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Self-Assembly of a Tetrapodal Adamantane with Carbazole Branches into Hollow Spherical Aggregates in Organic Media

Masahide Tominaga,*[†] Tetsuro Yoneta,[†] Kazuaki Ohara,[†] Kentaro Yamaguchi,[†] Tsutomu Itoh,[‡] Chihiro Minamoto,[§] and Isao Azumaya*[∥]

[†]Faculty of Pharmaceutical Sciences at Kagawa Campus, Tokushima Bunri University, 1314-1 Shido, Sanuki, Kagawa 769-2193, Japan

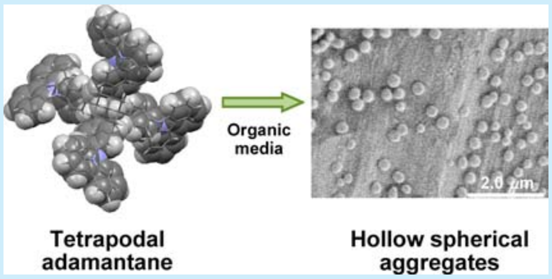
[‡]Center for Analytical Instrumentation, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan

[§]Department of Applied Chemistry and Biotechnology, Niihama National College of Technology, 7-1 Yakumo-cho, Niihama, Ehime 792-8580, Japan

[∥]Faculty of Pharmaceutical Sciences, Toho University, 2-2-1 Miyama, Funabashi, Chiba 274-8510, Japan

Supporting Information

ABSTRACT: A hydrophobic tetrapodal molecule is composed of carbazole units at the periphery linked by a phenyl spacer on an adamantane core. Tetrapodal adamantane self-assembles into hollow spherical aggregates with a multilayer membrane in organic media. The spherical assembly size is dependent on the organic solvent used. Hollow spheres can entrap guest molecules within their internal spaces. By increasing the concentrations of tetrapodal molecules, hollow spheres fused into necklace-shaped nanostructures and two-dimensional networks were obtained.



The self-assembly of planar π-conjugated aromatic molecules and dyes for the fabrication of nanostructures is an important topic in the diverse fields of materials science and supramolecular chemistry because of their applications in molecular devices of electronics, photonics, and optics.[1,2] Different morphological structures including fibers, tubes, rods, and helices can be obtained as a result of noncovalent interactions. Hollow spherical structures such as vesicles and micelles have attracted significant attention for use in light-harvesting systems and fluorescence sensors.[3−5] A wide variety of amphiphilic molecules bearing planar aromatic parts have been used to form vesicles through hydrophobic interactions, hydrogen bonds, and π-stacking.[6−8] These amphiphilic molecules are composed of both hydrophilic and hydrophobic segments within a single molecule. A few examples of vesicles that originate from nonamphiphilic molecules in aqueous and polar organic solvents have been reported, and they possess π-aromatic units and polar groups such as amides, hydroxyls, or urea groups.[9] However, the design of vesicular structures from organic molecules only containing hydrophobic portions without hydrophilic and polar divisions in organic solvents is challenging. This is because their molecular assemblies afford fundamental information about the relationship between the packing of individual molecules and the chemical and physical properties of the spherical nanostructures. Moreover, spherical assemblies such as nanocapsules and nanoreactors may possess an inclusion ability, and they may possess the catalytic activity of the guest molecules within their internal cavity in organic solutions.[10] We report that a tetrapodal adamantane bearing carbazole units, a hydrophobic molecule, afforded hollow spherical assemblies in organic media. The sizes of the spherical aggregates were modulated by changes in the *N*-heterocyclic branches of the tetrapodal skeleton and the properties of the organic media. The hollow spheres can encapsulate guest molecules within their internal cavities. Furthermore, the tetrapodal adamantane exhibited concentration-dependent morphology.

To realize the construction of hollow spherical assemblies from hydrophobic molecules, we designed a symmetrical tetrapodal molecule **1**. It is composed of carbazole units as the planar π-aromatic molecule at the periphery and is linked by a phenyl spacer on the bulky adamantane core (Figure 1).[11] Therefore, the tetrapodal adamantane contains two different types of aliphatic and aromatic divisions in a single molecule, and

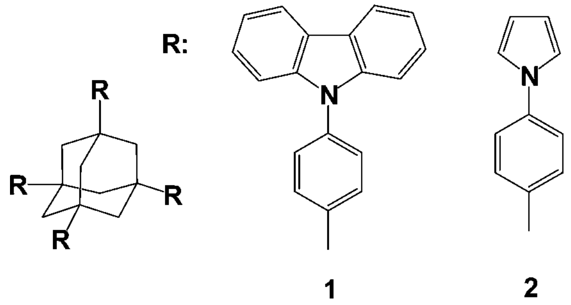


Figure 1. Adamantane-based tetrapodal molecules bearing carbazole (**1**) and pyrrole (**2**) branches.

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it is thus a hydrophobic molecule. The tetrapodal adamantane **1** was prepared by the copper(I)-catalyzed coupling of tetrakis(4-iodophenyl)adamantane with carbazole.

The tetrapodal molecule **1** was dissolved in various organic solvents including tetrahydrofuran, chloroform, and dichloromethane. The aggregation behavior of tetrapodal molecule **1** was examined in three organic solvents. Dynamic light scattering (DLS) measurements of tetrapodal molecule **1** in tetrahydrofuran (0.1 mM) at 25 °C indicated that the tetrapodal molecules formed large aggregates with an average diameter of 201 nm (Figure S1, Supporting Information). The diameters of the aggregates are larger than that of the tetrapodal molecule, implying that these aggregates are mainly vesicular-like structures.[12] Structural information about the aggregates was obtained from a solution of tetrapodal molecule **1** by field-emission scanning electron microscopy (FE-SEM) (Figure 2a). The SEM images revealed planar disklike shapes with a diameter of 220 nm after drying on a solid surface. The flattening of the spherical structures was likely caused by the removal of solvents within the hollow spheres under high vacuum.[13] Evidence for the hollow spherical structures was provided by transmission electron microscopy (TEM) studies (Figure 2b). The micrographs exhibited spherical forms with a diameter of 210 nm, and their hollow nature was confirmed by the contrast between the center and the periphery. The wall thickness was estimated to be 25−50 nm, indicating that the spherical aggregates possess a multilayer structure.

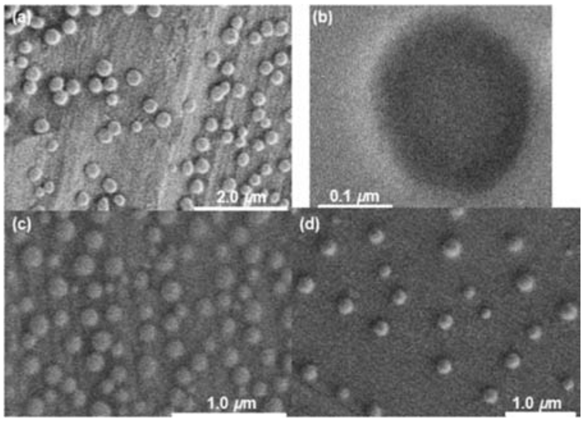


Figure 2. (a) SEM and (b) TEM images obtained from a tetrahydrofuran solution of **1**. SEM images obtained from chloroform (c) and dichloromethane (d) solutions of **1**.

The hollow spherical structures were similarly composed of **1** in other organic solvents. In the apolar chloroform and dichloromethane (0.1 mM) solvents, the SEM images showed spherical structures with a diameter of approximately 140 nm in both solvents (Figure 2c,d). Therefore, the aggregate sizes could be adjusted by the external environment through the properties of the organic solvents. The most striking feature is that spherical assemblies were obtained from the hydrophobic tetrapodal molecule in three organic media. Their spherical structures were stable without further solids precipitation, and this was confirmed by small changes in size over a period of 1 month in the three evaluated solvents.

The structure of tetrapodal molecule **1** was determined by single-crystal X-ray analysis (Figure 3). Colorless plate-shaped crystals of **1** were obtained by the vapor diffusion of hexane into chloroform solutions containing these compounds. X-ray crystallographic analysis revealed that the tetrapodal molecule has a size of 2.1 nm. The tetrapodal molecules formed one-dimensional columnar structures with a saddle-type arrangement (Figure 3a). These assembled into a molecular network via intermolecular CH/π interactions between the carbazole moieties. A rectangular cavity of 4.1 × 7.0 Å^2 in size was formed by the cyclic dimers of tetrapodal adamantane **1**, providing channel structures (Figure 3b). Two molecules of chloroform were encapsulated within the rectangular cavity where CH/π and CH/halogen interactions are evident between the chloroform and carbazole units. The chloroform molecules formed part of the one-dimensional (1D)-zigzag chains via halogen/halogen interactions directly along the channel axis.

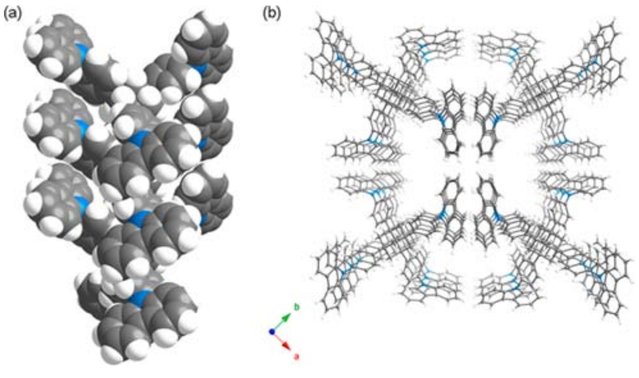


Figure 3. (a) Side view of the columnar structure in a space-filling model and (b) top view of the network structure in a packing diagram of crystal **1**. The chloroform molecules were omitted for clarity.

From X-ray analysis and TEM measurements, the tetrapodal molecule was 2.1 nm in size within the crystal structure, thus supporting the generation of hollow spherical structures bearing a multilayer membrane. On the basis of these results, the tetrapodal molecule self-assembled into vesicle-like structures that were generated by their alignment on the spherical surface. This occurred by the two- and three-dimensional packing of 1D columns of tetrapodal molecules that correspond to the 1D columns in the crystal structure (Figure 4). Because of the compatibility of the aromatic parts with the three organic solvents, the carbazole moieties on the tetrapodal skeleton were presumably located on the exterior of the spheres, while the

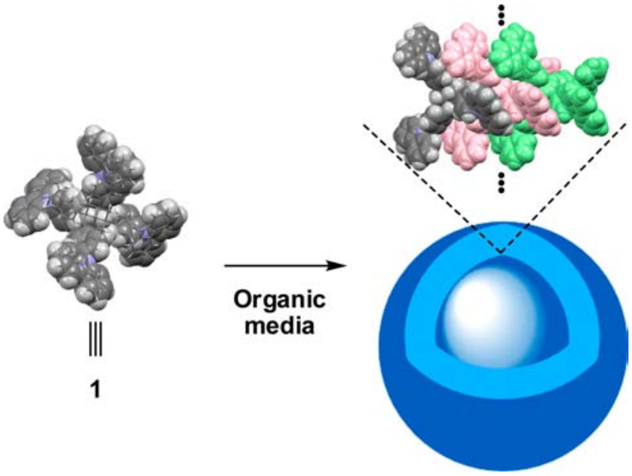


Figure 4. Schematic representation of hollow spherical structures with a multilayer membrane composed of tetrapodal adamantane **1** in organic solvents.

aliphatic adamantane core was located on the interior of the multilayer membranes. Furthermore, the distance between carbazole units in the columns of the crystal structure was 4.6 Å, which indicates that the carbazole moieties are not closely packed because of the bulkiness of the adamantane core. The spherical structures should thus be obtained without the production of 1D nanostructures such as fibers and tubes under these conditions.

The entrapment of guest molecules within the internal space of the hollow spherical aggregates can be achieved by the self-assembly of tetrapodal molecule **1**. Spherical structures including perylene as a hydrophobic fluorescent probe can be prepared and purified through dialysis. The inclusion of perylene within the hollow nanocapsules was verified by confocal laser scanning microscopy (CLSM), which showed the presence of colored spherical spots (Figure S2, Supporting Information). SEM measurements of the spherical assemblies containing the guest molecules revealed spheres with a diameter of ca. 200 nm, which is similar to the spherical structures without guest molecules (Figure S3, Supporting Information).

The tetrapodal adamantane with pyrrole units **2** is a reduced version of the *N*-heterocyclic moieties of **1**. In a tetrahydrofuran solution of **2** (0.1 mM), we observed the generation of hollow spherical assemblies with a multilayer membrane and with a diameter of ca. 110 nm. This was also confirmed by DLS, SEM, and TEM experiments (Figure 5 and S1, Supporting Information). Colorless plate-shaped crystals of **2** were obtained by the vapor diffusion of hexane into a chloroform solution of the compound. X-ray analysis revealed that the diameter of tetrapodal molecule **2** is 1.8 nm. Similarly, the 1D columnar structures derived from **2** were assembled into network structures through CH/π interactions. The small square cavities of 0.9×3.0 Å^2 in size were composed of cyclic tetramers of **2** (Figure S4, Supporting Information). Therefore, hollow spherical structures were generated from 1D columns, and this is supported by the columnar arrangements of **2**, as shown by X-ray analysis. Remarkably, the sizes of the spherical structures were modulated by altering the *N*-heterocyclic parts on the tetrapodal skeleton.

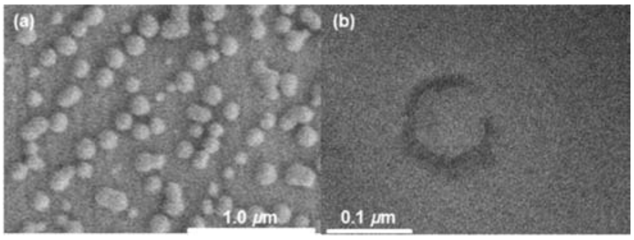
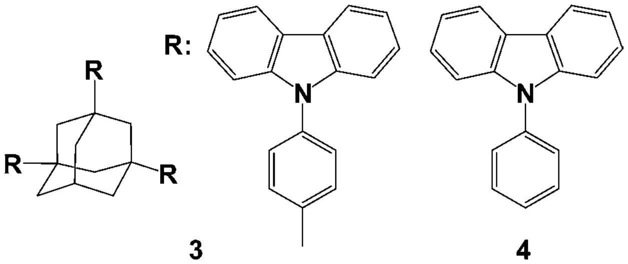


Figure 5. (a) SEM and (b) TEM images obtained from a tetrahydrofuran solution of **2** (0.1 mM).

To explain the formation of hollow spherical structures from tetrapodal adamantanes with *N*-heterocyclic parts, we investigated the assembly behavior of tripodal adamantane bearing carbazole units (**3**) and *N*-phenylcarbazole (**4**) in tetrahydrofuran (0.1 mM) (Figure 6). DLS and SEM studies of the tripodal adamantane **3** supported the production of spherical structures with a diameter of ca. 180 nm (Figure S1, 5, Supporting Information). However, spherical aggregates from *N*-phenylcarbazole (**4**) were not found by DLS and SEM measurements. Thus, the adamantane moieties in the tetrapodal molecule play essential roles in sphere formation in organic solutions.



3 **4**

Figure 6. Tripodal adamantane containing carbazole branches (**3**) and *N*-phenylcarbazole (**4**).

For insights into the driving force for the formation of spherical structures, UV−vis absorption measurements were obtained for **1**, **3**, and **4** in tetrahydrofuran (0.1 mM) (Figure S6, Supporting Information). Absorption bands were observed at 293, 327, and 340 nm for **4** and at 293, 328, and 342 nm for both **1** and **3**.[14] Fewer $\pi-\pi$ stacking intermolecular interactions are evident between the carbazole moieties of the tetra- and tripodal molecules in the spheres owing to the slight shift in the absorption bands. As a result, the driving force for the aggregation of adamantane-based molecules is mainly a solvophobic effect.

The morphology that results from the amphiphiles generally depends on the concentration in addition to the nature of the solvents. When tetrapodal molecule **1** afforded hollow spheres at a low concentration (0.1 mM) in tetrahydrofuran, a fusion phenomenon between the spherical assemblies was partly observed by SEM. It is thus likely that other highly aggregated structures will form at high concentrations of tetrapodal molecule **1**. For a concentration of **1** in tetrahydrofuran of 0.2 mM, from FE-SEM measurements necklace-like aggregates partially appeared in addition to spherical structures (Figure 7a). These are possibly produced by the fusion of individual spherical assemblies. For an even higher concentration (0.5 mM), SEM images revealed two-dimensional network assemblies composed of fibrous structures with a width of 200−400 nm (Figure 7b). Increasing the concentration of **1** facilitates the fusion of spherical assemblies, which induces necklace-shaped aggregates and these progressively form 1D fibrous assemblies leading to two-dimensional network structures.[15] Higher aggregates were generated by minimizing the interfacial free energy between the spherical assemblies and the organic solvent.

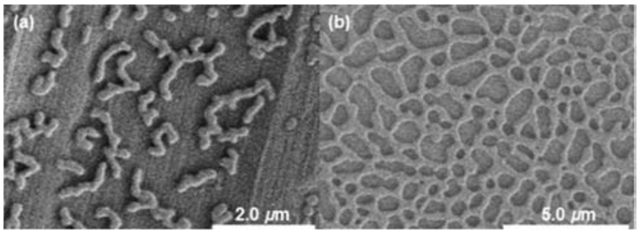


Figure 7. SEM images obtained from a tetrahydrofuran solution of **1** at (a) 0.2 mM and (b) 0.5 mM.

In conclusion, we designed tri- and tetrapodal adamantanes with carbazole and pyrrole moieties as hydrophobic molecules and examined their self-assembly behavior in organic solvents. We succeeded in the creation of tunable hollow spherical assemblies consisting of columnar structures from component molecules. The sizes of the hollow spherical structures were subject to the number of branched compartments, the character of the *N*-heterocyclic moieties, and the organic solvents. Studies into the exploitation of other tetrapodal adamantanes containing large π-aromatic molecules including pyrene and porphyrin and their self-assembly phenomenon in organic media are interesting subjects worthy of further investigation.

■ ASSOCIATED CONTENT

Supporting Information

Synthetic procedures, characterization data, DLS data, SEM, CLSM, and TEM images, UV−vis spectra, crystal data, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic data were deposited with the Cambridge Crystallographic Data Centre as CCDC 886345 and 886347.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: tominagam@kph.bunri-u.ac.jp.
*E-mail: isao.azumaya@phar.toho-u.ac.jp.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Grimsdale, A. C.; Müllen, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 5592−5629. (b) Iyoda, M.; Yamakawa, J.; Rahman, M. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 10522−10553. (c) Beaujuge, P. M.; Frĕchet, J. M. J. *J. Am. Chem. Soc.* **2011**, *133*, 20009−20029. (d) Maggini, L.; Bonifazi, D. *Chem. Soc. Rev.* **2012**, *41*, 211−241. (e) Görl, D.; Zhang, X.; Würthner, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 6328−6348.

(2) (a) Wilson, J. N.; Bunz, U. H. F. *J. Am. Chem. Soc.* **2005**, *127*, 4124−4125. (b) Zhang, W.; Jin, W.; Fukushima, T.; Saeki, A.; Seki, S.; Aida, T. *Science* **2011**, *334*, 340−343. (c) Huang, Z.; Kang, S.-K.; Banno, M.; Yamaguchi, T.; Lee, D.; Seok, C.; Yashima, E.; Lee, M. *Science* **2012**, *337*, 1521−1526. (d) Kartha, K. K.; Babu, S. S.; Srinivasan, S.; Ajayaghosh, A. *J. Am. Chem. Soc.* **2012**, *134*, 4834−4841.

(3) (a) Lim, Y.-b.; Moon, K.-S.; Lee, M. *Chem. Soc. Rev.* **2009**, *38*, 925−934. (b) Babu, S. S.; Praveen, V. K.; Ajayaghosh, A. *Chem. Rev.* **2014**, *114*, 1973−2129.

(4) (a) Hoeben, F. J. M.; Shklyarevskiy, I. O.; Pouderoijen, M. J.; Engelkamp, H.; Schenning, A. P. H. J.; Christianen, P. C. M.; Maan, J. C.; Meijer, E. W. *Angew. Chem., Int. Ed.* **2006**, *45*, 1232−1236. (b) Ajayaghosh, A.; Chithra, P.; Varghese, R. *Angew. Chem., Int. Ed.* **2007**, *46*, 230−233. (c) Tseng, K.-P.; Fang, F.-C.; Shyue, J.-J.; Wong, K.-T.; Raffy, G.; Guerzo, A. D.; Bassani, D. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 7032−7036.

(5) (a) Kim, J.-M.; Lee, Y. B.; Yang, D. H.; Lee, J.-S.; Lee, G. S.; Ahn, D. J. *J. Am. Chem. Soc.* **2005**, *127*, 17580−17581. (b) Zhang, X.; Rehm, S.; Safont-Sempere, M. M.; Würthner, F. *Nat. Chem.* **2009**, *1*, 623−629.

(6) (a) Hoeben, F. J. M.; Jonkheijm, P.; Meijer, E. W.; Schenning, A. P. H. J. *Chem. Rev.* **2005**, *105*, 1491−1546. (b) Ryu, J.-H.; Hong, D.-J.; Lee, M. *Chem. Commun.* **2008**, 1043−1054. (c) Fernández, G.; García, F.; Sánchez, L. *Chem. Commun.* **2008**, 6567−6569.

(7) (a) Yoshikawa, I.; Sawayama, J.; Araki, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 1038−1041. (b) Ke, D.; Zhan, C.; Li, A. D. Q.; Yao, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 3715−3719.

(8) (a) Charvet, R.; Jiang, D.-L.; Aida, T. *Chem. Commun.* **2004**, 2664−2665. (b) Shklyarevskiy, I. O.; Jonkheijm, P.; Christianen, P. C. M.; Schenning, A. P. H. J.; Meijer, E. W.; Henze, O.; Kilbinger, A. F. M.; Feast, W. J.; Guerzo, A. D.; Desvergne, J.-P.; Maan, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 1112−1113.

(9) (a) Ajayaghosh, A.; Varghese, R.; Mahesh, S.; Praveen, V. K. *Angew. Chem., Int. Ed.* **2006**, *45*, 7729−7732. (b) Yoosaf, K.; Belbakra, A.; Armaroli, N.; Llanes-Pallas, A.; Bonifazi, D. *Chem. Commun.* **2009**, 2830−2832.

(10) (a) Kishimura, A.; Koide, A.; Osada, K.; Yamasaki, Y.; Kataoka, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 6085−6088. (b) Duan, Q.; Cao, Y.; Li, Y.; Hu, X.; Xiao, T.; Lin, C.; Pan, Y.; Wang, L. *J. Am. Chem. Soc.* **2013**, *135*, 10542−10549.

(11) (a) Galoppini, E.; Gilardi, R. *Chem. Commun.* **1999**, 173−174. (b) Plietzsch, O.; Schilling, C. I.; Tolev, M.; Nieger, M.; Richert, C.; Muller, T.; Bräse, S. *Org. Biomol. Chem.* **2009**, *7*, 4734−4743. (c) Beaudoin, D.; Maris, T.; Wuest, J. D. *Nat. Chem.* **2013**, *5*, 830−834.

(12) (a) Li, D.; Zhou, W.; Landskron, K.; Sato, S.; Kiely, C. J.; Fujita, M.; Liu, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 5182−5187. (b) Mahato, P.; Saha, S.; Choudhury, S.; Das, A. *Chem. Commun.* **2011**, 11074−11076.

(13) (a) Tanaka, Y.; Miyachi, M.; Kokube, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 504−506. (b) Yang, M.; Wang, W.; Yuan, F.; Zhang, X.; Li, J.; Liang, F.; He, B.; Minch, B.; Wegner, G. *J. Am. Chem. Soc.* **2005**, *127*, 15107−15111.

(14) (a) Yang, X.; Lu, R.; Xu, T.; Xue, P.; Liu, X.; Zhao, Y. *Chem. Commun.* **2008**, 453−455. (b) Yang, X.; Lu, R.; Gai, F.; Xue, P.; Zhan, Y. *Chem. Commun.* **2010**, 1088−1090.

(15) (a) Yan, L.; Xue, Y.; Gao, G.; Lan, J.; Yang, F.; Su, X.; You, J. *Chem.—Eur. J.* **2010**, *16*, 2250−2257. (b) Yao, Y.; Xue, M.; Chen, J.; Zhang, M.; Huang, F. *J. Am. Chem. Soc.* **2012**, *134*, 15712−15715.