

Palladium-Catalyzed Cross-Coupling Reaction of 1-Aryltriazenes with Aryl- and Alkenyltrifluorosilanes

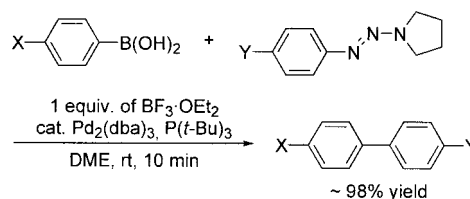
Tomoyuki Saeki,* Tadafumi Matsunaga, Eun-Cheol Son, Kohei Tamao*

International Research Center for Elements Science, Institute for Chemical Research, Kyoto University, Uji, Kyoto 611-0011, Japan
Fax: (+81)-774-38-3186, e-mail: tamao@scl.kyoto-u.ac.jp

Received: July 5, 2004; Accepted: November 1, 2004

Abstract: The palladium-catalyzed cross-coupling reaction of 1-aryltriazenes with aryl- and alkenyltrifluorosilanes occurs readily at room temperature to yield the corresponding biaryl and stilbene products in moderate to good yields. In contrast to the previous results for the reaction with areneboronic acids, in which an additional Lewis acid such as boron trifluoride is essential for the activation of the 1-aryltriazenes, the Lewis acidity of organotrifluorosilanes seems to be strong enough to directly activate the triazene moiety to enter into the palladium-catalyzed cross-coupling reaction without an extra Lewis acid.

Keywords: aryltriazene; biaryls; cross-coupling; palladium; stilbene; trifluorosilane



Scheme 1. General scheme for cross-coupling reaction of areneboronic acids with 1-aryltriazenes.

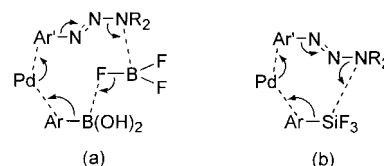


Figure 1. Schematic representations of a concerted-like mechanism for the formation of the diaryl-palladium intermediate.

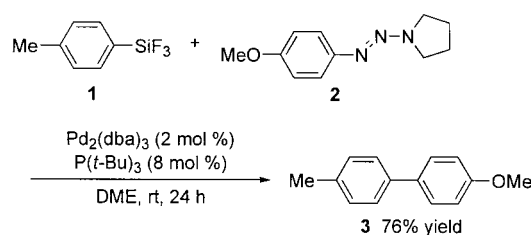
The transition metal-catalyzed cross-coupling reaction has become a promising synthetic tool for the construction of carbon–carbon and carbon–heteroatom bonds in the field of organic synthesis, material science, and pharmaceuticals.^[1]

We have recently reported that the 1-aryltriazenes can be employed as an electrophile in the palladium-catalyzed cross-coupling reaction with areneboronic acids,^[2] in which the addition of Lewis acids such as boron trifluoride is essential to enhance the reactivity of the triazene compounds toward the palladium catalyst (Scheme 1). The 1-aryltriazenes can readily be prepared from the corresponding arylamines,^[3] and the reaction is generally completed within 10 min at room temperature, thus providing a quick and organic halide-free coupling system under mild conditions.^[4] Although the actual reaction mechanism remains unclear, the boron trifluoride might play two crucial roles during the catalysis as depicted in Figure 1a: (i) as a *Lewis acid* toward the triazene to enhance the cleavage of the *sp*²-carbon–nitrogen bond and (ii) as a *fluoride source* to promote a transmetalation of the aryl substituent on the resulting borate moiety.

In the course of our research, we next examined the cross-coupling reaction of the 1-aryltriazenes with other

organometallic compounds, instead of the boronic acids, to construct a synthetically versatile reaction. Herein, we report the cross-coupling reaction of the 1-aryltriazenes with aryl- and alkenyltrifluorosilanes in the presence of a palladium catalyst and a phosphine ligand.

At the beginning of the investigation, we attempted the cross-coupling reaction of *p*-anisyltriazene **2** with various organosilicon compounds such as *p*-Tol-SiMe₃, -Si(OMe)₃, -SiCl₃, -SiMe₂F, -SiMeF₂, and -SiF₃ (**1**) under a catalyst system similar to that utilized for the areneboronic acids [Pd₂(dba)₃ (2 mol %), P(*t*-Bu)₃ (8 mol %), and BF₃·OEt₂ (1 equiv.)]^[2] to discover that only the trifluorosilane **1** having the highest Lewis acidity afforded the corresponding biaryl product **3** in 17% yield after 24 h stirring at room temperature; the other silicon compounds were totally ineffective.^[5] In sharp contrast to the previous results for the areneboronic acids, the additional Lewis acid turned out not to be necessary for the cross-coupling reaction of the trifluorosilanes. Thus, finally, the biaryl product **3** was obtained in 76% yield under the optimized catalyst system without boron trifluoride (Scheme 2). The direct acid–base interaction between the silicon atom of the trifluorosilane and the nitrogen atom at the 3-position of the triazene compound



Scheme 2. Cross-coupling reaction of *p*-tolyltrifluorosilane (1) with 1-(*p*-anisyl)triazene 2.

Table 1. Screening of catalyst system.^[a]

Entry	Catalyst	Ligand	Yield ^[b]
1	Pd ₂ (dba) ₃	none	37%
2	Pd ₂ (dba) ₃	PPh ₃	26%
3	Pd ₂ (dba) ₃	P(<i>o</i> -Tol) ₃	46%
4	Pd ₂ (dba) ₃	PCy ₃	28%
5	Pd ₂ (dba) ₃	P(<i>t</i> -Bu) ₃	76%
6	Pd ₂ (dba) ₃	dppb	9%
7	Pd ₂ (dba) ₃	dppf	41%
8	Pd(dba) ₂	P(<i>t</i> -Bu) ₃	62%
9	Pd(PPh ₃) ₄	none	26%

^[a] Reaction conditions: trifluorosilane **1** (0.20 mmol), aryltriazene **2** (0.24 mmol), catalyst (2 mol %), and ligand (8 mol %), DME (2.0 mL), room temperature.

^[b] Yields are determined by GC analysis with eicosane as an internal standard.

might be a crucial step in the catalysis as shown in Figure 1b, accounting for the effectiveness of the highly Lewis acidic trifluorosilane.^[6]

The screening of catalysts as summarized in Table 1 showed that the combination of Pd₂(dba)₃ with P(*t*-Bu)₃ was most effective (entry 5), whereas the triarylphosphines (entries 2 and 3) and bidentate ligands (entries 6 and 7) resulted in low yields. It is notable that, in the screening of solvents, the addition of methanol as a co-solvent was found to accelerate the reaction of the model case in Scheme 2 to give a slightly increasing yield of **3** (4 h, 90% yield). This acceleration effect was most remarkable in rather sterically hindered 1,2-disubstituted alkenyltrifluorosilanes, as will be mentioned below.^[7]

We next examined the scope of the cross-coupling reaction with respect to the substituents on the 1-aryltriazenes and aryltrifluorosilanes (Table 2). On the whole, triazenes with electron-donating substituents such as methyl and methoxy groups afforded the corresponding biaryl products in good yields, ranging from 63% to 76% (entries 1, 2, 6 and 7); it is noted that the bulky mesityl group can also be coupled. The diethylamino group, one of the most electron-donating substituents, exceptionally decreased the yield probably due to the undesired interaction between the nitrogen atom and the Lewis acidic silicon center to retard the coupling reaction (entry 8). Electron-withdrawing substituents de-

Table 2. Cross-coupling of aryltriazenes with aryltrifluorosilanes.^[a]

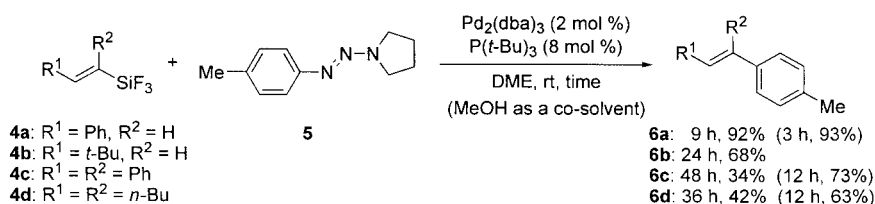
Entry	X	Y	Yield ^[b]
1	Me	<i>o</i> -Me	71%
2	Me	<i>m</i> -Me	74%
3	H	<i>p</i> -Me	74%
4	OMe	<i>p</i> -Me	60%
5	F	<i>p</i> -Me	82%
6	Me	2,4,6-Me ₃	63%
7	Me	<i>p</i> -OMe	76%
8	Me	<i>p</i> -NEt ₂	30%
9	Me	<i>p</i> -F	38%
10	Me	<i>p</i> -Cl	42%
11	Me	<i>p</i> -Br	trace
12	Me	<i>p</i> -I	0%
13	Me	<i>p</i> -OTf	36%
14	Me	<i>p</i> -C(O)Me	55%
15	Me	<i>p</i> -CO ₂ Me	22%

^[a] Reaction conditions: *p*-tolyltrifluorosilane (0.20 mmol), aryltriazene (0.24 mmol), Pd₂(dba)₃·CHCl₃ (2 mol %), and P(*t*-Bu)₃ (8 mol %), DME (2.0 mL), room temperature.

^[b] Yields are determined by GC analysis with eicosane as an internal standard.

creased the yields (entries 9–15); in the case of bromides and iodides, no product was obtained at all and most of the starting triazenes were recovered unchanged.^[8] In contrast, electron-withdrawing substituents on the aryltrifluorosilanes increased the yield to some extent, as observed for *p*-F-C₆H₄SiF₃ in comparison with *p*-OMe- and non-substituted analogues (entries 3–5). These results are consistent with our hypothetical mechanism shown in Figure 1b, in that the electron-withdrawing substituents on the aryltrifluorosilanes enhance the Lewis acidity of the silicon center making the silicon-nitrogen interaction more favored, and the electron-donating substituents on the triazene moiety then stabilize the cationic character of the aromatic group developed in the reaction intermediate (or transition state).^[9]

The reaction system was extended to the cross-coupling reaction of some *alkenyl*trifluorosilanes (**4a** – **d**) (Scheme 3).^[10,11] Among the alkenylsilanes examined, 2-substituted (*E*)-alkenyltrifluorosilanes **4a** and **4b** were more reactive, giving higher yields of coupling products **6** than 1,2-disubstituted alkenylsilanes **4c** and **4d**. The latter lower yields are probably due to the steric hindrance around the silicon center, preventing the interaction with triazene molecules. The addition of methanol was effective again to accelerate the reaction, especially for the sterically hindered 1,2-disubstituted alkenyltrifluorosilanes as shown in the parentheses in Scheme 3.^[7] The cross-coupling reactions of **4a** with var-



Scheme 3. Cross-coupling reaction of alkenylsilanes **4a** – **d** with 1-(*p*-tolyl)triazene **5**.

Table 3. Cross-coupling of (*E*)-styryltrifluorosilane (**4a**) with aryltriazenes.^[a]

Entry	X	Time	Yield ^[b]
1	Me	9 h	92%
2	OMe	9 h	95%
3	OTf	36 h	55% ^[c]
4	F	18 h	82%
5	Cl	18 h	85%
6	Br	48 h	52%
7	I	48 h	trace

^[a] Reaction conditions: (*E*)-styryltrifluorosilane (**4a**) (0.20 mmol), aryltriazene (0.24 mmol), Pd₂(dba)₃·CHCl₃ (2 mol %), and P(*t*-Bu)₃ (8 mol %), DME (2.0 mL), room temperature.

^[b] Yields are determined by GC analysis with eicosane as an internal standard.

^[c] Isolated yield.

ious triazenes are summarized in Table 3. In contrast to the results obtained for the aryltrifluorosilanes, not only the electron-donating groups but also the electron-withdrawing groups including halogen atoms were tolerated. Thus, the coupling reaction of **4a** with 4-bromophenyltriazene readily proceeded to give the bromine-substituted stilbene in 52% yield with good chemoselectivity (entry 6).

In conclusion, the palladium-catalyzed cross-coupling reaction of 1-aryltriazenes with aryl- and alkenyltrifluorosilanes has been achieved under mild conditions to give the corresponding biaryl and stilbene products in good yields. The Lewis acidity and the steric effect of the silicon compounds are responsible for the yields, thereby supporting our working hypothesis involving the direct acid-base interaction between the trifluorosilanes and the triazenes.

Experimental Section

Typical Procedure for the Cross-Coupling Reaction of Aryltriazenes with Trifluorosilanes

To a solution of *p*-anisyltriazene **2** (49 mg, 0.24 mmol) and Pd₂(dba)₃·CHCl₃ (4 mg, 0.004 mmol) in DME (2.0 mL) was

added P(*t*-Bu)₃ (10 wt % hexane solution, 32 mg, 0.016 mmol) and *p*-tolyltrifluorosilane **1** (35 mg, 0.2 mmol) at room temperature. The reaction was monitored by gas chromatography using eicosane (28 mg, 0.10 mmol) as an internal standard to confirm the formation of the desired biaryl product **3** in 76% yield after 18 h stirring. The reaction mixture was filtered through a pad of silica gel and the filtrate was evaporated under reduced pressure to give a viscous oil. The crude product was purified by HPLC using hexane/AcOEt (10:1) as an eluent to afford 4-methyl-4'-methoxybiphenyl (**3**); yield: 29 mg (0.15 mmol; 75%).

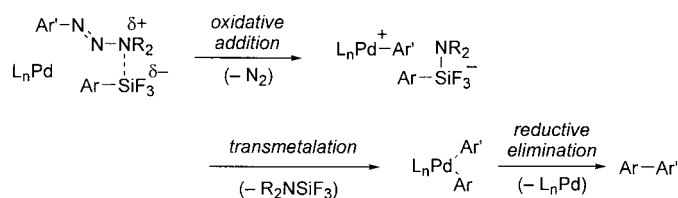
Acknowledgements

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 their gift of phosphine ligands.

References and Notes

- [1] a) *Metal-Catalyzed Cross-Coupling Reactions*, (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**; b) *Cross-Coupling Reactions: A Practical Guide* (Ed.: N. Miyaura), *Topics in Current Chemistry*, Vol. 219, Springer-Verlag, Heidelberg, **2002**; c) *30 Years of Cross-Coupling Reaction* (Eds.: K. Tamao, E.-i. Negishi, T. Hiyama), *J. Organomet. Chem. (Special Issue)* **2002**, 653.
- [2] T. Saeki, E.-C. Son, K. Tamao, *Org. Lett.* **2004**, 6, 617.
- [3] D. B. Kimball, M. M. Haley, *Angew. Chem. Int. Ed.* **2002**, 41, 3338 and references cited therein. **Caution:** the triazene compounds are carcinogenic; direct hand contact should be avoided.
- [4] Cross-coupling reactions of arenediazonium salts, one of the attractive candidates for halogen-free electrophiles, have been extensively studied: a) K. Kikukawa, K. Kono, F. Wada, T. Matsuda, *J. Org. Chem.* **1983**, 48, 1333; b) S. Sengupta, S. Bhattacharya, *J. Org. Chem.* **1997**, 62, 3405; c) M. B. Andrus, C. Song, *Org. Lett.* **2001**, 3, 3761.
- [5] This result is in sharp contrast to the fluoride ion-promoted Hiyama coupling in which aryldifluorosilanes are more reactive than aryltrifluorosilanes: Y. Hatanaka, K. Goda, Y. Okahara, T. Hiyama, *Tetrahedron* **1994**, 50, 8301.
- [6] An alternative reaction mechanism based on the generally accepted three-step mechanism is also possible: the Lewis acid-base interaction between the silicon atom

and the nitrogen atom enhances the oxidative addition of the sp^2 -carbon–nitrogen bond to the zero-valent palladium complex to form a cationic aryl-palladium intermediate. Then, transmetalation of the aryl substituent on the resulting pentacoordinate silicon atom and subsequent reductive elimination afford the biaryl product.



[7] The role of the methanol has not been clarified at the present time, but it can be assumed that the oxygen atom of methanol coordinates to the silicon center to form a pentacoordinate silicon species, and the resulting acidic hydrogen atom on the methanol interacts with the nitrogen atom of the triazene to enhance the oxidative addition to palladium complex.

[8] A competitive reaction between *p*-anisyltriazenes **2** and *p*-bromoanisole, in the reaction with *p*-tolyltrifluorosilane (**1**), afforded the corresponding biaryl **3** in satisfactory yield and the aryl bromide was recovered unchanged. Chemoselective differential reactions of 4-bromobenzene diazonium salts have been reported: See refs. [4b,10a, 11a]

[9] The electron-donating substituents can also stabilize the cationic aryl-palladium species generated as an initial intermediate in the three-step mechanism.^[6]

[10] Synthesis of symmetrical stilbene compounds *via* a double Heck reaction of arenediazonium salts, generated *in situ* from 1-aryltriazene, with vinyltriethoxysilane has been reported: a) S. Sengupta, S. K. Sadhukhan, *Org. Synth.* **2002**, 79, 52; b) S. Sengupta, S. Bhattacharyya, S. K. Sadhukhan, *J. Chem. Soc. Perkin Trans. 1* **1998**, 275.

[11] It is widely accepted that the palladium-catalyzed coupling reaction of arenediazonium salts with vinylsilanes proceeds by a Mizoroki–Heck-type addition-elimination mechanism: a) K. Kikukawa, K. Ikenaga, F. Wada, T. Matsuda, *Chem. Lett.* **1983**, 1337; b) K. Ikenaga, S. Matsumoto, K. Kikukawa, T. Matsuda, *Chem. Lett.* **1990**, 185.