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Organosilatrane building blocks

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ABSTRACT

Phenylsilatrane analogues containing reactive amino, bromo, boronic ester, and alkynyl functional groups for coupling reactions have been prepared. Pinacol boronic ester and ethynyl analogues were synthesized from 4-bromophenylsilatrane by palladium catalyzed reactions. The silatrane functional group was shown to be stable during the palladium catalysis procedures and silica-gel purification, making the molecules amenable to further synthetic manipulation. The described phenylsilatranes are useful building blocks for forming more complex organosilatrane species.

Modifying metal oxides with an organic molecule is a common route to alter specific properties and add novel functionalities to a particular system. It is a fundamental aspect of technologies such as modified silica columns for HPLC and for dye-sensitized solar cells. Organosilatranes have recently been explored as a new method for preparing robust organosiloxane monolayers on metal oxides.[1,2] Silatranes are tricyclic trialkoxysilanes prepared using triethanolamine analogues. The general synthesis involves reaction of a trialkoxy- or trichloro-silane with a triethanolamine derivative as shown in Figure 1. The versatility of silatranes has been expanding as new applications and properties are exploited. They have been investigated in biological,[3,4] materials,[5] and energy applications,[1,2] among others. A recent review paper highlights the broad range of silatrane derivatives and their uses.[6]

The silicon in a silatrane is more stable to nucleophiles than silicon in an open-chain analogue. This is due to both the cyclic nature of the molecule and the coordination of the nitrogen lone-pair of electrons to the silicon, forming a trans-annular dative bond and producing an electron-rich pentacoordinate silicon species as shown in Figure 2.[7] Silatranes are known to be stable to more extreme hydrolytic conditions than the open chain analogues, and we have shown they are capable of being purified by silica-gel chromatography.[7,1] In addition, their general increase in stability in aqueous solutions makes them air-stable. These advantageous features open up simplified synthetic avenues for relatively complex siloxyl-containing molecules that do not require strict anhydrous conditions and take advantage of chromatographic purification techniques.

One advantage of silatranes over trialkoxysilanes is for surface modification of metal oxides with synthetically complex molecules. Historically, trichlorosilanes or trialkoxysilanes such as aminopropyltriethoxysilane have been used to form a siloxane monolayer on a metal oxide surface that is then further modified by coupling to a more complex molecule.[8] This two-step method can be tedious, and is prone to silane polymerization that can form regions with greater than monolayer coverage.[9] Recently, we found that silatranes react on metal oxides with mild heating to form siloxy-linked monolayers, and without silane polymerization.[1]

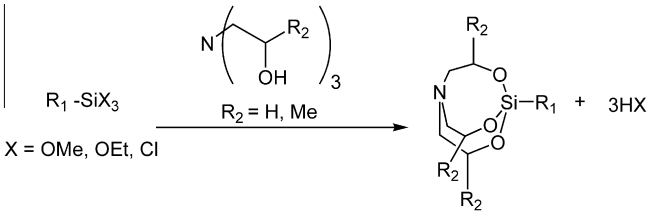

Figure 1. Synthesis of silatranes.

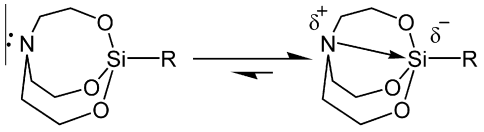

Figure 2. Trans-annular bonding.

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Due to the ability of silatranes to be purified using silica-gel chromatography, ruthenium polypyridyl and porphyrin dyes with silatrane functional groups can be synthesized, purified, and then bound to metal oxide surfaces.[1,2]

The use of a silatrane permits a single step reaction with the metal oxide to form a monolayer of the desired dye, removing the uncertainty of a multi-step reaction with the surface. In addition, the surface-bound porphyrin species were determined to be more stable under alkaline hydrolytic conditions than both carboxylate and phosphonate analogues on anatase TiO_2.[2] Aqueous stability of anchored molecules on metal oxides is an important feature for photodriven water splitting cells,[10] and commonly used carboxylate and phosphonate anchors do not efficiently bind to semiconductors such as TiO_2 at near-neutral pHs.[11] Thus, siloxyl-anchored molecules have a significant advantage in this respect.

The range of reactions for coupling silatranes to other moieties is growing.[12,1,2] In the above examples, amide and Heck couplings were used to functionalize the dye molecules with a silatrane. Here, the synthesis and characterization of silatrane derivatives capable of undergoing other coupling reactions are reported. The bromophenyl **1**, pinacol boronic ester **2**, ethynylphenyl **4** (Scheme 1), and aminophenyl analogues **5** and **6** (Fig. 3) were prepared, and are versatile starting materials for forming more complex silatrane derivatives. This is the first characterization of a silatrane functionalized with a boronic ester, a widely used functional group for cross-coupling reactions. We also characterize the 3- and 4-substituted aminophenyl silatrane analogues.

Initial formation of the organosilatranes from triethanolamine and a trimethoxy- or triethoxy-silane can be performed neat when the silane is liquid, or in toluene. The reaction is driven by the removal of the alcohol product by distillation during the synthesis. Simple recrystallizations and washes allow for moderate yields, with multi-gram scale reactions.

Reaction of 4-bromophenyltrimethoxysilane with triethanolamine to form the useful reagent 4-bromophenylsilatrane **1** occurs in 88% yield with minimal workup.[13] Silatrane **1** is capable of cross-coupling reactions, and is a building block for further transformations as shown in Scheme 1. Reaction of **1** with bis(pinacolato)diboron in DMSO using $Pd(DPPF)Cl_2$ catalyst and potassium acetate allowed for efficient gram-scale synthesis of the pinacol-boronic ester derivative **2** in 65% yield after silica-gel chromatography.[14]

In addition to borylation, the reaction of **1** with trimethylsilylacetylene using $Pd_2(dba)_3$ catalyst with triphenylphosphine, copper(I) iodide, and triethylamine in DMF formed the TMS-protected ethynylphenylsilatrane **3** in 44% yield after silica-gel chromatography.[15] Selective deprotection was efficient in a mixture of dichloromethane and methanol with potassium carbonate

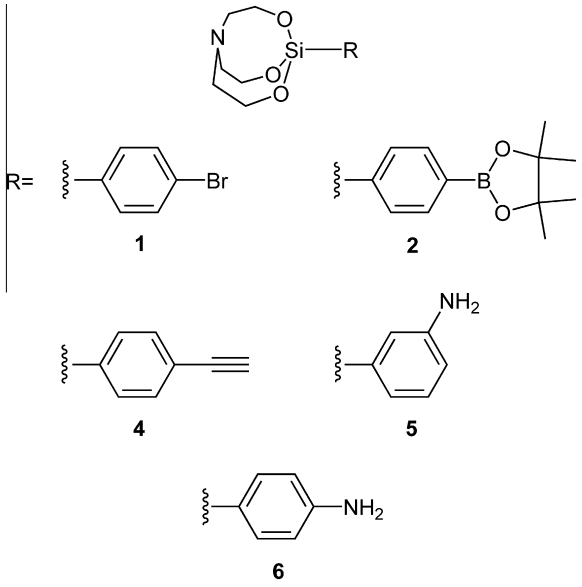


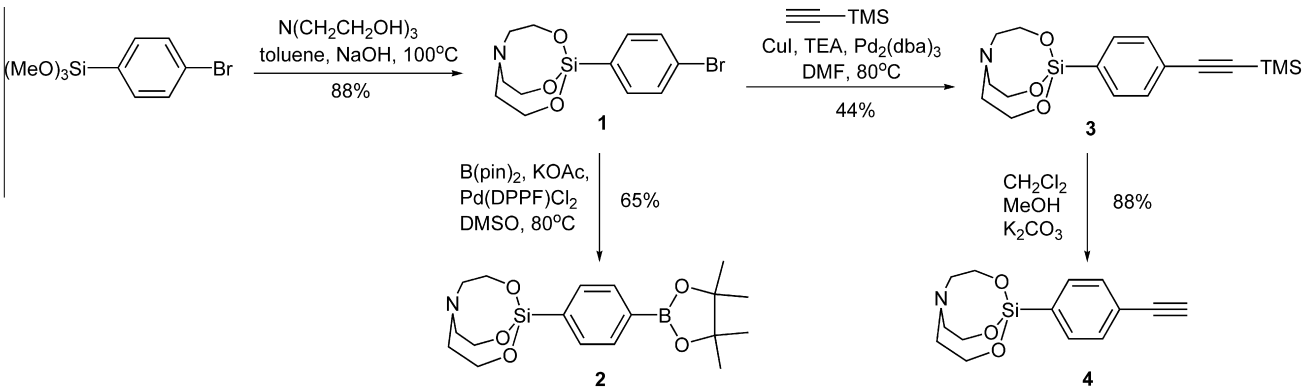
Figure 3. Synthesized silatrane derivatives.

to yield ethynylphenylsilatrane **4**.[16] This is an improved route to **4** over a previously-published synthesis that had an increased number of synthetic steps from commercially available precursors, formed the silatrane later in the synthetic process, and had lower overall yields.[4] Thus, use of the palladium catalyzed reaction allowed for a more straightforward route using the bromophenylsilatrane as a building block.

Aniline derivatives **5** and **6** were prepared from the aminophenyltrimethoxysilane precursors and triethanolamine in moderate yield after recrystallization.[17,18] Derivative **6** has been analyzed for medicinal applications, but not formally characterized.[19]

Both the boronic ester **2** and alkyne **4** are useful reagents capable of coupling to a variety of aryl halides via the Suzuki–Miyaura,[20] Sonogashira,[21] azide–alkyne cycloaddition,[22] and other reactions. The aniline derivatives **5** and **6** are similar to the widely used aminopropyltrialkoxysilane derivatives. Much like the saturated aminopropyl analogue, the aniline derivatives are capable of amide couplings among others. However, if used as an electronic linker between a semiconductive metal oxide surface and an electroactive molecule, aryl derivatives have the advantage of being much more conductive than alkyl. Such issues of electronic connectivity have arisen in our research and that of others.[1,23–25]

In summary, the molecules synthesized herein contain functional groups for common coupling reactions, providing possible



Scheme 1. Formation of boronic ester and alkyne derivatives.

synthetic conduits for attachment of phenylsilatrane species. Stability of the silatrane moiety to palladium catalysts and silica-gel chromatography provided simple routes to boronic ester- and alkyne-functionalized silatrane building blocks. Strategies and routes to a variety of complex molecules, functional surfaces, and materials are currently being examined for applications of these silatrane species. With surface-functionalized metal oxides being increasingly applied in a variety of applications, silatranes will undoubtedly be utilized as reagents for these transformations.

Acknowledgments

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Supplementary data

Supplementary data (synthesis and characterization of the described molecules) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.12.082.

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13. 4-Bromophenyl silatrane. To a dry round bottom flask were added 20 mL of toluene, 4.65 g of 4-bromophenyltrimethoxysilane (1.68×10^{-2} mol), 2.51 g of triethanolamine (1.68×10^{-2} mol), and a catalytic amount of sodium hydroxide (5 mg). A reflux condenser was attached and the mixture was stirred under a nitrogen atmosphere at 100 °C. After 2 h, the reflux condenser was removed and methanol byproduct was distilled under a nitrogen atmosphere. After 1 h, the reaction was cooled and the precipitate was collected by filtration and washed with toluene and methanol to yield a white solid (4.86 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.60 (d, J = 8.2 Hz, 2H, Ar-H), 7.38 (d, J = 8.2 Hz, 2H, Ar-H), 3.89 (t, J = 5.9 Hz, 6H, O-CH_2), 2.92 (t, J = 5.9 Hz, 6H, N-CH_2). ^{13}C (100 MHz, $CDCl_3$, δ): 141.2, 136.0, 130.2, 122.3, 57.6, 51.1. HRMS (API, QTOF) m/z calcd for $C_{12}H_{17}BrNO_3Si$ $[M+H]^+$, 330.0156; Found, 330.0160.
14. 4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl silatrane. To a dry round bottom flask were added 1.50 g 4-bromophenyl silatrane (4.5×10^{-3} mol), 1.27 g bis(pinacolato)diboron (5.0×10^{-3} mol), and 1.34 g potassium acetate (1.4×10^{-2} mol). DMSO (40 mL) was purged with nitrogen, 150 mg (1.8×10^{-4} mol) of [1,1′-bis-(diphenylphosphino)ferrocene]Pd(II) chloride ($Pd(DPPF)Cl_2$) was added, and the solution was added to the round bottom flask. The mixture was purged with nitrogen and then heated at 80 °C. After 6 h, the reaction was cooled and 120 mL of water was added. The precipitate was filtered and washed with water. The solid was dissolved in chloroform and filtered, and the filtrate was dried under reduced pressure. The crude solid was chromatographed on a silica column using chloroform eluent containing 3% ethanol. Fractions containing the desired product were combined and dried under reduced pressure to yield a white solid (1.106 g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.73 (d, J = 7.4 Hz, 2H, Ar-H), 7.70 (d, J = 7.4 Hz, 2H, Ar-H), 3.89 (t, J = 5.9 Hz, 6H, O-CH_2), 2.91 (t, J = 5.9 Hz, 6H, N-CH_2), 1.32 (s, 12H, CH_3). ^{13}C (100 MHz, $CDCl_3$, δ): 145.6, 133.6, 133.4, 83.3, 57.8, 51.2, 24.8. HRMS (API, QTOF) m/z calcd for $C_{18}H_{29}BNO_5Si$ $[M+H]^+$, 378.1903; Found, 378.1909.
15. 4-((Trimethylsilyl)ethynyl)phenyl silatrane. To a dry round bottom flask were added 23 mg copper(I) iodide (1.2×10^{-4} mol), 72 mg triphenylphosphine (2.7×10^{-4} mol), 1.00 g 4-bromophenyl silatrane (3.0×10^{-3} mol), 5 mL triethylamine, and 15 mL DMF. The solution was purged with nitrogen, and 55 mg (6.0×10^{-5} mol) of tris(dibenzylideneacetone) dipalladium ($Pd_2(dba)_3$) was added along with 1.0 mL (7.1×10^{-3} mol) trimethylsilylacetylene. A reflux condenser was attached, and the system was purged with nitrogen and heated at 80 °C for 23 h. The reaction was cooled and transferred to a separatory funnel with 60 mL of dichloromethane. The solution was washed with water, and the solvent was distilled under reduced pressure to yield a brown solid. The solid was redissolved in dichloromethane, and filtered through Celite®, and the solvent was distilled under reduced pressure. The crude material was chromatographed on a silica gel column using dichloromethane eluent and fractions were collected. Fractions containing the desired product were combined and dried under reduced pressure to yield a pale yellow solid (463 mg, 44%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.66 (d, J = 8.2 Hz, 2H, Ar-H), 7.36 (d, J = 8.2 Hz, 2H, Ar-H), 3.89 (t, J = 5.9 Hz, 6H, O-CH_2), 2.91 (t, J = 5.9 Hz, 6H, N-CH_2), 0.23 (s, 9H, Si-CH_3). ^{13}C (100 MHz, $CDCl_3$, δ): 143.1, 133.9, 130.7, 122.1, 106.5, 92.8, 57.7, 51.1, 0.11. HRMS (API, QTOF) m/z calcd for $C_{17}H_{26}NO_3Si_2$ $[M+H]^+$, 348.1446; Found, 348.1448.
16. 4-Ethynylphenyl silatrane. To a mixture of 3 mL dichloromethane and 3 mL methanol in a dry round bottom flask were added 50 mg 4-((trimethylsilyl)ethynyl)phenyl silatrane (1.4×10^{-4} mol) and 22 mg of powdered anhydrous potassium carbonate (1.6×10^{-4} mol). The mixture was sonicated briefly, stirred under nitrogen atmosphere for 13 h, and then quenched with 10 μL of glacial acetic acid (1.75×10^{-4} mol). The solution was placed into a separatory funnel and washed twice with water, and the organic layer was dried under reduced pressure to yield a pale yellow solid (34 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.69 (d, J = 8.2 Hz, 2H, Ar-H), 7.39 (d, J = 8.2 Hz, 2H, Ar-H), 3.89 (t, J = 5.9 Hz, 6H, O-CH_2), 3.00 (s, 1H, CH), 2.90 (t, J = 5.9 Hz, 6H, N-CH_2). ^{13}C (100 MHz, $CDCl_3$, δ): 143.8, 134.1, 130.8, 120.8, 84.9, 76.2, 57.6, 51.0. HRMS (API, QTOF) m/z calcd for $C_{14}H_{18}NO_3Si$ $[M+H]^+$, 276.1050; Found, 276.1048.
17. 3-Aminophenyl silatrane. To a dry round bottom flask was added 5.21 g 3-aminophenyltrimethoxysilane (2.4×10^{-2} mol) dissolved in 10 mL toluene. To the solution was added 3.65 g triethanolamine (2.4×10^{-4} mol) and a catalytic amount of sodium hydroxide (2 mg). A reflux condenser was attached and the mixture was heated to 110 °C while stirring under a nitrogen atmosphere. After 2 h, the reaction was cooled and filtered to yield a crude solid. This was boiled for 10 min in 30 mL of chloroform and cooled, and 10 mL hexanes were added. The precipitate was filtered to yield a white solid (4.43 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.15 (dt, J = 7.4 Hz, 1.2 Hz, 1H, Ar-H), 7.10–7.07 (m, 2H, Ar-H), 6.60 (ddd, J = 7.8 Hz, 2.3 Hz, 1.2 Hz, 1H, Ar-H) 3.90 (t, J = 5.9 Hz, 6H, O-CH_2), 3.50 (br s, 2H, NH_2), 2.91 (t, J = 5.9 Hz, 6H, N-CH_2). ^{13}C (100 MHz, $CDCl_3$, δ): 145.2, 142.6, 128.3, 124.7, 121.2, 115.2, 57.8, 51.2. HRMS (API, QTOF) m/z calcd for $C_{12}H_{19}N_2O_3Si$ $[M+H]^+$, 267.1159; Found, 267.1159.
18. 4-Aminophenyl silatrane. To a dry round bottom flask were added 2.15 g 4-aminophenyltrimethoxysilane (1.00×10^{-2} mol) and 1.52 g triethanolamine (1.02×10^{-2} mol). A reflux condenser was attached and the mixture was heated to 115 °C while stirring under a nitrogen atmosphere. After 3 h, the reaction was cooled and the methanol was removed under reduced pressure to yield a crude solid. This was recrystallized twice from chloroform and filtered to yield a white solid (1.68 g, 62%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.53 (d, J = 8.6 Hz, 2H, Ar-H), 6.63 (d, J = 8.6 Hz, 2H, Ar-H), 3.87 (t, J = 5.9 Hz, 6H, O-CH_2), 3.53 (br s, 2H, NH_2), 2.88 (t, J = 5.9 Hz, 6H, N-CH_2). ^{13}C (100 MHz, $CDCl_3$, δ): 146.1, 135.3, 130.3, 114.6, 57.9, 51.2. HRMS (API, QTOF) m/z calcd for $C_{12}H_{19}N_2O_3Si$ $[M+H]^+$, 267.1159; Found, 267.1166.
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