

## Palladium-Catalyzed Cocyclization of Arynes with Alkynes: Selective Synthesis of Phenanthrenes and Naphthalenes

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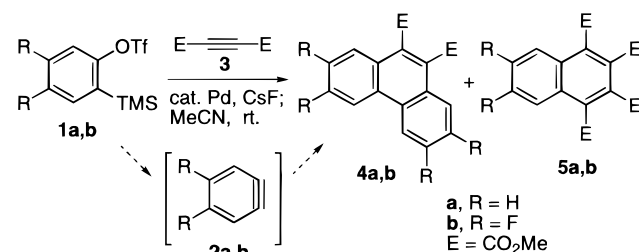
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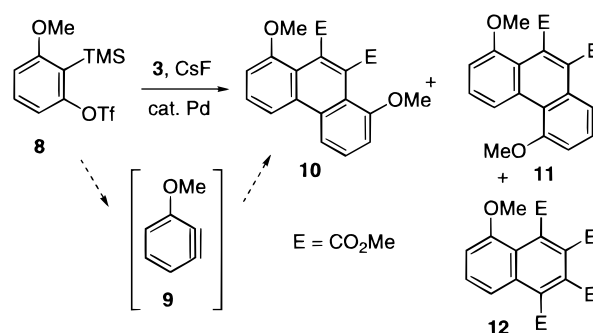
Reactions mediated by transition metals have played a crucial role in the development of synthetic methodology during the last quarter of this century. A paradigm of the synthetic potential of these transformations is the metal-catalyzed cyclotrimerization of alkynes to afford aromatic compounds.<sup>1</sup> This extensively exploited reaction has been studied from the mechanistic point of view and has been expanded in scope to embrace cocyclizations of alkynes, alkenes, nitriles, and other species. Our experience in aryne chemistry led us to consider the possibility of using transition metals to catalyze cycloaddition reactions of arynes,<sup>2,3</sup> a possibility recently confirmed by the finding that aryne can be transformed into triphenylenes by efficient palladium(0)-catalyzed cyclotrimerization.<sup>4</sup> To explore further the scope of this novel palladium-mediated aryne chemistry, we have investigated the cocyclization of aryne with other species. Here we report preliminary results on the cocyclization of aryne and alkynes to afford phenanthrenes and naphthalenes.

In our earlier work<sup>4</sup> we found that Pd(0) complexes are the catalysts of choice for trimerization of benzyne, which is strongly electrophilic. By contrast, there are few published examples of the cyclotrimerization of alkynes using Pd(0) complexes, and those that have been reported are mostly limited to electron-poor alkynes.<sup>5–7</sup> We envisaged that the difference between aryne and alkynes as regards reactivity with Pd(0) complexes, rather than being a disadvantage, might provide the chemoselectivity required for a synthetically useful cocyclization reaction. With this in mind we started our study with the reactions of aryne with an electron-deficient alkyne, dimethyl acetylenedicarboxylate (DMAD, **3**), catalyzed by Pd(0) complexes (Schemes 1 and 2).

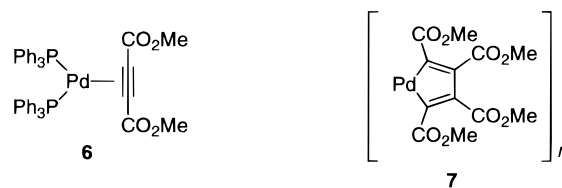
Scheme 1



Scheme 2



We found that slow generation of benzyne, by treatment of **1a** with CsF in acetonitrile at room temperature, in the presence of **3** and catalytic amounts of Pd(0), afforded mixtures of phenanthrene **4a**, naphthalene **5a**, and minor amounts of triphenylene. Various reaction conditions were tried in order to direct the reaction toward the formation of either the phenanthrene or the naphthalene. The best yield of **4a** was obtained using 1.4 equiv of the alkyne and Pd(PPh<sub>3</sub>)<sub>4</sub> as catalyst (Table 1, entry 1). Larger excesses of the alkyne produced less phenanthrene and more naphthalene, but selective formation of **5a** was not achieved even with 10 equiv of alkyne. TLC monitoring of these experiments showed the initial formation and eventual disappearance of a compound that upon isolation was characterized as complex **6**<sup>8</sup> and is assumed to be one of the intermediates in the formation of **4a** and **5a**. Naphthalene **5a** was obtained in good yield and with very good selectivity when Pd<sub>2</sub>(dba)<sub>3</sub> was used as the catalyst (entry 2). It is possible that reaction of DMAD with Pd<sub>2</sub>(dba)<sub>3</sub> gave complex **7**, as previously reported,<sup>6,9</sup> and that **5a** resulted from reaction of **7** with a molecule of benzyne.



The same chemoselectivity was observed when DMAD was reacted with the substituted aryne **2b** and **9** under similar reaction conditions. Thus, generation of 4,5-difluorobenzyne (**2b**) by treatment of triflate **1b** with CsF, in the presence of excess DMAD and 0.1 equiv of Pd(PPh<sub>3</sub>)<sub>4</sub>, afforded a mixture of phenanthrene **4b** (64%), naphthalene **5b** (9%), and 2,3,6,7,10,11-hexafluoro-triphenylene (8%) (Table 1, entry 3). The use of Pd<sub>2</sub>(dba)<sub>3</sub> as

(8) The formation of complexes of this kind by reaction of Pd(PPh<sub>3</sub>)<sub>4</sub> and electron-deficient alkynes has been described previously: Greaves, E. O.; Lock, C. J. L.; Maitlis, P. M. *Can. J. Chem.* **1968**, *46*, 3879–3891.

(9) (a) Moseley, K.; Maitlis, P. M. *J. Chem. Soc., Chem. Commun.* **1971**, 1604–1606. (b) Moseley, K.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1974**, 169–175.

(1) (a) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539–556. (b) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081–1119. (c) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G. Eds.; Hegedus, L. H., volume Ed.; Pergamon: Oxford, 1995; Vol. 12, pp 741–770.

(2) For general reviews on aryne chemistry, see: (a) Hoffmann, R. W. *Dehydrobenzene and Cycloalkynes*; Academic Press: New York, 1967. (b) Hart, H. In *The Chemistry of Functional Groups, Suppl. C2: The Chemistry of Triple-Bonded Functional Groups*; Patai, S., Ed.; Wiley: Chichester, 1994; pp 1017–1134.

(3) For recent reviews on transition metal complexes of aryne, see: (a) Buchwald, S. L.; Broene, R. D. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Hegedus, L. H., volume Ed.; Pergamon: Oxford, 1995; Vol. 12, pp 771–784. (b) Bennett, M. A.; Wenger, E. *Chem. Ber./Recueil* **1997**, *130*, 1029–1042.

(4) Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 2659–2661.

(5) Maitlis, P. M. *Pure Appl. Chem.* **1973**, *33*, 489–512.

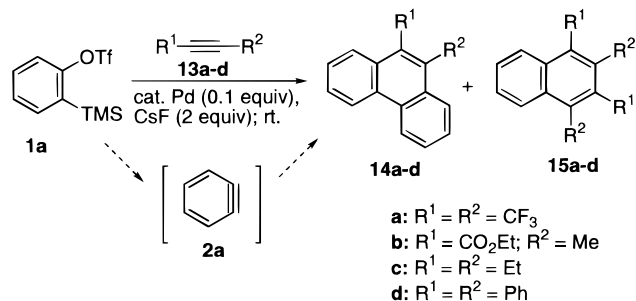
(6) Very electron-deficient alkynes (e.g., DMAD) undergo cycloaddition reactions when palladacyclopentadiene complexes are used as precursors of Pd(0) catalysts: (a) Brown, L. D.; Itoh, K.; Suzuki, H.; Hirai, K.; Ibers, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 8232–8238. (b) Stephan, C.; Munz, C.; Dieck, H. *J. Organomet. Chem.* **1993**, *452*, 223–227.

(7) Cyclization of alkynes by Pd(0) complexes and AcOH occurs via a different mechanism, involving Pd(II)–H complexes as active catalysts: (a) Negishi, E.; Harring, S. L.; Owczarczyk, Z.; Mohamud, M. M.; Ay, A. *Tetrahedron Lett.* **1992**, *33*, 3253–3256. (b) Brown, S.; Clarkson, S.; Grigg, R.; Sridharan, V. *Tetrahedron Lett.* **1993**, *34*, 157–160.

**Table 1.** Pd-Catalyzed Cocyclization of Benzyne and 4,5-Difluorobenzyne with DMAD<sup>a</sup>

entry	<b>1</b>	Pd(0) cat. (0.1 equiv)	product yields, % <sup>b</sup>		
			<b>4</b>	<b>5</b>	Triphenylene
1	<b>1a</b>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	84 ( <b>4a</b> )	7 ( <b>5a</b> )	2
2	<b>1a</b>	Pd <sub>2</sub> (dba) <sub>3</sub>	10 ( <b>4a</b> )	83 ( <b>5a</b> )	
3	<b>1b</b>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	64 ( <b>4b</b> )	8 ( <b>5b</b> )	8 <sup>c</sup>
4	<b>1b</b>	Pd <sub>2</sub> (dba) <sub>3</sub>	9 ( <b>4b</b> )	54 ( <b>5b</b> )	

<sup>a</sup> See Scheme 1. <sup>b</sup> Yield of isolated product. <sup>c</sup> 2,3,6,7,10,11-Hexafluorotriphenylene.

**Scheme 3**

catalyst resulted in the formation of naphthalene **5b** as the major product (54%), while **4b** was isolated in 9% yield (entry 4). In the case of 3-methoxybenzyne (**9**), treatment of triflate **8** with CsF in the presence of DMAD and catalytic Pd(PPh<sub>3</sub>)<sub>4</sub> led to the isomeric phenanthrenes **10** and **11** in 23 and 60% yield, respectively, together with the naphthalene **12** in 6% yield. Selective formation of naphthalene **12** in 82% yield was again achieved using Pd<sub>2</sub>(dba)<sub>3</sub> as catalyst; in these conditions phenanthrenes **10** and **11** were isolated in 3 and 11% yield, respectively.

These results show that the reaction of aryne with DMAD can easily be switched between the formation of phenanthrenes and the formation of naphthalenes by appropriate selection of the catalyst. This chemoselectivity is highly remarkable in a purely intermolecular [2 + 2 + 2] cocycloaddition reaction.<sup>10</sup>

Reaction of benzyne with other alkynes (Scheme 3) afforded lower yields of cycloaddition products despite exhaustive efforts at optimization (the main results are summarized in Table 2). The best results were obtained with the reaction of hexafluoro-2-butyne (**13a**) with benzyne in the presence of Pd(PPh<sub>3</sub>)<sub>4</sub> to give phenanthrene **14a** and triphenylene (the expected naphthalene **15a** was not detected). Although this reaction was complicated by polymerization of the alkyne, the yield increased from 55 (entry 1) to 65% when toluene was employed as solvent (entry 2). Less electrophilic alkynes showed much lower reactivity: reaction of **13b-d** with benzyne in the presence of Pd(PPh<sub>3</sub>)<sub>4</sub> at room temperature afforded triphenylene almost exclusively, only minor

(10) Selective cotrimerization between alkynes of different steric or electronic characters is possible in some cases, but more typically, mixtures of cotrimers and homotrimers are obtained; see, for example, Abdulla, K.; Booth, B. L.; Stacey, C. J. *Organomet. Chem.* **1985**, 293, 103.

(11) The formation of a dihydrophenanthrene by reaction of benzyne with a nickelaindane has been described: Cámpora, J.; Llevaría, A.; Moretó, J. M.; Poveda, M. L.; Carmona, E. *Organometallics* **1993**, 12, 4032–4038.

(12) This alternative pathway is reminiscent of the mechanism of the Pd-catalyzed annelation of aryl iodides with acetylenes: (a) Wu, G.; Rheingold, A. L.; Geib, S. J.; Heck, R. F. *Organometallics* **1987**, 6, 1941–1946. (b) Larock, R. C.; Doty, M. J.; Tian, Q.; Zenner, J. M. *J. Org. Chem.* **1997**, 62, 7536–7537.

**Table 2.** Pd-Catalyzed Cocyclization of Benzyne and Alkynes<sup>a</sup>

entry	<b>13</b>	Pd(0) cat.	Solvent	product yields, % <sup>b</sup>		
				<b>14</b>	<b>15</b>	Triphenylene
1	<b>13a</b>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	MeCN	55 ( <b>14a</b> )		20
2	<b>13a</b>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	PhMe <sup>c</sup>	65 ( <b>14a</b> )		20
3	<b>13b</b>	Pd <sub>2</sub> (dba) <sub>3</sub>	MeCN	63 ( <b>14b</b> )	8 ( <b>15b</b> ) <sup>c</sup>	10
4	<b>13c</b>	Pd <sub>2</sub> (dba) <sub>3</sub>	MeCN	28 ( <b>14c</b> )		23
5	<b>13d</b>	Pd <sub>2</sub> (dba) <sub>3</sub>	MeCN	16 ( <b>14d</b> )	1 ( <b>15d</b> )	42
6	<b>13d</b>	Pd <sub>2</sub> (dba) <sub>3</sub>	PhMe <sup>d</sup>	34 ( <b>14d</b> )	2 ( <b>15d</b> )	26

<sup>a</sup> See Scheme 3. <sup>b</sup> Yield of isolated product. <sup>c</sup> Mixture of regioisomers (major product **15b**). <sup>d</sup> 18-Crown-6 (3 equiv) was added.

amounts of the cocyclization products **14** and **15** being detected. However, satisfactory yields of the phenanthrenes **14b-d** were isolated after rational modification of the reaction conditions: hypothesizing that the bulky, highly nucleophilic and strongly coordinated ligand PPh<sub>3</sub> might prevent the coordination and subsequent reaction of these less electron-deficient alkynes, we again resorted to the “lightly stabilized” complex Pd<sub>2</sub>(dba)<sub>3</sub>. In the reaction of benzyne with **13b** this afforded **14b** in 63% yield together with an 8% yield of a mixture of the three possible naphthalenes, of which **15b** was the major regioisomer (entry 3). 3-Hexyne (**13c**) and diphenylacetylene (**13d**) also reacted under these conditions (entries 4 and 5), giving the corresponding phenanthrenes, **14c** and **14d**, in 28 and 16% yield, respectively; the reduction in yield can be attributed to the lesser ability of these alkynes to coordinate to palladium, which was also reflected by the precipitation of inactive palladium black during the reactions. Use of the phosphines P(*o*-tol)<sub>3</sub> and dppe to stabilize the catalyst did not give better results, but a better yield of **14d** was obtained when the reaction was carried out in toluene (entry 6), probably due to the greater solubility of alkyne **13d** in this solvent.

Although further investigation is needed to determine the precise mechanism of these reactions, we suggest that it may be similar to the one generally accepted for alkyne cyclotrimerizations.<sup>1</sup> This proposal is consistent with previous reports on the reactivity of aryne complexes of group 10 elements.<sup>3e,11</sup> An alternative mechanism initiated by oxidative addition of the triflate to Pd<sup>12</sup> is unlikely, since in the absence of CsF starting materials remained unaltered, even in the presence of other bases, such as triethylamine, or when alkenes were used as reaction partners.

In conclusion, this work shows that aryne can undergo palladium-catalyzed cocyclization with alkynes to afford phenanthrenes and, in the case of the reaction with DMAD, naphthalenes also. Remarkably, the reactions with DMAD can be selectively directed toward the formation of phenanthrenes or the formation of naphthalenes by changing the catalyst. This unusual selectivity makes the palladium-catalyzed cocyclization of aryne and alkynes a promising tool for the synthesis of polycyclic aromatic compounds.

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**Supporting Information Available:** Spectroscopic data and experimental procedures for the synthesis of compounds **1b**, **8**, **4a-b**, **5a-b**, **10**, **11**, **12** and **14a-d** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.