J|A|C|S
COMMUNICATIONS

Published on Web 01/10/2007

Microtubule Formation Using Two-Component Gel System

Ho Yong Lee, Seong Ryong Nam, and Jong-In Hong*

Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151-747, Korea

Received October 25, 2006; E-mail: jihong@snu.ac.kr

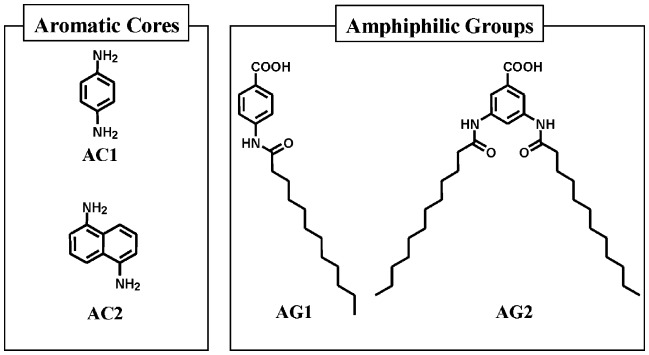
Self-assembly is a powerful tool for constructing various types of nano- and microstructures. Uniform self-assembled tubular structures can potentially be applied in the controlled generation of novel nano- or microscopic materials and devices.[1] Moreover, hollow tubular structures are abundant in nature and perform diverse biological functions.[2] Therefore, considerable attention is currently being focused on the fabrication of uniform tubular structures. Since the discovery of carbon nanotubes,[3] there have been reports on a variety of inorganic[4] and organic tubules.[5] Among them, self-assembled organic tubular structures have a lot of advantages such as a low-temperature fabrication process and easy modification.

Recently, there has been enormous interest in the development of a low molecular weight gelator (LMWG) for use in organic solvents.[6] The gelation process is accompanied by one-dimensional growth of the gelator in various types of fibers, strands, tapes, and tubes. There are an increasing number of reports about nanotubular structures being developed in the gelation process.[7] However, uniform microtubular structures are still rare.[8] In contrast with single LMWG gel systems, new gelation systems using two components have been developed.[9] In these systems, two components that serve as gelators are held together by noncovalent interactions. The most important feature of the two-component systems is the ease with which the properties and structures of the gel can be modulated by changing the molar ratio of the two components or by changing one of the two components. Excellent examples have been reported by Smith et al.[9a−g] They used a dendritic building block based on an amino acid in combination with an aliphatic diamine and examined the properties and structures of the resulting gel. In this study, we report a two-component gel system in which an amphiphile group and aromatic cores act as organic gelators by the process of self-assembly. The shape and size of the aromatic cores have a pronounced effect on the gel properties and on structures such as fibers and microtubules.

A two-component gel system is composed of aromatic cores (AC1, AC2) and amphiphile groups (AG1, AG2) (See Scheme 1). We have selected phenyl- and naphthyl-based aromatic groups (AC1, AC2). These two aromatic molecules are different in shape and size and are expected to show different packing patterns and strength when combined with the amphiphile groups. The aromatic core has amine groups, which are able to interact with the benzoic acid of the amphiphile group using hydrogen bonds. The amphiphile group is composed of four parts: a carboxylic acid, amide group, long alkyl chain (dodecyl), and phenyl ring. Benzoic acid forms a hydrogen bond with the amine group of the aromatic core. The amide groups act as additional hydrogen-bonding sites to enable further assembly of the complex between AC and AG. AG1 has one alkyl group, while AG2 has two alkyl groups.

The gelation behavior of the complexes between AC and AG were tested in various organic solvents. Gelation did not occur in polar protic and aprotic solvents because the hydrogen-bonded complexes between AC and AG might be disturbed in the polar solvents. Furthermore, gelation did not occur in aromatic solvents

Scheme 1



such as toluene and xylene which disrupt the further stacking of the complex between AC and AG. However, the complexes between AG2 and the aromatic cores showed a high gelation behavior in nonaromatic hydrocarbon solvents such as cyclohexane and decalin. The complexes between AG1 and the aromatic cores showed a poor gelation ability only in decalin. This indicates that an amide alkyl chain plays an important role in the gelation ability of a two-component system. Gelation was not observed when only one of the two components was present. Thus, the complex between the AC and AG groups is essential for gel formation.

The gelation ability of the two-component system in cyclohexane was investigated under various concentrations (Figure 1). All the gels were thermoreversible. The temperature (gel-to-sol temperature, T_{gel}) at which the gel vanishes was investigated under various concentrations. The T_{gel} value increased with the molar concentration. As reported elsewhere, T_{gel} reaches a plateau region above a certain concentration. All mixtures have a similar threshold concentration of approximately 25 mM, although they have different shapes and sizes. Another interesting feature is that T_{gel} changes according to the type of the aromatic core. In all the investigated concentrations, T_{gel} increased with the aromatic size of the AC group. The T_{gel} value of the complex between AC1 and AG2 is 42 °C at 10 mM, while that of the complex between AC2 and AG2 is 55 °C. The average change in T_{gel} is approximately 15 °C. A

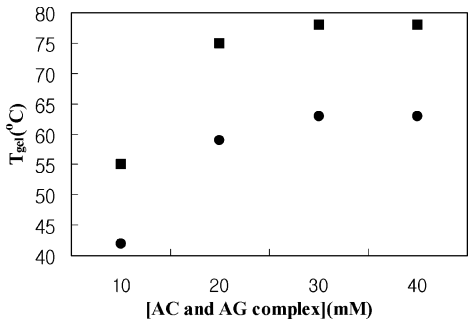


Figure 1. Effect of concentration on the gel−sol transition temperature of the gel in cyclohexane. AC and AG were mixed in a ratio of 1:2 (●, AC1 + AG2; ■, AC2 + AG2).

10.1021/ja0676197 CCC: $37.00

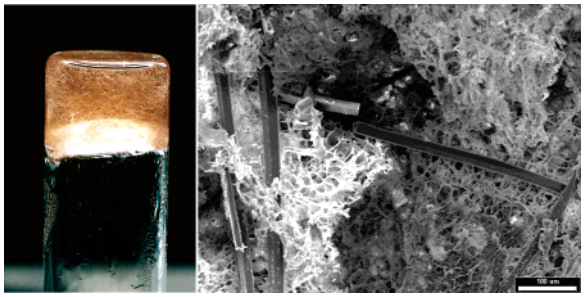


Figure 2. Gel images of the AC2 and AG2 mixture in an inversed vial (left). The image was captured by a digital camera ([AC2 + 2AG2] = 20 mM). SEM image of dried gel (right). (bar = 100 μm.) AC2 and AG2 were mixed in a ratio of 1:2 in cyclohexane.

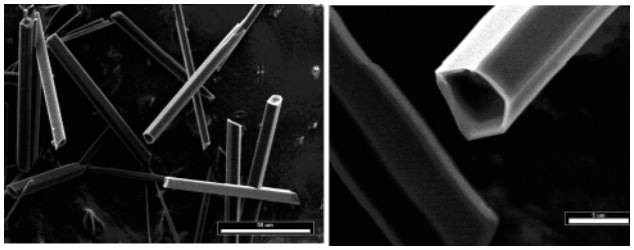


Figure 3. SEM images of the dried AC2 and AG2 mixture in a ratio of 1:2 in decalin (left, bar = 50 μm; right, bar = 5 μm).

dramatic change in T_{gel} was observed by the addition of one aromatic ring. Therefore, we can deduce that the $\pi-\pi$ interactions between the aromatic cores may play an important role in stabilizing the gel.

The microstructures of the two-component gel aggregates were significantly changed by the replacement of the AC groups. The scanning electron microscopy (SEM) image of the mixture of AC1 and AG2 in cyclohexane and decalin showed fiberlike structures.[10] A 1:2 mixture of AC1 and AG2 results in a clear gel.

However, in the case of the mixture of AC2 and AG2 in cyclohexane, fibrous structures in the gel medium, which were revealed to be microtubules, were observed with the naked eye (Figure 2, left). The SEM image of a dried gel shows two distinct microstructures (fibrous and tubular structures). The fibrous structures contribute to the gelation of cyclohexane and tubular structures pass through them. Microtubules can be separated by filtration after vigorously stirring the diluted gel. In most cases, the microtubular structures were collapsed or were deprived of their tubular function without a solvent. However, the separated microtubules retained their hollow tubular structure without the solvent and were stable in air. The photomicroscope and SEM images clearly show hollow tubular structures with uniform external diameters of 30−40 μm and wall thicknesses of 2−3 μm. The length of the longest tubule is 5 mm. We performed the same tests more than twenty times and obtained the same reproducible results. The reproducible formation of microtubules implies that the tubular structures have a definite composition of AC2 and AG2. The flat structure and hydrogen-bonding sites in the amphiphile group (AG2) are likely to facilitate the $\pi-\pi$ interactions of the aromatic cores.

We could also observe microtubules in the gel of AC2 and AG2 in delcalin, which were smaller than those in the cyclohexane gel. The SEM images clearly show a hollow space (Figure 3). Microtubules have external diameters of 5−10 μm, lengths of 20−70 μm, and wall thicknesses of 0.5−1 μm. The microtubules formed in decalin are faceted, while those formed in cyclohexane show a round shape. In the case of the delcalin gel, we failed to separate the microtubules in the gel medium. The microtubules in decalin have smaller external diameters and wall thicknesses than those in cyclohexane. This implies that the solvent affects the microscopic structure of the gelators.

In conclusion, we have developed a new gelation system for organic solvents by the self-assembly of aromatic amines and amphiphile groups. The thermal and morphological properties dramatically changed according to the solvent and the size and shape of the aromatic groups. The microtubular structure formed during gel formation is unique and reproducible. We expect that our results can be applied to the preparation of various types of microstructures by using different aromatic cores and amphiphile groups.

Acknowledgment. We thank the MOCIE (Grant No. 10022945) for financial support. Partial support from the Seoul R&BD is also acknowledged. H.Y.L. and S.R.N. are grateful to the Ministry of Education for a BK 21 fellowship.

Supporting Information Available: Experimental details, additional SEM images, and photomicroscope images. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) van Bommel, K. J. C.; Friggeri, A.; Shinkai, S. *Angew.Chem., Int. Ed.* **2003**, *42*, 980−999. (b) Reches, M.; Gazit, E. *Nature* **2003**, *300*, 625−627. (c) Kijima, T.; Yoshimura, T.; Uota, M.; Ikeda, T.; Fujikawa, D.; Mouri, S.; Uoyama, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 228−232.

(2) (a) Eisenberg, B. *Acc. Chem. Res.* **1998**, *31*, 117−123. (b) Sigler, P. B.; Xu, Z.; Rye, H. S.; Burston, S. G.; Fenton, W. A.; Horwich, A. L. *Annu. Rev. Biochem.* **1998**, *67*, 581−608. (c) Horwich, A. L.; Weber-Ban, E. U.; Finley, D. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 11033−11040. (d) Zwickl, P.; Voges, D.; Baumeister, W. *Philos. Trans. R. Soc. London, Ser. B* **1999**, *354*, 1501−1511.

(3) (a) Iijima, S. *Nature* **1991**, *354*, 56−58. (b) Ajayan, P. M. *Chem. Rev.* **1999**, *99*, 1787−1800.

(4) (a) Suenaga, K.; Colliex, C.; Demoncy, N.; Loiseau, A.; Pascard, H.; Willaime, F. *Science* **1997**, *278*, 653−655. (b) Chopra, N. G.; Luyken, R. J.; Cherrey, K.; Crespi, V. H.; Cohen, M. L.; Louie, S. G.; Zettl, A. *Science* **1995**, *269*, 966−967. (c) Stephan, O.; Ajayan, P. M.; Colliex, C.; Redlich, P.; Lambert, J. M.; Bernier, P.; Lefin, P. *Science* **1994**, *266*, 1683−1685. (d) Remskar, M.; Mrzel, A.; Skraba, Z.; Jesih, A.; Ceh, M.; Demšar, J.; Stadelmann, P.; Le'vy, F.; Mihailovic, D. *Science* **2001**, *292*, 479−481. (e) Hacohen, Y. R.; Grunbaum, E.; Tenne, R.; Sloan, J.; Hutchison, J. L. *Nature* **1998**, *395*, 336−337.

(5) (a) Bong, D. T.; Clark, T. D.; Granja, J. R.; Ghadiri, M. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 988−1011. (b) Kim, Y.; Mayer, M. F.; Zimmerman, S. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 1121−1126. (c) Vauthey, S.; Santoso, S.; Gong, H.; Watson, N.; Zhang, S. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5355−5360.

(6) Reviews: (a) Abdallah, D. J.; Weiss, R. G. *Adv. Mater.* **2000**, *12*, 1237−1247. (b) van Esch, J. H.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2000**, *39*, 2263−2267. (c) Terech, P.; Weiss, R. G. *Chem. Rev.* **1997**, *97*, 3133−3160. (d) Shimizu, T. Macromol. *Rapid Commun.* **2002**, *23*, 311−331. (e) Gronwald, O.; Shinkai, S. *Chem.—Eur. J.* **2001**, *7*, 4329−4334.

(7) (a) John, G.; Masuda, M.; Okada, Y.; Yase, K.; Shimizu, T. *Adv. Mater.* **2001**, *13*, 715−718. (b) Hafkamp, R. J. H.; Feiters, M. C.; Nolte, R. J. M. *J. Org. Chem.* **1999**, *64*, 412−426. (c) Fuhrhop, J.−H.; Spiroski, D.; Boettcher, C. *J. Am. Chem. Soc.* **1993**, *115*, 1600−1601. (d) Masuda, M.; Shimizu, T. *Langmuir* **2004**, *20*, 5969−5977.

(8) Self-assembled microtubes: (a) Wong, G. C. L.; Tang, J. X.; Lin, A.; Li, Y.; Janmey, P. A.; Safinya, C. R. *Science* **2000**, *288*, 2035−2039. (b) Yan, D.; Zhou, Y.; Hou, J. *Science* **2004**, *303*, 65−67. (c) Shimizu, T.; Kosigo, M.; Masuda, M. *Nature* **1996**, *383*, 487−488. (d) Shimizu, T.; Kosigo, M.; Masuda, M. *J. Am. Chem. Soc.* **1997**, *119*, 6209−6210. (e) Douliez, J.-P.; Gaillard, C.; Navailles, L.; Nallet, F. *Langmuir* **2006**, *22*, 2942−2945.

(9) (a) Smith, D. K. *Chem. Commun*. **2006**, 34−44. (b) Patridge, K. S.; Smith, D. K.; Dykes, G. M.; McGrail, T. P. *Chem. Commun*. **2001**, 319−320. (c) Hirst, A. R.; Smith, D. K.; Feiters, M. C.; Geurts, H. P. M.; Wright, A. C. *J. Am. Chem. Soc.* **2003**, *125*, 9010−9011. (d) Hardy, J. G.; Hirst, A. R.; Smith, D. K.; Brennan, C.; Ashworth, I. *Chem. Commun*. **2005**, 385−387. (e) Hirst, A. R.; Smith, D. K.; Feiters, M. C.; Geurts, H. P. M. *Chem. Eur. J.* **2004**, *10*, 5901−5910. (f) Hirst, A. R.; Smith, D. K. *Chem.—Eur. J.* **2005**, *11*, 5496−5508. (g) Hirst, A. R.; Smith, D. K.; Harrington, J. P. *Chem.—Eur. J.* **2005**, *11*, 6552−6559. (h) Yagai, S.; Nakajima, T.; Kishikawa, K.; Kohmoto, S.; Karatsu, T.; Kitamura, A. *J. Am. Chem. Soc.* **2005**, *127*, 11134−11139. (i) Oda, R.; Huc, I.; Candau, S. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 2689−2691. (j) Zemb, T.; Dubois, M.; Demé, B.; Gulik-Krzywicki, T. *Science* **1999**, *283*, 816−819.

(10) See the Supporting Information.

JA0676197