Self-Aggregation of Amphiphilic Dendrimer in Aqueous Solution: The Effect of Headgroup and Hydrocarbon Chain Length

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ABSTRACT: The self-aggregation of amphiphilic dendrimers GQPAMC
n
m based on poly(amidoamine) PAMAM possessing the same hydrophilic group but differing in alkyl chain length in aqueous solution was investigated. Differences in the chemical structures lead to significant specificities in the aggregate building process. A variety of physicochemical parameters presented monotonous regularity with the increase in alkyl chain length in multibranched structure, as traditional amphiphilic molecules. A significant difference, however, existed in the morphology and the microenvironment of the microdomain of the aggregates, with GQPAMC
m
with an alkyl chain length of 16 intending to form vesicles. To obtain supporting information about the aggregation mechanism, the thermodynamic parameters of micellization, the free Gibbs energy ΔG
mic
and the entropy ΔS
mic
were derived subsequently, of which the relationship between the hydrophobic chain length and the thermodynamic properties indicated that the self-assembly process was jointly driven by enthalpy and entropy. Other than traditional surfactants, the contribution of enthalpy has not increased identically to the increase in hydrophobic interactions, which depends on the ratio of the alkyl chain length to the radius in the headgroup. Continuous increases in the hydrophobic chain length from 12 to 16 lead to the intracoherence of the alkyl chain involved in the process of self-assembly, weakening the hydrophobic interactions, and the increase in −ΔH
mic
which offers an explanation of the formation of vesicular structures.

1. INTRODUCTION

Dendrimers with branched and symmetrical structure possess a very high concentration of surface functional groups. The properties of dendrimers, such as the reactivity, solubility, and thermal properties, are strongly influenced by the nature of these terminal functionalities. Amphiphilic dendrimers including more than one hydrophobic or hydrophilic group in the structure may combine the properties of low-molecular-weight surfactants and macromolecules and self-assemble in aqueous solution, forming micellike aggregates. In comparison with small molecular amphiphiles, dendritic amphiphiles can exhibit more stable micellar aggregates and even yield unimolecular micelles. The ability to self-assemble into nanometer dimensions, discrete size, and tailorable structures has led to their exploration for a range of applications, e.g., scaffolds for drug delivery, carriers for gene transfection, biosensors, and so on. Therefore, an understanding of supramolecular assemblies, especially the self-assembly process of the transition from small molecules to macrosurfactants, offers very deep insight into the intermolecular connections of molecular organization, which is a key requirement in the fabrication of advanced soft materials. In earlier work, our group has focused on the effect of the hydrophobic alkyl chain, the spacer, and the conformation on the aggregation properties of single and gemini surfactants in aqueous solution and obtained some regularity. With the development of novel surfactants with high efficiency and effectiveness, there is a great need to study the macrosurfactants and even polymeric surfactants which in principle permit us to achieve more stable self-assembled aggregates, larger loading capacities, longer ranges of repulsion between colloidal particles in suspension, and so on. With accurate control of the structure and chemical tailoring of the end groups, amphiphilic dendrimers will help to illuminate the structure–property relationship from small molecules to macromolecules. Water-soluble amphiphilic dendrimers GQPAMC
n
m
(n = 1−3; m = 8, 12, 16), with different hydrophobic groups (n) and hydrophobic chain lengths (m) based on the PAMAM dendrimer, were prepared by our group (Figure 1). In this article, the

Received: July 29, 2014
Revised: February 3, 2015
Published: February 9, 2015

DOI: 10.1021/la504949f
Langmuir 2015, 31, 7919−7925
Thermodynamics plays an important role in researching the self-assembly of surfactants and the effects of temperature, ionic strength, and, in particular, the alkyl chain length and the structure of surfactants on the molecular self-assembly process, by which a more detailed examination of the constituent parts of the free energy, i.e., the enthalpy and entropy of micellization, could lead to a deeper understanding of the complex patterns in inter- and intramolecular interactions and the driving forces involved in the self-assembly process. Therefore, it is necessary for us to study the effects of temperature, ionic strength, and, in particular, the alkyl chain length and the structure of surfactants on the molecular self-assembly process, for which one of the major concerns is embodied in controlling the number of terminal groups. In this work, we will illustrate the aggregation behaviors of a series of amphiphilic dendrimers in order to explore the relationship between structure and property. Studies on these characteristics will focus further on the effect of molecular shape on the self-assembly process, for which one of the major concerns is embodied in controlling the number of terminal groups. In this work, we will illustrate the aggregation behaviors of a series of amphiphilic dendrimers in order to explore the relationship between structure and property. Studies on these characteristics will focus further on the effect of molecular shape on the self-assembly process, for which one of the major concerns is embodied in controlling the number of terminal groups. In this work, we will illustrate the aggregation behaviors of a series of amphiphilic dendrimers G_nQPAMC_m in which n represents the dendrimer generation and m represents the alkyl chain length after the modification of the end group; here n = 1, m = 8, 12, 16, and G_nQPAMC_m was abbreviated as G_nQPAMC_m).

Figure 1. Chemical structure of amphiphilic dendrimer G_nQPAMC_m (in which n represents the dendrimer generation and m represents the alkyl chain length after the modification of the end group; here n = 1, m = 8, 12, 16, and G_nQPAMC_m was abbreviated as G_nQPAMC_m).

2. EXPERIMENTAL SECTION

Materials. Amphiphilic dendrimers with different alkyl chain lengths G_nQPAMC_m (m = 8, 12, 16) were synthesized and purified by our group (Figure 1). Pyrene and DPH (1,6-diphenyl-1,3,5-hexatriene) were purchased from Aldrich and recrystallized from ethanol. Ultrapure water (resitivity > 18.2 MΩ cm) was used in all experiments and measurements.

Surface Tension and Related Parameters. The equilibrium surface tension was examined using the Wilhelmy plate method (Data Physics DCA T2, Germany) using a platinum plate of ~5 cm perimeter. The solutions were immersed in a constant-temperature bath at the desired temperature of 30.0 ± 0.05°C. The instrument was calibrated with doubly distilled water, and the standard deviation for surface tension measurements was less than 0.2 mN/m. Sets of measurement were taken at certain intervals until the surface tension was constant for ~0.5 h. The critical micelle concentration (c_m) values were obtained according to the static surface tension versus the log of the bulk concentration as mentioned.18 The maximum surface excess concentration (Γ_max) was calculated according to the Gibbs adsorption (eq 1). The minimum average surface area/surfactant molecule (A_min) was obtained from the saturated adsorption by eq 2, where γ is the surface tension in mN m⁻¹, C is the concentration of the surfactant in the solution, Γ is the adsorption amount in μmol/m², N_A is Avogadro’s constant, T is the absolute temperature, R = 8.314 J mol⁻¹ K⁻¹, and dy/d(ln C) is the maximal slope in each case. For the ionic dendrimers with four branches, n = 4 is taken. Meanwhile, the number of molecules per micelle can be estimated by eq 3, using the value of the hydrophobic tail length L.20

\[
\Gamma = \frac{1}{2.303nRT} \int \frac{dy}{\ln C}
\]

(1)

\[
A_{\text{min}} = \left( \frac{N_A \Gamma_{\text{min}}}{\mu} \right)^{-1}
\]

(2)

\[
N_m = \frac{4\pi L^2}{A_{\text{min}}}
\]

(3)

Cryogenic Transmission Electron Microscopy (Cryo-TEM). The G_nQPAMC_m samples were embedded in a thin layer of vitreous ice on freshly carbon-coated holey TEM grids by blotting the grids with filter paper and then plunging them into liquid ethane cooled by liquid nitrogen. Frozen hydrated specimens were imaged by using an FEI Tecnai 20 electron microscope (LaB6) operated at 200 kV in low-dose mode (about 2000 e/Å²) and a nominal magnification of 50 000. For each specimen area, the defocus was set to 1 to 2 μm. Images were recorded on Kodak SO 163 films and then digitized by a Nikon 9000 with a scanning step of 2000 dpi corresponding to 2.54 Å/pixel.

Fluorescence Spectroscopy with Pyrene and DPH. Both pyrene and DPH were employed as fluorescent probes at a concentration of 1 μM, and the sample solutions were stirred at room temperature overnight before measurement. Steady-state fluorescence spectra were obtained with a Hitachi F-4500 spectrophotometer at ambient temperature. The emission spectra were scanned for pyrene from 350 to 550 nm using a 335 nm excitation wavelength. The width of the emission slit was 2.5 nm. The ratio of the intensities of the third (384 nm) to the first (373 nm) vibronic peaks (I_3/I_1) in the emission spectra was used to estimate the polarity of the pyrene microenvironment. In the case of DPH, the excitation wavelength was 430 nm and the emission wavelength was set at 430 nm. The emission of DPH excited at 360 nm as a function of amphiphilic concentration was useful for determining the presence of a hydrophobic environment.

Isothermal Titration Microcalorimetry (ITC). An isothermal titration calorimeter with a Thermostat TAM III (four channels, TA Instruments) was used to evaluate the thermodynamics of aggregation of G_nQPAMC_m in aqueous solution. The instrument was calibrated electrically with a precision of better than ±0.1%. Considering the low c_m value for G_nQPAMC_m solutions obtained by the Wilhelmy plate method, a 20 μL reaction cell was chosen to ensure an adequately dilute solution. The sample cell and the reference cell of the microcalorimeter were both initially loaded with 18 mL of pure water. The calorimetric titration experiments consisted of a series of consecutive additions of concentrated solutions above their c_m values into 18 mL of pure water. The titrating solution was automatically added in aliquots of 5–10 μL from a gastight Hamilton syringe controlled by a precision syringe pump with a control module (P/N 3810-5) through a thin stainless steel capillary until the desired range of concentration had been covered. During the whole titration process, the system was stirred at 100 rpm with a gold propeller, and the interval between two injections was 15 min for the signal to return to the baseline. All measurements were performed at 25.0 ± 0.01°C. Each experiment was repeated at least three times. The heat evolved per injection was integrated using software especially designed for TAM III in the plot of thermal power against time.
Table 1. cmc_{SFT}, A_{min}, Theoretical Alkyl Chain Length, and Ionization Degree (α) of G1QPAMC_m

<table>
<thead>
<tr>
<th>sample</th>
<th>cmc_{SFT}  \text{ (mol/L)}</th>
<th>cmc_{conduc} \text{ (mol/L)}</th>
<th>A_{min} \text{ (Å/molike)}^a</th>
<th>theoretical alkyl chain length (Å)</th>
<th>aggregation number N_{agg}</th>
<th>ionization degree α \text{d}</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1QPAMC_8</td>
<td>8.0 × 10^{-5}</td>
<td>6.0 × 10^{-5}</td>
<td>205</td>
<td>10.16</td>
<td>6</td>
<td>0.68</td>
</tr>
<tr>
<td>G1QPAMC_{12}</td>
<td>5.0 × 10^{-5}</td>
<td>4.5 × 10^{-5}</td>
<td>222</td>
<td>15.24</td>
<td>13</td>
<td>0.83</td>
</tr>
<tr>
<td>G1QPAMC_{16}</td>
<td>6.3 × 10^{-6}</td>
<td>4.0 × 10^{-6}</td>
<td>280</td>
<td>20.32</td>
<td>18</td>
<td>0.79</td>
</tr>
</tbody>
</table>

^a cmc_{SFT} (Wilhemy plate) and A_{min} are from ref 18. cmc_{conduc} was obtained from the conductivity experiment. N_{agg} was calculated with eq 3. α was obtained from the conductivity experiment.

3. RESULTS AND DISCUSSION

Properties of the Amphiphilic Dendrimer Solution.

According to the static surface tension versus log of the bulk concentration for G1QPAMC_m, all parameters such as cmc_{SFT}, Γ, and A_{min} were obtained and listed in Table 1.

As described previously, the cmc_{SFT} values decrease with increasing hydrophobic tail length for similar surfactants. Especially for the ionic surfactants, the cmc values decrease by half upon increasing each −CH_{10}− group on the hydrophobic chain, when the number of carbon atoms in the hydrophobic chain is in the range of 8−16. The rule can be described by the following empirical equation (eq 4)\textsuperscript{24}

\[ \log \text{cmc} = A - Bn \]  
(4)

in which A and B are positive empirical constants and n is the number of carbon atoms in the hydrophobic chain. Parameter B reflects the contribution of micelle formation ability as the n value increases. For presently studied amphiphilic dendrimers G1QPAMC_m, the cmc and Γ_{mc} values decrease with the increase in alkyl chain carbon number as mentioned before.\textsuperscript{18} However, the effect of the hydrophobic chain length on the surfactivity has not presented a good linear relationship. Parameter B is obtained from the curve fitting of log cmc versus the effective number of carbon atoms (n_{eff}) in the hydrophobic chains (A = 2.88, B = 0.03), which is smaller than for traditional surfactants,\textsuperscript{25} meaning that the contribution to micelle formation is relatively small with every increase in the number of carbon atoms in the alkyl chain.

In general, for ionic surfactants in aqueous solution, there is a substantial change in slope on the conductivity curve at the onset of aggregation. The conductivity against concentration plots for aqueous solutions of G1QPAMC_m (m = 8, 12, and 16) are shown in Figure S1, and the ionization degree (α) of micelles was estimated from the ratio of the slopes above and below the intersection (Table 1).\textsuperscript{26} The calculated α values increase from about 0.68 to 0.83 when the alkyl chain length increases from 8 to 12 but decrease only 0.04 with increases of the same alkyl chain length from 12 to 16, presenting a very different trend for conventional single quaternary ammonium surfactants.\textsuperscript{27} In particular, the breaks before and after are not obvious with the hydrophobic chain length increase, and the curves of κ vs C are close to the x axis in the case of G1QPAMC_{12} and G1QPAMC_{16}, indicating that the ion-pairing phenomenon is significant.\textsuperscript{28} For the κ vs C curve, the change in slope is not the commonly observed sharp transition, which is attributed to the fact that the micelles have a lower aggregation number (Table 1).

Morphology of the Aggregates.

For quaternary ammonium surfactants, the micelle shape is affected by both the spacer and the degree of oligomerization. The monomeric micelles are known to remain spherical or spheroidal even at very high concentration or ionic strength. With the increase in the number of branches, such as the cases of trimers and tetramers, branched wormlike micelles were observed.\textsuperscript{29,30} For G1QPAMC_m studied in the present work, spherical aggregates with a particle size of 50−100 nm were observed by cryo-TEM, which is of the same order of magnitude as that investigated by DLS (Figure S2). Taking into account the effect of the hydrophobic chain on the morphology, two kinds of aggregates emerged with the increase in the hydrophobic chain length. As shown in Figure 2, in the case of G1QPAMC_8, the aggregates are irregularly spherical and increase in number with increasing concentration. However, spherical aggregates become quite regular in the solution of G1QPAMC_{12} and G1QPAMC_{16}. It is particularly interesting that 50−100 nm vesicles with clear boundaries are observed in the bulk of G1QPAMC_{16} but are not found in the G1QPAMC_8 system, indicating that different aggregation behaviors occur.

Aggregate Microenvironment. Different fluorescent probes can provide different information about hydrophobic domain characteristics, such as the micropolarity and viscosity.\textsuperscript{31} To obtain as much information as possible, two fluorescent probes Py and DPH were used to characterize the hydrophobic domains of the amphiphilic dendrimers. For the emission spectra of Py, the relative intensities of the first (373 nm) and third vibronic peaks (384 nm) (I_1/I_3 or I_2/I_0) are sensitive to the environmental polarity and are frequently used to determine the microdomain polarity of aggregates. DPH is a very hydrophobic probe which has almost no fluorescence in aqueous solution (it is practically water-insoluble), but it is highly fluorescent in a hydrophobic environment. On account of its insolubility and lack of fluorescence emission in water
solutions, any measurable value for DPH intensity in the presence of an amphiphile will indicate the solubilization of the probe in the hydrophobic microdomain of that amphiphile.32

Figure 3a shows the variation of Py fluorescence in response to the amphiphilic dendrimer concentration, as obtained from emission spectra, namely, the ratio \( I_3/I_1 \). The measurable value for DPH intensity in the presence of G1QPAMC will indicate the solubilization of the probe into the hydrophobic microdomain, which is exhibited in Figure 3b. The increase in alkyl chain length results in a lower polarity and a higher solubilization ability of microdomains, being noticed between C8 and C12. Surprisingly, the microenvironment polarity of the microdomain presented a reverse change trend with the increase in alkyl chain length from C12 to C16, namely, the ratio \( I_3/I_1 \) increased with concentration. In the presence of DPH, however, a much sharper increase in its emission intensity occurs even in the case in which there is a weak hydrophobic microdomain microenvironment sensed by the Py probe, meaning that the microdomain of G1QPAMC16 aggregates has a significant ability to solubilize very hydrophobic probe DPH. Considering the rigid structure of Py, the higher polarity of the microdomain for G1QPAMC16 compared to that of G1QPAMC12 is reasonably attributed to the fact that a boundary structure (bilayer or multilayer) exists within the aggregates. However, DPH with flexible structure was not hindered by the boundary, which can be solubilized into the microdomain generated by intermolecular and intramolecular hydrophobic interactions, inducing a sharp increase in its emission intensity in the case of G1QPAMC16.

Calorimetric Study of G1QPAMCm in Aqueous Solution. As previously mentioned for conventional surfactants,35 when the overall concentration is in the premicellar range, the added micelles from a concentrated solution dissociate into monomers and the monomers are further diluted. In the case in which the concentration was above the cmc, the added micelles merely became diluted without dissociating into monomers. The large exothermic or endothermic enthalpy changes observed for the injections were associated mainly with micelle dilution, demicellization, and the dilution of surfactant molecules. It has been well known that the cmc values and the enthalpy of micelle formation \( \Delta H_{\text{mic}} \) can be extracted from the plots of \( \Delta H_{\text{obs}} \) against surfactant concentration, as obtained by ITC.34,35 Microcalorimetric curves for the dilution of concentrated solutions were performed at 25.0 ± 0.01 °C.

Figure 3. Influence of alkyl chain length on the fluorescence properties of pyrene (a) and DPH (b) for amphiphilic dendrimers G1QPAMCm as a function of concentration at room temperature.

Figure 4. Calorimetric titration curves for the variation of the observed enthalpies of dilution with G1QPAMCm concentration in aqueous solution.
$G_{1QPAMC_m}$ ($m = 8, 12, and 16$) into water are shown in Figure 4, where the change in the observed enthalpies of dilution ($\Delta H_{obs}$) were plotted as a function of amphiphilic dendrimer concentration and the corresponding enthalpy of micellization $\Delta H_{mic}$ was determined according to the calculation method reported.36

The endothermic processes are observed in the dilution process of solutions, indicating that the enthalpies of micelle formation ($\Delta H_{mic}$) are all exothermic for $G_{1QPAMC_m}$. The pattern of enthalpy changes on dilution is very similar to that of conventional surfactants, as we have observed a break corresponding to some kind of aggregation which suggests that micelle-like clusters consisting of branched alkyl chains of dendrimers are forming. This should be attributed to the balance of inter- or intramolecular hydrophobic interactions and the electrostatic repulsive interactions. We denote the concentration on the breaking point of the observed enthalpy curve ($\Delta H_{obs}$ vs C) at which aggregation starts as the cmcITC of the dendrimers.

It was observed that the $\Delta H_{mic}$ values for $G_{1QPAMC_8}$, $G_{1QPAMC_{12}}$, and $G_{1QPAMC_{16}}$ were $-2.3$, $-8.5$, and $-5.2$ kJ/mol, respectively. The negative enthalpy change indicates that the self-assembly process of the amphiphilic dendrimer is driven jointly by enthalpy and entropy. It is worth noting that the $\Delta H_{mic}$ values of $G_{1QPAMC_m}$ change nonlinearly, presenting a maximum value with the increase in the alkyl chain length. When the alkyl chain length is $m \leq 12$, the enthalpy changes significantly from $-2.3$ to $-8.5$ kJ/mol, indicating the effect of enhanced hydrophobic interactions. In another case, the absolute value of the enthalpy decreases with the alkyl chain length $m$ increasing from 12 to 16, showing an opposite feature. Under the condition of other groups being equal, taking the great headgroup into consideration, which is fully extended with a radius of 19.77 Å, the ratios of theoretical alkyl chain length/radius are 10.16/19.77 < 1 for $G_{1QPAMC_8}$, 15.24/19.77 < 1 for $G_{1QPAMC_{12}}$, and 20.32/19.77 > 1 for $G_{1QPAMC_{16}}$ (Figure 1 and Table 1), indicating that diverse conformations for the headgroup exist in the process of micellization and that the hydrophobic interaction is not the only contribution to the enthalpy change. In that way, what are the contributions of each hydrophobic/hydrophilic group and each increased carbon atom to the aggregation, especially for complex system? To explore this question, it is necessary to investigate the micellization free energy of $G_{1QPAMC_m}$

The free energy of micellization of a traditional surfactant has been widely determined using the relationships37

$$\Delta G_{mic} = RT \ln \text{cmc}$$

(5)

$$\Delta G_{mic} = RT(1 + \beta) \ln \text{cmc}$$

(6)

Recently, surfactants that contain several alkyl chains and an equal or unequal number of charged groups are emerging. Different expressions of $\Delta G_{mic}$ can be applied depending on the nature of the surfactant. The correct analysis of the free-energy change using the proper relationship is very important. Zana had derived an equation relating $\Delta G_{mic}$ to the cmc for a very general type of ionic surfactant18 in which the number of charged groups $i$, the valency of charged group $z_i$, the number of alkyl chains $j$, and the valency of the counterion $z_c$ were considered. The equation is

$$\Delta G_{mic} = RT \left( \frac{1}{j} + \beta \frac{1}{j} \right) \ln \text{cmcITC} + RT \left( \frac{1}{j} \right) \ln \left( \frac{z_i}{j} \right) - \ln \left( \frac{z_i}{j} \right)$$

(7)

Amphiphilic dendrimer $G_{1QPAMC_m}$ is made of one polar group connected by the level of four charged groups, four alkyl chains, and four monovalent counterions. Therefore, $i = j = 4$ and $z_i = z_c = 1$. $\Delta G_{mic}$ can be determined from eq 8:

$$\Delta G_{mic} = RT \left( \frac{1}{4} + \beta \right) \ln \text{cmcITC} - RT \ln \left( \frac{4}{4} \right)$$

(8)

The thermodynamic parameters are summarized in Table 2, and their variations with alkyl chain length are also plotted in Figure 5.

<p>| Table 2. Thermodynamic Parameters of $G_{1QPAMC_m}$ Obtained from ITC Measurements at 25.0 ± 0.01 °C |
|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|</p>
<table>
<thead>
<tr>
<th>sample</th>
<th>cmcITC (mol/L)</th>
<th>$\beta$</th>
<th>$\Delta H_{mic}$ (kJ/mic)</th>
<th>$\Delta G_{mic}$ (kJ/mic)</th>
<th>$T \Delta S_{mic}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1QPAMC8</td>
<td>9.0 × 10^{-6}</td>
<td>0.32</td>
<td>-2.3 ± 0.2</td>
<td>-17.3</td>
<td>15.0</td>
</tr>
<tr>
<td>G1QPAMC12</td>
<td>7.4 × 10^{-6}</td>
<td>0.17</td>
<td>-8.5 ± 0.1</td>
<td>-13.2</td>
<td>4.7</td>
</tr>
<tr>
<td>G1QPAMC16</td>
<td>4.7 × 10^{-6}</td>
<td>0.21</td>
<td>-5.1 ± 0.2</td>
<td>-14.8</td>
<td>9.7</td>
</tr>
</tbody>
</table>

* $\beta$ values were obtained from conductivity. ** $\Delta G_{mic}$ was calculated with eq 8. $T \Delta S_{mic}$ was calculated with $\Delta G_{mic} = \Delta H_{mic} - T \Delta S_{mic}$. 

Figure 5 in which the changing tendency of the Gibbs free energy with alkyl chain length is in accordance with that of enthalpy. The increase in the alkyl chain length causes an increase in all thermodynamic parameters, $-\Delta H_{mic}$ and $-\Delta G_{mic}$ at $m \leq 12$, and the large negative values of the Gibbs free energy are primarily due to the entropic contribution. As the $m$ value increases from 12 to 16, there is a small variance in the values of the Gibbs free energy. From another point of view, the contributions of $\Delta H_{mic}$ to $\Delta G_{mic}$ are 13.3% for $G_{1QPAMC_8}$, 64.4% for $G_{1QPAMC_{12}}$, and 34.5% for $G_{1QPAMC_{16}}$. It is noteworthy that although the hydrophobic interactions increase substantially, the contribution of enthalpy has not increased identically, which is especially obvious for the situation of $m = 12$, as also consistent with the results presented above. As to the internal differences in the molecular structure of $G_{1QPAMC_m}$, the alkyl chain length/headgroup ratio should be the key factor in the regularity, which determines the conformation of $G_{1QPAMC_m}$ in solution. When the alkyl chain length/headgroup ratio is smaller than 1, the intermolecular hydro-
phobic interactions are enhanced and the extent of increase depends on the conformation of the headgroup. As an example of a greater alkyl chain length/headgroup ratio, \( \text{G}_{1}\text{QPAMC}_{16} \) exhibits aggregation behavior with a remarkable intermolecular hydrophobic interaction inducing an intracohesion conformation; accordingly, the effects of electric repulsion and hydrogen bonds weaken the contribution of enthalpy. On the basis of the above results, it is reasonable to speculate that the self-assembly behaviors of amphiphilic dendrimers are dependent not only on the hydrophobic chain length but also on the headgroups. Irregular spherical micelles are formed for short alkyl chains, as the intermolecular hydrophobic interaction is the dominant force in the aggregation. However, for a long alkyl chain system such as \( \text{G}_{1}\text{QPAMC}_{16} \) the ratio of the theoretical alkyl chain length/radius is above 1, inducing an intermolecular hydrophobic interaction so that the intracohesion of the alkyl chain is involved in the process of self-assembly and thus vesicular structures tend to form. The representation of the molecular self-assembly process is shown in Figure 6.

![Figure 6. Schematic representation of the organization of amphiphilic dendrimers with different alkyl chain lengths in the process of self-assembly.](image)

4. CONCLUSIONS

Differences in chemical structures generate obvious specificities in the process of self-aggregation with the increase in alkyl chain length in multibranched structures. In particular, various morphologies of aggregates were observed in the system, and vesicular structures with clear boundaries take shape in \( \text{G}_{1}\text{QPAMC}_{16} \) solutions. Various fluorescence probes showed that a lower polarity and higher solubilization ability of microdomains occurred with the increase in alkyl chain length from C8 to C12, indicating the enhancement of the hydrophobic microenvironment. Surprisingly, the polarity of the microdomain presented a reverse change trend in the case of \( \text{G}_{1}\text{QPAMC}_{16} \), whereas the solubilization ability increased sharply, which can provide evidence for the boundary structure of vesicular aggregates. The thermodynamic properties and related parameters, \(-\Delta H_{\text{mic}}\) and \(-\Delta G_{\text{mic}}\), illustrated the contributions of enthalpy and entropy with the increase in alkyl chain length in the self-aggregation process. One can also conclude that the contributions of the hydrophobic interaction to aggregation involving intramolecular and intermolecular interactions depend not only on the hydrophobic chain but also on the alkyl chain length/radius ratio. Especially for \( \text{G}_{1}\text{QPAMC}_{16} \) with an alkyl chain length/radius > 1, the intermolecular hydrophobic interaction is a priority, inducing an intracohesion of alkyl chain involved in the process of self-assembly, of which the conformation is conducive to forming vesicles. Accordingly, the effect of electric repulsion and hydrogen bonds in the headgroup will likely weaken the contribution of enthalpy. It is reasonably concluded that the nature of headgroups together with the hydrophobic tails of the amphiphilic dendrimer are dominant factors in molecular self-assembly.

**ASSOCIATED CONTENT**

Supporting Information

Conductivity measurements, dynamic light scattering (DLS) measurements, and characterization data of aggregates. This material is available free of charge via the Internet at http://pubs.acs.org/.

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Notes

The authors declare no competing financial interest.

**ACKNOWLEDGMENTS**

We are thankful for financial support from the Important National Science and Technology Specific Project (2011ZX05024-004-03) of China and the Knowledge Innovation Project of the Chinese Academy of Sciences (KJCX-1YW-21-03). This work also received support from the National Natural Science Foundation of China (project no. 21273061).

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