JOC Article

Application of Directed Orthometalation toward the Synthesis of Aryl Siloxanes

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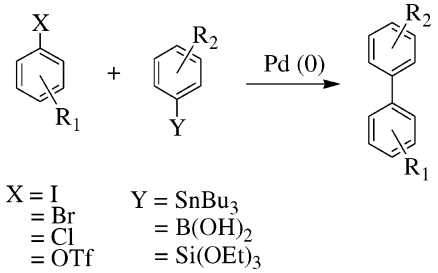
A selection of ortho-substituted aryl siloxanes have been prepared by directed orthometalation protocols. These siloxanes can be prepared in high yields and purity by use of a diverse selection of ortho-directing groups and electrophilic siloxane derivatives. The siloxanes are employed in palladium-catalyzed cross-coupling reactions with aryl bromides to generate unsymmetrical ortho-substituted biaryls in good to excellent yields.

Introduction

Palladium-catalyzed coupling reactions of metalloid derivatives are one of the most useful synthetic tools for the construction of unsymmetrical biaryl derivatives. Of the available methodologies, the Suzuki−Miyaura[1] (organoboron) and the Stille[2] (organostannane) coupling reactions have been the most widely employed due to their generality and overall good yields (Scheme 1). However, these coupling technologies have their limitations: boronic acids can prove difficult to synthesize and purify, and organostannanes suffer from toxicities of the tin reagents and byproducts.

Research in our laboratory[3] and others[4] has focused on the use of hypervalent siloxane reagents in palladium-catalyzed cross-coupling. This methodology has proven to be excellent for aryl−aryl couplings and can also be used for the arylation of allylic esters.[5] The major limitation of this approach has been the synthesis of the aryl siloxane reagents. Classically, synthesis of aryl siloxanes is accomplished by treatment of Grignard or organolithium reagents with a silicon electrophile, typically tetraethyl orthosilicate.[6] More recently, Pd(0)-[7] or Rh(I)-[8] catalyzed silylation reactions of aryl halides have been reported; however, both of these methods mandate the use of a suitable aryl halide as the substrate for siloxane synthesis.

SCHEME 1



As part of our development of the siloxane coupling methodology, we were interested in synthesizing highly functionalized aryl siloxane derivatives for application in natural product total synthesis. In several instances, the desired substitution pattern on the aromatic ring precluded the efficient synthesis of the requisite aryl halide. An orthometalation[9] strategy, on the other hand, presented an alternative for the preparation of these complex aryl siloxanes (Scheme 2). Organoboranes and organostannanes have been prepared by orthometalation; however, aryl siloxanes had never been prepared by this method.[10] The results summarized in this report demonstrate the scope and limitations of directed orthometa-

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(6) For several recent examples, see (a) Berlekamp, U. H.; Mix, A.; Neumann, B.; Stammler, H. G.; Jutzi, P. *J. Organomet. Chem.* **2003**, *667*, 167−175. (b) Pak, J. J.; Greaves, J.; McCord, D. J.; Shea, K. J. *Organometallics* **2002**, *21*, 3552−3561. (c) Kano, N.; Komatsu, F.; Kawashima, T. *J. Am. Chem. Soc.* **2001**, *123*, 10778−10779. (d) Cerveau, G.; Chappellet, S.; Corriu, R. J. P.; Dabiens, B. *J. Organomet. Chem.* **2001**, *626*, 92−99.

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

(9) For several recent reviews, see (a) Anctil, E. J. G.; Snieckus, V. *J. Organomet. Chem.* **2002**, *653*, 150−160. (b) Beak, P.; Kerrick, S. T.; Gallagher, D. J. *J. Am. Chem. Soc.* **1993**, *115*, 10628−10636. (c) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879−933. (d) Snieckus, V. *Heterocycles* **1980**, *14*, 1649−1676. (e) Chinchilla, R.; Najera, C.; Yus, M. *Chem. Rev.* **2004**, *104*, 2667−2722.

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SCHEME 2

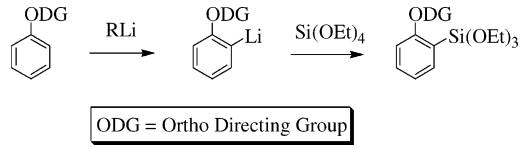
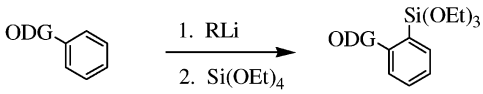


TABLE 1. Synthesis of Aryl Siloxanes via Orthometalation



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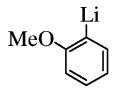
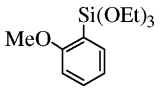
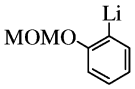
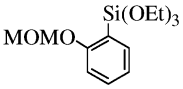
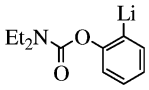
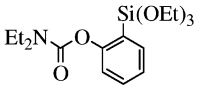
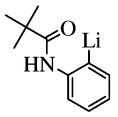
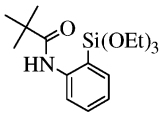
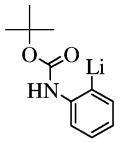
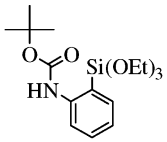
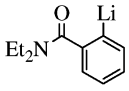
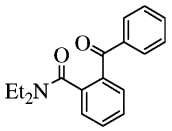
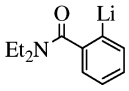
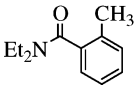
1		$Si(OEt)_4$		62
2		$Si(OEt)_4$		61
3		$Si(OEt)_4$		57
4		$Si(OEt)_4$		63
5		$Si(OEt)_4$		61
6		$Si(OEt)_4$		94
7		CH_3I		85

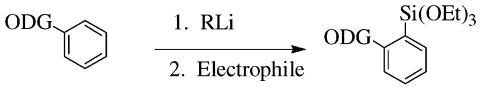
[a] For detailed metalation procedures for each substrate see Experimental Section. [b] Yield of purified product.

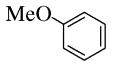
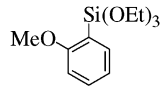
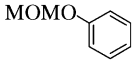
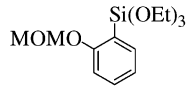
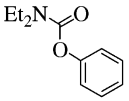
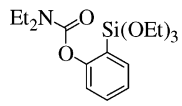
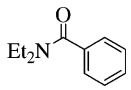
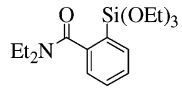
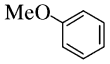
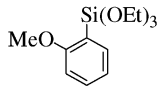
lation for the synthesis of aryl siloxanes and the coupling reactions of the resulting derivatives.

Results and Discussion

Initial studies have focused on surveying ortho-directing groups (ODG) that have proven effective in other instances, and the results are summarized in Table 1. Ethers (entries 1 and 2) and carbamates (entries 3 and 5, respectively) smoothly yielded the desired siloxanes in good yields. In addition, the *N*-pivaloate (entry 4) served as a suitable substrate for the formation of the requisite siloxane. However, *N*,*N*-diethylbenzamide siloxane proved elusive (entry 6). The only product obtained from a multitude of reaction conditions was the benzophenone derivative, which arose from nucleophilic attack of the lithiated benzamide species with another benzamide molecule. To show that the lithiated benzamide species was being generated, the reaction was quenched with CH_3I (entry 7). This led to the formation of the expected ortho-substituted product in 85% yield. It was thought that the inability to form the desired ortho-substituted benzamide siloxane was due to the poor electrophilicity of tetraethyl orthosilicate. We proposed that a more electrophilic siloxane source would give the desired siloxane in preference to the benzophenone adduct.

TABLE 2. Use of Alternative Silicon Electrophiles



Entry	Substrate	Electrophile	Product	Yield (%)
1		TfO-$Si(OEt)_3$		88
2		TfO-$Si(OEt)_3$		83
3		TfO-$Si(OEt)_3$		86
4		TfO-$Si(OEt)_3$		0
5		$SiCl_4$[a]		69

[a] Lithiated arene was quenched with $SiCl_4$ followed by the addition of anhydrous EtOH to obtain the desired siloxane. See Experimental Section for full reaction details.

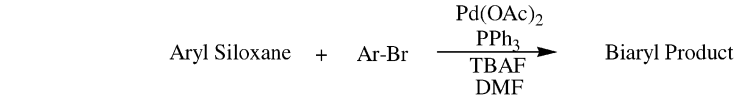
To this end, several silicon electrophiles were surveyed and the results are presented in Table 2. The most promising proved to be triethoxysilyltriflate. This reagent is readily obtained from treatment of allyltriethoxysilane with triflic acid.[11] Yields of the *o*-methoxy, *o*-MOM, and *o*-(*O*-carbamate) siloxanes were markedly increased with this electrophile (entries 1−3). Unfortunately, there was no reaction with the benzamide substrate (entry 4). The use of another silane electrophile, $SiCl_4$ (entry 5), produced only a marginal increase in yield over $Si(OEt)_4$ (69% vs 62%). Like the silyl triflate, no benzamide siloxane product was obtained with $SiCl_4$.

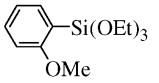
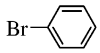
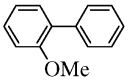
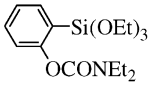
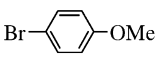
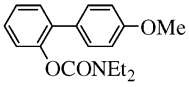
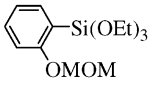
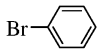
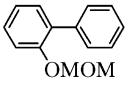
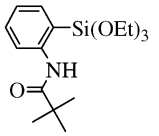
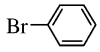
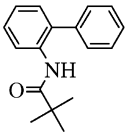
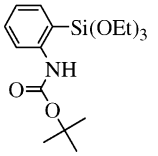
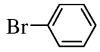
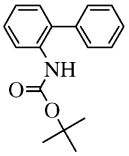
Having synthesized a variety of ortho-substituted aryl siloxanes, attention turned to assessing their ability to participate in palladium-catalyzed cross-coupling. The results of these cross-coupling studies are presented in

(10) For several examples, see (a) Beaulieu, F.; Snieckus, V. *Synthesis* **1992**, 112−118. (b) Chauder, B.; Green, L.; Snieckus, V. *Pure Appl. Chem.* **1999**, *71*, 1521−1529.

(11) Uhlig, W. *J. Organomet. Chem.* **1993**, *452*, 29−32.

TABLE 3. Palladium-Catalyzed Cross Coupling of Aryl Siloxane Derivatives



Entry	Aryl Siloxane	Ar-Br	$Pd(OAc)_2$[a] (mole %)	Biaryl Product	Yield[b] (%)
1			50(10)		75(39)
2			50(10)		49(12)
3			50(10)		87(54)
4			10		86
5			10		88

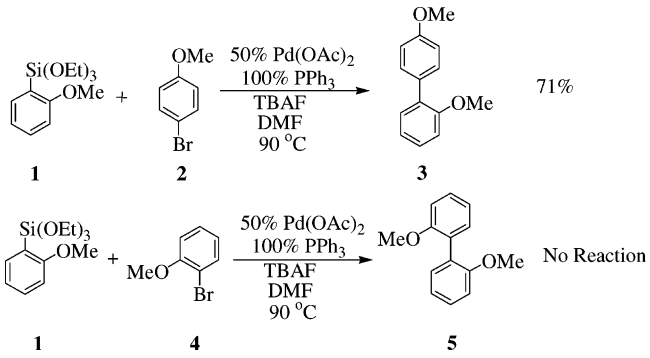
[a] In all cases, ratio of $Pd(OAc)_2$ to PPh_3 was 1:2. Reactions performed with 50 mol % catalyst were complete in less than 15 min at 90 °C, and reactions performed with 10 mol % catalyst were complete after 4 h at 90 °C. [b] Yield in parentheses is the yield obtained with 10 mol % catalyst.

Table 3, and data indicate that siloxanes possessing either *o*-ether (entries 1 and 3) or *o*-(*O*-carbamate) (entry 2) functionalities couple poorly with aryl bromides in the presence of 10 mol % catalyst. Previous studies in our lab had shown that the presence of ortho substituents on the aryl siloxane often led to poor yields of coupled product; however, the results can be significantly improved by increasing the catalyst loading to 50 mol %.[12]

The low yields of coupled product obtained by use of 10 mol % catalyst with *o*-phenolic derivatives (Table 3, entries 1−3) was due to competitive protodesilylation of the siloxane. However, in the case of the aniline derivatives of the siloxane (entries 4 and 5, respectively), excellent yields of coupled products are observed with only 10 mol % catalyst, with no detectable protodesilylation.

The cross-coupling reactions were found to be extremely sensitive to the presence of *o*-substituents in the aryl halide partners. For example, cross-coupling of *o*-methoxysiloxane **1** to *p*-bromoanisole **2** proceeded in good yield to generate biaryl **3**; however, attempted coupling of siloxane **1** to *o*-bromoanisole **4** was not successful (Scheme 3). This result indicates that these disubstituted substrates will not effectively couple under the current reaction conditions. We are presently engaged

SCHEME 3

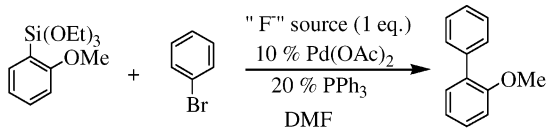


in the search for reaction conditions that will lead to improved yields in this important reaction.

In an attempt to elucidate the source of the hydrogen and the mechanism of protodesilylation, several control experiments were performed. Studies with deuterium-labeled solvents showed that solvent was not the source of the proton. Commercially available (Aldrich) solutions of TBAF in THF contain approximately 5% water and we thought that water in the TBAF may be serving as the proton source for protodesilyation. Accordingly, alternative anhydrous fluoride sources were investigated and the results of these studies are presented in Table 4. In most cases (entries 1−4 and 8−11) neither cross-coupling nor protodesilylation occurred upon treatment with the fluoride reagent, and the siloxane was recovered unchanged.

(12) Handy, C. J. In Preparation and NMR Studies of Hypervalent Silicates and Their Use in Palladium-Catalyzed Cross Coupling Reactions, Ph.D. Dissertation, University of Maryland, College Park, 2002.

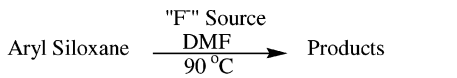
TABLE 4. Use of Alternative Fluoride Sources[a]

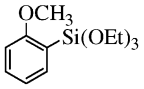
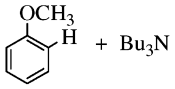
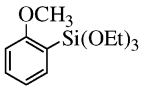
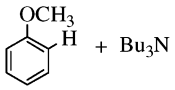
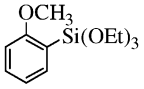
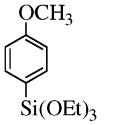


Entry	F Source	Yield of Coupled Product (%)
1	LiF	0[b]
2	NaF	15[c]
3	KF	20[c]
4	CsF	17[c]
5	TBAF (1.0 M in THF)[d]	40[e]
6	$TBAF{\cdot}3H_2O$	42[e]
7	$TMAF{\cdot}4H_2O$	41[e]
8	TMAF (anhydrous)[f]	0[g]
9	TASF	0[g]
10	$NaBF_4$	0[g]
11	Bu_4NBF_4	0[g]

[a] Reactions were performed at 90 °C for 4 h. [b] No reaction occurred. [c] Trace amounts of protodesilylated siloxane were present; remainder of siloxane was unreacted. [d] Contains 5% water. [e] Remainder of siloxane was hydrolyzed. [f] Purchased from Aldrich. [g] Greater than 70% of the starting siloxane was recovered from the reaction.

TABLE 5. Search for the Source of the Proton for Protodesilylation



Aryl Siloxane	"F⁻" Source	Products[a]
	$Bu_4NF{\bullet}3H_2O$	
	$Bu_4NF{\bullet}3D_2O$	
	$Me_4NF{\bullet}4D_2O$	
	$Bu_4NF{\bullet}3H_2O$	No Reaction

[a] Yields of products are greater than 90%.

It was found that if the siloxane was heated in the presence of tetrabutylammonium fluoride trihydrate ($TBAF{\cdot}3H_2O$), rapid and efficient protodesilylation occurred with the generation of tributylamine (Table 5). This result clearly indicated that a proton was abstracted from the tetrabutylammonium cation in a Hoffman-like elimination to generate tributylamine and butene. Further support for the hypothesis that this reaction was the source of the proton for protodesilylation was obtained from deuterium studies. $TBAF{\cdot}3H_2O$ was recrystallized from D_2O to give $TBAF{\cdot}3D_2O$, the structure of which was confirmed by IR. When $TBAF{\cdot}3D_2O$ was utilized in these experiments, no deuterium incorporation was observed in the product. For comparison, *p*-methoxysiloxane is stable for 24 h in the presence of $TBAF{\cdot}3H_2O$.

The protodesilylation mechanism was further probed by use of $TMAF{\cdot}4D_2O$. This reagent does not possess β-hydrogens and thus would not be able to undergo Hoffman elimination. However, rapid protodesilylation still occurred in this instance, also with no deuterium incorporation. This result indicated that the α-proton was abstracted from the tetramethylammonium cation generating the ylide, which can then undergo Stevens rearrangement to generate dimethylethylamine.[13]

In conclusion, directed orthometalation protocols have been developed for the synthesis of aryl siloxane derivatives. Subsequent cross-coupling of the resulting aryl siloxanes has been achieved. For phenolic derivatives, high catalyst loading is required for good yields of product. On the other hand, aniline derivatives underwent cross-coupling under standard conditions. The application of this methodology in the synthesis of several natural products is currently underway.

Experimental Section

2-(Triethoxysilyl)anisole (Table 1, entry 1). To a colorless solution of anisole (0.523 mL, 5.00 mmol) in Et_2O (10 mL), was added 0.906 mL of TMEDA (6.00 mmol). The reaction was cooled to 0 °C, and 3.75 mL of a 1.60 M solution *n*-BuLi in hexane was added. The resulting yellow solution was stirred at room temperature for 1 h. The dark yellow ethereal solution was added to 3.35 mL (15.0 mmol) of $Si(OEt)_4$ in 15 mL of Et_2O at −78 °C. The solution was stirred at −78 °C for 1 h and then allowed to warm to room temperature for an additional hour. A saturated aqueous solution of NH_4Cl (50 mL) was added and the aqueous layer was extracted with 50 mL of ether (×3), dried ($MgSO_4$), and concentrated in vacuo to give a yellow oil. Kugelrohr distillation (125 °C, 0.9 mmHg) yielded pure siloxane as a colorless oil (62%). The ^1H and ^{13}C NMR and IR spectra match those reported by Manoso and DeShong.[14]

2-(Triethoxysilyl)methoxymethoxybenzene (Table 1, entry 2). Title compound was synthesized by a modified metalation procedure of Barve.[15] Methoxymethoxybenzene (0.718 g, 5.00 mmol) and TMEDA (0.755 mL, 5.00 mmol) were dissolved in 10 mL of ether. The solution was cooled to 0 °C and 3.13 mL (5.00 mmol) of a 1.60 M n-BuLi solution in hexanes was added slowly, inducing the formation of a yellow slurry. The mixture was stirred for a further 30 min at 0 °C. The lithiated arene was then transferred via cannulation to a solution of tetraethyl orthosilicate (2.23 mL, 10.0 mmol) in 10 mL of ether at −78 °C. The reaction was stirred for 1 h at −78 °C and then allowed to warm to room temperature over a period of 1 h. The reaction was quenched with saturated aqueous NH_4Cl (50 mL). The aqueous layer was then extracted with ether (50 mL × 2) and dried ($MgSO_4$), and the solvent was removed in vacuo to give a pale yellow oil. Kugelrohr distillation (130 °C, 0.9 mmHg) yielded pure siloxane as a colorless oil (61%). IR (CCl_4) 2974 (m), 2926 (m), 2895 (m), 1591 (m), 1474 (m), 1230 (m), 1156 (m), 1105 (s), 1080 (s), 1006 (s); ^1H NMR ($CDCl_3$) δ 1.22 (t, J = 7.2 Hz, 9H), 3.49 (s, 3H), 3.83 (q, J = 7.2 Hz, 6H), 5.23 (s, 2H), 6.98 (t, J = 7.0 Hz, 1H), 7.13 (d, J = 7.0 Hz, 1H), 7.42 (t, J = 7.0 Hz, 1H), 7.60 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 18.2, 56.0, 58.6, 94.2, 113.1, 120.0, 121.5, 132.1, 137.5, 162.2; LRMS (FAB^+) *m/z* 300 (M^+, 25), 255 (60), 210 (100), 163 (35), 139 (30), 107 (35), 79 (28), 45 (97); HRMS (FAB^+, M^+) *m/z* calcd for $C_{14}H_{24}O_5Si$ 300.1393, found 300.1387.

(13) For a review of the Stevens rearrangement, see Pine, S. H. *Org. React.* **1970**, *18*, 403−464.
(14) Manoso, A. S.; DeShong, P. *J. Org. Chem.* **2001**, *66*, 7449−7455.
(15) Narasimhan, N. S.; Chandrachood, P. S.; Barve, M. V. *Synthesis* **1979**, 589−590.

2-(Triethoxysilyl)phenyl *N*,*N*-diethylcarbamate (Table 1, entry 3). Title compound was synthesized by a modified metalation procedure of Snieckus and co-workers.[16] A solution of *O*-phenyl diethylcarbamate (0.966 g, 5.00 mmol) in 5 mL of THF was added dropwise to a stirred solution of *sec*-BuLi (4.01 mL, 5.50 mmol) and TMEDA (0.830 mL, 5.50 mmol) in 50 mL of THF at −78 °C. The reaction was stirred for 1 h at −78 °C and was then slowly added to a stirred solution of tetraethyl orthosilicate (3.35 mL, 15.0 mmol) in 30 mL of THF at −78 °C. The reaction was stirred at −78 °C for 2 h, followed by 2 h at room temperature. Saturated aqueous NH_4Cl (50 mL) was added to the reaction mixture. The aqueous layer was then extracted with ether (50 mL × 2) and dried ($MgSO_4$), and the solvent was removed in vacuo to give a dark yellow oil. Kugelrohr distillation (135 °C, 0.9 mmHg) yielded pure siloxane as a colorless oil (57%). IR (CCl_4) 2978 (w), 2929 (w), 2885 (w), 1718 (s), 1421 (m), 1200 (m), 1155 (s), 1103 (s), 1086 (s); ^{1}H NMR ($CDCl_3$) δ 1.19−1.28 (m, 15H), 3.38 (q, J = 7.2 Hz, 2H), 3.53 (q, J = 7.2 Hz, 2H), 3.82 (q, J = 7.2 Hz, 6H), 7.17−7.26 (m, 2H), 7.43−7.45 (m, 1H), 7.71−7.30 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.3, 14.0, 18.0, 41.6, 42.0, 58.4, 122.4, 122.9, 124.6, 131.7, 137.0, 154.0, 156.5; LRMS (EI$^+$) m/z 355 (M$^+$, 5), 309 (30), 100 (100), 72 (25); HRMS (EI$^+$, M$^+$) m/z calcd for $C_{17}H_{29}O_5NSi$ 355.1815, found 355.1822.

2-(Triethoxysilyl)pivalanilide (Table 1, entry 4). Pivalanilide (886 mg, 5.00 mmol) was dissolved in a 50:50 solution of THF/Et_2O. To this colorless solution at 0 °C was added 12.4 mL of a 1.21 M solution of *n*-BuLi in hexane (15.0 mmol). The pale yellow solution was stirred at 25 °C for 20 h. The resulting white slurry was cooled to 0 °C and diluted with 50 mL of THF. Tetraethyl orthosilicate (3.35 mL, 15.0 mmol) was then added via syringe. The reaction was stirred for a further 4 h at room temperature. The solvent was removed in vacuo and the residue was dissolved in ether. The ether was washed with saturated aqueous NH_4Cl (50 mL) twice and dried ($MgSO_4$), and the solvent was removed in vacuo to give a pale yellow oil. Column chromatography (9:1 hexanes/EtOAc, TLC R_f = 0.28) yielded a pale yellow oil (62%). IR (CCl_4) 3368 (s), 3054 (w), 2971 (s), 2922 (s), 2895 (s), 1683 (s), 1576 (s), 1535 (s), 1431 (s), 1300 (s), 1159 (s), 1103 (s), 1076 (s), 962 (s); ^{1}H NMR ($CDCl_3$) δ 1.24 (t, J = 8.0 Hz, 9H), 1.30 (s, 9H), 3.88 (q, J = 8.0 Hz, 6H), 7.07 (t, J = 8.0 Hz, 1H), 7.41 (m, 1H), 7.55 (m, 1H), 8.33 (d, J = 8.4 Hz, 1H), 8.99 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.1, 27.6, 39.8, 59.1, 119.1, 121.0, 123.2, 131.7, 135.6, 144.1, 177.0; LRMS (FAB$^+$) m/z 339 (M$^+$, 10), 294 (100); HRMS (FAB$^+$, M$^+$) m/z calcd for $C_{17}H_{29}O_4NSi$ 339.1866, found 339.1860.

2-(Triethoxysilyl)-*N*-(*tert*-butoxycarbonyl)aniline (Table 1, entry 5). A solution of *t*-BuLi (4.20 mL, 6.30 mmol) was added dropwise to a stirred, colorless solution of *N*-(*tert*-butoxycarbonyl)aniline (500 mg, 2.52 mmol) in 10 mL of THF. The yellow solution was stirred at −20 °C for 2 h. The solution was diluted with 20 mL of THF and cooled to −78 °C, and tetraethyl orthosilicate (1.69 mL, 7.56 mmol) was then added via syringe. The reaction was then allowed to warm to room temperature overnight and quenched with saturated aqueous NH_4Cl (50 mL). The aqueous layer was then extracted with ether (50 mL × 2), decolorized with activated carbon, and dried ($MgSO_4$), and the solvent was removed in vacuo to give a dark yellow oil. Column chromatography (9:1 hexanes/EtOAc, TLC R_f = 0.33) yielded a colorless oil (61%). IR (CCl_4) 3337 (m), 3054 (w), 2978 (s), 2926 (m), 2888 (m), 1725 (s), 1580 (m), 1535 (m), 1438 (m), 1369 (m), 1300 (m), 1159 (s), 1079 (s), 958 (m); ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 6.8 Hz, 9H), 1.51 (s, 9H), 3.89 (q, J = 6.8 Hz, 6H), 7.01 (t, J = 7.6 Hz, 1H), 7.38−7.42 (m, 1H), 7.49−7.51 (m, 1H), 8.12 (d, J = 8.4 Hz, 1H), 8.72 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.0, 28.4, 29.5, 59.0, 118.6, 122.0, 131.8, 135.5, 144.7, 153.1; LRMS (FAB$^+$) m/z 355 (M$^+$, 42), 310 (22), 299 (40), 254 (100), 210 (45), 57 (25); HRMS (FAB$^+$, M$^+$) m/z calcd for $C_{17}H_{29}O_5NSi$ 355.1815, found 355.1826.

2-(Diethylcarbamoyl)benzophenone (Table 1, entry 6). *N*,*N*-Diethylbenzamide (500 mg, 2.82 mmol) in 20 mL of THF was added slowly to a solution of *sec*-BuLi (2.38 mL, 3.10 mmol) and TMEDA (0.468 mL, 3.10 mmol) in 40 mL of THF at −78 °C. The reaction was stirred at −78 °C for 1 h. The reaction mixture was then added to $Si(OEt)_4$ (1.89 mL, 8.46 mmol) in 100 mL of THF at −78 °C. The reaction was stirred for 1 h at −78 °C and quenched with saturated aqueous NH_4Cl (100 mL). The aqueous layer was then extracted with ether (50 mL × 2) and dried ($MgSO_4$), and the solvent was removed in vacuo to give a dark yellow oil. Column chromatography (1:1 hexanes/EtOAc, TLC R_f = 0.29) yielded a white solid (95%), mp 76.8−77.2 °C (lit. 76−77 °C).[17] IR (neat) 3059 (w), 2975 (w), 2935 (w), 2866 (w), 1660 (m), 1620 (s), 1591 (m), 1428 (m), 1268 (s), 1083 (m), 927 (m); ^{13}C NMR ($CDCl_3$) δ 12.2, 13.7, 38.8, 43.2, 126.8, 128.1, 128.3, 129.8, 130.3, 130.7, 133.0, 137.0, 137.2, 138.8, 169.9, 196.7; LRMS (FAB$^+$) m/z 282 (M$^+$, 95), 209 (100), 105 (32), 72 (32), 57 (19); HRMS (FAB$^+$, M$^+$) m/z calcd for $C_{18}H_{20}O_2N$ 282.1499, found 282.1507. The ^{1}H NMR matches that reported by Snieckus and co-workers.[17]

***N*,*N*-Diethyl-*o*-toluamide (Table 1, entry 7).** Title compound was synthesized by a modified metalation procedure of Beak and Brown.[18] *N*,*N*-Diethylbenzamide (570 mg, 3.22 mmol) in 10 mL of THF was added slowly to a solution of *sec*-BuLi (2.58 mL, 3.53 mmol) and TMEDA (0.533 mL, 3.53 mmol) in 40 mL of THF at −78 °C. The reaction was stirred at −78 °C for 1 h. Methyl iodide (0.501 mL, 8.05 mmol) was then added via syringe. The solution was then allowed to warm to room temperature. The reaction was quenched with saturated aqueous NH_4Cl (50 mL). The aqueous layer was then extracted with ether (50 mL × 2) and dried ($MgSO_4$), and the solvent was removed in vacuo to give a dark yellow oil. Kugelrohr distillation (85 °C, 0.3 mmHg) yielded the title compound as a colorless oil (85%). IR (CCl_4) 3061 (w), 3026 (w), 2974 (w), 2933 (w), 2871 (w), 1635 (s), 1552 (m), 1473 (m), 1455 (m), 1428 (m); ^{13}C NMR ($CDCl_3$) δ 12.9, 14.0, 18.8, 38.7, 42.6, 125.4, 125.8, 128.5, 130.3, 133.8, 137.1, 170.8. The ^{1}H NMR spectrum matches that reported by Beak and Brown.[18]

Palladium-Catalyzed Cross-Coupling Reactions of Aryl Siloxanes with Aryl Bromides, Representative Procedure. To a solution of siloxane (1.5 mmol), aryl bromide (1.0 mmol), $Pd(OAc)_2$ (0.10 mmol), and PPh_3 (0.20 mmol) in DMF (10 mL) is added 1.5 mL of TBAF in THF (1.0 M solution, 1.5 mmol). The reaction is heated at 90 °C for 4 h. The reaction is poured into 25 mL of water, and the aqueous layer is extracted with ether (25 mL ×3). The combined organic layers are dried ($MgSO_4$) and concentrated in vacuo. The biaryl product is then purified via column chromatography.

2-Methoxybiphenyl (Table 3, entry 1). Column chromatography (19:1 hexanes/EtOAc, TLC R_f = 0.37) yielded a colorless oil (39%). The ^{1}H and ^{13}C NMR and IR spectra match those reported by Buchwald and co-workers.[19]

4′-Methoxy-2-(*N*,*N*-diethyl-*O*-carbamoyl)biphenyl (Table 3, entry 2). Column chromatography (4:1 hexanes/EtOAc, TLC R_f = 0.27) yielded a colorless oil contaminated with a small amount of hexanes (12%): IR (CCl_4) 3078 (w), 3036 (w), 2971 (w), 2926 (w), 2867 (w), 2829 (w), 1718 (s), 1555 (m), 1521 (m), 1417 (m), 1272 (m), 1248 (m), 1196 (m), 1155 (m); ^{1}H NMR ($CDCl_3$) δ 1.04 (t, J = 6.5 Hz, 6H), 3.26 (q, J = 6.5 Hz, 4H), 3.83 (s, 3H), 6.92 (d, J = 8.0 Hz, 2H), 7.18−7.36 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 13.9, 13.2, 41.6, 41.9, 55.3, 113.5, 123.2, 125.5, 127.9, 130.2, 130.5, 134.7, 148.5, 154.1, 158.8; LRMS (EI$^+$) m/z 299 (M$^+$, 78), 294 (23), 100 (100), 72 (21); HRMS (EI$^+$, M$^+$) m/z calcd for $C_{18}H_{21}O_3NSi$ 299.1521, found 299.1518.

2-Methoxymethoxybiphenyl (Table 3, entry 3). Column chromatography (19:1 hexanes/EtOAc, TLC R_f = 0.28) yielded a colorless oil (54%): IR (CCl_4) 3061 (w), 3026 (w), 2992 (w),

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2954 (w), 2926 (m), 2895 (m), 2847 (m), 1480 (s), 1435 (m), 1228 (m), 1190 (m), 1148 (m), 1076 (s), 1017 (s). The ^{1}H and ^{13}C NMR spectra match those reported by Reinhoudt.[20]

2-Pivalanilinebiphenyl (Table 3, entry 4). Column chromatography (9:1 hexanes/EtOAc, TLC R_f = 0.27) yielded a yellow solid. Recrystallization from ethanol yielded a white solid (86%), mp 70.2−70.5 °C (lit. 69.7−70.1 °C).[20] ^{1}H NMR ($CDCl_3$) δ 1.09 (s, 9H), 7.14−7.16 (m. 1H), 7.24−7.2 (m, 1H), 7.36−7.48 (m, 7H), 8.36 (1H); ^{13}C NMR ($CDCl_3$) δ 27.4, 39.8, 120.9, 123.9, 128.1, 128.5, 129.1, 129.4, 129.7, 132.1, 135.2, 138.1, 176.3; LRMS (EI$^+$) *m*/*z* 254 (M$^+$, 20), 253 (100), 196 (15), 169 (67), 168 (25), 57 (45); HRMS (EI$^+$, M$^+$) *m*/*z* calcd for $C_{17}H_{20}ON$ 254.1545, found 254.1543. The IR spectrum matches that reported by Ohashi.[21]

2-*N*-(*tert*-Butoxycarbonyl)biphenyl (Table 3, entry 5). Column chromatography (19:1 hexanes/EtOAc, TLC R_f = 0.25) yielded a white solid (88%), mp 72.3−73.1 °C. IR (CCl_4) 3426 (m), 3067 (w), 3009 (w), 2978 (w), 2926 (w), 2898 (w), 1738 (s), 1590 (m), 1514 (s), 1493 (m), 1445 (s), 1162 (s); ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 9H), 6.49 (s, 1H), 7.07−7.12 (m, 1H), 7.18−7.21 (m, 1H), 7.32−7.42 (m, 4H), 7.48 (t, J = 7.2 Hz, 2H), 8.10 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.3, 30.0, 119.8, 123.1, 127.8, 128.4, 129.1, 129.3, 130.2, 130.9, 132.0, 135.3, 138.4; LRMS (FAB$^+$) *m*/*z* 269 (M$^+$, 65), 214 (100), 170 (78), 169 (52), 57 (45); HRMS (FAB$^+$, M$^+$) *m*/*z* calcd for $C_{17}H_{19}O2N$ 269.1420, found 269.1429.

4-Methoxy-2′-methoxybiphenyl (3). Column chromatography (9:1 hexanes/EtOAc, TLC R_f = 0.30) yielded a white solid (71%), mp 69.7−70.4 °C (lit. 69−70 °C).[22] The ^{1}H and ^{13}C NMR and IR spectra match those reported by Denmark.[22]

General Procedure for the Synthesis of Aryl Siloxanes by Use of Triethoxysilyltriflate. Triflic acid (3.50 mmol) is added dropwise to a stirred solution of allyltrimethoxysilane (3.50 mmol) in 50 mL of CH_2Cl_2 at −20 °C. After addition is complete, the solution is stirred at −20 °C for 1 h, followed by a further hour at room temperature. The solvent is removed in vacuo and the residue is dissolved in 50 mL of THF. After cooling to −78 °C, the silyltriflate is added dropwise to the aryllithium (3.50 mmol) in 100 mL of THF at −78 °C. The resulting solution is stirred at −78 °C for 1 h, held at room temperature for 1 h, and then quenched with 100 mL of saturated aqueous NH_4Cl. The aqueous layer was then extracted with ether (50 mL × 2) and dried ($MgSO_4$), and the solvent was removed in vacuo. The siloxane is purified as stated above.

General Procedure for the Synthesis of Aryl Siloxanes by Use of Silicon Tetrachloride. Lithiated arene (5 mmol) is prepared as described above and cooled to −78 °C. The lithiated arene is then added via cannula to a stirred solution of $SiCl_4$ (10 mmol) in 100 mL of THF at −78 °C. The reaction is stirred at −78 °C for 1 h. Dry EtOH (100 mmol) is then added via syringe, and the resulting mixture is stirred at room temperature for 15 min. The reaction is then quenched with 100 mL of saturated aqueous NH_4Cl. The aqueous layer was then extracted with ether (100 mL × 2) and dried ($MgSO_4$), and the solvent was removed in vacuo. The siloxane is purified as stated above.

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Supporting Information Available: General experimental procedures and spectral data for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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