Reversible helical polymerization of supramolecular toroidal objects†

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Although great efforts have been made to construct reversible helical supramolecular polymers through self-assembly, the hierarchical helical polymerization of toroidal objects still remains a challenge. Herein, we report that the toroidal architectures assembled from achiral dimeric macrocyclic building blocks are able to undergo reversible helical polymerization through spiral opening in response to heating–cooling cycles. In the presence of enantiomerically pure 2-butanol as a chiral regulator, the polymerization of achiral toroids generates helical polymers with a preferred handedness due to chirality transfer.

Hierarchical assembly of toroidal proteins to form quaternary structures has been discovered in many biological processes and plays essential roles in living organisms.1,2 Among the assembly models of toroidal proteins, the hypothesis for nucleation and growth of tobacco mosaic virus in which toroidal proteins are converted into open-ended spirals (‘spiral opening’) via RNA binding has attracted intense interest.3,4 In addition to the natural toroidal proteins, a variety of supramolecular toroidal architectures have been created through the self-assembly of amphiphiles,5,6 polymers,7,8 peptides9,10 and proteins.11 Although some examples of switchable toroids which stack into tubular structures12 or reassemble into coiled nanostructures driven by external stimuli have been reported recently,13,14 the helical polymerization of synthetic toroids via spiral opening has rarely been investigated.

Recently, we reported that toroidal structures formed by 1 in aqueous solution can be autonomously polymerized upon energy supply (Fig. 1a).14 Heat treatment as an energy source drives closed toroids to open out into spirals. Consequently, the spirally opened toroids undergo helical polymerization through end-to-end connection. When the supplied energy has been consumed, the helical polymers collapse to recover discrete toroids. Thus, the helical polymers transiently exist for only as long as energy is supplied. However, the energy-mediated polymerization-depolymerization is a very slow process, on time scales of 4 to 12 days at room temperature, resulting in limitations for further applications. Here we report the reversible helical polymerization of supramolecular toroids in rapid response to heating through spiral opening. Upon cooling to ambient temperature, the helical polymers immediately collapse to recover the original toroids without thermal hysteresis (Fig. 1). Notably, the polymerization of the achiral toroidal objects in the presence of a chiral guest generates optically active helical polymers through chirality transfer to toroid frameworks.

†Electronic supplementary information (ESI) available. See DOI: 10.1039/c9py01473j

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Fig. 1 (a) Molecular structure of amphiphiles 1 and 2. (b) Schematic representation of reversible hierarchical helical polymerization and depolymerization of supramolecular toroid 2 with rapid response to heating–cooling cycles.
The toroidal assembly of 1, which contains hydrophilic dendrons with a methyl stereogenic group, undergoes helical polymerization at a temperature above the lower critical solution temperature (LCST; 60 °C), similar to energy-mediated polymerization at room temperature. However, this occurs very slowly (~2 h) even with heating above the LCST. Moreover, the helical polymers easily collapse to irregular aggregates owing to solubility limitation (Fig. S1†). We considered that the slow polymerization and depolymerization process and the stability limitation arise from the steric effect between the hydrophobic methyl side groups in the oligoether chains. To rule out the influence of such obstacles arising from the methyl side groups on the helical polymerization, we synthesized macrocyclic amphiphile 2, which lacks the methyl side groups in the hydrophilic dendron (Fig. 1, Fig. S2 and S3†).

We initially investigated the aqueous self-assembly of amphiphile 2 using transmission electron microscopy (TEM). The image showed toroidal structures with a highly uniform external diameter of 12 nm in aqueous solution including 6% tetrahydrofuran (THF), indicating that the modification of the oligoether dendron does not disturb the formation of toroidal assemblies (Fig. 2a). The absorption and emission spectra of the solution of 2 in both molecularly dissolved and assembled states showed identical results to those of 1 (Fig. S4†), demonstrating that the toroids consist of perpendicularly stacked dimeric macrocycles with eclipsed molecular conformation. It is well known that oligoether chains undergo a thermal transition because of dehydration on heating. As expected, upon heating to 47 °C, the solution of 2 showed a phase transition, indicating that the oligoether chains show LCST behavior due to thermal dehydration (Fig. S5†). Upon dehydration of the oligoether dendrons, the dehydrated dendritic chains strengthen hydrophobic interactions, thus leading to slipped conformation of the dimeric macrocycles, which is reflected in the red-shifted absorption maximum (Fig. 2b and Fig. S6†). The slipped conformation of macrocycles would force the closed toroids to be spirally open to reduce ring strain. Consequently, the spirally open toroids can be helically polymerized through end-to-end connection between the open ends. Moreover, the lack of the hydrophobic methyl side groups in the dendritic chains would render the long polymer chains stable, without precipitation even above LCST.

To corroborate the helical polymerization of the toroids upon heating, we performed TEM experiments with the solution of 2 at 50 °C (Fig. 2c and Fig. S7†). Upon heating to 50 °C, the toroids are polymerized rapidly to form elongated helical structures, as evidenced by TEM, which showed the formation of helical polymers with ~400 nm length and 12 nm width. The perfect match between the external diameters of helix and toroids indicates that the helix retains the toroidal curvature. The degree of polymerization is assumed to be ~70 considering the pitch length is 6 nm. Consistent with the TEM results, dynamic light scattering (DLS) experiments from the solution of 2 revealed that the size of aggregates increases remarkably in hydrodynamic diameter from 12 nm to ~100 nm upon heating to 50 °C (Fig. 2d), supporting the idea that the toroids are readily polymerized upon heating. To gain insight into the mechanism of the helical polymerization, we performed polymerization experiments at slightly lower temperatures with increased THF content to slow down the polymerization (Fig. 2e and Fig. S8†). Upon heating to 40 °C without standing, the TEM image revealed that dispersed toroids with intact structure coexist with short helical polymers with opened terminals, suggesting that the polymerization occurs through the end-to-end connection of the spirally opening toroids rather than reassembly from free molecules. When the solution is cooled, the size of the aggregates dramatically decreases, as confirmed by DLS (Fig. 2d), demonstrating that the helical polymer chains rapidly collapse to recover the original toroidal objects upon cooling to room temperature. This is further illustrated by TEM, which showed immediate recovery into toroidal objects when the polymer solution was cooled to room temperature (Fig. 2f). These observations demonstrate
that the polymerization and depolymerization processes occur in rapid response to heating-cooling cycles, which is in great contrast to the slow process for 1.

Owing to the lack of a stereogenic center in the dendritic chains, the helical polymerization of the toroid of 2 generates a racemic mixture of left- and right-handed helices, as reflected by the absence of circular dichroism (CD) [Fig. S9†]. One strategy for controlling the symmetry breaking of the racemic mixture of the helical handedness is chirality transfer from chiral solvent molecules.16,18 To induce optically active helical polymers using a chirality transfer approach, we selected enantiomerically pure (S)(+)- and (R)(−)-2-butanol, which shows good solubility in H2O and is compatible with the oligoether chains. Upon addition of 2-butanol (5 vol%) into the solution of 2, TEM revealed that the toroidal objects were maintained without any structural changes, indicating that 2-butanol does not have an influence on maintaining toroidal structure [Fig. S10†]. To monitor the chirality induction on helical polymerization, we performed temperature-dependent CD experiments in the presence of 5 vol% (R)(−)-2-butanol (Fig. 3a). Upon heating the solution above 40 °C, an obvious increase in the intensity of the bisignate Cotton effect was observed. This result demonstrates that chirality transfer from the chiral guest leads to a slipped conformation in a preferred direction upon heating.20 Consequently, the slipped packing of the aromatic macrocycles would drive the closed toroids to open spirally in a favored direction, and the open-ended spirals would then, in turn, be interconnected to form optically active helical polymers. To identify the structural resolution of the helical polymers, TEM experiments were performed with the solution of 2 with 5 vol% of (R)(−)-2-butanol (Fig. 3b). When the solution was heated to 40 °C, right-handed helical polymers were formed preferentially, indicating that the chirality of the 2-butanol is communicated to the toroid frameworks to induce preferential opening and eventually to form helical polymers with a preferred handedness. When the identical experiments were carried out with (S)(+)-2-butanol, the CD spectra showed a mirror-image relationship to the R form, indicative of chirality transfer from 2-butanol (Fig. S11†).

To investigate the mechanism of chirality transfer, temperature-dependent UV experiments were performed with solutions of 2 containing different ratios of 2-butanol (Fig. S12†). Upon addition of 5 vol% 2-butanol to the toroid solution, the LCST is decreased to 37 °C, suggesting that 2-butanol diffuses into the oligoether dendritic segments.21 Upon heating, thermal dehydration of the oligoether chains occurs, capturing 2-butanol molecules within the dehydrated dendritic chains [Fig. 3d]. Consequently, the chirality of the captured guest molecules in the dehydrated dendrons is communicated to the aromatic segments to induce helical polymer chains with a preferred handedness. To corroborate the interactions between 2-butanol and the oligoether chains, temperature-dependent UV experiments were performed with solutions of 2 containing different ratios of 2-butanol (Fig. S11†). Upon addition of 3 vol% of enantiomerically pure 2-butanol (Fig. 3c and Fig. S13†). Upon heating, the 1H NMR resonances associated with the oligoether chains broadened, indicative of dehydration of the oligoether chains. In addition, correlation peaks between 2-butanol and the oligoether chains were detected, indicative of close proximity between the oligoether chains and 2-butanol in space. To confirm that the chirality transfer originates from the spatial confinement of a chiral guest rather than hydrogen-bonding between the oligoether chains and 2-butanol, butylene oxide was selected as an alternative chiral guest which is unable to form hydrogen bonds. Upon heating to 40 °C, similar CD induction was observed upon the addition of 3 vol% of enantiomerically pure butylene oxide [Fig. S14†], indicating that the chirality transfer mainly arises from the spatial confinement effect.

Notably, upon cooling of the solution of 2 containing chiral 2-butanol to room temperature, the induced CD signal rapidly disappeared, to restore the room temperature signal without any thermal hysteresis [Fig. 4a], demonstrating that the chirality transfer does not occur when the oligoether chains are rehydrated. This result indicates that CD signals can be used to monitor the process of helical polymerization. To confirm this, temperature-dependent CD intensities at 238 nm were monitored with a slow heating and cooling cycle (Fig. 4b). In the heating curve, the CD intensity increased rapidly until the temperature reached 35 °C and then leveled off, indicating that the preferential slipping of the macrocycles generates optically active helical polymers. Upon cooling from 40 °C, the CD intensity was immediately reduced without any hysteresis effect, demonstrating that the dimeric macrocycles with

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**Fig. 3** (a) Temperature-dependent CD spectra of 2 (0.01 wt%) in H2O (containing 6% THF) in the presence of 5 vol% (R)(−)-2-butanol. (b) Negatively-stained TEM image of 2 in the presence of 5 vol% (R)(−)-2-butanol upon heating. (c) 1H-and 1D NOE-NMR spectra of oligoether dendrons with 1 vol% 2-butanol at 60 °C. (d) Schematic representation of chirality induction from chiral 2-butanol upon heating.
slipped packing convert rapidly into an eclipsed conformation, followed by depolymerization. Upon subsequent heating of the depolymerized solution, bisignate CD signals were induced repeatedly, indicating that the new cycle of polymerization takes place without compromised response efficiency. This result demonstrates that the helical polymerization of the toroids is fully reversible and occurs repeatedly with subsequent heating–cooling cycles.

Conclusions

In conclusion, our results show that toroidal objects formed from dimeric macrocyclic amphiphile 2 undergo reversible helical polymerization and depolymerization in rapid response to heating–cooling cycles. Upon heating, helical polymers are formed through the end-to-end connection of spirally opened toroids. When the solution is cooled to room temperature, the helical polymers rapidly collapse to recover discrete toroidal objects. Notably, enantiomerically pure 2-butanol as a chiral regulator can induce helical polymerization with a preferred handedness. The reversible polymerization of supramolecular toroidal objects with controllable helicity in rapid response to heating–cooling cycles gives a new opportunity to design novel hierarchical supramolecular assemblies.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (21634005 and 51473062) and Jilin University Funding (JLUSTIRT).

Notes and references