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# Improved Synthesis of Aryltrialkoxysilanes via Treatment of Aryl Grignard or Lithium Reagents with Tetraalkyl Orthosilicates

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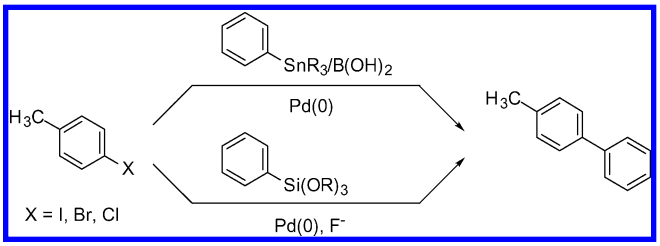
General reaction conditions for the synthesis of aryl(trialkoxy)silanes from aryl Grignard and lithium reagents and tetraalkyl orthosilicates ($Si(OR)_4$) have been developed. Ortho-, meta-, and para-substituted bromoarenes underwent efficient metalation and silylation at low temperature to provide aryl siloxanes. Mixed results were obtained with heteroaromatic substrates: 3-bromothiophene, 3-bromo-4-methoxypyridine, 5-bromoindole, and *N*-methyl-5-bromoindole underwent silylation in good yield, whereas a low yield of siloxane was obtained from 2-bromofuran, and 2-bromopyridine failed to give silylated product. The synthesis of siloxanes via organolithium and magnesium reagents was limited by the formation of di- and triarylated silanes ($Ar_2Si(OR)_2$ and $Ar_3SiOR$, respectively) and dehalogenated (Ar−H) byproducts. Silylation at low temperature gave predominantly monoaryl siloxanes, without requiring a large excess of the electrophile. Optimal reaction conditions for the synthesis of siloxanes from aryl Grignard reagents entailed addition of arylmagnesium reagents to 3 equiv of tetraethyl- or tetramethyl orthosilicate at −30 °C in THF. Aryllithium species were silylated using 1.5 equiv of tetraethyl- or tetramethyl orthosilicate at −78 °C in ether.

## Introduction

The metal-catalyzed cross-coupling reaction for the formation of carbon−carbon bonds between unsaturated centers is an indispensable synthetic tool for the preparation of useful industrial and pharmaceutical materials. Of the many combinations of organometallic nucleophiles and organic electrophiles in the literature,[1−3] the Stille[4] (organostannane) and Suzuki−Miyaura[5] (organoborane) coupling methodologies are the most widely employed for the synthesis of unsymmetrical biaryl derivatives and substituted alkenes due to the generally excellent yields, high stereoselectivities, and superior functional group tolerance (Scheme 1). Nonetheless, arylsilane derivatives have emerged as powerful alternatives to conventional arylmetalloids for the Pd(0)-catalyzed aryl−aryl coupling reaction with organohalides and organo(pseudo)halides. Aryl silanes avoid the inherent limitations associated with traditional methodologies: the Stille tin reagents and byproducts are toxic, and the Suzuki boron reagents can be difficult to synthesize and purify.

**SCHEME 1**




Previous studies from our group[6−14] and others[15−22] have shown that a variety of silicon derivatives undergo fluoride-mediated, Pd(0)-catalyzed aryl group transfer

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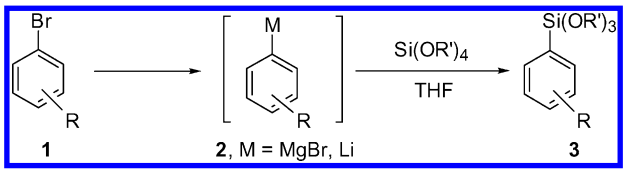
**SCHEME 2**




reactions. These earlier reports have demonstrated the relative mildness, wide-ranging functional group compatibility, and ease of workup of the siloxane-based cross-coupling process. However, the primary limitation of the siloxane protocol is the synthesis of the aryl siloxane reagents. Existing methods for the synthesis of aryl siloxanes fall into two categories: (1) treatment of an aryl Grignard or lithium reagent with a silicon electrophile (Scheme 2) and (2) silylation of an aryl iodide or bromide by triethoxysilane ($H-Si(OEt)_3$) in the presence of a Pd(0)[23,24] or Rh(I)[25] catalyst. The metalloid reaction, as presently constituted, is limited by the generally inferior yields of siloxane, most likely due to competing formation of di- and triarylated products (over-arylation). A general method for the synthesis of arylsiloxanes from aryllithium or magnesium reagents has not been reported, nor has a systematic study of this reaction been performed. We recently reported the preparation of ortho-substituted aryl siloxanes using directed orthometalation protocols.[14] The goal of the study reported herein was to develop a practical, general synthetic technique for the synthesis of aryl(trialkoxy)silanes utilizing standard organometallic reagents generated from the corresponding aryl halide by metal−halogen exchange.

## Results and Discussion

Traditionally, the synthesis of aryl siloxanes has been accomplished by the treatment of Grignard or organolithium reagents with either $SiCl_4$ (followed by alcoholysis),[16,26−34] $Cl-Si(OR)_3$,[30,35−37] or $Si(OR)_4$.[16,29,34,36,38−42] The use of $Si(OR)_4$ for the one-step preparation of aryl-siloxanes via the organometallic approach has several advantages, including the commercial availability, low cost, and ease of handling and storage of tetraalkoxy-orthosilicates.[43] The use of $SiCl_4$ as the silicon electrophile is of limited practicality for a number of reasons that include (a) moderate to poor product yield for the overall, two-step conversion, (b) the difficult transfer and handling of moisture-sensitive reagents and intermediates, and (c) multiple substitution results in the formation of difficult to separate byproducts.[26,30] In the past, large quantities of electrophile (20+-fold excess) have been employed to mitigate polyarylation; however, this leads to difficulties in product isolation and HCl contamination.[30] Treatment of the arylmetalloid with $Cl-Si(OR)_3$ should favor the formation of monoaryl siloxanes by preferential displacement of chloride from silicon.[30,35−37] As reported in the literature, not only are the yields somewhat better than the $SiCl_4$/alcoholysis technique, but the reaction involves a single step from the formation of the organometalloid.[37] However, use of $Cl-Si(OR)_3$ as the silicon electrophile still has several significant drawbacks: (1) unlike $SiCl_4$, $Cl-Si(OR)_3$ compounds are not commercially available and are tedious to prepare;[44−46] (2) while less reactive than the tetrachloride, chloro(trialkoxy)silane reagents still require careful handling to avoid hydrolysis of the reactive Si−Cl bond; and (3) surprisingly, even when excess electrophile is used or low temperatures are employed, over-arylation of silicon occurs, resulting in inseparable di- and triarylated byproducts.[30,43] Typically, the reaction of organometallic reagents with alkoxy silanes is more selective than the reaction with chlorosilanes.[43] Treatment of the arylmetalloid with the less reactive electrophile $Si(OEt)_4$ should favor the formation of monoaryl siloxanes because alkoxide is more difficult to displace from silicon than chloride.

For our studies, 4-methoxyphenylmagnesium bromide was selected as the initial nucleophile to be investigated in the metalation methodology (Table 1). The inexpensive, commercially available electrophiles tetramethyl orthosilicate ($Si(OMe)_4$), tetraethyl orthosilicate ($Si(OEt)_4$), and tetrachlorosilane ($SiCl_4$) were each evaluated for their efficacy in the formation of the Si−Ar bond. The results are summarized in Table 1. The temperature at which the Grignard reagent was added to the electrophile had a marked effect on the reaction. As seen in entries 1, 4, and 5, at temperatures above −30 °C a significant amount of the diaryl(dialkoxy)silane impurity **4** was formed, although no triaryl(alkoxy)silane was observed over the tested temperature range. The remainder of the reaction mixture was anisole, which resulted from the aqueous quench of unreacted arylmagnesium bromide. However, longer reaction time or elevated temper-

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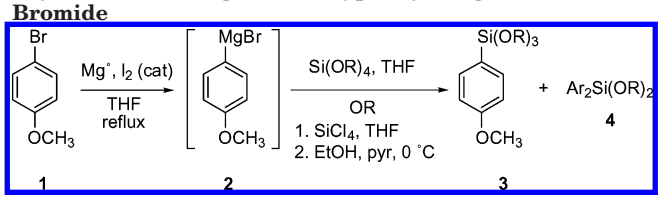
**TABLE 1. Optimization of the Synthesis of Arylsiloxanes Using 4-Methoxyphenyl Magnesium Bromide**




| | conditions[a] | | yield (%)[b,c] | |
|---|---|---|---|---|
| entry | silane/equiv | $T$ (°C) | 3 | 4 |
| 1 | $Si(OMe)_4$/3.0 | 25 | 47 | 47 |
| 2 | $Si(OMe)_4$/3.0 | −30 | 76 | 3 |
| 3 | $Si(OMe)_4$/1.5 | −30 | 65 | 4 |
| 4 | $Si(OEt)_4$/3.0 | 0 | 72 | 23 |
| 5 | $Si(OEt)_4$/3.0 | −10 | 70 | 23 |
| 6 | $Si(OEt)_4$/3.0 | −30 | 83 | 3 |
| 7 | $Si(OEt)_4$/1.5 | −30 | 76 | 2 |
| 8 | $Si(Cl)_4$/3.0[d] | −30 | 70[d] | 3 |

[a] Reactions of *p*-methoxy magnesium bromide **2** (1.0 equiv) with $Si(OR)_4$ or $SiCl_4$ (1.5 to 3.0 equiv) were allowed to stir at the given temperature in THF. The reaction mixture was stirred at the indicated temperature for 1 h and then at room temperature for 12 h. [b] GC yields were calculated using an internal standard (naphthalene); see Experimental Section. [c] Remainder of the product was anisole. [d] Yield of 4-(triethoxysilyl)anisole (**3**). The crude, concentrated 4-(trichlorosilyl)anisole was converted to the siloxane **3** by dropwise addition of the chlorosilane to EtOH/pyridine at 0 °C.

ature did not improve the yield. In addition, the amount of anisole remained constant regardless of the electrophile. It is likely that reduction occurs at least in part during the in situ formation of the Grignard reagent.

The best result was obtained when the Grignard reagent was treated at −30 °C with 3.0 equiv of the electrophile $Si(OEt)_4$ (83% yield, Table 1, entry 6); under identical reaction conditions, $Si(OMe)_4$ (76% yield, entry 2) and $SiCl_4$ (followed by alcoholysis) (70%, entry 8) also performed well (the yields were determined by GC analysis). In contrast, Shibata observed a 60% yield of siloxane using the two-step $SiCl_4$/alcoholysis method for the silylation of *p*-(4-propylcyclohexyl)phenylmagnesium bromide but only a 35% yield of siloxane via direct silylation with $Si(OMe)_4$.[16] The reaction conditions employed by Shibata were addition of the Grignard reagent to 1.5 equiv of silane at 0 °C.[16] In our study, a 2-fold decrease in the concentration of the electrophile slightly decreased the yield of the desired monoarylated silane but surprisingly did not stimulate the formation of diarylated byproduct (Table 1, entries 3 and 7).

Preliminary studies using commercial phenylmagnesium bromide indicated that increasing the concentration of the electrophile from 3 to 5 to 30 equiv did not improve the reaction outcome and only served to complicate product isolation. Little reaction improvement was observed with alternative ether solvents, and poor results were obtained with toluene or hexane. Ultimately, THF rather than lower-boiling $Et_2O$ was employed as the solvent in order to facilitate in situ formation of the Grignard reagent (which required heating to progress efficiently).

To demonstrate the scope of the Grignard reaction, a variety of substituted aryl bromides was examined (Table 2). The isolated yields obtained in our laboratories were generally better than those reported in the literature. Only trace amounts of diaryl(dialkoxy)silane contaminants were observed for all entries. Again, the remaining yield was of reduced (dehalogenated) aryl halide. As expected, tetramethyl orthosilicate and tetraethyl orthosilicate worked equally well (entries 1 and 2, 6 and 7).

Surprisingly, the results were comparable with o-, m-, and p-substituted anisyl and tolyl Grignard reagents (entries 2−4, and 7−9, respectively); all yields were approximately 80%. Also, 3,4-(methylenedioxy)bromobenzene underwent smooth conversion to the siloxane (entry 5, 74% yield). This result contradicts the findings of Selin and co-workers, who observed acceptable yields of *o*- and *p*- but not *m*-(triethoxysilyl)toluene. The reaction conditions employed by Selin entailed addition of the Grignard reagent to 2.0 equiv of tetraethyl orthosilicate at reflux.[38]

Several researchers have reported acceptable yields of arylsiloxane using Barbier reaction conditions, the in situ formation of the reactive Grignard intermediate in the presence of the silicon electrophile.[36,47−49] Ideally, Barbier conditions are a method of controlling multiple substitution at silicon, because the Grignard reagent is immediately consumed and never present in excess. For example, Shea and co-workers combined magnesium metal, a crystal of iodine, and 4 equiv of tetraethyl orthosilicate and THF and brought the mixture to reflux.[48] A solution of *p*-bromoanisole in THF was then added slowly, and the mixture was allowed to reflux for 12 h; a 74% isolated yield of 4-(triethoxysilyl)anisole was obtained without mention of byproducts. This result was not reproducible in our laboratories: under identical Barbier reaction conditions, only 50% yield at 80% conversion was achieved; although no diarylated silane was observed, the remaining yield was of reduced arene.

In continuing pursuit of our goal of synthesizing a variety of highly functionalized siloxane derivatives for use in aryl coupling reactions, we turned our efforts to determining the scope and limitations of the synthesis of aryl siloxanes from lithium reagents. For our studies, 4-lithiotoluene (Table 3) was selected as the initial nucleophile for investigation of the formation of the Si−Ar bond. The electrophile tetraethyl orthosilicate ($Si(OEt)_4$) was chosen for initial study, in lieu of tetramethyl orthosilicate ($Si(OMe)_4$), which freezes at the low temperatures required for the formation of aryllithium reagents, or tetrachlorosilane ($SiCl_4$), because the subsequent alcoholysis step had proven to be problematic (low yielding and complicated by polymerization). Both ether and THF were evaluated for their suitability in the silylation of aryllithium intermediates, although ether was the solvent of choice for practical reasons. The higher-boiling THF was preferred for the Grignard protocol because it allowed for heating the reaction to initiate formation of the Grignard reagent. The more reactive lithium reagents rapidly decompose at ambient temperatures and do not require higher-boiling solvents. The results of the silylation reactions are shown in Table 3.

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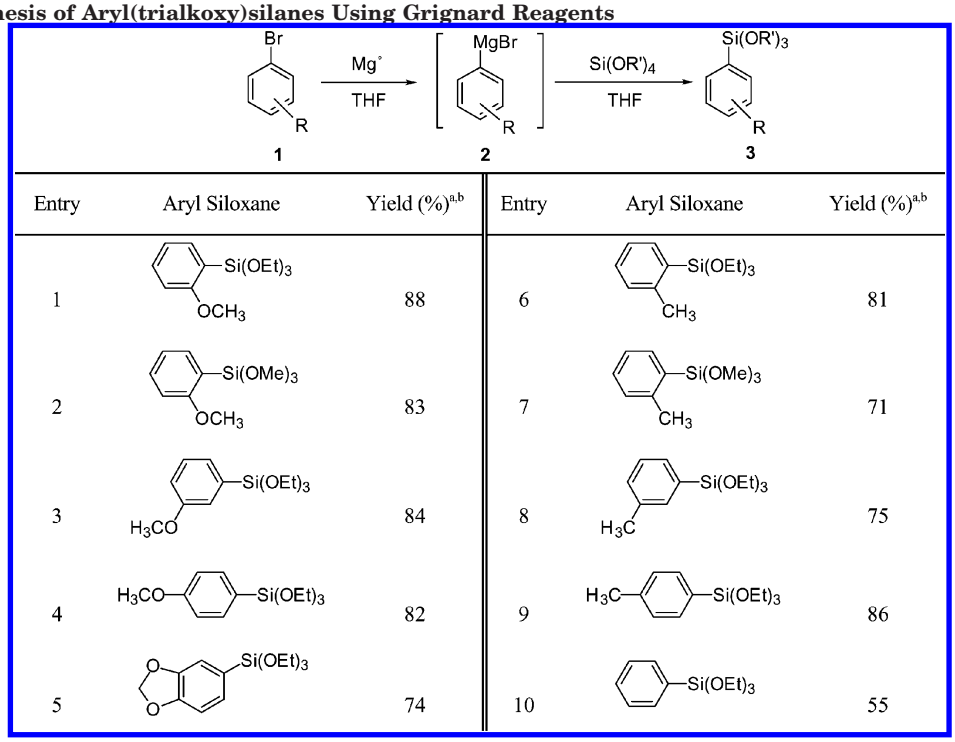
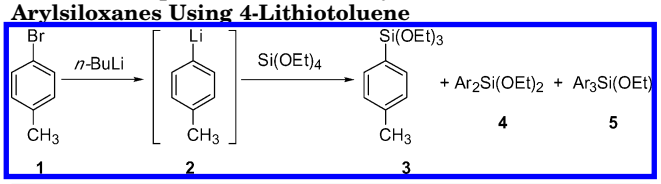
**TABLE 2. Synthesis of Aryl(trialkoxy)silanes Using Grignard Reagents**




| Entry | Aryl Siloxane | Yield (%)[a,b] | Entry | Aryl Siloxane | Yield (%)[a,b] |
|---|---|---|---|---|---|
| 1 |  | 88 | 6 |  | 81 |
| 2 |  | 83 | 7 |  | 71 |
| 3 |  | 84 | 8 |  | 75 |
| 4 |  | 82 | 9 |  | 86 |
| 5 |  | 74 | 10 |  | 55 |

[a] Reactions of arylmagnesium bromide **2** (1.0 equiv) with $Si(OEt)_4$ or $Si(OMe)_4$ (3.0 equiv) were allowed to stir at −30 °C in THF for 1 h and then at room temperature for 12 h. [b] Yields of **3** are after distillation (purity > 95%). The remainder of the product was of the reduced (dehalogenated) arene.

**TABLE 3. Optimization of the Synthesis of Arylsiloxanes Using 4-Lithiotoluene**




| | conditions[a] | | | yield (%)[b,c] | | |
|---|---|---|---|---|---|---|
| entry | equiv of $Si(OEt)_4$ | solvent | $T$ (°C) | **3** | **4** | **5** |
| 1 | 1.5 | THF | 0 | 7 | 25 | 54 |
| 2 | 1.5 | THF | −30 | 74 | 12 | 1 |
| 3 | 1.5 | $Et_2O$ | −30 | 77 | 6 | 0 |
| 4 | 1.5 | THF | −78 | 81 | 9 | 0 |
| 5 | 1.5 | $Et_2O$ | −78 | 82 | 5 | 1 |
| 6 | 3.0 | $Et_2O$ | −78 | 86 | 3 | 1 |

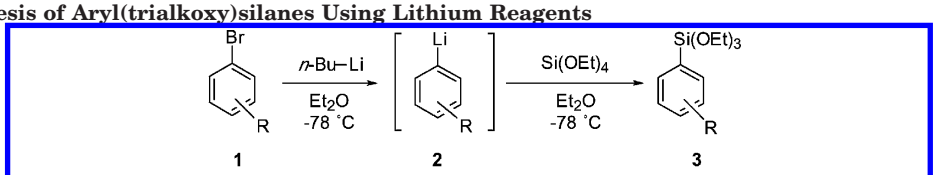
[a] Reactions of *p*-tolyllithium **2** (1.0 equiv) with $Si(OEt)_4$ (1.5−3.0 equiv) were allowed to stir at the given temperature; the reaction was complete in 1 h. [b] GC yields were calculated using an internal standard (naphthalene); see Experimental Section. [c] Remainder of the product was toluene.

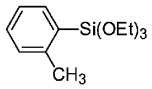
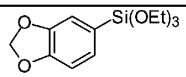
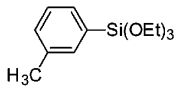
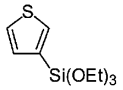
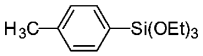
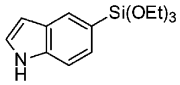
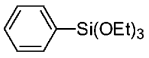
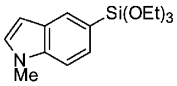
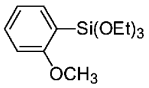
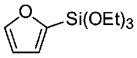
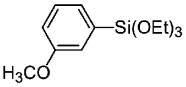
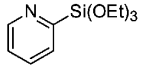
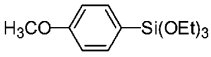
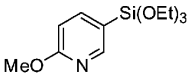
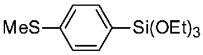
Like the Grignard approach, the temperature at which the lithium reagent was added to the electrophile dramatically effected the reaction outcome. As seen in entries 1−3, at temperatures above −78 °C a significant amount of the diaryl(dialkoxy)silane impurity **4** was formed. In addition, trialkylated product **5** was observed. Note that the analogous transformation employing Grignard reagents did not lead to the formation of trialkylated products, because of the significantly lower reactivity of Grignard reagents. At 0 °C (entry 1), the major product was tris-*p*-tolyl(ethoxy)silane (**5**). In contrast, at −30 °C (entries 2 and 3) and −78 °C (entries 4−6), formation of the trialkylated silane **5** was effectively suppressed, although diarylated silane **4** was formed. As in the Grignard reaction, reduction (dehalogenation) of the starting material also was observed. At low temperature, the reaction was essentially insensitive to the solvent ($Et_2O$ and THF were tolerated, entries 4 and 5) and only a small excess of the electrophile was needed (1.5−3.0 equiv were equally effective, entries 5 and 6).

The best result was obtained when the lithium reagent in ether was added to 3.0 equiv of the electrophile $Si(OEt)_4$ at −78 °C (86% yield, entry 6). Experience garnered applying these reaction conditions to other substrates would show that more than 1.5 equiv was unnecessary to achieve the optimum yield of siloxane. The electrophile and the lithium reagent were allowed to stir at −78 °C until the reaction ceased to progress. Quenching the reaction at −78 °C before allowing the mixture to slowly warm to room-temperature mitigated formation of di- and triarylated byproducts.

To demonstrate the scope of the optimized silylation reaction, a variety of substituted aryl bromides were examined (Table 4). Only trace amounts of diaryl(dialkoxy)silane contaminants were observed for most entries; again, the remaining yield was of reduced (dehalogenated) aryl halide. The best results were obtained with less reactive (less electron-rich) aryllithium derivatives: the less electron-rich tolyl series (entries 1−3) and electron-neutral phenyl (entry 4) outperformed the more electron-rich anisyl/thioanisyl series (entries 5−8). Bearing two electron-donating substituents, the 3,4-(methylenedioxy)phenyllithium intermediate (entry 9) proved to be highly reactive: the major product was the diarylated silane. Reducing the temperature to −110 °C or increasing the concentration of $Si(OEt)_4$ failed to improve the yield. Note that the analogous Grignard

**TABLE 4. Synthesis of Aryl(trialkoxy)silanes Using Lithium Reagents**




| Entry | Aryl Siloxane (**3**) | % Yield[a,b] | Entry | Aryl Siloxane (**3**) | % Yield[a,b] |
|---|---|---|---|---|---|
| 1 |  | 79 | 9 |  | 30[c] |
| 2 |  | 71 | 10 |  | 50 |
| 3 |  | 85 | 11 |  | 70 |
| 4 |  | 74 | 12 |  | 60 |
| 5 |  | 60 | 13 |  | 22[d] |
| 6 |  | 66 | 14 |  | 0 |
| 7 |  | 67 | 15 |  | 25[c] |
| 8 |  | 50 | | | |

[a] Reactions of aryllithium **2** (1.0 equiv) with $Si(OEt)_4$ (1.5 equiv) were allowed to stir at −78 °C for 1 h in $Et_2O$. [b] Yields of **3** are after distillation or chromatography (purity > 95%). [c] Major product was $Ar_2Si(OEt)_2$. [d] GC analysis indicated a 2:1:1 ratio of mono-:di-:triarylalkoxysilanes.

reagent underwent clean silylation (Table 2, entry 5), affording 74% yield of triethoxy(3,4-methylenedioxyphenyl)silane. Again, as with magnesium reagents, the reaction using aryllithium intermediates was insensitive to the position of substituents: o-, m-, and p-substituted arenes underwent silylation with equal efficiency (Table 4, entries 1−3 and 5−8).

Mixed results were obtained for silylation of heteroaromatic systems (entries 10−15). For example, acceptable yields of siloxane were obtained from the corresponding bromothiophene and indole derivatives (entries 10−12), whereas silylation of 2-bromofuran was inefficient and 2-bromopyridine failed to give any of the desired siloxane (entries 13 and 14). The yield of 2-(triethoxysilyl)furan was compromised by the formation of di- and triarylated products, indicating that 2-lithiofuran was successfully formed in situ but was highly reactive. In contrast, attempted silylation of 2-bromopyridine led to exclusive formation of pyridine, indicating successful formation of the organolithium intermediate but unsuccessful silylation. The nearly quantitative formation of 2-lithiopyridine under our reaction conditions was confirmed by capture with the more reactive electrophiles TMS−Cl and benzaldehyde. In an effort to increase the nucleophilicity of the pyridine metalloid, silylation of 3-bromo-4-methoxypyridine (entry 15) was attempted with dramatic results. The desired monopyridinyl siloxane was isolated in 25% yield, in addition to significant quantities of dipyridinyl- and tripyridinyl siloxanes.[50]

The results with pyridine derivatives were not surprising given the literature precedence. Using analogous reaction conditions, Schmidbaur and co-workers synthesized 2- and 3-(triethoxysilyl)pyridine in 10 and 16% yield, respectively.[51] Zeldin carefully examined the synthesis of 3-pyridinyl-substituted ethoxysilane monomers, focusing on the preparation of diethoxy(methyl)(3-pyridinyl)silane ($PyrSiMe_2(OEt)$).[30] A variety of silicon electrophiles were evaluated, most notably $MeSiCl_3$ (followed by alcoholysis), $MeSi(OEt)_2Cl$, and $MeSi(OEt)_3$, under different metalation conditions. Three significant conclusions were drawn: (1) $MeSi(OEt)_3$ (3 equiv) was ideal for the methyl(diethoxy)silylation of 3-pyridinylmagnesium

(50) Handy, C. J. Doctoral Dissertation, University of Maryland, College Park, Maryland, 2002.
(51) Riedmiller, F.; Jockisch, A.; Schmidbaur, H. *Organometallics* **1998**, *17*, 4444−4453.

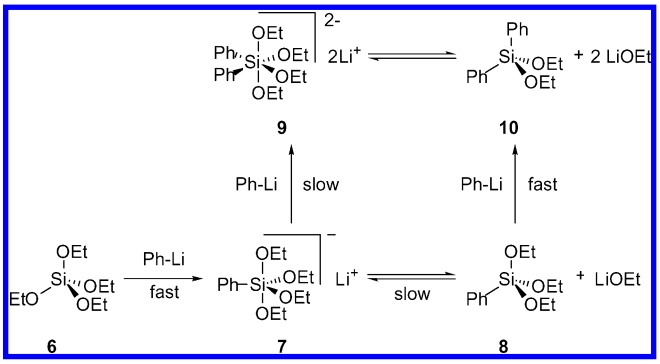
bromide, yielding 45% of the desired monosubstitution product and no diarylated adduct; (2) in contrast, a 20-fold excess of $MeSiCl_3$ was required to mitigate multiple substitution by 3-lithiopyridine and, as with $MeSi(OEt)_2Cl$, still yielded a significant amount of the diarylated silane and led to the formation of mixed silanes and silicates; and (3) the use of pyridinyllithium reagents led to the formation of a pentacoordinate anionic species between the silane product and LiOEt formed in the displacement reaction.[30] Zeldin obtained the best results when the pyridinyl Grignard reagent was generated under Barbier conditions; in fact, when the *preformed* 3-pyridinylmagnesium bromide was treated with $MeSi(OEt)_3$, no reaction was observed.[30] Given that pyridinyl Grignard reagents are reputed to be unreactive toward most electrophiles,[52,53] Zeldin's result is striking. Unfortunately in our laboratories, using the Barbier reaction conditions reported by Zeldin but substituting $Si(OEt)_4$ as the electrophile led to unsuccessful preparation of 3-(triethoxy)pyridine. The only products obtained were the homocoupled product 3,3′-dipyridyl and pyridine. Homocoupling (Wurtz-type coupling) is a common side-reaction of organomagnesium reagents.[54]

With both Grignard and lithium reagents, the formation of di- and triarylated silanes was best controlled by employing reduced reaction temperatures. In contrast, change of solvent or the use of large excesses of the electrophile had relatively little impact on the reaction outcome. It is unlikely that the temperature effect observed in the arylation is due solely to the attenuation of organometalloid reactivity at reduced temperature. Contrary to expectation, lower temperatures have been shown to increase the reactivity of the organometallic species toward electrophiles by causing deaggregation of the organometalloid.[54] This phenomenon would clearly favor multiple arylation of the silane. Instead, a reduction in diarylation was observed when the temperature was reduced; therefore, the reactivity of the nucleophile must not be greatly altered within the temperature range studied. In fact, it has been observed that phenyllithium does not change its aggregation state until temperatures as low as −100 °C are reached.[54]

The relative rates of reaction of alkoxysilanes with organometallic reagents follows the order of silane electrophilicity $Si(OEt)_4 > RSi(OEt)_3 > R_2Si(OEt)_2 > R_3Si(OEt)$; the same order is observed with chlorosilanes.[43] Given the relative reactivities, polyarylation should be stoichiometrically controllable or mitigated by slow addition of the organometallic reagent to the electrophile. On the contrary, even at low temperature, with less than 1 equiv of organometallic reagent, diarylated and even triarylated byproducts are observed, suggesting that factors other than organometalloid reactivity or electrophile electronics are at play.[55]

The accepted mechanism of alkylation comprises formation of pentacoordinate adduct **7** as shown in Scheme 3.[43,55,56] Diarylation is the result of either direct attack

**SCHEME 3**




of a second aryl nucleophile on the pentacoordinate silicate **7** to form hexacoordinate intermediate **9** or attack on the tetracoordinate monoaryl silane **8**.

Again, it was observed that at lower temperatures the formation of diaryl products was minimal. We propose that at reduced temperature, the pentacoordinate silicate **7** formed by initial attack of the metalloid reagent does not decompose (with loss of alkoxide) to give the neutral monoaddition product **8**. The stable, anionic monoaryl silicate **7** is less reactive than its neutral monoaryl silane counterpart **8**; in effect, the monoaryl silane **8** is "protected" as the pentacoordinate silane against multiple arylation. This result is quite different than what has been observed for chlorosilanes, where the analogous pentacoordinate tetrachloroaryl silicate ($Ar-SiCl_4^-$) has been found to be more reactive than the neutral tetracoordinate monoaryl silane ($Ar-SiCl_3$).[43,55,56]

## Conclusion

General reaction conditions for the synthesis of aryl(trialkoxy)silanes from aryl Grignard and lithium reagents and functionalized silanes have been developed. Although examples in the literature have described the use of a range of silicon electrophiles (including $SiCl_4$ and $Cl-Si(OR)_3$), our studies have demonstrated that tetraalkyl orthosilicates ($Si(OR)_4$) allow for the most direct and convenient synthesis of arylsiloxanes in that they are commercially available, inexpensive, and air and moisture stable and generally give an excellent yield of the desired siloxanes without subsequent transformations (i.e., conversion of the trichlorosilane to the siloxane). Using the reaction conditions developed herein, we observed o-, m-, and p-substituted bromoarenes to undergo efficient metalation and silylation. Mixed results were obtained with heteroaromatic substrates: 3-bromothiophene, 3-bromo-4-methoxypyridine, 5-bromoindole, *N*-methyl-5-bromoindole all underwent silylation in good yield, whereas low yields of siloxanes were obtained from 2-bromofuran and 2-bromopyridine failed to be silylated. The key feature of these reactions was the use of low temperatures during addition of the orthosilicate, which allowed for the formation of predominantly monoarylated siloxanes, without requiring more than 1.5−3.0 equiv of the electrophile.

The methodology reported above can be employed for the synthesis of highly functionalized aryl siloxane

(52) French, H. E.; Sears, K. *J. Am. Chem. Soc.* **1951**, *73*, 469−470.
(53) Fischer, F. C.; Havinga, E. *Recl. Trav. Chim. Pays-Bas.* **1965**, *84*, 439−439.
(54) Schlosser, M. In *Organometallics in Synthesis A Manual*, 2nd ed.; Schlosser, M., Ed.; John Wiley and Sons: New York, 2002; p 1−352.
(55) Gilman, H.; Brannen, C. *J. Am. Chem. Soc.* **1951**, *73*, 4640−4641.
(56) Corriu, R. J. P.; Guérin, C.; Moreau, J. J. E. *Top. Stereochem.* **1984**, *15*, 43−198.

derivatives for the siloxane coupling technologies, and we have recently reported initial studies for the synthesis of the antitumor antibiotics streptonigrin and lavendamycin.[12] Additional studies in this area are underway, and as always, the results will be reported in due course.

## Experimental Section

**Optimization of the Synthesis of 4-(Triethoxysilyl)-anisole Using 4-Bromomagnesium Anisole (Table 1).** A 10 mL, three-neck, pear-shaped flask was fitted with an addition funnel, a reflux condenser, a rubber septum, and a stir bar. The flask was then charged with freshly washed magnesium turnings (134 mg, 5.50 mmol), flame-dried under vacuum, and back-filled with argon. THF (1.0 mL) was added to the magnesium turnings via syringe. The addition funnel was charged with 4-bromoanisole (935 mg, 628 $\mu$L, 5.00 mmol) in 2.0 mL of THF. The reaction was initiated by addition of 5−10 drops of the bromoanisole solution to the magnesium turnings with stirring, followed by gentle heating. The rest of the bromoanisole solution was then added at such a rate that the THF maintained a moderate reflux. Upon final addition, the solution was allowed to stir at room temperature for 1 h, at which point GC analysis of a quenched aliquot of the reaction mixture indicated complete consumption of 4-bromoanisole. The 4-(bromomagnesium)anisole solution was then transferred via cannula to a second flame-dried addition funnel, to which was fitted a 50 mL round-bottom flask containing the indicated silane (1.5−3.0 equiv) and the internal standard naphthalene (64 mg, 0.50 mmol) in 10.0 mL of THF. The silane solution was cooled to the indicated temperature, and then the 4-(bromomagnesium)anisole solution was added dropwise (1 drop per second). The solution was allowed to stir at the indicated temperature for 1 h and then at room temperature for 12 h. Progress was monitored by GC analysis of aliquots of the quenched reaction mixture. GC response factors relative to the internal naphthalene standard were determined, and the observed percentages of products were normalized accordingly. The reduced product anisole was identified by comparison of the GC retention time to that of an authentic sample. Diarylated products were identified by GCMS; triarylated products were not observed. Aliquots of the crude, concentrated 4-(trichlorosilyl)anisole were converted to the siloxane by dropwise addition (1 drop per second) of the chlorosilane to EtOH/pyridine at 0 °C.

**General Procedure for Synthesis of Siloxanes from Grignard Reagents (Table 2).** Unless otherwise indicated, all reactions were performed on a 5 mmol scale. A 10 mL, three-neck, pear-shaped flask was fitted with an addition funnel, a reflux condenser, a rubber septum, and a stir bar. The flask was then charged with freshly washed magnesium turnings (134 mg, 5.50 mmol), flame-dried under vacuum, and back-filled with argon. THF (1.0 mL) was added to the magnesium turnings via syringe. The addition funnel was charged with the aryl halide (5.00 mmol) in 2.0 mL THF. The reaction was initiated by addition of 5−10 drops of the aryl halide solution to the magnesium turnings with stirring, followed by gentle heating. The rest of the aryl halide solution was then added at such a rate that the THF maintained a moderate reflux. Upon final addition, the solution was allowed to stir at room temperature until GC analysis of a quenched aliquot of the reaction mixture indicated complete consumption of aryl halide. The arylmagnesiumhalide solution was then transferred via cannula to a second flame-dried addition funnel, to which was fitted a 50 mL round-bottom flask containing tetraethyl orthosilicate or tetramethyl orthosilicate (15.00 mmol) in 10.0 mL of THF. The silane solution was cooled to −30 °C, and then the 4-arylmagnesiumhalide solution was added dropwise (1 drop per second). The solution was allowed to stir at the indicated temperature for 1 h and then at room temperature for 12 h. The crude reaction mixture was then poured into 50 mL of pentane in a 200 mL separatory funnel. The amber solution was washed with 3 × 25 mL of water, dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification of the residue by bulb-to-bulb distillation yielded the siloxane.

**2-(Triethoxysilyl)anisole (Table 2, Entry 1).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using 2-bromoanisole (935 mg, 623 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetraethyl orthosilicate (3.13 g, 3.35 mL, 15.0 mmol) in THF. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 1.19 g (88%) of 2-(triethoxysilyl)anisole as a colorless oil: IR (neat) 3067 (m), 2967 (s), 2922 (s, 2891 (s), 2829 (m), 2780 (w), 2762 (w), 1590 (s), 1569 (s), 1459 (s), 1241 (s) $cm^{-1}$; $^1H$ (NMR) ($CDCl_3$) $\delta$ 1.21 (t, $J$ = 7.2, 9H), 3.79 (s, 3H), 3.84 (q, $J$ = 7.2, 6H), 6.83 (d, $J$ = 8.2, 1H), 6.95 (t, $J$ = 7.2, 1H), 7.38 (m, 1H), 7.63 (dd, $J$ = 1.6, 7.2, 1H); $^{13}C$ (NMR) ($CDCl_3$) $\delta$ 18.2, 55.1, 58.7, 109.6, 119.2, 120.5, 132.2, 137.5, 164.3; MS (*m/z*) 271 ($M^+ + 1$, 42), 225 (100), 195 (21), 181 (36), 139 (25), 119 (21), 91 (24), 77 (14); HRMS for $C_{13}H_{23}O_4Si$ calcd 271.1366 ($M^+ + 1$), found 271.1354.

**2-(Trimethoxysilyl)anisole (Table 2, Entry 2).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using 2-bromoanisole (935 mg, 623 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetramethyl orthosilicate (2.28 g, 2.21 mL, 15.0 mmol) in THF. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 948 mg (83%) of 2-(trimethoxysilyl)anisole as a colorless oil: IR (neat) 2970 (s), 2920 (m), 1570 (m), 1486 (w), 1078 (s) $cm^{-1}$; $^1H$ (NMR) ($CDCl_3$) $\delta$ 3.61 (s, 9H), 3.80 (s, 3H), 6.87 (d, $J$ = 8.3, 1H), 6.97 (t, $J$ = 7.2, 1H), 7.42 (m, 1H), 7.59 (dd, $J$ = 1.7, 7.2, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 50.4, 54.9, 109.4, 117.7, 120.3, 132.2, 137.0, 164.1; MS (*m/z*) 228 (100), 196 (61) 167 (55), 137 (18), 121 (44), 91 (45), 58 (29); HRMS for $C_{10}H_{16}O_4Si$ calcd 228.0818, found 228.0809.

**3-(Triethoxysilyl)anisole (Table 2, Entry 3).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using 3-bromoanisole (935 mg, 633 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetraethyl orthosilicate (3.13 g, 3.35 mL, 15.0 mmol) in THF. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 1.14 g (84%) of 3-(triethoxysilyl)anisole as a colorless oil: IR (neat) 2975 (s), 2927 (m), 2887 (m), 1572 (m), 1482 (w), 1410 (w), 1391 (w), 1284 (w), 1249 (m), 1234 (m), 1167 (m), 1078 (vs) $cm^{-1}$; $^1H$ (NMR) ($CDCl_3$) $\delta$ 1.25 (t, $J$ = 7.0, 9H), 3.81 (s, 3H), 3.87 (q, $J$ = 7.0, 6H), 6.96−6.98 (m, 1H), 7.21−7.33 (m, 3H); $^{13}C$ (NMR) ($CDCl_3$) $\delta$ 18.3, 55.1, 58.8, 116.1, 119.8, 127.1, 129.2, 132.4, 159.0; MS (*m/z*) 270 (100), 256 (12), 255 (70), 226 (28), 225 (64), 211 (23), 197 (13), 182 (11), 181 (41), 169 (37), 168 (13), 167 (29), 163 (10), 154 (16), 153 (27), 149 (22), 147 (61), 139 (20), 137 (14), 136 (55), 135 (95); HRMS for $C_{13}H_{22}O_4Si$ calcd 270.1287, found 270.1282.

**4-(Triethoxysilyl)anisole (Table 2, Entry 4).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using 4-bromoanisole (935 mg, 626 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetraethyl orthosilicate (3.13 g, 3.35 mL, 15.0 mmol) in THF. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 1.11 g (82%) of 4-(triethoxysilyl)anisole as a colorless oil: IR (neat) 2975 (s), 2926 (m), 2894 (m), 1597 (s), 1505 (m), 1282 (m), 1249 (m), 1167 (s), 1127 (vs), 1104 (vs), 1080 (vs) $cm^{-1}$; $^1H$ (NMR) ($CDCl_3$) $\delta$ 1.24 (t, $J$ = 7.0, 9 H), 2.34 (s, 3H), 3.86 (q, $J$ = 7.0, 6 H), 6.92 (d, $J$ = 8.6, 2 H), 7.61 (d, $J$ = 8.6, 2 H); $^{13}C$ (NMR) ($CDCl_3$) $\delta$ 18.1, 54.9, 58.6, 113.6, 122.0, 136.4, 161.4; MS (*m/z*) 270 (52), 255 (53), 225 (38), 211 (25), 181 (28), 169 (27), 149 (22), 147 (100), 135 (32); HRMS for $C_{13}H_{22}O_4Si$ calcd 270.1287, found 270.1261. The IR and $^1H$ and $^{13}C$ NMR data were identical to published spectral data.[23]

**4-(Triethoxysilyl)-1,2-(methylenedioxy)benzene (Table 2, Entry 5).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using 4-bromo-1,2-(methylenedioxy)benzene (1.01 g, 602 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetraethyl orthosilicate (3.13 g, 3.35 mL, 15.0 mmol) in THF. Bulb-to-bulb

distillation (125 °C, 0.5 Torr) afforded 1.00 g (74%) of 4-(triethoxysilyl)-1,2-(methylenedioxy)benzene as a colorless oil: IR ($CCl_4$) 2976 (s), 2926 (m), 2886 (s), 1613 (w), 1503 (w), 1487 (m), 1422 (m), 1237 (m), 1168 (m), 1080 (s), 1045 (m) $cm^{-1}$; $^1H$ (NMR) ($CDCl_3$) $\delta$ 1.24 (t, $J$ = 6.8, 9H), 3.85 (q, $J$ = 6.8, 6H), 5.95 (s, 2H), 6.86 (d, $J$ = 7.6, 1H), 7.12 (s, 1H), 7.19 (d, $J$ = 7.6, 1H); $^{13}C$ (NMR) ($CDCl_3$) $\delta$ 18.1, 59.9, 100.8, 108.8, 114.2, 123.9, 129.6, 147.6, 149.7; MS (*m/z*) 284 (100), 239 (39), 226 (28), 211 (10), 195 (14), 183 (25), 167 (18), 153 (13), 149 (24), 148 (14), 147 (75), 135 (12); HRMS for $C_{13}H_{20}O_5Si$ calcd 284.1080, found 284.1083.

**2-(Triethoxysilyl)toluene (Table 2, Entry 6).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using 2-bromotoluene (855 mg, 601 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetraethyl orthosilicate (3.13 g, 3.35 mL, 15.0 mmol) in THF. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 1.03 g (81%) of 2-(triethoxysilyl)toluene as a colorless oil: IR ($CCl_4$) 3054, 2971, 2922, 2881, 1442, 1393, 1283, 1162, 1079 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.26 (t, $J$ = 7.0, 9H), 2.26 (s, 3H), 3.87 (q, $J$ = 7.0, 6H), 7.17 (m, 2H), 7.32 (m, 1H), 7.74 (m, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 18.2, 22.4, 58.5, 124.7, 129.7, 129.9, 130.5, 136.5, 144.5, MS (*m/z*) 254 (48), 209 (44), 208 (19), 162 (55), 147 (100), 119 (51), 91 (50), 79 (15); HRMS for $C_{13}H_{22}O_3Si$ calcd 254.1349, found 254.1338. The IR and $^1H$ and $^{13}C$ NMR data were identical to published spectral data.[38]

**2-(Trimethoxysilyl)toluene (Table 2, Entry 7).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using 2-bromotoluene (855 mg, 601 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetramethyl orthosilicate (2.28 g, 2.21 mL, 15.0 mmol) in THF. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 754 mg (71%) of 2-(trimethoxysilyl)toluene as a colorless oil: IR (neat) 3052 (w), 3008 (w), 2942 (s), 2840 (s), 1592 (m), 1471 (m), 1456 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.48 (s, 3H), 3.61 (s, 9H), 7.17 (m, 2H), 7.31 (m, 1H), 7.67 (d, $J$ = 7.5, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 22.2, 50.4, 124.7, 128.4, 129.7, 130.6, 136.3, 144.4; MS (*m/z*) 212 (61), 151 (16), 121 (100), 60 (73); HRMS for $C_{10}H_{16}O_3Si$ 212.0869, found 212.0859.

**3-(Triethoxysilyl)toluene (Table 2, Entry 8).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using 3-bromotoluene (855 mg, 607 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetraethyl orthosilicate (3.13 g, 3.35 mL, 15.0 mmol) in THF. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 954 mg (75%) of 3-(triethoxysilyl)toluene as a colorless oil: IR (neat) 2975 (s), 2926 (s), 2885 (s), 1577 (w), 1480 (w), 1442 (m), 1390 (m), 1295 (w), 1225 (w), 1167 (s), 1104 (vs), 1079 (vs) $cm^{-1}$; $^1H$ (NMR) ($CDCl_3$) $\delta$ 1.25 (t, $J$ = 7.2, 9H), 2.36 (s, 3H), 3.87 (q, $J$ = 7.2, 6H), 7.23−7.29 (m, 2H), 7.46−7.48 (m, 2H); $^{13}C$ (NMR) ($CDCl_3$) $\delta$ 18.4, 21.7, 58.9, 128.0, 130.8, 131.4, 132.0, 135.6, 137.4; MS (*m/z*) 254 (41), 239 (6), 209 (52), 195 (6), 162 (44), 147 (100), 119 (53), 91 (42), 66 (6); HRMS for $C_{13}H_{22}O_3Si$ calcd 254.1338, found 254.1331.

**4-(Triethoxysilyl)toluene (Table 2, Entry 9).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using 4-bromotoluene (855 mg, 638 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetraethyl orthosilicate (3.13 g, 3.35 mL, 15.0 mmol) in THF. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 1.09 g (86%) of 4-(triethoxysilyl)toluene as a colorless oil: IR ($CCl_4$) 2975 (s), 2926 (m), 2885 (m), 1167(s), 1124 (vs), 1103 (vs), 1080 (vs) $cm^{-1}$; $^1H$ (NMR) ($CDCl_3$) $\delta$ 1.24 (t, $J$ = 7.0, 9 H), 2.36 (s, 3 H), 3.86 (q, $J$ = 7.0, 6 H), 7.19 (d, $J$ = 7.9, 2 H), 7.57(d, $J$ = 7.9, 2 H); $^{13}C$ (NMR) ($CDCl_3$) $\delta$ 18.2, 21.5, 58.6, 127.4, 128.6, 134.8, 140.2; MS (*m/z*) 254 (23), 209 (38), 181 (5), 165 (16), 162 (30), 153 (19), 147 (100), 135 (17); HRMS for $C_{13}H_{22}O_3Si$ calcd 254.1363, found 254.1338. The IR and $^1H$ and $^{13}C$ NMR data were identical to published spectral data.[23]

**Triethoxyphenylsilane (Table 2, Entry 10).** The general procedure for synthesis of siloxanes from Grignard reagents was followed using bromobenzene (785 mg, 527 $\mu$L, 5.00 mmol), magnesium turnings (134 mg, 5.50 mmol), and tetraethyl orthosilicate (3.13 g, 3.35 mL, 15.0 mmol) in THF. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 661 mg (55%) of triethoxyphenylsilane as a colorless oil: spectral data is reported above; IR ($CCl_4$) 3140 (w), 2976 (s), 2928 (m), 2941 (m), 1431 (m), 1391 (m), 1129 (s), 1102 (s), 1094 (s), 1080 (s) $cm^{-1}$; $^1H$ (NMR) ($CDCl_3$) $\delta$ 1.25 (t, $J$ = 7.0, 9 H), 3.88 (q, $J$ = 7.0, 6 H), 7.3−7.5 (m, 3 H), 7.6−7.8 (m, 2 H); $^{13}C$ (NMR) ($CDCl_3$) $\delta$ 18.1, 58.7, 127.8, 130.2, 131.1, 134.7; MS (*m/z*) 240 (16), 195 (38), 181 (13), 162 (28), 147 (100), 139 (33), 135 (33); HRMS for $C_{12}H_{20}O_3Si$ calcd 240.1182, found 240.1141. The IR and $^1H$ and $^{13}C$ NMR data were identical to published spectral data.[23]

**Optimization of the Synthesis of 4-(Triethoxysilyl)-toluene Using 4-Lithioanisole (Table 3).** A solution of *n*-BuLi (1.5 M in pentane, 3.33 mL, 5.00 mmol) was added dropwise (1 drop per second) to a stirring solution of 4-bromotoluene (855 mg,615 $\mu$L, 5.00 mmol) in $Et_2O$ (15.0 mL) at room temperature. After 1 h, the solution was cooled to −78 °C and added via cannula to a stirring solution of tetraethyl orthosilicate (1.5−3.0 equiv) and the internal standard biphenyl (77 mg, 0.50 mmol) in $Et_2O$ (15.0 mL) at −78 °C. Progress was monitored by GC analysis of aliquots of the quenched reaction mixture. GC response factors relative to the internal standard were determined, and the observed percentages of products were normalized accordingly. The reduced product toluene was identified by comparison of the GC retention time to that of an authentic sample. Polyarylated products were identified by GCMS.

**General Procedure for Synthesis of Siloxanes from Lithium Reagents Using *n*-BuLi (Table 4).** Unless otherwise indicated, all reactions were performed on a 5 mmol scale. A solution of *n*-BuLi (1.6 M in pentane, 3.1 mL, 5.0 mmol) was added dropwise (1 drop per second) to a stirring solution of the aryl halide (5.00 mmol) in $Et_2O$ or THF (7.0 mL) at room temperature. After 1 h, the solution was cooled to −78 °C and added via cannula to a stirring solution of tetraethyl orthosilicate (1.56 g, 1.68 mL, 7.50 mmol) in $Et_2O$ or THF (7.0 mL) at −78 °C. After 1 h, the reaction was quenched with $H_2O$ (5 drops) at −78 °C and allowed to slowly warm to room temperature. The crude reaction mixture was then extracted with 3 × 50 mL $Et_2O$. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by either column chromatography or by bulb-to-bulb distillation.

**2-(Triethoxysilyl)toluene (Table 4, Entry 1).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 3.1 mL, 5.0 mmol), 2-bromotoluene (855 mg, 601 $\mu$L, 5.00 mmol), and tetraethyl orthosilicate (1.56 g, 1.68 mL, 7.50 mmol) in $Et_2O$. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 1.00 g (79%) of 2-(triethoxysilyl)toluene as a colorless oil. Spectral data is reported above.

**3-(Triethoxysilyl)toluene (Table 4, Entry 2).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 3.1 mL, 5.0 mmol), 3-bromotoluene (855 mg, 607 $\mu$L, 5.00 mmol), and tetraethyl orthosilicate (1.56 g, 1.68 mL, 7.50 mmol) in $Et_2O$. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 903 mg (71%) of 3-(triethoxysilyl)toluene as a colorless oil. Spectral data is reported above.

**4-(Triethoxysilyl)toluene (Table 4, Entry 3).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 3.1 mL, 5.0 mmol), 4-bromotoluene (855 mg, 638 $\mu$L, 5.00 mmol), and tetraethyl orthosilicate (1.56 g, 1.68 mL, 7.50 mmol) in $Et_2O$. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 1.08 g (81%) of 4-(triethoxysilyl)toluene as a colorless oil. Spectral data is reported above.

**Triethoxyphenylsilane (Table 4, Entry 4).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 3.1 mL, 5.0 mmol),

bromobenzene (785 mg, 527 μL, 5.00 mmol), and tetraethyl orthosilicate (1.56 g, 1.68 mL, 7.50 mmol) in $Et_2O$. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 889 mg (74%) of triethoxyphenylsilane as a colorless oil. Spectral data is reported above.

**2-(Triethoxysilyl)anisole (Table 4, Entry 5).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 3.1 mL, 5.0 mmol), 2-bromoanisole (935 mg, 623 μL, 5.00 mmol), and tetraethyl orthosilicate (1.56 g, 1.68 mL, 7.50 mmol) in $Et_2O$. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 811 mg (60%) of 2-(triethoxysilyl)anisole as a colorless oil. Spectral data is reported above.

**3-(Triethoxysilyl)anisole (Table 4, Entry 6).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 3.1 mL, 5.0 mmol), 3-bromoanisole (935 mg, 633 μL, 5.00 mmol), and tetraethyl orthosilicate (1.56 g, 1.68 mL, 7.50 mmol) in $Et_2O$. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 892 mg (66%) of 3-(triethoxysilyl)anisole as a colorless oil. Spectral data is reported above.

**4-(Triethoxysilyl)anisole (Table 4, Entry 7).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 3.1 mL, 5.0 mmol), 4-bromoanisole (935 mg, 626 μL, 5.00 mmol), and tetraethyl orthosilicate (1.56 g, 1.68 mL, 7.50 mmol) in $Et_2O$. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 906 mg (67%) of 4-(triethoxysilyl)anisole as a colorless oil. Spectral data is reported above.

**4-(Triethoxysilyl)thioanisole (Table 4, Entry 8).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 6.1 mL, 9.8 mmol), 4-bromothioanisole (1.99 g, 9.80 mmol), and tetraethyl orthosilicate (6.13 g, 6.56 mL, 29.4 mmol) in $Et_2O$ (20 mL). Extraction and flash chromatography (30 mm, 15 cm, 33% $CH_2Cl_2$/hexanes) afforded 1.40 g (50%) of 4-(triethoxysilyl)thioanisole as a colorless oil: TLC $R_f$ = 0.25 (33% $CH_2Cl_2$/hexanes); IR ($CCl_4$) 2976 (m), 2925 (m), 1585 (m), 1487 (m), 1440 (m), 1103 (s), 1080 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.24 (t, $J$ = 6.8, 9H), 2.48 (s, 3H), 3.86 (q, $J$ = 6.8, 6H), 7.25 (d, $J$ = 7.9, 2H), 7.58 (d, $J$ = 7.9, 2H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 15.0, 18.2, 58.7, 125.3, 126.7, 135.1, 141.4; MS (*m/z*) 287 ($M^+ + 1$, 22), 286 (100), 241 (19), 227 (17), 195 (19), 147 (49), 124 (17), 119 (17); HRMS for $C_{13}H_{22}O_3SSi$ calcd 286.1059, found 286.1063.

**4-(Triethoxysilyl)-1,2-(methylenedioxy)benzene (Table 4, Entry 9).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 3.1 mL, 5.0 mmol), 4-bromo-1,2-(methylenedioxy)-benzene (1.01 g, 602 μL, 5.00 mmol), and tetraethyl orthosilicate (1.56 g, 1.68 mL, 7.50 mmol) in $Et_2O$. Bulb-to-bulb distillation (125 °C, 0.5 Torr) afforded 427 mg (30%) of 4-(triethoxysilyl)-1,2-(methylenedioxy)benzene as a colorless oil. Spectral data is reported above.

**3-(Triethoxysilyl)thiophene (Table 4, Entry 10).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.6 M in pentane, 7.50 mL, 12.0 mmol), 3-bromothiophene (1.96 g, 1.12 mL, 12.0 mmol), and tetraethyl orthosilicate (7.50 g, 8.05 mL, 36.0 mmol) in $Et_2O$ (20 mL). Extraction and flash chromatography (30 mm, 15 cm, 17% $CH_2Cl_2$/hexanes) gave 1.48 g (50%) of 3-(triethoxysilyl)thiophene as a colorless oil: TLC $R_f$ = 0.25 (17% $CH_2Cl_2$/hexanes); IR ($CCl_4$) 2975 (m), 2926 (m), 1553 (m), 1542 (m), 1103 (s), 1081 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.24 (t, $J$ = 7.2, 9H), 3.87 (q, $J$ = 7.2, 6H), 7.29 (d, $J$ = 4.8, 1H), 7.40 (dd, $J$ = 4.8, 2.0, 1H), 7.74 (d, $J$ = 2.0, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 18.2, 58.7, 125.7, 131.7, 131.8, 135.5; MS (*m/z*) 247 ($M^+ + 1$, 17), 246 (100), 202 (30), 201 (46), 158 (51), 145 (30), 135 (73); HRMS for $C_{10}H_{18}O_3SSi$ calcd 246.0746, found 246.0743.

**5-(Triethoxysilyl)indole (Table 4, Entry 11).** To a solution of KH (35% dispersion in mineral oil, 292 mg, 2.55 mmol) in THF (5.0 mL) was added dropwise (1 drop per second) a solution of 5-bromoindole (498 mg, 2.54 mmol) in THF (5.0 mL). The reaction mixture was stirred for 15 min and then cooled to −78 °C. A solution of *t*-BuLi (1.7 M in pentane, 3.0 mL, 5.0 mmol) was then added via cannula. A white precipitate immediately formed. The mixture was stirred for 10 min, followed by dropwise (1 drop per second) addition of a solution of tetraethyl orthosilicate (1.06 g, 1.13 mL, 5.08 mmol) in THF (2 mL). The reaction mixture was stirred for 30 min at −78 °C and then allowed to slowly warm to room temperature. The reaction mixture was poured into 10 mL of ice water and then extracted with ether (3 × 15 mL). The combined organic extracts were dried over $MgSO_4$ and then concentrated in vacuo. Column chromatography (4:1 hexanes/EtOAc) afforded 497 mg (70%) of 5-(triethoxysilyl)indole as a pale yellow oil: TLC $R_f$ = 0.32 (4:1 hexanes/EtOAc); IR ($CCl_4$) 3489 (s), 2976 (s), 2926 (m), 1885 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.38 (br s, 1H), 8.03 (s, 1H), 7.48 (d, $J$ = 8.1 Hz, 1H), 7.39 (d, $J$ = 8.1 Hz, 1H), 7.16 (t, $J$ = 2.6 Hz, 1H), 6.56 (s, 1H), 3.89 (q, $J$ = 7.0, 6H), 1.26 (t, $J$ = 7.0, 9H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 137.2, 128.5, 127.7, 127.6, 124.2, 120.0, 110.9, 102.7. 58.6, 18.2; MS (*m/z*) 280 (70), 234 (42), 206 (14), 190 (21), 163 (100), 144 (78), 117 (58); HRMS for $C_{14}H_{21}NO_3Si$ calcd 280.1369, found 280.1381.

**5-(Triethoxysilyl)-1-methyl-indole (Table 4, Entry 12).** A solution of *t*-BuLi (1.50 M in pentane, 3.76 mL, 5.64 mmol) was added dropwise (1 drop per second) to a stirring solution of 5-bromo-1-methylindole (987 mg, 4.70 mmol) in $Et_2O$ (10.0 mL) at −78 °C. After 15 min, the solution was added dropwise (1 drop per second) via cannula to a solution of tetraethyl orthosilicate (6.25 g, 6.69 mL, 30.0 mmol) in 5 mL of $Et_2O$ cooled to −78 °C. After 1 h, the reaction was allowed to slowly warm to room temperature. The reaction mixture was quenched by the addition of 50 mL of water. The crude reaction mixture was then extracted with 4 × 50 mL of $Et_2O$. The combined organic extracts were dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (30 mm, 15 cm, 33% $CH_2Cl_2$/hexane) gave 840 mg (60%) of 5-(triethoxysilyl)-1-methyl-indole as a yellow oil: TLC $R_f$ = 0.37 (33% $CH_2Cl_2$/hexane); IR ($CCl_4$) 2975 (s), 2923 (m), 2882 (m), 1611 (m), 1556 (s), 1518 (m), 1480 (m), 1104 (s), 1080 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 1.25 (t, $J$ = 7.2, 9H), 3.79 (s, 3H), 3.88 (q, $J$ = 7.2, 6H), 6.52 (d, $J$ = 2.8, 1H), 7.05 (d, $J$ = 2.8, 1H), 7.36 (d, $J$ = 7.9, 1H), 7.52 (d, $J$ = 7.9, 1H), 8.00 (s, 1H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 18.2, 32.6, 58.5, 101.3, 108.9, 119.4, 127.3, 128.2, 128.6, 128.8, 137.9; MS (*m/z*) 294 ($M^+ + 1$, 29), 293 ($M^+$, 100), 278 (10), 131 (23). HRMS for $C_{15}H_{23}NO_3Si$ calcd 293.1447, found 293.1439.

**2-Furyltriethoxysilane (Table 4, Entry 13).** A solution of *t*-BuLi (1.50 M in pentane, 16.00 mL, 24.00 mmol) was added dropwise (1 drop per second) to a stirring solution of the furan (1.36 g, 1.46 mL, 20.0 mmol) and TMEDA (2.32 g, 3.02 mL, 20.0 mmol) in $Et_2O$ (40.0 mL) at 0 °C. After 2 h, the solution was cooled to −78 °C and tetraethyl orthosilicate (6.25 g, 6.69 mL, 30.0 mmol) was added dropwise (1 drop per second). After 1 h, the reaction was quenched with $H_2O$ (1 mL) at −78 °C and allowed to slowly warm to room temperature. The crude reaction mixture was then extracted with 2 × 200 mL $Et_2O$. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (30 mm, 15 cm, 10% EtOAc/hexanes) gave 1.01 g (22%) of 2-furyltriethoxysilane as a colorless oil: TLC $R_f$ = 0.71 (10% EtOAc/hexane); IR ($CCl_4$) 2974 (s), 2926 (s), 2891 (s), 1455 (m), 1390 (m), 1169 (s), 1100 (s), 1079 (s), 965 (m); $^1H$ (NMR) ($CDCl_3$) $\delta$ 1.23 (t, $J$ = 7.0, 9H), 3.87 (q, $J$ = 7.0, 6H), 6.39 (dd, $J$ = 1.3, 3.3, 1H), 6.87 (d, $J$ = 3.3, 1H), 7.65 (d, $J$ = 1.3, 1H); $^{13}C$ (NMR) ($CDCl_3$) $\delta$ 18.1, 59.0, 109.3, 123.2, 147.4, 151.3; MS (*m/z*) 231 ($M^+ + 1$, 5), 230 ($M^+$, 28), 215 (100), 203 (14), 185 (28), 147 (80), 119 (52), 113 (55), 79 (47), 63 (27); HRMS for $C_{10}H_{18}O_4Si$ calcd 230.0979, found 230.0974.

**5-Triethoxysilyl-2-methoxypyridine (Table 4, Entry 15).** The general procedure for synthesis of siloxanes from lithium reagents was followed using *n*-BuLi (1.4 M in pentane,

6.5 mL, 8.8 mmol), 5-bromo-2-methoxypyridine (1.66 g, 1.14 mL, 8.83 mmol), and tetraethyl orthosilicate (2.76 g, 2.95 mL, 13.3 mmol) in $Et_2O$ (20 mL). Extraction and flash chromatography (9:1 hexanes/EtOAc) afforded 527 mg (22%) of 5-triethoxysilyl-2-methoxypyridine as a colorless oil: TLC $R_f$ = 0.28 (9:1 hexanes/EtOAc); IR ($CCl_4$) 2976 (s), 2927 (m), 2887 (m), 1589 (s), 1491 (w), 1442 (m), 1390 (w), 1356 (m), 1286 (s), 1082 (vs) $cm^{-1}$; $^1H$ (NMR) ($CD_3CN$) $\delta$ 1.20 (t, $J$ = 7.0, 9H), 3.83 (q, $J$ = 7.0, 6H), 3.87 (s, 3H), 6.73−6.75 (m, 1H), 7.76−7.78 (m, 1H), 8.32−8.35 (m, 1H); $^{13}C$ (NMR) ($CD_3CN$) $\delta$ 18.6, 53.9, 59.5, 111.5, 130.8, 118.2, 145.5, 154.3, 166.5; MS (*m/z*) 272 (100), 240 (13), 226 (31), 170 (11), 163 (11), 136 (15), 119 (6), 91 (5), 79 (14); HRMS for $C_{12}H_{22}ONSi$ calcd 272.1318, found 272.1311.

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**Supporting Information Available:** General experimental procedures and $^1H$ NMR (400 MHz) spectra for all compounds (these compounds were prepared using the lithiation method). This material is available free of charge via the Internet at http://pubs.acs.org.

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