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Separation of asymmetrically capped double-decker silsesquioxanes mixtures

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ABSTRACT

A synthetic path to asymmetric side-capped double-decker shaped silsesquioxanes (DDSQ) and subsequent isolation is described. By strategically using a combination of dichloro and trichlorosilane capping agents, a resultant product with mixed silanol functionalities was obtained. The use of preparatory liquid chromatography (LC) cleanly separated DDSQ compound with asymmetric functionality, and HPLC provided a quantitative technique to analyze mixture ratios. These mixture ratios did not follow the expected statistical trend due to the steric effects on the rate of capping. As a consequence, a decreased amount of the desired asymmetric DDSQ was observed in some cases. This was overcome by varying the ratio of capping agents. Overall, this work demonstrates access to asymmetric DDSQ cages is feasible, and LC is an effective separation technique.

1. Introduction

Functionalized double-decker silsesquioxanes, DDSQs, are building blocks for diverse applications such as polymer chain modifiers [1–5]. Polymer chains modified with DDSQ can obtain low dielectric constant, enhanced hydrophobicity, and elevated degradation temperature [3,4,6,7]. These materials are derived from the tetrasilanol double-decker silsesquioxane or DDSQ$(OH)_4$ (**1**). This compound is composed of two cyclic *syn-cis*-1,3,5,7-tetraoltetraphenyltetrasilsesquioxane bridged by two oxygens and can be functionalized by a side-capping reaction with dichlorosilanes, Scheme 1, to produce DDSQs that are the building blocks in many polymer applications [4,7–9].

Side-capping with a dichlorosilane that has two distinct R-groups results in symmetric *cis* and *trans* isomers [8,9]. The products are symmetric because both sides are capped with the same capping agent. Separation of these *cis* and *trans* isomers using fractional crystallization (FC) has been reported [5,8,9]. FC is a technique that allows separation based on solubility differences between two or more analytes in a solution [10]. For example, *cis* and *trans*-DDSQ side-capped with 4-(dichloro(methyl)silyl)aniline were separated with high purity when the initial ratio between *cis* and *trans* isomers was different than 50% to 50% *cis*:*trans* using THF as the good solvent and hexane as the poor solvent [8]. DDSQ side-capped with isobutyl trichlorosilane was first separated using FC, and then subsequently polymerized using mostly a single isomer type was studied [5]. Also, separation of mostly *trans* isomer from the mixture obtained after side-capping of DDSQ$(OH)_4$ with methyldichlorosilane was done using FC [9]. However, Schoen et al. and Hoque et al. reported that further purification via liquid chromatography (LC) was needed, which for polar DDSQ isomers is a separation technique with superior resolution in comparison to FC [5,8].

LC is a technique that allows isolation of individual molecular compounds even with a partial overlap in retention times [11–13]. For many applications, this technique is faster than FC [14]; furthermore, industrially LC is less expensive despite the differences in initial cost. LC is based mainly on interactions between analytes, stationary phase, and mobile phase [11,15]. Among the many LC operation modes, normal phase (NP) and reverse phase (RP) have been widely used [16–19]. Separation for both NP and RP depend on polarity differences between the analytes. However, in NP analytes interact with a polar stationary phase and a low polar mobile phase [11]. Despite the advantages of LC, there are no reports for the separation of DDSQ compounds using LC except for further purification after FC.

The use of LC to isolate a DDSQ compound with asymmetric functionalities, ie the **AB** compound in Scheme 2, is proposed as an engineering solution to expand the field of application for functionalized DDSQs. In this work DDSQ$(OH)_4$ was side-capped with

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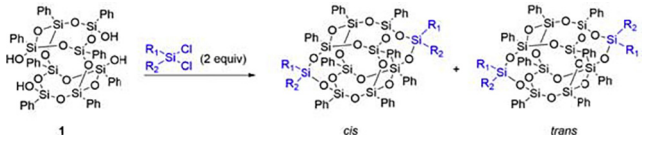


Scheme 1. Side capping of DDSQ(OH)$_4$ (1) with a dichlorosilane.

two different chlorosilanes which would produce a mixture 3 products, **AA**, **AB**, and **BB**. These DDSQ products have zero, one, and two hydroxyl groups after hydrolysis, and are separable by NP due to their polarity differences. Synthetic procedures, separation technique, and identification of the new **AB** compounds will be described in the following sections.

2. Experimental

2.1. General Information

All commercially available chemicals were used as received unless otherwise indicated. $(C_6H_5)_8Si_8O_{10}(OH)_4$ 5,11,14,17-Tetra(hydro)octaphenyltetracyclo[7.3.3.-3^{3,7}]octasilsesquioxane or DDSQ(OH)$_4$ was purchased from Hybrid Plastics. Dimethyldichlorosilane $(CH_3)_2SiCl_2$, vinylmethyldichlorosilane $(CH_3)(C_2H_3)SiCl_2$, methyldichlorosilane $(CH_3)HSiCl_2$, and 3-chloropropylmethyldichlorosilane $(CH_3)(C_3H_6Cl)SiCl_2$ were purchased from Gelest. Methyltrichlorosilane $(CH_3)SiCl_3$ was purchased from Sigma-Aldrich. Triethylamine (Et_3N) was purchased from Avantor and distilled over calcium hydride before use. Deuterated chloroform with 1 vol.% of tetramethylsilane $CDCl_3$-TMS and deuterated acetone acetone-D_6 were purchased from Cambridge isotopes laboratories. Tetrahydrofuran (THF) was refluxed over sodium/benzophenone ketyl and distilled. Reagent grade dichloromethane (DCM) and n-hexanes were degassed with helium for HPLC experiments. The previously listed solvents were purchased from Avantor. Si-gel P-60 was obtained from Silicycle. ^{1}H, ^{13}C, and ^{29}Si were recorded on 500 MHz NMR spectrometers.

2.2. General procedures

2.2.1. General procedure A: synthesis of symmetric DDSQ

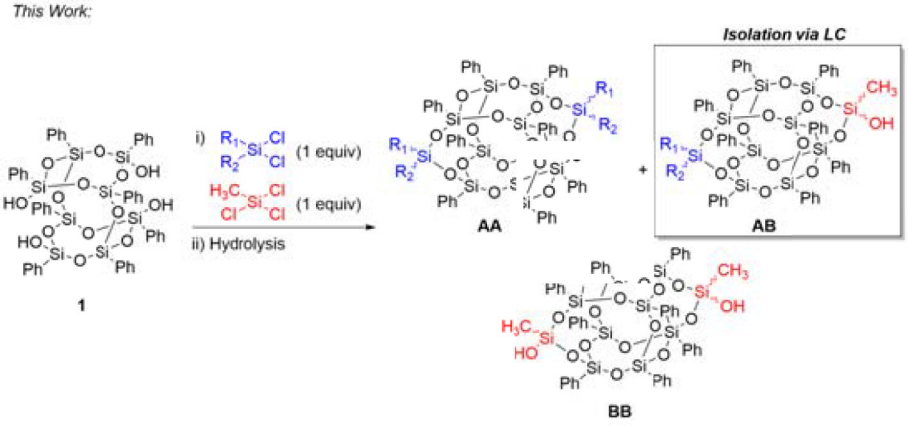
DDSQ(CH_3)(R) was synthesized following the reaction shown in Scheme 1. In a 250 ml flask purged with dry N_2 for 15 min, DDSQ(OH)$_4$ (**1**) (2 g, 1.87 mmol, 1 equiv) was dissolved in THF (60 mL) at room temperature. Dichlorosilane or trichlorosilane (3.74 mmol, 2 equiv.) was added to the DDSQ(OH)$_4$ solution. Et_3N (1.04 mL, 7.48 mmol, 4 equiv.) was added dropwise to the stirring solution. The addition of triethylamine took 5 min in total; a cloudy white suspension was formed and stirred for 4 h. The solution was then filtered through a fine fritted-funnel-filter to remove the solid triethylamine hydrochloride. The solution was dried in a rotary evaporator and then passed through a silica-gel column using DCM as the solvent. It should be noted that all chlorosilane intermediates hydrolyze upon exposure to silica. The volatiles were removed from the resulting solution and further dried at 0.4 mbar and 50 °C for 12 h to afford DDSQ(CH_3)(R) as a white powder. It should be noted the reported spectra are of the *cis*/*trans* mixtures. Full experimental details and product characterization were in the Supporting Information section.

2.2.2. General procedure B: synthesis of DDSQ symmetric and asymmetric mixtures

The synthesis of DDSQ mixture was done following the Scheme 2. In a 250 ml flask purged with dry N_2 for 15 min, DDSQ (OH)$_4$ (**1**) (2 g, 1.87 mmol) was dissolved in THF (60 ml) at room temperature. (CH_3)(R)$SiCl_2$ (1.87 mmol, 1 equiv.) and $(CH_3)SiCl_3$ (1.87 mmol, 0.24 ml, 1 equiv.) were added to the DDSQ(OH)$_4$ solution and stirred for 5 min. Et_3N (1.04 mL, 7.48 mmol, 4 equiv.) was added dropwise to the stirring solution. The addition of triethylamine took 5 min in total which created a cloudy white suspension which was stirred continuously for additional four hours. After, the solution was filtered through a fine fritted-funnel-filter to remove the solid triethylamine hydrochloride. Volatiles was removed from the resulting solution which produced a white powder. This powder was a mixture of three products as shown in Scheme 2. The powder was dissolved in a minimum amount of DCM and passed through a silica-gel column using DCM as the solvent. The silica column hydrolyzed the chlorosilanes into silanols which were isolated. The three separated products were dried at 0.4 mbar and 50 °C for 12 h. Full experimental details and product characterization were in the Supporting Information section.

2.3. Separation of DDSQ mixtures by LC

A glass preparatory chromatography column with 500 ml round top reservoir (L = 60 cm, D = 4 cm) was packed with Si-gel (60 g, H = 40 cm). DCM was flushed through the packed bed under pressure generated by a dry N_2 stream. The packed bed wetting was stopped after no air bubbles, and dry spaces were observed. A concentrated solution of DDSQ mixture in DCM (5 ml, 0.2 g/ml) was gently injected from the top of the wetted Si-gel bed and eluted into the packed bed until no solution was above the packed bed. The column was then gently charged with 500 ml of DCM and then



Scheme 2. Side capping of DDSQ(OH)$_4$ (1) with two chlorosilanes.

flushed using the N_2 stream with an average flow rate of 10 ml/min. Fractions of 5 ml were collected in the bottom of the column until the DCM reached the top of the bed. Each fraction was injected in 5 cm TLC plates of Si-gel supported in Aluminum. TLC was evaluated with DCM and then analyzed under a 245 nm UV-lamp. The graphic description of the TLC separation is shown in the Supporting Information.

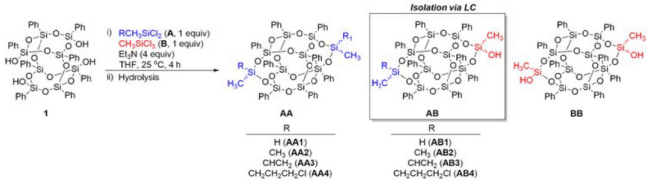
2.4. Characterization of DDSQ materials

Identification of components and their ratios in the mixture, as well as the fractions separated by LC, were done using an Agilent 1110 HPLC system. The samples were first dissolved in DCM and 5 ml injected into a Supelcosil column (L = 250 mm, ID = 4 mm) and separated at 1 ml/min with DCM as the mobile phase. The components were detected in a UV detector at 245 nm. Mixtures and separated samples were evaluated by NMR taking advantage of the three nuclei of the molecules: ^{1}H, ^{13}C, and ^{29}Si. Dry samples (0.2 g) were dissolved in 0.6 ml of $CDCl_3$-1%TMS and placed in a Variant UNITY Innova 600 at 589 MHz for ^{1}H, and 119.16 MHz for ^{29}Si. Fractions were also characterized by mass spectroscopy in a Waters Xevo G2-XS. The ionization was performed by atmospheric pressure chemical ionization (APCI) using acetonitrile as solvent.

3. Results and discussion

3.1. Separation by LC

To obtain asymmetric DDSQ, a dichlorosilane ($R(CH_3)SiCl_2$, **A**) and methyltrichlorosilane (CH_3SiCl_3, **B**) were added to DDSQ $(OH)_4$ (**1**) as is shown in Scheme 3. In addition to the desired **AB** product, two symmetric byproducts are obtained (**AA** and **BB**). This is because the two reactive sides of $DDSQ(OH)_4$ are 7 Å apart; thus after capping one side, there is no additional selectivity toward either capping agent **A** or **B**. Assuming the capping rate is independent of chlorosilane used, the probability to bond any chlorosilane to one of the sides is ½ and the probability of the same type of chlorosilane capping the second side is ½. This indicates that probability to synthesize **AA** or **BB** is 25% for each, and the probability to synthesize AB is ½ or 50% when equimolar amounts of **A** and **B** react with $DDSQ(OH)_4$ which provides an expected isomer ratio of 25:50:25 **AA**:**AB**:**BB**. However, by using methyltrichlorosilane as the **B** capping agent, the mixture of products will have zero, one and two chloro moieties. During the workup, hydrolysis of the resulting chloro group occurs readily leaving zero, one, and two silanols; thus, the final products contain a varying number of silanol groups and separation can be achieved based on polarity. Hydrolysis of the chlorosilane moiety can be achieved by mixing the crude reaction mixture with water; however, similar yields were obtained when the crude was simply added to silica (see SI for details). This indicates rapid hydrolysis occurs on silica. With silica-gel used as the stationary phase, compound **BB,** with two silanol groups, migrates slower than compounds **AB1-4** which in turn migrate slower than compounds **AA1-4**. This technique allows separation of the product mixtures as long as R on the **A** capping agent is non-polar. This is demonstrated by the retardation factor (R_f) on TLC. A R_f of 0.74 for **BB**, 0.83 for **AB1-4** and 0.93 for **AA1-4** was calculated. These R_f values were independent of the R moiety used in the synthesis.



Scheme 3. Proposed synthesis to obtain a mixture of AA, AB, and BB.

3.2. HPLC identification

Chromatograms for independently synthesized **AA1-4** exhibit a single peak at t_r = 2.6 min as shown in Fig. 1a–d. This finding agrees with TLC results, where R does not have an apparent effect on retention times. Two peaks (t_r = 18 min, t_r = 23 min) were observed for **BB** as shown in Fig. 1e. These peaks correspond to the *trans/cis* configurations. This behavior was reported previously in the separation of DDSQ cages side-capped with phenylamines [8]. Chromatograms for reactions following Scheme 3 have four peaks (t_r = 2.6 min, t_r = 6.5 min, t_r = 18 min, t_r = 23 min) as seen in Fig. 1f–i. Products **AA1-4** and **BB** are present in the reaction mixtures as confirmed by the retention times for independently synthesized compounds (see SI for experimental details). Excitingly, the peak at 6.5 min indicates the presence of asymmetric DDSQs **AB1-4**. To date, no literature in the separation of systems with similar DDSQs has been reported. Nevertheless, previous work in the separation of relatively large or bulky molecules by HPLC using a Si-gel stationary phase were developed for polyols and polymers with a varying number of hydroxyl groups [20,21].

The peaks observed in HPLC chromatograms were sufficiently resolved, so the relative ratio of the three compounds was evaluated. Since each compound has the same number of chromophores, UV was used for quantification. The results are shown in Table 1. As discussed above, we expected a statistical ratio of 25:50:25 for **AA**:**AB**:**BB**; however, significant variations were observed in the HPLC ratios. These variations were usually favoring capping of the chlorosilane with lower steric hindrance. The smallest chlorosilane in this work was methyldichlorosilane, when this competed with methyltrichlorosilane the highest yield of **AA** was produced. On the other hand, the bulkiest chlorosilane explored in this work was chloropropyl-methyldichlorosilane, when this

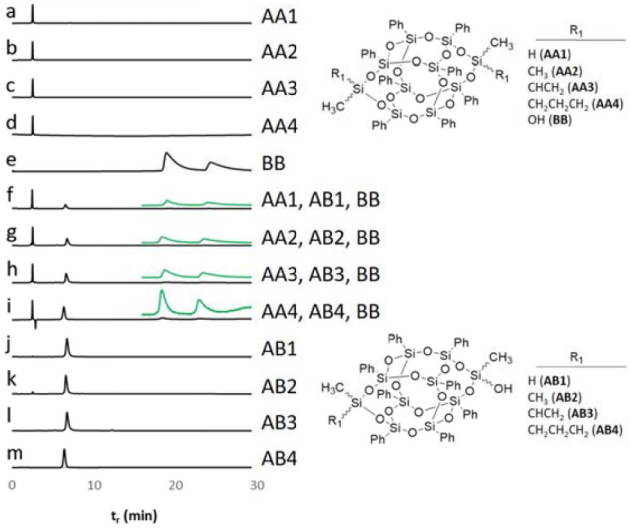


Fig. 1. Chromatograms for products of pure $(C_6H_5)_8Si_{10}O_{14}(CH_3)_2(R)_2$ obtained following Scheme 1 (a–e). Chromatograms for mixtures of $(C_6H_5)_8Si_{10}O_{14}(CH_3)_2(R)_2$, $(C_6H_5)_8Si_{10}O_{14}(CH_3)_2(R)(OH)$, and $(C_6H_5)_8Si_{10}O_{14}(CH_3)_2(OH)_2$ following synthesis proposed in Scheme 2. The absorbance in the region between 15 and 30 min is zoomed for reader convenience (f–i). The second fraction separated by LC corresponding to $(C_6H_5)_8Si_{10}O_{14}(CH_3)_2(R)(OH)$ (j–m).

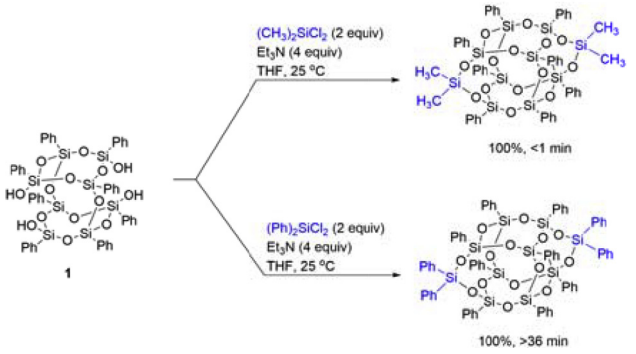
Table 1
The calculated ratio of products in DDSQ mixtures after separation by HPLC.

R	$(C_6H_5)_8Si_{10}O_{14}(CH_3)_2(R)_2$ AA (%)	$(C_6H_5)_8Si_{10}O_{14}(CH_3)_2(R)(OH)$ AB (%)	$(C_6H_5)_8Si_{10}O_{14}(CH_3)_2(OH)_2$ BB (%)
H	42.0	38.8	19.2
CH_3	32.3	48.1	19.6
$CHCH_2$	27.6	50.9	21.5
$CH_2CH_2CH_2Cl$	15.3	39.7	45.0

competed against methyltrichlorosilane the lowest yield of **AA** was obtained. Overall, the results in Table 1 show that as the sterics of the **A** dichlorosilane increase the amount of **AA** product decreases. This indicates that the rate of side-capping is significantly affected by the sterics of the capping agent.

To verify this, two capping agents, $(CH_3)_2SiCl_2$ and $(Ph)_2SiCl_2$, with distinct steric profiles were selected and reacted with DDSQ $(OH)_4$, Scheme 4. These reactions were followed by ^1H NMR and ^{29}Si NMR. It was found that DDSQ$(OH)_4$ was completely converted to DDSQ$(CH_3)_4$ before 59 seconds when the first ^1H NMR was collected. However, full capping of DDSQ$(OH)_4$ with diphenyldichlorosilane took between 36 min and 100 min to complete; thus, conclusively demonstrating that the sterics of the chlorosilanes significantly affect the rate of the capping reaction.

An unfortunate byproduct of the non-statistical ratios is that in cases where there is a significant difference in sterics between the **A** and **B** capping agent, the ratio of desired **AB** product suffered. For example in the first and last entry of Table 1, ~10% loss of **AB** product was observed. To see if this shortcoming could be overcome, we varied the ratios of $H(CH_3)SiCl_2$:$(CH_3)SiCl_3$ from 1.5:0.5 to 0.5:1.5. The HPLC ratios and the mass percentages after separation by liquid chromatography are summarized in Table 2. In every case, HPLC ratios match closely with the isolated masses from LC. The data in Table 2 indicates a preference towards the formation



Scheme 4. Side-capping of DDSQ$(OH)_4$ with chlorosilanes having moieties with different sterics, 100% conversion time for capping with $(CH_3)_2SiCl_2$ less than 1 min, 100% conversion time for capping with $(C_6H_5)SiCl_2$ higher than 36 min.

Table 2
Mass fraction analysis of products (in percent) after DDSQ mixtures synthesis with different ratios of methyldichlorosilane and methyltrichlorosilane. *HPLC column is calculated based on HPLC peak analysis and Mass column is calculated based on analytic balance measurement after separation by preparatory liquid chromatography Mass.

$H(CH_3)SiCl_2$: $(CH_3)SiCl_3$	**AA1** (%)		**AB1** (%)		**BB** (%)	
	*HPLC	*Mass	*HPLC	*Mass	*HPLC	*Mass
1.5:0.5	64.1	65.1	26.7	27.9	9.2	7.0
1.2:0.8	49.5	42.3	37.1	45.4	13.4	12.3
1: 1	42.0	45.2	38.8	32.5	19.2	22.2
0.8:1.2	36.6	24.3	44.9	50.7	18.5	25
0.5:1.5	6.4	6.0	28.9	30.0	64.7	64.0

of DDSQ capped in both sides with methyldichlorosilane just as in Table 1. However, this is mitigated when an excess of methyltrichlorosilane is used. Excitingly, close to the expected probability of 25:50:25 is obtained when a ratio of 0.8:1.2 was used.

4. Conclusions

When two different chlorosilanes compete for capping sites on DDSQ$(OH)_4$, mixtures of **AA**, **AB**, and **BB** are produced. The separation of these products was possible because a varied number of hydroxyl groups are present in each molecule. HPLC, a valid method to quantify the ratios of products, showed deviations from the expected statistical ratio of 25:50:25 **AA**:**AB**:**BB**. These deviations are due to the rate of side-capping being significantly affected by the sterics of the capping agent. In some cases, this deviation adversely affected the amount of desired **AB** product produced. This was overcome by changing the ratios of the capping agents such that the more sterically hindered capping agent was in excess. Overall, our technique provides a route to **AB** DDSQ systems with an average yield of 30%. This can be further optimized by modifying the ratio between chlorosilanes or modifying the reaction conditions. Isolation of **AB** DDSQ is a step forward to reach block copolymers linked by a single asymmetric DDSQ. Present research efforts are focused on finding a direct synthesis of difunctional DDSQ and exploring the properties of DDSQ based block copolymers.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.poly.2018.08.016.

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