

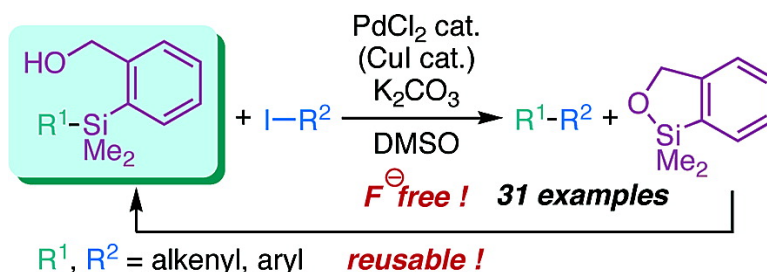
Communication

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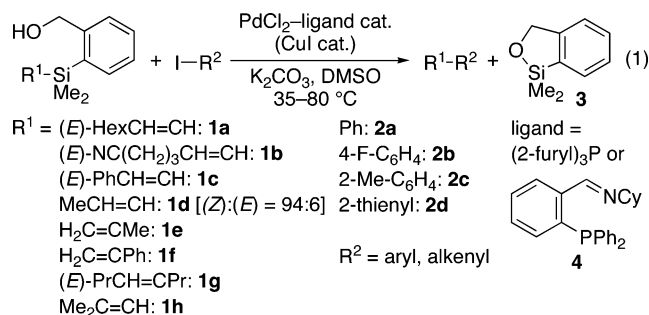
Alkenyl- and Aryl[2-(hydroxymethyl)phenyl]dimethylsilanes: An Entry to Tetraorganosilicon Reagents for the Silicon-Based Cross-Coupling Reaction

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In the past decade, the silicon-based cross-coupling reaction has gained increasing interest among metal-catalyzed cross-coupling reactions due to the ease of preparation and handling, stability, chemoselectivity, and nontoxicity associated with organosilicon compounds.¹ Nevertheless, the use of expensive fluoride activators, which are incompatible with several functional groups, including common silyl protectors, as well as that of relatively labile silicon reagents having oxygen or halogen atoms on silicon, has limited the widespread application of this protocol. Successful fluoride-free processes have been suggested using chlorosilanes and alkoxy-silanes, which are sensitive to heat, moisture, base, and/or acid.² Alternatively, silanols also undergo the cross-coupling reaction without fluoride activators.³ Although tetraorganosilicon reagents are desirable in view of their stability and easy handling,⁴ reported examples of their fluoride-free process show that they require a stoichiometric amount of transition-metal promoters⁵ or strong bases.^{4f} On the other hand, intramolecular activation has been reported to promote the coupling reaction under very mild conditions even with alkenyl(trimethyl)silanes, though a carboxyl group *cis* to the silyl group is required for successful coupling.⁶ Herein, we report that readily accessible and highly stable alkenyl- and aryl[2-(hydroxymethyl)phenyl]dimethylsilanes cross-couple with various aryl and alkenyl iodides under mild conditions with a general scope of substrates (eq 1).⁷ The reaction tolerates a gram-scale synthesis, and the silicon residue, cyclic silyl ether **3**, is readily recovered and reused.



We first examined the reaction of (*E*)-1-octenylsilane **1a** (1.1 mmol)⁸ with 4-iodobenzonitrile (1.0 mmol) in the presence of PdCl₂ (1.0 mol %), tri-2-furylphosphine (2.0 mol %), and K₂CO₃ (2.2 mmol) in DMSO at 35 °C for 20 h and obtained the corresponding coupling product in 93% yield (entry 1 of Table 1). Aryl iodides having such functional groups as ester, keto, formyl, nitro, chloro, and methoxy also underwent the reaction in good yields (entries 2–7). It is worth noting that both silyl-protected and unprotected hydroxyl groups tolerated the present protocol (entries 8 and 9). Ortho-substituents did not affect the reaction (entries 10 and 11). Such heteroaryl iodides as 3-iodopyridine and 2-iodothiophene reacted in good yields (entries 12 and 13). Other mono- and disubstituted alkenylsilanes **1b**–**1h** also reacted with ethyl 4-iodo-

Table 1. Cross-Coupling of **1** with Aryl and Alkenyl Iodides^a

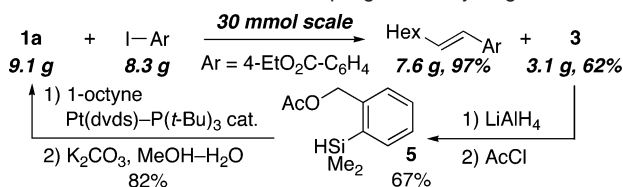
entry	alkenylsilane	R ²	time (h)	yield (%) ^b
1	1a	4-NC-C ₆ H ₄	20	93
2	1a	4-EtO ₂ C-C ₆ H ₄	18	96
3	1a	4-Me(O)C-C ₆ H ₄	17	94
4	1a	4-H(O)C-C ₆ H ₄	20	94
5	1a	4-O ₂ N-C ₆ H ₄	26	99
6	1a	4-Cl-C ₆ H ₄	19	93
7	1a	4-MeO-C ₆ H ₄	40	89
8	1a	3- <i>t</i> -BuMe ₂ SiOCH ₂ -C ₆ H ₄	23	98
9	1a	3-HOCH ₂ -C ₆ H ₄	47	88
10	1a	2-Me-C ₆ H ₄	47	94
11	1a	1-naphthyl	23	91
12	1a	3-pyridyl	23	80
13	1a	2-thienyl	23	99
14	1b	4-EtO ₂ C-C ₆ H ₄	19	95
15	1c	4-EtO ₂ C-C ₆ H ₄	19	88
16	1d	4-EtO ₂ C-C ₆ H ₄	19	91 ^c
17	1e	4-EtO ₂ C-C ₆ H ₄	24	96
18	1f	4-EtO ₂ C-C ₆ H ₄	25	95
19 ^{d,e}	1f	4-MeO-C ₆ H ₄	12	80 ^f
20 ^d	1g	4-EtO ₂ C-C ₆ H ₄	29	92
21	1h	4-EtO ₂ C-C ₆ H ₄	25	96
22 ^g	1b	(<i>E</i>)-HexCH=CH	3	73
23 ^g	1b	(<i>Z</i>)-HexCH=CH	2	78

^a The reaction was carried out using **1** (1.1 mmol), an aryl iodide (1.0 mmol), K₂CO₃ (2.2 mmol), PdCl₂ (10 μmol), and (2-furyl)₃P (20 μmol) in DMSO (2.5 mL) at 35 °C. ^b Isolated yields based on the aryl iodide. ^c *Z*:*E* = 94:6 by GC. ^d The reaction was carried out at 50 °C. ^e **1f** (1.3 mmol) was used. ^f *Cine*-product was obtained in ~4% yield. ^g **4** (10 μmol) was used as a ligand.

benzoate in stereo- and regiospecific manners, giving the desired products in good yields (entries 14–21). Especially, regiospecific reaction of **1f** with both activated and unactivated aryl iodides is remarkable in view that the corresponding coupling of fluorosilanes results in *cine*-substitution to some extent (entries 18 and 19).⁹ The reactions of **1b** with (*E*)- and (*Z*)-octenyl iodides proceeded stereospecifically in acceptable yields in the presence of *N*-(2-diphenylphosphinobenzylidene)cyclohexylamine (**4**) as a ligand (entries 22 and 23).¹⁰

A gram-scale synthesis was examined using 9.1 g (33 mmol) of **1a** and 8.3 g (30 mmol) of ethyl 4-iodobenzoate under identical conditions. Cyclic silyl ether **3** was recovered by distillation in 62% yield based on the aryl iodide; the residue was chromatographed to give the desired coupling product in 97% yield. Reduction of silicon residue **3** thus obtained with LiAlH₄ followed by acetylation in situ afforded **5**, which underwent the hydrosilylation of 1-octyne¹¹ to give **1a** in 82% yield after deacetylation (Scheme 1). Thus, the silyl residue of this protocol is successfully recovered and reused. Namely, *the metal residue of the cross-coupling is demonstrated for the first time to be reused for the next coupling.*

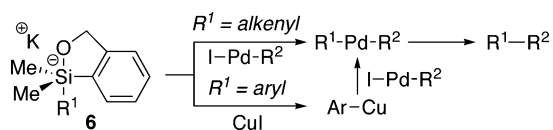
We further examined the cross-coupling of arylsilanes **2** (Table 2). After several modifications of the reaction conditions, we found that the reaction of phenylsilane **2a** with 4-iodobenzonitrile in the presence of PdCl₂ (3.0 mol %), iminophosphine ligand **4** (4.0 mol %), CuI (10 mol %), H₂O, and K₂CO₃ in DMSO at 50 °C for 7 h

Scheme 1. Gram-Scale Cross-Coupling and Recycling of **3**Table 2. Cross-Coupling of **2** with Aryl Iodides^a

entry	arylsilane	R ²	time (h)	yield (%) ^b
1	2a	4-NC-C ₆ H ₄	7	97
2	2a	4-MeO-C ₆ H ₄	16	99
3	2a	2,6-Me ₂ -C ₆ H ₃	13	94
4	2a	2-pyridyl	13	96
5	2a	2-thienyl	13	93
6	2b	4-EtO ₂ C-C ₆ H ₄	3	91
7 ^c	2c	4-EtO ₂ C-C ₆ H ₄	5	81
8	2d	4-EtO ₂ C-C ₆ H ₄	10	93

^a The reaction was carried out using **2** (0.81 mmol), an aryl iodide (0.70 mmol), K₂CO₃ (1.4 mmol), H₂O (1.4 mmol), CuI (70 μmol), PdCl₂ (21 μmol), and **4** (28 μmol) in DMSO (4 mL) at 50 °C. ^b Isolated yields based on the aryl iodide. ^c The reaction was carried out at 80 °C.

Scheme 2. Plausible Reaction Pathway



gave the desired biaryl in 97% yield (entry 1).^{12,13} It is highly intriguing that the phenyl group was transferred exclusively among two different aromatic groups on silicon; no trace of the coupling product derived from the 2-hydroxymethylphenyl group was detected. The reactions of **2a** with other aryl iodides proceeded in excellent yields irrespective of the electronically and sterically unactivated nature of substrates (entries 2 and 3). Heteroaryl iodides also coupled with **2a** in excellent yields (entries 4 and 5). Less nucleophilic 4-fluorophenyl, sterically hindered 2-methylphenyl, and labile 2-thienyl^{14c} groups coupled with ethyl 4-iodobenzoate successfully using the corresponding arylsilanes **2b–2d** (entries 6–8).

Although details remain yet to be clarified, we propose that pentacoordinated silicate intermediates, such as **6**, having a rather electron-withdrawing alkenyl or phenyl group at an axial position might be responsible for the selective aryl transfer (Scheme 2).¹⁴ In the case of arylsilanes, transmetalation from silicon to copper appears likely rather than direct transmetalation from silicon to palladium.¹⁵

In summary, we have introduced alkenyl- and aryl[2-(hydroxymethyl)phenyl]dimethylsilanes as a novel type of silicon cross-coupling reagents, which successfully react with a broad range of aryl and alkenyl iodides without any fluoride activators. Mild reaction conditions employing inexpensive and readily available base and catalyst and the reusable silicon residue would make the present protocol highly attractive from a viewpoint of practical synthesis. Further efforts to expand the scope¹⁶ as well as mechanistic studies are current issues in our laboratory.

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Supporting Information Available: Detailed experimental procedures including spectroscopic and analytical data (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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