Platinum Oxide Catalyzed Silylation of Aryl Halides with Triethylsilane: An Efficient Synthetic Route to Functionalized Aryltriethylsilanes
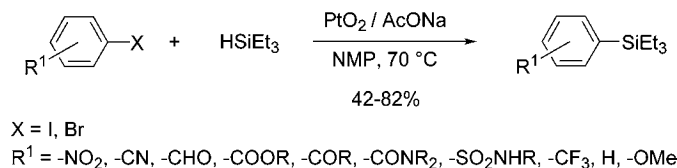
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ABSTRACT

X = I, Br
R^1 = -NO$_2$, -CN, -CHO, -COOR, -COR, -CONR$_2$, -SO$_2$NHR, -CF$_3$, H, -OMe

The first platinum-catalyzed selective silylation of aryl halides including aryl iodides and bromides having an electron-withdrawing group is described. The reaction takes place rapidly in NMP with triethylsilane as a silicon source and sodium acetate to provide functionalized aryltriethylsilanes in moderate to good yields. Heteroaromatic halides also were found to be readily silylated with triethylsilane. The procedure is chemoselective and tolerates a wide variety of functional groups.

Arylsilanes are valuable intermediates in organic synthesis, and their use has been demonstrated in a number of reviews which deal with Hiyama[1] coupling and other related transition-metal-catalyzed coupling reactions.[2]

Accordingly, many synthetic efforts have been devoted to their preparation. Classical synthetic routes to arylsilanes consist of the reaction of aryl Grignard or aryllithium compounds with silicon electrophiles.[3] More recent strategies involve the conversion of an sp^2-carbon−halogen bond to an sp^2-carbon−silicon bond under transition-metal catalysts.

Typically, the palladium-catalyzed cross-coupling reaction of aryl halides with disilanes as silicon sources has proven to be a useful route to functionalized arylsilanes.[4] Silylation[5] with hydrosilanes has also been reported, indicating their potential use as silylating reagents in the presence of transition-metal complexes. Masuda[6] and DeShong[7] reported the palladium-catalyzed silylation of aryl halides (I, Br) with triethoxysilane.[8] These reactions are effective with electron-rich and -neutral para-substituted aryl halides. However, with

(1) For selected reviews on the Hiyama cross-coupling reaction, see: (a) Hiyama, T. *in Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; p 421. (b) Hiyama, T.; Shirakawa, E. In *Topics in Current Chemistry*; Miyaura, N., Ed.; Springer-Verlag: Heidelberg, 2002; Vol. 219, p 61. (c) Horn, K. A. *Chem. Rev.* **1995**, *95*, 1317−1350. (d) Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845−853. (e) Pierrat, P.; Gros, P.; Fort, Y. *Org. Lett.* **2005**, *7*, 697−700. (f) Ito, H.; Sensui, H.; Arimoto, K.; Hosomi, A. *Chem. Lett.* **1997**, 639−640. (g) Fu, J. M.; Snieckus, V. *Can. J. Chem.* **2000**, *78*, 905−919. (h) Yoshikawa, E.; Radhakrishnan, K. V.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 729−731.

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

(3) (a) Lulinski, S.; Serwatowski, J. *J. Org. Chem.* **2003**, *68*, 9384−9388. (b) Nishide, K.; Miyamoto, T.; Kumar, K.; Ohsugi, S. I.; Node, M. *Tetrahedron Lett.* **2002**, *43*, 8569−8573. (c) Manoso, A. S.; Ahn, C.; Soheili, A.; Handy, C. J.; Correira, R.; Seganish, W. M.; DeShong, P. *J. Org. Chem.* **2004**, *69*, 8305−8314. (d) Schlosser, M.; Heiss, C. *Eur. J. Org. Chem.* **2003**, 4618−4624. (e) Oestreich, M.; Auer, G.; Keller, M. *Eur. J. Org. Chem.* **2005**, 184−195.

(4) (a) Denmark, S.; Kallemeyn, J. M. *Org. Lett.* **2003**, *5*, 3483−3486. (b) Goo-en, L. K.; Ferwanah, A.-R. S. *Synlett* **2000**, 1801−1803 and references therein.

(5) For a recent review, see: Handy, C. J., Manoso, A. S.; McElroy, W. T., Seganish, W. M., DeShong, P. *Tetrahedron* **2005**, *61*, 12201−12225.

(6) Murata, M.; Suzuki, K.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **1997**, *62*, 8569−8571.

(7) Manoso, A., S.; DeShong, P. *J. Org. Chem.* **2001**, *66*, 7449−7455.

electron-deficient aryl halides the side reduction of the carbon−halogen bond predominated. Murata[9] reported that a limited number of electron-deficient aryl bromides and iodides also react with triethoxysilane in the presence of Rh(I) catalyst. Quite recently, triethylsilane[10] has been used as a silylating reagent to achieve the silylation of aryl halides under palladium catalysis,[11] but again, this procedure is restricted to electron-rich and -neutral para-substituted aryl iodides.[12] Yamanoi also mentioned that the presence of a para electron-withdrawing group (e.g., −NO$_2$) on the aromatic ring interfered with the coupling reaction. Therefore, it would be desirable to develop a new selective procedure that would tolerate a wide range of functional groups to achieve the direct trialkylsilyl transfer to electron-deficient aryl halides.

During the course of our study on the PtO$_2$-catalyzed hydrosilylation reaction of halogenated internal arylalkynes,[13] we found that besides the H−Si bond addition, a side halogen/silicon exchange-reaction occurred. A survey of the literature revealed, to the best of our knowledge, that there is no report of platinum-catalyzed silicon-aryl carbon bond formation from aryl halides[14] using hydrosilane derivatives. Herein we report a useful and convenient synthetic route to functionalized aryltriethylsilanes by PtO$_2$-catalyzed silylation of aryl halides including aryl iodides and bromides substituted with an electron-withdrawing group (Scheme 1).

Scheme 1
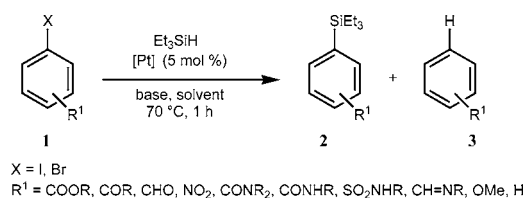
Initially, the silylation of ethyl 4-iodobenzoate **1a**, as a model substrate, was examined under various conditions. This study showed that the selectivity of the reaction (silylation vs reduction) depends greatly on the solvent, the base, and the platinum catalyst. The results are summarized in Table 1.

The reaction of **1a** with triethylsilane (1.5 equiv) in the presence of PtO$_2$ (5 mol %) in NMP (N-methyl-2-pyrroli-

(8) Triethoxysilane is highly toxic, and contact with the eyes may cause blindness; see: *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 7, p 5083.

(9) Murata, M.; Ishikura, M.; Nagata, M.; Watanabe, S.; Masuda, Y. *Org. Lett.* **2002**, *4*, 1843−1845.

(10) Triethylsilane generally works as a reducing reagent in the presence of a palladium catalyst; see: Boukherroub, R.; Chatgilialoglu, C.; Manuel, G. *Organometallics* **1996**, *15*, 1508−1510. See also ref 6.

(11) Yamanoi, Y. *J. Org. Chem.* **2005**, *70*, 9607−9609.

(12) For the coupling of butyldiethylsilane polystyrene with Boc-4-iodophenylalanine methyl ester in the presence of palladium catalyst, see: Gu, W.; Liu, S.; Silverman, R. B. *Org. Lett.* **2002**, *4*, 4171−4174.

(13) Hamze, A.; Provot, O.; Alami, M.; Brion, J.-D. *Org. Lett.* **2005**, *7*, 5625−5628.
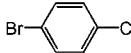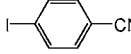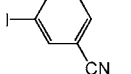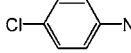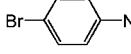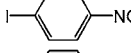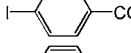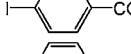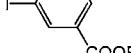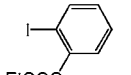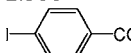
(14) For the Pt-catalyzed coupling of silane Si−H bonds with aromatic and aliphatic C−H bonds, see: (a) Tsukada, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 5022−5023. For Ru-catalyzed silylation of aromatic C−H bonds, see: (b) Kakiuchi, F.; Matsumoto, M.; Tsuchiya, K.; Igi, K.; Hayamizu, T.; Chatani, N.; Murai, S. *J. Organomet. Chem.* **2003**, *686*, 134−144.

Table 1. Optimization Reaction of Ethyl 4-Iodobenzoate **1a** with Triethysilane under Various Conditions[a]

entry	base	solvent	[Pt]	yield[b] (%) 2a	3a
1	i-Pr$_2$NEt	NMP	PtO$_2$	54[c]	22
2	Et$_3$N	NMP	PtO$_2$	50	16
3	N-Me-piperidine	NMP	PtO$_2$	66	16
4	Cs$_2$CO$_3$	NMP	PtO$_2$	5[d]	9
5	AcOK	NMP	PtO$_2$	67	14
6	AcONa	NMP	PtO$_2$	90[e]	8
7	AcONa	DMA	PtO$_2$	72	28
8	AcONa	DMF	PtO$_2$	65	26
9	AcONa	DMPU[f]	PtO$_2$	67	19
10	AcONa	CH$_2$Cl$_2$	PtO$_2$	0	0
11	AcONa	dioxane	PtO$_2$	0	0
12	AcONa	neat	PtO$_2$	12	7
13	AcONa	NMP	Pt(PPh$_3$)$_4$	20[g]	29
14	AcONa	NMP	Pt/C	87[h]	13
15	AcONa	NMP	PtCl$_2$	30	70
16	AcONa	NMP	H$_2$PtCl$_6$	17	83

[a] Reactions of ethyl 4-iodobenzoate **1a** (1.0 mmol) with triethylsilane (1.5 mmol) were performed at 70 °C for 1 h in 3 mL of solvent by using PtO$_2$ (5 mol %) and base (3 mmol). [b] Yields were determinated by GC analysis. [c] No reaction occurred at room temperature. [d] 15% conversion were observed by GC analysis after 1 h. [e] **2a** was easily purified by flash chromatography on silica gel; isolated yield of **2a** 73%. [f] DMPU: 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone. [g] 49% conversion were observed by GC analysis after 1 h. [h] Isolated yield of **2a** 70%.

dinone) was first evaluated with i-Pr$_2$NEt as a base. Thus, at room temperature, no silylation occurred and starting material **1a** was recovered unchanged. However, at 70 °C for 1 h, the reaction proceeded to give a mixture of the silylated derivative **2a** and the reduced byproduct **3a** (entry 1, Table 1). It should be noted that this selectivity markedly in favor of the desired product **2a** was dependent on the nature of the base (entries 2−6). Thus, in the presence of tertiary amine, especially N-methylpiperidine, the formation of **2a** was improved (entry 3), whereas the use of mineral base Cs$_2$CO$_3$ induced a lowering of the conversion rate and the selectivity (entry 4). The use of sodium acetate was found to be the most effective base for the selective formation of arylsilane **2a** (entry 6). Under these conditions, pure compound **2a** was obtained in a 73% isolated yield. It should be noted that decreasing the amount of sodium acetate from 3.0 to 1.5 equiv had no effect on the yield and the selectivity of the silylation (72% vs 73%). The influence of the solvent was next investigated. Among several polar solvents tested including DMA (N,N-dimethylacetamide), DMF, or DMPU (entries 7−9), NMP is the unrivaled solvent choice for this silylation. No reaction occurred in other solvents, such as CH$_2$Cl$_2$ or dioxane (entries 10 and 11).

In addition, the effect of platinum catalysts on the catalytic activity was also evaluated. The use of Pt(PPh$_3$)$_4$ produced an equal mixture of the arylsilane **2a** and the reduced derivative **3a** (entry 13). In the presence of Pt/C, as catalyst, however, the silylation reaction of **1a** was effective, affording a selectivity similar to that obtained with PtO$_2$ catalyst (compare entries 6 and 14), and **2a** was obtained in a 70%

isolated yield. When the reaction is carried out in the presence of PtCl$_2$ or H$_2$PtCl$_6$ as catalysts, the formation of undesirable **3a** predominated (entries 15 and 16). These results clearly indicated that platinum catalysts with a chlorine atom had a strong tendency to produce competitively the reduced byproduct **3a**. Accordingly, when exposing **1a** to Et$_3$SiH (1.5 equiv) in NMP at 70 °C for 2 h in the presence of BnNBu$_3$Cl (1 equiv), Pt/C (5 mol %), and AcONa (3 equiv), the reduced byproduct **3a** became dominant. The GC analysis of the reaction mixture indicated the formation of a mixture of **1a/2a/3a** in a 30:30:40 ratio.

Finally, the effect of other hydrosilanes under our optimized conditions (PtO$_2$, AcONa, NMP, 70 °C) was examined. The use of triethoxysilane induced a lowering of the reactivity and prevented the formation of the siloxane derivative.[15] Other hydrosilanes[16] including, PhMe$_2$SiH, Me$_2$-EtOSiH, Ph$_2$MeSiH, and i-Pr$_3$SiH were also examined in this reaction, but none of these reagents were more effective than Et$_3$SiH. Our study demonstrates that triethylsilane under PtO$_2$ catalyst selectively acted as a silicon source for the coupling of electron-deficient aryl iodide **1a**. Moreover, since the desired functionalized aryltriethylsilane **2a** and the reduced byproduct **3a** were easily separated by flash chromatography on silica gel, this new silylation complements the previous procedure[11] and provides a simple and widely available route to functionalized aryl-triethylsilanes **2**.

To demonstrate the scope of this new platinum-catalyzed silylation reaction, a variety of representative aryl halides was examined. Results summarized in Table 2 show that the yield of the silylation reaction was affected by the electronic and steric characteristics of the substrates used. On the contrary, of the previous palladium-catalyzed silylations,[11] best yields of aryltriethylsilane **2** were obtained for aryl halides with a π-electron-withdrawing group. As expected, the reactivity of aryl bromides was moderate in comparison with aryl iodides (compare entries 1, 2 and 5, 6), but unfortunately, the corresponding electron-deficient aryl chloride did not have enough reactivity, and as a consequence, compound **1e** was recovered unchanged (entry 4). Interestingly, the presence of a wide variety of electrophilic functional groups (e.g., −CO$_2$R, −CN, −NO$_2$, −SO$_2$-NHR, −CH=NPh, −COR, −CHO, ...) on the aryl halides **1** did not interfere with the outcome of the present reaction at 70 °C since the triethylsilane reactant was inert to many functional groups (entries 1−17) even to the formyl functionality[17] (entry 15). The position of the substituent greatly impacted the reaction outcome. Silylation of electron-deficient para- and meta-substituted aryl halides gave in moderate to good yields functionalized aryltriethylsilanes, whereas the reaction with the ortho-substituted derivatives
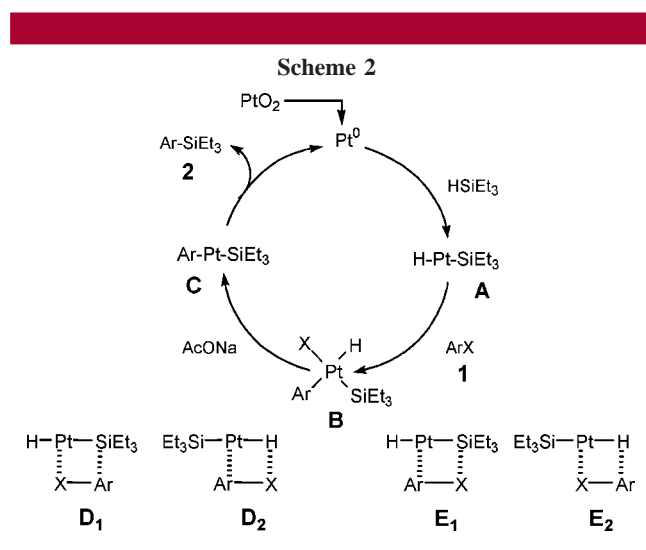
(15) The GC analysis of the reaction mixture indicated the only formation of the reduced product (15%) and starting halide (85%) after stirring for 1 h.

(16) Silylation yields of **1a** with other hydrosilanes under the catalytic conditions (PtO$_2$ 5 mol %, AcONa 3 equiv in NMP at 70 °C) are as follows: PhMe$_2$SiH **2x**, 36%; Me$_2$EtOSiH, traces; Ph$_2$MeSiH, traces; i-Pr$_3$-SiH, traces.

(17) Exposing 4-iodobenzaldehyde **1p** to Et$_3$SiH at 70 °C for 2 h in the absence of PtO$_2$ catalyst gave 4-iodobenzyl alcohol (30%) and starting halide (70%) after GC analysis of the reaction mixture.

Table 2. PtO$_2$-Catalyzed Silylation of Various Aryl Halides **1**: Synthesis of Functionalized Aryltriethylsilanes **2**

entry	aryl halide **1**		yields of **2** (%)[a,b]
1	**1b**	Br—⟨⟩—CN	50
2	**1c**	I—⟨⟩—CN	72
3	**1d**	I—⟨⟩ (CN)	60
4	**1e**	Cl—⟨⟩—NO$_2$	0
5	**1f**	Br—⟨⟩—NO$_2$	64
6	**1g**	I—⟨⟩—NO$_2$	80
7	**1h**	I—⟨⟩—CO$_2$-(CH$_2$)$_2$NMe$_2$	82
8	**1i**	I—⟨⟩—CO$_2$Me	70
9	**1j**	I—⟨⟩ (COOEt)	66
10	**1k**	I—⟨⟩ (COOEt, EtOOC)	10[c]
11	**1l**	I—⟨⟩—CONEt$_2$	42
12	**1m**	I—⟨⟩—CONHPr	71
13	**1n**	I—⟨⟩—SO$_2$NHPr	68
14	**1o**	I—⟨⟩—COBu	59
15	**1p**	I—⟨⟩—CHO	64
16	**1q**	I—⟨⟩—CF$_3$	48
17	**1r**	I—⟨⟩—CH=N—Ph	61[d]
18	**1s**	I—⟨⟩	70
19	**1t**	I—⟨⟩—OMe	0[e]
20	**1u**	Br-quinoline	50
21	**1v**	I—pyridine—Cl	67
22	**1w**	I—pyridine	48

[a] Reactions of aryl halide (1.0 mmol) with triethylsilane (1.5 mmol) were performed at 70 °C in NMP (3 mL) in the presence of PtO$_2$ (5 mol %) and sodium acetate (3 mmol). [b] Isolated yield of silylated product after flash chromatography on silica gel. [c] Yield was determined by GC analysis. [d] After purification, sensitive imine **2r** was contaminated with a substantial amount (22%) of aldehyde **2p**. [e] Starting material was recovered unchanged.

gave poor yields of the silylated product due to a chelation and/or a steric hindrance (entry 10).

The reaction was also effective with neutral aryl iodides and silylation of iodobenzene gave 70% of the corresponding phenyltriethylsilane (entry 18). However, in contrast to electron-deficient and -neutral para-substituted aryl iodides, no silylation occurred with electron-rich para-substituted aryl iodides and starting material was recovered unchanged (Table 2, entry 19). In the following examples, it is interesting to note that heteroaromatic iodides and bromides were readily silylated with triethylsilane without any difficulty. For instance, 3-bromoquinoline (**1u**), 2-chloro-5-iodopyridine (**1v**) and 3-iodopyridine (**1w**) afforded the corresponding 3-triethylsilanylquinoline (**2u**), 2-chloro-5-triethylsilanylpyridine (**2v**), and 3-triethylsilanylpyridine (**2w**) in 50%, 67%, and 48% yield, respectively (Table 2, entries 20−22).

Although there is no clear experimental evidence, we suppose that the reaction proceeds as shown in Scheme 2.

Scheme 2

Initially, the PtO_2[18] catalyst is probably reduced to metal platinum and triethylsilane would add to the metal catalyst to generate the $H-Pt^{II}-SiEt_3$ complex **A**.[19] Then a further oxidative addition of Ar−X would form a platinum(IV)

intermediate **B**, in view of the high reactivity of Pt(II) toward aryl halides demonstrated for some systems to give Pt(IV) species.[20] Accordingly, the formation of the intermediate **B** via an oxidative addition process would be favorable in the case of electron-deficient aryl halides and unfavorable with electron-rich aryl halides. Reductive elimination of **B** in the presence of AcONa would lead to a Pt(II) species **C**. A subsequent reductive elimination[21] of **C** produces the aryl-silane product **2** and regenerates the platinum catalyst. The reduced byproduct **3** would occur in the case that reductive elimination of Et_3SiX[22] from **B** proceeded. However, at present, we cannot rule out an alternative possibility that the aryl halide and the Pt(II) species **A** evolve according to a σ-bond metathesis between Si−Pt bond and C−X bond. Species D_1/D_2 would produce the arylsilanes **2** and species **E1/E2** would give the reduced byproduct **3**. However, since there are many factors governing this elemental step, it is not easy to conclude any clear rationale at this stage.

In conclusion, the present paper shows for the first time that PtO_2 proved to be a powerful and efficient catalyst for the direct trialkylsilyl transfer to a variety of electron-deficient and -neutral aryl halides using triethylsilane as silylating reagents in the presence of AcONa. The procedure is chemoselective and was also effective in the case of heteroaromatic halides. This coupling reaction complements the previous procedures[11] and provides a new and efficient synthetic route to a wide range of functionalized arytriethylsilanes. The investigations for silylation with other organic halides or pseudo halides are currently in progress in our laboratory.

Supporting Information Available: Experimental procedures and spectroscopic data of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Similar results were obtained when the silylation of **1a** was carried out in the presence of PtO_2 or Pt/C catalysts; compare entries 6 and 14 in Table 1.

(19) For the formation of platinum metal silyl hydride complexes, see: (a) Chan, D.; Duckett, S. B.; Heath, S. L.; Khazal, I. G.; Perutz, R. N.; Sabo-Etienne, S.; Timmins, P. L. *Organometallics* **2004**, *23*, 5744−5756. (b) Heyn, R. H.; Tilley, D. T. *J. Am. Chem. Soc.* **1992**, *114*, 1917−1919. (c) Braddock-Wilking, J.; Levchinsky, Y.; Rath, N. P. *Organometallics* **2000**, *19*, 5500−5510.

(20) (a) Canty, A. J.; Patel, J.; Rodemann, T.; Ryan, J. H.; Skelton, B. W.; White, A. H. *Organometallics* **2004**, *23*, 3466−3473. (b) Yahav, A.; Goldberg, I.; Vigalok, A. *Organometallics* **2005**, *24*, 5654−5659. (c) Anderson, C. M.; Puddephatt, R. J.; Fergusson, G.; Lough, A. J. *J. Chem. Soc., Chem. Commun.* **1989**, 1297−1298. (d) Canty, A. J.; Honeyman, R. T.; Skelton, B. W.; White, A. H. *J. Organomet. Chem.* **1990**, *389*, 277−288. (e) Canty, A. J.; Patel, J.; Skelton, B. W.; White, A. H. *J. Organomet. Chem.* **2000**, *599*, 195−199.

(21) For the C(sp²)−Si reductive elimination from Pt(II) species, see: Ozawa, F.; Tani, T.; Katayama, H. *Organometallics* **2005**, *24*, 2511−2515.

(22) Roy, A. K.; Taylor, R. B. *J. Am. Chem. Soc.* **2002**, *124*, 9510−9524.