, R. C. *Pure Appl. Chem.* **1999**, *71*, 1425.

(9) For related papers published by our group, see: (a) Liu, Z.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2005**, *127*, 15716. (b) Waldo, J. P.; Zhang, X. *J. Org. Chem.* **2008**, *73*, 6679. (c) Worlikar, S. A.; Larock, R. C. *Curr. Org. Chem.* **2011**, *15*, 3214 , (review).

(10) For related papers published by other groups, see: (a) Jeganmohan, M.; Bhuvaneswari, S.; Cheng, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 391. (b) Pi, S.; Tang, B.; Li, J.; Liu, Y.; Liang, Y. *Org. Lett.* **2009**, *11*, 2309. (c) Bhuvaneswari, S.; Jeganmohan, M.; Yang, M.; Cheng, C. *Chem. Commun.* **2008**, 2158. (d) Henderson, L. J.; Edwards, S. A.; Greaney, F. M. *Org. Lett.* **2007**, *9*, 5589. (e) Xie, C.; Zhang, Y.; Huang, Z.; Xu, P. *J. Org. Chem.* **2007**, *72*, 5431. (f) Jayanth, T. T.; Cheng, C. H. *Chem. Commun.* **2006**, 894. (g) Guitián, E.; Pérez, D.; Peña, D. *Top. Organomet. Chem.* **2005**, *14*, 109. (h) Yoshikawa, E.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 173. (i) Quintana, I.; Boersma, J. A.; Peña, D.; Pérez, D.; Guitián, E. *Org. Lett.* **2006**, *8*, 3347. (j) Parthasarathy, K.; Han, H.; Prakash, C.; Cheng, C.-H. *Chem. Commun.* **2012**, *48*, 6580. (k) Lin, Y.; Wu, L.; Huang, X. *Eur. J. Org. Chem.* **2011**, 2993. (l) Pi, S.-F.; Yang, X.-H.; Huang, X.-C.; Liang, Y.; Yang, G.-N.; Zhang, X.-H.; Li, J.-H. *J. Org. Chem.* **2010**, *75*, 3484.

(11) (a) Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem., Int. Ed.* **1998**, *19*, 37. (b) Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *J. Org. Chem.* **2000**, *65*, 6944.

(12) Gerfaud, T.; Neuville, L.; Zhu, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 572.

(13) (a) Yoshida, H.; Ikadai, J.; Shudo, M.; Ohshita, J.; Kunai, A. *Organometallics* **2005**, *24*, 156. (b) Matsubara, T. *Organometallics* **2003**, *22*, 4297. (c) Yoshida, H.; Tanino, K.; Ohshita, J.; Kunai, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 5052. (d) Retbøll, M.; Edwards, A. J.; Rae, A. D.; Willis, A. C.; Bennett, M. A.; Wenger, E. *J. Am. Chem. Soc.* **2002**, *124*, 8348.

(14) (a) Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *J. Am. Chem. Soc.* **1999**, *121*, 5827. (b) Yoshida, H.; Sugiura, S.; Kunai, A. *Org. Lett.* **2002**, *4*, 2767. (c) Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 2659. (d) Yoshida, H.; Ikadai, J.; Shudo, M.; Ohshita, J.; Kunai, A. *J. Am. Chem. Soc.* **2003**, *125*, 6638.

(15) (a) Gimbert, C.; Vallribera, A. *Org. Lett.* **2009**, *11*, 269. (b) Barbero, N.; Carril, M.; SanMartin, R.; Domínguez, E. *Tetrahedron* **2007**, *63*, 10425. (c) Kofink, C. C.; Blank, B.; Pagano, S.; Götz, N.; Knochel, P. *Chem. Commun.* **2007**, 1954. (d) Evindar, G.; Batey, A. R. *J. Org. Chem.* **2006**, *71*, 1802. (e) Ladziata, U.; Koposov, Y. A.; Lo, Y. K.; Willging, J.; Nemykin, N. V.; Zhdankin, V. V. *Angew. Chem., Int. Ed.* **2005**, *44*, 7127. (f) Pedersen, M. J.; Bowman, W. R.; Elsegood, R. J. M.; Fletcher, J. A.; Lovell, J. P. *J. Org. Chem.* **2005**, *70*, 10615.

(16) Cho, S. H.; Yoon, J.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 5996.

(17) Cipiciani, A.; Linda, P.; Macciantelli, D.; Lunazzi, L. *J. Chem. Soc., Perkin Trans. 2* **1979**, *8*, 1045.