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Synthesis of unsymmetrical dialkoxydiarylsilanes and diarylsilanediods from tetraalkoxysilane having a dioxasilepane unit†

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The tetraalkoxysilane carrying a stable seven-membered dioxasilepane moiety and two trifluoroethoxy groups undergoes reliable iterative substitution of the two trifluoroethoxy groups by sequential treatment with different aryl Grignard reagents while keeping the seven-membered structure intact. The process results in the synthesis of unsymmetrical dialkoxydiarylsilanes and eventually diarylsilanediods after proper hydrolysis.

Silanediods constitute a class of compounds characterized by two hydroxy groups attached to a silicon atom. These compounds are known for their unique ability to donate hydrogen bonds and have therefore attracted interest as a core structure of organocatalysts^{1–7} as well as a substructure of bioactive compounds that is biosoteric to a hydrated carbonyl group (Fig. 1A).^{8–13} The hydrolysis of dialkoxyxilanes represents a well-established method for the synthesis of these silanediods (Fig. 1B).¹⁴ In an ideal scenario, such dialkoxyxilanes could be synthesized *via* sequential reactions from a tetraalkoxysilane and organometallic reagents, wherein two substituents are sequentially introduced to the silicon center. Nevertheless, a significant challenge persists in controlling the sequential substitutions. An earlier solution for the selective synthesis of alkyl or aryl trialkoxysilanes involved the reaction of an excess amount of tetraalkoxysilane with Grignard reagent at low temperature (Fig. 1C).¹⁵ The necessity of the excess amount of an alkoxyxilane underscores the similar reactivity for the first nucleophilic substitution of an alkoxy group compared to the second introduction of an aryl group to form a dialkoxy diarylsilane. Moreover, dialkoxyxilanes readily react with organometallic reagents to introduce the third substituent (Fig. 1D).¹⁶ As a result, the controlled stepwise introduction of two different carbon substituents into a tetraalkoxysilane remains a major challenge.

Thus, we considered the use of a seven-membered dialkoxyxil moiety, the dioxasilepanyl group to circumvent this drawback.¹⁷ This functional moiety was designed to provide both kinetic and thermodynamic stability to the alkoxyxil moiety, allowing it to survive the reaction even when using butyllithium or LiAlH₄ (Fig. 1E). The seven-membered dialkoxy moiety also imparts unique reactivity to this silyl group. The methoxy group on the silicon atom can be cleanly substituted with an aryl group upon treatment with aryllithiums, and a hydrosilane can be used for C–H silylation of aryls. The silyl group can then be converted *via* the Hiyama cross-coupling reaction upon activation with AgF. In this context, here we report a reliable strategy for the sequential introduction of different aryl groups by carefully selecting a leaving alkoxy group onto the silicon center of a dioxasilepane moiety. Our method has successfully demonstrated the synthesis of a series of unsymmetrical dialkoxy diarylsilanes, which are practical precursors of diarylsilanediods (Fig. 1F).

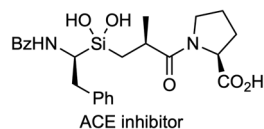
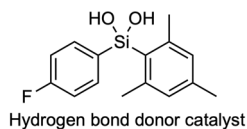
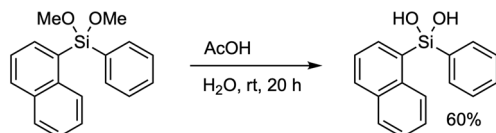
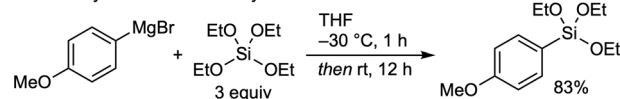
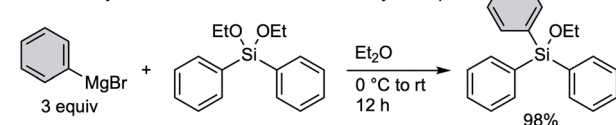
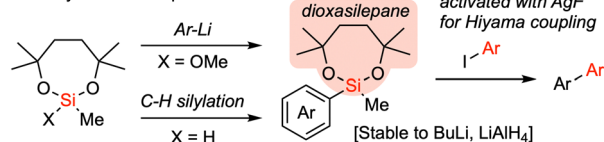
The nucleophilic substitution reaction involving a tetraalkoxysilane **1**, bearing a dioxasilepane unit, was initially explored (Scheme 1A). Using a 4-*t*Bu phenyl Grignard reagent, the reaction involving dimethoxy dioxasilepane **1-OMe** proceeded, with the methoxy group serving as the leaving group to give **2a-OMe**. At the same time, the overreaction yielded diarylsilane **3aa** in 25% yield (entry 1). This tendency to give a mixture showed a partial improvement with the ethoxy-substituted **1-OEt** as a substrate, decreasing the yield of the diarylsilane **3aa** due to the slower introduction of the second aryl group (entry 2). Isopropoxy group as a leaving group was not examined because the substrate **1-OiPr** could not be synthesized. Interestingly, the use of the tetraalkoxysilane **1-OTFE**, substituted with two trifluoroethoxy groups, showed satisfactory selectivity. Our mechanistic rationale for this phenomenon is that the first arylation of the silicon center is enhanced due to the electron withdrawing nature of the two trifluoroethoxy groups. In addition, the introduction of the second aryl group is slowed by the steric hindrance of the first aryl group and the remaining trifluoroethoxy group, which kinetically delays further nucleophilic attack.

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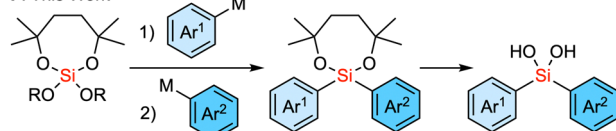
† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d4cc02051k>



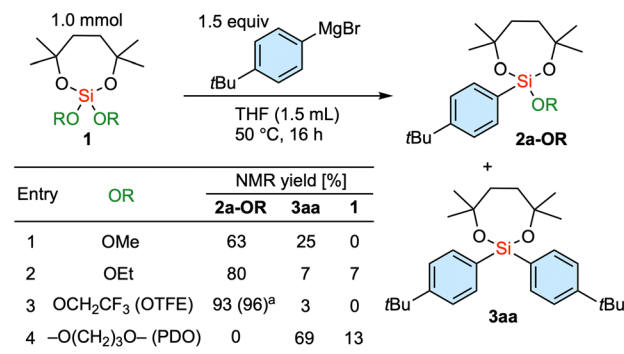
A. Functional Silanediols

B. Hydrolysis of a Dialkoxysilane¹⁴C. Monoarylation of Tetraethoxysilane¹⁵D. Potentially Viable Introduction of the Third Aryl Group¹⁶E. Utility of Dioxasilepane Unit¹⁷

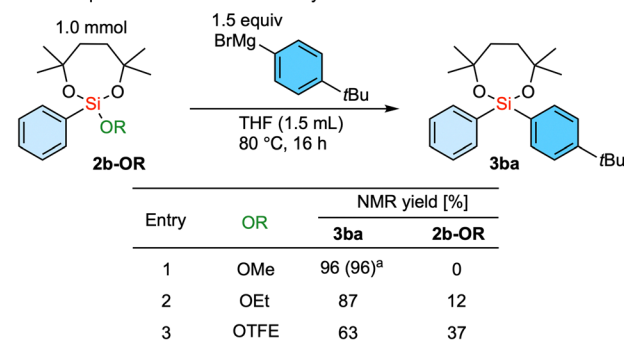
F. This Work



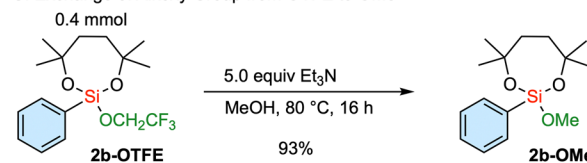
A. Nucleophilic Substitution of Tetraalkoxysilane 1



B. Nucleophilic Substitution of Trialkoxysilane 2b-OR



C. Exchange of Alkoxy Group from OTFE to OMe



Scheme 1 Exploration of alkoxy substituents on silicon center for the reaction with Grignard reagents. ^aIsolated yield. OTFE = 2,2,2-trifluoroethoxy, PDO = 1,3-propanediol.

Fig. 1 Overview of the current study.

Thus, a single substitution product **2a-OTFE** was obtained in 93% NMR yield along with a trace amount of **3aa** (entry 3). In essence, the combination of the 7-membered ring structure and the trifluoroethoxy group successfully controlled the single substitution reaction. Of note, this seven-membered moiety helps to improve the stability of alkoxy silanes,¹⁷ which are normally labile during chromatography and on contact with air and water. It is interesting to note that the substrate with the cyclic 1,3-propanediol diether (**1-PDO**) only led to the selective formation of disubstituted diarylsilane **3aa**. The reaction would probably proceed through the first substitution and the formation of a cyclic biscoordinating magnesium complex, which would further facilitate the leaving of a propanediolate through the second arylation.

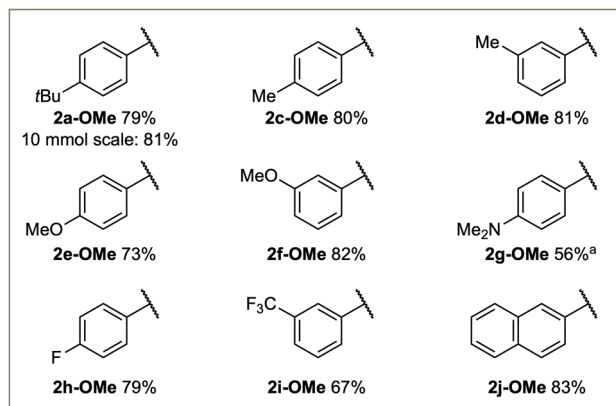
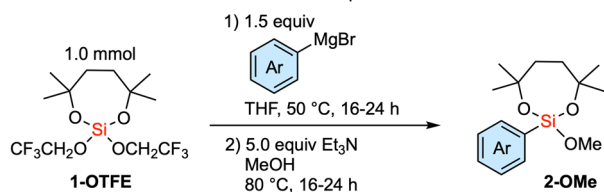
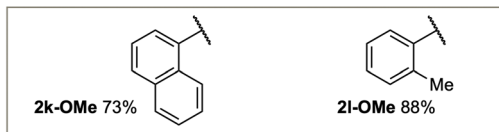
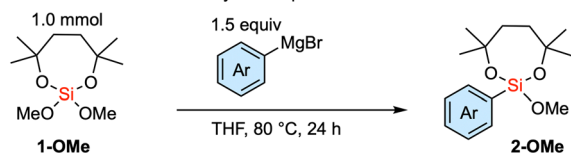
Next, we embarked on the exploration of the introduction of the second aryl group (Scheme 1B). In this case, the methoxy-substituted substrate **2b-OMe** gave the product **3ba** in very high yield (entry 1). In contrast, the ethoxy substrate **2b-OEt** resulted in a diminished reactivity as demonstrated above (entry 2), and the trifluoroethoxy-substituted **2b-OTFE** underwent the even more sluggish introduction of the second aryl group (entry 3).

Thus, the methoxy group serves as the optimal leaving group for the introduction of the second aryl group.

In an attempt to combine these two findings for selective sequential diarylation, the exchange of the remaining alkoxy group from trifluoroethoxy to methoxy was investigated. This transformation was achieved upon treatment with triethylamine in methanol (Scheme 1C).^{18,19} Therefore, the established protocol involves the use of a trifluoroethoxy group as a leaving group for the first aryl introduction. Subsequently, the remaining alkoxy group is converted to a methoxy group, which is then followed by the introduction of the second aryl group through the substitution of the methoxy group. It is of note that the dioxasilepane moiety remained unaffected during the introductions of the two aryl groups as well as the transalkoxylation. This underlines the fact that the introduction of the third aryl group is completely suppressed in the current process.

Based on the established method, we investigated the introduction of an array of aryl groups to the structure of diaryl silanes. Scheme 2A delineates the reaction of bis(trifluoroethoxy) dioxasilepane **1-OTFE** with a variety of aryl Grignard reagents. In

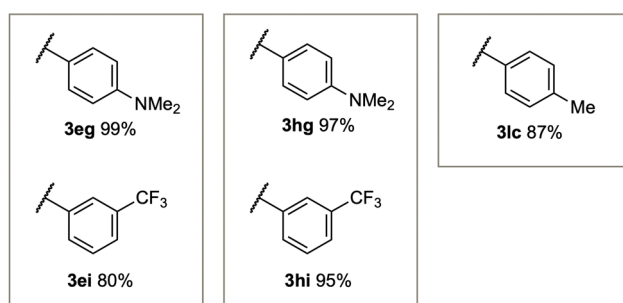
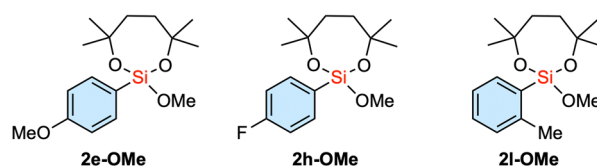
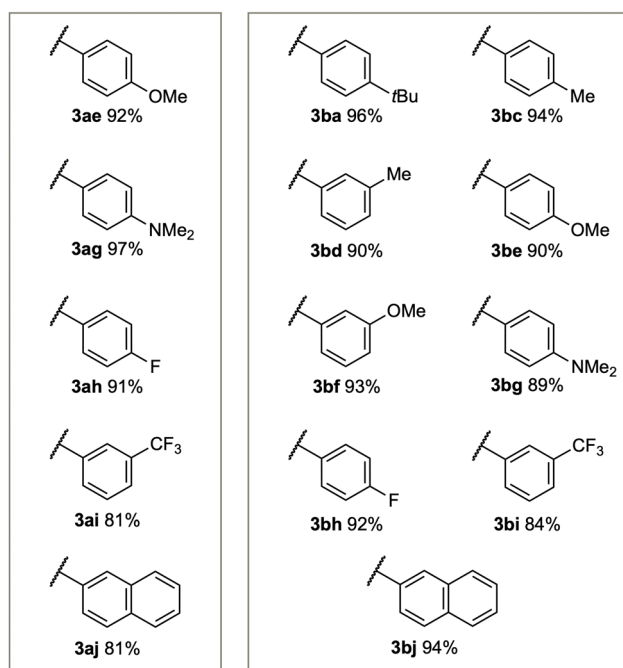
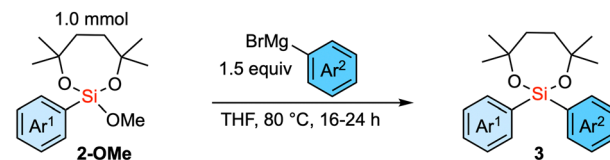


A. Reaction of **1-OTFE** with Various NucleophilesB. Reaction of **1-OMe** with Bulky Nucleophiles

Scheme 2 Scope of the first arylation with respect to the substituent on the aryl groups. ^aSecond step: 72 h.

this instance, a trace amount of diarylsilane **3** is formed, which complicates the purification of the product **2-OTFE**. Consequently, the crude **2-OTFE** was directly subjected to transalkoxylation to yield its methoxy form **2-OMe**, with the 2-step yields indicated in Scheme 2A. The reaction proceeds with a series of aryl Grignard reagents that are substituted with either electron-donating or electron-withdrawing substituents. The reaction can be scaled up to 10 mmol, providing **2a-OMe** in 81% yield. In the case of 4-dimethylaminophenylmagnesium bromide, a decrease in the yield was observed. This phenomenon can be attributed to the decreased efficiency of transalkoxylation due to the increased electron density on the silicon atom, culminating in the sluggish formation of **2g-OMe**. In the case of the bulky Grignard reagents, the above protocol resulted in a very slow conversion. Therefore, the more reactive **1-OMe** was used for those bulky nucleophiles (Scheme 2B). Thus, single substitution of **1-OMe** was observed in the case of 1-naphthyl and *o*-tolyl Grignard reagents as nucleophiles.

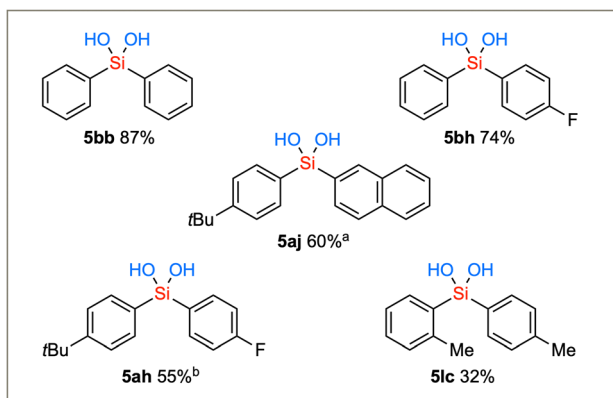
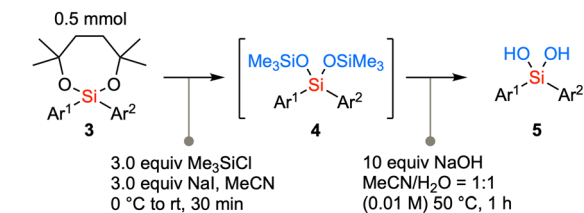
We subsequently scrutinized the scope of the nucleophilic substitution reaction concerning the structural variation of the initially introduced aryl group, denoted as Ar^1 , and the second



Scheme 3 Substrate scope of the reaction with respect to Ar^1 and Ar^2 groups.

aryl group, Ar^2 . As the substrate, we employed **2a-OMe** ($\text{Ar}^1 = 4$ -*t*-Bu-phenyl), **2b-OMe** ($\text{Ar}^1 =$ phenyl), **2e-OMe** ($\text{Ar}^1 = 4$ -OMe-phenyl), **2h-OMe** ($\text{Ar}^1 = 4$ -F-phenyl), and sterically demanding **2l-OMe** ($\text{Ar}^1 = 2$ -Me-phenyl). In any of these substrates, aryl





Scheme 4 Hydrolysis of diaryl dioxasilanes *via* the transesterification generates diarylsilane diols. ^aReaction time was 6 h for the second step. ^bReaction time was 2 h for the second step.

Grignard reagents (Ar^2MgBr) with electron-donating or electron-withdrawing substituents successfully gave the product diarylsilanes (Scheme 3).

The diarylsilanes synthesized *via* the aforementioned methodology were subjected to conversion into silane diols (Scheme 4). Due to the confirmed stability of diaryl dioxasilanes, the removal of the seven-membered structure was initially not successful using the conventional acidic conditions (TsOH, TFA, AcOH, or PPTS in CH_2Cl_2). Therefore, the removal of the cyclic structure was achieved by first converting the compound to bis-trimethylsilyl ether under conditions using a combination of chlorotrimethylsilane and NaI in acetonitrile to generate Me_3SiI *in situ*.²⁰ The cyclic structure was swiftly removed to afford the bis(trimethylsilyloxy)silane intermediate **4**. The TMS group can be readily hydrolyzed with aqueous NaOH in acetonitrile under mild basic conditions,²¹ resulting in the conversion to diarylsilane diols **5**. Not only the parent diphenylsilane diol **5bb** but also diarylsilane diols such as **5bh**, **5aj**, **5ah**, and **5lc** can be synthesized from the corresponding diarylsilane **3**.

In conclusion, we have discovered a method for the controlled nucleophilic substitution of two alkoxy groups on a tetraalkoxysilane having a dioxasilane moiety. Even two different aryl groups can be introduced sequentially to the central silicon atom. We have also established a method for the cleanly removing the seven-membered ring structure of the

product diarylsilane using TMS iodide and a mild conversion method for deprotecting diarylsilane diols. Thus, a general method for the synthesis of a variety of unsymmetrical diarylsilane diols has been established.

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Data availability

The data supporting this article have been included as part of the ESI.†

Conflicts of interest

There are no conflicts to declare.

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