ChemPubSoc Europe
DOI: 10.1002/ejic.201600454
EurJIC European Journal of Inorganic Chemistry
Communication

Siloxanes

Unexpected Selectivity in Cyclotetrasiloxane Formation by the Hydrolytic Condensation Reaction of Trichloro(phenyl)silane

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Abstract: The hydrolytic condensation reaction of $PhSiCl_3$ in aqueous solution forming cyclotetrasiloxane $[C_6H_5SiO(OH)]_4$ was studied in detail. The reaction, originally reported by J. F. Brown, was believed to provide only one cyclotetrasiloxane diastereomer, *cis*,*cis*,*cis*-isomer **1**. However, our detailed study clearly showed not only the formation of **1** (55.5 % yield) but also the formation of two other diastereomers, the *cis*,*cis*,*trans* isomer (11.9 % yield) and the *cis*,*trans*,*cis* isomer (4.3 % yield), without the formation of the last conceivable *trans*,*trans*,*trans* isomer (<0.1 % yield). A possible mechanism for the selective formation of the three diastereomers was proposed, in which it was assumed that the cyclotetrasiloxanes were formed by cyclization exclusively through the *meso* diastereomer of the linear tetrasiloxanes but not through the DL diastereomer. This selective cyclization was reasonably explained by considering the stable conformations of the linear tetrasiloxanes in a highly polar aqueous medium.

Introduction

Phenyl-substituted silsesquioxane materials have been explored since the pioneering work of Brown and co-workers[1] because of their structural diversity[2] and interest in clarifying their structures and the mechanisms by which they are formed. Such materials are widely used in industry, and their importance is increasing owing to their usefulness as incorporated ingredients in organosiloxane polymers for a wide range of applications such as sealing materials for light-emitting diodes and organic electroluminescence diodes and as antireflective layers for extreme lithography in forefront semiconductor production.[3] Organosiloxane polymers are generally produced by hydrolytic condensation of organochlorosilanes or organoalkoxysilanes, which usually provides uncontrolled random structures. To improve their properties, structural control of such polymers is inevitable, and for that purpose, understanding the details of the condensation reaction including precise structural understanding of the intermediate oligomer species is important. Despite the long history of research on organosiloxane polymers,[2] even the initial stage of the condensation reaction of silsesquioxane materials is not well understood.

Brown reported the formation of cyclotetrasiloxane **1** by hydrolytic condensation of $PhSiCl_3$ in aqueous medium.[1d] 1,3,5,7-Tetrahydroxy-1,3,5,7-tetraphenylcyclotetrasiloxanes exist as four stereoisomers, that is, compounds **1**–**4**, as shown in Figure 1. Brown assigned the structure of the cyclotetrasiloxane he obtained as *cis*,*cis*,*cis* diastereomer **1** on the basis of derivatization experiments by reaction with Me_2SiCl_2 and $(ClMe_2Si)_2O$. Although the structural assignment of one of the derivatized products was wrong,[4] the stereochemistry of the cyclotetrasiloxane product was later proved to be correct.[5] There is no description on the possible formation of cyclotetrasiloxane diastereomers **2**–**4** in this original report.

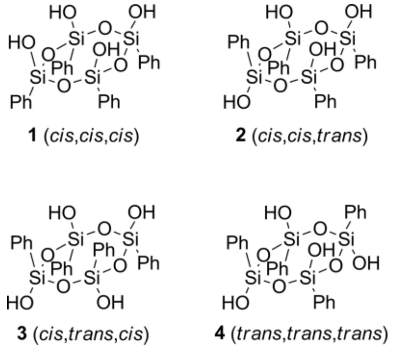
1 (*cis*,*cis*,*cis*)
2 (*cis*,*cis*,*trans*)
3 (*cis*,*trans*,*cis*)
4 (*trans*,*trans*,*trans*)

Figure 1. Structures of cyclotetrasiloxane diastereomers **1**–**4**.

Although some reports suggested the formation of other cyclotetrasiloxane diastereomers from $PhSiCl_3$ (**5**),[6] the reaction conditions and product distribution were not specified, and therefore, there are no reports that clearly describe the formation of cyclotetrasiloxane diastereomers other than **1** under Brown's conditions. Considering the highly attractive structural features and widespread applicability of these cyclotetrasiloxanes, it is very regrettable that the details of the hydrolytic condensation reaction have not yet been clarified and that produc-

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Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under http://dx.doi.org/10.1002/ejic.201600454.

tion of **1** as the sole product of the reaction still seems to be widely accepted half a century after Brown's first report.[5,7]

As a part of our research on organosiloxane polymers, we recently studied the acid-catalyzed condensation reaction of phenylsilanetriol[8] (**6**) in organic solvents, in which we unexpectedly found the formation of cyclotrisiloxane **11** as a major product and succeeded in its isolation and structural characterization.[9] On the other hand, as mentioned above, cyclotetrasiloxane **1** was obtained by hydrolytic condensation of **5** in aqueous medium. In the latter reaction, **6**, the same compound as that in the abovementioned study, was expected as an intermediate of the condensation reaction. On this basis, we carefully reinvestigated the hydrolytic condensation of **5** under Brown's conditions to determine unambiguously the structures of the products and to clarify the factors that determine the reaction products. In this report, we describe the unexpected formation of three diastereomers, **1**, **2** and **3**, out of four possible cyclotetrasiloxanes and provide a possible explanation for the selective formation of these three diastereomers.

Results and Discussion

Silanol-containing compounds are generally considered to be unstable because of their tendency to undergo self-condensation, and there are not many examples of their chromatographic analysis.[6a,9,10] However, as described by Klement'ev[10] and in our previous report,[9] reverse-phase HPLC is a very convenient and reliable method that can be used to analyze silsesquioxane-forming condensation reactions, especially for mixtures of oligomers bearing silanol groups.

The condensation reaction of **5** in aqueous acetone (Brown's conditions) was carefully analyzed by HPLC. A solid suspension started to form after about 1 h, and the resinous suspension observed after a sufficient reaction period (one to several days) was collected. Successive treatment with CS_2, drying under vacuum, and recrystallization from acetone afforded almost-pure **1**. Figure 2 shows chromatograms for the solid and solution parts of each step, and a possible reaction pathway for the hydrolytic condensation of **5** is shown in Scheme 1.

It is clearly shown that a crystalline product separated from the original reaction mixture (Figure 2, a) and that obtained after CS_2 treatment (Figure 2, c) consisted not only of *cis*,*cis*,*cis* isomer **1** (t_R = 5.23 min) but also of diastereomers **2** (t_R = 4.57 min) and **3** (t_R = 4.27 min). The structural assignment of the observed peaks will be discussed later, but it is unquestionable that no significant amount of fourth diastereomer **4** was included (less than 1:100 relative to **3**).[11] This observation clearly suggested that the hydrolytic condensation reaction of **5** afforded not a single diastereomer but a mixture of cyclotetrasiloxane diastereomers. Treatment with CS_2 increased the relative concentration of **1** in the solid mixture, and as a result, further purification by recrystallization became successful and afforded almost-pure **1** (96.5 % purity, Figure 2, e) in 15.6 % yield based on **5**.

The four peaks observed in the aqueous solution (Figure 2, b) were easily assigned to acetone (t_R = 0.32 min), phenylsilanetriol (**6**, t_R = 0.34 min), disiloxane **7** (t_R = 1.37 min), and trisiloxane **8** (t_R = 2.87 min) by comparison with the chromatograms for the mixture of the acid-catalyzed condensation reaction of **6** in organic solvents described in our previous report.[9] Very small peaks corresponding to **2** at t_R = 4.59 min and **1** at t_R = 5.27 min were also observed, which showed that the solubility of the cyclotetrasiloxanes in aqueous solution was very low.

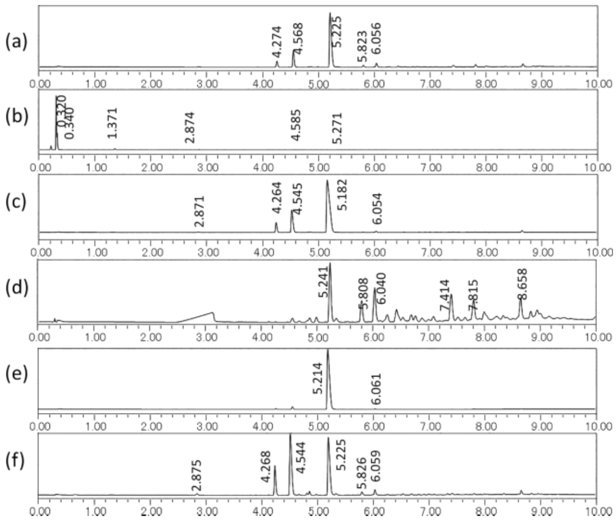
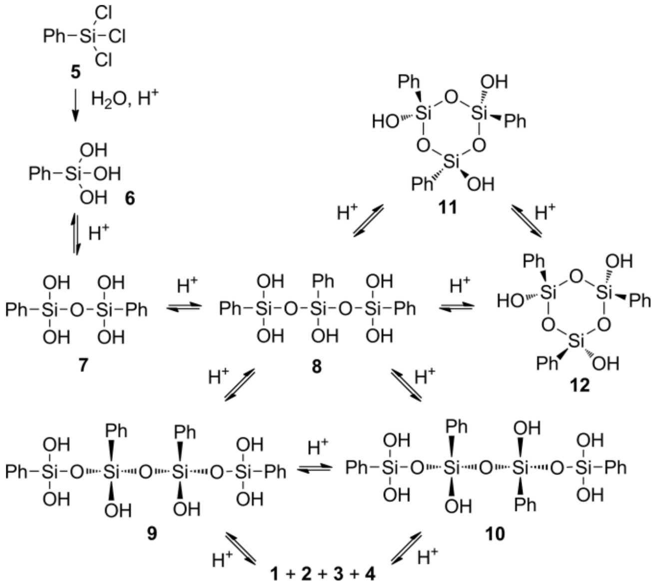


Figure 2. HPLC charts of (a) a mixture of four diastereomers obtained by the acid-catalyzed isomerization reaction, (b) the aqueous phase, (c) after CS_2 treatment, (d) the CS_2 solution part, (e) the crystalline product obtained after recrystallization from diethyl ether, and (f) the diethyl ether solution part after recrystallization.



Scheme 1. A possible reaction pathway for the formation of silsesquioxane oligomers.

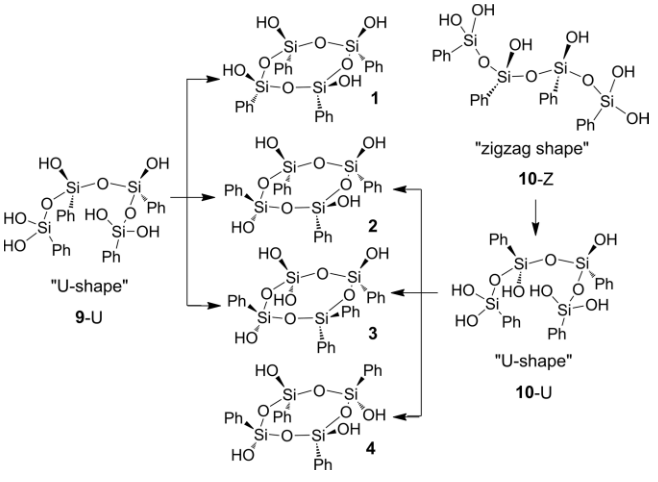
Although there are reports on the structural assignment of diastereomers **1**–**4**,[6,10] isolation and structural assignment of **1**–**4** were done by us to exclude ambiguity. A solution consisting of all four diastereomers was obtained by the acid-catalyzed isomerization [methanesulfonic acid (MSA) in THF] of the crystalline product after CS_2 treatment (Figure 2, c). Diastereomers

1–**4** were all isolated as pure crystals by silica-gel column chromatography with hexane/ethyl acetate mixture as the eluting solvents (eluted in the order **4**, **3**, **2**, and **1**) and subsequent crystallization. Figure S1 (Supporting Information) shows HPLC chromatograms of the mixture after isomerization and each isolated pure isomer. Among the four diastereomers, the structures of **3** and **4** were unambiguously determined by single-crystal X-ray analysis. Figures S2 and S3 show the molecular structure of **3** and its arrangement in the crystal through hydrogen bonds, respectively.[12] X-ray structure analysis of **4** was reported by Kawakami,[6a] and our results were almost identical. Further structural assignment of **1**–**4** was based on LC–MS (ESI-TOF) (Figures S5 and S6) and ^{1}H NMR, ^{13}C NMR, and ^{29}Si NMR spectroscopy (Figures S23–S37). Each isomer was further characterized by thermogravimetric analysis differential thermal analysis (TGA-DTA), differential scanning calorimetry (DSC), IR spectroscopy, and Raman spectroscopy (Figures S7–S22). Our assignments are consistent with those in previous reports.[6,10]

On the basis of the above observations, the presence of only a negligible amount of isomer **4** (less than 0.1 % yield) in the condensation reaction products became clear, and it was confirmed by repeated experiments. As a result, it was concluded that the solid products consisted only of diastereomers **1**, **2**, and **3**, and they were considered as the kinetic products of the original condensation reaction but not the equilibrium products of the acid-catalyzed isomerization reaction, because the latter results in the formation of all four diastereomers (see below). A possible explanation for the selective formation is described below.

It is quite reasonable to consider that the cyclotetrasiloxane framework is produced through the intramolecular condensation reaction of two terminal silanol groups of the linear tetrasiloxanes, *meso*-isomer **9** and/or DL-isomer **10**, as shown in Scheme 2. If it is assumed that no configurational inversion occurs at the central two silicon atoms during the cyclization process, *meso*-isomer **9** can produce only three diastereomers **1**, **2**, and **3** but not **4**, because the products must contain at least one *cis*-1,3-dihydroxy-1,3-diphenyldisiloxane unit in the molecule. On the other hand, DL-diastereomer **10** can produce only **2**, **3**, and **4** but not **1**, because the products must contain at least one *trans*-1,3-dihydroxy-1,3-diphenydisiloxane unit in the molecule. Consequently, the selective formation of **1**, **2**, and **3** without **4** can be explained by assuming that the cyclotetrasiloxanes are produced through the exclusive cyclization of *meso*-isomer **9**.

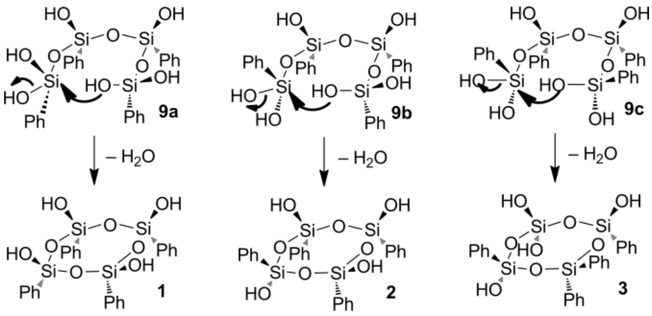
Such a selective cyclization reaction producing **1**–**3** can be explained by considering the differences in the stable conformations of linear tetrasiloxanes **9** and **10** in a strongly hydrophilic aqueous medium [acidic water/acetone (>20:1) mixture]. Under such conditions, the linear tetrasiloxanes are expected to prefer to adopt conformations having hydrophilic hydroxy groups and hydrophobic phenyl groups located on opposite sides of the molecular plane. As shown in Scheme 2, *meso*-diastereomer **9** would prefer "U-shape" conformation **9**-U, which is easy to cyclize by condensation between the terminal $PhSi(OH)_2$ moieties. On the other hand, DL-diastereomer **10** would prefer "zigzag-shape" conformation **10**-Z, which is difficult to cyclize. We suppose that **10** is converted into **9** by inversion of configuration of one of the central two silicon atoms by acid catalysis and then the latter further cyclizes to the cyclotetrasiloxanes. The high yields of formation of cyclotetrasiloxane diastereomers **1**–**3** (72 %) through only diastereomer **9** can reasonably be interpreted by considering such isomerization. A long reaction period for the completion of the condensation (more than 20 h) seems likely to suggest that the formation of linear tetrasiloxanes **9** and **10** is slow relative to the rate of cyclization of **9**, because no detectable amounts of **9** and/or **10** were observed by HPLC analysis of the reaction mixture.



Scheme 2. Cyclization of linear tetrasiloxanes, *meso*-isomer **9** and DL-isomer **10**, to form cyclotetrasiloxane diastereomers.

For further confirmation of our hypothesis, additional experiments were performed to exclude other possibilities. One of the other possible pathways for the selective formation of diastereomers **1**–**3** without **4** is selective crystallization of the three diastereomers from the reaction mixture containing all four diastereomers and rapid equilibration of remaining **4** in the solution under the reaction conditions. To examine this possibility, crystallization of an equilibrated mixture consisting of all four diastereomers (**1**/**2**/**3**/**4** = 10.8:48.4:22.3:16.7 %) was tested by pouring an acetone solution of the mixture into an aqueous solution containing the same concentration of hydrochloric acid as the condensation reaction mixture. HPLC analysis of the precipitated solid (64 % recovery) clearly showed the presence of all diastereomers **1**–**4** (**1**/**2**/**3**/**4** = 21.6:49.6:17.2:9.4 %) and not only three. Therefore, the possibility of selective crystallization of **1**–**3** and rapid equilibration of **4** was excluded.

The product distribution of diastereomers **1**, **2**, and **3** in the original solid mixture (65.5, 14.1, and 5.1 %, respectively) can be explained qualitatively by considering the stabilities of conformers **9a**, **9b**, and **9c** (Scheme 3). As discussed above, conformers having a greater number of hydroxy (or equally phenyl) groups on one side of the molecular plane are considered to be more stable in hydrophilic aqueous media. Diastereomer **1** will be formed through "U-shaped" conformer **9a**, which is considered to be the most stable one among the three conformers by the arrangement of four hydrophilic hydroxy groups on one side and all four hydrophobic phenyl groups on the opposite side of the molecular plane. Diastereomer **2** will be formed through moderately stable conformer **9b** having three hydroxy groups on one side of the molecular plane, and diastereomer **3** will be formed through least-stable conformer **9c** having two hydroxy groups on one side of the molecular plane.



Scheme 3. A plausible cyclization process forming cyclotetrasiloxane diastereomers **1**, **2**, and **3** from conformers **9a**, **9b**, and **9c** of *meso*-diastereomer **9**.

Stereochemical interconversion of the cyclotetrasiloxanes was examined by the reaction of **1** in THF with MSA as a catalyst. Figure 3 shows the time-dependent changes in the relative concentrations of the diastereomers, as monitored by HPLC. The curves for the changes in the relative abundances in the diastereomers are not far different from those reported by Klement'ev[10] for the similar reaction of **1** in acetone with Me_3SiCl as a catalyst. One of the distinctive differences is the presence of induction periods for the formation of **3** and **4**. This strongly suggests stepwise conversion of the diastereomers, as shown in Scheme 4. Diastereomer **2** is produced by inversion of configuration of one of the four silicon atoms in **1**. Diastereomers **3** and **4** are successively formed by further inversion of configuration of the silicon atoms in **2** at the adjacent and diagonal positions, respectively, of the initially inverted silicon atom. Klement'ev suggested that the isomerization proceeds directly from **1** to **3** and **4** with dissociation of the cyclotetrasiloxane ring in addition to the stepwise manner. However, our results suggest the isomerization proceeds, at least mainly, without dissociation of the cyclotetrasiloxane ring.

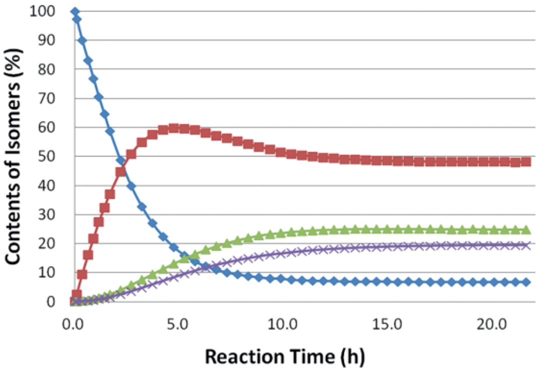
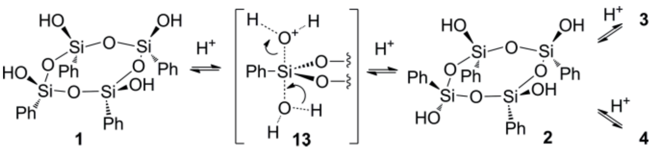


Figure 3. Time-dependent changes in the relative concentrations of the diastereomers (blue: **1**, red: **2**, green: **3**, purple: **4**) in the acid-catalyzed isomerization reaction of **1** (5.3 mg) with 1000 ppm MSA in THF (1.0 mL) at 5 °C.

Considering these observations and detailed studies about the reaction stereochemistry on silicon atoms by Corriu[13] and the involvement of hypervalent species by Bassindale,[14] we propose a S_N2-Si[15] mechanism for this interconversion, which includes protonation of a hydroxy group and backside attack of a water molecule to the silicon atom with inversion of configuration through transition state **13**, as shown in Scheme 4.



Scheme 4. A proposed mechanism for the stereochemical isomerization reaction of the cyclotetrasiloxane diastereomers.

The acid-catalyzed isomerization reaction reached equilibrium after 20 h. According to the relative ratio of the components, the relative free-energy differences (ΔG) were calculated, as shown in Table 1. It is clearly shown that *cis*,*cis*,*trans*-isomer **2** is the most stable isomer and that the *cis*,*cis*,*cis* isomer is the least stable one.

Table 1. Relative composition of diastereomers **1**–**4** in the equilibrium mixture determined by HPLC and their free-energy differences.

Diastereomer	Relative composition	ΔG [kJ mol^{-1}]
1	0.142	4.8
2	1.000	0.0
3	0.518	1.6
4	0.404	2.2

Conclusions

The condensation reaction of **5** in aqueous medium under Brown's conditions was revealed to provide three cyclotetrasiloxane diastereomers, that is, **1**–**3**, without the formation of a possible forth diastereomer, that is, **4** (<0.1 %), and not only **1**, as was believed since the original report.[1d] This was explained reasonably by assuming a cyclization process to form the cyclotetrasiloxanes exclusively from linear tetrasiloxane *meso*-diastereomer **9**, which was considered to adopt a U-shaped conformation in hydrophilic aqueous media and to be more suitable for cyclization than DL-diastereomer **10**. The distribution of diastereomers **1**–**3** in the original product mixture was also reasonably explained by considering the stability of the conformers of **9** leading to the cyclotetrasiloxanes. We believe this investigation provides a firm and reliable basic understanding of the initial stage of the silsesquioxane condensation reaction process, including the stereochemistry of the intermediates. These findings should contribute not only to the progress of basic siloxane chemistry but also to the industrial production of siloxane materials having superior properties.

Acknowledgments

This work was supported by the Ministry of Economy, Trade and Industry, Japan (METI) (Development of Innovative Catalytic Processes for Organosilicon Functional Materials project, grant to K. S.) and by the New Energy and Industrial Technology Development Organization (NEDO). The authors thank Dr. Y.-K. Choe for helpful discussions.

Keywords: Cyclization · Silicon · Cyclotetrasiloxane · Diastereoselectivity

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[11] Compounds observed at retention times of 5.82 and 6.06 min in Figure 1 (a) were not fully identified, but they are supposed to be pentasiloxanes having a cyclotetrasiloxane or a cyclopentasiloxane ring, as determined by MS (ESI-TOF) measurements.

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Received: April 19, 2016

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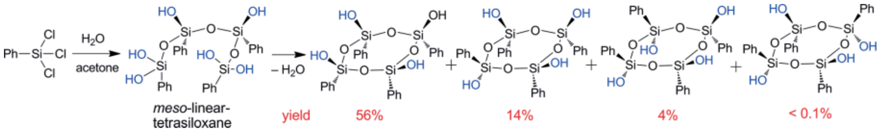

Selective cyclization: Hydrolytic condensation of $PhSiCl_3$ in aqueous medium affords only three cyclic tetrasiloxane diastereomers out of four conceivable ones. This phenomenon can reasonably be explained by exclusive cyclization through the *meso*-linear-tetrasiloxane.

DOI: 10.1002/ejic.201600454