ORGANIC LETTERS

2004
Vol. 6, No. 4
617−619

# Boron Trifluoride Induced Palladium-Catalyzed Cross-Coupling Reaction of 1-Aryltriazenes with Areneboronic Acids

**Tomoyuki Saeki,* Eun-Cheol Son, and Kohei Tamao***

*International Research Center for Elements Science, Institute for Chemical Research, Kyoto University, Uji, Kyoto 611-0011, Japan*

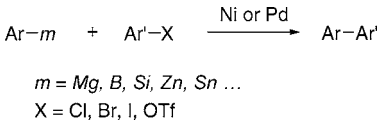
*tamao@scl.kyoto-u.ac.jp*

**Received December 15, 2003**

## ABSTRACT


**Aryltriazenes are directly coupled with areneboronic acids in the presence of a catalytic amount of $Pd_2(dba)_3$ and $P(tBu)_3$ together with 1 equiv of $BF_3$·$OEt_2$ in DME to afford the corresponding biaryl products in up to 98% yield. A carbonylative cross-coupling reaction under a carbon monoxide atmosphere is also found to give the corresponding diaryl ketone with a similar catalyst system.**

Nickel- or palladium-catalyzed cross-coupling reactions have been widely used as one of the most powerful synthetic tools for the construction of carbon−carbon and carbon−heteroatom bonds.[1] Although a variety of organometallic reagents have been explored, electrophilic counterparts have been substantially limited to organic halides and triflate.




Carbon−nitrogen compounds may be a third candidate as electrophilic counterparts in cross-coupling reactions.[2] In 1977,[3a] Kikukawa et al. reported the synthetic utility of arenediazonium salts in palladium-catalyzed Mizoroki−Heck-type reactions.[3] Since then, coupling reactions of arenediazonium salts with organometallic reagents have also been developed.[4] The arenediazonium salts, however, are prone to decompose upon storage, which is a critical disadvantage for practical use. Recently, 1-aryltriazenes, which can be easily prepared from the corresponding arylamines,[5] have been employed by Sengupta et al. as an arenediazonium surrogate in the Mizoroki−Heck-type reaction;[6] the triazenes are pretreated with trifluoroacetic acid (TFA) or tetrafluoroboric acid ($HBF_4$) to revert to the

(1) (a) *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998. (b) *Cross-Coupling Reactions: A Practical Guide*; Miyaura, N., Ed.; Springer-Verlag: Heidelberg, 2002; *Top. Curr. Chem.*, Vol. 219. (c) 30 Years of Cross-Coupling Reaction. Tamao, K.; Hiyama, T.; Negishi, E.-i., Eds., *J. Organomet. Chem.* **2002**, *653* (Special Issue).

(2) In addition to the arenediazonium salts and aryltriazenes as the main subject of this paper, arylammonium salts have been recently used for the Suzuki−Miyaura-type coupling reaction: Blakey, S. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 6046.

(3) (a) Kikukawa, K.; Matsuda T. *Chem. Lett.* **1977**, 159. (b) Sengupta, S.; Bhattacharya, S. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1943. (c) Sengupta, S.; Bhattacharya, S.; Sadhukkan, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 275. (d) Sengupta, S.; Sadhukkan, S. K. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2235. (e) Andrus, M. B.; Song, C.; Zhang, J. *Org. Lett.* **2002**, *4*, 2079.

(4) (a) Kikukawa, K.; Ikenaga, K.; Wada, F.; Matsuda, T. *Chem. Lett.* **1983**, 1337. (b) Kikukawa, K.; Kono, K.; Wada, F.; Matsuda, T. *J. Org. Chem.* **1983**, *48*, 1333. (c) Ikenaga, K.; Matsumoto, S.; Kikukawa, K.; Matsuda, T. *Chem. Lett.* **1990**, 185. (d) Sengupta, S.; Bhattacharya, S. *J. Org. Chem.* **1997**, *62*, 3405. (e) Andrus, M. B.; Song, C. *Org. Lett.* **2001**, *3*, 3761.

(5) Kimball, D. B.; Haley, M. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 3338 and references therein.

(6) (a) Bhattacharya, S.; Majee, S.; Mukherjee, R.; Sengupta, S. *Synth. Commun.* **1995**, *25*, 651. (b) Sengupta, S.; Sadhukkan, S. K. *Tetrahedron Lett.* **1998**, *39*, 715. (c) Sengupta, S.; Sadhukkan, S. K. *Org. Synth.* **2002**, *79*, 52.

10.1021/ol036436b CCC: $27.50 
**Published on Web 01/20/2004**

corresponding diazonium species and subsequently coupled with olefins. This methodology was extended by Bräse et al. to solid-phase organic synthesis.[7] However, the use of strong protic acids such as TFA and $HBF_4$ should still be a significant limitation considering their compatibility with functional groups and organometallic reagents. Actually, the Suzuki−Miyaura-type coupling reaction with phenylboronic acid was attempted, but the results were not necessarily satisfactory, as described by the authors themselves.[7a]

Reported herein is the first observation that the 1-aryltriazenes can be directly coupled with areneboronic acids in the presence of a palladium catalyst, phosphine ligand, and boron trifluoride. Our working hypothesis for the Lewis acid induced cross-coupling reaction, in which a diaryl-palladium intermediate is formed in a concerted process, is depicted in Figure 1. It can be expected here that the boron trifluoride

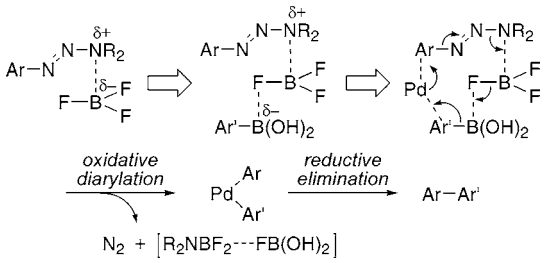
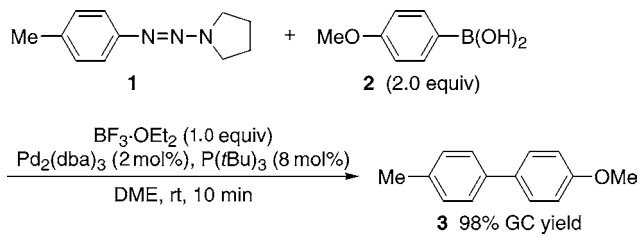



**Figure 1.** Schematic representation of a direct formation of diaryl-palladium intermediate in a concerted mechanism.

plays two roles during the reaction: (1) the boron trifluoride serves as a Lewis acid toward the 1-aryltriazene to form an aryltriazene-boron trifluoride complex to enhance the reactivity of the $sp^2$-carbon−nitrogen bond, and then (2) the resulting aminotrifluoroborate moiety serves as a fluoride base to promote a transmetallation of the areneboronic acid. Hence, the diaryl-palladium species can be directly formed from the zerovalent palladium complex.

After several tentative experiments, the desired cross-coupling of 1-(*p*-tolyl)triazene (**1**) with *p*-anisylboronic acid (**2**) was achieved with a catalytic amount of $Pd_2(dba)_3$ (4 mol %) and P(*t*Bu)$_3$ (8 mol %) together with 1 equiv of $BF_3$·$OEt_2$ in DME to afford the biphenyl product **3** in 98% GC yield within 10 min at room temperature, as shown in Scheme 1.[8]

**Scheme 1**




The Lewis acid was essential for the formation of the biphenyl product; without $BF_3$·$OEt_2$, no reaction occurred at all. In a control reaction, the 1-aryltriazenes did not react with boron trifluoride in the absence of either the palladium catalyst or boronic acids, implying that a concerted process may be involved. The choice of solvent also significantly affected the product yield, as shown by the results [solvent and GC yield (1 h): DME, 98%; THF, 96%; dioxane, 94%; toluene, 66%; DMF, trace; NMP, 0%]; satisfactory results were obtained only in ethereal solvents and we chose DME as the general solvent on the basis of the reaction rate.

The screening of catalysts and phosphine ligands revealed that the catalyst system with $Pd_2(dba)_3$ and P(*t*Bu)$_3$ was the most effective, regardless of their ratio, giving rise to the coupling product in a yield of 98% (Table 1, entries 1 and 2).

**Table 1.** Optimization of Catalyst System[a]

| entry | Pd complex | ligand | yield [%][b] 10 min, 1 h |
|---|---|---|---|
| 1 | $Pd_2(dba)_3$ | P(*t*Bu)$_3$ | 98, 98 (91)[d] |
| 2 | $Pd_2(dba)_3$ | P(*t*Bu)$_3$[c] | 95, 95 |
| 3 | $Pd_2(dba)_3$ | none | 69, 79 |
| 4 | $Pd_2(dba)_3$ | $PPh_3$ | 80, 83 |
| 5 | $Pd_2(dba)_3$ | dppb | 64, 70 |
| 6 | $Pd_2(dba)_3$ | dppf | 72, 79 |
| 7 | $Pd_2(dba)_3$ | PBiph(*t*Bu)$_2$[c] | 28, 47 |
| 8 | $Pd(PPh_3)_4$ | P(*t*Bu)$_3$ | 49, 59 |
| 9 | $Pd(OAc)_2$ | P(*t*Bu)$_3$ | 19, 37 |

[a] Reaction conditions: **1** (0.50 mmol), **2** (1.0 mmol), catalyst [Pd content] (4 mol %), ligand (8 mol %), $BF_3$·$OEt_2$ (0.50 mmol), room temperature, DME (5.0 mL). [b] Yields are determined by GC analysis with eicosane as an internal standard. [c] Using 4 mol %. [d] Isolated yield.

The phosphine-free Pd(0) catalyst gave the coupling product in 79% yield (entry 3). Whereas the addition of $PPh_3$ and bisphosphines hardly influenced the yield (entries 4−6), the more bulky ligand, PBiph(*t*Bu)$_2$, significantly suppressed the reaction process (entry 7). Other precatalysts such as $Pd(PPh_3)_4$ and $Pd(OAc)_2$ were less effective (entries 8 and 9).

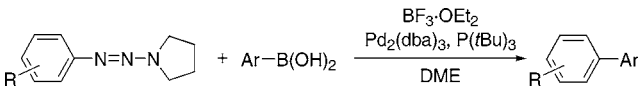
The scope of the coupling reaction with respect to the substituent on the 1-aryltriazenes and areneboronic acids was examined (Table 2).

Aryltriazenes having electron-donating groups at the *ortho*, *meta*, and *para* positions and a sterically hindered mesityl and naphthyl groups smoothly underwent the coupling reaction (entries 1−5 and 13). On the other hand, electron-withdrawing groups such as halogens, triflate, and acetyl substituents decreased the yields to some extent (entries 6−11). Notably, the triazene moiety showed a higher chemoselectivity over the triflate group as well as the bromine atom[9,10] as a leaving group under the stated reaction

(7) (a) Bräse, S.; Schroen, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 1071. (b) Bräse, S.; Kirchhoff, J. H.; Köbberling, *Tetrahedron* **2003**, *59*, 885.

(8) Triazenes having a diethylamino or morpholino moiety at the 3-position were less effective under the reaction conditions, and areneboronic esters were completely inert.

**Table 2.** Cross-coupling Reaction of 1-Aryltriazenes with Areneboronic Acids[a]



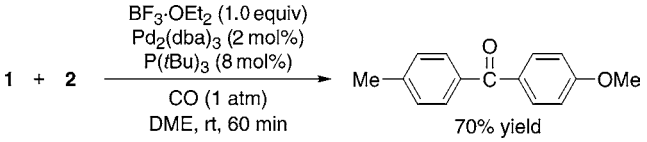

| entry | R | Ar | yield [%][b] 10 min, 1 h |
|---|---|---|---|
| 1 | *o*-Me | *p*-MeO-$C_6H_4$ (**2**) | 81, 91(72)[d] |
| 2 | *m*-Me | *p*-MeO-$C_6H_4$ (**2**) | 88, 92(80)[d] |
| 3 | *p*-Me (**1**) | *p*-MeO-$C_6H_4$ (**2**) | 98, 98(91)[d] |
| 4 | *p*-MeO | *p*-Me-$C_6H_4$ | 94, 94 |
| 5 | *2,4,6*-$Me_3$ | *p*-MeO-$C_6H_4$ (**2**) | 85, 90 |
| 6 | *p*-F | *p*-MeO-$C_6H_4$ (**2**) | 73, 81 |
| 7 | *p*-Cl | *p*-MeO-$C_6H_4$ (**2**) | 64, 74(68)[d] |
| 8[c] | *p*-Br | *p*-MeO-$C_6H_4$ (**2**) | 30, 40 |
| 9[c] | *p*-I | *p*-MeO-$C_6H_4$ (**2**) | tr, tr |
| 10 | *p*-TfO | *p*-MeO-$C_6H_4$ (**2**) | 43, 52(41)[d] |
| 11 | *p*- MeCO | *p*-MeO-$C_6H_4$ (**2**) | 31, 58 |
| 12 | *p*-$Et_2N$ | *p*-MeO-$C_6H_4$ (**2**) | 97, 97 |
| 13 | *p*-Me (**1**) | 1-naphthyl | 88, 90(78)[d] |
| 14 | *p*-Me (**1**) | 2-thienyl | 94, 94(84)[d] |
| 15 | *p*-Me (**1**) | 2-furyl | 0, 0 |

[a] Reaction conditions: 1-aryltriazene (0.50 mmol), areneboronic acid (1.0 mmol), $Pd_2(dba)_3$ (2 mol %), P(*t*Bu)$_3$ (8 mol %), $BF_3$·$OEt_2$ (0.50 mmol), room temperature, DME (5.0 mL). [b] Yields are determined by GC analysis with eicosane as an internal standard. [c] Using 5 mol % of $Pd_2(dba)_3$ without phosphine ligand. See ref 11. [d] Isolated yields.

conditions, giving the corresponding products in moderate yields (entries 8 and 10).[11] The lack of reactivity of the iodophenyltriazene (entry 9) remained to be clarified. It is noted that the electron-rich substituents such as the methoxy, diethylamino, and thienyl groups were also tolerated under the Lewis acidic conditions (entries 4, 12, and 14), whereas the furyl group showed a lack of compatibility (entry 15).

A carbonylative cross-coupling reaction[12] was also examined under a carbon monoxide atmosphere. The reaction condition was not optimized, but the carbonylative cross-coupling of **1** and **2** was found to give the corresponding diaryl ketone in 70% isolated yield (77% GC yield) as shown in Scheme 2.

**Scheme 2**




In summary, we have shown that the 1-aryltriazenes can be directly employed in Lewis acid induced palladium-catalyzed cross-coupling reactions with areneboronic acids. Although the actual reaction mechanism is not yet clear at the present time, the present reaction with a nitrogen-based leaving group has a potential utility in organic synthesis, providing a quick and halogen-free cross-coupling process under very mild conditions.

**Acknowledgment.** We thank the Ministry of Education, Culture, Sports, Science and Technology, Japan, for the Grant-in-Aid for COE Research on Elements Science, no. 12CE2005, and Hokko Chemical Industry Co., Ltd. for the gift of phosphine ligands.

**Supporting Information Available:** Detailed descriptions of experimental procedures and spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL036436B

(9) The competitive reaction of aryltriazene **1** with *p*-bromotoluene in the reaction with areneboronic acid **2** afforded biphenyl product **3** in 90% yield, together with the aryl bromide being recovered unchanged.

(10) Chemoselective differential reactions of 4-bromobenzene diazonium salt and 4-bromophenyltriazene have been already reported; see refs 4a,d and 6c.

(11) An increased amount of catalyst (5 mol %) without phosphine ligand was necessary: only a trace amount of product was obtained in the presence of phosphine ligand. The reason is not clear.

(12) (a) Kikukawa, K.; Kono, K.; Wada, F.; Matsuda, T. *Chem. Lett.* **1982**, 35. (b) Kikukawa, K.; Idemoto, T.; Katayama, A.; Kono, K.; Wada, F.; Matsuda, T. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1511. (c) Andrus, M. B.; Ma, Y.; Zang, Y.; Song, C. *Tetrahedron Lett.* **2002**, *43*, 9137.