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Palladium-Catalyzed Arylation of Enynes and Electron-Deficient Alkynes Using Diaryliodonium Salts

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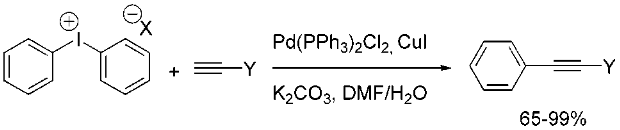
ABSTRACT



A new single-pot procedure for the synthesis of aryl alkynes is described. Palladium catalyzes the coupling reaction of diaryliodonium compounds with enynes and electron-deficient alkynes to give aryl alkynes in good yields.

The palladium-catalyzed coupling of terminal alkynes with aryl iodides to give arylalkynes is an important reaction in organic chemistry (Sonogashira coupling).[1,2] Alkynes obtained in these reactions are useful building blocks in organic and materials chemistry.[3] However, this reaction has limitations. Alkynes containing an electron-withdrawing group (directly attached to the ethynyl carbon) do not react significantly with aryl iodides;[4] therefore, not many reports appear in the literature.[5] Also, palladium-catalyzed arylation of enynes occurs only in moderate yields.[6] Herein, we report a new, efficient, and mild palladium-catalyzed method for the arylation of enynes and electron-deficient alkynes using diaryliodonium salts.

Iodonium compounds are widely available and generally prepared under mild conditions.[7] Aryliodonium salts show superior reactivity compared to aryl halides. The highly electron withdrawing nature of the PhI^+ moiety in iodonium compounds activates the carbon−iodine bond toward various reactions.[7] Diaryliodonium salts **1a** and **1b** were prepared by a literature procedure.[8]

First, we investigated the coupling of a diaryliodonium compound (**1a**) with a methyl enyne (**2a**) in the presence of palladium as a catalyst and copper as a cocatalyst. Different palladium sources and solvents were examined for this coupling reaction; the $PdCl_2(PPh_3)_2$/CuI/K_2CO_3 system was found to be superior to other combinations. With this catalytic system, reaction occurred at rt to give essentially a quantitative yield of the aryl-substituted enyne **3a** using either triflate or tosylate as the counterion (Table 1, entries 1 and 2).

Terminal alkynes containing an electron-withdrawing group directly attached to the ethynyl carbon atom do not react significantly with aryl halides. Therefore, generally an alternative methodology is used to prepare aryl propiolic

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[1] *Metal-Catalyzed Cross Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: London, 1998.

[2] (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467−4470. (b) Nakamura, K.; Okubo, H.; Yamaguchi, M. *Synlett* **1999**, 549−550.

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[5] Eckert, T.; Ipaktschi, J. *Synth. Commun.* **1998**, *28*, 327−335.

[6] Iwasawa, N.; Satoh, H. *J. Am. Chem. Soc.* **1999**, *121*, 7951−7952.

[7] (a) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123−1178. (b) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: London, 1997. (c) Wirth, T.; Hirt, U. H. *Synthesis* **1999**, 1271−1287.

[8] (a) Koser, G. F.; Wettach, R. H.; Smith, C. S. *J. Org. Chem.* **1980**, *45*, 1543−1544. (b) Stang, P. J.; Zhdankin, V. V.; Tykwinski, R.; Zefirov, N. S. *Tetrahedron Lett.* **1991**, *32*, 7497−7498.

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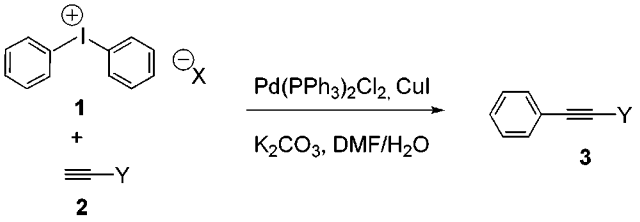
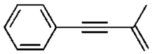
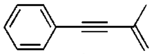
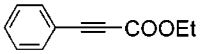
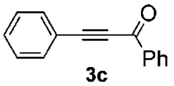
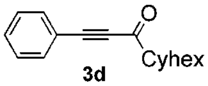
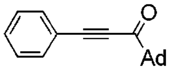
Table 1. Palladium-Catalyzed Arylation of Alkynes[9]



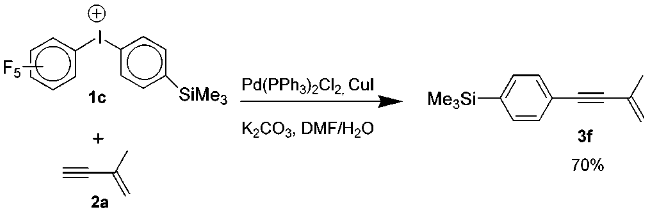
entry	X	Y	Product	Yield[a]
1	OTf **1a**	(CH$_3$)C=CH$_2$ **2a**	 **3a**	99%
2	OTs **1b**	(CH$_3$)C=CH$_2$ **2a**	 **3a**	99%
3	OTf **1a**	-COOEt **2b**	 **3b**	80%
4	OTs **1b**	-CO-Ph **2c**	 **3c**	70%
5	OTs **1b**	-CO-cyhex **2d**	 **3d**	65%
6	OTf **1a**	-CO-Ad **2e**	 **3e**	71%

[a] Isolated yields: cyhex, cyclohexane, Ad, adamantane.

esters[4b] and acetylenic ketones.[4c,10] In contrast, the aryliodonium salts underwent coupling with alkynes containing electron-withdrawing groups such as ester **2b** and ketones **2c**,[11] **2d**, and **2e** to give arylated products in good yield (Table 1, entries 3–6).

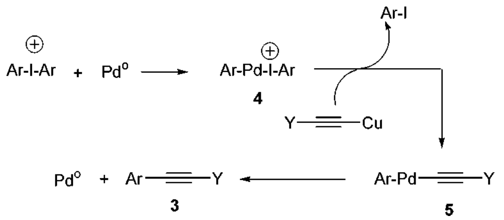
It was also of interest to study this reaction using unsymmetrically substituted iodonium salts. Aryliodonium **1c** was obtained using a modified literature procedure.[12] Coupling of iodonium salt **1c** and methyl enyne **2a** proceeded smoothly to give product **3f** (70%) (Scheme 1). The phenyl ring with the electron-donating group (TMS) underwent coupling to give the corresponding arylated product.

Scheme 1. Unsymmetrical Iodonium–Enyne Coupling



A plausible mechanism for this coupling reaction is depicted in Scheme 2. The reaction most likely begins with the oxidative addition of Pd^0 to the iodonium compound to give arylpalladium species **4** which on reaction with copper acetylide leads to the aryl(alkynyl)palladium species **5** that on extrusion of Pd^0 leads to the formation of aryl alkyne **3**. Both the palladium and copper(I) iodide were essential catalysts for this reaction. The aryl iodides obtained as byproduct lends support to our mechanism.

Scheme 2. Proposed Mechanism of Coupling Reactions



In summary, we have developed a new, superior, and mild protocol for the arylation of enynes and electron-deficient alkynes using aryliodonium salts as the electrophilic coupling partners, where aryl iodides either do not work or give only low yields of products.

Acknowledgment. We thank the NIH (GM-57052) for financial support.

Supporting Information Available: A description of experimental details and ^{1}H NMR spectra of the compounds **3d**, **3e**, and **3f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) **Typical procedure:** To a mixture of PdCl$_2$(PPh$_3$)$_2$ (0.021 g, 0.03 mmol), **1a** (0.643 g, 1.5 mmol), CuI (0.04 mmol), and K$_2$CO$_3$ (0.276 g, 2 mmol) in DMF/H$_2$O (6:1) (14 mL) was added enyne **2a** (0.099 g, 1.5 mmol) at rt under an N$_2$ atmosphere, and the solution was stirred at rt for 2–3 h. The reaction was quenched by an aqueous NH$_4$Cl solution; workup and column chromatography (silica gel, hexane) gave **3a** (0.21 g, 99%).

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(12) Kuehl, C. J.; Bolz, J. T.; Zhdankin, V. V. *Synthesis* **1995**, 312–316.