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Synthesis of Tetrasubstituted Naphthalenes by Palladium-Catalyzed Reaction of Aryl Iodides with Internal Alkynes

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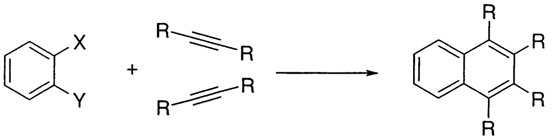
Abstract: The 1:2 coupling of aryl iodides with acetylenedicarboxylate esters and diphenylacetylene efficiently proceeds in the presence of a palladium catalyst with use of silver carbonate as base to produce the corresponding tetrasubstituted naphthalenes.

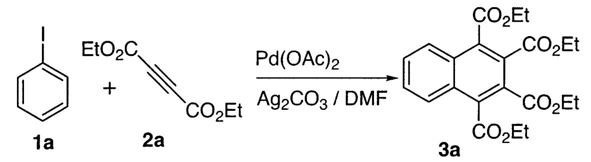
Selective synthesis of substituted polycyclic aromatic hydrocarbons has become increasingly important since they have been finding increasing application as π-conjugated functional materials.[1,2] Among modern potential strategies to prepare condensed aromatics is the metal-promoted or -catalyzed coupling reaction of mono- or difunctionalized aromatic substrates with two alkyne molecules that proceeds via arylmetal species (Scheme 1).[3−7]

SCHEME 1



We recently demonstrated that in the presence of an iridium catalyst, aroyl chlorides (X = COCl, Y = H) efficiently react with dialkyl- and diarylacetylenes accompanied by decarbonylation to produce the corresponding tetrasubstituted naphthalenes and anthracenes.[7] However, the reaction with electron-deficient alkynes, such as acetylenedicarboxylates, did not proceed. In contrast to the iridium catalysis, it was reported that palladium species can mediate the 1:2 coupling of iodobenzene with the latter alkynes,[6a] while no naphthalenes are formed with use of dialkylacetylenes.[4c,6b,8] However, the turnover number in the reaction with acetylenedicarboxylate esters was only ca. 2. In the course of our study of transition metal-catalyzed arylation reactions,[7,9] we have found an effective protocol for preparing naphthalenetetracarboxylates by the palladium-catalyzed coupling, which is reported herein.

TABLE 1. Reaction of Iodobenzene (1a) with Diethyl Acetylenedicarboxylate (2a)[a]



entry	temp (°C)/time (h)	% yield of **3a**[b]
1[c]	100/48	5
2	100/24	81
3	80/24	72
4[d]	80/24	25
5	120/8	90 (75)
6[e]	100/24	79
7[e,f]	100/22	17

[a] Reaction conditions: [**1a**]:[**2a**]:[$Pd(OAc)_2$]:[Ag_2CO_3] = 1:4:0.05:1 (in mmol), in DMF under N_2. [b] GLC yield based on the amount of **1a** used. Value in parentheses indicates isolated yield. [c] Cs_2CO_3 was used in place of Ag_2CO_3. [d] [**2a**] = 2 (mmol). [e] Reaction in the presence of P(2-furyl)$_3$ (0.15 mmol). [f] Reaction in *o*-xylene.

When iodobenzene (**1a**) was treated with diethyl acetylenedicarboxylate (**2a**) (4 equiv) in the presence of Pd(OAc)$_2$ (5 mol %) with Cs_2CO_3 (1 equiv), which is an effective base for the 1:1 coupling with dialkylacetylenes,[8] in DMF at 100 °C for 48 h, a small amount of tetraethyl naphthalene-1,2,3,4-tetracarboxylate (**3a**) (5%) was formed (entry 1 in Table 1). Interestingly, use of Ag_2CO_3 in place of Cs_2CO_3 remarkably improved the yield of **3a** up to 81% (entry 2). While lowering temperature to 80 °C only slightly affected the yield (entry 3), decreasing the amount of **2a** to 2 equiv considerably retarded the reaction (entry 4). At a higher temperature of 120 °C, **1a** was consumed completely within 8 h to give **3a** in 90% yield (entry 5). It is noted that in each run, detectable byproduct derived from **2a** by GC-MS was only a trace amount of its trimer.

Table 2 summarizes the results for the reactions of various aryl iodides with alkyne **2a**, using Ag_2CO_3 as base. In the reaction of 4-iodotoluene (**1b**) at 100 °C, tetraethyl 6-methylnaphthalene-1,2,3,4-tetracarboxylate (**3b**) was obtained in a comparable yield to that of **3a** (entry 1), but unexpectedly, it was decreased at 120 °C (entry 2). Thus, other 4-substituted iodobenzenes **1c**−**e**

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(4) X = OTf, Y = SiMe$_3$: (a) Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 2659. (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.

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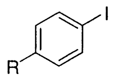
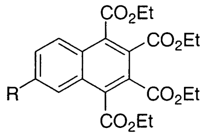
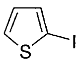
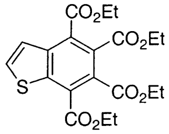
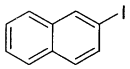
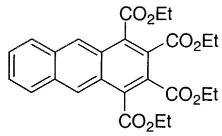
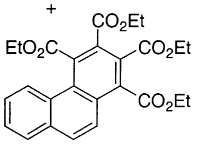
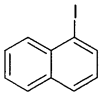
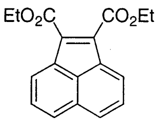
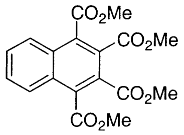
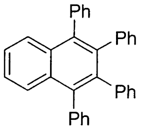
TABLE 2. Reaction of Aryl Iodides 1 with Diethyl Acetylenedicarboxylate (2a)[a]

entry	iodide	time (h)	product(s), % yield [b]
			
1	**1b**: R = Me	8	**3b**: R = Me, 81 (71)
2 [c]	**1b**: R = Me	8	**3b**: R = Me, 56
3 [d]	**1c**: R = OMe	8	**3c**: R = OMe, 73 (60)
4	**1d**: R = Cl	24	**3d**: R = Cl, 64 (54)
5	**1e**: R = Br	24	**3e**: R = Br, 55 (49)
6 [d]	 **1f**	24	 **3f**, (22)
7 [d]	 **1g**	24	 **3g**, 45 (41) +  **4**, 7 (4)
8 [d]	 **1h**	8	 **5**, 54 (37) + **4**, 22 (17)

[a] Reaction conditions: [**1**]:[**2a**]:[Pd(OAc)$_2$]:[Ag$_2$CO$_3$] = 1:4:0.05:1 (in mmol), in DMF at 100 °C under N$_2$. [b] GC yield based on **1** used. Value in parentheses indicates isolated yield. [c] Reaction at 120 °C. [d] P(2-furyl)$_3$ (0.15 mmol) was added.

TABLE 3. Reaction of Iodobenzene (1a) with Alkynes 2b and 2c[a]

entry	alkyne	solvent	temp (°C) / time (h)	product, % yield [b]
	$\mathrm{MeO_2C{-}{\equiv}{-}CO_2Me}$ **2b** (4 equiv)			
1 [c]		DMF	100 / 24	**6**, (56)%
	$\mathrm{Ph{-}{\equiv}{-}Ph}$ **2c** (2 equiv)			
2		DMF	80 / 24	**7**, 44
3		*o*-xylene	80 / 8	**7**, 87 (80)
4 [c]		*o*-xylene	80 / 24	**7**, 2
5 [d]		*o*-xylene	80 / 68	**7**, 54

[a] The reaction was carried out with **1a** (1 mmol), Pd(OAc)$_2$ (0.05 mmol), P(2-furyl)$_3$ (0.15 mmol), and Ag$_2$CO$_3$ (1 mmol). [b] GC yield based on **1a** used. Value in parentheses indicates isolated yield. [c] Without P(2-furyl)$_3$. [d] 2:1 coupling product (7%) was also formed.

(R = OMe, Cl, and Br) were reacted at 100 °C (entries 3−5). In each run, the corresponding naphthalene was obtained in good yield. The bromo moiety in **1e** was not attacked under these conditions. The reaction of 2-iodothiophene (**1f**) yielded benzothiophene **3f**, although the yield was low (entry 6).

Iodonaphthalenes were found to react with **2a** to form tricyclic compounds as expected (entries 7 and 8). The reaction of 2-iodonaphthalene (**1g**) gave tetraethyl anthracene-1,2,3,4-tetracarboxylate (**3g**) as the major product along with a small amount of the corresponding phenanthrene **4**. On the other hand, the reaction of 1-iodonaphthalene (**1h**) preferred 1:1 coupling to 1:2 coupling to produce diethyl acenaphthylene-1,2-dicarboxylate (**5**) as the major product along with **4**. It is noted that for the reactions of **1c** and **1f**−**h**, P(2-furyl)$_3$ was added as ligand, so that the product yields were improved by 6−13%. However, no positive effect of the posphine addition was observed in the other runs (e.g. entry 6 in Table 1). Dimethyl acetylenedicarboxylate (**2b**) reacted with **1a** to give naphthalene **6**, as expected (entry 1 in Table 3).

It has been reported that the palladium-catalyzed reaction of **1a** with diphenylacetylene (**2c**) gives rise to not only 1:2 product (1,2,3,4-tetraphenylnaphthalene, **7**)[6b] but also 2:1[10] and 1:1[11] products (9,10-diphenylphenanthrene and 9-benzylidenefluorene, respectively). While the latter two compounds were prepared with good yields by employing appropriate conditions, it appeared to be difficult to obtain **7** selectively.[6b,10b] Consequently, the reaction was carried out under the present conditions. It was of interest that treatment of **1a** with **2c** (2 equiv) in the presence of P(2-furyl)$_3$ selectively gave **7** (44%) as the single product, no other coupling products being formed (entry 2 in Table 3). It was also found that use of *o*-xylene as solvent in place of DMF improved both the reaction rate and product yield. Thus, **7** was produced exclusively in 87% yield within 8 h (entry 3). In this case, addition of the phosphine was essential to make the reaction catalytic (entry 4). The reaction with Cs$_2$CO$_3$ in place of Ag$_2$CO$_3$ was relatively slow and was accompanied by the formation of the 2:1 coupling product (entry 5).

A plausible mechanism for the reaction of aryl iodide **1** with alkyne **2** is illustrated in Scheme 2 (neutral ligands are omitted). Oxidative addition of **1** to Pd(0) species generated in situ gives an arylpalladium(II) intermediate **A**. Then, syn-addition of the Ar−Pd bond in **A** to the triple bond of **2** to give a vinylpalladium species **B**, followed by cyclopalladation affords a five-membered palladacycle **C**. The subsequent reaction with **2** and reductive elimination affords the corresponding annulated product with regeneration of Pd(0) species. As in the iridium-catalyzed naphthalene synthesis,[7] participation of another route, which involves successive inser-

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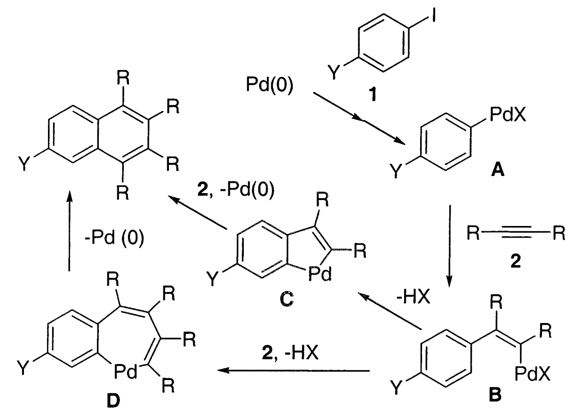
SCHEME 2



tion of two molecules of **2** and the subsequent cyclopalladation to form a seven-membered palladacycle **D**, cannot be excluded.

Anyway, Ag_2CO_3 appears to remove iodide ligand from the Pd center to promote alkyne insertion as well as cyclopalladation.[12] However, the origins of significant effects with use of *o*-xylene and P(2-furyl)$_3$ in the reaction with alkyne **2c** are not definitive at this stage, since in the case of **2a**, the solvent was not preferable (entry 7, Table 1) and the ligand showed no or only somewhat positive effects. It is worth noting that in the reaction of 1-iodonaphthalene (**1h**) (entry 8 in Table 2), cyclopalladation occurs preferably at its 8-position rather than 2-position.[13] A six-membered palladacycle thus formed undergoes reductive elimination prior to the reaction with the second alkyne molecule to afford **5** predominantly.

In summary, we have developed a useful method for the palladium-catalyzed coupling of aryl iodides with acetylene dicarboxylate esters as well as diphenylacetylene to produce tetrasubstituted naphthalene derivatives. The use of an appropriate base such as Ag_2CO_3 has been found to be critical to conduct the reaction efficiently and selectively.

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Supporting Information Available: Standard experimental procedure and characterization data for compounds **3b**–**g** and **4**–**7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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