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Self-division of 2-D sheets in aromatic macrocycle assembly†

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We report that the aqueous self-assembly of aromatic macrocycle amphiphiles containing oligo(ethylene oxide) dendrimers generates switchable 2-D sheet structures. Upon heating, the flat sheets split into uniform nanofibers and subsequent cooling leads to full recovery of the flat sheet, indicative of reversible lengthwise division.

The construction of well-defined nanostructures by molecular design is a major challenge in supramolecular chemistry.^{1,2} A variety of supramolecular architectures has been created by self-assembly of amphiphilic molecules.^{3,4} Among self-assembly building blocks, shape persistent aromatic macrocycles have received great attention owing to their intrinsic pore structures and novel properties.^{5–8} The rigid aromatic macrocycles are able to generate π -stacking assembled nanostructures in solution, nanoporous solids, and fluid phases which have promise for applications in areas ranging from nanotechnology to biotechnology.^{9–12} These macrocycles possess an internal void volume due to their rigid shape which allows the formation of porous structures.^{13,14} The aggregation properties of the shape persistent aromatic macrocycle can be easily modified by grafting side chains which contain various functional properties to endow the macrocycle assembly with specific functions.¹⁵ A wide variety of supramolecular assemblies based on the aromatic macrocycles with a well-defined size and shape including vesicles,^{16,17} nanosheets,¹⁸ nanofibrils,¹⁹ and nanotubes,^{20–22} as well as topologically nontrivial assemblies,²³ have been reported to form in solution.

Among various supramolecular structures, a 2-D sheet structure is particularly interesting because the sheet assembly is able to switch into curved structures with a hollow interior,²⁴ in which the internal cavities are able to perform various functions.^{25,26} For example, self-assembled flat ribbons which are composed of laterally assembled elementary fibrils in methanol folded into closed tubules in response to the addition of a carbohydrate guest.²⁷ Consequently, the 2-D

structures are able to capture a specific carbohydrate by folding into hollow tubules. In addition, we have demonstrated that 2-D structures are able to be spontaneously curved to form hollow capsules by budding in response to curved aromatic guests such as corannulene.²⁸ Recently, we have reported static and dynamic nanosheets formed from selective self-assembly of non-planar aromatic macrocycles based on anthracene units.²⁹ The *transoid* macrocycle isomer generates dynamic rolled sheets which are reversibly unrolled upon stimulation by a thermal signal, while the *cisoid* isomer forms static planar sheets. Furthermore, the mixed solution of the two isomers exhibits self-sorting behavior, leading to the coexistence of the two independent self-assembled structures, the planar sheets and the folded scrolls. This geometric contrast allows each isomer to be readily separated. The rolled sheet structures of the *transoid* macrocycle stem from twist packing of the anthracene unit to match steric requirement of non-planar aromatic macrocycle. This result stimulated us to investigate the switchable self-assembling behavior of planar aromatic macrocycle amphiphiles. Here, we report that 2-D sheet structures formed from the self-assembly of a planar aromatic macrocycle amphiphile are able to reversibly break up into nanofibers upon heating/cooling cycles. In aqueous solution, the amphiphilic aromatic macrocycle self-assembles into stable flat sheet structures through lateral association of primary fibrils with a uniform thickness of 2.0 nm. Upon heating, the sheet structures undergo self-division into uniform nanofiber structures (Fig. 1).

The molecules that form switchable sheets consist of planar aromatic macrocycles and oligoether dendrons grafted at both sides were synthesized in a stepwise fashion according to the procedures described in Scheme 1. The macrocycle amphiphiles were synthesized starting with an etherification reaction of 2,5-diiodophenol and a tosylated oligoether chain. The aromatic intermediate (**3**) was further modified by Suzuki reaction and iodination reaction to obtain the precursor molecule **5**. The final macrocycles *cis-1* and *trans-1* were prepared

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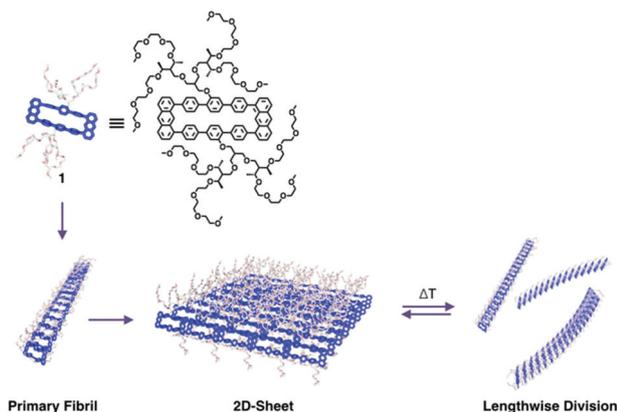
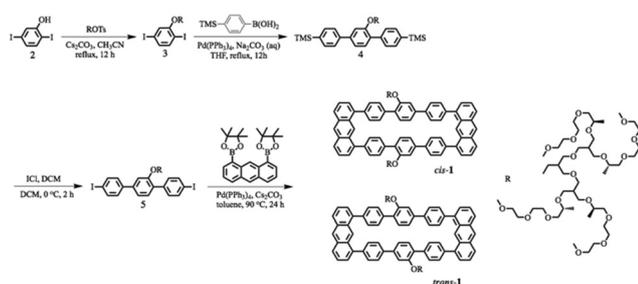


Fig. 1 Molecule **1** and schematic representation of the formation of the 2-D sheet that undergoes reversible break-up into nanofibrils.



Scheme 1 Synthetic method for macrocycle amphiphiles *cis-1* and *trans-1*.

from the Suzuki coupling reaction of **5** and an anthracene derivative in the presence of Pd as a catalyst. The macrocyclization under these conditions led to the generation of two geometric isomers, that is, *cis* (*cis-1*) and *trans* (*trans-1*) isomers which were confirmed by high-pressure chromatography (HPLC) and $^1\text{H-NMR}$ (Fig. 2a and b). To isolate each isomer, we performed HPLC using Prominence LC-20AP (SHIMADAZU) and a YMC C8 reverse phase column (250 × 4.6 mm ID, S 5 μm , 12 nm and 250 × 20.0 mm ID, S 5 μm , 12 nm). The chromatogram showed two peaks that can be attributed to the macrocyclization producing two geometric isomers. The *cis* isomer was eluted faster than the *trans* isomer under our experimental conditions. The chemical structure of each isomer was confirmed by $^1\text{H-NMR}$ measurements. The fraction eluted at 28.2 min showed a singlet peak at 8.80 ppm due to molecular symmetry, indicative of a *trans* isomer (Fig. 2b).

The macrocycle isomers can exhibit supramolecular assembly behavior in a selective solvent for the hydrophilic flexible dendrons because of its amphiphilic characteristics. To investigate the self-aggregation behavior of *cis-1* (0.01 wt%), we performed UV-vis and fluorescence spectroscopy experiments. The absorption maximum of the macrocycle in aqueous solution is red-shifted with respect to that recorded in CHCl_3 , and the fluorescence is quenched (Fig. 2c), which indicates slipped packing of the aromatic segments.³⁰ Time-dependent fluorescence spec-

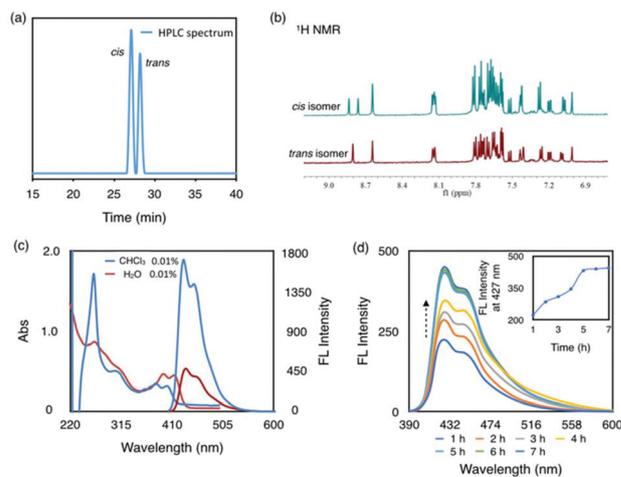


Fig. 2 (a) HPLC traces of *cis* and *trans* isomers. (b) $^1\text{H-NMR}$ spectra of *cis* and *trans* isomers. (c) Absorption and emission spectra of *cis-1* in CHCl_3 (blue line) and aqueous solution (red line). (d) Temperature dependent emission spectrum of *cis-1* in aqueous solution. The inset shows the change of fluorescence intensity with time at 427 nm.

troscopy measurements of *cis-1* revealed that the dynamic self-assembly behavior was stabilized up to 5 h (Fig. 2d), which suggests the presence of aggregates in a water environment. The solution of *trans-1* in aqueous solution exhibited a similar absorption and emission behavior to *cis-1* (Fig. S4†).

The formation of self-assembled nanostructures of the macrocycle amphiphile was investigated with the aqueous solution of *cis-1* using transmission electron microscopy (TEM) and atomic force microscopy (AFM). The TEM image of *cis-1* showed flat 2-D sheet structures with uniform sheet thickness (Fig. 3a). Closer examination of the images showed that the sheet consists of longitudinal stripes with a regular spacing of 3.5 nm, demonstrating that the sheet assembly originates from the lateral association of preformed fibrils (Fig. 3a, inset). The formation of the planar sheet nanostructures was further confirmed using cryogenic TEM (Cryo-TEM) with the vitrified aqueous solution, which provides further evidence that the aggregates exist as flat 2-D sheets in bulk solution (Fig. 3b). Additional structural information of the sheets was obtained by atomic force microscopy (AFM) measurements on a hydrophilic mica substrate in the completely dried state (Fig. 3c). The AFM image of *cis-1* revealed single-layered planar sheets with a thickness of 2.0 nm, which is consistent with the molecular dimensions of **1** (Fig. 3d).

These results demonstrate that the macrocycle amphiphiles self-assemble into stable, single-layered 2-D sheet structures through lateral association of primary fibrils in aqueous solution (Fig. 3e). The formation of the 2-D sheet structure consisting of lateral association of preformed fibrils arises from the tendency of π -stacking of rectangular plate shaped aromatic macrocycles and consequent space-filling requirements.³¹ The molecular architecture comprising a rectangular plate-shaped aromatic segment and a flexible dendrimer segment drives a nanophase separation due to large chemical differences

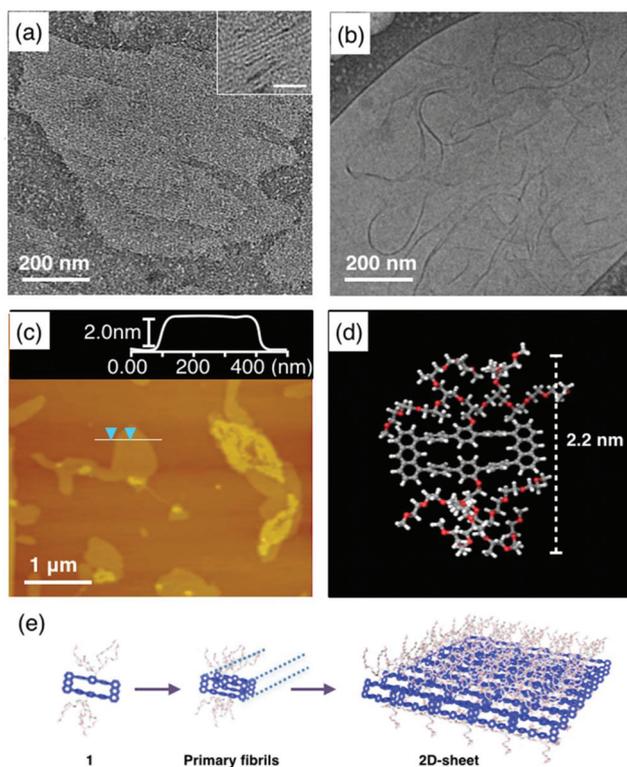


Fig. 3 (a) Negatively stained TEM image of 2D sheets from 0.01 wt% aqueous solution of *cis*-1. The inset shows a magnified image, scale bar: 20 nm. (b) Cryo-TEM image of *cis*-1 from 0.01 wt% aqueous solution. (c) AFM image of *cis*-1 from 0.01 wt% aqueous solution. (d) Molecular modeling of *cis*-1. (e) Schematic representation of the formation of 2D sheet structures through lateral association of elementary fibrils.

between each segment. However, fully overlapped stacks of the plate-like aromatic parts would confine grafting junctions to a flat and continuous interface with a high density of grafting sites, resulting in strong spatial crowding with chain deformation. To minimize chain deformation and fill space efficiently, the fully overlapped aromatic stacks would slip by splaying the flexible chains to provide larger interfacial area, giving rise to a long fibril with slipping aromatic parts (Fig. 3e). The slipped packing of the aromatic macrocycles is reflected in a red-shifted absorption maximum upon aggregation (Fig. 2c). As a result of the hydrophobic aromatic side faces, the elementary fibrils further assemble through side-by-side hydrophobic interactions to generate a planar sheet structure with a thickness of 2.0 nm (Fig. 3e). The single layered sheet structures were found to be very stable without further aggregation because the 2-D aromatic arrangement is covered by hydrophilic oligoether dendrimer chains. Similar to *cis*-1, the *trans* isomer, *trans*-1, forms a 2-D sheet structure in aqueous solution, as confirmed by TEM and AFM. TEM investigations revealed that *trans*-1 was self-assembled into 2-D sheet structures as large as several hundred nanometers (Fig. S5a†), which was further confirmed by AFM measurements (Fig. S5b†).

The formation of the single layered 2-D sheets covered by oligoether surfaces suggests that the aromatic sheets would

have thermo-responsive characteristics in aqueous solution due to the thermal dehydration behavior of the oligoether chains.^{24,29,32} Indeed, fluorescence emission showed quenching at 40 °C, indicative of thermo-responsive behavior (Fig. 4a). This result implies that the thermal dehydration of the dendritic segments leads to closer aromatic packing caused by the hydrophobic environment. To corroborate the structural changes of the 2-D sheet structures, TEM experiments were performed on the aqueous solution of *cis*-1 at 40 °C. In contrast to the image taken at room temperature, the image revealed thin fibrils with a uniform diameter of 4 nm (Fig. 4b), which was further confirmed by AFM measurements (Fig. 4c). This result demonstrates that the sheets are able to split up into uniform nanofibers in response to heating. The splitting of the 2-D sheet upon heating is attributed to the thermal dehydration of the dendritic ethylene oxide chains in aqueous media. At room temperature, the aromatic side faces of the primary fibers are not entirely surrounded by hydrophilic chains. To reduce the contact between aromatic segments and water molecules, the nanofibers laterally assemble into 2-D planar structures. On heating, however, the shrunken oligoether chains taking a globular shape caused by dehydration would make the planar sheet unstable owing to steric crowding between the dehydrated dendritic globules with a larger cross-section on the 2-D flat surfaces; the planar structure transforms into nanofibers to reduce the steric crowding (Fig. 4d). Upon cooling to room temperature and then 24 h resting, complete recovery to the original sheets was observed (Fig. S8a†), indicating that the sheets undergo reversible splitting between sheet and nanofiber states (Fig. 4e). The thermal dynamic behavior of *trans*-1 shows similar results with *cis*-1 (Fig. S6, S7 and S8b†).

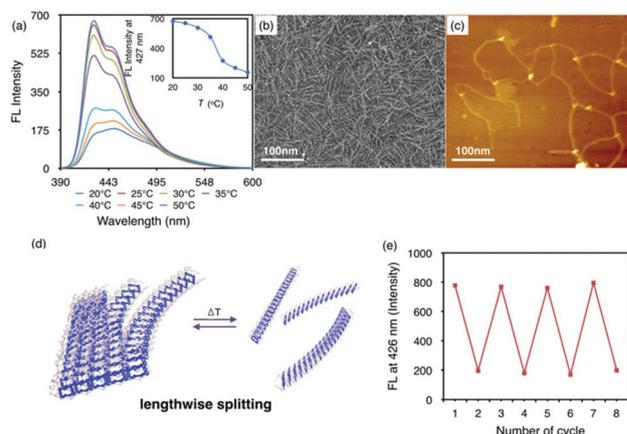


Fig. 4 (a) Temperature-dependent emission spectra of *cis*-1 from 0.01 wt% aqueous solution. The inset shows the change of fluorescence intensity with temperature at 427 nm. (b) Negative-stain TEM image and (c) AFM image of *cis*-1 from 0.01 wt% aqueous solution at 40 °C. (d) Schematic representation of the reversible structural change between sheet and fibers. (e) The reversible induction of emission intensity with the heating/cooling cycles.

In summary, we were able to synthesize macrocycle amphiphiles consisting of a planar aromatic macrocycle segment and hydrophilic dendrimers. The macrocyclization of the precursor molecule afforded two geometric isomers, that is, *cis* and *trans* isomers, which were isolated using HPLC. Both *cis* and *trans* isomers self-assemble into 2-D sheet structures which undergo reversible splitting of the planar sheet structure into long nanofibers triggered by heating-cooling cycles. The dynamic switching behavior of the sheets is attributed to the hydrophilic to hydrophobic environmental changes of the oligoether dendron chains due to thermal dehydration. This unique supramolecular structural change into smaller nanostructures in response to external stimuli might provide a new strategy for rational design and synthesis of intelligent aqueous materials.

Conflicts of interest

There are no conflicts to declare.

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