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Highly Efficient Route to Fused Polycyclic Aromatics via Palladium-Catalyzed Aryne Annulation by Aryl Halides

Zhijian Liu and Richard C. Larock*

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

larock@iastate.edu

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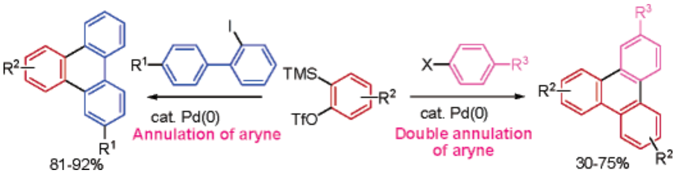

Polycyclic aromatic and heteroaromatic hydrocarbons have been synthesized in high yield by two different processes involving the Pd-catalyzed annulation of arynes. The first process involves a Pd-catalyzed annulation of arynes by 2-halobiaryls and related vinylic halides. The second process utilizes a Pd-catalyzed double annulation of arynes by simple aryl halides. Both processes appear to involve the catalytic, stepwise coupling of two very reactive substrates, an aryne and an organopalladium species, to generate excellent yields of cross-coupled products.

Introduction

Polycyclic aromatic and heteroaromatic hydrocarbons have been widely studied for their unique properties in material science.[1] Recently, these polycyclic aromatic compounds have been discussed as potential candidates for optoelectronic devices[2] and π-conjugated functional materials.[1a] Among these, triphenylenes are the most often synthesized and widely studied. Recently, the Pd-catalyzed cyclotrimerization of arynes, generated in situ, has been shown to be a very novel and useful approach to the synthesis of symmetrical triphenylenes.[3] However, an efficient synthesis of unsymmetrical and functionally substituted triphenylenes remains elusive.

Transition metal-catalyzed annulation processes have proven very useful in organic synthesis.[4] Alkynes have been frequently used as substrates for Pd-catalyzed annulations with functionally substituted aryl and vinylic halides to synthesize a wide variety of carbocycles and heterocycles.[5] These very useful transition metal-catalyzed annulation processes have only recently been extended to arynes. The obvious difficulty is that arynes are very reactive substrates compared with ordinary alkynes and they readily undergo cyclotrimerization under Pd catalysis to form polycyclic aromatic hydrocarbons.[3,6] However, the Pd-catalyzed cocyclotrimerization of arynes with alkynes,[7] arynes with allylic halides,[7c,8] and arynes with alkynes and allylic halides[9] has recently been reported. All examples of the carbopalladation of arynes reported thus far have involved very stable π-allylpalladium intermediates.[7c,8,9] The inherent instability and high reactivity of aryl and vinylic palladium species obtained by oxidative addition to Pd(0) and the high reactivity and propensity of arynes to cyclotrimerize in the presence of Pd(0) do not bode well for annulation processes requiring these species to react with one another.

Nevertheless, we have recently reported that *o*-haloarenecarboxaldehydes readily react in the presence of a Pd catalyst with

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[1] For reviews, see: (a) Watson, M. D.; Fethtenkotter, A.; Mullen, K. *Chem. Rev.* **2001**, *101*, 1267. (b) Chandrasekhar, S. *Liq. Cryst.* **1993**, *14*, 3. (c) Chandrasekhar, S.; Kumar, S. *Sci. Spectra* **1997**, *8*, 66. (d) Pérez, D.; Guitián, E. *Chem. Soc. Rev.* **2004**, *33*, 274. (e) Buess, C. M.; Lawson, D. D. *Chem. Rev.* **1960**, *60*, 313. (f) Watson, M.; Fechtenkötter, A.; Müllen, K. *Chem. Rev.* **2001**, *101*, 1267.

[2] Boden, N.; Bissell, N.; Clements, J.; Movaghar, B. *Liq. Cryst. Today* **1996**, *6*, 1.

[3] Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 2659.

[4] (a) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635. (b) Rubin, M.; Sromek, A. W.; Gevorgyan, V. *Synlett* **2003**, 2265.

[5] (a) Larock, R. C. *Pure Appl. Chem.* **1999**, *71*, 1435. (b) Larock, R. C. In *Topics in Organometallic Chemistry*; Springer: Berlin, Germany, 2005; p 147.

[6] (a) Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *Org. Lett.* **1999**, *1*, 1555. (b) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E.; Castedo, L. *Org. Lett.* **2000**, *2*, 1629.

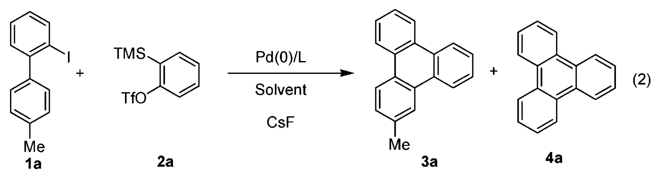
[7] (a) Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *J. Am. Chem. Soc.* **1999**, *121*, 5827. (b) Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *J. Org. Chem.* **2000**, *65*, 6944. (c) Yoshikawa, E.; Radhakrishnan, K. V.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7280. (d) Radhakrishnan, K. V.; Yoshikawa, E.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 7533.

[8] Yoshikawa, E.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 173.

[9] Yoshikawa, E.; Radhakrishnan, K. V.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 729.

10.1021/jo0619534 CCC: $37.00

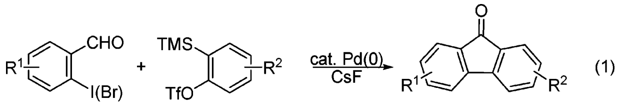
TABLE 1. Optimization of the Pd-Catalyzed Annulation of Benzyne (eq 2)[a]



entry	catalyst (0.05 equiv)	P(*o*-tolyl)$_3$ (equiv)	**2a** (equiv)	CsF (equiv)	solvent (MeCN/ toluene)	**3a**[b] (%)	**4a**[c]
1	Pd(dba)$_2$	0.05	2.0	3.0	100:0	12[d]	+
2	Pd(dba)$_2$	0.05	2.0	3.0	3:1	15[d]	+
3	Pd(dba)$_2$	0.05	2.0	3.0	1:1	38[d]	+
4	Pd(dba)$_2$	0.05	0.33	3.0	1:1	42	+
5	Pd(dba)$_2$	0.05	5.0	5.0	1:1	30	+
6	Pd(dba)$_2$	0.05	2.0	3.0	1:3	52	
7	**Pd(dba)$_2$**	**0.05**	**2.0**	**3.0**	**1:9**	**92**	**T**
8	Pd(dba)$_2$	0.05	2.0	3.0	0:100	trace[d]	
9	Pd(dba)$_2$	0.10	2.0	3.0	1:9	82[d]	T
10	Pd(dba)$_2$	0.02	2.0	3.0	1:9	87[e]	T
11	Pd$_2$(dba)$_3$	0.05	2.0	3.0	1:9	73	T
12	Pd(PPh$_3$)$_4$	0	2.0	3.0	1:9	84[d]	T

[a] All reactions were run using substrate **1a** (0.30 mmol) at 110 °C for 24 h unless otherwise specified. [b] Isolated yield. [c] Key: +, **4a** was the major product; T, a trace amount of **4a** was detected. [d] **1a** was recovered. [e] Pd(dba)$_2$ (0.02 equiv) was employed.

arynes, generated in situ by the reaction of *o*-(trimethylsilyl)aryl triflates and CsF, to afford fluoren-9-ones (eq 1).[10] We have also found that 2-halobiaryls react with arynes under Pd catalysis to generate the corresponding functionalized triphenylenes in very good yields.[11] This process appears to involve the catalytic, stepwise coupling of two very reactive substrates, an aryne and an organopalladium species, to generate excellent yields of cross-coupled products. Herein, we wish to provide a full account of the scope and limitations of that process and our mechanism studies of this novel Pd-catalyzed annulation chemistry. We also wish to report for the first time the Pd-catalyzed double annulation of arynes by simple aryl halides, which affords polycyclic aromatic compounds in good yields.[12]

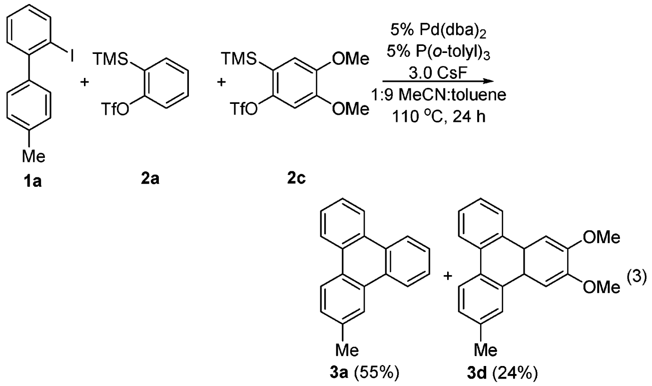


Results and Discussion

Synthesis of Fused Polycyclic Aromatics by the Pd-Catalyzed Annulation of Arynes Using 2-Halobiaryls and Related Vinylic Halides. We first allowed 2-iodo-4′-methylbiphenyl (**1a**) to react with 2.0 equiv of *o*-(trimethylsilyl)phenyl triflate (**2a**), 5 mol % of Pd(dba)$_2$, 5 mol % of P(*o*-tolyl)$_3$, and 3.0 equiv of CsF in 4.0 mL of MeCN at 110 °C for 24 h. The desired annulation product **3a** was obtained in a 12% yield, and considerable triphenylene byproduct was obtained (eq 2; Table 1, entry 1). It was our hypothesis that the concentration of benzyne, which can readily undergo cyclotrimerization to generate triphenylene,[3] was probably too high under these reaction conditions to allow for formation of the requisite arylpalladium halide intermediate. As a consequence, the benzyne reacted with itself in the presence of the palladium catalyst to generate a high yield of triphenylene (**4a**).

Subsequent work focused on optimization of this annulation chemistry. The key results are summarized in Table 1. During this process, we have found that the slow generation of benzyne by treatment of **2a** with CsF in the appropriate solvent system is crucial to the success of this annulation chemistry (compare entries 1−3, 6, and 7). By increasing the amount of toluene in the MeCN/toluene solvent system, one can slow generation of the benzyne and improve the yield of the annulation product **3a**. This presumably occurs because CsF, while highly soluble in MeCN, is only poorly soluble in toluene, which in turn slows generation of the benzyne. For example, when the reaction was performed in a 1:9 ratio of MeCN/toluene, while keeping all other parameters unchanged, the corresponding annulation compound **3a** was obtained in a 92% yield with no triphenylene byproduct (entry 7). However, using toluene as the only solvent provided only a trace of arene **3a**, and most of the starting materials were recovered (entry 8). We believe that MeCN may act as both a ligand and a cosolvent in our reaction system (compare entries 7 and 9). The yield of annulation product could not be improved simply by changing the ratio of the starting materials **1a** and **2a** (entries 4 and 5). If a low loading of the Pd catalyst (2 mol %) is used, the annulation product is still obtained in an 87% yield (entry 10). Other Pd catalysts, such as Pd$_3$(dba)$_2$•CHCl$_3$ (entry 11) and Pd(PPh$_3$)$_4$ (entry 12), have also been employed in this annulation reaction, but Pd(dba)$_2$ (entry 7) has given the highest yield of **3a**.

We have also examined the annulation of substituted arynes. When the 4,5-dimethoxy- and 4,5-dimethyl-substituted aryne precursors **2c** and **2d** (see Table 2 for these structures) were employed for this annulation process, we needed to increase the amount of MeCN in the solvent system in order to obtain good yields of the corresponding annulation products. We believe that generation of the arynes is significantly slower using these aryne precursors. To obtain evidence for this hypothesis, we allowed 2-iodo-4′-methylbiphenyl (**1a**) to react with 2.0 equiv of **2a** and 2.0 equiv of **2c** under our “optimal” reaction conditions. Indeed, we obtained a 55% yield of **3a** and only a 24% yield of **3d**, suggesting that benzyne itself is formed roughly twice as fast as the methoxy-substituted aryne under the same reaction conditions (eq 3).



On the basis of the above optimization efforts, the combination of 1 equiv of the 2-halobiaryl **1a** (0.3 mmol), 2 equiv of silylaryl triflate **2a**, 5 mol % of Pd(dba)$_2$, 5 mol % of P(*o*-tolyl)$_3$,

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[10] Zhang, X.; Larock, R. C. *Org. Lett.* **2005**, *7*, 3973.

[11] Liu, Z.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2005**, *127*, 15716.

[12] After our previous communication was published, a communication appeared that reported the synthesis of substituted triphenylenes by using aryl halides and two arynes: Jayanth, T. T.; Cheng, C.-H. *Chem. Commun.* **2006**, 894.

TABLE 2. **Pd-Catalyzed Annulation of Arynes**[a]

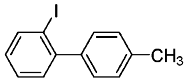
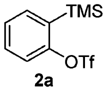
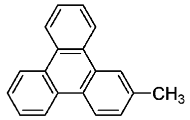
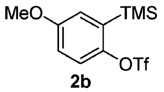
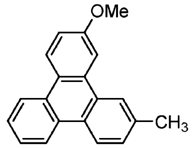
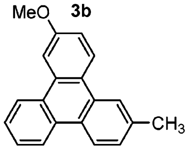
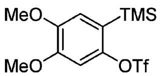
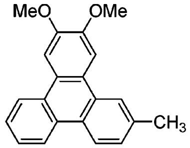
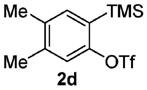
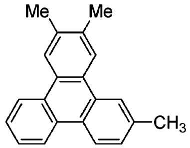
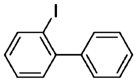
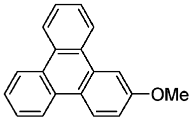
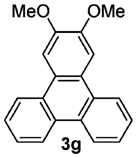
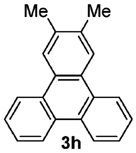
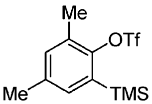
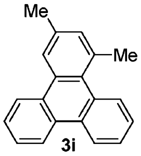
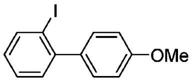
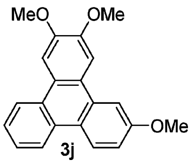
entry	substrate	aryl triflate	product(s)	% isolated yield[b]
1	 **1a**	 **2a**	 **3a**	92
2	**1a**	 **2b**	 **3b**  **3c**	86 (1:1)[c]
3	**1a**	 **2c**	 **3d**	88[d]
4	**1a**	 **2d**	 **3e**	98[d]
5	 **1b**	**2b**	 **3f**	83
6	**1b**	**2c**	 **3g**	82[d]
7	**1b**	**2d**	 **3h**	83[d]
8	**1b**	 **2e**	 **3i**	84[d]
9	 **1c**	**2a**	**3f**	83
10	**1c**	**2c**	 **3j**	81[d]

Table 2 (Continued)

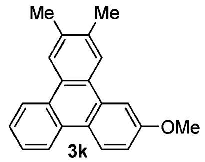
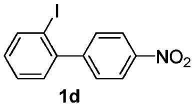
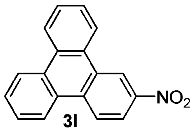
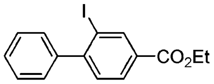
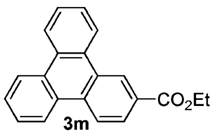
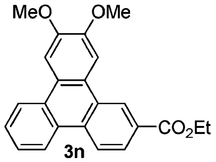
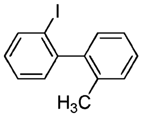
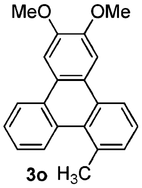
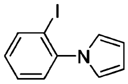
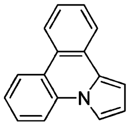
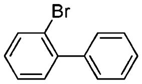
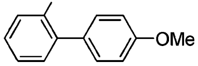
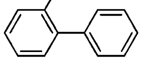
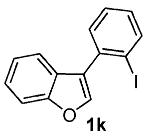
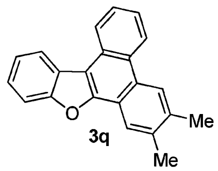
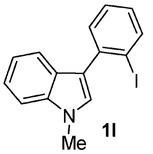
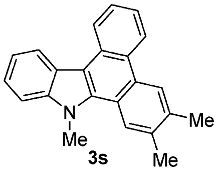
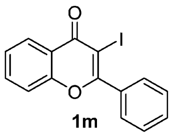
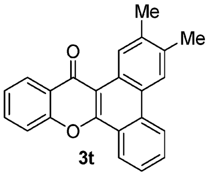
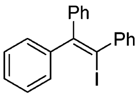
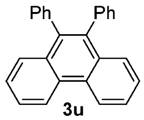
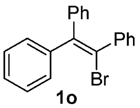
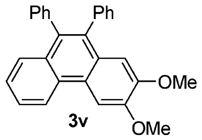
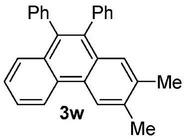
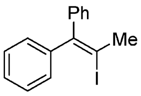
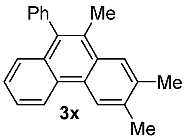
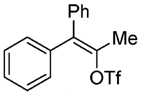
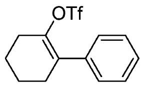
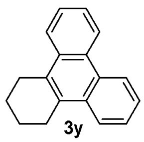
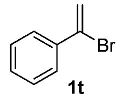
entry	substrate	aryl triflate	product(s)	% isolated yield[b]
11	**1c**	**2d**	 **3k**	93[d]
12	 **1d**	**2a**	 **3l**	75
13	 **1e**	**2a**	 **3m**	81
14	**1e**	**2c**	 **3n**	80[d]
15	 **1f**	**2c**	 **3o**	38[d,e]
16	 **1g**	**2a**	 **3p**	63[f]
17	 **1h**	**2c**	**3g**	81[d]
18	**1h**	**2d**	**3h**	79[d]
19	 **1i**	**2a**	**3f**	75
20	 **1j**	**2c**	no reaction	0[e]
21	 **1k**	**2d**	 **3q**	75[d]

Table 2 (Continued)

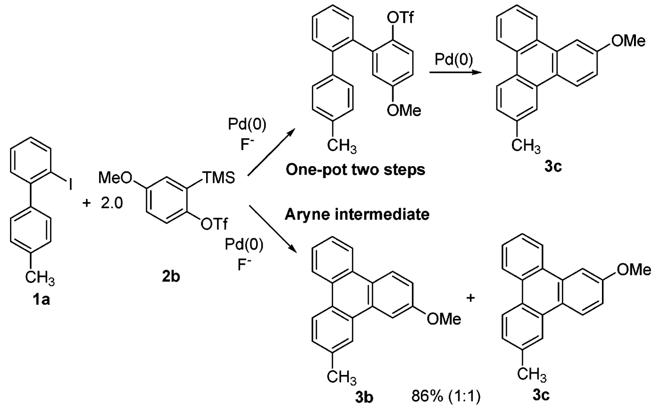
entry	substrate	aryl triflate	product(s)	% isolated yield[b]
22	 **1l**	**2d**	 **3s**	95[d]
23	 **1m**	**2d**	 **3t**	81[d]
24	 **1n**	**2a**	 **3u**	92
25	 **1o**	**2a**	**3u**	91
26	**1o**	**2c**	 **3v**	92[d]
27	**1o**	**2d**	 **3w**	93[d]
28	 **1p**	**2d**	 **3x**	38[d]
29	 **1q**	**2d**	**3x**	29[d]
30	 **1s**	**2a**	 **3y**	28
31	 **1t**	**2c**	messy	0

[a] All reactions were run using 0.30 mmol of the organic halide, 0.60 mmol of the aryne precursor, 5 mol % of Pd(dba)$_2$, 5 mol % of P(*o*-tolyl)$_3$, and 3.0 equiv of CsF in 4.0 mL of 1:9 MeCN/toluene at 110 °C for 24 h unless otherwise specified. [b] Isolated yield. [c] The ratio of products was determined by ^{1}H NMR spectral analysis. [d] MeCN/toluene = 1:3. [e] Starting material left. [f] Compound **3p** is unstable.

and 3 equiv of CsF in 4.0 mL of the mixed solvent (1:9 MeCN/toluene) at 110 °C for 1 d gave the best results (Table 1, entry 7). The mixed solvent needs to be changed from 1:9 to 1:3 in order to obtain good yields of the corresponding annulation products when employing the 4,5-dimethoxy- and 4,5-dimethyl-substituted aryne precursors **2c** and **2d** in this annulation process.

Having gained an understanding of the factors that influence the Pd-catalyzed annulation process, we wanted to know whether

SCHEME 1



our annulation process really involved an aryne intermediate, since another mechanism is also possible. It is conceivable that the compound 2-iodo-4′-methylbiphenyl (**1a**) and the benzyne precursor **2a** could first undergo a Hiyama cross-coupling[13] to generate the terphenyl triflate, which could then undergo Pd-catalyzed cyclization to afford compound **3a**. We, therefore, allowed 2-iodo-4′-methylbiphenyl (**1a**) to react with the 4-methoxy-substituted aryne precursor **2b** to gain evidence as to which mechanism is involved. When the 4-methoxy-substituted aryne precursor **2b** was allowed to react with 2-iodo-4′-methylbiphenyl (**1a**), two isomers **3b** and **3c** were obtained in a 1:1 ratio, clearly suggesting the intermediacy of an aryne in our reaction system. The other possibility, a one-pot, two-step Hiyama cross-coupling, followed by intramolecular cyclization, should afford a single product **3c**,[13] which is not observed (Scheme 1).

The scope and limitations of this Pd-catalyzed aryne annulation process were next examined using various aromatic and vinylic halides and aryne precursors. The results are summarized in Table 2. We first allowed 2-iodo-4′-methylbiphenyl (**1a**) to react with several different aryne precursors (**2a**−**d**). All of the aryne precursors work well in our annulation chemistry and give very high yields of the corresponding annulation products (entries 1−4). The parent 2-iodobiphenyl also afforded excellent yields with several aryne precursors (entries 5−8).

Biaryl substrates bearing both electron-donating and electron-withdrawing groups efficiently undergo this aryne annulation process to generate high yields of the corresponding polycyclic aromatics (Table 2, entries 9−14). The nitro-substituted biaryl is noteworthy, since Pd-catalyzed cyclizations onto such electron-deficient aromatic rings often proceed in significantly lower yields. When 2-iodo-2′-methylbiphenyl (**1f**) was allowed to react with aryne precursor **2c**, only a 38% yield of the corresponding annulation product was obtained (entry 15). The low yield of this reaction can easily be explained by the steric effect of the methyl group, which forces the two phenyl rings out of coplanarity, disfavoring the final cyclization step. The heteroatom-containing substrate **1g** also reacts well with the benzyne precursor **2a** to afford the anticipated annulation product **3p** in a 63% yield, although this product appears rather unstable. Interestingly, normally relatively unreactive 2-bromobiphenyl also reacts well with the aryne precursors **2c** and **2d** to afford the corresponding annulation products in very good yields (entries 17 and 18). The analogous methoxy-substituted bromobiphenyl has also afforded good results (entry 19). However, 2-chlorobiphenyl proved unreactive in this annulation chemistry under the same reaction conditions (entry 20).

A number of heterocycles, including a benzofuran, an indole, and a chromone, have also successfully been employed in this process, affording excellent yields of the corresponding polycyclic materials (Table 2, entries 21−23). This latter chromone substrate is particularly interesting, since it has been previously shown by us that this substrate reacts with diphenyl acetylene in the presence of a Pd catalyst to afford a furan product arising by alkyne insertion and attack of the resulting vinylpalladium intermediate on the carbonyl oxygen.[14] It is also particularly noteworthy that vinylic halides, such as chromone **1m** and the simple vinylic halides **1n** and **1o**, provide excellent yields of annulation products (entries 23−27). On the other hand, vinylic iodide **1p** and vinylic triflates **1q** and **1s** do not afford good yields of aryne annulation products under our reaction conditions (entries 28−30). It is possible that the initial vinylpalladium intermediate derived from the former substrate **1p** is undergoing rapid β-hydride elimination to generate an allene, although we have no direct evidence for this. The problem with the triflates is unclear. The vinylic bromide **1t** gave a messy reaction (entry 31). The anticipated product from vinylic bromide **1t** may simply be undergoing a further Heck reaction to produce a mixture of products.

On the basis of the known chemistry of arynes and previous work on the Pd-catalyzed annulation of alkynes,[5] we suggest two possible mechanisms (cycles **A** and **B**) to account for the present aryne annulation process (Scheme 2). The main difference between these two mechanisms is the first Pd oxidative addition step. In cycle **A**, the Pd(0) complex initially undergoes oxidative cyclization with the aryne **a** to generate palladacycle **b**.[15] Subsequent reaction with **1a** affords intermediate **d** (or perhaps initially an organopalladium(IV) intermediate, which undergoes rapid reductive elimination to **d**), which undergoes intramolecular C−H activation to generate the palladacycle **e**.[16] Subsequent reductive elimination yields the observed annulation product **3a** and regenerates the Pd(0) catalyst. Cycle **B** involves initial oxidative addition of 2-iodo-4′-methylbiphenyl (**1a**) to Pd(0) to generate arylpalladium intermediate **c**, which then reacts with the aryne to afford the same intermediate **d** (cycle **A**), which goes on to product. Both mechanisms afford reasonable routes to the corresponding annulation product.

In an effort to obtain further evidence regarding the mechanism, we have prepared the palladium intermediate **c′**, illustrated in cycle **B**, by reacting 2-iodo-4′-methylbiphenyl (**1a**) with $Pd(dba)_2$ and PPh_3.[15c] When palladium intermediate **c′** was allowed to react with 2.0 equiv of the benzyne precursor **2a** and 3.0 equiv of CsF in the usual solvent mixture, the desired annulation product **3a** was obtained in a 22% yield, alongside a 35% yield of triphenylene (eq 4). While this result is consistent with the mechanism illustrated in cycle **B**, we still cannot rule out the mechanism shown in cycle **A**.

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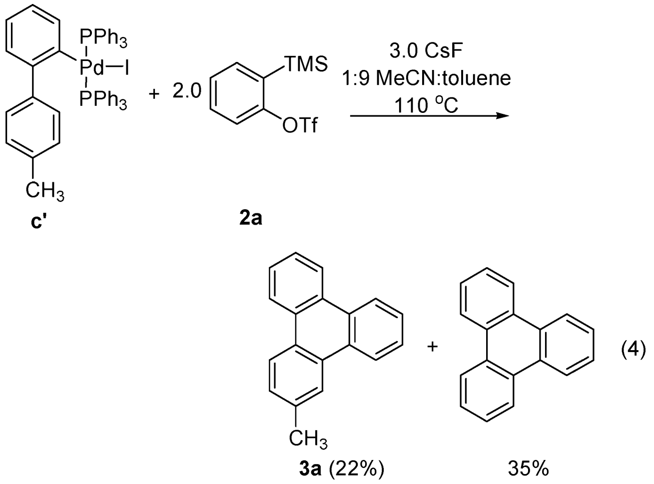
(13) (a) Hiyama, T. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998. (b) Hiyama, T. *J. Organomet. Chem.* **2002**, *653*, 58. (c) Denmark, S. E.; Sweiss, R. F. *Acc. Chem. Res.* **2002**, *35*, 835. (d) Spivey, A. C.; Gripton, C. J. G.; Hannah, J. P. *Curr. Org. Synth.* **2004**, *1*, 211.

(14) Larock, R. C.; Tian, Q. *J. Org. Chem.* **1998**, *63*, 2002.

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

(16) (a) Campeau, L.-C.; Parisien, M.; Jean, A.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 581. (b) Parisien, M.; Damien, V.; Fagnou, K. *J. Org. Chem.* **2005**, *70*, 7578.

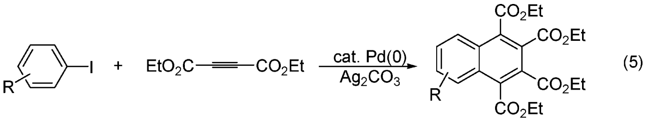


c' **2a**

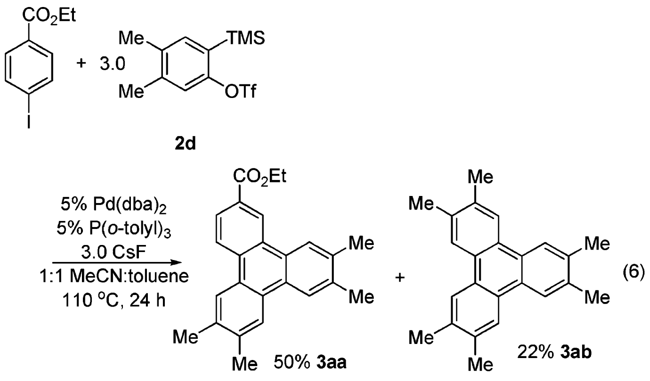
3a (22%) 35%

(4)

Synthesis of Fused Polycyclic Aromatics by the Pd-Catalyzed Double Annulation of Arynes Using Simple Aryl Halides. Recently, the Pd-catalyzed double annulation of an internal alkyne by simple aryl halides to synthesize multisubstituted naphthalenes has been reported (eq 5).[17] Our success in using 2-halobiaryls to annulate arynes and previous Pd-catalyzed cyclotrimerizations[3] suggested to us that we might also be able to generate polycyclic aromatics by the reaction of an aryl iodide and two arynes.[11] During the course of these studies, analogous work was reported by Jayanth and Chen.[12] We first allowed ethyl 4-iodobenzoate to react with 3.0 equiv of the aryne precursor **2d**, 5 mol % of Pd(dba)$_2$, 5 mol % of P(*o*-tolyl)$_3$, and 3.0 equiv of CsF in 2.0 mL of MeCN and 2.0 mL of toluene at 110 °C for 24 h. The desired double annulation product **3aa** was obtained in a 50% yield, alongside 22% of the cyclotrimer **3ab** (eq 6). Although this double annulation process only affords a 50% yield of the desired compound, it nevertheless provides a very short, efficient route to synthesize multisubstituted triphenylenes.



(5)



2d

50% **3aa** 22% **3ab**

(6)

Subsequent work focused on optimization of this double annulation chemistry. To minimize formation of the cyclotrimer, the ratio of the MeCN to toluene solvent mixture was changed from 1:1 to 1:3. Our assumption was that increasing the amount of toluene should slow generation of the aryne and thus formation of the cyclotrimer **3ab**, while increasing the likelihood of generating the arylpalladium intermediate and thus the product **3aa**. Indeed, the reaction furnished a 58% yield of the desired product and a reduced amount of the cyclotrimer. Further changes in the ratio of the solvents failed to improve the yield of the desired double annulation product.

The effect of different palladium catalysts and phosphine ligands on the outcome of the reaction has also been studied. We found that Pd(OAc)$_2$ gave a higher yield of the desired product than other palladium catalysts, such as Pd(PPh$_3$)$_4$, Pd(dba)$_2$, PdCl$_2$(PPh$_3$)$_2$, and Pd$_2$(dba)$_3$·CHCl$_3$. The ligand dppf gave better results than the other ligands studied (dppe, dppp, P(*o*-tolyl)$_3$, PCy$_3$, PPh$_3$). On the basis of the above optimization efforts, the combination of ethyl 4-iodobenzoate (0.3 mmol), 3.0 equiv of aryne precursor, 5 mol % of Pd(OAc)$_2$, 5 mol % of dppf, and 4.0 equiv of CsF, in 1.0 mL of MeCN and 2.0 mL of toluene at 110 °C for 1 d, gave the best yield of double annulation compound **3aa**, affording a 66% yield.

Having gained an understanding of the factors that influence the Pd-catalyzed double annulation process, we have explored

SCHEME 2

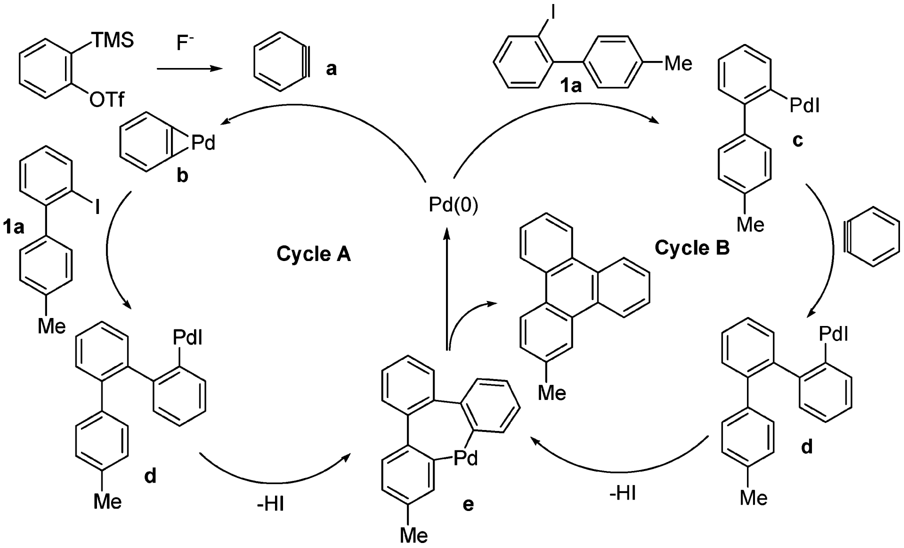


TABLE 3. Pd-Catalyzed Double Annulation of Arynes[a]

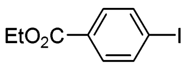
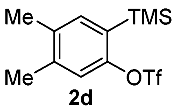
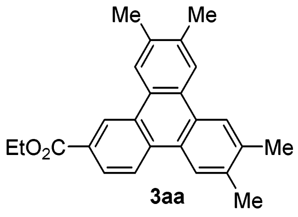
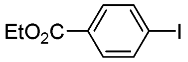
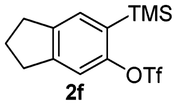
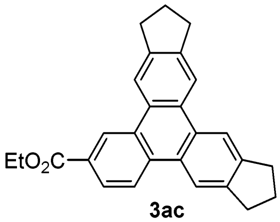
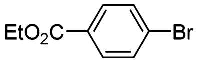
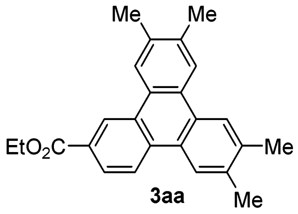
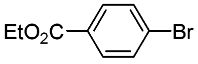
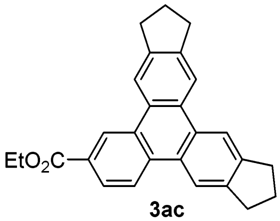
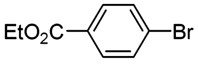
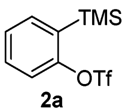
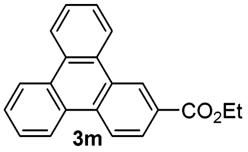
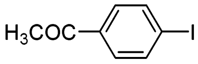
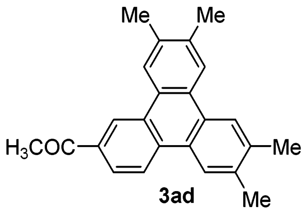
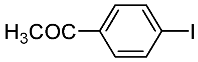
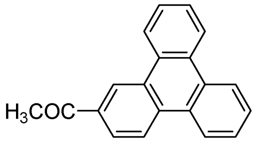
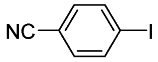
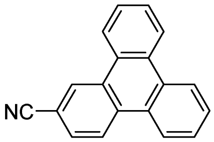
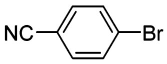
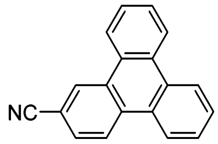
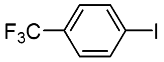
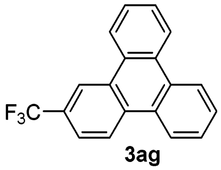
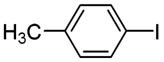
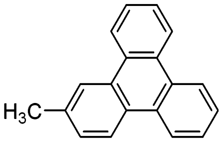
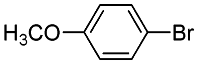
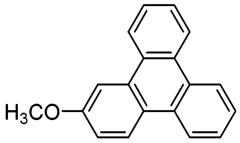
entry	aryl halide	silyl triflate	product	% isolated yield[b]
1		 **2d**	 **3aa**	66
2		 **2f**	 **3ac**	68
3		**2d**	 **3aa**	76
4		**2f**	 **3ac**	79
5		 **2a**	 **3m**	61[c]
6		**2d**	 **3ad**	54
7		**2a**	 **3ae**	51[c]
8		**2a**	 **3af**	48[c]

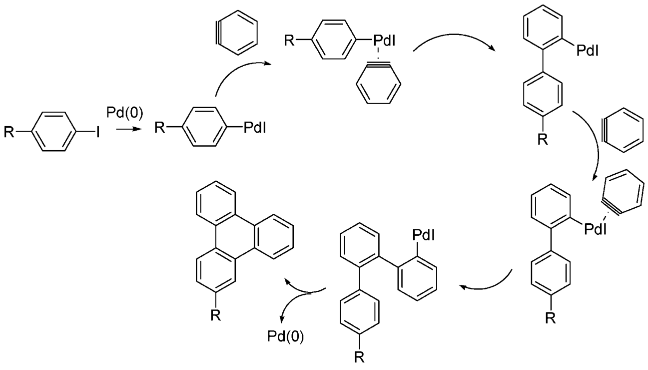
Table 3 (Continued)

entry	aryl halide	silyl triflate	product	% isolated yield[b]
9		**2a**	 **3af**	52[c]
10		**2a**	 **3ag**	43[c]
11		**2a**	 **3a**	36[c]
12		**2a**	 **3f**	38[c,d]

[a] All reactions were run using 0.30 mmol of aryl halide, 0.9 mmol of aryne precursor, 5 mol % of $Pd(OAc)_2$, 5 mol % of dppf, and 4.0 equiv of CsF in 4.0 mL of 1:3 MeCN/toluene at 110 °C for 24 h unless otherwise specified. [b] Isolated yield. [c] MeCN/toluene = 1:9. [d] If *p*-iodoanisole was used, the reaction was very messy.

the scope and limitations of this methodology. The results are summarized in Table 3. Aryl halides bearing electron-withdrawing groups efficiently undergo this aryne double annulation process to generate moderate to good yields of the corresponding multisubstituted polycyclic aromatics (Table 3, entries 1−10). For example, ethyl 4-iodobenzoate reacts with the aryne precursor **2f** to generate the corresponding double annulation product in a 68% yield (entry 2). Interestingly, we have found that the corresponding aryl bromide, which is usually significantly less reactive than the iodide, afforded even better results (compare entries 1 and 3 and 2 and 4). For example, ethyl 4-bromobenzoate reacts with aryne precursor **2d** to produce the double annulation product **3aa** in a 76% yield (entry 3), while the corresponding iodide gave only a 66% yield. Similar results have been obtained with other substrates. We have established that the lower yield from the iodide is due to the more facile reduction of this compound to ethyl benzoate. Fagnou has also recently observed that aryl bromides can often afford better results than the corresponding iodides in palladium-catalyzed intramolecular arylation.[16a] Benzyne precursor **2a** can also be employed in this double annulation process, although the yields of the corresponding annulation products are a little lower than those obtained using other aryne precursors (entries 5 and 7−12). Aryl halides bearing electron-donating methyl and methoxy groups do not work well in this double annulation process (entries 11 and 12). *p*-Iodotoluene and benzyne precursor **2a** afford only a 36% yield of the annulation product. If *p*-iodoanisole was employed under our reaction conditions, a messy reaction ensued and a low yield of the desired annulation product was obtained (entry 12).

SCHEME 3



The mechanism shown in Scheme 3 is proposed for this Pd-catalyzed double annulation process. It consists of the following key steps: (1) oxidative addition of the aryl halide to the Pd(0) catalyst, (2) arylpalladium coordination of the aryne and then insertion of the aryne to form a biarylpalladium intermediate, (3) biarylpalladium coordination to another aryne and then

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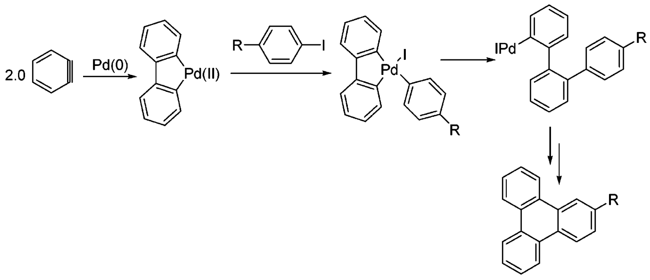
(17) For the Pd-catalyzed formation of naphthalenes from an aryl halide and two alkynes, see: (a) Kawasaki, S.; Satoh, T.; Miura, M.; Nomura, M. *J. Org. Chem.* **2003**, *68*, 6836. (b) Wu, G.; Rheingold, A. L.; Geib, S. L.; Heck, R. F. *Organometallics* **1987**, *6*, 1941.

SCHEME 4



insertion of the aryne to form a terarylpalladium intermediate, (4) intramolecular cyclization to afford a palladacyclic intermediate, and (5) reductive elimination to furnish the double annulation product and regenerate the Pd(0) catalyst. Another possibility involves the formation of a palladacycle intermediate via oxidative cyclization of two arynes on a Pd(0) species,[18] which then undergoes oxidative addition of the iodoarene to afford an organopalladium(IV) intermediate, which by reductive elimination and cyclization affords the triphenylene product (Scheme 4).[19] We tend to favor the former process but have no specific evidence to favor one over the other.

Conclusions

In summary, we have developed a novel, high yielding synthesis of fused polycyclic aromatics, which involves the Pd-catalyzed carboannulation of arynes by aryl and vinylic halides. This methodology provides an exceptionally efficient route to a wide variety of substituted polycyclic aromatic and heteroaromatic compounds from readily available starting materials and should find use in the construction of molecules with interesting properties and applications in material science.

Experimental Section

General Procedure for the Palladium-Catalyzed Annulation of Arynes Using 2-Halobiaryls. To a solution of the 2-halobiaryl (0.30 mmol), Pd(dba)$_2$ (0.015 mmol), P(*o*-tolyl)$_3$ (0.015 mmol), and the silylaryl triflate (0.60 mmol) in a mixed solvent system (4.0 mL) consisting of acetonitrile and toluene was added CsF (0.90 mmol). The reaction mixture was allowed to stir at 110 °C for 24 h under Ar. The resulting solution was washed with brine (20 mL) and extracted with diethyl ether (20 mL). The combined ether fractions were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired product.

2-Methyltriphenylene (3a). The indicated compound was obtained in a 92% yield (66.8 mg) as a white solid: mp 100−102 °C (lit.[20] mp, 101−103 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.56 (s, 3H), 7.42 (dd, J = 8.4, 1.5 Hz, 1H), 7.44−7.57 (m, 4H), 8.39 (s, 1H), 8.47 (d, J = 8.4 Hz, 1H), 8.54−8.62 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.1, 130.1, 130.0, 129.9, 129.6, 128.9, 127.7, 127.4, 127.3 (2C), 127.0, 123.6, 123.5 (2C), 123.4, 123.3, 22.1; IR ($CDCl_3$, cm^{-1}) 3081, 3026, 2923, 2854, 1742, 1437; HRMS *m*/*z* 242.1098 (calcd $C_{19}H_{14}$, 242.1095).

General Procedure for the Palladium-Catalyzed Double Annulation of Arynes Using Aryl Halides. To a solution of the aryl halide (0.30 mmol), Pd(OAc)$_2$ (0.015 mmol), dppf (0.015 mmol), and the silylaryl triflate (0.90 mmol) in a mixed solvent system (4.0 mL) consisting of acetonitrile and toluene was added CsF (1.20 mmol). The reaction mixture was allowed to stir at 110 °C for 24 h. The resulting solution was washed with brine (20 mL) and extracted with diethyl ether (20 mL). The combined ether fractions were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired product.

Ethyl 6,7,10,11-Tetramethyltriphenylene-2-carboxylate (3aa). The indicated compound was obtained in a 66% yield (71 mg) as a white solid: mp 148−150 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.48 (t, J = 7.2 Hz, 3H), 2.41 (s, 3H), 2.42 (s, 3H), 2.43 (s, 3H), 2.45 (s, 3H), 4.48 (q, J = 7.2 Hz, 2H), 8.08−8.18 (m, 4H), 8.29 (s, 1H), 8.46 (d, J = 8.7 Hz, 1H), 9.17 (d, J = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 137.3, 136.6, 136.0, 135.8, 133.0, 129.2, 128.8, 128.1, 128.0, 127.4, 126.9, 126.6, 125.2, 124.5, 124.1, 123.7, 123.6, 123.1, 61.3, 20.6, 20.5, 20.4 (2C), 14.7; IR ($CDCl_3$, cm^{-1}) 3019, 2874, 2918, 1710, 1612; HRMS *m*/*z* 356.1781 (calcd $C_{25}H_{24}O_2$, 356.1776).

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Supporting Information Available: Detailed experimental procedure and characterization data for all previously unknown products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0619534

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[18] (a) Belzen, R. V.; Klein, R. A.; Kooijman, H.; Veldman, N.; Spek, A.; Elsevier, C. J. *Organometallics* **1998**, *17*, 1812. (b) Catellani, M. *Synlett* **2003**, 298.

[19] We thank a referee for suggesting this mechanistic possibility.

[20] Mandelbaum, A.; Cais, M. *J. Org. Chem.* **1961**, *26*, 2633.