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Protecting and Leaving Functions of Trimethylsilyl Groups in Trimethylsilylated Silicates for the Synthesis of Alkoxysiloxane Oligomers

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Abstract: The concept of protecting groups and leaving groups in organic synthesis was applied to the synthesis of siloxane-based molecules. Alkoxy-functionalized siloxane oligomers composed of SiO_4, $RSiO_3$, or R_2SiO_2 units were chosen as targets; however, synthetic methods are limited. Here we describe a novel synthesis of alkoxysiloxane oligomers based on the substitution reaction of trimethylsilyl (TMS) groups with alkoxysilyl groups. Oligosiloxanes possessing TMS groups were reacted with alkoxychlorosilane in the presence of $BiCl_3$ as a catalyst. TMS groups were substituted with alkoxysilyl groups, leading to the synthesis of alkoxysiloxane oligomers. Siloxane oligomers composed of $RSiO_3$ and R_2SiO_2 units were synthesized more efficiently than those composed of SiO_4 units, suggesting that the steric hindrance around the TMS groups of the oligosiloxanes makes a difference in the degree of substitution. This reaction uses TMS groups as both protecting and leaving groups of $SiOH/SiO^-$ groups.

In organic synthesis, precise molecular design has been widely developed by using protection and deprotection of functional groups.[1] Silyl groups, most typically trimethylsilyl, are commonly used as protecting groups for –COH groups because C–O–Si bonds can be easily cleaved at the O–Si bond. We were inspired to apply this methodology to siloxane-based inorganic synthetic chemistry in order to advance and stimulate the field. It is well known that trialkylsilyl (–SiR_3) groups are useful for capping $SiOH/SiO^-$ groups; however, their use as protecting groups for the controlled synthesis of siloxane-based compounds has not been reported. One of the more challenging and unprecedented issues requiring investigation is the selective cleavage of the Si–O–SiR_3 linkages (deprotection) for subsequent reactions in multistep synthesis.

The target molecules in this study are well-defined oligosiloxanes used as building blocks for siloxane-based materials. Silicone, silsesquioxanes, and silica have applications in a wide range of fields. Using building blocks for the preparation of these materials is an effective methodology to construct siloxane structures that cannot be achieved by using monomeric silanes, which enables the development of materials with novel properties and functionalities.[2] In particular, oligosiloxanes possessing alkoxy groups (hereafter called alkoxysiloxane oligomers) are important because of their ability to form Si–O–Si networks with controlled compositions and nanostructures by hydrolysis and polycondensation of the alkoxy groups.[3] However, selective methods for the synthesis of alkoxysiloxane oligomers are quite limited.

Alkoxysiloxane oligomers are generally synthesized by alkoxysilylation of monomeric silanes or oligosiloxanes (Scheme 1a). The formation of siloxane bonds and the introduction of alkoxy groups are conducted simultaneously in these reactions.[4] However, the instability of the alkoxy groups against hydrolysis limits the reaction conditions and types of precursors available. Additionally, the synthesis and isolation of the reactants containing Si–OH groups are difficult. Although non-hydrolytic routes (Scheme 1b) have also been developed,[5] the structures of the alkoxysiloxane oligomers reported so far have been limited. To address these issues, we propose a new synthetic route in which the formation of siloxane bonds and the introduction of alkoxy groups are done separately, as shown in Scheme 1c. The terminal reactive sites ($SiOH/SiO^-$) of oligosiloxanes are first protected with trialkylsilyl groups, allowing the facile isolation of a variety of oligosiloxanes as stable compounds. The trialkylsilyl groups are then substituted with alkoxysilyl groups (deprotection). Trimethylsilylated derivatives of oligosiloxanes are rich in diversity, and various structural types such as linear, branched, ladder, and cubic have been reported. However, methods for the substitution step have not been developed yet. Although the substitution reaction of dimethylsilyl groups with other trialkylsilyl groups was reported,[6] this reaction cannot be adopted for the synthesis of alkoxysiloxane oligomers because the reaction is conducted under hydrolytic conditions.
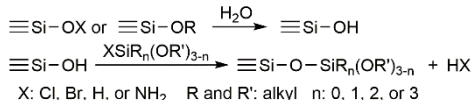
Herein, we report the nucleophilic substitution reaction of TMS groups with alkoxysilyl groups as a novel synthetic method for the synthesis of alkoxysiloxane oligomers (Scheme 1c). We confirmed the leaving group ability of the TMS groups of $QM_4^†$ by substituting with dimethoxy(methyl)silyl groups using a Lewis acid catalyst ($BiCl_3$) (Scheme 2a). The scope of the reaction was then investigated by using several oligosiloxanes possessing TMS groups as starting materials (Scheme 2a, b). Finally, we synthesized tris(dimethoxy(methyl)siloxy)(vinyldimethoxysiloxy)-silane ($QT^{Me}_3T^{Vinyl}$) from tris(trimethylsiloxy)silanol (QM_3) (Scheme 3). QM_3 can be considered as the protected compound of $Si(OH)_4$ with three TMS groups. To the best of our knowledge, this is the first report where the concept of protecting and leaving groups is applied to the synthesis of siloxane-based compounds.

The fact that TMS groups act as a leaving group in the substitution reaction of QM_4 with incoming dimethoxy(methyl)silyl groups was confirmed by the following
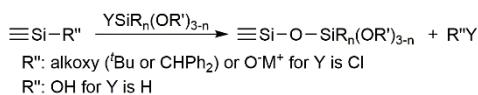
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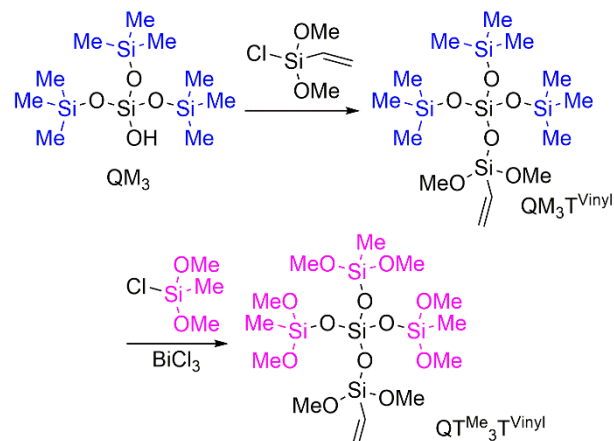# COMMUNICATION

Scheme 1. Conventional synthetic routes to alkoxysiloxane oligomers and a novel route proposed in this study.
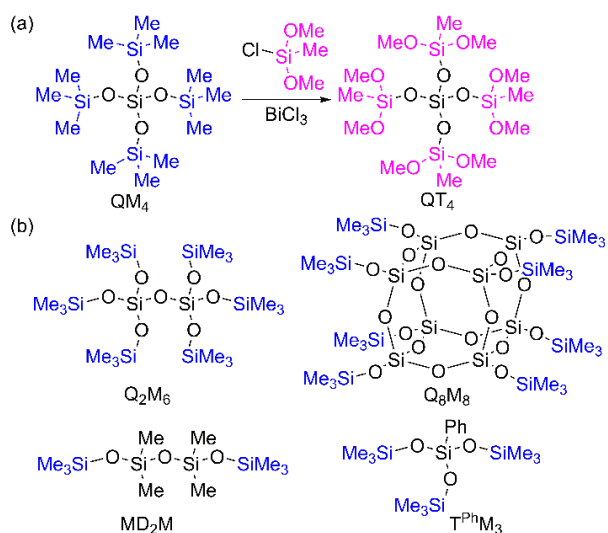
Scheme 2. (a) Syntheses of alkoxysiloxane oligomer based on the substitution reaction of TMS groups with alkoxysilyl groups. (b) Oligosiloxanes possessing TMS groups used as starting materials.

Scheme 3. Synthesis of an alkoxysiloxane oligomer with a vinyl group using TMS groups as protecting and leaving groups.

Table 1. Reaction conditions for the substitution of TMS group of QM_4.

Entry	Temperature / °C	Time / d	Product	Conversion of TMS groups / %
1	25	1	QM_2T_2, QMT_3, QT_4	84
2	25	7	QM_2T_2, QMT_3, QT_4	84
3	60	7	QMT_3, QT_4	98

two evidences. The formation of trimethylchlorosilane (TMCS) as a byproduct and the formation of QM_2T_2, QMT_3, and QT_4 as products were confirmed by NMR spectroscopy of the reaction mixture (Figs. S4a–S6a).

The ^{29}Si NMR spectrum of the purified sample derived from the QM_4/(MeO)$_2$MeSiCl/BiCl$_3$ reaction system (entry 1, Fig. S7a) shows signals corresponding to QM_2T_2, QMT_3, and QT_4. The starting QM_4 was not observed. The formation of these compounds is also supported by their ^1H and ^{13}C NMR spectra (Figs. S8 and S9), and high-resolution ESI-MS data (Table S1). The conversion ratio of TMS groups is 84%, which is calculated by Eq. (1) based on the signal intensities of M and T silicon atoms.

Conversion (%) = Sum of signal intensities of T silicon atoms
/ Sum of signal intensities of M and T silicon atoms × 100 Eq. (1)

The conversion did not change (84%) when the reaction time was increased from 1 d to 7 d (entry 2, Fig. S7b). This can be attributed to the equilibrium of the substitution reaction. The conversion of TMS groups was much lower (3%) without BiCl$_3$ under otherwise identical conditions (Figs. S10–S12), indicating that BiCl$_3$ catalyzes the substitution reaction of TMS groups.

In order to determine whether the substitution reaction of TMS groups is an equilibrium reaction or not, the reverse reaction of the substitution of TMS group of QM_4 with (MeO)$_2$MeSiCl was conducted by reacting QT_4, which was synthesized in a different manner (see the Experimental Section of SI), with TMCS. The ^1H, ^{13}C, and ^{29}Si NMR spectra (Figs. S13–S15) of the obtained mixture show signals corresponding to a large amount of unchanged QT_4 and a small amount of QMT_3, suggesting that the reverse reaction slightly proceeded. These results explain why some of the TMS groups were not substituted with alkoxysilyl groups in the QM_4/(MeO)$_2$MeSiCl/BiCl$_3$ reaction system.

To improve the conversion of TMS groups, the substitution reaction was conducted at the boiling point of the byproduct (TMCS) to bias the reaction equilibrium by removing TMCS from the reaction mixture (entry 3). The ^1H, ^{13}C, and ^{29}Si NMR spectra of the liquid, removed from the reaction mixture, show signals corresponding to TMCS, suggesting that it was successfully removed from the reaction mixture (Figs. S16–S18). The ^{29}Si NMR spectrum of the purified sample (entry 3, Fig. S7c) shows

signals corresponding to QMT_3 and QT_4, while the signal due to QM_2T_2 has disappeared. The conversion of TMS groups was 98%, indicating that the reaction equilibrium was successfully biased by removing the TMCS from the mixture.

The substrate versatility of the substitution reaction of TMS groups was investigated by using Q_2M_6 and Q_8M_8. Q_2M_6 and Q_8M_8 were reacted with $(MeO)_2MeSiCl$ in the presence of $BiCl_3$ at 60 °C for a week. In both cases, although the substitution reaction proceeded, TMS groups partially remained, as determined by NMR and MS spectroscopies (Q_2M_6: Figs. S19–S21 and Table S2; Q_8M_8: Figs. S22–S24 and Table S3). The conversions of TMS groups for Q_2M_6 and Q_8M_8 were 34% and 39%, respectively, and were not improved by increasing the reaction time. Such relatively low conversions may be caused by the increase in the steric hindrance around the oxygen atoms linked to the TMS groups with the progress of the substitution reaction, as described later in the reaction mechanism section. These results suggest this substitution reaction of TMS groups has a certain limit on the substrate tolerance.
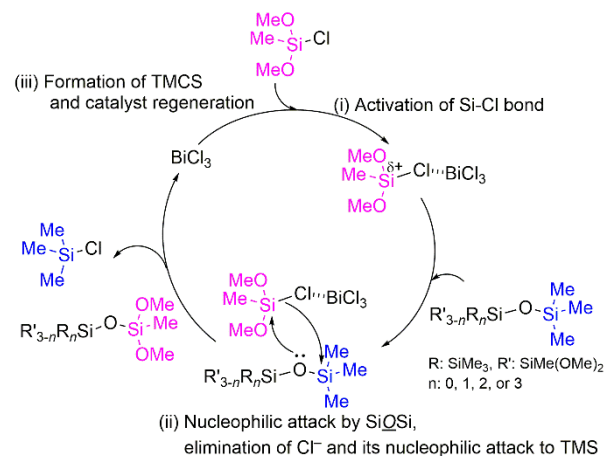
Scheme 4 shows the proposed reaction mechanism of the substitution reaction of TMS groups with alkoxysilyl groups ($QM_4/(MeO)_2MeSiCl/BiCl_3$ reaction system was used as a model case.). This mechanism is based on previous mechanistic studies of Lewis acid-catalyzed siloxane-bond-formation reactions between SiOR (R = Me or Et) and SiX (X = Cl or Br).[7] This reaction mechanism consists of the following three steps: (i) the Si–Cl bond of the alkoxychlorosilane is activated by $BiCl_3$; (ii) an oxygen atom of QM_4 attacks the silicon atom of the alkoxychlorosilane and chloride ion is eliminated, which attacks the silicon atom of a trimethylsilyl group; (iii) TMCS is formed and eliminated, and $BiCl_3$ is regenerated.

In the cases of Q_2M_6 and Q_8M_8 as starting materials, the oxygen atoms, which are not linked to TMS groups (Si_Q–O–Si_Q), were not involved in the reaction as suggested by the lack of signals in the NMR and MS spectra corresponding to the molecules formed by cleaving the Si_Q–O–Si_Q bonds. The oxygen atoms of Si_Q–O–Si_Q bonds are more sterically hindered and electron-poorer than those of S_Q–O–Si_M(TMS) bonds; therefore, the oxygen atoms in Si_Q–O–Si_Q bonds are less capable of attacking alkoxychlorosilanes nucleophilically.

The relatively low reactivities of Q_2M_6 and Q_8M_8 in the substitution reactions may be due to the steric hindrance around the oxygen atoms linked directly to TMS groups, which reduces their ability to attack the alkoxychlorosilane nucleophilically. In fact, when MD_2M, a compound with decreased steric hindrance than Q_2M_6, was used as a starting material, the conversion of TMS groups was 100% based on the ^{29}Si NMR spectrum (Figure S25). However, the reaction products were partially polymerized (details are shown below.).

To investigate the effects of the electron density, the TMS groups of $T^{Ph}M_3$ were substituted with dimethoxy(methyl)silyl groups. The Si atom linked to TMS groups of $T^{Ph}M_3$ is more electron-rich than those of QM_4 and Q_2M_6. The conversion of TMS groups of $T^{Ph}M_3$ was higher (100%) than those of QM_4 and Q_2M_6, based on the ^{29}Si NMR spectrum (Figure S28), suggesting that the nucleophilic attack of the oxygen atoms linked to TMS groups is the key step of the substitution reaction of TMS groups.

The conversions of TMS groups of MD_2M and $T^{Ph}M_3$ were

Scheme 4. Proposed reaction mechanism of the substitution reaction of TMS groups with alkoxysilyl groups.

high, however, partial polymerization of the reaction products was confirmed by NMR spectroscopy (Figure S25–S27 and S28–S30), while the same could not be confirmed for QM_4. This polymerization may be caused by a functional group exchange reaction between incoming -SiMe(OMe)$_2$ and -SiCl groups of dimethoxy(methyl)chlorosilane, and the following substitution reaction of TMS groups (Scheme S2). Alkoxy groups linked to electron-rich Si atoms are more easily exchanged with chloro groups than those linked to electron-poor Si atoms;[8] therefore, polymerized compounds were formed in the reactions of MD_2M and $T^{Ph}M_3$. Despite the low stability of the reaction products in the cases of MD_2M and $T^{Ph}M_3$, the concept of this study, that is the substitution of TMS groups with alkoxysilyl groups, was demonstrated.

The leaving group ability of TMS groups linked to –OSi was confirmed as mentioned above, therefore, the synthesis of alkoxysiloxane oligomers was conducted with TMS groups as protecting and leaving groups. As shown in Scheme 3, tris(trimethylsiloxy)silanol (QM_3) was chosen as a starting material because it can be considered as the protected compound of $Si(OH)_4$ with three TMS groups. Firstly, the remaining silanol group of QM_3 was alkoxysilylated with chlorodimethoxy(vinyl)silane to obtain QM_3T^{Vinyl}. Then, the TMS groups of QM_3T^{Vinyl} were substituted with dimethoxy(methyl)silyl groups while retaining the vinyldimethoxysilyl group. The formations of the target compound and the molecule with one remaining TMS group were confirmed by ^{29}Si NMR spectroscopy (Fig. 1). These results were also supported by ^1H, ^{13}C NMR (Figs. S31 and S32), and MS spectroscopies. The reason for this selective substitution of TMS groups can be explained by lower nucleophilicity of $–OSi(CH=CH_2)(MeO)_2$ group than that of TMS group at the stage (ii) in Scheme 4. The conversion of TMS groups was calculated as 97% and the synthesis of the target compound was achieved in high yield (94%); therefore, TMS groups can be used as protecting and leaving groups for the synthesis of siloxane-based molecules. Although the substrate scope of the reaction for oligosiloxanes composed of SiO_4 units is still limited as the conversion ratio depends on the structure of the starting trimethylsilylated silicates, the concept of protecting

groups has been achieved using this reaction. This approach is a novel synthetic strategy of alkoxysiloxane oligomer using designed precursors for siloxane-based
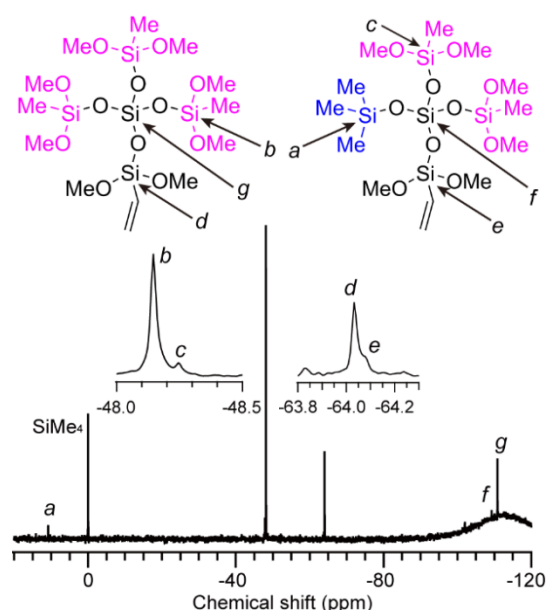
Figure 1. ^{29}Si NMR spectrum of the $QM_3T^{vinyl}/(MeO)_2MeSiCl/BiCl_3$ reaction system.

materials.

The substitution reaction of TMS groups is similar to the alkoxysilylation of *tert*-butoxysilane with alkoxychlorosilane.[5d-f] Leaving groups are substituted with alkoxysilyl groups in both reactions. The difference of conversion in these two reactions was investigated by reacting $(MeO)_2MeSiCl$ with QM_4 or $Si(O^tBu)_4$ under the same conditions (at room temperature for a day). The ^1H, ^{13}C, and ^{29}Si NMR spectra show that all the ^tBu groups are substituted with dimethoxy(methyl)silyl groups (Figs. S33–S35). On the other hand, TMS groups partly remained after the substitution reaction as mentioned above. This difference is caused by the existence of the reverse reaction. As already mentioned, the substitution of TMS groups progresses reversibly. In the case of ^tBu groups, the reverse reaction does not occur because the tertiary carbon atom of ^tBuCl (byproduct of the reaction) is not reactive under substitution conditions due to steric hindrance. In this sense, ^tBu group has an advantage over TMS group in terms of conversions; however, there are a couple of concerns on the use of ^tBuO groups. Functional group exchange between ^tBuO groups and chloro groups in starting materials unavoidably occurs, lowering the yields of target molecules. Furthermore, as mentioned in the introduction, trimethylsilylated oligosiloxanes are rich in diversity. These compounds can be used as building blocks for siloxane-based materials by introducing alkoxysilyl groups using the reaction developed here; therefore, this synthetic method is expected to be a fruitful methodology for the synthesis of siloxane compounds and siloxane-based materials derived from those compounds.

In conclusion, the leaving group ability of TMS groups in oligosiloxanes was confirmed by reacting several oligosiloxanes possessing TMS groups with alkoxychlorosilane in the presence of $BiCl_3$ as catalyst. The TMS groups of oligosiloxanes are substituted with alkoxysilyl groups, and alkoxysiloxane oligomers were successfully synthesized. Trimethylsilyl-terminated oligosiloxanes can be synthesized from natural and synthetic silicates, and their siloxane structures are rich in diversity (linear, branched, cyclic, and cubic). The expansion of this reaction's substrate scope by future studies will lead to a novel fruitful synthetic method for alkoxysiloxane oligomers. The present work demonstrates that the concept of protecting groups in synthetic organic chemistry is applicable to siloxane-based molecules. Further studies on the viability of this reaction will contribute to a precise synthetic chemistry of siloxane-based molecules.

† Symbols Q^n, T^n, D^n, and M^n denote the bonding state of Si atoms; Q^n: $Si(OSi)_n(OH, OR, or O^-)_{4-n}$ (n = 0, 1, 2, 3, or 4), T^n: R'$Si(OSi)_n(OH, OR, or O^-)_{3-n}$ (n = 0, 1, 2, or 3), D^n: R'$_2Si(OSi)_n(OH, OR, or O^-)_{2-n}$, (n = 0, 1, or 2) and M^n: R'$_3Si(OSi)_n(OH, OR, or O^-)_{1-n}$ (n = 0 or 1). In addition, the superscripts of these symbols, such as T^{Me} and T^{Ph}, denote the functional groups linked to the Si atoms (R') in this paper.
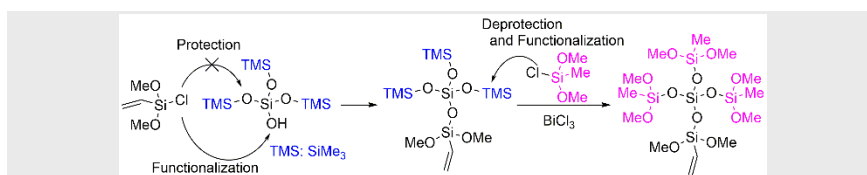
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Protecting group in siloxane-based inorganic synthetic chemistry: The concept of protecting groups in organic synthesis is applied for the synthesis of siloxane oligomers with alkoxy groups. Several alkoxysiloxane oligomers were successfully synthesized by substitution reaction of trimethysilyl groups with alkoxysilyl groups.

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