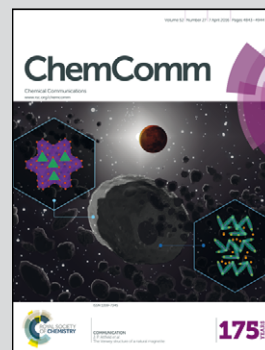


Showcasing research from Yun Yan's laboratory, Peking University, Beijing, China.

Allostery in molecular self-assemblies: metal ions triggered self-assembly and emissions of terthiophene

Binding of metal ions to the head of a coordinating amphiphile substantially changes the emission color of the terthiophene group attached to the chain end *via* a conformation triggered change of self assembly, in high analogy of the allostery of proteins in which binding a ligand to one site may affect its performance at another site through conformational change.

As featured in:



See Jianbin Huang, Yun Yan et al., *Chem. Commun.*, 2016, 52, 4876.



Cite this: *Chem. Commun.*, 2016, 52, 4876

Received 18th January 2016,  
Accepted 5th February 2016

DOI: 10.1039/c6cc00492j

www.rsc.org/chemcomm

## Allostery in molecular self-assemblies: metal ions triggered self-assembly and emissions of terthiophene†

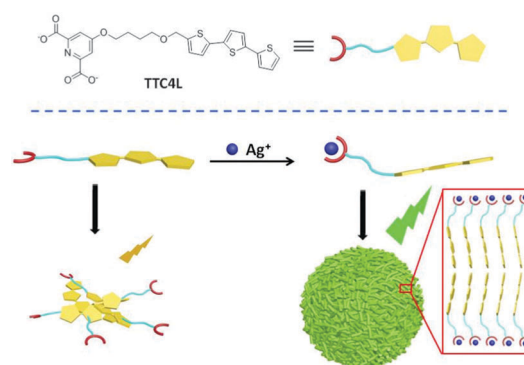
Shuai Liu,<sup>a</sup> Li Zhao,<sup>b</sup> Yunlong Xiao,<sup>a</sup> Tian Huang,<sup>a</sup> Jie Li,<sup>a</sup> Jianbin Huang<sup>\*a</sup> and Yun Yan<sup>\*a</sup>

**Binding of metal ions to the head of a coordinating amphiphile TTC4L substantially changes the emission color of the terthiophene group attached to the chain end via a conformation triggered self-assembly. This is in analogy with the allostery of proteins in which binding a ligand to one site may affect its performance at another site through conformational change.**

Allostery is a well-known phenomenon in biology.<sup>1–3</sup> Generally speaking, binding a ligand at one site of a protein modifies the performance at a distant site through conformational or dynamic changes.<sup>4–6</sup> Similar allostery was also found in DNA in recent years, where the deformation of a double-helical structure is the origin of DNA allostery.<sup>7–9</sup> Since DNA is a supramolecular self-assembly of many base-pairs, it suggests that allostery may have a general effect on molecular self-assemblies. Although extensive studies have been done on various aspects of self-assemblies,<sup>10–14</sup> less is known about their allostery, which is normally considered to be a mere biological phenomenon. Although it is well-known that the metal ions may trigger the change of the conformation of ligands, it only causes an allosteric effect on the molecular level.<sup>15–18</sup> In fact, many artificial molecular systems have been verified amazingly similar to bio-systems,<sup>19–22</sup> and bio-systems have inspired a number of elegant artificial designs. For instance, Rowan *et al.* reported the mechanical responsive hydrogels may mimic the behaviors of sea cucumber,<sup>23</sup> Yan *et al.* fabricated a breathing vesicle with fluorescence on-off just like jellyfish,<sup>24</sup> or even the growth of inorganic materials can be made in great analogy with the growth of plants.<sup>25</sup> In contrast, allostery has not been reported for molecular self-assemblies, namely, studies about molecular conformation triggered change in self-assembled structures and their properties have not been recognized. This is to a large extent due to the lack

of proper molecules which display conformation-dependent self-assembled structures.

Herein we report upon the employment of an amphiphile that exhibits distinct conformational related fluorescence, allostery in a molecular self-assembly can be achieved. This design employs the unique intermolecular distance dependent fluorescence of the terthiophene group. Blue, green and violet emissions may occur one by one with the intermolecular distance being 3–4 Å,<sup>26,27</sup> 4–7 Å,<sup>28,29</sup> and larger than 7 Å,<sup>30</sup> respectively. In this study, the hydrophobic terthiophene group was tethered to a hydrophilic coordinating head by a butyl group to form an amphiphile TTC4L (Scheme 1). TTC4L alone can hardly self-assemble into any well-defined structure; however, upon binding with metal ions, they self-assemble into mesoscale structures which are highly dependent on the metal ions. Meanwhile, the emission color changes accordingly. Molecular modelling suggests that both the change of the self-assembled structure and the emission colors are closely related to the metal ion triggered conformational change of TTC4L. This is in high analogy with the conformational related property change of protein or DNA. In this way, we generate an elegant case of allostery in molecular self-assembly.



**Scheme 1** Structure of TTC4L and the schematic representation of the change of emissions of TTC4L triggered by Ag<sup>+</sup>.

<sup>a</sup> Beijing National Laboratory for Molecular Sciences, Institution College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, China. E-mail: yunyan@pku.edu.cn, jbhuan@pku.edu.cn

<sup>b</sup> School of Food and Chemical Engineering, Beijing Technology and Business University, Beijing, 100048, China

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c6cc00492j



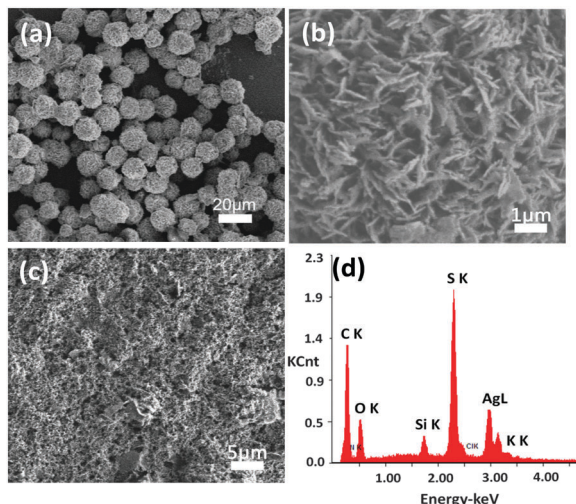


Fig. 1 SEM images of the assemblies of (a) TTC4L-Ag<sup>+</sup> and (c) TTC4L. (b) is a highly magnified image of the surface of a TTC4L-Ag<sup>+</sup> microsphere. (d) X-ray energy dispersive spectroscopy (EDS) of TTC4L-Ag<sup>+</sup> assemblies on silicon sheets. The concentrations of TTC4L and silver ions are all 0.50 mM.

TTC4L was synthesized in our lab.<sup>31</sup> The fresh solution of TTC4L in ethanol-water mixed solvent (1:1, v/v) is clear. However, upon addition of metal ions, such as Ag<sup>+</sup>, the solution immediately turns turbid, indicating the formation of large particles. SEM images in Fig. 1a shows the formation of uniform microspheres in the TTC4L-Ag<sup>+</sup> system with a nearly monodispersed size of about 10 μm. A zoomed in observation in Fig. 1b reveals that these spheres are the hierarchical self-assembled structures of nanosheets. Such highly ordered structure is in clear contrast to the amorphous structures of native TTC4L (Fig. 1c). Meanwhile, energy-dispersive spectroscopy (EDS, Fig. 1d and Table S1, ESI<sup>†</sup>) demonstrates that the molar ratio between TTC4L and Ag<sup>+</sup> is close to 1:1, suggesting that the basic units in the microspheres are the 1:1 coordinated TTC4L and Ag<sup>+</sup>.

Furthermore, CLSM observation reveals that these spheres emit bright green color (Fig. 2a), which is completely different from the dark orange color of native TTC4L (Fig. 2b). Since the emission colors of TTC4L are highly dependent on the self-assembly status of the terthiophene groups<sup>32</sup> at the chain end, the present results indicate that we may encounter an allosteric effect in this self-assembled system, which is generally recognized in protein and DNA systems.

In order to gain physical insights into this unusual allosteric effect in the TTC4L-Ag<sup>+</sup> coordinating self-assembly, fluorescence measurements were performed. Solid TTC4L on its own displays a broad emission with the strongest peak at 438 nm. (Fig. 2c, black line) The coexisting shoulder peaks at 420 nm, 450 nm, and 540 nm suggest that the molecular packing in the TTC4L system is rather ill-defined, which is in accordance with the structures observed in SEM (Fig. 1c). In contrast, in the TTC4L-Ag<sup>+</sup> system the strongest emission occurs at 470 nm which is accompanied by a shoulder peak at 502 nm (Fig. 2c, red line). These are the characteristics of terthiophene excimers,<sup>29</sup> in accordance with the green emissions observed in Fig. 1b.

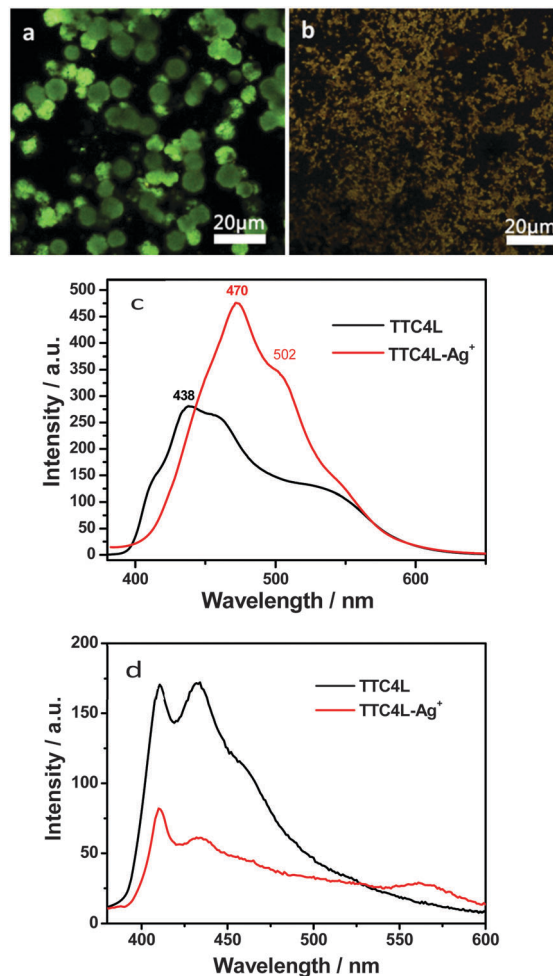
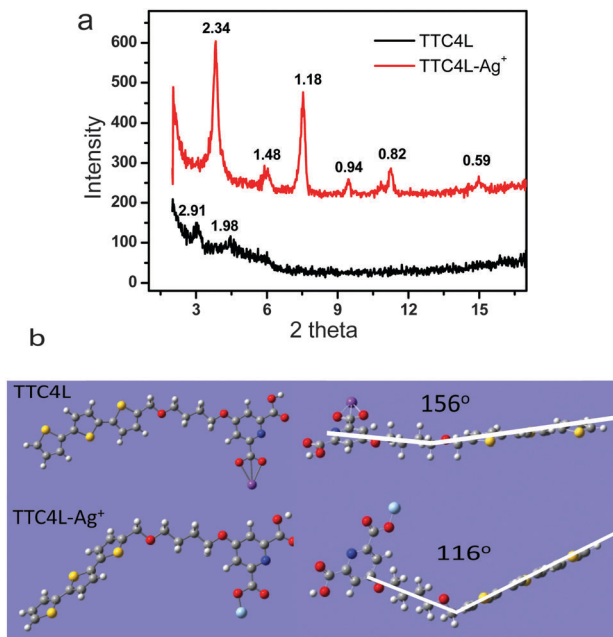


Fig. 2 Comparison of the CLSM images and fluorescence spectra for the TTC4L-Ag<sup>+</sup> assembly and for TTC4L. (a) CLSM image of TTC4L-Ag<sup>+</sup>; (b) CLSM image for TTC4L. The concentration of TTC4L and silver ions are all 0.50 mM. (c) The solid fluorescence emission spectra for the TTC4L-Ag<sup>+</sup> microsphere; (d) the emission of the molecularly dissolved TTC4L-Ag<sup>+</sup> coordinating complex in ethanol. ( $\lambda_{\text{ex}}$  = 365 nm).

To further verify that the self-assembled structures play important roles in the change of the emissions, the TTC4L-Ag<sup>+</sup> self-assembled particles were completely dissolved in ethanol. It is found that Ag<sup>+</sup> ions only slightly influence the emission of native TTC4L. The emission peaks are not shifted, except for the occurrence of a strong excimer emission (Fig. 2d, red). Obviously, the emission of the self-assemblies in Fig. 2c is drastically different from that of the dissolved TTC4L-Ag<sup>+</sup> (Fig. 2d). This means that the change of the emission colors is indeed triggered by the self-assembly of the TTC4L-Ag<sup>+</sup>.

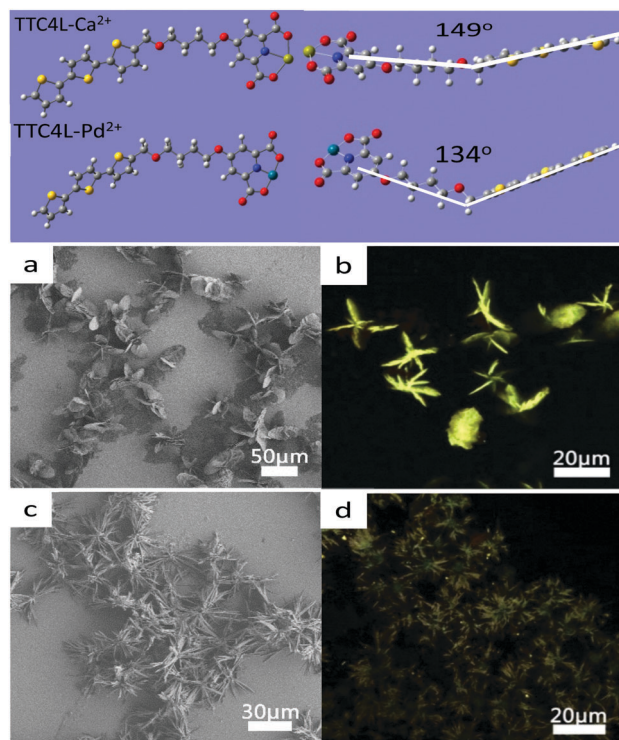
Next, XRD measurements were made to examine the molecular arrangements in the microspheres. Fig. 3a shows that different from the native TTC4L system, the TTC4L-Ag<sup>+</sup> system exhibit sharp Bragg's peaks corresponding to the distances of 2.4, 1.6, 1.2, 9.5 nm. These can be assigned as 002, 003, 004, and 005 diffractions, respectively, revealing a typical lamellar feature where the TTC4L molecules are in parallel packing.<sup>33–35</sup> This means that binding of Ag<sup>+</sup> has changed the molecular arrangement of



**Fig. 3** (a) XRD patterns for TTC4L and TTC4L-Ag<sup>+</sup> microspheres. (b1)–(b4) Molecular modelling of the conformation of TTC4L and TTC4L-Ag<sup>+</sup>. (b1) and (b2) are the front views of TTC4L (binding with 1 K, b1) and TTC4L-Ag<sup>+</sup> system (b2), (b3) and (b4) are the side views of TTC4L and TTC4L-Ag<sup>+</sup> systems, respectively.

TTC4L. The distance of 4.8 nm for the 001 diffraction (Fig. S1, ESI<sup>†</sup>) is two-fold the length of native TTC4L. Therefore, the repeating unit in the microspheres is the bilayer of TTC4L-Ag<sup>+</sup>.

In order to find the origin of the metal ion triggered bilayer arrangement of TTC4L, the restricted density function method<sup>36</sup> was employed to understand the effect of coordination on the molecular conformation of TTC4L. This method does not require assumptions but calculations of the conformation of TTC4L upon binding of Ag<sup>+</sup> to the coordinating head. Fig. 3b shows the front and the side views of the conformations. In the left column we compared the conformational difference for TTC4L alone (where 1 K is bound), and TTC4L-Ag<sup>+</sup> systems. Obviously, the plane of terthiophene twists upon addition of Ag<sup>+</sup>. This tendency can be further evidenced in the side views. In the right column we show that the twisting angle between the terthiophene plane and the butyl group for the primitive TTC4L is about 156°, whereas in the presence of Ag<sup>+</sup>, the twisting angle becomes 116°. Further calculations suggest that no specific interaction, such as  $\pi$ - $\pi$  stacking, exists between the twisted TTC4L-Ag<sup>+</sup>. This indicates that the hydrophobic interaction should be the driving force for the self-assembly of the twisted TTC4L-Ag<sup>+</sup>. Since hydrophobic interaction often drives the parallel alignment of the lipid molecules, the TTC4L-Ag<sup>+</sup> coordinating unit tends to self-assemble into bilayered structures. On the other hand, the coordination also affected the conformation of the terthiophene group. The calculated conformation suggests that Ag<sup>+</sup> triggered a planar terthiophene, which further affect their packing in the bilayers. As a result, the intermolecular distance between terthiophene groups, which is at the opposite end of TTC4L, was dramatically affected so that different emission colors occurred. This means that the Ag<sup>+</sup>



**Fig. 4** Molecular modelling of the conformation of TTC4L coordinating systems with Ca<sup>2+</sup>, Pd<sup>2+</sup>, and Cu<sup>2+</sup>. (a and c) and (b and d) are the SEM and corresponding CLSM images of the self-assembled structures in the TTC4L-Ca<sup>2+</sup> and TTC4L-Pd<sup>2+</sup> systems, respectively.

triggered a self-assembled structure and the corresponding distinct fluorescence is indeed an allosteric effect.

Most strikingly, we found that each different conformation of TTC4L triggered by specific metal ions could lead to a distinct self-assembled structure (Fig. 4 and Fig. S2 and S3, ESI<sup>†</sup>) with the corresponding emission colors. For instance, TTC4L-Ca<sup>2+</sup> self-assemble into microflowers (Fig. 4a) with yellow emission (Fig. 4b), and TTC4L-Pd<sup>2+</sup> star anises (Fig. 4c) with yellow-green emission (Fig. 4d). Compared with previous studies that modify the intermolecular distance between TTC4L by inserting surfactant molecules between them,<sup>31</sup> the prominent feature of this allosteric effect lies in the change of molecular conformation of TTC4L, which is the origin of different molecular packing, different self-assembled structures, and different emission colors.

In summary, we demonstrated a case of allostery in a molecular self-assembly using a coordinating amphiphile TTC4L that contains a terthiophene group at the chain end. It was found that binding of Ag<sup>+</sup> at the coordinating head resulted in distinct twisting of the terthiophene group at the chain end, which further affected the arrangement and intermolecular distances between the terthiophene groups, and finally led to a different fluorescence. A similar effect can be triggered by other metal ions, such as Ca<sup>2+</sup>, Pd<sup>2+</sup> etc., demonstrating that each specific metal ion can trigger distinct self-assembled structures and emission colors. This is in great analogy with protein allostery in which binding a ligand at one site will affect the performance at a distant site. Therefore, this work demonstrated an elegant case of allosteric self-assembly.

We envisage that bio-inspired allosteric self-assembly may act as a new strategy to control the self-assembled structures and their functions, which will open a new vista in the field of nanoscience, self-assembly and related materials science.

This work was supported by the National Natural Science Foundation of China (21422302, 21273013, 21573011), the National Basic Research Program of China (973 Program, 2013CB933800) and the Research Fund for the Doctoral Program of Higher Education of China.

## Notes and references

- 1 B. M. Forman, K. Umeson, J. Chen and R. M. Evans, *Cell*, 1995, **81**, 541–550.
- 2 T. Xiao, J. Takagi, B. S. Coller, J.-H. Wang and T. A. Springer, *Nature*, 2004, **432**, 59–67.
- 3 K. Gunasekaran, B. Ma and R. Nussinov, *Proteins*, 2004, **57**, 433–443.
- 4 D. Strickland, K. Moffat and T. R. Sosnick, *Proc. Natl. Acad. Sci. U. S. A.*, 2008, **105**, 10709–10714.
- 5 P. Ojeda-May, Y. Li, V. Ovchinnikov and K. Nam, *J. Am. Chem. Soc.*, 2015, **137**, 12454–12457.
- 6 R. Nussinov and C.-J. Tsai, *Curr. Opin. Struct. Biol.*, 2015, **30**, 17–24.
- 7 E. M. Jacobson, P. Li, A. LeondelRio, M. G. Rosenfeld and A. K. Aggarwal, *Genes Dev.*, 1997, **11**, 198–212.
- 8 S. Kim, E. Brostromer, D. Xing, J. S. Jin, S. S. Chong, H. Ge, S. Y. Wang, C. Gu, L. J. Yang, Y. Q. Gao, X. D. Su, Y. J. Sun and X. S. Xie, *Science*, 2013, **339**, 816–819.
- 9 A. Porchetta, A. Idili, A. Vallee-Belisle and F. Ricci, *Nano Lett.*, 2015, **15**, 4467–4471.
- 10 J. K. Klosterman, Y. Yamauchi and M. Fujita, *Chem. Soc. Rev.*, 2009, **38**, 1714–1725.
- 11 G. M. Whitesides and B. Grzybowski, *Science*, 2002, **295**, 2418–2421.
- 12 C. F. J. Faul, *Acc. Chem. Res.*, 2014, **47**, 3428–3438.
- 13 Z. Wu, Y. Yan and J. B. Huang, *Langmuir*, 2014, **30**, 14375–14384.
- 14 R. Verduzco, X. Y. Li, S. L. Peseka and G. E. Steinc, *Chem. Soc. Rev.*, 2015, **44**, 2405–2420.
- 15 A. M. Lifschitz, M. S. Rosen, C. M. McGuirk and C. A. Mirkin, *J. Am. Chem. Soc.*, 2015, **137**, 7252–7261.
- 16 S. Ulrich, A. Petitjean and J. M. Lehn, *Eur. J. Inorg. Chem.*, 2010, 1913–1928.
- 17 S. Nakamura, H. Kimura, T. Okuhara, M. Yamamura and T. Nabeshima, *J. Am. Chem. Soc.*, 2016, **138**, 794–800.
- 18 S. Le Gac, J.-F. Picron, O. Reinaud and I. Jabin, *Org. Biomol. Chem.*, 2011, **9**, 2387–2396.
- 19 S. Xu, Z. Yan, K.-I. Jang, W. Huang, H. Fu, J. Kim, Z. Wei, M. Flavin, J. McCracken and R. Wang, *Science*, 2015, **347**, 154–159.
- 20 Y. Habibi, L. A. Lucia and O. J. Rojas, *Chem. Rev.*, 2010, **110**, 3479–3500.
- 21 Y. Duan, X. Liu, L. Han, S. Asahina, D. Xu, Y. Cao, Y. Yao and S. Che, *J. Am. Chem. Soc.*, 2014, **136**, 7193–7196.
- 22 X. Gao, X. Yan, X. Yao, L. Xu, K. Zhang, J. Zhang, B. Yang and L. Jiang, *Adv. Mater.*, 2007, **19**, 2213.
- 23 J. R. Capadona, K. Shanmuganathan, D. J. Tyler, S. J. Rowan and C. Weder, *Science*, 2008, **319**, 1370–1374.
- 24 R. Dong, B. Zhu, Y. Zhou, D. Yan and X. Zhu, *Angew. Chem., Int. Ed.*, 2012, **51**, 11633–11637.
- 25 W. L. Noorduin, A. Grinthal, L. Mahadevan and J. Aizenberg, *Science*, 2013, **340**, 832–837.
- 26 W. W. Tsai, L. S. Li, H. G. Cui, H. Z. Jiang and S. I. Stupp, *Tetrahedron*, 2008, **64**, 8504–8514.
- 27 V. Percec, M. Glodde, T. K. Bera, Y. Miura, I. Shiyonovskaya, K. D. Singer, V. S. K. Balagurusamy, P. A. Heiney, I. Schnell, A. Rapp, H. W. Spiess, S. D. Hudson and H. Duan, *Nature*, 2002, **419**, 384–387.
- 28 S. De Feyter, J. van Stam, F. Imans, L. Viaene, F. C. De Schryver and C. H. Evans, *Chem. Phys. Lett.*, 1997, **277**, 44–50.
- 29 W. Mroz, J. P. Bombenger, C. Botta, A. O. Biroli, M. Pizzotti, F. De Angelis, L. Belpassi, R. Tubino and F. Meinardi, *Chem. – Eur. J.*, 2009, **15**, 12791–12798.
- 30 V. Deepak and P. R. Sundararajan, *J. Phys. Chem. B*, 2011, **115**, 8458–8464.
- 31 L. Zhao, X. Cheng, Y. Ding, Y. Yan and J. Huang, *Soft Matter*, 2012, **8**, 10472–10478.
- 32 M. Fujitsuka, D. W. Cho, J. Ohshita, A. Kunai and T. Majima, *J. Phys. Chem. C*, 2007, **111**, 1993–1998.
- 33 N. Kameta, M. Masuda, H. Minamikawa, N. V. Goutev, J. A. Rim, J. H. Jung and T. Shimizu, *Adv. Mater.*, 2005, **17**, 2732–2736.
- 34 N. Kameta, M. Masuda, H. Minamikawa and T. Shimizu, *Langmuir*, 2007, **23**, 4634–4641.
- 35 H. Yui, H. Minamikawa, R. Danev, K. Nagayama, S. Kamiya and T. Shimizu, *Langmuir*, 2008, **24**, 709–713.
- 36 Y. J. Wang, X. D. Gao, Y. L. Xiao, Q. Zhao, J. Yang, Y. Yan and J. B. Huang, *Soft Matter*, 2015, **11**, 2806–2811.