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Responsive Nanostructures from Aqueous Assembly of Rigid−Flexible Block Molecules

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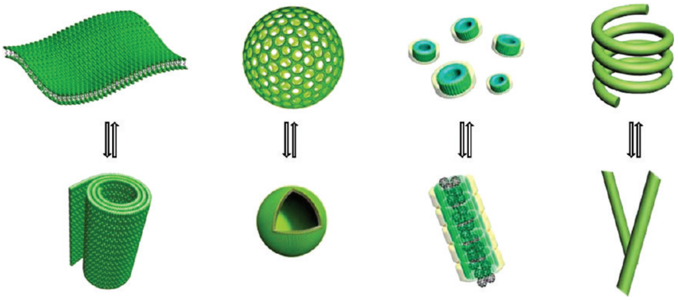
CONSPECTUS



During the past decade, supramolecular nanostructures produced via self-assembly processes have received considerable attention because these structures can lead to dynamic materials. Among these diverse self-assembly systems, the aqueous assemblies that result from the sophisticated design of molecular building blocks offer many potential applications for producing biocompatible materials that can be used for tissue regeneration, drug delivery, and ion channel regulation. Along this line, researchers have synthesized self-assembling molecules based on ethylene oxide chains and peptide building blocks to exploit water-soluble supramolecular structures. Another important issue in the development of systems that self-assemble is the introduction of stimuli-responsive functions into the nanostructures. Recently, major efforts have been undertaken to develop responsive nanostructures that respond to applied stimuli and dynamically undergo defined changes, thereby producing switchable properties. As a result, this introduction of stimuli-responsive functions into aqueous self-assembly provides an attractive approach for the creation of novel nanomaterials that are capable of responding to environmental changes.

This Account describes recent work in our group to develop responsive nanostructures via the self-assembly of small block molecules based on rigid−flexible building blocks in aqueous solution. Because the rigid−flexible molecules self-assemble into nanoscale aggregates through subtle anisometric interactions, the small variations in local environments trigger rapid transformation of the equilibrium features. First, we briefly describe the general self-assembly of the rod amphiphiles based on a rigid−flexible molecular architecture in aqueous solution. We then highlight the structural changes and the optical/macroscopic switching that occurs in the aqueous assemblies in response to the external signals. For example, the aqueous nanofibers formed through the self-assembly of the rod amphiphiles respond to external triggers by changing their shape into nanostructures such as hollow capsules, planar sheets, helical coils, and 3D networks. When an external trigger is applied, supramolecular rings laterally associate and merge to form 2D networks and porous capsules with gated lateral pores. We expect that the combination of self-assembly principles and responsive properties will lead to a new class of responsive nanomaterials with many applications.

Introduction

Aqueous assembly of amphiphilic molecules has great advantages to the creation of desired materials in terms of biological applications and environmentally friendly processability.[1−4] Examples of molecular building blocks for aqueous assembly include block copolymers, surfactants, peptide derivatives, and lipid molecules.[5−7] Depending on the external environments, molecular structures and shapes, and relative volume fraction of hydrophilic and hydrophobic parts, these molecules self-assemble into diverse supramolecular architectures, such as spherical or cylindrical micelles, vesicles, ribbons, and tubules. Besides the formation of interesting structures at nanoscale dimen-

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sions, the molecular assembly of the amphiphilic molecules through weak noncovalent interactions including hydrogen bonding, electrostatic interaction, and hydrophobic effect is ideally suitable for the construction of the responsive materials since the dynamic and reversible conformational changes can be triggered by external environments. Normally, this change is fully reversible once the stimulus has been removed. Numerous possible applications in the fields of environmental sciences, biomedical sciences, and nanodevices have been described for stimulus-responsive materials.[8−11]

A number of dynamic supramolecular systems have been developed and can be changed in their topologies and properties upon exposure to external triggers such as temperature, light, pH, and redox potential.[12−14] For example, microgel particles based on thermoresponsive poly(*N*-isopropylacrylamide) (PNIPAm) exhibit a conformational transition depending on temperature variation, which has been widely explored for a variety of material applications including drug delivery and sol−gel interconversion.[15] The photoresponsive azobenzene derivatives have been employed for another strategy to construct responsive self-assemblies. The azobenzene-functionalized amphiphiles form helical assemblies with phototunable helical pitches and chiroptical properties by conformational change between *trans*-azobenzene and its *cis*-isomer.[16,17] The applied magnetic field can also trigger the deformation of supramolecular assemblies. The capsule-like structures formed from bolaamphiphilic oligothiophenes deform into oblate spheroids resulting from the orientation of anisotropic thiophene segments along the applied magnetic field.[18]

Among a variety of self-assembling building blocks, rod amphiphiles, consisting of rigid rod and flexible coil segments, are excellent candidates for creating well-defined supramolecular structures in selective solvents for flexible side chains.[19] For the aqueous self-assembly of rigid−flexible block molecules, the amphiphilic combination of hydrophilic coil and hydrophobic rod segments leads to the formation of a well-defined nanostructure with rigid hydrophobic core surrounded by flexible hydrophilic chains.[20,21] In contrast to coil−coil systems, the rod−coils can form well-ordered structures even at very low molecular weights of each block because a stiff rod-like conformation of the rod segments imparts orientational organization. The packing arrangements of these small anisotropic rod segments are able to rapidly transform into their equilibrium states when faced with very small environmental changes, which is an essential prerequisite for construction of responsive nanostructures.

Our group has employed rigid−flexible block systems consisting of oligo(*para*-phenylene) rod units as a rigid segment and flexible chains such as poly(propylene oxide) (PPO), poly(ethylene oxide) (PEO), or alkyl chains for the construction of various self-assembled structures in bulk.[22−27] As an extension of the bulk-state supramolecular structures, we have pioneered diverse aqueous assemblies such as tubules, toroids, porous capsules, and helical fibers.[28−33] These nanostructures are able to respond to applied stimuli such as certain guests, pH, solvent, and temperature by changing their shape or macroscopic properties. We have focused on two features in these aqueous self-assembling systems to construct stimuli-responsive nanostructures. The first feature is that the rigid aromatic rods have a strong tendency to arrange with an anisotropic orientation. Small environmental changes are expected to significantly affect the details of aromatic rod packing and thus the structural nature of supramolecular assemblies. The second feature is that ethylene oxide segments are well-known for a lower critical solution temperature (LCST) property, exhibiting a hydration−dehydration transition in response to relatively small changes in temperature.[34] Combination of these two features in one system allows the self-assembled nanostructures to exhibit stimuli-responsive properties.

In this Account, we describe our recent progress on the development of aqueous rigid−flexible amphiphilic systems with the aim of the creation of stimuli-responsive smart nanostructures. Then we describe how these nanostructures undergo abrupt structural and property changes in response to small variation of applied stimuli.

Aqueous Nanofibers from Rod Amphiphiles

Among the diverse morphologies from aqueous self-assemblies, the construction of well-defined 1D nanostructures such as fibers, tubes, and helical coils is one of the important research topics in materials science and biorelated science. The incorporation of a stimuli-responsive moiety into the molecular building blocks leads to the formation of responsive nanofibers exhibiting changes in shape and physical properties. Stupp et al. reported the formation of quadruple helical fibers from peptide amphiphiles substituted by a nitrobenzyl group.[35] Upon photocleavage of the nitrobenzyl group, the multiplehelices transform into single nanofibers. Ajayaghosh et al. reported the self-assembly of tripodal squaraines into hollow spherical structures that change to form nanohelices upon binding with Mg^{2+} or Ca^{2+}.[36] Cationic charge repulsion is responsible for the transformation into the helical extended assemblies. Schenning and co-workers reported that achiral naphthalene guest molecules can bind to

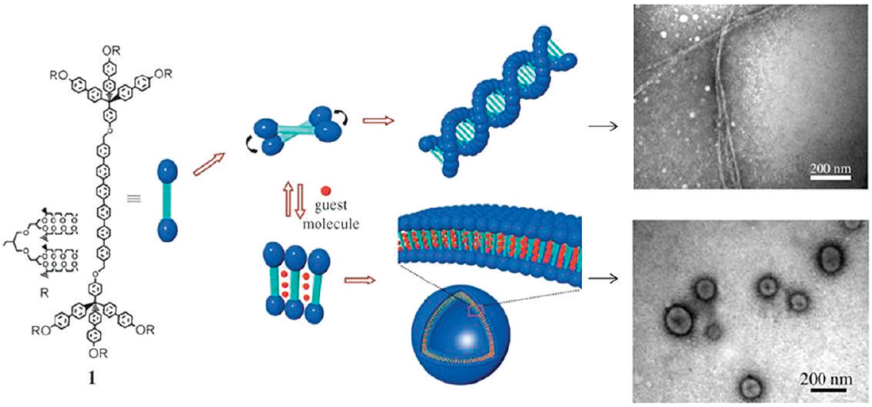

FIGURE 1. Molecular structure of amphiphilic dumbbell-shaped molecule **1** and representation of the reversible interconversion of helical fibers into nanocapsules. Adapted from ref 38 with permission. Copyright 2006 Wiley-VCH.

oligothymine strands to construct helical structures with a pH-switchable stability and supramolecular helicity as a result of protonation of the guest.[37]

We have been devoted to developing novel amphiphilic block molecules that self-assemble into various 1D nanostructures in aqueous solution. For example, we have shown that incorporation of a conjugated rod into an amphiphilic dumbbell-shaped molecule gives rise to the formation of helical nanostructures.[32] We have also shown that rigid–flexible diblock macrocycles self-assemble into a left-handed coiled tubular assembly.[30] As an extension of our efforts toward the construction of 1D nanostructures from the self-assembly of rigid–flexible diblock molecules, we have explored responsive characteristics of the self-assembled nanofibers such as their structural changes and related physical property changes in response to external stimuli. A typical example is provided by helical fibers and their reversible interconversion into spherical nanocapsules by intercalation of aromatic guest molecules (Figure 1).[38] We synthesized the amphiphilic dumbbell-shaped molecules **1** consisting of a hexa(*para*-phenylene) rod block and aliphatic oligoether dendritic chains with chiral carbon centers and investigated their self-assembly behavior in aqueous solution by transmission electron microscopy (TEM) and circular dichroism (CD). When molecular dumbbell **1** was dissolved in aqueous solution, the rod segments stacked on top of each other with mutual rotation in the same direction to avoid steric hindrance between the bulky dendritic chains. This stacking of the aromatic rod segments leads to helical objects comprising hydrophobic aromatic cores surrounded by hydrophilic dendritic segments. Remarkably, these helical fibers transform into hollow capsules triggered by the addition of aromatic guest molecules such as 4-bromonitrobenzene, which are selectively intercalated between aromatic segments. This intercalation of the guest molecules enlarges the distance between the adjacent rods segments. Subsequently, the twisted packing of the rod segments is rearranged into a parallel stacking, leading to the transformation of the fibers into hollow capsules. This reversible interconversion between helical fibers and hollow capsules was easily executed by extraction of guest molecules.

Molecular dumbbell **2** consisting of a carbazole end-capped phenanthrene as a rigid stem and chiral oligoether segments, self-assembles into nonchiral nanofibers that can be reversibly switched to a chiral fiber, triggered by temperature variation (Figure 2).[39] The TEM image of aqueous solution of **2** revealed 1D elongated fibers with a uniform diameter of 5 nm. Remarkably, the CD spectra of **2** at room temperature displayed inactive signal; however, upon heating the CD spectra displayed a strong Cotton effect, indicative of the transformation of the fibers with supramolecular chirality. This chirality switching of the fibers is attributed to the LCST behavior of oligoether chains in aqueous medium.[34] At room temperature, the ethylene oxide chains are fully hydrated and thus hydrophilic. Above the LCST, however, the ethylene oxide chains would be dehydrated due to the breaking of the hydrogen bonding between ether oxygens and water molecules. Consequently, the ethylene oxide chains would collapse into molecular globules due to dehydration. As confirmed by UV/vis and fluorescence measurements, the resulting shrinkage of the oligoether side chains leads the rod packing to the enhanced strength of the $\pi-\pi$ stacking interactions, giving rise to the helical stacking with restricted rotational freedom between the adjacent rods. Consequently, the nonchiral fibers, upon heating above the LCST, are reversibly transformed into helical fibers, indicating that the fibers act as a supramolecular device with chiroptical switching behavior.

The introduction of a branched alkyl chain and a linear PEO chain into each end of a wedge-shaped rigid aromatic seg-

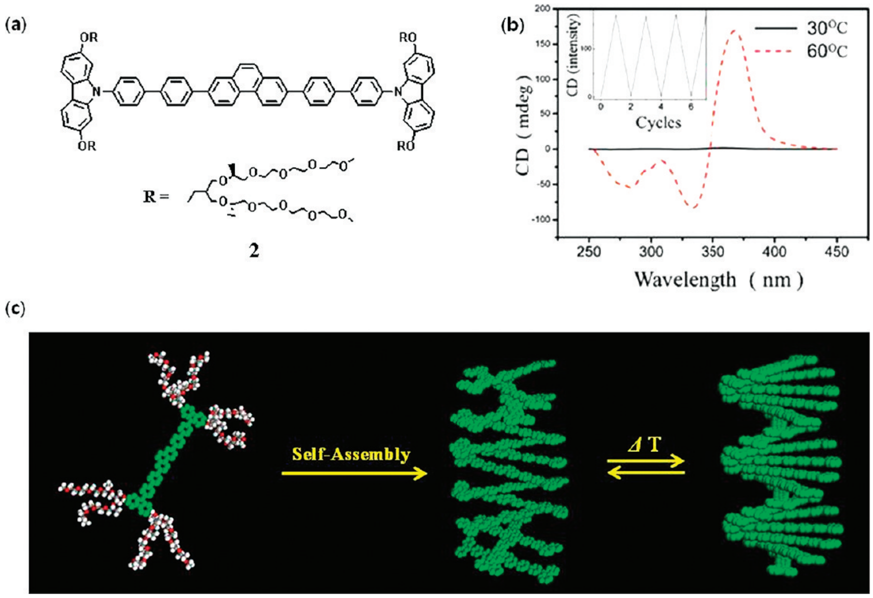

FIGURE 2. (a) Molecular structure of **2**, (b) CD spectra and reversible switching cycles of the intensity at 370 nm in an aqueous solution of **2** (0.01 wt %), and (c) schematic representation of the reversible transformation from achiral extended to chiral compressed states of the cylindrical stack. Adapted from ref 39 with permission. Copyright 2009 Royal Society of Chemistry.

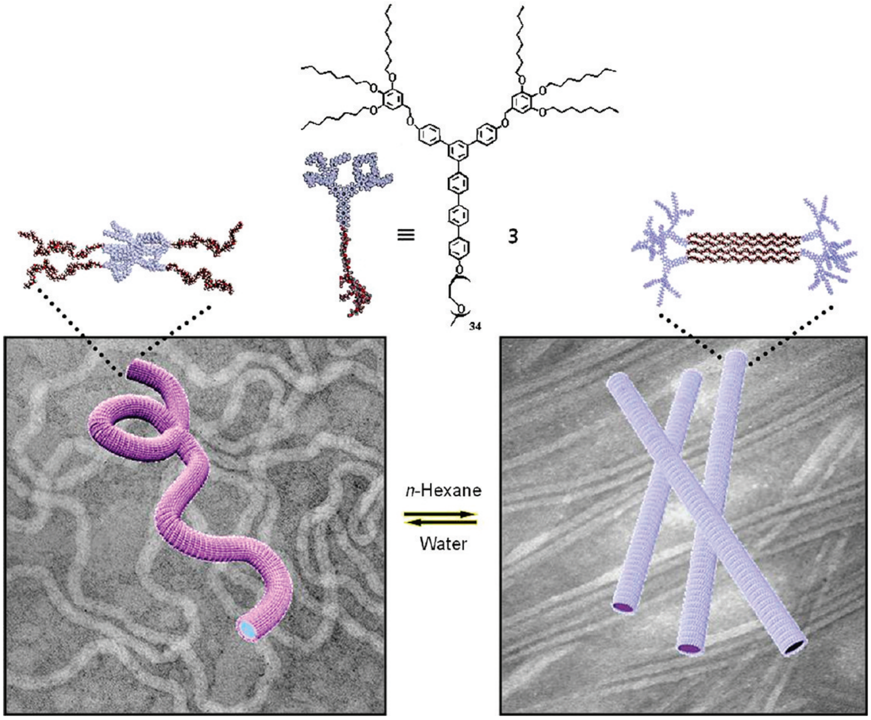

FIGURE 3. Schematic representation and TEM images of the transformation between flexible coil-like and stiff rod-like nanofibers of wedge–coil molecules **3**. Adapted from ref 40 with permission. Copyright 2006 Wiley-VCH.

ment gives rise to amphiphilic molecule **3**. Interestingly, this wedge–coil molecule **3** self-assembles into dynamic nanofibers exhibiting reversible switching between rigid rod-like fibers and flexible coil-like fibers triggered by solvent polarity (Figure 3).[40] In polar aqueous solution, the core of the nanofibers consists of noncrystallizable branched alkyl chains, leading to highly flexible nanofibers with an amorphous core. In nonpolar *n*-hexane solution, however, the core of the fibers consists of highly crystallizable PEO chains. The wide-angle X-ray scattering (WAXS) and FTIR experiments indicate that the PEO chains in hexane solution adopt a highly ordered crystalline packing. Eventually, high crystallinity of the core leads to stiff nanofibers. This result indicates that the structural inversion drives the flexible nanofibers to be highly stiff.

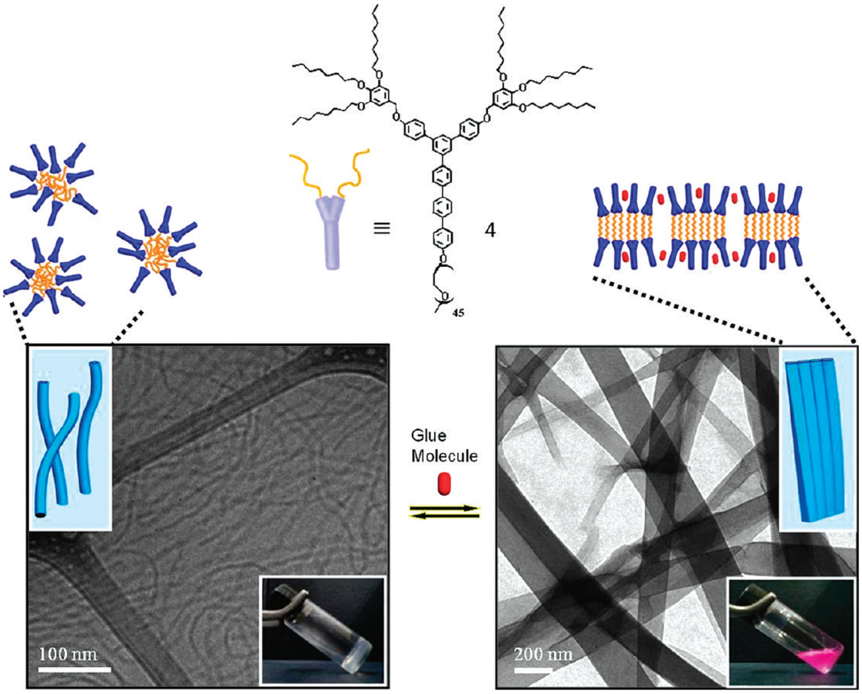

FIGURE 4. Schematic representation and TEM images of the transformation of single nanofibers to flat ribbons driven by addition of aromatic guest molecules. Adapted from ref 41 with permission. Copyright 2008 Wiley-VCH.

Collectively, the nanofibers can be considered to recognize solvent polarity by changing their stiffness.

The flexible nanofibers formed in aqueous solution entangle with each other to form stable gels. Interestingly, the gels respond to guest addition by changing into fluid solution (Figure 4).[41] Similar to **3**, wedge–coil molecule **4** self-assembles into flexible fibers with a uniform diameter that subsequently, entangle with each other to form gels. The TEM image of **4** (from a 0.01 wt % solution) showed cylindrical fibers with a diameter of 19 nm, and the cryo-TEM image revealed dark cylindrical fibers with a uniform diameter of 10 nm, suggesting that the hydrophobic core consists of twice the length of the hydrophobic segments including the aromatic moiety and alkyl chains. Considering these TEM results and Corey–Pauling–Koltun (CPK) models, it can be concluded that the aromatic segments in the cylindrical cores are arranged in a radial arrangement, which allows space-filling requirements for the long PEO chains. However, addition of aromatic guest molecules, Nile red, triggers the flexible nanofibers to transform into flat ribbon structures, resulting in gel–sol interconnection. This is because the addition of guest molecules into the hydrophobic core enforces the radial arrangement of the aromatic segments to be parallel packing to bind the guest efficiently. Eventually, the parallel packing of the rod segment endows the elementary fibers with hydrophobic side faces. To reduce the hydrophobic side faces that are exposed to water environment, the elementary fibers laterally associate to form a rigid ribbon structure with disentanglement. This disentanglement of the 1-D structure drives the gels to transform into fluid solution. As a result, the nanofibers can be considered to be intelligent nanomaterials that are responsive to an external stimulus by changing their macroscopic properties.

Dynamic Nanostructures from Laterally Grafted Rod Amphiphiles

The construction of hollow tubular structures by molecular self-assembly has been the subject of intense study in recent years for potential applications in areas ranging from optoelectronic devices to bioactive channels.[42,43] The tubular structure can be easily constructed by self-assembly of stiff macrocycles. An alternative strategy to construct a hollow 1D structure includes rolling-up of 2D sheets in one direction to form tubular scrolls.[44] Recently, we reported an example of the thermoresponsive formation of tubular structures by scrolling of planar sheets, which is based on the 2D self-assembly of rationally designed rod amphiphiles **5** (Figure 5).[45] The laterally grafted rod amphiphile **5** consists of a hepta(*p*-phenylene) rod in which hydrophilic oligoether dendrons and hydrophobic branched heptyl chains are grafted opposite to each other at the midpoint of the rod segment. The cryo-TEM and atomic force microscopy (AFM) revealed that the thickness of 2D sheets is about 5.4 nm, indicating that the amphiphilic rods are packed in a bilayer arrangement, in which the rods are arranged parallel to the 2D planes.

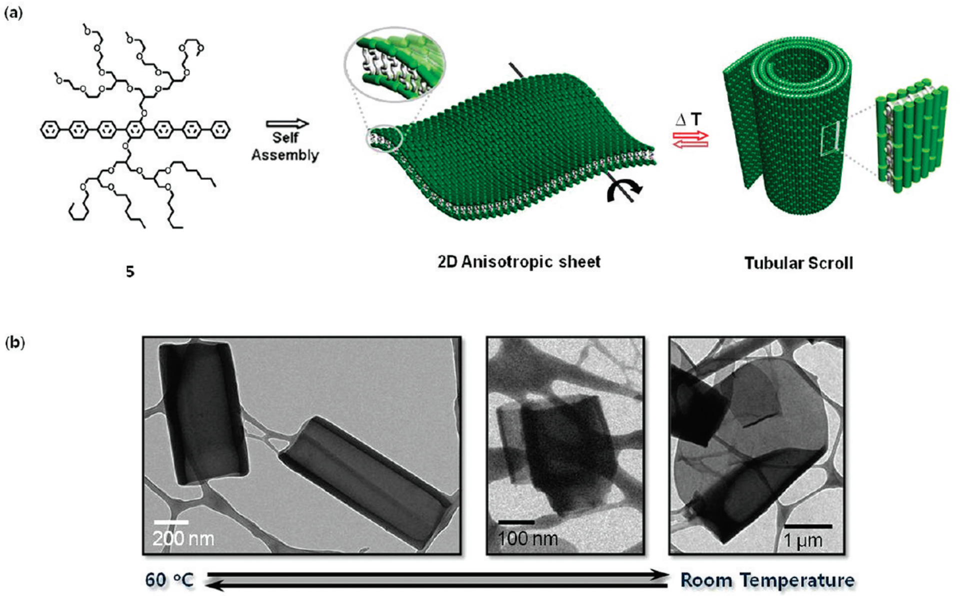

FIGURE 5. (a) Molecular structure and schematic representation and (b) TEM images of thermoreversible scrolling of anisotropic planar sheets of **5**. Adapted from ref 45 with permission. Copyright 2009 Wiley-VCH.

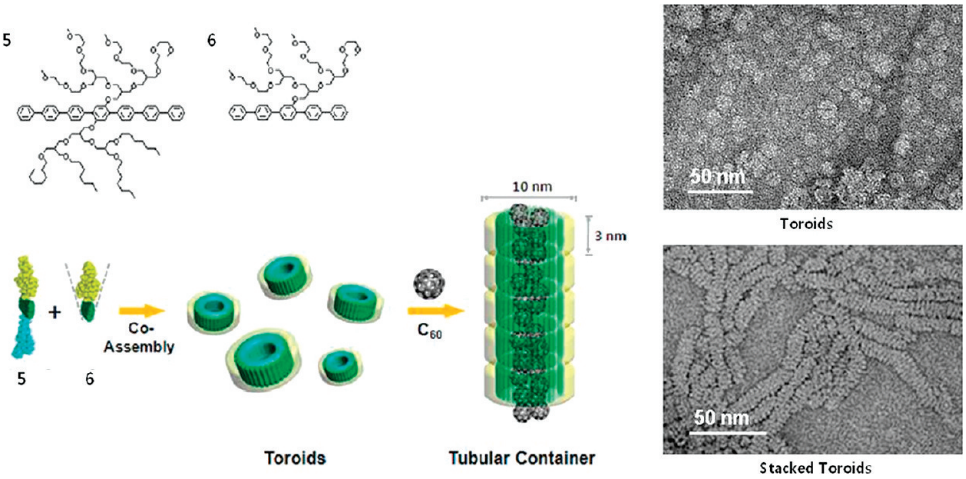

FIGURE 6. Schematic illustration and TEM images of the stacking of toroids in a 1D manner upon addition of C_{60} guest molecules. Adapted from ref 46 with permission. Copyright 2009 American Chemical Society.

Remarkably, as shown in TEM and scanning electron microscopy (SEM) experiments, the planar sheets of **5** roll up into tubular scrolls upon heating to 60 °C. After cooling to room temperature, the tubular structures are fully recovered into the planar sheets. This reversible structural change is attributed to the LCST behavior of oligoether chains.[34] Above LCST, the planar sheets, where the aromatic rod segments are aligned parallel to the sheet plane, would be unstable owing to the enhanced surface energies resulting from the hydrophobicity of the dehydrated oligoether chains. To reduce unfavorable contact between hydrophobic surfaces and water, the planar sheets roll up along the direction of the rod axis to form tubular scrolls. This unique structural transformation arises from in-plane orientational order of the rod segments. The resulting anisotropic sheets, upon heating, spontaneously roll up along the rod axis to form tubular scrolls. Thus the design of rod amphiphiles with lateral chains provides a novel opportunity to construct hollow 1D nanostructures.

In a subsequent work, we have found the formation of water-soluble toroids with a hydrophobic cavity by coassembly of laterally grafted amphiphiles and their tubular stacking triggered by guest (C_{60}) encapsulation (Figure 6).[46] As we described above, **5** self-assembles into infinite sheets. Notably, the sheets break-up into toroidal micelles upon addition of rod amphiphile **6** containing only a hydrophilic chain, indicating that the 2D structure transforms into discrete nanostructures with hollow interior triggered by coassembly. The transformation into the discrete toroids is attributed to the increasing volume fraction of hydrophilic segments through coassembly inducing the highly curved interfaces, to relieve steric crowding at the flat rod–coil surfaces of the sheets. The observed dimension of the internal cavity together with the molecular length indicates that the toroids have hydrophobic interiors. The formation of the water-soluble toroids with a hydrophobic cavity stimulated us to investigate whether the toroids encapsulate hydrophobic C_{60} molecules in aqueous solution. Notably, the addition of hydrophobic C_{60} molecules into aqueous toroidal solution drives the toroidal rings to stack on top of one another to form a 1D tubular assembly. As shown the TEM image of the mixed solution containing 30 mol % C_{60}, individual toroids with a height of 3.3 nm stack along the cylinder axis to form a tubular container with a diameter of 10 nm. The 1D stacking of toroids results from enhanced hydrophobicity in the up and down of the toroids due to the encapsulation of hydrophobic C_{60} molecules. To reduce the contact of the hydrophobic parts of the toroids to a water environment, the toroids are stacked together to form tubules in which C_{60} molecules are arranged in one dimension along the tubular cavity. This result represents a good example of directional assembly of discrete nanostructures triggered by an external stimulus.

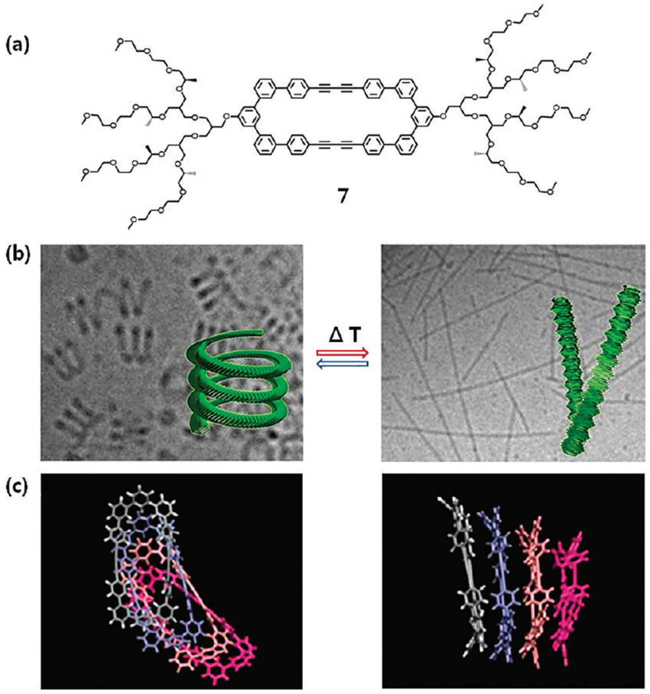

FIGURE 7. (a) Molecular structure and (b) schematic representation of reversible transformation of helical coils and straight rods of **7** and (c) molecular modeling of **7** indicating that boat conformations of macrocycles stabilize the helical coil structure: top view (left) and side view (right). Adapted from ref 49 with permission. Copyright 2009 American Chemical Society.

Switching between Helical Coils and Straight Rods

Most shape-persistent macrocycles self-assemble into hollow cylindrical micelles.[47,48] A major challenge in assembling rigid cyclic molecules into the nanostructures lies in their capability to respond to external stimuli. To obtain controlled aggregates that are able to respond to external stimuli, however, a more elaborated design of the corresponding building blocks is required. Accordingly, we have synthesized amphiphilic molecules based on an elliptical macrocycle that can endow aggregates with a responsive character through a conformational change. Elliptical macrocycle **7** self-assembles into helical coils (Figure 7). Remarkably, this curved structure showed, upon heating, extension to transform into straight rods.[49] At room temperature, the TEM image of aqueous solution revealed that **7** self-assembles into cylindrical fibers with a cross-sectional diameter of ~3 nm, which subsequently form highly curved helical coils with a diameter of ~30 nm and a pitch of ~10 nm. The CD spectra of the resulting helical assembly exhibit a strong Cotton effect over the absorption ranges, indicating the formation of helical aggregates with a preferred handedness. Upon heating to 50 °C (LCST), cryo-TEM of the solution of **7** revealed the transformation into straight rod-like cylinders with a uniform diameter of ~3 nm, indicating that the helical coils spontaneously unfold into straight rods. This switching behavior between helical coils and straight rods could be explained by considering a conformational change of the elliptical macrocycle caused by LCST of the oligoether chains. At room temperature, the elliptical macrocycle adopts a boat conformation, as confirmed by MD simulations (Figure 7b). The resulting nonplanar macrocycles are stacked with a slightly slipped and staggered orientation with respect to their neighbors to form highly curved helical coils. Above LCST, hydrophobic side chains drive the cycles with a boat conformation to be extended to a planar conformation that stack together to form straight rod-like fibers. This thermoresponsive feature of the helical structures represents a significant contrast to other dynamic helical fibers, which show a simple extension–contraction motion or unfold into a random coil conformation with loss of supramolecular chirality.[50,51] This switching behavior of the nanofibers provides a significant example showing how the subtle conformational change in molecular modules triggers a remarkable structural change at a supramolecular level.

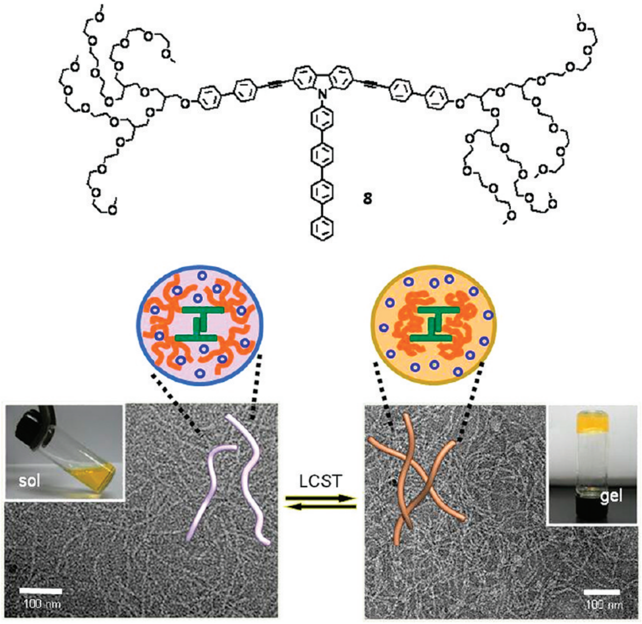

FIGURE 8. Stimulus-responsive sol–gel phase transition of self-assembled supramolecular nanofibers. Adapted from ref 52 with permission. Copyright 2007 Wiley VCH.

Stimuli-Responsive Gels from T-Shaped Molecules

It has been observed that the induced conformational transition often results in changes in the optical and macroscopic properties of the material. Therefore, many researches are focused on the fabrication of smart functional materials where physical properties and functions emerge from stimuli-responsive supramolecular structures. Recently, our group initiated a new strategy to prepare thermoresponsive 3D networks giving rise to a reversible sol–gel transition (Figure 8).[52] The T-shaped aromatic amphiphile **8** based on oligo(ethylene oxide) dendrons self-assembles into a fibrillar structure consisting of aromatic cores in which the T-shaped aromatic segments are packed with dimeric association to maximize $\pi-\pi$ interactions and hydrophilic dendritic corona that are exposed to the aqueous environment. This fibrillar structure of the T-shaped amphiphile with a hydrophilic oligoether dendritic exterior has temperature-dependent solution behavior, which induces a reversible phase transition from the fluid state to a gel with increasing temperature. Upon heating, the oligoether dendrons are dehydrated due to LCST behavior, which results in the nanofibers being hydrophobic. The resulting nanofibers entangle with each other through hydrophobic interactions to form 3D networks. In addition, the hydrogel transforms into a fluid solution by addition of hydrophobic guest molecules because of the breakup of long fibrils into discrete micelles caused by the packing frustration of the T-shaped aromatic segments by intercalation of the guest molecules. In great contrast to conventional fibrillar gels that dissolve upon heating, it is worth noting that the thermoresponsive fibers lead to gelation upon heating.

Structural Changes of Nanorings and Porous Nanostructures

Recently, we have prepared a series of asymmetric dumbbell-shaped rod amphiphiles containing oligoether dendrons at one end and hydrophobic alkyl dendrons at the other end of the stiff rod segment with systematic variation in the length of the hydrophobic alkyl chain.[53,54] The self-assembled structures from these amphiphiles in aqueous solution change from spheres to toroids then to planar nets and finally to vesicles, as the length of hydrophobic alkyl chain increases. The oligoether chains provide a great interest as they exhibit a thermoresponsive property related to LCST behavior in aqueous solution, as we mentioned earlier. Accordingly, the dumbbell-shaped molecules have been systemically investigated to determine whether they would exhibit the reversible structural changes in response to temperature variation (Figure 9).

Dumbbell-shaped rod molecule **9** based on a hexyl chain ($f_{\mathrm{alkyl/EO}} = 0.71$) gives rise to the formation of toroids with a cross-sectional diameter of 15 nm and average size diameter of ~115 nm, as confirmed by TEM. Considering the CPK model of **9** and the cross-sectional diameter of the toroids shown in cryo-TEM images, it can be concluded that the inner core of the toroid consists of a hydrophobic rod and alkyl chains surrounded by hydrophilic dendrons. A further increase in the length of the alkyl chain to a decyl group drives the toroids to transform into 2-D sheets. The cryo-TEM showed that the sheets consist of in-plane nanopores, indicating that the toroidal structure is able to transform directly into planar nets through lateral association. Indeed, upon heating to 70 °C, the toroids coalesced into large planar sheets with in-plane nanopores. The planar nets fully recovered into a toroidal structure upon cooling to room temperature, indicating that this structural change is completely reversible. In addition, the network structure of **10** transforms into hollow capsules with multiwalls at 60 °C. Upon heating above the LCST, the ^{1}H NMR resonances demonstrate the loss of hydrogen bonding interactions between ether oxygens and water molecules. Consequently, the anisotropic rod segments are packed more closely in a parallel fashion within the core owing to the dehydration of the oligoether dendritic chains, resulting in the exposure of the hydrophobic side faces of nanostructures to water. To reduce this unfavorable contact, the discrete toroids and 2D nets transform into 2D porous sheets and closed 2D vesic-

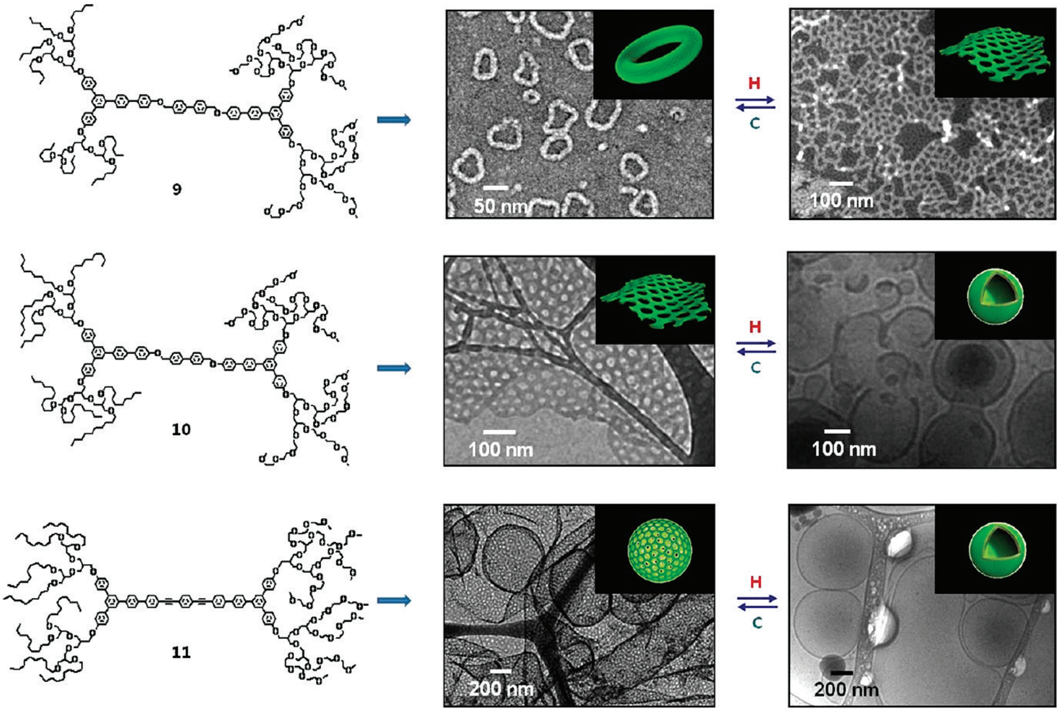

FIGURE 9. Thermoresponsive structural transitions of self-assembled structures of **9**−**11**. Adapted in part from ref 53 with permission. Copyright 2008 American Chemical Society. Adapted in part from ref 54 with permission. Copyright 2010 Wiley-VCH. Adapted in part from ref 55 with permission. Copyright 2008 Wiley-VCH.

ular structures, respectively, through lateral hydrophobic interactions (Figure 9).

This concept can be extended to construct porous capsules with reversibly gated lateral pores. Dumbbell-shaped rod amphiphile **11** self-assembles into hollow spheres with reversibly gated nanopores in the shell.[55] These pores undergo a reversible transition from the open state to the closed state upon heating, and are capable of entrapping cargoes with preservation of their hollow spherical structure. The cryo-TEM images revealed that **11** self-assembles into a capsule structure ranging from several hundreds to a few micrometers in diameter with a uniform pore size of about 25 nm. Upon heating to 65 °C (LCST), the porous capsules transform spontaneously into closed ones without any noticeable changes in spherical shape. Above the LCST, the ethylene oxide segments are dehydrated to collapse into molecular globules, which leads to a decrease in the effective volume fraction of the oligoether chains. To meet space filling requirements, the porous structure with a highly curved local interface transforms into a closed structure with flat local interface to reduce interfacial energy associated with unfavorable segmental contacts. We anticipate that the porous capsules with gated lateral pores offer novel opportunities for biological applications including controlled delivery vehicles.

Conclusion/Outlook

Stimuli-responsive nanostructures are the materials of the future. These materials hold great promise for the fabrication of intelligent nanodevices, nanoelectronics, and nanobiomaterials. We have described our current progress in the development of stimuli-responsive nanomaterials based on rigid−flexible block molecules based on hydrophilic oligoether chains. In fact, stimuli-responsive materials have also been widely explored in polymers, peptides, and various amphiphiles. Every system has its own features and merits. One of the most salient features of the rod amphiphiles comes from its unique anisotropic molecular shape and strong aggregation tendency due to the presence of additional $\pi-\pi$ stacking interactions, which have enabled the construction of highly versatile and dynamic nanostructures. Hence, variations in the molecular structure and local environment, albeit small, allow the rapid transformation of equilibrium morphology. Another advantage of our amphiphilic rods arises from the oligoether oxide flexible chains exhibiting a LCST behavior. Small temperature variations trigger large structural and property changes of the self-assembled nanostructures, giving rise to intelligent nanomaterials. Therefore, the rod amphiphiles based on oligoether chains should be a good starting point in developing responsive materials. The efficient microphase separation even at low molecular weight is the added advantage of rigid–flexible combination into a self-assembling module. Because of the relatively small molecular weight, it has been possible to synthesize highly homogeneous or monodisperse rod–coil building blocks, which is likely to enable facile stimuli-responsive nanostructural transformation and to improve batch to batch reproducibility. For the field to advance further, efforts are necessary in various aspects. One of them is to find the generalizable rules governing self-assembly of rigid–flexible block molecules. Since the field is relatively young, more extensive studies are necessary to find the exact relationship between the building block structure and the physical properties of self-assembled nanostructure. Moreover, diverse materials responsive to various types of conceivable external stimuli, such as electricity, light, and ionic strength as well as temperature, pH, and guest encapsulation state, should be consistently investigated. Finally, the stimuli responsive nanomaterials should be used in appropriate applications carefully and wisely.

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BIOGRAPHICAL INFORMATION

Ho-Joong Kim received a bachelor degree (2002) and his Ph.D. degree in chemistry (2009) under the supervision of Prof. Myongsoo Lee from Yonsei University, Korea. Currently he is carrying out postdoctoral studies as a member of Prof. Lee's group at Seoul National University. He received the Award for Excellent PhD Thesis of the Polymer Society of Korea (2009) and Excellent Thesis Award from Yonsei University (2009). His current research focuses on the development of stimuli-responsive nanostructures through supramolecualr assembly of well-defined organic molecules.

Taehoon Kim received a bachelor degree (2007) in chemistry from Yonsei University, Korea, and now is a first year graduate student pursuing his Ph.D. degree at Seoul National University under the supervision of Prof. Myongsoo Lee. His current research focuses on the development of functional nanostructures through self-assembling behavior of aromatic macrocyclic amphiphiles.

Myongsoo Lee received a bachelor degree in Chemistry from Chungnam National University, Korea, in 1982 and his Ph.D. degree in Macromolecular Science from Case Western Reserve University in 1993. After short postdoctoral appointments at University of Illinois at Urbana–Champaign, he joined the Faculty of Chemistry at Yonsei University (1994) and then moved to Seoul National University in 2009, where he is presently Fellow Professor of Chemistry. In 2002, he became a director of National Creative Research Initiative Center for Supramolecular Nano-Assembly. He received the PSK-Wiley Polymer Science Award for Young Scientist (2001), Yonsei Academy Award (2003), Scientist Award of This Month, Korea Ministry of Science & Technology (2006), Samsung Polymer Science Award (2008), and KCS Academy Award (2009). He currently serves as Editorial Board Member for *Chemistry—an Asian Journal* and *Journal of Polymer Science: Polymer Chemistry*. His main research interests include self-assembling molecules, controlled supramolecular structures, and peptide assembly.

FOOTNOTES

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