

Methoxy Dioxasilepane: A Versatile and Stable Synthetic Precursor of Trimethoxysilane

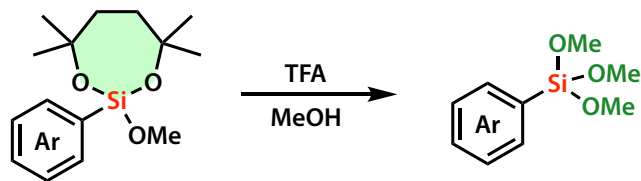
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[stability under acidic/basic conditions] [versatile silanetriol precursor]
[multiple synthetic pathways] [applicable to multistep synthesis]

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Abstract This study introduces an aryl methoxy dioxasilepane as a versatile and stable precursor for aryltrimethoxysilanes. We conducted a quantitative assessment of the stability of this silicon moiety under acidic and basic conditions, demonstrating its superior stability compared to triethoxysilane, and methyl- or trifluoroethoxy dioxasilepanes. The synthetic utility of the methoxy dioxasilepane unit was further elucidated through an examination of its orthogonality and selective functionalization capabilities. Notably, we developed an efficient method for the conversion of a methoxy dioxasilepane to a trimethoxysilane. This method underscores the potential of a methoxy dioxasilepane as a surrogate in multistep syntheses of silanetriols, which offer advantages in the development of silicon-based bioisosteres for medicinal chemistry applications.

Key words Silanol, Silanetriol, Alkoxysilane, Bioisostere, Dioxasilepane

The silicon-switch strategy is a method for identifying new biologically active compounds with different physical and biological characteristics.¹ This is accomplished by replacing the central carbon atom of a specific known candidate molecule with a silicon atom. Since Tacke first proposed this strategy, numerous biologically active compounds have been discovered, resulting in significant advancements in the development of silicon-containing drug-like molecules. Silanols represent a class of molecules that are of significant interest as a target for this strategy.² This approach allows for the identification of potential bioisosteres of the hydrated states of the corresponding carbonyl groups, offering a design of a new biologically active compound bearing a silanediol or silanetriol moiety. Thus, highly potent compounds have already been developed,³ exemplified by peptide-mimetic compound **1**, an angiotensin-converting enzyme (ACE) inhibitor (Figure 1A).^{3a,c} Despite these advances, there is still room for improving the synthetic methodologies used to access structurally complex silanediols or silanetriols.

Previously, we have demonstrated that the seven-membered dialkoxysilane unit, dioxasilepane, exhibits considerable steric bulk and exceptional stability.⁴ Building upon

this methodology, we have recently devised a novel synthetic route to silanediols (Figure 1B).⁵ Our research has identified tetraalkoxysilane **2**, which incorporates a dioxasilepane moiety and two trifluoroethoxy groups, as a valuable precursor for the selective synthesis of monoarylsilanes through a controlled reaction with aryl Grignard reagents. Subsequent conversion of the remaining trifluoroethoxy group to a methoxy substituent, yielding trialkoxysilane **3**, facilitates the introduction of a second aryl group through an additional treatment with Grignard reagent. Ultimately, this method furnishes unsymmetrical dialkoxysilanes **4**. This synthetic sequence has proven to be an invaluable tool for the preparation of diarylsilanediols **5**, with the development of a method for the final cleavage of the seven-membered cyclic structure. Here, further exploration was envisioned to elucidate the chemistry of silanetriol, a compound bearing an additional hydroxy moiety on the silicon atom. Silanetriol represents a valuable active species employed in diverse applications, notably as a precursor to silicon-containing compounds such as polyhedral oligomeric silsesquioxane (POSS).⁶ Moreover, the utilization of silanetriol as a bioisostere augments its significance. Silanetriol exhibits a structural configuration postulated to mimic hydrolytic intermediates of esters and carboxylic acids (Figure 1C). An early exemplar of bioisosteric silanetriol was reported by Pratt,⁷ wherein compound **6** was designed based on the corresponding carboxylic acid, albeit with insufficient biological activity. Subsequently, Pietschnig demonstrated the efficacy of cyclohexanesilanetriol **7** and arylsilanetriol **8**, as acetylcholinesterase (AChE) inhibitors.⁸ Furthermore, these compounds have been shown to exhibit minimal toxicity to humans. This research has established a foundation for the potential development of biologically active compounds incorporating silanetriol moieties. For the synthesis of these silanetriols, hydrolysis of trichlorosilanes or trimethoxysilanes has been predominantly employed (Figure 1D). However, the inherent synthetic instability of these reactive species impedes the synthesis of complex substrates, potentially hindering the

development of a diverse array of silanetriols. To facilitate the synthesis of a wide spectrum of silanetriols, it is imperative that novel synthetic methodologies for these precursor molecules be developed. The intermediate **3**, which was confirmed useful in the synthesis of silanediols, is an arene substituted with a methoxy dioxasilepane unit. This moiety has the structure of a trialkoxysilane and is expected to be qualitatively stable during the conventional organic synthetic operations. It is therefore anticipated that the molecules that has methoxy dioxasilepanes are stable. Thus, the objective of this study was to quantitatively confirm the stability of the methoxy dioxasilepane unit in **3** and to ascertain whether this functional unit could be converted to the trimethoxysilane **9**, which is a potential synthetic precursor of a silanetriol (Figure 1E).

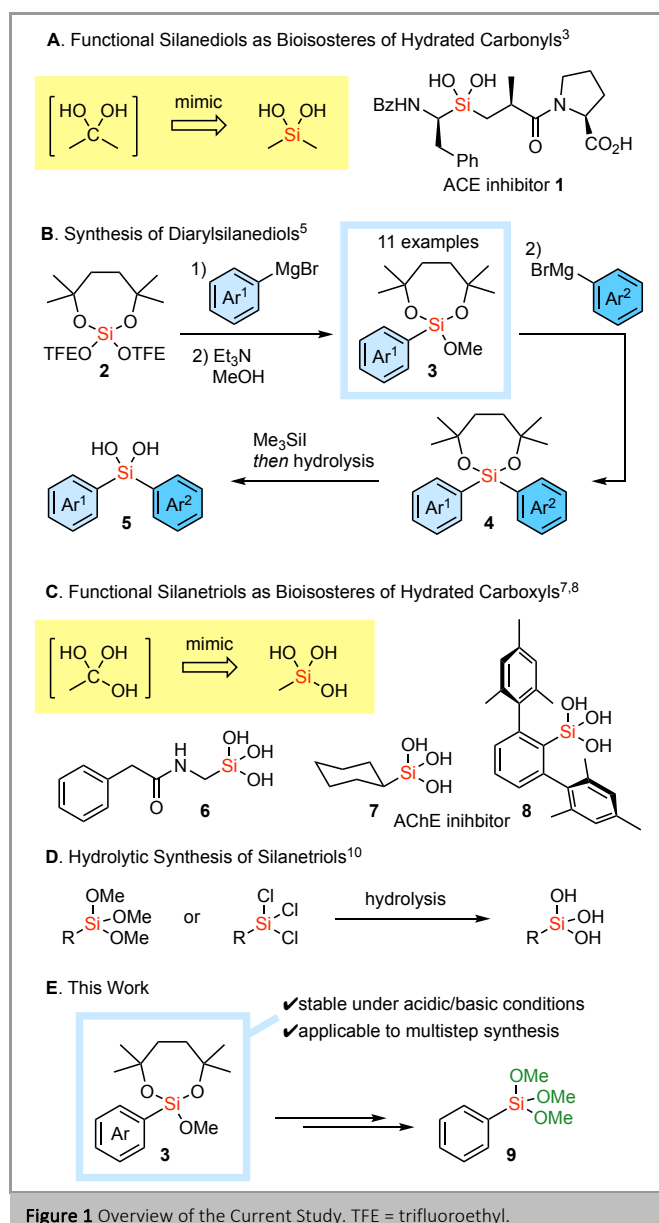


Figure 1 Overview of the Current Study. TFE = trifluoroethyl.

The stability of alkoxy silyl moieties, which were synthetically related to Ph-Si(OMe)_3 , was quantitatively assessed under acidic and basic conditions (Figure 2). Stability check studies were conducted under identical acidic (0.1 mol% TFA in $\text{CD}_3\text{CN}/\text{D}_2\text{O}$ NMR) or basic (10 mol% NaOD in $\text{CD}_3\text{CN}/\text{D}_2\text{O}$ NMR)

reaction conditions and the amount of the remaining starting material was monitored by NMR. In the case of acidic decomposition, Ph-Si(OEt)_3 **10** exhibited the degradation of about 70% of the starting material within 180 min. Ph-Si(pan)Me (Si(pan) = dioxasilepane) **11** also demonstrated pronounced instability, decomposing completely at approximately 60 min. The Ph-Si(pan)OR derivatives demonstrated enhanced stability under acidic conditions, with 74% of Ph-Si(pan)OMe **12**, 81% of Ph-Si(pan)OEt **13**, and even 98% of Ph-Si(pan)OTFE **14** remaining intact after 180 min. However, under basic conditions, Ph-Si(pan)OTFE **14** proved most susceptible to decomposition with over 80% degradation observed after 180 min. The reason for this tendency is unclear. However, this outcome can be attributed to either the fact that OTFE enhances the Lewis acidity of the silicon center or facilitates an efficient removal from the silicate intermediate. The degradation of Ph-Si(OEt)_3 **10** was approximately 15% after 180 min, while that of Ph-Si(pan)Me **11** was 4%, indicating the superior stability of Ph-Si(pan)Me **11** under basic conditions. Notably, Ph-Si(pan)OMe **12** and Ph-Si(pan)OEt **13** exhibited negligible degradation under basic conditions. These findings indicate that the trialkoxysilanes - Si(pan)OMe and - Si(pan)OEt demonstrate enhanced stability compared to - Si(pan)Me that is unstable under acidic conditions. This results indicate the possibility of - Si(pan)OR to be used as a key functional unit with synthetic utility.

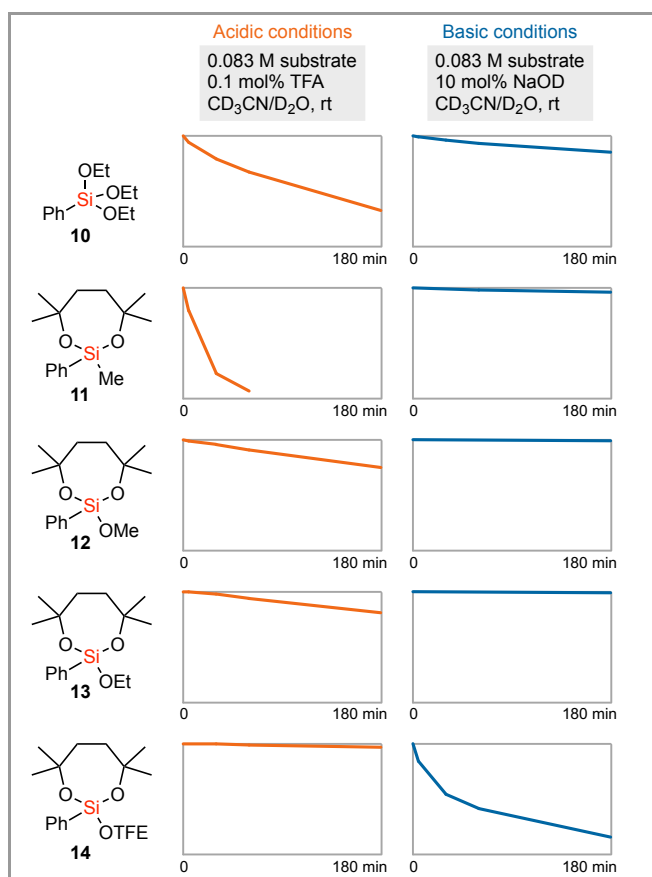


Figure 2 Time Course for Hydrolysis of Alkoxy silanes. The progression of the reaction was monitored over time by NMR analysis of the amount of the remaining starting material.

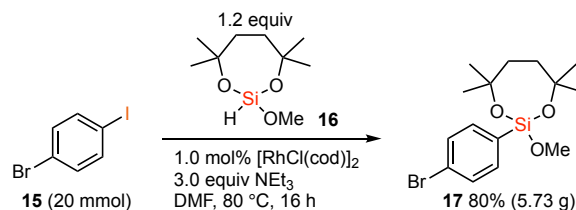
We chose - Si(pan)OMe for further study because of higher accessibility of **3** whose synthesis has already been

reported. To determine the synthetic utility of -Si(pan)OMe, we examined the method for introduction and the check of the stability of this functional unit under other conditions. Initially we examined to develop another synthetic method for **3** for more functional group compatibility. Therefore, we have chosen to implement the methodology developed by Masuda for the synthesis of aryltriethoxysilanes utilizing triethoxysilane and aryl iodides in the presence of a rhodium catalyst (Scheme 1A).⁹ We examined the use of H-Si(pan)OMe **16** as a coupling reagent. Our result demonstrates that the reaction proceeds selectively with iodide in the case of *p*-bromoiodobenzene **15**, affording the corresponding arylsilane *p*-Br-Ph-Si(pan)OMe **17** in excellent yield without touching the aryl bromide moiety.

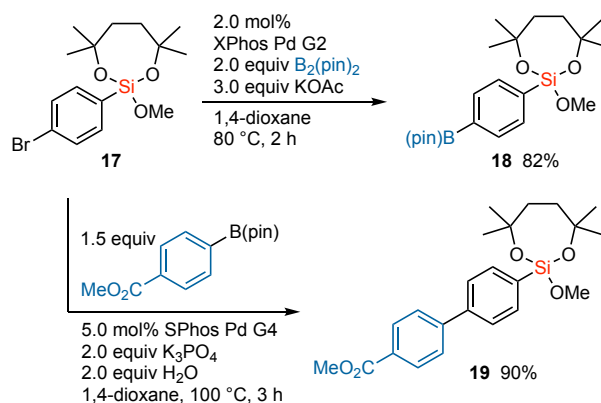
We also examined the transformations of carbon-bromine bonds in arylsilane **17** without loss of the silicon unit (Scheme 1B). The reactions were carried out using a palladium catalyst, via Ishiyama–Miyaura borylation and Suzuki–Miyaura cross-coupling reactions. These processes yielded the corresponding functionalized arylsilanes **18** and **19**, respectively in good yields. The results demonstrate that the silicon unit -Si(pan)OMe exhibits sufficient stability against nucleophilic conditions. Furthermore, -Si(pan)OMe was investigated for activation toward a coupling reaction. Thus, we confirmed that phenyltrialkoxysilane **12** underwent Hiyama cross-coupling reaction with *p*-iodoanisole under the established conditions, using a copper cocatalyst in the presence of AgF as a specially active base.⁴ This resulted in the formation of the biaryl product **20** (Scheme 1C).

It is anticipated that aryl-Si(pan)OMe **21** will serve as a stable precursor for the synthesis of a silanetriol. However, given that silanetriols easily undergo spontaneous self-condensation under both acidic and basic conditions,^{6c,d} the direct hydrolysis of aryl-Si(pan)OMe **21** would present a significant challenge for the selective synthesis of aryl silanetriol **23**. Following Tyler's report that demonstrates trimethoxysilyl arenes could serve as reliable precursors for silanetriols, similar results have been reported for the isolation of aryl- and alkylsilanetriols from trimethoxy- or trichlorosilanes.¹⁰ Therefore, facile preparation of trimethoxysilanes **22** can be considered optimal for the transformation to silanetriols **23**. An effort was made to convert the methoxy dioxasilepane **21** into the corresponding trimethoxysilane **22** (Scheme 1D). It was subsequently determined that the desired conversion proceeded with remarkable selectivity when TFA in methanol was employed as an acid source. After the conversion, TFA and methanol were evaporated, and the trimethoxysilyl analog was isolated through brief column chromatography to remove the liberated diol and polar byproducts. In the current study, substrates employed for conversion included phenyl-Si(pan)OMe (**12**) and *p*-bromophenyl-Si(pan)OMe (**17**), as well as *o*-tolyl-Si(pan)OMe (**21c**)⁵ that was synthesized through Grignard reaction. Additionally, the substrate **19** that has been synthesized in this study via Suzuki coupling reaction was used. All the substrates were successfully converted to the corresponding trimethoxysilanes **22a–d** in good yields. These results demonstrate that the aryl methoxy dioxasilepane that is capable of withstanding multistep synthesis, can serve as a viable surrogate for an aryl trimethoxysilane.

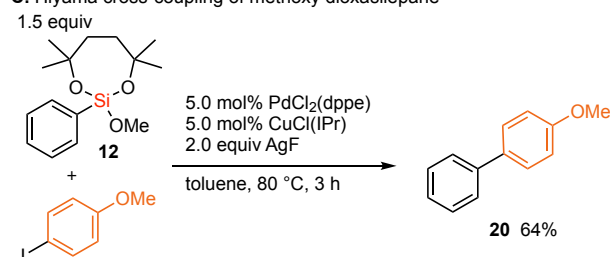
A. Rhodium-catalyzed silylation for methoxy dioxasilepane



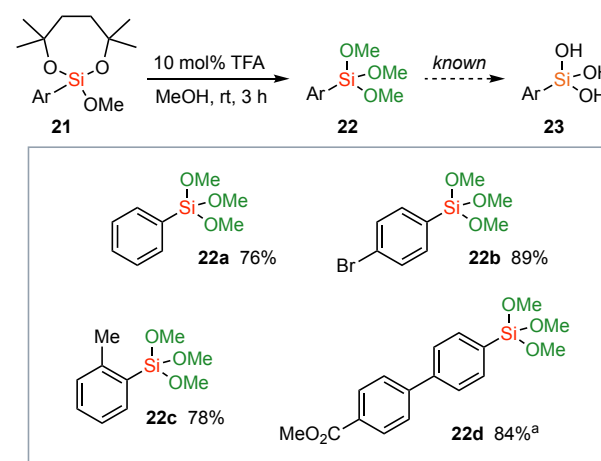
B. Stability of methoxy dioxasilepane under coupling reaction conditions



C. Hiyama cross-coupling of methoxy dioxasilepane



D. Acid-catalyzed exchange of alkoxides



Scheme 1 Study of Stability and Reactivity of Methoxy Dioxasilepane. ^a20 mol% TFA, 5 h.

In conclusion, we have demonstrated the synthetic utility of the methoxy dioxasilepane (-Si(pan)OMe) with respect to its introduction and transformation. This silicon unit exhibited enhanced stability compared to the methyl-substituted dioxasilepane (-Si(pan)Me) under both acidic and basic aqueous conditions, thus corroborating its superior stability during conventional organic chemistry processes. Moreover, upon activation, this silicon unit demonstrates efficacy in Hiyama-type

cross-coupling reactions. The stable silicon unit developed in this study can be readily converted to a trimethoxysilane, thereby confirming its potential utility as a precursor for silanetriols.

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All non-aqueous reactions were carried out under an inert atmosphere of N₂ gas in oven-dried glassware unless otherwise noted. Dehydrated solvent (DMF, 1,4-dioxane, toluene and MeOH) were purchased from FUJIFILM Wako Pure Chemical Corporation and stored under nitrogen atmosphere. Dehydrated DCM was purchased from Kanto Chemical Co., Inc. and stored under nitrogen atmosphere. **11**,⁴ **12**,⁵ **13**,⁵ **14**,⁵ and **21c**⁵ were prepared according to the literature. All other reagents were commercially available and used without further purification unless otherwise noted.

Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25-mm thick, silica gel 60 F₂₅₄. Preparative flash chromatography was performed using Silica Gel (Wakosil® C-300 purchased from FUJIFILM Wako Pure Chemical Corporation, or CHROMATOREX DIOL MB100-40/75 purchased from FUJI SILYSIA CHEMICAL LTD.) and Alumina (activated 200 purchased from Nacalai Tesque, Inc.). Preparative recycling gel permeation chromatography (GPC) was performed on a JAI LC-9260 II NEXT system using CHCl₃ as the eluent.

¹H NMR (600 MHz) and ¹³C NMR (151 MHz) spectra were recorded on a JEOL ECZ-600 spectrometer. Chemical shifts in ¹H NMR spectra were recorded in delta (δ) units, parts per million (ppm) relative to residual CHCl₃ (δ = 7.26 ppm) and C₆HD₅ (δ = 7.15 ppm). Chemical shifts in ¹³C NMR spectra were recorded in delta (δ) units, parts per million (ppm) relative to CDCl₃ (δ = 77.00 ppm) and C₆D₆ (δ = 128.00 ppm). C₆D₆ was used after distillation from CaH₂. The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

High resolution mass spectra (HRMS) were obtained on a Bruker microTOF II-KR spectrometer in Atmospheric Pressure Chemical Ionization (APCI) method using "LC/MS tuning mix, for APCI, low concentration" (Agilent Technologies, Inc.) as the internal standard. For all spectroscopic studies, spectroscopic grade solvents were used as purchased unless otherwise noted.

2-Methoxy-4,4,7,7-tetramethyl-1,3,2-dioxasilepane (16)

An oven-dried 1-L two-necked round-bottomed flask equipped with a magnetic stirring bar was charged with 2,5-dimethyl-2,5-hexanediol (14.7 g, 101 mmol), trichlorosilane (10.1 mL, 99.9 mmol), and DCM (300 mL). After the mixture was stirred at 0 °C for 5 min, triethylamine (27.9 mL, 200 mmol) was slowly added to the reaction and the resulting mixture was allowed to warm to room temperature. The reaction mixture was stirred at room temperature for 2 h, then MeOH (8.10 mL, 200 mmol) was added at 0 °C. Triethylamine (16.7 mL, 120 mmol) was added dropwise to the solution at 0 °C and the reaction mixture was stirred at room temperature for 12 h. Pentane (300 mL) was added to the flask and the mixture was vigorously stirred for 1 min. The precipitate was filtered off by using a Büchner funnel. The filtrate was concentrated under reduced pressure. Distillation of the resulting residue (75 °C / 12 torr) afforded **16** as a colorless oil (10.3 g, 50.5 mmol, 51%); *R*_f: 0.31 (hexane/EtOAc = 20/1).

¹H NMR (C₆D₆, 600 MHz): δ 4.61 (s, 1H), 3.40 (s, 3H), 1.55 (br, 4H), 1.26 (s, 6H), 1.23 (s, 6H).

¹³C NMR (C₆D₆, 151 MHz): δ 74.8, 49.5, 37.9, 30.5 (br, four methyl groups).

HRMS (APCI-MS, positive): *m/z* [M-H]⁺ calcd for C₉H₁₈O₃Si 203.1098; found: 203.1094.

2-(4-Bromophenyl)-2-methoxy-4,4,7,7-tetramethyl-1,3,2-dioxasilepane (17)

An oven-dried 300-mL two-necked round-bottomed flask equipped with a magnetic stirring bar was charged with [RhCl(cod)]₂ (98.6 mg, 0.200 mmol), aryl iodide **15** (5.66 g, 20.0 mmol), hydrosilane **16** (4.90 g, 24.0 mmol), triethylamine (8.37 mL, 60.0 mmol), and DMF (80 mL). The resulting solution was stirred at 80 °C for 16 h in an oil bath. The mixture

was poured into a separatory funnel with Et₂O (50 mL), water (50 mL) and partitioned. The organic phase was collected, and the aqueous phase was extracted with Et₂O (50 mL × 2). The combined organic extract was washed with brine (30 mL), dried over Na₂SO₄ (ca. 20 g), filtered, and concentrated under reduced pressure. The residue was passed through pads of silica gel and alumina (1 cm each) with Et₂O (50 mL) as an eluent. The resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/CHCl₃ = 10/1 to 2/1) to give **17** (5.73 g, 15.9 mmol, 80%) as a colorless oil; *R*_f: 0.30 (hexane/CHCl₃ = 2/1).

¹H NMR (CDCl₃, 600 MHz): δ 7.52 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 3.46 (s, 3H), 1.83 (br, 4H), 1.37 (s, 6H), 1.24 (s, 6H).

¹³C NMR (CDCl₃, 151 MHz): δ 136.2, 131.8, 130.8, 124.8, 75.0, 50.3, 37.5, 30.4 (br, four methyl groups).

HRMS (APCI-MS, positive): *m/z* [M]⁺ calcd for C₁₅H₂₃O₃Si⁸¹Br 360.0575; found: 360.0571.

2-Methoxy-4,4,7,7-tetramethyl-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1,3,2-dioxasilepane (18)

An oven-dried 20-mL Schlenk tube was charged with bis(pinacolato)diboron (254 mg, 1.00 mmol), XPhos Pd G2 (7.9 mg, 10 μmol), KOAc (147 mg, 1.50 mmol), and 1,4-dioxane (1.0 mL). **17** (180 mg, 0.501 mmol) was added to the tube, and 1,4-dioxane (1.0 mL) was then added to wash the inner side of tube. The resulting mixture was stirred at 80 °C for 2 h. The reaction mixture was cooled to room temperature and passed through pads of silica gel and alumina (1 cm each) with hexane/EtOAc (10/1, 50 mL) as an eluent. The resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc = 30/1) to give **18** (167 mg, 0.411 mmol, 82%, 98% purity) as a white solid; mp 134.2 - 139.5 °C; *R*_f: 0.35 (hexane/EtOAc = 10/1).

¹H NMR (CDCl₃, 600 MHz): δ 7.78 (d, *J* = 7.6 Hz, 2H), 7.67 (d, *J* = 7.6 Hz, 2H), 3.45 (s, 3H), 1.82 (br, 4H), 1.37 (s, 6H), 1.34 (s, 12H), 1.23 (s, 6H).

¹³C NMR (CDCl₃, 151 MHz): δ 136.3, 133.8, 133.7, 83.7, 74.8, 50.3, 37.5, 30.4 (br, four methyl groups), 24.8 (Carbon bearing boron atom was hardly observed due to the quadrupolar relaxation mechanism of ¹¹B nucleus).

HRMS (APCI-MS, positive): *m/z* [M+H]⁺ calcd for C₂₁H₃₆BO₅Si 407.2424; found: 407.2424.

Methyl 4'-[2-methoxy-4,4,7,7-tetramethyl-1,3,2-dioxasilepan-2-yl]-[1,1'-biphenyl]-4-carboxylate (19)

An oven-dried 100-mL Schlenk tube was charged with 4-methoxycarbonylphenylboronic acid pinacol ester (1.18 g, 4.50 mmol), SPhos Pd G4 (119 mg, 0.150 mmol), K₃PO₄ (1.28 g, 6.03 mmol) and 1,4-dioxane (12 mL). **17** (1.08 g, 3.01 mmol) and H₂O (108 μL, 5.99 mmol) were added to the tube, then 1,4-dioxane (6.0 mL) was added to wash the inner side of tube. The resulting mixture was stirred at 100 °C for 3 h. The reaction mixture was cooled to room temperature and passed through pads of silica gel and alumina (1 cm each) with EtOAc (50 mL) as an eluent. The resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/acetone = 1/0 to 30/1) and then GPC (eluent: CHCl₃) to give **19** (1.12 g, 2.70 mmol, 90%) as a colorless oil; *R*_f: 0.30 (hexane/acetone = 10/1).

¹H NMR (CDCl₃, 600 MHz): δ 8.10 (d, *J* = 8.2 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 2H), 3.94 (s, 3H), 3.51 (s, 3H), 1.86 (br, 4H), 1.40 (s, 6H), 1.28 (s, 6H).

¹³C NMR (CDCl₃, 151 MHz): δ 167.0, 145.6, 141.2, 135.3, 132.8, 130.1, 129.0, 127.1, 126.4, 74.9, 52.1, 50.4, 37.5, 30.5 (br, four methyl groups).

HRMS (APCI-MS, positive): *m/z* [M+H]⁺ calcd for C₂₃H₃₁O₅Si 415.1935; found: 415.1936.

4-Methoxy-1,1'-biphenyl (20): Hiyama Cross-Coupling Reaction

An oven-dried 20-mL Schlenk tube was charged with 4-iodoanisole (117 mg, 0.500 mmol), PdCl₂(dppe) (14.4 mg, 0.0250 mmol), CuCl(IPr) (12.2 mg, 0.0250 mmol), AgF (127 mg, 1.00 mmol), and toluene (1.0 mL). **12**

(210 mg, 0.749 mmol) was added to the tube, then toluene (1.0 mL) was added to wash the inner side of tube. The resulting mixture was stirred at 80 °C for 3 h. The reaction mixture was cooled to room temperature and passed through pads of silica gel and alumina (1 cm each) with EtOAc (50 mL) as an eluent. The resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/CHCl₃ = 30/1 to 10/1) to provide **20** as a white solid (58.5 mg, 0.318 mmol, 64%); mp 87.8–88.4 °C; *R*_f: 0.37 (hexane/CHCl₃ = 3/1).

All the resonances in ¹H NMR and ¹³C NMR spectra were consistent with the reported value.¹¹

Trimethoxy(phenyl)silane (**22a**): Typical Procedure for Transformation of Methoxydioxasilepane to Trimethoxysilane under Acidic Conditions

The synthesis of **22a** is representative. An oven-dried 20-mL Schlenk tube was charged with arylsilane **12** (140 mg, 0.499 mmol) and MeOH (1.5 mL). Trifluoroacetic acid (3.8 μL, 0.050 mmol) was added to the mixture, then MeOH (1.0 mL) was added to wash the inner side of tube. The resulting mixture was stirred at room temperature. After 3 h, dry toluene (2.5 mL) was added to the mixture and the mixture was stirred for 1 min. The resulting solution was concentrated under reduced pressure. The residue was purified by passing through a pad of silica gel (CHROMATOREX DIOL MB100-40/75, 1 cm) with an eluent (hexane/EtOAc = 20/1 to 5/1) to provide **22a** as a colorless oil (75.0 mg, 0.378 mmol, 76%); *R*_f: 0.63 (hexane/EtOAc = 5/1).

¹H NMR (CDCl₃, 600 MHz): δ 7.65 (d, *J* = 7.6, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 3.63 (s, 9H).

¹³C NMR (CDCl₃, 151 MHz): δ 134.7, 130.6, 129.4, 128.0, 50.8.

HRMS (APCI-MS, positive): *m/z* [M]⁺ calcd for C₉H₁₄O₃Si 198.0707; found: 198.0713.

(4-Bromophenyl)trimethoxysilane (**22b**)

Obtained as a colorless oil (124 mg, 0.446 mmol, 89%) from **17** (180 mg, 0.501 mmol). Purification was done by passing through a pad of silica gel (CHROMATOREX DIOL MB100-40/75, 1 cm) with an eluent (hexane/EtOAc = 20/1 to 5/1); *R*_f: 0.48 (hexane/EtOAc = 10/1).

¹H NMR (CDCl₃, 600 MHz): δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 3.61 (s, 9H).

¹³C NMR (CDCl₃, 151 MHz): δ 136.3, 131.2, 128.3, 125.7, 50.8.

HRMS (APCI-MS, positive): *m/z* [M]⁺ calcd for C₉H₁₃O₃Si⁸¹Br 278.9813; found: 278.9813.

Trimethoxy(*o*-tolyl)silane (**22c**)

Obtained as a colorless oil (82.9 mg, 0.390 mmol, 78%) from **21c** (147 mg, 0.499 mmol). Purification was done by passing through a pad of silica gel (CHROMATOREX DIOL MB100-40/75, 1 cm) with an eluent (hexane/EtOAc = 20/1 to 5/1); *R*_f: 0.44 (hexane/EtOAc = 10/1).

¹H NMR (CDCl₃, 600 MHz): δ 7.67 (d, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.22–7.16 (m, 2H), 3.62 (s, 9H), 2.49 (s, 3H).

¹³C NMR (CDCl₃, 151 MHz): δ 144.5, 136.4, 130.7, 129.8, 128.5, 124.8, 50.5, 22.3.

HRMS (APCI-MS, positive): *m/z* [M]⁺ calcd for C₁₀H₁₆O₃Si 212.0863; found 212.0861.

Methyl 4'-(trimethoxysilyl)-[1,1'-biphenyl]-4-carboxylate (**22d**)

Obtained as a white solid (139 mg, 0.418 mmol, 84%) from **19** (207 mg, 0.499 mmol) by using trifluoroacetic acid (7.7 μL, 0.10 mmol). Reaction time was 5 h. Purification was done by passing through a pad of silica gel (CHROMATOREX DIOL MB100-40/75, 1 cm) with an eluent (hexane/EtOAc = 20/1 to 5/1); mp 54.0–55.7 °C; *R*_f: 0.38 (hexane/EtOAc = 5/1).

¹H NMR (CDCl₃, 600 MHz): δ 8.11 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 3.95 (s, 3H), 3.66 (s, 9H).

¹³C NMR (CDCl₃, 151 MHz): δ 166.8, 145.2, 142.0, 135.3, 130.1, 129.21, 129.16, 127.0, 126.7, 52.1, 50.8.

HRMS (APCI-MS, positive): *m/z* [M+H]⁺ calcd for C₁₇H₂₁O₅Si 333.1153; found: 333.1156.

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Supporting Information

Supporting information for this article is available online.

Primary Data

NO.

Conflict of Interest

The authors declare no conflict of interest.

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