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## (Citation)

Reactive and Functional Polymers, 67(11):1264-1276

## (Issue Date)

2007-11

## (Resource Type)

journal article

## (Version)

Accepted Manuscript

## (URL)

<https://hdl.handle.net/20.500.14094/90000841>



*A paper manuscript for Reactive and Functional Polymers*

## **Silicone as an Organosilicon Reagent for the Palladium-Catalyzed Cross-Coupling Reaction**

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This paper is dedicated to Professor Teiji Tsuruta on the occasion of his 88th birthday.

**Keywords:** Silicone · Cross-Coupling · Silver oxide · tetrabutylammonium fluoride ·  
Potassium Carbonate

**Abstract:** Silicone, poly(diorganosiloxane), serves as an organosilicon reagent for palladium-catalyzed cross-coupling reactions. Treatment of poly[(aryl)methylsiloxane], poly[(alkenyl)methylsiloxane], or cyclic oligosiloxanes with various aryl iodides in the presence of silver(I) oxide ( $\text{Ag}_2\text{O}$ ) or tetrabutylammonium fluoride (TBAF) and a catalytic amount of palladium affords the corresponding cross-coupling product in a good to excellent yield. The reaction of silicone with aryl chlorides in the presence of  $\text{K}_2\text{CO}_3/\text{H}_2\text{O}$  as an activator proceeded to afford biaryl derivatives in moderate to excellent yields. A wide range of aryl chlorides bearing an electron-donating or electron-withdrawing substituent on the aromatic ring are tolerated.

## 1. Introduction

Silicone has been widely utilized as materials with unique characteristics caused by the strength and flexibility of the Si-O bond. The thermal and chemical stability of the siloxane bond has led to the wide applicability as silicone rubber, grease, and oil. Silicone and its copolymer bearing a functional group on the organic substituent of the silicon atom also serve as various specialty polymers [1-2]. A number of silicone compounds with various organic substituents are now readily available in silicone industry.

On the other hand, organosilicon compounds have been demonstrated to be valuable carbon-carbon bond forming reagents in organic synthesis [3-5]. Several types of organosilanes such as fluoro, chloro, alkoxy, hydroxy, and alkylsilanes react as an organometallic reagent with organic electrophiles in palladium-catalyzed cross-coupling reactions [6-27]. Nevertheless, polysiloxanes (silicone) have not been recognized as a organosilicon reagent for such transition metal-catalyzed coupling reactions so far. Accordingly, the use of poly(organosiloxane) as a source of the pseudo organometallic reagent in carbon-carbon bond-forming reaction can be a novel application of silicone materials in organic synthesis.

In our preliminary communications, we have demonstrated that poly(methylphenylsiloxane), which is a commercially available silicone oil with a high thermal stability, is available as an organosilicon reagent for the palladium-catalyzed cross-coupling reaction with organic electrophiles [28-29]. Herein, we describe scope and limitation of the coupling reaction of silicone using a variety of poly(organosiloxane)s and cyclic

siloxanes bearing aryl and alkenyl groups in an organic moiety of the silicon substituent.

## 2. Experimental

### 2.1. Materials and instruments

All reactions were carried out under an argon atmosphere. Cross-coupling reactions were carried out with standard Schlenk technique. Tetrahydrofuran (THF), 1,4-dioxane, *N*-methyl-2-pyrrolidone (NMP), and toluene were distilled from sodium/benzophenone. 2,4,6-Trimethyl-2,4,6-triphenylcyclotrisiloxane ( $D_3^{\text{Ph}}$ ), and 2,4,6,8-tetramethyl-2,4,6,8-tetraphenylcyclotetrasiloxane ( $D_4^{\text{Ph}}$ ) were kindly donated by Shin-Etho Chemical Co. Ltd. Poly(methylphenylsiloxane) was donated by Chisso Chemicals Co. Ltd ( $M_w = 2500\text{-}2700$ ). Poly(methylhydrosiloxane) (PMHS) was purchased from Aldrich Chemicals Co. Ltd. The average degree of polymerization of PMHS was estimated to be ca. 45-50 by  $^1\text{H}$  NMR analysis. Silver(I) oxide ( $\text{Ag}_2\text{O}$ ) was purchased from Wako Pure Chemical Inc. and used without further purification. Tetrabutylammonium fluoride (TBAF) (1 M THF solution) was purchased from Aldrich Chemicals Co. Ltd. NMR spectra were measured on a Varian Mercury 300 spectrometer with  $\text{CDCl}_3$  as a solvent at ambient temperature. The chemical shifts were recorded in parts per million downfield from tetramethylsilane ( $\delta = 0$  ppm) or based on residual  $\text{CHCl}_3$  ( $\delta = 7.26$  ppm) as an internal standard.  $^{13}\text{C}$  NMR spectra were recorded at 75.5 MHz with  $\text{CDCl}_3$  as a solvent with the central line of the solvent ( $\delta = 77.0$  ppm) as a reference and the coupling constant

(*J*) in herz. Infrared spectra were recorded on a Shimadzu FTIR-8000A spectrometer and are presented in  $\text{cm}^{-1}$ .

Size exclusion chromatography (SEC) was carried out with JASCO 800 HPLC system equipped with UV detector using THF as an eluent: flow rate,  $1.0 \text{ mL} \cdot \text{min}^{-1}$  with a Shodex column. Molecular weights and molecular weight distributions were estimated on the basis of the calibration curve obtained by standard polystyrene. X-ray diffraction (XRD) patterns were measured with Rigaku X-RAY DIFFRACTIOMETER RINT Ultima+/PC.

*2.2.1. General Procedure for the cross-coupling reaction of siloxane with an aryl iodide in the presence of silver(I) oxide (Conditions A)*

To a mixture of  $[\text{Ph}(\text{Me})\text{SiO}]_n$  **1** (1.36 g, 10.0 mmol),  $\text{Ag}_2\text{O}$  (0.46 g, 2.0 mmol) and  $\text{Pd}(\text{PPh}_3)_4$  (116 mg, 5 mol%) in 3 mL of THF was added aryl iodide (2.0 mmol). After the mixture was stirred at  $60^\circ\text{C}$  for 24 h, 20 mL of diethyl ether was added to the resulting mixture and stirring was continued for 10 min. The mixture was passed through a Celite pad to remove the silver residue. The pad was washed with 20 mL of diethyl ether. Concentration of the combined filtrate left a crude oil, which was chromatographed on silica gel (hexane:toluene = 10:1) to afford the corresponding coupling product.

*2.2.2. General Procedure for the cross-coupling reaction of a siloxane with an aryl iodide in the presence of TBAF (Conditions B)*

To a solution of **1** (0.97 g, 6.0 mmol) in 20 mL of THF was added TBAF (6 mL of 1 M THF solution, 6.0

mmol) at room temperature under an argon. To the mixture were successively added aryl iodide (5.0 mmol) and  $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$  (125 mg, 2 mol%). The solution was heated at 60 °C and the reaction was continued for 3 h. After being cooled to an ambient temperature, the resulting mixture was passed through a Celite pad. The filtrate was concentrated *in vacuo* to leave a dark brown liquid, which was purified by chromatography on silica gel to afford the corresponding coupling product.

*2.2.3. General procedure for the cross-coupling reaction of a siloxane with an aryl iodide in the presence of silver(I) oxide in 1,4-dioxane (Conditions C)*

To a solution of **1** (49 mg, 0.36 mmol; per unit) in 1,4-dioxane (2 mL) were added aryl iodide (0.3 mmol),  $\text{Ag}_2\text{O}$  (70 mg, 0.3 mmol) and  $\text{Pd}(\text{PPh}_3)_4$  (17 mg, 5 mol%) under an argon atmosphere. The resulting solution was degassed via three freeze-pump-thaw cycles and heated in an oil bath at 100 °C. After the mixture was stirred for 1 h, the reaction mixture was diluted with diethyl ether and passed through a Celite pad. The plug was washed with diethyl ether and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography on silica gel to afford the corresponding coupling product.

*2.2.4. Poly[4-methoxyphenyl(methyl)siloxane] (3)*

To a solution of  $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$  (93 mg, 1.5 mol%) and  $\text{P}(o\text{-tol})_3$  (110 mg, 6 mol%) in dry NMP (12 mL) was added 4-iodoanisole **2b** (1.4 g, 6 mmol), diisopropylentylamine (3.06 mL, 18 mmol) and PMHS (361 mg, 6 mmol; per unit). After the mixture was stirred for 16 h at 100 °C, the resulting solution was filtered off. The

filtrate was concentrated under reduced pressure to leave a crude oil, which was further treated at 170 °C/0.6 mmHg to afford **3** (760 mg) as a brown oil.

SEC analysis showed  $M_n$  of 8800 ( $M_w/M_n = 2.92$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.064\text{--}0.23$  (br, 3 H), 3.75 (br, 2.58 H), 6.71 (br, 1.97 H), 7.37 (br, 2.18 H). IR (neat):  $\nu = 2961.1, 1597.3, 1504.7, 1280.9, 1250.0, 1124.6, 1034.0\text{ cm}^{-1}$ .

#### 2.2.5. Poly[methyl(4-methylphenyl)siloxane] (**4**)

Synthesis of **4** was carried out in a similar manner to that of **3**: SEC analysis showed  $M_n$  of 9600 ( $M_w/M_n = 2.88$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 0.045\text{--}0.20$  (br, 3 H), 2.31 (br, 2.28 H), 6.97 (br, 1.92 H), 7.35 (br, 1.99 H). IR (neat):  $\nu = 2964.9, 1605.0, 1261.6, 1120.8, 1022.4\text{ cm}^{-1}$ .

#### 2.2.6. Poly[methyl(2-phenylethenyl)siloxane] (**5**)

To a screw-capped tube equipped with a magnetic stirring bar were added  $(\text{Bu}_4\text{N})_2\text{PtCl}_6$  (9 mg, 0.01 mmol), phenylacetylene (2.0 g, 20 mmol), and PMHS (1.2 g; 20 mmol per unit). The resulting mixture was heated at 60 °C for 24 h to form crude **5**, which was confirmed by  $^1\text{H}$  NMR. SEC analysis showed  $M_n$  of 8500 ( $M_w/M_n = 3.22$ ).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = -0.2\text{--}0.4$  (br, 3 H), 5.7 (br, 2 H), 5.47 (br d,  $J = 20\text{ Hz}$ , 1 H), 6.1 (br, 1 H).

#### 2.2.7. Poly[methyl(1-octen-1-yl)siloxane] (**6**)

Synthesis of **6** was carried out in a manner to that of **5**. SEC analysis showed  $M_n$  of 3100 ( $M_w/M_n = 1.54$ ).  $^1\text{H}$



NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0-0.3 (br s, 3 H), 0.88 (br s, 3 H), 1.3 (br, 8 H), 2.05 (br, 2 H), 5.47 (br d,  $J$  = 20 Hz, 1 H), 6.1 (br, 1 H).

#### 2.2.8. 2,4,6,8-tetramethyl-2,4,6,8-tetra(2-phenylethenyl)cyclotetrasiloxane (**9**)

To a screw-capped tube equipped with a magnetic stirring bar were added (Bu<sub>4</sub>N)<sub>2</sub>PtCl<sub>6</sub> (9 mg, 0.01 mmol), phenylacetylene (2.0 g, 20 mmol), and D<sub>4</sub><sup>H</sup> (1.2 g; 20 mmol per unit). The resulting mixture was heated at 60 °C for 24 h to form crude **9**, which was confirmed by <sup>1</sup>H NMR and directly used for further reactions without purification. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.1-0.5 (br, 12 H), 5.7-6.0 (br, 4H), 6.2-6.4 (br, 4 H), 6.8-7.6 (br, 20 H).

#### 2.2.9. 2,4,6,8-tetramethyl-2,4,6,8-tetra(1-octen-1-yl)cyclotetrasiloxane (**10**)

Synthesis of **10** was carried out in a similar manner to that of **9**. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0-0.3 (m, 12 H), 0.89 (br, 12 H), 1.2-1.5 (br, 32 H), 2.0-2.2 (br, 8 H), 5.5 (br,  $J$  = 20 Hz, 4 H), 6.1-6.3 (br, 4 H).

These compounds were used for the cross-coupling reactions without further purification.

#### 2.2.10. 1,1,1,3,5,5,5-Heptamethyl-3-phenyltrisiloxane (**11**)

To a solution of hexamethylcyclotrisiloxane (D<sub>3</sub>) (445 mg, 2.0 mmol) in Et<sub>2</sub>O (18 mL) was slowly added MeLi (5.77 mL, 6.0 mmol, 1.04 M in diethyl ether) at 0 °C. After the mixture was stirred at rt for 12 h, PhMeSiCl<sub>2</sub> (0.48 mL, 3.0 mmol) was added slowly at 0 °C. The mixture was allowed to warm to room temperature, and stirring was continued for an additional 7 h. After the organic phase was separated, the

aqueous phase was extracted with diethyl ether (30 mL x 2). The combined extracts were washed with brine (30 mL), dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane:ethyl acetate = 50:1) and bulb-to-bulb distillation under reduced pressure to afford **11** (116 mg, 0.39 mmol, 13% yield). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.103 (s, 18 H), 0.27 (s, 3H), 7.24-7.38 (m, 3 H), 7.53-7.57 (m, 2 H).

#### 2.2.11. Measurement of the molecular weight after treatment of **5**

To a solution of **5** (39 mg; 0.24 mmol per unit) in 3 mL of THF was added TBAF (0.24 mL, 0.24 mmol as 1 M THF solution) at room temperature. The resulting mixture was stirred at room temperature for 1 h and poured into a mixture of 20 mL of diethyl ether. Two phases were separated and the aqueous layer was extracted twice with 10 mL of dichloromethane. The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure to leave a crude oil. SEC analysis showed  $M_n$  of 2300 ( $M_w/M_n=1.25$ ).

#### 2.3.1. General Procedure for the cross-coupling reaction of a siloxane with an aryl chloride in the presence of $K_2CO_3$

To a toluene (3 mL) solution of **1** (204 mg, 1.5 mmol) was added  $K_2CO_3$  (414 mg, 3.0 mmol) in water (0.5 mL). After stirring at rt for 1 h, 1-chloro-4-methoxybenzene **12a** (43 mg, 0.3 mmol) and  $PdCl_2(PCy_3)_2$  (11 mg, 0.015 mmol) were added and then the resulting yellow mixture was stirred at 120 °C for 39 h. After cooling

the mixture to rt, the organic layer was separated and aqueous layer was extracted with Et<sub>2</sub>O (2 x 10 mL). The combined organic layer was washed with 1 M HCl (10 mL), sat. aq NaHCO<sub>3</sub> (10 mL), and brine (10 mL), and then dried over anhydrous MgSO<sub>4</sub>. Removal of the solvent left a crude oil, which was purified by chromatography on silica gel (reverse phase, MeOH:H<sub>2</sub>O = 3:1) to yield 52.5 mg of 4-methoxy-biphenyl (95%).

#### *2.4.1. Preparation of a sample for XRD analysis*

The procedure described for the cross-coupling reaction was followed using **1** (49 mg, 0.36 mmol; per unit), 4-iodoanisole **2b** (70 mg, 0.3 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (17 mg, 5 mol%), and Ag<sub>2</sub>O (70 mg, 0.3 mmol). The mixture involving a black precipitate was filtered off and washed with ethanol and then diethyl ether. The resulting solid was dried under reduced pressure to give a black powder, which was subjected to a glass plate for the XRD analysis and set in the diffractometer. The results were shown below.

#### *2.4.2. Residue with the cross-coupling reaction of a polysiloxane **1** with a **2b***

2θ (rel intensity): 22.393, 23.729, 25.364, 32.846, 39.250, 42.692, 45.648, 46.364.

#### *2.4.3. Ag<sub>2</sub>O for XRD analysis*

2θ (rel intensity): 7.718 (927), 8.478 (502), 9.640 (221), 12.841 (263), 21.321 (433), 22.360 (757), 23.259 (234), 23.702 (1777), 25.320 (329), 25.905 (136), 28.941 (209), 32.857 (357), 39.200 (1308), 42.640 (284), 46.320 (630).

#### 2.4.4. AgI for XRD analysis

2 $\theta$  (rel intensity): 23.070 (100), 39.133 (60), 46.308 (30), 56.667 (6), 62.258 (8), 71.028 (8), 76.082 (6), 84.285 (4), 89.100 (4), 97.186 (4), 125.101 (4).

### 3. Results and Discussion

We first examined the reaction of a polysiloxane bearing a phenyl group, which was commercially available as a highly thermo-resistant silicone oil (Scheme 1). The results are summarized in Table 1. The reaction with an aryl iodide was examined using silver(I) oxide (Ag<sub>2</sub>O) or tetrabutylammonium fluoride (TBAF). We have previously shown that Ag<sub>2</sub>O is an effective activator for the cross-coupling reaction of silanols and silanediols [13-14]. TBAF has also been employed frequently for the cross-coupling reaction of organofluorosilanes di- or trifluorosilanes and silanols [15-27]. The reaction of poly(methylphenylsiloxane) **1** with 4-iodoacetophenone **2a** in the presence of 5 mol% of Pd(PPh<sub>3</sub>)<sub>4</sub> and Ag<sub>2</sub>O at 60 °C in THF for 20 h afforded the corresponding coupling product in 67% yield (Conditions A). TBAF was also found to be an efficient activator for the coupling reaction, which proceeded with 2.5 mol% of Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (Conditions B). Under these conditions, aryl iodides bearing an electron-donating or -withdrawing substrate on the aromatic ring underwent the coupling reaction in good yields [28].

Scheme 1

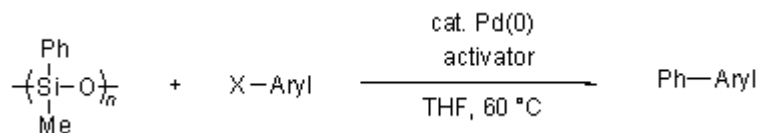
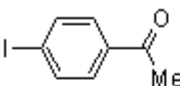
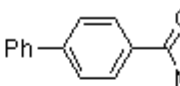
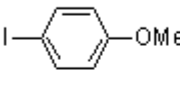
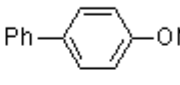
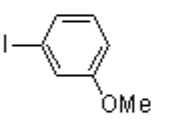
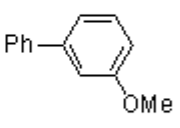
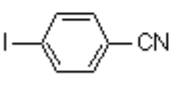
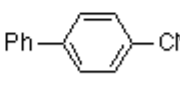
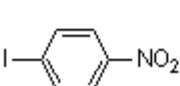
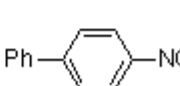


Table 1 Cross-coupling of a polysiloxane **1** with iodides in THF<sup>a</sup>

entry	I-Aryl	activator <sup>b</sup>	time/h	product	%yield <sup>c</sup>
1		Ag <sub>2</sub> O	20		67
2		TBAF	20		53
3		Ag <sub>2</sub> O	20		52
4		TBAF	20		79
5	 (2c)	Ag <sub>2</sub> O	24		96
6	 (2d)	Ag <sub>2</sub> O	24		59
7	 (2e)	Ag <sub>2</sub> O	24		97

(a) The reaction was carried out at 60 °C in THF (3 mL) using **1** (1.0 mmol; per unit) or **2** (0.2 mmol) and aryl iodide (0.2 mmol).

(b) Conditions A: Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%), Ag<sub>2</sub>O (0.2 mmol), conditions B: Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (2.5 mmol%), TBAF (0.24 mmol).

(c) Isolated yield based on the aryl iodide.

Although cross-coupling of silicone **1** was found to proceed in THF at 60 °C, the reaction was required to use excess amounts of **1** toward the aryl iodide. However, further optimization of reaction conditions revealed to achieve the reaction with a smaller amount of **1**. The reaction completed within a shorter reaction period when the coupling reaction was carried out at higher temperature with 1,4-dioxane as a solvent. As summarized in Table 2, 1.2 equiv of polysiloxane **1** reacted with various aryl iodides in 1,4-dioxane at 100 °C (Conditions C). The reaction of aryl iodides bearing an electron-donating or electron-withdrawing substituent on the phenyl ring afforded the corresponding coupling products in good yields. Aryl iodides bearing a substituent at the 2- or 3-position were also found to tolerate to give the coupling product in good yields (entries 5 and 6).

Table 2 Cross-coupling reaction of polysiloxane **1** with aryl halides in 1,4-dioxane <sup>a</sup>

entry	X-Aryl		time/h	product	%yield
1		X = I	1		71
2			1		64 <sup>b</sup>
3		Br	44		<2
4		Cl	72		0
5			1		64
6			1		65
7			1.5		73
8			1.5		74
9			1.5		57
10			24		96 <sup>c</sup>

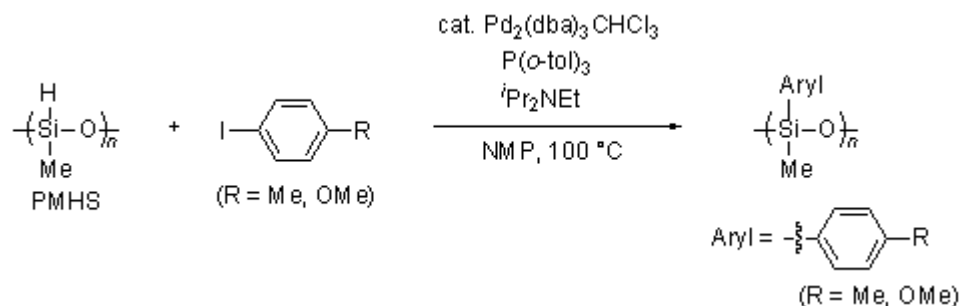
(a) The reaction was carried out at 100 °C using **1** (0.36 mmol; per unit), aryl iodide (0.3 mmol), Ag<sub>2</sub>O (0.3 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 2 mL of 1,4-dioxane (Conditions C).

(b) The reaction was carried out at 100 °C using **1** (2.4 mmol; per unit), aryl iodide (2.0 mmol), Ag<sub>2</sub>O (2.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%).

(c) The reaction was carried out at 60 °C in THF (3 mL) using **1** (1.0 mmol; per unit), aryl iodide (0.2 mmol), Ag<sub>2</sub>O (0.2 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%).

In addition to the polysiloxane **1**, which was a readily available reagent, our concern was then turned to the reaction of silicone reagents of several other aryl groups. Although polysiloxanes bearing a substituted aryl group are not available commercially, such compounds can be synthesized using a commercially available polysiloxane bearing a silicon-hydrogen bond, PMHS [30-33] by employing the palladium-catalyzed arylation of triethoxysilane with aryl iodides developed by Masuda [34-35]. The method was applied for the arylation of PMHS as a silane species. As shown in Scheme 2, the arylation of PMHS with 4-iodoanisole or 4-iodotoluene using 2.5 mol% of  $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$  as a catalyst proceeded to afford the corresponding coupling product poly[methyl(4-methoxyphenyl)siloxane] **3** or poly[methyl(4-methylphenyl)siloxane] **4** smoothly. Contents of arylation in the crude product were estimated by  $^1\text{H}$  NMR indicating to be 85% and 75%, respectively.

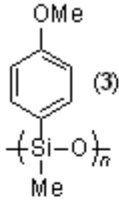

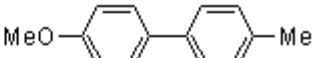
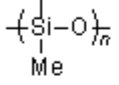
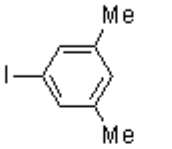
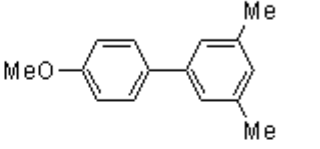
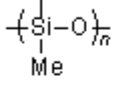
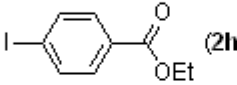
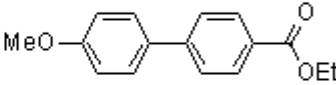
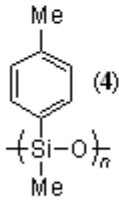
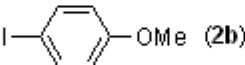
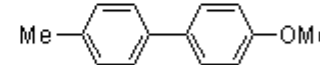
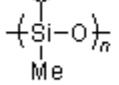
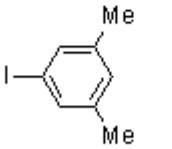
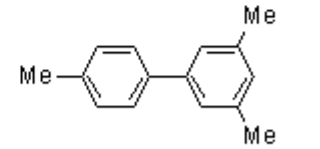
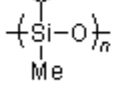
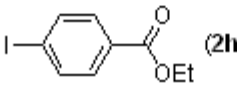
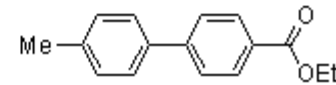
*Scheme 2*





Although the attempted purification of the arylated polysiloxane was unsuccessful, the cross-coupling reaction with the crude polysiloxane was found to produce the corresponding coupling products. In addition, these polysiloxane could be stored under an aerobic condition at room temperature for several months. Indeed, the obtained **3** and **4** were subjected to the palladium-catalyzed cross-coupling reactions with several aryl iodides in the presence of silver(I) oxide to afford the corresponding biaryls in moderate to good yields. These results are summarized in Table 3.

Table 3 Cross-coupling reaction of poly(arylsiloxane)s with aryl iodides <sup>a</sup>

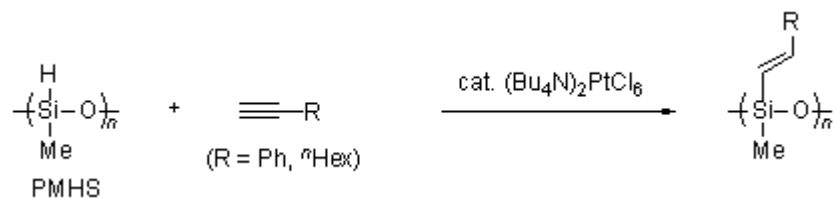
entry	silicone	I-Aryl	time/h	product	%yield
1	 ( <b>3</b> )	 ( <b>2g</b> )	4		67
2	 ( <b>3</b> )	 ( <b>2i</b> )	10		52
3	 ( <b>3</b> )	 ( <b>2h</b> )	1		94
4	 ( <b>4</b> )	 ( <b>2b</b> )	5		41
5	 ( <b>4</b> )	 ( <b>2i</b> )	22		25
6	 ( <b>4</b> )	 ( <b>2h</b> )	24		56

(a) The reaction was carried out using **3** or **4** (0.3 mmol; per unit), aryl iodide (0.3 mmol), Ag<sub>2</sub>O (0.3 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 2 mL of 1,4-dioxane.

Polysiloxanes bearing an alkenyl group were also found to be obtained easily from PMHS. The hydrosilylation of a terminal alkyne with PMHS using a catalytic amount of (Bu<sub>4</sub>N)<sub>2</sub>PtCl<sub>6</sub> [36] proceeded smoothly to afford poly[methyl(2-phenylethenyl)siloxane] **5** or poly[methyl(1-octen-1-yl)siloxane] **6** as

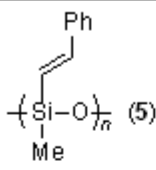
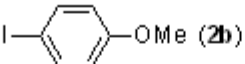
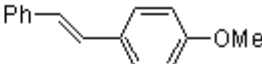
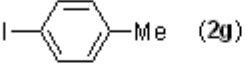
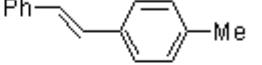
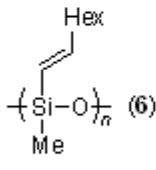

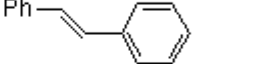
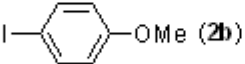
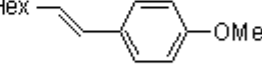
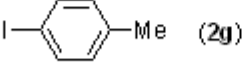
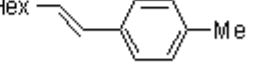
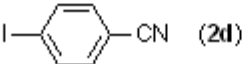
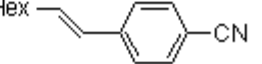
shown in Scheme 3.

Scheme 3



Measurement of  $^1\text{H}$  NMR showed that the alkenyl group was introduced in a quantitative manner although the attempted purification of polysiloxanes **5** and **6**, which were stored at an ambient temperature in air, was not successful. The obtained **5** or **6** were employed for the palladium-catalyzed coupling reactions as shown in Table 4. TBAF was found to be a suitable activator in the coupling of alkenylsiloxanes, which took place faster than that of phenylsiloxanes. Indeed, the reaction of alkenylsiloxane proceeded within 1-2 h to give the desired products in excellent yields. The coupling reaction with use of a slight excess (1.2 equiv) of siloxanes also underwent smoothly.

Table 4 Cross-coupling reaction of poly(alkenylsiloxane)s with aryl iodides <sup>a</sup>

entry	silicone	I-Aryl	time/h	product	%yield
1	 ( <b>5</b> )	 ( <b>2b</b> )	1		80 (>99) <sup>b</sup>
2			1		94 <sup>c</sup>
3		 ( <b>2g</b> )	1		>99
4	 ( <b>6</b> )	 ( <b>2b</b> )	1		97
5			1		90 (>99) <sup>b</sup>
6		 ( <b>2b</b> )	1		98 <sup>c</sup>
7		 ( <b>2g</b> )	1		51 (>99) <sup>b</sup>
8		 ( <b>2d</b> )	2		90

(a) Unless otherwise noted, the reaction was carried out using 1.0 mmol (5 equiv per unit) of **5** or 0.2 mmol of **6**, 0.2 mmol of aryl iodide, 0.24 mmol of TBAF, and 5 mol% of Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> at 60 °C in 3 mL of THF.

(b) Isolated yield by silica gel chromatography. The yield estimated by <sup>1</sup>H NMR is given in parentheses.

(c) The amount of employed polysiloxanes was 0.24 mmol (1.2 equiv per unit).

In addition to the polysiloxanes, a commercially available cyclic siloxane bearing phenyl groups,

2,4,6-trimethyl-2,4,6-triphenylcyclotrioxane;

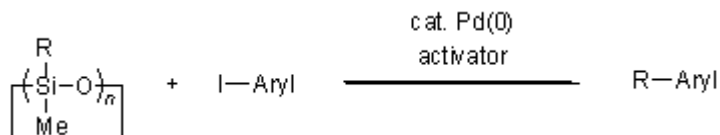
(D<sub>3</sub><sup>Ph</sup>)

**7**

or

2,4,6,8-tetramethyl-2,4,6,8-tetraphenylcyclotetrasiloxane; ( $D_4^{\text{Ph}}$ ) **8**, which had been used as a precursor of silicone polymers by ring opening polymerization [1], was also found to be reactive in the coupling reaction (Scheme 4).

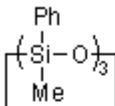
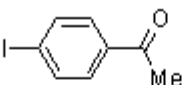
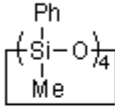
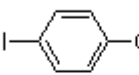
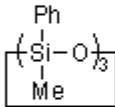
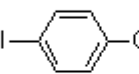
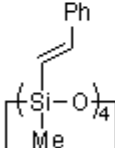

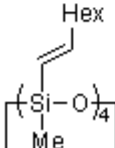
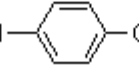
Scheme 4



Denmark reported vinyl-substituted cyclic oligosiloxanes are the effective vinylation reagents of aryl and alkenyl iodides in the presence of TBAF [37-38]. Recently, Fugami also reported cross-coupling reaction of hexaarylcyclotrisiloxane by the addition of aqueous potassium hydroxide in good yield [39]. The high temperature afforded the corresponding coupling product within 1 h (entry 4). This temperature dependence was closely similar to the reactivity of polysiloxane. Furthermore, a cyclic siloxane bearing alkenyl groups, 2,4,6,8-tetramethyl-2,4,6,8-tetra(2-phenylethenyl)cyclotetrasiloxane **9** ( $R=\text{Ph}$ ) and 2,4,6,8-tetramethyl-2,4,6,8-tetra(1-octen-1-yl)cyclotetrasiloxane **10** ( $R=\text{Hex}$ ) were synthesized by the similar hydrosilylation with the corresponding cyclic hydrosiloxane, 2,4,6,8-tetramethylcyclotetrasiloxane ( $D_4^{\text{H}}$ ). The

reaction of cyclic siloxane bearing alkenyl groups at 60 °C proceeded within 1-3 h to afford corresponding coupling product in excellent yield (entries 5-9). Under these conditions, the reactivity of cyclic siloxanes bearing alkenyl groups was much higher than that of phenyl groups. A palladium catalyst with  $\text{Pd}(\text{PPh}_3)_4$  and  $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$  without phosphine ligand was found to be equally effective for the coupling of alkenylsiloxanes (entries 7 and 9). These results are summarized in Table 5.

Table 5 Cross-coupling reaction of cyclic siloxanes with aryl iodides <sup>a</sup>

entry	silicone	I-Aryl	activator	temp/°C	time/h	%yield
1	 (7)	 (2a)	Ag <sub>2</sub> O	60	24	55
2			TBAF	60	40	36
3	 (8)	 (2b)	Ag <sub>2</sub> O	60	120	39
4	 (7)	 (2b)	Ag <sub>2</sub> O	100	1	75 <sup>b</sup>
5	 (9)	 (2b)	TBAF	60	1	99
6			TBAF	60	1	85 <sup>c</sup>
7	 (10)	 (2b)	TBAF	60	1	88
8			TBAF	60	1	79 <sup>c</sup>
9			TBAF	60	3	96 <sup>d</sup>

(a) Unless otherwise noted, the reaction was carried out using 1.0 mmol (5 equiv per unit) of 0.2 mmol of cyclic siloxane of aryl iodide, 0.24 mmol of activator, and 5 mol% of Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> at 60 °C in 3 mL of THF.

(b) The reaction was carried out at 100 °C in 1,4-dioxane.

(c) The amount of employed siloxane was 0.24 mmol (1.2 equiv per unit).

(d) 5 mol% of Pd(PPh<sub>3</sub>)<sub>4</sub> was used as a palladium catalyst.

Cross coupling of silicone of different degrees of polymerization, whose terminal was protected with the trimethylsilyl group, was carried out with **2b**. Employing the average molecular weight of 2500-2700 (ca. 20 mer), 700-900 (ca. 6 mer), and 350-450 (ca. 2 mer) cross-coupling was examined. These results are summarized in Table 6. The yield of the reaction with Ag<sub>2</sub>O as an activator was found to decrease as the degree of polymerization is smaller when 1.2 equiv of silicone toward **2b** was used. However, the reaction with 2 equiv of silicone afforded the corresponding biaryl in good yield irrespective of the degree of polymerization (entries 4 and 7). We then examined the reaction of phenyltrisiloxane **11**, whose terminals are trimethylsilyl groups, with 1.2 and 2 equivalents of **2b** (entries 9 and 10). Under similar conditions to polysiloxanes, the reactions were found to afford coupling product in rather lower yields. The results suggest that the activation of silicone with Ag<sub>2</sub>O hardly occurs at the trimethylsilylated end group. On the other hand, the cross-coupling reaction of trimethylsilylated disiloxane has been shown to occur by Denmark [40] when TBAF was employed as an activator. Indeed, the reaction of silicone with different degrees of polymerization was found to show little influence for the reactivity.



Table 6 Cross-coupling reaction of silicone of different degrees of polymerization <sup>a</sup>

$$\text{TMS-O}-\left(\text{Si}\begin{array}{c} \text{Ph} \\ | \\ \text{O} \\ | \\ \text{Me} \end{array}\right)_n-\text{TMS} + \text{I}-\text{C}_6\text{H}_4-\text{OMe} \xrightarrow[\text{activator}]{\text{cat. Pd(0)}} \text{Ph}-\text{C}_6\text{H}_4-\text{OMe}$$

entry	silicone	$M_w$	activator	equiv of Ph	time/h	%yield
1	$\left(\text{Si}\begin{array}{c} \text{Ph} \\   \\ \text{O} \\   \\ \text{Me} \end{array}\right)_{20}$	2500-2700	$\text{Ag}_2\text{O}$	1.2	1	71
2			TBAF	3.0	1.5	59
3	$\left(\text{Si}\begin{array}{c} \text{Ph} \\   \\ \text{O} \\   \\ \text{Me} \end{array}\right)_6$	700-900	$\text{Ag}_2\text{O}$	1.2	1.5	62
4			$\text{Ag}_2\text{O}$	2.0	1	72
5			TBAF	3.0	19	63
6	$\left(\text{Si}\begin{array}{c} \text{Ph} \\   \\ \text{O} \\   \\ \text{Me} \end{array}\right)_2$	350-450	$\text{Ag}_2\text{O}$	1.2	2	56
7			$\text{Ag}_2\text{O}$	2.0	1.5	73
8			TBAF	1.2	1.5	60
9	$\left(\text{Si}\begin{array}{c} \text{Ph} \\   \\ \text{O} \\   \\ \text{Me} \end{array}\right)_1$ ( <b>11</b> )	298	$\text{Ag}_2\text{O}$	1.2	24	15
10			$\text{Ag}_2\text{O}$	2.0	24	13

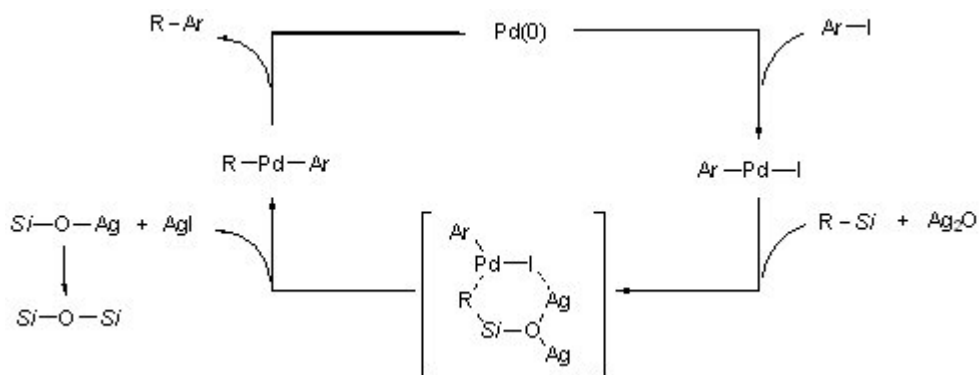
(a) Unless otherwise noted, the reaction was carried out using silicone, 4-iodoanisole **2b** (0.3 mmol), activator (0.3 mmol), and  $\text{Pd}(\text{PPh}_3)_4$  (5 mol%) in 2 mL of 1,4-dioxane.

When polyalkenysiloxane **5** ( $M_n = 8500$ ) was treated with TBAF and stirred at room temperature for 1 h, size exclusion chromatography (SEC) analysis of the resulting mixture showed the number average molecular

weight ( $M_n$ ) of 2300. The result indicates that polysiloxanes would be cleaved into smaller segments but not converted completely to monomeric species. Accordingly, we consider that a certain oligomer would be involved by the activation with TBAF in the cross-coupling reaction. On the contrary, the molecular weight did not change after treated with  $\text{Ag}_2\text{O}$  even at 100 °C.

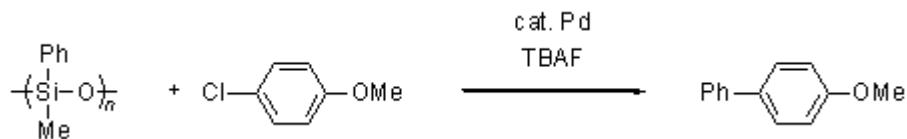
Recently, we reported the plausible reaction mechanism in the cross-coupling reaction of silanols with an aryl iodide [14]. In the reaction of silanols, silver oxide would interact with intermediary organopalladium(II) iodide complex produced by the oxidative addition of aryl iodide to palladium(0) due to the strong affinity of iodine with silver. Silver oxide may act as a nucleophilic activator of silicone to form pentacoordinate silicate species, which also facilitate the transfer of an organic group on silicon to palladium (transmetalation). In case of polysiloxane, similar intermediate seem to be generated in the reaction system. XRD analysis showed existence of AgI in the reaction mixture. The plausible reaction mechanism is illustrated in Figure 1.

Figure 1 Plausible mechanism of the cross-coupling reaction with an Organosilicon reagent.



Since aryl chlorides are one of the most attractive substrates for the transition metal-catalyzed cross-coupling reaction due to the lower cost compared to aryl bromide or aryl iodide counterparts [41-45], our focus was directed to modify the reaction protocol of silicone in order to cross-couple with aryl chlorides. These results are summarized in Table 7.

The reaction of **1** with 1-chloro-4-methoxybenzene **12a** in the presence of 5 mol% of  $\text{PdCl}_2(\text{PCy}_3)_2$  [46-48], which possessed electron-donating and bulky phosphine ligands and was shown to be effective for several cross-coupling reaction of aryl chlorides, was first examined using TBAF as an activator (Scheme 5) [29].



Scheme 5

According to the procedure for the cross-coupling of aryl iodides, the reaction was carried out using an equimolar amount of TBAF relative to the silicon atom of **1** in toluene at 120 °C for 39 h. However, no coupling product was obtained at all (entry 1). Dramatic improvement was observed by addition of water to afford the desired cross-coupling product in 65% yield (entry 2). Moreover, it is effective to stir the silicone **1** in the presence of TBAF/H<sub>2</sub>O at rt for 1 h before the addition of the palladium catalyst and **12a** to accomplish the cross-coupling reaction giving coupling product in 78% yield (entry 3). On the other hand, the coupling reaction did not proceed with the palladium catalyst in the absence of a phosphine ligand and in the presence of triphenylphosphine (entries 4 and 5). These results are explained in terms of the lower reactivity of aryl chlorides compared to that of aryl iodides toward a palladium complex [40-44]. Ethereal solvent such as 1,4-dioxane was similarly effective for the biaryl formation to furnish the desired coupling product in 81% yield (entry 6). Lowering the temperature to 70 °C also caused cross-coupling to give coupling product in 46% yield (entry 7) and increasing the amount of TBAF (2 equiv) resulted in lowering the yield of coupling product (entry 8).

Table 7 Palladium-catalyzed cross-coupling reaction of **1** with 1-chloro-4-methoxybenzene <sup>a</sup>

entry	cat. Pd	solvent	temp/°C	activator	%yield <sup>b</sup>
1	PdCl <sub>2</sub> (PCy <sub>3</sub> ) <sub>2</sub>	toluene	120	TBAF	0
2	PdCl <sub>2</sub> (PCy <sub>3</sub> ) <sub>2</sub>	toluene	120	TBAF/H <sub>2</sub> O	65
3	PdCl <sub>2</sub> (PCy <sub>3</sub> ) <sub>2</sub>	toluene	120	TBAF/H <sub>2</sub> O	78 <sup>c</sup>
4	Pd <sub>2</sub> (dba) <sub>3</sub>	toluene	120	TBAF/H <sub>2</sub> O	0 <sup>d</sup>
5	Pd(PPh <sub>3</sub> ) <sub>4</sub>	toluene	120	TBAF/H <sub>2</sub> O	0
6	PdCl <sub>2</sub> (PCy <sub>3</sub> ) <sub>2</sub>	1,4-dioxane	100	TBAF/H <sub>2</sub> O	81
7	PdCl <sub>2</sub> (PCy <sub>3</sub> ) <sub>2</sub>	1,4-dioxane	70	TBAF/H <sub>2</sub> O	46
8	PdCl <sub>2</sub> (PCy <sub>3</sub> ) <sub>2</sub>	1,4-dioxane	100	TBAF/H <sub>2</sub> O	61 <sup>e</sup>

(a) Unless otherwise noted, the reaction was carried out using **1** (1.5 mmol/unit), **12a** (0.3 mmol), 5 mol% of palladium catalyst, and TBAF (1.5 mmol) in the presence of water (0.5 mL) for 39 h.

(b) The yield was determined by <sup>1</sup>H NMR using diphenylmethane as an internal standard.

(c) Stirring **1** with TBAF at rt for 1 h before starting reaction.

(d) Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (2.5 mol%) was employed.

(e) TBAF (3.0 mmol) was used.

Screening of fluoride-free [49-56] additive for the cross-coupling reaction revealed that  $\text{Cs}_2\text{CO}_3$  or  $\text{K}_2\text{CO}_3$  served as an effective activator as summarized in Table 8. The reaction in the presence of  $\text{CsCO}_3$  produced the cross-coupling product in 73% yield (entry 1). It should be pointed out that use of  $\text{K}_2\text{CO}_3$  lead to the complete consumption of **12a** to afford the corresponding coupling product in a quantitative yield (entry 3). The reaction with  $\text{K}_2\text{CO}_3$  proceeded at higher temperature (100 °C) in 1,4-dioxane (entry 5). Another inorganic activator such as NaOH was also found to be applicable (entry 6). On the other hand, no coupling product was obtained when  $\text{Ag}_2\text{O}$  was employed (entry 7). This result is ascribed to the inferior interaction ability between silver and chlorine atom compared with the iodide case. Decreasing the amount of  $\text{K}_2\text{CO}_3$  from 2.0 equivalents to 1.0 equivalent relative to **1** was found to be less effective to afford a smaller amount of the cross-coupling product (entry 2). Similarly, the reaction was suppressed to some extent with increasing the amount of  $\text{K}_2\text{CO}_3$  from 2.0 equivalents to 3.0 equivalents (entry 4) suggesting that the reaction was significantly influenced by the amount of activator employed.

Table 8 Effect of additive in the cross-coupling of silicone **1**<sup>a</sup>

entry	additive	Additive/silicone	%yield <sup>b</sup>
1	Cs <sub>2</sub> CO <sub>3</sub>	2	73
2	K <sub>2</sub> CO <sub>3</sub>	1	65
3	K <sub>2</sub> CO <sub>3</sub>	2	>99
4	K <sub>2</sub> CO <sub>3</sub>	3	70
5	K <sub>2</sub> CO <sub>3</sub>	2	64 <sup>c</sup>
6	NaOH	2	>99
7	Ag <sub>2</sub> O	1	0

(a) Unless otherwise noted, the reaction was carried out in 3 mL of toluene and 0.5 mL of water for 39 h at 120 °C using silicone (1.5 mmol; per unit), aryl chloride (0.3 mmol), 5 mol% of PdCl<sub>2</sub>(PCy<sub>3</sub>)<sub>2</sub>, and additive.

(b) The reaction yield was estimated by <sup>1</sup>H NMR.

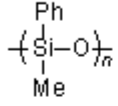
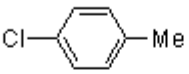
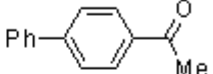
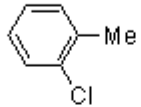
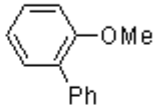

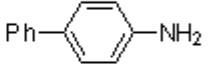
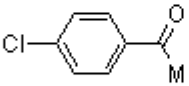
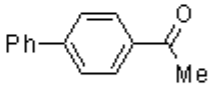
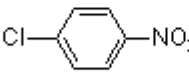
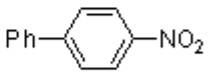
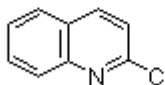
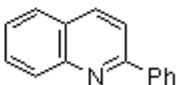
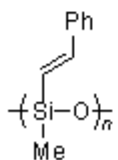
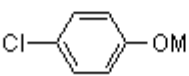
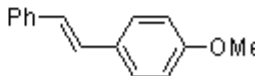
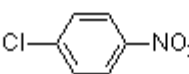
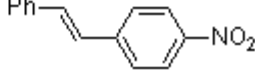
(c) The reaction was carried out at 100 °C in 1,4-dioxane.

Various aryl chlorides were treated with **1** to provide the corresponding coupling products in moderate to excellent yields. As illustrated in Table 9, aryl chlorides bearing an electron-donating or electron-withdrawing substituent on the aromatic ring underwent the cross-coupling reaction in good yields. Sterically hindered aryl

chloride **12c** was also tolerated to produce the corresponding product in 43% yield (entry 2). A heteroaromatic substrate such as 2-chloroquinoline **12g** reacted to afford corresponding coupling product in 68% yield (entry 6). Furthermore, **5** also served as a substrate for the alkenylation to afford stilbene derivatives in good yields (entries 7 and 8).



Table 9 Cross-coupling of silicone with various aryl chlorides <sup>a</sup>

$\begin{array}{c} \text{R} \\   \\ \text{-(Si-O)}_n \\   \\ \text{Me} \end{array} + \text{X-Aryl} \xrightarrow[\text{toluene, 120 }^\circ\text{C}]{\text{cat. PdCl}_2(\text{PCy}_3)_2, \text{K}_2\text{CO}_3\text{-H}_2\text{O}} \text{R-Aryl}$				
entry	silicone	Cl-Aryl	product	%yield <sup>b</sup>
1	 (1)	 (12b)		92
2		 (12c)		43
3		 (12d)		53
4		 (12e)		>99
5		 (12f)		77
6		 (12g)		68
7	 (5)	 (12a)		97
8		 (12f)		70

(a) Unless otherwise noted, the reaction was performed in toluene (3 mL) for 29-48 h at 120 °C using silicone

(1.5 mmol; per unit), aryl chloride (0.3 mmol), 5 mol% of PdCl<sub>2</sub>(PCy<sub>3</sub>)<sub>2</sub>, and 3 mmol of K<sub>2</sub>CO<sub>3</sub>-H<sub>2</sub>O.

(b) The yield was determined by <sup>1</sup>H NMR analysis using diphenylmethane as an internal standard.

#### 4. Conclusion

In conclusion, silicone bearing an aryl and alkenyl groups was revealed to be available as a practical organosilicon reagent for the palladium-catalyzed cross-coupling reactions. In particular, poly(methylphenylsiloxane), which is a highly thermally stable silicone oil, allows the coupling reaction with aryl halides leading to biaryls efficiently. Polysiloxanes with a different molecular weight and several cyclic siloxanes bearing a phenyl group were also subjected to the cross-coupling. Furthermore, siloxanes with other aryl group and alkenyl group were found to be synthesized from PMHS and to be subjected to the palladium-catalyzed coupling reactions. Silver(I) oxide, TBAF, and aqueous  $K_2CO_3$  serves as an effective activator for the silicone reagents. Organic synthesis with a transition metal-catalyst is a new class of utilization of silicone, which is an environmentally friendly and less expensive reagent.

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