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A Linear-Hyperbranched Supramolecular Amphiphile and Its Self-Assembly into Vesicles with Great Ductility

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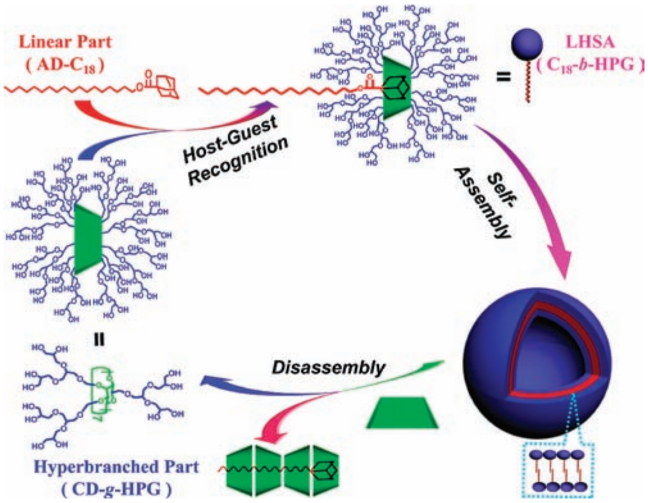
Ⓢ *Supporting Information*

ABSTRACT: A linear-hyperbranched supramolecular amphiphile was synthesized through the noncovalent coupling of adamantane-functionalized long alkyl chain (AD-C_n, n = 12, 18, 30) and hyperbranched polyglycerol grafted from β-cyclodextrin (CD-*g*-HPG) by the specific AD/CD host−guest interactions. The obtained supramolecular C_n-*b*-HPGs self-assembled into unilamellar vesicles with great ductility that could be disassembled readily under a competitive host of β-CD.

Linear-dendritic block copolymers (LDBCs) consisting of a linear chain attached to a dendritic block have received great interest in both academic and industrial fields due to their peculiar structures, properties, and applications.[1] As a mimic of nature, LDBCs very much resemble trees in their architecture and include two types: linear-dendrimer block copolymers and linear-hyperbranched block copolymers (LHBCs).[1,2] The former, pioneered by Gitsov and Fréchet, have well-defined structure but require a relatively tedious multistep synthesis process.[3] The latter, pioneered by Kricheldorf and being less perfect in structure, are much easier to prepare and have properties comparable to those of the former.[4] LHBCs can be synthesized by the "chain-first", "hyperbranched-first", and "hypergrafting" strategies.[4,5] For example, Frey and co-workers first used the "hypergrafting" strategy to prepare the LHBCs containing hyperbranched polyglycerol (HPG) blocks.[5b,6] However, hitherto, all reported linear-hyperbranched molecules including LHBCs involve covalent connection between the linear and hyperbranched segments. In addition, only spherical or rod-like micelles have been reported from the solution self-assembly of these hybrid molecules despite the burgeoning interest in those assembled strutures.[1,7]

Recently, supramolecular amphiphiles formed by connecting micromolecular or polymeric segments through noncovalent bonds have received much attention.[8−12] In this paper, we report for the first time on the construction of linear-hyperbranched supramolecular amphiphiles (LHSAs) through noncovalent coupling of HPG grafted from β-cyclodextrin (CD-*g*-HPG) and adamantane-functionalized long alkyl chain (AD-C_n, n = 18) AD-C_{18} by the specific AD/CD host−guest interactions (Scheme 1). Like LHBCs, the obtained supramolecular C_{18}-*b*-HPG consists of a C_{18} block and a HPG block and is a linear-hyperbranched block molecule in spite of the oligomeric nature of the C_{18} chain. This LHSA further self-assembled into vesicles in water, and the vesicles disassembled into unimers with the addition of a competitive host of β-CD. In addition, the vesicles demonstrated an unexpected great ductility and deformed readily. To our knowledge, this is also the first report on the self-assembly of vesicles from linear-hyperbranched amphiphiles.

Scheme 1. Preparation, Self-Assembly, and Disassembly Processes of C_{18}-*b*-HPG



CD-*g*-HPG ($M_{n,PS}$ = 4500 Da, $M_{n,NMR}$ = 5900 Da, DP_n = 65, PDI = 1.30, DB = 0.6) was synthesized via an anionic ring-opening multibranching polymerization method as reported by Frey, using β-CD as a multi-hydroxyl initiator together with a slow monomer addition technique (Figures S1−S3, Supporting Information (SI)).[13,14] AD-C_{18} was synthesized by the esterification reaction between octadecanol and adamantanecarbonyl chloride (Figure S4, SI). Since AD-C_{18} was insoluble in water, we selected water-soluble sodium 1-adamantanecarboxylate (AD-COONa) and trimethyloctadecylammonium chloride (C_{18}−N^+) as the model compounds to investigate the complexation behaviors between CD-*g*-HPG and AD-C_{18}. In the system of CD-*g*-HPG and AD-COONa, the 2D NOESY spectrum (Figure S7, SI) proves the intermolecular correlations between the internal H3, H5 protons of β-CDs and the protons of AD groups, and the ^{1}H NMR titration experiments (Figure S8, SI) show a low-field shift of the proton signals of AD groups with continuous addition of CD-*g*-HPG. Both results confirm

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the complexation between the β-CD groups in CD-*g*-HPG and AD groups in AD-COONa. The molecular complexation constant (K_C) calculated by the Benesi–Hildebrand equation is about 1.7 × 10^3, which is lower than the typical K_C ($\sim10^4$) between β-CD and AD groups.[15] Evidently, the grafted HPG in CD-*g*-HPG weakens the AD/CD host–guest interaction. However, in the system of CD-*g*-HPG and C_{18}–N^+, no obvious intermolecular correlations or chemical shift dependence of the C_{18} proton signals on the CD-*g*-HPG concentration was observed in the 2D NOESY (Figure S9, SI) or ^{1}H NMR titration spectra (Figure S10, SI). Thus, the β-CD groups in CD-*g*-HPG are difficult to complex with the C_{18} chains, probably due to the steric hindrance of the grafted HPG chains.

According to results of the model compound study, AD-C_{18} and CD-*g*-HPG should form the LHSA of C_{18}-*b*-HPG through the host–guest recognition between AD and CD groups. In addition, C_{18}-*b*-HPG may further self-assemble into superstructures due to its inherent amphiphilicity.[10,16] As proof-of-principle experiments, the complexation and self-assembly of AD-C_{18} and CD-*g*-HPG were performed by adding water dropwise into a DMF solution of them, followed by dialysis against water to remove DMF. A stable aqueous solution with a bluish tint and a final polymer concentration of 1 mg/mL was obtained. The DLS result indicates the formation of aggregates with a broad size distribution from 60 to 600 nm (Figure 1b and the inset). AD-C_{18} is insoluble, while CD-*g*-HPG is water-soluble and exists in the form of unimers of around 2 nm diameter over a wide range of temperatures (Figure 1a and Figure S11, SI). Thus, the big aggregates were believed to originate from the self-assembly of supramolecular C_{18}-*b*-HPG. This was further proved by the pyrene excimer experiments (Figure S12, SI). As further evidence, the aggregates were collected by freeze-drying and characterized by ^{1}H NMR measurement in DMSO-d_6 (Figure 1d). All the proton signals assigned to AD-C_{18} and CD-*g*-HPG were clearly discerned, and the molar ratio between them was close to the theoretical value of 1:1 (Figure S13, SI).

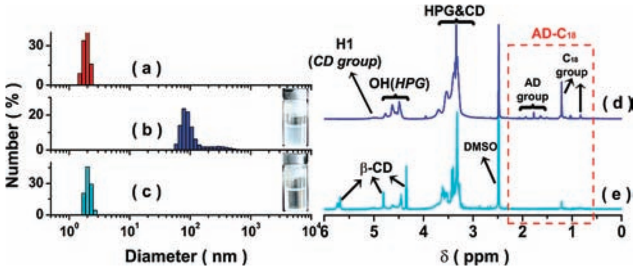

Figure 1. (Left) Number-averaged size distribution of the aqueous solutions of CD-*g*-HPG (a), C_{18}-*b*-HPG (b), and C_{18}-*b*-HPG with β-CD (c). (Right) ^{1}H NMR spectra of the freeze-dried C_{18}-*b*-HPG aggregates (d) and recovered unimers (e) in DMSO-d_6.

C_{18}-*b*-HPG also demonstrated the ability to reversibly assemble and disassemble like other supramolecular amphiphiles.[9b,11a] When a competitive host of β-CD with a stronger complexation capacity was added to the self-assembly system, the aggregates disappeared and a transparent unimer solution (Figure 1c and the inset) with precipitate was obtained. The WAXD result (Figure S14, SI) suggests that the precipitate consists of the pseudorotaxanes derived from the inclusion complexes between β-CD and AD-C_{18}.[17] The matter in the recovered unimer solution was freeze-dried and then analyzed by ^{1}H NMR (Figure 1e; Figure S13, SI), and it consisted of CD-*g*-HPG and excess β-CD with only a few AD-C_{18} residuals (dotted rectangle area). Thus, β-CD can incorporate AD-C_{18} from C_{18}-*b*-HPG and trigger the disassembly process as shown in Scheme 1.

The morphology of the aggregates formed by C_{18}-*b*-HPG was observed SEM, TEM, and AFM (Figure 2). The SEM image in Figure 2a shows spherical particles, and the presence of the concave feature (white arrows) in some particles indicates a possible hollow structure of the spheres. The TEM image in Figure 2b indicates the particles are unilamellar vesicles according to a contrast difference between the particle skin and the inner pool.[18] Such a skin/pool structure was further proved by the cryo-TEM measurements (inset in Figure 2b). The AFM images (Figure 2c) of the dried particles show the height-to-diameter ratio is up to 1:20, indicating a thin-layered and collapsed vesicle structure.[11b] The hollow lumens of the vesicles were also directly observed in the AFM images (Figure S15, SI).

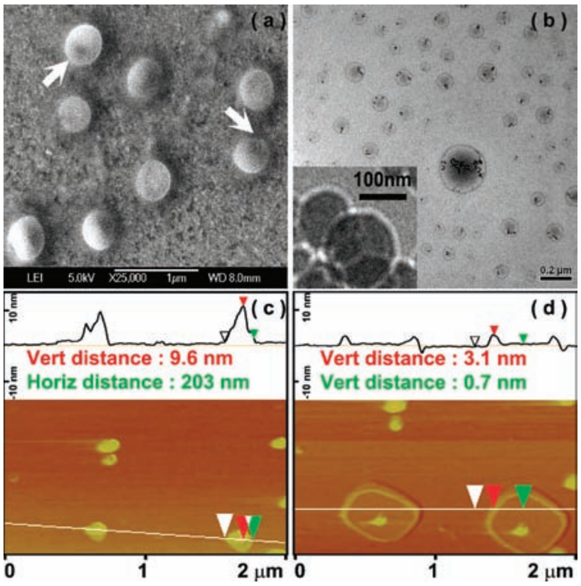

Figure 2. Self-assemblies captured by SEM (a), TEM (b), cryo-TEM (inset in b), and AFM (c,d). The force was increased to 2.1 nN on AFM tip in image (d).

Although the vesicle size is polydisperse according to the DLS and TEM results (Figures 1b and 2b), the vesicle wall thickness is almost uniform, about 8 ± 1.4 nm through the statistical analysis of 30 vesicles from the TEM images. Considering that the extended length of C_{18}-*b*-HPG calculated with Chem3D is around 3.7 nm (Figure S16, SI), the vesicles may possess a bilayer structure with two hydrophilic HPG shell layers and one hydrophobic alkyl chain core layer, as shown in Scheme 1. Solution-state ^{1}H NMR measurements provide direct evidence to support the core–shell structure. With the addition of D_2O into the CD-*g*-HPG/AD-C_{18} DMSO-d_6 solution, the vesicular self-assembly occurred, and the proton signals of AD-C_{18} were almost totally shielded by the strong HPG proton signals (Figure S17, SI). At present, we cannot explain why such a LHSA favors the formation of vesicles, and we hope to disclose it in the near future by a theoretical simulation study.

The colloidal stability of the vesicles is excellent, so no morphology and size changes (Figures S18 and S19, SI) were observed for half a year after the vesicle solution was prepared. Interestingly, the vesicles deformed greatly when the force of the AFM tip was increased in the tapping-mode AFM experiments. For example, the two vesicles in Figure 2c (white line) show an expansion of about 300% in radii after deformation (Figure 2d). The heights of the periphery and center of the deformed vesicle are about 3 and 0.7 nm, respectively. The former is approximately the size of a C_{18}-*b*-HPG molecule, and the latter is close to the size of CD-*g*-HPG with a collapsed structure. Thus, we speculated that the vesicle deformation was induced by the sliding or decomplexation of C_{18}-*b*-HPGs under external force. The largest vesicle deformation is about 450%. In addition, we found the vesicles, after being kept in solution for half a year, also possessed such good ductility (Figure S19, SI). The vesicle ductility is a good demonstration of the unique dynamic property of supramolecular amphiphiles.

Besides C_{18}-*b*-HPG, we also prepared the LHSAs of C_{12}-*b*-HPG and C_{30}-*b*-HPG through the noncovalent coupling between AD-C_{12} and CD-*g*-HPG or between AD-C_{30} and CD-*g*-HPG, and we found that both of them self-assembled in water into vesicles of around 100 nm in diameter (Figures S5, S6, S20, S21, and S22, SI).

In summary, we have prepared supramolecular linear-hyperbranched block molecules through noncovalent host—guest coupling between the CD-functionalized HPGs and AD-functionalized long alkyl chains. The obtained supramolecular amphiphiles further self-assemble into vesicles in water, which can be disassembled readily by the introduction of competitive hosts. The vesicles are very stable and flexible, and they show great ductility under external force. We believe this work will cast a new light on supramolecular amphiphiles based on hyperbranched polymers.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental materials and instruments; syntheses and characterizations of CD-*g*-HPG, AD-C_n, and supramolecular C_n-*b*-HPG; complexation behaviors of model molecules; WAXD spectrum of rotaxane; vesicle characterizations. This material is available free of charge via the Internet at http://pubs.acs.org.

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