



Cite this: DOI: 10.1039/c5cc10617f

Received 28th December 2015,  
Accepted 21st January 2016

DOI: 10.1039/c5cc10617f

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## Construction of pillar[6]arene-based CO<sub>2</sub> and UV dual-responsive supra-amphiphile and application in controlled self-assembly†

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**A gas and photo dual-responsive host–guest recognition motif was established based on a water-soluble pillar[6]arene and an azobenzene derivative in an aqueous medium. This smart inclusion complex was further applied for the construction of a supra-amphiphile, which could reversibly self-assemble into vesicles upon UV/vis irradiation or bubbling with N<sub>2</sub>/CO<sub>2</sub>.**

Stimuli-responsive vesicles have recently attracted significant attention not only because they are ubiquitous building blocks in living systems but also because of their promising applications in the fields of chemistry, biology and materials science, such as biomimetic systems, controllable drug transport, gene delivery, micro-reactors and light-harvesting systems.<sup>1</sup> As a typical type of intelligent assembly, the fabrication of smart vesicles which can undergo reversible chemical/physical changes and modulate their self-assembled nanostructures in response to external-stimuli, such as pH, light, temperature, redox and enzyme, is becoming an extraordinarily fascinating topic.<sup>2</sup> Up to now, a wide variety of molecular building blocks have been exploited for the construction of vesicles. Besides the irreversible covalent route, the supramolecular approach paves an alternative way to build “supramolecular amphiphiles” which are more promising in developing stimuli-responsive nano-carriers due to the existing inter- and intramolecular noncovalent interactions including multiple hydrogen bondings, hydrophobic interactions, charge-transfers,  $\pi$ - $\pi$  interactions, metal–ligand coordination, *etc.*<sup>3</sup> However, these frequently employed noncovalent interactions are not always effective in fabricating assemblies in aqueous media with good biocompatibility, which is essential for biotechnological applications. Compared with other noncovalent interactions, host–guest interactions possess more stimuli-responsive properties and higher thermostability which endowed them with multitudinous

applications in various fields. Therefore, the construction of supra-amphiphiles through macrocycle-based host–guest recognition is of particular interest and significant importance.<sup>4</sup>

Pillararenes,<sup>5,6</sup> a novel class of emerging macrocyclic hosts, which are next to crown ethers, cyclodextrins, calixarenes and cucurbiturils,<sup>7,8</sup> have been attracting widespread attention since their discovery in 2008. The unique rigid pillar structures and accessible functionalizations of pillararenes endowed them with prominent superiority in host–guest recognition. Recently, a series of external-stimuli have been applied in the construction of sophisticated pillararene-based supramolecular systems exhibiting desirable assembly and disassembly processes by controllable association and dissociation, which could be employed in various fields, including liquid crystals, chemo-sensors, supramolecular polymers, and drug delivery systems.<sup>9</sup> Among them, gas and photo-responsive systems are of special interest. Carbon dioxide (CO<sub>2</sub>), as one of the most important metabolic substances of body, is an environmentally friendly trigger for stimuli-responsive systems due to its excellent biocompatibility and membrane permeability.<sup>10</sup> Additionally, photo-responsive self-assemblies have a profound influence on the biological field due to their easy operation, high sensitivity and excellent controllability.<sup>11</sup> Owing to chasing complex controllability and convenient applications under various conditions, multiple stimuli-responsive systems are now undergoing extensive investigation.

It is affirmed that tertiary amine-containing units can react with CO<sub>2</sub> in water to form charged ammonium bicarbonate, which can be recovered upon CO<sub>2</sub> removal (bubbling with N<sub>2</sub>).<sup>12</sup> Herein, pillar[6]arene **DEAP6** with six tertiary amine groups on both rims was designed and prepared as shown in Fig. 1. Upon bubbling with CO<sub>2</sub>, **DEAP6** was protonated into cationically charged pillararene (**CP6**) and became soluble in water, making it a desired host for an anionic guest. According to a previous report,<sup>13</sup> the cavity size of pillar[6]arene is suitable for *trans*-azobenzene, while it is too small for *cis*-azobenzene, so a photo-controllable threading–dethreading switch based on a pillar[6]arene/azobenzene recognition motif can be achieved due to the photoisomerization of the azobenzene unit. As shown

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† Electronic supplementary information (ESI) available: Synthetic procedures, characterizations, determination of association constants, UV-vis data and other materials. See DOI: 10.1039/c5cc10617f

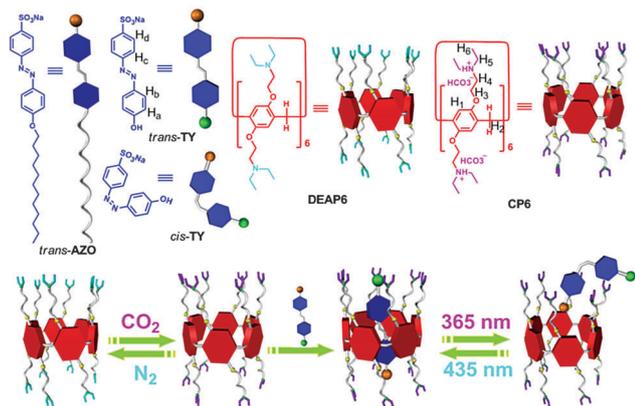


Fig. 1 Chemical structures of the compounds used here and the cartoon representation of the stimuli-responsive host-guest recognition.

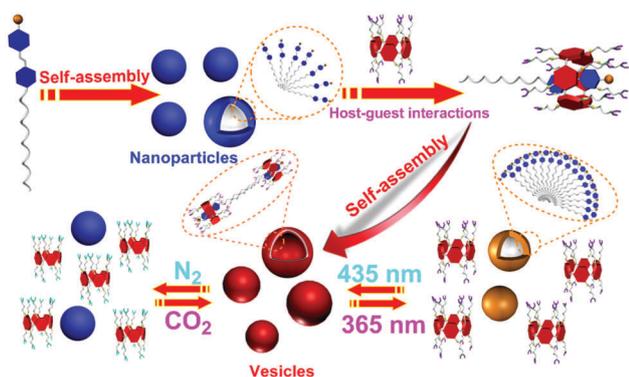


Fig. 2 Cartoon representation of the stimuli-responsive self-assembly.

in Fig. 1, *trans*-tropaeolin Y (*trans*-TY) is selected as the azobenzene-containing guest, and its host-guest properties with CP6 were fully investigated. In order to apply this smart recognition motif in stimuli-responsive self-assembly, an amphiphilic azobenzene derivative *trans*-AZO was designed. Interestingly, supramolecular vesicles were obtained from this supra-amphiphile (CP6  $\supset$  *trans*-AZO) in water and could be destroyed upon UV irradiation or bubbling with N<sub>2</sub> (Fig. 2). Oppositely, upon irradiation with 435 nm light or bubbling with CO<sub>2</sub>, the vesicles could form again. To the best of our knowledge, this is the first report on CO<sub>2</sub> and photo dual-responsive supramolecular vesicles, and it is expected that they will have wide range of applications in the future.

Pillararene DEAP6 was prepared referring to a previously reported paper and characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, LRESIMS and HR-LRESIMS (Fig. S1–S3, ESI<sup>†</sup>).<sup>12</sup> In order to protonate DEAP6, CO<sub>2</sub> (0.4 MPa, 1 min) was bubbled into the solution with well-dispersed DEAP6 treated by ultrasound. The host-guest interaction between CP6 and *trans*-TY in water was firstly studied by <sup>1</sup>H NMR spectroscopy. Compared with the spectrum of free *trans*-TY (Fig. 3a), the resonance peaks related to the protons H<sub>a</sub>, H<sub>b</sub>, H<sub>c</sub> and H<sub>d</sub> of *trans*-TY displayed substantial upfield shifts in the presence of an equivalent amount of CP6 (Fig. 3b). The reason was that these protons were shielded by the electron-rich cavity upon forming a

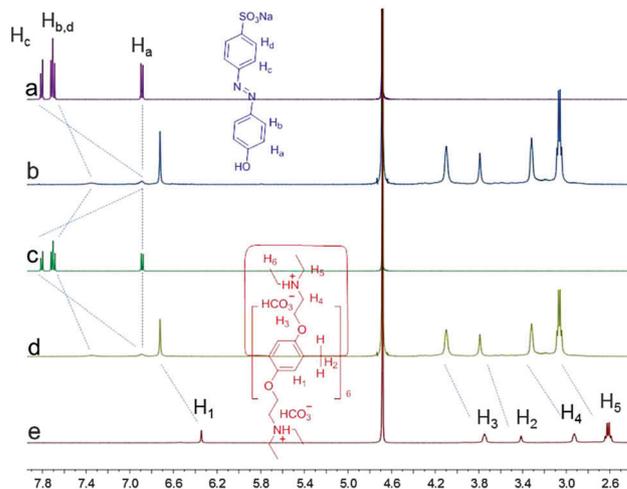


Fig. 3 Partial <sup>1</sup>H NMR spectra (400 MHz, D<sub>2</sub>O, 295 K): (a) *trans*-TY (2.00 mM); (b) CP6 (2.00 mM) and *trans*-TY (2.00 mM); (c) after bubbling b with N<sub>2</sub>; (d) after bubbling c with CO<sub>2</sub>; (e) CP6 (2.00 mM).

threaded structure between CP6 and *trans*-TY.<sup>6b</sup> Moreover, extensive broadening effects were observed for the peaks corresponding to the protons on *trans*-TY due to complexation dynamics. On the other hand, the protons on CP6 also exhibited slight chemical shift changes due to the interactions between CP6 and *trans*-TY.

2D NOESY NMR spectroscopy is a useful tool to study the relative positions of the components in host-guest inclusion complexes. Nuclear overhauser effect (NOE) correlations were observed between the signals related to the protons H<sub>a–d</sub> on the azobenzene unit of *trans*-TY and the protons H<sub>1,2</sub> on CP6 (Fig. S9, ESI<sup>†</sup>), suggesting that protons H<sub>a–d</sub> were located in the cavity of CP6. Isothermal titration calorimetry (ITC) experiments were performed to provide thermodynamic insight into the inclusion complexation between CP6 and *trans*-TY. From Fig. S10 (ESI<sup>†</sup>), the *K*<sub>a</sub> value of CP6  $\supset$  *trans*-TY was determined to be  $(3.73 \pm 0.23) \times 10^5 \text{ M}^{-1}$  in a 1 : 1 complexation stoichiometry. The driving forces for this host-guest system can be attributed to the cooperation of multiple electrostatic interactions between the cationic groups on the rigid pillar[6]arene receptor platform and the anionic sulfonate part of the guest and hydrophobic interactions between the azobenzene and the host. Furthermore, the enthalpy and entropy changes were obtained ( $\Delta H^\circ < 0$ ;  $T\Delta S^\circ > 0$ ;  $|\Delta H^\circ| > |T\Delta S^\circ|$ ), indicating that this complexation was primarily driven by the enthalpy change with entropy assistance (Fig. S10, ESI<sup>†</sup>).

As mentioned above, tertiary amine-containing units can react with CO<sub>2</sub> in water to form a charged ammonium bicarbonate, which can be recovered upon CO<sub>2</sub> removal (bubbling with N<sub>2</sub>). On the other hand, the photoisomerization of the azobenzene unit can induce the threading-dethreading behaviors between pillar[6]arene and azobenzene derived guest, thereby endowing the CP6  $\supset$  *trans*-TY complex with photo and CO<sub>2</sub> dual-responsiveness. <sup>1</sup>H NMR provided direct evidence for the UV and gas-controlled complexation between CP6 and *trans*-TY. Compared with the spectrum of *trans*-TY and CP6 in water, the signals on CP6 disappeared after bubbling with N<sub>2</sub>, and the corresponding signals on *trans*-TY returned to their

uncomplexed state, indicating that the *trans*-TY dethreaded from the cavity of CP6 (Fig. 3c). As expected, the resonance peaks related to the protons H<sub>a</sub>, H<sub>b</sub>, H<sub>c</sub> and H<sub>d</sub> of *trans*-TY displayed substantial upfield shifts again upon bubbling with CO<sub>2</sub> (Fig. 3d). Parallely, the photo-responsive host-guest complexation was also studied. Due to the low efficiency of photo-isomerization of *trans*-TY in aqueous solution upon UV irradiation, another azobenzene derivative *trans*-TY-1 was prepared (Fig. S7, ESI†). When the *trans*-TY-1 solution was irradiated with UV light for 30 min, the proton signals of *cis*-TY-1 appeared and the ratio of the *trans* to *cis* forms changed to about 20 : 80 (Fig. S7, ESI†). Upon irradiation with 435 nm light for sufficient time, *cis*-TY-1 converted back to *trans*-TY-1, and the proton signals of the spectrum shown in Fig. S7c (ESI†) were the same as those of the spectrum shown in Fig. S7a (ESI†). According to a previous report, the *cis* form of azobenzene is too large to be complexed by pillar[6]arene, so UV-responsive host-guest complexation could also be obtained in this case.

After the establishment of the stimuli-responsive recognition motif between CP6 and *trans*-TY, we further utilized it to construct a supra-amphiphile and investigated its responsive self-assembly in water. An amphiphilic azobenzene derivative *trans*-AZO was designed and its critical aggregation concentration (CAC) was determined to be  $3.00 \times 10^{-5}$  M (Fig. S11, ESI†) by using the concentration-dependent conductivity measurements. As revealed by TEM, *trans*-AZO itself self-assembled into nanoparticles with an average diameter of  $\sim 40$  nm (Fig. 4a). In the presence of CP6, the supra-amphiphile was formed with the pillar[6]arene head as the hydrophilic portion and the alkyl chain on *trans*-AZO as the hydrophobic part. The critical aggregation concentration of CP6  $\supset$  *trans*-AZO increased to be  $4.36 \times 10^{-5}$  M (Fig. S12, ESI†), and the enhancement of the CAC value was attributed to the stable host-guest complexation between CP6 and *trans*-AZO. The self-assembly morphologies of CP6  $\supset$  *trans*-AZO in water were investigated *via* TEM and DLS. DLS results showed that the

aggregates of CP6  $\supset$  *trans*-AZO have an average diameter of 250 nm with a narrow size distribution (Fig. 4c), and this result was confirmed by TEM. Hollow spherical assemblies with a thin shell were observed from the TEM images (Fig. 4b), indicating that CP6  $\supset$  *trans*-AZO self-assembled into vesicles in water. Notably, the wall thickness of the vesicles was measured to be about 16 nm based on an enlarged TEM image (Fig. 4d).

Just as expected, when the solution was irradiated with UV light for 30 min, the vesicles collapsed into nanoparticles due to the dethreading of *cis*-AZO from the cavity of CP6, causing a change in the packing arrangement of the amphiphilic building blocks and resulting in the change of the self-assembly morphology (Fig. 5a). Moreover, upon irradiation with 435 nm visible light, the nanoparticles turned back to vesicles again (Fig. 5b). Coincidentally, the vesicles collapsed into irregular assemblies upon bubbling with N<sub>2</sub> due to the precipitation of DEAP6 resulted from the deprotonation process of CP6 (Fig. 5c). Reversely, upon bubbling with CO<sub>2</sub> for 5 minutes, the irregular assemblies disappeared and vesicular aggregates emerged again (Fig. 5d).

In conclusion, a gas and photo dual-responsive host-guest recognition motif was established based on a water-soluble pillar[6]arene and an azobenzene derivative in an aqueous medium. This smart inclusion complex was further applied for the construction of a supra-amphiphile that could reversibly self-assemble into vesicles as a smart carrier for stimuli-responsive controlled release upon UV/vis irradiation or bubbling with N<sub>2</sub>/CO<sub>2</sub>. It is anticipated that utilizing green stimuli methods to realize a unique self-assembly behavior in aqueous solution may offer new possibilities in “on demand” release or absorption of chemicals such as drugs. As both CO<sub>2</sub> and light are crucial for living organisms, the system also provides inspiration for biomimicry by using synthetic supra-molecular systems.

This work was supported by the Fundamental Research Funds for the Central Universities.

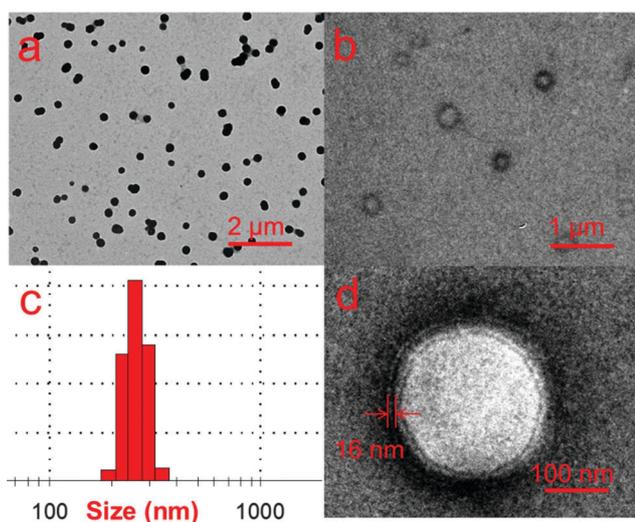


Fig. 4 (a) TEM image of (a) *trans*-AZO; (b) TEM image of CP6  $\supset$  *trans*-AZO; (c) DLS result of CP6  $\supset$  *trans*-AZO; and (d) enlarged TEM image of CP6  $\supset$  *trans*-AZO.

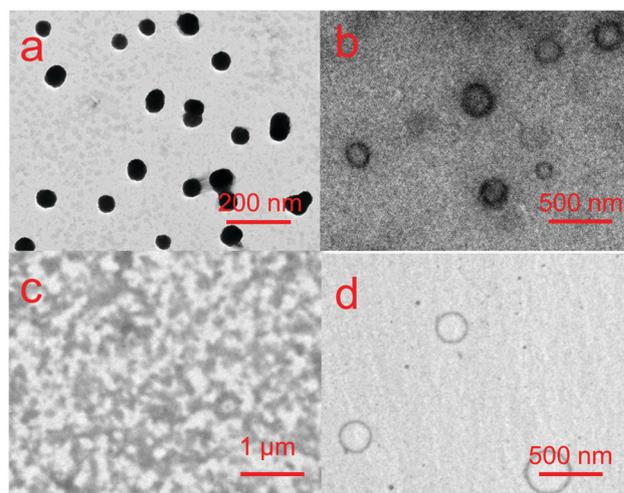


Fig. 5 (a) TEM image of (a) CP6  $\supset$  *trans*-AZO after irradiation with UV light at 365 nm; (b) after further irradiation with visible light at 435 nm of (a); (c) TEM image of CP6  $\supset$  *trans*-AZO after bubbling with N<sub>2</sub>; (d) TEM image of c after bubbling with CO<sub>2</sub>.

## Notes and references

- (a) A. Mueller and D. F. O'Brien, *Chem. Rev.*, 2002, **102**, 727; (b) S. Zhou, C. Burger, B. Chu, M. Sawamura, N. Nagahama, M. Toganoh, U. E. Hackler, H. Isobe and E. Nakamura, *Science*, 2001, **291**, 1944; (c) X. Zhang, S. Rehm, M. M. Safont-Sempere and F. Würthner, *Nat. Chem.*, 2009, **1**, 623.
- (a) J. Z. Du and S. P. Armes, *J. Am. Chem. Soc.*, 2005, **127**, 12800; (b) Q. Yan, J. Y. Yuan, W. Z. Yuan, M. Zhou and C. Y. Pan, *Chem. Commun.*, 2008, 6188; (c) X. K. Liu and M. Jiang, *Angew. Chem., Int. Ed.*, 2006, **118**, 3930; (d) N. Ma, Y. Li, H. P. Xu, Z. Q. Wang and X. Zhang, *J. Am. Chem. Soc.*, 2010, **132**, 442.
- (a) Y. Wang, N. Ma, Z. Wang and X. Zhang, *Angew. Chem., Int. Ed.*, 2007, **46**, 2823; (b) Y. H. Ko, E. Kim, I. Hwang and K. Kim, *Chem. Commun.*, 2007, 1305; (c) X. Zhang and C. Wang, *Chem. Soc. Rev.*, 2011, **40**, 94; (d) C. Wang, Z. Wang and X. Zhang, *Acc. Chem. Res.*, 2012, **45**, 608; (e) G. Yu, K. Jie and F. Huang, *Chem. Rev.*, 2015, **115**, 7240.
- (a) B. Jing, X. Chen, X. Wang, C. Yang, Y. Xie and H. Qiu, *Chem. – Eur. J.*, 2007, **13**, 9137; (b) Q. Yan, J. Yuan, Z. Cai, Y. Xin, Y. Kang and Y. Yin, *J. Am. Chem. Soc.*, 2010, **132**, 9268.
- Selective publications about pillar[5]arenes: (a) C. Li, L. Zhao, J. Li, X. Ding, S. Chen, Q. Zhang, Y. Yu and X. Jia, *Chem. Commun.*, 2010, **46**, 9016; (b) C. Li, Q. Xu, J. Li, F. Yao and X. Jia, *Org. Biomol. Chem.*, 2010, **8**, 1568; (c) Z. Zhang, Y. Luo, J. Chen, S. Dong, Y. Yu, Z. Ma and F. Huang, *Angew. Chem., Int. Ed.*, 2011, **50**, 1397; (d) 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; (e) X.-Y. Hu, X. Wu, Q. Duan, T. Xiao, C. Lin and L. Wang, *Org. Lett.*, 2012, **14**, 4826; (f) X.-B. Hu, Z. Chen, G. Tang, J.-L. Hou and Z.-T. Li, *J. Am. Chem. Soc.*, 2012, **134**, 8384; (g) Y. Yao, M. Xue, J. Chen, M. Zhang and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 15712; (h) 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; (i) Y. Fang, L. Wu, J. Liao, L. Chen, Y. Yang, N. Liu, L. He, S. Zou, W. Feng and L. Yuan, *RSC Adv.*, 2013, **3**, 12376; (j) K. Wang, C.-Y. Wang, Y. Wang, H. Li, C.-Y. Bao, J.-Y. Liu, X.-A. Zhang and Y.-W. Yang, *Chem. Commun.*, 2013, **49**, 10528; (k) H. Li, D.-X. Chen, Y.-L. Sun, Y. Zheng, L.-L. Tan, P. S. Weiss and Y.-W. Yang, *J. Am. Chem. Soc.*, 2013, **135**, 1570; (l) C. Li, K. Han, J. Li, H. Zhang, J. Ma, X. Shu, J. Chen, L. Weng and X. Jia, *Org. Lett.*, 2012, **14**, 42; (m) X. Wang, Y. Wang, Z. Chen, Y. Lin, L. Weng, K. Han, J. Li, X. Jia and C. Li, *Chem. Commun.*, 2015, **51**, 3434.
- Selective publications about pillar[n]arenes ( $n > 5$ ): (a) D. Cao, Y. Kou, J. Liang, Z. Chen, L. Wang and H. Meier, *Angew. Chem., Int. Ed.*, 2009, **48**, 9721; (b) Y. Ma, X. Chi, X. Yan, J. Liu, Y. Yao, W. Chen, F. Huang and J.-L. Hou, *Org. Lett.*, 2012, **14**, 1532; (c) T. Ogoshi, K. Kida and T. A. Yamagishi, *J. Am. Chem. Soc.*, 2012, **134**, 20146; (d) G. Yu, M. Xue, Z. Zhang, J. Li, C. Han and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 13248; (e) J. Yang, X. Chi, Z. Li, G. Yu, J. He, Z. Abliz and F. Huang, *Org. Chem. Front.*, 2014, **1**, 630.
- (a) Q.-C. Wang, D.-H. Qu, J. Ren, K. Chen and H. Tian, *Angew. Chem., Int. Ed.*, 2004, **43**, 2661; (b) Y. J. Jeon, H. Kim, S. Jon, N. Selvapalam, D. H. Seo, I. Oh, C.-S. Park, S. Jung, R. D.-S. Koh and K. Kim, *J. Am. Chem. Soc.*, 2004, **126**, 15944; (c) W.-H. Huang, P. Y. Zavalij and L. Isaacs, *Angew. Chem., Int. Ed.*, 2007, **46**, 7425; (d) W. Jiang, A. Schäfer, P. C. Mohr and C. A. Schalley, *J. Am. Chem. Soc.*, 2010, **132**, 2309; (e) D.-S. Guo and Y. Liu, *Chem. Soc. Rev.*, 2012, **41**, 5907; (f) X. Zeng, J. Ma, L. Luo, L. Yang, X. Cao, D. Tian and H. Li, *Org. Lett.*, 2015, **17**, 2976; (g) G. Nie, Y. Sun, F. Zhang, M. Song, D. Tian, L. Jiang and H. Li, *Chem. Sci.*, 2015, **6**, 5859.
- (a) J. Cao, Z.-P. Song, X.-Z. Zhu and C.-F. Chen, *Tetrahedron Lett.*, 2010, **51**, 3112; (b) Y.-K. Tian, L. Chen, Y.-J. Tian, X.-Y. Wang and F. Wang, *Polym. Chem.*, 2013, **4**, 453; (c) M. Song, Z. Sun, C. Han, D. Tian, H. Li and J. S. Kim, *Chem. – Asian J.*, 2014, **9**, 2344.
- (a) N. L. Strutt, R. S. Forgan, J. M. Spruell, Y. Y. Botros and J. F. Stoddart, *J. Am. Chem. Soc.*, 2011, **133**, 5668; (b) Q. Duan, Y. Cao, Y. Li, X. Hu, T. Xiao, C. Lin, Y. Pan and L. Wang, *J. Am. Chem. Soc.*, 2013, **135**, 10542; (c) H. Zhang, X. Ma, K. T. Nguyen and Y. Zhao, *ACS Nano*, 2013, **7**, 7853; (d) G. Yu, Y. Ma, C. Han, Y. Yao, G. Tang, Z. Mao, C. Gao and F. Huang, *J. Am. Chem. Soc.*, 2013, **135**, 10310; (e) J. Yang, Z. Li, Y. Zhou and G. Yu, *Polym. Chem.*, 2014, **5**, 6645.
- (a) Q. Yan, R. Zhou, C. Fu, H. Zhang, Y. Yin and J. Yuan, *Angew. Chem., Int. Ed.*, 2011, **50**, 4923; (b) Q. Yan, J. Wang, Y. Yin and J. Yuan, *Angew. Chem., Int. Ed.*, 2013, **52**, 5070.
- (a) C. Park, K. Lee and C. Kim, *Angew. Chem., Int. Ed.*, 2009, **48**, 1275; (b) T. Dvir, M. R. Banghart, B. P. Timko, R. Langer and D. S. Kohane, *Nano Lett.*, 2010, **10**, 250; (c) M. J. Tucker, J. R. Courter, J. Chen, O. Atasoylu, I. A. B. Smith and R. M. Hochstrasser, *Angew. Chem., Int. Ed.*, 2010, **49**, 3612.
- K. Jie, Y. Yao, X. Chi and F. Huang, *Chem. Commun.*, 2014, **50**, 5503.
- G. Yu, C. Han, Z. Zhang, J. Chen, X. Yan, B. Zheng, S. Liu and F. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 8711.