Self-Assembly of Octaaminoamido Derivatives of Resorcin[4]arene in Water – A "Cell-Like" Submicron-Scale Hydrogel Structure

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We have prepared four new octaaminoamide resorcin[4]-arenes having hydrocarbon chains of different lengths (**1**, **2**: R = CH_3; **3**, **4**: R = $C_{11}H_{23}$) and different terminal groups (**1**, **3**: NH_2; **2**, **4**: NMe_2). The surface tension and self-assembly of aqueous solutions of **2**–**4** were studied and their critical micelle concentrations (CMC) were determined. At the water/air interface, compound **2** forms a multilayer structure, whereas compound **3** forms a bilayer and compound **4** a monolayer structure. In addition, we found that compound **3** has a second CMC (CMC_2). A dynamic light scattering study indicated that, at a concentration of 0.1 wt% (i.e., > CMC_2), **3** forms nanodimensional aggregates; increasing the concentration up to 1.2 wt% results in the formation of strong transparent gels. For hydrogels having 5 wt% of **3**, SEM images demonstrated the formation of submicron-scale "cell-like" aggregates.

Introduction

Resorcin[4]arenes are well-known macrocyclic compounds that feature a hydrophobic aromatic cavity; the upper part of this cavity can be modified, by introducing convergent functional groups, to obtain 3D host molecules that possess additional binding centers besides the cavity.[1] The hydrophobic/hydrophilic balance of those hosts can be adjusted by condensing aliphatic aldehydes that have carbon chains of various lengths.[2] This procedure can be used to prepare structures that have the ability to form aggregates of different shapes, e.g., bilayers, tubes, and sheets. Recently, Reinhoudt and coworkers presented several examples of calixarene mono- and bilayers prepared on metallic surfaces.[3] Increased attention to the synthesis and properties of water-soluble calixarenes[4] has been caused by their high potential for mimicking and understanding biological self-assembly and recognition processes. There are, however, only a few reports describing the self-assembly of calixarene hosts in aqueous media,[5] and it still remains necessary to acquire sufficient amounts of information concerning their structure-property relationships before applying rational design strategies for the preparation of intelligent materials based on calixarene aggregates.

In this paper, we report the synthesis and self-assembly of new octaaminoamide resorcin[4]arenes that have a different chain lengths (**1**, **2**: R = CH_3; **3**, **4**: R = $C_{11}H_{23}$) and terminal groups (**1**, **3**: NH_2; **2**, **4**: NMe_2).

Compounds **1**–**4** are crystalline substances and their solubilities in a variety of solvents are listed in Table 1. Each compound is soluble in water, alcohols, and chloroform, with the exception of the initial amine **1**, which is soluble only in aqueous solutions of hydrochloric and acetic acids. Substance **3**, when dissolved in water or THF, forms gels, whereas only compound **4** is soluble, when heated, in aromatic solvents and ethyl acetate.

To determine some structure–property correlations, and to explain the solubilities of compounds **2**–**4**, we measured the surface tensions of their aqueous solutions, in the concentration range from 10^{-6} to 10^{-2} M, at the water/air interface.

Figure 1 presents diagrams of the dependence of the surface tension on ln *C*; the break points correspond to the critical micelle concentration (CMC; see also Table 2). We observe, for compounds **2** and **4**, that an increase in the length of the alkyl chain on the lower rim of the resorcinarene cavity (from CH_3 to $C_{11}H_{23}$) results in a 25-fold decrease of the CMC; for compounds differing only by an alkylamino substituent on the upper rim, alteration from H (**3**) to CH_3 (**4**) results in a threefold increase of the CMC. In contrast to compounds **2** and **4**, there are two break points observed in the surface tension curve of **3**; they correspond

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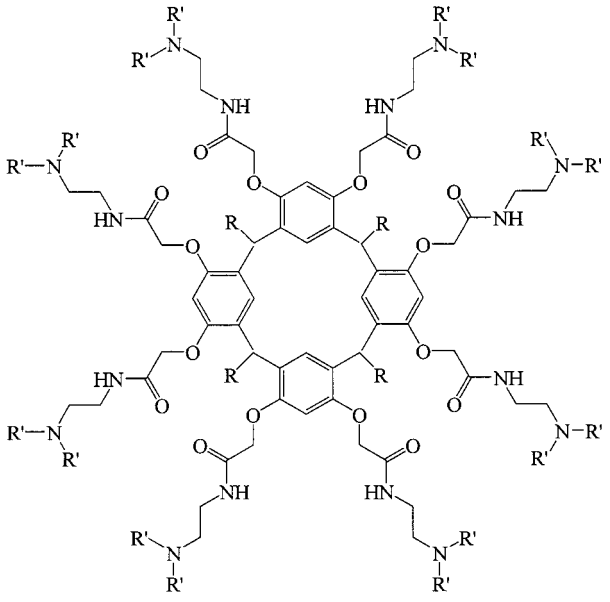
Table 1. Solubilities of compounds **1**−**4** in various solvents

Solvent[a]	**1**	**2**	**3**	**4**
Toluene	I[b]	I	I	S
Benzene	I	I	I	S (t)[c]
Carbon tetrachloride	I	I	I	S (t) → P
Chloroform	I	S	S	S
Dichloromethane	I	S	I	S
Acetone	I	S	S	S (t)
Ethyl acetate	I	I	I	S (t)
Dioxane	I	S (t)	S	S (t)
Tetrahydrofuran	I	S	S (t) → G	S (t)
Methanol	I	S	S	S
Ethanol	I	S	S	S
Butanol	I	S	S	S
Pentanol	I	S	S	S
Acetonitrile	I	S (t)	I	S (t)
Dimethyl sulfoxide	I	S (t)	S	S (t)
Dimethylformamide	I	S (t)	S (t)	S (t)
Water	S (pH < 5)	S (t)	S (t) → G	S (t)

[a] Amounts of compounds **1**−**4** were taken so as to obtain 3-wt% solutions. [b] S: soluble; I: insoluble; P: precipitates; G: gelation. [c] t: heating (to reflux) is required to dissolve this substance.



1 R = CH_3, R' = H
2 R = CH_3, R' = CH_3
3 R = $C_{11}H_{23}$, R' = H
4 R = $C_{11}H_{23}$, R' = CH_3

to a CMC_1 of 5.2×10^{-6} M and a CMC_2 of 2.9×10^{-4} M. Because of the distinct separation of the hydrophobic and hydrophilic parts in these resorcinarenes, even tetramethylresorcinarene **2** forms aggregates at concentrations lower than those found by Shinkai and coworkers[5a] for charged calix[*n*]arenes (n = 4, 6, 8). In addition, for long-chain derivatives, the values of the CMC of resorcinarenes are approximately one order of magnitude lower than those of calixarenes. The surface tension isotherms we obtained were used to calculate experimental adsorption parameters (Table 2) according to procedure described previously;[6] we compared these parameters to theoretical adsorption parameters calculated from a thermodynamic model based on the molecular mass and density of amphiphile. The thickness of the monolayer and the diameter of the adsorption sites were also estimated by means of molecular modeling (MM+ force field).

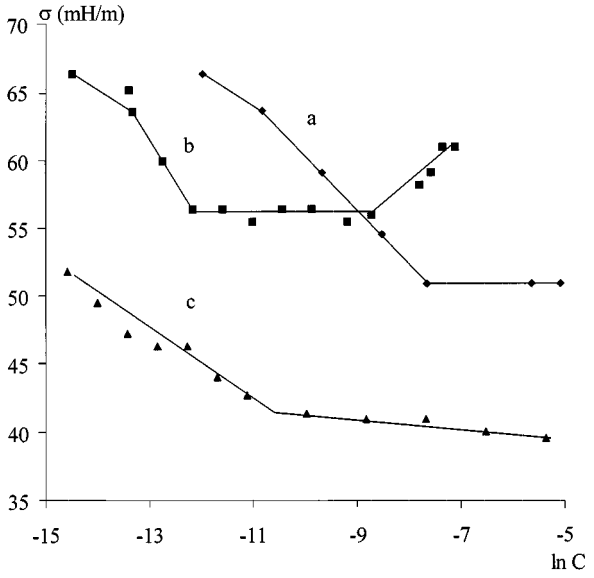


Figure 1. Plots of surface tension vs. ln concentration at 20 °C: (A) **2**, (B) **3**, and (C) **4**

Table 2. Absorption and micellization parameters of aqueous solutions of **2**−**4** at 20 °C

Compound		**2**	**3**	**4**
Γ_∞ [mol cm^{-2}]	exp.	1.6×10^{-10}	1.7×10^{-10}	9.7×10^{-11}
	calcd.[a]	1.2×10^{-10}	8.3×10^{-11}	8.2×10^{-11}
CMC [M]		5.1×10^{-4}	7.9×10^{-6}	2.2×10^{-5}
$(\sigma - \sigma_0)$/CMC		4×10^4	2.2×10^6	1.42×10^6
d (Å)[b]	exp.	12	11	15
	calcd.[a]	15	16	16
	MM+[c]	10	10	10
δ (Å)[b]	exp.	22	29	18
	calcd.[a]	13	14	15
	MM+[c]	5	15	15
ΔG^0_m [kJ·mol^{-1}][b]		−28.9	−39.2	−36.7

[a] Thermodynamic model, calculated according to Equation (1). [b] d: Diameter of the hydrophilic area; δ: thickness of a monolayer; ΔG°_m: free energy of micellization. [c] Thickness of monolayer was estimated by molecular modeling (MM+).

For resorcinarene **2**, the thickness of the corresponding monolayer, estimated by molecular modeling, is ca. 5 Å (Figure 2), but the estimations according to experimental data give a value of δ of ca. 22 Å. This discrepancy can be attributed to the formation of a multilayer structure at the water/air interface, in which the molecules of resorcinarene **2** adopt "boat" conformations and are arranged in a "tail-

to-tail'' manner.[7] In the case of **3**, the experimentally determined layer thickness (δ) is almost twice that calculated by molecular modeling for a single molecule. This observation suggests the formation of a bilayer or, possibly, to a nonuniform distribution of resorcinarene molecules of the surface layer as a result of the strong intramolecular interactions. The calculated values of δ for compound **4** are in a good agreement with those obtained from the surface tension measurements, which suggests that a saturated surface layer forms at the air/solution interface even at concentrations above the CMC.

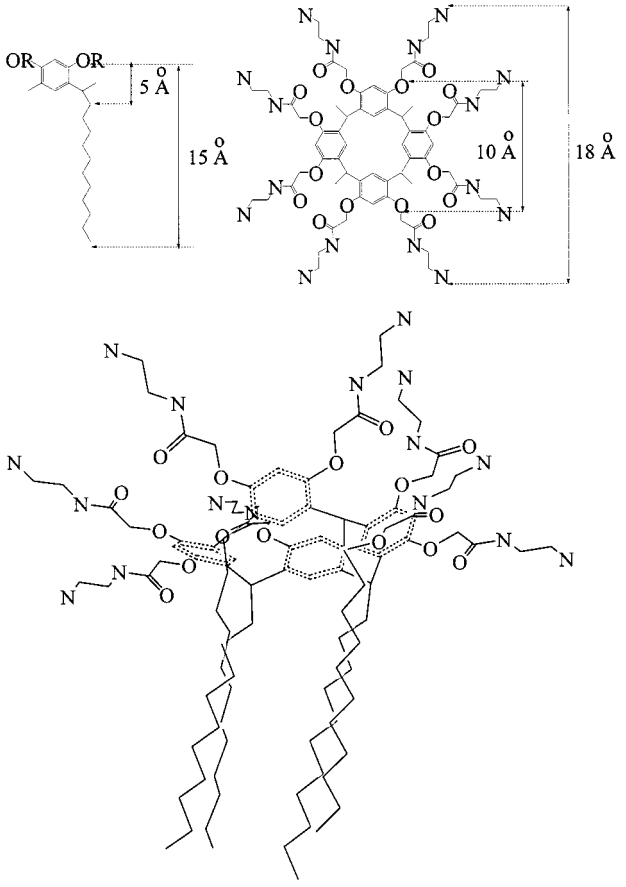


Figure 2. The dimension of hydrophilic and hydrophobic parts of resorcinarenes and schematic model of resorcinarene **3** prepared by HyperChem

As we observe in Figure 1 (B), increasing the concentration of **3** in solution above CMC_2 causes an increase in the surface tension as a result of depletion of the surface layer. This effect is caused by the formation of a continuous 3D gel net in the bulk of the solution. At concentrations of **3** above 4.17×10^{-4} M, the solution becomes viscous and then a transparent gel forms. The tendency of **3** to aggregate correlates well with both the surface activity parameter $(\sigma - \sigma_0)/CMC$[6] and the free energy of micellization (ΔG^0_m) calculated from the surface tension measurements.

To estimate the aggregate dimensions in the area before gel formation (above $CMC_2 = 2.9 \times 10^{-4}$ M), we studied the dynamic light scattering of a 0.1 wt% solution (5.245×10^{-4} M) of **3** (Figure 3, left and right, respectively). DLS measurements at different angles (30 and 90°) allowed the registration of the particles of different size. The simultaneous presence of small (Ø = 102−178 nm) and large particles (Ø = 407−826 nm) in solution suggests the existence of as equilibrium between them. Apparently, the smaller particles are substructures of the larger aggregates. The presence of a second sufficiently shifted peak in DLS spectra is common evidence that the sample is polydisperse (broad particle size distribution of aggregates). Because the particle size in a DLS experiment is often similar to the wavelength used, the results obtained are strongly affected by both the shape of the macromolecules and the observation angle. Therefore, we used an angle of 30° to register the smaller particles; for the larger particles, measurements at 90° were suitable. Fusion of the aggregates at concentrations above 1 wt% (5.245×10^{-3} M) resulted in the formation of the gel.

A large number of articles have been published that describe low-molecular-weight gelators, which include calix[8]arenes.[8] It has been found that their 3D nets are formed through noncovalent interactions between aggregates. These low-weight gelators seem to be very promising materials for preparing strong, thermo-reversible hydrogels useful in drug delivery,[8a] as templates for new silicon materials,[9] and for the design of membrane filters.[8a] Sugars,[10] bile acids,[11] azobenzenes,[12] and amino acids[13] have all been used successfully as hydrogelators.

As we mentioned above, resorcinarene **3** forms a strong clear gel even at a concentration of 1.2 wt%, which means that one molecule of the gelator immobilizes 10000 water molecules! In contrast to the results of a previous study,[11] where a hydrogel was obtained from solutions of bile acid derivatives in the presence of acidic acid, the addition of methanol and organic acids (acidic, oxalic, succinic, citric, or glucuronic acids) as a co-solvent for **3** did not result in the formation of new gel.

The thermal stability of hydrogel **3** ($T_{gel-sol}$) was determined with the help of viscometry (Figure 4). The value of $T_{gel-sol}$ decreases upon decreasing the concentration of **3**: it is 45 °C at 1.2 wt% (see a in Figure 4) and 35 °C for 0.75 wt% solutions (see b in Figure 4). The thermal reversibility of the hydrogel depends on the time required for the "melting−cooling'' cycle. No gel was formed when a 1.2-wt% solution of **3** that was heated to T_{gel} was poured rapidly into a cold glass; instead, a thick opaque form covers the top of the solution. Presumably such an abrupt decrease of temperature does not favor the formation of the noncovalent bonds, which did formed when this solution was left to cool slowly in a warm glass.

Comparing the IR spectrum of the gel of **3** to that of its xerogel obtained by vacuum drying of the respective hydrogel, we found that the latter contains residual water, which appears as a band at 1638 cm^{-1}. We found also that the viscosity and thermal stability of the hydrogel prepared from the xerogel of **3** were higher ($T_{gel-sol}$ = 60 °C; Figure 3, c) than those measured for the 1.2-wt% hydrogel of **3** (curve a). Presumably, the increased viscosity and thermal stability of the "second'' gel are due to the "memory effect''

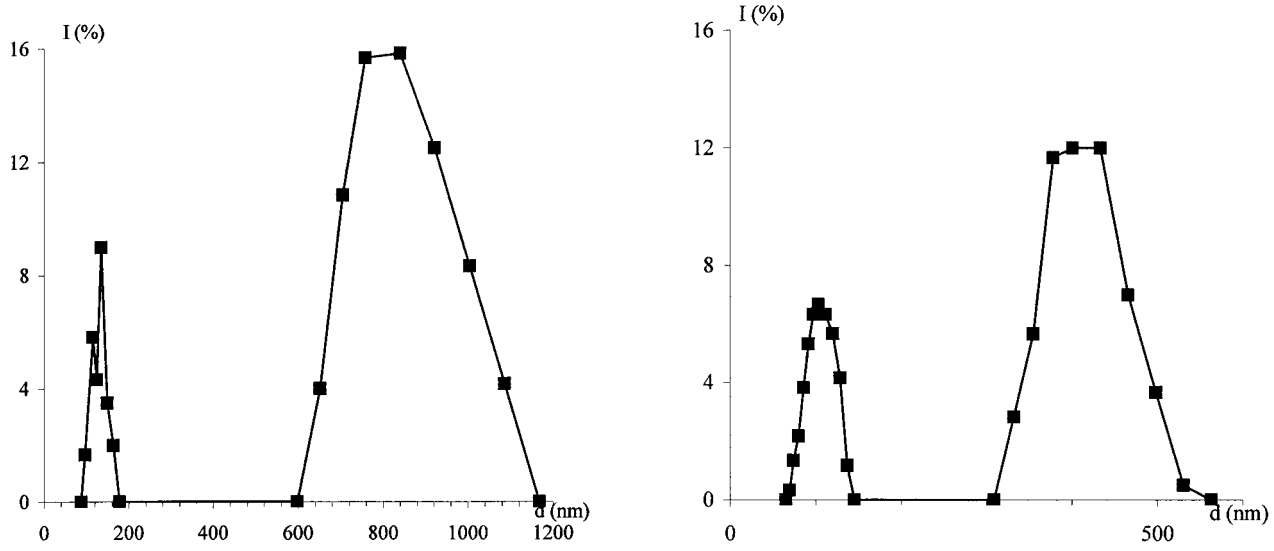


Figure 3. DLS data obtained from a 0.1% aqueous solution of **3** at 30° (left) and at 90° (right). *d*: diameter of particles; *I*: intensity of signal

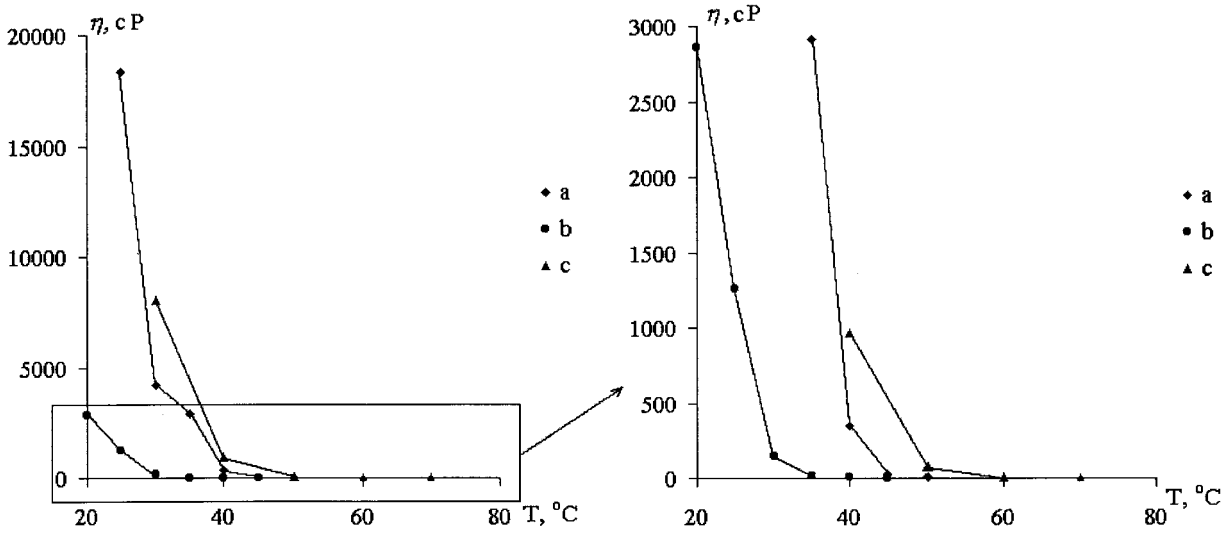


Figure 4. Plot of the viscosity of an aqueous solution of **3** vs. the experimental temperature: (a) 1.2 wt%, (b) 0.75 wt%, and (c) 1 wt% solution of the xerogel

of the retained intermolecular 3D net and, thereby, it is reinforced in the "second" gel structure. To define the structural fragments of **3** that are responsible for its gelator properties, we compared the IR spectra of the gel, xerogel, and pure **3** (Table 3). We observe that the adsorption and vibration peaks of the amino and amido groups of resorcinarene are affected by gelation, which indicates their participation in intramolecular hydrogen bonding.[10,13] The appearance of an uncompensated band at 1638 cm^{-1} in the hydrogel's spectrum with water compensation confirmed the presence of ordered water molecules bound noncovalently to the polar fragments of **3**. Keeping in mind that acidification of aqueous solutions of **3** prevents their gelation, we suggest that formation of the gel is driven by intramolecular hydrogen bonding between the polar groups of **3** [the NH_2 and C(O)NH units] with water and with each other on one side and by hydrophobic interactions between the long aliphatic chains on the other.

The form and structure of the gel were examined by obtaining scanning electron micrographs (SEM) of the xerogel derived from the 3-wt% (1.6×10^{-2} M; Figure 5, a–c) and 5-wt% (2.6×10^{-2} M; Figure 5, d–f) hydrogels of **3**. SEM images of the xerogel at the water/air interface are provided in Figure 5. We observe "cell-like" aggregates that have submicron dimensions (Ø = 40–100 μm) that are separated from each other by diaphragms (Ø = 5–13 μm). Images of the xerogel cross-section (Figure 5, b and c) demonstrate that the diaphragms do not separate "cells" completely, but they form a wall-thick (ca. 5 μm) inner compartment (width = 40 μm).

Table 3. IR spectroscopic data for pure **3** and its hydrogel and xerogel

	ν(OH) H_2O	ν(NH_2)	ν(NH) amide	ν(CH)	Amide I	δ(OH) H_2O	δ(NH_2)	Amide II
3	–	3389	3294	2922 2853	1666	–	1581	1534
Hydrogel **3**[a]	–	3392	3317	2924 2845	1661	1638	1580	1542
Xerogel **3**	–	3395	3297	2924 2854	1665	1638	1583	1539
Water	3321					1634		

[a] Spectra with compensation of water molecule adsorption peaks.

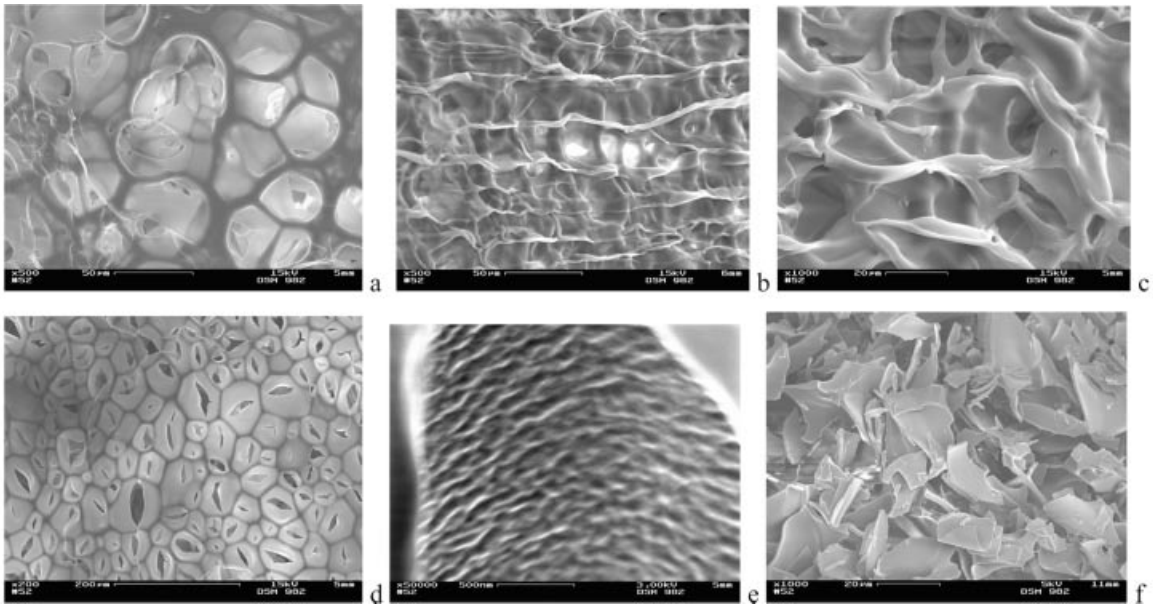


Figure 5. Scanning electron microscopy (SEM) images of 3-wt% (a, b, c) and 5-wt% (d, e, f) dried hydrogels of **3**; magnifications: (a) × 500, (b) × 500, (c) × 1000, (d) × 200, (e) × 50,000, (f) × 1000

Vesicular aggregates on the surface of the xerogel, prepared from the 5-wt% hydrogel (Figure 5, d), have a strong resemblance to plant cells; each cell has a polygonal form that that arises from the pressure exerted by the neighboring cells. The diameters of the aggregates are between 20 and 800 μm. Most of the aggregates feature ripped slits that were caused by the extraction of water during the preparation of the xerogel sample in vacuo; obviously, while in the gel state, the aggregates were separated by diaphragms filled with water. The stratified structures of the inner walls of the aggregates can be seen through these slits (Figure 5, e). We estimate from SEM images that the thickness of the walls in the "cell-like" aggregates is in the range 0.4−1.3 μm. Since dimensions of one resorcinarene molecule do not exceed 30 Å, we conclude that these walls are formed by multilayers of 100 to 400 molecules of **3**, which is similar to the degree of aggregation observed for the crown-appended cholesterol derivatives in an organic or acetic acid medium.[9]

It is clear that the presence of the hydrophobic moeities of molecules **2**, **3**, and **4** (when compared with **1**) provides hydrophobic dispersion interactions and, thereby, aggregation of the amphiphile, which promotes their solubility in the neutral aqueous medium. Here we have described the first example of the gelation of a neutral aqueous solution by the presence of an amphiphilic aminoamide octa derivative of resorcin[4]arene **3**. We found the following features to be crucial for effecting the gelation properties of **3**:

1) The presence of the amido- and apical NH_2 groups, which provide intermolecular interactions at the hydrophilic domain of the amphiphile and promote the formation *of big aggregates* as a result of intramolecular interactions occurring even above the CMC_2.

2) Fusion of aggregates (micelles) into a gel net, which occurs as a result of the interactions between the apical NH_2 groups and the water molecules held by the nascent xerogel.

Analysis of the wall thicknesses of the "cell-like" aggregates revealed that they possess a multilayer structure, which, according to rough estimations for the gel prepared at a 5-wt% concentration, consists of 100−400 molecules of **3**.

Experimental Section

4,6,10,12,16,18,22,24-Octakis(ethoxycarbonylmethoxy)-2,8,14,20-tetramethylcalix[4]arene and 4,6,10,12,16,18,22,24-octakis(ethoxycarbonylmethoxy)-2,8,14,20-tetraundecylcalix[4]arene were synthesized as described previously.[7b]

4,6,10,12,16,18,22,24-Octakis{[*N*-(2-aminoethyl)amido]methoxy}-2,8,14,20-tetramethylcalix[4]arene (1): 4,6,10,12,16,18,22,24-Octakis(ethoxycarbonylmethoxy)-2,8,14,20-tetramethylcalix[4]arene (1.0 g, 0.81 mmol) was dissolved in ethylenediamine (30 mL) and the solution was stirred at room temperature for 7 days. The precipitate obtained was filtered and washed with acetone (2 × 50 mL). The product, a white powder, was dried in vacuo (0.68 g, 62%). M.p. > 350 °C. MS: *m*/*z* = 1346 [M + H$^+$], 1368 [M + Na$^+$].

4,6,10,12,16,18,22,24-Octakis{[*N*-[2-(dimethylamino)ethyl]amido]-methoxy}-2,8,14,20-tetramethylcalix[4]arene (2): 4,6,10,12,16,18,22,24-Octakis(ethoxycarbonylmethoxy)-2,8,14,20-tetramethylcalix[4]arene (1.5 g, 1.2 mmol) was dissolved in dimethylethylenediamine (30 mL). The solution was stirred at room temperature for 4 h and then at 60 °C for 6 days. The precipitate obtained was filtered and washed with acetone (2 × 100 mL). The product, a white powder, was dried in vacuo (1.83 g, 96%). M.p. 251−253 °C. ^{1}H NMR (300 MHz, D_2O, 25 °C): δ = 7.07 (s, 4 H), 6.83 (s, 4 H), 6.38 (s, 4 H), 5.75 (s, 4 H), 3.49−3.46 (m, 16 H), 3.36 (s, 16 H), 2.55 (t, *J* = 5.74 Hz, 8 H), 2.37 (t, *J* = 5.74 Hz, 8 H), 2.22 (s, 48 H), 1.24 (d, *J* = 6.57 Hz, 12 H) ppm. MS: *m*/*z* = 1572.8 [M + H$^+$], 1594.9 [M + Na$^+$], 1610.9 [M + K$^+$].

4,6,10,12,16,18,22,24-Octakis{[*N*-(2-aminoethyl)amido]methoxy}-2,8,14,20-tetraundecylcalix[4]arene (3): 4,6,10,12,16,18,22,24-Octakis(ethoxycarbonylmethoxy)-2,8,14,20-tetraundecylcalix[4]arene (2 g, 1.1 mmol) was dissolved in ethylenediamine (50 mL). The solution was stirred at room temperature for 4 h and then at 60 °C for 3 days. The solution was concentrated in vacuo and the precipitate obtained was washed with dioxane (2 × 100 mL). The product, a white powder, was dried in vacuo (2.63 g, 86%). M.p. 214−217 °C. ^{1}H NMR (300 MHz, D_2O/CD_3COOD, 25 °C): δ = 7.01 (s, 4 H), 6.50 (s, 4 H), 6.20 (s, 4 H), 5.74 (s, 4 H), 3.36−3.20 (m, 32 H), 2.97 (s, 16 H), 0.91 (s, 80 H), 0.53 (br. s, 12 H) ppm. MS: *m*/*z* = 1908.5 [M + H$^+$], 1930.8 [M + Na$^+$], 1946.8 [M + K$^+$].

4,6,10,12,16,18,22,24-Octakis{[*N*-[2-(dimethylamino)ethyl]amido]-methoxy}-2,8,14,20-tetraundecylcalix[4]arene (4): 4,6,10,12,16,18,22,24-Octakis(ethoxycarbonylmethoxy)-2,8,14,20-tetraundecylcalix[4]arene (2.8 g, 1.6 mmol) was dissolved in dimethylethylenediamine (50 mL). The solution was stirred at room temperature for 10 days and then at 60 °C for 5 h. The solution was concentrated in vacuo and the precipitate obtained was washed with acetone (50 mL). The product, a white powder, was dried in vacuo (2.32 g, 65%). M.p. 127−130 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.20 (s, 4 H), 6.63 (br., 8 H), 6.28 (s, 4 H), 4.55 (t, *J* = 7.05 Hz, 4 H), 4.07−4.02 (m, 16 H), 3.38−3.34 (t, *J* = 5.85 Hz, 16 H), 2.42−2.38 (t, *J* = 6.27 Hz, 16 H), 2.16 (s, 48 H), 1.31 (br. s, 8 H), 1.22 (s, 80 H), 0.85 (t, *J* = 6.06 Hz, 12 H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$, 25 °C): δ = 167.9, 154.4, 128.8, 126.4, 103.5, 69.7, 57.9, 45.1, 36.8, 35.9, 34.8, 31.7, 30.1, 29.7, 29.6, 29.5, 29.2, 22.5, 13.8 ppm. MS: *m*/*z* = 2129 [M + H$^+$].

Preparation of Hydrogel: A weighed amount of **3** and the solvent (1 cm^3) were heated in a sealed test tube until dissolution of the solid occurred. The hot solution was cooled to room temperature. Gelation was considered successful if the sample became transparent and had a solid-like form that showed no apparent flow upon inversion of the test tube.

Preparation of a Xerogel for Viscometry and FT-IR Spectroscopy Experiments: The xerogel was obtained from the 1.2-wt% hydrogel by vacuum drying at 80 °C for 12 h.

Surface Tension Measurements: The surface tensions of aqueous solutions of **2**−**4** were estimated in pure water at 20 °C by using a Wilhelmy method.[5]

Before effecting the measurements, the aqueous solutions of **2**−**4** were aged for 72 h to receive completely formed surface. The surface tension was estimated as an average of three measurements (standard deviation did not exceed ±2 dynes/cm). The values of the CMC were determined graphically from plots of σ(ln *C*) (σ, surface tension; *C*, concentration of surfactant). The value of the maximum surface adsorption (Γ_∞), the surface area per molecule (S_m), the diameter per molecule (*d*), and the surface thickness (δ) were found from the Gibbs adsorption equation, as has been described previously [Equation (1) and Equation (2)]:[6]

$$\Gamma_\infty = (-1/RT)(d\sigma/d\ln C) \quad (1)$$

$$S_m = 1/(\Gamma_\infty \cdot N_A),\ d = (4S/\pi)^{1/2},\ \delta = M_r \cdot \Gamma_\infty/\rho \quad (2)$$

where R is the gas constant, *T* is the absolute temperature (293 K), and M_r is the molecular mass of substance. The value of the density of the resorciarenes (ρ = 1.13 g/cm^3) was taken from the literature.[14]

The free energy of micellization was calculated from Equation (3).[6]

$$\Delta G^0_m = RT\ln cmc \quad (3)$$

The theoretical values of Γ_∞ and *S* were found by using the following Equation (4).[6]

$$\Gamma_\infty = 1/(S_m \cdot N_A) = (M/\rho)^{-2/3} \cdot N_A^{-1/3} \quad (4)$$

Geometric parameters of the studied molecules were estimated by means of HyperChem software (HyperChem® Release 5.0, N 500−10001026, Hypercube Inc.) by applying the MM+ force field and the Polak−Ribiere optimization algorithm for minimization in vacuo. The final gradient was 0.090578 for **1**, 0.009296 for **2**, 0.09086 for **3**, and 0.008331 for **4**.

Viscosity Measurements: The viscosities of the 1.2- and 0.75-wt% aqueous solutions of **3** and for the 1.0-wt% xerogel of **3** were measured using a Geppler viscometer. Hot solutions (ca. 50 mL) were placed in the viscometer (Ø of the tube: 16 mm; length of the tube: 200 mm) and then cooled to room temperature before being thermostatted at the experimental temperature. A metal ball (weight, 16.0581 g; density, 8.131 g/cm^3; ball constants, $K_{forward}$ = 0.12264 cP·cm^3·g·s, K_{back} = 0.12239 cP·cm^3·g·s) was placed on the gel surface. Full gel disintegration, which is measured as occurring when the metal ball undergoes a practically instant fall to the bottom of the tube, was observed for the 1.2-wt% solution at 45 °C (the falling time of the ball was 23 s), for the 0.75-wt% solution at 35 °C (22 s), and for the 1.0-wt% xerogel at 60 °C (13 s). The viscosity (η) was calculated according to the following Equation (5):

$$\eta = t(Q - \rho)K \quad (5)$$

where t is the time taken for the ball to pass through the measured part of the tube, Q is the ball's density, ρ is the solvent's density, and K is a ball constant.

Dynamic Light Scattering: The dynamic light scattering (DLS) measurements were performed on a transparent aqueous solution of **3** (5.245×10^{-4} M) using a DLS 700 instrument (Otsuka, Japan) at scattering angles of 30 and 90°.

Scanning Electron Microscopy: Scanning electron microscopy images were taken using a Gemini microscope (Zeiss, Germany). Samples were prepared from 3- and 5-wt% hydrogels of **3** dropped on an aluminum support and freeze-dried at −50 °C in vacuo for 4 h. All images were taken at a voltage of 4 kV.

FT-IR Spectra: FT-IR spectra were recorded using an AVATAR 360 FT-IR spectrometer. Spectra of the hydrogel, xerogel, and a solid sample of **3** were measured in the reflection regime and were corrected for water.

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