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Palladium-Catalyzed Silylation of Aryl Chlorides with Bulky Dialkoxydisilanes

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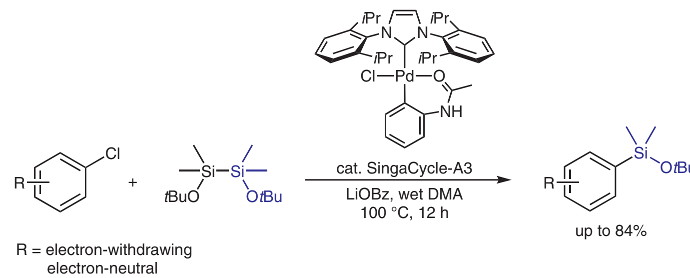

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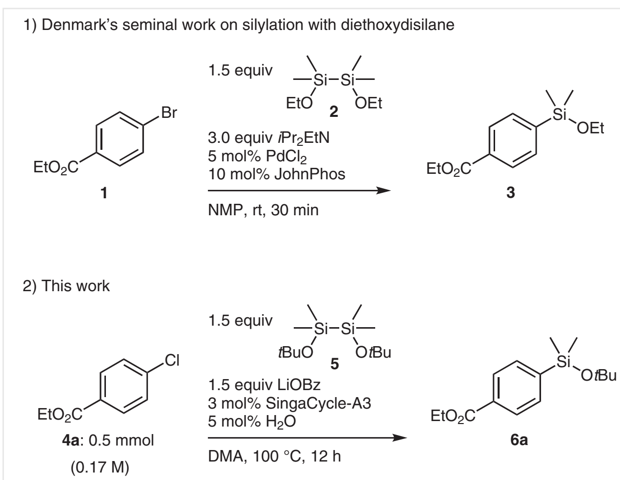
Abstract Arylsilanes bearing a bulky alkoxy group on the silicon were synthesized from aryl chlorides and dialkoxydisilanes under reaction conditions utilizing SingaCycle-A3 as a palladium precatalyst and lithium benzoate in wet DMA. This report proposes the first direct and catalytic method for introducing *tert*-butoxy- or 1-adamantyloxysilyl groups onto various aryl moieties through the silylation reaction.

Key words palladium, alkoxysilane, disilane, arylsilane

Due to their unique chemical reactivity and potential synthetic utility, organosilicon compounds have frequently been the target of synthetic studies.[1] In the current framework of organic synthesis, silicon functional groups should become more balanced in terms of stability and ease of activation. Some are rather too stable for facile transformations; others are too labile to manage during standard synthetic manipulations. Therefore, prompting better balances between stability and ease of activation would widen the possibility of using silyl groups as alternative key functional groups in organic synthesis. One of the promising solutions to this dilemma is the use of bulky alkoxy substituents to balance them.[2] Our research focus has thus turned to a tBuOMe$_2$Si[3,4] group, as a candidate for such a balanced functional group. The special feature of this silyl group is its exceptional stability against water or bases in contrast to other labile primary or secondary alkoxy silyl groups. This silyl group is therefore expected to serve as a reliable functional group that can survive during multistep synthetic transformations. We accordingly focused on the development of a general method to introduce a tBuOMe$_2$Si group via silylation of aryl halides. Typical silylation reagents for aryl halides include hydrosilanes,[5] silylboranes,[6] and disilanes.[5d,7] We chose to employ the corresponding disilane **5** as the silicon source for our cross-coupling-type silylation reaction. Compound **5** can be easily prepared in one step,[3b] and this reagent is now commercially available. Among the previously reported conditions for silylation between an aryl halide and a dialkoxydisilane[5d,7g,7i–l], Denmark's seminal work was the first and only method to introduce an alkoxysilyl group (Scheme 1, eq. 1) wherein aryl bromide **1** reacted with diethoxydisilane **2** using a $PdCl_2$/JohnPhos catalytic system to give arylsilane **3**.[5d] As such, introduction of a silyl group with a more bulky tertiary alkoxy group such as tBuO has yet to be reported. Herein, we report our research on a palladium-catalyzed method for introducing a tBuOMe$_2$Si group through the silylation of aryl chloride with the corresponding disilane **5** (Scheme 1, eq. 2).



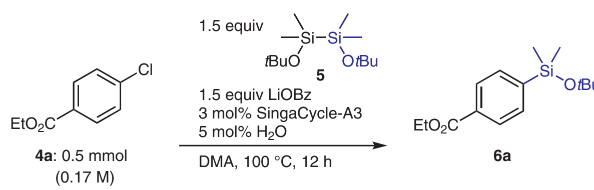
Scheme 1 Catalytic alkoxysilylation of aryl halide with dialkoxydisilane

As a result of our optimization of palladium-catalyzed silylation of ethyl *p*-chlorobenzoate (**4a**) with disilane **5**, we eventually devised the standard conditions for the reaction:

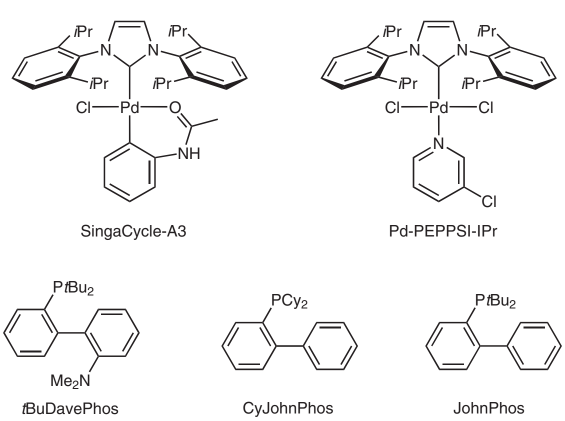
4a (0.17 M), 1.5 equiv disilane **5**, 3 mol% SingaCycle-A3[8], 1.5 equiv LiOBz , 5 mol% H_2O, DMA, 100 °C, 12 h.[9] Table 1 shows results associated with differences based on the deviations listed. Under the standard conditions, arylsilane **6a** was obtained in 75% NMR yield (75% isolated yield) along with the formation of the corresponding homocoupling product, diethyl 1,1′-biphenyl-4,4′-dicarboxylate, in 4% yield. Pd-PEPPSI-IPr[10] was also applicable albeit with a slower reaction rate (entry 2). When the ligand was changed to *t*Bu-DavePhos or CyJohnPhos, the reaction became even more sluggish (entries 3, 4). With JohnPhos that gave a good result in Denmark's report,[5d] a low conversion was observed (entry 5).

The amount of the base heavily affected the reaction outcome. With 0.1 equiv of LiOBz, the minimum necessary amount for activating SingaCycle-A3, only a 13% yield of the product was obtained (Table 1, entry 6). This is in contrast with our previous report on the base-free silylation of aryl chloride with silylsilatrane,[7m] in which we proposed the reaction proceeds through the four-membered transition

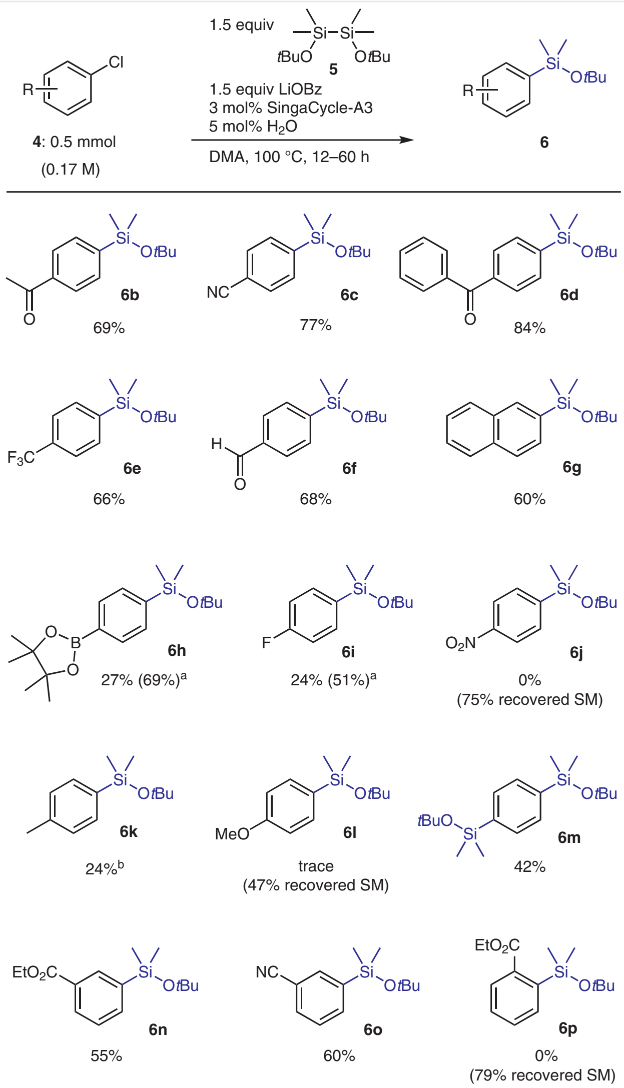
Table 1 Optimization of Silylation Conditions



Entry	Deviations from the standard conditions	Yield (%)[a]		
		4a	**6a**	Biaryl
1	none	0	75 (75[b])	4
2	Pd-PEPPSI-IPr instead of SingaCycle-A3	7	65	2
3	3.0 mol% *t*BuDavePhos, 1.5 mol% $Pd_2(dba)_3$ instead of SingaCycle-A3	20	48	3
4	3.0 mol% CyJohnPhos, 1.5 mol% $Pd_2(dba)_3$ instead of SingaCycle-A3	12	49	6
5	3.0 mol% JohnPhos, 1.5 mol% $Pd_2(dba)_3$ instead of SingaCycle-A3	57	17	<1
6	0.1 equiv instead of 1.5 equiv LiOBz	59	13	0
7	Et_3N instead of LiOBz	84	3	0
8	LiOAc instead of LiOBz	12	55	1
9	LiOPiv instead of LiOBz	5	53	1
10	Li_2CO_3 instead of LiOBz	68	12	0
11	NaOBz instead of LiOBz	0	54	11
12	KOBz instead of LiOBz	0	31	43
13	NMP instead of DMA	0	71	<1
14	DMF instead of DMA	29	50	3
15	1,4-dioxane instead of DMA	90	0	0

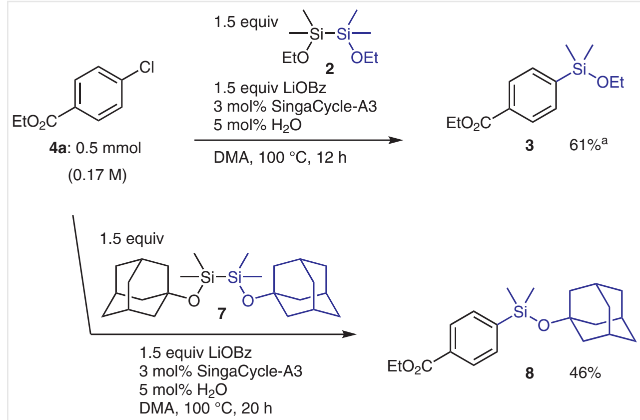


[a] Determined by [1]H NMR analysis using 1,3,5-trimethoxybenzene or mesitylene as an internal standard.
[b] Isolated yield.



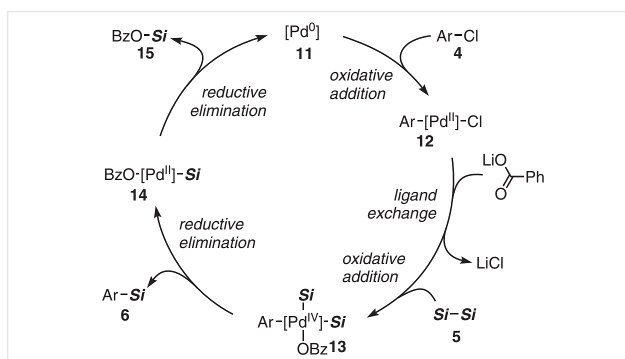
Scheme 2 Scope of reaction with respect to aryl chloride. *Reagents and conditions*: **4** (0.5 mmol, 0.17 M), **5** (1.5 equiv), SingaCycle-A3 (3 mol%), LiOBz (1.5 equiv), H_2O (5 mol%), DMA, 100 °C, 12–60 h. Isolated yields are given. [a] Determined by ^{1}H NMR analysis using 1,3,5-trimethoxybenzene or mesitylene as an internal standard. [b] SingaCycle-A3 (6 mol%).

state. The screening of bases disclosed Et_3N to be ineffective in the current transformation (entry 7). Lithium acetate or pivalate showed a lower efficiency compared to benzoate (entries 8, 9). A much lower yield was observed with lithium carbonate, indicating the importance of carboxylate bases (entry 10). Sodium and potassium benzoates did not give better yields than lithium benzoate (entries 11, 12). Other solvents were also examined. The reaction efficiency is similar in NMP (entry 13), and a slower reaction was observed in DMF (entry 14). The reaction completely stopped in 1,4-dioxane (entry 15). Under strictly dehydrated conditions, the reduced conversion rate was observed to indicate the importance of water for the reproducible results in the current transformation, though the exact reason is unclear. Thus, the conditions in Table 1, entry 1 were confirmed to be optimal.



Scheme 3 Silylation with diethoxy- or diadamantyloxydisilane. [a] Determined by GC analysis.

Scheme 2 shows the substrate scope under the optimized conditions. Silylation products were obtained in good yields when the *para* position was substituted with electron-withdrawing groups such as acetyl (**6b**[11]), cyano (**6c**[12]), benzoyl (**6d**), CF_3 (**6e**), and formyl (**6f**). A naphthyl substituent was also applicable (**6g**). It is intriguing that the Bpin substituent in **6h** survived the reaction conditions although some decomposition, probably at the boron unit, was observed during purification on silica gel. Fluoro-substituted product **6i** was obtained albeit with a loss of the material and was obtained in only a 24% yield. With a nitro group, none of product **6j** was observed while most of the aryl chloride starting material was recovered. With an electron-donating methyl (**6d**) or methoxy (**6h**) substituents, conversion was very sluggish. Product bearing *m*-ethoxycarbonyl group (**6n**) or *m*-cyano group (**6o**) was obtained in moderate yield. The *ortho* substitution seems to be retarding the silylation, and no ethoxycarbonyl product **6p** was observed. Heteroaromatic substrate (2-chloroquinoline) or alkenyl chloride (4-*tert*-butyl-1-chlorocyclohex-1-ene) gave no corresponding silylated product.



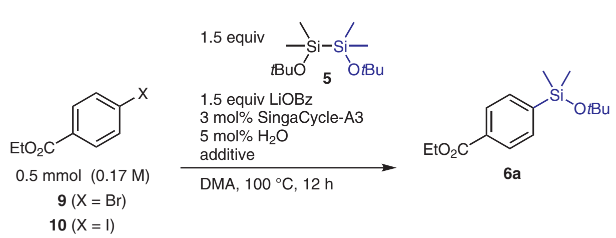
Scheme 4 Proposed reaction mechanism

Other dialkoxydisilanes could also be used for this silylation reaction (Scheme 3). 1,2-Diethoxy-1,1,2,2-tetramethyldisilane (**2**), which was reactive under Denmark's conditions,[5d] reacted similarly under our optimized conditions. However, product **3** was not stable enough for chromatographic purification, and the yield (61%) was determined by gas chromatography. Also, we have synthesized 1,2-bis(adamantan-1-yloxy)-1,1,2,2-tetramethyldisilane(**7**) as a crystalline dialkoxydisilane.[13] Under the standard conditions, **7** could also be applied to the silylation reaction of **4a** to afford **8** in 46% yield.

Bromides and iodides were examined for our silylation reaction (Table 2). Under the standard conditions for aryl chloride, bromide **9** and iodide **10** were converted into the corresponding arylsilane **6a** only in 27% and 3% respective yields (entries 1, 2). In the presence of additional LiCl, yields were slightly improved (27% to 48% for bromide **9** and 3% to 21% for iodide **10**; entries 3 and 4). The reason for the importance of chloride ion is not clear in the current state.

A plausible reaction mechanism for the silylation is shown in Scheme 4. Pd(0) species **11** generated from the precatalyst would be subjected to oxidative addition to yield **12**. Maji reported a mechanistic investigation by DFT calculations for his palladium-catalyzed C–H silylation with hexamethyldisilane, in which the chloride substituent on Pd(II) was replaced with a carboxylate to facilitate the activation of the disilane to give a Pd(IV) intermediate.[14] Keeping in mind that carboxylate bases were indispensable for the current silylation, the reaction of **12** with disilane **5** would similarly form Pd(IV) carboxylate species **13** and reductive elimination to generate arylsilane **6**.[15] Finally, reductive elimination from **14** would generate silyl carboxylate **15** and Pd(0) species **11** to close the catalytic cycle.

Table 2 Applications to Aryl Bromide and Iodide



Entry	Halide	Additive	Yield (%)[a] 9 or 10	6a	Biaryl
1	**9**	none	46	27	5
2	**10**	none	73	3	4
3	**9**	1.5 equiv LiCl	26	48	2
4	**10**	1.5 equiv LiCl	58	21	1

[a] Determined by ^1H NMR analysis using mesitylene as an internal standard.

In conclusion, conditions for palladium-catalyzed silylation reaction between aryl chlorides and bulky dialkoxydisilanes were developed. These NHC-Pd-catalyzed conditions newly allowed the introduction of bulky *tert*-alkoxysilyl groups to arenes bearing electron-neutral or electron-withdrawing substituents.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690877.

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(9) **Ethyl 4-(*tert*-butoxydimethylsilyl)benzoate (6a) – Typical Procedure**
An oven-dried 30 mL Schlenk tube was charged with LiOBz (96.0 mg, 0.75 mmol), SingaCycle-A3 (10.0 mg, 0.015 mmol), and DMA (1.5 mL) under nitrogen atmosphere. Ethyl 4-chlorobenzoate (**4a**, 92.3 mg, 0.50 mmol), 1,2-di-*tert*-butoxy-1,1,2,2-tetramethydisilane (**5**, 235 μL, 0.75 mmol), and H_2O stock solution (0.17 M in DMA, 0.15 mL, 25 μmol) were sequentially added to the mixture. DMA (1.35 mL) was added to wash the inner side of the tube. The reaction mixture was stirred at 100 °C for 12 h and quenched with sat. aq $NaHCO_3$ (10 mL). The mixture was poured into a separatory funnel with EtOAc (20 mL) and partitioned. The organic phase was collected and washed with sat. aq $NaHCO_3$ (10 mL), sat. aq NH_4Cl (10 mL), brine (10 mL), dried over anhydrous Na_2SO_4 (ca. 5 g), filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel with an eluent (hexane and hexane/EtOAc = 100:1) to afford **6a** (105.6 mg, 0.38 mmol, 75%) as colorless oil. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 8.01 (d, *J* = 8.2 Hz, 2 H), 7.67 (d, *J* = 8.2 Hz, 2 H), 4.38 (q, *J* = 6.9 Hz, 2 H), 1.39 (t, *J* = 6.9 Hz, 3 H), 1.25 (s, 9 H), 0.39 (s, 6 H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ = 167.0, 146.8, 133.4, 131.0, 128.6, 73.2, 61.0, 32.2, 14.5, 1.5. HRMS: *m/z* calcd for $C_{15}H_{25}O_3Si$ [M + H]$^+$: 281.1567; found: 281.1569.

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(11) **1-[4-(*tert*-Butoxydimethylsilyl)phenyl]ethan-1-one (6b)**
Reaction time was 12 h. Column chromatography with an eluent (hexane to hexane/EtOAc = 30:1) afforded **6b** as colorless oil (85.9 mg, 0.34 mmol, 69%) from **4b** (77.3 mg, 0.50 mmol). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.92 (d, *J* = 8.2 Hz, 2 H), 7.70 (d, *J* = 8.2 Hz, 2 H), 2.61 (s, 3 H), 1.26 (s, 9 H), 0.39 (s, 6 H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ = 198.6, 147.3, 137.5, 133.7, 127.3, 73.2, 32.2, 26.8, 1.5. HRMS: *m/z* calcd for $C_{14}H_{23}O_2Si$ [M + H]$^+$: 251.1462; found: 251.1461.

(12) **4-(*tert*-Butoxydimethylsilyl)benzonitrile (6c)**
Reaction time was 12 h. Column chromatography with an eluent (hexane to hexane/EtOAc = 100:1) afforded **6c** as colorless oil (89.6 mg, 0.38 mmol, 77%) from **4c** (68.8 mg, 0.50 mmol). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.68 (d, *J* = 8.2 Hz, 2 H), 7.62 (d, *J* = 8.2 Hz, 2 H), 1.26 (s, 9 H), 0.39 (s, 6 H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ = 147.4, 133.9, 131.1, 119.3, 112.7, 73.4, 32.2, 1.5. HRMS: *m/z* calcd for $C_{13}H_{20}NOSi$ [M + H]$^+$: 234.1309; found: 134.1304.

(13) X-ray crystallographic analysis revealed the bulky adamantyloxy groups are antiperiplanar across the Si–Si bond. See the Supporting Information for details.

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(15) We could not deny the possibility that disilane **5** reacts with Pd(II) benzoate through a concerted six-membered transition state to give silyl benzoate **15** and an Ar–Pd(II)–$SiMe_2$(O*t*Bu) species, which would then generate arylsilane **6** via reductive elimination.