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Pd-Catalyzed Reactions of *o*-Diiodoarenes with Alkynes for Aromatic Ring Extension

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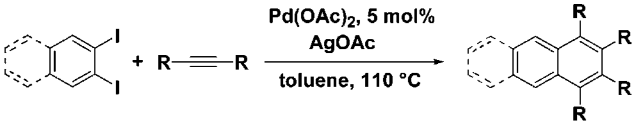
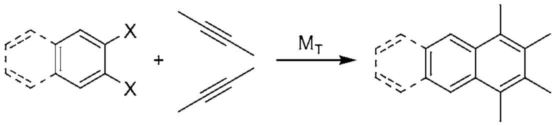
ABSTRACT



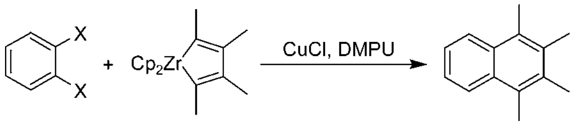
A new and efficient palladium-catalyzed reaction of *o*-diiodoarenes with internal alkynes produces naphthalenes or anthracenes in good to excellent yields. This procedure provides a simple, catalytic, and straightforward ring-extension method for constructing substituted polycyclic aromatic compounds.

Development of synthetic methods of linearly fused aromatic compounds has received considerable attention in organic synthesis[1] because of their increasing importance in the field of organic electroactive materials.[2] Among possible strategies to construct acene skeletons, a straightforward aromatic ring extension reaction as shown in eq 1 seems the simplest and the most attractive one.



(1)

During the course of our investigations of the reactions of zirconacyclopentadienes,[3,4] we developed a general coupling reaction of dihaloarenes with zirconacyclopentadienes in the presence of CuCl (eq 2).[4]



(2)

However, this reaction needs a stoichiometric amount of the zirconium reagent and CuCl. So far, catalytic aromatic ring extension from dihaloarenes has never been reported, although some catalytic reactions using mono- or difunctionalized benzene are known.[5,6]

In this paper, we report the first efficient palladium-catalyzed aromatic ring extension reaction of *o*-diiodoarenes

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[1] (a) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901. (b) Watson, M. D.; Fethtenkötter, A.; Müllen, K. *Chem. Rev.* **2001**, *101*, 1267. (c) Fu, P. P.; Harvey, R. G. *Chem. Rev.* **1978**, *78*, 317.

[2] (a) Katz, H. E.; Bao, Z.; Gilat, S. L. *Acc. Chem. Res.* **2001**, *34*, 359. (b) Dimitrakopoulos, C. D.; Malenfant, P. R. L. *Adv. Mater.* **2002**, *14*, 99.

[3] Benzannulations with zirconacyclopentadienes: (a) Takahashi, T.; Ishikawa, M.; Huo, S. *J. Am. Chem. Soc.* **2002**, *124*, 388. (b) Duan, Z.; Nakajima, K.; Takahashi, T. *Chem. Commun.* **2001**, 1672. (c) Takahashi, T.; Kitamura, M.; Shen, B.; Nakajima, K. *J. Am. Chem. Soc.* **2000**, *122*, 12876. (d) Takahashi, T.; Tsai, F.-Y.; Li, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **1999**, *121*, 11093. (e) Takahashi, T.; Xi, Z.; Yamazaki, A.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **1998**, *120*, 1672. (f) Takahashi, T.; Kotora, M.; Xi, Z. *Chem. Commun.* **1995**, 361. (g) Xi, Z.; Li, Z.; Umeda, C.; Guan, H.; Li, P.; Kotora, M.; Takahashi, T. *Tetrahedron* **2002**, *58*, 1107. (h) Kotora, M.; Noguchi, Y.; Takahashi, T. *Collect. Czech. Chem. Commun* **1999**, *64*, 1119.

[4] Condensations of zirconacyclopentadienes with dihaloarenes: (a) Takahashi, T.; Li, Y.; Stepnicka, P.; Kitamura, M.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **2002**, *124*, 576. (b) Takahashi, T.; Hara, R.; Nishihara, Y.; Kotora, M. *J. Am. Chem. Soc.* **1996**, *118*, 5154.

[5] Benzannulation from monofunctionalized benzenes: (a) Sakakibara, T.; Tanaka, Y.; Yamasaki, S.-I. *Chem. Lett.* **1986**, 797. (b) Wu, G.; Rheingold, A. L.; Geib, S. J.; Heck, R. F. *Organometallics* **1987**, *6*, 1941. (c) Yasukawa, T.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2002**, *124*, 12680. (d) Kawasaki, S.; Satoh, T.; Miura, M.; Nomura, M. *J. Org. Chem.* **2003**, *68*, 6836.

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with alkynes, which produces naphthalenes or anthracenes in good to excellent yields.

A representative procedure is as follows (Scheme 1): To a solution of *o*-diiodobenzene **1a** (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), and AgOAc (2.0 mmol) in toluene (6 mL) was added 3-hexyne **2a** (6.0 mmol) at room temperature. After the mixture was stirred for 6 h at 110 °C, 1,2,3,4-tetraethylnaphthalene **3a** was formed in 92% GC yield along with the formation of hexaethylbenzene (0.16 mmol). At room temperature the reaction did not proceed. An excess amount of alkyne was needed in these reactions to consume **1a** completely. As a catalyst, $Pd(OAc)_2$ gave better results than $Pd_2(dba)_3$, $Pd(PPh_3)_4$, $[PdCl(\pi\text{-allyl})]_2$, and $PdCl_2$ (Table 1).

Scheme 1

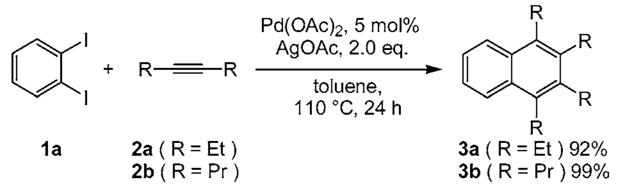


Table 1. Palladium-Catalyzed Reaction of *o*-Diiodobenzene **1a** with 4-Octyne **2b**[a]

entry	amount of **2b** (equiv)	Pd catalyst[b] (mol %)	yield of **3b**[c] (%)
1	3.0	$Pd(OAc)_2$ (5.0)	63[d]
2	6.0	$Pd(OAc)_2$ (5.0)	99 (80)
3	6.0	$Pd_2(dba)_3$ (2.5)	93
4	6.0	$Pd(PPh_3)_4$ (5.0)	63
5	6.0	$[PdCl(C_3H_5)]_2$ (2.5)	78
6	6.0	$PdCl_2(PBu_3)_2$ (5.0)	75
7	6.0	$PdCl_2$ (5.0)	83

[a] The reaction was performed using *o*-diiodobenzene **1a** (1.0 mmol) and 4-octyne **2b** in the presence of Pd catalyst and AgOAc (2.0 mmol) in toluene at 110 °C for 24 h unless otherwise noted. [b] Amounts of Pd catalysts are based on the amount of **1a** used. [c] GC yields. Isolated yield is given in parentheses. [d] 3.0 mmol of AgOAc was used.

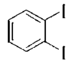
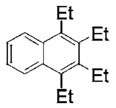
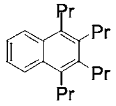
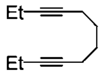
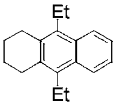
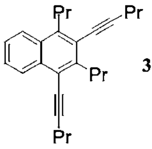
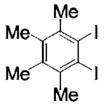
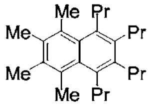
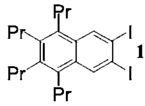
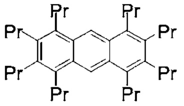
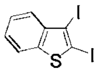
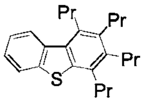
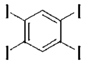
It is worth noting that the silver additive plays an important role in this reaction as shown in Table 2. It is known that silver salts produce Pd cation species.[7] In the absence of additives, this reaction could not proceed (entry 1). If the amount of AgOAc was less than 2.0 equiv, **1a** could not be consumed completely, and the yield of **3b** was relatively lower (entry 2). The other silver salts such as Ag_2CO_3, Ag_3-

Table 2. Effect of Additives on Palladium-Catalyzed Ring Extension Reactions of *o*-Diiodoarenes with Alkynes[a]

entry	additive	amount (equiv)	yield of **3b**[b] (%)
1	none	–	0
2	AgOAc	1.0	46
3	AgOAc	2.0	99
4	Ag_3PO_4	0.7	38
5	Ag_2CO_3	1.0	47
6	$AgNO_3$	2.0	19
7	K_2CO_3	1.0	7
8	Cs_2CO_3	1.0	8
9	Et_3N	6.0	0

[a] The reaction was performed using *o*-diiodobenzene **1a** (1.0 mmol) and 4-octyne **2b** (6.0 mmol) in the presence of Pd $(OAc)_2$ (0.05 mmol) in toluene at 110 °C for 24 h. [b] The yields were determined by GC analyses and based on the amount of **1a**.

Table 3. Palladium-Catalyzed Ring Extension Reactions of Various *o*-Diiodoarenes with Alkynes[a]

Entry	Iodoarene		Alkyne	Product		Yield/% [b]
1[c]		**1a**	Et—≡—Et **2a**		**3a**	92
2[c]	**1a**		Pr—≡—Pr **2b**		**3b**	99
3[d]	**1a**		 **2c**		**3c**	(83)
4	**1a**		Pr—≡—≡—Pr **2d**		**3d**	45[e]
5		**1b**	**2b**		**3f**	68 (42)
6		**1c**	**2b**		**3g**	71 (62)
7		**1d**[f]	**2b**		**3h**	(68)
8[g]		**1e**	**2b**	**3g**		37

[a] Unless otherwise noted, diiodoarene (1.0 mmol), alkyne (6.0 mmol), $Pd(OAc)_2$ (0.05 mmol), and AgOAc (2.5 mmol) were refluxed in toluene for 48 h. [b] GC or NMR yields. Isolated yields are given in parentheses. [c] 2.0 mmol of AgOAc was used and refluxed for 24 h. [d] 3.0 mmol of diynes **2c** was used. [e] Another isomer, 1,4-dipropyl-2,3-dipentyn-1-ylnaphthalene (**3e**), was also obtained in 25% GC yield. [f] Reference 10. [g] **2b** (12 mmol), $Pd(OAc)_2$ (0.1 mmol), and AgOAc (6.0 mmol) were used.

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(6) Benzannulation from difunctionalized benzenes: (a) Iwasawa, N.; Shido, M.; Maeyama, K.; Kusama, H. *J. Am. Chem. Soc.* **2000**, *122*, 10226. (b) Larock, R. C.; Tian, Q.; Oletnev. A. A. *J. Am. Chem. Soc.* **1999**, *121*, 3238. (c) Tian, Q.; Pletnev, A. A.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 339. (d) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650. (e) Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 2659. (f) Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *J. Am. Chem. Soc.* **1999**, *121*, 5827. (g) Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *J. Org. Chem.* **2000**, *65*, 6944. (h) Yoshikawa, E.; Radhakrishnan, K. V.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7280.

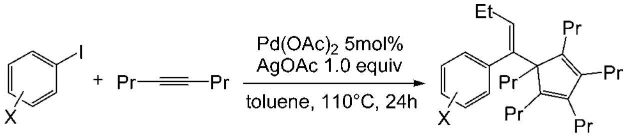
(7) Bebgoa, E. G.; Cuerva, J. M.; Echavarren, A. M.; Martorell, G. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 767.

PO_4, and $AgNO_3$ gave **3b** in much lower yields than AgOAc (entry 4−6). In addition, common bases such as K_2CO_3, Cs_2CO_3, and triethylamine showed little or no efficiency for the reaction (entries 7−9).

Table 3 summarizes the results of the reactions of various *o*-diiodoarenes with alkynes catalyzed by $Pd(OAc)_2$ in the presence of AgOAc. *o*-Diiodoarenes can be easily prepared from either direct iodination of aromatic compounds with iodine and periodic acid[8] or condensation of 1,2,4,5-tetraiodobenzene and zirconacyclopentadienes as we reported previously.[4a] When diyne **2c** was employed for the reaction, the tricyclic compound **3c** was formed in high yield (entry 3). The reaction with conjugated diyne **2d** gave the corresponding bisalkynylnaphthalene as a mixture of regioisomers (entry 4). Highly congested persubstituted naphthalene **3f** could be prepared from diiodotetramethylbenzene **1b** in a good yield (entry 5). The reaction could be applied to not only diiodobenzenes but also to diiodonaphthalene **1c** to afford the corresponding anthracene **3g** in 71% yield (entry 6). In this case, no phenanthrene derivative was detected in the reaction mixture. Furthermore, the reaction similarly proceeded with heteroaromatic diiodide **1d** to produce the corresponding dibenzothiophene **3h** in 68% isolated yield (entry 7). A double-benzannulation reaction was also possible with 1,2,4,5-tetraiodobenzene to produce the corresponding anthracene derivative **3g** (entry 8).

Among the investigated dihaloarenes, *o*-dibromobenzene and *o*-bromoiodobenzene showed much lower reactivity for the reactions with 4-octyne (**2b**) under the same reaction conditions as used here. Naphthalene **3b** was formed in 13 and 24% yields, respectively, while *o*-dichlorobenzene did not react. On the other hand, when the same reactions were carried out with *mono*iodobenzene, *o*-chloroiodobenzene, and *p*-diiodobenzene, the corresponding cyclopentadiene derivatives **4a**, **4b**, and **4c** were obtained in 67, 93, and 21% yields, respectively (Scheme 2).[9] The formation of the cyclopentadiene ring is consistent with the results reported by Heck.[5b] These results clearly show that the good leaving group at the ortho position on the haloarene ring is essential for the present benzannulation reaction.

Scheme 2



4a X = H, 67%
4b X = *o*-Cl, 93%
4c X = *p*-I, 21%

In conclusion, this new catalytic procedure provides a simple and straightforward ring extension method for constructing substituted polycyclic aromatic compounds. Further study to elucidate precise mechanism of this reaction and to extent the scope of synthetic utility for construction of multisubstituted polycyclic aromatic compounds are now in progress.

Supporting Information Available: Details of the experimental procedure and analytical data for compounds **3a−j** and **4a−c**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL049176M

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[8] (a) Mattern, D. L. *J. Org. Chem.* **1984**, *49*, 3051. (b) Suzuki, H. *Org. Synth.* **1971**, *51*, 94 and references therein.

[9] The structures of compounds **3d**,**e** and **4a−c** were characterized by NMR and NOE experiments. See the Supporting Information.

[10] Muraki, T.; Togo, H.; Yokoyama, M. *Synlett* **1998**, 286.