

Palladium-Catalyzed Silylation of Electron-Deficient Aryl Iodides Using Triorganosilane in the Presence of Pyridine and LiCl

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Palladium-catalysed silylation of aryl iodides with electron-withdrawing groups was efficiently achieved using pyridine and lithium chloride as additives and conducting the reaction at room temperature. Functionalized aryl[2-(hydroxymethyl)-phenyl]dimethylsilanes were also prepared by palladium-catalysed reaction using THP-protected [2-(hydroxymethyl)-

phenyl]dimethylsilane as a silylating agent followed by deprotection. Rhodium-catalysed 1,4-addition of the arylsilane was carried out using cyclohexenone as an enone in excellent yield.

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Introduction

The silicon-based cross coupling has become an important method for carbon–carbon bond formation, and the reaction is now widely used (Hiyama coupling).^[1] Various arylsilanes have been employed for the coupling partners and the transition-metal-catalysed silylation of aryl halides should be one of the most versatile and chemoselective methods to prepare arylsilanes.^[2] Recently, Yamanoi reported the palladium-catalysed silylation of aryl halides using *t*Bu₃P as a ligand (Figure 1).^[2h] Trialkylsilyl groups can be successfully transferred by the reaction; however, the reaction is not applicable to aryl halides with an electron-withdrawing group. Murata et al. also reported a palladium-catalysed silylation of aryl halides with electron-donating groups using triorganosilanes.^[2e] Alami et al. reported a platinum oxide catalysed trialkylsilylation of various aryl halides,^[2f] but there has been no successful report of palladium-catalysed silylations of aryl halides with electron-withdrawing groups.

In connection with our recent study on the selective transformation of arylsilanes,^[3] we investigated the selective silylation of aryl halides with various functional groups catalysed by palladium.

Results and Discussion

We first investigated the palladium-catalysed silylation of 4-iodonitrobenzene (**1**), which was considered to be the most challenging substrate for the selective silylation as shown in Figure 1. In order to avoid the formation of reduced product **3**, various reaction conditions were screened, and conditions free of phosphane ligands were suggested to be favorable. After the screening of various reaction conditions, we found that the use of pyridine and lithium chloride as additives is effective for selective silylation.

When 1-iodo-4-nitrobenzene (**1**) was treated with Et₃SiH in the presence of Pd(OAc)₂ (4 mol-%), pyridine (2.5 equiv.) and LiCl (4 equiv.) in DMI (*N,N*-dimethylimidazolin-2-one), silylated nitrobenzene **2** was obtained in 51% yield, and the ¹H NMR analysis of the crude material indicated a ratio of **2/3** = 8:2 (Table 1, Entry 1). The use of other solvents such as NMP or DMF gave poorer **2/3** ratios (Table 1, Entries 2, 3). When Et₃N was employed instead of pyridine, no formation of **2** was observed, and only **3** was produced (Table 1, Entry 4). The absence of base also resulted in no formation of **2** (Table 1, Entry 5). The use of NaOAc, LiBr, or LiI as an additive was not effective for the formation of **2**, and only **3** was formed (Table 1, Entries 6–8). On the other hand, the use of Et₄NCl was effective like LiCl, and **2** was obtained in 56% yield (Table 1, Entry 9). When the amount of LiCl was reduced to 1 equiv., the ratio of **2/3** decreased (Table 1, Entry 10). Thus, pyridine was found to be essential for selective formation of **2**, and also chloride anions play an important role for the selective transfer of a silyl group.

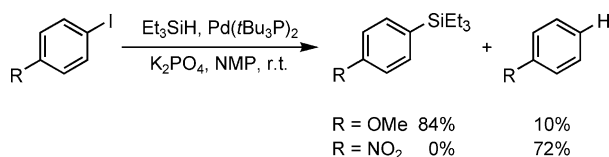
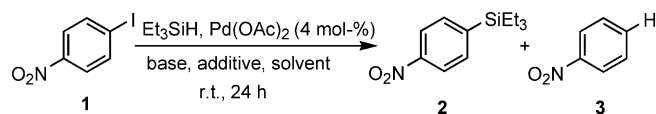


Figure 1. Side reaction in the silylation of iodoarenes.^[2h]

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Table 1. Palladium-catalyzed silylation of 1-iodo-4-nitrobenzene.



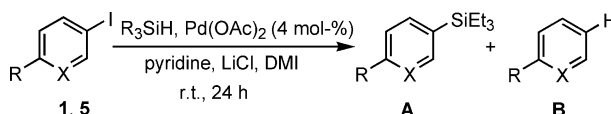
Entry	Base	Additive	Solvent	2/3 ^[a]	Yield (%) of 2 ^[b]
1	pyridine	LiCl (4 equiv.)	DMI	8:2	52
2	pyridine	LiCl (4 equiv.)	NMP	7:3	—
3	pyridine	LiCl (4 equiv.)	DMF	6:4	—
4	Et ₃ N	LiCl (4 equiv.)	DMI	0:10	—
5	—	LiCl (4 equiv.)	DMI	0:10	—
6	pyridine	NaOAc	DMI	0:10	—
7	pyridine	LiBr	DMI	0:10	—
8	pyridine	LiI	DMI	0:10	—
9	pyridine	Et ₄ NCl	DMI	8:2	56
10	pyridine	LiCl (1 equiv.)	DMI	6:4	—

[a] Estimated by ¹H NMR spectroscopy. [b] Isolated yields.

Further investigations were carried out for the silylation of various aryl iodides using several silanes. On 1-iodo-4-nitrobenzene (**1**), the use of PhMe₂SiH gave almost similar results with Et₃SiH, and **A** (**2b**) was isolated in 45% yield (Table 2, Entry 1). When Ph₃SiH was used, the yield of **A** (**2c**) was improved to 70% (Table 2, Entry 2). The reaction of 4-iodobenzonitrile (**5a**) with Et₃SiH gave **A** (**6a**) in 46% yield (Table 2, Entry 3). The use of PhMe₂SiH improved the yield of **A** (**6b**) up to 94%, and no formation of **B** was observed (Table 2, Entry 4). The reaction using Ph₃SiH gave **A** (**6c**) in 64% yield with no formation of **B** (Table 2, Entry 5). The reaction of 4-iodoacetophenone (**5b**) with Et₃SiH gave a 1:1 mixture of **A/B**, and the desired **A** (**7a**) was isolated in 38% yield (Table 2, Entry 6). When PhMe₂SiH was used, the ratio of **A/B** was improved to 8:2, and **A** (**7b**) was obtained in 73% yield (Table 2, Entry 7). The use of Ph₃SiH gave the best result, and **A** (**7c**) was obtained in 85% yield with no formation of **B** (Table 2, Entry 8). The reaction of methyl 4-iodobenzoate (**5c**) with Et₃SiH gave a 6:4 mixture of **A/B**, and **A** (**8a**) was isolated in 35% yield (Table 2, Entry 9). The use of PhMe₂SiH gave a 9:1 mixture of **A/B**, and **A** (**8b**) was isolated in 82% yield (Table 2, Entry 10). The use of Ph₃SiH showed an excellent selectivity, and **A** (**8c**) was obtained in 91% yield with no formation of **B** (Table 2, Entry 11). 3-Iodopyridine (**5d**) was also treated with PhMe₂SiH, and the corresponding silylated pyridine **9** was obtained in 87% yield (Table 2, Entry 12). The use of phenyl-substituted silanes showed better selectivities, and this tendency was also suggested by Murata's report.^[2e] At this moment, the silylation of an electron-rich aryl halide such as 4-iodoanisole was unsuccessful under our reaction conditions, and only a trace amount of silylated product was isolated.

With respect to the mechanism of the silylation reaction, two types of pathways have been suggested: (i) σ -bond metathesis, (ii) Pd^{IV} intermediate involvement.^[2a,2g] At this moment, it is not clear how pyridine and LiCl effectively form the silylated products; however, the combination is suggested to be favorable for the transition state of the metathesis or the formation of Pd^{IV} species.

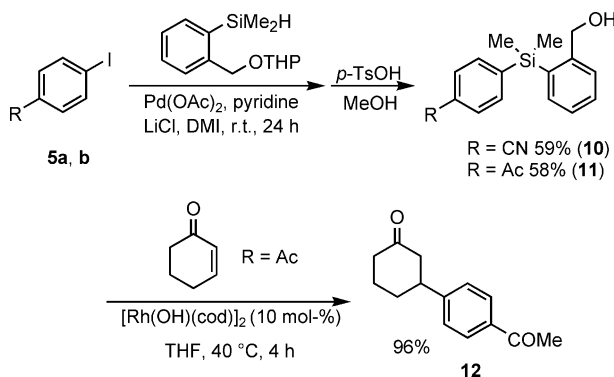
Table 2. Palladium-catalyzed silylation of iodoarenes.



Entry	R	X	1 or 5	R ₃ SiH	A/B ^[a]	Yield (%) of A ^[b]
1	NO ₂	CH	1	PhMe ₂ SiH	9:1	45 (2b)
2	NO ₂	CH	1	Ph ₃ SiH	—	70 (2c) ^[c]
3	CN	CH	5a	Et ₃ SiH	—	46 (6a)
4	CN	CH	5a	PhMe ₂ SiH	10:0	94 (6b)
5	CN	CH	5a	Ph ₃ SiH	10:0	64 (6c)
6	COMe	CH	5b	Et ₃ SiH	5:5	38 (7a)
7	COMe	CH	5b	PhMe ₂ SiH	8:2	73 (7b)
8	COMe	CH	5b	Ph ₃ SiH	10:0	85 (7c)
9	COOMe	CH	5c	Et ₃ SiH	4:6	35 (8a)
10	COOMe	CH	5c	PhMe ₂ SiH	9:1	82 (8b)
11	COOMe	CH	5c	Ph ₃ SiH	10:0	91 (8c)
12	H	N	5d	PhMe ₂ SiH	—	87 (9)

[a] Estimated by ¹H NMR spectroscopy. [b] Isolated yields. [c] DMF was used as a solvent.

Our next interest was focused on the formation of aryl[2-(hydroxymethyl)phenyl]dimethylsilanes, which recently were reported to be excellent aryl donors for various transition-metal-catalysed reactions.^[4] The THP-protected [2-(hydroxymethyl)phenyl]dimethylsilane was treated with 4-iodobenzonitrile (**5a**) and 4-iodoacetophenone (**5b**) followed by the treatment with *p*-TsOH to remove THP protective group, and the silylated arenes **10** and **11** were obtained in 59% and 58% yields, respectively. The [2-(hydroxymethyl)phenyl]silylated acetophenone **11** was then treated with cyclohexenone in the presence of a rhodium catalyst which gave the 1,4-adduct **12** in 96% yield (Scheme 1).



Scheme 1. Selective transformation of arylsilanes.

Conclusions

Palladium-catalysed silylation of aryl iodides with electron-withdrawing groups was efficiently achieved using pyridine and lithium chloride as additives and conducting the reaction at room temperature. Aryl[2-(hydroxymethyl)phenyl]dimethylsilanes were also prepared by palladium-catalysed reaction using protected [2-(hydroxymethyl)phenyl]dimethylsilane as a silylating agent followed by de-

protection. Rhodium-catalysed 1,4-addition of the arylsilane was carried out using cyclohexenone in excellent yield. Further investigations on the scope and limitations of the palladium-catalysed silylation and mechanistic studies are underway.

Supporting Information (see footnote on the first page of this article): Experimental procedure and spectroscopic data of synthesized compounds.

Acknowledgments

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- [1] a) T. Hiyama, in *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**, p. 421; b) T. Hiyama, E. Shirakawa, in *Topics in Current Chemistry* (Ed.: N. Miyaoura), Springer-Verlag, Heidelberg, **2002**, vol.

- 219, p. 61; c) K. A. Horn, *Chem. Rev.* **1995**, 95, 1317; d) Y. Hatanaka, T. Hiyama, *Synlett* **1991**, 845.
[2] a) M. Murata, H. Yamasaki, K. Uogishi, S. Watanabe, Y. Masuda, *Synthesis* **2007**, 2944; b) Y. Yamanoi, T. Taira, J. Sato, I. Nakamura, H. Hishihara, *Org. Lett.* **2007**, 9, 4543; c) M. Murata, K. Oka, H. Yamasaki, S. Watanabe, Y. Masuda, *Synlett* **2007**, 1387; d) M. Murata, H. Yamasaki, T. Ueta, M. Nagata, M. Ishikura, S. Watanabe, Y. Masuda, *Tetrahedron* **2007**, 63, 4087; e) M. Murata, H. Ohara, R. Oiwa, S. Watanabe, Y. Masuda, *Synthesis* **2006**, 1771; f) A. Hamze, O. Provot, M. Alami, J.-D. Brion, *Org. Lett.* **2006**, 8, 931; g) D. Karchtedt, A. T. Bell, T. D. Tilley, *Organometallics* **2006**, 25, 4471; h) Y. Yamanoi, *J. Org. Chem.* **2005**, 70, 9607; i) S. E. Denmark, J. M. Kallemeyn, *Org. Lett.* **2003**, 5, 3483; j) W. Gu, S. Liu, R. B. Silverman, *Org. Lett.* **2002**, 4, 4171; k) A. S. Manoso, P. J. DeShong, *J. Org. Chem.* **2001**, 66, 7455; l) M. Murata, K. Suzuki, S. Watanabe, Y. Masuda, *Tetrahedron Lett.* **1999**, 40, 9255; m) M. Murata, K. Suzuki, S. Watanabe, Y. Masuda, *J. Org. Chem.* **1997**, 62, 8569.
[3] K. Suzawa, M. Ueno, A. E. H. Wheatley, Y. Kondo, *Chem. Commun.* **2006**, 4850.
[4] a) Y. Nakao, H. Imanaka, A. H. Sahoo, A. Yada, T. Hiyama, *J. Am. Chem. Soc.* **2005**, 127, 6952; b) Y. Nakao, J. Chen, H. Imanaka, T. Hiyama, Y. Ichikawa, W.-L. Duan, R. Shintani, T. Hayashi, *J. Am. Chem. Soc.* **2007**, 129, 9137; c) Y. Nakao, J. Chen, M. Tanaka, T. Hiyama, *J. Am. Chem. Soc.* **2007**, 129, 11694.

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