

# Hybrid Organic/Inorganic Dendritic Triblock Copolymers: Synthesis, Nanostructure Characterization, and Micellar Behavior

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**ABSTRACT:** A new class of amphiphilic dendritic ABA triblock copolymers, which is based on organic linear polyethylene oxide (PEO) and inorganic dendritic carbosiloxane (CSO) was synthesized. The strategy used in synthesizing these materials is based on divergent method using hydrosilylation-alcoholysis cycles. The reaction conditions and structural features of dendrimers were analyzed by different physicochemical techniques such as: GPC, NMR, UV spectroscopy, DSC, and viscometry. The generational limit of dendrimer after the first generation, OSC-D<sub>G<sub>1</sub></sub>-PEO-D<sub>G<sub>1</sub></sub>-CSO, forced us to employ HSiCl<sub>2</sub>CH<sub>3</sub> as branching reagent. Also further hydrosilylation of the third generation yielded an irregular structure species. Self-assembling and morphological studies of first, OSC-D<sub>G<sub>1</sub></sub>-PEO-D<sub>G<sub>1</sub></sub>-CSO, and second, OSC-D<sub>G<sub>2</sub></sub>-PEO-D<sub>G<sub>2</sub></sub>-CSO, generations in aqueous medium were monitored by using

fluorescence, TEM and DLS techniques. However, the dendritic block copolymer with third generation, OSC-D<sub>G<sub>3</sub></sub>-PEO-D<sub>G<sub>3</sub></sub>-CSO, could not be dispersed in aqueous phase. The diameters of dendritic micelles had a narrow distribution in the ranges of 69 and 88 nm, respectively. Although the micelles were stable even in first generation, partition equilibrium constants of pyrene and critical micelle concentration in both of dendritic micelles imply that the micellar behaviors of the supramolecules strongly depend on the hydrophobic block's size in which increasing generation effectively promoted the micelle formation. © 2010 Wiley Periodicals, Inc. *J Appl Polym Sci* 117: 1085–1094, 2010

**Key words:** block copolymers; dendrimers; micelles; synthesis

## INTRODUCTION

Flory's theory of highly branched polymers was a turning point in developing some of dendritic structures over the past two decades.<sup>1–3</sup> Chemists have recently combined linear and dendritic structures to synthesize novel block copolymers. It can be speculated that the targeted dendritic architectures with hydrophilic and hydrophobic segments will have micellar features that can be tailored for a certain application.<sup>4–9</sup> Recently Fréchet et al. have designed the formation of dendritic conjugates with different kinds of hydrolytically labile linkages based on 2,2-bis(hydroxymethyl)propanoic acid. These types of dendrimers are hybrid macromolecules consisting of PEO as core and dendritic polyester moieties as terminal blocks. In these types of structures, the effi-

cacy of the macromolecules as drug carriers depends on the size of the dendritic end groups. The other types have reverse composition in which the PEO represented the peripheral groups.<sup>10–12</sup>

On the other hand, structure-biocompatibility relationship for some of dendritic micelles illustrates that, regardless of internal unit structure, dendrimers with cationic end groups induced hemolysis and these dendrimers are cytotoxic. However, dendrimers with anionic end groups as well as carbosilane dendrimers grafted by PEO were not hemolytic up to a concentration of 2 mg/mL.<sup>13</sup>

Currently, researches into dendrimers are developing into an interface between polymer, organic, inorganic chemistry, and nanosciences.<sup>14</sup> Carbosiloxane dendrimers, as one of the most important classes of silicon-based dendrimers, have received much attention due to their excellent chemical and thermal stability.<sup>15</sup> They are hybrids between pure inorganic and organic materials and exhibit properties of both organic moiety and inorganic framework, because they contain flexible Si–O backbones and the organic substituents attached to the silicon atoms.<sup>16–22</sup>

On the other hand, due to lack of researches on applications of carbosiloxane-based dendritic block

Additional Supporting Information may be found in the online version of this article

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copolymers and necessity to further investigations, we were motivated to design new amphiphilic linear-dendritic triblock copolymer with organic/inorganic identity. This work, based on our previous investigations, reports synthesis of carbosiloxane-based dendritic macromolecules by using the hydrosilylation-alcoholysis methodology.<sup>23–27</sup> PEO was chosen because of its distinguished effects on biocompatibility and solubility of copolymers especially in the field of bioapplications.<sup>28</sup>

To establish this system as a suitable carrier, micellar properties of the dendritic amphiphilic copolymers in aqueous media were studied by fluorescence techniques and dynamic light scattering. Also, considering their characteristic reaction chemistry, micellar properties in aqueous phase, and development for potential applications were examined. The solubility capacity of the micellar aggregates were evaluated using pyrene as a highly hydrophobic compound. These results indicated that the dendritic micelles can be considered as promising carrier systems for targeting delivery of lipophilic drug molecules (Fig. 1).

#### A note on symbolism

The following examples illustrate the symbolism used:

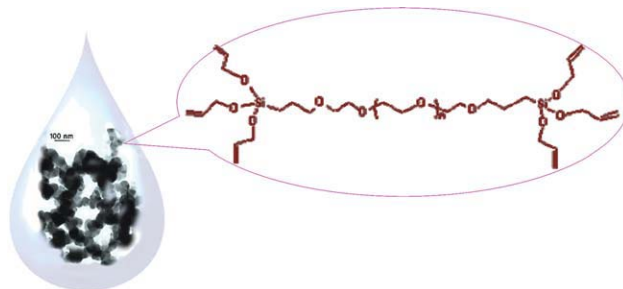
OSC- $D_{G_2}$ -PEO- $D_{G_2}$ -CSO ( $G_2$ ) and Cl-SiC- $D_{G_2}$ -PEO- $D_{G_2}$ -CSi-Cl ( $G_2$ -Cl) stand for dendritic triblock copolymers with second generation ( $D_{G_2}$ ), obtained by two terminal carbosiloxane blocks, which contains Si—O bonds that arise from allyl alcohol (OSC— or —CSO) and Si—Cl bonds (Cl—SiC or CSi—Cl), respectively. These copolymers contain a PEO block with  $M_n$  1000 as the core.

Allylated PEO and PEO containing two silicon atoms called as  $G_0$  and  $G_1$ , respectively, to facilitate the representation of data in different sections of the manuscript.

## EXPERIMENTAL

### Materials

All glasswares were thoroughly dried with vacuum and all reactions were carried out under dried argon atmosphere using standard Schlenk techniques. Karstedt catalyst (Aldrich; platinum–divinyltetramethyldisiloxane complex) was used as received. PEO (Merck; molecular weight 1000) was precipitated from methylene chloride into *n*-hexane and dried in vacuum. Allyl bromide (Merck) was vacuum-distilled over calcium chloride, allyl alcohol (Merck) was distilled from Na metal and both of them were stored on molecular sieves 4 Å. TMEDA (Merck; tetramethyl ethylene diamine) was refluxed with KOH



**Figure 1** A graphical abstract of amphiphilic ABA type carbosiloxane-based triblock copolymer as dendritic micelle in first generation. [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]

and freshly distilled. Trichlorosilane (Merck), methyldichlorosilane (Aldrich), and pyrene (Merck) were used without further purification. Sodium hydride (Merck; 80% in mineral oil). All solvents were purified by a procedure described in the literature.<sup>22</sup>

### Instruments

Nuclear magnetic resonance (NMR)

$^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra were carried out on a Bruker AC 400 MHz spectrometer.

Gel permeation chromatography (GPC)

Molecular weights and molecular weight distributions were determined with a gel permeation chromatograph (GPC, WATERS-150 C) equipped with a 410 RI detector, a 510 HPLC pump, and m-Styragel columns with pore sizes of  $10^2$ ,  $10^3$ , and  $10^4$  Å. The eluent was THF, and the molecular weights were calibrated with polystyrene standards.

### Micelle preparation

Micelles of the triblock copolymers were prepared in aqueous solution. The triblock copolymer of 0.2 g was dissolved in THF and of 5.0 mL in a 100 mL flask and after that redistilled water 40 mL was added at the rate of one drop every 10 s under vigorous stirring. Subsequently, the THF in the aqueous solution was removed with a rotary evaporator under vacuum for 3 h. The remained micelle solution was diluted with redistilled water to 100 mL. For the fluorescence measurement, pyrene solution in THF ( $1.2 \times 10^{-3}\text{M}$ ) was added to redistilled water to give a pyrene concentration of  $12 \times 10^{-7}\text{M}$  and then THF was removed. All the samples were sonicated for 10 min and were allowed to stand for 1 day before fluorescence measurements. The stock solution was further diluted to yield sample solutions of  $10^{-4}$  to  $5 \times 10^{-1}$  mg/mL for the copolymer.

### Fluorescence measurements

All the fluorescence measurements were performed using a JASCO FP-750 spectrofluorometer using thermostat cell unit. The solutions were kept at room temperature for 24 h to reach solubility equilibrium of pyrene in the aqueous phase. Excitation was carried out at 237 nm, and emission spectra were recorded at 377 nm. A critical micellar concentration (cmc) value was determined from intersection of the tangent to the curve at the inflection with horizontal tangent through the points at low concentration.

### Transmission electron microscopy (TEM)

TEM experiments were carried out on a LEO 906 Instrument operating at an acceleration voltage of 100 kV. TEM sample was prepared by dipping a copper grid with Formvar film into the freshly prepared nanoparticles solution (0.5 mg/mL). After the deposition, the aqueous solution was blotted away with a strip of filter paper and dried in air.

### Dynamic light scattering measurements (DLS)

The hydrodynamic diameter of micellar particles was determined with a He-Ne Laser Light Scattering (Photon Correlation Spectroscopy-SEMATECH). A scattering angle of 90° was used for dynamic light scattering (DLS) evaluations at  $k = 632.8$  nm. Size and size distribution of particles were estimated by cumulant method.

### Differential scanning calorimetry (DSC)

DSC measurements were carried out on a DSC Lines DSC L63. It is equipped with a refrigerated cooling system. All the samples equilibrate at  $-110^{\circ}\text{C}$  and then start to warm with a ramp of 10 K/min up to  $350^{\circ}\text{C}$ .

### UV-Vis spectrophotometry

UV spectra were measured by a SHIMADZU UV-1700 Pharmaspec UV-Vis spectrophotometer.

### Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF)

MALDI spectra were obtained using a Voyager-Elite time-of-flight mass spectrometer (PerSeptive Biosystem) operated at 25 kV accelerating voltage in reflectron mode with positive ionization. The samples were prepared both as sample matrix solutions (3,5-dihydroxy benzoic acid, THF) and as sample matrix silver trifluoroacetate (AgTFA) solutions (dithranol 10 mg/mL, AgTFA 0.1%, THF).

### Viscometry measurements

Viscosity measurements were carried out with Ubbelohde type viscometer equipped with a capillary of 0.45 mm diameter. Solutions were filtered prior to any measurements and apparatus was thermostated at  $25^{\circ}\text{C}$ .

### Procedure for hydrosilylation reaction

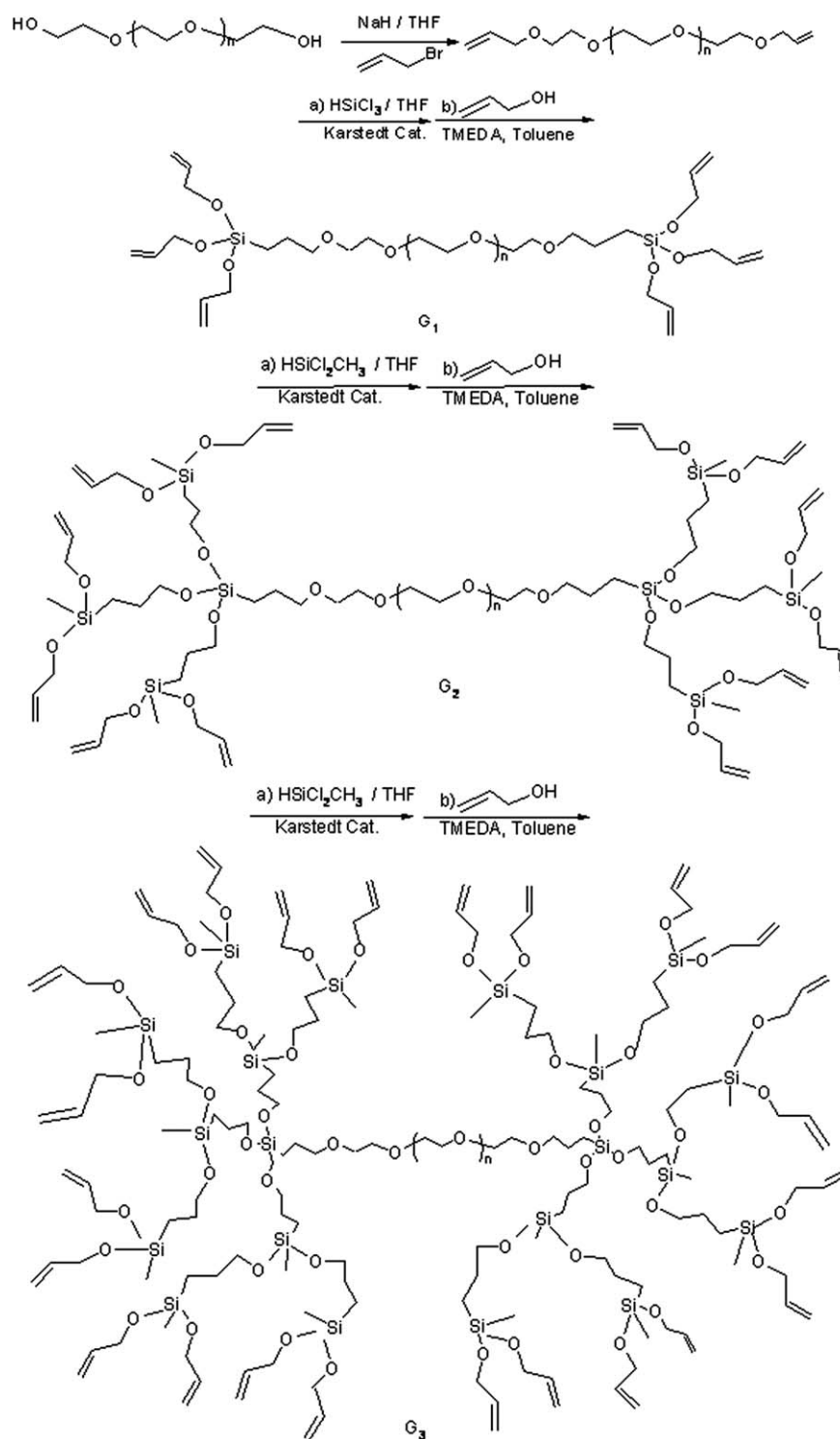
Hydrosilylation process was carried out with Karstedt's catalyst [Pt(0)-divinyltetramethyldisiloxane complex] with Schlenk-type material purged with argon. Combination of hydrosilylation and alcoholysis reactions has been recently reported.<sup>22</sup> Here, only a model example of the modified procedure for the preparation of all dendrimers is shown.

### Synthesis of diallyl PEO ( $G_0$ )

Sodium hydride (7.8 g, 80% in mineral oil, 195 mmol) in THF (100 mL) was added very slowly to a solution of PEO (20 g, 20 mmol) in THF (150 mL) at  $5^{\circ}\text{C}$  (caution: otherwise the solution produces bubbles and starts to rise), temperature was raised up to ambient temperature gently. The reaction mixture stayed at this temperature for 6 h with vigorous agitation. After the evolution of  $\text{H}_2$  ceased, a solution of allyl bromide (23.6 g, 195 mmol) in THF (150 mL) was added to the reaction mixture and then stirred at  $35^{\circ}\text{C}$  for 24 h. The crude product with light brown color was filtered through sintered glass filter and finally the solvent was evaporated and diallylated product was purified by repeated precipitation from methylene chloride into cold *n*-hexane obtaining a white powder (yield: 87%).

### Synthesis of Cl-SiC- $D_{G_1}$ -PEO- $D_{G_1}$ -CSi-Cl ( $G_1$ -Cl)

The operations were carried out in an inert argon atmosphere. Karstedt catalyst ( $12.6 \times 10^{-5}$  mmol, 0.05 mL) was added to a solution of  $G_0$  (1.95 g, 1.80 mmol), trichlorosilane (0.63 g, 20 mmol), and anhydrous THF (50 mL). The mixture was kept at  $20^{\circ}\text{C}$  for 1 h under vigorous magnetic stirring and additionally at  $40^{\circ}\text{C}$  until no allyl groups were detected by FTIR ( $1635\text{ cm}^{-1}$  typically 17 h). Excess trichlorosilane and THF were removed under reduced pressure at  $22^{\circ}\text{C}/3\text{ mmHg}$  and  $G_1$ -Cl was obtained as a colorless liquid and immediately was exposed to reactions of next step. Further purification was not available in this stage due to obtained materials sensitivity against moisture.



**Scheme 1** Synthetic method of carbosiloxane-based dendritic copolymers utilizing hydrosilylation-alcoholysis process.

### Synthesis of OSC-D<sub>G<sub>1</sub></sub>-PEO-D<sub>G<sub>1</sub></sub>-CSO (G<sub>1</sub>)

Allyl alcohol (0.63 g, 108 mmol) in toluene (15 mL) was slowly added to a mixture of Cl-Si-C-D<sub>G<sub>1</sub></sub>-PEO-D<sub>G<sub>1</sub></sub>-CSi-Cl (1.94 g, 1.80 mmol) and TMEDA (1.25 g, 10.80 mmol) in toluene (40 mL) at a rate of 30 drops per minute. When adding of materials were finished, the reaction mixture was warmed to 27°C for 5 h

and additional 30 min at 50°C. When the reaction was completed by <sup>1</sup>H-NMR, the salt was filtered off and washed with pentane. The volatile components were removed under reduced pressure, leaving a colorless liquid. The product was purified by repeated precipitation from THF into cold *n*-hexane and further purification was carried out by column



**TABLE I**  
**Reaction Conditions and Results for the Hydrosilylation-Alcoholysis Cycles of Three Generations of Carbosiloxane-Based Dendritic Copolymers (Si-H:C=C, 1 : 1 Molar Ratio)**

| Entry | Generation     | Catalyst/C=C ratio     | Hydrosilylation <sup>a</sup> |                     |                    |                     | Alcoholysis <sup>a</sup> |                     |                    |                     | CH=CH <sub>2</sub> conversion (%) <sup>b</sup> |
|-------|----------------|------------------------|------------------------------|---------------------|--------------------|---------------------|--------------------------|---------------------|--------------------|---------------------|--|
|       |                |                        | t <sub>1</sub> (h)           | T <sub>1</sub> (°C) | t <sub>2</sub> (h) | T <sub>2</sub> (°C) | t <sub>1</sub> (h)       | T <sub>1</sub> (°C) | t <sub>2</sub> (h) | T <sub>2</sub> (°C) |  |
| 1     | G <sub>1</sub> | 1.2 × 10 <sup>-5</sup> | 1                            | 25                  | 17                 | 35                  | 2                        | 35                  | 1                  | 45                  | 80   |
| 2     | G <sub>1</sub> | 1.2 × 10 <sup>-5</sup> | 1                            | 20                  | 17                 | 40                  | 2                        | 35                  | 1                  | 45                  | 66   |
| 3     | G <sub>1</sub> | 3.5 × 10 <sup>-5</sup> | 1                            | 20                  | 17                 | 40                  | 2                        | 35                  | 1                  | 45                  | 83   |
| 4     | G <sub>1</sub> | 3.5 × 10 <sup>-5</sup> | 1                            | 20                  | 17                 | 40                  | 5                        | 27                  | 0.5                | 50                  | 100  |
| 5     | G <sub>2</sub> | 3.5 × 10 <sup>-5</sup> | 1                            | 20                  | 17                 | 40                  | 5                        | 27                  | 0.5                | 50                  | 50   |
| 6     | G <sub>2</sub> | 3.5 × 10 <sup>-5</sup> | 1                            | 20                  | 17                 | 50                  | 5                        | 27                  | 0.5                | 50                  | 50   |
| 7     | G <sub>2</sub> | 3.5 × 10 <sup>-5</sup> | 1                            | 20                  | 17                 | 50                  | 24                       | 30                  | 1                  | 50                  | 100  |
| 8     | G <sub>3</sub> | 3.5 × 10 <sup>-5</sup> | 1                            | 20                  | 17                 | 50                  | 24                       | 30                  | 1                  | 50                  | 28   |
| 9     | G <sub>3</sub> | 3.5 × 10 <sup>-5</sup> | 1                            | 20                  | 17                 | 50                  | 36                       | 30                  | 1                  | 50                  | 30   |
| 10    | G <sub>3</sub> | 3.5 × 10 <sup>-5</sup> | 1                            | 20                  | 17                 | 50                  | 48                       | 30                  | 2                  | 50                  | 100  |

<sup>a</sup> t<sub>1</sub> and t<sub>2</sub> are reaction times; T<sub>1</sub> and T<sub>2</sub> are temperatures for hydrosilylation and alcoholysis reactions in THF and toluene, respectively.

<sup>b</sup> Determined by <sup>1</sup>H-NMR spectroscopy.

chromatography on silica gel with methanol/chloroform (5/95, v/v) as an eluent. After evaporation of the solvents, leaving 8.41 g (8.60 mmol, 65%), obtained pure product G<sub>1</sub> was a very light yellow waxy matter (Table II).

#### Synthesis of Cl-SiC-D<sub>G<sub>2</sub></sub>-PEO-D<sub>G<sub>2</sub></sub>-CSi-Cl (G<sub>2</sub>-Cl)

Operations were carried out in an inert argon atmosphere. Karstedt catalyst (0.06 mL, 1.407 × 10<sup>-5</sup> mmol) was added to a solution of G<sub>1</sub> (0.1 g, 0.07 mmol), methylchlorosilane (0.21 mL, 2.01 mmol), and dry THF (50 mL). Mixture was kept at 20°C for 1 h under vigorous magnetic stirring and then was continued at 50°C until no allyl groups were detected by FT IR (1635 cm<sup>-1</sup>, ~ 17 h). Excess meth-

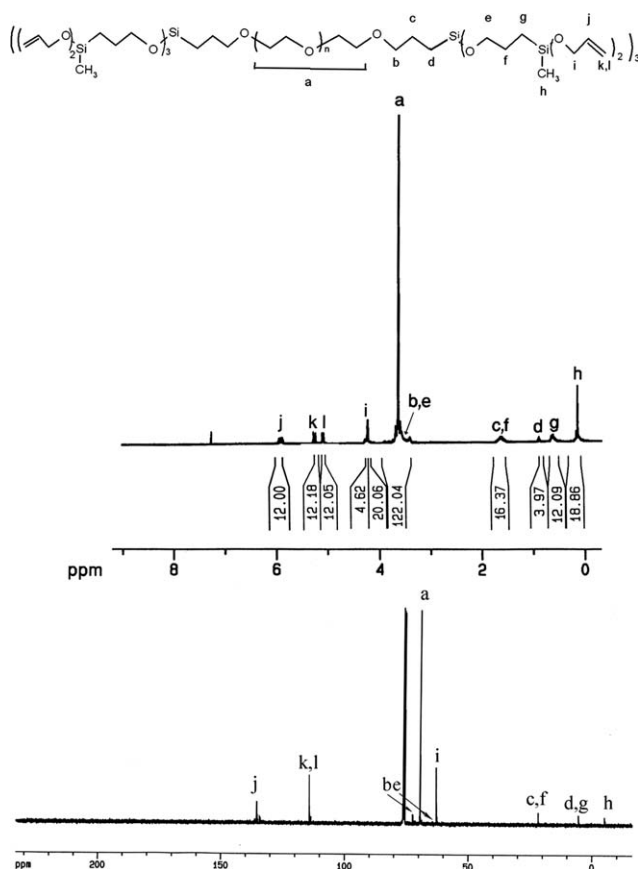
ylchlorosilane and THF were removed under reduced pressure at 30°C/3 mmHg and obtained product was a colorless liquid, which was immediately exposed to reaction of the next step. Further purification was not available in this stage because of its sensitivity against moisture.

#### Synthesis of OSC-D<sub>G<sub>2</sub></sub>-PEO-D<sub>G<sub>2</sub></sub>-CSO (G<sub>2</sub>)

The synthesis procedure of G<sub>2</sub> was similar to that of G<sub>1</sub>. Only difference was that reaction was prolonged to 24 h at 30°C and additional 1 h at 50°C, due to steric hindrance effects of Cl-SiC-D<sub>G<sub>2</sub></sub>-PEO-D<sub>G<sub>2</sub></sub>-CSi-Cl were more than that of Cl-SiC-D<sub>G<sub>1</sub></sub>-PEO-D<sub>G<sub>1</sub></sub>-CSi-Cl. Obtained product G<sub>2</sub> was a light yellow slightly viscous liquid weighted 0.36 g (0.15 mmol, yield: 45%).

**TABLE II**  
**NMR Spectroscopic Data of the Carbosiloxane-Based Dendritic Copolymers Measured in CDCl<sub>3</sub>**

| Generation              |                 | G <sub>0</sub>      | G <sub>1</sub>      | G <sub>2</sub>      | G <sub>3</sub>      |
|-------------------------|-----------------|---------------------|---------------------|---------------------|---------------------|
| PEO                     | <sup>1</sup> H  | 3.58–3.65 (m, 103H) | 3.55–3.68 (m, 105H) | 3.54–3.67 (m, 106H) | 3.58–3.74 (m, 105H) |
|                         | <sup>13</sup> C | 69.54               | 69.52               | 69.52               | 69.62               |
| CH <sub>2,allylic</sub> | <sup>1</sup> H  | 3.99–4.02 (m, 4H)   | 4.26–4.30 (m, 12 H) | 4.20–4.22 (m, 24H)  | 4.16–4.27 (m, 48H)  |
|                         | <sup>13</sup> C | 68.66               | 62.94               | 62.94               | 62.72               |
| CH=                     | <sup>1</sup> H  | 5.84–5.94 (m, 2H)   | 5.87–5.96 (m, 6 H)  | 5.86–5.95 (m, 12H)  | 5.86–6.06 (m, 24H)  |
|                         | <sup>13</sup> C | 136.28              | 136.29              | 136.29              | 136.37              |
| =CH <sub>trans</sub>    | <sup>1</sup> H  | 5.22–5.28 (m, 2H)   | 5.23–5.25 (m, 6H)   | 5.22–5.27 (m, 12H)  | 5.25–5.31 (m, 24H)  |
|                         | <sup>13</sup> C | 114.21              | 114.18              | 114.18              | 114.39              |
| =CH <sub>cis</sub>      | <sup>1</sup> H  | 5.14–5.18 (m, 2H)   | 5.06–5.18 (m, 6H)   | 5.07–5.10 (m, 12H)  | 5.08–5.17 (m, 24H)  |
|                         | <sup>13</sup> C | 114.21              | 114.18              | 114.18              | 114.39              |
| CH <sub>2</sub> -O      | <sup>1</sup> H  | –                   | 3.40–3.43 (t, 4H)   | 3.40–3.46 (m, 16H)  | 3.40–3.49 (m, 24H)  |
|                         | <sup>13</sup> C | –                   | 72.10               | 72.21, 64.34        | 72.34, 64.42        |
| CH <sub>2</sub>         | <sup>1</sup> H  | –                   | 1.64–1.73 (m, 4H)   | 1.53–1.68 (m, 16H)  | 1.58–1.60 (m, 36H)  |
|                         | <sup>13</sup> C | –                   | 22.36               | 22.59               | 22.69               |
| CH <sub>2</sub> -Si     | <sup>1</sup> H  | –                   | 0.66–0.70 (m, 4H)   | 0.56–0.91 (m, 16H)  | 0.64–0.95 (m, 36H)  |
|                         | <sup>13</sup> C | –                   | 6.12                | 6.28                | 6.35                |
| Si-CH <sub>3</sub>      | <sup>1</sup> H  | –                   | –                   | 0.08–0.18 (m, 18H)  | 0.06–0.18 (m, 54H)  |
|                         | <sup>13</sup> C | –                   | –                   | –5.02               | –4.68, –4.95        |



**Figure 2**  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra of OSC- $\text{D}_{\text{G}_2}$ -PEO- $\text{D}_{\text{G}_2}$ -CSO ( $\text{G}_2$ ).

### Synthesis of Cl-SiC- $\text{D}_{\text{G}_3}$ -PEO- $\text{D}_{\text{G}_2}$ -CSi-Cl ( $\text{G}_3$ -Cl)

The procedure was the same that carried out to synthesis Cl-SiC- $\text{D}_{\text{G}_2}$ -PEO- $\text{D}_{\text{G}_2}$ -CSi-Cl.

### Synthesis of OSC- $\text{D}_{\text{G}_3}$ -PEO- $\text{D}_{\text{G}_2}$ -CSO ( $\text{G}_3$ )

The same synthetic method for the preparation of  $\text{G}_2$ , was applied with prolonged reaction times 48 h at  $30^\circ\text{C}$  and additional 2 h at  $50^\circ\text{C}$ . Obtained product was a light yellow liquid weighted 0.12 g (0.028 mmol, yield: 37%).

**TABLE III**  
UV Spectroscopic Data of the Carbosiloxane-Based Dendritic Copolymers Measured in THF

| Generation <sup>a</sup> | $n$ | $\lambda_{\text{max}}$ (nm) | $\epsilon_{\text{max}}$ (L/mol cm) | $\epsilon_{\text{max}}/n$ |
|-------------------------|-----|-----------------------------|------------------------------------|---------------------------|
| $\text{G}_0$            | 2   | 238                         | 595.4                              | 297.72                    |
| $\text{G}_1$            | 6   | 239                         | 1703                               | 283.83                    |
| $\text{G}_2$            | 12  | 241                         | 3658                               | 304.66                    |
| $\text{G}_3$            | 24  | 241                         | 6832                               | 284.66                    |

$n$ , number of functionalities.

<sup>a</sup> All compounds were colorless solution in THF.

## RESULTS AND DISCUSSION

### Overview of structures and synthetic strategies

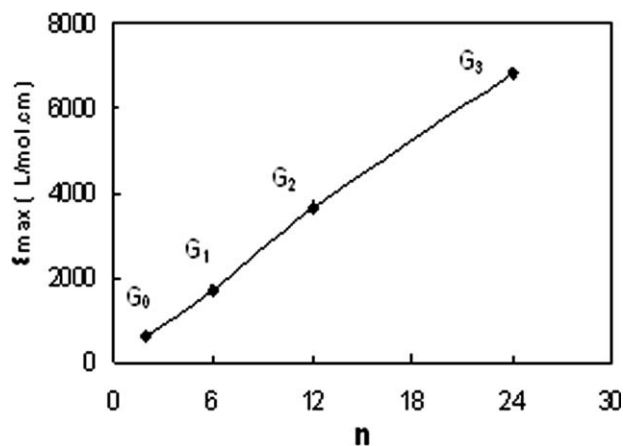
PEO is one of the most popular core molecules due to its unique characteristics, which lead to carbosiloxane dendrimers of symmetrical dumbbell-shaped topology.<sup>28</sup> Our attempts were failed to synthesis second and third generations with trichlorosilane branches. To overcome this drawback, here we report a dendrimer with an open structure, which was obtained using trichlorosilane merely for synthesizing the first generation and methyldichlorosilane for the second and third generations, with expectations that further development in generations will come around. However, it was difficult to synthesis higher generation than third generation on such core structure as a result of high-steric hindrance in using methyldichlorosilane as hydrosilylation reagent.

The basic procedure for the preparation of dendritic carbosiloxane containing block copolymers is outlined in Scheme 1.

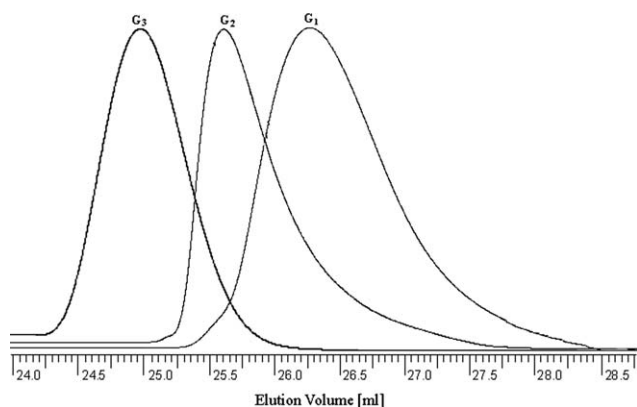
In this direction, several reaction conditions were tested (temperature, Catalyst/C=C ratio,  $t_1$ ,  $t_2$ ,  $T_1$ ,  $T_2$  and  $\text{CH}=\text{CH}_2$  conversion) and results for the best conditions were collected in Table I.

As seen in Table I, certain reaction conditions such as reaction temperatures and medium, were adjusted to maximize  $-\text{CH}=\text{CH}_2$  conversion yields and to minimize the other unwanted side reactions resulting from dehydrogenative addition reaction. Accordingly, with applying low-reaction temperatures in appropriate times and a polar solvent (THF), dehydrogenative addition reaction could be suppressed effectively.

Based on our observation only a very small quantity of Karstedt catalyst were sufficient; typically, the



**Figure 3** The contribution of UV spectroscopy to evaluate generation development in the carbosiloxane-based dendritic copolymers.  $\epsilon_{\text{max}}$  is the molar absorption coefficient and  $n$  is the number of the functionalities.



**Figure 4** GPC chromatogram of the cabosiloxane-based dendritic copolymers for the developed generations.

amounts were in the region of  $10^{-5}$  catalyst/ $\text{CH}=\text{CH}_2$ , but in some cases the ratio of  $10^{-7}$  catalyst/ $\text{CH}=\text{CH}_2$  has been used successfully.<sup>29</sup>

Another important key to develop subsequent generation returns to alcoholysis conditions. Based on our experience, this reaction can be maintained at mild conditions by carefully controlling the dropping speed.  $^1\text{H-NMR}$  spectra for the all generations terminated with allyloxy groups depicted that the desired products were obtained successfully. TMEDA as the base and catalyst can facilitate the  $\text{SiCl}/\text{OH}$  condensation.<sup>20</sup> Also the crude product can be purified by repeating precipitation in appropriate solvent/nonsolvent system and then further purification by column chromatography. Results can be determined by disappearance of hydroxyl group signal bond of allyl alcohol in FTIR spectrum of the desired products.

### Characterization

Block copolymers synthesized in this work have ABA type triblocks consisted of dendritic-linear-dendritic parts. Completion of hydrosilylation reactions

were monitored by FTIR spectroscopy, which confirmed the consumption of peripheral allyloxy groups in systems.

Structural characterization was performed by  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectroscopy (Table II and Fig. 2; see also supporting information).

In  $^1\text{H-NMR}$  spectra,  $H_{\text{allyloxy}}/H_{\text{PEO}}$  (the ratio of peak integrations of allyloxy protons) at regions between 5.14, 5.22, and 5.84 ppm increased with subsequent generation of dendritic carbosiloxane block. For the second and third generations, methyl protons connected to silicon atoms as well as methylene protons between silicon and oxygen atoms appeared approximately at 0.08, 0.64, 1.58, and 3.40 ppm. Pattern of the methyl and methylene protons does not change; however, these peaks do become broader as the generations become larger.

Calculated number-average molecular weight ( $M_n$ ) of triblock copolymers could be determined by a comparison of integration in certain regions such as the protons in dendritic moiety approximately at 4.20, 5.07, 5.22, and 5.86 ppm and methylene protons in PEO at 3.54 ppm.

To investigate the unified character and molecular weight of the dendrimers, UV spectroscopy is a suitable technique.<sup>19</sup> UV spectroscopy could make interesting results based on increasing number of peripheral double bonds, which are proportional to increasing generation number. The molar absorption coefficients ( $\epsilon_{\text{max}}$ ) of all dendrimers are represented in Table III.

This implies that the terminal allyloxy groups in each generation could have contribution to the UV radiation. Therefore, UV spectroscopy was employed as a helpful method to monitor the perfection of this type of dendrimers (Fig. 3).

Furthermore, the GPC experiments clearly exhibit that molecular weights of allyloxy functionalized copolymers have narrow distribution, implying formation of regular structures. However for dendritic and hyperbranched polymers, hydrodynamic radii

**TABLE IV**  
Physicochemical Properties of the Carbosiloxane-Based Dendritic Copolymers

| Generation     | Physical form | $n$ | $[\eta]^a$ (dL g $^{-1}$ ) | $M_{n,\text{theor}}^b$ | $M_{n,\text{calcd}}^c$ | Hydrophobic block ( $X_w\%$ ) <sup>d</sup> | PDI <sup>e</sup> |
|----------------|---------------|-----|----------------------------|------------------------|------------------------|--|------------------|
| G <sub>0</sub> | Powder        | 2   | 0.96                       | 1082                   | 1096                   | 7.76                                       | –                |
| G <sub>1</sub> | Waxy mater    | 6   | 0.72                       | 1488                   | 1503                   | 32.93                                      | 1.08             |
| G <sub>2</sub> | Oil           | 12  | 0.44                       | 2332                   | 2349                   | 57.20                                      | 1.10             |
| G <sub>3</sub> | Liquid        | 24  | 0.19                       | 4324                   | 4340                   | 76.91                                      | 1.11             |

$n$ , number of functionalities.

<sup>a</sup> Intrinsic viscosity,  $[\eta]$ , in a solution of THF at 25°C.

<sup>b</sup>  $M_{n,\text{theor}} = M_{n,\text{PEO}} + M_{n,\text{CSO}}$ ;  $M_{n,\text{PEO}}$  and  $M_{n,\text{CSO}}$  are the molecular weight of the each block.

<sup>c</sup>  $M_{n,\text{calcd}} = M_{n,\text{PEO}} + M_{n,\text{CSO}}$ ;  $M_{n,\text{PEO}}$  and  $M_{n,\text{CSO}}$  calculated from  $^1\text{H-NMR}$  spectra.

<sup>d</sup> Calculated for hydrophobic carbosiloxane block.

<sup>e</sup> GPC.

are smaller than that of their linear analogues with comparable molecular weights. This phenomenon is related closely to the degree of branching of polymers (Fig. 4).<sup>21,22</sup>

The physicochemical characteristics of species were collected in Table IV.

Thermal behavior of PEO-allylated ( $G_0$ ) and other copolymers were reported in Table V. The  $G_3$  was liquid at room temperature and it was an oily form for  $G_2$ . Nevertheless, melting-like transition temperature ( $T_m$ ) for all of generations measured by using DSC. As seen in Table V, with increasing in generation number, a logical drop in the  $T_m$ s takes place. It was expected due to increasing in carbosiloxane block of copolymers which illustrate the development of generations from  $G_0$  to  $G_3$ . A similar effect on the glass transition temperature ( $T_g$ ) of copolymers was observed. Indeed, this relationship between  $T_m$  and  $T_g$ , in one hand and the generations development on the other hand seems to be approximately in a linear trend.

As represented in Table V, all copolymers clearly show three transitions. The lowest transitions situated between  $-70^\circ\text{C}$  and  $-30^\circ\text{C}$  in all of these systems, which are due to the glass transition of copolymers arising from inorganic carbosiloxane block.<sup>4</sup> An interesting aspect is that a decrease in  $T_g$ s still continues with development of generations, for instance  $-64.1^\circ\text{C}$  and  $-42.0^\circ\text{C}$  for  $G_3$  and  $G_1$ , respectively (Table V).

The MALDI-TOF mass spectrum of the first generation showed ion peak at 1493.67 (m/z) that agrees approximately with theoretical value (Table IV). However, MALDI-TOF mass spectra of higher generation dendrimers did not show molecular ion peaks of the synthesized compounds, implying that the products are not stable enough in this mass-measuring condition. Similar intricacies in obtaining mass spectroscopic data have frequently been encountered in analysis of carbosiloxane dendrimers (supporting information).<sup>19-21,30-33</sup>

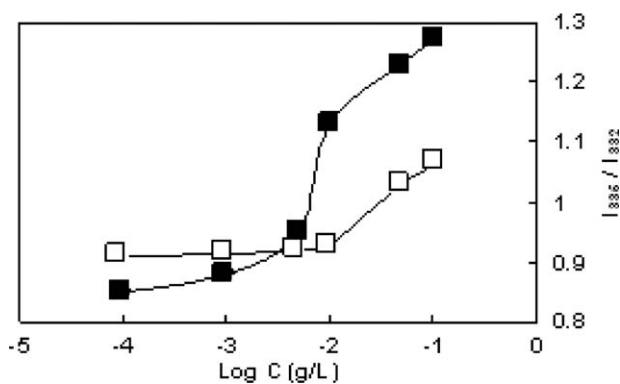
### Micellar behavior

The concept of carbosiloxane-based dendritic delivery system implies that hydrophobic species are

**TABLE V**  
Thermal Behavior of the Carbosiloxane-Based Dendritic Copolymers

| Generation | $T_g$ | $T_m$ | $T_d^a$ |
|------------|-------|-------|---------|
| $G_0$      | -31.9 | 44.0  | 231.1   |
| $G_1$      | -42.0 | 36.8  | 235.1   |
| $G_2$      | -54.0 | 27.2  | 243.8   |
| $G_3$      | -64.1 | -12.6 | 244.6   |

<sup>a</sup> Temperature of decomposition.

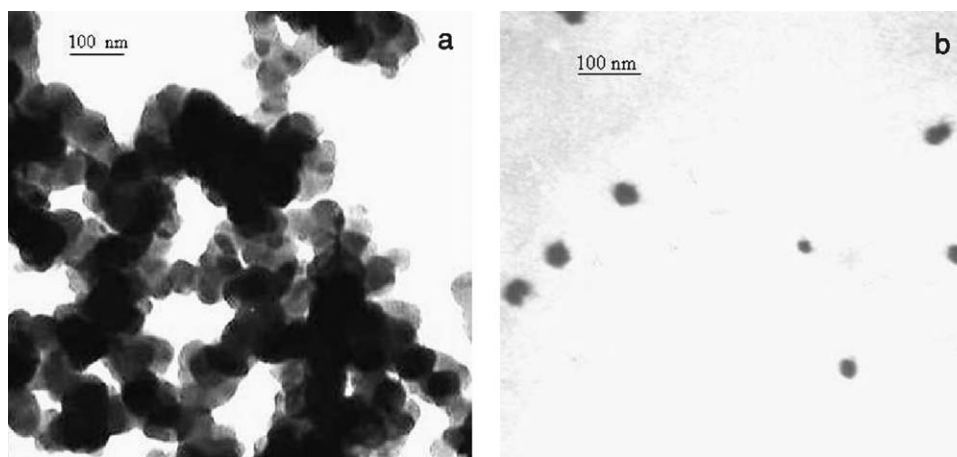


**Figure 5** Plot of  $I_{336}/I_{332}$  from pyrene excitation spectra versus  $\log C$  for first ( $\square$ ) and second ( $\blacksquare$ ) generations of dendritic micelles.

noncovalently incorporated in the dendritic micelles in aqueous media. Pyrene was used as fluorescent probe. As a result, significant changes in the spectroscopic properties were observed upon transfer of probe from the aqueous environment to the nonpolar microenvironment of the dendritic micelle. Thus, the characteristic feature of pyrene excitation spectra, band (0, 0), was a red shift of band from 332 to 336 nm with concentration of the dendrimers. Second, pyrene excitation spectra of  $G_2$ 's micellar aggregates represented slightly broad band comparison to those of  $G_1$  counterpart. This phenomenon was due to the fact that  $G_1$  is less hydrophobic than  $G_2$ . However,  $G_3$  did not exhibit micellar aggregate possibly owing to the high ratio of hydrophobic carbosiloxane block. Finally, changes in the fluorescence and absorption spectra of pyrene have been employed to estimate cmc. Figure 5 depicts the comparative plot of  $I_1/I_3$  ratio of pyrene excitation fluorescence with concentration of  $G_1$  and  $G_2$ . Therefore, the corresponding cmc's of  $G_1$  and  $G_2$  micellar aggregates were obtained from the intersection of the tangents to  $I_{336}/I_{332}$  versus  $\log C$ . The cmc values so were determined for  $G_1$  and  $G_2$  were 12 and 1.6 mg/L, respectively. These cmc values are lower than those reported for other polymeric micelles and comparable with dendritic micelles.<sup>10,11,34</sup> This comparison implies a very strong tendency of carbosiloxane triblock dendritic copolymers toward micelle formation and their relatively thermodynamically stable entities. This result could be accounted by strong hydrophobicity of carbosiloxanic micellar aggregates without charges as well as the location of the end hydrophobic blocks.<sup>35</sup> Consequently, as the hydrophobic blocks became larger, the cmc's of the generations became smaller.

To exploit micelles as suitable carriers, it is vital to determine the hydrophobicity of the micelles.  $K_{\nu}$ , partition equilibrium constant, of pyrene can be estimated by using the method of Wilhelm et al.<sup>36</sup> The





**Figure 6** TEM micrographs of (a) OSC-D<sub>G1</sub>-PEO-D<sub>G1</sub>-CSO (G<sub>1</sub>) and (b) OSC-D<sub>G2</sub>-PEO-D<sub>G2</sub>-CSO (G<sub>2</sub>) aqueous micelles containing 0.5 g/L.

comprehensive theoretical model for this goal could be formulated as:

$$(F - F_{\min}) / (F_{\max} - F) = K_v C X_{w,(\text{CSO})} / 10^3 \rho$$

where  $F$  is intensity ratio in the intermediate dendrimer concentration region,  $F_{\min}$  and  $F_{\max}$  are the average values of the intensity ratio of  $I_{336}/I_{332}$  in the low- and high-dendrimer concentrations,  $C$  is the dendrimer concentration,  $X_{w,(\text{CSO})}$  is the weight fraction of hydrophobic CSO in the copolymer, and  $\rho$  is the density of CSO block in the micelles, which is assumed to take the same value as dendritic CSO (1.082 g/mL)\*.

The  $K_v$  values of G<sub>1</sub> and G<sub>2</sub> were  $0.264 \times 10^{-5}$  and  $2.771 \times 10^{-5}$ , respectively, suggesting that pyrene is strongly favored to stay in hydrophobic part of the dendritic micelles. On the other hand, with increase of generation of hydrophobic dendritic block,  $K$  increases as well. The  $K_v$  of G<sub>2</sub> is comparable with the linear triblock copolymers such as: PMMA-*b*-PEO-*b*-PMMA ( $1.37$  to  $2.65 \times 10^{-5}$ ) PHPMA-*b*-PCL-*b*-PHPMA ( $2.3$  to  $2.6 \times 10^5$ ) and PVP-*b*-PCL-*b*-PNP ( $3.2$  to  $4.2 \times 10^{-5}$ ) in which PVP and PHPMA stand for poly(*N*-vinyl-2-pyrrolidone) and poly(*N*-(2-hydroxypropyl)-metacryl amide), respectively.<sup>11,31</sup> It is notable that  $K_v$  of G<sub>1</sub> is lower than that of sodium dodecyl sulfate (SDS) micelle ( $1.2 \times 10^5$ ). This phenomenon might be attributed to the flexible architecture of dendritic hydrophobic block, where SDS displays a contrasting view of stacking arrangement with their linear hydrophobic chains.<sup>10</sup>

Morphology and size of the dendritic micelles analyzed by TEM observation revealed that particles in first and second generations were spherical, smooth,

and regular with diameters of  $\sim 60$ – $75$  and  $80$ – $95$  nm, respectively (Fig. 6).

DLS measurement depicted the diameters ( $d$ ) of micelles as 69 and 88 nm, respectively. This increase in the diameters obtained from DLS analysis with increasing the generation, was in good agreement with the TEM observation.

The micelles formed in aqueous solution seems to be in a rosette shape with hydrophobic carbosiloxane core and PEO loop corona.<sup>37</sup> Polydispersity factor,  $\mu_2/\Gamma^2$  estimated by the cumulant method, suggests a narrow size distribution as shown in Table VI.

## CONCLUSIONS

Carbosiloxane-based ABA triblock copolymers with well-defined dendritic structure were successfully developed using a fairly straightforward strategy in different generations. The obtained dendritic copolymers also had ability to react by using peripheral Si-Cl or allyloxy double bonds.

The obtained results indicated that the hydrophobic blocks make a significant influence on the morphological, physicochemical, and micellar characteristics of the supramolecules. Accordingly, the capacity to solubilize hydrophobic species can be readily controlled. Thus, these functionalized

**TABLE VI**  
Micellar Properties of Carbosiloxane-Based Dendritic Copolymers in First and Second Generations

| Generation     | cmc <sup>a</sup> (mg/L) | $d^b$ (nm) | $\mu_2/\Gamma^{2c}$ | $K_v$ ( $\times 10^{-5}$ ) |
|----------------|-------------------------|------------|---------------------|----------------------------|
| G <sub>1</sub> | 12                      | 69         | 0.082               | 0.264                      |
| G <sub>2</sub> | 1.6                     | 88         | 0.099               | 2.771                      |

<sup>a</sup> Measured at 25°C.

<sup>b</sup> Diameter measured by dynamic light scattering in water.

<sup>c</sup> Polydispersity factor.

\*Densitometry was carried out for second generation with Me<sub>2</sub>SiCl<sub>2</sub> and HSiMeCl<sub>2</sub> as core and branching reagent, respectively, at 25°C.

dendritic micelles are expected to attract a great interest as new supramolecular architectures.

Our experiments to test their hydrolytic behavior as potential utilities in biomedical applications including targeted delivery and surface modification through the coupling of drug models are ongoing.

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