RSC Advances

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

**ARTICLE TYPE**

# Supramolecular Hydrogel Based on Amphiphilic Calix[4]arene and Its Application in the Synthesis of Silica Nanotubes

Song Song,[a] Jinhua Wang,[a] Hai-Tao Feng,[a] Zhi-Hua Zhu,[a] and Yan-Song Zheng*[a]

*Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX*

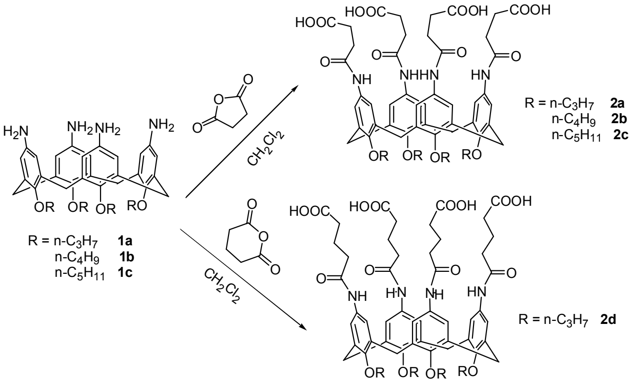
**DOI: 10.1039/b000000x**

**Novel amphiphilic calix[4]arenes bearing four carboxylic groups at the upper rim and four alkyl chains at the lower rim were synthesized. It was found for the first time that a hydrogel could form by leaving the suspension of the amphiphilic calix[4]arene in aqueous media to stand at room temperature for a period of time. Unlike most of supramolecular gel which resulted from the aggregation of a solute in hot solution upon cooling, this kind of hydrogel was produced through a dissolution-reassembly process from nanospheres to nanofibers, which could be used as a template for preparation of silica nanotubers.**

## Introduction

Recently, supramolecular gels based on low-molecular-mass gelators (LMMGs) have attracted great attention due to a large variety of potential applications,[1] such as sensing,[2] catalysis,[3] electronic devices,[4] drug delivery,[5] regenerative medicine,[6] tissue engineering,[7] and templates for the synthesis of nanoporous organic[8] and inorganic materials[9] *etc*. To endow the gels with more functionalities, many macrocyclic compounds, such as crown ethers,[10] cyclodextrins,[11] calix[4]pyrroles,[12] and so on, have been used to prepare gel.

Besides acting as well known macrocyclic host compounds, calixarenes can also easily self-assembly[13] into supramolecular nanostructures including micelles,[14] vesicles,[15] capsules,[16] rotaxanes,[17] and nanotubes.[18] Some gels resulted from the self-assembling of calixarene derivatives have also been gained. For example, Shinkai and coworkers have reported that calix[n]arenes (n = 4, 6, 8) bearing long acyl groups at the upper rim are excellent gelators for various organic solvents.[19] Xu and coworkers have found a simple method for preparing a novel and stable metallogel based on 3-pyridine-azo-calix[4]arenes.[20] Zheng et al have found that chiral calix[4]arenes bearing S-1-phenylethylamine groups at the lower rim can enantioselectively form heat-set gels with D-2,3-dibenzoyltartaric acid in cyclohexane,[21] and calix[4]arene bearing L-2,3-dibenzoyltartaric acid groups at the lower rim can enantioselectively self-assemble into a gel only with one enantiomer of chiral amines in chloroform.[22] Recently, more calix[4]arene gelators for organic solvents were reported.[23] Although aqueous media is beneficial to the preparation of drug carrier, biomolecule sensor, and tissue engineering which need to be carried out in water, the calixarene hydrogels in aqueous media were very rare.[24] Here we report that amphiphilic calix[4]arenes bearing four carboxylic groups at the upper rim and four alkyl chains at the lower rim are synthesized and can form a gel in aqueous media. This kind of hydrogel can be used as a template for the preparation of silica nanotubes.



**Scheme 1** The synthetic routes of the amphiphilic calix[4]arenes **2a** – **2d**.

## Result and discussion

### Synthesis of the amphiphilic calix[4]arenes 2a – 2d

The starting materials calixarene amines bearing four alkyl groups at the lower rim **1a** – **1c** were easily prepared according to the procedure in literatures.[25] By acylization of the amino groups with dicarboxylic anhydride, amphiphilic calix[4]arenes bearing four carboxylic groups at the upper rim **2a** – **2d** were obtained in excellent yield (Scheme 1). In the synthetic process of either the calix[4]arene amines or the amphiphilic calix[4]arenes, re-crystallization instead of column chromatography was used for the purification of all the products, which would be beneficial for their preparation on the large scale. They were fully characterized by $^{1}$H NMR spectra, $^{13}$C NMR spectra, IR spectra, HRMS spectra and melting points (ESI). The NMR spectra of the amphiphilic calix[4]arenes indicated that they were all in cone conformation.

### Gelation behaviors of compounds 2a – 2d

Gelation behavior of amphiphlic calix[4]arenes in a mixed solvent of deionized water and ethanol was studied. To the solution of the amphiphlic calix[4]arenes (2.5 mM) in ethanol water was rapidly added, which instantly gave rise to a suspension. The suspension was left to stand for more than 4 h at room temperature. It was found that **2a** and **2b** could gelate the mixed solvent of water and ethanol while **2c** and **2d** only led to precipitates (Table 1). When the pH was decreased to 3 from 6, calixarene **2a** could not arouse a gel in this mixed solvent. Using other organic solvents that are miscible with water, such as acetone and THF, no gelation was observed.

**Table 1** Gelation behaviours of **2a – 2d** in the mixed solvent of water and ethanol[a]

| Entry | Compound | Amount (mg)[b] | pH | Result |
|---|---|---|---|---|
| 1 | **2a** | 5.3 | 6 | G |
| 2 | **2a** | 5.3 | 3 | P |
| 3 | **2b** | 5.6 | 6 | G |
| 4 | **2c** | 5.8 | 6 | P |
| 5 | **2d** | 5.6 | 6 | P |

[a] [**2**] = 2.5 mM; water/ethanol 9:1 v/v.

[b.] The amount of **2a – 2d** in 2 mL of the mixed solvent.

[c.] G = gel; P = precipitates.

Just like most of supramolecular gels, the hydrogels of **2a** and **2b** are responsive to temperature. When the gel was heated, it became a suspension. Upon standing the suspension at room temperature, it became a gel (Fig. 1). This process could be repeated for many times. At the same concentration (2.5 mM), the gel from **2a** and **2b** had a suspension–gel transition temperature of 80 °C and 30 °C, respectively, in water/ethanol (4:1 v/v) solvent.

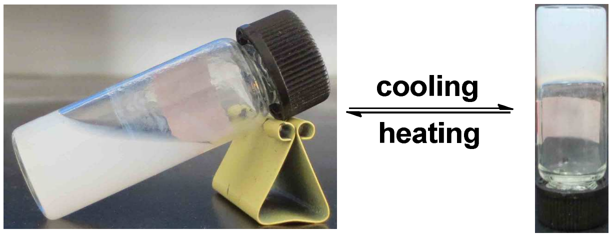


**Fig. 1** The reversible suspension–gel transition of **2a** (2.5 mM) in water/ethanol (4:1 v/v) solvent.

**Table 2** Gelation behavior of **2a** in water with different ethanol fraction.[a]

| Entry | EtOH (v%) | Result | $T_g$ (°C)[b] |
|---|---|---|---|
| 1 | 5 | G | 30 |
| 2 | 10 | G | 100 |
| 3 | 15 | G | 90 |
| 4 | 20 | G | 80 |
| 5 | 25 | G | 60 |
| 6 | 30 | P | — |
| 7 | 35 | P | — |
| 8 | 40 | P | — |
| 9 | 45 | P | — |
| 10 | 50 | S | — |

[a] [2] = 2.5 mM.

[b.] $T_g$ = suspension–gel transition temperature.

[c.] G = gel; P = precipitates; S = solution.

The effect of the ethanol fraction in water on the gelation behavior of **2a** was studied (Table 2). When the ethanol fraction in water is less than 30%, gel could form. However, in the mixed solvent with more than 30% ethanol fraction, **2a** precipitated. A solution was obtained after the ethanol fraction was increased to 50%. It was found that the thermostability (suspension-gel transition temperature) of gel increased as the ethanol fraction decreased. The suspension-gel transition temperature increased from 84 °C to 100 °C when the ethanol fraction was reduced to 10% from 25%. However, when the ethanol fraction was further reduced to 5%, the suspension-gel transition temperature was only 30 °C. This probably resulted from partial precipitation of **2a** in the mixed solvent with less ethanol fraction, which reduced the concentration of the suspension that could form the gel.

### Micro-structure of the hydrogel and its formation mechanism

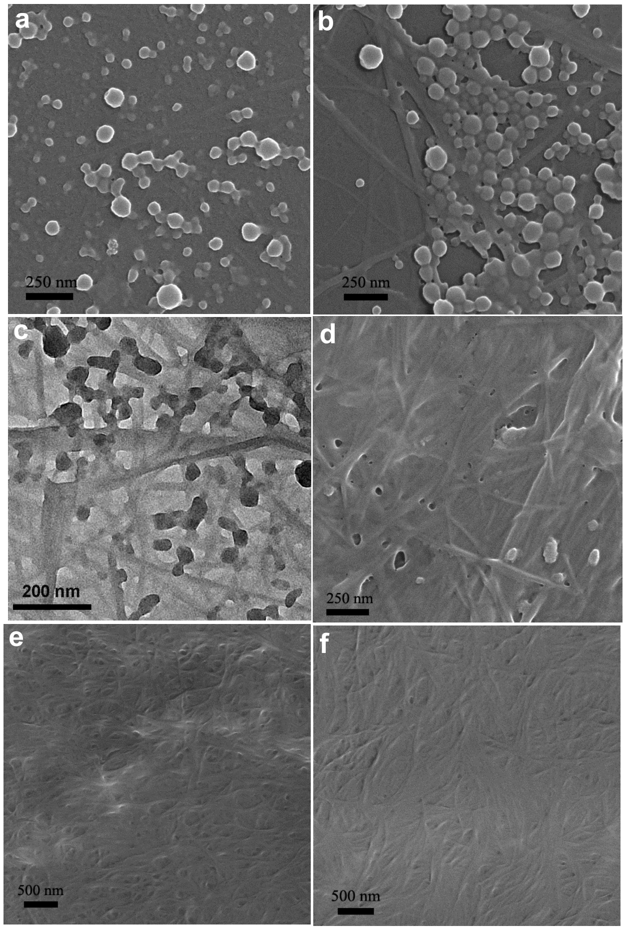


**Fig. 2** The FE-SEM and TEM images of the suspensions and the gels from **2a** (2.5 mM) in water and ethanol 9:1 v/v after standing for different time. FE-SEM images (a, b, d–f) and TEM image (c). Standing time, a, 5 min; b, 1 h; c, 2h; d, 4 h; e, 12 h; f, 24 h.

The micro structure of the suspensions and the gels from **2a** was studied *via* FE-SEM and TEM measurements. As shown in Fig. 2a, spherical particles were observed in the FE-SEM images when the suspension resulted from the addition of water into the solution of **2a** in ethanol was left to stand for 5 minutes. The diameter of the nanospheres was in a range of 50 nm to 140 nm. After the suspension was allowed to stand for 1 h, nanofibers appeared besides the major nanospheres (Fig. 2b). By standing the suspension for 2 h, more nanofibers formed while the isolated nanospheres became into fusing ones (Fig. 2c). Four hours of standing was the critical time at which a gel started to emerge from the suspension, and the nanofibers became the major structure while only very few of nanospheres could be observed from TEM images. After 12 h of standing, a stable gel formed, which was completely composed of nanofibers and no any nanosphere remained (Fig. 2e – 2f).

Dynamic light scattering (DLS) of the suspension of **2a** in water and ethanol (9:1, v/v) after standing for different time at room temperature was investigated (Fig. 3). At initial stage of 10 min, the aggregates had a diameter of about 90 nm, which was in accordance with the observation from the electron microscope (Fig. 3a). After standing for 1 h and 2 h, the diameters of the aggregates were increased up to 200 nm and 600 nm, respectively (Fig. 3b and 3c). By standing the suspension for 4 h at which the gel started to form, the aggregates had a size of 1500 nm (Fig. 3d). This confirmed that the aggregates of **2a** in water/ethanol could truly become bigger ones as the standing time increased.

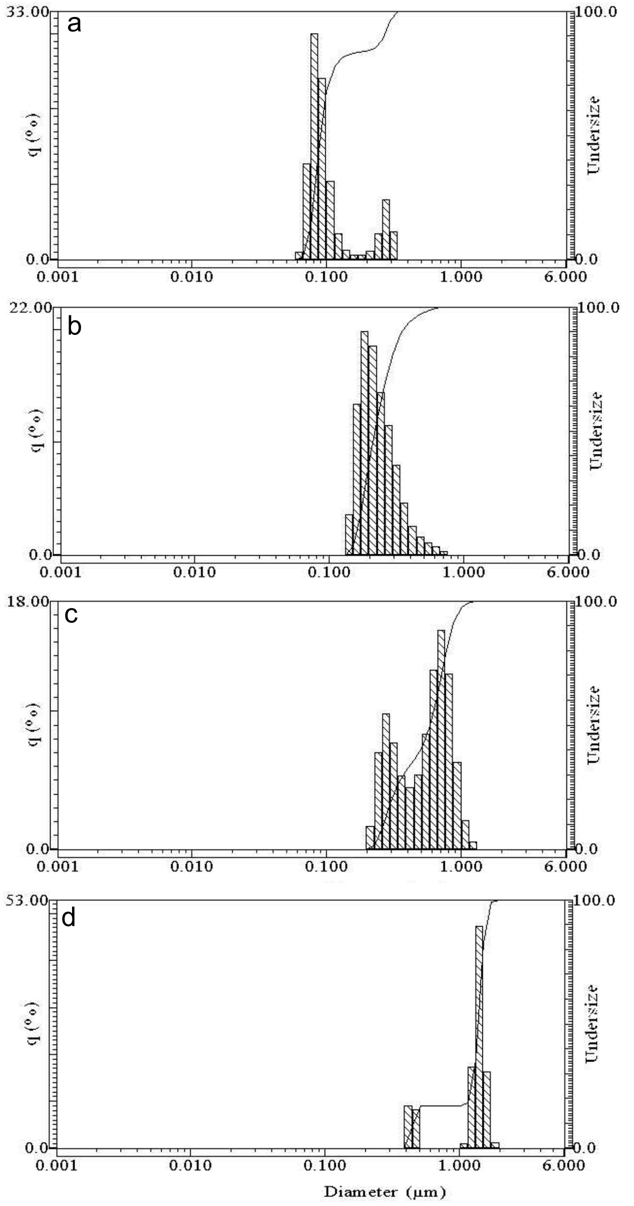


**Fig. 3**. Dynamic light scattering (DLS) diagrams of the suspension of **2a** in water and ethanol (9:1, v/v) after standing for (a) 10 min, (b) 1 h, (c) 2h, and (d) 4 h at room temperature. [**2a**] = $3.0\times10^{-4}$ M.

It could be inferred that the aggregation of **2a** was so fast that it only produced nanosphere by aggregating around an initially formed tiny particle when water was rapidly added into the solution of **2a**. However, the nanospheres in the suspension were not stable and could dissolve and re-aggregated into the stable nanofibers. This kind of dissolution-reassembly process could be confirmed by the following experimental facts. First, the suspension could not be transformed into a gel if it was allowed to stand at less than 15 °C. At lower temperature, the nanospheres were difficult to dissolve. Second, when the ethanol fraction in water was reduced to 5%, the resultant gel was obviously less stable than that in the mixed solvent with higher ethanol fraction. With less ethanol fraction, some of **2a** became precipitates which was bulky and had a less solubility. Finally, the nanofibers had a less diameter (about 10 nm) than that of the nanospheres (about 100 nm), and were also more uniform than the nanospheres. This results indicated that the nanofibers were not produced by fusion of the nanospheres one by one although the fusion of the two or three nanospheres was observed. If the nanofibers resulted from the fusion of several nanospheres, nanorods instead of nanofibers with high aspect ratio (10 nm wide and more than 2000 nm long) formed. In addition, no any incompletely fused nanospheres were found in a nanofiber. Therefore, nanofibers were produced by a dissolution-reassembly process. These nanofibers with high aspect ratio were cross-linked and interwoven together to form a 3D network which could fix the aqueous solvent and form a hydrogel (Fig. 4).[26]

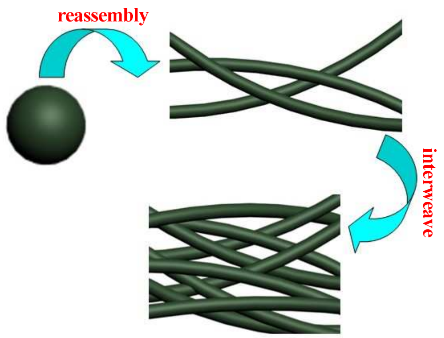


**Fig. 4** Schematic transformation from nanospheres to nanofibers and formation of 3D network that gave a gel.

## Using the hydrogel as template for preparation of silica nanofibers

Due to the hydrophilicity, the carboxylic groups of **2a** should be exposed to the surface of the nanofibers in the aqueous solvent. According to Che's reports,[27] a co-structure-directing agent, 3-aminopropyl trimethoxysilane (APTMS), would be attracted by the carboxylic groups due to acid–base interaction. Then a main silication agent, tetraethoxysilane (TEOS), would join into the co-structure-directing agent to form a layer of silica on the surface of the nanofibers due to the formation of silicon oxide networks through hydrolysis and condensation. Hollow nanotubes would be obtained after the organic nanosphere template was removed by washing.

Based on the above considerations, APTMS and TEOS were added to the hydrogels of **2a** in the mixed solvent of water and ethanol (9:1 v/v). The resultant mixture was gently stirred for 5 minutes (about 60 r/min) before it was left to stand for 12 hours in order to make the hydrolysis and condensation complete. The precipitates were collected and washed by centrifugation. As revealed by the TEM measurement, the solid was made of hollow nanotubes (Fig. 5) with an inner diameter of about 10 nm, which was in accordance with the diameter of the nanofibers in the hydrogel.

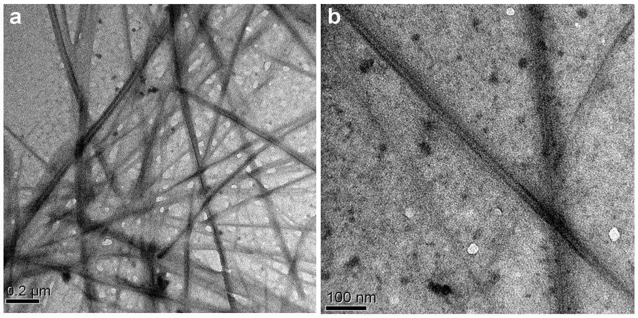


**Fig. 5** TEM images of the silica hollow nanotubes from the hydrogels of **2a** after APTMS and TEOS were added.

## Conclusions

Novel amphiphilic calix[4]arenes bearing four carboxylic groups at the upper rim and four alkyl chains at the lower rim were synthesized and could form a gel in aqueous media. Unlike most of supramolecular gel which resulted from the cooling of a hot solution, this kind of hydrogel formed by standing a suspension of **2a** in aqueous media at room temperature through a dissolution-reassembly process. During the process, unstable nanospheres could spontaneously transfer into nanofibers which aroused a gelation of the aqueous solvent. This kind of hydrogel could be used as a template for preparation of silica nanotubes. Other application potential of this hydrogel is under development.

## Acknowledgments

We thank the National Natural Science Foundation of China ( No. 20872040 and 21072067) for funding support and the Analytical and Testing Centre at Huazhong University of Science and Technology for measurement.

## Notes and references

[a] *School of Chemistry and Chemical Engineer, Huazhong University of Science and Technology, Wuhan 430074, China. Fax: +86-27-87543632; Tel: +86-27- 87543632; E-mail: zyansong@hotmail.com*

† Electronic Supplementary Information (ESI) available: Synthesis of compounds and experiment details for preparation of TEM and FE-SEM sample; $^{1}$H NMR, $^{13}$C NMR, IR, HRMS spectra of compounds **2a** – **2d**; fabrication of **2a** hydrogels. See DOI: 10.1039/b000000x/

1 P. Terech and R. G. Weiss, *Chem. Rev.*, 1997, **97**, 3133; P. Dastidar, *Chem. Soc. Rev.*, 2008, **37**, 2699; M. George and R. G. Weiss, *Acc. Chem. Res.*, 2006, **39**, 489; D. J. Abdallah and R. G. Weiss, *Adv. Mater.*, 2000, **12**, 1237.

2 P. Mukhopadhyay, Y. Iwashita, M. Shirakawa, S.-i. Kawano, N. Fujita and S. Shinkai, *Angew. Chem. Int. Ed.*, 2006, **45**, 1592.

3 F. Rodriguez-Llansola, J. F. Miravet and B. Escuder, *Chem. Commun.*, 2009, **45**, 7303.

4 A. R. Hirst, B. Escuder, J. F. Miravet and D. K. Smith, *Angew. Chem. Int. Ed.*, 2008, **47**, 8002.

5 J. J. Panda, A. Mishra, A. Basu and V. S. Chauhan, *Biomacromolecules*, 2008, **9**, 2244.

6 R. M. Capito, H. S. Azevedo, Y. S. Velichko, A. Mata and S. I. Stupp, *Science*, 2008, **319**, 1812.

7 S. Banerjee, R. K. Das and U. Maitra, *J. Mater. Chem.*, 2009, **19**, 6649.

8 Q. Wei and S. L. James, *Chem. Commun.*, 2005, **41**, 1555.

9 Y. Ono, K. Nakashima, M. Sano, Y. Kanekiyo, K. Inoue, S. Shinkai and J. Hojo, *Chem. Commun.*, 1998, **34**, 1477.

10 E. Noh, S. Park, S. Kang, J. Y. Lee and J. H. Jung, *Chem. Eur. J.*, 2013, **19**, 2620; Z. Qi, C. Wu, P. Malo de Molina, H. Sun, A. Schulz, C. Griesinger, M. Gradzielski, R. Haag, M. B. Ansorge-Schumacher and C. A. Schalley, *Chem. Eur. J.*, 2013, **19**, 10150.

11 W. Deng and D. H. Thompson, *Soft Matter*, 2010, **6**, 1884; L. Tan, Y. Liu, W. Ha, L.-S. Ding, S.-L. Peng, S. Zhang and B.-J. Li, *Soft Matter*, 2012, **8**, 5746.

12 B. Verdejo, F. Rodriguez-Llansola, B. Escuder, J. F. Miravet and P. Ballester, *Chem. Commun.*, 2011, **47**, 2017.

13 A. Wei, *Chem. Commun.*, 2006, **42**, 1581.

14 H. Huang, D.-M. Li, W. Wang, Y.-C. Chen, K. Khan, S. Song and Y.-S. Zheng, *Org. Biomol. Chem.*, 2012, **10**, 729.

15 M. Strobel, K. Kita-Tokarczyk, A. Taubert, C. Vebert, P. A. Heiney, M. Chami and W. Meier, *Adv. Funct. Mater.*, 2006, **16**, 252.

16 J. J. Rebek, *Chem. Commun.*, 2000, **36**, 637.

17 A. Arduini, R. Bussolati, A. Credi, A. Secchi, S. Silvi, M. Semeraro and M. Venturi, *J. Am. Chem. Soc.*, 2013, **135**, 9924.

18 Q. Liang, G. Chen, B. Guan and M. Jiang, *J. Mater. Chem.*, 2011, **21**, 13262.

19 M. Aoki, K. Nakashima, H. Kawabata, S. Tsutsui and S. Shinkai, *Journal of the Chemical Society, Perkin Transactions 2*, 1993, 347.

20 B. Xing, M.-F. Choi and B. Xu, *Chem. Commun.*, 2002, **38**, 362; B. Xing, M.-F. Choi, Z. Zhou and B. Xu, *Langmuir*, 2002, **18**, 9654.

21 J.-L. Zhou, X.-J. Chen and Y.-S. Zheng, *Chem. Commun.*, 2007, **43**, 5200.

22 Y.-S. Zheng, S.-Y. Ran, Y.-J. Hu and X.-X. Liu, *Chem. Commun.*, 2009, **45**, 1121.

23 X. Cai, K. Liu, J. Yan, H. Zhang, X. Hou, Z. Liu and Y. Fang, *Soft Matter*, 2012, **8**, 3756; D. Hwang, E. Lee, J. H. Jung, S. S. Lee and K.-M. Park, *Cryst. Growth Des.*, 2013, **13**, 4177; C.-C. Tsai, K.-C. Chang, I. T. Ho, J.-H. Chu, Y.-T. Cheng, L.-C. Shen and W.-S. Chung, *Chem. Commun.*, 2013, **49**, 3037; X. Cai, Y. Wu, L. Wang, N. Yan, J. Liu, X. Fang and Y. Fang, *Soft Matter*, 2013, **9**, 5807; C.-C. Tsai, Y.-T. Cheng, L.-C. Shen, K.-C. Chang, I. T. Ho, J.-H. Chu and W.-S. Chung, *Org. Lett.*, 2013, **15**, 5830.

24 T. Becker, C. Yong Goh, F. Jones, M. J. McIldowie, M. Mocerino and M. I. Ogden, *Chem. Commun.*, 2008, **44**, 3900; C. Y. Goh, T. Becker, D. H. Brown, B. W. Skelton, F. Jones, M. Mocerino and M. I. Ogden, *Chem. Commun.*, 2011, **47**, 6057; J. Zhang, D.-S. Guo, L.-H. Wang, Z. Wang and Y. Liu, *Soft Matter*, 2011, **7**, 1756.

25 F. Sansone, E. Chierici, A. Casnati and R. Ungaro, *Org. Biomol. Chem.*, 2003, **1**, 1802; Z. Li, J. Ma, J. Chen, Y. Pan, J. Qiang and L. Wang, *Chin. J. Chem.*, 2009, **27**, 2031.

26 S. Dong, Y. Luo, X. Yan, B. Zheng, X. Ding, Y. Yu, Z. Ma, Q. Zhao and F. Huang, *Angew. Chem. Int. Ed.*, 2011, **50**, 1905; S. Dong, B. Zheng, D. Xu, X. Yan, M. Zhang and F. Huang, *Adv. Mater.*, 2012, **24**, 3191; X. Yan, D. Xu, X. Chi, J. Chen, S. Dong, X. Ding, Y. Yu and F. Huang, *Adv. Mater.*, 2012, **24**, 362.

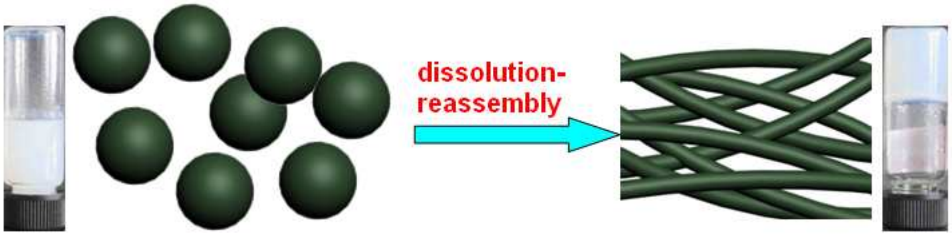
27 H. Qiu, Y. Inoue and S. Che, *Angew. Chem. Int. Ed.*, 2009, **48**, 3069.

# Table of contents entry

# Supramolecular Hydrogel Based on Amphiphilic Calix[4]arene and Its Application in the Synthesis of Silica Nanotubes

**Song Song,**[a] **Jin-Hua Wang,**[a] **Hai-Tao Feng,**[a] **Zhi-Hua Zhu**[a] **and Yan-Song Zheng***[a]

[a] School of Chemistry and Chemical Engineer, Huazhong University of Science and Technology, Wuhan, China. E-mail: zyansong@hotmail.com



**A hydrogel could be formed by leaving a suspension of novel amphiphilic calix[4]arene in aqueous media to stand at room temperature through a dissolution-reassembly process.**