ChemComm

COMMUNICATION

View Article Online
View Journal

Construction of giant branched nanotubes from cyclodextrin-based supramolecular amphiphiles†

Xiaotong Fan,[a] Liang Wang,[b] Quan Luo,[b] Linlu Zhao,[b] Jiayun Xu,[b] Junqiu Liu*[b] and Qingchuan Zheng*[a]

Cite this: DOI: 10.1039/c5cc01414j

Received 15th February 2015,
Accepted 9th March 2015

DOI: 10.1039/c5cc01414j

www.rsc.org/chemcomm

Giant branched nanotubes were successfully constructed using cyclodextrin-based amphiphiles. The 'backbone' of the nanotubes could branch out into two or multiple branches, from which thinner branches grow out.

Molecular self-assembly, which is very common in nature, plays an important role in the formation process of many highly organized and functionalized biological macromolecules such as viruses and cytomembranes. Inspired by the wisdom of nature, a tremendous effort has been devoted to designing complicated nanostructures in the past decades. Supramolecular amphiphiles with the advantage of easy preparation attracted considerable attention. The amphiphilic supermolecules, which carry hydrophobic and hydrophilic segments within one complex structure, can self-assemble into a variety of configurations. For example, vesicles, nanorings, nanofibers and micelles.[1] The exciting morphologies mainly depend on the architecture of the molecules and noncovalent driving forces, such as electrostatic attraction, hydrogen bonding, charge transfer interaction, metal–ligand coordination, host–guest recognition, and coiled–coil peptide interaction.[2] However, it is still a great challenge to see how to utilize the driving forces discovered to construct more sophisticated nanostructures.

Herein, we successfully constructed a novel kind of nanostructure: branched giant nanotubes. The newly developed structure is triggered by direct self-assembly of superamphiphiles formed by cyclodextrin-based host–guest chemistry. The 'backbone' of the giant nanotube could smartly branch out into two or more branches, from which thinner branches could grow out continually.

β-Cyclodextrin (β-CD), a macrocyclic cavitand consisting of seven glucopyranose units, has a hydrophobic cavity that can serve as a perfect receptor for an adamantanol group. Since this typical host–guest pair could form stable 1 : 1 complexes in aqueous solution, by directly mixing the host molecule β-CD and the guest molecule adamantanol moieties, it has been widely used in the construction of supramolecular assemblies. As an example, Ravoo's group prepared vesicles using amphiphilic cyclodextrins that could recognize adamantanol carboxylate *via* host–guest interaction.[3] Shi *et al.* reported a pseudo block copolymer formed by adamantine-end poly(*N*-isopropylacrylamide) and β-CD-end poly(4-vinylpyridine) though β-CD–adamantane interaction. Micelles formed by the pseudo block copolymer could transform into vesicles *via* changing the pH.[4] Nanotubes based on cyclodextrins arouse considerable attention in these years, for example, Liu *et al.* prepared hollow tubular architectures as nanoreactors though host–guest interaction between the host molecule phthalocyanine-bridged β-cyclodextrins and the guest molecule carboxylated porphyrin.[5] Kim's group demonstrated that vesicles formed by dentron-like molecules could transform into nanotubes upon directly adding CDs into the solution of vesicles *via* host–guest interaction.[6] Yuan and co-workers constructed light-responsive nanotubes though α-CD–*trans*-azobenzene interaction between *trans*-azobenzene-end poly(acrylic acid) and α-CD-end poly(caprolactone).[7]

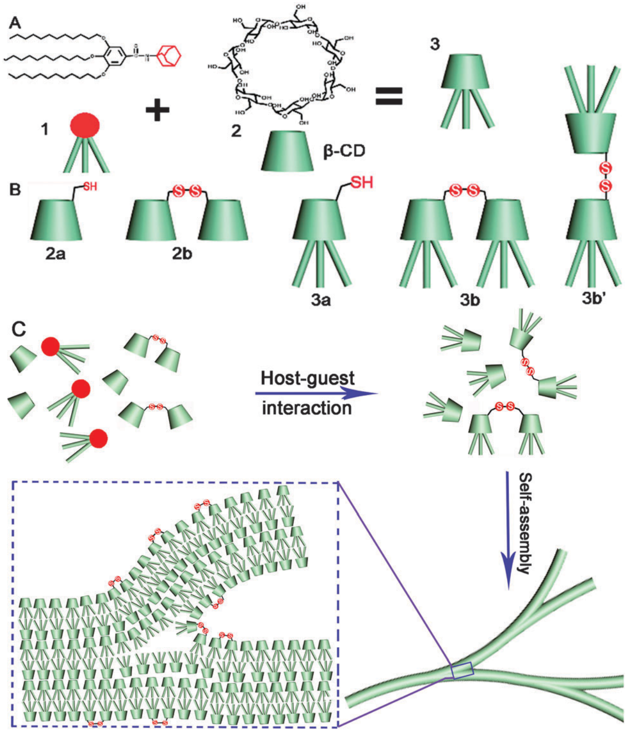
Our previous work has suggested that CD and adamantanol hydrophobic moieties can assemble into unusual giant nanotubes with the large diameter of 500 nm and length of about 20 μm.[8] Inspired by this work, we wondered whether the nanotubes can be controlled to generate branched giant nanotubes. The idea is very challenging, because except for steric straight organic nanotubes, fabricating more sophisticated tubular structures is very difficult and has not yet been explored. To fulfill this purpose, a disulfides linked β-CD dimer, as one of host molecules, was introduced to the assemblies and adamantanol-1-3,4,5-trihydroxybenzoicamide **1** was also used as the guest molecule,

---

[a] *International Joint Research Laboratory of Nano-Micro Architecture Chemistry, State Key Laboratory of Theoretical and Computational Chemistry, Institute of Theoretical Chemistry, Jilin University, Changchun 130012, China. E-mail: zhengqc@jlu.edu.cn*

[b] *State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun 130012, China. E-mail: junqiuliu@jlu.edu.cn*

† Electronic supplementary information (ESI) available: Synthetic procedures and characterization of new compounds, and spectroscopic studies (UV, fluorescence, DLS, NMR). See DOI: 10.1039/c5cc01414j



Scheme 1 Structures of (A) guest molecule **1**, host molecule β-CD **2**, and supramolecular amphiphile **3** formed by **1** and **2** and (B) 6-thio-β-CD **2a**, disulfide linked β-CD dimer **2b** and supramolecular amphiphiles **3a**, **3b** and **3b′**. (C) Schematic representation of the self-assembly of the branched nanotube and proposed self-assembled branched multilayers.

as shown in Scheme 1. We hoped that the giant nanotubes would generate branches when the disulfides linked β-CD dimer was introduced in the self-assembly system.

The disulfide linked β-CD dimer (CD-S-S-CD) was obtained by adding excess H_2O_2 to the aqueous solution of thiolated CD (CD–SH). CD–SH was synthesized from 6-OTs-CD and thiourea *via* refluxing for 50 hours.[9] Details of the reaction procedure and characterization data are outlined in ESI.†

We firstly prepared the amphiphiles using CD–SH and adamantanol-1-3,4,5-trihydroxybenzoicamide. As expected, after self-assembly, we get a straight giant tubular architecture with the length of 20–30 μm observed by optical microscope (Fig. 1b). Transmission electron microscopy (TEM) analysis (Fig. 1e) confirms the nanotube structure. Similarly to the nanostructure formed by CD and adamantanol-1-3,4,5-trihydroxybenzoicamide (Fig. 1a), the inner and outer diameters of these nanotubes here are large, up to 400 nm and 460 nm, respectively, and the thickness of the wall is about 30 nm. The molecule packing mode of these tubes was further investigated by X-ray diffraction (XRD; Fig. 2a). Based on the calculation result from the Bragg equation, we get the bilayer thickness of 3.8 nm. We deduce that the unusual giant nanotubes wall is made up of about eight bilayers of the superamphiphiles. When CD-S-S-CD acts as the host molecule, we discovered that giant branched aggregates with lengths of up to 100 μm emerged (see Fig. 1c), surprisingly.

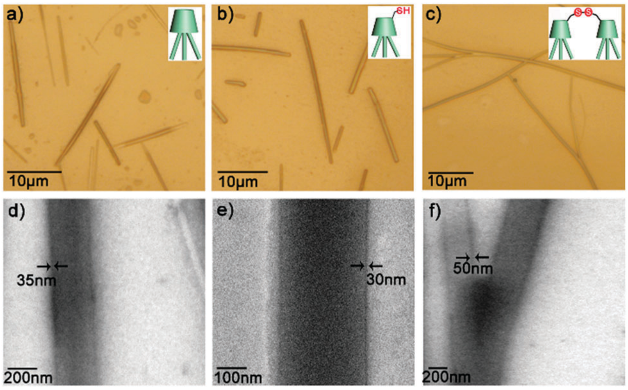


Fig. 1 Images of self-assembled giant nanotubes. Optical microscopy images: (a) the assemblies of **3**, (b) the assemblies of **3a** and (c) the assemblies of **3b**. Transmission electron microscopy images: (d) the assemblies of **3**, (e) the assemblies of **3a** and (f) the assemblies of **3b**. The concentration of β-cyclodextrin units is 5 × 10^{-5} mol L^{-1}.

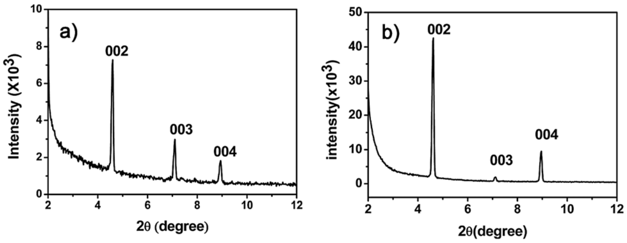


Fig. 2 XRD scan of (a) the nanotubes formed by **3a** and (b) the branched nanotubes formed by **3** with **3b** at a ratio of 4 : 1.

When the disulfides linked β-CD dimer, as one of the host molecules of the amphiphiles, participates in self-assembly, the unbranched nanotubes transform into branch-like aggregates when the β-CD : CD-S-S-CD ratio equals 4 : 1 (Fig. 3c).

The preparation of branch-like aggregates is similar to that of straight giant nanotubes.[8] Typically, the host molecules β-CD (**2**, 22.7 mg) and CD-S-S-CD (**2b**, 46 mg), and guest molecule adamantanol-1-3,4,5-trihydroxybenzoicamide (**1**, 16.16 mg) were, respectively, dissolved in 2 mL DMF. Then, 16 μL of **2**, 4 μL of **2b** and 24 μL of **1** were mixed together to prepare the complex. Then, when the DMF solution of the amphiphile was diluted by deionized water to a final concentration of 0.01 mM under the

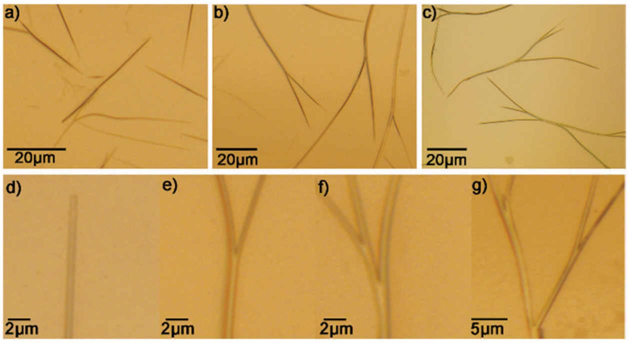


Fig. 3 Optical microscopy images of the branched nanotubes with β-CD : CD-S-S-CD, as the host molecules, at a molar ratio of (a) 10 : 1, (b) 8 : 1 and (c) 4 : 1. (d–g) The magnified structures of the branched nanotubes. The concentration of β-cyclodextrin units is 5 × 10^{-5} mol L^{-1}.

condition of ultrasonication at 30 °C, a novel kind of architecture emerged. Giant dendritic aggregates were observed by optical microscope with a drop of the sample solution placed on a slide and air-dried. The optical microscopy image in Fig. 3c reveals that a great change is made in comparison with that observed in Fig. 1a. We could clearly see that the branch-like architecture emerged with the large length up to 100 μm. It should be noted that the novel structure presents softness and flexibility, this may be attributed to the wiggle of disulfide bonds.

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) were utilized to explore the morphology of these branch-like architectures and provide direct characterization of the 'branched nanotube'. The image of Fig. 3c clearly reveals that the two sides of the 'backbone', respectively, branch out into two branches (named first branch), from which thinner branches (named second branch) grow out. The magnified image of the branched nanotubes (Fig. 3d–g) clearly shows the details of the novel assemblies, the 'backbone' could grow out with two or multiple branches. The SEM analysis (Fig. S2, ESI†) shows that the diameter of the backbone is large, up to more than 1 μm, but the diameter after the first branch is thinner, about 1 μm and 500 nm, respectively. Though the two branches are not the same size, they adopt a similar way to grow out the thinner branches. It should be pointed out that the junction is very smooth, indicating that the aggregate obtained is a whole structure. From the TEM image in Fig. 1f we could clearly see the obvious contrast between the periphery and the central part of the junction, which is typical for the biforked hollow tube structure. Thus, we provide solid evidence that we obtained giant branched nanotubes. It should be noted that the wall thickness of the 'backbone' or the 'branches' is the same size. We deduce that they may adopt the same molecule packing mode in the wall of the nanotubes. The inner and outer diameters of the 'backbone' are large, at 450 and 550 nm, respectively. The thickness of the wall is about 50 nm. X-ray diffraction (XRD; Fig. 2b) was employed to investigate the molecule packing mode of the dendritic structure. Based on the calculation result from the Bragg equation, we get the bilayer thickness of 3.8 nm. We demonstrate that the wall of the branched nanotube is, just like the giant nanotube mentioned above, made up of about thirteen bilayers of the superamphiphiles. This means that the disulfide bonds have no influence on the structure of the bilayers. As we know, the disulfides linked β-CD dimer has two different molecular conformations owing to the wiggle of disulfide bonds: 'head to head' (Scheme 1, **3b′**) and 'shoulder to shoulder' (Scheme 1, **3b**). The two different conformations could induce the bilayers to pack in two different directions, thus, it provides the possibility that the nanotubes grow out branches. As shown in Scheme 1C, a possible arrangement of the supramolecular amphiphile is that one of the cyclodextrin units of CD-S-S-CD is located in the multilayers of one branch, the other unit is located in the multilayers of the other branch of the nanotube. The two cyclodextrin units of the β-CD dimer induce the nanotube to grow in two different directions. In other words, the disulfide bond acts as the linker of the two branches.

In order to exploit the effect of the disulfides linked dimer on self-assembly, a series of complexes with different β-CD : CD-S-S-CD ratios were prepared. We discovered that the extent of nanotube branching was proportional to the amount of CD-S-S-CD in the host molecule. When the β-CD : CD-S-S-CD ratio was 10 : 1 (Fig. 3a), the assemblies presented the trend to branch out, but unbranched nanotubes still accounted for the majority of the assemblies. As the CD-S-S-CD component increased, there became more and more branched structures. At a β-CD : CD-S-S-CD ratio of 8 : 1, obvious branched nanotubes emerge, but most nanotubes only show the first branch (Fig. 3b). When the β-CD : CD-S-S-CD ratio reached 4 : 1, a large area of dentritic aggregates was obtained, and the nanotubes could grow until the second branches (Fig. 3c). We can also observe the structure with multiple branches: the two sides of the 'backbone', respectively, branch out into two branches from which thinner branches grow out. These phenomenon imply that the disulfide bond is crucial for the formation of the branched structure, the nanotube branching out branches should be attributed to the disulphide linked dimer.

To summarize, for the first time, we fabricated giant dendritic nanotubes based on the cyclodextrin-based amphiphiles. The nanotube could generate two branches, from which thinner branches grow out. Meanwhile, this approach of constructing giant dendritic nanotubes is economical, simple, and environmentally benign. It is anticipated that this new finding will provide a new strategy for constructing more diverse nanostructures for material application.

This work was supported by the Natural Science Foundation of China (No: 21234004, 21420102007, 21221063 and 21474038), 111 project (B06009), the Chang Jiang Scholars Program of China.

Notes and references

1 (*a*) J. D. Hartgerink, E. Beniash and S. I. Stupp, *Science*, 2001, **294**, 1684–1688; (*b*) C. Wang, Y. S. Guo, Y. P. Wang, H. P. Xu, R. J. Wang and X. Zhang, *Angew. Chem., Int. Ed.*, 2009, **48**, 8962–8965; (*c*) J. K. Kim, E. Lee, Z. Huang and M. Lee, *J. Am. Chem. Soc.*, 2006, **128**, 14022–14023; (*d*) J. Z. Du, H. Y. Long, Y. Y. Yuan, M. M. Song, L. Chen, H. Bi and J. Wang, *Chem. Commun.*, 2012, **48**, 1257–1259; (*e*) J. W. Sadownik, J. Leckie and R. V. Ulijn, *Chem. Commun.*, 2011, **47**, 728–730.

2 (*a*) C. Wang, Y. S. Guo, Y. P. Wang, H. P. Xu and X. Zhang, *Chem. Commun.*, 2009, 5380–5382; (*b*) X. Zhang and C. Wang, *Chem. Soc. Rev.*, 2011, **40**, 94–101; (*c*) G. S. Chen and M. Jiang, *Chem. Soc. Rev.*, 2011, **40**, 2254–2266.

3 P. Falvey, C. W. Lim, R. Darcy, T. Revermann, U. Karst, M. Giesbers, A. T. M. Marcelis, A. Lazar, A. W. Coleman, D. N. Reinhoudt and B. J. Ravoo, *Chem. – Eur. J.*, 2005, **11**, 1171–1180.

4 J. Zeng, K. Shi, Y. Zhang, X. Sun and B. Zhang, *Chem. Commun.*, 2008, 3753–3755.

5 Z. Q. Li, Y. M. Zhang, Y. Chen and Y. Liu, *Chem. – Eur. J.*, 2014, **20**, 8566–8570.

6 C. Park, M. S. Im, S. Lee, J. Lim and C. Kim, *Angew. Chem., Int. Ed.*, 2008, **47**, 9922–9926.

7 Q. Yan, Y. Xin, R. Zhou, Y. W. Yin and J. Y. Yuan, *Chem. Commun.*, 2011, **47**, 9594–9596.

8 Y. Tang, L. P. Zhou, J. X. Li, Q. Luo, X. Huang, P. Wu, Y. G. Wang, J. Y. Xu, J. C. Shen and J. Q. Liu, *Angew. Chem., Int. Ed.*, 2010, **49**, 3920–3924.

9 B. Tang, H. L. Liang, K. H. Xu, Z. Mao, X. F. Shi and Z. Z. Chen, *Anal. Chim. Acta*, 2005, **554**, 31–36.