JOC Article

Synthesis of Substituted Carbazoles, Indoles, and Dibenzofurans by Vinylic to Aryl Palladium Migration

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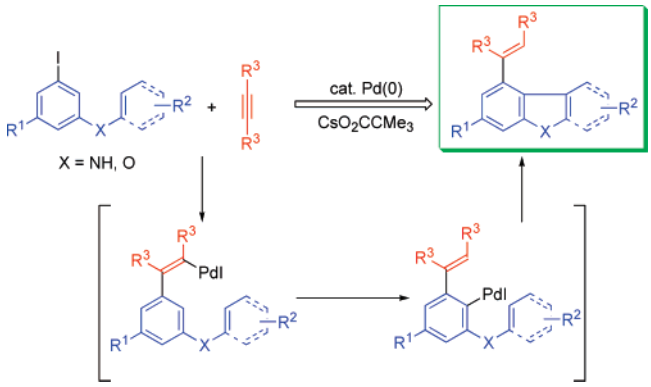
Received April 5, 2006



Substituted carbazoles, indoles, and dibenzofurans are readily prepared in moderate to excellent yields by the palladium-catalyzed cross-coupling of alkynes and appropriately substituted aryl iodides. This process proceeds by carbopalladation of the alkyne, heteroatom-directed vinylic to aryl palladium migration, and ring closure via intramolecular arylation or a Mizoroki−Heck reaction. Results from the deuterium labeling experiments are consistent with the proposed mechanism.

Introduction

The palladium-catalyzed activation of unfunctionalized C−H bonds is considered a highly atom-efficient and environmentally friendly strategy for organic synthesis.[1] Recently, a number of palladium migration examples involving intramolecular C−H activation have been disclosed by our group and others. This through-space shift of palladium appears to be fairly general and can take place between a wide variety of carbon atoms. Specifically, vinylic to aryl,[2] aryl to aryl,[3] alkyl to aryl,[4] and vinylic to aryl to allylic[5] palladium migration processes have been reported. These novel palladium migration processes are not only mechanistically important but also synthetically useful because they afford an alternative way to introduce a palladium moiety into an organic molecule.

Recently, we reported a nitrogen-directed vinylic to aryl palladium migration, which provides an efficient way to prepare biologically interesting carbazoles as shown in Scheme 1.[2c,6] This process proceeds by carbopalladation of the internal alkyne, and then the palladium moiety migrates from the vinylic position to the aryl position through an intramolecular C−H activation

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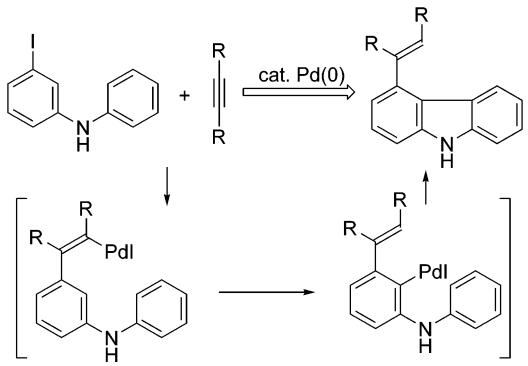
10.1021/jo060727r CCC: $33.50
Published on Web 06/17/2006

SCHEME 1. Synthesis of Substituted Carbazoles via Vinylic to Aryl Palladium Migration

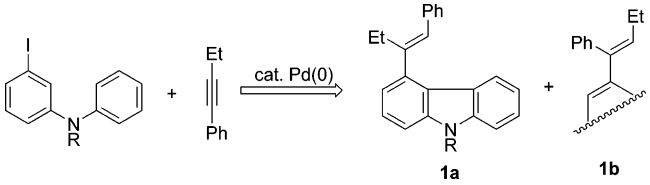


process. The arylpalladium intermediate generated subsequently undergoes intramolecular arylation to afford the carbazole products. Herein, we wish to report a complete account on this nitrogen-directed palladium migration, an extension of this methodology to the synthesis of biologically interesting dibenzofurans,[7] and the synthesis of indoles[8] in which the arylpalladium intermediate is trapped by an intramolecular Mizoroki−Heck reaction. Furthermore, substrates labeled with deuterium have also been prepared and employed in this process to explore the mechanistic details of this rearrangement.

Results and Discussion

1. Optimization of Reaction Conditions. In our initial work on this carbazole synthesis, we treated *N*-phenyl-3-iodoaniline and 1 equiv of 1-phenyl-1-butyne with 5 mol % of $Pd(OAc)_2$, 10 mol % of PPh_3, and 2 equiv of NaOAc in *N*,*N*-dimethylformamide (DMF) at 100 °C for 24 h (Table 1, entry 1). Unfortunately, only a trace amount of the desired carbazole product **1a** was observed by GC-MS analysis. This reaction was subsequently carried out using both an inorganic base Na_2CO_3 (entry 2) and an organic base NEt_3 (entry 3), but none of the desired carbazole product was observed. When 1 equiv of *n*-Bu_4NCl (TBAC) was added to the NaOAc reaction, a 20% yield of a 10:1 ratio of isomeric carbazoles **1a** and **1b** was obtained (entry 4). We next conducted the model reaction in the presence of 2 equiv of CsO_2CCMe_3 (CsPiv) because of its superior solubility in DMF. To our delight, a 60% yield of the desired products was obtained (entry 5). By simply replacing PPh_3 with a bidentate ligand bis(diphenylphosphino)methane (dppm), we isolated a 73% yield of the two regioisomers by flash chromatography (entry 6). We then repeated the same reaction in the presence of 1 equiv of TBAC, but it appears that the presence of a chloride source is unnecessary for this transformation (entry 7). The lack of a substituent on the aniline nitrogen is also crucial because the corresponding amines with Me and Ph substituents produced none of the anticipated carbazoles (entries 8 and 9). In conclusion, the "optimal" reaction conditions for this nitrogen-directed vinylic to aryl palladium migration utilize 5 mol % of $Pd(OAc)_2$, 5 mol % of bis(diphenylphosphino)methane (dppm), and 2 equiv of CsO_2CCMe_3 (CsPiv) in DMF at 100 °C.

TABLE 1. Optimization of the Carbazole Synthesis



entry	R	base	ligand	additive	time (h)	% yield (**1a**:**1b**)[a]
1	H	2NaOAc	10% PPh_3		24	trace
2	H	$2Na_2CO_3$	10% PPh_3		24	0
3	H	$2NEt_3$	10% PPh_3		24	0
4	H	2NaOAc	10% PPh_3	1TBAC	24	20 (10:1)
5	H	2CsPiv	10% PPh_3		12	60[b] (10:1)
6	H	2CsPiv	5% dppm		6	73 (10:1)
7	H	2CsPiv	5% dppm	1TBAC	6	71[b] (10:1)
8	Me	2CsPiv	5% dppm		12	trace
9	Ph	2CsPiv	5% dppm		12	0

[a] All reactions were conducted on a 0.25 mmol scale at 100 °C in 4 mL of DMF, and the ratio of aryl iodide to alkyne was 1:1 (sealed vial, under Ar). The ratio of **1a** to **1b**, as determined by ^1H NMR spectroscopy, is reported in parentheses. [b] GC yield.

2. Synthesis of Carbazoles by Nitrogen-Directed Vinylic to Aryl Palladium Migration. We next examined the reaction using various internal alkynes to determine the scope and limitations of this process. The results are shown in Table 2. Theoretically, when 4,4-dimethyl-2-pentyne was allowed to react with *N*-phenyl-3-iodoaniline, the previously reported consecutive vinylic to aryl to allylic palladium migration could also occur, and a π-allylpalladium complex **I** would be generated as shown in Scheme 2.[5] However, as determined by GC-MS analysis, only the expected carbazole product was found, and a 44% yield of one regioisomer **2a** was isolated (Table 2, entry 2). When 4-octyne was employed as the starting material, the reaction was very messy, and only a 35% yield of the carbazole **3** was obtained (entry 3). In this system, the vinylpalladium intermediate generated from carbopalladation may undergo β-H elimination to afford an allene, which may account for the low yield of carbazole in this reaction. To avoid loss of the volatile alkyne (the boiling point of 4,4-dimethylpentyne is only 70 °C) or possible β-H elimination, 2,2-dimethyl-3-octyne was prepared and allowed to react with our diarylamine. However, only a 48% yield of the desired product **4a** was isolated (entry 4). 1-Phenyl-1-propyne afforded a 65% yield of two regioisomers **5a** and **5b** in a 12:1 ratio (entry 5). In the case of diphenylacetylene, the arylpalladium intermediate formed by vinylic to arylpalladium migration might be expected to undergo direct arylation of one of the phenyl groups of the diphenylacetylene, affording phenylamino-substituted benzylidenefluorenes **II** or **III** (Scheme 2).[2] Surprisingly, a 69% yield of a single isomer **6** was isolated from this reaction (entry 6), and no benzylidenefluorene products were observed. We have also examined the reaction of this aniline with a couple of other aryl acetylenes bearing diverse functionalities on the arene. When 1-(4-nitrophenyl)-1-butyne was employed in our carbazole synthesis, a very messy reaction was observed and none of the desired product was evident by GC-MS analysis (entry 7). However, when a moderate electron-withdrawing ester group (CO_2Et) was present on the phenyl ring of the alkyne, a 71% yield of a single regioisomer **7a** was isolated by flash chromatography (entry 8).

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TABLE 2. Synthesis of Substituted Carbazoles[a]

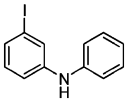
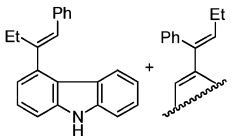
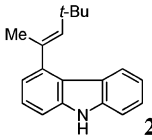
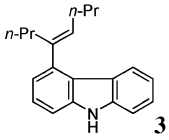
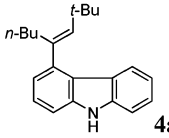
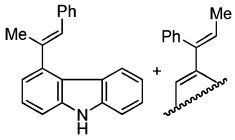
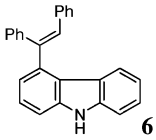
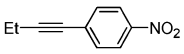
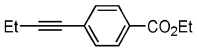
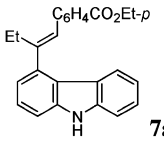
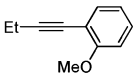
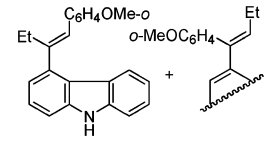
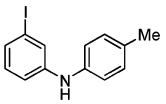
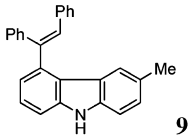
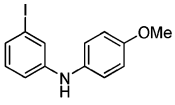
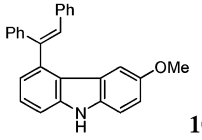
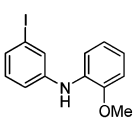
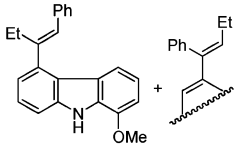
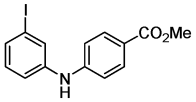
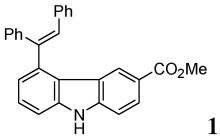
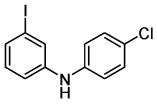
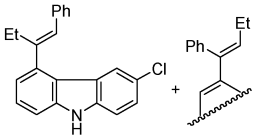
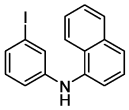
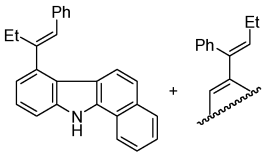
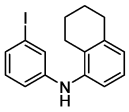
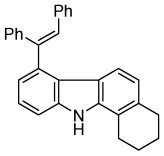
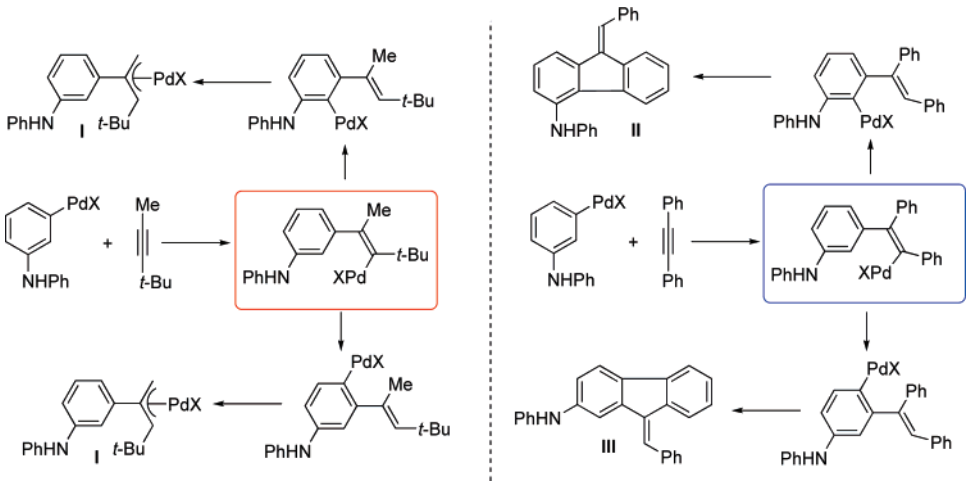
entry	aryl iodide	alkyne	time (h)	product(s)	% yield (**a**:**b**)[b]
1			6	 **1a** **1b**	73 (10:1)
2			6	 **2a**	44
3			6	 **3**	35[c]
4			6	 **4a**	48
5			6	 **5a** **5b**	65 (12:1)
6			6	 **6**	69
7			12	-	0
8			6	 **7a**	71
9			6	 **8a** **8b**	68 (10:1)
10			24	-	0
11			6	 **9**	61
12			6	 **10**	75
13			6	 **11a** **11b**	77 (10:1)

Table 2 (Continued)

entry	aryl iodide	alkyne	time (h)	product(s)	% yield (**a**:**b**)[b]
14			6	 **12**	71
15			6	 **13a** **13b**	65 (10:1)
16			6	 **14a** **14b**	64 (10:1)
17			12	 **15**	68

[a] All reactions were conducted on a 0.25 mmol scale at 100 °C, using 5 mol % of $Pd(OAc)_2$, 5 mol % of bis(diphenylphosphino)methane (dppm), and 2 equiv of CsO_2CCMe_3 (CsPiv) in DMF (4 mL), and the ratio of aryl iodide to alkyne was 1:1 (sealed vial, under Ar). [b] The ratio of **a** to **b**, as determined by ^1H NMR spectroscopy, is reported in parentheses. [c] The isolated products contain impurities, which cannot be separated by flash chromatography, thus the yield has been determined by GC analysis.

SCHEME 2. Other Possible Palladium Migration Reactions

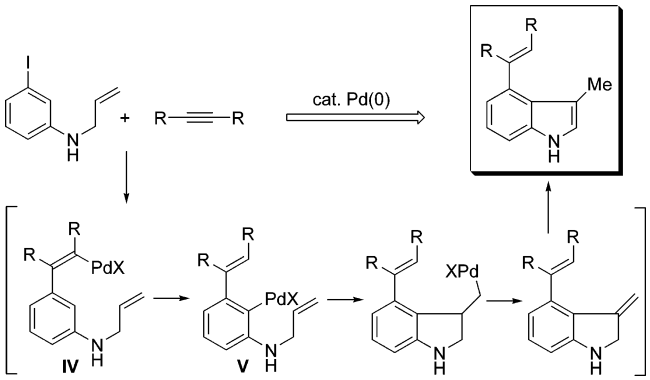


Presumably, the improved regioselectivity is due to the fact that the electron-withdrawing group tends to stabilize the vinylpalladium intermediate generated[9] and thus enhances the regioselectivity of carbopalladation. We can only surmise that the presence of the NO_2 group stabilizes the resulting vinylpalladium intermediate so much that it no longer undergoes palladium migration and side reactions ensue, consuming all starting materials. An analogous alkyne bearing an *ortho*-methoxy group on the arene afforded a 68% yield of the anticipated 10:1 mixture of carbazoles **8a** and **8b**, respectively (entry 9). When methyl phenylpropynoate was employed in this process, after a 24 h reaction, none of the desired carbazole product was evident (entry 10).

(9) Zhou, C.; Emrich, D. E.; Larock, R. C. *Org. Lett.* **2003**, *5*, 1579.

We have also examined the reaction of a number of anilines bearing functionality on the aromatic ring undergoing substitution by the arylpalladium intermediate generated by the vinylic to aryl palladium migration (see the later mechanistic discussion). The reaction of *N*-(4-methylphenyl)-3-iodoaniline and diphenylacetylene afforded a 61% yield of carbazole **9** (entry 11). A more electron-rich substrate bearing a methoxy group afforded a 75% yield of a single carbazole product **10** (entry 12). The reaction of *N*-(2-methoxyphenyl)-3-iodoaniline and 1-phenyl-1-butyne was also studied (entry 13). Statistically, the methoxy group ortho to the nitrogen would be expected to reduce the opportunities for intramolecular arylation, plus the favored molecular configuration for the arylpalladium intermediate is expected to be one in which the aromatic ring is

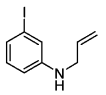
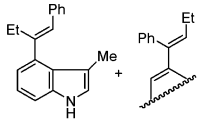
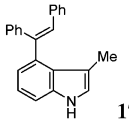
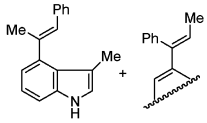
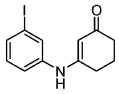
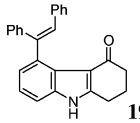
SCHEME 3. Synthesis of Substituted Indoles



perpendicular to the other aromatic ring, which should disfavor intramolecular arylation. However, a 77% yield of a 10:1 mixture of regioisomeric carbazoles was obtained, probably because the oxygen atom of the methoxy group coordinates to the palladium moiety and perhaps stabilizes the arylpalladium intermediate generated. Substrates bearing either an electron-withdrawing 4-methoxycarbonyl or a 4-chloro group also afforded a 71% yield of carbazole **12** and a 65% yield of two isomeric carbazoles **13a** and **13b** in a 10:1 ratio, respectively (entries 14 and 15). We have also examined the regioselectivity of ring closure by employing *N*-(3-iodophenyl)naphthalen-1-amine (entry 16). Here, cyclization might occur at either the 2 position or the 8 position of the naphthalene ring. However, the only products observed are those formed by ring closure at the 2 position of the naphthalene by the presumed intermediacy of a six-membered ring palladacycle, as opposed to the analogous seven-membered ring palladacycle required to generate the product of attack at the 8 position of the naphthalene. A tetrahydronaphthylamine compound was also prepared and allowed to react with diphenylacetylene, and a 68% yield of carbazole **15** was isolated by flash chromatography (entry 17).

3. Synthesis of Substituted Indoles by Vinylic to Aryl Palladium Migration Followed by an Intramolecular Mizoroki−Heck Reaction. The arylpalladium intermediates generated by aryl to aryl palladium migration have been shown to undergo an intermolecular Mizoroki−Heck reaction and a Suzuki−Miyaura reaction,[10] and the arylpalladium species generated from alkyl to aryl palladium migration have also been shown to be easily trapped by an intermolecular Mizoroki−Heck reaction.[4] An arylpalladium species generated from vinylic to aryl palladium migration has also been trapped by a Stille coupling reaction.[2c] Because the intramolecular Mizoroki−Heck reaction is a very powerful method for C−C bond formation in organic synthesis and a plethora of natural products and biologically interesting compounds have been synthesized employing this methodology,[11] we were encouraged by our carbazole synthesis to examine possible intramolecular Heck reactions as a trap for the arylpalladium intermediate generated. As shown in Scheme 3, after carbopalladation, vinylpalladium intermediate **IV** is generated. Once the palladium moiety undergoes nitrogen-directed vinylic to aryl migration to afford arylpalladium species **V**, an intramolecular Heck reaction, followed by aromatization, should generate indole derivatives. *N*-Allyl-3-iodoaniline and 1 equiv of 1-phenyl-1-butyne were allowed to react with 5 mol % of $Pd(OAc)_2$, 5 mol % of dppm, and 2 equiv of CsO_2CCMe_3 in 4 mL of DMF at 100 °C. After 3 h, the aryl iodide was completely consumed and a 45% yield of two isomeric indoles **16a** and **16b** was obtained in a 10:1 ratio (Table 3, entry 1). Two equiv of *N*-allyl-3-iodoaniline was allowed to react with this alkyne. However, a lower yield was obtained. We have been very reluctant to dramatically change the reaction conditions because the palladium migration chemistry is generally very sensitive to variations in the reaction conditions, especially the base. However, we did try a few things to optimize the reaction conditions to achieve higher yields. The reaction was conducted at both 80 °C and 125 °C, in more concentrated or diluted solutions, in the presence of TBAC or Ag_2CO_3, and using electron-rich ligands, such as P(*t*-Bu)$_3$. Unfortunately, none of our efforts were fruitful. A set of other alkynes and imine starting materials have been screened, and only moderate yields (26−40%) have been obtained (entries 2−4). The major problem in this process is probably the fact that the arylpalladium intermediate generated by oxidative addition, the vinylpalladium intermediate **IV**, and the arylpalladium intermediate **V** can all react with *N*-allyl-3-iodoaniline. Although the desired process is an intramolecular reaction, which should have some advantage over those intermolecular processes, at this time we are unable to get higher yields. An additional complication is that the vinylic to aryl palladium migration is presumably the slow step in this domino process, which leaves plenty of time for side reactions.

TABLE 3. Synthesis of Substituted Indoles[a]

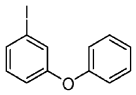
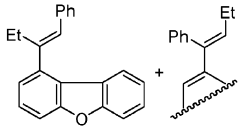
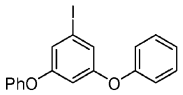
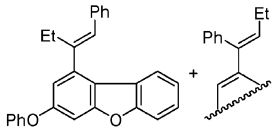
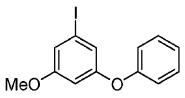
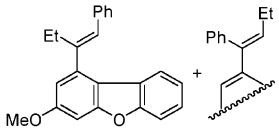
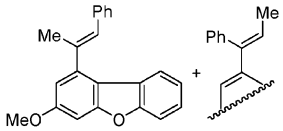
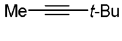
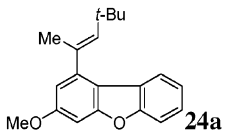
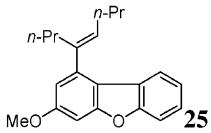
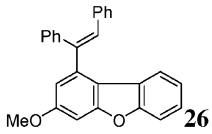
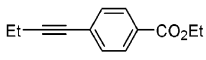
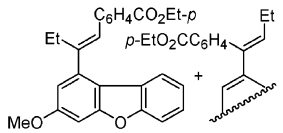
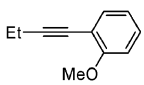
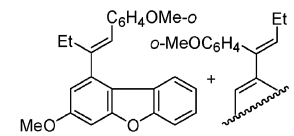
entry	aryl iodide	alkyne	product	% yield (**a**:**b**)[b]
1			 **16a** **16b**	45 (10:1)
2			 **17**	31
3			 **18a** **18b**	26 (15:1)
4			 **19**	40[c]

[a] These reactions were conducted on a 0.25 mmol scale at 100 °C for 3 h, using 5 mol % of $Pd(OAc)_2$, 5 mol % of bis(diphenylphosphino)methane (dppm), and 2 equiv of CsO_2CCMe_3 (CsPiv) in DMF (4 mL), and the ratio of aryl iodide to alkyne was 1:1 (sealed vial, under Ar). [b] The ratio of **a** to **b**, as determined by ^{1}H NMR spectroscopy, is reported in parentheses. [c] The reaction was conducted at 125 °C, using 10 mol % of $Pd(OAc)_2$, 10 mol % of bis(diphenylphosphino)methane (dppm), and 2 equiv of CsO_2CCMe_3 (CsPiv) in DMF (2 mL) for 24 h.

(10) Campo, M. A.; Zhang, H.; Yao, T.; McCulla, R. D.; Huang, Q.; Zhao, J.; Jenks, W. S.; Larock, R. C. *J. Am. Chem. Soc.*, submitted.

(11) (a) Negishi, E. *Handb. Organopalladium Chem. Org. Synth.* **2002**, *1*, 1223 and references therein. (b) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons: England, 2004; p 135. (c) Odle, R.; Blevins, B.; Ratcliff, M.; Hegedus, L. S. *J. Org. Chem.* **1980**, *45*, 2709. (d) Larock, R. C.; Babu, S. *Tetrahedron Lett.* **1987**, *28*, 5291. (e) Caddick, S.; Kofie, W. *Tetrahedron Lett.* **2002**, *43*, 9347.

TABLE 4. Synthesis of Substituted Dibenzofurans[a]

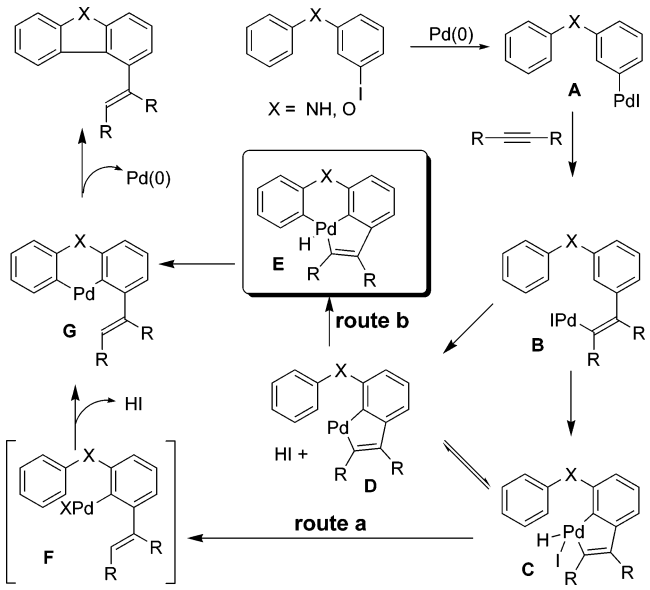
entry	aryl iodide	alkyne	product(s)	% yield (**a**:**b**)[b]
1			 **20a** **20b**	30
2			 **21a** **21b**	75 (9:1)
3			 **22a** **22b**	80 (9:1)
4			 **23a** **23b**	78 (9:1)
5			 **24a**	42
6			 **25**	44
7			 **26**	76
8			 **27a** **27b**	60 (15:1)
9			 **28a** **28b**	37 (7:1)

[a] All reactions were conducted on a 0.25 mmol scale at 100 °C for 12 h, using 5 mol % of $Pd(OAc)_2$, 5 mol % of bis(diphenylphosphino)methane (dppm), and 2 equiv of CsO_2CCMe_3 (CsPiv) in DMF (4 mL), and the ratio of aryl iodide to alkyne was 1:1 (sealed vial, under Ar). [b] The ratio of **a** to **b**, as determined by ^{1}H NMR spectroscopy, is reported in parentheses.

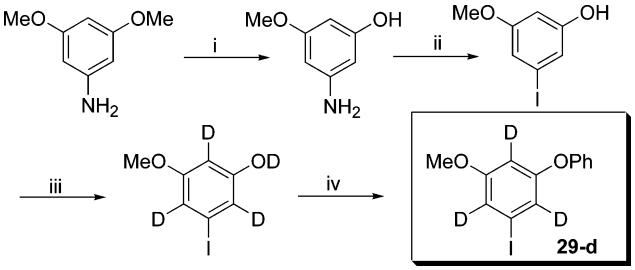
4. Synthesis of Substituted Dibenzofurans. After having investigated the nitrogen-directed vinylic to aryl palladium migration, we wondered if we could expand this protocol to the synthesis of substituted dibenzofurans, although Pd−O coordination would be expected to be much weaker than Pd−N coordination. 3-Iodophenyl phenyl ether and 1-phenyl-1-butyne were treated with 5 mol % of $Pd(OAc)_2$, 5 mol % of dppm, and 2 equiv of $Cs_2O_2CCMe_3$ in DMF at 100 °C; however, the reaction was very messy, and only a 30% yield of an 8:1 mixture of two isomeric dibenzofurans **20a** and **20b** was observed by GC-MS analysis (Table 4, entry 1). Previous aryl to aryl palladium migration studies in our group have indicated that palladium tends to reside on the more electron-rich aromatic ring. Thus, we felt that an increase in electron density in the arene undergoing vinylic to aryl palladium migration should facilitate this through-space migration. Indeed, the reaction of 1-iodo-3,5-diphenoxybenzene with 1-phenyl-1-butyne afforded a 75% yield of a 9:1 mixture of two regioisomeric dibenzofurans **21a** and **21b** (entry 2). The increased reaction efficiency could be a result of the increased electron density of the arene favoring Pd migration. However, this process may also be more efficient because migration to either of the two ortho positions of the arene is now possible, doubling the probability of intramolecular arylation. To further examine the effect of an electron-rich substituent, 3-iodo-5-phenoxyanisole was prepared and allowed to react with 1-phenyl-1-butyne. A 78% yield of two isomeric dibenzofurans **22a** and **22b** was obtained (entry 3), which clearly suggests that an increase in the electron density of the arene is the major reason for the improved reaction efficiency. Several other internal alkynes have been allowed to react with this iodoarene, and moderate to excellent yields have generally been obtained. 1-Phenyl-1-propyne afforded a 78% yield of two regioisomers **23a** and **23b** in a 9:1 ratio (entry 4). 4,4-Dimethyl-2-pentyne afforded a 42% yield of a single regioisomer **24**, as expected (entry 5). 4-Octyne afforded a 44% yield of dibenzofuran **25** (entry 6). When employing diphenylacetylene, a 76% yield of a single isomer **26** was obtained (entry 7). When methyl 4-(but-1-ynyl)benzoate was employed in this reaction, a 60% yield of two isomeric dibenzofurans **27a** and **27b** was obtained in a 15:1 ratio (entry 8). An analogous alkyne bearing an *ortho*-methoxy group afforded a 37% yield of a 7:1 mixture of dibenzofuran products **28a** and **28b** (entry 9).

5. Mechanism. A plausible mechanism for this palladium rearrangement is proposed in Scheme 4. Intermediate **A** is first generated by oxidative addition of the aryl iodide to Pd(0). Subsequent intermolecular carbopalladation would be expected to afford intermediate **B**. The resulting vinylic palladium intermediate **B** might then undergo palladium migration from the vinylic position to an aryl position to generate intermediate **F**, possibly through an organopalladium(IV) hydride **C** (route a), although such Pd(IV) hydride intermediates have not previously been reported.[12] An equilibrium between organopalladium(IV) hydride **C** and organopalladium(II) intermediate **D** is also possible, although palladacycle **D** could also be generated directly from intermediate **B**. Intermediate **F** eventually undergoes either palladium insertion into the C−H bond of the neighboring arene or electrophilic aromatic substitution to afford the six-membered ring palladacycle **G**. Alternatively, intermediate **D** can undergo intramolecular C−H activation to generate an interesting organopalladium(IV) hydride **E**; subsequent reductive elimination could also generate intermediate **G** (route b). When R is a phenyl group, the palladium moiety can migrate to either of two ortho positions of the arene originally bearing the iodo group and then be trapped by arylation to generate either the observed carbazole (dibenzofuran) or a fluorene. Although we have previously reported such a fluorene synthesis,[2] only the carbazole (dibenzofuran) products are observed, which suggests that the palladium only migrates to the position ortho to the heteroatom. This interesting selectivity may be due to coordination between the ortho heteroatom and the palladium moiety, which is not available if the palladium migrates to the position para to the heteroatom. Alternatively, the palladium may prefer the position ortho to the heteroatom due to stabilization of the arylpalladium intermediate by inductive electron withdrawal, as suggested by recent results in our laboratories, which are supported by calculations.[10]

SCHEME 4. Proposed Mechanism



SCHEME 5. Synthesis of Deuterated Compound 29-d[a]



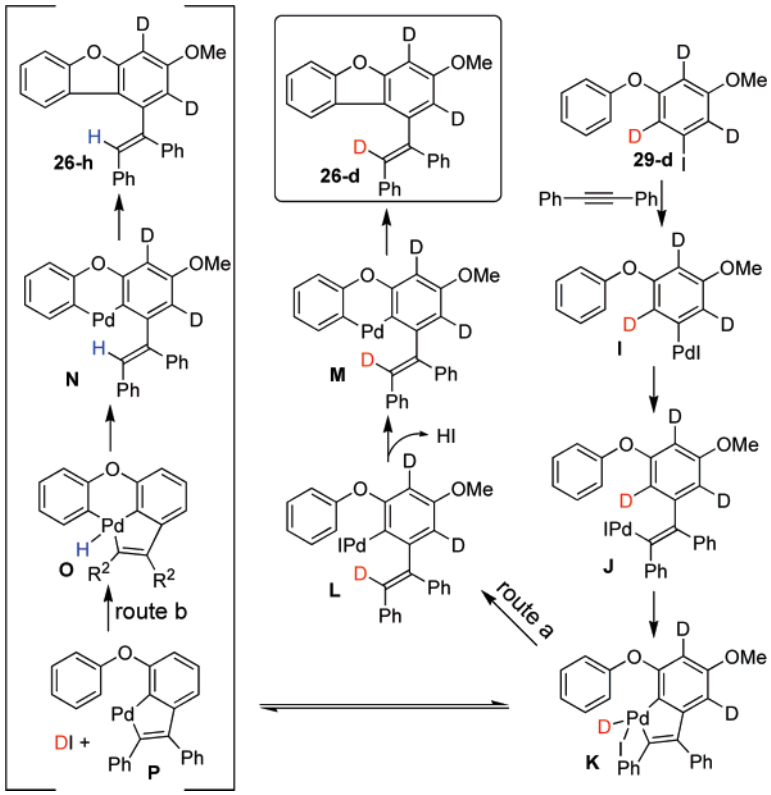
[a] (i) NaSMe, DMA, 140 °C; (ii) (a) $NaNO_2$, HCl, (b) Kl; (iii) CF_3CO_2D, reflux; (iv) 4CsF, 1.1 2-(trimethylsilyl)phenyl trifluoromethanesulfonate, MeCN.

6. Deuterium Labeling Experiments. To clarify the ambiguities in the mechanism, we prepared the deuterium labeled starting material **29-d** (90% deuterium incorporation in each position of the arene, as shown in Scheme 5)[13] and allowed this compound to react with diphenylacetylene under our usual palladium migration conditions. According to the proposed

(12) Other organopalladium(IV) species are well-known, however. See: Canty, A. J. *Acc. Chem. Res.* **1992**, *25*, 83.

(13) For the preparation of 3-hydroxy-5-methoxyaniline, see: Wendt, M. D.; Rockway, T. W.; Geyer, A.; McClellan, W.; Weitzberg, M.; Zhao, X.; Mantei, R.; Nienaber, V. L.; Stewart, K.; Klinghofer, V.; Giranda, V. *J. Med. Chem.* **2004**, *47*, 303.

SCHEME 6. Deuterium Labeling Experiment



mechanism shown in Scheme 6, if the reaction only proceeds through route a, the deuterium originally ortho to the oxygen atom and the iodine atom will shift to the vinylic position after the vinylic to aryl palladium migration. Thus, we should obtain dibenzofuran **26-d**. On the other hand, if this reaction only goes through the mechanism described in route b, product **26-h** should be obtained. Indeed, an 80% yield of dibenzofuran **26-d** was isolated by flash chromatography, with 70% deuterium incorporation in the vinylic position (determined by ^{1}H NMR spectroscopy). This result clearly suggests the involvement of route a. The loss of deuterium could be due to H−D exchange through an equilibrium between palladacycle **K** and palladacycle **P** or to the direct H−D exchange between intermediate **K** and an H source in the reaction solution. Alternatively, it could be due to the involvement of route b because the aryl deuterium presumably would be washed out upon formation of intermediate **P**. To address these issues, we conducted the same reaction in the presence of 10 equiv of D_2O, and 85% deuterium incorporation was observed in the vinylic position of the isolated dibenzofuran product **26-d**, which suggests that the previous deuterium loss was probably the result of H−D exchange in intermediate **K**, instead of the result of the alternative mechanistic route b.

Conclusions

In conclusion, we have established the scope and limitations of a mechanistically important palladium migration process, which affords an efficient way to prepare biologically interesting carbazoles, indoles, and dibenzofurans. The advantage of this chemistry is that an alkenyl substituent can be efficiently incorporated into the heterocyclic ring during the course of the cyclization, which can be still further modified to other functional groups. This reaction is quite general for the synthesis of carbazoles; however, only moderate yields can be obtained in the synthesis of indoles, and excellent yields can be achieved in the synthesis of dibenzofurans only if electron-rich aryl iodides are employed. The relatively modest regiochemistry of alkyne insertion also presents problems. The results of deuterium labeling experiments showed a high degree of deuterium incorporation in the vinylic position of the dibenzofuran product obtained, affording convincing evidence for the proposed palladium migration mechanism. The H−D exchange also suggests that the migration process involves an equilibrium between Pd(II) and Pd(IV) intermediates, which is consistent with a previously reported consecutive vinylic to aryl to allylic palladium migration[5] and does not favor the direct Pd−H shift mechanism reported elsewhere.[2d]

Experimental Section

Representative Procedure for the Palladium-Catalyzed Migration Reactions. The appropriate aryl iodide (0.25 mmol), $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), 1,1-bis(diphenylphosphino)methane (dppm) (4.8 mg, 0.0125 mmol), and CsO_2CCMe_3 (CsPiv) (0.117 g, 0.5 mmol) in DMF (4 mL) were stirred under Ar at 100 °C for the specified period of time. The reaction mixture was allowed to cool to room temperature, diluted with diethyl ether (25 mL), and washed with 5% aq Na_2CO_3 (25 mL). The aqueous layer was reextracted with diethyl ether (25 mL) twice. The organic layers were combined, dried ($MgSO_4$), and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel.

(*E*)-4-(1,2-Diphenylvinyl)-9*H*-carbazole (6). Purification by flash chromatography (5:1 hexane/EtOAc) afforded 59.5 mg (69%) of the product as a light yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.03−7.14 (m, 3H), 7.23−7.42 (m, 14H), 8.03 (s, 1H), 8.37 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) 109.8, 110.8, 119.6, 121.3, 121.7, 123.0, 123.4, 125.7, 125.9, 127.3, 127.7, 128.5, 128.7, 129.8, 130.2,

131.1, 137.6, 140.0, 140.3, 140.4, 140.7, 141.3; IR ($CDCl_3$) 3414, 3054, 1599, 1455 cm^{-1}; HRMS *m*/*z* 345.1522 (calcd for $C_{26}H_{19}N$, 345.1518).

(*E*)-3-Methyl-4-(1-phenylbut-1-en-2-yl)-1*H*-indole (16a). Purification by flash chromatography (2:1 hexane/EtOAc) afforded 28.2 mg (45%) of the product as a light yellow oil: ^1H NMR ($CDCl_3$) δ 1.09 (t, $J = 7.2$ Hz, 3H), 2.36 (s, 3H), 2.77 (q, $J = 7.2$ Hz, 2H), 6.47 (s, 1H), 6.96−6.99 (m, 2H), 7.18 (t, $J = 7.8$ Hz, 1H), 7.27−7.32 (m, 2H), 7.41 (d, $J = 4.1$ Hz, 4H), 7.93 (s, 1H); ^{13}C NMR ($CDCl_3$) 13.2, 13.4, 27.1, 110.0, 112.5, 119.7, 121.7, 122.9, 125.6, 126.6, 128.5, 128.98, 129.0, 137.3, 137.9, 138.4, 144.4; IR ($CDCl_3$) 3418, 3021, 2964, 1598 cm^{-1}; HRMS *m*/*z* 261.1518 (calcd for $C_{19}H_{19}N$, 261.1521).

(*E*)-1-(1,2-Diphenylvinyl)-3-methoxydibenzofuran (26). Purification by flash chromatography (10:1 hexane/EtOAc) afforded 71.4 mg (76%) of the product as a colorless oil:^1H NMR ($CDCl_3$) δ 3.86 (s, 3H), 6.72 (s, 1H), 7.06−7.37 (m, 14H), 7.54 (d, $J = 8.1$ Hz, 1H), 7.92 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 56.0, 95.7, 111.5, 112.8, 115.8, 122.0, 122.8, 124.5, 125.9, 127.5, 127.9, 128.5, 128.8, 129.8, 130.3, 131.6, 137.1, 140.0, 140.1, 140.9, 156.8, 158.2, 159.6; IR ($CDCl_3$) 3054, 3022, 2958, 1629 cm^{-1}; HRMS *m*/*z* 376.1470 (calcd for $C_{27}H_{20}O_2$, 376.1463).

Acknowledgment. We deeply appreciate the financial support of the National Science Foundation and thank Johnson Matthey, Inc. and Kawaken Fine Chemical Co. for donations of $Pd(OAc)_2$.

Supporting Information Available: Preparation and characterization of the aryl iodides and characterization of the carbazole, indole, and dibenzofuran products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO060727R