JOC*Note*

Palladium-Catalyzed Silylations of Hydrosilanes with Aryl Halides Using Bulky Alkyl Phosphine

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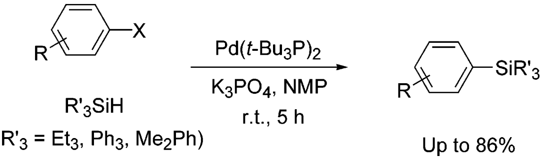
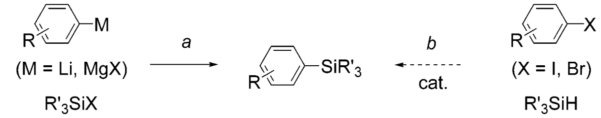


A palladium-catalyzed direct trialkylsilyl transfer to aryl halides has been developed. In the presence of Pd(t-Bu$_3$P)$_2$ and K$_3$PO$_4$, electron-rich para- or meta-substitute aryl iodides were coupled efficiently with triethylsilane, triphenylsilane, and dimethylphenylsilane to afford the corresponding silylated products in moderate to good yields.

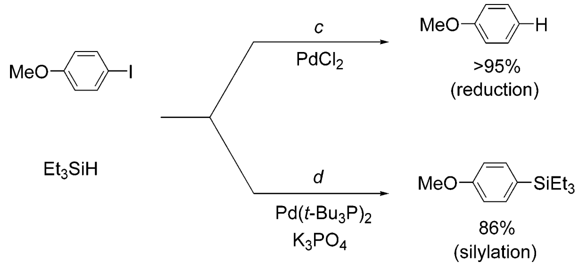
Arylsilanes are one of the most fundamental and widespread classes of intermediates in modern organic chemistry, and numerous preparation methods have been proposed.[1] One of the great strengths and sources of creativity in synthetic chemistry is the availability of a number of viable routes to the same or similar chemical products. On the basis of this idea, much interest has been focused on the development of a methodology for the introduction of silicon into organic molecules, because such a methodology would be valuable for the preparation of novel silicon-containing materials.

The traditional method of generating arylsilanes is through the reaction of chlorosilanes with aryllithium or aryl Grignard reagents (Scheme 1, route a).[2] On the other hand, hydrosilane derivatives are also thought to have potential utility as silylating reagents in the presence of transition-metal complexes. Palladium-catalyzed reactions are especially versatile methods for carbon−carbon bond formation due to their generality and ability to tolerate a wide range of important organic functional groups.[3] However, to the best of our knowledge, there have been a few successful reports of palladium-catalyzed silicon−aryl carbon bond formation (Scheme 1, route b).[4,5] This is because hydrosilanes generally work as reducing reagents in the presence of a palladium catalyst. For instance, Chatgilialoglu et al. reported that the addition of palladium dichloride (5−10 mol %) to a mixture of 4-iodoanisole and triethylsilane in ether at room temperature gave the corresponding reduction product, anisole, in an almost quantitative yield (Scheme 2, route c; reduction).[6,7] Murata, Masuda, and co-workers reported the synthesis of aryltriethoxysilanes via palladium-catalyzed silylation of aryl iodides with triethoxysilane in the presence of base.[4a,b,8] However, they also mentioned that triethylsilane was not suitable as a silylating reagent because of its strong reducing power in their palladium-catalyzed silylation of aryl halides. DeShong and Komuro and their co-workers also reported the Pd(0)-catalyzed silylation of aryl halides with triethoxysilane, but there was no information about the coupling of triethylsilane with aryl halide.[4c,d] Therefore, the development of a coupling procedure utilizing trialkylsilane

SCHEME 1. Different Synthetic Routes to Arylsilanes



SCHEME 2. Reaction of 4-Iodoanisole with Triethylsilane in the Presence of Palladium Catalyst



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[1] For reviews, see: (a) Horn, K. A. *Chem. Rev.* **1995**, *95*, 1317. (b) Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845.

[2] *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley & Sons: New York, 2000.

[3] For representative reviews, see: (a) Trost, B. M. *Science* **1991**, *234*, 1471. (b) Tsuji, J. *Palladium Reagents and Catalysis: New Perspective for the 21st Century*; Wiley & Sons: New York, 2004. (c) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., de Meijere, A., Bäckvall, J. E., Cacchi, S., Hayashi, T., Ito, Y., Kosugi, M., Murahashi, S.-I., Oshima, K., Yamamoto, Y., Eds.; Wiley & Sons: New York, 2002. (d) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (e) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263.

[4] (a) Murata, M.; Suzuki, K.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **1997**, *62*, 8569. (b) Murata, M.; Watanabe, S.; Masuda, Y. *Tetrahedron Lett.* **1999**, *40*, 9253. (c) Manoso, A. S.; DeShong, P. *J. Org. Chem.* **2001**, *66*, 7449. (d) Komuro, K.; Ishizaki, K.; Suzuki, H. *Touagousei-kenkyu-nenpo* **2003**, *6*, 24. (e) Denmark, S. E.; Kallemeyn, J. M. *Org. Lett.* **2003**, *5*, 3483.

[5] Silverman reported the coupling of butyl diethylsilane polystyrene with Boc-4-iodophenylalanine methyl ester in the presence of Pd$_2$(dba)$_3$·CHCl$_3$ and KOAc. See: Gu, W.; Liu, S.; Silverman, R. B. *Org. Lett.* **2002**, *4*, 4171.

[6] Boukherroub, R.; Chatgilialoglu, C.; Manuel, G. *Organometallics* **1996**, *15*, 1508.

[7] For other reducing systems based on the combination of silanes/transition-metal complexes, see: (a) Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1992**, *57*, 3751. (b) Barr, K. J.; Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1994**, *59*, 4323. (c) Breeden, S. W.; Lawrence, N. J. *Synlett* **1994**, 833. (d) Keinan, E. *Pure Appl. Chem.* **1989**, *61*, 1737. (e) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188. (f) Chatgilialoglu, C. *Chem. Rev.* **1995**, *95*, 1229 and references therein.

[8] Murata and Masuda also reported the silylation of aryl halide with triethoxysilane in the presence of Rh(I) catalyst. See: Murata, M.; Ishikura, M.; Nagata, M.; Watanabe, S.; Masuda, Y. *Org. Lett.* **2002**, *4*, 1843.

10.1021/jo051131r CCC: $30.25

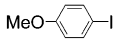
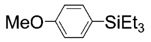
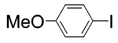
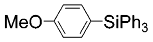
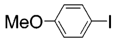
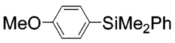
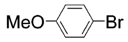
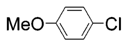
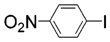
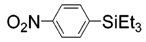
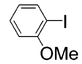
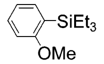
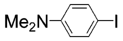
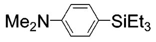
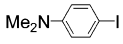
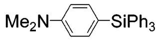
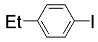
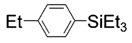
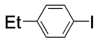
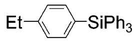
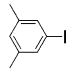
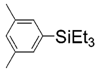
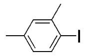
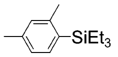
represents an interesting challenge in the field of organic synthesis.[5,9]

Our group and others have recently demonstrated that palladium catalysts coordinated with bulky, electron-rich tri-*tert*-butylphosphine can exhibit high reactivity in a range of coupling processes.[10−12] During the course of our study, we found that trialkylsilanes show *different reactivity* toward aryl halides in the presence versus the absence of $Pd(t\text{-}Bu_3P)_2$ (Scheme 2, route d; *silylation*).[13] In this report, I attempt to describe the palladium-catalyzed silicon−aryl bond formation using aryl iodides with hydrosilanes in the presence of a catalytic amount of $Pd(t\text{-}Bu_3P)_2$ and provide the information on the scope and limitations of this reaction.

The coupling reaction of 4-iodoanisole with triethylsilane was selected to optimize the reaction conditions. It was found that, among the catalysts tested, $Pd(t\text{-}Bu_3P)_2$ was the most effective palladium source.[14a] The reaction proceeded smoothly even at 1 mol % catalyst loading. After screening bases, we recognized K_3PO_4 as the most effective.[14b] The desired silylated product was obtained in low yield, and the reduced one was dominantly observed without base. Among the solvents examined, the use of 1-methyl-2-pyrrolidinone (NMP) was essential for this silylation. Room temperature was found to be optimal for the reaction. The optimized conditions were 4-iodoanisole (1.0 equiv), triethylsilane (1.1 equiv), K_3PO_4 as base (3.0 equiv),[14c] and 1 mol % of $Pd(t\text{-}Bu_3P)_2$ in NMP at room temperature under a nitrogen atmosphere, which afforded the silyl product in an 84% isolated yield along with a small amount of anisole (ca. 10%).[15]

TABLE 1. Reaction of Organic Halides with R_3SiH in the Presence of a Catalytic Amount of $Pd(t\text{-}Bu_3P)_2$[a]

$$\mathrm{ArX} + \mathrm{R_3SiH} \xrightarrow[\mathrm{K_3PO_4,\ NMP}\ \mathrm{r.t.,\ 5\ h}]{\mathrm{Pd}(t\text{-}\mathrm{Bu_3P})_2} \mathrm{ArSiR_3}$$

Entry	ArX	R_3	Product		Yield (%) [b]	
1		Et_3		(**1**)	84	(10)
2		Ph_3		(**2**)	65	(21)
3		$PhMe_2$		(**3**)	72	(16)
4		Et_3	(**1**)		49	(34)
5		Et_3	(**1**)		12	(20)[c]
6		Et_3		(**4**)	— [d]	(72)
7		Et_3		(**5**)	(trace)[e]	(78)
8		Et_3		(**6**)	86	(7)
9		Ph_3		(**7**)	79	(10)
10		Et_3		(**8**)	76	(9)
11		Ph_3		(**9**)	53	(29)
12[f]		Et_3		(**10**)	51	(36)
13		Et_3		(**11**)	(trace)[e]	(83)

[a] Reaction conditions: aryl halide 0.55 mmol, R_3SiH 0.60 mmol, K_3PO_4 1.65 mmol, $Pd(t\text{-}Bu_3P)_2$ 0.0055 mmol, NMP 1 mL. [b] Isolated yield of silylated product. Other major products were reduction ones, and the GC yield is shown in parentheses. [c] Starting material was recovered in 61% (GC yield). [d] The silylated product could not be detected by GC−MS. [e] GC yield. The silylated product could be detected by GC−MS, but could not be isolated. [f] The reaction time was 60 h.

To clarify the generality and scope of this coupling reaction, the silylations of a wide variety of aryl halides and trialkylsilanes were examined under these conditions. The results are summarized in Table 1. The electronic and steric characteristics of the substrates significantly affected the reactions. Aryl iodides were significantly more reactive than bromides and chlorides (entries 1, 4, and 5). The presence of an electron-withdrawing group on the aromatic ring interfered with the coupling reaction (entry 6). On the other hand, electron-rich aryl iodide afforded moderate to good product yields (entries 1, 8, and 10), although the prolonged reaction time was required for meta-substituted aryl iodide (entry 12).[16,17] This is in contrast to a typical palladium-catalyzed cross-coupling process, where electron-rich aryl halide furnished lower product yields. Additionally, the presence of a group at the ortho-position of the aromatic ring afforded no silylated product due to the steric hindrance (entry 7). This reaction was applicable

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(9) Quite recently, Tsukada and Hartwig reported the direct silylation of benzene with triethylsilane in the presence of platinum complex. See: Tsukada, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 5022.

(10) For recent reviews, see: (a) Fu, G. C. *J. Org. Chem.* **2004**, *69*, 3245. (b) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176.

(11) (a) Suzuki reaction: Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3378. (b) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020. (c) Heck reaction: Littke, A. F.; Fu, G. C. *J. Org. Chem.* **1999**, *64*, 10. (d) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989. (e) Stille reaction: Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 2411. (f) Littke, A. F.; Schwarz, L.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 6343. (g) Sonogashira reaction: Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett.* **2000**, *2*, 1729. (g) Negishi reaction: Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719.

(12) For a pioneering study on the use of t-Bu_3P in palladium-catalyzed coupling reactions, see: (a) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 617. (b) Yamamoto, T.; Nishiyama, M.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 2367. (c) Watanabe, M.; Nishiyama, M.; Koie, Y. *Tetrahedron Lett.* **1999**, *40*, 8837. (d) Watanabe, M.; Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **2000**, *41*, 481.

(13) $Pd(t\text{-}Bu_3P)_2$ is available from Strem Chemicals (catalog number 46-0252).

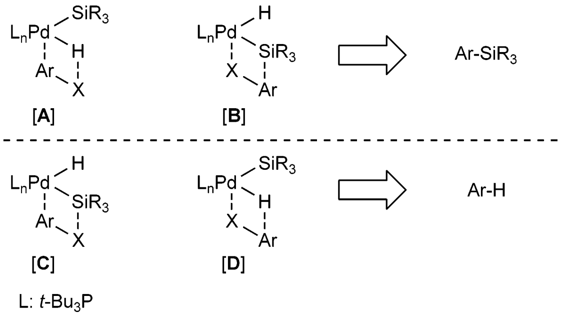
(14) Notes: (a) The yields of the silylation of 4-iodoanisole with triethylsilane in the presence of other palladium catalysts (1 mol %) and K_3PO_4 (3.0 equiv) are as follows. $Pd(PPh_3)_4$: trace, $PdCl_2(PPh_3)_2$: trace, and $Pd[(C_6H_{11})_3P]_2$: 56% ($Pd[(C_6H_{11})_3P]_2$ is available from Strem Chemicals, catalog number 46-0260). (b) The yields of the silylation of 4-iodoanisole with triethylsilane in the presence of $Pd(t\text{-}Bu_3P)_2$ (1 mol %) and other bases (3.0 equiv) are as follows. Et_3N: 47%, i-Pr_2NEt: 59%, K_2CO_3: 80%, Na_2CO_3: 75%, KOAc: 34%, and without base: 29%. (c) The yields of the silylation of 4-iodoanisole with triethylsilane in the presence of $Pd(t\text{-}Bu_3P)_2$ (1 mol %) and K_3PO_4 (x equiv) are as follows. 1.0 equiv: 26%, 2.0 equiv: 59%, 3.0 equiv: 84%, and 4.0 equiv: 82%.

(15) The yield of anisole was estimated by GC−MS using an internal standard.

(16) 4-Iodo-*N*,*N*-dimethylaniline was prepared from 4-iodoaniline by reductive methylation with formaldehyde and $NaBH_3CN$ in the presence of acetic acid. (a) Jian, H.; Tour, J. M. *J. Org. Chem.* **2003**, *68*, 5091. (b) Giumanini, A. G.; Chiavari, G.; Musiani, M. M.; Rossi, P. *Synthesis* **1980**, *9*, 743.

(17) Note: On a 20 mmol scale, the silylation depicted in entry 8 of Table 1 proceeds in 73% yield (3.45 g of product). See Supporting Information for detailed preparation.

SCHEME 3. Tentative Intermediates A−D for the Silylation Reaction



to not only triethylsilane but triphenylsilane and dimethylphenylsilane as well (entries 2, 3, 9, and 11).[18]

Although the mechanistic details of the reaction are not yet clear, at the initial step oxidative addition of hydrosilane to the Pd(0) catalyst generates the $R_3Si-Pd^{II}-H$ complex,[19] which reacts with Ar−X to form the intermediates **A**−**D**. Through the σ-bond metathesis reaction of these species, the silylated product ($ArSiR_3$) would be produced from the intermediates **A** or **B**, reduction product would be generated from the intermediates **C** or **D**, and active Pd(0) species would be needed to complete the catalytic cycle (Scheme 3).[4d,20] The bond dissociation energies for Ar−X are as follows: Cl = 96 kcal/mol, Br = 81 kcal/mol, and I = 65 kcal/mol.[21] Accordingly, a decrease in the bond energy between carbon and halide leads to an increase in the reactivity of σ-bond metathesis. In addition, the steric hindrance (ortho and para) plays a significant role in this transformation.

In summary, a catalyst system that achieves the direct trialkylsilyl transfer to aryl halides has been developed. This study provides further evidence of the usefulness of bulky, electron-rich phosphines in palladium-catalyzed coupling reaction. Detailed mechanistic investigations and additional studies of related transformations are under investigation.

Experimental Section

A Typical Experimental Procedure for Palladium-Catalyzed Silylation Reaction. To a solution of Pd(t-Bu$_3$P)$_2$ (2.8 mg, 0.0055 mmol) and K_3PO_4 (350 mg, 1.65 mmol) in dry and degassed NMP (1.0 mL), trialkylsilane (0.60 mmol) and aryl halide (0.55 mmol) were added under a nitrogen atmosphere. After being stirred for 5 h at room temperature, the reaction mixture was quenched with water, extracted with CH_2Cl_2 three times, and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and column chromatography on silica gel afforded the spectroscopically pure silylated product.

Acknowledgment. I thank Professor Gregory C. Fu, Massachusetts Institute of Technology, and Professor Hiroshi Nishihara, The University of Tokyo, for their helpful discussion and encouragement throughout this research work. I also thank Ms. Kimiyo Saeki, the Elemental Analysis Center of The University of Tokyo, for the measurement of elemental analysis. This work was financially supported in part by the Japan Society for the Promotion of Science (JSPS) for a postdoctoral fellowship from 2000 to 2001.

Supporting Information Available: Spectral data for all silylated products (**1**−**3** and **6**−**10**) and an experimental procedure for the large-scale preparation of **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[18] Under the same reaction conditions, triethoxysilane is not a suitable coupling partner.

[19] Corey, J. Y.; Braddock-Wilking, J. *Chem. Rev.* **1999**, *99*, 175.

[20] Kunai and Ishikawa reported that the reaction of triethylsilane with alkyl and phenyl iodides in the presence of a catalytic amount of $PdCl_2$ at room temperature afforded alkyl- and phenyl-substituted iodosilane in high yields as well as reduced products. They also reported that the reaction of dialkylsilane with *alkyl iodide* brought out the formation of a Si−C bond through the σ-bond metathesis reaction between the Si−Pd bond and the C−I bond. Kunai, A.; Sakurai, T.; Toyoda, E.; Ishikawa, M.; Yamamoto, Y. *Organometallics* **1994**, *13*, 3233.

[21] Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 1047 and references therein.