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Switchable Aromatic Nanopore Structures: Functions and Applications

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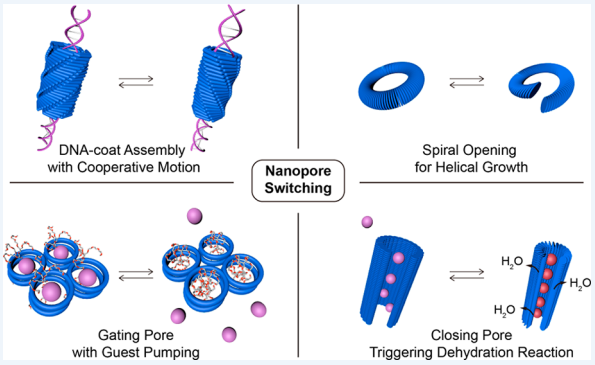
CONSPECTUS: Nanopore structures in nature play a crucial role in performing many sophisticated functions such as signal transduction, mass transport, ion channel, and enzyme reaction. Inspired by pore-forming proteins, considerable effort has been made to design self-assembling molecules that are able to form nanostructures with internal pores in aqueous media. These nanostructures offer ample opportunity for applications because their internal pores are able to perform a number of unique functions required for a confined nanospace. However, unlike nanopore assembly in nature, the synthetic nanopore structures are mostly based on a fixed pore that impedes performing adaptable regulation of properties to environmental change. This limitation can be overcome by integration of hydrophilic oligo(ethylene oxide) dendrons into aromatic building blocks for nanopore self-assembly, because the dendritic chains undergo large conformational changes triggered by environmental change. The transition of the oligoether chains triggers the aromatic nanopore assembly to undergo reversible pore deformation through closing, squeezing, and shape change without structural collapse. These switching properties allow the aromatic nanopore structures to perform adaptable, complex functions which are difficult to achieve using a fixed pore assembly.



In this Account, we summarize our recent progress in the development of switchable nanopore structures by self-assembly of rigid aromatic amphiphiles grafted by hydrophilic oligo(ethylene oxide) dendrons in aqueous media. We show that combining oligoether chains into aromatic segments generates switchable aromatic nanopore structures in aqueous media such as hollow tubules, toroidal structures, and 2D porous sheets depending on the shape of the aromatic building block. Next, we discuss the chemical principle behind the switching motion of the aromatic nanopore structures triggered by external stimuli. We show that the internal pores of the aromatic nanostructures are able to undergo reversible switching between open−closed or expanded−contracted states triggered by external stimuli such as temperature, pH, and salts. In the case of toroidal structures, closed ring-like aromatic frameworks can be spirally open triggered by heat treatment, which spontaneously initiate helical polymerization. Additionally, we discuss switchable functions carried out by the aromatic nanopores such as driving helicity inversion of DNA, consecutive enzymatic action, reversible actuation of lipid vesicles, and pumping of captured guests out of internal pores. By understanding the underlying chemical principle required for dynamic mechanical motion, aromatic assembly can be exploited more broadly to create emergent nanopore structures with functions as complex as those of biological systems.

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1. INTRODUCTION

Protein assemblies with internal cavities in nature are highly dynamic and play a crucial role in performing many sophisticated biological functions such as signal transduction, mass transport, ion channels, and enzyme reactions.[5,6] Inspired by pore-forming proteins, considerable effort has been made to design self-assembling molecules that are able to form nanostructures with internal cavities such as capsules,[7] toroids,[8] tubules,[9] and nanoporous sheets,[10,11] because their internal pores are able to perform a number of unique functions required for a confined nanospace. For example, the hollow interior of supramolecular capsules can be used to encapsulate guest molecules or ions, with potential for subsequent application as nanoscale reaction containers.[12] When tubular assembly forms transmembrane channels, the internal nanopores can mimic biological functions such as control of ion exchange, signal transduction, and molecular transport.[13] Among self-assembling systems, the synthesis of supramolecular structures with internal cavities using aromatic rod building blocks is one of the most attractive topics in organic nanomaterials, because the aromatic building blocks not only endow the pore walls with enhanced stability but also exhibit unique electronic and photonic properties as a result of π-conjugation.[14−16]

When conjugated with hydrophilic segments, the hydrophobic aromatic building blocks self-assemble into supramolecular structures with well-defined internal cavities in aqueous media.[17,18] Nevertheless, the self-assembled structures in aqueous solution cannot yet compete with dynamic pore architectures found in natural systems, especially with regard to open−closed gating, size and shape control of internal pores, reversible mechanical motion, and hierarchical porous structure formation. Therefore, the important issue to synthesize supramolecular structures with hollow interior is the integration of response characteristics adaptable to environmental changes.[19,20] The combination of responsive hydrophilic chains into aromatic building blocks can endow the internal pores with adaptable and switchable functions that are difficult to achieve using nanostructures based on a fixed internal cavity. To construct switchable nanostructures in aqueous media, we have grafted oligo(ethylene oxide) dendrons as a hydrophilic segment into hydrophobic aromatic building blocks to generate aromatic amphiphiles that form responsive nanostructures.[21,22] It is well-known that the oligo(ethylene oxide) dendrons exhibit a thermal transition between hydration and dehydration states which is the so-called lower critical solution temperature (LCST).[23] Upon heating, oligoether dendrons are dehydrated due to breaking of H-bonds between water and ether oxygens, resulting in the collapse into hydrophobic globular conformations. The transition associated with the dehydrative collapse of dendritic oligoether chains occurs in a milder temperature range, typically between 30 and 50 °C, than linear counterparts that show a transition at much higher temperatures due to higher energy requirement for dehydration.[24] The shape and hydrophilicity changes of the grafted oligoether dendrons give rise to fluctuation in the packing arrangement and orientation of aromatic segments, thus resulting in the reversible switching of aromatic self-assembly (Figure 1).[4,25,26] The change of

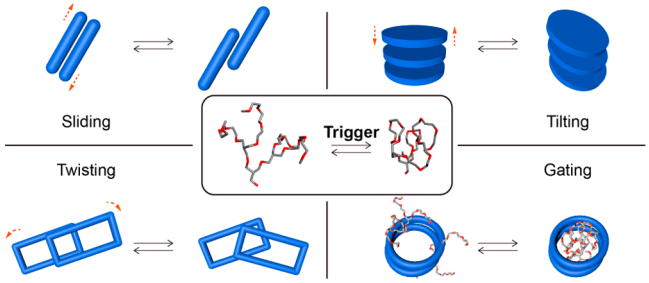

Figure 1. Representative switchable packing modes of aromatic segments triggered by phase transition of oligo(ethylene oxide) dendrons.

packing mode in the aromatic assembly includes slipping of rod building blocks, tilting of disc-shaped building blocks, and twisting of aromatic macrocycles. The oligoether dendrimers exhibit not only a temperature-responsive property but also a salting-out effect in response to salt addition, a hydrophobic collapse behavior similar to a thermal transition. Therefore, salts and hydrophilic small biomolecules such as peptides and carbohydrates can also be used as a trigger for supramolecular switching.[27]

In this Account, we focus on our recent progress in the development of switchable nanopore structures formed through self-assembly of aromatic amphiphiles based on hydrophilic oligo(ethylene oxide) dendrons in aqueous media. The nanopore structures originate from either the stacks of aromatic macrocycles formed by covalent bonds or noncovalent interactions or the curvature driven by the asymmetric arrangement of hydrophilic chains between the basal planes of aromatic stackings. The switchable nanopore structures include tubules, toroids, and porous 2D sheet structures in which their internal pores can be reversibly closed, squeezed, or changed in shape in response to external stimuli. We also summarize how their internal nanopores engender complex functions associated with their switchable properties.

2. SWITCHABLE TUBULAR PORES

2.1. Tubular Structures Based Noncovalent Macrocycles

The realization of complexity of tubular assemblies requires the creation of dynamic nanostructures with controllable functions. Self-assembly of aromatic building blocks provides a facile platform to construct switchable nanostructures with responsive features.[28,29] In contrast to the self-assembling systems based on H-bonds or coordination interactions that make it hard to conduct a dynamic structural switch without bond breaking, self-assembly based on nonspecific aromatic interactions allows neighboring aromatic segments to readily rearrange with each other in response to external stimuli, leading to a switchable nanostructure without structural collapse.[4,25,26] The aromatic tubular assembly with switchable internal pores can be rationally designed and synthesized by using the combination of bent-shaped aromatic building blocks and hydrophilic oligo(ethylene oxide) dendrimers (Figure 2). The bent-shaped molecular geometry with an internal angle of 120° is well fitted into a hexameric noncovalent macro-

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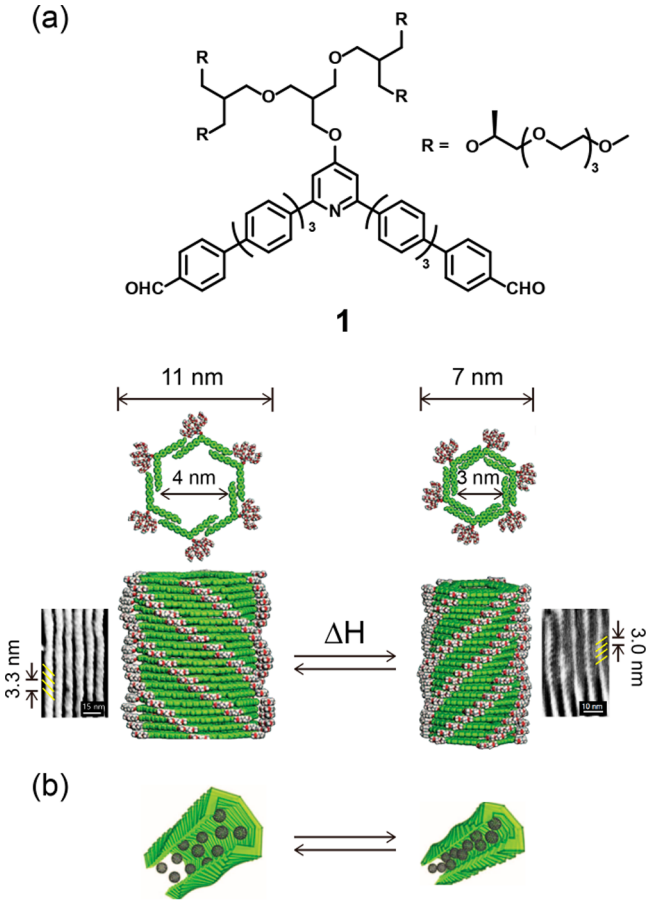

Figure 2. Reversible expanded−contracted switching of the tubular assembly with chirality inversion. (a) Chemical structure of bent-shaped aromatic amphiphile **1**. (b) Schematic representation of the expansion−contraction process with the chirality inversion and the regulated guest−guest interactions. Reproduced with permission from ref 25. Copyright 2012 The American Association for the Advancement of Science.

cycle.[30−33] When they are grafted by hydrophilic chains at the apex such as molecule **1**, the noncovalent macrocycles are surrounded by hydrophilic chains outside the aromatic frameworks.[25] Subsequently, the aromatic macrocycles are stacked on top of each other through hydrophobic interactions to form helical tubules with hydrophilic exterior and hydrophobic interior. The chirality of the helical stacking of the macrocycles is regulated by chirality transfer from chiral dendritic chains. Interestingly, introduction of a pyridine unit on the concave side of the apex of the bent-shaped aromatic segment induces adjacent molecules to slide into a looser packing because pyridine can form water clusters by H-bonding. Consequently, the slipped arrangement of the aromatic segments leads the helical stacks to be expanded with an 11 nm external diameter and a 4 nm internal diameter. The expanded tubules with oligoether dendritic exterior and pyridine interior can be reversibly squeezed through a sliding motion among the adjacent aromatic segments because of thermally regulated dehydration in both the oligoether chains and the pyridine units. The dehydration allows sliding of the aromatic segments from slipped into fully overlapped packings to maximize aromatic $\pi-\pi$ stacking interactions. As a result, heating the solution drives expanded tubules to be squeezed with a 47% internal cavity reduction in cross-sectional area compared to that at room temperature. This size change is fully reversible on cooling and subsequent heating cycles. Notably, this squeezable motion of the tubules is accompanied by chirality inversion from right- to left-handed helical structures, and also reversibly regulates guest−guest interactions encapsulated inside the internal cavity (Figure 2b).

The tubular structure can surround DNA through cooperative interactions to protect DNA against enzymatic degradation and transfect cells with considerable efficiency.[34] The cooperativity can also endow the DNA−coat assembly with simultaneous structural change. When DNA is included inside the tubules, the helicity switching of the tubules drives DNA to undergo cooperative motion (Figure 3).[3] The tubular structure with internal pyridinium cation units is able to wrap the natural DNA molecule inside the hollow cavity through electrostatic interaction between a pyridinium cation and the

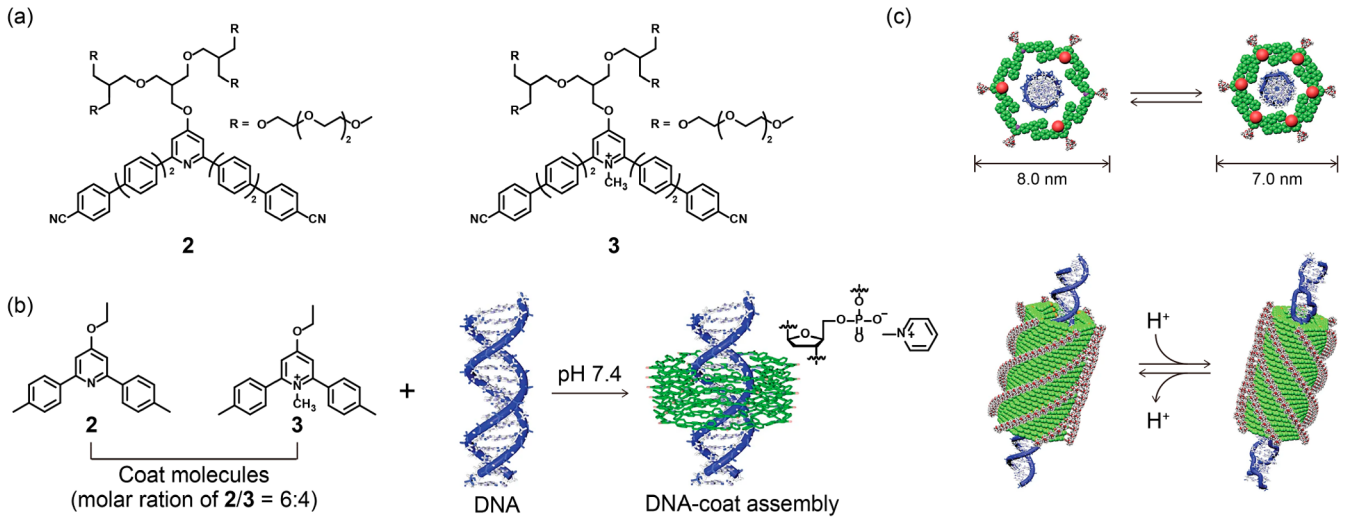

Figure 3. Collective helicity switching of the DNA-coat assembly. (a) Chemical structure of coat molecules **2** and **3**. (b) Schematic representation of the interactions between coat molecules and DNA to form the assembly at pH 7.4. (c) Schematic representation of the collective motion of the DNA−coat assembly with a helicity inversion by a pH change. Reproduced with permission from ref 3. Copyright 2017 Springer Nature.

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phosphate anion of DNA. The switching of the tubular coat assembly can drive helicity inversion of DNA from natural right-handed to highly unstable left-handed DNA.[35] To wrap DNA through electrostatic interactions, we prepared the achiral pyridine-based molecule **2** and pyridinium-based cationic molecule **3** as coat molecules.

When double-stranded DNA is added to an achiral **2** and **3** mixture solution (6/4 molar ratio) at a neutral condition (pH = 7.4), double-stranded DNA induces a helical DNA-coat assembly with an 8.4 nm diameter, demonstrating that the expanded coat assembly based on slipped packings of the coat molecules wraps a single DNA molecule (Figure 3b). The coat assembly based on achiral molecules shows a right-handed helical structure, indicating that the helicity information on the DNA transfers to the coat assembly, and thereby leads to a helical coat assembly with identical handedness to a canonical B-DNA.

When the pH value is lowered, the DNA−coat assembly undergoes collective helicity switching to an opposite handedness which is accompanied by a reversible contraction of the coat assembly (Figure 3c). Because of the pyridine unit in molecule **2** with a pK_a of 5.8, a lower pH can protonate the pyridine unit, causing increased positive charge at the coat interior. Consequently, more positive charges provide a higher binding affinity to DNA and weaken the electrostatic repulsion among DNA phosphates, which stabilizes DNA in a left-handed Z form, relative to a right-handed B form.[36] Moreover, a more efficient confinement of DNA in the tubular coat contributed to a stronger multivalent binding with phosphate anions, driving the relative stability of the two forms to be inverted because of the lower conformational entropy in the Z form with a reduced diameter.[37] As a result, the coat assembly is squeezed through a sliding motion between the adjacent aromatic units to fit the Z-DNA with a reduced diameter. The collective helicity switching can also be triggered by internalization of the DNA−coat assembly into a cell by endocytosis because of the lower pH in intracellular environments. This observation may add some insights into the puzzling biological role of the higher-energy conformer Z DNA within cells.

When the volume fraction of the oligoether dendrimer decreases compared to molecule **1**, the tubular pores are able to be closed−triggered by the H-bonding guest (Figure 4).[38] Aromatic amphiphile **4**, based on decreased chain length in the dendritic segment, forms uniform nanofiber structures based on dimeric micellar stacks with a diameter of 5 nm. Notably, triggered by a hydrogen-bonding guest *p*-phenylphenol, the nanofibers reversibly inflate into tubular structures by forming hollow cavities. The reversible inflation of the nanofibers stems from the packing rearrangements in the aromatic cores from *transoid* dimers to *cisoid* macrocycles triggered by the reversible H-bonding interactions between the pyridine units and the guest molecules.

2.2. Tubular Structures Based on Aromatic Macrocycle Amphiphiles

Nanopore structures in nature undergoing open−closed gating perform various vital processes to regulate biological activities.[39−41] With this in mind, we have synthesized switchable tubular structures with open−closed gating of the internal pores by using aromatic amphiphiles consisting of a disc-shaped aromatic macrocycle and oligoether dendrons (Figure 5).[4] The disc-shaped aromatic amphiphile, **5**, self-assembles into hollow tubules with a 9 nm external diameter

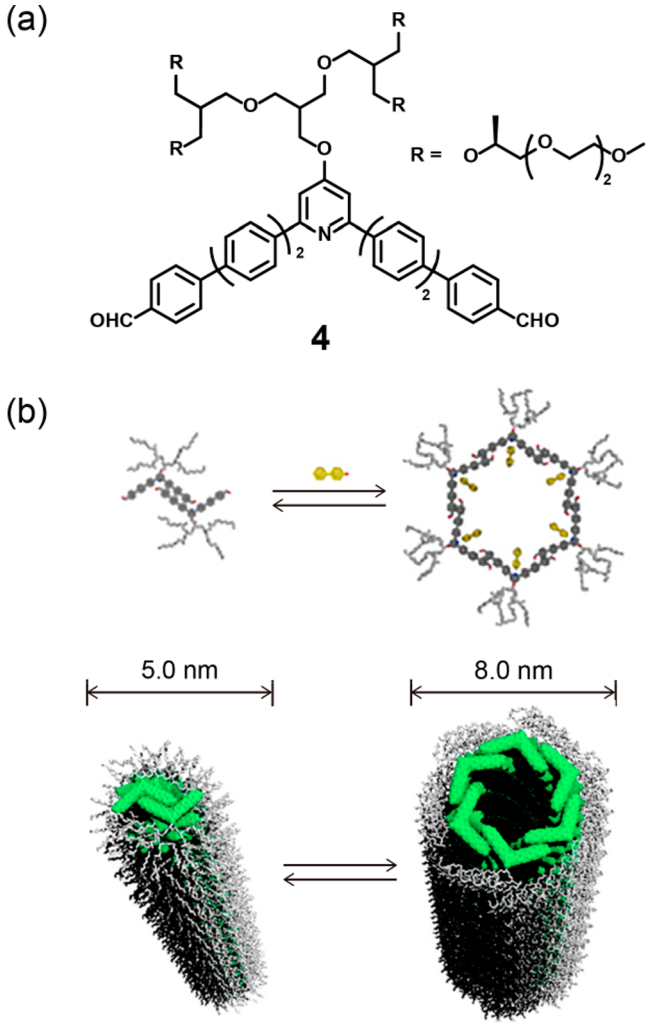

Figure 4. Reversible inflation of a self-assembled nanofiber into a hollow tubule. (a) Chemical structure of bent-shaped aromatic amphiphile **4**. (b) Schematic representation of the inflation process triggered by the guest. Reproduced with permission from ref 38. Copyright 2014 American Chemical Society.

and a 1.8 nm internal diameter. The tubular walls consist of the lateral association of the primary fibrils formed at initial self-assembly conditions. The curvature required to form a tubule has been proven to arise from the asymmetric arrangements of hydrophilic chains between the basal planes caused by the mutual rotation of stacked aromatic discs.

The tubular pores can perform a rapid switching between open and closed states in aqueous solution stimulated by heat (Figure 5b). Upon heating, the dendritic chains become hydrophobic and collapse into a globular conformation, driving the packing mode of the disc stacking from a normal of fiber axis to a tilted state, which can reduce the steric hindrance of the globules with a greater cross section. The tilting of the aromatic discs leads to drastic shrinkage of the tubules in cross section, and thus the internal pores are closed. Considering that closing the tubular pores is accompanied by water pumping action out of the interior, the pore switching can be used for the abiotic dehydration of encapsulated biomolecules (Figure 5c). When the tubules encapsulate AMP inside the cavities and then heat, the closed tubules perform dehydrative cyclization of the encapsulated AMP to yield cyclized AMP (cAMP) without the help of additional catalysts. By

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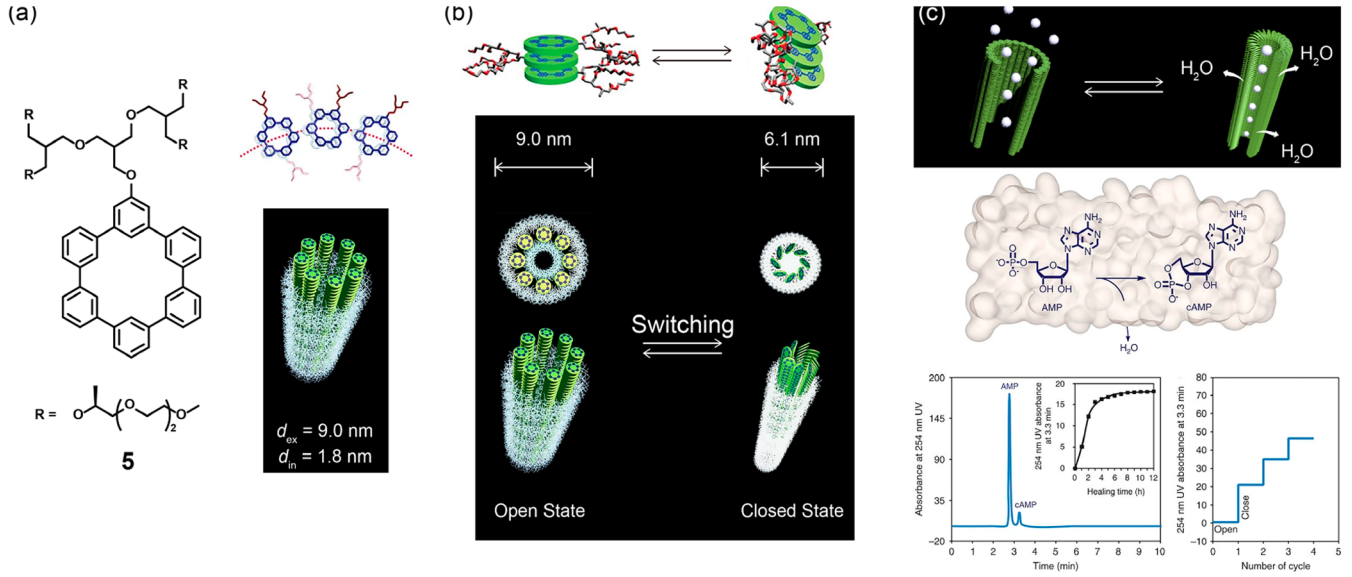

Figure 5. Open−closed gating of the tubular pores. (a) Chemical structure of disc-shaped aromatic amphiphile **5**. (b) Schematic representation of the open−closed switching caused by the slipped aromatic packing triggered by heat. (c) Dehydrative cyclization of AMP to yield cAMP in the closed tubule by water pumping action. Reproduced with permission from ref 4. Copyright 2015 Springer Nature.

conducting several cycles of cooling and heating, the cAMP amount increases consecutively, indicating that in the open state, free AMP diffuses into the tubular pores and then in the closed state the reaction occurs repeatedly. Hydrophobic interior and space confinement in the closed state driven by thermal dehydration of oligoether dendrons are the main driving forces to accelerate dehydrative cyclization inside the tubular cavities. This dynamic switchable pore structure, which can perform a unique water pumping action, may raise new insight into the utilization of hollow structures to encapsulate biomolecules with size-selectivity and convert them into target molecules, to regulate important cellular functions.[42]

The hollow tubules are also able to form by rolling-up infinite 2D sheet structures.[26] Aromatic amphiphile, **6**, consisting of a nonplanar aromatic macrocycle and oligoether dendrimer side groups self-assembles into scrolled tubules in aqueous solution (Figure 6). TEM revealed that **6** self-assembles into scrolled tubules with a ca. 40 nm external diameter. The formation of a highly curved scrolled tubule originates from the slipped and twisted stacking of the adjacent anthracene units in the aromatic macrocycle segments. This twisted packing of the anthracene units which are arranged perpendicular to the layer plane gives rise to rolling the sheets with the axis perpendicular to the fiber direction. The scrolled tubules undergo reversible unfolding at 40 °C. Upon heating, the tightly packed scrolls loosen gradually and subsequently transform into open sheet. Cryo-TEM images show flexible sheet structures at higher temperature, meaning that the scrolls unfold into flat sheets with a thermal stimulation. The original scrolls could be completely recovered after staying at room temperature for 12 h, indicating that the scrolls can undergo a reversible switch between folded and unfolded states. This result provides a nice example in which the internal pores of scrolled tubules are able to reversibly open through unrolling the two-dimensional walls.

3. SWITCHABLE TOROIDAL NANOSTRUCTURES

Toroidal nanostructures in nature such as β-barrels and β-helical bundles accomplish many adaptive functions including transmembrane channels, DNA replications, and microtubule severing.[43,44] By moving from nature to artificial systems, toroidal structures can by synthesized by self-assembly of amphiphilic block copolymers, DNAs, rod−coil amphiphiles, peptides, and proteins.[45] Construction of toroidal structures requires the induction of high interfacial curvature of 1-dimensional nanostructures. This can be achieved by grafting bulky flexible chains into the center of the rigid building block. For example, introducing a hydrophilic dendritic chain to the middle part of the hydrophobic segments, such as *p*-oligophenylene rods or β-sheet peptides, can induce the curvature at the interface of the hydrophobic segments to reduce the steric repulsion of the bulky hydrophilic parts, causing rod-like aromatic segments or short peptide to self-assemble into highly curved toroidal structures.[46,47] Another approach is provided by self-assembly of curved aromatic amphiphiles. For example, bent-shaped aromatic amphiphiles with bulky hydrophilic dendrons generate ring-like non-covalent macrocycles.[25,48] Although a number of toroidal structures have been constructed by self-assembling processes of synthetic molecules, most toroidal assembly exists as a fixed form, and thus is incapable of performing dynamic complex functions required for open-closed switching. One approach to overcome this limitation is applying the adaptable nature of living systems to the artificial toroidal assembly.[49]

To construct switchable toroidal structures, we have designed and synthesized a hexa-*m*-phenylene macrocycle dimeric amphiphile to form toroidal structures which are able to switch between closed toroid and spirally open toroid driven by heat treatment (Figure 7).[1] In aqueous solution, the macrocycle dimer **7** adopts a wedge-shaped conformation through eclipsed folding of the aromatic macrocycles, which is essential molecular geometry. Consequently, **7** with a wedge-shaped conformation self-assembles into highly stable, uniform toroidal structures with a 12 nm external diameter. The toroids

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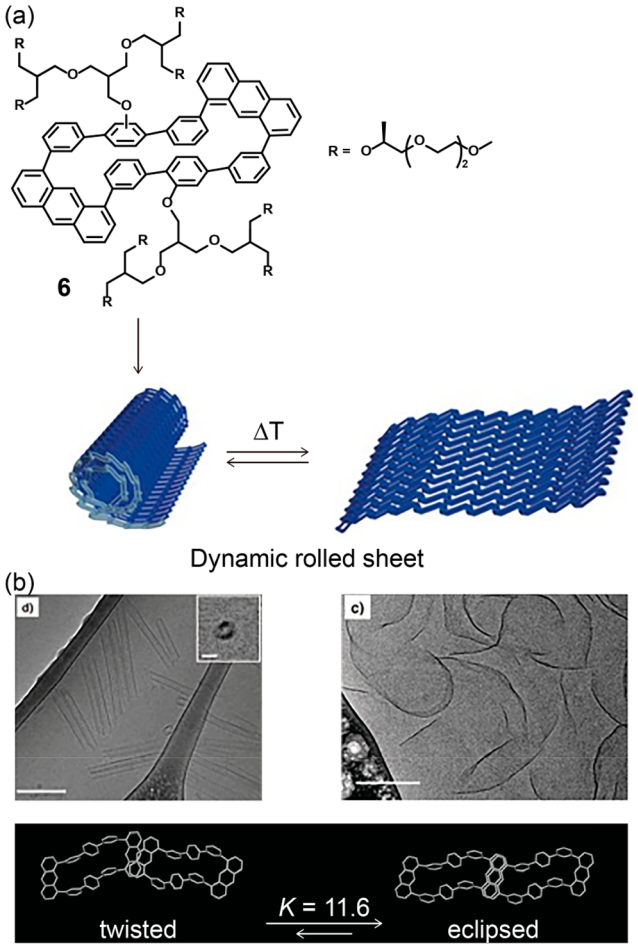

Figure 6. Dynamica rolling behaviors between scrolled tubules and flat sheets. (a) Chemical structure of aromatic amphiphile **6**. (b) Cryo-TEM images and molecular dynamics simulations of the reversible switching between folded and unfolded states (scale bar: 100 nm). Reproduced with permission from ref 26. Copyright 2016 Wiley.

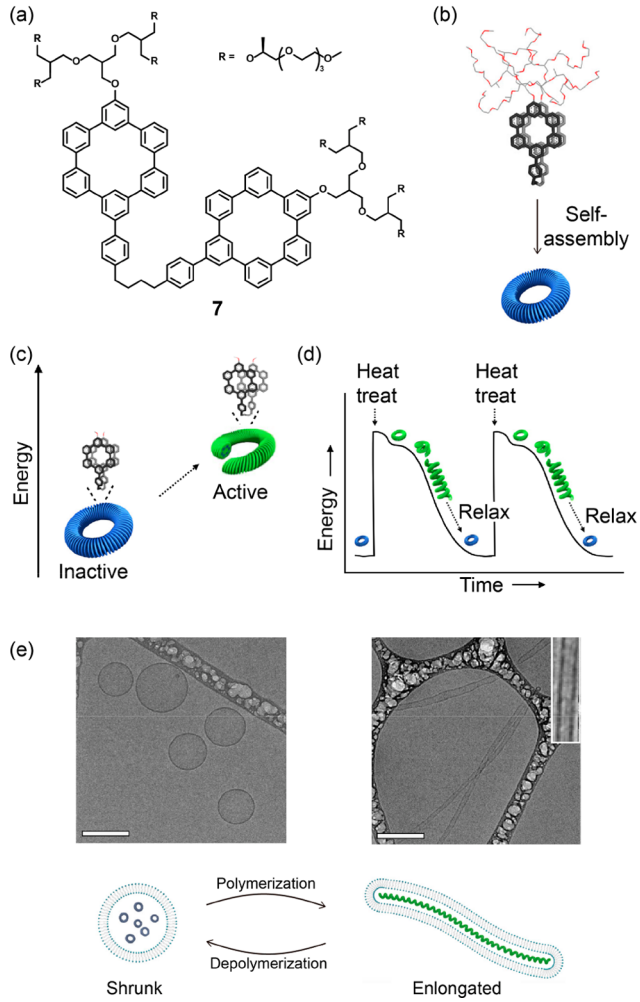

Figure 7. Heat-fueled dissipative helical assembled polymers. (a) Chemical structure of macrocycle dimeric amphiphile **7**. (b) Schematic representation of the toroidal assembly through an eclipsed conformation. (c) Tilting transition of the toroids active by heat. (d) Energy landscape of polymerization/depolymerization cycles. (e) Cryo-TEM images and schematic representation of the elongated–contracted motion of the vesicle with the toroids inside by spontaneous polymerization/depolymerization (scale bar: 200 nm). Reproduced with permission from ref 1. Copyright 2019 Springer Nature.

are able to spirally open accompanied by molecular slipping upon heat treatment (Figure 7c). The spirally open toroid has a high kinetic stability, characterized by a large hysteresis. In the kinetically trapped state, the toroidal objects undergo spontaneous helical polymerization over 4 days (Figure 7d). When the relaxation to a stable state occurs, the helical polymers are unable to sustain. From the fifth day, the helical polymers become shorter with irregular chain scission and finally collapse into the initial intact toroidal objects. The polymerization/depolymerization cycle indicates that energy input triggers helical polymerization of stable toroids via switching into spirally open toroids. After the spirally open subunits are polymerized into a helical polymer over 4 days, the subunits based on slipped packing begin to relax into the equilibrium state by recovery of the eclipsed packing with releasing energy. Thus, the energy stored in the helical polymer is dissipated as the helical chains are depolymerized to recover stable toroids in equilibrium. Upon the subsequent heat treatment, a new cycle of polymerization occurs to form helical chains with the same response efficiency, demonstrating that the deactivated toroids can be repeatedly activated by subsequent heat treatments. Therefore, the helical polymers exist out of equilibrium, only with an energy supply.

By encapsulating the toroids into the lipid vesicles, the helical growth of the toroids can push the membrane of the vesicle into an elongated form, causing a reversable shape change of the vesicle (Figure 7e). TEM showed that the spherical vesicles including the toroids inside are largely deformed into elongated tubules, indicating that the helical growth in the vesicles forces the vesicular membranes to elongate through dimensional response. Subsequent depolymerization allows the elongated vesicles to recover their spherical shape. This result proves that switching into the out-of-equilibrium state can enable the static object to perform spontaneous polymerization/depolymerization as well as the conversion of external stress into mechanical work.

4. 2D SINGLE LAYERED POROUS SHEET WITH OPEN–CLOSED GATING

Single-layered porous sheets have become imperative for separation, transport, pollutant capture, delivery, and catalytic

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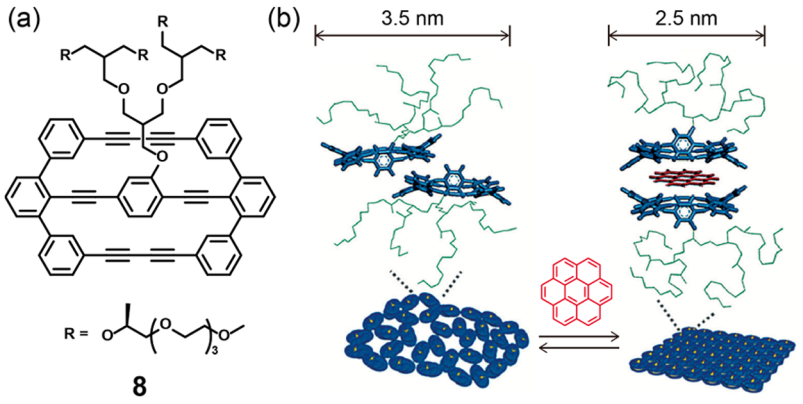

Figure 8. Dynamic motion of 2D porous sheets between open and closed states. (a) Chemical structure of aromatic amphiphile **8**. (b) Schematic representation of the switch between a nanoporous sheet and a closed sheet triggered by guest intercalation. Reproduced with permission from ref 54. Copyright 2013 Wiley.

applications.[50,51] However, most of the single-layered porous materials show poor stability in solution caused by the strong tendency of aromatic stacks of large 2D layers. The layer stacks engender pore block or deformation, thus leading to insufficient pore performance. Therefore, the construction of stable single-layered porous sheets is essential to maintain high pore performance. One approach to prevent sheet stacking is to cover 2D aromatic surfaces by hydrophilic chains.[52] We have demonstrated that, when covered by hydrophilic chains on the 2D surfaces, single-layered nanoporous sheets are very stable in solution without further aggregation and, thus, exhibit nearly perfect pore performance in encapsulation of linear substrates and their macrocyclization.[53]

Besides stability, one important point for 2D planar materials is the integration of dynamic responsive characteristics following the environmental change. The combination of 2D porous structures with responsive properties would generate switchable nanomaterials with extensive application potentials. To address the challenge to construct responsive 2D porous nanostructures, we synthesized an aromatic macrobicycle with a face-on grafted oligoether dendron (Figure 8).[54] The face-on grafted hydrophilic chains can direct the flat aromatic segments to arrange in two dimensions by preventing continuous aromatic stacks in one dimension. In aqueous solution, aromatic amphiphile **8** forms a faced dimer with a slipped packing arrangement in which the hydrophilic chains are located up and down the aromatic basal plane and hydrophobic aromatic side faces. Subsequently, the dimeric micelles grow laterally through side-to-side hydrophobic interactions to form 2D sheets with irregular lateral pores. The irregular internal cavities of the sheet structure are formed between the dimeric micelles because the weak lateral association of the thin dimeric micelles causes in-plane defects. The resulting pores undergo reversible switching between open and closed states triggered by the intercalation of a flat aromatic guest. When coronene as a guest is added into the sheet aqueous solution, the solution readily solubilizes coronene by intercalation while maintaining the 2D structure. The coronene guest sandwiched between the two aromatic basal planes of the faced dimers drives the internal cavities to be closed due to strengthened lateral packing of the dimeric micelles. With the removal of the guest coronene, the original porous sheets are fully recovered. Thus, the in-plane nanopores are able to switch between open and closed states triggered by guest addition without affecting the 2D structure.

The porous nanosheet structures with well-defined internal pores can be constructed by self-assembly of face-on grafted aromatic macrocycle amphiphiles (Figure 9).[2] Aromatic macrocycles are intrinsically well-defined pore structures, thus ideal building blocks for the construction of porous materials with uniform pore size. Molecule **9** with a nonplanar macrocycle conformation self-assembles into homochiral porous sheets in which the pores originate from a faced macrocycle dimer with twisted stacking. The twisted stacking in a preferred rotation generates the chiral pore interior through chirality transfer from chiral dendritic chains. The chiral dimeric macrocycle pores in turn grow laterally through side-to-side hydrophobic interactions to form stable 2D homochiral sheet structures with a well-defined pore size. The pores of the sheets undergo open−closed gating triggered by salt addition. When ammonium acetate is added, the chiral pores of the sheets can be closed by collapse of the dendrimer chains into the macrocycle interior due to the salting out effect, and thus, the pores are closed (Figure 9b).[55] The gated chiral pores preferentially absorb one enantiomer over the other in the open state with more than 96% uptake capacity (Figure 9c). The absorbed enantiomer can be pumped out of the pores by pore closing with the addition of ammonium acetate. In addition to open−closed gating, the porous sheets absorb selectively one enantiomer with very fast absorption in a racemic guest solution, with only one molecular discrimination event, either binding or nonbinding. This is different from the mechanism of current materials for enantioseparation, which rely on a series of interactions between a racemic mixture and the pore walls.[56] This capability of enantioseparation in a single molecular event could allow 2D materials to become a highly efficient alternative to current separation methods.

5. CONCLUSIONS AND OUTLOOK

Aromatic self-assembly to form nanopore structures in aqueous media provides a valuable addition to nanoporous materials for applications in selective binding of substrates, transport, and confined chemical reactions. When integrated with hydrophilic oligo(ethylene oxide) dendrons, aromatic pore structures are able to undergo reversible switching such as open−closed gating and expansion−contraction motion in response to environmental changes such as temperature, pH, and salt addition. The pore switching stems from packing changes between aromatic segments in their assembly state such as

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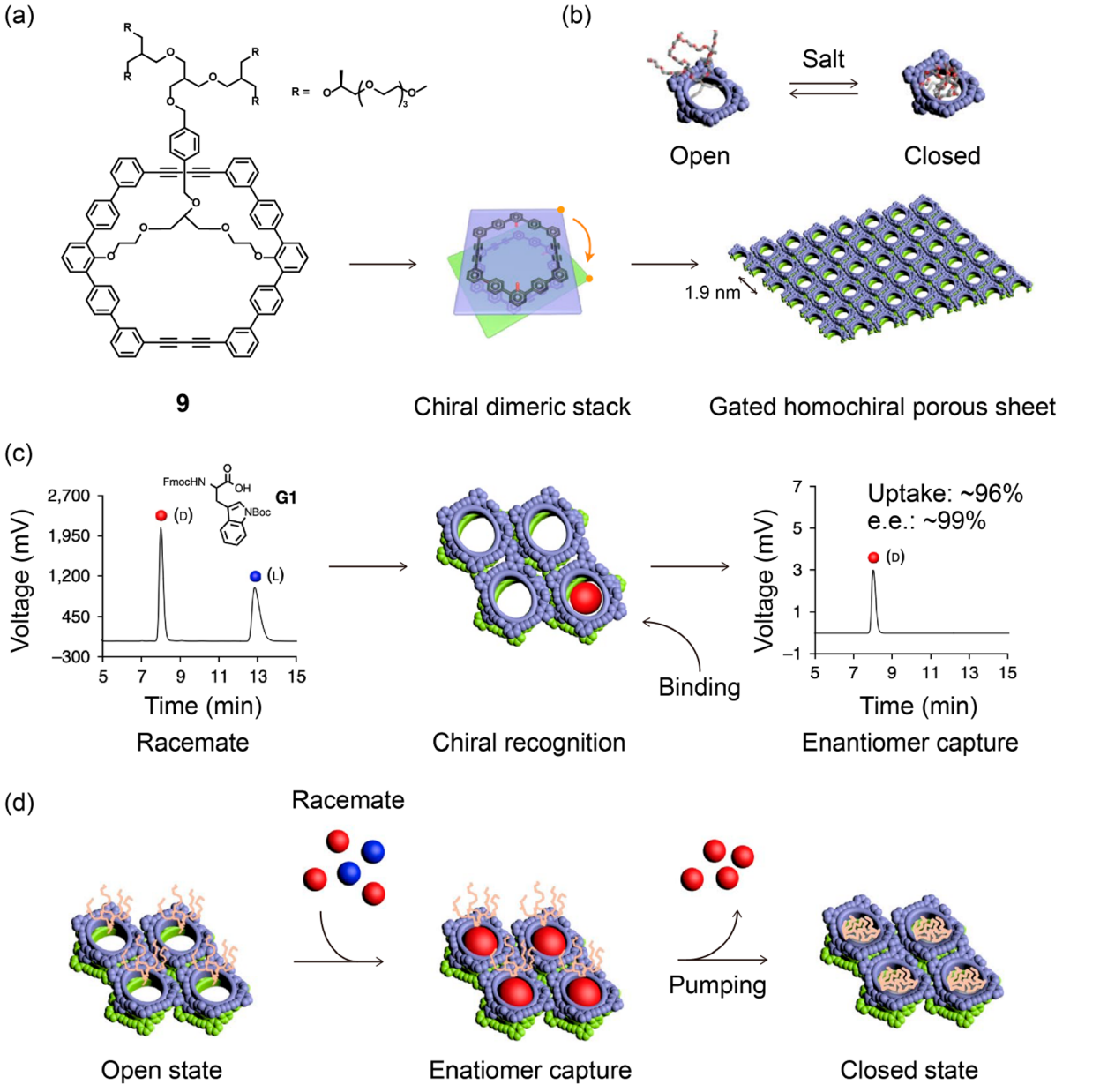

Figure 9. Open−closed gating of homochiral porous nanosheets for enantiomer sieving. (a) Chemical structure of aromatic macrocycles **9** and schematic representation of the formation of homochiral porous nanosheets. (b) Open−closed gating behavior triggered by salt. (c) Chiral recognition and macroscopic separation. (d) Chiral recognition, enantiomer sieving, and pumping action by addition of salt. Reproduced with permission from ref 2. Copyright 2018 Springer Nature.

sliding, tilting, and twisting. Subsequently, the switching properties allows the pore structures for performing complex functions. For example, squeezable tubules can regulate encapsulated guest interactions and, thus, photophysical properties. Tubular switching can also direct helicity switching of encapsulated DNA from natural B-DNA to highly unstable, left-handed Z-DNA through collective motion. Tubules with open−closed gating are able to perform consecutive dehydrative cyclization of a biomolecule through water pumping action. Toroidal structures with polymerization−depolymerization switching, when they are encapsulated inside lipid vesicles, can lead to dynamic actuation of the vesicles by reversible elongation. Moving from single pore structures to porous 2D materials, the multiple pores show nearly perfect enantiomer separation performance with pumping-out of the absorbed enantiomer.

Although the findings above furnish significant insight into the understanding of the driving forces behind dynamic self-assembly, more efforts are still necessary to discover subtle motion using aromatic building blocks with a rational design. Particularly, the responsibility of the switchable self-assembled pores should be extended to other types of external stimuli, in addition to temperature and pH. The pore structures with bioactive parts such as carbohydrates and peptides will be an ideal candidate to understand the structural basis of internal pores regarding how to precisely control and regulate complex biological functions in cells. In this aspect, the bioactive pore structures of the aromatic amphiphiles capable of switching may allow the exploration of obscure bioprocesses and expand

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the range of biomaterials applications. Another important issue to address is how to apply the out-of-equilibrium nature to synthetic assembly to create emergent functions.[57−61] With energy input, pore assembly is able to perform a variety of complex functions, similar to natural pore structures. However, most supramolecular assembly exists in a global minimum state, incapable of exhibiting such complex behaviors. The static nature of synthetic mimics severely restricts dynamic action for the evolution of biomimetic complexity, not yet explored by artificial systems. Translating the out-of-equilibrium feature of biological systems into artificial assembly would be an answer to provide an approach for creating dynamic pore materials with emergent properties far beyond what static systems can allow. The realization of such emergent functions through synthetic pore assembly still remains a great challenge.

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