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COMMUNICATION

Cyclic Azobenzene-Containing Amphiphilic Diblock Copolymers: Solution Self-Assembly and Unusual Photo-Responsive Behaviors

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A novel amphiphilic diblock copolymer containing cyclic-azobenzene has been synthesized and self-assembled into sphere micelles with triple tunable responses. Interestingly, the multifunctional copolymer and its micellar aggregates show unusual photo-responsive behaviors.

Azobenzene-containing functional materials have played a critical role in the field of nano-optics and attracted considerable attention in the recent years. By accurately incorporation of functional azobenzene units into targeted molecules, chemists may develop the ability to design and predict their photoresponsive properties during the reversible *cis-trans* photoisomerization of azobenzene moieties. So far, extensive efforts have been devoted to the rational design and facile synthesis of diverse azobenzene-containing organic materials with unparalleled functions and properties, such as amphiphiles, liquid crystal polymers, and dendrimers.^[1] The constant demand for improved properties of azobenzene-based functional soft matters in various applications inspires people to develop new strategies for preparing these cutting edge materials with diverse modified azobenzene derivatives. Current strategies for the construction of such new modified azobenzene units generally focus on the chemical functionalizations of their substituents with electron-donating or electron-withdrawing as well as other functionalized groups.^[2] The amphiphilic polymers containing azobenzene groups can self-assemble into micellar structures in a selective solvent due to the microphase separation between two immiscible blocks. The formed micellar aggregates could undergo the size change and morphological transformation triggered by light, since the reversible *trans-cis* isomerization of azobenzene can result in large changes of azobenzene polarity, further influencing the hydrophilic-hydrophobic ratio of whole macromolecule.^[3] In the past decades, a lot of work has been devoted to the exploitation aimed at assembling azobenzene-containing copolymers with promising applications, such as photoswitches and drug delivery in biochemical systems, have been presented.^[4] So far, the self-assembly of azobenzene-

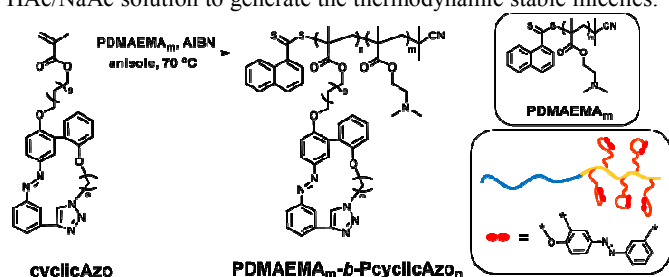
containing copolymers with different architectures, such as block polymers, random copolymers, dendritic polymers and star-like polymers and so on, has been well documented.^[1b,1c,1h] Alternatively, it is anticipated that the non-linear shaped azobenzene molecules could also lead to new physical properties and interesting photo-isomerization behaviors. A typical example is that the *cis*-form isomeric azobenzene could be significantly stabilized by the ring strain when azobenzene is exposed into a cyclic structure.^[5] In recent years, cyclic azobenzene has used as one of the most versatile building blocks towards various new azobenzene-based functional materials. Some applications of them have been impressively presented in the optical field, such as liquid-crystal displays, chiroptical switches and switchable gels.^[6] More importantly, the emergence of cyclic azobenzene molecules also provides new opportunities to achieve functional macromolecules with unparalleled properties and unique photo-responsive behaviors. In 2013, our group have prepared a homopolymer with cyclic azobenzene pendants via reversible addition-fragmentation chain transfer (RAFT) polymerization.^[7] The stringent rigidity of the cyclic azobenzene pendants resulted in the significant improved macromolecular properties, including higher T_g and larger modulation depth (M.D.) of photoinduced surface relief grating (SRG) compared with its analogue with linear-azobenzene pendants. Considering that introducing cyclic azobenzene as monomer into polymeric materials could greatly affect their physical properties, it is thus highly desirable to construct other kinds of cyclic azobenzene-containing macromolecules for the further study on their structure-property relationships.

In this communication, we report our efforts in the synthesis and characterization of a new class of amphiphilic diblock copolymers containing multiple cyclic azobenzene pendants as the hydrophobic part as well as PDMAEMA as a hydrophilic block. The resulting copolymer could self assemble into sphere micelles at the mixture of DMF and HAc/NaAc buffer solution (pH = 3.0) with triple tunable responses under the stimuli of temperature, pH, and light. The

unusual photo-responsive behaviors of the copolymer and their self-organized micelles were also fully investigated.

The synthetic route of copolymers PDMAEMA_m-*b*-PcyclicAzo_n is shown in Scheme 1. The monomer (cyclicAzo), methacrylate containing cyclic azobenzene were prepared according to our previous work.^[7] Firstly, homopolymer PDMAEMA was synthesized via the RAFT polymerization of DMAEMA using 2-cyanoprop-2-yl 1-dithionaphthalate (CPDN) as a chain transfer agent in anisole, and then two kinds of well-controlled diblock copolymers with the same DMAEMA block length (*m*) and different cyclicAzo block lengths (*n*) were prepared via RAFT chain-extension in anisole using PDMAEMA as the macro-RAFT agent and cyclicAzo as monomer. The structures of resulting copolymers were confirmed via Gel permeation chromatography (GPC) by contrasting the polymer (PDMAEMA₁₀₁) before chain extending reaction (Fig. S1(A)). The ¹H NMR (Fig. S1(B)), FT-IR (Fig. S2) and ¹³C NMR spectra (Fig. S3) further confirmed the successful synthesis of copolymer. The repeated DMAEMA units (*m*) and cyclicAzo units (*n*) of PDMAEMA_m-*b*-PcyclicAzo_n were calculated based on the ¹H NMR spectra of copolymers, as presented in SI (Supporting Information). The macromolecular characterizations of two prepared copolymers are summarized in Table S1.

The self-assembly of the resulting PDMAEMA₁₀₁-*b*-PcyclicAzo₃₁ was performed in the mixed solution of DMF and HAc/NaAc solution to generate the thermodynamic stable micelles.^[8]



Scheme 1 Synthetic route of the copolymer PDMAEMA_m-*b*-PcyclicAzo_n

The detailed process is described in SI. Notably the mixed aggregates, including sphere micelles, colloidal particles and aggregated hollow-sphere colloidal particles, were formed by using PDMAEMA₁₀₁-*b*-PcyclicAzo₈₃, which consists of a higher volume fraction of the hydrophobic domain, under precisely the same condition (Fig. S4). This might be that the decreased volume fraction of hydrophilic block in diblock amphiphiles may generate more flat surface curvature of the self-assembled aggregates, resulting in such kinds of morphologies.^[9]

The obtained micellar nanoparticles of PDMAEMA₁₀₁-*b*-PcyclicAzo₃₁ were carefully investigated utilizing transmission electron microscopy (TEM) and dynamic light scattering (DLS) techniques. Fig. 1(A) shows the bright field TEM image of sphere micelles with average diameter of (29.1±3.7) nm, which was also fully supported by DLS result (Fig. 1(A), inset). The formed sphere micelles are quite stable in the buffer solution for more than 4 months.

The multi-responses of the formed sphere micelles to external stimuli, *i.e.* temperature, pH and light were then investigated.^[10,11] The micellar morphology of PDMAEMA₁₀₁-*b*-PcyclicAzo₃₁ in

aqueous solution at various pH values and temperatures was tracked by TEM. For example, the pH-induced phase transition behavior of micellar solution was observed in the alkaline aqueous solution, probably due to the deprotonation of N,N-dimethylaminoethyl groups. As TEM image shown in Fig. 2(A), we found that all sphere micelles basically transformed into vesicles aggregates when the micelles solution stirred for 8 hours at pH 9.5, which is in good agreement with the increased hydrophobicity of the whole molecules. A yellow precipitate could be observed when pH value of solution rose to 10 because of a more hydrophobic nature of PDMAEMA block in copolymer. The vesicles aggregates can return to original sphere micelles when solution was re-adjusted into pH 3 and stirred 1 day (Fig. 2(B)). In addition, the temperature-induced incomplete phase transition from spheres to vesicles was also presented when the micelle solution was kept at 65 °C for 3 days, as TEM image shown in Fig. 2(C). It is considered that the degree of hydration of PDMAEMA block decreases with the increasing temperature so that the whole macromolecule becomes more hydrophobic, which leads the more flat surface curvature formation of the supramolecular structures. The incomplete phase transition process might be due to the very slow movement of the hydrophobic segment during the re-assembly process in the acidity solution. We might observe single vesicular micelles after a long enough time.

Moreover, the photo-responsive behavior of prepared polymeric micelles was also investigated. It was observed that similar spherical micelles with smaller size appeared after exposing under the 365 nm UV light for 70 min, and then returned to the initial sizes in the dark (Fig. 1). We try to count 100 typical micellar particles in TEM image for each kind of micelle to precisely analyze its size distribution. It was found that the diameters for the freshly prepared micelles, micelles after irradiation, and irradiated micelles after dark recovery are (29.1±3.7) nm, (24.1±2.8) nm, and (28.5±3.0) nm, respectively. Considering the difference in the size of distinct micelles (before and after light irradiation, and staying in dark for a long time) is quite small, DLS technique is not possible to be applicable for accurately analyzing this photo-response process. Such interesting micellar size changing can be explained by the unique dipole moment change of cyclic azobenzene pendants during the *trans-to-cis* photoisomerization process.^[2a,12] The difference in dipole moment between *cis* and *trans* isomers of azobenzene can alter the hydrophilic/hydrophobic balance of amphiphilic copolymers in selective solvent.^[11] To better understand the photo-responsive behavior of the micelle aggregates in this work, we calculated the dipole moments of *cis* and *trans* isomers of the cyclic azobenzene pendants of the hydrophobic block at the level of B3LYP/6-31G(d) level with Gaussian 03.^[13,11a] The detailed calculation is described in SI. Interestingly, a decrease of the dipole moment of the cyclic azobenzene pendants was found during *trans-to-cis* photoisomerization process, in which the *trans* configuration is 5.3 D while *cis* form is 4.0 D. For the comparison purpose, we also supposed a linear structure obtained by opening C-N bond between triazole and alkyl chain in cyclic azobenzene for further calculating the dipole moments of its *cis* and *trans* configuration (*cis*, 4.859D, *trans*, 4.750D, as listed in Table S2). The optimized configurations of the cyclic and hypothetical linear structures were also simulated at the level of the B3LYP/6-31G(d),^[13] as depicted in Fig. 3((a)and(b))

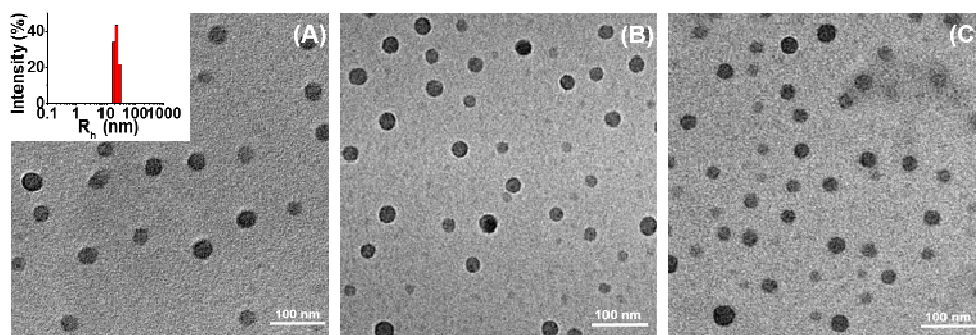


Fig. 1 TEM images of the sphere micelles formed by PDMAEMA₁₀₁-*b*-PcyclicAzo₃₁ in the mixed solution of DMF and HAC/NaAc solution (0.1M, PH=3) (1.0 mg/mL initial concentrations of block copolymer in DMF, and buffer solution content was 80% (wt%)): (A) initial micelle solution, the inset in (A) is hydrodynamic radius ($R_{h,DLS}$) distributions of initial micelle solution determined by DLS (scattering angle = 90°); (B) the micelle solution was exposed under the 365 nm light for 70 min; (C) the micelle solution was recovered in the dark for 114 h.

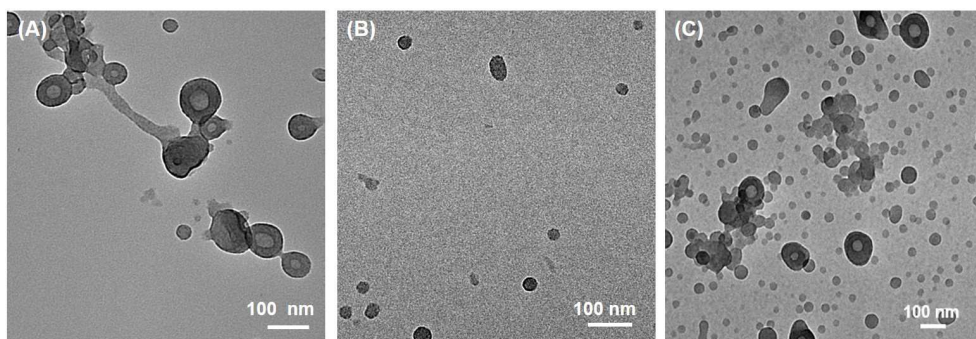


Fig. 2 TEM images of the micelles solution of PDMAEMA₁₀₁-*b*-PcyclicAzo₃₁ (A) at pH 9.5; (B) re-adjusted into pH 3; (C) at 65 °C for 3 days.

and Fig.S5, respectively. Based on this analysis, it is clear that a decrease of polarity (hydrophily) of the hydrophobic PAzo block in the micellar cores, resulting in the hydrophilic/hydrophobic ratio shifts in an opposite direction under UV light irradiation. As a result, it is reasonable that *trans-to-cis* photoisomerization of azobenzene segments in cyclic pendants is favorable for compact packing of micelles aggregates.^[11a]

The photoisomerization kinetics of cyclic azobenzene-containing diblock copolymer in THF solution and in its micelle solution were performed by UV-*vis* spectra, under 365 nm light irradiation and staying in dark, respectively (Fig. S6). Based on the absorbance at 345 nm in Fig. S6, the first-order kinetics curves were plotted (Fig. S7), and the rate constants (k_e and k_H) of *trans-to-cis* and *cis-to-trans* were calculated. The results show that the k_e values is 14.8 and 5.4 ($k_e \times 10^{-2}$, min^{-1}) the THF solution, and the k_H values is 3.2 and 2.0 ($k_H \times 10^{-2}$, h^{-1}), for the micelle solution, respectively. We note that the both k_H of the copolymer in THF and in its micelle solution are much smaller than respective k_e (*i.e.* recovery time of *cis-to-trans* in the dark of up to 46 h and 114h for two solutions (Fig. S6)), indicating that the *cis*-isomers of the cyclic azobenzene pendants have very slow thermally-driven back-isomerization compared with traditional copolymers containing linear azobenzene pendants.^[1b, 11] This can be attributed to the more stable conformation of *cis*-isomeric cyclic azobenzene pendants compared with that of its *trans*-analogue. The ring tension energy of the *cis* and *trans* isomers was estimated by the B3LYP/6-31G(d) level with Gaussian 03, respectively.^[13] The ring strain energy of *cis*-isomer is smaller with a value of 3.28 kcal/mol than that of *trans*-isomer, which perfectly

match with the above-mentioned thermodynamically more stable *cis* state. Moreover, compared with copolymer in THF solution, the rate of *trans-to-cis* photoisomerization for micelles solution is also much slower due to the compact structure of cyclicAzo in the aggregated cores.

Furthermore, we also examined the fluorescence change of copolymer in THF solution and in its micelles solution before and after UV irradiation as well as in the dark for additional information on their photoresponsive behaviors. It is clearly found that no fluorescence can be generated by diblock copolymer in THF solution before or after prolonged irradiation with 365 nm light (Fig. 3(C)). It is because that *cis-trans* photoisomerization of cyclic azobenzene induced a non-radiative relaxation process for the excited *trans* azobenzene.^[14] Similar result was reported by Han's group.^[2a] In our system, the *cis* configuration of cyclic azobenzene has a smaller dipole moment than its *trans* analogue and displays very slow thermally-driven back-isomerization due to its sufficient lifetimes, causing no fluorescence generation during *trans-to-cis* photoisomerization. The distinct fluorescence emission is observed in the micelle solution, which can be attributed to the molecular compact stacking in the micelles aggregates restricts the non-radiative relaxation channel of azobenzene. For example, it was clearly observed that the fluorescence emission is continually enhanced with increasing the amount of HAC/NaAc buffer in the mixture solution until it reaches to 1600% (v/v, with respect to DMF) (Fig.S8(A)), indicating the formed self-assembled micellar aggregates could induce the fluorescence emission, as further confirmed by TEM images in Fig.S8(B).^[15] Unlike linear

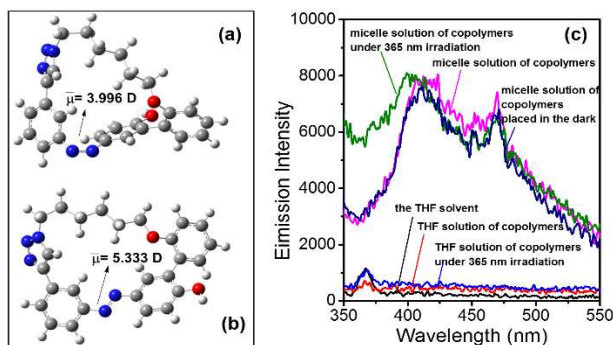


Fig. 3 The optimized configurations of (a) *cis*-isomer and (b) *trans*-isomer of cyclic azobenzene. (c) Fluorescence spectra of the THF solution of PDMAEMA₁₀₁-*b*-PcyclicAzo₃₁ and its micelle solution before and after UV irradiation as well as in the dark for a long time at an excitation wavelength of 330 nm.

azobenzene-containing aggregates,^[11b] we note that the fluorescence intensity of the micelles solution slightly increased around 350-400 nm after UV irradiation and then got back to original state after sample was placed in the dark for a period of time. This fluorescence enhancement is possibly resulted from the more compact packing of cyclic azobenzene pendants in hydrophobic PcyclicAzo core due to a decrease of its hydrophilicity through the *trans*-to-*cis* photoisomerization, as described above. This is also another evidence to support the formation of smaller sized micellar aggregates after exposing under the 365 nm UV light, as observed in Fig. 1.

In summary, novel amphiphilic diblock copolymers of containing multiple cyclic azobenzene pendants and their uniform sphere micelles were successfully prepared. The multi-responses of formed sphere micelles to temperature, pH and light were fully investigated. The present copolymer and its micellar aggregates show distinct photo-responsive behaviors compared with those of conventional amphiphilic block copolymers of containing linear azobenzene pendants. Firstly, both of the copolymer and related micelles demonstrate very slower thermally-driven back-isomerization, especially much slower for micelles solution since the *cis*-form isomer of cyclic azobenzene pendants presents a thermodynamic more stable conformation compared with that of *trans*-form one. Secondly, the micelle solution of copolymer exhibit fluorescence enhancement after 365 nm light irradiation, which can attributed to the more compact packing in hydrophobic PcyclicAzo core due to a decrease of dipole moment through the transformation from *trans* isomer to its *cis* analogue of cyclic azobenzene. The unprecedented results in this work are of interest to conduct future studies on the functionality of copolymers containing azobenzene and their biomedical applications. The related studies are currently underway in our research group.

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Notes and references

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†Electronic Supplementary Information (ESI) available: Materials, synthesis and characterization of PDMAEMA, PDMAEMA_m-*b*-PcyclicAzo_n, UV-vis absorption spectra, related TEM images and calculation of dipole moments. See DOI: 10.1039/c000000x/

- (a) M. Han and M. Hara, *J. Am. Chem. Soc.*, 2005, **127**, 10951-10955; (b) Y. Cai, J. Lu, F. Zhou, X. Zhou, N. Zhou, Z. Zhang and X. Zhu, *Macromol. Rapid Commun.*, 2014, **35**, 901-907; (c) N. Li, Y. Li and X. Wang, *Macromolecules*, 2011, **44**, 8598-8606; (d) Y. Yu, M. Nakano and T. Ikeda, *Nature*, 2003, **425**, 145; (e) Y. Wang and Q. Li, *Adv. Mater.*, 2012, **24**, 1926-1945; (f) W. Sun, X. He, C. Gao, X. Liao, M. Xie, S. Lin and D. Yan, *Polym. Chem.*, 2013, **4**, 1939-1949; (g) F. Vögtle, S. Gestermann, R. Hesse, H. Schwierz and B. Windisch, *Prog. Polym. Sci.*, 2000, **25**, 987-1041; (h) K. Han, W. Su, M. Zhong, Q. Yan, Y. Luo, Q. Zhang and Y. Li, *Macromol. Rapid Commun.*, 2008, **29**, 1866-1870.
- (a) M. R. Han, Y. Hirayama and M. Hara, *Chem. Mater.*, 2006, **18**, 2784-2786; (b) D. Bléger, J. Schwarz and A. M. Brouwer, *J. Am. Chem. Soc.*, 2012, **134**, 20597-20600.
- (a) Y. Zhao, *Macromolecules*, 2012, **45**, 3647-3657; (b) G. Wang, X. Tong and Y. Zhao, *Macromolecules*, 2004, **37**, 8911-8917; (c) O. Boissiere, D. Han, L. Tremblay and Y. Zhao, *Soft Matter*, 2011, **7**, 9410-9415; (d) G. Shen, G. Xue, J. Cai, G. Zou, Y. Li, M. Zhong and Q. Zhang, *Soft Matter*, 2012, **8**, 9127-9131; (e) Y. Zhang, W. Wu, G. Shen, J. Gao and Q. Zhang, *Micro Nano Lett.*, 2014, **9**, 390-394; (f) L. Lin, Z. Yan, J. Gu, Y. Zhang, Z. Feng and Y. Yu, *Macromol. Rapid Commun.*, 2009, **30**, 1089-1093.
- (a) W. Shen, M. Xing, Z. Zhang, W. Zhang, Z. Cheng and J. Zhu, *J. Macromol. Sci. A*, 2012, **49**, 834-844; (b) J. Rao and A. Khan, *J. Am. Chem. Soc.*, 2013, **135**, 14056-14059; (c) O. Sadovskii, A. B. Beharry, F. Zhang and G. A. Woolley, *Angew. Chem., Int. Ed.*, 2009, **48**, 1484-1486.
- (a) R. Siewertsen, H. Neumann, B. Buchheim-Stehn, R. Herges, C. Näther, F. Renth and F. Temps, *J. Am. Chem. Soc.*, 2009, **131**, 15594-15595; (b) Y. Norikane, K. Kitamoto and N. Tamaoki, *Org. Lett.*, 2002, **4**, 3907-3910.
- (a) Y. Norikane, Y. Hirai, and M. Yoshida, *Chem. Commun.*, 2011, **47**, 1770-1772; (b) K. Takaiishi, A. Muranaka, M. Kawamoto and M. Uchiyama, *Org. Lett.*, 2012, **14**, 276-279; (c) R. Reuter and H. A. Wegner, *Chem. Commun.*, 2013, **49**, 146-148.
- J. Li, N. Zhou, Z. Zhang, Y. Xu, X. Chen, Y. Tu, Z. Hu, X. Zhu, *Chem. Asian. J.*, 2013, **8**, 1095-1100.
- Z. Wang, Y. Li, X. Dong, X. Yu, K. Guo, H. Su, K. Yue, C. Wesdemiotis, S. Z. D. Cheng and W. Zhang, *Chem. Sci.*, 2013, **4**, 1345-1352;
- Y. Mai and A. Eisenberg, *Chem. Soc. Rev.*, 2012, **41**, 5969-5985.
- V. Bütün, S. P. Armes and N. C. Billingham, *Polymer*, 2001, **42**, 5993-6008.
- (a) X. Tong, G. Wang, A. Soldera and Y. Zhao, *J. Phys. Chem. B*, 2005, **109**, 20281-20287; (b) R. Dong, B. Zhu, Y. Zhou, D. Yan and X. Zhu, *Polym. Chem.*, 2013, **4**, 912-915.
- G. S. Kumer and D. C. Neckers, *Chem. Rev.*, 1989, **89**, 1915-1925.
- M. J. Frisch, et. al. *Gaussian 03*, Revision B.04; Gaussian, Inc.: Wallingford, CT, 2003. [Full reference given in SI]
- H. Rau, *Angew. Chem., Int. Ed.*, 1973, **12**, 224-235.
- Q. Bo and Y. Zhao, *Langmuir*, 2007, **23**, 5746-5751.