

A cationic water-soluble pillar[6]arene: synthesis, host-guest properties, and self-assembly with amphiphilic guests in water†

Cite this: *RSC Adv.*, 2013, **3**, 23953Received 29th August 2013
Accepted 11th October 2013

DOI: 10.1039/c3ra44727h

www.rsc.org/advances

Yingjie Ma, Jie Yang, Jinying Li, Xiaodong Chi and Min Xue*

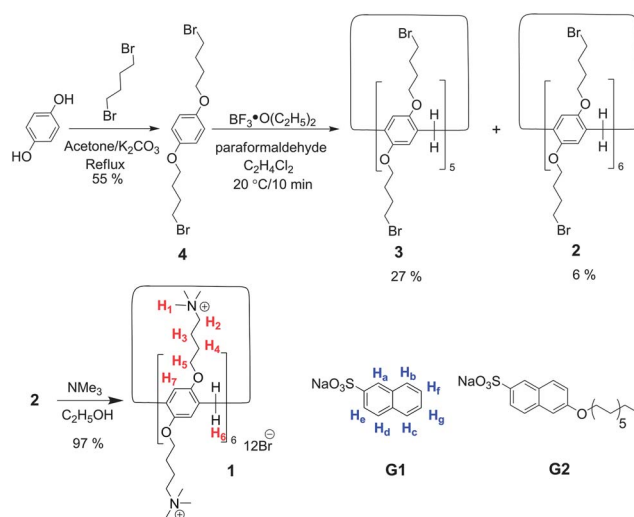
The facile and efficient preparation of a cationic water-soluble pillar[6]arene was achieved, which shows a high affinity for sodium 2-naphthalenesulfonate and could encapsulate an amphiphilic guest containing the 2-naphthalenesulfonate unit as the hydrophilic part to change the aggregation of the amphiphilic guests in water, giving regular and uniform micelles.

The development of supramolecular chemistry leads to synthesis of new host compounds for a manifold of substrates,¹ such as crown ethers, cyclodextrins, cucurbiturils, calixarenes and pillararenes. Pillararenes,^{2–6} as a new kind of macrocyclic host, display a lot of fascinating properties in the preparation of supramolecular polymers,^{3d} vesicles,³ⁱ artificial transmembrane channels,^{4b} nano tubes,³ⁱ and other interesting supramolecular systems. However, most of the work about pillararenes were studied in organic solvents, but less in aqueous media, especially about pillar[6]arenes. Pillar[6]arenes consist of six arene rings covalently linked at the *para*-positions to give a well-formed cavity,^{3b,r} which would make them have both a high affinity and a high selectivity for the binding of guests in water. Until now, only few examples of water-soluble pillar[6]arenes has been reported by Prof. Huang^{3u} and Prof. Li.⁵ By introducing carboxylate anionic groups on both rims of pillar[6]arenes, Huang *et al.* synthesized the water-soluble pillar[6]arenes for the first time, which could be used in the pH-controlled reversible dispersion of multiwalled carbon nanotubes in water and reducing the toxicity of paraquat efficiently.

Hence, in order to gain insight into the host-guest properties of pillar[6]arenes in aqueous solution, we report the synthesis of a cationic water-soluble pillar[6]arene (**1**, Scheme 1) and a novel molecular recognition between **1** and 2-naphthalenesulfonate

(**G1**, Scheme 1) in water, mainly driven by hydrophobic, π - π stacking interactions and electrostatic interactions. Furthermore, we utilized this new recognition motif in self-assembly between **1** and an amphiphilic guest (**G2**, Scheme 1) bearing a hydrophilic 2-naphthalenesulfonate unit. **G2** itself could form micelles in aqueous solution by self-assembly. However, the host-guest system of **1** and **G2** could form larger, regular and uniform micelles in water.

In our previous work,^{3b} we reported a method of synthesis of pillar[5]arene decabromide. By a modified method, not only pillar[5]arene decabromide (**3**) but also pillar[6]arene dodecaboride (**2**) could be prepared (Scheme 1). The preparation concerned the reaction of **4** and paraformaldehyde in 1,2-dichloroethane in the presence of boron trifluoride diethyl etherate. After stirring at 20 °C for 10 min, the reaction was quenched with saturated NaHCO₃ aqueous solution and worked up as usual to give a solid residue. After column chromatography, **2** and **3** were obtained in 27% and 6%,

Scheme 1 Synthesis of a water-soluble pillar[6]arene (WP6, **1**).

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China. E-mail: xuemin@zju.edu.cn; Fax: +86-571-8795-3189

† Electronic supplementary information (ESI) available: Characterization data of new compounds; determination of the association constants (K_a) for complex **1**⊃**G1**. See DOI: 10.1039/c3ra44727h

respectively. **3** was a white solid, while **2** was a colorless oil. It was found that the reaction time and temperature were the key factors for the formation of pillar[6]arene. And 20 °C and 10 min were the best condition for the formation of pillar[6]arenes. Higher temperature and longer reaction time could only lead to **3**, but not **2**. Owing to the reversibility of the Friedel–Crafts alkylation reaction,⁶ this is a thermodynamic controlled reaction, thus allowing **3** to be obtained in high yields. Bearing twelve alkyl bromide terminal groups makes **2** be easily functionalized to generate derivatives of pillar[6]arene. Treatment of **2** with excess trimethylamine in ethanol gave compound **1** containing twelve trimethylammonium groups at upper and lower rims (97% yield). **1** has a very good solubility in water to give a colorless solution.

Compound **1** possesses both a hydrophobic cavity and twelve charged substituents, thus providing a very efficient recognition motif for guests with multiple functional groups such as 2-naphthalenesulfonate **G1**. A detailed study of the inclusion property of **1** with the anionic guests revealed that compound **1** displayed high affinities for **G1** in water. As shown in Fig. 1, the 1 : 1 mixture of **1** and **G1** in D₂O had significant chemical shift changes in the ¹H NMR signals compared with the free host and free guest under the same condition. And only one set of peaks was found for the solution of **1** and **G1**, indicating fast-exchange complexation on the ¹H NMR time scale. The protons (H_a–H_g) on **G1** moved upfield sharply, indicating the formation of host–guest complex. Binding of **G1** made the shielding effect on H₃ of **1** a little diminished, causing the signals of H₃ to move downfield, while leaving the other peaks (H₁, H₂, H₄–H₇) of **1** unchanged. The 2D NOESY NMR spectrum of an equimolar mixture of **1** and **G1** (Fig. 2) showed correlations between phenyl protons H₇ of **1** and all the protons (H_a–H_f) of **G1**. Besides, there were correlations between protons H₃/H₄ or H₆/H₅ of **1** and all the protons of **G1**, respectively. These phenomena suggested that **G1** was fully encapsulated by **1** to form a [2]pseudorotaxane with the hydrophobic naphthalene group located at the deep cavity of **1** and the sulfonic acid group positioned at the

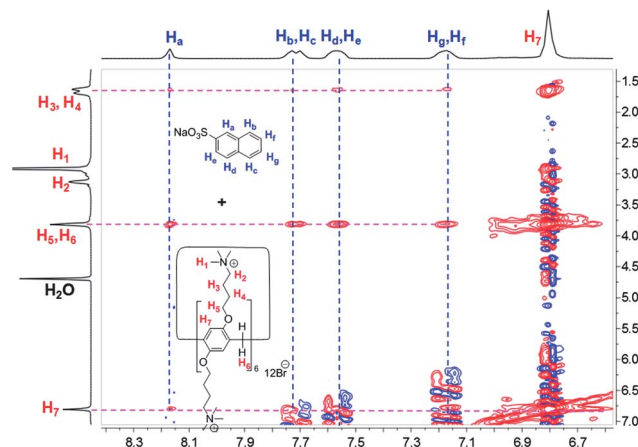


Fig. 2 2D NOESY NMR spectrum (400 MHz, D₂O, 298 K, mixing time = 1.0 s) of 4.00 mM **1** and **G1**.

entrance of the cavity. The formation of the complex might be mainly driven by electrostatic interactions between the anionic sulfonate moieties and the cationic ammonium groups of the host, π – π stacking interactions between the benzene rings on the pillar[6]arene host and the naphthalene group on **G1**, and the hydrophobic interactions between the benzene ring of **G1** and the hydrophobic cavity of **1** in aqueous solution.^{3h,6c}

For the estimation of the association constant for the complexation between **1** and **G1**, fluorescence titrations of **1** with **G1** were carried out with the concentration of **G1** kept constant at 1.00×10^{-4} M and that of **1** varied from 0 to 1.77×10^{-4} M at room temperature. Addition of **1** to a solution of **G1** in water resulted in a substantial decrease in the intensity of the emission band at 339 nm (Fig. S13[†]), because of the formation of host–guest complex. And it was found that the stoichiometry of the complex was 1 : 1 (Fig. S13[†]). By using the Stern–Volmer equation, the association constant (K_a) of **1** with **G1** was calculated to be $(2.45 \pm 0.20) \times 10^4$ M⁻¹. In our previous work, we reported the complexation of the sodium 1-octanesulfonate guest by a cationic water-soluble pillar[5]arene bearing trimethylammonium groups, the K_a value of which is $(1.33 \pm 0.94) \times 10^4$ M⁻¹.^{3h} This K_a value is close to that of **1**⊃**G1**.

After the establishment of the new host–guest recognition motif in aqueous solution, we further applied it to construct a supra-amphiphile and utilized it in self-assembly. **G2** itself is an amphiphilic molecule which contains a long alkyl chain as

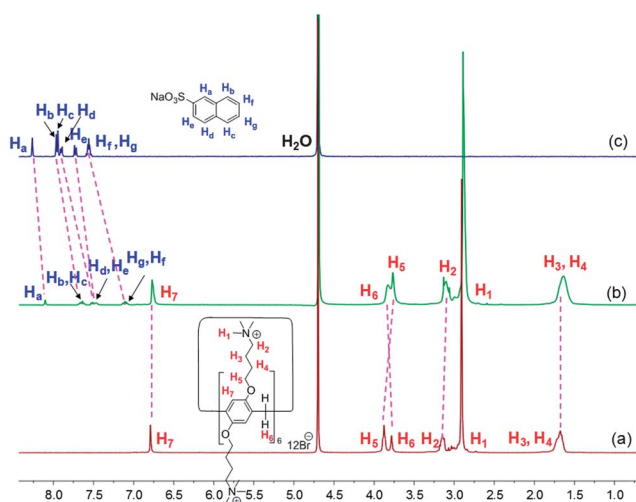


Fig. 1 ¹H NMR spectra (D₂O, 293 K, 400 MHz) of (a) 4.00 mM **G1**; (b) 4.00 mM **1** + 4.00 mM **G1**; (c) 4.00 mM **1**.

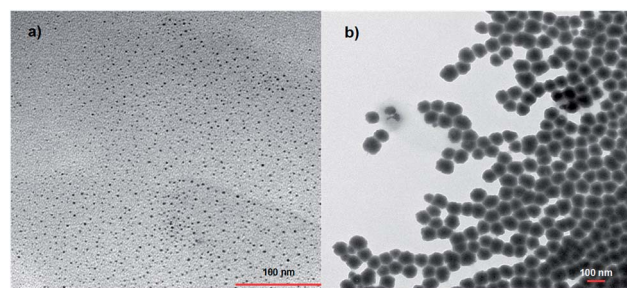


Fig. 3 TEM images of (a) **G2** aggregates, and (b) **1**⊃**G2**.

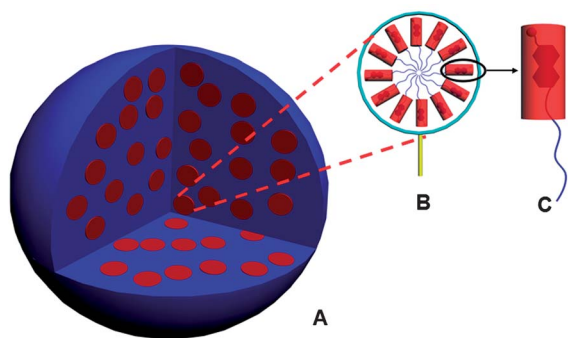


Fig. 4 Cartoon representation of the structure of large multimolecular micelles formed by **1** and **G2** in water.

hydrophobic part and naphthalenesulfonate unit as hydrophilic part. In order to investigate the self-assembled aggregates in water, an aqueous solution of **G2** was prepared with a concentration of 1.00×10^{-4} M. According to transmission electron microscopy (TEM), small spherical micelles were observed with a diameter of ~ 2 nm (Fig. 3a). These micelles had a regular spherical morphology. Interestingly, upon addition of 1 equiv. of **1**, regular micelles with a diameter of ~ 100 nm were observed, drastically different from the smaller micelles formed by **G2** alone. How can molecules of **1** and **G2** self-assemble into the large micelles around 100 nm? The self-assembly process might be that **1** bonds **G2** to form a host-guest complex which is considered as a new amphiphilic molecule (Fig. 4C) and self-assembles into small micelles in water (Fig. 4B); the small micelles further aggregate together to form large multi-molecular micelles (Fig. 3b and 4A). That is to say, the large micelles are a type of multimicelle aggregates with the basic building units (Fig. 4B).⁷

Conclusions

In conclusion, we have reported the synthesis and full characterization of a pillar[6]arene dodecabromide, which could serve as a good precursor for functionalized pillar[6]arene derivatives. The precursor was obtained starting from easily accessible compounds by a modified method reported by us previously. By introduction of trimethylammonium groups at both upper and lower rims of the pillar[6]arene dodecabromide, a new cationic water-soluble pillar[6]arene was synthesized, which showed a high affinity to 2-naphthalenesulfonate in water. They could form a stable 1 : 1 [2]pseudorotaxane in aqueous solution, driven by electrostatic interactions, hydrophobic interactions, and π - π stacking interactions. This novel recognition motif was further used to control the aggregation of an amphiphilic derivative of 2-naphthalenesulfonate (**G2**) in water. In contrast to the small sphere micelles formed by amphiphilic molecule **G2**, the host-guest complex **1**⊃**G2** self-assembled into much larger regular sphere micelles in water. This new recognition motif based on the cationic water-soluble pillar[6]arene should be helpful for the investigation of the application of pillararenes.

Notes and references

- (a) F. Huang, F. R. Fronczek and H. W. Gibson, *J. Am. Chem. Soc.*, 2003, **125**, 9272–9273; (b) F. Huang, H. W. Gibson, W. S. Bryant, D. S. Nagvekar and F. R. Fronczek, *J. Am. Chem. Soc.*, 2003, **125**, 9367–9371; (c) F. Huang, J. W. Jones, C. Slebodnick and H. W. Gibson, *J. Am. Chem. Soc.*, 2003, **125**, 14458–14464; (d) F. Huang and H. W. Gibson, *J. Am. Chem. Soc.*, 2004, **126**, 14738–14739; (e) F. Huang, K. A. Switek, L. N. Zakharov, F. R. Fronczek, C. Slebodnick, M. Lam, J. A. Golen, W. S. Bryant, P. E. Mason, A. L. Rheingold, M. Ashraf-Khorassani and H. W. Gibson, *J. Org. Chem.*, 2005, **70**, 3231–3241; (f) X.-Z. Zhu and C.-F. Chen, *J. Am. Chem. Soc.*, 2005, **127**, 13158–13159; (g) Y. Yang, H.-Y. Hua and C.-F. Chen, *Tetrahedron Lett.*, 2007, **48**, 3505–3509; (h) C. Zhang, S. Li, J. Zhang, K. Zhu, N. Li and F. Huang, *Org. Lett.*, 2007, **9**, 5553–5556; (i) D. J. Hoffart, J. Tiburcio, A. Torre, L. K. dela Knight and S. J. Loeb, *Angew. Chem., Int. Ed.*, 2008, **47**, 97–101; (j) F. Wang, C. Han, C. He, Q. Zhou, J. Zhang, C. Wang, N. Li and F. Huang, *J. Am. Chem. Soc.*, 2008, **130**, 11254–11255; (k) L. M. Klivansky, G. Koshkakarayan, D. Cap and Y. Liu, *Angew. Chem., Int. Ed.*, 2009, **48**, 4185–4189; (l) W. Jiang and C. A. Schalley, *Proc. Natl. Acad. Sci. U. S. A.*, 2009, **106**, 10425–10429; (m) Z. Ge, J. Hu, F. Huang and S. Liu, *Angew. Chem., Int. Ed.*, 2009, **48**, 1798–1802; (n) F. Wang, J. Zhang, X. Ding, S. Dong, M. Liu, B. Zheng, S. Li, K. Zhu, L. Wu, Y. Yu, H. W. Gibson and F. Huang, *Angew. Chem., Int. Ed.*, 2010, **49**, 1090–1094; (o) S. Li, J. Chen, B. Zheng, S. Dong, Z. Ma, H. W. Gibson and F. Huang, *J. Polym. Sci., Part A: Polym. Chem.*, 2010, **48**, 4067–4073; (p) 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**, 1905–1909; (q) Z. Niu, C. Slebodnick, K. Bonrad, F. Huang and H. W. Gibson, *Org. Lett.*, 2011, **13**, 5411; (r) Z. Niu, C. Slebodnick and H. W. Gibson, *Org. Lett.*, 2011, **13**, 5410; (s) Y. Liu, Z. Wang and X. Zhang, *Chem. Soc. Rev.*, 2012, **41**, 5922–5932; (t) D.-S. Guo and Y. Liu, *Chem. Soc. Rev.*, 2012, **41**, 5907–5921; (u) L. Chen, Y.-K. Tian, Y. Ding, Y.-J. Tian and F. Wang, *Macromolecules*, 2012, **45**, 8412–8419; (v) B. Zheng, F. Wang, S. Dong and F. Huang, *Chem. Soc. Rev.*, 2012, **41**, 1621–1636; (w) X. Yan, F. Wang, B. Zheng and F. Huang, *Chem. Soc. Rev.*, 2012, **41**, 6042–6065; (x) D.-S. Guo, K. Wang, Y.-X. Wang and Y. Liu, *J. Am. Chem. Soc.*, 2012, **134**, 10244–10250; (y) Y.-K. Tian, L. Chen, Y.-J. Tian, X.-Y. Wang and F. Wang, *Polym. Chem.*, 2013, **4**, 453–457.
- (a) T. Ogoshi, S. Kanai, S. Fujinami, T. A. Yamagishi and Y. Nakamoto, *J. Am. Chem. Soc.*, 2008, **130**, 5022–5023; (b) T. Ogoshi, M. Hashizume, T. Yamagishi and Y. Nakamoto, *Chem. Commun.*, 2010, **46**, 3708–3710.
- (a) Z. Zhang, B. Xia, C. Han, Y. Yu and F. Huang, *Org. Lett.*, 2010, **12**, 3285–3287; (b) C. Han, F. Ma, Z. Zhang, B. Xia, Y. Yu and F. Huang, *Org. Lett.*, 2010, **12**, 4360–4363; (c) Z. Zhang, Y. Luo, B. Xia, C. Han, Y. Yu, X. Chen and F. Huang, *Chem. Commun.*, 2011, **47**, 2417–2419; (d) Z. Zhang, Y. Luo, J. Chen, S. Dong, Y. Yu, Z. Ma and

- F. Huang, *Angew. Chem., Int. Ed.*, 2011, **50**, 1397–1401; (e) Z. Zhang, G. Yu, C. Han, J. Liu, X. Ding, Y. Yu and F. Huang, *Org. Lett.*, 2011, **13**, 4818–4821; (f) Y. Ma, Z. Zhang, X. Ji, C. Han, J. He, Z. Abliz, W. Chen and F. Huang, *Eur. J. Org. Chem.*, 2011, 5331–5335; (g) B. Xia, J. He, Z. Abliz, Y. Yu and F. Huang, *Tetrahedron Lett.*, 2011, **52**, 4433–4436; (h) Y. Ma, X. Ji, F. Xiang, X. Chi, C. Han, J. He, Z. Abliz, W. Chen and F. Huang, *Chem. Commun.*, 2011, **47**, 12340–12342; (i) Y. Yao, M. Xue, J. Chen, M. Zhang and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 15712–15715; (j) G. Yu, M. Xue, Z. Zhang, J. Li, C. Han and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 13248–13251; (k) M. Xue, Y. Yang, X. Chi, Z. Zhang and F. Huang, *Acc. Chem. Res.*, 2012, **45**, 1294–1308; (l) C. Han, G. Yu, B. Zheng and F. Huang, *Org. Lett.*, 2012, **14**, 1712–1715; (m) Y. Yao, M. Xue, X. Chi, Y. Ma, J. He, Z. Abliz and F. Huang, *Chem. Commun.*, 2012, **48**, 6505–6507; (n) G. Yu, Z. Zhang, C. Han, M. Xue, Q. Zhou and F. Huang, *Chem. Commun.*, 2012, **48**, 2958–2960; (o) Z. Zhang, C. Han, G. Yu and F. Huang, *Chem. Sci.*, 2012, **3**, 3026–3031; (p) C. Han, G. Yu, B. Zheng and F. Huang, *Org. Lett.*, 2012, **14**, 1712–1715; (q) S. Dong, C. Han, B. Zheng, M. Zhang and F. Huang, *Tetrahedron Lett.*, 2012, **53**, 3668–3671; (r) Y. Ma, X. Chi, X. Yan, J. Liu, Y. Yao, W. Chen, F. Huang and J.-L. Hou, *Org. Lett.*, 2012, **14**, 1532–1535; (s) C. Han, Z. Zhang, G. Yu and F. Huang, *Chem. Commun.*, 2012, **48**, 9876–9878; (t) G. Yu, Z. Zhang, J. He, Z. Abliz and F. Huang, *Eur. J. Org. Chem.*, 2012, 5902–5907; (u) G. Yu, C. Han, Z. Zhang, J. Chen, X. Yan, B. Zheng, S. Liu and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 8711–8717; (v) C. Han, Z. Zhang, X. Chi, M. Zhang, G. Yu and F. Huang, *Acta Chim. Sin.*, 2012, **70**, 1775–1778; (w) P. Wei, X. Yan, J. Li, Y. Ma, Y. Yao and F. Huang, *Tetrahedron*, 2012, **68**, 9179–9185; (x) G. Yu, X. Zhou, Z. Zhang, C. Han, Z. Mao, C. Gao and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 19489–19497; (y) P. Wei, X. Yan, J. Li, Y. Ma and F. Huang, *Chem. Commun.*, 2013, **49**, 1070–1072; (z) L. Gao, C. Han, B. Zheng, S. Dong and F. Huang, *Chem. Commun.*, 2013, **49**, 472–474.
- 4 (a) X.-B. Hu, L. Chen, W. Si, Y. Yu and J.-L. Hou, *Chem. Commun.*, 2011, **47**, 4694–4696; (b) W. Si, L. Chen, X.-B. Hu, G. Tang, Z. Chen, J.-L. Hou and Z.-T. Li, *Angew. Chem., Int. Ed.*, 2011, **50**, 12564–12568; (c) C. Li, X. Shu, J. Li, S. Chen, K. Han, M. Xu, B. Hu, Y. Yu and X. Jia, *J. Org. Chem.*, 2011, **76**, 8458–8465; (d) C. Li, K. Han, J. Li, H. Zhang, J. Ma, X. Shu, Z. Chen, L. Weng and X. Jia, *Org. Lett.*, 2011, **14**, 42–45; (e) C. Li, S. Chen, J. Li, K. Han, M. Xu, B. Hu, Y. Yu and X. Jia, *Chem. Commun.*, 2011, **47**, 11294–11296; (f) H. Tao, D. Cao, L. Liu, Y. Kou, L. Wang and H. Meier, *Sci. China, Ser. B: Chem.*, 2012, **55**, 223–228; (g) N. L. Strutt, H. Zhang, M. A. Giesener, J. Lei and J. F. Stoddart, *Chem. Commun.*, 2012, **48**, 1647–1649; (h) P. J. Cragg and K. Sharma, *Chem. Soc. Rev.*, 2012, **41**, 597–607; (i) Q. Duan, W. Xia, X. Hu, M. Ni, J. Jiang, C. Lin, Y. Pan and L. Wang, *Chem. Commun.*, 2012, **48**, 8532–8534; (j) Y. Guan, M. Ni, X. Hu, T. Xiao, S. Xiong, C. Lin and L. Wang, *Chem. Commun.*, 2012, **48**, 8529–8531; (k) X.-Y. Hu, P. Zhang, X. Wu, W. Xia, T. Xiao, J. Jiang, C. Lin and L. Wang, *Polym. Chem.*, 2012, **3**, 3060–3063; (l) K. Wang, L.-L. Tan, D.-X. Chen, N. Song, G. Xi, S. X.-A. Zhang, C. Li and Y.-W. Yang, *Org. Biomol. Chem.*, 2012, **10**, 9405–9409; (m) H. Deng, X. Shu, X. Hu, J. Li, X. Jia and C. Li, *Tetrahedron Lett.*, 2012, **53**, 4609–4612; (n) X.-Y. Hu, X. Wu, Q. Duan, T. Xiao, C. Lin and L. Wang, *Org. Lett.*, 2012, **14**, 4826–4829; (o) H. Zhang, X. Ma, J. Guo, K. T. Nguyen, Q. Zhang, X.-J. Wang, H. Yan, L. Zhu and Y. Zhao, *RSC Adv.*, 2013, **3**, 368–371; (p) B. Xia, B. Zheng, C. Han, S. Dong, M. Zhang, B. Hu, Y. Yu and F. Huang, *Polym. Chem.*, 2013, **4**, 2019–2024; (q) G. Yu, Y. Ma, C. Han, Y. Yao, G. Tang, Z. Mao, C. Gao and F. Huang, *J. Am. Chem. Soc.*, 2013, **135**, 10310–10313; (r) X. Yan, S. Li, T. R. Cook, X. Ji, Y. Yao, J. B. Pollock, Y. Shi, G. Yu, J. Li, F. Huang and P. J. Stang, *J. Am. Chem. Soc.*, 2013, **135**, 14036–14039; (s) Q. Duan, Y. Cao, Y. Li, X. Hu, T. Xiao, C. Lin, Y. Pan and L. Wang, *J. Am. Chem. Soc.*, 2013, **135**, 14036–14039; (t) Y. Yao, M. Xue, Z. Zhang, M. Zhang, Y. Wang and F. Huang, *Chem. Sci.*, 2013, **4**, 3667–3672.
- 5 During the preparation of this manuscript, a similar synthetic approach was reported for the synthesis of pillar[6]arenes decabromide, see: W. Chen, Y. Zhang, J. Li, X. Lou, Y. Yu, X. Jia and C. Li, *Chem. Commun.*, 2013, **49**, 7956–7958.
- 6 (a) M. Holler, N. Allenbach, J. Sonet and J. F. Nierengarten, *Chem. Commun.*, 2012, **48**, 2576–2578; (b) X. Hu, Z. Chen, L. Chen, L. Zhang, J.-L. Hou and Z.-T. Li, *Chem. Commun.*, 2012, **48**, 10999–11001; (c) Y. Ma, M. Xue, Z. Zhang, X. Chi and F. Huang, *Tetrahedron*, 2013, **69**, 4532–4535; (d) L. Gao, B. Zheng, Y. Yao and F. Huang, *Soft Matter*, 2013, **9**, 7314–7319; (e) M. Pang and M. Xue, *Eur. J. Org. Chem.*, 2013, 4787–4793.
- 7 (a) H. Hong, Y. Mai, Y. Zhou, D. Yan and J. Cui, *Macromol. Rapid Commun.*, 2007, **28**, 591–596; (b) M. R. Radowski, A. Shukla, H. von Berlepsch, C. Böttcher, G. Pickaert, H. Rehage and R. Haag, *Angew. Chem., Int. Ed.*, 2007, **46**, 1265–1269.